On the Reaction of 5-Aminopyrimidine with Diazonium Salts (1,2)

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Received October 31, 1980

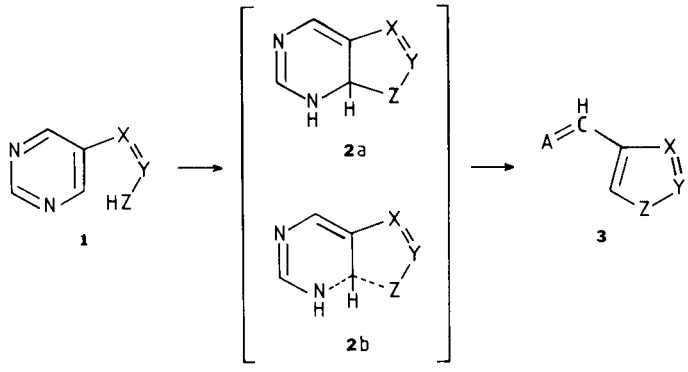
The reaction of 5-aminopyrimidine with benzenediazonium chloride, *p*-methylbenzenediazonium chloride and *p*-bromobenzenediazonium chloride is described. The reaction leads to a mixture of compounds, *i.e.* 1-aryl-3-(pyrimidin-5-yl)triazene (**6**), 5-amino-4-aryl-6-arylazopyrimidine (**7**) and 4-aryl-6-arylazo-5-hydroxypyrimidine (**8**). The yields are found to be strongly dependent on the substituent present in the diazonium salt. Attempts to rearrange 1-(*p*-bromophenyl)-3-(pyrimidin-5-yl)triazene (**6c**) under basic and acidic conditions into a 1,2,3-triazole derivative failed.

J. Heterocyclic Chem., 18, 1639 (1981).

Introduction and Results.

Ring interconversion of heterocycles is well described for five-membered nitrogen-containing rings (3). Rearrangements of the 5-substituted pyrimidine derivative (**1**) into the five-membered heterocycle (**3**) have also been found: the formation of pyrazoles (4,5) from **1** (X=Y-ZH : -CH=N-NH_2), isoxazoles (4) from **1** (X=Y-ZH : -CH=N-OH) and imidazoles (6) from **1** (X=Y-ZH : -N=CH-NH_2).

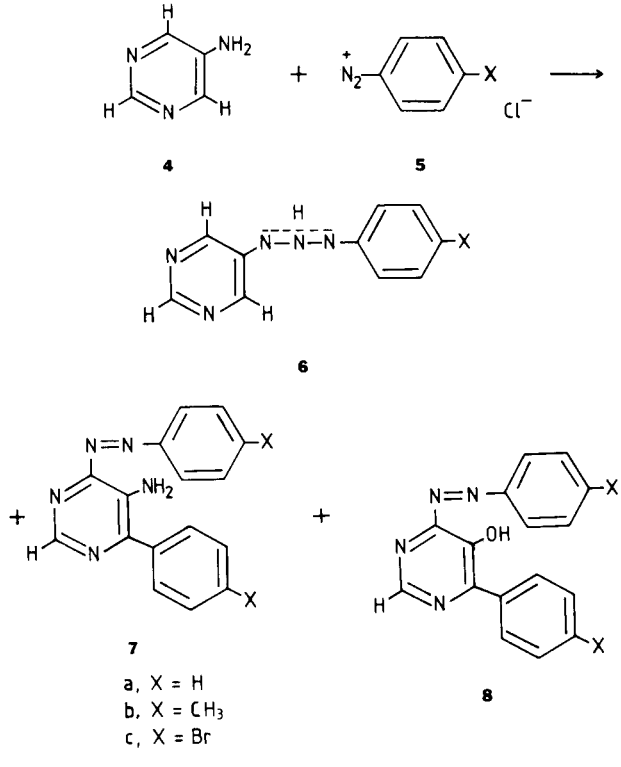
Scheme 1



In the rearrangement **1**→**3** a bicyclic intermediate **2** can be suggested as intermediate (7) although an intermediary step in which bond formation and bond breaking occur "simultaneously" cannot be excluded (6,8). Attempts to isolate bicyclic intermediate **2a** met with little success, probably due to the fact that aromatization of **2**→**3** is a low-energy-requiring step and thus easily takes place.

In this paper we describe the preparation of 1-aryl-3-(pyrimidin-5-yl)triazene (**1**, X=Y-ZH : -N=N-NH-C_6H_4-*p*X) and our unsuccessful attempts to rearrange this compound into a 4-substituted *N*-aryl-1,2,3-triazole. On reacting 5-aminopyrimidine (**4**) with the three diazonium salts **5a** (X = H), **5b** (X = CH_3) and **5c** (X = Br) in aqueous acid buffered with sodium acetate, we observed that in the reaction of **4** with **5c** 1-(*p*-bromophenyl)-3-(pyrimidin-5-yl)-triazene (**6c**) was obtained in a reasonable yield (63%), that with **5b** no triazene was formed and that with **5a** only in a small yield (2%) the triazene **6a** was yielded (see Table I). Furthermore it was found that in these three reactions two additional products (although in varying yields) were formed; they were identified as 5-amino-4-*p*-X-phenyl-6-*p*-X-phenylazopyrimidine (**7a**, **7b** and **7c**) and 5-hydroxy-4-*p*-X-phenyl-6-*p*-X-phenylazopyrimidine (**8a**, **8b** and **8c**).

