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CHEMICAL FORMS OF IODINE IN CARRIER FREE PREPARATIONS OF Na<sup>131</sup>I

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## SUMMARY

Various forms of iodine have been separated chromatographically and their  $R_F$  values determined. The formation of unidentified components in the systems:  $^{131}\text{I}/\text{I}_2$ ,  $^{131}\text{I}/\text{IO}_3^-$ ,  $^{131}\text{I}/\text{IO}_4^-$ , has been investigated as a function of the concentration of the reagent, the pH of the medium, the aging time of the solution and the temperature, by employing a paper chromatographic method.

## INTRODUCTION

Radioactive iodine-131 is obtained by irradiating tellurium:  $^{130}\text{Te}(n,\gamma)^{131}\text{Te} \xrightarrow{\beta} ^{131}\text{I}$ . The final form of the preparation is as Na<sup>131</sup>I in a reducing solution: Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub>, NaHCO<sub>3</sub> and Na<sup>131</sup>I in NaOH (refs. 1 and 2).

In addition to the known stable forms: IO<sub>3</sub><sup>-</sup>, IO<sub>4</sub><sup>-</sup> and I<sub>3</sub><sup>-</sup>, commercial preparations of iodide can also contain a certain quantity of unidentified noniodide components<sup>3</sup>.

On investigating the valency state of the iodine, obtained by neutron irradiation of tellurium, the percentage of oxidised and reduced forms of iodine was found to vary considerably depending on the chemical form of the target and the pH value of the medium in which the irradiated target is dissolved<sup>4</sup>. It was found that part of the radioiodine can be in the form of unstable IO<sub>2</sub><sup>-</sup> ions. This form is fixed by the addition of inactive IO<sub>3</sub><sup>-</sup>, IO<sub>4</sub><sup>-</sup> and I<sub>2</sub>, as carriers, to a neutral solution of the irradiated target, in which it remains stable for a long time.

The chemical behaviour of iodine in very small concentrations differs considerably from its known behaviour in macro quantities. Unstable oxidation products such as HIO and HIO<sub>2</sub> are much more stable in carrier-free solutions<sup>5</sup>.

In preparations of high specific activity, the free hydrogen and OH-radicals built up by water radiolysis change the chemical form of the radioisotopes<sup>6</sup>. We have also observed this phenomenon on investigating radioiodide preparations produced at the Boris Kidrič Institute by one-dimensional ascending chromatography. Investigation on preparations from Oak Ridge have shown that after aging for 4 weeks the percentage of unidentified components considerably increases<sup>3</sup>. Various workers have

given these components different names: "Extraneous band", "S-material", and "Unknown"<sup>7-9</sup>.

In medicine, iodine is used for examining the function of the thyroid gland and for treating some forms of hyperthyreosis. In biology, it is used for the radiobiological investigations of enzymes. As the thyroid only fixes iodine in the form of iodide, the use of a radioiodide preparation in medicine for diagnostic and therapeutic purposes can, in cases where other forms of iodine are present, lead to wrong conclusions.

The purpose of this work is to investigate the conditions which bring about the formation of unidentified components in radioiodide preparations and to attempt to identify them.

The reactions:  $I^-/IO_3^-$ ,  $I^-/IO_4^-$  and  $I^-/H_2O_2$  have been investigated as a function of the concentration of the reacting agent, the pH of the medium, aging and temperature.

#### EXPERIMENTAL

An ascending paper chromatographic method was used, which according to the literature data, is suitable for investigating slow exchange reactions ( $I^-/IO_3^-$ )<sup>10,11</sup> and instantaneous exchanges ( $I_2/I^-$ )<sup>12</sup>, in which the exchange is completed prior to chromatographic separation.

This method allows for quantitative separation of the substances present in very low concentrations. Carrier-free amounts of the radioisotope behave as macro quantities, while the  $R_F$  values remain constant up to concentrations of  $10^{-12}$  moles/l.

Mixtures of various concentrations of the components tested,  $I^-/IO_3^-$  and  $I^-/IO_4^-$ , were made. The pH values were adjusted by means of suitable buffer solutions. The samples investigated at room temperature as a function of time and heated at high temperatures were sealed in quartz ampoules.

In order to investigate the fast exchange reactions in the system  $I_2/I^-$  and observe the appearance of higher polyiodides ( $I_5^-$ ,  $I_7^-$ ,  $I_9^-$ )<sup>13</sup>, equal volumes of  $I_2$  in nitrobenzene or benzene solutions of fixed concentrations were equilibrated with aqueous solutions of NaI. The phases were separated by centrifugation.

In all the experiments the NaI solutions were labelled with iodine-131 produced in the Boris Kidrič Institute. The specific activity of the reaction mixture amounted from several tens to several hundreds of mCi/ml.

Aliquots of 1-5  $\mu$ l of each sample were taken, depending on the specific activity of the sample, and spotted on a 30  $\times$  2.5 cm chromatographic strip at a distance of 2.5 cm from the end of the strip.

Whatman papers No. 1, No. 3 MM, No. 31 and washed Whatman No. 1 paper were examined (the paper was washed with 2 N HCl by ascending chromatography and then with distilled water until the reaction to Cl ion disappeared). As the type of paper did not have any effect on the separation of the forms of iodine investigated, except in the case when washed Whatman No. 1 paper was used and where the  $R_F$  values were slightly higher, we used Whatman No. 1 chromatographic paper for our investigations.

