119.53, 121.44, 121.58, 126.99, 134.46, 135.79, 136.17, 173.25; mass spectrum (CI, $CH_4$), $m/e$ 259 (M + 1, 100%); high-resolution mass spectrum, $m/e$ 258.1369 ($C_{15}H_{18}N_2O_2$ requires 258.1368).

**2-Methyl-3-(methoxycarbonyl)-1,9-dimethyl-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]indole (18a, 18b).** $N_a$,$N_b$-Dimethyltryptophan methyl ester **17** (0.014 g, 0.057 mmol), acetaldehyde dimethyl acetal **10a** (0.010 g, 0.11 mmol), and trifluoroacetic acid (0.012 g, 0.11 mmol) were stirred for 12 days to provide **18a,b** as a dark oil (0.0155 g, 0.057 mmol, 100%); the cis/trans ratio was measured by $^1H$ NMR analysis to be 14:86 (c/t): $^1H$ NMR ($CDCl_3$) $\delta$ 1.52 (3 H, d, $J$ = 6.9 Hz, $CHCH_3$ cis and trans), 2.47 (2.6 H, s, $NCH_3$ trans), 2.57 (0.4 H, s, $NCH_3$ cis), 2.90-3.18 (2 H, m), 3.62 (3 H, s), 3.63-4.04 (2 H, m including a singlet (3 H) at 3.72), 7.01-7.50 (4 H, m); mass spectrum (CI, $CH_4$), $m/e$ 273 (M + 1, 100%).

***trans*-2-Benzyl-3-(methoxycarbonyl)-1-phenyl-1,2,3,4-tetrahydro-9*H*-pyrido[3,4-*b*]indole (16b).** $N_b$-Benzyltryptophan methyl ester **11e** (0.308 g, 1.0 mmol), benzaldehyde dimethyl acetal **10b** (0.310 g, 2.0 mmol), and trifluoroacetic acid (0.228 g, 2.0 mmol) were stirred for 48 h to provide a dark yellow oil, which was flash chromatographed on silica gel (hexane/EtOAc, gradient) to provide a light yellow oil (0.375 g, 95%) whose proton NMR and IR spectra were identical with those of the trans diastereomer **16b**[4] obtained from the reaction of $N_b$-benzyltryptophan methyl ester (**11c**) and benzaldehyde in refluxing benzene.[4] No other products were observed in this reaction by TLC or from the NMR spectrum of the crude material.

**Acknowledgment.** We wish to thank the NIH (NS-22287) and the NIMH (MH-36644) for generous financial support. We also wish to thank Dr. Suzanne Wehrli and Frank Laib for the NMR and mass spectra, respectively. We also acknowledge helpful discussions with Carol Gorst and thank Anju Gupta for preparation of this manuscript.

**Registry No.** **7a**, 99708-04-0; **7b**, 81095-85-4; **8a**, 123050-53-3; **8b**, 123050-54-4; **8c**, 123050-55-5; **9a**, 123050-56-6; **9b**, 123050-57-7; **9c**, 123050-58-8; **10a**, 534-15-6; **10b**, 1125-88-8; **11a**, 7303-49-3; **11b**, 123003-67-8; **11c**, 73327-10-3; **11d**, 123003-68-9; **12a**, 50302-68-6; **12a** (R′ = $CH_2Ph$), 123003-76-9; **12b**, 75196-51-9; **12b** (R′ = $CH_2Ph$), 123003-77-0; **13a**, 123003-69-0; **13b**, 123003-70-3; **14a**, 93712-65-3; **14b**, 93712-66-4; **15a**, 123003-71-4; **15b**, 123003-72-5; **16b**, 123050-52-2; **17**, 123003-73-6; **18a**, 123003-74-7; **18b**, 123003-75-8; H-DL-Trp-OMe, 7303-49-3; $PhCH_2CHO$, 122-78-1.

