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Extraction Equilibria of Butyric Acid with Organic Solvents

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ABSTRACT

Fourteen solvents (five with a tertiary amine and different diluents, four C8–C18 alcohols, dibutylether, two hydrocarbons, and two vegetable oils) have been tested for the extraction of butyric acid. The highest distribution coefficient for butyric acid is shown by solvents with tertiary amines. A ternary solvent with amine extractant, *n*-alkanes as diluent, and higher alcohol as modifier can be advantageous in this procedure. Amines enable the extraction of acid at a pH above the pK_a value up to about pH 5.6. With an increase of the molecular weight of alcohol, the value of the distribution coefficient decreases. Its value for pure alcohols is independent of the concentration of acid in the aqueous phase. Equilibrium data suggest that the stoichiometry of the acid–alcohol complex is 2:1, and only undissociated acid is extracted.

INTRODUCTION

Solvent or reactive extraction techniques are nowadays of more and more interest. This results from their possible applications not only in the chemical industry but also in the biotechnological production of some substances (1–6). The production of organic acids such as citric (2, 3), lactic (4), and butyric (5) acids as well as penicilline (1) can be given as examples. Extraction can be employed not only in downstream separations but also integrated with fermentations. An advantage of on-line extraction in fermentation technology is the removal of products which often have an inhibitory effect, thereby permitting a continuous process.

Extraction of some carboxylic acids has been studied using hydrocarbon solvents, phosphorus-bonded oxygen donor extractants, and aliphatic amine extractants as presented in the review of Kertes and King (7). The authors described extraction characteristics of selected extractants. Hydrocarbon solvents are usually used as diluents of phosphorus or amine extractants (3, 8, 14–16). Hano et al. (8) described the reactive extraction of some carboxylic acids with the solvating extractant tri-*n*-octylphosphine oxide (TOPO) in several diluents. It was found that for monocarboxilic acids, the molar ratio of acid to TOPO is 1:1. Tamada and King (22, 23) investigated the extraction of carboxylic acids with amine extractants. Their results show that the molar ratio monocarboxylic acid:amine is m:1, where $m = 1, 2, 3$, or 4, depending on the acid (22–26).

There are also works available which evaluate a series of solvents, especially for one or two carboxylic acids. The distribution coefficients and solvation numbers were estimated in these works. The most suitable reactive extractants seem to be tri-*n*-octylphosphine oxide or tertiary (*n*-octyl, *n*-decyl) amines. Among diluents, alkanes or alcohols are mostly used. These data refer to citric (3), lactic (14, 15), propionic, or acetic (16) acids.

A detailed evaluation of solvents for butyric acid extraction is not available in literature. Only a few distribution coefficient values are available. For example, Davison and Thompson (17) determined that the distribution coefficient of butyric acid and butanol for oleyl alcohol is nearly the same and is about 3. A low value of the distribution coefficient, 0.56, was determined for vegetable oils (21). Hano et al. (8) determined the values of the extraction constant for several acids. For butyric acid it was 51.9 L/mol.

Our main interest focused on butyric acid because of its wide use in industry. This acid is employed in the diary or food industries to increase the fragrance of beverages or foodstuffs (9, 10), in the pharmaceutical industry, and as a raw material for the production of biodegradable polymers based on β-hydroxybutyrate. This makes the biotechnological production of butyric acid interesting.

But there is a problem connected with the unstability of acidogenesis during the fermentation process and with the low final concentration of product because of an inhibitory effect of the undissociated acid (11–13).

This problem can be solved by in-situ (on-line) solvent extraction or pertraction through liquid membranes of undissociated butyric acid from the fermentation broth. In this way it is possible to control the pH in the fermentor and the level of undissociated butyric acid which is inhibitory for the fermentation process. Moreover, the desirable product in the final solution can be isolated and concentrated. In this respect, evaluation of extractive reagents and better understanding of the extraction process is necessary. Such evaluation has been made for lactic (14, 15), citric (3), acetic, and propionic (16) acids, and also for butanol and acetone production (17, 19). A negative effect of some solvents for many types of microorganisms (18–20, 27) has been observed.

The aim of this presented work was the screening of solvents for the extraction of butyric acid and examination of the most prospective solvents in more detail.

