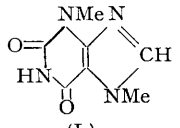
131. *An Investigation of Some Coloured Iminazolidines derived from Theobromine.*

By A. R. Todd and N. Whittaker.

The pentachloride (II) prepared by the action of chlorine on theobromine reacts with aromatic amines to give brightly coloured iminazolidine derivatives, the allophanic acid residue being eliminated. Aniline gives rise to 2-*imino*-4 : 5-*bisphenylimino*-3-*phenyl*-1-*methyliminazolidine* (V; R = Ph) and 2-*imino*-4 : 5-*bisphenylimino*-1 : 3-*diphenyliminazolidine* (VII; R = Ph) and corresponding compounds are obtained using *p*-toluidine. The structure of these compounds has been established by hydrolytic degradation and the mechanism of their formation is discussed. In the course of some synthetic experiments 4 : 5-*bisphenylimino*-2-*ketoiminazolidine* was prepared by the action of ethyl chloroformate on oxalbisphenylamidine (cyananiline).

The action of chlorine on a boiling suspension of theobromine (I) in chloroform was first studied by Fischer and Frank (*Ber.*, 1897, **30**, 2604). From the yellow solution produced in this way they isolated a colourless crystalline halogen-containing compound for which they could obtain no consistent analytical values. This difficulty in analysis they ascribed to its instability; on treatment with cold water it was converted to theobromuric acid, $C_7H_8O_5N_4$, to which they tentatively ascribed structure (III). Many years later Biltz (*Ber.*, 1934, **67**, 1856) re-examined these products and showed that the initial reaction product is to be regarded as *N*-(2 : 4 : 5 : 5-tetrachloro-1-methyl-Δ^2-iminazolinyl-4)-*N*-methylallophanic acid chloride (II), and theobromuric acid as (III) in accordance with the view of Fischer and Frank; he also showed that the main reason for the unsatisfactory analytical results obtained by the latter authors lies in the fact that (II) when isolated from the reaction mixture contains 1 mol. of chloroform of crystallisation which it loses very easily. In the course of an examination of various degradations of theobromine we repeated the work of Biltz and confirmed it in all essential particulars. For the production of the pentachloride (II) trichloroethylene proved

as effective as chloroform (the product containing trichloroethylene of crystallisation) but carbon tetrachloride was unsatisfactory as a reaction medium. In an attempt to characterise (II) we treated it with ammonia but obtained only resinous products. With aromatic amines, however, (II) yielded crystalline brightly coloured products and the study of these forms the subject of this communication.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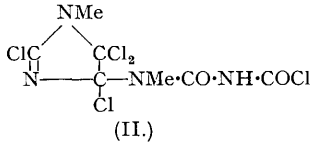
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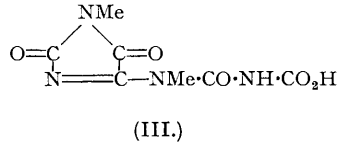
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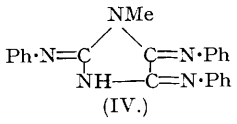
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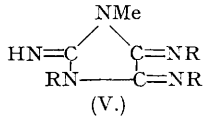
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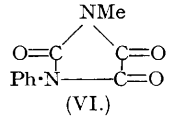
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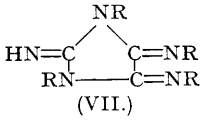
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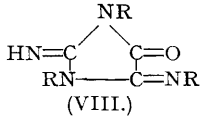
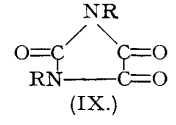

(VIII.)


(IX.)

When a solution of aniline in benzene was added to a suspension of (II) in the same solvent, rapid reaction occurred with separation of a mixture of aniline and methylamine hydrochlorides. From the orange coloured reaction solution two yellow crystalline substances, (*A*) needles, $C_{22}H_{19}N_5$, and (*B*) plates, $C_{27-28}H_{21-23}N_5$, were isolated together with *s*-diphenylbiuret. By varying the relative proportions of the reactants and the rate of addition of the aniline it was possible to obtain either *A* or *B* in large excess. This proved to be the only really satisfactory way of preparing them in any quantity in a pure condition since similar solubilities and behaviour on chromatographic analysis made separation of mixtures of *A* and *B* in anything like equal proportions very tedious. When *p*-toluidine replaced aniline in the above reaction two yellow products, $C_{25}H_{25}N_5$ and $C_{31-32}H_{29-31}N_5$, corresponding to *A* and *B* were obtained, but when *p*-bromoaniline was used only one coloured product, $C_{22}H_{16}N_5Br_3$, corresponding to *A* was isolated.

