SYNLETT
Spotlight 149

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

$Cu(BF_4)_2{\cdot}xH_2O$: A Versatile Catalyst

Compiled by Raj Kumar Khunger

Raj Kumar was born in 1979. He received his B. Pharm. in 2001 from Maharshi Dayanand University, Rohtak, Haryana, India. He started to study chemistry in 2001 at the Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Punjab, India, where he completed his M.S. (Pharm) thesis under the supervision of Prof. Asit K. Chakraborti, FRSC. After completion of his degree in 2003 he joined Discovery Research, Dr. Reddy's Laboratories Ltd, Hyderabad, India as a research chemist. He then returned to NIPER and is currently working on his Ph.D. thesis, again under the guidance of Prof. Chakraborti. His primary research interests focus on the synthesis of small heterocyclic compounds of medicinal importance and the development of new methodologies.

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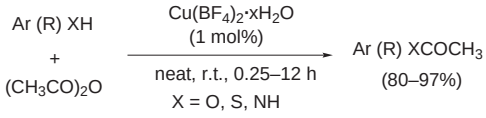
Introduction

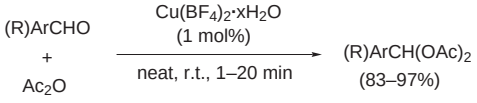
Copper(II) tetrafluoroborate hydrate $Cu(BF_4)_2{\cdot}xH_2O$ [CAS: 314040-98-7] is a corrosive, moisture-sensitive, blue crystalline solid readily soluble in water and sparingly soluble in alcohols. $Cu(BF_4)_2{\cdot}xH_2O$ is readily available and widely used as the starting material for homometallic, trinuclear heteroscorpionate[1] complexes applied in the studies of electronic and magnetic properties. It causes decomposition of 9-diazofluorene in acetonitrile solvent.[2] As it does not require special storage conditions and is safe and stable under normal environmental conditions, $Cu(BF_4)_2{\cdot}xH_2O$ has emerged as one of most useful reagent in various transformations such as acylation reactions and 1,1-diacetate formations. In all the cases, this reagent has been found to be superior to other available Lewis acids such as triflates, tetrafluoroborates and perchlorates with regard to short reaction times, requirement of stoichiometric amount of reagent, mild reactions conditions, solvent-free conditions and low cost. Further, the distinct advantage of the use of $Cu(BF_4)_2.xH_2O$ as a catalyst for thia-Michael addition reactions[3] with α,β-unsaturated carbonyl compounds is evidenced by the fact that the reaction of 3-methylcyclohexenone with thiophenol afforded the product in 45 minutes while the corresponding reaction did not proceed in the presence of an ionic liquid.[4]

Abstract

(A) *Acylation reactions:* Acetylation[5] of structurally diverse phenols, alcohols, thiols, and amines with stoichiometric amounts of Ac_2O under solvent-free conditions at room temperature has been efficiently catalyzed by $Cu(BF_4)_2{\cdot}xH_2O$. Excellent chemoselectivity was observed during reaction with secondary and tertiary alcohols without any competitive dehydration and no rearrangement took place with allylic and propargylic substrates.



(B) *Diacetate formation:* A strong catalytic effect of $Cu(BF_4)_2{\cdot}xH_2O$ has also been observed in the formation of aldehyde 1,1-diacetates[6] from aldehydes and acetic anhydride under solvent-free conditions at room temperature. The rate of reaction was found to be very fast and in most of the cases the reaction was completed in 1–20 minutes in excellent yields, which could make this method more attractive and industrially viable.



