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The Unexpected Formation of 9,9,10,10-Tetrafluoro-1,2,4,12-tetraphenyl[2.2]paracyclophan-1-ene

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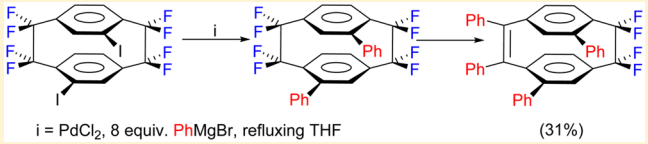
Supporting Information

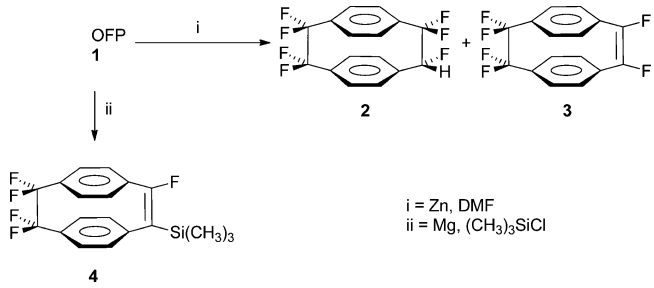
ABSTRACT: An investigation of the palladium-catalyzed Kumada cross-coupling reaction between PhMgBr and (pseudo-*ortho*) 4,12-diiodo-1,1,2,2,9,9,10,10-octafluoro[2.2]-paracyclophane revealed that in addition to the expected cross-coupled product, an unintended major product was generated. The product was determined to be 9,9,10,10-tetrafluoro-1,2,4,12-tetraphenyl[2.2]paracyclophan-1-ene by X-ray crystallography and is proposed to be formed via the first reported example of reductive defluorination by a Grignard reagent.



Cyclophanes are a general class of compounds where aromatic rings are connected by multiple aliphatic bridges.[1] The most famous of these compounds is undoubtedly [2.2]paracyclophane,[2] whose chemistry has been thoroughly studied and reviewed over the last six decades.[3−5] This field continues to thrive because of the increasingly successful application of these molecules in the areas of chiral catalysis and material science.[6] Our own interest in this broad field has been in the realm of fluorinated paracyclophanes, and convenient synthetic routes generating 1,1,2,2,9,9,10,10-octafluoro[2.2]-paracyclophane (OFP, **1**)[7−9] and, more recently, the perfluoroparacyclophane (PFP)[10] have been reported.[11] In addition to the commercial value and industrial potential of such molecules (e.g., for use as monomers for fluoroparylene polymers),[12] such practical and convenient syntheses have permitted the exploration of the chemistry of these interesting fluorinated phanes.[13−15]

It is important to note that over the past 20 years, almost all of the published reports concerning the reactions of OFP and its derivatives have focused on transformations occurring at the aromatic rings,[16−18] whereas very little has been reported concerning chemistry occurring at the signature octafluorinated bridges of these molecules. In fact, there are only two reports of such chemistry in the literature (Scheme 1). The first report was in 2000, where we showed that compounds **2** and **3** were generated as byproducts in the reaction of Zn with $ClCF_2PhCF_2Cl$ during the synthesis of OFP (**1**).[7] These products were both clearly the result of reductive defluorination of the target molecule **1**. The generation of **3** in this reaction was actually at the time an annoyance, since this significant impurity (6% under normal conditions) needed to be removed from the desired product **1** (by $KMnO_4$ oxidation). In that same publication, we reported that extended exposure of **1** to zinc in refluxing THF increased the yield of **3** to 14%. More recently, a magnesium-promoted defluorinative silylation

Scheme 1. Previous Examples of Reductive Defluorination of OFP 1



reaction of **1** was reported by Amii, Uneyama, and co-workers,[19] who were able to attain an X-ray crystal structure of the trimethylsilylated pentafluoro[2.2]paracyclophan-1-ene product **4**. This highly strained molecular structure revealed a remarkably long CF_2-CF_2 bond length of 1.64 Å.

