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A simple catalyst system for the palladium-catalyzed coupling of aryl halides with terminal alkynes

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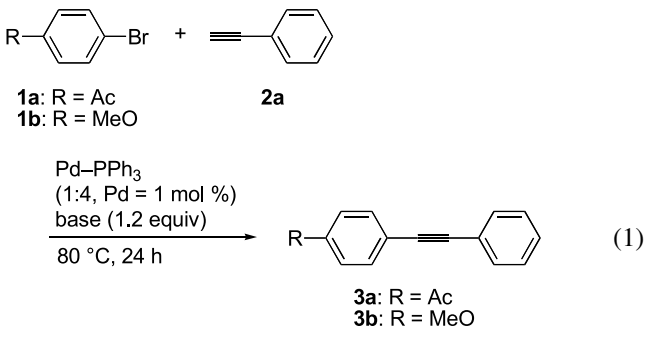
Abstract—A convenient catalyst system consisting of $Pd(OAc)_2$, PPh_3, K_3PO_4 and DMSO was found to be effective for the coupling reaction of aryl halides with terminal alkynes as well as the deacetonative coupling reaction using a 4-aryl-2-methylbut-3-yn-2-ol as a terminal alkyne precursor. An iminophosphine as a ligand worked more effectively for some combination of substrates than triphenylphosphine.

1. Introduction

The palladium-catalyzed alkynylation of aryl and alkenyl halides using terminal alkynes has become one of the most convenient methods to prepare arylalkynes and conjugated enynes,[1,2] which are important precursors for natural products,[3] pharmaceuticals[4] and molecular organic materials.[5] The two earliest studies in this field were reported independently by the Heck's Group[6] and Cassar[7] in 1975. Heck and co-workers used a $Pd(OAc)_2$–PPh_3 complex as a catalyst and triethylamine or piperidine as a base and a solvent, which are based on the Mizoroki–Heck reaction, namely the palladium-catalyzed arylation or alkenylation of alkenes. On the other hand, a palladium catalyst coordinated by PPh_3 in combination with sodium methoxide as a base and DMF as a solvent was disclosed in the Cassar's report. The both methods generally require high temperature (up to 100 °C). Later but in the same year, Sonogashira and Hagihara reported that addition of a catalytic amount of CuI greatly accelerates the reaction to enable the alkynylation at room temperature.[8] Thereafter the Sonogashira–Hagihara coupling, alternatively called simply as to the Sonogashira coupling, had expelled all other protocols from the field of the palladium-catalyzed coupling of aryl or alkenyl halides with terminal alkynes. However, copper-free protocols have recently emerged as matches for the Sonogashira coupling reaction. In 1993, Alami and Linstrumelle found that cyclic amines such as pyrrolidine and piperidine[9] as a base and a solvent enhanced the reaction rate to promote the coupling even at room temperature.[10] Numerous studies on copper-free protocols have followed it, the protocols being called as to the copper-free Sonogashira coupling but not as to the Heck and/or Cassar coupling.

The copper-free protocols thus far reported should be classified into two groups on the basis of reagents used. The first group, which includes the original methods developed by Heck or Cassar, utilizes a simple system consisting of an easily available palladium precursor, a conventional phosphine ligand such as triphenylphosphine, a simple base and a usual solvent. The second group uses expensive and/or elaborated compounds, for example, (1) stoichiometric amount of activators such as silver(I) oxide and ammonium salts,[11] (2) a special medium such as ionic liquids,[12] (3) expensive, difficult to handle ligands such as tri(*t*-butyl)phosphine,[13] or (4) special catalysts such as palladacycles.[14] Most of the methods in the second group achieve higher efficiency and/or wider scope but require one or more compounds that have low accessibility and/or difficulty in handling. Some protocols seem to spoil the



(1)

Keywords: Alkynes; Aryl halides; Coupling reactions; Palladium and compounds.
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Table 1. Palladium-catalyzed coupling of 4-bromoacetophenone or 4-bromoanisole with phenylacetylene[a]

