# Preparation and Thermal Behavior of 3,3,4,4-Tetrafluorocyclobutane-1,2-diols: A New Family of Cyclobutane-1,2-diols

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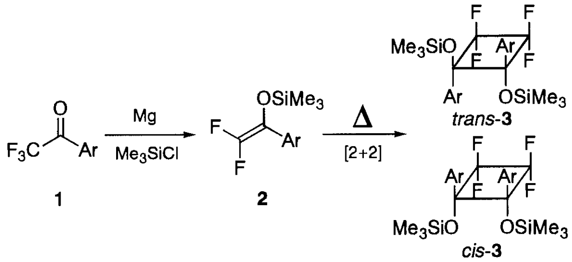
Thermal dimerization of 2,2-difluoro enol silyl ethers led to 3,3,4,4-tetrafluorocyclobutanes. The [2+2] cycloaddition proceeded in a "head-to-head" fashion to afford the cyclobutanes containing the *trans* and *cis* stereoisomers. The cyclobutanes were transformed to tetrafluorocyclobutane-1,2-diols by desilylation.

Fluorine containing cyclobutanes are interesting precursors for bioactive compounds or functionalized polymers.[1–3] Thermal [2+2] cycloaddition is one of the well-known methods to produce cyclobutanes from α,α-difluoroolefins.[4–7] However, there is no report on tetrafluorocyclobutanediol. Herein, we report the thermal dimerization of 2,2-difluoro enol silyl ethers **2** to give 3,3,4,4-tetrafluorocyclobutane-1,2-diols derivatives **3**, which are considered to be promising bifunctional molecules possessing two silyl-protected hydroxyl functionalities.

Recently, we have reported Mg(0)-promoted selective defluorination of readily available trifluoromethyl ketones **1** in the presence of chlorotrimethylsilane by means of a process involving C–F bond cleavage (Scheme 1),[8,9] which provides an easy access to a variety of 2,2-difluoro enol silyl ethers **2**.



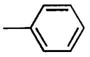
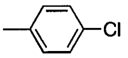
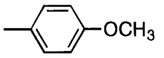
**Scheme 1.**

The preparation procedure of cyclobutanes **3** from **2** is very simple. Heating neat **2a** under an Ar atmosphere at 110 °C for 6 h[10] gave a mixture of *trans* and *cis* isomers of **3a** in good yield (Table 1). On heating **2** in air at the same temperature, however, a complex mixture of no fluorine containing compounds was obtained as strong yellow and high viscous oil.

The intermolecular [2+2] cycloaddition of **2** proceeded predominantly in a head-to-head fashion. It is well-known that the thermal [2+2] cycloaddition reactions of fluoroolefins proceed via radical intermediates.[5–7] The preference for the head-to-head adduct formation can be explained by assuming that the ring open-chain biradical intermediates generated from radical coupling at the 2-positions (head-to-head coupling) of **2**, are much more stable than that of head-to-tail coupling due to the stabilization of both of the radical centers of the intermediates by the aromatic and siloxy group.

Other examples of formation of **3** are given in Table 1.

**Table 1.** Thermal dimerization of difluoroenol silyl ethers **2**

| Entry | Ar | Product | Yield /%[a] | *trans*:*cis*[b] |
|---|---|---|---|---|
| 1 |  | **3a** | 89 | 53:47 |
| 2 |  | **3b** | 63 | 63:37 |
| 3 |  | **3c** | 64 | 56:44 |

[a]Isolated yield. [b]Determined by $^{19}$F NMR.

The enol ethers **2** that possess either electron-withdrawing (entry 2) and electron-donating (entry 3) on the aryl ring provided **3** in good yields. In all cases, the cyclobutanes **3** were obtained as a mixture of *trans* and *cis* isomers in an approximate ratio 1:1. The diastereomeric mixture of **3** was separable by column chromatography on silica gel.[11] When the enol silyl ether **2a** was heated at 150 °C for 6 h, *trans* and *cis*-**3a** were obtained in 54% yield in a ratio of 10:1, indicating that thermal decomposition of *cis*-**3a** took place. In fact, the compounds of *trans*- and *cis*-**3a** showed different thermal stability at high temperature. On thermogravimetric analysis (TGA) for each isomers under nitrogen atmosphere, the weight loss of *cis*-**3a** started at 115 °C, whereas no weight loss up to 150 °C in the case of

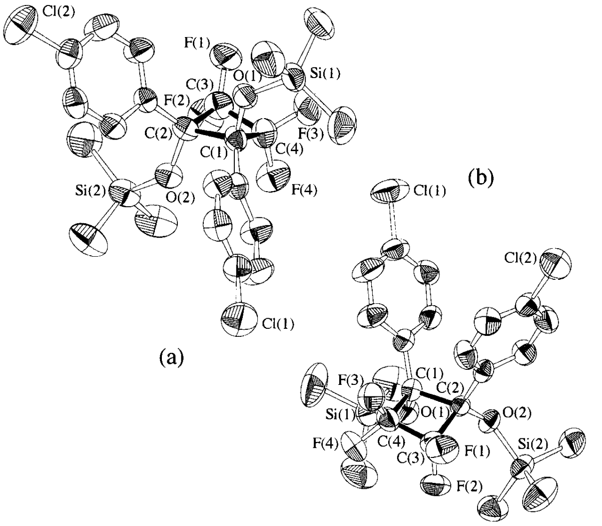
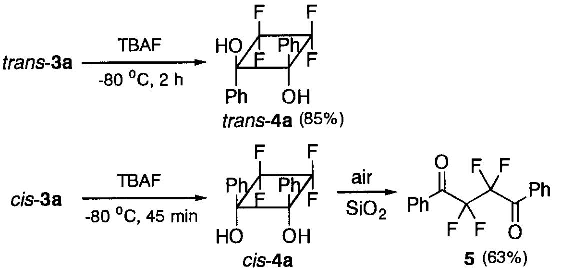


