Synthesis and Solvolysis of Arylidene-1-methyl-1*H*-tetrazol-5-ylhydrazidic Bromides: A Route to 6-Aryl-3-methyl[1,2,4]triazolo[4,3-*d*]tetrazoles [1]

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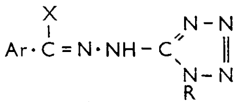
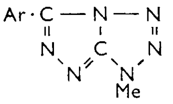
Bromination of arylidene-1-methyl-1*H*-tetrazol-5-ylhydrazines yielded the corresponding hydrazidic bromides. Solvolysis of these materials in aqueous solvents resulted in the formation of fused triazolotetrazoles. This reaction which involves the tetrazole ring as a nucleophile was, under appropriate conditions, competed against by the solvent water, or by added nucleophiles such as acetate, and it was eliminated when a highly nucleophilic solvent such as aniline was used. Some further reactions of the hydrazidic bromides are also discussed.

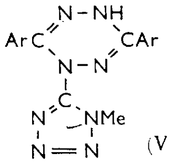
REACTION of substituted arylidene hydrazines with bromine in acetic acid results in the formation of hydrazidic halides. We have recently [2] examined the mechanism of this reaction using arylidene arylhydrazines and have demonstrated the importance therein of the nature of the substituent in the hydrazine moiety of the substrate. With arylidene heterocyclic hydrazines, the behaviour on treatment with bromine can be more complex. With a monoaza-ring system (pyridyl) hydrazidic bromination apparently failed, the product being an *N*-bromo-compound.[3] With a polyaza-system (tetrazolyl) we have previously encountered both hydrazidic substitution [4a] and under special conditions, aza-ring cleavage to form isocyanogen dibromides.[4b]



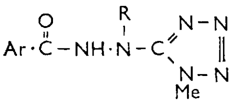
	X	R
(I) *	Br	Me
(II)	H	Me
(III)	H	Me, HBr
(IV)	Br	H
(VIII)	NHPh	Me
(X)	OAc	Me



(V)

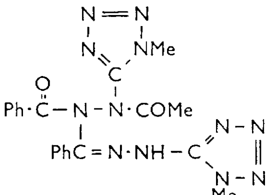


(VI)



(VII: R = H)

(IX: R = Ac)



(XI)

In the present work we have used arylidene-1-methyl-1*H*-tetrazol-5-ylhydrazines (II) † as substrates and have found that bromination to yield hydrazidic bromides (I) occurs smoothly in acetic acid solution at ambient temperatures, the reaction being facilitated by the electron donating property of the methyl substituent. This substituent also has the added effect of preventing fragmentation of the tetrazole nucleus thus affording an overall cleaner reaction. The increased nucleophilicity resulting from the presence of the methyl group gives rise to the formation, as minor products, of the hydrobromides (III) of those hydrazones containing *p*-electron donating substituents. The formation of these hydrobromides was sensitive to slight variations in experimental conditions and in some apparently duplicate preparations they were not (inexplicably) encountered. The results of these bromination reactions are summarised in the Experimental section (Table 3).

The nature of the hydrazine moiety also plays a key role in the behaviour of the hydrazidic halides. Thus the tetrazole ring in tetrazolyl hydrazidic bromides of type (IV) determines the nature of the products in the solvolysis reactions of these materials, the products being in fact triazolyl azides [6] resulting from cleavage of the tetrazole ring arising from its nucleophilic involvement at the carbon–bromine reaction site. The rate determining step in these reactions is the complete or partial ionisation of the carbon–bromine bond with the development of an azocarbonium ion.[6,7] With a methyl group replacing the tetrazole hydrogen atom as in compound (I) while tetrazole involvement at the carbon–bromine site again remains the dominant characteristic in the reactions of these compounds a marked difference in this case is the absence of ring fragmentation, the tetrazolyl involvement resulting instead in the formation of novel fused triazolotetrazoles (V).

When compound (Ia) was briefly heated under reflux in aqueous ethanolic or aqueous dioxan solution intractable gums resulted. However, performing the reactions at ambient temperatures afforded crystalline products. Thus, the substance (Ia) after reaction for 100 min. in 50% (v/v) dioxan–water or acetone–water containing

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* The letters a—e are used to modify symbols throughout. These letters carry the following implications, where a is used Ar = C_6H_5, for b Ar = C_6H_4Cl-*p*, for c Ar = C_6H_4Br-*p*, for d Ar = C_6H_4Me-*p*, and for e Ar = $C_6H_4Pr^i$-*p*.

† The arylidene-1-methyl-1*H*-tetrazol-5-ylhydrazines were obtained by the methylation of the parent arylidene-1*H*-tetrazol-5-ylhydrazines. The structure of each material was established by an unequivocal preparation; for details see ref. 5.

