TABLE I

SUMMARY OF PROPERTIES OF NEW COMPOUNDS

Compound	B.P. °C.	Mm. Hg	M.P., °C.	n_D^{20}	d_4^{20}	Molar Refraction Calcd.[a]	Found	AR_F Calcd.
n-$C_3F_7CH_2CH_2I$	112–113	628	−5	1.3771	1.918	38.10	38.89	1.21
	77.8	185						
	44.3	47						
n-$C_3F_7CH_2CH_2OCOCH_3$	132	633		1.3283	1.4135	35.49	36.8	1.24
n-$C_3F_7CH_2CH_2OH$	116–117	632		1.3151	1.506	26.83	27.81	1.24
	62–63	111						
n-$C_3F_7CH_2COOH$	170–172[b]	630	10	1.3202	1.604	26.84	28.21	1.31
	62.3	6						
n-$C_3F_7CH_2CONH_2$			92.5–93					
n-$C_3F_7(CH_2)_2CONH_2$			96.5–97					
n-$C_3F_7(CH_2)_3CONH_2$			102.5–103					
n-$C_3F_7COCH_2Cl$	97–98	625		1.3240	1.580	30.18	31.8	1.21
	61	178						
n-$C_3F_7COCH_2Br$	118	631		1.3436	1.818	33.08	33.88	1.22
	80.2	213						
$C_2F_5COCH_2Cl$	74	634		1.3088	1.348	26.55	27.8	1.34

[a] Calculated from the Lorenz-Lorentz formula with 1.1 as AR_f for fluorine. [b] With dec.

Method II. Twenty-three grams (0.1 mole) of C_3F_7COCl dissolved in 150 ml. of sodium-dried ether was added dropwise to 500 ml. of ethereal diazomethane (prepared from 35 g. of *N*-methylnitrosourea) contained in a 1-l. three-neck flask fitted with a dropping funnel and stirrer. The third neck was protected with a calcium chloride drying tube. The reaction mixture was kept cold (0° to −10°) during the addition of the acid chloride.

When the addition was completed the mixture was allowed to warm to room temperature and allowed to stand for 8 hr. The dropping funnel was replaced by a gas inlet tube, and a bubbler was attached to the drying tube outlet. Anhydrous hydrogen chloride, passed successively through a safety trap, a concentrated sulfuric acid scrubber, and a second safety trap, was passed slowly into the solution. When the evolution of nitrogen ceased, the flow of hydrogen chloride was discontinued. The solution was then worked up as described in Method I. The yield of $C_3F_7COCH_2Cl$ (b.p. 98.5–99.5°/632 mm.) was 7 g. (28.5%).

Preparation of heptafluoropropyl bromomethyl ketone. This reaction was carried out under conditions similar to that described for $C_3F_7COCH_2Cl$ (Method I). Twenty-eight grams (0.1 mole) of C_3F_7COBr was used. The fraction boiling at 80–81° at 213 mm. was collected. The yield of α-bromoketone was 6 g. (20%), n_D^{20} 1.3436; d_4^{20} 1.818.

Anal. Calcd. for $C_5H_2BrF_7O$: C, 20.64; H, 0.69; Br, 27.46. Found: C, 20.69; H, 0.80; Br, 27.80.

Pentafluoroethyl chloromethyl ketone was prepared in a manner similar to that used for the preparation of $C_3F_7COCH_2Cl$.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF COLORADO]

Action of Aluminum Chloride on Hexafluoropropene

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Aluminum chloride has been found to react with hexafluoropropene to yield $CF_3CF{=}CFCl$, $CF_3CF{=}CCl_2$, $CF_2ClCF{=}CCl_2$, $CFCl_2CF{=}CCl_2$, $CCl_3CF{=}CCl_2$ and $CCl_3CCl{=}CCl_2$. A mechanism for the reactions involving replacement as well as rearrangement is postulated.

The reaction of aluminum chloride with chlorofluoroalkanes to replace fluorine by chlorine has been reported by Henne[2,3] and Miller and his coworkers.[4–6] In the present work, the action of aluminum chloride on hexafluoropropene was studied to ascertain the order of replacement of the organically bound fluorine atoms by chlorine and the de-

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velopment of this method as a simple procedure for the synthesis of various chlorofluoropropenes.

