95. *Optically Active Mixed Benzoins derived from (+)Mandelonitrile.*

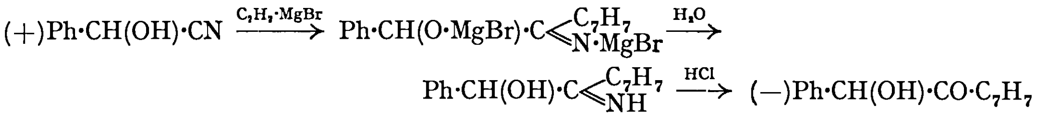
By Alex. McKenzie and Andrew L. Kelman.

The antimeric benzoins were prepared by the action of phenylmagnesium bromide on (—) and (+)mandelamides (McKenzie and Wren, J., 1908, **93**, 309; Wren, J., 1909, **95**, 1583, 1593), and (—)mandelamide also served for the preparation of (—)propionylphenylcarbinol and (—)phenacetylphenylcarbinol (Roger, *Helv. Chim. Acta*, 1929, **12**, 1060) and of (—)acetylphenylcarbinol (Roger, *Biochem. Z.*, 1931, **230**, 320). The action of Grignard reagents on optically active acid amides had also been utilised for the preparation of the methyl ether of (—)benzoin from (—)α-methoxyphenylacetamide, and of (+)benzoylbenzylcarbinol from (+)α-hydroxy-β-phenylpropionamide (McKenzie, Martin, and Rule, J., 1914, **105**, 1583), whilst recently (—)*o*-ethoxymandelamide has been converted into (—)*oo'*-diethoxybenzoin (Weissberger and Dym, *Annalen*, 1933, **502**, 74).

Whilst in those examples the method proved itself to be a practical one, it did not appear to lend itself readily in certain cases for the preparation of optically active mixed benzoins derived from the mandelamides; thus, the yields of *r-p*-toluoylphenylcarbinol and of *r-o*-toluoylphenylcarbinol from *r*-mandelamide were so small that no attempts were made at the time to prepare the corresponding optically active isomerides (McKenzie, Martin, and Rule, *loc. cit.*).

Meanwhile, however, optically pure (+)mandelonitrile has been isolated from amygdalin by Dr. Isobel Agnes Smith (*Ber.*, 1931, **64**, 427), and this has been applied by her for preparing (—)benzoin. The yield of the latter compound was rather less than by the older method, but the operations involved are fewer. The possibility that optically active mixed benzoins could be prepared was thus suggested, and the action of various Grignard reagents on (+)mandelonitrile was accordingly undertaken. Certain racemic mixed benzoins of the type Ph·CH(OH)·COR (where R is an aliphatic radical), which cannot be obtained by the condensation of benzaldehyde and aliphatic aldehydes by means of potassium cyanide, have also been prepared from *dl*-mandelonitrile.

The normal action may be represented as occurring by the following stages, for example, in the preparation of (—)*p*-toluoylphenylcarbinol:



$$(+)\mathrm{Ph{\cdot}CH(OH){\cdot}CN} \xrightarrow{\mathrm{C_7H_7{\cdot}MgBr}} \mathrm{Ph{\cdot}CH(O{\cdot}MgBr){\cdot}C}{<}\begin{smallmatrix}\mathrm{C_7H_7}\\ \mathrm{N{\cdot}MgBr}\end{smallmatrix} \xrightarrow{\mathrm{H_2O}}$$

$$\mathrm{Ph{\cdot}CH(OH){\cdot}C}{<}\begin{smallmatrix}\mathrm{C_7H_7}\\ \mathrm{NH}\end{smallmatrix} \xrightarrow{\mathrm{HCl}} (-)\mathrm{Ph{\cdot}CH(OH){\cdot}CO{\cdot}C_7H_7}$$

The formation of an intermediate ketimine in the reaction $R{\cdot}CN + R'{\cdot}MgX \rightarrow R{\cdot}CO{\cdot}R'$ (Blaise) was demonstrated by Moureu and Mignonac (*Compt. rend.*, 1913, **156**, 1801; *Ann. Chim.*, 1920, **14**, 322). It must, however, be recognised that an aryl group can sometimes be substituted for the CN group by means of a Grignard reagent, for example, $NC{\cdot}CO{\cdot}OEt \xrightarrow{Ph{\cdot}MgBr} Ph{\cdot}CPh_2{\cdot}OH$ (McKenzie and Duff, *Ber.*, 1927, **60**, 1335), but in the course of the present research there was no evidence that a secondary alcohol was formed on the lines $R{\cdot}CH(OH){\cdot}CN \longrightarrow R{\cdot}CH(OH){\cdot}R'$.

