[Chem. Pharm. Bull. 27(12)3123—3129(1979)]

UDC 547.512.04 : 547.517.04

# Studies on Organic Fluorine Compounds. XXX.[1] Ring Opening Reaction of Acetoxydifluorocyclopropanes with Various Nucleophiles

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(Received August 8, 1979)

Ring opening reactions of acetoxydifluorocyclopropanes with various nucleophiles were investigated. Alkaline hydrolysis of acetoxydifluorocyclopropane afforded the $\alpha,\alpha$-difluoro ketone, $\alpha$-fluoro enone and, in the case of **4**, $\alpha$-fluoro-$\beta$-methoxy ketone (**8**), while reactions with $CH_3Li$, Grignard reagent and $LiAlH_4$ gave the corresponding fluoro allyl alcohol derivatives (**15**) exclusively, in good yields. The reaction of **3** with $CH_3MgI$ in the presence of CuBr afforded 2-fluoro-3-methylcyclotridecanone (**21**).

**Keywords**——acetoxydifluorocyclopropanes; $\alpha,\alpha$-difluoro ketone; $\alpha$-fluoro enone; fluoro allyl alcohols; 2-fluoro-3-methylcyclotridecanone

Carbon-chain extension and ring enlargement of dihalocyclopropanes, formed by the addition of dihalocarbene to carbon-carbon double bonds, are well-known reactions and have been widely utilized in synthetic organic chemistry.[3–13] Dichloro- and dibromocyclopropanes rather than the difluoro derivatives have been well studied owing to the low reactivity of the difluoro analog. In the course of our studies to explore new synthetic reactions utilizing difluorocyclopropanes including the synthesis of fluorinated biological active compounds, we examined the reactions of acetoxydifluorocyclopropanes with various nucleophiles. Recently we reported the synthesis of 24,24-difluoro-25-hydroxyvitamin $D_3$ (**1**) *via* a ring opening reaction of the difluorocyclopropane (**2**).[14]

Acetoxydifluorocyclopropanes (**3**, **4**, and **5**) were obtained in good yields by the reaction of the corresponding enol acetates with difluorocarbene, generated by pyrolysis of sodium

1) Part XXIX: Y. Kobayashi, H. Hamana, S. Fujino, A. Ohsawa, and I. Kumadaki, *J. Am. Chem. Soc.*, in press
2) Location: *Horinouchi, Hachioji, Tokyo 192-03, Japan.*
3) For reviews, see: *a*) W.E. Parham and E.E. Schweizer, "Organic Reactions," Vol. 13, ed. by A.C. Cope, John Wiley and Sons, Inc., New York, 1963, p. 55; *b*) C.D. Gutsche and R. Redmore, "Carbocyclic Ring-Expansion Reactions," Academic Press, Inc., New York, 1968, p. 127; *c*) R. Bartlet and Y. Vo-Quang, *Bull. Soc. Chim. Fr.*, **1969**, 3729.
4) W.E. Parham and J.F. Dooley, *J. Am. Chem. Soc.*, **89**, 985 (1967).
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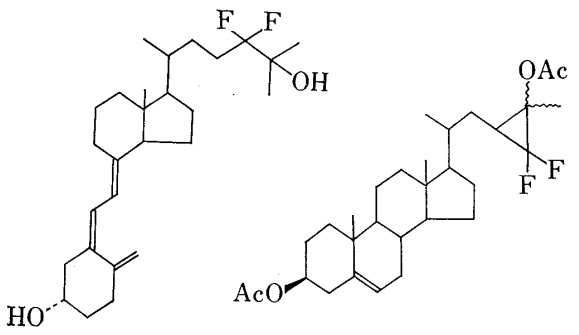

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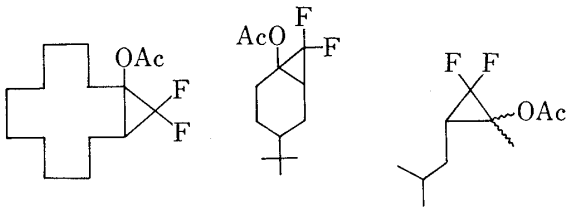
Chart 1



