The Use of Glucose as Alternative Reducing Agent in Copper-Catalyzed Alkyne-Azide Cycloaddition

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Abstract: 1,2,3-triazoles were synthesized using several alkynes and azides as starting materials in the presence of glucose and catalytic amounts of Fehling reagent. This process is carried out under ambient pressure and temperature with good yields.

Keywords: Alkynes, azides, Fehling reagent, glucose, 1,2,3-triazoles.

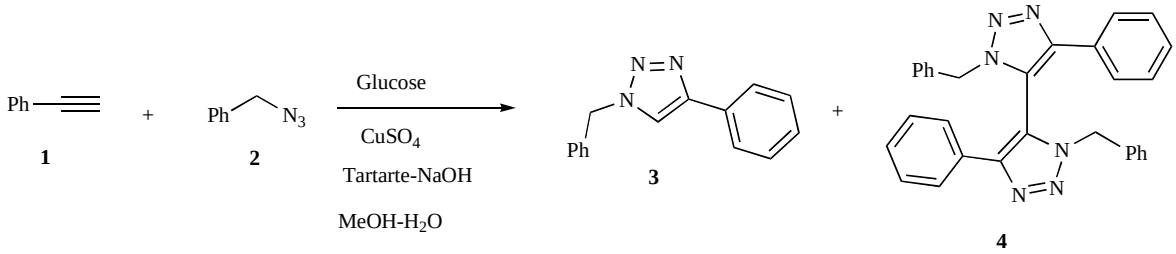
Copper-catalyzed Alkyne-azide cycloaddition (CuAAC) is the most used "click" reaction and one of the most important ligation methods developed in the 21st century [1, 2]. This reaction offers the best method to obtain 1,4-disubstituted-1,2,3-triazoles which have interesting biological activities [3]. One of the advantages of CuAAC is the combination of mild conditions with high yields and regioselectivities, together with high efficiency in terms of atom economy.

The most used protocols to perform this kind of reactions were developed by the groups of Meldal [4] and Sharpless-Fokin [5]. Although both procedures are widespread in application, research and developing in new copper catalysts are important.

In connection with other projects, some time ago we initiated the studies on the synthesis of 1,2,3-triazoles by CuAAC, focused on searching alternative catalytic systems, more economical and compatible to the environment. Inspired by the preceding works of Sharpless and Fokin [5], we sought alternative copper bioreductants which were suitable for click reaction.

In this regard, we were attracted by the Fehling reaction, a process where a copper (II) tartrate complex is reduced by reducing sugars [6]. This reaction is widely used as an identification test. However, as far we know, this process has not been used like a source of copper (I) for catalysis. Motivated by these facts, we decided to investigate the feasibility of this idea and its possible application in CuAAC. Herein is described a summary of our recent endeavours in this area.

In a model study, benzyl azide **2**, which in turn was prepared from benzyl chloride and sodium azide, was reacted with phenylacetylene **1** at room temperature using a catalytic system which was prepared *in situ* by successive addition of glucose, tartrate-NaOH solution (Fehling A Solution), and $CuSO_4$ solution (Fehling B solution) [7]. After 2 h, a mixture of triazole **3**, and bistriazole **4** was obtained. This behaviour



Scheme 1. Cu- catalyzed cycloaddition between azide **2** and alkyne **1**.

has been observed by Angell and Burgess using diverse inorganic bases as additives [8]. On the other hand, when the reaction time was extended to 24 h, only triazole **3** was obtained.

In addition, we prepared a study about the role of the glucose concentration in the Click reaction. In previous works with sodium ascorbate, the group of Sharpless and Fokin discovered a significant influence between the amount of sodium ascorbate and the reaction yield, and they realized that this reaction proceeds with an excess of sodium ascorbate to keep the Cu(I) ion in the reaction, which is the catalytic species in this process. With this precedent, several experiments were carried out using different concentrations

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of glucose (Table **1**). From these results, it was observed that the amount of glucose is important, and the best results were obtained using 0.25 molar equivalents of glucose, increasing the yield to 79.5%.

