[Contribution from the Department of Chemistry, Purdue University, Lafayette, Ind.]

Preparation and Reactivity of Polyfluorinated β,β-Disubstituted α,β-Unsaturated Acids and Esters[1]

By E. T. McBee, Y. S. Kim and H. P. Braendlin

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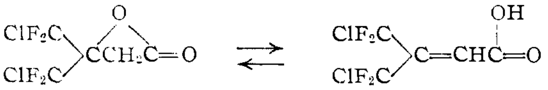
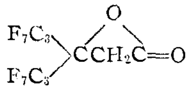
The Knoevenagel reaction of some fluorinated ketones with malonic acid gave fluorinated β,β-dialkyl-β-hydroxyacids. Some of these acids and their esters dehydrated with difficulty. Ethyl 3-methyl-4,4,4-trifluorocrotonate reacted with certain carbanions to yield fluorinated neopentyl derivatives. Methylmagnesium iodide reacted with the carbonyl group of methyl 3-methyl-4,4,4-trifluorocrotonate in 1,2-fashion.

The considerable reactivity of β-perfluoroalkyl-α,β-unsaturated acids and esters toward nucleophiles[2,3] has been ascribed to the pronounced electropositivity of the β-carbon atom, which arises from the electron withdrawal exerted in opposite direction by the perfluoroalkyl (inductive) and carboxyl (resonance polar) groups, respectively.[2] This reactivity was expected to be retained by fluorinated β,β-dialkyl-α,β-unsaturated compounds, leading on attack of selected carbanions on the β-carbon atom to neopentyl derivatives of theoretical and practical interest.

For the preparation of the unsaturated materials we chose the Knoevenagel procedure with malonic acid, which was shown to be superior to the Reformatsky reaction.[3,4] No true condensation occurs in either reaction, *i.e.*, not unsaturates normally isolated with non-fluorinated carbonyl compounds, but β-hydroxy derivatives are obtained. The −I effect of the fluorine cluster, which shortens the carbon–hydroxyl bond, is held responsible for this. However, β-perfluoroalkyl-β-hydroxyacids and esters dehydrate with relative ease at elevated temperatures with agents such as phosphoric anhydride.[3,4] Although the reaction of several fluorinated ketones with malonic acid presented no difficulties, the fluorinated β,β-dialkyl-β-hydroxyacids thus prepared, and their esters, dehydrated with surprising reluctance: $CF_3C(CH_3)OHCH_2CO_2Et$ (I) gave only a small amount of $CF_3C(CH_3){=}CHCO_2Et$ (II) on vigorous treatment with phosphoric anhydride; $(CF_2Cl)_2COHCH_2CO_2Et$ (III) and $(C_3F_7)_2COHCH_2CO_2Et$ (IV) did not react. On treating IV with phosphorus pentachloride, furthermore, no hydrogen chloride was evolved and the ester was recovered. This points to steric shielding of the hydroxyl group as the main deterrent to the dehydration of fluorinated β,β-disubstituted β-hydroxyesters. On the other hand, $CF_3C(CH_3)OHCH_2CO_2H$ (V) yields the olefinic acid $CF_3C(CH_3){=}CHCO_2H$ (VI).[4] Where the ester is reluctant, the acid obviously reacts by esterification of the carboxyl group with phosphoric anhydride, with subsequent pyrolysis leading to unsaturation. An interesting comparison could be drawn from this and results obtained on treating the acids corresponding to III and IV with phosphoric anhydride. Whereas $(CF_2Cl)_2COHCH_2CO_2H$ (VII) yielded an equilibrium mixture of lactone VIII and olefinic acid IX, dehydration of $(C_3F_7)_2COHCH_2CO_2H$ (X) resulted in the lactone XI only. Moreover, XI underwent exclusive acyl oxygen fission; for instance, the acid-catalyzed reaction with ethanol gave the β-hydroxyester IV. On the other hand, esterification of mixture VIII-IX and of VI gave good yields of $(CF_2Cl)_2C{=}CHCO_2Et$ (XII) and II, respectively. It appears that relatively slight changes in the electronic and steric properties of polyfluoroalkyl groups can considerably affect the behavior of adjacent reaction centers.

