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Double elimination protocol for aryleneethynylenes*

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Abstract: A variety of aryleneethynylenes are synthesized by double elimination reaction of β-substituted sulfones. The acetylenic bond is formed from readily available aromatic aldehydes and benzylic sulfones. A sequence of aldol reaction, trapping of the aldolates with a leaving group, and eliminations proceeds in one pot. The utility of this protocol is exemplified by synthesis of dihalo diphenylacetylenes, 5,6,11,12-tetradehydrodibenzo[a,e]cyclooctene, and double-helical aromatic acetylenes.

Keywords: double elimination; aryleneethynylenes; β-substituted sulfones; dihalo diphenylacetylenes; tetradehydrodibenzo[a,e]cyclooctene; double-helical aromatic acetylenes.

INTRODUCTION

The aryleneethynylene array is an important component for organic materials such as liquid crystals [1], photoluminescent compounds [2], and carbon-rich materials [3]. The compounds are mostly prepared by Sonogashira coupling [4] while other transition-metal-catalyzed reactions like acetylene metathesis, Suzuki–Miyaura coupling, and Negishi coupling are invoked occasionally. These protocols, though being very versatile, suffer from some drawbacks. Namely, chemically labile terminal acetylenes should be employed, resulting in self-coupling to diynes. Moreover, it is difficult to remove completely the transition-metal catalyst residues from the products.

Previously, we put forth a double elimination reaction which leads to polyenes and acetylenes (Scheme 1) [5]. That is, aldol-type products obtained from benzyl sulfones and aldehydes are trapped by leaving groups such as acetates, phosphates, silyl ethers, etc. Treatment of these β-substituted sulfones with an excess amount of base induces the double elimination reaction to give polyenes or acetylenes. The bifurcation arises at the stage of vinyl sulfone intermediates that were formed by abstraction of the α-proton to the sulfonyl group. 1,3-Dienes result from the isomerization of these intermediates to allylic sulfones, followed by 1,4-elimination. Alternatively, if the isomerization is not allowed, 1,2-elimination of vinyl sulfones occurs to provide alkynes. The stepwise procedures were originally employed where the respective intermediates were isolated and purified. Later, these reactions were integrated into a one-pot process starting from benzyl sulfones and aldehydes by in situ trapping of the aldolate anion with Ac_2O, TMSCl, or $ClP(O)(OEt)_2$ followed by direct addition of a base to this reaction mixture (Scheme 2) [6]. The products are free from the diyne impurities and, of course, transition-metal residues. This protocol was found to be useful for synthesis of a variety of acetylenes. Herein are described applications to some synthetically important and structurally interesting acetylene compounds.

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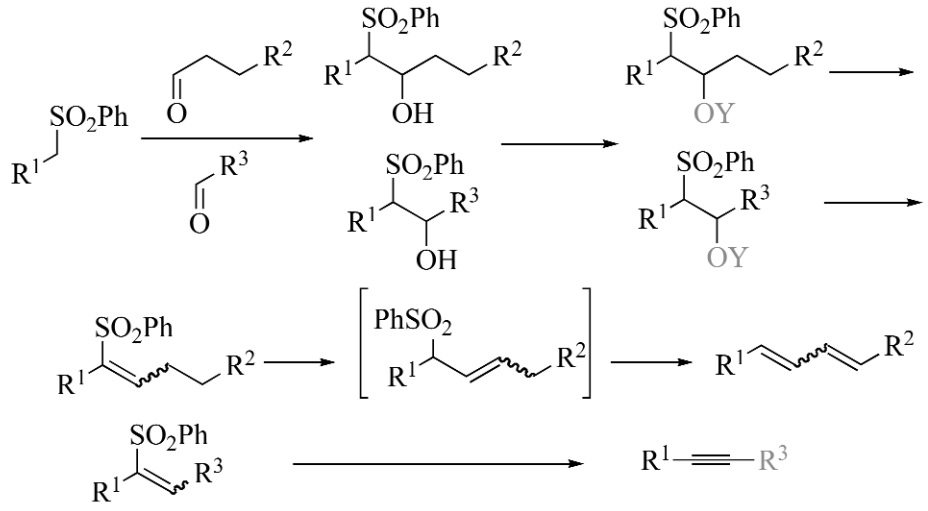
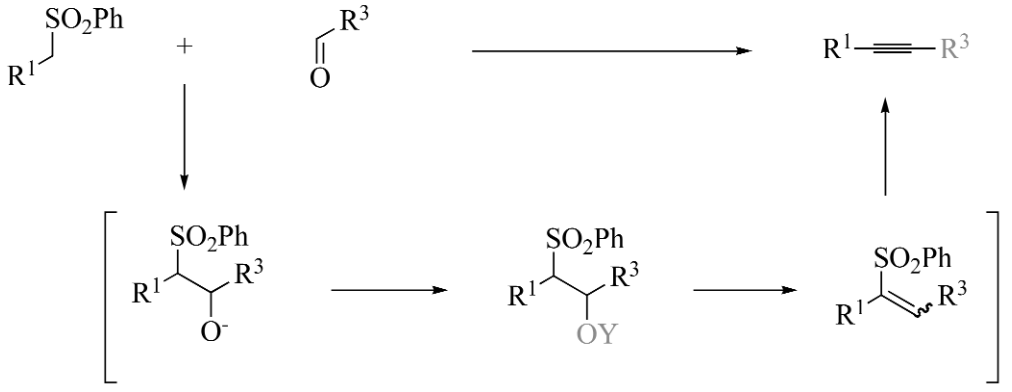


Scheme 1

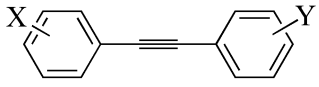


Scheme 2

RESULTS AND DISCUSSION

Synthesis of dihalo diphenylacetylenes [7]

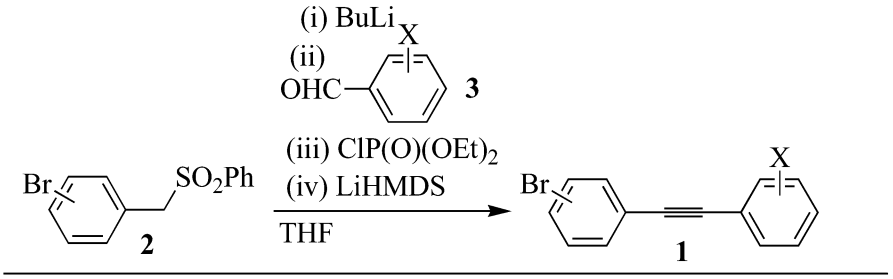
Dihalo diphenylacetylenes **1** (Fig. 1) are versatile building blocks for constructing phenyleneethynylenes. In particular, those with different halogen substituents on the respective phenyl rings (**1**, X ≠ Y) are expected to serve for designing tailor-made phenyleneethynylenes with regulated structure and composition because different, and hence selective, C–C bond formations are feasible on both sides of the molecules on account of different reactivities of the halogens.

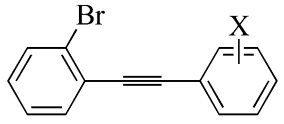


X, Y = Cl, Br and I

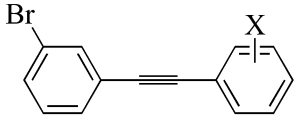
Fig. 1 Dihalo diphenylacetylenes.

The synthesis of the dihalo diphenylacetylenes by the double elimination protocol is straightforward. Combination of 2- and 3-bromobenzyl sulfones **2a**,**b** and halobenzaldehydes **3** furnished the corresponding products **1a**–**q** in good yields irrespective of the position of halogens in **3** (Scheme 3). When 4-bromobenzyl sulfone **2c** was employed, however, dibromo stilbene **4** formed in 88 % yield (Scheme 4). Fortunately, this reaction was suppressed by use of LiHMDS instead of BuLi as a base to generate the α-sulfonylbenzyl anion, and the desired dihalo diphenylacetylenes **1f**,**n**,**r–u** were obtained in good yields (Scheme 5). This modification also allowed the use of iodo benzyl sulfones which are liable to dehalogenation with BuLi, and the desired coupling products were obtained without loss of the halogen (Scheme 6).



