# One-pot transformation of Me<sub>3</sub>Si-/Ph<sub>2</sub>P(O)-protected ethynes to unsymmetrical arylethynes

## Li-fen Peng<sup>a</sup>, Jia-ying Lei<sup>a</sup>, Li Wu<sup>a</sup>, Zi-long Tang<sup>a</sup>\*, Zhi-peng Luo<sup>a</sup>, Yin-chun Jiao<sup>a</sup> and Xin-hua Xu<sup>b</sup>

<sup>a</sup>Key Laboratory of Theoretical Organic Chemistry and Functional Molecule of Ministry of Education, Hunan Provincial Key Laboratory of Controllable Preparation and Functional Application of Fine Polymers, School of Chemistry and Chemical Engineering, Hunan University of Science and Technology, Xiangtan 411201, P.R. China. <sup>b</sup>State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha 410082, P.R. China.

 $Me_3Si-/Ph_2P(0)$ -protected ethynes were successfully transformed to unsymmetrical arylethynes *via* a one-pot  $Ph_2P(0)$ -deprotection/ [Pd(dppf)Cl\_2]-catalysed coupling and one-pot  $Me_3Si$ -deprotection/Sonogashira coupling under mild conditions and in high yield. Unsymmetrical phenylethynes, unsymmetrical extended phenylene ethynylenes and unsymmetrical anthrylethynes were successfully synthesised in good to excellent yields.

Keywords: one-pot, unsymmetrical ethynes, protecting group, deprotection, Sonogashira coupling

Highly  $\pi$ -conjugated unsymmetrical arylethynes, which have rigid structures and highly extended  $\pi$ -systems, are important organic materials used in organic field-effect transistors,<sup>1</sup> organic light-emitting diodes,<sup>2-4</sup> liquid crystals<sup>5</sup> and dye-sensitised solar cells<sup>6,7</sup>. The Sonogashira coupling is a powerful method for synthesising arylethynes from the corresponding aryl halide and terminal ethynes as starting materials. The traditional synthesis of unsymmetrical arylethynes often suffers from severe drawbacks, such as the difficult separation of the products that have similar  $R_{\rm f}$  values to the starting materials and by-products as well as low overall yields and long synthetic steps.<sup>8</sup> Although trialkylsilyl groups such as trimethylsilyl (TMS) and t-butyldimethylsilyl (TBDMS) and the 2-hydroxy-2-propyl group are routinely used as protecting groups for terminal ethynes, the phosphoryl group (Ph<sub>2</sub>P(O)) has been developed as a new protecting group.<sup>9-13</sup> The high polarity of the phosphoryl group enables the easy separation of the desired products from the less-polar hydrocarbon by-products.<sup>10,12</sup> Recently, a short one-pot synthesis of unsymmetrical arylethynes has been developed involving dephosphorylation followed by Sonogashira couplings. However, the isolation of products was tedious because

of the similar  $R_{\rm f}$  values of the products and by-products, and the yields of products required improvement.<sup>10</sup>

Therefore, a more efficient procedure leading to unsymmetrical arylethynes under mild reaction conditions, with easy purification and high yields was required. We now report our work on developing an efficient route to unsymmetrical arylethynes from Me<sub>3</sub>Si-/ Ph<sub>2</sub>P(O)-protected arylethynes *via* a one-pot Ph<sub>2</sub>P(O)-deprotection [Pd(dppf)Cl<sub>2</sub>]-catalysed coupling followed by a one-pot Me<sub>3</sub>Si-deprotection/Sonogashira coupling under mild conditions, with easy purification and in high yield.

#### **Results and discussion**

First, we tried a selective  $Ph_2P(O)$ -deprotection/ $[Pd(dppf)Cl_2]$ catalysed coupling and Me\_3Si-deprotection/Sonogashira coupling of the Me\_3Si-/Ph\_2P(O)-protected phenylethyne **1**. When **1** was treated successively with MeMgBr and then with the phenyl halide **2** and Pd catalyst, the corresponding Sonogashira coupling product **3** was obtained. The crude product **3** was subjected to a KOHcatalysed desilylation/[Pd, Cu]-catalysed Sonogashira coupling to afford product **5** as shown in Table 1. In the above procedure,



<sup>\*</sup> Correspondent. E-mail: 1060137@hnust.edu.cn

a filtration of **3** through a thin pad of silica gel was required. Otherwise, the residual oxidised transition metal catalyst(s) affected the second one-pot step and produced a low yield of **5**. m-, p- and o-substituted unsymmetrical phenyl ethynes were successfully synthesised in excellent yields, and the products were easily isolated (Table 1, **5a**-**c**).

