

Nickel Chloride Promoted Glaser Coupling Reaction in Hot Water

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Abstract: A Glaser coupling reaction of terminal alkynes in the presence of nickel chloride without any organics and bases in hot water has been developed, which produces the corresponding homo-coupling products in good yields.

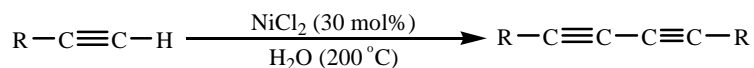
Keywords: Glaser coupling reaction, terminal alkynes, nickel chloride, hot water.

Diacetylene and its derivatives are very important intermediates and target molecules in biological, polymer and material science¹. A classical, effective and useful method for preparing diacetylenes was discovered by Carl Glaser in 1869, which involves a cuprous salt (CuCl) promoted oxidative homo-coupling of terminal alkynes in the presence of oxygen, ammonia and ammonium chloride². Subsequent studies indicated that a variety of copper salts (including cuprous and cupric salts, generally used in stoichiometric amount) are effective mediators for the coupling reaction, which is generally carried out in organic solvents such as methanol, acetone, pyridine, methyl cellosolve, benzene and toluene³, which often pose environmental problems. In addition, the bad smell piperidine, pyridine, diethylamine and triethylamine, which are usually required in Glaser reaction, added to the environmental burden. Recently we reported that an energy efficient modification of the Glaser coupling by using cupric chloride doped on KF/Al₂O₃ under solventless reaction conditions⁴. However, to the best of knowledge, there is no report on the Glaser coupling reaction promoted by nickel (II) salt.

Organic reactions carried out in water have received much attention in recent years⁵. Unfortunately most organic compounds are poorly soluble in water at ambient temperature. Nonetheless, the unique properties of water near its critical point ($T_c = 374^\circ\text{C}$, $P_c = 221$ bar) promoted the researchers to study the possibility of alternating the organic solvents by the water in its critical point in organic synthesis. There are increasing numbers of papers, which suggested that near-critical water could be used as excellent solvent for organic reactions⁶.

Here, we wish to report a Glaser coupling reaction of terminal alkyne in the presence of nickel chloride (30 mol %) without any organics and bases under hot water conditions. The reaction affords the corresponding coupling products in good yields.

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In our optimization process investigation, phenylacetylene was chosen as a model compound. The results are summarized in **Table 1**.

As shown in **Table 1**, the reaction temperature plays an important role in the oxidative homo-coupling reaction of terminal alkyne. It is evident that phenylacetylene could not be completely oxidized and subsequently coupled to form a homo-coupling product without any organics and bases in the presence of nickel chloride in water below 170°C (entry 7, **Table 1**), and only a moderate yield of diacetylene was obtained at 250°C, because of the polymerization (entry 3, **Table 1**). A good yield of product was observed at temperature in the range of 190–210°C. The ratio of nickel chloride to phenylacetylene was also examined. The results showed that when the ratio of nickel chloride to phenylacetylene was less than 0.1:1, the reaction was not completed (entries 8 and 9, **Table 1**) and while the ratio equaled or was more than 0.2:1, the satisfactory results were obtained (entries 10, 11 and 1, **Table 1**). The effect of the reaction time on the Glaser coupling reaction indicated that the reaction was not completed when the reaction time was less than 1 h (entry 12, **Table 1**). However, no increase of yield was observed when reaction time was prolonged more than 2 h. It is surprising to find that the isolated yield of Glaser coupling product was not increased when the reaction was carried out in the presence of bases under hot water conditions (entries 15 and 16, **Table 1**). The best reaction conditions for the oxidative coupling of phenylacetylene were found to be NiCl₂ (0.3 mmol), phenylacetylene (1 mmol), H₂O (10 mL) at 200°C for 2 h.

Table 1 Optimization reaction conditions for Glaser coupling of phenylacetylene in water

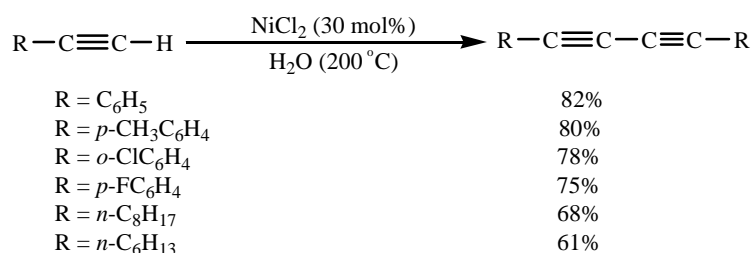
Entry	Nickel salt	Salt amount (mol %)	Temp. (°C)	Time (h)	Yield (%) ^b
1	NiCl ₂	30	200	2	82
2	NiSO ₄	30	200	2	72
3	NiCl ₂	30	250	2	58
4	NiCl ₂	30	230	2	73
5	NiCl ₂	30	210	2	81
6	NiCl ₂	30	190	2	80
7	NiCl ₂	30	170	2	71
8	NiCl ₂	0	200	2	trace
9	NiCl ₂	10	200	2	60
10	NiCl ₂	20	200	2	82
11	NiCl ₂	50	200	2	82
12	NiCl ₂	30	200	1	68
13	NiCl ₂	30	200	3	81
14	NiCl ₂	30	200	5	80
15	NiCl ₂ ^c	30	200	2	71
16	NiCl ₂ ^d	30	200	2	74

^a Reaction conditions: Phenylacetylene (1 mmol), nickel(II) salt (30 mol%), tap water (10 mL) in a high *T/p* batch reactor system. ^b Isolated yields. ^c In the presence of NaOAc (2 mmol). ^d In the presence of Na₂CO₃ (2 mmol).

A variety of terminal alkynes were successfully coupled using the above optimizing reaction conditions. The results are listed in **Scheme 1**. In the presence of nickel chloride (30 mol%) without any organics and bases in water at 200°C, homo-coupling of terminal alkyne occurs smoothly to produce the desired diacetylene in moderate to good yields. Substituent effect was also examined. The results indicated that the reaction is relatively insensitive to the electronic nature (electron-donating or electron-withdrawing) of substituents on the aromatic rings.

In conclusion, a reliable procedure for the synthesis of diacetylenes *via* a Glaser coupling reaction was developed which involves the use of nickel chloride (30 mol%) in hot water (200°C) without any organics and bases. The reaction is novel and environmentally friendly.

Scheme 1



General procedure for the preparation of diacetylenes: Terminal alkyne (1.00 mmol) and nickel chloride (39 mg, 0.3 mmol) were added to a high *T/p* stainless steel autoclave reactor charged with tap water (10 mL) with stirring. The reactor was heated at 200°C for 2 h. After cooling, ether (10 mL×2) was added for extracting the products. After the organic layer was dried over anhydrous sodium sulfate, the solvents were evaporated under reduced pressure. The product was purified by flash chromatography.

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Correction

X. Q. LIN, X. H. JIANG, L. P. LIU, "DNA Nano-netting Intertexture on Carbon Electrodes", Vol. 15, No. 8, pp997-1000. On page 998, in **Figure 1a** one part of the cyclic voltammetry was missed. **Figure 1a** should be:

