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A straightforward and sustainable synthesis of 1,4-disubstituted 1,2,3-triazoles *via* visible-light-promoted copper-catalyzed azide–alkyne cycloaddition (CuAAC)†

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A simple and green synthesis of 1,4-disubstituted 1,2,3-triazoles through the effective reduction of copper(II) assisted by organic dyes and promoted by visible light was developed. This reaction was performed under very mild conditions, using water as solvent, under a non-inert atmosphere, with low catalyst precursor loading, and in the absence of any additive. Copper and solvent recycling was successfully achieved at least three times without loss of efficiency. In addition, a safer one-step one-pot procedure was designed with very good yield.

Introduction

Over the past decades, interest in the synthesis of 1,2,3-triazoles has significantly increased. Although these five-membered heterocycles are not normally found in nature, several and interesting biological activities have been attributed to them.[1] They are stable against numerous reaction conditions, such as oxidation, hydrolysis and reduction, turning them into an amide mimetic group.[2] On the other hand, they can interact with molecules through hydrogen bonding and dipole–dipole interactions.[3] Due to these particular properties, they are increasingly employed in several areas of chemistry such as new drug discovery,[4] biochemistry,[5] dendrimers,[6] polymer chemistry,[7] and materials science.[8] Currently, the copper-catalyzed azide–alkyne cycloaddition (CuAAC) is the method most commonly used for the synthesis of 1,2,3-triazoles.[9] This reaction was developed simultaneously by Sharpless[10] and Meldal,[11] and allowed affording exclusively the 1,4-disubstituted regioisomer.

CuAAC reactions are within the group of reactions defined by Sharpless as "click".[12] These reactions are easy to carry out, have a broad synthetic scope, high yield and specificity, are easily purified, do not generate secondary products or are harmful to the environment or health, require starting materials available and easily handled, and can often be developed in benign solvents such as water or alcohols.

It is widely demonstrated that Cu(I) is the catalytically active species which leads to the exclusive formation of 1,4-disubstituted 1,2,3-triazole in CuAAC reactions.[13] Several copper sources can be used: for example, elemental copper either in wire form or nanoparticles;[14] or Cu(0) combined with a source of Cu(II) to promote comproportionation.[15] Other methodologies directly employ a Cu(I) source; yet, an inert atmosphere is often required to avoid cation oxidation. In these cases, the addition of nitrogenous base or a ligand is needed to stabilize active Cu(I) and prevent its oxidation or disproportionation.[16] In addition, the use of organic solvents such as MeCN, THF, dichloromethane, and toluene is often required. Despite that, the *in situ* Cu(I) formation at the expense of a Cu(II) source is the most simple and convenient method. This methodology ensures a high concentration of Cu(I) throughout the reaction. The most widespread catalytic system is CuSO$_4$ (as a Cu(II) source) and sodium ascorbate (as a reducing agent). The limitation is shown when aerobic conditions are employed in aqueous media, where the oxidation of Cu(I) to the inactive Cu(II) species is favoured. To overcome this drawback, larger amounts of Cu(II) (5–20 mol%) and ascorbate, up to five times the amounts of Cu(II), must be employed. In addition, the use of reducing agents such as sodium ascorbate is limited in biological systems, since it could affect protein chains[17] and DNA structure.[18] To deal with this issue, protocols where Cu(I) species are generated *in situ* by the photoinduced reduction of Cu(II) have been developed. This allows the application of CuAAC not only in biological environments, but also in materials science, thanks to the perfect spatial and temporal control offered by these methodologies.[19] Generally, two ways of using the light to promote reduction of Cu(II) salts are reported: (i) irradiating with UV light (or visible light to a lesser extent) metal complexes

