Reduction of a Ketone by Lithium Di-n-butylcuprate

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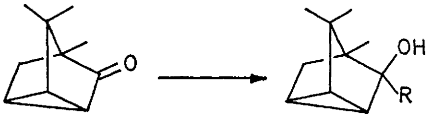
Summary Lithium di-n-butylcuprate reduces pericyclocamphor to the corresponding secondary alcohol, whereas lithium dimethylcuprate gives a tertiary alcohol by addition of methyl to the carbonyl group.

ORGANO-COPPER compounds have been widely investigated in recent years as reagents for many carbon–carbon bond-forming operations.[1] In particular, the conjugate addition of lithium dialkylcuprates to $\alpha\beta$-unsaturated ketones has been studied extensively, although ketones lacking olefinic conjugation have generally been considered unreactive towards these reagents.[1–3] We have found, in contrast, that pericyclocamphor (**1**)[4] does react with lithium dialkylcuprates[5] at 0° and that the reaction course depends markedly on the specific reagent employed.



(1) (2)

Lithium di-n-butylcuprate reduces ketone (**1**) at 0° in 1 h to the secondary alcohol (**2**; R = H)[†][‡][6] in high yield. Hindered ketones often suffer carbonyl reduction on treatment with Grignard reagents,[7] although with the ketone (**1**), Bu^nMgCl gives equal amounts of reduction and addition[†] products; Bu^nLi adds quantitatively (see Table).

Lithium dimethylcuprate, MeMgCl, and MeLi all yield the tertiary alcohol (**2**; R = Me)[†] as the sole product from (**1**) (see Table). At 0°, only the MeLi reaction reaches completion within 1 h; with excess of lithium dimethylcuprate the disappearance of starting material has a half life of many hours at this temperature. Absence of the reduction product (**2**; R = H) in the dimethylcuprate reaction suggests a β-hydrogen-transfer mechanism for reduction of (**1**) by lithium di-n-butylcuprate, although the intermediacy of copper hydride[8] cannot be excluded.

TABLE

Reagent[a]	Product (**2**)[b]
$LiBu^n_2Cu$	R = H
Bu^nMgCl[c]	R = H + R = Bu^n (1:1)
Bu^nLi	R = Bu^n
$LiMe_2Cu$[d]	R = Me
MeMgCl[c]	R = Me
MeLi	R = Me

[a] All reactions were conducted in Et_2O with a several-fold excess of reagent for 1 h at 0°, unless otherwise indicated. [b] Good yields (>70%) were realized in all cases; no other products were detected by g.l.c. [c] Grignard reactions were run at 25° for 1 h; at 0° these reactions did not reach completion within 1 h. [d] After 20 h at 0°, this reaction had still not reached completion.

Clearly, pericyclocamphor (**1**) displays several special structural features; the carbonyl group is strained, hindered, non-enolizable, and conjugated with a cyclopropane ring. The extent to which each of these features affects the reaction with lithium dialkylcuprates is not yet known.

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[†] The combustion analysis, i.r., n.m.r., and mass spectral properties of this compound are all consistent with the structure assigned $Eu(dpm)_3$ induces a relatively large shift in the n.m.r. signal for two of the three methyl groups, while the third methyl signal shifts very little. We believe this observation to be consistent with the *exo*-orientation of the OH group and inconsistent with the *endo*.

[‡] This reduction product is identical to that obtained by treatment of (**1**) with $LiAlH_4$; m.p. 175—177°.

[1] For a review see: J. F. Normant, *Synthesis*, 1972, 63.

[2] C. Jallabert, N. T. Luong Thi, and H. Riviere, *Bull. Soc. chim. France*, 1970, 797.

[3] Apparent intramolecular additions of organo-copper intermediates to saturated ketones have been reported: E. J. Corey and I. Kuwajima, *J. Amer. Chem. Soc.*, 1970, **92**, 395.

[4] Prepared by treatment of αα-dibromocamphor with Et_2Zn in benzene: L. T. Scott and W. D. Cotton, *J. Amer. Chem. Soc.*, in the press.

[5] Lithium dialkylcuprates were prepared as described by E. J. Corey and G. H. Posner, *J. Amer. Chem. Soc.*, 1967, **89**, 3911.

[6] Reduction of (**1**) with Na–EtOH reportedly gives an alcohol, m.p. 174—176°, whereas catalytic hydrogenation over Pt gives a different alcohol, m.p. 181°: M. Lipp, *Chem. Ber.*, 1941, **74**, 6.

[7] M. S. Kharasch and O. Reinmuth, 'Grignard Reactions of Nonmetallic Substances,' Prentice-Hall, New York, 1954, pp. 147–166.

[8] G. M. Whitesides, E. R. Stedronsky, C. P. Casey, and J. San Filippo, jun., *J. Amer. Chem. Soc.* 1970, **92**, 1426.