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# LI.—Conversion of Racemic Acid into a Mixture of Racemic and d-Tartaric Acids by Means of 1-Malic Acid.

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ACCORDING to Pasteur, ammonium hydrogen *d*-tartrate combines with ammonium hydrogen *l*-malate to form a crystalline compound, which, when dissolved in aqueous ammonia, has the same rotatory power as is possessed by a mixture of equimolecular quantities of the two salts.

This statement led the author to attempt the resolution of optically inactive acids by combining them with active acids instead of with the active bases which are usually employed for the On the basis of Pasteur's observation, if ammonium purpose. hydrogen racemate were combined with ammonium hydrogen *l*-malate, two compounds would probably be produced, namely, (a) ammonium hydrogen d-tartrate + ammonium hydrogen l-malate (Pasteur's salt), and (b) ammonium hydrogen l-tartrate + ammonium hydrogen *l*-malate. Since complexes of this nature are not enantiomorphously related, their separation might be effected in virtue of the difference in solubility, which would doubtless exist between them. In this connexion the remark of Pasteur that the ammonium hydrogen salt of *l*-tartaric acid does not form a compound with the ammonium hydrogen salt of *l*-malic acid is significant, indicating, as it does, that salt (b) is more soluble in water than salt (a).

In the course of an investigation of this problem the unexpected results, which are described in the present paper, were encountered.

Racemic acid (1 mol.) was neutralised with aqueous potassium hydroxide, and *l*-malic acid (1 mol.) was added. The crystalline product which separated was dextrorotatory, and consisted of a mixture of potassium hydrogen racemate and potassium hydrogen *d*-tartrate.

Now the addition of a nucleus of an optically active compound to a solution of the inactive form is known in certain cases to cause the deposition of optically active crystals. Gernez, for example, found that, when a nucleus of sodium ammonium d-tartrate is added to a supersaturated solution of sodium ammonium racemate, the resulting crystals consist of the d-salt, whereas, when a nucleus of the *l*-tartrate is added, the *l*-salt separates (*Compt.* rend., 1866, **63**, 843). Other cases of this extension of Pasteur's original method of mechanical separation are afforded in the resolution of zinc ammonium lactate (Purdie, T., 1893, **63**, 1143) and of

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the phenylbenzylhydrazones of erythrose (Ruff, Ber., 1901, **34**, 1362). Moreover, Ostromisslenski (Ber., 1908, **41**, 3035) has shown that *l*-asparagine causes the crystallisation of sodium ammonium *d*-tartrate when a nucleus of it is added to a supersaturated solution of the racemate, whilst Kipping and Pope (T., 1909, **95**, 103), in a series of experiments on the crystallisation of externally compensated mixtures, have shown that nuclei present in the dust of the atmosphere of the laboratory induce crystallisation in a solution of sodium ammonium racemate, the crystals formed being sometimes dextrorotatory and sometimes lævorotatory.

The most probable explanation of the activation of racemic acid by malic acid would naturally be sought for on these lines. The phenomenon must, however, be ascribed to some other cause. In no case has potassium hydrogen racemate been crystallised from water alone so as to cause the deposition of an optically active salt.

One other observation may be recorded at the present time. Van't Hoff has suggested the possibility of activating an inactive compound by crystallising it from an optically active solvent. This idea has now been experimentally realised in the following manner. When potassium hydrogen racemate is crystallised from an aqueous solution of l-malic acid, the crystals which separate are dextrorotatory, and consist of a mixture of potassium hydrogen racemate and potassium hydrogen d-tartrate.

### EXPERIMENTAL.

The racemic acid used in each case was tested to make certain that it was optically inactive. No optical activity was detected with a concentrated aqueous solution. Two grams of the acid were dissolved in water and neutralised by potassium hydroxide; the whole of the solution was polarimetrically examined in a 2-dcm. tube, and found to be inactive.

Experiment I.—A solution of 10 grams of racemic acid (1 mol.) in water was neutralised by the calculated quantity of potassium hydroxide, and made up to 500 c.c. Eight grams of *l*-malic acid (1 mol.) were then dissolved in the solution of potassium racemate which had previously been warmed, and crystals began to separate before the liquid was cold. The whole was then stirred vigorously, and allowed to remain for two days at the ordinary temperature. The crystals were collected, washed with 10 c.c. of water, dried on porous plate, and then at  $100^{\circ}$  for one hour. The yield was 11 grams (crop A).

0.2394 required 47.25 c.c. of baryta  $(N/40 \times 1.077)$  for neutralisation, whereas  $CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CO_2K$  requires 47.26 c.c.

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Two grams of A were neutralised by potassium hydroxide and made up to the bulk necessary to fill a 1-dem. tube (8.1 c.c.). The solution was distinctly dextrorotatory, giving  $\alpha_{\rm D} + 0.44^{\circ}$ . Eleven c.c. of N-sulphuric acid were then added, and the resulting salt (1.8 grams) was collected and crystallised from 100 c.c. of water. The crystals which separated amounted to 1.4 grams. They were neutralised, and the solution of the potassium salt examined in a 1-dcm. tube. The dextrorotation was still slight but definite  $(+0.08^{\circ})$  after this treatment.

