392. *The Absorption of Some Organic Bases by Carboxylic Acid Ion-exchange Resins. Part I. Equilibrium Studies.*

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Quantitative studies of the equilibrium distributions of a number of organic bases between their solutions (aqueous and alcoholic) and weak acid ion-exchange resins have been made. The volume changes of the resin caused by changing the solvent and by absorption of bases have also been observed.

The distribution results have been presented, after calculation of molar concentrations per unit volume of the bases in both resin and solution phases. Mathematical relations between these equilibirum concentrations have been developed.

An analogy between the logarithmic form of the equilibrium distribution equation which fits most of the results, and the dose-response equation of quantitative biology, is indicated.

WORK reported previously (*J.*, 1950, 2915) has been extended by the study of the absorption of a number of organic bases from aqueous, water–ethanol, or ethanolic solutions by various carboxylic acid ion-exchange resins. We now describe the results of studies of the equilibrium distributions of some bases between their solutions and the resins. Observations have also been made of the swelling of the resins caused by saturating them with the different bases.

The word absorption has been used in this paper to describe the uptake of bases by the resin, since this involves the transfer of material from bulk solution to bulk resin phase. We suggest that the term adsorption should be reserved to describe the uptake of macromolecular materials by highly cross-linked resins, a process which occurs mainly at the resin particle–solution interface.

Since the above paper was published, several accounts of further work with the weak acid type of resin have appeared. For example, Talboys (*Nature*, 1950, **166**, 1077) has reported the use of the sodium salt of the resin for purifying a bacterial pectinase, and Lee Huyck (*Amer. J. Pharm.*, 1950, **122**, 228) has reported that Amberlite IRC50 is a good absorbing medium for a base such as ephedrine. Weiss (*Nature*, 1950, **166**, 66) has suggested that weak acid resins can be used in the dissociated, *e.g.*, sodium, form as an absorbing material for organic anions.

EXPERIMENTAL

Except where otherwise stated all the work has been carried out with a large, uniform batch of Amberlite IRC50. Resin samples were dried at 110° to constant weight and weighed as this dry, hydrogen form; heating to this temperature has been shown to have no measurable effect on the absorption properties of the resin. Before use, the weighed dried sample was saturated overnight with the appropriate solvent, containing some hydrochloric acid to ensure complete conversion into the hydrogen form. It was then washed thoroughly with pure solvent, surface-dried by being spread on filter-paper, and put into the solution of base under investigation. In some cases, before being washed, the resin was cycled between ammonium and hydrogen forms several times; this variation was also found to have no observable effect on absorption properties.

Methacrylic acid resins were prepared by copolymerising redistilled methacrylic acid and divinylbenzene, as described by Topp and Pepper (*J.*, 1949, 3299). These resins were weighed as the 110°-dried hydrogen form and saturated with solvent before use, as described above.

Both Amberlite IRC50 and the methacrylic acid resins showed the typical sodium hydroxide titration curves of weak acid resins (cf. Topp and Pepper, *loc. cit.*).

The following organic bases were obtained in the purest form available and were subsequently dried and fractionally distilled in an all-glass apparatus, precautions being taken to prevent contamination with moisture or carbon dioxide; appropriate fractions were collected, having the following properties : piperidine, d_4^{20} 0·8608, n_D^{20} 1·4532 ; benzylamine, d_4^{19} 0·9822, n_D^{20} 1·5400, b. p. 183·5° ; *n*-butylamine, d_4^{20} 0·7405, n_D^{20} 1·4068, b. p. 78° ; pyridine, d_4^{20} 0·9820, n_D^{20} 1·5092, b. p. 115° ; aniline, d_4^{20} 1·0220, n_D^{20} 1·5862, b. p. 184° ; dimethylaniline, d_4^{20} 0·9560, n_D^{20} 1·5582, b. p. 193·5°.

