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Formation of F^{18}-Labeled Fluoro-Organic Compounds by the $F^{19}(n, 2n)$ Reaction

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Fluoro-organic compounds were subject to irradiation by fast neutrons produced in a nuclear reactor; fluoroderivatives labeled with F^{18} were produced and their yield was determined. It was found that labeling yields of fluoro-organic compounds were substantially higher than those of other organic compounds exposed to fluorine 18 produced extramolecularily, either by the $O^{16}(H^3, n)$ or by the $F^{19}(n, 2n)$ reactions. The extent of substitution of a hydrogen atom by radiofluorine was found more than 100 times higher than that of a fluorine atom. It was shown that the labeling occurs mainly in the same part of the molecule which carried the original fluorine atom. In some cases it was shown that it is the same atom which is transformed to a radionuclide.

When fluoroorganic compounds were irradiated in solution, a constant molecular labeling yield was observed. This yield which was obtained in dilute solutions in water, acetic acid or ethanol, was found independent of solute concentration; moreover, it was not affected by the presence of scavengers. The labeling yield of the aliphatic solvents was lower when exposed to fluorine 18 produced from an organically bound fluorine than from a fluoride ion.

It is difficult to interpret the experimental results without assuming that a genuine retention of the transformed fluorine 18 in the parent molecule takes place. It is suggested that the $(n, 2n)$ reaction proceeds, in part at least, as a spallation-type reaction, forming an excited F^{18} nucleus which does not undergo any recoil. The excited F^{18} is subsequently converted to the ground state following gamma emission; the recoil energy of many of these gammas is not sufficient to cause an irreversible cleavage of the C–F bond.

INTRODUCTION

THE reactions of atoms which have undergone nuclear transformations have been subject to extensive investigations.[1,2] Several mechanisms have been proposed, including the reactions of "hot atoms,"[3] diffusive thermalized atoms, "billiard ball" replacements,[4] ionic interactions,[5] and hot spot diffusive reactions.[6] The main experimental tools to distinguish between the different mechanisms are the identification of products, the effects of dilution in liquid and gas phase[7] and the effects of scavengers on the radiochemical yield of labeled products. Surprisingly enough, no substantial differences in labeling yield were observed in many systems, when the same compounds were subject to different nuclear transformations,[8–10] e.g., (n, γ) *I.T.*, (d, p) or $(n, 2n)$. This result implies that the labeling reaction occurs at the terminal stage of lifetime of the newly transformed atom, irrespective of its previous history.

In certain systems, however, different results were obtained with isotopic radionuclides formed by different nuclear processes.[11,12] In both cases cited, the labeling yield of the nuclide produced by the $(n, 2n)$ reaction was higher than that formed by either (n, γ) or (γ, n) reactions. The result is rather surprising in view of the fact that the recoil energy of the $(n, 2n)$ produced radionuclide is expected to be substantially higher than that produced by the (n, γ) reaction, but it is lower than the product of the (γ, n) process. It was of interest to compare the radiochemical behavior of the same radionuclide produced by two different nuclear processes, one involving an isotopic transformation and the other being a transmutation from another element; in this case, "extramolecular" and "intramolecular" labeling processes could be compared. Fluorine 18 may be produced by both the F^{19} $(n, 2n)$ and the O^{16} (H^3, n) reactions, thus it might be an appropriate example for such a comparative study.

In the irradiation of fluorobenzene by fast neutrons, 36% of the fluorine activity was found in the organic phase[13]; the mechanism of this retention has not been elucidated. In an extensive study[14] of the chemical behavior of fluorine 18 produced by the O^{16} (H^3, n) F^{18} reactions, it has been shown that fluorine atoms in a thermalized state are the active species in the labeling process. The labeling yields were, however, much lower than those observed in the case of the F^{19} $(n, 2n)$ F^{18} reactions.[13] It became of interest to investigate the mechanism of retention of the latter process. In the

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following study, fluoroorganic compounds were irradiated by fast neutrons generated in a nuclear reactor, and their labeling yields in pure state and in solution were measured. From these results it became possible to interpret the difference in behavior of fluorine 18 in the two systems and to elucidate the mechanism of retention in the $(n, 2n)$ process.

