STUDIES ON THE NATURE OF THE RACEMIC MODIFICATIONS OF OPTICALLY ACTIVE COMPOUNDS IN THE SOLID STATE

Part VI. The Nature of the Racemic Modifications of 3-Nitro-*p*-toluidino-, 5-Iodo-*o*-toluidino-, 4-Nitro-*o*-toluidino-, Oxy-, 2-Nitro-*p*-toluidino-, 3-Nitro-4-chloroanilino-, 2 : 5-Dichloroanilino- and 4-Chloro-*o*-toluidino-methylenecamphors

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IN this paper we have described our investigation of the nature of the racemic modifications of oxymethylenecamphor and its condensation products with 3-nitro-*p*-toluidine, 5-iodo-*o*-toluidine, 4-nitro-*o*-toluidine, 2-nitro-*p*-toluidine, 3-nitro-4-chloroaniline, 2 : 5-dichloroaniline and 4-chloro-*o*-toluidine.

A racemic modification may exist in the solid state in one of the following three forms: (1) a mechanical mixture (conglomerate) of the *d*- and *l*-forms; (2) a true racemic compound of the *d*- and *l*-forms; and (3) a solid solution (mixed crystal) of the optically active and opposite forms.

Three methods have been devised for determining the nature of the racemic modification. Two of these methods based on measurements of freezing-point and solubility of the racemic modification and its mixtures with its *d*- or *l*-form are due to Roozeboom and Bruni.[1] The third Biochemical Method, which depends upon the different actions of the optically active and opposite forms on micro- and higher-organisms, has been devised by one of us.[2]

We have employed Roozeboom's freezing-point (melting-point) method in this investigation. A melting-point-composition-diagram for mixtures of the racemic modification and its *d*- or *l*-form is prepared: a racemic mixture of the *d*- and *l*-forms gives a diagram consisting of two curves with a minimum of temperature, the eutectic point (Type I); the racemic compound gives a diagram consisting of three curves with two minima (eutectic points) and a maximum of temperature (Type II); and the solid solution (mixed crystal) of the *d*- and *l*-isomers will give a single continuous curve joining the melting-points of the optically active and opposite forms

(Type III). In the present investigation we have not come across an example of Type III.

The nature of the middle branch (Type II) often indicates the degree of stability of the compound; if the compound is sufficiently stable, the middle branch forms the greater part of the whole curve and rises and falls abruptly. When the compound is extremely unstable, the middle branch of the curve is smaller and is much flatter in appearance. We have applied these considerations in indicating the degree of stability of the racemic forms.

Experimental

The *dextro-*, *lævo-* and *racemic*-forms of the substances were prepared by methods already described.[3] The melting-point determinations were carried out by preparing an intimate mixture of accurately weighed quantities of the racemic modification and its *d-* or *l*-form and determining the melting-point of the mixture by the capillary-tube method. The melting-points (in °C.) are given in Tables I–VIII.

Discussion

3-*Nitro*-p-*toluidinomethylenecamphor*.—The melting-point determinations are given in Table I. The melting-point-composition-diagram (Fig. 1) consists of two symmetrical curves with a eutectic point. This shows that the racemic modification is a true *dl*-mixture and conforms to Type I mentioned above.

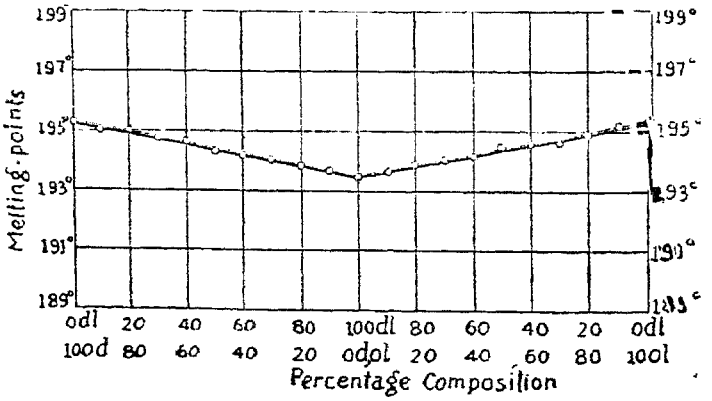

Fig. 1. 3-Nitro-*p*-toluidinomethylenecamphors

5-*Iodo*-o-*toluidinomethylenecamphor*.—The melting-point determinations are given in Table II. The melting-point-composition-diagram (Fig. 2) consists of three curves with two eutectic points. Therefore, the racemic modification is a true *dl*-compound and conforms to Type II mentioned above. It is very stable, and the range of stability is very large as the middle branch is very steep and occupies almost the whole of the diagram.

