

## The Preparation and Reactions of Some Fluorinated Cyclobutane Carboxylic Acids

J. D. Park\* and F. E. Rogers\*\*

Department of Chemistry, University of Colorado Boulder, Colorado 80302, U. S. A.

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**Abstract** Diethyl itaconate was found to react with tetrafluoroethylene, trifluorochloroethylene, and 1, 1, -difluoro-2, 2-dichloroethylene quite readily at 180° to form 1-carboxy-2, 2, 3, 3-tetrahalo-cyclobutane ethanoic acid derivatives ( $\text{CX}_2\text{-CF}_2\text{-CH}_2\text{-C}(\text{COOEt})\text{-CH}_2\text{COOEt}$ , where X is Cl or F). Diethylcitraconate failed to yield any cycloaddition products. The physical and chemical properties of the above esters and their derivatives are characterized and compared with other similar ring compounds.

### Introduction

The literature on the synthesis of fluorinated cyclobutanes and cyclobutenes by cycloaddition reactions of fluorinated alkenes to alkenes and fluorinated alkene to alkyne has been well reviewed elsewhere.<sup>1-3</sup>

The present study was undertaken to study the cycloaddition of diethyl itaconic and diethyl citraconate with various fluoro-olefins.

### Discussion

Diethyl itaconate undergoes cycloaddition quite readily with tetrafluoroethylene, trifluorochloroethylene and 1, 1-difluoro-2, 2, dichloroethylene at 180° to form cyclobutane derivative of the type  $\text{CX}_2\text{-CX}_2\text{-CH}_2\text{C}(\text{COOEt})\text{-CH}_2\text{COOEt}$ . By an indirect method it is shown that the

structure of the adducts resulting from  $\text{CF}_2=\text{CFCl}$  and  $\text{CF}_2=\text{CCl}_2$  is probably  $\text{CX}_2\text{CF}_2\text{CH}_2\text{C}(\text{COOEt})\text{CH}_2\text{COOEt}$  (where X=F, Cl).

Fluorinated olefins of the structure,  $\text{CF}_2=\text{CX}_2$  thermally dimerize to form derivatives of cyclobutane. These fluorinated cyclic structures are generally more stable than their hydrocarbon analogs. The dimers  $\text{CF}_2\text{-CF}_2\text{-CF}_2\text{-CF}_2$  and  $\text{CF}_2\text{CF}_2\text{-CFCl-CFCl}$  did not equilibrate with their monomers at 300° to 500°. The increased stability of these compounds resides in the effect that fluorine has when substituted for the hydrogen atoms in an alkane. It is interesting to note that the bond strengthening effect of fluorine substitution seems to be restricted largely to the C-C bonds of a molecule and not the C-H or C-X bonds (where X=Cl, Br, I).

Thus, the presence of fluorine atoms at a C-C single bond appears to cause appreciable strengthening of that bond, while those bonds to Cl, Br and H are unaffected. Herein may lie the reason why fluorinated olefins form cyclobutane rings so easily; the two new C-C bonds formed are so energetically favored that any strain involved in the formation of the

\*At present, president of the Korea advanced Institute of Science, Seoul, Korea

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four membered ring is more than compensated for. How the presence of fluorine affects the energy of the surrounding bonds is also illustrated in the chlorination studies of Lacher, Park, et al.<sup>8</sup> who report the heat of chlorination of tetrafluoroethylene as 57.3 kcal./mole while this value for ethylene is 43.6. where this energy difference resides is not known, however, if the new bond dissociation energies<sup>6,7</sup> for  $\text{CF}_2\text{Cl}$  are correct, the C-Cl bonds in the product  $\text{CF}_2\text{ClCF}_2\text{Cl}$  are probably "normal." Again it is interesting to consider the kinetic studies on the dimerization of tetrafluoroethylene.<sup>5</sup> It was found that tetrafluoroethylene did not equilibrate with the cyclic dimer octafluorocyclobutane between 300° and 500°.

Thus, in this temperature range, and probably at lower temperatures, the cyclobutane ring is more stable than the olefin. Similarly, ethylene is less stable than cyclobutane but this strain is relieved by polymerization rather than cyclic dimerization. Therefore, in fluorinated compounds there must be an added "plus-factor" which makes cyclization so easy. This added incentive may reside in the fact that the formation of a fluorinated C-C bond gives rise to a stronger bond than the corresponding hydrogen-containing bond, so that stability and ease of formation are enhanced.

Why the fluorinated olefins prefer one dominant isomeric structure may be plausibly explained on the basis of the formation on the lowest energy diradical<sup>9</sup> when two similar or dissimilar olefins react to form the cyclobutane structure.

