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Studies on Organic Fluorine Compounds. XL.[1] Ring-Opening Reactions of *gem*-Difluorocyclopropyl Carbinols

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Three types of ring-opening reactions of *gem*-difluorocyclopropyl carbinols are described; 1) reaction with hydrobromic acid, 2) reaction with acetic acid in the presence of *p*-toluenesulfonic acid, and 3) rearrangement through a mesylate. Ring-opening reactions of **1a**, **d**, **e** having an electron-donating substituent at C_3 were found to give β,β-difluorohomoallyl derivatives derived from C_1–C_3 bond scission. On the other hand, reactions of **1b**, **c** having hydrogen atoms or a methyl group at C_3 were not selective or afforded α,α-difluorohomoallyl derivatives (C_1–C_2 bond scission) preferentially.

Keywords——*gem*-difluorocyclopropyl carbinol; Julia-Johnson synthesis; ring-opening reaction; β,β-difluorohomoallyl derivative; α,α-difluorohomoallyl derivative

The ring-opening reactions of cyclopropanes provide efficient methods for homologation of carbon chains and for ring-enlargement in organic syntheses.[2] Dihalocyclopropane derivatives, readily obtained by addition of dihalocarbene to olefinic compounds undergo a wide variety of reactions, in which a halogen atom behaves as either a good leaving group or a potential oxidant against organometallic reagents. In contrast to many reported examples of the reactions of dichloro- and dibromocyclopropanes, only a limited number of reactions of the difluoro analogues have been reported.[3]

In the course of our studies to explore synthetic reactions utilizing difluorocyclopropane derivatives,[4] we have investigated the ring-opening reactions of *gem*-difluorocyclopropyl carbinols. Rearrangement of a cyclopropyl carbinol system is an especially useful reaction for construction of a homoallyl bromide unit in isoprenoid syntheses (Julia-Johnson synthesis).[5] Similar types of ring-opening of difluorocyclopropyl carbinols would be expected to lead to new methodology for the syntheses of fluorinated biologically active compounds.[6] In the ring-opening reaction of difluorocyclopropyl carbinol (**1**) two different types of ring-cleavage, C_1–C_3 bond cleavage (a nucleophile attacks C_3) and C_1–C_2 bond cleavage (a nucleophile attacks C_2), may be possible through an intermediary cyclopropyl carbinyl cation (Chart 1).

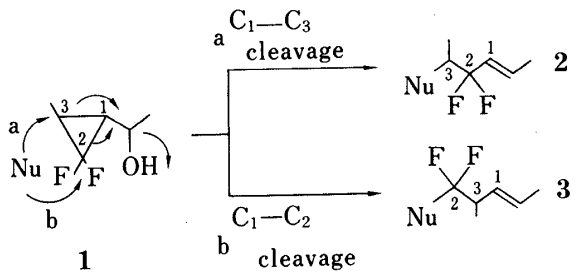


Chart 1

In this paper we will desribe the following reactions; 1) reaction with hydrobromic acid, 2) reaction with acetic acid in the presence of *p*-toluenesulfonic acid, and 3) rearrangement through a mesylate. The reaction course was found to be strongly influenced by the nature of

the substituent(s) at the C_3 position, and this can be explained in terms of the stability of the intermediary carbonium ion.

Results and Discussion

gem-Difluorocyclopropyl Carbinols[7)]

Difluorocyclopropyl carbinols (**1a—d**) were easily obtained by the addition of difluorocarbene generated by pyrolysis (diglyme reflux) of sodium chlorodifluoroacetate ($ClCF_2COONa$) to allyl acetates (**4a—d**) followed by alkaline hydrolysis (KOH, methanol–THF) as shown in Chart 2. In the difluorocyclopropanation of **4d** (R_1 = Me, R_2 = Me, R_3 =

