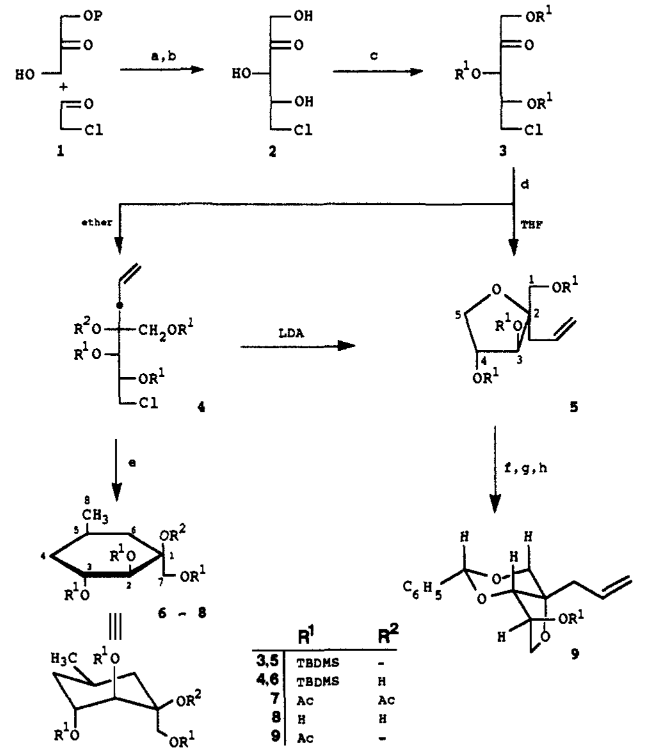
Scheme I[a]



	R^1	R^2
3,5	TBDMS	-
4,6	TBDMS	H
7	Ac	Ac
8	H	H
9	Ac	-

[a] Reagents and conditions: (a) RAMA; (b) acid phosphatase, 50%; (c) TBDMSiOTf/Et_3N, 67%; (d) allylmagnesium bromide, 79%; (e) Bu_3SnH/AIBN, 75%, Δ; (f) TBAF, 96%; (g) $C_6H_5CH(OCH_3)_2$/TsOH; (h) Ac_2O/Pyr/DMAP.

D-threo (3*S*,4*R*) stereochemistry.[8-10] The aldol condensation between DHAP and chloroacetaldehyde **1** catalyzed by RAMA proceeds rapidly[9] and conveniently generates 5-deoxy-5-chloro-*threo*-pentulose (**2**) on a gram scale. Enzymatic dephosphorylation of **2** in situ with acid phosphatase (AP; EC 3.1.3.2) and protection of the hydroxyl groups as *tert*-butyldimethylsilyl ethers leads to **3**. Reaction of **3** with allylmagnesium bromide shows an interesting solvent dependence: in dry tetrahydrofuran (THF), the Grignard addition leads to an easily separable 2.7:1 mixture of *threo*-pentulose-*C*-allylglycoside **5** and the branched chain alditol **4**; in dry diethyl ether, this reaction gives **4** exclusively in 79% yield. Radical ring closure[11] starting from **4** forms the cyclitol **6**.[12]

We assigned the stereocenters in **4** and **6** in several ways. First, we transformed the alditol **4** into the *C*-glycoside **5** by treatment with LDA; this transformation establishes that the stereochemistry generated by the Grignard reaction is the same in **4** and **5**. Since the branched-chain alditol **4** can be converted to the cyclitol derivative **6**, the stereochemistry at the quaternary center in **6** must be the same as that of the anomeric center in **5**. This assignment was supported by NOE studies on **9**,[13] which showed a syn relationship between the hydrogen at C-3 and the allyl moiety at the "anomeric" center. The conformation shown in Scheme I is consistent with $J_{3,4} \sim 0$ Hz for **9**. ^1H NMR and NOE experiments on **6** showed $J_{2,3} = 3.3$ Hz and indicated a trans diaxial arrangement of the silyloxy groups at C-2 and C-3. The axial attachment of the hydrogen at C-5 was assigned on the basis of the large coupling constant of this proton to the proton H-6ax ($J = 12.5$ Hz), and because there was a significant NOE effect (4.2%) between H-5 and the CH_2 protons at C-7. These observations define the conformation of **6** unambiguously.[14] Since RAMA-catalyzed aldol condensations produce vicinal diols having only the 3*S*,4*R* stereochemistry, we were thus able to assign all the stereocenters.

The synthetic route outlined in Scheme I demonstrates an efficient approach to both cyclitols and *C*-glycosides based on catalysis by RAMA. Other aldolases generate other stereochemistries in the original aldol adduct.[15] Investigations directed toward expansion of these strategies are under way.

Supplementary Material Available: Experimental procedures for all compounds, ^1H and ^{13}C NMR data for **2–7**, **8** (^1H), and **9**, high-resolution mass spectra for **3**, **5**, and **6**, and elementary analysis for **3–6** (7 pages). Ordering information is given on any current masthead page.

