# One-Pot, Three-Component Synthesis of 1-(2-Hydroxyethyl)-1*H*-1,2,3-triazole Derivatives by Copper-Catalyzed 1,3-Dipolar Cycloaddition of 2-Azido Alcohols and Terminal Alkynes under Mild Conditions in Water

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A safe, efficient, and improved procedure for the regioselective synthesis of 1-(2-hydroxyethyl)-1*H*-1,2,3-triazole derivatives under ambient conditions is described. Terminal alkynes reacted with oxiranes and $NaN_3$ in the presence of a copper(I) catalyst, which is prepared by *in situ* reduction of the copper(II) complex **4** with ascorbic acid, in $H_2O$. The regioselective reactions exclusively gave the corresponding 1,4-disubstituted 1*H*-1,2,3-triazoles in good to excellent yields. This procedure avoids the handling of organic azides as they are generated *in situ*, making this already powerful click process even more user-friendly and safe. The remarkable features of this protocol are high yields, very short reaction times, a cleaner reaction profile in an environmentally benign solvent ($H_2O$), its straightforwardness, and the use of nontoxic catalysts. Furthermore, the catalyst could be recovered and recycled by simple filtration of the reaction mixture and reused for ten consecutive trials without significant loss of catalytic activity. No metal-complex leaching was observed after the consecutive catalytic reactions.

**Introduction.** – *Huisgen*'s 1,3-dipolar cycloaddition of an organic azide and an alkyne is an efficacious way for multifarious syntheses of the 1*H*-1,2,3-triazole ring system [1]. This reaction has important uses in bio-orthogonal bioconjugation [2–5], polymer [6][7] and dendrimer syntheses [8], and the construction of peptide-bond surrogates [9] and powerful pharmacophores. The reaction takes place in the presence of a copper(I) catalyst to afford the 1,4-disubstituted 1*H*-1,2,3-triazoles exclusively, which contrasts with the thermal reaction requiring high temperature and, prolonged reaction time and resulting in the two regioisomeric 1,4- and 1,5-disubstituted 1*H*-1,2,3-triazoles. The copper(I) catalysts are directly formed from $Cu^I$ salts in the presence of ligands [5][10], or prepared *in situ* by reduction of $Cu^{II}$ salts with ascorbate [11], or oxidation of copper(0) metal [12], or by comproportionation of $Cu^0$ and $Cu^{II}$ [13].

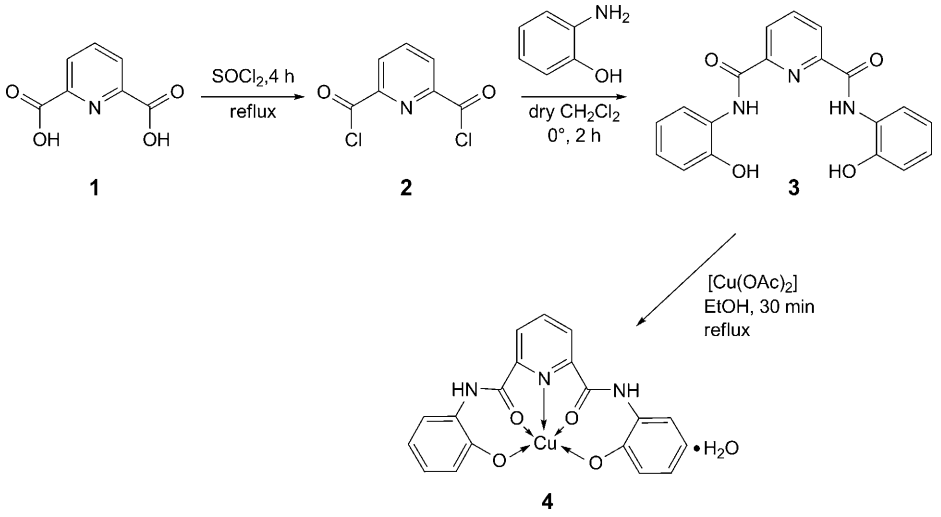
The development of heterogeneous catalysts for the synthesis of fine chemicals has become a major area of research recently, as the potential advantages of these materials over homogeneous systems can have a major impact on the environmental performance of a synthesis [14]. To improve the recovery and reuse, copper species have been immobilized onto various supports such as activated carbon [15], amine-functionalized polymers [16], zeolites [17], amine-functionalized silica [18], and aluminium oxyhydroxide fiber [19].

Although organic azides are generally stable under most reaction conditions such as in the presence of $H_2O$ and $O_2$ [20], isolation or purification of low-molecular-mass organic azides or polyazides can be problematic. Therefore, a procedure that avoids isolation of organic azides is desirable. Recently, some examples were reported for *in situ* generation of organic azides by means of a one-pot procedure to prepare 1*H*-1,2,3-triazole derivatives based on three-component coupling reaction [18][21].

Since 1-(2-hydroxyethyl)-1*H*-1,2,3-triazole derivatives have become increasingly useful and important in drugs and pharmaceuticals [22], the development of a simple and efficient method for their synthesis in a single-step operation is desirable. Here, we wish to report an efficient, safe, and environmentally benign one-pot synthesis of 1-(2-hydroxyethyl)-1*H*-1,2,3-triazole derivatives from oxiranes, $NaN_3$, and alkynes in $H_2O$ in the presence of catalytic amounts of a heterogeneous $Cu^{II}$ complex by way of a three-component reaction, proceeding *via* the formation of 2-azido alcohols from the oxiranes and $NaN_3$. Pleasantly, azides generated *in situ* from the corresponding oxiranes led efficiently to triazoles.

**Results and Discussion.** – As part of our continuing attempts to broaden the scope of heterogeneous catalyst and transition-metal complexes [23], we recently reported the efficiency of a copper complex in the synthesis of benzimidazole derivatives [24]. The extraordinary stability of this complex toward heat, oxygen, and moisture prompted us to test them in the *Huisgen* cycloaddition. Three simple steps were required to prepare [Cu(bhppda)$H_2O$] (**4**) from **1** *via* **2** and **3**, as [24] shown in *Scheme 1* (bhppda = $N^2$,$N^6$-bis(2-hydroxyphenyl)pyridine-2,6-dicarboxamidato(2−).

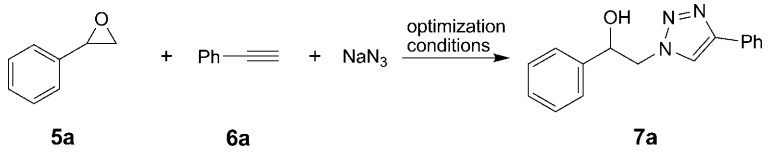
*Scheme 1*




To establish the optimum conditions for the *Huisgen* 1,3-dipolar cycloaddition, initially, various metal complexes were examined in a model reaction between styrene oxide (=2-phenyloxirane; **5a**), $NaN_3$, ascorbic acid, and phenylacetylene

(=ethynylbenzene; **6a**) in $H_2O$ as solvent at room temperature *via* a three-component reaction (*Scheme 2*).

*Scheme 2*




**5a** **6a** **7a**

The copper complex **4** was found to be the most effective catalyst in terms of reaction rate, regioselectivity, and yield of the product (*Table 1*, *Entry 1*). The reaction proceeded smoothly to give the corresponding (2-hydroxyethyl)triazole **7a** in high yield. In addition, [$Cu(OAc)_2$] [25] and [Cu(II)(salen)] were also examined as catalysts for this reaction; however, they were less effective compared to **4** and afforded **7a** in 10% and 75% yields, respectively, thereby indicating the important role of the ligand system (*Entries 6* and *7*). The attempts to carry out the reaction without a copper catalyst did not give the expected triazole, even after long reaction times (*Entry 8*). In the absence of ascorbic acid, the reaction time increased (*Entry 9*).