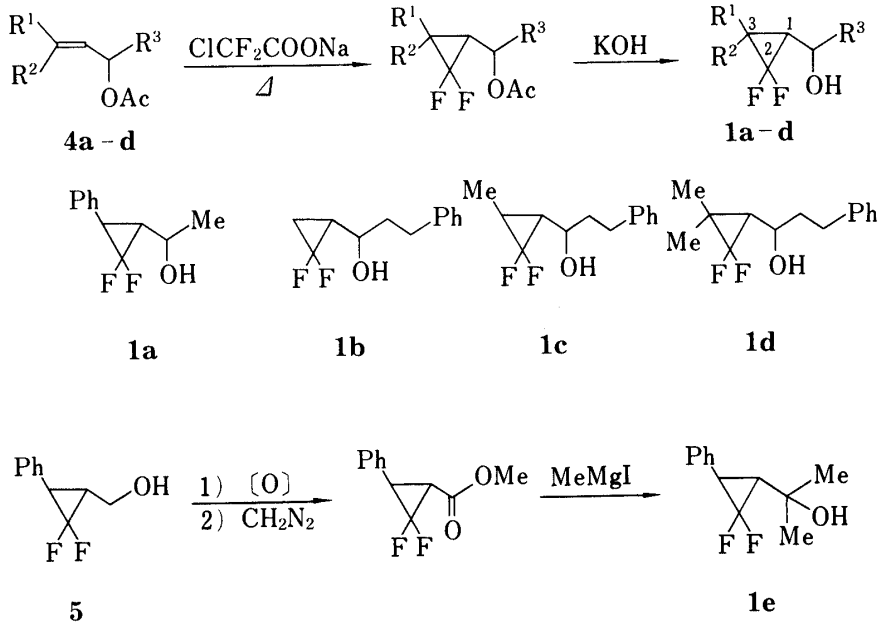


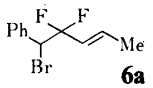
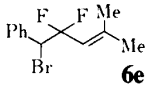
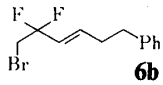
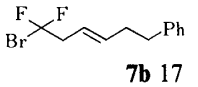
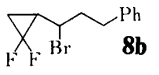
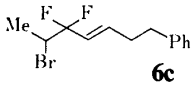
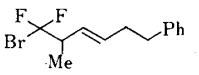
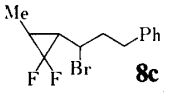
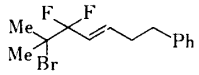
Chart 2

$PhCH_2CH_2$–) the reaction temperature must be controlled at 150 °C, because at a higher temperature the solvolysis of **4d** occurred to form olefinic compounds, which further reacted with difluorocarbene. A tertiary carbinol (**1e**) was synthesized from the cyclopropyl carbinol (**5**), which was obtained by the reaction of cinnamyl acetate with difluorocarbene. The cyclopropane (**5**) was oxidized with Jones reagent to the carboxylic acid and esterified with diazomethane, followed by Grignard reaction (MeMgI) to afford the tertiary carbinol (**1e**). The stereochemical relationships between substituents at C_1 and C_3 in **1a**, **c**, **e** were *trans* due to the stereospecific *cis*-addition of difluorocarbene[8)] to the *trans*-allyl acetates, and **1a—d** were diastereoisomeric mixtures as reported in the previous paper.[4e)]

Reactions of *gem*-Difluorocyclopropyl Carbinols (1) with Hydrobromid Acid

The reaction of the difluorocyclopropyl carbinol (**1a**) possessing a phenyl substituent at C_3 with 48% hydrobromic acid at 55 °C for 3 h gave the β,β-difluorohomoallyl bromide (**6a**) in 39% yield along with recovery of the starting cyclopropane (18%). Similarly, the tertiary carbinol (**1e**) on treatment with hydrobromic acid (in methylene chloride, reflux, 4 h) afforded **6e** in 39% yield (**1e** was recovered in 31% yield). These reactions show the selectivity of bond cleavage in the case of difluorocyclopropyl carbinols possessing a phenyl substituent at C_3 (C_1–C_3 bond cleavage). On the other hand, in the cases of **1b** and **1c** the ring-opening reactions were not selective; these reactions gave mixtures of β,β-difluorohomoallyl bromides (**6b** and **6c**) and α,α-difluorohomoallyl bromides (**7b** and **7c**) derived from C_1–C_2 bond cleavage in

TABLE I. Reactions of *gem*-Difluorocyclopropyl Carbinols (**1**) with Hydrobromic Acid

Difluorocyclopropyl carbinol (**1**)	Conditions			Products, Yield (%) [Yield (%)][a]	
	Solvent	Temp.	Time		
1a	—	55°C	3 h	 **6a**	39 [48]
1e	CH_2Cl_2	Reflux	4 h	 **6e**	39 [57]
1b	CCl_4	Reflux	5 h	 **6b**	6.4 [6.7]
				 **7b**	17 [26]
				 **8b**	11 [17]
1c	CCl_4	Reflux	3 h	 **6c**	15[b] [19]
				 **7c**	12 [15]
				 **8c**	19[b] [23]
1d	*n*-Hexane	Reflux	10 h	 **6d**	[20]

a) Based on the conversion of **1**.
b) Calculated from the relative intensities of ^{19}F-NMR signals of a mixture of **6c** and **8c**.

ratios of 21 : 79 and 56 : 44, respectively. Since the bromides (**8b** and **8c**) were also obtained, the ring-opening reactions of **1b** and **1c** seem to be slower than those of **1a** and **1e**. In the reaction of **1d** possessing *gem*-dimethyl substituents at C_3, the ring-opening product was β,β-difluorohomoallyl bromide (**6d**), and no minor product derived from C_2–C_3 bond cleavage was isolated. These results are shown in Table I.