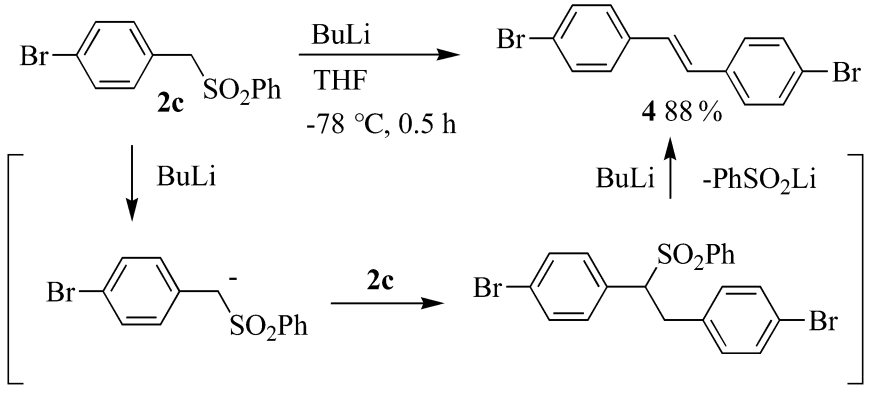


X=2-Cl (**1a**), 74 %: 3-Cl (**1b**), 84 %: 4-Cl (**1c**), 85 %
=2-Br (**1d**), 83 %: 3-Br (**1e**), 89 %: 4-Br (**1f**), 82 %
=2-I (**1g**), 78 %: 3-I (**1h**), 84 %: 4-I (**1i**), 82 %

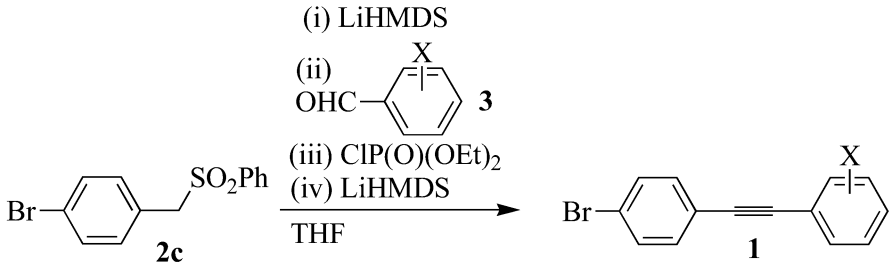


X=2-Cl (**1j**), 85 %: 3-Cl (**1k**), 88 %: 4-Cl (**1l**), 82 %
=2-Br (**1e**), 82 %: 3-Br (**1m**), 82 %: 4-Br (**1n**), 86 %
=2-I (**1o**), 81 %: 3-I (**1p**), 81 %: 4-I (**1q**), 83 %

Scheme 3

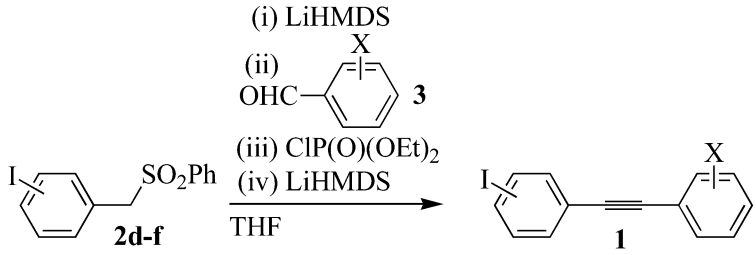


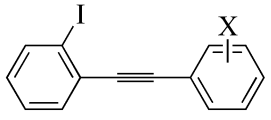
Scheme 4



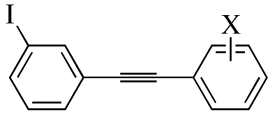
X=2-Cl (**1r**), 84 %: 3-Cl (**1s**), 87 %: 4-Cl (**1t**), 74 %
=2-Br (**1f**), 78 %: 3-Br (**1n**), 75 %: 4-Br (**1u**), 77 %

Scheme 5

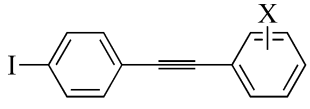




X=2-Br (**1g**), 61 %: 3-Br (**1o**), 82 %: 4-Br (**1v**), 76 %
=2-I (**1w**), 60 %



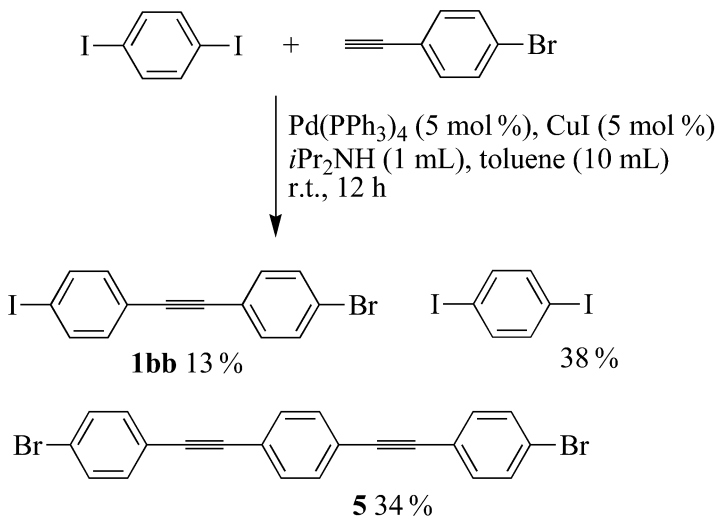
X=2-Br (**1h**), 79 %: 3-Br (**1p**), 83 %: 4-Br (**1x**), 86 %
=2-I (**1y**), 71 %: 3-I (**1z**), 75 %: 4-I (**1aa**), 73 %



X=2-Br (**1i**), 84 %: 3-Br (**1q**), 78 %: 4-Br (**1bb**), 84 %
=2-I (**1cc**), 72 %: 4-I (**1dd**), 76 %

