Tetrahedron Letters,Vol.27,No.10,pp 1205-1208,1986 0040-4039/86 $3.00 + .00
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Cu^{2+}/BH_4^- REDUCTION SYSTEM: SYNTHETIC UTILITY AND MODE OF ACTION

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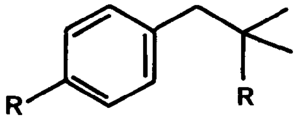
ABSTRACT: Cu^{2+}/BH_4^- offers a mild, method of reduction for aromatic and aliphatic tertiary nitro groups. Its mode of action has been studied, in comparison with related reagents, by deuterium isotope experiments.

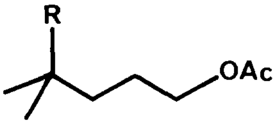
Transition metal/Borohydride reagent systems have found use in the reduction of a variety of functionality in recent years$^{(1-6)}$ viz., aryl nitro, cyanide or amide groups, with Co^{2+} and Ni^{2+} as the metal ions most often used. Cu^{2+}/BH_4^- however, has received scant attention and the mechanism of action of each of these systems has been poorly understood.$^{(3)}$ In this report attention is turned to each of these points and the applicability of Cu^{2+}/BH_4^- reduction to certain aliphatic functionality studied.

Unlike Co^{2+} or Ni^{2+}/BH_4^-, Cu^{2+}/BH_4^- was found to be unreactive toward cyanide and amide groups and was also inert to esters. It did however, effectively reduce a general selection of substituted aromatic nitro compounds and aliphatic nitro attached to tertiary carbon (e.g. 1 and 3 were reduced in 75-80% yield to 2 and 4 respectively).



1 R = NO_2

2 R = NH_2



3 R = NO_2

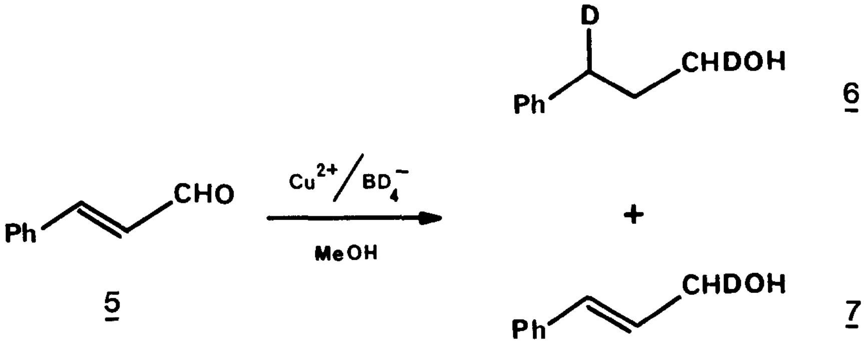
4 R = NH_2

Corresponding reductions with Co^{2+} or Ni^{2+} ions often led to azoxy derivatives or other unidentifiable products. Reductions of primary nitro groups produced a complex mixture of products, including major amounts of azoxy dimer, independent of the metal ion used. Secondary nitro compounds only yielded some unreacted starting material.

The mode of action of each reagent was tested using deuterium isotope experiments in the reduction of cinnamaldehyde 5. Treatment of 5 with BH_4^- alone, led to reduction of the carbonyl group only.

Cu^{2+}/BH_4^-

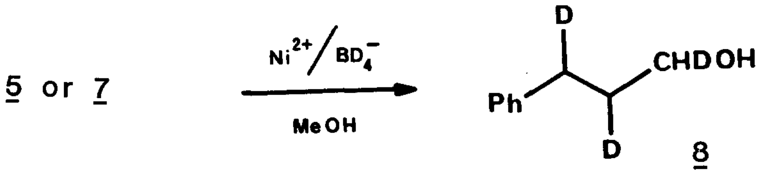
Reaction is always accompanied by the formation of a black solid and Cu^{2+}/BD_4^- in MeOH gave the following reaction with 5.



A mixture of 1,4 and 1,2 attack by "D^-" was observed. The system almost certainly acts by coordination of 5 to the solid followed by hydride attack, or by reaction with a surface bound hydride. Homogeneous reaction can be excluded since the solid (presumably a copper boride complex in analogy with the known result for cobalt and nickel) can be isolated, washed with MeOH, resuspended in MeOH (containing a trace of BD_4^- to mop up any free Cu^{2+}ions) and addition of 5 followed by BD_4^- again gives 6 and 7, although the proportion of Michael derived product drops due to the smaller available surface area as compared to the precipitate formed *in situ*. The reagent is therefore not a copper hydride of the type studied by Whitesides(7) or Semmelhack.(8) In addition, the aforementioned copper boride solid was found to be incapable of catalytically hydrogenating nitroaromatics or olefins at room temperature, in EtOH, under a hydrogen atmosphere.

Ni^{2+}/BH_4^-

Reaction is normally accompanied by formation of a black solid (Nickel Boride after Brown and Brown(9)) and Ni^{2+}/BD_4^- in MeOH gave the following reaction with 5 and 7.



Co^{2+}/BH_4^-

Similarly Co^{2+}/BD_4^- in MeOH reduced 5 and 7 to 8, again with the formation of a black solid. Both Ni^{2+} and Co^{2+}/BH_4^- reagents give hydrogenation of the double bond rather than hydride addition.

It was observed that during slow addition of BH_4^- to a solution of Co^{2+} and 5, the solution remained pink during reduction of the carbonyl group, after which it became darkly discoloured. Continued stirring however, led to the regeneration of a dull pink solution and fully reduced product. This argues for homogenous reduction, in contrast with the work of Heinzman and Ganem(3) on the reduction of aryl nitriles where a heterogeneous route was demonstrated. Initial reduction of the aldehyde in 5 with Ni^{2+}/BH_4^- also proceeded homogeneously, with no precipitation or discolouring of the solution, whilst it was also observed that change of solvent from MeOH to EtOH in the reduction of aryl nitro compounds again gave homogeneous reduction.

Conclusion

Cu^{2+}/BH_4^- is an efficient, mild reagent for the reduction of aryl and tertiary aliphatic nitro groups in the presence of other functionality. There is a clear difference in its mode of action in comparison with Co^{2+} or Ni^{2+}/BH_4^- (monohydride addition vs hydrogenation).

Whether homogeneous or heterogeneous reduction is observed for the latter two systems is strongly dependent on the nature of the functional groups present and on reaction conditions.

Procedure for Cu^{2+}/BH_4^- Reduction of 1 to 2

280 mg 1 were dissolved in 15 ml MeOH and 5 ml of a saturated solution of $Cu(OAc)_2$, (containing some solid) added. Small portions of $NaBH_4$ (up to 500mg) were added with stirring at r.t. until the reaction was complete, followed by immediate addition of 30 ml Et_2O. The reaction mixture was washed with $NaHCO_3$, the aqueous layer extracted with a further 10ml Et_2O and the combined Et_2O fractions dried (Na_2SO_4), filtered and solvent removed to yield 162 mg (79%) 2 which was then recrystallised from CH_2Cl_2/hexane.

Acknowledgements

I thank S.E.R.C. and St. John's College, Cambridge for financial support, and Dr J K M Sanders for helpful advice.

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(Received in UK 17 January 1986)