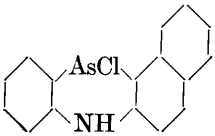
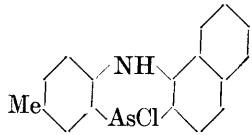
CCXCVI.—10-*Chloro*-5 : 10-*dihydrophenarsazine and its Derivatives. Part III. Homologues and Amino-, Chloro-, and Cacodyl Derivatives.*

By HAROLD BURTON and CHARLES STANLEY GIBSON.

THE reaction between arsenious chloride and diphenylamine and its homologues has already been shown (Burton and Gibson, this vol., pp. 455, 466) to be of general applicability. The condensations of arsenious chloride with phenyl-β-naphthylamine, with *p*-tolyl-α-naphthylamine and with p-tolyl-β-naphthylamine, yielding 12-*chloro*-7 : 12-*dihydrobenzophenarsazine* (I), 7-*chloro*-9-*methyl*-7 : 12-*dihydrobenzophenarsazine* (II), and 12-*chloro*-10-*methyl*-7 : 12-*dihydrobenzophenarsazine* (III), respectively, are further instances of the general



(I.)



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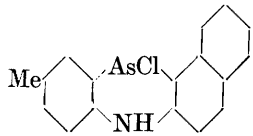
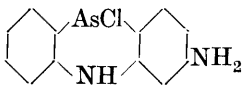


(III.)

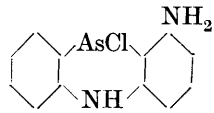
reaction and are described in the present communication. The compound obtained by condensing arsenious chloride with phenyl-α-naphthylamine, namely, 7-chloro-7 : 12-dihydrobenzophenarsazine, is isomeric with (I) and has already been described by Lewis and Hamilton (*J. Amer. Chem. Soc.*, 1921, **43**, 2218; compare Burton and Gibson, this vol., p. 470).

Wieland and Rheinheimer (*Annalen*, 1921, **423**, 1) showed that *m*-aminodiphenylamine condenses readily with arsenious chloride and they assign formula (IV), 10-chloro-3-amino-5 : 10-dihydro-

phenarsazine, to the product. There is the possibility of the formation of an isomeric compound, (V), 10-chloro-1-amino-5 : 10-dihydrophenarsazine, but like the previous workers we have been unable to isolate a second product from the reaction. (This and the other amino-derivatives are most conveniently isolated in the form of the hydrochlorides.) The probable correctness of formula (IV) follows from the work of Roberts and Turner (J., 1925, **127**, 2005), who have shown that 3 : 10-dichlorophenoxarsine (VI) is exclusively formed when *m*-chlorodiphenyl ether is condensed with arsenious chloride.



(IV.)



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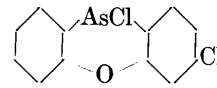
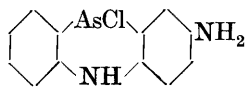
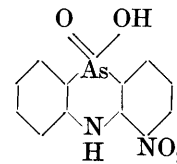


(VI.)

A second amino-derivative was obtained by Wieland and Rheinheimer (*loc. cit.*) by reducing the mononitrophenarsazinic acid, obtained from 10-chloro-5 : 10-dihydrophenarsazine by nitration and subsequent oxidation, first to the amino-acid and then to the chloroaminodihydrophenarsazine. To this compound they assigned the formula (VII), 10-chloro-2-amino-5 : 10-dihydrophenarsazine.

(VII.)




(VIII.)

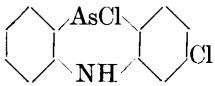
We have obtained the same compound by condensing arsenious chloride with *p*-aminodiphenylamine and thereby proved the correctness of the constitution assigned to it by Wieland and Rheinheimer.

By the nitration of phenarsazinic acid, Wieland and Rheinheimer obtained a nitrophenarsazinic acid to which they ascribed constitution (VIII), 4-nitrophenarsazinic acid. They also obtained the corresponding amino-acid. We have carried the reduction one stage further and obtained the corresponding 10-chloro-compound, the third of this series. This compound, which is different from either (IV) or (VII), cannot be 10-chloro-4-amino-5 : 10-dihydrophenarsazine corresponding to the constitution of Wieland and Rheinheimer's nitrophenarsazinic acid. On diazotisation, the amino-acid from which it is prepared does not yield a triazole derivative but a product which couples normally with β-naphthol. Consequently, the chloro-compound prepared from the nitration product of phenarsazinic acid must be 10-chloro-1-amino-5 : 10-dihydrophenarsazine

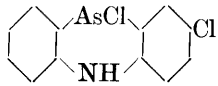
(V) referred to above, and the product of the nitration of phenarsazinic acid obtained by us must be 1-nitrophenarsazinic acid.