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† Electronic supplementary information (ESI) available: Experimental procedure, characterization data and copies of ¹H and ¹³C NMR spectra for all the products (**3a–r**). See DOI: 10.1039/c7ra06390c
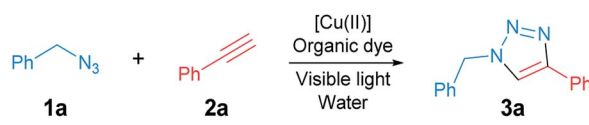
which contain nitrogenous or carboxylates ligands;[20] and (ii) using a photoinitiator, which fragments under irradiation.[21] Other methodologies reported are less widespread, but more beneficial since they use visible light exclusively.[22] In these cases, an organic chromophore[23] or a transition metal complex[24] is employed, which can be reduced by a donor sacrificial reagent, usually triethylamine (TEA), when electronically excited by light. The reduced species can transfer one electron to Cu(II) cation and Cu(I) species is thus generated triggering CuAAC reaction. The present work represents a novel example in the use of organic dyes and visible light to assist the reduction of Cu(II) ions, merging the concepts of photoredox[25] and transition metal catalysis applied to the synthesis of 1,4-disubstituted 1,2,3-triazoles. This new protocol is carried out in water as solvent, under air atmosphere, at room temperature, and in short reaction times. In addition, a lower catalyst loading is used in comparison to conventional CuAAC protocols, and additives such as bases, proton source, sophisticated ligands, and copper complexes or nanostructures are not required.

Results and discussion

We set out benzylazide **1a** and phenylacetylene **2a** as model reagents in water as solvent to test the CuAAC reaction. Some copper(II) salts were used as a copper source, and organic dyes as a visible light-promoted reducing agent (Chart 1). Preliminarily, we found that eosin Y disodium salt (EY) promoted an efficient photochemical reduction of Cu(II) to Cu(I) which afterward participated as catalyst in the copper-catalyzed azide–alkyne cycloaddition reaction, yielding the 1,4-disubstituted 1,2,3-triazoles **3a** as unique product. Thus, optimization and control reactions were performed (Table 1).

In the starting condition, Cu(II) and organic dye were initially used at 5 mol%. The mixture was placed under green-LED light

Chart 1 Structures of organic dyes employed for the optimizing reactions conditions.

Table 1 Optimization and control reactions

Entry[a]	Dye (mol%)	[Cu(II)] (mol%)	$h\nu$ (nm)	Time (h)	Yield 3a[b] (%)
1	EY (5)	CuSO$_4$ (5)	530	1	58
2	—	CuSO$_4$ (5)	530	15	Traces
3	EY (5)	—	530	15	—
4	EY (5)	CuSO$_4$ (5)	—	15	Traces
5	EY (1)	CuSO$_4$ (1)	530	1	66 (56)[c]
6	EY (0.4)	CuSO$_4$ (0.4)	530	2	86
7	FL (0.4)	CuSO$_4$ (0.4)	467	2	49 (31)[d]
8	RB (0.4)	CuSO$_4$ (0.4)	530	2	67
9	R6G (0.4)	CuSO$_4$ (0.4)	530	2	5
10	MB (0.4)	CuSO$_4$ (0.4)	625	2	21 (13)[d]
11	EY (0.4)	Cu(NO$_3$)$_2$ (0.4)	530	2	82
12	EY (0.4)	Cu(OAc)$_2$ (0.4)	530	2	68
13	**EY (0.4)**	**CuCl$_2$ (0.4)**	**530**	**2**	**95**
14	EY (0.1)	CuCl$_2$ (0.1)	530	2	71

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.25 mmol), water (2 mL), room temperature, ambient air. [b] Isolated yield. [c] Reaction performed under nitrogen. [d] Reaction irradiated with green LED (530 nm).

(530 nm) for 1 h to give **3a** in 58% yield (Table 1, entry 1). Subsequently, control experiments were performed at considerably longer reaction times. The absence of the organic dye, copper source, or irradiation inhibited the formation of **3a**, since under these conditions the Cu(I) active species fails to form (Table 1, entries 2–4).

When catalyst precursor loading was decreased to 1%, a slight improvement in yield of **3a** to 66% was observed (Table 1, entry 5); whereas in inert N$_2$ atmosphere, no significant advantages against aerobic conditions were noticed. Since a decrease in catalyst precursor loading showed a slight improvement in yield of **3a**, Cu(II) salt was reduced to 0.4% and irradiation time was increased to 2 h. In these conditions, **3a** was obtained in 86% yield (Table 1, entry 6).

