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A New C−F Bond-Cleavage Route for the Synthesis of Octafluoro[2.2]paracyclophane

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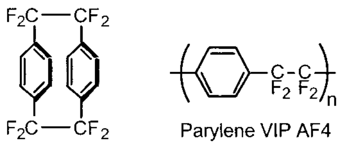
Introduction

Fluoropolymers have received intense attention with implications for material science. Some of them possess potentially important and interesting properties as an electronic device. For example, poly(α,α,α′,α′-tetrafluoro-*p*-xylylene) (**2**), known in the industry as Parylene VIP AF4, is endowed with fascinating material properties such as low dielectricity (dielectric constant: 2.36 ± 0.5),[1] high thermal and oxidative stability (450 °C in air),[2] low moisture absorption, and chemical inertness due to the nature of C−F bonds (Chart 1). Thus, the Parylene AF4 polymer **2** satisfies many of the exacting requirements for high-temperature applications and shows considerable promise as an on-chip dielectric interlayer medium and as a coating of an electrical component near an automobile engine.

Chart 1

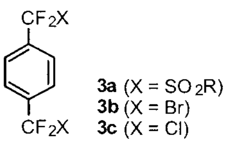


AF4 (**1**)

Parylene VIP AF4
2

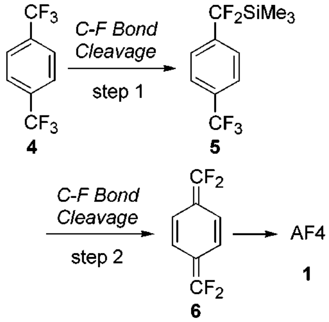
Octafluoro[2.2]paracyclophane (AF4, **1**), which is an excellent precursor of the high-purity parylene polymer **2** via vapor deposition (CVD) process,[3] is a key compound of significant commercial interest. Despite its desirability in the market, there have been few methodologies to synthesize the cyclophane **1** (the precursors are summarized in Chart 2); (a) pyrolytic/reductive processes of **3a**−**c**,[4,5] (b) reductive debromination of **3b** using low-valent titanium,[6a] or (c) using a stoichiometric amount of $Bu_3Sn-SiMe_3$/CsF. [6b]

Chart 2



3a (X = SO_2R)
3b (X = Br)
3c (X = Cl)

Very recently, Dolbier et al. reported inexpensive and highly scalable preparation of AF4 by (d) a reaction of *p*-bis(chlorodifluoromethyl)benzene (**3c**) with Zn under non-high-dilution conditions,[6c] and they also demonstrated the functionalization of the benzene ring of AF4.[7] However, to our knowledge, there has been no commercially available precursor to AF4 (**1**). By taking advantage of the use of readily available trifluoromethylated compounds, selective defluorination of 1,4-bis(trifluoromethyl)benzene (**4**) would provide a highly efficient access to cyclophane **1**.[8] Herein, we report a conceptually new route for the synthesis of AF4 involving successive C−F bond cleavage processes of commercially available **4** as a starting material (eq 1).



(1)

Results and Discussion

The First C−F Bond Cleavage Process for AF4. Mg(0)-promoted defluorinative silylation of 1,4-bis(trifluoromethyl)benzene (**4**) affording α-trimethylsilyl-α,α,α′,α′,α′-pentafluoroxylene (**5**) has been examined. In general, the cleavage of a C−F bond is not easy due to the large bond energy (ca. 552 kJ mol^{-1}).[9] However, the bond breaking does occur rather easily when a CF_3 group is attached to the π-system because electron acceptance into a benzene ring and subsequent extrusion of a fluoride ion may make large contributions to the driving force for the reaction.[10] Clavel et al. reported the selective synthesis of $PhCF_2SiMe_3$ via an electrochemical reduction of $PhCF_3$ in the presence of chlorotrimethylsilane.[11] For the synthesis of $PhCF_2SiMe_3$ from $PhCF_3$, the chemical metal reduction methods did not work well due

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[8] Carbon−fluorine bond cleavage of 1,4-bis(trifluoromethyl)benzene catalyzed by 1,4-bis(bromodifluoromethyl)benzene and zinc metal in the synthesis of poly(tetrafluoro-*p*-xylene), see: Wu, P. K.; Yang, G.-R.; You, L.; Mathur, D.; Cocoziello, A.; Lang,; C.-I.; Moore, J. A.; Lu, T.-M. *J. Electron. Mater.* **1997**, *26*, 949. However, in this reaction, special apparatus was required and the metal surface is corroded by molecular fluorine.

[9] For recent reviews on metal-mediated C−F bond activation, see: (a) Burdeniuc, J.; Jedlicka, B.; Crabtree, R. H. *Chem. Ber./Recueil* **1997**, *130*, 145−154. (b) Richmond, T. G. In *Activating of Unreactive Bonds and Organic Synthesis. Topics in Organometallic Chemistry*; Murai, S., Ed.; Springer-Verlag: Berlin, 1999; Vol. 3, p 243.

