

Synthesis of Differentially Substituted Hexaethynylbenzenes Based on Tandem Sonogashira and Negishi Cross-Coupling Reactions

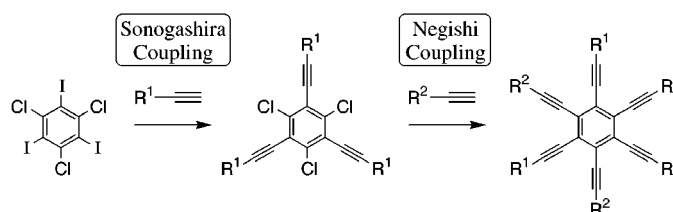
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ABSTRACT



Synthesis of polyethynyl-substituted aromatic compounds was achieved efficiently by the use of the Negishi cross-coupling reaction, and this method, coupled with the Sonogashira reaction, was applied to the synthesis of differentially substituted hexaethynylbenzenes from chloriodobenzenes.

Much attention has been focused in recent years on the hexaethynylbenzene derivatives because of their potential as liquid crystals,¹ nonlinear optical materials,² core structures for dendritic³ as well as light-harvesting materials,⁴ and building blocks for two-dimensional carbon networks (e.g., graphyne).⁵ Differentially substituted hexaethynylbenzenes, in which the ethynyl ends possess different functional groups,

are attractive because it would be possible to change the above properties by modifying the substitution pattern of the terminal groups. In this connection, we and Rubin reported independently approaches to the differentially substituted hexaethynylbenzenes of C_{2v} symmetry based on the Diels–Alder reaction of tetraethynylcyclopentadienones.⁶ A method for the synthesis of hexaethynylbenzenes of D_{3h} symmetry was also developed by Rubin.⁷ Recently, Anthony reported the synthesis of a D_{2h} symmetric hexaethynylbenzene from tetrabromobenzoquinone.⁸

As a part of our research program on the construction of extended π -electronic systems, we planned to develop an efficient method for the synthesis of hexaethynylbenzene derivatives from polyhalogenated benzenes using the Negishi

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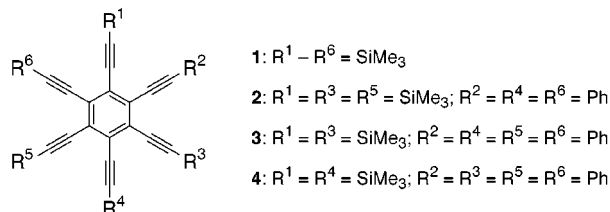
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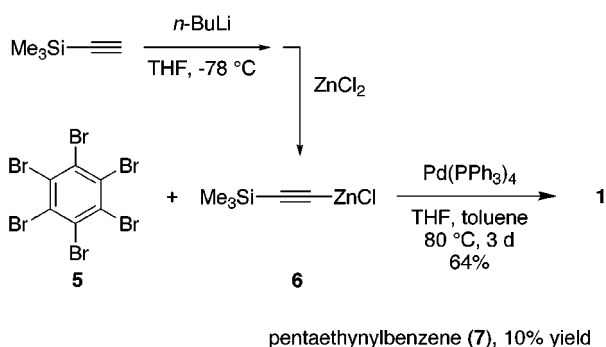
coupling reaction⁹ as a pivotal step. In this context, we report herein the efficient synthesis of polyethynyl-substituted aromatic compounds, hexakis[(trimethylsilyl)ethynyl]benzene (**1**) and 2,4,6-tris[(trimethylsilyl)ethynyl]-1,3,5-triazine (**9**), using the Negishi protocol and its application to a new route to the differentially substituted hexaethynylbenzenes from chloriodobenzenes by ingenious combination with the Sonogashira reaction.¹⁰



To test the efficiency of the Negishi reaction in the multiple substitution on the aromatic core, we chose hexaethynylbenzene **1**¹¹ and triethynyltriazine **9**¹² as the first targets, because (i) these compounds have not been prepared efficiently by the Sonogashira method¹³ and (ii) removal of the trimethylsilyl group of these compounds and subsequent coupling with appropriate aromatic halides would lead to a variety of extended π systems.

