XVIII.—*Studies on the Walden Inversion. Part VII. The Influence of the Solvent on the Sign of the Product in the Conversion of α -Bromo- β -phenylpropionic Acid to α -Amino- β -phenylpropionic Acid (Phenylalanine). Iminodiphenyldipropionic Acid.*

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IN previous papers (Senter and Drew, T., 1915, **107**, 638; 1916, **109**, 1091; Senter and Tucker, this vol., 140) it has been shown that when the halogen atom in phenylchloro- and phenylbromo-acetic acid is displaced by the amino-group by the direct action of ammonia, the optical sign of the resulting amino-acid depends on the nature of the solvent in which the reaction occurs. In the case of the bromo-acid (Senter and Tucker, *loc. cit.*), the amino-acid obtained from liquid ammonia and from acetonitrile has the same sign as the bromo-acid taken, whereas from the other solvents an amino-acid of the opposite sign to the original bromo-acid is produced.

In both the acids referred to the phenyl group is directly attached to the asymmetric carbon atom, and in order to find how the results would be affected by a phenyl group further from the point at which substitution occurs, a similar investigation has now been carried out with α -bromo- β -phenylpropionic acid (benzylbromo-acetic acid), $C_6H_5 \cdot CH_2 \cdot CHBr \cdot CO_2H$, and the results are described in the present paper.

The acid was resolved by a slight modification of the method described by Fischer and Carl (*Ber.*, 1906, **39**, 4000); the most

active specimens gave for $[\alpha]_D^{17}$ the value -10.2° , as compared with $[\alpha]_D^{20} - 8.3^\circ$, the highest value obtained by Fischer and Carl. Most of the measurements were made with two preparations of the *l*-acid of activity $[\alpha]_D^{17} - 8.8^\circ$ and -10.2° respectively; in a few cases, a dextrorotatory acid of lower activity was used.

The main reaction between ammonia and the ammonium salt of the bromo-acid proceeds according to the equation

but in all the solvents a certain proportion of cinnamic acid, $\text{CHPh}\cdot\text{CH}\cdot\text{CO}_2\text{H}$, is formed by elimination of hydrogen bromide. Further, an imino-acid, which is shown to be *α -imino- $\beta\beta$ -diphenyl-dipropionic acid*, $\text{CH}_2\text{Ph}\cdot\text{CH}(\text{CO}_2\text{H})\cdot\text{NH}\cdot\text{CH}(\text{CO}_2\text{H})\cdot\text{CH}_2\text{Ph}$, was isolated from the products of reaction in all the solvents used. This imino-acid, which has not hitherto been described, may be regarded as being formed by the interaction of two molecules of the ammonium salt and one molecule of ammonia, according to the equation

The method used in isolating the amino-acid in a pure condition, and the identification and properties of the imino-acid, are fully described in the experimental portion of the paper. The reaction in all cases took place at the ordinary temperature, and as the halogen in this case is much less reactive than in phenylbromoacetic acid (compare Senter and Martin, T., 1917, **111**, 447), the reacting substances were kept in sealed tubes for two or three weeks in the case of liquid and aqueous ammonia and acetonitrile, and for some months in the case of the alcohols, in order to ensure that the changes were practically complete.

The optical activity of the products was determined for the mercury green ($\lambda=5461$) as well as for sodium light. The measurements with phenylalanine were made in aqueous solution, the concentration in all cases except one (product from benzonitrile, $c=0.646$) being about 1 per cent. ($c=1.0$). The measurements with the imino-acid, on account of its very sparing solubility in water and in dilute hydrochloric acid (p. 162), were made in $1.082 \times N/20$ -sodium hydroxide. Owing to the small yields of the imino-acid from certain solvents, very dilute solutions had in some cases to be used for the activity measurements, and it was therefore not convenient to make up the solutions to the same concentration, as in the case of the amino-acid. The main results of the investigation are summarised in table I.

TABLE I.

