154. *The Resolution of* dl-*Menthyl* (−)*Mandelate.*

By ALEX. MCKENZIE and E. MARGARET LUIS.

WHEN an alcoholic solution of equal weights of (−)menthyl (−)mandelate and (−)menthyl (+)mandelate was evaporated, the product was identical with the ester which can be obtained more readily by the direct esterification of *r*-mandelic acid by (−)menthol and has been designated as (−)menthyl *r*-mandelate. It was shown by one of us that the latter ester belongs to Ladenburg's type of " partially racemic " compounds; it is well defined and homogeneous, and not a simple mixture, and it remains unchanged in melting point and rotatory power after repeated crystallisations (McKenzie, J., 1904, **85**, 378, 1249). The transition temperature at which this partial racemate breaks up into a conglomerate of two diastereoisomerides probably lies below −15° (Findlay and Hickmans, J., 1909, **95**, 1386).

Closely related to it are (−)menthyl *dl*-phenylchloroacetate (McKenzie and Smith, J., 1923, **123**, 1962), (−)menthyl *dl*-phenylbromoacetate (McKenzie and Smith, J., 1924, **125**, 1582), and (−)menthyl *dl*-α-naphthylglycollate (McKenzie and Gow, J., 1933, 32). These esters cannot be crystallised unchanged, but separation into diastereoisomerides occurs in each case. They are thus in marked contrast to (−)menthyl *r*-mandelate.

Accordingly, since *dl*-menthol is now readily available, it was of interest to make a more extended study of the menthyl mandelates, and it has now been found that dl-*menthyl* (−)*mandelate* is not partially racemic but undergoes resolution into its diastereoisomerides. (+)*Menthyl* (−)*mandelate* is the more sparingly soluble of the two, and it was isolated in a state of optical purity. Incidentally, a method is here provided for obtaining (+)menthol by resolution of *dl*-menthol (cf. Read and Grubb, J., 1931, 188; *J. Soc. Chem. Ind.*, 1932, **51**, 329T).

dl-Menthyl (−)mandelate and r-*menthyl* r-*mandelate* were also isolated.

EXPERIMENTAL.

(+)*Menthyl* (−)*Mandelate.*—A mixture of (−)mandelic acid (30 g.) and *dl*-menthol (90 g.) was heated on the water-bath for 16 hours in the presence of hydrogen chloride. The ethereal solution of the product was washed with dilute aqueous sodium bicarbonate until all the acid was removed, the ether expelled, and the residue distilled in steam to remove unattacked menthol. The yield of crude ester was 56 g. A portion of it (4 g.) was crystallised six times from aqueous acetic acid (65%), the crystals obtained giving in ethyl alcohol $[\alpha]_D^{18^\circ}$ − 2·7° (c = 2·967). It thus appeared that (+)menthyl (−)mandelate is less soluble in aqueous acetic acid than is its diastereoisomeride, (−)menthyl (−)mandelate, which has $[\alpha]_D$ − 138·6° (McKenzie, *loc. cit.*). The main amount of the crude ester (52 g.) was then crystallised nine times from aqueous acetic acid (65%); the final crystals (5·8 g.), m. p. 96—98°, gave in ethyl alcohol $[\alpha]_D^{17\cdot5^\circ}$ + 1·6° (c = 4·638). Although this product was not far removed from optical purity, the separation of traces of the strongly lævorotatory diastereoisomeride was tedious, but by fractional crystallisation from aqueous ethyl alcohol (66%) about 4 g. of the optically pure compound were obtained.

(+)*Menthyl* (—)*mandelate* separates from ethyl alcohol in glassy rectangular prisms, and from light petroleum (b. p. 40—60°), in which it is more sparingly soluble than in alcohol, in long needles, m. p. 98—99° (Found: C, 74·6; H, 9·0. $C_{18}H_{26}O_3$ requires C, 74·4; H, 9·0%). In ethyl alcohol: $l = 1$, $c = 4{\cdot}639$, $\alpha_{5791}^{20{\cdot}5^\circ} + 0{\cdot}42^\circ$, $[\alpha]_{5791}^{20{\cdot}5^\circ} + 9{\cdot}1^\circ$; $\alpha_{5893}^{20{\cdot}5^\circ} + 0{\cdot}45^\circ$, $[\alpha]_{5893}^{20{\cdot}5^\circ} + 9{\cdot}6^\circ$; $\alpha_{5461}^{20{\cdot}5^\circ} + 0{\cdot}42^\circ$, $[\alpha]_{5461}^{20{\cdot}5^\circ} + 9{\cdot}1^\circ$.