The coupling constants of olefinic protons of homoallyl bromides (15—16 Hz for both **6** and **7**) in the NMR spectra indicate the *trans*-stereoselectivity of these reactions, and the corresponding *cis*-isomers were not detected at all. In the reactions of difluorocyclopropyl carbinols possessing a phenyl or dimethyl group at C_3, in which the C_3-carbonium ion is stabilized by substituent(s), C_1–C_3 bond cleavage occurred selectively. On the other hand in the case of a methyl group or hydrogen atom at C_3, a decrease of the stability of the C_3-carbonium ion resulted in an increase in the C_1–C_2 bond cleavage.

Reactions with Acetic Acid in the Presence of *p*-Toluenesulfonic Acid

When a solution of tertiary carbinol (**1e**) and 0.2 eq. of *p*-toluenesulfonic acid (*p*-TsOH) in acetic acid was heated at 70 °C for 7.5 h, the expected **9e** (C_1–C_3 bond cleavage) was obtained in 71% yield along with a similar product (**10e**) attacked by *p*-TsOH (13%). In this reaction, the enone derivative (**11e**) was also isolated (11%). Compared with that of **1e**, the

reaction of the secondary carbinol (**1a**) proceeded relatively slowly to afford the corresponding ring-opening products in moderate yield. The ratio of the products (**9** to **11**) depends on the reaction conditions; under vigorous conditions the solvolytic cleavage of the allylic carbon-fluorine bond to form **11** increased. However, in the reactions of **1b** and **1c** no ring-opening products were obtained and the result was the formation of acetates of **1b** and **1c** with recovery of the starting carbinols under the same conditions (70—80 °C, 7 h). As indicated above the acetolytic ring-opening of **1** in the presence of *p*-TsOH was found to proceed in the case of the carbinol having a phenyl substituent at C_3 *via* selective cleavage of the C_1–C_3 bond (Chart 3).

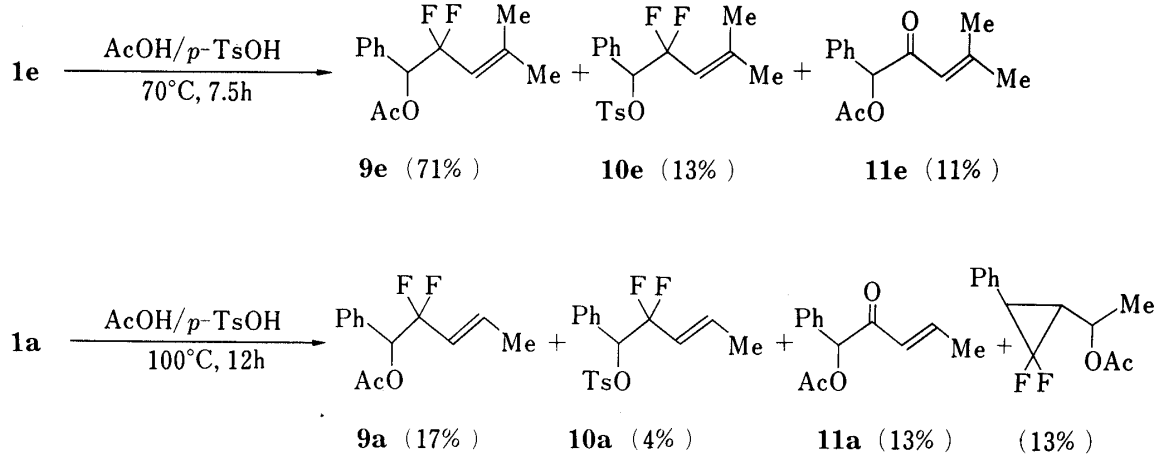


Chart 3

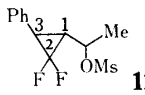
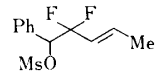
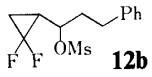
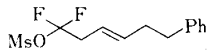
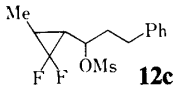
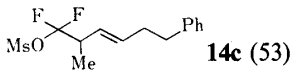
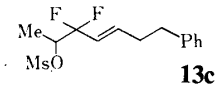
Rearrangements of Mesylates of Difluorocyclopropyl Carbinols

Similar regioselectivity of ring-opening reactions of difluorocyclopropyl carbinols was clearly found in rearrangements of mesylates of **1** as shown in Table II. For example, mesylate (**12a**) which was obtained by treatment of **1a** with methanesulfonyl chloride and triethylamine in methylene chloride, selectively afforded **13a** derived from C_1–C_3 bond cleavage in 86% yield under reflux in *n*-hexane for 2 h. This reaction also took place easily at room temperature overnight without solvent. Since the chemical shifts of **12** and **13** in the ^{19}F-NMR spectrum were quite different, the rearrangement of cyclopropanes can be readily monitored by ^{19}F-NMR analysis of the reaction mixture.

