

SYNLETT Spotlight 149

Cu(BF₄)₂·xH₂O: A Versatile Catalyst

Compiled by Raj Kumar Khunger



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

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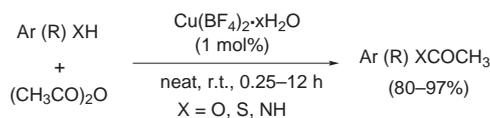
Introduction

Copper(II) tetrafluoroborate hydrate Cu(BF₄)₂·xH₂O [CAS: 314040-98-7] is a corrosive, moisture-sensitive, blue crystalline solid readily soluble in water and sparingly soluble in alcohols. Cu(BF₄)₂·xH₂O is readily available and widely used as the starting material for homometallic, trinuclear heteroscorpionate¹ complexes applied in the studies of electronic and magnetic properties. It causes decomposition of 9-diazafluorene in acetonitrile solvent.² As it does not require special storage conditions and is safe and stable under normal environmental conditions, Cu(BF₄)₂·xH₂O 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

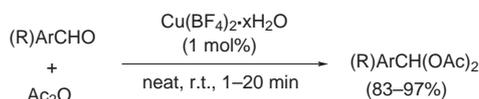
been found to be superior to other available Lewis acids such as triflates, tetrafluoroborates and perchlorates with regard to short reaction times, requirement of stoichiometric amount of reagent, mild reactions conditions, solvent-free conditions and low cost. Further, the distinct advantage of the use of Cu(BF₄)₂·xH₂O as a catalyst for thia-Michael addition reactions³ 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

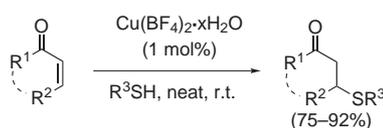
(A) *Acylation reactions*: Acetylation⁵ of structurally diverse phenols, alcohols, thiols, and amines with stoichiometric amounts of Ac₂O under solvent-free conditions at room temperature has been efficiently catalyzed by Cu(BF₄)₂·xH₂O. Excellent chemoselectivity was observed during reaction with secondary and tertiary alcohols without any competitive dehydration and no rearrangement took place with allylic and propargylic substrates.



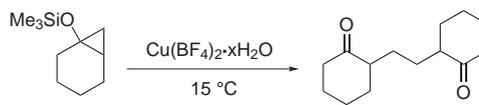
(B) *Diacetate formation*: A strong catalytic effect of Cu(BF₄)₂·xH₂O has also been observed in the formation of aldehyde 1,1-diacetates⁶ from aldehydes and acetic anhydride under solvent-free conditions at room temperature. The rate of reaction was found to be very fast and in most of the cases the reaction was completed in 1–20 minutes in excellent yields, which could make this method more attractive and industrially viable.



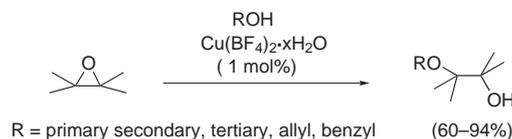
(C) *Conjugate addition*: $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$ has been found to be a new and highly efficient catalyst for Michael addition of thiols³ to α,β -unsaturated carbonyl compounds under solvent-free conditions.



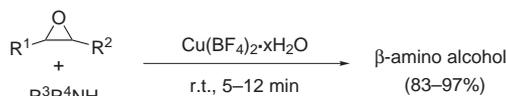
(D) *Electrophilic ring opening*: A ring opening of siloxycyclopropane,⁷ via β -copper substituted ketone intermediate, is efficiently catalyzed by $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$ leading to the formation of a 1,6-diketone. The reaction takes place in 0.5–1 hour at 15 °C in Et_2O .



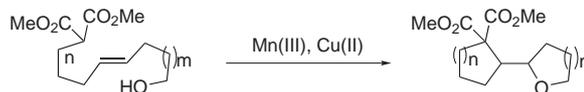
(E) *Epoxide ring opening by alcohols*: A general, simple and efficient protocol⁸ has been developed for ring opening of different epoxides by reaction with various alcohols under the catalytic influence of $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$. The reactions were carried out at room temperature and offered the use of cheap and commercially available copper tetrafluoroborate.