EXPERIMENTAL

Materials

Organic reagents used for irradiation were of cp grade and were further purified by recrystallization or distillation as necessary. Special fluoroderivatives, not available commercially, were made available to us by Dr. Z. Pelchovich from the Institute of Biological Research, Nes-Ziona. Each reagent was tested for purity by checking on its physical properties, e.g., melting point or refractive index. Organic reagents of cp grade were used for the preparation of derivatives without further purification. Inorganic reagents used were of analytical grade and did not undergo any further purification. Triple distilled, conductivity-tested water was used as solvent. Lithium salts of monofluoro- and trifluoracetic acids and of *p*-fluorobenzoic acid were prepared by neutralizing the acid with lithium hydroxide. The water was then evaporated under vacuum and the lithium salt was dried until constant weight. Li^6 96% and Li^7 99.98% were obtained from Oak Ridge National Laboratory. $H_3B^{10}O_3$ was prepared by oxidation of elementary boron 10 99.5% by nitric acid.

Irradiation of Samples

One to two grams of the solid material or 5–10 ml of liquid material or of solution were encapsulated and sealed in polyethylene containers and irradiated in the pneumatic tube of the Israel Research Reactor 1 (swimming-pool-type reactor). The thermal neutron flux of irradiation was 7.10^{11} $n/cm^2/sec$. The samples were irradiated for 6 min, resulting in an irradiation dose $2.5.10^{14}$ nvt/cm^2. When thermal neutron flux was exclusively used for irradiation, the samples were irradiated in the thermal column of the same reactor with 60 cm of graphite separating the sample from the reactor core. The thermal neutron flux was about 10^{10} $n/cm^2/sec$ and the samples were irradiated for 2 h.

Chemicals Procedure and Radioassay

The irradiated samples were dissolved in water (or in 50% ethanol), and 1 ml of 0.001 M NaF solution was added as a hold-back carrier. The solutions at *p*H 7–8 were passed through a column of chromatographic alumina, carrier sodium fluoride was added again and the procedure was repeated once or twice until constant specific activity was attained. The chromatographic alumina columns were shown to hold back fluoride activity better than 98% on a single passage. After removing the fluoride activity, the organic compound labeled with F^{18} was isolated and purified as described below. When alcoholic solutions were irradiated, the alcohol was separated by distillation after passing through alumina columns; the fraction boiling up to 90°C was collected and subsequently dried over potassium carbonate. The solutes of the alcoholic solutions were separated from the fluoride free nondistilled solutions. In cases where the organic substrate did not contain any fluorine before labeling, the original compound was isolated, assuming that the fluoroderivative which is present at extremely low concentrations, will follow the bulk material without losses. This has been found to be true as no changes in the specific activities of such mixtures were observed on different physical or chemical treatments. To check on this assumption in the cases where fluoroacetic and fluorobenzoic acids were isolated from the irradiated samples, mono-fluoroacetic acid or a mixtureof *o*-, *m*-, and *p*-fluorobenzoic acids were added. The fluoroderivatives were isolated and their radioactivity was found equal to that obtained without addition of carriers.

The activity was determined in a NaI well-type scintillation counter with a discriminator setting at 0.4 MeV. The activity of each sample was measured for 6 h at 1-h intervals, starting about 2 h after end of irradiation, and then at 20 and 28 h after end of irradiation. The measured activity was plotted graphically and corrected for radiocontaminants, e.g. Na^{24}. After correcting for the longer-lived activities, the points were found to correspond to a half-life of 105–115 min. The activity at time zero (stop of irradiation) was obtained by graphical extrapolation, using a slope corresponding to $t_{\frac{1}{2}}=112$ min. Following this procedure, there was no necessity for further corrections, due to the presence of short-lived radiocontaminants in the irradiated samples. All activities referred to in the following presentation are activities at zero time.

