

CONVENIENT SYNTHESIS OF BIS(TRIPHENYLPHOSPHINE) COPPER(I) TETRAHYDROBORATE AND REDUCTION OF ACID CHLORIDES TO ALDEHYDES

G.W.J. Fleet, and P.J.C. Harding

Dyson Perrins Laboratory, Oxford University,
South Parks Road, Oxford, UK

There is considerable interest in the application of transition metal hydrides in selective reduction. Reagents derived from treatment of halides of titanium¹, other first row transition elements², and zirconium³ with lithium aluminum hydride have been studied in the reduction of epoxides, alkenes, alkynes and alkyl halides. Examples of the use of transition metal tetrahydroborates in organic synthesis are, however, rare: a lanthanide tetrahydroborate has been implicated in the reduction of α, β -unsaturated ketones to allylic alcohols⁴ and bis(cyclopentadienyl)chlorotetrahydroborate zirconium (IV) has been shown to reduce aldehydes and ketones.⁵ Bis(triphenylphosphine) copper(I) tetrahydroborate, $(\text{Ph}_3\text{P})_2\text{CuBH}_4$, has been demonstrated to give good isolated yields of aromatic aldehydes from the corresponding acid chlorides;^{6,7} this communication shows that a very wide range of aldehydes may be conveniently prepared by the reaction (Table).

One major disadvantage of bis(triphenylphosphine) copper(I) tetrahydroborate, which only provides one hydride equivalent per mole, is its molecular weight of 603; large scale preparations by previously reported procedures^{6,7,8,9} are inconvenient, slow and use large excess of either (or both) triphenylphosphine and sodium tetrahydroborate. The method detailed below allows large quantities to be made quickly from copper(I) chloride, triphenylphosphine, and sodium tetrahydroborate in the molar ratio of 1:2:1. Tris(triphenylphosphine) copper(I) chloride, $(\text{Ph}_3\text{P})_3\text{CuCl}$, can be isolated quantitatively as a by-product after the reduction of acid chlorides and it is easily recycled to the tetrahydroborate complex; thus the problem of loss of large quantities of triphenylphosphine during the reaction is easily overcome.

Saturated alicyclic and aliphatic acid chlorides are readily reduced to the corresponding aldehydes in good yields with no further reduction to the alcohols taking place; the major problem is the separation of the aldehyde from the reaction mixture. Experimental procedures are given for the preparation of decanal from decanoyl chloride (purified by distillation) and of 3,4-dimethoxybenzaldehyde (purified by removal of triphenylphosphine as the triphenylphosphinecopper(I) chloride complex). Pivalaldehyde was prepared by performing the reaction in a high boiling solvent (triglyme) and distilling the aldehyde out of the reaction mixture directly. Terephthalaldehyde was isolated by aqueous extraction.

TABLE

<u>Acid Chloride</u>	<u>Aldehyde</u>	<u>Yield%</u> ^a
hexanoyl	hexanal	71
decanoyl	decanal	79 (91)
pivaloyl	pivalaldehyde	60
cyclohexanecarbonyl	cyclohexanecarboxaldehyde	72 (86)
adipoyl	adipaldehyde	(b)
	cyclopentene-1-aldehyde	71
α -acetoxypropionyl	α -acetoxypropionaldehyde	23
crotonoyl	crotonaldehyde	33
cinnamoyl	cinnamaldehyde	78 (86)
benzoyl	benzaldehyde	78 (81)
3,4-dimethoxybenzoyl	3,4-dimethoxybenzaldehyde	79
4-tert butylthiazole-5-carbonyl ¹⁰	4-tert-butylthiazole-5-aldehyde	51 ^c
terephthaloyl	terephthalaldehyde	53
phthaloyl	(b)	-

a) Isolated yields of pure aldehydes; yields in parenthesis refer to quantitative glc yields, using an internal standard

b) see text

c) yield based on acid as starting material without isolation of acid chloride

The reduction of several diacid chlorides was investigated. Reduction of adipoyl chloride gave on distillation a good yield of cyclopentene-1-aldehyde¹¹ (nmr δ 9.75, 1H, s, 6.90, 1H, br. s; ir 1680 cm^{-1}) the crude reaction mixture before distillation contained none of the cyclised product but only adipaldehyde (nmr δ 9.60, t; ir 1725 cm^{-1}) which could be isolated as its bisdinitrophenyl-hydrazone.¹² The only product isolated from the reduction of phthaloyl chloride was phthalide (o-hydroxymethylbenzoic acid lactone) ir 1750 cm^{-1} , m.p. 74-76^o 13); no evidence was found for the formation of phthalaldehyde - the crude reaction mixture showed no aldehyde proton in the nmr nor a carbonyl stretch in the ir consistent with phthalaldehyde. In contrast, terephthaloyl chloride is reduced to terephthalaldehyde.