## Primary Polyfluoroallylic Alcohols. Preparation and Isomerization into 2-Fluoroacrylic Acid Fluoride and 1-Fluoro Vinyl Ketones

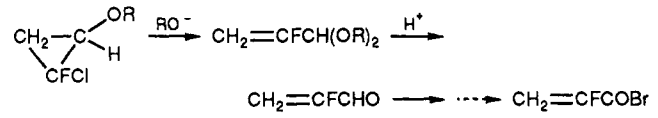
T. Nguyen* and C. Wakselman

*CNRS-CERCOA 2 à 8, rue Henri Dunant, 94320 Thiais, France*

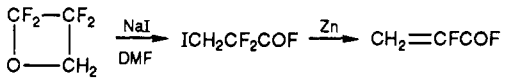
*Received March 6, 1989*

Alkyl and aryl 2-fluoroacrylic acid esters have been used as starting materials for number of coating agents, dental polymers,[1] and special glass.[2] These esters have been commonly prepared from 2-fluoroacrylic acid halides $CH_2$=CFCOX (X = Cl,[3] Br,[4] F[5]). The recent processes for having these intermediates involved the rearrangement

**Scheme I**



**Scheme II**

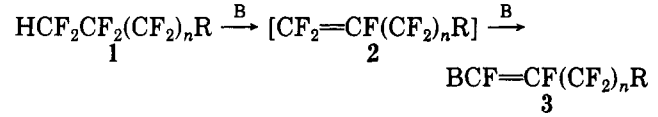


of an alkoxycyclopropane[4] (Scheme I) or the opening of and oxetane by a nucleophile[5] (Scheme II).

These two reactions brought great improvements over the previous method which used as starting material the very toxic 2-fluoroacetic derivatives.[6] The cyclopropane route needs nevertheless several steps, and the oxetane[7] is also toxic. Another possible way of obtaining 2-fluoroacrylic acid halides should be a rearrangement of 2-fluoroacrylic alcohols CXY=CFCH$_2$OH if these alcohols are available. The allylic rearrangements were already performed on secondary and tertiary fluoroallylic alcohols,[8] but not on a primary alcohol. The reason was certainly an absence of a practical method of preparation of these alcohols. Therefore we were searching a convenient method of obtaining primary polyfluoroallylic alcohols.

A few years ago, we showed that 1-H perfluoroalkyl chains are transformed into fluorinated olefins by action of strong bases like lithium dialkylamides[9] or organolithium reagents[10] (Scheme III).

**Scheme III**



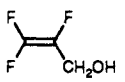
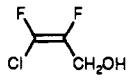
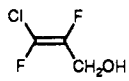
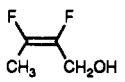
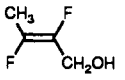
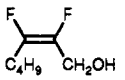
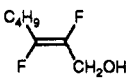
This conversion was observed with alcohols $HCF_2CF_2(CF_2)_nCH_2OH$ when $n$ was equal to 2, 4, or 6. The vinylic intermediate **2** was not isolated. This fluorinated olefin, activated by the electron-withdrawing difluoromethylene group, was steadily attacked by the organolithium reagent. However, the case of the alcohol $HCF_2CF_2CH_2OH$ **4** corresponding to $n$ equal to zero, was not examined at that time. Recently we were asking ourselves what could be the reactivity of the intermediate olefin **5** which is not activated by an adjacent electronegative group. Is it possible to stop the condensation at the intermediate step **5** in order to get the allylic alcohol **7** after hydrolysis? (See Scheme IV.)

We report here that this transformation can be performed under controlled conditions of temperature and reaction time. Addition of methyllithium to the alcohol **4** in diethyl ether at 0 °C and stirring during 5 h at room temperature led, after hydrolysis, to a mixture containing 74% of **7**, 16% of **8**, and 10% of the starting material **4** as shown by an NMR analysis. If the condensation is allowed to go to completion when the addition is performed at room temperature the substituted allylic alcohol **8** can