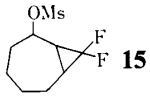
In contrast, in the case of **12b**, which forms a more unstable carbonium ion on C_3 than that of **12a**, the selectivity of ring-opening altered and **14b** (C_1–C_2 bond cleavage) was obtained selectively in 71% yield. Cyclopropane (**12c**) in which the carbonium ion on C_3 was stabilized by a single methyl group gave a mixture of **14c** (53%) and **13c** (19%) in preference to C_1–C_2 bond cleavage. The ring-opening rearrangement of the bicyclo[5,1,0]octanol derivative (**15**) did not proceed under forcing conditions. In this derivative the trans anti-parallel arrangement of the breaking bonds (C–OMs and C_1–C_2 or C_1–C_3) is difficult because of the rigid bicyclic structure.

In conclusion, it appears that the regioselectivity of the ring-opening reactions of difluorocyclopropyl carbinols observed in the present study is highly dependent on the substituent on the cyclopropane ring (C_3) and that the stereoselectivity of the C–C double bond of the products is exclusive trans, as in the Julia-Johnson synthesis. Since these reactions proceed through cationic intermediate(s), the electronic factor which determines the reaction course of ring-opening is the relative stability of the carbonium ions on C_3 and C_2 bearing fluorine atoms, namely, the effect of the substituent at C_3. In the cases of a difluorocyclopropyl carbinol possessing an electron-donating substituent at C_3 (*e.g.* phenyl, *gem*-dimeth-

TABLE II. Rearrangements of Mesylates of Difluorocyclopropyl Carbinols (**12**)

Mesylate	Conditions			Products (Yield, %)
	Solvent	Temp.	Time	
 **12a**	*n*-Hexane	Reflux	2 h	 **13a** (86)
	none	R. temp.	Overnight	
 **12b**	*n*-Hexane	Reflux	18 h	 **14b** (71)[a]
 **12c**	*n*-Hexane	Reflux	3.5 h	 **14c** (53)
				 **13c** (19)

a) The yield of **14b** is based on the carbinol (**1b**).

 **15**

yl) the bond (C_1–C_3) opposite to the difluoromethylene group is cleaved to afford β,β-difluorohomoallyl derivatives (**2**), whereas in the cases of the difluorocyclopropyl carbinol possessing a methyl group or hydrogen atom at C_3 ring-opening is not selective or occurs on an adjacent bond (C_1–C_2) to give α,α-difluorohomoallyl derivatives (**3**) preferentially.

Experimental

Melting points were taken on a hot-stage microscope (Yanagimoto) and are uncorrected. Infrared (IR) spectra were recorded using a Jasco IRA-1 spectrophotometer. Proton magnetic resonance (^{1}H-NMR) spectra were recorded on a Varian EM360L, EM390L or JEOL JNH-PS-100 spectrometer. Chemical shifts are reported in parts per million (ppm) on the δ scale relative to tetramethylsilane internal standard. Fluorine magnetic resonance (^{19}F-NMR) spectra were recorded on a Varian EM360L spectrometer. Chemical shifts are reported in parts per million relative to benzotrifluoride internal standard, and a plus sign indicates high field. Mass spectra (MS) were recorded on a Hitachi RMU-7L instrument. *p*-TsOH refers to *p*-toluenesulfonic acid, and MsCl to methanesulfonyl chloride.

Reaction of 2,2-Difluoro-1-(1-hydroxyethyl)-3-phenylcyclopropane (1a) with Hydrobromic Acid——A mixture of **1a** (198 mg, 1 mmol) and 48% HBr (0.4 ml) was stirred for 3 h at 55 °C. The reaction mixture was neutralized with $NaHCO_3$ aq., extracted with ether and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the residue was chromatographed on silica gel to give (*E*)-1-bromo-2,2-difluoro-1-phenylpent-3-ene (**6a**) (100.9 mg, 39%) and recovered **1a** (18%). **6a**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3040—2830, 1670, 1495, 1445. ^{1}H-NMR ($CDCl_3$) δ: 1.7 (3H, m, CH_3), 5.0 (1H, t, J=12 Hz, CH), 5.53 (1H, dt, J=15 and 12 Hz, CF_2CH=), 6.1 (1H, dqt, J=15, 6 and 1.5 Hz, =CH), 7.2—7.63 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +34.5 (dd, J=12 and 12 Hz). MS *m/e*: 262 and 260 (M^+), 181, 171, 169, 161, 146, 91. High-resolution MS Calcd for $C_{11}H_{11}BrF_2$: 260.0011. Found: 259.9981.