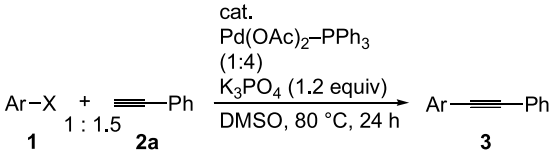
Entry	Aryl bromide	Solvent	Base	**2a/1**	Conv. (%)[b]	Yield (%)[c]
1[d]	**1a**	DMF	NaOMe	1.5	>99	35
2		DMF	NaOMe	1.5	>99	43
3		DMF	K_3PO_4	1.5	>99	83
4		DMSO	K_3PO_4	1.5	>99	89
5		1,4-Dioxane	K_3PO_4	1.5	87	63
6		Toluene	K_3PO_4	1.5	80	56
7		DMSO	Et_3N	1.5	>99	92
8		Piperidine	—	1.5	>99	96
9	**1b**	DMSO	K_3PO_4	1.5	>99	81
10		DMSO	Et_3N	1.5	79	51
11		Piperidine	—	1.5	67	59
12	**1a**	DMSO	K_3PO_4	1.2	>99	87
13	**1b**	DMSO	K_3PO_4	1.2	>99	78

[a] The reaction was carried out in a solvent (1.6 mL) at 80 °C for 24 h using 4-bromoacetophenone or 4-bromoanisole (0.80 mmol), phenylacetylene (1.2 mmol) and a base (0.96 mmol) in the presence of $Pd(OAc)_2$ (8.0 μmol) and PPh_3 (32 μmol).
[b] Determined by the yield of the recovered aryl bromide.
[c] Isolated yield based on the aryl bromide.
[d] A combination of $PdCl_2(PPh_3)_2$ (8.0 μmol) and PPh_3 (16 μmol) was used instead of $Pd(OAc)_2$–PPh_3.

merit to omit the copper catalyst. Consequently, the simplest methods to couple aryl and alkenyl halides with terminal alkynes thus far available should be the following three procedures: (1) the Heck's method with an amine as a base and a solvent,[15] (2) its descendant using a cyclic amine as a base and a solvent reported by Alami and Linstrumelle,[10,16] and (3) the Cassar's method featuring an inorganic base.[17,18] All of these do not require any commercially unavailable reagents except for the substrates themselves. The Cassar's method is hardly explored in contrast that the amine-based methods seem to have become mature. Here, we report a convenient system, based on the Cassar's original report, for the coupling reaction of aryl or alkenyl halides with terminal alkynes, consisting solely of commercially available and easy to handle materials.

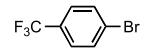
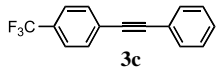
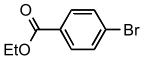
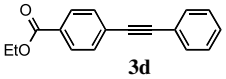
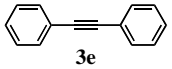
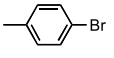
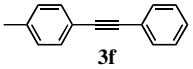
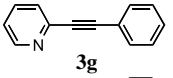
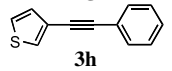
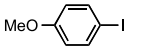
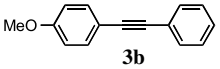
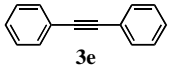
2. Results and discussion

We first examined the effect of bases and solvents in the coupling of 4-bromoacetophenone (**1a**) with phenylacetylene (**2a**) using a catalyst (1 mol%) consisting of a palladium precursor and PPh_3 (4 equiv to Pd) at 80 °C for 24 h (Eq. 1). Under the Cassar's conditions,[7] which employ $PdCl_2(PPh_3)_2$–PPh_3 (1/2) as a catalyst, NaOMe as a base, and DMF as a solvent, the reaction of **1a** with **2a** (1:1.5) afforded only 35% yield of 4-acetylphenyl(phenyl)acetylene



(2)

Table 2. Coupling of aryl halides with phenylacetylene[a]