Several different solvent mixtures for the separation procedures were investigated, for example: *n*-butanol-acetic acid-water (78:5:17); isoamyl alcohol saturated with 2 N  $NH_4OH$ ; *n*-butanol-dioxan-2 N  $NH_4OH$  (50:12.5:37.5), methanol-water (70:30).

The best separation of the unidentified forms of iodine was obtained with the following solvent mixtures: butanol saturated with 3 *N* NH<sub>4</sub>OH and butanol-ethanol-2 *N* NH<sub>4</sub>OH (5:1:2).

The chromatograms were developed in glass cylinders at room temperature for about 17 h. After the chromatograms had been developed and dried, the distribution of the radioactivity along the chromatogram was determined by scanning the strip under the window of a GM counter, with constant 2-π geometry, at 1/2 cm intervals. The percentage of each form of iodine was determined by measuring the radioactivity on the chromatography strips relative to the total activity of the band or by determining the areas covered by the curves of the separated components obtained with an instrument for automatic activity registration.

#### SEPARATION OF THE COMPONENTS AND DETERMINATION OF THEIR *R<sub>F</sub>* VALUES

The *R<sub>F</sub>* value of each form of iodine, which can occur in radioiodide preparations, was determined. Na<sup>131</sup>IO<sub>3</sub> was obtained by oxidising the radioiodide solution with hypochlorite in a slightly acid medium and by addition of a small quantity of inactive iodide (as carrier). Oxidation to Na<sup>131</sup>IO<sub>3</sub> is fast and quantitative. The Na<sup>131</sup>IO<sub>3</sub> obtained in this way is further oxidised to Na<sup>131</sup>IO<sub>4</sub> by introducing chlorine in strong alkaline solutions<sup>14</sup>. Na<sup>131</sup>I<sub>3</sub> is obtained by dissolving I<sub>2</sub> in a NaI solution labelled with Na<sup>131</sup>I.

The *R<sub>F</sub>* values of each particular form (I<sup>-</sup>, I<sub>3</sub><sup>-</sup>, IO<sub>3</sub><sup>-</sup>, IO<sub>4</sub><sup>-</sup>) were identical with those obtained with the mixture of all forms on chromatographic separation.

The formation of unidentified components in the solution was observed in several solutions of radioiodide produced by the Boris Kidrič Institute after various

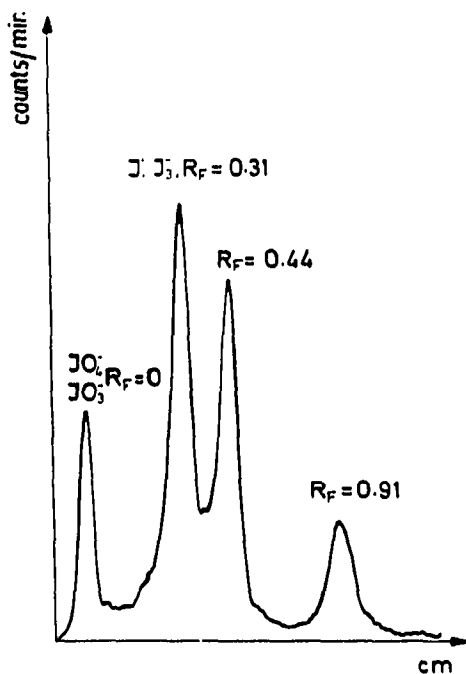


Fig. 1. Chromatographic separation of stable forms of iodine IO<sub>3</sub><sup>-</sup>, I<sup>-</sup>, I<sub>3</sub><sup>-</sup> from unidentified species. Solvent: butanol saturated with 3 *N* NH<sub>4</sub>OH, for 17 h on Whatman No. 1 chromatographic paper.

TABLE I

EFFECT OF AGING THE Na<sup>131</sup>I PREPARATION ON THE FORMATION OF STABLE OXIDATION FORMS OF IODINE AND FORMS WITH AN  $R_F$  VALUE OF 0.44

Reducing solution	pH of the solution	Activity mCi/ml	On production day		30 days later	
			Unidentified $R_F = 0.44$ (%)	$IO_3^-$ (%)	Unidentified $R_F = 0.44$ (%)	$IO_3^-$ (%)
NaOH	10.7	7	0	2	3	2
NaOH	10.7	14	1	0	2	1
NaOH	8.7	8	2	2	2	2
NaOH	8.0	3	0	1	5	4
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	9.2	9	2	1	6	3
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	8.0	15	2	0	24	13
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	8.0	4	1	0	8	5
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	8.0	4	4	0	10	6
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	7.8	15	2	0	24	13
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	7.6	14	3	0	10	13
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	7.4	9	3	1	4	7
Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>	7.2	15	2	3	25	10

periods of time. Apart from the above mentioned stable forms, there are two unidentified forms of iodine whose  $R_F$  values are 0.44 and 0.91.

Using the solvent mixture butanol saturated with 3 N NH<sub>4</sub>OH, we separated four components with the following  $R_F$  values:  $IO_3^-$  and  $IO_4^-$ ,  $R_F = 0$ ; I<sup>-</sup> and I<sub>3</sub><sup>-</sup>,  $R_F = 0.31$ ; and two unidentified spots,  $R_F = 0.44$  and 0.91. The butanol-ammonia solvent system mentioned above was used in all subsequent investigations.