Table 1. *Investigation of Various Metal Complexes* (5 mol-%) *in the Synthesis of 1-(2-Hydroxyethyl)-1*H*-1,2,3-triazole Derivative* **7a** *from 2-Phenyloxirane* (**5a**; 1 mmol), *Phenylacetylene* (**6a**; 1 mmol), *$NaN_3$* (1.2 mmol), *and Ascorbic Acid* (0.2 mmol) *in $H_2O$ at Room Temperature*

| *Entry* | Catalyst | Time [h] | Yield of **7a**[a]) [%] |
|---|---|---|---|
| *1* | [$Cu(bhppda)H_2O$] (**4**) | 2 | 90 |
| *2* | [$Mn(bhppda)H_2O$] | 7 | 40 |
| *3* | [$Co(bhppda)H_2O$] | 7 | – |
| *4* | [$Cd(bhppda)H_2O$] | 7 | – |
| *5* | [$Fe(bhppda)H_2O$] | 7 | 20 |
| *6* | [$Cu(OAc)_2$] | 7 | 10 |
| *7* | [Cu(II)(salen)] | 7 | 75 |
| *8* | –[b]) | 24 | – |
| *9* | –[c]) | 7 | 45 |

[a]) Yield of isolated product. [b]) Under the same conditions, but without catalyst. [c]) Under the same conditions in the presence of **4**, but in the absence of ascorbic acid.

Then, we turned our attention to the investigation of the effect of the solvent on our model reaction (*Table 2*). Organic solvents such as MeCN, DMF, THF, *t*BuOH, and toluene were not effective (*Entries 1–5*). By changing the solvent to DMSO, which enhances the solubility of $NaN_3$, the product was obtained in only 10% yield (*Entry 6*). However, when the reaction was carried out in the 1:1 mixture of an organic solvent and $H_2O$, we observed formation of the triazole in 45% and 40% yield after 5 h (*Entries 7* and *8*). Pleasantly, a strong acceleration and an excellent yield were observed in $H_2O$ (*Entry 9*). This is probably due to the high solubility of ascorbic acid and $NaN_3$ in $H_2O$. It should be noted that the optimal catalyst loading in the synthesis of **7a** is at a concentration of 5 mol-%.

Table 2. *Investigation of the Effect of Various Solvents on the Synthesis of 1-(2-Hydroxyethyl)-1*H*-1,2,3-triazole Derivative* **7a** *from 2-Phenyloxirane* (**5a**; 1 mmol), *Phenylacetylene* (**6a**; 1 mmol), *$NaN_3$* (1.2 mmol), *Ascorbic Acid* (0.2 mmol), *and Catalyst* **4** (5 mol-%) *at Room Temperature*

| *Entry* | Solvent | Time [h] | Yield of **7a**[a]) [%] | *Entry* | Solvent | Time [h] | Yield of **7a**[a]) [%] |
|---|---|---|---|---|---|---|---|
| *1* | MeCN | 5 | trace | *6* | DMSO | 5 | 10 |
| *2* | DMF | 5 | 5 | *7* | DMSO/$H_2O$ | 5 | 45 |
| *3* | THF | 5 | 5 | *8* | $^t$BuOH/$H_2O$ | 5 | 40 |
| *4* | $^t$BuOH | 5 | 5 | *9* | $H_2O$ | 2 | 90 |
| *5* | toluene | 5 | – | | | | |

[a]) Yield of isolated product.

To generalize the methodology, we focused our attention on the use of other oxiranes **5** and alkynes **6** that can act as substrates for the synthesis of 1,4-disubstituted 1*H*-1,2,3-triazoles of type **7**. For this purpose, also new alkynes containing thioxanthone (see **6h** and **6i**), anthraquinone (see **6o**), azacrown ether (see **6n**), *etc.*, were synthesized. As expected, all reactions of **6** with **5a** proceeded smoothly at room temperature and led to the regioselective formation of the desired (2-hydroxyalkyl)-triazoles **7** in good to excellent yield (*Table 3*, *Entries 2–15*). In this study, aryl propargyl ethers (= prop-2-yn-1-yloxy)benzenes) **6b**–**6e** were chosen to investigate not only the influence of the aryloxy linkage in the coupling by changing the electronic nature of the alkyne but also as a way to obtain new 1-(2-hydroxyalkyl)-1*H*-1,2,3-triazoles. In these cases, the assembly proceeded to completion in reaction times no longer than 4 h leading to the 1,4-disubstituted 1,2,3-triazoles **7b**–**7e** with high yields (*Table 3*, *Entries 2–5*). As a second approach for the synthesis of new 1-(2-hydroxyalkyl)-1*H*-1,2,3-triazoles, the propargylamines **6f** and **6g** were used in the cycloaddition reaction with **5a** and $NaN_3$, leading to **7f** and **7g** with similarly good results (*Entries 6* and *7*). In a similar manner, propargyloxyheteroarene derivatives gave the corresponding products **7h**–**7j** in high yields (*Entries 8–10*). The methodology was also applied to the aliphatic alkynes **6k**–**6m**. For example, the sterically bulky **6l** (*Entry 12*) reacted without any problems to give the corresponding triazole **7l** in 80% yield. A sterically hindered propargylamine, *i.e.*, the azacrown ether derivative **6n**, allowed, through our methodology, to prepare a new azacrown ether that is attached to 1-(2-hydroxyethyl)-1*H*-1,2,3-triazole (*Entry 14*). The 1,3-dipolar *Huisgen* cycloaddition reaction was also applicable to substrates containing two reactive sites such as bis(propargyloxy)anthraquinone **6o**, which furnished the corresponding product **7o** in good yield (*Entry 15*).

Encouraged by the results achieved with 2-phenyloxirane (**5a**), we turned our attention to various other oxiranes (*Table 3*, *Entries 16–19*). The formed triazoles from the aliphatic oxiranes **5b** and **5c** were also obtained from the terminal attack of the azide nucleophile (*Entries 16* and *17*). The 2-cyclohexyloxirane (**5d**) also reacted with $NaN_3$ and phenylacetylene (**6a**) or propargyl ether **6p** to produce the 1-cyclohexyl-1*H*-triazole **7r** or **7s**, respectively, in excellent yield (*Entries 18* and *19*); the configuration of the products was found to be *trans* from the coupling constants of the cyclohexane H-atoms [26].

As expected, disubstituted alkynes, *e.g.*, **6q** and **6r**, did not react; this behavior is in agreement with a mechanism involving the formation of a copper(I) acetylide species (*Table 3*, *Entries 20* and *21*).

To check the feasibility of this procedure on a preparative scale, we carried out the cycloaddition of 2-phenyloxirane (**5a**) and $NaN_3$ with phenylacetylene (**6a**) on a 30-mmol scale in the presence of $Cu^{II}$ complex **4**. As expected, the reaction proceeded similarly to the experiment on a smaller scale, except that a little prolonged reaction time was required (2.3 h).

To confirm that this process is heterogeneous, the catalyst **4** and the product **7a** were separated by simple filtration, and the solid mixture was washed with excess of AcOEt to remove the product from the catalyst. This catalyst was directly used for further recycling experiments. From *Table 4*, it is very clear that the catalytic activity of the present system is intact even after 10 cycles.

The proposed mechanism for the formation of 1-(2-hydroxyethyl)-1*H*-1,2,3-triazoles may comprise two possible pathways in which the copper complex has a dual catalytic role: *A* and *B*. *Pathway A* includes the copper-complex-catalyzed 2-azido-1-phenylethanol formation from $NaN_3$ and 2-phenyloxirane (**5a**; *Scheme 3*). The participation of a metal azide as the catalytically active species suggests that the mechanism of oxirane-ring opening involves azide delivery from the catalyst as well as oxirane activation by the Cu catalyst. We propose a mechanism involving catalyst activation of both nucleophile and electrophile. Moreover, based on our previous studies [27], it can be concluded that the reaction rate in the present reaction should be affected not only by complexation of $NaN_3$ with copper complex, but also by dissociation of the $N_3^-$ anion from the adduct and simultaneous activation of the oxirane and azide by two different catalyst molecules.

For *Pathway B*, firstly the 'copper(II)/ascorbate system', the active catalyst $[CuL_n]^+$, is generated *in situ* from the copper complex **4** *via* reduction with ascorbic acid. Then, activation of the terminal alkyne takes place by insertion of the copper complex to the terminal alkyne, forming copper(I) acetylide **I** [28]. Having the concerted pathways eliminated, we propose that the azide binds to the copper atom *via* the N-atom proximal to the C-atom, forming intermediate **II**. In the next step, protonolysis of **III** releases the 1,2,3-triazole **IV**, thereby completing the catalytic cycle [12] (*Scheme 3*, *Pathway B*).

