118. *The Isomeric Mandelohydrazones of Benzoin.*

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r-Benzoin condenses with *r*-mandelohydrazide on the lines :

$$Ph{\cdot}CH(OH){\cdot}COPh + Ph{\cdot}CH(OH){\cdot}CO{\cdot}NH{\cdot}NH_2 = H_2O + Ph{\cdot}CH(OH){\cdot}CPh{:}N{\cdot}NH{\cdot}CO{\cdot}CHPh{\cdot}OH$$

Following on this observation, (−)*benzoin* (−)*mandelohydrazone*, (+)*benzoin* (+)*mandelohydrazone*, (−)*benzoin* (+)*mandelohydrazone*, and (+)*benzoin* (−)*mandelohydrazone* were prepared, and a resolution of *r*-benzoin by the agency of the optically active mandelohydrazides is also described.

Two isomeric r-*benzoin* r-*mandelohydrazones* were isolated.

For the preparation of the optically active benzoins the method of McKenzie and Wren (J., 1908, **93**, 309; compare Wren, J., 1909, **95**, 1593) has proved itself to be useful, and has been employed in numerous researches. This method involves the following stages, for example in the preparation of (−)benzoin :

$$(-)Ph{\cdot}CH(OH){\cdot}CO_2H \longrightarrow (-)Ph{\cdot}CH(OH){\cdot}CO_2R \quad [R = Me \text{ or } Et]$$
$$\longrightarrow (-)\,Ph{\cdot}CH(OH){\cdot}CO{\cdot}NH_2 \xrightarrow{\text{by PhMgBr}} (-)\,Ph{\cdot}CH(OH){\cdot}COPh$$

The optically active mandelic acids form the starting point for those changes, and we now describe another method, namely, one of resolution, *in which the same acids are also employed.*

r-Benzoin was warmed with a solution of *r*-mandelohydrazide in dilute acetic acid. On cooling, crystals of *r*-benzoin *r*-mandelohydrazone gradually separated, and by heating this compound with dilute hydrochloric acid *r*-benzoin was regenerated.

(−)*Benzoin* (−)*mandelohydrazone*, prepared from (−)benzoin and (−)*mandelohydrazide*, is of interest from the point of view of rotatory dispersion. Thus, in methyl-alcoholic solution, $[\alpha]_D$ gave the value − 33°, whereas $[\alpha]_{5461}$ was very slightly less, namely − 32·2°, under similar conditions of concentration and temperature. The sign of rotation swung round to dextro- when violet light was used, the value $[\alpha]_{4358}$ + 36·3° being noted. A similar behaviour was observed with (+)*benzoin* (+)*mandelohydrazone*.

The antimeric (−)*benzoin* (+)*mandelohydrazone* and (+)*benzoin* (−)*mandelohydrazone*, which were crystallised from ethyl alcohol, contained each 1 mol. of ethyl alcohol of crystallisation, which was expelled only after prolonged heating at 90—100° in a vacuum. The rotatory powers are high. The rotatory powers of the isomeric optically active benzoin mandelohydrazones in methyl-alcoholic solution are given in the following table.

	l.	*c.*	$\alpha_D^{14°}$.	$[\alpha]_D^{14°}$.	$\alpha_{5461}^{14°}$.	$[\alpha]_{5461}^{14°}$.	$\alpha_{4358}^{17°}$.	$[\alpha]_{4358}^{17°}$.		
(−)Benzoin (−)mandelohydrazone	1	1·365	−0·45°	−33°	−0·44°	−32·2°	—	—		
	1	1·433	—	—	—	—	+0·52°	+36·3°		
			$\alpha_D^{17°}$.	$[\alpha]_D^{17°}$.	$\alpha_{5461}^{17°}$.	$[\alpha]_{5461}^{17°}$.	$\alpha_{4358}^{17°}$.	$[\alpha]_{4358}^{17°}$.		
(+)Benzoin (+)mandelohydrazone	1	1·401	+0·46°	+32·8°	+0·45°	+32·1°	—	—		
	1	1·403	—	—	—	—	−0·44°	−31·3°		
									$\alpha_{5791}^{17°}$.	$[\alpha]_{5791}^{17°}$.
(−)Benzoin (+)mandelohydrazone (containing 1 mol. EtOH)	1	1·488	+2·53	+170	+3·15	+212	+6·79	+456	+2·68°	+180°
(+)Benzoin (−)mandelohydrazone (containing 1 mol. EtOH)	1	1·606	−2·74	−171	−3·39	−211	−7·22	−450	−2·89	−180°