THEORY

Extraction of weak organic acids from the aqueous phase into the organic phase can occur as a result of physical and/or chemical interactions in the system. Partition of undissociated acid molecules (HA) can be formally described by the reaction

$$\mathrm{HA} \Leftrightarrow \overline{\mathrm{HA}} \tag{1}$$

where the overbar denotes the organic phase species. When the organic phase–solvent contains solvating or an other complexing extractant (S), the complex of organic acid is formed according to the overall reaction

$$m\mathrm{HA} + n\overline{\mathrm{S}} \Leftrightarrow \overline{(\mathrm{HA})_m\mathrm{S}_n} \tag{2}$$

with the related apparent equilibrium–extraction constant

$$K_{mn} = \frac{[\overline{\mathrm{HA}_m\mathrm{S}_n}]}{[\mathrm{HA}]^m[\overline{\mathrm{S}}]^n} \tag{3}$$

where brackets express concentration in molar units. In the case where there is a single extractant molecule per complex molecule (m, 1), stoichiometry as it is reported for monocarboxylic acids (8, 23), Eq. (3), can be written as

$$K_{m1} = \frac{[\overline{\mathrm{HA}_m\mathrm{S}}]}{[\mathrm{HA}]^m[\overline{\mathrm{S}}]} \tag{4}$$

In a two-phase system, other chemical reactions can proceed. This has to be taken into account, especially dissociation of the acid in the aqueous phase:

$$HA \Leftrightarrow H^+ + A^- \tag{5}$$

$$K_a = \frac{[H^+][A^-]}{[HA]} \tag{6}$$

and dimerization of acid in the organic phase:

$$2\overline{HA} \Leftrightarrow \overline{(HA)_2} \tag{7}$$

$$K_d = \frac{[\overline{(HA)_2}]}{[\overline{HA}]^2} \tag{8}$$

If a water-insoluble alcohol is present in the solvent, the distribution coefficient of monocarboxylic acids is higher in compared to pure hydrocarbon diluents. This is a consequence of a strong donor–acceptor interaction. Thus the extracted acid will dimerize only to a small extent, or not at all (7). Hence, dimerization of butyric acid in alcohols can be neglected.

The distribution coefficient is defined as the ratio of total acid concentration in all possible forms in the aqueous and organic phases:

$$D = c_S^*/c_F^* \tag{9}$$

According to Eq. (2), ionization of acid strongly depends on pH_F in the aqueous phase. This equation can be transformed into a form of the concentration ratio of undissociated acid to the total acid concentration in the aqueous phase:

$$\frac{[HA]}{c_F} = \frac{[H^+]}{K_a + [H^+]} = \{1 + 10^{(pH - pK_a)}\}^{-1} \tag{10}$$

For butyric acid, $pK_a = 4.63$ at 25°C (8). From Eq. (10) it follows that the dissociation of butyric acid is negligible at pH_F lower than 2.7. Undissociated acid concentration under this pH is more than 99% of total acid concentration.

If pure hydrocarbons or alcohols are used as the organic phase, only butyric acid in undissociated form is extracted (7, 24). An amine extractant forms an ion pair or a hydrogen bond with the first acid, and the second acid forms a hydrogen bond with the carboxylate of the first acid (23). Solvation of the complex by the diluent is an important factor in the extraction of acids. Amine complexes of acids have a low solubility in nonpolar diluents, and a second organic phase can be formed.

EXPERIMENTAL

A mixture of trialkylamines with *n*-octyl and *n*-decyl alkyl groups, with a mean molecular weight of 395 and a density of 0.81 at 20°C, was used as a reactive extractant (Hostarex A327, Hoechst, D). As solvents or modifiers, *n*-octanol (Lachema, CZ), isodecanol, and isotridecanol (technical products, UNIPAR, NL) were used. Further solvents tested were oleyl alcohol (Merck, D), sunflower oil (Palma-Tumis, SK), rape seed oil (Palma-Tumis, SK), di-*n*-butylether (Lachema, CZ), and toluene (Lachema, CZ). As a diluent or solvent, *n*-alkanes (narrow dodecane fraction with C10–C13 *n*-alkanes with a density of 0.764 $g \cdot cm^{-3}$ at 25°C, Slovnaft, SK) were used. Ammonia (Mikrochem, SK) and HCl (Lachema, CZ) had concentrations of 26 and 36 wt% respectively. Butyric acid (Reachim, Russia) and propionic acid (Lachema, CZ) were of analytical grade.