The structures of the adducts of diethyl itaconate and  $\text{CF}_2=\text{CF}_2$ ,  $\text{CF}_2=\text{CFCl}$  and  $\text{CF}_2=\text{CCl}_2$  were proved by an indirect route. The possibility existed that diethyl itaconate rearranged to diethyl citraconate which subsequently reacted with the olefin to form a structure,  $\text{CF}_2\text{CF}_2\text{CH}(\text{COOEt})\text{C}(\text{CH}_2)\text{COOEt}$ . This route was ruled out when it was observed that first, diethyl

itaconate could be recovered from the reaction mixture, and second, citraconic anhydride did not undergo cycloaddition with  $\text{CF}_2=\text{CCl}_2$  under conditions that gave the adduct with diethyl itaconate. The importance of the terminal  $\text{CH}_2=$  group is also illustrated by the failure of both diethyl maleate and fumarate to form cyclobutane derivatives with  $\text{CF}_2=\text{CF}_2$ . When 1,3-pentadiene was reacted with  $\text{CF}_2=\text{CF}_2$  at 100-125° only the terminal double bond was involved in the cyclization product  $\text{CH}_3\text{CH}=\text{CH}-\text{CH}-\text{CH}_2\text{CF}_2$ .<sup>3</sup> To check the susceptibility of 1,2-disubstituted ethylenes, butene-2 was reacted with  $\text{CF}_2=\text{CF}_2$  to give the addition product  $\text{CH}_3-\text{CHCH}(\text{CH}_3)-\text{CF}_2\text{CF}_2$  in only 5% yield while propene gave the corresponding cyclobutane in 72% yield.

With the possibility of a structure involving citraconic acid ruled out, it remained to prove whether the adduct possessed the structure  $\text{CF}_2\text{CX}_2\text{CH}_2\text{C}(\text{COOR})\text{CH}_2\text{COOR}$  or  $\text{CX}_2\text{CF}_2\text{CH}_2\text{C}(\text{COOR})\text{CH}_2\text{COOR}$  (X=Cl, F).

Some information as to the nature of the structure resulting from ethyl itaconate and olefins of the type  $\text{CF}_2=\text{CX}_2$  can be obtained from an examination of similar work. It was found that 1,3-butadiene undergoes cycloaddition with  $\text{CF}_2=\text{CFCl}$  to give a structure  $\text{CFCICF}_2\text{CH}_2\text{CH}-\text{CH}=\text{CH}_2$  wherein the  $\text{CF}_2$  group is adjacent to the  $\text{CH}_2$  group.<sup>9</sup> The preference for this arrangement was also supported by the investigation on the cyclization of this same unsymmetrical olefin with acrylonitrile. It was found that the inhibited thermal cycloaddition of these two olefins gave a product of the structure  $\text{CFCICF}_2\text{CH}_2\text{CHCN}$  and not the isomeric product  $\text{CF}_2\text{CFCICH}_2\text{CHCN}$ . The structure of the adduct was proven after the manner of Barney, et al.<sup>10</sup> by ring cleavage to  $\alpha, \alpha$ -difluoroglutaric acid.

Roberts<sup>11,12</sup> has shown that in the thermal

cycloaddition of phenylacetylene with  $\text{CF}_2=\text{CCl}_2$  or  $\text{CF}_2=\text{CFCl}$ , the CF group prefers the terminal carbon atom of the triple bond to form  $\overset{1}{\text{CX}_2\text{CF}_2\text{CH}=\overset{1}{\text{C}}-\phi$  (where X=F, Cl). Work in this laboratory also indicates that the proximity of the  $\text{CF}_2$  and  $\text{CH}_2$  groups in the final product is independent of the bond dipole of the unfluorinated olefin used. It was found that  $\text{CF}_2=\text{CFCl}$  reacted with both acrylonitrile<sup>13</sup> and vinyltrimethylsilane<sup>14</sup> to give a cyclobutane with the  $\text{CF}_2$  and  $\text{CH}_2$  groups adjacent on the ring. Since the dipole of the former olefin is  $\overset{+}{\text{C}}\text{H}_2-\overset{-}{\text{C}}\text{HCN}$  as shown by the addition of HX, it would be expected to give a different product than the latter olefin which has the opposite dipole,  $\overset{+}{\text{C}}\text{H}_2=\overset{-}{\text{C}}\text{HSiMe}_3$ . It would appear then that the direction of the bond dipole is not an important factor in the mechanism of cyclization under ordinary conditions.

When the olefins  $\text{CF}_2=\text{CFCl}$ , and  $\text{CF}_2=\text{CCl}_2$  are thermally dimerized separately only the "head-to-head" adducts are obtained.<sup>15</sup> This mode of addition also prevails when the olefins are codimerized. In light of this knowledge it would seem reasonable that the results obtained with one of these olefins could be extrapolated to include the other olefin. Thus, if  $\text{CF}_2=\text{CFCl}$  gave such a product as  $\overset{1}{\text{CFCICF}_2\text{CH}_2\text{CH-R}}$ , the olefin,  $\text{CF}_2=\text{CCl}_2$  would yield a similar structure  $\overset{1}{\text{CCl}_2\text{CF}_2\text{CH}_2\text{CH-R}}$ . In this investigation the dimer resulting from ethyl itaconate and  $\text{CF}_2=\text{CCl}_2$  was chosen for investigation.