Solvent.	Value of $[\alpha]_D^{20}$ for bromo-acid used.	Value of $[\alpha]_D^{20}$ for phenylalanine.	Value of $[\alpha]_{5461}$ for imino-acid
Water (35 per cent. NH_3) ...	- 8.8°	+ 26°	34° ($c = 0.292$)
Water + NH_4Br	- 8.8	+ 27	
Liquid ammonia	- 8.8	+ 10	
"	- 10.2	+ 7	
Liquid Ammonia)	- 8.8	+ 25	
+ NH_4Br .....)	- 10.2	+ 30	
$\text{CH}_3\cdot\text{CN}$	- 8.8	+ 9	
"	+ 5.8	- 8	+ 11 ($c = 1.10$)
$\text{C}_6\text{H}_5\cdot\text{CN}$	+ 6.2	- 7	
$\text{CH}_3\cdot\text{OH}$	- 8.8	+ 23	- 34 ($c = 0.219$)
$\text{C}_2\text{H}_5\cdot\text{OH}$	- 8.8	+ 25	- 35 ($c = 0.542$)
$\text{C}_3\text{H}_7\cdot\text{OH}$ (n) ...	- 8.8	+ 24	- 34 ($c = 0.591$)
$\text{C}_4\text{H}_9\cdot\text{OH}$ (n) ...	- 8.8	+ 19	- 33 ($c = 0.458$)
$(\text{CH}_3)_3\text{C}\cdot\text{OH}$ ...	- 8.8	+ 22	- 28 ($c = 0.909$)
$\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{OH}$ ...	+ 6.2	practically inactive.	+ 30 ($c = 0.168$)

The value $[\alpha]_D^{16}$ for pure *d*-phenylalanine in 2.03 per cent. aqueous solution is +35.1° (Fischer and Mouneyrat, *Ber.*, 1900, **33**, 2383).

Although, owing to its solubility in water, the amino-acid cannot be isolated quantitatively from the products of reaction, there is no doubt that the numbers given in the table represent fairly accurately the relative activities of the products from the different solvents. As the solubility of the inactive acid is considerably less than that of the active acid (p. 159), a greater proportion of the latter will, as a rule, be removed during the washing of the products with water, and therefore the numbers in the table must be rather lower than those for the amino-acid formed. The yields of phenylalanine from the solutions in benzonitrile and in benzyl alcohol are so small (0.07 and 0.06 gram respectively) that not much confidence can be placed in the results from a quantitative point of view, as the active acid would be largely removed during washing with water.

Fischer and Carl (*loc. cit.*), by the action of aqueous ammonia on a bromo-acid of activity $[\alpha]_D^{20} - 8.3$, obtained phenylalanine with $[\alpha]_D^{20} + 31.78^\circ$. The slightly higher value as compared with ours is probably to be accounted for partly by a difference in the amount of washing and partly by the fact that they carried out the early stages of the reaction at a very low temperature.

The formation of an imino-acid in the reaction was overlooked by Fischer and Carl.

Discussion of Results.

The main result of the investigation, so far as the formation of amino-acid is concerned, is that with all the ten solvents used the amino-acid obtained has the same sign, opposite to that of the bromo-acid taken. Further, except in the case of solutions in liquid ammonia, acetonitrile, and benzonitrile, the displacement of bromine by NH_3 takes place without marked racemisation; for reasons already given, the racemisation is even less than appears from the numbers in the table. The effect of ammonium bromide (about 4 grams in 15 c.c.) on the reaction was examined, with remarkable results. Whereas this salt has practically no influence on the activity of the amino-acid obtained from aqueous ammonia, it greatly diminishes the racemisation of the product from liquid ammonia (p. 160).