Table 1. Effect of Glucose in 1,2,3-triazole Formation

Entry	mmol glucose / mmol alkyne	% Yield
1	0.05	56
2	0.10	59.4
3	0.15	71.9
4	0.20	75
5	0.25	79.5
6	0.30	78

On the other hand, the influence of the concentration of basic tartrate/NaOH solution was analyzed. Burgess [8] found a dependence of the base concentration in alkyne-azide cycloaddition, which occurs in alkaline conditions. Therefore, several experiments were made using different volumes of solution of sodium tartrate/NaOH (Table **2**), in order to find the best reaction conditions. A noteworthy feature is that using 0.1 mL of the solution/mmol alkyne, the reaction yield was increased to 95% (see Table **2**, entry 10). The tartrate/NaOH solution is important in this process, because it provides a buffer which stabilizes the cuprous ion in solution.

Table 2. Effect of Tartrate-NaOH Solution in 1,2,3-triazole Formation

Entry	ml tartrate-NaOH / mmol alkyne	% Yield
1	0.025	78
2	0.05	81
3	0.075	88
4	0.10	95
5	0.15	93

In order to explore the reaction scope, several triazoles were synthesized using diverse alkynes and azides (Table **3**). The results show that 1,2,3-triazoles are major products and , in many cases, the only products. However, in some cases (entries 1,6), the presence of bistriazole was also noted. In these examples, the yields were not higher than 20%.

All compounds were fully characterized by conventional spectroscopic techniques, and 1-Benzyl-4-p-tolyloxymethyl-[1,2,3]triazole (entry 6, Table **3**) was obtained as a crystalline solid which was studied by X-ray crystallography, confirming the proposed structure for this compound (Fig. **1**).

Furthermore, we found that certain alkynes and azides gave exclusively bistriazoles, whereas triazoles were not detected. This kind of compounds might be obtained by an oxidative process; such as Angell and Burgess have proposed, however, the mechanistic details are not already clear [8]. Currently, our group is studying the mechanism and some reaction conditions in order to develop a selective procedure for the synthesis of triazoles or bistriazoles.

In conclusion, this report shows that 1,2,3- triazoles are efficiently synthesized from the appropriately constituted alkynes and azides using a catalytic system prepared from Fehling reagent and glucose. This procedure represents an alternative and inexpensive methodology to obtain triazolyl compounds, which are useful points of departure enroute to novel libraries and compounds with triazole moiety. These elements suggest a widespread application.

EXPERIMENTAL

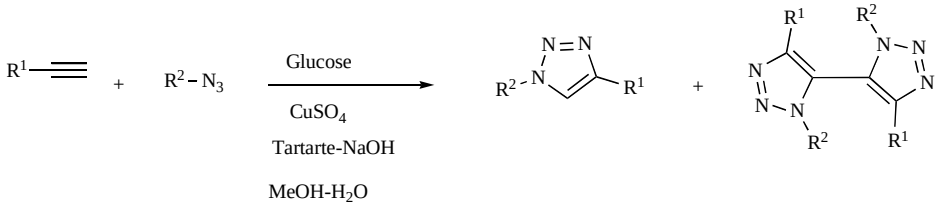
The starting materials were purchased from Aldrich Chemical Co. and were used without further purification. The organic azides were prepared according to the literature [10-12]. Solvents were distilled before use. The tartrate-NaOH solution (Fehling B solution) was prepared dissolving sodium hydroxide (23.5g, 0.04 mol), tartaric acid (18.3 g, 0.012 mol) in H_2O (100 mL). The $CuSO_4$ solution (Fehling A solution) was prepared dissolving $CuSO_4{\cdot}5H_2O$ (9.89g, 0.039 mol) in H_2O (100 mL). Silica gel (230–400 mesh) was purchased from Merck. Silica plates of 0.20 mm thickness were used for thin layer chromatography. Melting points were determined with a Fischer-Johns Scientific melting point apparatus and they are uncorrected. ^1H and ^{13}C NMR spectra were recorded using a Varian 500 MHz, The chemical shifts (δ) are given in ppm relative to TMS as internal standard (0.00). For analytical purposes the mass spectra were recorded on a JEOL JMS-5X 10217 in the EI mode, 70 eV, 200 °C *via* direct inlet probe. Only the molecular and parent ions (m/z) were reported. IR spectra were recorded on a Nicolet Magna 55-X FT instrument.

