Nucleophilic Displacement Reactions on the New Acyl System, 1-Bromo-1-(alkyl- or arylthio)-4-aryl-2,3-diazabuta-1,3-diene

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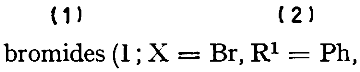
Reaction of 1,1-dibromo-4-aryl-2,3-diazabuta-1,3-dienes (1,1-dibromoazines) with aliphatic or aromatic thiols yielded products resulting from thiolysis of one or two bromine atoms. The monobromoazine (1-bromo-1-alkylthio-4-aryl-2,3-diazabuta-1,3-diene) is very reactive undergoing replacement of bromine by primary and secondary amines, phenylhydrazine, water, azide ion, alcohols, and phenols to give a variety of novel thiodiaza-systems. The kinetics of displacement by water has been studied in detail in 40% dioxan at 25°. The effect of substituents on the S–Ar ring ($\rho = -1{\cdot}0$) is consistent with thioazacarbonium-ion formation as is the observation of a large solvent effect and rate enhancement by the presence of salts other than those containing bromide ion (which causes a rate depression). Direct S_N2 displacement of bromide ion is also rendered unlikely by the fact that hydrolysis is slightly slower at high hydroxide ion concentration.

It has been well established that nucleophilic substitution of acyl chlorides can occur by several mechanisms, dependent on substrate structure and reaction conditions.[1] In good ionizing solvents and with compounds which have electron-donating substituents, acylium-ion intermediates are formed, while S_N2 displacement (or addition–elimination, with rate-determining formation of the intermediate) occurs in less aqueous solvents.[2] A change in mechanism can clearly be observed in solvents of intermediate ionizing ability and curvature of linear free-energy plots results.[3] Although less well documented, the aza-analogues (1) show the same general behaviour. Ugi and his co-workers [4] in a study of the reactive imidoyl chlorides (1; X = Cl, R^1 and R^2 = alkyl or aryl) concluded that an azocarbonium ion-pair is formed in solvolysis because of the large stabilizing power of electron-donating substituents in R^1 and R^2. More recently Rappoport [5] has proposed that imidoyl chlorides which have electron withdrawing substituents (in R^1 or R^2) may undergo direct S_N2 displacement (or tetrahedral intermediate formation) by amine bases in benzene solution. Further stabilization of the potential carbonium-ion centre is provided when R^2 = NHR^3 and indeed there is substantial evidence that



$$\overset{X}{R^1C}{=}NR^2 \xrightarrow{Y^-} \overset{Y}{R^1C}{=}NR^2$$

(1) (2)

hydrazonyl bromides (1; X = Br, R^1 = Ph, R^2 = $NHC_6H_4NO_2$-*p*, for example) solvolyse by an azocarbonium-ion pathway.[6] For these compounds the observed base-

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[1] S. L. Johnson, *Adv. Phys. Org. Chem.*, 1967, **5**, 237.

[2] R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, 1969, **91**, 6031.

[3] E. W. Crunden and R. F. Hudson, *J. Chem. Soc.*, 1956, 501.

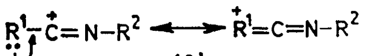
[4] I. Ugi, F. Beck, and V. Fetzer, *Ber.*, 1962, **95**, 126.

[5] Z. Rappoport and R. Ta-Shma, *Tetrahedron Letters*, submitted for publication. We are indebted to Prof. Rappoport for a copy of this paper prior to its publication.

[6] A. F. Hegarty, M. Cashman, and F. L. Scott, *J. Chem. Soc.* (*B*), 1971, 1607.

catalysed reaction was shown recently[7] to involve 1,3-dipolar ion formation from the hydrazonyl bromide anion, rather than direct S_N2 attack by hydroxide ion.

Stabilization of an intermediate acylium ion (3) is also enhanced if the substituents attached to carbon carry lone-pair electrons. In the present study the synthesis



(3)

of a series of compounds with this potential, the mercaptohydrazonyl bromides where $R^1 = S$-alkyl or S-aryl, is described together with some of the reactions of this novel system and an investigation of the mechanism of their solvolysis.

EXPERIMENTAL

Materials.—All inorganic chemicals were AnalaR grade. Sodium perchlorate, sodium azide, sodium nitrate, and sodium bromide were dried at 120° for 3 h before use. The solvent used for the kinetic experiments, 40% dioxan, was prepared by mixing 40 volumes dioxan and 60 volumes water at 25°. Other dioxan–water mixtures were similarly prepared. The dioxan was B.D.H. AnalaR grade, while the water had been passed through a mixed cation-anion exchange resin and then distilled from potassium perpermanganate.

