A Thermodynamic Investigation on the Racemization of Tartaric Acid

THOMAS ROSENBERG

Physico-Chemical Institute, University of Copenhagen, Denmark

The basis of the thermodynamic treatment of the racemization process is the energetic identity of the optical antipodes. On this basis, Brønsted[1] in a paper on the racemization of potassium tartrate has shown and realized various possibilities for the determination of the affinity of the process, *inter alia* by means of solubility determinations of the optically active and the racemic forms. This method is well suited for such determinations, provided that the gas laws hold for the saturated solutions in question. In the mentioned investigations, this condition has been fulfilled, a strong salt solution being used as a solvent in which the solubility of potassium tartrate and racemate was very low.

In the present investigation the racemization of crystalline tartaric acid into racemic acid (*dl*-tartaric acid) is investigated; the process is represented by the scheme

$$d \longrightarrow r \tag{1}$$

One mole of *d*-tartaric acid, *l*-tartaric acid, and racemic acid are denoted by *d*, *l*, and *r*, respectively, and identical values are used for the molecular weights of racemic acid and tartaric acid. A hydrate of racemic acid, which is obtained by crystallization in aqueous medium and which contains 1 mole of H_2O per 150 g acid, is denoted by *rh*.

While in the case of potassium tartrate the deviations from the ideal conditions almost exclusively are caused by the fact that the ions, in view of their electric charge, affect each other, the conditions in the system tartaric acid — racemic acid are different. The electrolytic dissociation of tartaric acid is relatively low ($K_1 \sim 10^{-3}$), and its solubility in water is rather high, much higher than the solubility of racemic acid. The deviations from the ideal conditions are, therefore, preponderantly due to a solvent effect in addition to

the mutual influence of the molecules, their association, etc., factors which cannot be eliminated in the aqueous medium. Consequently, determinations according to the mentioned principle necessitate the choice of another well suited solvent. A determination of the racemization affinity on the basis of the knowledge of the saturation conditions in aqueous medium can, however, be performed if the degree of deviation from the ideal conditions can be determined quantitatively, for example, by determining the activity coefficients.

<p style="text-align:center">THEORETICAL BASIS</p>

Racemization of an optically active crystalline compound generally does not occur spontaneously at ordinary temperature. Without changing the energetic conditions we can, however, assume that half of the observed quantity of the d-compound, for example $\frac{1}{2}$ mole, is converted into the l-compound and, instead of (1), we may write

$$\tfrac{1}{2}\, d + \tfrac{1}{2}\, l \longrightarrow r \qquad (2)$$

This process, which is thermodynamically equivalent to (1), will occur spontaneously if a small amount of a solvent is present, the effect of which may be considered as catalytic.

Different possibilities exist for the determination of the affinity of process (2), *viz.*

1. It can be treated analogously to the double salt formation whose formal similarity to (2) is immediately obvious.

2. It can be understood by analogy to the allotropic transformation, the mixture of equal parts of the d- and the l-form being the one modification which is converted into the stable racemic form.

Brønsted [2] has described a method for the affinity determination in double salt formation which, in the present work, is used for the determination of the racemization affinity. The method is based upon the following principle;

Let us assume that process (2) is performed by transferring $\frac{1}{2}$ mole d from a solution saturated with respect to d (s—d) and $\frac{1}{2}$ mole l from a solution saturated with respect to l (s—l) into a solution saturated with respect to r (s—r). The affinity for this process is given by

$$A^* = \tfrac{1}{2}\left(\mu_{d\,(s-d)} - \mu_{d\,(s-r)}\right) + \tfrac{1}{2}\left(\mu_{l(s-l)} - \mu_{l\,(s-r)}\right) \qquad (3)$$

where the chemical potentials are denoted by μ. Thus, $\mu_{d(s-d)}$ is the chemical potential of d-tartaric acid in a solution saturated with d-tartaric acid. The
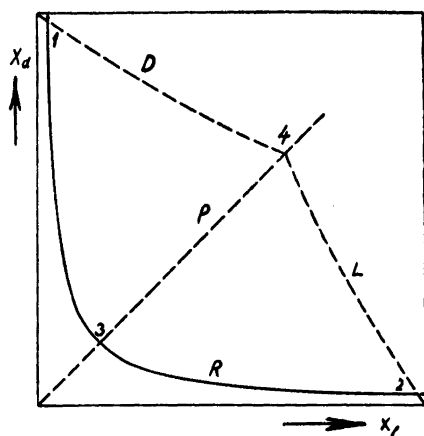
Fig. 1. Schematic solubility diagram in a system with optically active components.

conditions are most clearly illustrated by means of a solubility diagram (Fig. 1).