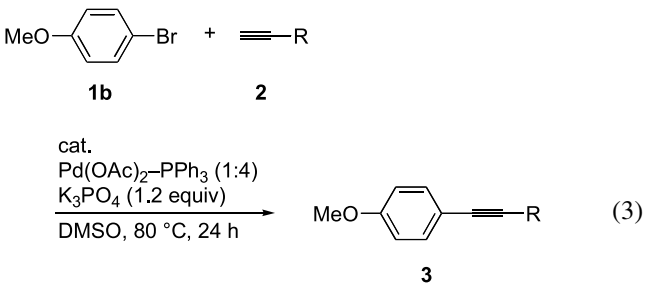
Entry	Aryl halide **1**	Pd (mol%)	Product **3**	Yield (%)[b]
1		3	 **3c**	94
2		3	 **3d**	93
3		1	 **3e**	81
4		1	 **3f**	80
5		1	 **3g**	89
6		3	 **3h**	84
7[c]		3	 **3b**	80
8		3	 **3e**	89

[a] The reaction was carried out in DMSO (1.6 mL) at 80 °C for 24 h using an aryl halide (0.80 mmol), phenylacetylene (1.2 mmol), K_3PO_4 (0.96 mmol), $Pd(OAc)_2$ and PPh_3 (4.0 equiv to Pd).
[b] Isolated yield based on the aryl halide.
[c] The reaction was carried out at 60 °C.

(**3a**) with a complete consumption of **1a** (entry 1 of Table 1). As $Pd(OAc)_2$, a more easily available precursor than $PdCl_2(PPh_3)_2$, in combination with PPh_3 (4 equiv to Pd) scored a comparable yield (entry 2), we used $Pd(OAc)_2$–PPh_3 as a catalyst thereafter. The change of the base from NaOMe to K_3PO_4 raised the yield to 83% (entry 3).[19] Then we compared DMF with other solvents to find that DMSO[20] was rather superior to DMF, and much more effective than 1,4-dioxane and toluene (entries 4–6). Use of triethylamine instead of K_3PO_4 in DMSO, which recalls the Heck's method,[6] also was found to be effective (entry 7), and piperidine as a solvent and a base, the system of Alami and Linstrumelle,[10] was even more efficient (entry 8). However, with these organic bases, an electron-rich aryl halide, 4-bromoanisole (**1b**), coupled sluggishly with **2a** to give only $<60\%$ yield of **3b** after 24 h, whereas K_3PO_4 worked well also with **1b** (entries 9–11). The coupling of **1a** or **1b** with a decreased amount of **2a** resulted in a slightly lower yield (entries 12 and 13).

The protocol can be applied to various combinations of substrates, though some reactions required 3 or 5 mol% of the catalyst for completion within 24 h. Phenylacetylene coupled with phenyl bromides having an electron-withdrawing or -donating group other than acetyl or methoxy at the *para* position in high yields (Eq. 2 and entries 1–4 of Table 2). The reaction is applicable also to heteroaryl bromides in addition to an aryl iodide and a triflate (entries 5–8), where a lower temperature raised the yield in the reaction of an active electrophile such as 4-iodoanisole.

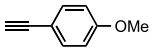
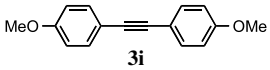
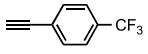
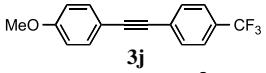
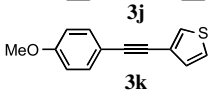
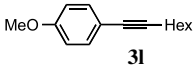
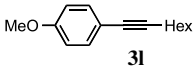
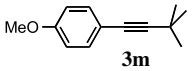
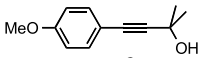
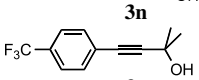
Next, we examined the scope on terminal alkynes in the coupling with 4-bromoanisole (**1b**) (Eq. 3 and Table 3). Phenylacetylenes substituted by an electron-withdrawing or -donating group as well as a heteroarylacetylene also participated in the coupling reaction (entries 1–3). In addition to diarylacetylenes, alkyl(aryl)acetylenes were obtained from aliphatic alkynes (entries 4–6). In the coupling of 1-octyne, use of increased amounts of K_3PO_4 and the alkyne was much more effective than that of an increased amount of the palladium catalyst. The Pd–PPh_3 catalyst is applicable also to the coupling of 2-methylbut-3-yn-2-ol, whose coupling products are known to undergo deacetonation to give terminal alkynes (entry 7).[21] 4-Bromo(trifluoromethyl)benzene also coupled with 2-methylbut-3-yn-2-ol, where a lower reaction temperature was found to be more suitable (entry 8).



