XLIX.—*The Arrangement in Space of the Groups Combined with the Tervalent Nitrogen Atom.*

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THE discussion as to the cause of the existence of isomeric oximes and of that of certain other derivatives of tervalent nitrogen, which for so many years occupied a prominent place in current chemical literature, apparently came to an end some time ago; at any rate, the occurrence of such isomerides now excites but little interest, and is, in fact, taken as a matter of course, and the usual "*syn*" and "*anti*" configurations having been respectively assigned to the two isomerides, the matter is dismissed from further consideration.

It is far from our intention to attempt to make any review of the literature of this subject, as it would occupy far too much space even were we merely to refer in the briefest manner to the views of the principal workers in this field, or to recapitulate quite cursorily the various arguments which have led to the adoption of the "*syn*" and "*anti*" configurational formulæ for isomeric derivatives of tervalent nitrogen; it is necessary, however, in order to explain one of the objects of this investigation, to briefly recall the meaning and consequences of such stereochemical representations.

According to Hantzsch and Werner (*Ber.*, 1890, 23, 11), the existence of this type of isomerides is to be explained by assuming that the groups around a tervalent nitrogen atom are situated at the corners of a regular tetrahedron, of which the nitrogen atom itself occupies the fourth corner; the "*syn*" and "*anti*" configurations are thus respectively represented by the following symbols:

Now this hypothesis, which seems to be generally accepted by chemists as a means of explaining the phenomenon in question, involves, or seems to involve, certain consequences which are by no means confirmed by experimental evidence.

In the first place, this conception premises the existence of isomerides in the case of a great number of compounds which hitherto have been obtained in only one form (compare Hantzsch and Werner, *loc. cit.*). Azobenzene, for example, as far as is known, does not exhibit stereoisomerism, and yet the existence of *syn*- and *anti*-forms of this and of azo- and azoxy-compounds generally would be in accordance with theory; as a matter of fact, the only cases of isomerism in such compounds which have yet been described are those of *p*-azoxytoluene and trinitrazotoluene (Janovski and Reimann, *Ber.*, 1889, 22, 40, and Janovski, *Ber.*, 1889, 22, 1172), and it would appear that even these may be capable of some other explanation. Many other examples of a similar absence of conceivable isomerides might be quoted, but it is unnecessary to do so; Hantzsch, himself, has tried to obtain isomeric compounds containing doubly-linked nitrogen in many cases where their existence seemed a probable consequence of his and Werner's theory (compare *Ber.*, 1893, 26, 926).

The question which more immediately concerns our work, however, is that of the possibility of existence of isomerism in compounds of the type $\text{NR}_1\text{R}_2\text{R}_3$; if the three atoms or groups combined with trivalent nitrogen are situated at the angles of a regular tetrahedron, secondary and tertiary nitrogen bases which are of the above type, that is to say, in which the three atoms or groups are all different from one another, should exist in enantiomorphously related forms, and the latter in all probability would be optically active; such forms would be represented respectively by the configurational formulæ:

The possibility of the existence of such isomerides has been previously considered, and, in fact, experiments have already been made in order to try and obtain such optically active compounds. Kraft (*Ber.*, 1890, 23, 2780), at the suggestion of Hantzsch, attempted to resolve benzylethylamine and *p*-tolylhydrazine by fractionally crystallising their hydrogen tartrates, whereas Behrend and König (*Annalen*, 1891, 263, 175; *Ber.*, 1891, 24, 447c) carried out similar and additional

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experiments with β -benzylhydroxylamine, whilst Ladenburg (*Ber.*, 1893, 26, 864) investigated methylaniline, tetrahydroquinoline, and tetrahydropyridine; all these investigations, and likewise some experiments of Le Bel (*Compt. rend.*, 1891, 112, 11), were, however, uniformly unsuccessful.

Now it may be observed in connection with the investigations just referred to that the point actually put to the test of experiment was not so much the existence of isomeric tervalent as that of quinquevalent derivatives of nitrogen containing two identical groups or atoms. Even had isomeric salts been obtained, the latter might not have afforded enantiomorphously related bases when decomposed with alkalis, because in passing from the quinquevalent to the tervalent state a complete rearrangement in space of the nitrogen "valencies" might occur, and both the isomeric salts might give the same compound or the same mixture of isomerides.

These considerations led us to undertake the present work in the hope of adding to our knowledge of the configuration of tervalent nitrogen. Our first experiments were directed towards an investigation of the products obtained by the action of an externally compensated acid chloride on certain primary and secondary amines. A *dl*-acid chloride, such as *dl*-phenylchloroacetyl chloride, gives with a *dl*-base, such as *dl*-hydrindamine, a mixture of two isomeric phenylchloroaceto-hydrindamides, which can be separated by fractional crystallisation (Kipping and Hall, *Trans.*, 1901, 79, 444); this is due, of course, to the formation of the four compounds,

which are enantiomorphously related in pairs, and which crystallise together, forming two different *dl*-isomerides. An externally compensated acid chloride may therefore be employed for the detection of asymmetry in bases, a fact which in the first place we confirmed by proving that *dl*-benzylmethylacetyl chloride gives with *dl*-hydrindamine a mixture of isomeric *dl*-substituted amides from which the two compounds may be isolated without much difficulty.