In Fig. 1, the concentrations of d and l as mole fractions are are the co-ordinates. The three solubility curves D, L, and R give the composition of the solutions in equilibrium with solid d, l, and r, respectively. The points of intersection 1, 2, and 4 denote the composition of solutions in equilibrium with two crystalline compounds. If the racemic compound is dissolved in the pure solvent until saturation is reached, a solution of composition 3 is obtained. The line P divides the diagram into two symmetrical parts in view of the thermodynamic identity of the optically active forms. The transferring process mentioned above can obviously be performed from arbitrary points on the curves D and L to an arbitrary point on the curve R. In the present case, it is most advantageous to transfer d and l from 1 and 2, respectively, to 3. Hence, we obtain for the affinity, according to (3),

$$A^* = \tfrac{1}{2} \left(\mu_{d(1)} - \mu_{d(3)} \right) + \tfrac{1}{2} \left(\mu_{l(2)} - \mu_{l(3)} \right) \tag{4}$$

For symmetry reasons, however, the two potential differences in the equation (4) are equal and (4) can be simplified to

$$A^* = \mu_{d(1)} - \mu_{d(3)} \tag{5}$$

From (5) it results that the affinity determination presupposes the knowledge of the change in potential of the d-form along curve R between 1 and 3.

The present case involves the complication that racemic acid is present as a hydrate in equilibrium with the solutions, so that R may represent the

saturation curve of *rh*. If $\frac{1}{2}$ mole *d* and $\frac{1}{2}$ mole *l* are transferred to 3, apart from one mole *r*, 1 mole H_2O will disappear from the solution, which must be replaced by addition of 1 mole H_2O from outside to 3. The affinity of this process which obviously has to be included in the affinity of the total process depends on from where this water is taken. If it is taken from a mixture of *r* and *rh* (*r—rh*), the total process will consist in the formation of 1 mole *r*, in agreement with (2).

In view of this addition of H_2O the expression (5) for the affinity must be extended to

$$A^* = \mu_{d(1)} - \mu_{d(3)} + (\mu_{H_2O(r \longrightarrow rh)} - \mu_{H_2O(3)}) \tag{6}$$

Along the saturation curve of *rh* we have

$$d\mu_{rh} = \tfrac{1}{2} d\,\mu_d + \tfrac{1}{2} d\,\mu_l + d\,\mu_{H_2O} = 0 \tag{7}$$

and, furthermore, Gibbs-Duhem's equation

$$n_d\, d\mu_d + n_l\, d\mu_l + n_{H_2O}\, d\mu_{H_2O} = 0 \tag{8}$$

where *n* is the number of moles of the respective component in the solution.

Consequently, we obtain

$$\mu_{d(1)} - \mu_{d(3)} = \int_3^1 d\mu_d = \int_1^3 \frac{n_{H_2O} - 2n_l}{n_d - n}\, d\mu_{H_2O}$$

and by means of (6):

$$A^* = \int_1^3 \frac{n_{H_2O} - 2n_l}{n_d - n_l}\, d\mu_{H_2O} + (\mu_{H_2O(r \longrightarrow rh)} - \mu_{H_2O(3)}) \tag{9}$$

A rough calculation by means of van der Waals' equation for water vapour shows that the gas laws can here be applied. (The constants *a* and *b* are taken from Landolt-Börnstein: $a = 5.47$ and $b = 0.0305$, *p* being given in atmospheres and *v* in litres.) For the vapour, we have

$$\left(\frac{d\mu}{dp}\right)_T = v = RT\left(\frac{1}{p} + \frac{d\ln f}{dp}\right)$$

where *f* is the activity coefficient of the water vapour, and $\dfrac{d\ln f}{dp}$ is calculated by means of a and b to -0.00815 atm.$^{-1}$. In the pressure range observed, this correction term is of the order of magnitude of 0.2 $^0/_{00}$ and, thus, without significance.

Introducing the relation between the chemical potential and the vapour pressure in (9), we obtain

$$A^* = RT \left[\int_1^3 \frac{1 - x_A - 2x_l}{x_A - 2x_l} \, d\ln p + \ln \frac{p_{r-rh}}{p_3} \right] \tag{10}$$

where

$$x_A = \frac{n_d + n_l}{n_{H_2O} + n_d + n_l} \quad \text{and} \quad x_l = \frac{n_l}{n_{H_2O} + n_d + n_l}$$

SOLUBILITY DETERMINATIONS

Equation (10) shows that for the calculation of the affinity we must know the interdependence of vapour pressure and composition for solutions which are saturated with respect to rh and in which $n_d \geqq n_l$. The method applied in the present work leads only to corresponding values of the vapour pressure and the total quantities of d, r, and H_2O in the system containing a certain amount of rh in solid form. In order to arrive at the composition of the solution from these total quantities, solubility determinations of rh had to be performed in solutions with varying x_d. Two methods have been used, viz.

