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Extraction of Thallium with Butyl Acetate

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ABSTRACT

Experimentally obtained extraction isotherms of the system thallium–sulfuric acid–sodium chloride–butyl acetate are presented. The influence of the sulfuric acid and chloride anion concentrations on the extraction equilibria of thallium was investigated. An increase in the acidity of the aqueous phase results in steeper extraction isotherms, and the amount of thallium extracted generally increases. The influence of chloride anions on the equilibrium is more complex. It was found that the extraction equilibria is not influenced by the chloride ion concentration, provided that the Cl/Tl ratio in the aqueous phase is ≥ 4. If this ratio is less than 4, the concentration of chloride anions significantly influences the extraction isotherms. The results obtained are discussed in terms of the composition of the complex in the organic phase. An apparent reaction constant equation is proposed for the prediction of the extraction equilibria.

Key Words. Thallium; Butyl acetate; Extraction; Production of radiopharmaceuticals; ^{201}TlCl

INTRODUCTION

The radionuclide ^{201}Tl, a close chemical analogue of potassium, is widely used in nuclear medicine for investigating potassium metabolism, especially for myocardial imaging (1, 2). It can be obtained by proton-induced nuclear

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reactions from $^{205}Tl(p,5n)^{201}Pb \rightarrow {}^{201}Tl$ or, more conveniently, from $^{203}Tl(p,3n)^{201}Pb \rightarrow {}^{201}Tl$, followed by subsequent target processing. Due to the extremely high toxicity of thallium and the high specific activity required, the key step in the production of the radiopharmaceutical $^{201}TlCl$ is the separation of tracer amounts of ^{201}Pb (the parent of ^{201}Tl) from the irradiated target material, metallic ^{203}Tl.

Many methods, such as precipitation, coprecipitation, ion exchange, solvent extraction, and their combinations, have been proposed for the purpose (3–16). The highest tolerable concentration of inactive thallium in radiopharmaceutical preparation is 2 or 5 $mg \cdot dm^{-3}$, defined by the *United States* and *European Pharmacopoeia*, respectively (17, 18). For a target weighing 1.0 g ^{203}Tl, a decontamination factor of 2.5×10^4 has to be assured in the shortest possible time. None of the reported techniques can assure such a high decontamination factor in a single step. Additionally, most of the proposed methods require complex operations inside hot cells, which cannot be done using simple automatic devices.

One of the most promising techniques for the separation of thallium from lead is solvent extraction using butyl acetate (BuAc). A complete technological scheme based on extraction has been reported for the routine production of radiopharmaceutic $^{201}TlCl$ (12, 13). However, no systematic investigation of the extraction equilibria applied in this method has been carried out. The aim of this paper is to present the results of a thorough investigation of the system sulfuric acid–sodium chloride–thallium–BuAc as a starting point for optimization of the separation process.

EXPERIMENTAL

The investigation of the extraction equilibria was carried out by equilibrating water solutions containing Tl^{3+}, NaCl, and H_2SO_4 with different volumes of BuAc, followed by subsequent chemical analysis of the phases. It is well known that thallium can be extracted by organics in the form of $HTlCl_4$ (19–22). Since the reported technique for the extraction of thallium by BuAc (12, 13) presumes the necessity of a high concentration of Cl^- in the aqueous phase, we decided to investigate the influence of Cl^- concentration on the extraction equilibria. The separation of tracer levels of ^{201}Pb from the bulk of the metallic target ^{203}Tl is usually preceded by dissolution of the target material in 5.0 $mol \cdot dm^{-3}$ H_2SO_4, and the extraction is carried out from this acidic solution. Therefore, we investigated the influence of H_2SO_4 on the equilibria as well. All the results presented in this paper were obtained by extracting thallium from an aqueous phase containing a known initial (total) concentration of H_2SO_4 and Cl^-.