In conclusion, we developed a safe and efficient protocol for the regioselective generation of 1-(2-hydroxyalkyl)-1*H*-1,2,3-triazole derivatives *via* a three-component reaction of an oxirane, $NaN_3$, and an alkyne in an environmentally benign solvent, $H_2O$. By executing several reaction steps in a one-pot reaction and purifying only at the final stage, this procedure avoids the isolation of the azide intermediate, which significantly reduced the synthetic process time and improved the overall yield. The process showed the considerable synthetic advantages in terms of product diversity, mild reaction condition, simplicity of the reaction procedure, and good to excellent yields. Furthermore, copper(II) catalyst **4** can be recovered and recycled by simple filtration of the reaction mixture and reused for at least ten consecutive trials without decrease in activity.

Table 3. *One-Pot Synthesis of 1-(2-Hydroxyethyl)-1*H*-1,2,3-triazole Derivatives* **7** *from Oxiranes* **5** (1 mmol), *Alkynes* **6** (1 mmol), $NaN_3$ (1.2 mmol), *Ascorbic Acid* (0.2 mmol), *and Catalyst* **4** (5 mol-%) *in* $H_2O$ *at Room Temperature*

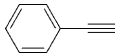
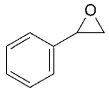
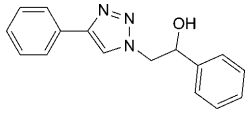
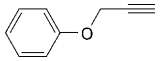
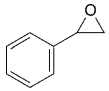
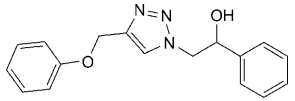
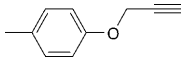
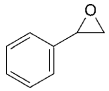
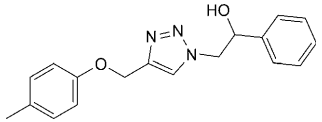
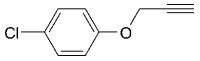
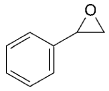
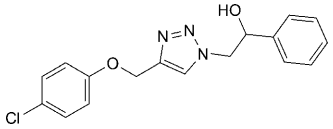
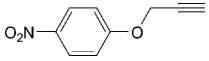
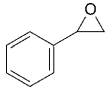
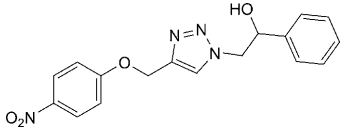
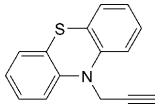
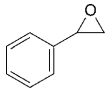
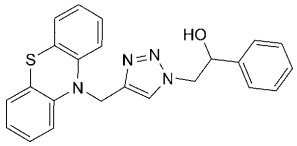
| *Entry* | Alkyne | | Oxirane | | Product | | Time [h] | Yield[a]) [%] |
|---|---|---|---|---|---|---|---|---|
| *1* | **6a** |  | **5a** |  | **7a** |  | 2 | 90 |
| *2* | **6b** |  | **5a** |  | **7b** |  | 4 | 90 |
| *3* | **6c** |  | **5a** |  | **7c** |  | 3 | 87 |
| *4* | **6d** |  | **5a** |  | **7d** |  | 2.5 | 88 |
| *5* | **6e** |  | **5a** |  | **7e** |  | 2.3 | 90 |
| *6* | **6f** |  | **5a** |  | **7f** |  | 5.6 | 78 |

*Table 3* (cont.)

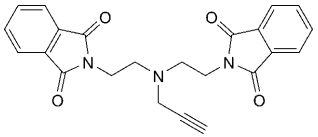
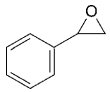
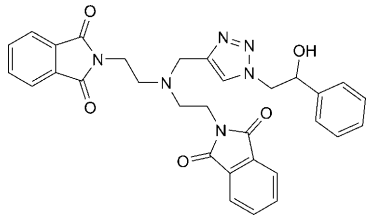
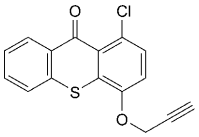
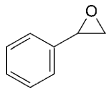
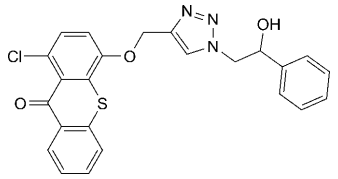
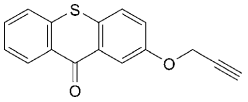
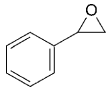
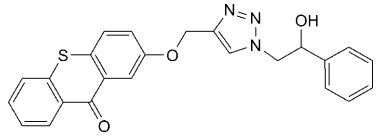
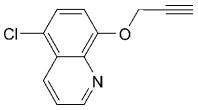
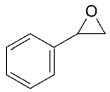
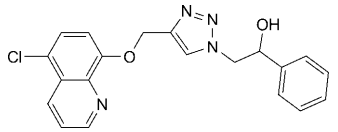
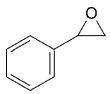
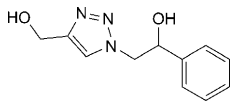
| *Entry* | Alkyne | Oxirane | Product | Time [h] | Yield[a]) [%] |
|---|---|---|---|---|---|
| *7* | **6g**  | **5a**  | **7g**  | 4 | 86 |
| *8* | **6h**  | **5a**  | **7h**  | 3 | 84 |
| *9* | **6i**  | **5a**  | **7i**  | 2.5 | 81 |
| *10* | **6j**  | **5a**  | **7j**  | 3 | 87 |
| *11* | **6k**  | **5a**  | **7k**  | 4.5 | 85 |

*Table 3* (cont.)

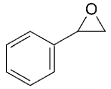
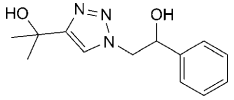
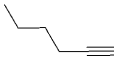
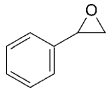
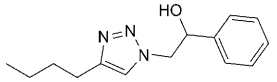
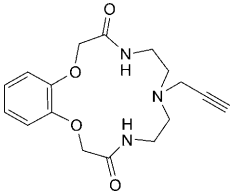
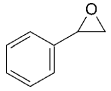
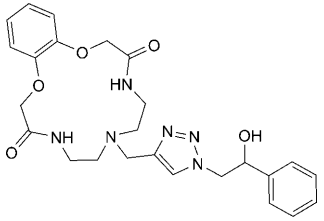
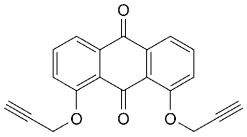
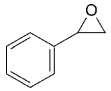
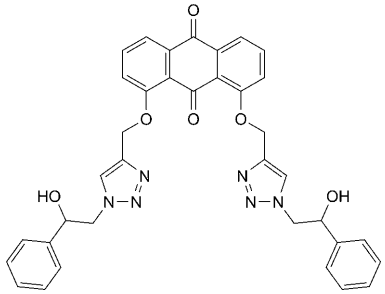
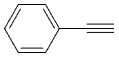
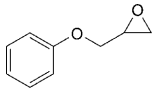
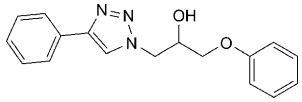
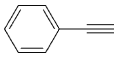
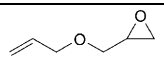
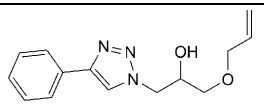
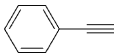
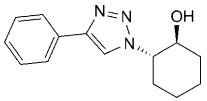
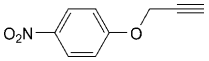
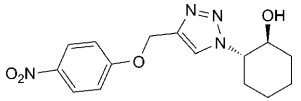
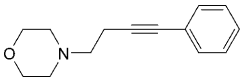
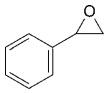
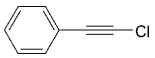
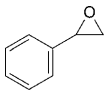
| *Entry* | Alkyne | Oxirane | Product | Time [h] | Yield[a]) [%] |
|---|---|---|---|---|---|
| *12* | **6l**  | **5a**  | **7l**  | 4.5 | 80 |
| *13* | **6m**  | **5a**  | **7m**  | 4.5 | 80 |
| *14* | **6n**  | **5a**  | **7n**  | 5 | 79 |
| *15* | **6o**  | **5a**  | **7o**  | 5.5 | 85 |
| *16*[b]) | **6a**  | **5b**  | **7p**  | 7 | 78 |

*Table 3* (cont.)

| *Entry* | Alkyne | Oxirane | Product | Time [h] | Yield[a]) [%] |
|---|---|---|---|---|---|
| *17* | **6a**  | **5c**  | **7q**  | 4.1 | 80 |
| *18* | **6a**  | **5d**  | **7r**  | 4 | 83 |
| *19* | **6p**  | **5d**  | **7s**  | 4.5 | 84 |
| *20* | **6q**  | **5a**  | – | no reaction | 24 | – |
| *21* | **6r**  | **5a**  | – | no reaction | 24 | – |

[a]) Yield of isolated product. [b]) Under the same conditions, but at 50°.