When (−)benzoin (−)mandelohydrazone was heated with N-hydrochloric acid, the resulting benzoin was considerably racemised under the conditions described in the experimental section, its rotation in acetone being only $[\alpha]_D$ −73·9°, whereas the value for (−)benzoin is − 117·5°. This marked racemisation had doubtless taken place, to some extent at least, after the liberation of the benzoin from the hydrazone, since (−)benzoin

itself did not entirely survive after being heated for 1 hour with 2N-hydrochloric acid, the rotation in acetone being then $[\alpha]_D$ −100·8°.

r-Benzoin was resolved by means of (+)*mandelohydrazide* by dissolving the latter in hydrochloric acid, then adding an alcoholic solution of *r*-benzoin and heating for 30 minutes. Prolonged heating is inadvisable. The resulting (+)benzoin (+)mandelohydrazone, which separated first, was decomposed by warming for ¾ hour with 0·3N-sulphuric acid, and gave a good yield of optically pure (+)benzoin. Under these conditions no racemisation was detected. (−)Benzoin (+)mandelohydrazone was also isolated as another product from the resolution.

In some cases, however, the resolution was found to proceed on lines different from the above; for example, one experiment is recorded where (−)mandelohydrazide was used as the resolving agent. Here the crystals first obtained consisted of (+)benzoin (−)mandelohydrazone, from which (+)benzoin was obtained on hydrolysis, whilst (−)benzoin (−)mandelohydrazone was isolated from the filtrate. In fact, from the results recorded and also from the results of other resolutions which need not be stated, it became clear that the resolution takes an irregular course. This we ascribe to the presence of nuclei which in due course had infected the atmosphere and initiated the crystallisation of the ethyl-alcoholic solutions, and this is all the more likely since crystallisation is slow in starting from the cold solutions. The difficulty in resolving *r*-phenylchloroacetic acid with morphine (McKenzie and Clough, J., 1908, **93**, 811; 1909, **95**, 777) may probably be ascribed to a similar cause (compare Ostromisslensky, *Ber.*, 1908, **41**, 3035).

It may be observed that at least four isomeric racemates of benzoin mandelohydrazone are theoretically possible, since geometrical isomerism on the basis of the Hantzsch–Werner hypothesis may play a rôle. In the light of the following observations we were led to examine the possibility of the existence of isomeric racemates.

An ethyl-alcoholic solution of a mixture of equal quantities of (−)menthyl (+)mandelate, m. p. 98—99°, and (+)menthyl (−)mandelate, m. p. 98—99°, gave, on expulsion of the solvent, prisms of the optically inactive ester designated as *r*-menthyl *r*-mandelate, m. p. 80—81° (McKenzie and Luis, J., 1934, 715). This racemic compound is, however, different from that obtained by dissolving a mixture of equal quantities of (−)menthyl (−)mandelate, m. p. 81—82°, and (+)menthyl (+)mandelate, m. p. 81—82°, in acetone, and expelling the solvent. The product, which was optically inactive, consisted of silky needles, m. p. 103—104°, and was provisionally designated as *dl*-menthyl *r*-mandelate (McKenzie and Luis, *Ber.*, 1936, **69**, 1118). Later, *three* optically inactive isomeric menthyl esters of *o*-nitromandelic acid were described and designated as the α-, β-, and γ-forms (Abbot, McKenzie, and Stewart, *Ber.*, 1937, **70**, 456), whilst *three* optically inactive isomeric bornyl mandelates were also isolated (Luis and McKenzie, *ibid.*, p. 2161). On those lines, *two* optically inactive benzoin mandelohydrazones are described in the present paper. The α-form, m. p. 183—184° (decomp.), is dimorphous, crystallising in prisms or in silky needles, whilst the β-form, m. p. 156—157° (decomp.), crystallises in prisms.

