

Anal.—Calc. for $C_{12}H_{12}O_2$: C, 81.99; H, 11.18. Found: C, 81.90; H, 11.10.

The benzoate derivative had m.p. 292–294°; $[\alpha]_D^{25} +35.7^\circ$; IR spectrum: ν_{max}^{KBr} 5.97 and 7.95 (OBz), 6.10 and 12.40 ($>C=CH$) μ .

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Conductimetric Studies of Interactions of Optically Active Ions I: Interactions of Amphetamine with Mandelic and Tartaric Acids

NICOLAS H. CHOULIS

Abstract □ The conductances of 0.006 *M* aqueous solutions of *d*- and *l*-amphetamine were measured in equimolar aqueous solutions of *d*- and *l*-mandelic acid and *d*- and *l*-tartaric acid. Conductivity changes were recorded, and the results were interpreted in terms of ionic associations.

Keyphrases □ Amphetamine-mandelic acid interaction—conductimetric study of optically active ions □ Amphetamine-tartaric acid interaction—conductimetric study of optically active ions □ Optically active ions—amphetamine with mandelic or tartaric acid, conductivity changes □ Conductivity changes—optically active ions, amphetamine with mandelic and tartaric acids, ionic associations

The observed phenomena that optically active compounds such as bases may be used to resolve racemic acids (and vice versa) suggested that even under aqueous conditions a *d*-acid associates with an optically active base differently than does the corresponding *l*-acid. Conductimetric studies (1) of the association of *d*- and *l*-tris(ethylenediamine)-cobalt (III) iodide in a 0.003 *M* solution of both *d*- and *l*-sodium tartrate in water showed significant differences in mobility between the two cobalt isomers in the solutions of optically active tartrates.

Conductivity was used also to examine molecular associations of some organic salts at different concentrations (2). This method was chosen because association of the cations and anions would be expected to lead to a definite change in the conductivity of the solutions. Similar studies for isotopic lithium chlorides at various concentrations showed a 0.35% greater mobility for the ^6Li than for the ^7Li ions (3).

The purpose of the present report is to present the results of a series of measurements of the conductance of 0.006 *M* amphetamine solutions in equimolar solutions of optically active mandelic and tartaric acids.

EXPERIMENTAL

Materials—The following were used: *d*-mandelic acid¹, m.p. 133.5° [lit. (4) m.p. 133.8°] and specific rotation +156° [lit. (4) +156° in H₂O]; and *l*-mandelic acid¹, m.p. 132.5° [lit. (4) m.p. 132.8°] and specific rotation -156.2° [lit. (4) -156.2° in H₂O]. Mandelic acids were recrystallized from ethyl alcohol, filtered through sintered-glass funnels, and dried before melting points and optical rotations were taken. Also used were: *d*-tartaric acid², m.p. 169.5° [lit. (5) m.p. 168–170°] and specific rotation +12° [lit. (5) +12° in H₂O]; and *l*-tartaric acid², m.p. 169.5° [lit. (5) m.p. 168–170°] and specific rotation -12° [lit. (5) -12° in H₂O]. Tartaric acids were recrystallized from absolute alcohol, filtered, and dried in a desiccator before melting points and optical rotations were taken. *d*-Amphetamine, puriss.³, b.p. 204° [lit. (4) b.p. 203–204°] and n_D^{25} 1.517 [lit. (4) 1.517]; and *l*-amphetamine, puriss.³, b.p. 204° [lit. (4) b.p. 203–204°] and n_D^{25} 1.5172 [lit. (4) 1.517] were also used. The conductivity water of low CO₂ content was prepared by boiling distilled water for about 5 min. and cooling rapidly.

Apparatus and Methods³—Aqueous solutions of the bases and of the acids at exactly 0.006 *M* concentrations were prepared, and the individual resistances were measured at constant temperatures. Then 20 ml. of each base solution was added to exactly 20 ml. of each acid solution in beakers and were mixed well using magnetic stirrers. After temperature equilibrium, the resistances were taken.

¹ Eastman Organic Chemicals.

² Aldrich.

³ A Conductoscop E 365 B (Metrohm A. G.) was used with a Jones cell, model EA-655 (cell constant $c = 7.4 \text{ cm}^{-1}$).