Table 4. *Catalyst-Recyclability Studies on the Synthesis of 1-(2-Hydroxyethyl)-1*H*-1,2,3-triazole Derivative* **7a** *from 2-Phenyloxirane* (**5a**; 1 mmol), *Phenylacetylene* (**6a**; 1 mmol), *$NaN_3$* (1.2 mmol), *Ascorbic Acid* (0.2 mmol), *and* **4** (5 mol-%) *in $H_2O$ at Room Temperature*

| Number of uses | Yield[a]) [%] | Recovery of catalyst [%] | Number of uses | Yield[a]) [%] | Recovery of catalyst [%] |
|---|---|---|---|---|---|
| 1 | 90 | > 98 | 6 | 89 | 97 |
| 2 | 90 | > 98 | 7 | 87 | 95 |
| 3 | 90 | > 98 | 8 | 87 | 95 |
| 4 | 90 | > 98 | 9 | 87 | 95 |
| 5 | 89 | 97 | 10 | 85 | 94 |

[a]) Yield of isolated product.

## Experimental Part

*General*. Chemical materials were either prepared in our laboratories or were purchased from *Fluka*, *Aldrich*, or *Merck*. The purity determination of the substrates and reaction monitoring were accomplished by TLC (silica gel *PolyGram SILG/UV$_{254}$* plates). Column chromatography (CC): short glass columns (Ø 2 – 3 cm) of silica gel *60* ($SiO_2$; 70 – 230 mesh); 15 – 30 g of $SiO_2$ for 1 g of crude mixture. M.p.: open capillary; *Büchi-535* circulating-oil melting-point apparatus. IR Spectra: *Shimadzu-FT-IR 8300* spectrophotometer; in $cm^{-1}$. NMR Spectra: *Bruker-Avance-DPX-250* ($^1$H at 250 and $^{13}$C at 62.9 MHz) in pure deuterated solvents with $Me_4Si$ as internal standard; $\delta$ in ppm, $J$ in Hz. MS: *Shimadzu-GCMS-QP-1000-EX* instruments at 70 or 20 eV; in $m/z$ (rel. %).

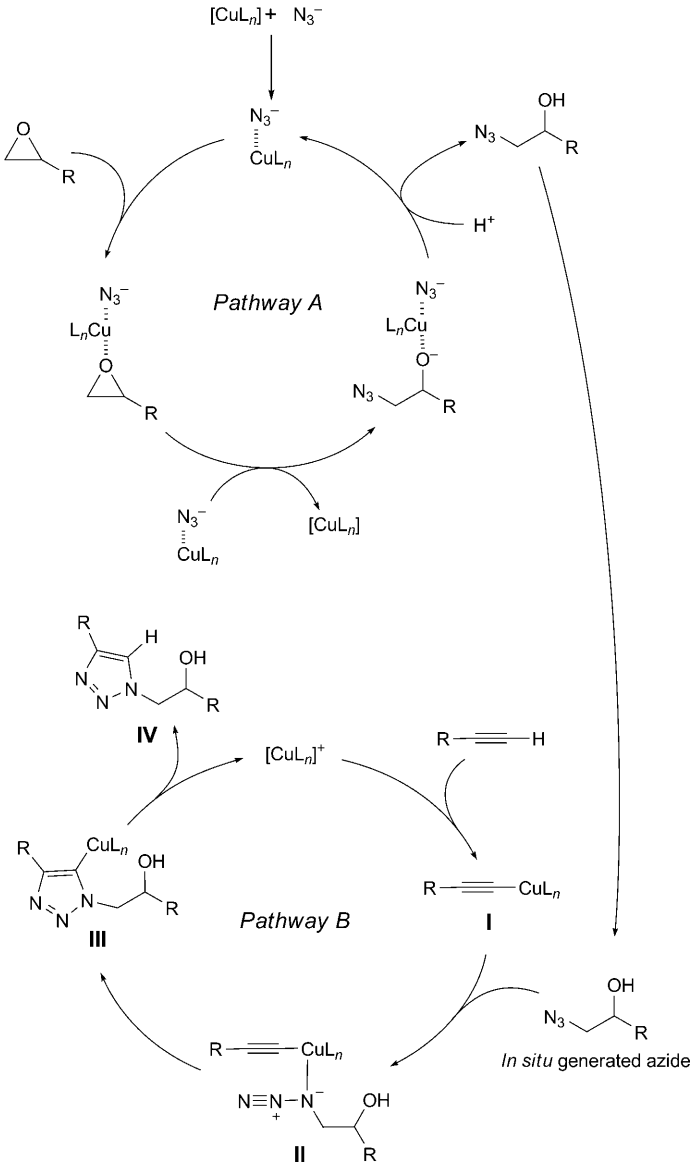
*1-(2-Hydroxyalkyl)-1*H*-1,2,3-triazole Derivatives: General Procedure.* The [Cu(bhppda)$H_2O$] (**4**) [24] catalyst was subjected to ten successive reuses under the following conditions: For each reaction, oxirane **5** (1 mmol), alkyne **6** (1 mmol), and $NaN_3$ (1.2 mmol) were mixed and stirred in $H_2O$ (1 ml) in the presence of **4** (5 mol-%) and ascorbic acid (10 mol-%) at r.t. in an uncapped vial. After the completion of the reaction (TLC (hexane/AcOEt 4 : 1) monitoring), the mixture was diluted by $H_2O$ (5 ml), then the whole mixture was directly passed through a *Celite* pad and rinsed with AcOEt (3 × 10 ml). The combined org. layer was washed with sat. brine, dried ($Na_2SO_4$), and concentrated and the residue recrystallized from EtOH/$H_2O$ 3 : 1 or purified by CC ($SiO_2$, hexane/AcOEt 4 : 1): pure **7**.

*α,4-Diphenyl-1*H*-1,2,3-triazole-1-ethanol* (**7a**): Yield 238.5 mg (90%). Colorless solid. M.p. 125.5 – 126.5°. IR (KBr): 3398 (br.), 3093*m*, 2928*m*, 1458*s*, 1427*m*, 1223*m*, 1118*w*, 1076*s*, 1049*s*, 1030*m*, 760*s*, 694*s*. $^1$H-NMR ($CDCl_3$): 3.62 (*s*, 1 H); 4.15 (*dd*, $J$ = 12.7, 3.8, 1 H); 4.56 (*dd*, $J$ = 12.4, 8.2, 1 H); 5.60 (*dd*, $J$ = 8.2, 3.7, 1 H); 7.17 – 7.26 (*m*, 5 H); 7.28 (*s*, 1 H); 7.29 – 7.34 (*m*, 2 H); 7.62 – 7.69 (*m*, 3 H). $^{13}$C-NMR ($CDCl_3$): 64.7; 67.3; 120.7; 126.0; 127.2; 128.2; 128.8; 129.0; 130.2; 136.2; 147.4. EI-MS: 267 (0.2, $[M+2]^+$), 266 (2.9, $[M+1]^+$), 265 (6.9, $M^+$), 218 (3.7), 206 (43.1), 178 (9.5), 116 (100.0), 77 (40). Anal. calc. for $C_{16}H_{15}N_3O$ (265.31): C 72.43, H 5.70; found: C 72.56, H 5.67.

*4-(Phenoxymethyl)-α-phenyl-1*H*-1,2,3-triazole-1-ethanol* (**7b**): Yield 265.8 mg (90%). Colorless solid. M.p. 78 – 79°. IR (KBr): 3421 (br.), 2870*w*, 1597*m*, 1458*m*, 1223*s*, 1134*w*, 1053*s*, 860*m*, 756*s*, 706*s*. $^1$H-NMR ($CDCl_3$): 3.25 (*s*, 1 H); 3.98 (*dd*, $J$ = 12.3, 3.9, 1 H); 4.36 (*dd*, $J$ = 12.3, 8.4, 1 H); 4.94 (*s*, 2 H); 5.44 (*dd*, $J$ = 8.2, 3.9, 1 H); 6.72 – 6.76 (*m*, 3 H); 6.99 – 7.16 (*m*, 7 H); 7.40 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 61.9; 64.2; 65.8; 114.8; 116.2; 121.4; 123.9; 127.6; 128.8; 129.0; 130.1; 136.2; 143.6; 158.0. EI-MS: 297 (1.0, $[M+2]^+$), 296 (3.2, $[M+1]^+$), 295 (10.6, $M^+$), 236 (4.5), 202 (42.3), 174 (23.4), 144 (48.0), 121 (100.0), 103 (84.6), 77 (75.9), 54 (73.2). Anal. calc. for $C_{17}H_{17}N_3O_2$ (295.34): C 69.14, H 5.80; found: C 69.17, H 5.82.