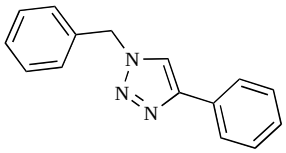
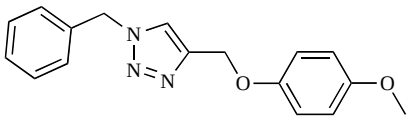
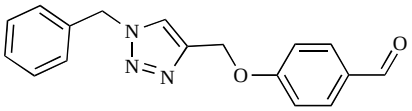
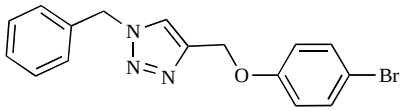
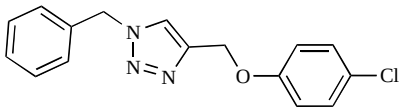
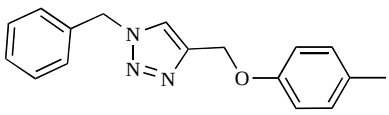
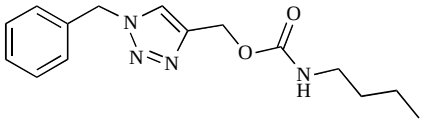
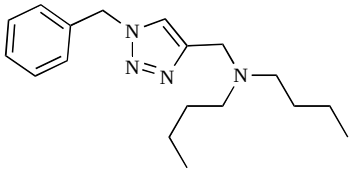
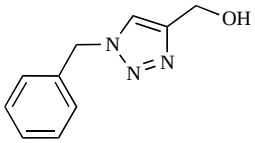
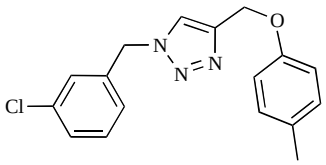
For the RX difraction studies, crystals of compound 1-Benzyl-4-p-tolyloxymethyl-[1,2,3]triazole (entry 6, Table **3**), were obtained by slow evaporation of a dilute EtOH solution, and the reflections were acquired with a Bruker difractometer. Three standard reflections every 97 reflections were used to monitor the crystal stability. The structure was solved by direct methods; missing atoms were found by difference-Fourier synthesis, and refined on F2 by a full-matrix least-squares procedure using anisotropic displacement parameters using SHELX-97. Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (CCDC No. 841826). Copies of available materials can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 IEZ, UK (facsimile: (44) 01223 336033); e-mail: deposit@ccdc.ac.uk.

Synthesis of 1,2,3-triazoles catalyzed by glucose-Fehling Reagent

Typical procedure. The corresponding azide (1 mmol) and alkyne (1 mmol) were added to a solution of glucose (0.045g, 0.25 mmol) in H_2O (1 mL) and MeOH (5 mL). The mixture was treated successively with tartrate-NaOH solution (Fehling B solution, 0.1 mL) and $CuSO_4$ solution (Fehling A solution, 0.25 mL, 0.1 mmol). The resulting mixture was stirred at room temperature for 24 h. The solvent was removed *in vacuo* and the final product was

Table 3. Triazoles Synthesized from Alkynes and Azides Using Catalytic Fehling-Glucose



