Anal. Calcd for $C_{21}H_{17}O_7N$: C, 63.79; H, 4.33; N, 3.54. Found: C, 63.81; H, 4.40; N, 3.50.

Registry No.—**7**, 27391-06-6; **8**, 27391-07-7; **9**, 27391-08-8; **10**, 27391-09-9; **11**, 27391-10-2; **12**, 27391-11-3; **13**, 27425-46-3; **14**, 27425-47-4; **15**, 27425-48-5; **16**, 27391-12-4; **17**, 27391-13-5; **18**, 27391-14-6; **19**, 27425-49-6; **20**, 27415-61-8; **23**, 27415-62-9; **24**, 27415-63-0; **32**, 27415-64-1; **36**, 27371-68-2; **37**, 27415-66-3; **38**, 27415-67-4; **39**, 27425-50-9; **40**, 27415-68-5; **41**, 27415-69-6; **42**, 27415-70-9; **43**, 27415-71-0; **44**, 27415-72-1; **45**, 27415-73-2; **46**, 27415-65-2.

The Synthesis of 1-Fluorocycloalkenes

DONALD R. STROBACH* AND G. A. BOSWELL, JR.

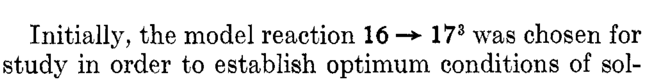
Contribution No. 1713 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

Received August 24, 1970

The reaction of anhydrous, neutral alumina, activity grade I, with a 1,1-difluorocycloalkane produces the corresponding 1-fluorocycloalkene in 20–70% yield. In this way, 1-fluorocyclopentene, 1-fluorocyclohexene, 1-fluorocycloheptene, 1-fluorocyclooctene, 1-fluorocyclododecene, and 4-methoxy-1-fluorocyclohexene were prepared and characterized, principally by proton and fluorine nmr and infrared spectra. The starting difluoro compounds were obtained by the action of sulfur tetrafluoride on the cyclic ketone. Thus, a facile, two-step entry into this elusive class of vinyl fluorides is provided.

Although linear vinyl fluorides are a well-known class of organic compounds, their cyclic counterparts are little described in the chemical literature. To our knowledge, the only example reported is 1-fluorocyclohexene (**6**).[1] We wish to report that the action of anhydrous, neutral alumina on a *gem*-difluorocycloalkane is a convenient, general route to cyclic vinyl fluorides. The difluoro compounds are obtained readily from the corresponding cyclic ketone and sulfur tetrafluoride[2] and this synthetic approach is outlined in Scheme I.

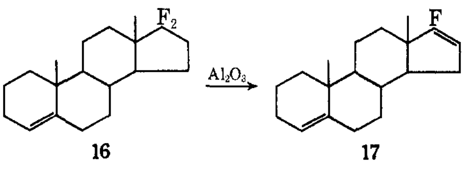
SCHEME I
SYNTHESIS OF 1-FLUOROCYCLOALKENES



1, $n = 3$	**2**, $n = 3$	**3**, $n = 3$
4, $n = 4$	**5**, $n = 4$	**6**, $n = 4$
7, $n = 5$	**8**, $n = 5$	**9**, $n = 5$
10, $n = 6$	**11**, $n = 6$	**12**, $n = 6$
13, $n = 10$	**14**, $n = 10$	**15**, $n = 10$

