combined, washed one time with saturated $Na_2S_2O_3$, dried ($MgSO_4$), and evaporated to give 0.12 g (87%) of 4-hydroxy-3-methyl-4-phenyl-2-butanone (**8**) as a nearly colorless oil: IR (thin film) 3450, 1700, 1450, 1360, 1180, 1020, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.07 (3 H, d, $J = 6$), 2.05 (3 H, s), 2.8 (1 H, dq, $J = 6$, 4), 3.4 (1 H, br s), 4.93 (1 H, d, $J = 4$), 7.18 (5 H, s). An analytical sample was prepared by chromatography on silica gel (50% ether/hexanes).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.03; H, 7.89.

1-Hydroxy-2-methyl-1-phenyl-3-pentanone (2). The foregoing procedure was repeated, using ethyllithium instead of methyllithium. Aldol **2** was obtained in 65% yield as a colorless oil after chromatography: IR (thin film) 3450, 1700, 1450, 1010, 980, 770, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.97 (3 H, t, $J = 7$), 1.05 (3 H, d, $J = 7$), 2.4 (2 H, dq), 2.9 (1 H, dq, $J = 4$, 7), 4.93 (1 H, d, $J = 4$), 7.22 (5 H, s).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.14; H, 8.38.

1-Hydroxy-2-methyl-1-phenyl-3-heptanone (9). The foregoing procedure was employed using *n*-butyllithium. Aldol **9** was obtained in 88% yield as a colorless oil after chromatography: IR (thin film) 3450, 1700, 1450, 1020, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (3 H, d, $J = 7$), 2.4 (2 H, m), 2.9 (1 H, dq, $J = 4$, 7), 4.90 (1 H, d, $J = 4$), 7.23 (5 H, s).

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.55; H, 9.16.

Acknowledgment. This reasearch was supported by a grant from the United States Public Health Service (Grant AI-15027).

Registry No. 2, 71699-15-5; **4**, 72507-50-7; **6**, 71699-17-7; **7** (isomer 1), 75600-08-7; **7** (isomer 2), 75658-53-6; **8**, 75600-09-8; **9**, 75600-10-1; benzaldehyde, 100-52-7; dihydropyran, 110-87-2; *erythro*-2,5-dihydroxy-2,4-dimethyl-1-phenyl-3-pentanone, 72658-44-7.

Preparation of Thermally Stable and Soluble Mesitylcopper(I) and Its Application in Organic Synthesis

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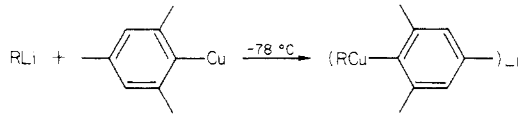
Received June 11, 1980

Copper(I) *tert*-butoxide, *t*-BuOCu,[1] which is the first example of thermally stable copper(I) alkoxide has been frequently used in organic synthesis as a metalation reagent[2] and as a "holding group" in a mixed lithium cuprate reagent (R_TCuOBu-*t*)Li.[3] However, in the metalation reaction, the liberation of *tert*-butyl alcohol from *t*-BuOCu puts a limitation to the variety of active-hydrogen compounds to be metalated. Moreover, the relatively low solubility of *t*-BuOCu in organic solvents is inconvenient for its use. Here we report the preparation of thermally stable and soluble mesitylcopper(I) (**1**) and its utilization in organic synthesis as an efficient metalation reagent and as a useful "holding group" in the mixed lithium cuprate reagents.

