SEPARATION OF PYRIDINE COMPOUNDS ON ION-EXCHANGE RESINS

I. MAXIMUM PARTITION COEFFICIENTS AND SEPARATION OF SOME PYRIDINE COMPOUNDS

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UDC 547.82+543.544.42:543.544.6

The reaction of pyridine compounds (pyridine, 4-methylpyridine, 4-hydroxypyridine, 4-carboxypyridine, pyridine-4-aldehyde, and pyridine-4-aldoxime) with KU-2 cation-exchange resins in the H^+, K^+, and NH_4^+ forms and with AV-17 anion-exchange resins in the OH^- and Cl^- forms was investigated. A dependence of the maximum partition coefficients of the pyridine compounds on the composition and concentration of the eluent was found. The chromatogram of the separation of a mixture of pyridine compounds on AV-17 (Cl^- form) is presented.

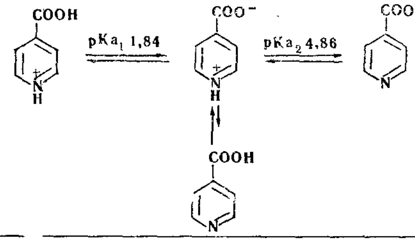
A number of investigations have been devoted to the separation and quantitative determination of pyridine compounds (PC) by paper [1, 2], thin-layer [3, 4], sedimentation [5, 6], and gas-liquid [7-18] chromatography. Ion-exchange resins have been used for the separation of PC only in individual cases. A few studies have been devoted to the investigation of pyridine sorption by ion-exchange resins [19, 20] and to the isolation of nicotinamide by an ion-exchange method [21].

The separation of PC, particularly the high-boiling and unstable compounds, on solid sorbents, including ion-exchange resins, is of interest for analytical and preparative purposes if one considers the certain limitedness in this respect of the gas-liquid method.

The aim of this investigation was therefore to study the possibility of the separation on ion-exchange resins of some PC formed primarily in the vapor-phase oxidation of 4-methylpyridine [22].

We investigated the chromatographic behavior of pyridine (I), 4-methylpyridine (II), 4-carboxypyridine (III), pyridine-4-aldoxime (IV), 4-hydroxypyridine (V), and pyridine-4-aldehyde (VI) on KU-2 cation-exchange resins in the H^+, K^+, and NH_4^+ forms and on anion-exchange resins AV-17 in the OH^- and Cl^- forms.

The basicity of the nitrogen atom in the heterocyclic ring of I changes as a function of the nature and position of the substituent. Thus, the methyl group in II increases the ionization constant of the basic group of I by +0.79 units (Table 1) as a result of mesomeric (+M) and inductive (+I) effects. A hydrogen atom is transferred from the substituent to the ring nitrogen atom in PC which contain acid groups in the substituent with ionization constants which are lower than the ionization constants of the base [23]. Among such PC are III-V which exist in aqueous solution primarily in the form of inner salts, i.e., as zwitterions. For example, depending on the solution pH, III ionizes as follows:



Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR, Riga. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 220-224, February, 1971. Original article submitted March 4, 1969.

TABLE 1. Maximum Partition Constant (P_0) between KU-2 H^+ and 2 N HCl and Ionization Constants of Some 4-Substituted Pyridine Compounds

Compound	P_0	Ionization constants		
		pk_{a1}	pk_{a2}	literature
VI	7,6	4,77	(12,2)	24
III	16	1,84	4,86	25
I	17	5,23	—	26
IV	23	4,77	9,99	27
V	25	3,27	11,09	28
II	27	6,02	—	29