An an example of an aldehyde which might possibly be resolved by means of the optically active mandelohydrazides, we selected *dl*-hydratropaldehyde for the reason that the deamination of nor-(+)-ψ-ephedrine gives (+)hydratropaldehyde as one of the products (McKenzie, Luis, and Mitchell, *Ber.*, 1932, **65**, 798). An attempt made by Wootton (J., 1910, **97**, 405) to resolve this aldehyde by (+) 4-bromo-3-aminophenyl-α-camphoramic acid was unsuccessful, since the compounds did not interact.

dl-Hydratropaldehyde condenses with *r*-mandelohydrazide to give *r*-hydratropaldehyde *r*-mandelohydrazone. When (+)mandelohydrazide was used, *r*-hydratropaldehyde (+)mandelohydrazone was isolated, but since this compound appears to be " partially racemic " the attempt to resolve the aldehyde by this means was a failure.

In the literature there are only a few examples recorded for the resolution of externally compensated aldehydes and ketones by the agency of compounds of known constitution. Neuberg (*Ber.*, 1903, **36**, 1192) used (−)menthylhydrazine for the resolution of *r*-arabinose. The experience of Marckwald and McKenzie on the isolation of the optically pure (−)amyl alcohol present in fusel oil (*Ber.*, 1901, **34**, 485) enabled Neuberg and Federer (*Ber.*, 1905, **38**, 866) to obtain a 94% pure (−)alcohol, by means of which they prepared (+)amyl-

phenylhydrazine (probably not quite pure), which was then applied with success to the resolution of *r*-arabinose and *r*-galactose (*Ber.*, 1905, **38**, 868). More recently, Hopper and Wilson (J., 1928, 2483) employed (+) and (−)δ-α-phenylethylsemicarbazide for the resolution of *r*-benzoin, which was also carried out by (−)δ-menthylsemicarbazide (Crawford and Wilson, J., 1934, 1122) and by (+) and (−)δ-α-phenylpropylsemicarbazide (Little, McLean, and Wilson, J., 1940, 336). *dl-p*-Methoxyhydratropaldehyde has been resolved by Betti (*Ber.*, 1930, **63**, 874) by means of (+)phenyl-2-hydroxy-α-naphthylmethylamine (compare also Betti and Pratesi, *Atti R. Accad. Lincei*, 1931, **13**, 646, for the resolution of *p*-methylhydratropaldehyde, and Betti and Pratesi, *Biochem. Z.*, 1934, **274**, 1, for a rather imperfect resolution of *dl*-glyceraldehyde). Finally, Woodward, Kohman, and Harris (*J. Amer. Chem. Soc.*, 1941, **63**, 120) have recently resolved *r*-camphor by means of (−)menthyl *N*-aminocarbamate.

From the preparative standpoint the method of obtaining the antimeric benzoins described in the present paper as well as the methods of Wilson and his colleagues are not nearly so practical as the method of McKenzie and Wren (*loc. cit.*). It may also be recalled that a method for preparing (−)benzoin from (+)mandelonitrile has been devised by Smith (*Ber.*, 1931, **64**, 427). The yield is not so good as that provided by the older method starting with the optically active mandelic acids, but it is more expeditious, since the time involved in converting amygdalin into (−)benzoin is much less than that demanded by the older method. If the latter method from (+)mandelonitrile is employed, it should, however, be noted that this nitrile is exceedingly susceptible to catalytic racemisation, and the necessary care must be taken to avoid this.

It is possible that the optically active mandelohydrazides or other hydrazides of simply constituted, optically active acids may prove to be of service in the future for the resolution of aldehydes and ketones.

Experimental.

Action of r-*Mandelohydrazide on* r-*Benzoin.*—When *r*-mandelohydrazide (Curtius and Müller, *Ber.*, 1901, **34**, 2794) crystallised from ethyl alcohol, it separated in two dimorphous forms. The bulk formed glistening plates, m. p. 132—133°, and silky, prismatic needles, m. p. 132—133°, separated from the filtrate overnight. The compound is described by Curtius and Müller as forming colourless leaflets, m. p. 132°, but the solvent is not given.

