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HYDRAZIDIC HALIDES, PART IV (1). THE SOLVOLYSES OF p-SUBSTITUTED BENZHYDRAZIDIC BROMIDES

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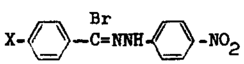
p-Substituted benzhydrazidic bromides (I) can be made by bromination of the appropriate arylidine p-nitrophenylhydrazones in acetic acid solution.


I


II

The reaction conditions used generally involved treating a suspension of the appropriate hydrazone (4 m.moles) in 100 ml. of glacial acetic acid with a solution of 8 m.moles of bromine in 20ml. of the same solvent (added slowly with vigorous stirring). The benzhydrazidic bromides (I) are formed in ca. 60% yields. More vigorous reaction conditions, in particular the use of a four-fold excess of bromine and higher reaction temperatures leads to the introduction of an additional bromine atom meta to the nitro group. The only previous report on the bromination of an arylidine p-nitrophenylhydrazone was that of Gibson (2). He used the benzaldehyde derivative and reported the formation of a dibromo compound.

Compounds of type I are readily hydrolysed to the corresponding aroyl hydrazides (II), after being refluxed in 50% aqueous dioxan solution. The yields and melting points of the appropriate compounds of types I and II are summarized in Table I.

Table I

Benzhydrazidic halides (I) and their hydrolysis products (II)

Substituent	(I)	m.p.°C	(II)	m.p.°C	Yield %	Reflux time hrs.
H	A	190	A	194(3)	96	1.5
CH_3	B	192	B	230	93	1
$(CH_3)_2CH$	C	167	C	225-227	90	1
Br	D	236-237	D	247-249	97	4
Cl	E	222-223	E	242-248	98	4
VA		172	VC	202	95	2

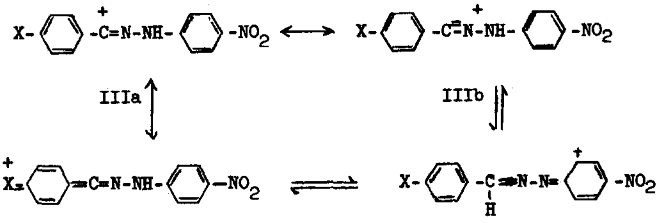
The rates of these hydrolytic reactions have been measured in aqueous dioxan, and these data, and the thermodynamic data they provide, are summarized in Table II.

Table II

Compound	$10^5 k$ sec^{-1} (50°)	$10^4 k$, sec^{-1} (75°)	$\Delta H^{\pm}$	$\Delta S^{\pm}$
IA	1.2	1.33	20.8	-16.6
IB	1.57	1.78	21	-15.3
IC	1.85	1.95	20.4	-16.2
ID	0.84	1.90	19.3	-21.0
IE	0.67	0.72	19.1	-19.7
VA	0.79	0.36	35.8	-41.0

These rate data correspond to a Hammett ρ of -0.93 ($r=0.984$, $s=0.036$) at 50°, and a ρ of -0.92 ($r = 0.987$, $s = 0.04$) at 75°. During the rate runs , the instantaneous values of the rate constants drifted downwards slowly and the rate constants cited above are derived by extrapolating the drifting values to 0% reaction. The negative $\Delta S^{\ddagger}$ values obtained while they imply an ordered transition state, are not unequivocally diagnostic of mechanism (4).

The negative sign of ρ implies the development of carbonium ion character during the hydrolysis. Ionization to a stabilized carbonium ion of type (III) may be involved.

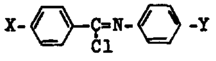


IIIc IIId

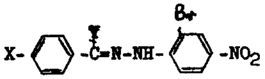
Stabilization of such carbonium ions can be achieved by delocalization of the positive charge onto the hydrazino nitrogen, and into the aryl ring (containing X), and via a tautomerization, even into the p-nitrophenyl ring, (as in IIId). Undoubtedly the low value of ρ represents an overall effective delocalization of charge in the transition state rather than poor development of carbonium ion character therein.

The kinetics of hydrolysis of diarylimidic halides (IV) have been studied recently (5) and from the data reported we calculate a ρ of -1.2 ($\pm$ 0.1), for the reaction response to variations in X, and a ρ of -0.7 ($\pm$ 0.3) for the response to variation of Y. The negative sign of ρ in both cases supports Ugi's postulate of an ionization mechanism.

