Chemical Use of the Absorption of Soft γ-Rays, β-Ray-excited X-Rays and K-Capture X-Rays. III. Application to Column-chromatographic Separation of Halogen Compounds

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Column-chromatographic separation of colorless compounds always involves a tedious procedure or requires a special instrument[1]. With such a method, usually only frontal analysis is possible, and no information concerning the behavior of each compound in the column is offered. Even where colored compounds are concerned, a small overlap of two adsorption zones is often overlooked and the observation of their behavior in the column is ambiguous. In this paper, the author will indicate that utilization of the absorption phenomenon of soft γ-rays, β-ray-excited X-rays and K-capture X-rays offers a very useful technique for the column-chromatographic separation of iodine-, bromine- or chlorine-containing substances, which are mostly colorless. Frontal analysis is thus made always possible regardless of the use of the solvent consisting of lighter elements than oxygen. With iodine- or bromine-containing compounds, nondestructive determination of the location of each compound in the column is made possible. As shown in Table I, a photon-beam of a suitable energy is absorbed strongly by bromine or iodine, but only slightly by column-wall substances, adsorbents and solvents; these usually consist of elements of a low atomic number. Nondestructive determination of the location of the compounds at a given time is named "in-situ determination".

TABLE I. ABSORPTION COEFFICIENT (cm^2/g.)

Source	Substance				
	C	Al	Cl	Br	I
^{55}Fe	4.5	48	ca. 110	>100	>300
Bγ-β	1.3	ca. 15	42	ca. 30	ca. 90
Ce-β	0.23	0.89	ca. 1.5	12	ca. 30
RaD	0.19	0.46	0.68	5.22	14.79
^{204}Tl	0.17	0.24	0.35	1.9	5.17

Outline of the Technique.—Figure 1 shows the measuring device. Useful sources are listed in Table II. (For convenience, the β-ray-excited X-rays of element M are written as M-β in this paper.)

As shown in Table II, the source for the in-situ determination of iodine or bromine must be chosen according to the diameter of the column or the concetration of the solution.

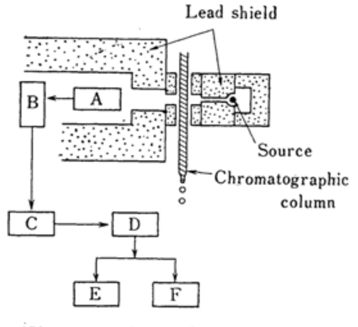

Fig. 1. Measuring device.

A: Detector head B: Preamplifier
C: Linear amplifier
D: Single channel analyzer
E: Scaler F: Automatic recorder

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1) E. g., E. Lederer and M. Lederer, "Chromatography", Elsevier Pub. Co., Amsterdam (1955), p. 41.

2) R. Adams, "Organic Syntheses", Vol. VIII (1928), p. 42.

TABLE II. USEFUL PHOTON-BEAM SOURCES

	In-situ determination	Frontal analysis
Chlorine	Unsuccessful	^{55}Fe, Sr-β, Br-β
Bromine	Ce-β[a)], Ba-β[a)] RaD[b)]	Ba-β, Sn-β, Mo-β
Iodine	RaD[c)] ^{204}Tl[d)] ^{203}Hg[e)]	RaD, Ce-β

a) When a small amount of bromine is adsorbed.
b) When a large amount of bromine is adsorbed.
c) When the column diameter is small (less than 3 cm.).
d) When the column diameter is large (3 to 8 cm.).
e) When the column diameter is still larger.

For the in-situ determination of iodine, the following method is useful for a column of a larger diameter: a fine polyethylene tube is placed at a suitable position in the adsorbent along the direction of the tube, so that a point source can be moved in the tube and the absorption of the photon-beam by the material can be measured at a given location in the column. This method is one of the techniques that are made possible only by utilizing a radio-isotope rather than an X-ray generator. For the in-situ determination of bromine of a smaller concentration, Ba-β or Ce-β should be used in spite of the ease with which the photon-beam is absorbed by other materials than the compounds in question. Hence, the column should preferably be made of polyolefine, and, whenever possible, the adsorbent should be charcoal or carbohydrate. When a large amount of bromine compounds is to be separated, it is preferable to carry out, in the first place, both the in-situ determination and the frontal analysis by the use of a small column and of a minor portion of the compounds. The behavior of the compounds in the column, including the retention volumes and the relation between the results of both determinations, are thus made clear. The major portion is then separated on a large scale with the aid of only frontal analysis.

Unfortunately, the in-situ determination of chlorine is very difficult because of the more pronounced absorption of the soure photon-beam by other materials than the compounds in question.