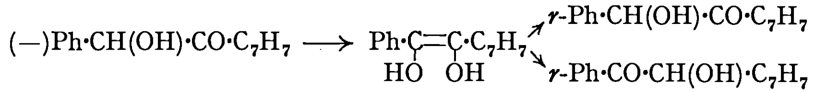
The formation of optically active mixed benzoins from (+)mandelonitrile is invariably accompanied by a change of sign of rotation.

(+)Mandelonitrile is more readily racemised than is the configuratively related (—)mandelamide, and precautions have to be taken when optically active mixed benzoins are prepared from it, not for this reason alone but also because the ketols themselves undergo racemisation with ease. Both (—)p- and m-*toluoylphenylcarbinols* were obtained optically pure when an ethereal solution of the nitrile was in each instance added to an excess of the Grignard reagent. But, when the reverse procedure was adopted by adding the Grignard reagent to the nitrile, the former exerted a racemising influence; for example, the *p*-toluoylphenylcarbinol formed under these conditions gave after crystallisation a product which had only $[\alpha]_{5461}$ — 52·5° in acetone, whereas the pure substance has $[\alpha]_{5461}$ — 103·6°.

In spite of the precautions observed, we were entirely unsuccessful in obtaining optically active *o*-toluoylphenylcarbinol: in other cases also *o*-tolylmagnesium bromide behaves abnormally. Stoermer (*Ber.*, 1906, **39**, 2288) was unable, for example, to obtain a glycol by the action of *o*-tolylmagnesium bromide on ethyl *dl*-lactate, and Roger and McKay (J., 1931, 2229) had a similar experience with ethyl *r*-mandelate, although they found that the action proceeded quite smoothly with both *p*- and *m*-tolylmagnesium bromides. Again, the latter authors observed that, although (+)*o*-tolylhydrobenzoin (α-form) can be obtained from (−)benzoin, it is invariably accompanied by considerable amounts of *r*-benzoin, whilst no such racemisation was detected in the preparation of the *p*- and *m*-isomerides. In our attempts to isolate optically active *o*-toluoylphenylcarbinol, we obtained 2-*methylbenzil*. Similarly, phenyl α-naphthyl diketone was obtained as a by-product from the action of α-naphthylmagnesium bromide on *dl*-mandelonitrile (cf. the formation of *p*-dimethylaminobenzil from *r*-4-dimethylaminobenzoin and from *r*-4′-dimethylaminobenzoin; Luis, J., 1932, 2547).

The optically active mixed benzoins now described resemble the ketones obtained by semipinacolinic changes (McKenzie, Roger, and Wills, J., 1926, 779; McKenzie and Dennler, *Ber.*, 1927, **60**, 220; Roger and McKenzie, *Ber.*, 1929, **62**, 272; McKenzie and Mills, *Ber.*, 1929, **62**, 284) in undergoing catalytic racemisation by the addition of a few drops of alcoholic potash.*

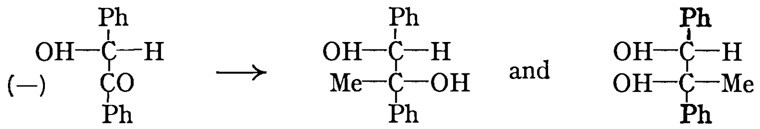
The product in each case is a mixture of the racemic ketols; thus, with (−)*p*-toluoylphenylcarbinol the product is a mixture of *r*-*p*-toluoylphenylcarbinol and *r*-benzoyl-*p*-tolylcarbinol:



$$(-)\mathrm{Ph{\cdot}CH(OH){\cdot}CO{\cdot}C_7H_7} \longrightarrow \mathrm{Ph{\cdot}\underset{HO}{C}{=}\underset{OH}{C}{\cdot}C_7H_7}\begin{matrix}\nearrow r\text{-}\mathrm{Ph{\cdot}CH(OH){\cdot}CO{\cdot}C_7H_7}\\ \searrow r\text{-}\mathrm{Ph{\cdot}CO{\cdot}CH(OH){\cdot}C_7H_7}\end{matrix}$$

This is in harmony with the observations of Luis (*loc. cit.*), who effected the interconversion of certain racemic mixed benzoins, for example, anisbenzoin → benzanisoin, and 4′-dimethylaminobenzoin → 4-dimethylaminobenzoin.