1. At relatively low d-concentrations ($x_d < 0.05$), weighed quantities of d, r, and H_2O are shaken for 1—2 days in a thermostat at 20° C. Subsequently, a weighed quantity of the saturated solutions is titrated with 0.1 N NaOH and phenolphtalein as an indicator. The distribution of the weighed substances between solution and solid phase is seen from the following table, where the quantities of the substances are given in g, and M denotes the molecular weight.

	Tartaric Acid (t)	Racemic Acid	H_2O
Total amounts taken	a	b	e
Amounts in the solid phase	—	$y \cdot M_r/M_{H_2O}$	y
Amounts in the solution	a	$b - y \cdot M_r/M_{H_2O}$	$e-y$

By titration we find the sum of the tartaric acid concentration and the racemic acid concentration, viz.

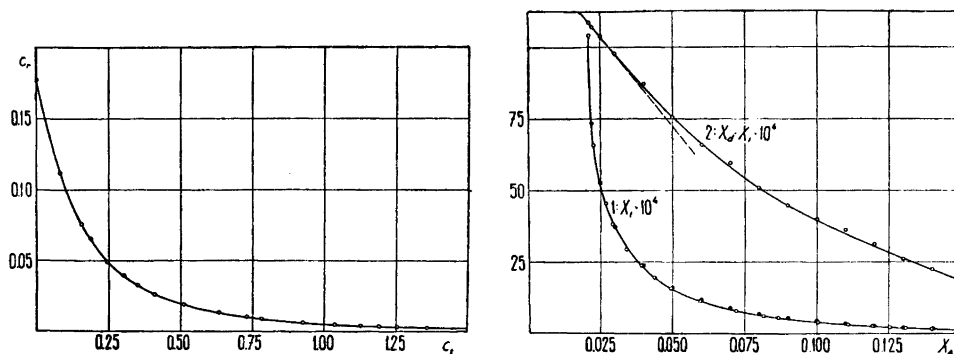$$c_A = \frac{g \cdot \text{total acid}}{g \cdot H_2O} = \frac{a + b - y \dfrac{M_r}{M_{H_2O}}}{e - y}$$

Fig. 2a and 2b. Solubility of racemic acid in solutions of tartaric acid.
O : experimental values
● : calculated from (15)

From this, we derive

$$y = \frac{a + b - e \cdot c_A}{\dfrac{M_r}{M_{H_2O}} - c_A}$$

and, for the solubility of the racemic acid in the same concentration units, we obtain

$$c_r = \frac{b - y\dfrac{M_r}{M_{H_2O}}}{e - y} = \frac{c_A\left(\dfrac{M_r}{M_{H_2O}} \cdot e - b\right) - a\dfrac{M_r}{M_{H_2O}}}{\dfrac{M_r}{M_{H_2O}} \cdot e - b - a}$$

With increasing x_d the solubility of the racemic acid decreases and, consequently, the inaccuracy of the titration method increases. For $x_d > 0.05$, the following procedure was therefore used.

2. Known amounts of d and r are placed in a weighed flask. Somewhat less H_2O than necessary to dissolve all racemic acid is added. The flask is rotated in the thermostat at 20° C and water is added by the drop until all racemic acid is dissolved. By renewed weighing of the flask the added amount of water is found and, thereby, the composition of the solution.

The results of the two experimental series are given in Figs. 2a and 2b. The preparations used were Kahlbaum's *p. a.* The racemic acid was repeatedly recrystallized. Titration proved that the preparations were pure (100 %).
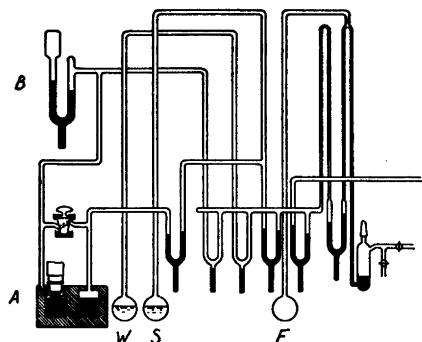
3

Fig. 3. Apparatus for the measurement of vapour pressures.
A Mercury manometer
B Mercury manometer
F Recipient
S Flask containing the system under investigation
W Flask containing water

The solubility determinations of racemic acid were continued in the range supersaturated with respect to tartaric acid.

Furthermore, the solubility of tartaric acid in H_2O was determined by titration to be $c_d = 1.36$.

MEASUREMENTS OF VAPOUR PRESSURES

Measuring principle

A flask containing weighed quantities of tartaric acid and racemic acid and an unknown quantity of H_2O is evacuated and, then, connected with the manometer by means of which the vapour pressure is measured. Subsequently, part of the water is distilled off and weighed. The vapour pressure at the new concentration is measured and the procedure is continued until the solution is saturated with both acids. The apparatus is shown in Fig. 3 which gives the details.