Now if instead of a base such as *dl*-hydrindamine, which owes its asymmetry to a carbon group, some primary or secondary base, such as *p*-toluidine or methylaniline, were treated with a *dl*-acid chloride, it seems reasonable to suppose that two isomeric substituted amides should be obtained, provided that the three nitrogen valencies are not arranged in one plane, but, as surmised by Hantzsch and Werner in the case of the oximes; the *d*-component of the acid chloride would give equal or approximately equal quantities of the two compounds,

which are not enantiomorphously related, whilst the *l*-component would give rise to two analogous isomerides; these would then crystallise in pairs, just as in the case of the hydrindamides, giving two different *dl*-substituted amides.

The experiments were tried with methylaniline, *p*-toluidine, phenylhydrazine, and benzyaniline, the acid chloride being *dl*-benzylmethylacetyl chloride; in no case, however, could we observe the least indication of the formation of isomerides.

In all these examples, if non-enantiomorphously related isomerides were produced at all, each of the four compounds which might conceivably have been formed would contain one group enantiomorphously related to that in one of its isomerides; thus, although *dBdA* and *dBIA* are not enantiomorphously related, a portion of the molecule of the one does bear such a relationship to a portion of that of the other; similarly with *lBIA* and *lBdA*. This might condition the formation of a double racemic salt $\left\{ \begin{array}{l} \textit{dBdA}, \textit{dBIA} \\ \textit{lBIA}, \textit{lBdA} \end{array} \right\}$ such as is possibly produced from *dl*-hydrindamine and *dl*-mandelic acid (Kipping and Hall, *Trans.*, 1901, 79, 442), and thus account for the failure of our attempts to separate isomerides.

In order to limit such a possibility to some extent, we next made experiments on the behaviour of some primary and secondary bases towards optically active benzylmethylacetyl chloride, and examined the substituted amides derived from *p*-toluidine and benzyaniline; no evidence of the formation of isomerides *dBdA* and *lBdA*, however, could be obtained.

Our last and most conclusive experiments on these lines were made with optically active bases and optically active benzylmethylacetyl chloride. If, in the case of asymmetric carbon groups, the two enantiomorphously related compounds are generally separable as soon as an asymmetric radicle is substituted for one of the atoms or radicles in each of the groups, it would seem highly probable that the introduction of a second centre of asymmetry would greatly enhance the difference between the two isomerides as regards their solubility, &c., and thus greatly facilitate their separation by fractional crystallisation.

Now when an optically active base such as *l*-menthylamine is treated with *d*-benzylmethylacetyl chloride, the resulting substituted amide contains two centres of asymmetry due to carbon; if, in addition,

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the three nitrogen valencies are so arranged as to condition a third centre of asymmetry, two very different isomerides, represented respectively by the following configurational formulæ, should be obtained :

The bases examined in this way were *d*-hydrindamine, *l*-methylhydrindamine, *l*-menthylamine, and *l*-phenylethylamine ; in all cases, however, the product seemed to consist of one substance only, and when crystallised fractionally from various solvents retained its uniform character.

We conclude from these results that the three radicles, together with the tervalent nitrogen atom itself, are situated in one plane ; that two of the radicles are symmetrically grouped with respect to the third, and that in all probability this is true of any two, that is to say, the whole arrangement is the most symmetrically possible one.

Examination of Oximes.—Having failed to detect any indication of isomerism in the case of saturated tervalent nitrogen compounds which would be in accordance with the theory of Hantzsch and Werner, we next turned our attention to the oximes themselves.

Assuming that the isomerism of the *syn*- and *anti*-forms is structural and that the two compounds are represented by the formulæ

an asymmetric carbon group, would exist in enantiomorphously related forms. If, then, an optically active acyl group were substituted for the hydrogen atom, two non-enantiomorphously related optically active isomerides should be obtained, whereas by employing a *dl*-acyl chloride two different *dl*-compounds should be produced.

Intending, subsequently, to investigate the benzaldoximes, we first studied the action of the *dl*-acid chloride on benzoinoxime, a substance which crystallises well, and the derivatives of which, it was thought, would show a similar behaviour. The reaction, however, proceeded in a manner altogether abnormal ; instead of obtaining an acyl derivative by the simple displacement of the oximic hydrogen atom, we got a number of other products, namely, benzil, benzoin, benzaldehyde, benzonitrile, ammonium chloride, hydrogen chloride, benzylmethylacetic acid, and a compound melting at 126° ; this decomposition of the oxime made it impossible, of course, to accomplish the objects in view, but the result is not without interest as showing how easily the

benzoin molecule—which is generally so stable—may undergo decomposition.

