

Cu (MeCN)₄BF₄ Catalyzed Addition of 2-Pyridylzinc Bromide to Acid Chlorides

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ABSTRACT

The 2-pyridylzinc bromide was easily prepared via the direct insertion of active zinc into the corresponding bromopyridines. The subsequent addition reaction of the resulting 2-pyridyl zinc bromide to aryl acid chloride was catalyzed by several copper (I) complex catalyst. We have prepared benzoyl derivatives of pyridine using tetrakis acetonitrile copper (I) tetrafluoroborate as efficient catalyst under mild condition.

Keyword : Highly Active Zinc Metal, 2-Pyridylzinc Bromide, Acid Chloride, Copper(I) Complex.

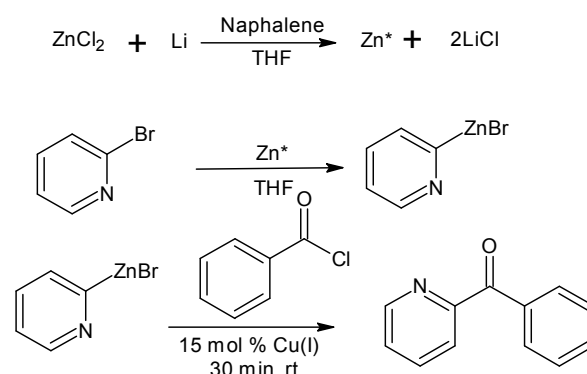
I. INTRODUCTION

Organozinc reagents are most useful organometallic reagent for organic transformation and occupied unique position in synthetic organometallic chemistry due to large number of functional group tolerance and easy formation and transmetalation.¹⁻⁶ The organozinc halides undergo transmetalation by number of transition metal salt or complex such as copper, palladium and nickel etc.⁷⁻¹² They undergo major pathway for carbon-carbon bond formation as conjugate addition to α , β unsaturated carbonyl compounds, cross coupling,¹⁴ addition to acetylene and nucleophilic displacement of halides, sulphonates, allylic acetates.¹⁵ The remarkable advantage offered by reagent is built up polyfunctional molecules without protection and deprotection.²¹⁻²²

Pyridine ring system is widely distributed in nature in the form of pyridine derivatives and many important alkaloids. A number of pyridine derivatives have been used in pharmaceutical, agrochemical, medicinal chemistry and in material chemistry.²³⁻²⁷ The 2-pyridyl derivatives have been prepared using the Suzuki, Still, Grignard and Negishi coupling reaction catalyzed by transition metal.²⁸⁻³⁴ The reike zinc metal is easily prepared by reduction of anhydrous zinc chloride using lithium in the presence of a catalytic amount of naphthalene in THF at room temperature.³⁵ The resulting active zinc is highly reactive metal and readily undergoes oxidative addition with 2-bromopyridine.³⁶

II. RESULT AND DISCUSSION

We have prepared active zinc metal by reduction of zinc chloride using lithium naphthalene known as reike zinc. This is the highest active form of zinc used for oxidative insertion in 2-bromopyridine after 1 hr reflux condition. LiCl in THF not only solubilize the benzylic zinc halide but also assist the zinc insertion into 2-bromopyridine. The 2-bromopyridine zinc bromide was added to various acid chlorides at room temperature in presence of different copper (I) complex as catalyst i.e. catalyst screening. We have observed that Cu(MeCN)₄BF₄ found to be best catalyst for this addition reaction. Among the product 1a,2a,3a and 4a from table number 2 are formed without catalyst in moderate yield³⁷ but use of catalyst enhance the yield.



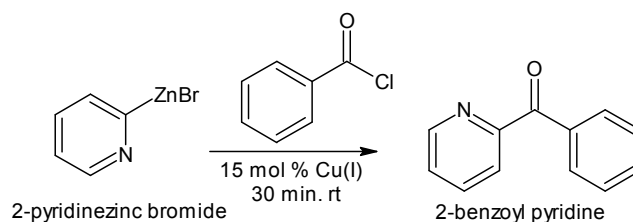
Scheme 1. Synthesis of 2-benzoyl pyridine derivatives.