It has been previously reported that a palladium-catalyzed Kumada cross-coupling reaction of diiodide **5** generated products **6** and **7** in 20% and 21% yield, respectively.[15] We were motivated to revisit this reaction for two reasons. First, we had a general desire to improve the efficiency and yield of this reaction. Second, given the recently reported propensity of PhMgBr to promote homocouplings in related systems,[20] we were curious to see whether this method could similarly produce tris(OFP) or larger poly(OFP)-type molecules starting from difunctional **5**.

In this regard, a study of reaction conditions was explored, and it was discovered that using dropwise addition of the Grignard reagent in refluxing THF increased the yields of the cross-coupled products **6** and **7** to 30% (Scheme 2). However,

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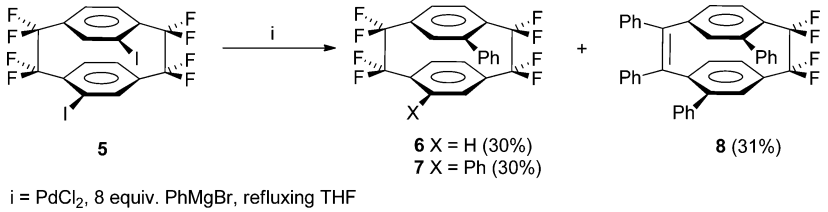
Scheme 2. Formation of Intended and Unintended Products



this investigation also alerted us to the formation of an additional, unexpected molecule that in fact was the major isolated product of this reaction. The new product exhibited two AB quartet patterns in the ^{19}F NMR spectrum, characteristic of a disubstituted OFP derivative (yet different from the expected compound **7**),[15] but the electron ionization mass spectrum of the new product lacked the characteristic "split in half" xylylene fragmentation pattern typical for such paracyclophanes.[1,14] On the contrary, this product displayed only a dominant peak at m/z 582 with minimal fragmentation. After isolation by column chromatography and further characterization, our product was proposed to be molecule **8**, and then the molecular structure was determined by X-ray crystallography.

Structure Description and Comparisons. The molecular structure of **8** is shown in Figure 1 as an ORTEP drawing.

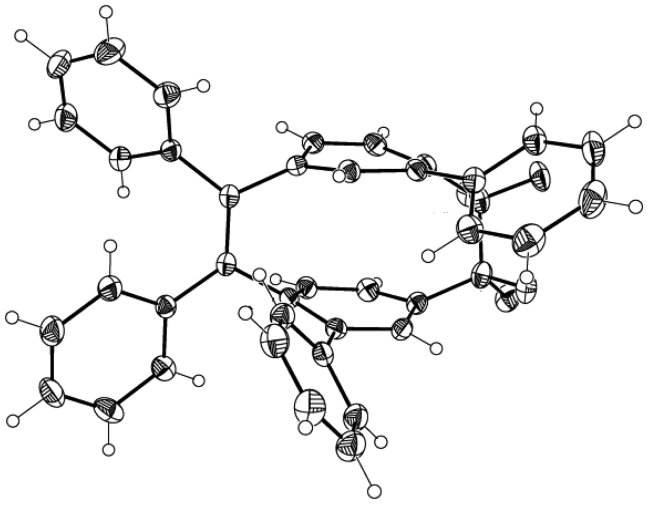
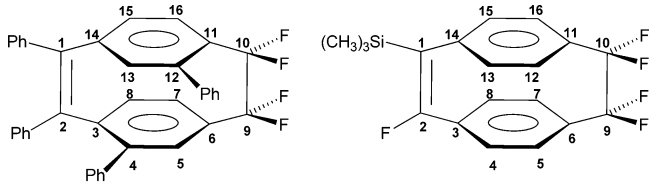


Figure 1. ORTEP representation of the molecular structure of **8** with thermal ellipsoids set at 50% probability.

The overall structure of **8** is typical of a highly strained [2.2]paracyclophane, with the aryl rings being characteristically[1,21] bent out of planarity into boatlike conformations. A summary of the most pertinent bond lengths is reported in Table 1, along with corresponding values for two closely related structures for comparison. The bond length of the CF_2−CF_2 bridge in **8** was found to be 1.60 Å, which is slightly longer than the corresponding bond length in OFP (1.58 Å) and shorter than the extremely long CF_2−CF_2 bond length reported for **4** (1.64 Å). As expected, the bridge containing the C═C double bond in **8** is shorter than the tetrafluoroethylene bridge, with a bond length of 1.36 Å. The corresponding C═C bridge in **4** is slightly shorter at 1.34 Å. For both **8** and **4**, the distances between the upper and lower rings are smaller proximate to the C═C bridge end and correspondingly larger proximate to the tetrafluoroethylene bridge end.