When (−)benzoin was acted on by methylmagnesium iodide, it was pointed out by McKenzie and Wren (J., 1910, **97**, 473) that two diastereoisomeric methylhydrobenzoins might on theoretical grounds be formed, since the carbon atom of the carbonyl group is rendered asymmetric, thus:



But these authors showed that the reaction proceeded one-sidedly and only a single glycol was isolated, as was also the case when (−)benzoin was acted on by ethylmagnesium bromide, results which should not, however, be designated as examples of asymmetric syntheses. Now, Tiffeneau and Lévy (*Bull. Soc. chim.*, 1927, **41**, 1351) have shown that when a racemic ketol of the type Ph·CH(OH)·CO·R is acted on by a Grignard reagent, R′·MgX, the resulting glycol, ${}^{\mathrm{Ph}}_{\mathrm{H}}{>}\underset{\mathrm{HO}}{\mathrm{C}}{-}\underset{\mathrm{OH}}{\mathrm{C}}{<}{}^{\mathrm{R}}_{\mathrm{R'}}$, is different from that obtained by the action of R·MgX on the ketol Ph·CH(OH)·CO·R′ (cf. McKenzie, Luis, Tiffeneau, and Weill, *Bull. Soc. chim.*, 1929, **45**, 414). The two isomeric glycols are designated by Tiffeneau as α- and β- respectively. When the radical R attached to the ketonic group of the ketol

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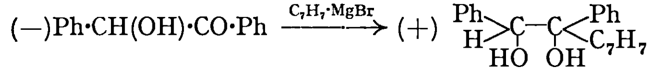
* The interpretations previously suggested for this type of racemisation (cf., for example, McKenzie and Wren, J., 1919, **115**, 602; McKenzie and Smith, J., 1922, **121**, 1348; *Ber.*, 1925, **58**, 894) not only with ketones but also with esters and acid amides have received much support from the researches of other authors, more particularly with enolates (Scheibler and Voss, *Ber.*, 1920, **53**, 388; Scheibler and Ziegner, *Ber.*, 1922, **55**, 789; Staudinger and Meyer, *Helv. Chim. Acta*, 1922, **5**, 656; Hückel, *Z. angew. Chem.*, 1926, **39**, 842; Hückel and Goth, *Ber.*, 1925, **58**, 447; Müller, *Annalen*, 1930, **491**, 251; Schlenk, Hillemann, and Rodloff, *Annalen*, 1931, **487**, 135).

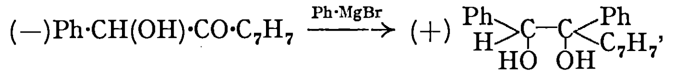
Ph•CH(OH)•CO•R has a smaller molecular weight than the radical R′ introduced by the action of R′MgX, then the glycol obtained is the α-form, whereas when R has a greater molecular weight than R′, the β-glycol is obtained. The optically active methylhydrobenzoin prepared from (—)benzoin is thus the β-form, whereas the isomeride from (—)acetylphenylcarbinol and phenylmagnesium bromide (Neuberg and Ohle, *Biochem. Z.*, 1922, **127**, 327; Roger, *ibid.*, 1931, **230**, 320) is the α-form.

The α-form of (+)*p*-tolylhydrobenzoin was prepared by Roger and McKay (*loc. cit.*) by the action of *p*-tolylmagnesium bromide on (—)benzoin :



$$(-)\mathrm{Ph{\cdot}CH(OH){\cdot}CO{\cdot}Ph} \xrightarrow{\mathrm{C_7H_7{\cdot}MgBr}} (+)\ \mathrm{Ph(H)C(OH){-}C(OH)(Ph)C_7H_7}$$

The β-*form* from phenylmagnesium bromide and (—)*p*-toluoylphenylcarbinol,



$$(-)\mathrm{Ph{\cdot}CH(OH){\cdot}CO{\cdot}C_7H_7} \xrightarrow{\mathrm{Ph{\cdot}MgBr}} (+)\ \mathrm{Ph(H)C(OH){-}C(OH)(Ph)C_7H_7},$$

has now been prepared. Like the α-form, it is strongly dextrorotatory, a change of sign taking place in its formation. A comparison of the rotatory powers of these α- and β-glycols shows a somewhat remarkable concordance: the α-form has $[\alpha]_{5461}$ + 252·6°, + 308·4°, + 260·4°, and + 264·5° in acetone, benzene, chloroform, and ethyl alcohol respectively, whereas the corresponding values for the β-form are + 252°, + 305·7°, + 259·3°, and + 266·4° respectively. Now, Roger and McKay (*loc. cit.*) from a study of the rotatory dispersions of (+)*o*-, *m*-, and *p*-tolylhydrobenzoins (α-forms) and (+)triphenylethylene glycol have shown that the new asymmetric centres arising from the formation of the tolylhydrobenzoins from (—)benzoin have little, if any, influence on the rotatory powers exhibited by the glycols themselves in various solvents. The question whether the new asymmetric centre in a glycol such as (+)*p*-tolylhydrobenzoin (β-form) is really a centre of optical activity is an interesting one.

