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THE REACTION OF ALKYLCOPPER(I) COMPLEXES WITH CARBON MONOXIDE: A NEW KETONE SYNTHESIS

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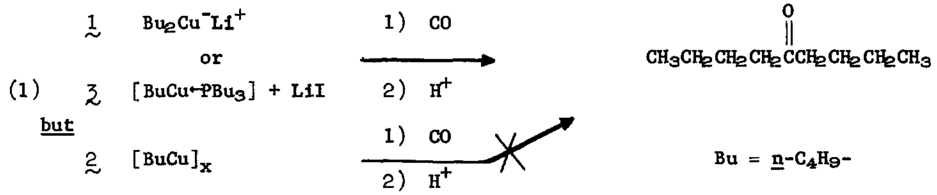
The use of alkylcopper(I) "ate" complexes for alkylation of a wide variety of organic substrates continues to be a subject of active interest.[1,2] In this context, we wish to report our observations concerning the reaction of several of such complexes with carbon monoxide, a reaction which, under appropriate conditions, results in high yields of symmetrically substituted ketones. These studies have shown that while lithium di-n-butylcuprate (1) absorbs one equivalent of carbon monoxide (based on starting millimoles of copper) to give 5-nonanone in 70% yield upon hydrolysis, butylcopper(I) (2) yields no ketone on similar treatment with carbon monoxide. We also note that n-butyl(tri-n-butylphosphine)copper(I) (3), in ether, absorbs one equivalent of carbon monoxide but yields 5-nonanone on hydrolysis only when lithium halide is present in the reaction mixture (Eq. 1). When lithium iodide is removed by precipitation with dioxane,[3] tri-n-butylphosphine butylcopper(I) complex (3) does absorb one equivalent of CO and, on hydrolysis, yields butane and n-octane but essentially no ketone. These observations are consistent with the interpretation that the copper(I) species which reacts with CO to yield ketone is lithium di-n-butylcuprate and that this reagent is produced from n-butyl(tri-n-butylphosphine)copper(I) according to the equilibrium reaction shown in



$$(1)\quad \begin{array}{ll} 1\ \ Bu_2Cu^-Li^+ & \\ \quad\text{or} & \xrightarrow[2)\ H^+]{1)\ CO}\ CH_3CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2CH_2CH_3 \\ 3\ \ [BuCu\leftarrow PBu_3] + LiI & \\ \underline{\text{but}} & \\ 2\ \ [BuCu]_x & \xrightarrow[2)\ H^+]{1)\ CO}\ \times \qquad Bu = \underline{n}\text{-}C_4H_9\text{-} \end{array}$$

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Equation (2). Evidence in support of a similar equilibrium reaction involving

$$(2) \qquad 8[\mathrm{BuCu{\leftarrow}PBu_3}] + 4\ \mathrm{LiI} \rightleftarrows 4\ \mathrm{Bu_2Cu^-Li^+} + [\mathrm{ICu{\leftarrow}PBu_3}]_4 + 4\ \mathrm{PBu_3}$$

(tri-*n*-butylphosphine)carbonylcopper(I) complexes is provided by the fact that if a halide-free[3] ethereal solution of *n*-butyl(tri-*n*-butylphosphine)copper(I), which has absorbed one equivalent of carbon monoxide, is divided into halves, formation of 5-nonanone occurs in the aliquot to which freshly prepared lithium iodide is introduced but does not occur in the other aliquot. In no case was *n*-valeraldehyde detected as a reaction product. The results of typical experiments are summarized in Table I. Yields of 5-nonanone, based on butyllithium, were found to be substantially higher for reaction of CO with lithium di-*n*-butylcuprate than they were for similar treatment with *n*-butyl(tri-*n*-butylphosphine)copper(I) in the presence of lithium iodide. It has been reported[4,5] that 6-butyl-5-decanone is the major product of reaction between CO and butyllithium. However, in no instance did reaction between CO and various butylcopper(I) complexes yield this ketone in greater than trace amounts. It is entirely possible that this product arises from small amounts of excess

