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Preparation of Aldehydes from Acid Chlorides Using Copper Tetrahydroborate Complexes[1]

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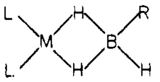
It has been proposed previously that covalent, transition-metal tetrahydroborate complexes constitute a new class of stoichiometric reducing agents for organic synthesis. Thus, tetrahydroborate complexes of copper having phosphine and phosphite ligands are prepared from sodium borohydride, cuprous chloride, and the appropriate ligand in chloroform–ethanol solution. It is demonstrated that these compounds reduce acid chlorides to aldehydes in acetone containing excess triphenylphosphine under mild conditions and in high yields. The reactivity for the complexes L_2CuBH_4 increases in the series $Ph_3P < (i\text{-}C_3H_7O)_3P < (CH_3O)_3P$, parallel to the increasing electron-donor ability of the ligands L.

The chemistry of transition-metal tetrahydroborate complexes has been the subject of numerous investigations over the past several years, focused primarily upon the unusual bonding and fluxional characteristics such compounds possess.[2] The development of the reaction chemistry of these complexes has lagged far behind, although the catalytic properties of the metal ions in such compounds have been examined. Recently, we proposed that covalent metal–borohydride complexes **1**, like their ionic congeners, should possess a reducing capability which might be readily varied according to the nature of the ligands, L and R, or of the metal ion, M.[3]



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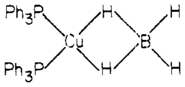
To date, only two such complexes have been studied. Bis(triphenylphosphine)tetrahydroboratocopper(I) (**2**) reduces carboxylic acid chlorides to aldehydes under mild conditions,[3-5] and bis(cyclopentadienyl)chlorotetrahydroboratozirconium(IV) (**3**) functions as a benzene-soluble analogue of sodium borohydride, reducing aldehydes and ketones to the corresponding alcohols in the presence of other functional groups.[6]



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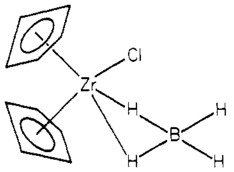

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This paper summarizes the work on the copper complex **2** as well as its phosphite-substituted derivatives.[7]

Results and Discussion

Bis(triphenylphosphine)tetrahydroboratocopper(I) [$(Ph_3P)_2CuBH_4$, **2**] is readily prepared from cuprous chloride, triphenylphosphine, and sodium borohydride in chloroform–ethanol solution. The reaction may be scaled conveniently to produce up to 0.3 mol of reagent which, being inert to both oxygen and water, has an indefinite shelf life. The reagent is unreactive toward all common functional groups with the exception of acid halides and iminium salts.[5]

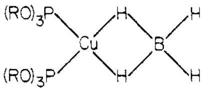
Reduction of acid chlorides to aldehydes occurs smoothly at 25 °C within 1 h and yields are usually good to excellent (Table I). The ideal solvent is acetone in which **2** is only slightly soluble. In most cases, 2 additional equiv of triphenylphosphine are added, one to bind to the copper byproduct and the other to trap liberated BH_3 (eq 1).

$$(Ph_3P)_2CuBH_4 + RCOCl \xrightarrow[\text{acetone, 25 °C}]{2Ph_3P} (Ph_3P)_3CuCl + RCHO + Ph_3PBH_3 \quad (1)$$

Since $(Ph_2P)_3CuCl$ is only sparingly soluble in acetone, it is easily removed by filtration and can be recycled to **2**.[5] If excess triphenylphosphine is not supplied, the inorganic product is $[(Ph_3P)_2CuCl]_2$ while the borane is removed presumably by reaction with the solvent.

We established earlier that the reagent supplied only a single hydride ion during the reduction.[3] The molecular weight of 603 for $(Ph_3P)_2CuBH_4$ therefore requires that large quantities are necessary for preparative-scale reactions. However, because of its ease of manipulation, $(Ph_3P)_2CuBH_4$ is one of the more useful reagents for carrying out the transformation: acid chloride → aldehyde.[8] The workup for a liquid product comprises a simple distillation, while for a solid, excess triphenylphosphine is removed by stirring a chloroform solution of the crude product with cuprous chloride, and the product is recrystallized.