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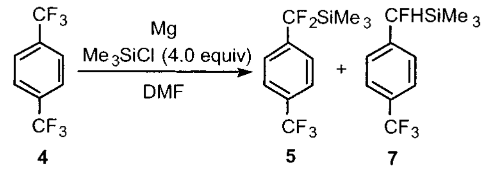
Table 1. Mg-Promoted Defluorinative Silylation of 4



entry	Mg (equiv)	conditions	product (% yield)[a] 5	7
1	1.1	rt, 3 h	35	7
2	2.0	rt, 0.5 h	64 (48)[b]	5
3	2.0	rt, 1 h	58	15

[a] NMR yield, which was calculated by ^{19}F NMR integration of product **5** relative to the 2,2,2-trifluoroethanol internal standard. [b] Isolated yield (in parentheses).

to the lack of chemoselectivity resulting in contamination with the persilylated products. Independently, we developed the electroreductive methods for silyl difluoroenol ethers and difluoroenamines and α-silyldifluoroacetates using trifluoromethyl ketones and imines and trifluoroacetates as a starting material.[12] Recently, we found Mg(0) metal proves useful for the C−F bond-breaking process of trifluoromethyl ketones to provide a highly efficient access to a variety of 2,2-difluoroenol silyl ethers.[13] We have thus tried to apply our Mg(0) method as a convenient reduction system to the cleavage of benzylic C−F bond of **4**.

1,4-Bis(trifluoromethyl)benzene (**4**) was treated with magnesium (1.1 equiv) and chlorotrimethylsilane (4.0 equiv) in DMF at room temperature for 3 h. Defluorinative silylation took place to afford not only the desired α,α-difluorobenzylsilane **5** in 35% yield but the further defluorination product **7** in 7% yield (Table 1, entry 1).

The best result [**5** (64% yield) + **7** (5% yield) by ^{19}F NMR] was obtained by the use of 2.0 equiv of Mg with 30 min of stirring (48% isolated yield after distillation, >95% purity) (Table 1, entry 2), while a longer reaction time (1 h) promoted the formation of undesired product **7** [**5** (58%) + **7** (15%)] (Table 1, entry 3). Raising the reaction temperature (>80 °C) and using large amounts of Mg (>8 equiv) resulted in very sluggish reactions. Although we could not prevent trace contamination with **7** because of close reduction potentials between the starting material **4** and the product **5**,[11b] the reaction described here presents a simple and versatile example of a practical synthetic method involving C−F bond cleavage without any requirement of special techniques and reagents.

The Second C−F Bond Cleavage Process for AF4. Conjugative elimination is one of the most versatile and efficient methods for the generation of *o*- and *p*-xylylene intermediates. Ito et al. reported the generation of *o*-xylylene intermediates by fluoride anion induced 1,4-eliminaion of *o*-(trimethylsilylalkyl)benzyltrimethylammonium halides for use in Diels−Alder reactions.[14] A key feature of this methodology is the mildness of the reaction conditions to generate *o*-quinodimethanes, which are attributed to the use of the trigger fluoride ion by virtue of the large bond energy between silicon and fluorine. In most cases, a stoichiometric amount of fluoride is required for these reactions due to the decreased ability of the leaving groups to attack the silicon atom of the precursors. By contrast, when the conjugative elimination of **5** occurs and the leaving group is a fluoride ion that can react again with **5**, the process should be catalytic with respect to fluoride. We have explored a catalytic version of fluoride anion induced 1,6-elimination of **5** to generate tetrafluoro-*p*-xylylene (**6**) (Scheme 1).

Scheme 1. Fluoride Anion-Catalyzed 1,6-Elimination of 5

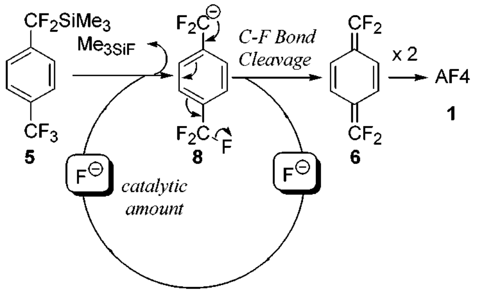
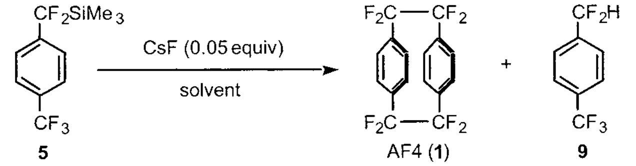


Table 2. CsF-Catalyzed 1,6-Elimination of 5[a]



entry	solvent	conditions	additive	product (% yields)[b] 1	9
1	toluene	110 °C, 24 h		trace	42
2	*o*-xylene	140 °C, 24 h		21	*c*
3	mesitylene	160 °C, 24 h		33	*c*
4	anisole	160 °C, 24 h		20−45	*c*
5	anisole	160 °C, 24 h	$Pd_2(dba)_3\cdot CHCl_3$/TBC[a]	61 (53)[e]	*c*

[a] All reactions were carried out with 0.05 M concentration of 5. [b] NMR yield, which was calculated by ^{19}F NMR integration of product **1** relative to the 2,2,2-trifluoroethanol internal standard. [c] Not determined. [d] $Pd_2(dba)_3\cdot CHCl_3$ (0.00125 equiv) and TBC (5.0 10-5 in anisole) were used. [e] Isolated yield (in parentheses).