Fig. 1 shows a chromatogram for the separation of the stable forms of iodine from the unidentified forms.

In order to discover the reason for the variation in the percentages of the oxidised and unidentified forms of iodine, we analyzed the radioiodide preparations in a reducing medium of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and in NaOH solutions to determine the dependence on the pH of the medium, the specific activity, and the aging time of the preparation. Results of these investigations are shown in Table I.

Table I shows that the unidentified component with  $R_F = 0.44$  and the stable oxidised form  $IO_3^-$  are mainly formed in the reducing solution Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (on standing, the dilute solution decomposes), at lower pH values and in preparations of higher specific activity.

The unidentified form with  $R_F = 0.91$  appears in negligible amounts in solutions which have aged only a short time.

Most of the radioiodide preparations investigated, with pH above 10, were stable even after long storage and they only contained iodide.

Figs. 2 and 3 show the distribution of radioactivity over a chromatogram obtained by analysing the Na<sup>131</sup>I solution in Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, pH = 7.8, and with an activity of 15 mCi/ml. The percentage of the unidentified form whose  $R_F$  value is 0.44 increases to 24% after aging for 30 days, while the percentage of the oxidised form increases to 13%.

The spectrometric analysis of the chromatogram strips, by means of a 256-channel analyzer, confirmed that the activity of the unidentified forms belongs to iodine-131.

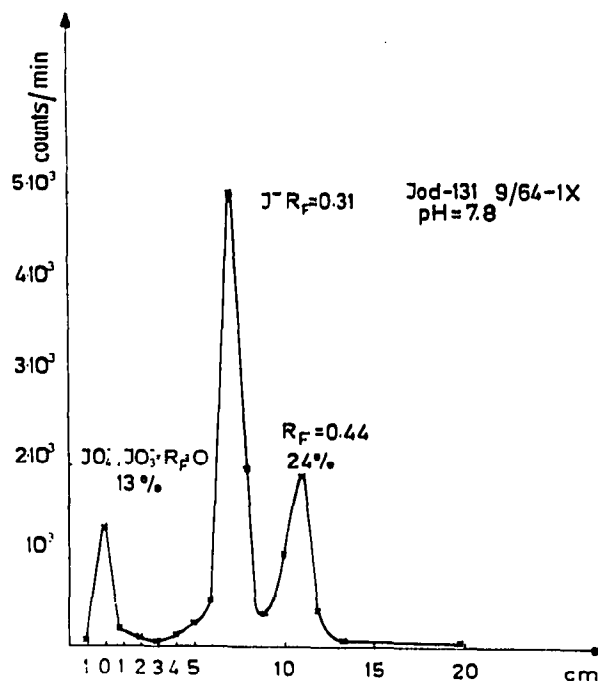
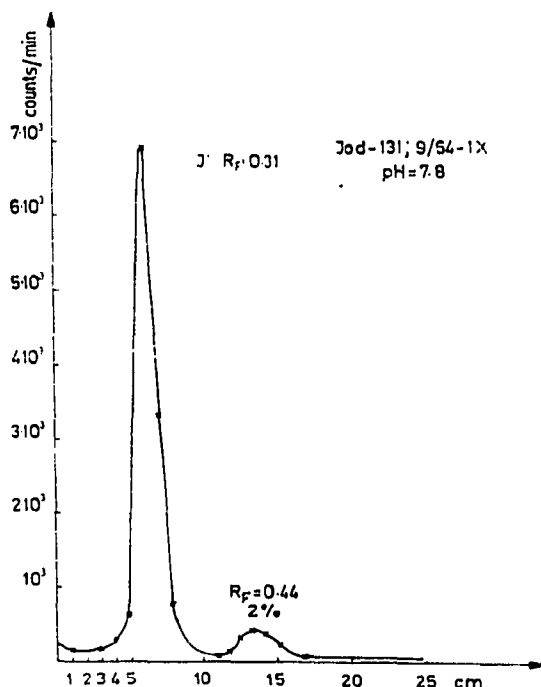


Fig. 2 Chromatogram showing the distribution of activity for each form of iodine in the radioiodide preparation YVI-131/IX produced at the Boris Kidrič Institute, Vinča. Chromatogram of preparation on the production day.

Fig. 3. Chromatogram showing the distribution of activity of each form of iodine in a radioiodide preparation of YVI-131/IX. Preparation aged for 30 days.

#### INVESTIGATION OF THE CONDITIONS UNDER WHICH THE UNIDENTIFIED FORMS WITH $R_F$ VALUES 0.91 AND 0.44 ARE FORMED

##### *Oxidation of iodide to $I_2$ with iodate*

In acid medium this reaction proceeds according to the following equation:



Mixtures of the reacting components of the following concentration ratios of  $IO_3^-$  to  $I^-$  were made:  $5 \cdot 10^{-2} M / 1 \cdot 10^{-2} M$ ;  $5 \cdot 10^{-2} M / 1 \cdot 10^{-5} M$ ;  $5 \cdot 10^{-2} M / 1 \cdot 10^{-8} M$ ;  $5 \cdot 10^{-2} M / \text{carrier free}$ ;  $5 \cdot 10^{-5} M / 1 \cdot 10^{-5} M$ . Solutions with pH values of 1.2, 3.4 and 7 were investigated.