Experiments were performed in double-walled glass funnels with an internal volume of 250 mL. The minimal volume of organic or aqueous phases was 25 mL. For measurements of distribution coefficients, the initial volume of both phases was 25 mL and the initial pH of the aqueous phase was 2.4. In experiments where the concentration dependence of the distribution coefficient was measured, the volume of the aqueous phase was changed while both the volume of the organic phase and the initial pH of the aqueous phase were always the same (25 mL and 2.4, respectively). In the case of determination of the influence of pH on the distribution coefficient, the initial volume of both phases was 25 mL and the initial pH was adjusted to a chosen value with the aid of an NH_3 solution. The initial concentration of butyric acid was in most cases about 1 mol/L, with the exception of the last measurements with pure alcohols where the concentration dependence of the distribution coefficient was measured (initial concentration was 2.45 mol/L).

The duration of equilibration in shaking funnels was 5 hours and the temperature was kept at 30°C. Then the phases were separated after 5–12 hours of settling at 30°C. The pH of the aqueous phases was measured, and the phases were stored at 4°C for analytical assays. The organic phases were stripped with an aqueous NaOH solution with an excess of alkali. After 10 minutes of shaking the phases were separated and the aqueous phase was analyzed.

The concentration of butyric acid in aqueous solutions was determined by gas chromatography (GC). Analyses were performed after appropriately acidifying of samples ($pH < 2.5$) with HCl and adding of an exact amount of propionic acid as an internal standard on the gas chromatograph Chrom 5 (Laboratory Instruments, CZ). A packed column with Porapak Q (length 1.5 m and internal diameter 3 mm) was used. As the carrier gas, N_2 with a pressure of 160 kPa was used. The flow rate of H_2 was 26 mL/min. The temperature of the FID detector and injection space was 240°C, and the temperature of the column was 220°C.

The value of the distribution coefficient was calculated from Eq. (9). Values of c_F^* were obtained directly by GC analysis. Acid concentration in the organic phase was obtained after stripping the organic phase with a NaOH solution and GC analysis of the aqueous phase. c_S^* was calculated by the following equation:

$$c_S^* = \frac{c_R V_R}{V_{Ss}} \tag{11}$$

based on the mass balance of acid, where the volume of solution after stripping was different from its initial volume due to the transfer of butyric acid (which is a liquid). Volumes of phases after extraction were calculated from equations based on the experimentally proven assumption of additivity of volumes as follows:

$$V_R = \frac{V_{R0}\rho_b}{(\rho_b - c_R M_w)} \tag{12}$$

$$V_F^* = \frac{V_{F0}(\rho_b - c_{F0} M_w)}{(\rho_b - c_F^* M_w)} \tag{13}$$

$$V_S^* = V_{S0} + (V_{F0} - V_F^*) \tag{14}$$

The mass balance was checked by the mass balance ratio, defined as

$$\Delta = \frac{c_F^* V_F^* + c_S^* V_S^*}{V_{F0} c_{F0}} \tag{15}$$

In the ideal case the value of Δ should be 1.

RESULTS AND DISCUSSION

Screening of Solvents

Fourteen solvents have been tested for extraction of butyric acid. They are ranked in Table 1 according to the distribution coefficient value. Butyric acid is quantitatively stripped from the solvent phase into a NaOH solution with a stoichiometric excess of alkali. This is documented with the mass balance ratio, Δ, whose value was close to 1 as shown in Table 1. For most of the data listed in Table 1, the pH of the aqueous phase in equilibrium was lower than 2.7 when the dissociation of butyric acid was negligible.