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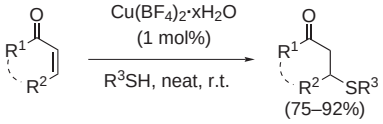
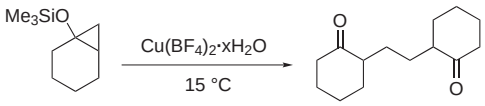
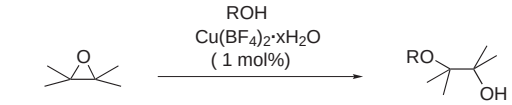
(C) *Conjugate addition:* $Cu(BF_4)_2{\cdot}xH_2O$ has been found to be a new and highly efficient catalyst for Michael addition of thiols[3] to α,β-unsaturated carbonyl compounds under solvent-free conditions.



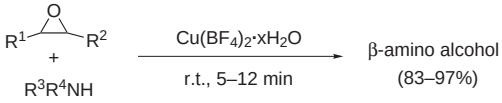
(D) *Electrophilic ring opening:* A ring opening of siloxycyclopropane,[7] via β-copper substituted ketone intermediate, is efficiently catalyzed by $Cu(BF_4)_2{\cdot}xH_2O$ leading to the formation of a 1,6-diketone. The reaction takes place in 0.5–1 hour at 15 °C in Et_2O.



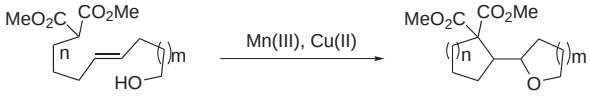
(E) *Epoxide ring opening by alcohols:* A general, simple and efficient protocol[8] has been developed for ring opening of different epoxides by reaction with various alcohols under the catalytic influence of $Cu(BF_4)_2{\cdot}xH_2O$. The reactions were carried out at room temperature and offered the use of cheap and commercially available copper tetrafluoroborate.



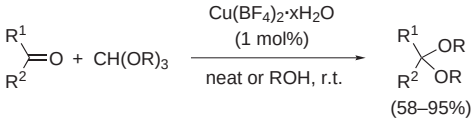
(F) *Epoxide ring opening by amines:* Another mild, efficient and selective ring opening of epoxides[9] has been effected by amines leading to the synthesis of β-amino alcohols under the catalytic effect of $Cu(BF_4)_2{\cdot}xH_2O$. The mild reaction conditions, short reaction times, solvent-free conditions, and excellent regio-, diastereo-, and chemoselectivity are the important features of this method.



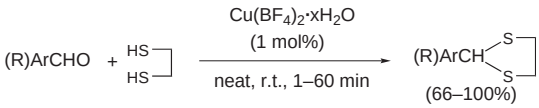
(G) *Cyclization:* Exposure of unsaturated malonates bearing pendant alcohols to $Cu(BF_4)_2{\cdot}xH_2O$[10] and $Mn(OAc)_3$ gives rise to the formation of carbocycles linked to oxygen heterocycles. The use of copper(II) salts bearing poorly coordinating anions has a profound influence on the product distribution.



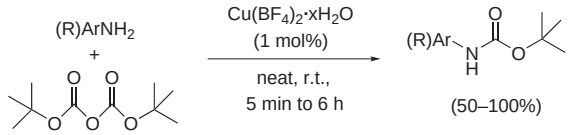
(H) *Acetal formation:* Dimethyl/diethyl acetal formation[11] in high yields from aldehydes and ketones by reaction with trimethyl/triethyl orthoformate at room temperature and in short reaction time has been successfully carried out in the presence of a catalytic amount of $Cu(BF_4)_2{\cdot}xH_2O$ which can be recycled.



(I) *1,3-Dithiolane/dithiane formation:* Recently, $Cu(BF_4)_2{\cdot}xH_2O$ has emerged as an extremely efficient catalyst for 1,3-dithiolane/dithiane formation from aromatic, heteroaromatic and aliphatic aldehydes and cyclic saturated ketones under solvent-free conditions at room temperature.[12]



(J) *Carbamate formation:* N-*tert*-Butoxycarbonylation[13] of amines by reaction with di-*tert*-butyldicarbonate under solvent-free conditions and at room temperature was successfully carried out in the presence of a catalytic amount of $Cu(BF_4)_2{\cdot}xH_2O$ in high yield.



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