(1) Masahiro, P.; Shimishi, I. Jpn. Pat. 60158137 (1985); *Chem. Abstr.* **1977**, *86*, 50564y. Shigeru, M.; Masahiko, O. Eur. Pat. 168032 (1986).
(2) Bloch, B.; Cavalli, C.; Charrier, D. German Patent (DOS) 2950490; *Chem. Abstr.* **1981**, *94*, 16336.
(3) Boguslavkaya, L. S.; Tchouvatkin, N. N.; Morozova, T. B.; Pariteleeva, I. Y.; Kartaelov, A. B.; Sineskov, K. P. *Zh. Org. Khim.* **1987**, *23*, 1173. Heumuller, R.; Herbrechtsmeier, P.; Siegemund, G.; Groh, W. D.E.3 620 050 A1 (1987); *Chem. Abstr.* **1988**, *108*, 205235a.
(4) Molines, H.; Nguyen, T.; Wakselman, C. *Synthesis* **1985**, 755.
(5) Ohmori, A.; Takaki, S.; Kitahara, T. Eur. Pat. 136668 (1985).
(6) Gault, H.; Rouge, D.; Gordon, E. *Compt. Rend. Acad. Sci. Fr.* **1960**, *250*, 1073. Hudlicky, M. *Tetrahedron Lett.* **1960**, *14*, 21. Tolman, V.; Veres, K. *Collect. Czech. Chem. Commun.* **1964**, *29*, 234.
(7) Weinmayr, V. *J. Org. Chem.* **1963**, *28*, 492.
(8) Sterlin, R. N.; Yatsenko, R. D.; Knunyants, I. L. *Khim. Nauka i. Promy* **1958**, *3*, 540; *Chem. Abstr.* **1959**, *53*, 4195. Drakesmith, F. G.; Richardson, R. D.; Stewart, O. I.; Tarrant, P. *J. Org. Chem.* **1968**, *33*, 286. Normant, J. F.; Foulon, J. P.; Masure, D.; Sauvêtre, R.; Villieras, J. *Synthesis* **1975**, 122.
(9) Wakselman, C.; Nguyen, T. *J. Org. Chem.* **1977**, *42*, 565.
(10) Nguyen, T.; Rubinstein, M.; Wakselman, C. *Synth. Commun.* **1983**, *13*(1), 81.

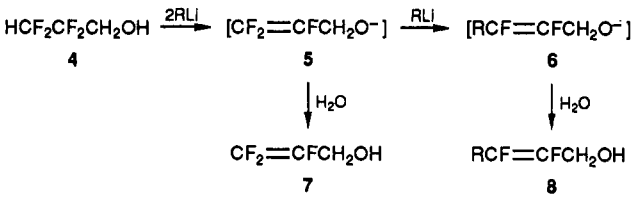
0022-3263/89/1954-5640$01.50/0 

**Table I. NMR Spectral Data of Polyfluoroallylic Alcohols $XCF{=}CFCH_2OH$**

| compounds | chemical shifts,[a] δ | | | | coupling constants[b] | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | F | F | Y | $CH_2CH$ | $J_{FF}$ | $^3J_{FF}$ | $^3J_{FF}$ | $^3J_{FCH_2OH}$ | $^4J_{FCH_2OH}$ | $^3J_{FY}$ | $^4J_{FY}$ |
|  **7** | 104 | 121 | 179 | 4.4 | 84 | 32 | 120 | 22 | 3 | | |
|  **10E** | 104 | 141 | | 4.4 | | 14 | | 22 | | | |
|  **10Z** | 122 | 152 | | 4.4 | | | 138 | 22 | 2 | | |
|  **8Z** | 126.5 | 147.5 | 2 | 4.2 | | 8 | | 24 | 4 | 20 | 2.5 |
|  **8E** | 145 | 161 | 2 | 4.3 | | | 134 | 25 | 5 | 19 | |
|  **8′Z** | 133 | 145 | 2.25<br>1.45<br>0.95 | 4.2 | | 10 | | 26 | | 26 | |
|  **8′E** | 150 | 161 | 2.4<br>1.5<br>0.98 | 4.4 | | | 132 | 26 | 6 | 26 | 6 |

[a] Chemical shifts are expressed in ppm from TMS and $CFCl_3$ as external references. [b] Coupling constants are expressed in hertz.

**Scheme IV**




be obtained with 56% yield. Similar transformation of alcohol **9** into alcohol **10** has been also observed.

$$HCFClCF_2CH_2OH \underset{9}{\rightarrow} CFCl{=}\underset{10}{CFCH_2OH} \xrightarrow{H^+} CH_2{=}\underset{11}{CFCOF}$$

Since alcohols **4** and **9** were easily available,[11,12] this process for having polyfluoroallylic alcohols appeared very attractive. One valuable development was the allylic rearrangement which occurs steadily in acidic medium. From alcohol **7**, 2-fluoroacrylic acid fluoride **11** was obtained in good yield. Likewise was for alcohol **10**. In the case of **10**, the superior ability of chlorine over fluorine as leaving atom was obvious. Allylic rearrangement occurred equally with alcohols **8**; 1-fluorovinyl ketones **12** resulted (Scheme V).