Reaction of 2,2-Difluoro-1-(1-hydroxy-1-methylethyl)-3-phenyl-cyclopropane (1e) with Hydrobromic Acid——A solution of **1e** (165 mg, 0.78 mmol) and 48% HBr (1.0 ml) in CH_2Cl_2 (3 ml) was refluxed for 4 h. After extractive work-up as described above, the extract was chromatographed on silica gel to give **6e** (83.1 mg, 39%) and recovered **1e** (31%). **6e**, IR ν_{max}^{NaCl} cm^{-1}: 3040—2840, 1670. ^{1}H-NMR ($CDCl_3$) δ: 1.73 (6H, m, $CH_3\times2$), 5.07 (1H, dd, J=10 and 13 Hz, CH), 5.33 (1H, tm, J=15 Hz, CH=), 7.23—7.67 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +28.7 (m), +29.5 (m). MS *m/e*: 276 and 274 (M^+), 195, 175, 171, 169, 160, 140, 105. High-resolution MS Calcd for $C_{12}H_{13}BrF_2$: 195.0984. Found: 195.0966.

Reaction of 2,2-Difluoro-1-(1-hydroxy-3-phenylpropyl)cyclopropane (1b) with Hydrobromic Acid——A solution of **1b** (162.3 mg, 0.77 mmol) and 48% HBr (0.88 ml) in CCl_4 (3.6 ml) was refluxed for 5 h. After extractive work-up,

the extract was chromatographed on silica gel to give (*E*)-1-bromo-2,2-difluoro-6-phenylhex-3-ene (**6b**) (9.3 mg, 4.4%), (*E*)-1-bromo-1,1-difluoro-6-phenylhex-3-ene (**7b**) (36.2 mg, 17%), 2,2-difluoro-1-(1-bromo-3-phenylpropyl)cyclopropane (**8b**) (23.5 mg, 11%) and recovered **1b** (34%). **6b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3010, 2920, 1670, 1260, 1020, 700. ^{1}H-NMR (CCl_4) δ: 2.28—2.88 (4H, m, CH_2CH_2), 3.45 (2H, t, J=12 Hz, $BrCH_2$), 5.6 (1H, dt, J=16 and 12 Hz, CF_2CH=), 6.2 (1H, dt, J=16 and 7 Hz, =CH), 7.00—7.37 (5H, m, aromatic). ^{19}F-NMR (CCl_4) δ: +33.7 (dt, J=12 and 12 Hz). MS *m/e*: 276 and 274 (M^+), 205, 91. High-resolution MS Calcd for $C_{12}H_{13}BrF_2$: 274.0167. Found: 274.0158. **7b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3060—2840, 1600, 1500, 1450. ^{1}H-NMR ($CDCl_3$) δ: 2.2—2.83 (4H, m, CH_2CH_2), 3.03 (2H, dt, J=6 and 13.5 Hz, CBr_2FCH_2), 5.47 (1H, dt, J=15 and 7 Hz, CH=), 5.8 (1H, dt, J=15 and 6 Hz, =CH), 7.03—7.47 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: −18.3 (t, J=13.5 Hz). MS *m/e*: 276 and 274 (M^+), 195, 175, 145, 131, 91. High-resolution MS Calcd for $C_{12}H_{13}BrF_2$: 274.0168. Found: 274.0164. **8b**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3080—2840, 1600, 1500, 1465. ^{1}H-NMR ($CDCl_3$) δ: 1.03—2.47 (5H, m, cyclopropane and CH_2), 2.73—3.03 (2H, m, $PhCH_2$), 3.47—3.9 (1H, m, BrCH), 7.17—7.47 (5H, s, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +60.7 (d, J=158 Hz), +79.3 (d, J=158 Hz). MS *m/e*: 276 and 274 (M^+), 195, 91. High-resolution MS Calcd for $C_{12}H_{13}BrF_2$: 274.0168. Found: 274.0194.