[1] Part of this work has been previously published in communication form, F. L. Scott, R. N. Butler, and D. A. Cronin, *Angew. Chem. Internat. Edn.*, 1965, **4**, 950.

[2] A. F. Hegarty and F. L. Scott, *Tetrahedron Letters*, 1965, 3801; *J. Chem. Soc.* (*B*), 1966, 672.

[3] M. S. Gibson, *Tetrahedron*, 1963, **19**, 1587.

[4] (*a*) F. L. Scott, W. N. Morrish, and J. Reilly, *J. Org. Chem.*, 1957, **22**, 692; (*b*) F. L. Scott and D. A. Cronin, *Chem. and Ind.*, 1964, 1757.

[5] R. N. Butler and F. L. Scott, *J. Org. Chem.*, 1966, **31**, 3182.

[6] F. L. Scott and D. A. Cronin, *Tetrahedron Letters*, 1963, 715.

[7] F. L. Scott and J. B. Aylward, *Tetrahedron Letters*, 1965, 841.

one equivalent of sodium acetate, gave three compounds; compound (Va) in 70% yield, a material of m. p. 262—264° in 4% yield, which we have not yet unequivocally identified but to which we tentatively assign the structure (VIa) as that which best fits our data * to date, and finally benzoic acid (2%), and some gum. When this solvolysis reaction was performed in the absence of sodium acetate the yield of compound (Va) was reduced to 50% with an increase in the extent of decomposition, the yield of benzoic acid was 13%. When compound (Va) was treated with one equivalent of hydrobromic acid or one equivalent of sodium acetate under the appropriate conditions, compound (VIa) and gums were obtained, the material (Va) being recovered in yields similar to those obtained in the solvolysis reactions of the hydrazidic bromide (Ia). This suggests that the decomposition encountered in these solvolysis reactions occurred subsequent to the formation of the triazolotetrazole (Va).

TABLE 1

Solvolysis of the hydrazidic bromides (I)

		Triazolotetrazoles			Other products		
Bromide	Time [c] (min.)	Compound	Yield (%) [d]	M. p.[e]	Compound	Yield (%)	M. p.
(Ia) [a]	(i) 20 (ii) 80	(Va)	50	157°	(VIa)	6	262—264°
(Ia) [b]	(i) 20 (ii) 80	(Va)	56	157	(VIa)	8	262—264
(Ib) [a]	(i) 30 (ii) 75	(Vb)	84	173	(VIIb)	2·5	193—194
(Ib) [b]	(i) 30 (ii) 75	(Vb)	75	173	(VIIb)	2	193—194
(Ic) [a]	(i) 30 (ii) 60	(Vc)	50	174	(VIIc)	12	203—205
(Ic) [b]	(i) 15 (ii) 240	(Vc)	66	174	(VIIc)	3	203—205
(Id) [a]	(i) 3 (ii) 120	(Vd)	74	156—158	(VId)	3	272—274
(Id) [b]	(i) 3 (ii) 120	(Vd)	82	156—158	(VId)	4	272—274 [f]
(Ie) [b]	(i) 30	(Ve)	37	120	(VIe)	0	

[a] Solvent is acetone–water (50 : 50 v/v mixture). [b] Solvent is dioxan–water (90 : 10 v/v mixture). [c] Procedures 1 and 2 describe the consecutive treatment the solutions were given; (i) indicates the period of stirring at 50° and (ii) the period of subsequent stirring at ambient temperatures. [d] All runs involved the formation of various quantities of gums. [e] Recrystallised from ether. Methyl isocyanide gas was evolved at the melting point leaving a residue which on further heating changed to a clear liquid at 300—320°. [f] Recrystallised from 95% ethanol.

The materials (V) were also obtained by the oxidative cyclisation of the hydrazones (II) with lead tetra-acetate. (cf. refs. 8*a* and *b*).

The results of a study of the solvolysis reactions of compounds (I) in the absence of added salts are summarised in Table 1. The most suitable conditions for these reactions were found to be, heating the reaction mixture at 50° for short periods to ensure the dissolution of the compound followed by stirring the solution at ambient temperatures. The rates of solvolysis of the hydrazidic bromides (I) in dioxan–water (90 : 10 (v/v) mixture) at 25·0 (±0·2)° were as follows (hydrazidic bromide, $k \times 10^4$ sec.$^{-1}$); (Ia) 1·0, (Ib) 0·25, (Ic) 0·26, (Id) 1·9, and (Ie) 1·8. These rate data, which corresponded to a Hammett ρ value of −2·2, indicate that the solvolytic reaction mechanism is essentially the same as for the unmethylated analogue,[6] *i.e.*, the rate determining step involves the ionisation of the carbon–bromine bond with subsequent nucleophilic attack at this site by the tetrazole ring.