Results and Discussion

Initially, the model reaction **16** → **17**[3] was chosen for study in order to establish optimum conditions of solvent, temperature, and type of alumina. This reaction proceeded under very mild conditions[4] and no side reactions were observed. In addition, integration of H-4 *vs.* H-16, which are well resolved in the 60-MHz nmr spectrum of **17**, provided accurate quantitative data. By this method, it was established that hydrocarbon solvents gave high yields of **17**, whereas polar solvents, *e.g.*, acetonitrile, ethyl acetate, and dimethyl sulfoxide, gave essentially no product under identical reaction conditions. The source of the alumina was critical. Several samples were tested but only Woelm or Guilini[5] neutral alumina,[6] activity grade I, gave good results. Woelm basic alumina gave lower yields and Woelm acidic alumina and other samples of alumina from various commercial sources returned only unchanged **16**. The reactivity of an alumina sample probably is a function of available Lewis acid and base sites on the alumina surface, since we have shown that blocking the former sites with pyridine *or* the latter sites with tetracyanoethylene[7] completely inhibited the above reaction. Additional evidence in support of active sites is the fact that alumina is required in stoichiometric amount. No more than about 1 mmol of difluoro compound per 5 g of alumina can be dehydrofluorinated under the conditions used, and, if this ratio is exceeded, a mixture of starting material and product is obtained.



16 **17**

When alumina was suspended in a hexane solution of 1,1-difluorocyclohexane (**5**) at reflux temperature, starting material was consumed completely, and a single volatile product was formed as evidenced by gas–liquid chromatography. However, it was not possible to separate product from solvent by careful distillation, and essentially all the product was lost in fractions over the boiling range of 80–92°. To circumvent this difficulty, neat **5** was admixed with alumina without solvent and heated in an oil bath in a nitrogen atmosphere after which the reaction vessel was evacuated through a cold trap. The volatile material in the trap was shown to be a mixture of 96% of **6** and 4% of cyclohexene by nmr, mass spectrum, and glc analysis. The yield was 63% compared to 66%[8] in the solvent-mediated reaction

---

[1] (a) G. N. Valkanas and H. Hopff, U. S. Patent 3,093,692 (1963); *Chem. Abstr.*, **59**, 11291*e* (1963). (b) G. Wittig and B. Mayer, *Ber.*, **96**, 329 (1963).

[2] (a) W. R. Hasek, W. C. Smith, and V. A. Engelhardt, *J. Amer. Chem. Soc.*, **82**, 543 (1960); (b) D. G. Martin and F. Kagan, *J. Org. Chem.*, **27**, 3164 (1962).

[3] The preparation of steroid vinyl fluorides will be the subject of a separate communication from this laboratory.

[4] In hexane at room temperature, yields of **17** were 50 and 60% after 1 and 18 hr, respectively. At reflux temperature, the yield was 95–98% in 1 hr.

[5] Supplied by Bodman Chemical Co., Narberth, Pa.

[6] Hereafter designated as alumina.

[7] F. Figueras Roca, A. Nohl, L. de Mourges, and Y. Trambourze, *C. R. Acad. Sci.*, **266**, 1123 (1968).

[8] Gas–liquid chromatographic analysis.

described above. Similarly, pure 1-fluorocyclopentene (**3**) was obtained from 1,1-difluorocyclopentane (**2**) in 67% yield.

However, when this technique was applied to 1,1-difluorocycloheptane, no volatile products collected in the cold trap. A complex mixture of nonvolatile products was removed from the alumina with ether and a mixture of ether and methanol, from which cycloheptanone was isolated in 40% yield. The residual 35–40% of products was not identified, but spectral evidence indicated that, in part, they were condensation products of cycloheptanone.[9] Ketones were formed in all dehydrofluorination reactions reported herein, presumably by hydrolysis of the difluoro compound on the alumina surface but only the seven-membered ring gave ketone as the major product. The desired product **9** was finally obtained in 20% yield along with 42% of cycloheptanone by use of hexane solvent at reflux temperature.

