220. *Studies in Stereochemical Structure. Part VIII. The Stereochemical Relationship of the α- and the β-Forms of Substituted Hydrobenzoins.* (a) *Ethylhydrobenzoin* (α-*Form*).

By Robert Roger.

Acree (*Amer. Chem. J.*, 1905, **33**, 193) first described the action of ethylmagnesium bromide on benzoin and showed that it gave *r*-ethylhydrobenzoin. McKenzie and Wren (J., 1910, **97**, 473) later synthesised a dextrorotatory ethylhydrobenzoin from *D*(—)benzoin, but foresaw the possible formation of two diastereoisomeric forms:

Only one form was isolated by the latter authors from the Grignard action. Tiffeneau and Lévy (*Bull. Soc. chim.*, 1927, **41**, 1351) found, however, that the action of phenylmagnesium bromide on phenylpropionylcarbinol, $C_6H_5{\cdot}CH(OH){\cdot}CO{\cdot}C_2H_5$, gave once again a homogeneous product, but this, though isomeric, was not identical with the glycol isolated by Acree. Later, Roger (*Helv. Chim. Acta*, 1929, **12**, 1060) obtained two optically active ethylhydrobenzoins by the actions of ethylmagnesium bromide and phenylmagnesium bromide on *D*(—)benzoin and *D*(—)phenylpropionylcarbinol respectively. Only one form of the glycol was isolated in each action, and, starting from *D*(—)mandelic acid, both of these forms were dextrorotatory in the solvents examined. The melting points and magnitude of the rotatory powers in various solvents showed that these two forms of the glycol were quite distinct. Similarly, Roger (*Biochem. Z.*, 1931, **230**, 320) examined the forms of methylhydrobenzoin obtained from *D*(—)benzoin and *D*(—)phenylacetylcarbinol and showed, not only that they were quite distinct, but that neither form was identical with the (+)αα-diphenylpropylene-αβ-glycol obtained by the action of phenylmagnesium bromide on (+)ethyl lactate.

Glycol.	M. p.	$[\alpha]_{5893}^{20°}$ in EtOH.	$[\alpha]_{5893}^{20°}$ in $COMe_2$.
D(+)Methylhydrobenzoin (from phenylacetylcarbinol, α-form)	92—93°	+40·6°	+ 31·1°
D(+)Methylhydrobenzoin [from *D*(—)benzoin, β-form]	80—81	+21·3	+ 30·9
(+)αα-Diphenylpropylene-αβ-glycol	92—93	—	+132·7

This point is important, since it was possible that one of the ketols (particularly the phenylacetylcarbinol) might have undergone rearrangement during the Grignard action, with the resultant formation of some αα-diphenylpropylene-αβ-glycol:

$$CHPh(OH){\cdot}CO{\cdot}CH_3 \longrightarrow CH_3{\cdot}CH(OH){\cdot}COPh \longrightarrow CH_3{\cdot}CH(OH){\cdot}C(OH)Ph_2$$

In fact, Favorsky and Temnikova (*Bull. Soc. chim.*, 1935, **2**, 253) found that the methylbenzoylcarbinol, $CH_3{\cdot}CH(OH){\cdot}CO{\cdot}C_6H_5$, did undergo transformation during the action of phenylmagnesium bromide, giving a mixture of glycols. They also found, however, that phenylacetylcarbinol was not transformed during the Grignard action.

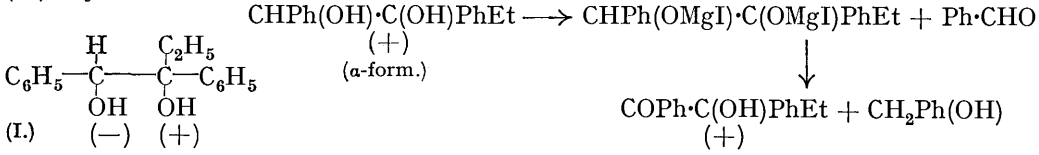
The existence of stereoisomeric forms * of the substituted hydrobenzoins has also been confirmed in the following cases: the *m*- and *p*-tolylhydrobenzoins (McKenzie, Roger, and McKay, J., 1932, 2597; Roger and McKay, J., 1933, 332; McKenzie and Kelman, J., 1934, 413), the benzylhydrobenzoins (Roger, *loc. cit.*), the anisylhydrobenzoins (McKenzie and Kelman, *loc. cit.*; McKenzie, Luis, Tiffeneau, and Weill, *Bull. Soc. chim.*, 1929, **45**, 414); and since the work of McKenzie and Wren it has been accepted implicitly that the two forms are diastereoisomers. No proof of this point has ever been brought forward, nor have the actual configurations of any of the forms been determined. Actually, Roger and McKay (*loc. cit.*) showed that the contribution of the new-born centre of asymmetry to the evident rotatory power of the tolylhydrobenzoins (α-forms) was small. This was later confirmed by the fact that phenyl-*p*-tolylglycollic acid has a very small rotatory power (McKenzie, Christie, and Ritchie, J., 1935, 153). The problem of the configuration of the two forms was tackled generally on the principle of converting the mandelyl complex into a symmetric system whilst the new asymmetric system was left unchanged. This was tried in two ways: (1) by conversion of the mandelyl complex into the benzyl system, and (2) by the oxidation of the mandelyl complex to the benzoyl group:

$$Ph{\cdot}CO{\cdot}CPhEt{\cdot}OH \xleftarrow{O} OH{\cdot}CHPh{\cdot}CPhEt{\cdot}OH \xrightarrow{H_2} CH_2Ph{\cdot}CPhEt{\cdot}OH$$