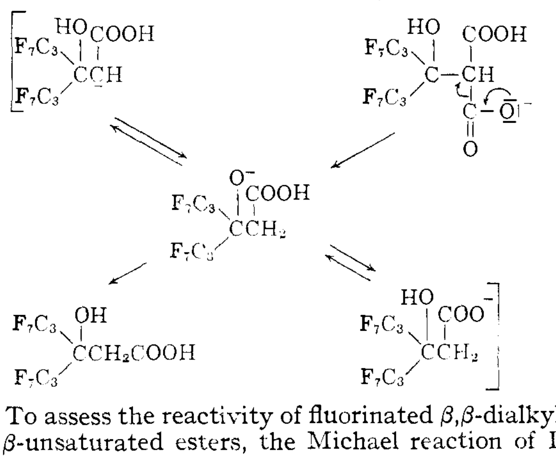


VIII IX



XI

Walborsky, *et al.*,[4] explained the unusual Knoevenagel reaction with fluorinated compounds by a modification of Corey's[5] one-step mechanism of decarboxylative hydroxyl elimination. They assumed the formation of a "loose ion pair" between the hydroxyl group and the incipient olefin, which subsequently collapsed to yield the acid. However, the failure of X to dehydrate renders such a process unlikely in at least the case of the bis-(perfluoropropyl) substituted derivative. We prefer an alternate mechanism wherein decarboxylative hydroxyl elimination is withstood and an intermediate anion is formed on decarboxylation.



To assess the reactivity of fluorinated β,β-dialkyl-α,β-unsaturated esters, the Michael reaction of II

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(1) From a thesis submitted by You Sun Kim to the Graduate School of Purdue University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

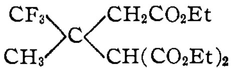
(2) E. T. McBee, O. R. Pierce and D. D. Smith, *J. Am. Chem. Soc.*, **76**, 3722, 3725 (1954).

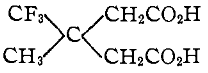
(3) E. T. McBee, C. W. Roberts and G. Wilson, Jr., *ibid.*, **79**, 2323 (1957).

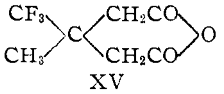
(4) H. M. Walborsky, M. Baum and D. F. Loncrini, *ibid.*, **77**, 3637 (1955).

(5) E. J. Corey, *ibid.*, **74**, 5897 (1952).

and XII with diethyl malonate, the Reformatsky reaction of II with ethyl difluoroacetate, and the Grignard reaction of II with methylmagnesium iodide were carried out. Compound II underwent reaction with diethyl malonate to give the neopentyl derivative XIII, identified by hydrolytic decarboxylation to the diacid XIV, from which the corresponding anhydride XV could be obtained. No reaction took place with a catalytic amount of sodium ethoxide. With an equivalent amount of base, 51% of XIII was obtained, as compared to 90% of product from $C_3F_7CH{=}CHCO_2Et$.[3] Reduction of the base concentration to half the equivalent increased the yield of XIII to 71%.

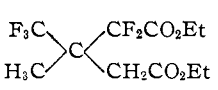

XIII

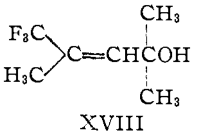

XIV


XV

Compound XII underwent reaction with diethyl malonate, but in addition to sodium chloride only an impure product was obtained with an approximate formula of $C_{14}H_{17}O_6ClF_4$ (XVI). Acid hydrolysis of XVI gave β-carboxyglutaric acid, *i.e.*, complete hydrolysis of the perhalomethyl groups took place with subsequent decarboxylation. The instability of activated perfluoromethyl groups in dilute acid is known[6] and may explain the hydrolysis result. On treatment of XII with other nucleophiles, such as pyridine, iodide and fluoride ion, a reaction occurred in each instance, giving chloride ion, decomposition products and starting materials.

Kennedy[7] and Resconich[8] recently have studied the reaction of various polyhaloacetates with carbonyl compounds by the Reformatsky procedure, using magnesium amalgam as condensation agent. Resconich concluded that the active species is an enolate ion $[^-CF_2CO_2Et \rightleftarrows CF_2{=}C(OEt)\text{-}O^-]$, similar to the one proposed in the normal Reformatsky reaction.[9] Further evidence for this was obtained when II reacted with ethyl difluoroacetate and magnesium amalgam to give the neopentyl derivative XVII.[10]


