Studies on 5-Arylidene-3-phenyl-2-methylmercaptohydantoins

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The action of ammonium acetate on 5-arylidene-3-phenyl-2-methylmercaptohydantoins **1g,h** in acetic acid led to the formation of the 5-arylidene-3-phenylhydantoin derivatives **4a,b**. In absence of a solvent, ring opening and rearrangement took place with the formation of the 5-arylidene-N^2-phenylglycocyamidine derivatives **7a-c**. Compounds **7a-c** reacted with methyl iodide to afford the corresponding 3-methyl derivatives **9a-c**. The structures of the synthesised products were established and the mechanism proposed for the rearrangement reaction was discussed.

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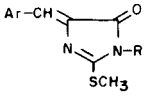
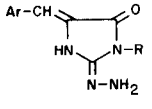
The action of hydrazine on 5-arylidene-2-methylmercaptohydantoins **1a,b** and the 3-methyl derivative **1d** has been shown to give the corresponding 2-hydrazones **2a-c** [2,3]. However, the 3-phenyl derivatives **1g-i** were recently shown to undergo an interesting rearrangement upon treatment with the same reagent to give the 5-arylidene-3-amino-N^2-phenylglycocyamidine derivatives **3a-c** [4].



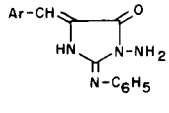
I

a, Ar = C_6H_5, R = H
b, Ar = $C_6H_4OCH_3$-p, R = H
c, Ar = $C_6H_4CH_3$-p, R = H
d, Ar = C_6H_5, R = CH_3
e, Ar = $C_6H_4OCH_3$-p, R = CH_3
f, Ar = $C_6H_4CH_3$-p, R = CH_3
g, Ar = R = C_6H_5
h, Ar = $C_6H_4OCH_3$-p, R = C_6H_5
i, Ar = $C_6H_4CH_3$-p, R = C_6H_5



2

a, Ar = C_6H_5, R = H
b, Ar = $C_6H_4OCH_3$-p, R = H
c, Ar = C_6H_5, R = CH_3



3

a, Ar = C_6H_5
b, Ar = $C_6H_4OCH_3$-p
c, Ar = $C_6H_4CH_3$-p

Our interest has now been extended to study the possible reaction of compounds **1g-i** with ammonia in different media. It has been reported that amines react with compounds **1a-c** to give the corrresponding glycocyamidines **7a-c** [4]. We have now found that compounds **1g-i** do not react to any appreciable extent with ammonia or ammonium acetate in refluxing ethanol for 10 hours. However, in acetic acid, compounds **1g,h** react with ammonium acetate to give the corresponding 5-arylidene-3-phenylhydantoins **4a,b**. On the other hand, fusion of compounds **1g-i** with ammonium acetate afforded the corresponding 5-arylidene-N^2-phenylglycocyamidines **7a-c**. The structure of compounds **4a,b** and **7a-c** was established by their independent synthesis according to the reported procedures from compounds **1g,h** [4,6] and **1a-c** [2,4,5].

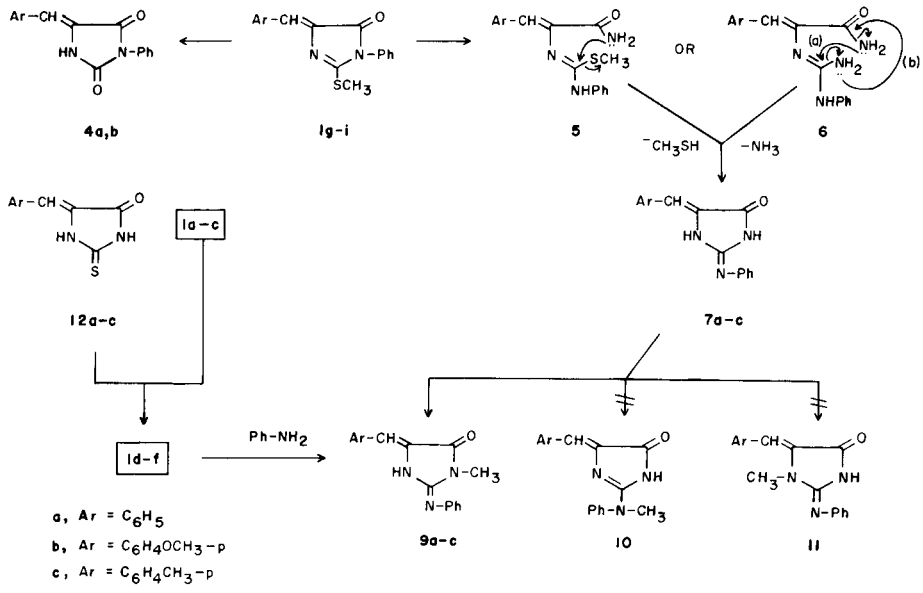
The rearrangement of compounds **1g-i** with ammonium acetate might be expected to proceed *via* an acyclic compound resulted from the nucleophilic attack of ammonia