Five solvents with tertiary amine Hostarex A327 exhibit the highest distribution coefficient values. The distribution coefficient value decreases with decreasing amine concentration and increasing molecular weight of alcohol diluent, (see Table 1). For pure alcohols, the value of D is lower. Di-*n*-butylether has a distribution coefficient similar to that of oleyl alcohol. Somehow, D is smaller for toluene. The distribution

TABLE 1
Distribution Coefficient of Butyric Acid for Solvents Tested. pH_F^* was Lower Than 2.8 in Most Cases. Kinematic Viscosity of Some Solvents at 25°C Is Presented

Solvent	*D*	c_F^* (mol·L^{-1})	Δ	$\nu^{25} \times 10^6$ m^2·s^{-1}
Hostarex A327 (30 wt%) in isodecanol	13.40	0.070	1.04	16.8
Hostarex A327 (20 wt%) in isodecanol	9.57	0.096	1.04	
Hostarex A327 (20 wt%), isodecanol (30 wt%) in n-alkanes	7.90	0.100	1.03	3.9
Hostarex A327 (20 wt%) in isotridecanol	6.57	0.100	0.96	
Hostarex A327 (20 wt%) in oleyl alcohol	6.40	0.133	0.99	
n-Octanol	6.31	0.137	1.02	9.2
Isodecanol	5.60	0.156	1.04	14.7
Isotridecanol	4.82	0.170	1.04	30.8
Di-*n*-butylether	2.96	0.259	1.03	
Oleyl alcohol	2.85	0.259	0.99	27.2
Toluene	2.40	0.293	0.98	
Rape seed oil	1.02	0.510	0.99	
Sunflower oil	0.99	0.523	1.00	
n-Alkanes	0.71	0.605	0.98	1.7

coefficient of butyric acid for vegetable oils has a value of about 1, and for *n*-alkanes it reaches the lowest value of 0.71.

Besides extraction properties, biocompatibility, among others, is also important in biotechnological applications. Aromatic hydrocarbons, ethers, and also *n*-octanol are toxic for microorganisms (18–20). Further testing of the biocompatibility of solvents with production strains is very important for their application in biotechnology.

Based on extraction properties and medium or low toxicity, higher alcohols and solvents with tertiary amines were selected for more detailed study.

Alcohols

The distribution coefficient of butyric acid decreases with increasing molecular weight of alcohols. A plot of the distribution coefficient vs the number of carbon atoms in the molecule of alcohols is linear, as shown

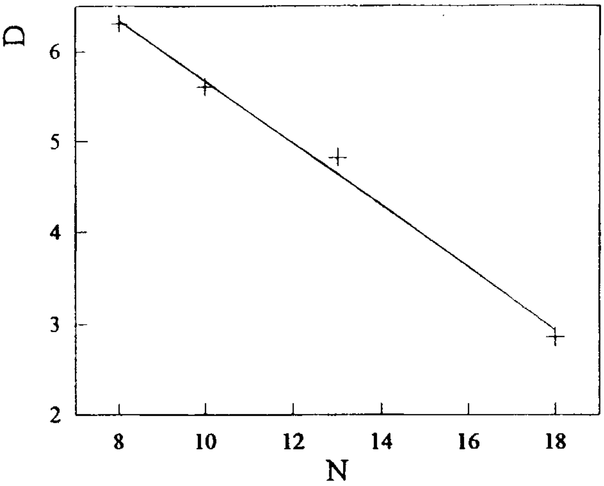

FIG. 1 Distribution coefficient of butyric acid between water and alcohols vs number of carbons in alcohol molecule.

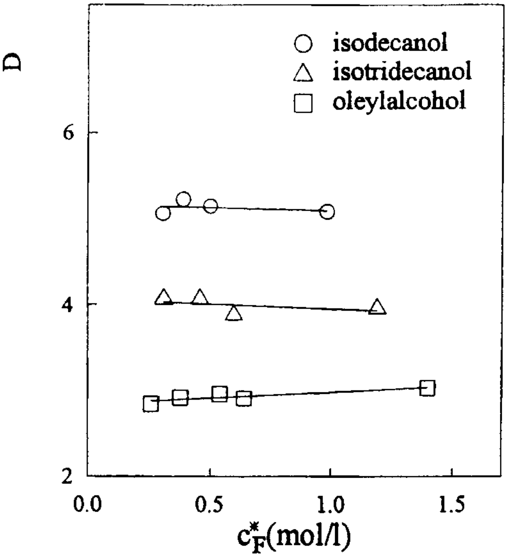

FIG. 2 Distribution coefficient of butyric acid between water and alcohols vs equilibrium concentration of butyric acid in the aqueous phase.

in Fig. 1. The distribution coefficient values for alcohols are practically independent of the acid concentration in the interval tested (Fig. 2).