*4-[(4-Methylphenoxy)methyl]-α-phenyl-1*H*-1,2,3-triazole-1-ethanol* (**7c**): Yield 265.9 mg (87%). Colorless solid. M.p. 94 – 95°. IR (KBr): 3418 (br.), 2870*w*, 1608*w*, 1508*s*, 1458*m*, 1292*w*, 1234*s*, 1176*m*, 1007*s*, 957*m*, 860*m*, 822*s*, 705*s*, 517*m*. $^1$H-NMR ($CDCl_3$): 2.15 (*s*, 3 H); 4.04 (*dd*, $J$ = 12.1, 4.0, 1 H); 4.07 (*s*, 1 H); 4.39 (*dd*, $J$ = 11.9, 8.4, 1 H); 4.95 (*s*, 2 H); 5.55 (*dd*, $J$ = 8.2, 3.8, 1 H); 6.71 (*d*, $J$ = 8.5, 2 H); 6.93 (*d*, $J$ = 8.3, 2 H); 7.08 – 7.21 (*m*, 5 H); 7.53 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 20.5; 61.9; 64.5; 67.2; 114.7; 123.7;

*Scheme 3*




125.9; 128.8; 130.0; 130.5; 136.1; 143.9; 156.1. EI-MS: 311 (1.2, $[M+2]^+$), 310 (3.2, $[M+1]^+$), 309 (10.8, $M^+$), 250 (4.2), 202 (23.4), 174 (42.3), 144 (42.4), 121 (100.0), 103 (80.7), 77 (73.9), 54 (88.5). Anal. calc. for $C_{18}H_{19}N_3O_2$ (309.15): C 69.88, H 6.19; found: C 69.86, H 6.16.

*4-[(4-Chlorophenoxy)methyl]-α-phenyl-1*H*-1,2,3-triazole-1-ethanol* (**7d**): Yield 290.1 mg (88%). Colorless solid. M.p. 83–84°. IR (KBr): 3105 (br.), 2928*w*, 2854*w*, 1716*w*, 1593*w*, 1493*s*, 1250*s*, 1053*s*, 829*m*, 748*w*, 698*m*. $^1$H-NMR ($CDCl_3$): 3.94 (*dd*, *J* = 12.1, 4.2, 1 H); 4.28 (*dd*, *J* = 12.1, 8.4, 1 H); 4.32 (*s*, 1 H), 4.83 (*s*, 2 H); 5.47 (*dd*, *J* = 8.3, 4.1, 1 H); 6.62 (*dd*, *J* = 6.9, 2.1, 2 H); 6.96 (*dd*, *J* = 6.8, 2.2, 2 H);

6.99–7.10 (*m*, 5 H); 7.48 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 61.9; 64.2; 67.4; 116.1; 123.9; 126.0; 127.3; 128.8; 128.9; 129.4; 129.6; 129.9; 136.1; 143.2; 156.8. EI-MS: 331 (0.3, $[M+2]^+$), 330 (0.7, $[M+1]^+$), 329 (1.4, $M^+$), 271 (0.3), 270 (1.1), 209 (1.1), 210 (0.6), 144 (22.0), 121 (37.6), 103 (42), 83 (100.0), 54 (44.4). Anal. calc. for $C_{17}H_{16}ClN_3O_2$ (329.78): C 61.91, H 4.89; found: C 61.90, H, 4.87.

*4-[(4-Nitrophenoxy)methyl]-α-phenyl-1*H-*1,2,3-triazole-1-ethanol* (**7e**): Yield 306.2 mg (90%). Brown solid. M.p. 108–109°. IR (KBr): 3333 (br.), 3151*w*, 2835*w*, 1593*s*, 1504*s*, 1384*s*, 1254*s*, 1176*w*, 1111*s*, 1061*m*, 1003*s*, 868*s*, 841*s*, 752*s*, 690*s*. $^1$H-NMR ($CDCl_3$): 3.62 (*s*, 1 H); 4.19 (*dd*, *J* = 12.2, 3.9, 1 H); 4.56 (*dd*, *J* = 12.2, 8.4, 1 H); 5.24 (*s*, 2 H); 5.68 (*dd*, *J* = 8.2, 3.8, 1 H); 7.02 (*d*, *J* = 9.2, 2 H); 7.21–7.35 (*m*, 5 H); 7.69 (*s*, 1 H); 8.15 (*d*, *J* = 9.2, 2 H). $^{13}$C-NMR ($CDCl_3$): 62.3; 64.7; 67.3; 114.8; 124.0; 125.9; 127.1; 129.1; 129.2; 135.7; 141.8; 142.6; 163.1. EI-MS: 310 (2.4), 281 (2.3), 228 (2.6), 202 (55.9), 156 (31.5), 144 (92.9), 129 (48.5), 121 (100.0), 103 (78.9), 91 (54.6), 77 (39.9), 54 (32.5). Anal. calc. for $C_{17}H_{16}N_4O_4$ (340.33): C 59.99, H 4.74; found: C 59.97, H 4.72.

*4-[(10*H*-Phenothiazin-10-yl)methyl]-α-phenyl-1*H-*1,2,3-triazole-1-ethanol* (**7f**): Yield 312.3 mg (78%). Colorless solid. M.p. 151–152°. IR (KBr): 3418 (br.), 3059*w*, 2870*w*, 1589*w*, 1458*s*, 1335*m*, 1284*w*, 1223*m*, 1130*m*, 1053*m*, 748*s*, 702*m*. $^1$H-NMR ($CDCl_3$): 2.81 (*s*, 1 H); 4.13 (*dd*, *J* = 12.4, 3.8, 1 H); 4.49 (*dd*, *J* = 12.4, 8.4, 1 H); 5.20 (*s*, 2 H); 5.54 (*dd*, *J* = 8.2, 3.7, 1 H); 6.74 (*d*, *J* = 8.0, 2 H); 6.88 (*t*, *J* = 7.4, 2 H); 6.99–7.10 (*m*, 5 H); 7.09 (*dd*, *J* = 7.5, 1.5, 2 H); 7.28 (*dd*, *J* = 5.4, 1.7, 2 H); 7.29 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 44.9; 64.9; 67.1; 115.3; 122.8; 123.5; 124.0; 126.7; 127.2; 128.8; 128.9; 136.0; 144.2; 144.9. EI-MS: 402 (0.7, $[M+2]^+$), 401 (6.0, $[M+1]^+$), 400 (13.1, $M^+$), 280 (1.1), 236 (8.5), 198 (100.0), 121 (14.5), 103 (17.9), 83 (29.1), 55 (55.4). Anal. calc. for $C_{23}H_{20}N_4OS$ (400.50): C 68.98, H 5.03; found: C 68.96, H 5.05.

*2,2'-{{{[1-(2-Hydroxy-2-phenylethyl)-1*H-*1,2,3-triazol-4-yl]methyl}imino}diethane-2,1-diyl}bis[1*H-*isoindole-1,3(2*H*)-dione]* (**7g**): Yield 485.4 mg (86%). Oil. IR (neat): 3464 (br.), 2847*w*, 1770*s*, 1709v*s*, 1400*s*, 1219*w*, 1049*w*, 756*s*, 717*s*. $^1$H-NMR ($CDCl_3$): 2.67–2.77 (*m*, 4 H); 3.59–3.65 (*m*, 4 H); 3.70 (*s*, 1 H); 3.80 (*s*, 2 H); 4.07 (*dd*, *J* = 12.3, 3.8, 1 H); 4.45 (*dd*, *J* = 12.3, 8.4, 1 H); 5.49 (*dd*, *J* = 8.4, 3.7, 1 H); 7.11–7.26 (*m*, 5 H); 7.35 (*s*, 1 H); 7.54–7.57 (*m*, 8 H). $^{13}$C-NMR ($CDCl_3$): 31.8; 47.8; 51.2; 64.8; 66.9; 122.9; 123.4; 125.9; 127.9; 128.5; 128.8; 131.8; 133.7; 136.4; 143.6; 168.1. Anal. calc. for $C_{31}H_{28}N_6O_5$ (564.591): C 65.95, H 5.00; found: C 65.75, H 4.98.

