

Photoreactivity of Diazines. Part III.¹ Pyrimidines. Part XXXVIII.² Photoamination of Halogenopyrimidines

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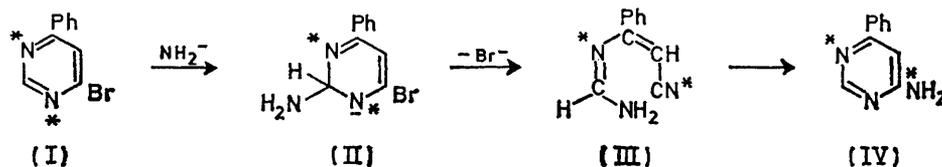
The hitherto unknown u.v. induced amination of 4-X-6-phenylpyrimidines (V; X = Cl, Br, or I) to give 4-amino-6-phenylpyrimidine (VI), using liquid ammonia as solvent and reactant, is described. The reactivity order is found to be I > Br > Cl. Evidence is presented that the photoamination does *not* occur according to an S_N(ANRORC) or an S_N(AE) mechanism. Since an inhibitory effect of the radical scavenger di-*t*-butyl nitroxide is observed in the photoamination, a reaction pathway involving a radical as intermediate is postulated.

THE conversion of 2- and 4-halogeno-6-phenylpyrimidines into the corresponding 2- or 4-amino-6-phenylpyrimidine by potassium amide in liquid ammonia clearly points to the occurrence of the novel S_N(ANRORC) mechanism (Addition of Nucleophile, Ring Opening, Ring Closure).³ An essential feature of this S_N(ANRORC) mechanism (Scheme 1) is the initial addition

of the amide ion to the unoccupied electron-deficient position, adjacent to the nitrogen, which in the case of 4-bromo-6-phenylpyrimidine (I) leads to the anionic intermediate (II). On release of bromide ion ring opening occurs yielding the rather unstable aminocynoaza-

butadiene (III) which is strongly inclined to give a fast ring closure into (IV). Support for this mechanism has been obtained by using the ¹⁵N-labelled pyrimidine (I), since in compound (IV) the ¹⁵N is found divided between the nitrogen of the ring and the amino-group.

Like bromobenzene,⁴ the 4-halogeno-6-phenylpyr-



SCHEME 1

imidines (V) are completely stable in liquid ammonia. However, on exposure of a solution of 4-chloro-6-phenylpyrimidine (V; R = Ph, X = Cl) in liquid ammonia for 5 h to u.v. light, 3% of 4-amino-6-phenylpyrimidine

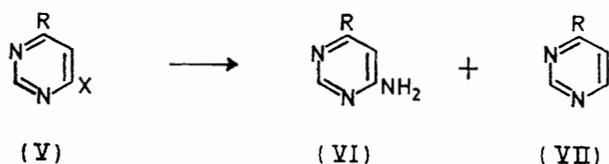
¹ Part II, R. A. F. Deeleman and H. C. van der Plas, *Rec. Trav. chim.*, 1973, **92**, 317.

² Part XXXVIII, E. A. Oostveen, H. C. van der Plas and H. Jongejan, *Rec. Trav. chim.*, in the press.

³ J. de Valk and H. C. van der Plas, *Rec. Trav. chim.* (a), 1971, **90**, 1239; (b) 1972, **91**, 1414; (c) A. P. Kroon and H. C. van der Plas, *ibid.*, 1973, **92**, 1020; (d) A. P. Kroon and H. C. van der Plas, *ibid.*, in the press.

⁴ R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, 1973, **38**, 1407.

(VI; R = Ph) is formed; 95% of the starting material could be recovered (see the Table). The 4-bromo- and



4-iodo-compounds (V; R = Ph, X = Br or I) reacted somewhat differently; the yield of the 4-amino compound (VI; R = Ph) is considerably increased, and both compounds also undergo dehalogenation leading to 4-phenylpyrimidine (VII; R = Ph) (see Table). It is evident from the yields of recovered substrates (V; R = Ph) that the 4-iodo-compound is the most reactive and the 4-chloro-compound the least reactive (I > Br > Cl). It is further established that (VI; R = Ph) is not formed by photoamination of (VII).

