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A novel method for the synthesis of aromatic *E*-β-chlorovinylketones

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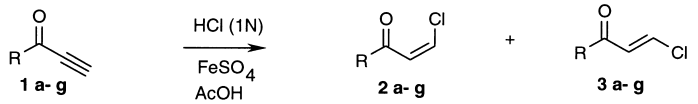
Abstract

The reaction of aromatic acetylenic ketones with aqueous HCl promoted by catalytic $FeSO_4$ gave a *E,Z*mixture of β-chlorovinylketones which isomerized almost exclusively to the *E*-β-isomer upon heating

β-Chlorovinylketones have proved to be versatile and valuable materials in organic synthesis.[1] The synthesis of β-chlorovinylketones has been performed under a diversity of conditions[2] although a mixture of *E* and *Z* isomers is often obtained. Recent methods have used LiCl for the preparation of such compounds but the yields were poor and the selectivity low.[2d] Gaseous HCl is also known to afford *E* or *Z*-chlorovinylketones depending on the reaction temperature.[2e]

We report herein a novel and cost effective method for the preparation of aromatic β-chlorovinylketones from terminal acetylenic ketones that were readily prepared from the corresponding acid chlorides.[3] Thus the reaction of aromatic acetylenic ketones (Eq. (1)) with aqueous HCl in the presence of a catalytic amount of $FeSO_4$ in acetic acid as solvent afforded the corresponding mixture of *E,Z*-chlorovinylketones which was easily converted by heating the reaction mixture for several hours, exclusively to the *E*-isomer **3** (Table 1). We have observed that prior to heating, the *Z*-isomer **2** was the major product formed along with a small amount of **3** which is the thermodynamically more stable compound.[2e]



(1)

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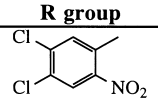
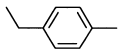
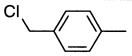
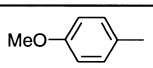
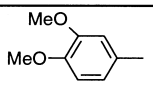
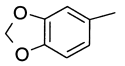
Table 1
Preparation of *E*,β-chlorovinylketones **3a–g**

Entry	R group	Yield [a]	Ratio (2: 3)[b]	Conditions
3a		65%	1: 99	18 h, 80°C
3b		70%	1: 99	6 h, 60°C
3c		73%	1: 99	5 h, 50°C
3d		78%	1:99	5 h, 35°C
3e		74%	1:99	3 h, 75°C
3f		64%	1:99	3 h, 80°C
3g	$Cl(CH_2)_4$-	64% [c]	1: 2.5	24 h, 80°C

[a] Yield of isolated, chromatographically pure β-chlorovinyketones. [b] ratio determined by ^{1}H-NMR of the crude mixture. [c] yield of the *Z, E* mixture.

A variety of acetylenic ketones were submitted to these reaction conditions and the results are summarized in Table 1. While aromatic ketones gave satisfactory results, substrates with aliphatic **R** groups showed little or no formation of the desired product. When **R** = Cl-$(CH_2)_4$ (entry 3g), the reaction proceeded at 80°C for 24 h to yield a mixture of isomers which did not undergo isomerization.

When the substates depicted in Table 1 were treated with aqueous HCl (1N) in AcOH in the absence of $FeSO_4$ no reaction took place which suggests that Fe(II) coordinates with the carbonyl group and/or the triple bond activating the alkyno ketones. On the other hand, equimolecular or excess amount of Fe(II) increased the rate of the reaction.

Typical preparation of β-E-chlorovinylketones: to a stirring solution of acetylenic ketone (Table 1) in acetic acid was added 1.1 equivalents of aqueous HCl (1N) at room temperature followed by 0.1 equiv. of $FeSO_4$. The reaction mixture was then heated (see conditions; Table 1) for several hours. When completed, water was added followed by EtOAc at ambient temperature. The organic layer was separated and washed with H_2O. After drying over $MgSO_4$, the solution was concentrated under vacuum to give a residue which was purified by flash chromatography (EtOAc:hexane, 1:10).[4]

In conclusion, we have described an efficient and cost effective method for the synthesis of aromatic β-chlorovinylketones from the acetylenic precursors.

Acknowledgements

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References

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4. All compounds were characterized by spectroscopic and analytical methods.