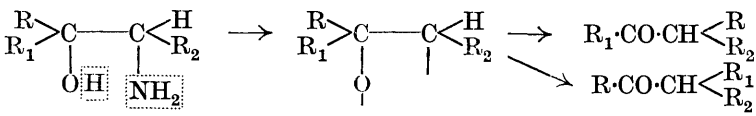
CVI.—*Elimination of the Amino-group of Tertiary Amino-alcohols. Part III. A New Method for the Preparation of Optically Active Ketones.*

By ALEX. MCKENZIE, ROBERT ROGER, and GEORGE OGILVIE WILLS.

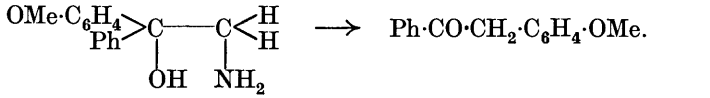
PREVIOUS research (McKenzie and Richardson, J., 1923, **123**, 79; McKenzie and Roger, J., 1924, **125**, 844; McKenzie and Dennler, J., 1924, **125**, 2105; McKenzie and Wills, J., 1925, **127**, 283) carried out in this laboratory on the behaviour of certain tertiary amino-alcohols towards nitrous acid has demonstrated that in no case was the glycol corresponding with the amino-alcohol isolated, although such glycols are readily enough accessible in other ways. The action is thus an abnormal one, the product invariably being a ketone (a dehydration product of the glycol). At once the simplest and the most obvious interpretation would be based on the assumption that the glycol is formed as an intermediate phase and then undergoes dehydration. This is an assumption which is, however, untenable, and the experimental evidence is conclusive in proving that a hydrocarbon residue migrates from one carbon atom to another adjacent to it. A process, such as this, for effecting the migration of groups was designated by McKenzie and Roger as "semipinacolinic deamination" from its analogy with the semipinacolinic changes which have come under the observation of Tiffeneau, Orékhov, and their colleagues.

The latter chemists, as well as Meerwein, have studied the dehydration of glycols where the two hydroxyl groups are bound to contiguous carbon atoms by gripping forces which vary in intensity. Wherever the variation of this gripping force is very great, that is to say, when the one hydroxyl group is very firmly and the other very loosely bound, the investigation of the dehydration of a glycol does occasionally provide a good indication of the migrational aptitude of groups. But, especially in other cases, semipinacolinic deamination is proving of service where the evidence deduced from the dehydration of glycols as to migrational aptitude is rather inconclusive. In fact, the method possesses the advantage of being a general one for testing the migrational aptitude of groups, as the elimination of the amino-group necessarily involves group transposition :

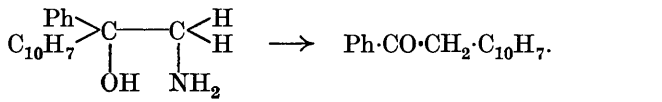


An extension of the method has lately been published by Orékhov

and Roger (*Compt. rend.*, 1925, **180**, 70) to embrace tertiary amino-alcohols where the amino-group is attached to a secondary carbon atom. Thus, the action of nitrous acid on β-hydroxy-ββ-diphenylethylamine leads to the formation of deoxybenzoin and not of *as*-diphenylethylene oxide, whilst the interpretation advanced by us agrees with that of Orékhov and Roger. Again, the superiority of the migrational aptitude of the *p*-anisyl as compared with the phenyl group is shown by the formation of *p*-methoxydeoxybenzoin from β-hydroxy-β-phenyl-β-anisylethylamine:

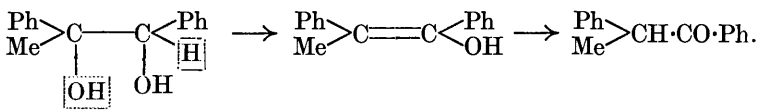


Further, when β-phenyl-β-(α-)naphthylethylamine is deaminated (Luce, *Compt. rend.*, 1925, **180**, 145), the naphthyl group wanders more readily than does the phenyl group, since ω-α-naphthylacetophenone is formed:



In the present paper, an application of our method to optically active amino-alcohols is described. The products are ketones, and it is remarkable that *optical activity is preserved in spite of the molecular rearrangement which is involved.*

