

A Thesis Entitled

STUDIES ON SOME HETEROCYCLIC COMPOUNDS

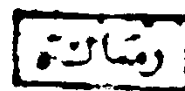
Studies on 2-Thiohydantoins

Submitted by

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Faculty of Science
Ain Shams University



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STUDIES ON SOME HETEROCYCLIC COMPOUNDS

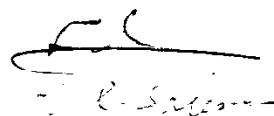
"Studies on 2-Thiohydantoins"

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Head of Chemistry Department



N O T E

Besides the work carried out in this thesis, the candidate has attended post-graduate courses for one year in organic chemistry including the following topics:

- 1) Reaction Mechanisms.
- 2) Electronic, Infrared, Raman, N.M.R. and Mass Spectroscopy of Organic Molecules.
- 3) Organic Reactions.
- 4) Heterocyclic Compounds.

He has successfully passed an examination in these topics.

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S U M M A R Y

2-Thiohydantoin (1) reacts with primary amines, namely, methyl-, n-propyl-, iso-propyl, n-butyl, and benzylamines to give α -thioureido-N-alkyl-acetamides (2a - e).

Similarly 2-thiohydantoin (1) reacts with piperidine and morpholine to give α -thioureido-N-piperidino (3a) and α -thioureido-N-morpholinacetamide (3b) respectively.

5-Arylidene-2-thiohydantoins (4a and b) were reacted with methyl-, n-propyl-, n-butyl, and benzylamines to give the corresponding 2-N-alkyl-imino-5-arylidene-hydantoin (5).

Similarly 5-arylidene-2-thiohydantoins (4a and b) were reacted with piperidine and morpholine to give 4-arylidene-2-piperidinyl- (7a and b) and 4-arylidene-2-morpholinyl-2-imidazolinone-5 (8a and b), respectively.

Leannich condensation with 2-thiohydantoin was also investigated.

2-Thiohydantoin (1) reacts with formaldehyde and piperidine or morpholine to give 1,3-N-dipiperidinomethyl (12a), and 1,3-N-dimorpholinomethyl-2-thio-

hydantoin (12b), respectively.

The structure of the above products was confirmed by studying their infrared spectra.

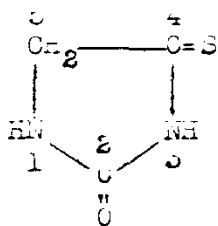
REVIEW OF LITERATURE

THIOHYDANTOINS AND PSEUDOTHIOHYDANTOINS

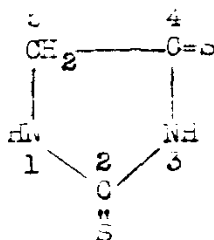
Closely allied to hydantoins are the 2-thiohydantoins. It has seemed desirable to consider these two types of compound more or less together, since they undergo analogous reactions in the presence of the same or of similar reagents.

Moreover, 2-thiohydantoin and its various derivatives are readily converted into the corresponding oxygen compounds. This last statement is of particular importance, since the sulfur hydantoins are frequently not only prepared and isolated more easily than the oxygen compounds, but also more reactive.

Also 4-thiohydantoins and 2,4-dithiohydantoins have been prepared; these also have chemical properties similar to those of the corresponding oxygen compounds.



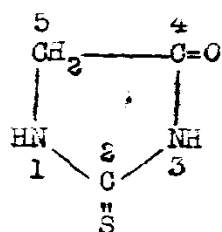
4-Thiohydantoin



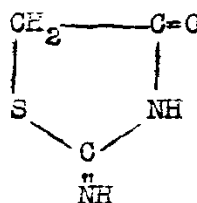
2,4-Dithiohydantoin

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Pseudothiohydantoins are isomeric with 2-thiohydantoins:



2-Thiohydantoin



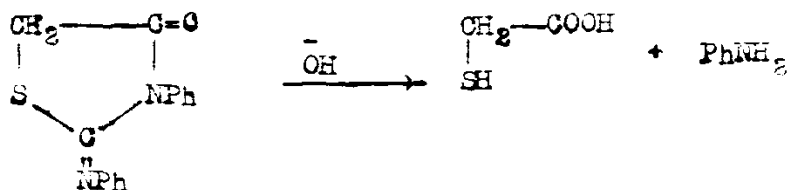
Pseudothiohydantoin

The difference between 2-thiohydantoins and pseudothiohydantoins was first recognized in 1879 by Liebermann and Lange^{1,2}. Further study of the structural differences was made by Aschan³, and by Dixon⁴.

One of the principal methods of preparation of pseudothiohydantoins is through the interaction of a thiourea with chloroacetic acid; this reaction was studied by a number of investigators between 1873 and 1879, and was believed to lead to the formation of 2-thiohydantoins⁵⁻¹¹. It was soon found, however, that these compounds gave unexpected results when hydrolyzed¹², oxidized¹⁵, or treated with metallic oxides in attempts to desulfurize them^{10,11}. It was the hydrolysis of a diphenyl derivative of pseudothiohydantoin to form

3.

aniline and thioglycollic acid which led Liebermann and Lange to conclude that their "diphenylthiohydantoin" had been incorrectly formulated¹.



METHODS OF SYNTHESIS OF THIOHYDANTOINS

A) From aminoacids and alkali thiocyanates.

2-Thiohydantoins are prepared from the reaction of potassium thiocyanate with α -aminoacids.

It was reported by Kleson¹⁴, and later confirmed by Johnson¹⁵, that 2-thiohydantoin (I) was formed when the hydrochloride of glycine ethyl ester (II) and potassium thiocyanate are heated together at 140 - 150°C, without solvent. Ethyl thiohydantoate was also isolated by Johnson from the reaction products, but the fact that he was unable, as were Harries and Weiss^{16,17}, to bring about ring closure of this ester to 2-thiohydantoin (I), indicates that ethyl thiohydantoate is not an intermediate product in the formation of 2-thiohydantoin (I).

It was reported by Komatsu¹⁸ that thiohydantoic acid had been obtained by heating glycine with potassium thiocyanate in acetic anhydride solution, and that 2-thiohydantoin (I) could be prepared by heating thiohydantoic acid with hydrochloric acid. Since it had been found impossible to bring about the cyclization of ethyl thiohydantoate with mineral acid, this reaction was investigated