

REACTION OF HYDRAZINE HYDRATE WITH SUBSTITUTED HYDANTOINS

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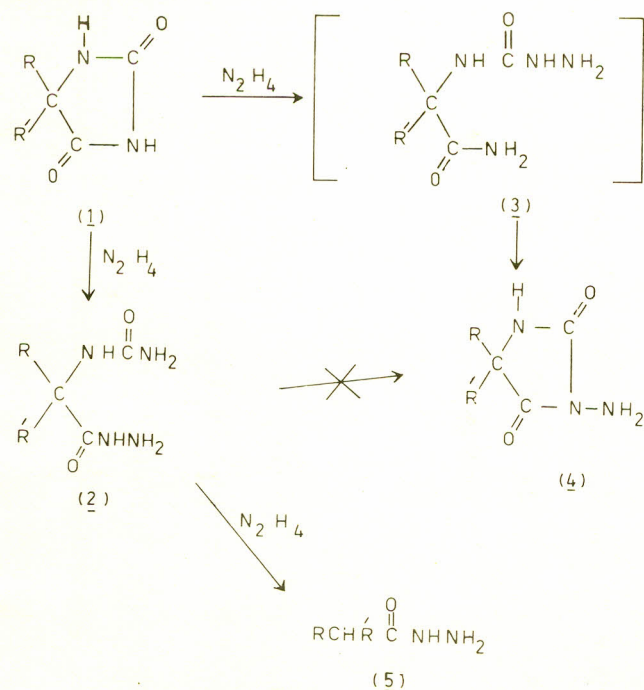
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INTRODUCTION

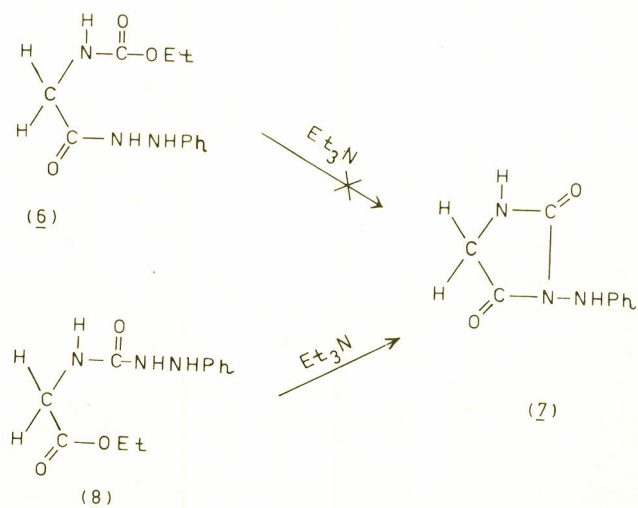
The reaction between hydrazine hydrate and $C_{5,5}$ -disubstituted hydantoin (1), to give N_3 -aminohydantoin (4) was first reported by Davidson [1] and then Winstead [2]. Neither the mechanism of amination nor the general applicability of the reaction to the C_5 -substituted hydantoin as a class has been mentioned. Accordingly, we propose to extend the above reaction over a large number of C_5 -substituted hydantoin and to postulate the mechanism of the reaction.

Different products were obtained from the $C_{5,5}$ -disubstituted and C_5 -monosubstituted hydantoin. The $C_{5,5}$ -disubstituted gave the corresponding N_3 -aminohydantoin, while the C_5 -monosubstituted hydantoin yielded the C_2 -substituted hydantoinic acid hydrazides. On either extending the reaction time between C_5 -monosubstituted hydantoin and hydrazine hydrate or employing a concentrated solution of the reagent the corresponding phenylacetic acid hydrazides are obtained. These conversions are summarized in the following scheme.



The mechanism of the reaction is believed to proceed at least in two stages *viz.* ring cleavage and ring closure. It is proposed that the ring opening for C_5 -mono and $C_{5,5}$ -disubstituted hydantoin proceed by different initial nucleophilic attack on $C_4=O$ and $C_2=O$ carbon atoms yielding a ureido (2) and carbohydrazide (3) types of compounds, respectively. Product (2) was isolated while the intermediate (3) is postulated. This is believed to be due to steric effect whereby the disubstituents prevent the more favourable $C_4=O$ from nucleophilic attack by hydrazine.

As for the ring closure, the postulated carbohydrazido compounds (3) cyclize *in situ* by expulsion of ammonia to give 3-aminohydantoin (4) by analogy to several work [3–8] which employ the compounds with carbohydrazide moiety to prepare 3-aminohydantoin. The isomeric ureido compound (2) was difficult to cyclize to 3-aminohydantoin and this is supported by the observation of Duane *et al.* [8] that the carboethoxyglycinephenylhydrazine (6) was difficult to cyclize to 3-anilinohydantoin (7) whereas the isomeric *N*-carboxyphenylhydrazidoglycine derivative (8) cyclized readily under the same conditions as shown in the following equation.



Some of the products of hydrazinolysis of C_5 -monosubstituted hydantoin are given in Table 1*. The products

Table 1*. Products of hydrazinolysis of C₅-monosubstituted hydantoins.

No	R	R	Time ^a (hr)	Yield (%)	m.p. ^b (°C)	Formula ^c
2	Me(CH ₂) ₆	H	8	60	180-1	C ₁₀ H ₂₂ N ₄ O ₃
2	Ph	H	7	55	208-10	C ₉ H ₁₂ N ₄ O ₂
2	4-MeOPh	H	8	60	200-1	C ₁₀ H ₁₄ N ₄ O ₃
2	3-ClPh	H	7	65	176	C ₉ H ₁₁ N ₄ O ₂ Cl
2	4-ClPh	H	7	55	208-10	C ₉ H ₁₁ N ₄ O ₂ Cl
2	4-OHPh	H	10	60	228-9	C ₉ H ₁₂ N ₄ O ₃
5	4-ClPh	H	2d	65	167-9 ^e	
5	4-OHPh	H	3d	70	200-2 ^f	

a. Time of refluxing the reaction mixture., b. M.p.s were determined on an electrothermal apparatus and are uncorrected. c. Where the formula is given, the compounds were analysed for C,H,N and analytical results are within +0.4% of calculated values., d. Reaction was conducted in high concentration of the reagent., e. lit. m.p. 170^o [9], f. lit. m.p. 200-2^o [10].

*Mechanism of the formation of phenylacetic acid hydrazides will be the subject of a detailed discussion in another communication.

from 5,5-disubstituted hydantoins are not dealt with in this paper.

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