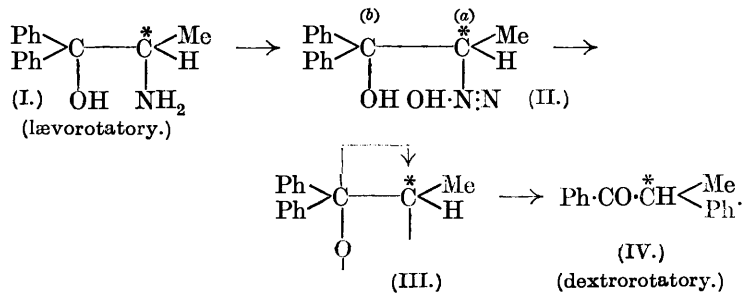
It may be recalled that in the formation of diphenylacetone from β-hydroxy-αβ-diphenylpropylamine a phenyl group migrates from a carbon atom to the adjacent one to which a phenyl group is already attached, and it would not therefore be anticipated (since diphenylacetone does not possess an asymmetric carbon atom) that the resulting ketone would be optically active if the starting point were the optically active amino-alcohol. The action of concentrated sulphuric acid on methylhydrobenzoin, the glycol corresponding with the above amino-alcohol, forms a striking contrast to the above, inasmuch as there is no group wandering, the change being what Tiffeneau calls "vinyl dehydration":



Now when the dextrorotatory methylhydrobenzoin, obtained by acting on *l*-benzoin with magnesium methyl iodide, is dehydrated with concentrated sulphuric acid, the resulting methyldeoxybenzoin is optically inactive, as it would necessarily be if the mechanism of

the action were that of vinyl dehydration. But McKenzie and Roger (J., 1924, **125**, 2148) have shown that, when the dehydrating agent is dilute sulphuric acid, the optical activity does not disappear; the product is not, however, an optically active methyldeoxybenzoin, but the lævorotatory diethylenic oxide, $\left(\begin{matrix}\text{CPhMe·CHPh}\\ \text{└—O—┘}\end{matrix}\right)_2$. It is possible that the *r*-methyldeoxybenzoin, which is formed when concentrated sulphuric acid is employed, is produced from the lævorotatory diethylenic oxide formed as an intermediate phase, whilst racemisation accompanies the transformation of the oxide into the *r*-ketone.

In the experimental section, the preparation of *d*-methyldeoxybenzoin is described. *d*-Alanine was converted into its ethyl ester hydrochloride, from which l-β-*amino*-αα-*diphenyl*-n-*propyl alcohol* was obtained by the action of magnesium phenyl bromide.* When the amino-alcohol, with $[\alpha]_D - 82°$ in chloroform, is acted on by nitrous acid, it gives the *d*-ketone with $[\alpha]_D + 207°$ in the same solvent. On the interpretation of semipinacolinic deamination, the following mechanism is suggested:



In a discussion of the Walden inversion, Biilmann (*Annalen*, 1912, **388**, 330) depicts the action of silver nitrate on α-bromopropionic acid as taking place between the silver ion and the acid ion on the lines:

$$CH_3\cdot CHBr\cdot CO\cdot \bar{O} \text{ and } Ag^+ \longrightarrow CH_3\cdot \overset{+}{C}H\cdot CO\cdot \bar{O} \text{ and } AgBr.$$

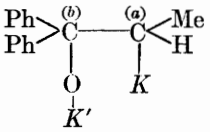
The resulting "Zwitterion" then combines with the hydroxyl ion from water:

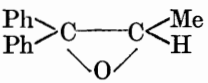
$$CH_3\cdot \overset{+}{C}H\cdot CO\cdot \bar{O} \text{ and } (OH)^- \longrightarrow CH_3\cdot CH(OH)\cdot CO\cdot \bar{O}.$$

* The designations *d*- and *l*- throughout this paper mean dextrorotatory and lævorotatory, respectively, and do not refer to configurative relationships. The dextrorotatory alanine is converted in the above case into a lævorotatory amino-alcohol which is, however, configuratively related to the parent amino-acid.

Biilmann advanced this idea as a basis of some generalisations which are untenable, as they were framed on an imperfect recognition of the literature and were not in accordance with the experimental facts. McKenzie and Clough (J., 1913, **103**, 687), in their criticism of Biilmann's paper, pointed out that since a "Zwitterion" is supposed to be electrically neutral, it cannot even be urged that a free electric charge plays the part of the fourth grouping which is necessary for the retention of asymmetry. At the same time, the conclusion was drawn that if Biilmann's idea were accepted, the formation of an optically active structure containing a tervalent carbon atom must be admitted, a view for which there was not the slightest experimental evidence.

It might be submitted that such evidence is now forthcoming in the retention of asymmetry during the formation of *d*-methyldeoxybenzoin (IV) from *l*-β-amino-αα-diphenyl-*n*-propyl alcohol (I). Various interpretations could be advanced, and of these the one which we favour as being the least unsatisfactory is the following. After the elimination of the nitrogen from (II), the carbon atom (*a*), from which the nitrogen has been detached, retains an electric charge K; the oxygen atom attached to the contiguous carbon atom (*b*) also retains an electric charge K', so that (III) would be written thus (A):

(A.) 

