Well-Defined Diimine Copper(I) Complexes as Catalysts in Click Azide-Alkyne Cycloaddition Reactions

Jordi Markalain Barta † and Silvia Díez-González *

Department of Chemistry, Imperial College London, Exhibition Road, South Kensington, SW7 2AZ London, UK; E-Mail: j_markalain@hotmail.com

† Erasmus Student from the Universidad de Barcelona, Barcelona 08130, Spain.

* Author to whom correspondence should be addressed; E-Mail: s.diez-gonzalez@imperial.ac.uk; Tel.: +44-207-549-699.

Received: 29 June 2013; in revised form: 21 July 2013 / Accepted: 23 July 2013 / Published: 26 July 2013

Abstract: A series of 1,4-disubstituted 1,2,3-triazoles have been prepared in high yields while respecting the stringent Click criteria. In these reactions, highly stable pre-formed complexes bearing diimine ligands were used.

Keywords: ligand; diimine; copper(I); Click; dipolar cycloaddition; azide

1. Introduction

The introduction of copper(I) catalysts in the cycloaddition of azides and terminal alkynes represents one of the latest success stories of organometallic catalysis [1–4]. Not only is this transformation high yielding and completely regioselective, but also it exemplifies the utility and importance of Click chemistry [5]. Whereas this cycloaddition reaction has been applied in a plethora of fields, the efforts to develop efficient catalytic systems, respectful of the Click criteria, have been significantly fewer. Nevertheless, the use of ligands in the cycloaddition of alkynes and azides has been shown to stabilize the copper(I) centre, increase the catalytic activity, and even modulate it [6]. Among the different families of ligands applied in this reaction, nitrogen-based ones are arguably the most widely used. Whereas Meldal et al. used diisopropylethylamine in their groundbreaking report [1], \(N,N',N''\)-pentamethylenetriamine (PMDETA) and tris-triazoles are also very popular choices [6]. However, examples of well-defined catalysts containing nitrogen based remain scarce [7–11]. Most
reported examples employ polydentate ligands such as polytriazoles or tren ligands (Figure 1). Particularly relevant to this work are complexes bearing bis(aryl)acenaphthenenquinonedimine (Ar-BIAN) ligands C. These have been shown to lead to the formation of triazoles in conversion ranging from modest to good in THF at 50 °C [11].

**Figure 1.** Reported preformed copper(I) catalysts with N-ligands.

Herein, we report the catalytic activity of pre-formed copper(I) complexes bearing one or two \( \alpha \)-diimine ligands in the preparation of 1,2,3-triazoles from azides and terminal alkynes. The structures of the screened complexes are shown in Figure 2. These complexes are all highly stable and easy to prepare from simple diazabutadiene compounds [12].

**Figure 2.** Copper(I) catalysts used in this study.
2. Results and Discussion

We started our optimization studies with the screening of different solvents. We chose cationic complex 1 and benzyl azide (9a) and phenylacetylene as the model reaction. Using 5 mol% of the copper catalyst, virtually no conversion of the starting materials was observed with MeCN, cyclohexane, or ethyl acetate, whereas poor results were obtained in MeOH or under neat conditions (Table 1). Satisfyingly, complete conversions into triazole 10a were obtained on water and in acetone (Table 1, entries 8 and 9). Similar results were observed in THF or in a mixture water/t-BuOH, however, reactions in these solvents were not always reproducible and they were not studied further (Table 1, entries 6 and 7).

In order to determine the best reaction medium for this reaction, the copper loading was next reduced to 2 mol% with acetone and water (Table 1, entries 10 and 11). A higher conversion of 86% was observed in acetone and hence it was kept as solvent for the rest of the study. It is important to note that all tested solvents were technical grade, and in particular, the acetone employed here was the one normally used for cleaning the glassware in the laboratory.

**Table 1.** Solvent screening.

| Entry | Solvent             | [Cu] (mol%) | Conv. (%) a |
|-------|---------------------|-------------|-------------|
| 1     | MeCN                | 5           | <5          |
| 2     | Cyclohexane         | 5           | <5          |
| 3     | Ethyl Acetate       | 5           | <5          |
| 4     | MeOH                | 5           | 52          |
| 5     | Neat                | 5           | 13          |
| 6     | THF                 | 5           | 84 to <5    |
| 7     | Water/t-BuOH        | 5           | >95 to 9    |
| 8     | Water               | 5           | >95         |
| 9     | Acetone             | 5           | >95         |
| 10    | Water               | 2           | 52          |
| 11    | Acetone             | 2           | 86          |

*a 1H-NMR conversions are the average of at least two independent reactions.

