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Copper(I)-catalysed Acylation of Terminal Alkynes

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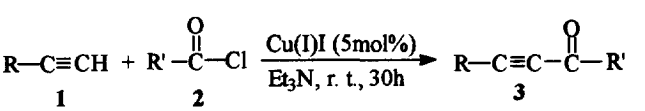
Abstract: *A facile synthesis of conjugated acetylenic ketones is reported, involving Copper(I) catalysed acylation of terminal alkynes with acyl halides.* Copyright © 1996 Elsevier Science Ltd

Conjugated acetylenic ketones have evoked considerable interest because of their utility as synthetic intermediates[1-2]. Also, many of them are of biological interest[3-4]. Because of their importance, a number of methods have been developed for the synthesis of conjugated acetylenic ketones[5]. Recent trends have been the synthesis of α,β-acetylenic ketones by palladium-catalysis from 1-alkynes and acyl chlorides[6] or from 1-alkynes and aryl or vinyl halides in the presence of carbon monoxide[7]. The acylation of alkynyl zincs[8] and alkynyl stannanes[9] with acyl chlorides in the presence of palladium catalysts leading to α,β-acetylenic ketones has also been reported. This communication describes a very facile method for the synthesis of α,β-acetylenic ketones by the reaction of 1-alkynes with acyl halides in the presence of catalytic amounts of copper(I) salts only (Scheme-1).

Scheme-1



1 **2** **3**

As can be seen from Table-1, good yields of α,β-acetylenic ketones could be obtained by treating a mixture of the alkyne **1** and acid chloride **2** in triethylamine with cuprous iodide at room temperature. It is to be observed that the reaction does not take place in the absence of the copper catalyst (entry 1). However, it is equally applicable to terminal alkynes substituted either with aryl (entries 2-6), heteroaryl (entry 7) or alkyl (entries 9, 10) substituents. The reaction was found to be tolerant of other functional groups, e. g. , hydroxyl (entry 10), nitro (entry 4) and silyl (entry 8).

The reaction is characterised by its simplicity of operation. A typical reaction procedure is as follows : to a mixture of dimethyl propargyl alcohol (2.5 mmol) and cuprous iodide (5 mol %, 0.125 mmol) in

triethylamine, p-toluoyl chloride (3.12 mmol) was added. The mixture was stirred at room temperature for 30h under argon atmosphere. After removal of the solvent, methanol (2.5ml) was added and the mixture was further stirred for five minutes. After usual work-up, the product was purified by chromatography over silica-gel (60-120 mesh) with 10% EtOAc in chloroform as eluent.

Table-1. Copper(I)-Catalysed Synthesis of α,β-Acetylenic Ketones.

Entry	R—C≡CH (R)	R'—C(=O)—Cl[a] (R')	3[%][b]	Entry	R—C≡CH (R)	R'—C(=O)—Cl[a] (R')	3[%][b]
1[c]	Ph	p-CH_3,C_6H_4	0	6	1-naphthyl	p-Cl, C_6H_4	62
2	Ph	p-CH_3, C_6H_4	83	7	2,4-dimethoxy-pyrimidin-5-yl	p-CH_3, C_6H_4	65
3	Ph	Ph	78	8	$SiMe_3$	p-CH_3, C_6H_4	79
4	Ph	p-$NO_2C_6H_4$	82	9	n-butyl	Ph	44
5	Ph	$(CH_3)_2CH$	48	10	$(CH_3)_2C(OH)$	p-CH_3, C_6H_4	71

[a]The reaction did not work with straight chain aliphatic acid chlorides (e. g. acetyl, propionyl and butyryl chlorides).

[b]Yields based on terminal alkynes were determined after isolation of spectroscopically pure products using chromatography over silica-gel (60-120 mesh).

[c]Entry 1 was carried out without Copper(I) iodide.

Thus, we have described a very simple method for the synthesis of α,β-acetylenic ketones. The method is characterised by (i) its simplicity of operation (one step procedure), (ii) the ready availability of starting materials, (iii) modest to excellent yields of the products and (iv) tolerance of other functional groups (OH, NO_2, silyl).It is certainly superior to methods which involve the use of metal salts of the alkynes or their silylated or stannyl derivatives.

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