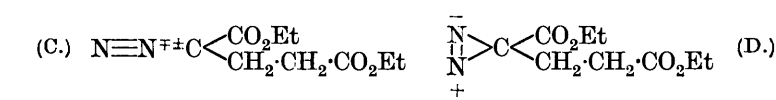
 (B.)

Were those charges of opposite kinds, positive and negative, the formation of diphenylpropylene oxide (B) would have been anticipated instead of that of the isomeric methyldeoxybenzoin. Now diphenylpropylene oxide (Stoermer, *Ber.*, 1906, **39**, 2288) is a stable compound, which under the experimental conditions adopted would have been isolated if it had been formed. Since it is not formed, the assumption—a very problematical one—is made that the electric charges as pictured above are of the same sign, and repel one another. During the transposition of a phenyl group to carbon atom (*a*), we are dealing with a reaction of substitution, the charge K playing the part of a group and being displaced by a phenyl group which may or may not occupy the position vacated by the amino-group, so that on this picture *a Walden inversion is possible within the molecule itself.*

There is no evidence available as to whether *d*-methyldeoxybenzoin has the same configuration as the *d*-alanine from which it is prepared; so far as is known, it may equally well have the

opposite configuration. Now one of us in the course of work on the Walden inversion has shown that displacement racemisation very frequently accompanies the displacement of groups in optically active compounds, especially in such as have a phenyl group attached to the asymmetric carbon atom, and it is thus rather significant that the crude product from the deamination of the *l*-amino-alcohol gave a value for its specific rotation which is considerably below that of the optically pure ketone (see experimental part). In this product we probably had to deal with a mixture of the *r*- and *d*-ketones, from which the latter was easily isolated by repeated crystallisation.

There are several examples on record where an electric charge is put forward as playing the part of a group in retaining asymmetry. For example, Marvel and Noyes (*J. Amer. Chem. Soc.*, 1920, **42**, 2259) point out that the electronic formula for an aliphatic diazo-compound suggests the possibility of such a compound exhibiting optical activity, although this is not apparent from the formulæ either of Curtius or of Angeli and Thiele. Chiles and Noyes (*J. Amer. Chem. Soc.*, 1922, **44**, 1798) claim to have obtained several optically active aliphatic diazo-compounds which do not contain an asymmetric atom in the old sense of the term, thus diethyl diazoglutarate is formulated as (C) on the basis of the Angeli-Thiele scheme,

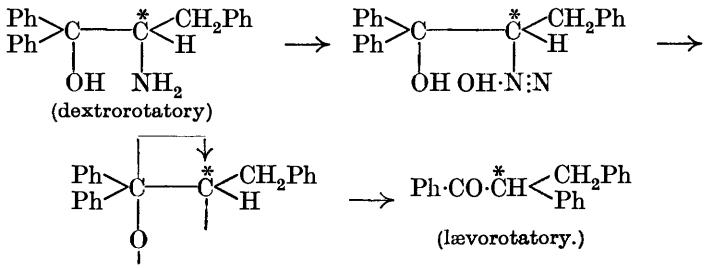


(C.) (D.)

which is in better agreement with the modern views of Lewis and Langmuir than is (D) on the Curtius scheme. Further observations by Levene and Mikeska (*J. Biol. Chem.*, 1922, **52**, 485; 1923, **55**, 795) on diethyl diazosuccinate indicate that a compound of the type $N_2{=}C{<}^{R_1}_{R_2}$ can exhibit optical activity, whilst Phillips (J., 1925, **127**, 2552) has described an optically active form of ethyl *p*-toluenesulphinate, $EtO{\cdot}\overset{+}{S}(\cdot\overset{-}{O}){\cdot}C_7H_7$. In a recent historical survey (*Die Naturwissenschaften*, 1925, 331) Walden has also directed attention to the asymmetry of the sulphur, selenium, and tin compounds prepared by Pope, and suggests that the sulphur atom in the optically active methylethylthetine ion, $CH_3{>}S{<}^{CH_2{\cdot}CO_2H}_{C_2H_5}$, for example, has an electric charge which plays the part of a group.

