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A Novel, Non-High-Dilution Method for Preparation of 1,1,2,2,9,9,10,10-Octafluoro[2.2]paracyclophane

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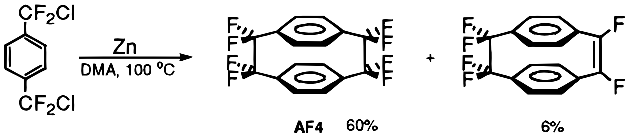
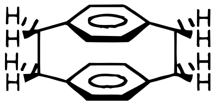
ABSTRACT



A novel synthesis of octafluoro[2.2]paracyclophane (AF4), one that remarkably does not require the use of high dilution methodology, is presented. Using this unprecedented methodology, AF4 is produced in 60% yield in a reaction of Zn with 0.35 M *p*-bis(chlorodifluoromethyl)-benzene in DMA at 100 °C. The process comprises a convenient, inexpensive, and highly scaleable preparation of AF4 for both research and commercial purposes.

Since their first designed synthesis in 1951,[1] [2.2]paracyclophanes have been considered valuable compounds for testing theories of bonding, ring strain, and π-electron interactions.[2−4] A number of methods have been devised for the relatively convenient synthesis of parent hydrocarbon **1**, all of which require the use of high dilution methodology.[5−7]



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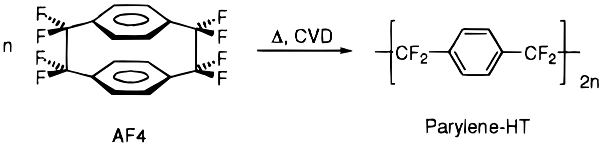
In addition, it has been recognized since the mid-1960s that [2.2]paracyclophanes are useful chemical vapor deposition (CVD) precursors of thin film polymers, known in the industry as "parylenes".[8] Such parylenes are ideally suited for use as conformal coatings in a wide variety of applications, such as in the electronics, semiconductor, automotive, and medical industries. Parylene coatings are inert and transparent and have excellent barrier properties. Parylene N, which is generated from the parent hydrocarbon **1**, has been found to be useful at temperatures up to 130 °C.

1,1,2,2,9,9,10,10-Octafluoro[2.2]paracyclophane, **2**,[9] the bridge-fluorinated version of **1** (and known in the industry as AF4), is the CVD precursor of Parylene-HT polymer, poly(α,α,α′,α′-tetrafluoro-*p*-xylylene). The Parylene-HT polymer combines a low dielectric constant (2.25)[10] with high thermal stability (<1 wt % loss/2 h at 450 °C), low moisture absorption (<0.1%), and other advantageous properties.[10,11] With such properties and because its in vacuo deposition



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[1] Cram, D. J.; Steinberg, H. *J. Am. Chem. Soc.* **1951**, *73*, 5691.
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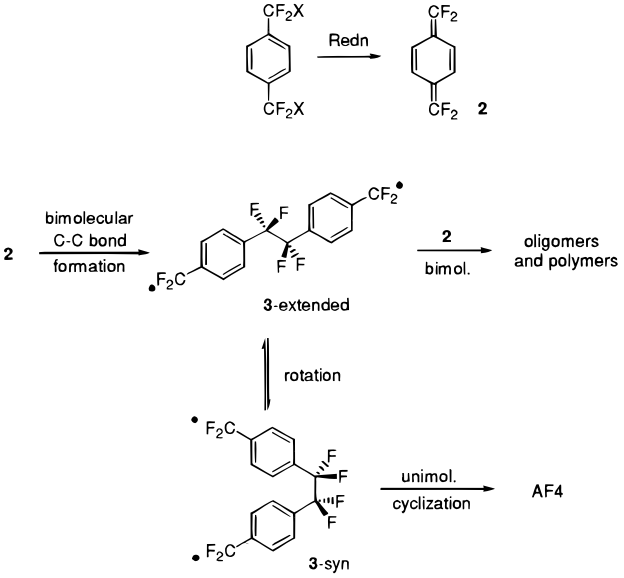
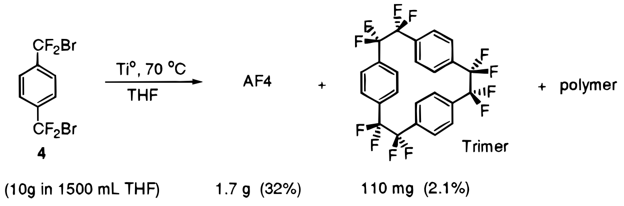
process ensures conformality to microcircuit features and superior submicron gap-filling capability, Parylene-HT continues to show considerable promise as an interlayer dielectric for on-chip high-speed semiconductor device interconnection.

Heretofore, a significant aspect of methods for synthesis of virtually every [2.2]paracyclophane has been the necessity to carry out such reactions using high dilution conditions. The classic and still most commonly used method of preparing [2.2]paracyclophanes involves generation of a *p*-xylylene intermediate such as **2**, which then dimerizes to form the paracyclophane, as exemplified in Scheme 1 for the general synthesis of AF4. Use of high dilution conditions is generally required in such processes in order to provide the optimal kinetic environment to allow *unimolecular* cyclization of intermediate diradical **3** to compete effectively with undesired *bimolecular* oligomerization.

