STUDIES ON THE NATURE OF THE RACEMIC MODIFICATION OF OPTICALLY ACTIVE COMPOUNDS

Part V. Roozeboom Solubility Composition Isotherms for Mixtures of Active and Inactive Camphoric Acids in Water at 25° C., 45° C., and 100° C.

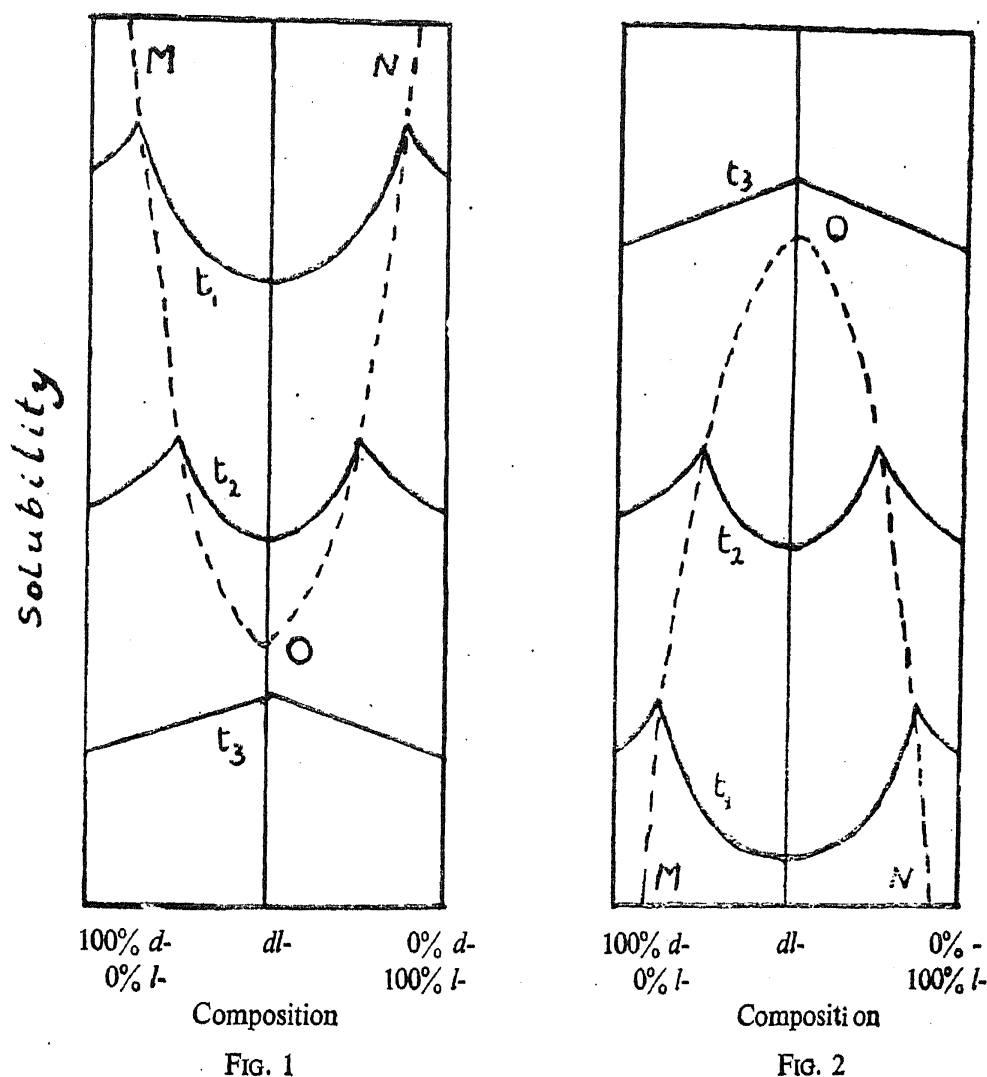BY BAWA KARTAR SINGH, F.A.Sc., AND BAL KISHORE K. NAYAR

(*From the Panjab University Institute of Chemistry, Lahore, and the Department of Chemistry, University of Allahabad*)

THE present work is in continuation of Part III in this series.[1] The solubility-composition isotherms for mixtures of active and inactive camphoric acids in water at 25° C., 45° C. and at the boiling points of the solutions have been determined with a view to ascertain the variation of the solubility isotherms with temperature, and if possible, to find out the temperature of transition of the rasemic compound into the racemic mixture.