0.24 $mol \cdot dm^{-3}$ solutions of Tl_2SO_4 (Fluka, p.a. grade) were prepared in 2.0, 3.0, 5.0, and 8.0 $mol \cdot dm^{-3}$ H_2SO_4 (Merck, p.a. grade) in twice distilled water with the addition of the required amount of NaCl (Merck, p.a. grade). Trivalent thallium, which is appropriate for extraction with BuAc, was obtained by oxidation with an excess of $KBrO_3$ (Merck, p.a. grade) prior to extraction. The reaction preceding the extraction experiment starts with the oxidation of thallium:

$$5Tl^+ + 2BrO_3^- + 12H^+ = 5Tl^{3+} + Br_2 + 6H_2O \tag{1}$$

while the excess of BrO_3^- further reacts with the available Cl^- ions:

$$10Cl^- + 2BrO_3^- + 12H^+ = 5Cl_2 + Br_2 + 6H_2O \tag{2}$$

The released gaseous Br_2 and Cl_2 were removed from the solutions by refluxing for 5 minutes.

The stoichiometry of the above reactions was checked by argentometric titration of the remaining Cl^-. Thallium was removed before the titration by neutralization of the acid with NaOH up to pH 12. The precipitated Tl_2O_3 was stripped off by filtration (22). This procedure was also used for determination of Cl^- after the extraction equilibria. In order to determine the concentration of Cl^- in the organic phase after equilibration, 5 cm^3 of distilled water was added to the separated BuAc and the emulsion was boiled until all of the BuAc was distilled. In this way the organic extract was quantitatively transferred to the aqueous phase.

The extraction experiments were always done in 5 cm^3 vials using a 1-cm^3 aqueous phase and a 0.2–2 cm^3 organic phase. The stoppered vials were agitated using a mechanical shaker at room temperature (22 ± 1°C). The phases were separated by first using a micropipet to remove 0.1 cm^3 of the organic phase that was used for analytical purposes. The rest of the organic phase was removed by a micropipet as well, together with a small amount of the aqueous phase, and discarded in order to free the aqueous phase from traces of BuAc.

The distribution of thallium between the aqueous and organic phases was traced by labeling the initial aqueous solution with $^{201}TlCl$ (CIS bio international) followed by subsequent determination of the specific activities of both phases using an automated γ-counter (LKB WaLLac, CompuGama Model 1282-001). The initial activity of ^{201}Tl was high enough in each experiment to allow at least 10,000 counts per 0.1 cm^3 for both phases.

A series of experiments was carried out in order to determine the time needed to reach equilibrium. It was found that equilibrium was practically reached within 10 minutes. However, all the experiments presented in this paper were carried out with 20 minutes agitation to avoid any influence of kinetic parameters on the equilibrium.

The concentration of thallium in the aqueous phase after equilibration was determined in several series of experiments by ICP-AES (Perkin-Elmer Model 6500) using the initial solution as a reference standard. The linearity of the instrument response had been previously tested by a series of measurements and was found to be better than ±2% in the region of interest. The correlation between the results obtained by these different techniques was within the experimental error.

RESULTS AND DISCUSSION

The estimated experimental error in determining equilibrium concentrations is not greater than 4% in the aqueous phase and not greater than 6% in the organic phase. The higher uncertainty in the concentrations of the organic phase are due to the volatility of BuAc.

Figure 1 presents the extraction isotherms of thallium as a function of total H_2SO_4 concentration in the aqueous phase while the concentration of Cl^- was kept constant. The initial molar ratio of Cl/Tl in the aqueous phase was 4 in these experiments. By increasing the H_2SO_4 concentration the extraction isotherms became steeper and the distribution ratio (defined as $C_{\mathrm{Tl,org}}/C_{\mathrm{Tl,aq}}$) increased for the same equilibrium concentration of thallium in the aqueous phase. This behavior is expected if one accepts the belief that thallium persists

