Diels−Alder Reactions of Tetraethynylcyclopentadienones. An Approach to Differentially Substituted Hexaethynylbenzenes of C_{2v} Symmetry

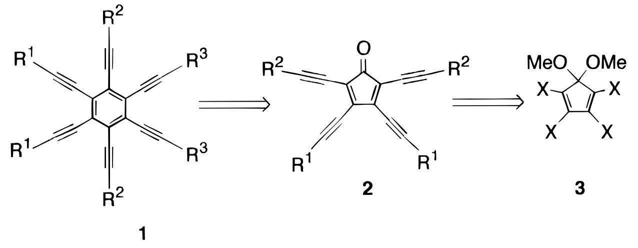
Yoshito Tobe,* Kouzoh Kubota, and Koichiro Naemura

Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan

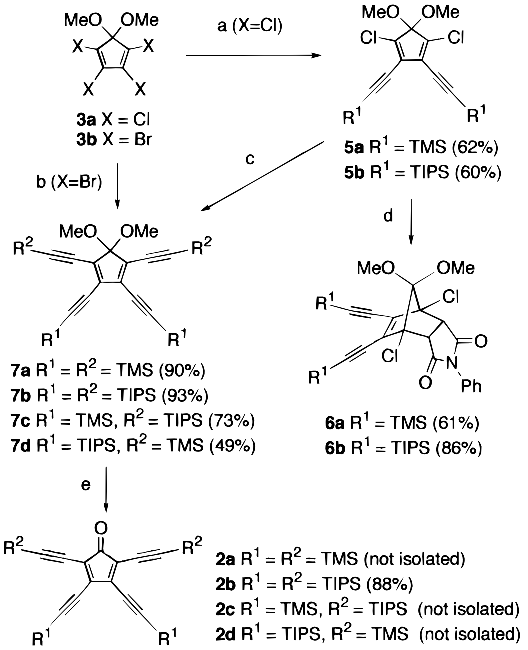
Received February 19, 1997

Hexaethynylbenzene[1] and its derivatives have received extensive attention over the last decade owing to their intriguing properties as liquid crystals[2] and nonlinear optical materials[3] as well as their potential as precursors to a two-dimensional carbon network (e.g., graphyne)[4] and carbon-rich polymeric materials.[5] These properties would be modified if electron-donating or -accepting alkyne end-groups are introduced at specific positions on the benzene ring. However, the reported syntheses, which are based on palladium(0)−copper(I)-catalyzed substitution of hexahalobenzene with acetylene derivatives, are not suited for the preparation of specifically substituted hexaethynylbenzenes because regioselectivity is not expected in this kind of substitution strategy.[1,2b,3,5a,6] In this respect, we planned to develop a method to prepare hexaethynylbenzenes **1** of C_{2v} symmetry possessing three different substituents R^1-R^3 (Scheme 1),[7] which is based on the Diels−Alder reaction of $\alpha,\alpha',\beta,\beta'$-tetraethynylcyclopentadienone **2** with a hexatriyne synthon[8] preceded by a regioselective substitution of tetrahalocyclopentadienone acetal **3** with appropriate acetylenes.[9,10] We expected that Pd(0)−Cu(I)-catalyzed substitution of dienone acetal **3** would take place regioselectively at the β,β' positions, since it has been demonstrated that β-haloenones are more reactive than α-halo enones in Pd(0)-catalyzed coupling reactions.[11]

Scheme 1



Scheme 2[a]



[a] Reagents: (a) TMS-C≡CH (**4a**) or TIPS-C≡CH (**4b**) (2 equiv), $Pd(PPh_3)_4$, CuI, $BuNH_2$, THF, rt; (b) **4a** or **4b** (5 equiv), Pd $(PPh_3)_4$, CuI, *i*-Pr_2NH, THF, rt; (c) for **5a**, **4b**, $PdCl_2(PhCN)_2$, CuI, *i*-Pr_2NH, 50 °C; for **5b**, **4a**, $PdCl_2(PPh_3)_2$, CuI, PPh_3, Et_3N, 89 °C; (d) *N*-phenylmaleimide, toluene, reflux; (e) TFA, CH_2Cl_2 rt.

