



Copper(I) Catalyzed Azide-Alkyne Click Reaction: Synthesis and Metal-Ion Binding Studies of Some 1,2,3-Triazole Derivatives

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Click chemistry involving 1,3-dipolar cycloaddition reaction of an azide and a terminal alkyne has gained much attention in the field of science to design new materials for various applications. Recently, ability of 1,2,3-triazole ring to participate in complexation with metal ions has been recognized. The demand for selective receptors for specific cations especially sensors that monitor toxic heavy metal ions selectively have been continuously increasing. Therefore, we report herein, the synthesis of some 1,2,3-triazole derivatives through the click reaction. All the newly synthesized compounds thus obtained have been characterized by IR, ^1H NMR, ^{13}C NMR and mass spectral studies and screened for their recognition properties towards various metal ions.

Keywords: Click reaction, Binding studies, Chemosensor.

INTRODUCTION

Owing to great biological and environmental importance, a large number of receptors for sensing metal ions has been designed and synthesized. Though metal ions are essential for various biological and other processes, concentration of these ions plays crucial role in feasibility of such processes. On the other hand, the contamination of some toxic metal ions such as mercury and lead from industries and other sources poses major threats for environment and human health. Thus, there is a great demand for such compounds which can show sensitivity and selectivity for a particular metal ion as compared to other metal ions. In past decade, considerable efforts have been made to design new ligands for selective recognition of metal ions [1]. In recent past, the ability of 1,2,3-triazole ring to participate in complexation with metal ions has been recognized [2-4]. Consequently, various receptors have been developed showing the coordination properties of 1,2,3-triazole ring with metal ions [5-23]. Though various synthetic methods are available for 1,2,3-triazoles, Huisgen *et al.* [24] reported that the 1,3-dipolar cycloaddition between terminal alkynes and organic azides is the most common and traditional method. Their approach lead to a mixture of 1,4- and 1,5-disubstituted 1,2,3-triazoles. However, the reaction yields 1,4-disubstituted 1,2,3-triazoles regioselectively in presence of Cu(I) as a catalyst discovered recently by Meldal *et al.* [25] and Sharpless *et al.* [26] independently. In view of above mentioned facts, herein, we designed and synthesized various 1,2,3-triazole receptors and studied their metal ion recognition properties.

EXPERIMENTAL

Melting points of compounds synthesized are uncorrected, recorded in $^{\circ}\text{C}$ by open capillary method. FT-IR spectra were recorded on Shimadzu FT-IR spectrometer using KBr (potassium bromide) powder and values are given in cm^{-1} . The ^1H NMR and ^{13}C NMR spectra were recorded on Bruker 300 MHz NMR spectrometer, in deuterated chloroform *versus* tetramethyl silane (TMS) as an internal standard (chemical shift in δ , ppm). The completion of reactions were monitored by using silica gel 60 F-254 thin layer chromatography (TLC) plates and visualized under ultraviolet lamp.

Absorption spectra were recorded on Perkin Elmer Lambda bio-20 double-beam spectrophotometer. All spectrophotometric measurements were performed in quartz cells at 25°C . Stock solutions of compounds **4a**, **4b**, **4c**, **4d** and **4e** were prepared in $\text{CHCl}_3/\text{MeOH}$ (7:3, v/v) just before the experiments. The aliquots of metal solution were added to a cuvette containing 2.5 mL solution of the appropriate receptor and UV-visible absorbance spectra were recorded after 15 min intervals. The titration was continued until no further change in the spectrum was observed. The salts employed for the binding studies were $\text{Hg}(\text{ClO}_4)_2$, $\text{Cd}(\text{ClO}_4)_2$, $\text{Zn}(\text{ClO}_4)_2$, $\text{Cu}(\text{ClO}_4)_2$, $\text{Co}(\text{ClO}_4)_2$, $\text{Pb}(\text{ClO}_4)_2$ and $\text{Mg}(\text{ClO}_4)_2$.

General procedure for the synthesis of 1,2,3-triazole based receptors: To a stirred solution of benzyl azide (**3**) (250 mg, 0.43 mmol) in 30 mL of *t*-BuOH was added propargyl derivatives (**2a-2e**) (0.95 mmol) followed by $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (10

mol %), sodium ascorbate (20 mol %) and 3 mL of H₂O. The solution was stirred at 50 °C for 14 h. The solvent was evaporated under vacuum and the residues obtained were dissolved in 30 mL of CHCl₃ and washed with H₂O (10 mL) and then with brine (10 mL) and dried over anhydrous Na₂SO₄. The solvent was evaporated completely under vacuum and the crude product was purified by column chromatography over silica-gel (30 % ethyl acetate in hexane) to get the desired 1,2,3-triazole receptors (**4a-4e**).

