Microwave-accelerated solventless Sonogashira-like coupling reaction of 1,1-dibromo-1-alkenes with organic halides on nickel(0) powder-doped KF/Al_2O_3

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Under solvent free and microwave irradiation reaction conditions, a Sonogashira-like coupling reaction of 1,1-dibromo-1-alkenes with organic halides on nickel(0) powder-doped KF/Al_2O_3 has been developed, which generates the corresponding alkynes in moderate to good yields.

Keywords: Sonogashira-like reaction, nickel(0) powder, KF/Al_2O_3

The Sonogashira coupling reaction of terminal alkynes and aryl or alkenyl halides is an efficient route to aryl alkynes.[1] Numerous applications to natural product syntheses have been reported by using Sonogashira coupling reaction, including the construction of complex enediyne antibiotics.[2] The classic Sonogashira reaction is generally carried out in organic solvents such as amines, benzene, dioxane, and DMF along with the complex palladium catalysts which are soluble in these solvents. These soluble palladium reagents tend to be expensive and sometimes difficult to manipulate and recover. In addition, amines such as piperidine, diethylamine and triethylamine are required in most Sonogashira reactions which add to the environmental burden.

Alumina is a particularly useful reagent in organic synthesis because it can be modified in variety of ways that enhance its reactivity. It also obviates a number of environmental problems. For example, using a commercially available alumina potassium fluoride mixture to which we added palladium(0) powder, we were able to carry out Suzuki and Sonogashira coupling reaction on a wide variety of aromatic moieties without the use of solvents.[3]

1,1-Dibromo-1-alkenes, easily prepared from a simple reaction of an aldehyde with carbon tetrabromide and triphenylphosphine,[4] are important starting materials in organic synthesis. There are a few reports on the Pd-catalysed cross coupling reaction of 1,1-dibromo-1-alkenes with organoboronic acids,[5] organoalanes,[6] and organozinc and Grignard reagents,[7] which provide a convenient and straightforward route for the preparation of polysubstituted alkenes. On the other hand, Pd-catalysed hydrogenolysis of 1,1-dibromo-1-alkenes with tributyltin hydride,[8] reductive reaction with hydride anion,[9] reductive debromination with indium metal to vinyl monobromides,[10] and reductive debromination followed rearrangement to alkynes with samarium diiodide[11] have been also surveyed. In addition, 1,1-dibromo-1-alkenes can also be used as equivalents of 1-bromo-1-alkynes in palladium catalysed reaction.[12] However, to the best our knowledge, there is not any report on the cross-coupling reaction of 1,1-dibromo-1-alkenes (as a terminal alkynes synthon equivalents) with organic halides catalysed by zero valent nickel. Here, we report a microwave-accelerated solventless Sonogashira-like coupling reaction of 1,1-dibromo-1-alkenes with organic halides on nickel(0) powder-doped KF/Al_2O_3, which affords the corresponding alkynes in moderate to good yields.

Earlier studies revealed that potassium fluoride is an effective base and palladium(0) powder is an efficient catalyst for solid-phase Sonogashira coupling reaction, and microwave irradiation can accelerate this transformation and save energy.[3d] The Sonogashira-like coupling reaction of 1,1-dibromo-1-alkenes with organic halides was carried out smoothly under solventless and microwave irradiation reaction conditions on nickel(0) powder-doped KF/Al_2O_3. A variety of organic halides, such as *m*-iodonitrobenzene, *p*-iodoanisole, *p*-iodoacetophenone, and *p*-bromonitrobenzene, coupled with a variety of 1,1-dibromo-2-aryl-1-alkenes, such as 1-chloro-4 (2',2'-dibromovinyl)benzene, 1-methyl-4-(2',2'-dibromovinyl) benzene, 1-bromo-3-(2',2'-dibromovinyl)benzene and 2, 2-dibromovinylbenzene to afford the corresponding alkynes in moderate to good yields. Substituent effects were also investigated in series of 1,1-dibromo-2-aryl-1-alkenes as well as aromatic iodides. The results indicated that the reaction is relatively insensitive to the electronic nature of substituents and the substitution pattern on the aromatic rings. Although the addition of CuI greatly accelerates the reaction, it also introduces the homo-coupling byproduct of terminal alkyne (reaction intermediate). The ratio of homo-coupling byproduct to cross-coupling product decreases with decreased amount of CuI used. Halogens in 1,1-dihalo-1-alkenes other than bromine were also examined, as well as in aromatic halides, however, 1,1-dichloro-2-aryl-1-alkenes and chlorobenzene or fluorobenzene are far less reactive, probably due to the stronger carbon–chlorine and carbon–fluorine bonds.

