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Convenient synthesis and single-crystal X-ray structures of two tetrafluoro[2,2]paracyclophane isomers

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Abstract—Fluorinated [2,2]paracyclophanes are useful precursors to poly(*p*-xylylene) polymers. The cyclophanes 1,1,9,9-tetrafluoro[2,2]*p*-cyclophane (**3a**) and 1,1,10,10-tetrafluoro[2.2]*p*-cyclophane (**3b**) can be readily prepared via a convenient two-step synthesis from the parent hydrocarbon [2,2]*p*-cyclophane (**1**). The structures of **3a** and **3b** are confirmed via single crystal X-ray analysis.

The functionalization of the methylene bridge carbons of the prototypical hydrocarbon [2,2]*p*-cyclophane (**1**) (Fig. 1) has been of interest for many years.[1] For example, bridge-functionalized **1** has recently been used as a poly(*p*-phenylenevinylene) (PPV) precursor.[2] In addition, fluorinated [2,2]*p*-cyclophanes have been attracting increased attention. Poly(*p*-xylylene) polymers formed via the vapor deposition polymerization of cyclophane precursors that are either fully[3] or partially[4] fluorinated at their methylene carbons are materials of current technological interest. Compound **2** (Fig. 1), for example, is a precursor to a polymer (Parylene AF4)[5] which has exhibited promise as an interlayer dielectric material in high-speed integrated circuits due to its low dielectric constant.[6] An obstacle to the commercialization of the fluorinated parylenes is the multistep syntheses required to obtain the fluorinated cyclophane precursors. Recently, an exciting new methodology allowing for the large scale synthesis of **2** was reported.[7]

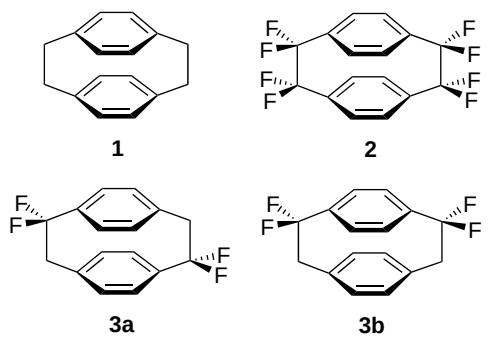
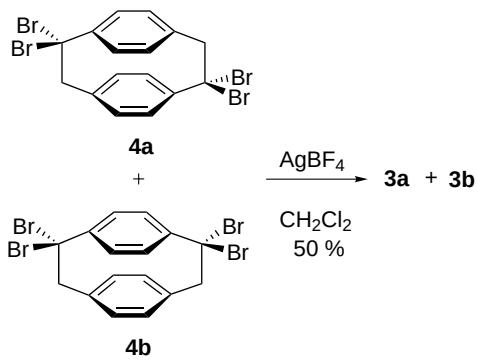


Figure 1. Structures of [2,2]-*p*-cyclophane (**1**) and its fluorinated derivatives.

The parylene derived from partially fluorinated **3a** (Fig. 1) is also of interest for technological applications, for example as a coating with enhanced oxidative and thermal stability.[8] Previously, Itoh and coworkers synthesized **3a** via a five-step sequence from **1**.[4] The more recent patented procedure for the preparation of **3a** involved a three-step bromination–oxidation–fluorination sequence starting with the bromination of **1**, followed by separation of the isomers, oxidation with AgOAc or NaOAc and fluorination with SF_4 or Et_2NSF_3.[8] Herein, we report a mild, convenient two-step synthesis of a separable mixture of **3a** and **3b** (Fig. 1).

Known compounds **4a** and **4b** were prepared via the bromination of [2,2]-*p*-cyclophane (**1**) according to



Scheme 1. Conversion of known tetrabromides **4a** and **4b** to the fluorinated targets **3a** and **3b** in a 2:3 ratio.

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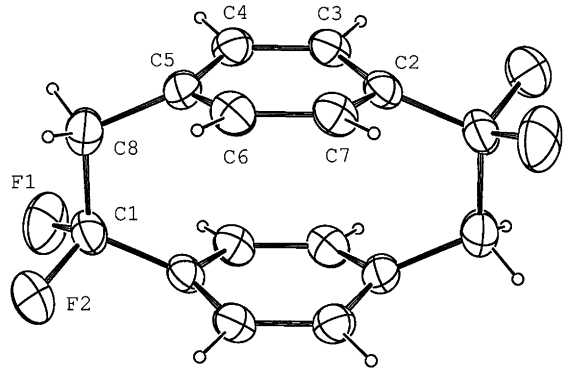
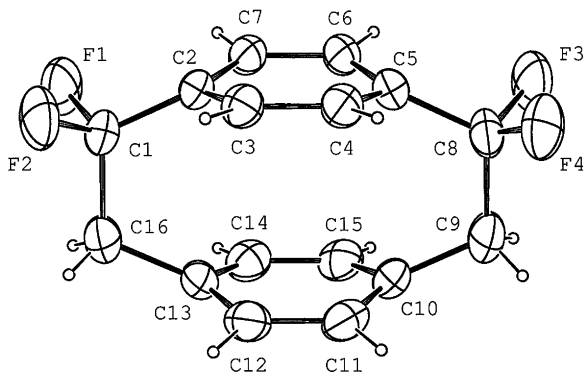


3a



3b

Figure 2. X-Ray structures of **3a** and **3b**.

Cram's procedure in a 2:3 ratio, respectively.[1a] We reasoned that a mild, direct functional group interconversion of **4a** and **4b** to the difluorides would be more efficient and less costly than the prior syntheses,[4,8] thereby affording a more attractive alternative for industrial preparation.