When a trace was dissolved in concentrated sulphuric acid at the ordinary temperature a pink coloration appeared very slowly. On warming, the solution assumed an orange tint.

r-Benzoin (2·4 g.) was dissolved in a warm solution of the hydrazide (2 g.) in a mixture of water (24 c.c.) and glacial acetic acid (12 c.c.). The solid which separated after 3 days was crystallised from methyl alcohol. Yield, 1·2 g.

r-*Benzoin* r-*mandelohydrazone* formed clusters of colourless prisms, m. p. 183—184° (decomp.) (Found: C, 73·5; H, 5·7; N, 8·0. $C_{22}H_{20}O_3N_2$ requires C, 73·3; H, 5·6; N, 7·8%). On heating 1·2 g. on the water-bath for 1 hour with dilute hydrochloric acid, and then crystallising the resulting solid from ethyl alcohol, *r*-benzoin (0·6 g.) was obtained with m. p. 132—133°, not depressed by an authentic sample.

Action of Hydrazine Hydrate on the Optically Active Ethyl Mandelates.—Ethyl (+)mandelate (40 g.) was dissolved at the ordinary temperature in 160 c.c. of 50% aqueous hydrazine hydrate. The solid which separated overnight was crystallised from ethyl alcohol. Yield, 27 g.

(+)*Mandelohydrazide* formed elongated prisms, m. p. 152—153° (Found: N, 16·9. $C_8H_{10}O_2N_2$ requires N, 16·9%). In methyl alcohol ($l = 1$, $c = 2·585$): $\alpha_D^{16°}$ + 1·35°, $[\alpha]_D^{16°}$ + 52·2°; $\alpha_{5461}^{16°}$ + 1·58°, $[\alpha]_{5461}^{16°}$ + 61·1°.

(−)*Mandelohydrazide*, prepared in a similar manner from ethyl (−)mandelate (10 g.), crystallised from ethyl alcohol in elongated prisms, m. p. 152—153° (Found: C, 57·8; H, 5·8; N, 17·1. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·1; N, 16·9%). In methyl alcohol ($l = 1$, $c = 2·637$): $\alpha_D^{16°}$ −1·39°, $[\alpha]_D^{16°}$ − 52·7; $\alpha_{5461}^{16°}$ − 1·62°, $[\alpha]_{5461}^{16°}$ − 61·4°. Yield, 7·5 g.

Condensation of the Optically Active Mandelohydrazides with the Optically Active Benzoins.—(−)Mandelohydrazide (2 g.) was dissolved in glacial acetic acid (12 c.c.), and the solution diluted with an equal bulk of water. (−)Benzoin (2·4 g.), prepared by the action of phenylmagnesium bromide on (−)mandelamide (McKenzie and Wren, *loc. cit.*), was dissolved in the warm solution. The solid which separated after 5 days at the ordinary temperature was crystallised from ethyl alcohol. Yield, 0·4 g.

(−)*Benzoin* (−)*mandelohydrazone* formed colourless, elongated prisms, m. p. 166—167° (decomp.) (Found : C, 72·9; H, 5·6; N, 7·9. $C_{22}H_{20}O_3N_2$ requires C, 73·3; H, 5·6; N, 7·8%). The rotatory powers of this compound and those of its optically active isomerides are given in the introduction.

For the preparation of the antimeride, an aqueous solution of sodium acetate (0·55 g.) was added to a solution of (+)mandelohydrazide (0·7 g.) in glacial acetic acid diluted with an equal volume of water. A warm ethyl-alcoholic solution of (+)benzoin (0·9 g.), prepared from (+)mandelamide, was added, and the mixture was heated for 2 hours on the water-bath. After 1 day at the ordinary temperature, the solid which separated was crystallised from ethyl alcohol. Yield, 0·8 g.

(+)*Benzoin* (+)*mandelohydrazone* formed colourless, elongated prisms, m. p. 166—167° (decomp.) (Found : C, 73·2; H, 5·5; N, 7·8%).

Attempts to prepare the hydrazones which are diastereoisomeric with the preceding two presented some difficulty, the products from some experiments being gummy oils from which crystals were obtained in traces only. The following conditions led to the desired result. An aqueous solution of sodium acetate (0·8 g.) was added to a solution of (+)mandelohydrazide (1 g.) in N-hydrochloric acid (6 c.c.). To the warm solution a warm ethyl-alcoholic solution of (−)benzoin (1·3 g.) was added, and the mixture heated for ¾ hour on the water-bath. At the ordinary temperature crystallisation proceeded very slowly, and after 5 days the resulting solid (1·5 g.) was crystallised from ethyl alcohol. Again crystallisation was slow. Yield, 1·1 g.

