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A NEW APPROACH FOR THE CONVERSION OF THIOHYDANTOIN TO HYDANTOIN DERIVATIVES

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Abstract: The reaction of thiohydantoins with 1-(bromoacetyl)benzenes afforded the corresponding hydantoin derivatives and 1-(mercaptoacetyl)benzenes instead of the expected oxoimidazothiazoles.

Fused heterocyclic systems containing thiazole ring are ranked among the versatile heterocyclic compounds and a wide variety of procedures have been developed for their synthesis[1a]. During the course of our research work we were interested in some derivatives of oxoimidazothiazoles.

Earlier, the synthesis of 5-arylidene-6-oxoimidazothiazoles[2] has been carried out using 3-acetic acid-2-iminothiazole and aldehydes in acetic acid. The reaction of 2-amino thiazole with chloroacetyl chloride affords the 6-oxoimidazothiazoles, for which, some structural discrepancy has been recorded[1b]. Further

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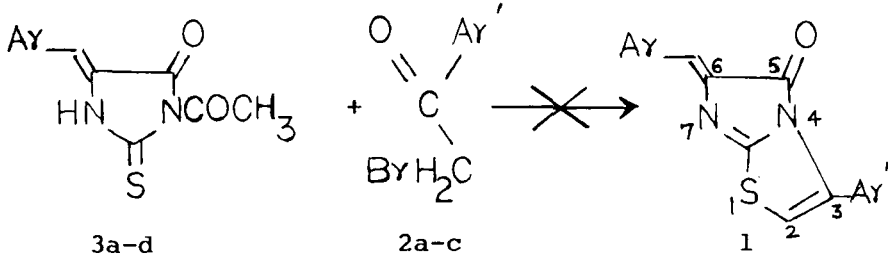
building up of thiazole moiety on thiohydantoin i.e. 4-oxo-2-thioxoimidazolidene, has been reported. For example, the reaction of thiohydantoin with 1,2-dihaloalkanes in ethanol/NaOH gives a mixture of 5-oxo- and 6-oxo-imidazothiazolidenes[3] and with $ClCH_2COOR$ (R=H, CH_3) in ethanol gives oxoimidazothiazolidene derivatives[4].

Since we were interested in 5-oxoimidazothiazole derivatives **1**, the strategy was planned involving the reaction of thiohydantoin derivatives and 1-(bromoacetyl)benzenes **2** using Hantzsch synthesis. The 3-acetyl-5-arylidene-2-thiohydantoins[5] **3** were the preferred choice[6] and thus treated with **2**, however, some undesired results were obtained which are summarized herein.



3a-d **2a-c** **1**

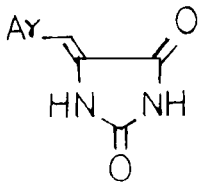
The experimental procedure involves the reaction of equimolar amounts of 3-acetyl-5-benzylidene-2-thiohydantoin **3a** and 1-(bromoacetyl)-4-methoxybenzene **2a** in ethanol at reflux temperature for 5 hrs. Work up of the reaction mixture and column purification gave two products ***A*** and ***B*** [R_f ***A*** 0.09; R_f ***B*** 0.56; Solvent system 5:95, acetone-benzene]. Data for compound ***A*** (yield 64%) includes m.p. 220-2°; PMR(DMSO-d_6) : 3.3 (s, 1H, NH), 6.4 (s, 1H, CH), 7.05-7.7 (m, 5H, Ar-H); MS M^+ 188

(78%), 117 (100%); elemental analysis: C 63.01, H 4.31, N 15.06%. The data was not in accordance with the expected structure **1** [Ar=C_6H_5; Ar´=(p-OCH_3)C_6H_4-]. On the basis of above ***A*** was assigned the structure as 5-benzylidene hydantoin **4a**. The structure **4a** was finally confirmed by its comparison [m.p. 220-1° (lit.[7] m.p. 220°), m.m.p., co-IR] with an authentic sample prepared by condensation of hydantoin with benzaldehyde.

