

FLUORO-KETONES. III. SYNTHESIS OF ARYL PERFLUOROALKYLETHERS
KETONES BY THE FRIEDEL-CRAFTS ACYLATION

KALATHIL C. EAPEN* and CHRIST TAMBORSKI
Air Force Materials Laboratory, Wright-Patterson Air Force Base,
Ohio 45433 (U.S.A.)

and

THEODORE PSARRAS
PCR Inc., Gainesville,
Florida 32602 (U.S.A.)

SUMMARY

The first successful application of aliphatic perfluoroacid halides containing an ether function, in the Friedel-Crafts acylation is reported.

INTRODUCTION

Acid halides of poly- and perfluorinated aliphatic as well as aromatic acids have been successfully employed in the Friedel-Crafts acylations of aromatic substrates [1-3]. There has been however no report of a Friedel-Crafts acylation using an acid halide containing a perfluoroalkylether function. Attempts in this direction might have been discouraged by the reported substitution of fluorine α - to the oxygen atom by chlorine when a perfluoro ether is heated with anhydrous aluminum chloride at 150-200° [4].

*National Research Council Senior Postdoctoral Associate 1976-1978. Present Address: University of Dayton Research Institute, 300 College Park, Dayton, Ohio, USA

We now report the successful Friedel-Crafts acylations of aromatic compounds with perfluoroalkylether acid halides in presence of anhydrous aluminum chloride. Oligomeric acid halides from hexafluoropropene oxide, $C_3F_7O[CF(CF_3)CF_2O]_nCF(CF_3)C(O)X$ (where $X = F, Cl$) [5] and tetrafluoroethylene oxide, $C_2F_5O(CF_2CF_2O)_4CF_2C(O)F$ [6] have been employed, and under the conditions used ($<100^\circ$), α -substitution was negligible. In addition, a diketone [9] was prepared from perfluoroglutaryl chloride.

RESULTS AND DISCUSSION

A number of ketones prepared in this study have been prepared earlier by organometallic reactions [7]. Table 1 lists all the ketones prepared along with their analytical data. Among the oligomeric acid halides used, those from hexafluoropropene oxide gave the best yields. Acid fluorides could be used directly with 2-4 molar equivalents of aluminum chloride as they were readily converted to the acid chlorides during the reaction. This was confirmed by reacting $C_3F_7OCF(CF_3)C(O)F$ (VII) with aluminum chloride at $50-55^\circ$ to yield $C_3F_7OCF(CF_3)C(O)Cl$ (VIII) (76% yield).

In most of the reactions benzene was used as the aromatic substrate. The yield of the ketones varied with the amount of aluminum chloride, temperature and time of reaction. One of the reactions viz. the acylation of benzene with $C_3F_7OCF(CF_3)C(O)F$ (VII) was studied in detail to optimize reaction conditions, and the data are presented in Table 2. Heating VII and aluminum chloride in the mole ratio 1:3 with excess of benzene at 50° for 2 h. was a convenient way of realizing the best yield of

TABLE 1

PERFLUOROALKYLETHYL ARYL KETONES

Ketone (a)	B.P.	Elemental Analysis		IR (C=O) cm ⁻¹	M.S. (Found) (b)
		(Calc./Found) C	H		
C ₆ H ₅ C(O)CF(CF ₃)OC ₃ F ₇ (I)	80°/18mm [7]	$\frac{36.94}{37.10}$	$\frac{1.29}{1.16}$	1710	M ⁺
C ₆ H ₅ C(O)CF(CF ₃)OCF ₂ (CF ₃)OC ₃ F ₇ [II]	112°/20mm [7]	$\frac{32.40}{32.40}$	$\frac{0.90}{0.90}$	1710	M ⁺
C ₆ H ₅ C(O)CF(CF ₃) [OCF ₂ CF(CF ₃)] ₂ OC ₃ F ₇ [III]	114°/5mm [7]	$\frac{29.93}{29.80}$	$\frac{0.70}{0.62}$	1710	M ⁺
C ₆ H ₅ C(O)CF ₂ [OCF ₂ CF ₂] ₄ OC ₂ F ₅ [IV] [nc]	90°/0.45mm	$\frac{28.66}{28.51}$	$\frac{0.67}{0.68}$	1725	M ⁺
(p-)C ₆ H ₅ OC ₆ H ₄ C(O)CF(CF ₃)OC ₃ F ₇ [V] [nc]	304° (c)	$\frac{44.81}{45.22}$	$\frac{1.87}{1.72}$	1700	M ⁺
C ₆ H ₅ C(O)(CF ₂) ₃ (O)CC ₆ H ₅ [VI]	140°/0.5mm [9] [m.p. 50-51°]	--	--	1705 (Doublet)	M ⁺