Roozeboom[2] and also Bruni[3] have theoretically discussed, from the phase rule standpoint, the solubility relations existing between optical isomerides and their racemic forms (mixtures, compounds, or solid solutions). The solubility composition isotherm for a simple mixture of *d*- and *l*-isomers without the formation of a racemic compound would give a curve consisting of two parts having a maximum of solubility at the isothermal invariant point for the *d*- and *l*-forms. In the case of a racemic compound, the curve would consist of three parts with two invariant points, one for the *d-dl*-system, the other for the *l-dl*-system.

It may be pointed out that the Bruni-Roozeboom solubility isotherms of mixtures of optically active and inactive forms in a given solvent at different temperatures would form a family of curves in which the isothermal invariant points would all lie on a smooth curve (MON) symmetrical about the *dl*-axis and cutting it at some point O (Figs. 1 and 2). The temperature at which the solubility of the *dl*-form corresponds to this point of intersection (O) gives the transition point. At all temperatures where the solubility of the inactive form lies on the concave side of the curve (MON) connecting the invariant points, the racemic form exists as a *dl*-compound; at all temperatures on the convex side, as a *dl*-mixture.

100% d-   dl-   0% d-
0% l-   100% l-

Composition

FIG. 1

100% d-   dl-   0% -
0% l-   100% l-

Composition

FIG. 2

Camphoric acids[1] and camphor-β-sulphonic acids[4] are the only cases, in which as far as we are aware, Roozeboom solubility-composition isotherms giving the solubility relations which exist between the optical enantiomorphs and the racemic forms have been investigated, and the exact shape and slopes of the curves determined. The inactive acids in both cases were shown to be *dl*-compounds, a result in complete agreement with our previous studies by the Roozeboom freezing point method.[5] In the present paper we adduce further data in support of the racemic camphoric acid being a *dl*-compound. It is also shown that the transition temperature (from racemic compound to racemic mixture) of camphoric acid-water system lies considerably above 100° C.

EXPERIMENTAL

The *d-*, *l-* and *dl*-camphoric acids were prepared and purified by the methods described by Singh and Mahanti.[6] The measurements of solubility at 25° C. and 45° C. were made in the apparatus described in Part III.

Bawa Kartar Singh and others

The measurements of solubility at the boiling points were made in an apparatus similar in principle to one described by Seidel.[7] Ebullition kept the solution well stirred and mechanical agitation was also employed to ensure proper release of supersaturation, if any. The maximum temperature during steady boiling was noted. For transferring the solution suction was used.[8] A tube containing fused calcium chloride was inserted between the receiver and the point where suction was applied, to absorb any water vapour escaping from the transferred solution during suction. The acid in solution was estimated directly by titration. For determination of the isothermal invariant points, 10 c.c. of alcohol was added to the receiver and the total volume made upto 100 c.c. so that the solution contained approximately 10% alcohol. A portion of the solution was used for polarimetric analysis and another portion for titration. The specific rotation of

TABLE I

Solubility of mixtures of d- *and* dl-*camphoric acids in water at 45° C.*

Amount of acid (gm.)/100 gm. of solution	Amount of acid (gm.)/100 gm. of solvent	Amount of d-acid	Amount of dl-acid	Percentage composition	
				d-acid	dl-acid
1·127	1·140	1·140	..	100·0	0·0
1·151	1·164	1·102	·062	94·6	5·4
1·163	1·177	1·101	·076	93·5	6·5
0·885	0·893	0·804	·089	90·1	9·9
0·750	0·756	0·668	·088	88·4	11·6
0·620	0·624	0·533	·091	85·5	14·5
0·494	0·497	0·400	·097	80·6	19·4
0·386	0·388	0·267	·121	68·9	31·1
0·339	0·340	0·134	·206	39·2	60·8
0·317	0·318	..	·318	0·0	100·0