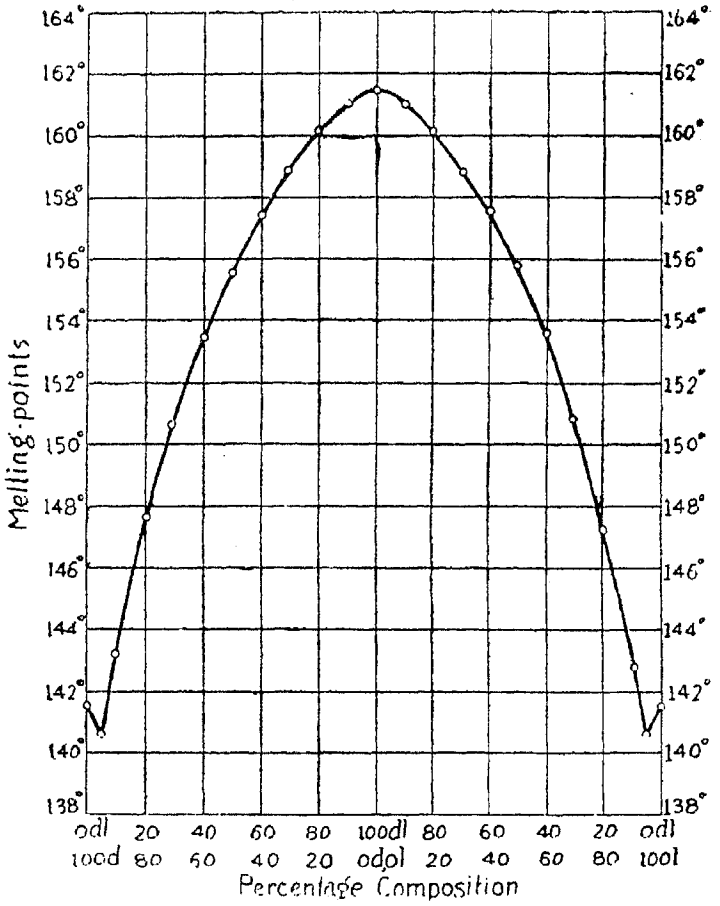

FIG. 2. 5-Iodo-*o*-toluidinomethylenecamphors

4-*Nitro*-o-*toluidinomethylenecamphor*.—The melting-point determinations are given in Table III. The melting-point-composition-diagram (Fig. 3) shows that the racemic modification is a true *dl*-compound (Type II). The shape of the middle branch indicates that it is fairly stable and that the range of stability is fairly large.

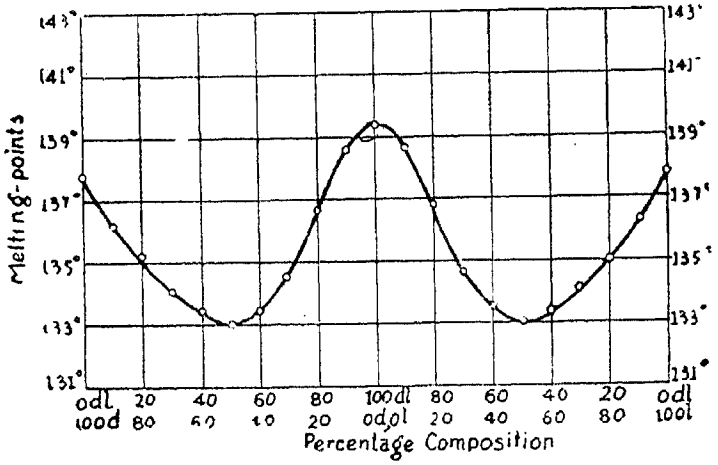

FIG. 3. 4-Nitro-*o*-toluidinomethylenecamphors

Oxymethylenecamphor.—The melting-point determinations are given in Table IV. The melting-point-composition-diagram (Fig. 4) shows that the racemic modification is a true *dl*-compound (Type II). It is stable but the range of stability is small.