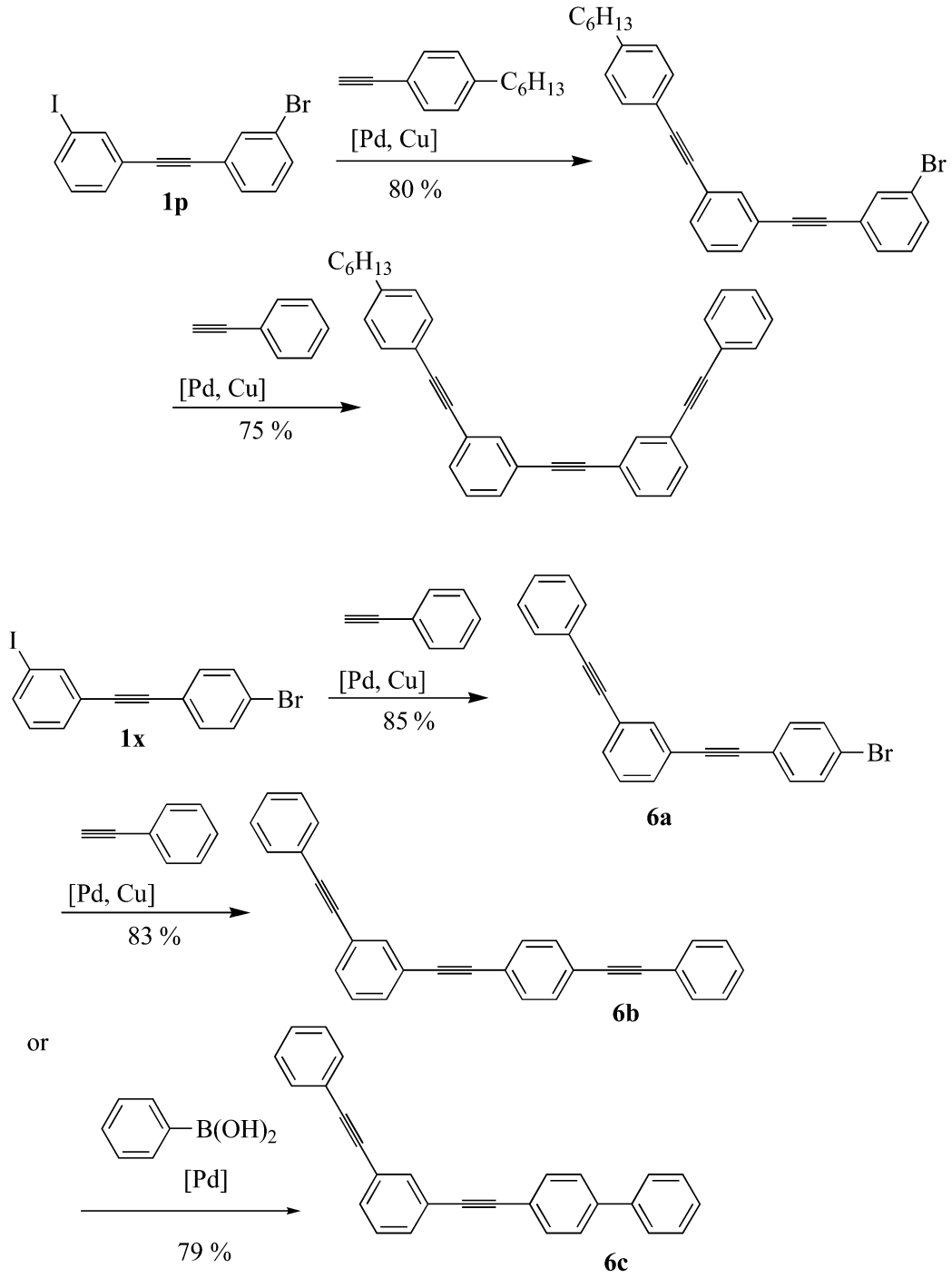
Scheme 6

The utility of the double elimination route for the dihalo diphenylacetylenes is apparent from comparison with the Sonogashira protocol (Scheme 7). When 1,4-diiodobenzene was subjected to Sonogashira coupling with 4-bromophenylacetylene in a 1:1 ratio, the desired coupling product **1b** was contaminated by double-coupling product **5** together with unreacted diiodobenzene. Separation of **1** from these contaminants was difficult on account of their similar polarity and solubility in organic solvents, and the repeated column chromatography was necessary for isolation of the pure compound. Apparently, it is difficult to differentiate the same halogen functions in the Sonogashira reaction. The other route by which to arrive at the same target is combination of 4-bromoiodobenzene and 4-iodophenylacetylene. However, unfavorable self-coupling of the 4-iodophenylacetylene competes with the desired intermolecular reaction under normal conditions.

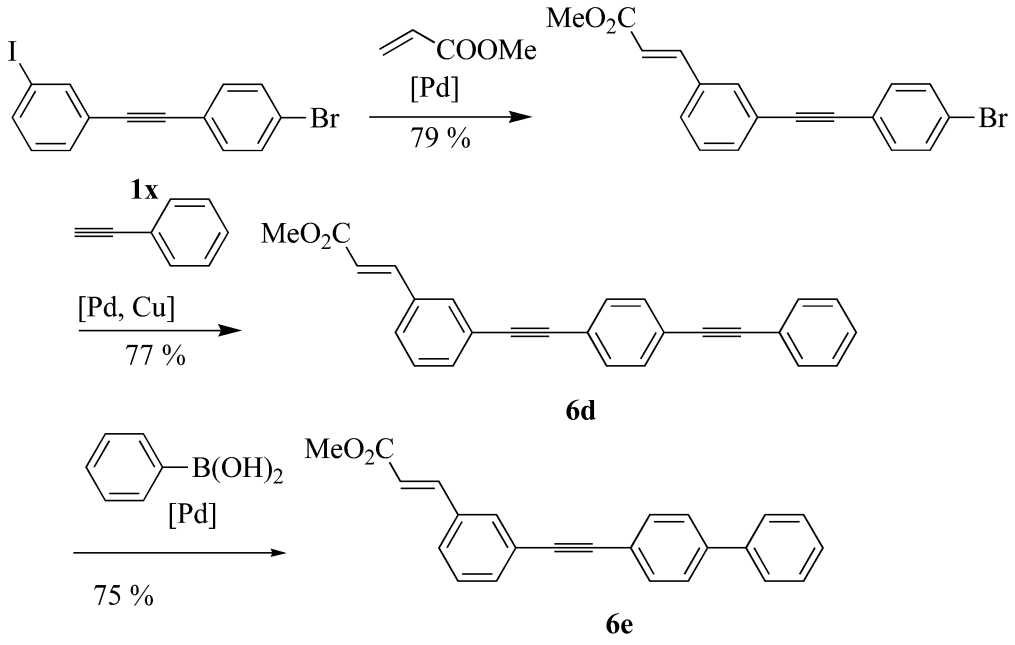


Scheme 7

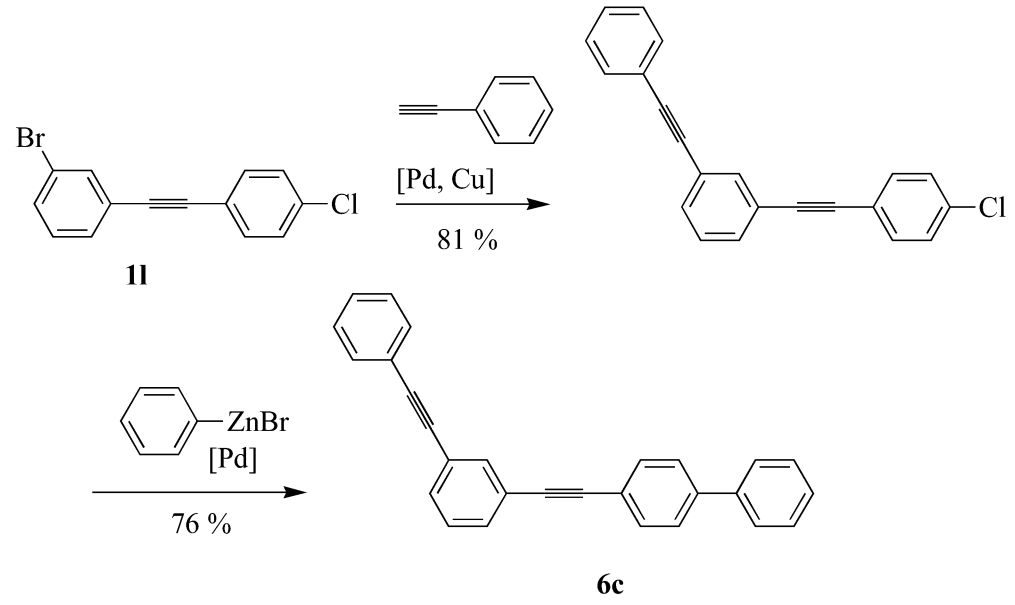
With the above compounds in hand, we turned our attention to demonstrating their synthetic potential as building blocks for a wide spectrum of higher homologues of phenyleneethynylenes. Sonogashira coupling between bromo iodo diphenylacetylenes with aryl acetylenes occurred on the iodide exclusively (Scheme 8). Subjection of these monobromides to additional Sonogashira reaction led to **6a** and **6b**, respectively. The positions of the ethynyl groups on the aromatic rings can be controlled by choosing appropriate dihalo diphenylacetylenes. Substituents like the hexyl group can also be incorporated at whichever positions depending on the substituents of the starting sulfone and aldehyde. Suzuki–Miyaura coupling was employable for the second reaction as well, and a biphenylacetylene derivative **6c** was obtained. Mizoroki–Heck reaction also worked well (Scheme 9). The reaction of the bromo iodo substrate **1x** with methyl acrylate proceeded exclusively on the iodide to afford a monobromide. Subjection of this compound to Sonogashira reaction provided an ene-yne **6d**, while conjunction with Suzuki–Miyaura coupling furnished the corresponding biphenyl derivative **6e**. Combination of bromo and chloro functions is also useful for selective C–C bond formations. Subjection of bromo chloro substrate **1l** to Sonogashira reaction led to a monochloride, which then underwent Negishi coupling to afford a biphenyl derivative **6c** (Scheme 10).