Reaction of 2,2-Difluoro-1-(1-hydroxy-3-phenylpropyl)-3-methylcyclopropane (1c) with Hydrobromic Acid——A solution of **1c** (132.59 mg, 0.59 mmol) and 48% HBr (0.6 ml) in CCl_4 (2.5 ml) was refluxed for 3 h. After extractive work-up, the extract was chromatographed on silica gel to give a mixture of **6c** and **8c** (58 mg, 34%, **6c**:**8c**=1:1.3 by NMR), **7c** (19.9 mg, 12%) and recovered **1c** (19%). Further purification of a mixture of **6c** and **8c** by high performance liquid chromatography (HPLC) gave analytically pure samples. **6c**, bp 78—88 °C/4 mmHg (bulb to blub distillation). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3040, 2940, 1680, 1500, 1450. ^{1}H-NMR ($CDCl_3$) δ: 1.63 (3H, d, J=7 Hz, CH_3), 2.27—2.92 (4H, m, CH_2CH_2), 4.0 (1H, m, CH), 5.65 (1H, dt, J=15 and 12 Hz, CF_2CH=), 6.22 (1H, dt, J=15 and 6 Hz, =CH), 7.03—7.4 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +37.7 (m), +38.7 (m). MS *m/e*: 290 and 288 (M^+), 91. *Anal.* Calcd for $C_{13}H_{15}BrF_2$: C, 53.99; H, 5.23; Br, 27.64; F, 13.14. Found: C, 54.17; H, 5.38; Br, 27.54; F, 12.97. **8c** (diastereoisomeric mixture), ^{1}H-NMR ($CDCl_3$) δ: 1.2 (3H, m, CH_3), 1.1—1.8 (2H, m, cyclopropane), 2.03—2.4 (2H, m, CH_2), 2.67—2.93 (2H, m, CH_2Ph), 3.7 (1H, m, CH), 7.1—7.33 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +73 (m), +74.3 (m), +78.3 (m). MS *m/e*: 290 and 288 (M^+), 209, 189, 131, 129, 117, 105, 91. **7c**, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3060—2840, 1500, 1450. ^{1}H-NMR ($CDCl_3$) δ: 1.2 (3H, d, J=7.5 Hz, CH_3), 2.12—3.05 (5H, m, CH_2CH_2 and CH), 5.37 (1H, dd, J=6 and 15 Hz, CH=), 5.7 (1H, dt, J=15 and 6 Hz, =CH), 6.83—7.6 (5H, s, aromatic), ^{19}F-NMR ($CDCl_3$) δ: −14.0 (d, J=9.4 Hz). MS *m/e*: 290 and 288 (M^+), 209, 189, 169, 131, 91. High-resolution MS Calcd for $C_{13}H_{15}BrF_2$: 288.0324. Found: 288.0324.

Reaction of 2,2-Difluoro-1-(1-hydroxy-3-phenylpropyl)-3,3-dimethylcyclopropane (1d) with Hydrobromic Acid——A solution of **1d** (65.1 mg, 0.27 mmol) and 48% HBr (0.6 ml) in *n*-hexane (2 ml) was refluxed for 10 h. After extractive work-up, the extract was chromatographed on silica gel to give **6d** (16.48 mg, 20%), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3060—2860, 1670. ^{1}H-NMR ($CDCl_3$) δ: 1.73 (6H, s, $CH_3\times2$), 2.3—2.97 (4H, m, CH_2CH_2), 5.83 (1H, dt, J=15 and 12 Hz, CF_2CH=), 6.27 (1H, dt, J=15 and 7.5 Hz, =CH), 7.07—7.43 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +41.7 (d, J=12 Hz). MS *m/e*: 304 and 302 (M^+), 284, 282, 223, 203, 183, 181, 161, 141. High-resolution MS Calcd for $C_{14}H_{17}BrF_2$: 302.0481. Found: 302.0483.