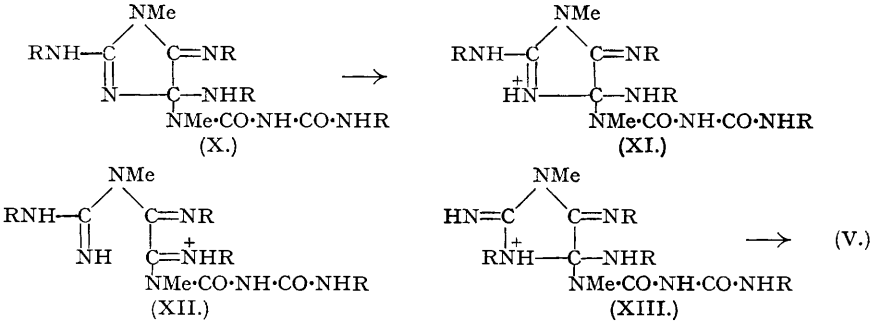
From the analytical data it was evident that *A* contained three and *B* four aryl residues together, probably, with the iminazole portion of (II). Reaction of aniline with the acid chloride grouping in (II) followed by elimination of the side chain would have been expected to yield *N*-phenyl-*N'*-methylbiuret; presumably this reacted further with aniline to give *s*-diphenylbiuret and methylamine, just as *N*-phenylbiuret reacts with aniline to give *s*-diphenylbiuret and ammonia (Schiff, *Annalen*, 1907, **352**, 78). At first sight it seemed likely that *A* would have structure (IV) but this was not borne out by the results of hydrolytic degradation. On warming *A* for a short time with dilute alcoholic hydrochloric acid the red colour of the solution was replaced by yellow, and a pale yellow product, $C_{16}H_{14}ON_4$, could be isolated. On refluxing this product or the original substance *A* with alcoholic hydrochloric acid a colourless compound, $C_{10}H_8O_3N_2$, was produced, together with ammonia and aniline. The compound $C_{10}H_8O_3N_2$ decomposed further on warming with barium hydroxide solution yielding oxalic acid and *N*-phenyl-*N'*-methylurea. It followed that the substance $C_{10}H_8O_3N_2$ must be N-*phenyl*-N'-*methylparabanic acid* (VI). Andreasch (*Ber.*, 1898, **31**, 138) claimed to have prepared this substance by desulphurising *N*-phenyl-*N'*-methyl-2-thioparabanic acid and recorded m. p. 148°, whereas our product had m. p. 210°. We therefore synthesised (VI) by condensation of phenylurea with ethyl oxalate followed by methylation; the synthetic material proved identical with that obtained from *A*. The nature of Andreasch's product remains unknown, but it evidently was not *N*-phenyl-*N'*-methylparabanic acid. The results of hydrolytic degradation make it clear that *A* is 2-*imino*-4 : 5-*bisphenylimino*-3-*phenyl*-1-*methyliminazolidine* (V; R = Ph). The yellow compound obtained by mild hydrolysis of *A* is consequently 2-imino-4- or -5-phenylimino-5- or -4-keto-3-phenyl-1-methyliminazolidine, the exact position of the keto-group being undetermined. In the same way the compounds $C_{25}H_{25}N_5$ and $C_{22}H_{16}N_5Br_3$ obtained from the reaction between (II) and *p*-toluidine and *p*-bromoaniline respectively were hydrolysed to N-p-*tolyl*-N'-*methylparabanic acid* and N-p-*bromophenyl*-N'-*methylparabanic acid*. They are therefore respectively 2-*imino*-4 : 5-*bis*-p-*tolyl*-*imino*-3-p-*tolyl*-1-*methyliminazolidine* (V; R = C_6H_4Me) and 2-*imino*-4 : 5-*bis*-p-*bromophenylimino*-3-p-*bromophenyl*-1-*methyliminazolidine* (V; R = C_6H_4Br).

There now remained the problem of the structure of *B* prepared from aniline and the pentachloride (II) and of the corresponding product from *p*-toluidine. Analytical values and molecular weight determinations by the Rast method failed to distinguish with certainty between the C_{27} and C_{28} formulæ for *B* and it was only after degradative experiments had been carried out that the formula of *B* was definitely established as $C_{27}H_{21}N_5$ and that of the *p*-toluidine product as $C_{31}H_{29}N_5$. Landgrebe (*Ber.*, 1877, **10**, 1593; 1878, **11**, 975) showed that 2 : 4 : 5-tri-imino-1 : 3-diphenyliminazolidine heated with aniline hydrochloride in alcoholic solution yields 4 : 5-di-imino-2-phenylimino-1 : 3-diphenyliminazolidine. On heating (V; R = Ph) with aniline hydrochloride in alcohol, *B* is produced in moderate yield; in analogous fashion (V; R = C_6H_4Me) can be converted by means of *p*-toluidine hydrochloride into the product $C_{31}H_{29}N_5$. That simple replacement

of the 2-imino-group had not occurred in these two cases was, however, shown when degradative experiments were carried out; as a matter of convenience these were done on the *p*-toluidine derivative.

