Preparation and properties of 1:4(or 1:5)-dimethylglyoxaline and 1:3-dimethylpyrazole / by Hooper Albert Dickinson Jowett and Charles Etty Potter.

L.—*Preparation and Properties of* 1 : 4(*or* 1 : 5)-*Dimethylglyoxaline and* 1 : 3-*Dimethylpyrazole.*

By Hooper Albert Dickinson Jowett and Charles Etty Potter.

During the course of the investigation by one of us on the constitution of pilocarpine (see preceding paper), it was found necessary for the purpose of comparison to prepare certain derivatives of 1-methylglyoxaline and 1-methylpyrazole. Accordingly, 1 : 4(or 1 : 5)-dimethylglyoxaline and 1 : 3-dimethylpyrazole have been prepared and characterised, and their behaviour with certain reagents studied.

1 : 4(or 1 : 5)-*Dimethylglyoxaline* was prepared from 4(or 5)-methylglyoxaline, which in turn was obtained from the corresponding mercaptan according to the method of Gabriel and Pinkus (*Ber.*, 1893, **26**, 2203). This latter base, which had hitherto been described as a liquid, was obtained in crystals melting at 55°. The new base is a liquid forming crystalline salts. With bromine at the ordinary

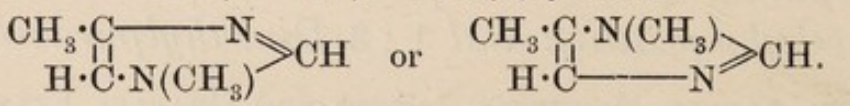
temperature, it forms a crystalline dibromo-derivative, but with excess of the reagent at 100° under pressure, further action occurs, a crystalline acid containing both nitrogen and bromine being formed. Chromic acid does not attack the base, but potassium permanganate oxidises it, producing ammonia, methylamine, and acetic acid. When the methiodide is heated with aqueous caustic potash in a sealed tube at 180°, methylamine and acetic acid are formed.

1 : 3-*Dimethylpyrazole* was prepared through its methiodide from 3-methylpyrazole, which was obtained by the condensation of formylacetone with hydrazine (Knorr and Macdonald, *Annalen*, 1894, **279**, 225). Knorr also obtained this base (*loc. cit.*, 231), but had doubts as to its purity, and did not further investigate it. The base is a colourless liquid forming crystalline salts. With bromine, either at the ordinary temperature or at 100° under pressure, the dibromo-derivative is formed; in the latter respect, the base differs from the isomeric glyoxaline, which is decomposed by excess of bromine at 100°. With potassium permanganate, the corresponding pyrazolemonocarboxylic acid is formed, and the methiodide is not readily decomposed by aqueous caustic potash; in both these reactions the pyrazole behaves differently from the glyoxaline.

Professor C. R. Marshall has examined these compounds physiologically, but neither of them was found to possess any action analogous to that of pilocarpine. It was also found necessary to characterise the isomeric 1 : 2-dimethylglyoxaline which had been previously prepared (*Ber.*, 1883, **16**, 448), inasmuch as the physical constants of its salts had not been recorded.

Experimental.

1 : 4(or 1 : 5)-*Dimethylglyoxaline*,



This base was prepared from 4(or 5)-methylglyoxaline by the method (B) given by Titherley for the preparation of monoalkyl-substituted amides (Trans., 1901, **79**, 401); it was, however, extracted with ether instead of with benzene. The dark-coloured and oily residue, which was distilled under 20—25 mm. pressure, boiled almost entirely between 110° and 117°, the yield being 60 to 70 per cent. of the theoretical. The product was rectified, and a fraction boiling at 116° under 25 mm. pressure analysed with the following result:

0·1058 gave 0·2426 CO_2 and 0·0824 H_2O. C = 62·5; H = 8 6.
0·1250 „ 0·2850 CO_2 „ 0·0962 H_2O. C = 62·2; H = 8·5.
0·0808 „ 20 c.c. nitrogen at 14° and 747 mm. N = 28·9.

$C_5H_8N_2$ requires C = 62·5; H = 8·3; N = 29·2 per cent.

The base, which distilled at 203° under the ordinary pressure, is a colourless liquid, soluble in water, alcohol, and ether in all proportions, and has a characteristic odour recalling both that of pyridine and of trimethylamine; it has a sp. gr. 1·003 at 15°/15°.

1 : 4(or 1 : 5)-Dimethylglyoxaline was obtained by the following methods: (i) by the action of methyl iodide on the silver derivative of 4(or 5)-methylglyoxaline, in methyl-alcoholic solution, in a sealed tube at 160°; (ii) by the action of sodium methyl sulphate on the sodium derivative of the methylglyoxaline in boiling amyl-alcoholic solution; but in neither of these two cases was the yield of dimethyl compound so satisfactory as in the method just described.

The *aurichloride* formed yellow needles, which, when crystallised from alcohol, melted at 176°, but after remaining in a desiccator over sulphuric acid for two or three days, the crystals melted at 214—215°.