2-[(1-Benzyl-1H-1,2,3-triazol-4-yl)methoxy]benzaldehyde (4a): Yield 89.60 %, ¹H NMR (300 MHz, CDCl₃): δ 5.32 (s, 2H, methylene CH₂ α-N), δ 5.57 (s, 2H, methylene CH₂ α-O), δ 7.042-7.385 (m, 7H, ArH), δ 7.56 (s, 1H, 1,2,3-triazole), δ 7.706-7.845 (2H, ArH), δ 10.439 (s, 1H, CHO). ¹³C NMR (75 MHz, CDCl₃): δ 54.51 (C-α to N), δ 62.48 (C-α to O), δ 113.04, δ 121.3, δ 125.08, δ 128.64, δ 128.88, δ 129.15, δ 134.25 (C5-triazole), δ 135.92 (C4-triazole), δ 160.39, δ 189.51. MS (ESI) *m/z*: 294 (M+1).

2-[(1-Benzyl-1H-1,2,3-triazol-4-yl)methoxy]benzoic acid (4b): Yield 91.2 %, ¹H NMR (300 MHz, CDCl₃): δ 5.436 (s, 2H, CH₂ methylene α-N), δ 5.564 (s, 2H, CH₂ methylene α-O), δ 7.123-7.542 (m, 2H, ArH), δ 7.566 (s, 1H, 1,2,3-triazole), δ 7.59-8.149 (2H, ArH). ¹³C NMR (75 MHz, CDCl₃): δ 54.48 (C-CH₂-φ), δ 63.44 (O-CH₂), δ 113.42, δ 122.61, δ 128.18, δ 129.03, δ 129.28, δ 133.72, δ 134.04, δ 135.09, δ 156.9, δ 172 (COOH). MS (ESI) *m/z*: 310 (M+1).

1-[(1-Benzyl-1H-1,2,3-triazol-4-yl)methoxy]naphthalene-2-carbaldehyde (4c): Yield 78 %, ¹H NMR (300 MHz, CDCl₃): δ 5.47 (s, 2H, CH₂ methylene α-N), δ 5.565 (s, 2H, CH₂ methylene α-O), δ 7.282-7.78 (m, 9H, ArH, 1H, triazole), δ 7.809-8.08 (m, 1H, ArH), δ 9.239-9.268 (m, 1H, ArH), δ 10.859 (s, 1H, CHO). ¹³C NMR (75 MHz, CDCl₃): δ 54.49 (C-CH₂ α-N), δ 63.44 (C-CH₂ α-O), δ 113.85, δ 117.23, δ 124.91, δ 125.01, δ 128.09, δ 128.26, δ 128.81, δ 128.93, δ 129.2, δ 129.92, δ 131.4, δ 134.17 (Triazole), δ 137.61, δ 162.54, δ 191.85 (CHO). MS (ESI) *m/z*: 344 (M+1).

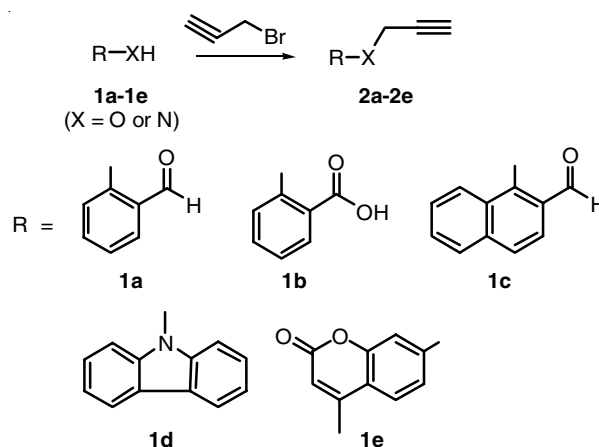
9-[(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl]-9H-carbazole (4d): Yield 86.50 %, IR: (KBr, ν_{max}, cm⁻¹): 3061 (C-H), 2923, 1449 (C-C), 1270 (C-N). m.p.: 159-16 °C; ¹H NMR (300 MHz, CDCl₃): δ 5.329 (s, 2H, CH₂ methylene α-N), δ 5.589 (s, 2H, CH₂ methylene α-φ), δ 7.018-8.09 (m, 13H, ArH, 1H, triazole). ¹³C NMR (75 MHz, CDCl₃): δ 38.96 (C-CH₂ α to carbazole), δ 54.15 (C-CH₂ α to φ), δ 108.8, δ 119.44, δ 120.42, δ 121.45, δ 123.08, δ 125.97, δ 127.87, δ 128.72, δ 129.06, δ 134.38 (triazole), δ 140.05, δ 144.9. MS (ESI) *m/z*: 339 (M+1).

