Oxidation of Some 4-Substituted *N*-Aminopyridinium Salts

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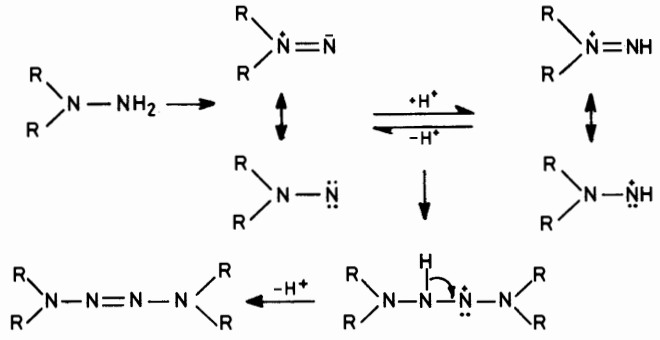
Oxidation of 4-substituted *N*-aminopyridinium salts with aqueous bromine yields either the corresponding 1,1′-azopyridinium salts or 1-pyridiniopyridinium salts depending upon the nature of the 4-substituent. Thus *N*-amination and subsequent oxidation of 4-dimethylamino-, 4-methylphenylamino-, 4-methoxy-, and 4-methylthio-pyridine yields the corresponding tetrazenes, but similar treatment of 4-t-butyl- and 4-methyl-pyridine yields the corresponding 1-pyridiniopyridinium salts.

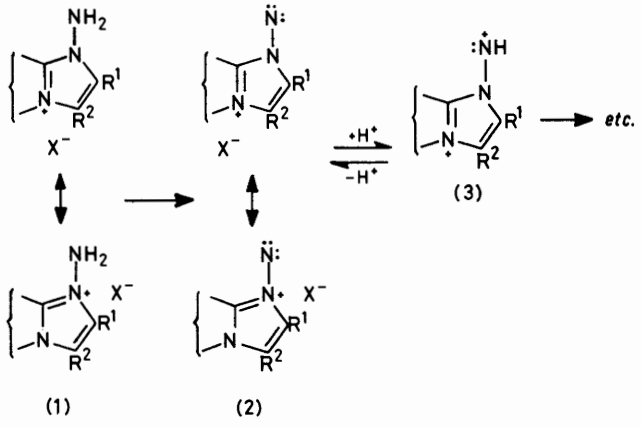
THE formation of tetrazenes by oxidation of 1,1-disubstituted hydrazines, with bromine produced by acidification of potassium bromate, has been shown [1] to proceed *via* an aminonitrene which couples with its conjugate acid as shown in the Scheme; such coupling is inhibited by both strongly basic and strongly acidic solutions.



SCHEME

A variety of quaternary *N*-aminoimidazoles and fused *N*-aminoimidazoles (1) have been shown [2-7] to yield tetrazenes on oxidation with aqueous bromine. The use of saturated aqueous bromine (pH *ca.* 2.5) in these instances and its effective use in the cases previously referred to [1] suggests a common mechanism for tetrazene formation. The observation that the perbromide (26) obtained by treating the *N*-amino-salt [2] (25) with saturated aqueous bromine is identical with that obtained by similar treatment of the corresponding tetrazene [2] (27) provides additional evidence that tetrazene formation from the *N*-amino-salt occurs in the aqueous bromine rather than *via* a brominated intermediate and the agency of the boiling acetone used for subsequent decomposition of the perbromide. Further, in the case of the 2-methyl compounds (28) [2] and (29),[7] in which ready bromination occurred in the five-membered ring, precipitation of the perbromides of the respective bromo-*N*-amino-salts (30) and (31) inhibited oxidation to the tetrazene.

Presumably in the oxidation of the *N*-aminoimidazole derivatives [2-7] (1) mesomeric distribution of the charge on the quaternary centre is sufficient to allow protonation of the initially formed aminonitrene (2), giving a doubly charged conjugate acid (3). Subsequent coupling with unprotonated aminonitrene would then yield the corresponding tetrazene. We were interested in the



degree of charge distribution necessary in quaternary *N*-amino-compounds in order that protonation of the derived aminonitrene and subsequent conversion into the corresponding tetrazene could occur. For our study we chose the 4-substituted pyridines (4)—(9), which were *N*-aminated in good yield with *O*-*p*-tolylsulphonylhydroxylamine.[6] Treatment of the 4-methoxy- and 4-methylthio-*N*-aminopyridinium salts (12) and (13) and also the

[1] W. R. McBride and E. M. Bens, *J. Amer. Chem. Soc.*, 1959, **81**, 5546.
[2] E. E. Glover and M. Yorke, *J. Chem. Soc.* (*C*), 1971, 3280.
[3] D. C. Bishop, E. E. Glover, and K. T. Rowbottom, *J.C.S. Perkin I*, 1972, 2927.
[4] E. E. Glover and K. T. Rowbottom, *J.C.S. Perkin I*, 1973, 842.
[5] E. E. Glover and K. D. Vaughan, *J.C.S. Perkin I*, 1974, 1137.
[6] E. E. Glover and K. T. Rowbottom, *J.C.S. Perkin I*, 1976, 367.
[7] D. G. Doughty, E. E. Glover, and K. D. Vaughan, *J.C.S. Perkin I*, 1977, 78.