TABLE I

TYPICAL RESULTS

Copper(I) Compound (1 mmole)	M equiv. CO Absorbed	Reaction Time (min)	% Yield‡	
			5-nonanone	5-nonanol
BuCu(solid)	None	45	-	-
$\mathrm{Bu_2Cu^-Li^+}$	0.95	45	73.0	1.0
$\mathrm{Bu_2Cu^-Li^+}$	Injection[7]	60	77.4	2.0
$\mathrm{Bu_3P{\rightarrow}CuBu}$				
a) LiI present	0.96	60	32.0	3.0
b) LiI absent[3]	0.98	55	not analyzed	
c) LiI present	Injection[7]	60	68.0	2.4
d) LiI absent[3]	Injection[7]	60		
1) Then add LiI		30	58.8	8.5
2) Then no LiI added		30	1.4	0.0

‡ These yields are based on butyllithium. The remainder of the butyllithium was accounted for as organocopper(I) hydrolysis (butane) and thermal decomposition (butane, 1-butene and *n*-octane) products.[1,3,8] Absolute yields of products were calculated from sharp peak heights using internal standard techniques with response factors obtained with authentic samples.

butyllithium present in solution with the alkylcopper(I) species. In related experiments, the production of cyclopentanone from 1,4 tetramethylenedilithium,[6] copper(I) complexes, and CO in 18% yield was realized.

In a typical experimental procedure,[9] butylcopper(I) was prepared[1] in a pyrex centrifuge tube from bis(di-n-butylsulfide)iodocopper(I) and butyllithium at -78°. The resulting two-phased solution was swirled vigorously, and, immediately, a bright yellow precipitate of butylcopper(I) formed. The reaction mixture was then centrifuged in a cooled bucket and the ethereal supernatant was removed via pressurized siphoning through a hollow needle. The precipitate was washed several times with diethyl ether which had been previously cooled to -78°. The golden yellow butylcopper(I) was then suspended in diethyl ether which had been cooled to -78°. One equivalent of butyllithium was added quickly. As the reaction mixture slowly warmed from -78° to 0°, the suspension of butylcopper(I) slowly dissolved to yield an initially light yellow and finally a light violet solution of lithium di-n-butylcuprate. The ethereal solution of lithium di-n-butylcuprate was stable for several hours if stored below 0°.

In other experiments, the solution of n-butyl(tri-n-butylphosphine)copper(I) in diethyl ether was prepared[3] from iodo(tri-n-butylphosphine)copper(I) at -78°. The light yellow ethereal solution prepared in this way could then be made halide-free by precipitation of lithium iodide as the dioxane adduct.

The reaction between CO and the organocopper reagent was initiated by injection of an ethereal solution of the organometallic into a Schlenk tube connected to a buret filled with this gas at a constant pressure of 1 atm. The reaction mixture was maintained at -22°, and rapid uptake of CO ensued.[7] When absorption of gas ceased (typically greater than 0.97 equiv absorbed), excess CO was removed through repeated evacuation and introduction of nitrogen. The deeply colored resulting solution was then treated with either gaseous HCl or water to yield a colorless ethereal solution which was then analyzed by gas chromatography. In all reaction sequences, the identity of each component was determined through coinjection with authentic material. Chromatographically pure samples of ketone products were collected, and each displayed an IR spectrum identical with that obtained from authentic material.

We are presently studying the mechanism of this interesting synthetic reaction and are exploring routes which may prove useful in the synthesis of unsymmetrically substituted ketones. We are also investigating the use of alkylcopper complexes as alkylating agents for molecules isoelectronic with CO.

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7. Alternatively, one equiv of CO could be injected, using a gas-tight syringe, into a vessel containing a solution of the organocopper(I) reagent to produce, upon protonolysis, high yields of the ketone.
8. We could not separate 1-butene from *n*-butane by vpc. We could not determine, therefore, the *relative* yields of hydrolysis and thermal decomposition products of butylcopper(I) species.
9. All reactions were performed in diethyl ether which was freshly distilled from LAH. Except where carbon monoxide was used as a reagent, the atmosphere present was dry nitrogen. Vapor phase chromatographical analyses were obtained using an 8' x 1/4" column packed with 5% carbowax 20 M on 80/100 Chromosorb P.
10. From S.B. Thesis, MIT, May, 1966.