Weighed amounts of the irradiated compounds or measured amounts of the irradiated solutions were taken for radioassay. Aliquots of the aqueous solutions were taken before and after passing through alumina columns. The final derivatives of the organic labeled compounds were weighed after being dried to a constant weight and their molar activities determined.

Calculation of the Labeling Yield of Organic Compounds[14]

A. Pure Compounds

The labeling yield was calculated by relating the total activity of F^{18} in the irradiated sample to the organically bound activity found in the purified labeled compound or in its derivative. *The total* F^{18} *activity per mole* T was calculated from the initial specific activity S_i (c/min/g) of the irradiated compound, multiplied

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by the molecular weight M; $T = S_i \times M$. *The molar activity of the final product* F was calculated from the final specific activity S_f multiplied by the molecular weight of the final derivative M_d; $F = S_f \times M_d$. In cases when the original compound did not contain fluorine and no fluoro derivative was added as carrier, M_d was taken for the fluorine-free final derivative. The *percent yield of labeling* is defined $Y = 100\,F/T = 100\,S_f M_d / S_i M$. This mode of calculation was adopted because in many cases the purified derivative of the labeled product, the activity of which was determined, had a different molecular weight than the originally irradiated compound.

B. Solutions

The labeling yield in solutions Y_s containing C moles *per gram* organic solute was calculated from the total activity T_s produced *per gram* solution, compared with the molar activity of the pure labeled solute F, $Y_s = 100\,FC/T$.

Isolation of Fluorine Labeled Pure Compounds and Derivatives

(1) Monofluoroacetic, trifluoacetic, acetic, and propionic acids were separated as their *p*-bromophenacyl esters,[15a] which were washed and recrystallized. When acetic acid was irradiated, monofluoroacetic acid was added as carrier and its *p*-bromophenacyl ester was precipitated. No change in the activity separated was found when fluoroacetic acid was isolated with acetic or monofluoroacetic acid as carrier. Acetic and propionic acid were also separated as their silver salts in the presence of fluoride carrier. The silver salt was separated by centrifuge and subsequently dissolved in nitric acid; next it was precipitated by adding ammonia. This procedure was repeated three times. The specific activities of the silver salt did not change between the second and third precipitation.

(2) Benzoic and *p*-fluorobenzoic acids, 2-carboxy-3-fluorophenyl naphthyl ketone and 5-fluorouracil were precipitated by acidification of their alkaline solutions in the presence of fluoride hold-back carrier. When benzoic acid was irradiated, a mixture of ortho, meta, and para fluorobenzoic acids 1:1:1 was added as carrier. When a mixture of benzoic acid and fluorobenzoic acids 1:1:1:1 was recrystallized from hot water, it was shown spectrophotometrically, that the fractionation per recrystallization did not exceed 2%. The compounds were then recrystallized three times from water.

(3) 2-carboxy-3-fluorophenyl naphthyl ketone was also determined as its 2,4-dinitrophenyl hydrazone which was then recrystallized from alcohol.[15b] This was done in order to find out whether labeled decomposition products are formed, which could have been precipitated with the mother-compound in acid form as described under 2.

(4) Aliphatic alcohols were separated by distillation from alkaline solutions containing fluoride hold-back carrier, next they were dried over anhydrous sodium sulphate, the 3,5-dinitrobenzoate[15c] derivatives were then separated and recrystallized.

(5) Fluorophenols were separated as their *o*-acetic acid derivatives formed in alkaline solution with chloroacetic acid.[15d]

(6) Fluorobenzene, *p*-fluorotoluene, benzyl fluoride, alpha-fluoro- and trifluoroacetophenone, *p*-fluorobenzyl alcohol and hexane were separated by distillation after repeated washings with dilute sodium fluoride solution.

(7) 1-fluoro-9-methylanthracene was precipitated from alcoholic solution by adding water. This procedure was repeated three times.