Table

Characterization Data of **1e,f** and **9a-c**

Product [a]	Mp, °C [a]	Yield % [c]	Formula (Mol wt)	Analysis % Calcd./Found C	H	N	S
1e [b]	140	[i] 75	$C_{13}H_{14}N_2O_2S$	59.54	5.34	10.68	12.21
		[ii] 82	(262)	59.70	5.30	10.50	12.10
1f	120	[i] 80	$C_{13}H_{14}N_2OS$	63.41	5.69	11.38	13.01
		[ii] 82	(246)	63.30	5.70	11.50	13.20
9a	210	[iii] 65	$C_{17}H_{15}N_3O$	73.64	5.41	15.16	—
		[iv] 90	(277)	73.40	5.20	15.20	—
9b	218	[iii] 52	$C_{18}H_{17}N_3O_2$	70.36	5.54	13.68	—
		[iv] 89	(307)	70.10	5.50	13.80	—
9c	210	[iii] 50	$C_{18}H_{17}N_3O$	74.23	5.84	14.43	—
		[iv] 92	(291)	74.40	5.70	14.20	—

[a] Compound **9a**, ir (potassium bromide): 3330, 1702, 1652, 1605 cm^{-1}; nmr (deuteriochloroform): δ 1.55 (s, 1H, NH), exchangeable with deuterium oxide, 3.3 (s, 3H, N-CH_3), 6.55 (s, 1H, Ar-CH=) and 6.8-7.4 (m, 10H, ArH) ppm; Compound **9b**, ir (potassium bromide): 3330, 1702, 1652, 1605 cm^{-1}; nmr (deuteriochloroform): δ 1.5 (s, 1H, N-H), 3.25 (s, 3H, NCH_3), 3.75 (s, 3H, OCH_3), 6.45 (s, 1H, Ar-CH=), 6.8-9.3 (m, 9H, ArH's) ppm; Compound **9c**, ir (potassium bromide): 3300, 1700, 1650, 1605 cm^{-1}; nmr (deuteriochloroform): δ 1.55 (s, 1H, NH), 2.5 (s, 3H, Ar-CH_3), 3.3 (s, 3H, N-CH_3), 6.7 (s, 1H, Ar-CH=) and 7.2-7.4 (m, 9H, ArH's) ppm. [b] Compound **1e** reported mp 198-202° [3]; nmr (deuteriochloroform): δ 2.7 (s, 3H, SCH_3), 3.18 (s, 3H, N-CH_3), 3.85 (s, 3H, OCH_3), 6.85 (s, 1H, Ar-CH=), 6.95 (d, 2H, ArH's) and 8.15 (d, 2H, ArH's) ppm. [c] [i] Yield from methylation of **12b,c**; [ii] yield from methylation of **1b,c** [iii] yield from methylation of **7a-c** and [iv] yield obtained by reacting aniline with **1d-f**.



on position 4 of compounds **1g-i** (similar to that proposed for the action of hydrazine [4]). Two possible acyclic intermediates **5** and **6** can be expected to lead to the final products **7a-c**. Intermediate **5** leads to **7a-c** *via* elimination of methylmercaptan, however, the other intermediate **6** leads to the same products by attack of NH_2 and elimination of ammonia molecule. The formation of compounds **4a,b** in acetic acid is the result of acid hydrolysis which is well documented for such systems [7].