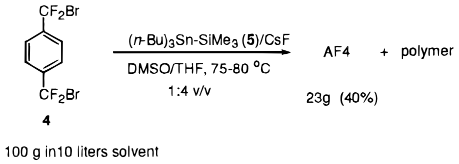
Scheme 1



In our initially reported Ti* process, although the use of traditional high dilution methodology allowed preparation of gram quantities of AF4 for the first time, it also essentially precluded significant scale-up of the procedure.[12]

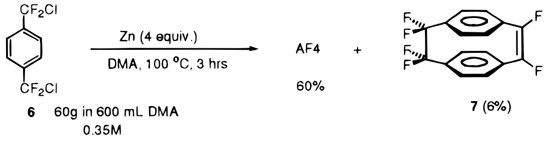


Subsequently, we found that a process involving use of (trimethylsilyl)tributyltin, **5**, with cesium fluoride allowed one to circumvent conventional high dilution technology with the result that both high yield and scale-up were feasible.[13] Nevertheless, use of this process has been inhibited by the high costs of the required AF4 precursor, *p*-bis(bromodifluoromethyl)benzene, **4**, and the tinsilane reagent **5**, as well as by the lack of a good scale-up procedure for **4**.



Thus, work has continued to find a convenient, inexpensive, and scaleable method for synthesis of AF4, a goal made all the more important since methods have recently been reported for mono- and multisubstituted ring derivatization of AF4,[14,15] which opens up a number other potential applications of AF4 and its derivatives. In this Letter, we are pleased to report an exciting new method for the synthesis of AF4, one that moreover describes what we believe is the first example of the synthesis of a [2.2]paracyclophane by a method that *does not require the use of high dilution technology*.

It has been found that heating a mixture of 4 equiv of zinc dust and 0.35 M *p*-bis(chlorodifluoromethyl)benzene, **6**, in dimethylacetamide, for 4 h at 100 °C produces AF4 in a yield of ~60%, with some apparent oligomeric side products but little insoluble polymer being formed. A typical small scale procedure is given in ref 18, but the reaction can be scaled proportionally to virtually any magnitude.[16]



Significantly, when the reaction is carried out under typical high dilution conditions, little or no AF4 is formed. Moreover, use of dibromide precursor, **4** (which was essential to the success of both the Ti* and tinsilane processes), in place of dichloride **6** leads to a greatly diminished (~10%) yield of AF4. Numerous other metals, including Mg, were examined, but zinc proved to be unique in giving good yields in the reaction. The presence of O_2 inhibits the reaction. It should also be mentioned that the conditions of this reaction unfortunately proved inappropriate for synthesis of parent [2.2]paracyclophane **1** from *p*-bis(chloromethyl)benzene (yield < 5%), although numerous ring-substituted derivatives of **6** proved to be decent substrates for the reaction, albeit none so efficacious as **6** itself.

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Note that small amounts of unusual bridge-unsaturated compound **7** are formed in the reaction as it is run.[17] If desired, one can modify the reaction conditions to form larger quantities of **7**, at the expense of AF4. Thus, carrying out the reaction in refluxing THF for 2 days gives 14% of **7** and only 6% of AF4.

It is apparent that the mechanism of this [2.2]paracyclophane-forming reaction cannot involve free α,α,α′α′-tetrafluoroxylylene, **2**, undergoing its usual mechanism of dimerization and cyclization as depicted in Scheme 1. Rather we believe that the reaction is occurring on the surface of the zinc metal and that dimerization is occurring without the intermediacy of free **2**. Further studies, presently underway, should shed additional light on the mechanism of the reaction.

Combining the ease of the new AF4-forming process with the fact that dichloro precursor **6** is much more readily prepared (photolytically or thermally initiated chlorination of α,α,α′α′-tetrafluoroxylene)[9] than its dibromo analogue **4**, the current overall methodology for synthesis of AF4 should enable convenient, inexpensive, and highly scaleable preparation of AF4 for both research and commercial purposes.

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(17) NMR (in $CDCl_3$) characterization of **7**: ^{1}H, δ 7.06 and 7.15 (AB, $J_{AB} = 8.7$ Hz); ^{19}F, δ −115.98 (s, 4F), −118.68 (s, 2F).

(18) **Experimental procedure:** Into a 1 L three-necked round-bottomed flask are added 600 mL of *N*,*N*-dimethylacetamide (DMA), *p*-bis(chlorodifluoromethyl)benzene (**6**) (60 g, 0.24 mol), and zinc dust (61 g, 0.96 mol). The mixture is heated over a period of 40 min to 100 °C under vigorous stirring and an N_2 atmosphere, and it was maintained at that temperature for 4 h, after which no **6** remained and the solution had become yellow. The reaction mixture was then cooled to room temperature and filtered, washing the resulting oligomeric solids with two 50 mL portions of DMA to extract small amounts of AF4. Combining these washings with the original DMA filtrate, the impurities **7** (~6% yield) and heptafluoro[2.2]paracyclophane (<1%) were removed by stirring the combined DMA solution at room temperature with 5 g of $KMnO_4$ overnight, followed by again filtering the mixture to obtain a clear, colorless DMA solution. The crude AF4 product was then obtained by evaporating the DMA filtrate at 100 °C under full vacuum. After washing the resulting residue with water and cold methanol, the crude product was extracted with benzene, the benzene was evaporated, and the residue was recrystallized from hexane to give >99% pure AF4 (25.6 g, 60.5%).