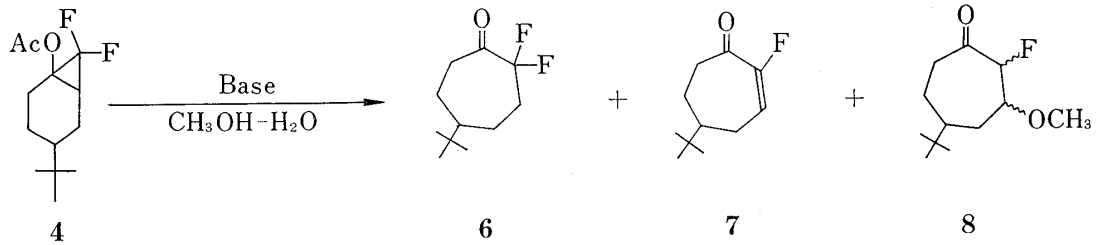
3 (quant.) 4 (87%) 5 (51%)

Chart 2

chlorodifluoroacetate[15] as shown in Chart 2. These cyclopropanes show large geminal F–F coupling ($J$=140—150 Hz) in the $^{19}$F-NMR spectrum.

Though solvolytic ring opening of dichloro- or dibromocyclopropanes derived from an enol acetate, silyl enol ether, vinyl ether or enamine led to the formation of the homologous α-chloro or α-bromo enone, the formation of an α,α-difluoro ketone was observed in the alkaline hydrolysis of acetoxydifluorocyclopropane; the mechanism of this reaction was also discussed by Crabbé and his co-workers.[13] In the course of the synthesis of 24,24-difluoro-25-hydroxyvitamin $D_3$ (**1**), we have also examined the alkaline hydrolysis of acetoxydifluorocyclopropane and found that the base and solvent affect the hydrolysis of **3** and **4**.

Reaction of **4** with LiOH in aqueous methanol gave the α,α-difluoro ketone (**6**), α-fluoro enone (**7**) and α-fluoro-β-methoxy ketone (**8**) in 58, 18 and 18% yields, respectively. When NaOH was used in this reaction, the yield of **6** decreased to 41%, but the monofluoro compounds, **7** and **8**, were obtained in a total yield of 47% (see Table I). Since **6** was not converted to **7** or **8** under the conditions of hydrolysis of **4**, **6** is not an intermediate, which suggests that the formation of **7** and **8** may involve a concerted ring opening of **4** to the allyl cation (**9**).




4 6 7 8

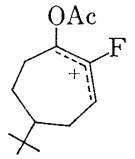


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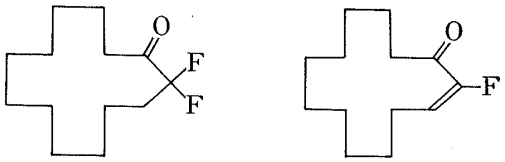
Chart 3

Reaction of **3** with LiOH in aqueous methanol (the reaction mixture was heterogeneous) afforded α,α-difluoro ketone (**10**) and α-fluoro enone (**11**) in 48 and 29% yields, respectively,

15) *a*) W.M. Wagner, *Proc. Chem. Soc., London*, **1959**, 229; *b*) J.M. Birchall, G.W. Cross, and R.M. Hazeldine, *ibid.*, **1960**, 18.

Table I. Alkaline Hydrolysis of **4**

| Base | Products (Yield %) | | |
|---|---|---|---|
| | **6** | **7** | **8** |
| LiOH | 58 | 18 | 18 |
| NaOH | 41 | 11 | 36 |



**10** **11**

Chart 4

based on the conversion of **3**. When the reaction system was made homogeneous by the addition of tetrahydrofuran, the yield of **10** decreased to 21%. No significant difference in the ratio of **10** and **11** was found on changing the base (see Table II). It should be noted that **10** could not be converted to **11** under the conditions of hydrolysis of **3**.