In order to circumvent the molecular-weight problem and to examine the effect of different ligands on the reactivity of **2**, we have prepared the trimethyl and triisopropyl phosphite analogues **4**. The synthesis of these



4a, R = CH_3
b, R = $CH(CH_3)_2$

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[1] Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the University Research Council of UNC for support of this research.

[2] T. J. Marks and J. R. Kolb, *Chem. Rev.*, **77**, 99 (1970).

[3] T. N. Sorrell and R. J. Spillane, *Tetrahedron Lett.*, 2473 (1978).

[4] G. W. J. Fleet, C. J. Fuller, and P. J. C. Harding, *Tetrahedron Lett.*, 1437 (1978).

[5] G. W. J. Fleet and P. J. C. Harding, *Tetrahedron Lett.*, 975 (1979).

[6] T. N. Sorrell, *Tetrahedron Lett.*, 4985 (1978).

[7] Abbreviations used in this paper are: Ph, phenyl; 2,4-DNP, 2,4-dinitrophenylhydrazine; Ⓟ-H, cross-linked polystyrene; THF, tetrahydrofuran.

[8] For large-scale reductions, the Rosenmund reaction is still the method of choice. See C. A. Buchler and D. E. Pearson, "Survey of Organic Syntheses", Vol. 1, Wiley, New York, 1970, p 571. Other reagents include $LiAlH(O\text{-}t\text{-}C_4H_9)_3$ (H. C. Brown and R. F. McFarlin, *J. Am. Chem. Soc.*, **78**, 252 (1956), $Na_2Fe(CO)_4$ (W. O. Siegl and J. P. Collman, *ibid.*, **94**, 2516 (1972), and $HFe(CO)_4^-$ (T. E. Cole and R. Pettit, *Tetrahedron Lett.*, 781 (1977)).

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Table I. **Preparation of Aldehydes from Acid Chlorides with Tetrahydroboratocopper(I) Complexes**[a]

	% yield[b]		
aldehyde	$(Ph_3P)_2CuBH_4$	$[(CH_3O)_3P]_2CuBH_4$[c]	$[(i\text{-}C_3H_7O)_3P]_2CuBH_4$[c]
nonanal	76 (90)	72	77
cinnamaldehyde	77 (82)	(11)	(40)
benzaldehyde	83 (90)	82 (100)	70 (81)
4-chlorobenzaldehyde	80 (100)	53 (56)	74 (76)
4-nitrobenzaldehyde	57 (63)	(0)[d]	(17)
furfural	78 (82)	(50)	56 (72)

[a] Additional examples may be found in ref 3–5. [b] Isolated yields of pure aldehydes; numbers in parentheses refer to GC yields using an internal standard. [c] Isolated yields are for the 2,4-DNP derivatives. [d] 4-Nitrobenzyl alcohol observed.

compounds, isolated as quasistable oils, followed the method of Bommer and Morse[9] in which a chloroform solution of cuprous chloride and the trialkyl phosphite is treated with an ethanolic solution of sodium borohydride. We found it convenient to store complex **4** as a cold (−20 °C) solution in acetone and to remove aliquots for the reactions with organic substrates.

The reactions of **4a** and **4b** with carboxylic acid chlorides proceed smoothly to the aldehyde stage within 2 and 15 min, respectively. Acetone is used as the solvent again, and 2 equiv of triphenylphosphine are added. Yields are given in Table I. The use of the phosphite-ligated reagents **4** is inconvenient in terms of the workup since it is extremely difficult to separate excess ligand from the organic product; therefore, aldehydes prepared by this method are isolated as their 2,4-DNP derivatives.

Unlike the phosphine complex **2**, the trimethyl phosphite derivative is capable of reducing aldehydes to the corresponding alcohols.[10] However, that reaction is much slower, requiring at least 24 h to proceed to completion. Therefore, using 1 equiv of reagent, one is able to stop the reaction at the aldehyde stage.[11] An exception is *p*-nitrobenzoyl chloride which reacts apparently via an electron transfer from the copper, and *p*-nitrobenzyl alcohol is the only observable product under all conditions.