**Scheme V**

$$RCF{=}\underset{8}{CFCH_2OH} \xrightarrow{H^+} CH_2{=}\underset{12}{CFCOR}\ (R = CH_3, C_4H_9)$$

Ketones of this type were prepared by a carbene route[13] or by organometallic condensations.[14,15] The present process was comparatively straightforward.

In conclusion, we are reporting a simple way to prepare primary polyfluoroallylic alcohols **7**, **8**, and **10**, which use the easily accessible 3-hydropolyfluoropropanol **4** and **9** as starting materials. We have performed the allylic rearrangement of alcohols **7** and **10** into 2-fluoroacrylic acid fluoride **11**, a valuable synthon in the preparation of 2-fluoroacrylic polymers. By extension of the method to alcohols **8** which were obtained by the same process, 1-fluorovinyl ketones **12** were prepared.

## Experimental Section

$^1H$ and $^{19}F$ NMR spectra were recorded on a Varian EM360L instrument, and chemical shifts were reported in ppm from TMS in δ scale for $^1H$, from $CFCl_3$ in φ scale for $^{19}F$. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer. Elemental analyses were carried out in the Laboratoire Central d'Analyse of CNRS(Lyon). 3-H tetrafluoropropanol was purchased from TCI Tokyo, Japan, alkyllithium from Janssen Chimica Beerse Belgium, and chlorotrifluoroethylene from Matheson Oevel Belgium.

**Trifluoroallylic Alcohol, 7.** To a solution of alcohol **4** (20 g, 151 mmol) in 20 mL of anhydrous diethyl ether was added dropwise, at 0 °C, 320 mmol of methyllithium (1.2 M solution in ether); over a period of 1 h, the temperature was allowed to reach room temperature. Stirring was continued for 5 h; afterward the reaction flask was again cooled to 0 °C. Concentrated HCl

(11) Joyce, R. N. U.S. 2559628 (1951). Lazerte, J. D.; Koshar, R. J. *J. Am. Chem. Soc.* **1955**, *77*, 910. Beer, A. A.; Zaforets, P. A.; Inozentsev, V. F.; Povkh, Gr. S.; Popov, A. I. *Zeftekhimiya* **1962**, *2*, 617; *Chem. Abstr.* **1963**, *58*, 8885e.

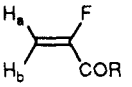
(12) Frantisek, L.; Simek, S. *Collect. Czech. Chem. Commun.* **1970**, *35*, 1752.

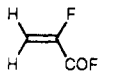
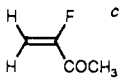
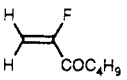
(13) Buddrus, J.; Nerdel, F.; Hentochal, P. *Tetrahedron Lett.* **1966**, 379. Molines, H.; Wakselman, C. *Tetrahedron* **1976**, *32*, 2099. Bessière, Y.; Savary, D. N. H.; Schlosser, M. *Helv. Chim. Acta* **1977**, *60*, 1739. Blanco, L.; Rousseau, Cr. *Bull. Soc. Chim. Fr.* **1985**, 455.

(14) Elkik, E.; Dahan, R.; Parlier, A. *Bull. Soc. Chim. Fr.* **1981**, Part I, *2*, 353.

(15) Chuit, C.; Sauvêtre, R.; Masure, D.; Baudry, M.; Normant, J. F.; Villieras, J. *J. Chem. Res.* **1977**, 104.