TABLE 1

Physical data for 1-bromo-1-arylthio-4-aryl-2,3-diazabuta-1,3-dienes, $XC_6H_4{\cdot}CH{=}N{\cdot}N{=}CBr{\cdot}S{\cdot}C_6H_4Y$

Substituent			Found (%)						Required (%)				
X	Y	M.p. (°C)	C	H	Br	N	S	Formula	C	H	Br	N	S
p-NO_2	H	95—97	46·1	2·7	22·0		8·7	$C_{14}H_{10}BrN_3O_2S$	46·5	2·7	22·0		8·4
p-NO_2	p-Cl	115—116	42·2	2·3	20·1		8·2	$C_{14}H_9BrClN_3O_2S$	42·6	2·3	20·4		8·0
p-NO_2	p-Br	119	37·8	2·0	36·3		7·1	$C_{14}H_9Br_2N_3O_2S$	37·9	2·0	36·1		7·2
p-NO_2	p-F	110	43·7	2·4	20·8		8·5	$C_{14}H_9BrFN_3O_2S$	44·0	2·3	21·0		8·4
p-NO_2	p-Me	108—109	47·8	3·0	21·0		8·6	$C_{15}H_{11}BrN_3O_2S$	47·7	3·2	21·1		8·5
p-Cl	p-Me	56—57	49·3	3·4		7·9		$C_{15}H_{10}BrClN_2S$	49·0	3·3		7·6	
p-Cl	H	63	47·5	2·9		8·2		$C_{14}H_{10}BrClN_2S$	47·5	2·8		7·9	
p-Cl	p-F	119—120	45·7	2·5		7·8		$C_{14}H_9BrClFN_2S$	45·4	2·4		7·5	
p-Cl	p-Cl	110—111	43·3	2·4		7·1		$C_{14}H_9BrCl_2N_2S$	43·3	2·3		7·2	
p-Cl	p-NO_2	160	42·2	2·3		10·3		$C_{14}H_9BrClN_3O_2S$	42·2	2·3		10·5	

TABLE 2

Physical properties of 1-bromo-1-alkylthio-4-(p-nitrophenyl)-2,3-diazabuta-1,3-dienes, p-$NO_2{\cdot}C_6H_4{\cdot}CH{=}N{\cdot}N{=}CBr{\cdot}SR$

		Found (%)					Required (%)			
R	M.p. (°C)	C	H	Br	S	Formula	C	H	Br	S
CH_2Ph	122	47·6	3·2	21·2	8·2	$C_{15}H_{12}BrN_3O_2S$	47·4	3·3	21·1	8·5
Et	120	37·6	3·4	24·9	10·4	$C_{15}H_{12}BrN_3O_2S$	37·8	3·2	25·3	10·1
Pr^n	117	40·4	3·5	24·5	9·4	$C_{11}H_{12}BrN_3O_2S$	40·0	3·6	24·7	9·7
Bu^n	120	41·7	4·1	23·5	9·0	$C_{12}H_{14}BrN_3O_2S$	41·9	4·1	23·2	9·3
Bu^t	125	41·9	4·1	23·0	9·5	$C_{12}H_{14}BrN_3O_2S$	41·9	4·1	23·2	9·3

Substrates

1-*Bromo*-1-(p-*chlorophenylthio*)-4-(p-*nitrophenyl*)-2,3-*diazabuta*-1,3-*diene* (9; $Ar^1 = p$-$NO_2C_6H_4$; $R^1 = p$-ClC_6H_4).—To a solution of 1,1-dibromo-4-(p-nitrophenyl)-2,3-diazabuta-1,3-diene (0·67 g, 2 mmol) in dry benzene (30 ml) was added p-chlorothiophenol (0·289 g, 2 mmol) in dry benzene (10 ml), followed by triethylamine (0·275 ml, 2 mmol). The solution was stirred for 3 h at 50° and the triethylamine hydrobromide (0·30 g, 75% of theoretical) which separated was filtered off. The benzene was evaporated from the filtrate to leave a mustard-coloured solid, m.p. 95—100°. On recrystallization the 1-*bromo*-1-(p-*chlorophenylthio*)-4-(p-*nitrophenyl*)-2,3-*diazabuta*-1,3-*diene* had m.p. 115—116° [from light petroleum (40—60°)]. (See Table 1 for analytical data).

The above procedure is typical of that used to synthesize these 4-(p-nitrophenyl)-substituted diazabutadienes. In Table 1 are listed m.p. and analytical data for the compounds prepared.

1-*Bromo*-1-*phenylthio*-4-(p-*chlorophenyl*)-2,3-*diazabuta*-1,3-*diene* (9; $Ar = p$-ClC_6H_4; $R^1 = C_6H_5$).—The following general procedure was used to synthesise the 4-(p-chlorophenyl)-substituted compounds which were unreactive under the conditions used for the p-nitro-analogues above. Sodium (0·23 g, 0·01 g-atom) was added to methanol (10 ml) followed by thiophenol (1·10 g, 10 mmol). The sodium thiophenoxide solution was added dropwise to a solution of 1,1-dibromo-4-(p-chlorophenyl)-2,3-diazabuta-1,3-diene (3·25 g, 10 mmol) in dry ether (250 ml). The resultant milky solution was stirred at room temperature for 8 h when the precipitated sodium bromide (0·80 g, 78%) was filtered off. The brown oil which remained on evaporation of the filtrate was dissolved in pentane (*ca.* 25 ml) and a light yellow solid (2·1 g, 59%), m.p. 50—59°, was precipitated by cooling the mixture to —15°. Repeated recrystallization from pentane gave the *monobromo-product*, m.p. 63° (1·60 g, 45%). See Table 1 for analytical data for this compound and other related materials (in which X = Cl) which were prepared by this same general method. The S-alkyl analogues were similarly prepared (see Table 2).

