Optimization of the Synthesis of Copper(I) Phenylacetylide

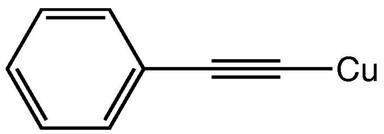
Valentina Duque Castano,[1] Kian B. Muldoon,[1] Daniel J. LeMay,[1] Greg G. Ciangiotto,[1] Wheeler J. Smith,[1] Robert Papoular,[2] and A. Timothy Royappa,[1]

[1] Department of Chemistry, Hall Marcus College of Engineering , University of West Florida

[2] CEA-Saclay, France

INTRODUCTION

Copper(I) phenylacetylide is a chemical compound that plays an important role in medicinal chemistry, pharmaceutical manufacturing, drug development, and general chemical synthesis (1-4). The structure of this compound is shown below:



It has a characteristic yellow color in the solid state, making it easy to identify. Copper(I) phenylacetylide is produced from the reaction of basic copper(I) oxide, Cu_2O, with the weak acid phenylacetylene in ethanol, with a sulfuric acid catalyst.

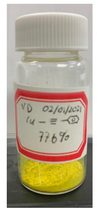
Available methods for making these compound are difficult, time-consuming and require environmentally hazardous solvents. We have found a new way to synthesize Copper(I) phenylacetylide by a simple, quick and "green" synthesis. Our method offers multiple advantages, since no reducing agent is needed and no air-free conditions are required during filtration. The starting materials are all available commercially at a good price and the solvent used, 95% ethanol, is environmentally friendly.

EXPERIMENTAL METHOD

The starting method (that was further optimized) was the following: 220 µl phenylacetylene is added to 10 ml of ethanol in a 25 ml round bottom flask (RBF) with a stir bar and fitted with a rubber septum. The flask is flushed with N_2. 0.143 g of Cu_2O is added to this solution, and the flask is flushed again with N_2. Finally, 125 µl of 1 M H_2SO_4 are added and the flask is flushed one last time with N_2. The rubber septum is replaced with a greased stopper and the reaction mixture is allowed to stir for 3 hrs. The mixture is transferred into a beaker by performing rinsing the flask repeatedly with 5 mL of water and 5 mL of ethanol. 200 µl of 1 M H_2SO_4 are added, and the mixture is stirred for 1 hr. The product is suction filtered using P8 filter paper and washed on the Büchner funnel with 20 ml of water and 15 ml of 95% ethanol. The collected product is left to air-dry overnight. The yield is measured and sample purity is determined by elemental analysis.

RESULTS

In order to optimize the synthesis of copper(I) phenylacetylide the method was extensively modified. The following timeline shows the different modifications in the method along with the results of each modification. The vials show the product and list the yield for each reaction and the table shows how many percent off the elemental analysis was for each sample.



02/01

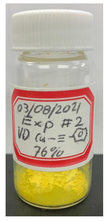
Starting Method

C	H	N	S
-3.34	-0.38	-0.06	0.10

03/08

Reaction time 12 h; purity within range

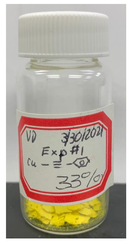
C	H	N	S
-0.12	-0.04	-0.14	0.01



03/30

1000 µl 1 M H_2SO_4 in initial reaction; purity increased compared with starting point but yield significantly decreased

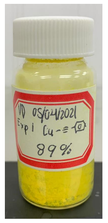
C	H	N	S
-0.93	-0.08	-0.12	0.03



05/04

Reaction time 12 h, 20 min wash; better yield and purity within range

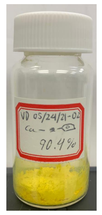
C	H	N	S
-0.38	-0.17	0.11	0.11



05/24

Reaction time 12 h, 20 min wash, P2 filter paper, better yield

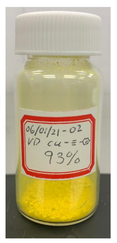
C	H	N	S
-0.99	-0.23	0.09	0.10



06/01

Reaction time 12 h, wash conducted in same reaction flask, 75 min wash, P2 filter paper, better yield

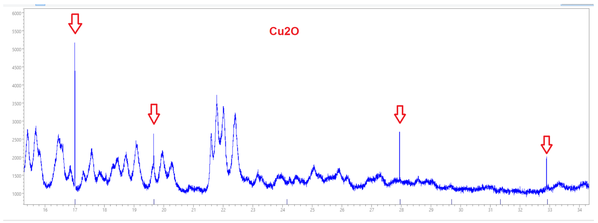
C	H	N	S
-0.64	-0.37	0.01	0.09



CONCLUSIONS

To conclude, it can be seen how increasing the initial stirring time results in a product with higher purity. As the amount of sulfuric acid added to the initial reaction setup is increased so does the purity by the yield is significantly decreased. Longer washes result in lower yields while a finer filter paper results in higher yields.

A further analysis of sample VD-05-04-21 was made at the synchrotron SOLEIL in Paris to test for purity. The diffractogram is shown below. This analysis revealed the presence of a small amount of Cu_2O impurity in the sample. Considering this, our future aim is to modify the acid wash and to reduce the surface tension with ethanol so that the acid can dissolve the coated Cu_2O fragments present.



Diffractogram of sample VD-05-04-2021; peaks marked with red arrows correspond to the presence of unreacted Cu_2O in the sample

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