Table II. Alkaline Hydrolysis of **3**

| Base | Solvent | Conversion (%) | Products (Yield %) | |
|---|---|---|---|---|
| | | | **10** | **11** |
| LiOH | $CH_3OH$–$H_2O$ | 55 | 48 | 29 |
| LiOH | $CH_3OH$–$H_2O$–THF | 72 | 21 | 27 |
| NaOH | $CH_3OH$–$H_2O$–THF | 75 | 29 | 36 |
| KOH | $CH_3OH$–$H_2O$–THF | 80 | 33 | 41 |

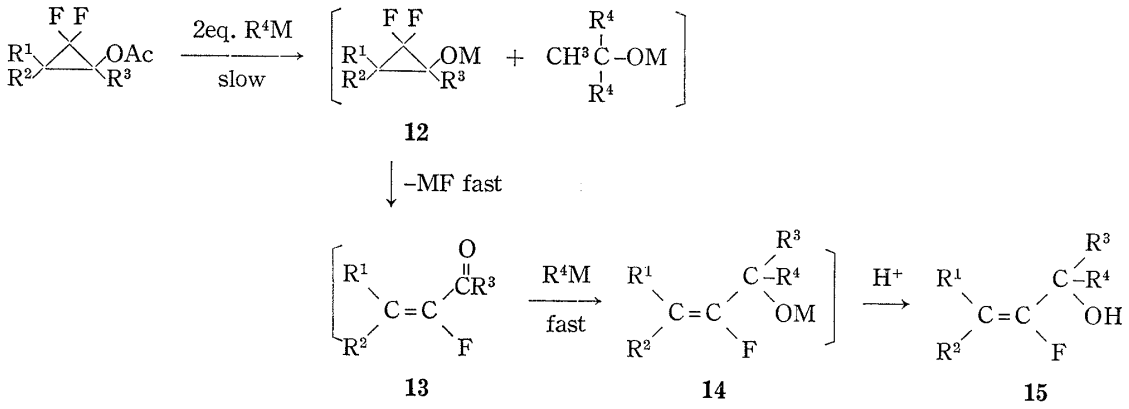
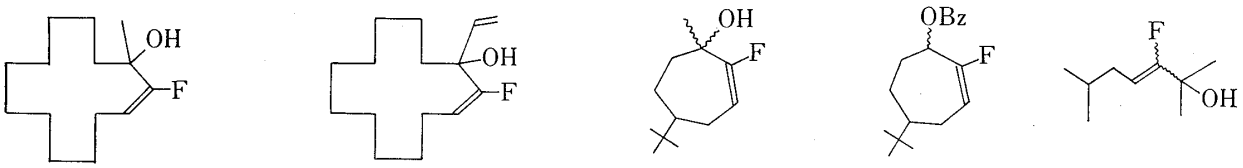


Chart 5

In contrast to the above-mentioned alkaline hydrolysis of acetoxydifluorocyclopropanes, reactions with $CH_3Li$, Grignard reagent or $LiAlH_4$ afforded the corresponding fluoro allyl alcohol derivatives (**15**) exclusively; no cyclopropanol, difluoro ketone or fluoro enone was obtained, even if these reactions were performed at low temperature for a short time. Fluoro allyl alcohol derivatives (**15**) may be formed through ring opening to the α-fluoro enone (**13**) and subsequent nucleophilic attack at the carbonyl group as depicted in the following scheme (Chart 5). For example, the reaction of **3** with excess $CH_3Li$ in ether at −78° for 10 min afforded 1-methyl-2-fluoro-2-cyclotridecenol (**16**) in 78% yield. On the other hand, the reaction of **3** with 0.9 mol equivalent of $CH_3Li$ gave **16** in 24% yield, with 64% recovery of **3**, but no cyclopropanol, difluoro ketone (**10**) or fluoro enone (**11**) could be detected. The reaction of **3** with methyl magnesium iodide in ether at room temperature proceeded rather slowly and gave **10** in 84% yield. In the course of this reaction, only **16** and **3** were detected by TLC and GLC. These results suggest that the ring opening of difluorocyclopropoxide (**12**) to α-fluoro enone (**13**) and the subsequent reaction of **13** thus formed with $CH_3Li$ or

$CH_3MgI$ are faster than nucleophilic attack of these reagents at the ester group of the starting acetoxydifluorocyclopropane. The results of the reactions of **3**, **4** and **5** with $CH_3Li$, Grignard reagent and $LiAlH_4$ are summarized in Table III.