Experimental data for solvent extraction of butyric acid were analyzed using the relation

$$\log \frac{[\overline{HA_mS}]}{[\overline{S}]} = \log K_{m1} + \log[HB]^m \tag{16}$$

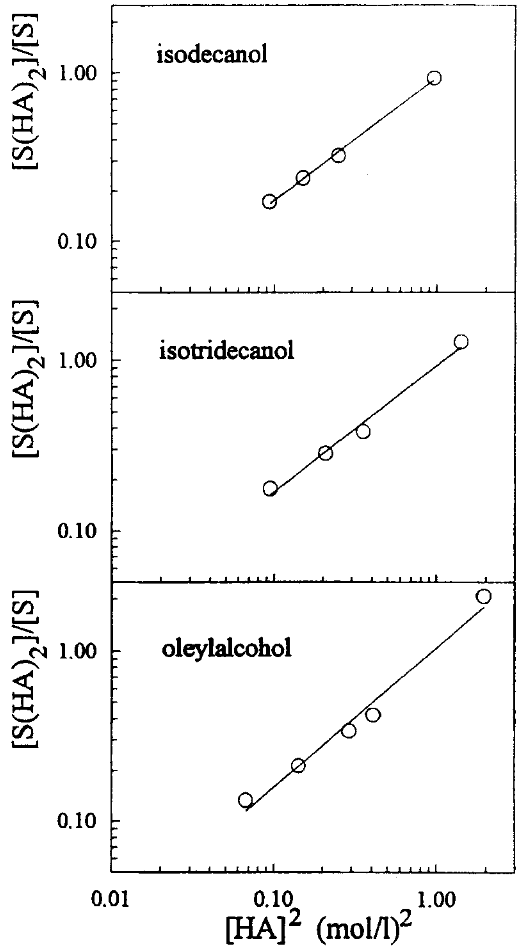

FIG. 3 Extraction of butyric acid with alcohols. Plots based on Eq. (9) for $m = 2$. Extraction constants are given in Table 2.

TABLE 2
Extraction Constants of Butyric Acid for Higher Alcohols According to Eq. (4) and Acid-to-Alcohol Stoichiometry 2:1

Solvent	K_{21} ($L^2 \cdot mol^{-2}$)	r
Isodecanol	0.842	1.00
Isotridecanol	0.835	0.99
Oleyl alcohol	1.084	0.98

which was derived from Eq. (4). The results suggest that the stoichiometry of acid to alcohol in the complex is 2:1 ($m = 2$), as shown in Fig. 3. Corresponding values of the extraction constant are given in Table 2.

Figure 4 reveals that the distribution coefficient values in isotridecanol and oleyl alcohol decrease with increasing pH of the aqueous phase. This supports the assumption that only undissociated acid molecules are extracted by these solvating extractants.

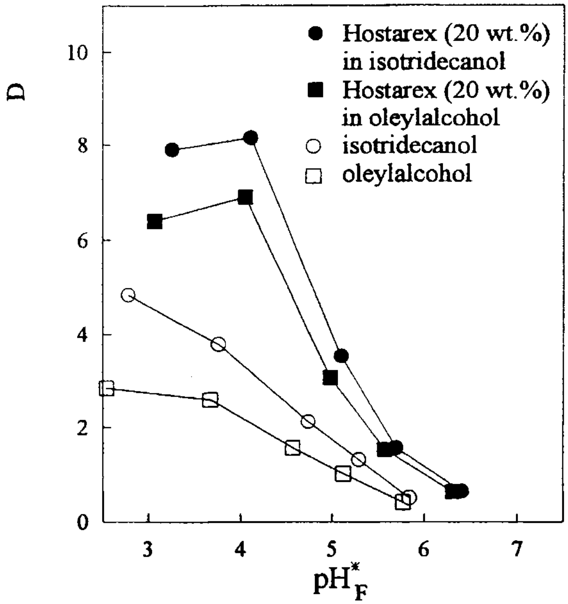

FIG. 4 Distribution coefficient of butyric acid between water and various solvents vs equilibrium pH of the aqueous phase. C_{F0} = 1 mol/L.