From the foregoing discussion, a reasonable assumption is that the  $\text{CF}_2=\text{CCl}_2$  and  $\text{CF}_2=\text{CClF}$  dimers have the structure  $\overset{1}{\text{CX}_2\text{CF}_2\text{CH}_2\overset{1}{\text{C}}(\text{COOEt})\text{CH}_2\text{COOEt}$ , where X=F, Cl. Previous studies indicated that some halogens on cyclobutane are easily hydrolyzed with ring cleavage following. Roberts<sup>11</sup> reports that the acid hydrolysis of the allylic fluorines in  $\overset{1}{\text{CCl}_2\text{CF}_2\text{CH}=\overset{1}{\text{C}}\phi$  takes place readily at 100° in a period of eleven

minutes.

The product cyclobutenone was easily opened by warming with dilute alkali to give beta-dichloromethylcinnamic acid. We found that the nonallylic fluorine in 3,3-difluorophenylcyclobutane was also hydrolyzed with concentrated sulfuric acid in fifteen minutes.

Barney and Cairns<sup>10</sup> reported that 20 % sodium hydroxide was capable of hydrolyzing the  $\text{CF}_2$  group of  $\overset{1}{\text{CF}_2\text{CF}_2\text{CH}_2\text{CHCN}}$  to cause ring opening and the formation of  $\alpha, \alpha$  difluoroglutaric acid.

Subsequent work<sup>13</sup> indicated the  $\overset{1}{\text{CHCICF}_2\text{CH}_2\overset{1}{\text{C}}\text{HCN}}$  yielded to acid and basic hydrolysis to form  $\alpha, \alpha$ -difluoroglutaric acid. In the ozonolysis reaction of  $\overset{1}{\text{CFCICF}_2\text{CH}_2\text{CH-CH}=\text{CH}_2$ , the expected acid was not isolated, only that acid which resulted from hydrolysis and ring cleavage,  $\alpha, \alpha$ -difluoroglutaric acid.<sup>16</sup> Hydrolysis started when the ozonide was decomposed with slightly acidic hydrogen peroxide and completed with 10 % sodium hydroxide at room temperature.

In striking contrast to the aforementioned results, it was found that the compound,  $\overset{1}{\text{CCl}_2\text{CF}_2\text{CH}_2\overset{1}{\text{C}}(\text{COOEt})\text{CH}_2\text{COOEt}$  (I) was remarkably stable toward both acid and basic hydrolysis. The dimer (I) was treated with concentrated hydrochloric acid on a steam bath for a period of three days. The major product from the reaction was half ester and some di-acid. The stability of the second ester group toward hydrolysis supports the structure (I) which shows that the carboxy on the tertiary carbon is somewhat hindered and hence less reactive than the more available ester group. The structure of the half ester was supported by a neutralization equivalent determination, elemental analysis and the appearance of two types of carbonyl absorption in the infrared spectrum. The diester (I) was treated with an excess of 10 % alcoholic sodium hydroxide:

at reflux. When the reaction was complete as signified by a constant titer of standard acid, the di-acid was isolated in 93 % yield. In a further attempt to cleave the di-acid  $\text{CCl}_2\text{CF}_2\text{CH}_2\text{C}(\text{COOH})\text{CH}_2\text{COOH}$  was heated at  $190^\circ$  with concentrated sulfuric acid for seven hours. The effluent gases were collected in a water bubbler. At the completion of reaction the water gave a positive test for both fluoride and chloride ions but 80 % of the starting di-acid was recovered from the reaction mixture. It is evident, therefore, that the decomposition of the acid proceeds at a very slow rate under these drastic conditions. The unusual stability of this compound as compared to similar molecules may be a function of the protective shielding provided by the neighboring  $-\text{CH}_2\text{COOH}$ , and  $-\text{COOH}$  group; the lack of an alpha-hydrogen or the inherent stability of  $\text{CCl}_2$  over a  $\text{CFCl}$  or  $\text{CF}_2$  structure. Barney et al.<sup>10</sup> felt that the  $\alpha$ -hydrogens were important in this elimination-degradation process and proposed a mechanism expected for such a haloacid in which the driving force for the reaction is the formation of a carbanion by abstraction of a proton ultimately resulting in the formation of  $\alpha, \alpha$ -difluoroglutaric acid.

In the diacid,  $\text{CCl}_2\text{CF}_2\text{CH}_2\text{C}(\text{COOH})\text{CH}_2\text{COOH}$  no alpha hydrogen is present, hence elimination is prohibited.

In a further effort to elucidate the structure of the diacid  $\text{CCl}_2\text{CF}_2\text{CH}_2\text{C}(\text{COOH})\text{CH}_2\text{COOH}$  an attempt was made to oxidize off the carboxymethyl side chain.

Oxidation under conditions with almost neutral permanganate yielded no isolable product although only 54 % of the starting material was recovered.

When the di-potassium salt of the above diacid was heated in ethylene glycol at  $180^\circ$ , some carbon dioxide was evolved but only a

black solid was isolated.

The Hunsdiecker reaction was successful when applied to the half ester,  $\text{CCl}_2\text{CF}_2\text{CH}_2\text{C}(\text{OOEt})\text{CH}_2\text{COOH}$ . This half ester was chosen in preference to the alternate because a literature survey revealed carboxy groups on tertiary carbons other than bridgehead carbon do not give normal products, thus silver pivalate gave no products when reacted with bromine<sup>17</sup> and triphenylacetic gave trityl alcohol in one case and trityl triphenylacetate in another.<sup>18</sup> The product gave the correct analysis for the compound,  $\text{CCl}_2\text{CF}_2\text{CH}_2\text{C}(\text{CH}_2\text{Br})\text{COOEt}$ . Since the structure of the bromide depends on that of the half ester used, a study of the carbonyl absorptions was made. The assignments as tabulated below give further support to the proposed structure for the half ester.

