Anomalous Racemates of Malic Acid

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The system (+)-malic acid − (−)-malic acid has been studied by melting-point diagrams and X-ray powder photographs. Besides the normal racemic compound in the ratio 1:1, the enantiomers form anomalous racemates in the ratio 1:3.

In 1927 two Japanese chemists reported the discovery of four optically active forms of β-hydroxy-γ-benzoylamino-butyric acid. As the compound has only one asymmetric carbon, the authors suggested that the occurrence of supernumerary isomers might be explained by some kind of restricted rotation.[1] On reinvestigation, Bergmann and Lissitzin [2] found that the forms with the highest rotations are the real enantiomers while the other two, which crystallise with one mole of water, are molecular compounds of the enantiomers in the ratio 1:2. It is well-known that enantiomers often crystallise together in the ratio 1:1, giving true racemic compounds. For molecular compounds of enantiomers in other ratios, Bergmann and Lissitzin proposed the name *anomalous racemates* or *anomalous racemic compounds*.

One of the present authors (A.F.) has found similar molecular compounds in the case of α,α'-dimethylglutaric acid.[3] They manifest themselves as special curve branches in the melting-point diagram of the antipodes. As they melt incongruently, the diagram gives no information as to the composition of the compounds. However, the α,α'-dimethylglutaric acid gives quasi-racemates with some other acids and the diagrams give indication for the existence of further molecular compounds in addition to those in the ratio 1:1. In the diagram of the system (+)-α,α'-dimethylglutaric acid − (−)-dilactic acid, a well-developed maximum at 75 mole-% of the former acid displayed the existence of an *anomalous quasi-racemate*.[4] As this is formed in the ratio 3:1 it is probable that the anomalous racemates of the α,α'-dimethylglutaric acid have the same composition.
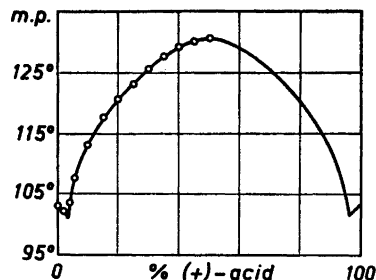
Fig. 1. Melting-point diagram of the system (+)- and (−)-malic acid.

It seems that anomalous racemates are very rare. We can, however, report that such compounds are formed by the well-known and much investigated malic acid.

The melting-point diagram of the system (+)- and (−)-malic acid has been studied by Timmermans and Vesselovsky,[5] who found that the inactive acid is a true racemic compound; as the diagram must be symmetrical, only the region 0—50 % (+)-acid was investigated. In connection with current work on the conditions for racemate formation, we had occasion to study their data and noted that some melting-points in the vicinity of 25 % (+)-acid don't fit quite well into the diagram, thus indicating some kind of irregularity. We reinvestigated the system very carefully and found a pronounced maximum at 50 % and a eutectic point at about 3.5 % (Fig. 1). The general shape of the curve is, however, rather unusual, showing a discontinuity or an inflexion at about 25 % (+)-acid. X-Ray powder photographs of a series of mixtures of (−)-malic acid and racemic malic acid revealed the existence of three crystalline phases, *viz.* the pure enantiomer, the normal racemate and a phase containing 25 % of the (+)-form, thus clearly indicating the formation of a molecular compound of the enantiomers in the ratio 1:3, that is an anomalous racemate.

It is obvious that the existence of a such compound may easily be over-looked if the melting-points of the diagram are not recorded very carefully or if the distances between adjacent points are too large. It is therefore possible that anomalous racemic compounds are less rare than it seems.

On the other hand, there are reasons to believe that they cannot be very common. The formation of a true racemic compound is certainly due to a combination of geometrical and polar factors, resulting in a closer packing, a more symmetrical structure and a more stable lattice than can be realised in the case of the pure enantiomers. Very often the (+)- and (−)-molecules are arranged in pairs having a centre of symmetry. A combination in another ratio than 1:1 can never attain the same symmetry and probably not the same close packing as the true racemic compound. It is therefore quite reasonable that normal racemic compounds are much more common, and that the anomalous racemates, if they are formed at all, melt incongruently and play a rather insignificant rôle in the melting point diagrams.