With the hydrazidic halides the substituents in the N-aryl moiety again influence the overall rate of hydrolysis (and do so with a negative ρ). We have not sufficient data to calculate this value, but the rate of solvolysis of VA (compared with IA) does indicate a rate depression with the introduction of an additional electron attracting group into the N-aryl function. When the N-aryl group is replaced by a heterocyclic ring, the overall reaction may be effected in several ways. Thus, with N-tetrazolylhydrazidic halides, (1) the tetrazolyl moiety becomes involved with the carbonium ion centre and is itself opened thereby. The behaviour of other hetero rings is also of interest. Arylidene-2-pyridylhydrazones proved resistant to bromination in the hydrazidic position and no effects could be studied with that system (6). We have now prepared a hydrazidic halide of the 1,2,4-triazolyl type (VIB), as follows. The hydrazone (VIA) (7) was treated with bromine in the standard manner described earlier. From the reaction mixture a hydrobromide, m.p. 203-205° separated (in 87%) yield). This, on distribution between ether and water, afforded the triazolylhydrazidic bromide (VIB), m.p. 168-170°. When 1.4 m.moles of compound(VIB) was refluxed for six hours with 100 ml. of acetic acid in the presence of an equivalent of anhydrous sodium acetate, the bicyclic compound (VII) (8) m.p. 258°, was obtained in 5% yield as well as 15% 1,4-dibenzoylaminoguanidine and small quantities of other unidentified materials. The formation of VII in such very small yield suggests either relatively ineffective triazolyl anchimerism or that, unlike the tetrazole ring, the 1,2,4-triazole moiety is a poor competitor (compared to solvent etc.) for a nearby carbonium ion centre. The relative reactivities of the tetrazolyl, triazolyl, and aryl hydrazidic bromides are in the order : tetra zolyl,>triazolyl > p-nitrophenyl, with the overall rate differences being of the order of a factor of 10.



IV



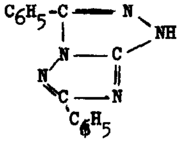
V,A, X = H, Y = Br

B X = H, Y = OR

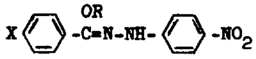
C X = H, Y = OH

VI, A, X=H

B, X=Br



VII



VIII

When the solvolyses of compounds of type I and type (VA) are effected in 95% alcohol buffered with one equivalent of sodium acetate, under reflux conditions, a new class of compounds, the hydrazidic ethers (VIII) and (VB) are formed.

Table III summarizes the yields and melting points of these materials. These ethers are cleaved by acids. Thus, when 1.3 m.moles of compound V (X=H Y=OC_2H_5) is refluxed in 100 ml. of 95% ethanol in the presence of 1.3 m.moles of hydrobromic acid for three hours, work-up yielded 25% of the corresponding hydrazide

VC, 10% benzoic acid and 35% of 1,1-diethyl-2-(2'-bromo-4'-nitrophenylhydrazine. The hydrazidic ethers are however more stable than the comparable imidic compounds.

Table III

Hydrazidic Ethers

Compound	m.p.°C	Yield	Reflux time in hours
VIII (X=H, R=C_2H_5)	182°	47	1.5
VIII (X=Br, R=C_2H_5)	181°	61	2.0
V (X=H), Y=OC_2H_5	146-147°	65	1.5
V (X=H, Y= OCH_3)	125-126°	15	1.5
V (X=H, Y=OC_3H_7)	77-78°	56	1.5
V (X=Cl, Y= OC_2H_5)	190°	73	2.5
V (X=$(CH_3)_2CH$, Y=OC_2H_5)	60°	51	1.0

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REFERENCES

1. The papers, F.L.Scott, and N.M. Holland, Proc.Chem.Soc., 106,(1962), F.L.Scott and D.A.Cronin, Tetrahedron Letters No.11, 715 (1963), F.L.Scott and D.A. Cronin, Chemistry and Industry, 1757 (1964) are to be regarded as parts I, II, and III in this series.
2. J.M. Burgess and M.S. Gibson, Tetrahedron, 18, 1001 (1962).

3. Reported m.p. 193°C. E. Hyde, *Ber.* **32**, 1811 (1899).

4. See L.L.Schalaeger and F.A.Long, *Advances in Physical-Organic Chemistry No. 1.* Edited by V.Gold, Academic Press, New York (1963).

5. I.Ugi,F.Beck and U.Fetzer, *Chem.Ber.* **95**, 126 (1962).

6. M.S.Gibson, *Tetrahedron* **19**, 1587 (1963).

7. This hydrazone, m.p. 262°C, was prepared by the method of E. Hoggarth, *J.Chem.Soc.* 612 (1950).

8. This material was prepared unambiguously by the oxidation of VIA with lead tetraacetate in glacial acetic acid using the method of J.D.Bower and F.P.Doyle, *J.Chem.Soc.* 727 (1957) see also H.Gemlen and G.Robisch *Liebigs Ann.Chem.* **660**, 148 (1962).