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A New and Practical Synthesis of Octafluoro[2.2]paracyclophane

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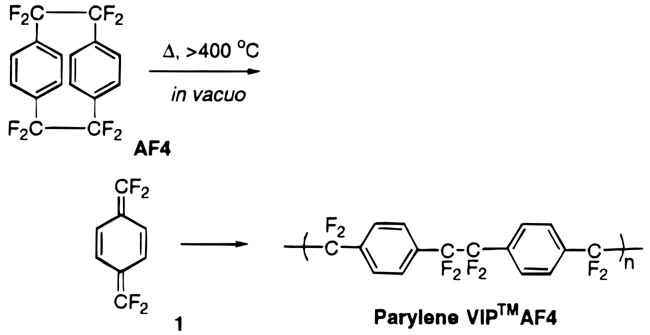
Per-α-fluoro[2.2]paracyclophane (**AF4**), being the precursor to the organic, vapor-deposited parylene polymer, poly(α,α,α′,α′-tetrafluoro-*p*-xylylene (Parylene VIP AF4) (Scheme 1), is a material of considerable commercial interest.[1]

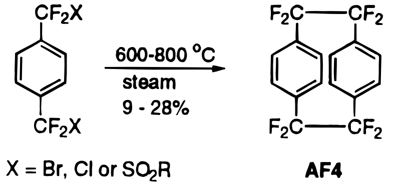
The Parylene AF4 polymer combines low dielectric constant (2.25; normal to the film plane)[2−4] with high thermal stability (<1% wt loss/2 h at 450 °C)[2,3,5] and low moisture absorption (<0.1%).[3] With such properties and because its *in vacuo* deposition process assures conformality to microcircuit features and superior submicron gap-filling capability, the Parylene AF4 polymer shows considerable promise as an interlayer dielectric for on-chip high speed semiconductor device interconnection.[2,3]

Such a market would require that the AF4 dimer precursor be available in commercial quantities. However, until now AF4 has only been able to be synthesized in gram quantities by two alternative methods, one an awkward pyrolytic/reductive process developed by Union Carbide in the 1960's to first synthesize AF4 (Scheme 2),[6,7] and the other, a much improved reductive method which uses a complex, low-valent form of Ti to effect debromination of 1,4-bis(bromodifluoromethyl)benzene, **2**, a process which allows relatively easy preparation of gram quantities of AF4 in an acceptable (32%) yield (Scheme 3).[8] Nevertheless, the high dilution technology required in the latter process proved not amenable to scale up, a result which frustrated attempts at large scale preparation of AF4 by this method.[9]

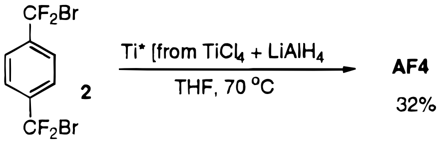
Scheme 1. Parylene Vapor Deposition Process



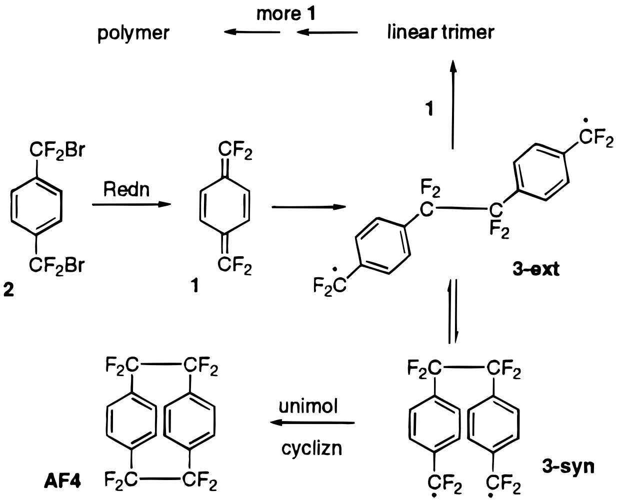
Scheme 2. 1969 Union Carbide Process



Scheme 3. 1992 Dolbier Process



Scheme 4. Overall Mechanistic Scheme for AF4 Formation



An important aspect of any method for [2.2]paracyclophane synthesis is the necessity to carry out the reaction under high dilution conditions. In the Ti* process, such high dilution was maintained by traditional methods, which included very slow, simultaneous addition of both dibromide and Ti* to a large surplus of solvent. As such, 10 g of dibromide **2** in 500 mL of THF and 3.5 equiv of reduced Ti in 500 mL of THF were added over a period of 10 h to 500 mL of refluxing THF to give 1.7 g of AF4 (32%).