When the α- and β-forms of (+)*m*-tolylhydrobenzoin are contrasted, the divergence in rotatory power is more pronounced than with the *p*-tolyl glycols, the α-form having $[\alpha]_{5461}$ some 20° higher than the β-form in the solvents examined.

The β-*form* of (+)anisylhydrobenzoin is also described.

EXPERIMENTAL.

In the majority of the preparations involving (+)mandelonitrile the crude crystalline product obtained by the action of sulphuric acid on amygdalin was employed (Smith, *loc. cit.*). Occasionally the optically pure nitrile obtained by crystallising the crude product from light petroleum(b. p. 40—60°)–carbon disulphide was used.

(—)p-*Toluoylphenylcarbinol.*—An ethereal solution of (+)mandelonitrile (8 g.) was added within 10 minutes to the Grignard reagent prepared from *p*-bromotoluene (39 g.), and the mixture heated for 15 minutes. On cooling, decomposition of the additive complex was effected by ice–concentrated hydrochloric acid (60 c.c.). The ethereal layer, containing *p*-ditolyl but practically no ketol, was separated as quickly as possible after the solid had dissolved. The aqueous solution was kept in the ice-chest for 2 days, the hydrolysis of the ketimine hydrochloride taking place somewhat slowly in this case. The precipitated solid (7 g.) was crystallised four times from light petroleum (b. p. 60—80°)–ethyl alcohol until it was optically pure. Yield, 3·5 g.

(—)p-*Toluoylphenylcarbinol* separates in needles, m. p. 102—103° (Found : C, 79·2; H, 6·2. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%). In acetone : $l = 2$, $c = 1$, $\alpha_D^{17^\circ}$ — 1·73°, $[\alpha]_D^{17^\circ}$ — 86·5°; $l = 2$, $c = 1{\cdot}004$, $\alpha_{5461}^{25^\circ}$ — 2·08°, $[\alpha]_{5461}^{25^\circ}$ — 103·6°. In ethyl alcohol : $l = 2$, $c = 1{\cdot}005$, $\alpha_{5461}^{25^\circ}$ — 2·41°, $[\alpha]_{5461}^{25^\circ}$ — 120°. A trace of the ketol when warmed with concentrated sulphuric acid gave a yellowish-green coloration.

Catalytic Racemisation of (—)p-*Toluoylphenylcarbinol.*—Five drops of *N*-ethyl-alcoholic potash were added to the solution used in the preceding polarimetric determination :

$\alpha_{5461}^{25^\circ}$	−1·71°	−1·45°	−1·19°	−1·05°	−0·97°	−0·54°	−0·30°
Time (mins.)	28	43	60	73	87	177	23 (hrs.)

Three additional drops of alcoholic potash caused the solution to become optically inactive after 30 minutes. After expulsion of the alcohol the residue after treatment with water was an oily solid consisting of a mixture of *r*-*p*-toluoylphenylcarbinol and *r*-benzoyl-*p*-tolylcarbinol. The aqueous solution from which this mixture was separated gave on acidification with mineral acid a mixture of benzoic and *p*-toluic acids, the ketols having undergone some alcoholic scission.

Action of Phenylmagnesium Bromide on (−)p-*Toluoylphenylcarbinol.*—The Grignard reagent prepared from bromobenzene (17 g.) was gradually added to an ethereal solution of (−)*p*-toluoylphenylcarbinol (4 g.). After heating for 3 hours, the product was treated with ice and dilute sulphuric acid, the ethereal solution dried (sodium sulphate), and the ether removed. The oily product gradually solidified after the addition of light petroleum and the solid was then crystallised from light petroleum (b. p. 80—100°)–ethyl alcohol. Yield, 2·5 g.

(+)p-*Tolylhydrobenzoin* (β-*form*) separates in needles, m. p. 135·5—136° (Found : C, 83·0; H, 6·8. $C_{21}H_{20}O_2$ requires C, 82·9; H, 6·6%), whereas the isomeric (+)α-form has m. p. 120—121° (Roger and McKay, *loc. cit.*). (The melting points of these and other substituted hydrobenzoins, however, vary according to the rate of heating, some dehydration taking place at elevated temperatures.) A trace of the β-form gives a pale green coloration when added to concentrated sulphuric acid.