Since the addition of boric acid to *d*-tartaric acid is known to enhance the rotatory power of the latter, a mixture of 2 grams of A and 1.5 grams of boric acid was heated with water, and the solution examined in a 2-dcm. tube. The value  $\alpha_D + 1.34^\circ$  was observed.

*Experiment II.*—Ten grams of racemic acid were neutralised and acted on with *l*-malic acid as before. After twenty-four hours the crystals (crop B) amounted to 9.5 grams.

6.5 Grams of B were neutralised by potassium hydroxide, and the solution was examined in a 2-dcm. tube. Found,  $\alpha_{\rm D} + 1.3^{\circ}$ .

Since ordinary tartar emetic is strongly dextrorotatory, a mixture of 2.9 grams of B and 2.2 grams of antimony oxide were made into a paste with water and heated on the water-bath for half-an-hour, water being added at intervals. The product was then boiled with water and filtered. After being kept overnight, the crystals amounted to 3.3 grams, whilst the filtrate gave  $\alpha_{\rm D} + 5.4^{\circ}$  in a 2-dcm. tube.

Experiment III.—100 C.c. of an aqueous solution of potassium racemate, prepared from 5 grams of racemic acid, were heated at  $80^{\circ}$ , and 4 grams of *l*-malic acid were added. The product (C) amounted to 5.5 grams:

0.693 (dried at 130°) gave 0.3188  $K_2SO_4$ . K = 20.6.

 $C_4H_5O_6K$  requires K=20.7 per cent.

One gram of C was neutralised by potassium hydroxide, and the solution made up to 20 c.c. The observed value was  $a_{\rm D} + 0.22^{\circ}$  (l=2), and this corresponds with  $[a]_{\rm D} + 1.8^{\circ}$  when referred to the normal potassium salt, whereas potassium *d*-tartrate has, according to Landolt,  $[a]_{\rm D} + 27.39^{\circ}$ .

The filtrate, from which C had been removed, amounted to 90 c.c., a portion of it in a 2-dcm. tube giving  $\alpha_{\rm D} - 0.82^{\circ}$ .

3.8 Grams of C were dissolved by boiling with 100 c.c. of water. The crystals which separated overnight were neutralised as usual, and the solution was made up to 20 c.c., a portion of which in a 2-dcm. tube gave  $\alpha_{\rm p} + 0.34^{\circ}$ ; the filtrate from which the crystals had been removed was also dextrorotatory.

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Experiment IV.-2.3 Grams of racemic acid (1 mol.) were neutralised and made up to 100 c.c. 3.8 Grams of *l*-malic acid (2 mols.) were added. The crystals (2.5 grams) were treated as in experiment I. Found,  $a_{\rm p} + 0.5^{\circ}$ .

Experiment V.—1.6 Grams of *l*-malic acid were neutralised, and 2 grams of racemic acid were added to the solution. Volume = 100 c.c. Crystals=2 grams; treated as in experiment I; found,  $\alpha_{\rm D} + 0.44^{\circ}$ .

## Crystallisation of Potassium Hydrogen Racemate from an Aqueous Solution of 1-Malic Acid.

Racemic acid was neutralised by aqueous potassium hydroxide and the acid salt was precipitated by the addition of sulphuric acid. The salt was crystallised from water; the potassium salt, obtained from the recrystallised acid salt, was optically inactive.

A solution of 3.2 grams of *l*-malic acid (1 mol.) in 210 c.c. of water was heated to boiling, and 4.4 grams of recrystallised potassium hydrogen racemate (1 mol.) were added. The solution was boiled for five minutes, and the clear solution then poured into a beaker and stirred. After twenty-four hours, the crystals, which had separated, were collected (filtrate=190 c.c.), washed with 10 c.c. of water, and dried at 100° for one hour. Yield, 3.2 grams: 0.2784 required 55 c.c. of baryta ( $N/40 \times 1.077$ ) for neutralisa-

tion. CO<sub>2</sub>H·CH(OH)·CH(OH)·CO<sub>2</sub>K requires 54.96 c.c.

2.844 Grams of the salt were neutralised by the calculated quantity of potassium hydroxide, and the solution was made up to 16 c.c., the bulk necessary to fill a 2-dcm. tube. The solution was distinctly dextrorotatory, giving  $a_{\rm D} + 0.39^{\circ}$ . It was then made up to 50 c.c., and the salt was precipitated by the addition of 16 c.c. of N-sulphuric acid. After three hours' keeping, the filtrate was treated with 16 c.c. of N-sulphuric acid, and evaporated to the bulk necessary to fill a 1-dcm. tube; the solution was slightly dextrorotatory, giving  $a_{\rm D} + 0.09^{\circ}$ . The crystals were crystallised from 100 c.c. of boiling water. The product (1.9 grams) was dissolved in potassium hydroxide, and then gave  $a_{\rm D} + 0.08^{\circ}$  in a 2-dcm. tube.

This work is being continued.

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