In order to try and throw some light on this extraordinary reaction, we next studied the action of benzoyl chloride on benzoinoxime, but found that interaction proceeded in a normal manner, giving a benzoinoxime benzoate in which the benzoyl group had displaced the oximic hydrogen atom; the constitution of the product was established by preparing the oxime of the benzoylbenzoin described by Zinin (*Annalen*, 1857, 104, 117); the latter, which would necessarily have the constitution $C_6H_5 \cdot CH(OBz) \cdot CPh : N \cdot OH$, is not identical with the benzoyl derivative of benzoinoxime, so that our compound must be represented by the formula $C_6H_5 \cdot CH(OH) \cdot CPh : N \cdot OBz$.

Failing to obtain the desired results with benzoinoxime, we made a few experiments with α -benzaldoxime, but were unable to prepare the benzylmethylacetyl derivative owing to the decomposition of the aldoxime into benzonitrile.

The Resolution of dl-Bases with the aid of d-Benzylmethylacetyl Chloride.

The resolution of a *dl*-base by fractionally crystallising the salt obtained by combining it with an optically active acid is very often unsuccessful owing to the fact that the two salts *dBdA* and *lBdA* or *dBIA* and *lBIA* may differ so slightly in solubility that no appreciable separation occurs, or, again, they may unite to form a partially racemic compound. Judging from the many cases which have been examined in this laboratory, it would seem that it is rather the exception than the rule for a resolution to take place, and were all the negative results of investigators on record, this conclusion would probably be amply substantiated; contrary to the views sometimes held, the use, in such experiments, of a relatively weak acid also seems to be just as likely to give satisfactory results as that of a relatively strong one, since hydrolytic dissociation seldom plays any important part, the difference in solubility of the salts being practically the only factor of importance.

The investigations carried out during the last few years on the behaviour of *dl*-hydrindamine have shown that the resolution of this base presents more than the usual difficulties, and that ordinary fractional crystallisation of its salts with *d*-bromocamphorsulphonic, *d*-chlorocamphorsulphonic, Reychler's *d*-camphorsulphonic, *l*-mandelic, and *d*-tartaric acids fails to effect a separation of the two isomerides. In these circumstances, it occurred to one of us that a resolution might be accomplished by using an optically active acid chloride which would probably give isomeric substituted amides differing considerably in solubility; this expectation proved to be well-founded, inasmuch as

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the product of interaction of *dl*-hydrindamine and *d*-benzylmethylacetyl chloride was easily separated into two isomerides having different specific rotations.

d-Benzylmethylacetyl chloride was also employed for the resolution of *dl*-phenylethylamine, and in this case also the two isomeric amides corresponding with the *d*- and *l*-bases respectively are separated without much difficulty.

Judging from these examples, an optically active acid chloride may be employed with success when the use of an acid gives unsatisfactory results, but it will be necessary to wait until a greater number of cases have been tried before concluding that such a method is universally applicable. One great drawback to the use of the acid chloride is that it may be impossible to obtain the optically active bases themselves, either because the substituted amides are so stable that they cannot be hydrolysed, or because so high a temperature is required to bring about hydrolysis that the bases undergo racemisation. Thus, in the case of the benzylmethylacetohydrindamide, all attempts to regenerate the base were unsuccessful; the amides are exceedingly stable towards ordinary hydrolysing agents at moderate temperatures, and although change occurs at high temperatures, it results in the formation of indene and ammonia.

The application of an optically active acid chloride for the resolution of *dl*-alcohols or other *dl*-hydroxy-compounds has not yet been tried.

EXPERIMENTAL.

dl Hydrindamine and *dl*-Benzylmethylacetyl Chloride. Isolation of Two Isomerides.

In order to satisfy ourselves that *dl*-benzylmethylacetyl chloride would prove serviceable in detecting asymmetry, we first tried its action on *dl*-hydrindamine, a base which is very prone to form partially racemic salts, and which is resolved into its enantiomorphously related components only with great difficulty.

On adding the *dl*-benzylmethylacetyl chloride to the *dl*-base, both in ethereal solution, a development of heat occurred, and the hydrochloride of the base separated in crystals; after filtering, washing with water, and evaporating the ethereal solution, the substituted amide was obtained as an oil which rapidly solidified.

When crystallised fractionally from methyl alcohol, ether, and other solvents, this product, which at first melts indefinitely at about 70°, is finally resolved into two isomerides. One of these crystallises in thick, transparent prisms melting at 110–111°, but when the partially melted substance is allowed to cool it immediately solidifies, and when heated again melts at about 126°; it is therefore dimorphous.

This amide is very readily soluble in cold methyl alcohol, moderately so in ether, but dissolves very sparingly in light petroleum (b. p. 40—60°).

0.1615 gave 0.4857 CO₂ and 0.1090 H₂O. C = 82.0; H = 7.5.

C₁₉H₂₁ON requires C = 81.7; H = 7.5 per cent.

The second isomeride crystallised from aqueous methyl alcohol in felted masses of needles melting sharply at 119.5°; it seems to be far less soluble in cold ether than the preceding compound.

0.1497 gave 0.4484 CO₂ and 0.0996 H₂O. C = 81.7; H = 7.4.

C₁₉H₂₁ON requires C = 81.7; H = 7.5 per cent.

