97. *Optical Isomerism due to symmetrically placed Hydrogen and Deuterium Atoms. Part II.*

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The paper is a contribution to the question of the possible optical activity of organic compounds due to the difference between hydrogen and deuterium in their molecules.

In view of the negative or indecisive results hitherto recorded it was decided to attack the problem along the lines of the successful resolution of αγ-diphenyl-αγ-dinaphthylallene by Maitland and Mills (J., 1936, 987). Attempts to obtain an active allene by dehydration of either *αγ-diphenyl-γ-pentadeuterophenyl-α-*1-*naphthylallyl alcohol* (VII, R = C_6D_5) and *αγ-diphenyl-α-pentadeuterophenyl-γ-*1-*naphthylallyl alcohol* (II, R = C_6D_5) with *d*-camphorsulphonic acid, however, gave negative results. Furthermore, the isomeric alcohols, *αγ-diphenyl-α-*p-*tolyl-γ-*1-*naphthylallyl alcohol* (II, R = *p*-tolyl) and *αγ-diphenyl-γ-*p-*tolyl-α-*1-*naphthylallyl alcohol* (VIII, R = *p*-tolyl), also gave negative results in attempts at asymmetric dehydration, although in the light of the success of Maitland and Mills, the latter alcohol at any rate was expected to give a positive result.

d-Tartaric and *d*- and *l*-mandelic acids act as asymmetric dehydrating agents on αγ-diphenyl-αγ-di-1-naphthylallyl alcohol.

*Phenyl β-phenyl-β-*p-*tolylvinyl ketone* (VI, R = *p*-tolyl) has been obtained as a mixture of two well-defined geometrical isomers, the dipole moments of which have been measured in order to decide their configurations.

The question of optical activity of organic compounds due to the difference between hydrogen and deuterium atoms in their molecules has engaged the interest of several workers. All compounds of the type $CHDR_1R_2$ hitherto prepared have either been inactive or have given such small rotations as to be controversial and most of the experiments have been indecisive. It was then thought that a compound, the dissymmetry of whose molecules depended on the difference between two radicals, one containing wholly hydrogen atoms and the other wholly or partly deuterium atoms, ought to give more conclusive results. The reported resolution of α-pentadeuterophenylbenzylamine by Clemo and (the late) McQuillen (J., 1936, 808) has been criticised on the ground that the hexadeuterobenzene used as the starting material was impure: the work was repeated by Adams (*J. Amer. Chem. Soc.*, 1938, **60**, 1260) with negative results. Hydrogen has been replaced by deuterium in active compounds by Young and Porter (*ibid.*, 1937, **59**, 328, 1437), who observed a decrease in rotatory power. Other such cases have been reported (*e.g.*, by Erlenmeyer and Schenkel, *Helv. Chim. Acta*, 1936, **19**, 1199), but the dissymmetry is not due to symmetrically placed hydrogen and deuterium, and these are not true cases of optical activity caused by such an arrangement.

The separation of an allene hydrocarbon into its optical antipodes by Maitland and Mills (J., 1936, 987), and the very high rotations observed for the *d*- and the *l*-form, suggested another method of examining the problem. We thought that, if there should be an appreciable asymmetric difference between the " heavy " and the " light " phenyl group attached to the α-carbon atom in *αγ-diphenyl-α-pentadeuterophenyl-γ-*1-*naphthylallyl alcohol* (II, R = C_5D_5), dehydration might well proceed asymmetrically here also when brought about by *d*-camphorsulphonic acid. Furthermore, the deuterium compound can be easily prepared without the use of reagents likely to cause appreciable exchange of deuterium and hydrogen.

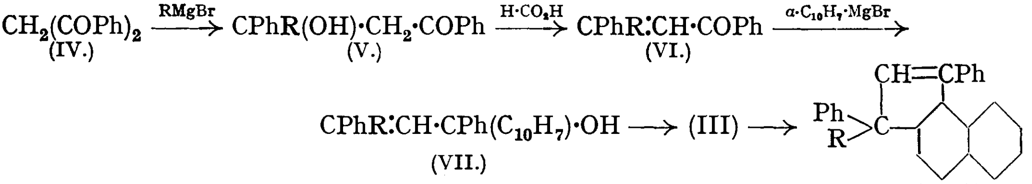
$CPh(C_{10}H_7){:}CH{\cdot}COPh$	$CPh(C_{10}H_7){:}CH{\cdot}CPhR{\cdot}OH$	$CPh(C_{10}H_7){:}C{:}CPhR$
(I.)	(II.)	(III.)

