CuSCN-mediated homocoupling of terminal alkynes to 1,3-diynes using 4-nitrobenzenediazonium tetrafluoroborate as oxidant

Haidong Liu[a,c], Bo Chen[a], Jin Cai[b], Junqing Chen[b] and Min Ji[a,c]*

[a]*School of Biological Science and Medical Engineering, Southeast University, Si Pai Lou 2#, Nanjing city 210096, P.R. China*
[b]*School of Chemistry and Chemical Engineering, Southeast University Si Pai Lou 2#, Nanjing city 210096, P.R. China*
[c]*Suzhou Key Laboratory of Biomaterials and Technologies & Collaborative Innovation Center of Suzhou Nano Science and Technology, Suzhou, 215123, P.R. China*

Eleven 1,3-diynes have been prepared by a highly efficient base-catalysed homocoupling of terminal alkynes mediated by a novel combination of CuSCN/4-nitrobenzenediazonium tetrafluoroborate.

Keywords: 4-nitrobenzenediazonium tetrafluoroborate, homocoupling reaction, oxidant, terminal alkynes, 1,3-diynes, CuSCN, DBU

1,3-Diyne derivatives play a very important role in natural products,[1] oligomers and polymers,[2] molecular recognition processes,[3] industrial and pharmaceutical intermediates,[4] and in electronic and optical materials.[5] Homocoupling of terminal alkynes to give 1,3-diynes was pioneered by Glaser in 1869.[6,7] In recent years, Cu(I) or Cu(II) salt mediated Glaser coupling and related modified methods are still widely applied in the synthesis of conjugated diynes.[8] Traditional homocoupling is catalysed by copper salts in the presence of a base and a stoichiometric amount of an oxidant such as O_2[9,10] an α-halocarbonyl compound,[11–13] nitrobenzene,[14] iodine,[15–17] and others.[18–20] However, to the best of our knowledge, the study of 4-nitrobenzenediazonium tetrafluoroborate (NBDTF) as an oxidant in Glaser coupling reactions has not been reported.

In this paper, we report a highly efficient preparation of symmetrical 1,3-diynes from terminal alkynes in the presence of a strong base and Cu(I)/NBDTF.

Results and discussion

Recently, our research interest has focused on Sonogashira cross-coupling reactions.[21,22] Our initial study was to attempt the addition reaction of phenylacetylene to 4-nitrobenzenediazonium tetrafluoroborate **2a** in the presence of 1.0 equiv. CuSCN and 1.0 equiv. TMEDA without use of palladium reagent under argon. However, no desired product was observed in the presence of Cs_2CO_3 in DMF at various temperatures. Interestingly, the homocoupling product of phenylacetylene was isolated in 87% yield. This encouraging result led us to explore the homocoupling reaction of phenylacetylene (I; R = Ph) using arenediazonium salts as oxidant.

In order to optimise the yield, the reaction conditions were varied by adjusting several parameters, including oxidant, solvent, base and copper salt loading. The homocoupling reaction of phenylacetylene **1a** was chosen as the model. As listed in Table 1, the oxidant plays an important role in the reaction. When the model reaction was performed in the presence of CuSCN (1.0 equiv.) and TMEDA (1.0 equiv.) in DMF at room temperature (25–30 °C), 4-nitrobenzenediazonium tetrafluoroborate exhibited the highest reactivity, and an 87% yield of the desired oxidative coupling product **3a** was isolated (entry 1). 4-Methylbenzenediazonium tetrafluoroborate **2b** and benzenediazonium tetrafluoroborate **2c** were found to be inferior, and only 11–34% yields of **3a** were obtained (entries 2–3). Then the effect of solvent on the model reaction was examined. In MeCN, a 91% yield of **3a** was obtained (entry 4). When the reaction was performed in toluene or

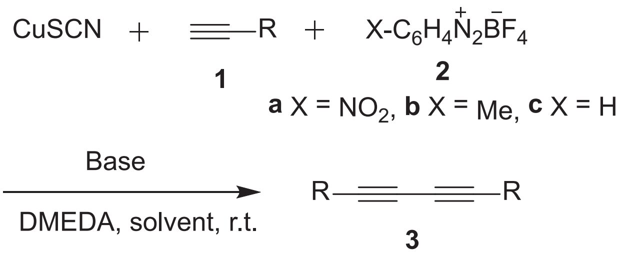
Table 1 Effect of variation of solvent, base and catalyst-loading on the yield of 1,4-diphenyldiyne (**3a**; R = H) formed by the homocoupling of phenylacetylene (**1a**; R = H) catalysed by CuSCN/DMEDA in the presence of X-benzenediazonium tetrafluoroborate **2a–c** (Scheme 1)[a]

