

Extraction of 7-Aminocephalosporanic Acid with Secondary, Tertiary, and Quaternary Amines

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Extraction of 7-aminocephalosporanic acid (7-ACA) has been investigated using secondary and tertiary amines and a quaternary ammonium salt (Aliquat-336) as the carriers. The values of the distribution coefficients have been reported in a range of aqueous-phase pH values and concentrations of 7-ACA using different carriers in *n*-butyl acetate as the diluent. As expected, ion-pair extraction with secondary and tertiary amines exhibits lowerings of the distribution coefficient with increase of pH, whereas the ion exchange extraction with quaternary ammonium chloride (Aliquat-366) exhibits an opposite but more pronounced pH dependence, providing at the same time higher values of distribution coefficient at high values of pH. Both the extraction principles can be exploited to achieve extraction and reextraction of 7-ACA in the pH range of 5 to 8 in which it is relatively stable.

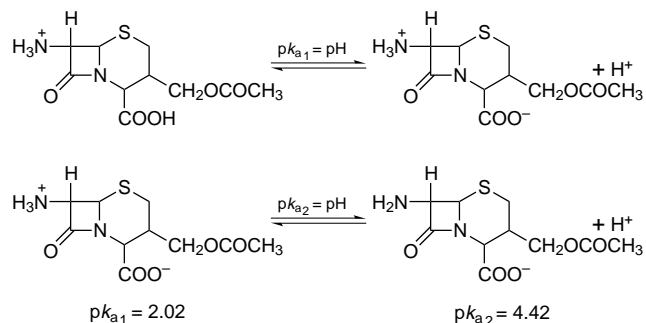
Introduction

7-Aminocephalosporanic acid (7-ACA) is an important intermediate for semisynthetic cephalosporins such as cephaloglycin, cephalothin, cephapirin, etc. It is usually made by chemical deacylation of cephalosporin-C (CPC), which is a fermentation product of *Cephalosporium acremonium* (Huber et al., 1972). In the classical process, 7-ACA is isolated from the reaction mixture by removal of the solvent under vacuum, dissolution of the residue in water, acidification, and precipitation at the isoelectric point (pH = 3.5) of 7-ACA. However, such methods involve capital and energy intensive operations particularly when a dilute solution is dealt with. Since 7-ACA is an amphoteric molecule, physical (solvent) extraction is difficult. Various methods of extraction and purification of cephalosporin antibiotics have been discussed in our recent review (Ghosh et al., 1997). Reactive extraction has been thought to be a potential method for recovery of lactam antibiotics from a complex culture broth (Ghosh et al., 1996, 1997; Hano et al., 1992). We have been trying to exploit the principle of reactive extraction for developing liquid membrane processes for various cephalosporin antibiotics (Ghosh et al., 1995; Sahoo et al., 1996, 1997). Data on equilibrium and kinetics of reactive extraction are useful for optimizing the operating condition of liquid membrane processes. We have recently reported the use of Aliquat-336 for reactive extraction of 6-aminopenicillanic acid (Bora et al., 1997). In this paper, we report complementary studies on reactive extraction of 7-ACA using secondary and tertiary amines as well as a Aliquat-336 with butyl acetate as the solvent.

Extraction Equilibrium

7-ACA is an amphoteric molecule, and in aqueous solution, it exists in ionic forms of different charges

depending on the pH of the media: It does, however, show unstable behaviour at high pH (Yamane and Tsuji, 1976). At pH below 2.02, the predominant form is cationic, at pH above 4.42, it is anionic, and in the range 2.02 < pH < 4.42, the zwitterion as a whole is predominant as evident from the scheme shown below



The pH at which the amino group ionizes keeps the carboxyl group in the COO^- form.

The reactive extraction of 7-ACA with aliphatic amines can proceed as follows. 7-ACA (HP) dissociates in the aqueous phase to give an anion, P^- , and a proton, H^+ , as



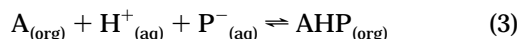
The dissociation constant, K_a , is given by

$$K_a = \frac{C_{\text{H}^+} C_{\text{P}^-}}{C_{\text{HP}}} \quad (2)$$

where C_{H^+} , C_{P^-} , and C_{HP} are concentrations of H^+ , P^- , and HP, respectively.

The amine, A, dissolved in the organic phase reacts with 7-ACA anion, P^- , and the proton, H^+ , in the aqueous phase. In a simple (1:1) stoichiometry, the reaction is given by

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where AHP is the amine-7-ACA complex.

