[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AT THE OHIO STATE UNIVERSITY]

Difluoromalonic Derivatives from Difluoropentane

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To prepare a fluorinated compound containing an oxygenated function, we have consistently introduced the fluorine atoms in a non-oxygenated compound first, then created the oxygenated function afterwards. In so doing, we have frequently been able to take advantage of the directing power of the fluorinated cluster. The syntheses of CF_3CO_2H, and of $HO_2C(CF_2)_nCO_2H$, are examples of this procedure.[1,2]

We have now prepared difluoromalonic acid and some of its derivatives by the following sequence. Diethyl ketone was transformed into 3,3-difluoropentane; due to the directing effect of the CF_2 group away from the alpha hydrogen atoms,[3] moderate chlorination gave preferentially the 1,5-dichloro derivative $CH_2ClCH_2CF_2CH_2CH_2Cl$. Aided by the stronger acidity of the hydrogen atoms in 2 and 4 positions, the removal of two molecules of hydrogen chloride proved quite easy and yielded a diene $CH_2{=}CHCF_2CH{=}CH_2$. Alkaline permanganate oxidation of the diene gave difluoromalonic acid which, although fairly stable, was nevertheless handled as its di-ester and characterized as its crystalline diamide.

In the process of chlorinating 3,3-difluoropentane, the various mono- and di-chloro derivatives were isolated and characterized; their relative abundances were determined, and agreed with the expectations based on the directing influence of the CF_2 group. All chlorides beyond the dichlorinated stage were further treated for complete transformation into the perchlorinated form $C_2Cl_5CF_2C_2Cl_5$, a well crystallized product. From this, the non-conjugated pentadiene $CCl_2{=}CClCF_2CCl{=}CCl_2$ was prepared, and its formula demonstrated by oxidation to difluoromalonic acid. It is proposed to use this diene as an intermediate toward $CF_2{=}CFCF_2CF{=}CF_2$, a perfluorinated non-conjugated diene, the polymerization of which may offer new characteristics.

Experimental

Synthesis of $C_2H_5CF_2C_2H_5$.—Diethyl ketone was treated with phosphorus pentachloride to obtain a mixture of $C_2H_5CCl_2C_2H_5$ and $C_2H_5CCl{=}CHCH_3$. Since the latter is more advantageous for the subsequent treatment with hydrogen fluoride, operations were adjusted to obtain as favorable a ratio as possible. In a five-liter, three-necked flask maintained at 12 to 14° by a water-bath was placed 1342 g. (6.45 moles) of phosphorus pentachloride; this was agitated by a Hershberg stirrer driven by a motor strong enough to plow through the dry material. From a dropping funnel, 500 g. (5.8 moles) of diethyl ketone was fed over a period of two to two and one-half hours; the mixture was stirred overnight, then progressively brought to boiling under constant stirring, and maintained at the boiling point for forty-five minutes. After cooling, the reaction mixture was delivered dropwise into vigorously boiling water, held in a five-liter, three-necked flask. Superheated steam was supplied continuously to the bottom through one neck, and the vapors were led from the other neck to a condensing system adequately cooled. The organic material steamed over was decanted, neutralized, and dried to yield 582 g. of product. Distillation gave 439 g. b. 87–95° ($CH_3CH_2CCl{=}CHCH_3$) and 110 g. b. 127–135° ($C_2H_5CCl_2C_2H_5$). The average yield was 73% of chloropentene, and 14% of dichloropentane or 88% of usable material. The dichloride was transformed into more chloro-olefin by treating its boiling alcoholic solution (2.4 moles in 600 cc.) with a solution of 2.6 moles of potassium hydroxide in 700 cc. of alcohol; this treatment gave a 36% conversion and a 55% recovery of unreacted dichloride, which was treated again.

