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Modified *Glaser* Reaction of Terminal Alkynes on KF/Alumina

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Summary. A variety of 1,3-diyne compounds are prepared in a solvent-free reaction on KF/alumina in the presence of catalytic amounts of $Cu(OAc)_2 \cdot H_2O$ with up to 96% yields at room temperature.

Keywords. *Glaser* Reaction; Alkynes; Homocoupling; KF/Alumina; Solvent-free Synthesis.

Introduction

The *Glaser* reaction, first reported in 1869 [1] involves self-coupling of terminal alkynes promoted by cupric salts. The resulting diacetylenes are important building blocks in the synthesis of natural products [2], monomers, polymers, fundamental host molecules [3], and supramolecular materials useful in electronic and optical industries [4].

Traditionally, the classical oxidative dimerization is carried out in organic solvents such as methanol, acetone, pyridine, cyclohexylamine, and toluene. Recent procedures, however, focused on more environmentally friendly methods applying supercritical fluids [5], water [6], and ionic liquids [7] to minimize using of organic solvents. Efforts to completely eliminate the need for organic solvents by carrying out the reaction on the surface of solid-supports have also been documented [8]. The active surface of some solid-supports including montmorillonite, silica gel, clayfen, and alumina has been confirmed as a practical alternative to organic solvents. The milder conditions, increased selectivity, decreased side reactions, and eco-friendly conditions make this modern procedure more and more attractive. Among others, alumina seems to be a particularly useful reagent, as it can be modified in a variety of ways which enhance its application [9]. For example KF/alumina developed by *Ando et al.* [10] has found a broad application in

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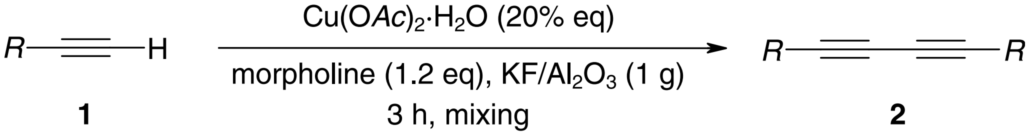


Scheme 1

organic reactions [11], such as elimination [12], addition [13], condensation [14], and epoxidation [15]. *Kabalka et al.* have used this system for the homocoupling of terminal acetylenes in a solvent-free reaction, enhanced by microwave irradiation [8]. They have reported that the best reaction conditions for the *Glaser* reaction using KF/alumina were found to be $CuCl_2$ (3.7 eq) and KF/alumina (40% by weight, 0.6 g) for one mmol terminal alkyne under microwave irradiation for 8 minutes. Although this method benefits from the solvent-free conditions, the use of excess Cu catalyst for only good to moderate yields (up to 75%) suggests a need for further improvement.

We have previously reported that this method can be modified by using of catalytic amounts of a copper halide and alumina under microwave irradiation with moderate yields [16]. We now wish to report that high to excellent yields can be obtained, if the terminal acetylenes are treated on KF/alumina, in the presence of $Cu(OAc)_2 \cdot H_2O$ and morpholine at room temperature (Scheme 1).

Results and Discussions

A variety of terminal alkynes including aliphatic and aromatic acetylenes, propargylamines, and ethers were successfully coupled. The results are summarized in Table 1.

All of the known products exhibit physical and spectral characteristics in accord with literature values. The high yields show that this method is an efficient approach to 1,3-diynes. For example, the treatment of phenylacetylene (**1a**) in the presence of 0.2 eq $Cu(OAc)_2 \cdot H_2O$ on KF/alumina afforded the corresponding 1,4-diphenyl-1,3-butadiyne in 96% yield, obviously more than that reported by *Kabalka* (75%) [8] under microwave irradiation and *Glaser* (40%) [1] by the classical method in organic solvents. The more recent methods using ionic liquids are hardly more efficient [7].

