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A Novel Cu(II)-Mg-System for Allylation and Reduction of Carbonyl Compounds

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Abstract: Allylation of a variety of carbonyl compounds with allylic halides could be induced by Cu(II)-Mg to give corresponding homoallylic alcohols with high chemoselectivity. Cu(II)-Mg/THF-H₂O was found to be an efficient reduction system of aldehyde to alcohol.

Intensive studies have been carried out on the regio and stereoselective allylation¹ and reduction² of carbonyl compounds. The allylation of carbonyl compounds to homoallylic alcohols is of synthetic importance and a number of metals have been used to promote Barbier-type allylation of carbonyl compounds with allyl halides³. An useful application of the reagent copper(II) chloride dihydrate to promote Barbier-type allylation and reduction of carbonyl compounds has come to light. In continuation with our earlier studies on application of metal reagents⁴, we found that CuCl_{2.}2H₂O-Mg is a facile system for the allylation, Scheme 1 as well as reduction, Scheme 2, of carbonyl compounds at room temperature under mild reaction conditions.



The reaction procedure is extremely simple. To a suspension of magnesium powder (73mgs, 3mmol), CuCl₂.2H₂O (510mgs, 3mmol) and carbonyl compound (2mmol) in tetrahydrofuran (10ml) was

added allyl halide (3mmol) at room temperature. The reaction mixture was stirred for 3-12 hs while monitoring by TLC. The reaction mixture was quenched with dilute hydrochloric acid (5%) and the product was extracted with dichloromethane. Purification of the reaction products was carried out using preparative chromatography to afford the corresponding homoallylic alcohols, Table 1. A mixture of $CuCl_22H_2O$ (510mgs, 3mmol), Mg(73mgs, 3mmol) and aldehyde (1.5mmol) in THF (5ml) was stirred at room temperature. Water (2ml) was added dropwise to the reaction mixture over a period of 5 minutes. An exothermic reaction took place with the liberation of hydrogen. The reaction mixture was stirred for 5-8 hs. After the reaction was completed (monitored by TLC), usual work up yielded the corresponding alcohols, Table 2.

The yields of the reaction of carbonyl compounds with allyl bromide were better as compared to allyl chloride. Allyl chloride was found to be less reactive and requires longer reaction period to obtain moderate yields. Allylation of ketones (entries 6-9) occured only with allyl bromide and gave corresponding homoallylic alcohols with moderate yield. The reaction of allyl halide with cinnamaldehyde (entry 5) occurred at the γ -position and an α , β -unsaturated aldehyde afforded a regiospecific 1, 2-addition homoallylic alcohol which subsequently dehydrated during work up with dil. HCI in Table 1. The reaction did not proceed when either CuCl₂.2H₂O or Mg or anhydrous CuCl₂-Mg was employed. However, addition of water (0.1ml) to the anhydrous system of CuCl₂.2H₂O-Mg/THF-H₂O system. In case of α , β -unsaturated aldehydes, reduction occurred only at the C=O position (entries-6, 7) in Table 2 whereas carbon-carbon double bond remains intact. It is therefore evident from the above findings that the water of crystallisation of CuCl₂.2H₂O plays a vital role for the allylation to occur. However, the water of crystallisation does not suffice for the reduction of the aldehyde. Addition of water to the system facilitates the reduction process.

It has been observed that a combination of a stoichiometric amount of metallic copper and magnesium leads to a successful allylation of carbonyl compounds with allyl halides. The reaction mechanism is not clear at present, but the findings suggests a possibility of activation of allyl halides with magnesium. Meanwhile magnesium would be a promising metal for the generation of Cu(O) from Cu(II) since magnesium is less electronegative than copper so as to reduce in principle Cu(II) to Cu(O). The active zero-valent copper could induce allylation and reduction effectively.

Because of ready access of reagents, mild reaction conditions, good yields, easy work up and general applicability, CuCl₂.2H₂O-Mg-THF/THF-H₂O system will be an useful addition to the existing procedures for allylation and reduction.

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| Entry | Carbonyl Compound | % Yield ^a , Time/hs | %Yield ^b , Time/hs | Product ^C |
|-------|---|-----------------------------------|----------------------------------|----------------------|
| | | | | OH |
| 1. | PhCHO | 99, 6 | 70, 12 | Ph OH |
| 2. | p-ClPhCHO | 95, 4 | 70, 8 | p-CIPh |
| 3. | УСНО СНО | 75, 7 | 87, 12 | |
| 4. | | 99, 5 | 80, 12 | $\sim\sim\sim\sim$ |
| 5. | PhCH=CHCHO | 95, 3 | 85, 10 | Ph |
| 6. | PhCOCH ₃ | 70, 4 | | |
| 7. | CH ₃ CO(CH ₂) ₅ CH ₃ | 48, 10 | | |
| 8. | Ô | 50, 10 | | |
| 9. | | 52, 6 | | |

Table 1. Allylated Products of Carbonyl Compounds with Allyl halides.^{a,b}

a. Allyl bromide b. Allyl chloride c. All the products are confirmedby spectral data.

| Table 2. Reduction of aldehydes with CuCl ₂ .2H ₂ O-Mg/THF-H ₂ O | | | | |
|---|-------------|----------------------|------------------|--|
| Entry | Aldehyde | Product* | % Yield, Time/hs | |
| 1. | PhCHO | PHCH ₂ OH | 90, 6 | |
| 2. | p-CIPhCHO | p-CIPhCH2OH | 95, 5 | |
| 3. | p-OCH3PhCHO | p-OCH3PhCH2OH | 92, 5 | |
| 4. | СНО | УЛУ ОН | 78, 7 | |
| 5. | СНО | | 92, 6 | |
| 6. | СНО | ОН | 85, 8 | |
| 7. | Ph CHO | Ph | 70, 8 | |

* All the products are confirmed by spectral data and compared with authentic sample.

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