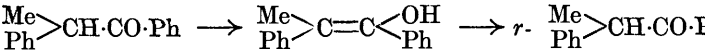
Other examples of the application of semipinacolinic deamination for the preparation of optically active ketones are now described. Whereas *d*-alanine gives, by the action of magnesium phenyl bromide on its ester hydrochloride, an amino-alcohol of the opposite

sign of rotation, the amino-alcohol obtained from *d*-phenylalanine by the same method has the same sign of rotation as that of the parent amino-acid, namely, dextrorotatory, and it has the same configuration. The deamination, however, caused a change of sign, *d*-β-amino-αα-diphenyl-β-benzylethyl alcohol giving *l*-benzyldeoxybenzoin:



Thus, whilst dextrorotatory alanine gives dextrorotatory methyldeoxybenzoin, the ketone derived from dextrorotatory phenylalanine is lævorotatory. In a similar manner, *l*-phenylalanine was converted into a lævorotatory amino-alcohol which gave *d*-benzyldeoxybenzoin. The configuration of the *d*- and *l*-benzyldeoxybenzoins in relationship to the parent amino-acids is unknown owing to the possibility of an intramolecular Walden inversion during the deamination of the amino-alcohol.

The optically active ketones described are very readily racemised at the ordinary temperature when a few drops of alcoholic potash are added to their alcoholic solutions. For comparison, the effect of the catalyst on *l*-benzoin is described. The catalytic racemisation of *l*-benzoin was first interpreted by Wren (J., 1909, **95**, 1593) on the basis of a desmotropic change caused by the migration of a hydrogen atom, and on this assumption *d*-methyldeoxybenzoin undergoes racemisation through an enolic complex:



Subsequent work by McKenzie and Wren on the hydrolysis of optically active esters by alcoholic potash (compare McKenzie and Smith, *Ber.*, 1925, **58**, 894) and by McKenzie and Smith on the catalytic racemisation of optically active acid amides (J., 1922, **121**, 1348) has provided evidence that the catalyst is potassium ethoxide, and it is suggested that the hypothetical enolic isomeride is formed only after the catalyst has combined with the ester or amide. A similar interpretation can be advanced with regard to ketones like methyldeoxybenzoin which contain (*a*) a phenyl group attached to the asymmetric carbon atom, and also (*b*) a hydrogen

atom attached to the asymmetric carbon atom which in turn is attached directly to a carbonyl group. The point is emphasised that *the latter hydrogen atom has no migrational tendency in the ketone itself, and does not become mobile until an additive complex with potassium ethoxide has first been formed.*

We are continuing our work on semipinacolinic deamination, more particularly with reference to the preparation of optically active ketones derived from phenylaminoacetic acid, phenylalanine and alanine. A few additional observations on the action of magnesium benzyl chloride on *d*-benzyldeoxybenzoin, ethyl *r*-alanine hydrochloride, and ethyl *r*-phenylaminoacetate hydrochloride, respectively, and on the deamination of *r*-β-amino-β-phenyl-αα-dibenzylethyl alcohol are recorded at the end of the experimental section.

EXPERIMENTAL.

Optically Active Methyldeoxybenzoin.

Action of Magnesium Phenyl Bromide on Ethyl d-*Alanine Hydrochloride.*—The final purification of the *d*-alanine employed was effected by dissolving the amino-acid in hot water, and then adding rectified spirit until crystallisation started. The amino-acid separated in long, silky needles, and, for comparison with the value of the specific rotation quoted by Fischer (*Ber.*, 1906, **39**, 464), 0·8000 g. was made up to 10 c.c. with *N*-hydrochloric acid; this solution gave $\alpha_D + 1{\cdot}17°$ in a 1-dcm. tube, whence $[\alpha]_D + 10{\cdot}4°$ for the hydrochloride ($c = 11{\cdot}276$), a value identical with Fischer's.

d-Alanine ethyl ester hydrochloride (15 g., 1 mol.) was added in instalments to an ethereal solution of magnesium phenyl bromide prepared from bromobenzene (150 g., 10 mols.), and the mixture was heated for 5 hours. The additive complex underwent slow decomposition when ice, ammonium chloride, and ammonia were added. When the decomposition was completed, the mixture was extracted several times with ether, the ethereal solution was dried with anhydrous sodium sulphate, the ether was expelled, and the resulting oil recrystallised from light petroleum. The crystals obtained were washed with light petroleum, and then consisted of the optically pure amino-alcohol (5·8 g.). The light petroleum was evaporated from the filtrates, the diphenyl was removed by distillation in steam, and the residual oil was extracted with ether. The oil resulting from the ethereal solution was dissolved in hot aqueous alcohol, and a mixture of oil and crystals separated on cooling. The oil was separated from the crystals by means of light petroleum, and in this manner an additional 5·2 g. of the amino-alcohol were obtained. Total yield = 11 g.

