THE DISTRIBUTION OF SOME ALKALOIDS IN HETEROGENEOUS SYSTEMS

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As has been shown in a preceding paper [1], the pK_a values of some alkaloids are not connected with their pH transitions on extraction from chloroform solution by buffer solutions with various pH values. Consequently, we have studied in more detail the nature of the distribution of the bases of *Vinca erecta* and a number of other alkaloids in systems consisting of chloroform and buffer solutions of various pH values under equilibrium conditions. It was established by special experiments that in all cases the distribution process is accompanied by pure salt-formation: in the chloroform (or benzene) layer there are no alkaloids in the form of salts, and in the aqueous layer there are none in the form of bases. We have determined the concentration of alkaloids in the buffer solution (C_1) and in the organic solvent (C_2). In each case, the same result was obtained in three parallel experiments. The main distribution criterion, of course, is the distribution coefficient (K) calculated from the formula

$$K=\frac{C_1}{C_2}.$$

As can be seen from Table 1, K changes from 0 to 10 and more according to the pH of the buffer solution, while for none of the alkaloids investigated did these figures coincide. From the values of the distribution coefficient we plotted a graph of $K = f(\mathrm{pH})$. The graph shows the relationship for vincanine.

The results on distribution were compared with the pH value of the buffer solution that would extract precisely half the alkaloids from the organic solvent phase, $pH_{1/2}$ [2]. The values of $pH_{1/2}$ for each base was found from a graph of $K = f(\mathrm{pH})$. The sequence of arrangement of the alkaloids with respect to their $pH_{1/2}$ values differs considerably from that according to their pK_a values (Table 2) and is identical with the sequence of passage into the buffer in the separation of the combined alkaloids.

TABLE 1. Distribution Coefficients of Alkaloids in Chloroform–Buffer Solution Systems

pH	Vincamine	Vincanine	Vincarine	Akuammidine	Vincanidine	Tombosine
8,0	0	0	0	0	0	0
7,5	0	0	0	0	0	0
7,0	0	0	0	0	0,07	0,3
6,5	0	0	0	0	0,36	0,5
6,0	0	0,062	0	0,14	0,50	1,3
5,5	0	0,13	0,2	0,80	2,0	5,0
5,0	0,007	0,17	0,6	1,30	8,80	17,0
4,5	0,18	0,35	3,1	2,60	29,0	+
4,0	0,41	0,59	5,3	5,0	+	+
3,5	0,76	1,2	17,0	23,0	+	+
3,0	2,14	12,0	+	+	+	+
2,5	6,05	33,0	+	+	+	+
2,0	13,1	+	+	+	+	+

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TABLE 2. Basic Strength of the Alkaloids of *V. erecta*

$pH_{1/2}$ from chloroform	Base	pK_a [3]
6,35	Tombosine	7,54
5,80	Vincanidine	6,84
5,35	Akuammidine	6,66
4,90	Vincarine	6,91
3,60	Vincanine	7,79
3,30	Vincamine	6,62

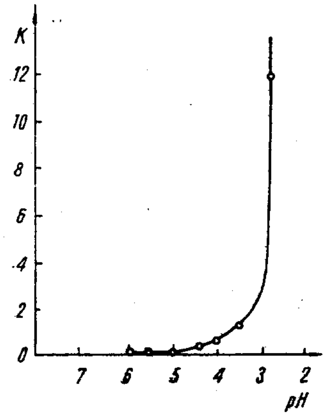

Fig. 1. Distribution of the base vincanine between chloroform and buffer solutions with various pH values.

Although the value of $pH_{1/2}$ depends on many factors (the properties of the substance being separated, the nature of the heterogeneous system, etc.), one of the factors determining $pH_{1/2}$ values is undoubtedly the basic strength of the alkaloid. Consequently, the differentiation of the basic strength of alkaloids according to their $pH_{1/2}$ values may be extremely useful for the distribution of alkaloids in heterogeneous systems with the formation of salts.

We have also found the values of K and of $pH_{1/2}$ for the main opium alkaloids, for which the pK_a values are known from the literature [3], and also for salsoline and salsolidine, the pK_a values of which we determined ourselves.