Reactions of 1-*Bromo*-1-*phenylthiodiazabutadienes*.—(a) *With aniline*. To 1-bromo-1-phenylthio-4-(p-nitrophenyl)-2,3-diazabuta-1,3-diene (0·37 g, 1 mmol) in benzene solution (50 ml) was added aniline (0·19 ml, 2 mmol). The solution was refluxed for 2 h and on cooling the precipitate (0·272 g), m.p. 245—246° (from ethanol), was filtered

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[7] A. F. Hegarty, M. P. Cashman, and F. L. Scott, *Chem. Comm.*, 1971, 689.

off. This proved to be the *hydrobromide of* 1-(p-*nitrobenzylidene*)-3,4-*diphenylisothiosemicarbazide* (Found: C, 52·9; H, 3·7; S, 6·7. $C_{20}H_{16}BrN_4O_2S$ requires C, 52·5; H, 3·5; S, 7·0%). The free base was prepared from this by suspending it in 70% ethanol and adding a dilute solution of sodium carbonate. On recrystallization from ethanol the dark red powder (11; $Ar^1 = p\text{-}NO_2C_6H_4$; $Ar^2 = Ph$) had m.p. 155° (Found: C, 63·5; H, 4·4; S, 8·1. $C_{20}H_{16}N_4O_2S$ requires C, 63·8; H, 4·2; S, 8·5%).

1-(p-*Nitrophenylbenzylidene*)-4-*phenyl*-3-(p-*chlorophenyl*)-*isothiosemicarbazide* was similarly prepared, m.p. 158° (70% yield) (Found: C, 58·8; H, 4·1; S, 7·4. $C_{20}H_{15}ClN_4O_2S$ requires C, 58·5; H, 3·6; S, 7·8%).

(b) *With a secondary amine*. *N*-Benzylmethylamine (0·242 ml, 2 mmol) was added to 1-bromo-1-(*p*-chlorophenylthio)-4-(*p*-nitrophenyl)-2,3-diazabuta-1,3-diene (0·398 g, 1 mmol) in benzene (40 ml); the solution was maintained at 50° for 15 min. The amine hydrobromide which precipitated was filtered off (0·36 g, 80%) and the filtrate evaporated to leave an oil which on extraction with light petroleum (b.p. 60—80°) gave 1-(p-*chlorophenylthio*)-1-*benzyl*(*methyl*)*amino*-4-(p-*nitrophenyl*)-2,3-*diazabuta*-1,3-*diene* [12; $Ar^1 = p\text{-}NO_2C_6H_4$; $Ar^2 = p\text{-}ClC_6H_4$; $NR_2 = N(Me)CH_2Ph$] (0·27 g, 68%) as a yellow solid, m.p. 92—93° (Found: C, 59·9; H, 4·4; S, 7·2. $C_{22}H_{19}ClN_4O_2S$ requires C, 60·3; H, 4·3; S, 7·3%).

TABLE 3

Analytical and m.p. data for the aryl- and alkyl-thiocarbonylhydrazines, $XC_6H_4\cdot CH{=}N\cdot NH\cdot CO\cdot SR$

Substituents				Found (%)				Repuired (%)		
X	R	M.p. (°C)	Yield (%)	C	H	N	Formula	C	H	N
p-NO$_2$	C$_6$H$_5$	179	87	55·8	3·6	10·3	$C_{14}H_{11}N_3O_3S$	56·0	3·7	10·7
p-NO$_2$	*p*-ClC$_6$H$_4$	190	95	50·2	2·9	9·75	$C_{14}H_{10}ClN_3O_3S$	50·2	2·9	9·5
p-NO$_2$	*p*-BrC$_6$H$_4$	194	85	44·4	2·8	8·9	$C_{14}H_{10}BrN_3O_3S$	44·2	2·8	8·45
p-NO$_2$	*p*-FC$_6$H$_4$	182	92	52·6	3·0	10·4	$C_{14}H_{10}FN_3O_3S$	52·6	3·1	10·1
p-NO$_2$	*p*-MeC$_6$H$_4$	201	75	56·9	4·3	10·2	$C_{15}H_{13}N_3O_3S$	57·1	4·1	10·2
p-Cl	*p*-MeC$_6$H$_4$	204—205	81	57·4	4·3	9·3	$C_{15}H_{13}ClN_2OS$	57·3	4·2	8·9
p-Cl	Ph	189—190	85	57·8	3·6	9·7	$C_{14}H_{11}ClN_2OS$	57·8	3·8	9·6
p-Cl	*p*-FC$_6$H$_4$	208—209	88	54·2	3·2	9·5	$C_{14}H_{10}ClFN_2OS$	54·5	3·3	9·1
p-Cl	*p*-ClC$_6$H$_4$	206—207	90	51·4	3·2	8·7	$C_{14}H_{10}Cl_2N_2OS$	51·7	3·1	8·6
p-NO$_2$	CH$_2$Ph	197	90	56·9	4·2	10·5	$C_{15}H_{13}N_3O_3S$	57·1	4·1	10·2
p-NO$_2$	Et	182	69	47·7	4·3	13·2	$C_{10}H_{11}N_3O_3S$	47·4	4·3	12·8
p-NO$_2$	Pr^n	187	94	49·2	5·0	12·2	$C_{11}H_{13}N_3O_3S$	49·2	4·9	12·0
p-NO$_2$	Bu^n	188	85	49·9	5·3	11·6	$C_{12}H_{15}N_3O_3S$	50·0	5·3	11·3
p-NO$_2$	Bu^t	174	87	50·3	5·3	11·0	$C_{12}H_{15}N_3O_3S$	50·0	5·3	11·3