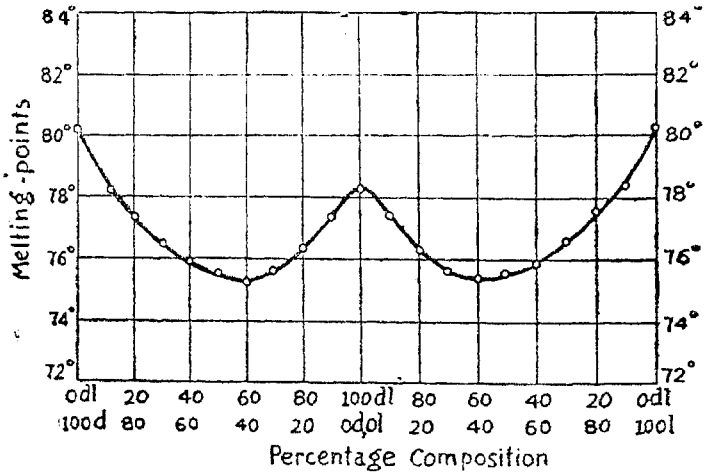

FIG. 4. Oxymethylenecamphors

2-*Nitro*-p-*toluidinomethylenecamphor.*—The melting-point determinations are given in Table V. The melting-point-composition-diagram (Fig. 5) shows that the racemic modification is a true *dl*-compound (Type II). It is stable but the range of stability is small as is clear from the shape of the middle branch of the diagram.

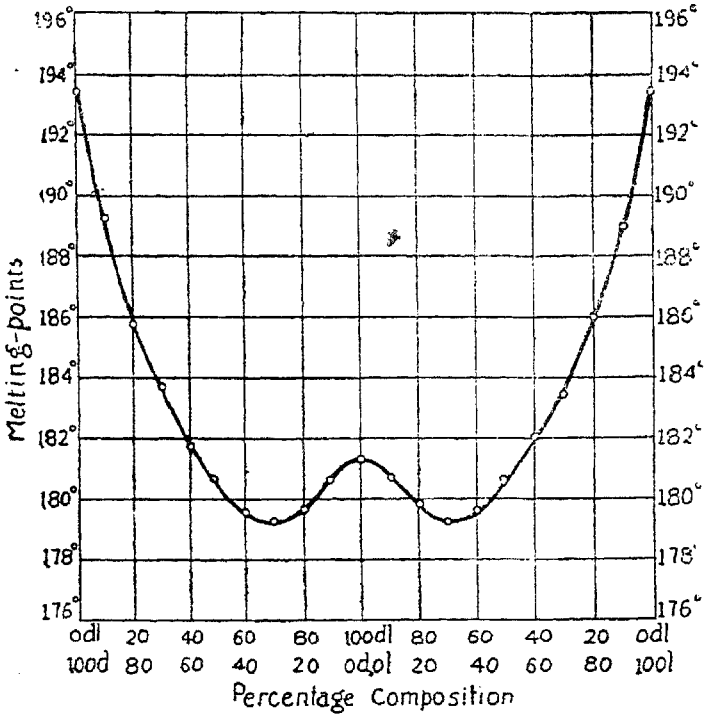

FIG. 5. 2-Nitro-*p*-toluidinomethylenecamphors

3-*Nitro*-4-*chloroanilinomethylenecamphor*.—The melting-point determinations are given in Table VI. The melting-point-composition-diagram (Fig. 6) shows that the racemic modification is a true *dl*-compound (Type II). It is much less stable as the middle curve is flatter in appearance.