*1-Chloro-4-{[1-(2-hydroxy-2-phenylethyl)-1*H-*1,2,3-triazol-4-yl]methoxy}-9*H-*thioxanthen-9-one* (**7h**): Yield 403.9 mg (87%). Yellow solid. M.p. 102–103°. IR (KBr): 3387 (br.), 2920*w*, 1643*s*, 1578*m*, 1431*s*, 1296*s*, 1250*s*, 1045*s*, 748*s*. $^1$H-NMR ($CDCl_3$): 3.75 (*s*, 1 H); 4.11–4.15 (*m*, 1 H); 4.47–4.55 (*m*, 1 H); 5.18 (*s*, 2 H); 5.53 (*dd*, *J* = 7.7, 3.2, 1 H); 6.99 (*d*, *J* = 8.7, 1 H); 7.14–7.30 (*m*, 7 H); 7.39 (*t*, *J* = 7.7, 2 H); 7.69 (*s*, 1 H); 8.21 (*d*, *J* = 8.5, 1 H). $^{13}$C-NMR ($CDCl_3$): 62.4; 63.7; 66.3; 112.7; 123.2; 124.7; 125.2; 125.5; 126.1; 126.8; 127.8; 128.0; 128.2; 129.4; 130.9; 134.1; 134.9; 150.3; 178.8. EI-MS: 423 (0.1), 389 (0.1), 366 (0.1), 346 (0.2), 312 (0.1), 295 (16.7), 222 (8.6), 193 (17.5), 167 (16.2), 149 (73.6), 117 (69.5), 77 (100), 57 (53.6). Anal. calc. for $C_{24}H_{18}ClN_3O_3S$ (463.937): C 62.13, H 3.91; found: C 61.98, H 4.06.

*2-{[1-(2-Hydroxy-2-phenylethyl)-1*H-*1,2,3-triazol-4-yl]methoxy}-9*H-*thioxanthen-9-one* (**7i**): Yield 347.8 mg (81%). Yellow solid. M.p. 161–162°. IR (KBr): 3433*s*, 3132*w*, 2920*w*, 1624*s*, 1589*s*, 1473*m*, 1338*m*, 1215*m*, 1119*w*, 1007*w*, 744*m*. $^1$H-NMR ($CDCl_3$): 3.75 (*s*, 1 H); 4.07–4.23 (*m*, 1 H); 4.52 (*dd*, *J* = 12.4, 2.8, 1 H); 5.22 (*s*, 2 H); 5.58 (*dd*, *J* = 8.2, 3.8, 1 H); 7.14–7.64 (*m*, 11 H); 8.21 (*d*, *J* = 2.8, 1 H); 8.53 (*dd*, *J* = 8.6, 0.8, 1 H). $^{13}$C-NMR ($CDCl_3$): 62.0; 64.9; 67.3; 111.6; 122.7; 125.9; 126.1; 127.2; 127.4; 128.7; 129.1; 132.0; 135.9; 137.4; 156.8; 179.4. EI-MS: 431 (3.7, $[M+2]^+$), 430 (10.6, $[M+1]^+$), 429 (23.0, $M^+$), 404 (1.3), 370 (3.5), 342 (1.4), 309 (1.7), 281 (3.1), 265 (9.0), 228 (100), 200 (27.6), 174 (1.3), 144 (23.8), 121 (44.6), 103 (36.7), 77 (23.6), 54 (41.9). Anal. calc. for $C_{24}H_{19}N_3O_3S$ (429.492): C 67.12, H 4.46; found: C 66.93, H 4.66.

*4-{[(5-Chloroquinolin-8-yl)oxy]methyl}-α-phenyl-1*H-*1,2,3-triazole-1-ethanol* (**7j**): Yield 331.2 mg (87%). Colorless solid. M.p. 170–172°. IR (KBr): 3310 (br.), 31248*m*, 2943*s*, 2862*w*, 1439*s*, 1238*s*, 1088*s*, 1057*s*, 980*w*, 771*s*, 698*s*. $^1$H-NMR ($CDCl_3$): 3.24 (*s*, 1 H); 4.13–4.16 (*m*, 1 H); 4.43–4.52 (*m*, 1 H); 5.43 (*s*, 2 H); 5.53 (*dd*, *J* = 8.2, 3.9, 1 H); 7.08–7.30 (*m*, 5 H); 7.42–7.48 (*m*, 3 H); 7.64 (*s*, 1 H); 8.45 (*dd*, *J* = 8.6, 1.6, 1 H); 8.84 (*d*, *J* = 2.8, 1 H). $^{13}$C-NMR ($CDCl_3$): 62.9; 64.9; 67.3; 109.9; 122.3; 124.3; 126.4; 127.2; 129.1; 133.1; 135.8; 140.6; 143.5; 149.7. EI-MS: 382 (2.8, $[M+2]^+$), 381 (2.1, $[M+1]^+$), 380 (6.7, $M^+$), 321 (6.2), 231 (8.5), 189 (8.1), 179 (100), 151 (22.1), 121 (34.0), 103 (36.7), 54 (42.3). Anal. calc. for $C_{20}H_{17}ClN_4O_2$ (380.832): C 63.08, H 4.50; found: C 62.89, H 4.67.

*4-(Hydroxymethyl)-α-phenyl-1*H-*1,2,3-triazole-1-ethanol* (**7k**): Yield 180.5 mg (85%). Colorless solid. M.p. 110–111°. IR (KBr): 3340 (br.), 3167*s*, 2932*w*, 2893*w*, 1454*s*, 1234*m*, 1119*s*, 1084*s*, 1011*s*, 849*m*, 795*m*, 702*s*. $^1$H-NMR ($CDCl_3$): 4.03 (*dd*, *J* = 12.3, 3.6, 1 H); 4.33–4.46 (*m*, 3 H); 4.52 (*s*, 2 H); 5.58 (*dd*, *J* = 8.8, 3.8, 1 H); 7.13–7.30 (*m*, 5 H); 7.52 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 53.1; 64.5; 67.1; 122.9; 125.9; 127.1; 128.9; 136.0; 147.3. Anal. calc. for $C_{11}H_{13}N_3O_2$ (219.240): C 60.26, H 5.98; found: C 60.22, H 6.04.

*4-(1-Hydroxy-1-methylethyl)-α-phenyl-1*H-*1,2,3-triazole-1-ethanol* (**7l**): Yield 197.7 mg (80%). Colorless solid. M.p. 119.5–120.5°. IR (KBr): 3356 (br.), 3128*m*, 2970*m*, 1458*w*, 1358*w*, 1165*s*, 1076*s*, 957*m*, 860*m*, 721*m*, 698*m*. $^1$H-NMR ($CDCl_3$): 1.53 (*s*, 6 H); 2.99 (*s*, 2 H); 4.09 (*dd*, *J* = 12.7, 3.7, 1 H); 4.50 (*dd*, *J* = 12.3, 8.4, 1 H); 5.54 (*dd*, *J* = 8.3, 3.6, 1 H); 7.15–7.31 (*m*, 5 H); 7.43 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 30.1; 64.7; 67.2; 68.2; 120.3; 127.2; 128.9; 136.1; 155.2. EI-MS: 247 (0.8, $M^+$), 246 (3.3), 232 (36.8), 216 (20.8), 188 (28.7), 170 (41.3), 149 (14.2), 130 (42.5), 103 (100.0), 84 (70.7), 55 (47.8). Anal. calc. for $C_{13}H_{17}N_3O_2$ (247.293): C 63.14, H 6.93; found: C 63.09, H 6.98.

