undecanoic Acid.—11-Fluoro-3-methylundecanoic acid (15.0 g., 0.069 mole), methyl hydrogen azelate (28.0 g., 0.139 mole), sodium (0.23 g., 0.01 g. atom) and methanol (70 ml.) were electrolyzed by the usual procedure at 1.7 amp. for 4.5 hr. The crude reaction product, after isolation in the usual way, was heated under reflux with 10% sodium hydroxide (200 ml.) for 3 hr. The mixture was separated into neutral and acidic fractions, and the extracts were dried over sodium sulfate. The neutral extract on distillation yielded 1,20-difluoro-9,12-dimethyleicosane (2.8 g., 23%), b.p. 149–150° (0.15 mm.), n_D^{25} 1.4438. The acidic extract on distillation gave a fraction (3.6 g.) of b.p. 148–154° (0.025 mm.), presumed to be impure Vb, and hexadecanedioic acid (7.2 g., 36%), b.p. 184–188° (0.07 mm.), colorless crystals from methanol, m.p. 123–124°; Chuit[14] reports m.p. 124–124.2°. The sample of impure Vb was heated under reflux for 16 hr. with methanol (20 ml.), ethylene chloride (25 ml.) and concentrated sulfuric acid (0.2 ml.).[15] After dilution with water, the ethylene chloride layer was separated and distilled through a short Vigreux column to yield methyl fluorotuberculostearate (2.5 g., 11.5%), b.p. 149–150° (0.10 mm.), n_D^{25} 1.4433.

Anal. Calcd. for $C_{20}H_{39}O_2F$: C, 72.68; H, 11.90. Found: C, 72.88; H, 11.90.

(b) **From 14-Fluoro-6-methyltetradecanoic Acid.**—A mixture of 14-fluoro-6-methyltetradecanoic acid (2.0 g., 0.0077 mole), methyl hydrogen adipate (2.5 g., 0.0156 mole), sodium (0.035 g., 0.0015 g. atom) and methanol (75 ml.) was electrolyzed at 1.5 amp. for 50 minutes. Isolation and distillation of the products in the usual way gave two fractions: (1) dimethyl sebacate (1.08 g., 30%), b.p. 76–78° (0.02 mm.), n_D^{25} 1.4368; Stahl and Pessen[16] report n_D^{25} 1.4368. (2) Methyl fluorotuberculostearate (0.62 g., 25.5%), b.p. 126–127° (0.02 mm.), n_D^{25} 1.4433. The distillation residue was too small to allow of the isolation of pure 1,26-difluoro-9,18-dimethylhexacosane.

18-Fluoro-10-methyloctadecanoic Acid (Fluorotuberculostearic Acid) (Vb).—A portion of Va was hydrolyzed with 10% sodium hydroxide in the usual manner to yield the free acid, a colorless liquid of b.p. 159–160° (0.05 mm.), n_D^{25} 1.4500. The acid solidified just below room temperature.

Anal. Calcd. for $C_{19}H_{37}O_2F$: C, 72.10; H, 11.79; F, 6.00; neut. equiv., 316.5. Found: C, 72.14; H, 11.68; F, 5.7; neut. equiv., 318.2.

The sodium salt was prepared as follows: the acid (1.3 g.), dissolved in ethanol (20 ml.), was titrated with 0.25 *N* sodium hydroxide to a faint pink end-point, using phenolphthalein as an external indicator. A few drops of Vb in ethanol were then added to return the solution to the acid side of the indicator. The solution was evaporated on a steam-bath, forming a colorless solid. After drying in a vacuum desiccator, the sodium salt was found to be non-hygroscopic and sufficiently soluble in water for biological testing.