Other organic dyes such as fluorescein (FL), rose bengal (RB), rhodamine 6G (R6G), and methylene blue (MB) were tested (Chart 1, Table 1, entries 7–10). The best results were obtained when the mixtures were irradiated at the wavelength whose organic dye shows maximum absorption. The formation of Cu(I) was assisted more efficiently by EY where the best yield for **3a** was observed. The absence of **3a** was noticed when R6G was used (Table 1, entry 9), attributed to two possible reasons: (i) inability to form Cu(I) from Cu(II) due to the negligible intersystem crossing quantum yield ($\Phi_{ISC} = 0.002$),[26] or (ii) absence of free carboxyl groups which could act as ligands of the catalytically active cations.[27] Then, other Cu(II) sources such as Cu(NO$_3$)$_2$, Cu(OAc)$_2$, and CuCl$_2$ were used (Table 1, entries 11–13 respectively). CuCl$_2$ was the most efficient, giving an excellent isolated yield of **3a** (95%). Even though the effect of the counterion in the copper source should be negligible in the
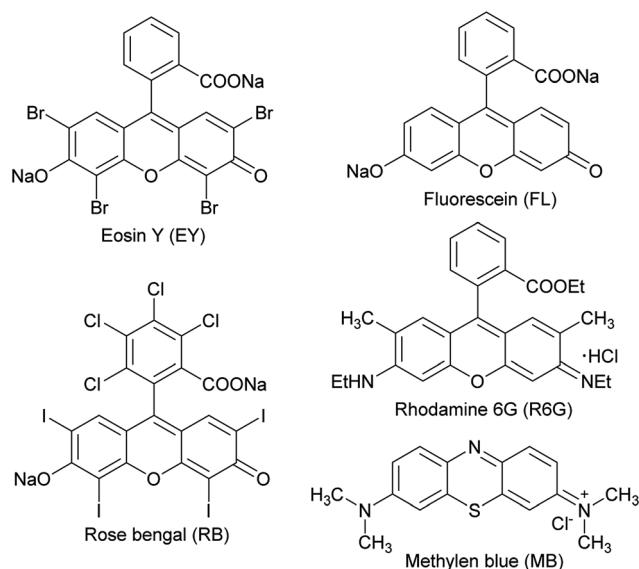
CuAAC reaction, our results suggested that the *in situ* photoinduced reduction of Cu(II) is indeed affected by the anions. This effect is reasonable by considering that ligands with a pronounced tendency to complex with metal ions considerably reduces the reduction potential of the Cu(II)/Cu(I) redox couple.[28] Under these conditions, and if the entire amount of Cu(II) would be reduced to Cu(I) by EY, a TON (turn over number) of at least 240 would be obtained, which is much higher than the TONs of most CuAAC reactions carried out in conventional systems. Finally, when a catalyst precursor loading of 0.1 mol% was tested (Table 1, entry 14), **3a** was afforded in 71% yield (TON = 710). This proves the high efficiency of our system, since acceptable yields can be obtained using the smallest catalyst amount that we could use.

On the other hand, the presence of certain additives was also tested to improve efficiency, reducing, for instance, irradiation time. Organic and inorganic bases and acids (and their combination) were employed to assist the deprotonation or protonation steps in CuAAC reaction.[9] However, a significant inhibition was found when triethylamine (TEA) and triethanolamine (TEOA), or its combination with AcOH at 5 mol%, were used. When TEOA or TEOA/AcOH was employed, **3a** was obtained in around 14% yield, whereas a quantitative recovery of substrates was noticed when TEA or TEA/AcOH was employed. A decrease in yield of **3a** (65%) was observed when the inorganic base K_2CO_3 (2 mol%) was used. To improve the solubility of substrates, organic co-solvents such as ethanol, isopropanol, *tert*-butanol, and PEG 300 were evaluated; however, **3a** was not detected under these conditions.

To study the reaction scope, benzyl, phenacyl, alkyl and aryl azides, as well as aryl, and alkyl terminal alkynes were tested under optimized conditions. Scheme 1 shows triazoles obtained by this methodology. For some substrates, experimental conditions were slightly modified so as to improve reaction yields.

The reaction between **1a** and **2a** gave an excellent yield of **3a** in 95% under standard conditions as mentioned above (condition A, Scheme 1). Less than 50% yield was observed when the irradiation time was 2 h for the other benzylic azides, but was considerably improved when the irradiation time was duplicated. Thus, triazoles achieved from benzyl azides with a methyl (**3b**), methoxy (**3c**), nitro (**3e**), and cyano (**3f**) group in their aromatic ring showed very good to excellent yields (73–100%). Triazoles from benzyl azides with iodine (**3d**) and trifluoromethyl (**3g**) substituent were obtained close to 50% yield, (condition A, Scheme 1). In all cases, a satisfactory mass balance was found even when yields were not quantitative, in these cases unreacted starting material and no by-products were detected.