In another preparation the procedure was varied as follows. *d*-Alanine ethyl ester hydrochloride (8 g.) was added gradually to the Grignard reagent prepared from bromobenzene (98 g.), and the mixture after 3 hours' heating was decomposed by ice and dilute hydrochloric acid. In this case the diphenyl remained in the ethereal layer, which was separated from the aqueous layer containing the solution of the hydrochloride of the amino-alcohol. The latter solution was then decomposed by ammonia, but the precipitate which formed contained, not only the free amino-alcohol, but also some of its hydrochloride; the latter was removed by treatment with hot water. Yield of pure amino-alcohol = 4 g. The homogeneity of the amino-alcohol from this and from the preceding preparation was established by repeatedly crystallising from aqueous alcohol and examining the crystals polarimetrically. The amino-alcohol prepared from *d*-alanine is lævorotatory in chloroform, or in ethyl alcohol.

l-β-*Amino*-αα-*diphenyl*-n-*propyl alcohol*, $CH_3 \cdot CH(NH_2) \cdot CPh_2 \cdot OH$, separates from aqueous alcohol in needles, m. p. 101·5—102·5°. The *r*-isomeride (McKenzie and Wills, *loc. cit.*) also melts at 101·5—102·5°. The *l*-amino-alcohol is very sparingly soluble in water or in light petroleum, and readily soluble in ethyl alcohol, chloroform, benzene, toluene, or acetone (Found: C, 79·1; H, 7·7. $C_{15}H_{17}ON$ requires C, 79·3; H, 7·5%). Its colour reaction with concentrated sulphuric acid is similar to that exhibited by the *r*-isomeride. Its specific rotation was determined in chloroform: $l = 2$, $c = 1{\cdot}6776$, $\alpha_D^{16^\circ} - 2{\cdot}76^\circ$, $[\alpha]_D^{16^\circ} - 82{\cdot}3^\circ$; $\alpha_{5461}^{15{\cdot}5^\circ} - 3{\cdot}32^\circ$, $[\alpha]_{5461}^{15{\cdot}5^\circ} - 99{\cdot}0^\circ$. In ethyl alcohol: $l = 2$, $c = 1{\cdot}6628$, $\alpha_D^{16{\cdot}5^\circ} - 2{\cdot}11^\circ$, $[\alpha]_D^{16{\cdot}5^\circ} = -63{\cdot}4^\circ$; $\alpha_{5461}^{16{\cdot}5^\circ} = -2{\cdot}51^\circ$, $[\alpha]_{5461}^{16{\cdot}5^\circ} - 75{\cdot}5^\circ$.

The Action of Nitrous Acid on l-β-*Amino*-αα-*diphenyl*-n-*propyl Alcohol*.—A solution of sodium nitrite (2 g.) in water (10 c.c.) was added drop by drop in the course of ¾ hour to 2·2 g. of the amino-alcohol dissolved in 75 c.c. of 25% acetic acid, the temperature being kept at 0° during the addition. The whole was kept at 0° for 5 hours. The oil, which at first separated, crystallised slowly in needles, which were collected, washed with water, and as usual dried in a vacuum over sulphuric acid before a polarimetric determination was made. Yield: 1·9 g. In chloroform: $l = 2$, $c = 2{\cdot}0092$, $\alpha_D^{17^\circ} + 6{\cdot}33^\circ$, $[\alpha]_D^{17^\circ} + 158^\circ$. Thus the lævorotatory amino-alcohol gave a dextrorotatory ketone. After one crystallisation of the product from aqueous alcohol, fine, silky needles were obtained giving the following value in chloroform: $l = 2$, $c = 2{\cdot}0096$, $\alpha_D^{16^\circ} + 7{\cdot}15^\circ$, $[\alpha]_D^{16^\circ} + 178^\circ$. As the substance, however, was not yet optically pure, the deamination of the amino-alcohol was conducted in three additional experiments with 2·5 g., 4·3 g.,

and 5·2 g., respectively. The 9 g. of crude ketone thus obtained were crystallised repeatedly from aqueous alcohol until determinations of the rotatory power showed that the ketone had been obtained pure. Five crystallisations were necessary. Yield = 4 g.

d-*Methyldeoxybenzoin*, $C_6H_5 \cdot CH(CH_3) \cdot CO \cdot C_6H_5$, crystallises from aqueous alcohol in glistening, silky plates or needles, m. p. 34—35° (Found: C, 85·5; H, 6·7. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7%). It is readily soluble in the commoner organic solvents. It gives a pale yellowish-green coloration when a trace is dissolved in cold concentrated sulphuric acid. Determinations of its specific rotation gave the following results. In chloroform for $c = 1{\cdot}0715$ ($l = 2$):

λ	6563	5893	5461	4861	4358
$\alpha^{17°}$	+3·39°	+4·44°	+5·57°	+7·99°	+11·86°
$[\alpha]^{17°}$	+158°	+207°	+260°	+373°	+553°

In ethyl alcohol:

$$l = 2,\ c = 2{\cdot}2320,\ \alpha_D^{18°} + 9{\cdot}41°,\ [\alpha]_D^{18°} + 210{\cdot}8°.$$

After 1 day at the ordinary temperature, the solutions exhibited no autoracemisation.