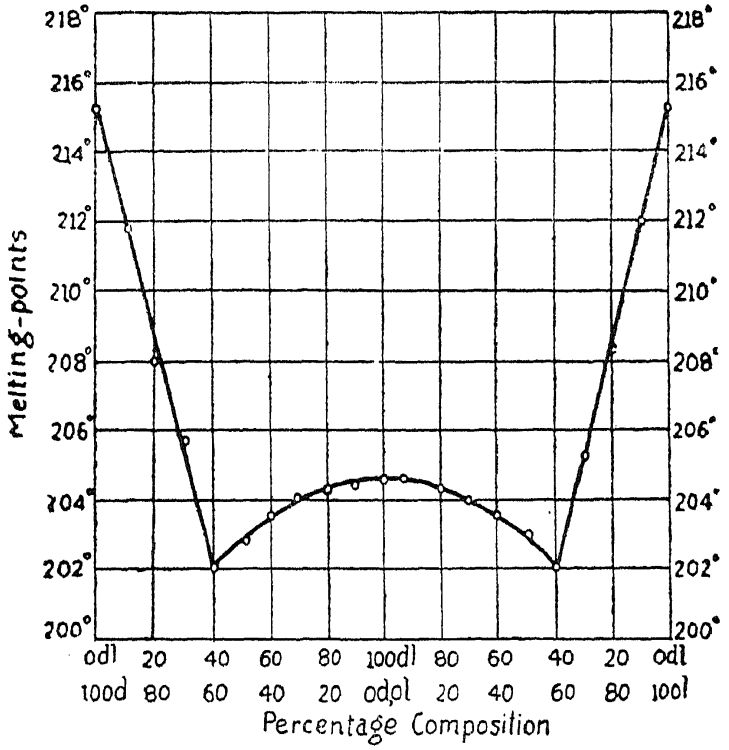

FIG. 6. 3-Nitro-4-chloroanilinomethylenecamphors

2: 5-*Dichloroanilinomethylenecamphor*.—The melting-point determinations are given in Table VII. The melting-point-composition-diagram (Fig. 7) shows that the racemic modification is a true *dl*-compound (Type II) of low stability and that the range of stability is small.

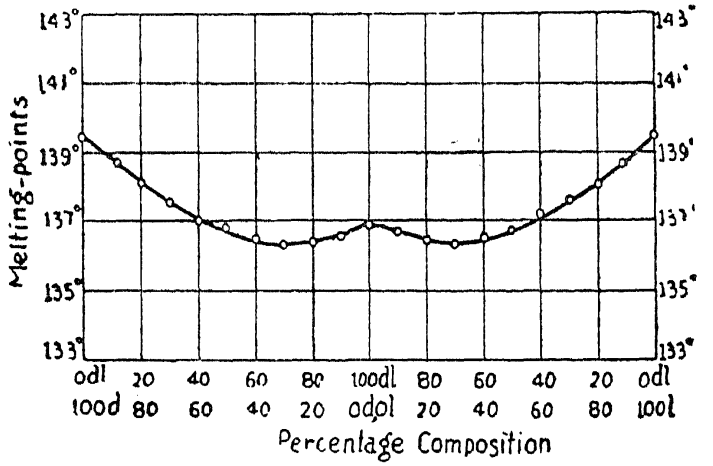

FIG. 7. 2 : 5-Dichloroanilinomethylenecamphors

4-*Chloro*-o-*toluidinomethylenecamphor*.—The melting-point determinations are given in Table VIII. The melting-point-composition-diagram (Fig. 8) shows that the racemic modification is a true *dl*-compound (Type II)

of little stability. The range of stability is very small as indicated by the flat nature of the middle curve.

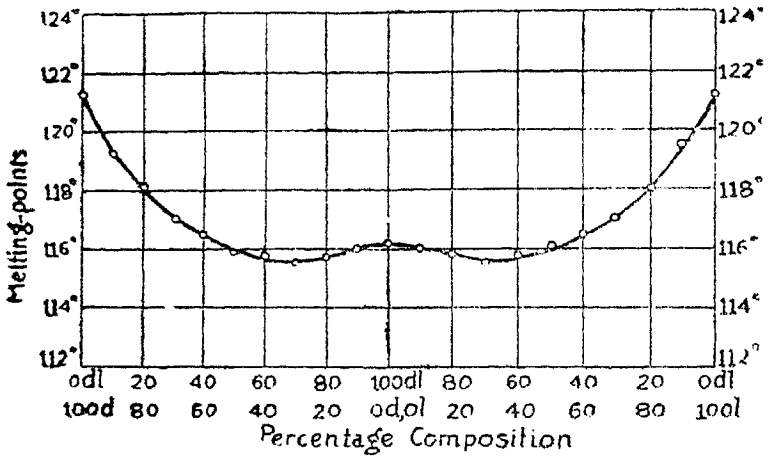

FIG. 8. 4-Chloro-*o*-toluidinomethylenecamphors

TABLE I

*3-Nitro-*p*-toluidinomethylene-camphors*

Mixed melting-points of the racemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	193·4°
90	10	193·6
80	20	193·8
70	30	194·0
60	40	194·2
50	50	194·3
40	60	194·6
30	70	194·7
20	80	195·0
10	90	195·0
0	100	195·2
90	10*l*	193·6
80	20	193·8
70	30	194·0
60	40	194·1
50	50	194·4
40	60	194·5
30	70	194·6
20	80	194·8
10	90	195·1
0	100	195·2