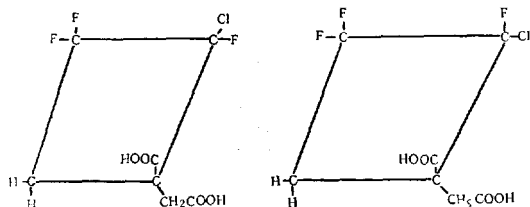
Compound		Carbonyl Absorption( $\mu$ )	
$\begin{array}{c} \text{CF}_2-\text{CCl}_2 \\   \\ \text{CH}_2-\text{CCOOEt} \\   \\ \text{CH}_2\text{COOEt} \end{array}$	I	5.68 (shoulder)	5.72
$\begin{array}{c} \text{CF}_2-\text{CCl}_2 \\   \\ \text{CH}_2-\text{CCOOEt} \\   \\ \text{CH}_2\text{COOH} \end{array}$	II	5.68	5.82
$\begin{array}{c} \text{CF}_2-\text{CCl}_2 \\   \\ \text{CH}_2-\text{CCOOEt} \\   \\ \text{CH}_2\text{Br} \end{array}$	III	5.68	

One carbonyl peak has remained unchanged in all the reactions. The proximity of a negative group to a carboxy group tends to increase the frequency<sup>19</sup> of absorption for that carbonyl group. On this basis, the carboxy group directly attached to the ring is assigned the constant absorption peak at 5.68 and the carboxy group which is shielded from the ring by a methylene group is assigned the 5.82 micron peak in the half ester (II). These con-

clusions are in accord with the notion that the most accessible ester group was hydrolyzed when the diester (I) was treated with concentrated hydrochloric acid.

An effort was made to determine if the dimer resulting from  $\text{CF}_2=\text{CFCl}$ , which is assigned the structure  $\text{CFCICF}_2\text{CH}_2\text{C}(\text{COOEt})\text{CH}_2\text{COOEt}$  (IV), was also stable to hydrolytic reaction. The cyclic dimer IV, was heated on a steam bath with concentrated hydrochloric acid for three days. Two dibasic acids were isolated, one melting at  $179.5\text{--}180^\circ$ , and the other at  $119\text{--}122^\circ$ . The neutralization equivalent and elemental analysis for both acids agreed with the structure of the expected diacid,  $\text{CFCICF}_2\text{CH}_2\text{C}(\text{COOH})\text{CH}_2\text{COOH}$ .

Since this acid has two asymmetric carbon atoms the products isolated are evidently geometrical isomers. The diagram below illustrates these isomers.



No attempt was made to relate the structures and melting points. Gas chromatography using a silicone oil column failed to resolve the geometric diesters.

When the diester (IV) was subjected to prolonged hydrolysis with 10% ethanolic sodium hydroxide only a mixture of the geometrical diacids was obtained. While the resulting diacid was not treated for a prolonged period with hot concentrated sulfuric acid, the somewhat milder conditions indicate that the acid is reasonably stable.

The cyclic dimer,  $\text{CF}_2\text{CF}_2\text{CH}_2\text{C}(\text{COOEt})\text{CH}_2\text{COOEt}$  was reduced to the corresponding diol

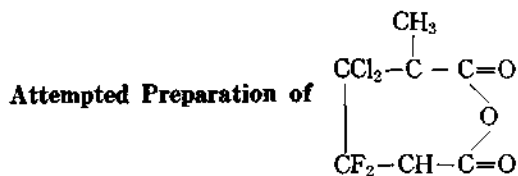
with lithium aluminum hydride.

Supporting evidence for the assigned structures of the chlorocyclobutane derivatives arises from the observation that no dehydrochlorination took place when the cyclic dimers were treated with alkali as would be expected if they had the structure,  $\text{CF}_2\text{-CX}_2\text{CH}_2\text{C}(\text{COOR})\text{CH}_2\text{COOR}$ .

### Experimental Results

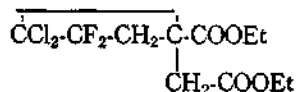
**Ethyl Itaconate** Itaconic acid (130 grams, 1 mole), absolute ethanol (200 grams, 4.35 mole) and dry benzene (500ml.) were placed in a one liter flask fitted with a thermometer and a Dean-Starke moisture trap. The solution was heated to reflux. The azeotrope (water-ethanol-benzene) was drawn off periodically. The reaction was discontinued when the azeotrope stopped collecting in the moisture trap. Complete esterification required the formation of two moles of water. However, a total of about 80ml. was collected in the moisture trap indicating that this liquid contained ethanol and benzene. The solvent was removed at atmospheric pressure until the pot temperature rose to  $110^\circ$ , then the remainder was distilled in vacuo. Low temperature prevented the rearrangement of the itaconate to citraconate. The diester (164 grams, 88%) was collected at a b. p.  $110.5$  (13mm),  $n_D^{20}$  1.4362 (lit.,  $n_D^{24}$  1.4367, b. p.  $111^\circ$  (13mm)).