(8) *p*-fluorobenzyl alcohol was oxidized by alkaline permanganate solution,[15e] to *p*-fluorobenzoic acid which was then purified by recrystallization. The same treatment was performed on alpha-fluoro- and trifluoroacetophenone after hydrolysis in alkaline solution. In a kinetic test it was shown that under the experimental conditions *p*-fluorobenzyl alcohol is completely oxidized to *p*-fluorobenzoic acid just like benzyl alcohol to benzoic acid. It may be inferred that the difference in the rates of oxidation of fluoroaromatic derivatives as compared to nonfluoroaromatics, does not induce any fractionation in our oxidation and precipitation procedure. A mixture of *o*, *m*, and *p*-fluorobenzoic acids was added to the oxidized solution as carriers as described above. These oxidations were carried out in order to determine the distribution of fluorine between the aromatic ring and the aliphatic group.

(9) Ortho and para fluorophenol irradiated in solution of *n*-hexane were gas chromatographically analyzed for their labeled products. The irradiated solution was passed through an alumina column, then a mixture 1:1:1 of the three isomeric fluorophenols was added. The solution was passed over a silicone grease column at 100°C, using nitrogen as carrier gas. It was difficult to separate the meta from the para isomer, thus these two isomers were analyzed as a single fraction. Each fraction was completely collected in a toluene-containing test tube which was then measured in the well-type scintillation counter.

RESULTS

Organic compounds were labeled with fluorine 18 produced by the F^{19} $(n, 2n)$ F^{18} reaction; the results are summarized in Table I. Two types of neutron fluxes were applied, a flux of mixed energies obtained in the pneumatic tube and a thermal flux in the thermal

[15] A. I. Vogel, *Practical Organic Chemistry* (Longmans, Green & Company, Ltd., London, 1959), 3rd ed. (a) p. 362; (b) p. 344; (c) p. 262; (d) p. 682; (e) p. 520.

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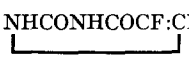
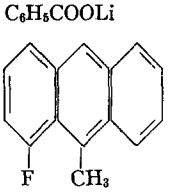
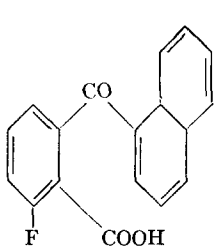
TABLE I. Formation of F^{18} labeled fluorocompounds.

	Compound	Yield of labeling
1.1	CH_2FCOOH	10.0
1.2	$CH_2FCOOLi^7$	9.5
1.3	$CH_2FCOOLi^7+10\%(CH_3O)_3B$	9.2
1.4	$CH_2FCOOLi^6$	1.4
1.5	$CH_2FCOOLi^a$	2.7
1.6	CH_3COOLi	3.0
1.7	$CH_3COOH+NH_4F$	2.9
1.8	CF_3COOH	2.8
1.9	CF_3COOLi^a	0.07
1.10	CF_3COOLi	2.0
1.11	CF_3COOLi^7	3.2
1.12	$C_2H_5OH+NH_4F$	3.6
1.13	$C_2H_5OH+Li^6OH$	3.5
1.14		8.0
1.15	$C_6H_5CH_2F$	11.0
1.16	C_6H_5F	14.5
1.17	p-$FC_6H_4CH_3$	17.0
1.18	o-FC_6H_4OH	16.0
1.19	p-$FC_6H_4CH_2OH$	13.0[b]
1.20	$C_6H_5COCH_2F$	15.0[c]
1.21	$C_6H_5COCF_3$	12.0[d]
1.22	p-FC_6H_4COOH	20.0[e]
1.23	p-$FC_6H_4COOLi^7$	19.0
1.24	p-FC_6H_4COOLi	6.5
1.25	p-$FC_6H_4COOLi^6$	3.2
1.26	C_6H_5COOLi	2.8
1.27		19.5
1.28		21.0