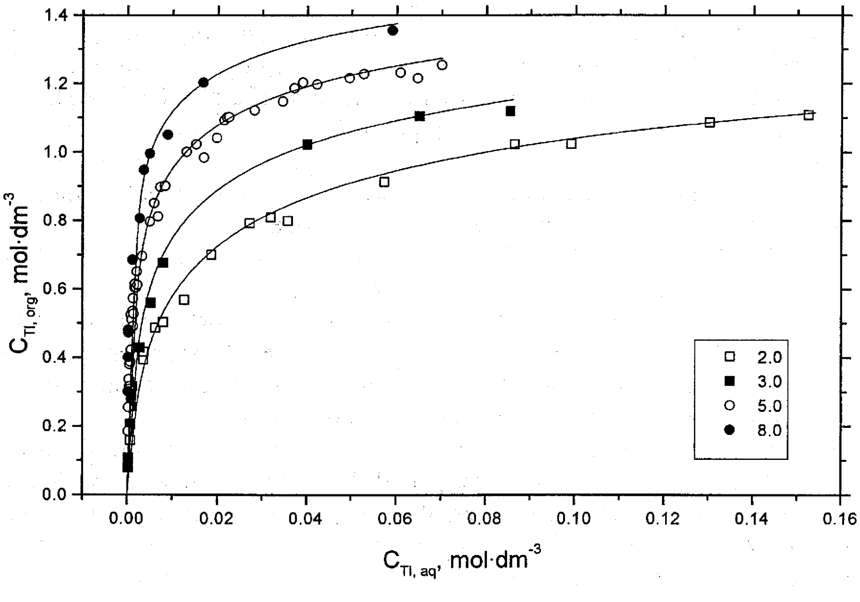

FIG. 1 Extraction isotherms of thallium with BuAc for indicated initial sulfuric acid concentrations in the aqueous phase (mol·dm^{-3}). The initial Cl/Tl molar ratio in the aqueous phase was 4.0.

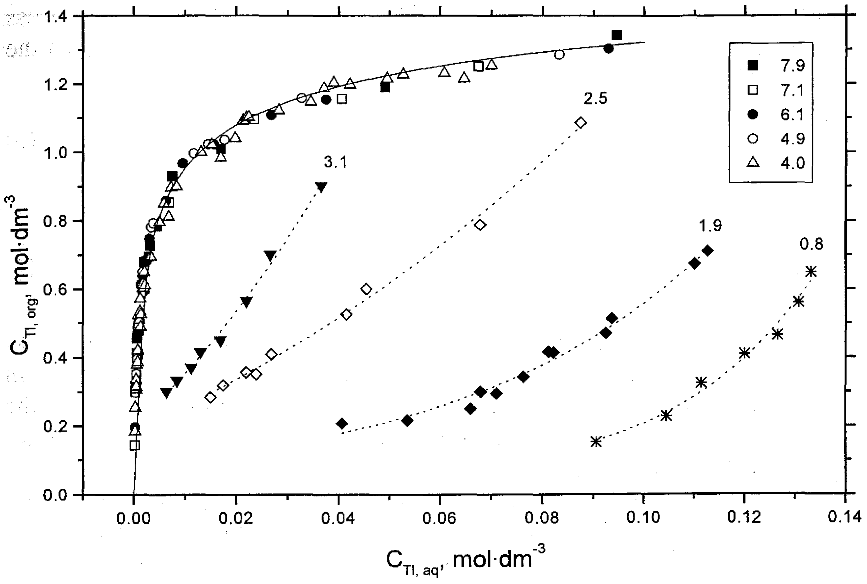

FIG. 2 Extraction isotherms of thallium with BuAc for indicated initial Cl/Tl molar ratios in the aqueous phase. The initial concentration of sulfuric acid in all cases was 5.0 mol·dm^{-3}.

in the organic phase in the form of $HTlCl_4$ since sulfuric acid suppresses the dissociation of this weak acid and thus expels it from the aqueous phase.

Figure 2 presents the extraction isotherms of thallium as a function of the initial Cl/Tl molar ratio in the aqueous phase while the initial concentration of H_2SO_4 was kept constant (5.0 mol·dm^{-3}). It can be seen that the extraction mechanism is quite different if the Cl/Tl molar ratio is below 4, while it has no effect on the extraction mechanism if this ratio is greater than 4. This is also in line with the assumption that the optimal form of thallium in the organic phase is $HTlCl_4$ (19). If the Cl/Tl molar ratio is below 4, only part of the thallium can be extracted in this form; the rest will be extracted to much lower extent, probably in the form of sulfate. Due to the high sulfuric acid concentration, all of the $HTlCl_4$ in the aqueous phase is in molecular form, therefore the salting-out effect, expected by increasing the Cl^- concentration in the aqueous phase, was not observed when the Cl/Tl molar ratio exceeded 4.