Entry	Oxidant (equiv.)	CuSCN (equiv.)	Solvent	Base (equiv.)	Yield/(%)[b]
1	**2a** (1.1)	1.0	DMF	Cs_2CO_3, 1.0	87
2	**2b** (1.1)	1.0	DMF	Cs_2CO_3, 1.0	11
3	**2c** (1.1)	1.0	DMF	Cs_2CO_3, 1.0	34
4	**2a** (1.1)	1.0	MeCN	Cs_2CO_3, 1.0	91
5	**2a** (1.1)	1.0	Toluene	Cs_2CO_3, 1.0	65
6	**2a** (1.1)	1.0	DCM	Cs_2CO_3, 1.0	38
7	**2a** (1.1)	1.0	MeCN	K_2CO_3, 1.0	83
8	**2a** (1.1)	1.0	MeCN	DBU, 1.0	97
9	**2a** (1.1)	0.2	MeCN	DBU, 1.0	37
10	**2a** (1.1)	1.0	MeCN	DBU, 1.0	94
11	**2a** (1.1)	–	MeCN	DBU, 1.0	–
12	–	1.0	MeCN	DBU, 1.0	–
13	**2a** (1.1)	1.0	MeCN	DBU, 1.0	83[c]
14	nitrobenzene (1.1)	1.0	MeCN	DBU, 1.0	–

[a]Reaction conditions: (**1a**; R = H) (1.0 mmol), **2a–c** (1.1 mmol) and CuSCN/DMEDA in solvent (4 mL) within 20 min under an air atmosphere. [b]Isolated yield.
[c]In the absence of TMEDA.

---

* Correspondent. E-mail: 101010516@seu.edu.cn



Scheme 1

dichloromethane, lower yields of **3a** was observed (entries 4–6). We screened three bases and observed a clear activation tendency in the following order: K_2CO_3 < Cs_2CO_3 < DBU (entries 7, 4 and 8). When the ratio of CuSCN to **1a** was 0.2:1 and 1:1 (entries 9, 10), 37 and 94% of cross-coupled conjugated 1,3-diyne **3a** was obtained. We also performed three control experiments: (1) in the absence of CuSCN, no homocoupling product **3a** was observed (entry 11); (2) in the absence of 4-nitrobenzenediazonium tetrafluoroborate **2a**, no desired product **3a** was obtained (entry 12); (3) in the absence of TMEDA, only 83% of the corresponding 1,3-diyne **3a** was obtained (entry 13); and (4) no homocoupling product **3a** was obtained when using nitrobenzene as the oxidant (entry 14).

With the optimised conditions in hand (Table 1, entry 8), we examined the generality and scope of this method for the homocoupling of various substituted terminal alkynes. Gratifyingly, the reaction demonstrated wide scope for the structure of terminal alkynes and the yields and rates depended upon the substrates. Terminal aromatic alkynes with various alkyl substituents successfully underwent the homocoupling to produce the corresponding products in very good to excellent yields (Table 2, entries 2–4). For halophenyl alkynes **1e–f**, the corresponding products were obtained in slightly lower yields due to the sublimation of the corresponding 1,3-diynes (entries 5–6). In the case of 4-methoxyphenylacetylene, the reaction was sluggish due to the low solubility of the corresponding copper acetylide, but when the reaction was performed in DMF, a good yield was obtained (entry 7). For aliphatic alkynes **1h–j** and propargyl alcohol **1k**, the corresponding products were also obtained in moderate to good yields (entries 8–11). All compounds are known and were characterised by their m.p., MS, and ^{1}H and ^{13}C NMR spectra.[23–30]

Table 2 Yields of 1,4-aryldiynes **3a–k** formed by the homocoupling of arylacetylenes **1a–k** catalysed by CuSCN/DMEDA in the presence of 4-nitrobenzenediazonium tetrafluoroborate **2a**[a]