A study of the chlorofluoroolefins isolated, $CF_3CF{=}CFCl$, $CF_3CF{=}CCl_2$, $CF_2ClCF{=}CCl_2$, $CFCl_2CF{=}CCl_2$, $CCl_3CF{=}CCl_2$ and $CCl_3CCl{=}CCl_2$, reveals that only one isomer was obtained. This seems to rule out the possibility of random substitution.

Miller[6] has shown the singular example of the rearrangement of $CFCl_2CF{=}CF_2$ to $CF_2ClCF{=}CFCl$ under the catalytic influence of aluminum chloride without reporting experimental conditions or finding the isomer $CF_3CF{=}CCl_2$ as one of the intramolecular rearrangement products.

In this study the stability of the chlorofluoro groupings toward replacement and/or rearrangement reactions with aluminum chloride in the perhalopropenes was found to be in the following order:

$$-\overset{F}{C}{=} > CF_3{-} > CF_2Cl{-} > CFCl_2 > {=}C\langle^{F}_{Cl} > {=}C\langle^{F}_{F}$$

The fluorine atom on the central carbon atom showed the greatest resistance to replacement by chlorine. In contrast to this, Miller[5] found that the fluorine atom on the central carbon atom in $CF_2ClCFClCF_2Cl$ was most easily replaceable or rearranged to $CF_3CCl_2CF_2Cl$ and $CF_3CCl_2CCl_3$.

Under the conditions of our study, $CF_3CF{=}CCl_2$ and $CCl_3CF{=}CCl_2$ were obtained in the largest quantities. The olefins, $CF_3CF{=}CFCl$, $CF_2ClCF{=}CCl_2$ and $CFCl_2\text{-}CF{=}CCl_2$, were found in small amounts. Since the remarkable chemical stability of the CF_3- and CCl_2-groups is well-known in these aluminum chloride reactions,[5,7] the greater yield of $CF_3CF{=}CCl_2$ (in comparison to $CF_2ClCF{=}CCl_2$ and $CFCl_2CF{=}CCl_2$) may be attributed to this factor. These results parallel the stability of the above groups toward chlorine replacement by reagents such as antimony fluoride.

EXPERIMENTAL

Hexafluoropropene was obtained from the pyrolysis of $CF_3CF_2CF_2COONa$ according to the method of Hals, Reed, and Smith.[8]

Action of $AlCl_3$ on hexafluoropropene at low temperatures. The reaction between $AlCl_3$ and $CF_3CF{=}CF_2$ was first investigated by heating the reactants in a Pyrex combustion tube at a series of temperatures ranging from 0° to 150°. The temperature range, 50–60°, gave the best conversion of $CF_3CF{=}CF_2$ to chlorofluoropropenes with the least amount of tar formation.

About 266 g. (2 moles) of anhydrous granular aluminum chloride (Baker C.P.) was first placed in a 500 ml. capacity Parr bomb and then evacuated. After cooling the bomb to −78°, about 150 g. (1 mole) of $CF_3CF{=}CF_2$ was added. The bomb and its contents were allowed to warm gradually to room temperature under agitation and the temperature gradually raised to 50°. A maximum pressure of 200–250 p.s.i.g. was obtained in the first hour which gradually decreased to 150–200 p.s.i.g. during the next 4 hours with the temperature still at 50–60°. After being cooled to room temperature, the bomb was chilled to −20°, after which the gases were vented into a trap cooled to −78°. The recovery was 47 g. of hexafluoropropene.

The bomb was opened and the liquid products decanted from the solid residue. In 3 similar runs, a total of 450 g. (3 moles) of $CF_3CF{=}CF_2$ and 798 g. (6 moles) of $AlCl_3$ were used. The recovery was 125 g. of $CF_3CF{=}CF_2$ and 131 g. of liquid products. The solid residue, which contained a considerable amount of tar, weighed 927 g. The over-all material recovery for the 3 runs was 1183 g. as against an original total charge of 1248 g. The recovery was 94.8%.