The determination of the Cl/Tl molar ratio in the organic phase led us to the same conclusion, since this ratio was (within the limits of experimental error) always the same as in the aqueous phase when it did not exceed 4. In cases when this ratio was greater than 4 in the aqueous phase, the Cl/Tl molar ratio in the organic phase was always equal to 4, regardless on the Cl/Tl ratio in the aqueous phase.

Based on these findings, one can assume that the overall extraction process can be described by the following stoichiometric equation, assuming that the initial Cl/Tl molar ratio is greater than or equal to 4 in the aqueous phase:

$$H^+ + TlCl_4^- + n\text{BuAc} = HTlCl_4\cdot n\text{BuAc} \qquad (3)$$

with the corresponding thermodynamic equilibrium constant defined by

$$K = \frac{a_{HTlCl_4\cdot n\text{BuAc,org}}}{a_{H^+,\text{aq}}\cdot a_{TlCl_4^-,\text{aq}}\cdot a^n_{\text{BuAc,org}}} \qquad (4)$$

where $a_{HTlCl_4\cdot n\text{BuAc,org}}$ stands for the activity of the complex formed in the extraction process in the organic phase, a_{H^+} is the activity of hydronium ions in the aqueous phase, $a_{TlCl_4^-}$ is the activity of the thallous chloride anion in the aqueous phase, while a_{BuAc} stands for the activity of the noncomplexed (free) BuAc in the organic phase.

Assuming that the dissociation of $HTlCl_4$ is highly suppressed by sulfuric acid and taking into account that the acidity is only slightly changed by the extraction (the initial stoichiometric concentration of H^+ was at least 10 times higher than that of thallium in the experiments), the thermodynamic Eq. (4) can be replaced by an apparent equation:

$$Q = \frac{C_{HTlCl_4\cdot n\text{BuAc,org}}}{C_{HTlCl_4,\text{aq}}\cdot C^n_{\text{BuAc,org}}} \qquad (5)$$

where the reaction constant Q (not a thermodynamic constant) is dependent on the total concentration of the sulfuric acid in the aqueous phase. Combining Eq. (5) with the mass balance Eq. (6):

$$C^{\text{tot}}_{\text{BuAc,org}} = C_{\text{BuAc,org}} + n\cdot C_{HTlCl_4\cdot n\text{BuAc,org}} \qquad (6)$$

one will get Eq. (7) which describes the extraction process in terms of $C_{\text{BuAc,org}}$:

$$n\cdot Q\cdot C_{HTlCl_4,\text{aq}}\cdot C^n_{\text{BuAc,org}} + C_{\text{BuAc,org}} - C^{\text{tot}}_{\text{BuAc,org}} = 0 \qquad (7)$$

Solving Eq. (7) for different n, Q, and $C_{HTlCl_4,\text{aq}}$ values ($C^{\text{tot}}_{\text{BuAc,org}} = 7.59$ mol·dm^{-3} for pure BuAc) and introducing the $C_{\text{BuAc,org}}$ values obtained in Eq. (5), one can calculate the extraction isotherm as

$$C_{HTlCl_4\cdot n\text{BuAc,org}} = f(n, Q, C^{\text{tot}}_{\text{BuAc,org}}, C_{HTlCl_4,\text{aq}}) \qquad (8)$$

Using a nonlinear least square fitting algorithm, Eq. (8) can be used for determination of the best n and Q values by comparing the experimentally ob-