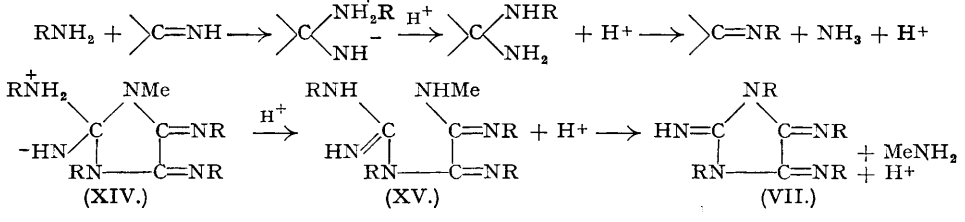
Mild hydrolysis of $C_{31}H_{29}N_5$ with aqueous hydrochloric acid gave, with elimination of one *p*-toluidine residue, a yellow compound, $C_{24}H_{22}ON_4$, while more drastic treatment with alcoholic hydrochloric acid gave a colourless substance, $C_{17}H_{14}O_3N_2$, which was evidently *NN'*-di-*p*-tolylparabanic acid (IX; R = C_6H_4Me) since it yielded *NN'*-di-*p*-tolylurea and oxalic acid on fission with alkali. Furthermore, on refluxing the original yellow product $C_{31}H_{29}N_5$ with alcoholic hydrochloric acid until the colour of the solution just disappeared, then making alkaline for a few minutes and reacidifying, *NN'*-di-*p*-tolylguanidine was isolated. There can therefore be no doubt but that the original compound is 2-*imino*-4 : 5-*bis*-p-*tolylimino*-1 : 3-*di*-p-*tolyliminazolidine* (VII; R = C_6H_4Me), and the yellow partial hydrolysis product is 2-*imino*-4-p-*tolylimino*-5-*keto*-1 : 3-*di*-p-*tolyliminazolidine* (VIII; R = C_6H_4Me). In accordance with this conclusion a re-examination of the reaction between *p*-toluidine hydrochloride and (V; R = C_6H_4Me) showed that methylamine hydrochloride was produced in addition to (VII; R = C_6H_4Me). By analogy with the *p*-toluidino-compound it is concluded that compound *B* prepared from aniline and the pentachloride (II) is 2-*imino*-4 : 5-*bisphenylimino*-1 : 3-*diphenyliminazolidine* (VII; R = Ph).

The production of compounds of types (V) and (VII) from the pentachloride (II) was rather unexpected and calls for some comment. If we consider first the production of (V) it seems certain that an intermediate opening of the heterocyclic ring and re-closure in a different direction has occurred; an alternative mechanism involving the migration of an aryl group seems most unlikely. Presumably the initial step is the production of (X) by reaction of (II) with 4 mols. of arylamine and formation of 5 mols. of hydrogen chloride. It is suggested that (X) then forms a salt whose highly resonant ion may be written as (XI) or in a mesomeric form (XII) in which the tendency to change over to (XIII) by addition of the arylamino-group [located at C_2 in the initial product (X)] to C_4 is evident. (XIII) is the ion of a much weaker base than is (XI) (just as aniline is a weaker base than guanidine) and readily loses a proton from the ring nitrogen; presumably the side chain is simultaneously ejected from C_4 yielding (V) as final product of the reaction.



The formation of (VII) from (V) with elimination of methylamine as hydrochloride clearly involves a second ring-opening. A possible explanation can be given on the basis of the following normal mechanism for the acid catalysed replacement of an imino-group by an arylimino-group.

In the case of (V) the initial step would be formation of the complex (XIV). In this complex there are three other nitrogen atoms attached to the carbon atom of (V) which has been attacked by the arylamine, *i.e.*, the basicity of the molecule is not really concentrated in the NH⁻ group as represented in (XIV). Whilst any of these three nitrogen atoms might in theory receive the first proton it may be assumed that the tendency

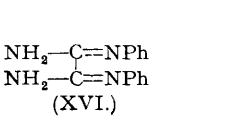


will be for it to be taken by the most nucleophilic, *i.e.*, N^1 carrying the methyl group, with a consequent opening of the labile iminazolidine ring to give (XV). Further reaction will then proceed in the direction of a stable product (VII) with loss of methylamine, ring-closure in this manner being favoured by the greater basicity of the arylamino-group as compared with the imino-group. On this view the formation of (VII) in the reaction between the pentachloride (II) and excess of arylamine in benzene solution would proceed through (V) as an intermediate. It is interesting to note that (V; R = Ph) does not react in benzene solution with aniline hydrochloride; presumably the conversion of (V) into (VII) in the original reaction of (II) with aniline occurs rapidly before protons are removed from the mixture as the insoluble aniline hydrochloride.

