

Proceeding Paper

Synthesis of 1,2,3-Triazoles from Alkyne-Azide Cycloaddition Catalyzed by a Bio-Reduced Alkynylcopper (I) Complex †

Josué Varela-Palma ¹, Jaime González ¹, Gustavo Lopez-Téllez ^{1,2}, M. V. Basavanag Unnamatla ^{1,2}, Marco A. García-Eleno ^{1,2} and Erick Cuevas-Yañez ^{1,2,*}

¹ Centro Conjunto de Investigación en Química Sustentable UAEM-UNAM, Carretera Toluca-Atlacomulco Km. 14.5, Toluca 50200, Estado de México, Mexico; jvarelap@alumno.uaemex.mx (J.V.-P.); arratia_9@hotmail.com (J.G.); glopezt@uaemex.mx (G.L.-T.); mvbasavanagu@uaemex.mx (M.V.B.U.); magarciae@uaemex.mx (M.A.G.-E.)

² Facultad de Química, Universidad Autónoma del Estado de México. Paseo Colón esq. Paseo Tollocan, Toluca 50120, Mexico

* Correspondence: ecuevasy@uaemex.mx; Tel.: +52-722-276-6610 (ext. 7734); Fax: +52-722-217-5109

† Presented at the 24th International Electronic Conference on Synthetic Organic Chemistry, 15 November–15 December 2020; Available online: <https://ecsoc-24.sciforum.net/>.

Abstract: A small library of 1,2,3-triazoles was synthesized from diverse alkynes and azides using catalytic amounts of an alkynylcopper (I) complex, which in turn was prepared from direct treatment of phenylacetylene with a Fehling reagent in the presence of glucose as a reducing agent. The results suggest that copper-catalyzed azide alkyne cycloaddition (CuAAC) reactions require only 0.5 mg/mmol copper (I) phenylacetylde without any further additives.

Keywords: 1,2,3-triazole; alkynylcopper(I) complex; click chemistry; bio-reduced catalyst

Citation: Varela-Palma, J.; González, J.; Lopez-Téllez, G.; Unnamatla, B.; García-Eleno, M.A.; Cuevas-Yañez, E. Synthesis of 1,2,3-Triazoles from Alkyne-Azide Cycloaddition Catalyzed by a Bio-Reduced Alkynylcopper (I) Complex. *Chem. Proc.* **2021**, *3*, 54. <https://doi.org/10.3390/ecsoc-24-08384>

Academic Editors: Julio A. Seijas and M. Pilar Vázquez-Tato

Published: 14 November 2020

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2020 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).

1. Introduction

For more than 15 years, copper-catalyzed azide alkyne cycloaddition (CuAAC) has been the most extended “click” reaction providing a successful method for molecular assembly as well as a growing approach for drug design and materials discovery [1–4]. In this reaction, the copper catalyst plays an essential role in driving the formation of 1,2,3-triazole, recognized as the main CuAAC product serving as a molecular scaffold in these processes [5,6].

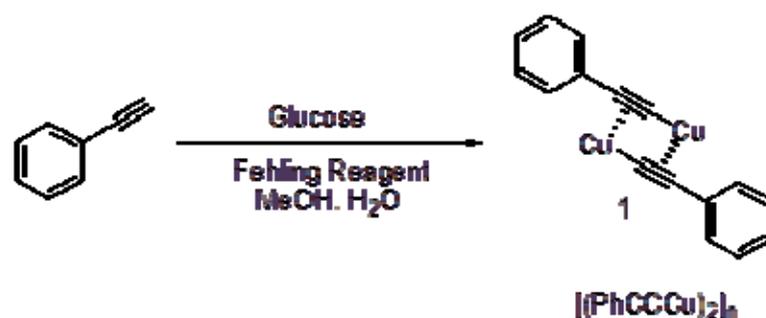
In this regard, diverse copper catalysts have been designed, prepared, and used in CuAAC reactions for several reaction conditions; among these catalysts, alkynylcopper (I) complexes, namely copper acetylides, have been identified as efficient catalysts in these reactions [7]. Although first reports described that metal acetylides are explosives [8], recent reports show some stable copper acetylides with excellent catalytic properties in CuAAC reactions [9–12].