Scheme 2



Structure Identification.

We will describe in more detail the structure assignments of the *p*-bromo compounds **6c**, **7c** and **8c**. The structure of the compounds **6a**, **7a**, **7b**, **8a** and **8b** were established similarly. All physical data supporting

the structures are collected in Table I.

The mass spectrum of **6c** showed in the parent peak and in several fragmentation peaks the presence of one bromine atom. The exact mass measurements and the microanalytical data indicate the molecular formula $C_{10}H_8BrN_5$. That in this compound the pyrimidine positions 2,4 and 6 are unsubstituted was proved by ^{1}H-nmr spectroscopy, showing a 2:1 ratio of the H-(4,6) singlet (δ 8.82) and the H-2 singlet (δ 8.92).

Mass spectrometry of the compound, being assigned structure **7c**, indicated the presence of two bromine atoms. Thus the compound must contain two phenyl groups. Exact mass measurement and micronalysis prove the molecular formula $C_{16}H_{11}Br_2N_5$, supporting the presence of two *p*-bromophenyl groups. In the low field region of the ^{1}H-nmr spectrum of **7c** one singlet at δ 8.62 was observed besides the phenylmultiplets at δ 7.4-7.9. This singlet was ascribed to H-2 of the pyrimidine ring. That this assignment was correct was confirmed by the ^{13}C-nmr coupled spectrum of **7b** (X = CH_3), showing a doublet at δ 148.0 with a coupling constant ^1J (C-H) of 206.1 Hz, being characteristic for coupling between hydrogen and the carbon atom at position 2 of the pyrimidine ring (9). Moreover in the ^{13}C-nmr spectrum of **7b** (X = CH_3) in the region of δ 21-22 two different methyl groups were found, indicating again the presence of two aryl groups in compound **7**. The presence of the amino group in **7c** was proved by the broad singlet around δ 5.8-5.9. Microanalysis and exact mass measurement of **8c** show the molecular formula $C_{16}H_{10}Br_2N_4O$. The ^{1}H-nmr spectrum is nearly identical to that of **7c** showing in addition to the phenyl multiplets the low yield singlet (δ 8.95). We do not observe a C=O stretching frequency in the ir spectrum leading to the conclusion that the position 5 and not position 4 or 6 of the pyrimidine ring is occupied by the hydroxy group.

Attempts at Rearrangements.

Several attempts were made to convert the triazene **6c** into a 1,2,3-triazole derivative under various reaction conditions. We used the following solvents and reagents: ammonia/acetone, potassium hydroxide/ethanol, potassium hydroxide/xylene, potassium hydroxide/DMSO, hydrogen chloride/chloroform, hydrogen chloride/methanol, hydrogen chloride/water, phosphorus oxychloride/chloroform. Under reflux conditions all these attempts failed. Only small amounts of pyrimidine derivatives and benzene derivatives were isolated.

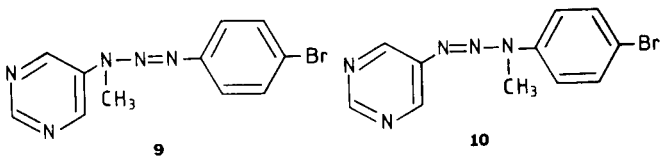
We also tried to rearrange both *N*-methyl derivatives **9** and **10**. They were prepared by reacting **6c** with methyl iodide in basic medium. Two isomers were formed, which could be separated by column chromatography. The isomer with the mp 149-150° was assigned structure **10** since treatment of this isomer with HCl/methanol gave *i.a.*, *N*-methyl-*p*-bromoaniline as proved by mass spectrometry. Acid treatment of the isomer with mp 142-144° (structure **9**) only showed the formation of some coloured decomposition products. Thus, in these reactions too, no indication was found for the formation of a triazole derivative.

Table I

Physical Data of the 1-Aryl-3-(pyrimidin-5-yl)triazenes (**6**), the 5-Amino-4-aryl-6-arylazopyrimidine (**7**) and 5-Hydroxy-4-aryl-6-arylazopyrimidine (**8**)

