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CuI/iodine-mediated homocoupling reaction of terminal alkynes to 1,3-diynes

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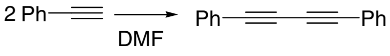
ABSTRACT

A facile and efficient pathway for CuI/iodine-mediated homocoupling reaction of terminal alkynes to symmetrical 1,4-disubstituted 1,3-diynes in good to excellent yields was reported.

Homocoupling reaction of terminal alkynes to give 1,3-diynes is highly important for a number of applications, particularly in the construction of linearly π-conjugated acetylenic oligomers and polymers,[1] natural products,[2] supramolecular materials,[3] and molecular recognition processes.[4] Traditional methods for the synthesis of 1,3-diynes include Glaser oxidative dimerization of terminal alkynes,[5] various improved Glaser oxidative homocoupling reactions of terminal alkynes,[6–8] and Sonogashira coupling.[9] Catalytic systems mediated by palladium, Pd(0) or Pd(II), are arguably the most mild, efficient, and selective for homocoupling reactions of terminal alkynes.[10–17] However, palladium reagents are expensive, and they often required air-sensitive and expensive phosphine ligands as well as amine reagents. Here, we report our finding of CuI/iodine mediated homocoupling reaction of terminal alkynes in detail.

Recently, our research interest focused on Baylis-Hillman chemistry.[18] Our initial study was to attempt the addition reaction of phenylacetylene to Baylis-Hillman adducts. However, no product was observed in the presence of Na_2CO_3 in DMF under various temperature. Subsequently, we tried to further activate phenylacetylene with CuI and iodine. Interestingly, after addition of CuI (10 mol %) and iodine (10 mol %) to the above reaction system, the homocoupling product of phenylacetylene was detected. This encouraging result led us to explore the homocoupling reaction of phenylacetylene. After some optimization (Scheme 1, Table 1), the best result for homocoupling of phenylacetylene leading to 1,4-diphenyl-1,3-butadiyne in 99% yield was afforded using phenylacetylene (1 mmol), CuI (1 mmol), I_2 (1 mmol), Na_2CO_3 (2 mmol) in DMF (1 mL) at 80 °C for 3 h (Table 1, entry 6). We have also performed a number of control experiments: (1) in the absence of CuI, no homocoupling product of phenylacetylene was observed, with only (iodoethynyl)benzene was obtained in 35% yield (Table 1, entry 8); (2) in the presence of CuI (5–70 mol %), the reaction proceeded slowly in relatively low yields (Table 1, entries 2–5); (3) in the absence of iodine or at room temperature, the poor yields were obtained (Table 1, entries 7, 9); (4) a 96% yield was observed when Na_2CO_3 was replaced by NaOAc (Table 1, entry 10); (5) when Na_2CO_3 was replaced by Et_3N, the reaction conducted slowly, and a low yield was observed (Table 1, entry 11).



Scheme 1.

Under above optimized condition, we have examined the substrate scope of this reaction. Our experiments indicate that a variety of terminal alkynes including aliphatic and aromatic acetylenes successfully underwent the homocoupling to produce the corresponding 1,3-diynes in good to excellent yields (Scheme 2, Table 2). Also, the reaction was sluggish in the case of the aliphatic alkyne, propargyl alcohol, giving a relatively low yield after a longer reaction time (Table 2, entries 8–11). Especially, the homocoupling of 1-ethynyl-4-fluoro- benzene needed prolonged reaction time (10 h, Table 2, entry 7). This is likely due to the presence a fluoro atom which decreases the reactivity of 1-ethynyl-4-fluorobenzene.