While the tetrazole ring plays a dominant role in determining the products formed in the reactions of the tetrazolyl hydrazidic bromides (I), it is not always the exclusive nucleophile. Thus, with hydrazidic bromides containing *p*-electron withdrawing substituents, *e.g.*, (Ib) and (Ic), small quantities of the hydrazides (VII) [10] were obtained. The formation of these materials may be attributed to either a direct hydrolysis of the hydrazidic bromide or to an effective competition between water and the tetrazole ring for the azocarbonium ion. The decreased stability of the carbonium ion resulting from the presence of the electron withdrawing substituents would enchance such a competition. The use of a solvent of even greater nucleophilic character for these reactions might be expected to result in even more effective competition with tetrazole ring involvement. This was realised when quantitative yields of the hydrazidines (VIII) were obtained on solvolysis of the hydrazidic bromides (I) in aniline as solvent. The possibility that compounds (VIII) were formed in this reaction subsequent to the formation of the triazolotetrazoles (V) was excluded when it was found that greater than 90% of compound (Va) could be recovered from the reaction of this material with aniline under the appropriate solvolytic conditions. Thus, the nucleophilic aniline environment eliminated the tetrazole ring involvement.

The formation of the tetrazines (VI), in the present reactions appears to occur only with hydrazidic bromides containing *p*-electron donating substituents. Tetrazine formation by the condensation of nitrilamine intermediates is well-established in the reactions of hydrazidic halides.[11] We envisage their formation in our present work as involving (*a*) the degradation of com-

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* Microanalytical data indicate the formula $C_{16}H_{14}N_8$. The i.r. spectrum of the material shows —C=N absorption at 1630 cm.$^{-1}$ and a weak N–H band at 3080 cm.$^{-1}$. In the u.v. the material has $\lambda_{max.}$ 278 mμ. The nuclear magnetic resonance (n.m.r.) spectrum shows the presence of two benzene nuclei and one N–CH_3 group (τ 5·52) located in a tetrazole nucleus (cf. refs. 5 and 9). The i.r. spectrum of the analogous compound (VId) shows similar bands and the n.m.r. spectrum of this material shows absorptions due to eight aromatic protons, two C–CH_3 groups (*p*-tolyl) (τ 7·53 and 7·59) and one N–CH_3 group (τ 5·55).

[8] (*a*) F. L. Scott and R. N. Butler, *J. Chem. Soc.* (*C*), 1966, 1202; (*b*) J. D. Bower and F. P. Doyle, *J. Chem. Soc.*, 1957, 727.

[9] J. H. Markgraf, W. T. Bachmann, and D. P. Hollis, *J. Org. Chem.*, 1965, **30**, 3472.

[10] R. N. Butler and F. L. Scott, *J. Chem. Soc.* (*C*), 1966, 1319.

[11] R. Huisgen, E. Aufderhaar, and G. Wallbillich, *Chem. Ber.*, 1965, **98**, 1476; R. Huisgen, R. Grashey, E. Aufderhaar, and R. Kunz, *ibid.*, p. 642.

pound (I) to a reactive diazo * entity, (*b*) followed by a 1,3-dipolar coupling (cf. refs. 12*a* and 13) of this species with the parent nitrilamine to produce tetrazines such as (VI).

The reactions of the hydrazidic bromides (I) with acetate ion (Table 2) proved complex. With aqueous dioxan or aqueous acetone as the solvent the role of the acetate ion was to buffer the hydrobromic acid eliminated during the reaction and thus increase the yields of the material (V). With 95% ethanol or acetic acid as the solvent, acetate ion competed with the tetrazole ring for the carbonium ion. Thus, the major products from the solvolysis of the compounds (Ib) and (Id) in the presence of sodium acetate were the triazolotetrazoles (Vb) and (Vd) and the *N*-acetyl-*N'*-benzoylhydrazines (IXb) and (IXd). We have recently discussed the structure of these latter materials,[8a] which in this instance are formed by a 1,4-acyl migration [14] in the intermediate hydrazidic acetate (X). Similar O–N acyl migrations have been well established for imidic acetate intermediates [15] and recently 1,4-acyl migrations have also been found to occur with *O*-acyl oximes.[16] Curtin and his co-workers [17] have succeeded in isolating and studying some of these reactive *O*-acyl intermediates with selected compounds in which acyl migration is sterically hindered.