Acknowledgments.—The work described herein was carried out under Contract (DRB X-24) with the Defence Research Board of Canada, to whom grateful acknowledgment is made for financial assistance and for permission to publish this work. The authors wish also to express their indebtedness to the National Research Council of Canada for the award of a bursary to R.G.W.; to Mr. J. B. Stothers for valuable help in the preliminary phases of the investigation; to Dr. I. G. Walker, Defence Research Medical Laboratories, Toronto, for carrying out the toxicity determinations; and to Parke, Davis and Co., Detroit, Mich., for screening sodium fluorotuberculostearate against *M. tuberculosis*.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WESTERN ONTARIO]

Toxic Fluorine Compounds. XVI.[1] Branched ω-Fluorocarboxylic Acids

BY F. L. M. PATTISON AND R. G. WOOLFORD

RECEIVED DECEMBER 3, 1956

Six branched ω-fluorocarboxylic acids, $F(CH_2)_nCHMe(CH_2)_mCOOH$, were prepared by anodic coupling reactions. The toxicological results may be explained on the basis of two modes of breakdown: (1) when *m* is odd, the compounds form intermediate oxidation products which in turn break down to give ω-fluorocarboxylic acids containing a total of *n* carbon atoms; (2) when *m* is even, β-oxidation occurs in the usual way, resulting in toxicity figures comparable to those of the unbranched ω-fluorocarboxylic acids, $F(CH_2)_{n+m+1}COOH$. Thus, compounds in which *n* is the same have approximately the same toxicity, irrespective of *m* and hence of the total length of the chain.

The unique pharmacological properties of the ω-fluorine atom in aliphatic compounds have been outlined in earlier reports in this series. By an examination of the toxicity of members of any series $F(CH_2)_nX$, it has been possible to deduce the probable metabolic fate of the group X. As an extension of this work, we have now prepared some branched ω-fluorocarboxylic acids (Table II), in order to obtain information regarding the metabolism of the corresponding unfluorinated branched-chain acids.

The value of unsymmetrical anodic coupling reactions in the synthesis of fluorine compounds has already been indicated.[2,3] The procedure used in the present work to obtain the compounds listed in Table I was essentially the same as that described earlier. In general, ω-fluorocarboxylic acids were electrolyzed in the presence of an excess of the appropriately substituted glutaric acid half-ester

$$F(CH_2)_{n-1}COOH + HOOCCH_2CHMeCH_2COOCH_3 \longrightarrow F(CH_2)_nCHMeCH_2COOCH_3 \longrightarrow F(CH_2)_nCHMeCH_2COOH$$

Simple homologation of II by means of the Arndt–Eistert synthesis yielded 11-fluoro-4-methylundecanoic acid (V). The preparation of 18-fluoro-10-methyloctadecanoic acid (VI) has been described in an earlier report.[3]

The results presented in Table II indicate that compounds in which *n* is odd are non-toxic whereas those in which *n* is even are toxic, irrespective of *m* and hence of the total length of the carbon chain. It is convenient to discuss this observation and the

(1) Part XV, THIS JOURNAL, **79**, 1959 (1957). Issued as DRB Report No. SW-36.

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(3) F. L. M. Pattison and R. G. Woolford, *ibid.*, **79**, 2306 (1957).

TABLE I

UNSYMMETRICAL ANODIC COUPLING REACTIONS

Product	Reactants	Yield, %	Symmetrical by-products (yield, %) ω,ω'-Difluoroalkane	Dicarboxylic acid
$F(CH_2)_6CHMeCH_2COOH$ (I)	$F(CH_2)_4COOH$ $HOOCCH_2CHMeCH_2COOCH_3$	30	$F(CH_2)_8F$ (10)	$HOOCCH_2CHMe(CH_2)_4CHMeCH_2COOH$ (36)
$F(CH_2)_7CHMeCH_2COOH$ (II)	$F(CH_2)_6COOH$ $HOOCCH_2CHMeCH_2COOCH_3$	42	$F(CH_2)_{12}F$ (20)	$HOOCCH_2CHMe(CH_2)_3CHMeCH_2COOH$ (35)
$F(CH_2)_8CHMeCH_2COOH$ (III)	$F(CH_2)_7COOH$ $HOOCCH_2CHMeCH_2COOCH_3$	45	$F(CH_2)_{14}F$ (20)	$HOOCCH_2CHMe(CH_2)_2CHMeCH_2COOH$ (37)
$F(CH_2)_5CMe_2CH_2COOH$ (IV)	$F(CH_2)_4COOH$ $HOOCCH_2CMe_2CH_2COOCH_3$	30	$F(CH_2)_8F$ (10)	$HOOCCH_2CMe_2(CH_2)_2CMe_2CH_2COOH$ (38)