The equilibrium constant, K_P , and the distribution coefficient, K_d , are given by

$$K_P = \frac{C_{PG} - C_{P-}}{(C_{AG} - C_{PG} + C_{P-})C_{H-C_{P-}}} \quad (4)$$

$$K_d = \frac{(C_{PG} - C_{P-})}{C_{P-}} \quad (5)$$

where C_{AG} and C_{PG} are the overall concentrations of acid and amine, respectively.

Considering physical extraction of undissociated 7-ACA, the following equations (Reschke and Schugerl, 1984) were used for theoretical prediction of K_d and K_P

$$K_d = \frac{C_{PG}}{C_{P-} (1 + 10^{pK_s - \text{pH}})} - 1 \quad (6)$$

$$K_P = \frac{C_{P,G} - C_{P,z}}{C_H C_P (C_{AG} - C_{PG} + C_{P,z})} \quad (7)$$

where pK_s is defined as $-\log(K_a)$ and C_P and z can be derived as

$$C_P = -0.5 \left(\frac{C_{A,G} - C_{P,G}}{z} + \frac{1}{K_P C_H} \right) + \left\{ 0.25 \left(\frac{C_{A,G} - C_{P,G}}{z} + \frac{1}{K_P C_H} \right)^2 + \frac{C_{P,G}}{K_P C_H z} \right\}^{1/2} \quad (8)$$

$$z = 1 + 10^{pK_s - \text{pH}} + c 10^{pK_s - \text{pH}} \quad (9)$$

where c is the partition coefficient of physical extraction as determined separately during the experiments.

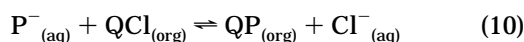
$$C_{PG} = C_P + C_{HP(\text{aq})} + C_{HP(\text{org})} + C_{AHP}$$

$$C_{AG} = C_A + C_{AHP}$$

$$C_{AHP} = C_{PG} - (C_P + C_{HP(\text{aq})}) \left(1 + \frac{c}{1 + 10^{pK_s - \text{pH}}} \right)$$

where C_{AHP} is the concentration of amine-7-ACA complex.

In the case of Aliquat-336, the reaction of dissociated 7-ACA anion, P^- , and the carrier, QCl , dissolved in the organic phase takes place in a simple stoichiometry as follows



The equilibrium constant, K_P , of this reaction is given by

$$K_P = \frac{C_{QP} C_{Cl}}{C_P C_{QCl}} \quad (11)$$

where C_{QCl} , C_P , C_{QP} , and C_{Cl} are the concentrations of Aliquat-336, 7-ACA anion, 7-ACA complex of Aliquat, and chloride ion, respectively, where the charge of the ions is omitted for simplicity. Since $C_{QP} = C_{Cl}$, it follows (in the absence of the measurement of C_{Cl}) that

$$K_P = \frac{(C_{PG} - C_P)^2}{C_{QCl,G} C_P - C_{PG} C_P + C_P^2} \quad (12)$$

Table 1. Specifications of Carriers Investigated

carrier	molecular weight	purity	supplier
secondary amine			
di- <i>n</i> -octylamine	241.5	98%	Fluka
Amberlite LA-1	375	laboratory grade	Fluka
Amberlite LA-2		-do-	Fluka
tertiary amine			
tri- <i>n</i> -octylamine	353.68	95%	Fluka
quaternary amine			
Aliquat-336	417-442	analytical grade	Fluka

The distribution coefficient, K_d , is defined as

$$K_d = \frac{C_{QP}}{C_P} \quad (13)$$

Rearrangement of eqs 11 and 13 gives

$$\log K_d = \log K_P + \log \frac{C_{QCl}}{C_{Cl}} \quad (14)$$

Experimental Section

Materials. Table 1 shows the pertinent properties of the carriers investigated in this work. 7-ACA was procured from Aldrich Chemical Co. (United States). Butyl acetate, acetic acid, sodium mono/diphosphate, citric acid, NaCl, etc., were procured from E. Merck (India) and were of analytical grade and were used without further purification.