(a) NMR spectra were consistent with structures indicated.

(b) M.S. by chemical ionization.

(c) B.P. by Siwoloboff's method. Isolated by preparative GLC ¹H NMR data suggested p-substitution.

TABLE 2

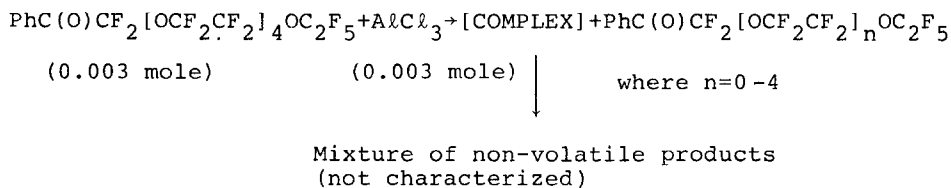
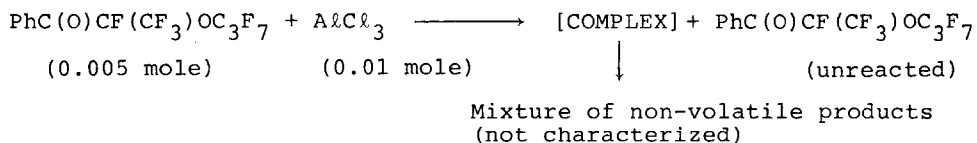
EXCESS BENZENE + C₃F₇OCF(CF₃)C(O)F(VII) + ANH. AlCl₃

TEMPERATURE (°C)	TIME (h)	RATIO R _f OR C(O)F: AlCl ₃	YIELD OF KETONE (I) (%)*
50	0.5	1:3	25.4
50	1.0	1:3	38.4
50	1.5	1:3	47.3
50	2.0	1:3	57.0
50	2.0	1:2	42.3
50	2.0	1:1	33.2
50	2.0	1:5	44.8
50	7.5	1:3	57.6
50	18.0	1:3	56.5
65-70	0.5	1:3	43.4
65-70	1.0	1:3	52.5
65-70	2.0	1:3	44.5
75-80	1.0	1:3	40.9
Ambient	70.0	1:3	43.8

* The yields were determined by GLC using n-octane as standard, and represent the average of two experiments.

about 57%. Though longer reaction time, under the same temperature and ratio of reactants, did not substantially alter the yield, higher or lower ratio of aluminum chloride reduced the yield of $C_6H_5C(O)CF(CF_3)OC_3F_7$ [I].

In addition to the main product, the ketone, all acylation reactions with $C_3F_7O[CF(CF_3)CF_2O]_nCF(CF_3)C(O)F$ gave varying amounts of solid secondary products. These were not detected by GLC as they were non-volatile, but could be partially separated by thin layer chromatography on silica. These secondary products were too complex to be purified and identified. Reaction of the pure ketone $C_6H_5C(O)CF(CF_3)OC_3F_7$ [I] with aluminum chloride also gave similar non-volatile solids as a complex mixture. With $C_2F_5O[CF_2CF_2O]_4CF_2C(O)F$ [XI], in addition to these secondary products, there were ketones with lower molecular weights. GLC/MS data suggested that they might be formed by unzipping of the oligomeric perfluoroalkylether chain. Reaction of the ketone $C_6H_5C(O)CF_2[OCF_2CF_2]_4OC_2F_5$ [IV] with aluminum chloride also indicated formation of volatile by-products due to unzipping and a mixture of non-volatile solids.