We next performed a catalyst screening in acetone at room temperature using 2 mol% of different diimine copper complexes (Scheme 1). All the tested complexes performed well in the model reactions with conversion ranging from 42% to complete. For complexes bearing aromatic groups on the ligands, steric hindrance proved to be more beneficial to the reaction outcome than the presence of electron donating groups. In general, cationic complexes performed better than their neutral analogues, except for complexes bearing adamantyl imine ligands 5 and 6. Additionally, the best performing
complexes had aliphatic substituents on the diimine ligand(s). Hence, complexes 5, 7 and 8 led to total conversions and further experiments were run with these in order to determine the best performing one.

**Scheme 1.** Catalyst screening

\[
\text{Ph} = \text{Ph}_3 \text{N}^+ \quad \text{Ph} + \text{Cu} \quad \text{BF}_4^- \quad \text{RT, 20 h, air} \to \text{Ph} \text{Ph}_3 \text{N} \quad \text{Ph}_3 \text{N}
\]

1, 86%  
2, 82%  
3, 42%  
4, 68%  
5, <95%  
6, 57%  
7, <95%  
8, <95%

\(^a\) \(^1\)H-NMR conversions are the average of at least two independent reactions.

First, the metal loading was further reduced (Table 2). Similar results were obtained with 1 mol% [Cu], but at 0.5 mol% [Cu] it became apparent that complexes bearing either one or two cyclohexyl diimine ligands 7 and 8 displayed a better activity than complex 5, with adamantyl substituents. Gratifyingly, complex 8 could still achieve total conversion in a more concentrated reaction (1 M rather than 0.5 M), and it was chosen as the optimal catalyst within the tested series.

With an optimized catalytic system in hand, the scope of the reaction was then explored. All reactions were carried out in technical grade acetone, in air and in no cases oxidation to copper(II) or disproportionation to copper(0) and copper(II) were observed. Also, no other by-products were formed and the prepared triazoles could be easily isolated as pure products in high yields after a simple extraction (Scheme 2).

A number of functional groups were well tolerated, such as alcohols, amines, alkenes and nitriles. Benzyl, alkyl and aryl azides well suitable cycloaddition partners, as well as electron rich or electron poor alkynes. In some cases, total conversions were not reached under the optimized conditions. However, a slight increase in the reaction temperature (from RT to 40 °C) or the metal loading was enough to ensure a high isolated yield.
Table 2. Final optimization reactions.

| Entry | [Cu] Concentration (M) | Conv. (%) a |
|-------|------------------------|-------------|
| 1     | 5, 1 mol%              | 0.5         | <95         |
| 2     | 7, 1 mol%              | 0.5         | <95         |
| 3     | 8, 1 mol%              | 0.5         | <95         |
| 4     | 5, 0.5 mol%            | 0.5         | 63          |
| 5     | 7, 0.5 mol%            | 0.5         | 92          |
| 6     | 8, 0.5 mol%            | 0.5         | <95         |
| 7     | 7, 0.5 mol%            | 1.0         | 93          |
| 8     | 8, 0.5 mol%            | 1.0         | <95         |

a 1H-NMR conversions are the average of at least two independent reactions.

Scheme 2. Preparation of 1,2,3-triazoles catalyzed by complex 8.a.

3. Experimental Section

3.1. General

All reagents were commercially available and used as received. 1H-NMR (400 MHz) and 13C-NMR (100 MHz) spectra were recorded in CDCl3 on a Bruker AVANCE400 spectrometer at room
temperature. Chemical shifts (δ) are reported in ppm and referenced to tetramethylsilane (1H) and deuterated chloroform (13C), respectively. All reactions were carried out in air and using technical solvents with no particular precautions to exclude oxygen or moisture. All reported yields are isolated yields and are the average of at least two independent reactions. Benzyl azide (9a) [13] 2-azidoethyl-disopropylamine (9b) [14], 2-(2-azidoethyl)-1,3-dioxolane (9c) [15], (2-azidoethyl)benzene (9d) [13], 3-(azidoprop-1-en-yl)benzene (9e) [16], phenyl azide (9f) [17], 6-azidohexanenitrile (9g) [18] and (1-azidoethyl)benzene (9h) [13] are known in the literature and the corresponding spectroscopic data for all these compounds were in good agreement with the reported data.