Its optical purity was established in two ways. (1) Its antimeric form, (—)menthyl (+)mandelate (McKenzie, *loc. cit.*; Findlay and Hickmans, *loc. cit.*; Roger, J., 1932, 2168), was examined under the same conditions as the above, giving $\alpha_{5791} - 0{\cdot}43^\circ$, $\alpha_{5893} - 0{\cdot}44^\circ$, $\alpha_{5461} - 0{\cdot}42^\circ$. (2) A 1 dcm. tube containing a solution of (+)menthyl (—)mandelate ($c = 4{\cdot}639$) was placed in the polarimeter trough, and behind it in another 1 dcm. tube the solution of (—)menthyl (+)mandelate of the same concentration. No optical activity was detected for λ 5791, 5893 or 5461.

Saponification of (+)*Menthyl* (—)*Mandelate.*—Alcoholic sodium hydroxide (18 c.c.) containing 1·1 g. of sodium hydroxide was added to a solution of the ester (3·7 g.) in ethyl alcohol (50 c.c.). After heating for 3 hours, the bulk of the alcohol was removed, and the residue distilled in steam. The resulting (+)menthol was separated by filtration from the distillate. Yield: 1·5 g. It had m. p. 42—43°, and was optically pure. In ethyl alcohol: $l = 1$, $c = 2{\cdot}045$, $\alpha_{D}^{16^\circ} + 1{\cdot}02^\circ$, $[\alpha]_{D}^{16^\circ} + 49{\cdot}9^\circ$. Read and Grubb (J., 1931, 188) give $[\alpha]_{D}^{25^\circ} + 49{\cdot}9^\circ$ ($c = 1{\cdot}9550$) in the same solvent. The mandelic acid was recovered, and according to expectation was very largely racemised, giving $[\alpha]_{D}^{15^\circ} - 54{\cdot}7^\circ$ ($c = 6{\cdot}736$) in water.

Esterification of (—)*Mandelic Acid by* (+)*Menthol.*—The (+)menthol used was recovered from an experiment on the fractional esterification of *r*-α-naphthylglycollic acid (McKenzie and Gow, *loc. cit.*). (—)Mandelic acid (0·7 g.) was heated with (+)menthol (2 g.) and the crude ester was obtained as previously described for the esterification of *dl*-menthol. After two crystallisations from ethyl alcohol the ester obtained had m. p. 98—99° (Found: C, 74·6; H, 8·9. Calc.: C, 74·4; H, 9·0%). In ethyl alcohol: $[\alpha]_D + 9{\cdot}4^\circ$ ($c = 4{\cdot}648$). The ester was thus identical with that obtained from the resolution.

dl-*Menthyl* (—)*Mandelate.*—A mixture of 0·2952 g. of (+)menthyl (—)mandelate, m. p. 98—99°, and 0·2952 g. of (—)menthyl (—)mandelate, m. p. 81—82° (McKenzie, *loc. cit.*), was dissolved in acetone, and the solvent expelled by evaporation at the ordinary temperature. After drying under diminished pressure, the *ester* had m. p. 76—77° (Found: C, 74·5; H, 9·1. $C_{18}H_{26}O_3$ requires C, 74·4; H, 9·0%). In ethyl alcohol: $l = 1$, $c = 4{\cdot}646$, $\alpha_{D}^{20^\circ} - 2{\cdot}99^\circ$, $[\alpha]_{D}^{20^\circ} - 64{\cdot}4^\circ$. This value is practically identical with that calculated from the values + 9·6° and — 138·6° for the diastereoisomerides.

The ester (0·5 g.) was crystallised from light petroleum (b. p. 40—60°). The crystals (0·2 g.) which separated had $[\alpha]_{D}^{20^\circ} = -48^\circ$ ($c = 5{\cdot}76$), a value which showed that resolution had occurred, and that (+)menthyl (—)mandelate predominated in the mixture.

r-*Menthyl* r-*Mandelate.*—An ethyl-alcoholic solution of a mixture of 0·93 g. of (+)menthyl (—)mandelate, m. p. 98—99°, and 0·93 g. of (—)menthyl (+)mandelate, m. p. 98—99°, was evaporated to dryness at the ordinary temperature, and was then crystallised from aqueous ethyl alcohol. r-*Menthyl* r-*mandelate* separated in rectangular prisms, m. p. 80—81° (Found: C, 74·4; H, 8·8. $C_{18}H_{26}O_3$ requires C, 74·4; H, 9·0%).

UNIVERSITY COLLEGE, DUNDEE.
UNIVERSITY OF ST. ANDREWS.

[*Received, March* 17*th*, 1934.]