To obtain triazoles with a phenacyl moiety, a reduced group of α-azidoacetophenones was employed. Under standard conditions, only **3i** could be isolated in a very good yield (91%), whereas **3h** and **3j** were detected in traces with a partial consumption of the corresponding organic azide. However, with an increase in concentration of about five times (0.4 mL final volume) very good yields were obtained for **3h** and **3j**, 70% and 86% respectively after 4 h of irradiation (condition B, Scheme 1).
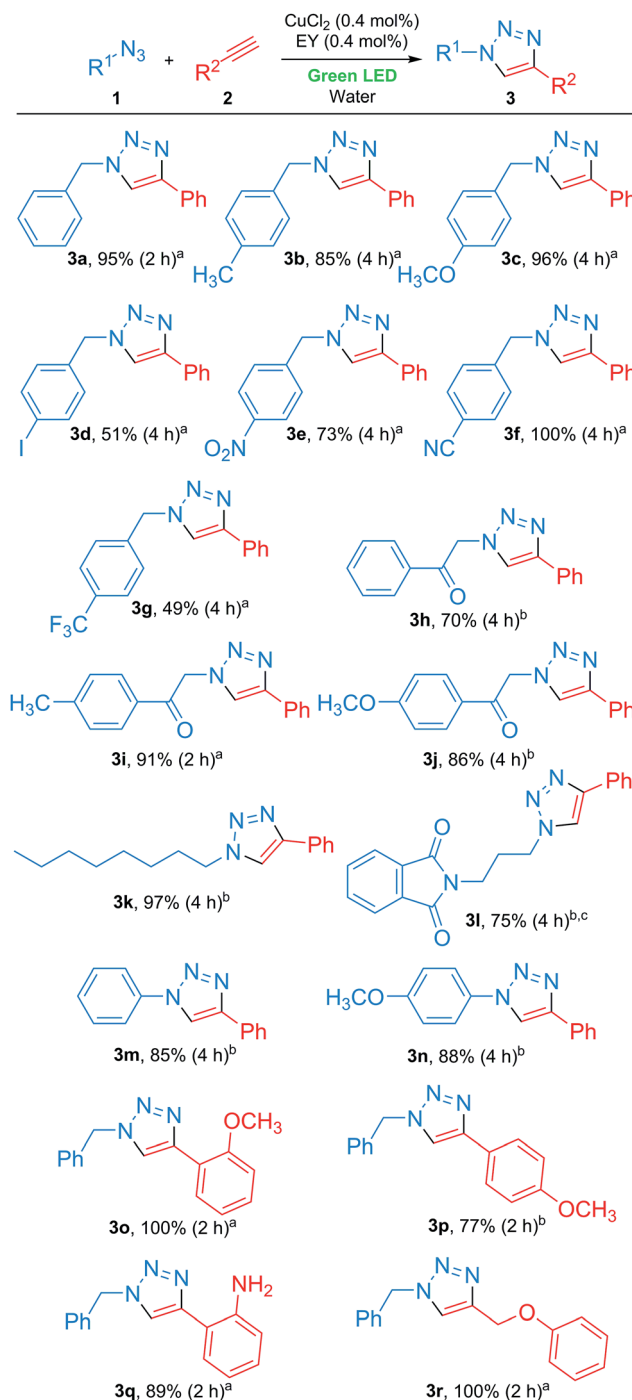
Scheme 1 Synthesis of 1,4-disubstituted 1,2,3-triazoles *via* visible-light promoted CuAAC reaction. Reaction conditions: [a]condition A: organic azide **1** (0.25 mmol), terminal alkyne **2** (0.25 mmol), $CuCl_2$ (0.4 mol%), EY (0.4 mol%) in water (2 mL) irradiated with green LED (530 nm) for the time in parenthesis indicated. Isolated yields were reported. [b]Condition B: idem condition A, except that 0.4 mL of water were used instead of 2 mL. [c]Condition C: reaction performed in two steps: a mixture of $CuCl_2$ (0.4 mol%) and EY (0.4 mol%) was irradiated for 1 h, then organic azide and terminal alkyne were added and stirred for 4 h in the dark.