Products from dl-Benzylmethylacetyl Chloride and Primary or Secondary Bases.

Having proved that evidence of asymmetry due to a carbon group is easily obtained with the aid of *dl*-benzylmethylacetyl chloride, we studied the products of the action of this compound on some primary and secondary bases.

Methylaniline and the *dl*-chloride interact readily in ethereal solution. The resulting substituted amide remained in an oily condition for a long time, but ultimately solidified completely; it was fractionally crystallised from warm light petroleum (b. p. 30—40°) in which it was readily soluble, and was thus obtained in lustrous, transparent prisms melting sharply at 54—55°; all the fractions had the same appearance, and except the last, which melted a few degrees below 54°, liquefied at the same temperature. *Benzylmethylaceto-methylanilide* exists, therefore, in only one form; it is readily soluble in all ordinary organic solvents.

p-Toluidine and *dl*-benzylmethylacetyl chloride interact vigorously in ethereal solution; the *benzylmethylaceto-p-toluidide*, which is thus formed, solidified readily, and was fractionally crystallised from aqueous alcohol; it separated in concentrically grouped needles melting at 130°. The very last mother liquors gave traces of a product melting about 2° lower than the rest, but there was no evidence of the existence of isomerides. *Benzylmethylaceto-p-toluidide* is readily soluble in all ordinary organic solvents with the exception of light petroleum (b. p. 30—40°), in which it dissolves somewhat sparingly.

Benzylaniline and *dl*-benzylmethylacetyl chloride give a product which is at first rather difficult to obtain in a crystalline condition, but which afterwards crystallises easily from aqueous alcohol in ill-defined prisms; the compound was separated into a number of fractions, but the latter were all identical in appearance and melting point.

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Benzylmethylacetobenzylanilide is readily soluble in most organic solvents and melts at 69—70°.

0.1452 gave 0.4457 CO₂ and 0.0921 H₂O. C = 83.7; H = 7.05.
 C₆H₅·CH₂·CH(CH₃)·CO·N(C₇H₇)·C₆H₅ requires C = 83.9; H = 7.0 per cent.

Phenylhydrazine, when treated with the *dl*-chloride in ethereal solution, readily yielded *benzylmethylacetophenylhydrazide*, which crystallised from methyl alcohol in large, transparent, lustrous prisms melting at 116—117° and readily soluble in ethyl acetate; fractional crystallisation failed to indicate the presence of an isomeride.

Products from d-Benzylmethylacetyl Chloride and Primary or Secondary Bases.

For the reasons already stated, we next examined the products obtained with the aid of the optically active chloride; in doing so, it was found that even when the acid chloride had the highest specific rotation previously observed, namely, $[\alpha]_D + 18^\circ$ in ethereal solution (Kipping and Hunter, *Trans.*, 1903, 83, 1005), it still contained a small quantity of the *l*-isomeride, owing, doubtless, to the occurrence of racemisation during its preparation, and gave rise to some of the *dl*-substituted amide; the presence of the latter was a serious disadvantage because, although the main portions of the active and inactive amides could be separated without much difficulty, there still remained a considerable quantity of mixed products in which the required isomeric active compound might conceivably be concealed. In the later and more important experiments, therefore, the active acid chloride was prepared from very carefully purified acid by a method which should exclude the possibility of racemisation (p. 447).

p-Toluidine and *d*-benzylmethylacetyl chloride gave a product which, when repeatedly fractionally crystallised from aqueous alcohol, was resolved into two compounds, one of which, however, was present in relatively small proportions; this was the amide of the *dl*-acid and melted at 130° (p. 445). The main component, namely, *d*-benzylmethylaceto-*p*-toluidide, crystallised in large, flat, transparent, well-defined prisms melting at 115—116°; it was readily soluble in cold alcohol and in ethyl acetate.

0.2364, dissolved in alcohol and the solution diluted to 25 c.c., gave, in a 200 mm. tube, $\alpha + 3.17^\circ$, whence $[\alpha]_D + 167.6^\circ$.

0.5150, dissolved in chloroform and the solution diluted to 20 c.c., gave, in a 200 mm. tube, $\alpha + 5.67^\circ$, whence $[\alpha]_D + 110.1^\circ$.

During the fractional crystallisation, no compound other than the

two already mentioned was obtained, and we concluded that optically active isomerides were not produced. The experiment was subsequently repeated, using a sample of *d*-chloride free from the *l*-isomeride, and in this case only one compound, namely, that melting at 115—116°, was obtained.

Benzylaniline and *d*-benzylmethylacetyl chloride gave a product which was very difficult to crystallise even when the acid chloride had been prepared by the special method to be described later. This was due to the fact that the product retained benzylaniline very tenaciously, and repeated washing with warm hydrochloric acid was required before the whole of this base was removed. Finally, however, the amide solidified to a crystalline mass, which was fractionally crystallised from light petroleum and from aqueous alcohol. The several fractions of *d*-benzylmethylacetobenzylanilide,

thus obtained melted at the same temperature (69—70°), which is also the melting point of the inactive amide already described (p. 446); moreover, a mixture of the crystals of the active and inactive amides also melted at 69—70°.