Scheme 8 Sonogashira/Sonogashira or Suzuki–Miyaura coupling.



Scheme 9 Mizoroki–Heck/Sonogashira or Suzuki–Miyaura coupling.

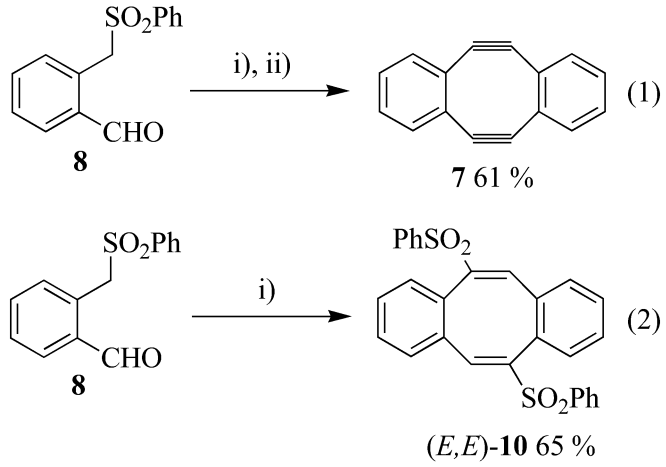


Scheme 10 Sonogashira/Negisha coupling.

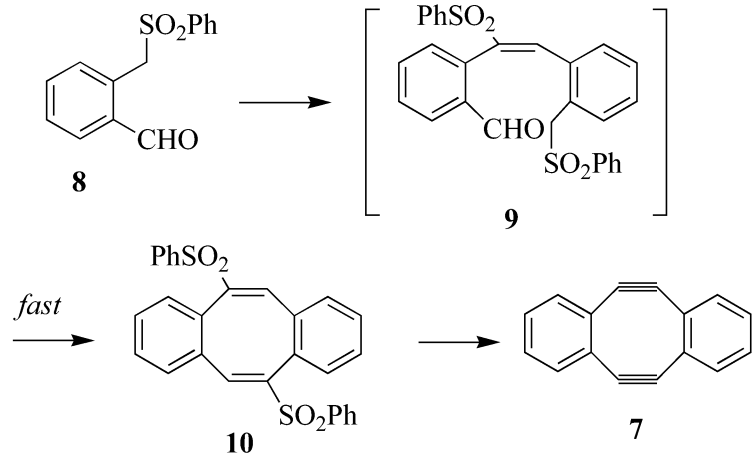
Synthesis of 5,6,11,12-tetradehydrodibenzo[a,e]cyclooctene [8]

5,6,11,12-Tetradehydrodibenzo[a,e]cyclooctene (**7**) is the smallest cyclophane with alternate aryleneethynylene linkage. As expected, this compound was found to possess highly bent acetylenic bonds (155.7°) on the basis of X-ray analysis [9]. Quite naturally, such acetylenic bonds are highly reactive. The synthesis of **7** was first achieved by Sondheimer et al. [10]. Bromination of *sym*-dibenzocyclooctatetraene with irradiation (~75 % yield) followed by dehydrobromination of the resulting tetrabromide with *t*-BuOK (48 % yield) furnished **7**. Besides a relatively low overall yield (36 %) in this process, two procedures for preparing *sym*-dibenzocyclooctatetraene with recourse to Wittig [11] and Knoevenagel [12] condensations were reported to result in less than 20 % yield starting from *o*-phthalaldehyde. As such, the Sondheimer process is not efficient. This process was modified recently by Wudl et al. [13]. Youngs et al. invoked Sonogashira coupling to dimerize an *o*-ethynyl iodobenzene derivative with bulky substituents at ortho positions, yet only a 10 % yield of the desired cyclophane was obtained [14]. The low yield was ascribed to the highly reactive acetylenic bonds of the product under the reaction conditions. It is apparent, therefore, that the direct C–C bond formation at terminal acetylenes is not easy to generate cyclic acetylenes on account of the propensity of the sp carbon to adopt the linear disposition. Such a drawback is particularly conspicuous with small rings like **7**. In the double elimination process, the initial C–C bond is formed between sp^3 carbons and the successive eliminations follow, giving rise to sp^2 and finally sp carbons in a stepwise manner. Accordingly, it is reasonable to assume that involvement of bent sp^3 or sp^2 carbons allows this protocol to construct aryleneethynylene cyclophane skeletons more easily than the terminal acetylene coupling modes.

Our procedure is quite simple (Scheme 11, eq. 1). A mixture of *o*-(phenylsulfonylmethyl)benzaldehyde (**8**) and $(EtO)_2P(O)Cl$ was treated with $LiN(TMS)_2$ (LiHMDS) at –78 °C ~room temperature (rt). Then, the reaction mixture was exposed to lithium diisopropylamide (LDA) at –78 °C to afford **7** in 61 % yield. Notably, all operations were performed in one pot and the selection of the above combination of bases is crucial. The starting material **8** could be readily obtained from commercially available tolunitrile (see Experimental section). A plausible reaction pathway is shown in Scheme 12. Initially, **8** undergoes phosphonation and subsequent intermolecular Wittig–Horner reaction to afford mono(vinylsulfone) intermediate **9** that probably consists of (*E*)- and (*Z*)-isomers. Only the (*E*)-isomer can undergo the second intramolecular Wittig–Horner reaction to arrive at bis(vinylsulfone) **10** while the (*Z*)-counterpart presumably oligomerizes as a result of intermolecular condensations. In fact, when the reaction was quenched before addition of LDA, **10** was isolated in 65 % yield after column chromatography (Scheme 11, eq. 2). Thin-layer chromatograpy (TLC) monitoring of the reaction exhibited highly polar material presumably due to the oligomers derived from (*Z*)-**9**. X-ray diffraction study confirmed the (*E*,*E*)-structure for **10**. Apparently, the *E*-geometry of **9** is crucial for arriving at **10** so that the second formyl and sulfonylmethyl groups could get close to each other, whereas no effective interaction between these two groups are feasible with *Z*-geometry. The failure of all attempts to isolate **9** suggests that this intermediate was consumed as soon as it had been generated. Obviously, the rigid *E*-geometry is responsible for the acceleration of the second Wittig–Horner reaction.