Methods. 1. Measurement of Distribution Coefficient. The distribution coefficient (K_d) was measured in a 50-mL stoppered flask provided with magnetic stirrer. The experiments were carried out at 25 °C by mixing 10 mL each of the aqueous 7-ACA solution and butyl acetate solution of the carrier. The pH values of the aqueous phase maintained by using standard buffer solution ranged from 4 to 8. Carbonate-bicarbonate buffer was used to maintain the aqueous phase pH of 9.0, while phosphate buffer was used for pH values of 6, 7, and 8. Citrate-phosphate buffer was used to maintain the pH values at 2.5, 3, 4, and 5. Carbonate-bicarbonate buffer was prepared by using 0.2 M solution of sodium carbonate and 0.2 M solution of sodium bicarbonate. 4.0 mL of 0.2 M sodium carbonate was mixed with 46.0 mL of sodium bicarbonate, and the solution was diluted to a total volume of 200 mL to obtain a pH of 9.0. For phosphate buffer, 5.3, 39.00, and 87.7 mL of 0.2 M monobasic sodium phosphate solutions were mixed with 94.7, 61, and 12.3 mL of 0.2 M dibasic sodium phosphate solutions, and the resulting solutions were diluted to a total volume of 200 mL each to obtain pH values of 8, 7, and 6, respectively. Similarly for citrate-phosphate buffer, 44.6, 39.8, 30.7, and 24.3 mL of 0.2 M citric acid solution were mixed with 5.4, 10.2, 19.3, and 25.7 mL of 0.2 M dibasic sodium phosphate solution, and the resulting solutions were diluted to a total volume of 100 mL each to obtain pH's of 2.5, 3, 4, and 5, respectively. The concentrations of 7-ACA in the aqueous phase and that of the carriers in the organic phases were varied over a wide range in order to assess the concentration effect. An equilibration time of 2 h was provided in each experiment. After attainment of the equilibrium and phase separation, the concentration of 7-ACA and the pH change were determined. 7-ACA concentration was determined in a UV-visible recording spectrophotometer (model UV 160A Shimadzu), which was calibrated at 264 nm. Analysis was done in triplicate, and the reproducibility was within $\pm 1\%$.

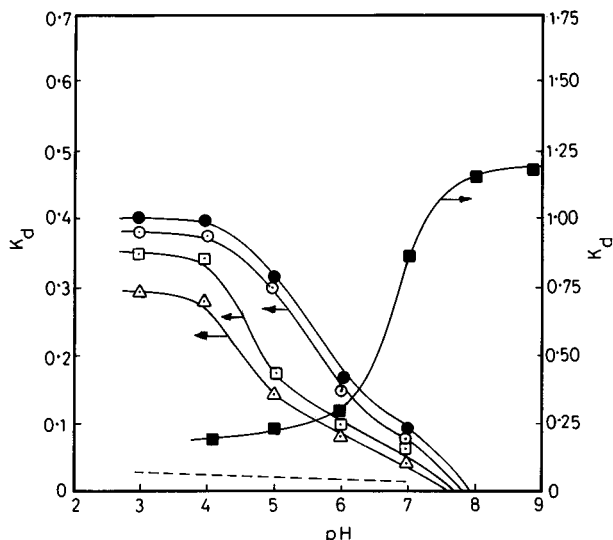


Figure 1. Effect of carrier on the pH dependence distribution coefficient (K_d): $C_A = C_P = 1.0 \times 10^{-3}$ mol/L; (○) dioctylamine; (□) Amberlite LA-1; (●) Amberlite LA-2; (△) tri-*n*-octylamine; (■) Aliquat-336; (---) $C_A = 0$.

Results and Discussion

Effect of Carrier. For discussion on carrier effect and pH dependence of K_d , experimental data generated with butyl acetate were considered, as this being a proton-donating diluent leads in general to stability of the acid-carrier complex owing to the formation of hydrogen bond with the diluent (Bizek et al., 1993).

Primary amines have not been used as they are amenable for formation of stable emulsion and are too soluble in water. The pH dependence of K_d for various carriers is shown in Figure 1 for the pH range of 5–8 where 7-ACA is relatively stable. As shown in the figure, K_d for ion-pair extraction with amine decreases with an increase of pH and ultimately drops to zero at certain values of pH. The most effective amine carrier appears to be Amberlite LA-2, which, however, exhibits weaker and opposite pH dependence of K_d as compared to that achieved with Aliquat-336, which provides a liquid-liquid ion-exchange extraction. Table 2 shows the experimental equilibrium constant (K_P) values for the carriers, and it is apparent that, out of the secondary and tertiary amines studied, trioctylamine exhibits the highest K_P values and stronger pH dependence, implying that smaller pH gradient may be adequate for extraction and reextraction. It may be inferred from Figure 1 that Aliquat-336 should be the preferred choice for the reactive extraction of 7-ACA as both extraction and back-extraction can be performed easily at pH values of 8 and 5, respectively, and it provides finite extraction at both low and high pH unlike the behavior exhibited by the secondary and tertiary amines. For extraction of carboxylic acids, Aliquat-336 was supposed to extract both the dissociated and undissociated forms of the acid (Yang et al., 1991), whereas a tertiary amine, such as Alamine 336, extracts only the undissociated acid. Using any of the amines, larger pH shift will be required for the extraction and reextraction of 7-ACA. The extraction equilibrium behavior of 7-ACA with various carriers at appropriate pH conditions is shown in Figure 2, from which stoichiometry of the complexation reactions can be inferred as will be discussed below in a subsequent section.