The specific rotation of the *d*-anilide was determined in chloroform solution: 0.3079, dissolved in chloroform, the solution diluted to 20 c.c. and examined in a 200 mm. tube, gave $\alpha + 0.27^\circ$ whence $[\alpha]_D + 8.8^\circ$; in methyl-alcoholic solution the specific rotation was $[\alpha]_D + 16^\circ$.

Although only one active compound was isolated, and although there was no evidence of the formation of an isomeride in the above experiment, we are unable to state positively that only one substance was produced, as a portion of the product from the last mother liquors crystallised badly and had a brown colour, doubtless owing to atmospheric oxidation.

Preparation of d-Benzylmethylacetyl Chloride.

Owing to the readiness with which the *d*-acid chloride is racemised under the influence of heat (Kipping and Hunter, *Trans.*, *loc. cit.*), the compound prepared in the usual manner is almost invariably mixed with more or less of the *l*-isomeride, the presence of which is very objectionable in such experiments as those already described, where it is a question of the existence of isomeric amides. In order to prepare the active compound in an optically pure condition, it is necessary to keep the temperature as low as possible and then to remove the phosphorus oxychloride from the product without the application of heat. This can be accomplished by passing a current of dry air through the mixture under greatly reduced pressure, but the operation requires a considerable time before the last portions of phosphorus oxychloride

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are removed. The *d*-chloride thus prepared has a specific rotation in light petroleum $[\alpha]_D + 26.2$, a value which is a trifle higher than that previously obtained (*loc. cit.*).

This method of preparation does not remove every trace of phosphorus compounds, for the acid chloride still gives a slight reaction with ammonium molybdate, probably due to the presence of phosphoric acid; this impurity, however, is of little consequence, as it is easily eliminated by washing with water, when the acid chloride is used for the preparation of a substituted amide.

Products from d-Benzylmethylacetyl Chloride and Optically Active Bases.

1. *l*-Phenylethylamine.—The active base, prepared by the method recently described (Kipping and Hunter, *Trans.*, 1903, 83, 1147), was dissolved in dry ether and the active acid chloride added gradually, when a reaction immediately occurred, and the hydrochloride separated in crystals. This salt was removed by filtration, and the ethereal solution washed successively with dilute hydrochloric acid, water, sodium carbonate, and water, by which treatment any remaining hydrochloride, free base, or free acid is removed. After evaporating off the ether, the crude product, which immediately solidified, was then fractionally crystallised from benzene and thus separated into at least nine fractions, but one and the same compound melting at 122° was obtained throughout, and no indication whatever of the presence of isomerides was observed. *d*-Benzylmethylaceto-*l*-phenylethylamide, $C_6H_5 \cdot CH_2 \cdot CH(CH_3) \cdot CO \cdot NH \cdot CH(CH_3) \cdot C_6H_5$, crystallises from benzene in beautiful, long, silky needles melting at 122.5° . It is readily soluble in ethyl acetate, chloroform, methyl alcohol, ether, or alcohol, but only sparingly so in light petroleum.

0.4315, dissolved in ether and diluted to 20 c.c., gave, in a 200 mm. tube, $\alpha + 0.37^\circ$, whence $[\alpha]_D + 8.6^\circ$.

2. *l*-Methylhydrindamine.—The reaction was conducted in dry ethereal solution, and since the product was not readily soluble in ether the solvent was allowed to evaporate and the residue washed at the pump with dilute hydrochloric acid, hot water, dilute sodium carbonate, and hot water successively. The substance, which then melted at 150 – 152° , was now subjected to fractional crystallisation from benzene and separated into at least eight portions, but in this case, as before, only one compound was found to be present, although the last fractions had their melting point lowered slightly through the presence of a trace of unavoidable impurity.

d-Benzylmethylaceto-*l*-methylhydrindamide crystallises from benzene and alcohol in long, silky needles very similar to those of the acid

amide of *l*-phenylethylamine and melting at 152° ; it is readily soluble in hot benzene, alcohol, chloroform, or ether.

0.4071, dissolved in chloroform and diluted to 20 c.c., gave, in a 200 mm. tube, $\alpha - 1.08^{\circ}$, whence $[\alpha]_D - 26.5^{\circ}$.

3. *l*-Menthylamine.—The optically pure base, prepared from its *d*-bromocamphorsulphonate (Tutin and Kipping, Trans., 1904, 85, 65) dissolved in ether, was added to an ethereal solution of *d*-benzylmethylacetyl chloride, when a vigorous reaction occurred; the deposited menthylamine hydrochloride was separated by filtration and the ethereal solution washed with dilute hydrochloric acid, sodium carbonate, and water successively. The product was fractionally crystallised from benzene and separated into at least six fractions, but the first and last fractions were identical in crystalline form and melting point.

d-Benzylmethylaceto-*l*-menthylamide crystallises from benzene in long needles melting at 140° ; it is readily soluble in all the ordinary organic solvents.