Throughout these cases, the use of an exact exponential absorption curve is not essential, unless an accurate determination of the compound is to be made in the column.

Discussion on the Usefulness of the Technique.—By the use of the in-situ determination, the following important information for column-chromatographic separation can be obtained in the early stage of adsorption (when only a small quantity of the original solution has been treated): (1) the retention volume of each compound, (2) minimum recovery of most weakly adsorbed substance in a pure state without elution, and also without elution tailing, (3) maximum quantity of the original solution which can be treated in one lot for complete separation under the given conditions, (4) the necessary quantity of an eluent for eluting each of the compounds. An almost ideal case (without marked elution tailing) is exemplified by the separation of iodobenzene and 4-iodobiphenyl described below.

When a pronounced elution tailing is observed, complete separation is usually impossible. But a part of the most weakly adsorbed compound is obtained in a pure state, leaving a mixture in the column. For molecules having a similar functional group, it is generally true that the stronger the affinity with an adsorbent, the less the solubility in a given solvent. Thus, for the separation of a binary mixture, a method consisting of the following procedures is useful; (1) the mixture is dissolved in a suitable solvent of a quantity sufficient for complete dissolution of the more soluble compound I; (2) when the less soluble compound II remains undissolved, it is obtained in a pure state by filtration and, whenever necessary, by recrystallization; (3) a part of pure I is obtained chromatographically; (4) the mixture of I and II is completely eluted with a solvent with a strong eluting power; (5) the solvent is removed from this effluent to give a solid mixture, which is submitted to the same process again to give further I and II in a pure state. Step 3, the most important procedure, can be made easier by the use of the photon-beam absorption technique for colorless bromine and iodine compounds. Such a case is exemplified by the preparation of 4-iodobiphenyl and 4, 4′-diiodobiphenyl by direct iodination of biphenyl and their separation (see below).

Column chromatography is also useful for purifying some kinds of material. Crude halogen compounds prepared by the Sandmeyer reaction always contain impurities (e. g., phenols and oxidation products of the amines), which are much more easily adsorbed than the halogen compounds themselves. When the halogen compound is colorless, the photon-beam absorption provides a valuable tool in its chromatographic purification. Such a process is exemplified by the purification of 2-chloro-*p*-terphenyl (see below).

Separation of Iodobenzene and 4-Iodobiphenyl.—Figure 2 shows the behavior of iodobenzene

(A) (724 mg.) and 4-iodobiphenyl (B) (555 mg.) which have been dissolved in petroleum benzine (50 ml.). The column was 13.5 mm. in diameter and contained alumina (38 g.; apparent length: 30 cm.). The adsorption heads of the two substances move at a definite rate according to the volume of both the solution and the eluent (5.0 mm. per ml. for A, 2.0 mm. per ml. for B). Iodobenzene gives some elution tailing, though not pronounced, and 4-iodobiphenyl gives a marked tailing.

When the rate of migration of substance I, which is eluted easier, and that of substance II are denoted by R_{I} and R_{II} (in cm. per ml.) respectively, and the length of the adsorbent is L (cm.), the retention volumes of the substances V_{I} and V_{II} (ml.) are:

$$V_{\mathrm{I}}=L/R_{\mathrm{I}} \qquad V_{\mathrm{II}}=L/R_{\mathrm{II}} \tag{1}$$

In the absence of tailing, there are the following approximate relationships between the maximum treatable quantity of the original solution for complete separation, Q (ml.), and the minimum volume of the eluent necessary for complete elution of I under the given condition, S (ml.):

$$L=(Q+S)R_{\mathrm{II}}=SR_{\mathrm{I}}$$

Thus,

$$Q=L/R_{\mathrm{II}}-L/R_{\mathrm{I}}=V_{\mathrm{II}}-V_{\mathrm{I}} \tag{2}$$

$$S=L/R_{\mathrm{I}}=V_{\mathrm{I}} \tag{3}$$

Since L, R_{I} and R_{II} are 30, 0.50 and 0.20 respectively, V_{I} and V_{II} are 60 and 150 respectively; without tailing of *I*, Q and S should be 90 and 60 respectively. When the elution tailing of I is as in Fig. 2, Q is 70 to 75 and S about 75.

