A Study of the Recoil Labeling of Fluothane with ^{82}Br during Neutron Irradiation

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1,1,1-Trifluoro-2-chloro-2-bromoethane labeled with ^{82}Br (fluothane-^{82}Br) was purely separated from neutron-irradiated fluothane by means of a gas-chromatographic technique. The maximum radiochemical yield of fluothane-^{82}Br was 38.3% when the target material was irradiated with neutrons to nvt of 3.4×10^{16} n·cm^{-2}. Of the many organic species produced by the recoil events following the radiative neutron capture and subsequent (I.T.) processes, CF$_3$^{82}Br and CF$_3$CHBr^{82}Br were also identified. In order to elucidate the mechanism of recoil labeling, the scavenger effects were examined in the CF$_3$CHClBr–Br$_2$ system, Br$_2$ being used as a radical scavenger. The "high-energy" yields of CF$_3$CHCl^{82}Br thus estimated were approximately 3.6 to 4.8%. It was suggested that most of the ^{82}Br-labeled species were formed through the "thermal" processes including the reaction of ^{82}Br with the organic radicals produced by the radiolysis of the parent fluothane.

Fluothane (1,1,1-trifluoro-2-chloro-2-bromoethane) is a volatile anesthetic, and its metabolism has attracted much interest in biological research.[1] Fluothane labeled with radioisotopes has been used for the investigation of the behavior of anesthetics *in vivo*. Carbon-14 labeled fluothane has been synthesized starting with chloroacetic-1-^{14}C acid and used for the studies of metabolism.[2,3]

The aim of the present work is to investigate the feasibility of the recoil labeling of fluothane with ^{82}Br during neutron irradiation. The method is expected to be convenient for preparing labeled compounds with short-lived radioisotopes. Several factors leading to the preparation of fluothane-^{82}Br, determined by means of a gas chromatographic analysis, will be described in this article.

Fluothane is, on the other hand, an interesting substance in the fields of recoil and radiation chemistry, because C–H, C–F, C–Cl, C–Br, and C–C bonds coexist in a molecule. To compare the reactivity to a recoil atom among different kinds of chemical bonds may give important information for elucidating the mechanism of recoil labeling. The fundamental chemical behavior of ^{82}Br recoil atoms produced in neutron-irradiated fluothane will be discussed, with emphasis laid on the radiation and scavenger effects as well as on the reactivity of recoil atoms.

Experimental

1,1,1-Trifluoro-2-chloro-2-bromoethane (fluothane) from Takeda Chemical Industries, containing 0.01% of thymol, was purified at room temperature by means of a vacuum line with an approximate pressure of 10^{-3} mmHg. The vaporized portion of the material, the vapor pressure of which was 242 mmHg at 20 °C, was condensed in a cold trap. No impurity was observed in the gas chromatogram for the material thus trapped, although trace amounts of signals considered to be due to impurities[4] were observed in the mass spectrum even after the purification. The target material, 5 or 10 μl of liquid fluothane, or a mixture of it with bromine (0.5—70% Br$_2$ by molar ratio), was sealed in a 0.3—0.5 ml quartz ampoule *in vacuo* (0.9×10^{-3} mmHg) and then irradiated in the T-pipe of the JRR-4 reactor of the Japan Atomic Energy Research Institute, operated at 2.5 MW, at an ambient reactor temperature ~50 °C. The thermal neutron flux at the irradiation position was 2.8×10^{13} n·cm^{-2} s^{-1}, with an approximate γ-ray dose rate of 0.8×10^{8} rad·hr^{-1}. The neutron-irradiated samples were left in the cooling water of the reactor for more than 24 hr. A γ-ray irradiation facility with 45 kCi of ^{60}Co sources was utilized when the target materials were exposed to γ rays for the study of radiolysis. Ten microliters of liquid fluothane sealed in the same way as in the neutron irradiation were exposed to ^{60}Co γ-rays at room temperature (dose, 2.1×10^{21} and 1.0×10^{22} eV·g^{-1}).

