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Conjugate addition Reactions of Two New Copper Reagents

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Abstract

Two new copper reagents containg sulfur atom are described. Although there have been many reports on the copper reagents, little is known on the disulfinyl copper reagents. In this communication, we wish to report conjugate addition reactions of two new copper reagents to α, β-unsaturated carbonyl compounds.

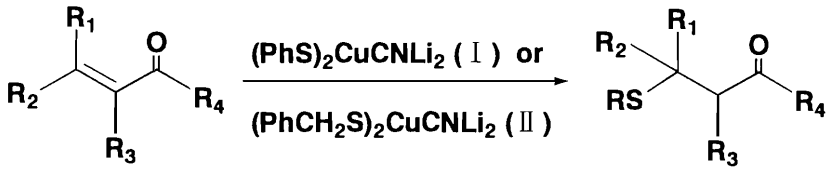
Introduction

One of the most important reactions is conjugate addition reactions in organic chemistry and biochemistry[1]. On these foundation enormous amount of organocopper reagents has been reported for the last several decades[2]. But no report concerning sulfides built in organocopper reagent is curious. Conjugate addition of a sulfide to an electron deficient olefin to form a sulfur-carbon introduce a new asymmetric center and is derivated to a variety of compounds, olefine, alcohol etc. We now report the first example of copper analogs cotaining two sulfur atoms to the conjugate addition reaction.

Result and Discussion

Although conjugate addition of sulfur compounds has been widely studied about a thiol[3], these reactions have been proposed in acidic or basic conditions. These conditions are not suitable for a synthesis of complicated natural products which possess many functional groups sensitive to acid and base at the same compound. Now reported are the two new organocopper reagents cotaining two sulfur atoms, $(PhS)_2CuCNLi_2$ (Ⅰ) and $(PhCH_2S)_2CuCNLi_2$ (Ⅱ), which carried under neutral condition[4].

Initially, we investigated the addition of two new copper reagents to α, β-unsaturated ketones (Scheme 1). The results are summarized in Table 1.



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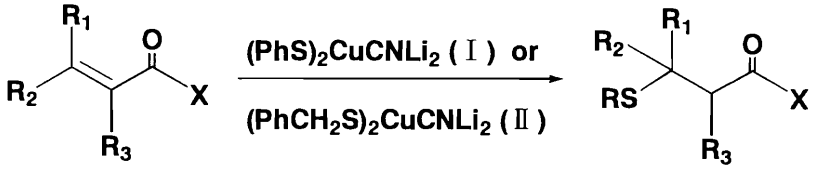
Scheme 1. Conjiugate Addition of Copper Reagents (Ⅰ) and (Ⅱ) to α, β-unsaturated ketones

Table 1. Conjiugate Addition of Copper Reagents (Ⅰ) and (Ⅱ) to α, β-unsaturated ketones

Entry	R_1	R_2	R_3	R_4	Yield of 2a	Yield of 2b
1	C_6H_5	H	H	CH_3	80	99
2	H	H	H	CH_3	57	100
3	H	H	CH_3	CH_3	88	78
4	C_6H_5	C_6H_5	H	CH_3	64	74

We also tested α, β-unsaturated ester and amide compound (Scheme 2). Both of results were satisfied (Table 2).



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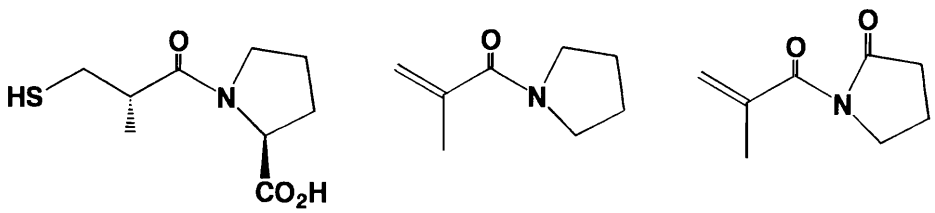
Scheme 2. Conjiugate Addition of Copper Reagents (Ⅰ) and (Ⅱ) to α, β-unsaturated carbonyl compounds

Table 2. Conjiugate Addition of Copper Reagents (Ⅰ) and (Ⅱ) to α, β-unsaturated carbonyl compounds

Entry	R_1	R_2	R_3	X	Yield of 4a	Yield of 4b
1	H	H	H	OCH_3	80	86
2	H	H	H	$N(CH_3)_2$	87	80

As a model experiment of asymmetric synthesis of Captopril (5), inhibitor of angiotensin

converting enzyme (ACE)[5], we tried conjugate addition of pyrrolidine derivatices (6). Although conjugate addition of (6) was 73% recovery, pyrrolidone derivatices (7) was 70% yield (Scheme 3). In Comparison with entry 2 (Table 2), these results were strange.



(5) (6) (7)

Scheme 3

Appended to above results, we obtained interesting result. Usually conjugate addition of t-butyl mercaptane to α, β -unsaturated carbonyl compounds, e.g. pyroglutamate derivative, was not easy (in our case, recovery was 90%). But this type reagent, $(t\text{-BuS})_2CuCNLi_2$, gave excellent yield (92%).

Acknowledgments

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(4) The tpical reaction is followed; To a solution of thiol (1.4mmol) in tetrahydrofuran (THF; 1ml) was added a solution of n-BuLi (1.4ml) in hexane at -78℃. The reaction mixture was stirred for 10 min at this temperature and then CuCN (0.8mmol) was added at the same temperature. The resulting suspension was allowed to warm to -30℃ and a homogeneous solution was obtained. The solution was cooled to -78℃ and α, β -unsaturated compound (0.4mmol) was added at this temperature. After a few minites the reaction was quenched with saturated aqueous NH_4Cl. The usual work-up gave the crude product, which was purified by Thin Layer Chromatography on silicagel, affording sulfide compound.

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