Entry	triazole	% triazole	% bistriazole
1		95	2
2		57	--
3		80	--
4		53	--
5		89	--
6		72	20
7		70	--
8		47	--
9		73	--
10		65	--

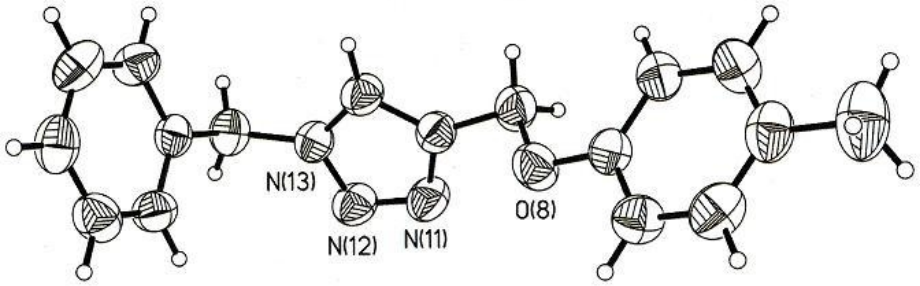
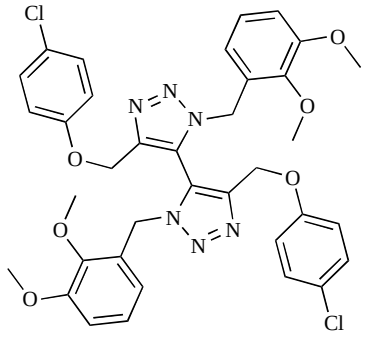
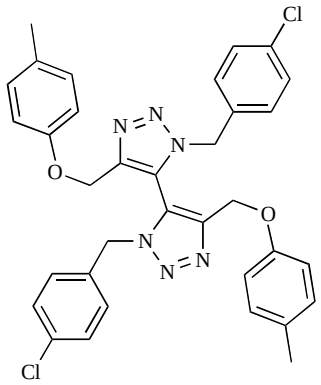
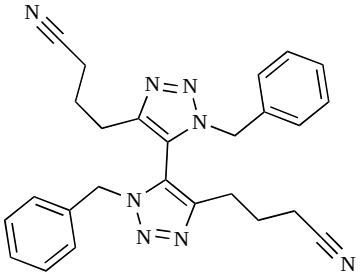


Fig. (1). ORTEP representation for triazole in entry 6, Table **3**.

Table 4. Bistriazoles Synthesized from Alkynes and Azides Using Catalytic Fehling-Glucose

Entry	Bistriazole	% Yield
1		35
2		16
3		53

purified by crystallization or column chromatography (SiO_2, hexane/AcOEt 8:2).

1-Benzyl-4-phenyl-1,2,3-triazole (3)

White solid; mp 130°C (lit. 130-130.9ºC);[9] IR (KBr): ν= 1220, 1350, 1450, 3100 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.79 (m, 2H), 7.69 (s, 1H), 7.40-7.35 (m, 3H), 7.32-7.29 (m, 5H), 5.56 (s,2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 148.0, 134.5, 130.4, 128.9, 128.6, 128.6, 128.0, 127.9, 125.5, 54.0. MS [EI+] m/z (%) 235 $[M]^+$ (20), 206 $[M - HN_2]^+$ (50), 116 $[M - C_7H_7N_2]^+$ (100), 91 $[C_6H_5CH_2]^+$ (85) .

3,3'- Dibenzyl -5, 5'- diphenyl - 3H, 3'H-[4,4'] bi [[1,2,3 triazolyl] (4)

White solid, mp. 65ºC (MeOH).[8] IR (KBr): ν= 1220, 1350, 1450, 3100 cm^{-1}. 1H NMR ($CDCl_3$, 500 MHz) δ 7.45 (m, 4H), 7.28-7.20 (m, 6H), 7.14 (m, 2H), 7.09 (m, 4H), 6.81 (d, 4H, J = 8.0 Hz), 4.70 (d, 2H, J = 14.5 Hz), 4.64 (d, 2H, J

= 14.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 147.8, 132.9, 129.2, 128.9, 128.8, 128.7, 128.7, 128.1, 125.8, 119.8, 52.6. MS [EI+] m/z (%) 468 $[M]^+$ (40), 349 $[M - C_7H_7N_2]^+$ (35), 321 $[M - C_7H_7N_4]^+$ (35), 91 $[C_6H_5CH_2]^+$ (100).

