Tetrahedron Letters Vol. 21, pp 813 - 816
0040-4039/80/0222-0813$02.00/0

μ-BIS(CYANOTRIHYDROBORATO)-TETRAKIS(TRIPHENYLPHOSPHINE) DICOPPER(I). A NEW, SELECTIVE, pH DEPENDENT REDUCING AGENT

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Abstract: The title compound selectively reduces acid chlorides to aldehydes under neutral conditions and aldehydes and ketones to alcohols in acidic media. 4-tert-Butylcyclohexanone is reduced to the trans alcohol with a high degree of stereoselectivity (94:6).

The combination of hydride transfer agents and transition metal derivatives has attracted increasing interest as an approach toward modifying the reducing ability of a number of reagents.[1] However, no investigations have appeared concerning cyanotrihydridoborate (cyanoborohydride) coupled with transition metals although a number of stable complexes have been synthesized and structurally investigated.[2] This report describes preliminary results with one such complex, μ-bis(cyanotrihydroborato)-tetrakis(triphenylphosphine) dicopper ($([(C_6H_5)_3P]_2CuBH_3CN)_2$ (1) as a reagent for the chemoselective conversion of acid chlorides to aldehydes and, in acidic media, aldehydes and ketones to alcohols.

The reagent is conveniently prepared by treating cupric sulfate hydrate sequentially with excess triphenylphosphine and sodium cyanoborohydride in ethanol.[3] The structure is a novel eight-membered ring dimer in which both a hydrogen and nitrogen from each BH_3CN ligand are coordinated to the Cu atoms.[4] Dispersal of negative charge toward the Cu(I) atoms evidently moderates the hydride transfer ability of the boron in 1 (compared to $NaBH_3CN$) since acid chlorides are cleanly converted to aldehydes with 1 under neutral conditions while the latter reagent affords alcohols.[5] Table I presents a variety of representative conversions of both aromatic and aliphatic examples and the experimental procedure is illustrated below for the reduction of p-bromobenzoyl chloride to p-bromobenzaldehyde.

p-bromobenzaldehyde. A mixture of p-bromobenzoyl chloride (2.18 g, 9.93 mmol) and 1 (9.34 g, 14.9 mmol) in 50 mL of dry acetone was stirred at room temperature for 3 hrs and then evaporated at reduced pressure. The residue was treated with 50 mL of methanol, the precipitate was filtered and washed thoroughly with methanol, and the solvent removed at reduced pressure. The residue was dissolved in 25 mL of chloroform, 2 gms of cuprous chloride was added and the mixture stirred at room temperature for 30 min. The mixture was then filtered, the filtrate concentrated and the residue flash distilled at reduced pressure (Kugelrohr apparatus) to afford 1.42 g (77%) of p-bromobenzaldehyde, identical (ir, nmr) to an authentic sample. In a similar run (2 mmol of p-bromobenzoyl chloride), the reaction mixture was filtered, the precipitate washed with ether and the filtrate analyzed by glpc using an internal standard; the yield was 83%.

The inertness of the reagent suggests synthetic applications which necessitates maximum chemoselectivity.

Table I. Reduction[a] of Acid Chlorides to Aldehydes with $([(C_6H_5)_3P]_2CuBH_3CN)_2$

Acid Chloride	% Yield Aldehyde[b] (Isolated)[c]
C_6H_5COCl	84(56)
o-ClC_6H_4COCl	75
p-ClC_6H_4COCl	92(92)
p-BrC_6H_4COCl	83(77)
p-$CH_3OC_6H_4COCl$	71
p-$O_2NC_6H_4COCl$	48
$CH_3(CH_2)_8COCl$	82
$C_6H_5CH_2COCl$	55
$H_2C{=}CH(CH_2)_8COCl$	60
$C_6H_5CH{=}CHCOCl$	61

(a) Reactions were 0.2 M in the acid chloride, 0.3 M in the metal complex in acetone; stirred at room temperature for 3 hrs. (b) Yields represent glpc determinations using internal standards and corrected for detector response. (c) Purified by distillation or recrystallization.

In analogy with the parent sodium cyanoborohydride, the reducing ability if 1 is enhanced in acidic media. Thus, in THF at pH ca. 3, aldehydes and ketones (except diaryl ketones) are reduced to alcohols in good yields as demonstrated in Table II and illustrated below for the reduction of p-nitrobenzaldehyde to p-nitrobenzyl alcohol.

p-nitrobenzyl alcohol. A mixture of p-nitrobenzaldehyde (314 mg, 2.08 mmol), 1 (2.41 g, 3.84 mmol) and tetradecane (internal standard, 380 mg, 1.92 mmol) in 10 mL of dry THF was acidified to pH ca. 3 with concentrated HCl (methyl orange indicator) and stirred at room temperature for 3 hrs. The mixture was filtered, the precipitate washed with ether and the filtrate evaporated to ca. 10 mL under a stream of nitrogen. Analysis by glpc indicated a 77% yield of p-nitrobenzyl alcohol.

We envisioned that the bulky transition metal-triphenylphosphine appendage might provide a reagent sufficiently encumbered to give stereoselective equatorial attack on cyclohexanones.[6] Surprisingly, however, reduction of 4-tert-butylcyclohexanone afforded a 94:6 mixture of the trans : cis isomeric alcohols, respectively, an even higher ratio than that obtained with sodium cyanoborohydride (92:8)! In fact, the predominance of the trans isomer is one of the highest observed for metal hydride reagents[6] and recommends the reagent for such synthetic conversions.

Current interests involve the incorporation of chiral phosphine ligands into the metal complex to provide optically active reagents for the asymmetric reduction of ketones.

Table II. Reduction of Aldehydes and Ketones to Alcohols with $([(C_6H_5)_3P]_2CuBH_3CN)_2$ in Acidic THF.[a]

Carbonyl Compound	% Yield of Alcohol[b](Isolated)[c]
C_6H_5CHO	75
<u>o</u>-ClC_6H_4CHO	77
<u>m</u>-$O_2NC_6H_4CHO$	83
<u>p</u>-$O_2NC_6H_4CHO$	77(59)
$CH_3(CH_2)_8CHO$	84
$CH_3CO(CH_2)_5CH_3$	74
$C_6H_5COCH_3$	68
$(C_6H_5)_2CO$	32
4-<u>tert</u>-butylcyclohexanone	80[d]

(a) Reactions were 0.2 M in the carbonyl compound, 0.37-0.40 M in the metal complex in dry THF, acidified to ca. pH 3 (methyl orange indicator) with concentrated HCl; stirred at room temperature for 3 hrs. (b) Yields determined by glpc using internal standards and corrected for detector response. (c) Purified by distillation. (d) trans/cis ratio 94/6 determined by glpc and corrected for detector response. An analogous reduction using sodium cyanoborohydride afforded an 83% yield of the alcohols and a 92/8 ratio of the trans/cis isomers.

Acknowledgements. We wish to thank Thiokol, Ventron Division and The National Science Foundation for support of our programs on hydride chemistry.

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(Received in USA 15 November 1979)