Although the detailed reaction mechanism is not clear, the reaction presumably proceeds through the Ni(0)-catalysed debromination of 1,1-dibromo-1-alkene to form the corresponding terminal alkyne intermediate under the reaction conditions, similar to that of the debromination catalysed by palladium.[12b] This intermediate subsequently coupled with

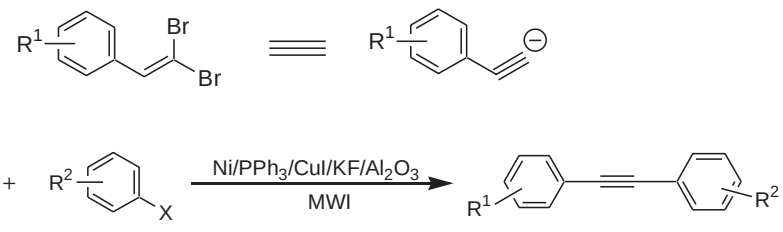

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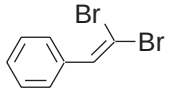
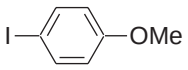
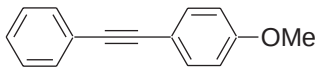
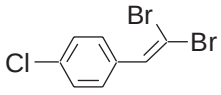
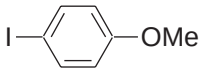
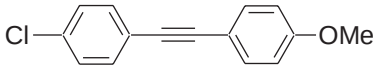
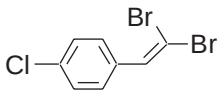
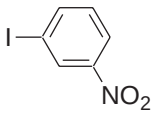
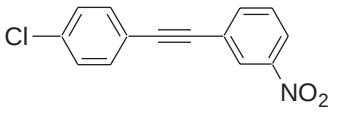
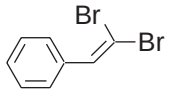
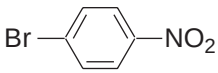
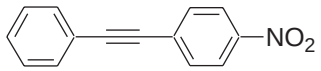
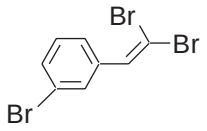
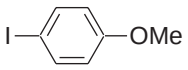
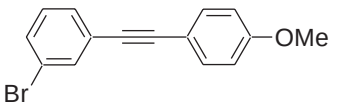
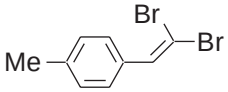
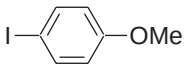
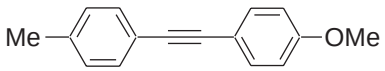
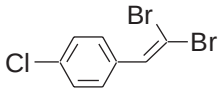
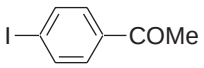
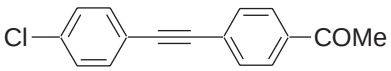
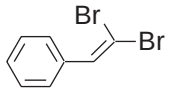
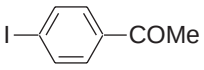
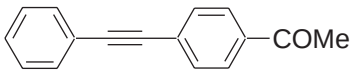
Table 1 Sonogashira-like coupling reaction of 1,1-dibromo-1-alkenes with aromatic halides[a]

Entry	1,1-Dibromo-1-alkenes	Aromatic halides	Products	Yields/% [b]
1				61
2				71
3				70
4				68
5				53
6				75
7				66
8				56

[a]Reactions were carried out by mixing 1 mmol of 1,1-dibromo-1-alkene with 1 mmol of organic halide and 1 g of 40 % KF/Al_2O_3 mixed with 18 mg of nickel(0) powder, 10 mg of cuprous iodide and 156 mg of triphenylphosphine irradiated in a 900W microwave oven (Glanze WD900SL23-2) at medium power and 2450 MHz for 3 min. [b] Isolated yields.

organic halide to generate the cross-coupling product in classic Sonagashira reaction manner. Further investigation is underway.

In conclusion, a novel, reliable and practical synthetic procedure for the preparation of alkynes has been developed, which involves the Sonogashira-like coupling reaction of 1,1-dibromo-1-alkenes with organic halides on nickel(0) powder-doped KF/Al_2O_3 under solvent free and microwave irradiation reaction conditions.

Experimental

Melting points were recorded on a WRS-1B melting point apparatus and are uncorrected. A commercial available Glanze WD900SL23-2, 900W microwave oven was utilised at 2450 MHz. All ^{1}H NMR spectra were recorded on a 60 MHz JEOL MY 60 FT-NMR or a 300 MHz Bruker AZ 300 spectrometer using $CDCl_3$ as solvent. Chemical shift are given as δ value with reference to tetramethylsilane (TMS) as internal standard. IR spectra were obtained by using a Nicolet NEXUS 470 spectrophotometer. The reagents were received from commercial supply without purification prior to use. Products were purified by flash column chromatography.

