

Double Elimination Protocol for Access to Unsymmetrical Di(phenylethynyl)benzenes

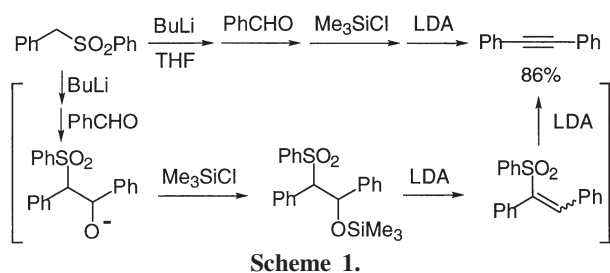
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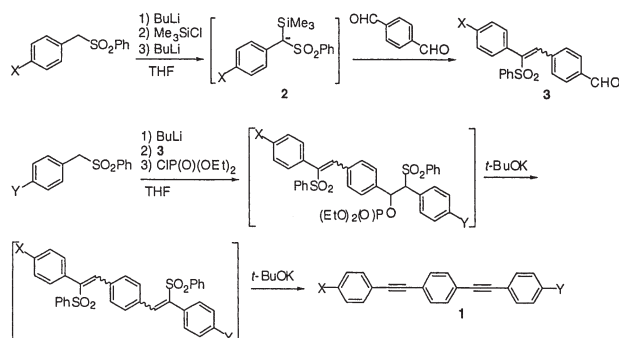
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For facile access to phenylene-ethynylenes, a new methodology for construction of unsymmetrically substituted di(phenylethynyl)benzenes has been established by taking advantage of double elimination protocol of α -sulfonyl aldolates.

Phenylene-ethynylenes have received great attention as organic materials like liquid crystal¹ and photo-² and electroluminescent compounds.³ Although it is well recognized that the organic liquid crystal is composed of rigid and flexible parts, it is greatly fascinating that the phenylene-ethynylene serves as a rigid moiety in some cases⁴ and as a flexible one in the other.⁵ A number of preparative methodologies for acetylenes have been developed so far.⁶ Although the Sonogashira coupling between aryl halides and acetylenes have been utilized routinely for access to phenylene-ethynylenes,⁷ this methodology requires either separate or in situ protection-deprotection operations for construction of unsymmetrically substituted phenylene-ethynylenes.⁸ On the other hand, we reported a double elimination protocol by use of sulfone and aldehyde as starting compounds (Scheme 1).⁹



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 sulfone are integrated in one-pot. We postulated that discriminative stepwise reactions with dialdehydes would enable access to unsymmetrically substituted



phenylene-ethynylenes **1** (Scheme). In this process, key intermediate **3** would be easily separated from the remaining starting aldehyde and/or a possible co-product divinylsulfone, if any, because of high polarity of the phenylsulfonyl group. This is indeed the case, and the consecutive Peterson olefination and double elimination give rise to the formation of the desired unsymmetrically substituted phenylene-ethynylenes **1**.

An anion of α -trimethylsilylbenzylsulfone (**2a**) prepared in situ reacted with terephthalaldehyde (1.0 equiv.) at -78°C to furnish a formylvinylsulfone **3a** ($X = \text{H}$) in 75% yield as a 39 : 61 mixture of geometrical isomers. Notably, discrimination proceeded quite efficiently to provide **3** without protection-deprotection technology.¹⁰ In sharp contrast, it has been described that discriminative C–C bond formation by use of the Sonogashira coupling is difficult even if an excess of dihaloarene is used.¹¹ Consecutive addition of anion of *p*-methoxybenzylphenylsulfone, chlorophosphate and *t*-BuOK to **3a** gave the desired unsymmetrically substituted di(phenylethynyl)benzene **1a** ($X = \text{H}$, $Y = \text{MeO}$) in 91% yield (Table 1, entry 1). According to this two-step procedure, several diynes were obtained successfully as shown in Table 1.¹² The unsymmetrically substituted diynes are accessed irrespective of addition order of the sulfone (entries 1 and 2, 3 and 4, 5 and 6, 7 and 8), yet initial addition of sulfones bearing a more electron-withdrawing group resulted in better yields than those of the reversed order except the combination shown in entries 7 and 8.

