LXVII. SYNTHESIS OF 4-(OR 5-) CARBAMIDOGLYOXALINE

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THE preparation from guanine of a substance regarded as 4-(or 5-)guanidinoglyoxaline has been reported by one of us: the corresponding carbamido-compound was also described [1936]. The synthesis of the latter from 4-(or 5-)nitroglyoxaline is here reported, and its identity with the previously described compound established. The synthesis takes the following course:

After the failure of several attempts to isolate the aminoglyoxaline (II) from the mixture resulting from reduction of (I), it was finally decided to attempt the synthesis without the isolation of (II); the reduction mixture was therefore treated directly with cyanic acid, in presence of a slight excess of acetic acid, to yield 4-(or 5-)carbamidoglyoxaline (III).

The course of synthesis was readily followed by application of the Koessler and Hanke diazo-test. 4-(or 5-)Aminoglyoxaline, like 4-(or 5-)guanidinoglyoxaline, yields a methylene blue-like colour when coupled with sodium diazobenzene-*p*-sulphonate. The carbamido-compound, on the other hand, yields a brilliant red. As the condensation progresses, the blue diazo-test is gradually replaced by the red.

The 4-(or 5-)carbamidoglyoxaline is obtainable as a silver salt, insoluble in slight excess of $\text{Ba}(\text{OH})_2$. When the solution, freed from silver, is heated with excess of picric acid, a beautifully crystalline picrate is obtained on cooling. The pure hydrochloride is obtained as large flat plates and spars, by the usual procedures, from the picrate.

The identity of the substance with that already described is proved by analysis and M.P. and mixed M.P. of the hydrochlorides.

EXPERIMENTAL

1 g. of 4-(or 5-)nitroglyoxaline [Fargher & Pyman, 1919] was suspended in 100 ml. methyl alcohol and reduced by shaking in the dark at ordinary temperature with 50 g. of 3% sodium amalgam.¹ The reaction mixture acquired a dense blue colour. Reduction was judged complete at the end of 2 hours when a small aliquot of the mixture gave a maximum blue colour with the diazo-reagent.

The solution was decanted from the mercury, made faintly acid to litmus by addition of glacial acetic acid and treated with 1.4 g. of pulverized KCNO . It

¹ For the above reduction Na amalgam was found to be more efficient than Al amalgam, Zn or Sn and HCl, or catalytic hydrogenation using platinum black as catalyst.

was kept in the dark at ordinary temperature with occasional shaking for 3 days. At the end of this time the original blue diazo-test was entirely replaced by a brilliant red.

The reaction mixture was centrifuged and filtered in order to remove the precipitate and the blue pigment which had been formed. The dark brown alcoholic filtrate was evaporated *in vacuo* and the residue taken up in about 20 ml. water. The solution was boiled with charcoal and again filtered.

The filtrate and washings were made to about 300 ml. with water and the solution definitely acidified with 5 *N* HNO_3 . 10 % AgNO_3 was added to excess as shown by the appearance of brown Ag_2O when a drop of the filtered solution was tested with $\text{Ba}(\text{OH})_2$. The large precipitate of unknown decomposition products carried with it nearly all the pigment from the solution. After standing for some time in a refrigerator this precipitate was removed by centrifuging. A further small precipitate was obtained by partial neutralization with 10 % NaOH . The ice-cooled filtrate obtained from the faintly acid solution was now treated with hot $\text{Ba}(\text{OH})_2$ to precipitate the silver salt of 4-(or 5-)carbamidoglyoxaline. A slight excess only of alkali is necessary for its complete precipitation.

Care must be taken in the silver fractionation. The appreciable precipitate formed in the acid solution tends to adsorb some of the carbamidoglyoxaline. In order to minimize this occlusion, the volume of the solution was kept fairly large, the AgNO_3 solution was added drop by drop to the well agitated solution, and NaOH was used instead of $\text{Ba}(\text{OH})_2$ to bring the solution to faint acidity to litmus.

The silver salt was well washed with cold, dilute $\text{Ba}(\text{OH})_2$, immediately suspended in water and the mixture made just acid with H_2SO_4 . The silver was removed with H_2S in the usual manner. The H_2S was removed by distillation *in vacuo*, the solution neutralized by the addition of $\text{Ba}(\text{OH})_2$ and the BaSO_4 removed. The solution was boiled with charcoal and the filtrate reduced *in vacuo* to a volume of about 2 ml. An excess of picric acid was added, the precipitate dissolved by heat and crystallization allowed to take place by slow cooling. Long robust needles of the picrate were obtained.

The crystals were collected on a sintered glass funnel and well washed with alcohol; yield 0.23 g., m.p. 200° , of crystals contaminated with brown pigment. The impurity is not readily removed by recrystallization and no attempt was made to obtain the pure picrate at this stage. On the basis of this picrate the yield is about 8 % of the theoretical.

1.23 g. of picrate, collected from various batches as above, were suspended in about 30 ml. of water, HCl was added and the picric acid removed by shaking with ether. The resulting solution was evaporated *in vacuo* to a small volume and boiled with charcoal. It was then further concentrated to about 3 ml. and 3 vol. of absolute ethyl alcohol were added. The hydrochloride crystallized as large flat pigmented plates; yield 0.26 g. It was dissolved in about 5 ml. of water, boiled with charcoal and recrystallized as above. 0.20 g. of pure 4-(or 5-)carbamidoglyoxaline hydrochloride, with characteristic faint pink tinge, was obtained. m.p. 210° . (Found: N, 34.24, 34.49; Cl, 21.97, 21.87 %. $\text{C}_4\text{H}_6\text{ON}_4 \cdot \text{HCl}$ requires N, 34.46; Cl, 21.80 %.)

A mixture with the compound obtained from guanine had m.p. 210° .

REFERENCES

- Fargher & Pyman (1919). *J. chem. Soc.* 115, 227.
 Hunter (1936). *Biochem. J.* 30, 1183, 1201.