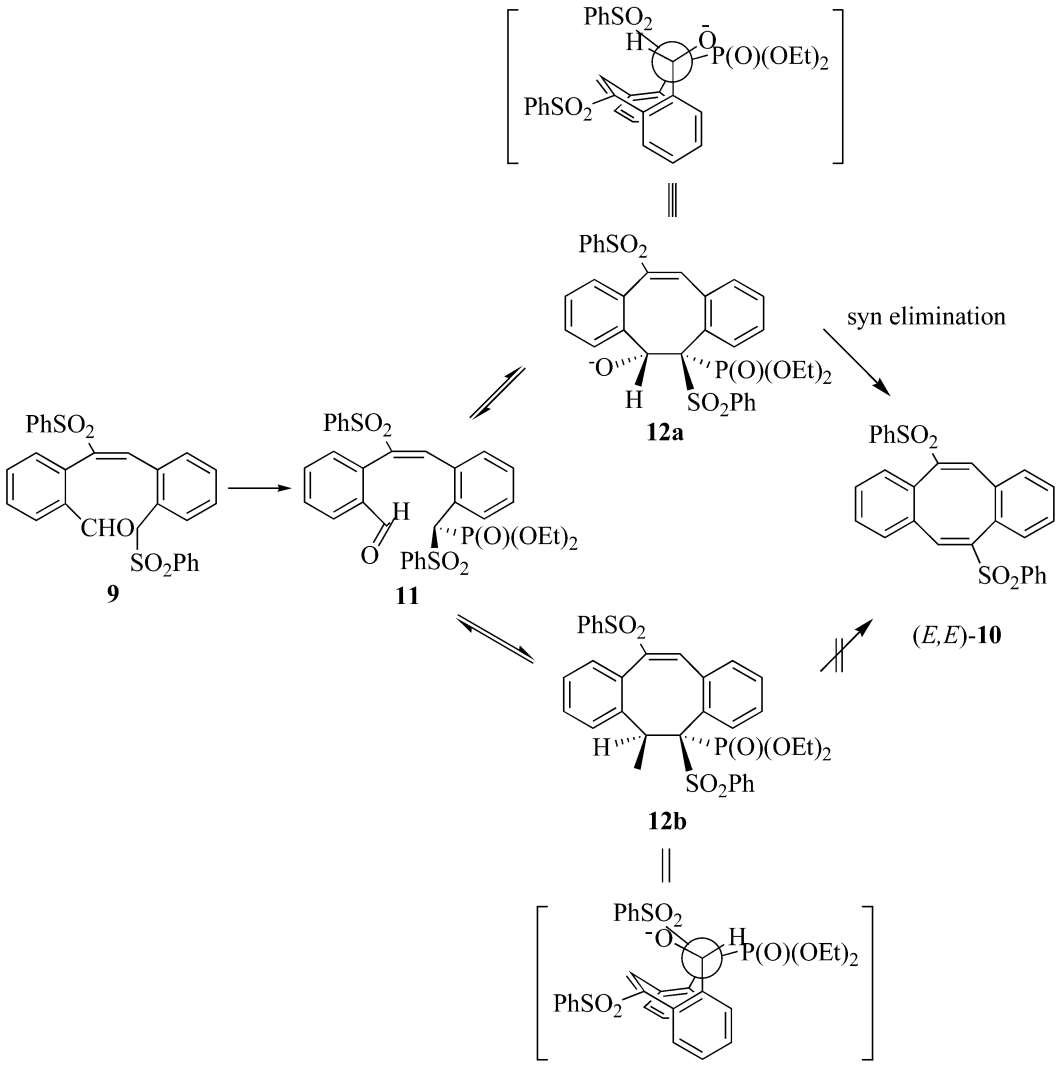


Scheme 11



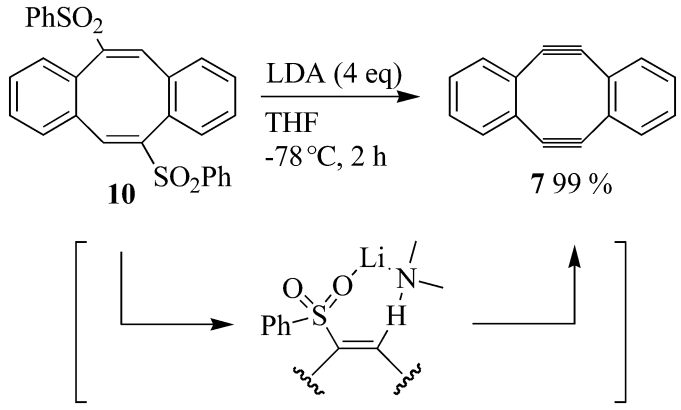
Scheme 12

The generation of (*E*,*E*)-**10** can be accounted for on the basis of the equilibration as shown in Scheme 13. The intermediate **9** is converted to **11** through consecutive lithiation, phosphonation, and the second lithiation. The anion **11** undergoes intramolecular C–C bond formation to give **12**. The diastereomer **12a** is readily transformed to (*E*,*E*)-**10** through *syn*-elimination via a four-membered intermediate, while the analogous elimination is not allowed for **12b** due to the conformational rigidity arising from the pre-existing (*E*)-sulfonyl alkene linkage. Since **12a** and **12b** are involved in an equilibrium via **11** due to the well-recognized fluttering of α-sulfonylbenzyl anion [15] as well as rotation of the aryl-formyl bond, the equilibrium is biased in favor of **12a**.



Scheme 13

The elimination of **10**, upon treatment with LDA (4 equiv), proceeded completely to give **7** even at –78 °C (Scheme 14). Such facile reaction has never been encountered since the elimination of vinyl sulfones usually demands higher reaction temperatures (rt ~60 °C) and the yield is not so high as in the present case [5,6]. Furthermore, the progress of the reaction itself is counterintuitive in terms of the increase in the ring strain as the elimination advances. The uphill variation is apparent from the heats of formation calculated by PM3 [16] for relevant species (Fig. 2) [17]. Hence, the high reactivity should be accounted for on the kinetic grounds. Probably, the facile *syn*-elimination [18] as depicted in Scheme 14 is responsible. It should be noted that the difference of the heat of formation ($\Delta\Delta H_f$) is larger in the first elimination than in the second one (Fig. 2) [19]. This is in accord with experimental results that no mono(vinylsulfone) species was detected even by use of lesser amounts of LDA, indicating much faster second elimination than the first one.



Scheme 14

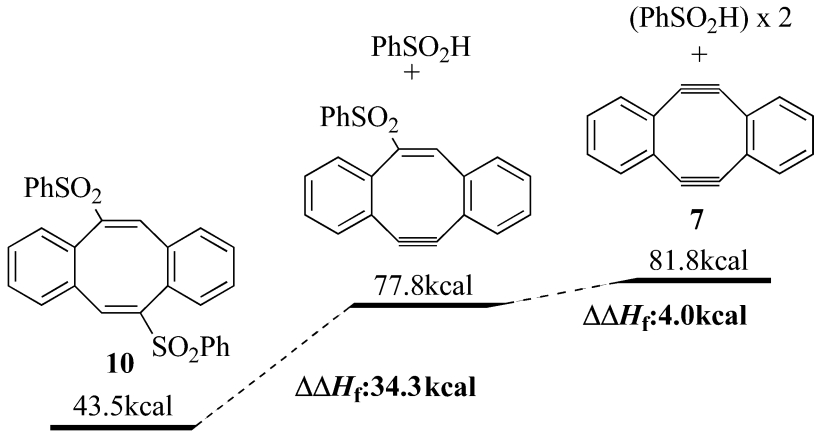
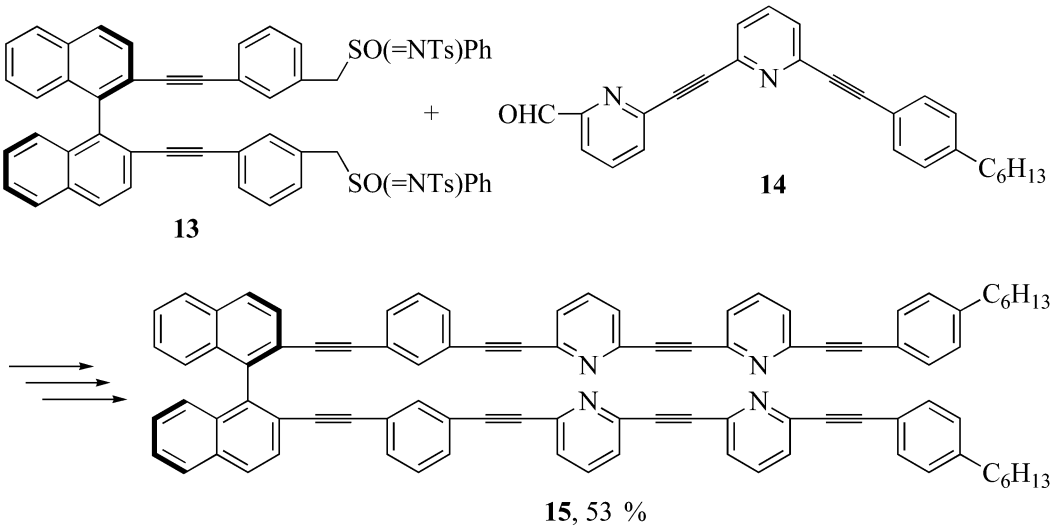


Fig. 2 PM3-calculated heat of formation.