(c) *With sodium azide*. To 1-bromo-1-(*p*-chlorophenylthio)-4-(*p*-nitrophenyl)-2,3-diazabuta-1,3-diene (0·398 g, 1 mmol) in dioxan (20 ml) was added sodium azide (0·13 g, 2 mmol) in water (5 ml). The deep red solution which formed was refluxed for 2 h and allowed to cool. Ice-cold water (500 ml) was added to precipitate 5-(p-*chlorophenylthio*)-1-(p-*nitrobenzylideneamino*)*tetrazole* (15; $Ar = p\text{-}NO_2C_6H_4$; $R = p\text{-}ClC_6H_4$) (0·223 g, 62%) as a yellow solid, m.p. 111—113° (from acetone–pentane) (Found: C, 46·2; H, 2·6; N, 22·7; S, 9·0. $C_{14}H_9ClN_6O_2S$ requires C, 46·6; H, 2·5; N, 22·4; S, 8·9%).

(d) *With sodium methoxide*. Sodium methoxide (10 ml, 0·20N; 2 mmol) was added to 1-bromo-1-(*p*-chlorophenylthio)-4-(*p*-nitrophenyl)-2,3-diazabuta-1,3-diene (0·398 g, 1 mmol) dissolved in dry methanol (80 ml) and refluxed for 1·5 h. On cooling *p*-nitrobenzaldehyde azine (0·05 g, 16%) was precipitated. The methanolic solution was evaporated *in vacuo* to give 1-*methoxy*-1-(p-*chlorophenylthio*)-4-(p-*nitrophenyl*)-2,3-*diazabuta*-1,3-*diene* (18; $Ar^1 = p\text{-}NO_2C_6H_4$; $Ar^2 = p\text{-}ClC_6H_4$; $R = Me$) as a grey solid (0·21 g, 62%), m.p. 188° (from diethyl ether) (Found: C, 51·8; H, 3·75; S, 8·95. $C_{15}H_{12}ClN_3O_3S$ requires C, 51·5; H, 3·4; S, 9·2%).

(e) *With water*. To a solution of 1-bromo-1-(*p*-chlorophenylthio)-4-(*p*-nitrophenyl)-2,3-diazabuta-1,3-diene (0·398 g, 1 mmol) in dioxan (70 ml) was added water (30 ml); the resulting solution was maintained at 75 °C for 6 h. Ice-cold water was added to the cooled solution and the resulting suspension was stirred to coagulate the precipitate which was filtered off to give *N'*-(*p*-nitrobenzylidene)-*N*-(*p*-chlorophenylthiocarbonyl)hydrazine (23; $Ar = p\text{-}NO_2C_6H_4$; $R = p\text{-}ClC_6H_4$), m.p. 189—190 °C (from ethanol) (yield 95%).

Hydrolysis of the other bromoazines listed in Tables 1 and 2 under these conditions also gave the corresponding hydrazines (see Table 3 for analytical, reaction yield, and m.p. data).

(f) *With phenylhydrazine*. Phenylhydrazine (0·65 ml) was added to a suspension of 1-bromo-1-(*p*-chlorophenylthio)-4-(*p*-nitrophenyl)-2,3-diazabuta-1,3-diene (1·18 g, 3 mmol) in 95% ethanol (50 ml) and the mixture was stirred for four days at room temperature, during which time the colour of the suspension changed from yellow to deep red. A small amount of unchanged substrate (0·01 g) was filtered off and the solution was evaporated *in vacuo* to *ca.* 50% of its original volume. A red-brown precipitate separated (0·178 g, 42%), m.p. 141—146°. On recrystallization from methanol the 1-*phenyl*-3-(p-*chlorophenylthio*)-5-(p-*nitrobenzylidene*)*formazan* (21; $Ar^1 = p\text{-}NO_2C_6H_4$; $Ar^2 = p\text{-}ClC_6H_4$) had m.p. 154° (Found: C, 56·6; H, 3·4; N, 16·9; S, 7·8. $C_{20}H_{14}ClN_5O_2S$ requires C, 56·7; H, 3·3; N, 16·5; S, 7·6%). Further evaporation of the ethanolic solution gave another crop of the formazan which was obtained in total yield of 83%.