We succeeded in the synthesis of the unsymmetrical phenylene ethynylene **8** with an extended  $\pi$ -system using Ph<sub>2</sub>P(O)deprotection/[Pd(dppf)Cl<sub>2</sub>]-catalysed coupling and a Me<sub>3</sub>Sideprotection/Sonogashira coupling procedure. Treatment of **6** with MeMgBr, 1-bromo-4-methoxybenzene and a Pd catalyst afforded the intermediate **7**. After filtration, the crude intermediate **7** was subjected to a KOH-catalysed desilylation/ [Pd, Cu]-catalysed Sonogashira coupling with 4-iodobenzonitrile to afford product **8** in 78% yield as shown in Scheme 1.

The  $Ph_2P(O)$ -deprotection/ $[Pd(dppf)Cl_2]$ -catalysed coupling and  $Me_3Si$ -deprotection/Sonogashira coupling protocol was also applied to synthesise unsymmetrical anthrylethynes as well as phenylethynes. Unsymmetrical anthryl ethynes **10a** and **10b** were obtained in good yields from  $Me_3Si$ -/ $Ph_2P(O)$ protected anthrylethyne **9** through MeMgBr-catalysed dephosphination/ $[Pd(dppf)Cl_2]$ -catalysed coupling followed by a KOH-catalysed desilylation/[Pd, Cu]-catalysed Sonogashira coupling (Scheme 2).

### Conclusion

We have developed an efficient procedure for the synthesis of unsymmetrical arylethynes from Me<sub>3</sub>Si-/Ph<sub>2</sub>P(O)-protected arylethynes through a one-pot Ph<sub>2</sub>P(O)-deprotection/[Pd(dppf)Cl<sub>2</sub>]-catalysed coupling and one-pot Me<sub>3</sub>Si-deprotection/Sonogashira coupling. Unsymmetrical phenylethynes, unsymmetrical extended phenylene ethynylenes and unsymmetrical anthrylethynes were synthesised successfully in good to excellent yields. The mild reaction conditions, short synthetic route, facile isolation of products and excellent yields provide a convenient method to prepare these important unsymmetrical arylethynes.

#### Experimental

Dry solvents, reagents and catalysts were purchased as analytical grade and were used without further purification. Me<sub>3</sub>Si-/Ph<sub>2</sub>P(O)-protected arylethynes **1a–c**, **6** and **9** were synthesised according to literature procedures.<sup>11</sup> Analytical TLC was performed with silica gel 60 F254 plates. Column chromatography was carried out using silica gel 60 (200–300 mesh). Melting points were measured on a



Scheme 1 Synthesis of unsymmetrical extended phenylene ethynylene.



Scheme 2 Synthesis of unsymmetrical anthrylethynes.

SGW X-4 (INESA) melting point apparatus and are uncorrected. All NMR spectra were recorded on a Bruker AV-II 500 MHz NMR spectrometer operating at 500 MHz for <sup>1</sup>H and 125 MHz for <sup>13</sup>C. Tetramethylsilane (TMS) was used as internal reference for <sup>1</sup>H and <sup>13</sup>C chemical shifts and CDCl<sub>3</sub> was used as solvent. Mass spectra (MS) were obtained using EI mass spectrometer on a Bruker MicroTof II mass spectrometer.

# Synthesis of unsymmetrical arylethynes **5a–c**, **8**, **10a** and **10b**; general procedure (representative procedure for **5a**)