Arsenious chloride readily reacts with both *m*- and *p*-chlorodiphenylamines and the condensation products, 3 : 10-*dichloro*-5 : 10-*dihydrophenarsazine* (IX) and 2 : 10-*dichloro*-5 : 10-*dihydrophenarsazine* (X) respectively, have very similar properties to those of the parent substances. In a similar manner, 2 : 8 : 10-*trichloro*-5 : 10-*dihydrophenarsazine* (XI) has been prepared by condensing arsenious chloride with the now completely identified *pp'*-dichlorodiphenylamine.*

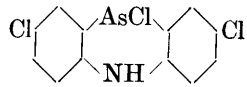
Hypophosphorous acid reduces the more soluble of these derivatives, either in the form of the chloro-compounds or as the phenarsazinic acids, in aqueous acetone–alcohol or acetic acid solution to the corresponding cacodyl compounds. Of these, only 10 : 10'-



(IX.)



(X.)



(XI.)

bis-5 : 10-*dihydrophenarsazine* and the corresponding *diacetyl* derivative are now described. These two sparingly soluble compounds are moderately stable and do not change during isolation under ordinary conditions. On the other hand, the cacodyl compounds obtained in a similar manner from 10-chloro-2-methyl-5 : 10-dihydrophenarsazine and 3-aminophenarsazinic acid are too unstable to be isolated easily in a pure condition.

10 : 10'-Bis-5 : 10-dihydrophenarsazine is converted by bromine in carbon tetrachloride solution into 10-bromo-5 : 10-dihydrophenarsazine and, when suspended in boiling xylene with free access of air, it is oxidised in a short time to the colourless phenarsazinic acid.

EXPERIMENTAL.

12-*Chloro*-7 : 12-*dihydrophenarsazine* (I) was prepared by boiling for 8 hours a mixture of phenyl-β-naphthylamine (10·9 g.), arsenious chloride (10 g.) and *o*-dichlorobenzene (30 c.c.). The crude compound (14·8 g.) was recrystallised from *s*-tetrachloroethane and

* The following compounds do not react directly with arsenious chloride to give dihydrophenarsazine derivatives: *o*-aminodiphenylamine, *pp'*-diaminodiphenylamine, *o*-, *m*-, and *p*-nitrodiphenylamines, *oo'pp'*-tetrachlorodiphenylamine. These negative results taken in conjunction with the positive results we have obtained indicate that arsenious chloride will condense with substituted diphenylamines as with diphenylamine, only when all the ortho-positions with respect to the nitrogen atom are free and when no nitro-substituting group is present. This does not hold, however, in the case of phenylene-substituting groups (compare this vol., p. 455).

obtained in yellow needles, m. p. 249—250° (Found : As, 22·6. $C_{16}H_{11}NClAs$ requires As, 22·9%).

7-*Chloro*-9-*methyl*-7 : 12-*dihydrobenzophenarsazine* (II) was prepared in a similar manner from *p*-tolyl-α-naphthylamine. Recrystallised from toluene, it was obtained in deep yellow needles, m. p. 252—255° (decomp.) (Found : As, 21·8. $C_{17}H_{13}NClAs$ requires As, 21·95%).

12-*Chloro*-10-*methyl*-7 : 12-*dihydrobenzophenarsazine* (III) was prepared similarly from *p*-tolyl-β-naphthylamine. The substance was obtained in yellow needles, m. p. 266—267° (decomp.), by recrystallisation from *s*-tetrachloroethane (Found : As, 21·8. $C_{17}H_{13}NClAs$ requires As, 21·95%).

On repeating the preparation of the hydrochloride of 10-chloro-3-amino-5 : 10-dihydrophenarsazine (IV) the product was found to be homogeneous. A mixture of *m*-aminodiphenylamine * (5 g.) and arsenious chloride (8 g.) was heated for 5 hours, the temperature of the oil-bath being gradually raised from 140° to 170°. The powdered residue was washed with dry ether and recrystallised from alcoholic hydrochloric acid. The compound (5 g.) crystallised in pale yellow prisms which do not melt below 300° (Found : Cl, 21·5. $C_{12}H_{11}N_2Cl_2As$ requires Cl, 21·6%).

The hydrochloride of 10-chloro-2-amino-5 : 10-dihydrophenarsazine (VII) was prepared in a similar manner from *p*-aminodiphenylamine. The product separated from alcoholic hydrochloric acid in greenish-yellow plates which do not melt below 300° (Found : Cl, 21·7. Calc. for $C_{12}H_{11}N_2Cl_2As$: Cl, 21·6%). This compound was identical with the compound prepared in a different manner by Wieland and Rheinheimer.

