SHORT PAPER

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Copper-catalysed cross coupling reaction under microwave irradiation conditions[†]

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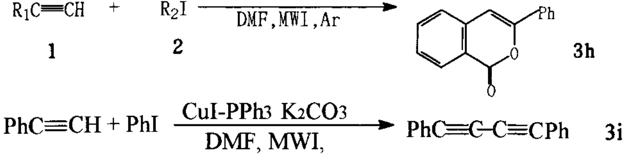
Copper-catalysed cross coupling of aryl iodies with terminal alkynes was readily achieved using CuI–PPh_3 as catalyst in the presence of potassium carbonate in DMF at 375W for 10 minutes under microwave irradiation.

The palladium-catalysed[1–4] coupling reaction of aryl halides with terminal alkynes is a useful tool for preparation of unsymmetrical acetylenes and is now widely used for synthesis of biologically active enyne-compounds.[5,6] The reaction is usually carried out using palladium complexes as catalysts,[l,7] some use copper(I) iodide as co-catalyst.[8–10] On the other hand, the reaction of aryl iodides with copper(I) acetylides[11] and vinyl halides with terminal alkynes in the presence of a stoichiometric amount of the copper species to produce arylacetylenes and enynes[12] are also known. The reaction also proceeds efficiently in the presence of a catalytic amount of copper(I) iodide when an appropriate amount of triphenylphosphine is added.[13] However, in all of these the reaction time is long enough for full conversion.

In recent years, microwave-induced rate acceleration technology is becoming a powerful tool in organic synthesis, because of milder reaction conditions, reduction of reaction times, enhanced selectivity and associated ease of manipulation. Microwave irradiation has also been applied to several organic reactions. It has been used for a great variety of organic reactions such as Reformatsky, Knoevenagel, Bischler-Napieralski, etherification esterification, oxidation, hydrolysis, Diels–Alder reactions and solid-phase peptide synthesis *etc*. Some important reviews have been published.[14] However, few practical applications have been devised for the coupling reaction in the presence of palladium.[15,16] There are no reports on the use of CuI–PPh_3 as catalyst for the coupling reaction of aryl halides with terminal alkynes under microwave irradiation conditions. In continuation of our studies on organic synthesis under microwave irradiation,[17–18] we decided to explore copper-catalysed cross coupling reaction using microwaves and compare the results with classical conditions. We now report a very simple, fast and general method for the copper-catalysed cross coupling of aryl iodies with terminal alkynes in the presence of potassium carbonate under microwave irradiation conditions. The reactions are shown in Scheme l and results are summarized in Table l.



Scheme 1

The results in Table l show that in the presence of CuI–PPh_3, a variety of terminal alkynes have been converted to the corresponding unsymmetrical acetylenes in good yields under microwave irradiation conditions. Under these conditions, 2-iodobenzoic acid (entry 8) is converted exclusively to 3-phenylisocoumarin (**3h**). However, under the same condions but without the Ar protection, the product is **3i** (entry 9).

Using the synthesis of **3a** (entry l) as an example, we have investigated the effect of different catalysts on the reaction. It was found that the activities of the catalysts are in the following sequence: CuI/PPh_3>CuBr/PPh_3>CuCl/PPh_3>PPh_3.The efficiency of various solvents on the formation of **3a** was studied using microwave irradiation. DMF was found to be an effective solvent for the reaction. The effect of various solvents in the synthesis of **3a** is in the following order: DMF>DMSO>CH_3CN>EtOH>benzene. We have also investigated the effects of irradiation power and time on the reaction. It was found that the highest yield of compound **3a** is obtained at a power level of 375 W for 10 min continuous irradiation.

The impact of the microwave irradiation and conventional heating for the formation of compounds **3a–h** has been compared and the results are summarized in Tables 2 and 3. The results showed that the synthesis of compounds **3a–h** under microwave irradiation were 48–144 times faster than under conventional heating.