Entry	1	Yield/%[b]
1	Phenylacetylene (**1a**)	97
2	4-Methylphenylacetylene (**1b**)	94
3	4-Ethylphenylacetylene (**1c**)	93
4	1-Ethynyl-4-pentylbenzene (**1d**)	95
5	4-Fluorophenylacetylene (**1e**)	89
6	4-Chlorophenylacetylene (**1f**)	86
7	4-Methoxyphenylacetylene (**1g**)	92[c]
8	1-Hexyne (**1h**)	85
9	1-Heptyne (**1i**)	87
10	1-Octyne (**1j**)	88
11	Propargyl alcohol (**1k**)	76

[a] Reaction conditions: A mixture of (**1a–k**) (1.0 mmol), **2a** (1.1 mmol), and CuSCN/DMEDA in MeCN (4 mL) was treated at r.t. for 20 min under an air atmosphere.

[b] Isolated yield.

[c] The reaction was performed in DMF.

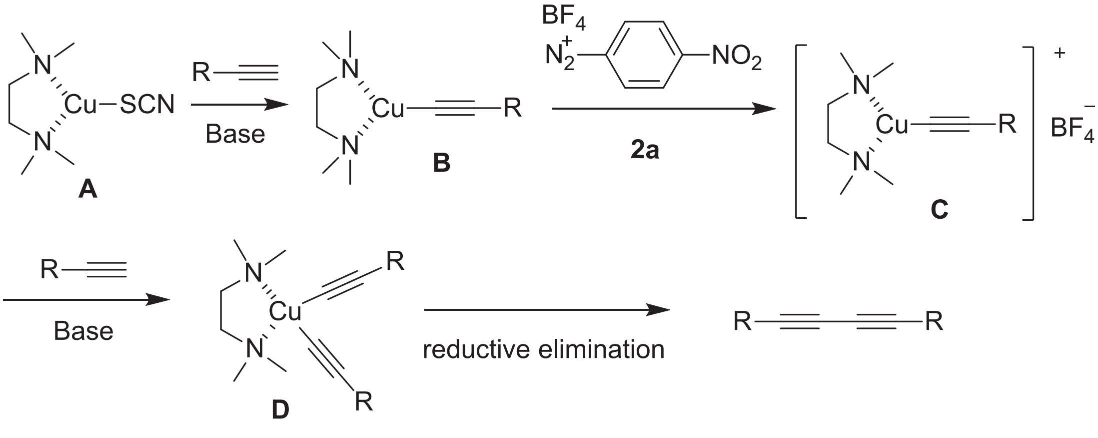
Based on previous reports,[22] a possible mechanism for the sp–sp homocoupling reaction of terminal alkynes is depicted in Scheme 2. The initial reaction of a terminal alkyne with intermediate **A** results in the formation of intermediate **B**. Next, the intermediate **C** was formed by its oxidation by 4-nitrobenzenediazonium tetrafluoroborate **2a** with release of nitrobenzene (which was unambiguously characterised by MS and ^{1}HNMR). The intermediate **C** further reacted with a terminal alkyne to give the intermediate **D**, reductive elimination of which afforded the corresponding 1,3-diyne.

Experimental

All reagents including analytical-grade solvents were purchased from Sigma–Aldrich (USA), Aladdin (P.R. China), or Sinopharm Chemical Reagent (P.R. China) and used without further purification. Melting points are uncorrected. NMR spectra were obtained on a Bruker 400 MHz spectrometer (^{1}H NMR at 400 Hz, ^{13}C NMR at 100 Hz) in $CDCl_3$ or DMSO-d_6 using TMS as internal standard. Chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. Mass spectra (MS) were obtained from Finnigan (USA) MAT-95 Spectrometry Services. Silica gel (200–300 µm) for flash chromatography was purchased from Qingdao Haiyang Chemical (P.R. China).