The irradiated sample was directly introduced into a radio-gas chromatograph by means of a specially-designed ampoule breaker,[5] so that both the gaseous and the liquid substances were injected successfully into the column. Organic species labeled with ^{82}Br were separated by a gas-chromatographic set-up consisting of a thermal conductivity detector (TCD) and a glass column 2.5 m in length and with an inner diameter of 5 mm, packed with dioctyl phthalate (20% on chromosorb W, 60—80 mesh). Helium was used as the carrier gas at the flow rate of 120 ml·min^{-1}. The temperature at the TCD was 115 °C, while that of the glass column was kept at 60 °C. The latter was gradually raised to 110 °C after the signal of fluothane was observed.

The radioactivity of ^{82}Br of the gases leaving the TCD was detected using a single-channel pulse-height analyzer with a NaI(Tl) detector (well-type, 1.75″$\phi\times$2″). The radioactivity signals were registered both on a ratemeter, feeding a signal to a two-channel recorder, and on a digital printer. In the determination of the product yields, the radioactivities adsorbed both on potassium ferrocyanides (for inorganic products) and on activated carbons (for organic products), placed before and after the gas-chromatographic column, were measured.

In identifying the chromatographically-separated species, a gas chromatograph and mass spectrometer (GC-MS) from the Japan Electron Optics Laboratory, at Miyagi University of Education, was used. When the neutron-irradiated sample was analyzed by means of the GC-MS, the sample was stored in a vessel filled with ice for more than 3 months before analysis.

Results and Discussion

In neutron-irradiated fluothane, more than 20 organic products labeled with ^{82}Br, including fluothane-^{82}Br (CF$_3$CHCl^{82}Br), CF$_3$^{82}Br, and CF$_3$CHBr^{82}Br, were found. The gas chromatogram, of both the radioactivity and the mass signals, of fluothane irradiated

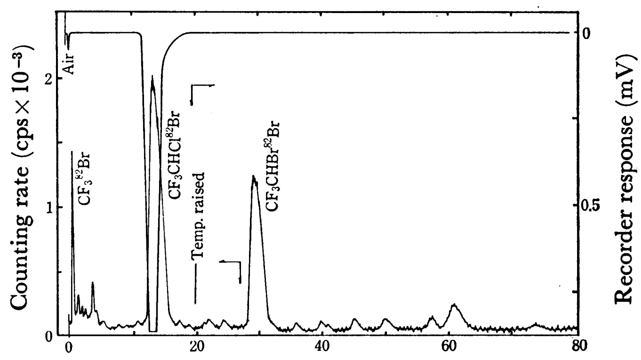

Fig. 1. Gas chromatograms of fluothane irradiated for 30 s in the JRR-4 reactor. The temperature of the gas chromatographic column was kept at 60 °C, although it was raised gradually up to 110 °C after the signal of $CF_3CHClBr$ was observed.

for 30 s in the JRR-4 reactor is illustrated in Fig. 1, where a 10 μl portion of the neutron-irradiated sample was subjected to analysis. Of the many radioactivity peaks, $CF_3CHCl^{82}Br$ showed the highest emergence. None of the mass peaks except for fluothane was found in the chromatogram, within the limits of detection.

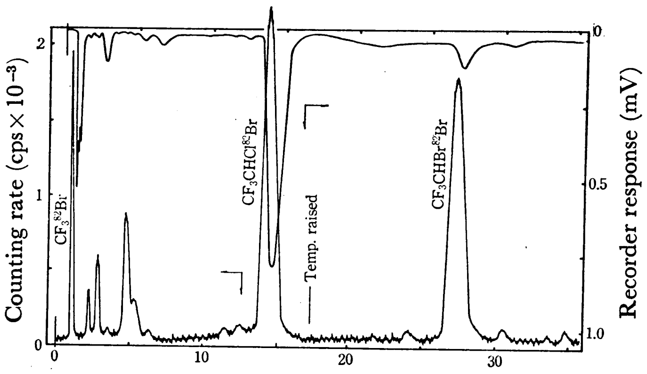

Fig. 2. Gas chromatograms of fluothane irradiated for 20 min in the JRR-4 reactor. The separation condition was identical with that of Fig. 1.