Synthesis of Bis-sulphides.—(a) *From* 1-*bromo*-1-(*alkyl- or aryl-thio*)-4-*aryl*-2,3-*diazabuta*-1,3-*dienes*. Thiophenol (0·22 ml, 2 mmol) and triethylamine (0·275 ml, 2 mmol) were added successively to a solution of 1-bromo-1-(*p*-chlorophenylthio)-4-(*p*-nitrophenyl)-2,3-diazabuta-1,3-diene (0·79 g, 2 mmol) in dry benzene (50 ml). The amine hydrobromide was filtered off after 2 h and the benzene was evaporated to leave a yellow gummy solid. Repeated recrystallization from pentane–diethyl ether gave 1-*phenylthio*-1-(*p*-*chlorophenylthio*)-4-(p-*nitrophenyl*)-2,3-*diazabuta*-1,3-*diene* (10; $Ar = p\text{-}NO_2C_6H_4$; $R^1 = p\text{-}ClC_6H_4$; $R^2 =$

Ph) (0·54 g, 68%), m.p. 94° (Found: C, 56·6; H, 3·3; N, 9·9; S, 15·5. $C_{20}H_{14}ClN_3O_2S_2$ requires C, 56·2; H, 3·2; N, 9·8%; S, 14·9).

(b) *From* 1,1-*dibromo*-4-*aryl*-2,3-*diazabuta*-1,3-*diene*. Toluene-α-thiol (0·75 ml, 6 mmol) and triethylamine (0·55 g, 4 mmol) were added successively to 1,1-dibromo-4-(*p*-nitrophenyl)-2,3-diazabuta-1,3-diene (0·67 g, 2 mmol) in dry benzene (30 ml). After 1 h at reflux, triethylamine hydrobromide was filtered off and evaporation of the filtrate gave 1,1-*bisbenzylthio*-4-(p-*nitrophenyl*)-2,3-*diazabuta*-1,3-*diene* (10; Ar = *p*-$NO_2C_6H_4$; $R^1 = R^2 = PhCH_2$) as a yellow solid, m.p. 130° (from ether) (Found: C, 62·8; H, 4·3; N, 10·2. $C_{22}H_{19}N_3O_2S_2$ requires C, 62·7; H, 4·5; N, 10·0%).

Table 4 contains m.p., yield, and analytical data for the dithiols prepared by routes (a) and/or (b) above.

TABLE 4

The bis-sulphides, *p*-$NO_2{\cdot}C_6H_4{\cdot}CH{=}N{\cdot}N{=}C(SR^1){\cdot}SR^2$

				Found (%)				Calc. (%)		
R^1	R^2	M.p. (°C)	Yield (%)	C	H	N	Formula	C	H	N
p-ClC_6H_4	Ph	94	68	56·4	3·2	9·5	$C_{20}H_{14}ClN_3O_2S_2$	56·2	3·2	9·8
CH_2Ph	CH_2Ph	130	56	62·6	3·4	9·9	$C_{22}H_{19}N_3O_2S_2$	62·7	3·5	9·9
Et	Et	90	48	48·5	5·0	14·2	$C_{12}H_{15}N_3O_2S_2$	48·4	5·0	14·1
CH_2Ph	*p*-ClC_6H_4	121	41	54·5	3·7	9·2	$C_{21}H_{16}ClN_3O_2S_2$	54·4	3·6	9·5

Kinetic Method.—The kinetics of hydrolysis of the monobromo-azines (9) were followed in aqueous dioxan using a Unicam SP 800 spectrophotometer. Usually the decrease in absorption at 310 nm due to disappearance of the starting material was used. In all cases the reaction cells were thermostatted at 25 °C unless otherwise stated. Ionic strength was normally maintained at a constant value of 0·1M. Since the hydrolysis rates for most of the compounds studied were independent of the pH of the solution (within wide limits) the solutions used were unbuffered. In the one case where buffers were necessary (with the *p*-nitro-derivative, see text) a combined pH stat-spectrophotometric technique was used in which a Radiometer pH-stat was fitted into a Cary 14 IR spectrometer.[8] Reaction was initiated in all cases by the addition of a drop of a concentrated (10^{-2}M) solution of the substrate in dioxan to the solvent in the reaction cell.

Except in the case of the *p*-nitro-derivative (9; R^1 = *p*-$NO_2C_6H_4$) mentioned above (where subsequent reaction intervened) the observed optical density *vs.* time plots fitted exactly a pseudo-first-order kinetic form and stable and reproducible infinity values were obtained. Repetitive scans of the u.v. region showed that the conversion of (9) to (23) was characterised by tight isosbestic points; the build-up of intermediate products was therefore excluded. The rate constants were determined graphically using either (*a*) the experimental infinity value or (*b*) the method of Guggenheim, the optical density charge being measured to *ca.* 3 half-lives.

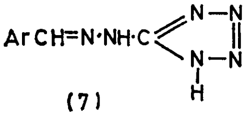
In some earlier probe kinetic experiments, the rates of hydrolysis were also followed in 80% dioxan at elevated temperatures. The course of the reaction was monitored by titration of the bromide ion released using the Volhard technique. To achieve reliable end-point detection the substrate was of necessity more concentrated than required using the spectrophotometric technique. Typically 10^{-2}M-solutions were used; this had the dual disadvantage: (*a*) the solubility of some of the substrates was too low under these conditions to permit measurement and (*b*) the calculated pseudo-first-order rate constants were not constant during a kinetic experiment but drifted upwards as the reaction proceeded. In these cases the rate constant at zero time was obtained by extrapolating a plot of the observed rate constants *vs.* time back to time = 0.