Isotopic exchange between iodides and iodates is a comparatively slow reaction and depends on the pH of the solution. In neutral medium no exchange takes place at room temperature. Exchange occurs only in acid medium and the exchange rate decreases sharply with decreasing acidity of the solution.

Aliquots from the solutions with a pH of 1.2 were taken, at room temperature, at intervals from 0.5 to 72 h, and from the solutions with a pH of 3.4 they were taken at intervals from 0.5 to 96 h. Neutral solutions of the reacting components were heated from 8 to 60 h at  $228^\circ$ ; aliquots for analysis being taken after the solution had cooled to room temperature.

Investigation results of the iodide-iodate exchange and the formation of unidentified forms under the above conditions are given in Table II.

TABLE II

ACTIVITY DISTRIBUTION BETWEEN THE IODATE AND UNIDENTIFIED IODINE FORMS IN THE  $^{131}\text{I}^-/^{10}_3^-$  SYSTEM AS A FUNCTION OF THE pH OF THE MEDIUM, CONCENTRATION AND TIME

pH of the solution	% $^{10}_3^-$						% $R_F = 0.44$						% $R_F = 0.91$						Concentration ratio of $^{10}_3^-/^{131}\text{I}^-$					
	0.5 h	3 h	6 h	24 h	48 h	72 h	96 h	0.5 h	3 h	6 h	24 h	48 h	72 h	96 h	0.5 h	3 h	6 h	24 h		48 h	72 h	96 h		
1.2	7	9	13	—	—	65	—	0	0	0	—	—	0	—	0	10	20	23	—	—	8	—	$5 \cdot 10^{-2}/1 \cdot 10^{-2}$	
	7	7	10	—	—	38	—	0	0	0	—	—	0	—	0	9	9	9	—	—	4	—	$5 \cdot 10^{-2}/1 \cdot 10^{-5}$	
	6	6	6	—	—	38	—	0	0	0	—	—	0	—	0	6	6	8	—	—	4	—	$5 \cdot 10^{-2}/1 \cdot 10^{-8}$	
	0	0	0	—	—	20	—	0	0	0	—	—	0	—	0	0	0	0	—	—	12	—	$5 \cdot 10^{-2}/^{131}\text{I}^-$	
	0	0	0	—	—	10	—	0	0	0	—	—	0	—	0	0	0	0	—	—	10	—	$5 \cdot 10^{-5}/1 \cdot 10^{-5}$	
3.4	5	—	5	11	11	—	11	0	—	0	0	0	0	—	0	8	—	8	8	8	—	8	—	$5 \cdot 10^{-2}/1 \cdot 10^{-2}$
	7	—	7	11	11	—	11	5	—	5	16	16	—	21	1	—	1	8	12	12	—	20	—	$5 \cdot 10^{-2}/1 \cdot 10^{-5}$
	6	—	6	11	16	—	16	0	—	0	7	14	—	19	1	—	1	8	15	15	—	18	—	$5 \cdot 10^{-2}/1 \cdot 10^{-8}$
	0	—	7	11	—	—	—	0	—	0	2	—	—	—	0	—	0	2	—	—	—	—	—	$5 \cdot 10^{-5}/^{131}\text{I}^-$
	0	—	0	3	—	—	—	0	—	0	0	0	—	—	0	—	0	0	0	—	—	—	—	$5 \cdot 10^{-5}/1 \cdot 10^{-5}$

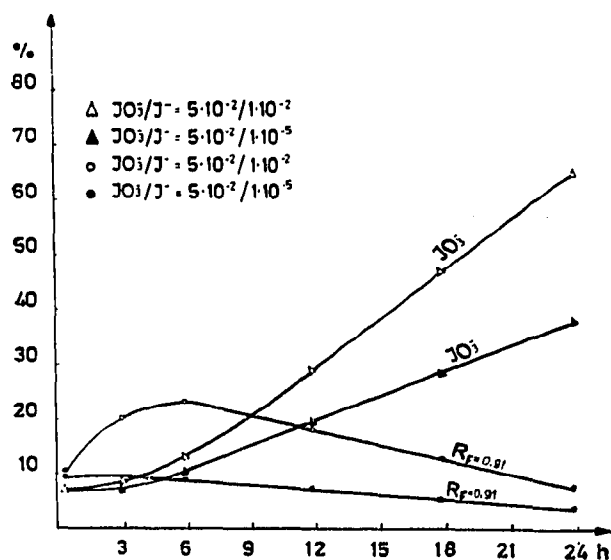


Fig. 4. Percentage content of  $^{131}\text{IO}_3^-$  and the component with  $R_F = 0.91$  in an  $\text{IO}_3^-/^{131}\text{I}^-$  system as a function of the  $^{131}\text{I}^-$  concentration and aging time of the solution at  $\text{pH} = 1.2$ .

It can be seen that the unidentified forms of iodine with  $R_F$  values 0.91 and 0.44, appearing in carrier-free radioiodide solutions, form on isotopic exchange between iodide and iodates.

