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A NEW REACTIVE GROUP OF HALIDES - AMINOHYDRAZIDIC BROMIDES

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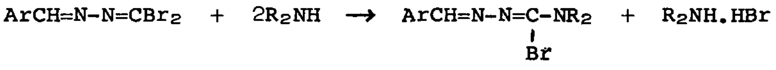
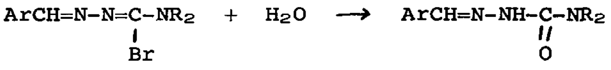
Hydrazidic halides which are very useful synthetic intermediates (e.g. in 1,3-dipolar additions) have their utility limited by their general methods of preparation, namely halogenation of an aldehydic hydrazone or reaction of a hydrazide with a phosphorus pentahalide. We now report a third route to such systems and describe the synthesis of the first of new classes of compounds derived in this way, namely aminohydrazidic halides.

We have found that isocyanogen dibromides (I) (1) react with secondary amines in benzene solution to yield (2) aminohydrazidic bromides. (II). The rate of this addition-elimination process depends upon the steric requirements of the amine - morpholine and piperidine reacting exothermically and rapidly at room temperature while the sterically less favoured amines such as dimethyl and diethylamine reacted only after the reaction mixture had been maintained at 75°C for one hour.



$$\mathrm{ArCH{=}N{-}N{=}CBr_2} + \mathrm{2R_2NH} \longrightarrow \mathrm{ArCH{=}N{-}N{=}}\underset{\mathrm{Br}}{\underset{|}{\mathrm{C}}}\mathrm{{-}NR_2} + \mathrm{R_2NH.HBr}$$

I II



$$\mathrm{ArCH{=}N{-}N{=}}\underset{\mathrm{Br}}{\underset{|}{\mathrm{C}}}\mathrm{{-}NR_2} + \mathrm{H_2O} \longrightarrow \mathrm{ArCH{=}N{-}NH{-}}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{{-}NR_2}$$

II III

The hydrolysis of compounds (II) in dioxan-water formed the 4,4-disubstituted semicarbazones (III) in good yield and this reaction constitutes a useful route to these materials. We have examined the rates of such hydrolyses in aqueous dioxan (data summarized in Table I). A Bronsted-type plot (i.e. of log k_ψ , hydrolysis rate-constant, vs. pKa of the amine group) showed a rectilinear relationship ($\beta = 0.4$, $r = 0.99$) indicating the dependence of the solvolysis rate-constant upon the proton basicity of the amine group.

A similar result was obtained when a Taft plot of log k_ψ vs. $\Sigma\sigma^*$ for the amine groups was made with a ρ^* of -0.97 (r = 0.98). The ρ^* for the protonation of the analogous amines is -3.23 (3). Both of these results are consistent with the involvement of an amine stabilised carbonium ion (IV) in

$$\mathrm{ArCH{=}N{-}N{=}\underset{+}{C}{-}NR_2} \longleftrightarrow \mathrm{ArCH{=}N{-}\underset{+}{N}{\equiv}C{-}NR_2} \longleftrightarrow \mathrm{ArCH{=}N{-}N{=}C{=}\underset{+}{N}R_2}$$

IVa IVb IVc

the solvolyses; with the comparatively small ρ^* value (compared to protonation) suggesting the form IVc cannot play a predominant role.

Table I

Data for Aminohydrazidic Bromides : $\mathrm{NO_2C_6H_4CH{=}N{-}N{=}\underset{Br}{C}{-}NR_2}$ and solvolysis in 80% aqueous dioxan at 25°C.

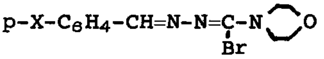
NR_2	Substrate m.p. °C	HNR_2pKa	$\Sigma\sigma^*$	Solvoly.rate 10^4k.sec.$^{-1a}$	Product m.p. °C
morpholine	183	8.36	1.16	2.85	179
benzylmethyl	111	9.58	0.69	5.00	113
diethyl	103	10.98	0.31	18.00	146
di-n-propyl	95	11.00	0.25	25.00	123
di-iso-propyl	94	11.05	0.15	26.91	125
piperidine	133	11.22	0.35	32.92	170

[a] run 3-4 times, precision ± 2%

We examined briefly, using a range of binary dioxan-water mixtures (the dioxan content varying from 60 to 95 vol%), the sensitivity of the hydrolysis of a typical aminohydrazidic bromide (II, Ar = p-$NO_2C_6H_4$, NR_2 = $C_6H_5CH_2NCH_3$) to solvent variation. Applying the Grunwald-Winstein treatment to these data gave a solvent sensitivity parameter m, value of 0.81 (r = 0.991). This again is strongly suggestive of carbonium ion character in the transition state

Table II

Hydrolysis data for



$p\text{-}X\text{-}C_6H_4\text{-}CH{=}N\text{-}N{=}\underset{Br}{C}\text{-}N\;\;O$ (V)

in 80% aqueous dioxan at 25°C.

Substituent X	Substrate m.p. °C	σ	Solvolysis rate 10^4k sec^{-1}	Product m.p. °C
OCH_3	103	-0.268	9.5	168
H	127	0.0	5.7	136
Cl	137	+0.227	4.9	164
Br	145	+0.232	5.3	182
NO_2	183	+0.778	2.8	179

Finally we examined the attenuation effects achieved by the azavinyl (-C = N-) group. To do this we synthesised a series of aryl-substituted morpholino hydrazidic halides (V) and examined the rates of their solvolysis in 80% aqueous dioxan (Table II). These rate data correspond to a Hammett ρ of -0.4, r = 0.984. When these data were compared to the rate data for the solvolysis of a series of aryl formamidine halides ($ArN = C(Cl)NR_2$)(4), insertion of the azavinyl group reduced the ρ from -0.6 to -0.4, i.e. it reduced it by one - third. The corresponding vinyl insertion from C_6H_5COOH to $C_6H_5CH{=}CH\text{-}COOH$ (ρ from 1.0 to 0.46) reduced the ρ by more than 50%. This easier transmission of the azavinyl system is to be expected on spectroscopic evidence also (5).

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