**Citraconic Anhydride** The procedure is that of Shriner et al. wherein itaconic acid (166 grams, 1.28 mole) was heated at  $180\text{--}185^\circ$  until no water collected in an attached Dean-Starke moisture trap. The elapsed time was



three hours. Distillation gave pure citraconic anhydride, b. p. 121–122° (43mm),  $n_D^{25}$  1.4690 (lit., b. p. 105–110° (23mm),  $n_D^{24.2}$  1.4697). Citraconic anhydride (14 grams, 0.125mole) and  $\text{CF}_2=\text{CCl}_2$  (13 grams, 0.102 mole) were heated in a combustion tube with a small amount of terpene "B" inhibitor for twelve hours at 125°, eight hours at 150°, three hours at 165° and finally twelve hours at 180°. Only starting anhydride was recovered.

## Preparation of

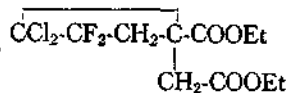


$\text{CF}_2=\text{CCl}_2$  (40 grams, 0.3 mole), ethyl itaconate (35 grams, 0.185mole) and terpene "B" inhibitor (0.5 ml.) were sealed in an evacuated pyrex combustion tube. The tube was heated in a furnace at 180° for fourteen hours. The colored product was vacuum distilled to yield unreacted ethyl itaconate (4 grams) and the cyclobutane diester (40.2 grams, 76%), b. p. 122°C. (4.3 mm),  $n_D^{25}$  1.4436,  $d_4^{25}$  1.3300,  $MR_D$ : calcd. 64.04, obsd. 63.84.

Anal.: Calcd. for  $\text{C}_{11}\text{H}_{14}\text{Cl}_2\text{F}_2\text{O}_4$ : C, 41.39; H, 4.38; Cl, 22.24.

Found: C, 41.44; H, 4.49; Cl, 21.95

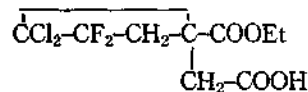
## Acid Hydrolysis of



Into a flask fitted with a stirrer, thermometer and a reflux condenser were charged the diester (7.5 grams, 0.0235 mole) and concentrated hydrochloric acid (60 ml.). The heterogeneous system was heated 100–105° with rapid stirring. After one day, more hydrochloric acid (conc. 25 ml.) was added. The solution was still heterogeneous but the organic layer had darkened. The reaction was discontinued after three days. The organic layer gradually solidified on solution was filtered on a sintered-glass funnel and the precipitate washed with a small amount of

water. The collected crystals were air-dried to constant weight (5 grams), m. p. 69–77°. Two recrystallizations from Skelly "C" gave white crystals (2.1 grams), m. p. 77.2–78°. These water insoluble crystals were soluble in 10%  $\text{NaHCO}_3$  indicating an acid. This solid was identified as the half ester on the basis of neutralization equivalent, analysis, and infrared spectrum.

Neutralization Equivalent: Calcd. for:



Calcd.: 291.2. Found: 285.5

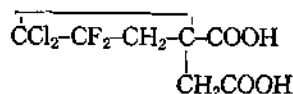
Anal.: Calcd. for  $\text{C}_9\text{H}_{10}\text{Cl}_2\text{F}_2\text{O}_4$ : C, 37.12; H, 3.46; F, 13.05; Cl, 24.38.

Found: C, 36.94; H, 3.65; F, 13.20; Cl, 24.45.

The infrared spectrum showed two types of carbonyl groups; a peak at 5.68 microns was assigned to the -COOEt groups attached to the ring and another peak at 5.82 microns which was assigned to the carbonyl stretching in the -CH<sub>2</sub>COOH group.

The original acid solution from the hydrolysis was diluted with water and extracted four times with fifty milliliter portions of ether. Evaporation of the ether yielded an oil which gradually crystallized over a two day period. These crystals (1.95 grams) were recrystallized from hot toluene to yield a white solid (1.35 grams), m. p. 149.5–150°. Another recrystallization from hot toluene gave a solid dibasic acid, m. p. 150–150.3°.

Neutralization Equivalent: Calcd. for:



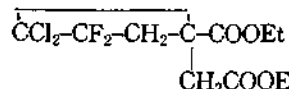
Calcd.: 131.5. Found: 134.1.

Anal.: Calcd. for  $\text{C}_7\text{H}_6\text{Cl}_2\text{F}_2\text{O}_4$ : C, 31.95; H, 2.30; F, 14.44; Cl, 26.98.

Found: C, 31.84; H, 2.26; F, 14.22;  
27.23.

The above reaction was repeated. Heating and stirring were carried out for two days. Only starting diester, the half ester and the diacid were isolated.

#### Basic Hydrolysis of

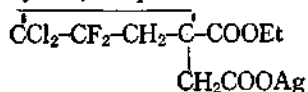


A solution of U. S. P. potassium hydroxide (28 grams, 0.5 mole) in 60 % ethanol (300 ml.) was placed in a flask with the diester (30 grams, 0.094 mole). The solution was heated at reflux on a steam bath until the titer a one milliliter aliquot of the reaction mixture was constant. At this point, no further hydrolysis was taking place, so the reaction was discontinued. The titrations were performed with standard HCl, however any dilute acid could be used since this technique is only qualitative.