Reaction of 1e with Acetic Acid in the Presence of *p*-TsOH——A mixture of **1e** (104 mg, 0.49 mmol), acetic acid (230 mg), acetic anhydride (80 mg) and *p*-TsOH (20.2 mg) was stirred for 7.5 h at 70 °C. The reaction mixture was neutralized with $NaHCO_3$ aq. and extracted with ether. The organic layer was washed with brine, and then dried over $MgSO_4$. The solvent was removed *in vacuo*, and the residue was chromatographed on silica gel to give 1-acetoxy-2,2-difluoro-4-methyl-1-phenylpent-3-ene (**9e**) (89 mg, 71%), 2,2-difluoro-4-methyl-1-phenyl-1-tosyloxypent-3-ene (**10e**) (23 mg, 13%) and 1-acetoxy-4-methyl-2-oxo-1-phenylpent-3-ene (**11e**) (12 mg, 11%). **9e** bp 92—96 °C/3 mmHg (bulb to bulb distillation). IR ν_{max}^{NaCl} cm^{-1}: 3060, 3040, 2980, 2950, 1755, 1680, 1500, 1460. ^{1}H-NMR ($CDCl_3$) δ: 1.68 (6H, m, $CH_3\times2$), 5.17 (1H, tm, J=14 Hz, CH=), 5.98 (1H, t, J=11 Hz, CH), 7.17—7.55 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +36.8 (dd, J=11 and 14 Hz). MS *m/e*: 149, 105, 77. *Anal.* Calcd for $C_{14}H_{16}F_2O_2$: C, 66.13; H, 6.34; F, 14.94. Found: C, 66.26; H, 6.43; F, 14.81. **10e**, mp 83—83.5 °C (from cyclohexane), IR ν_{max}^{KBr} cm^{-1}: 3080—2820, 1680, 1500, 1460. ^{1}H-NMR ($CDCl_3$) δ: 1.67 (6H, m, $CH_3\times2$), 2.37 (3H, s, CH_3), 5.2 (1H, t, J=16 Hz, CH=), 5.5 (1H, t, J=10 Hz, CH), 7.00—7.77 (10H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +36.3 (m). MS *m/e*: 261, 155, 105. *Anal.* Calcd for $C_{19}H_{20}F_2O_3S$: C, 62.29; H, 5.50; F, 10.37; S, 8.73. Found: C, 61.99; H, 5.49; F, 10.15; S, 8.66. **11e**, IR ν_{max}^{NaCl} cm^{-1}: 3070, 3040, 2980, 2940, 2920, 1760—1740, 1700, 1620, 1500, 1450, 1380. ^{1}H-NMR ($CDCl_3$) δ: 1.83 (3H, s, CH_3CO), 2.17 (6H, br s, $CH_3\times2$), 5.97 (1H, s, CH), 6.03 (1H, m, CH=), 7.37 (5H, br s, aromatic). MS *m/e*: 232 (M^+), 195, 172, 149, 107. High-resolution MS Calcd for $C_{14}H_{16}O_3$: 232.1098. Found: 232.1096.

Reaction of 1a with Acetic Acid in the Presence of *p*-TsOH——A solution of **1a** (272.4 mg, 1.38 mmol) and *p*-TsOH (55.9 mg) in acetic acid (3 ml) was stirred for 12 h at 100 °C. After extractive work-up as described above, the extract was chromatographed on silica gel to give **9a** (56.8 mg, 17%), **10a** (18.96 mg, 4%), **11a** (40.4 mg, 13%) and the acetate of **1a** (13%). **9a**, bp 83—101 °C/2 mmHg (bulb to bulb distillation). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3040—2840, 1750, 1670. ^{1}H-NMR ($CDCl_3$) δ: 1.75 (3H, m, CH_3), 2.15 (3H, s, CH_3CO), 5.50 (1H, dtm, J=14 and 14 Hz, CF_2CH=), 5.80—6.24 (1H, m, =CH), 5.97 (1H, t, J=10 Hz, CH), 7.38 (5H, br s, aromatic), ^{19}F-NMR ($CDCl_3$) δ: +42.0 (m), +42.5 (m). MS *m/e*: 149, 107. *Anal.* Calcd for $C_{13}H_{14}F_2O_2$: C, 64.99; H, 5.80; F, 15.80. Found: C, 64.86; H, 5.90; F, 15.66. **10a**, mp 90—91.5 °C (from cyclohexane), IR ν_{max}^{KBr} cm^{-1}: 3080, 3040, 2960—2920, 1680, 1600, 1500, 1380, 1350, 1180.

^{1}H-NMR (CCl_4) δ: 1.75 (3H, m, CH_3), 2.37 (3H, s, CH_3), 5.2—5.63 (1H, m, $CF_2CH=$), 5.4 (1H, dd, J=9 and 11 Hz, CH), 5.97 (1H, dqt, J=16, 6 and 2 Hz, =CH), 7.0—7.67 (10H, m, aromatic). ^{19}F-NMR (CCl_4) δ: +40.8 (m), +42.7 (m). MS *m/e*: 261, 155, 91. *Anal.* Calcd for $C_{18}H_{18}F_2O_3S$: C, 61.36; H, 5.15; F, 10.79; S, 9.08. Found: C, 61.62; H, 5.17, F, 10.60; S, 8.94. **11a**, bp 107—118 °C/3 mmHg (bulb to bulb distillation). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3050, 2830, 1745—1740, 1705—1690, 1630. ^{1}H-NMR ($CDCl_3$) δ: 1.83 (3H, dd, J=1 and 7 Hz, CH_3), 2.2 (3H, s, CH_3CO), 6.17 (1H, s, CH), 6.23 (1H, dd, J=1 and 15 Hz, COCH=), 7.03 (1H, dq, J=15 and 7 Hz, =CH), 7.43 (5H, s, aromatic). MS *m/e*: 219 (M^++1), 190, 176, 149, 107. *Anal.* Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.34; H, 6.50.