The connections in the system are made with mercury valves which are operated by means of a pressure-vacuum-system (not shown in the figure). A is a mercury manometer drilled out of an iron block and kept at 25° C by means of an interior thermostat arrangement, in order to prevent condensation of water. Readings are made by focussing a microscope upon the picture of a radiating slit, which it is itself projecting upon the mercury surface (Prytz's optical contact principle [3]). The accuracy is 0.002 mm Hg.

The 2 flasks W and S contain water and the system under investigation, respectively. They are placed in a thermostat at 20° C and connected with a shaking mechanism. To measure the vapour pressure, the 2 flasks are connected to each side of A. B is a mercury manometer with microscope reading and nonius graduation. It is connected to W and serves as a control. Water

is distilled from S to the recipient F, which is kept cold in ice. After the last reading, S is weighed in order to determine the amount of remaining water. Using this value, we can calculate the composition for all previous measurements in the same series.

Measurements

First, three series were made with solutions of d-tartaric acid without addition of racemic acid. The measurements extend to the range of supersaturation. The results, given in Fig. 4, are later applied to a calculation of the solubility of racemic acid in solutions of tartaric acid.

The pressure is always given in mm Hg. The vapour pressure of the solution is calculated on the basis of $p_0 = 17.535$ mm for pure H_2O. The activity coefficient of water is obtained from the relation

$$f_{H_2O} = \frac{p}{(1-x)\, p_0}$$

In the homogeneous system d-tartaric acid — water, the calculation of the composition of the solutions is performed directly from the total quantities. In systems which besides tartaric acid contain racemic acid in solid and in dissolved form, the determination of the composition of the liquid, on the basis of the total amounts, is made graphically by means of the solubility curve shown in Fig. 2a as follows, the amounts of the respective substances being given in g and the concentrations (c) in g dissolved substance per g H_2O in solution:

	Tartaric acid (t)	Racemic acid	H_2O
Total amounts in the system	a	b	e
Amounts in the solid phase	—	$y\, \dfrac{M_r}{M_{H_2O}}$	y
Amounts in the solution	a	$b - y\, \dfrac{M_r}{M_{H_2O}}$	$e - y$

$$c_r = f\,(y) = \frac{b - \dfrac{M_r}{M_{H_2O}} \cdot y}{e - y}$$

$$c_t = F\,(y) = \frac{a}{e - y}$$

$$c_r = \psi\ (c_t) = c_t \cdot \left(\frac{b}{a} - \frac{M_r}{M_{H_2O}} \cdot \frac{e}{a}\right) + \frac{M_r}{M_{H_2O}}$$

The relation $c_r = \psi\ (c_t)$ represents a straight line containing the point which gives the composition. The dependence between c_t and c_r on the basis of the solubility determination, however, is represented by the curve Fig. 2a. Consequently, the composition of a given solution is obtained from the point of intersection of this curve and the straight line $c_r = \psi\ (c_t)$.

Two series of measurements were performed, the results of which are shown in Fig. 4, where they are plotted together with the results from the tartaric acid series.

The results indicate that the vapour pressure within the limits of the experimental accuracy depends only on the total acid concentration, irrespective of the quantities of acid present in the d-form and in the l-form, respectively. This result suggests that the specific forces between the d- and the l-form, which are preponderant in the racemic crystals, are of no significance in the solutions investigated, or — less plainly spoken — that the racemic acid is not present in demonstrable amounts as a racemic compound in solution. Raoult [4], when examining this question by means of the more sensitive freezing point method, has found that a solution of 14.23 g anhydrous racemic acid in 100 g H_2O has a freezing point of $-1.807°$ C, while a tartaric acid solution of the same concentration has a freezing point of $-1.862°$ C. From this result he calculated that 6 per cent of the racemic acid at this concentration is present as a racemic compound. Apart from the fact that Raoult in his calculations erroneously uses $M_r = 376$ instead of 300, the solubility of racemic acid in water at $0°$ C., according to the available solubility determinations [5, 6] amounts to 8.25 g anhydrous racemic acid in 100 g H_2O; thus, Raoult's racemic acid solution has been considerably supersaturated. His result may probably be due to beginning crystallization and, therefore, it cannot be taken as a proof of the existence of a racemic compound in solution.

Furthermore, the vapour pressure of the saturated rh-solution without addition of d (p_3) and of a mixture of crystalline r and rh (p_{r-rh}) was measured. The first was determined in the same apparatus as described above, the second one by means of an ordinary manometer filled with liquid paraffin, the specific gravity of which was determined to be 0.888 g/cm^3. The results were as follows

$$p_3 = 17.149\ \text{mm Hg}$$
$$p_{r-rh} = 19.88\ \text{cm paraffin} = 13.03\ \text{mm Hg}$$

The vapour pressure measurement of $r-rh$ incipiently gave low and slowly increasing values and it took several weeks until equilibrium was reached.
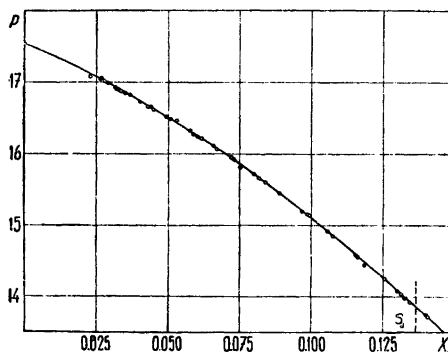
Fig. 4. Vapour pressure of solutions of d-tartaric acid in water (○) and in saturated racemic acid solutions (●).