1-Benzyl-4-(4-methoxy-phenoxymethyl)-[1,2,3]triazole (entry 2, Table 3)

m.p. 78°C (MeOH). IR (KBr, cm) ν= 1508, 1458, 1228 cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.49 (s, 1H), 7.33(m, 5H), 6.89 (d, 2H, J=8.5Hz), 6.78 (d, 2H, J=8.5Hz), 5.47 (s, 2H), 5.10 (s, 2H),3.76 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz) δ ppm: 154.5, 154.2, 144.8, 129.1, 128.7, 128.0, 122.6, 116.1, 134.5, 115.9, 114.6, 62.8, 56.5, 55.5. MS [EI+] m/z (%): 295 $[M]^+$ (20), 144 $[M - C_7H_7N_2O_2]^+$ (35), 123 $[M - C_9H_8N_3]^+$ (100), 91 $[C_6H_5CH_2]_+$ (50). HRMS (EI+): for $C_{17}H_{17}N_3O_2$ calcd. 295.1321, found 295.1325.

4-(1-Benzyl-1H-[1,2,3]triazol-4-ylmethoxy)-benzaldehyde (entry 3, Table 3)

White solid (80%); mp 79-80 °C (MeOH). IR (KBr): ν= 1252, 1508, 1680 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.89(s, 1H), 7.83 (d, 2H, J= 8 Hz), 7.80 (m, 2H), 7.58(s, 1H), 7.36 (m, 3H), 7.08(d, 2H, J= 8 Hz), 5.53 (s, 2H), 5.25 (s, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 190.7, 163.14, 163.1, 143.5, 134.3, 130.3, 129.1, 128.9, 128.0, 122.9, 115.1, 62.1, 55.9. MS [EI+] m/z 293 $[M]^+$ (10), 172 $[M - C_7H_9N_2]^+$ (75), 144 $[M – C_7H_7N_2O]^+$ (80), 91 $[C_6H_5CH_2]^+$ (100). HRMS (EI+): for $C_{17}H_{15}N_3O_2$ calcd. 293.1164, found 293.1165.

1-Benzyl-4-(4-bromo-phenoxymethyl)-1H-[1,2,3]triazole (entry 4, Table 3)

White solid (53%); mp 109-111 °C(MeOH). IR (KBr): ν= 1241, 1491, 1601, 3080, cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.52 (s, 1H), 7.37 (m, 2H), 7.28 (m, 2H), 7.19 (m, 1H), 6.93 (m, 2H), 6.84 (m, 2H), 5.54 (s, 2H), 5.16 (s, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 158.8, 144.0, 134.8, 134.3, 130.2, 129.1, 128.8, 128.1, 122.6, 121.4, 115.4, 113.1, 62.2, 54.2. MS [EI+] m/z 345 $[M+2]^+$ (5), 343 $[M]^+$ (5), 172 $[M-C_6H_4BrO]^+$ (15), 144 $[M-C_8H_8BrO]^+$ (65), 91 $[C_6H_5CH_2]^+$ (100). HRMS (EI+): for $C_{16}H_{14}BrN_3O$ calcd. 343.0320, found 343.0324.