The ethanol was removed on a steam bath and the aqueous solution acidified to a pH of 2-3 with 10 % sulfuric acid.

The acidified solution was extracted five times with 50 ml. portions of ether. The combined extracts were dried over "Drierite" and the ether removed on a steam bath. A colored oil remained which gradually crystallized on standing. The crude diacid (23 grams, 92.7 %) melted at 143-145°. Recrystallization from hot toluene gave white crystals, m. p. 140-150°.

#### The Reaction of



with bromine (Hunsdiecker) The acid ester (11 grams, 0.038 mole) was taken up in acetone and an excess of alkali-free, freshly prepared silver oxide was added. The slurry was heated gently for fifteen minutes and allowed to stand for one hour. The solution was filtered to remove the unreacted silver oxide. Acetone was evaporated on the steam bath leaving the solid

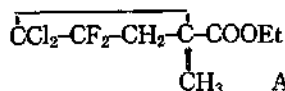
silver salt of the acid ester. The pale yellow solid was dried to constant weight in a vacuum-desiccator at 90°, to give 13.6 grams (91 %).

Bromine (7 grams, 0.044 mole) and anhydrous carbon tetrachloride were charged to a flask fitted with a reflux condenser and an air-powered stirrer. The silver salt was placed in an Erlenmeyer flask connected to a neck of the flask via a piece of rubber tubing. A small amount of the silver salt was added to the stirred bromine solution at room temperature. When carbon dioxide started to evolve the remainder of the silver salt was added at such a rate so as to maintain a moderate flow of the gas through a bubbler. After addition of the salt was complete, the slurry (silver bromide formed a slurry during reaction) was heated at 50° until no more gas was evolved. The solid, collected in a Soxhlet thimble, was extracted with 100 ml. of carbon tetrachloride\* for two hours. The extract was combined with the filtrate and washed with 5 % sodium hydroxide to remove bromine and any acid formed, then extracted twice with water. The carbon tetrachloride solution was dried over "Drierite" and distilled. The bromide  $\text{CCl}_2\text{CF}_2\text{CH}_2\text{C}(\text{CH}_2\text{Br})\text{COOEt}$  (6.6 grams, 59 %) was collected over the boiling range of 109-112° at 13mm; most of this fraction distilled at 110° with  $n_D^{25}$  1.4678 and  $d_4^{25}$  1.6137,  $MR_D$ : calcd. 56.10, obsd. 55.83.

Anal.: Calcd. for  $\text{C}_8\text{H}_9\text{BrCl}_2\text{F}_2\text{O}_2$ : C, 29.45;  
H, 2.76.

Found: C, 29.64; H, 2.62

#### Attempted Preparation of

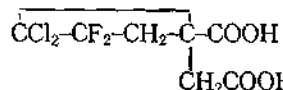


A solution of potassium borohydride (1 gram, 0.018 mole) in 75 % (volume) methanol (40 ml.) was placed in a

\* The anhydrous solvent was obtained by distillation of the technical grade of carbon tetrachloride and discarding the forerun (a carbon tetrachloride-water azeotrope).

metro-ware flask fitted with a dropping funnel, stirrer and a condenser. This solution was warmed until hydrogen began to evolve, then 1-bromomethyl-1-carbomethoxy-2,2-dichloro-3,3-difluorocyclobutane (6 grams, 0.018 mole) in methanol (10 ml.) was added over a period of five minutes. The reaction mixture became warm and some refluxing took place. The solution was allowed to stir overnight. The reaction mixture was diluted with water and extracted three times with 50 ml. portions of ether. The extracts were combined and extracted with water, then dried over "Drierite." Distillation yielded only the starting bromide (3.5 grams).

#### Action of Concentrated Sulfuric Acid on

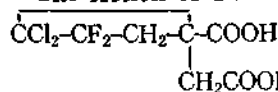


In an attempt to hydrolyze the halogens of the diacid with concentrated sulfuric acid as Roberts et al.<sup>11,12</sup> have done, three different sets of conditions were chosen; twenty-five minutes at 95°, fourteen hours at 155°, and seven and one-half hours at 190°. The latter, the most vigorous, will be described in detail.

The crude diacid (m. p. 147-149°, 4.1 grams) and concentrated sulfuric acid (30 grams) were placed in a flask fitted with a condenser and heated in an oil bath at 190° for seven and one-half hours. The effluent gases were led through water. After one hour some gas began to evolve slowly. At the end of the reaction, the water gave a positive qualitative test for both chloride and fluoride ions thus indicating that some hydrolysis and/or decomposition had taken place. The acid solution was made up to 200 ml. with water and extracted five times with 75 ml. portions of ether. The ether solutions were combined and dried over "Drierite." Evaporation of the ether left an oily residue which gradually solidified, (3.45 grams, m. p.

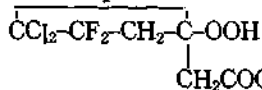
141-145°). A second recrystallization from hot toluene gave the starting diacid, m. p. 146-147.5°. This solid did not depress the melting point of an authentic sample.