Cinnamoyl chloride is reduced to cinnamaldehyde in good yield. However, relatively poor yields of crotonaldehyde were obtained from crotonyl chloride; the low yield is not due to further reaction of crotonaldehyde with either triphenylphosphine or the reducing agent. The low yield of α -acetoxypropionaldehyde was due to the difficulty of its separation from the reaction mixture.

In every case the rate of reduction of the acid chloride with bis(triphenylphosphine) copper(I) tetrahydroborate was increased in the presence of a two-fold excess of triphenylphosphine; in several cases, the yield of aldehyde was also increased. The increased rate may be due to nucleophilic catalysis involving an intermediate acyl phosphonium salt;⁶ the rate of reduction

was also increased by addition of alkyl phosphites, aryl phosphites and tertiary amines. However, although triethylamine catalysed the reduction of benzoyl chloride to benzaldehyde, the use of pyridine as a catalyst greatly reduced the yield of aldehyde - presumably because the intermediate acyl pyridinium salt is attacked on the pyridine ring. Although imines are not affected by $(\text{Ph}_3\text{P})_2\text{CuBH}_4$, iminium salts are readily reduced to the corresponding tertiary amines e.g. N-Methylquinolinium iodide is regiospecifically reduced to N-methyl-1,2-dihydroquinoline.¹⁴

Although large scale reductions using stoichiometric amounts of the complex copper tetrahydroborate involve a large physical bulk of reagent, the reaction is easily carried out on 0.3 mole of acid halide. It is not necessary, nor is it an advantage, to perform the reduction under homogeneous conditions. The most suitable solvent is acetone; during the reaction, the majority of the tetrahydroborate and of the complex copper chloride products are not in solution. Satisfactory yields may also be obtained in nitrobenzene, toluene, triglyme, toluene and ether. In chloroform and in dichloromethane, some benzyl alcohol was produced in the reduction of benzoyl chloride, although benzaldehyde was not reduced to benzyl alcohol by bis(triphenylphosphine) copper tetrahydroborate; in contrast, 4-nitrobenzaldehyde was reduced to 4-nitrobenzyl alcohol under similar conditions.

The ease of making, handling, storing and using bis(triphenylphosphine) copper tetrahydroborate, together with its compatibility with a large number of functional groups, makes this reagent an attractive and general alternative to the present range of methods for the reduction of acid chlorides to aldehydes.^{15,16,17}

Experimental

Bis(triphenylphosphine) copper(I) tetrahydroborate

Finely powdered copper(I) chloride (40 g, 0.4 mol) was added to a stirred solution of triphenylphosphine (216 g, .82 mol) in chloroform (1500 ml) over five minutes. The reaction mixture was stirred until the copper chloride had dissolved (15 min), treated with a suspension of sodium tetrahydroborate (15.2 g, 0.4 mol) in ethanol (150 ml), stirred for a further fifteen minutes, and then added to water (300 ml). The chloroform layer was then washed with water (2 x 250 ml), dried (magnesium sulphate) and treated with diethyl ether (2000 ml). Bis(triphenylphosphine) copper(I) tetrahydroborate was precipitated immediately, collected by filtration and washed with ether to give white needles, m.p. 172-4° (lit.⁸ 177°), 225g, .37 mol, 93% yield. The preparation can be accomplished readily within one hour. $(\text{Ph}_3\text{P})_2\text{CuBH}_4$ may also be prepared from the filter cake* of tris(triphenylphosphine) copper(I) obtained in the reduction reaction below as follows:

The filter cake of crude tris(triphenylphosphine) copper(I) chloride (300 g, 0.34 mol) was dissolved in chloroform (1500 ml) and treated with a suspension of sodium tetrahydroborate (12.9 g, 0.34 mol) in ethanol (150 ml). The resulting reaction mixture was stirred for ten minutes, washed with water (3 x 250 ml), and dried (magnesium sulphate). Addition of ether precipitated bis(triphenylphosphine) copper(I) tetrahydroborate as fine white needles, m.p. 170-4.

