Double Elimination Protocol for Access to Pyridine-Containing Arylene–Ethynylenes

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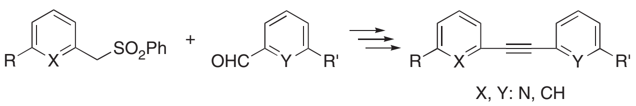
The arylene–ethynylene arrays involving pyridine were constructed successfully by taking advantage of double elimination reaction of β-substituted sulfones (sulfoximines) which are easily accessible from arylmethyl sulfones (sulfoximines) and aromatic aldehydes. This protocol was utilized for synthesis of an enantiopure arylene–ethynylene framework bearing a binaphthyl stereogenic core.

Pyridine derivatives have received great attention as building blocks for supramolecules[1] and ligands for transition metal catalysts[2] and luminecent complexes.[3] Especially great interest has been focused on pyridylene–ethynylenes. Although such array is usually formed by the Sonogashira coupling between bromopyridines and terminal acetylenes, a more versatile methodology is still in demand particularly for pyridylene–ethynylenes having functional groups.[1b] In this context, we have developed a new synthetic process for acetylenes by utilizing double elimination of β-substituted sulfones which could be easily derived from sulfones and aldehydes. In this process, a series of reactions such as aldol-type C–C bond formation, protection of the resulting aldolate and double elimination of the β-substituted sulfones are integrated in one-pot. Based on this protocol, various types of acetylenes such as unsymmetrically substituted aromatic polyynes[4] and highly strained[5] and chiral acetylenic cyclophanes[6] were obtained. We expected that this protocol would be useful for construction of pyridylene–ethynylene units having various functional groups (Scheme 1).

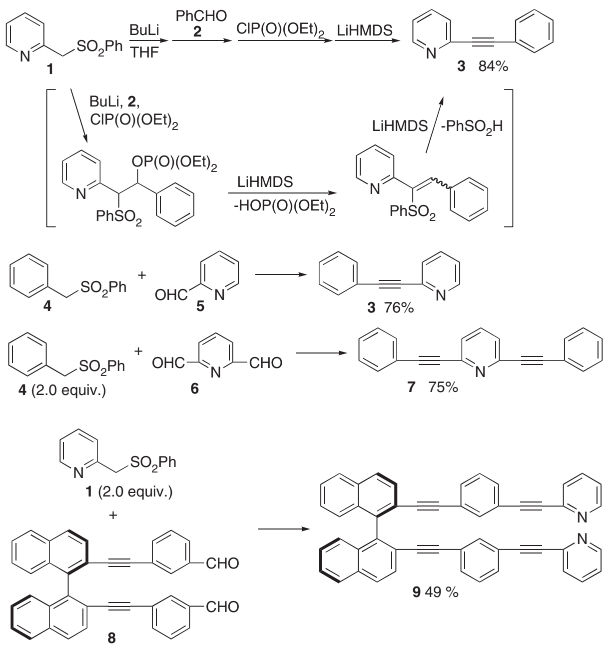


Scheme 1.

Herein, we describe the double elimination protocol for pyridine-containing arylene–ethynylenes. First of all, we conducted the reaction of 2-pyridylmethyl sulfone **1** with benzaldehyde (**2**) (Scheme 2). This reaction proceeded smoothly giving rise to formation of the desired pyridylacetylene **3**. An alternative combination of benzyl sulfone **4** and 2-pyridinecarboxaldehyde (**5**) produced **3** in 76% yield. Dialdehydes were employable as well. Treatment of **4** with 2,6-pyridinedicarboxaldehyde (**6**) afforded the desired diyne **7**, and enantiopure dialdehyde **8** reacted with **1** to provide tetrayne **9**.

With these results in hand, we tackled to prepare enantiopure pyridine-containing arylene–ethynylene **10** which had been revealed to form a unique double helicate **A** upon complexation with copper(I) and silver(I).[7] Previously, this compound was synthesized by the Sonogashira coupling, yet repetition of the Sonogashira coupling resulted in coloration of the product and required repeating column chromatography for purification. When a model reaction for incorporation of a triple bond between pyridines was attempted by use of **1** and **5** (for route A in Figure 1), only a trace amount of the desired dipyridylacetylene was produced together with a number of byproducts.

In sharp contrast to this disappointing result, acetylene formation was effected by use of sulfone **11** and **2** though in a modest yield (for route B in Figure 1, Scheme 3). However, when benzyl sulfoximine **13** and a pyridinecarboxaldehyde derivative **14** were combined, the same product **12** was prepared in 83% yield (Scheme 3). These results prompted us to employ route B for construction of the target compound **10**. Enantionpure disulfoximine **15** was prepared according to the procedure previ-



Scheme 2.