TABLE II

TOXICOLOGICAL RESULTS AND POSTULATED METABOLIC DEGRADATIONS OF $F(CH_2)_nCHMe(CH_2)_mCOOH$

Acid	L.D. 50,[a] mg./kg.	L.D. 50[a,b] of corresponding unbranched acid,[c] mg./kg.	Suggested metabolic route[d]	Suggested intermediary metabolite	L.D. 50,[a,b] mg./kg.
$F(CH_2)_5CHMeCH_2COOH$ (I)	118	0.64	1	$F(CH_2)_4COOH$	>100
$F(CH_2)_7CHMeCH_2COOH$ (II)	65	1.5	1	$F(CH_2)_6COOH$[e]	40
$F(CH_2)_8CHMeCH_2COOH$[f] (III)	2.42	57.5	1	$F(CH_2)_7COOH$[g]	0.64
$F(CH_2)_5CMe_2CH_2COOH$ (IV)	121	0.64	Blocked	.....	....
$F(CH_2)_7CHMeCH_2CH_2COOH$ (V)	52	57.5	2	$F(CH_2)_6COOH$	40
$F(CH_2)_8CHMe(CH_2)_8COONa$[f] (VI)	2.7	5.7	2	$F(CH_2)_7COOH$	0.64

[a] Intraperitoneal injection into mice. [b] Reported previously.[4] [c] General formula $F(CH_2)_{n+m+1}COOH$. [d] Outlined in the Discussion. [e] L.D. 50 of 9-fluoro-2-nonanone, $F(CH_2)_7COCH_3$, 16 mg./kg.[5] [f] Reported previously.[3] [g] L.D. 50 of 10-fluoro-2-decanone, $F(CH_2)_8COCH_3$, 1.2 mg./kg.[5]

resultant biochemical conclusions under two main headings.

(1) **When *m* is Odd (Compounds I–IV).**— The most striking feature apparent in this class of compounds is the pronounced difference in toxicity between the branched and the corresponding unbranched ω-fluorocarboxylic acids. The mere introduction of one or more methyl groups in the β-position results in the complete reversal of the toxicological pattern. Clearly, β-oxidation of the main chain is not occurring in the usual manner. Originally, it was considered likely that methyl ketones were formed[6,7] as intermediates by loss of two carbon atoms ($F(CH_2)_nCHMeCH_2COOH \rightarrow F(CH_2)_nCOMe$). While it is possible that this is indeed the case to a certain extent, it is nevertheless unlikely that methyl ketones are the sole or even the main intermediates, since the toxicities of II and III are not sufficiently similar to those of the anticipated methyl ketones[5] (Table II) to justify drawing any such definite conclusion. Additional evidence against this simple ketone formation is supplied by the report[8] that β-methyl-*n*-valeric acid forms, not methyl ethyl ketone, but acetone. An alternative mode of breakdown is suggested by the observation of Barker,[9] as a result of work with *Clostridium kluyveri* extracts, that fatty acids can give rise to the corresponding β-unsaturated acids; if this mechanism be applied to compounds I–III, the postulated intermediate, $F(CH_2)_{n-1}CH{=}CMeCH_2COOH$, could on subsequent oxidation form the ω-fluorocarboxylic acid containing a total of *n* carbon atoms. In short, the nature of the intermediary metabolites is uncertain, and the most reasonable interpretation of the toxicity results is that the members under consideration form ω-fluorocarboxylic acids containing a total of *n* carbon atoms, presumably through the intermediate formation of oxidation products which may or may not include the above-mentioned ketones and unsaturated acids. That the toxic members ultimately form fluoroacetate is indicated[10] by the high citric acid level in the tissues of animals poisoned by III.