TABLE 2

Reactions of hydrazidic bromides (I) with acetate ion

			Products						
Bromide	Time (min.) [e]	Temp.	Compound	Yield (%) [g]	Compound	Yield (%)	M. p.	Compound	Yield (%)
(Ia) [a]	(i) 20	50°	(Va)	70				(VIa)	6
	(ii) 50	15—18 [f]							
(Ia) [b]	(i) 3	30			(XI)	56	141°	(VIa)	7
	(ii) 30	15—18 [f]							
(Ia) [c]	(i) 15	50			(XI)	47	141		
	(ii) 90	15—18 [f]							
(Ib) [a]	(i) 30	50	(Vb)	80				(VIIb)	2·5
	(ii) 75	15—18 [f]							
(Ib) [b]	(i) 5	40	(Vb)	18·5	(IXb)	46	182—184	(VIIb)	1
	(ii) 60	15—18 [f]							
(Id) [d]	(i) 40	15—18 [f]	(Vd)	76				(VId)	4
(Id) [c]	(i) 120	15—18 [f]	(Vd)	43	(IXd)	26	169—171		

[a] Solvent was 50% (v/v) acetone–water. Molar ratio, hydrazidic bromide : sodium acetate was 1 : 1. [b] Solvent was 95% ethanol. Molar ratio, hydrazidic bromide : sodium acetate was 1 : 1. [c] Solvent was acetic acid. Molar ratio, hydrazidic bromide : sodium acetate was 1 : 3. [d] Solvent was 80% (v/v) acetone–water. Molar ratio, hydrazidic bromide : sodium acetate was 1 : 1·1. [e] Procedures 1 and 2 describe the consecutive treatment the solutions were given. Ambient. [g] All runs involved the formation of various quantities of gums.

When compound (Ia) was treated with acetate ion in 95% ethanol or acetic acid, the main product formed was the material (XI), with compound (VIa) also being isolated in 7% yield from the reaction in ethanol. Compound (XI) on reaction with 3·7 equivalents of hydrobromic acid in aqueous solution for 45 min. at ambient temperatures (followed by 8 min. at 70°) yielded 56% of the hydrazine (IXa) and 9% of compound (VIa) along with some gum. On heating under reflux in benzene for 75 min., compound (XI) broke down to give a 98% yield of the triazolotetrazole (Va) and 53% of compound (IXa), (based on 100% formation of only the two degradation products). The formation of the material (XI) can be rationalised as follows. The halide (Ia) undergoes ionisation, partial or complete, to give an azocarbonium ion, which is then attacked by acetate ion and after O–N acetyl migration compound (IXa) results. This material is acidic and its anion once formed competes more effectively for the carbonium ion than did acetate ion. Hence compound (IXa) as it is formed attacks the ion pair yielding the adduct (XI). We have verified this sequence by treating the compounds (Ia) and (IXa) with base under the appropriate conditions, when compound (XI) is readily formed.

The factors which govern the formation of compounds of type (XI) are the acidity of the *N*-acetyl-*N'*-benzoylhydrazine (IX) and the nucleophilicity of the anion of this material. Since the substituted hydrazidic bromides (Ib) and (Id) do not form the corresponding adducts (XI), and since electron donating and withdrawing substituents will affect the factors mentioned inversely, it appears that a delicate balance of these effects in the unsubstituted compound allows for the formation of compound (XI). We have as yet no satisfactory explanation for the remarkably different behaviour of acetate ion toward the azocarbonium ion in the different solvents.

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* For the generation of diazo-intermediates from hydrazones, see ref. 12.

[12] (*a*) F. L. Scott and F. J. Lalor, *Chem. and Ind.*, 1966, 420; and (*b*) W. F. Bamford and T. S. Stevens, *J. Chem. Soc.*, 1952, 4735; W. Kirmse, B. G. von Bülow, and H. Schepp, *Annalen*, 1966, **691**, 41; K. W. Wiberg and J. M. Lavanish, *J. Amer. Chem. Soc.*, 1966, **88**, 365.

[13] R. Huisgen, *Angew. Chem. Internat. Edn.*, 1963, **2**, 575.

[14] I. T. Barnish and M. S. Gibson, *J. Chem. Soc.*, 1965, 2999; J. M. Burgess and M. S. Gibson, *ibid.*, 1964, 1500.

[15] F. Cramer and K. Baer, *Chem. Ber.*, 1960, **93**, 1231; D. Martin, *ibid.*, 1965, **98**, 3286.

[16] N. E. Alexandrou and D. N. Nicolaides, *Tetrahedron Letters*, 1966, 2497; G. Just and K. Dahl, *ibid.*, p. 2441.

[17] D. Y. Curtin and L. L. Miller, *Tetrahedron Letters*, 1965, 1867; D. Y. Curtin and N. Alexandrou, *Tetrahedron*, 1963, **19**, 1697.