TABLE 1

N-Aminopyridinium salts

Reactants	Product	X	Yield (%)	M.p. (°C)	Cryst. solvent	Found (%) C	H	N	Reqd. (%) C	H	N
(4) (1.0 g) in $CHCl_3$ (30 ml) + TSH [a] (3.0 g) [b] in $CHCl_3$ (30 ml) [c,d]	(10)	$C_7H_7SO_3$ [e]	88	95—97	$CHCl_3$–Et_2O	55.8	5.8	10.0	55.7	5.75	10.0
(5) (5.0 g) in $CHCl_3$ (30 ml) + TSH [a] (10.7 g) [b] in $CHCl_3$ (100 ml) [c,d]	(11)	$C_7H_7SO_3$ [e]	94	118—120	$CHCl_3$–Et_2O	59.5	7.05	8.6	59.6	6.9	8.7
(6) (0.3 g) in $CHCl_3$ (15 ml) + TSH [a] (0.78 g) [b] in $CHCl_3$ (11 ml) [c,f]	(12) *	$C_7H_7SO_3$ [e]	97	132—134	$CHCl_3$–Et_2O	52.8	5.2	9.5	52.7	5.4	9.5
(7) (3.62 g) in $CHCl_3$ (30 ml) + TSH [a] (8.7 g) [b] in $CHCl_3$ (87 ml) [c,g]	(13) †	ClO_4	72	140—143	EtOH–Et_2O	30.2	3.4	11.55	29.9	3.8	11.6
(8) (1.0 g) in $CHCl_3$ (20 ml) + TSH [a] (2.3 g) [b] in $CHCl_3$ (46 ml) [c,h]	(14)	ClO_4	67	178—179	MeOH–Et_2O	35.5	4.9	17.8	35.4	5.1	17.7
(9) [i] (0.5 g) in $CHCl_3$ (30 ml) + TSH [a] (0.75 g) [b] in $CHCl_3$ (30 ml) [c,j]	(15)	ClO_4	61	127	MeOH–Et_2O	48.2	4.5	14.0	48.1	4.7	14.0

[a] *O*-*p*-Tolylsulphonylhydroxylamine. [b] Weight of ethyl *O*-*p*-tolylsulphonylacetohydroximate from which the TSH was derived.[6] [c] The TSH solution was added in bulk. [d] The mixture was stirred for 1 h after which ether was added to incipient precipitation. The mixture was treated with more ether (50 ml). The product which separated on cooling was then filtered off and recrystallized. [e] Toluene-*p*-sulphonate. [f] The mixture was stirred for 1.5 h and then treated with ether to incipient precipitation. Trituration and cooling gave a solid which was filtered off and recrystallized. [g] The mixture was stirred for 1 h after which ether (150 ml) was added and the yellow solution decanted from the red oil which had separated. The oil was then dissolved in boiling ethanol (50 ml) and 70% perchloric acid (5 ml) added. Addition of ether followed by cooling and trituration gave the product, which was filtered off and recrystallized. [h] The mixture was stirred for 1 h, then ether (200 ml) was added and the mixture cooled to 0 °C for 0.5 h. The solid which separated was filtered off, dissolved in methanol, and treated with 70% perchloric acid (35 drops). Addition of ether precipitated the product, which was filtered off and recrystallized. [i] Obtained by heating a mixture of 4-chloropyridine (2.5 g) and redistilled *N*-methylaniline (5.0 g) under reflux on a boiling water bath for 2 h. The resulting viscous red oil was cooled and triturated, yielding a brown solid which was filtered off and dissolved in water (20 ml). The aqueous layer was extracted with ether and then basified with concentrated aqueous ammonia before extraction with chloroform. The dried (Na_2CO_3) chloroform extract was then evaporated and the residue distilled giving the *base* as an oil, b.p. 154—156 °C at 4 mmHg and 124—126 °C at 0.7 mmHg (3.0 g, 74%) (Found: C, 78.0; H, 6.7; N, 15.3. $C_{12}H_{12}N_2$ requires C, 78.2; H, 6.6; N, 15.2%). The *picrate* crystallized from ethanol and had m.p. 152—153 °C (Found: C, 52.3; H, 3.6; N, 16.9. $C_{12}H_{12}N_2$, $C_6H_3N_3O_7$ requires C, 52.3; H, 3.7; N, 16.95%). [j] The mixture was stirred for 3 h and then treated with ether (250 ml). The gum which precipitated was separated and dissolved in methanol (30ml). Addition of 70% perchloric acid (12 drops) followed by ether, with subsequent trituration, gave the perchlorate, which was filtered off and recrystallized.

* $\lambda_{max.}$ (H_2O) 224 and 251 nm ($\log_{10}\varepsilon$ 4.13 and 4.08). † $\lambda_{max.}$ (H_2O) 232 and 308 nm ($\log_{10}\varepsilon$ 3.89 and 4.30).