Reactive Extraction with Secondary Amine *n*-Butyl Acetate Systems. The variation of K_d with pH of 7-ACA solution for the dioctylamine-*n*-butyl acetate system is

Table 2. Equilibrium Constants for Various Carriers in Butyl Acetate

pH	K_P		
	experimental	calculated	
Dioctylamine			
3	1.82×10^6	1.90×10^6	$K_P/(\text{L}^2 \cdot \text{mol}^{-2})$
4	2.51×10^6	2.62×10^6	
5	2.05×10^6	2.12×10^6	
6	1.63×10^6	1.91×10^6	
7	1.20×10^6	1.11×10^6	
8	1.03×10^6	1.05×10^6	
Amberlite LA1			
3	1.77×10^6	1.92×10^6	$K_P/(\text{L}^2 \cdot \text{mol}^{-2})$
4	2.30×10^6	2.19×10^6	
5	1.73×10^6	1.53×10^6	
6	1.10×10^6	1.19×10^6	
7	1.01×10^6	1.03×10^6	
8	1.002×10^6	1.02×10^6	
Amberlite LA2			
3	1.91×10^6	2.02×10^6	$K_P/(\text{L}^2 \cdot \text{mol}^{-2})$
4	3.36×10^6	3.49×10^6	
5	2.80×10^6	2.53×10^6	
6	1.86×10^6	1.39×10^6	
7	1.66×10^6	1.33×10^6	
8	1.34×10^6	1.67×10^6	
Trioctylamine			
3	2.11×10^6	2.25×10^6	$K_P/(\text{L}^2 \cdot \text{mol}^{-2})$
4	3.98×10^6	3.70×10^6	
5	3.26×10^6	3.12×10^6	
6	2.45×10^6	2.22×10^6	
7	2.15×10^6	1.10×10^6	
8	1.86×10^6	1.70×10^6	
Aliquat 336			
5	6.25×10^{-3}	5.60×10^{-3}	K_P
6	1.40×10^{-2}	1.12×10^{-2}	
7	1.17×10^{-1}	1.20×10^{-1}	
8	2.00×10^{-1}	2.17×10^{-1}	

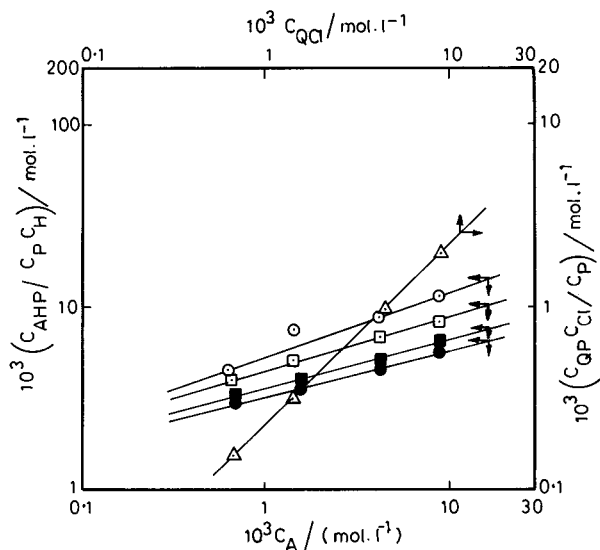


Figure 2. Determination of extraction equilibrium of 7-ACA with different carriers in butyl acetate as the solvent: $C_P = (1-1.5) \times 10^{-3}$ mol·L⁻¹; $C_A = (1-10) \times 10^{-3}$ mol·L⁻¹; pH = 8, (△) Aliquat-336; pH = 4, (○) Amberlite LA-2; (●) Amberlite LA-1; (■) dioctylamine; (□) tri-*n*-octylamine.

shown in Figure 3a, from which the effect of carrier concentration, C_A , is quite apparent. At fixed pH and 7-ACA concentrations, K_d increases for an increase of C_A , the effect being more pronounced at low pH, whereas at high pH K_d tends to attain asymptotic values of similar orders of magnitude. As compared to dioctylamine, Amberlite LA-1 exhibits relatively low pH dependence of K_P