EXPERIMENTAL

Melting points were measured on an Electrothermal apparatus. Molecular weights were determined by vapour pressure techniques. Infrared spectra were measured on a Perkin-Elmer Infracord (model 137E) spectrophotometer with sodium chloride optics. Solids were examined as discs with potassium bromide. N.m.r. spectra were recorded on a Varian HA-100 spectrometer with tetramethylsilane as internal reference and deuteriochloroform as solvent.

(a) *Bromination of Arylidene*-1-*methyl*-1H-*tetrazol*-5-*ylhydrazines* (II) *.—The following is a typical example. Bromine (1·62 ml.) in glacial acetic acid (20 ml.) was added, with stirring, over a period of 90 min. to a solution of benzylidene-1-methyl-1*H*-tetrazol-5-ylhydrazine (IIa) (2 g.), (prepared as described elsewhere [5]), in 60 ml. of the same solvent. The mixture was stirred for a further 2·5 hr., and the yellow solid which had precipitated (226 mg., 8%) m. p. 218—220° (filtrate A) was removed and washed with ether. This material which separated as a white crystalline *solid* of m. p. 221—222° on recrystallisation from acetic acid, is compound (IIIa) (Found: C, 38·1; H, 3·8; Br, 28·4; N, 29·9. $C_9H_{11}BrN_6$ requires C, 38·15; H, 3·9; Br, 28·3; N, 29·7%).

The filtrate (A) was added slowly with stirring to 200 ml. of water cooled with crushed ice. The flocculent precipitate (1·9 g., 68%) (m. p. 145°) was washed with small quantities of water and ether. This material [m. p. 147° from 50% (v/v) benzene–chloroform] is the *hydrazidic bromide* (Ia) (Found: C, 38·3; H, 3·2; Br, 28·6; N, 30·4. $C_9H_9BrN_6$ requires C, 38·3; H, 3·5; Br, 28·4; N, 29·8%).

The above was the general procedure followed in the reactions outlined in Table 3. In the bromination of the hydrazone (IId) the hydrazidic bromide (Id) and the hydrobromide (IIId) separated as a mixture. The former compound was removed by elution of the mixture with warm benzene in which the latter material is insoluble.

The hydrobromides (III) were also prepared, in quantitative yield, by adding 48% (w/w) hydrobromic acid solution, with stirring to a solution of the hydrazone in glacial acetic acid containing sufficient acetic anhydride to keep the solution dry. The hydrobromides separated immediately as white crystalline solids.

(b) *Solvolysis of the Hydrazidic Bromides* (I).—The following are typical examples. (i) A solution of *p*-bromobenzylidene-1-methyl-1*H*-tetrazol-5-ylhydrazidic bromide (Ic), (900 mg.), in 60 ml. of 50% (v/v) acetone–water was heated at 50° for 30 min., stirred at ambient temperatures for 1 hr. and cooled in an ice-bath. The solid (290 mg., m. p. 165°) (filtrate A) which separated was recrystallised from ether to give white *crystals* of compound (Vc), m. p. 174° (Found: C, 38·8; H, 2·75; Br, 28·35; N, 30·1%; *M*, 278. $C_9H_7BrN_6$ requires C, 38·7; H, 2·5; Br, 28·7; N, 30·1%; *M*, 279).

The filtrate (A) was distributed between ether (100 ml.) and water (100 ml.) and the layers were separated. The aqueous layer (solution B) was further extracted with 2 × 100 ml. aliquots of ether. The combined ethereal solutions were concentrated to 100 ml. and cooled to yield *compound* (VIIc) (35 mg.), m. p. 203—205° (Found: C, 36·7; H, 3·0; Br, 26·8; N, 28·1; O, 5·65. $C_9H_9BrN_6O$ requires C, 36·4; H, 3·1; Br, 27·0; N, 28·3; O, 5·4%). The ethereal filtrate was evaporated and the residue (300 mg.), a white crystalline solid mingled with a reddish gum was swirled in ether to remove the gum. The remaining solid (230 mg.) had m. p. 165—180°. Repeated recrystallisations of this material from 50-ml. aliquots of ether yielded a further 100 mg. of compound (Vc), (total yield, 390 mg., 50%) and 40 mg. of compound (VIIc) which did not dissolve in the ether. Evaporation of the final ethereal filtrate yielded a trace of a white solid of m. p. 249—250° which appears to be *p*-bromobenzoic acid (lit.,[18] 251°).