Enantiopure aryleneethynylene double helicates [20]

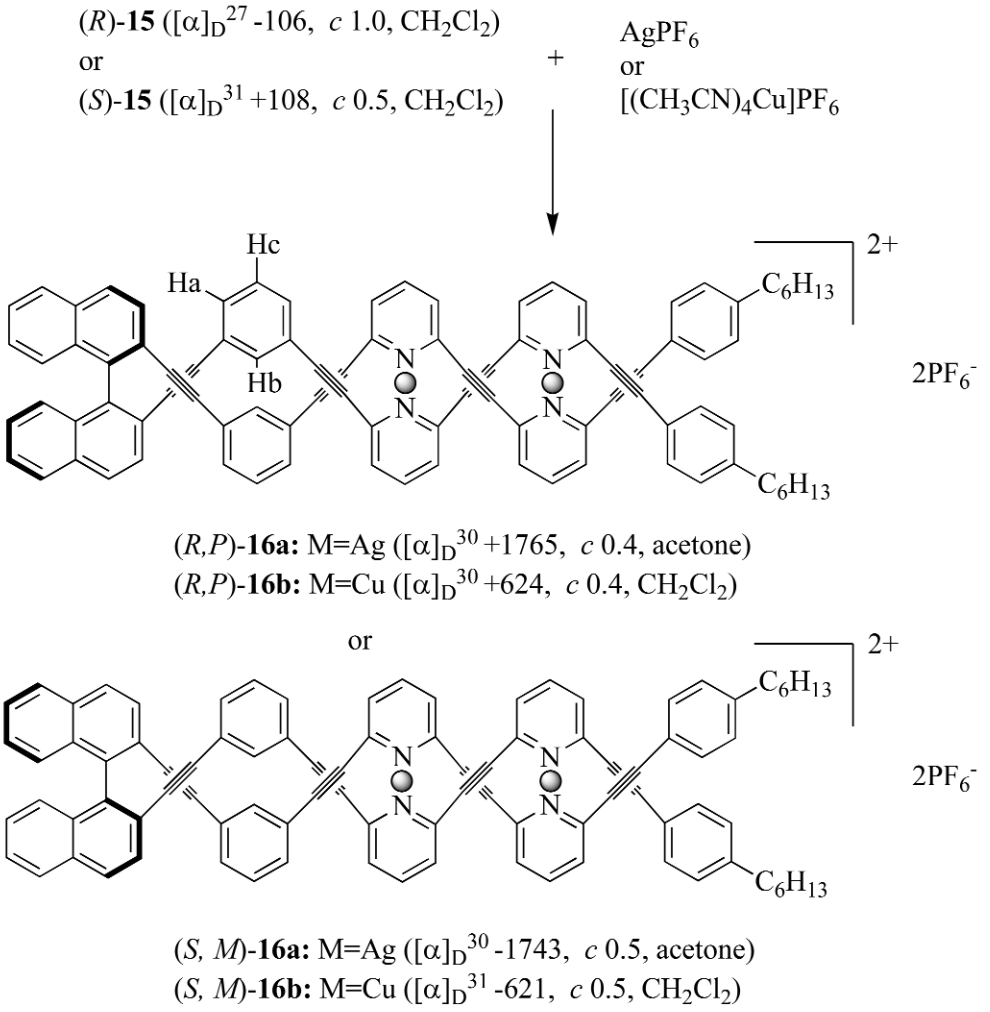
Extensive attention has been paid to the self-assembly of double helicates, some now available even in enantiomerically pure form [21]. Metal coordination chemistry has played a pivotal role for this purpose since the pioneering work by Lehn et al. [22]. The most common way to arrive at homochiral helicates is to introduce a chiral center into the backbone of the ligand strand [23]. Spontaneous resolution is also effective on some occasions [24]. Another strategy is to attach ligand strands to a chiral template as developed by Cozzi, Siegel et al. [25]. During a project on aryleneethynylene chemistry, we reported the synthesis of an enantiopure double-helical phenyleneethynylene cyclophane [26]. Consequently, we have become interested in acyclic analogs because no such motif is known in contrast to extensive work on the relevant single helices [27]. Inspection of molecular models suggested to us that the double-helix arrangement would be feasible if the strands with alternating ethynylene/*meta*-arylene arrays were connected to the 2- and 2'-positions of a 1,1'-binaphthalene template. However, preliminary experiments soon revealed that no helical structures could be attained by use of simple phenyleneethynylene chains due to the lack of effective interactions between them. We were then intrigued by the Cozzi–Siegel strategy. On the basis of molecular modeling, pyridine was found to be a suitable donor unit due to fitness of the metal-nitrogen coordination bond in the rigid aryleneethynylene double-helical systems. The binaphthyl group was a stereogenic template of choice because of its facile

availability [28]. The aldol-type coupling between an enantiopure disulfoximine **13** and pyridylcarboxaldehyde **14** followed by double elimination of the resulting β-substituted sulfoximine furnished the desired acetylene **15** in 53 % yield (Scheme 15) [29]. Notably, the product thus formed suffered from no coloration and enjoyed facile purification. When the corresponding disulfone was employed instead of **13**, yellowish product **15** was obtained only in 30 % yield.



Scheme 15

Metal complexation was straightforward. To a THF solution of either (*R*)- or (*S*)-**15** (1 equiv) was added a THF solution of $AgPF_6$ (2.2 equiv) in the dark at rt (Scheme 16). The complex **16a** precipitated immediately as a white solid. The ^{1}H NMR spectrum of **16a** revealed that H_a and H_c experienced an appreciable upfield shift relative to **15**, while H_b resonance was shifted downfield. In the complex, H_a and H_c are situated in the diamagnetic region of the binaphthyl group, and H_b is deshielded by a phenyl ring of the counterpart strand. These shifts suggest that the freely moving strands in **15** are immobilized as in **16a**. The corresponding Cu(I) complexes **16b** were obtained analogously as yellow precipitates when (*R*)- or (*S*)-**15** was added to $[(CH_3CN)_4Cu]PF_6$ (2.2 equiv) in CH_2Cl_2. NMR spectra of these complexes exhibited slightly broad signals, possibly due to dynamic dissociation. Such slight instability may be ascribed to the two-coordinate metal complex [23f,30]. Some two-coordinate Cu(I) and Ag(I) complexes are known, and a dynamic change of bonding mode was suggested for Cu(I) and Ag(I) complexes. Confirmation of the 2:1 metal/**15** stoichiometry of the complexes **16a** and **6b** was attempted by electrospray and matrix-assisted laser desorption ionization with time-of-flight mass spectrometries (MALDI-TOFs). However, both methods gave rise to no parent peak, but a peak appeared assignable to the 1:1 species corresponding to **15**/Ag^+ or **15**/Cu^+ in which one of the metal ions and all PF_6 anions had been removed from **16a** and **16b** probably because of weak coordination bonding and possibly metal–metal repulsion in the multimetal coordination. This nevertheless does not mean that **16a** and **16b** possess a 1:1 composition. The 2:1 stoichiometry is supported by titration experiments in circular dichroism (CD) spectra (vide infra). Furthermore, ^{1}H NMR spectrum of a 1:1 mixture of **15** and $AgPF_6$ exhibited only broad signals in contrast to the sharp signals of **16a**.