In conjunction with other research, we observed the *in situ* formation of 1,2,3-triazole copper complexes by a straightforward mixing of alkyne, azide, and a copper (I) salt [13]. From these studies, we detected the formation of a copper acetylde and we decided to investigate in detail this process, aiming to prepare efficient catalysts for the synthesis of 1,2,3-triazoles through CuAAC reactions. Herein is disclosed a summary of our recent findings about this challenge.

2. Results and Discussion

A particular chemical process that has drawn our attention is the bio-reduction of copper (II) sulfate promoted by glucose as a reducing agent, which has been used as a catalytic source for CuAAC reactions [14]. Inspired by these features, we proceeded to

adapt the methodologies developed by our group to obtain exclusively copper acetylides. Thus, the successive addition of Fehling A and B solutions to a mixture of glucose–phenylacetylene produced a characteristic yellow precipitate, which was identified as phenylethynylcopper (I) **1**, presenting the same physical data described in the literature (Scheme 1) [12,13]. In addition, XPS analysis of compound **1** displays a signal 2p 3/2 at 935 eV corresponding to a copper species with an oxidation number (I) in agreement with previous reports (Figure 1) [13–17], whereas a signal at 533.8 eV (spectrum b, Figure 1) suggests a Cu–C interaction [18,19]; moreover, the C 1s bond energy at 285.8 eV assigned to aromatic carbons confirmed the formation of copper (I) phenylacetylide **1**, which was used in the following steps.



Scheme 1. Preparation of copper phenylacetylide **1**.

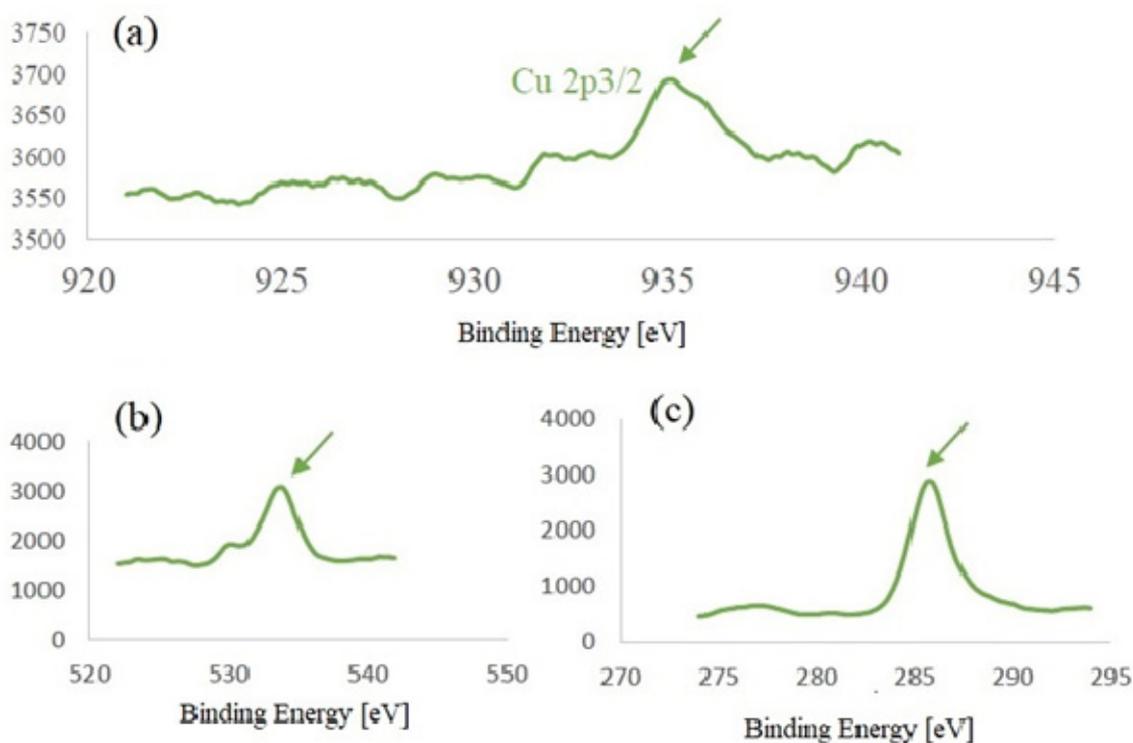
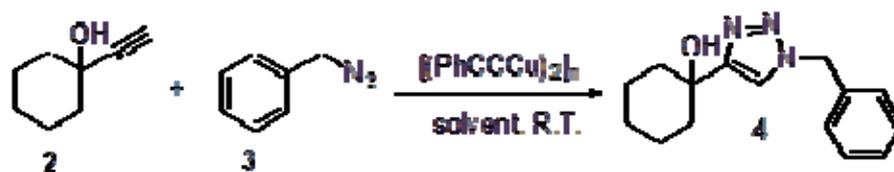