Furthermore, alkyne **2a** was tested with two aliphatic azides, *n*-octyl azide, and 3-azidopropylphthalimide. For the former, triazole **3k** was obtained in 97% yield in 4 h under condition B.

However, for the latter, **3l** was not found under any of the above conditions, and a partial consumption of the corresponding organic azide was observed. In the substrate with a strong electron-withdrawing group, a reduction event from the electronically excited eosin (EY*) could take place,[25a] protecting Cu(II) and avoiding the formation of Cu(I) catalytically active species. Despite this, reduction products from these azides were not observed by GC-MS. For this reason, the reaction between 3-azidopropylphthalimide and **2a** was performed in two steps (condition C, Scheme 1): a first step in presence of light, where a mixture of CuCl$_2$ (0.4 mol%) and EY (0.4 mol%) was irradiated with green-LED light in 0.4 mL of water for 1 h, to achieve *in situ* formation of the Cu(I) catalytically active species; and a second step under the dark, where the substrates were added, stirring at room temperature and without irradiation (dark condition) for additional 4 h. Under two-step reaction conditions, **3l** was obtained in 75% isolated yield. Similarly, phenacyl azides were retested under condition C but **3h** and **3j** showed no improvement. Unfortunately, the phenacyl azides with nitro and cyano group on their aromatic ring (not shown in Scheme 1) failed to achieve their corresponding triazoles, even under two-step reaction conditions. Aromatic azide with no substituents in its aromatic ring (phenyl azide) was used to obtain **3m** in 85% yield. When the aromatic azide had a methoxy group (4-methoxyphenyl azide), the corresponding triazole was isolated in 88% yield (**3n**) (condition B, Scheme 1).

On the other hand, different terminal alkynes were also employed. When *ortho*-methoxyazidobenzene was used, a quantitative yield of **3o** was obtained under condition A. For the aryl acetylene with the methoxy group at *para* position, triazole **3p** was achieved in 77% yield under condition B. When 2-ethynylaniline was used as terminal alkyne, **3q** was isolated in 89% yield under standard conditions. Finally, propargylic alkyne 3-phenoxy-1-propyne reacted with **1a** to give **3r** in an excellent 100% yield.

Recycling of catalyst and solvent reaction was also studied. The substrate models **1a** and **2a** were used for this assay. After the first cycle (irradiation for 2 h with green-LED light), **3a** was extracted with diethyl ether and a new charge of substrates was added again to the aqueous layer. The yield of the second catalytic cycle dropped dramatically when aqueous layer was not treated; however, when 0.4 mol% of EY was added again after extraction and before a new catalytic cycle, recycling was possible up to three times without considerable yield loss (Scheme 2). EY could not be recovered since a large amount of

this dye does not have a formal charge under the reaction conditions,[29] and could be removed from the aqueous layer after each cycle. In addition, since our system does not involve the use of ligands or additives, bare Cu(I) species is not stable under aerobic conditions, thus a new addition of EY is required to promote photoreduction in the next cycle.

Organic azides with a medium and high molecular weight are stable in aqueous media and air, although storage at low temperatures is advised to avoid decomposition. Aliphatic azides are more stable than aromatic, vinyl or those attached to a carbonyl group. While they are mostly easily handled, low molecular weight azides could be volatile, unstable, and even explosive, hindering their store and handle. Accordingly, methodologies that avoid the manipulation of organic azides have been reported by *in situ* generation in a one-pot procedure.[30] These methods are environmentally friendly since they avoid synthesis steps and their isolation, reducing waste and ensuring greater safety. Here, we could perform the synthesis of **3a** by a one-step one-pot procedure, using benzyl bromide (**4**), sodium azide (**5**) and phenylacetylene (**2a**), in presence of CuCl$_2$ and EY, under standard conditions (Scheme 3). In a first approximation, 0.25 mmol of **4** was placed in the presence of a slight excess of **5** (1.1 equiv.). In this case, the complete consumption of **4**, concomitant with a quantitative formation of **1a** but the absence of **3a**, was observed when the mixture was irradiated for more than 5 h (Scheme 3a). The one-pot procedure was then repeated but using 0.25 mmol of **5** and 1.1 equiv. of **4**, where the NaN$_3$ was the limiting reagent. Fortunately, the desired triazole **3a** was obtained in 88% yield (Scheme 3b). The one-pot reaction was also performed on a gram scale (with 5 mmol of NaN$_3$). Unlike smaller-scale reactions, in the large-scale one-pot reaction, 8 mL of water were employed and the mixture was irradiated for 8 h. Under these conditions **3a** was isolated in 80% yield (Scheme 3c).