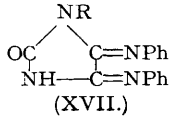
Arising from the above considerations it seemed that by heating (V; R = C_6H_4Me) with *m*-nitroaniline

hydrochloride it would be possible to obtain a compound analogous to (VII; R = C_6H_4Me) in which one of the cyclic nitrogen atoms bore a *m*-nitrophenyl group. In fact on refluxing an equimolecular mixture of (V; R = C_6H_4Me) and *m*-nitroaniline hydrochloride in alcohol, *p*-toluidine hydrochloride was produced together with a yellow *compound*, $C_{24}H_{22}O_2N_6$. This new product was evidently formed by replacement of a *p*-tolylimino-group at C_4 or C_5 by a *m*-nitrophenylimino-group since it yielded on hydrolysis *N*-*p*-tolyl-*N'*-methylparabanic acid. Whether the *m*-nitrophenylimino-group is attached to C_4 or C_5 remains uncertain, but it is probable that the group which it has displaced is the same as that which is readily removed from (V; R = C_6H_4Me) on mild hydrolysis. An analogous product, $C_{24}H_{23}ON_5$, was formed on heating (V; R = C_6H_4Me) with *p*-aminophenol hydrochloride in acetone; on hydrolysis it, too, yielded *N*-*p*-tolyl-*N'*-methylparabanic acid showing that the *p*-hydroxyphenylimino-residue is located at C_4 or C_5.

At an early stage in the investigation of the nature of the compound *A* from aniline and the pentachloride, it was thought possible that it might in fact be 2 : 4 : 5-trisphenylimino-1-methyliminazolidine (IV), and experiments were commenced with a view to the synthesis of this compound. Before they had been completed it was realised that our product was in fact (V; R = Ph) and as the preparation of intermediates in quantity was rather arduous the synthesis of (IV) was abandoned. Since the work actually carried out involved an iminazolidone synthesis of a new type the results obtained are recorded.



(XVI.)



(XVII.)

The route selected for the projected synthesis of (IV) was condensation of oxalbisphenylamidine (XVI) with ethyl chloroformate which by analogy with the condensation of ethyl chloroformate and malondiamidine (Howard, Lythgoe, and Todd, *J.*, 1944, 476) to 4 : 6-diamino-2-hydroxypyrimidine might yield (XVII; R = H). From (XVII; R = H) it was proposed to obtain (IV) by introduction of an anilino residue at C_2 before or after methylation of one heterocyclic nitrogen atom.

Oxalbisphenylamidine (XVI), commonly known as cyananiline after its preparation from cyanogen and aniline (Hofmann, *Annalen*, 1848, **66**, 132), has been prepared by a variety of methods; of these we found that described by Nef (*Annalen*, 1895, **287**, 282) the most convenient for preparation in quantity. On refluxing with excess of ethyl chloroformate, oxalbisphenylamidine yielded a substance, $C_{26}H_{30}O_8N_4$, presumably the *tetracarbethoxy*-derivative of oxalbisphenylamidine, while the same reaction carried out in the cold in presence of pyridine gave the *dicarbethoxy*-derivative. When equimolecular proportions of ethyl chloroformate and oxalbisphenylamidine were dissolved in pyridine and kept, the product consisted of a mixture of the dicarbethoxy-derivative and a pale yellow substance, evidently 4 : 5-*bisphenylimino*-2-*ketoiminazolidine* (XVII; R = H) since it gave on hydrolysis parabanic acid and aniline. Methylation of (XVII; R = H) with methyl iodide and methanolic sodium methoxide gave a mixture of 4 : 5-*bisphenylimino*-2-*keto*-1-*methyliminazolidine* (XVII; R = Me) and 4 : 5-*bisphenylimino*-2-*keto*-1 : 3-*dimethyliminazolidine*. (XVII; R = Me) reacted smoothly with phosphoryl chloride but the projected synthesis of (IV) was not further pursued.

Experimental.

Pentachloride (II) *from Theobromine.*—(a) *In chloroform.* Chlorine was passed through a boiling suspension of theobromine in chloroform until evolution of hydrogen chloride ceased, and the mixture worked up according to Biltz (*loc. cit.*). Yield of crystalline pentachloride, colourless plates, m. p. *ca.* 136° (decomp.), was 85%; material prepared in this way was used throughout the investigations described in this paper.

(b) *In trichloroethylene.* The procedure of Biltz (*loc. cit.*) applied to a suspension of theobromine in trichloroethylene gave a 75% yield of the pentachloride as needles, m. p. *ca.* 143° (decomp.), containing trichloroethylene. With alcohol the product gave ethyl theobromurate and with water theobromuric acid, trichloroethylene being liberated in each reaction.

Reaction of the Pentachloride (II) *with Aniline.*—(*a*) A solution of aniline (53 g. ≡ 9 mols.) in dry benzene (100 c.c.) was added within 2 minutes to a vigorously stirred suspension of the pentachloride (30 g. ≡ 1 mol.) in dry benzene (500 c.c.) at room temperature. Vigorous reaction ensued causing the benzene to reflux and the mixture became first red then orange and a white powder separated. When the reaction subsided the mixture was refluxed for 30 minutes and filtered from a mixture of aniline and methylamine hydrochloride (36 g.; theoretical, 37 g.). The filter residue was washed with warm benzene, and the combined filtrate and washings were concentrated to 150 c.c. then left overnight; a mass of colourless needles separated. These were collected and recrystallised from alcohol giving *s*-diphenylbiuret (11 g.), m. p. and mixed m. p. 208—209° (Found: C, 66·0; H, 5·2; N, 16·8. Calc. for $C_{14}H_{13}O_2N_3$: C, 65·9; H, 5·1; N, 16·5%).