When only the original solution is passed through the column until the adsorption head of II reaches the lower end of the column with the aim of obtaining a part of I in a pure state, the yield, Y, is expressed by:

$$Y>(V_{\mathrm{II}}-V_{\mathrm{I}})/V_{\mathrm{II}} \tag{4}$$

This is because the concentration of I at the location where only I is adsorbed is higher than that at the location where both I and II are present, owing to the displacement of I by II. Moreover, this relation is always valid regardless of the presence of tailing. When this mixture is submitted to such a treatment,

$$(V_{\mathrm{II}}-V_{\mathrm{I}})/V_{\mathrm{II}}=0.60$$

but the true value of Y, which is easily obtainable from Fig. 2 and the quantity of the substances present, should be about 0.75.

When elution is carried out to such a degree that an incomplete separation is caused, an approximate value of Y can be estimated by the use of the in-situ determination.

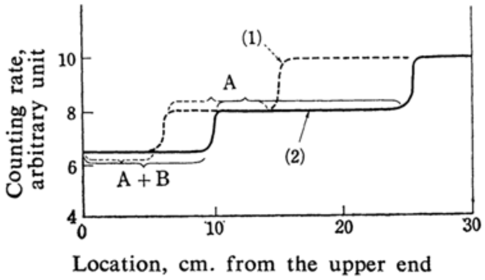

Fig. 2-1. Behavior of iodobenzene (A) and 4-iodobiphenyl (B) in a column.

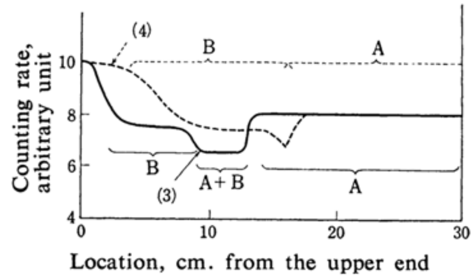

Fig. 2-2. Behavior of iodobenzene (A) and 4-iodobiphenyl (B) in a column.

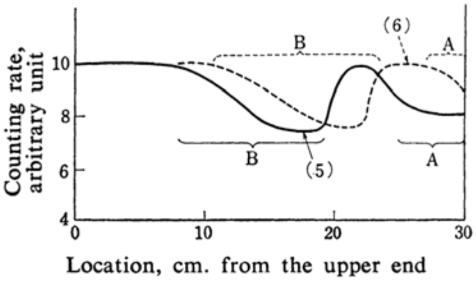

Fig. 2-3. Behavior of iodobenzene (A) and 4-iodobiphenyl (B) in a column.

(1); 30 ml. adsorption
(2); 50 ml. adsorption
(3); 50 ml. adsorption and 15 ml. elution
(4); 50 ml. adsorption and 30 ml. elution
(5); 50 ml. adsorption and 45 ml. elution
(6); 50 ml. adsorption and 60 ml. elution

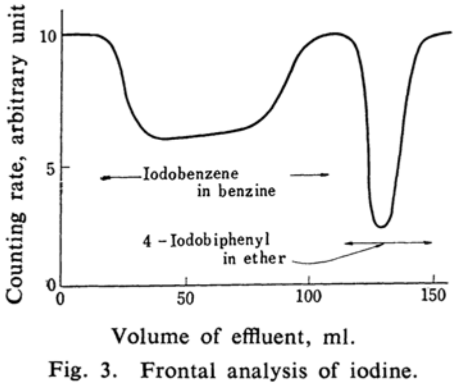

Fig. 3. Frontal analysis of iodine.

Frontal analysis was also carried out successfully, the results being shown in Fig. 3. When all of A came out, ether was caused to pass in order to elute B rapidly.

Similar results were obtained with bromobenzene and 4-bromobiphenyl.

Preparation of 4-Iodobiphenyl and Similar Compounds.—4-Iodobiphenyl and 4-bromobiphenyl are useful for the synthesis of polyphenyl compounds. Direct bromination of biphenyl offers 4-bromobiphenyl contaminated with 4, 4′-dibromobiphenyl, which can be only with difficulty removed. Thus, the standard method[2] for the synthesis of pure 4-bromobiphenyl is the reaction of the diazotization product of 4-bromoaniline with benzene in an alkaline medium. 4-Iodobiphenyl is prepared by the Sandmeyer reaction from 4-aminobiphenyl, which must be synthesized from biphenyl.

Direct iodination of biphenyl can be attained easily in acetic acid with the aid of nitric acid. Column-chromatographic separation offers both 4-iodobiphenyl and 4, 4′-diiodobiphenyl in a good yield and with a satisfactory purity.

For the bromine compounds, the separation method is less effective, because the adsorbing power of an adsorbent toward 4-bromobiphenyl and 4, 4′-dibromobiphenyl differs less than in the case of corresponding iodo-compounds, and because the in-situ determination of bromine is less easy than that of iodine. For most synthetic purposes, however, the use of 4-iodobiphenyl is preferable to that of 4-bromobiphenyl.