When a mixture of hexabromobenzene (**5**) and 10 equiv of [(trimethylsilyl)ethynyl]zinc chloride (**6**), prepared by treatment of (trimethylsilyl)acetylene with butyllithium followed by zinc chloride,^{9a} in the presence of Pd(PPh₃)₄ (20 mol %) was heated in THF¹⁴ at 80 °C for 3 days, hexaethynylbenzene **1** was obtained in 64% isolated yield (Scheme 1).¹⁵ The yield of **1** is much better than those reported previously.¹¹

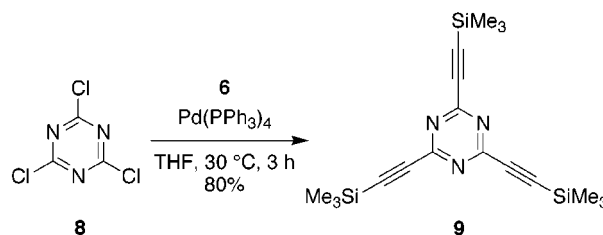
Scheme 1



Similarly, the reaction of 2,4,6-trichloro-1,3,5-triazine (**8**) with ethynylzinc chloride **6**, in the presence of the palladium

catalyst, proceeded smoothly at room temperature to give triethynyltriazine **9** in 80% yield (Scheme 2).

Scheme 2



With these results in hand, we applied the Negishi coupling reaction to the synthesis of differentially substituted hexaethynylbenzenes from chloriodobenzenes. Our plan is based on the combination of two coupling methods, the Sonogashira and Negishi cross-coupling reactions, taking advantage of the difference between the reactivity of the halogen atoms of aryl halides. Namely, the first Sonogashira reaction of chloriodobenzenes would take place selectively at iodine, and subsequent coupling at chlorine would be achieved by the use of the Negishi method. In general, chloroarenes are known to exhibit significant low reactivities to palladium-catalyzed cross-coupling in the absence of activating factors.^{16,17} However, we expected that the weakly electron-withdrawing ethynyl groups introduced by the Sonogashira coupling would activate the remaining C–Cl bonds toward oxidative addition of Pd(0).¹⁸

We reported that the reaction of 1,3,5-trichloro-2,4,6-triiodobenzene (**11**), derived from 1,3,5-trichlorobenzene (**10**) by iodination with periodic acid,¹⁹ with (trimethylsilyl)acetylene under the Sonogashira coupling conditions gave

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(13) The synthesis of **9** and its derivatives has been accomplished by the use of expensive trifluorotriazine (with ethynyllithium reagents: ref 12 and Wortmann, R.; Glania, C.; Krämer, P.; Matschiner, R.; Wolff, J. J.; Kraft, S.; Treptow, B.; Barbu, E.; Längle, D.; Görlitz, G. *Chem. Eur. J.* **1997**, *3*, 1765) or a potentially toxic ethynyltin reagent (with trichlorotriazine **8**: Faust, R.; Göbelt, B. *Tetrahedron Lett.* **1997**, *38*, 8017).

(14) We employed ca. 40% toluene as a cosolvent with THF to raise the reflux temperature.

(15) As a byproduct, pentakis[(trimethylsilyl)ethynyl]benzene (**7**) was isolated in 10% yield (see ref 11b).

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(18) Recently the utility of zinc reagents in palladium-catalyzed cross-coupling reactions of aryl chlorides was reported by Fu. However, alkynylzinc reagents were reported to be unsuitable coupling partners: Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719.

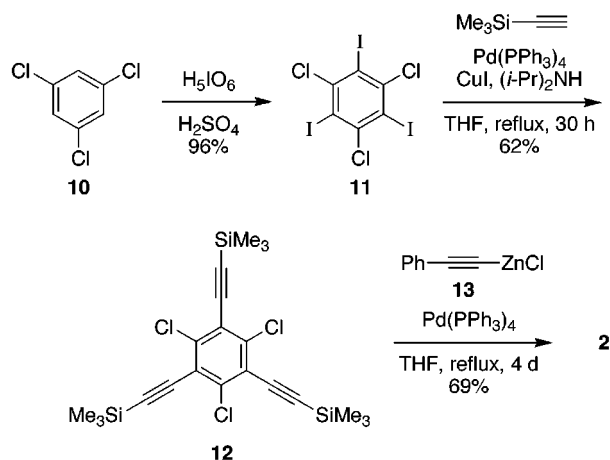
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(9) (a) King, A. O.; Negishi, E.-I.; Villani, F. J., Jr.; Silveira, A., Jr. *J. Org. Chem.* **1978**, *43*, 358. For a review, see: (b) Negishi, E.-I.; Liu, F. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 1–48.