*4-Butyl-α-phenyl-1*H-*1,2,3-triazole-1-ethanol* (**7m**): Yield 196.2 mg (80%). Oil. IR (neat): 3302 (br.), 3093*m*, 2932*m*, 1551*w*, 1454*s*, 1229*m*, 1072*m*, 756*m*, 702*s*. $^1$H-NMR ($CDCl_3$): 0.89 (*t*, *J* = 7.3, 3 H); 1.24–1.41 (*m*, 2 H); 1.53–1.65 (*m*, 2 H); 2.65 (*t*, *J* = 7.5, 2 H); 3.73 (*s*, 1 H); 4.15 (*dd*, *J* = 12.3, 3.9, 1 H); 4.53 (*dd*, *J* = 12.3, 8.4, 1 H); 5.60 (*dd*, *J* = 8.2, 3.8, 1 H); 7.18–7.37 (*m*, 6 H). $^{13}$C-NMR ($CDCl_3$): 13.8; 22.3; 25.1; 31.3; 64.7; 68.1; 121.5; 127.6; 128.6; 128.8; 136.5; 148.1. Anal. calc. for $C_{14}H_{19}N_3O$ (245.320): C 68.54, H 7.81; found: C 68.44, H 7.69.

*5,6,7,8,9,10-Hexahydro-7-{[1-(2-hydroxy-2-phenylethyl)-1*H-*1,2,3-triazol-4-yl]methyl}-2*H-*1,13,4,7,10-benzodioxatriazacyclopentadecine-3,11(4*H,*12*H)-*dione* (**7n**): Yield 390.6 mg (79%). Colorless solid. M.p. 105–106°. IR (KBr): 3398*s*, 2932*w*, 2854*w*, 1682v*s*, 1535*s*, 1504*s*, 1439*w*, 1257*s*, 1219*w*, 1126*m*, 1053*m*, 756*m*. $^1$H-NMR ($CDCl_3$): 2.77 (*t*, *J* = 5.3, 4 H); 3.48 (*t*, *J* = 5.3, 4 H); 3.77 (*s*, 2 H); 4.07 (*dd*, *J* = 12.3, 3.9, 1 H); 4.36 (*s*, 4 H); 4.44 (*dd*, *J* = 12.3, 8.5, 1 H); 4.50 (*s*, 1 H); 5.54 (*dd*, *J* = 8.3, 3.8, 1 H); 6.81–7.01 (*m*, 4 H); 7.08–7.11 (*m*, 2 H); 7.26–7.29 (*m*, 3 H); 7.49 (*s*, 1 H); 7.59 (*s*, 2 H). $^{13}$C-NMR ($CDCl_3$): 35.5; 44.9; 52.4; 64.7; 67.1; 112.9; 122.2; 123.1; 125.8; 126.9; 128.8; 129.1; 136.1; 143.5; 146.3; 167.5. EI-MS: 496 (1.2, $[M+2]^+$), 495 (3.2, $[M+1]^+$), 494 (16.0, $M^+$), 422 (2.5), 408 (3.6), 373 (2.5), 314 (1.9), 293 (11.4), 292 (29.5), 245 (11.9), 228 (11.5), 203 (12.9), 167 (12.9), 137 (28.4), 121 (59.3), 103 (45.3), 83 (100.0), 56 (99.8). Anal. calc. for $C_{25}H_{30}N_6O_5$ (494.543): C 60.72, H 6.11; found: C 60.89, H 6.08.

*1,8-Bis{[1-(2-hydroxy-2-phenylethyl)-1*H-*1,2,3-triazol-4-yl]methoxy}anthracene-9,10-dione* (**7o**): Yield 530.9 mg (85%). Yellow solid. M.p. 167–168°. IR (KBr): 3394 (br.), 2932*w*, 2878*w*, 2338*w*, 1670v*s*, 1585*s*, 1454*m*, 1315*m*, 1277*m*, 1242*s*, 1053*m*, 980*m*, 744*m*, 702*w*. $^1$H-NMR ($CDCl_3$): 4.10 (*dd*, *J* = 12.3, 3.8, 2 H); 4.15 (*s*, 1 H); 4.45–4.56 (*m*, 3 H); 5.18 (*s*, 4 H); 5.66–5.71 (*m*, 2 H); 7.13–7.23 (*m*, 6 H); 7.30–7.35 (*m*, 4 H); 7.44 (*t*, *J* = 8.2, 2 H); 7.47 (*s*, 2 H); 7.69 (*d*, *J* = 7.6, 2 H); 7.90 (*d*, *J* = 6.8, 2 H). $^{13}$C-NMR ($CDCl_3$): 63.9; 64.6; 67.2; 119.9; 120.6; 124.3; 127.1; 128.7; 128.9; 134.0; 134.6; 136.1; 143.4; 157.8; 183.2. Anal. calc. for $C_{36}H_{30}N_6O_6$ (642.660): C 67.28, H 4.71; found: C 67.42, H 4.87.

*α-(Phenoxymethyl)-4-phenyl-1*H-*1,2,3-triazole-1-ethanol* (**7p**): Yield 230.3 mg (78%). Colorless solid. M.p. 125–126°. IR (KBr): 3425 (br.), 3074*w*, 2920*w*, 1724*w*, 1597*m*, 1493*w*, 1250*s*, 1119*w*, 1080*m*, 1041*m*, 752*s*, 690*s*. $^1$H-NMR ($CDCl_3$): 3.88 (*s*, 1 H); 4.01–4.05 (*m*, 2 H); 4.55 (*dd*, *J* = 12.7, 3.5, 2 H); 4.68–4.77 (*m*, 1 H); 6.90–7.02 (*m*, 3 H); 7.6–7.02 (*m*, 5 H); 7.69–7.72 (*m*, 2 H); 7.85 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 53.5; 68.6; 68.9; 114.5; 121.4; 121.6; 125.5; 128.1; 128.8; 129.6; 130.0; 147.2; 158.2. EI-MS: 297 (1.6, $[M+2]^+$), 296 (4.4, $[M+1]^+$), 295 (7.1, $M^+$), 279 (7.3), 243 (3.7), 222 (5.1), 202 (9.0), 167 (22.1), 149 (62.5), 117 (35.7), 94 (24.2), 77 (51.8), 57 (100.0). Anal. calc. for $C_{17}H_{17}N_3O_2$ (295.336): C 69.14, H 5.80; found: C 68.98, H 5.93.

*4-Phenyl-α-[(prop-2-en-1-yloxy)methyl]-1*H-*1,2,3-triazole-1-ethanol* (**7q**): Yield 236.2 mg (80%). Colorless solid. M.p. 71.5–72°. IR (KBr): 3356 (br.), 3128*m*, 2970*m*, 1458*w*, 1358*w*, 1165*s*, 1076*s*, 957*m*, 860*m*, 721*m*, 698*m*. $^1$H-NMR ($CDCl_3$): 3.19 (*d*, *J* = 5.0, 2 H); 3.70 (*d*, *J* = 5.4, 2 H); 3.96–4.11 (*m*, 2 H); 4.27 (*dd*, *J* = 13.2, 2.6, 1 H); 4.51 (*s*, 1 H); 4.93 (*dd*, *J* = 17.2, 10.3, 1 H); 4.99–5.01 (*m*, 1 H); 5.53–5.64 (*m*, 1 H); 6.94–7.06 (*m*, 3 H); 7.36 (*dd*, *J* = 8.2, 1.7, 2 H); 7.58 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 53.5; 68.9; 71.3; 72.3; 117.4; 121.0; 125.4; 128.0; 128.7; 129.7; 134.2; 147.0. EI-MS: 260 (5.4, $[M+1]^+$), 259 (10.5, $M^+$), 230 (4.8), 203 (11.1), 158 (14.9), 132 (16.0), 116 (100.0), 93 (4.2), 77 (46.2), 57 (37.7). Anal. calc. for $C_{14}H_{17}N_3O_2$ (295.304): C 64.85, H 6.61; found: C 64.97, H 6.49.

rel-*(1*R,*2*R*)-2-(4-Phenyl-1*H-*1,2,3-triazol-1-yl)cyclohexanol* (**7r**): Yield 201.9 mg (83%). Colorless solid. M.p. 179–180°. IR (KBr): 3310 (br.), 3124*m*, 2943*s*, 2862*w*, 1439*s*, 1238*s*, 1088*s*, 1057*s*, 980*w*, 771*s*,

698*s*. $^1$H-NMR ($CDCl_3$): 1.39–2.25 (*m*, 8 H); 4.09–4.17 (*m*, 3 H); 7.23–7.36 (*m*, 3 H); 7.36 (*dd*, $J = 8.2$, 1.7, 2 H); 7.69 (*s*, 1 H). $^{13}$C-NMR ($CDCl_3$): 24.1; 24.8; 31.5; 33.8; 67.4; 72.5; 120.1; 125.4; 127.9; 128.7; 130.2. EI-MS: 245 (0.3, $[M+2]^+$), 244 (2.6, $[M+1]^+$), 243 (6.7, $M^+$), 215 (1.5), 203 (2.6), 174 (1.7), 158 (3.7), 117 (100.0), 81 (55.7), 55 (23.5). Anal. calc. for $C_{14}H_{17}N_3O$ (243.307): C 69.11, H 7.04; found: C 69.03, H 6.89.