1-benzyl-4-(4´-chlorophenoxymethyl)-1,2,3-triazole (entry 5, Table 3)

White solid (82%); mp 102-103°C(MeOH). IR (KBr): ν= 1241, 1491, 1599, 3083, cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.52 (s, 1H), 7.37 (m, 2H), 7.28 (m, 2H), 7.19 (m, 1H), 6.93 (m, 2H), 6.84 (m, 2H), 5.54 (s, 2H), 5.16 (s, 2H), ^{13}C NMR ($CDCl_3$, 125 MHz) δ 158.8, 144.0, 134.8, 134.3, 130.2, 129.1, 128.8, 128.1, 122.6, 121.4, 115.4, 113.1, 62.2, 54.2. MS [EI+] m/z (%) 301 $[M +2]^+$ (5), 299 $[M]^+$ (15), 144 $[M – C_6H_4ClN_2O]^+$ (50), 91 $[C_6H_5CH_2]^+$ (100). HRMS (EI+): for $C_{16}H_{14}ClN_3O$ calcd. 299.0825, found 299.0827.

1-Benzyl-4-p-tolyloxymethyl-[1,2,3]triazole (entry 6, Table 3)

White solid (75%); mp 92-93°C (MeOH). IR (KBr): ν = 1572, 1475, 1276 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.51(s, 1H), 7.36 (d, 2H, J=8 Hz), 7.26 (d, 2H, J=8 Hz), 7.06 (d, 2H, J=8 Hz), 6.84 (d, 2H, J=8 Hz), 5.52(s, 2H), 5.15 (s, 2H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.1, 144.9, 134.5, 129.9, 129.1, 128.8, 128.1, 122.4, 114.6, 62.2, 54.2, 20.4. MS [EI+] m/z (%) 279 $[M]^+$ (40), 144 $[M – C_7H_7N_2O]^+$ (70), 91 $[C_6H_5CH_2]^+$ (100). HRMS (EI+): for $C_{17}H_{17}N_3O$ calcd. 279.1372, found 279.1377.

Crystal data: formula: $C_{17}H_{17}N_3O$; FW 279.34; crystal system: Orthorhombic; space group: $P2_12_12_1$; temp, K=296(2); λ, Å=1.54178; Unit cell dimensions a, Å=5.7275(6); b, Å=8.1375(8); c, Å= 32.067(3); α, deg= 90; β, deg= 90; γ, deg= 90; V, Å^3=1494.6(3); Z=4; $\rho_{calcld.}$, g·cm^{-3}=1.241; μ, mm^{-1}=0.632; F(000)= 592; crystal size, mm^3=0.2 x 0.05 x 0.05; θ range for data collection, deg= 2.76 to 66.37; index ranges: $– 6 \leq h \leq 5$, $– 9 \leq k \leq 9$, $– 37 \leq l \leq 38$; Reflections collected: 14063; Independent reflections (R_{int})= 2582 (0.0287); no. of data / restraints / parameters=2582 / 0 / 190; GoF on F^2=1.073; Final R indices [$I>2\sigma(I)$] R_1=0.0300, wR_2=, 0.0817; R_1, wR_2 (all data): 0.0303, 0.0820; largest diff. peak / hole, e·Å^{-3}=0.107 / –0.109.

In addition, the reaction afforded 3,3'-Dibenzyl-5,5'-bis-p-tolyloxymethyl-3H,3'H-[4,4']bi[[1,2,3]triazolyl] as a White solid (20%); 56-57°C (MeOH). IR (KBr): ν = 1260, 1300, 1560, 3125 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.27 (m, 6H), 6.96 (d, 4H), 6.88 (d, 4H), 6.49 (m, 4H), 4.96 (d, 2H), 4.55 (d, 2H), 4.49 (d, 2H), 4.30 (d, 2H), 2.24 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.5, 146.0, 138.8, 130.6, 129.8, 129.0, 128.9, 128.1, 114.2, 60.9, 52.5, 20.4. [EI+] m/z (%) 556 $[M]^+$ (10), 91 $[C_6H_5CH_2]^+$ (100). HRMS (EI+): for $C_{34}H_{32}N_6O_2$ calcd. 556.2587, found 556.2590.