**16** **17** **18** **19** **20**

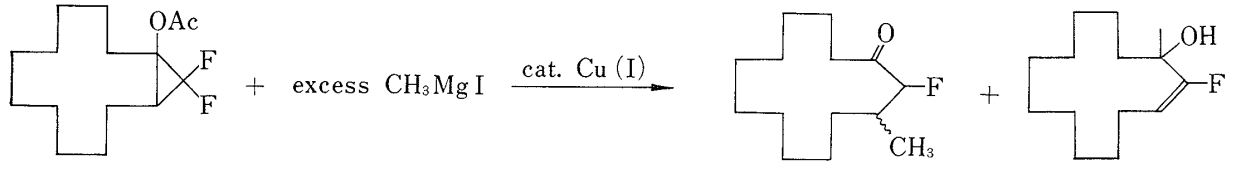
Chart 6

Table III. Reactions of Acetoxydifluorocyclopropane with $CH_3Li$, Grignard Reagent and $LiAlH_4$

| Cyclopropane | Reagent | Reaction temp. (°C) | Conditions time | Product (Yield %)[a] | |
|---|---|---|---|---|---|
| **3** | $CH_3Li$ | −78 | 10 min | **16** | (78) |
| **3** | $CH_3MgI$ | r. temp. | 10 hr | **16** | (84) |
| **3** | ⁄⁄\MgBr | r. temp. | 10 hr | **17** | (35) |
| **4** | $CH_3Li$ | −78 | 10 min | **18** | (70) |
| **4** | $LiAlH_4$ | r. temp. | 1.5 hr | **19**[b] | (68) |
| **5** | $CH_3Li$ | −78 | 10 min | **20** | (68) |

*a*) Isolation yield.
*b*) The alcohol formed by the reaction of **4** with $LiAlH_4$ was isolated as its benzoate (**19**).

The path of the reaction of **3** with $CH_3MgI$ mentioned above suggests that the homologous β-methyl-α-fluoro ketone (**21**) is obtained by the reaction of $CH_3MgI$ in the presence of Cu(I) salt through conjugate addition of organo copper reagent to the intermediary α-fluoro enone (**11**).[16] Indeed, the reaction of **3** with $CH_3MgI$ in the presence of a catalytic amount of CuBr in ether gave 2-fluoro-3-methylcyclotridecanone (**21**) in 32% yield accompanied by the formation of the 1,2-addition product (**16**) in 26% yield, as shown in Chart 7.




**3** **21** **16**

Chart 7

The effects of other copper salts or additives were also examined, and the results are summarized in Table IV. Though the yield of the 1,4-addition product was not good, this reaction provides a simple method for the ring enlargement of cyclic ketone accompanied by the introduction of a methyl group at the β-position.

In conclusion, alkaline hydrolysis of acetoxydifluorocyclopropane afforded the homologous α,α-difluoro ketone, α-fluoro enone and, in the case of **4**, α-fluoro-β-methoxy ketone (**8**). On the other hand, reactions with $CH_3Li$, Grignard reagent and $LiAlH_4$ gave the corresponding fluoro allyl alcohol derivatives exclusively, in good yields. The reaction of **3** with

16) *a*) H.O. House, W.L. Respess, and G.M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966); G.H. Posner, "Organic Reactions," Vol. 19, ed. by W.G. Dauben, John Wiley and Sons, Inc., New York, 1972, p. 1.

Table IV. Reaction of 3 with $CH_3MgI$ in the Presence of Cu Salts

| Additive | Products (Yield %) | |
|---|---|---|
| | 1,4-Addition (**21**) | 1,2-Addition (**16**) |
| CuBr | 32 | 26 |
| CuI | 24 | 22 |
| CuI $Ph_3P$ | 14 | 73 |
| CuBr $(CH_3)_2S$ | 19 | 64 |

$CH_3MgI$ in the presence of Cu(I) salt afforded 2-fluoro-3-methylcyclotridecanone through conjugate addition to the intermediary α-fluoro enone.