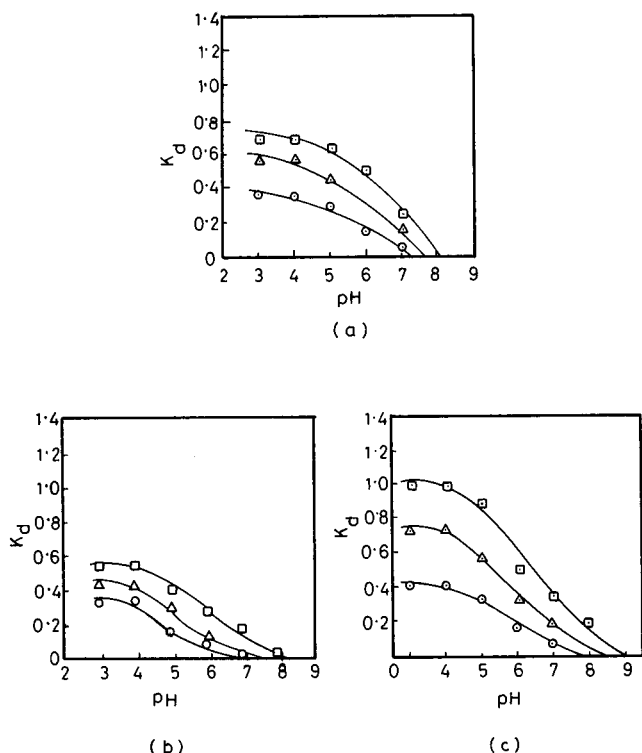
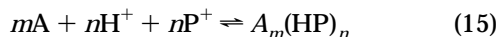


Figure 3. Distribution coefficient (K_d) as a function of pH at different concentrations of secondary amine: (a) dioctylamine, (b) Amberlite LA-1, and (c) Amberlite LA-2: $C_P = 1.0 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (\odot) $C_A = 2 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (Δ) $C_A = 5 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (\square) $C_A = 10 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$.

as shown in Figure 3b. For Amberlite LA-2, an increase in carrier concentration (Figure 3c) increases the pH dependence of K_d and the magnitude of K_d values are higher than those of dioctylamine and Amberlite LA-1 in the pH range of 5 to 8. Thus, the extraction can be carried out at pH 5 and reextraction at pH 8, and the extraction efficiency can be controlled by the concentration of the carrier. Stronger pH dependence of K_d was reported also for the extraction of Penicillin-G by Amberlite LA-2 (Schugler and Degener, 1992). This is advantageous as the extraction and reextraction can be achieved through a shift in the pH value of the aqueous phase. The other advantage is that for a fixed carrier concentration and aqueous-phase pH value, K_d increases with a decrease in the 7-ACA concentration, and thus reactive extraction will be more effective at low concentration such as that encountered in fermentation broth.

In Figures 3 a–c, the smoothed curves are calculated values whereas the experimental points are represented by the symbols. For all the secondary amines, the agreement between measured and calculated profiles of K_d vs pH cannot be considered reasonable possibly because of the deviation from a 1:1 reaction stoichiometry.

For this extraction, a nonstoichiometric reaction model can be suggested as follows



for which the equilibrium constant, K_P , is given by (Reschke and Schugler, 1984)

$$K_P = \frac{(1/n)(C_{P,G} - C_P)}{C_H^n C_P^n \{C_{AG} - (m/n)(C_{PG} + C_P)\}^m} \quad (16)$$

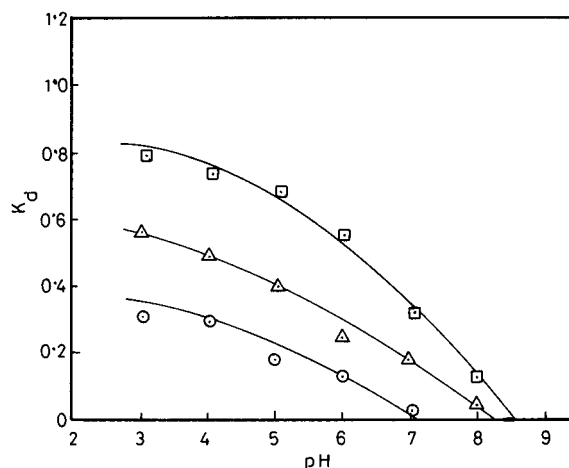


Figure 4. Distribution coefficient (K_d) as a function of the pH at various concentrations of trioctylamine: $C_P = 1 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (\odot) $C_A = 1 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (Δ) $C_A = 5 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (\square) $C_A = 10 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$.