3.2. Catalytic Results

**General Procedure for the [3+2] Cycloaddition of Azides and Terminal Alkynes**

In a vial fitted with a screw cap, azide 9 (1 mmol), alkyne (1 mmol), acetone (1 mL) and 8 (3 mg, 0.5 mol%) were loaded. The reaction was allowed to proceed at room temperature overnight (20 h). The reaction mixture was then hydrolyzed with a saturated aqueous solution of NH₄Cl (1 h) and extracted with EtOAc. In all examples, the crude products were estimated to be greater than 95% pure by 1H-NMRs.

1-Benzyl-4-phenyl-1H-1,2,3-triazole (10a). Using the general procedure 223 mg (95%) of the title compound were prepared from benzyl azide (9a, 125 μL) and phenylacetylene (112 μL). Spectroscopic data for 10a were consistent with previously reported data for this compound [19]. 1H-NMR (CDCl₃): δ 7.80 (d, J = 7.0 Hz, 2H, H Ar), 7.66 (s, 1H, NCH = C), 7.42–7.37 (m, 5H, H Ar), 7.34–7.31 (m, 3H, H Ar), 5.59 (s, 2H, PhCH₂). 13C-NMR (CDCl₃): δ 148.2 (C, =C–Ph), 134.7 (C, C Ar), 130.5 (C, C Ar), 129.1 (CH, CH Ar), 128.8 (CH, CH Ar), 128.1 (CH, CH Ar), 128.0 (CH, CH Ar), 125.7 (CH, CH Ar), 119.5 (CH, NCH=), 54.2 (CH₂).

1-Benzyl-4-butyl-1H-1,2,3-triazole (10b). Using the general procedure 199 mg (92%) of the title compound were prepared from benzyl azide (9a, 125 μL), 1-hexyne (115 μL), and 8 (12 mg, 2 mol%) at 40 °C. Spectroscopic data for 10b were consistent with previously reported data for this compound [10]. 1H-NMR (CDCl₃): δ 7.40–7.34 (m, 3H, H Ar), 7.26–7.24 (m, 2H, H Ar), 7.18 (s, 1H, NCH=C), 5.50 (s, 2H, PhCH₂N), 2.69 (t, J = 7.5 Hz, 2H, C≡CNCH₂), 1.62 (quintet, J = 7.5 Hz, 2H, CH₂CH₂CH₂), 1.37 (sextet, J = 7.3 Hz, 2H, CH₂CH₃), 0.91 (t, J = 7.3 Hz, 3H, CH₃). 13C-NMR (CDCl₃): δ 149.8 (C, NC≡C-butylyl), 135.0 (C, C Ar), 129.0 (CH, CH Ar), 128.0 (CH, CH Ar), 128.6 (CH, CH Ar), 127.9 (CH, CH Ar), 120.9 (CH, NCH=), 54.0 (CH₂, PhCH₂), 31.4 (CH₂), 25.4 (CH₂), 22.3 (CH₂), 13.8 (CH₃).

1-Benzyl-4-(2-hydroxypropan-2-yl)-1H-1,2,3-triazole (10c). Using the general procedure 183 mg (84%) of the title compound were prepared from benzyl azide (9a, 125 μL), 2-methylbut-3-yn-2-ol (100 μL), and 8 (6 mg, 1 mol%) at 40 °C. Spectroscopic data for 10c were consistent with previously reported data for this compound [19]. 1H-NMR (CDCl₃): 7.39–7.35 (m, 3H, H Ar), 7.34 (s, 1H, NCH=C), 7.31–7.27 (m, 2H, H Ar), 5.51 (s, 2H, CH₂), 2.34 (br s, 1H, OH), 1.61 (s, 6H, CH₃). 13C-NMR (CDCl₃): δ 156.0 (C, NC≡C–), 134.6 (C, C Ar), 129.2 (CH, CH Ar), 128.6 (CH, CH Ar), 128.2 (CH, CH Ar), 119.1 (CH, NCH=), 68.3 (C, C(OH)Me₂), 54.2 (CH₂, PhCH₂), 30.5 (CH₃).
1-(2-Diisopropylaminoethyl)-4-phenyl-1H-1,2,3-triazole (10d). Using the general procedure 232 mg (85%) of the title compound were prepared from azide 9b (170 mg) and phenylacetylene (112 μL).