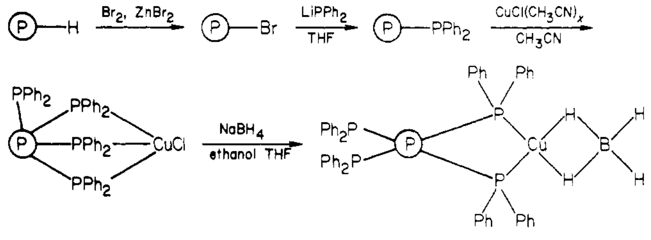
The increased reactivity of **4a** compared to **2** is best rationalized on the basis of the ligand strengths of trimethyl phosphite vs. triphenylphosphine. The former is a better π donor and a poorer σ acceptor than is Ph_3P,[12] leading to increased electron density at the metal and hence greater reactivity of the B–H bond. This is analogous to the reactivity of the simple borohydride derivatives BH_3CN^- and $BH(C_2H_5)_3^-$ in which an electron-withdrawing group decreases the reactivity of the hydride while electron-donating groups have the opposite effect.[13]

Finally, in an effort to provide an easier workup for reaction 1, we attached **2** to an insoluble support as shown in Scheme I. The yield for the reduction of benzoyl chloride to benzaldehyde by **5** was slightly lower than that obtained in solution; moreover, the quantity of reagent necessary to effect the transformation makes its use inconvenient on a preparative scale.

Conclusions

We have examined the reactivity of a series of copper(I) tetrahydroborate complexes having phosphite or phosphine ligands for the reduction of acid chlorides to aldehydes. The results verify our original hypothesis, namely, that changing the ligand of covalent tetrahydroborate complexes results in a change in the reactivity of the boron hydride moiety. Unfortunately, for this case, the range of usable ligands is very narrow due to the instability of the copper complex toward reduction to the metal, so the observed differences in reactivity are modest.

Scheme I



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Experimental Section

General Procedures. Unless otherwise stated, all reagents and solvents were obtained commercially and used without further purification. Cuprous chloride was synthesized by the literature method,[14] using only a fraction of the solvent so that large quantities could be prepared. Acetonitrile was distilled from CaH_2 and THF was distilled from sodium–benzophenone, both under a nitrogen atmosphere.

Gas chromatographic analysis of the reaction mixtures was performed by using a Hewlett-Packard Model 5380A GC with a thermal-conductivity detector. The samples were calibrated with dodecane as an internal standard and the separation was carried out with a 6-ft column of 10% OV-101 on Chromosorb W. All isolated compounds had NMR spectra identical with those of commercial samples. Melting points were obtained on a Fisher-Johns apparatus and are corrected. Analyses were obtained from Galbraith Laboratories, Inc., and from Integral Microanalytic Laboratories, Inc., in Raleigh, NC.

Bis(triphenylphosphine)tetrahydroboratocopper(I) (2). The previously reported[5] large-scale preparation of this material was not consistently reproducible in our hands; therefore, we present this alternative method. To a stirred solution of 216 g (0.82 mol) of triphenylphosphine dissolved in 1.5 L of chloroform was added 40 g (0.4 mol) of cuprous chloride over a period of 5 min. After the solution had become homogeneous, a suspension of 15.2 g (0.4 mol) of sodium borohydride in 150 mL of 95% ethanol was added slowly. The resulting mixture was stirred for 15 min and poured into 300 mL of water, and the organic layer separated. The resulting solution was washed twice with 250 mL of water, dried over $MgSO_4$, filtered, and treated with 2 L of diethyl ether. The precipitate (mp 158–162 °C) was collected and dissolved in 1.5 L of chloroform containing 50 g of triphenylphosphine. A slurry of 12.8 g of $NaBH_4$ in 150 mL of 95% ethanol was added, the mixture was stirred for 20 min, and an additional 450 mL of 95% ethanol was added. The filtered solution was evaporated with a rotary evaporator until crystals began to form. The precipitate was collected, washed with ether, and allowed

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(9) J. C. Bommer and K. W. Morse, *Inorg. Chem.*, 17, 3708 (1978).