Reaction of tetrachlorodienone acetal **3a**[12] with 2 equiv of (trimethylsilyl)acetylene (**4a**) in the presence of Pd$(PPh_3)_4$, CuI, and $BuNH_2$ in THF at room temperature proceeded regioselectively to give β,β'-disubstituted compound **5a** (Scheme 2). Similarly, reaction of **3a** with (triisopropylsilyl)acetylene (**4b**) gave **5b**. The regiochemistry of the substitution was established by converting **5a** and **5b** to the respective Diels−Alder adducts **6a** and **6b** with *N*-phenylmaleimide, whose ^{13}C NMR signals of the bridgehead carbons appeared at relatively low field (δ 73.3 for **6a** and 73.9 for **6b**).[13] The Pd(0)−Cu(I)-catalyzed substitution with tetrabromo derivative **3b**[14] gave a mixture of mono-, di-, and trisubstituted products. However, when 5 equiv of acetylene **4a** or **4b** was employed, the corresponding tetrasubstituted dienone acetals **7a** and **7b** were obtained in excellent yields.[9c,d] The second substitution of **5a** with **4b** took place smoothly using $PdCl_2(PhCN)_2$ and CuI as catalysts and diisopropylamine as a base at 50 °C to give **7c** (74%), while substitution of **5b** with **4a** was accomplished at 85 °C

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* To whom correspondence should be addressed. Phone: +81-6-850-6227. Fax: +81-6-850-6229. E-mail: tobe@chem.es.osaka-u.ac.jp.

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(13) *N*-Phenylmaleimide adducts of **3a** and **7a** exhibit the ^{13}C NMR signals of the bridgehead carbons at 75.1 and 56.1 ppm, respectively.

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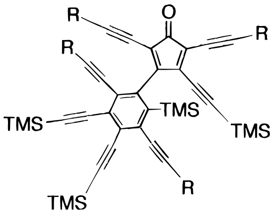
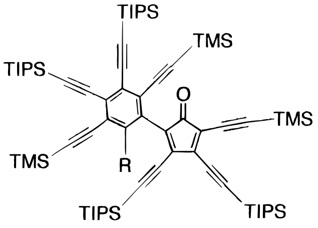
with $PdCl_2(PPh_3)_2$ and PPh_3 in Et_3N, giving **7d** in 49% yield. Hydrolysis of the acetals **7a-d** afforded the corresponding dienones **2a**−**d**, although only the tetrakis-TIPS derivative **2b** was isolated as a stable compound in 88% yield (Scheme 2).[9c,d] The other dienones **2a**, **2c**, and **2d** were not isolated because they readily underwent dimerization at room temperature to give the homo dimers **8a** (26%), **8c** (80%), and **8d** (ca. 68%), respectively.[15,16] The IR and UV−vis spectra of the homo dimers indicated the presence of the cylopentadienone moiety. The ^{13}C NMR spectra of **8a** and **8c** exhibited one signal each at relatively low field (δ 160.3 for **8a** and 161.3 for **8c**) due to the phenyl-substituted β carbon of the dienone ring,[17] indicating that the β acetylene moiety was involved in the Diels−Alder dimerization as a 2π component. On the other hand, the dimer **8d**, which was contaminated with desilylated compound **8d′**, did not show vinyl carbon signals at such low-field region, suggesting that the α triple bond participated in the dimerization. It appears that TMS-substituted triple bonds are reactive enough to undergo [4 + 2] addition to the cyclopentadienone moieties regardless of their position (α or β) in the ring.