XVII


XVIII

Methylmagnesium halide is known to react with the carbonyl group of $CF_3CH{=}CHCO_2Et$ in 1,4-fashion,[2] undoubtedly because of the considerable electropositivity of the β-carbon atom which forces the nucleophilic portion of the organometallic into that position. Significantly, the analogous reaction with $CF_3C(CH_3){=}CHCO_2Me$ gave the 1,2-addition product XVIII.[11] This complete reversal of reactivity is interesting, resembling the different behavior on dehydration of $CF_3CHOHCH_2CO_2Et$ (easy)[2] and II (difficult), and must be explained primarily by steric hindrance exerted by the second β-substituent. Another factor, partial reduction of the positive charge on the β-carbon atom due to the +I effect exerted by methyl, probably plays a smaller part: the carbonyl group in *trans*-$C_3F_7CH{=}CHCO_2Et$ recently was shown to react with methylmagnesium halide also in 1,2-fashion only[12]; C_3F_7, although nearly equally inductive as CF_3, is considerably larger.

Trifluoroiodomethane, known to homolyze and to add to a variety of unsaturates,[13] did not react with II and $CF_3CH{=}CHCO_2Et$, the latter less hindered sterically. Apparently, the electron deficiency around the double bond, which comes in good stead in ionic reactions, rendered attack of the electrophilic free radical impossible. In conclusion, attack on the β-carbon atom in fluorinated β,β-dialkyl-α,β-unsaturated acids and esters is reserved for nucleophiles; organometallics react with the carboxy or carbethoxy function and free radicals do not react.

Experimental[14]

Starting Materials.—1,1,1-Trifluoropropanone-2 was prepared according to the procedure reported by Swarts.[15] Tetradecafluoroheptanone-4 was prepared according to the procedure reported by Hauptschein and Braun.[16] 1,3-Dichloro-1,1,3,3-tetrafluoroacetone was obtained from Allied Chemical Co. and distilled before use. Trifluoroacetaldehyde was prepared according to the procedure reported by Pierce and Kane.[17] 3-Methyl-4,4,4-trifluorocrotonic acid was prepared according to the procedure reported by Walborsky, Baum and Loncrini.[4] Ethyl 4,4,4-trifluorocrotonate was prepared according to the procedure reported by McBee, Pierce and Smith.[2] The yields and physical properties of all products are listed in Table I.

Condensation of Malonic Acid with Fluorinated Aldehydes and Ketones.—The reaction with 1,1,1-trifluoropropanone-2 will serve as an example: A solution of malonic acid (260 g., 2.5 moles) and 5 ml. of piperidine in 500 ml. of pyridine was treated with 280 g. (2.5 moles) of trifluoroacetone slowly distilled through a gas inlet tube into the solution over a period of 4 hours and under vigorous stirring. The reaction mixture was stirred for an additional 12 hours, kept at gentle reflux for 4 hours and distilled under pressure to remove pyridine. The residue was acidified with a 50% (by volume) solution of sulfuric acid, the solution was extracted with ether and the ether solution dried over anhydrous sodium sulfate. The ether was removed and the residue fractionated

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[6] E. Wertyporoch, *Ann.*, **493**, 153 (1932).

[7] R. J. Kennedy, Ph.D. Thesis, Purdue University, 1958.

[8] S. Resconich, Ph.D. Thesis, Purdue University, 1961.

[9] R. L. Shriner, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1957, p. 1.

[10] Hydrolysis of XVII did not afford a solid diacid, but a viscous oil. Reaction of XVII with hydrazine hydrate gave an unidentifiable material. Dehydration of the hydrolysis product did give a material revealing characteristic anhydride absorption in the infrared, but the product could not be purified for identification. The reason for the failure to purify these materials may be sought in the fact that the central carbon atom is asymmetric and that XVII and its derivatives are inseparable racemic mixtures.

[11] The methyl ester was employed because in prior attempts with II separation of product from starting material was unsuccessful.

[12] A. Pohland, M.S. Thesis, Purdue University, 1960.

[13] (a) A. L. Henne and M. Nager, *J. Am. Chem. Soc.*, **73**, 5527 (1951); (b) R. N. Haszeldine, *J. Chem. Soc.*, 3761 (1953); (c) J. D. Park, R. J. Sefel and J. R. Lacher, *J. Am. Chem. Soc.*, **78**, 59 (1956).

[14] All melting points and boiling points are uncorrected. Analyses were performed by Dr. C. S. Yeh, Purdue University. The infrared spectra were determined by Mrs. W. Dilling, Purdue University, on a Perkin-Elmer model 21 spectrophotometer. The vapor phase chromatograms were obtained with a Perkin-Elmer model 154 vapor fractometer, using a copper column packed with Carbowax on firebrick.