rel-*(1*R*,2*R*)-2-{4-[(4-Nitrophenoxy)methyl]-1*H*-1,2,3-triazol-1-yl}cyclohexanol* (**7s**): Yield 264.1 mg (83%). Brown solid. M.p. 143.5–144°. IR (KBr): 3394 (br.), 2951*w*, 2878*w*, 1589*s*, 1512*s*, 1493*s*, 1458*w*, 1338*s*, 1296*m*, 1254*s*, 1223*m*, 1169*m*, 1111*m*, 984*m*, 864*m*, 837*m*, 748*w*. $^1$H-NMR ($CDCl_3$): 1.34–1.49 (*m*, 3 H); 1.84–1.94 (*m*, 3 H); 2.15–2.20 (*m*, 2 H); 3.09 (*s*, 1 H); 3.92–4.02 (*m*, 1 H); 4.12–4.22 (*m*, 1 H); 5.22 (*s*, 2 H); 7.03 (*dd*, $J = 7.2, 2.1, 2$ H); 7.73 (*s*, 1 H); 8.16 (*dd*, $J = 7.2, 2.1, 2$ H). $^{13}$C-NMR ($CDCl_3$): 23.9; 24.7; 31.7; 34.0; 62.4; 67.0; 72.5; 114.8; 123.2; 125.9; 141.8; 163.1. EI-MS: 320 (0.4, $[M+2]^+$) 319 (0.5, $[M+1]^+$), 180 (27.2), 152 (79.4), 108 (17.5), 81 (100.0), 56 (55.5). Anal. calc. for $C_{15}H_{18}N_4O_4$ (318.33): C 56.60, H 5.70, N 17.60; found: C 56.62, H 5.71, N 17.58.

## REFERENCES


[1] R. Huisgen, in '1,3-Dipolar Cycloaddition Chemistry', Ed. A. Padwa, J. Wiley & Sons, New York, 1984, Vol. 1, pp. 1–176.
[2] Q. Wang, T. R. Chan, R. Hilgraf, V. V. Fokin, K. B. Sharpless, M. G. Finn, *J. Am. Chem. Soc.* **2003**, *125*, 3192.
[3] A. J. Link, M. K. S. Vink, D. A. Tirrell, *J. Am. Chem. Soc.* **2004**, *126*, 10598.
[4] A. E. Speers, B. F. Cravatt, *Chem. Biol.* **2004**, *11*, 535.
[5] T. R. Chan, R. Hilgraf, K. B. Sharpless, V. V. Fokin, *Org. Lett.* **2004**, *6*, 2853.
[6] D. D. Díaz, S. Punna, P. Holzer, A. K. McPherson, K. B. Sharpless, V. V. Fokin, M. G. Finn, *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 4392.
[7] A. J. Scheel, H. Komber, B. I. Voit, *Macromol. Rapid Commun.* **2004**, *25*, 1175.
[8] P. Wu, A. K. Feldman, A. K. Nugent, C. J. Hawker, A. Scheel, B. Voit, J. Pyun, J. M. J. Fréchet, K. B. Sharpless, V. V. Fokin, *Angew. Chem., Int. Ed.* **2004**, *43*, 3928.
[9] W. S. Horne, M. K. Yadav, C. D. Stout, M. R. Ghadiri, *J. Am. Chem. Soc.* **2004**, *126*, 15366.
[10] C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057; F. Pérez-Balderas, M. Ortega-Muñoz, J. Morales-Sanfrutos, F. Hernández-Mateo, F. G. Calvo-Flores, J. A. Calvo-Asín, J. Isac-García, F. Santoyo-González, *Org. Lett.* **2003**, *5*, 1951; J. Meng, V. V. Fokin, M. G. Finn, *Tetrahedron Lett.* **2005**, *46*, 4543; B. Gerard, J. Ryan, A. B. Beeler, J. A. Porco Jr., *Tetrahedron* **2006**, *62*, 6405; J. Broggi, S. Díez-González, J. L. Petersen, S. Berteina-Raboin, S. P. Nolan, L. A. Agrofoglio, *Synthesis* **2008**, 141; A. Marra, A. Vecchi, C. Chiappe, B. Melai, A. Dondoni, *J. Org. Chem.* **2008**, *73*, 2458.
[11] V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem., Int. Ed.* **2002**, *41*, 2596.
[12] F. Himo, T. Lovell, R. Hilgraf, V. V. Rostovtsev, L. Noodleman, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2005**, *127*, 210.
[13] S. Quader, S. E. Boyd, I. D. Jenkins, T. A. Houston, *J. Org. Chem.* **2007**, *72*, 1962.
[14] N. Mizuno, M. Misono, *Chem. Rev.* **1998**, *98*, 199; G. Sartori, R. Ballini, F. Bigi, G. Bosica, R. Maggi, P. Righi, *Chem. Rev.* **2004**, *104*, 199; M. Wang, P. Li, L. Wang, *Eur. J. Org. Chem.* **2008**, 2255.
[15] B. Lipshutz, B. R. Taft, *Angew. Chem., Int. Ed.* **2006**, *45*, 8235.
[16] C. Girard, E. Önen, M. Aufort, S.Beauvière, E. Samson, J. Herscovici, *Org. Lett.* **2006**, *8*, 1689.
[17] S. Chassaing, M. Kumarraja, A. S. S. Sido, P. Pale, J. Sommer, *Org. Lett.* **2007**, *9*, 883.
[18] T. Miao, L. Wang, *Synthesis* **2008**, 363.
[19] I. S. Park, M. S. Kwon, Y. Kim, J. S. Lee, J. Park, *Org. Lett.* **2008**, *10*, 497.
[20] E. Saxon, C. R. Bertozzi, *Science (Washington, DC, U.S.)* **2000**, *287*, 2007.
[21] V. D. Bock, H. Hiemstra, J. H. van Maarseveen, *Eur. J. Org. Chem.* **2006**, 51; S. Díez-González, A. Correa, L. Cavallo, S. P. Nolan, *Chem.–Eur. J.* **2006**, *12*, 7558; P. Appukkuttan, W. Dehaen, V. V. Fokin, E. Van der Eycken, *Org. Lett.* **2004**, *6*, 4223; K. Kacprzak, *Synlett* **2005**, 943; Y.-B. Zhao, Z.-Y. Yan, Y.-M. Liang, *Tetrahedron Lett.* **2006**, *47*, 1545.

[22] A. Brik, J. Alexandratos, Y.-C. Lin, J. H. Elder, A. J. Olson, A. Wlodawer, D. S. Goodsell, C.-H. Wong, *ChemBioChem* **2005**, *6*, 1167.
[23] H. Sharghi, M. H. Beyzavi, M. M. Doroodmand, *Eur. J. Org. Chem.* **2008**, 4126; H. Sharghi, M. Aberi, M. M. Doroodmand, *Adv. Synth. Catal.* **2008**, *350*, 2380; H. Sharghi, R. Khalifeh, M. M. Doroodmand, *Adv. Synth. Catal.* **2009**, *351*, 207.
[24] H. Sharghi, M. Hosseini-Sarvari, F. Moeini, *Can. J. Chem.* **2008**, *86*, 1044.
[25] K. R. Reddy, C. U. Maheswari, K. Rajgopal, M. L. Kantam, *Synth. Commun.* **2008**, *38*, 2158.
[26] J. S. Yadav, B. V. S. Reddy, B. Jyothirmai, M. S. R. Murty, *Tetrahedron Lett.* **2005**, *46*, 6559.
[27] H. Sharghi, A. R. Hassani Nejad, M. A. Nasseri, *New J. Chem.* **2004**, *28*, 946.
[28] M. Kinugasa, S. Hashimoto, *J. Chem. Soc., Chem. Commun.* **1972**, 466; M. Miura, M. Enna, K. Okuro, M. Nomura, *J. Org. Chem.* **1995**, *60*, 4999; M. M.-C. Lo, G. C. Fu, *J. Am. Chem. Soc.* **2002**, *124*, 4572.

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