[CONTRIBUTION FROM THE COLLEGE OF ENGINEERING, THE UNIVERSITY OF FLORIDA, AND THE SCHOOL OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE COLLEGE]

Fluorocarbon Aromatic Ketones

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Following a procedure modified after the one used by Simons and Ramler,[1] a series of fluorocarbon aromatic ketones were prepared, and their properties determined. Some of these compounds were found to make the usual ketone derivatives.

Discussion

Simons and Ramler[1] first prepared a fluorocarbon aromatic ketone by a Friedel–Crafts type reaction in the presence of aluminum chloride. They found that trifluoroacetyl chloride served as an acylating agent.

Our investigation was concerned with an extension of this type reaction to include other aromatic nuclei as well as other fluorocarbon acid chlorides.

The preparation of fluorocarbon aromatic ketones is accomplished by the use of fluorocarbon acid chlorides using aluminum halides as catalysts. The small amount of fluoride ion found in some, but not all reaction products, in all probability resulted from hydrolysis of impurities in the fluorocarbon carboxylic starting material.[2]

The physical properties of *p*-trifluoromethyl tolyl ketone lead us to agree with the observations of Nes and Burger[3] that *o*-trifluoromethyl tolyl ketone was prepared by Jones[4] instead of trifluoromethyl benzyl ketones, as reported. We are, therefore, including *o*-trifluoromethyl tolyl ketone in Table II.

TABLE I

Compound	B.p., °C.	Mm.	$n^{25}D$	d^{25}_4	Chlorine, % Calcd.	Found
CF_3COCl[5]	−27		...	..	...	...
C_2F_5COCl	5.0–5.5	760	...	..	19.43	19.42
C_3F_7COCl[6]	38–39	740	1.288	1.55	...	...
C_4H_9COCl	67.5–68.0	760	...	..	12.52	12.50
$C_5H_{11}COCl$	85.8–86.0	760	1.327	1.66	10.67	10.64

Experimental

Preparation of Acid Chlorides.—The acid chlorides were prepared by the reaction of the corresponding acids with phosphorus pentachloride. The physical properties of the acid chlorides are reported in Table I.

Preparation of Ketones. Procedure A. Acid Chlorides Boiling below 40°.—In a 250-ml. flask equipped with magnetic stirrer, thermometer, and a Dry Ice–acetone Dewar type reflux condenser, were placed the aromatic compound and aluminum chloride and cooled to −10°. The acid chloride was bubbled through the mixture over a period of 6 hr. The flask was allowed to warm to 0° with the introduction of the acid chloride and maintained at 0° during the entire addition, after which the flask was warmed to 10° and stirred for 2 additional hr., until there was no longer any evolution of hydrogen chloride. The reaction mixture was poured onto an ice–hydrochloric acid mixture and ether added for extraction. The water layer was tested for fluoride ion. The ether extractions were dried over calcium chloride and distilled at reduced pressure through a 50-cm. column, 8 mm. inside diameter, packed with $^1/_{16}$ in. glass helices.

Procedure B. Acid Chlorides Boiling Above 40°.—Aluminum chloride and the aromatic compounds were placed in a 250-ml. flask which was equipped with magnetic stirrer, thermometer and a water condenser. The flask was warmed to 50°, and the acid chloride was added dropwise during a period of 4 hr. The reaction mixture was cooled to room temperature, poured into an ice–hydrochloric acid mixture, and ether added for extraction. The water layer was tested for fluoride ion. The ether extractions were dried over calcium chloride and fractionated as in procedure A.

Procedure C.—The apparatus was the same as in procedure B. Aluminum bromide was substituted for aluminum chloride. The aluminum bromide was prepared by adding bromine dropwise to small pieces of aluminum metal containing one piece of aluminum amalgam. A mixture of acid chloride and aromatic compound was then added dropwise to the aluminum bromide during a period of 2 hr. The reaction was maintained at 50°. After the reaction was complete, procedure B was followed.

After hydrolysis of the reaction mixture with ice and hydrochloric acid, fluoride ion was found only in reactions involving nonafluorovaleryl chloride and undecafluorocaproyl chloride, and in these cases in only small amount.

Trifluoromethyl tolyl ketone had a penetrating disagreeable odor. The other ketones had little odor.