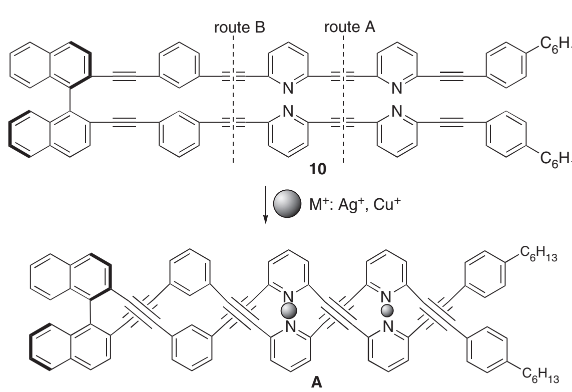
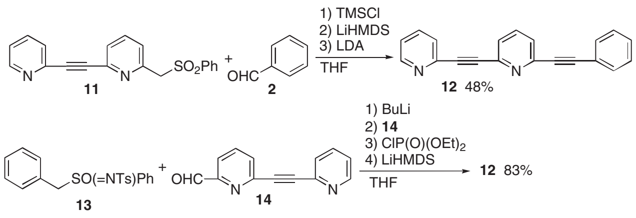
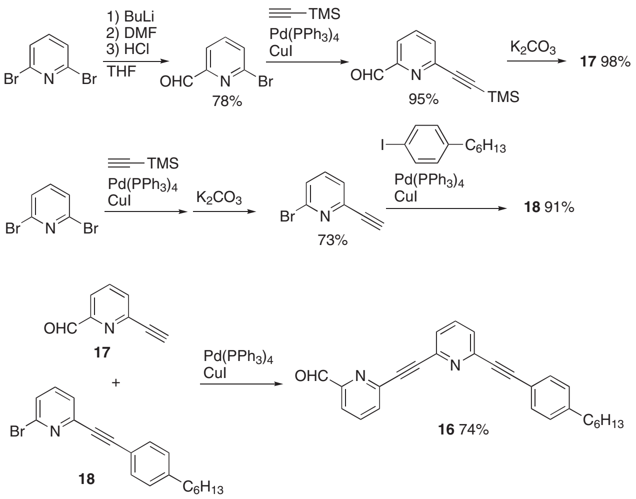


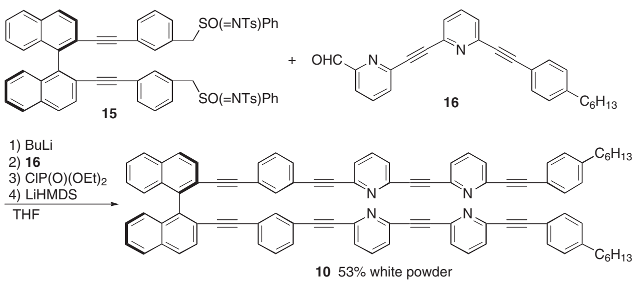
Figure 1.



Scheme 3.



Scheme 4.



Scheme 5.

ously reported.[6b] A pyridylcarboxaldehyde **16** was accessible by repeating the Sonogashira coupling as shown in Scheme 4.

The aldol-type coupling between an enantiopure disulfoximine **15** and pyridylcarboxaldehyde **16** followed by double elimination of the resulting β-substituted sulfoximine furnished the desired acetylene **10** in 53% yield (Scheme 5).[8] Notably, the product thus formed suffered from no coloration and enjoyed facile purification. When the corresponding disulfone was employed instead of **15** yellowish product **10** was obtained only in 30% yield.

In summary, the double elimination protocol has proved to be effective for synthesis of pyridylacetylenes.

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References and Notes

1 a) C. A. Schalley, A. Lützen, and M. Albrecht, *Chem.—Eur. J.*, **10**, 1072 (2004). b) C. Tschierske, *Angew. Chem., Int. Ed.*, **39**, 2454 (2000). c) J.-M. Lehn, *Chem.—Eur. J.*, **6**, 2097 (2000).

2 a) T. Kawano, T. Shinomaru, and I. Ueda, *Org. Lett.*, **4**, 2545 (2002). b) T. Kawano, J. Kuwana, T. Shinomaru, C.-X. Du, and I. Ueda, *Chem. Lett.*, **2001**, 1230.

3 a) X. Shen, T. Moriuchi, and T. Hirao, *Tetrahedron Lett.*, **44**, 7711 (2003). b) A. Khatyr and R. Ziessel, *Tetrahedron Lett.*, **43**, 7431 (2002). c) H. S. Joshi, R. Jamshidi, and Y. Tor, *Angew. Chem., Int. Ed.*, **38**, 2722 (1999). d) V. Balzani, A. Juris, and M. Venturi, *Chem. Rev.*, **96**, 759 (1996).

4 a) F. Ye, A. Orita, A. Doumoto, and J. Otera, *Tetrahedron*, **59**, 5635 (2003). b) A. Orita, F. Ye, A. Doumoto, and J. Otera, *Chem. Lett.*, **32**, 104 (2003).

5 A. Orita, D. Hasegawa, T. Nakano, and J. Otera, *Chem.—Eur. J.*, **8**, 2000 (2002).

6 a) D.-L. An, T. Nakano, A. Orita, and J. Otera, *Angew. Chem., Int. Ed.*, **41**, 171 (2002). b) A. Orita, D. Hasegawa, D.-L. An, T. Nakano, J. Yaruva, N. Ma, and J. Otera, *Chem.—Eur. J.*, **8**, 2005 (2002).

7 A. Orita, T. Nakano, D.-L. An, K. Tanikawa, K. Wakamatsu, and J. Otera, *J. Am. Chem. Soc.*, **126** 10389 (2004).

8 To a THF solution (3 mL) of disulfoxime **15** (213.9 mg, 0.20 mmol) was added BuLi (0.33 mL, 1.35 M hexane solution, 0.46 mmol) at −78 °C, and the mixture was stirred for 0.5 h. To this solution was added a THF solution (3 mL) of **16** (164.8 mg, 0.42 mmol), and the mixture was stirred for 1.5 h. After $ClP(O)(OEt)_2$ (0.064 mL, 0.44 mmol) had been added, the reaction mixture was stirred at RT for 2 h. After lithium hexamethyldisilazide (3.0 mL, 1.0 M THF solution, 3.0 mmol) had been added at −78 °C, the mixture was stirred at −78 °C for 1 h and at RT for 1 h. After usual workup with sat. NH_4Cl aq/CH_2Cl_2, the combined organic layer was washed with brine and dried over anhydrous soudium sulfate. The organic layer was evaporated under vacuum, and the residue was subjected to column chromatography to give **10** (130.1 mg, 53%).

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