#### The Action of Potassium Permanganate on



The diacid (5 grams, 0.016 mole), and a solution of potassium hydroxide (assay 87.4%, 1.22 grams, 0.018 mole) in water (50 ml.) were placed in a flask fitted with a condenser. Potassium permanganate (4 grams, 0.025 mole) in water (150 ml.) was added over a period of one hour. The purple solution was heated at 60° for twenty-four hours and for seven hours at reflux. The purple color at this stage had completely disappeared. The manganese dioxide was removed by filtration, the filtrate was colorless. The filtrate was acidified with 10% sulfuric acid and extracted four times with 50 ml. portions of ether. The combined extracts were dried over "Drierite" and the ether then removed. A colorless oil remained which gradually crystallized on standing to yield white crystals (2.7 grams), m. p. 146.5-147.5°. A rexed melting point with pure starting diacid showed no depression.

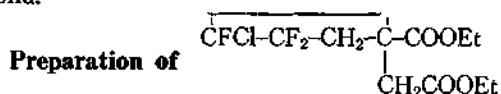
#### Attempted Decarboxylation of



The diacid (18 grams, 0.068 mole) was taken up in water and titrated with standard potassium hydroxide to the phenolphthalein end point. The water was evaporated leaving the di-potassium salt (22.8 grams, 98%). The dry salt and ethylene glycol were placed in a flask fitted with a condenser. The exit tube of this condenser was connected first to an air-cooled trap, then to a dry ice-acetone cooled trap. The mixture was heated to 180-190° and held for one day. At 150° some gas evolved which was not condensed in the dry ice trap (carbon dioxide). The only volatile:



products collected were removed from the air-cooled trap; these were water and glycol. The remaining glycol was azeotropically distilled with chlorobenzene leaving a black, intractable solid.

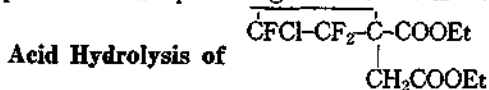


Ethyl itaconate (59 grams, 0.33 mole),  $\text{CF}_2=\text{CFCI}$  (43 grams, 0.43 mole) and terpene "B" inhibitor (1 gram) were heated together in a sealed tube at  $190^\circ$  for fifteen hours. Hydrogen fluoride vapors emanated from the tube on opening. The reaction mixture was vacuum distilled and the fraction, boiling at  $75\text{--}95^\circ$  (0.38 mm), collected. Redistillation of this fraction yielded the cyclobutane diester (35.5 grams, 36.2%), b. p.  $91^\circ$  (1.5 mm),  $n_D^{25}$  1.4182,  $p_D^{25}$  1.2804,  $\text{MR}_D$ : calcd. 59.59, obsd. 59.53,

Anal.: Calcd. for  $\text{C}_{11}\text{H}_{14}\text{ClF}_3\text{O}_4$ : C, 3.63; H, 4.66; Cl, 11.71,

Found: C, 43.30; H, 4.85; Cl, 11.53,

The infrared spectrum indicated strong  $\text{C}=\text{O}$  absorption and no  $\text{C}=\text{C}$  bond. Gas chromatography using a silicone column failed to separate the two possible geometrical isomers.



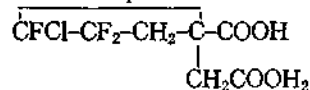
The diester (6.9 grams, 0.023 mole) and concentrated hydrochloric acid (70 ml.) were placed in a flask. The heterogeneous mixture was stirred on a steam bath for three days. At the end of this time a small amount (ca 0.5 gram) of an organic liquid remained undissolved. The aqueous layer was diluted with water and extracted four times with fifty milliliter portions of ether. The combined extracts were dried over "Drierite." Evaporation of the ether left an oily residue which gradually crystallized on standing overnight. This solid was recrystallized from hot toluene. Air-drying overnight gave a solid which started to melt at  $122^\circ$  and

cleared at  $150^\circ$ .

The white crystals (2.3 grams) were taken up in toluene (20 ml.), shaken for fifteen minutes and filtered. This material was air-dried (1.5 grams) and then taken up in hot toluene. On standing at room temperature, some crystals deposited which were filtered and air-dried (0.8 gram), m. p. ca  $168\text{--}175^\circ$ . The mother liquor was concentrated by evaporation and allowed to stand at room temperature for a day. Some crystals (0.34 gram) deposited which were filtered and air-dried, m. p.  $118\text{--}125^\circ$ .

The high melting solid was recrystallized from warm toluene to yield a solid, m. p.  $172\text{--}178^\circ$ . This solid was taken up in hot water. The second crop of crystals which deposited after cooling in the ice box ( $1^\circ\text{C}$ .) were collected and air dried, m. p.  $179.5\text{--}180^\circ$ .

Neutralization Equivalent: Calcd. for:



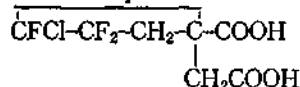
Calcd.: 123.2. Obsd.: 127.3.

Anal.: Calcd. for  $\text{C}_7\text{H}_6\text{ClF}_3\text{O}_4$ : C, 34.09; Cl, 14.40.