Compound	Formula	Mp (°C) Solvent for Crystallization	Yield %		Analytical Data C	H	N	NMR-Chemical Shifts (δ)
7a	$C_{16}H_{13}N_5$ (275.31)	130-133 ethanol	7.6	Calcd.	69.80	4.76	25.44	(deuteriochloroform) 8.70 s (H-2 pyrimidine), 7.2-8.0 m (phenyl groups), 5.9 s (NH_2 group)
				Found	69.85	4.72	24.95	
8a	$C_{16}H_{12}N_4O$ (276.29)	105-110 ethanol	7.0	Calcd.	69.55	4.38	20.28	(deuteriochloroform) 8.91 s (H-2 pyrimidine), 7.8-8.3 m (H-*ortho*, phenyl groups) and 7.3-7.6 m (H-*meta*, *para*, phenyl groups)
				Found	69.86	4.18	20.48	
7b	$C_{18}H_{17}N_5$ (303.36)	190-192 ethanol	10.2	Calcd.	71.27	5.65	23.08	(deuteriochloroform)8.65 s (H-2 pyrimidine), 7.2--8.0 pairs of doublets (phenyl groups), 5.9 s (NH group), 2.4 s (CH_3 groups)
				Found	71.27	5.60	23.07	
8b	$C_{18}H_{16}N_4O$ (304.35)	168-173 ethanol	9.6	Calcd.	71.03	5.30	18.41	(deuteriochloroform) 8.91 s (H-2 pyrimidine), 7.1-7.5, 7.7-8.2 pairs of doublets (phenyl groups) 2.4 s (CH_3 groups)
				Found	71.05	5.19	18.43	
6c	$C_{10}H_8BrN_5$ (278.01)	215 purified by acid precipitation	63.01	Calcd.	43.17	2.90	25.19	(DMSO) 8.92 s (H-2 pyrimidine), 8.82 s (H-4.6 pyrimidine), 7.3-7.7 (phenyl groups), 12.8 s (NH group)
				Found	43.25	2.68	25.46	
7c	$C_{16}H_{11}Br_2N_5$ (432.95)	191-193 ethanol	3.7	Calcd.	44.35	2.56	16.18	(deuteriochloroform) 8.62 s (H-2 pyrimidine), 7.4-7.9 (phenyl groups), 5.8 s (NH_2 group)
				Found	44.42	2.38	16.15	
8c	$C_{16}H_{10}Br_2N_4O$ (433.93)	240-242 chloroform	1.2	Calcd.	44.25	2.32	12.91	(deuteriochloroform) 8.95 s (H-2 pyrimidine), 7.4-8.2 pairs of doublets (phenyl groups)
				Found	44.01	2.14	13.15	

Scheme 3



9 10

EXPERIMENTAL

The Coupling Reaction.

To a solution of 1.04 g (0.012 mole) of 5-aminopyrimidine (**4**) and 5 g of sodium acetate in 50 ml of water and 3 ml of glacial acetic acid a solution of aryl diazonium chloride (prepared from 0.01 mole of the corresponding aryl amine and 0.690 g (0.01 mole) of sodium nitrite in 5.5 ml of 10% hydrochloric acid) was added with stirring below 5°. After addition the reaction mixture was allowed to stand for 12 hours, then extracted with chloroform and separated on the silica gel column. The reaction mixture obtained on reaction of **4** with **5c** was filtered. The crystalline product was refluxed with chloroform and crude **6c**, being insoluble in chloroform, was separated by filtration. All compounds were obtained in such quantities that microanalytical and nmr data could be obtained; except **6a** which was isolated in such an amount (2%) that only a melting point and an exact mass measurement could be made (mp 197-198°; theor. 199.0859; exp. 199.0858).

1-(*p*-Bromophenyl)-3-methyl-3-(pyrimidin-5-yl)triazine (**9**) and 3-(*p*-Bromophenyl)-3-methyl-1-(pyrimidin-5-yl)triazene (**10**).

One g (0.0036 mole) of triazene **6c** was dissolved in 10% methanolic potassium hydroxide, 2.5 g (0.015 mole) of methyliodide was added and this mixture was refluxed for 1 hour. The reaction products were separated by column chromatography. The yields, the physicochemical data and the solvent used for crystallization are given in Table II.

Acknowledgement.

We are indebted to Dr. C. A. Landheer for measuring the mass spectra and to Mr. A. van Veldhuizen for measuring the ^{13}C-nmr spectra.

REFERENCES AND NOTES

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(2) Part **87** on Pyrimidines from this Laboratory; for part **86** see reference 1.

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(9) J. B. Stothers, "Carbon-^{13}C-nmr Spectroscopy", Academic Press, New York, 1972, p. 343.

Table II

Physical Data of the *N*-Methyltriazenes **9** and **10**

Compound	Formula	Mp (°C) Solvent for Crystallization	Yield %	Analytical Data	C	H	NMR Chemical Shift (δ)
9	$C_{11}H_{10}BrN_5$ (292.03)	142-144 ethyl acetate	15.3	Calcd.	42.21	3.45	(deuteriochloroform 8.92 s (H-2 pyrimidine), 8.8 s
				Found	45.21	3.29	(H-4,6 pyrimidine), 7.43 s (phenyl group) 3.6 s (CH_3 group)
10	$C_{11}H_{10}BrN_5$ (292.03)	149-150 ethanol	16.1	Calcd.	45.21	3.45	(deuteriochloroform) 8.92 s (H-2 pyrimidine), 8.8 s
				Found	44.96	3.29	(H-4,6 pyrimidine), 7.1-7.6 pair of doublets (phenyl group), 3.6 s (CH_3 group)