



Efficient route to synthesize Triazoles using copper on carbon catalyst via click chemistry

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Abstract : One of the most popular reactions within the click chemistry concept is the azide alkyne Huisgencycloaddition using a Copper (Cu) catalyst at room temperature. Reactions for the synthesis of triazoles have been carried out by using 2 eq. of an alkyne/allene, copper sulfate and sodium ascorbate. In situ reduction of copper(II) salts such as CuSO₄•5H₂O with sodium ascorbate in aqueous alcoholic solvents allows the formation of 1,4-triazoles at room temperature in high yield, with < 2 mol % catalyst loading. In order to attain more atom economy and lower amount of hazardous solvents and other chemicals, the reaction is tried with copper nitrate on carbon. Reaction can be carried out at much lower equivalent of reagents and catalysts because of the spreading of copper salt on to the carbon surface.

Key words : Click Chemistry, Copper on Carbon, Cicerarietinum.

Introduction:

Click chemistry is a term applied to chemical synthesis tailored to generate substances quickly and reliably by joining small units together. Click chemistry is not a single specific reaction, but describes a way of generating products that follows examples in nature, which also generates substances by joining small modular units. The term was coined by K. Barry Sharpless in 1998, and was first fully described by Sharpless, Hartmuth Kolb, and M.G. Finn¹⁻³.

One of the most popular reactions within the click chemistry concept is the azide alkyne Huisgencycloaddition using a Copper (Cu) catalyst at room temperature. The copper-catalyzed reaction was later expanded using a bimetallic catalyst so that 1,4,5-substituted triazoles could be obtained from seemingly internal alkynes.

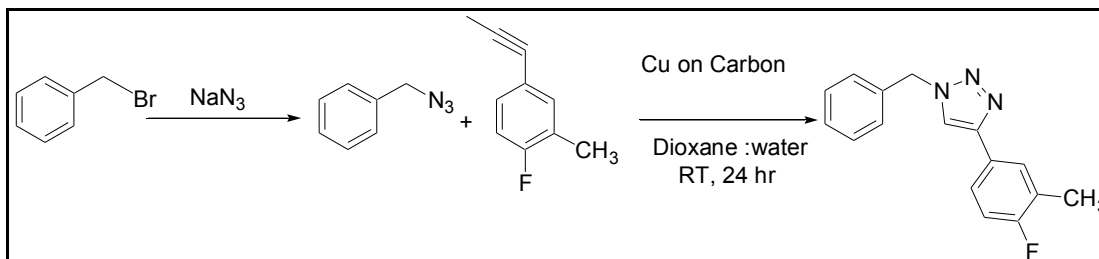
Experimental:

Reactions were carried out using 100 mg of azide, 1.1 equivalent of alkyne and varying amount of Copper-On-Carbon in solvents with different polarity. The mixture was stirred for 24 hrs at room temperature. It was filtered and filtrate was dried over anhydrous sodium sulphate, purified on column chromatography (as and when required) and the product was isolated.

Results and Discussion:

In order to evaluate various reaction parameters such as selection of solvents and minimal quantity of metal on carbon a model reaction of 3-methyl-4- fluoro phenyl acetylene and benzyl bromide was carried out (Scheme 1).

Scheme 1



Selection of Solvent:

Various solvent systems are used to find out most suitable system. When 10 % Cu-on-carbon is used, quantitative yields of product are observed. Dioxane, very common aprotic dipolar solvent, indicates zero dipole moment. Similarly, THF, aprotic dipolar solvent shows dipole moment of 1.7 which is close to methanol, 1.69. The substrate is semi polar which dissolves in the above solvents to similar extent and product is formed in nearly similar percentage. However, the solubility of substrate is significant in dioxane-water (3:1) system which has maximum yield. Water being protic polar, substrate has less solubility. So, yield of the product is less.

With increasing amount of Cu-on-Carbon, there is gradual increase in yield in dioxane, dioxane-water, methanol and water while yield in THF remains same. The results are shown (Table 1).

Table 1: Yields of adduct using varying amount of Cu-on –Carbon

Amount of Cu on carbon (mg)	% Yield in various solvents				
	Dioxane	Dioxane: water 3:1	Methanol	THF	Water
10	89	92	88	88	76
20	90	93	89	88	79
30	91	93	91	88	79

From Table 1, it is evident that the reaction worked very well with mixture of dioxane and water (3:1) as a solvent. Low yields in water as a solvent indicates that an aprotic polar solvent is necessary for dissolution. It also confirms that the output of the reaction increases with increase in amount of Cu-on-carbon. Thus, the optimum conditions for the reaction would be the use of dioxane:water (3:1) as a solvent and 30 mg. of Cu-on-carbon as a catalyst.

Optimization of metal on Carbon:

There is no vast difference in the yields with respect to change in carbon. Yields with commercial carbon (COM 1) are on slightly higher side as compared to C600, C800 and MIP. All these carbons are prepared using same raw material, Cicerarietinum. C600 is prepared by carbonization at 600°C under Nitrogen, C800 is prepared by carbonization at 800 °C under Nitrogen while MIP is prepared by first carbonization of the material at 600°C followed by treatment with phosphoric acid. Results are presented (Table 2).

Table 2: Reaction yields using various carbons

Carbon used for Cu-on- Carbon	% Yield
C600	93
C800	92
MIP	93
COM1	94

Conclusions:

Increasing amount of catalyst (Cu-on-Carbon) increases the yield of reaction. Very minute change in yields even when there is great increase in surface area and other properties, going from C600 to COM1 carbon, indicates that Cu salt does not penetrate the pores of the carbon and is deposited only on the surface. Surface active groups help in stabilizing the salt on its surface. The amount required for carrying out reaction using Cu-on-Carbon as compared to only Copper salt underlines the importance of carbon to increase the available surface for reaction.

References:

1. Kolb H. C., et al., *Angew. Chem. Int. Ed.*, 2001, 40, 2004-2021.
2. Evans R. A., *Australian Journal of Chemistry*, 2007, 60(6), 384-395.
3. Kolb H. C., et al., *Drug Discovery Today*, 2003, 8, 1128-1137.