RESULTS AND DISCUSSION

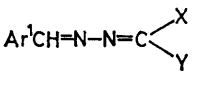
Direct chlorination of aldehyde azines (4) (1,4-diaryl-2,3-diaza-1,3-butadienes) may result in replacement of one or two methine hydrogens by chlorine to give (5) and (6) depending on reaction conditions.[9] Direct bromination, however, is more difficult and considerable cleavage of the azine to regenerate the aldehyde results.[10] Also when an unsymmetrical azine is used two monosubstituted products are possible. The required monobrominated thiol substituted azines (9) were, therefore, prepared indirectly.

$ArCH{=}N{-}N{=}CHAr$ (4) $ArCCl{=}N{-}N{=}CHAr$ (5) $ArCCl{=}N{-}N{=}CClAr$ (6)

Bromination of the tetrazolylhydrazones (7) in aqueous acetic acid results in oxidative cleavage of the tetrazole ring and formation of 1,1-dibromo-4-aryl-2,3-diaza-1,3-butadienes (8) (*i.e.* 1,1-dibromoazines).[11] We have recently found that under suitable conditions the halogens may be successively replaced by various oxygen and nitrogen nucleophiles.[12] We have now found that replacement of one bromine by thiols to give (9) is also possible. Under more vigorous reaction conditions, in addition to (9), the disubstituted product (10) was also isolated. The only similar materials reported [13] result



(7)



(8) X = Y = Br
(9) $X = SR^1$, Y = Br
(10) $X = SR^1$, $Y = SR^2$
(11) $X = SAr^2$, Y = NHPh
(12) $X = SAr^2$, $Y = NR_2$

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[8] A. F. Hegarty, M. P. Cashman, and F. L. Scott, *J.C.S. Perkin II*, 1972, 44.

[9] K. Issleib and A. Balszweit, *Ber.*, 1966, **99**, 1316; R. Stolle and K. Thoma, *J. prakt. Chem.*, 1906, **73**, 288.

[10] F. L. Scott and P. A. Cashell, unpublished results.

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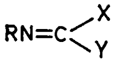
[12] F. L. Scott, J. A. Cronin, and J. Donovan, *Tetrahedron Letters*, 1969, 4615.

[13] E. Kuehle, *Angew. Chem. Internat. Edn.*, 1962, **1**, 339; 1969, **8**, 20.

from the reaction of thiolate ions with isocyanogen dichlorides (13) which yields the 1-chlorothioformimidates

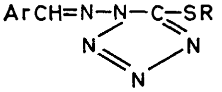


(13) X = Y = Cl

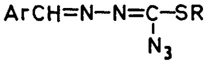
(14) X = SR; Y = Cl

(14). Under appropriate conditions displacement of Br in (9) could be achieved by a wide range of nucleophiles, yielding products which are difficult to synthesize by alternative routes. Thus the bromides (9) reacted in refluxing benzene with aniline to yield an *S*-substituted isothiosemicarbazide (11) (which is also an isothiourea derivative). Seondary amines react in a similar manner to yield *N*,*S*-alkyl or aryl derivatives (12). This reaction parallels that of *N*-sulphonyl imino-thioesters.[14] Reactions of compounds with the group $ArS(NR_2)C$ attached to either carbon or nitrogen have been widely investigated.[15]

The bromides (9) also react with sodium azide to give the novel 5-mercaptotetrazoles (15), presumably formed by the spontaneous cyclization of the isomeric azide (16). The tetrazole structure (15) is supported by i.r. evidence

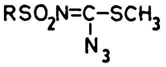


(15)



$$ArCH{=}N{-}N{=}\underset{N_3}{C}{-}SR$$

(16)

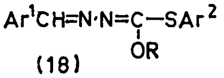


$$RSO_2N{=}\underset{N_3}{C}{-}SCH_3$$

(17)

and by the absence of the characteristic azide-stretching absorption at *ca.* 2200 cm^{-1}. It has been reported[16] that the reaction of sulphonyl-1-chlorothioimidates with azide ion yields the corresponding azides (17) without cyclization. Clearly then cyclization is dependent on the donor properties of the imino nitrogen in (16).

Reaction of alkoxide ions with compounds (9) yields the compounds (18), which could also be prepared by



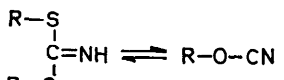
$$Ar^1CH{=}N{\cdot}N{=}\underset{OR}{C}{-}SAr^2$$

(18)

starting with the dibromide (8) and replacing the Br groups in the reverse order, *i.e.* firstly by the alcohol and then by the thiol. The only other account of the synthesis of such iminothiocarbonates is recent and involves the addition of an alcohol or thiol to an alkyl thiocyanate (19) or alkyl cyanate (20) respectively.[17]

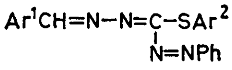
R–S–CN

(19)



(20)

The formazan (21) was formed by the reaction of (9) with phenylhydrazine in 95% alcohol at room temperature. The formazan (21) is the *S*-aryl sulphide of dithizone (22) which is of considerable utility in analytical chemistry.[18]



$$Ar^1CH{=}N{-}N{=}\underset{N{=}NPh}{C}{-}SAr^2$$

(21)

$ArN{=}N{\cdot}CS{\cdot}NH{\cdot}NHPh$

(22)

Kinetic Studies.—Hydrolysis of the *S*-aryl or *S*-alkyl monobromoazines (9; R^1 = aryl or alkyl) occurred smoothly in aqueous dioxan and in all cases the corresponding novel aryl or alkylthio-carbonylhydrazines (23) were formed in good yield. Typical reaction conditions involved refluxing the substrate in 60% dioxan for 1 h. A longer reaction time (or the addition of acid or base) resulted in subsequent cleavage of (23) to give the symmetrical azine, ArCH=N–N=CHAr, as major product. Azine formation was most pronounced when the hydrazine (23) had a good leaving thiolate group (*e.g.* R^1 = *p*-$NO_2C_6H_4$).