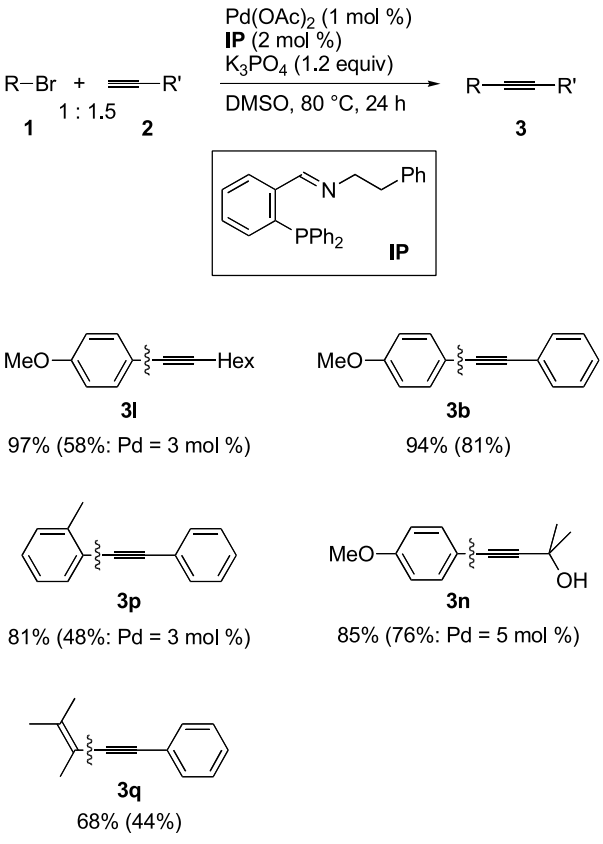
(3)

As we have described thus far, a palladium complex coordinated by triphenylphosphine, one of the most common phosphine ligands, conveniently catalyzes the coupling of various combinations of aryl halides with alkynes. However, sometimes the yields are not sufficient. For such cases, a palladium complex having *N*-(2-diphenylphosphinobenzylidene)-2-phenylethylamine (**IP**)[22] as a ligand was found to be more effective. **IP** can be easily prepared by condensation of 2-(diphenylphosphino)benzaldehyde[23] with 2-phenylethylamine, both of which are commercially available. The results using $Pd(OAc)_2$ and **IP** in a 1:2 ratio compared with those with

Table 3. Coupling of aryl bromides with terminal alkynes[a]

Entry	Alkyne **2**	Pd (mol%)	Product **3**	Yield (%)[b]
1		3	 **3i**	82
2		3	 **3j**	71
3		3	 **3k**	72
4		3	 **3l**	58
5[c]		1	 **3l**	84
6		3	 **3m**	86
7		5	 **3n**	76
8[d]		5	 **3o**	77

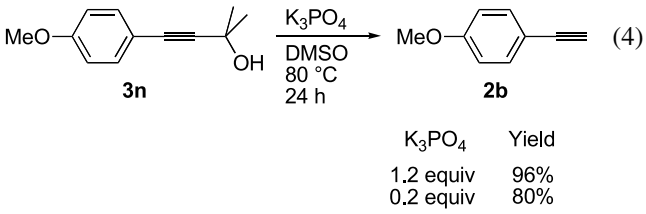
[a] The reaction was carried out in DMSO (1.6 mL) at 80 °C for 24 h using an aryl bromide (0.80 mmol), a terminal alkyne (1.2 mmol), K_3PO_4 (0.96 mmol), $Pd(OAc)_2$ and PPh_3 (4.0 equiv to Pd).
[b] Isolated yield based on the aryl bromide.
[c] K_3PO_4 (1.6 mmol) and 1-octyne (1.6 mmol) were used.
[d] 4-Bromo(trifluoromethyl)benzene was used instead of 4-bromoanisole. Reaction temperature = 70 °C.