$$F(CH_2)_nCHMeCH_2COOH \longrightarrow [\text{intermediate}] \longrightarrow F(CH_2)_{n-1}COOH$$

(2) **When *m* is Even (Compounds V and VI).**— In contrast to the compounds described above, the toxicity of the two members of this class are very similar to those of the corresponding unbranched acids, within the limits of biological variation. Thus the introduction of the methyl group causes no change in the general toxicological pattern of the unbranched ω-fluorocarboxylic acids. The obvious conclusion is that these branched acids, after initial formation of the thiol-ester of coenzyme A, progressively lose two carbon atoms by β-oxidation until an acid possessing an α-methyl substituent is produced; this can then undergo further β-oxidation, since an α-methyl substituent apparently results in no interference with the normal process.[11–14] Thus the branched acids of this class show toxicity figures very similar to those of the unbranched acids, $F(CH_2)_{n+m+1}COOH$.

$$F(CH_2)_nCHMeCH_2CH_2COOH \longrightarrow F(CH_2)_nCHMeCOOH \longrightarrow F(CH_2)_{n-1}COOH$$

(4) F. L. M. Pattison, S. B. D. Hunt and J. B. Stothers, *J. Org. Chem.*, **21**, 883 (1956).

(5) R. R. Fraser, J. E. Millington and F. L. M. Pattison, THIS JOURNAL, **79**, 1959 (1957).

(6) K. Bloch, *J. Biol. Chem.*, **155**, 255 (1944).

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(10) R. A. Peters, *Proc. Roy. Soc. (London)*, **B139**, 143 (1952).

(11) H. D. Kay and H. S. Raper, *Biochem. J.*, **18**, 153 (1924).

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(14) M. J. Coon and N. S. B. Abrahamsen, *ibid.*, **195**, 805 (1952).

The fundamental distinction between the above two metabolic mechanisms is well illustrated in the case of the two isomeric acids III and V, which differ only in the position of the methyl group. The simple shift of the methyl group to the adjacent carbon atom results in one acid being over 20 times more toxic than the other.

It is also of interest to consider the progressive substitution of 8-fluoroöctanoic acid. The unsubstituted acid previously has been reported[4] to be very toxic. The substitution of one methyl group on the β-carbon atom (I) results in a remarkable drop in toxicity (nearly 200 fold), as explained by mechanism 1 above. The substitution of two methyl groups on the β-carbon atom results in another non-toxic acid (IV), the lack of toxicity of which probably is associated with complete blockage of the β-oxidation process. The latter derivative (IV) is analogous to ethyl 4-fluoro-3,3-dimethylbutanoate, $FCH_2CMe_2CH_2COOEt$, which previously has been reported[15] to be non-toxic, presumably for the same reason.

It is probably justifiable to extend the above mechanisms of intermediary metabolism to unfluorinated branched acids, $CH_3(CH_2)_nCHMe(CH_2)_mCOOH$. Thus, if m is even, the acid will be metabolized by essentially the same route as the unsubstituted acid, $CH_3(CH_2)_{n+m+1}COOH$; whereas if m is odd, the probable end-products of metabolism will be formed by β-oxidation of $CH_3(CH_2)_{n-1}COOH$.

The results and conclusions presented provide further examples of the ω-fluorine atom acting as a "tag" in the elucidation of metabolic mechanisms. The general method is of wide application, and readily could provide information regarding the metabolism of many different types of branched and unbranched aliphatic compounds.