## Experimental

**1-Acetoxy-13,13-difluorobicyclo[10,1,0]tridecane** (**3**)——A solution of 25.5 g (167 mmol) of sodium chlorodifluoroacetate in 80 ml of diglyme was added dropwise during 1 hr to a refluxing solution of 5.36 g (23.9 mmol) of 1-acetoxy-1-cyclododecene[17] in 20 ml of diglyme and the reaction mixture was refluxed for 20 min. The reaction mixture cooled to room temperature then poured into 400 ml of ice-water and extracted with 450 ml of *n*-hexane. The organic layer was washed with water three times and dried over $Na_2SO_4$. The solvent was removed *in vacuo*, the residue was chromatographed on silica gel (dichloromethane–*n*-hexane 1: 1 v/v eluent) to give 6.533 g (quantitative) of **3**, bp 103—105° (25 mmHg). **3** is a stereoisomeric mixture as indicated by its $^{19}F$ NMR spectrum. NMR ($CCl_4$) $\delta$: 1.96 (s, Ac); $^{19}F$ NMR ($CCl_4$)[18] +88.0 (d, $J_{F-F}=145$ Hz) and +70.5 (d, $J_{F-F}=145$ Hz) for one isomer, +82.7 (d, $J_{F-F}=149$ Hz) and +72.3 (d, $J_{F-F}=149$ Hz) for another isomer; MS *m/e*: 274 ($M^+$), 254 ($M^+-HF$), 231 ($M^+-Ac$). *Anal.* Calcd. for $C_{15}H_{24}F_2O_2$: C, 65.67; H, 8.82; F, 13.85. Found: C, 65.80; H, 8.83; F, 14.11.

**1-Acetoxy-4-*t*-butyl-7,7-difluorobicyclo[4,1,0]heptane** (**4**)——As described for the preparation of **3**, reaction of 3.92 g of 1-acetoxy-4-*t*-butylcyclohexene[19] with 11.44 g of sodium chlorodifluoroacetate in refluxing diglyme afforded 4.307 g (88%) of **4**, bp 83—84° (3 mmHg). NMR ($CCl_4$) $\delta$: 0.83 (s, *t*-Bu), 2.00 (s, Ac); $^{19}F$ NMR +75.2 (dd, $J_{F-F}=144$, $J_{F-H}=17$ Hz), +84.8 (d, $J_{F-F}=144$ Hz). MS *m/e*: 246 ($M^+$), 231 ($M^+-CH_3$), 203 ($M^+-Ac$). *Anal.* Calcd. for $C_{13}H_{20}F_2O_2$: C, 63.39; H, 8.19; F, 15.43. Found: C, 63.17; H, 8.28; F, 15.67.

**1-Acetoxy-1-methyl-2,2-difluoro-3-isobutylcyclopropane** (**5**)——As described for the preparation of **3**, the reaction of 3.597 g of 2-acetoxy-5-methyl-2-hexene with 15.26 g of sodium chlorodifluoroacetate in refluxing diglyme gave 2.393 g (51%) of **5**, bp 101—102° (48 mmHg). NMR ($CCl_4$) $\delta$: 2.00 (s, Ac); $^{19}F$ NMR +83.2 (dm, $J_{F-F}=149$ Hz) and +69.9 (dm, $J_{F-F}=149$ Hz) for one isomer, +81.6 (dm, $J_{F-F}=140$ Hz) and +72.7 (dm, $J_{F-F}=140$ Hz) for another isomer. MS *m/e*: 206 ($M^+$). *Anal.* Calcd. for $C_{10}H_{16}F_2O_2$: C, 58.24; H, 7.82. Found: C, 58.25; H, 7.77.

**Reaction of 3 with KOH**——A solution of 112 mg of KOH and 274 mg of **3** in a mixture of methanol (2.1 ml), water (4.8 ml) and tetrahydrofuran (2.0 ml) was stirred for 20 hr at room temperature. The reaction mixture was diluted with d-HCl and extracted with dichloromethane. The organic layer was washed with water and dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel (dichloromethane–*n*-hexane 1: 1 v/v eluent) to give 62 mg (27%) of 2,2-difluorocyclotridecanone (**10**) which was recrystallized from methanol, mp 30—31°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1740 (C=O). $^{19}F$ NMR ($CCl_4$) +44.0 (t, $J=14$ Hz). MS *m/e*: 232 ($M^+$), 214, 188, 146, 140, 135, 126, 121, 112, 98, 84. *Anal.* Calcd. for $C_{13}H_{22}F_2O$: C, 67.21; H, 9.55; F, 16.36. Found: C, 67.10; H, 9.74; F, 16.11. The second fraction gave 56 mg (20%) of the starting cyclopropane (**3**). The third fraction gave 20 mg (9%) of *E*-2-fluoro-2-cyclotridecenone (**11***E*) as a colorless oil. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1710, 1645. NMR ($CCl_4$) $\delta$: 5.46 (dt, $J_{H-F}=24$, $J_{H-H}=8$ Hz, olefinic H); $^{19}F$ NMR ($CCl_4$) +54 (d, $J=24$ Hz). MS *m/e*: 212 ($M^+$). The last fraction gave 48 mg (23%) of *Z*-2-fluoro-2-cyclotridecenone (**11***Z*) which was recrystallized from methanol, mp 61—62°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1675, 1650. NMR ($CCl_4$) $\delta$: 6.10 (dt, $J_{H-F}=34$, $J_{H-H}=8$ Hz, olefinic H); $^{19}F$ NMR +66.0 (d, $J=34$ Hz). MS *m/e*: 212 ($M^+$). *Anal.* Calcd. for $C_{13}H_{21}FO$: C, 73.54; H, 9.97; F, 8.95. Found: C, 73.63; H, 10.13; F, 8.71.