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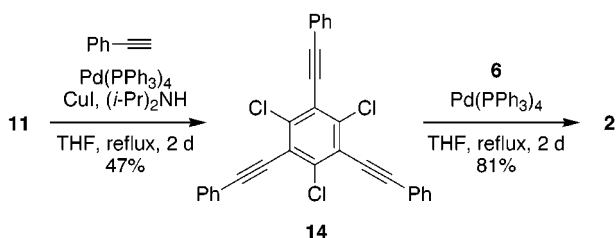
1,3,5-trichloro-2,4,6-tris[(trimethylsilyl)ethynyl]benzene (**12**) in 62% isolated yield.²⁰ As we expected, the reaction of **12** with 20 equiv of (phenylethynyl)zinc chloride (**13**) and 26 mol % of Pd(PPh₃)₄ in THF at the reflux temperature proceeded to give 1,3,5-tris[(trimethylsilyl)ethynyl]-2,4,6-tris(phenylethynyl)benzene (**2**)⁷ with *D*_{3h} symmetry in 69% isolated yield (Scheme 3).

Scheme 3



The synthesis of **2** was also achieved by altering the order of the use of the acetylenes. Namely, the reaction of **11** with 4 equiv of phenylacetylene by the Sonogashira coupling gave (1 mol % of Pd(PPh₃)₄) 1,3,5-trichloro-2,4,6-tris(phenylethynyl)benzene (**14**) in 47% yield. The reaction of **14** with the ethynylzinc chloride **6** gave **2** in 81% yield (Scheme 4).

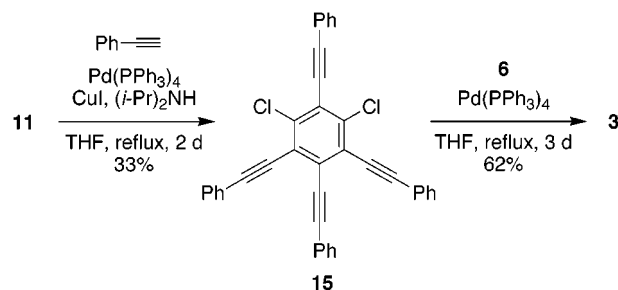
Scheme 4



Interestingly, in the reaction of **11** with phenylacetylene, the use of an excess amount (5.2 equiv) of phenylacetylene and a relatively large amount (10 mol %) of Pd(PPh₃)₄ resulted in tetraethynylation to give **15** in 33% yield as a principal product (Scheme 5). Ethynylation of the remaining chloro substituents of **15** afforded *C*_{2v} symmetric hexaethynylbenzene (**3**).

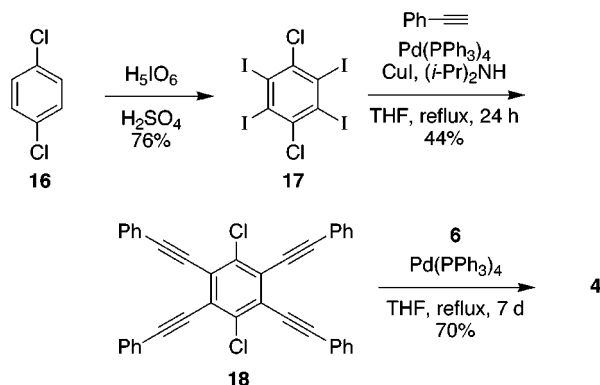
In the same manner, we also prepared a *D*_{2h} symmetric hexaethynylbenzene from 1,4-dichloro-2,3,5,6-tetraiodobenzene (**17**), prepared from 1,4-dichlorobenzene (**16**) by

Scheme 5



periodination. Compound **17** reacted with phenylacetylene under Sonogashira coupling conditions to afford tetrakis(phenylethynyl)benzene **18** in 44% isolated yield. Subsequent reaction of **18** with ethynylzinc chloride **6** under Negishi coupling conditions afforded **4** of *D*_{2h} symmetry in 70% isolated yield (Scheme 6).

Scheme 6



In summary, we demonstrated the utility of ethynylzinc reagents for polyethynylation of aromatic compounds, in particular, differentially substituted hexaethynylbenzenes. With this polyethynylation method, the synthesis of many polyethynyl-substituted aromatic compounds with specific substitution patterns would become possible.

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Note added in proof: After submission of this Letter, the authors became aware of the recent paper by Haley et al., which reported an improvement of the Sonogashira reaction in the perbutadiynylation of hexaiodobenzene by the use of Pd[P(*o*-Tol)₃]₂: Wan, W. B.; Haley, M. M. *J. Org. Chem.* **2001**, 66, 3893.

Supporting Information Available: Experimental procedures and spectral data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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