Experimental[16]

Equipment and Intermediates.—The electrolyses were carried out in the cell and by the general procedure described previously.[2] The ω-fluorocarboxylic acids were prepared[2,4] by hydrolysis of ω-fluoronitriles[17] or by oxidation of ω-fluoroalcohols.[18] Methyl hydrogen β-methylglutarate was prepared as described by Linstead, Lunt and Weedon.[19] Methyl hydrogen β,β-dimethylglutarate (b.p. 153–154° (14 mm.), $n^{25}D$ 1.4398) was prepared from β,β-dimethylglutaric acid[20] by conversion to the anhydride followed by treatment with anhydrous methanol.[21] Diazomethane was prepared[22] from N-methyl-N-nitroso-*p*-toluenesulfonamide.

8-Fluoro-3-methyloctanoic Acid (I).—5-Fluorovaleric acid (20.0 g., 0.167 mole) and methyl hydrogen β-methylglutarate (53.4 g., 0.334 mole) were electrolyzed by the general procedure for unsymmetrical couplings.[2] Methyl hydrogen β-methylglutarate (13.5 g.) and sodium (0.57 g., 0.025 mole) were dissolved in methanol in the electrolysis cell, and a current of 1.7 amp. was applied. A methanolic solution of the remainder of the starting materials was added slowly and at such a rate as to maintain the current at 1.7 amp. Total volume of methanol used was 70 ml. When the reaction solution became slightly alkaline to litmus (*ca.* 10 hours), the electrolysis was stopped. The solution was diluted with water, acidified with glacial acetic acid, and extracted with ether. After removal of the ether, the residue was hydrolyzed by heating under reflux with 10% sodium hydroxide (300 ml.) for three hours. The resultant mixture was separated into neutral and acidic fractions using aqueous sodium carbonate, and the ether extracts of each were dried over sodium sulfate. The neutral fraction on distillation yielded 1,8-difluoroöctane (1.30 g., 10%), b.p. 70° (10 mm.), $n^{25}D$ 1.3943. We have previously reported[2] b.p. 75–75.5° (13 mm.) and $n^{25}D$ 1.3933. Distillation of the acidic fraction through a short Vigreux column gave 8-fluoro-3-methyloctanoic acid (8.9 g., 30%), b.p. 97–98° (0.15 mm.), $n^{25}D$ 1.4287.

Anal. Calcd. for $C_9H_{17}FO_2$: C, 61.35; H, 9.73. Found: C, 61.45; H, 9.53.

Further distillation of the acidic residue yielded β,β'-dimethylsuberic acid (12.2 g., 36%), b.p. 172–174° (0.4 mm.), m.p. 87–90°. Linstead, Lunt and Weedon[23] report m.p. 90–92° for a mixture of stereoisomeric β,β'-dimethylsuberic acids.

10-Fluoro-3-methyldecanoic Acid (II).—A mixture of 7-fluoroheptanoic acid (12.0 g., 0.081 mole), methyl hydrogen β-methylglutarate (26.0 g., 0.163 mole), sodium (0.28 g., 0.012 mole) and methanol (70 ml.) was electrolyzed, as above. The reaction was complete after 4.5 hours at a current of 1.7 amp. After isolation and hydrolysis in the usual way, the resultant mixture was separated into neutral and acidic fractions. The ethereal solution of each was dried over sodium sulfate. The neutral fraction on distillation yielded 1,12-difluorododecane (1.69 g., 20%), b.p. 120° (10 mm.), $n^{25}D$ 1.4177. We have previously reported[2] b.p. 120° (10 mm.) and $n^{25}D$ 1.4170. Distillation of the acidic fraction through a short Vigreux column gave 10-fluoro-3-methyldecanoic acid (7.0 g., 42%), b.p. 120–121° (0.50 mm.), $n^{25}D$ 1.4392.

Anal. Calcd. for $C_{11}H_{21}FO_2$: C, 64.67; H, 10.36. Found: C, 64.85; H, 10.29.

