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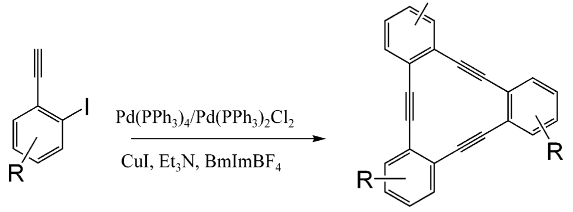
Efficient Synthesis of Tribenzohexadehydro[12]annulene and Its Derivatives in the Ionic Liquid

Yang Li,† Jiyong Zhang,† Wenkuan Wang,† Qiang Miao,†
Xuegong She,*,†,‡ and Xinfu Pan*,†

Department of Chemistry, National Key Lab of Applied Organic Chemistry, Lanzhou University, Lanzhou, P.R. China, and State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China

shexg@lzu.edu.cn; panxf@lzu.edu.cn

Received December 8, 2004



A simple and efficient synthesis of tribenzohexadehydro[12]-annulene and related derivatives in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate is described. A Sonogashira coupling reaction is the key step. In this system, the amount of CuI normally used can be reduced so that homocoupling is minimized.

Arylacetylene macrocycles have attracted intense attention in the field of supermolecular chemistry and materials science over the past decade[1] due to their novel properties and potential applications. Tribenzohexadehydro[12]annulene (tribenzocyclyne) **(1a)** and its derivatives are structural units of *graphyne*.[2] The annulenes can be prepared by several procedures including palladium-catalyzed co-cyclization of 1,2-diiodobenzene with acetylene,[3] palladium-catalyzed trimerization of 4-(2-bromophenyl)-2-methylbutyn-2-ol,[4] Stephens−Castro coupling of copper (2-iodophenyl)acetylide,[5] a combination of a Witting reaction and a bromination procedure,[6] and alkyne metathesis.[7] Recently, the Iyoda group reported a novel synthetic procedure of **1a** and some derivatives employing a coupling reaction of acetylenes with iodoarenes in the presence of catalytic amounts of CuI and PPh_3, together with 3 equiv of K_2CO_3 in DMF at 160 °C.[8] Despite considerable efforts to improve procedures, the synthesis of **1a** and its derivatives still remains troublesome.

Although the Sonogashira reactions of phenylacetylene with bromo- or iodobenzene produce diphenylacetylene in a quantitative yield,[9] cyclotrimerization by normal Sonogashira coupling of (2-iodophenyl)acetylene is still challenging. At present, few cyclotrimerization reactions under Sonogashira conditions were successful according to several reports.[1,8] The problem is that cyclotrimerization under Sonogashira conditions affords tribenzocyclyne in a very low yield due to a preferential homocoupling between alkynes.[10] After many trials, we discovered that cyclotrimerizations to **1a**−**c** (Figure 1) occur in satisfactory yield in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ($BMIMBF_4$)[11] under Sonogashira conditions.

We reasoned that employing the ionic liquid $BMIMBF_4$ as the solvent may have prominent advantages for the cyclotrimerization. The solvent might neutralize the donor electronic ability of methoxy groups, which are disadvantageous for Sonogashira coupling. Moreover $BMIMBF_4$ may reduce the need for CuI, which is mainly responsible for homocoupling.[1,10,11] Furthermore, $BMIMBF_4$ can activate and stabilize the catalytically active palladium species.[11,12] The above possibilities stimulated our study of cyclotrimerizations carried out in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate.[11]

Our initial strategy involved the preparation of the precursor **2a**, **2b**, and **2c** starting from the appropriate arylaldehyde. Adapting the procedure developed by Corey,[13] the arylaldehyde was treated with the CBr_4/triphenylphosphine reagent (350 mol %) affording a quantitative yield of the corresponding 1,1-dibromoarylene, which was transformed into arylacelene **3a**−**c** with butyllithium. Adapting the conditions of Brandsma,[14] *o*-iodoarylacetylenes **2a**−**c** were obtained in a moderate

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† Lanzhou Uinivesity.

‡ Chinese Academy of Sciences.

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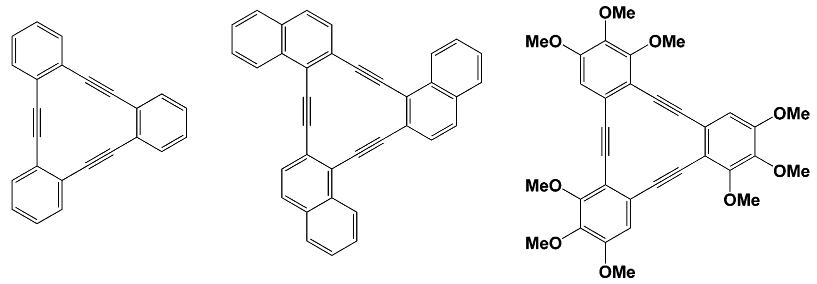
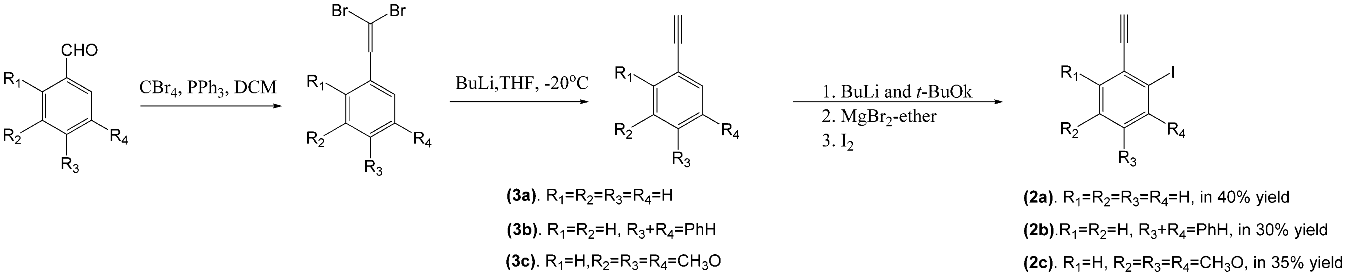


1a **1b** **1c**

FIGURE 1. Tribenzohexadehydro[12]annulene and its derivatives **1a**, **1b**, and **1c**.