It is instructive to compare these results with those obtained with phenylbromoacetic acid, as the two acids differ mainly as regards the relative position of the phenyl group with reference to the asymmetric carbon atom (or to the bromine atom). With phenylbromoacetic acid, racemisation was pronounced in all solvents; the amino-acid from liquid ammonia and from acetonitrile had the same sign as the original bromo-acid, whereas in all other solvents it had the opposite sign; finally, whereas ammonium bromide had little effect on the activity of the amino-acid from aqueous ammonia, it produced complete racemisation as regards the amino-acid from liquid ammonia. At first sight there does not seem to be much resemblance in the behaviour of the two acids towards ammonia, but a little consideration puts the matter in a different aspect. The most significant fact appears to be that the phenylalanine from liquid ammonia and from acetonitrile is racemised to a greater extent than that from other solvents, and it is just in those two solvents that the action of ammonia on phenylbromoacetic acid yields an amino-acid opposite in sign to that obtained from all the other solvents. This is most readily accounted for on the assumption that, as compared with other solvents, these two solvents favour the formation of an amino-acid of the same sign as the original bromo-acid, but whereas with *l*- α -bromo- β -phenylpropionic acid the result is the formation of a considerable proportion of both *d*- and *l*-phenylalanine, the product as a whole being dextrorotatory, with *l*-phenylbromoacetic acid the tendency to the formation of the *l*-amino-acid is so much greater that the product as a whole is levorotatory.

The remarkable effect of ammonium bromide on the two reactions in liquid ammonia can be represented on similar lines; the assump-

tion in this case is that the salt favours the production of an amino-acid having the opposite sign to that of the original bromo-acid. In the case of *l*- α -bromo- β -phenylpropionic acid, the result is a diminution in the racemisation of the resulting *d*-phenylalanine, whilst with *l*-phenylbromoacetic acid, the resulting amino-acid is practically inactive as compared with the formation of a *l*ævorotatory acid in the absence of the salt. It appears justifiable, therefore, to draw the conclusion that the same solvents produce similar effects, of different magnitudes, on the action of ammonia on the active phenylbromoacetic and phenylbromopropionic acids. This conclusion receives strong support from the fact, established in a recent paper (Senter and Martin, T., 1917, **111**, 447), that there is a close analogy in the action of water on the two acids and on their sodium salts.

The same considerations apply to the results with the different alcohols as solvents. The tendency to the formation of an amino-acid of the same sign as that of the original bromo-acid is so much greater in the case of phenylbromoacetic acid that whereas the *d*-phenylalanine from *l*-bromo- β -phenylpropionic acid is scarcely racemised, the amino-acid from *l*-phenylbromoacetic acid, although dextrorotatory, is in most cases only slightly active. In the same circumstances, *l*-phenylchloroacetic acid yields an amino-acid which is slightly *l*ævorotatory.

These results are perhaps best accounted for on the hypothesis that the action of ammonia on the halogen-substituted acids proceeds as two simultaneous reactions, giving rise to *d*- and *l*-amino-acids respectively; for example,

and that one or the other action predominates, depending on the nature of the halogen acid, the nature of the solvent, and other conditions. The nature of these reactions will be discussed when fuller experimental data are available.

The investigations of Franklin and Kraus (*J. Amer. Chem. Soc.*, 1905, **27**, 191) furnish an interesting analogy to the slight influence of ammonium haloids on the effect of aqueous ammonia as compared with liquid ammonia in the reactions just discussed. Both liquid ammonia and aqueous ammonia react with mercuric chloride as follows:

In liquid ammonia, the presence of a small quantity of ammonium

chloride prevents the formation of the ammonio-basic salt ($\text{NH}_2 \cdot \text{HgCl}$), whilst in aqueous ammonia a large excess of ammonium chloride is necessary to ensure a pure precipitate of the compound $\text{HgCl}_2, 2\text{NH}_3$.

The above considerations throw some light on the question of the occurrence of racemisation in reactions involving displacement of groups, a subject about which very little is known. This type of racemisation is quite distinct from catalytic racemisation; for example, the conversion of active to inactive mandelic acid by heating with alkali. Catalytic racemisation has in some cases been satisfactorily accounted for on the basis of the formation of intermediate compounds not containing an asymmetric carbon atom (compare Werner, "Stereochemie," p. 52; Lowry, *Rep. Brit. Assoc.*, 1904; McKenzie and Widdows, T., 1915, **107**, 704), and an explanation on similar lines may be found applicable in some cases of displacement racemisation. The results described in this paper, however, make it probable that the racemisation accompanying the displacement of the halogen atom in the phenylhalogenacetic acids is due to the occurrence of two simultaneous reactions, resulting in the formation of *d*- and *l*-amino-acids respectively, and this explanation will probably be found applicable to other examples of displacement racemisation.