1H-NMR (CDCl3): δ 7.84–7.81 (m, 3H, HAr), 7.45 (t, J = 6.4 Hz, 2H, HArd), 7.35 (t, J = 6.4 Hz, 1H, HArd), 4.38 (t, J = 6.5 Hz, 2H, CH₂), 3.04 (septet, J = 6.5 Hz, 2H, CH₂), 0.99 (d, J = 6.5 Hz, 12H, CH₃); 13C-NMR (CDCl3): δ 147.1 (NCH=C), 130.9 (C, C Ar), 128.8 (CH, CHAr), 127.9 (CH, CHAr), 125.7 (CH, CHAr), 120.8 (CH, NCH=), 51.2 (CH₂, CH₂N), 48.7 (CH, CHN), 45.7 (CH₂, CH₂N), 20.8 (CH₃). HRMS calculated for C₁₆H₂₅N₄: 273.2079; found 273.2086 [(M+H)+].

Ethyl 1-(2-(1,3-dioxolan-2-yl)ethyl)-1H-1,2,3-triazole-4-carboxylate (10e). Using the general procedure 203 mg (84%) of the title compound were prepared from azide 9c (143 mg), ethyl propiolate (102 μL), and 8 (6 mg, 1 mol%). Spectroscopic data for 10e were consistent with previously reported data for this compound [20].

1H-NMR (CDCl₃): δ 8.12 (s, 1H, NC=H), 4.93 (t, J = 4.0 Hz, 1H, OCHO), 4.58 (t, J = 7.0 Hz, 2H, CH₂), 4.43 (q, J = 7.0 Hz, 2H, CH₂), 4.03–3.93 (m, 2H, OCH₂CH₂O), 3.93–3.83 (m, 2H, OCH₂CH₂O), 2.33 (dt, J = 4.0; 7.0 Hz, CH₂), 1.41 (t, J = 7.0 Hz, 3H, OCH₃). 13C-NMR (CDCl₃): δ 160.2 (C, C=O), 139.3 (C, =C–CO₂Et), 127.5 (CH, CH=C), 127.5 (CH, O–CH–O), 64.55 (CH₂, O–CH₂–CH₂–O), 64.48 (CH₂, O–CH₂–CH₂–O), 60.6 (CH₂, OCH₂–CH₂), 45.0 (CH₂, CH₂–CH₂–N), 33.2 (CH₂, CH₂–CH₂–N), 13.7 (CH₃).

N,N-Dimethyl-1-(1-phenethyl-1H-1,2,3-triazol-4-yl)methanamine (10f). Using the general procedure 202 mg (88%) of the title compound were prepared from (2-azidoethyl)benzene (9d, 147 mg), dimethylprop-2-ynylamine (111 μL) and 8 (6 mg, 1 mol%). Spectroscopic data for 10f were consistent with previously reported data for this compound [20].

1H-NMR (CDCl₃): δ 7.31–7.21 (m, 4H, HAr + NC=H), 7.09 (d, J = 7.0 Hz, 2H, HAr), 4.58 (t, J = 7.0 Hz, 2H, PhCH₂), 3.57 (s, 2H, CH₂NMe₂), 3.21 (t, J = 7.0 Hz, 2H, PhCH₂CH₂), 2.23 (s, 6H, NMe₂). 13C-NMR (CDCl₃): δ 144.7 (C, NCH=C), 137.0 (C, C Ar), 128.7 (CH, CHAr), 128.6 (CH, CHAr), 126.9 (CH, NCH=), 54.2 (CH₂, PhCH₂CH₂N), 51.4 (CH₂, CH₂NMe₂), 44.9 (CH₂, PhCH₂), 36.6 (CH₃).