[15] F. Swarts, *Bull. soc. acad. Belg.*, **8**, 343 (1922).

[16] H. M. Hauptschein and R. A. Braun, *J. Am. Chem. Soc.*, **77**, 4930 (1955).

[17] O. R. Pierce and T. Kane, *ibid.*, **76**, 300 (1954).

Table I

Yields and Physical Properties of Fluorinated Knoevenagel Products and Derivatives

Compound	Yield, %	B.p., °C. (mm.)	M.p., °C.	n^{20}D	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Fluorine, % Calcd.	Fluorine, % Found
$CF_3CHOHCH_2CO_2H$	70		78–79[a]							
$CF_3CHOHCH_2CO_2Et$	80	81–83 (15)		1.3742[b]						
$CF_3C(CH_3)OHCH_2CO_2H$ (V)	73[c,d]	103–104 (7)[c]	32[c,e]							
$CF_3C(CH_3)OHCH_2CO_2Et$ (I)	84	69–70 (15)		1.3789	42.00	41.89	5.00	5.43		
$CF_3C(CH_3)OHCH_2CONHNH_2$			131–132		32.26	32.14	4.84	5.14[f]		
$CF_3C(CH_3){=}CHCO_2Et$ (II)	70	129–130		1.3741	46.16	46.42	4.98	5.22		
$CF_3C(CH_3){=}CHCO_2Me$	48	110–111		1.3717	42.86	42.90	4.16	4.21	33.93	33.81
$EtO_2CCH(CO_2Et)C(CF_3)(CH_3)CH_2CO_2Et$ (XIII)	71	146–147 (8)		1.4165	49.12	48.85	6.14	5.90		
$CF_3C(CH_3)(CH_2CO_2H)_2$ (XIV)	77		121–122		39.21	39.57	4.23	4.41[g]		
(XIV)-Anhydride (XV)	83		130		42.86	43.00	3.58	3.79	29.08	28.80
$HO_2CCF_2C(CF_3)(CH_3)CH_2CO_2H$ (XVII)	41	91–92 (24)		1.4002	43.13	43.43	4.90	4.91		
$CF_3C(CH_3){=}CHC(CH_3)_2OH$ (XVIII)	49	139–140		1.3903	50.00	50.03	6.55	6.70	33.93	33.85
$CF_3C(C_6H_5)OHCH_2CO_2H$	59		133–134[e]		51.28	51.41	3.85	4.33		
$(CF_2Cl)_2COHCH_2CO_2H$ (X)	69		106–107[e]		23.17	23.04	1.54	1.40[h]		
$(CF_2Cl)_2COHCH_2CO_2Et$ (III)	80	91–92 (2)		1.4050	28.92	29.19	2.79	2.73	26.48	26.20[i]
$(CF_2Cl)_2C{=}CHCO_2Et$ (XII)	72	56–57 (2)		1.4031	31.23	31.48	2.23	2.54	28.25	28.01[j]
$(C_3F_7)_2COHCO_2CO_2H$ (X)	61		103–104[e]		25.35	25.31	0.94	1.19		
$(C_3F_7)_2COHCH_2CO_2Et$ (IV)	79	65–66 (3)		1.3351[k]						
$(C_3F_7)_2CCH_2COO$ (XI)	46	65–66 (3)		1.3157	26.47	26.40	0.49	0.69	65.20	65.24
$(C_3F_7)_2COHCH_2CONHNH_2$			95		24.54	24.56	1.37	1.33	60.45	60.11[l]

[a] McBee, Pierce and Smith[2] report m.p. 78–90°. [b] Ref. 2 reports b.p. 81–82° (15 mm.), m.p. 25.5°, n^{20}D 1.3720. [c] Walborsky, Baum and Loncrini[4] report 75% yield, b.p. 75–76° (2 mm.), m.p. 30°. [d] Yield was increased to 83% when the reaction was carried out under pressure (autoclave) but otherwise under the same conditions. [e] Recrystallized from petroleum ether (60–70°). [f] % N calcd. 15.05, found 15.22. [g] Neut. equiv. calcd. 107, found 109.5. [h] % Cl calcd. 27.41, found 27.01. [i] % Cl calcd. 24.74, found 24.50. [j] % Cl calcd. 27.14, found 26.91. [k] McBee, Pierce and Christman, *J. Am. Chem. Soc.*, **77**, 1581 (1955), report b.p. 65–66° (3 mm.), n^{20}D 1.3348. [l] % N, calcd. 6.36, found 6.70.

under reduced pressure through a column to give 314 g. (73%) of the β-hydroxyacid boiling at 103–104° (7 mm.). The crude product solidified on standing and was recrystallized from benzene. (Note: in the reaction with trifluoroacetaldehyde, the latter underwent initial polymerization but depolymerized on continued reaction.)