[a] Thermal neutron flux only.
[b] p-FC_6H_4COOH obtained by oxidation of p-$FC_6H_4CH_2OH$ showed a labeling yield of 11.0%.
[c] C_6H_5COOH obtained by oxidation of $C_6H_5COCH_2F$ showed a labeling yield of 3.0%.
[d] C_6H_5COOH obtained by oxidation of $C_6H_5COCF_3$ showed a labeling yield of 3.7%.
[e] Yield after annealing at 150° for 1 h increased to 27.0%.

column. The flux of neutrons in the thermal column was free of neutrons with energies above 10.5 MeV; this was proved by irradiating trifluoroacetic acid under conditions similar to those of the irradiation of lithium trifluoroacetate—the *total* activity produced in the latter compound was more than 100 000 times higher than that of the irradiated pure acid. In the pneumatic tube, on the other hand, comparable *total* activities were obtained when equal quantities of lithium acetate or monofluoroacetic acid were irradiated for the same time.

The yields of labeling were compared with those obtained with F^{18} produced by the Li^6 $(n, He^4)H^3$, O^{16} $(H^3, n)F^{18}$ reactions. It is evident that the labeling yield of fluoroacetic acid by the F^{19} $(n, 2n)$ reaction is much higher than that obtained by the irradiation of its lithium salt by thermal neutrons only (1.1–1.5). This difference cannot be accounted by the difference between the acid and its salt, as lithium 7 fluoroacetate gives the same labeling yield (1.1–1.2). The difference between yields of labeling by the two processes becomes even more conspicuous when lithium 7 fluoroacetate is compared with its lithium 6 analog (1.2–1.4). This change in yields of labeling cannot be due to local radiation damage due to the Li^6 $(n, \alpha)H^3$ reaction. This is proved by the fact that boron 10 at an equivalent concentration does not affect the labeling yield of fluoroacetic acid. (1.2–1.3–1.5) by its B^{10} $(n, \alpha)Li^7$ reaction. Ten percent methyl borate yield the same number of heavy particles per gram as natural lithium fluoroacetate. It has also been shown[14] that the yield of fluorine-labeled decomposition products by the Li^6 (n, α) reaction does not exceed 10% of the organically bound F^{18}. When the source of fluorine, on the other hand, was extramolecular, comparable yields were obtained disregarding the source of the fluorine 18; acetic acid or ethanol were labeled by fluorine produced by the $(n, 2n)$ reaction, with yields of labeling comparable to those obtained for fluorine produced by the (H^3, n) reaction (1.6–1.7, 1.12–1.13). The labeling yields of fluorouracyl and benzyl fluoride are comparable to that of fluoroacetic acid (1.1–1.14, 1.15).

Trifluoroacetic acid was labeled to a smaller extent than the monofluoro acid (1.1–1.8, 1.2–1.11). Irradiation of lithium trifluoroacetate with thermal neutrons (1.9) resulted in a very low labeling yield, which means that the fluorine atoms produced by the O^{16} (H^3, n) reaction are not efficient in substituting fluorine on carbon. This result is in accordance with the diminished yield of labeling when natural lithium trifluoroacetate was irradiated with neutrons of mixed energies (1.10–1.8, 1.11).

The yields of labeled derivatives of irradiated fluoroaromatic compounds is higher than that of fluoroaliphatic compounds (1.1–1.16, 1.17). The labeling yield of fluorobenzene found was 14.5 after distillation, a "yield" of 45% was, however, obtained, when the irradiated samples were subject to repeated extractions

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only (cf. reference 13). The yield of aromatic fluoroderivatives ranges from 13 to 20% in different aromatic compounds (1.16 to 1.19, 1.22, 1.23, 1.27, 1.28). The yield of labeling of aliphatic radicals in aliphatofluoroaromatic compounds was found small compared to that of the aromatic nucleus (1.19). On the other hand, when the aliphatic radical contained the fluorine atom like in α-fluoroacetophenone, the aromatic nucleus was labeled with a low yield (1.20, 1.21). The labeling yields of the nonfluorinated parts of the molecules was found equal to that of nonfluorinated compounds labeled by extramolecular fluorine.[14] When a lithium 6 salt of a fluoroaromatic compound was irradiated by a mixed-neutrons flux, a considerably lower yield was observed, compared to the lithium 7 salt (1.23–1.25); this demonstrates again the fact that fluorine is not substituted by F^{18} to any appreciable extent. The irradiation of solid fluoroderivatives gave a little higher yield of labeling especially after annealing (1.22, 1.23, 1.27, 1.28).

