

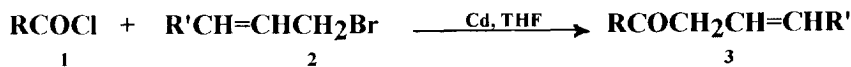
Cadmium Promoted Allylation of Acid Chlorides : Synthesis of β,γ -Unsaturated Ketones

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Abstract: A new and efficient method for the preparation of β,γ -unsaturated ketones has been achieved by a simple reaction of an acid chloride with allyl and crotyl bromide and cadmium powder in absolute tetrahydrofuran. Copyright © 1996 Published by Elsevier Science Ltd

Synthesis of β,γ -unsaturated ketones is complicated, inter alia, by a proclivity toward prototropic rearrangement producing conjugated isomeric α,β -unsaturated ketones¹. Although deconjugation of α,β -unsaturated ketones can be achieved by a variety of methods², mixtures of α,β and β,γ -unsaturated isomers are often produced. Thus the reaction conditions 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 generated³. Certain transition metal mediated synthesis have been partially successful, but they also suffer from poor regioselectivity⁴. Among other methods, direct oxidation of homoallylic alcohols produced via allylboration have been demonstrated to be successful for specific classes⁵. Allylic ketones have also been prepared by the reaction of allylic organometallic of silicon⁶, copper⁷, rhodium⁸, manganese⁹, titanium¹⁰ and mercury¹¹ with acyl halides, but these reactions are of limited application, not being very simple and straightforward. In view of the synthetic importance of these ketones, it is desirable to have a general convenient methodology for their synthesis especially from readily available material¹². Herein we report a new and efficient procedure for the synthesis of various β,γ -unsaturated ketones through the allylation of acid chlorides using allyl and crotyl bromide and cadmium powder in absolute tetrahydrofuran at room temperature¹³.



In a typical case, cadmium metal powder¹⁴ (0.112g, 1 mmol) was added to a stirred solution of allyl bromide (0.12g, 1 mmol) in 10ml of dry tetrahydrofuran and the stirring was continued for 30 mins at room temperature. Freshly distilled benzoyl chloride¹⁵ (0.14g, 1 mmol) in 5ml of THF was then added dropwise and the progress of the reaction was monitored by tlc to avoid any chance of further addition to produce alcohols. After 3 hrs the reaction mixture was quenched with a few drops of water and the product was isolated by extraction with dichloromethane and purification by column chromatography on silica gel gave allylic ketone **3** (entry 1) in 90% yields exclusively and there was no evidence for the formation of any isomeric conjugated α,β -unsaturated ketone as reported by earlier workers. When crotyl bromide was used in place of allyl bromide in the above reaction the corresponding (E)-isomer¹⁶ (entry 2) was obtained in 85% yields, without the formation of any rearranged products. A double bond present elsewhere in the molecule also remain unaffected (entry 10). Similar treatment of other acid chlorides gave the corresponding β,γ -unsaturated ketones in 70-90% yields and the typical results are summarised in the table. All the compounds obtained were characterised by infrared and ¹H NMR spectroscopy and finally by comparison with authentic samples.

In conclusion, the present procedure for the synthesis of β,γ -unsaturated ketones provides much improvements over the existing methods and will make a useful and important addition to the present methodologies. The main advantages of this new method are mild reaction conditions tolerance to olefinic double bond, no protropic isomerisation during the reaction and excellent yields of the products.

Table: Synthesis of β,γ -unsaturated ketones 3.

Entry	Acid chloride R	Allyl halides	Time (hrs)	Yield (%) ^a
1	C ₆ H ₅	CH ₂ =CH-CH ₂ Br	3	90
2	C ₆ H ₅	(E)-MeCH=CH-CH ₂ Br	2.5	85
3	p-NO ₂ C ₆ H ₄ -	(E)-MeCH=CH-CH ₂ Br	3.5	88
4	p-BrC ₆ H ₄	CH ₂ =CH-CH ₂ Br	4	86
5	p-BrC ₆ H ₄	(E)-MeCH=CHCH ₂ Br	3.5	80
6	p-CH ₃ OC ₆ H ₄	CH ₂ =CH-CH ₂ Br	2	90
7	PhCH ₂	CH ₂ =CH-CH ₂ Br	3.5	70
8	n-C ₃ H ₇	CH ₂ =CH-CH ₂ Br	2	82
9	n-C ₃ H ₇ CCl	(E)-MeCH=CH-CH ₂ Br	2.5	70
10	(E)-Me(CH ₂) ₇ CH=CH(CH ₂) ₇	CH ₂ =CH-CH ₂ Br	3.5	90

^aYields refer to pure isolated products, characterized by IR & ¹H NMR.

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- Cadmium powder used was of commercial grade and procured from Central Drug House (Pvt.) Ltd., New Delhi-110002.
- Acid chlorides either were obtained commercially or prepared according to known procedures and distilled before use.
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