In the case of AF4, all methods which have been used for its preparation involve, we believe, the intermediacy of α,α,α′,α′-tetrafluoro-*p*-xylene, **1**, as a reactive monomeric species.[10] As shown in Scheme 4, this reactive species must be generated under reaction conditions wherein it will survive until it encounters molecule of **1** to form the dimer diradical **3**.

3 will most likely be formed in an extended form such as **3-ext** which will need to undergo an entropy unfavor-

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[1] Beach, W. F.; Lee, C.; Bassett, D. R.; Austin, T. M.; Olson, R. A. Xylylene Polymers In *Wiley Encylopedia of Polymer Science and Technology*; Wiley: New York, 1989; Vol. 17, pp 990−1025.

[2] Majid, N.; Dabral, S.; McDonald, J. F. *J. Electron. Mater.* **1989**, *18*, 301−311.

[3] Wary, J.; Olson, R. A.; Beach, W. F. VMIC Conference, Santa Clara; Feb, 1996; paper 6-B.

[4] Gaynor, J.; Chen, J.; Nguyen, H.; Brown, G.; Taylor, K.; Luttmer, J. D.; Plano, M. A.; Cleary, T.; Wing, J.; Kelly, *Proceedings of the 191st Meeting of the Electrochemical Society, Symposium F: Low and High Dielectric Constant Materials*, *97*-1, 325, paper no. 259.

[5] Williams, K. R. *J. Thermal Anal.* **1997**, *49*, 589−594.

[6] Chow, S. W.; Pilato, L. A.; Wheelwright, W. L. *J. Org. Chem.* **1970**, *35*, 20−22.

[7] A recent modification of the Chow process which substitutes helium for steam: Grechkine, E. V.; Soohilian, V. A.; Pebalk, A. V.; Kardash, I. E. *Zh. Org. Khim.* **1993**, *29*, 1999−2001.

[8] Dolbier, W. R., Jr.; Asghar, M. A.; Pan, H.-Q.; Celewicz, L. *J. Org. Chem.* **1993**, *58*, 1827−1830.

[9] Whereas it proved relatively easy to get 2 grams of pure AF4 by this method, attempts to scale the process up to produce greater than 10 g per run led to formation of increasing amounts of trimer and polymer at the sacrifice of desired dimer.

[10] Monomer **1** has been previously isolated at −180 °C: Pebalk, A. V.; Kardash, I. e.; Kozlova, N. V.; Zaitseva, E. L.; Kozlov, Yu. A.; Pravednikov, A. N. *Vysokomol. Soedin. Ser. A* **1980**, *22*, 972−976; *Chem. Abstr.* **1983**, *93*, 132917j.

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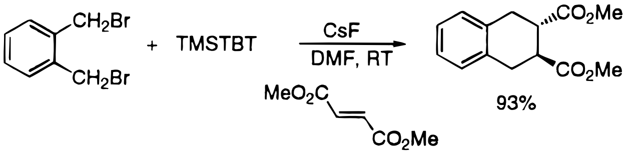
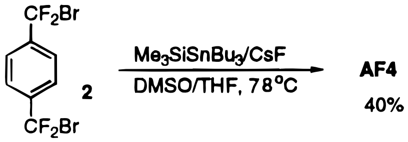
Scheme 5. Mori's Study



Scheme 6. New AF4 Synthesis



able conformational change to the *syn* conformer, **3-syn**, before it can undergo unimolecular cyclization to the desired paracyclophane product, AF4. If **3** encounters another molecule of monomer **1** before it can cyclize, it will react to form the linear trimer diradical which, having an even smaller probability of undergoing cyclization, usually, but not always, continues on to form AF4 polymer. This polymer has no appreciable solubility in any solvent yet tested. The high dilution conditions are designed to provide the optimal kinetic environment for allowing unimolecular cyclization of **3** to compete effectively with bimolecular oligomerization.

Recognizing the need for an improved synthesis of AF4, we have continued to pursue new reductive methodologies toward that end, with the result that we now wish to report a new and improved method for synthesis of AF4, using as a reductant the active species generated *in situ* by reaction of (trimethylsilyl)tributyltin (TMSTBT) with cesium fluoride (CsF). Furthermore, it has been demonstrated that this method is scaleable and thus should be able to be utilized to readily make kilogram quantities of AF4.