Hydrolysis of the solid residue. A 3-l. three-neck flask was equipped with a dropping funnel, a feed-tube for solids and a reflux condenser with a gas delivery outlet leading to a series of traps cooled in an ice water and a dry ice acetone bath. Dilute hydrochloric acid and the solid residue were fed into the flask and allowed to react in an excess of the acid. An oil separated from the aqueous reaction mixture along with a large amount of tar. The gases which were liberated and collected in the traps amounted to 21 g. The aqueous acid solution containing the oil-tar layer was neutralized with dilute base and after cooling extracted with Skelly Solve B and the extract dried over sodium sulfate. Distillation of the 21 g. of gaseous products combined with the 131 g. of liquid yielded the following cuts: 2.9 g. of $CF_3CF{=}CFCl$;[9] 28 g. of $CF_3CF{=}CCl_2$;[10] 4.1 g. of $CF_2ClCF{=}CCl_2$; b.p. 79.6°/627 mm.; n_D^{20} 1.4046; d_D^{20} 1.6084.

Anal. Calcd. for $C_3Cl_3F_3$: C, 18.05; Cl, 53.5. Found: C, 18.03; Cl, 53.1.

3.6 g. of $CFCl_2CF{=}CCl_2$; b.p. 121°/627 mm.; n_D^{20} 1.4891; d_4^{20} 1.6562.

Anal. Calcd. for $C_3Cl_4F_2$: C, 16.66; Cl, 65.71. Found: C, 17.05; Cl, 65.70.

Distillation of the oil obtained from the hydrolysis of the solid residue yielded only small quantities of the above olefins. The main fraction was 116 g. of $CCl_3CF{=}CCl_2$.[11]

Action of aluminum chloride on hexafluoropropene at high temperatures. The reaction of $AlCl_3$ with $CF_3CF{=}CF_2$ was also studied at 75°, 100°, 150°, and 450°. The results showed a large increase in tar formation and the isolation of only $CCl_3CF{=}CCl_2$.

The reaction of 530 g. (3.43 moles) of $CF_3CF{=}CF_2$ and 693 g. (5.21 moles) of $AlCl_3$ was studied at 450° after 6 hr. of continuous stirring, the bomb was brought to room temperature, and vented into traps. About 201 g. of $CF_3CF{=}CF_2$ was recovered. No liquid products were recovered on opening the bomb. The solid residue was hydrolyzed with dilute HCl and treated as previously described. Fractionation yielded 19.5 g. of $CCl_3CF{=}CCl_2$ and about 50 g. of $CCl_3{-}CCl_3$ along with a higher polymeric material, m.p. 222–223°, which was not characterized.

In another run, about 19.4 g. (0.084 moles) of $CCl_3CF{=}CCl_2$ and 3.99 g. (0.028 moles) of $AlCl_3$ was placed in a 50 ml. round-bottom flask equipped with a reflux condenser and allowed to reflux for 18 hr. Hydrolysis of this reaction mixture and treatment as previously described yielded 2.6 g. of $CCl_3CF{=}CCl_2$ and 11.8 g. of $CCl_3CCl{=}CCl_2$.

Proof of structure. The proofs of structure of the various olefins were obtained by comparison of the physical properties and infrared spectra of our compounds with those of known structure previously described in the literature. The works of Miller,[6] Henne *et al.*,[9] and Whaley and Davis[7] along with our studies gave stimulus for the consideration of the following mechanism.

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1. $CF_3CF{=}CF_2 + AlCl_3 \longrightarrow AlCl_3F^- + \overset{+}{C}F_2{-}CF{=}CF_2$

2. $\overset{+}{C}F_2{-}CF{=}CF_2 + AlCl_3F^- \longrightarrow CF_2Cl{-}CF{=}CF_2 + AlCl_2F$

3. $CF_2ClCF{=}CF_2 \xrightarrow{AlCl_3} CF_3CF{=}CFCl$

4. $CF_3CF{=}CFCl + AlCl_2F \longrightarrow \overset{+}{C}F_2{-}CF{=}CFCl + AlCl_2F_2^-$