1 was prepared as a pale yellow solid by the reaction of mesitylmagnesium bromide with copper(I) chloride. **1** is thermally stable up to 100 °C. **1** reacted with allyl bromide in hexamethylphosphoric triamide (HMPA) at 90 °C to give allylmesitylene almost quantitatively. At 120 °C, **1** partly decomposed in HMPA to produce bimesityl. Ordinary organocoppers(I) including alkylcoppers(I) are insoluble in common organic solvents due to their associations.[4] **1** is highly soluble in various organic solvents such as benzene, ether, tetrahydrofuran (THF), and HMPA and is partly soluble in *n*-pentane and *n*-hexane. Recently an *o*-methyl-substituted phenylcopper(I) has been shown to have a high thermal stability and a low degree of association.[5]

On metalation of active-hydrogen compounds, **1** releases mesitylene which is inert and easily removable. On the basis of this property together with its high solubility and stability, **1** functions as an efficient metalation reagent to produce various types of copper(I) complexes without the concurrent production of salts. The metalation reactivity of **1** is higher than that of *t*-BuOCu. **1** easily metalates primary and secondary amines whereas *t*-BuOCu cannot metalate these amines. For example, evaporation of a THF solution of **1** and diethylamine in vacuo after an overnight reaction at ambient temperature gave copper(I) diethylamide. To our knowledge, this is the first example of isolation of a copper(I) amide derived from an ordinary amine.[6] **1** also metalated *tert*-amyl mercaptan and *tert*-butyl alcohol to produce copper(I) *tert*-amylmercaptide and *tert*-butoxide, respectively.

Several mixed lithium cuprate reagents (R_TCuR)Li having a nontransferable ligand R (a holding group) have been developed for the purpose of saving a valuable transferring group.[3,7] Recently Corey et al. have reported the use of soluble $MeOC(CH_3)_2C{\equiv}CCu$ as a precursor for mixed cuprates.[8] **1** was found to be effective for the formation of a soluble mixed cuprate reagent (**2**) in which the mesityl group acts as a nontransferable holding group. **2a** and **2b** effected a selective conjugate addition of the R group to cyclohexenone (Table I). In **2c**, however, both mesityl and *tert*-butyl groups were transferred at a comparable ratio. The conjugate addition of organocuprate reagents to α,β-unsaturated aldehydes has not been widely studied.[9] **2a** caused the conjugate addition to *trans*-2-hexenal, transferring its *n*-butyl group selectively (Table I).



1

2a, R = *n*-Bu
b, R = *sec*-Bu
c, R = *t*-Bu

Recently several complex copper hydride reagents such as LiCuRH,[10] $LiAl(OCH_3)_3H$–CuI,[11] and Li_2CuH_3[12] have

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[1] Tsuda, T.; Hashimoto, T.; Saegusa, T. *J. Am. Chem. Soc.* **1972**, *94*, 658.

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[6] Various copper(I) amides derived from ordinary amines including ammonia and aniline have been prepared by the metalation using **1**, which will be published elsewhere together with their characterizations.

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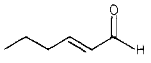
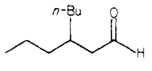
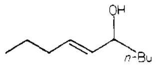
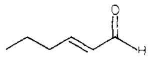
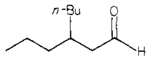
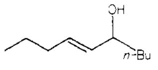
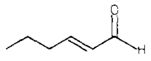
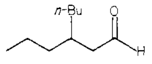
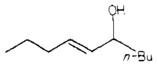
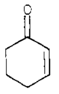
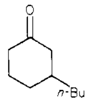
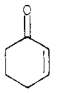
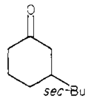
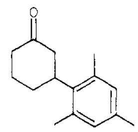
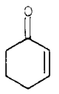
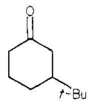
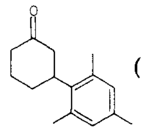
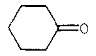
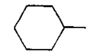
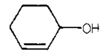
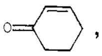
Table I. Reactions of Lithium Organocuprate Reagents with α,β-Unsaturated Carbonyl Compounds^a

cuprate reagents	α,β-unsaturated carbonyl compounds	products^b (yields, %)^c	
2a		 (64)	 (2)
2n-BuLi-CuCl		 (8)	 (15)
2n-BuLi-CuI		 (42)	 (7)
2a		 (90, 79^d)	
2b		 (85)	 (trace)
2c		 (26)	 (19)

^{a} Cuprate reagent ca. 2 mmol, α,β-unsaturated carbonyl compound/cuprate reagent = 1.2, temp −78 °C, time 3 h, THF solvent, 10 mL. ^{b} Satisfactory infrared, proton magnetic resonance, and mass spectral data were obtained for each product. ^{c} Yields were determined by GLC and were based on copper. ^{d} An isolated yield in the reaction using 5.90 mmol of 2a.