A toluene solution of **5** containing a catalytic amount (0.05 equiv) of CsF was stirred at 110 °C only to give the protodesilylation product ($HCF_2C_6H_4CF_3$, **9**) in 42% yield (Table 2, entry 1). After several attempts, we succeeded in the generation of tetrafluoro-*p*-xylylene **6** to provide cyclophane **1** by raising the reaction temperature. The desired 1,6-elimination occurred in refluxing mesitylene or anisole (160 °C) affording AF4 (**1**) in 20−45% yield (Table 2, entries 3 and 4). A higher reaction temperature is considered to be essential to the elimination of the poor leaving group such as a fluoride because the bond energy

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of a C−F bond is much larger than that of other C−X bonds (X: good leaving groups).

Interestingly, the yield of AF4 dramatically increased to 61% (53% isolated yield) when the reaction was conducted in the presence of a very small amount of Pd(0) catalyst[15] with good reproducibility (Table 2, entry 5). Pd(0) catalyst is considered to accelerate the intramolecular coupling reaction of the diradical intermediate.[6]

In conclusion, a new sequence was developed in which two C−F bonds were cleaved, the first through Mg(0)-promoted defluorinative silylation and the second by subsequent conjugative 1,6-elimination induced by the *catalytic* use of CsF. The present example demonstrates a promising application of selective C−F bond cleavage processes in material science.

Experimental Section

^{1}H and ^{19}F NMR spectra were recorded at 200 and 188 MHz, respectively, using $CDCl_3$ as a solvent. The chemical shifts are reported in δ (ppm) values relative to TMS (δ 0 ppm for ^{1}H NMR) and C_6F_6 (d 0 ppm for ^{19}F NMR). Coupling constants are reported in hertz (Hz). Commercially available Mg turnings (Nacalai tesque, Inc.) were used without further activation of the magnesium surface, such as iodine, dibromoethane, or ultrasound treatment. All air- and/or water-sensitive reactions were carried out under argon atmosphere with dry, freshly distilled solvents using standard syringe-cannula/septa techniques. DMF, toluene, xylene, mesitylene, and anisole were distilled from CaH_2. All other reagents and solvents were employed without further purification.

α-Trimethylsilyl-α,α,α′,α′,α′-pentafluoroxylene (5). To a mixture of Mg (1.73 g, 72 mmol) and chlorotrimethylsilane (15.6 g, 144 mmol) in distilled DMF (80 mL) was added 1,4-bis(trifluoromethyl)benzene (**4**) (7.70 g, 36 mmol) dropwise, and then the mixture was stirred for an additional 20−30 min under an argon atmosphere at room temperature. H_2O was added to quench the reaction, the reaction mixture was extracted with hexane, and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated. Kugelrohr distillation afforded **6** as a colorless oil (4.64 g, 48%): bp 100 °C (30 mmHg); ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.15 (s, 9H), 7.46 (d, $J = 8.6$ Hz, 2 H), 7.68 (d, $J = 8.6$ Hz, 2 H); ^{19}F NMR (188 MHz, $CDCl_3$, C_6F_6 as an internal standard): δ 48.7 (s, 2F), 99.0 (s, 3F). Anal. Calcd for $C_{11}H_{13}F_5Si$: C, 49.24; H, 4.88. Found: C, 49.18; H, 5.14.

1,1,2,2,9,9,10,10-Octafluoro[2.2]paracyclophane (AF4, 1). A mixture of **5** (3.21 g, 12 mmol) and CsF (91.2 mg, 0.6 mmol) and $Pd_2(dba)_3\cdot CHCl_3$ (24.7 mg, 24 μmol) in anisole (80 mL; contaminated with 1.8 mg of 4-*tert*-butylcatechol) was heated at reflux for 24 h. The cooled reaction mixture was filtered through a pad of Celite. Anisole was removed by distillation. Kugelrohr distillation afforded **1** as a colorless solid (1.12 g, 53%): bp 150 °C (3 mmHg); mp 261 °C (lit.[6] mp 262 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.16 (s, 8 H); ^{19}F NMR (188 MHz, $CDCl_3$ C_6F_6 as an internal standard) δ 43.5 (s, 8 F). Anal. Calcd for $C_{16}H_8F_8$: C, 54.56; H 2.29. Found: C, 54.86; H, 2.44.

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