Figure 2 shows the gas chromatogram of fluothane irradiated with neutrons for 20 min. In this case, a 5 μl portion of the sample was subjected to analysis. The pattern of the radioactivity signal was identical with that in Fig. 1, while a few additional peaks were seen in the mass signal. Separation was performed by means of the gas chromatograph under the same conditions as in the previous case. Additional mass peaks were observed in the sample irradiated for more than 2 min, and the intensity increased with an increase in the irradiation time. The results suggest the occurrence of the radiolysis of the parent fluothane.

In order to examine the radiation effect, fluothane was exposed to ^{60}Co γ-rays at doses of 2.1×10^{21} and 1.0×10^{22} eV·g^{-1}. These γ-ray doses corresponded to the doses given the target material irradiated in the reactor for 25 min and 2 hr respectively. Various peaks of the radiolytic products from fluothane appeared in the gas chromatograms for both cases of γ-irradiation, although the intensities of all the peaks except for that of the parent fluothane were rather small in the former case. The pattern of the gas chromatogram for the latter case, illustrated in Fig. 3, was comparable enough with that of Fig. 2. The separation conditions of the gas chromatograph were identical with those of neutron-irradiated samples. It is noticeable that the radiolysis of fluothane is more sensitive to the irradiation in the reactor than to exposure to ^{60}Co γ-rays. This may be explained in terms of the internal radiation effect due to the recoil particles, such as ^{38}Cl, ^{80m}Br, ^{80}Br, ^{82m}Br, and ^{82}Br itself, produced in the neutron-irradiated sample. Details of the study of the radiolysis will be discussed elsewhere.[6)]

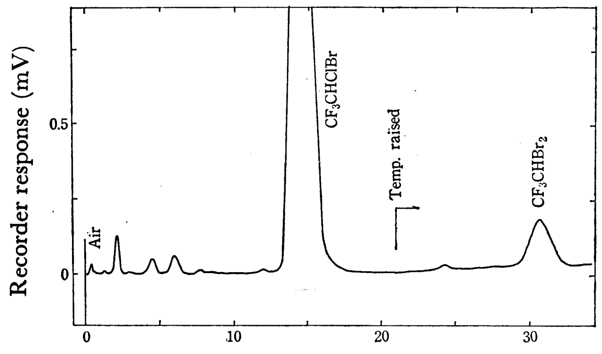

Fig. 3. Gas chromatogram of fluothane irradiated with ^{60}Co γ-rays to dose of 1.0×10^{22} eV/g. Only the liquid portion of the sample was subjected to the analysis.

The chemical distribution of ^{82}Br-labeled species resulting from the recoil processes in fluothane was investigated as a function of the irradiation time in the reactor. The radiochemical yields of the inorganic and organic products, including $CF_3CHCl^{82}Br$, are plotted against the irradiation time in Fig. 4. The overall organic yield increased abruptly around the irradiation time of 2 min and then reached a plateau at 95%, while the inorganic yield decreased from 32.6 to 5.5% in the same range of irradiation times. The yield of

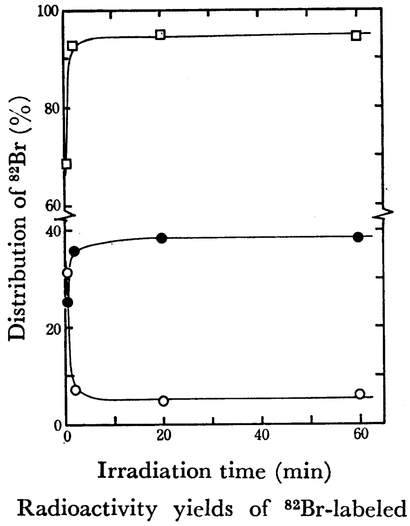

Fig. 4. Radioactivity yields of ^{82}Br-labeled products as a function of the irradiation time in the reactor. □, Overall organic products; ○, inorganic products; ●, $CF_3CHCl^{82}Br$.