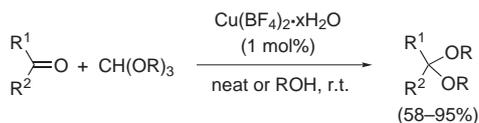
(F) *Epoxide ring opening by amines*: Another mild, efficient and selective ring opening of epoxides⁹ has been effected by amines leading to the synthesis of β -amino alcohols under the catalytic effect of $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$. The mild reaction conditions, short reaction times, solvent-free conditions, and excellent regio-, diastereo-, and chemoselectivity are the important features of this method.



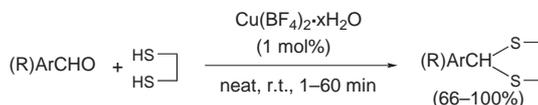
(G) *Cyclization*: Exposure of unsaturated malonates bearing pendant alcohols to $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$ ¹⁰ and $\text{Mn}(\text{OAc})_3$ gives rise to the formation of carbocycles linked to oxygen heterocycles. The use of copper(II) salts bearing poorly coordinating anions has a profound influence on the product distribution.



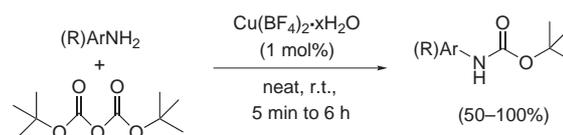
(H) *Acetal formation*: Dimethyl/diethyl acetal formation¹¹ in high yields from aldehydes and ketones by reaction with trimethyl/triethyl orthoformate at room temperature and in short reaction time has been successfully carried out in the presence of a catalytic amount of $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$ which can be recycled.



(I) *1,3-Dithiolane/dithiane formation*: Recently, $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$ 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*-Butoxycarbonylation¹³ 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 $\text{Cu}(\text{BF}_4)_2 \cdot x\text{H}_2\text{O}$ in high yield.



References

- Higgs, T. C.; Spartalian, K.; O'Connor, C. J.; Matzanke, B. F.; Carrano, C. J. *Inorg. Chem.* **1998**, *37*, 2263.
- Ahmad, I. *Int. J. Chem. Kinet.* **1984**, *17*, 763.
- Garg, S. K.; Kumar, R.; Chakraborti, A. K. *Tetrahedron Lett.* **2005**, *46*, 1721.
- Ranu, B. C.; Dey, S. S. *Tetrahedron* **2004**, *60*, 4183.
- Chakraborti, A. K.; Shivani, R. G. *Synthesis* **2004**, 111.
- Chakraborti, A. K.; Thilagavathi, R.; Kumar, R. *Synthesis* **2004**, 831.
- Ryu, I.; Ando, M.; Ogawa, A.; Murai, S.; Sonoda, N. *J. Am. Chem. Soc.* **1983**, *105*, 7192.
- Barluenga, J.; Vazquez-Villa, H.; Ballesteros, A.; Gonzalez, J. M. *Org. Lett.* **2002**, *4*, 2817.
- Kamal, A.; Ramu, R.; Azhar, M. A.; Khanna, G. B. R. *Tetrahedron Lett.* **2005**, *46*, 2675.
- Hulcoop, D. G.; Sheldrake, H. M.; Burton, J. W. *Org. Biomol. Chem.* **2004**, 965.
- Kumar, R.; Chakraborti, A. K. *Tetrahedron Lett.* **2005**, *46*, 8319.
- Besra, R. C.; Rudrawar, S.; Chakraborti, A. K. *Tetrahedron Lett.* **2005**, *46*, 6213.
- Chanckeshwara, S. V.; Chakraborti, A. K. *Tetrahedron Lett.* **2006**, *47*, 1087.