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A Remarkably Efficient Synthesis of Pure *cis*-Stilbenoid Hydrocarbons Using *trans*-Dibromoalkenes via Palladium Catalysis

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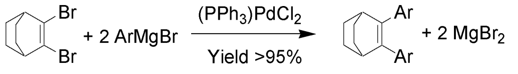
cis-Stilbenoid hydrocarbons containing highly substituted phenyl groups (such as pentamethylphenyl) form molecular clefts that are especially efficacious for trapping small analytes such as nitric oxide and metal cations.[1−3] These hydrocarbons are also potentially useful as photochromic molecular switches for molecular-electronics applications.[4] Despite the extensive need for such molecules, there are no reported general procedures for preparation of pure *cis*-stilbenoid frameworks. Synthesis of highly substituted stilbenoid hydrocarbons is generally accomplished by using either McMurry coupling or the dimerization of carbenes in rather minuscule yields.[5] It is noteworthy that these procedures are nonstereospecific and thus produce mixtures of *cis*- and *trans*-stilbenes.

Presently, palladium catalysts are extensively investigated because of their important role in the formation of C−C bonds, especially between sp^2-hybridized carbons.[6] We have recently observed that the *cis*-1,2-dibromobicyclo[2.2.2]oct-2-ene undergoes an efficient coupling with various aryl Grignard reagents in the presence of bis(triphenylphosphine)palladium dichloride to afford 1,2-diarylbicyclo[2.2.2]oct-2-enes in excellent yields[7] (eq 1).

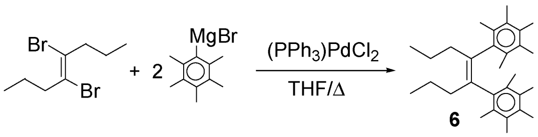


(eq.1)

Ar = Phenyl, Tolyl, Mesityl, Pentamethylphenyl

Unfortunately, only a handful of *cis*-dibromoalkenes are known which are generally prepared via multistep synthetic procedures.[8] In sharp contrast, the *trans*-1,2-dibromoalkenes with a broad array of substituent are readily available from a simple bromination of the corresponding acetylenes.[9]

We now report that, under reaction conditions depicted in eq 1, the coupling of aryl Grignard reagents (bearing ortho methyl groups) with acyclic *trans*-1,2-dibromoalkenes readily affords in each case a single isomer of pure *cis*-1,2-diarylalkenes (vide infra) in nearly quantitative yields (see Table 1), for example, eq 2

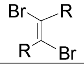
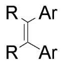
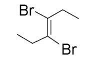
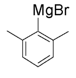
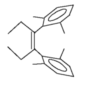
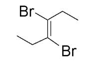
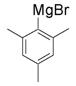
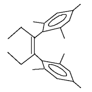
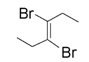
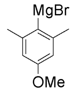
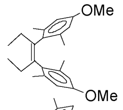
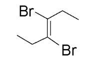
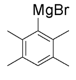
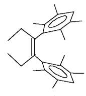
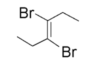
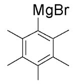
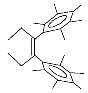
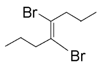
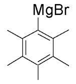
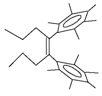
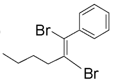
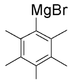
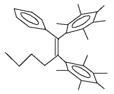
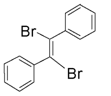
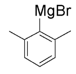
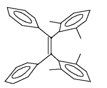
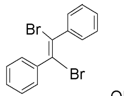
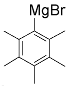
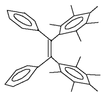
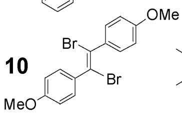
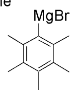
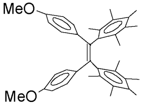


6

(eq. 2)