Bloodworth and Mitchell previously developed a halogen–exchange reaction of geminal dichlorides and diiodides to the corresponding difluorides employing $AgBF_4$.[9] Based on their procedure we are able to transform the mixture of **4a** and **4b** (4.72 g, 9 mmol) to the corresponding tetrafluorides **3a** and **3b** in 50% isolated yield in a 2:3 ratio via stirring with $AgBF_4$ (4 equiv.) in CH_2Cl_2 at rt for 20 h[10,11] (Scheme 1). Interestingly, the 50% yield for the difluorination of **4a** and **4b** is higher than those reported for unstrained dihalides.[9] Separation of **3a** and **3b** by flash chromatography followed by recrystallization from a 1:1 benzene:hexane solution affords X-ray quality crystals.

Compounds **3a** and **3b**, along with **1** and **2**, are a homologous series of structurally-related cyclophanes. The crystal structures of **1** and **2** were previously studied together and were shown to exhibit remarkably similar features. The X-ray crystal structures of **3a** and **3b** (Fig. 2) complement the prior X-ray studies of **1**[12] and **2**.[12c] 1,1,9,9-Tetrafluoro-[2,2]-*p*-cyclophane **3a** crystallizes in the monoclinic system with $a=13.8709(5)$, $b=7.8354(5)$, $c=11.6450(9)$ Å, $\beta=99.898(4)°$, space group $C2/c$, and $Z=4$ molecules per cell. 1,1,10,10-Tetrafluoro-[2,2]-*p*-cyclophane **3b** crystallizes in the monoclinic system with $a=27.656(2)$, $b=8.1496(9)$, $c=11.364(1)$ Å, $\beta=102.841(8)°$, space group $C2/c$, and $Z=8$ molecules per cell. Both refinements were based on data collected on an Enraf–Nonius CAD4 diffractometer to $\theta=75°$ with Cu Kα radiation, yielding $R=0.053$ for all 1281 data for **3a** and $R=0.063$ for all 2576 data for **3b**. The molecule of **3a** lies on a crystallographic inversion center, while that of **3b** lies in a general position. The carbon skeletons of **3a** and **3b** are very similar. The C–C bridge distance in **3a** is 1.545(3) Å, while those in **3b** are 1.537(3) and 1.538(4) Å. In **3a**, C2 and C5 lie 0.130(2) and 0.162(2) Å, respectively, out of the plane of the other four atoms of the phenyl ring. For **3b**, analogous distances are 0.135(2) Å for C2, 0.143(2) Å for C5, 0.158(2) Å for C10, and 0.161(2) Å for C13. The perpendicular distances between these four-atom planes are 3.088(2) Å in **3a** and 3.086(2) Å in **3b**. C–F distances range 1.359(2)–1.363(2) Å in **3a** and 1.353(3)–1.370(3) Å in **3b**. The F–C–F angle is 104.3(2)° in **3a**, and those in **3b** are 104.4(1) and 103.6(2)°.

In conclusion, room temperature treatment with $AgBF_4$ is a mild and convenient technique for introducing fluorines at cyclophane methylene bridge carbons. Parylene precursor cyclophanes **3a** and **3b** can be directly prepared at room temperature via the corresponding tetrabromide precursors in just two steps from commercially available **1**.

Acknowledgements

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11. 1,1,9,9-Tetrafluoro[2,2]-*p*-cyclophane (**3a**) and 1,1,10,10-tetrafluoro[2,2]-*p*-cyclophane (**3b**). The mixture of **4a**:**4b** (2:3 4.72 g, 9 mmol) is stirred in anhydrous CH_2Cl_2 (200 mL) under Ar. $AgBF_4$ (7.4 g, 38 mmol) is added in small portions through a solid addition funnel. The mixture is stirred 20 h at rt and concentrated in vacuo. The black residue was extracted with hot benzene affording a yellowish solid (2.3 g). The residue is sublimed (70°C, 0.01 mm Hg) affording a white solid (1.25 g, 50%). Column chromatography on silica gel (50 g, 200 mesh) eluting with 1:4 benzene:hexane produced X-ray quality crystals of **3b**. Recrystallization of the 1:1 mixture of **3a**:**3b** with 1:1 benzene:hexane followed by column chromatography on silica gel (20 g, 200 mesh) eluting with 1:4 benzene:hexane affords X-ray quality crystals of **3a**. Data for **3a**: mp: 191–193°C; ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.61 (t, $J=14.8$ Hz, 4H), 6.96 (dd, 6.80, 8H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 51.21 (t, $J=33.1$ Hz), 125.86 (t, $J=254.2$ Hz), 129.56 (t, $J=5.8$ Hz), 133.77 (s), 135.03 (t, $J=26.9$ Hz), 138.92 (t, $J=5.1$ Hz) ppm. ^{19}F NMR (235 MHz, $CDCl_3$) δ: −91.74 (t, $J=14.8$ Hz, 4F) ppm. HRMS calcd 280.0875, found 280.0874. Data for **3b**: mp: 160–161°C; ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.59 (t, $J=15$ Hz, 4H), 6.63 (s, 4H), 6.96 (s, 4H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 50.95 (t, $J=34.0$ Hz), 125.99 (t, $J=254.3$ Hz), 129.65 (t, $J=6.3$ Hz), 133.68 (s), 136.81 (t, $J=26.9$ Hz), 137.40 (t, $J=5.3$ Hz) ppm. ^{19}F NMR (235 MHz, $CDCl_3$) δ: −92.29 (t, $J=15$ Hz, 4F) ppm. HRMS calcd 280.0875, found 280.0865
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