The component with an  $R_F$  value of 0.44 is formed only in solutions at  $\text{pH} 3.4$  for iodide concentrations less than  $1 \cdot 10^{-5} M$ . Under these conditions exchange proceeds to 15% after 96 h. If the iodide concentration exceeded  $1 \cdot 10^{-5} M$  this form did not appear; however, in acid medium at  $\text{pH} 1.2$ , although the exchange reaches the highest percentage, up to 65% after 72 h, this form was not present.

The component with an  $R_F$  value of 0.91 (it moves with the solvent front) is formed in solutions at  $\text{pH} = 1.2$  and 3.4 for all iodide concentrations cited. The percentage of this component depends on the aging time and iodide concentration, as shown in Fig. 4.

As Fig. 4 shows the radioactivity of this component increases in the beginning but after several hours of aging it decreases, while the iodate content permanently increases, being faster with larger iodide concentrations.

In the above ratios of the reacting agents, the iodate ion was always in excess.

TABLE III

EXCHANGE RATE OF  $^{131}\text{I}^-$  AND  $\text{IO}_3^-$  IN NEUTRAL MEDIUM AT  $228^\circ$

Heating time (h)	Concentration (moles/l)		Exchange degree $x/c$	Exchanged part $x/c(1 + b/a)$	Nonexchanged part $1 - x/c(1 + b/a)$
	$\text{NaIO}_3$	$\text{Na}^{131}\text{I}$			
8	$5 \cdot 10^{-2}$	$1 \cdot 10^{-2}$	0.07	0.091	0.91
20	$5 \cdot 10^{-2}$	$1 \cdot 10^{-2}$	0.19	0.228	0.77
41	$5 \cdot 10^{-2}$	$1 \cdot 10^{-2}$	0.35	0.420	0.58
60	$5 \cdot 10^{-2}$	$1 \cdot 10^{-2}$	0.47	0.560	0.44
41	$5 \cdot 10^{-2}$	$1 \cdot 10^{-5}$	0.00	—	—
41	$5 \cdot 10^{-2}$	$1 \cdot 10^{-8}$	0.00	—	—

If the iodide ion was in excess in the reaction mixtures, the presence of the components with  $R_F$  values 0.91 and 0.44 was not detected by chromatographic analysis. Analysis of these solutions furnish data only for the presence of triiodide ion ( $R_F = 0.31$ ).

In neutral medium, isotopic exchange is, even at a temperature of 228°, a slow reaction, and it is only obtained for the concentrations of the reacting components  $1 \cdot 10^{-2} M Na^{131}I/5 \cdot 10^{-2} M NaIO_3$ . The results are shown in Table III.

On the basis of the exchange rate equation<sup>10</sup>,

$$R = - \frac{2.3}{t(a+b)} \log \left[ 1 - \frac{x}{c} \left( 1 + \frac{b}{a} \right) \right] \text{ l} \cdot \text{mol}^{-1} \text{h}^{-1} \quad (2)$$

where:  $t$  = time;  $x/c$  = exchange degree;  $x/c(1 + b/a)$  = exchanged part,  $1 - x/c(1 + b/a)$  = unexchanged part, and from the experimental data in Table III, we calculated the rate constant for the reverse bimolecular isotopic exchange reaction:  $Na^{131}I + NaIO_3 \rightarrow NaI + Na^{131}IO_3$ .  $R = 0.216 \text{ l} \cdot \text{mol}^{-1} \text{h}^{-1}$ .

#### Oxidation of iodide with periodate

In solutions with a  $pH > 3$ , the reaction between iodides and periodates proceeds according to the equation:



As seen in equation (3), the components appearing in the solution are:  $IO_4^-$ ,  $IO_3^-$ ,  $I^-$  and  $I_2$ . By chromatographic separation with the system of solvents described

TABLE IV

ACTIVITY DISTRIBUTION BETWEEN THE IODATE AND THE UNIDENTIFIED IODINE FORMS IN THE  $^{131}I/IO_4^-$  SYSTEM AS A FUNCTION OF THE  $pH$  OF THE MEDIUM, THE CONCENTRATION AND TIME

$pH$ of the solution	Time	Content of $IO_3^-$ (%)	Content of $R_F = 0.91$ (%)	Content of $R_F = 0.44$ (%)	Ratio of $IO_4^-/I^-$
3.4	2 min; 1 h; 24 h	8; 36; 95	20; 0; 0	0; 0; 0	$5 \cdot 10^{-2}/1 \cdot 10^{-2}$
		5; 9; 10	0; 2; 2	0; 8; 10	$5 \cdot 10^{-2}/1 \cdot 10^{-5}$
		4; 4; 7	2; 2; 2	7; 7; 13	$5 \cdot 10^{-2}/1 \cdot 10^{-8}$
5.5-7.5	2 min; 1 h; 24 h	80; 100; —	0; 0; —	0; 0; —	$5 \cdot 10^{-2}/1 \cdot 10^{-2}$
		38; 56; 100	2; 2; 0	12; 6; 0	$5 \cdot 10^{-2}/1 \cdot 10^{-5}$
		— 7; 61	— 2; 6	— 10; 3	$5 \cdot 10^{-3}/1 \cdot 10^{-5}$
		7; 11; 11	0; 2; 2	7; 60; 60	$5 \cdot 10^{-3}/1 \cdot 10^{-8}$
10	2 min; 1 h; 24 h	52; 100; —	11; 0; —	0; 0; —	$5 \cdot 10^{-2}/1 \cdot 10^{-2}$
		0; 0; 5	0; 0; 0	0; 0; 0	$5 \cdot 10^{-5}/1 \cdot 10^{-5}$
	2h at 95°	93; — —	0;	0;	$5 \cdot 10^{-5}/1 \cdot 10^{-5}$
	2 min; 1 h; 24 h	17; 71; 100	5; 2; 0	8; 3; 0	$5 \cdot 10^{-2}/1 \cdot 10^{-8}$
	— — 24 h	—; —; 0	—; —; 0	—; —; 0	$5 \cdot 10^{-5}/1 \cdot 10^{-8}$
	2 h at 95°	59	0	0	$5 \cdot 10^{-5}/1 \cdot 10^{-8}$
2 min; 1 h; 24 h	13; 21; 75	11; 15; 3	15; 19; 6	$5 \cdot 10^{-2}/^{131}I^-$	



