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Cyclopentadienones as intermediates for the synthesis of highly functionalized biaryls☆

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Abstract—A new approach to the synthesis of substituted biaryls, via Diels–Alder reaction between cyclopentadienones and arylacetylenes, is described.

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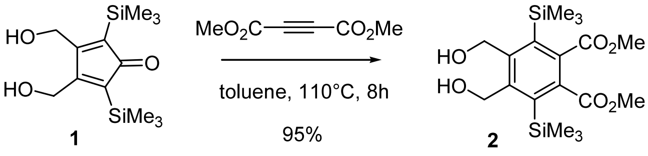
1. Introduction

Biaryls are important subunits in a broad range of natural product molecules,[1] as well as ligands used in asymmetric catalysis,[2,3] and materials structures.[3] Numerous methods have been developed for the construction of these molecules, mostly by direct coupling of two suitably activated aromatic moieties.[1,4] Nonetheless, alternative approaches to these structures that allow introduction of dense functionality, as well as the potential for generating chiral biaryl structures, represent useful additions to the currently available methodology. One such approach might be the reaction of a cyclopentadienone derivative with a suitably functionalized alkyne, which is known[5] to generate aromatic molecules by a Diels–Alder cycloaddition followed by cheletropic extrusion of carbon monoxide. While this reaction has been reported for alkynes such as dimethyl acetylenedicarboxylate, as far as we are aware there have been no reports of its application to biaryl synthesis, wherein an arylalkyne is used as the dienophile. This paper reports our initial investigations into this reaction, which appears to provide a potentially useful alternative approach to biaryl synthesis.

We recently reported a method for preparing unsymmetrically substituted cyclopentadienones by a silicon tethered [2+2+1] cyclocarbonylation reaction of two alkynes promoted by pentacarbonyliron.[6] This reaction has the potential to afford a broad range of cyclopentadienones that are versatile intermediates for organic synthesis, because the silicon tether can be removed under conditions that are non-invasive toward the reactive cyclopentadienone. The symmetrically substituted compound **1** was chosen as a substrate for the present study in order to circumnavigate regiochemical issues in the synthesis of the target biaryl structures.

2. Results and discussion

In order to ensure that **1** is a suitable substrate for Diels–Alder reaction/CO extrusion to afford aromatic molecules, we examined its reaction with dimethyl acetylenedicarboxylate, which proceeded smoothly in toluene at 110°C to afford the hexasubstituted benzene derivative **2**. It should be mentioned that, since we have access to a wide range of cyclopentadienone structures using the aforementioned cyclocoupling methodology, this procedure could in principle afford numerous hexasubstituted aromatic compounds. Moreover, the known chemistry of arylsilanes,[7] such as ipso electrophilic substitution, is expected to generate a rich chemistry for these products.



Our first attempt to utilize **1** as a precursor to biaryls examined its reaction with the simple methyl phenylpropiolate (**3**), a known compound that was prepared by esterification of the corresponding acid. No reaction

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Keywords: biaryl; cyclopentadienone; alkyne; cycloaddition.

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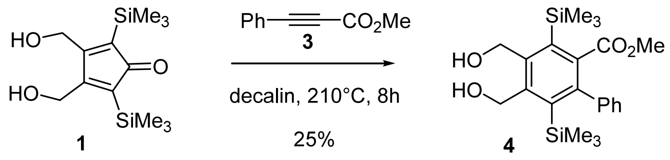
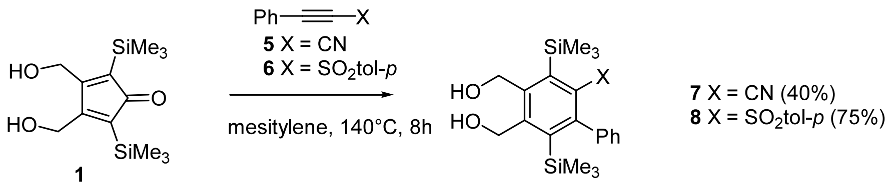




was observed in toluene at 110°C, or in mesitylene at 140°C, but higher temperature (decalin, 210°C, 8 h) promoted the formation of biaryl **4**, in low yield (25%). Owing to its less electron deficient nature, alkyne **3** is a less effective dienophile than dimethyl acetylenedicarboxylate, and we therefore investigated activating groups other than ester in an effort to generate biaryls in good yield under somewhat milder reaction conditions. Compounds **5**[8] and **6**[9] were prepared by published procedures and subjected to Diels–Alder reaction with **1**: **5** in mesitylene for 8 h at 140°C afforded biaryl **7** in 40% yield, while **6** under identical conditions produced **8** in 75% yield.

