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BROMINATION OF PYRIMIDINE IN THE GAS PHASE*

by
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Forty years ago it was found by one of us (d.H.) together with J.P.Wibaut, that bromination of gaseous pyridine at ~ 300°C leads to the formation of a mixture consisting mainly of 3-bromo- and 3,5-dibromopyridine, whereas at ~ 500°C 2-bromo- and 2,6-dibromopyridine are obtained in high yield together with some 2,4,6-tribromopyridine (1). This discovery was an incentive for examining halogenations of both arenes (2) and hetarenes (3) in the vapour phase with the purpose to elucidate the change of the reaction type when elevating the temperature. Thus far little work has been done on reactions of hetarenes other than pyridine and derivatives of this substance (4). A comparative investigation has now been started in this laboratory on gas phase brominations of a series of azahetarenes. In this paper some orientating experiments on the bromination of pyrimidine are described.

Preheated gaseous pyrimidine and bromine, diluted with nitrogen, were passed through a vertical glass tube (length 60 cm, diameter 2 cm) externally heated by a furnace. Reaction products were analysed quantitatively, applying GLC and identified spectrometrically or by comparison with authentic specimens.

Results obtained are summarized in the table.

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[*] XXVIIth Communication from this laboratory on derivatives of pyrimidine.

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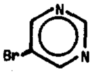
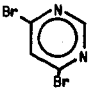
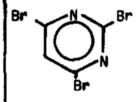
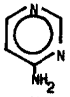
Temp.	Molar ratio $\frac{C_4H_4N_2}{Br_2}$	Contact sub-stance	Contact time (sec)	Products (%, calculated on the amount of pyrimidine introduced)				
				 I	 II	 III	 IV	 V
220°	1/1.5	---	80	10-15	5	---	---	10
220°	1/1.5	pumice	55	---	60	---	---	---
300°	1/1	---	70	15-20	5	---	---	15
300°	1/1.5	pumice	45	---	35-40	---	---	---
400°	1/1	---	60	15-20	10	---	---	15-20
400°	1/2	pumice	30	---	15-20	---	---	5-10
500°	1/1	---	50	---	---	3	---	3
500°	1/3	---	55	---	---	15-20	30-35	---

5-Bromopyrimidine (II, m.p. 73-74°C) was shown to be identical with an authentic specimen prepared as described by Bredereck et al. (5).

The structure of 4,6-dibromopyrimidine (III, m.p. 48-50°C) followed from the elemental analysis and its PMR-spectrum, showing singulets at 1.40 ppm (2-proton) and at 2.30 ppm (5-proton); reference TMS = 10 ppm.

2,4,6-Tribromopyrimidine (IV, m.p. 112-113°C) and 4-aminopyrimidine (V, m.p. 150-151°C) were found to be identical with authentic specimens (Cf. (6) and (7) respectively).

As in the bromination of pyridine two reaction types can be distinguished i.e. the formation of the bromo derivative in which bromine is attached to the least positively charged carbon atom (C_5), occurring at temperatures up to 300°C in the presence of a contact substance and the formation of derivatives in which bromine is bound to the more positively charged carbon atoms 2, 4 and 6, occurring in an empty tube.

There is an essential discrepancy, however, in the behaviour of pyridine and pyrimidine. By brominating pyridine in an empty tube at slightly elevated temperatures a mixture is obtained from which together with small amounts of β-substituted bromopyridines, 4-aminopyridine can be isolated. The last-mentioned substance results from the reaction of primarily formed 4-bromopyridine with pyridine, leading to N-(4-pyridyl)pyridinium bromide and subsequent decomposition of the last-mentioned compound when working up the reaction mixture in basic medium. At more elevated temperatures 2-bromo-, 2,6-dibromo- and some 2,4,6-tribromopyridine come forth, stable products being formed above 400°C in high yields.

Pyrimidine (I) is attacked in the empty tube mainly at position 4 (=6), yielding the presumably unstable 4-bromopyrimidine (VI). Analogously to what happens in the bromination of pyridine, VI is converted by pyrimidine (I) into N-(4-pyrimidyl)pyrimidinium bromide, from which compound in basic medium 4-aminopyrimidine (V) and ammonia are generated. V is formed in the whole temperature range investigated. Thus, also at high temperatures there is a preference for attack at C-4 (=6) which atom, in contrast with C_4 in pyridine, occupies an ortho as well as a para position towards a ring nitrogen atom. When at 500°C an excess of bromine is used, however, the rate of introduction of a second bromine atom into the nucleus of 4-bromopyrimidine (VI) surpasses that of its reaction with pyrimidine. Thus, in this case the stable brominated pyrimidines III and IV are obtained in fair yields. Still a considerable amount of pyrimidine changes into undefined products.

As for the conversion of pyrimidine (I) into 5-bromopyrimidine (II) this reaction requires, like the transformation of pyridine into β-substituted bromopyridines, the presence of a contact substance. It was established that II is transformed in an empty tube by bromine into less stable compounds again. The formation of ammonia and some 5-bromo-4-hydroxypyrimidine (m.p. 198-199°C) points to the initial generation of 4,5-dibromopyrimidine, probably being converted in a secondary process into a N-(pyrimidyl) pyrimidinium compound.

The investigation is being continued.

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