Table I—Direct Conductivity Measurements of the Optically Active Amphetamine, Mandelic Acid, and Tartaric Acid

Compounds	Conductivity Readings, mho/cm. $\times 10^{-3}$
<i>d</i> -Amphetamine	13.708
<i>l</i> -Amphetamine	13.764
<i>d</i> -Mandelic acid	51.615
<i>l</i> -Mandelic acid	51.663
<i>d</i> -Tartaric acid	73.590
<i>l</i> -Tartaric acid	73.815

All experiments were carried out in triplicate (at $23 \pm 0.2^\circ$), giving practically identical results.

RESULTS AND DISCUSSION

Direct conductivity measurements (Table I) for the individual compounds were found using Eq. 1:

$$L = R \times S \times C \quad (\text{Eq. 1})$$

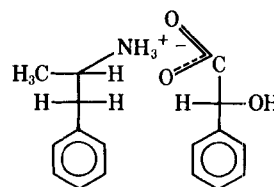
where L = true conductivity reading, R = reading on scale, S = range factor, and C = cell constant (7.4 cm^{-1} for the present experiment). Results are expressed in mhos/cm.

By taking into consideration the direct conductivity readings of the individual compounds (Table I), the theoretical conductances for the various salts can be calculated by adding the conductances of the components of the salts. The theoretical and direct values are summarized in Table II.

By comparing the theoretical and direct conductances of the various salts, it is indicated that a large number of ions are associated even in dilute solutions. It is known that when a salt formed from a reasonably strong acid and base is dissolved in water, complete ionization should be expected. However, when organic bases and acids are involved, it does not follow that there is complete dissociation. Moreover, when a given electrolyte is added to a solution of a second electrolyte and no significant change in volume or temperature takes place, the conductance of the resulting solution is expected to increase or decrease, the direction of the change depending largely upon the mobility of the ions and whether ionic interac-

Table II—Comparison of Direct and Theoretical Conductivity Measurements of the Various Salts in Solution

Salt	Direct Conductivity Readings, mho/cm. $\times 10^{-3}$	Theoretical Conductivity Readings, mho/cm. $\times 10^{-3}$
<i>d</i> -Amphetamine- <i>l</i> -mandelic acid	16.006	65.371
<i>d</i> -Amphetamine- <i>d</i> -mandelic acid	16.356	65.323
<i>l</i> -Amphetamine- <i>l</i> -mandelic acid	16.350	65.427
<i>l</i> -Amphetamine- <i>d</i> -mandelic acid	16.000	65.379
<i>d</i> -Amphetamine- <i>d</i> -tartaric acid	26.399	87.298
<i>d</i> -Amphetamine- <i>l</i> -tartaric acid	26.099	87.523
<i>l</i> -Amphetamine- <i>d</i> -tartaric acid	26.055	87.354
<i>l</i> -Amphetamine- <i>l</i> -tartaric acid	26.427	87.579



Scheme 1—Suggested position of acid-base association in solution: amphetamine mandelate

tion occurs. It was observed earlier (2, 6) that association of organic acids and bases is present in solution and that this association involves interaction of the hydrocarbon moieties of the molecules as well as electrostatic attractions of the solvated cationic and anionic heads of the molecules in the fashion depicted in Scheme 1.

The observed differences between the theoretical and direct conductance values is indicative of the quantity of electrolytes in the solution and also the degree of the acid-base association or ion-pair formation. Moreover, this degree varies among the various salts in the solution, depending on the optical rotation of the antipodes involved. This difference, which is much larger than the expected maximum experimental error of 0.1%, establishes that the mobilities of the various isomers are not equal. The results indicate that a *d/l*-diastereoisomer will have smaller mobility than a *d/d*. Consequently, within the experimental errors, the same is true when these ions are replaced by their optical antipodes, i.e., *l/d* and *l/l*, respectively.

The solubility of the *d/l* (or *l/d*) is higher than that of the *d/d* (or *l/l*) and, in fact, this is the way the salts are resolved.

Studies of the optical isomers of these acids with racemic amphetamine (and vice versa) did not show any significant conductimetric differences. Presumably the dilute solutions at the experimental conditions did not permit any resolution. *meso*-Tartaric was not examined, since this form of the acid is unresolved and, consequently, does not form optical isomers.

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