The mechanism of 1,4-disubstituted 1,2,3-triazole formation by cycloaddition reaction from organic azides and terminal alkynes catalyzed by Cu(I) is well known and accepted by organic chemists.[13] For this reason, some research groups have centred on finding Cu(I) catalytic systems, designing and synthesizing highly sophisticated metal complexes which stabilize the metal, avoiding its oxidation and modulating its reactivity. On the other hand, other methodologies adopt more stable and cheaper Cu(II) sources, whereas the use of a reducing agent is necessary for Cu(I) formation. In the latter case, the amount of
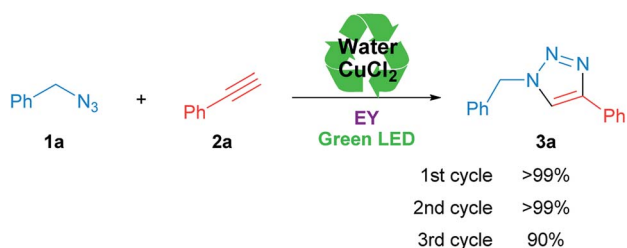
**Scheme 2** Reusability of copper catalyst and solvent in CuAAC reaction.
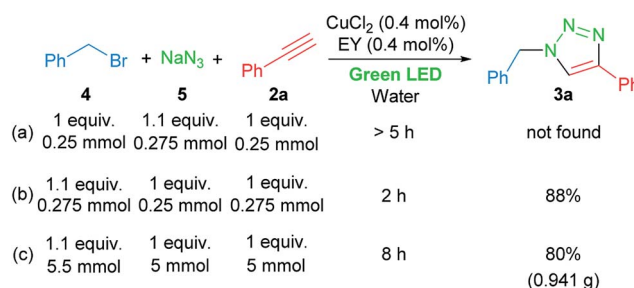
Scheme 3 Synthesis of **3a** *via* a one-pot one-step procedure.

reducing agent is often higher than Cu(ɪɪ). In our system, reducing agent is the EY dye, which is electronically excited by visible light (530 nm) forming $^3EY^*$ after the inter system crossing (ISC), finally promoting Cu(ɪɪ) reduction (oxidative quenching cycle (a) in Scheme 4). The lack of reactivity in the singlet excited state of EY ($^1EY^*$) was tested by fluorescence experiments, where a modification of the quantum fluorescence yield (Φ_F) was not found with successive addition of Cu(ɪɪ). We also observed that R6G could not be able to give Cu(ɪ) from Cu(ɪɪ), since the energy absorbed during irradiation was entirely emitted by fluorescence as its Φ_{ISC} is close to zero. Thus $^3R6G^*$ cannot be formed and reduction of Cu(ɪɪ) is not achieved. On the other hand, thermal electron transfer was ruled out, since EY UV-Vis spectra did not show significant changes with the addition of CuCl$_2$ in water and **3a** was neither observed under dark conditions (Table 1, entry 4). Furthermore, results shown in Scheme 3(a) suggest that Cu(ɪɪ) reduction occurs from the triplet state ($^3EY^*$) since, when a strong triplet quencher such as N$_3^-$ anion is present,[31] the Cu(ɪɪ) photoreduction step to Cu(ɪ) is not favoured and CuAAC is not carried out (reductive quenching cycle (b) in Scheme 4). Molecular oxygen (O$_2$) dissolved in water is also a potential $^3EY^*$ quencher, but its concentration (0.26 mM) is lower than excess azide ions and Cu(ɪɪ) concentrations in standard condition shown in Scheme 3 (12.5 mM and 0.5 mM respectively). An energy transfer quenching is possible by O$_2$ (giving $^1O_2$ which does not affect CuAAC reaction nor products), where EY ground state is recovered.