The chloro-olefin was treated with hydrogen fluoride in a manner which would minimize the formation of the mere addition product ($C_2H_5CClFC_2H_5$) in favor of the desired $C_2H_5CF_2C_2H_5$. In a 1500-ml. steel vessel were placed 700 g. (6.7 moles) of chloro-olefin cooled to −80°, then 660 g. (33 moles) of liquefied hydrogen fluoride also cooled to −80°. A 45-cm. length of pipe bearing the customary thermometer well, pressure gage, and releasing needle valve was screwed on; the pipe was cooled by means of a sleeve through which cold water was passed. Warming to room temperature caused the pressure to rise rapidly to 12 atmospheres, due to formation of hydrogen chloride. This was reduced to 8 atmospheres by slow release of the gases through a wash train. The temperature was progressively raised to 60° and held there as long as the pressure could be kept around 8 atmospheres while slowly bleeding off the hydrogen chloride formed in the reaction. After cooling, the remaining pressure was released, then the contents of the vessel were poured into a slurry of 30% sodium hydroxide–ice, washed three times by siphoning, steam-distilled and dried, giving 579 g. of organic material. Distillation gave 524 g. (4.85 moles) b. 55–65° ($C_2H_5CF_2C_2H_5$); 5 g. b. 65–85°; 12 g. b. 85–95° (recovered $C_2H_5CCl{:}C_2H_4$); 15 g. b. 95–105° ($C_2H_5CFClC_2H_5$) and 18 g. of residue. Average yields were similarly between 67 and 73%, an appreciable improvement over those in the literature.[4,5]

Monochlorination of $C_2H_5CF_2C_2H_5$.—Chlorine was led into liquid difluoropentane floating over water, in a Pyrex flask equipped with a reflux condenser, until the increase in weight corresponded to about 70% of monochlorination. A 480 g. batch (4.6 moles) took about ten hours to reach this stage (585 g.). Distillation gave 160 g., b. 54–67° (recovered $C_2H_5CF_2C_2H_5$); 7 g., b. 67–97°; 91 g., b. 97–101° ($C_2H_5CF_2CHClCH_3$); 13 g., b. 101–114°; 198 g., b. 114–119° ($C_2H_5CF_2CH_2CH_2Cl$) and 115 g. of higher chlorides. The average of several such operations gave a ratio $C_2H_5CF_2CH_2CH_2Cl/C_2H_5CF_2CHClCH_3$ of about 2. The formula of the two monochlorides was derived from chlorine analysis, differences of boiling points similar to those observed in the butane series[3,6] and reactions with alcoholic potassium hydroxide, which was much stronger for the higher boiling isomer.[3,6]

Dehydrochlorination of $C_2H_5CF_2CH_2CH_2Cl$ was performed by dripping into its hot alcoholic solution a very concentrated alcoholic solution of potassium hydroxide, and adjusting the reflux in such a way as to allow only the olefin $C_2H_5CF_2CH{=}CH_2$, b. 51° to distil out of the reaction mixture. This olefin was used successfully to

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(1) Henne and Trott, THIS JOURNAL, **69**, 1820 (1947).

(2) Henne and Zimmerschied, *ibid.*, **69**, 281 (1947).

(3) Henne and Hinkamp, *ibid.*, **67**, 1194 (1945).

(4) Renoll, *ibid.*, **64**, 1115 (1942).

(5) Henne and Plueddeman, *ibid.*, **65**, 1271 (1943).

(6) Henne and Hinkamp, *ibid.*, **67**, 1197 (1945).

PHYSICAL PROPERTIES OF NEW COMPOUNDS

	F. p., °C.	B. p., °C., 760 mm.	n^{20}_D	d^{20}_4	*MR*	*AR*F
$C_2H_5CF_2CHClCH_3$		99.4 ± 0.1	1.3788	1.1085	29.7	0.9
$C_2H_5CF_2CH_2CH_2Cl$		117.9 ± 0.2	1.3859	1.1278	29.7	.9
$CH_3CH_2CF_2CHClCH_2Cl$		146.7 ± 0.1	1.4140	1.2840	34.5	.8
$CH_2ClCH_2CF_2CHClCH_3$		154.8	1.4179	1.2899	34.6	.9
$CH_2ClCH_2CF_2CH_2CH_2Cl$	− 24.9 ± 0.2	176.3 ± 0.1	1.4261	1.3179	34.4	.8
$CH_2{=}CHCF_2CH{=}CH_2$	−135.3 ± 0.2	46.8	1.3552	0.9368	24.2	1.0
$CCl_2{=}CClCF_2CCl{=}CCl_2$	− 40.8 ± 0.2	101–102 (13 mm.)	1.5171	1.7480	53.8	1.2
$C_2Cl_5CF_2C_2Cl_5$	89.6 ± 0.2					
$CF_2(CO_2CH_3)_2$	about − 35°	58–59 (9 mm.)	1.3721	1.3059	29.2	1.4
$CF_2(CONH_2)_2$	206.4 ± 0.2					

synthesize $C_2H_5CF_2CHClCH_2Cl$, needed for contrast with other dichlorides, and also $C_2H_5CF_2CO_2H$ to test its response to oxidation.[2]

