CHEMISTRY

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1960

SovietRxiv

Abstract

Full Text

CHEMISTRY

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SYNTHESIS OF SOME 8,9-PENTAMETHYLENEPURINES

(Presented by Academician M. M. Shemyakin, March 9, 1960)

The presence of purine compounds in nucleic acids, as well as the high biological activity of 6-substituted purines and alkaloids of the dioxypurine series, has in recent years aroused great interest in the synthesis of purine derivatives, including compounds with tricyclic systems containing the purine nucleus ([1,2]). This prompted us to synthesize, for biological study, certain representatives of a new series of 8,9-polymethylenepurines and, first of all, 8,9-pentamethylenepurines (I, $n = 3$):

8,9-polymethylenepurine skeleton
with substituents X and Y, and an annelated $-(CH_2)_n-$ chain
(I)

We set ourselves the task of obtaining structural analogues of such biologically important purines as adenine, guanine, kinetin (6-furfurylaminopurine), 6-mercaptopurine, and others. For this purpose an attempt was made to carry out the synthesis of I by condensation of uramil (II) with O-methylcaprolactim (III):

$$\text{uramil (II)} + \text{O-methylcaprolactim (III)} \xrightarrow[-CH_3OH]{} [\text{intermediate condensation product}] \xrightarrow[-H_2O]{} \text{8,9-pentamet}$$

However, in a series of experiments on the condensation of II with III under various conditions, it was not possible to bring about their interaction, and in all cases II and III were recovered completely. To carry out the synthesis of I, another possible variant was subsequently studied, consisting in the condensation of III with α-amino-α-cyanoacetamide (IV):

$$\alpha\text{-amino-}\alpha\text{-cyanoacetamide (IV)} + \text{O-methylcaprolactim (III)} \xrightarrow[-CH_3OH]{} \begin{cases} [\text{intermediate (V)}] \longrightarrow \text{cyclized p} \\ \text{isomeric product (VII)} \end{cases}$$

On brief heating of III with IV in ethyl cellosolve (method A), a substance with m.p. 272–274° (decomp.) was obtained; because of the possibility of

condensation of III at the NH_2 group of IV, and also because of the ability of III to react with compounds containing an active CH_2 group ([3]), its structure could correspond to one of three mutually isomeric compounds V, VI, and VII. When the condensation of III with IV was carried out in a boiling solution of alcoholic HCl, a hydrochloride with m.p. 257–259° was isolated. The same hydrochloride was obtained from the dihydrochloride of aminomalonamidoamidine (VIII) ([4]), likewise by heating with III:

$$\text{(VIII)} \xrightarrow[-CH_3OH]{+III} [\text{intermediate}] \cdot 2HCl \xrightarrow[-NH_4Cl]{} VI \cdot HCl$$

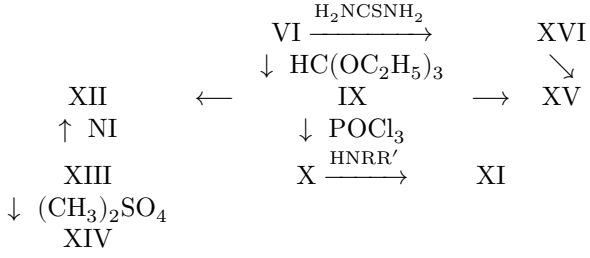
From these two hydrochlorides one and the same base was isolated, with m.p. 272–274°, identical with the substance obtained by method A. The IR spectrum of this substance showed that it contains no CN group, while absorption bands characteristic of NH_2 and H_2NCO groups are present (2.95; 3.04; 3.15 and 6.12 μ). Thus, for the product of condensation of III

Table 1

Substance	IX	X	XIa	XIb	XIc	XId	XIe	XII	XIII*	XIV	XV
M.p., °C	308–311 (decomp.)	141–143	226.5–228.5	142–144	153–155	168–170	177–179	290–292 (decomp.)	99–101	139–141	> 360

* Picrate, m.p. 166–169°.

with IV, structures V and VII are excluded, and structure VI remains. The final proof of the structure of this substance as the amide of 1,2-pentamethylene-5-aminoimidazole-4-carboxylic acid follows from a series of transformations of VI into various derivatives of 8,9-pentamethylenepurine (see the scheme and Table 1).



XIa $R = R' = \mathrm{H}$,
b $R = R' = \mathrm{CH_3}$,
c $R = \mathrm{H}$, $R' = \mathrm{CH_2C_6H_5}$,
d $R = \mathrm{H}$, $R' = \mathrm{CH_2}$–furyl,
e $R = R' = \mathrm{CH_2CH_2OH}$.

The UV spectra of IX and XII proved to be identical to the spectra of hypoxanthine and 6-mercaptopurine. It is interesting to note that, on fusion of VI with thiourea, instead of the expected XVI, 8,9-pentamethyleneguanine (XV) was obtained, whose UV spectrum corresponded to that of guanine.

All-Union Scientific Research
Chemical-Pharmaceutical Institute
named after S. Ordzhonikidze

Received
29 II 1960

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Note: Figure translations are in progress. See original paper for figures.