This can be explained by assuming that the transformation of the crystal lattice of the hydrate to that of the anhydrous substance is a rather slow process. The equilibrium value was checked by repeatedly increasing and decreasing the temperature, by which procedure the above value was corroborated. Partington[7] has determined $p_{r\rightarrow rh}$ by means of a dynamic method at various temperatures. From his results we find by interpolation to 20° C, the value of 5.42 mm Hg, which is less than half of the value obtained in the present work. Already when taking into consideration that the racemic acid hydrate effloresces under normal conditions, Partington's result appears to be very dubious. If we, moreover, keep in mind the conditions observed at the adjustment of equilibrium, it becomes obvious that a dynamic method is inapplicable to the measurement of the vapour pressure of this system.

CALCULATION OF THE RACEMIZATION AFFINITY

For the calculation of the integral in equation (10), the interdependence of $\log p$ and $y = \dfrac{1 - x_A - 2x_l}{x_A - 2x_l}$ must be known. This is represented in the curve of Fig. 5.

For $p = p_3$, $y = \infty$, so that for pressure values near p_3, the integral cannot be calculated without further assumptions. Therefore, the integration was performed by calculating two partial integrals I_1 and I_2. For the range $0.03 \leqq x_A \leqq 0.1367$, the following empirical formula was used:

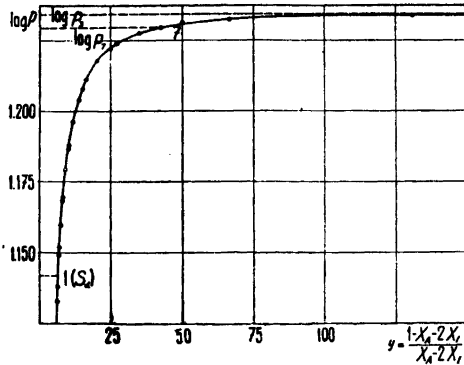$$\log p = 1.2391 - \frac{2.14}{6}\frac{1}{y}\frac{1}{y} - \frac{122}{72}\frac{1}{y^2} \tag{11}$$

Fig. 5. Vapour pressure of solutions of
d-tartaric acid in saturated racemic acid.
O : experimental values
● : calculates from (11)

The values calculated according to (11) are plotted in Fig. 5. For the integral in equation (10) we obtain, for the part of the curve considered, by insertion of (11)

$$I_1 = \int_1^7 \frac{1 - x_A - 2x_l}{x_A - 2x_l}\, d\ln p = \int_1^7 2.303\, y\, \frac{d\,\log\,p}{d\,y}\, dy$$

$$= \int_1^7 2.303 \left(\frac{2.14}{6}\frac{1}{y} + \frac{244}{72}\frac{1}{y^2} \right) dy$$

Insertion of $y_1 = 6.370$ and $y_7 = 42.63$ gives

$$I_1 = 2.604$$

From Fig. 2b, curve 2, it appears that the product $x_d \cdot x_l$ to a good approximation varies linearly with x_A between $x_A = 0.02$ and $x_A = 0.03$. This relation was used in the calculation of the other partial integral, I_2. From

$$(x_A - x_l)\, x_l = -\frac{b}{4} x_A - \frac{a}{4} \tag{12}$$

we obtain

$$x_l = \frac{1}{2} \left(x_A - \sqrt{a + bx_A + x_A{}^2} \right) \text{ and}$$

$$x_A - 2x_l = \sqrt{a + bx_A + x_A{}^2} = \sqrt{z}$$

Insertion of this expression gives, for I_2,

$$I_2 = \int_7^3 \frac{1 - x_A - 2x_l}{x_A - 2x_l} \frac{d\ln p}{dx_A} dx_A = \int_7^3 \frac{1 - 2x_A + \sqrt{Z}}{\sqrt{Z}} \frac{d\ln p}{dx_A} dx_A$$

For $\qquad \dfrac{d\ln p}{dx_A} = -\dfrac{1}{1 - x_A} + \dfrac{d\ln f_{H_2O}}{dx_A}$ we insert

$$\frac{d\ln p}{dx_A} = k - 1 - x_A - x_A^2$$

using

$$\frac{1}{1 - x_A} = 1 + x_A + x_A^2 \text{ and}$$

$$\frac{d\ln f_{H_2O}}{dx_A} = k \ (cf. \text{ Fig. 6, curve 1}).$$

Consequently, we obtain for the whole expression

$$I_2 = \int_7^3 \frac{(1 - 2x_A + \sqrt{Z})(k - 1 - x_A - x_A^2)}{\sqrt{Z}} dx_A$$

where $Z = a + bx_A + x_A^2$.