Found: C, 34.45; Cl, 14.36.

The low melting solid ( $118\text{--}125^\circ$ ) was recrystallized from Skelly "C" -ethanol mixture. The solid was vacuum dried, m. p.  $115.5\text{--}117.5^\circ$ . The mother liquor yielded crystals, m. p.  $119\text{--}122^\circ$ . This latter material showed  $-\text{COOH}$  absorption in the infrared spectrum. Repeated recrystallizations would not give a constant melting solid. Some of the crystals, m. p.  $119\text{--}122^\circ$ , were used for element analysis and a neutralization equivalent.

Neutralization Equivalent.: Calcd. for:



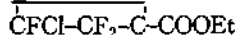
Calcd.: 123.2. Obsd.: 122.9

Anal.: Calcd. for  $\text{C}_7\text{H}_6\text{ClF}_3\text{O}_4$ : C, 34.09; H, 2.45; Cl, 14.40

Found: C, 35.36; H, 3.06; Cl, 14.62.

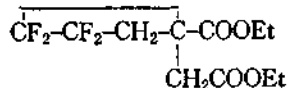
While this low melting material bears a close resemblance to the solid, m. p. 182°, its impurity as manifest in the carbon analysis makes any definitive statement impossible, however the possibility of cis-trans isomers must be considered.

#### Alkaline Hydrolysis of



$\text{CH}_2\text{COOEt}$  The diester (7 grams, 0.0285 mole), sodium hydroxide (U. S. P. 5 grams) and 60 % ethanol (50 ml.) were placed in a flask fitted with a condenser and refluxed on a steam bath for eighteen hours. A distillation head was attached to the flask and the ethanol removed. The aqueous solution was acidified with 10 % sulfuric acid and extracted five times with twenty-five ml. portions of ether. The combined ether extracts were set on a steam bath and the ether removed. An oily liquid remained which gradually crystallized during a three hour period. The white crystals were dried yielding the crude mixture of diacids (5.2 grams, 91.5 %), m. p. 122-145°. Since a similar mixture of acids was separated in the acid hydrolysis experiment no further work was done on this batch.

#### Preparation of



Ethyl itaconate (38 grams, 0.21 mole), terpene "B" (0.5 gram) and hydroquinone (0.2 gram) were charged into a pyrex combustion tube. The tube was cooled in liquid nitrogen and evacuated, then tetrafluoroethylene (20 grams, 0.2 mole) was distilled in. The tube was sealed and heated in a furnace at 190° for fifteen hours. The reaction product was brownish-red with a greenish-blue fluorescence in visible light and a light blue fluorescence in ultraviolet light. It should be noted that the inhibitors terpene "B" and hydroquinone also fluoresce.

Rectification yielded the product (41.8 grams, 72 %) which contained some entrained ethyl itaconate as indicated by the infrared spectra.

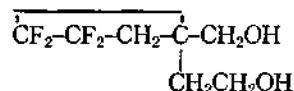
To remove any starting ester the product was treated with bromine (1 gram) in carbon tetrachloride and allowed to stand for two hours at room temperature. The red solution was washed once with sodium thiosulfate then twice with water. The organic material was dried over "Drierite" and transferred to a flask with a little anhydrous ether and distilled. The pure diester was collected at 73.2-73.8° (1.1mm) with  $n_D^{25}$  1.3942,  $d_4^{25}$  1.2423,  $M_R^D$ : calcd. 54.50, obsd. 55.08, saponification equivalent: calcd. 143.0, obsd. 142.8.

Anal.: Calcd. for  $\text{C}_{11}\text{H}_{14}\text{F}_4\text{C}_4$ : C, 46.15; H, 4.92

Found: C, 45.93; H, 5.11.

The infrared spectrum indicated strong C=O absorption, C-H but no C=C peak. This pure material does not fluoresce in ultraviolet or visible light.

#### Preparation of



2, 2, 3, 3-Tetrafluoro-1-carbomethoxy-1-carbomethoxymethylcyclobutane (19.2 grams, 0.063 mole) in anhydrous ether (100 cc.) was added to a solution of lithium hydride (4.5 grams, 0.12 mole) in ether (200 cc.) over a period of two hours. The slurry was stirred overnight. Water (75 cc.) was added carefully and the solution filtered to remove the oxides. The aqueous layer was extracted continuously for sixteen hours with ether. The combined ether solutions were dried over "Drierite" and then the ether was removed. A clear, very viscous residue remained which could not be fractionated in a long path column. Vacuum distillation through a short path column gave the crude glycol (5 grams), reflux b. p. 198° (625mm),  $n_D^{25}$  1.4128. The 3,5 dinitrobenzoate derivative was prepared for analysis in

the same manner as that for  $C_3F_7CH_2CH(OH)-CH_2CH$ . The bis-(3,5-dinitrobenzoate) of the glycol melted at 122.5-123.5°.

Anal.: Calcd. for  $C_{21}H_{14}F_4N_4O_{12}$ : C, 42.55;  
H, 2.37; F, 12.88  
Found: C, 42.60; H, 2.51; F, 12.70.

#### Acknowledgment

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