Figure 4 indicates the behavior of 4-iodobiphenyl (I) and 4, 4′-diiodobiphenyl (II) including by-product (III) of the iodination reaction of biphenyl. Both I and II are partly replaced by III, which forms a visible zone. The head of the zone of II becomes less clear with the progress of elution owing to the elution tailing of I. Frontal analysis is useless in such a case.

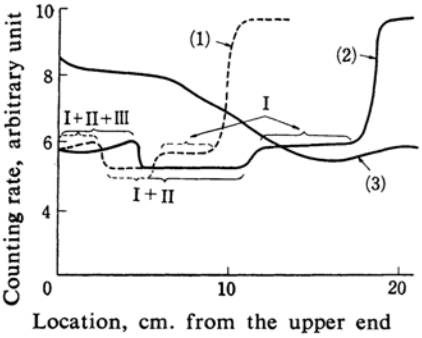

Fig. 4. Behavior of 4-iodobiphenyl (I), 4,4′-diiodobiphenyl (II) and by-product (III) in a column.
(1); 20 ml. adsorption
(2); 40 ml. adsorption
(3); 40 ml. adsorption and 20 ml. elution

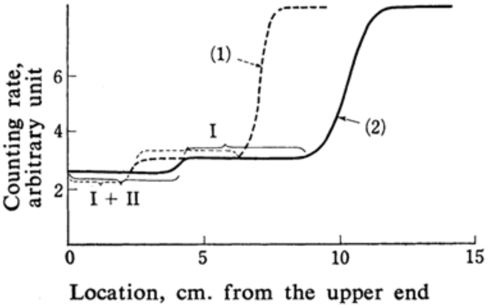

Fig. 5. Adsorption of 4-iodobiphenyl (I) and 4, 4′-diiodobiphenyl (II).
(1); 320 ml. adsorption
(2); 500 ml. adsorption

Figure 5 shows the behavior of the same iodine compounds, from which the by-product has been removed by a preliminary treatment. In this case, all the substances in the column are easily eluted with benzene or, preferably, with ethyl acetate, and the alumina can be reused after heat treatment at 200 to 250°C under a reduced pressure. The impurity in the eluted I appears to consist of a small quantity of remaining biphenyl or, more probably, 2-iodobiphenyl simultaneously formed. The impurity, however, can be removed, by recrystallization and pure I is obtained easily in a good yield. This synthesis of I is definitely superior to the Sandmeyer reaction with 4-aminobiphenyl with respect to the saving of time, labor and expense. The product will contain no trace of II.

Direct iodination of *p*-terphenyl is similarly attained by using a larger amount of the solvent. 4-Iodo-*p*-terphenyl is obtained from the product, by a similar, process, but with a disadvantage due to its lower solubility. Benzene must be used in place of benzine despite the much smaller retention volume, which always decreases the quantity of materials treated in one lot. This method, however, is preferable for preparing a small quantity (less than a few grams) of pure 4-iodo-*p*-terphenyl, which must otherwise be synthesized through many tedious steps[3].

Purification of Mono-halogeno-*p*-terphenyls.—Figure 6 shows the results of the frontal analysis of 2′-chloro-*p*-terphenyl prepared by the Sandmeyer reaction. The size, shape and mode of attachment of the adsorption cell are very important in determining the real concentration of chlorine in the effluent at a given instant. Some other mono-halogeno-*p*-terphenyls prepared by the same reaction were

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[3] T. Nozaki et al., This Bulletin, 33, 1329 (1960).

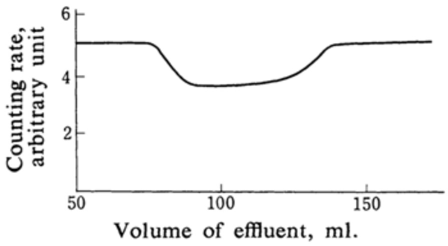

Fig. 6. Frontal analysis of chlorine.

similarly purified with the aid of the absorption technique, and their properities are now under investigation.

The technique was, however, unsatisfactory for the separation of a mixture of 2-, 3- and 4-chloro-*p*-terphenyl, prepared by the decomposition of 4-(*N*-nitrosoacetamido)-biphenyl in chlorobenzene because of the marked elution tailing.