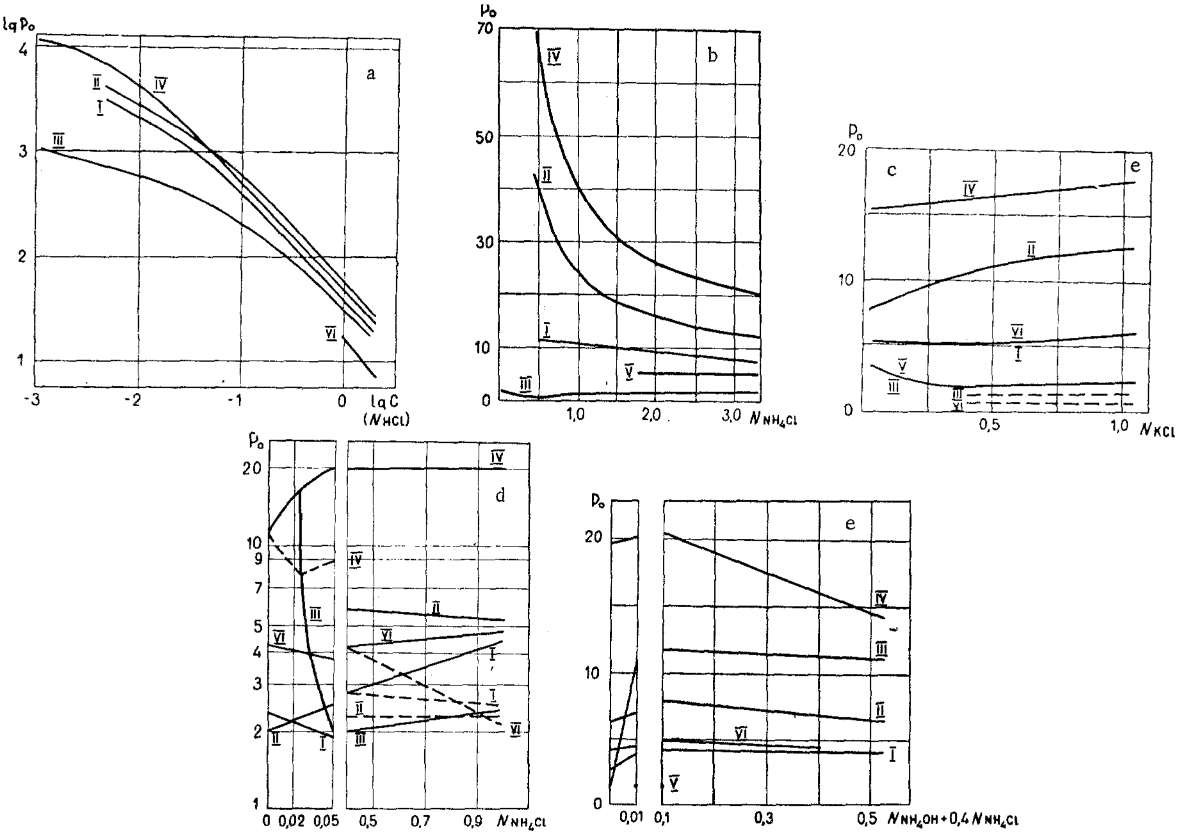


Fig. 1. Changes in the maximum coefficients of partition of pyridine compounds between an ion-exchange resin and a solution as a function of the eluent concentration: a) KU-2 H^+, HCl eluent; b) KU-2 NH_4^+, NH_4Cl eluent; c) KU-2 K^+, KCl eluent; d) AV-17 Cl^-, NH_4Cl eluent; and e) AV-17 Cl^-, NH_4OH + NH_4Cl eluent.

Compound VI does not have zwitterion character; in aqueous solution it is in equilibrium with the hydrated form. In acid media the equilibrium is shifted to favor the hydrated form, while the unhydrated form is favored in alkaline media.

As a result of partition between the solution and the ion-exchange membrane, in accordance with the membrane (Donnan) equilibrium, the PC forms a complex with KU-2 H^+ with the hydrogen ion located there. This complex is positively charged and remains in the resin at the same site where the hydrogen ion was.

$$[PC] + H^+ - KU\text{-}2 \rightleftarrows [PC \cdot H]^+ - KU\text{-}2$$

Thus, the absorption of the PC by the ion-exchange resin depends not only on partition in accordance with the membrane equilibrium, but chiefly on the stability of the complex formed. If the external solution also contains H^+ ions, which form a complex with the PC, the absorption of the latter by cation-exchange resin depends on the H^+ ion concentration in solution and on the stabilities of the complexes in solution and in the

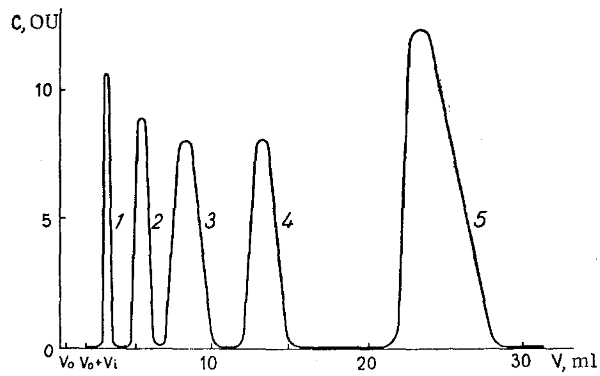


Fig. 2. Separation of 4-substituted pyridines on AV-17 Cl^-: 1) V; 2) I; 3) II; 4) III; 5) IV [column 39 cm by 0.078 cm^2; resin grain diameter 0.05-0.06 mm; eluent 0.4 N NH_4Cl + 0.01 N NH_4OH; eluent passage rate 0.73 ml/cm^2-min; C is the concentration of each component in optical units (OU)].

ion-exchange resin. The quantity of absorbed molecules is limited by the ion-exchange capacity of the resin. According to [20], the absorption of I by the sulfo groups of KU-2 H^+ is equal to the capacity of the ion-exchange resin.

Figure 1a shows the dependence of the maximum partition coefficients (P_0) of PC on KU-2 H^+ on the HCl concentration in an equilibrium solution. It is apparent from the figure that the PC are strongly absorbed by the cation-exchange resin. It is apparent from a comparison of the P_0 values obtained in 2 N HCl with the ionization constants of the PC in solution (Table 1) that, as a result of interaction with the ion-exchange resin matrix, the order of stability of the PC complexes in the resin, viz., VI < III < I < IV < V < II, does not correspond to the order of increase in the pK_{a_1} of the PC (III < V < VI, IV < I < II).