A THF solution (10.0 mL) of 1a (1.0 mmol) was treated with MeMgBr (1.0 mmol). After the mixture had been stirred for 30 min under nitrogen at 0 °C, 2a (1.0 mmol) and Pd(dppf) Cl<sub>2</sub>-CH<sub>2</sub>Cl<sub>2</sub> (0.05 mmol) were added at 0 °C. The mixture was stirred under nitrogen at 80 °C for 6 h. After workup with CH<sub>2</sub>Cl<sub>2</sub> and aqueous NH<sub>4</sub>Cl, the organic layer was washed with brine and dried over MgSO4. After filtration, the solvents were evaporated. The crude product was filtered through a thin pad of silica gel to give the product 3 in sufficiently pure form for further reaction. A THF solution (10.0 mL) of the crude product 3 was treated with TBAF (1.0 mmol) at 0 °C. After the mixture had been stirred for 4 h under nitrogen at room temperature, 4a (0.95 mmol), Pd(PPh<sub>2</sub>), (0.05 mmol), CuI (0.05 mmol), toluene (15.0 mL) and diisopropylamine (0.5 mL) were added sequentially. The mixture was stirred under nitrogen at 60 °C for 15 h. After workup with CH<sub>2</sub>Cl<sub>2</sub> and aqueous NH<sub>4</sub>Cl, the organic layer was washed with brine and dried over MgSO<sub>4</sub>. After filtration, the solvents were evaporated. The crude product was subjected to column chromatography on silica gel (hexane/CH<sub>2</sub>Cl<sub>2</sub>, 3:1) to afford **5a** in a pure form (yield 86%).

**5a**: Pale yellow powder; m.p. 170–172 °C (lit.<sup>9</sup> 169–171 °C); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  3.86 (s, 3H), 6.89 (d, *J* = 9.0 Hz, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.47–7.53 (m, 4H), 7.601–7.67 (m, 4H), 7.71 (s, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  55.29, 86.97, 88.09, 90.37, 92.96, 111.59, 114.00, 114.07, 114.85, 118.48, 122.46, 124.18, 127.97, 128.58, 131.04, 131.95, 132.09, 133.13, 134.56, 159.81.

**5b**: White powder; m.p. 150–152 °C (lit.<sup>10</sup> 151–153 °C); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  0.88 (d, J = 6.75 Hz, 6H), 0.94 (d, J = 6.45 Hz, 3H), 1.15–1.36 (m, 6H), 1.52–1.62 (m, 2H), 1.67–1.68 (m, 1H), 1.81–1.87 (m, 1H), 3.83 (s, 3H), 3.97–4.06 (m, 2H), 6.87–6.89 (m, 4H), 7.44–7.48 (m, 8H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  19.62, 22.59, 22.65, 24.64, 27.97, 29.82, 36.08, 37.26, 39.21, 55.23, 66.39, 87.85, 87.94, 91.12, 91.26, 114.02, 114.56, 114.85, 115.17, 122.99, 123.12, 131.28, 133.05, 133.07, 159.34, 159.72.

**5c**: Colourless oil (lit.<sup>14</sup> colourless oil); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 3.83 (s, 3H), 6.87 (d, J = 8.7 Hz, 2H), 7.26–7.28 (m, 2H), 7.33–7.36 (m, 3H), 7.53 (d, J = 8.7 Hz, 2H), 7.54–7.58 (m, 4H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 55.32, 87.11, 88.54, 93.42, 93.83, 114.01, 115.55, 123.43, 125.61, 126.27, 127.66, 128.07, 128.42, 131.63, 131.72, 131.85, 133.11, 159.80.

**8**: White powder; m.p. 216–218 °C; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 3.84 (s, 3H), 6.89 (d, J = 8.6 Hz, 2H), 7.31–7.38 (m, 2H), 7.46–7.48 (m, 3H), 7.50–7.55 (m, 3H), 7.60–7.68 (m, 5H), 7.71 (s, 1H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ 55.34, 74.06, 74.70, 80.44, 81.26, 86.86, 88.52, 90.47, 92.39, 111.80, 114.02, 114.09, 114.86, 118.44, 121.85, 122.36, 122.81, 124.23, 127.77, 131.77, 132.10, 132.15, 132.92, 133.13, 133.17, 135.23, 135.53, 159.85; HRMS (ESI) m/z calcd for C<sub>34</sub>H<sub>19</sub>NO: [M + H]<sup>+</sup>: 458.1467; found: 458.1471. **10a**: White powder; m.p. 235–236 °C (lit.<sup>12</sup> 234–235 °C); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  3.88 (s, 3H), 6.97 (d, J = 8.8 Hz, 2H), 7.61–7.66 (m, 4H), 7.69–7.73 (m, 4H), 7.81 (d, J = 8.2 Hz, 2H), 8.56–8.62 (m, 2H), 8.66–8.71 (m, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  55.35, 85.18, 91.01, 100.18, 103.42, 111.56, 114.22, 115.28, 116.36, 118.58, 120.28, 126.73, 127.17, 127.48, 128.27, 131.76, 131.97, 132.18, 132.26, 133.25, 160.12.

