Tetrahedron Letters No.22, pp. 1879-1880, 1970. Pergamon Press. Printed in Great Britain.

NEW HETEROCYCLIC SYSTEMS WITH INCORPORATED HYDROXYGUANIDINE

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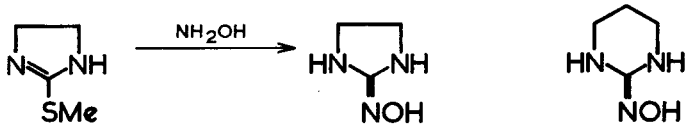
(Received in UK 13 March 1970; accepted for publication 9 April 1970)

Very little is known on hydroxyguanidine and its N-substituted derivatives, prepared first by Praetorius (1) and Braun (2). The isolation of canavanine, a natural aminoacid with a hydroxyguanidine fragment, as well as the possibility of the direct introduction of guanidine into aromatic systems using hydroxyguanidine sulphonate (3), has stimulated chemical research on such compounds. Nevertheless, no heterocyclic systems incorporating hydroxyguanidine have been investigated as yet.

Two simple heterocyclic compounds of the type, (I) viz., N,N′-ethylene-N′′--hydroxyguanidine and its propylene homologue (Ia) were prepared by substituting the hydroxyimino group for the methylthio group in the corresponding derivatives of isothiourea:

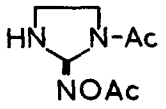


I Ia

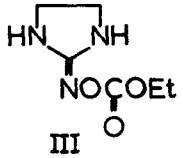
Both bases I and Ia were unstable. The preparation was, therefore, carried out in an excess of acetic acid, or with the hydroiodide or hydrochloride salt of one of the reactants. The acetate of I and Ia readily underwent O-acylation and O,N-diacetyl derivatives (II and IIa respectively) were obtained when acetic anhydride was used in excess.

Acylation of I with ethyl chloroformate carried out in aq. solution in the presence of potassium carbonate yielded O-carbethoxy-2-oximino-imidazolidine (III); further cyclization of the latter to a bicyclic system failed. Compound Ia readily gave under the same conditions 5,6,7,8-tetrahydro-[1,2,4]-oxadi-

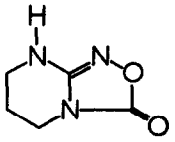
azolo[3,4-a]pyrimidine-3-one (IVa).



II

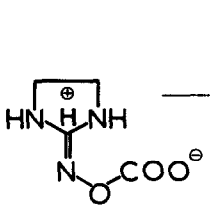


III

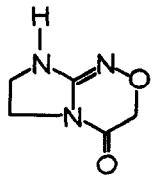


IVa

Bicyclic systems were also prepared from S-methylisothiourea derivatives and aminooxyacetic acid, the latter being used instead of hydroxylamine (4). Best yields of V and Va, which can be considered as O-carboxymethyl derivatives of I and Ia, were obtained when dimethylformamide was used as the solvent. Attempted esterification of V and Va resulted in the formation of bicyclic compounds, 3,4,6,7-tetrahydroimidazo[2,1-c]1,4,2-oxadiazine-4-one (VI) and 3,4,5,7-tetrahydropyrimido[2,1-c]1,4,2-oxadiazine-4-one (VIa), respectively. With an excess of diazomethane VII and VIIa were obtained.

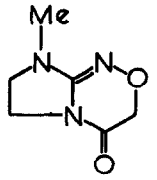


V



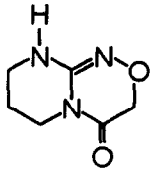
VI

or



VII

Va



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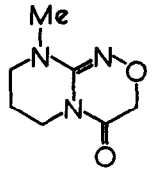

VIa VIIa

Structural assigments of the new compounds were based upon elemental analysis and ir and NMR spectra.

References

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