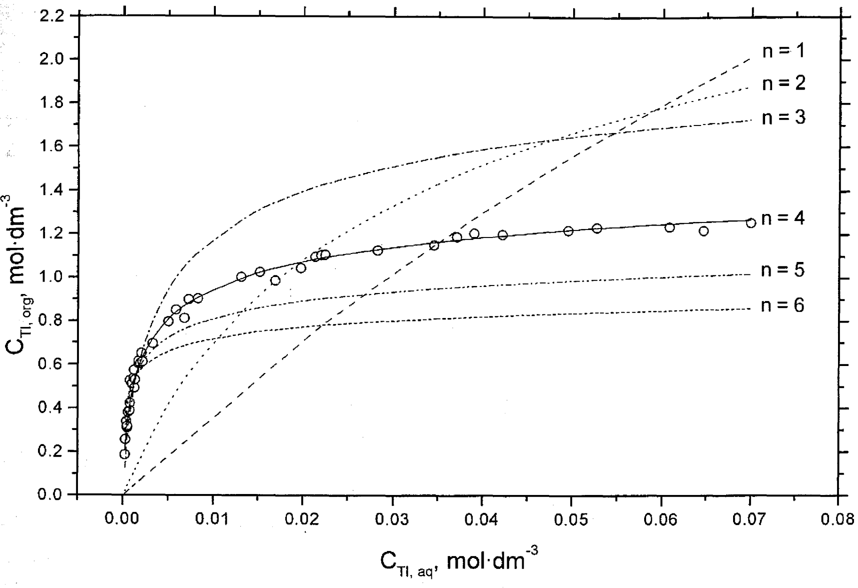

FIG. 3 Illustration of the best fit results for different solvation numbers indicated on the figure. The experimental data were obtained with an initial sulfuric acid concentration of 5.0 mol·dm^{-3} and an initial Cl/Tl molar ratio of 4.0 in the aqueous phase.

tained and calculated $C_{HTlCl_4,org}$ values. For $n = 1$, 2, and 3, Eq. (7) can be explicity solved (23), and the fitting procedure can be accomplished by any standard software package for nonlinear least square fitting. However, the best fit results obtained for $n = 1$, 2, and 3 were unsatisfactory, as shown by Fig. 3, leading to the conclusion that the complex of thallium in the BuAc phase contains more than three BuAc molecules ($n \geq 4$).

In order to prove this conclusion, an algorithm was developed that includes the numerical solution of Eq. (7) for any real value of n. As one can see from Fig. 3, the best fit was obtained with $n = 4$ (the full lines in Figs. 2 and 3 are also calculated by this procedure). Assuming that the four chlorine atoms are equivalent in the complex, it seems that the interaction between BuAc and $HTlCl_4$ occurs through dipole–dipole interactions between chlorine atoms and esteric groups.

Table 1 presents the reaction constants obtained for different sulfuric acid solutions. As expected, these values are strongly influenced by the acid concentration: the higher the initial concentration of the acid, the higher is the reaction constant. However, this correlation is not linear due to the high ionic strength of the aqueous phase.

TABLE 1
Best Fit Values of the Equilibrium Constant (defined by Eq. 5) for Different Initial Sulfuric Acid Concentrations, While the Initial Concentration of Chloride Anions in the Aqueous Phase Was 0.96 mol·dm^{-3} (Cl/Tl molar ratio = 4.0). σ Is the Relative Standard Deviation between the Experimental and Calculated Values

$C^{tot}_{H_2SO_4,aq}$ (mol·dm^{-3})	Q (mol^{-4}·dm^{12})	σ (%)
2.0	0.0758	4.8
3.0	0.1499	4.9
5.0	0.4708	4.0
8.0	1.2071	5.3

The simple model presented in this paper does not take into account the hydration of the complex formed in the organic phase, although it has been shown that water will be coextracted when thallium is extracted by sulfoxides (20). Since the model presented fits satisfactorily the experimentally obtained extraction isotherms (the relative standard deviation between the measured and calculated isotherms is less than 5%), we believe that the coextracted water in the organic phase can be treated as an inert diluent (24) that does not affect the equilibria.

CONCLUSION

The experimental results presented in this paper allow the extraction equilibria in the system thallium–sulfuric acid–sodium chloride–butyl acetate to be understood. The results clearly show that the extraction equilibria are not affected by the concentration of chloride anions in the aqueous phase, provided that the Cl/Tl molar ratio exceeds 4. Below this ratio the extraction process has quite a different mechanism. The effect of the sulfuric acid concentration on the extraction equilibria is significant: an increase in the acidity enhances the extractability of trivalent thallium with BuAc.

It was shown that the extraction equilibria can be described by a simple apparent equation. A special algorithm was developed, and the reaction constants were numerically determined. Based on the results of the fitting procedure, it was found that the thallous complex in the organic phase contains four BuAc molecules. This apparent equation can be used for the prediction of the extraction equilibria and for the optimization of the process for separation of thallium from the aqueous phase, the most important step in the production of the radiopharmaceutical ^{201}TlCl.

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