Fluoro Ketones. IV. Mechanism of Thermal Decomposition of Fluoroacetone Hemiketal Esters[1]

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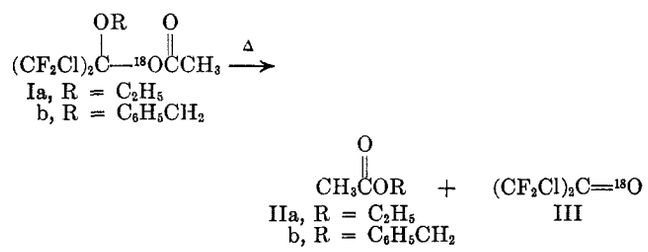
Pyrolysis of oxygen-18-labeled ethyl and benzyl dichlorotetrafluoro hemiketal acetates Ia, b gave labeled fluoroacetone and unlabeled ethyl and benzyl acetates (IIa, b). The sulfur analogs (IVa, b) also decomposed similarly to give the fluoroacetone and the corresponding thiol acetates (Va, b). Solvent studies showed that the rates of decomposition parallel the ionizing power of the solvent. These results are rationalized on the basis of a cyclic four-membered transition state.

The formation of fluoroacetone hemiketal esters *via* acetylation of the corresponding hemiketals[2] proceeds readily and in good yield.[1] We have found these esters to be thermally unstable and suggested a mechanism which is formally analogous to that of normal ester pyrolysis.[3] Since this mechanism was advanced only by analogy, we decided to utilize oxygen-18 as a tracer to provide information on the actual mechanism of the decomposition.

Results and Discussion

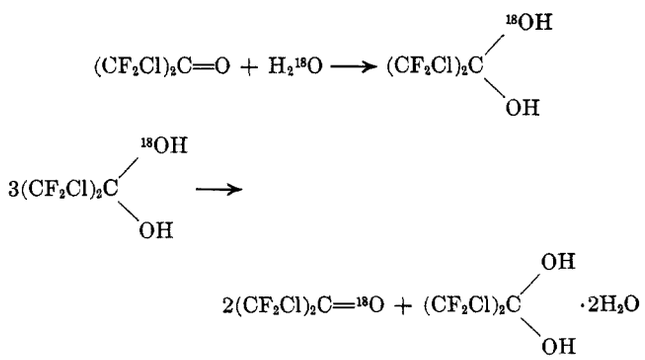
Labeled *sym*-dichlorotetrafluoroacetone was conveniently prepared by the hydration[4] of the unlabeled ketone with oxygen-18-enriched water[5] followed by disproportionation of the monohydrate as shown in Scheme I.[6]

The labeled ketone (2.6 ^{18}O atom %) was treated with the appropriate alcohol to give the hemiketal which was acetylated with acetyl chloride in the manner previously described.[1,2] Pyrolysis of the resultant fluoro ketone hemiketal acetates (I) gave the fluoro ketone (III) and simple nonfluorinated esters (II).



The mass spectra of the ethyl and benzyl acetates (IIa, b) recovered from the pyrolysis of the corresponding oxygen^{18}-labeled hemiketal acetates[7] were compared with the spectra of samples of normal isotopic composition and were found to be nearly identical. Relative parent peak heights ($\times 10^3$) for pyrolysate and normal IIa, b were 5.2 and 5.3 for IIa (90/88) and 1.9 and 1.9 for IIb (152/150) (Table I). The fragmentation pattern of III was very complex owing largely to the presence of chlorine isotopes. All of the detectable

SCHEME I



excess oxygen-18 (2.6 ^{18}O atom %)[8] was found to reside in the fluoro ketone (III). The determination was based on the $C_3F_4ClO^+$ fragment corresponding to a loss of Cl from the molecular ion. The intensity of this peak was 20 times that of the parent peak allowing for greater precision. A correction was made for the contribution of the ^{37}Cl isotope to the *m/e* 165 peak by using a ^{35}Cl abundance of 75.7%.[9]

TABLE I

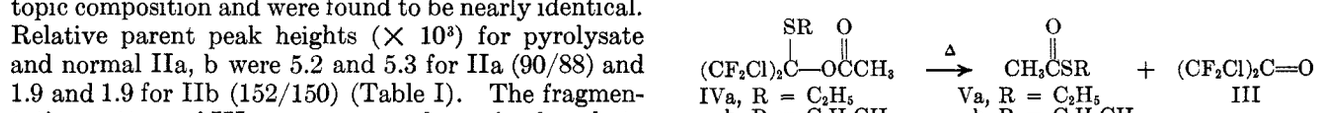
RELATIVE PEAK HEIGHT RATIOS ($^{18}O/^{16}O \times 10^3$)

m/e 90/88		*m/e* 152/150		*m/e* 165/163	
IIa (normal)	5.3[a]	IIb (normal)	1.9[a]	III (normal)	6.50
IIa (pyrolysate)	5.2[a]	IIb (pyrolysate)	1.9[a]	III (labeled) (2.6 atom %)[b]	27.0
				III (pyrolysate) (2.6 atom %)[b]	26.5