Ephedrine and (+)-ψ-ephedrine were purified by recrystallisation from ether, giving ephedrine, m. p. 38·0°, and (+)-ψ-ephedrine, m. p. 116·5°, $[\alpha]_{20}^{D}$ +51·0° (in ethanol). Quinine was purified as already described (*J.*, 1950, 2915). Nicotine was fractionally distilled under reduced pressure in the presence of nitrogen, and had d_4^{20} 1·0096, n_D^{20} 1·5278, $[\alpha]_D^{20}$ −168°.

n-Heptylamine and α- and β-naphthylamine were not further purified. The materials used had the following properties : *n*-heptylamine, $n_D^{26·5}$ 1·4195, d_4^{20} 0·7768 ; α-naphthylamine, m. p. 49·5° ; β-naphthylamine, m. p. 112·5°. Caffeine, recrystallised from hot water and then heated to constant weight at 110°, had m. p. 235·5°. Dodecylamine was fractionally frozen until of m. p. 27·5°.

Densities were determined by means of a 10-ml. pycnometer, appropriate buoyancy corrections being applied to the weighings ; refractive indices were measured by means of an Abbé refractometer.

The solvents used were freshly distilled water, 50% (by vol.) water–ethanol mixtures, and "absolute" ethanol (referred to subsequently as ethanol), containing 0·5% of water.

Equilibrium Studies.—These were carried out by making up solutions of the various bases in the appropriate solvents by conventional volumetric techniques, and adding to these known amounts of resin saturated with the solvent (all resin weights referring to the 110°-dried hydrogen form) and surface-dried, as already described. Well-stoppered flasks containing resin and base solution were set aside, with intermittent shaking, in a room whose temperature was controlled to 20°±2°, until no further changes in solution concentration occurred (up to 10—12 days with the weaker bases). Blanks consisting of solutions without resin were kept for similar periods to ensure that no changes of concentration other than those due to absorption of base by the resin occurred. Other blanks consisting of resin and pure solvent were also set aside to ensure that no detectable amounts of material were dissolved out of the resin under the conditions of the experiments.

When the resin–solution mixtures had reached equilibrium, the solutions were analysed for base content. From these and the initial solution concentrations, the amounts of base absorbed by the resin were calculated. In a few cases, a small correction had to be applied to allow for the decrease in solution volume caused by the swelling of the resin during absorption.

Methods of Analysis.—Several different analytical methods were used. Quinine and nicotine were determined polarimetrically in a 10-cm. tube with the D-line from a sodium lamp ; rotation–concentration curves for these bases in the different solvents were prepared. All the other bases were determined by means of a Rayleigh interference refractometer, a 1 cm. cell and white light illumination being used, the vernier readings of this instrument being converted into concentrations from previously prepared reading–concentration curves for each base in each solvent.

In addition to analyses by the above methods, the stronger bases such as piperidine and the ephedrines were determined by volumetric titration with standard acid ; pyridine was determined by means of a photoelectric turbidimeter, after precipitation with phosphotungstic acid ; caffeine was determined by evaporating the solutions to dryness and heating the residues to constant weight at 105°.

Concentrations in the Resin Phase.—In order to present the results in a uniform manner, the equilibrium concentrations of bases have been expressed as moles per litre of total external phase volume in both resin and solution phases. To evaluate concentrations in the resin phase it has been necessary to determine "specific volumes" of the resin in the different solvents used and to measure the swelling of the resin on absorption of the different bases.

Swelling of the Resin.—The saturation swelling of the resin, *i.e.*, the swelling produced by prolonged contact with a concentrated solution of the base, has been determined for all the bases in the solvents used in the equilibrium work. These determinations have been carried out by two methods.

(i) The first was based on direct microscopic observation. A spherical particle of solvent-saturated, hydrogen form of the resin was picked out from a sample and held between optically flat glass plates under the objective of a microscope fitted with a micrometer eyepiece. The microscope was focused so as to give the particle a sharp periphery, and its diameter was measured in two mutually perpendicular directions. During this measurement, the space between the glass plates was filled with solvent. A concentrated solution of base was then allowed to flow round the particle from a reservoir consisting of a tap-funnel connected to a hypodermic needle inserted between the glass plates. When no further change of the particle size occurred, the perpendicular diameters were again measured. The linear swellings measured by this method were found to be completely reversible; *i.e.*, when acid dissolved in the same solvent flowed round a resin particle saturated with base, it regained its original diameter, showing that no slow flattening of the particle between the plates had occurred.

With aqueous solutions of the stronger bases, the particles often ruptured before complete saturation. When this occurred, the technique was reversed; a sample of resin was saturated with the base solution, a spherical particle was selected, and the decrease in mean diameter produced by flow of solvent containing acid around it, for a long time, was measured.