Table 1. Selected Structural Data for 8 and Related Structures[a]



8 **4**

	distance (Å)		
atoms	**8**	**4**	**1**
C9−C10	1.60	1.64	1.58
C1−C2	1.36	1.34	
C3−C14	2.71	2.76	2.80
C6−C11	2.89	2.84	
C4−C13	3.16	3.10	3.09
C5−C12	3.23	3.11	
C8−C15	3.07		
C7−C16	3.11		

[a]Values for the structures of **4** and **1** were taken from refs 19 and 21.

One of the more obvious differences in the structure of **8** relative to those of **1** and **4** is that the 4,12- (pseudo-*ortho*-) substitution pattern of the sterically demanding phenyl substituents causes the aryl rings of the cyclophan-1-ene to no longer be level with each other; instead, they are "slanted", with the result that the "back" carbons on the unsubstituted edge of the rings (i.e., C7,C8 and C16,C15) are closer in space than the corresponding "front" carbons (i.e., C4,C5 and C12,C13).

As shown in Scheme 3, the formation of product **8** presumably starts with the originally desired double palladium-catalyzed Kumada coupling of diiodide **5** and PhMgBr to generate the intended cross-coupled product **7**. It seems likely that the excess PhMgBr then acts as a reductant, promoting reductive defluorination of **7** to generate the corresponding paracyclophan-1-ene **9**, and in turn the remaining excess PhMgBr then performs two sequential vinylic substitutions of the fluorines to generate the final product **8**.

The sequential reductive defluorination and nucleophilic substitution of fluorine in our proposed reaction is reminiscent of the famous reaction reported by MacNicol and Robertson[22] in which perfluorodecalin is converted into octa(phenylthio)-naphthalene by excess NaSPh (Scheme 4). Reductive defluorination is an established "Achilles' heel" of fluoroalkyl groups, which are often otherwise perceived to be chemically unreactive.[23] This area has been reviewed, and common reagents for reductive defluorination include metals (e.g., Fe, Hg, Mg, Na, Al, Zn), metal complexes (e.g., $CsCoF_3$),

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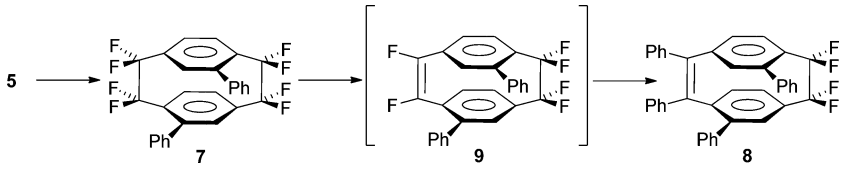
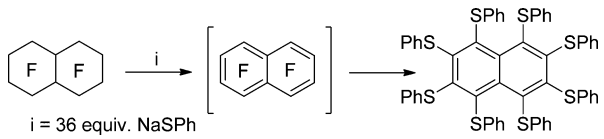
Scheme 3. Proposed Pathway for Formation of 8



Scheme 4. Reductive Defluorination and Subsequent Substitution



metallocenes, activated carbon, organic radical anions, $LiAlH_4$, and other SET agents (e.g., iodide ion, aromatic amines).[23] For perfluoroalkanes, the electron transfer is into the low-lying σ^* orbital of the carbon−fluorine bond, whereas in our reaction of **7**, the electron donation is undoubtedly facilitated by the π system adjacent to the tetrafluoroethylene bridge.[3] The electrochemical reduction of **1** to its radical anion has been reported in the literature.[24] Grignard reagents are known to act as SET agents,[25] but we are not aware of any previous reports of Grignard reagents causing reductive defluorination from a fluoroalkyl system.