Figure 1. XPS narrow spectra of phenylacetylide **1** for (a) Cu 2p 3/2, (b) Cu–C at the O (1s) level, and (c) C 1s regions.

The reaction between 1-ethynylcyclohexanol **2** and benzylazide **3** was used as a model to evaluate the catalytic activity of phenylacetylide **1** (Scheme 2). In all cases, 1-(1-benzyl-1,2,3-triazol-4-yl)cyclohexanol **4** was obtained as the only reaction product. The results showed in Table 1 indicate that the best conditions were obtained using a 0.5 mg/mmol catalyst after 24 h of using CH_2Cl_2 as a solvent. The conditions found were extended to a series of diverse alkynes and both benzyl azide **3** and 1,3-diazidopropan-2-ol,

affording the corresponding 1,2,3-triazoles in 70–90% yields (Table 2) with a broad functional group tolerance and without other kinds of additives.



Scheme 2. Synthesis of 1,2,3-triazole 4 catalyzed by copper phenylacetylide 1.

Table 1. Synthesis of triazole 4 catalyzed by phenylacetylide 1.

Entry	Catalyst Ratio (mg/mmol)	Solvent	Reaction Time (h)	%Yield
1	0.25	CH ₃ OH	24	50
2	0.25	Acetone	24	58
3	0.25	CH ₂ Cl ₂	24	60
4	0.25	CH ₃ OH	48	51
5	0.25	Acetone	48	55
6	0.25	CH ₂ Cl ₂	48	63
7	0.5	CH ₃ OH	24	72
8	0.5	Acetone	24	70
9	0.5	CH ₂ Cl ₂	24	75
10	0.5	CH ₃ OH	48	71
11	0.5	Acetone	48	71
12	0.5	CH ₂ Cl ₂	48	76
13	1	CH ₃ OH	24	74
14	1	Acetone	24	72
15	1	CH ₂ Cl ₂	24	77
16	1.5	CH ₃ OH	24	74
17	1.5	Acetone	24	74
18	1.5	CH ₂ Cl ₂	24	76

Table 2. 1,2,3-triazole yields catalyzed by copper phenylacetylide 1.

Compound	Alkyne	Azide	% Yield
4	CH ₂ (CH ₂ CH ₂) ₂ C(OH)C≡CH	PhCH ₂ N ₃	77
5	PhC≡CH	PhCH ₂ N ₃	80
6	4-ClC ₆ H ₄ OCH ₂ C≡CH	PhCH ₂ N ₃	70
7	4-NO ₂ C ₆ H ₄ OCH ₂ C≡CH	PhCH ₂ N ₃	87
8	4-BrC ₆ H ₄ OCH ₂ C≡CH	PhCH ₂ N ₃	72
9	4-CH ₃ C ₆ H ₄ OCH ₂ C≡CH	PhCH ₂ N ₃	82
10	C ₁₀ H ₇ OCH ₂ C≡CH	PhCH ₂ N ₃	80
11	CH ₂ (CH ₂ CH ₂) ₂ C(OH)C≡CH	N ₃ CH ₂ CH(OH)CH ₂ N ₃	83
12	PhC≡CH	N ₃ CH ₂ CH(OH)CH ₂ N ₃	92
13	4-ClC ₆ H ₄ OCH ₂ C≡CH	N ₃ CH ₂ CH(OH)CH ₂ N ₃	89

A particular group of triazoles synthesized by this protocol contains a 1,3-bis-(1,2,3-triazol-1-yl)-propan-2-ol core, which has been recognized as a potential building block to antifungal compound development due to its similarity to the fluconazole structure [20]. Thus, compounds 11–13 were obtained in 80–92% through this simple and mild protocol, opening possibilities to develop new potential antifungal drugs; hence, future studies are glimpsed to determine biological properties for these compounds.