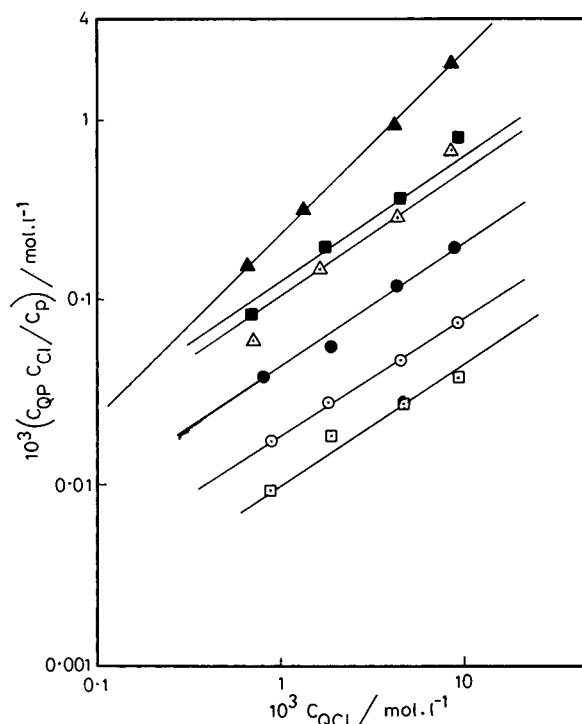


Figure 5. Equilibrium behavior and solvent effect on extraction of 7-ACA with Aliquat-336: $C_A = (1-10) \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; $C_P = 1 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; pH = 8; (\blacktriangle) butyl acetate; (\blacksquare) 1-octanol; (Δ) dichloromethane; (\bullet) chloroform; (\odot) cyclohexane; (\square) benzene.

By using the calculated K_P vs pH curve to the measured curves, a formal complex composition can be established. In this way, the identified complex compositions are $A_{1:4}^-(HP)$ for dioctylamine, $A_{1:5}(HP)$ for Amberlite LA-1, and $A_{1:3}(HP)$ for Amberlite LA-2. The calculated slopes of the lines in Figure 2 are also less than unity for all these three amines implying the validity of a nonstoichiometric model in the reaction.

Reactive Extraction with Tertiary Amine. In this work, trioctylamine was used as the only tertiary amine for the which the results on K_d are shown in Figure 4. In this case also, the agreement between experimental data and the computed profiles based on simple stoichiometric eq 3 appears unsatisfactory. The formal complex composition computed by fitting the data on K_P has been found to

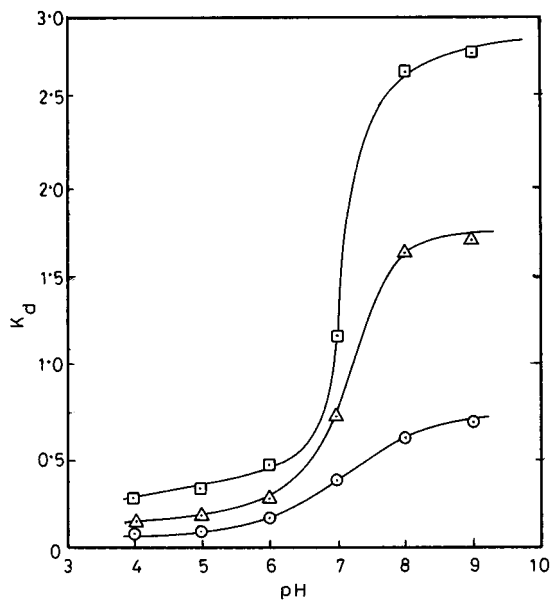


Figure 6. Distribution coefficient (K_d) as a function of the pH of 7-ACA solution at various concentrations of Aliquat-336: $C_P = 1 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (\odot) $C_A = 1 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (Δ) $C_A = 5 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (\square) $C_A = 10 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$.

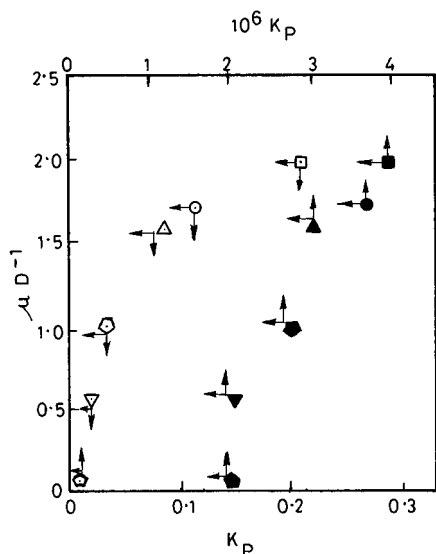


Figure 7. Variation of extraction equilibrium constant with relative permittivity (μD^{-1}) of solvents at pH = 8 for Aliquat-336 and pH = 4 for tri-*n*-octylamine: $C_P = (1-1.5) \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; $C_A = (1-10) \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (\square , \blacksquare) butyl acetate; (\odot , \bullet) 1-octanol; (Δ , \blacktriangle) dichloromethane; (inverted dotted \diamond , inverted \blacklozenge) chloroform; (∇ , \blacktriangledown) cyclohexane; (dotted \diamond , \bullet) benzene (open and closed symbols for Aliquat-336 and tri-*n*-octylamine, respectively).

be (A)_{1:4}(HP). The validity of the nonstoichiometric model is also apparent from the slope (<1) of the corresponding line in Figure 2. The values of K_d and their pH dependence are quite low as compared to those for secondary amine, and thus trioctylamine will be less effective for reactive extraction of 7-ACA.