Evaporation of the benzene mother liquors after removal of the *s*-diphenylbiuret gave a red resin which was dissolved in hot alcohol (150 c.c.) and the solution set aside for 3 days. The yellow needles which separated were thrice recrystallised from alcohol giving 2-*imino*-4 : 5-*bisphenylimino*-3-*phenyl*-1-*methyliminazolidine* (5·5 g.), m. p. 153—154° (Found: C, 74·8; H, 5·3; N, 20·2; *M* (Rast), 390. $C_{22}H_{19}N_5$ requires C, 74·8; H, 5·4; N, 19·8%; *M*, 353). The substance dissolved in cold alcoholic hydrochloric acid to a red solution from which it was precipitated unchanged on dilution with water. On catalytic hydrogenation using a platinum oxide catalyst it absorbed 2·8 mols. of hydrogen giving an unstable colourless product.

(*b*) When the above procedure was repeated using aniline (18 g. ≡ 11 mols.) and pentachloride (8 g. ≡ 1 mol.) the products were *s*-diphenylbiuret (2·5 g.) and 2-*imino*-4 : 5-*bisphenylimino*-1 : 3-*diphenyliminazolidine* (2·7 g.), the latter crystallising from alcohol as yellow plates, m. p. 177—178° (Found: C, 77·9; H, 5·4; N, 16·8; *M* (Rast), 422. $C_{27}H_{21}N_5$ requires C, 78·0; H, 5·1; N, 16·9%; *M*, 415. $C_{28}H_{23}N_5$ requires C, 78·3; H, 5·4; N, 16·3%; *M*, 429).

The substance dissolved in cold alcoholic hydrochloric acid to a red solution from which it was precipitated unchanged on dilution with water.

(*c*) Variation in the proportion of aniline and pentachloride between those used in (*a*) and (*b*) gave mixtures of approximately equal quantities of the two yellow compounds, as also did slower addition of the aniline solution (10 or more minutes).

Reaction of the Pentachloride (II) *with* p-*Toluidine*.—(*a*) The reaction was carried out exactly as in the case of the aniline experiment (*a*) above using *p*-toluidine (60 g. ≡ 9 mols.) and pentachloride (30 g. ≡ 1 mol.). After removal of *p*-toluidine and methylamine hydrochlorides and crystallisation of the *s*-di-*p*-tolylbiuret, the benzene solution was evaporated, and the residue stirred with water (200 c.c.) and again evaporated to remove any residual benzene and *p*-toluidine. The residue was dissolved in hot alcohol (180 c.c.) and left for 24 hours, and the crystalline precipitate was collected and recrystallised twice from alcohol. 2-*Imino*-4 : 5-*bis*-p-*tolylimino*-3-p-*tolyl*-1-*methyliminazolidine* (V; R = C_6H_4Me) was obtained in yellow hexagonal plates (6·8 g.), m. p. 169° (Found : C, 76·4; H, 6·2; N, 17·7. $C_{25}H_{25}N_5$ requires C, 76·0; H, 6·3; N, 17·7%). It closely resembled (V; R = Ph) in properties.

Water (10 c.c.) was added to the alcoholic mother liquor remaining after separation of (V; R = C_6H_4Me). After 24 hours the crystalline precipitate was collected and twice recrystallised from alcohol giving yellow needles (2·6 g.) of 2-*imino*-4 : 5-*bis*-p-*tolylimino*-1 : 3-*di*-p-*tolyliminazolidine* (VII; R = C_6H_4Me), m. p. 178—179° (Found : C, 79·0; H, 6·3; N, 14·8. $C_{31}H_{29}N_5$ requires C, 79·0; H, 6·2; N, 14·9%). The compound contained no *N*-methyl groups.

(*b*) As in (*a*) using *p*-toluidine (45 g. ≡ 10 mols.) and pentachloride (20 g. ≡ 1 mol.) the product was (VII; R = C_6H_4Me), m. p. 178—179° (7 g.); there appeared to be very little (V; R = C_6H_4Me) present.

Reaction of the Pentachloride (II) *with* p-*Bromoaniline*.—The reaction was carried out in the normal fashion using *p*-bromoaniline (55 g. ≡ 10 mols.) and pentachloride (15 g. ≡ 1 mol.) in benzene. The only coloured product isolated was 2-*imino*-4 : 5-*bis*-p-*bromophenylimino*-3-p-*bromophenyl*-1-*methyliminazolidine* (V; R = C_6H_4Br) which, thrice crystallised from glycol monoethyl ether, formed orange plates (4·2 g.), m. p. 261—262° (Found : C, 45·1; H, 2·7; N, 11·5; Br, 40·3. $C_{22}H_{16}N_5Br_3$ requires C, 44·8; H, 2·7; N, 11·8; Br, 40·7%).

