

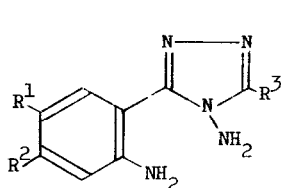
FORMATION OF NOVEL 1,5-DIAMINO-1H-[1,2,4]TRIAZOLO[1,5-c] QUINAZOLINIUM BROMIDES

R. A. BOWIE and D. A. THOMASON  
Imperial Chemical Industries Limited, Pharmaceuticals Division, Alderley Park,  
Macclesfield, Cheshire, SK10 4TG

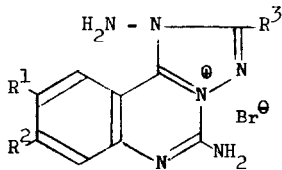
and J. A. J. JARVIS  
Imperial Chemical Industries Limited, Corporate Laboratory, P.O. Box No. 11,  
The Heath, Runcorn, Cheshire

(Received in UK 19 March 1973; accepted for publication 28 March 1973)

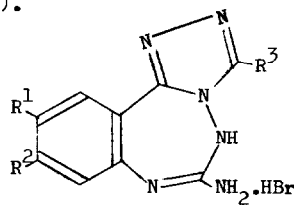
4-Chloroquinazolines re-arrange with hydrazine hydrate to yield 4-amino-4H-1,2,4-triazoles<sup>1</sup> (1a-k). Cyanogen bromide reacts with ortho-phenylene diamine to give 2-aminobenzimidazoles<sup>2</sup> and its reaction with the triazoles (1a-k) in ethanol at 70 - 80°C. gave in good yield (60 - 90%) products which, by analogy to the condensation of the triazoles with trialkylorthoesters<sup>1</sup>, would be expected to have been the 6-amino-5H-1,2,4-triazolo[4,3-d][1,3,4]benzotriazepines hydrobromides (3a-k). However, we provide evidence that the products are the isomeric 1,5-diamino-1H-1,2,4-triazolo[1,5-c] quinazolinium bromides (2a-k).



(1)



(2)



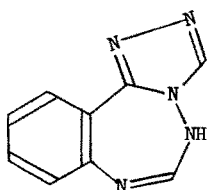
(3)

	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
(a)	H	H	H
(b)	H	H	Me
(c)	H	H	Et
(d)	H	H	Pr <sup>n</sup>

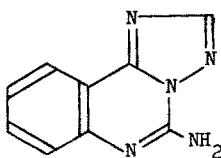
	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
(e)	H	H	Pr <sup>i</sup>
(f)	H	H	CH <sub>2</sub> Ph
(g)	H	H	Ph
(h)	Cl	H	H

	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
(i)	Me	H	H
(j)	H	Cl	H
(k)	H	Cl	Me

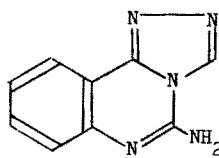
Support for structures (2a-k) came when compound (2a) m.p. 227°C., was found to have a high basic strength ( $pK_a > 11$ ) in agreement with the proposed quaternary structure whilst 5H-1,2,4-triazolo[4,3-d][1,3,4] benzotriazepine (4) had only a  $pK_a$  of 1.7. Even with an amino group in position 6 (3a), the increase in basicity would only be in the region of 2 - 4 units<sup>3</sup>. Also, compound (2a) deaminated in nitrous acid to yield 5-amino-1,2,4-triazolo[1,5-c] quinazoline (5) and not (6) in agreement with the deamination of quaternary 4-amino-1,2,4-triazole salts to 1,2,4-triazoles under nitrous acid conditions<sup>4</sup>. The mass spectrum of (2a), apart from its mass ion at 281, was identical to that of (5). Compound (5) was synthesised from (7) and cyanogen bromide; NMR data differentiated between (5) and the isomeric (6).



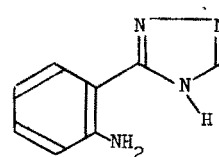
(4)



(5)



(6)



(7)

The precise molecular configuration of (2a) was finally established using X-ray crystallographic techniques which proved conclusively that compound (2a) has the structure shown and not (3a).

Satisfactory analyses and spectral data were obtained for all new compounds.

#### References

1. R. A. Bowie and D. A. Thomason, *J.C.S. Perkin I*, 1972, 1842.
2. N. J. Leonard, D. Y. Curtin and K. M. Beck, *J. Amer. Chem. Soc.*, 1947, **69**, 2459.
3. See D. D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution", Butterworths, London, 1965, for typical heterocycle and 2-aminoheterocycle  $pK_a$  values.
4. H.G.O. Becker, H. Boettcher, T. Roethling and H. J. Timpe, *Wiss. A. Tech. Hochschule Chem. Leuna-Merseburg*, 1966, **8**, 22; *Chem. Abs.*, 1966, **64**, 19596d.