TABLE II

Compound	Procedure	Yield, %	B.p., °C.	M.p., °C.	$n^{25}D$	d^{25}_4	Analysis of ketones Theory C, %	Found C, %	Theory F, %	Found F, %	Derivatives 2,4-Dinitrophenylhydrazones M.p., °C.	Analysis of 2,4-Dinitrophenylhydrazones Theory N, %	Found N, %
$CF_3COC_6H_5$[1]	A	..	152[d]	....	1.4583[a]	1.279[a]	..	..	..	..	94.5–95.5	...	...
$C_2F_5COC_6H_5$	A	44.2	161.2	....	1.4245	1.372	48.2	47.9	42.5	42.1	119–120	13.86	13.80
$C_3F_7COC_6H_5$	A	41.3	173.5	....	1.4130[a]	1.473[a]	43.8	43.7	48.5	48.8	133–135[b]	13.17[c]	13.10
$C_4F_9COC_6H_5$	B	32.8	188.5	....	1.3990	1.517	40.8	40.7	52.8	52.3	133–136	11.11	11.07
$C_5F_{11}COC_6H_5$	B	43.6	204 sl. dec.	....	1.3910	1.538	38.5	38.2	55.8	55.7	144–145	10.11	10.06
p-$CF_3COC_6H_4CH_3$	A	32.4	179.2	3.5	1.4664	1.240	57.5	57.4	33.0	33.2	187–188	15.22	15.02
o-$CF_3COC_6H_4CH_3$[3]	..	..	163–163.5[e]	....	1.4625	....	..	..	..	..	.....	...	...
p-$C_2F_5COC_6H_4CH_3$	A	43.8	181.4	4.0	1.4380	1.317	50.4	50.4	39.9	39.8	162–163	13.40	13.61
p-$C_3F_7COC_6H_4CH_3$	A	27.1	193	0.5	1.4230	1.384	46.2	46.1	46.2	45.9	141–142	11.97	12.14
p-$C_4F_9COC_6H_4CH_3$	B	21.0	211	−16.5	1.4126	1.445	42.9	42.8	50.6	50.3	152–153	10.81	10.78
p-$C_5F_{11}COC_6H_4CH_3$	B	65.5	217.3 sl. dec.	−13.5	1.4039	1.504	40.4	40.5	55.3	55.3	160–161	9.86	9.81
2,4-$(CH_3)_2C_6H_3COC_5F_{11}$	C	81.0	217	....	1.4421	1.438	50.5	50.5	52.0	51.9	.....	...	...

[a] Determined at 20°. [b] Semicarbazone. [c] Analysis of semicarbazone. Nitrogen analysis by Clark Microanalytical Laboratory, Urbana, Ill. [d] 730 mm. [e] 741 mm.

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(1) J. H. Simons and E. O. Ramler, THIS JOURNAL, 65, 389 (1943).

(2) E. A. Kauck and A. R. Diesslin, *Ind. Eng. Chem.*, 43, 2332 (1951).

(3) W. R. Nes and A. Burger, THIS JOURNAL 72, 5409 (1950).

(4) R. C. Jones, *ibid.*, 70, 143 (1948).

(5) J. M. Tinker, U. S. Patent 2,257,868, October 7, 1941.

(6) "Heptafluorobutyric Acid," Technical Bulletin, Minnesota Mining & Mfg. Co., 1949.

The ketones are insoluble in water and concentrated sulfuric acid and soluble in ether, ethanol, benzene and bisnonafluorobutyl oxide.

2,4-Dinitrophenylhydrazone and semicarbazone derivatives were prepared, but all attempts to prepare bisulfite addition products were unsuccessful.

The yields of ketone found in the various preparations are listed in column 3 of Table II.

Derivatives

Preparation of 2,4-Dinitrophenylhydrazones.—A solution of 2,4-dinitrophenylhydrazine was prepared by adding 0.5 g. of 2,4-dinitrophenylhydrazine to 10 ml. of 50% sulfuric acid, followed by the addition of 10 ml. of 95% ethanol. To this solution, 0.5 g. of ketone was added and allowed to stand for one week instead of the usual few hours. The crystals were filtered and recrystallized three times from ethanol and water. The highest yields of the 2,4-dinitrophenylhydrazones were obtained when a solution of 50% sulfuric acid was used.

Preparation of Semicarbazone.—The semicarbazone was prepared by refluxing a solution of semicarbazide hydrochloride, water, ethanol and ketone for one hour, after which the solvents were removed under vacuum. The solution must be refluxed at least one hour to obtain an appreciable yield of semicarbazone. The semicarbazone was crystallized from ether after being decolorized with activated charcoal.

Degradation.—The ketones reacted vigorously with a solution of concentrated potassium hydroxide to give a haloform-type splitting reaction, yielding a monohydrofluorocarbon. Upon acidification, the sole organic product was an aromatic acid. In every case, benzoic acid, *p*-toluic acid or 2,4-dimethylbenzoic acid, was obtained and identified by its melting point and neutral equivalent. The monohydrofluorocarbons obtained were identified by their physical properties.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Hydrolysis of Ethyl Fluoroacetates[1]

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Ethyl monofluoroacetate is hydrolyzed more slowly than ethyl acetate in 70% aqueous acetone with 0.1 *M* hydrochloric acid as a catalyst. Ethyl difluoroacetate and ethyl trifluoroacetate, on the other hand, are hydrolyzed more rapidly than ethyl acetate, and are susceptible to fairly rapid hydrolysis even in initially neutral medium. The significance of these results is discussed. Reaction rate constants are given at 25° and two other temperatures, and energies of activation have been calculated.