With the further data now available, the interconversion of the halogen and amino-derivatives of the two acids in question can be summarised as follows (compare Fischer and Carl, *loc. cit.*; McKenzie and Clough, T., 1909, **95**, 777; Frankland, T., 1913, **103**, 731):

These results are very puzzling, and there appears to be little advantage in discussing them more fully until further information as to the mechanism of the reactions involved has been obtained. These investigations are now in progress.

It may be mentioned that Werner, in the course of his investigations on stereoisomeric cobalt compounds (*Annalen*, 1912, **386**, 57), has found that the displacement of a halogen atom in the inner sphere by the NH_3 -group takes place more often abnormally than normally (that is, a *cis*-compound is usually obtained from a

trans-, and vice versa), and this is the case both with liquid ammonia and aqueous ammonia as substituting agents.

α -Imino- $\beta\beta$ -diphenyldipropionic Acid.—In the case of the *l*-phenylhalogenoacetic acids (Senter and Drew, *loc. cit.*; Senter and Tucker, *loc. cit.*), it was shown that the action of ammonia in all the solvents examined produced an imino-acid which was dextro-rotatory in *N*-hydrochloric acid solution. The imino-acid produced by the action of ammonia on *l*- α -bromo- β -phenylpropionic acid in all the solvents examined is laevorotatory in *N*/20-sodium hydroxide solution. The latter imino-acid is not sufficiently soluble in *N*-hydrochloric acid to be examined in this solvent, but phenyliminoacetic acid was shown to be dextrorotatory in both *N*-hydrochloric acid and *N*/20-sodium hydroxide; thus, a specimen having $[\alpha]_{5461}^{17} + 190^\circ$ in *N*-hydrochloric acid ($c=0.15$) gave $[\alpha]_{5461}^{17} + 167^\circ$ in 1.082*N*/20-sodium hydroxide ($c=0.09$). The nature of the solvent is therefore without influence on the sign of the resulting imino-acid in the case of the two acids in question. The theoretical bearing of these results is briefly discussed in the preceding paper (Senter and Tucker, this vol., p. 145).

It is clear from the graphic formula of α -imino- $\beta\beta$ -diphenyldipropionic acid (p. 152) that optical inactivity may be due either to the presence of equal amounts of the *d*- and *l*-acid or to internal compensation. The fact that the melting point of the partly active imino-acid is close to and a few degrees below that of the inactive acid obtained from *r*- α -bromo- β -phenylpropionic acid would accord with the view that the latter acid is the racemic form, but this argument is, of course, not conclusive.

EXPERIMENTAL.

Resolution of r- α -Bromo- β -phenylpropionic Acid.

The pure *r*-acid was prepared by Fischer's method (compare Senter and Martin, T., 1917, 111, 447), and was resolved with brucine by a modification of the method of Fischer and Carl (*loc. cit.*), which consisted in redissolving the precipitated brucine salt at the ordinary temperature in a mixture of alcohol and water (in which it is more readily soluble than in either of the pure solvents) instead of in alcohol at 25° (Fischer and Carl). The details of one experiment are as follows. Thirty grams of the *r*-bromo-acid were dissolved in 150 c.c. of alcohol, and 51.5 grams of anhydrous brucine added, with shaking, at 16°. The solution was filtered, and 900 c.c. of water were added, with stirring. An oil was deposited, which solidified after twenty-four hours. The solid, after being collected

and dried, weighed 53 grams. It was redissolved in a mixture of 250 c.c. of alcohol and 50 c.c. of water, and the solution poured into 1600 c.c. of water. The dried salt finally obtained weighed 26 grams. The acid prepared from it by decomposing with dilute hydrochloric acid and extracting with ether had $\alpha_D^{18} - 13.06^\circ$ for $l=1$, corresponding with $[\alpha]_D^{18} - 8.80$, and contained the theoretical proportion of bromine. The acid obtained from the first mother liquor was a yellow oil, which gradually deposited a little of the solid τ -acid. The remainder gave for $\alpha_D^{18} + 8.54^\circ$, $l=1$.