4-Phenyl-1-(3-phenyl-2-propenyl)-1H-1,2,3-triazole (10g). Using the general procedure 250 mg (96%) of the title compound were prepared from azide 9e (159 mg) and phenylacetylene (112 μL). Spectroscopic data for 10g were consistent with previously reported data for this compound [21].

1H-NMR (CDCl₃): δ 7.84–7.82 (m, 3H, HAr + NC=H), 7.43–7.39 (m, 4H, HAr), 7.36–7.32 (m, 4H, HAr), 6.72 (d, J = 16.0 Hz, 1H, PhCH=CH), 6.40 (dt, J = 16.0, 6.5 Hz, 1H, PhCH=CH), 5.20 (d, J = 6.5 Hz, 2H, CH₂NMe₂), 3.21 (t, J = 7.0 Hz, 2H, PhCH₂CH₂), 2.23 (s, 6H, NMe₂). 13C-NMR (CDCl₃): δ 148.0 (C, NCH=C), 135.4 (C, C Ar), 135.2 (C, CHAr), 130.5 (C, CAr), 128.7 (CH, CHAr), 128.6 (CH, CHAr), 128.4 (CH, CHAr), 128.0 (CH, CHAr), 126.6 (CH, PhCH=), 125.6 (CH, PhCH=CH), 121.8 (CH, CHAr), 119.3 (CH, NCH=), 52.3 (CH₂, CH₂NMe₂).

Dimethyl(1-phenyl-1H-1,2,3-triazol-4-yl)methanamine (10h). Using the general procedure 196 mg (97%) of the title compound were prepared from phenyl azide (9f, 107 μL) and dimethylprop-2-ynylamine (111 μL). Spectroscopic data for 10h were consistent with previously reported data for this compound [22].

1H-NMR (CDCl₃): δ 7.95 (s, 1H, NCH=C), 7.74 (d, J = 8.0 Hz, 2H, HArd), 7.53 (t, J = 8.0, 2H, HArd), 7.43 (t, J = 8.0 Hz, 1H, HArd), 3.71 (s, 2H, CH₂NMe₂), 2.34 (s, 6H, NMe₂). 13C-NMR (CDCl₃): δ 146.0 (C, NCH=C), 137.0 (C, CAr), 129.6 (CH, CHAr), 128.5 (CH, CHAr), 120.4 (CH, NCH=), 120.3 (CH, CHAr), 54.3 (CH₂, CH₂N), 45.2 (CH₃).
6-(4-Phenyl-1,2,3-triazol-1-yl)hexanenitrile (10i). Using the general procedure 227 mg (94%) of the title compound were prepared from 6-azidohexanenitrile (9g, 138 mg) and phenylacetylene (112 μL). Spectroscopic data for 10i were consistent with previously reported data for this compound [23].

$^1$H-NMR (CDCl$_3$): $\delta$ 7.85–7.82 (m, 2H, H$_{Ar}$), 7.76 (s, 1H, NCH=), 7.45–7.42 (m, 2H, H$_{Ar}$), 7.36–7.31 (m, 1H, H$_{Ar}$), 4.44 (t, $J$ = 7.0 Hz, 2H, CH$_2$N), 2.36 (t, $J$ = 7.0 Hz, 2H, CH$_2$CN), 2.08–1.97 (m, 2H, CH$_2$H$_2$), 1.77–1.67 (m, 2H, CH$_2$H$_2$), 1.59–1.48 (m, 2H, CH$_2$).

$^{13}$C-NMR (CDCl$_3$): $\delta$ 147.8 (C, C=C–Ph), 130.5 (C, C$_{Ar}$), 128.8 (CH, C$_{Ar}$), 128.1 (CH, C$_{Ar}$), 125.6 (CH, C$_{Ar}$), 119.5 (CH, CH=C–Ph), 119.3 (C, CN), 49.8 (CH$_2$, CH$_2$–N), 29.5 (CH$_2$), 25.5 (CH$_2$), 24.7 (CH$_2$), 17.0 (CH$_2$).