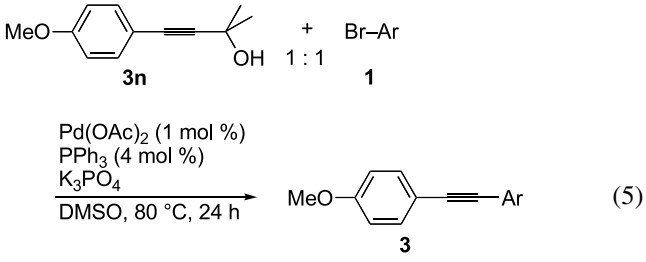


Scheme 1. Palladium–**IP**-catalyzed coupling of organic halides with terminal alkynes. The results using PPh_3 (4.0 equiv to Pd) instead of **IP** are shown in parenthesis.

triphenylphosphine are summarized in Scheme 1. The yield in the coupling of an aliphatic alkyne drastically increased without use of increased amounts of some of the reagents, though the effect of **IP** was not so drastic in the reaction of phenylacetylene. A sterically hindered aryl bromide, 2-methylbut-3-yn-2-ol and an alkenyl bromide also received the benefit of the iminophosphine ligand.

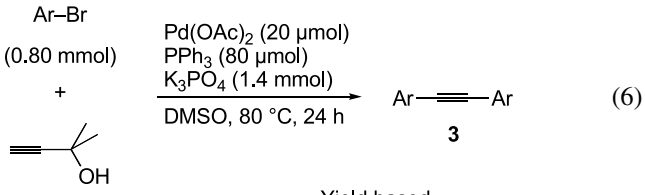
2-Methylbut-3-yn-2-ol can be regarded as a masked acetylene, one of whose acetylenic protons is protected with a hydroxy(dimethyl)methyl group. The protecting group can be removed as acetone by treatment of a base such as KOH or NaOH.[21] We expected that K_3PO_4, the base used in our coupling reaction, also would mediate the deacetonation, and found that arylpropargyl alcohol **3n** underwent deacetonation by treatment of 0.2 or 1.2 equiv of K_3PO_4 in DMSO at 80 °C for 24 h, giving 4-methoxyphenylacetylene in 80% or 96% yield, respectively (Eq. 4). However, any examination aiming the K_3PO_4-mediated deacetonation in the presence of a palladium catalyst failed. Thus, the coupling-deacetonation sequence using 2-methylbut-3-yn-2-ol in combination with 4-methoxyphenyl or 4-(trifluoromethyl)phenyl bromide afforded only a trace amount of the corresponding terminal alkyne,[24] probably because most of them were consumed through the influence of the palladium catalyst. In sharp contrast, in the presence of an aryl bromide, the deacetonation proceeded successfully, being accompanied by the coupling reaction to give diarylacetylenes (Eq. 5). The deacetonative coupling effectively proceeded with phenyl bromide in addition to that having an electron-withdrawing group, whereas the coupling reaction with 4-bromoanisole resulted in a low yield, which was recovered in some extent by using an excess amount of K_3PO_4.



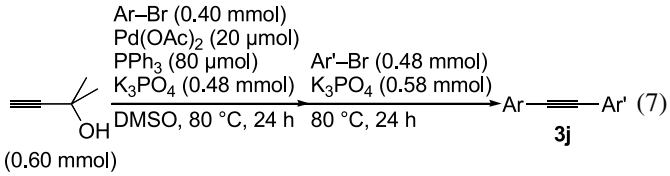


Ar	Amount of K_3PO_4	Yield	Product
Ph	1.2 equiv	84%	**3b**
4-CF_3-C_6H_4	1.2 equiv	93%	**3j**
4-MeO-C_6H_4	1.2 equiv	60%	**3i**
4-MeO-C_6H_4	3.0 equiv	73%	**3i**