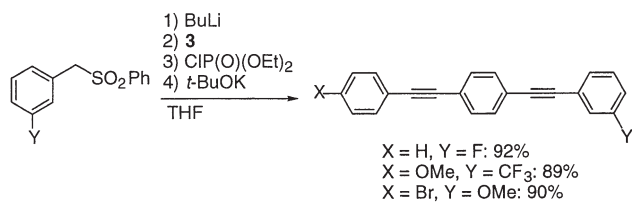
Table 1. Preparation of vinylsulfones **3** and di(phenylethynyl)benzenes **1** according to Scheme

Entry	X	Yield of 3 /%	Y	Yield of 1 /%	Total yield/% ^a
1	H	75	MeO	91	68 (75 × 91)
2	MeO	71	H	75	53 (71 × 75)
3	F	82	H	89	73 (82 × 89)
4	H	75	F	80	60 (75 × 80)
5	Br	76	MeO	87	66 (76 × 87)
6	MeO	71	Br	69	49 (71 × 69)
7	CF ₃	67	MeO	67	45 (67 × 67)
8	MeO	71	CF ₃	86	61 (71 × 86)

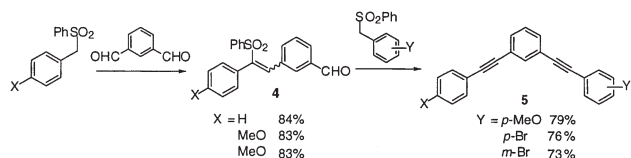
^aIsolated yield.

Subjection of **3** to the double elimination reaction with *meta*-substituted sulfones afforded the corresponding *meta*-substituted derivatives (Scheme 3). When isophthalaldehyde was utilized as a starting compound, this two-step protocol served quite well to afford the desired *meta*-substituted phenylene-ethynylene derivatives (Scheme 4).

In summary, we have succeeded in the convenient syntheses of unsymmetrically substituted phenylene-ethynylenes. Further application of this protocol is underway in our laboratory.



Scheme 3.



Scheme 4.