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(9) Bednarski, M. D.; Simon, E. S.; Bischofberger, N.; Fessner, W.-D.; Kim, M.-J.; Lees, W.; Saito, T.; Waldmann, H.; Whitesides, G. M. *J. Am. Chem. Soc.* **1989**, *111*, 627–635.

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(14) Compound **6** has an unusual conformation; it contains three (rather than two) axial substituents. This assignment agrees with an analogous one by Paulsen and co-workers.[3] The same conformation is observed for **7** and **8**.

(15) Ozaki, A.; Toone, E. J.; von der Osten, C. H.; Sinskey, A. J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1990**, *112*, 4970–4971.

Thermal Rearrangement of Fluorinated Dioxoles[1]

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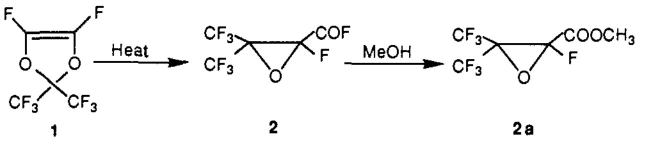
Du Pont has recently developed Teflon-AF,[2] a family of amorphous copolymers of 2,2-bis(trifluoromethyl)-4,5-difluoro-1,3-dioxole[3] (**1**) and tetrafluoroethylene. These polymers are similar to poly(tetrafluoroethylene) in chemical and thermal stability but have superior physical properties and optical clarity and lower dielectric constants. In addition, they are soluble in selected fluorinated solvents, thus allowing the preparation of thin cast films.[4] The dioxole monomer **1** and related dioxoles undergo a number of surprising reactions. We report the unusual thermal rearrangement of these dioxoles to substituted acyl epoxides.



1 **2** **2a**

Perfluoro-2,3-epoxy-3-methylbutyryl fluoride (**2**) was isolated in greater than 85% yield when **1** was heated at 250 °C over glass beads in a flow system. The acyl fluoride **2** was characterized by infrared absorption bands at 1887 (C=O) and 1462 cm^{-1} (oxirane) and by its ^{19}F NMR spectrum (Table I). Treatment of **2** with methanol yielded methyl perfluoro-2,3-epoxy-3-methylbutyrate (**2a**), characterized by infrared absorption bands at 1792 (C=O) and 1466 cm^{-1} (oxirane) and also by its ^{19}F NMR spectrum (Table I).

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(1) The Chemistry of Fluorinated Dioxoles and Dioxolanes. Part I.

(2) Trademark of E. I. du Pont de Nemours and Company.

(3) Resnick, P. R. U.S. Pat. 3,865,845, 1975; U.S. Pat. 3,978,030, 1976.

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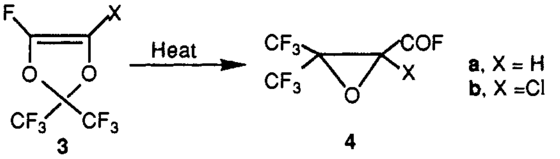
0002-7863/90/1512-9671$02.50/0

Table I. Yield and ^{19}F Nuclear Magnetic Resonance Data of Epoxy Acid Fluorides[a]

compd	yield,[b] %	bp, °C	^{19}F NMR[c]
2	86	35	−68.9 (3 F), −71.1 (3 F), −148.6 (1 F), +28.7 (1 F)
2a	72	91	−68.6 (3 F), −71.3 (3 F), −145.8 (1 F); 3.80[d]
4a	72	73	−69.8 (3 F), −74.5 (3 F), +37.8 (1 F); 4.18[d]
4b	88	63	−67.6 (3 F), −71.2 (3 F), +25.0 (1 F)
5c	90	45	−68.0 (3 F), −83.8 (3 F), −118.9 (2 F), −149.7 (1 F), +27.2 (1 F) (major isomer); −70.3 (3 F), −84.0 (3 F), −117.0 (2 F), 147.5 (1 F), +27.8 (1 F) (minor isomer)
5d	90	55	−114.0 (4 F), −82.0 (6 F), −145.7 (1 F), +25.8 (1 F)
12	100	45	−66.7 (3 F), −68.0 (3 F), −71.3 (3 F), +37.7 (1 F)

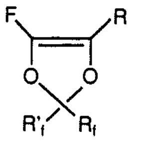
[a] All new compounds have been fully characterized by spectral means and elemental compositions determined by combustion analysis or high-resolution mass spectrometry. [b] Isolated yields. [c] Neat, $CFCl_3$ as reference. [d] ^{1}H NMR, tetramethylsilane as reference.

Thermal rearrangement of dioxoles **3a** and **3b**[5] resulted in the formation of acyl fluorides **4a** and **4b**, respectively, as the sole products. No aldehyde or acid chloride was detected.



