Res Chem Intermed
DOI 10.1007/s11164-013-1042-2

Synthesis of symmetrical 1,3-diynes in water-soluble ionic liquid [DMIM]Me_2PO_4

**Wensheng Zhang · Wenjing Xu · Fei Zhang ·
Hui Jin · Yuzhe Wang · Jitao Li**

Received: 23 December 2012 / Accepted: 10 January 2013

Abstract Treatment of a variety of arynes in water-soluble ionic liquid [DMIM]-Me_2PO_4 in the presence of catalytic amount of CuI and inexpensive $NH_3 \cdot H_2O$ under aerobic conditions afforded the corresponding symmetrical 1,3-diynes in high yields. The ionic liquid could be reused for at least five times without apparent decrease of the yield.

Keywords Diyne · Glaser reaction · CuI · Synthesis · Ionic liquid

Introduction

Conjugated diynes are recurring building blocks for the synthesis of natural products, pharmaceuticals, and bioactive compounds with antiinflammatory, antifungal, anti-HIV, antibacterial, or anticancer activities [1–9]. In addition, conjugated diynes have found wide applications in the construction of industrial intermediates and materials, particularly macrocyclic annulenes, organic conductors, supramolecular switches, and carbon-rich materials [10–14]. Therefore, much attention [15–36] has been devoted to the development of new and efficient methods for the synthesis of diynes. A classical and effective route for preparing symmetrical 1,3-diynes has been the homocoupling of volatile and savory terminal alkynes [37].

W. Zhang (✉) · W. Xu · Y. Wang · J. Li
School of Biological and Chemical Engineering, Jiaozuo Teachers' College, Shanyang Road 998,
Jiaozuo 450001, China
e-mail: tongjizws@163.com

F. Zhang
Jiaozuo Vocational Education Center, Huayuan Road 57, Jiaozuo 454001, China

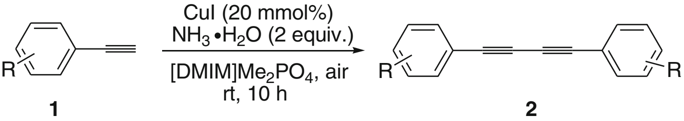
H. Jin
School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University,
Shanghai 200240, China

Ionic liquids have become solvents of choice in many applications [38–39]. More often than not, symmetrical 1,3-diynes were obtained in organic solvents such as DMF, DMSO, and MeCN. Yadav's group reported that terminal alkynes undergo oxidative-coupling smoothly in the presence of the CuCl–TMEDA catalytic system in water-insoluble ionic liquid [BMIM]PF_6 under aerobic conditions [39]. In this article, with the desire to avoid the use of toxic organic solvent, we developed a facile method for the synthesis of symmetrical diynes **2** from commercially available arynes in water-soluble ionic liquid [DMIM]Me_2PO_4 (1,3-dimethylimidazolium dimethylphosphate) (Scheme 1) in the presence of CuI and inexpensive $NH_3 \cdot H_2O$.

Results and discussion

Our initial attempt began with an effort to optimize reaction conditions for the oxidation coupling of terminal acetylenes. Phenylacetylene **1a** and $NH_3 \cdot H_2O$ were chosen as the model substrate and base, respectively, for the optimization process (Table 1, entries 1–8). The experiment was carried out with **1a** (1 mmol), CuI (20 mmol %), and $NH_3 \cdot H_2O$ (2 equiv.) in water-insoluble ionic liquids (10 mL). The reaction mixture was stirred at room temperature for 10 h. A series of water-insoluble ionic liquids including 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM]PF_6), 1-hexyl-3-methylimidazolium tetrafluoroborate ([HMIM]BF_4), 1-ethyl-3-methylimidazolium bis[(trifluoromethyl) sulfonyl]imide ([EMIM]Tf_2N), and 1-butyl-3-methylimidazolium trifluoromethanesulfonate ([BMIM]OTf) were screened. The expected product **2a** was afforded in only 22–37 % yields (Table 1, entries 1–4). Fortunately, when water-soluble [DMIM]Me_2PO_4 was used, an excellent yield of the desired **2a** was obtained (Table 1, entry 5). The screening of various bases (Table 1, entries 6–9) revealed that $NH_3 \cdot H_2O$ was the best choice and organic bases such as Et_3N, DBU, DABCO, and Et_2NH were less effective for the water-soluble ionic liquid system.

Other terminal acetylenes besides phenylacetylene were employed successfully using the optimized conditions (Table 2, entries 9–12). This ionic liquid system proved to be applicable for arynes bearing both electron-donating groups such as Me and MeO and electron-withdrawing groups like Cl, Br, and F, affording products **2b**–**2i** in 80–94 % yields (Table 2, entries 2–9). The steric hindrances of the substituents like Cl, Br, and OMe on the *ortho*- position of the aromatic ring did not alter the efficiency of the reaction (Table 2, entries 7–9).