TABLE II

Solubility of mixtures l- *and* dl-*camphoric acids in water at 45° C.*

Amount of acid (gm.)/100 gm. of solution	Amount of acid (gm.)/100 gm. of solvent	Amount of l-acid	Amount of dl-acid	Percentage composition	
				l-acid	dl-acid
1·132	1·145	1·145	..	100·0	0·0
1·148	1·161	1·111	0·050	95·7	4·3
1·165	1·179	1·101	0·078	93·4	6·6
0·730	0·735	0·649	0·086	88·2	11·8
0·576	0·579	0·486	0·093	83·9	16·1
0·432	0·434	0·323	0·111	74·5	25·5
0·343	0·344	0·162	0·182	46·9	53·1
0·317	0·318	..	0·318	0·0	100·0

TABLE III

Solubility of mixtures of d- *and* dl-*camphoric acids in water at* 25° C.

Amount of acid (gm.)/100 gm. of solution	Amount of acid (gm.)/100 gm. of solvent	Amount of *d*-acid	Amount of *dl*-acid	Percentage composition	
				d-acid	*dl*-acid
0·725	0·730	0·730	..	100·0	0·0
0·725	0·730	0·699	0·031	95·7	4·3
0·727	0·732	0·692	0·040	94·5	5·5
0·535	0·538	0·495	0·043	92·0	8·0
0·410	0·412	0·371	0·041	90·0	10·0
0·314	0·315	0·247	0·068	78·5	21·5
0·235	0·236	0·123	0·113	52·3	47·7
0·228	0·229	0·049	0·180	21·5	78·5
0·226	0·227	..	0·227	0·0	100·0

TABLE IV

Solubility of mixtures of l- *and* dl-*camphoric acids in water at* 25° C.

Amount of acid (gm.)/100 gm. of solution	Amount of acid (gm.)/100 gm. of solvent	Amount of *l*-acid	Amount of *dl*-acid	Percentage composition	
				l-acid	*dl*-acid
0·718	0·723	0·723	..	100·0	0·0
0·726	0·731	0·700	0·031	95·7	4·3
0·727	0·732	0·692	0·040	94·5	5·5
0·363	0·364	0·313	0·051	86·0	14·0
0·251	0·252	0·156	0·096	62·2	37·8
0·229	0·230	0·078	0·152	33·9	66·1
0·226	0·227	..	0·227	0·0	100·0

TABLE V

Solubility of camphoric acids at boiling point of water

Solubility of *dl*-camphoric acid in water (100·2° C.) = 2·412 gm./100 gm. solution

Solubility of *d*-camphoric acid in water (100·4° C.) = 8·325 gm./100 gm. solution

Solubility of *l*-camphoric acid in water (100·4° C.) = 8·429 gm./100 gm. solution

Solubility at the invariant point (100·4° C.) (*d*+*dl*-) = 8·954 gm./100 gm. solution

Solubility at the invariant point (100·4° C.) (*l*+*dl*-) = 9·015 gm./100 gm. solution

Specific rotation in 10% alcohol $[\alpha]_{5461}^{35°} = \pm 55°$

The percentage of *d*-acid at invariant point = 87·5

The percentage of *l*-acid at invariant point = 88·1

TABLE VI

The percentage composition of camphoric acid at the isothermal invariant point at different temperatures

Temperature (°C.)	Iso. Inv. point of *d-dl*-system	Iso. Inv. point of *l-dl*-system
25	94·5 *d*-acid	94·5 *l*-acid
35	94·1 ,,	94·0 ,,
45	93·3 ,,	93·4 ,,
100	87·5 ,,	88·1 ,,

camphoric acid in " 10% " alcohol, at approximately the same concentration, was determined to calculate the amount of the active form corresponding to the rotation measured for the invariant points.