Decanal

Decanoyl chloride (20 g, 0.1 mol) in acetone (50 ml) was added over a period of five minutes to a stirred slurry of bis(triphenylphosphine) copper(I) tetrahydroborate, (63g, 0.105 mol) and triphenylphosphine (55 g, 0.21 mol) in acetone (250 ml). The reaction mixture became warm and some gas evolution was observed. The course of the reaction was followed by glc which showed a yield of 67% after 5 min increasing to 91% after 25 min. After half an hour, the precipitate* of tris(triphenylphosphine) copper(I) chloride was removed by filtration and the filter cake washed with ether. The solvents were then removed under reduced pressure and the residue extracted with methanol (150 ml). The methanol was removed and the residue distilled under reduced pressure to yield decanal, 13.0 g, 79%, b.p. 64° at 0.4mm Hg, identical with an authentic sample.

3,4-Dimethoxybenzaldehyde

Bis(triphenylphosphine) copper(I) tetrahydroborate (30 g, 0.05 mol) was added to a stirred solution of 3,4-dimethoxybenzoyl chloride (10 g, 0.05 mol) and triphenylphosphine (26 g, 0.1 mol) in acetone (200 ml). The reaction mixture was stirred for one hour and the precipitate was then removed by filtration. The filter cake was washed with ether and the solvents removed from the combined filtrates; the residue was extracted with methanol, the methanol removed under reduced pressure and the residue dissolved in chloroform (60 ml). The chloroform solution was stirred over finely powdered copper(I) chloride (9 g) for 30 min in order to remove free triphenylphosphine as triphenylphosphinecopperchloride, $\text{Ph}_3\text{PCuCl}^6$; the reaction mixture was filtered, the chloroform filtrate evaporated to dryness and the residue crystallised from petrol (b.p. 60-80) to yield 3,4-dimethoxybenzaldehyde (6.5 g, 79%), m.p. 54-56° (lit 58°).

We are pleased to acknowledge a CASE award with ICI Pharmaceuticals, Macclesfield.

REFERENCES

1. J.E. McMurry, M.G. Silvestri, T. Hoz, and M.W. Grayston, *J.Org.Chem.*, 1978, 43, 3249.
2. E.C. Ashby, and J.J. Lin, *J.Org.Chem.*, 1978, 43, 1263, 2567.
3. F. Sato, S. Sato, and M. Sato, *J.Organometal.Chem.*, 1976, 122 C-25.
4. J.L. Luche, *J.Amer.Chem.Soc.*, 1978, 100, 2226.
5. T.N. Sorrell, *Tetrahedron Lett.*, 1978, 4985.
6. G.W.J. Fleet, C.J. Fuller, and P.J.C. Harding, *Tetrahedron Lett.*, 1978, 1437
7. T.N. Sorrell, and R.J. Spillane, *Tetrahedron Lett.*, 1978, 2226.
8. J.M. Davidson, *Chem.Ind.(London)*, 1964, 2021
9. F. Cariati, and L. Naldini, *Gazz.Chim.Ital.*, 1965, 95, 3.
10. Experiment performed by Mr. P. Kaye.
11. J.B. Brown, H.B. Henbest, and E.R.H. Jones, *J.Chem.Soc.*, 1950, 3634
12. R. Pappo, D.S. Allen, Jr., R.U. Lemieux, and W.S. Johnson, *J.Org.Chem.*, 1956, 21, 478.
13. J.H. Gardner, and C.A. Naylor, *Organic Syntheses, Collected Vol.2*, p.526, Wiley, 1943.
14. G.W.J. Fleet, and E.M. Irving, unpublished results.
15. R.A.W. Johnstone, and R.P. Telford, *J.Chem.Soc., Chem.Commun.*, 1978, 354.
16. H.C. Brown and B.C. Subba Rao, *J.Amer.Chem.Soc.*, 1958, 80, 5377.
17. C.A. Buehler and D.E. Pearson, *Survey of Organic Syntheses, Vol.2*, p.499 Wiley, 1977.

(Received in UK 29 December 1978)