Rearrangement of Mesylate (12a)——To a solution of **1a** (150 mg, 0.76 mmol) and triethylamine (194 mg, 1.9 mmol) in CH_2Cl_2 (6 ml) was added a solution of MsCl (191 mg, 1.6 mmol) in CH_2Cl_2 (2 ml) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C, and then at room temperature for 30 min. The reaction mixture was diluted with dil. HCl and extracted with ether. The organic layer was washed with $NaHCO_3$ aq., brine, and then dried over $MgSO_4$. Removal of the solvent *in vacuo* gave the mesylate (**12a**) in quantitative yield. A solution of **12a** (46.6 mg, 0.17 mmol) in *n*-hexane (4 ml) was refluxed for 2 h. After the removal of the solvent, the residue was chromatographed on silica gel to give (*E*)-2,2-difluoro-1-mesyloxy-1-phenylpent-3-ene (**13a**) (40.3 mg, 86%), IR ν_{max}^{NaCl} cm^{-1}: 3040, 2840, 1675, 1500, 1380—1340, 1180. ^{1}H-NMR ($CDCl_3$) δ: 1.63—1.87 (3H, m, CH_3), 2.87 (3H, s, CH_3), 5.60 (1H, dt, J=12 and 15 Hz, $CF_2CH=$), 5.67 (1H, t, J=9 Hz, CH), 6.20 (1H, dqt, J=15, 6 and 2 Hz, =CH), 7.5 (5H, s, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +41.7 (m). MS *m/e*: 276 (M^+), 185, 181, 161, 107, 105, 91. High-resolution MS Calcd for $C_{12}H_{14}F_2O_3S$: 276.0631. Found: 276.0638.

Rearrangement of Mesylate (12b)——The reaction of **1b** (198.5 mg, 0.94 mmol) with MsCl (216 mg, 1.9 mmol) and triethylamine (191 mg, 1.89 mmol) in CH_2Cl_2 (5 ml) gave **12b**. A solution of **12b** in *n*-hexane (10 ml) was refluxed for 18 h. After the removal of the solvent the residue was chromatographed on silica gel to give (*E*)-1,1-difluoro-1-mesyloxy-6-phenylpent-3-ene (**14b**) (193.2 mg, 71%), IR ν_{max}^{NaCl} cm^{-1}: 3020, 2920, 1600, 1500, 1380, 1200. ^{1}H-NMR ($CDCl_3$) δ: 2.2—3.03 (6H, m, CH_2 × 3), 3.1 (3H, s, CH_3), 5.4 (1H, dt, J=15 and 6 Hz, CH=), 5.78 (1H, dt, J=15 and 6 Hz, CH=), 7.1—7.47 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +5.7 (t, J=12 Hz). MS *m/e*: 290 (M^+), 194, 130, 103, 91. High-resolution MS Calcd for $C_{13}H_{16}F_2O_3S$: 290.0786. Found: 290.0769.

Rearrangement of Mesylate (12c)——A solution of **12c** (103.2 mg, 0.34 mmol) in *n*-hexane (4 ml) was refluxed for 3.5 h. After the removal of the solvent, the residue was chromatographed on silica gel to give **14c** (54.6 mg, 53%) and **13c** (19.8 mg, 19%). **14c**, IR ν_{max}^{NaCl} cm^{-1}: 3010, 2940, 1600, 1500, 1380, 1200. ^{1}H-NMR ($CDCl_3$) δ: 1.17 (3H, d, J=7 Hz, CH_3), 2.20—3.0 (5H, m, CH_2CH_2+CH), 3.12 (3H, s, CH_3), 5.35 (1H, dd, J=7 and 15 Hz, CH=), 5.75 (1H, dt, J=15 and 6 Hz, =CH), 7.03—7.45 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) δ: +12.5 (d, J=9.4 Hz), MS *m/e*: 304 (M^+), 208, 130, 117, 91. High-resolution MS Calcd for $C_{14}H_{18}F_2O_3S$: 304.0943. Found: 304.0924. **13c**, IR ν_{max}^{NaCl} cm^{-1}: 3020, 2920, 1670, 1600, 1500, 1350, 1180. ^{1}H-NMR ($CDCl_3$) δ: 1.36 (3H, d, J=7 Hz, CH_3), 2.30—2.90 (4H, m, CH_2CH_2), 3.0 (3H, s, CH_3), 4.78 (1H, tq, J=8 and 7 Hz, CH), 5.54 (1H, dt, J=16 and 12 Hz, $CF_2CH=$), 6.24 (1H, dt, J=16 and 6 Hz, =CH), 7.04—7.44 (5H, m, aromatic). ^{19}F-NMR ($CDCl_3$) +44.0 (m). MS *m/e*: 304 (M^+), 208, 188, 130, 91. High-resolution MS Calcd for $C_{14}H_{18}F_2O_3S$: 304.0944. Found: 304.0955.

References and Notes

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