0.7704, dissolved in chloroform and diluted to 20 c.c. in a 200 mm. tube, gave $\alpha + 0.58^{\circ}$, whence $[\alpha]_D + 7.5^{\circ}$.

4. *d*-Hydrindamine.—The reaction was conducted as in the case of the former active bases and the product fractionated from benzene. Six fractions were thus obtained, but no difference in appearance or melting point could be observed on comparing the first and last deposits.

d-Benzylmethylaceto-*d*-hydrindamide crystallises from benzene in long, colourless needles melting at $148-149^{\circ}$; it is readily soluble in methyl alcohol, chloroform, acetone or ethyl acetate; moderately so in ether, and dissolves sparingly in light petroleum.

0.8580, dissolved in methyl alcohol and the solution diluted to 20 c.c., gave, in a 200 mm. tube, $\alpha - 1.33^{\circ}$, whence $[\alpha]_D - 15.5^{\circ}$.

1.2482, dissolved in chloroform and the solution diluted to 20 c.c., gave, in a 200 mm. tube, $\alpha + 0.76^{\circ}$, whence $[\alpha]_D + 6.1^{\circ}$.

Action of dl-Benzylmethylacetyl Chloride on Benzoinoxime.

Benzoinoxime was covered with dry ether or light petroleum and slowly treated with one molecular proportion of *dl*-benzylmethylacetyl chloride. No appreciable development of heat was observed, but the gradual progress of the reaction was indicated both by the conglomeration of the benzoinoxime into a united whole, and also by the slow evolution of hydrogen chloride. If the mixture is warmed to the boiling point of the solvent, the reaction is considerably accelerated, the

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whole of the oxime dissolves, and a crystalline product is deposited in small quantities.

The crystalline product was fractionally crystallised from alcohol; the first deposit consisted of beautiful, long, lemon-yellow crystals which were evidently pure and melted at 95° , being thus identified as benzil. The second deposit of crystals consisted of a mixture of small, colourless needles and of a white, fluffy, crystalline substance. The latter, which was immediately dissolved on washing with water, consisted of ammonium chloride. The residue, when crystallised, yielded colourless needles identified as benzoin (m. p. 134°). The alcoholic mother liquors yielded further quantities of these three products only.

The ethereal solution gave, on evaporation, a yellow oil, which was washed with dilute aqueous sodium carbonate until the extracts were found to be free from acid. The substance thus removed was precipitated from the alkaline solution by the addition of dilute sulphuric acid, extracted with ether, and distilled under reduced pressure (18 mm.). It consisted almost entirely of benzylmethylacetic acid, boiling at 164° . The ethereal solution, which had been extracted with sodium carbonate, gave, on evaporation, an oil, which had a strong odour of bitter almonds and which was distilled under atmospheric pressure, the fractions being collected at $179-190^{\circ}$ and $190-200^{\circ}$. The residue was then distilled under reduced pressure (17 mm.) and the distillate solidified to a yellow mass, which, when crystallised from alcohol, melted at 95° , and proved to be benzil, the presence of which among the products of the reaction had been previously observed. The two fractions, boiling at $179-190^{\circ}$ and $190-200^{\circ}$ respectively, were too small for further fractional distillation, but as the former had the strong odour and boiling point of benzaldehyde, it was treated with phenylhydrazine in acetic acid solution, when benzaldehydephenylhydrazone (m. p. 154°) was obtained. The second fraction, boiling at $190-200^{\circ}$, was found to be hydrolysed by prolonged boiling with an aqueous solution of sodium hydroxide, a copious evolution of ammonia taking place; the alkaline solution, when neutralised, yielded a crystalline precipitate, which was identified as benzoic acid. This fraction therefore consisted chiefly of benzonitrile.

We have thus shown that the products of the interaction of benzoin-oxime and benzylmethylacetyl chloride are: (1) benzylmethylacetic acid; (2) benzaldehyde; (3) benzonitrile; (4) benzoin; (5) benzil; (6) ammonium chloride; and (7) hydrogen chloride.

This decomposition of the molecule of benzoinoxime by the acid chloride is somewhat obscure, but apparently decomposition occurs in two different directions simultaneously. In the first instance, the molecule is severed between the two central carbon atoms with the

formation of benzaldehyde and its oxime, the latter of which by dehydration is converted into benzonitrile. This decomposition may be indicated thus :

In the second place, the decomposition of the benzoinoxime takes place by the elimination of ammonia and the formation of benzil according to the equation :

In any case, the above decomposition of benzoinoxime at the ordinary temperature is a reaction of some interest, inasmuch as it affords one of the few known examples whereby the benzoin condensation of benzaldehyde is reversed. Zinin (*Ber.*, 6, 1207), by repeated distillation of benzoin, obtained a decomposition into benzaldehyde, benzil, deoxybenzoin, and water according to the equation :

whilst the same products were obtained by passing benzoin vapour through a red-hot tube (compare also Knoevenagel and Tomaszewski (*Ber.*, 1903, 36, 2829).