TABLE II

*5-Iodo-*o*-toluidinomethylene-camphors*

Mixed melting-points of the racemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	161·4°
90	10	161·0
80	20	160·1
70	30	158·9
60	40	157·4
50	50	155·5
40	60	153·4
30	70	150·6
20	80	147·6
10	90	143·2
5	95	140·6
0	100	141·5
90	10*l*	161·0
80	20	160·0
70	30	158·8
60	40	157·6
50	50	155·8
40	60	153·6
30	70	150·8
20	80	147·2
10	90	142·8
5	95	140·6
0	100	141·5

TABLE III

4-Nitro-o-toluidinomethylenecamphors

Mixed melting-points of the racemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	139·4°
90	10	138·6
80	20	136·6
70	30	134·5
60	40	133·4
50	50	133·0
40	60	133·4
30	70	134·0
20	80	135·2
10	90	136·2
0	100	137·8
90	10*l*	138·6
80	20	136·8
70	30	134·6
60	40	133·5
50	50	133·0
40	60	133·4
30	70	134·1
20	80	135·0
10	90	136·3
0	100	137·8

TABLE IV

Oxymethylenecamphors

Mixed melting-points of the recemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	78·2°
90	10	77·3
80	20	76·3
70	30	75·6
60	40	75·3
50	50	75·6
40	60	75·9
30	70	76·4
20	80	77·3
10	90	78·2
0	100	80·2
90	10*l*	77·3
80	20	76·3
70	30	75·5
60	40	75·3
50	50	75·5
40	60	75·9
30	70	76·5
20	80	77·5
10	90	78·3
0	100	80·2

TABLE V

2-Nitro-p-toluidinomethylenecamphors

Mixed melting-points of the recemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	181·3°
90	10	180·6
80	20	179·7
70	30	179·2
60	40	179·7
50	50	180·6
40	60	181·8
30	70	183·7
20	80	185·8
10	90	189·2
0	100	193·4
90	10*l*	180·6
80	20	179·9
70	30	179·2
60	40	179·6
50	50	180·6
40	60	182·0
30	70	183·4
20	80	186·0
10	90	189·0
0	100	193·4

TABLE VI

3-Nitro-4-chloroanilinomethylenecamphors

Mixed melting-points of the racemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	204·5°
90	10	204·4
80	20	204·2
70	30	204·0
60	40	203·4
50	50	202·7
40	60	202·0
30	70	205·6
20	80	208·0
10	90	211·8
0	100	215·2
90	10*l*	204·4
80	20	204·2
70	30	203·9
60	40	203·5
50	50	202·9
40	60	202·0
30	70	205·2
20	80	208·4
10	90	212·0
0	100	215·2

TABLE VII

2 : 5-*Dichloroanilinomethylene-camphors*

Mixed melting-points of the racemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	136·8°
90	10	136·6
80	20	136·4
70	30	136·2
60	40	136·4
50	50	136·7
40	60	137·0
30	70	137·5
20	80	138·1
10	90	138·7
0	100	139·4
90	10*l*	136·6
80	20	136·3
70	30	136·2
60	40	136·4
50	50	136·6
40	60	137·1
30	70	137·5
20	80	138·0
10	90	138·7
0	100	139·4

TABLE VIII

4-*Chloro*-o-*toluidinomethylene-camphors*

Mixed melting-points of the racemic modification with its *d*- or *l*-form.

Wt. % of the racemic modification	Wt. % of the *d*- or *l*-form	Melting-point of the mixture
100	0*d*	116·2°
90	10	116·0
80	20	115·7
70	30	115·5
60	40	115·7
50	50	115·9
40	60	116·4
30	70	117·0
20	80	118·1
10	90	119·2
0	100	121·2
90	10*l*	116·0
80	20	115·8
70	30	115·5
60	40	115·7
50	50	116·1
40	60	116·5
30	70	117·1
20	80	118·0
10	90	119·5
0	100	121·2

SUMMARY

The racemic modification of 3-nitro-*p*-toluidinomethylenecamphor is a true *dl*-mixture whereas the racemic modifications of 5-iodo-*o*-toluidino-, 4-nitro-*o*-toluidino-, oxy-, 2-nitro-*p*-toluidino-, 3-nitro-4-chloroanilino-, 2 : 5-dichloroanilino- and 4-chloro-*o*-toluidino-methylenecamphors are all true *dl*-compounds.

The stability of the racemic forms is also discussed.

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