(10) The triphenylphosphine reagent **2** is capable of reducing the acid chloride to the alcohol if a solvent other than acetone is used. For example, benzoyl chloride is reduced partially to benzyl alcohol in chloroform solution, although benzaldehyde itself is apparently inert.

(11) The reduction of aldehydes to alcohols can be carried out with acetone as the solvent, raising the possibility that **4** will selectively reduce aldehydes in the presence of ketones. Work in this area is continuing.

(12) W. A. G. Graham, *Inorg. Chem.*, 7, 315 (1968).

(13) H. C. Brown and S. Krishnamurthy, *J. Am. Chem. Soc.*, **95**, 1669 (1973).

(14) R. N. Keller and H. D. Wycoff, *Inorg. Synth.*, 2, 1 (1946).

to air dry to yield 200 g (83%), mp 173–175 °C (lit.[15] mp 177 °C).

Preparation of Aldehydes Using 2. (1) Liquid Product. A solution of 3.52 g of furfuryl chloride (27 mmol) in 40 mL of acetone was added to a suspension of 20 g (33 mmol) of **2** and 15.2 g (60 mmol) of triphenylphosphine in 100 mL of acetone. After 1 h, the solution was filtered, and the filter cake was washed with three 50-mL portions of ether. The combined filtrates were evaporated to dryness at reduced pressure. The residue was dissolved in ether, and the solution was filtered and then evaporated to give an oil. Evaporation distillation at reduced pressure gave 2.06 g (78%) of furfural.

(2) Solid Product. To a stirred solution of 4.6 g (25 mmol) of *p*-nitrobenzoyl chloride and 13.0 g (50 mmol) of triphenylphosphine in 50 mL of acetone was added 15.5 g (26 mmol) of **2** in one portion. After 1 h, the solution was filtered, and the filter cake was washed with three 50-mL portions of ether. The combined filtrates were evaporated to dryness, and the residue was dissolved in 40 mL of chloroform. The resulting solution was treated with 6 g of commercial cuprous chloride, allowed to stir for 1 h, and filtered. The solvent was evaporated at reduced pressure, and the residue was crystallized from aqueous ethanol to give 2.14 g (57%) of *p*-nitrobenzaldehyde.

Bis(trimethyl phosphite)tetrahydroboratocopper(I) (4a). To a stirred solution of 25 mL of trimethyl phosphite and 5 g (50 mmol) of CuCl in 250 mL of chloroform was added dropwise a solution of 2.47 g (65 mmol) of $NaBH_4$ in 175 mL of absolute ethanol. The resulting solution was stirred for 15 min, filtered, and evaporated at reduced pressure to give a colorless oil. The oil was dissolved in a mixture of 25 mL of methylene chloride and 175 mL of pentane, and the resulting solution was filtered and cooled to −78 °C. The supernatant was decanted from the oil and the procedure repeated. The oil was placed under high vacuum until it just began to darken, and then it was dissolved in acetone and stored at −20 °C or used immediately. The solution is stable for 1–2 weeks.

Bis(triisopropyl phosphite)tetrahydroboratocopper(I) (4b). The same procedure described for the trimethyl phosphite complex was followed except that the product did not oil from solution at −78 °C. Thus, the solvent was evaporated and the oil placed under high vacuum until it just began to darken.

Preparation of Aldehydes Using 4a and 4b. A solution of 0.33 g (2.35 mmol) of benzoyl chloride and 0.6 g (2.3 mmol) of triphenylphosphine in 15 mL of acetone was treated with 12.5 mL of 0.2 M **4a** in acetone. The solution was stirred for 15 min and evaporated to dryness. The residue was dissolved in methanol and the resulting solution filtered, concentrated, and treated with 2,4-dinitrophenylhydrazine reagent.[16] The 2,4-DNP derivative was filtered and then crystallized from aqueous ethanol to yield 0.547 g (83%) of benzaldehyde 2,4-dinitrophenylhydrazone, mp 235–237 °C (lit.[17] mp 237 °C).