TABLE 3

Summary of bromination reactions

	Hydrazidic bromide			Hydrobromide		
Hydrazone	Compound	Yield (%)	M. p.	Compound	Yield (%)	M. p.
(IIa)	(Ia)	68 (73) [b]	147°	(IIIa)	8	221—222°
(IIb)	(Ib)	75	159 [c]			
(IIc)	(Ic)	82	160 [c]			
(IId)	(Id)	55·5	143 [c]	(IIId)	17	224—225
(IIe) [a]	(Ie)	50 (63)	138 [d]	(IIIe)	14	214

[a] In this reaction the molar ratio, bromine–hydrazone was 1 : 1. In all of the other reactions this ratio was 3 : 1. [b] Figures in parentheses represent the yields obtained when compounds (III) were not formed. [c] Recrystallised from benzene. [d] Recrystallised from benzene–pentane (60—80°) (50% v/v).

The aqueous solution (B) was evaporated to 10 ml. at 80°, which on cooling in ice gave a further crop (19 mg.) (m. p. 198—200°) of compound (VIIc) (total yield, 90 mg., 12%).

(ii) A solution of compound (Ia) (1 g.) in 90% (v/v) dioxan–water (100 ml.) was heated at 50° for 20 min., stirred at ambient temperatures for 80 min., treated with water (80 ml.) and cooled in ice. The flocculent precipitate (45 mg., 8%) (filtrate A) which separated had m. p. 259—262° raised to 262—264° by recrystallisations from chloroform–pentane in the cold. This material is *compound* (VIa) (Found: C, 59·15; H, 4·21; N, 35·4%; *M*, 451 measured in phenol and 817 measured in benzene indicating considerable association presumably through hydrogen bonding. $C_{16}H_{14}N_8$ requires C, 60·4; H, 4·4; N, 35·2%; *M*, 318). [It was found difficult to purify this material satisfactorily. Even after numerous recrystallisations microanalytical data measured on extensively dried samples of the material showed the presence of approximately 1% oxygen due possibly to resistant water trapping. A similar phenomenon was also observed with compound (VId), Table 4.]

The filtrate (A) was distributed between ether (150 ml.) and water (150 ml.) and the layers were separated. The aqueous layer (solution B) was further extracted with 2 × 100 ml. aliquots of ether and the combined ethereal solutions after being washed with water were dried and evaporated. The residue (470 mg.), a white crystalline solid mingled with a small quantity of a yellow gum, was swirled in ether (10 ml.) to remove the gum. The remaining solid (400 mg., 56%) (m. p. 154°) was recrystallised from ether to give pure compound (Va), m. p. 157°.

The aqueous solution (B) was evaporated to 10 ml. at 80° which, on cooling in ice, gave benzoic acid (20 mg., 4·5%) m. p. 120—122°.

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* We are indebted to Dr. D. A. Cronin who carried out this reaction with compound (Ia).

[18] " Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., Cleveland, Ohio, 1959.

Table 1 summarises the reactions in which this general procedure was followed. For an alternative synthesis of, and microanalytical data on the compounds (Va), (Vb), (Vd), and (Ve) see refs. 8*a* and 10.

(iii) *Reaction of compound* (Va) *with hydrobromic acid.* A solution of compound (Va) (200 mg.) in 50% (v/v) acetone–water (30 ml.) containing 0·06 ml. of 48% (w/w) hydrobromic acid was heated at 50° for 10 min., stirred at ambient temperatures for 1 hr., and cooled in an ice-bath. The solid (17 mg., 10%) (m. p. 258—262°) (filtrate A) which separated was shown to be the material (VIa) by a mixed m. p. and a comparison of its i.r. spectrum.

The filtrate (A) was extracted with ether. Work-up of the ethereal solution in the manner described above yielded compound (Va) (128 mg., 64%) and a yellow gum (20 mg.).

TABLE 4

Analytical data

Compound	Found (%) C	H	Br	N	Formula	Required (%) C	H	Br	N
(Ib) [a]	34·6	2·8	24·8	26·9	$C_9H_8BrClN_6$	34·3	2·5	25·4	26·6
(Ic)	30·1	2·45	44·2	23·5	$C_9H_8Br_2N_6$	30·0	2·2	44·4	23·2
(Id)	40·85	3·7	26·8	28·3	$C_{10}H_{11}BrN_6$	40·7	3·7	27·1	28·5
(Ie)	44·05	4·7	24·9	26·2	$C_{12}H_{15}BrN_6$	44·55	4·6	24·8	26·0
(IIId)	39·9	4·5	27·05	28·2	$C_{10}H_{13}BrN_6$	40·4	4·4	26·95	28·3
(IIIe)	44·6	5·2	24·1	25·8	$C_{12}H_{17}BrN_6$	44·3	5·2	24·6	25·8
(VId) [b]	60·7	5·0		34·0	$C_{18}H_{18}N_8$	62·4	5·2		32·4

[a] (Found: Cl, 11·2. Required Cl, 11·25). [b] (Found: *M*, 337. Required *M*, 346).