We observed that when an authentic sample of proposed intermediate **7** was subjected to the same reaction conditions (6 equiv of PhMgBr/$PdCl_2$/reflux/THF), product **8** was again produced, isolated in 20% yield from a complex mixture of products via column chromatography. When purified **8** was exposed to further analogous conditions, only 15% of the starting material remained, accompanied by numerous (>10) unidentified products. GC−MS analysis of the complex product mixture indicated that the other unidentified products were dimeric or higher oligomeric materials, which seems to be in agreement with the results of the previously described magnesium-promoted defluorinative silylation reaction.[19] In our above reactions, we were not able to observe the presence of intermediate **9** (the expected ^{19}F NMR signal for such bridge vinylic fluorines is around $\delta_F = -118$ ppm[7]), nor did we detect any paracyclophan-1,9-diene-based structures.

The demonstrated use of phenylmagnesium bromide to achieve reductive defluorination provides an alternative and complementary method to access the interesting and rare paracyclophan-1-ene structural skeleton. Such compounds hold great potential as building blocks leading to other more exotic phane molecules. Additionally, such molecules may also find uses in materials applications[26,27] and also as ROMP monomers.[28,29]

In conclusion, we have reported a palladium-catalyzed Kumada reaction that in addition to forming the intended cross-coupling product also generated an unexpected product as the major isolated product. It has been proposed that the remaining excess organometallic reagent promoted reductive defluorination of one of the tetrafluoroethylene bridges of the intended product **7** and then trapped the putative paracyclophan-1-ene intermediate **9** via double vinylic substitution of the fluorines. The unintended product **8** was confirmed to be 9,9,10,10-tetrafluoro-1,2,4,12-tetraphenyl[2.2]paracyclophan-1-ene by X-ray crystallography. The proposed mechanism contains the first example of a Grignard reagent causing reductive defluorination of a fluoroalkyl group. This reaction, along with the previously reported Mg-[19] and Zn-promoted[7] reductive defluorination reactions, clearly demonstrates the ability to perform chemistry on the tetrafluoroethylene bridges of such fluorinated paracyclophanes and its future potential, which to this point have been relatively unexplored.

EXPERIMENTAL SECTION

9,9,10,10-Tetrafluoro-1,2,4,12-tetraphenyl[2.2]paracyclophan-1-ene (8). A degassed THF solution (30 mL) containing 4,12-diiodo-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane[15] (**5**) (1.80 g, 2.98 mmol) and palladium dichloride (63 mg, 0.36 mmol) was stirred and brought to reflux under a nitrogen atmosphere. A 1 M THF solution of phenylmagnesium bromide (24.0 mL, 24.00 mmol) was added via syringe and syringe pump over a period of 4 h, and the black solution was heated to reflux overnight. Evaporation of the solvent was followed by the addition ice water, and the precipitated solids were chromatographed on silica gel (hexane/dichloromethane 9/1) to give (R_f = 0.44) 4-phenyl-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane (**6**) (386 mg, 30%), (R_f = 0.37) 4,12-diphenyl-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane (**7**) (454 mg, 30%), and (R_f = 0.29) 9,9,10,10-tetrafluoro-1,2,4,12-tetraphenyl[2.2]paracyclophan-1-ene (**8**) (542 mg, 31%). White solid, mp above 200 °C. ^1H NMR (300 MHz, acetone-d_6) δ: 7.92 (d, ^3J = 7.5 Hz, 2H); 7.62−7.11 (m, 22H); 7.00 (dd, ^3J = 7.5 Hz, ^4J = 3.3 Hz, 2H). ^{19}F NMR (300 MHz, acetone-d_6) δ: −99.6 (d, ^2J = 237.4 Hz, 1F); −108.6 (d, ^2J = 237.4 Hz, 1F); −112.0 (d, ^2J = 237.6 Hz, 1F); −114.0 (d, ^2J = 237.6 Hz, 1F). MS: m/z 582 (M^+, 100%). Full ^{13}C NMR data could not be obtained because of solubility issues. The molecular structure of **8** was determined by X-ray crystallography. Anal. Calcd for $C_{40}H_{26}F_4$: C, 82.46; H, 4.50. Found: C, 82.45; H, 4.57. Products **6** and **7** were identified by comparison of their ^{19}F and ^1H NMR spectra and GC−MS analyses with published literature data[14,15] and additionally were found to be identical to previously prepared authentic samples.

ASSOCIATED CONTENT

Supporting Information

NMR spectra and MS data for compounds **6**−**8** as well as microanalysis data and crystallographic data (.cif) for compound **8**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00657.

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Notes

The authors declare no competing financial interest.

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