When N$_3^-$ ions are present, formation of cycloaddition products is totally suppressed, since these anions could be able to give EY$^{\bullet-}$ from $^3EY^*$ by electron-transfer quenching. Similarly, an important drop in the triazole yield was evidenced when TEA (or TEOA) was added as additive since these amines are also electron donors (cycle (b) in Scheme 4). Even Cu(ɪ) could be formed at the expense of EY$^{\bullet-}$ by electron transfer to Cu(ɪɪ) in the presence of TEA, TEOA or N$_3^-$. Dissolved oxygen could also be reduced to superoxide (O$_2^{\bullet-}$) and subsequent formation of H$_2$O$_2$ promoted Cu(ɪ) deactivating through its oxidation disfavouring CuAAC reaction (cycle (b) in Scheme 4).
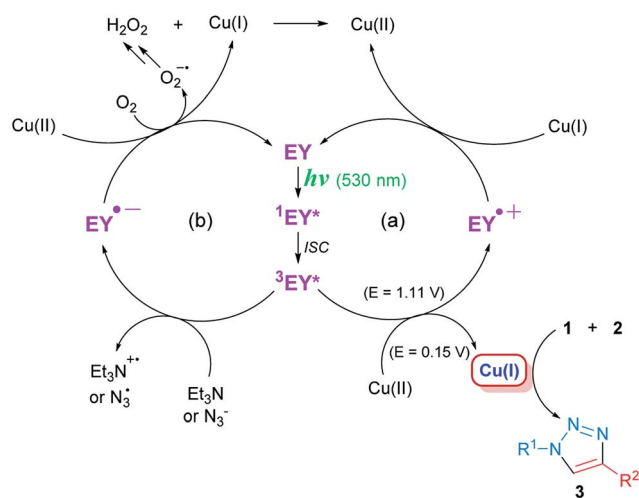
Scheme 4 Plausible mechanism of Cu(ɪ) formation.

Summing up, based on our experimental evidence, active Cu(ɪ) formation pathway is shown in oxidative quenching cycle (a) in Scheme 4, as well as the pathways where Cu(ɪ) species are converted into inactive Cu(ɪɪ). Based on thermodynamic grounds $^3EY^*$ is able to reduce Cu(ɪɪ) to Cu(ɪ), generating EY$^{\bullet+}$, with a very exergonic Gibbs free energy change (ΔG°_{ET}) close to -29 kcal mol^{-1} ($\Delta E = 1.26$ V), under the Rehm–Weller approximation.[32] Oxidized EY does not interfere in the normal progress of CuAAC reaction, except when the amount of Cu(ɪɪ) is higher than EY. When **1a** and **2a** were placed in the presence of 0.8 mol% of CuCl$_2$ and 0.4 mol% EY (Cu(ɪɪ) in excess), yield of **3a** was strongly affected (13%), probably by a back electron transfer reaction. However, when 0.4 mol% of CuCl$_2$ and 0.8 mol% of EY were used, **3a** was obtained in 92% yield. Thus, the amount of EY needs to be equimolar (or higher) than Cu(ɪɪ). Reduction was favoured and the subsequent Cu(ɪ) oxidation was apparently inhibited. On the other hand, carboxylic groups in EY could act as ligands allowing stabilization and activity modulation of Cu(ɪ) in CuAAC reaction.[25]

Conclusions

The use of organic dyes as a Cu(ɪɪ) reducing agent by photoredox reactions which promote Cu(ɪ) production for its application in CuAAC reaction was reported as a novel methodology in the synthesis of 1,4-disubstituted 1,2,3-triazoles in this work. This protocol is environmentally friendly and respects several green chemistry principles: water is used as a renewable and non-toxic solvent, avoiding the use of organic solvents; the amount of catalyst precursor (and organic dye as a reducing agent) is much lower than that found in conventional methodologies (TON = 710); metal and solvent can be recycled for up to three times without a considerable loss of efficiency; visible light through LED is used, which is inexpensive and safer compared with methodologies which employ UV light to promote Cu(ɪɪ) reduction; and lack of additives such as bases, ligands, proton sources, phase transfer agents, and sacrificial reducers, improving the atom economy. In addition, an efficient one-step one-pot procedure was designed and carried out on a small and large scale with very good results, avoiding synthesis step and the handling of organic azides that could be hazardous.