earlier, the activity for IO<sub>3</sub><sup>-</sup> and IO<sub>4</sub><sup>-</sup> is determined as the sum at the starting point of the chromatogram; the iodate does not separate from the periodate. In these investigations we have also used a solvent which separates IO<sub>3</sub><sup>-</sup> from IO<sub>4</sub><sup>-</sup> (ref. 14); the chromatogram was developed in separate experiments using both solvents. In this way we could obtain results for all the components present.

Table IV shows the results of these investigations, under various conditions of pH, concentration of reacting agent, and aging time. The iodide and periodate concentrations varied. The iodide concentration gradually decreased to carrier free radioiodide concentration, while periodate occurred in excess.

Results showed that isotopic exchange between iodides and periodates does not take place in solutions with pH = 3.4; 5.5-7.5 and 10. The unidentified form whose *R<sub>F</sub>* value is 0.44 appears in solutions with the above pH values if the iodide concentration is below 1 · 10<sup>-5</sup>. In neutral solutions for the concentration ratio 1 · 10<sup>-8</sup> M I<sup>-</sup> / 5 · 10<sup>-3</sup> M IO<sub>4</sub><sup>-</sup> the percentage of the unidentified form, with *R<sub>F</sub>* = 0.44, increases even as far as 60 % of the total radioactivity. The form with *R<sub>F</sub>* = 0.91 was present under all the above conditions, irrespective of the iodide concentration.

TABLE V

RATE OF IODATE FORMATION ACCORDING TO REACTION (3)  
0.06 M NaIO<sub>4</sub>, 0.12 M NaI labelled with <sup>131</sup>I<sup>-</sup>. Precipitation with Ba(NO<sub>3</sub>)<sub>2</sub> at 60°.

<i>NaIO<sub>4</sub> added to Na<sup>131</sup>I solution in presence of Ba(NO<sub>3</sub>)<sub>2</sub></i>	<i>Radioactivity of precipitate as a function of time of addition of Ba(NO<sub>3</sub>)<sub>2</sub> to reaction mixture after</i>					<i>Precipitation in presence of NH<sub>4</sub>NO<sub>3</sub> (pH = 7) after 600 sec</i>
	<i>4 sec</i>	<i>10 sec</i>	<i>30 sec</i>	<i>90 sec</i>	<i>160 sec</i>	
<i>imp./min</i> 1.185	6.153	11.788	16.203	16.500	16.580	2.612

In order to obtain more data for the conditions in which the unidentified form of iodine appears, we investigated the rate of iodate formation, according to equation (3), by separating the iodate produced from the reaction mixture, using Ba(NO<sub>3</sub>)<sub>2</sub>. The radioactivity of the iodate precipitate was determined as a function of the time of the addition of barium salt as precipitating agent. By treating the mixture of radioiodide and barium nitrate with inactive periodate solution, a slightly radioactive precipitate is obtained (periodate reacts with iodide before barium precipitates periodate from the reaction mixture).

If barium nitrate is added after the solution of radioiodide and inactive periodate is left to react for some time, one obtains an iodate precipitate whose activity depends on the time when the Ba(NO<sub>3</sub>)<sub>2</sub> was added to the reaction mixture. Results are shown in Table V.

As can be seen from the results, the activity of the iodate increases and after some time it remains constant. On addition of barium nitrate the primary reaction (3) in which iodate is formed stops, because periodate precipitates as well as iodate. Further formation of iodate proceeds according to the secondary reactions:



The rate of the secondary reaction decreases with decreasing pH of the solution. Under our experimental conditions the addition of barium salts decreases the pH of the solution from 10 to 6.

According to the results obtained by MAGNIER *et al.*<sup>15</sup>, who investigated the mechanism of reaction (3), only the elementary iodine formed in this reaction is radioactive and is produced from the I<sup>-</sup> ion. Iodine atoms in an iodate molecule are exclusively formed from periodates and they are inactive. Radioactive iodate is then formed from radioactive I<sub>2</sub> by the secondary reactions (4) and (5).

If precipitation with barium nitrate in the presence of ammonium nitrate (pH = 7) proceeds even after 10 min, the radioactivity of the precipitate obtained is weak and the solution above the precipitate is radioactive, its colour is brown and is characteristic of the presence of an I<sup>-</sup> and I<sub>2</sub> mixture.