[a] Parent peak corrected for 2-^{13}C atoms; reproducibility ±5%. [b] Estimated error ± 0.2 atom %; corrected for ^{37}Cl contribution.[9]

Similarly, the thiohemiketal esters (IVa, b) were prepared by the acetylation of the appropriate thiohemiketal.

An appreciable amount of Vb was obtained on vac-



uum distillation of IVb indicating poorer thermal stability of the sulfur analogs. This was substantiated

(1) Part III: P. E. Newallis and P. Lombardo, *J. Org. Chem.*, **30**, 3834 (1965).

(2) H. E. Simmons and D. W. Wiley, *J. Amer. Chem. Soc.*, **82**, 2288 (1960).

(3) C. H. Depuy and R. W. King, *Chem. Rev.*, **60**, 431 (1960).

(4) C. Woolf, Abstracts, the 132nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1957, p 23M.

(5) Contained 5.15% ^{18}O atom and was purchased from Yeda Research and Development Co., Rehovoth, Israel.

(6) We are indebted to Dr. C. Woolf and W. J. Cunningham for this procedure.

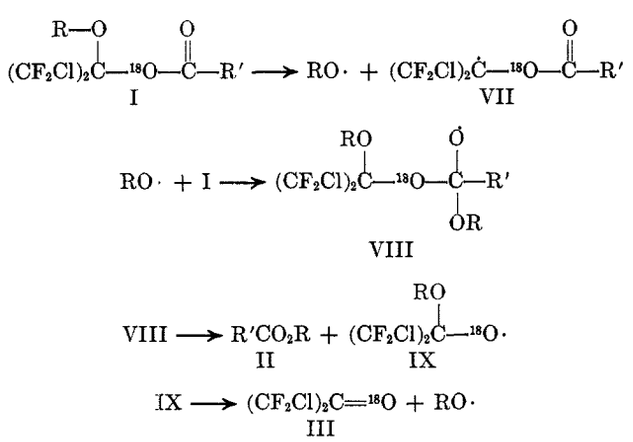
(7) These samples were doubly distilled and checked for purity by gas chromatography on two different columns.

(8) The accuracy of this determination is estimated to be ±0.2 atom %. Since 2.6 ^{18}O atom % was found to be present in III obtained from the pyrolysis of I as well as that used in the synthesis of I, any errors very likely would be canceled. Furthermore, our failure to find any of the excess ^{18}O in II requires that the excess ^{18}O be present in the only other product, namely III.

(9) Determined independently by measuring the $C_3F_4Cl^+$ fragment *m/e* 147/149 from 1,2-dichlorohexafluorocyclobutane which is in good agreement with the previously reported value of 75.8% [S. Meyerson, *Anal. Chem.*, **33**, 964 (1961)].

by the lower temperatures required for the controlled pyrolysis of the sulfur analogs compared with their oxygenated counterparts. It is significant that the thiol esters V were obtained from the pyrolysis of IV, not II. Thus, the sulfur atom serves as a label in this case.

The probability of a clean radical reaction being involved in these decompositions was ruled out based on the following results. We would have expected at least small amounts of radical-type products from the pyrolysis of a wide variety of hemiketal esters[1,10] which included the cyclopropylcarbinol, β-phenethanol, and allylcarbinol derivatives. Evidence for ring opening of cyclopropylcarbinyl radicals[11] and ring closure[11b,12] or isomerization[11b,13] of allylcarbinyl radicals has been reported. The stability of primary, secondary, and tertiary, as well as benzyl, radicals has been discussed and illustrated by many examples.[11b,14] Moreover, no evidence of radicals was observed when the decomposition was followed by esr spectroscopy. Monitoring a neat sample of Ib at 200° over a 30-min period showed only a constant base line.[15] Free-radical mechanisms involving alkyl radicals would place the oxygen label in the ester which is contrary to our results. An interesting radical process involving alkoxy radicals[16a] rather than alkyl radicals is given below.



The attractive feature of this mechanism is that it would give the ^{18}O-enriched ketone (III) which is consistent with our results. However, it would require that this sequence occur within the solvent cage and not abstract hydrogen from hydrocarbon solvent. Considering the reactivity of alkoxy radicals[16b] and the absence of any by-products of any type, this process seems less attractive.