In the reaction of the ketones with aluminum chloride, it could be observed that there is an initial fast consumption of the ketone and further amounts of ketone are not used up with time. The amount and complexity of the non-volatile products however increased with time. It would appear therefore that the ketone once formed, complexes with the available aluminum chloride as is known for hydrocarbon analogs, and it is the instability of this complex that leads to the secondary reaction products.

Reactions of other aromatic substrates with the acid fluoride VII were also investigated. Chlorobenzene reacted slowly at 65-70° and gave <5% of the expected ketone [GLC/MS only] in addition to other unidentified products. Bromobenzene reacted vigorously at 90° with considerable charring. At 60° the reaction was more tractable and after 1 h., the reaction mixture contained approximately 10% of benzene, 6% of the ketone(I) derived from benzene and 18% of dibromobenzenes [GLC/MS only] These are explained on the basis of the reported isomerization of bromobenzene with aluminum chloride [8] to yield benzene and dibromobenzenes. Reaction of diphenylether at room temperature for 90 h. gave a low yield (6%) of the p-substituted ketone along with non-volatile solid products which remain unidentified.

Other catalysts investigated, such as HF and BF₃ were not successful in these acylations.

EXPERIMENTAL

The oligomeric acid fluorides were distilled and stored under dry nitrogen before use. Anhydrous aluminum chloride (Fisher Scientific) was used without further purification. The ketones formed were characterized by NMR (¹⁹F and ¹H), IR, MS (chemical ionization) and elemental analysis and/or comparison with

authentic samples. GLC analysis was performed on a Hewlett-Packard Model 700 instrument using 6' or 12" stainless steel columns (1/4"d) packed with 10% SE-30 or Apiezon L on chromosorb W.

A typical procedure for the Friedel-Crafts acylation is given below. Table 3 gives the conditions and yields of all the reactions studied. The aromatic substrate was taken in large excess and served as solvent.

1. Acylation of benzene with $C_3F_7OCF(CF_3)C(O)F$ [VII]

A mixture of benzene (200 ml) and anhydrous $AlCl_3$ (98.5 g; 0.74 mole) was placed in a three-necked flask fitted with a water condenser, thermometer and an addition funnel. While stirring under N_2 with an efficient magnetic stirrer, the contents were heated to 50° . $C_3F_7OCF(CF_3)C(O)F$ [VII] (91.5 g; 0.275 mole) was slowly added to the hot stirred mixture during 30 min. HCl was evolved and the mixture slowly turned black. Heating was continued for another 2 h. The reaction mixture was cooled, added slowly to ice-cold 30% HCl and extracted repeatedly with $CFCl_2CF_2Cl$. The extract was distilled to yield 61.0g (57% yield) of pure $C_6H_5C(O)CF(CF_3)OC_3F_7$ [I] boiling at $80^\circ/18$ mm Hg. The pot residue was a brown solid which on TLC silica showed a complex mixture of components which could not be characterized.

2. Preparation of $C_3F_7OCF(CF_3)C(O)Cl$ [VIII]

Anhydrous $AlCl_3$ (38.5 g; 0.29 mole) was placed in a 3-necked flask fitted with a water condenser, thermometer and addition funnel. While keeping a flow of N_2 through the flask and stirring with a magnetic stirrer, $C_3F_7OCF(CF_3)C(O)F$ [VII] (74.0 g; 0.223 mole) was added during 30 min. The contents were