#### *Oxidation of iodide with H<sub>2</sub>O<sub>2</sub>*

In addition to iodate and periodate as radiochemical impurities in radioiodide preparations, hydrogen peroxide also occurs as the product of water radiolysis, especially in preparations of high specific activity. On oxidising carrier-free radioiodide preparations with H<sub>2</sub>O<sub>2</sub>, we also found, by chromatographic separation, in addition to iodates some unidentified components with  $R_F = 0.44$  and  $0.91$ . As in cases of iodide oxidation with iodate and periodate, the form with  $R_F = 0.44$  is present only in solutions in which the iodide concentration was below  $1 \cdot 10^{-5}$ , while the component with  $R_F = 0.91$  appears in solutions for all the iodide concentrations investigated. On oxidising a radiochemically pure preparation with a 3% solution of H<sub>2</sub>O<sub>2</sub> in acid medium (2 N H<sub>2</sub>SO<sub>4</sub>), a component containing 13% of the activity and with  $R_F = 0.44$  appears within 10 min of aging. After 40 min the activity of this form increases to 24% and does not change even after aging for 24 h. The activity of iodate is constant and amounts to about 7%.

#### *The effect of the concentration ratio I<sub>2</sub>/<sup>131</sup>I<sup>-</sup> on the appearance of the unidentified component with $R_F = 0.91$ .*

Further investigations of the properties of the unidentified components have shown that, on extraction with organic solvents, the component with  $R_F = 0.44$  remains in the aqueous phase.

The unidentified form which on chromatography has an  $R_F$  value of 0.91 goes quantitatively to the organic phase together with the triiodide ion ( $R_F = 0.31$ ).

It is known that the solvents in which iodine solubility is greatest, favour the formation of higher polyiodides. In our investigations nitrobenzene was chosen as such a solvent. The aqueous phase, NaI, labelled with <sup>131</sup>I<sup>-</sup> was equilibrated with the organic phase, I<sub>2</sub> in nitrobenzene. Two series of experiments were made. In the first series the concentrations of [I<sup>-</sup>] > [I<sub>2</sub>] and in the second series [I<sup>-</sup>] < [I<sub>2</sub>], the concentration of NaI was  $1 \cdot 10^{-1}$  and  $1 \cdot 10^{-5}$  M respectively. The I<sub>2</sub> concentration varied from  $1 \cdot 10^{-1}$  to  $1 \cdot 10^{-5}$  M. In this case we assumed that the exchange between the iodide and iodine atom, which are components of the polyiodide, is instantaneous<sup>12</sup>. After separating the phases, the organic phase of the solutions was investigated chromatographically. In the case where the ratio [I] > [I<sub>2</sub>], it was found that only the triiodide ion with  $R_F = 0.31$  was present. Under these conditions, the unidentified form with  $R_F = 0.91$  does not appear.

In the solutions where the concentration ratio was  $[I_2] > [I^-]$ , an unidentified form with an  $R_F$  value of 0.91 was found in addition to the triiodide ion in the organic phase. The percentage of this form decreases with increasing  $I_2$  concentration. Results of these investigations are shown in Fig. 5. As shown in the diagram, the amount of the component with  $R_F = 0.91$  increases with decreasing  $I_2$  concentration, so that for  $1 \cdot 10^{-4} M I_2$  it is 73 % of the total radioactivity, while the amount of the triiodide ion is proportionally smaller. The aqueous phase contained only iodide.

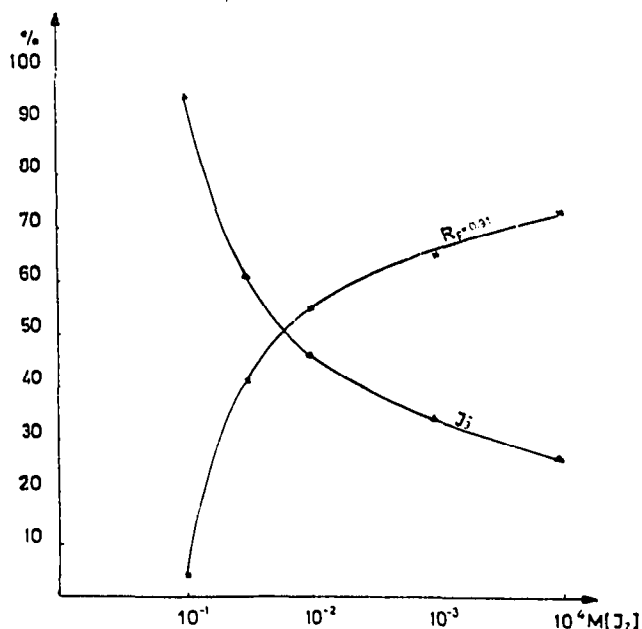


Fig. 5. Percentage content of  $^{131}I_3^-$  and component with  $R_F = 0.91$  in the organic phase of the system  $I_2$  in nitrobenzene, aqueous solution of  $Na^{131}I$ , as a function of  $I_2$  concentration.  $[I_2] > [I^-] = 1 \cdot 10^{-5} M$ .

The conditions for the formation of this form were also investigated by equilibrating the aqueous phase  $Na^{131}I$  with an organic phase of  $I_2$  in benzene. The ratio of the concentrations of  $I^-$  in aqueous phase to  $I_2$  in benzene was the same as that in the preceding experiments with nitrobenzene.