General Procedure. In a typical procedure, a freshly prepared solution of pentamethylphenylmagnesium bromide (1.0 M, 105 mmol) was mixed with a solution of *trans*-4,5-dibromooct-4-ene (50 mmol) in anhydrous tetrahydrofuran (50 mL) containing a catalytic amount of bis(triphenylphosphine)palladium(II) chloride[6a] (0.1 mol %) under an argon atmosphere at 25 °C. The resulting pale-yellow solution was refluxed for 8−16 h and cooled to room temperature. The resultant reaction mixture was diluted with water (50 mL) and extracted with dichloromethane (3 × 50 mL). Drying of the organic layer and evaporation of the solvent, followed by recrystallization from ethanol−dichloromethane mixture afforded bis-4,5-(pentamethyl-phenyl)oct-4-ene (**6**) in essentially quantitative yield (49.2 mmol, 98%).

Table 1. Pd-Catalyzed Coupling of ArMgBr with *trans*-Dibromoalkenes[a]

Entry		ArMgBr		Time[b] (h)	% Yield[c]
1				8	96
2				8	98
3				12	96
4				8	97
5				8	98
6				8	94
7				8	92
8				10	96
9				10	91
10				12	92

[a] All reactions were performed using the general procedure (see text). [b] Progress of the reactions was monitored by GC and TLC. [c] Isolated yield.

The generality of this surprisingly simple procedure (in eq 2) is demonstrated by the preparation of a variety of *cis*-stilbenoid hydrocarbons having different substituents (see Table 1). Moreover, it is important to emphasize that this synthesis of *cis*-diarylalkenes, according to the general procedure described above (eq 2 and Table

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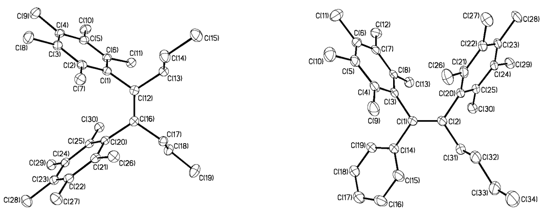
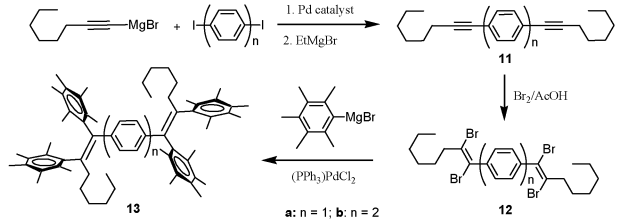


Figure 1. ORTEP diagrams of bis(pentamethylphenyl)-octene **6** (left) and bis(pentamethylphenyl)phenylhexene **7** (right) showing the *cis*-juxtaposition of pentamethylphenyl moieties.

Scheme 1. Synthesis of Multichromophoric Stilbenoid Hydrocarbons

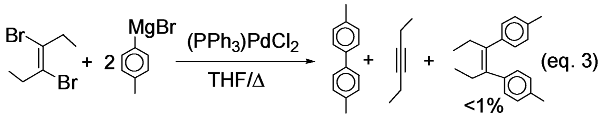


1), did not produce even a trace amount of the *trans*-isomer in all cases. The structures of various *cis*-diarylalkenes were established by NMR spectroscopy[10] and further confirmed by X-ray crystallography (see Figure 1 for representative X-ray structures[11]).

The versatility of this simple procedure is further demonstrated by an easy three-step preparation of bichromophoric stilbenoid ligands **13a** and **13b** from readily available starting materials (see Scheme 1 and Supporting Information). These ligands contain multiple stilbenoid clefts which are especially efficacious for binding a variety of metal cations and other analytes such as NO and NO_2.[3] For example, bifunctional ligands **13a** and **13b** readily incorporate two metal cations, such as Ag^+, with high binding efficiency.[12] We are currently exploring the physical and chemical properties of these materials for potential usage as molecular switches and intervalence compounds.[13]