The action of sulfur tetrafluoride on cyclooctanone gave pure 1,1-difluorocyclooctane in about 0.5% yield, and our studies of this substance were limited. In pentane solution at room temperature, **11** was consumed rapidly by alumina, and at least three volatile products were formed as shown by glc analysis. By use of a combined gas chromatograph–mass spectrometer, the most abundant of the three products was shown to be the only one which contained fluorine. A small sample was collected by preparative glc. An exact mass measurement gave the formula $C_8H_{13}F$, and in pentane solution the fluorine resonance was a triplet ($J_{FCCH} = 22.5$ Hz) of doublets ($J_{FC=CH} = 18.0$ Hz) centered at 99.1 ppm. The vinyl proton was a doublet ($J_{HF} = 18.0$ Hz) of triplets ($J_{HH} = 8.6$ Hz) which confirmed strong coupling between fluorine and the vinyl proton. These data are most consistent with the *cis*-1-fluorocyclooctene structure.[10]

Finally, treatment of 1,1-difluorocyclododecane with alumina in hexane solution under conditions similar to those used for **9** revealed that vinyl fluorides are also dehydrofluorinated by alumina. The major product was cyclododecyne contaminated with one or more cyclic dienes.[11] 1-Fluorocyclododecene was prepared by increasing the amount of **14** per gram of alumina and was obtained in 46% yield as a colorless oil contaminated with starting difluoro compound. Since the product was characterized by infrared, nmr, and mass spectra, preparative glc was not carried out and **15** was not obtained in pure form.

Spectral Data.—The main features of the nmr spectra of the 1-fluorocycloalkenes are presented in Table I.[12] Although the spectra of 1-fluorocyclopentene are not well resolved, the spectra of the remaining members of the series essentially define the structure. It is difficult to interpret the strong doublet coupling between the fluorine atom and vinyl proton as the result of other than a vinyl fluoride. The magnitude of $J_{(FC=CH)}$ is consistent with the expected cis stereochemistry at the carbon–carbon double bond of the cyclopentene through cyclooctene compounds; the $J_{(FC=CH)} = 37$ Hz of 1-fluorocyclododecene suggests a trans structure. Unfortunately, the more intriguing aspects of the nmr spectra, such as the large variation of fluorine chemical shift *vs.* ring size, cannot be explained at this time.

TABLE I

NMR PARAMETERS FOR 1-FLUOROCYCLOALKENES[a]

Ring size	Chemical shift: F, ppm	Chemical shift: Vinyl H, δ	J, Hz: CH=CF	J, Hz: CH₂CF=	J, Hz: CH₂CH=
5	122.7	4.92	*b*	*b*	*b*
6	101.1	5.14	17	*c*	*c*
d	103.1	5.00	16	*e*	3.5
7	91.9	5.35	21.5	11.5	6.0
8	99.1	5.10	18.0	22.5	8.6
12	112.5	4.53	37.0	16.0	7.5

[a] Additional nmr data for these compounds are given in the Experimental Section. [b] *J* values are small. Proton and fluorine resonances are narrow (10 Hz) multiplets. [c] Pattern is too complex to analyze. [d] 4-Methoxy-1-fluorocyclohexene. [e] Not resolved.

Each of the fluoroenes gave a molecular ion as the most important feature in the low-resolution mass spectrum and the molecular weight of the dehydrofluorination products was confirmed in this way. However, the fragmentation patterns were of little use for determination of structure. It should be noted that the mass spectra of a 1-fluorocycloalkene and the corresponding 1,1-difluorocycloalkane are very similar. The difluoro compounds lose the elements of hydrogen fluoride and give M − 20 as the ion of highest mass in the spectrum. Some of our initial, small-scale studies were confused by this fact.

Experimental Section

General Methods.—Proton (60 MHz) and fluorine (56.4 MHz) nmr spectra were recorded as solutions in deuteriochloroform with tetramethylsilane and fluorotrichloromethane as internal references. Fluorine chemical shifts are in ppm upfield from the reference. The notation s, d, t, q, and m refers to singlet, doublet, triplet, quartet, and multiplet, respectively. Gas–liquid chromatography was carried out with a 6 ft × 0.25 in. column of Dow Corning silicone oil, FS 1265, 20% on Gas-Chrom R (60–80 mesh). Infrared spectra were recorded on neat films. Mass spectra were obtained on a Bendix time-of-flight mass spectrometer which was equipped to sample from a glc unit. Mass measurements were confirmed with higher resolution instruments when necessary.