(10) P. Lombardo, unpublished results.

(11) (a) J. D. Roberts and R. H. Mazur, *J. Amer. Chem. Soc.*, **73**, 2509 (1951); E. Renk, P. R. Shafer, W. H. Graham, R. H. Mazur, and J. D. Roberts, *ibid.*, **83**, 1987 (1961); W. H. Urry, D. J. Strecker, and H. D. Harzler, *J. Org. Chem.*, **29**, 1663 (1964). (b) C. Walling in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, New York, N. Y., 1963.

(12) T. A. Halgren, M. E. H. Howden, M. E. Medof, and J. D. Roberts, *J. Amer. Chem. Soc.*, **89**, 3051 (1967).

(13) L. K. Montgomery and J. W. Matt, *ibid.*, **89**, 3050 (1967); L. K. Montgomery, J. W. Matt, and J. R. Webster, *ibid.*, **89**, 923 (1967).

(14) (a) C. Walling, "Free Radicals in Solution," John Wiley & Sons, Inc., New York, N. Y., 1957; (b) W. H. Urry and N. Nicolaides, *J. Amer. Chem. Soc.*, **74**, 5163 (1952); (c) D. H. Barton, *ibid.*, **82**, 2640 (1960).

(15) Control experiments have shown that the decomposition of Ib does occur at temperatures around 200°; however, the concentration of the radical species may be too low to detect.

(16) (a) Suggested by one of the referees. (b) For a discussion of the fate of alkoxy radicals, see C. Walling, *Pure Appl. Chem.*, **15**, 69 (1967).

A study of the decomposition of 0.1 *M* solutions of Ib in sealed ampoules at 185° showed a significant effect of solvent on the rate of reaction. The decompositions proceeded more rapidly in dipolar aprotic solvents[17] than in nonpolar solvents (Table II).

TABLE II

EFFECT OF SOLVENT ON THE THERMAL DECOMPOSITION OF 0.1 *M* SOLUTIONS OF Ib AT 185°

Solvent	3 hr, % decompn	5 hr, % decompn
Benzene	14	
Cumene	27	
Dioxane	58[a]	65[b]
Tetrahydrofuran	67	
Acetonitrile	97	
Dimethylformamide	100[c]	

[a] 0.65 *M*, 75%; 0.05 *M*, 55%. [b] 0.02 *M*, 60%. [c] Decomposed 75% in 1 hr; indication that generated fluoro ketone may have reacted with the DMF.

Rates of decomposition and the activation parameters for Ib in dioxane were determined gas chromatographically and are recorded in Table III. Good first-order plots were obtained for over 60% reaction.

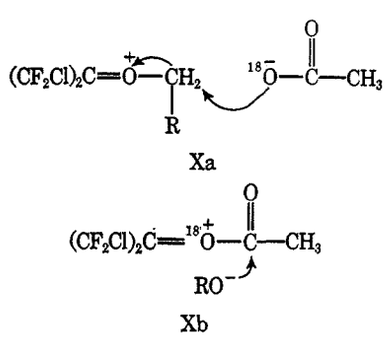
TABLE III

KINETICS OF DECOMPOSITION OF Ib IN DIOXANE

Temp,[a] °C	$k \times 10^{-5}$,[b] sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
177.2	4.74	27.1	−18.9
185.0	8.05		
197.2	18.1		

[a] Temperature variation $\leq \pm 0.2°$. [b] Determined by the method of least-squares analysis.

The entropy of activation is consistent with values obtained for reactions involving cyclic transition states[18] formed from neutral species and may reflect a crowded environment. These results also could be indicative of some charge separation in the transition state, suggestive of the ion pairs (X) or similar ionic pathways.



Xa

Xb

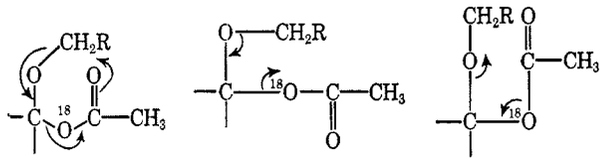
Ion pair Xb would give labeled fluoro ketone as we observed but would invoke a highly destabilized carbonium ion due to the six adjacent halogens. Since acetate is a better leaving group than alkoxide, Xa would be more reasonable. However, in view of the absence of scrambling of oxygen-18 which we would

(17) The solvent studies may have been complicated by the high reactivity of the fluoro ketones. For an excellent review of the reactions of fluoro ketones, see N. P. Gambaryan, E. M. Rokhlin, Y. V. Zeifman, C. Ching-Yun, and I. L. Knunyants, *Angew. Chem. Intern. Ed. Engl.*, **5**, 947 (1966).