Henne and Pelley[2] reported recently that the acetate esters of alcohols containing fluorine atoms in the β- or γ-positions are hydrolyzed more slowly than the corresponding unsubstituted esters in 50% acetone and 0.1 *M* hydrochloric acid, the decrease in rate being about tenfold or less. This paper reports the investigation of a series of compounds in which substitution is at the α-position of the acid, namely, the series ethyl monofluoroacetate, ethyl difluoroacetate and ethyl trifluoroacetate. The effect of this type of substitution is more varied and more profound.

Experimental

Materials.—In order to avoid systematic errors, several samples of each ester were prepared and used interchangeably, except in the case of ethyl monofluoroacetate, the toxicity of which made it advisable to keep manipulation at a minimum. Ethyl monofluoroacetate (Monsanto Chemical Co.) and ethyl difluoroacetate (Columbia Chemicals, Inc.) were purified by treatment with dilute aqueous sodium bicarbonate to remove excess acid and then with a large excess of anhydrous calcium chloride to remove water and alcohol. Ethyl trifluoroacetate was prepared from trifluoroacetic acid and ethyl alcohol. Each ester was rectified at least once through a 4-ft. helices-packed "Todd" distillation column, and the product collected for use was no more than the middle third of the fraction boiling over a 0.5° range. The saponification equivalent (sapn. equiv.) was determined by treatment with 1–2 *M* sodium hydroxide at room temperature for 2–12 hours.[3] These are representative properties: ethyl monofluoroacetate, b.p. 114° (750 mm.), $n^{24}\text{D}$ 1.3737, sapn. equiv. 106.5 (calcd. 106.1); ethyl difluoroacetate, b.p. 98.8° at 740 mm., $n^{20}\text{D}$ 1.34713,[4] sapn. equiv. 123.7 (calcd. 124.1); ethyl trifluoroacetate, b.p. 60.7° (740 mm.), $n^{20}\text{D}$ 1.30735,[4] sapn. equiv. 142.1 (calcd. 142.1). The purification of acetone, ethyl acetate, trifluoroacetic acid and difluoroacetic acid has been described elsewhere.[5] All other reagents were C.P. or of analytical grade.

Composition and Properties of Reaction Medium.—The reaction medium contained in all cases 70.0 ml. (54.9 ± 0.1 g.) acetone; to this were added about 1 ml. of ethyl acetate and the catalyzing acid, and enough water to make 100 ml. To correct for changes in volume in experiments at temperatures other than 25°, the following densities were assumed: 0°, 0.916 g./ml.; 15°, 0.898; 25°, 0.888; 35°, 0.879; 50°, 0.864.[6]

Temperature Regulation.—Temperatures were checked with a thermometer calibrated by the Bureau of Standards, and maintained with the tolerances: 0.00 ± 0.02°; 15.0 ± 0.1°; 25.00 ± 0.05°; 35.00 ± 0.05°; 50.2 ± 0.1°.

Ethyl Acetate and Ethyl Monofluoroacetate.—The rates of reaction at 25° were determined essentially as described elsewhere,[5] except that in these experiments the solutions were approximately 0.1 *M* in ethyl acetate. Measurements at 35° were made as follows (procedure A): the reaction mixture was made up at 25°, and aliquot portions were immediately titrated; the mixture was then allowed to come to equilibrium at the higher temperature, and other aliquot portions were withdrawn and titrated at appropriate intervals; the ester concentration and zero-time titer were calculated by allowing for the expansion of the solvent. Measurements at 50° were made as follows (procedure B): all reagents except ethyl monofluoroacetate were mixed at 25°, diluted to 99.0 ml., and allowed to come to equilibrium at

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(1) Presented before the Division of Organic Chemistry, 123rd National Meeting of the American Chemical Society, Los Angeles, Calif., March 15–19, 1953.

(2) A. H. Henne and R. L. Pelley, THIS JOURNAL, **74**, 1426 (1952).

(3) After each determination, the solution was tested with the zirconium-alizarin sulfonate reagent (F. P. Treadwell and W. T. Hall, "Analytical Chemistry," Vol. I, 9th ed., John Wiley and Sons, Inc., New York, N. Y., p. 439) and the fluorine present as fluoride ion amounted to less than 0.5%.

(4) Determined with a Bausch and Lomb Precision Refractometer by Mr. J. P. Wright.

(5) O. R. Pierce and G. Gorin, THIS JOURNAL, **75**, 1749 (1953).

(6) The values at 0–25° were calculated from the formula given in "International Critical Tables," Vol. III, p. 112, taking the percentage of acetone by weight as 62% (the weight of water required to make 100.0 ml. of solution with no other reagents added was 33.25 ± 0.15 g). The values at 35° and 50° were estimated by extrapolation.