4-Cyclopropyl-1-(1-phenylethyl)-1H-1,2,3-triazole (10j). Using the general procedure 183 mg (85%) of the title compound were prepared from azide 9h (147 mg), ethynylcyclopropane (87 μL) and 8 (6 mg, 1 mol%) at 40 °C. Spectroscopic data for 10j were consistent with previously reported data for this compound [23].

$^1$H-NMR (CDCl$_3$): $\delta$ 7.40–7.28 (m, 3H, H$_{Ar}$), 7.27–7.24 (m, 2H, H$_{Ar}$), 7.11 (s, 1H, NCH=C), 5.76 (q, 1H, $J$ = 7.0 Hz, PhCH), 1.95 (d, 3H, $J$ = 7.0 Hz, CH$_3$), 1.93–1.87 (m, 1H, CH$_{cyclopropyl}$), 0.94–0.87 (m, 2H, CH$_2$), 0.84–0.79 (m, 2H, CH$_2$).

$^{13}$C-NMR (CDCl$_3$): $\delta$ 150.2 (C=C$_{cyclopropyl}$), 140.1 (C, C$_{Ar}$), 128.9 (CH, C$_{Ar}$), 128.3 (CH, C$_{Ar}$), 126.4 (CH, CH$_{Ar}$), 118.3 (CH, N–CH=C), 58.9 (CH, PhCH), 21.2 (CH$_3$), 7.6 (CH, CH$_{cyclopropyl}$), 6.7 (CH$_2$, CH$_2$).

4. Conclusions

Diimine copper(I) complexes are highly efficient catalysts for the [3+2] cycloaddition of azides and terminal alkynes. Low copper loadings were enough to ensure high isolated yields of 1,2,3-triazoles at room temperature, in air and in technical grade acetone. Furthermore, purification by column chromatography was not necessary, and a simple extraction was enough to isolate pure triazoles. The reported catalysts are noticeably more active than related Ar-BIAN complexes. This might be attributed to two factors: (1) the presence of alkyl groups on the diimine ligands; which in these series systematically outperformed aryl diimines; or (2) the increased chemical stability of simple diimine scaffolds, in particular towards oxidation and reduction reactions.

Acknowledgments

Imperial College London is acknowledged for financial support. J.M.B. thanks the Universidad de Barcelona for an Erasmus Scholarship.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Tornøe, C.W.; Christensen, C.; Meldal, M. Peptidotriazoles on solid phase: [1,2,3]-Triazoles by regiospecific copper(I)-catalyzed 1,3-dipolar cycloaddition of terminal alkynes to azides. *J. Org. Chem.* **2002**, *67*, 3057–3064.
2. Rostovtsev, V.V.; Green, L.G.; Fokin, V.V.; Sharpless, K.B. A stepwise huisgen cycloaddition process: Copper(I)-catalyzed regioselective “ligation” of azides and terminal alkynes. *Angew. Chem. Int. Ed.* 2002, 41, 2596–2599.

3. L’abbe, G. Are azidocumulenes accessible? *Bull. Soc. Chem. Belg.* 1984, 93, 579–592.

4. Special Issue on Click Chemistry. *Chem. Soc. Rev.* 2010, 39, 1221–1408.

5. Kolb, H.C.; Finn, M.G.; Sharpless, K.B. Click chemistry: Diverse chemical function from a few good reactions. *Angew. Chem. Int. Ed.* 2001, 40, 2004–2021.

6. Diez-González, S. Well-defined copper(I) complexes for Click azide-alkyne cycloaddition reactions: One Click beyond. *Catal. Sci. Tech.* 2011, 1, 166–178.

7. Donnelly, P.S.; Zanatta, S.D.; Zammit, S.C.; White, J.M.; Williams, S.J. “Click” cycloaddition catalysts: Copper(I) and copper(II) tris(triazolylmethyl)amine complexes. *Chem. Commun.* 2008, 2008, 2459–2461.

8. Chan, T.R.; Fokin, V.V. Polymer-supported copper(i) catalysts for the experimentally simplified azide-alkyne cycloaddition. *QSAR Comb. Sci.* 2007, 26, 1274–1279.

9. Öżçubukçu, S.; Ozkal, E.; Jimeno, C.; Pericás, M.A. A highly active catalyst for Huisgen 1,3-dipolar cycloadditions based on the tris(triazolyl)methanol-Cu(I) structure. *Org. Lett.* 2009, 11, 4680–4683.