Materials.—Cyclic ketones were commercial samples used without purificaton except 4-methoxycyclohexanone, which was obtained by catalytic reduction of *p*-methoxyphenol to 4-methoxycyclohexanol followed by dichromate oxidation to the ketone, bp 78–79° (11 mm) [lit.[13] bp 84–85° (14 mm)]. Hexane was ACS grade and Woelm or Guilini[5] neutral alumina, activity grade I, was used.

1,1-Difluorocyclopentane (**2**).—Literature procedures[2] were used with slight modification. A mixture of **1** (1.0 mol), hydrogen fluoride (1.0 mol), sulfur tetrafluoride (1.0 mol), and 150 ml of dichloromethane was agitated for 120 hr in a Hastelloy C pressure vessel at 30° and autogenous pressure. The vessel was opened and the reaction mixture was washed with water, 10% sodium bicarbonate solution, and water. The organic layer was dried ($CaSO_4$) and was flash-distilled on a rotary evaporator. The flash distillate was dried again and was fractionated carefully through a spinning-band column to give 39% of **2**: bp 69–70°; $n^{25}D$ 1.3612; fmr was a quintet at 93.4 ppm, $J_{HF} = 14.0$ Hz.

Anal. Calcd for $C_5H_8F_2$: C, 56.61; H, 7.60; F, 35.82. Found: C, 57.8; H, 7.75; F, 35.7.

1,1-Difluorocyclohexane (**5**).—The above procedure was used with **4** (2.5 mol), hydrogen fluoride (3.0 mol), sulfur tetrafluoride

---

(9) A. T. Nielsen and W. J. Houlihan, *Org. React.*, **16**, 1 (1968).

(10) The low-temperature fluorine nmr of this substance is the subject of a separate communication from this laboratory: F. J. Weigert and D. R. Strobach, *Org. Magn. Resonance*, **2**, 303 (1970).

(11) The elimination of 2 mol of hydrogen fluoride was also noted with linear systems such as 2,2-difluorooctane, which gave 2-octyne as a major product.

(12) For comparison, the nmr spectra of the series, cyclopropene through cyclooctene, have been recorded and discussed: K. B. Wiberg and J. Nist, *J. Amer. Chem. Soc.*, **83**, 1226 (1961).

(13) N. A. Milas and C. P. Priesing, *ibid.*, **79**, 6295 (1957).

(2.0 mol), and 300 ml of dichloromethane with a reaction time of 48 hr. The yield of **5** was 70%: bp 99-100°; $n^{25}D$ 1.3904 (lit.[2a] values are bp 98-99°, $n^{25}D$ 1.3890); fmr was a quintet at 96.0 ppm, J_{HF} = 14.0 Hz.

1,1-Difluoro-4-methoxycyclohexane.—As above, 4-methoxycyclohexanone (0.195 mol), hydrogen fluoride (0.50 mol), sulfur tetrafluoride (0.37 mol), and dichloromethane (50 ml) were agitated for 18 hr. The yield of product was 57%, bp 65-67° (45 mm). Fmr was an AB quartet at 93.2 ppm (equatorial) and 101.7 ppm (axial), J_{FF} = 236 Hz.

Anal. Calcd for $C_7H_{12}F_2O$: C, 55.98; H, 8.05; F, 25.30. Found: C, 56.6; H, 8.08; F, 25.9.

1,1-Difluorocycloheptane (8).—As above, **7** (0.45 mol), hydrogen fluoride (1.0 mol), sulfur tetrafluoride (0.56 mol), and dichloromethane (100 ml) were agitated for 24 hr. The yield of **8** was 79%: bp 130-131°; $n^{25}D$ 1.4058; fmr was a quintet at 85.3 ppm, J_{HF} = 16.0 Hz.

Anal. Calcd for $C_7H_{12}F_2$: C, 62.65; H, 9.02; F, 28.33. Found: C, 62.7; H, 9.09; F, 28.3.

