SHORT PAPER

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A convenient synthesis of conjugated acetylenic ketones by copper(I)-catalysis under microwave irradiation†

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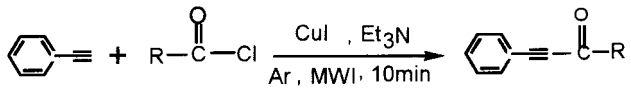
A rapid and efficient synthesis of conjugated acetylenic ketones is reported involving copper(I)-catalysed aroylation of phenylacetylene with aroyl chloride under microwave irradiation.

Keywords: conjugated acetylenic ketones

Alkynyl ketones are useful precursors and intermediates in synthetic organic chemistry[1] and have evoked considerable interest. A number of methods for the synthesis of conjugated acetylenic ketones involving the reaction of a metal acetylide with an acyl chloride or another carboxylic acid derivative have been developed.[2] Recently, the synthesis of α,β-conjugated acetylenic ketones by Pd(II)[3] catalysed or by copper(I)-Pd(II)[4] catalysed reactions of 1-alkynes and acyl chlorides have been described. The acylation of terminal alkynes by acyl chlorides in the presence of catalytic amounts copper(I) salts leading to α,β-conjugated acetylenic ketones has also been reported.[5] However, many of these reactions suffer from high pressure (17 atm),[3] long reaction time (30 h)[5] and require low temperatures (–78°C).[2i] Our work involves the synthesis of conjugated acetylenic ketones via the reaction of terminal alkynes with aroyl chlorides in the presence of cuprous iodide under microwave irradiation.

In recent years, interest has been shown in the study of microwave assisted organic reaction and some important reviews have been published.[6] Microwave irradiation has also been applied to several organic reactions. In previous papers, we have reported on the microwave-assisted etherification[7] and nucleophilic ring opening of oxiranes.[8,9] But so far, there have not been any reports of the synthesis of conjugated acetylenic ketones under microwave irradiation conditions.

We have now found that substituted conjugated acetylenic ketones can be obtained from terminal alkynes and aroyl chlorides using copper(I) salts as catalysts under microwave irradiation. A comparative study on the reaction of conjugated acetylenic ketones shows that this method offers the possibility of considerably decreasing the reaction time and improving the yield compared to conventional conditions. This method is simple, rapid and affords good yield. The reactions are shown in Scheme 1 and results are summarized in Table 1.



1 **2a-i** **3a-i**
3a R=C_6H_5, **3b** R=4-ClC_6H_4, **3c** R=4-BrC_6H_4,
3d R=4-$CH_3C_6H_4$, **3e** R=C_6H_5CH=CH, **3f** R=2-ClC_6H_4,
3g R=2-BrC_6H_4, **3h** R=4-$CH_3OC_6H_4$, **3i** R=1-$C_{10}H_7$

Scheme 1

Using the synthetic reaction of phenylacetylene with benzoyl chloride as an example, we investigated the effects of various solvents on the reaction. When triethylamine is used as solvent, the yield of compounds **3a–i** is high (76–93%), whereas, the yield is very poor when the reaction is carried out in benzene or DMF and triethylamine (v/v=5 ml: 5 ml). There is no reaction when benzene, CH_2Cl_2, CH_3CN are used as solvents and triethylamine as base. If K_2CO_3 or K_3PO_4 are used as base and the other solvent, there is also no reaction. We have also investigated the effects of irradiation power and time on the reaction. It was found that the highest yield of

Table 1 Preparation of α,β-conjugated acetylenic ketones compounds **3a–i** under microwave irradiation[a]

Entry	Product	Yield[(b)](%)	M.p.°C/Lit
3a	$C_6H_5COC{\equiv}CC_6H_5$	87	47–48(46–48[10])
3b	4-Cl-$C_6H_4COC{\equiv}CC_6H_5$	91	103–104(105[11])
3c	4-Br-$C_6H_4COC{\equiv}CC_6H_5$	93	106–107(110[12])
3d	4-CH_3-$C_6H_4COC{\equiv}CC_6H_5$	85	67–68(71[13])
3e	C_6H_5CH=$CHCOC{\equiv}CC_6H_5$	76	72–73(73.5–74[4])
3f	2-Cl-$C_6H_4COC{\equiv}CC_6H_5$	80	Oil[c]
3g	2-Br-$C_6H_4COC{\equiv}CC_6H_5$	83	Oil[d](Oil[14])
3h	4-CH_3O-$C_6H_4COC{\equiv}CC_6H_5$	79	98–99(100[11])
3i	1-$C_{10}H_7COC{\equiv}CC_6H_5$	82	93–94(95[13])