7-[(1-Benzyl-1H-1,2,3-triazol-4-yl)methoxy]-4-methyl-2H-chromen-2-one (4e): Yield 76 %, ¹H NMR (300 MHz, CDCl₃): δ 2.382 (s, 3H, CH₃), δ 5.216 (s, 2H, CH₂ methylene α-N), δ 5.549 (s, 2H, CH₂ methylene α-O), δ 6.129-7.671 (m, 9H, ArH, 1H, triazole). ¹³C NMR (75 MHz, CDCl₃): δ 18.68 (C-CH₃), 54.65 (C-CH₂ α to φ), 62.23 (C-O-CH₂), 102.4, 112.26, 112.44, 114.06, 125.71, 128.22, 128.91, 129.2, 134.29 (triazole), 152.5, 155.09, 161.11, δ 161.19 (C=O). MS (ESI) *m/z*: 348 (M+1).

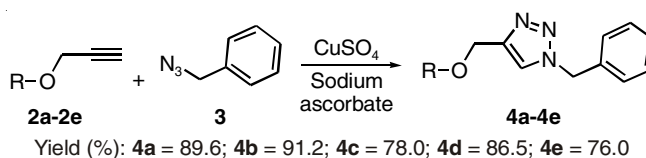
RESULTS AND DISCUSSION

Various terminal alkynes and 1,2,3-triazoles were synthesized according to **Scheme-I** and **II**, respectively. The terminal

alkynes (**2a-2e**) were prepared by treating corresponding starting materials (**1a-1e**) with propargyl bromide by following the literature procedure [27] (**Scheme-I**). 1-Benzyl triazoles (**4a-4e**) were synthesized according to **Scheme-II**.



Scheme-I: Synthesis of various alkynes (**2a-2e**)



Scheme-II: Synthesis of 1-benzyl triazoles (**4a-4e**)

The benzyl based 1,2,3-triazole receptors were synthesized by the 1,3-dipolar cycloaddition reactions of benzyl azide (**3**) with O-propargylsalicylaldehyde (**1a**), O-propargylsalicylic acid (**1b**), O-propargylnaphthaldehyde (**1c**), N-propargylcarbazole (**1d**) and O-propargylcoumarin (**1e**) in presence of CuSO₄ (20 mol %) and sodium ascorbate (40 mol %) in *t*-BuOH/H₂O (1:1) at 50 °C to yield compounds **4a**, **4b**, **4c**, **4d** and **4e**, respectively.

All the synthesized 1,2,3-triazoles were well characterized by employing various spectroscopic techniques *viz.* FTIR, ¹H NMR, ¹³C NMR and MS.

Metal ion binding studies: The metal ion binding property of receptors **4a**, **4b**, **4c**, **4d** and **4e** was investigated by UV-visible titration method. The changes in the absorbance bands after addition of perchlorate salt of various metal ions to the solution of receptors were monitored to determine the binding affinity of these receptors towards metal ions.

We investigated the affinity of receptor **4a** towards Cu²⁺ ion in detail, by monitoring the absorbance changes on addition of Cu(ClO₄)₂ (1.5 × 10⁻³ M) to the solution of receptor **4a** (5 × 10⁻⁵ M) in CHCl₃/MeOH (7:3, v/v). As shown in Fig. 1, the absorbance bands around 256 and 319 nm decreased and around 278 nm increased with three sharp isosbestic points at 268, 287 and 358 nm, on the incremental addition of Cu²⁺ ion (0-10 equiv). Jobs plot [Fig. 2(a)] shows 1:1 complex formation between receptor and metal.