(1-Benzyl-1,2,3-triazol-4-yl)methyl butylcarbamate (entry 7, Table 3)

White solid (43%); mp 82-83°C (MeOH). IR (KBr): ν = 1536, 1610, 1710, 2954 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.99 (s, 1H), 7.28-7.41 (m, 5H), 7.26 (s, 2H), 5.54 (s, 1H, NH), 5.22 (s, 2H), 4.59 (s, 2H), 3.15 (m 2H),1.44 (m, 2H), 1.25 (m, 2H), 0.86 (t, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.2, 143.9, 134.6, 129.7, 128.5, 127.9, 120.4, 57.6, 52.9, 40.7, 31.9, 19.8, 13.7. MS [EI+] m/z (%) 288 $[M]^+$ (10), 144 $[M – C_5H_{10}N_3O_2]^+$ (20), 91 $[C_6H_5CH_2]^+$ (100). HRMS (EI+): for $C_{15}H_{20}N_4O_2$ calcd. 288.1586, found 288.1583.

(1-Benzyl-1H-[1,2,3]triazol-4-ylmethyl)-dibutyl-amine (entry 8, Table 3)

White solid (65%); mp 66-67°C °C (MeOH). IR (KBr): ν = 1577, 1473, 1276 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.6 (s, 1H), 7.26-7.47 (m, 5H), 5.52 (s, 2H), 3.8 (s, 2H), 2.5 (s, 4H), 1.5 (m, 4H), 1.26 (m, 4H), 0.89 (t, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 134.7, 132.4, 129.1, 129.0, 128.9, 127.9, 58.5, 54.1, 52.8, 27.9, 20.4,13.9. MS [EI+] m/z (%)300 $[M]^+$ (5), 257 $[M-C_3H_7]^+$ (45), 144 $[M-C_{10}H_{21}N]^+$ (45), 91 $[M-C_{11}H_{21}N_4]^+$ (100), 73 $[M-C_{14}H_{17}N_3]^+$ (65). HRMS (EI+): for $C_{18}H_{28}N_4$ calcd. 300.2314, found 300.2319.

(1-Benzyl-[1,2,3]triazol-4-yl)-methanol (entry 9, Table 3)

White solid (73%); mp 76-77°C (lit. 76-77°C);[10] IR (KBr): ν = 1276, 1475, 1572, 3330 cm^{-1} . ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.47(s, 1H), 7.32 (m, 3H), 7.21 (m, 2H), 5.44(s, 2H), 4.68 (s, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 148.3, 134.5, 129.0, 128.7, 128.0, 121.9, 55.9, 54.0. MS [EI+] m/z (%) 189 $[M]^+$ (40), 91 $[C_6H_5CH_2]^+$ (100).

1-(3-Chloro-benzyl)-4-p-tolyloxymethyl-[1,2,3]triazole (entry 10, Table 3)

White solid (65%); mp 67-69 °C(MeOH). IR (KBr): ν = 1276, 1471, 1577 cm^{-1} . ^1H NMR ($CDCl_3$, 500 MHz) δ 7.54 (s, 1H), 7.31 (m, 3H), 7.14 (dt, 1H), 7.06 (d, 2H), 6.85 (d, 2H), 5.49 (s, 2H), 5.14 (s, 2H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.0, 145.1, 136.4, 135.1, 130.6, 130.4, 129.9, 129.3, 128.1, 126.1, 122.5, 114.6, 62.2, 53.5, 20.9. MS [EI+] m/z (%) 315 $[M+2]^+$ (10), 313 $[M]^+$ (30), 178 $[M - C_8H_8N_3]^+$ (80), 125 $[M - C_{10}H_{10}N_3O]^+$ (100). HRMS (EI+): for $C_{17}H_{16}ClN_3O$ calcd. 313.0982, found 313.0986.