(−)*Benzoin* (+)*mandelohydrazone* formed large, colourless prisms which, when dried in a vacuum at the ordinary temperature, melted indefinitely at 111—124° (Found : C, 71·1; H, 6·5; N, 7·0. $C_{22}H_{20}O_3N_2,C_2H_5{\cdot}OH$ requires C, 70·9; H, 6·5; N, 6·9%). The alcohol of crystallisation is removed from this compound only after prolonged heating. After 20 hours at 70—90° in a vacuum, 0·3829 g. lost 0·0336 g. and further heating at 90—100° for 14 hours was necessary before constancy in weight was obtained, the total loss in weight being 0·0405 g., the amount calculated for 1 mol. of $C_2H_5{\cdot}OH$ being 0·0433 g. At this stage the product still melted indefinitely, and was now faintly yellow (Found : C, 73·0; H, 5·8; N, 7·7. $C_{22}H_{20}O_3N_2$ requires C, 73·3; H, 5·6; N, 7·8%). The rotation was taken in methyl alcohol ($l = 1$, $c = 1{\cdot}487$) : $\alpha_D^{18°}$ + 2·73°, $[\alpha]_D^{18°}$ + 184°; $\alpha_{5791}^{18°}$ + 2·92°, $[\alpha]_{5791}^{18°}$ + 196°; $\alpha_{5461}^{18°}$ + 3·42°, $[\alpha]_{5461}^{18°}$ + 230°; $\alpha_{4358}^{18°}$ + 7·21°, $[\alpha]_{4358}^{18°}$ + 485°.

(+)*Benzoin* (−)*mandelohydrazone*, prepared from (+)benzoin (1·3 g.) and (−)mandelohydrazide (1 g.), crystallised from ethyl alcohol in bulky, colourless prisms which melted indefinitely after being dried in a vacuum at the ordinary temperature. Like its antimeride, it contained 1 mol. of ethyl alcohol of crystallisation (Found : C, 70·9; H, 6·5; N, 6·8%). Yield, 1 g.

Like its antimeride, this compound lost weight on heating in a vacuum at 99—100°, the loss corresponding with 1 mol. of EtOH of crystallisation, the product giving in methyl alcohol $[\alpha]_{5461}^{18°}$ − 230° ($c = 1{\cdot}497$). From the latter, on crystallisation from ethyl alcohol, the hydrazone containing 1 mol. of ethyl alcohol of crystallisation was regenerated. Ethyl alcohol was the only solvent which was found suitable as a crystallising medium for this hydrazone and its antimeride.

Racemisation Phenomena.—The catalytic racemisation of (−)benzoin occurs in ethyl-alcoholic solution containing a trace of sodium ethoxide (Wren, *loc. cit.*; McKenzie, Roger, and Wills, J., 1926, 789), and the racemisation of the optically active benzoins by various agents has been studied in some detail by Roger and McGregor (J., 1934, 1545). We now find that partial racemisation takes place under the following conditions when (−)benzoin (−)mandelohydrazone is decomposed by dilute hydrochloric acid. The hydrazone (0·2 g.) was heated with N-hydrochloric acid (10 c.c.) for 1 hour on the water-bath. The benzoin which separated on cooling melted indefinitely at 122—126°, and gave in acetone $[\alpha]_D^{17°}$ − 73·9° ($l = 1$, $c = 1{\cdot}056$). Racemisation was thus considerable, since optically pure (−)benzoin has m. p. 132·5—133·5° and $[\alpha]_D^{10·5°}$ − 117·5° ($c = 1{\cdot}2508$) in acetone (McKenzie and Wren, *loc. cit.*). It seems probable that this partial racemisation had taken place, at least to some extent, after the liberation of the benzoin from the hydrazone, since (−)benzoin itself undergoes partial racemisation under the following conditions. (−)Benzoin (0·6 g.) was heated for 1 hour on the water-bath with 2N-hydrochloric acid (30 c.c.). On cooling, the liquid was filtered, and the benzoin thus recovered was not optically pure, since it melted at 128—131°, and gave in acetone $[\alpha]_D^{6°}$ −100·8° ($l = 1$, $c = 1{\cdot}3$). It gave the optically pure (−)benzoin after two crystallisations from methyl alcohol.