The *picrate* immediately crystallised in long, yellow needles, which, after crystallisation from hot water, melted sharply at 167°, and were not altered by further crystallisation.

The *platinichloride* slowly separated from solution in orange-coloured, laminar crystals, which, after recrystallisation, melted and decomposed at 239°:

0·0972 gave 0·032 Pt. Pt = 32·9.

$(C_5H_8N_2)_2,H_2PtCl_6$ requires Pt = 32·4 per cent.

The *hydrochloride* was obtained on evaporating the aqueous solution in a vacuum over caustic potash, as a mass of very hygroscopic, colourless crystals melting at 145°.

The *methiodide* was prepared by heating the 4(or 5)-methylglyoxaline in a sealed tube at 110° for 3 or 4 hours with methyl iodide and methyl alcohol. On evaporation, the methiodide of dimethylglyoxaline slowly crystallised. It was redissolved in absolute alcohol, boiled with animal charcoal, filtered, and dry ether cautiously added to the solution while still warm, when the methiodide crystallised in fine needles. This operation was repeated until the product was colourless, and the melting point constant at 156°:

0·2538 gave 0·2494 AgI. I = 53·1.

$C_5H_8N_2,CH_3I$ requires I = 53·3 per cent.

Action of Bromine.

(1) *In Acetic Acid Solution.*—Dibromodimethylglyoxaline was prepared in a similar manner to dibromo*iso*pilocarpine (Trans., 1901, 79, 580), and formed long, colourless needles, which melted sharply at 127°, and are soluble in alcohol and ether, but insoluble in water;

0·1416 gave 0·2103 AgBr. Br = 63·2.

$C_5H_6N_2Br_2$ requires Br = 63·0 per cent.

An attempt to reduce a small quantity of dibromodimethylglyoxaline with sodium and amyl alcohol gave a negative result.

(2) *In Aqueous Solution under Pressure.*—A preliminary experiment on a small quantity of dimethylglyoxaline showed that with excess of bromine in aqueous solution at 100° under pressure, no dibromodimethylglyoxaline was formed, but a crystalline acid was produced, containing both nitrogen and bromine, together with small quantities of ammonia and methylamine. The reaction will be further studied.

Oxidation with Potassium Permanganate.—2·5 grams of dimethylglyoxaline were oxidised with potassium permanganate at the ordinary temperature, and the products of the reaction isolated in the usual manner. The colour of the permanganate was not discharged immediately, but disappeared on allowing the mixture to stand a short time. The reaction may be represented by the equation :

$$C_5H_8N_2 + 2O_2 + 2H_2O = NH_3 + NH_2{\cdot}CH_3 + CH_3{\cdot}CO_2H + 2CO_2.$$

The amount of permanganate required, according to this equation, should be 11 grams, the amount actually used was 11·2 grams.

The bases formed were identified as ammonia and methylamine, the yield being theoretical ; the platinichloride of the latter was isolated and analysed (Pt = 41·1 per cent.).

The acid formed was identified as acetic acid by the formation of ethyl acetate. The products of this oxidation are therefore ammonia, methylamine, and acetic acid.

Action of Aqueous Caustic Potash on the Methiodide.—Dimethylglyoxaline methiodide was heated with 20 per cent. caustic potash in a sealed tube at 180°, and the products of the reaction, which were isolated in the usual manner, were identified as acetic acid and methylamine, the latter being isolated in the form of its platinichloride (Pt = 40·9 per cent.).

1 : 3-*Dimethylpyrazole*, $\begin{matrix} HC{\cdot}N(CH_3) \\ \| \quad\quad \\ HC{\cdot}C(CH_3) \end{matrix}\!\!>\!N.$

1 : 3-Dimethylpyrazole was prepared from 3-methylpyrazole by the agency of the methiodide as follows. Ten grams of 3-methylpyrazole were dissolved in methyl alcohol, 34·5 grams of methyl iodide added, and the mixture heated in a sealed tube at 110° for 4 or 5 hours. When cold, a large quantity of crystalline dimethylpyrazole methiodide separated, this product being collected and washed with alcohol and

ether. The mother liquor, when treated with ether, gave a further quantity of methiodide, the total yield being almost quantitative.

The methiodide, when purified by repeated crystallisation from alcohol and ether, forms white, prismatic needles which melt at 256°; it is very soluble in water and ethyl alcohol, less so in methyl alcohol, and quite insoluble in ether :

0·2374 required 10 c.c. $N/10$ $AgNO_3$. I = 53·5.
$C_5H_8N_2,CH_3I$ requires I = 53·3 per cent.

When subjected to dry distillation, the methiodide fused and decomposed, giving the dimethylated base and methyl iodide. The base was separated from a certain amount of methiodide, which volatilised, by treating the distillate with dry ether, filtering, drying over potassium carbonate, and redistilling. After removing the ether, nearly all the residue distilled between 140° and 150°, the yield being theoretical. After twice fractionating, a portion boiling at 148° was analysed. It was a colourless, mobile liquid with a slight pyridine-like odour, and a burning taste ; it was quite neutral to litmus, and had a sp. gr. = 0·965 at 15°/15°.