(18) J. S. Meek and J. S. Fowler, *J. Org. Chem.*, **33**, 226 (1968); C. A. Kingsbury and D. J. Cram, *J. Amer. Chem. Soc.*, **82**, 1810 (1960), and references cited therein.

anticipate,[19] processes such as Xa are untenable. Further support for this view can be found in our studies on the decomposition of thio hemiketal esters (IV). The thio ketone and II would be the expected products from Xa; instead, only III and V were produced. Bimolecular reactions were also considered unlikely based on the labeling experiments and the fact that the decomposition was not significantly dependent upon concentration.

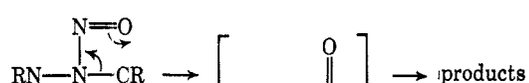
Finally, three cyclic intramolecular mechanisms which would account for this over-all reaction were considered. Path XI invokes a cyclic six-membered transition state similar to that proposed for normal ester pyrolysis and would require that the excess ^{18}O appear in the carbonyl function of the resultant ester.



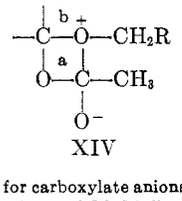
XI XII XIII

If mechanism XII were operative, the excess ^{18}O would be found in the ether oxygen of the ester, while the presence of the excess ^{18}O in fluoro ketone would be in accord with mechanism XIII as the correct pathway for these decompositions. The only mechanism consistent with the mass spectral data is XIII which invokes a cyclic four-membered transition state in which there is probably considerable charge separation in contrast to the nonfluorinated esters.[20] The ease of these decompositions[21] is attributed to the electronegative influence of the halogen atoms on the carbon–oxygen bonds, resulting in the generation of the fluoro ketone.

Mechanistically these pyrolyses are more analogous to the first step in the thermal elimination of N_2 or N_2O from nitroso and nitro amides which have been extensively studied by White,[22] Huisgen,[23] and Hey.[24]



We suggest that the transition state very likely resembles XIV with cleavage of bond a being well advanced.



XIV

Hemiketal esters derived from secondary alcohols decompose in a similar fashion to give II and III and apparently *via* the same mechanism. Pyrolysis of the tertiary alcohol derivatives (*e.g.*, *t*-butyl), however, gave III, olefin, and acid.[1] The effect of structure in determining the products of the decomposition of the hemiketal esters and their mechanistic implications are now under investigation.

Experimental Section

Boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 337 spectrophotometer and the esr studies were conducted with a Varian V-4502 instrument. Unless otherwise specified, gas chromatographic analyses were carried out using an F & M Model 700 or 720 instrument with either 0.125- or 0.25-in.-diam, 6-ft columns packed with 10% DC-200 on Chromosorb W.

Preparation of ^{18}O-Labeled Dichlorotetrafluoroacetone.—*sym*-Dichlorotetrafluoroacetone (100 g 0.5 mol) was placed in a 250-ml three-necked flask equipped with stirrer, condenser, thermometer, and addition funnel. The ^{18}O-enriched water,[5] 9.0 g (5.15% ^{18}O, 0.56% ^{17}O), was added dropwise with stirring over 15 min. After completion of the addition, the mixture was stirred for an additional hour and then distilled at atmospheric pressure. A 67% yield (44.0 g) of labeled ketone was obtained.

Preparation of the ^{18}O-Labeled Hemiketal Esters. 1-Benzyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—To 10.0 g (0.05 mol) of ^{18}O-labeled *sym*-dichlorotetrafluoroacetone was added dropwise 5.4 g (0.05 mol) of benzyl alcohol. After the addition was completed, 50 ml of anhydrous ethyl ether was added, and the reaction mixture was cooled to 5°. A solution of 3.9 g (0.05 mol) of acetyl chloride in 10 ml of ether was then added rapidly, followed by dropwise addition of a solution of 3.9 g (0.5 mol) of pyridine in 50 ml of ether. The mixture was then stirred overnight at room temperature. After washing with water and drying over anhydrous magnesium sulfate, the ether was distilled leaving a residue of 16 g of an oil. Distillation of the crude product gave 10.0 g (57%) of a water-white liquid, bp 100–102° (0.9 mm) [lit.[1] bp 106° (0.95 mm)].

1-Ethoxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—Using the procedure described above, a 0.05 *M* run gave 9.7 g (67%) of product, bp 45–46° (2.0 mm) [lit.[1] bp 42–43° (1.2 mm)].