Esterification. Standard Procedure.—A mixture of β-hydroxyacid (0.5 mole), 200 ml. of absolute ethanol (or methanol) and 5 g. of concentrated sulfuric acid was stirred for 24 hours at room temperature and for 4 hours at reflux. The organic layer was separated and the aqueous portion repeatedly extracted with ether. The combined organic portions were washed twice with a 5% sodium carbonate solution, then with distilled water, and dried over anhydrous magnesium sulfate. Solvent was removed and the residue fractionated through a column to give the ester. From I, the hydrazide was obtained on heating the ester with an equimolar amount of 100% hydrazine hydrate for 20 minutes on a steam-bath, then adding 5 ml. of absolute ethanol, refluxing for 30 minutes, concentrating, and recrystallizing from chloroform.

Ethyl 3-Methyl-4,4,4-trifluorocrotonate (II). A.—A mixture of I (40.2 g., 0.2 mole) and phosphoric anhydride (28.2 g., 0.2 mole) was heated from 100 to 200° over a period of 6 hours. Distillation of the sirupy solution gave 17.2 g. of I, 3.1 g. of crude II, b.p. 120–125°, and a tarry residue. Attempts at improving the yield by the use of solvents, such as ether, dibutyl ether and ethanol, failed.

B.—Concentrated sulfuric acid (98 g.) was added dropwise over a period of 3 hours, under vigorous stirring, to 154 g. (1.0 mole) of 3-methyl-4,4,4-trifluorocrotonic acid[4] and 5.0 moles of absolute ethanol. During the addition of the acid, the flask was kept in an ice–water-bath. After complete addition, the reaction mixture was stirred at room temperature for 24 hours and subsequently kept at reflux for 4 hours. The organic layer was separated and the aqueous layer repeatedly extracted with ether. The combined organic material was washed twice with a 5% sodium carbonate solution and with distilled water. After drying over anhydrous magnesium sulfate, the ether was removed and the residue fractionated to give II.

Reaction of 3-Chlorodifluoromethyl-3-hydroxy-4-chloro-4,4-difluorobutyric Acid (VII) with Phosphoric Anhydride.—A mixture of 25.6 g. (0.1 mole) of VII and 7 g. (0.05 mole) of phosphoric anhydride was heated at 180–190° for 14 hours. Direct distillation gave 15.8 g. of a fraction (VIII–IX) boiling at 168–170°, n^{20}D 1.4089. The infrared spectrum showed peaks at 5.38, 5.40, 5.60 and 5.75 μ. The gas chromatogram showed two distinct peaks.

α,α-Di-(heptafluoropropyl)-β-propiolactone (XI).—A mixture of 42 g. (0.1 mole) of X and 7 g. (0.05 mole) of phosphoric anhydride was well stirred and heated at 130–140° for 12 hours. Distillation under reduced pressure gave 4.08 g. (0.01 mole) of XI; 4 g. of 100% hydrazine hydrate was heated on a steam-bath for 20 minutes, and 5 ml. of absolute ethanol was added. After refluxing for 30 minutes, evaporation of alcohol and cooling for 2 days, the solid hydrazide, recrystallized from chloroform, was obtained.

Ethyl 3-Chlorodifluoromethyl-4-chloro-4,4-difluorocrotonate (XII).—A mixture of 96 g. (0.4 mole) of VIII–IX, 184 g. of absolute ethanol and 39.2 g. of concentrated sulfuric acid was allowed to react as in procedure B for the preparation of ethyl 3-methyl-4,4,4-trifluorocrotonate. Distillation through a spinning band column gave pure XII.