Reactive Extraction with Aliquat-336. The phenomenological behavior of ion-exchange extraction with Aliquat-336 is different from that of ion-pair extraction with amines. A logarithmic plot in $[C_{QP}/C_{Cl}]$ vs C_{QCl} is shown in Figure 7 as well as in Figure 5 from which the slope of the lines is calculated to be 1, implying that 7-ACA anion complexes with Aliquat-336 in a 1:1 ratio. The variations of K_d with aqueous-phase pH are shown in Figure 6, which

Table 3. Equilibrium Constants (K_P) for Extraction of 7-ACA in Different Solvents^a

solvent	$10^2 K_P$ (Aliquat-336)	$10^6 K_P$ (tri- octylamine)/ $\text{L}^2\cdot\text{mol}^{-2}$	relative permittivity μD^{-1}
butyl acetate	20.00	3.98	1.98
1-octanol	11.00	3.7	1.71
dichloromethane	7.05	3.01	1.6
chloroform	3.7	2.94	1.01
cyclohexane	1.71	2.09	0.55
benzene	1.11	1.75	0.0

^a $C_P = 1 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$, and $C_A = (1-10) \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$.

shows also the effect of carrier concentration. An increase of pH and carrier concentration increases K_d , the pH effect being attributable to the large fraction of dissociated 7-ACA anion at high pH values. Furthermore, the pH dependence of K_d is appreciably higher than that obtained with any of the amines within the pH range of interest. Thus, the extraction can be controlled by properly maintaining the pH value of the 7-ACA solution and the carrier concentration in the organic phase. The measured and calculated K_d values agree fairly well at low carrier concentrations, but deviation seems to occur at higher carrier concentration. The curves were calculated with a predetermined K_P value of 1.65 under the studied experimental conditions. This deviation may be attributed to the coextraction of buffer anion, an effect being inferred also from the observed pH shift of buffered 7-ACA solution. Indeed, the coextraction of anions such as OH^- , CO_3^{2-} , SO_4^{2-} , and PO_4^{3-} by Aliquat-336 was found to be comparable to that of amino acid extraction (Hano et al., 1990; Haensel et al., 1986) at the pH under at which the amino acids exist in the anionic form.

Solvent Effect. Solvent effect was studied using *n*-butyl acetate, *n*-octanol, dichloromethane, cyclohexane, chloroform, and benzene with Aliquat-336 and tri-*n*-octylamine at pH 8 and pH 4, respectively. The observation of our study on solvent effect is dissimilar to that obtained for extraction of organic acid using tri-*n*-octylamine (Puttemans et al., 1985), in which case the efficiency of the solvent was found to be in the order: dichloromethane, pentanol, chloroform, methyl isobutyl > butyl acetate > hexane. We have attempted to correlate the K_P values with solvent relative permittivity (μD^{-1}), where μ and D are the dipole moment and debye unit, respectively, and the relationship can be understood from Table 3 and Figure 7. It appears that for both ion-exchange and ion-pair extractions, the values of K_P increase with increase of dipole moment implying that extraction probably occurs via solvation of the complex based on dipole-dipole interaction. Similar solvent effect was observed for amine extraction of citric acid (Bizek et al., 1993).

Loading Effect of Carriers. Loading of the extractant, Z , is defined as the ratio of the total concentration of acid, 7-ACA (all forms), in the organic phase to the total concentration of carrier (all forms) in the organic phase, at equilibrium. Thus for amines

$$Z = \frac{C_{P,\text{org}}}{C_{A,\text{org}}} = \frac{C_{\text{HP,org}}}{C_{A,\text{org}}} \quad (17)$$

and for Aliquat-336

$$Z = \frac{C_{P,\text{org}}}{C_{\text{QCl,org}}} = \frac{C_{\text{QP,org}}}{C_{\text{QCl,org}}} \quad (18)$$