General procedure for the Sonogashira-like coupling reaction of 1, 1-dibromo-1-alkenes with organic halides: To a mixture of KF/Al_2O_3 (1.00 g, 40 % by weight), nickel(0) powder (18 mg, 99.9+% as nanosize activated powder, 0.3 mmol) and cuprous iodide (10 mg, 0.052 mmol) contained in a clean, dry, round-bottomed flask was added 1,1-dibromo-2-aryl-1-alkene (1.0 mmol), triphenylphosphine (156 mg, 0.6 mmol), and organic halide (1.0 mmol). The solid mixture was stirred at room temperature in the open air until homogeneous. The mixture was stirred at room temperature for an additional 15–20 min to ensure efficient mixing.

The flask was then fitted with a septum (punctured by an 18 gauge needle), placed in a Glanze WD900SL23-2 microwave oven and irradiated at medium power and 2450 MHz for 3 min. After cooling, a small quantity of hexane was added and the slurry stirred at room temperature for an additional 20–30 min to ensure product removal from the surface. The mixture was vacuum filtered through a sintered glass funnel and then the product isolated *via* flash chromatography to yield the corresponding coupling product.

(4-Acetylphenyl)phenylacetylene: m.p. 94–96°C (lit.[13] 95–96°C); IR (KBr) ν_{max}: 3040, 2980, 2940, 2870, 2215, 1690, 1600, 1480; ^{1}H NMR ($CDCl_3$) δ: 7.95 (d, *J* = 7.4 Hz, 2H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.56–7.53 (m, 2H), 7.38–7.35 (m, 3H), 2.60 (s, 3H).

(4-Nitrophenyl)phenylacetylene: m.p. 120–121°C (lit.[13] 120–122°C); IR (KBr) ν_{max}: 3030, 2970, 2935, 2234, 1610, 1490; ^{1}H NMR ($CDCl_3$) δ: 8.21 (d, *J* = 7.6 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.59–7.55 (m, 2H), 7.41–7.37 (m, 3H).

(4-Methoxyphenyl)phenylacetylene: m.p. 58–60°C (lit.[14] 57–61°C); IR (KBr) ν_{max}: 3035, 2982, 2925, 2208, 1600, 1480, 1380; ^{1}H NMR ($CDCl_3$) δ: 7.63–7.34 (m, 7H), 6.83 (d, *J* = 7.0 Hz, 2H), 3.82 (s, 3H).

1-(4-Methoxyphenyl)-2-(4-methylphenyl)acetylene: m.p. 125–126°C (lit.[15] 125.5–126°C); IR (KBr) ν_{max}: 3080, 3045, 2983, 2212, 1600, 1480, 1380; ^{1}H NMR ($CDCl_3$) δ: 7.54–7.48 (m, 4H), 7.18 (d, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 7.2 Hz, 2H), 3.78 (s, 3H), 2.42 (s, 3H).

1-(4-Methoxyphenyl)-2-(4-chlorophenyl)acetylene:[16] m.p. 120.5–121°C; IR (KBr) ν_{max}: 3075, 3030, 2978, 2930, 2224, 1605, 1490, 1385; ^{1}H NMR ($CDCl_3$) δ: 7.52–7.30 (m, 6H), 6.90 (d, *J* = 7.2 Hz, 2H), 3.78 (s, 3H).

1-(4-Methoxyphenyl)-2-(3-bromophenyl)acetylene: m.p. 113–115°C; IR (KBr) ν_{max}: 3050, 3025, 2974, 2209, 1606, 1480, 1380; ^{1}H NMR ($CDCl_3$) δ: 7.56–7.38 (m, 6H), 6.78 (d, *J* = 7.2 Hz, 2H), 3.75 (s, 3H). Anal. Calcd. for $C_{15}H_{11}BrO$: C, 62.74; H, 3.86. Found: C, 62.97; H, 3.53.

1-(4-Acetylhenyl)-2-(4-chlorophenyl)acetylene: m.p. 114–116°C; IR (KBr) ν_{max}: 3038, 2978, 2218, 1695, 1596, 1478, 1382; ^{1}H NMR ($CDCl_3$) δ: 7.67–7.22 (m, 8H), 2.68 (s, 3H). Anal. Calcd. for $C_{16}H_{11}ClO$: C, 75.45; H, 4.35. Found: C, 75.28; H, 4.53.

1-(4-Chlorophenyl)-2-(3-nitrophenyl)acetylene: m.p. 96.5–97.2°C; IR (KBr) ν_{max}: 3083, 3032, 2984, 2928, 2205, 1600, 1400; ^{1}H NMR ($CDCl_3$) δ: 8.02–7.38 (m, 8H). Anal. Calcd. for $C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44. Found: C, 65.55; H, 3.33; N, 5.63.

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