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4,5-DEHYDROPYRIMIDINES. I

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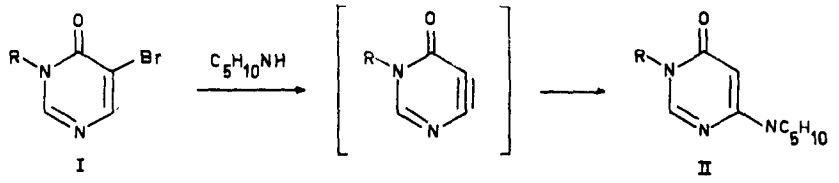
Much work has been done in recent years to extend the chemistry of benzyne to the field of N-heteroaromatic compounds [1-3]. Nevertheless, few results dealing with the occurence of 4,5-dehydropyrimidines have been reported [4-8]. In this connection, it seems worth while to mention an anomalous nucleophilic substitution reaction displayed by two 5-bromopyrimidines.

When 5-bromo-4-hydroxypyrimidine (I, R=H) [9] was refluxed for 4 hours in neat piperidine, the sole product that we could isolate, in low yield (33%), was 4-hydroxy-6-piperidinopyrimidine (II, R=H) (m.p.259-263° dec.)*. Paper



I II

chromatography of the reaction mixture in two solvent systems (dimethylformamide - aqueous ammonia 28% - isopropyl alcohol 25:10:65 [10] and n-butyl alcohol - water 90,8:9,2) reveals that the starting material is still present in large amounts. No isomeric 4-hydroxy-5-piperidinopyrimidine has so far been detected.

The structure of the rearranged product (II, R=H) was established from its N.M.R. spectrum (see table) and by comparison with a specimen prepared by the following route : 4-chloro-6-piperidinopyrimidine [11] was converted into 4-methoxy-6-piperidinopyrimidine (b.p.112-115°/1,5mm) which, on acid hydrolysis,

*Analytical values for all the compounds described in this paper are consistent with the indicated structures.

TABLE.

Compounds	Solvent	δ	H	Multiplicity	J(c/s)	Assignment
I (R=H)	DMSO	~ 4,58		broad band		>NH
		8,23	1	doublet	$J_{2,6}$ ±0,2	H_2 *
		8,33	1	doublet		H_6 *
II (R=H)	DMSO	5,22	1	doublet	$J_{2,5}$ 0,5	H_5
		7,87	1	doublet		H_2
I ($R=CH_3$)	$DCCl_3$	3,80	3	singlet		>N-CH_3
		8,10	1	broadened singlet		H_2 *
		8,21	1	broadened singlet		H_6 *
II ($R=CH_3$)	$DCCl_3$	1,62	6	broad band		3 CH_2
		3,41	3	singlet		>N-CH_3
		3,52	4	broad band		2 CH_2
		5,43	1	doublet	$J_{2,5}$ ±0,3	H_5
		7,82	1	doublet		H_2
IV	$DCCl_3$	6,49	1	quartet	$J_{3;5'}$ 0,7	$H_{4'}$
		6,78	1	doublet	$J_{4;5'}$ 1,8	$H_{3'}$
		7,47	4	multiplet	$J_{3;4'}$ 3,5	$H_{5'}$ (δ 7,53) H_m and H_p of the C_6H_5 group
		8,47	2	multiplet		H_o of the C_6H_5 group
		9,03	2	singlet		H_4 and H_6

All N.M.R. spectra were measured at 60 Mc.. Chemical shifts are expressed in p.p.m. downfield from internal tetramethylsilane.

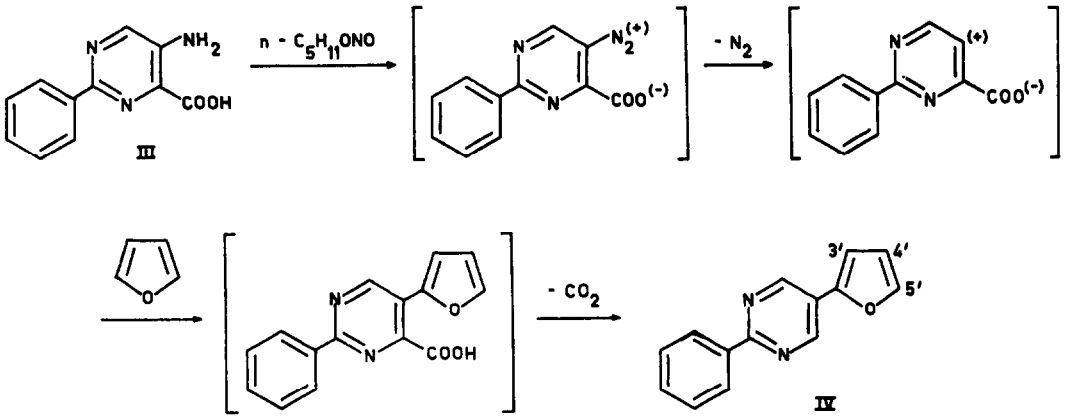
* These assignments are based on the width of the signals, assuming that the broader line arises from the proton in position 2.

gave 4-hydroxy-6-piperidinopyrimidine (II, R=H).

5-Bromo-4-hydroxy-6-methylpyrimidine [12] is completely inert under the same experimental conditions. This result provides good evidence that the former reaction proceeds via an elimination - addition mechanism involving a 4,5-dehydropyrimidine intermediate.

On the other hand, 5-bromo-3,4-dihydro-3-methyl-4-pyrimidinone (I, $R=CH_3$) [13] (m.p.152-154°), obtained by bromination of 3,4-dihydro-3-methyl-4-pyrimidinone [14], reacts easily with piperidine. The 6-piperidino-compound II ($R=CH_3$) (m.p.166-168°) was isolated in yields up to 62%. Its structure was deduced from its N.M.R. spectrum (see table).

In an other set of experiments, we have tried to produce a 4,5-dehydropyrimidine intermediate according to the method of Friedman and Logullo [15] 5-Amino-2-phenyl-4-pyrimidine-carboxylic acid (III) [16] was thus prepared by a modified procedure. This derivative was treated with n-amyl nitrite in dioxane and the mixture refluxed in the presence of a large excess of furan. All attemps to characterise the expected adduct, 5,8-endoxy-5,8-dihydro-2-phenylquinazoline, have so far been unsuccessful. However, we have isolated, in 13,5% yield, an isomeric product which was identified from its N.M.R. spectrum (see table) and mass spectrum (M^+ 222) as 5-(2-furyl)-2-phenylpyrimidine (IV) (m.p.153-154°). A likely explanation for the formation of this compound appears to be the following :



This scheme is reminiscent of a modified Gomberg synthesis of 2-arylfurans described by Johnson [17].

A detailed account of our work will be published at a later date.

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