Experiments were first carried out to observe the effect of reducing the amount of phenylmagnesium bromide required for the preparation of *ααγ-triphenyl-γ-*1-*naphthylallyl alcohol* (II, R = C_6H_5) from phenyl β-phenyl-β-1-naphthylvinyl ketone (I) prepared by the method of Maitland and Mills (*loc. cit.*). It was found that, by adding a solution of this ketone to the boiling Grignard reagent, only two equivalents of the latter were required, and as the same conditions held for the preparation of the deuterium isomer (II, $R = C_6D_5$), only one half of the amount of bromopentadeuterobenzene at first thought necessary was required.

No optical activity was observed when 4·5 g. of the carbinol (II, $R = C_6D_5$) were dehydrated with *d*-camphorsulphonic acid. A reason for this negative result is obvious if the ingenious theory of asymmetric dehydration put forward by Maitland and Mills (*loc. cit.*) is correct. Another explanation is that the *αγ-diphenyl-α-pentadeuterophenyl-γ-1-naphthylallene* (III, $R = C_6D_5$), even if it is completely resolvable, may show only a very small activity and thus, under the conditions of asymmetric dehydration, where usually only 1 or 2% excess of one of the enantiomorphous forms results, the resulting activity may be very small. In this connection it is significant that, although (III, $R = C_6D_5$) and (III, $R = C_{10}H_7$) have similar absorption spectra, the latter shows a much higher extinction coefficient at the peak of the band in the near ultra-violet region.

The theory of Maitland and Mills suggests that the alcohol is esterified by the camphorsulphonic acid and, further, that both the *d*- and the *l*-form of the resulting ester consist of a mixture of *cis*- and *trans*-isomers. When the ester group is in the configuration necessary for the *trans*-elimination of the camphorsulphonic acid, the orientation of the camphorsulphonic group in the molecule is very closely defined, being surrounded by three aromatic groups. It can well be understood that in a molecule possessing this *trans*-configuration, an interchange of the phenyl and the pentadeuterophenyl group on the asymmetric carbon atom (the interchange necessary to represent the other antimeric form of the ester molecule in the *trans*-form) would have a smaller effect on the rates of elimination of the camphorsulphonic acid molecule from the two antimeric forms of the alcohol, than would be the case were the pentadeuterophenyl group replaced by the naphthyl group as in the *carbinol* (VII, $R = C_6D_5$). Hence, if the phenyl and the pentadeuterophenyl group show a spatial difference, this alcohol ought to give rise to a greater excess of one of the antimeric forms of the corresponding allene than the isomeric alcohol (II, $R = C_6D_5$). This, however, could not be demonstrated.

In the synthesis of the alcohol (VII, $R = C_6D_5$), the pentadeuterophenyl group was introduced in the first stage. This entailed a slight modification in the usual method of dehydrating the substituted *propiophenone* (V, $R = C_6D_5$) with hydrochloric acid, in order to minimise the possibility of the replacement of deuterium by hydrogen. Formic acid (*d* 1·2) readily dehydrated the deutero-alcohol in half an hour.



$$\underset{\text{(IV.)}}{CH_2(COPh)_2} \xrightarrow{RMgBr} \underset{\text{(V.)}}{CPhR(OH)\cdot CH_2\cdot COPh} \xrightarrow{H\cdot CO_2H} \underset{\text{(VI.)}}{CPhR\colon CH\cdot COPh} \xrightarrow{\alpha\text{-}C_{10}H_7\cdot MgBr}$$

$$\underset{\text{(VII.)}}{CPhR\colon CH\cdot CPh(C_{10}H_7)\cdot OH} \longrightarrow (III) \longrightarrow$$

(VIII.)

In order to study this mechanism of dehydration further, we decided to synthesise the two isomeric *alcohols* (II, R = *p*-tolyl) and (VII, R = *p*-tolyl). The asymmetric dehydration of the latter alcohol would be expected to give a greater excess of one of the active forms of the corresponding allene and hence the product in this case should display a higher optical activity than the product in the former case, since there is greater similarity between the phenyl and the *p*-tolyl group in (II, R = *p*-tolyl) than between the phenyl and the naphthyl group attached to the asymmetric carbon atom in (VII, R = *p*-tolyl).