Such a remarkably efficient and quantitative isomerization of a *trans*-alkene to the corresponding *cis*-diarylalkene, during the aryl coupling, in the presence of a catalytic amount (0.1 mol %) of $(PPh_3)_2Pd(II)Cl_2$ in eq 2 is unprecedented. It is, however, important to note that the success of this transformation (eq 2) clearly depends on the presence of ortho methyl groups on the aryl Grignard reagent. For example, when the reaction of *trans*-dibromoalkenes is carried out with arylmagnesium bromides lacking ortho substituents, they produced largely (>95% yield) the corresponding biaryls and dialkylacetylene, for example, eq 3.[14]

This transformation in eq 3 is in sharp contrast with the reactions



presented in eq 1 with *cis*-1,2-dibromobicyclooctene and other *cis*-dibromoalkenes,[15] which yield the *cis*-diarylalkenes with both unsubstituted and substituted arylmagnesium bromides in excellent yields.

Moreover, the reaction with *cis*-dibromoalkenes[15] proceeded in a stepwise manner, that is, first one aryl group adds to yield 1-bromo-2-arylcycloalk-1-ene followed by the coupling of the second aryl group to afford 1,2-diarylcycloalk-1-ene. Contrastingly, when a reaction of pentamethylphenylmagnesium bromide was carried out with an excess of *trans*-dibromohexene (100 fold) according to the general procedure in eq 2, it yielded only the *cis*-diarylalkene **5** and none of the monoarylated bromoalkene could be detected by a careful GC and GC/MS analysis. While a detailed study of the mechanism of this reaction is in progress, these preliminary experiments suggest that the coupling of two aryl groups to the *trans*-dibromoalkenes (in the presence of a palladium catalyst) is either simultaneous or that the addition of second aryl group is much faster than the first one.

In summary, we have developed a novel and versatile procedure for the preparation of pure *cis*-diarylalkenes from readily available *trans*-dibromoalkenes. We believe that this new versatile synthesis of *cis*-stilbenoid hydrocarbons will allow the exploration of these novel cleft-containing materials for the development of practical optoelectronic devices for the detection and quantification of various analytes such as NO, NO_2, Ag^+, and so forth.

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Supporting Information Available: Experimental procedures and spectral data for **1**−**13** (PDF) and the X-ray crystallographic data for **6** and **7** (PDF/CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(3) Various highly substituted stilbenoid hydrocarbons in Table 1 effectively bind NO and NO_2 upon oxidative activation. Rathore, R.; Deselnicu, M. I. (unpublished results).

(4) (a) For a recent review, see: Masahiro, I. *Chem. Rev.* **2000**, *100*, 1685 and references therein. (b) Also see: *Introduction to Molecular Electronics*; Petty, M. C., Bryce, M. R., Bloor, D., Eds.; Oxford University Press: New York, 1995.

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(9) Pincock, J. A.; Yates, K. *Can. J. Chem.* **1970**, *48*, 3332.

(10) It is noteworthy that the chemical shifts for the methylene protons of the alkyl groups in *cis*-stilbenoid hydrocarbons are shifted downfield as compared to the corresponding trans analogues; see: Leimner, H.; Weyerstahl, P. *Chem. Ber.* **1982**, *115*, 3697.

(11) X-ray crystallography data for **6** and **7** are on deposit with Cambridge Crystallographic Data Center as supplementary publication nos. CCDC169899 and CCDC169900, respectively.

(12) Bifunctional ligands **13a**−**b** readily incorporate two Ag^+ cation in the stilbenoid clefts as judged by the simple ^1H NMR spectra, which suggest that two Ag^+-bound stilbenoid moieties are chemically equivalent in solution at 22 °C. An X-ray crystallographic study in progress will establish this point.

(13) Preliminary electrochemical and UV−vis spectral studies on **13a**−**b** suggest that a single hole (formed by removal of an electron) is delocalized over both stilbenoid moieties; Rathore, R.; Deselnicu, M. I.; Burns, C. L (unpublished results).

(14) The structure of the trace amount of *cis*-3,4-ditolylhex-3-ene obtained in eq 3 was established by comparison with an authentic sample.[10]

(15) 1,2-Dibromocyclohex-1-ene and 1,2-dibromocyclopent-1-ene showed reactivity analogous to that of 1,2-dibromobicyclooct-2-ene (see eq 1).

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