## SYNLETT <br> Spotlight 320

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

## Copper(II) Sulfate

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## Introduction

Copper(II) sulfate $\left(\mathrm{CuSO}_{4}\right)$ exists as a series of compounds that differ in their degree of hydration. The anhydrous form is a gray-white powder, whereas the pentahydrate, the most commonly encountered salt and commercially available, is bright blue. The hydrated copper sulfate occurs in nature as chalcanthite ${ }^{1}$ (pentahydrate), and two more rare ones: bonattite (trihydrate) ${ }^{2}$ and boothite (heptahydrate). ${ }^{3}$ It can be made by the action of
sulfuric acid on a variety of copper(II) compounds, for example the basic copper(II) oxide or by electrolyzing sulfuric acid using copper electrodes. The anhydrous salt, prepared by previous heating of the pentahydrate salt, is used in transacetalization reactions as a dehydrating component. ${ }^{4}$ Copper(II) sulfate pentahydrate is used in many organic transformations under mild and convenient conditions to afford the products in high yields. In addition, copper(II) sulfate pentahydrate is a source to prepare copper complexes. ${ }^{5,6}$

## Abstracts

(A) Preparation of 1,4-Disubstituted 1,2,3-Triazoles:

The copper-catalyzed azide-alkyne cycloaddition (CuAAC) broadly know as 'click reaction' has found a widespread use. ${ }^{7}$ The reaction is carried out in a mixture of organic and aqueous systems employing copper(II) sulfate pentahydrate and a reducing agent. The triazole formed is essentially chemically inert to reactive conditions, such as oxidation, reduction and hydrolysis.
(B) Preparation of 3,5-Disubstituted Isoxazoles.

The copper(I)-catalyzed cycloaddition between nitrile oxides and terminal acetylenes gives 3,5 -disubstituted isoxazoles. ${ }^{8}$ This 'click' reaction is a convenient one-pot, three-step procedure using stoichiometric amounts of the reagents minimizing the formation of byproducts.

(C) N-Arylation of Imidazoles:

A simple, highly efficient, economical, and environmentally friendly protocol for copper-catalyzed N -arylation of imidazoles in water has recently being reported. ${ }^{9}$ The catalytic system can be easily generated using a mixture of $\mathrm{CuSO}_{4} \cdot 5 \mathrm{H}_{2} \mathrm{O}$ and bidentate $\mathrm{N}, \mathrm{N}$-ligands to promote the N -arylation of imidazoles with aryl halides with up to 95\% yield.

(D) Formation of Ynamides:

A general and efficient method for the coupling of a wide range of amides with alkynyl bromides also involves a catalytic protocol using $\mathrm{CuSO}_{4} \cdot 5 \mathrm{H} 2 \mathrm{O}$ and a ligand to produce a diverse array of ynamides. ${ }^{10}$ The catalyst system directs the sp $\mathrm{C}-\mathrm{N}$ bond formation leading to the desired product.

(E) Epoxidation:

Epoxidation of trisubstituted steroid olefins by a nonconcerted pathway was promoted by a mixture $\mathrm{CuSO}_{4}$ and $\mathrm{KMnO}_{4}$ in $t$ - BuOH and $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ at reflux (Parish reagent). ${ }^{11}$ During epoxidations with the Parish oxidizing mixture there is considerable evolution of oxygen; however, without copper (II), little oxygen is evolved and little or no epoxide is formed.

(F) Deprotection of Acetals, Etherifications, and Iodolactonizations:
Deprotection of acetals, catalyzed by a convenient system of $\mathrm{CuSO}_{4}$ and NaI has been developed. ${ }^{12}$ The oxidation of NaI using $\mathrm{CuSO}_{4}$ in acetone generates $\mathrm{I}_{2}$ in situ that allows chemoselective deprotection of acetals. Other applications include etherifications and iodolactonizations.


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