$CF_3CHCl^{82}Br$ was about 26% for the target irradiated for less than 30 s; it increased to 38% at irradiation times above 2 min. Table 1 is a list of the detailed yields of the ^{82}Br-labeled products in neutron-irradiated fluothane. It is noteworthy that the yield of $CF_3CHBr^{82}Br$ was as high as 25% in the target irradiated for more than 2 min. The change in the chemical distribution of ^{82}Br-labeled species was investigated as a function of the elapsed time between 25 and 170 hr after the neutron-irradiation, but little change was observed when the irradiated samples were stored below room temperature. The results shown in Fig. 4 and Table 1 are the mean values of the experimental data, without any particular correction.

Table 1. Chemical distribution of ^{82}Br-labeled species in neutron-irradiated $CF_3CHClBr$ as a function of the irradiation time

Irradiation time	Fractional yield, %				
	Inorganic species	Organic species			
		CF_3-^{82}Br	CF_3CHCl-^{82}Br	CF_3CHBr-^{82}Br	Others
10 s	32.6	1.1	27.4	17.9	21.0
30 s	31.4	1.2	25.6	18.5	23.3
2 min	7.3	1.1	35.8	26.6	29.2
20 min	5.0	2.3	38.3	24.7	29.7
1 h	6.2	2.9	37.9	25.5	27.5
5 h	5.2	2.8	19.9	25.6	46.5

Bromine-82 is produced by both the radiative neutron capture of Br and the isomeric transition (I.T.) of the resulting ^{82m}Br. By the time the ^{82m}Br nuclei with a half-life of 6.1 min have decayed, 90% of the surviving ^{82}Br (35.34 hr half-life[7]) will have come from the isomeric transition and 10% directly from the (n, γ) activation.[8] The primary recoil event of the ^{82}Br recoil atom is almost always followed by the Auger effect, since the 0.06 MeV transition of ^{82m}Br to its ground state has an internal conversion coefficient of 382.[8,9] Several studies have shown that, in the liquid phase, the organic yields from the converted isomeric transition process occurring in bromine nuclides are higher than the organic yields from the (n, γ) recoil processes.[10–13] The relatively high yield of CF_3CHCl-^{82}Br obtained in this experiment may be attributed to the contribution of the (I.T.) process. In this article, however, the problems involving the difference in the primary recoil events are not discussed in detail.

Two chemical processes are, on the whole, involved in the mechanism of recoil labeling: a high-energy (or "hot") process and a thermal process including radical reactions. In order to estimate the ratio of a high-energy process to the thermal processes, the scavenger effect was examined in connection with the chemical distribution of ^{82}Br-labeled products in neutron-irradiated fluothane, in which Br_2 was used as the radical scavenger. As is shown in Fig. 5, typical scavenger curves were obtained for the $CF_3CHClBr$–Br_2 system irradiated for 30 s in the reactor. By extrapolating the almost linear portion of the curves to the zero bromine concentration, 4.8±0.5% of $CF_3CHCl^{82}Br$ was estimated to be produced through the "high-energy" process. As is listed in Table 2, the "high-energy" yield of $CF_3CHCl^{82}Br$ estimated for the 20 min-irradiated target was 3.6±0.5%. A small difference in the "high-energy" yield was observed between the 30 s- and 20 min-irradiated targets. This difference was also found in the "high-energy" yields of $CF_3CHBr^{82}Br$: 4.0±0.5 and 2.4±0.5% for the targets irradiated for 30 s and 20 min respectively. If the "high-energy" yield estimated from the scavenger curve represents the yield due to a hot-atom reaction, it should be rather constant, independent of the irradiation time. The difference in the "high-energy" yield thus obtained may be correlated with the caging effect which is expected in the reaction of bromine atoms in the condensed phase. Because of this effect, the radical scavenger is considered to be inhibited in some portion from reacting with the thermalized ^{82}Br atoms. The decrease in the "high-energy" yield in a longer irradia-