The use of TMSTBT/CsF for the purpose of debromination has been previously reported in Mori's study of the generation of *o*-quinodimethanes for use in Diels–Alder reactions (Scheme 5).[11,12]

The new method uses a unique approach to circumvent the need for conventional high dilution technology. It allows one to add in most of the ingredients together rather quickly, while maintaining the necessary low concentration of monomer via control of its rate of *in situ* generation. As was the case for the earlier two methods, **2** is the preferred precursor to monomer **1** in the new synthesis. In a typical reaction, 55 g (0.36 mol) of CsF, 105.5 g (0.28 mol) of TMSTBT, and 100 g (0.32 mol) of dibromide **2** were added consecutively to a mixture of 8 L of THF and 2 L of DMSO at 78 °C. After stirring and refluxing for 12 h, another 57.5 g (0.16 mol) of tinsilane was added, followed by a third 52.5 g (0.14 mol) dose after 6 h more. After an additional 10 h of reflux, the reaction was worked up to give 25 g of crude AF4 product, which upon recrystallization from 10:1 CHCl$_3$–hexane provided 22.7 g (40%) of >99% pure AF4 (Scheme 6). In subsequent development studies, the reaction has been able to be scaled up to produce as much as 1 kg of AF4 in a single run.

The above-described conditions have been optimized with respect to choice of solvent and reaction conditions. Under otherwise identical conditions, carrying out the reaction in pure THF gave but an 8% yield, whereas use of HMPA in place of the DMSO (again 8:1) led to a 16% yield. If KF was used in place of CsF, only a 5% yield was obtained. Attempts to substitute other ethereal solvents, such as diethyl ether, dioxane, or diglyme, for THF also led to much poorer results.

It is believed that the active reducing agent in this reaction is generated *in situ* by the reaction of fluoride ion, F$^-$, with TMSTBT. Because Me$_3$SiF and Bu$_3$SnBr are formed as a result of the overall reaction, it is assumed that the process begins by attack of the TMSTBT by fluoride ion. That being the case, the actual active reducing agent could be either the complex anion **4** or the tributyltin anion itself, **5** (Scheme 7).

The suggestion that **4** is the possible active agent which effectively "delivers" Bu$_3$Sn$^-$ to dibromide **2** has precedent in that Olah has found that CF$_3$SiMe$_3$ + fluoride ion effectively "delivers" a CF$_3^-$ anion in reactions with carbonyl compounds without apparently passing thorough a free CF$_3^-$ anionic species (Scheme 8).[13]

Indeed we have found, in a control study, that treatment of **2** with pregenerated Li$^+$SnBu$_3^-$ under high dilution conditions does not lead to formation of significant amounts of AF4. Mori also made the same type of observation in his Diels–Alder study depicted in Scheme 5.[11]

It is believed that the success of our new procedure derives from the limited solubility of CsF in the solvent mixture at 70 °C and that the required slow but consistent generation of the active reducing agent is controlled by the slow, steady dissolution of the CsF which generates this active agent.

The actual nature of the debrominative process also remains ambiguous as to whether there is a direct formation of Bu$_3$SnBr by a bimolecular reaction of the active reducing agent with dibromide **2**, or there is a single electron transfer (SET) process involved between **4** (or **5**) with **2**. Consistent with this latter possibility is the fact that the two best cosolvents with THF have been found to be DMSO and HMPA, both recognized to be excellent facilitators of SET reactions. The truth is, though, that the emphasis in this work has been development of a good synthesis, with little effort of a mechanistic nature having been made.

The fact that the major competing reaction in this new process is formation of polymer, with most of the remaining material being accounted for as "reduction" products, where one or both of the CF$_2$Br groups of **2** have been reduced to CF$_2$H groups, provides good evidence for the intermediacy of monomer **1** in the reaction. Another piece of evidence along that line derives from an experiment in which pure DMSO was used as the solvent at 70 °C, with gradual addition of CsF. In this case no AF4 was observed, but there was instead a high yield conversion to the pentafluoro-*p*-xylene, **6**, most likely via fluoride interception of monomer **1**, followed by abstraction of a proton from DMSO (Scheme 9).

Experimental Section

Anhydrous THF and DMSO were obtained from Fisher Scientific, cesium fluoride (anhydrous, 99%) from CM Chemical Products, Inc., and tri-*n*-butyltin chloride and trimethylsilyl chloride from Aldrich Chemical Co.

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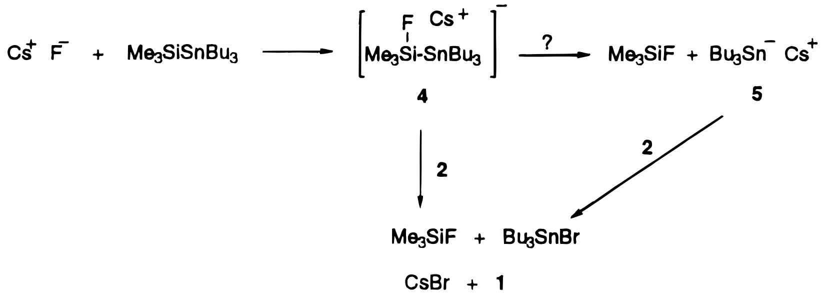
(11) Sato, H.; Isono, N.; Okamura, K.; Date, T.; Mori, M. *Tetrahedron Lett.* **1994**, *35*, 2035–2038.