Table II. Conjugate Reductions of Cyclohexenone by the Combination of 1 and $LiAlH_4$^{a}

			product yields, %^{c}			recovered
1/$LiAlH_4$	solvent	time, min				, %
0	THF	180	7	12	57	0
1	THF	180	43	22	13	0
1^b	THF	180	36	6	9	0
0	THF-HMPA	180	23	8	4	0
1	THF-HMPA	180	77	7	0	0
0.1	THF-HMPA	180	72 (65^d)	5	0	0
0	THF-HMPA	5	21	9	14	10
0.1	THF-HMPA	5	69	8	1	0

^{a} $LiAlH_4$ ca. 1-2 mmol, 2-cyclohexenone/$LiAlH_4$ = 1.1, solvent, 5 mL (THF-HMPA solvent consists of 4 mL of THF and 1 mL of HMPA), temp −78 °C. ^{b} An equimolar mixture of $LiAlH_4$ and 1 in THF was added to cyclohexenone. Unless otherwise noted, cyclohexenone was added to the reducing reagent. ^{c} Yields were based on the LiH moiety in $LiAlH_4$. Products were identified by the agreement of their infrared and proton magnetic resonance spectra with those of the authentic samples. ^{d} An isolated yield in the reaction using 6.22 mmol of $LiAlH_4$.

been introduced for conjugate reduction of enones. However, most of them are not easily prepared and must be used in excess of the substrate. We found that a reagent produced by an equimolar reaction of 1 and $LiAlH_4$ achieved the conjugate reduction of cyclohexenone (Table II). The reduction in THF was not highly regioselective. However, addition of HMPA as a cosolvent to THF (THF/HMPA, 4/1) strikingly improved the regioselectivity of the 1,4-reduction. Interestingly, 1 even catalyzed the rapid 1,4-reduction of cyclohexenone by $LiAlH_4$. Mesityl oxide and *trans*-4-phenyl-3-buten-2-one also underwent the efficient conjugate reduction catalyzed by 1. Thus, the combination of 1 and $LiAlH_4$ provides a convenient method for the conjugate reduction of enones.[13]

Experimental Section

All operations described below were carried out under nitrogen.

Preparation of Mesitylcopper(I) (1). The reaction mixture resulting from the addition of 100 mL of a 1.0 M THF solution of mesitylmagnesium bromide (100 mmol) to a suspension of CuCl (10.9 g, 110 mmol) in 100 mL of THF at −20 °C was allowed to react overnight at ambient temperature under stirring. The filtrate obtained after the addition of 50 mL of dioxane to complete the precipitation of MgBrCl was evaporated under reduced pressure to produce a solid residue. Dissolution of this solid in 50 mL of benzene, filtration of a small amount of insoluble matters, and evaporation of the filtrate in vacuo at ambient temperature gave a pale yellow solid of 1 (13.7 g, 75 mmol): Cu content by iodometry 34.0% (calcd 34.8%); mesitylene formation by acetolysis 98%; NMR (C_6D_6) δ 6.54 (phenyl protons, m, 2 H), 2.80 (*o*-methyl protons, s, 6 H), 1.90 (*p*-methyl protons, s, 3 H); IR (Nujol) 1592 (C=C), 845 cm^{-1} (C=CH).