Optically Active Benzyldeoxybenzoins.

Resolution of r-*Phenylalanine.*—The method of Fischer and Schoeller (*Annalen*, 1907, **357**, 1) was employed. Formyl-*r*-phenylalanine was resolved by brucine in methyl-alcoholic solution, and the resulting *d*- and *l*-formyl-acids were hydrolysed by hydrobromic acid. The *d*-phenylalanine obtained gave in aqueous solution: $l = 2$, $c = 2{\cdot}043$, $\alpha_D^{16°} + 1{\cdot}43°$, $[\alpha]_D^{16°} + 35{\cdot}0°$, whilst the *l*-amino-acid gave in the same solvent: $l = 2$, $c = 2{\cdot}043$, $a_D - 1{\cdot}42°$, $[\alpha]_D - 34{\cdot}8°$. The values quoted by Fischer and Schoeller are: for the *d*-acid, $[\alpha]_D^{20°} + 35{\cdot}14°$, and for the *l*-acid, $[\alpha]_D - 35{\cdot}09°$.

For the preparation of the optically active phenylaminoacetic acids, the resolution of the *r*-acid by Reychler's *d*-camphorsulphonic acid * was in our experience (McKenzie and Wills, *loc. cit.*) more practicable than that described by Fischer and Weichhold (*Ber.*, 1908, **41**, 1286) through the agency of the formyl-*r*-acid. Accordingly, attempts were made to prepare the optically active phenylalanines on similar lines. The homogeneous *dAd*B salt was obtained by combining the *r*-amino-acid with an equimolecular quantity of *d*-camphorsulphonic acid, and then crystallising the salt several times until the rotation was constant in value.

d-*Phenylalanine* d-*camphorsulphonate* separates from water in

* Recent work on the constitution of Reychler's acid indicates that the sulphonic group occupies the 10-position in the camphor molecule with sulphonation of the methyl group (Wedekind, Schenk, and Stüsser, *Ber.*, 1923, **56**, 633).

needles. In aqueous solution: $l = 2$, $c = 2{\cdot}0200$, $\alpha_D^{18{\cdot}5^\circ} + 0{\cdot}74^\circ$, $[\alpha]_D^{18{\cdot}5^\circ} + 18{\cdot}3^\circ$. We did not, however, find that this was a convenient method for effecting the resolution. Crystallisation took place too sluggishly, whether effected from water, benzene, aqueous alcohol or aqueous acetone, and the yield of the pure salt was small.

The enantiomorphous salt was prepared by combining *l*-phenylalanine with *l*-camphorsulphonic acid in methyl-alcoholic solution.

l-*Phenylalanine* l-*camphorsulphonate* separates from methyl alcohol in plates, m. p. 109—110°. In aqueous solution: $l = 2$, $c = 2{\cdot}0208$, $\alpha_D^{18{\cdot}5^\circ} - 0{\cdot}74^\circ$, $[\alpha]_D^{18{\cdot}5^\circ} - 18{\cdot}3^\circ$.

The Action of Nitrous Acid on l-β-*Amino-αα-diphenyl-β-benzylethyl Alcohol.*—The *l*-amino-alcohol was prepared by the action of magnesium phenyl bromide on *l*-phenylalanine (compare the preparation of the *d*-amino-alcohol, McKenzie and Wills, *loc. cit.*). The mixture of 1·9 g. of the *l*-amino-alcohol and 40 c.c. of 25% acetic acid was warmed until most of the solid had dissolved, and was then cooled to 0°. The gradual addition of a solution of sodium nitrite (1·3 g. in 10 c.c. of water) during 30 minutes caused the separation of a voluminous solid, which was kept for 4 hours at 0° in contact with the solution. This solid (1·25 g.) was strongly *dextrorotatory*, giving in chloroform solution $[\alpha]_D + 233^\circ$ for $c = 1{\cdot}346$ ($l = 2$). It consisted of the almost pure ketone, and was recrystallised twice from ethyl alcohol.

d-*Benzyldeoxybenzoin*, $CH_2Ph{\cdot}CHPh{\cdot}CO{\cdot}Ph$, is sparingly soluble in ethyl alcohol, from which it separates in silky needles, m. p. 121—121·5° (Found: C, 88·3; H, 6·5. $C_{21}H_{18}O$ requires C, 88·1; H, 6·3%). It is readily soluble in chloroform, ether, or acetone. Its specific rotation was determined in chloroform: $l = 2$, $c = 1{\cdot}348$, $\alpha_D^{16^\circ} + 6{\cdot}50^\circ$, $[\alpha]_D^{16^\circ} + 241^\circ$. In ethyl alcohol: $l = 2$, $c = 0{\cdot}392$, $\alpha_D^{16^\circ} + 1{\cdot}90^\circ$.