3 **4**

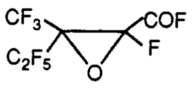
The rate of rearrangement increased as the size of the substituents at the 2-position of the 1,3-dioxole ring increased. Rearrangement of **1**, **5a**, and **5b**[6] at 100 °C were followed chromatographically.[7] After 0.5 h, dioxole **1** was unchanged, while 11–12 mol % of **5a** and 28–29 mol % of **5b** had rearranged to the corresponding epoxides, **5c**, two isomers in a ratio of 3.2:1.0, and **5d**, respectively. The difference in rate may be due to increased steric congestion in the series of **1**, **5a**, and **5b** as the electronic effects of trifluoromethyl and pentafluoroethyl groups are quite similar.[8]



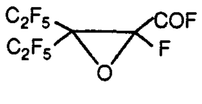
5a, R = F, R$_f$ = CF_3, R'$_f$ = C_2F_5,

5b, R = F, R$_f$ = C_2F_5, R'$_f$ = C_2F_5,

6, R = CF_3, R$_f$ = CF_3, R'$_f$ = CF_3



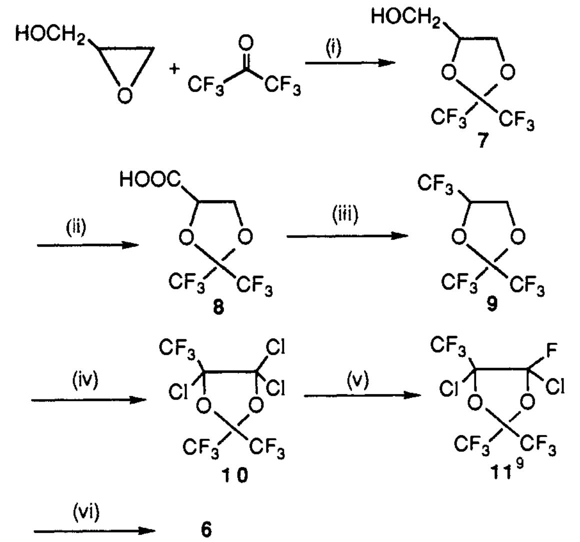
5c



5d

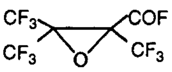
Dioxole **6** was synthesized in six steps from hexafluoroacetone as shown in Scheme I. Heating **6** at 200 °C for 15 min followed by heating at 240 °C for 30 min resulted in almost quantitative conversion to the acid fluoride **12**, characterized by its ^{19}F NMR spectrum, (Table I). None of the isomeric ketone, **13**, was observed.

Scheme I[a]

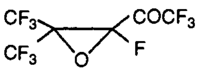


[a] Reagents and conditions: (i) n-Bu_4NBr, 0.15%, H_2O, 0.15%, 125 °C, 5 h, 93%; (ii) $KMnO_4/Na_2CO_3$/water, 25 °C, 16 h, 82%; (iii) SF_4/HF, 85 °C, 6 h, 58%; (iv) Cl_2, neat, 120 °C, 87%; (v) $SbF_3/SbCl_5$, neat, 100–110 °C, 8 h, 70%; (vi) $LiAlH_4/TiCl_4$/THF, 25–35 °C, 1–2 h, 88%.

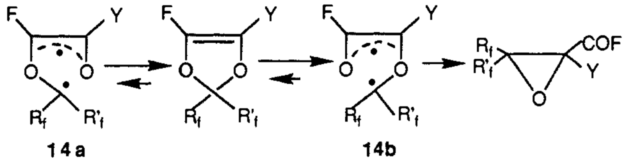
One plausible mechanism for this rearrangement involves the formation of a biradical intermediate followed by ring closure to give the epoxide product. The increased stability of **14b** over **14a** is apparently large enough to result in the high regioselective formation of acyl fluorides. An analogous rearrangement of 2,2-bis(trifluoromethyl)-1,3-dioxole was not observed.



12



13



14a **14b**

Y = F, H, Cl, Br, CF_3

In a typical experiment, a 1-ft glass tube with a 1-in. diameter was filled with glass beads and heated to 280 °C, and dioxole **1** (17.4 g, 71 mmol) was added at a rate of 0.48 mL/min. The effluent was trapped at −78 °C and distilled to give epoxide **2** (15.0 g, 86% yield) as a clear, colorless liquid, boiling at 35 °C.

In conclusion, we have discovered an unusual thermal rearrangement reaction that involves the conversion of a fluorinated dioxole to an epoxy acid fluoride. These epoxy-containing acyl compounds are highly useful in further synthetic applications.

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(6) Hung, M.-H. U.S. Pat. 4,908,461, 1990.

(7) Six feet × 1/4 in. 20% OV-210 on Chromosorb P (AW-DMCS) at 100 °C.

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(9) Compound **11** was obtained as an isomeric mixture with the mole ratio Z/E = 7:1. This isomeric mixture was used directly for next step synthesis. For compound (Z)-**11**: ^{19}F NMR (neat, $CFCl_3$) −54.3 (m, 1 F). For (E)-**11**: −40.7 (m, 1 F).

A Silicon-Directed Aldol Condensation. Synthesis of Enantiomerically Pure Anti Aldols

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A new type of aldol addition reaction involving the direct condensation of O-silyl ketene N,O-acetals with aldehydes is re-