In the integration we take no account of a cubic term:

$$I_2 = \left(k - 1 - \frac{b}{2} + bk + \frac{3}{8}b^2 - \frac{a}{2}\right) \ln \left(\sqrt{Z} + x_A + \frac{b}{2}\right)$$

$$+ \left(1 - 2k + \frac{x_A}{2} - \frac{3b}{4}\right) \sqrt{Z} + kx_A - x_A - \frac{x_A^2}{2} - \frac{x_A^3}{3} \Bigg|_{x_7}^{x_3}$$

If we introduce the limiting values $x_7 = 0.03$ and $x_3 = 0.02087$ and also

$$a = -5.403 \cdot 10^{-4}$$
$$b = 5.04 \cdot 10^{-3}$$
$$k = 1.61 \cdot 10^{-1}$$

which three values we obtain from Fig. 2b, curve 2, and Fig. 6, we get
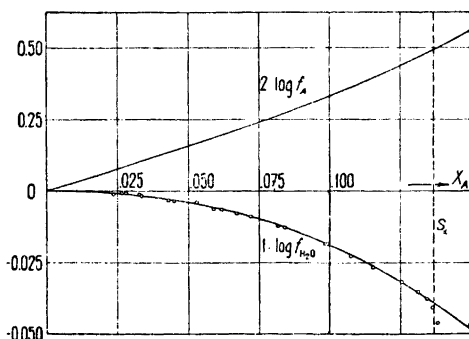
$$I_2 = 0.969$$

Fig. 6. Activity coefficients of tartaric acid and of water. Curves drawn according to (17) and (18).
O : *experimental values*

Hence, for the first term on the right side of equation (10) we get:

$$RT\ (2.604 + 0.969) = A_2{}^* = 2080\ \text{cal}$$

$A_2{}^*$ is the affinity for the formation of 168 g rh from 75 g d, 75 g l, and 18 g H_2O, which are taken from solution 3 saturated with rh.

Consequently we obtain for the total affinity,

$$A^* = 2080 + RT\ \ln \frac{13.03}{17.15} = 1920\ \text{cal}$$

CALCULATION OF THE SOLUBILITY OF RACEMIC ACID IN TARTARIC ACID SOLUTIONS

The vapour pressure of mixtures of d- and l-solutions depends — as shown — upon the total acid concentration only and not on the relative quantities of the components. Consequently, the activity coefficients for both forms in a given mixture must be equal. Therefore, the solubility of racemic acid in tartaric acid solutions of varying concentration can be calculated on the basis of the vapour pressure curve of tartaric acid solutions and of the solubility of racemic acid in water. According to the law of mass action, we have for a solution saturated with respect to rh:

$$x_d \cdot f_d \cdot x_l \cdot f_l\ (1 - x_A)^2\ f_{H_2O}^2 = K'_a \tag{13}$$

an equation which also may be written as

$$(x_A - x_l)\ x_l \cdot f_A^2 \cdot p^2 = K_a \tag{14}$$

where K'_a and K_a are constants.

From (14) we derive, for the dependence between x_l and x_A,

$$x_l = \frac{x_A}{2} - \frac{1}{2} \sqrt{x_A^2 - \frac{4Ka}{f_A^2 \cdot p^2}} \tag{15}$$

f_A is found from $f_{H_2O} = \dfrac{p}{(1-x_A)\, p_0}$ by means of Gibbs-Duhem's equation

$$x_A \frac{d \log f_A}{dx_A} + (1-x_A) \frac{d \log f_{H_2O}}{dx_A} = 0$$

$$\log f_{A(i)} = \int_0^{x_{A(i)}} - \frac{1-x_A}{x_A} \frac{d \log f_{H_2O}}{dx_A} \, dx_A \tag{16}$$

The values of $\log f_{H_2O}$ are plottet against x_A, giving a curve (Fig. 6), which may be represented by the empirical equation

$$\log f_{H_2O} = -1.60\ x_A^2 - 164\ x_A^{4.85} \tag{17}$$

According to (16) and (17) we obtain

$$\log f_A = \log f_{H_2O} + 3.20\ x_A + 207\ x_A^{3.85} \tag{18}$$

From the solubility of rh in pure H_2O we find $K_a = 0.04347$, the pressure being expressed in mm Hg. By means of this value, x_l was calculated for a series of values of x_A. The results of these calculations together with the results found in the solubility determinations are given in Fig. 2b, curve 1. The excellent agreement between these values confirms the absence of a specific association of the d- and l-compound.

