Reaction of Lithium Dialkylcuprates with *S*-2-Pyridyl Thioates in the Presence of Oxygen. A Carboxylic Ester Synthesis

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Summary Reaction of lithium dialkylcuprates with *S*-2-pyridyl thioates in the presence of oxygen affords carboxylic esters in high yields, whereas under nitrogen it affords ketones.

S-2-PYRIDYL THIOATES have recently attracted a great deal of attention as active acylating agents in the synthesis of peptides,[1] ketones,[2] macrocyclic lactones,[3] and β-lactams.[4] It has been reported recently that organocopper reagents react with *S*-2-pyridyl thioates to afford ketones during the total synthesis of erythronolide A [5] and monensin.[6]

While examining the scope and limitation of this useful procedure for a ketone synthesis, we observed that treatment of *S*-2-pyridyl thioates in the presence of oxygen with lithium dialkylcuprates surprisingly results in the formation of carboxylic esters in high yields. Although oxygen-containing products are obtained as byproducts from oxidations of many aryl copper reagents with oxygen,[7] this observation is in striking contrast with earlier findings that oxidations of organocopper reagents with oxygen give the symmetric coupling products.[8]

Lithium dialkylcuprate, which is prepared in diethyl ether under nitrogen by the known procedure is further stirred at −78 °C for 5 min under a balloon-filled atmosphere of oxygen, and the resulting organocopper reagent (1 mmol) is added to the *S*-2-pyridyl thioate (1 mmol) in diethyl ether containing oxygen at −78 °C with stirring. The resulting mixture is allowed to attain room temperature gradually. Within 3 h the reaction is normally complete and the product is isolated in the usual manner.

Some experimental results are summarized in the Table and demonstrate the general applicability of this procedure.

TABLE. Isolated yields of carboxylic esters and ketones.

R–CO–S–py	$LiCuR'_2$	% Yield	
R	R′	RCOOR′	RCOR′
Ph	Me	71	85
Ph	Bu^n	99	99
Ph	Bu^t	43^a	96
$PhCH_2$	Bu^n	89	87
Bu^n	Bu^n	82	90
Pr^i	Bu^n	71	79
Bu^t	Bu^n	57^b	70

[a] With recovery of 40% of starting material. [b] With recovery of 19% of starting material.

Of special synthetic significance is the exclusive ester formation without contamination of the ketone and the fact that no appreciable amounts of byproducts are observed in most instances. When *S*-n-butyl benzenethioate is treated with lithium di-n-butylcuprate in the same manner, n-butyl benzoate is obtained in only 23% yield with recovery of starting material in 66% yield. Thus, it seems that the 2-pyridyl moiety is essential to the high-yield ester formation and stabilizes the copper species by internal complexation.

In additional experiments using a similar procedure under nitrogen at −78 °C, the ketones are generally obtained in high yields without contamination of the esters as shown in Table. Thus, the ester formation is attributed to oxidation of the organocopper reagents with oxygen. However, despite much available data on organocopper reactions we cannot yet say what species is responsible for the observed oxidation. Presumably the reaction proceeds *via* an intermediate copper alkoxide.

In conclusion, this procedure represents a unique and efficient method for converting *S*-2-pyridyl thioates into either esters or ketones and has wide applications because *S*-2-pyridyl thioates can be easily prepared in high yields under mild conditions.[9]

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