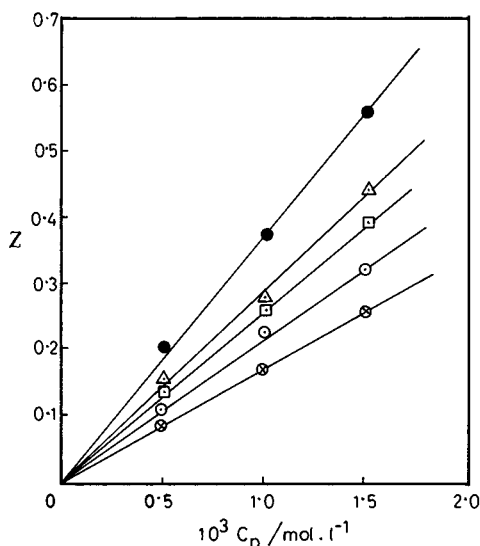


Figure 8. Loading effect for reactive extraction of 7-ACA. pH = 4 for secondary and tertiary amines and pH = 8 for Aliquat-336. $C_A = 2 \times 10^{-3} \text{ mol}\cdot\text{L}^{-1}$; (○) Amberlite LA-1; (△) Amberlite LA-2; (□) dioctylamine; (⊙) Tri-*n*-octylamine; (●) Aliquat-336.

Table 4. Decomposition Rate of 7-ACA in Aqueous Solution with Solvent and/or Carrier

pH	carrier and/or solvent ^a	k/h^{-1}	decomposition % in 10 h
4		1.00×10^{-2} ^a	
5		0.90×10^{-2} ^a	
6		0.90×10^{-2} ^a	
8		0.90×10^{-2} ^a	
9		1.00×10^{-2}	
5	butyl acetate	0.90×10^{-2}	3.21
5	Aliquat-336	0.95×10^{-2}	3.21
6	-do-	1.28×10^{-2}	3.28
7	-do-	1.21×10^{-2}	4.20
8	-do-	1.37×10^{-2}	4.80
5	Amberlite LA-2	1.20×10^{-2}	3.25
6	-do-	1.37×10^{-2}	4.80
7	-do-	1.40×10^{-2}	5.00

^a Carrier and/or solvent with which the solution is saturated.

^b Data from Yamane et al. (1976).

The loading curve is a plot of Z versus $C_{P,org}$ as shown in Figure 8. For all the amines and Aliquat-336 studied in this work, no overloading ($Z < 1$) was observed, implying that complexes with not more than one acid molecule per amine molecule have been formed. One 7-ACA molecule may complex with more than one amine molecule. It may be presumed that the systems are characterized by only one amine per complex, which is further evidenced by the observation of no effect of total amine concentration on the loading. These results also indicate that the systems do not exhibit aggregation even at the pH that provides a higher degree of extraction.

Stability of 7-ACA. The stability of 7-ACA in aqueous solution is affected by specific H^+ ion catalyzed, spontaneous, and specific hydroxide ion catalyzed degradation. The spontaneous degradation rate could be influenced by the dissociation of the ammonium group. However, the stability is not known under reactive extraction conditions. The effect of carrier and *n*-butyl acetate on the 7-ACA stability was studied by first equilibration of 7-ACA solution with equimolar ($10 \times 10^{-3} \text{ mol/L}$) carrier in *n*-butyl acetate and then mixing the organic solution with fresh 7-ACA solution at two levels of pH (5 and 8) for an extended period of time, during which 7-ACA concentrations were monitored peri-

odically. The first-order decomposition rate constant, k , given by

$$\ln(C_P/C_{P,0}) = -kt \quad (19)$$

was evaluated from the experimental profiles of $C_P/C_{P,0}$ vs time, t , where $C_{P,0}$ is the initial concentration of 7-ACA. The results are shown in Table 4 only for Amberlite LA-2 and Aliquat-336. The values of decomposition rate constants within the pH range of interest remain essentially constant at 0.9×10^{-2} for 7-ACA solution alone. The solvent as such appears to have no effect on the stability. However, the presence of carrier diminishes the stability of 7-ACA particularly at high pH, and the value of the rate constant is increased by a factor of 1.5 at pH 8 over that obtained without using a carrier. Aliquat-336 is, however, better than Amberlite LA-2 from stability consideration.

Conclusions

Secondary, tertiary, and quaternary amines can be used as the carriers for reactive extraction of 7-ACA in the pH range of 5 to 8 in which 7-ACA is relatively stable. In case of extraction with secondary and tertiary amines, the distribution coefficient, K_d , decreases with an increase of pH of 7-ACA solution. An opposite but more pronounced pH dependence of K_d is obtained for extraction with Aliquat-336, which also provides values of K_d higher than those of secondary and tertiary amines in the above pH range. Unlike the secondary and tertiary amines, Aliquat-336 complexes with 7-ACA anion in a simple 1:1 stoichiometric ratio. Stability of 7-ACA should be considered while performing reactive extraction with the carriers.

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