We investigated the affinity of receptor **4a** towards Mg²⁺ ion in detail, by monitoring the absorbance changes on addition of Mg(ClO₄)₂ (1.5 × 10⁻³ M) to the solution of receptor **4a** (5 × 10⁻⁵ M) in CHCl₃/MeOH (7:3, v/v). As shown in Fig. 3, the absorbance bands around 256 and 319 nm decreased and

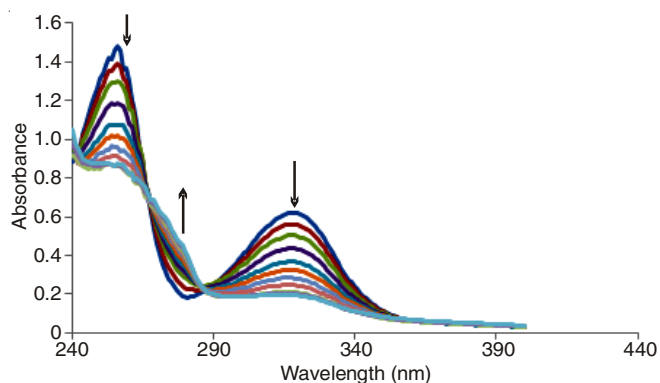


Fig. 1. Absorbance spectra of compound **4a** (5×10^{-5} M) in $\text{CHCl}_3/\text{MeOH}$ (7:3, v/v) in the presence of Cu^{2+} (0-10 equiv)

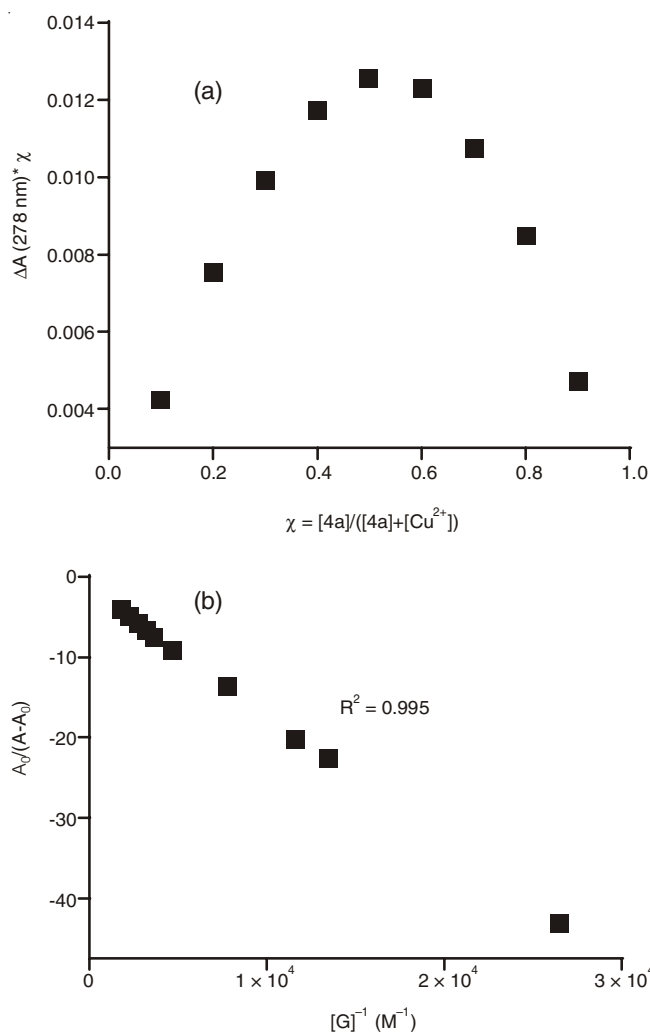


Fig. 2. (a) Jobs plot showing 1:1 complex formation between compound **4a** and Cu^{2+} ; (b) Hildebrand-Benesi plot [28] based on the 1:1 binding model: $A_0/(A-A_0)$ versus $[G]^{-1}$

around 278 nm increased with two sharp isosbestic points at 269 and 286 nm, on the incremental addition of Mg^{2+} ion (0-10 equiv).

Compound **4a** also shows good binding affinity with Hg^{2+} as shown in Fig. 4.

Compounds **4c** and **4d** show change in absorbance due to masking effect of heavy metal Hg^{2+} as shown in Figs. 5 and 6.