Experimental

Adsorbent and Reagents.—Freshly purchased commercial alumina (Kantō Chem. Co. for chromatographic purpose) was used without further treatment. Too great an activity of alumina sometimes caused a slight decomposition of the iodine compounds. All solvents were of the first grade and were used after having been kept in contact with a small quantity of highly activated alumina for several days. In some cases, extremely purified solvents were also used, but no significant difference in the behavior of the compounds was observed. Other reagents were also of a commercial first grade.

Measurement Device.—For the in-situ determination, a collimated photon-beam was caused to pass along cross-section of the chromatographic column to enter the scintillation crystal or the counter tube (Fig. 1). For the frontal analysis of chlorine, the outlet of the tube was connected to a polypropylene absorption cell of a suitable dimension, while for that of iodine, the alumina near the outlet was replaced by cotton wool. The output pulse of the scintillation head or the counter tube was amplified by a linear amplifier, and the photo-peak was counted by the use of a single channel analyzer and a scaler or an automatic recorder.

For the analysis of chlorine Br-β was adopted and the photon-beam was measured by a xenon-filled proportional counter tube. For other sources a scintillation counter was used.

Preparation of 4-Iodobiphenyl and 4, 4′-Diiodobiphenyl.—A mixture of 20 g. of biphenyl and 20 g. of iodine in acetic acid (150 ml.) containing nitric acid (d=1.38, 25 ml.) was boiled gently under reflux (for about 1.5 hr.) until the color of iodine disappeared. After the mixture had been poured into water, the separated solid was filtered off, washed with an aqueous alkali solution and dried. About 40 g. of a faintly yellowish hydrophobic powder was obtained, which was recrystallized from 200 ml. benzene. On filtration and washing of the precipitate with ethanol, 8 g. of fairly pure 4,4′-diiodobipenyl (II) was obtained (m. p. and mixed m. p. 203∼205°C). The mother liquor was caused to pass through a column of alumina (ca. 200 g.) to remove the yellow material, from which a small quantity of 4-nitrobiphenyl was isolated by further purification, including recrystallization. Benzene was then removed from the effluent, aud the colorless residual solid was digested with 600 ml. of petroleum benzine. The insoluble solid offered 2 g. of fairly pure II. Moreover, the mother liquor was submitted to column-chromatographic separation with the aid of the adsorption technique by using a column 6 cm. in diameter containing 300 g. of alumina.

Alter all the solution had been passed through, petroleum benzine was caused to pass through the column for elution until the adsorption head of II reached the lower end of the column. The effluent gave, on removal of the solvent, 20 g. of solid melting at 107∼112°C. This gave, however, after a single recrystallization from a small quantity of ethanol, 15 g. of pure 4-iodobiphenyl (I) (m. p. and mixed m. p. 113∼114°C). The column was eluted with ethylacetate to offer 6 g. of solid with ease after removal of the solvent. This solid gave, on a treatment similar to that above under a diminished scale, 1 g, of II, 3 g. of I and 2 g. of their mixture. The I obtained at this time was pure enough without recrystallization from ethanol. Thus, from 20 g. of biphenyl and 20 g. of iodine, 18 g. of I and 11 g. of II were obtained in a fairly pure state along with 2 g. of their mixture.

Another experiment which did not involve the removal of the yellow material (nitro-compounds) was also carried out. About 4 g. of the crude iodination mixture was treated with 80 ml. of petroleum benzine, and, after removal of the insoluble II, the solution was submitted to column chromatography. Both the in-situ determination and the frontal analysis were applied.

Purification of 2′-Chloro-*p*-terphenyl.—2′-Nitro-*p*-terphenyl (2 g.) prepared by the reaction of nitrosation product of 3-nitro-4-acetamidobiphenyl with benzene was reduced with tin(II) chloride, and the amine hydrochloride was diazotized and decomposed in concentrated hydrochloric acid with the aid or copper(I) chloride. The product was extracted with a mixture of petroleum benzine (40 ml.) and benzene (40 ml.), caused to pass through a column of alumina (40 g.), and eluted with the same solvent. The chlorine-containing part, which was recognized by frontal analysis, offered, on removal of the solvent, a colorless mass which was recrystallized from ethanol (25 ml.) into transparent square platelets (0.5 g.) [m. p. 101°C].

Summary

The absorption technique of soft γ-rays, β-ray-excited X-rays and K-capture X-rays was successfully applied to column-chromatographic separation and purification of halogen compounds. By this technique, the behavior of the iodine- and bromine-containing compounds

in the column was determined in situ, and important information for column chromatography, including the retention volume, was obtained at an early stage of adsorption. The technique was also satisfactorily applied to the frontal analysis of halogen compounds. An excellent method for the preparation of pure 4-iodobiphenyl by the use of the in-situ determination was provided.

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