Chlorination of $C_2H_5CF_2CH_2CH_2Cl$.—Chlorination was carried out to 60% of the next stage in the same manner as above. Fractionation of 598 g. of reaction product gave 91 g., b. up to 140°; 48 g., b. 140–148°, $C_2H_5CF_2$-$CHClCH_2Cl$, calcd. Cl, 40.4, found, Cl, 39.3; 12 g., b. 148–150°; 91 g., b. 150–155°, $CH_2ClCH_2CF_2CHClCH_3$, calcd. Cl, 40.4, found, Cl, 40.4; 34 g., b. 155–170°; 220 g., b. 170–173°, $CH_2ClCH_2CF_2CH_2CH_2Cl$, calcd. Cl, 40.4, found Cl, 41.0; 20 g., b. 173–179°, and 78 g. of residue (higher chlorides). By averaging, the following proportion of the possible dichlorides was found to be: $C_2H_5CF_2CH_2CHCl_2/C_2H_5CF_2CHClCH_2Cl/CH_3CHClCF_2$-$CH_2CH_2Cl/CH_2ClCH_2CF_2CH_2CH_2Cl$ 0/1/4/10. The tendency to affect the hydrogen *beta* to the CF_2 group is thus evident.

Chlorination of $C_2H_5CF_2CHClCH_3$.—Carried out in the same manner as above the results were, for 353 g. of chlorinated material: 70 g., b. up to 118°; 19 g., b. 118–122° ($CH_3CHClCF_2CHClCH_3$ or $C_2H_5CF_2CCl_2CH_3$); 26 g., b. 122–149°; 165 g., b. 149–154° ($CH_2ClCH_2CF_2$-$CHClCH_3$); 10 g., b. 154–166°; 35 g., b. 166–171° (a trichloride isomer); 6 g., b. 171–174°; and 20 g. of residue. Chlorination of $C_2H_5CF_2CHClCH_3$ proceeds almost exclusively to $CH_2ClCH_2CF_2CHClCH_3$, by preferred action on the hydrogen beta to the CF_2 group.

The identity of $CH_2ClCH_2CF_2CHClCH_3$ is derived from the facts that (1) it is obtained from both possible monochlorides, and (2) it differs from $C_2H_5CF_2CHCl$-CH_2Cl obtained by chlorine addition to the olefin.

Perchlorination.—Perchlorination was performed with a source of ultraviolet light immersed in the organic material, as shown before.[7] The chlorinator was, however, redesigned to permit its use at varied temperatures without risk of breakage due to the different coefficients of expansion of quartz and Pyrex glass (Fig. 1). The operation was carried out around 60°. Chlorination was pushed as fast as the consumption of the chlorine would permit. It was noted that after a period of continued chlorination the rate of absorption dropped very markedly. When this happened, the material solidified at room temperature. The crystals were separated from the oil by suction, and a sample, after repeated crystallization from alcohol, melted sharply at 62.3–62.8°, and analyzed for 72.6% chlorine. This is midway between $C_5F_2H_2Cl_8$ and $C_5F_2H_3Cl_7$. The formula was not further investigated. With alcoholic KOH, removal of two moles of hydrogen chloride occurred without loss of fluorine. The reaction product, b. 95–100° at 2 mm., d^4_{20} 1.7751, n^{20}_D 1.5162, was presumed to be mostly $CCl_2{=}CClCF_2$-$CCl{=}CCl_2$, and on this basis the computed value for *AR*F was 0.9, an acceptable value. Chlorine addition was performed at 70–80° and quantitatively yielded a solid material, which after recrystallization from absolute alcohol melted at 89.4–89.8° and analyzed for 78.6% chlorine; calculated for $C_5F_2Cl_{10}$, 78.4%.