3. Experimental

The starting materials were purchased from Aldrich Chemical Co. and were used without further purification. The solvents were distilled before use. Silica plates of 0.20 mm thickness were used for thin layer chromatography. Melting points were determined with a Krüss Optronic melting point apparatus, and they were uncorrected. ^1H and ^{13}C NMR spectra were recorded using a Bruker Avance 300-MHz; the chemical shifts (δ) are given in ppm relative to TMS as an internal standard (0.00). For analytical purposes, the mass spectra were recorded on a Shimadzu GCMS-QP2010 Plus in the EI mode, 70 eV, and 200 °C via direct inlet probe. Only the molecular and parent ions (m/z) are reported. IR spectra were recorded on a Bruker Tensor 27 equipment.

The XPS wide and narrow spectra were acquired with a JEOL JPS-9200, equipped with a Mg X-ray source (1253.6 eV) at 250 W over an analysis area of 3 mm² under vacuum on the order of 1×10^{-8} Torr for all samples. The spectra were analyzed using the specsurfTM software included with the instrument, and all spectra were charge-corrected by means of the carbon signal (C1s) at 284 eV. The Shirley method was used for background subtraction, whereas curve fitting was performed with the Gauss–Lorentz method. Samples were directly deposited on the sample holder and analyzed without any further preparation.

3.1. Copper (I) Phenylacetylide (1)

Phenylacetylene (0.109 mL, 0.102 g, 1 mmol) was added to a solution of glucose (0.45 g, 2.5 mmol) in H₂O (5 mL) and MeOH (15 mL). The mixture was treated successively with tartrate–NaOH solution (Fehling B solution, 1.0 mL) and CuSO₄ solution (Fehling A solution, 2.5 mL, 1.0 mmol). The resulting mixture was stirred for 24 h at room temperature. The solid was filtered and washed with cold diethyl ether (10 mL), MeOH (20 mL), and H₂O (20 mL). The product was dried under reduced pressure. Yield: 0.156 g (95%), m.p. 290 °C. IR (ATR) ν_{max} 3048, 2100 cm⁻¹. Elemental analysis calculated: C, 58.35; H, 3.06; found: C, 58.91; H, 3.19.

3.2. General Procedure for the Synthesis of 1,2,3-Triazoles Catalyzed by Copper Phenylacetylide

Copper (I) phenylacetylide **1** (0.05 g, 0.025 mmol) was added to a stirred solution containing the corresponding alkyne (1.0 mmol) and the appropriate azide (1.0 mmol) in CH₂Cl₂ (10 mL). The resulting reaction mixture was stirred at room temperature for 24 h. The mixture was filtered through celite. The solvent was removed under reduced pressure, and the final product was purified by crystallization.

3.2.1. 1-(1-Benzyl-1,2,3-triazol-4-yl)cyclohexanol **4**

1-Ethynylcyclohexanol and benzyl azide afforded 1-(1-benzyl-1,2,3-triazol-4-yl)-cyclohexanol **4** as a white solid, m.p. 150 °C. Yield: 0.198 g (77%). IR (ATR) ν_{max} 3386, 3291, 2930, 2855, 1604 cm⁻¹. ^1H NMR (300 MHz, DMSO-*d*₆) δ 7.98 (s, 1H), 7.39 (m, 5H), 5.60 (s, 1H), 4.92 (s, 1H), 1.92–1.46 (m, 10H); ^{13}C NMR (75 MHz, DMSO-*d*₆) δ 136.2, 128.7, 128.5, 128.0, 121.1, 68.0, 52.7, 37.8, 25.224, 21.6. MS [EI⁺] m/z (%): 257 [M]⁺ (20), 91 [C₆H₅CH₂]⁺ (100).