The reduction of the glycols was not successful. Reducing agents such as hydrogen and palladium or platinum, or zinc and dilute hydrochloric acid, were without action, and more powerful agents such as hydriodic acid caused dehydration of the glycols and yielded inseparable mixtures of products. At first, oxidation methods were unsuccessful also. Nitric acid caused dehydration of the glycol. No definite results were obtained by the use

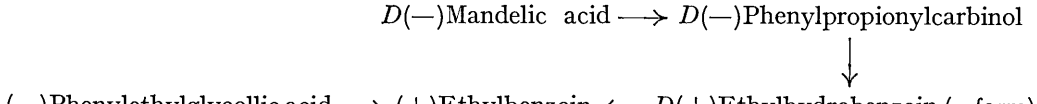
* The term "α-form" is applied to the glycol synthesised from the ketol of the smaller molecular weight, the term "β" to that from the ketol of greater molecular weight. Thus the ethylhydrobenzoin derived from phenylpropionylcarbinol is the α-form, and that from benzoin is the β-form.

of osmic acid or alkaline hypobromite. Lead tetra-acetate, chromic acid, aqueous pyridine and copper sulphate all caused scission of the glycol into simpler molecules. Finally, the method used was that of Gomberg and Bachmann (*J. Amer. Chem. Soc.*, 1930, **52**, 4966; see also Shankland and Gomberg, *ibid.*, 1930, **52**, 4973). The glycol was dissolved in ethylmagnesium iodide, and this solution was used to reduce benzaldehyde to benzyl alcohol, the glycol in its turn being oxidised to ethylbenzoin. Thus, the racemic form of ethylhydrobenzoin (α-form) gave *r*-ethylbenzoin, and the *D*(+)ethylhydrobenzoin gave (+)ethylbenzoin:



From this evidence the α-form of ethylhydrobenzoin would appear to have the structure (I) *provided* that no inversion of the mandelyl complex has occurred either during the conversion of *D*(−)mandelic acid into *D*(+)ethylhydrobenzoin, or in the solution of the glycol in the ethylmagnesium iodide preparatory to oxidation. So far, it has not been found possible to detect whether such an inversion has taken place.

The ethylbenzoin isolated from this action was the optical antipode of that obtained from (+)phenylethylglycollic acid by McKenzie and Ritchie (*Ber.*, 1937, **70**, 23), so the following relationships emerge:



This does not, however, enable one to connect the configurations of mandelic acid and phenylethylglycollic acid.

McKenzie and Ritchie (*loc. cit.*) observed that their (−)ethylbenzoin (in ethyl alcohol) became dextrorotatory in carbon disulphide. The configuration of the new centre of asymmetry would therefore appear to depend on the solvent used, particularly since the *D*(+)ethylhydrobenzoin (α-form) remains dextrorotatory in carbon disulphide. Roger and McGregor (J., 1934, 1545) found that asymmetric induction played a considerable part in determining the magnitude of rotatory power of *D*(−)benzoin in various solvents, for it

	D(−)Benzoin.	*D*(−)Phenylpropionylcarbinol.	Ethylbenzoin.	
$[\alpha]^{20°}_{5461}$ in EtOH	−162·4°	−199°	+253°	increasing
$[\alpha]^{20°}_{5461}$ in CS_2	−501	−361	−182	lævorotation

showed a striking increase in lævorotation in the passage from ethyl alcohol to carbon disulphide, and the (+)ethylbenzoin isolated here is showing the same tendency. This criticism, therefore, does not render the deductions from this oxidation invalid.

The oxidation of ethylhydrobenzoin (β-form) and other evidence regarding the relationship of the two forms of the glycol will be dealt with in future communications.

Experimental.

Ethylhydrobenzoin (α-form), prepared by the action of phenylmagnesium bromide on *D*(−)phenylpropionylcarbinol, had $[\alpha]^{18°}_{5461}$ + 42·1° (*c* = 3·278 in benzene, *l* = 1, $\alpha^{18°}_{5461}$ = + 1·38°).

The glycol (10 g.) was dissolved in the Grignard reagent prepared from ethyl iodide (30 g.). Benzaldehyde (15 g., twice distilled) in 50 c.c. of pure, dry benzene was added gradually. The mixture was kept overnight and then boiled for 1¼ hours. On decomposition with ice and sulphuric acid and extraction with ether, an oil was obtained from the ethereal layer, and was distilled in a vacuum. A fraction, b. p. 200—208°/20 mm., was collected which slowly became semi-solid. The addition of light petroleum with a small amount of ethyl alcohol caused separation of more solid. This was recrystallised from light petroleum and alcohol, coarse needles, m. p. 69—71° being formed. After several recrystallisations, the compound had m. p. 71°

and was constant in rotatory power : (1) in ethyl alcohol ($c = 1{\cdot}959$, $l = 1$), $\alpha^{20°}_{5461} = +4{\cdot}95°$, $[\alpha]^{20°}_{5461} = +252{\cdot}7°$; (2) in carbon disulphide ($c = 2{\cdot}078$, $l = 1$), $\alpha^{20°}_{5461} = -3{\cdot}79°$, $[\alpha]^{20°}_{5461} = -182{\cdot}4°$, $\alpha^{20°}_{5791} = -3{\cdot}23°$, $[\alpha]^{20°}_{5791} = -155{\cdot}5°$. McKenzie and Ritchie (*loc. cit.*) give for (−)ethylbenzoin, m.p. 69—70° : $[\alpha]^{17°}_{5461} = -250{\cdot}8°$ ($c = 2{\cdot}233$, $l = 1$) in ethyl alcohol, and $[\alpha]^{17°}_{5461} = +180{\cdot}5°$ ($c = 2{\cdot}216$, $l = 1$) in carbon disulphide.

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