To assay the effect of any contributor in the reaction, we have chosen the homoalkynylation reaction of phenylacetylene. The results are summarized in Table 2. In the absence of morpholine and Cu-catalyst no reaction occurred on KF/alumina (Entry 1). Addition of morpholine to KF/alumina raised the yield of the reaction to 17% (Entry 2). Without morpholine but in the presence of Cu-catalyst the yield is better (27%, Entry 3), but not high enough. As it is shown in Table 2, the presence of KF/alumina seems to be necessary (Entry 4). The best result was obtained by using KF/alumina, morpholine, and $Cu(OAc)_2 \cdot H_2O$ together (Entry 5). These results were confirmed with the homocoupling reaction of methyl-phenylprop-2-ynylamine (**1b**) and 4-(prop-2-ynyl)morpholine (**1d**) (Table 2, Entries 6–11). Avoiding microwave irradiation and performing of these reactions just at room temperature makes this method more attractive and practical.

Table 1. Oxidative homocoupling of terminal acetylenic compounds on KF/alumina at room temperature

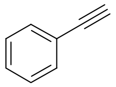
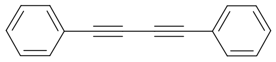
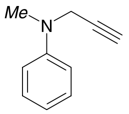
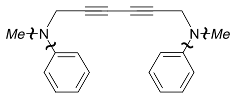
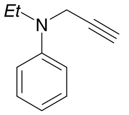
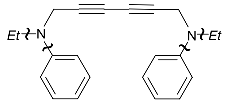
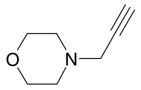
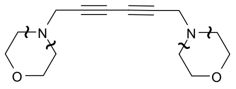
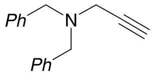
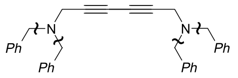
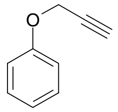
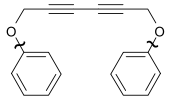
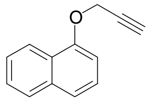
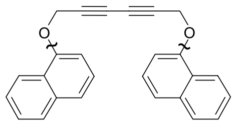
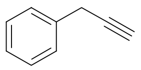
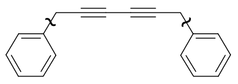
Entry	Substrate	No.	Product	No. Ref.	Yield/%
1		**1a**		**2a** [17]	96
2		**1b**		**2b** [18]	92
3		**1c**		**2c** [19]	93
4		**1d**		**2d** [20]	90
5		**1e**		**2e** [16]	90
6		**1f**		**2f** [21]	65
7		**1g**		**2g** [16]	60
8		**1h**		**2h** [22]	90

Table 2. The effects of reaction contributors

Entry	Alkyne (1.0 mmol)	KF/Alumina (1 g)	Morpholine (1.2 mmol)	$Cu(OAc)_2 \cdot H_2O$ (0.2 mmol)	Yield/%
1	**1a**	+	−	−	0
2	**1a**	+	+	−	17
3	**1a**	+	−	+	27
4	**1a**	−	+	+	64
5	**1a**	+	+	+	96
6	**1b**	+	−	−	0
7	**1b**	−	+	+	45
8	**1b**	+	+	+	92
9	**1d**	+	−	−	0
10	**1d**	−	+	+	43
11	**1d**	+	+	+	90

In addition of mild conditions, the time of the reaction is short enough for preparative purposes.

In summary, we have reported here a facile modified method of the *Glaser* reaction for the preparation of 1,3-diynes from terminal acetylenes in a solvent-free reaction at room temperature, with up to quantitative yields.

Experimental

KF/alumina was prepared as previously described [23]. Mps were determined on a hot stage or oil bath apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 80 MHz in $CDCl_3$ using *TMS* as internal standard. All known products were characterized by comparison of their melting points or NMR spectra with those in literature. The GC was performed with a Varian CP-3800 instrument.

General Procedure for Oxidative Homocoupling of Terminal Acetylenic Compounds on KF/Alumina at Room Temperature

A mixture of 1 mmol acetylenic compound, 1.2 mmol morpholine, and 0.2 mmol copper acetate monohydrate were ground with 1 g KF/alumina in a mortar. The mixture was transferred to a 25 cm^3 flask and stirred for 3 h. The progress of reaction was monitored by TLC and GC. Then the mixture was extracted with ethyl acetate. Evaporation of the solvent gave the crude product, which was purified by flash column chromatography (silica gel; eluent: petroleum ether).

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