3.2.2. 1-Benzyl-4-phenyl-1,2,3-triazole **5**

Phenylacetylene and benzyl azide afforded 1-Benzyl-4-phenyl-1,2,3-triazole **5** as a white solid, m.p. 131 °C. Yield: 0.188 g (80%). IR (ATR) ν_{max} 3250, 2850, 1650, 1600 cm⁻¹. ^1H NMR (300 MHz, CDCl₃) δ 7.82 (m, 2H), 7.68 (s, 1H), 7.41 (m, 4H), 7.33 (m, 1H), 5.59 (s, 2H); ^{13}C NMR (75 MHz, CDCl₃) δ 148.2, 134.6, 130.5, 129.1, 128.8, (2 X CH), 128.7, 127.9, 125.6, 119.5, 54.2. MS (EI⁺) m/z (%): 235[M]⁺ (21), 206 [M – HN₂]⁺ (74), 116 [M – C₆H₅N₃]⁺ (100).

3.2.3. 1-Benzyl-4-(4-chlorophenoxy)methyl-1,2,3-triazole **6**

1-Chloro-4-prop-2-ynyloxybenzene and benzyl azide afforded 1-benzyl-4-(4-chlorophenoxy)methyl-1,2,3-triazole **6** as a white solid, m.p. 103 °C. Yield: 0.207 g (70%). IR (ATR) ν_{max} 1650, 1600 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.38 (m, 3H), 7.27 (m, 2H), 7.22 (dd, 2H, $J = 3\text{Hz}$, $J = 9\text{Hz}$), 6.89 (dd, 2H, $J = 2\text{Hz}$, $J = 9\text{Hz}$), 5.54 (s, 2H), 5.16 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 54.2 (CH_2), 62.2 (CH_2), 116.0 ($2 \times \text{CH}$), 122.6 (CH), 126.1 (C), 128.0 ($2 \times \text{CH}$), 128.8, 129.4 ($2 \times \text{CH}$), 129.7 ($2 \times \text{CH}$), 134.3 (C), 144.1 (C), 156.7 (C). MS (EI^+) m/z (%): 299 [M] $^+$ (15), 91 [$\text{C}_6\text{H}_5\text{CH}_2$] $^+$ (100).

3.2.4. 1-Benzyl-4-(4-nitrophenoxy)methyl-1,2,3-triazole **7**

1-Nitro-4-prop-2-ynyloxybenzene and benzyl azide afforded 1-benzyl-4-(4-nitrophenoxy)methyl-1,2,3-triazole **7** as a white solid, m.p. 95 °C. Yield: 0.269 g (87%). IR (ATR) ν_{max} 3260, 3109, 3084, 2923, 2853, 2129, 1608, 1586, 1383, 1247 (m), 1105 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 8.24 (d, $J = 9\text{Hz}$, 2H), 7.38 (s, 1H), 7.25 (m, 2H), 7.16 (m, 4H), 5.16 (s, 2H), 4.53; ^{13}C NMR (75 MHz, CDCl_3) δ 164.5, 144.2, 140.1, 134.9, 129.7, 129.4, 128.8, 126.1, 116.0, 63.6, 53.7. MS (EI^+) m/z (%): 310 [M] $^+$ (5), 91 [$\text{C}_6\text{H}_5\text{CH}_2$] $^+$ (100).

3.2.5. 1-Benzyl-4-(4-bromophenoxy)methyl-1,2,3-triazole **8**

1-Bromo-4-prop-2-ynyloxybenzene and benzyl azide afforded 1-benzyl-4-(4-bromophenoxy)methyl-1,2,3-triazole **8** as a white solid, m.p. 110 °C. Yield: 0.246 g (72%). IR (ATR) ν_{max} 3260, 3040, 2954, 2926, 2873, 1581, 1487, 1105 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.51 (s, 1H), 7.38 (m, 3H), 7.30 (m, 2H), 7.25 (d, 2H, $J = 8.3\text{Hz}$), 6.81 (d, 2H, $J = 8.2\text{Hz}$), 5.52 (s, 2H), 5.14 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 157.3, 144.2, 134.4, 132.3, 129.2, 128.9, 128.1, 122.7, 116.6, 113.5, 62.2, 54.3. MS (EI^+) m/z (%): 343 [M] $^+$ (5), 91 [C_7H_7] $^+$ (100).

3.2.6. 1-Benzyl-4-p-tolyloxymethyl-1,2,3-triazole **9**

1-Methyl-4-prop-2-ynyloxybenzene and benzyl azide afforded 1-benzyl-4-p-tolyloxymethyl-1,2,3-triazole as a white solid, m.p. 111 °C. Yield: 0.228 g (82%). IR (ATR) ν_{max} 3212, 2954, 2919, 2869, 1607, 1287 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.50 (s, 1H), 7.34 (m, 3H), 7.24 (m, 2H), 7.04 (d, 2H, $J = 8.2\text{Hz}$), 6.83 (d, 2H, $J = 8.2\text{Hz}$), 5.50 (s, 2H), 5.54 (s, 2H), 5.15 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 156.1, 144.9, 134.5, 130.1, 129.9, 129.1, 128.7, 128.1, 122.5, 114.7, 62.3, 54.2, 23.5. MS (EI^+) m/z (%): 279 [M] $^+$ (20), 91 [C_7H_7] $^+$ (100).

3.2.7. 1-Benzyl-4-(naphthalen-1-yloxy)methyl-1,2,3-triazole **10**

1-Prop-2-ynyloxynaphthalene and benzyl azide afforded 1-benzyl-4-(naphthalen-1-yloxy)methyl-1,2,3-triazole **10** as a white solid, m.p. 76 °C. Yield: 0.252 g (80%). IR (ATR) ν_{max} 3126, 3084, 3066, 3040, 2956, 2924, 2874, 2854, 1579, 1460, 1378, 1267, 1240 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 8.20 (d, 1H), 7.82 (m, 2H), 7.65 (m, 2H), 7.59 (s, 1H), 7.38 (m, 3H), 7.30 (m, 3H), 6.95 (d, 1H), 5.55 (s, 2H), 5.39 (s, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 152.2, 143.1, 132.8, 127.4, 127.0, 126.3, 125.7, 124.1, 124.0, 123.5, 120.7, 120.2, 119.1, 103.7, 60.8, 52.5. MS (EI^+) m/z (%): 315 [M] $^+$ (10), 91 [C_7H_7] $^+$ (100).

3.2.8. 1,3-Bis-[4-(1-hydroxy)cyclohexyl-1,2,3-triazol-1-yl]propan-2-ol **11**

1-Ethynylcyclohexanol **2** and 1,3-diazidopropan-2-ol afforded 1,3-Bis-[4-(1-hydroxy)cyclohexyl-1,2,3-triazol-1-yl]propan-2-ol **11** as a white solid, m.p. 100 °C. Yield: 0.319 g (82%). IR (ATR) ν_{max} 3270, 3143, 3094, 2915, 2874, 1605 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 8.21 (s, 2H), 5.04 (s, 1H), 4.60–4.51 (m), 4.20–3.89 (m), 2.22–2.00 (m), 1.87–1.71 (m), 1.60–1.44 (m). ^{13}C NMR (75 MHz, CDCl_3) δ 149.1, 120.3, 72.8, 71.9, 52.9, 36.6, 25.5, 22.6. MS (EI^+) m/z (%): 390 [M] $^+$ (5), 210 [$\text{C}_{10}\text{H}_{16}\text{N}_3\text{O}$] $^+$ (100).

3.2.9. 1,3-Bis-(4-phenyl-1,2,3-triazol-1-yl)-propan-2-ol **12**

Phenylacetylene and 1,3-diazidopropan-2-ol afforded 1,3-bis-(4-phenyl-1,2,3-triazol-1-yl)-propan-2-ol **12** as a white solid, m.p. 200 °C. Yield: 0.318 g (92%). IR (ATR) ν_{max} 3368, 3123, 3094, 2936, 1610, 1579, 1557, 1147, 1126 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 8.53 (s, 2H), 7.85 (d, $J = 7.5$ Hz, 4H), 7.43 (t, $J = 8$ Hz, 4H), 7.31 (t, $J = 7.5$ Hz, 2H), 5.78 (d, $J = 5$ Hz, 1H), 4.60 (d, $J = 10.5$ Hz, 2H), 4.41 (d, $J = 10.5$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 146.1, 130.8, 128.8, 127.7, 125.0, 122.4, 68.2, 53.2. MS $[\text{EI}^+]$ m/z (%): 346 $[\text{M}]^+$ (100).

