

Studies in the Synthesis of Thiohydantoins: Part II*. Derivatives of 3-(Benzothiazole-2-yl) Thiohydantoins

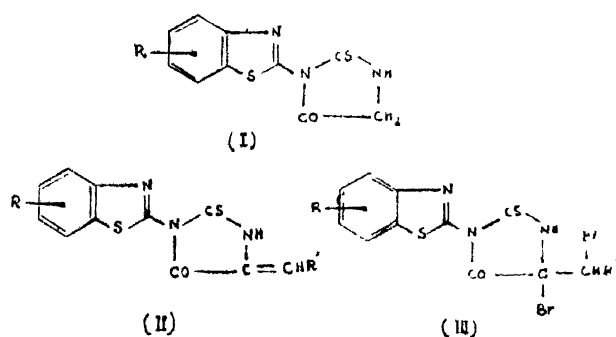
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Several substituted benzothiazolyl thiohydantoins (I), their arylidene derivatives (II) and dibromo compounds (III) have been synthesised.

IN view of the significant therapeutic importance of thiohydantoins and their derivative it was considered worthwhile to synthesise various thiohydantoins, their arylidene derivatives and dibromo compounds with a heterocyclic substituent (benzothiazole) in the position 3 of the thiohydantoin moiety. 2-Amino benzothiazoles, required for the synthesis of thiohydantoins were prepared from their aryl thiocarbamides with bromine according to Bhargava *et al.*¹. Acetone solution of the 2-amino benzothiazoles were converted into their respective thioureas with benzoylthiocyanate according to our previous communication². These thioureas on condensation with monochloro acetic acid furnished thiohydantoins (I) in the medium of pyridine. The thiohydantoins were condensed with aromatic aldehydes to get the arylidene compounds (II) which



have been brominated to (III) with bromine in chloroform. The structures of thiohydantoin and their arylidene derivatives have been confirmed from IR, which shows a batho-chromic shift in the carbonyl absorption in case of the arylidene derivatives because of conjugation due to unsaturation at 5-position. The magnitude of the shift is more when an electron donating substituent is present in the para position of the aldehyde and it is decreased by the introduction of an electron withdrawing substituent.

* Part I. This journal; communicated for publication.
† Deceased.

Experimental

All melting points are uncorrected. IR spectra of the compounds were taken on KBr discs.

N¹-(Substituted benzothiazole-2-yl) thioureas were prepared from 2-amino benzothiazoles with benzoyl thiocyanate according to our previous communication².

3-(Benzothiazole-2-yl) thiohydantoin (I; R = H)

A mixture of N¹-(benzothiazole-2-yl) thiourea (3.15 g) and monochloro acetic acid (2.3 g) in pyridine (10 ml) was warmed on a water bath for 2-3 min during which an exothermic reaction took place. It was kept as such till the vigour of the reaction got subsided and the whole mixture became viscous. It was treated with alcohol and refluxed on a water bath for 1 hr. The shining crystalline solid formed was filtered and crystallised from alcohol. Yield 60%, m.p.; 219° (Found: S, 25.06; C₁₀H₇N₃OS₂ requires S, 25.70%), λ_{max} (cm⁻¹); 1405 (CH deformation in CH₂), 1770 (C=O), 3400 (NH) broad.

The analytical data etc. of other thiohydantoins have been reported in Table I.

TABLE I. (THIOHYDANTOINS)

Nature of R.	Yield %	M.P. °C	% Sulphur	
			Found	Calc.
6-Chloro	65	232	11.07	11.28
6-Methyl	60	241	12.39	12.16
6-Methoxy	55	192	11.36	11.47
6-Nitro	50	260	10.73	10.88
6-Ethoxy	52	183	10.61	10.91
4-Chloro	55	173	11.46	11.28

3-(Benzothiazole-2-yl) 5-benzal thiohydantoin (II; R and R¹ = H)

A mixture of above thiohydantoin (0.25 g), benzaldehyde (0.2 g) and sodium acetate (0.5 g) was taken in glacial acetic acid (8 ml) and refluxed

