

chloride remains as shown by quenching the reaction mixture with absolute methanol which produces methyl benzoate). Storage at -20° for 1-1.5 hrs causes complete decomposition of cuprates 1.

Table I summarizes the substitution reactions achieved using tert-butoxy-alkylcuprates 1 and various acyl and alkyl halides.

Table I. Reaction of 1.2-1.3 Equiv of Lithium tert-butoxy-alkylcuprates 1 with 1 Equiv of Organic Halides in THF at -78° (Eq. 1a)

Organic Halide	Reaction Time (min)	Product	R, % Isolated Yield	
			<u>tert</u> -Bu	<u>sec</u> -Bu
C_6H_5COC1	20	$C_6H_5COR^a$	82	87
$Br(CH_2)_{10}COC1$	20	$Br(CH_2)_{10}COR$	78 ^b	83
$CH_3O_2C(CH_2)_2COC1$	20	$CH_3O_2C(CH_2)_2COR$	61 ^c	66 ^c
$n-BuCO(CH_2)_4COC1$	20	$n-BuCO(CH_2)_4COR$	73	86
$C_6H_5CH_2Br$	240	$C_6H_5CH_2R$	88 ^{c,d}	0 ^e
$n-C_8H_{17}I$	90	$n-C_8H_{17}R$	82 ^{c,f}	52 ^{c,f,g}
$n-C_8H_{17}Br$	240	$n-C_8H_{17}R$	83 ^{d,h}	0 ⁱ

^aIsobutyrophenone and valerophenone were formed in 80 and 70% yields respectively using lithium tert-butoxy-isopropylcuprate 1 and lithium tert-butoxy-n-butylcuprate 1. ^bThe yield was increased to 83% when 1.5 equiv of cuprate 1 were used. ^cYield was determined by quantitative VPC using internal standards. ^d5 Equiv of cuprate 1 were used. ^e90% Bibenzyl. ^f3 Equiv of cuprate 1 were used. ^gAfter 4 hrs at -78° the reaction was allowed to warm slowly to 0° (2 hrs). ^h -50° Reaction temperature. ⁱStarting material was recovered in good yield even after prolonged exposure to cuprate 1.

Several important conclusions can be drawn from the data in Table I: (1) formation of the tert-butoxy-alkylcuprate reagents 1 from equiv amounts of cuprous tert-butoxide and lithium alkyls is complete because no tert-butyl esters¹¹ and no alcohols¹² are observed; (2) the absence of tert-butyl esters and tert-butyl ethers indicate the specific transfer of only the alkyl group in the tert-butoxy-alkylcuprates 1; (3) replacement of acyl chlorine by a tertiary, or a secondary, or a primary alkyl group can be achieved equally well using the corresponding cuprates 1, but replacement of alkyl halogen is accomplished better with tert-butylcuprate 1 than with sec-butylcuprate 1; (4) n-alkyl ketones can be formed effectively using 1.2-1.3 equiv of tert-butoxy-n-alkylcuprates 1 (see Footnote a in Table I); (5) low temperature (-78°) and short time (20 min) allow conversion of 11-bromoundecanoyl chloride into the corresponding bromoketone (i.e. bromine not replaced by alkyl), whereas higher temperature (-50°) and longer time (4 hrs) effect replacement of bromine by the tert-butyl group.^{13,14}

It should be noted that trans-1-bromo-2-phenylethylene and 1-chloro-1-phenylethane are essentially inert to tert-butylcuprate 1 and that 2-octyl iodide and tosylate are converted to 2,2,3-trimethylnonane in less than 25% yield. Thus tert-butyl 1 is not useful in substitution of vinylic and secondary alkyl systems.

Conjugate addition of alkenyl groups to α,β -unsaturated carbonyl compounds has most recently been applied to synthesis of various prostaglandins.^{7b} To explore the potential utility of mixed alkoxy-alkenylcuprates(I) for 1,4 addition reactions, 1 equiv of cyclohexenone was added at -50° to 1.2-1.3 equivs of several tert-butoxy-alkylcuprates 1 in THF to give after 1-3 hrs 3-substituted cyclohexanones in varying isolated yields (2, R = n-Bu, 84%; R = sec-Bu, 77%; R = tert-Bu, 52%; and R = vinyl, low yield¹⁵). Although conjugate addition of primary, secondary, and tertiary alkyl groups is achieved effectively and economically (in terms of the alkyl group) using tert-butoxy-alkylcuprates 1, the low yield of conjugate vinyl adduct is disappointing.