Further distillation of the acidic residue yielded β,β'-dimethylsuberic acid (5.8 g., 35%), with the same physical constants as described above.

11-Fluoro-3-methylundecanoic Acid (III) has been previously described.[3] Its methyl ester, prepared as an intermediate in other work, was obtained as follows. The acid III (15.0 g., 0.069 mole), methanol (25 g.), ethylene chloride (75 ml.) and concd. sulfuric acid (0.8 ml.) were heated under reflux for 16 hours. The mixture was cooled and diluted with water. The ethylene chloride layer was washed with aqueous sodium carbonate and with water. Distillation yielded the methyl ester (14.7 g., 92%), b.p. 95.5–96° (0.2 mm.), $n^{25}D$ 1.4330.

Anal. Calcd. for $C_{13}H_{25}FO_2$: C, 67.20; H, 10.85. Found: C, 67.25; H, 10.90.

8-Fluoro-3,3-dimethyloctanoic Acid (IV).—A mixture of 5-fluorovaleric acid (20.0 g., 0.167 mole), methyl hydrogen β,β-dimethylglutarate (58.0 g., 0.333 mole), sodium (0.57 g., 0.025 mole) and methanol (70 ml.) was electrolyzed, as above. The reaction was complete after 10 hours at a current of 1.7 amp. After isolation and hydrolysis, the resultant mixture was separated into neutral and acidic fractions. The ethereal solution of each was dried over sodium sulfate. The neutral fraction on distillation yielded 1,8-difluoroöctane (1.27 g., 10%), with the same physical constants as described above. Distillation of the acidic fraction through a short Vigreux column gave 8-fluoro-3,3-dimethyloctanoic acid (9.5 g., 30%), b.p. 124–125° (1.0 mm.), $n^{25}D$ 1.4340.

Anal. Calcd. for $C_{10}H_{19}FO_2$: C 63.14; H, 10.07. Found: C, 63.28; H, 9.97.

The acidic residue was recrystallized from methanol to yield $\beta,\beta,\beta',\beta'$-tetramethylsuberic acid (14.6 g., 38%), m.p. 169–170°. Birch, *et al.*,[24] report m.p. 169.5°.

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10-Fluoro-3-methyldecanoyl Chloride.—10-Fluoro-3-methyldecanoic acid (6.0 g., 0.029 mole) was added dropwise to boiling thionyl chloride (4.8 g., 0.040 mole). The resultant mixture was heated for an additional two hours on a steam-bath. Fractional distillation of the product gave 10-fluoro-3-methyldecanoyl chloride (5.3 g., 81.5%), b.p. 112–114° (1.5 mm.), $n^{25}D$ 1.4410.

Anal. Calcd. for $C_{11}H_{20}ClFO$: C, 59.32; H, 9.05; Cl, 15.93. Found: C, 59.38; H, 9.04; Cl, 15.98.

11-Fluoro-4-methylundecanoic Acid (V).—A solution of 10-fluoro-3-methyldecanoyl chloride (5.3 g., 0.024 mole) in anhydrous ether (25 ml.) was added to a stirred ethereal solution of diazomethane (5.9 g., 0.14 mole) cooled in an ice-bath. Stirring was continued for three hours in the cold and then for three hours at 20–25°. The ether was removed *in vacuo* at 20–25°. The residual diazomethyl ketone, a bright yellow liquid, was dissolved in dioxane (100 ml.) and was added dropwise with stirring to a mixture of freshly prepared silver oxide (2 g.), sodium carbonate (5 g.) and sodium thiosulfate (3 g.) in water (200 ml.) at 70°. The mixture was stirred at 70° for two hours with occasional addition of fresh silver oxide. The temperature was then raised to 90° for 10 hours. The black silver residue was removed by filtration, and the filtrate was acidified with dilute nitric acid. The resultant solution was extracted with ether and separated into neutral and acidic fractions. After drying over sodium sulfate and removal of the ether, the acidic fraction was distilled through a short Vigreux column to yield 11-fluoro-4-methylundecanoic acid (1.4 g., 27%), b.p. 150–151° (0.2 mm.), $n^{25}D$ 1.4393.