Morphine is extracted completely from chloroform solution even by a buffer solution with pH 9.0. Consequently, its basic strength is higher than that of all the alkaloids of *V. erecta* and the opium bases, as can be seen by comparing Tables 1 and 3. Codeine and thebaine have $pH_{1/2}$ values comparable with those of vincanidine and vincanine. Papaverine and narcotine are not extracted from the chloroform even with a buffer solution having pH 1.5; they are weak bases and behave similar to substances of neutral nature, although their pK_a values are fairly high. For the alkaloids that we used it is possible to construct the following sequence with respect to $pH_{1/2}$ values on their extraction from chloroform: morphine, tombosine, codeine, vincanidine, akuammidine, vincarine, vincanine, vincamine, papaverine, narcotine.

We also determined the values of K and $pH_{1/2}$ for the alkaloids of *V. erecta* in heterogeneous systems consisting of benzene and buffer solution of various pH values in order to determine the influence of this change in the organic phase (Table 4).

A comparison of Tables 1 and 4 shows, in all cases, an increase in the $pH_{1/2}$ values of the alkaloids.

TABLE 3. Distribution Coefficients of Some Alkaloids in Chloroform–Buffer Solution Systems

pH	Morphine	Codeine	Thebaine	Papaverine	Narcotine	Salsoline	Salsolidine
9,0	Passes into the buffer completely	0	0	Does not pass into the buffer at any pH		0	0
8,5		0	0			0,34	0
8,0		0	0			1,24	0
7,5		0	0			4,79	0
7,0		0,13	0			20,5	0,06
6,5		0,22	0			+	0,62
6,0		0,7	0			+	2,79
5,5		1,5	0			+	4,74
5,0		4,42	0			+	23,0
4,5		+	0,14			+	+
4,0		+	0,52			+	+
3,5		+	1,6			+	+
3,0		+	15,8			+	+
2,5		+	+			+	+
2,0		+	+			+	+
$pH_{1/2}$	<9	5,75	3,70	<2	<2	8,45	6,45
pKa	7,87	7,95	7,00	5,90	6,18	8,46	7,71

TABLE 4. Distribution Coefficients of Alkaloids in Benzene—Buffer Solution Systems

pH	Vincamine	Vincanine	Vincarine	Akuammidine	Vincanidine	Tombosine
8,0	0	0	0	0	0	0,8
7,5	0	0	0	0	0	1,0
7,0	0	0	0	0	1,4	1,8
6,5	0	0	0,8	0,4	4,0	5,0
6,0	0	0	1,4	2,0	+	+
5,5	0,6	0,4	+	16,0	+	+
5,0	0,7	1,6	+	+	+	+
4,5	1,1	2,6	+	+	+	+
4,0	5,9	5,5	+	+	+	+
3,5	+	+	+	+	+	+
$pH_{1/2}$	4,6	5,7	6,3	6,3	7,1	7,5

EXPERIMENTAL

A solution of an alkaloid in chloroform with an accurately known concentration was prepared. Then aliquots were taken from this solution and exactly the same volume of a buffer solution with a pH from 9 to 2.0 was added.

The equilibrium distribution of the alkaloids was achieved by shaking for 1 h. After the separation of the phases, the organic phase was taken off and was washed with water. The wash-water contained no alkaloids.

The buffer phase was checked qualitatively with silicotungstic acid for the presence of alkaloids. If the reaction was positive, 1 ml of the organic phase was transferred to a beaker and was evaporated to dryness, and the residue was dissolved in methanol and titrated with 0.01 N HCl. The pH values of the buffer solutions were determined on a LPM-60M potentiometer.

SUMMARY

1. The distribution of the alkaloids investigated in the heterogeneous systems selected is accompanied by salt formation.

2. The distribution coefficients of the 13 alkaloïds studied change within wide limits (from 0 to 10 and more) according to the pH of the buffer solution, the heterogeneous system, the basic strengths of the alkaloids, etc.

3. In order to characterize the distribution of alkaloids in heterogeneous systems and to differentiate alkaloids with respect to their basic strength, the value of $pH_{1/2}$, in addition to pK_a, is proposed.

LITERATURE CITED

1. T. Artykova, Kh. N. Aripov, and T. T. Shakirov, Khim. Prirodn. Soedin., 57 (1973).
2. W. Bottomley and P. J. Mortimer, Austr. J. Chem., 7, No. 2, 189 (1954).
3. Handbook of Chemistry [in Russian], Vol. III, Khimiya, Moscow—Leningrad (1964), p. 98.