The investigations show that: (i) while non-protonic polar solvent is used, the yield of diphenylacetylene is good. DMF is a microwave–active solvent because it is benefical for efficient absorption of microwave energy. (ii) Both strong base NaOH and weaker base $NaHCO_3$ give low yields. The strong base cause the secondary reaction. Weaker base decrease the rate of deproton. Using K_2CO_3, the good yield is given. (iii) The reaction cannot proceed without copper(I) salt. The yield is high when CuI is used.

Experimental

In a typical procedure, a mixture of iodobenene (1.02 g, 5 mmol), phenylacetylene (0.77 g, 7.5 mmol), CuI (0.09 g, 0.5mmol), PPh_3 (0.262 g,1 mmol) and K_2CO_3 (1.04 g, 7.5 mmol) in DMF (10 ml) were taken in the reaction flask and then irradiated at 375W for 10 minutes. After cooling, the product mixture was poured into 30 ml diethyl ether, then filtered the residue was washed with ether. The combine ether was washed with the saturated brine (3 × 10 ml) and dried over magnesium sulfate. The dried ethereal solution was concentrated. The crude product was purified by column chromatography on silica gel using petroleum/ ethyl acetate (v/v =1:1) as the eluent.

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Table 1 Fast copper-catalysed coupling reaction of aryl iodides with terminal alkynes under microwave irradiation[a]

Entry	R_1	R_2	Product	Yield (%)[c]	mp/bp(Torr) (Lit.)°C
1	Ph	Ph	**3a**	91	61–62 (62.5)[20]
2	Ph	p-$CH_3C_6H_4$	**3b**	84	71–72 (70.9–71.8)[21]
3	Ph	o-$O_2NC_6H_4$	**3c**	83	43–44 (43–44)[11]
4	Ph	p-$O_2NC_6H_4$	**3d**	90	119–120 (119–120)[11]
5	Ph	p-HO_2CC_6H	**3e**	92	221–222 (221–222)[11]
6	Ph	p-ClC_6H_4	**3f**	80	82–83 (81.5-82)[22]
7	$HOCH_2$	CH_2=$CHCH_2$	**3g**	80	70–72(2.7 kPa) (70–72 2.7 kPa)[3]
8	Ph	o-$HO_2CC_6H_4$	**3h**	86	88–89 (89–91)[23]
9	Ph	Ph	**3i**	65[b]	87–88 (88)[24]

[a]The reactions were carried out in the presence of K_2CO_3 using CuI-PPh_3 as catalyst in DMF at 375 W for 10 min under argon. [b]Under the same conditions but without the Ar protection, the product is **3i**. [c]Isolated yield.

Table 2 Comparison of time and yields on the formation of compounds **a-h** using microwave and conventional heating[a]

Product	Conventional heating[b]		Microwave heating			
	t/min	Yield(%)[c]	Power/W	t/min	Yield (%)[c]	t_c/t_{mw}
3a	720	83	375	10	91	72
3b	1440	95	375	10	84	144
3c	600	84	375	10	83	60
3d	720	75	375	10	90	72
3e	600	85	375	10	92	60
3f	1440	92	375	10	80	144
3g	900	89	375	10	80	90
3h	480	91	375	10	86	48

[a]The reaction were carried out in the presence of K_2CO_3 using Cu-PPh_3 as catalyst in DMF under argon. [b]Reflux temperature. [c]Isolated yield.

Table 3 Effect of the reaction times on the formation of **3a** using microwave and conventional reflux[a]

Entry	Time (min)	Yield (%)[b]	
		Conventional heating[c]	Microwave irradiation
1	2	No reaction	22
2	5	No reaction	78
3	8	Trace	84
4	10	5	91

[a]The reaction were carried out in the presence of K_2CO_3 using Cu-PPh_3 as catalyst in DMF under argon. [b]Reflux temperature. [c]Isolated yield.

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