Experimental

Synthetic procedures

General experimental procedure for the synthesis of 1,4-disubstituted 1,2,3-triazoles *via* visible-light promoted CuAAC reaction in *one step*. Condition A. The reactions were carried out in a 10 mL glass vial, equipped with a rubber septum and a magnetic stirrer. Organic azide (**1**, 0.25 mmol), terminal alkyne (**2**, 0.25 mmol), and 1.6 mL of water were added. 200 μL EY (5 mM) and 200 μL CuCl$_2$ (5 mM) were added and the mixture was irradiated with green-LED (530 nm) and stirred under air atmosphere for the time indicated. Ethyl acetate (10 mL) and a saturated solution of NaHCO$_3$ (10 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10

mL). The combined organic extract was dried over anhydrous Na_2SO_4 and the products were isolated from the crude reaction mixture by flash column chromatography (silica gel, eluting with 1 : 1 pentane/dichloromethane (50 mL) and 1 : 1 dichloromethane/ethyl acetate (50 mL)).

General experimental procedure for the synthesis of 1,4-disubstituted 1,2,3-triazoles *via* visible-light promoted CuAAC reaction in *one step*. Condition B. The reactions were carried out in a 10 mL glass vial, equipped with a rubber septum and a magnetic stirrer. Organic azide (**1**, 0.25 mmol), terminal alkyne (**2**, 0.25 mmol). 200 μL EY (5 mM) and 200 μL $CuCl_2$ (5 mM) were added and the mixture was irradiated with green-LED (530 nm) and stirred under air atmosphere for the time indicated. Ethyl acetate (10 mL) and a saturated solution of $NaHCO_3$ (10 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic extract was dried over anhydrous Na_2SO_4 and the products were isolated from the crude reaction mixture by flash column chromatography.

General experimental procedure for the synthesis of 1,4-disubstituted 1,2,3-triazoles *via* visible-light promoted CuAAC reaction in *two steps*. Condition C. The reactions were carried out in a 2 mL glass vial, equipped with a rubber septum and a magnetic stirrer. A mixture of 200 μL EY (5 mM) and 200 μL $CuCl_2$ (5 mM) was irradiated with green-LED (530 nm) and stirred under air atmosphere for 1 h. Organic azide (**1**, 0.25 mmol) and terminal alkyne (**2**, 0.25 mmol) were then added and the mixture was stirred in dark for 4 h. Ethyl acetate (10 mL) and a saturated solution of $NaHCO_3$ (10 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic extract was dried over anhydrous Na_2SO_4 and the products were isolated by flash column chromatography.

Experimental procedure for the synthesis of 3a *via* one-step one-pot procedure. The reactions were carried out in a 10 mL glass vial, equipped with a rubber septum and a magnetic stirrer. Benzyl bromide (**4**, 0.275 mmol), NaN_3 (**5**, 0.25 mmol), and phenyl acetylene (**2a**, 0.25 mmol) were added and a suspension was observed when water (1.6 mL), 200 μL EY (5 mM) and 200 μL $CuCl_2$ (5 mM) were added. The mixture was irradiated with green-LED (530 nm) and stirred under air atmosphere for 2 h. Ethyl acetate (10 mL) and a saturated solution of $NaHCO_3$ (10 mL) were added and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic extract was dried over anhydrous Na_2SO_4 and **3a** was isolated by flash column chromatography.

Synthetic procedure and characterization data for novel 2-(3-(4-phenyl-1H-1,2,3-triazol-1-yl)propyl)isoindoline-1,3-dione (3l). Following the general procedure for the reaction in two steps, 2-(3-azidopropyl)isoindoline-1,3-dione (57.5 mg, 0.25 mmol) and phenyl acetylene (**2a**, 25.5 mg, 0.25 mmol) were placed in a glass vial. Then, 200 μL of both solutions of EY (5 mM) and $CuCl_2$ (5 mM) were added and the mixture was irradiated with green-LED (530 nm), stirring for 4 h. Purification was performed by flash column chromatography affording **3l** as a light brown solid

(62.3 mg, 75% yield). Mp = 146.5–147.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.38 (q, J = 6.6 Hz, 2H), 3.78 (t, J = 6.6 Hz, 2H), 4.45 (t, J = 6.6 Hz, 2H), 7.31 (t, J = 7.5 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.69–7.71 (m, 2H), 7.80–7.84 (m, 4H), 7.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.5, 35.2, 48.0, 120.4, 123.5, 125.9, 128.2, 128.9, 130.8, 132.0, 134.3, 147.8, 168.5. HRMS EI [M$^+$] calcd for $C_{19}H_{16}N_4NaO_2$: 355.1165, found 355.1181.

Notes and references

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