Synthesis of 1,3-diynes; general procedure

Terminal alkynes (1.0 mmol), CuSCN (1.0 mmol), MeCN (4 mL) and TMEDA (1.0 mmol) were added to a reaction bottle that was equipped



Scheme 2

with a stirrer bar under air. DBU (1.0 equiv.) was added to the reaction mixture dropwise over 10 min. The resulting mixture was stirred at ambient temperature (25–30 °C) for 10–30 min. A suspension of **2a** (1.1 equiv.) in MeCN (1 mL) was added to the reaction bottle under an air atmosphere over 20 min. The mixture was stirred at ambient temperature for 20 min, and then it was mixed with a small amount of silica gel and concentrated. It was purified by column chromatography using hexane to afford the pure products. All products **3a**–**k** are known and all the melting points are uncorrected.

1,4-Diphenylbutadiyne (**3a**)[23,24,26,29]

White powder, 98 mg (97%), m.p. 86–88 °C (hexane) [lit.[26] m.p. 86–87 °C]; $R_f = 0.9$ (hexane). ^{1}H NMR ($CDCl_3$): δ (ppm) 8.27 (m, 4H), 7.73 (m, 2H), 7.57 (m, 4H); ^{13}C NMR ($CDCl_3$): δ (ppm) 132.8, 129.2, 128.7, 121.9, 81.6, 74.0; MS (EI) for $C_{16}H_{10}$ $[M]^+$ calcd 202.1; found: 202.1.

1,4-Bis(4-methylphenyl)-1,3-butadiyne (**3b**)[23,25,26,29,31]

White powder, 108 mg (94%), m.p. 138–140 °C (hexane); $R_f = 0.9$ (hexane) [lit.[31] m.p. 138–140 °C]; ^{1}H NMR ($CDCl_3$): δ (ppm) 7.43 (d, $J = 8.0$ Hz, 4H), 7.15 (d, $J = 8.0$ Hz, 4H), 2.39 (s, 6H); ^{13}C NMR ($CDCl_3$): δ (ppm) 139.5, 132.1, 129.2, 118.9, 121.9, 81.6, 73.5, 21.6; MS (EI) for $C_{18}H_{14}$ $[M]^+$ calcd 230.1; found: 230.1.

1,4-Bis(4-ethylphenyl)-1,3-butadiyne (**3c**)[26,29]

White powder, 139 mg (93%), m.p. 96–97 °C (hexane) [lit.[26] m.p. 96–97 °C]; $R_f = 0.9$ (hexanes);.^{1}H NMR ($CDCl_3$): δ (ppm) 7.40 (d, $J = 8.0$ Hz, 4H), 7.18 (d, $J = 8.0$ Hz, 4H), 2.68 (d, $J = 7{,}6$ Hz, 4H), 1.26 (t, $J = 7.6$ Hz, 6H); ^{13}C NMR($CDCl_3$): δ (ppm) 145.7, 132.5, 128.0, 119.1, 81.6, 73.5, 28.9, 15.2; MS (EI) for $C_{20}H_{18}$ $[M]^+$ calcd 258.1; found: 258.1.

1,4-Bis(4-pentylphenyl)-1,3-butadiyne (**3d**)[26,29]

White powder, 163 mg (95%), m.p. 84–85 °C (hexane) [lit.[26] m.p. 84 °C]; $R_f = 0.9$ (hexane). ^{1}H NMR ($CDCl_3$): δ (ppm) 7.45 (d, $J = 8.4$ Hz, 4H), 7.16 (d, $J = 8.4$ Hz, 4H), 2.63 (t, $J = 7{,}6$, 8.0 Hz, 4H), 1.63 (t, $J = 7{,}2$, 7,6 Hz, 4H), 1.36 (m, 8H), 0.92 (t, $J = 6.8$ Hz, 6H); ^{13}C NMR ($CDCl_3$): δ (ppm) 144.5, 132.4, 128.5, 119.1, 81.6, 73.5, 36.0, 31.4, 22.5, 13.9; MS (EI) for $C_{26}H_{30}$ $[M]^+$ calcd 342.2; found: 342.2.

1,4-Bis(4-fluorophenyl)-1,3-butadiyne (**3e**)[26,29]

White powder, 106 mg (89%), m.p. 190–192 °C (hexane) [lit.[26] m.p. 192–193 °C]; $R_f = 0.9$ (hexane). ^{1}H NMR ($CDCl_3$): δ (ppm) 7.54 (m, 4H), 7.06 (m, 4H); ^{13}C NMR ($CDCl_3$): δ (ppm) 164.3, 161.8, 134.6, 117.9, 116.0, 80.4, 73.6; MS (EI) for $C_{16}H_8F_2$ $[M]^+$ calcd 238.1; found: 238.1.