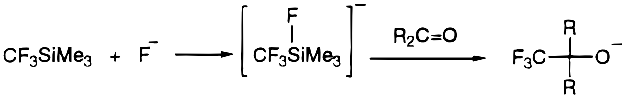
(12) Sato, H.; Isono, N.; Miyoshi, I.; Mori, M. *Tetrahedron* **1996**, *52*, 8143–8158.

(13) Prakash, G. K. S.; Krishnamurti, R.; Olah, G. A. *J. Am. Chem. Soc.* **1989**, *111*, 393–395.

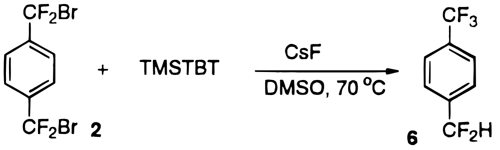
Scheme 7



Scheme 8. Olah's CF_3-Transfer Reaction



Scheme 9



(Tri-*n*-butylstannyl)lithium. To a dry, three-neck 12 L flask equipped with mechanical stirrer, condenser, and addition funnel, and maintained under argon, was added 3500 g (10.75 mol) of tri-*n*-butyltin chloride, followed by addition of 300 g (42.9 mol) of lithium chips and 20 g of sodium. The reaction mixture was stirred for 3 days at ambient temperature, with the flask becoming slightly warm to the touch. During this time the mixture turned dark. After the mixture was cooled to 5 °C, 3 L of THF was added using the addition funnel, the mixture turning green. Stirring continued for 4−5 days at ambient temperature after which the mixture was filtered through glass wool to remove the excess lithium metal.

(Trimethylsilyl)tributyltin.[14] The above described solution of (tributylstannyl)lithium was cooled to 5 °C with an ice bath and, using the addition funnel, 1750 g (16.1 mol) of chlorotrimethylsilane was added slowly, at a rate which maintains the temperature below 5 °C (approximately 2 h). The ice bath was then removed and the solution allowed to warm to room temperature, continuing stirring for 3 h. At that point 50 mL of n-propyl bromide was added and the mixture stirred an additional 2 h (to remove any *n*-Bu_3SnH which might have been formed). The mixture was filtered to remove LiCl, and the filtrate was distilled to remove the THF. Two liters of diethyl ether was then added and the mixture washed with water (2 × 500 mL), after which the solution was dried over $MgSO_4$. The ether was removed by rotary evaporation, and the product was distilled to obtain 2850 g of (trimethylsilyl)tributyltin (72.5% yield), bp 88 °C/0.2mm.

Octafluoro[2.2]paracyclophane (AF4). Eight liters of anhydrous THF, two liters of anhydrous DMSO, and 55.3 g (0.36 mol) of anhydrous CsF were added under an N_2 atmosphere to a dried, three-necked twelve liter round bottomed flask which was equipped with a mechanical stirrer, a condenser, and an N_2 inlet, and heated by a heating mantel. The mixture was stirred, the temperature allowed to rise to 70 °C, and the mixture stirred for an additional 30 min. To this mixture was added 105.5 g (0.28 mol) of (trimethylsilyl)tributyltin (TMSTBT) and the mixture stirred for 30 min at 70 °C. The solution was then brought to reflux (78 °C), and 100 g (0.32 mol) of 1,4-bis(bromodifluoromethyl)benzene (**2**) was added all at once. The mixture was then stirred for 12 h after which an additional 57.5 g (0.16 mol) of TMSTBT was added to the mixture, with a final portion of TMSTBT (52.5 g, 0.14 mol) being added after an additional 6 h. Upon stirring for an additional 10 h, it was determined by ^{19}F NMR that all of the dibromide **2** had been consumed.

Seven liters of the THF were then removed by distillation at atmospheric pressure. The resulting mixture was then cooled to rt and allowed to stand for 12 h, after which the precipitate was filtered off and the remaining THF was removed by rotary evaporation. The residual liquid was distilled under vacuum, with the distillate boiling above 70 °C (0.5 mm) being collected and placed in a refrigerator for 12 h to yield 25 g of crystalline AF4. The crude product was recrystallized from chloroform−hexane (10:1) (chilled at 0−10 °C for 12 h in the refrigerator) to yield 22.7 g of pure AF4 (40%); ^1H NMR ($CDCl_3$), δ 7.16 ppm (s); ^{19}F NMR ($CDCl_3$), δ −118.75 ppm (s); ^{13}C NMR ($CDCl_3$), δ 129.82 ppm (t, $J = 3.4$ Hz).

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[14] Lahournère, J.-C.; Valade, J. *J. Organomet. Chem.* **1970**, *22*, C3.