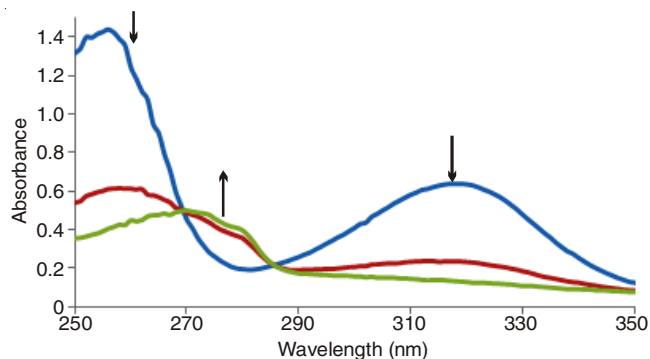


Fig. 3. Absorbance spectra of compound **4a** (5×10^{-5} M) in $\text{CHCl}_3/\text{MeOH}$ (7:3, v/v) in the presence of Mg^{2+} (0-10 equiv)

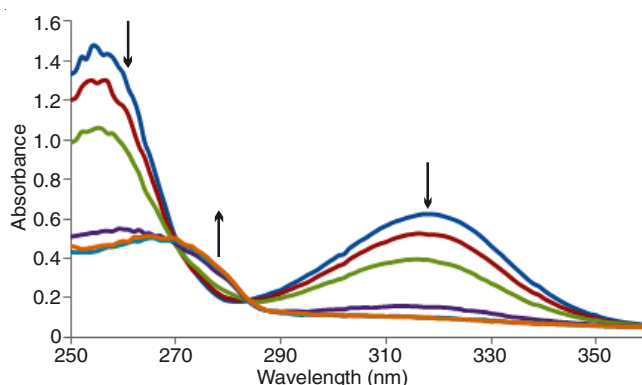


Fig. 4. Absorbance spectra of compound **4a** (5×10^{-5} M) in $\text{CHCl}_3/\text{MeOH}$ (7:3, v/v) in the presence of Hg^{2+} (0-10 equiv)

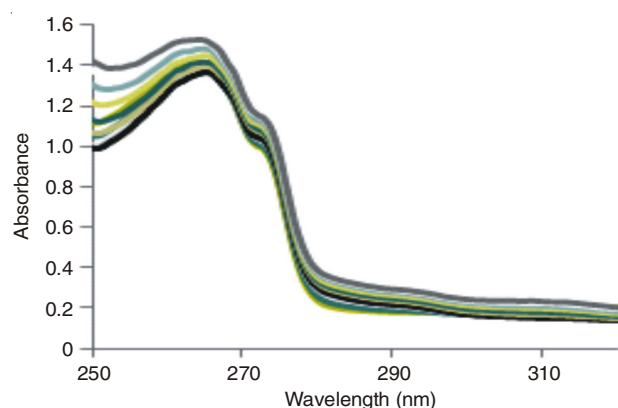


Fig. 5. Absorbance spectra of compound **4c** (5×10^{-5} M) in $\text{CHCl}_3/\text{MeOH}$ (7:3, v/v) in the presence of Hg^{2+} (0-10 equiv)

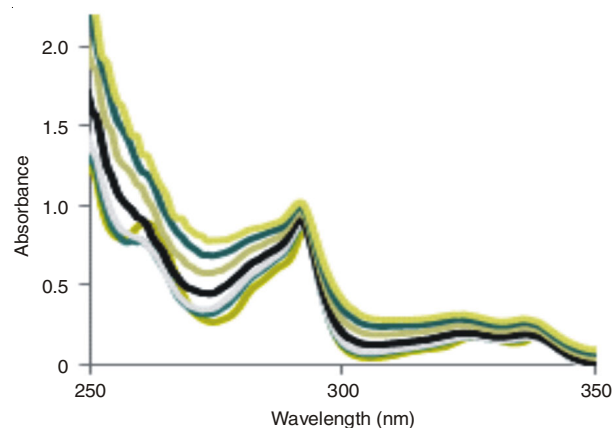


Fig. 6. Absorbance spectra of compound **4d** (5×10^{-5} M) in $\text{CHCl}_3/\text{MeOH}$ (7:3, v/v) in the presence of Hg^{2+} (0-10 equiv)

Conclusion

In summary, we have synthesized benzyl-based receptors containing 1,2,3-triazole units using Cu(I)-catalyzed click reaction and studied their binding properties towards various metal ions. UV-visible studies revealed that receptor **4a** showed the highest binding affinity for Cu²⁺, Mg²⁺ and Hg²⁺ metal ions, respectively. Interestingly, receptors **4c** and **4d** showed weak binding affinity for Hg²⁺ metal ion. While receptors **4b** and **4e** shows no binding affinity. These receptors particularly **4a** may find useful applications as chemosensor for the detection of toxic metal ions such as Hg²⁺.

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