0·1352 gave 0·3084 CO_2 and 0·1032 H_2O. C = 62·2 ; H = 8·5.
0·1062 ,, 0·2440 CO_2 ,, 0·0812 H_2O. C = 62·5 ; H = 8·5.
0·0610 ,, 14·6 c.c. nitrogen at 11° and 768 mm. N = 28·8.
$C_5H_8N_2$ requires C = 62·5 ; H = 8·3 ; N = 29·2 per cent.

The *aurichloride*, prepared in the ordinary way, crystallised in yellow needles, which softened at 165° and fused completely at 175°. The salt contains two molecules of water of crystallisation, which are lost, together with a molecule of hydrochloric acid, on heating at 115° :

0·1302 air-dried salt lost at 115° 0·0188 and gave 0·055 Au.
Loss in weight = 14·4 ; Au = 42·2.
$C_5H_8N_2,HAuCl_4,2H_2O$ requires Au = 41·8 and for loss of $2H_2O$,HCl 15·2 per cent.

The *platinichloride* formed orange-coloured cubes which melted at 234°.

The *hydrochloride*, obtained by evaporating the aqueous solution in a vacuum over caustic potash, separated in very hygroscopic, long, prismatic crystals ; it contained one molecule of water of crystallisation and melted at 160°, but dissociated slowly on heating at 100° :

0·02 required 13·2 c.c. $N/10$ Na_2CO_3; $C_5H_8N_2,HCl,2H_2O$ requires 13·9 c.c.

Action of Bromine.

(1) *In Acetic Acid Solution.*—Dibromodimethylpyrazole, which was prepared in the same manner as the dibromodimethylglyoxaline, formed long, white needles melting at 74°; these were very soluble in ethyl or methyl alcohol, and in ether or acetone, but insoluble in water:

0·2018 gave 0·3010 AgBr. Br = 63·4.

$C_5H_6N_2Br_2$ requires Br = 63 per cent.

(2) *In Aqueous Solution under Pressure.*—This reaction was found to yield the same product as the previous one.

Attempts to reduce the dibromodimethylpyrazole with zinc dust and glacial acetic acid, and also with sodium and boiling amyl alcohol, were unsuccessful.

Oxidation with Potassium Permanganate.

Dimethylpyrazole on oxidation with permanganate at 80° yielded no volatile base, but an acid forming colourless laminar crystals melting at 222°. The crystals were moderately soluble in hot water, and almost insoluble in cold:

0·1266 gave 0·2208 CO_2 and 0·0554 H_2O. C = 47·6; H = 4·8.

$C_5H_6O_2N_2$ requires C = 47·6; H = 4·8 per cent.

The product of oxidation was therefore *N*-methylpyrazolemonocarboxylic acid, $\begin{matrix}CH{-}{-}N(CH_3)\\ \|\quad\quad\\ CH\cdot C(CO_2H)\end{matrix}\!\!>\!N$.

Action of Caustic Potash under Pressure on the Methiodide.

This experiment was carried out in the usual manner, but as the amount of volatile bases formed was so minute, it was evident that the reaction had not taken place so readily or so completely as was the case with the glyoxaline; it was therefore not further investigated.

1 : 2-*Dimethylglyoxaline*, $\begin{matrix}CH\cdot N(CH_3)\\ \|\quad\quad\\ CH\text{———}N\end{matrix}\!\!>\!C\cdot CH_3$.

This compound was prepared in a precisely similar manner to that given above for the preparation of 1 : 4(or 1 : 5)-dimethylglyoxaline, that is, by the action of the sodium derivative of 2-methylglyoxaline on sodium methyl sulphate.

A fraction boiling at 205—206° was analysed with the following result:

0·1124 gave 0·2566 CO_2 and 0·0842 H_2O; C = 62·3; H = 8·3.
$C_5H_8N_2$ requires C = 62·5; H = 8·3 per cent.

The *aurichloride*, when recrystallised from dilute hydrochloric acid, formed orange-yellow needles which melted at 215°:

0·0932 salt dried at 100° gave 0·0426 Au. Au = 45·7.
$C_5H_8N_2,HAuCl_4$ requires Au = 45·3 per cent.

The *platinichloride*, recrystallised from dilute hydrochloric acid, formed orange-coloured needles which melted sharply and decomposed at 230°.

The *picrate*, which crystallised from hot water in fine, yellow, prismatic needles melting at 179°, was unchanged by further crystallisation from alcohol.

The *methiodide*, prepared by adding methyl iodide to the base, became solid immediately, with the evolution of much heat. When recrystallised from methyl alcohol and ether, it was obtained in white needles, which although slowly decomposed in the air, were not very hygroscopic, and did not melt below 300°.

In conclusion, we wish to reserve for future study the action of bromine under pressure on these glyoxalines.

THE WELLCOME CHEMICAL RESEARCH LABORATORIES.

R. CLAY AND SONS, LTD., BREAD ST. HILL, E.C., AND BUNGAY, SUFFOLK.