Decomposition of ^{18}O-Labeled 1-Benzyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoromethyl Acetate.—A 5-g sample (0.014 mol) of the above ester was placed in a 10-ml distilling flask attached to a Berl saddle packed, vacuum-jacketed semimicro column and distillation head. The distilling flask was immersed in an oil bath heated to 230°, and 1.8 g (63%) of the fluoro ketone was collected (bp 46–50°). The column was removed, and 1.5 g (70%) of benzyl acetate was collected (bp 220–225°).[25]

Decomposition of ^{18}O-Labeled 1-Ethoxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—Using the procedure and equipment described above, 4.0 g (0.014 mol) of the above ester was decomposed at 130° over a 22-hr period to give 1.8 g (65%) of the fluoro ketone and 0.7 g (57%) of ethyl acetate,[21] bp 75–77°.

1-Benzylthio-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—To 39.8 g (0.2 mol) of *sym*-dichlorotetrafluoroacetone dissolved in 100 ml of anhydrous ether was added dropwise 24.8 (0.2 mol) of benzyl mercaptan with stirring and cooling. After the addition was completed, 15.7 g (0.2 mol) of acetyl chloride was added followed by dropwise addition of 15.8 g (0.2 mol) of pyridine in 100 ml of anhydrous ether. The reaction mixture was stirred overnight, filtered, washed with water, and dried over anhydrous magnesium sulfate. The solvent was removed with a rotary evaporator, and the residual oil was distilled. The first fraction distilling at 68–80° (0.5 mm) was benzyl thiolacetate[25] (35%) followed by 6.4 g of an intermediate fraction at 82–114° (0.4 mm) and 22.9 g (31%) of the product

(19) Equilibration of ^{18}O for carboxylate anions has been well documented. See, for example, H. L. Goering and M. M. Pombo, *ibid.*, **82**, 2515 (1960); H. L. Goering and J. F. Levy, *ibid.*, **86**, 120 (1964), and references cited therein. Exceptions have been noted in special cases involving bridged species [D. B. Denney and D. G. Denney, *ibid.*, **79**, 4806 (1957)] and when the generated carbonium ion is of high energy [W. E. Doering, M. Levitz, A. Sayigh, M. Sprecher, and W. P. Whelan, *ibid.*, **75**, 1008 (1953)].

(20) R. Taylor, G. G. Smith, and W. H. Wetzel, *ibid.*, **84**, 4817 (1962).

(21) Electronic effects of acyl substituents on the stability of esters has been demonstrated. See, for example, W. J. Bailey and J. J. Howitt, *J. Org. Chem.*, **21**, 543 (1956); G. L. O'Connor and H. R. Nace, *J. Amer. Chem. Soc.*, **75**, 2118 (1953). For the effect of alkyl substituents, see G. G. Smith, F. D. Bagley, and R. Taylor, *ibid.*, **83**, 3647 (1961); C. H. DePuy and R. E. Leavy, *ibid.*, **79**, 3705 (1957).

(22) E. H. White and L. A. Dolak, *ibid.*, **88**, 3790 (1966); E. H. White and C. A. Aufdermarsh, *ibid.*, **83**, 1179 (1961); E. H. White, *ibid.*, **77**, 6011 (1955).

(23) R. Huisgen, *Ann.*, **574**, 184 (1951); R. Huisgen and H. Reimlinger, *ibid.*, **599**, 161 (1956).

(24) D. H. Hey, J. Stuart-Webb, and G. H. Williams, *J. Chem. Soc.*, 4657 (1952).

(25) The ir spectrum and vpc retention times of this sample were identical to those of an authentic sample.

at 113–115° (0.5 mm): $n^{25}D$ 1.4991; λ_{max}^{film} 5.6 (C=O) and 8.2–9.0 μ (C—F, very broad and intense).

Anal. Calcd for $C_{12}H_{10}Cl_2F_4O_2S$: C, 39.4; H, 2.74; Cl, 19.4. Found: C, 39.5; H, 2.85; Cl, 19.3.

Decomposition of Benzylthio-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—Into a distillation flask attached to a vacuum-jacketed Vigreaux column was placed 7.3 g (0.02 mol) of the ester. The flask was immersed in an oil bath at 170°, and 3.4 g of the fluoro ketone, bp 42–48°, was collected. Vacuum was then applied and the oil bath was heated to 210° until the high-boiling component appeared to be rising in the column. The bath temperature was then adjusted so that a smooth distillation could be carried out. The benzyl thiolacetate[25] (2.5 g) was collected at 50–52° (0.1 mm), leaving a residue of 0.5 g shown to be the undecomposed starting ester by gas chromatography.