**Table II. NMR Spectral Data of (1-Fluorovinyl)carbonyl Compounds 11 and 12**



| compounds | chemical shifts,[a] δ | | | | coupling constants[b] | | | |
|---|---|---|---|---|---|---|---|---|
| | $H_a$ | $H_b$ | F | R | $^2J_{HH}$ | $^3J_{FH_a}$ | $^3J_{FH_b}$ | $J_{FR}$ |
|  11 | 5.6 | 6 | −117 | +14 | | 12 | 46 | 18 |
|  12 | 4.9 | 5.4 | −116 | 2.3 | 4 | 17 | 46 | 3 |
|  12′ | 5.1 | 5.65 | −117 | 2.7<br>1.65<br>0.95 | 3 | 17 | 48 | 2 |

[a] Chemical shifts are expressed in ppm from TMS and $CFCl_3$ as external references. [b] Coupling constants are expressed in hertz. [c] These characteristics were in agreement with those given in the literature.[13]

(18 mL) was carefully added, and the pH was adjusted to 6 or 7. The solution was left for the night, and then the organic phase was separated, washed, and dried over magnesium sulfate. Diethyl ether was distilled off, leaving a crude oil which was flash distilled to give a clean liquid (bp 60 °C, 100 Torr; 17 g). By introduction of a known quantity of $CFCl_3$ in a sample of the distillate, one can evaluate the ratio of different fluorinated compounds obtained as in the following: 74% of **7**, 16% of **8**, and 10% of **4**. Purified alcohol **7** was obtained by a second distillation in the presence of hydroquinone (bp 98 °C, 12.5 g, yield 74%). The $^1H$ NMR and $^{19}F$ NMR data of **7** are found in Table I. Anal. Calcd for $C_3H_3F_3O$: C, 32.17; H, 2.70. Found: C, 32.34; H, 2.75.

**3-Chloro-2,3-difluoroallylic Alcohol, 10.** The same process applied to a solution of alcohol **9**, $CHClFCF_2CH_2OH$ (10 g, 68.4 mmol), in 10 mL of anhydrous diethyl ether, and 127 mmol of methyllithium, gave a crude distillate (bp 90–95 °C, 125 Torr; 7.8 g) from which alcohol **10** (bp 116 °C; 5.7 g) was isolated as two isomers (*E*/*Z* equal to 45/55). Their $^1H$ NMR and $^{19}F$ NMR data are found in Table I. IR ($CCl_4$): 3300 (OH), 1780 $cm^{-1}$ (CF=CFCl). Anal. Calcd for $C_3H_3ClF_2O$: C, 28.04; H, 2.35. Found: C, 28.18; H, 2.48.

**3-Methyl-2,3-difluoroallylic Alcohol, 8.** To a solution of 10 g (76 mmol) of alcohol **4** in 30 mL of diethyl ether was added dropwise with stirring 220 mmol of methyllithium. The stirring was continued overnight at room temperature. The solution was neutralized carefully and worked up as in the preparation of **7**. A fractionation of the crude distillate gave **7** (1 g, 9 mmol) and **8** (4.6 g, 42.7 mmol, yield 56%) as a mixture of two isomers (*E*/*Z* equal to 80/20). We cannot separate these isomers by VPC through a column of SE30 heated to 130 °C. The $^1H$ NMR and $^{19}F$ NMR data of these isomers are found in Table I. IR ($CCl_4$): 3300, 3230 (OH), 1740, 1710 $cm^{-1}$ (CF=CF). Anal. Calcd for $C_4H_6F_2O$: C, 44.48; H, 5.6; F, 35.18. Found: C, 44.77; H, 5.61; F, 34.12.

**3-Butyl-2,3-difluoroallylic Alcohol, 8′.** Similarly, a solution of 7 g (53 mmol) of alcohol **4**, 70 mL of diethyl ether, and 180 mmol of butyllithium (1.2 M solution in hexane) gave 6.8 g of crude distillate, bp 70–80 °C (15 Torr), from which 5.4 g (36 mmol) of **8′** were isolated, yield 68%. The isomers *E*, bp 176 °C, and *Z*, bp 188 °C, were separated by VPC through a column of SE 30 heated to 160 °C. The ratio *E*/*Z* was 77/23. The $^1H$ NMR and $^{19}F$ NMR data of these isomers are found in Table I. IR ($CCl_4$): 3300, 3230 (OH), 1732 $cm^{-1}$ (CF=CF). Anal. Calcd for $C_7H_{12}F_2O$: C, 56.05; H, 8.06; F, 25.33. Found: (*E*) C, 56.17, H, 8.13; F, 24.62; (*Z*) C, 55.87; H, 8.93.