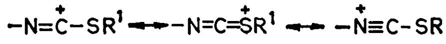
$ArCH{=}N{\cdot}NH{\cdot}CO{\cdot}SR^1$ (23)

The kinetics of hydrolysis of (9) to (23) were studied in 40% dioxan at 25°. Substituents in the remote Ar ring have little influence on the rate of hydrolysis of the related aminohydrazonyl bromides;[12] two series of compounds with Ar = *p*-ClC_6H_4 or Ar = *p*-$NO_2C_6H_4$ were chosen as being representative of the series. For the five substituted compounds (9) (with R^1 = *p*-fluoro, *p*-methyl, *p*-chloro, *p*-nitrophenyl and phenyl); the results obtained are presented in Table 5. The rate of solvolysis increases markedly with increasing electron donation from R^1; a plot of log *k vs.* the corresponding σ values of McDaniel–Brown[19] gave a ρ value of −1·0 (with *r* = 0·978). This represents the build-up of considerable positive charge on sulphur in the transition state. Since the adjacent nitrogen is also available to stabilize and delocalize the charge on carbon in the octet-stabilized form (24c), the total charge on the transition state must be considerable. It is interesting to compare the relative abilities of neighbouring oxygen

TABLE 5

Rate constants (s^{-1}) for the solvolysis of the mono-bromoazines (9; Ar = *p*-ClC_6H_4; R^1 = *p*-XC_6H_4) at 25° in 40% dioxan–water (μ = 0·10, $NaNO_3$)

Substituent X	10^4k
Me	67
H	51
F	37
Cl	19
NO_2	8·0



$$-N{=}\overset{+}{C}{-}SR^1 \longleftrightarrow -N{=}C{=}\overset{+}{S}R^1 \longleftrightarrow -\overset{+}{N}{\equiv}C{-}SR^1$$

(24a) (24b) (24c)

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[14] R. Niedlein and W. Haussman, *Ber.*, 1968, 553.

[15] R. Gompper and W. Elser, *Annalen*, 1969, **725**, 64.

[16] R. Neidlein and W. Haussman, *Tetrahedron Letters*, 1966, 5401.

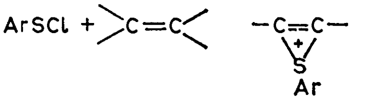
[17] W. D. Habicher and R. Mayer, *Angew. Chem. Internat. Edn.*, 1968, **7**, 67.

[18] H. M. N. Irving and U. S. Mahnot, *Talanta*, 1968, **15**, 811.

[19] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.

and sulphur in stabilizing a carbonium-ion centre. There is some evidence that while sulphur shows less tendency to delocalize its lone-pair electrons through π bond formation, this is more than compensated by the less electronegative character of sulphur (relative to oxygen).[20,21] Consistent with this, we have found in preliminary studies that the oxy-analogues of (9) solvolyse *ca.* 10 times more slowly (in 80% dioxan at 75°).

A ρ value of similar sign and magnitude ($-0{\cdot}66$) has been reported in the reaction of 4-substituted 2-nitrobenzenesulphenyl chloride with cyclohexene in acetic acid at 25°.[22] The proposed intermediate (25) also


(25)

involves charge distribution over three atoms. When the carbonium ion can be delocalized only between one carbon atom and sulphur the charge borne by sulphur is predictably higher. Thus Bordwell[21] has reported a ρ value of $-2{\cdot}6$ for the hydrolysis of $ArSCH_2Cl$ in water for the variation of Ar. Taken overall, the data presented on these compounds supports a mechanism involving direct ionization, *i.e.* formation of $Ar\overset{+}{S}CH_2$. The recent work of Queen[20] is also of interest. Data for the hydrolysis of chlorothioformates RSCOCl in water suggested the presence of the intermediate $RS\overset{+}{C}O$ and from his data we have calculated a Taft ρ^* value of $-2{\cdot}3$ (with $\delta = 0{\cdot}7$) for the variation of the alkyl substituent R. Although Taft and Hammett ρ values are not strictly comparable, this is in line with the results obtained in the present study.

Further evidence to support rate-determining thioazocarbonium-ion formation (24) is provided by the following: The solvolysis of the unsubstituted compound (9, $Ar = p\text{-}ClC_6H_4$; $R^1 = C_6H_5$) was studied in various dioxan–water and acetone–water mixtures (in all cases the ionic strength was maintained at 0·1M-$NaNO_3$), see Table 6. A plot of log k *vs.* the corresponding Y values of the solvent[23,24] gave Grunwald–Winstein m values of 1·15 ($r = 0{\cdot}999$) for dioxan–water and 1·10 ($r = 0{\cdot}997$) for acetone–water. This high dependence on the ionizing power of the solvent, greater than that of the standard compound t-butyl chloride[24] and approximately the same as for 1-adamantyl bromide,[25] is good evidence for appreciable charge formation in the transition state.