Two forms of *phenyl β-phenyl-β-*p*-tolylvinyl ketone* (VI, R = *p*-tolyl), easily prepared by dehydration of the corresponding substituted *propiophenone* derivative (V, R = *p*-tolyl), were obtained. These are geometrical isomers, and yield the corresponding *cis*- and *trans*-alcohols after treatment with *p*-tolylmagnesium bromide. The dipole moments of the two ketones, m. p. 108° and 85°, are μ 1·00 and 0·88 respectively; in the light of values already recorded for *cis*- and *trans*-isomers, this indicates that the ketone of m. p. 108° has the *cis*- and the ketone of m. p. 85° has the *trans*-configuration (with respect to the hydrogen atom and the *p*-tolyl group).

No activity, however, could be detected after dehydration of the two isomeric alcohols (II, R = *p*-tolyl) and (VII, R = *p*-tolyl) (3—20 g.) with *d*-camphorsulphonic acid, and this negative result led to the search for other asymmetric dehydrating agents. αγ-Diphenyl-αγ-di-1-naphthylallyl alcohol (II, R = $C_{10}H_7$), prepared as described by Maitland and Mills (*loc. cit.*), was asymmetrically dehydrated by *d*-tartaric and *d*- and *l*-mandelic acids, but the time required for complete dehydration in boiling benzene solution was 1—2 days, as compared with 5—10 minutes for dehydration with *d*-camphorsulphonic acid. Hence the tartaric and mandelic acids cannot act catalytically by protolysis, as it seems inconceivable that their hydrogen-ion concentrations in benzene are high enough to catalyse the reaction, and it is much more probable that esterification occurs first, followed by elimination of the acid molecule.

The possibility that the activity may be due to the formation of the optically active ester may be precluded, as the activity is not proportional to the amount of the acid used. Furthermore, the acids are recovered unchanged from the solution by cooling and the optical activity is not destroyed or diminished when the benzene solutions are shaken with warm, moderately concentrated sodium hydroxide or sodium carbonate solution.

d-Tartaric and *d*- and *l*-mandelic acids also dehydrate the alcohols (II, R = Ph or *p*-tolyl) and (VII, R = Ph or *p*-tolyl), but the resulting solutions are inactive and we have assumed that this *αγ-diphenyl-α-*p*-tolyl-γ-1-naphthylallene* (III, R = *p*-tolyl) does not display a high rotatory power, unlike αγ-diphenyl-αγ-di-1-naphthylallene (III, R = $C_{10}H_7$). In support of this statement may be mentioned the successful resolution of an allenic acid into its optical antipodes by Kohler and co-workers (*J. Amer. Chem. Soc.*, 1935, **57**, 1743): the specific rotation of the acid, 29·5°, is much lower than one would anticipate on comparing the structures of this allenic derivative and αγ-diphenyl-αγ-di-1-naphthylallene (III, R = $C_{10}H_7$).

αγ-Diphenyl-α-*p*-tolyl-γ-1-naphthylallene (III, R = *p*-tolyl) and ααγ-triphenyl-γ-1-naphthylallene (III, R = Ph) are not so stable as the αγ-diphenyl-αγ-di-1-naphthyl derivative (III, R = $C_{10}H_7$), since *p*-toluenesulphonic acid not only dehydrates the parent alcohols catalytically, but rapidly isomerises the allenes formed to the respective indene derivatives. *d*-Camphorsulphonic acid also partly converts the allene into the isomeric indene compound.

The *indene* derivative (VIII, R = *p*-tolyl) corresponding to αγ-diphenyl-γ-*p*-tolyl-α-1-naphthylallene (III, R = *p*-tolyl) shows the phenomenon of phototropism (Maitland and Mills, *loc. cit.*), but the *triphenyl* substituted indene (VIII, R = Ph) does not.

Crystals (m. p. 100°) of ααγ-triphenyl-γ-1-naphthylallene (III, R = Ph) and αγ-diphenyl-α-pentadeuterophenyl-γ-1-naphthylallene (III, R = C_6D_5) obtained from benzene–light petroleum solutions crumble to white powders after several weeks and the m. p. rises to 142° in each case. The transitions can be brought about in a few minutes by heating the allenes above their original melting points (100°). Analysis shows that the chemical compositions of the new modifications are unchanged, and on recrystallisation from benzene and light petroleum the allenes of m. p. 142° revert to the original forms, m. p. 100°. This shows the existence of dimorphism.