Besides the above two-pot reaction consisting of the coupling using 2-methylbut-3-yn-2-ol and the deacetonative coupling, the one-pot version through a coupling-deacetonation-coupling sequence also was found to be possible.[25,26] Symmetrical diarylacetylenes were obtained by treatment of an aryl bromide and 2-methylbut-3-yn-2-ol (2:1.1) with a catalytic amount of $Pd(OAc)_2$–PPh_3 (1/4) and K_3PO_4 at 80 °C for 48 h (Eq. 6). Although the propargyl alcohol coupled twice with 4-(trifluoromethyl)phenyl bromide eliminating acetone in a good yield, the reaction of 4-bromoanisole gave the desired diarylacetylene only in 42% yield, which was accompanied by formation of a considerable amount (ca. 20% estimated by ^1H NMR) of 1-(4-methoxylphenyl)-2-phenylethyne. The phenyl group of the unsymmetrical diarylacetylene must be derived from triphenylphosphine, where the 4-methoxyphenyl group in exchange for the phenyl group should be transferred from the bromine to the phosphorous atom of the phosphine through the palladium.[27] Unsymmetrical diarylacetylenes can be prepared in moderate yields with a similar procedure, where a second aryl bromide as well as two-thirds amount of K_3PO_4 were added after 24 h interval (Eq. 7). The order of adding aryl bromides did not affect so significantly the yields of 1-(4-methoxyphenyl)-2-[4-(trifluoromethyl)-phenyl]ethyne (**3j**).



Ar	Yield based on Ar–Br	Product
4-CF_3-C_6H_4	76%	**3r**
4-MeO-C_6H_4	42%	**3i**



Ar	Ar'	Yield based on Ar–Br
4-MeO-C_6H_4	4-CF_3-C_6H_4	62%
4-CF_3-C_6H_4	4-MeO-C_6H_4	52%

In conclusion, we have disclosed a simple catalyst system, consisting merely of commercially available, relatively inexpensive materials, for the palladium-catalyzed coupling reaction of aryl halides with terminal alkynes. The protocol is not only as simple as the Casser's original method but also shows much wider scope than that, where electron-rich and -poor aryl electrophiles having a bromide, iodide or triflate as a leaving group coupled with various aryl and aliphatic terminal alkynes. Another feature of this protocol is the simple catalyst system applicable also to the deacetonative coupling reaction of α-dimethyl-γ-arylpropargyl alcohols with aryl halides. Symmetrical and unsymmetrical diarylacetylenes can be obtained by simple one-pot procedures from aryl bromides and 2-methylbut-3-yn-2-ol without adding other reagents. We also described efficiency of **IP**, prepared from commercially available reagents in one step, in the present coupling reaction.

3. Experimental

3.1. General

All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard Schlenk technique under a nitrogen atmosphere. Nuclear magnetic resonance spectra were taken on a Varian Gemini 2000 (^{1}H, 300 MHz) or a JEOL JNM LA-500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) spectrometer using tetramethylsilane (^{1}H and ^{13}C) as an internal standard. Preparative recycling gel permeation chromatography was performed with JAI LC-908 equipped with JAIGEL-1H and -2H using chloroform as an eluent. Unless otherwise noted, reagents were commercially available and used without further purification. Anhydrous DMF, DMA, and DMSO were purchased from Aldrich Chemical Co. and Kanto Chemicals and used as received. Toluene and 1,4-dioxane were distilled from sodium/benzophenone ketyl. 3-Ethynylthiophene[28] and *N*-(2-diphenylphosphinobenzylidene)-2-phenylethylamine (**IP**)[22a] were prepared according to the literature methods.

3.2. Palladium-catalyzed coupling of aryl halides with terminal alkynes. A general procedure (Tables 2 and 3, and Scheme 1)

A solution of an aryl halide (0.80 mmol), an alkyne (1.2 mmol), $Pd(OAc)_2$, a ligand (PPh_3: 4.0 equiv to Pd, or **IP**: 2.0 equiv to Pd), and K_3PO_4 (204 mg, 0.96 mmol) in DMSO (1.6 mL) was degassed by four freeze-thaw cycles. After stirring at 80 °C for 24 h, water (30 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL×3). The combined organic layer was washed with brine (30 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification with PTLC, column chromatography, or gel permeation chromatography gave the corresponding arylalkyne.

3.2.1. 1-(4-Methoxyphenyl)-2-(3-thienyl)ethyne (3k). A pale yellow powder; mp 63–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3H), 6.84–6.90 (m, 2H), 7.18 (dd, J=5.0, 1.1 Hz, 1H), 7.28 (dd, J=5.0, 3.1 Hz, 1H), 7.42–7.47 (m, 2H), 7.48 (dd, J=3.1, 1.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 83.1, 88.8, 114.0, 115.3, 122.6, 125.2, 128.0, 129.9, 133.0, 160.0. Anal. Calcd for $C_{13}H_{10}OS$: C, 72.87; H, 4.70. Found: C, 73.14; H, 4.87.