Thinking that the decomposition of the benzoinoxime might be due to the action of the hydrogen chloride which is liberated, experiments were made in which an excess of dry quinoline was previously mixed with the oxime; the presence of this base, however, seemed to have little effect on the course of the reaction. It may be added that in many of the experiments the various products already enumerated were accompanied by very small quantities of a crystalline compound melting at 126°; this substance was not identified, but from its composition and reactions it seemed to be the substituted amide,

produced by intramolecular change.

In order to ascertain whether other acid chlorides would react normally with benzoinoxime giving acyl derivatives, or whether, like benzylmethylacetyl chloride, they would bring about a decomposition of the molecule, molecular proportions of benzoyl chloride and benzoinoxime were allowed to interact in ethereal solution. A gradual

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evolution of hydrogen chloride occurred, but the reaction was not vigorous. After keeping for several hours at the ordinary temperature, the ethereal liquid was separated from the solid by filtration. The filtrate contained unchanged benzoyl chloride together with approximately equal proportions of benzoin and benzil. The solid product consisted chiefly of benzoinoxime benzoate, but it also contained a moderate quantity of benzoin and hydroxylamine hydrochloride. The presence of the latter was shown, after the removal of the benzoate by crystallisation, by evaporating the alcoholic mother liquors and washing the residue with water. The aqueous extract immediately reduced Fehling's solution and also gave the reactions of a chloride.

Benzoinoxime benzoate is easily purified by crystallisation from alcohol, in which it is only slightly soluble (approximately 1 part in 30 parts of boiling alcohol); it is thus obtained in leaf-like plates melting at 165—166°.

0.1540 gave 0.4301 CO₂ and 0.0729 H₂O. C = 76.17; H = 5.26.

0.4795 „ 19.4 c.c. moist nitrogen at 21° and 750.3 mm. N = 4.6.

C₂₁H₁₇O₃N requires C = 76.13; H = 5.14; N = 4.2 per cent.

Benzoinoxime benzoate is hydrolysed by acids and alkalis giving benzoin, benzoic acid, and hydroxylamine. It is moderately soluble in chloroform and ethyl acetate; only slightly so in benzene.

The foregoing method of preparing the benzoyl derivative leaves open several possibilities with regard to its constitution. Since benzoinoxime contains two hydroxyl groups, it is uncertain whether the benzoyl group has entered the alcoholic or the oximic hydroxyl, or whether the benzoinoxime has undergone the Beckmann transformation prior to benzoylation. The latter possibility, however, is shown to be untenable by a study of the reactions of the product. Since, on hydrolysis, it yields benzoin and hydroxylamine, it cannot have the constitution C₆H₅·CH(OH)·CO·NBz·C₆H₅ or

but may be either

A decision between these two formulæ has been rendered possible by the fact that we have prepared the compound having the latter constitution by benzoylating benzoin prior to the introduction of the oxime group, a process which ensures the substitution of the hydrogen of the alcoholic hydroxyl group by the benzoyl radicle. In order to distinguish between the two isomerides, we have described them as benzoinoxime benzoate and benzoylbenzoinoxime respectively.

Benzoylbenzoin was prepared by heating molecular proportions of benzoin and benzoyl chloride at 150° for an hour (Zinin, *loc. cit.*); the reaction was always accompanied by oxidation with the formation of benzil (about 10 per cent.). The benzoylbenzoin was boiled in aqueous alcoholic solution with twice the theoretical quantities of sodium acetate and hydroxylamine hydrochloride, the heating being continued during 6—12 hours; when the greater portion of the alcohol was then distilled off and the residue poured into water, the semi-solid product, on crystallisation from alcohol, deposited globular clusters of crystals melting at 148° .

0.2400 gave 0.1122 H_2O and 0.6704 CO_2 . C = 76.18; H = 5.19.

0.5295 „ 20.3 c.c. moist nitrogen at 17.5° and 763.5 mm. N = 4.5.

$\text{C}_{21}\text{H}_{17}\text{O}_3\text{N}$ requires C = 76.13; H = 5.14; N = 4.2 per cent.

Benzoylbenzoinoxime is readily soluble in the ordinary organic solvents.

Action of Benzylmethylacetyl Chloride on α -Benzaldoxime.

When α -benzaldoxime, covered with light petroleum, is treated with benzylmethylacetyl chloride, the mixture becomes warm and hydrogen chloride is slowly evolved, while the transparent crystals of the oxime are converted into a fine, white powder. After leaving the mixture at the ordinary temperature for several hours, the solid is separated by filtration and identified as benzamide. On evaporation, the light petroleum solution gave an oil which had a strong odour of bitter almonds; on distilling in steam, a portion passed over and was identified as benzonitrile. The residue consisted of benzylmethylacetic acid.

In one experiment, 10.7 grams of acid chloride and 7.1 grams of benzaldoxime were used, from which 5 grams of benzonitrile, 2 grams of benzamide, and 9 grams of benzylmethylacetic acid were obtained.

In a second experiment, only 0.5 gram of benzamide was produced from 8.3 grams of benzaldoxime, with a corresponding increase in the quantity of benzonitrile.