Both phases were investigated chromatographically after they had been separated. The unidentified form with  $R_F = 0.91$  only accounts for  $\sim 5\%$  of the total activity for the largest concentration of  $I_2$  ( $1 \cdot 10^{-1} M I_2 / 1 \cdot 10^{-5} M I^-$ ), while 95 % was found in the form of triiodide ion with  $R_F = 0.31$ . The aqueous phase contained only iodide.

Results have shown that solutions of benzene whose dielectric constant is much smaller (2.3) compared with that of nitrobenzene (36.1) are not suitable for the formation of a component with an  $R_F$  value of 0.91.

#### CONCLUSIONS

Chromatographic investigations have shown that, besides the stable forms of iodine, two unidentified components occur in radioiodide preparations, depending on the aging period. With the solvent mixture butanol saturated with 3 N  $NH_4OH$ ,

stable forms of the two unidentified components could be separated chromatographically. The  $R_F$  values of the various forms were:  $\text{IO}_3^-$ ,  $\text{IO}_4^- = 0.0$ ;  $\text{I}^-$ ,  $\text{I}_3^- = 0.31$ ; unidentified forms = 0.44 and 0.91.

In order to investigate the conditions under which the unidentified components are formed, radioiodide solutions were oxidised with iodate, periodate and hydrogen peroxide. The concentrations of the reacting components were for iodide:  $1 \cdot 10^{-2} M$  to carrier free, while the amounts of  $\text{IO}_3^-$  and  $\text{IO}_4^-$  were higher than the same for respective  $\text{I}^-$  concentrations *viz*:  $5 \cdot 10^{-2}$ ,  $5 \cdot 10^{-3}$  and  $5 \cdot 10^{-5} M$ .

The unidentified component with  $R_F = 0.44$  is formed in the solutions when the iodide concentration is below  $1 \cdot 10^{-5} M$ ; in the system  $^{131}\text{I}^-/\text{IO}_3^-$  at  $\text{pH} = 3.4$ , and in the system  $^{131}\text{I}^-/\text{IO}_4^-$  in weakly acid, neutral and alkaline media. If the iodide concentration is above  $1 \cdot 10^{-5} M$  this form is not present.

The component with  $R_F = 0.91$  is formed on oxidation with iodate in acid solution and with periodate in acid, neutral and alkaline media, in presence of excess  $\text{IO}_3^-$  and  $\text{IO}_4^-$ , for all iodide concentrations investigated.

The rate constant  $R$  for the isotopic exchange  $^{131}\text{I}^-/\text{IO}_3^-$  in neutral medium at  $228^\circ$  was determined for the concentrations  $1 \cdot 10^{-2} M$   $^{131}\text{I}^-/5 \cdot 10^{-2} M$   $\text{IO}_3^-$  and its value is  $0.216 \text{ l} \cdot \text{mol}^{-1} \text{h}^{-1}$ .

Under our experimental conditions no exchange occurs between  $^{131}\text{I}^-/\text{IO}_4^-$ . As the formation of unidentified components is also followed by the presence of iodate, the rate of iodate formation in the system  $^{131}\text{I}^-/\text{IO}_4^-$  has been investigated. Iodine atoms in the iodate molecule formed from the periodate are inactive. Active iodate is formed from  $^{131}\text{I}_2$  by secondary reactions.

On extraction of reaction mixtures with nitrobenzene, the unidentified form with  $R_F = 0.91$  goes quantitatively to the organic phase together with the  $\text{I}_3^-$  ion, while the unidentified component with  $R_F = 0.44$  remains in aqueous phase together with the  $\text{I}^-$  and  $\text{IO}_3^-$  ions.

On equilibrating the aqueous phase  $\text{Na}^{131}\text{I}$  with the organic phase,  $\text{I}_2$  in nitrobenzene: when  $[\text{I}_2] > [\text{I}^-]$  in addition to  $\text{I}_3^-$  in the organic phase an unidentified form with  $R_F = 0.91$ , also appears as a result of instantaneous isotopic exchange, while the aqueous phase contains only iodide.

According to the results obtained, it can be assumed that in nitrobenzene solutions a mixture of polyiodides is formed:  $\text{I}_3^-$  ( $R_F = 0.31$ ) and an unidentified form with  $R_F = 0.91$  which is probably a mixture of higher polyiodides ( $\text{I}_5^-$ ,  $\text{I}_7^-$  and  $\text{I}_9^-$ ).

The unidentified form which remains in the aqueous phase, after extraction with organic solvents, and has an  $R_F$  value of 0.44, is stable in neutral solutions even after a long time. On addition of acid it disappears, while the amount of  $\text{IO}_3^-$  and the form with  $R_F = 0.91$  increase to the same amount. It does not reduce with  $\text{Na}_2\text{S}_2\text{O}_3$ , and the effect of sulphites and thiouracyl is negligible. Electrophoretic behaviour of this component shows that it is an anion whose migration differs from the known forms  $\text{IO}_3^-$ ,  $\text{IO}^-$  and polyiodide. This form appears as an intermediate product on oxidation of iodide or  $\text{I}_2$  to iodate, in solutions of low concentration where the reaction rate is reduced.

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