Reactions of 4-halogeno-6-R-pyrimidines (V) with liquid ammonia at -33° on exposure to u.v. light

Compound (V)	Recovered substrate (%)	4-NH ₂ -6-R-pyrimidine (VI) (%)	4-R-pyrimidine (VII) (%)
R = Ph, X = Cl	95	3	
R = Ph, X = Br	65	28	5
R = Ph, X = I		56	8
R = Bu ^t , X = Br		> 95	

An experiment with 4-bromo-6-t-butylpyrimidine (V; R = Bu^t, X = Br) indicated that the photoamination leads to a nearly quantitative yield of the 4-amino-compound (VI; R = Bu^t).

Considering the possible mechanism of the formation of the amino-compound (VI), we have established that in the photoamination of (V; R = Ph, X = Br) no heteroaryne-type intermediate, *i.e.* 4-phenyl-5,6-didehydropyrimidine (X) is involved; * on irradiation of a solution of 4-bromo-5-deuterio-6-phenylpyrimidine (VIII) (D-content 36.5%)[†] in liquid ammonia, the deuterium content at position 5 in the 4-amino-compound formed (IX) is the same as that in the starting substance, *i.e.* 36%.

The occurrence of a photo-stimulated S_N(ANRORC) mechanism as pictured in Scheme 1 for ground state reactions, can also be rejected; the 4-amino-compound (XI) obtained in the photoamination of [1(3)-¹⁵N]-4-bromo-6-phenylpyrimidine (I) still has all the ¹⁵N in the pyrimidine-ring.[‡]

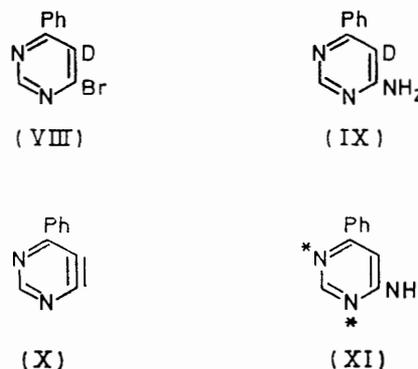
As it does not seem attractive to explain the light-

* If this were the case the addition of the amide ion to the 'aryne' bond would have to occur in one direction only. Theoretical calculations⁵ have made it clear that in an 'aryne' bond adjacent to the nitrogen (*e.g.* 2,3-didehydropyridine, 4,5-didehydropyrimidine) the addition of a nucleophile is strongly preferred at that carbon-atom which is adjacent to the nitrogen.
[†] The deuterium content was estimated by comparing the *M* + 1/*M* ratio of (VIII) with that of the unlabelled compound 4-bromo-6-phenylpyrimidine.

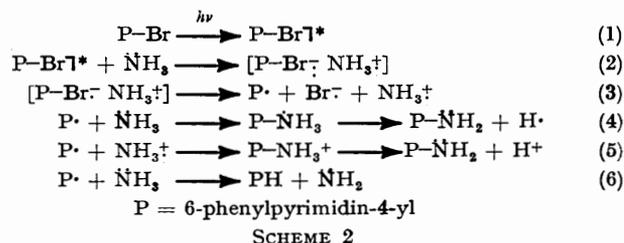
[‡] The method by which this can be established has been published previously.^{3a, b}

§ Preliminary e.s.r. measurements do indeed indicate that one or more radicals are involved in the photoamination.

induced amination only by a photo S_N(AE) mechanism we investigated the possible occurrence of a radical mechanism. Evidence that radicals are intermediates during the photoamination was obtained when the photoamination was carried out in the presence of di-*t*-butyl nitroxide, a radical scavenger.[§] In case of (V; R = Bu^t, X = Br), in the presence of di-*t*-butyl nitroxide the yield of the 4-amino-product (VI; R = Bu^t) dropped from >95 to 13%. A possible mechanism



which is most compatible with our observations is shown in Scheme 2.



The initiation step is an electron transfer from the lone pair of ammonia to the excited state of 4-bromo-6-phenylpyrimidine PBr[•]*; this leads to a charge-transfer complex (step 2). The formation of similar complexes during photoreduction with amines has been precedented.⁶ In this ion-pair complex the C-Br bond cleaves to generate a pyrimidinyl radical,⁷ which reacts further *via* a pyrimidinylamine radical [step (4)] {or possibly *via* a pyrimidinylammonium ion [step (5)]} to give 4-amino-6-phenylpyrimidine. The reaction of the pyrimidinyl radical P[•] with ammonia is very attractive since the ability of radicals to unite with nucleophiles to form radical ion intermediates⁸ is well-established, as is

⁵ W. Adam, A. Grimison, and R. Hoffmann, *J. Amer. Chem. Soc.*, 1969, **91**, 2590.