Metalation of Diethylamine. Diethylamine (0.64 mL, 6.20 mmol) was added at ambient temperature to 5 mL of THF containing 1 (0.227 g, 1.24 mmol). The mixture was stirred overnight at ambient temperature. GLC analysis of the resulting homogeneous solution showed the formation of mesitylene in 92% yield. The reaction mixture was evaporated in vacuo to produce a pale yellow solid of copper(I) diethylamide, which was washed with *n*-hexane (10 mL) and was dried in vacuo: Cu content by iodometry 47.0% (calcd 46.8%); NMR (C_6D_6, $P(OMe)_3$) δ 2.45 (q, 4 H), 1.00 (t, 6 H).

Representative Cuprate Reaction Using Mesitylcopper(I) (1). To 10 mL of a THF solution of 1 (0.366 g, 2.00 mmol) at −78 °C was added 1.61 mL of a 1.24 M *n*-hexane solution of

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[13] On the basis of the results of the conjugate reduction of enones by the system 1-$LiAlH_4$, other copper(I) salts such as CuCl, CuI, and *t*-BuOCu instead of 1 have been examined and found to be similarly effective; this will be reported elsewhere.

n-butyllithium (2.00 mmol). The resulting homogeneous solution was stirred for 30 min at −78 °C, and then *trans*-2-hexenal (0.26 mL, 2.20 mmol) was added. After being stirred for 3 h at −78 °C, the reaction mixture was treated with 5 mL of NH_4Cl-saturated aqueous solution. The organic layer was analyzed by GLC on a 20% Silicone DC 550 on Celite 545 column, using tetralin as an internal standard.

Conjugate Reduction of Cyclohexenone by $LiAlH_4$–Mesitylcopper(I) (1). To a suspension of $LiAlH_4$ (0.0378 g, 0.996 mmol) in 3 mL of THF at −78 °C was added 1 (0.0182 g, 0.0996 mmol) dissolved in a mixed solvent of 1 mL of THF and 1 mL of HMPA. The resulting reaction mixture was stirred for 30 min at −78 °C, and cyclohexenone (0.11 mL, 1.10 mmol) was added. After being stirred for 3 h at −78 °C, the reaction mixture was treated with 3 mL of NH_4Cl-saturated aqueous solution. The organic layer was analyzed by GLC on a 20% Silicone DC 550 on Celite 545 column and on a 20% PEG 20M on Celite 545 column, using tetralin as an internal standard.

Registry No. 1, 75732-01-3; butyllithium, 109-72-8; *sec*-butyllithium, 598-30-1; *tert*-butyllithium, 594-19-4; mesitylmagnesium bromide, 2633-66-1; mesitylene, 108-67-8; copper(I) diethylamide, 71426-07-8; *trans*-2-hexenal, 6728-26-3; 2-cyclohexenone, 930-68-7; 3-propylheptanal, 75732-02-4; 6-decen-5-ol, 75732-03-5; 3-butylcyclohexanone, 39178-69-3; 3-*sec*-butylcyclohexanone, 37172-15-9; 3-*tert*-butylcyclohexanone, 936-99-2; 3-mesitylcyclohexanone, 75732-04-6; cyclohexanone, 108-94-1; cyclohexanol, 108-93-0; 2-cyclohexen-1-ol, 822-67-3; CuCl, 7758-89-6.

The First Spectral Confirmation for the Structures of Anhydro Dimers of *o*-Hydroxybenzaldehydes

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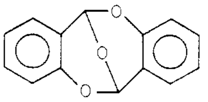
Received June 6, 1980

The anhydro dimers of *o*-hydroxybenzaldehydes have been known for over a century. The parent member of the series, "disalicylaldehyde", was first reported by Ettling[1] in 1845 and later by Cahours[2] in 1851 and by Perkin[3] in 1868. By now there are a dozen or more examples[4] of these anhydro dimers, which have been characterized by melting point, elemental analysis, and their tendency to revert to hydroxy aldehyde or a derivative thereof on acidolysis. It is assumed all possess the trioxabicyclo[3.3.1]nonane structure, by analogy with that originally proposed for



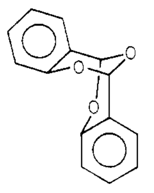
disalicylaldehyde in a publication by Adams, Fogler, and Kreger[5] in 1922. Yet to date there is apparently no information about their spectral properties. We have prepared four of the dimers 1–4 and report herein the results of measurement of their IR, UV, ^1H NMR, ^{13}C NMR, and mass spectra.