Attempts to methylate compounds **7a-c** with methyl iodide in refluxing ethanol in the presence of sodium ethoxide led to the formation of the 3-monomethyl derivatives **9a-c**. Of the three possible isomeric monomethyl derivatives **9-11**, only structure **9** was shown to be the sole reaction product. The structure of products **9a-c** was established by their independent synthesis by the action of aniline on 5-arylidene-3-methyl-2-methylmercaptohydantoins (**1d-f**). The latter compounds were prepared by methylation of either 5-arylidene-2-thiohydantoins **12a-c** or their 2-methylmercapto derivatives **1a-c** in ethanolic sodium ethoxide (*cf.* Chart).

EXPERIMENTAL

All melting points are uncorrected. The ir spectra (potassium bromide) were recorded with a Perkin-Elmer infrared spectrophotometer. The nmr (deuteriochloroform) spectra were obtained on a Varian T-60 NMR spectrophotometer and the uv spectra were recorded on SP 1750 spectrophotometer in methanol. Elemental analyses were carried out by the Microanalytical Center, Cairo University.

Action of Ammonium Acetate on 5-Arylidene-3-phenyl-2-methylmercaptohydantoins **1g-i**. (a) In Acetic Acid.

To a solution of each of **1g,h** (1 g) in acetic acid (20 ml) was added ammonium acetate (5 g). The reaction mixture was heated under reflux for 10 hours. The precipitate obtained upon dilution with water and cooling was collected by filtration and recrystallized from acetic acid. The products were identified as **4a,b** (mp and mixed mp determinations) [6].

(b) Without Solvent.

A mixture of each of **1g-i** (1 g) and ammonium acetate (5 g) was heated in an oil-bath at 150-160° for 5 hours. The solid obtained after cooling was washed with water, cold ethanol and then recrystallised from DMF to give pale yellow crystals of **7a-c** (mp and mixed mp determinations) [4].

5-Arylidene-3-methyl-N^2-phenylglycocyamidines (**9a-c**). (a) By the Methylation of **7a-c**.

A suspension of each of **7a-c** (0.001 mole) in ethanol (20 ml) containing sodium ethoxide (prepared from 0.03 g of sodium) and methyl iodide (0.2 g, 0.0014 mole) was heated under reflux for 10 hours. The solid precipitated after cooling and dilution with water was collected by filtration and crystallised from ethanol to give yellow crystals of **9a-c** (*cf.* Table).

(b) By the Action of Aniline on **1d-f**.

A mixture of each of **1d-f** (0.002 mole) and aniline (0.5 ml) was heated in an oil-bath at 160-170° for 3 hours. The solid obtained after cooling and addition of ethanol (5 ml) was collected by filtration and crystallised from ethanol to give yellow crystals of **9a-c**.

Compound **9a-c** obtained by both methods (a) and (b) showed identical mp, mixed mp and ir spectra (*cf.* Table), also uv spectra of **9a** obtained by both methods showed λ max (methanol) at 250 and 370 nm.

5-Arylidene-3-methyl-2-methylmercaptohydantoins **1d-f**. (a) By Methylation of 5-Arylidene-2-thiohydantoins **2a-c**.

3-Methyl-2-methylmercaptohydantoins **1e,f** listed in the Table were prepared by the action of methyl iodide (3.7 g, 0.026 mole) on each of **12b,c** (0.01 mole) in ethanol (20 ml) containing sodium ethoxide (prepared from 0.6 g, 0.02 g atom of sodium), following the same procedure previously described for the synthesis of compound **1d** [5]. Compounds **1e,f** (*cf.* Table) were crystallised from ethanol into yellow crystals.

(b) By Methylation of **1a-c**.

A solution of each of **1a-c** (0.01 mole) in ethanol (20 ml) containing sodium ethoxide (prepared from 0.03 g, 0.013 g atom of sodium) and methyl iodide (1.85 g, 0.013 mole) was heated under reflux for 6 hours. The solid precipitated upon cooling and dilution with water was filtered off and crystallised from ethanol to give **1d-f** (*cf.* Table). Compound **1d** gave the same melting point and mixed melting point [5].

REFERENCES AND NOTES

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