DISCUSSION

The results given in Tables I, II, III and IV are plotted in Fig. 3. The total solubility in 100 gm. of water is plotted against the percentage composition of the mixtures. The *l-dl*-portions of the graphs are drawn as mirror images of the *d-dl*-portions. The points corresponding to actual determination of the *l-dl*-system are found to fit on these curves. The solubility composition isotherm for 35° C., described in Part III, is also included for the sake of comparison.

It is found from the graphs that the curves for 25°, 35° and 45° C. are quite similar. In every case there are two invariant points and three curves. showing that the racemic form exists as a compound at all these temperatures The presence of the invariant points at the temperatures of boiling of the solution, indicates the existence of the racemic camphoric acid as a *dl*-compound at those temperatures also.

A study of the isothermal invariant points for the camphoric acid-water system at different temperatures (Table VI) shows that there is a slow shifting of these points nearer to the *dl*-axis with increasing temperature (thus corresponding to Fig. 2 discussed above). This points to the decreasing stability of the *dl*-camphoric acid as a compound as the temperature rises. The shift is not considerable, even over a temperature range of 75° C. Since at the transition point the percentage of the *dl*-compound is zero, we may expect that this temperature is high indeed.

A correlation is possible between the solubility curves and the melting point curves. The percentage composition at the eutectic points as deter-
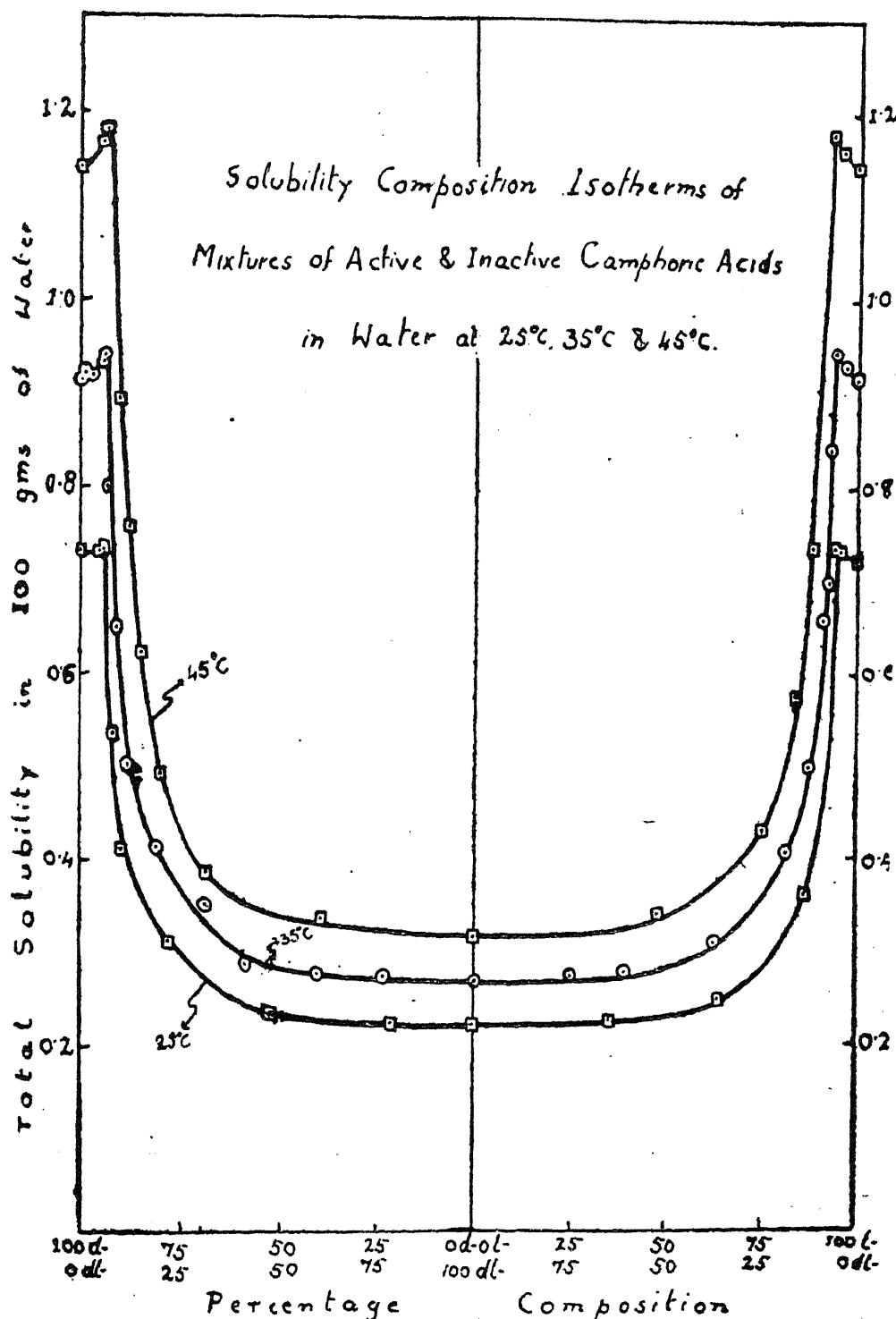
FIG. 3