Diethyl 2-Carbethoxy-3-trifluoromethyl-3-methylpentanedioate (XIII). A.—Diethyl malonate (69 g., 0.434 mole) was added to a solution of 7.5 g. (0.3 g. atom) of sodium in 200 ml. of absolute ethanol under vigorous stirring at room temperature. After stirring for 30 minutes at room temperature, 80.4 g. (0.44 mole) of II was added dropwise over a period of 4 hours. The mixture was kept at reflux for 10 hours under vigorous stirring and was acidified with 10% hydrochloric acid. The aqueous layer was extracted with ether and the combined organic portion dried over anhydrous sodium sulfate. The ether was removed and the residue fractionated under reduced pressure to give 77.7 g. (51%) of XIII.

B.—The reaction was repeated with 4.8 g. (0.25 g. atom) of sodium in 200 ml. of absolute ethanol, 80 g. (0.5 mole) of diethyl malonate and 91 g. (0.5 mole) of II under the conditions of procedure A to give 120 g. (71%) of XIII.

3-Trifluoromethyl-3-methylglutaric Acid (XIV).—A mixture of 102 g. (0.3 mole) of XIII and 500 ml. of 24% hydrochloric acid was vigorously refluxed under stirring until the organic layer disappeared (72 hours). Distillation under reduced pressure removed water and acid. The white solid residue was washed once with water and recrystallized from a 1:1 mixture of benzene and petroleum ether (60–70°) to give pure XIV.

3-Trifluoromethyl-3-methylglutaric Anhydride (XV).—A mixture of 10.7 g. (0.05 mole) of XIV and 7.1 g. (0.05 mole) of phosphoric anhydride was well stirred before heating for 4 hours on a steam-bath. After continued heating at 130–140° for 10 hours and cooling, the organic product was taken up in ether and the ethereal solution dried over anhydrous magnesium sulfate. After removal of the ether, the residue was recrystallized from petroleum ether (60–70°) to give pure XV (infrared, 5.65 μ).

Reaction of Ethyl 3-Chlorodifluoromethyl-4-chloro-4,4-difluorocrotonate (XII) with Diethyl Malonate.—Sodium (1.9 g., 0.08 atom) in 200 ml. of absolute ethanol, 24 g. (0.15 mole) of diethyl malonate and 40 g. (0.15 mole) of XII were allowed to react as described in the previous reaction, with the exception that addition occurred at 0° and that the mixture was then heated at 80–85° for 28 hours. Distillation gave 18.4 g. of a fraction boiling at 155–156° (17 mm.), $n^{20}\text{D}$ 1.4210, and 3.1 g. of a fraction boiling at 191–200° (17 mm.), $n^{20}\text{D}$ 1.4310. Both fractions had nearly identical infrared spectra, with absorptions at 3.35, 5.7, 6.8, 6.9, 9.8, 10.6, 11.7 and 13.45 μ. On repeated distillation of fraction 1 through a spinning band column, evolution of hydrogen chloride gas was observed. The gas chromatogram of the product showed mainly one peak with two small shoulders.

Anal. Calcd. for $C_{14}H_{17}O_6ClF_4$: C, 42.75; H, 4.33; Cl, 9.16; F, 19.34. Found: C, 43.12; H, 4.19; Cl, 5.70; F, 22.29.

The material (10.7 g.) was stirred at 110–120° with 100 ml. of 24% hydrochloric acid until the organic layer disappeared (37 hours). After concentration, extraction with ether, drying, removal of ether and recrystallization from benzene–ether, 3.4 g. of a white solid, m.p. 156–157°, was obtained (reptd.[18] for β-carboxyglutaric acid, m.p. 160°).

Anal. Calcd. for $C_6H_8O_6$: C, 40.91; H, 4.55; neut. equiv., 72. Found: C, 41.41; H, 4.70; neut. equiv., 68.

Ethyl 2,2-Difluoro-3-trifluoromethyl-3-methylglutarate (XVII).—Magnesium turnings (5 g., 0.2 g. atom) were placed in a flask equipped with a stirrer and nitrogen and hydrogen inlets. The system was flamed out under dry nitrogen, cooled, and 300 g. of mercury was added. After passing hydrogen gas for 15 minutes, the amalgam was stirred until the liberation of heat ceased. A solution of 12.4 g. (0.1 mole) of ethyl difluoroacetate and 18.2 g. (0.1 mole) of II in 200 ml. of anhydrous ether was added dropwise under vigorous stirring and cooling to 0°. After stirring for 12 hours at room temperature, the organic layer was decanted into 300 ml. of 3% sulfuric acid. The organic layer was separated and the aqueous layer extracted with ether. The combined organic portion was washed with 5% sodium bicarbonate, twice with distilled water, and dried over anhydrous magnesium sulfate. The ether was evaporated and the residue distilled under reduced pressure to give XVII which was purified by redistillation. The black viscous residue (15 g.) with a boiling range of 92–115° at 3 mm. was unidentifiable and probably polymeric.