**Reaction of 4 with Lithium Hydroxide**——A solution of 90 mg of $LiOH\cdot H_2O$ and 493 mg of **4** in methanol (6 ml) and water (4 ml) was stirred for 1 hr at room temperature and then acidified by addition of d-HCl. The reaction mixture was extracted with ether and the organic layer was washed with brine, then dried over

17) N.J. Leonald and F.H. Owens, *J. Am. Chem. Soc.*, **80**, 6039 (1958).
18) Chemical shifts were measured in ppm from benzotrifluoride as internal standard. + indicates high field.
19) M.M. Rogic, *Tetrahedron*, **21**, 2823 (1965).

$Na_2SO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel. The fraction eluted with dichloromethane–*n*-hexane (1: 3 v/v) gave 236 mg (58%) of 2,2-difluoro-5-*t*-butylcycloheptanone (**6**). bp 127—129° (13 mmHg) (bulb to bulb distillation). IR $\nu_{max}^{CH_2Cl_2}$ $cm^{-1}$: 1745. $^{19}F$ NMR ($CCl_4$) +36.4 (dt, $J_{F-F}=222$, $J_{H-F}=8$ Hz), +47.6 (ddd, $J_{F-F}=222$, $J_{H-F}=26$, $J_{H-F}=12$ Hz). MS *m/e*: 204 ($M^+$), 189 ($M^+-CH_3$), 169 ($M^+-CH_3$, HF). *Anal.* Calcd. for $C_{11}H_{18}F_2O$: C, 64.68; H, 8.88; F, 18.68. Found: C, 64.48; H, 8.98; F, 18.35. The next fraction, eluted with dichloromethane–*n*-hexane (1: 1 v/v), gave 64 mg (18%) of 2-fluoro-5-*t*-butyl-2-cycloheptenone (**7**) as a colorless oil. IR $\nu_{max}^{CH_2Cl_2}$ $cm^{-1}$: 1685, 1650. NMR ($CCl_4$) $\delta$: 6.27 (1H, ddd, $J_{H-F}=20$, $J_{H-H}=6$ Hz, olefinic H); $^{19}F$ NMR ($CCl_4$) +58.0 (dm, $J_{H-F}=20$ Hz). MS *m/e*: 184 ($M^+$), 169 ($M^+-CH_3$). The last fraction, eluted with the same solvent system as above, gave 79 mg (10%) of 2-fluoro-3-methoxy-5-*t*-butylcycloheptanone (**8**) as a colorless oil. IR $\nu_{max}^{CH_2Cl_2}$ $cm^{-1}$: 2830, 1740, 1725. NMR ($CCl_4$) $\delta$: 3.24 (3H, s, $OCH_3$), 3.80 (1H, dd, $J_{H-F}=20$, $J_{H-H}=6$ Hz, C<u>H</u>–$OCH_3$), 5.15 (d, $J_{H-F}=48$ Hz, C<u>H</u>–F). MS *m/e*: 184 ($M^+-CH_3OH$), 169 ($M^+-CH_3OH$, $CH_3$).