**Figure 1.** Molecular structure of *trans*-**3b** (a) and *cis*-**3b** (b) at 50% probability level. All hydrogen atoms are omitted for clarity. Selected distances (Å) and angles (deg): *trans*-**3b**: C(1)-C(2), 1.579(5); C(2)-C(3), 1.555(4); C(3)-C(4) 1.530(6); C(4)-C(1), 1.555(4); C(4)-C(1)-C(2), 87.4(1); C(1)-C(2)-C(3), 87.4(1); C(2)-C(3)-C(4), 89.2(1); C(3)-C(4)-C(1), 89.2(1). *cis*-**3b**: C(1)-C(2), 1.627(5); C(2)-C(3), 1.553(5); C(3)-C(4), 1.517(5); C(4)-C(1), 1.562(4); C(4)-C(1)-C(2), 87.6(2); C(1)-C(2)-C(3), 86.8(2); C(2)-C(3)-C(4), 92.0(3); C(3)-C(4)-C(1), 90.5(3).

*trans*-**3a**.

Besides the thermograms, the X-ray crystal structure analyses of *trans*- and *cis*-**3b**[12] also suggest the weakness of C(1)–C(2) bond since the bond lengths of C(3)–C(4) (1.52 Å (*trans*-**3b**) and 1.52 Å (*cis*-**3b**)) are shorter and the lengths of C(1)–C(2) (1.60 Å (*trans*-**3b**) and 1.63 Å (*cis*-**3b**)) are longer as compared with the reported average bond lengths of cyclobutanes (1.55 Å). As shown in Figure 1, *cis*-**3b** has a more strained 4-membered ring structure than *trans*-**3b**; the bond length of C(1)–C(2) of *cis*-**3b** (1.63 Å) is slightly longer than that of *trans*-**3b** (1.60 Å), and the longer C(1)–C(2) bond length in *cis*-**3b** would result in potentially reducing the thermal stability of *cis*-**3**.

Compound **3** could be converted into diol **4** (Scheme 2). Desilylation for **3a** with tetrabutylammonium fluoride (TBAF) was achieved at –80 °C for 2 h.[13] Different reactivity on this reaction was observed for *trans* and *cis*-**3a**. Desilylation with TBAF for *cis*-**3a** was faster than *trans*-**3a**. The higher reactivity of *cis*-**3a** is consistent with the result of TGA and X-ray analyses. Furthermore, ketone **5** was obtained from diol *cis*-**4a** (63% isolated yield) by treating with silica gel and $Na_2SO_4$ in $Et_2O$ at room temperature for 12 h.[14] On the other hand, diol *trans*-**4a** was scarcely converted to **5** under such conditions.



**Scheme 2.**

In summary, we have prepared tetrafluorocyclobutanes by thermal [2+2] dimerization of difluoro enol silyl ethers. The dimers were consisting of *trans* and *cis* stereoisomers. TMS deprotection of the dimers led to diols that could be derived to a wide range of 4-membered ring containing materials.

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## References and Notes

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10 Generally, intermolecular [2+2] cycloaddition of α,α-difluoroolefins occurs when heating at 100–700 °C, see ref 1.
11 $^{19}$F NMR ($CDCl_3$, 188 MHz, $C_6F_6$ as an internal standard) of *trans*-**3a**: δ (ppm) 40.8 (2 F, d, *J* = 201 Hz), 43.5 (2 F, d, *J* = 201 Hz). $^{19}$F NMR ($CDCl_3$, 188 MHz) of *cis*-**3a**: δ (ppm) 41.1 (2 F, d, *J* = 217 Hz), 42.4 (2 F, d, *J* = 217 Hz).
12 Crystal Data for *trans*-**3b**: $C_{22}H_{26}Cl_2F_4O_2Si_2$, MW = 525.52, monoclinic, space group $C_2/c$ (#15), $a$ = 12.4317(7), $b$ = 13.7899(8), $c$ = 14.3406(6) Å, β = 90.077(3)°, $V$ = 2629.9(2) Å$^3$, $Z$ = 4, $D_c$ = 1.327 g·cm$^{-3}$, $R$ = 0.0469, $R_w$ = 0.0603. Crystal Data for *cis*-**3b**: $C_{22}H_{26}Cl_2F_4O_2Si_2$, MW = 525.52, triclinic, space group $P1$ (#2), $a$ = 10.732(1), $b$ = 13.022(2), $c$ = 9.974(1) Å, α = 89.986(5)°, β = 100.734(7)°, γ = 105.270(9)°, $V$ = 1319.42 Å$^3$, $Z$ = 2, $D_c$ = 1.323 g·cm$^{-3}$, $R$ = 0.0569, $R_w$ = 0.0620. These structures were solved and refined with teXsan program package.
13 $^{19}$F NMR ($CDCl_3$, 188 MHz, $C_6F_6$ as an internal standard) of *trans*-**4a**: δ (ppm) 37.9 (2 F, d, *J* = 205 Hz), 39.3 (2 F, d, *J* = 205 Hz). $^{19}$F NMR ($CDCl_3$, 188 MHz) of *cis*-**4a**: δ (ppm) 35.2 (2 F, d, *J* = 218 Hz), 40.2 (2 F, d, *J* = 218 Hz).
14 We have found that ketone **5** was also obtained from 2,2-difluoro enol silyl ethers **2** by oxidative dimerization.