The Action of Nitrous Acid on d-β-*Amino-αα-diphenyl-β-benzylethyl Alcohol.*—The deamination was conducted as in the preceding case. The crude product (0·8 g.) obtained from the *d*-amino-alcohol (0·9 g.) was strongly *lævorotatory* in chloroform solution, giving $[\alpha]_D - 195^\circ$ for $c = 1{\cdot}5984$ ($l = 2$). It was crystallised thrice from ethyl alcohol until the optically pure ketone was obtained.

l-*Benzyldeoxybenzoin* crystallises from ethyl alcohol in silky needles, m. p. 121—121·5°. With concentrated sulphuric acid, a trace of the compound gives a faint greenish-yellow coloration. The following determinations of the specific rotation were made. In chloroform: $l = 1$, $c = 1{\cdot}258$, $\alpha_D^{16{\cdot}5^\circ} - 3{\cdot}04^\circ$, $[\alpha]_D^{16{\cdot}5^\circ} - 242^\circ$. In acetone: $l = 1$, $c = 1{\cdot}118$, $\alpha_D^{18^\circ} - 2{\cdot}45^\circ$, $[\alpha]_D^{18^\circ} - 219^\circ$; $\alpha_{5461}^{17^\circ} - 3{\cdot}00^\circ$, $[\alpha]_{5461}^{17^\circ} - 268^\circ$.

It is very unusual to find an optically active compound and

its inactive isomeride melting at practically the same temperature. Several such cases have been noted in the course of the present research; thus, *r*-β-amino-αα-diphenyl-β-benzylethyl alcohol melts at 144·5—145·5° (McKenzie and Richardson, J., 1923, **123**, 91), whereas the *d*-isomeride melts at 143—144° (McKenzie and Wills, *loc. cit.*, p. 293). *r*-Benzyldeoxybenzoin melts at 121·5—122° (McKenzie and Richardson, *loc. cit.*; McKenzie and Roger, J., 1924, **125**, 849), whereas the optically active isomerides melt at 121—121·5°, and reference has been already made to *l*- and *r*-β-amino-αα-diphenyl-*n*-propyl alcohols, which melt at 101·5—102·5°.

Catalytic Racemisation of Optically Active Ketones.

l-*Benzoin*.—This ketone was prepared by the action of magnesium phenyl bromide on *l*-mandelamide (McKenzie and Wren, J., 1908, **93**, 309). A determination was made of its specific rotation in ethyl-alcoholic solution: $l = 2$, $c = 1{\cdot}1550$, $\alpha_D^{16^\circ} - 3{\cdot}06°$, $[\alpha]_D^{16^\circ} - 132{\cdot}5°$. To this solution in a 2-dcm. tube, four drops of ethyl-alcoholic potash (0·4487*N*) were added, and quickly mixed. Polarimetric readings were taken at intervals, and after 1 hour three additional drops of the alcoholic alkali were added. The initial reading immediately after the addition of the alkali was $\alpha_D - 3{\cdot}05°$; t = interval (minutes) after addition of the catalyst, and $\theta°$ = observed angle:

t	15	30	45	60	65	80	100	120	140
$\theta°$ ...	−2·77	−2·68	−2·61	−2·61	−2·49	−2·26	−2·00	−1·82	−1·72
t	180	220	250	280	340	400	23 hrs.	31 hrs.	5 days
$\theta°$ ...	−1·48	−1·22	−1·06	−0·91	−0·70	−0·55	−0·24	−0·22	−0·22

d-*Methyldeoxybenzoin*.—An ethyl-alcoholic solution of the ketone ($c = 0{\cdot}8095$) gave $\alpha_D^{16^\circ} + 3{\cdot}37°$ in a 2-dcm. tube. Four drops of ethyl-alcoholic potash (0·4487*N*) were mixed with the solution, and the fall in rotation was noted as below:

t (mins.)	1	10	20	30	40	50	60	90	
$\theta°$	+3·36	+3·25	+3·13	+3·04	+2·94	+2·83	+2·74	+2·54	
t (hours)	2	3	4	5	6	7	7½	23½	29½	47½
$\theta°$	+2·32	+2·00	+1·70	+1·49	+1·25	+1·04	+0·94	+0·10	+0·07	+0·00

The alcohol was evaporated from the solution, and the solid was crystallised from ethyl alcohol; silky needles of *r*-methyldeoxybenzoin, m. p. 49·5—50·5°, separated.

