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NITROGEN BRIDGEHEAD COMPOUNDS. PART 60[1]. UNUSUAL AMINATION WITH SODIUM AZIDE.

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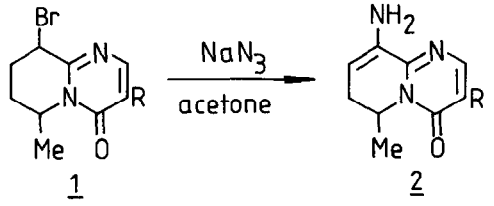
Summary: 9-Bromo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-ones react with sodium azide to afford 9-amino-6,7-dihydroanalogues. A mechanism involving a tricyclic tetrazine intermediate formed by neighbouring-group participation is suggested.

In our earlier publications we have described some interesting nucleophilic substitutions of 9-bromo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidin-4-ones[1-4]. Simple anions (I^-, CN^-, ^-OAc, RS^-, SCN^-) behaved as usual[1,4], but azide ion gave an unexpected result. If compounds 1a,b were allowed to react in acetone with an equimolar amount of sodium azide at 25 °C soon gas evolution occured and the mixture assumed a purple colour. The major component of the reaction could be isolated by filtering the precipitated product (2a,b) and its structure was identified by IR and NMR spectra.



1 2

2a M.p.: 162-163 °C (EtOH); Yield 42%
2b M.p.: 180-182 °C (EtOH); Yield 55%
a, R = $CONH_2$; b, R = CN

The IR spectra of compounds 2a,b revealed the lack of the N_3 band and the appearance of a NH_2 band, while the ^1H and ^{13}C NMR spectra indicated the presence of a double bond between C-8 and C-9 atoms.

To explain the reaction pathway we first assumed an azide intermediate (3) transformed into a nitrene by the loss of nitrogen. (It is worth noting that no record in the literature is available on such a facile thermal decomposition of azides). The nitrene intermediate could be stabilized by intramolecular H-9 insertion affording the imine tautomer of 2 (2').

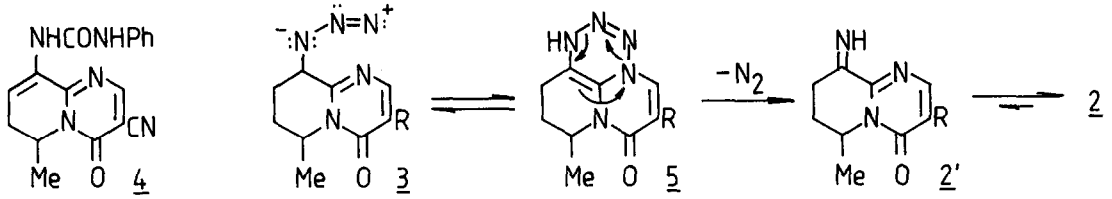
^{1}H NMR Chemical shifts — Jeol FX-100 — δ(TMS) = 0 ppm

Comp.	H-2	H-6	H-7$_{eq}$	H-7$_{ax}$	H-8	6-Me	NH$_2$	Solvent
2a	8.83s	5.22m	2.38ddd	2.86ddd	5.68dd	1.38d		$CDCl_3$ + CD_3OD
$^2J_{7,7}$=18.0; $^3J_{7eq,8}$=7.0; $^3J_{6,7eq}$=1.5; $^3J_{6,7ax}$=7.0; $^3J_{7ax,8}$=3.0; $^4J_{6,8}$=1.4Hz								
2b	8.28s	5.18m	2.32ddd	2.82ddd	5.51m	1.37d	3.95br	$CDCl_3$
$^2J_{7,7}$=18.0; $^3J_{7eq,8}$=7.1; $^3J_{6,7eq}$=1.1; $^3J_{6,7ax}$=7.1; $^3J_{7ax,8}$=3.2; $^4J_{6,8}$=1.3Hz								

^{13}C NMR Chemical shifts — Jeol FX-100 — $CDCl_3$ — δ(TMS) = 0 ppm

Comp.	C-2	C-3	C-4	C-6	C-7	C-8	C-9	C-9a	6-Me	3-CN
2b	159.0	101.6	157.7	46.0	26.9	105.9	133.8	153.6	17.7	113.9

Trapping of 3b with 1,3-dipolarophiles e.g. ethyl propiolate, phenylacetylene failed and although phenyl isocyanate gave a new compound (4)[5], this was formed by the acylation of 2b.



Another, perhaps more reasonable route can give acceptable explanation for the easy decomposition of 2 without assuming the existence of nitrene intermediate. We suggest the cyclization of the 9-azido group with C-9a and N-1 double bond forming the ring tautomer, a dihydro-1,2,3,4-tetrazine (5), which is unstable and loses nitrogen to give 2'. As to the 2'⇌2 equilibrium it is entirely shifted to the enamine form (2) as we have earlier observed with the similar 9-arylamino-6,7-dihydro-4H-pyrido[1,2-a]pyrimidin-4-ones[6].

REFERENCES and NOTES: 1. I. Bitter, B. Pete, G. Tóth, I. Hermecz, and Z. Mészáros, submitted for publication to Heterocycles. 2. I. Hermecz et.al, J. Med. Chem. 1983, 26, 1494. 3. T. Breining, I. Hermecz, B. Podányi, Z. Mészáros, and G. Tóth, J. Chem. Soc., Perkin Trans. 1, 1985, 1015. 4. I. Bitter, B. Pete, G. Tóth, I. Hermecz, and Z. Mészáros: Heterocycles in press. 5. Compound 4 is prepared by combining equimolar amounts of 1b, NaN_3 and PhNCO in dry acetone at 25 °C. Yield 45%. M.p.: 118-120 °C (EtOH). ^{1}H NMR ($CDCl_3$) Me 1.27d; EtO 1.32t, 4.32q; CH_2-7 2.3-3.0m; H-8 5.74dd (J=7.5 and 3.0Hz) H-6 5.20m; Ph 7.0-7.5m; NH 7.89s, and 8.29s; H-2 8.48s. 6. T. Breining, I. Hermecz, B. Podányi, and J. Sessi, J. Heterocyclic Chem. in press.

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