Anal. Calcd. for $C_{12}H_{23}FO_2$: C, 66.02; H, 10.61. Found: C, 66.02; H, 10.60.

18-Fluoro-10-methyloctadecanoic acid (VI) has been previously described.[3]

Acknowledgments.—The work described herein was carried out under Contract (DRB X-24) with the Defence Research Board of Canada, to whom grateful acknowledgment is made for financial assistance and for permission to publish this work. The authors wish also to express their indebtedness to the National Research Council of Canada for the award of a bursary to R. G. W.; and to Drs. J. M. Parker and I. G. Walker, Defence Research Medical Laboratories, Toronto, for carrying out the toxicity and citric acid determinations.

LONDON, ONTARIO, CANADA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WESTERN ONTARIO]

Toxic Fluorine Compounds. XVII.[1] Some 1-Fluoroalkanes, ω-Fluoroalkenes and ω-Fluoroalkynes

BY F. L. M. PATTISON AND J. J. NORMAN

RECEIVED DECEMBER 26, 1956

Some 1-fluoroalkanes (*n*-alkyl fluorides), ω-fluoroalkenes and ω-fluoroalkynes were prepared for biochemical studies, and for use as intermediates in the synthesis of other compounds. The even-chain 1-fluoroalkanes are very toxic. Whereas no clear-cut conclusions could be drawn regarding the biochemical breakdown of 1-alkenes, evidence was obtained for ω-oxidation of 1-fluoroalkanes, and, less convincingly, for hydration of 1-alkynes to the corresponding methyl ketones. Ethyl ω-fluorolactate, $FCH_2CH(OH)COOEt$, the preparation of which is described, was found to be non-toxic.

The three classes of monofluorinated hydrocarbons described in this paper were prepared for toxicological studies, and hence to obtain information regarding the breakdown *in vivo* of the unfluorinated analogs. ω-Oxidation had previously been postulated[2] in the biological degradation of certain fluoroketones; it was recognized that the study of 1-fluoroalkanes would provide additional evidence for this mechanism. The results presented here are in conformity with the suggestion. In an earlier report[3] was mentioned the toxicity of 11-fluoro-1-undecene; the inference was drawn that the alkene was converted to the intermediate 11-fluoro-1,2-undecanediol,[4] which in turn was oxidized with loss of one carbon atom. The toxicities of the ω-fluoro-1-alkenes presented below do not tally with this simple mechanism. In regard to the biological fate of the 1-alkynes, hydration to the corresponding methyl ketones was considered most likely; the toxicity figures shown in Table II, supplemented by some studies of citric acid accumulation, lend support for this prediction.

(1) Part XVI, THIS JOURNAL, **79**, 2308 (1957); issued as DRB Report No. SW-37.

(2) R. R. Fraser, J. E. Millington and F. L. M. Pattison, *ibid.*, **79**, 1959 (1957).

(3) F. L. M. Pattison, *Nature*, **174**, 737 (1954).

(4) F. L. M. Pattison, *ibid.*, **172**, 1139 (1953).

Preparation

The majority of the 1-fluoroalkanes were prepared from alkyl halides or alkyl sulfonates by treatment with potassium fluoride in diethylene glycol.[5–10] Special procedures, for example the cleavage of an alkyl *p*-toluenesulfonate with silver fluoride in acetonitrile, were used in a few instances, but none proved superior to the two above-mentioned methods, both of which already have been described. All the 1-fluoroalkanes have been prepared previously in other laboratories.

The ω-fluoroalkenes listed in Table I were prepared from ω-haloalkenes or from ω-methanesulfonoxyalkenes[10] by treatment with potassium fluoride in diethylene glycol. All four members were prepared by the former method, while 5-fluoro-1-pentene was obtained also by the latter method.[10]

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