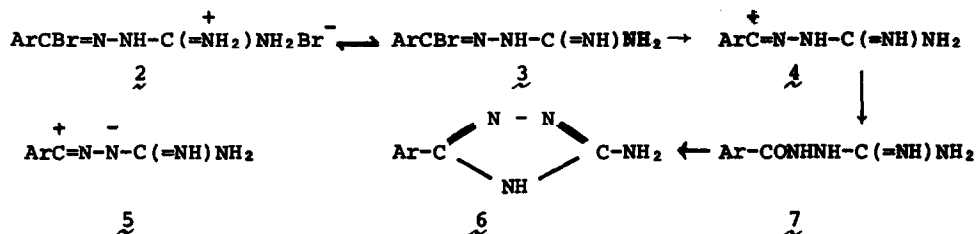


THE STEPWISE CYCLIZATION OF NOVEL N-AMIDINO HYDRAZONYL BROMIDES TO AMINO-TRIAZOLES.

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The reaction of arylidene arylhydrazines (ArCH=N-NH-Y, 1) with bromine can lead to hydrazonyl bromides (when Y is Ar)¹, or perbromides of 1 (when Y is CONMe₂)² or directly to ring closure products (when Y is CONH₂,^{3a} or CSNHR^{1b} or COAr^{3c}). We have now found that even when Y is a good nucleophile (-C(=NH)NH₂) it is possible to isolate the corresponding hydrazonyl bromides (2, see Table), stabilized as hydrobromide salts. As well as being the first group of acyl hydrazonyl bromides prepared in this way, these hydrazonyl bromides are solvolytically the most reactive yet examined.



On hydrolysis the bromides 2 were rapidly and smoothly converted to aroylamino-guanidine hydrobromides (7.HBr) (Table). Although complete within the time of mixing in water at 25°, the conversion of 2 to 7 could be studied in 3:1 dioxan water in acid solution. Over the pH range 1 to 3, the observed rate of hydrolysis of 2 (Ar = p-BrC₆H₄) increased with decreasing hydrogen ion concentration (such that a plot of log k_{obs} vs. pH was linear with a slope of +1.0). At pH 3, t_{1/2} for this compound was ca. 5s.

Under these reaction conditions the hydrazonyl bromides are present largely as the conjugate acids (2) since the free amidino compounds (3) are moderately strong bases. Thus the pK_a of the corresponding hydrazone (1, Ar = p-BrC₆H₄, Y = C(=NH₂)NH₂) which was used as a model for 2) is 8.72 in water (and 8.60 in 3:1 dioxan water). Assuming that the free base 3 is the reactive species (consistent with the observed pH-rate profile) a rate constant of ca. 10⁴ s⁻¹ can be calculated for the conversion of the free base, 3 to 7 in 3:1 dioxan-water. Such a rapid rate of reaction must reflect the efficiency of the neighbouring amidino group in stabilizing the azo-carbonium ion species 4.

TABLE. The hydrazoneyl bromide salts (2, Ar = 4-XC₆H₄) and their hydrolysis products (7.HBr, Ar = 4-XC₆H₄).

Substituent X	MeO	Me	Pr ⁱ	H	Cl	Br
Compounds <u>2</u> ^a (M.p./°C)	201-202 ^o	231-232	171-173	191-192	248-250	249-250
Compounds <u>7</u> .HBr (M.p./°C):	251-252	270	264-265	250-251	274	276

^a Prepared in >90% yield by reaction of 1 (Y=C(=NH)NH₂) with two equivalents of bromine in glacial acetic acid.

The involvement of the stabilized carbonium ion 4 is supported by the observed large increase in hydrolysis rate when the water content of the solvent was increased (k_{obs} increases 7-fold in 1:1 dioxan-water). The intermediate carbonium ion is also highly selective since the addition of bromide ion (at constant ionic strength) causes a rate depression such that a plot of $1/k_{obs}$ vs. $\{Br^-\}$ is linear; at $\{Br^-\} = 2 \times 10^{-2}M$ the back reaction of 4 with bromide ion reduces the overall rate of conversion of 3 to 7 by 100-fold.

Even at high pH, the direct cyclization of 3 to 6 does not occur. This is surprising since base catalysed dehydrohalogenation of 3 giving the 1,3-dipolar ion species 5 (which is characteristic of hydrazoneyl halides)^b would appear to provide an efficient direct route to 6; presumably the rapidity of the carbonium ion pathway (to form 7) is such that it dominates over the entire pH range.

The conversion of the hydrazides 7 to the aminotriazoles 6 does occur in aqueous solution, but at elevated temperatures, thus providing an indirect route from 3 to 6. In this case also the free base species alone is reactive, since the rate of conversion of 7 to 6 is pH independent at pH >9.5 and decreases rapidly as the pH is lowered below 8 (pK_a of 7) is 8.36); the rate of cyclization (measured at 75° or 90°) is relatively insensitive to the nature of the substituent present in Ar (Hammett $\rho = +0.44$).

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