1,4-Bis(4-chlorophenyl)-1,3-butadiyne (**3f**)[29,30]

White powder, 116 mg (86%), m.p. 256–257 °C (hexane) [lit.[30] m.p. 253 °C]; $R_f = 0.9$ (hexane). ^{1}H NMR ($CDCl_3$): δ (ppm) 7.46 (d, $J = 8.4$ Hz, 4H), 7.33 (d, $J = 8.8$ Hz, 4H); ^{13}C NMR ($CDCl_3$): δ (ppm) 133.7, 128.9, 114.0, 80.4, 74.7; MS (EI) for $C_{16}H_8Cl_2$ $[M]^+$ calcd 270.0; found: 270.0.

1,4-Bis(4-methoxyphenyl)-1,3-butadiyne (**3g**)[23,26,29,30]

White powder, 121 mg (92%), m.p. 140–142 °C (hexane); $R_f = 0.9$ (hexane) [lit.[30] m.p. 142 °C]; ^{1}H NMR ($CDCl_3$): δ (ppm) 7.49 (d, $J = 9.2$ Hz, 4H), 6.89 (d, $J = 8.8$ Hz, 4H), 3.85 (s, 6H); ^{13}C NMR ($CDCl_3$): δ (ppm) 160.3, 134.0, 124.2, 114.2, 81.23, 73.0. 55.3; MS (EI) for $C_{18}H_{14}O_2$ $[M]^+$ calcd 262.1; found: 262.1.

Dodeca-5,7-diyne (**3h**)[29]

Colourless oil, 69 mg (85%); $R_f = 0.9$ (hexane); ^{1}H NMR ($CDCl_3$): δ (ppm) 2.27 (t, $J = 6.8$ Hz, 4H), 1.51 (m, 8H), 0.91 (t, $J = 6.8$ Hz, 6H); ^{13}C NMR ($CDCl_3$): δ (ppm) 65.3, 30.4, 21.9, 19.7, 13.5; MS (EI) for $C_{12}H_{18}$ $[M]^+$ calcd 162.1; found: 162.1.

Tetradeca-6,8-diyne (**3i**)[26,29]

Colourless oil, 83 mg (87%); $R_f = 0.9$ (hexane); ^{1}H NMR ($CDCl_3$): δ (ppm) 2.26 (t, $J = 6.8$ Hz, 4H), 1.32–1.57 (m, 12H), 0.91 (t, $J = 6.8$ Hz, 6H); ^{13}C NMR ($CDCl_3$): δ (ppm) 65.3, 31.0, 28.0, 22.1, 19.2, 13.9; MS (EI) for $C_{14}H_{22}$ $[M]^+$ calcd 190.2; found: 190.2.

Hexadeca-7,9-diyne (**3j**)[23,27,29]

Colourless oil, 96 mg (88%); $R_f = 0.9$ (hexane); ^{1}H NMR ($CDCl_3$): δ (ppm) 2.27 (t, $J = 6.8$ Hz, 4H), 1.27–1.56 (m, 16H), 0.91 (t, $J = 6.8$ Hz, 6H); ^{13}C NMR ($CDCl_3$): δ (ppm) 65.3, 31.4, 28.3, 24.7, 22.3, 20.1, 13.8; MS (EI) for $C_{16}H_{26}$ $[M]^+$ calcd 218.2; found: 218.2.

Hexa-2,4-diyne-1,6-diol (**3k**)[23,28,30]

White powder, 58 mg (63%), m.p. 112–113 °C (ethyl acetate/hexane) [lit.[23] m.p. 112–114 °C]; $R_f = 0.9$ (ethyl acetate/hexane = 1:2). ^{1}H NMR (-$DMSOd_6$): δ (ppm) 4.83 (t, 1H), 3.50 (m, 2H), 2.39 (t, $J = 6.8$, 2H); ^{13}C NMR ($CDCl_3$): δ (ppm) 66.4, 59.9, 23.5; MS (EI) for $C_6H_6O_2$ $[M]^+$ calcd 110.0; found: 110.0.

We are grateful for financial support from the National Basic Research Program of China (No.2013AA032205).