10. Candelon, N.; Lastécouères, D.; Diallo, A.K.; Aranzaes, J.R.; Astruc, D.; Vincent, J.M. A highly active and reusable copper(I)-tran catalyst for the “click” 1,3-dipolar cycloaddition of azides and alkynes. *Chem. Commun.* 2008, 2008, 741–743.

11. Li, L.; Lopez, P.S.; Rosa, V.; Figueira, C.A.; Lemos, M.A.N.D.A.; Duarte, M.T.; Avilés, T.; Gomes, P.T. Synthesis and structural characterisation of (aryl-BIAN)copper(I) complexes and their application as catalysts for the cycloaddition of azides and alkynes. *Dalton Trans.* 2012, 41, 5144–5154.

12. Frutos Pedreño, R.; Markalain-Barta, J.; Vega Isa, E.; Diez-González, S. Manuscript in preparation, 2013.

13. Alvarez, S.G.; Alvarez, M.T. A practical procedure for the synthesis of alkyl azides at ambient temperature in dimethylsulfoxide in high purity and yield. *Synthesis* 1997, 1997, 413–414.

14. Engler, A.C.; Bonner, D.K.; Buss, H.G.; Cheung, E.Y.; Hammond, P.T. The synthetic tuning of clickable pH responsive cationic polypeptides and block copolypeptides. *Soft Matter* 2011, 7, 5627–5637.

15. Carboni, B.; Vaultier M.; Carrié, R. Etude de la chimioselectivité de la reaction des dichloroboranes avec les azides fonctionnels: une synthese efficace d’amines secondaires fonctionnalisees. *Tetrahedron* 1987, 43, 1799–1810.

16. Van Kalkeren, H.A.; Bruins, J.J.; Rutjes, F.P.J.T.; van Delft, F.L. Organophosphorus-catalysed staudinger reduction. *Adv. Synth. Catal.* 2012, 354, 1417–1421.

17. Rehse, K.; Cwiklicki, A. Antiaggregating and antithrombotic activities of new 1,2,3-triazolecarboxamides. *Arch. Pharm. Pharm. Med. Chem.* 2004, 337, 156–163.

18. Luo, L.; Wilhelm, C.; Sun, A.; Grey, C.P.; Lauher, J.W.; Goroff, N.S. Poly(diiododiacetylene): Preparation, isolation, and full characterization of a very simple poly(diacetylene). *J. Am. Chem. Soc.* 2008, 130, 7702–7709.
19. Appukkuttan, P.; Dehaen, W.; Fokin, V.V.; van der Eycken, E. A microwave-assisted Click chemistry synthesis of 1,4-disubstituted 1,2,3-triazoles via a copper(I)-catalyzed three-component reaction. *Org. Lett.* **2004**, *6*, 4223–4225.

20. Díez-González, S.; Nolan, S.P. [(NHC)$_2$Cu]X complexes as efficient catalysts for azide-alkyne Click chemistry at low catalyst loadings. *Angew. Chem. Int. Ed.* **2008**, *47*, 8881–8884.

21. Kamijo, S.; Jin, T.; Huo, Z.; Yamamoto, Y. A one-pot procedure for the regioconrolled synthesis of allyltriazoles via the Pd-Cu bimetallic catalysed three-component coupling reaction of nonactivated terminal alkynes, allyl carbonate, and trimethylsilyl azide. *J. Org. Chem.* **2004**, *69*, 2386–2393.

22. Yan, Z.Y.; Zhao, Y.B.; Fan, M.J.; Liu, W.M.; Liang, Y.M. General synthesis of (1-substituted-1H-1,2,3-triazol-4-ylmethyl)-dialkylamines via a copper(I)-catalyzed three-component reaction in water. *Tetrahedron* **2005**, *61*, 9331–9337.

23. Lal, S.; Díez-González, S. [CuBr(PPh$_3$)$_3$] for azide-alkyne cycloaddition reactions under strict Click conditions. *J. Org. Chem.* **2011**, *76*, 2367–2373.

*Sample Availability:* Not available.

© 2013 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 license (http://creativecommons.org/licenses/by/3.0/).