The following determinations were made at 25° for λ5461 (l = 2) :

Solvent.	*c*.	α.	[α].
Acetone	1·002	+ 5·05°	+252°
Benzene	2·0115	+12·3	+305·7
Chloroform	1·8935	+ 9·82	+259·3
Ethyl alcohol	1·725	+ 9·19	+266·4

The specific rotation in acetone decreased with increasing temperature (l = 2, c = 1) :

λ	4861	5461	5893	6563
[α] at 0°	+397·5°	+296·5°	+248°	+181°
[α] at 40°	+325·5°	+241°	+199·5°	+155°

A similar decrease with increasing temperature was also observed in acetone by Roger and McKay (*loc. cit.*) for the α-glycol :

t	0°	19·5°	30°
$[\alpha]_{5893}$	+232°	+210·6°	+205·1°

Action of Phenylmagnesium Bromide on r-p-*Toluoylphenylcarbinol.*—*r*-*p*-Toluoylphenylcarbinol, m. p. 109—110°, was prepared from *dl*-mandelonitrile and *p*-tolylmagnesium bromide according to Weissberger, Strasser, Mainz, and Schwarze (*Annalen*, 1930, **478**, 126), a method which gives a better yield than that of McKenzie, Martin, and Rule (*loc. cit.*) from *r*-mandelamide. 3 G. of the ketol (1 mol.) were acted upon by phenylmagnesium bromide (6 mols.). Yield of glycol, 2 g.

r-p-*Tolylhydrobenzoin* (β-*form*) separates from benzene–light petroleum in plates, m. p. 181—182° (Found : C, 82·9; H, 6·7. $C_{21}H_{20}O_2$ requires C, 82·9; H, 6·6%), whereas the isomeric α-form (McKenzie, Mills, and Myles, *Ber.*, 1930, **63**, 911) has m. p. 161—162°.

(−)m-*Toluoylphenylcarbinol.*—This compound was prepared from *m*-tolylmagnesium bromide and (+)mandelonitrile, the procedure being similar to that adopted for the *p*-toluoyl isomeride. It crystallised from light petroleum (b. p. 60—80°)–ethyl alcohol in needles, m. p. 73—73·5° (Found : C, 79·5; H, 6·1. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%), and gave an olive-green coloration on warming with concentrated sulphuric acid.

In acetone ($l = 2$, $c = 1·0015$) : $\alpha^{25°}_{5461}$ − 2·45°, $[\alpha]^{25°}_{5461}$ − 122·3°.

In ethyl alcohol ($l = 2$, $c = 1$) : $\alpha^{24°}_{5461}$ − 3·02°, $[\alpha]^{25°}_{5461}$ − 151°.

The addition of three drops of *N*-alcoholic potash caused the rotation of the latter solution to fall to − 0·50° after 7 hours. Over-night the rotation was unchanged. Four additional drops of alcoholic potash added to the neutral solution caused complete racemisation after 56 minutes.

r-m-*Toluoylphenylcarbinol.*—When the product from the action of *m*-tolylmagnesium bromide (3 mols.) on *dl*-mandelonitrile (1 mol.) was decomposed by ice and concentrated hydrochloric acid, and the aqueous solution separated as usual, the bulk of the ketimine hydrochloride was gradually deposited as a solid, which was decomposed by alcoholic hydrochloric acid.

r-m-*Toluoylphenylcarbinol* crystallises from light petroleum (b. p. 60—80°) in rectangular prisms, m. p. 69·5—70° (Found : C, 79·6; H, 6·5. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%).

Action of Phenylmagnesium Bromide on (−)m-*Toluoylphenylcarbinol.*—This action gave

(+)m-*tolylhydrobenzoin* (β-*form*), which separates from light petroleum–ethyl alcohol in needles, m. p. 125—126° (Found : C, 83·2; H, 6·5. $C_{21}H_{20}O_2$ requires C, 82·9; H, 6·6%), whereas the isomeric α-form has m. p. 106—108°. The following determinations were made at 25° (l = 2) :

Solvent.	*c.*	α_{5790}.	α_{5461}.	α_{4358}.	$[\alpha]_{5790}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.
Acetone	1·9975	+8·37°	+ 9·76°	+17·48°	+209·5°	+244·3°	+437·5°
Ethyl alcohol	2·003	+8·93	+10·19	—	+222·9	+254·4	—
Chloroform	2·0055	+8·56	+ 9·88	—	+213·4	+246·3	—
Benzene	1·1235	+5·53	+ 6·39	—	+246·1	+284·4	—

It gives a green coloration with concentrated sulphuric acid.

Action of Phenylmagnesium Bromide on r-m-*Toluoylphenylcarbinol*.—This action gave r-m-*tolylhydrobenzoin* (β-form), which crystallises from ethyl alcohol in long prisms, m. p. 123—124° (Found : C, 82·9; H, 6·7. $C_{21}H_{20}O_2$ requires C, 82·9; H, 6·6%), whereas the isomeric α-form, prepared from *m*-tolylmagnesium bromide and *r*-benzoin (Roger and McKay, *loc. cit.*), has m. p. 135—137°.