SCHEME 1. Synthesis of 2a, 2b, and 2c



yield. Since the iodination reaction does not show good regioselectivity due to the other isomers present, **2a**−**c** must be separated carefully from other byproducts (Scheme 1).

The cyclotrimerization of **2a**, **2b**, and **2c** was investigated under Sonogashira conditions with $Pd(PPh_3)_2Cl_2$, CuI, Et_3N in diverse solvents such as THF, DMF at room temperature or at reflux temperature, yet only a trace amount of **1a-1c** were obtained. The major product was the homocoupling product, which was confirmed by relative references[1,8] and NMR spectra. Employing $Pd(PPh_3)_4$ as a substitute for $Pd(PPh_3)_2Cl_2$ resulted in the formation of **1a** in 30% yield. However, under similar conditions, **2b** and **2c** produced a complex mixture of unidentified products. The low yield is attributed to the presence of the methoxy groups which are disadvantageous to the Sonogashira coupling reaction and which favor the homocoupling product.[1,8]

When the ionic liquid $BMIMBF_4$ is used as the reaction solvent, we found that the catalytic ability of both $Pd(PPh_3)_2Cl_2$ and $Pd(PPh_3)_4$ is enhanced dramatically. Furthermore, the amount of CuI can be reduced to 1 mol % in the Sonogashira coupling reaction. Under these conditions, homocoupling is minimized and cyclotrimerization formed dibenzohexadehydro[12]annulene in a satisfactory yield (Scheme 2 and Table 1). The reaction proceeded at 80 °C for 12 h to afford **1a** in a 37% yield. If $Pd(PPh_3)_2Cl_2$ (5 mol %) is used in place of $Pd(PPh_3)_4$, the yield decreased to 19%.

We tried the synthesis of an unsymmetric [12]annulene framework as found in **1b** and **1c.** This kind of framework was first synthesized through cyclotrimerization. As shown in Scheme 2, the cyclotrimerization of **2b** under the same conditions in the presence of CuI (1 mol %), $Pd(PPh_3)_4$ (5 mol %), and Et_3N (150 mol %) in $BMIMBF_4$ produced **1b** in a 23% yield and in a 17% yield with $Pd(PPh_3)Cl_2$ (5 mol %). The reaction under similar conditions produced **1c** in an 11% yield.

SCHEME 2. Synthesis of 1a, 1b, and 1c

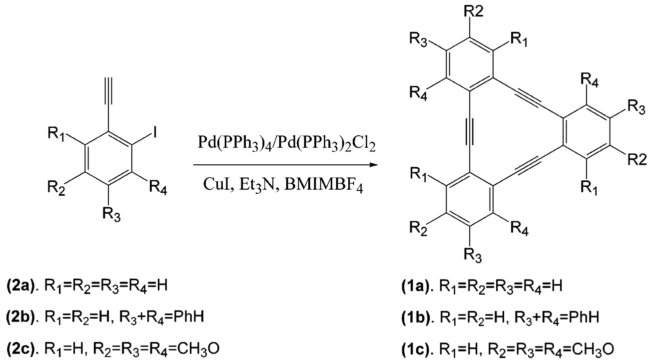


TABLE 1. Results of Sonogashira Coupling in THF and $BMIMBF_4$

entry	2	catalyst Pd (5 mol %)	solvent	product (%)
1	**2a**	$Pd(PPh_3)_4$	THF	**1a** (30)
2	**2b**	$Pd(PPh_3)_4$	THF	**1b** (trace)
3	**2c**	$Pd(PPh_3)_4$	THF	**1c** (trace)
4	**2a**	$Pd(PPh_3)_4$	$BMIMBF_4$	**1a** (37)
5	**2b**	$Pd(PPh_3)_4$	$BMIMBF_4$	**1b** (21)
6	**2c**	$Pd(PPh_3)_4$	$BMIMBF_4$	**1c** (11)
7	**2a**	$Pd(PPh_3)_2Cl_2$	$BMIMBF_4$	**1a** (19)
8	**2b**	$Pd(PPh_3)_2Cl_2$	$BMIMBF_4$	**1b** (16)
9	**2c**	$Pd(PPh_3)_2Cl_2$	$BMIMBF_4$	**1c** (5)

In summary, tribenzohexadehydro[12]annulene **1a** and unsymmetric [12]annulenes **1b** and **1c** have been synthesized via cyclotrimerization under Sonogashira conditions in the ionic liquid $BMIMBF_4$. A simple and efficient synthetic approach was developed in $BMIMBF_4$ to sup-

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press homocoupling. Further work will focus on methods to synthesize larger, more complex annulenes.

Acknowledgment. This work was supported by the Special Doctorial Program Funds of the Ministry of Education of China (20040730008), A Hundred Talents Program of CAS, NSFC (QT program), and SRF for ROCS SEM.

Supporting Information Available: General experimental methods and ^{1}H and ^{13}C NMR spectra for compounds **1a**–**c**, **2a**–**c**, and products derived from a homocoupling reaction. This material is available free of charge via the Internet at http://pubs.acs.org.

JO047836V