Scheme 1 Synthesis of symmetrical diynes from arynes in water-soluble ionic liquid

Table 1 Optimization of the reaction conditions based on **1a**

Entry	Solvent	Base	**1a** yield (%)[a]
1	[BMIM]PF_6	$NH_3·H_2O$	37
2	[HMIM]BF_4	$NH_3·H_2O$	33
3	[EMIM]Tf_2N	$NH_3·H_2O$	22
4	[BMIM]OTf	$NH_3·H_2O$	30
5	[DMIM]Me_2PO_4	$NH_3·H_2O$	94
6	[DMIM]Me_2PO_4	Et_3N	55
7	[DMIM]Me_2PO_4	DBU	48
8	[DMIM]Me_2PO_4	DABCO	49
9	[DMIM]Me_2PO_4	Et_2NH	55

[a] Isolated yield

Experimental

Melting points were recorded using a WRS-1B digital melting point apparatus and are uncorrected. ^1H NMR spectra were recorded using Bruker DPX-400 spectrometer in $CDCl_3$ with $SiMe_4$ as an internal standard. MS data were measured using a Varian-310 mass spectrometer. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with HuanghaiGF_{254} silica gel-coated plates. Column chromatography was carried out using 300- to 400-mesh silica gel at medium pressure.

1,3-Diynes (**2**); general procedure

Arynes **1** (1 mmol), $NH_3·H_2O$ (2 equiv.) and CuI (0.2 mmol) were dissolved in [DMIM]Me_2PO_4 (10 mL), and the reaction system was stirred at room temperature for 10 h. After the completion of the reaction screened by TLC, the mixture was filtered and extracted with Et_2O (10 × 3 mL). The ionic liquid layer was collected and dried under reduced pressure at 80 °C for 6 h before reuse. The combined ether layer was washed with water, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by column chromatography afforded products **2**. The structure of products **2** were fully consistent with their ^1H NMR data [15–36]. The IL could be reused for at least five times without effect of the yield.

1,4-Diphenylbuta-1,3-diyne (**2a**)

Yield: 182 mg (90 %); white solid; mp 86–86.5 °C (lit.[33] 86–87 °C); $R_f = 0.9$ (EtOAc-petroleum ether, 1:20). ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.32–7.37$ (m, 6H, ArH), 7.52–7.54 (m, 4H, ArH). MS (ESI): $m/z = 202$ [M^+].

1,4-Bis(4-methylphenyl)buta-1,3-diyne (**2b**)

Yield: 212 mg (92 %); white solid; mp 182.1–182.5 °C (lit.[34] 182–183 °C, lit.[35] 137–138 °C); $R_f = 0.85$ (EtOAc-petroleum ether, 1:20). ^1H NMR (400 MHz,

Table 2 Synthesis of symmetrical diynes **2** in [DMIM]Me_2PO_4

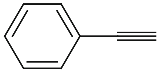
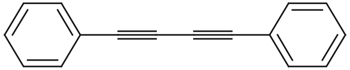
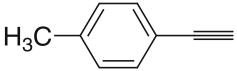
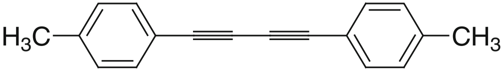
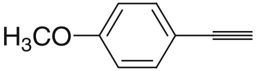
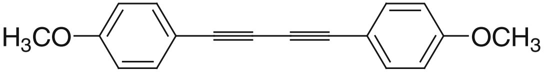
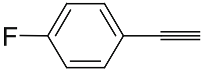
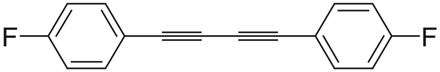
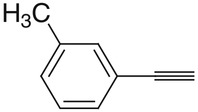
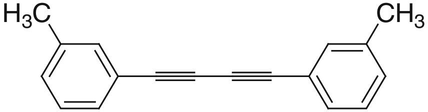
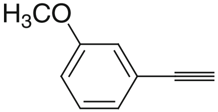
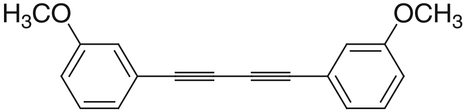
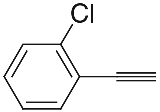
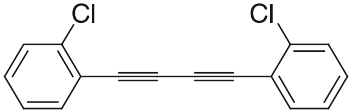
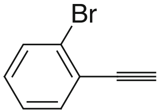
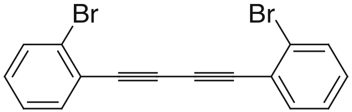
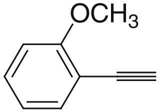
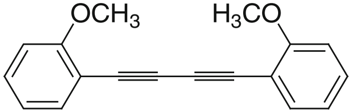
Entry	Substrate **1**		Product **2**		Yield of **2** (%)[a]
1		**1a**		**2a**	94
2		**1b**		**2b**	90
3		**1c**		**2c**	88
4		**1d**		**2d**	80
5		**1e**		**2e**	87
6		**1f**		**2f**	86