Of greater interest is the construction of biaryls containing substituents on both aromatic rings, especially at the *o* and *o′* positions, for which purpose the reaction between **1** and substituted phenylacetylenes was studied. Two dienophiles, **12a** and **12b**, were prepared via the Sonagashira procedure reported by Thorand and Krause[10] to access the intermediates **10a** and **10b**. The TMS group was removed from each intermediate by stirring with K_2CO_3 in methanol,[11] and the resulting arylacetylenes were converted to the nitriles using the electrophilic cyanation method described by Wu et al. (Scheme 1).[12]

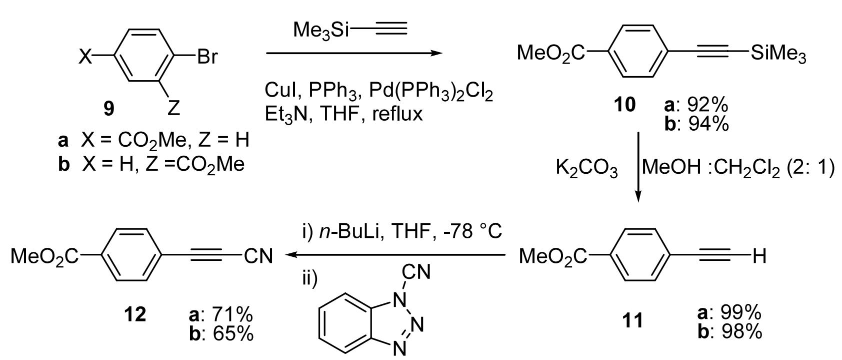
Reaction of **1** with **12a** and **12b** afforded similar yields of biaryl products **13** and **14** as observed for the unsubstituted phenylpropiolonitrile, indicating that the presence of an electron withdrawing group on the aromatic ring does not have a significant effect on the electronic nature of the dienophile, and that the presence of one ortho substituent does not lead to significant steric retardation of the cycloaddition reaction.

3. Conclusions

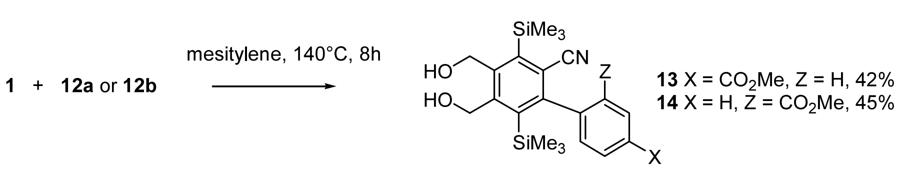
In summary, we have demonstrated that cyclopentadienones are potentially useful intermediates for the construction of multi-substituted biaryl structures. Clearly there is much to be done in further development of this protocol, which will form the basis for future studies in our laboratory.

4. Supplementary material

Spectroscopic characterization data for all new compounds, and copies of their ^1H and ^{13}C NMR spectra.



Scheme 1.



Acknowledgements

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References

1. For a recent review of biaryl synthesis as well as an overview of natural product structures based on biaryls, see: Lloyd-Williams, P.; Giralt, E. *Chem. Soc. Rev.* **2001**, *30*, 145.
2. Examples include the binaphthyl-derived ligands such as BINOL: Mikami, K.; Motoyama, Y. In *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L. A., Ed.; John Wiley and Sons: Chichester, 1995; Vol. 1, p. 403; Guiry, P. J.; McCarthy, M.; Lacey, P. M.; Saunders, C. P.; Kelly, S.; Connolly, D. J. *Curr. Org. Chem.* **2000**, *4*, 821.
3. Pu, L. *Chem. Rev.* **1998**, *98*, 2405.
4. Recent reviews: Bringmann, G.; Tasler, S. *Tetrahedron* **2001**, *57*, 331; Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359; Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314; Suzuki, A. *Pure Appl. Chem.* **1985**, *57*, 1749; Suzuki, A. *Pure Appl. Chem.* **1994**, *66*, 213; Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508; Miyara, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
5. (a) Allen, C. F. H.; Ryan, R. W., Jr.; VanAllan, J. A. *J. Org. Chem.* **1962**, *27*, 778; (b) Knolker, H. J.; Baum, E.; Heber, J. *Tetrahedron Lett.* **1995**, *36*, 7647; (c) Harano, K.; Yasuda, M.; Kanematsu, K. *J. Org. Chem.* **1982**, *47*, 4736 and references cited therein; (d) Jikyo, T.; Eto, M.; Harano, K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3463; (e) Jikyo, T.; Eto, M.; Harano, K. *Tetrahedron* **1999**, *55*, 6051.
6. Pearson, A. J.; Kim, J. B. *Org. Lett.* **2002**, *4*, 2837.
7. Fleming, I. In *Comprehensive Organic Chemistry* Jones, D. N., Ed.; Pergamon Press: Oxford, 1979; Vol. 3, Chapter 13.
8. Luo, F.-T.; Wang, R.-T. *Tetrahedron Lett.* **1993**, *34*, 5911.
9. Truce, W.; Wolf, G. C. *J. Org. Chem.* **1971**, *36*, 1727.
10. Thorand, S.; Krause, N. *J. Org. Chem.* **1988**, *63*, 8551.
11. Hirsh, K. A.; Wilson, S. R.; Moore, J. S. *J. Am. Chem. Soc.* **1997**, *119*, 10401.
12. Wu, Y.-Q.; Limburg, D. C.; Wilkinson, D. E.; Hamilton, G. S. *Org. Lett.* **2000**, *2*, 795.