1,1-Difluorocyclooctane (11).—As above, **10** (0.60 mol), hydrogen fluoride (2.25 mol), sulfur tetrafluoride (1.20 mol), and dichloromethane (150 ml) were agitated for 18 hr. An impure product was collected by distillation, 1.24 g (1.6%), bp 62-65° (35 mm). This was purified by preparative glc on a 6-ft column of 25% fluorosilicone on Gas-Chrom R. Column temperature was 75° and He flow rate was 500 ml per min. The product had 93.9-min retention time. Fmr was a quintet at 88.0 ppm, J_{HF} = 15.0 Hz (lit.[14] values are a quintet at 89.0 ppm, J_{HF} = 15.1 Hz in propene as solvent).

Anal. Calcd for $C_8H_{14}F_2$: F, 25.64. Found: F, 24.9.

1,1-Difluorocyclododecane (14).—As above, **13** (0.41 mol), hydrogen fluoride (0.50 mol), sulfur tetrafluoride (0.56 mol), and dichloromethane (150 ml) were agitated for 120 hr. The crude product could not be distilled and was passed over a column (4.8 × 43 cm) of Florisil with hexane as eluent. Fractions (50 ml) were collected and monitored by gravimetric analysis and tlc on silica gel. Appropriate fractions were combined, solvent was removed, and the residue was sublimed (bath temperature 60°, 0.10 mm) to give 19.2 g (23%) of colorless, crystalline, waxy solid, mp 42-44°. Fmr was a quintet at 91.7 ppm, J_{HF} = 14.5 Hz.

Anal. Calcd for $C_{12}H_{22}F_2$: C, 70.54; H, 10.86; F, 18.60. Found: C, 70.9; H, 10.89; F, 18.7.

1-Fluorocyclopentene (3).—1,1-Difluorocyclopentane (10.0 g, 0.094 mol) was added to a freshly opened, 500-g can of Woelm alumina and mixed for 15 min. The contents of the can were transferred to a flask which was heated in an oil bath (70°) for 15 hr under nitrogen. The flask was evacuated slowly to 5-mm pressure through a Dry Ice-acetone trap. The bath temperature was raised rapidly to 150°, and, after 1 hr, 5.40 g (66%) of colorless liquid was removed from the trap and dried ($CaSO_4$). The dried product was analytically pure, $n^{25}D$ 1.400, and had infrared bands at 2980 (s), 2870 (s), 1680 (s, CH=CF), 1450 (w), 1340 (s), 1160 (s), 950 (m), 870 (m), and 800 cm^{-1} (m, broad). Pmr was δ 2.00, m, 6 H. A small sample was distilled, bp 56°.

Anal. Calcd for C_5H_7F: C, 69.75; H, 8.19; F, 22.06. Found: C, 69.9; H, 8.29; F, 22.1.

1-Fluorocyclohexene (6).—The procedure used to prepare **3** was repeated with 1,1-difluorocyclohexane (10.4 g, 0.087 mol). The liquid in the trap weighed 5.46 g (63%) and was dried over $CaSO_4$, $n^{25}D$ 1.4251. The product gave a molecular ion (*m/e* 100) in the mass spectrum and was contaminated with 4% of cyclohexene, which was identified by mass spectrum (*m/e* 82) and glc retention time: infrared bands at 2970 (s), 2860 (s), 1700 (s, CH=CF), 1440 (m), 1360 (s), 1330 (m), 1140 (s), 970 (m), 920 (m), 910 (m), 860 (m), 840 (m), 800 (m), and 780 cm^{-1} (m); pmr resonance at δ 1.65 m, 4 H and 2.06, m, 4 H (CH_2C=).