⁶ (a) S. G. Cohen and H. M. Chao, *J. Amer. Chem. Soc.*, 1968, **90**, 165; (b) S. G. Cohen and J. I. Cohen, *J. Phys. Chem.*, 1968, **72**, 3782; (c) S. G. Cohen, A. Parola, and G. H. Parsons, jun., *Chem. Rev.*, 1973, **73**, 144; (d) J. Nasielski, A. Kirsch-Demesmaeker, and R. Nasielski-Hinskens, *Tetrahedron*, 1972, **28**, 3767; (e) J. Nasielski and A. Kirsch-Demesmaeker, *Tetrahedron*, 1973, **29**, 3153.

⁷ Carbon-halogen bond fragmentation in radical anions has recently been discussed by K. Alwair and J. Grimshaw, *J.C.S. Perkin II*, 1973, (a) 1150; (b) 1811.

⁸ D. J. Myers, G. G. Stroebel, P. R. Ortiz de Montellano, and P. D. Gardner, *J. Amer. Chem. Soc.*, 1973, **95**, 5832; and references cited therein.

found in reactions with ethoxide,⁸ azide,⁸ amide,⁹ cyanomethanide,⁹ enolate,^{10,11} and carbanions.¹¹ Step (6) in which NH_3 reacts as a hydrogen atom donor accounts for the substantial amounts of 4-phenylpyrimidine being formed during the reaction.

That bromobenzene survives exposure to near u.v. light in liquid ammonia⁴ but that in contrast 4-bromopyrimidines are quite reactive can be understood, since azines in general show an enhanced electron affinity in comparison with arenes, owing to the increased electron deficiency of the aromatic ring containing nitrogen,¹ making step (2) a more favourable reaction.

EXPERIMENTAL

G.l.c. analyses were carried out on a Becker chromatograph (Delft, the Netherlands) using an r.s. column, length 100 cm, o.d. 3/16 in, containing OV-17 on Anakrom ABS 70—80, weight ratio 20:80. The measurements of the ¹⁵N-contents were carried out on an A.E.I. MS 902 mass spectrometer.

Preparation of Starting Materials.—4-Bromo,^{3a} 4-chloro,¹² and 4-iodo-6-phenylpyrimidine,^{3b} [1(3)-¹⁵N]-4-bromo-6-phenylpyrimidine,^{3a} 4-amino-6-phenylpyr-

imidine,¹³ 4-amino-6-t-butylpyrimidine,¹³ and di-t-butyl nitroxide⁴ were synthesized as described in the literature.

4-Bromo-6-t-butylpyrimidine.—6-t-Butylpyrimidin-4-one (3 g, 0.020 mmol) was heated with phosphoryl bromide (15 g) at 100° for 3 h. After cooling, the mixture was poured on crushed ice and the solution obtained was extracted twice with ether. The ethereal extracts were washed with an aqueous sodium hydroxide solution and dried (MgSO_4). The ether was removed and the residue was distilled under reduced pressure to give the *bromo-compound* (1.7 g, 40%), b.p. 97—98° at 12 mmHg (Found: C, 44.9; H, 4.9. $\text{C}_8\text{H}_{11}\text{BrN}_2$ requires C, 44.7; H, 5.15%).

Irradiation Experiments.—The irradiations were carried out in a quartz glass reaction vessel containing a solution (250 ml) of the 4-halogenopyrimidine (0.004 mol) in boiling liquid ammonia (−33°), with a high pressure mercury arc lamp (Hanau TQ 150) as internal light source. After 5 h the liquid ammonia was evaporated off and the yields of reaction products in the residue were determined by g.l.c. The structure of the products was confirmed by comparison of their i.r. spectra with those of authentic specimens.

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⁹ (a) J. K. Kim and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1970, **92**, 7463; (b) J. K. Kim and J. F. Bunnett, *ibid.*, p. 7464; (c) R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, 1972, **37**, 3570.
¹⁰ R. A. Rossi and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1972, **94**, 683.

¹¹ R. A. Rossi and J. F. Bunnett, *J. Org. Chem.*, 1973, **38**, 3020.

¹² H. C. van der Plas and G. Geurtsen, *Tetrahedron Letters*, 1964, 2093.

¹³ H. C. van der Plas, *Rec. Trav. chim.*, 1965, **84**, 1101.