Table 2 continued

Entry	Substrate **1**		Product **2**		Yield of **2** (%)[a]
7		**1g**		**2g**	84
8		**1h**		**2h**	82
9		**1i**		**2i**	82

[a] Isolated yields based on arynes **1**

$CDCl_3$): δ = 2.36 (s, 6H, CH_3), 7.14 (d, *J* = 8.0 Hz, 4H, ArH), 7.42 (d, *J* = 8.0 Hz, 4H, ArH). MS (ESI): *m*/*z* = 230 [M^+].

1,4-Bis(4-methoxyphenyl)buta-1,3-diyne (**2c**)

Yield: 228 mg (87 %); white solid; mp 139–140.5 °C (lit.[34] 140–141 °C); $R_f = 0.8$ (EtOAc-petroleum ether, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 6H, CH_3), 6.85 (d, *J* = 8.8 Hz, 4H, ArH), 7.46 (d, *J* = 8.8 Hz, 4H, ArH).

1,4-Bis(4-fluorophenyl)buta-1,3-diyne (**2d**)

Yield: 138 mg (56 %); white solid; mp 187.3–188 °C (lit.[34] 194–195 °C, lit.[35] 187–189 °C); $R_f = 0.8$ (EtOAc-petroleum ether, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (t, *J* = 8.5 Hz, 4H, ArH), 7.49–7.53 (m, 4H, ArH).

1,4-Bis(3-methylphenyl)buta-1,3-diyne (**2e**)

Yield: 205 mg (89 %); white solid; mp 68–68.5 °C (lit.[34] 68–70 °C, lit.[36] 74–75 °C); $R_f = 0.85$ (EtOAc-petroleum ether, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.34 (s, 6H, CH_3), 7.17–7.35 (m, 8H, ArH).

1,4-Bis(3-methoxyphenyl)buta-1,3-diyne (**2f**)

Yield: 233 mg (89 %); yellow solid; mp 91.8–92.9 °C (lit.[34, 35] 92–93 °C); $R_f =$ 0.8 (EtOAc-petroleum ether, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 6H, CH_3), 6.93–7.24 (m, 8H, ArH).

1,4-Bis(2-chlorophenyl)buta-1,3-diyne (**2g**)

Yield: 230 mg (85 %); yellow solid; mp 139–140.5 °C (lit.[35] 138–140 °C); $R_f = 0.75$ (EtOAc-petroleum ether, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.33 (m, 4H, ArH), 7.42 (d, *J* = 9.2 Hz, 2H, ArH), 7.58 (d, *J* = 6.0 Hz, 2H, ArH).

1,4-Bis(2-bromophenyl)buta-1,3-diyne (**2h**)

Yield: 300 mg (83 %); yellow solid; mp 132.5–133.8 °C; $R_f = 0.8$ (EtOAc-petroleum ether, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.31 (m, 4H, ArH), 7.57–7.62 (m, 4H, ArH).

1,4-Bis(2-methoxyphenyl)buta-1,3-diyne (**2i**)

Yield: 223 mg (85 %); white solid; mp 137.8–149.5 °C (lit.[33] 138–140 °C); $R_f = 0.8$ (EtOAc-petroleum ether, 1:20). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (s, 6H, CH_3), 6.86–6.91 (m, 4H, ArH), 7.29–7.42 (m, 4H, ArH).

Conclusion

In conclusion, we have developed a new method for the synthesis of symmetrical 1,3-diynes from arynes catalyzed by CuI-$NH_3{\cdot}H_2O$ system in water-soluble ionic liquid [DMIM]Me_2PO_4. The ionic liquid could be reused at least five times.

Acknowledgments This study was supported by the Program for Science & Technology Innovation Talents in Universities of Henan Province (No. 2011HASTIT032), the Foundation of He'nan Educational Committee (No. 2011C150001), the Foundation of Jiaozuo Scientific and Technological Bureau (No. 201113), and the Foundation of Henan Scientific and technological Committee (No. 112300410236).

