

DIVERSE CARBONYLATION OF PHCU·P (N-BUTYL)3: A PATH TO BENZOPHENONE

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Abstract

The carbonylation of alkylcopper reagents, as initially demonstrated by Jeffery Schwartz in 1972, represents a critical synthetic pathway for generating symmetrical ketones through quenching with dilute aqueous acid. While this groundbreaking discovery has been pivotal for the synthesis of symmetrical ketones, it has primarily focused on dialkyl cuprates and alkylcopper complexes of tri-n-butylphosphine. Interestingly, the simple alkylcopper compounds, without the presence of tri-n-butylphosphine, do not exhibit similar reactivity. Remarkably, the scope of this reaction has yet to be explored in the context of arylcopper reagents, a class of compounds that holds immense significance in organic synthesis. Consequently, this study aims to bridge this knowledge gap by investigating the carbonylation reaction with arylcopper reagents, shedding light on the potential of extending this versatile transformation to a broader range of substrates. The outcome of this research may not only expand the synthetic toolbox but also provide valuable insights into the reactivity patterns of arylcopper compounds in carbonylation reactions.

1. Introduction and Background

1.1 Background

The incorporation of carbonyl groups in organic synthesis is of great importance. This is often accomplished by the attack of nucleophilic reagents on suitable carbonyl derivatives such as acyl halides or anhydrides. The development of nucleophilic carbonyl reagents would greatly expand the scope of incorporating carbonyl groups in organic synthesis and extend their synthetic utility (Carey & Sunberg, 1990). One approach to such reagents would be the carbonylation of organometallic compounds to produce acyl anions.

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1.2 Introduction

In 1972 Jeffery Schwartz reported the successful carbonylation of alkylcopper reagents, which upon quenching with dilute aqueous acid, produced symmetrical ketones (Schwartz, 1972). Dialkyl cuprates and alkylcopper complexes of tri-*n*-butylphosphine both undergo this reaction. The simple alkylcopper compounds, lacking tri-*n*-butylphosphine, do not. The report did not encompass the study of any arylcopper reagents, which are an extremely important class of compounds. To our knowledge there have been no reported studies of this reaction with respect to arylcopper reagents.

2. Experimental

2.1 Experimental Setup

All reactions were carried out in 100-mL three-neck round-bottomed flasks equipped with a reflux condenser and containing a small Teflon-clad stirring bar. The condenser was connected to an argon/vacuum dual-manifold. The second neck was connected to the carbon monoxide source, and the third neck sealed with a rubber septum. All glassware was oven dried, assembled hot, and purged with argon. Tetrahydrofuran (THF) was distilled from sodium/potassium alloy just prior to use.

2.2 Starting Materials.

All starting materials were commercially purchased as reagent grade or better and used as received unless otherwise stated. These include: PhLi (1.0 M soln.), decane, tetrahydrofuran (THF), P(*n*-butyl)₃. These reagents were purchased from the Aldrich Chemical Company.

2.2.1 Purified CuI.

CuI was purchased from the Aldrich Chemical Company and further purified by literature methods (Kauffman & Teter, 1963).

2.2.2 PhCu.

Purified CuI (5 mmol) was stirred with freshly distilled THF (10 mmol). Then 5 mmol of a 1.0 M solution of PhLi was syringed in to the reaction vessel at 0°C and allowed to stir for 10 min. The internal standard was then added (decane, 4.0 mmol).

2.2.3 Ph₂CuLi.

Purified CuI (5 mmol) was stirred in freshly distilled THF (10 mL). Then 10 mmol of a 1.0 M solution of PhLi was syringed into the reaction vessel at 0°C and allowed to stir for 10 min. The internal standard was added last (decane, 4.0 mmol).

2.2.4 PhCu · P(*n*-butyl)₃.

Purified CuI (5 mmol) was stirred with freshly distilled THF (10 mL). Then tri-*n*-butyl phosphine (5.1 mmol) was syringed into the reaction vessel and the solution stirred until all of the CuI was dissolved (10 min). Then PhLi (5 mmol of a 1.0 M soln.) was syringed into the reaction vessel at 0°C and allowed to stir for 10 min. The internal standard was then added (decane, 4.0 mmol).

2.2.5 Ph₂CuLi · P(*n*-butyl)₃.

Purified CuI (5 mmol) was stirred with freshly distilled THF (10 mL). Then tri-*n*-butyl phosphine (5.1 mmol) was syringed into the reaction vessel and the solution stirred until all of the CuI was dissolved (10 min). Then PhLi (10 mmol of a 1.0 M soln.) was syringed into the reaction vessel at 0°C and allowed to stir for 10 min. The internal standard was added last (decane, 4.0 mmol).