Racemic acid is seen to be very slightly soluble in saturated tartaric acid, its solubility being about 100 times lower in tartaric acid than in water. This fact can be utilized in the preparation of racemic acid from tartaric acid. After racemization of tartaric acid with NaOH the separation of racemic acid from simultaneously formed meso-tartaric acid and non-converted tartaric acid usually occurs via the Ca-salts and the acid K-salts [8]. This rather troublesome and not very efficient procedure can be replaced by the following. After racemization, HCl is added to the mixture until the color of added methyl orange has changed. d-tartaric acid is added until saturation, whereby racemic acid crystallizes almost quantitatively, while meso-tartaric acid remains in the

solution. The precipitate is filtered off and washed with a solution of 100 g of tartaric acid in 100 g water, and is then recrystallized from alcohol in which — as will be shown later — the solubility of tartaric acid can be assumed to be about 13 times higher than that of racemic acid.

OTHER METHODS OF AFFINITY CALCULATION

A calculation of the affinity, which in formal respect is somewhat simpler than that previously applied, can be performed on the basis of the principle of allotropic transformations. According to (2), a mixture of equal parts of d- and l-tartaric acid can be regarded as an instable modification of racemic acid, and the transformation affinity

$$
\begin{aligned}
A^* &= \tfrac{1}{2}\,\mu_{d(d)} + \tfrac{1}{2}\,\mu_{l(l)} - \mu_{r(r)} \\
&= \tfrac{1}{2}\,\mu_{d(d)} + \tfrac{1}{2}\,\mu_{l(l)} - (\tfrac{1}{2}\mu_{d(r)} + \tfrac{1}{2}\mu_{l(r)}) \\
&= \mu_{d(s\rightarrow d)} - \mu_{d(s\rightarrow r)}
\end{aligned}
\tag{19}
$$

is identical with the racemization affinity.

According to (6), we have

$$
A^* = \mu_{d(s\rightarrow d)} - \mu_{d(s\rightarrow rh)} + \mu_{H_2O(r\rightarrow rh)} - \mu_{H_2O(s\rightarrow rh)}
\tag{20}
$$

Hereby, $\mu_{d\,(s\rightarrow r)}$, the chemical potential of d in the instable solution saturated with anhydrous racemic acid in water, becomes accessible to calculation. From (19) and (20) we obtain

$$
\mu_{d(s\rightarrow r)} - \mu_{d(s\rightarrow rh)} = \mu_{H_2O(s\rightarrow rh)} - \mu_{H_2O(r\rightarrow rh)}
\tag{21}
$$

which can be transformed to

$$
RT\ln \frac{x_{d(s\rightarrow r)}\,f_{d(s\rightarrow r)}}{x_{d(s\rightarrow rh)}\,f_{d(s\rightarrow rh)}} = RT\ln \frac{p_3}{p_{(r\rightarrow rh)}}
\tag{22}
$$

By insertion of the values $x_{d\,(s\rightarrow rh)} = 0.01044$, $f_{d\,(s\rightarrow rh)} = 1.166$, $p_3 = 17.15$, and $p_{(r\rightarrow rh)} = 13.03$ we obtain

$$
x_{d\,(s\rightarrow r)}\,f_{d\,(s\rightarrow r)} = 0.01602
\tag{23}
$$

If we insert this value and $x_{d\,(s\rightarrow d)} = 0.137$ and $f_{d\,(s\rightarrow d)} = 3.13$ (according to equation (18)) into equation (19) transformed to

$$A^* = RT\ln \frac{x_{d\,(s-d)}\ f_{d\,(s-d)}}{x_{d\,(s-r)}\ f_{d\,(s-r)}} \qquad (24)$$

we obtain $A^* = 1910\ cal$ in agreement with the previously calculated value. The solubility of r in H_2O is calculated from (23) to

$$x_{r\,(s-r)} = 2x_{d\,(s-r)} = 0.0264$$

After transformation of the precipitate in the instable solution into the hydrate, the concentration decreases to $x_{r\,(s-rh)} = 0.0209$.

SOLUBILITY IN NON-AQUEOUS SOLVENTS

If the ideal laws can be applied to the saturated solutions, the equation (24) can be simplified to

$$A^* = RT\ln \frac{x_{d\,(s-d)}}{x_{d\,(s-r)}} = RT\ln \frac{2\ x_{d\,(s-d)}}{x_{r\,(s-r)}} \qquad (25)$$

It is a supposition for the applicability of (25) that the solubilities in the solvent concerned are low and that no mutual association of the tartaric acids occurs in the solutions. On the other hand, an association of the tartaric acids with the molecules of the solvent can be advantageous to the applicability of (25) by counteracting the mutual association. It is, therefore, natural to use a solvent of polar character, since the association tendency of tartaric acid must be assumed to originate from the presence of carboxyl groups and hydroxyl groups. The question whether the conditions for the validity of (25) are fulfilled is best decided by performing solubility experiments in different solvents, as the affinity and consequently the ratio $\dfrac{x_{d\,(s-d)}}{x_{d\,(s-r)}}$ must be independent of the solvent.