1-Ethylthio-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—To a solution of 39.8 g (0.2 mol) of *sym*-dichlorotetrafluoroacetone in 100 ml of anhydrous ether was added 12.4 g (0.2 mol) of ethyl mercaptan all at once with stirring and cooling. After stirring for 1 hr at room temperature, 15.7 g (0.2 mol) of acetyl chloride was added followed by dropwise addition of a solution of 15.8 g (0.2 mol) of pyridine in 50 ml of anhydrous ether. The reaction mixture was stirred overnight and quenched with water, and the organic layer was dried over anhydrous magnesium sulfate. Removal of solvent with a rotary evaporator left 48.2 g of an amber oil, which on distillation gave 46.2 g (76%) of a water-white liquid: bp 42–46° (0.15 mm); $n^{25}D$ 1.4352; λ_{max}^{film} 5.6 (C=O) and 8.2–9.2 μ (C—F, very broad and intense).

Anal. Calcd for $C_7H_8F_4O_2S$: C, 27.8; H, 2.64; Cl, 25.1. Found: C, 27.8; H, 2.57; Cl, 25.0.

Decomposition of 1-Ethylthio-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—A distilling flask attached to a vacuum-jacketed Vigreux column containing 9.1 g (0.03 mol) of ester was placed in an oil bath at 180–215°. The temperature of the bath was maintained so that smooth evolution of the fluoro ketone (1.6 g), bp 44°, occurred. An intermediate fraction (1.7 g), bp 65–90°, consisted largely of ethyl thiolacetate and a third fraction (2.3 g), bp 95–100°, was essentially pure ethyl thiolacetate.[25] The residue (2.1 g) was shown to be a 2:1 mixture of the starting material to ethyl thiolacetate by gas chromatography.

α-Methylbenzyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Propionate.—To a solution of 12.2 g (1.0 mol) of α-methyl benzyl alcohol in 100 ml of anhydrous ether was added 20.0 g (0.1 mol) of *sym*-dichlorotetrafluoroacetone with stirring and cooling. Propionyl chloride, 9.3 g (0.1 mol), was then added all at once followed by dropwise addition of 7.9 g (0.1 mol) of pyridine in 100 ml of anhydrous ether. The reaction mixture was stirred at room temperature for 6 hr. The solid was filtered, and the ethereal solution was washed with water and dried over anhydrous magnesium sulfate. The solvent was removed with a rotary evaporator, and the residual oil distilled to yield 33.0 g (87%): bp 89° (0.15 mm); $n^{20}D$ 1.4606; λ_{max}^{film} 5.6 (C=O) and 8.1–9.1 μ (C—F broad and intense).

Anal. Calcd for $C_{14}H_{14}Cl_2F_4O_3$: C, 44.6; H, 3.73; Cl, 18.8. Found: C, 44.9; H, 3.65; Cl, 18.6.

Decomposition of α-Methylbenzyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Propionate.—A distilling flask attached to a vacuum-jacketed Vigreaux column containing 5.4 g (0.015 mol) of ester was placed in an oil bath at 185°. The fluoro ketone (2.3 g) distilled smoothly over a 2-hr period. After the distillation had subsided, the bath temperature was lowered; vacuum was applied; and 1.8 g of α-methylbenzyl propionate[25] distilled at 64° (0.8 mm). The residue (approximately 0.5 g) was shown to be more undistilled decomposed ester, by ir spectroscopy and gas chromatography.

1-Phenethoxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Propionate.—This compound was made by the method described for Ib. Distillation of the crude product gave a 68% yield of colorless liquid: bp 87° (0.07 mm); $n^{20}D$ 1.4603; λ_{max}^{film} 5.65 (C=O) and 8.1–8.7 μ (C—F, very broad and intense).

Anal. Calcd for $C_{14}H_{14}Cl_2F_4O_3$: C, 44.6; H, 3.73; Cl, 18.8. Found: C, 44.3; H, 3.7; Cl, 18.6.

Decomposition of 1-Phenethoxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Propionate.—A distilling flask attached to a vacuum-jacketed Vigreaux column containing 5.0 g (0.013 mol) of the ester was placed in an oil bath at 140°. The fluoro ketone (2.2 g) distilled smoothly over a 4-hr period. After the distillation had subsided, the bath temperature was lowered; vacuum was applied; and 2.5 g of phenethyl propionate distilled at 104–105° (4.0 mm). There was no residue left.