4-Methoxy-1-fluorocyclohexene.—A stirred mixture of 375 g of alumina, 500 ml of hexane, and 8.0 g (0.053 mol) of 4-methoxy-1,1-difluorocyclohexane was refluxed for 16 hr under nitrogen when starting material was consumed (glc). The mixture was cooled and solids were removed and washed with hexane. The filtrates were concentrated on the water pump to give 3.00 g (43%) of colorless oil which was pure by glc analysis: infrared bands at 2920 (s), 2850 (s), 1700 (s, CH=CF), 1450 (s), 1360 (s), 1240 (m), 1190 (s), 1180-1080 (s, broad), 1030 (m), 1000 (m), 915 (m), 875 (m), 840 (s), 830 (s), 805 (m), 780 (m), and 710 cm^{-1} (m); pmr resonances at δ 1.88, m, 2 H (CCH_2COMe), 2.18, m, 4 H (CH_2C=), 3.28, s with m buried underneath, 4 H ($HCOCH_3$).

Anal. Calcd for $C_7H_{11}FO$: C, 64.57; H, 8.52; F, 14.60. Found: C, 64.8; H, 8.44; F, 14.1.

1-Fluorocycloheptene (9).—Using the amounts and procedure described above for the methoxy compound, 10.4 g (0.077 mol) of 1,1-difluorocycloheptane was agitated for 25 hr. The hexane solution and washes were concentrated by distillation, and the residues was distilled to give 2.0 g (20%) of **9**: bp 54° (60 mm); $n^{25}D$ 1.4359; infrared bands at 2920 (s), 2850 (s), 1700 (s, CH=CF), 1450 (s), 1370 (s), 1210 (m), 1150 (m), 1110 (m), 1090 (s), 1070 (s), 1010 (m), 840 (m), 815 (m), 800 (m), and 725 cm^{-1} (m); pmr resonance at δ 1.68, m, 6 H (ring CH_2 groups), 1.8-2.7, broad m, 4 H (CH_2C=).

Anal. Calcd for $C_7H_{11}F$: C, 73.62; H, 9.71; F, 16.64. Found: C, 73.7; H, 10.2; F, 16.0.

***cis*-1-Fluorocyclooctene (12).**—A mixture of approximately 0.3 ml of 1,1-difluorocyclooctane, 18.8 g of alumina, and 25 ml of pentane was shaken occasionally for 4 hr at room temperature. Glc indicated that **11** had been consumed and three new peaks were present. The mass spectrum of each peak showed that only the major product contained fluorine. A small sample was collected from the analytical gas chromatograph and the molecular formula was established by exact mass measurement (Calcd for $C_8H_{13}F$: 128.1001. Found: 128.0997.). The sample was not completely free of impurities and only the fmr spectrum and vinyl region of the pmr spectrum were recorded (Table I).

***trans*-1-Fluorocyclododecene (15).**—A mixture of 3.0 g (0.015 mol) of 1,1-difluorocyclododecane (**14**), 37.5 g of alumina, and 50 ml of hexane was agitated overnight at room temperature. The mixture was filtered, solvent was removed, and the residue was distilled to give 1.82 g of colorless liquid, bp 46-50° (0.25 mm). Glc and fmr analysis indicated that about 1.24 g (46% based on **14**) of **15** was present in the product mixture, the remainder being **14**. Strong bands at 2980, 1710 (CH=CF), and 1460 cm^{-1} were present in the infrared spectrum.

Registry No.—**2**, 1120-70-3; **3**, 27415-42-5; **5**, 371-90-4; **6**, 694-51-9; **8**, 27371-42-2; **9**, 27415-45-8; **11**, 23170-87-8; **12**, 27390-78-9; **14**, 27415-48-1; **15**, 27390-79-0; 1,1-difluoro-4-methoxycyclohexane, 27371-43-3; 4-methoxy-1-fluorocyclohexene, 27415-47-0.

Acknowledgments.—The authors are indebted to Dr. F. J. Weigert for assistance in interpretation of nmr spectra and to Mrs. S. Wheeler for valuable technical assistance. Mr. C. Matthews obtained the mass spectra and Messrs. L. Walther, L. Rizzardi, and D. Nickerson recorded the nmr spectra.

---

[14] J. E. Anderson, E. S. Glazer, D. L. Griffith, R. Knorr, and J. D. Roberts, *J. Amer. Chem. Soc.*, **91**, 1386 (1969).