Polymeric Bis(phosphine)tetrahydroboratocopper(I) (5). Polystyryldiphenylphosphine was prepared by the method of Regen.[18] Anal. Found: P, 7.27 (43% ring substitution).

Polystyryldiphenylphosphine (10 g) was added to 75 mL of dry tetrahydrofuran under a nitrogen atmosphere and allowed to swell. To this slurry was added 0.635 g (6.35 mmol) of CuCl in 20 mL of dry, degassed acetonitrile. After being stirred under N_2 for 48 h, the suspension was filtered under a nitrogen atmosphere, and the resin was washed with degassed THF, 1:1 THF–CH_3CN, and ether and then dried under vacuum. Anal. Found: P, 6.94; Cu, 3.68.

The above polymer (10.5 g) was suspended in 50 mL of chloroform and allowed to swell. A solution of 0.46 g of sodium borohydride in 50 mL of absolute ethanol was added dropwise and the slurry allowed to stir for 36 h. The resin was filtered, washed with $CHCl_3$, 2:1 $CHCl_3$–ethanol, 1:1 $CHCl_3$–ethanol, and ether. Anal. Found: B, 0.36.

Reduction of Benzoyl Chloride by 5. A solution of 141 mg (1.07 mmol) of benzoyl chloride in 7 mL of acetone was added to 2.4 g of polymeric reagent **5** in 15 mL of THF. After 90 min, GC analysis using an internal standard indicated a 73% yield of benzaldehyde.

Registry No. Nonanoyl chloride, 764-85-2; cinnamoyl chloride, 102-92-1; benzoyl chloride, 98-88-4; 4-chlorobenzoyl chloride, 122-01-0; 4-nitrobenzoyl chloride, 122-04-3; furfuryl chloride, 527-69-5; nonanal, 124-19-6; cinnamaldehyde, 104-55-2; benzaldehyde, 100-52-7; 4-chlorobenzaldehyde, 104-88-1; 4-nitrobenzaldehyde, 555-16-8; furfural, 98-01-1; $(Ph_3P)_2CuBH_4$, 16903-61-0; $[(CH_3O)_3P]_2CuBH_4$, 67784-66-1; $[(i\text{-}C_3H_7O)_3P]_2CuBH_4$, 74113-18-1.

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(15) J. M. Davidson, *Chem. Ind. (London)*, 2021 (1964).

(16) D. J. Pasto and C. R. Johnson, "Organic Structure Determination", Prentice-Hall, Englewood Cliffs, NJ, 1969, p 383.

(17) A. Vogel, "A Textbook of Practical Organic Chemistry", Longman, London, 1978, p 1192.

(18) S. L. Regen and D. P. Lee, *J. Org. Chem.*, **40**, 1669 (1975).

Indenone Chemistry. 4.[1] Synthesis of Substituted 1-Naphthalenols and 8-Oxoindeno[1,2-*c*]pyrroles: Mechanism of an Indenone–Naphthalenol Rearrangement

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Treatment of 2,3-bis(bromomethyl)-6-methoxy-1-indenone (**1**) with various nucleophiles constitutes a one-step synthesis of 2,4-disubstituted 1-naphthalenols **3**. The mechanism of this reaction has been explored. This study reveals the intermediacy of 3-(bromomethyl)-6-methoxy-2-methylene-1-indanones of type **7**, which are thought to be formed by a S_N2' substitution on the allylic bromide system of **1**. A second nucleophilic attack on **7** leads to cycloprop[*a*]inden-6-ones **9** via a homo S_N2' substitution. The latter rearrange spontaneously into the 1-naphthalenols **3**. With carefully controlled reaction conditions an intermediate of type **7** could be isolated; it has been used in separate experiments with other nucleophiles. Depending on the nucleophile, this leads either to naphthalenols **3** or to 8-oxoindeno[1,2-*c*]pyrrolidines **5**.

In order to synthesize heterocyclic compounds incorporating the indenone system, we tried to condense secondary amines with the indanone **2**, which had been prepared from the indenone **1** according to an earlier de-

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