TABLE 2

Nature of R	Nature of R'	Arylidene derivatives(II)				Dibromo compounds(III)			
		Yield %	M.P. °C	%Sulphur		Yield %	M.P. °C	%Bromine	
				Found	Calcd.			Found	Calcd.
H	H	—	—	—	—	52	240	32.01	32.19
-do-	<i>p</i> -CH ₃ O	72	238	16.74	17.54	50	238	30.16	30.36
-do-	<i>p</i> -Cl	70	195	17.42	17.22	45	243	37.61*	36.78
-do-	<i>p</i> -Br	60	211	14.70	15.38	40	264	41.89	41.67
-do-	<i>p</i> -NO ₂	65	231	16.52	16.74	50	244	29.65	29.52
-do-	<i>p</i> -(CH ₃) ₂ N	56	194	16.60	16.84	—	—	—	—
6-Cl	H	62	253	17.04	17.22	50	248	36.73*	36.78
-do-	<i>p</i> -CH ₃ O	60	246	15.26	15.94	45	141	34.65*	34.81
-do-	<i>p</i> -Cl	58	217	15.82	15.76	45	268	40.39*	40.11
-do-	<i>p</i> -Br	55	243	14.20	14.64	40	149	45.36*	45.12
-do-	<i>p</i> -NO ₂	50	260	15.06	15.36	40	250	33.29*	33.90
-do-	<i>p</i> -(CH ₃) ₂ N	60	254	15.30	15.44	—	—	—	—
6-CH ₃	H	60	210	18.74	18.24	50	192	31.20	31.31
-do-	<i>p</i> -CH ₃ O	60	213	16.20	16.80	50	193	29.38	29.57
-do-	<i>p</i> -Cl	55	198	16.42	16.60	45	177	35.72*	35.83
-do-	<i>p</i> -Br	50	217	15.06	14.88	40	229	40.42	40.67
-do-	<i>p</i> -NO ₂	55	250	16.72	16.16	40	243	28.69	28.77
-do-	<i>p</i> -(CH ₃) ₂ N	50	218	16.14	16.84	—	—	—	—
6-CH ₃ O	H	63	216	16.38	17.44	45	267	30.15	30.36
-do-	<i>p</i> -CH ₃ O	60	232	16.60	16.12	40	237	28.96	28.72
-do-	<i>p</i> -Cl	55	234	15.62	15.94	40	225	34.73*	34.81
-do-	<i>p</i> -Br	50	221	14.12	14.34	40	214	39.54	39.60
-do-	<i>p</i> -NO ₂	60	248	14.64	15.54	40	269	27.38	27.97
-do-	<i>p</i> -(CH ₃) ₂ N	55	185	15.06	15.60	—	—	—	—
6-NO ₂	H	60	250	—	—	40	208	29.32	29.52
-do-	<i>p</i> -CH ₃ O	60	250	—	—	45	250	27.18	27.97
6-C ₂ H ₅ O	H	60	208	16.24	16.50	50	144	—	—
-do-	<i>p</i> -CH ₃ O	65	174	—	—	50	153	28.37	28.02
-do-	<i>p</i> -NO ₂	55	218	—	—	45	237	—	—
-do-	<i>p</i> -Br	50	182	12.72	13.90	45	216	38.62	38.71
4-Cl	H	65	250	17.06	17.22	55	250	—	—
-do-	<i>p</i> -CH ₃ O	65	221	14.64	15.94	55	250	34.73*	34.81
-do-	<i>p</i> -Cl	60	260	—	—	50	250	—	—
-do-	<i>p</i> -Br	55	260	—	—	50	250	—	—
-do-	<i>p</i> -NO ₂	50	250	14.34	15.36	50	250	33.13*	33.90
-do-	<i>p</i> -(CH ₃) ₂ N	50	250	—	—	—	—	—	—

* Indicates halogen content.

for 2 hr. After cooling it was poured into water and the resulting yellow precipitate formed was crystallised from acetic acid. Yield 75%, m.p. >250°. (Found: S, 18.62; C₁₇H₁₁S₂ON₃ requires S, 18.98%) λ_{max} (cm⁻¹) 1560 (C=O), 1740 (C=O), 3400 (NH).

3-(Benzothiazole-2-yl) 5-bromo 5-(*z*-bromo) benzyl thiohydantoin (III, R and R' = H)

To a solution of benzylidene thiohydantoin in chloroform (0.2 g in 20 ml) bromine in chloroform (0.2 g in 5 ml) was added dropwise at 0° and kept overnight in the refrigerator. Excess of chloroform was removed and SO₂ gas was passed through the aqueous suspension. The slightly yellow coloured dibromo compound obtained was filtered, washed with ether and finally dried.

The analytical data, m.p. etc. of various compounds and their dibromo derivatives prepared

from different thiohydantoin have been recorded in Table 2.

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