TABLE 3

EXPERIMENTAL CONDITIONS FOR FRIEDEL-CRAFT'S ACYLATIONS

Substrate [R-H]	Acid Halide [A] $R_fOR_fC(O)X$	Catalyst [B]	Ratio A:B	Time (h)	Temp. (°C)	Yield of Ketone (%) $R_fOR_fC(O)R$ (a)
C_6H_6	$C_3F_7OCF(CF_3)C(O)F$ [VII]	HF	1:2.8	5.0	50	NIL
C_6H_6	$C_3F_7OCF(CF_3)C(O)F$ [VII]	BF_3	1:3.7	70.0	75	NIL
C_6H_6	$C_3F_7OCF(CF_3)C(O)F$ [VII]	$AlCl_3$	1:2.7	2.5	50	57 [I]
C_6H_6	$C_3F_7OCF(CF_3)C(O)Cl$ [VIII]	$AlCl_3$	1:3.0	1.5	50-70	44 [I]
C_6H_6	$C_3F_7OCF(CF_3)C(O)Cl$ [VIII]	$AlCl_3$	1:1.1	1.5	50-70	63 [I]
C_6H_6	$C_3F_7OCF(CF_3)CF_2OCF(CF_3)C(O)F$ [IX]	$AlCl_3$	1:2.5	1.0	70-80	70 [II]
C_6H_6	$C_3F_7O[CF(CF_3)CF_2O]_2CF(CF_3)C(O)F$ [X]	$AlCl_3$	1:2.1	1.0	70-80	73 [III]
C_6H_6	$C_2F_5O[CF_2CF_2O]_4CF_2C(O)F$ [XI]	$AlCl_3$	1:3.7	1.0	70-80	25 [IV] (b)
C_6H_6	$Cl(O)C[CF_2]_3C(O)Cl$ [XII]	$AlCl_3$	1:2.0	1.0	60-70	10 [V] [Diketone]
$C_6H_5OC_6H_5$	$C_3F_7OCF(CF_3)C(O)F$ [VII]	$AlCl_3$	1:3.0	90.0	Ambient	6 [VI] [p-substitution]
C_6H_5Cl	$C_3F_7OCF(CF_3)C(O)F$ [VII]	$AlCl_3$	1:3.0	1.0	65-70	<5 (c)
C_6H_5Br	$C_3F_7OCF(CF_3)C(O)F$ [VII]	$AlCl_3$	1:3.0	1.0	60	NIL (d)

(a) All reactions with $AlCl_3$ had varying amounts of non-volatile by-products which could not be characterized, (b) Ketones with shorter chain lengths were observed as volatile by-products, (c) Yield estimated and product characterized by GLC/MS, and (d) Among the by-products were I (~4%), C_6H_6 (~10%) and $C_6H_4Br_2$ (~18%), estimated and characterized by GLC/MS.

heated to 50-55° and maintained for a total of 6 h. GLC analysis of the liquid portion showed essentially the acid chloride.

The volatile portion of the reaction mixture was collected into two -78° traps under vacuum to yield the crude acid chloride [VIII] which was purified by fractionation. Yield = 59.2 g (76% yield) B.P. 76-78°.

4. Reaction of $C_6H_5C(O)CF(CF_3)OC_3F_7$ [I] with anhydrous $AlCl_3$

The ketone [I] (1.95 g; 0.005 mole) was dissolved in benzene (7.5 ml) and while stirring under N_2 heated to 50°. Anhydrous $AlCl_3$ (1.33 g; 0.01 mole) was added in one portion. The contents became deeply colored and turned black within 5 min. Heating was continued for a total of 30 min. The contents were then cooled and hydrolysed with dil. HCl and extracted three times with small amount of ether. To the ether extract, a weighed amount of n-octane was added as standard for quantitative GLC analysis. The amount of the unreacted ketone was determined as 1.337 g (68.5 %). TLC of the reaction mixture showed a complex mixture of products which were not volatile enough to be detected by GLC.

Identical experiments conducted with the same relative amounts of the reactants, but for longer duration (viz. 18 h.) did not show any substantial reduction in the ketone concentration beyond the initial consumption. The amount and complexity of the nonvolatile solid products increased with time.

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