1-Cyclopropylcarbinyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—This compound was made by the method described for Ib. Distillation of the crude product gave a 33% yield of water-white liquid: bp 55–56° (0.5 mm); $n^{25}D$ 1.4130; λ_{max}^{film} 5.6 (C=O) and 8.1–9.0 μ (C—F, very broad and intense).

Anal. Calcd for $C_9H_{10}Cl_2F_4O_3$: C, 34.5; H, 3.20; Cl, 22.7. Found: C, 34.4; H, 3.4; Cl, 22.4.

Decomposition of Cyclopropylcarbinyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—A 5-g sample (0.016 mol) of ester in a distilling flask attached to a vacuum-jacketed Vigreaux column was placed in an oil bath at 180°. The bath temperature was slowly raised to 225° over a 10-hr period. Four fractions[26] were collected containing 3.3 g of a mixture of fluoro ketone and cyclopropylcarbinyl acetate.[25,27] The residue (1.1 g) consisted of approximately a 3:5 mixture of cyclopropylcarbinyl acetate to starting ester and 0.5 g of black tar.

1-Allylcarbinyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—This compound was made by the method described for Ib. Distillation of the crude product gave a 40% yield of water-white liquid: bp 49° (0.2 mm); $n^{25}D$ 1.4072; λ_{max}^{film} 5.6 (C=O), 6.05 (C=C), and 7.8–9.0 μ (C—F, very broad and intense).

Anal. Calcd for $C_9H_{10}Cl_2F_4O_3$: C, 34.5; H, 3.20; Cl, 22.7. Found: C, 34.4; H, 3.1; Cl, 22.5.

Decomposition of 1-Allylcarbinyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl Acetate.—Six grams (0.019 mol) of esters in a distilling flask aattched to a vacuum-jacketed Vigreux column was placed in an oil bath at 180°. The bath temperature was slowly raised to 225° over a 7-hr period and maintained at 225–230° for the next 21 hr. Five fractions[26] were collected which contained 3.2 g of a mixture of fluoro ketone and allylcarbinyl acetate.[25,27] The residue (2.4 g) consisted of approximately 50% of allylcarbinyl acetate, 25% undecomposed ester, and 5% tar; the remainder was two other impurities.

Mass Spectrometric Data.—Measurements were made using a modified CEC 21-103 and an Atlas CH4-B mass spectrometer with an ionization energy of 70 eV. The samples were introduced at 50° into a metal inlet system, and the source temperature was 250°. The $C_3F_4ClO^+$ (*m/e* 163) fragment was used for the isotopic analysis of the fluoro ketone (III), which corresponds to the loss of Cl from the molecular ion. The absence of $C_3F_3{}^{37}Cl^+$ (*m/e* 167) from the untagged fluoro ketone eliminates the possibility of the *m/e* 163 peak being produced by a loss of $^{16}O + {}^{19}F$.

Kinetic and Solvent Studies.—Standard stock solutions approximately 0.1 *M* in Ib were prepared by weighing the appropriate quantity directly into 10-ml volumetric flasks and diluting to mark with solvent. Into a 5-ml ampoule was placed 0.5 ml of the standard solution, and the ampoule was sealed and immersed in a thermostated oil bath. The bath was controlled to ±0.1°. After a specified time period, the ampoules were removed and cooled in an ice bath, and the samples immediately analyzed by gas chromatography.

All vpc measurements were carried out on an F & M Model 700 gas chromatograph with dual thermal conductivity detectors using a 4 ft × 0.125 in. o.d. glass column packed with silicone oil DC-200 on Chromosorb G. Samples of 4 μl were injected with a syringe fitted with a Chaney adapter. Quantitative data were obtained by determining the decrease in peak area of Ib using a Disc integrator. All data represent an average of two or more separate determinations and were reproducible to ±2%.

Registry No.—IVa, 17497-44-8; IVb, 17528-33-5; α-methylbenzyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl propionate, 17497-45-9; 1-phenethoxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl propionate, 17497-57-3; 1-cyclopropylcarbinyloxy-

(26) Good separation of fluoro ketone from lower alkyl acetates is usually achieved with a packed column.

(27) A 6 ft × 0.125 in. o.d. stainless steel column packed with 10% diisodecyl phthalate on Chromosorb G was used isothermally at 110°. An authentic mixture of cyclopropylcarbinyl and allylcarbinyl acetates was conveniently separated with this column.

1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl acetate, 17497-46-0; 1-allylcarbinyloxy-1-(chlorodifluoromethyl)-2-chloro-2,2-difluoroethyl acetate, 17497-47-1.