Synthesis of $CH_2{=}CHCF_2CH{=}CH_2$.—An alcoholic solution of $CH_2ClCH_2CF_2CH_2CH_2Cl$ (277 g. or 1.56 moles in 450 ml. absolute alcohol) was treated with a solution of 3.42 moles of potassium hydroxide in one liter of alcohol, the addition and reflux being controlled in such a way as to permit only the diene to distil off. The distillate, after washing off alcohol and drying, amounted to 148 g. of which 110 g. was good diene, 30 g. was $CH_2ClCH_2CF_2CH{=}CH_2$ and the remainder unreacted dichloride. This is a conversion of 63% and a recovery of 83%. *Anal.* Calcd.: F, 36.4. Found: F, 35.0.

Synthesis of $CCl_2{=}CCl$-$CF_2CCl{=}CCl_2$.—The treatment of an alcoholic solution of $C_2Cl_5CF_2C_2Cl_5$ with zinc is too vigorous. However, if methylene chloride is added, its refluxing keeps the reaction at a temperature no higher than 40°, and the desired removal of four chlorine atoms takes place efficiently (91%). The reaction product boils at 101–102° under 13 mm., and analyzes for 68.3% chlorine, while theoretical for $C_5F_2Cl_6$ is 68.4%.

Difluoromalonic Acid and Derivatives.—In a small preliminary run, $CH_2{=}CH$—CF_2—$CH{=}CH_2$ was oxidized with alkaline permanganate in our conventional way.[1,2] Ether extraction gave a few grams of mushy material, from which filtration gave grayish crystals with a neutral equivalent of 77, while the mother liquid had an equivalent of 90; the calculated value for difluoromalonic acid is 70 and for difluoroacetic acid is 96. On standing the crystals became liquid; this was interpreted as a slow decarboxylation of difluoromalonic acid to difluoroacetic acid, and in further tests the free acid was avoided.

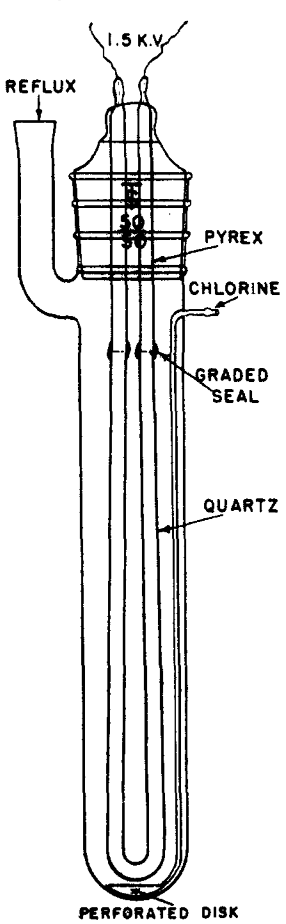

Fig. 1.—Ultra-violet light chlorinator.

The oxidation of the diene (21 g. or 0.2 mole) was exceedingly vigorous and exothermic, necessitating cooling of the oxidation mixture during addition to maintain the temperature at 60°. Within fifteen minutes after completion of the addition, oxidation was complete. Treatment of the reaction mixture with sulfur dioxide followed the conventional practice, and so did the ether extraction. However, at this point, the free acid was esterified by dripping its ether solution into an ether solution of diazomethane. Fractional distillation under reduced pressure gave 7 g. of a lighter boiling material, presumed to be

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[7] Henne and Zimmerschied, THIS JOURNAL, **67**, 1235 (1945).

methyl difluoroacetate, and 24 g. of dimethyl difluoromalonate (*Anal.* Calcd.: F, 22.6. Found: F, 22.5), a 67% yield. A solution of 2 g. of this ester in 8 g. of ethyl ether was treated at 0° with anhydrous ammonia. White crystals formed at once, and 1.6 g. of amide, m. 206.5–206.7°, was collected, the theoretical yield. Nitrogen analysis indicated 20.1% (calculated, 20.3%).

The same amide (as determined by mixed melting point) was also obtained by oxidation of $CCl_2{=}CClCF_2CCl{=}CCl_2$ but this oxidation was slow; it required long heating, and the yield was poor. Better operating conditions were not worked out.