Partial Hydrolysis of (V; R = Ph).—The substance (1 g.) was dissolved in a mixture of alcohol (20 c.c.) and concentrated hydrochloric acid (4 c.c.) and the solution warmed to 60° until the red colour was replaced by yellow (*ca.* 5 minutes). It was now diluted with water (60 c.c.) and cooled, and the precipitate was collected, dried, dissolved in chloroform (15 c.c. containing 1% alcohol), and chromatographed on activated alumina, the same solvent being used for developing. The product moved fairly rapidly down the column as a compact yellow band which was washed through; the eluate so obtained was evaporated, and the residue recrystallised from alcohol. Pale yellow needles, m. p. 203° (Found : C, 68·8; H, 5·3; N, 19·9. $C_{16}H_{14}ON_4$ requires C, 69·1; H, 5·0; N, 20·1%). On refluxing with alcoholic hydrochloric acid the substance rapidly formed *N*-phenyl-*N'*-methylparabanic acid, m. p. 210°.

Hydrolysed in exactly similar fashion (V; R = C_6H_4Me) gave pale yellow needles, m. p. 235° (Found : C, 70·8; H, 5·9; N, 17·8. $C_{18}H_{18}ON_4$ requires C, 70·6; H, 5·9; N, 18·3%). Refluxed with alcoholic hydrochloric acid the substance readily gave *N*-*p*-tolyl-*N'*-methylparabanic acid, m. p. 202°.

N-*Phenyl*-N'-*methylparabanic Acid from* (V; R = Ph).—The compound (0·5 g.) was dissolved in hot alcohol (20 c.c.), concentrated hydrochloric acid (2 c.c.) added, and the mixture refluxed for 20 minutes. On cooling the colourless solution plates (0·08 g.) separated, m. p. 210° (Found : C, 58·6; H, 3·9; N, 14·1. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 3·9; N, 13·7%). The substance showed no depression in m. p. when mixed with synthetic *N*-phenyl-*N'*-methylparabanic acid (see below). On warming the substance (0·2 g.) with aqueous barium hydroxide (0·8 g. in 50 c.c. water) to 50° it gradually dissolved (10 minutes) and barium oxalate separated. After removal of the barium oxalate the solution was warmed to 80° and neutralised with sulphuric acid; barium sulphate was centrifuged off, and the clear solution concentrated to small bulk (8 c.c.). On cooling, *N*-phenyl-*N'*-methylurea separated in small colourless plates; recrystallised from water it had m. p. 150—151° undepressed in admixture with an authentic specimen (m. p. 150—151°).

From the hydrolysis mother liquor left after removal of *N*-phenyl-*N'*-methylparabanic acid, it was possible to isolate, after bromination, tribromoaniline (0·9 g. Calc. for 2 mols. of aniline, 0·93 g.). Ammonia was liberated from the hydrolysis liquors on making alkaline with potassium hydroxide.

N-*Phenyl*-N'-*methylparabanic Acid*.—Sodium (0·75 g.) was dissolved in absolute alcohol (30 c.c.) and the solution added to a mixture of phenylurea (4 g.) and ethyl oxalate (4·3 g.) with shaking. Soon after all had gone into solution the sodium salt of phenylparabanic acid separated as a crystalline solid; methyl iodide (4·6 g.) and absolute alcohol (20 c.c.) were added and the mixture was refluxed for 30 minutes and allowed to cool. Colourless plates (1·4 g.) of *N*-phenyl-*N'*-methylparabanic acid separated and were recrystallised from alcohol; they had m. p. 210°, undepressed in admixture with the hydrolysis product of (V; R = Ph).

N-p-*Tolyl*-N'-*methylparabanic Acid*.—Prepared in the same manner as the *N*-phenyl analogue but using *p*-tolylurea as starting material. The *acid* crystallised from alcohol in colourless plates (yield, 90%), m. p. 202° undepressed in admixture with the product, m. p. 202°, obtained by hydrolysis of (V; R = C_6H_4Me) (Found : C, 60·6; H, 5·0; N, 12·6. $C_{11}H_{10}O_3N_2$ requires C, 60·5; H, 4·6; N, 12·8%).

N-p-*Tolyl*-N'-*methylparabanic Acid from* (V; R = C_6H_4Me).—Hydrolysed in the same manner as the corresponding aniline derivative, (V; R = C_6H_4Me) (0·5 g.) gave *N*-*p*-tolyl-*N'*-methylparabanic acid (0·1 g.), m. p. and mixed m. p. 202°.

N-p-*Bromophenyl*-N'-*methylparabanic Acid from* (V; R = C_6H_4Br).—Hydrolysis was carried out with alcoholic hydrochloric acid as described for the aniline derivative. (V; R = C_6H_4Br) (0·5 g.) gave N-p-*bromophenyl*-N'-*methylparabanic acid* (0·1 g.), m. p. 255° (Found : C, 42·2; H, 2·8; N, 10·3; Br, 27·9. $C_{10}H_7O_3N_2Br$ requires C, 42·4; H, 2·5; N, 9·9; Br, 28·3%).