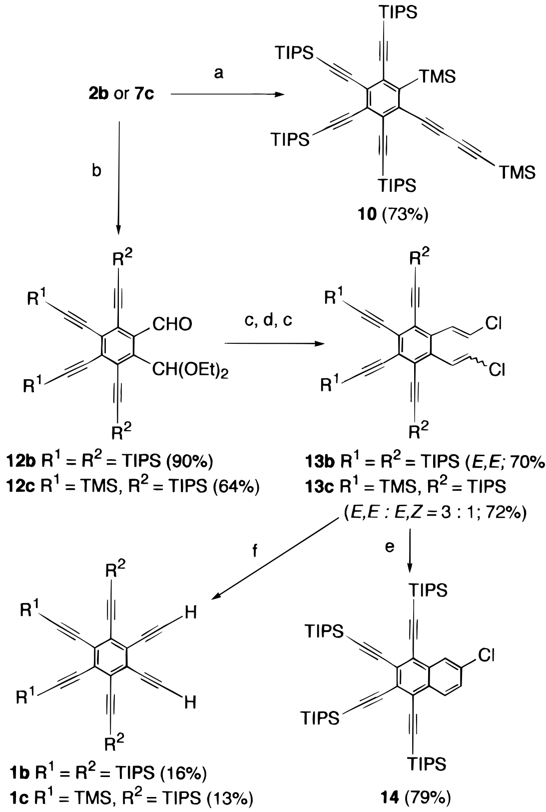
8a R = TMS
8c R = TIPS



8d R = TMS
8d′ R= H

We used stable dienone **2b** as a model in order to find a route for the conversion of cyclopentadienone **2** to hexaethynylbenzene **1** (Scheme 1). First, dienone **2b** was heated with bis(trimethylsilyl)hexatriyne (**9**),[18] in the hope of preparing a tetrakis-TIPS, bis-TMS-substituted hexaethynylbenzene system in a single step. To our dismay, however, the adduct obtained as the sole product turned out to be unsymmetrical **10**, which was formed by reaction at the terminal triple bond of the triyne **9**. Consequently, diethoxybutynal (**11**)[19] was used as a hexatriyne synthon. Thus, reaction of **2b** with **11** in refluxing toluene afforded the Diels-Alder adduct **12b** in 90% yield (Scheme 3). Homologation of **12b** was achieved by stepwise chloromethylenation,[20] since neither dibromomethylenation[21] nor dichloromethylenation[22] worked. Thus, treatment of **12b** with (chloromethylene)triphenylphosphorane gave an (*E*)-chloro alkene in 93% yield. Subsequent deprotection with TFA followed by another chloromethylenation afforded (*E,E*)-diene **13b**. Difficulty was encountered in the final conversion of **13b** to the hexayne system **1b**. Treatment of **13b** with LDA at −78 °C yielded cleanly the naphthalene derivative **14** as a single product in 79% yield.[23] Reaction with BuLi resulted in the formation of a mixture of intractable tarry materials. Finally, by using MeLi at room temperature, we achieved the conversion of **13b** to **1b**, albeit in low yield (16%). The same set of reactions was similarly applied to bis-TMS, bis-TIPS dienone **2c**. Namely, after deprotection of acetal **7c**, the resulting dienone **2c** was directly subjected, without isolation, to reaction with excess dienophile **11** to afford **12c**. Double chloromethylenation of **12c** gave diene **13c**, which was converted to hexaethynylbenzene **1c**.

Scheme 3[a]



[a] Reagents: (a) for **2b**, TMS−C≡C−C≡C−C≡C−TMS (**9**), toluene, reflux; (b) for **2b**, $(EtO)_2CHC{\equiv}CCHO$ (**11**), toluene, reflux; for **7c**, TFA, CH_2Cl_2, rt, then **11**, toluene, reflux; (c) $ClCH_2PPh_3Cl$, BuLi, THF, −78 °C to rt; (d) TFA, CH_2Cl_2, rt; (e) for **13b**, LDA, THF, −78 °C; (f) MeLi, Et_2O, rt.

Acknowledgment. This work was supported in part by a Grant-in-Aid (No. 07651056) from the Ministry of Education, Science, Sports and Culture. The authors are grateful to Prof. Y. Rubin for sharing his results with us prior to publication. A generous gift of organosilicon reagents from Shin-Etsu Chemicals Co. is also gratefully acknowledged.

Supporting Information Available: Experimental procedures, characterization data, and selected ^1H and ^{13}C NMR spectra (40 pages).

JO970309+

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(15) In contrast, tetrakis-TIPS dienone **2b** is unreactive toward homo dimerization. It was recovered unchanged even when it was heated in refluxing toluene for 2 days.

(16) Higher oligomers of **2a**, **2c**, and **2d** were not detected presimably due to steric hindrance. Namely, since the cyclopentadienone and the benzene rings of the dimers **8a**, **8c**,and **8d** are orthogonal to each other, the π faces of their triple bonds are hindered by the substituents extruding from one another's ring.

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(23) The formation of **14** can be explained in terms of intramolecular addition of a carbenoid to the neighboring double bond and subsequent cleavage of the strained cyclopropane bond.