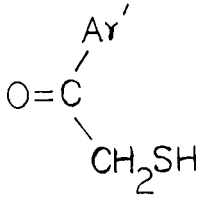
Compound ***B*** possessed following data: m.p. 57°; PMR ($CDCl_3$) : 1.5 (s, 1H, D_2O exchangeable), 3.82 (s, 3H, -OCH_3), 4.1 (s, 2H, -CH_2), 6.9 and 8.0 (each 'd' J=9Hz, 2x2H-ArH). Besides this it showed positive DNP test for >C=O and gave yellow color with DTNP reagent[8] [2,2´-dithiobis(5-nitropyridine)], a positive test, for thiol (-SH) group. On the basis of all these observations ***B*** was assigned the structure as 1-(mercaptoacetyl)-4-methoxybenzene **5a**.

Further reaction of the derivatives of **3** with any of the derivatives of **2** gave the corresponding hydantoins **4** and 1-(mercaptoacetyl)benzene derivatives **5****. All the structures **4a-d** were confirmed by comparison (m.p. m.m.p. co-IR) with authentic samples prepared from hydantoin and corresponding aldehydes.

***Only mercapto derivative **5a** could be isolated in minor quantities. Rest of the derivatives **5b-c** were qualitatively analyzed on TLC plate, by DNP (for >C=O) and DTNP (for -SH) tests. It was not possible to isolate **5b-c** in present set of conditions as they decompose readily[9] with evolution of H_2S.*



4a-d



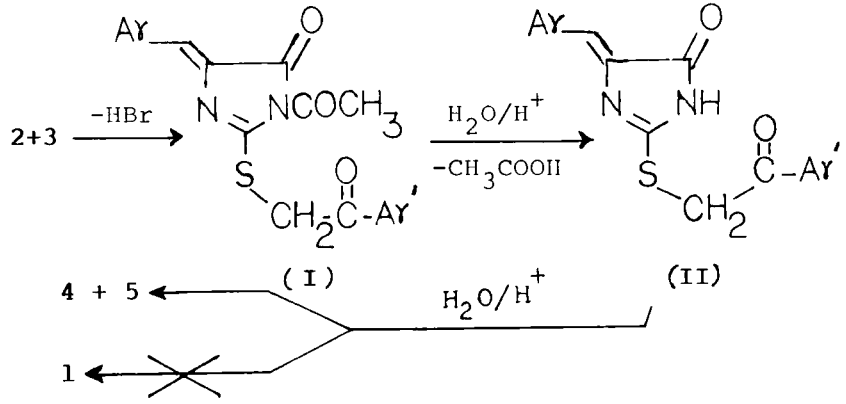
5a-c

	3,4 Ar	2,5 Ar'
a	C_6H_5-	(P-OCH_3)C_6H_4-
b	(P-CH_3)C_6H_4-	C_6H_5-
c	(P-Cl)C_6H_4-	(P-CH_3)C_6H_4-
d	2-Furfuryl	

The physical data (mol. for.; m.p.; yield) for compounds **4b-d** is as follows: **4b:** $C_{11}H_{10}N_2O_2$, 275°, 67%; **4c:** $C_{10}H_7ClN_2O_2$, 292°, 71%; **4d:** $C_8H_6N_2O_3$ 231-4°, 58%.

In above cases conversion of thiohydantoin to hydantoin has been observed. Earlier, such conversions have been effected under different conditions[10] e.g. Bromine water, alkaline $KMnO_4$, sodium hypochlorite etc.

It is believed that thiohydantoin **3a-d** give S-acyl intermediate-**I** on reaction with 1-(bromoacetyl)benzenes **2**, and HBr, thus released, induces the deacylation



SCHEME-1

process to give S-acyl intermediate-**II**. This is supported by the fact that 3-acetyl-5-arylidene-2-thiohydantoins on refluxing with HBr in ethanol give corresponding deacylated products[5]. Subsequently, rupture of the **C-S** bond of intermediate-**II** takes place to give the hydantoins **4** and mercapto derivatives **5**, instead of the expected thiazoles **1**. During the overall process the role of traces of water cannot be overlooked as depicted in scheme-1.

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