EXPERIMENTAL.

ααγ-Triphenyl-γ-1-naphthylallyl Alcohol (II, R = Ph).—Phenyl β-phenyl-β-1-naphthylvinyl ketone (I) (J., 1936, 993) (5 g.) in benzene (36 c.c.) was run during 15 minutes into a Grignard solution prepared from magnesium (1·44 g.), ether (36 c.c.), and bromobenzene (6·3 c.c.). After reaction was complete the mixture was diluted with benzene (36 c.c.), kept at 15—20° overnight, and decomposed with ice and ammonium chloride; the solution was dried (potassium carbonate), the solvents removed, light petroleum (15 c.c., b. p. 40—60°) added to the residue, and the turbidity cleared by addition of a few drops of benzene. The *alcohol* separated in colourless crystals (5 g.), m. p. 147—149°, raised to 150° by recrystallisation from benzene–light petroleum (Found: C, 90·0; H, 6·0. $C_{31}H_{24}O$ requires C, 90·3; H, 5·9%).

Dehydration. The alcohol (0·2 g.) and *d*-camphorsulphonic acid (5 mg.) were refluxed in benzene (10 c.c.) for 10 minutes, a yellow solution with violet edges being formed. This was evaporated, and light petroleum added; *triphenyl-1-naphthylallene* (III, R = Ph) separated, m. p. 100—102° after crystallisation from benzene–light petroleum (Found: C, 94·3; H, 5·6. $C_{31}H_{22}$ requires C, 94·4; H, 5·6%). The same allene was formed when the alcohol was dehydrated with *d*-tartaric acid or *l*-mandelic acid, but *p*-toluenesulphonic acid gave the isomeric *indene* (VIII, R = Ph), m. p. 234° (Found: C, 94·2; H, 5·7%). The allene was converted into the indene by refluxing with *p*-toluenesulphonic acid in benzene, or by hydrogen chloride in acetic acid.

*αγ-Diphenyl-α-pentadeuterophenyl-γ-*1*-naphthylallyl Alcohol* (II, R = C_6D_5).—The same vinyl ketone (0·77 g.) was added to a Grignard solution prepared as above from bromopentadeuterobenzene (0·75 g.) at 40—45°, and the mixture worked up in the same way after standing for 15 minutes, giving the *alcohol* as clusters of crystals (0·65 g.), m. p. 147—148°, raised to 149—150° by recrystallisation from benzene–light petroleum (Found: C, 89·1; water, 60·1. $C_{31}H_{19}D_5O$ requires C, 89·2; water, 53·0%).

Dehydration. The alcohol (0·5 g.) was dehydrated as above with *d*-camphorsulphonic acid (5 mg.). No optical activity was observed in several experiments. The *allene* (III, R = C_6D_5) (0·44 g.), m. p. 100—101°, was obtained on evaporation and addition of light petroleum (Found: C, 93·3: water, 55·3. $C_{31}H_{17}D_5$ requires C, 93·2; water, 50·8%).

β-Hydroxy-ββ-diphenylpropiophenone (V, R = Ph).—Dibenzoylmethane (1·45 g.) in benzene (3 c.c.) was added to phenylmagnesium bromide (from bromobenzene, 0·7 g.) at 10° during 15 minutes. The bright green solution became yellow overnight; it was decomposed (ice and ammonium chloride), the ethereal layer dried and evaporated, the residual gum dissolved in benzene (2 c.c.), and light petroleum (12 c.c., b. p. 40—60°) added. The solid obtained was crystallised from benzene–light petroleum; yield 1·25 g., m. p. 116—118° (Found: C, 83·2; H, 5·9. $C_{21}H_{18}O_2$ requires C, 83·4; H, 6·0%).