d-*Benzyldeoxybenzoin*.—An ethyl-alcoholic solution of the ketone ($c = 0{\cdot}392$) gave $\alpha_D^{16^\circ} + 1{\cdot}90°$ in a 2-dcm. tube, and this value was unchanged after 1 day at the ordinary temperature. Three drops (0·05 c.c.) of ethyl-alcoholic potash (0·4487*N*) were then mixed with the solution and the fall in rotation was noted as below:

t.	*θ.*	*t.*	*θ.*	*t*	*θ.*
1 min.	+1·87°	4 hours	+1·26°	24 hours	+0·31°
10 ,,	1·82	5 ,,	1·15	26 ,,	0·25
20 ,,	1·78	6 ,,	1·05	32 ,,	0·16
30 ,,	1·74	7 ,,	0·96	48 ,,	0·06
1 hour	1·63	8 ,,	0·88	54 ,,	0·05
2 hours	1·49	11 ,,	0·74	73 ,,	0·02
3 ,,	1·37	12 ,,	0·69		

Action of Magnesium Benzyl Chloride on d-*Benzyldeoxybenzoin.*—The mixture of the ketone (0·6 g.) and the Grignard reagent prepared from benzyl chloride (2 g.) was boiled for 6 hours and then decomposed by ice and dilute sulphuric acid. The ethereal layer was dried, the ether expelled, and the oil triturated with hot light petroleum. The resulting solid was crystallised from light petroleum (b. p. 80—100°), d-αβ-*diphenyl*-αβ-*dibenzylethyl alcohol*, $CH_2Ph{\cdot}CHPh{\cdot}CPh(OH){\cdot}CH_2Ph$, separating in rosettes of needles, m. p. 167—168° (Found: C, 88·6; H, 7·0. $C_{28}H_{26}O$ requires C, 88·8; H, 6·9%). In chloroform: $l = 1$, $c = 1{\cdot}306$, $\alpha_D^{17°} + 2{\cdot}02°$, $[\alpha]_D^{17°} + 155°$.

We are indebted to Mr. Arthur Kelman Mills for the following observations.

Action of Magnesium Benzyl Chloride on Ethyl r-*Alanine Hydrochloride.*—The ester hydrochloride (1 mol.) was heated for several hours with the Grignard reagent prepared from benzyl chloride (9 mols.). The mixture was decomposed by ice and ammonium chloride, the ether layer separated, the ether expelled, and the dibenzyl removed by steam distillation. The product was purified by crystallising first from light petroleum and then from rectified spirit.

r-β-*Amino*-αα-*dibenzyl*-n-*propyl alcohol*,

$$(PhCH_2)_2C(OH){\cdot}CHMe{\cdot}NH_2,$$

is moderately soluble in rectified spirit, from which it crystallises in plates, m. p. 93·5—94·5° (Found: C, 80·1; H, 8·4. $C_{17}H_{21}ON$ requires C, 80·0; H, 8·3%).

Action of Magnesium Benzyl Chloride on Ethyl r-*Phenylaminoacetate Hydrochloride.*—The ester hydrochloride (10 g., 1 mol.) was added to the Grignard reagent prepared from benzyl chloride (52·5 g., 9 mols.) and boiled for 3 hours. After decomposition with ice and ammonium chloride, the ethereal layer was separated and dried and from it an oil was obtained which was dissolved in hot light petroleum (b. p. 60—80°). 6·9 G. of solid crude amino-alcohol separated. This was recrystallised from rectified spirit; 6·0 g. of β-amino-αα-dibenzyl-β-phenylethyl alcohol, m. p. 125—126°, were then obtained. This compound has already been described by Thomas and Bettzieche (*Z. physiol. Chem.*, 1924, **140**, 244), who used somewhat different experimental conditions from the above.

Deamination of r-β-*Amino*-β-*phenyl*-αα-*dibenzylethyl Alcohol.*—To the solution of the amino-alcohol (4 g.) in 25% acetic acid (120 c.c.) an aqueous solution of sodium nitrite (3 g.) was added while the whole was maintained at 0°. The white solid which at first separated soon became viscous, and was extracted with ether. The product from the ethereal solution was dissolved in alcohol, and the solid which separated was crystallised twice from light petroleum (b. p. 40—60°). The resulting rosettes of needles consisted of benzyl αβ-diphenylethyl ketone, $CH_2Ph{\cdot}CHPh{\cdot}CO{\cdot}CH_2Ph$, m. p. 74—75°. For comparison, α-phenyl-ββ-dibenzylethylene glycol was prepared from ethyl *dl*-mandelate by the action of magnesium benzyl chloride, and dehydrated with concentrated sulphuric acid according to Orékhov (*Bull. Soc. chim.*, 1919, **25**, 111). When prepared in the latter manner, the ketone had m. p. 74—75° (Orékhov gives 75—76°), and there was no depression of the melting point when it was mixed with the product of the deamination.

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