Summary

Diethyl ketone was transformed into 3,3-difluoropentane and the latter subjected to chlorination. The directing effect of the CF_2 group upon the first two chlorine atoms entering the organic molecule was ascertained, before perchlorination was allowed to proceed. From saturated derivatives, two non-conjugated dienes were prepared, $CH_2{=}CHCF_2CH{=}CH_2$ and $CCl_2{=}CClCF_2CCl{=}CCl_2$, both of which were oxidized to difluoromalonic acid. The latter was transformed into its dimethyl ester by means of diazomethane, and characterized as its crystalline diamide.

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Polyfluoro Alkyl Ethers and their Preparation

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Alkyl ethers containing fluorine were previously prepared by Swartz[1-3] by the action of alcoholic caustic or metallic carbonate on polyfluorohaloethanes. This procedure was later modified by Gowland.[4] Aryloxy alkanes containing fluorine also were prepared by McBee and Bolt[5] by a similar reaction. In the present work, alkoxy-2-chloro-1,1,2-trifluoroethanes were prepared by the base-catalyzed addition of alcohol to chlorotrifluoroethylene carried out at room temperature and atmospheric pressure. This type of addition to fluoroölefins was first carried out by Hanford and Rigby[6] under autogenous pressure and at elevated temperatures in the presence of sodium alkoxide as a catalyst.

Starting Materials.—The various alcohols and chemicals used in this study were of technical grade. When deemed necessary they were purified by distilling before using. The compound, CF_2ClCCl_2F, used as an intermediate in the preparation of chlorotrifluoroethylene was of "refrigerant-grade" furnished us through the courtesy of Mr. R. J. Thompson of the Kinetic Chemicals, Inc. Chlorotrifluoroethylene was obtained by dehalogenation of CF_2ClCCl_2F with ethanolic zinc according to a known method.[7]

Fractionation of the product showed the pure olefin to boil at −34 to −35° at 630 mm. pressure.

Preparation of Ethers.—The general reaction involved is

$$ROH + CF_2{=}CFCl \longrightarrow ROCF_2CHFCl \quad (1)$$

According to Pauling's[8] bond energies, the vapor phase reaction should be exothermic to the extent of 5.7 kcal. The entropy change is not known but may be estimated by analogy with similar reactions,[9-12] to be around −28 e. u. The free energy change at 298°K. is +2.6 kcal. and becomes zero at 200°K. It is apparent, therefore, that an equilibrium would be favored by low temperatures and high pressures. Since the reaction was quite rapid at room temperature and slightly above, it was not necessary to employ high pressures. An excess of alcohol was used in all cases.

In the experimental arrangement finally chosen, the olefin, $CF_2{=}CFCl$, from a cylinder was bubbled through a dispersion disk at the bottom of a long vertical tube filled with a potassium hydroxide saturated solution of the alcohol. The outlet end of the tube was connected to an upright water condenser. The unreacted olefin escaping through the condenser was led into a second potassium hydroxide-alcohol solution. The flow of organic through the disk was so regulated that most of the reaction took place in the first reactor. The reaction was quite slow at first. However, as soon as some ether was formed, the rate increased quite rapidly with a resultant rise in temperature. After the necessary amount of olefin had reacted with the alcohol, the reaction mixture was poured into water. The excess alcohol was completely removed by washing with water and the heavier ether layer separated. The ether was then dried over "Drierite" and fractionated in a laboratory precision column.

The addition of alcohols to chlorotrifluoroethylene may proceed to give the product listed in equation I or the structure may be $ROCClFCHF_2$. It is believed that the structure containing the —CHFCl group is the more probable. This is indicated by the formation of CHFCl-COOH in the catalytic hydrolysis of the ethyl ether in the presence of silica gel.[6] The second structure is not consistent with the relative stabilities of the ethers (with the possibile exception of the isopropyl derivative). This structure would permit the elimination of hydrochloric acid quite easily with the formation of $ROCF{=}CF_2$. Such a compound was not isolated under our reaction conditions. If the addition of alcohols to chlorotrifluoroethylene leads to the thermodynamically most stable product, then considerably more heat must be liberated when the isomer containing the —CHFCl group is formed, in which case tables of bonding energies will not be sufficiently precise to determine the course of the reaction.

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