The Resolution of dl-Bases with the Aid of an Active Acid Chloride.

Action of d-Benzylmethylacetyl Chloride on dl-Hydrindamine.

On slowly adding a dry ethereal solution of hydrindamine (2 mols.) to an ethereal solution of benzylmethylacetyl chloride (1 mol.), pre-

pared from the *d*-acid in the ordinary way, a vigorous reaction ensues with development of heat and precipitation of hydrindamine hydrochloride, but after about half the base has been run in, the reaction moderates considerably. The solution, left overnight to ensure complete interaction, is then washed with water, the ether allowed to evaporate, and the crystalline product separated by filtration and washed with water until free from hydrochloride. On repeatedly crystallising the crude hydrindamide from methyl alcohol, the most sparingly soluble isomeride is obtained without much trouble; this compound crystallises from methyl alcohol in colourless needles or prisms melting at 148—149°; it is readily soluble in cold methyl alcohol, ethyl acetate, ether, and acetone, but practically insoluble, even in boiling water. This compound is laevorotatory in methyl-alcoholic solution, and is a derivative of *d*-hydrindamine, as is proved by the fact that it is identical with the *d*-benzylmethylaceto-*d*-hydrindamide already described (p. 449); its specific rotation was determined with the following results:

0.5766, in 25 c.c. methyl alcohol and in a 200 mm. tube, gave $\alpha - 0.74^\circ$, whence $[\alpha]_D - 16^\circ$.

0.1411 gave 0.4232 CO₂ and 0.0952 H₂O. C=81.79; H=7.5.

0.1419 „ 0.4266 CO₂ „ 0.1016 H₂O. C=82.0; H=7.9.

C₁₉H₂₁ON requires C=81.7; H=7.5 per cent.

The various mother liquors remaining after the isolation of the *d*-benzylmethylaceto-*d*-hydrindamide gave crystalline deposits, which, when submitted to fractional crystallisation, gave long, ill-defined needles melting at 119—120°; this substance is one of the externally compensated compounds identical with that prepared from *dl*-hydrindamine and the *dl*-acid chloride (p. 444). The later crystalline deposits yielded a compound which crystallised from methyl alcohol in well-defined prisms melting at 110—111°; this is the isomeric externally compensated compound previously described. The mother liquors which then remained gave crystalline deposits of very indefinite melting point, and from which, owing to their very great solubility, it seemed impossible to isolate the last component of the original product, namely, the derivative of the other active base. In these circumstances, the several most soluble deposits were collected, recrystallised until colourless, and then examined polarimetrically in methyl alcohol solution, when it was proved that these fractions contain a compound which was *dextro*-rotatory, and which therefore represents the derivative of the other active base, namely, the *l*-isomeride.

The acid chloride used in the above experiments had been distilled under reduced pressure, and contained a considerable quantity of the *l*-compound; the experiment was repeated, using the *d*-chloride pre-

pared as described in this paper (p. 447). In this case, the active amide melting at 148—149° was very easily isolated by two or three crystallisations from benzene, but again it was found almost impossible to obtain any quantity of a pure preparation of the isomeride from the mother liquors, although a few crystals were obtained melting at 113°. Attempts to hydrolyse the amide melting at 148—149° were unsuccessful; it seems to be quite stable towards boiling concentrated aqueous or alcoholic potash or aqueous baryta, and is only very slowly hydrolysed by boiling hydrochloric or dilute sulphuric acids, giving mere traces of ammonia and of indene; more concentrated sulphuric acid at 150° is much more rapid in its action, but ammonia is the only basic product; the liberated *d*-benzylmethylacetic acid is still optically active, thus indicating the stability of the asymmetric carbon group in this compound. The active hydrindamide, when heated in sealed tubes with alcoholic potash, hydrochloric acid, or sulphuric acid, or other hydrolysing agents, was decomposed into indene and ammonia.

Action of d-Benzylmethylacetyl Chloride on dl-α-Phenylethylamine.

The optically pure chloride of the *d*-acid was treated in dry ethereal solution with excess of freshly distilled base in the same solvent; a vigorous reaction took place, heat being developed and a bulky precipitate of the hydrochloride being formed. The ether was allowed to evaporate, and the residue heated with a little water to dissolve the salt formed, when a white, slightly viscid solid remained, which melted at 95—100°. The product was first crystallised from methyl alcohol; the sparingly soluble fraction, which separated in thick prisms, melted at 118—119°; this portion was first crystallised from light petroleum (b. p. 60—80°), in which it was very sparingly soluble, and then from benzene; the fine, long needles thus obtained melted at 119°, and were identical with those of the *d*-benzylmethylaceto-*l*-phenylethylamide previously described (p. 448).

0.2925, dissolved in 25 c.c. ether gave, in a 200 mm. tube, $\alpha + 0.24^\circ$, whence $[\alpha]_D + 10.3^\circ$.

The isomeric derivative of *d*-phenylethylamine was not isolated from the mother liquors, since it was found impossible to regain the active bases by the hydrolysis of their amides.

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