As seen from Table 1, the X-ray pattern of the normal racemate has relatively few lines compared to those of the enantiomer and the anomalous racemate; this indicates that even in the malic acid system the crystal lattice of the true racemate as expected has the higher symmetry.

Table 1. X-Ray powder data of (−)-malic acid, the normal racemate (ratio 1:1), and the anomalous racemate (ratio 1:3). (19 cm diameter Bradley camera, CrKα-radiation). The three strongest lines are designated I, II, and III. The relative intensities I are indicated as s, s− (strong), m+, m, m− (medium), w+, w, w− (weak) and w? (dubious).

	(−)-malic acid			racemic malic acid			anomalous racemate of malic acid (1:3)	
	d (Å)	I		d (Å)	I		d (Å)	I
	5.00	w−		4.79	w−		4.58	w
II	4.584	m+	I	4.405	s	I	4.30	s−
	4.431	w		4.238	w		4.207	w
	4.238	w+	II	3.761	s−		4.001	w?
	3.967	w+		3.654	w?	II	3.818	m+
I	3.648	s−		3.335	w−	III	3.695	m+
	3.421	w		3.227	m−		3.357	w−
	3.214	m−		2.727	m		3.198	w
	3.030	m		2.513	w+		3.043	w
	2.954	w−		2.416	w?		2.909	w+
	2.629	w+	III	2.393	m		2.771	w+
	2.515	w		2.240	w		2.688	w−
	2.425	w+		2.200	w−		2.630	w−
III	2.381	m+		2.153	w?		2.519	m−
	2.345	w−		2.082	w−		2.422	m
	2.287	w−		2.045	w−		2.382	m
	2.251	w+		2.008	w?		2.179	w−
	2.217	w−					2.147	w−
	2.169	w−					2.042	w?
	2.138	w−						
	1.988	w−						

As mentioned above, the anomalous racemates of Bergmann and Lissitzin [2] crystallise with one molecule of water. In this case, no melting-point diagram and no X-ray studies were reported. It would certainly be of interest to study this case more closely and to establish if the water is essential for the formation of the molecular compounds or if phases of the corresponding compositions are present also in the system of the anhydrous components.

EXPERIMENTAL

Melting point diagrams. The samples of laevorotatory and racemic malic acid were the best commercial products "for scientific purposes". Weighed mixtures of active and racemic acid were dissolved in a little acetone. After spontaneous evaporation at room temperature, the residue was powdered and dried in a desiccator. The melting-points were determined on a Leitz hot stage microscope. To avoid decomposition during the heating, the samples were introduced into the apparatus a little below the expected melting-points. The values were reproducible within 0.5°C.

X-Ray powder photographs. Using Phragmén-Hägg focusing cameras of the A and E type [6] and CrKα-radiation, X-ray powder patterns were recorded of (−)-malic acid, racemic malic acid and mixtures of the two compounds containing 40−33.3−30− 27.5−25−22.5−20 and 12.5 % (+)-malic acid. The samples used were prepared by evaporation at 50°C of aqueous solutions of weighed proportions of the two compounds, leaving the dry crystals at 50° overnight before specimens for the X-ray analyses were made. X-Ray powder patterns made directly from the commercially obtained preparations were identical to those described above. Evaporation to dryness at room-tempera-

ture gave poorly crystallized samples, from which only weak, diffuse and non-reproducible X-ray diagrams were obtained. The X-ray patterns of the mixtures containing more than 25 % (+)-malic acid could be identified as the superimposed patterns of *rac.* malic acid and the phase containing 25 % (+)-malic acid, respectively. The diagrams from mixtures containing less than 25 % of the (+)-acid consisted similarly of the superimposed patterns of the (−)-acid and the 25 % (+)-acid.

The X-ray patterns of the three phases, *viz.* (−)-malic acid, the normal racemate, and the anomalous racemate (ratio 1:3) were even recorded in a Debye-Scherrer camera; the results obtained are given in Table 1.

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