From these results percentage particle diameter increases (all based on the diameter of the hydrogen form in the solvent used) were found and the values were checked by determinations using several different particles. Observations were also made of the effects on the particle diameters of various forms of the resin of changing the solvent from water to ethanol.

Estimates of percentage volume changes were made from the percentage diameter changes by consideration of the fact that in the swelling experiments the particle will be unable to swell freely in one dimension, owing to the presence of the glass plates. In the shrinking experiments it will be able to contract freely from a sphere to a sphere of smaller diameter. The exact shape assumed by the resin particle when it swells between the glass plates is uncertain, and this produces some uncertainty in the conversion of linear into volume swellings.

(ii) The second method used for studying volume changes was by direct determination of the volume of 1 g. (weighed as dry, hydrogen form) of the resin, saturated with various liquids. The resin was removed from the liquid, rapidly surface-dried, and then put into the new volume of equilibrium liquid contained in a micro-burette; the change in burette reading gave a direct measure of the resin volume. Results obtained by this method showed reasonable agreement with those obtained by the microscope method.

Since this work was carried out, Gregor, Held, and Bellin (*Analyt. Chem.*, 1951, **23**, 620) have described various methods of measuring external volumes of ion-exchange resins. Despite the uncertainty concerning the factor for conversion of linear into volume swellings, the direct observation method is probably the soundest, for all methods depending on the removal of resin particles from their liquid environment involve other, and perhaps greater, uncertainties.

The following table shows the mean volume increases (%) of the hydrogen form of Amberlite IRC50 on saturation with various bases, in the solvents indicated.

Base	Water	50% Ethanol	Base	Water	50% Ethanol
Sodium hydroxide	53	—	Nicotine	40	20
Piperidine	51	37	Pyridine	25	10
Ephedrine	49	—	Aniline	7	—
(+)-ψ-Ephedrine	—	35	Caffeine	4	4
Ammonia	49	—			

In absolute ethanol, none of the bases caused swellings greater than 5% by volume. This result is of practical value in column work, since by working in ethanol solutions the jamming of the column caused by large volume changes can be avoided.

The hydrogen form of the resin was found to swell by 38% by volume on change from water to ethanol solvent and this increase was exactly reversed by passing back to water. The " specific volumes " (volumes per g. of the 110°-dried hydrogen form of the resin, IRC50) were found to be: 1·60 ml./g. in water, 2·10 ml./g. in 50% ethanol, and 2·25 ml./g. in ethanol.

Volume changes of the resin saturated with base, on changing from water to ethanol solvent, were of two types. For weak bases such as pyridine and caffeine, an increase of volume occurred as with the hydrogen form. For strong bases, however, such as sodium hydroxide, ammonia, or piperidine, a marked shrinkage on changing to ethanol solvent occurred. These results can be explained by considering that two main swelling mechanisms operate: (i) an effect due to the solvation of the hydrocarbon structure of the resin by organic solvents; (ii) an electrostatic effect due to the mutual repulsions of ionised carboxyl groups held close to one another in the macromolecular resin structure. A third, less important, effect is the swelling caused by the molecular size of the absorbate. The solvation effect causes the swelling of the hydrogen and weak-base forms of the resin, which are only slightly ionised, on changing from water to ethanol solvent. With the ionised strong-base forms of the resin, the electrostatic swelling will be a function of the dielectric constant of the solvent: on changing from water to ethanol this falls considerably and the repulsions between carboxyl groups are reduced, causing a shrinking of the resin which outweighs the solvation swelling.

The degree of cross-linking of methacrylic acid resins very much affects the amount of swelling observed (cf. Pepper, *J. Appl. Chem.*, 1951, **1**, 124; Gregor *et al.*, *loc. cit.*); *e.g.*, the volumes per g. (110°-dry hydrogen form) of various methacrylic acid resins containing divinylbenzene in the ratios 10 : 5 : 2·5 : 1, were found to be 3·5, 3·8, 5·1, and 7·3 ml./g., respectively, in 50% alcohol.