Organic compounds were labeled by the $(n, 2n)$ and the (H^3, n) reactions also in solution. The results are given in Table II. The labeling yield by F^{18} produced by the O^{16} (H^3, n) reaction in solution, is comparable with that of F^{18} produced from extramolecular fluorine by the $(n, 2n)$ reaction (2.1–2.2; 2.3–2.4). It was found that the labeling yield of fluoroderivatives in dilute solution is independent of their concentration (2.5, 2.6, 2.9, 2.10, 2.12, 2.13, 2.17, 2.18, 2.20, 2.22, 2.23) and is unaffected by free radical scavengers which were found to diminish considerably the labeling yield by the O^{16} (H^3, n) reaction in solution[14] (2.10–2.11; 2.18–2.19). The labeling yield by the latter process in solution is independent on the concentration of the labeled solute (2.14, 2.15; 2.16, cf. reference 14). It should be noted that the limiting value of the labeling yield of aromatic fluorocompounds is equal for different compounds and in different solvents (2.13, 2.20, 2.23, 2.24, 2.25, 2.26, 2.27, 2.28). In highly concentrated solutions, the labeling yield is higher than the limiting value in dilute solutions (2.21–2.22). Some labeling of the aliphatic solvent was also observed which is independent of solute concentration (2.22, 2.23), this labeling yield, is, however, lower than that observed for fluorine 18 produced from unbound F^{19} (1.12). The difference between the intra- and extramolecularly produced fluorine is again demonstrated when the lithium 6 salt of *p*-fluorobenzoic acid is compared with lithium 7 salt (2.7–2.16). Again it has been shown that the diminished yield in the presence of Li^6 is not due to radiation damage (2.7–2.8), as the radiation damage to the solution by 10% $H_3B^{10}O_3$ is two orders of magnitude greater than that of 0.2 M lithium 6. In this case there are equal chances for the Li^6 and B^{10} to cause radiation damage, as they are homogenously distributed in solution.

The identity of the product formed from an aromatic fluoroderivative in dilute solution was examined by analyzing the isomer distribution of the labeled product of ortho and para fluorophenol (2.27, 2.28). It has been shown that the original isomer is produced in the labeled form at an overwhelming yield compared with its other isomers.

DISCUSSION

The formation of organic compounds labeled with newly transformed radionuclides, has been considered in all the "classical" works on the subject as an exposure of the substrate compound to a flux of fast, epithermal or thermal radioactive atoms or ions. The selectivity of the point of attack and the sensitivity to scavengers, were used to assign the energy range of the attacking radionuclides.[1,2] In view of these postulations, the same labeling yields are expected, disregarding the mode of formation of the transformed radionuclides.

When these criteria were tested on fluorine 18 produced by the O^{16} (H^3, n) reaction, or by the F^{19} $(n, 2n)$ process in fluoride ions, equal yields of substituted derivatives were actually observed. When, however, the source of F^{18} was organically bound fluorine atoms transformed by the $(n, 2n)$ reaction, much higher yields of labeling were observed. "Intramolecular" labeling experiments show that the labeling yields of an aliphatic side chain by fluorine generated on the aromatic ring, as well as the labeling of an aromatic ring by fluorine generated on an aliphatic side chain, are comparable to those obtained by "extramolecular" fluorine 18, whereas the organic radical to which the fluorine was originally bound is labeled with a much higher yield. The retention of F^{18} in ortho and in para fluorophenol emphasizes even more the selectivity of the retention process.