Resolution of r-*Benzoin.*—(+)Mandelohydrazide (12 g.) was dissolved in 2N-hydrochloric

acid (36 c.c.). An ethyl-alcoholic solution of *r*-benzoin (12 g.) was added to the warm solution, sufficient alcohol being added to prevent deposition of solid. After heating for 30 minutes on the water-bath, the solid (15·5 g.) which had separated overnight was crystallised from methyl alcohol. The prisms (3·8 g.), which separated very slowly, were recrystallised from methyl alcohol. The product (2·2 g.) had m. p. 166—167° (decomp.) (Found : C, 73·5; H, 5·6. Calc. : C, 73·3; H, 5·6%). In methyl alcohol ($l = 1$, $c = 1{\cdot}361$) : $\alpha_D^{14°}$ +0·45°, $[\alpha]_D^{14°}$ +33·1°; $\alpha_{5461}^{14°}$ + 0·44°, $[\alpha]_{5461}^{14°}$ + 32·3°. After crystallisation from ethyl alcohol, there was no change in melting point or optical rotatory power. The compound was thus optically pure (+)benzoin (+)mandelohydrazone. An additional 1·5 g. were isolated from the filtrates. For the isolation of (+)benzoin, this hydrazone (2·2 g.) was warmed for ¾ hour on the water-bath with 40 c.c. of 0·3N-sulphuric acid, enough ethyl alcohol being added to bring about solution. The solid (I) (0·8 g.), which separated on cooling, gave (+)benzoin, m. p. 133—134° (alone or mixed with an authentic sample) after two crystallisations from ethyl alcohol. In acetone ($l = 1$, $c = 1{\cdot}504$) : $\alpha_D^{19°}$ + 1·76°, $[\alpha]_D^{19°}$ +117°; $\alpha_{5461}^{19°}$ +2·18°, $[\alpha]_{5461}^{19°}$ + 144·9°. Some additional (+)benzoin was obtained from the alcoholic filtrate, and some by heating the filtrate from (I) with dilute sulphuric acid. In all, 0·87 g. of optically pure (+)benzoin was obtained. Yield, 67%.

By fractional crystallisation of the filtrate from which the above 3·8 g. had been removed, crystals of optically pure (−)benzoin (+)mandelohydrazone (2·4 g.) were isolated.

In a second resolution of *r*-benzoin (25·6 g.) with (+)mandelohydrazide (20 g.) the experimental conditions were similar to the preceding except that the heating of the alcoholic solution was prolonged for 6 hours. On this occasion only 9·9 g. of crystals had been deposited after 1 week. These were dissolved in ethyl alcohol, and crystallisation was again slow. After 1 week optically pure (+)benzoin (+)mandelohydrazone (4·2 g.) separated, and optically pure (−)benzoin (+)mandelohydrazone (4·5 g.) was isolated from the filtrate.

Prolonged heating of the resolution mixture is inadvisable, since, when the heating was prolonged over 11 hours with the same quantities as in the preceding experiment, the product was a viscous yellow oil from which no solid was obtained.

In some other cases the resolution took a somewhat different course. Thus, an aqueous solution of sodium acetate (15·9 g.) was added to a solution of (−)mandelohydrazide (20 g.) in 2N-hydrochloric acid (60 c.c.), an ethyl-alcoholic solution of *r*-benzoin (25·6 g.) being then added, and the solution heated on the water-bath for 30 minutes. On cooling, a yellow oil, but no solid, separated. The whole was then heated for an additional 30 minutes, and after 2 days at the ordinary temperature, the viscous semi-solid, yellowish product (30 g.) was heated with ethyl alcohol (100 c.c.). On cooling, and removal of a small amount of insoluble solid, glassy prisms of optically pure (+)benzoin (−)mandelohydrazone (6·8 g.) gradually separated. This hydrazone (2 g.) was hydrolysed with sulphuric acid, optically pure (+)benzoin (0·63 g.) being isolated, m. p. 132—134°; in acetone ($c = 1{\cdot}5$, $l = 1$) : $[\alpha]_{5461}^{20°}$ +145·3°. Yield, 60%. From the filtrate from which the above-mentioned hydrazone had been removed, optically pure (−)benzoin (−)mandelohydrazone (2 g.) was obtained, m. p. 166—167° (decomp.), not depressed by an authentic sample.