Phenyl ββ-Diphenylvinyl Ketone (VI, R = Ph).—The above *propiophenone* (2 g.) was refluxed for 3 hours with concentrated hydrochloric acid (10 c.c.) and water (10 c.c.). The gum deposited on cooling was extracted with benzene, the extract dried (potassium carbonate), the solvent removed, and the residue crystallised from alcohol (10—15 c.c.), giving the *ketone* in golden-yellow prisms (1·8 g.), m. p. 85—87°, raised to 88° by a further crystallisation (Found: C, 88·4; H, 5·9. $C_{21}H_{16}O$ requires C, 88·7; H, 5·6%). The propiophenone (2 g.) can also be dehydrated by refluxing for ½ hour with formic acid (10 c.c., *d* 1·2); the product is diluted, extracted with benzene, and worked up as above.

*αγγ-Triphenyl-α-*1*-naphthylallyl Alcohol* (VII, R = Ph).—The above vinyl ketone (2·6 g.) in benzene (25 c.c.) was added drop by drop to a solution of 1-naphthylmagnesium bromide (from 1-bromonaphthalene, 5·1 c.c.) at 0° with stirring; the solution, after standing overnight, was decomposed (ice and ammonium chloride). The residue after removal of solvents was dissolved in ethyl acetate (3 c.c.), and alcohol (20 c.c.) added. The *alcohol* deposited (2·8 g.), m. p. 110—119°, was recrystallised from benzene–light petroleum; m. p. 124—126° (Found: C, 90·4; H, 5·9. $C_{31}H_{24}O$ requires C, 90·3; H, 5·9%).

β-Hydroxy-β-phenyl-β-pentadeuterophenylpropiophenone (V, R = C_6D_5) was prepared from dibenzoylmethane (0·4 g.) and bromopentadeuterobenzene (0·2 g.) in the same way as for the "light" compound described above, and crystallised from alcohol; yield 0·3 g., m. p. 115° (Found: C, 82·5; water, 54·8. $C_{21}H_{13}D_5O_2$ requires C, 82·1; water, 54·4%).

Phenyl β-phenyl-β-pentadeuterophenylvinyl ketone (VI, R = C_6D_5) (0·18 g.), m. p. 85—86°, was obtained by dehydrating the above "heavy" propiophenone (0·2 g.) with formic acid (5 c.c., *d* 1·2) in the same way as for the corresponding "light" compound (Found: C, 87·0; water, 58·7. $C_{21}H_{11}D_5O$ requires C, 87·2; water, 51·6%).

*αγ-Diphenyl-γ-pentadeuterophenyl-α-*1*-naphthylallyl Alcohol* (VII, R = C_6D_5).—The above "heavy" vinyl ketone (0·12 g.) in benzene (1 c.c.) was added during 5 minutes to a Grignard reagent (from 1-bromonaphthalene, 0·25 c.c.) and after 12 hours the solution was decomposed (ice and ammonium chloride), the dried solvents removed, and the residue taken up in the minimum amount of methyl alcohol. The *alcohol* (0·1 g.), m. p. 114—115°, was slowly deposited; it had m. p. 117—119° after recrystallisation from ethyl acetate–alcohol (Found: C, 88·7; water, 58·5. $C_{31}H_{19}D_5O$ requires C, 89·2; water, 53·0%).

Dehydration with *d*-camphorsulphonic acid gave the inactive allene (III, R = C_6D_5), m. p. 101°, identical with that obtained from (II, R = C_6D_5).

*αγ-Diphenyl-α-*p*-tolyl-γ-*1*-naphthylallyl Alcohol* (II, R = *p*-tolyl).—Phenyl β-phenyl-β-1-naphthylvinyl ketone (5 g.) in benzene (36 c.c.) was added during 15 minutes to a Grignard reagent (from *p*-bromotoluene, 7·5 c.c.). The usual treatment gave the *alcohol* (4·8 g.), which was crystallised from benzene (5 c.c.) and light petroleum (30 c.c.); m. p. 131—133° (Found: C, 89·8; H, 6·3. $C_{32}H_{26}O$ requires C, 90·1; H, 6·1%).

Dehydration. The alcohol (0·5 g.) and *d*-camphorsulphonic acid (5 mg.) were refluxed for

1½ hours, the solvent evaporated, and light petroleum added and allowed to evaporate. Two solids were obtained, namely, *αγ-diphenyl-γ-*p*-tolyl-α-*1*-naphthylallene* (III, R = *p*-tolyl), m. p. 119—122° (Found : C, 94·0; H, 6·05. $C_{32}H_{24}$ requires C, 94·1; H, 5·9%), and the isomeric *indene* (VIII, R = *p*-tolyl), m. p. 172—175° (Found : C, 94·2; H, 5·5%). The former was converted into the latter by hydrochloric acid in acetic acid. *l*-Mandelic acid gave the allene (m. p. 118—121°, mixed m. p. 118—120°), and *p*-toluenesulphonic acid the indene (m. p. 172—175°).