Action of o-*Tolylmagnesium Bromide on* (+)*Mandelonitrile*.—In the course of an attempt to obtain the ketol from (+)mandelonitrile (5 g.), a yellow oil was obtained which contained neither chlorine nor nitrogen and did not reduce Fehling's solution. It solidified in contact with light petroleum (b. p. 40—60°), and crystallised from this solvent in yellow hexagonal prisms, m. p. 57—58°. Yield, 1 g. The compound was *phenyl* o-*tolyl diketone* (*2-methylbenzil*) (Found : C, 80·1; H, 5·4. $C_{15}H_{12}O_2$ requires C, 80·3; H, 5·4%).

This diketone, synthesised from *o*-toluonitrile by the stages $o\text{-}C_6H_4Me{\cdot}CN \longrightarrow o\text{-}C_6H_4Me{\cdot}CO{\cdot}CH_2Ph \longrightarrow o\text{-}C_6H_4Me{\cdot}CO{\cdot}C(:N{\cdot}OH)Ph \longrightarrow o\text{-}C_6H_4Me{\cdot}CO{\cdot}CO{\cdot}Ph$, had m. p. 57—58° and gave no depression of m. p. when mixed with the product obtained from (+)mandelonitrile.

Several attempts were made to obtain the mixed benzoin from (+)mandelonitrile, but the crystalline product obtained in each case was optically inactive.

Action of Ethylmagnesium Bromide on (+)*Mandelonitrile*.—An ethereal solution of (+)mandelonitrile (10 g.) was gradually added to the cooled Grignard reagent prepared from ethyl bromide (33 g.), the whole kept at the ordinary temperature for 2 hours, ice and concentrated hydrochloric acid (65 c.c.) then added, and the ethereal layer separated. From the last a yellow oil (1·6 g.), b. p. 120—123°/14 mm., was obtained, whilst from the acid layer, which had been kept over-night, 3·4 g. of an oil, b. p. 120—126°/14 mm., were obtained. The products gradually solidified, and were then crystallised from light petroleum (b. p. 60—80°). The resulting (—)propionylphenylcarbinol (2 g.) separated in needles, m. p. 39—40°, and gave in chloroform (l = 1, c = 1·763) : $\alpha_{\mathrm{D}}^{25^\circ}$ — 7·58°, $[\alpha]_{\mathrm{D}}^{25^\circ}$ — 430°; $\alpha_{5461}^{25^\circ}$ — 9·39°, $[\alpha]_{5461}^{25^\circ}$ —533°. The ketol, obtained by Roger (*loc. cit.*) by the action of ethylmagnesium bromide on (—)mandelamide, had m. p. 39—40° and $[\alpha]_{\mathrm{D}}^{20^\circ}$ — 428° in chloroform (c = 1·35), whereas the *r*-isomeride (Tiffeneau and Lévy, *Bull. Soc. chim.*, 1925, **37**, 1247) from *r*-mandelamide has m. p. 32—33°.

Action of Methylmagnesium Iodide on (+)*Mandelonitrile*.—The oil obtained by decomposition of the additive complex from the action of the Grignard reagent prepared from methyl iodide (32 g.) on (+)mandelonitrile (8 g.) gave in ethyl-alcoholic solution (l = 2, c = 2·0615) : α_{5461} — 3·08°, $[\alpha]_{5461}$ — 74·7°. The rotation fell gradually to α_{5461} — 0·28° in the presence of a few drops of alcoholic alkali.

Wren (J., 1909, **95**, 1593) synthesised the corresponding *dl*-ketol by the action of methylmagnesium iodide on *r*-benzoin, and Roger (*Biochem. Z.*, 1931, **230**, 320) has applied this reaction to (—)benzoin, obtaining a ketol with $[\alpha]_{\mathrm{D}}$ — 154·8° in ethyl alcohol, whereas he obtained the value $[\alpha]_{\mathrm{D}}$ — 158° for the product by means of carboligase. The value of Neuberg and Ohle (*loc. cit.*) by the latter method is higher, namely $[\alpha]_{\mathrm{D}}$ — 176°, whilst the value — 108° given by Freudenberg, Schoeffel, and Braun (*J. Amer. Chem. Soc.*, 1932, **54**, 234) is low.

Our product was thus a partially racemised (—)acetylphenylcarbinol. The preparation was repeated several times, and partial racemisation was always detected.