In another experiment, in which the brucine salt was three times crystallised, the acid gave $\alpha_{5461}^{17} - 19.14^\circ$ and $\alpha_D^{17} - 15.22^\circ$ for $l=1$. The density of the liquid was found to be 1.487 at 17° and 1.479 at 25° ; hence $[\alpha]_{5461}^{17}$ is -12.9° and $[\alpha]_D^{17} - 10.2^\circ$. In order to obtain a comparison with Fischer's measurements at 20° , the effect of change of temperature on the rotation of another specimen was determined, with the following results: $\alpha_{5461}^{17.5} - 16.92^\circ$, $\alpha_{5461}^{25} - 17.52^\circ$, $\alpha_{5780}^{17.5} - 14.28^\circ$, $\alpha_{5780}^{25} - 14.86^\circ$ for $l=1$. The rotation of α -bromo- β -phenylpropionic acid therefore increases markedly with rise of temperature. The value of $[\alpha]_D$ for our most active specimen at 20° was therefore about -10.4° , as compared with -8.3° for the purest acid of Fischer and Carl. Even after prolonged keeping in a vacuum, our acid could not be obtained in the solid form, so it was probably not quite optically pure.

Method of Experiment.

The method of experiment was similar to that already employed in the case of phenylchloroacetic acid (T., 1916, 109, 1098). About 1 gram of the bromo-acid was dissolved in about 15 c.c. of the solvent, the solution saturated with dry ammonia, sealed up in a Jena-glass tube, and left at the ordinary temperature until the change was assumed to be complete. The solvent and excess of ammonia were then evaporated off at as low a temperature as possible (in some cases under diminished pressure), the residue was dissolved in water, made acid to Congo-red by addition of hydrochloric or hydrobromic acid, and the precipitate, consisting of the bulk of the imino-acid and cinnamic acid, collected and washed with cold water. From the precipitate, the pure imino-acid was isolated by extracting the cinnamic acid with ether.

The slightly acid aqueous filtrate containing the amino-acid, any unchanged bromo-acid, any hydroxy-acid or alkyloxy-acid formed in the course of the reaction, together with traces of imino-acid and cinnamic acid, was repeatedly extracted with ether, whereby all but the amino-acid and remaining imino-acid were removed. The

amino-acid was then freed from imino-acid and from ammonium chloride and bromide by evaporating the solution to dryness, dissolving in aqueous ammonia, again evaporating to dryness, and finally treating with small quantities of cold water until the filtrate was free from halogen salts. In this way, any remaining imino-acid was removed, since its ammonium hydrogen salt is stable and soluble in cold water.

The purity of the amino-acid was checked by determining its equivalent as hydrochloride, as described for phenylaminoacetic acid, and as in all cases practically theoretical results were obtained, it is unnecessary to quote the actual figures. In some cases the proportion of nitrogen was estimated by combustion.

As regards the different solvents, the results obtained with liquid ammonia, aqueous ammonia, and acetonitrile are of fundamental importance for the question of the replacement of halogen atoms by the amino-group, and the details of the experiments are therefore briefly summarised. As the remaining solvents, comprising a number of alcohols, all give very similar results, it seems unnecessary to describe the experiments in detail.

Aqueous Ammonia.

The velocity of reaction between inactive α -bromo- β -phenylpropionic acid and aqueous ammonia (35 per cent. NH_3) was determined approximately at 25° . From a solution containing 1.22 grams of the acid in 50 c.c. of the solution, about half the bromine was displaced in twenty-four hours. In a corresponding experiment with ethyl alcohol saturated with ammonia at 25° , about half the bromine was displaced in fourteen days.

In a preliminary experiment, in which 3 grams of the *r*-acid in 20 c.c. of aqueous ammonia (35 per cent. NH_3) was kept for seven days at 25° , 1.1 grams of pure *r*-phenylalanine and 0.1 gram of the imino-acid were obtained. The saturated solution of *r*-phenylalanine in water at 12° contains 1.24 grams in 100 c.c. of solution, about half that given by Fischer and Mouneyrat (*loc. cit.*) for the pure active forms.