The solvolysis of (9) is also very much dependent on the nature of added salts (see Table 7). The presence of 0·1M-sodium nitrate causes the rate of hydrolysis to increase 1·7-fold, but a similar concentration of sodium bromide decreases the rate of hydrolysis *ca.* 15-fold. When allowance is made for the rate enhancement due to increasing the ionic strength by the presence of sodium bromide, the overall rate-decrease due to the common-ion is *ca.* 26-fold. Such a large common-ion effect can only be explained in terms of the existence of a long-lived and discriminatory carbonium-ion species.

TABLE 6

Rate constants (s^{-1}) for the solvolysis of (9; $Ar = p\text{-}ClC_6H_4$, $R^1 = C_6H_5$) in various dioxan and acetone–water mixtures at 25° ($\mu = 0{\cdot}10$, $NaNO_3$)

Solvent	10^4k
30% Dioxan	186
40% Dioxan	51
50% Dioxan	12
60% Dioxan	1·6
70% Dioxan	0·26
40% Acetone	77
50% Acetone	21
60% Acetone	5·3

TABLE 7

Relative rates of solvolysis of (9; $Ar = p\text{-}ClC_6H_4$; $R^1 = C_6H_5$) at 25° in the presence of various added salts (in 40% dioxan)

(Salt)	Ionic strength	$k_{rel.}$*
	0	1
0·10M-$NaNO_3$	0·10	1·7
0·10M-NaBr	0·10	0·059
0·05M-NaBr	0·10	0·092
0·01M-NaBr	0·10	0·32
0·80M-$NaClO_4$	0·80	6·5
0·80M-NaOH	0·80	0·96
0·80M-$HClO_4$	0·80	21·9
0·08M-$HClO_4$	0·80	8·5

* k for {salt} = 0 is $3{\cdot}07 \times 10^{-3}\ s^{-1}$.

A possible S_N2-type displacement by water (or hydroxide ion) as observed in the case of the analogous acyl chlorides[26] is ruled out by the observed independence of the rate of hydrolysis of hydroxide ion concentration. In fact in 0·8M-hydroxide ion the solvolysis rate is remarkably similar to that in neutral solution (*i.e.* there is a small rate depression when allowance is made for the ionic strength of the medium). In the presence of 0·8M-perchloric acid there is a small rate increase (*ca.* 3-fold relative to sodium perchlorate) which may be due to the incursion of an acid-catalysed path or, more likely, due to a specific salt effect. Therefore, the rate of hydrolysis of (9) is very much independent of pH over the range 0—14; this is entirely consistent with the proposed formation of the resonance stabilized species (24) in the rate-determining step.

Comparable results were obtained using (9; $Ar = p\text{-}NO_2C_6H_4$, $R^1 = p\text{-}ClC_6H_4$) as substrate at 75° in 80%

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[20] A. Queen and T. A. Nour, *Canad. J. Chem.*, 1970, **48**, 522.

[21] F. G. Bordwell, G. D. Cooper, and H. Morita, *J. Amer. Chem. Soc.*, 1957, **79**, 376.

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[25] D. J. Raber, R. C. Bingham, J. M. Harris, J. L. Fry, and P. R. Schleyer, *J. Amer. Chem. Soc.*, 1970, **72**, 5977; D. N. Kevill, K. C. Kolwyck, and R. L. Weitl, *J. Amer. Chem. Soc.*, 1970, **92**, 7300.

[26] M. L. Bender and M. C. Chen, *J. Amer. Chem. Soc.*, 1963, **85**, 30.

dioxan (Table 8). In this case the rate constants were followed titrimetrically and consequently at higher substrate concentration (*viz.* 10^{-2} M). Since both the acid concentration and the ionic strength of the solution increase appreciably during the kinetic run the apparent first-order rate constants increased during a kinetic run. The values quoted were obtained by extrapolation back to zero percent reacted, *i.e.* they represent initial rates and are therefore less reliable than the spectrophotometrically measured rate constants.

TABLE 8

Rates of solvolysis of (9; Ar = p-$NO_2C_6H_4$; R^1 = p-ClC_6H_4) at 75° in aqueous dioxan

Salt *	None	$NaNO_3$	HNO_3	NaOH	NaBr	CH_3CO_2Na
$10^4k/s^{-1}$	3·1	5·3	8·8	0·95	1·4	1·0

* (Substrate) = (Salt) = 10^{-2}M.

The starting dibromoazine (8) is relatively unreactive in solvolysis; presumably the presence of the Br (rather than S–R) group destabilizes carbonium-ion formation. Compound (8) however does undergo S_N2 attack.[27] The monobromoazine (9) is, as shown in this study, very reactive under conditions which favour S_N1 reaction. Isolation of (9) therefore depends upon the use of reaction conditions where S_N2 attack by thiophenoxide is enhanced but S_N1 solvolysis is inhibited. The reaction of sodium thiophenoxides with the dibromoazines (8) in diethyl ether best satisfies these conditions.

[1/1687 *Received*, 15*th September*, 1971]

[27] D. A. Cronin, unpublished work.