Other coupling products are the compounds already reported in literature. Their spectroscopic data are as follows.

3.2.2. 1-(4-Acetylphenyl)-2-phenylethyne (3a).[13b] A white powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.62 (s, 3H), 7.35–7.41 (m, 3H), 7.52–7.58 (m, 2H), 7.59–7.65 (m, 2H), 7.92–7.98 (m, 2H).

3.2.3. 1-(4-Methoxyphenyl)-2-phenylethyne (3b).[29] A white powder; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.83 (s, 3H), 6.85–6.91 (m, 2H), 7.28–7.37 (m, 3H), 7.44–7.53 (m, 4H).

3.2.4. 1-Phenyl-2-[4-(trifluoromethyl)phenyl]ethyne (3c).[30] A white powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.41 (m, 3H,), 7.52–7.58 (m, 2H), 7.60–7.64 (m, 4H).

3.2.5. Ethyl 4-(phenylethynyl)benzoate (3d).[11c] A pale yellow powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (t, J=7.2 Hz, 3H), 4.39 (q, J=7.2 Hz, 2H), 7.34–7.40 (m, 3H), 7.52–7.62 (m, 4H), 8.00–8.06 (d, J=8.4, 2 H).

3.2.6. Diphenylethyne (3e).[31] A white powder; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31–7.37 (m, 6H), 7.52–7.56 (m, 4H).

3.2.7. 1-(4-Methylphenyl)-2-phenylethyne (3f).[31] A pale yellow powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3H), 7.13–7.19 (m, 2H), 7.30–7.39 (m, 3H), 7.40–7.46 (m, 2H), 7.50–7.56 (m, 2H).

3.2.8. 1-Phenyl-2-(2-pyridyl)ethyne (3g).[32] A colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22–7.28 (m, 1H), 7.34–7.40 (m, 3H), 7.51–7.56 (m, 1H), 7.58–7.64 (m, 2H), 7.65–7.73 (m, 1H), 8.61–8.65 (m, 1H).

3.2.9. 1-Phenyl-2-(3-thienyl)ethyne (3h).[33] A pale yellow powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (dd, J=4.8,

1.2 Hz, 1H), 7.30 (dd, J=4.8, 2.7 Hz, 1H), 7.32–7.39 (m, 3H), 7.49–7.55 (m, 3H).

3.2.10. Bis(4-methoxyphenyl)ethyne (3i).[26] A yellow powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.83 (s, 6H), 6.84–6.90 (m, 4H), 7.42–7.48 (m, 4H).

3.2.11. 1-(4-Methoxyphenyl)-2-[4-(trifluoromethyl)-phenyl]ethyne (3j).[31] A white powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.84 (s, 3H), 6.87–6.93 (m, 2H), 7.46–7.52 (m, 2H), 7.57–7.62 (m, 4H).

3.2.12. 1-(4-Methoxyphenyl)-1-octyne (3l).[34] A pale brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, J= 7.0 Hz, 3H), 1.25–1.39 (m, 4H), 1.40–1.51 (m, 2H), 1.53–1.66 (m, 2H), 2.38 (t, J=7.2 Hz, 2H), 3.79 (s, 3H), 6.79–6.82 (m, 2H), 7.28–7.35 (m, 2H).

3.2.13. 1-(4-Methoxyphenyl)-3,3-dimethyl-1-butyne (3m).[35] A pale yellow powder; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 9H), 3.79 (s, 3H), 6.77–6.83 (m, 2H), 7.29–7.35 (m, 2H).

3.2.14. 4-(4-Methoxyphenyl)-2-methylbut-3-yn-2-ol (3n).[34] A pale yellow powder; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.61 (s, 6H), 1.99 (s, 1H), 3.81 (s, 3H), 6.81–6.86 (m, 2H), 7.32–7.37 (m, 2H).