In a similar experiment with sodium acetate the recovery of compound (Va) was 75% with the material (VIa) being formed in 2% yield.

(iv) *Reaction of the hydrazidic bromides* (I) *with aniline.* *p*-Chlorobenzylidene-1-methyl-1*H*-tetrazol-5-ylhydrazidic bromide (Ib) (250 mg.) was made into a paste with 1·5 ml. of redistilled aniline. The mixture was heated on a water-bath at 70° for 10 min. and then digested with ether (50 ml.). The white solid which separated was leached with pentane (50 ml.) and water (50 ml.) in succession after which it had m. p. 233—235° (quantitative yield). Recrystallisation from 95% ethanol raised the m. p. of this *material* (VIIIb) to 234—235° (Found: C, 54·4; H, 4·6; Cl, 10·8; N, 29·7. $C_{15}H_{14}ClN_7$ requires C, 55·0; H, 4·3; Cl, 10·8; N, 29·9%. Similar reactions with compounds (Ia) and (Id) yielded *compound* (VIIIa), m. p. 212—214° (Found: C, 61·4; H, 5·3; N, 33·3. $C_{15}H_{15}N_7$ requires C, 61·4; H, 5·15; N, 33·4%) and *compound* (VIIId) m. p. 233—235° (Found: C, 62·7; H, 5·7; N, 31·3. $C_{16}H_{17}N_7$ requires C, 62·5; H, 5·5; N, 31·9%). When compound (Va) was treated with aniline in the manner described it was recovered unchanged in 90% yield on work-up of the mixture.

(c) *Reactions of the Hydrazidic Bromides* (I) *with Sodium Acetate.*—The reactions of the compounds (I) with sodium acetate in acetone–water solution were carried out as described in section (b) parts (i) and (ii). With 95% ethanol or acetic acid as solvents these reactions were carried out as follows. (i) A suspension of compound (Ib) (1 g.) in 95% ethanol (50 ml.) containing sodium acetate trihydrate (440 mg.) was heated at 40° for 5 min., stirred at ambient temperatures for 1 hr., and cooled in ice. The white crystals (137 mg., 18·5%) (m. p. 167°) which separated were washed with water and recrystallised from ether to yield pure compound (Vb), m. p. 173°.

Treatment of the filtrate (A) with water (80 ml.) yielded a brown precipitate (95 mg.) (m. p. 155—163°) (solid A). The filtrate from this material on standing for 2 hr. yielded white crystals (100 mg.) (m. p. 182—184°) (filtrate B) of *compound* (IXb). The filtrate (B) was extracted with ether (3 × 60 ml.). The ethereal layers were separated (aqueous solution C), washed, dried, and evaporated. The residue was compound (IXb) (230 mg.) (m. p. 180—182°) and a small quantity of a reddish oil which was removed in ether (10 ml.). The aqueous solution (C) was acidified with hydrochloric acid and evaporated to 5 ml. at 80°, which on cooling in ice gave compound (VIIb) (9 mg., 1%), m. p. 192°.

The solid (A) was dissolved in boiling ether (60 ml.) and the solution after being filtered to remove particles of an intractable material was concentrated to 10 ml. Further evaporation to 3 ml. with a current of air yielded 80 mg. of compound (IXb) (total yield, 410 mg., 45%), m. p. 182—184° (from aqueous alcohol). Evaporation of the ethereal filtrate to dryness yielded a greenish gum.

(ii) A solution of the hydrazidic bromide (Id) (360 mg.) in glacial acetic acid (30 ml.) containing anhydrous sodium acetate (280 mg.) was stirred at ambient temperatures for 2 hr. and then added slowly with stirring to 80 ml. of water cooled with crushed ice. A few mg. of unreacted hydrazidic bromide was removed and the solution was extracted with ether (3 × 100 ml.). The ethereal solution was washed thoroughly with water, extracted with aqueous sodium carbonate (solution A), dried, and evaporated. The residue (130 mg.), a white crystalline material mixed with a yellow oil, was swirled in cold ether (5 ml.) to remove the oil. The remaining solid (110 mg., 43%) had m. p. 145—152°, raised by recrystallisation from ether to 156°. This material was 6-*p-tolyl*-3-*methyl*[1,2,4]*triazolo*[4,3-d]*tetrazole* (Vd).

The alkaline extract (A) was acidified with hydrochloric acid and extracted with ether (3 × 80 ml.). The combined ethereal extracts were dried and evaporated. The residue, white needles mixed with a small quantity of a gum, was stirred in ether (5 ml.). The insoluble material (85 mg., 26%) was *compound* (IXd), m. p. 169—171°.