A solution of 1.02 grams of *l*- α -bromo- β -phenylpropionic acid in 22 c.c. of aqueous ammonia (35 per cent. NH_3), kept for forty-two days at the ordinary temperature, gave 0.45 gram of amino-acid, $[\alpha]_D^{15} + 24^\circ$ (m. p. $258\text{--}259^\circ$ decomp.; rapid heating). In another experiment, 0.77 gram of the *l*-bromo-acid in dilute aqueous ammonia (4 per cent. NH_3), kept for twenty-one days at the ordinary temperature, yielded only 0.09 gram of amino-acid, $[\alpha]_D^{16} + 17^\circ$. From the ethereal solution (compare the method of

experiment), crystals were obtained which, after recrystallisation from benzene, melted at 123—125° and gave in ethyl alcohol $[\alpha]_{5461}^{18.5} - 21.5^\circ$, $c = 0.373$. The substance is evidently nearly pure *l*- α -hydroxy- β -phenylpropionic acid, formed by the action of water on the ammonium salt of the bromo-acid. It has been shown by McKenzie and Wren (T., 1910, 97, 1355) that *l*- α -bromo- β -phenylpropionic acid gives a hydroxy-acid of the same sign when acted on by water, by aqueous sodium hydroxide, by water and calcium carbonate, and by water and silver oxide.

The effect of ammonium bromide on the activity of the resulting phenylalanine was determined as follows. A solution of 1.02 grams of the *l*-bromo-acid, $[\alpha]_D^{17} - 8.8^\circ$, and 4 grams of ammonium bromide in 22 c.c. of aqueous ammonia (35 per cent. NH_3) was kept for eleven days at the ordinary temperature. The yield of phenylalanine was 0.27 gram of $[\alpha]_D^{13} + 27^\circ$, which is practically the same as that obtained in the absence of ammonium bromide.

Liquid Ammonia.

A solution of 0.53 gram of the *l*-bromo-acid, $[\alpha]_D^{17} - 8.8^\circ$, in 16 c.c. of liquid ammonia, kept for fourteen days, gave 0.17 gram of amino-acid, $[\alpha]_D^{14} + 8.5^\circ$. 0.85 Gram of the *l*-bromo-acid, $[\alpha]_D^{17} - 8.8^\circ$, and 4 grams of ammonium bromide, dissolved in 13 c.c. of liquid ammonia and kept for fourteen days, gave 0.1 gram of amino-acid, $[\alpha]_D^{17} + 24.5^\circ$. It appears from these data that in the presence of ammonium bromide the resulting phenylalanine is racemised to a much smaller extent than in the absence of the salt. In order to place this important result beyond doubt, two exactly parallel experiments were carried out, as follows. Two tubes, each containing 0.86 gram of the *l*-bromo-acid, $[\alpha]_D^{17} - 10.2^\circ$, in 13 c.c. of liquid ammonia, and one containing 4 grams of ammonium bromide in addition, were kept for fourteen days. The ammonia was then allowed to evaporate, the residue in each case dissolved in water and made up to 50 c.c., and 4 grams of ammonium bromide were added to the solution which did not already contain the salt. The amino-acid was then isolated in the usual way. From the solution originally containing ammonium bromide, the yield of amino-acid was 0.12 gram, $[\alpha]_D^{10} + 30^\circ$. From the corresponding solution without ammonium bromide the yield of amino-acid was 0.14 gram, $[\alpha]_D^{10} + 6.5^\circ$, so that the previous result was fully confirmed.

Acetonitrile.

A solution of 1.08 grams of the *l*-bromo-acid, $[\alpha]_D^{18} - 8.8^\circ$, in 15 c.c. of acetonitrile was saturated with dry ammonia at 9° , whereby the volume increased by 1.2 c.c. The solution at first was clear, but a precipitate consisting of the ammonium salts of the amino-acid, the imino-acid, and cinnamic acid soon began to form. After twenty-four days, the precipitate was collected, and the amino-acid obtained as usual, the yield being 0.2 gram, $[\alpha]_D^{14} + 9^\circ$. The imino-acid was accidentally lost.