**10b**: White powder; m.p. 192–193 °C (lit.<sup>12</sup> 190–191 °C); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  7.08–7.11 (m, 4H), 7.19 (d, *J* = 7.6 Hz, 4H), 7.33 (t, *J* = 7.9 Hz, 4H), 7.57–7.68 (m, 8H), 7.96 (d, *J* = 7.6 Hz, 1H), 8.01 (s, 1H), 8.66–8.67 (m, 2H), 8.69–8.71 (m, 2H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  85.76, 88.08, 100.29, 103.43, 115.85, 116.82, 119.72, 122.16, 122.21, 123.76, 123.76 (q, *J* = 272.3 Hz), 124.39, 125.12 (q, *J* = 2.1 Hz), 126.66, 126.93, 127.04, 127.42, 128.26 (q, *J* = 3.6 Hz), 129.06, 129.46 (m), 131.12 (d, *J* = 32.5 Hz), 132.79, 132.20, 132.68, 134.69, 147.05, 148.38.

#### Acknowledgements

This work was supported by the Natural Science Fund Youth Project of Hunan Province (No. 2018JJ3145), the General Project of Hunan Education Department (17C0629), the Doctoral Foundation of Hunan University of Science and Technology (No. E51693), the Open Foundation of Key Laboratory of Theoretical Organic Chemistry and Functional Molecule of Ministry of Education, Hunan University of Science and Technology (No. E21630) and the National Natural Science Foundation of China (No. 21402048).

#### Received 24 April 2018; accepted 2 May 2018 Paper 1805397

https://doi.org/10.3184/174751918X15269925671284 Published online: 30 May 2018

#### References

- L. Fenenko, G. Shao, A. Orita, M. Yahiro, J. Otera, S. Svechnikov and C. Adachi, *Chem. Commun.*, 2007, 2278.
- 2 L.-F. Peng, J. Jiang, C. Peng, N.-N. Dai, Z.-L. Tang, Y.-C. Jiao, J.-Y. Chen and X.-H. Xu, *Chin. J. Org. Chem.*, 2017, **37**, 3013.
- 3 D. Matsuo, X. Yang, A. Hamada, K. Morimoto, T. Kato, M. Yahiro, C. Adachi, A. Orita and J. Otera, *Chem. Lett.*, 2010, **39**, 1300.
- 4 Y. Yamaguchi, T. Ochi, S. Miyamura, T. Tanaka, S. Kobayashi, T. Wakamiya, Y. Matsubara and Z. Yoshida, J. Am. Chem. Soc., 2006, 128, 4504.
- 5 M. Fischer, G. Lieser, A. Rapp, I. Schnell, W. Mamdouh, S.d. Feyter, F.C. Schryver and S. Höger, J. Am. Chem. Soc., 2004, 126, 214.
- 6 X. Yang, S. Kajiyama, J.-K. Fang, F. Xu, Y. Uemura, N. Koumura, K. Hara, A. Orita and J. Otera, *Bull. Chem. Soc. Jpn*, 2012, 85, 687.
- 7 Z.-Y. Yao, M. Zhang, H. Wu, L. Yang, R.-Z. Li and P. Wang, J. Am. Chem. Soc., 2015, 137, 3799.
- 8 F. Diederich, P.J. Stang and R.R. Tykwinski, Acetylene chemistry. Wiley-VCH, Weinheim, 2005.
- 9 X. Yang, D. Matsuo, Y. Suzuma, J.-K. Fang, F. Xu, A. Orita and J. Otera, *Synlett*, 2011, 16, 2402.
- 10 L.-F. Peng, F. Xu, Y. Suzuma, A. Orita and J. Otera, J. Org. Chem., 2013, 78, 12802.
- 11 L.-F. Peng, F. Xu, K. Shinohara, A. Orita and J. Otera, *Chem. Lett.*, 2014, 43, 1610.
- 12 L.-F. Peng, F. Xu, K. Shinohara, T. Nishida, K. Wakamatsu, A. Orita and J. Otera, Org. Chem. Front., 2015, 2, 248.
- 13 L.-F. Peng, S.-W. Zhang, B.-H. Wang, M.-S. Xun, Z.-L. Tang, Y.-C. Jiao and X.-H. Xu, Chin. J. Org. Chem., 2018, 38, 519.
- 14 P.W. Peterson, N. Shevchenko and I.V. Alabugin, Org. Lett., 2013, 15, 2238.