Isomeric Optically Inactive Benzoin Mandelohydrazones.—The preparation of the isomeride which we propose to designate as the α-form, and which crystallises in prisms, m. p. 183—184° (decomp.), has already been described. The compound was formed by the condensation of *r*-benzoin with *r*-mandelohydrazide. It was also synthesised as follows.

A mixture of (−)benzoin (−)mandelohydrazone (0·1546 g.) and (+)benzoin (+)mandelohydrazone (0·1546 g.) was dissolved in ethyl alcohol. The solution was allowed to evaporate spontaneously at the ordinary temperature; long, silky, colourless needles were gradually deposited and no other form of crystal could be detected. After the alcohol had evaporated, the residue was optically inactive in methyl-alcoholic solution. After one crystallisation from ethyl alcohol, long needles, m. p. 183—184° (decomp.), again separated, and there was no change in m. p. after a further crystallisation (Found : C, 73·6; H, 5·6; N, 7·8. $C_{22}H_{20}O_3N_2$ requires C, 73·3; H, 5·6; N, 7·8%). Although this product crystallised in needles, it gave no depression in the m. p. when mixed with the prisms, m. p. 183—184° (decomp.).

r-*Benzoin* r-*mandelohydrazone* (β-form) was prepared as follows. (−)Benzoin (+)mandelohydrazone (0·237 g.) and (+)benzoin (−)mandelohydrazone (0·237 g.) were mixed in ethyl-alcoholic solution. During spontaneous evaporation of the solvent crystals separated in sheaves of elongated prisms. After the solvent had disappeared, the residue was dried under diminished pressure, and then had m. p. 155—157° (decomp.). It was optically inactive in methyl-alcoholic solution. From ethyl alcohol it crystallised slowly in elongated, glassy, colourless prisms, m. p. 156—157° (decomp.), and the m. p. was unchanged after one further

crystallisation from ethyl alcohol. A mixture with the α-form melted indefinitely at 148—160° (decomp.). The β-*form* differed from the optically active isomerides from which it had been synthesised by crystallising without ethyl alcohol of crystallisation (Found: C, 73·5; H, 5·5; N, 7·8. $C_{22}H_{20}O_3N_2$ requires C, 73·3; H, 5·6; N, 7·8%).

r-Benzoin (10 g.) and *r*-mandelohydrazide (7·8 g.) were mixed in ethyl-alcoholic solution, and about 10 drops of glacial acetic acid added. After heating for 3 hours under reflux, both the α- and the β-form were isolated from the mixture, the former easily but the latter with some difficulty.

Action of r-*Mandelohydrazide on* dl-*Hydratropaldehyde.*—An ethyl-alcoholic solution of a mixture of *dl*-hydratropaldehyde (15·5 g.) and *r*-mandelohydrazide (19 g.) was heated for 15 minutes. The crystals (28 g.) which separated from the cold solution were recrystallised first from benzene and then from ethyl alcohol. Yield, 23 g.

r-*Hydratropaldehyde* r-*mandelohydrazone* formed colourless prisms, m. p. 138—139° (Found: C, 72·5; H, 6·6; N, 9·4. $C_{17}H_{18}O_2N_2$ requires C, 72·3; H, 6·4; N, 9·9%).

r-*Hydratropaldehyde* (+)*Mandelohydrazone.*—*dl*-Hydratropaldehyde (2 g.) was added to an ethyl-alcoholic solution of (+)mandelohydrazide (2·4 g.) and heated on the water-bath for 15 minutes. The crystals (3·3 g.) which separated from the cold solution were recrystallised from ethyl alcohol. The crystals (2·45 g.) had m. p. 150—152°, and gave in methyl alcohol $[\alpha]_D^{20°}$ + 78·8° (c = 1·917). After one more crystallisation, the product (1·5 g.) had m. p. 150—152°, and gave in methyl alcohol $[\alpha]_D^{20°}$ + 80·9° (c = 1·915). One further crystallisation gave colourless prisms (0·7 g.), m. p. 150—152°, with $[\alpha]_D^{18°}$ + 80·7° (c = 1·98) in methyl alcohol. These results suggest that we have to deal with a " partially racemic " compound.

r-*Hydratropaldehyde* (−)*mandelohydrazone*, prepared in a similar manner, formed colourless prisms, m. p. 150—152° (Found: C, 72·5; H, 6·4. $C_{17}H_{18}O_2N_2$ requires C, 72·3; H, 6·4%).

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