**Reaction of 3 with Methyllithium**——A 5% ethereal solution of methyllithium (5 ml) was added to a solution of 548 mg of **3** in dry ether (10 ml) at −78° under an argon atmosphere, then the reaction mixture was stirred for 10 min. After the addition of aqueous $NH_4Cl$, the reaction mixture was extracted with ether. After washing with brine, the extract was dried over $Na_2SO_4$ and chromatographed on silica gel (benzene eluent) to afford 167 mg (37%) of *E*-1-methyl-2-fluoro-2-cyclotridecenol (**16***E*) which was recrystallized from cyclohexane, mp 113—114°. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3220 (OH), 1675, 940. NMR (acetone-$d_6$) $\delta$: 4.95 (1H, ddd, $J_{H-F}=28$, $J_{H-H}=10$, $J_{H-H}=5$ Hz, olefinic H); $^{19}F$ NMR (acetone-$d_6$) +41.0 (dm, $J_{H-F}=28$ Hz). MS *m/e*: 228 ($M^+$), 210 ($M^+-H_2O$). *Anal.* Calcd. for $C_{14}H_{25}FO$: C, 73.64; H, 11.04; F, 8.32. Found: C, 73.58; H, 10.93; F, 8.19. The next fraction, eluted with benzene, gave 99 mg (22%) of an *E* and *Z* mixture of **16** and the last fraction gave 87 mg (19%) of the *Z* isomer of **16** as a colorless oil. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3420, 1700, 940. NMR ($CCl_4$) $\delta$: 4.84 (1H, dt, $J_{H-F}=38$, $J_{H-H}=7.4$ Hz, olefinic H); $^{19}F$ NMR +57.9 (d, $J_{H-F}=38$ Hz). MS *m/e*: 228 ($M^+$), 210 ($M^+-H_2O$).

**Reaction of 4 with Methyllithium**——In the manner described above, the reaction of 300 mg (1.22 mmol) of **4** with methyllithium (5.0 mmol) gave 177 mg (70%) of 1-methyl-2-fluoro-5-*t*-butyl-2-cycloheptenol, bp 100—102° (6 mmHg) (bulb to bulb distillation). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3600. NMR ($CCl_4$) $\delta$: 0.90 (9H, s, *t*-Bu), 1.33 and 1.36 (total 3H, each s, $CH_3$ at C-1), 5.25 (1H, m, olefinic H); $^{19}F$ NMR ($CCl_4$) +53.8 (d, $J_{H-F}=22$ Hz) for one isomer, +56.4 (d, $J_{H-F}=20$ Hz) for another isomer. MS *m/e*: 200 ($M^+$), 185 ($M^+-CH_3$), 182 ($M^+-H_2O$), 167 ($M^+-CH_3$, $H_2O$). *Anal.* Calcd. for $C_{12}H_{21}FO$: C, 71.96; H, 10.57; F, 9.49. Found: C, 71.61; H, 10.73; F, 8.71.

**Reaction of 5 with Methyllithium**——In the manner described above, the reaction of 556 mg (2.7 mmol) of **3** with methyllithium (11 mmol) afforded 295 mg (68%) of 2,5-dimethyl-3-fluoro-3-heptenol (**20**), which was identified as a 1: 1 *E* and *Z* mixture from its NMR spectrum, bp 95—115° (50 mmHg) (bulb to bulb distillation). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3580, 1690. NMR ($CCl_4$) $\delta$: 4.80 (dt, $J_{H-F}=36$, $J_{H-H}=8$ Hz, olefinic H of *Z* isomer), 4.98 (dt, $J_{H-F}=26$, $J_{H-H}=8$ Hz, olefinic H of *E* isomer); $^{19}F$ NMR ($CCl_4$) +56.6 (d, $J_{H-F}=36$ Hz), +42.6 (d, $J_{H-F}=26$ Hz). MS *m/e*: 160 ($M^+$), 145 ($M^+-CH_3$), 142 ($M^+-H_2O$). High-resolution MS Calcd. for $C_9H_{17}FO$; 160.1263. Found: 160.1272.