References

1. X. S. Jia, K. Yin, C. Li, J. Li, H. S. Bian, Green Chem. **13**, 2175 (2011)
2. M. L. Lerch, M. K. Harper, D. J. Faulkner, J. Nat. Prod. **66**, 667 (2003)
3. D. Lechner, M. Stavri, M. Oluwatuyi, R. Perda-Miranda, S. Gibbons, Phytochemistry **65**, 331 (2004)
4. C. P. Constable, G. H. N. Towers, Phytochemistry **55**, 35 (1989)
5. Y. Z. Zhou, H. Y. Ma, H. Chen, L. Qiao, Y. Yao, J. Q. Cao, Y. H. Pei, Chem. Pharm. Bull. **54**, 1455 (2006)
6. M. Ladika, T. E. Fisk, W. W. Wu, S. D. Jons, J. Am. Chem. Soc. **116**, 12093 (1994)
7. S. F. Mayer, A. Steinreiber, R. V. A. Orru, K. Faber, J. Org. Chem. **67**, 9115 (2002)
8. G. Zeni, R. B. Panatieri, E. Lissner, P. H. Menezes, A. L. Braga, H. A. Stefani, Org. Lett. **3**, 819 (2001)
9. A. Stüts, Angew. Chem., Int. Ed. Engl. **26**, 320 (1987)
10. M. Gholami, R.R. Tykwinski, Chem. Rev. **106**, 4997 (2006)
11. P. N. W. Baxter, R. Dali-Youcef, J. Org. Chem. **70**, 4935 (2005)
12. J. A. Marsden, M. M. Haley, J. Org. Chem. **70**, 10213 (2005)
13. Y. B. Jiang, C. X. Kuang, Prog. Chem. **24**, 1983 (2012)
14. J.D. Crowley, S.M. Goldup, A.L. Lee, D.A. Leigh, R.T. McBurney, Chem. Soc. Rev. **38**, 1530 (2009)
15. P. Siemsen, R. C. Livingston, F. Diederich, Angew. Chem., Int. Ed. **39**, 2632 (2000)
16. M. M. Haley, Pure Appl. Chem. **80**, 519 (2008)
17. A. S. Hay, J. Org. Chem. **27**, 3320 (1962)
18. E. Valenti, M. A. Pericas, F. Serratosa, J. Am. Chem. Soc. **112**, 7405 (1990)
19. Y. Liao, R. Fathi, Z. Yang, Org. Lett. **5**, 909 (2003)
20. T. Oishi, T. Katayama, K. Yamaguchi, N. Mizuno, Chem.-Eur. J. **15**, 7539 (2009)
21. S. Adimurthy, C. C. Malakar, U. Beifuss, J. Org. Chem. **74**, 5648 (2009)
22. G. Eglington, R. Galbraith, J. Chem. Soc. 889 (1959)
23. K. Sonogashira, Y. Tohda, N. Hagihara, Tetrahedron Lett. **50**, 4467 (1975)
24. J. Yan, J. Wu, H. Jin, J. Organomet. Chem. **692**, 3636 (2007)
25. Q. Zheng, R. Hua, Y. Wan, Appl.Organomet. Chem. **24**, 314 (2010)
26. P. Kuhn, A. Alix, M. Kumarraja, B. Louis, P. Pale, J. Sommer, Eur. J. Org. Chem. 423 (2009)
27. A. L. K. Shi Shun, R. R. Tykwinski, Angew. Chem., Int. Ed. **45**, 1034 (2006)
28. Z. Chen, H. Jiang, A. Wang, S. Yang, J. Org. Chem. **75**, 6700 (2010)
29. H. A. Stefani, A. S. Guarezemini, R. Cella, Tetrahedron **66**, 7871 (2010)
30. K. Kamata, S. Yamaguchi, M. Kotani, K. Yamaguchi, N. Mizuno, Angew. Chem., Int. Ed. **47**, 2407 (2008)
31. J. D. Crowley, S. M. Goldup, N. D. Gowans, D. A. Leigh, V. E. Ronaldson, A. M. Z. Slawin, J. Am. Chem. Soc. **132**, 6243 (2010)
32. K Homo-Balaraman, V. Kesavan, Synthesis **20**, 3461 (2010)
33. A. Coste, F. Couty, G. Evano, Synthesis **9**, 1500 (2010)
34. S. L. Zhang, X. Y. Liu, T. Q. Wang, Adv. Synth. Catal. **353**, 1463 (2011)
35. S. N. Chen, W. Y. Wu, F. Y. Tsai, Green Chem. **11**, 269 (2009)
36. K. Yin, C. J. Li, J. Li, X. S. Jia, Green Chem. **13**, 591 (2011)
37. C. Glaser, Ber. Dtsch. Chem. Ges. **2**, 422 (1869)

38. A.K. Burrell, R.E.D. Sesto, S.N. Baker, T.M. McCleskeya, G.A. Baker, Green Chem., **9**, 449 (2007) (and references therein)
39. J. S. Yadav, B. V. S. Reddy, K. B Reddy, K. Uma Gayathri, A. R. Prasad. Tetrahedron Lett. **44**, 6493 (2003)