The kinematic viscosity of higher alcohols is relatively great compared with that of hydrocarbons (*n*-alkanes); see Table 1. This can be disadvantageous in terms of the mass-transfer rate.

Solvents with Tertiary Amines

The value of the distribution coefficient of butyric acid for solvents with tertiary amines (Hostarex A327) sharply decreases with increasing concentration of acid in aqueous solution; see Fig. 5. Also, *D* has attractive values at higher concentrations (above 4 at pH below 2.8).

With an increase of pH of the aqueous phase above 4, the distribution coefficient rapidly decreases (Fig. 4). At a pH of about 5.5, which is a realistic value for fermentation, butyric acid is still extracted with a *D* of about 1.5. This value is acceptable for the separation of acid by solvent extraction or especially by pertraction through liquid membranes.

With increasing molecular weight of alcohol diluent, the distribution coefficient of butyric acid also decreases, as is observed for pure alcohols (Fig. 5). Table 1 shows that these solvents are relatively viscose. A ternary

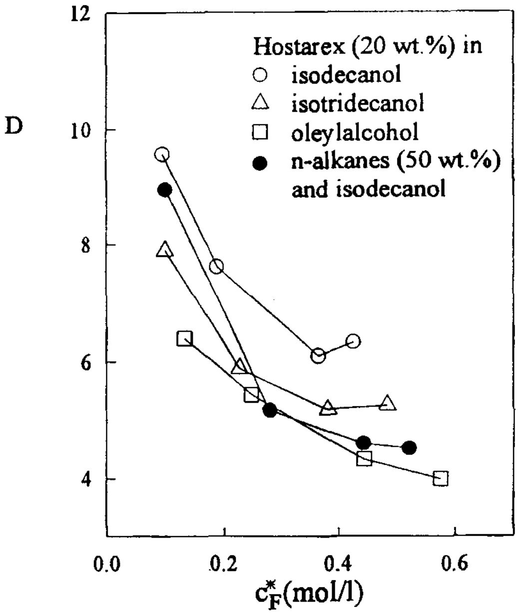

FIG. 5 Distribution coefficient of butyric acid for solvents with tertiary amines Hostarex A327 vs equilibrium concentration of butyric acid in the aqueous phase. pH_{F0} = 2.45 and equilibrium pH was below 2.8.

solvent with *n*-alkane diluent has a much lower viscosity in comparison with a binary solvent (Table 1), but also a slightly smaller distribution coefficient, as follows from Fig. 5.

CONCLUSIONS

Based on extractive properties, the best solvents for butyric acid from the series of 14 solvents tested are those with tertiary amines (Hostarex A327). The value of the distribution coefficient of acid sharply decreases with increasing pH and acid concentration. Tertiary amine extractants can effectively extract butyric acid at low pH (up to about 5.6). A ternary solvent with amine in an *n*-alkane diluent and with a higher alcohol modifier can be advantageous.

The distribution coefficient of butyric acid decreases with the number of carbons in the alcohol molecule and with increasing pH. This value, however, is independent of the concentration of acid. Stoichiometry of the acid–alcohol complex is 2:1, and only undissociated acid molecules are extracted.

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NOTATION

c	overall concentration of solute (butyric acid) (mol/L)
D	distribution coefficient (Eq. 9) (—)
K_a	dissociation constant of acid (—)
K_d	dimerization constant, Eq. (8) (L/mol)
K_{mn}	extraction constant, Eq. (3) $(\mathrm{L/mol})^{m+n-1}$
K_{m1}	extraction constant, Eq. (4) $(\mathrm{L/mol})^{m}$
m,n	number of molecules of acid and extractant per one molecule of complex (—)
M_w	molar weight of butyric acid (g/mol)
N	number of carbon atoms in chain (–)
r	correlation coefficient (–)
V	volume (L)
[ ]	molar concentration of species given in brackets (mol/L)

Δ	mass balance ratio (Eq. 15) (—)
ν	kinematic viscosity ($m^2 \cdot s^{-1}$)
ρ_b	density of butyric acid (g/L)

Subscripts and Superscripts

F	aqueous phase
R	stripping solution
s	sample
S	organic (solvent) phase
0	initial
*	equilibrium

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