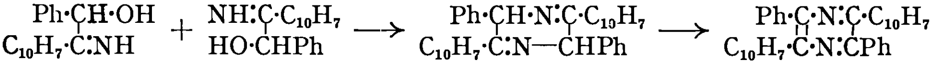
r-cyclo*Hexoylphenylcarbinol*.—*dl*-Mandelonitrile (11·5 g.) was added to the Grignard reagent prepared from *cyclo*hexyl bromide (50 g.). The oil obtained by the usual procedure was distilled, and the main fraction was nucleated by crystals obtained fortuitously in a preliminary experiment. The oil then solidified, and was crystallised several times from light petroleum (b. p. 40—60°). Yield, 3 g.

r-cyclo*Hexoylphenylcarbinol* separates in long silky needles, m. p. 62—63° (Found : C, 76·8; H, 8·5. $C_{14}H_{18}O_2$ requires C, 77·0; H, 8·3%).

Action of Phenylmagnesium Bromide on r-cyclo*Hexoylphenylcarbinol*.—The Grignard reagent prepared from bromobenzene (10 g.) was added to an ethereal solution of *r-cyclo*hexoylphenylcarbinol (2 g.). The oil resulting after the usual treatment crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 133—134°, of r-cyclo*hexylhydrobenzoin* (*β-form*) (Found: C, 80·7; H, 8·1. $C_{20}H_{24}O_2$ requires C, 81·0; H, 8·2%).

Action of cyclo*Hexylmagnesium Bromide on* (+)*Mandelonitrile.*—Several attempts were made to obtain the optically active ketol, in the course of which some of the *r*-ketol was isolated. The product of the highest optical rotatory power was an oil with $[\alpha]_{5461}^{20^\circ}$ − 134° (c = 1·019, in acetone), but this was not considered to be optically pure.

Action of α-Naphthylmagnesium Bromide on (+) *and on* dl-*Mandelonitrile.*—We were unsuccessful in isolating the ketols. The substance which separated from the decomposition with hydrochloric acid of the product from the (+)nitrile crystallised from alcohol–ether in needles, which melted mainly at 240—250° (decomp.), contained nitrogen and chlorine, and was optically inactive in alcoholic solution (c = 1·045). By the action of ammonia on a solution of this product in a mixture of methyl alcohol and water, a compound, which contained nitrogen but no chlorine and crystallised from benzene in needles, m. p. 260—260·5°, was isolated. It gave a deep blue coloration with concentrated sulphuric acid. By analogy with Gabriel's work on the formation of pyrazine derivatives from α-amino-ketones, this compound appears to be 2 : 5-*diphenyl*-3 : 6-*di-α-naphthylpyrazine*, formed by the condensation of the ketimine and oxidation of the resulting substituted dihydropyrazine, thus:



$$\begin{array}{c}\text{Ph·CH·OH}\\ \text{C}_{10}\text{H}_7\text{·C:NH}\end{array} + \begin{array}{c}\text{NH:C·C}_{10}\text{H}_7\\ \text{HO·CHPh}\end{array} \longrightarrow \begin{array}{c}\text{Ph·CH·N:C·C}_{10}\text{H}_7\\ \text{C}_{10}\text{H}_7\text{·C:N—CHPh}\end{array} \longrightarrow \begin{array}{c}\text{Ph·C·N:C·C}_{10}\text{H}_7\\ \text{C}_{10}\text{H}_7\text{·C·N:CPh}\end{array}$$

(Found: C, 88·9; H, 5·2; N, 5·6. $C_{36}H_{24}N_2$ requires C, 89·2; H, 5·0; N, 5·8%).

The oil from the *dl*-nitrile was distilled under a high vacuum, and the fraction, b. p. 185—230°, was crystallised from alcohol–light petroleum. The compound obtained was phenyl α-naphthyl diketone, $Ph·CO·CO·C_{10}H_7$, which crystallises in yellow rectangular prisms, m. p. 102·5—103° (Found: C, 82·9; H, 4·5. Calc. for $C_{18}H_{12}O_2$: C, 83·0; H, 4·7%), whereas Ruggli and Reinert (*Helv. Chim. Acta*, 1926, **9**, 67) give 101·5—102°. Its identity was established by its conversion by alcoholic potash into an acid (m. p. 146—147°), which gave a green coloration with concentrated sulphuric acid and exhibited no depression of melting point on admixture with a specimen of phenyl-α-naphthylglycollic acid prepared by the interaction of α-naphthylmagnesium bromide and ethyl benzoylformate (McKenzie and Tattersall, J., 1925, **127**, 2522).

