92. *Direct Production of Organic Compounds containing Artificial Radio-elements.*

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In view of the increased interest in the use of radioactive indicators for the investigation of biological and chemical reactions (see *e.g.*, Chiewitz and von Hevesy, *Nature*, 1935, **136**, 754; von Hevesy, Lindestrøm, and Olsen, *ibid.*, **137**, 66; Juliusburger, Topley, and Weiss, *J. Chem. Physics*, 1935, **3**, 437), we endeavoured to find new methods for the production of organic compounds with a relatively high percentage of radioactive substance.

After irradiating perchlorate, periodate, and permanganate with slow neutrons, we found, as experiments by Amaldi, d'Agostino, Fermi, Pontecorvo, Rasetti, and Segrè (*Proc. Roy. Soc.*, 1935, *A*, **149**, 538) would suggest, that no measurable activity remained in the original molecule, provided that the separation of the ejected active isotope was carried out with sufficient care. On the other hand, it is impossible to remove by aqueous extraction (Szilard and Chalmers, *Nature*, 1934, **134**, 462) or by an electric field (Fay and Paneth, preceding paper) all the active isotope from organic halides, and we found that in such cases between one-half and two-thirds of the activity could not be removed by repeated extraction with a reducing aqueous solution of the corresponding alkali halide. In Fermi's opinion (*loc. cit.*), the energy of the γ-ray recoil is sufficient to eject the active atom from its molecule, and it is therefore probable that the residual activity in organic substances is due to the ejected active atom entering another molecule. In order to be able to separate the minute quantities of any substances likely to be formed as the result of this re-entering process, we added to various organic liquids after irradiation small quantities of the respective isotopic compounds. After extraction of the free halogen, the organic liquid was separated again by distillation or other means into its various components, the activities of which were measured separately on a Geiger–Müller counter. The following is the description of a typical experiment.

32 C.c. (73 g.) of methyl iodide (after addition of a drop of methylene di-iodide and a small crystal of iodine for protection) were irradiated for 1 hour with a 340-mc. radon–beryllium source, the whole being surrounded by water to " slow down " the neutrons. After irradiation, 3 c.c. (10 g.) of methylene di-iodide and 11 c.c. (10 g.) of toluene (the latter to facilitate the separation by distillation of the two halides) were added. The whole was extracted with 46 c.c. (50 g.) of an aqueous solution of potassium iodide and sulphur dioxide. The aqueous extract was separated, 2 c.c. were transferred to a glass vessel with a bottom of aluminium foil (thickness 0·05 mm.), and the activity was measured. A second and a third similar extract were found to contain no measurable activity. The organic liquid was then dried over calcium chloride, and the activity of 2 c.c. of it was measured in a similar vessel. The rest was fractionated and the activities of the components were measured separately. The whole operation can be performed in less than ½ hour. The number of impulses per minute (corrected to zero time) were : 540 for the aqueous extract, 390 for the organic liquid after extraction, 400 for the methyl iodide, 0 for the toluene, 630 for the methylene di-iodide.

In considering these activities, it should be borne in mind that only 32 c.c. of methyl iodide were irradiated. If a larger quantity had been employed, under exactly the same conditions, the activity of the methylene di-iodide would have been several times the value given above. In order to compare the values, a correction must be applied for the concentration and density of the substances measured. We did this approximately by dividing by the ratio of the weight of substance irradiated to the weight of the liquid in which the product under consideration was measured.

The results tabulated below for several experiments show the percentage of the total activity (corrected as above) carried by each constituent.

	Percentage of total activity carried by constituents after separation.			
Substance irradiated.	Aqueous extract (free halogen).	Extracted organic liquid before distillation.	Original substance recovered.	New product found.
CH_3I at 15°	43	57	46	11 (CH_2I_2)
CH_3I at −195°	44	49	45	11 (CH_2I_2)
CH_3I at 15° (with cadmium + boron absorber)	41	55	48	11 (CH_2I_2)
CH_2Br_2	43	64	43	14 ($CHBr_3$)
$CHBr_3$	34	69	47	19 (CBr_4)
C_6H_5Cl	50	50	35	15 ($C_6H_4Cl_2$)
$CH_2Br{\cdot}CO_2H$	78	22	remained in aqueous extract	22 (CH_2Br_2)

(Cols. 2, 4, and 5 are made to add up to 100%, and it is seen that, within the limit of experimental error, the sum of cols. 4 and 5 is equal to col. 3.)

The actual percentage of the total activity carried after separation by the new product formed is comparatively small, but it should be remembered that this activity is contained in a small quantity of substance which, mass for mass, is often many times more active than the original substance irradiated.