Solubility determinations were performed in glacial acetic acid and in isobutyl alcohol. $C.$ 15 g of the solvent were shaken in a thermostat with an excess of the respective acid. $C.$ 10 g of the saturated solution were weighed accurately and evaporated in vacuo. The solubility was calculated from the evaporation residue. The results are given in Table 1.

From the values at 20° C the solubility quotient was calculated:

$$\underset{\substack{\text{glacial acetic}\\\text{acid}}}{\frac{x_{d\,(s-d)}}{x_{r\,(s-r)}}} = 12.80 \quad \text{and} \quad \underset{\substack{\text{isobutyl}\\\text{alcohol}}}{\frac{x_{d\,(s-d)}}{x_{r\,(s-r)}}} = 12.82$$

Table 1. Solubilities of tartaric acid and racemic acid in non-aqueous solvents.

Solute	Solvent	Temp °C	$\dfrac{\text{g acid}}{\text{g sol.}}$	x_A
tartaric acid	glac.acetic acid	20	0.01395	.005633
racemic acid	» » »	20	0.00110	.000440
tartaric acid	» » »	25	0.01662	.006716
racemic acid	» » »	25	0.00130	.000523
tartaric acid	iso-butylalcohol	20	0.04644	.02349
racemic acid	» »	20	0.00372	.00183

The agreement between these values is in favour of the applicability of equation (25). For the affinity we obtain, consequently,

$$A^* = RT\ln\ 25.62 = 1890\ cal$$

The agreement with previously found values must be considered satisfactory.

HEAT OF RACEMIZATION

The relation between racemization affinity and heat of racemization ΔH is given by the equation

$$\Delta H = T^2\ \frac{d\left(\dfrac{A^*}{T}\right)}{dT} \tag{26}$$

or, according to (25), by

$$\Delta H = RT^2\frac{d\ln\ \dfrac{x_{d\,(s-d)}}{x_{r\,(s-r)}}}{dT} = q_d - q_r \tag{27}$$

where q_d and q_r according to the method of derivation are the differential heats of solution per mole acid in the saturated solutions in question. The heat of racemization can, therefore, be determined on the basis of the temperature

coefficients of the solubilities. From the solubilities in glacial acetic acid at 20° C and 25° C given in Table 1 we calculate

$$q_d = 6150 \text{ cal} \qquad \text{and} \qquad q_r = 6000 \text{ cal}$$

Hence,

$$\Delta H = 150 \text{ cal}$$

This value is, however, rather uncertain, as ΔH is obtained as a difference between two much higher values. From these values, therefore, we can only conclude that the heat of racemization is low, much lower than the affinity. A transition temperature, if any, between $d + l$ and r, is therefore very far from the temperatures used here.

SUMMARY

1. The theoretical basis for the determination of the racemization affinity is discussed.

2. The solubility of racemic acid in tartaric acid solutions of varying concentrations is determined.

3. The vapour pressure of tartaric acid solutions and of saturated racemic acid in tartaric acid solutions is measured. The results show that no detectable specific association of the d- and l-form is found in solution.

4. The affinity of the process $d \longrightarrow r$ is calculated on the basis of the experimental results according to the principle of double salt formation. The value found is 1920 cal/150 g.

5. The solubility of racemic acid in tartaric acid solutions of different concentrations is calculated from the vapour pressure curve of tartaric acid and from the solubility of racemic acid in water. A method is outlined for the preparation of racemic acid, which is based upon the low solubility of racemic acid in strong tartaric acid solutions.

6. The racemization affinity is calculated according to the principle of allotropic transformation on the basis of the solubility of tartaric acid and of anhydrous racemic acid in water, glacial acetic acid, and isobutyl alcohol, respectively. The values found are 1910 cal/150 g and 1890 cal/150 g, respectively.

7. The heat of racemization is calculated on the basis of solubility determinations in glacial acetic acid to be 150 cal/150 g.

REFERENCES

1. Brønsted, J. N., *Kgl. Danske Videnskab. Selskabs., Naturvidenskab. math. Comm.* Series 7 **XII**, No. 6 (1915) 243.
2. Brønsted, J. N. *Kgl. Danske Videnskab. Selskab., Mat.-fys. Medd.* I, **5** (1918) 3.
3. Prytz, K. *Ann. Physik* **4** (1905) 16, 735.
4. Raoult, F. M. *Z. physik. Chem.* **1** (1887) 186.
5. Leidie, E. *Z. anal. Chem.* **22** (1883) 269.
6. Kuhn, R., and Wagner-Jauregg, T. *Ber.* **61** (1928) 487.
7. Partington, J. R. *J. Chem. Soc.* **99** (1911) 466.
8. *Cf. e. g. Org. Syntheses* **6** (1926) 82.