Maximum Exchange in N/4-*Solutions*.—The maximum absorption from N/4-solutions of bases by the resins (hereinafter abbreviated to N/4-absorptions) have been determined by measuring equilibrium absorptions when 100 ml. of N/4-base solution were put into contact with 1 g. of resin. The results are recorded in the following table. Col. 4 shows the N/4-absorptions of the bases per 10 m.-equiv. of carboxyl in the resin, the N/4-absorption for sodium hydroxide being used as a measure of the amount of exchangeable carboxyl present per g. of resin. Comparison of these value with those in col. 3 shows that, on this basis, the values for the two resins are quite similar.

" N/4-*Absorptions* " *of bases by carboxylic acid resins.*

Base	Solvent *	Methacrylic acid resin (with 10% of divinylbenzene)		Amberlite IRC50
		M.-moles/g.	M.-moles/10 m.-equiv. of CO_2H	M.-moles/g.
NaOH	H_2O	9·10	10·00	10·03
Nicotine	H_2O	5·06	5·50	5·60
	H_2O–EtOH	3·70	4·07	4·00
	EtOH	2·80	3·08	3·18
Pyridine	H_2O	3·68	4·04	4·10
	H_2O–EtOH	2·28	2·50	2·50
	EtOH	1·52	1·67	1·80
Piperidine	H_2O	8·02	8·82	9·20
	H_2O–EtOH	7·92	8·70	9·00
	EtOH	7·24	7·96	8·12
Ephedrine	H_2O–EtOH	7·30	8·02	8·20
	EtOH	4·90	5·38	5·45
Quinine	EtOH	1·90	2·08	2·07

* H_2O–EtOH = 50% mixture.

The N/4-absorptions of quinine and sodium hydroxide by methacrylic acid resins containing varying proportions of divinylbenzene, are shown below.

Divinylbenzene (approximate % in the resin)	NaOH, m-.moles/g.	Quinine, m.-moles/g.	Quinine, m.-moles/10 m.-equiv. of CO_2H
10	9·32	1·95	2·09
5	9·92	2·17	2·19
2·5	10·60	2·69	2·54
1	10·84	2·95	2·72

The value for sodium hydroxide being taken as a measure of the amount of exchangeable carboxyl per g., the N/4-absorption for quinine per 10 m.-equivs. of carboxyl group increases as the degree of cross-linking of the resin, *i.e.*, as the proportion of divinylbenzene present decreases.

Discussion

Equilibrium Distributions.—The reversible nature and definite character of the equilibrium distributions of bases between solution and resin have been demonstrated in the case of quinine by showing that the distribution is independent of resin particle size (*e.g.*, 1 g. of resin + 25 ml. of ethanol solution containing 6·17 m.-moles of quinine absorbed 2·07 m.-moles of quinine at equilibrium with 20—40 B.S.S. resin, 2·07 m.-moles with 40—60 B.S.S., and 2·08 with <60 B.S.S.) and also that they are in fact reversible. To show this with quinine, a sample of resin already saturated with the base was allowed to come to equilibrium with pure ethanol. Although the results of these reverse equilibrium experiments were not in exact agreement with distributions obtained in the forward direction, the discrepancies were not greater than could be accounted for by the larger errors of the reverse-direction measurements and were sufficient to establish that the absorption process is reversible. The systems studied can be classified into two groups; the first, consisting of very weak bases, follow a simple distribution law

$$\frac{\text{Concentration of base in resin}}{\text{Concentration in equilibrium solution}} = \text{constant} \quad . \quad . \quad . \quad . \quad (1)$$

in the second group, the distributions mostly follow a logarithmic law.

For uniformity, the concentrations of base in the two bulk phases have been expressed in the same units, moles per litre of total phase volume : C has been used to denote the concentration of base in the equilibrium solution in these units, and y denotes the corresponding base concentration in the resin phase, in moles of base per litre of total resin phase volume.