By irradiating methyl iodide at liquid-nitrogen temperature, the same result was obtained as in the experiment at room temperature, showing that the production of higher organic halides is not the result of ordinary chemical substitution, which under these conditions would be suppressed. This deduction is supported by the fact that high concentrations of activity were found in the organic substances containing one halogen atom more than the original compounds.

Modified experiments with perchloric acid and methyl iodide were made in order to ensure that the ejection of the active atom was actually produced by the γ-ray recoil and not by the impact of neutrons of medium velocity. The samples were surrounded in both cases by a 5% solution of cadmium chloride, and contained in solution about 5% of cadmium nitrate and methyl borate respectively. In both samples the activity was reduced to one-fifth, showing that at least four-fifths of the original activity was due to the slow neutrons. At the same time the percentages of the total activity carried by the separated constituents were in no way altered (see above table).

That the active halogen atom is always ejected from the molecule is not surprising, in view of the fact that the γ-ray energies already measured for other elements (Rasetti, *Z. Physik*, **1935**, **97**, 64) have values between 3·3 and $6{\cdot}6 \times 10^6$ e.v. Even in the case of periodate, in which, the equation $IO_4' \longrightarrow I' + 4O - 270$ cals. being assumed, the iodine has the greatest possible binding energy, the γ-ray energy required to disrupt the bond would be only $1{\cdot}7 \times 10^6$ e.v.

The ability of the activated atoms, ejected from their compounds with high energy, to enter other molecules permits the production of highly active compounds. We were thus able to extract from mixtures newly formed active products as shown below.

Mixtures irradiated.		Products separated with concentrated activity.
$C_2H_5{\cdot}OH + I_2$	(satd.)	CH_3I (6),[*] C_2H_5I (4).
$CH_3{\cdot}CO_2H + I_2$	(satd.)	CH_3I (10).
$C_6H_6 + CCl_4$	1 : 1	C_6H_5Cl (10).
$C_6H_6 + CBr_4$	1 : 1	C_6H_5Br (15).
$C_6H_5{\cdot}OH + CH_3Br$	1 : 1	CH_3Br (6), C_6H_5Br (2), $C_6H_4Br{\cdot}OH$ (2).
$C_6H_5{\cdot}NH_2,HBr$		C_6H_5Br (1), $C_6H_4Br{\cdot}NH_2$ (2).
$C_6H_6 + CH_3I$	10 : 1	C_6H_5I (15).

[*] The figures in parentheses denote the approximate percentage of the total activity carried by the constituents.

If one diminishes the possibility of an ejected halogen atom re-entering a molecule by greatly diluting the liquid to be irradiated with an inert substance, no activity should remain in the original liquid after extraction. A 4% solution (by vol.) of bromoform in carbon disulphide was irradiated, and after removal of the free bromine and the carbon disulphide, no measurable activity remained in the bromoform, showing that within the limit of our measurements every halogen atom which captures a neutron is ejected from its molecule. Use was made of this fact in the experiment with benzene and methyl iodide. By using a relatively large amount of benzene, the concentrated activity was obtained mainly as iodobenzene instead of as a mixture of the latter and methylene di-iodide, which would have been difficult to separate. It follows from the last table that the active halogen atom exchanges, not only with halogen or hydrogen, but also with the hydroxyl, amino-, carboxyl, and hydroxymethyl groups and probably many others whenever a stable compound is produced by the exchange.

A continuous supply of organic halides with highly concentrated activities can be obtained by a very convenient method in cases where the original substance irradiated is soluble in water and the product is insoluble and fairly volatile. As an example of the method, 800 c.c. of a saturated solution of potassium iodide in 80% acetic acid were irradiated to equilibrium, and a rapid current of air, saturated with methyl iodide vapour at 0°, was passed through the solution for 5 minutes. The issuing air, after passing through soda–lime and calcium chloride to remove acid and water vapours, was cooled in a U-tube immersed in liquid air, whereby the methyl iodide was frozen out. The liquid air was then removed, and the methyl iodide liquefied and run into one of the glass–aluminium vessels described above. About 1·5 c.c. were obtained, which gave an activity of 5 kicks per minute per mc. five minutes after the air-current had been stopped. By improving the conditions, still higher yields could be obtained. As the composition of the irradiated liquid remains unchanged, the method permits the production of an almost continuous and unlimited supply of active methyl iodide. This particular method of preparation may be of special interest for biological experiments, as most of these volatile organic halides produce anæsthesia and have specific effects on the various parts of the brain.

SUMMARY.

It is shown that when organic halogen compounds are irradiated with slow neutrons, the activated halogen atoms are ejected from their molecules with high energy and then enter other molecules. They replace not only other halogen atoms, but also hydrogen and univalent groups, thereby producing new halogen compounds which can be separated with a high concentration of activity.

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