Table 1. Different copper(I) catalyst screening

Sr. No.	Copper (I) Catalyst	% Yield
1	without catalyst	42 %
2	Cu(MeCN) ₄ BF ₄	88 %
3	Cu(MeCN) ₂ F ₃ CSO ₃	57%
4	Cu(MeCN) ₄ ClO ₄	61%
5	Cu(MeCN) ₄ NO ₃	58%
6	Cu(MeCN) ₄ PF ₆	48%

All the products are purified by column chromatography and yield was reported. They are known derivatives and confirm by melting point. The product was analyzed by

IR, ¹HNMR and ¹³CNMR The copper (I) catalyzed nucleophilic addition of 2-pyridine zinc bromide to acid chloride is an important reaction constitute a C-C bond formation and ketone functional group synthesis. The 2-benzoyl pyridine derivatives has tremendous potential in organic transformation i.e. versatile precursor in organic synthesis.

**Table 2.** Synthesis of 2-benzoyl pyridine using tetrakis acetonitrile copper (I) tetrafluoroborate as catalyst

Entry	Acid chloride	Product	Yield	M. P. °C
1			68%	45-47°C
2			74%	120-122°C
3			85%	liq.
4			78%	105-107°C
5			72%	115-117°C

6			56%	65-67°C
7			69%	120-125°C
8			52%	liq.
09			82%	liq.

III. CONCLUSION

We have introduced **tetrakis** acetonitrile copper (I) tetrafluoroborate as efficient catalyzes addition of 2-pyridylzinc bromide to acid chloride under mild condition.

Experimental Section

Precaution

- 1) Strictly anhydrous condition was maintained.
- 2) All glassware dried overnight 150°C before use.
- 3) All solvents were dried as per Vogel's practical book procedure.

Typical procedure for preparation of copper (I) catalyst

4g (0.028 mole) cuprous oxide mixed with 80 ml acetonitrile in RBF suspension was observed. 113 mmole acid was added slowly with constant stirring at room temp. exotherm observed. The reaction mixture was keep at 50°C for 30 min then filtered removing any unreacted copper (I) oxide. The colorless clear solution was then cooled at -10°C in a freezer and left overnight.

A white colored crystal settle at the bottom of RBF which was separated by filtration washed with diethyl ether under nitrogen atmosphere. Then the copper salt was recrystallised and store in acetonitrile. All the copper salts were confirmed by melting point.³⁸⁻⁴⁴

Typical procedure for preparation of reike zinc metal

One 50 ml two neck RBF was equipped with rubber septa, stopper and magnetic bar flush by nitrogen. A small amount freshly cut of lithium 0.05g (7.204 mmole), naphthalene 0.1 g (0.7813 mmole) and 5 ml dry THF was charged by syringe clear solution was observed. The mixture was stirred at room temp. colorless solution changes to dark green.

Second 50 ml two neck RBF was equipped with rubber septa, stopper and magnetic bar flush by nitrogen. Anhydrous Zinc chloride 0.5g (3.724mmole) was charged and 5ml dry THF added by syringe clear solution obtained. The zinc chloride solution was added to above dark green solution by syringe through septum. The mixture was stirred for 1 hr black-grey colored zinc metal observed in RBF. The weight of zinc metal

generated after reduction was 0.210 gram i.e.0.003211 mole.

Typical procedure for preparation of 2-pyridinezinc bromide and addition to acid chloride.

Anhydrous LiCl (2 equivalent) was dissolved in 2 ml dry THF and charged zinc metal (2.5 equivalent) solution by syringe. 2-pyridine bromide (1 equivalent) was dissolved in 2ml dry THF add to zinc metal solution and slowly allow to raise temp. reflux for 1 hr zinc insertion takes place. organozinc reagent formation confirm by TLC i.e. consumption of 2-bromopyridine. Again organozinc reagent containing solution cool to room temperature then substituted benzoyl chloride (1.1 eq.) was dissolved in 2 ml dry THF added by syringe and solid catalyst 15 mol %. The temperature of reaction mixture was stirred at room temperature for 30 min. Add 30 ml saturated ammonium chloride solution stir reaction mixture for 1 hr at rt and heat the reaction mixture to evaporate THF completely. The product was extracted in ethyl acetate wash by aq. NaHCO₃ and water dried organic layer over sodium sulphate. The product was purified using column chromatography and yield was reported.

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