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Total Synthesis of the Macrocyclic Lactone, Dideoxyzearalane

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Dideoxyzearalane, 2-(10-hydroxyundecyl)benzoic acid lactone (**2**), the simplest macrocyclic lactone having the same skeletal structure as the macrolide zearalenone (**1**) was totally synthesized. Condensation of 10-undecenoic anhydride with phthalic anhydride gave 3-(9-decenylidene)phthalide (**3**). The internal double bond of diene **3** was in effect reduced in alkali with sodium borohydride and the terminal double bond was hydrated with mercuric acetate and sodium borohydride to yield 3-(9-hydroxydecyl)phthalide (**5**). Saponification and catalytic hydrogenolysis of **5** gave 2-(10-hydroxyundecyl)benzoic acid (**7a**). (±)-Dideoxyzearalane (**2**) was obtained by lactonization of **7a** in benzene at high dilution with phosgene as cyclization agent. Optically active (+) **2** was obtained by hydrogenolysis of **10b**, the dibenzoxazolyl ether of zearalane (**10a**), derived from zearalenone (**1**). This (+) **2** and the totally synthesized (±) **2** are spectroscopically and chromatographically identical.

The structure of the macrolide zearalenone (**1**), the anabolic and uterotropic factor isolated from *Gibberella zeae*,[1] was established in these laboratories.[2] Total syntheses of zearalenone (**1**) and several derivatives have been reported.[3] The subject of this report is the total synthesis of dideoxyzearalane, 2-(10-hydroxyundecyl)benzoic acid lactone (**2**), the simplest macrocyclic lactone having the same skeletal structure as zearalenone (**1**).

The condensation of 10-undecenoic anhydride with phthalic anhydride in the presence of sodium acetate or sodium 10-undecenoate according to the procedure of Mowry, *et al.*,[4] gave 3-(9-decenylidene)phthalide (**3**). Saponification of **3** and reduction with sodium borohydride yielded 3-(9-decenyl)phthalide (**4**).

Markovnikov hydration of the terminal double bond of **4** *via* mercuric acetate addition followed by sodium borohydride demercuration by a modification of the procedure of Brown and Geoghegan[5] gave 3-(9-hydroxydecyl)phthalide (**5**). Alternatively, treatment of **3** with mercuric acetate followed by simultaneous demercuration and reduction in alkali with sodium borohydride yielded **5** directly. The crude product, however, was more complex and less readily purified when prepared in this manner. Hydration of **3** *via* formic acid addition[6] gave primarily the desired secondary alcohol resulting from normal Markovnikov hydration, but also appreciable amounts of other secondary alcohols.

Saponification of **5** yielded the salt of the dihydroxy acid **6** which was converted by catalytic hydrogenolysis[7] of the benzylic hydroxyl group into 2-(10-hydroxyundecyl)benzoic acid (**7a**). Methyl ester **7b** was prepared by reaction of **7a** with diazomethane.

In comparison with the relative ease of cyclization of several related hydroxy acids and esters,[3] the cyclization of hydroxy acid **7a** to lactone **2** proved unexpectedly difficult. Trifluoroacetic anhydride, dicyclohexylcarbodiimide, thionyl chloride, and *p*-toluenesulfonyl chloride all proved unsuitable as lactonization agents. Equally unsuccessful were attempted lactonizations of the hydroxy ester **7b** by transesterification employing aluminum isopropoxide, sodium ethoxide with molecular sieves, sodium triphenylmethoxide, sodium hydride, polymeric dibutyltin oxide, or *p*-toluenesulfonic acid as catalysts. Similar difficulties have recently been reported by Baker, Bycroft, and Roberts[8a] and by Musgrave, Templeton, and Munro[8b] in attempts to prepare di-O-methylcurvularin (**8**) by lactonization of hydroxy acid **9**.

Lactonization of hydroxy acid **7a** to (±)-dideoxyzearalane (**2**) was achieved using phosgene with triethylamine in benzene under high dilution conditions.[9] The major by-product appears to be a polymeric, cyclic ester (see below).

The structure of racemic dideoxyzearalane (**2**) was established by elemental analysis and direct comparison (nmr, ir, uv, and tlc) with an authentic sample of (+)-dideoxyzearalane (**2**). (+)-Dideoxyzearalane (**2**) was prepared by replacement of the phenolic groups of zearalane (**10a**) with hydrogen. This deoxygenation was accomplished by catalytic hydrogenolysis of **10b**, the dibenzoxazolyl ether of **10a**, by a modification of the method of Musliner and Gates.[10] Zearalane (**10a**) was obtained from natural zearalenone (**1**) as previously described.[2]

Hydrolysis of (+)-dideoxyzearalane (**2**) with sodium hydroxide in aqueous dimethyl sulfoxide yielded hy-

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