**2-Fluoroacryloyl Fluoride, 11.** Into a distillation flask containing 10 mL of concentrated sulfuric acid were added dropwise with stirring 2.5 g (22 mmol) of alcohol **7**. An exothermic reaction occurred. The volatile acryloyl fluoride **11** formed was distilled in vacuo (200 Torr) in a receiver cooled by a dry ice–acetone mixture. Obtained was 1.15 g (12.5 mmol), yield 55%. Similarly, 4.5 g (35 mmol) of alcohol **10** gave 2.78 g (29 mmol) of **11**. Yield 82%. The $^1H$ NMR and $^{19}F$ NMR data of **11** were in Table I. Treated by a solution of phenol in $CH_2Cl_2$ **11** gave the known phenyl 2-fluoroacrylic acid ester **2**.

**Fluorovinyl Methyl Ketone, 12.** A mixture of 2.4 g (18.9 mmol) of alcohol **8**, $CH_3CF{=}CF\text{-}CH_2OH$, 10 mL of tetrachloroethane, 0.5 mL of concentrated sulfuric acid, and hydroquinone was heated for half an hour on an oil bath at ca. 100 °C; it was then distilled in vacuo to give a crude distillate, bp 60–80 °C (100 Torr), 7.2 g. It contains 14.5 mmol (evaluated by $^{19}F$ NMR) of ketone **12**, which was separated by a second distillation in the presence of hydroquinone at room temperature under 15 Torr. Yield 1.3 g, 76%. The $^1H$ NMR and $^{19}F$ NMR spectra of **12** are in Table II. IR ($CCl_4$): 1730, 1710 (C=O), 1640 $cm^{-1}$ (C=CF). These characteristics were in agreement with those given in the literature.[13]

**1-Fluorovinyl *n*-Butyl Ketone, 12′.** A mixture of 2.1 g (14 mmol) of alcohol **8′**, *E* and *Z* $C_4H_9CF{=}CFCH_2OH$, 5 mL of $CH_2Cl_2$, 0.5 mL of concentrated sulfuric acid, and hydroquinone was heated for half an hour on an oil bath at ca. 100 °C and then distilled off in vacuo to give ketone **12′**, bp 75–80 °C (160 Torr), 1.2 g (8.6 mmol), yield 61%. The $^1H$ NMR and $^{19}F$ NMR data of **12′** are in Table II. IR ($CCl_4$): 1710 (C=O), 1640 $cm^{-1}$ (C=CF). Anal. Calcd for $C_7H_{11}FO$: C, 64.67; H, 8.33. Found: C, 64.00; H, 8.60.

**Registry No.** **4**, 76-37-9; **7**, 41578-52-3; (*E*)-**8**, 123028-47-7; (*Z*)-**8**, 123028-48-8; (*E*)-**8′**, 123028-51-3; (*Z*)-**8′**, 123028-52-4; **9**, 28885-04-3; (*E*)-**10**, 123028-49-9; (*Z*)-**10**, 123028-50-2; **11**, 60556-85-6; **12**, 2372-98-7; **12′**, 71150-92-0; $CH_3Li$, 917-54-4; $C_4H_9Li$, 109-72-8.

## Trimethylsilyl Polyphosphate for Intramolecular Friedel–Crafts Cyclizations

Ellen M. Berman* and H. D. Hollis Showalter

*Chemistry Department, Parke-Davis Pharmaceutical Research Division, Warner-Lambert Company, Ann Arbor, Michigan 48105*

*Received May 15, 1989*

In connection with studies directed toward the synthesis of a novel class of DNA intercalating agents,[1] we needed to prepare a series of 9*H*-selenoxanthen-9-ones. The

(1) Presented at the 78th Annual Meeting of the American Association for Cancer Research, Atlanta, GA, May 1987; Abstract No. 1197. Berman, E.; Klohs, W.; Leopold, W. R.; Plowman, J.; Sercel, A. D.; Shillis, J.; Showalter, H. D. H.; Werbel, L. M. *Proceedings Am. Assoc. Cancer Res.* **1987**, *28*, 302.

0022-3263/89/1954-5642$01.50/0 