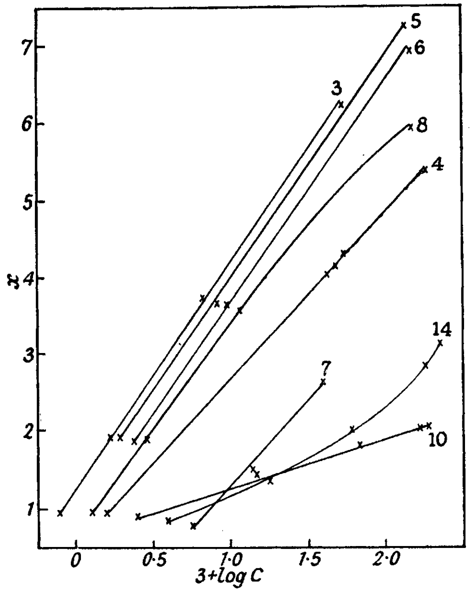


FIG. 1. *Equilibrium distributions of bases between Amberlite* IRC50 *and their solutions in ethanol.*

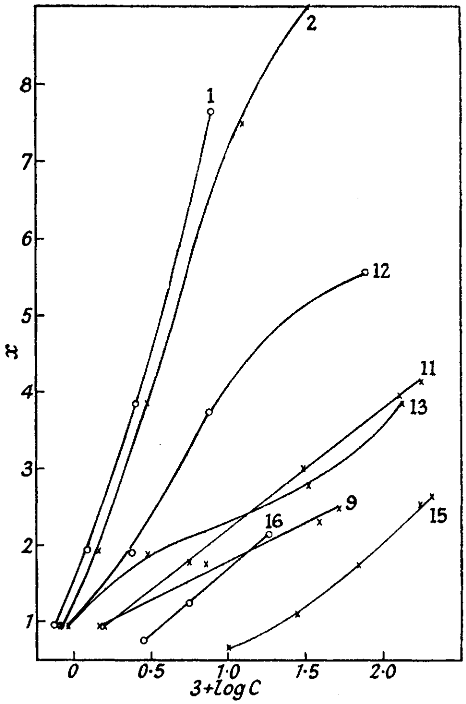


FIG. 2. *Equilibrium distributions of bases between Amberlite* IRC50 *and their solutions in water* (○) *and* 50% *ethanol* (×).

(Numbers indicate the bases listed in the table on p. 2117.)

The values of y have been calculated from x, the amount of base absorbed per g. of 110°-dried hydrogen form of the resin, the specific volume and swelling data already recorded being used. In the cases of systems following equation (1) the swelling effects are very small; y has been calculated on the assumption that the amount of swelling was proportional to the amount of base absorbed. An example of a system following the simple distribution law is given in the table below.

Equilibrium data for absorption of pyridine from alcoholic solution by Amberlite IRC50.

Initial concn., m.-moles/100 ml.	Wt. of resin, g./ 100 ml. of solution	M.-moles absorbed	y	C	y/C
3·09	3·15	0·71	0·100	0·0238	4·22
6·17	3·15	1·38	0·195	0·0479	4·07
12·34	3·15	3·05	0·430	0·0929	4·63
24·68	3·15	5·82	0·812	0·1886	4·33

Other solutions obeying equation (1) were found to be : (i) Aniline in 50% ethanol, const. = 2·2; (ii) dimethylaniline in 50% ethanol, const. = 2·2; (iii) α-naphthylamine in

FIG. 3. *Representing* $y = A \log C + B$.

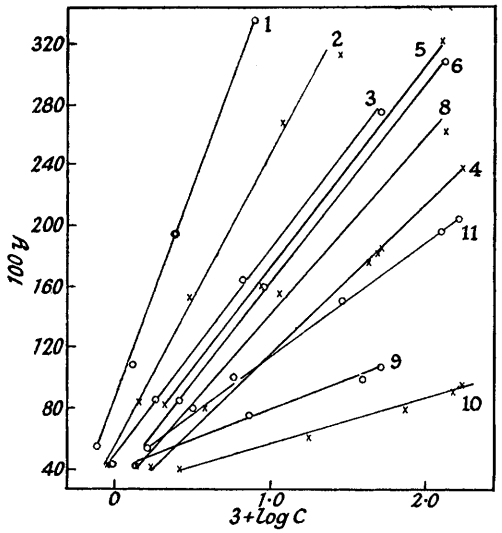
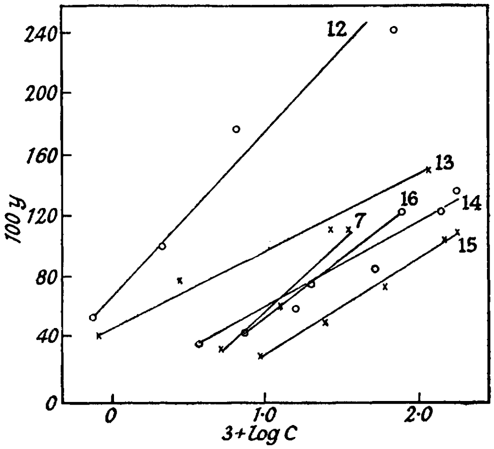


FIG. 4. *Representing* $y = A \log C + B$.