Received 19 February 2016; accepted 1 March 2016
Paper 1603930 doi: 10.3184/174751916X14622729380672

References

1 L.K. Annabelle and R.R. Tykwinski, *Angew. Chem. Int. Ed.*, 2006, **45**, 1034.
2 R.E. Martin and F. Diederich, *Angew. Chem. Int. Ed.*, 1999, **38**, 1350.
3 J. Breitenbach, J. Boosfeld and F. Vogtle, *Comprehensive supramolecular chemistry*, eds V. Vogtle. Pergamon, Oxford, 1996, Vol. 2, chap. 2, pp. 29–67.
4 M.M. Haley and R.R. Tykwinski, *Carbon-rich compounds: from molecules to materials*. Wiley-VCH, Weinheim, 2006.
5 F. Diederich, P.J. Stang and R.R. Tykwinski, *Acetylene chemistry: chemistry, biology and material science*. Wiley-VCH, Weinheim, 2005.
6 C. Glaser, *Ber. Dtsch. Chem. Ges.*, 1869, **2**, 422.
7 C. Glaser, *Ann. Chem. Pharm.*, 1870, **154**, 137.
8 K. Kamata, S. Yamaguchi, M. Kotani, K. Yamaguchi and N. Mizuno, *Angew. Chem. Int. Ed.*, 2008, **47**, 2407.
9 J.-H. Li, Y. Liang and Y.-X. Xie, *J. Org. Chem.*, 2005, **70**, 4393.
10 A.S. Batsanov, J.C. Collings and J.J. Zhu, *Org. Chem.*, 2005, **70**, 703.
11 A. Lei, M. Srivastava and X. Zhang, *J. Org. Chem.*, 2002, **67**, 1969.
12 W.A. Chalifoux, M.J. Ferguson and R.R. Tykwinski, *Eur. J. Org. Chem.*, 2007, **6**, 1001.
13 R. Rossi, A. Carpita and C. Bigelli, *Tetrahedron Lett.*, 1985, **26**, 523.
14 P. Siemsen, R.C. Livingston and F. Diederich, *Angew. Chem. Int. Ed.*, 2000, **39**, 2632.
15 J. Yan, F. Lin and Z. Yang, *Synthesis*, 2007, **9**, 130.
16 Q. Liu and D.J. Burton, *Tetrahedron Lett.*, 1997, **38**, 4371.
17 D.-f. Li, K. Yin, J. Li and X.-sh. Jia, *Tetrahedron Lett.*, 2008, **49**, 5918.
18 J.-H. Li, Y. Liang and X.-D. Zhang, *Tetrahedron*, 2005, **61**, 1903.
19 Y. Liao, R. Fathi and Z. Yang, *Org. Lett.*, 2003, **5**, 909.
20 S.V. Damle, D. Seomoon and P.H. Lee, *J. Org. Chem.*, 2003, **68**, 7085.
21 R. Chinchilla and C. Najera, *Chem. Rev.*, 2007, **107**, 874.
22 R. Chinchilla and C. Najera, *Chem. Soc. Rev.*, 2011, **40**, 5084.
23 T.-M. Wu, Sh.-H. Huang and F.-Y. Tsai, *Appl. Organometal. Chem.*, 2011, **25**, 395.
24 Q. Liu and D.J. Burton, *Tetrahedron Lett.*, 1997, **38**, 4371.
25 J.-H. Li, Y. Liang and X.-D. Zhang, *Tetrahedron*, 2005, **61**, 1903.
26 Y. Kun, L. Chunju, L. Jian and J. Xueshun, *Green Chem.*, 2011, **13**, 591.
27 S.V. Damle, D. Seomoon and P.H. Lee, *J. Org. Chem.*, 2003, **68**, 7085.
28 N.A. Milas and O.L. Mageli, *J. Am. Chem. Soc.*, 1953, **75**, 5970.
29 D.-f. Li., K. Yin, J. Li and X.-sh. Jia, *Tetrahedron Lett.*, 2008, **49**, 5918.
30 E. Merkul, D. Urselmann and T.J.J. Müller, *Eur. J. Org. Chem.*, 2011, **2**, 238.
31 J.-H. Li, Y. Liang and X.-D. Zhang, *Tetrahedron*, 2005, **61**, 1903.