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A Convenient Synthesis of β,γ -Unsaturated Ketones through Zinc-Mediated Allylation of Acid Chlorides

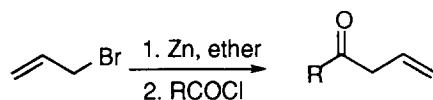
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Abstract: An efficient procedure for the preparation of β,γ -unsaturated ketones has been developed by a simple reaction of an acid chloride with allyl bromide and commercial zinc dust in ether.

β,γ -Unsaturated ketones have high versatility and wide applicability in natural product synthesis.¹ However, their synthesis is often complicated by the inherent lability of the double bond toward protropic rearrangement, producing conjugated isomeric α,β -unsaturated ketones.² Thus, the reaction conditions for the synthesis of this class of compounds need to be as mild as possible. Although a number of synthetic methods are available, only a few have proven useful and practical. Acylation of olefins frequently favours the production of β,γ -unsaturated ketones, but α,β -unsaturated ketones may also be generated.³ Certain transition metal mediated syntheses have been partially successful, but they also suffer from poor regioselectivity.⁴ Claisen rearrangement of α -alkoxy ketone enol derivatives provides β,γ -unsaturated ketones with good selectivity, but the procedure is tedious.⁵ Direct oxidation of homoallylic alcohols, produced via allylboration, has been demonstrated to be successful for specific classes.⁶ A recent method through allylation of z -1-halo-1-alkenyl-1,3,2-dioxaborolane is satisfactory; but it involves a number of steps.⁷ Allylic ketones have also been prepared by the reaction of allylic

organometallics of silicon,⁸ tin,⁹ copper,¹⁰ rhodium,¹¹ manganese,¹² titanium¹³ and mercury¹⁴ with acyl halides; but these reactions are of limited application, not being very simple and straightforward. Besides, some of these procedures entail the problems of corrosivity and effluent pollution. Recently, we have reported a simple zinc-mediated preparation of homoallylic alcohols¹⁵ and wish to disclose here another convenient procedure for the synthesis of β,γ -unsaturated ketones through allylation of acid chlorides using allyl bromide and commercial zinc dust (Scheme-1).


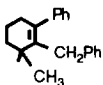


Scheme 1

In a typical procedure, allyl bromide (1 mmol) in ether (1 ml) was added to a stirring suspension of commercial zinc dust (1 mmol) in ether (3 ml) and stirring was continued for 30 min at room temperature. Acid chloride was then added drop wise to it and the reaction mixture was sonicated¹⁶ for a certain period of time as required for completion (monitored by TLC). The reaction mixture was then quenched with a few drops of water and the product was isolated by solvent extraction. A wide range of acid chlorides were converted to the corresponding allylic ketones by this procedure. The results are presented in Table 1. The reactions are reasonably fast and high-yielding. The reaction conditions are mild enough not to induce any isomerisation to conjugated α,β -unsaturated ketone. A double bond present elsewhere in the molecule also remains unaffected (entries 6 and 10). The reaction is found to be general being applicable to primary, secondary and tertiary acid chlorides; although for secondary and tertiary acid chlorides use of more than 1 equivalent (1.5) of allyl bromide/zinc reagent was needed to produce satisfactory results.¹⁷

In conclusion, the present method provides a very simple and convenient procedure for the preparation of β,γ -unsaturated ketones. The notable advantages of this methodology are mild condition (no use of acid or base), use of commercial zinc dust without any activation,¹⁸ fast reaction time (5 min to 10 h), tolerance to olefinic double bond, no prototropic isomerisation during reaction and high yield (75-90%) and thus, it offers significant improvements over other related procedures involving acylation of allylzinc species.¹⁹ We believe this will find significant application in the field of organic synthesis.

Table 1. Allylation of Acid Chlorides with Allyl Bromide and Zinc

entry	acid chloride R	time	yield of allyl ketone (%) ^a
1	CH ₃ (CH ₂) ₂ -	6 h	85
2	(CH ₃) ₂ CH-	2.5 h ^b	89
3	CH ₃ (CH ₂) ₆ -	10 h	87
4	PhCH ₂ -	1.5 h	92
5	Ph(CH ₂) ₂ -	1.5 h ^b	87
6	CH ₃ (CH ₂) ₇ CH=CH(CH ₂) ₇ -	5 min	90
7	PhCH ₂ CH(COCl)(CH ₂) ₃ -	45 min	89
8	Ph-	3 h	75
9		5 min ^b	92
10		1 h ^b	81

^a Yields refer to pure isolated products, fully characterized by IR and ¹H NMR.

^b The reaction was run at 5-10°C.

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16. Without sonication the reaction is very sluggish.
17. The progress of the reaction was monitored by TLC to avoid any chance of further addition to produce alcohols.
18. Usually, the preparation of allylzinc derivatives is reported to require activated zinc to initiate the reaction: Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, 56, 1445.
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