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Facile and Efficient Synthesis of Homoallylic Alcohols Using Allyl Bromide and Commercial Zinc Dust

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Abstract : An efficient procedure for the preparation of homoallylic alcohols has been achieved by a simple reaction of an aldehyde or a ketone with allyl bromide and commercial zinc dust in tetrahydrofuran.

Synthesis of homoallylic alcohols by allylation of carbonyl compounds is one of the most important processes in organic synthesis¹ since the homoallylic alcohols can be easily converted to many important building blocks for natural product synthesis.² Acyclic stereocontrol during the carbon-carbon bond formation has also increased the importance of this process.³ Different methods have been developed based on the use of a variety of metals such as magnesium, $\frac{4}{2}$ zinc⁵ and tin.⁶ However. zinc offers certain specific advantages being moderately reactive to allow the preparation of polyfunctional allylzinc derivatives⁷ and avoiding the formation of side products derived from the reductive coupling of the carbonyl compound such as the pinacol condensation, often observed using other reagents. $\frac{8}{100}$ However, the preparation of allylzinc derivatives is reported to require activated zinc to initiate the reactions,⁹ Several methods have been reported to activate zinc such as washing with HCI solution, ¹⁰ ultrasound irradiation in the presence of lithium, ¹¹ the use of Zn/Cucouple,¹² reduction of zinc chloride with alkali metals,¹³ or electroreduction of zinc chloride,⁹ among others. Considering the increasing importance of the allylzinc compounds in organic synthesis,¹ we sought to devise a simple and straighforward procedure for its preparation avoiding the additional step for preparation of activated zinc. Very interestingly, we have observed a clean and smooth reaction of allyl bromide with commercial zinc dust in tetrahydrofuran forming the allylzinc bromide which adds on to aldehyde or ketone to produce the corresponding homoallylic alcohol in excellent yield. To the best of our knowledge, we are not aware of any report of use of commercial zinc dust without being activated for an efficient allylation reaction.¹⁴ However, similar reactions in aqueous medium¹⁵ or in presence of some additive¹⁶ are known.

Br + O Zn OH

entry	carbonyl compound	time (h)	product	yield(%) ^a
1		1.5	но	80
2		3	HO	92
3		1	HO	84
4		0.5	HO	94
5	Ph	1	H0 Ph	85
6	Ph	2	H0 Ph	89
7	O Ph Ph	2.5	HO Ph Ph	91
8	С М ₆ Н	1.5	OH V ₆	88
9		3	OH Ph	90
10	ОЦН	1.5	OH OH	91 ^b
11	Ph H	e E		94

Table 1. Allylation of Carbonyl Compounds with Allyl Bromide and Zn-dust

Table 1 (contd....)



^aAll yields refer to pure isolated products. ^bThis compound decomposes during purification through column chromatography over silica gel. ^CThe reaction was carried out with crotyl bromide.

The experimental procedure is very simple and straightforward. The allyl bromide (1 mmol) in THF (1 ml) was added dropwise to a stirred suspension of commercial zinc dust (1 mmol) in THF (2 ml) at room temperature and the mixture was stirred for half an hour after which the carbonyl compound (1 mmol) in THF (1 ml) was added. Stirring was continued for a certain period of time as required to complete the reaction (TLC). The reaction mixture was decomposed with a few drops of water and extracted with ether. The ethereal extract was washed with brine, dried over Na₂SO₄ and evaporated to leave the crude product which was purified by filtering it through a short column of silica gel.

Several structurally different aldehydes and ketones underwent allylation by this procedure to produce the corresponding homoallylic alcohols in excellent yields. The results are summarized in Table 1. The reactions are reasonably fast and clean. The reaction condition is mild enough not to affect the conjugated as well as the isolated double bond and carboxylic ester functionality (entries 10-14). This procedure is also regionalective as the reaction of crotyl bromide with cyclohexanone gives only (>95%, ac) the Υ -addition product (entry 15).

Ally chloride is found to be much less reactive than ally bromide as it has been observed that the reactions of allyl chloride with cyclohexanone and 1-octanal under identical conditions are only 10-15% complete.¹⁴ Zinc dust from different sources are found to give the same results. Following the same procedure, the propargyl bromide also reacts with cyclohexanone and octanal to produce the correesponding acetylenic alcohols in very good yields. This demonstrates the further scope and potentiality of this simple procedure.

To sum up, the present procedure for allylation of carbonyl compounds using commercial zinc dust provides much improvement over the existing methods and thus, will make a useful and important addition to the present methodologies. Further investigations to find the useful applications of this methodology are in progress and will be reported shortly.

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4888

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