The extensive labeling of fluoroderivatives might be due to two alternative mechanisms. (1) A "billiard ball" replacement of organically bound fluorine by radiofluorine atoms. (2) The formation of long-lived residual organic radicals which recombine with the original transformed fluorine. The first mechanism is unlikely because of the comparable masses of F^{18} with those of C^{12}, N^{14}, or O^{16}, all of which may act as efficient moderators for epithermal fluorine atoms; moreover, it was unambiguously shown that no *fluorine* substitution takes place in either aromatic or aliphatic fluoroderivative with fluorine 18 produced by the O^{16} (H^3, n) reaction. The second mechanism which essentially postulates a "nest of radicals" is expected to be strongly affected by dilution and free-radical scavengers. These assumptions have been examined by investigating the labeling process in dilute solutions and in the presence of scavengers, and it has been found that a certain percentage of labeling yield is unaffected by dilution or by the presence of scavengers. This percentage being equal for all fluoroaromatic compounds tested in various solvents. If a "nest of radical" would be formed, the probability of recombination should be dependent on the reactivity of the different free

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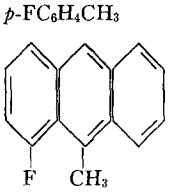
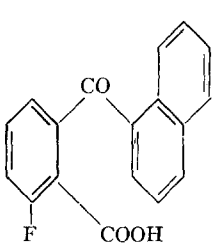
TABLE II. Formation of F^{18} labeled fluorocompounds in solutions.

	Solute	Solvent	Conc. (moles/liter)	Yield of labeling
2.1	$C_2H_5COOH+1M NH_4F$	H_2O	1.40	2.0
2.2	C_2H_5COOLi	H_2O	1.40	1.9
2.3	$C_6H_5COOH+1M NH_4F$	H_2O	0.38	0.7
2.4	C_6H_5COOLi	H_2O	0.40	0.6
2.5	p-FC_6H_4COOH	H_2O	0.29	3.0
2.6	p-FC_6H_4COOH	H_2O	0.24	3.5
2.7	p-$FC_6H_4COOLi^7$	H_2O	0.20	3.2
2.8	p-$FC_6H_4COOLi^7+10\%H_3B^{10}O_3$	H_2O	0.20	2.8
2.9	p-FC_6H_4COOH	H_2O	0.15	3.5
2.10	p-FC_6H_4COOH	H_2O	0.07	3.1
2.11	p-$FC_6H_4COOH+2M HCOOH$	H_2O	0.07	3.0
2.12	p-FC_6H_4COOH	H_2O	0.04	3.0
2.13	p-FC_6H_4COOH	H_2O	0.02	3.0
2.14	p-FC_6H_4COOLi[a]	H_2O	0.80	1.4
2.15	p-FC_6H_4COOLi[a]	H_2O	0.50	0.8
2.16	p-$FC_6H_4COOLi^6$	H_2O	0.20	0.3
2.17	p-FC_6H_4COOH	CH_3COOH	0.63	3.3
2.18	p-FC_6H_4COOH	CH_3COOH	0.31	3.2
2.19	p-$FC_6H_4COOH+2M HCOOH$	CH_3COOH	0.31	3.3
2.20	p-FC_6H_4COOH	CH_3COOH	0.20	2.9
2.21	C_6H_5F	C_2H_5OH	4.0	4.3[b]
2.22	C_6H_5F	C_2H_5OH	1.5	3.0[c]
2.23	C_6H_5F	C_2H_5OH	0.7	3.0[d]
2.24	p-$FC_6H_4CH_3$	C_2H_5OH	0.9	3.0[e]
2.25		C_2H_5OH	0.05	3.0
2.26		H_2O	0.08	2.9[f]
2.27	o-FC_6H_4OH	n-C_6H_{14}	0.5	2.6[g,h]
2.28	p-FC_6H_4OH	n-C_6H_{14}	0.5	2.7[i]

[a] Thermal neutrons only.
[b] Labeling yield of C_2H_5OH—0.5.
[c] Labeling yield of C_2H_5OH—2.0.
[d] Labeling yield of C_2H_5OH—2.0.
[e] Labeling yield of C_2H_5OH—2.2.
[f] Yield of labeled decomposition products including fluorophthalic acid<10% of the organically bound fluorine.
[g] Labeled yield of C_6H_{14}—4.7.
[h] Relative yield ortho:meta+para—14:1.
[i] Relative yield ortho:meta+para—1:13.