(iii) * A suspension of the hydrazidic bromide (Ia) (1·5 g.) in 95% ethanol (60 ml.) containing 764 mg. of sodium acetate trihydrate was heated at 30° for 3 min., stirred at ambient temperatures for 30 min., and cooled in ice. The precipitate (65 mg., 7%) m. p. 254—260° (filtrate A) which separated was washed with water. Three recrystallisations from chloroform–pentane raised the m. p. of the material, compound (VIa), to 262—264°.

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* We are indebted to Dr. D. A. Cronin who carried out this reaction with compound (Ia).

The filtrate (A) was distributed between ether (150 ml.) and water (150 ml.) and the layers were separated. The aqueous solution was re-extracted with ether (2 × 150 ml.). The combined ethereal extracts were washed, dried, and evaporated. The brown oily residue was stirred in cold ether (40 ml.) and the insoluble white solid (390 mg.) (m. p. 135°) was collected. Treatment of the ethereal filtrate with an equal volume of pentane yielded a further 185 mg. (total yield, 725 mg.; 56%) of this material, m. p. 134°. Recrystallisation from ether (100 mg.) (20 ml.) raised the m. p. of the material, *compound* (XI), to 141° (Found: C, 52·1; H, 4·6; N, 36·0; O, 7·3. $C_{20}H_{20}N_{12}O_2$ requires C, 52·2; H, 4·3; N, 36·5; O, 7·0%). Methyl isocyanide is evolved at its melting point.

The above reaction was carried out in acetic acid in a similar manner (results in Table 2). In the reaction of the hydrazidic bromide (Ia) with one equivalent of the hydrazine (IXa) in 95% ethanol containing 2 equivalents of sodium carbonate under the above conditions the material (XI) (identified by mixture m. p. and i.r. spectrum) was obtained in 52% yield.

(iv) *Degradation of compound* (XI). (*a*) A suspension of compound (XI) (246 mg.) in water (40 ml.) containing sodium bromide (206 mg.) and 98% sulphuric acid (1·1 ml.) was stirred at room temperature for 45 min., heated at 70° for 8 min., and cooled in an ice-bath. The precipitate (10 mg., 8%) (m. p. 248—252°) which was washed with water and recrystallised from chloroform–pentane (m. p. 258°) was identified as compound (VIa) by a mixture melting point and a comparison of its i.r. spectrum.

The filtrate (A) was extracted with ether (3 × 80 ml.). The ethereal solution was dried and evaporated. The residue (160 mg.) consisted of white needles and a gum, which was removed in ether (15 ml.) to leave white needles (78 mg., 56%) (m. p. 153—155°) of *compound* (IXa).

(*b*) A solution of compound (XI) (230 mg.) in benzene (30 ml.) was heated under reflux for 75 min., cooled and distributed between ether (30 ml.) and cold saturated sodium carbonate solution (40 ml.). The layers were separated and the benzene–ether layer (solution A) was re-extracted with aqueous sodium carbonate solution (40 ml.). The combined alkaline extracts were acidified with hydrochloric acid and extracted with ether. On evaporation the dried ethereal solution deposited white needles (68 mg., 53%) (m. p. 150—153°) of *N*-acetyl-*N*-(1-methyl-1*H*-tetrazol-5-yl)-*N*′-benzoylhydrazine (IXa).

Evaporation of solution (A) yielded a white crystalline solid (98 mg., 98%) (m. p. 155°) with a slight reddish tint which was identified as compound (Va) by a mixture melting point with an authentic sample and a comparison of its i.r. spectrum. The yields are calculated on the assumption that 100% of both degradation products (and these only) are formed. For an alternative synthesis of and microanalytical data on the compounds (IXa), (IXb), (IXd), and (VIIb) see ref. 8*a*.

(d) *Kinetic Studies.*—The rates of solvolysis of the hydrazidic bromides (I) were studied in 90 : 10 (v/v) dioxan–water solution at 25·0 (±0·2)°. The solvent was prepared by mixing 90 volumes of dioxan (B.D.H. AnalaR) with 10 volumes of distilled water both at 25°. The concentration of the hydrazidic bromide which was used in each case was 200 mg. in 50 ml. of solvent, the rates being followed by measuring the increasing concentration of bromide ion in the solution. Samples (5 ml.) were withdrawn at suitable time intervals, distributed between ether and water and the aqueous layer was tested for bromide ion by the Volhard method. Rate constants, which were calculated from the first order equation $k = 1/t \,.\, \ln a/(a - x)$, drifted downwards during the runs; the k values reported were calculated by extrapolating the plot of k *vs.* % reaction to 0% reaction.

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