2,4-Dimethyl-5,5,5-trifluoropent-3-en-2-ol (XVIII).—A solution of 0.45 mole of methylmagnesium iodide in 200 ml. of anhydrous ether was added at 0° to 25.2 g. (0.15 mole) of methyl 3-methyl-4,4,4-trifluorocrotonate. The mixture was stirred for 14 hours at that temperature and then refluxed for 3 hours. After hydrolysis with a saturated solution of ammonium chloride, the bulky precipitate was washed three times with ether and the organic portions combined and dried over anhydrous magnesium sulfate. Distillation and redistillation through a spinning band column gave pure XVIII. A Lucas test for a tertiary alcohol was positive (infrared, 2.9, 9.95 μ.)

Acknowledgments.—The financial support of the Westinghouse Electric Corporation and the Hooker Chemical Corporation is gratefully acknowledged.

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[18] German Chemical Society, "Beilstein, Handbuch der Organischen Chemie," Vol. II, p. 816.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY, LAFAYETTE, IND.]

The Kinetics of the Reaction between Polyfluoroalkyl Halides and Iodide Ion[1]

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The rates of reaction of 2,2,2-trifluoro-1-bromoethane, 3,3,3-trifluoro-1-bromopropane, 2,2,3,3,4,4,4-heptafluoro-1-bromobutane, 3,3,4,4,5,5,5-heptafluoro-1-bromopentane, allyl chloride and *trans*-4,4,4-trifluorocrotyl chloride with potassium or sodium iodide in dry acetone have been measured and the energies of activation, entropies of activation and frequency factors calculated. The results are discussed in terms of steric and electronic effects exerted by the fluorine substituents.

There are numerous reports of the striking influence exerted on organic reactions by fluorine in the molecule. The electron-withdrawing inductive effect caused by these strongly electronegative substituents was recognized at an early stage to be a predominant factor. When perfluoroalkyl groups are spaced adjacent to reaction centers, a second major factor, a steric effect, is thought to play a significant role. However, the latter is usually obscured by the profound influence of inductivity, and the cases are few where a steric effect has been demonstrated unambiguously, especially with trifluoromethyl as substituent. Evidence for steric hindrance exerted by longer-chain perfluoroalkyl groups was provided by Bender[2] who obtained, according to the equilibrium $R_fCO_2Et + MeO^- \rightleftharpoons R_fC(OMe)(OEt)O^-$, an expected percentage increase of methoxide ion addition to ethyl fluoroacetates with increasing fluorine content, but observed a sharp decrease in percentage addition when substituting pentafluoropropionate or heptafluorobutyrate for trifluoroacetate. This was ascribed to F-strain in the larger molecules.

The influence of perfluoroalkyl groups is reduced considerably when a methylene unit separates the reaction center from the fluorine cluster; when two methylene units shield the functional group, the effects are almost negligible. This was demonstrated by comparison of the ionization constants of selected fluorinated alcohols and acids with non-fluorinated analogs.[3] The decrease in acidity with increasing distance between the perfluoroalkyl group and the reaction center cannot be interpreted solely on the basis of inductivity. In a recent review,[4] Lagowski showed convincing support for the assumption that trifluoromethyl is less electron withdrawing than fluorine. Calculated electronegativity values for trifluoromethyl obtained both from comparison of group influences on C=O and P=O infrared absorption frequencies and from bond dissociation data, were consistently

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[1] From a thesis submitted by R. D. Battershell to the Graduate School of Purdue University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] M. L. Bender, *J. Am. Chem. Soc.*, **75**, 5986 (1953).

[3] (a) A. L. Henne and C. J. Fox, *ibid.*, **73**, 2323 (1951); (b) A. L. Henne and R. L. Pelley, *ibid.*, **74**, 1426 (1952); (c) A. L. Henne and W. C. Francis, *ibid.*, **75**, 991 (1953); (d) E. T. McBee, O. R. Pierce and D. D. Smith, *ibid.*, **76**, 3722 (1954).

[4] J. J. Lagowski, *Quart. Revs.*, **13**, 233 (1959).