3.2.15. 4-[4-(Trifluoromethyl)phenyl]-2-methylbut-3-yn-2-ol (3o).[36] A brown powder; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.63 (s, 6H), 2.03 (s, 1H), 7.49–7.59 (m, 4H).

3.2.16. 1-Phenyl-2-(2-tolyl)ethyne (3p).[31] A brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.52 (s, 3H), 7.13–7.21 (m, 1H), 7.22–7.25 (m, 2H), 7.30–7.40 (m, 3H), 7.47–7.58 (m, 3H).

3.2.17. 3,4-Dimethyl-1-phenylpent-3-en-1-yne (3q).[37] A brown oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.79 (s, 3H), 1.89 (s, 3H), 2.02 (s, 3H), 7.22–7.34 (m, 3H), 7.39–7.45 (m, 2H).

3.3. Deacetonation of 4-(4-methoxyphenyl)-2-methylbut-3-yn-2-ol (Eq. 4)

A solution of 4-(4-methoxyphenyl)-2-methylbut-3-yn-2-ol (**3n**, 76.6 mg, 0.403 mmol) and K_3PO_4 (102 or 16.3 mg, 0.48 or 0.077 mmol) in DMSO (0.80 mL) was degassed by four freeze-thaw cycles. After stirring at 80 °C for 24 h, water (30 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL×3). The combined organic layer was washed with brine (30 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification with PTLC (hexane/EtOAc=4:1) gave 4-methoxyphenylethyne.

3.4. Deacetonative coupling of 4-(4-methoxyphenyl)-2-methylbut-3-yn-2-ol with terminal alkynes (Eq. 5)

A solution of 4-(4-methoxyphenyl)-2-methylbut-3-yn-2-ol (**3n**, 76.3 mg, 0.401 mmol), an aryl bromide (0.40 mmol), $Pd(OAc)_2$ (0.90 mg, 4.0 μmol), PPh_3 (4.2 mg, 16 μmol), and K_3PO_4 (102 or 254 mg, 0.48 or 1.2 mmol) in DMSO (0.80 mL) was degassed by four freeze-thaw cycles. After stirring at 80 °C for 24 h, water (30 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL× 3). The combined organic layer was washed with brine (30 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification with PTLC (hexane/EtOAc=3:1 for **3b**, 2:1 for **3i**, 4:1 for **3j**) gave **3b**, **3i** or **3j**.

3.5. One-pot synthesis of symmetrical diarylacetylenes from an aryl bromide and 2-methylbut-3-yn-2-ol (Eq. 6)

A solution of an aryl bromide (0.80 mmol), 2-methylbut-3-yn-2-ol (37 mg, 0.44 mmol), $Pd(OAc)_2$ (4.5 mg, 20 μmol), PPh_3 (21 mg, 80 μmol), and K_3PO_4 (309 mg, 1.46 mmol) in DMSO (0.80 mL) was degassed by four freeze-thaw cycles. After stirring at 80 °C for 48 h, water (30 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL×3). The combined organic layer was washed with brine (30 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification with column chromatography (hexane for **3r**, hexane/EtOAc=10:1 for **3i**) gave **3r** or **3i**.

3.5.1. Bis[4-(trifluoromethyl)phenyl]ethyne (3r).[13f] A white powder; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62–7.67 (m, 8H).

3.6. One-pot synthesis of an unsymmetrical diarylacetylene from two different aryl bromides and 2-methylbut-3-yn-2-ol

A solution of an aryl bromide (0.40 mmol), 2-methylbut-3-yn-2-ol (50 mg, 0.60 mmol), $Pd(OAc)_2$ (4.5 mg, 20 μmol), PPh_3 (21 mg, 80 μmol), and K_3PO_4 (102 mg, 0.48 mmol) in DMSO (0.80 mL) was degassed by four freeze-thaw cycles. After stirring at 80 °C for 24 h, another aryl bromide (0.48 mmol) and K_3PO_4 (123 mg, 0.58 mmol) were added. After the reaction mixture was stirred at 80 °C for 24 h, water (30 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL×3). The combined organic layer was washed with brine (30 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification with column chromatography (hexane/EtOAc=5:1) gave **3j**.

Acknowledgements

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