(Numbers indicate the bases listed in the table on p. 2117.)

FIG. 5. *Correlation between A and* pK_B.

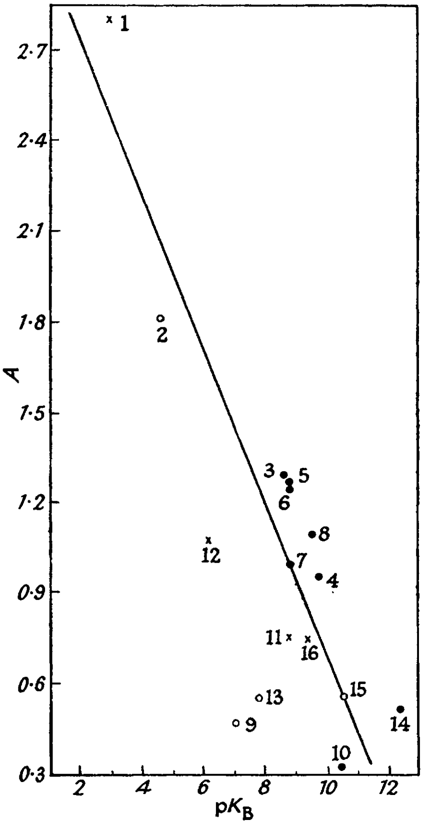
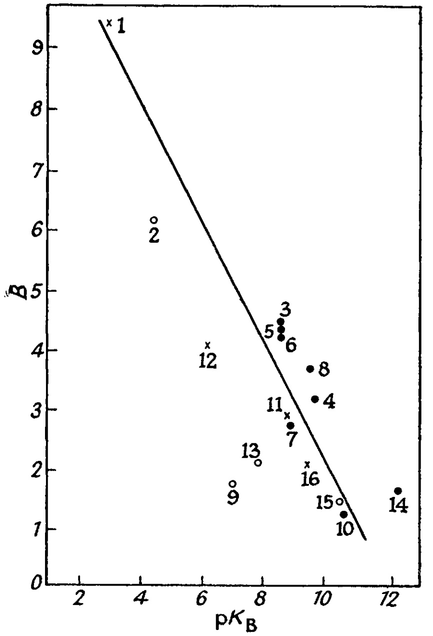


FIG. 6. *Correlation between B and* pK_B.



(Numbers and symbols as in Fig. 5.)

Solvents used: ×, *water;* ○, 50% *ethanol;* ●, *pure ethanol.*
(Numbers as on p. 2117.)

ethanol, const. = 2·0; (iv) β-naphthylamine in ethanol, const. = 2·2; (v) caffeine in water, const. = 13·6.

The homocyclic bases all give a very similar value of the constant. It must be remembered that the resin itself contains a certain amount of solvent and part of the constant of equation (1) will be due to a straightforward distribution of solute between solvent in solution and in the resin phase.

If a system follows equation (1) it seems likely that the absorption is a simple distribution of un-ionised base between resin and solution, *i.e.*, a molecular absorption, the un-ionised base presumably being held to the carboxyl groups of the resin by a dipole-association mechanism.

The equilibrium results for the systems containing stronger bases were mostly found to follow a logarithmic type of distribution law. The figures show the experimental curves relating x to log C.

The linearity of the plots in ethanol solution (see Fig. 1) is very clear, apart from the anomalous results for nicotine. Since none of the bases causes very much swelling of the resin when absorbed from ethanol solution, the y–log C plots are similar in form.