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References and Notes

- 1 S. Höger, V. Enkelmann, K. Bonrad, and C. Tschierske, *Angew. Chem., Int. Ed.*, **39**, 2268 (2000).
- 2 a) A. Kokil, I. Shivanovskaya, K. D. Singer, and C. Weder, *J. Am. Chem. Soc.*, **124**, 9978 (2002). b) Y. Morisaki and Y. Chujo, *Chem. Lett.*, **2002**, 194. c) O. Mongin, L. Porres, L. Moreaux, J. Mertz, and M. Blanchard-Desce, *Org. Lett.*, **4**, 719 (2002).
- 3 a) A. Kraft, A. C. Grimsdale, and A. B. Holmes, *Angew. Chem., Int. Ed.*, **37**, 403 (1998). b) R. Giesa, *JMS-Rev. Macromol. Chem. Phys.*, **C36**, 631 (1996). c) L. S. Swanson, F. Lu, J. Shinar, Y. W. Ding, and T. J. Barton, *Proc. SPIE-Int. Soc. Opt. Eng.*, **1910**, 101 (1993).
- 4 a) C.-H. Lee and T. Yamamoto, *Bull. Chem. Soc. Jpn.*, **75**, 615 (2002). b) C. Sekine, K. Iwakura, N. Konya, M. Minai, and K. Fujisawa, *Liq. Cryst.*, **28**, 1375 (2001).
- 5 a) D. J. Pesak and J. S. Moore, *Angew. Chem., Int. Ed. Engl.*, **36**, 1636 (1997).
- 6 a) K. Grela and J. Ignatowska, *Org. Lett.*, **4**, 3747 (2002). b) G. Brizius and U. H. F. Bunz, *Org. Lett.*, **4**, 2829 (2002). c) U. H. F. Bunz, *Acc. Chem. Res.*, **34**, 998 (2001). d) A. Fürstner and C. Mathes, *Org. Lett.*, **3**, 221 (2001). e) S. Z. Zard, *Chem. Commun.*, **2002**, 1555. f) A. R. Katritzky, J. Wang, N. Karodia, and J. Li, *J. Org. Chem.*, **62**, 4142 (1997). g) D. G. Brown, E. J. Velthuisen, J. R. Commerford, R. G. Brisbois, and T. R. Hoye, *J. Org. Chem.*, **61**, 2540 (1996).
- 7 a) K.-y. Tomizaki, R. S. Loewe, C. Kirmaier, J. K. Schwartz, J. L. Retsek, D. F. Bocian, D. Holten, and J. S. Lindsey, *J. Org. Chem.*, **67**, 6519 (2002). b) R. E. Bauer, V. Enkelmann, U. M. Wiesler, A. J. Berresheim, and K. Müllen, *Chem.—Eur. J.*, **8**, 3858 (2002). c) M. L. Yongge Wei, B. Xu, C. F.-C. Cheng, Z. Peng, and D. R. Powell, *Angew. Chem., Int. Ed.*, **41**, 1566 (2002).
- 8 a) M. J. Mio, L. C. Kopel, J. B. Braun, T. L. Gadzikwa, K. L. Hull, R. G. Brisbois, C. J. Markworth, and P. A. Grieco, *Org. Lett.*, **4**, 3199 (2002). b) T. M. Pappenfus and K. R. Mann, *Org. Lett.*, **4**, 3043 (2002). c) M. B. Nielsen, N. F. Utesch, N. N. P. Moonen, C. Boudon, J.-P. Gisselbrecht, S. Concilio, S. P. Piotto, P. Seiler, P. Günter, M. Gross, and F. Diederich, *Chem.—Eur. J.*, **8**, 3601 (2002).
- 9 a) A. Orita, D. Hasegawa, T. Nakano, and J. Otera, *Chem.—Eur. J.*, **8**, 2000 (2002). b) A. Orita, D. L. An, T. Nakano, J. Yaruva, N. Ma, and J. Otera, *Chem.—Eur. J.*, **8**, 2005 (2002). c) A. Orita, N. Yoshioka, P. Struwe, A. Braier, A. Beckmann, and J. Otera, *Chem.—Eur. J.*, **5**, 1355 (1999).
- 10 Although a small amount of divinylsulfone (11% yield) was also produced, its higher polarity enabled easy separation from **3a** by column chromatography.
- 11 a) S.-X. Liu, C. Michel, and M. Schmitt, *Org. Lett.*, **2**, 3959 (2000). b) O. Mongin, A. Schuwey, M.-A. Vallot, and A. Gossauer, *Tetrahedron Lett.*, **40**, 8347 (1999).
- 12 A typical procedure is as follows: To a THF solution (5 mL) of benzylphenylsulfone (232 mg, 1.0 mmol) was added a hexane solution of BuLi (1.60 M, 0.69 mL, 1.1 mmol) at -78°C , and the mixture was stirred for 0.5 h. Trimethylsilyl chloride (0.14 mL, 1.1 mmol) was added, and the mixture was stirred at rt for 1 h. BuLi (1.60 M, 0.69 mL, 1.1 mmol) was added at -78°C , and the mixture was stirred for 0.5 h. Terephthalaldehyde (134 mg, 1.0 mmol) was added and the mixture was stirred for 2 h. After usual workup with ethyl acetate and NH_4Cl aq, drying over MgSO_4 and evaporation, the residue was subjected to column chromatography to furnish **3a** as a 39 : 61 mixture of geometric isomers (261 mg, 75%). To a THF solution (5 mL) of *p*-methoxybenzylphenylsulfone (79 mg, 0.30 mmol) was added BuLi (1.60 M, 0.21 mL, 0.35 mmol), and the mixture was stirred for 0.5 h. A THF solution (3 mL) of **3a** (87 mg, 0.25 mmol) was added, and the mixture was stirred for 1 h. At -78°C , CIP(O)(OEt)₂ (0.05 mL, 0.30 mmol) was added, and the mixture was stirred at rt for 2 h. *t*-BuOK (421 mg, 3.75 mmol) was added at -78°C , and the mixture was stirred at -78°C for 1 h and at rt for 2 h. After usual workup with ethyl acetate and NH_4Cl aq, drying over MgSO_4 and evaporation, the residue was subjected to column chromatography to furnish **1a** (70 mg, 91%). **1a**: mp $175\text{--}177^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 3.83 (s, 3H), 6.89 (d, $J = 8.9$ Hz, 2H), 7.34–7.37 (m, 3H), 7.46–7.54 (m, 8H); ^{13}C NMR (CDCl_3) δ 55.3, 87.9, 89.2, 91.1, 91.3, 114.0, 115.1, 122.7, 123.1, 123.4, 128.4, 128.5, 131.3, 131.5, 131.6, 133.1, 159.8. Anal. Calcd for $\text{C}_{23}\text{H}_{16}\text{O}$: C, 89.58; H, 5.23. Found: C, 89.53; H, 5.06.