Table I. UV Spectral Data of Anhydro Dimers 1-4 ($CHCl_3$)

compd	λ (log ε), nm	UV of *o*-hydroxybenzaldehyde precursor
1	274.3 (3.51), 283.1 (3.44)	211.9 (4.12), 254.7 (3.96), 326.0 (3.49)
2	241.9 (3.86), 292.5 (3.64), 301.2 (3.62)	250 (3.6),[a] 290 (2.5), 342 (3.27)
3	239.6 (4.63), 266.4 (3.97), 277.5 (4.03), 290.2 (3.96), 315.5 (3.56), 330.5 (3.67)	225 (4.8),[b] 330 (3.9), 370 (3.7)
4	295.7 (4.29)	230 (3.92),[c] 258 (3.32), 310 (4.00)

[a] (EtOH) N. A. Valyashko and N. N. Valyashko, *Zh. Obsch. Khim.*, **18**, 1113 (1948). [b] (Isooctane) N. Melchior, *J. Am. Chem. Soc.*, **71**, 3647 (1949). [c] (EtOH) I. A. Kaye, R. S. Matthews, and A. A. Scala, *J. Chem. Soc.*, 2816 (1964).

The dimers, being head-to-tail bis acetals, have been prepared previously under a variety of conditions with dehydrating agents and acid catalysts. **1–3** were obtained by procedures already described; in the case of **4**, we were able to carry out the bimolecular acetalization of 5-nitrosalicylaldehyde under conditions[4b] which had not previously been successful. The anhydro dimer had been prepared earlier by nitration[6] of **1**. The fact that **4** has now been prepared by two independent routes serves to confirm its structure; in particular, it indicates the position of nitration in both rings to be para to the phenolic oxygen.



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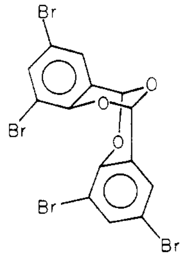
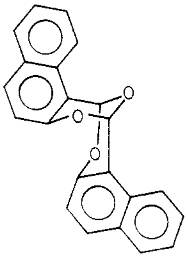
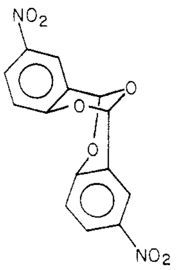


2



3



4

All of the spectral properties of **1–4** are consistent with the assigned structures. The IR spectra are devoid of OH and carbonyl stretching bands. The UV spectra of all four, collected in Table I, differ significantly from their precursors, the *o*-hydroxybenzaldehydes. A suitable model compound for **1** would be *o*-methoxybenzaldehyde acetal (**5**), which has apparently not been reported as a pure compound. It was shown by Melchior,[7] however, that the UV spectrum of *o*-methoxybenzaldehyde in acidified

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[1] Ettling, *Justus Liebigs Ann. Chem.*, **53**, 77 (1845).

[2] A. Cahours, *Justus Liebigs Ann. Chem.*, **78**, 225 (1851).

[3] W. H. Perkin, *Justus Liebigs Ann. Chem.*, **145**, 295 (1868).

[4] In addition to those specifically described in this paper, others have been reported in the following: (a) E. Rupp and M. Meyer, *Arch. Pharm.*, **253**, 379–383 (1915); (b) H. Fiedler, *ibid.*, **297**, 226 (1964); (c) E. Profft and W. Krause, *ibid.*, **298**, 148 (1965).

[5] R. Adams, M. F. Fogler, and C. W. Kreger, *J. Am. Chem. Soc.*, **44**, 1126 (1922).

[6] W. P. Bradley and F. B. Dains, *Am. Chem. J.*, **14**, 293 (1892).

[7] N. Melchior, *J. Am. Chem. Soc.*, **71**, 3651 (1949).

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