In 50% ethanol and in aqueous solution (see Fig. 2) the nicotine curves are again anomalous. The piperidine and pyridine plots show some curvature, but the remaining graphs do not deviate very greatly from linearity. In these solvents quite large resin volume changes occurred on absorption of base, and in order to calculate values of y from x, we have again assumed that the swelling is a linear function of base absorbed. An experimental check has indicated that in the case of the larger swellings, *e.g.*, piperidine in water, this assumption may introduce errors in y of the order of 5%.

The plots of y against log C are shown for all the systems in Figs. 3 and 4. The substitution of y for x improves the linearity in some cases. The following table shows the values of the constants A and B for the equation

$$y = A \log C + B \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

for the different systems, derived from the straight lines shown in Figs. 3 and 4.

Values of the constants of the equation, y = A log C + B

Curve in fig.	Base	Solvent	A	B	B/A
1	Piperidine	H_2O	2·80	9·35	3·34
2	Piperidine *	H_2O–EtOH	1·82	6·12	3·36
3	Piperidine	EtOH	1·30	4·47	3·44
4	(+)-*ψ*-Ephedrine	,,	0·97	3·14	3·24
5	*n*-Butylamine	,,	1·29	4·36	3·38
6	*n*-Heptylamine	,,	1·26	4·16	3·30
7	*n*-Dodecylamine	,,	1·01	2·65	2·62
8	Benzylamine *	,,	1·10	3·67	3·34
9	Quinine	H_2O–EtOH	0·48	1·70	3·71
10	Quinine	EtOH	0·33	1·23	3·74
11	Pyridine	H_2O	0·77	2·80	3·56
12	Nicotine †	,,	1·10	3·96	3·60
13	Nicotine †	H_2O–EtOH	0·55	2·12	3·86
14	Nicotine †	EtOH	0·52	1·63	3·14
15	Pyridine *	H_2O–EtOH	0·57	1·42	2·50
16	Aniline *	H_2O	0·76	1·99	2·62

* Distinct curvature of y–log C plot.
† Wide deviations from straight line plot of y against log C.

Figs. 5 and 6 show the way in which A and B vary with the dissociation constant exponents pK_B of the bases. The values of pK_B have been determined by potentiometric titration, corrections put forward by the authors (*J. Pharm. Pharmacol.*, 1951, **3**, 78, and in preparation) being used for the 50% ethanol and ethanol solutions. Both A and B decrease with decreasing base strength. The straight lines shown in Figs. 5 and 6 represent the regressions A/pK_B and B/pK_B, respectively.

The effect of molecular size on the values of A and B is illustrated by the results for butylamine, heptylamine, and dodecylamine (5, 6, and 7). These three bases all have similar dissociation constants, but their A and B values decrease markedly as molecular size increases.

The form of the logarithmic distribution equation (2) is analogous to that relating quantitative biological responses produced by physiologically active bases and other materials, to doses administered to animals (cf. Burn, "Biological Standardisation," Oxford Med. Pub., 1950, p. 19).

A provisional theory for the form of equation (2) can be developed by making the following assumptions: (1) That the base is completely ionised in the resin phase. This assumption is supported for smaller absorptions of base by Honda's measurements of the internal pH of Amberlite IRC50 by an indicator method; the results indicate a pH of about 4 in aqueous solutions (*J. Chem. Soc. Japan*, 1950, **71**, 440). (2) That the activity correcting factor in the equations derived is constant. (3) That the free energy required to ionise a carboxyl group in the resin phase increases linearly as the amount of base absorbed (*i.e.*, as y) increases. Ionisation of one carboxyl group by absorption of base is likely to affect neighbouring groups in the same way as the ionisation of one carboxyl group of a polybasic acid increases the free energy required to ionise the other groups. As a result, potential energy will be stored in the gel structure of the resin as ionisation proceeds, owing to the proximity of negatively charged carboxyl groups whose charges cannot be effectively shielded from one another by the gegen-ions, owing to the presence of the electrically neutral hydrocarbon structure of the resin. This is likely to provide a less effective shield between the negatively charged groups than the cations in the resin.

In some cases the stored potential energy appears as an appreciable swelling of the resin. The primarily electrostatic nature of the swellings of these weak acid resins is indicated by the observations (see table, p. 2113) that stronger bases all cause similar swellings and the sodium form of the resin shrinks when immersed in ethanol.

The potential or free-energy storage produced by the ionisation of a weak electrolyte gel may be a significant factor in some biosynthetic processes.

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