Scheme 16

While complexes **16a**, **b** exhibited no significant difference from free **15** in UV–vis spectra, $[\alpha]_D$ values were greatly altered (Scheme 16). The negative value of (*R*)-**15** was converted to large positive values upon complexation, and the reverse transition occurred on complexation of (*S*)-**15**. Since such enormous variation cannot be induced solely by deformation of the binaphthyl core, it is reasonable to conclude that the chirality has emerged from the strands as well. Similar behavior found in the Cozzi–Siegel protocol with oligo(bipyridine-ether) strands was attributed to double-helix formation [25].

Analysis of CD spectra also supported the emergence of chirality in the strands (Fig. 3). The strong Cotton effect with a zero point at 320 nm observed for (*R*)- and (*S*)-**15** disappeared in the complexes. Alternatively, the silver complexes exhibited a strong peak at 345 nm and a medium peak at 310 nm, whereas only a broad peak was observed at 310 nm in the copper complexes. Such spectral changes were characteristic of double-helix formation in our previous study on chiral acetylenic cyclophanes [26]. It is highly probable, therefore, that double helicates are formed in both silver and copper complexes. The completely reversed spectral profiles of the complexes derived from antipodal (*R*)- and (*S*)-**15** imply that the helical modes of strands in these complexes are heterochiral. The 2:1 metal/**15**

stoichiometry of the complexes was confirmed on the basis of CD spectra through titration with the metal (Fig. 4). Upon increasing the amount of the silver salt added to (*R*)-**15**, the negative sign band at 340 nm diminished gradually while a new positive sign band at 345 nm appeared. The intensity of this band reached an upper limit at the 2:1 metal/**15** ratio and experienced no more enhancement beyond this ratio.

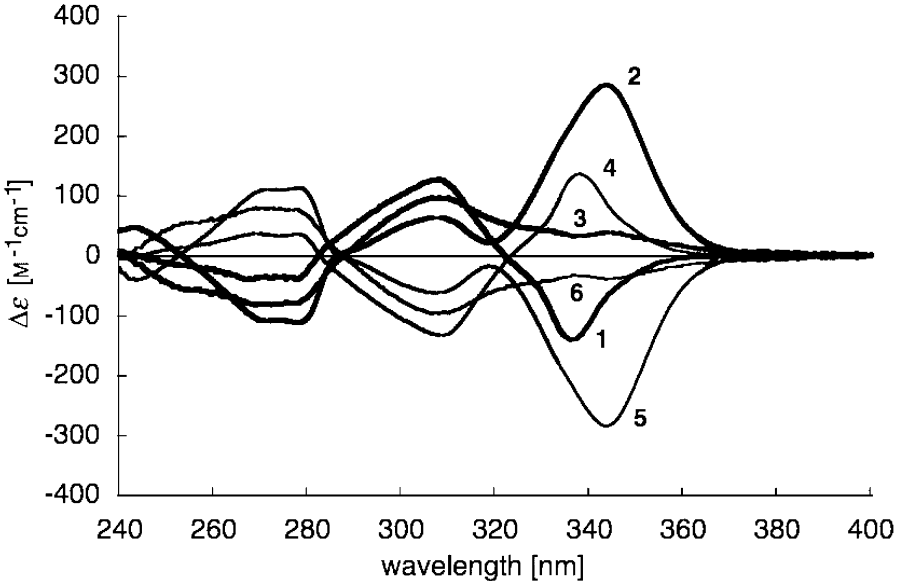


Fig. 3 CD spectra of **15** and **16**. (1) (*R*)-**15** in CH_2Cl_2; (2) (*R*,*P*)-**16a** in 95:5 $CHCl_3$/DMF; (3) (*R*,*P*)-**16b** in CH_2Cl_2; (4) (*S*)-**15** in CH_2Cl_2; (5) (*S*,*M*)-**16a** in 95:5 $CHCl_3$/DMF, (6) (*S*,*M*)-**16b** in CH_2Cl_2.

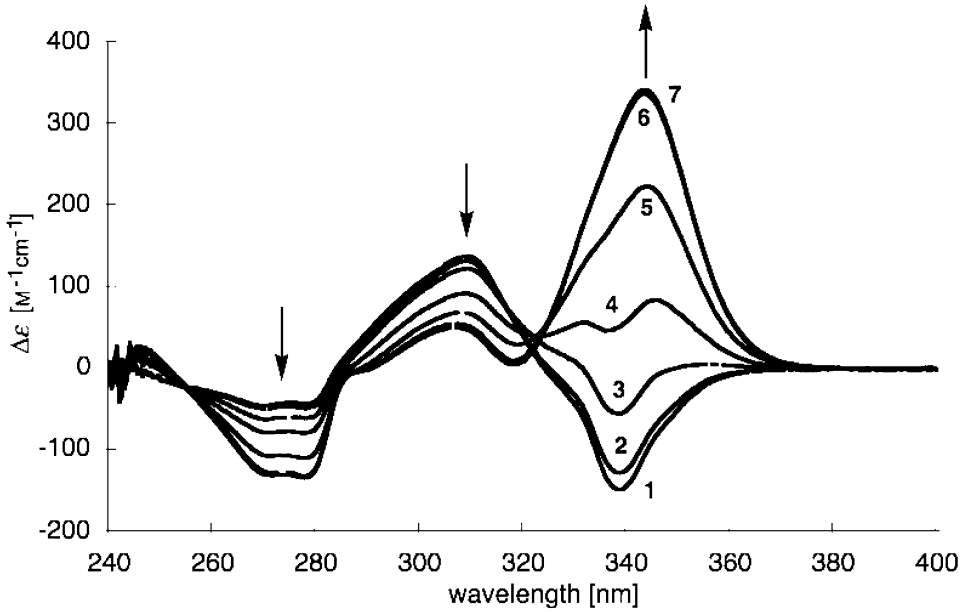


Fig. 4 CD spectral change upon titration of (*R*)-**15** with $AgPF_6$ in 95:5 $CHCl_3$/DMF. $AgPF_6$/(*R*)-**15**: (1) 0.0; (2) 0.4; (3) 0.8; (4) 1.2; (5) 1.6; (6) 2.0; (7) 2.4.

CONCLUSION

The double elimination reaction of β-substituted sulfones has proved to be useful for synthesis of various aryleneethynylenes. In particular, otherwise difficult-to-prepare diphenylacetylenes with different halogen substituents are accessible in a straightforward manner. These compounds are versatile building blocks for higher homologues of phenyleneethynylenes because various C–C bond formations like Sonogashira, Mizoroki–Heck, Suzuki–Miyaura, and Negishi couplings can be conducted sequentially on the different halogen functions. According to this strategy, various moieties can be incorporated at any desired positions because all substitution patterns of halogens are accessible for dihalo diphenylacetylenes. Notably, the substitution modes are readily controlled by suitable choice of substituted benzyl sulfones and benzaldehydes. As a consequence, a variety of aromatic acetylene compounds with regulated structure and composition can be tailored conveniently. We believe that the present protocol will find a wide range of utilization in synthesis of acetylenic materials.

The extremely concise, high-yielding process for 5,6,11,12-tetradehydrodibenzo[a,e]cyclooctene has been established according to the reaction pathway given in Scheme 11. It should be noted that an attempt for similar dimerization by Sonogashira coupling failed; the corresponding oligomers resulted. Apparently, the bond formation between sp^3 carbons followed by conversion to sp carbons in the double elimination protocol is a key factor for the successful dimerization.