Scheme 3 illustrates the proposed mechanism for the sp–sp homocoupling reaction of terminal alkynes. The alkynylcopper intermediate **A** is formed from the reaction of a terminal alkyne and CuI in the presence of Na_2CO_3, and then it undergoes smooth

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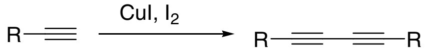
Table 1
Screening reaction parameters for the homocoupling of phenylacetylene

Entry	CuI (equiv)	Iodine (equiv)	Base (2 equiv)	Time (h)	Temp. (°C)	Yield[a] (%)
1	0.05	1.0	Na_2CO_3	24	rt	—[b]
2	0.05	1.0	Na_2CO_3	24	80	85
3	0.1	1.0	Na_2CO_3	24	80	87
4	0.5	1.0	Na_2CO_3	12	80	92
5	0.7	1.0	Na_2CO_3	8	80	95
6	1.0	1.0	Na_2CO_3	3	80	99
7	1.0	1.0	Na_2CO_3	24	rt	32
8	0	1.0	Na_2CO_3	24	80	—[c]
9	1.0	0	Na_2CO_3	24	80	18
10	1.0	1.0	NaOAc	3	80	96
11	1.0	1.0	Et_3N	20	80	72

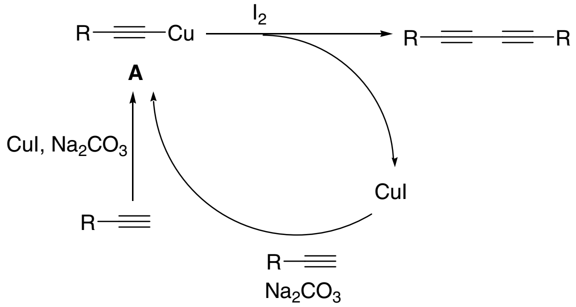
[a] Isolated yield.
[b] A trace amount of (iodoethynyl)benzene was formed.
[c] (Iodoethynyl)benzene was afforded in 35% yield.



Scheme 2.

Table 2
CuI/iodine-mediated homocoupling reaction of terminal alkynes

Entry	R	Time (h)	Isolated yield (%)
1	C_6H_5	3	99
2	$4\text{-}MeC_6H_4$	3	94
3	$4\text{-}EtC_6H_4$	3	96
4	$4\text{-}n\text{-}PrC_6H_4$	3	95
5	$4\text{-}n\text{-}C_5H_{11}C_6H_4$	3	92
6	$4\text{-}MeOC_6H_4$	3	93
7	$4\text{-}FC_6H_4$	10	92
8	$n\text{-}C_4H_9$	5	86
9	$n\text{-}C_5H_{11}$	5	87
10	$n\text{-}C_6H_{13}$	5	89
11	$HOCH_2$	5	70



Scheme 3.

oxidative dimerization with iodine to the sp–sp homocoupling product.

In conclusion, we have successfully developed a facile and efficient pathway for CuI/iodine-mediated homocoupling reaction of terminal alkynes.[19] The great attractiveness of the current method lies in simple procedure (without exclusion of air or moisture), the use of a solid base (Na_2CO_3) instead of amines and good to excellent yields. Furthermore, the application of this methodology for the cross-coupling of terminal alkynes is ongoing and will be reported in due course.

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19. To a stirred solution of alkyne (1 mmol) in DMF (1 mL), CuI (1 mmol), Na_2CO_3 (2 mmol), and iodine (1 mmol) were added successively. The resulting mixture was then allowed to react at 80 °C in air. Progress of this reaction was monitored by TLC. After completion of the reaction, 5 mL of ethyl acetate was added. The mixture was filtered through a pad of diatomite under reduced pressure, and the filtration residue was washed with ethyl acetate. The filtrate was then washed with saturated $Na_2S_2O_3$, saturated brine, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The residue was then was purified by TLC using petroleum ether as eluent to afford the corresponding 1,3-diynes. All of the products are known and were characterized by comparison of their spectral data with those of authentic samples.
Selected data of 1,4-bis(4-ethylphenyl)-1,3-butadiyne: IR (KBr): 3041, 2963, 2132, 1599, 1457, 1370, 828 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.44 (d, J = 8.0 Hz, 4H), 7.16 (d, J = 8.0 Hz, 4H), 2.65 (q, J = 7.5 Hz, 4H), 1.23 (t, J = 7.5 Hz, 6H). MS: m/z = 258 (M^+, 100%).