For the nitration of phenarsazinic acid a modification of Wieland and Rheinheimer's method was employed. A solution of phenarsazinic acid (20 g.) in hot glacial acetic acid (450 c.c.) was cooled rapidly to 15°, and fuming nitric acid (25 c.c.) added in small portions with thorough shaking, the temperature being maintained at 20—25°. After 1 hour, the yellow, crystalline solid was separated and washed with acetic acid and with ether. The crude nitrophenarsazinic acid (43 g. from two experiments) was dissolved in hot sodium hydroxide solution (500 c.c. containing 40 g. of NaOH), and the sodium salt allowed to crystallise. This salt was recrystallised from half the quantity of sodium hydroxide solution and, after separation, washed with dilute sodium hydroxide and finally

* The *m*-aminodiphenylamine was prepared by reducing *m*-nitrodiphenylamine with iron filings and acetic acid. It had m. p. 66—67° (Found : N, 15·4%). The m. p., 76—77°, given by Wieland and Rheinheimer is probably a misprint.

with water. The neutral sodium salt was converted into the *barium* salt in the usual manner and this was crystallised from water. It separated in silky, yellow needles containing seven molecules of water of crystallisation. The anhydrous barium salt had a beautiful bronze lustre (Found : H_2O, 14·4. $C_{24}H_{16}O_8N_4As_2Ba,7H_2O$ requires H_2O, 14·0%. Found in anhydrous salt : Ba, 17·7. $C_{24}H_{16}O_8N_4As_2Ba$ requires Ba, 17·7%). The barium salt, suspended in water, was treated with a slight excess of hydrochloric acid, and the nitrophenarsazinic acid (16·4 g.) filtered off, washed thoroughly with water, and dried. The acid, only slightly soluble in most solvents, can be conveniently crystallised from acetic acid, from which it separates in clusters of yellow needles which do not melt below 300°.

For the reduction to the amino-acid, a hot solution of the nitro-acid (9·5 g.) in dilute sodium hydroxide was added to a boiling suspension of ferrous hydroxide prepared by adding an excess of 25% sodium hydroxide solution to a hot solution of ferrous sulphate (50 g. in 150 c.c. of water). The mixture was well stirred for 10 minutes and, after filtration from ferric hydroxide, the amino-acid was isolated in quantitative yield by acidification of the filtrate. The solubility of the amino-acid in water is very small. The constitution of this amino-acid was proved by dissolving it in an excess of dilute hydrochloric acid and diazotising the solution in the cold with sodium nitrite; the resulting solution gave, with an alkaline solution of β-naphthol, a soluble red azo-compound.

The *dihydrochloride* was obtained by treating a suspension of the acid in hot alcohol with concentrated hydrochloric acid until crystalline matter began to separate. The dihydrochloride decomposed when heated to about 260° (Found : Cl, 21·5. $C_{12}H_{13}O_2N_2Cl_2As$ requires Cl, 21·5%).

The *hydrochloride* of 10-*chloro*-1-*amino*-5 : 10-*dihydrophenarsazine* (V) was obtained by dissolving the above amino-acid (8 g.) in a boiling mixture of alcohol (20 c.c.) and concentrated hydrochloric acid (10 c.c.) containing a trace of iodine. Sulphur dioxide was passed into the boiling solution until crystalline material separated. The crystals were filtered off and washed with alcoholic hydrochloric acid, absolute alcohol, and finally with ether. The hydrochloride of 10-chloro-1-amino-5 : 10-dihydrophenarsazine crystallises from alcoholic hydrochloric acid in yellow plates which begin to decompose at a high temperature (Found : Cl, 21·2. $C_{12}H_{11}N_2Cl_2As$ requires Cl, 21·6%).

m-Chlorodiphenylamine was made by the diazotisation treatment with cuprous chloride and subsequent hydrolysis of *N*-acetyl-*m*-aminodiphenylamine. It had b. p. 340°/766 mm. *p*-Chlorodi-

phenylamine was similarly prepared from *N*-acetyl-*p*-aminodiphenylamine. It was finally separated by steam distillation and had m. p. 66—67° (Ullmann, *Annalen*, 1910, **355**, 312, gives 74°).