3.2.10. 1,3-Bis-[4-(4-chlorophenoxymethyl)-1,2,3-triazol-1-yl]-propan-2-ol **13**

1-Chloro-4-prop-2-ynyloxybenzene and 1,3-diazidopropan-2-ol afforded 1,3-bis-[4-(4-chlorophenoxymethyl)-1,2,3-triazol-1-yl]-propan-2-ol **13** as a white solid, m.p. 119 °C. Yield: 0.421 g (89%). IR (ATR) ν_{max} 3397, 3128, 3095, 2923, 2853, 1578, 1487, 1386 cm^{-1} . ^1H NMR (300 MHz, CDCl_3) δ 7.75 (s, 1H), 7.38 (d, $J = 8.3$ Hz, 3H), 7.26 (d, $J = 1.4$ Hz, 3H), 6.87 (d, $J = 8.0$ Hz, 3H), 5.18 (s, 2H), 4.53 (d, $J = 14.9$ Hz, 1H), 4.38 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 158., 134.9, 130.3, 124.8, 121, 6, 68.5, 61.9, 53.1. MS $[\text{EI}^+]$ m/z (%) 474 $[\text{M}]^+$ (100).

4. Conclusions

1,3-Bis-1,2,3-triazol-1-yl-propan-2-ol-based compounds are easily available from CuAAC reactions using phenylacetylide **1** as an inexpensive catalyst obtained from glucose-promoted bio-reduction of a Fehling reagent in the presence of phenylacetylene through a mild synthetic protocol that does not require other additives with high functional group tolerance. The simplicity of this synthetic method suggests that this route to 1,2,3-triazoles will enjoy widespread application.

Author Contributions: Conceptualization, E.C.-Y.; methodology, J.V.-P. and J.G.; formal analysis, G.L.-T.; investigation, J.V.-P., J.G., E.C.-Y., G.L.-T., M.A.G.-E., and M.V.B.U.; resources, E.C.-Y.; data curation, G.L.-T., M.A.G.-E., and M.V.B.U.; writing—original draft preparation, E.C.-Y.; writing—review and editing, E.C.-Y.; supervision, E.C.-Y., M.A.G.-E., and M.V.B.U.; project administration, E.C.-Y.; funding acquisition, E.C.-Y. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by CONACYT-Mexico, project No. A1-S-18230.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: Financial support from CONACYT is gratefully acknowledged. The authors would like to thank N. Zavala, A. Nuñez, L. Triana, and M. C. Martínez for the technical support.

Conflicts of Interest: The authors declare no conflicts of interest.

References

- Chen, Y.; Tong, Z.R. *Click Chemistry: Approaches, Applications and Challenges*; Nova Science Publishers: New York, NY, USA, 2017.
- Chandrasekaran, S. *Click Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2016.
- El-Azab, A.S.; Abdel-Aziz, A.A.M. *Click Chemistry and Applications*; LAP Lambert Academic Publishing: Saarbrücken, Germany, 2014.
- Lahann, J. *Click Chemistry for Biotechnology and Materials Science*; John Wiley & Sons: Chichester, UK, 2009.
- Liang, L.; Astruc, D. The copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) “click” reaction and its applications. An overview. *Coord. Chem. Rev.* **2011**, *255*, 2933–2945.
- Bock, V.D.; Hiemstra, H.; van Maarseveen, J.H. Cu^I-Catalyzed Alkyne–Azide “Click” Cycloadditions from a Mechanistic and Synthetic Perspective. *Eur. J. Org. Chem. Soc.* **2006**, *2006*, 51–68.
- Buckley, B.R.; Dann, S.E.; Heaney, H. Experimental Evidence for the Involvement of Dinuclear Alkynylcopper(I) Complexes in Alkyne–Azide Chemistry. *Chem. Eur. J.* **2010**, *16*, 6278–6284.
- Sladkov, A.M.; Ukhin, L.Y. Copper and Silver Acetylides in Organic Synthesis. *Russ. Chem. Rev.* **1968**, *37*, 748–763.
- Buckley, B.R.; Dann, S.E.; Heaney, H.; Stubbs, E.C. Heterogeneous Catalytic Reactions “On Water” by Using Stable Polymeric Alkynylcopper(I) Pre-Catalysts: Alkyne/Azide Cycloaddition Reactions. *Eur. J. Org. Chem.* **2011**, *2011*, 770–776.