Substitution of alkyl or acyl halogen by a sec- or tert-alkyl group and conjugate addition of such groups is usually best accomplished using organocopper reagents.^{3,4} Although the easily prepared tert-butoxy-sec- and tert-alkylcuprates 1 described herein are thermally unstable above -50° , at or below -50° they are highly effective even when used in slight excess in converting functionalized acid chlorides selectively into the corresponding sec- and tert-alkylketones, in attaching a sec- and tert-alkyl group specifically at the β -carbon of α,β -unsaturated ketones, and in replacing primary alkyl iodide or bromide by the tert-alkyl group. The favorable stoichiometry and functional group specificity of these new alkoxy-alkylcuprate(I) reagents 1 make them welcome additions to the rapidly expanding collection of synthetically useful organometallic reagents.¹⁶

The chemistry of alkoxy-alkylcuprates(I) is being explored further.¹⁷

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References

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4. G. H. Posner, Org. React., 19, 1 (1972).
5. G. M. Whitesides, W. F. Fischer, Jr., J. San Filippo, Jr., R. W. Bashe, and H. O. House, J. Amer. Chem. Soc., 91, 4871 (1969): "For coupling reactions requiring tert-alkyl-copper(I) reagents, lithium di-tert-alkyl(tri-n-butylphosphine)copper(I) compounds are the only practical choice, despite the problems frequently encountered during work-up procedures" (emphasis added).
6. In most lithium diorganocuprate(I) reactions, only one of the two R groups in the R_2CuLi reagent is utilized effectively (see ref 4).

7. (a) $(RC\equiv C)(alkyl)CuLi$: J. F. Normant and M. Bourgain, Tetrahedron Lett., 1970, 2659 and J. F. Normant, Synthesis, 1972, 63;
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(c) $(norbornyl)(butyl)CuLi$: G. M. Whitesides, J. San Filippo, Jr., E. R. Stedronsky, and C. P. Casey, ibid, 91, 6542 (1969).
8. T. Tsuda, T. Hashimoto and T. Saegusa, J. Amer. Chem. Soc., 94, 658 (1972).
9. Complete details of preparation and reactions of these new alkoxy-alkylcuprate reagents will be reported shortly.
10. For an earlier report on ketone formation from acid chlorides and organocuprates(I), see G. H. Posner, C. E. Whitten, and P. E. McFarland, J. Amer. Chem. Soc., 94, 5106 (1972)
11. Phenoxy-copper species have been shown to convert acid chlorides to phenyl esters: T. Kawaki and H. Hashimoto, Bull. Chem. Soc. Japan, 45, 1499 (1972).
12. Lithium alkyls react rapidly with even hindered ketones at low temperatures; for the low temperature addition of tert-butyllithium to di-tert-butyl ketone see P. D. Bartlett and E. B. Lefferts, J. Amer. Chem. Soc., 77, 2804 (1955).
13. Conversion of acid chlorides to hindered ketones has been reported using tert-butyl-magnesium and tert-butyllithium reagents and cuprous salts as "catalysts".
(a) J. E. Dubois, M. Boussu, and C. Lion, Tetrahedron Lett., 1971, 829;
(b) J. A. MacPhee and J. E. Dubois, ibid, 1972, 467.
14. There is only one reported example of replacement of primary alkyl halogen by a tert-butyl group; that reaction involved a 500% excess of a phosphine complexed lithium di-tert-butylcuprate(I) and a tedious procedure for product isolation (ref 5).
15. Cyclohexenone is recovered in >60% yield.
16. Using our procedure as described in this communication, Dr. Joel Shulman (The Proctor and Gamble Co., Miami Valley Laboratories) has prepared several isopropyl ketones easily and in high yield from the corresponding acid chlorides and lithium tert-butoxy-isopropylcuprate(I).
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