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radicals formed in the spur; it is most unlikely that different phenyl radicals should compete with water, ethanol or acetic acid to the same extent and give the same labeling yield. It should be noted that the labeling yield of the aliphatic solvent was found substantially lower when the F^{18} originated from an organically bound fluorine, as compared to F^{18} produced from fluoride ions. This means that even in dilute solutions, the F^{18} formed by the $(n, 2n)$ process has better chances to recombine with the original molecule, (even with the particular part of the molecule which carried the fluorine and which might be less vulnerable to substitution by "extramolecular" F^{18} than with molecules of the solvent.

Unless one assumes genuine retention, it is hard to understand why a fluorine atom in an alcoholic medium should select the original compound for attack and behave quite differently from a fluorine atom generated by the same nuclear process from a fluoride ion. As long as the newly transformed radionuclide remains in the sphere of reactivity of the original molecule, we may refer to it as being actually retained by the parent molecule. It should be remembered that fluorine atoms in any energetic state are expected to be most reactive chemical species,[16] and it is hard to explain this selectivity of attack on the fragment of the original molecule, unless the transformed fluorine did not recede from the original molecule far enough to become equivalent with a free "extramolecular" fluorine atom.

A genuine retention of a transformed radionuclide following a $(n, 2n)$ reaction, may be explained by two principally different nuclear mechanisms; one involving the formation of a compound nucleus, and the other being a kind of spallation reaction. According to the first mechanism, the fast neutron interacts with the bound fluorine atom, imparting its large momentum to the fluorine atom; this momentum, of over 10.5 MeV, should undoubtedly break the C–F bond permanently.

The second mechanism postulates that the $(n, 2n)$ reaction proceeds as an elastic collision of the incoming neutron with a neutron in the nucleus resulting in the emission of two neutrons. The whole process takes a very short time (of the order of 10^{-22} sec) and the fluorine atom as a whole remains intact, as far as conservation of momentum is concerned; thus the C–F bond is not severed at this stage. The F^{18} nucleus might eventually remain in an excited state and will reach its ground state by the emission of gamma radiation. There are four close levels of excitation of F^{18} at 0.94, 1.043, 1.085, and 1.127 MeV[17]; further levels of excitation were determined at 1.7, 2.1, 2.53, and 3.06 MeV[17]; excitation to these levels as well as to the 5.61–5.67 doublet will undoubtedly result in irreversible rapture of C–F bond. If the excitation energy is of the order of 1 MeV, emitted as a single photon, the recoil energy of the F^{18} will be 30 eV.[4] This recoil energy may cause the rapture of the C–F bond, but the separated radiofluorine which will be most probably in the F^+ state (IP 17.5 eV) will recede with a kinetic energy of about 15 eV, which might bring it to a maximum distance of less than one angstrom unit from the original carbon.[18] This F^+ ion will undergo immediate neutralization by capturing a neighbouring electron. There are good chances for the F atom to recombine with the original free radical. This model of reaction may explain the experimental findings of genuine retention.

It should be emphasized that we do not exclude the model of a compound nucleus as a plausible mechanism for the $(n, 2n)$ reaction; it is most probably that a major part of the transformed fluorine atoms are formed by this mechanism and are ejected into the irradiated medium to a considerable distance from the original molecule.

It may be concluded that in the F^{19} $(n, 2n)F^{18}$ reaction, genuine retention of the transformed radiofluorine has been demonstrated and it was possible to imply information from the chemical fate of the daughter nucleus on the mechanism of the nuclear process, namely the existence of a spallation-like process occurring in a light nucleus, in a $(n, 2n)$ reaction at relatively low energies.

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