β-*Hydroxy*-β-*phenyl*-β-p-*tolylpropiophenone* (V, R = *p*-tolyl).—Dibenzoylmethane (7·2 g.) in benzene (36 c.c.) was added to a Grignard reagent (from *p*-bromotoluene, 25 g.) at 0—10° and, after standing overnight, the solution was treated with ice and dilute sulphuric acid and steam-distilled. The gum remaining was dissolved in ethyl acetate (4 c.c.), methyl alcohol (15 c.c.) added, and the whole cooled to 0° ; the *ketone* then separated, mixed with ditolyl. The latter was removed by crystallisation from ethyl acetate–alcohol, giving the ketone (6·5—6·8 g.), m. p. 109—111° (Found : C, 83·6; H, 6·7. $C_{22}H_{20}O_2$ requires C, 83·5; H, 6·3%).

Phenyl β-*Phenyl*-β-p-*tolylvinyl Ketone* (VI, R = *p*-tolyl).—The above crude propiophenone (5 g.) was refluxed for 3 hours with concentrated hydrochloric acid (25 c.c.) and water (25 c.c.). The gum deposited on cooling was washed (water) and extracted with benzene, the solvent removed, and the residue dissolved in alcohol (40 c.c.). On cooling, lemon-yellow prisms (2·3 g.), m. p. 105—107°, raised to 108—109° by recrystallisation from alcohol, separated (Found : C,88·7 ; H, 5·9. $C_{22}H_{18}O$ requires C, 88·6 ; H, 6·0%). The mother-liquor on standing deposited fine yellow needles (2·2 g.), m. p. 75°, raised to 85° by recrystallisation from alcohol (Found : C, 88·7; H, 6·3%).

*αγ-Diphenyl-γ-*p*-tolyl-α-*1*-naphthylallyl Alcohol* (VII, R = *p*-tolyl).—The above vinyl ketone (3 g., m. p. 108—109°) in benzene (25 c.c.) was added during 15 minutes to 1-naphthylmagnesium bromide (from 1-bromonaphthalene, 5·6 c.c.) at 0—10° with stirring. The resulting solution was left overnight and then decomposed in the usual way, and the solvents and free naphthalene removed by distillation under reduced pressure. The residual gum was dissolved in ethyl acetate (2 c.c.) and methyl alcohol (25 c.c.) and cooled to 0° ; the *alcohol* then separated (2·5 g.), m. p. 145°, raised to 150—152° by crystallisation from ethyl acetate–alcohol (Found : C, 89·8; H, 6·3. $C_{32}H_{26}O$ requires C, 90·1; H, 6·1%).

Dehydration. The alcohol (1 g.) and *d*-camphorsulphonic acid (10 mg.) were refluxed in benzene (10 c.c.) for ½ hour, the solvent removed, and the allene precipitated by alcohol from ethyl acetate solution. It had m. p. 119—120° and was identical with that obtained from (II, R = *p*-tolyl). *l*-Mandelic acid gave the same compound, but *p*-toluenesulphonic acid produced the isomeric indene.

*Dehydration of αγ-Diphenyl-αγ-di-*1*-naphthylallyl Alcohol* (Maitland and Mills, *loc. cit.*).—The alcohol (1 g.) was dehydrated by refluxing for 24 hours with *d*-mandelic acid (50 mg.) in benzene (20 c.c.). On cooling, most of the acid crystallised unchanged (m. p. 129—130°). After filtration the solution showed $\alpha^{17°}_{5461} = 2·04°$ and $\alpha^{17°}_{5780} = 1·7°$ ($l = 2$), not changed after 10 minutes' shaking with warm sodium carbonate (10%) or sodium hydroxide (10%) solution. Evaporation gave almost pure *dl*-allene (m. p. 240°). *l*-Mandelic acid gave a solution showing $\alpha^{18°}_{5461} = -1·0°$ ($l = 2$), and *d*-tartaric acid a solution showing $\alpha^{20°}_{5461} = 0·60°$ and $\alpha^{20°}_{5780} = 0·50°$ ($l = 2$).

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