10. Buckley, B.R.; Dann, S.E.; Harris, D.P.; Heaney, H.; Stubbs, E.C. Alkynylcopper(I) polymers and their use in a mechanistic study of alkyne–azide click reactions. *Chem. Commun.* **2010**, *46*, 2274–2276.
11. Evano, G.; Jouvin, K.; Theunissen, C.; Guissart, C.; Laouiti, A.; Tresse, C.; Heimbürger, J.; Bouhoute, Y.; Veillard, R.; Lecomte, M.; et al. Turning unreactive copper acetylides into remarkably powerful and mild alkyne transfer reagents by oxidative umpolung. *Chem. Commun.* **2014**, *50*, 10008–10018.
12. Díez-González, S. Copper(I)–Acetylides: Access, Structure, and Relevance in Catalysis. *Adv. Organomet. Chem.* **2016**, *66*, 93–141.
13. Ramírez-Palma, M.T.; Segura-Arzate, J.; López-Téllez, G.; Cuevas-Yañez, E. Ligand Synthesis Catalyst and Complex Metal Ion: Multicomponent Synthesis of 1,3-Bis(4-phenyl-[1,2,3]triazol-1-yl)-propan-2-ol Copper(I) Complex and Application in Copper-Catalyzed Alkyne-Azide Cycloaddition. *J. Chem.* **2016**, *2016*, 6432492.
14. García, M.A.; Ríos, Z.G.; González, J.; Pérez, V.M.; Lara, N.; Fuentes, A.; González, C.; Corona, D.; Cuevas-Yañez, E. The Use of Glucose as Alternative Reducing Agent in Copper-Catalyzed Alkyne-Azide Cycloaddition. *Lett. Org. Chem.* **2011**, *8*, 701–706.
15. Theunissen, C.; Lecomte, M.; Jouvin, K.; Laouiti, A.; Guissart, C.; Heimbürger, J.; Loire, E.; Evano, G. Convenient and Practical Alkynylation of Heteronucleophiles with Copper Acetylides. *Synthesis* **2014**, *46*, 1157–1166.
16. Okamoto, Y.; Kundu, S.K. Photoconductive Properties of Arylethynylcopper Polymers. Effects of Structure and Oxygen. *J. Phys. Chem.* **1973**, *77*, 2677–2680.
17. Velasco, B.E.; López-Téllez, G.; González-Rivas, N.; García-Orozco, I.; Cuevas-Yañez, E. Catalytic Activity of Dithioic Acid Copper Complexes in the Alkyne-Azide Cycloaddition. *Can. J. Chem.* **2013**, *91*, 292–299.
18. Alonso, F.; Moglie, Y.; Radivoy, G.; Yus, M. Click chemistry from organic halides, diazonium salts and anilines in water catalysed by copper nanoparticles on activated carbon. *Org. Biomol. Chem.* **2011**, *9*, 6385–6395.
19. Carley, A.F.; Dollard, L.A.; Norman, P.R.; Pottage, C.; Roberts, M.W. The reactivity of copper clusters supported on carbon studied by XPS. *J. Electron Spectrosc. Relat. Phenom.* **1999**, *98–99*, 223–233.
20. Zambrano-Huerta, A.; Cifuentes-Castañeda, D.D.; Bautista-Renedo, J.; Mendieta-Zerón, H.; Melgar-Fernández, R.C.; Pavón-Romero, S.; Morales-Rodríguez, M.; Frontana-Uribe, B.A.; González-Rivas, N.; Cuevas-Yañez, E. Synthesis and in vitro biological evaluation of 1,3-bis-(1,2,3-triazol-1-yl)-propan-2-ol derivatives as antifungal compounds fluconazole analogues. *Med. Chem. Res.* **2019**, *28*, 571–579.