Conversion of (V; R = Ph) *into* (VII; R = Ph).—A mixture of (V; R = Ph) (0·5 g.), aniline hydrochloride (0·25 g.), and alcohol (10 c.c.) was refluxed for 6 hours. On cooling the red solution, yellow plates (0·2 g.) separated which, after recrystallisation from alcohol, had m. p. 177—178° undepressed in admixture with (VII; R = Ph) (m. p. 177—178°). In exactly similar fashion (VII; R = C_6H_4Me) was prepared from (V; R = C_6H_4Me) by heating with *p*-toluidine hydrochloride in alcohol; the reaction mother liquor boiled with mercuric oxide did not yield ammonia, but methylamine was evolved on treatment with potassium hydroxide. The same product was obtained by heating the reactants in absence of solvent at 160° for 10 minutes.

Partial Hydrolysis of (VII; R = C_6H_4Me).—(VII; R = C_6H_4Me) (0·5 g.) was heated under reflux for 1 hour with water (10 c.c.) and concentrated hydrochloric acid (10 c.c.). The initial red coloration faded giving place to yellow, and a yellow crystalline solid separated. The solid was collected, dissolved in chloroform containing 1% of alcohol, and purified by chromatography on activated alumina and recrystallisation from alcohol. 2-*Imino*-4-p-*tolylimino*-5-*keto*-1 : 3-*di*-p-*tolyliminazolidine* (VIII; R = C_6H_4Me) was obtained as yellow plates, m. p. 249—250° (Found : C, 75·7; H, 6·1; N, 14·3. $C_{24}H_{22}ON_4$ requires C, 75·4; H, 5·8; N, 14·7%).

NN'-*Di*-p-*tolylparabanic Acid from* (VII; R = C_6H_4Me).—The following procedure was found most satisfactory. (VII; R = C_6H_4Me) (0·5 g.) was heated with alcohol (20 c.c.) and concentrated hydrochloric acid (3 c.c.) in a sealed tube at 100° during 1 hour. Evaporation of the solution and recrystallisation of the residue from aqueous alcohol gave colourless prisms of *NN'*-di-*p*-tolylparabanic acid, m. p. 135—136°. Landgrebe (*Ber.*, 1877, **10**, 1590) gives

m. p. 144° (Found: C, 69·9; H, 4·8; N, 9·7. Calc. for $C_{17}H_{14}O_3N_2$: C, 69·5; H, 4·8; N, 9·5%). Further evidence for the identity of this product was obtained by heating it at 80° for 3 minutes with aqueous alcoholic potassium hydroxide (*ca.* 2%). The product which separated on cooling crystallised from aqueous alcohol in colourless needles, m. p. 266—267° undepressed by authentic *NN'*-di-*p*-tolylurea.

NN'-*Di*-p-*tolylguanidine from* (VII; R = C_6H_4Me).—A mixture of (VII; R = C_6H_4Me) (1 g.), alcohol (30 c.c.), and concentrated hydrochloric acid (4 c.c.) was refluxed for 15 minutes. The pale yellow solution was made alkaline with potassium hydroxide, boiled for 5 minutes, and then acidified to Congo-red with hydrochloric acid. The solution was now evaporated under reduced pressure, the residue extracted with water (100 c.c.), and the filtered solution made alkaline with ammonia. Fine colourless needles separated on standing; these were collected after 2 days and recrystallised several times from light petroleum (b. p. 80—100°) giving *NN'*-di-*p*-tolylguanidine, m. p. 166—167°, undepressed in admixture with an authentic specimen (m. p. 167—168°) (Found: C, 75·0; H, 6·9; N, 18·0. Calc. for $C_{15}H_{17}N_3$: C, 75·3; H, 7·1; N, 17·6%).

Reaction of (V; R = C_6H_4Me) *with* m-*Nitroaniline Hydrochloride*.—A mixture of (V; R = C_6H_4Me) (1 g.), *m*-nitroaniline hydrochloride (0·45 g.), and alcohol (25 c.c.) was refluxed for 20 minutes, cooled, and set aside. After 2 hours the yellow plates which had separated were collected and recrystallised from alcohol. The *product* (0·2 g.) had m p. 225—227° (Found: C, 68·0; H, 5·3; N, 19·7. $C_{24}H_{22}O_2N_6$ requires C, 67·7; H, 5·2; N, 19·7%). From the neutralised mother liquors *p*-toluidine was isolated.

Reaction of (V; R = C_6H_4Me) *with* p-*Aminophenol Hydrochloride*.—A mixture of (V; R = C_6H_4Me) (0·5 g.), *p*-aminophenol hydrochloride (0·2 g.), and acetone (20 c.c.) was refluxed for 1 hour, filtered from solid hydrochlorides, and evaporated. The residue was dissolved in chloroform (20 c.c.) and chromatographed on activated alumina, the same solvent being used for developing. Unchanged starting material (0·26 g.) passed rapidly through the column leaving an orange band which was eluted with alcohol–acetone (1 : 1). Evaporation of the eluate and recrystallisation from alcohol gave the *product* as yellow needles (0·15 g.), m. p. 253—254° (Found: C, 72·0; H, 5·5; N, 17·8. $C_{24}H_{23}ON_5$ requires C, 72·5; H, 5·8; N, 17·6%). The substance was insoluble in aqueous but dissolved in alcoholic potassium hydroxide to a red solution from which it could be recovered by acidifying with hydrochloric acid and neutralising with ammonia.