The following is the method of preparation leading to the complete identification of pp'-*dichlorodiphenylamine*. A solution of *N*-formyl-*pp'*-diaminodiphenylamine (40 g.) in water (200 c.c.) and concentrated hydrochloric acid (100 c.c.) was cooled to 0° and diazotised with a solution of sodium nitrite (32 g.) in water. The diazo-solution was added gradually to a cold solution of cuprous chloride made from copper carbonate (24 g.), concentrated hydrochloric acid (240 c.c.), and excess of copper. After 5 hours, the crude formyl derivative was filtered off and extracted from inorganic matter with the minimum quantity of hot alcohol. Hydrolysis was effected by boiling the alcoholic solution for 1 hour with concentrated hydrochloric acid (100 c.c.). After removal of the alcohol, the dark-coloured residue was extracted with ether, the ethereal solution dried, and the ether distilled off. The crude dichloro-compound crystallised rapidly (31 g.) and was purified by extraction in the cold with ligroin (b. p. 40—60°). On concentrating this solution, *pp'*-dichlorodiphenylamine was obtained in almost colourless crystals, m. p. 71—72° (Found : Cl, 29·6. $C_{12}H_9NCl_2$ requires Cl, 29·8%).

3 : 10-*Dichloro*-5 : 10-*dihydrophenarsazine* (IX) was prepared by heating a mixture of *m*-chlorodiphenylamine (10·3 g.), arsenious chloride (10 g.), and *o*-dichlorobenzene (40 c.c.) under reflux for 7 hours. Hydrogen chloride was evolved steadily. On cooling, the crude chloro-compound separated in yellow needles (7·2 g.). 3 : 10-Dichloro-5 : 10-dihydrophenarsazine crystallised from benzene in yellow needles, m. p. 220—221° (decomp.) (Found : As, 23·9. $C_{12}H_8NCl_2As$ requires As, 24·0%).

2 : 10-*Dichloro*-5 : 10-*dihydrophenarsazine* (X) was prepared from *p*-chlorodiphenylamine in an exactly similar manner. The compound was recrystallised from glacial acetic acid and obtained in yellow needles, m. p. 230—231° (decomp.) (Found : As, 23·8. $C_{12}H_8NCl_2As$ requires As, 24·0%).

2 : 8 : 10-*Trichloro*-5 : 10-*dihydrophenarsazine* (XI) was prepared by boiling for 12 hours a mixture of *pp'*-dichlorodiphenylamine (11·9 g.), arsenious chloride (10 g.), and *o*-dichlorobenzene (20 c.c.). The product, which separated on cooling, crystallised from acetic acid in yellow needles, m. p. 273—274° (decomp.) (Found : As, 21·3; Cl, 30·1. $C_{12}H_7NCl_3As$ requires As, 21·6; Cl, 30·7%).

10 : 10'-*Bis*-5 : 10-*dihydrophenarsazine*, $[NH(C_6H_4)_2As]_2$, was prepared in two ways. (*a*) A hot solution of 10-chloro-5 : 10-dihydrophenarsazine (5·5 g.) in a mixture of alcohol (75 c.c.) and acetone

(100 c.c.) was treated with hypophosphorous acid (8 c.c., *d* 1·136) diluted with alcohol (15 c.c.). The solution became orange in colour, and, on cooling, orange-yellow needles of the cacodyl compound (2·7 g.) separated. (*b*) Phenarsazinic acid (5 g.) was dissolved in boiling acetic acid (120 c.c.) containing a trace of iodine. To the hot solution, hypophosphorous acid (quantity as above) was added. On cooling, crystals of the cacodyl compound (2·5 g.) separated identical in every respect with a sample prepared as above.

The cacodyl compound is very sparingly soluble in the usual organic solvents. It melts at 304—305° (decomp.) (Found : As, 30·8. $C_{24}H_{18}N_2As_2$ requires As, 31·0%). It is moderately stable under ordinary conditions, but when suspended in boiling acetone or xylene it is rapidly oxidised, producing the colourless phenarsazinic acid.

A suspension of the cacodyl compound (9·45 g.) in carbon tetrachloride was treated with a 10% solution of bromine in the same solvent. The colour of the bromine was discharged and crystals slowly separated which, after recrystallisation from acetic acid and then from toluene, were proved to be 10-bromo-5 : 10-dihydrophenarsazine by the m. p. and by the m. p. of a mixture with an authentic specimen.

10 : 10′-*Bis*-5-*acetyl*-5 : 10-*dihydrophenarsazine*, $[CH_3{\cdot}CO{\cdot}N(C_6H_4)_2As]_2$.

—*N*-Acetylphenarsazinic acid (5 g.) was dissolved in boiling acetic acid (50 c.c.) containing a trace of iodine. To the hot solution hypophosphorous acid (quantity as above) was added. On cooling, the cacodyl compound separated in clusters of almost colourless needles, m. p. 293—294° after previous decomposition (Found : As, 26·3. $C_{28}H_{22}O_2N_2As_2$ requires As, 26·4%).

GUY'S HOSPITAL MEDICAL SCHOOL,
LONDON, S.E. 1.

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