[a]Products generally were characterised by IR, ^{1}H NMR and MS, and comparison of their physical constants with those reported in literature. [b]Isolated yield. [c] 3f has not been reported previously (Found C, 74.98; H, 3.68; Cl, 14.58. $C_{15}H_9OCl$ requires C, 74.85; H,3.77; Cl,14.73%). IR_{max}.(neat): ν 2198(C≡C), 1652(C=O) cm^{-1}. ^{1}H NMR($CDCl_3$): δ 7.30–7.82(m, 8H), 8.06–8.18(m, 1H). MS(*m/z*): 242(M^+). [d]3g was characterised by IR, ^{1}HNMR and MS and the spectroscopic data are similar to those reported in the literature:[14] IR_{max}.(neat):ν 2196(C≡C), 1654(C=O) cm^{-1}. ^{1}H NMR($CDCl_3$): δ 7.32-8.20(m, 9H). MS(*m/z*): 284(M^+), 286(M^+).

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Table 2 Comparison of times and yield in synthesis of compounds **3a-i** using microwave and conventional heating

	Conventional heating			Microwave heating		
Products	t/h	Yield(%)	Power/W	*t*/min	Yield(%)	t_c/t_{mw}
3a	30	78	525	10	87	180
3b	30	80	525	10	91	180
3c	30	81	525	10	93	180
3d	30	76	525	10	85	180
3e	36	52	525	10	76	216
3f	30	67	525	10	80	180
3g	30	69	525	10	83	180
3h	30	65	525	10	79	180
3i	30	61	525	10	82	180

compounds **3a-i** is obtained at a power level of 525 W for 10 minutes continuous irradiation.

The effects of various catalysts used in the formation of α,β-conjugated acetylenic ketones was studied and Cu(I) was found to be the best catalyst for the reaction. The efficiencies of several catalysts studied are in the order: $Pd(PPh_3)_2Cl_2$-CuI > CuI ≈ CuCN > CuBr > CuCl. Since Pd(II) is very expensive, and CuCN is a poisonous reagent, we selected CuI as the best catalyst for our reactions. There was no reaction in the absence of catalyst. In conclusion, we have been developing a simple, rapid and economical method for synthesis of α,β-conjugated acetylenic ketones under microwave irradiation.

The impact of the microwave irradiation and conventional heating for synthesis of compounds **3a–i** have been compared and the results are summarized in Table 2. The results showed that the syntheses of compounds **3a–i** under microwave irradiation were 180–216 times faster than under conventional heating. The ratio between the reaction time using conventional reaction and microwave irradiation (t_c/t_{mw}) under the same conditions, quantifies the microwave heating effect.

Experimental

Infrared spectra were measured as KBr discs (or liquid film) using an Alpha centauri FT–IR spectrometer. ^{1}H NMR spectra (80 MHz) were recorded in $CDCl_3$ using an FT-80 spectrometer. Mass spectra were obtained on a QP-1000A GC–MS spectrometer using the electron impact mode ($70e^v$ or $20e^v$). Microwave irradiation was carried out with a commercial microwave oven GlanzWP 750B at 2450Hz. Melting points were determined with an Electrothermal micromelting point apparatus and were uncorrected.

*General procedure for the preparation of compounds **3a–i***: A mixture of aroyl chlorides (3.2 mmol), phenylacetylene (2.5 mmol), cuprous iodide (0.125 mmol) and triethylamine (10 ml) was irradiated at 525W for 10 minutes by microwave under an argon atmosphere. The mixture was cooled to room temperature, methyl alcohol (5 ml) was added and the mixture was stirred for 5 minutes. The solvent was removed under reduced pressure. Diethyl ether (20 ml) and water (20 ml) were added to the residue, the aqueous layer was extracted with diethyl ether (20 ml × 2), the combined organic extract was washed with water (20 ml × 3), 5% H_2SO_4(20 ml × 3), saturated $NaHCO_3$ (20 ml × 3) and brine (20 ml × 3) and then dried (magnesium sulfate). The dried diethyl ether solution was concentrated and the product was purified by column chromatography on silica gel (200–300 mesh) using petroleum (b.p. 60–90°C)/ethyl actate (v/v 10:1) as the eluent.

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