When benzylic sulfones give poor yields in the double elimination reactions, sulfoximines work better on some occasions. Incorporation of pyridine moieties into the aryleneethynylene strands attached to the binaphthyl chiral auxiliary was successfully realized by this protocol. The resulting strands formed a double helicate upon complexing with Ag(I) and Cu(I) salts. The helicate formation could be unambiguously elucidated by characteristic variations of $[\alpha]_D$ values and CD spectra.

As such, the double elimination protocol will find a wide spectrum of applications for synthesis of aryleneethynylenes.

EXPERIMENTAL

*Preparation of **1a** through double elimination of β-substituted sulfone derived from the reaction of **2a** with **3a** (representative)*: To a THF solution (5 mL) of 2-bromobenzyl phenyl sulfone **2a** (372 mg, 1.2 mmol) was added a hexane solution of BuLi (1.60 M, 0.75 mL, 1.2 mmol) at –78 °C, and the mixture was stirred for 0.5 h. A THF solution (3 mL) of 2-chlorobenzaldehyde **3a** (141 mg, 1.0 mmol) was added at –78 °C, and the mixture was stirred for 0.5 h. Diethyl chlorophosphate (0.14 mL, 1.0 mmol) was added at –78 °C, and the mixture was stirred at rt for 1 h. A THF solution of LiHMDS (1.0 M, 4.0 mL, 4.0 mmol) was added at –78 °C, and the mixture was stirred at rt for 2 h. After usual work-up with ethyl acetate and NH_4Claq, drying over $MgSO_4$ and evaporation, the residue was subjected to a thin pad of silica gel to furnish **1a** in a pure form (216 mg, 74 %).

*Preparation of **1r** through double elimination of β-substituted sulfone derived from the reaction of **2c** with **3a** (representative)*: To a THF solution (5 mL) of 4-bromobenzyl phenyl sulfone **2c** (372 mg, 1.2 mmol) was added a THF solution of LiHMDS (1.0 M, 1.2 mL, 1.2 mmol) at –78 °C, and the mixture was stirred for 0.5 h. A THF solution (3 mL) of 2-chlorobenzaldehyde **3a** (141 mg, 1.0 mmol) was added at –78 °C, and the mixture was stirred for 0.5 h. Diethyl chlorophosphate (0.14 mL, 1.0 mmol) was added at –78 °C, and the mixture was stirred at rt for 1 h. A THF solution of LiHMDS (1.0 M, 4.0 mL, 4.0 mmol) was added at –78 °C, and the mixture was stirred at rt for 2 h. After usual work-up with ethyl acetate and NH_4Claq, drying over $MgSO_4$ and evaporation, the residue was subjected to a thin pad of silica gel to furnish **1r** in a pure form (245 mg, 84 %).

*Preparation of **8***: (i) α-Bromotolunitrile: A 100-mL flask was charged with *o*-tolunitrile (2.37 mL, 20.0 mmol), *N*-bromosuccinimide (3.74 g, 21.0 mmol), AIBN (328 mg, 2.0 mmol), and CCl_4 (30 mL). After the mixture had been stirred at 80 °C for 5 min and at 90 °C for 2 h, the reaction mixture was cooled to rt and filtered. The filtrate was washed with aqueous $NaHCO_3$, dried over $MgSO_4$,

and filtered. The solvent was evaporated in vacuo, and the residue was chromatographed (1:9 AcOEt/hexane) to give 3.14 g of α-bromotolunitrile (80 %) as a white solid: ^{1}H NMR ($CDCl_3$) 500 MHz: δ 4.64 (s, 2H), 7.43 (dt, *J* = 1.6, 7.5 Hz, 1H), 7.55–7.63 (m, 2H), 7.68 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) 75 MHz: δ 29.30, 112.36, 116.70, 128.90, 130.41, 133.13, 133.22, 141.05. (ii) *o*-(Phenylsulfonylmethyl)benzonitrile: A 100-mL flask was charged with α-bromotolunitrile (3.92 g, 20.0 mmol), benzenesulfinic acid sodium salt dihydrate (4.80 g, 24.0 mmol), and dimethylformamide (DMF) (30 mL). After the mixture had been stirred at 80 °C for 2 h, the reaction mixture was cooled to rt. After usual work-up with water and ethyl acetate, the solvent was evaporated in vacuo, and the residue was subjected to recrystallization from AcOEt/hexane to give 4.58 g of *o*-(phenylsulfonylmethyl)benzonitrile (89 %) as colorless needles: m.p. 157–160 °C; ^{1}H NMR ($CDCl_3$) 300 MHz: δ 4.57 (s, 2H), 7.27–7.57 (m, 4H), 7.62–7.73 (m, 5H); ^{13}C NMR ($CDCl_3$) 75 MHz: δ 60.46, 114.33, 116.51, 128.67 (2C), 129.25 (2C), 129.36, 131.60, 132.18, 132.77, 132.93, 134.28, 137.48. (iii) *o*-(Phenylsulfonylmethyl)benzaldehyde (**8**): A 100-mL flask was charged with *o*-(phenylsulfonylmethyl)benzonitrile (1.29 g, 5.0 mmol) and CH_2Cl_2 (15 mL), and DIBAL-H (1.0 M in hexane, 11.5 mL, 11.5 mmol) was added at –78 °C. After the mixture had been stirred at this temperature for 2 h, aqueous NH_4Cl was poured into the mixture. After usual work-up with 1N HCl and CH_2Cl_2, the solvent was evaporated in vacuo, and the residue was subjected to filtration through a thin pad (SiO_2; CH_2Cl_2) and recrystallization from CH_2Cl_2/hexane gave 1.01 g of **8** (78 %) as colorless needles: m.p. 143–145 °C; ^{1}H NMR ($CDCl_3$) 300 MHz: δ 5.03 (s, 2H), 7.43–7.48 (m, 3H), 7.55–7.63 (m, 3H), 7.69-7.75 (m, 3H), 9.83 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 57.67, 128.68 (2C), 128.82, 128.85 (2C), 129.49, 133.57, 133.83, 133.88, 134.49, 134.61, 138.20, 192.04. MS (EI): [M^+] calcd. 260.0507, found 260.0510.

*Synthesis of **7** from **8***: A 100-mL flask was charged with **8** (260 mg, 1.0 mmol), $ClP(O)(OEt)_2$ (0.17 mL, 1.2 mmol) and THF (30 mL), and LiHMDS (1.0 M in THF, 2.0 mL, 2.0 mmol) was added at –78 °C. After the mixture had been stirred at –78 °C for 30 min and, then, at rt for 1.5 h, LDA (1.0 M in THF/hexane, 5.0 mL, 5.0 mmol) was added dropwise at –78 °C. The reaction mixture was stirred at this temperature for 2 h, and aqueous NH_4Cl was poured into the mixture. After usual work-up with water and AcOEt, the solvent was evaporated in vacuo, and the residue was chromatographed (2:3 CH_2Cl_2/hexane) to give 61 mg of **7** (61 %) as a yellow solid: ^{1}H NMR ($CDCl_3$) 300 MHz: δ 6.71–6.77 (m, 4H), 6.90–6.96 (m, 4H); ^{13}C NMR ($CDCl_3$) 75 MHz: δ 109.28, 126.68, 129.01, 132.83.

Synthesis of **15**: To a THF solution (3 mL) of disulfoxime **13** (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 **14** (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 work-up with sat. NH_4Claq/CH_2Cl_2, the combined organic layer was washed with brine and dried over anhydrous sodium sulfate. The organic layer was evaporated under vacuum, and the residue was subjected to column chromatography to give **15** (130.1 mg, 53 %).

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