Synthesis of Bistriazoles Catalyzed by Glucose-Fehling Reagent

Typical procedure. The corresponding azide (1 mmol) and alkyne (1 mmol) were added to a solution of glucose (0.045g, 0.25 mmol) in H_2O (1 mL) and MeOH (5 mL). The mixture was treated successively with tartrate-NaOH solution (Fehling B solution, 0.1 mL) and $CuSO_4$ solution (Fehling A solution, 0.25 mL, 0.1 mmol). The resulting mixture was stirred at room temperature for 48 h. The solvent was removed *in vacuo* and the final product was purified by column chromatography (SiO_2, hexane/AcOEt 8:2).

5,5'-Bis-(4-chloro-phenoxymethyl)-3,3'-bis-(2,3-dimethoxy-benzyl)-3H,3'H-[4,4']bi[[1,2,3]triazolyl] (entry 1, Table 4)

White solid (35%); mp 103-104°C (AcOEt). IR (KBr): ν = 1276, 1470, 1577 cm^{-1} . ^1H NMR ($CDCl_3$, 500 MHz) δ 7-7.2 (m, 8H), 6.8-6.99 (m, 8H), 5.59 (d, 4H), 5.07 (d, 4H), 3.84 (d, 6H), 3.80 (d, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 158.0, 152.1, 146.5, 143.1, 134.0, 131.8, 130.5, 127.7, 120.5, 115.6, 112.1, 61.8, 58.3, 55.5, 48.9. MS $[FAB]^+$ m/z (%): 718 $[M+1]^+$ (1), 360 $[M\text{-}C_{18}H_{17}ClN_3O_3]^+$ (40), 151 $[M\text{-}C_{27}H_{23}Cl_2N_6O_4]^+$ (100). (100). HRMS (FAB+): for $C_{36}H_{35}Cl_2N_6O_6$ calcd. 717.1995, found 717.1999.

3,3'-Bis-(4-chloro-benzyl)-5,5'-bis-p-tolyloxymethyl-3H,3'H-[4,4']bi[[1,2,3]triazolyl] (entry 2, Table 4)

White solid (16%); mp 109-110°C (AcOEt). IR (KBr): ν = 1276, 1473, 1577 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 7-7.2 (m, 8H), 6.8-6.99 (m, 8H), 5.59 (d, 4H), 5.07 (d, 4H), 3.84 (d, 6H), 3.8 (d, 6H).^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.3, 145.7, 135.0, 132.0, 130.8, 130.5, 129.4, 129.2, 122.2, 114.1, , 61.1, 51.7, 20.4. MS $[FAB]^+$ m/z (%): 625 $[M+1]^+$ (25), 517 $[M\text{-}C_7H_7O]^+$ (30), 154 $[M\text{-}C_{27}H_{24}ClN_4O_2]^+$ (65), 125 $[M\text{-}C_{27}H_{24}ClN_60_2]^+$ (100).HRMS (FAB+): for $C_{34}H_{31}Cl_2N_6O_2$ calcd. 625.1886, found 625.1888.

4-[3,3'-Dibenzyl-5'-(3-cyano-propyl)-3H,3'H-[4,4']bi [[1,2,3]triazolyl]-5-yl]-butyronitrile (entry 3, Table 4)

White solid (53%); mp 56-57°C (AcOEt). IR (KBr): ν = 1370, 1660, 2220, 3095 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37 (m, 6H), 7.26 (m, 4H), 5.52 (d, 4H), 3.07 (m, 2H), 2.87 (m, 2H), 2.66 (m, 2), 2.41 (m, 2H), 2.10 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 148.3, 134.6, 128.9, 128.0, 127.6, 121.1, 119.3, 52.9, 23.9, 16.49. MS $[EI]^+$ m/z (%):450 $[M]^+$ (5), 91 $[M\text{-}C_6H_5CH_2]^+$ (100). HRMS (EI+): for $C_{26}H_{26}N_8$ calcd. 450.5382, found 450.5388.

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