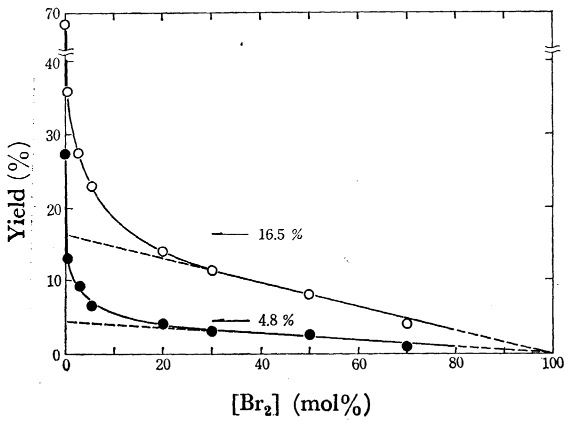

Fig. 5. Radioactivity yields of ^{82}Br-labeled product in the $CF_3CHClBr$–Br_2 system irradiated for 30 s in the JRR-4 reactor. ○, Overall organic products; ●, $CF_3CHCl^{82}Br$.

Table 2. Contribution of "thermal" and "high-energy" processes to the radiochemical yield of ^{82}Br-labeled species produced in neutron-irradiated $CF_3CHClBr$

Irradiation time	Radiochemical yield,[a] %					
	Overall organic		$CF_3CHCl^{82}Br$		$CF_3CHBr^{82}Br$	
	Y_t	Y_h	Y_t	Y_h	Y_t	Y_h
30 s	53.1±2.5	16.5±1.0	20.8±1.5	4.8±0.5	14.5±1.0	4.0±0.5
20 min	83.0±2.5	12.0±1.0	34.7±1.5	3.6±0.5	22.3±1.5	2.4±0.5

a) The Y_t and Y_h denote the "thermal" and "high-energy" yields, which were estimated from the scavenger curves obtained for the $CF_3CHClBr$–Br_2 system.

tion may be attributed to the contribution of the radiolytic organic radicals produced in the reaction zone.

At least, it can be pointed out that the high-energy yield of $CF_3CHCl^{82}Br$ is larger than that of $CF_3CHBr^{82}Br$. The high-energy yield of $CF_3{}^{82}Br$ is undoubtedly smaller than 1.1%, judging from the data listed in Table 1. Hardly any of the labeled product caused by ^{82}Br-for-F substitution was observed in this experiment. As a result, the order of the high-energy yields may be described as: $CF_3CHCl^{82}Br > CF_3CHBr^{82}Br > CF_3{}^{82}Br$ ($>$ ^{82}Br-for-F substituted species). This suggests that the high-energy reaction of ^{82}Br recoil atoms with $CF_3CHClBr$ has a close relation with the bond strength in the molecule, because the bond dissociation energies of the individual bond in $CF_3CHClBr$ should be in the order of: $C\text{–}Br < C\text{–}Cl < C\text{–}C < C\text{–}H < C\text{–}F$.[14)]

The abrupt increase in the overall organic yield at the irradiation time of around 2 min may be explained in terms of the thermal reactions of ^{82}Br with organic radicals. When the target material was irradiated for less than 30 s, the bulk concentration of the radiolytic organic radicals should be quite low, judging from the fact that hardly any mass signals of organic species except for fluothane were observed in the gas chromatogram in Fig. 1. In this case, the thermalized ^{82}Br atom should give rise to an inorganic compound, probably forming $H^{82}Br$, $Cl^{82}Br$, or $Br^{82}Br$, although we have not yet identified them. On the other hand, in the case of the irradiation for more than 2 min, the concentration of the organic radicals produced by the radiolysis of the parent molecules might be sufficiently high in the vicinity of the ^{82}Br recoil atoms, so that the thermalized ^{82}Br atom could react with those radicals to form organic compounds *via* shorter diffusion paths. In fact, the increase in the thermal yield of the overall organic products between 30 s- and 20 min-irradiation, 29.9%, is comparable with decrease in the inorganic yield of 26.4%, within the limits of experimental error.

Through the present study of the chemical behavior of ^{82}Br recoil atoms produced in neutron-irradiated fluothane, several factors which determine the chemical distribution of the ^{82}Br-labeled species were elucidated. Recoil labeling was revealed to be a feasible method for the preparation of fluothane-^{82}Br; some technical information related to the practical preparation will be reported in a forthcoming journal.[5)]

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