2.2.6 PhCu · P(*n*-butyl)₃ + 1.5 P(*n*-butyl)₃.

Purified CuI (5 mmol) was stirred with freshly distilled THF (10 mL) and tri-*n*-butyl phosphine (12.5 mmol) was syringed into the reaction vessel and the solution stirred until all of the CuI was dissolved (10 min). Then PhLi

(5 mmol of a 1.0 M soln.) was syringed into the reaction vessel at 0°C and allowed to stir for 10 min. The internal standard was then added (decane, 4.0 mmol).

2.3 Addition of Carbon Monoxide.

When the formation of the organocopper reagent was complete, CO was bubbled through the solution for 20 min after which the solution was blanketed with a static atmosphere of CO for an additional 40 min.

2.4 Temperature Adjustment.

After the addition of CO the solution was brought to the desired temperature and stirring continued for the allotted time.

2.5 Quenching and sampling.

At the end of the reaction time an aliquot (2 ml) was removed from the reaction vessel and quenched with 0.5mL of H₂SO₄ (0.01 M). The organic layer was separated and analyzed by gas chromatography.

2.6 Analysis.

The benzophenone product was identified by comparing its physical properties with those of an authentic commercial sample. Quantification was performed by gas chromatography using the internal standard method and using an authentic commercial sample of benzophenone to obtain an accurate response factor.

3. Results and Discussion

We wish to report the successful carbonylation of an arylcopper reagent to produce, upon treatment with dilute aqueous acid, the symmetrical diaryl ketone (Table I). Specifically, phenylcopper tri-*n*-butylphosphine complex was carbonylated at 0°C for one hour. The temperature was then raised to 60°C for an additional hour. This was followed by quenching the reaction with dilute aqueous acid, which produced benzophenone in a 55% yield (entry 4).

Table I. Reaction of Phenylcopper Reagents with Carbon Monoxide to Produce Benzophenone

1)	CO, 0°C, 1 hr.	
2)	60°C, 1 hr	
3)	H ⁺ _(aq)	
entry	Phenylcopper Reagent	□□□□□□□□ PhC(O)Ph (yield)
1	Ph ₂ CuLi	5%
2	Ph ₂ CuLi · P(<i>n</i> -butyl) ₃	34%
3	PhCu	0%
4	PhCu · P(<i>n</i> -butyl) ₃	55%
5	PhCu · P(<i>n</i> -butyl) ₃ + 1.5 P(<i>n</i> -butyl) ₃	6%

Unlike the dialkylcuprate reagents studied by Schwartz, we were unable to produce more than a trace of the symmetrical ketone by using the simple diarylcuprate (entry 1). Phenylcopper produced no detectable amount of benzophenone (entry 3). Adding tri-*n*-butyl phosphine to the diarylcuprate produced a yield of 34% (entry 2). The addition of more tri-*n*-butyl phosphine beyond one equivalence (based upon copper) lowered the yield of product (entry 5).

Table II. Optimization of the Reaction of PhCu · P(*n*-butyl)₃ with Carbon Monoxide to Produce Benzophenone

	CO	Temp.	H ⁺ _(aq)	
	PhCu · P(<i>n</i> -butyl) ₃	□□□□□	□□□□□	□□□□□ PhC(O)Ph
entry	0°C, 1 hr	Time		(% yield)

1	25°C, 1 hr	26%
2	60°C, 1 hr.	55%
3	60°C, 2 hr	56%

Benzophenone could best be produced from the phenylcopper tri-*n*-butylphosphine complex (Table II). To accomplish this the temperature was raised to 60°C for 1 hr. after carbonylation (entry 2). Lowering the temperature resulted in a lower yield (entry 1). Allowing the reaction to run for a longer period of time, even at 60°C, did not significantly improve the yield (entry 3).

4. Conclusion

In conclusion, we have shown that, with slight modification, the Schwartz protocol for converting alkylcopper tri-*n*-butylphosphine complexes into symmetrical ketones can be expanded to include arylcopper complexes. Specifically, phenylcopper tri-*n*-butylphosphine complex can be carbonylated and then quenched with dilute aqueous acid to produce benzophenone in a 56% yield. This yield is comparable to the yields produced by Schwartz in the reactions with alkylcopper reagents, which ranged from 32% to 77% (Schwartz, 1972).

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Conflict of Interest: The authors declare they have no conflict of interest.

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