Tetracarbethoxyoxalbisphenylamidine.—A mixture of oxalbisphenylamidine (2 g.) and ethyl chloroformate (6 c.c.) was refluxed for 15 minutes when the amidine dissolved and a pale yellow solid separated. Benzene (20 c.c.) was added and the precipitate of oxalbisphenylamidine hydrochloride collected and washed with benzene (10 c.c.). The combined filtrate and washings were evaporated and the residue was recrystallised from alcohol; the *tetracarbethoxy*-derivative formed colourless plates (0·6 g.), m. p. 144° (Found: C, 59·1; H, 5·7; N, 10·8; *M* (Rast), 495. $C_{26}H_{30}O_8N_4$ requires C, 59·3; H, 5·7; N, 10·7%; *M*, 526).

Dicarbethoxyoxalbisphenylamidine.—Ethyl chloroformate (5 c.c.) was added with shaking to a solution of oxalbisphenylamidine (2 g.) in dry pyridine (50 c.c.). After 3 hours the precipitated hydrochloride was filtered off and the yellow solution evaporated under reduced pressure. The residue was washed with dilute hydrochloric acid and recrystallised from alcohol; colourless needles (0·8 g.), m. p. 230—231° (Found: C, 63·1; H, 5·4; N, 14·3. $C_{20}H_{22}O_4N_4$ requires C, 62·8; H, 5·8; N, 14·7%).

4 : 5-*Bisphenylimino*-2-*ketoiminazolidine*.—Ethyl chloroformate (25 g. ≡ 1 mol.) was added during 10 minutes to a vigorously stirred suspension of oxalbisphenylamidine (55 g. ≡ 1 mol.) in dry pyridine (500 c.c.). After 3 days the red solution was filtered from precipitated hydrochloride and evaporated; the residue was extracted with dilute hydrochloric acid (4000 c.c. of N) by stirring at room temperature for several hours, and then extracted with hot alcohol (200 c.c.). The alcoholic solution yielded, on cooling, dicarbethoxyoxalbisphenylamidine (1·8 g.) while the undissolved residue, recrystallised from glycol monoethyl ether, gave pale yellow needles (2·7 g.) of 4 : 5-*bisphenylimino*-2-*ketoiminazolidine*, m. p. 284° (decomp.) (Found: C, 68·6; H, 4·5; N, 21·2. $C_{15}H_{12}ON_4$ requires C, 68·2; H, 4·6; N, 21·2%).

On refluxing the above iminazolidine (0·1 g.) with alcohol (20 c.c.) and concentrated hydrochloric acid (1 c.c.) for 10 minutes and evaporating to dryness, a residue was obtained which was then extracted with ether. The ethereal solution gave on evaporation parabanic acid, m. p. 240—241° (decomp.); mixed m. p. with authentic parabanic acid (m. p. 243°), 242°. The ether-insoluble residue consisted of aniline hydrochloride.

Methylation of 4 : 5-*Bisphenylimino*-2-*ketoiminazolidine*.—Methyl iodide (1 g.) was added to a refluxing solution of 4 : 5-bisphenylimino-2-ketoiminazolidine (0·55 g.) in methanolic sodium methoxide (4·7 c.c. of a solution made by dissolving 1 g. of sodium in 100 c.c. of methanol). After being heated for 30 minutes the solution was concentrated to half bulk and poured into water (100 c.c.). The yellow precipitate was dried, dissolved in chloroform (20 c.c. containing 1% alcohol), and chromatographed on activated alumina, the column being developed with the same solvent. Two distinct yellow bands were obtained in addition to a small amount of starting material located at the top of the column. Of these the lower, rather diffuse band, eluted with chloroform and evaporated, gave 4 : 5-*bisphenylimino*-2-*keto*-1 : 3-*dimethyliminazolidine* (0·07 g.) which crystallised from aqueous alcohol in yellow needles, m. p. 177° (Found: C, 70·2; H, 5·7; N, 19·6. $C_{17}H_{16}ON_4$ requires C, 69·9; H, 5·5; N, 19·2%).

The upper, sharply defined band was similarly eluted with chloroform and the solution evaporated. The residue, recrystallised from aqueous alcohol, gave small yellow prisms (0·15 g.) of 4 : 5-*bisphenylimino*-2-*keto*-1-*methyliminazolidine*, m. p. 183° (Found: C, 68·8; H, 5·3; N, 20·4. $C_{16}H_{14}ON_4$ requires C, 69·1; H, 5·0; N, 20·1%). A mixture with the above dimethyl compound had m. p. 151—157°.

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