mined by Singh and Perti was 80 *d-*: 20 *dl-*. This is quite in keeping with
our present results which give approximately 88 *d-*: 12 *dl-* at 100° C. The
transition temperature thus appears to be much higher than even the
melting points. The evidence for the existence of racemic compounds in
the liquid state is rather conflicting and it is, therefore, hazardous to make
any guess about the temperature of transition of inactive camphoric acid
from the *dl-*compound to the *dl-*mixture. An upper temperature limit for
the measurement of these solubility isotherms in the case of camphoric acids
is set as the acid changes into the anhydride above its melting point.

It is interesting to note here the latent heats of fusion of the three camphoric acids. According to Ross and Somerville,[9] the latent heats are 4,835 calories for the d- and l- forms and 13,840 calories for the dl- form. The great difference in the latent heats of the active and inactive forms points to the great stability of the dl- compound even at the melting point. Making allowance for the variation of latent heats for different melting points (188-89° C. for the active forms and 202-03° C. for the racemic) the extra heat consumed is likely to have been utilised for the breaking up of the dl- molecules into d- and l- forms. This dissociation being thus endothermic, we should expect by Le Chatelier's principle that rise in temperature will favour dissociation. The transition temperature may thus be expected to be beyond the temperatures of fusion, a result entirely in accordance with our present conclusion.

We wish to thank the University of Allahabad, where this work was carried out, for the grant of the Empress Victoria Readership to one of us (B.K.K.N.) which enabled him to take part in these investigations.

SUMMARY

1. The solubility composition isotherms of camphoric acids in water at 25° C., 45° C. and at the boiling points of the solutions have been determined. In each case three curves have been obtained showing that the racemic form is a true dl-compound at these temperatures.

2. The results obtained by the solubility method are in agreement with those already obtained from melting point data.

3. The temperature of transition of racemic camphoric acid from the compound into the mixture of optically active and opposite forms has been discussed.

REFERENCES

1. Singh, B. K., and Nayar, B. K. K...   *Proc. Ind. Acad. Sci.*, 1945, 22 A, 46.

2. Roozeboom, B.   *Ber.*, 1899, 32, 537 ; *Zeit. Physik. Chem.*, 1899, 28, 494.

3. Bruni   *Gazettā*, 1900, 30, 35.

4. Singh, B. K., and Perti, O. N.   *Proc. Ind. Acad. Sci.*, 1945, 22 A, 170.

5. —————   *Proc. Nat. Acad. Sci.*, 1944, 14 A, 79.

6. ——— and Mahanti, I.   *Proc. Ind. Acad. Sci.*, 1935, 2, 378.

7. —————   *Solubilities* by A. Seidell, 1919, 767–68.

8. —————   *Ibid.*, Walton and Judd, p. 764.

9. Ross and Somerville   *J. C. S.*, 1926, 2770.