5. $\overset{+}{C}F_2{-}CF{=}CFCl + AlCl_2F_2^- \longrightarrow CF_2Cl{-}CF{=}CFCl + AlClF_2$

6. $CF_2Cl{-}CF{=}CFCl \xrightarrow{AlCl_3} CF_3CF{=}CCl_2$

7. $CF_3CF{=}CCl_2 + AlCl_3 \longrightarrow AlCl_3F^- + \overset{+}{C}F_2{-}CF{=}CCl_2$

8. $\overset{+}{C}F_2{-}CF{=}CCl_2 + AlCl_3F^- \longrightarrow CF_2ClCF{=}CCl_2 + AlCl_2F$

Steps 3 and 6 involve intramolecular rearrangement. Step 8 continues stepwise until $CCl_3CF{=}CCl_2$ is ultimately formed. This latter compound, $CCl_3CF{=}CCl_2$, which resists quite strongly the action of $AlCl_3$ to convert it to $CCl_3{-}CCl{=}CCl_2$, may be partially explained on the basis of the peculiar geometry of the molecule which prevents the complexing of $AlCl_3$ with $CCl_3CF{=}CCl_2$.

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[CONTRIBUTION FROM THE LABORATORY FOR THE STUDY OF HEREDITARY AND METABOLIC DISORDERS, AND THE DEPARTMENTS OF BIOLOGICAL CHEMISTRY AND MEDICINE, UNIVERSITY OF UTAH]

Preparation and Properties of β-3-Indolyl Compounds Related to Tryptophan Metabolism[1]

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3-Indolylpyruvic acid was prepared from DL-tryptophan *via* the *N*-chloroacetyl derivative and 2-methyl-4-(3′-indolal)-5-oxazolone, and also from 3-formylindole *via* 2-methyl-4-(1′-acetyl-3′-indolal)-5-oxazolone. The pyruvic acid was converted to β-(3-indolyl)lactic and β-(3-indolyl)-α-oximinopropionic acids. β-(3-Indolyl)acrylic and β-(3-indolal)malonic acids were synthesized from 3-formylindole and malonic acid. 3-Indolylglyoxylic acid, amide, and methyl ester were prepared from indole and oxalyl chloride *via* 3-indolylglyoxylyl chloride. 3-Indolylglycolic acid was obtained as a stable sodium salt by reduction of the glyoxylic acid and the instability of the free glycolic acid was confirmed. 3-Indolylcarboxylic acid was prepared from 3-cyanoindole which was obtained from 3-indolylglyoxylic acid or from 3-formylindole *via* the aldoxime. 3-Indolylacetamide was synthesized from 3-indolylacetic acid *via* the acid chloride. The factors which influence the yield, stability, and purity of these compounds are considered in relation to inadequacies in earlier literature.

Only a minor portion of the tryptophan ingested by man follows the known metabolic paths, which lead to nicotinic acid or to serotonin, and the fate of the remainder is uncertain.[4] Varying small amounts of many indole compounds are present in human urine; an abnormal excretion of some of these compounds has been reported in cases of phenylketonuria,[5] malignant carcinoid tumor,[6,7] and Hartnup disease.[8] The preparation of several 3-indolyl compounds, which were required in a study of urinary indole acids and their possible significance in relation to other metabolic paths,[9] is reported in the present paper. New syntheses of indolepyruvic acid, sodium indoleglycolate, and indoleacetamide are presented, together with effective procedures for indoleacrylic, indolecarboxylic, indoleglyoxylic, and indolelactic acids. The conditions which influence the yield, stability, and purity of the compounds are considered. These factors have not been treated sufficiently in many of the earlier publications, and procedures frequently have not been described or are inadequate.

β-(3-Indolyl)pyruvic acid (I) was prepared in 43% overall yield from DL-tryptophan *via* its *N*-chloroacetyl derivative (II) and 2-methyl 4-(3′-indolal)5-oxazolone (III). Cooley and Wood[10] used this approach to make *N*-acetyldehydrotryptophan, but did not isolate I and III. I also was obtained in low yield *via* 2-methyl-4-(1′-acetyl-3′-indolal)-5-oxazolone by condensing 3-formylindole with acetylglycine. Bentley *et al.*[11] recently described the

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