Phenyl α-naphthyl diketone was also formed when the Grignard action was carried out in *m*-xylene instead of ether. The crude product after decomposition of the acid layer was washed with acetone, in which it was sparingly soluble, and a yellowish solid (m. p. 97—100°) containing neither nitrogen nor chlorine was obtained. This was slightly lævorotatory and the optical activity vanished after the addition of a trace of alcoholic potash. This indicated that some of the optically active mixed benzoin had been present. The main constituent of the product, m. p. 97—100°, was, however, the diketone.

(−)*Anisoylphenylcarbinol.*—After the addition of an ethereal solution of (+)mandelonitrile (9 g.) to the Grignard reagent prepared from anisyl bromide (38 g.), the mixture was decomposed in the usual manner, the ethereal solution (containing dianisyl and only a little of the ketol) neglected, and the acid solution of the ketimine hydrochloride kept for 3 days at the ordinary temperature.* The solid (7 g.) was separated and was crystallised from light petroleum (b. p. 80—100°), containing a little alcohol.

(−)*Anisoylphenylcarbinol* [(−)*benzanisoin*] forms prisms, m. p. 102·5—103·5° (Found: C, 74·1; H, 5·9. $C_{15}H_{14}O_3$ requires C, 74·3; H, 5·8%). In acetone (l = 2, c = 1·0005): $\alpha_{5461}^{20^\circ}$ − 1·53°, $[\alpha]_{5461}^{20^\circ}$ −76·5°. In ethyl alcohol (l = 2, c = 1·0055): $\alpha_{5461}^{20^\circ}$ −1·81°, $[\alpha]_{5461}^{20^\circ}$ − 90°. A trace gives a green coloration on warming with concentrated sulphuric acid.

Catalytic Racemisation of (−)*Anisoylphenylcarbinol.*—Five drops of *N*-ethyl-alcoholic potash were added to the preceding solution:

$\alpha_{5461}^{20^\circ}$	−1·73°	−1·57°	−1·36°	−1·25°	−1·16°	−1·08°	−0·95°	−0·84°
Time (mins.)	5	12	24	32	39	45	57	72
$\alpha_{5461}^{20^\circ}$	−0·67°	−0·43°	−0·29°	−0·13°	−0·07°	−0·03°	−0·00°	
Time (mins.)	98	121	172	239	301	351	411	

The reaction is unimolecular.

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* When this solution was kept for a shorter time, a varying amount of an orange-coloured solid generally separated. This consisted of the crude ketimine hydrochloride, as it gave the ketol when its warm alcoholic solution was decomposed by a little concentrated hydrochloric acid.

When the oily mixture of *r*-benzanisoin and *r*-anisbenzoin obtained after the evaporation of the alcohol was crystallised from rectified spirits, rosettes of needles separated (m. p. 105·5—106·5°), not depressed on admixture with a specimen of *r*-benzanisoin obtained by the action of alcoholic potassium cyanide on a mixture of benzaldehyde and anisaldehyde (McKenzie, Luis, Tiffeneau, and Weill, *loc. cit.*; Luis, *loc. cit.*).

Action of Phenylmagnesium Bromide on (—)*Benzanisoin.*—After decomposition of the product from this action by ice and hydrochloric acid, the ethereal solution was removed, the ether expelled, the diphenyl separated by steam distillation, the crude glycol extracted with ether, and the resulting product crystallised from light petroleum (b. p. 80—100°) containing a little alcohol.

(+)*Anisylhydrobenzoin* (β-*form*) separates in rosettes of fine needles, m. p. 146—147° (Found: C, 78·5; H, 6·4. $C_{21}H_{20}O_3$ requires C, 78·7; H, 6·3%). The *r*-isomeride (β-form) obtained from *r*-benzanisoin and phenylmagnesium bromide has m. p. 155—156°, and the *r*-isomeride (α-form) from *r*-benzoin and anisylmagnesium bromide has m. p. 203—204° (McKenzie, Luis, Tiffeneau, and Weill, *loc. cit.*). The following determinations were carried out in acetone ($l = 2$, $c = 1·0975$, $t = 20°$):

λ	6563	6162	5893	5461	5106	4861	4583	4358
α	+ 3·58°	+ 4·17°	+ 4·76°	+ 5·70°	+ 6·75°	+ 7·71°	+ 8·94°	+ 10·40°
[α]	+163·1°	+190°	+216·9°	+259·7°	+307·5°	+351·3°	+407·3°	+473·8°

The effect of temperature was pronounced: for the same solution as the above, where $\alpha_{5461}^{20°}$ + 5·70° was observed, the values at 0° and 40° were $\alpha_{5461}^{0°}$ + 6·14° and $\alpha_{5461}^{40°}$ + 5·11°, respectively, corresponding with $[\alpha]_{5461}^{0°}$ + 232·9° and $[\alpha]_{5461}^{40°}$ + 279·7°.

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