A second experiment with a less active bromo-acid ($[\alpha]_D^{18} + 5.8^\circ$) in more concentrated solution (3.9 grams in 17 c.c. of solvent), kept for twenty-one days, gave 0.35 gram of (recrystallised) phenylalanine, $[\alpha]_D^{20} - 8^\circ$, and 0.57 gram of imino-acid (compare the section on the imino-acid). It appears therefore that, as would be anticipated, the more concentrated the solution of bromo-acid the greater is the yield of imino-acid.

The Alcohols.

As the reaction in these solvents is very slow, the solutions were kept for 280—300 days before separating the products. In each case, 0.7—0.8 gram of active bromo-acid was used, and the yield of amino-acid (except with benzyl alcohol) varied from 0.15—0.25 gram. With methyl alcohol, the solutions remained clear throughout, showing that the amino-acid and imino-acid (or their ammonium salts) are soluble in this solvent. With the other alcohols, except benzyl alcohol, a small amount of precipitate formed after a time. The absence of a precipitate in the benzyl alcohol solution is probably due to the slow rate of reaction in this solvent, as only 0.06 gram of amino-acid and 0.02 gram of imino-acid were obtained, although the mixture was kept for 309 days. The relative activities of the amino-acids from the different solvents are given in the table. The properties of the partly active imino-acids obtained from these solvents are briefly dealt with in the next section.

 α -Imino- $\beta\beta$ -diphenyldipropionic Acid.

As this acid has not been previously obtained, it is desirable to describe its properties in some detail. Earlier experiments having shown that a good yield of the imino-acid was obtained from acetonitrile, 8.4 grams of the *r*-bromo-acid were dissolved in 20 c.c. of

this solvent, the solution being saturated with dry ammonia and kept for twenty-eight days. The precipitate was then collected, washed with ether, and the inactive imino-acid separated as already described (p. 158). After crystallisation from a mixture of acetone and water, in which it is very sparingly soluble, the compound forms stellar aggregates of elongated leaflets or needles melting and decomposing at 262—264°, with previous discoloration and shrinkage at 235°. Before analysis, it was dried for some hours at 100°:

0.2588 gave 0.6545 CO₂ and 0.1447 H₂O. C=69.0; H=6.27.

0.5561 „ 21.1 c.c. N₂ (moist) at 18° and 771 mm. N=4.5.

C₁₈H₁₉O₄N requires C=69.0; H=6.1; N=4.5 per cent.

α-Imino-ββ-diphenyldipropionic acid is very sparingly soluble in water, practically insoluble in dilute or concentrated hydrochloric acid, but readily soluble in dilute alkali hydroxide solution. This shows that, as would be anticipated, it is an extremely weak base, whereas its acidic character is fairly pronounced. An attempt to determine its equivalent by evaporating with hydrochloric acid gave an unsatisfactory result, as the hygroscopic hydrochloride decomposed on drying at 100°. Further, no definite results for the equivalent were obtained by titration, using phenolphthalein as indicator, or by evaporating with ammonia, in an attempt to prepare a pure ammonium salt. Evidence was obtained in some of the experiments with acetonitrile as to the dibasic character of the acid, since the solid imino-acid compound which separates from this solvent during the reaction, on treatment with water in the cold, gives off ammonia, forming an ammonium salt (the hydrogen ammonium salt) soluble in water.

The amount of active imino-acid obtained from most of the solvents was very small, on the average 0.05 gram (from trimethylcarbinol 0.1 gram), but the rotation measurements were quite definite. The various specimens decomposed on heating to 245—251°.

Summary.

- (1) The amino-acid obtained by the action of ammonia on optically active *α*-bromo-*β*-phenylpropionic acid in different solvents has in all cases the same sign, opposite to that of the original bromo-acid.
- (2) The amino-acid from liquid ammonia and acetonitrile is more racemised than that from other solvents.
- (3) The presence of ammonium bromide has little effect on the

activity of the product from aqueous ammonia; it greatly diminishes the racemisation when the reaction is carried out in liquid ammonia.

(4) α -Imino- $\beta\beta$ -diphenyldipropionic acid was isolated from the products of reaction in all solvents used, and its properties were investigated; the sign was in all cases the same as that of the original bromo-acid.

(5) The mechanism of displacement racemisation is discussed.

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