**Reaction of 4 with $LiAlH_4$**——Compound **4** (246 mg) was added to a solution of 114 mg of $LiAlH_4$ in 4 ml of ether at 0° under an argon atmosphere, and the reaction mixture was stirred for 1 hr at room temperature. Ethyl acetate (6 ml) was added to the reaction mixture to destroy excess $LiAlH_4$, followed by acidification with d-HCl and then extraction with ether. The organic layer was washed with brine, dried over $Na_2SO_4$ and then concentrated *in vacuo*. The residue was treated with 0.2 ml of pyridine and 169 mg of benzoyl chloride in dichloromethane (2 ml) at 0° for 1 hr. The reaction mixture was concentrated to dryness *in vacuo* and then subjected to prep. TLC (dichloromethane–*n*-hexane, 1: 2 v/v eluent, *Rf* 0.5—0.7) to give 183 mg (63%) of **19** as a colorless oil. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1695. NMR ($CCl_4$) $\delta$: 0.86 (9H, s, *t*-Bu), 5.30—5.90 (2H, broad, olefinic H and CHOBz), 7.40 (3H, m, aromatic), 7.90 (2H, m, aromatic); $^{19}F$ NMR ($CCl_4$) +42.6 (m). MS *m/e*: 290 ($M^+$), 223 ($M^+-C_4H_9$), 168 ($M^+-C_6H_5CO_2H$). High-resolution MS Calcd. for $C_{18}H_{23}FO_2$: 290.1682. Found: 290.1704.

**Reaction of 3 with Vinylmagnesium Bromide**——Compound **3** (2.74 g) was added to a THF solution (30 ml) of vinylmagnesium bromide (prepared from 1.90 g of magnesium and 9.08 g of vinyl bromide according to the literature[20]) under an argon atmosphere, and the reaction mixture was stirred for 10 hr at room temperature. The reaction mixture was poured into ice-water, acidified by the addition of d-HCl and extracted with ether. The organic layer was successively washed with d-HCl, 5% $NaHCO_3$ solution, and brine, and then dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel (dichloromethane–*n*-hexane 1: 2 v/v eluent) to give 1.213 g of crude **17** which was further purified by prep. TLC (dichloromethane–*n*-hexane 1: 1 v/v eluent, *Rf* 0.3—0.4) to afford 830 mg (35%) of **17** as a colorless oil. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 3580, 1640, 990, 910. NMR ($CCl_4$) $\delta$: 1.0—1.83 (20H, broad), 2.13 (1H, s, OH), 4.68 (1H, ddd, $J_{Ha-F}=36$, $J_{Ha-Hb}=10$, $J_{Ha-Hc}=7$ Hz, Ha, CHbHc–CHa=CF–), 5.08 (1H, d, $J_{Hd-Hf}=10$ Hz, Hd,

20) D. Seyferth "Organic Syntheses," Coll. Vol. IV, ed. by N. Rabjohn, John Wiley and Sons, Inc., New York, 1963, p. 258.

Hf, Hd, He ), 5.27 (1H, d, $J_{He-Hf}=18$ Hz, He), 6.0 (1H, dd, $J_{Hd-Hf}=10$, $J_{He-Hf}=18$ Hz, Hf). MS *m/e*: 240 ($M^+$).

**Reaction of 3 with $CH_3MgI$-CuBr**——An ethereal solution of $CH_3MgI$, prepared from 243 mg of Mg and 0.63 ml of $CH_3I$ in 10 ml of ether, was added to a solution of 548 mg (2 mmol) of 3 and 72 mg (0.5 mmol) of CuBr in 5 ml of ether at 0° under an argon atmosphere, and the reaction mixture was stirred for 10 hr at room temperature. The reaction mixture was treated with $NH_4Cl$ solution and extracted with ether. The organic layer was washed with brine, dried over $Na_2SO_4$ and then concentrated *in vacuo*. The residue was chromatographed on silica gel (dichloromethane–*n*-hexane 1: 3 v/v eluent) to afford 147 mg (32%) of 2-fluoro-3-methylcyclotridencanone, bp 130—139° (8 mmHg) (bulb to bulb distillation). IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1715. NMR ($CCl_4$) $\delta$: 1.05 (3H, ddm, $J_{H-H}=8$, $J_{H-F}=3$ Hz, $-CH_3$), 4.45 (1H, dd, $J_{H-F}=50$, $J_{H-H}=2$ Hz, CH–F). MS *m/e*: 228 ($M^+$). The fraction eluted with dichlomethane–*n*-hexane (1: 2 v/v) gave 118 mg (26%) of **16**.