By comparing the salt forms of the cation-exchange resin, we see that the PC are more strongly absorbed by the ammonium form (Fig. 1b) than by the potassium form (Fig. 1c), which may be explained by the higher affinity of the K^+ ion for the cation-exchange resin as compared with the NH_4^+ ion and also by the fact that the NH_4Cl solution is weakly acidic. It must be noted that in experiments for the determination of the P_0 values by a dynamic method on KU-2 K^+ with 0.4 and 1.0 N KCl as eluents, III and VI are separated into two peaks; i.e., under these conditions a pure substance simultaneously has two P_0 values; this is possibly explained by the existence in solution of two equilibrium forms of compounds with low rates of establishment of equilibrium between the forms. (In the figures, the P_0 values of the second form are designated by dash lines.)

As in the case of KU-2 H^+, the absorption of III, IV, and V by the strongly basic AV-17 in the OH^- form occurs via a complexing mechanism:

$$[\mathrm{PC}] + \mathrm{OH}^- \text{—AV-17} \rightleftharpoons [\mathrm{PC}]^- \text{—AV-17} + \mathrm{H_2O}.$$

When the P_0 values are high, absorption is limited by the ion-exchange capacity of the ion-exchange resin. The sorbed compound is eluted with a concentrated solution of a strong alkali. Compounds I, II, and VI are absorbed weakly on AV-17 OH^-, and their P_0 values during elution with water are 2.8, 4.8, and 13.5, respectively.

Except for IV, which is most strongly sorbed, P_0 between AV-17 Cl^- and NH_4Cl solution (Fig. 1d) differs little for the various PC. When the concentration of the NH_4Cl solution is decreased, P_0 decreases for IV but increases for III. The existence of two forms of PC is also observed under the investigated partition conditions.

The graph of the dependence of the P_0 of PC on AV-17 Cl^- on the composition and concentration of the eluting solution (Fig. 1e) indicates that the absorption of III increases sharply with alkalization of the eluent (NH_4Cl).

The determination of the P_0 between the various forms of ion-exchange resins and eluting solutions for the investigated PC makes it possible to select the most suitable conditions for their separation; conversely, knowing the ratios of the P_0 values of the separable components and the height of an equivalent theoretical plate of the chromatographic column, one can establish the length of the column for complete separation of a mixture and determine the volumes of the fraction of effluent solution in which each component will be contained. As an example, Figure 2 shows the chromatogram of the separation of an artificial mixture prepared from five PC on AV-17 Cl^- with 0.4 N NH_4Cl + 0.01 N NH_4OH as the eluent.

EXPERIMENTAL

Except for KU-2 in the H^+ form, the maximum partition coefficients (P_0) on the investigated forms of the ion-exchange resins were determined under dynamic conditions. P_0 was calculated from the expression [30]

$$P_0 = \frac{V_{max} - (v_i + v_0)}{m},$$

where P_0 is the weight maximum partition coefficient in milliliters per gram, V_{max} is the volume (in milliliters) of eluent passing through the column from the start of application of the sample to the appearance of the peak maximum, v_i is the free volume of the chromatographic column in milliliters (v_i in all of the experiments was taken as 40% of the total volume of the chromatographic column), v_0 is the volume (in milliliters) of the connecting tube from the chromatographic column to the detector (in our experiments, v_0 was 0.40 ml), and m is the weight of the air-dried ion-exchange resin in grams.

A chromatographic column with a length of 10-40 cm and a cross section of 0.08 cm^2 and ion-exchange resins with grains 0.05-0.06 mm were used in the experiments. The weight of the air-dried resin in the chromatographic column was calculated from the previously determined specific volume of the swelled resin (KU-2 H^+ 0.40 g/ml, AV-17 Cl^- 0.36 g/ml).

The column was brought into equilibrium with the eluent before application of the test solution (0.1-0.2 ml). The amount of applied compound on the column was ~ $1 \cdot 10^{-3}$ mg-equivalent, which was less than 0.1% of the ion-exchange resin capacity.

Detection was accomplished through light absorption in the UV region with a DPU-2 densitometer which was connected to an EPP-09 recording potentiometer with a 10-mV scale.

The P_0 values of the compounds on KU-2 H^+ were determined under static conditions from the ratio of the concentration of the compound in the resin in milligram-equivalents per gram of air-dried resin and the concentration in the equilibrium solution in milligram-equivalents per milliliter:

$$P_0 = \frac{(C_0 - C_1) \cdot V}{m}; \quad C_1 = \frac{\bar{C}}{C_1},$$

where C_0 and C_1 are the initial and equilibrium concentrations of the solution in milligram-equivalents per milliliter, C is the concentration in the resin in milligram-equivalents per gram of air-dried resin, and V is the volume of the solution, allowing for water in the swelled resin, in milliliters.

The absolute error (reproducibility) in the determination of P_0 was less than 5%.

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