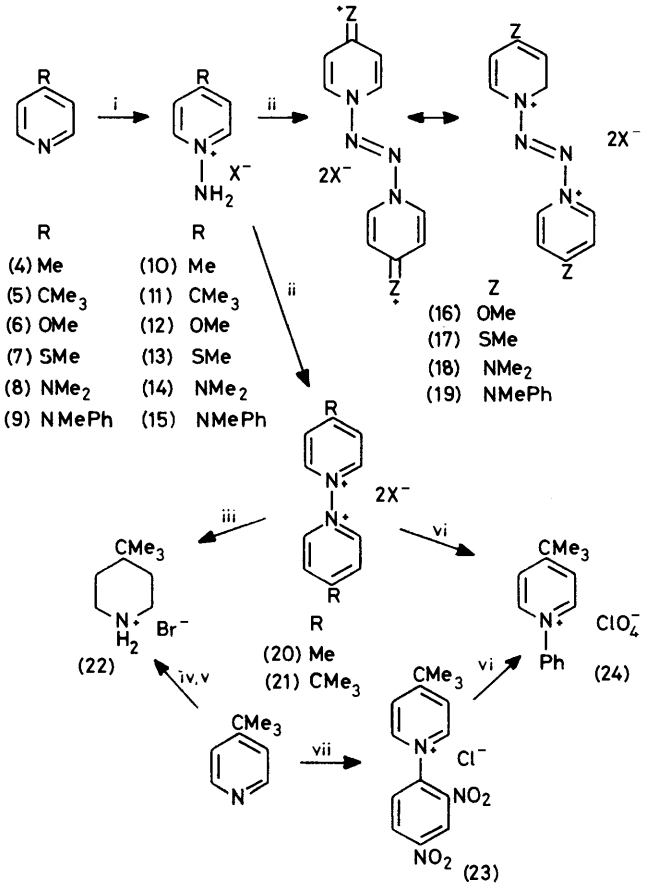
TABLE 2

1,1′-Azopyridinium salts

Reactants	Product	X	Yield (%)	M.p. (°C)	Cryst. solvent	Found (%) C	H	N	Reqd. (%) C	H	N
(12) [a] (0.25 g) in H_2O (3 ml) + sat.aq.Br_2 (30 ml) [b,c]	(16) [d]	Br	29	260 [e]	48% HBr–Me_2CO	33.8	3.7	13.2	34.0	3.8	13.2 [f]
	(16)	ClO_4 [g]		226—228	MeCN–Et_2O	32.2	3.1	12.4	32.4	3.2	12.6
(13) [h] (0.1 g) in H_2O (10 ml) + sat.aq.Br_2 (30 ml) [b,i]	(17) [j]	ClO_4	32	175—185 [k]	MeOH–Et_2O	30.0	3.2	11.5	30.2	3.0	11.7
(14) [h] (0.7 g) in H_2O (50 ml) + sat.aq.Br_2 (50 ml) [b,l]	(18) [m]	Br	56	272 [k]	MeOH–Et_2O	36.2	5.2	17.95	35.9	5.2	17.95 [n]
	(18)	$C_6H_2N_3O_7$ [o]		270	MeOH	42.5	3.3		42.9	3.3	
(15) [h] (0.3 g) in H_2O (20 ml) + sat.aq.Br_2 (80 ml) [b,p]	(19) [q,r]	Br	68	230—232 [k]	MeOH–Et_2O	48.7	4.4	14.2	48.7	4.8	14.2 [n]
	(19)	ClO_4 [s]		242—244 [k]	H_2O	47.9	4.0	13.85	48.4	4.1	14.1

[a] Toluene-*p*-sulphonate salt. [b] The saturated aqueous bromine was added in bulk. [c] The mixture was set aside for 0.25 h, after which the perbromide was filtered off, dried in the atmosphere, and then boiled with absolute acetone (20 ml). The resulting solid was filtered off and recrystallized. [d] $\lambda_{max.}$ (aq. 10% HBr) 345 nm ($\log_{10}\varepsilon$ 4.52). [e] Decomposed without melting at the temperature shown. [f] Monohydrate. [g] Obtained by treating a solution of the bromide in the minimum volume of methanol with 70% perchloric acid and cooling the solution. [h] Perchlorate salt. [i] The mixture was set aside for 17 h, after which the perbromide was filtered off and boiled with absolute acetone (10 ml). The solution was then cooled in ice and the acetone decanted from the gummy precipitate. The precipitate was dissolved in methanol (10 ml) and 70% perchloric acid (3 drops) added. Ether was then added to incipient precipitation and the solution cooled and triturated; the solid which separated was filtered off and recrystallized. [j] $\lambda_{max.}$ (10% $HClO_4$) 422 nm ($\log_{10}\varepsilon$ 4.51). [k] With decomp. [l] The mixture was set aside for a further 0.5 h after which the perbromide was filtered off and boiled with absolute acetone. The resulting bromide was then filtered off and recrystallized. [m] $\lambda_{max.}$(H_2O) 249, 277sh, and 408 nm ($\log_{10}\varepsilon$ 4.14, 3.91, and 4.8). [n] Dihydrate. [o] Picrate. [p] The mixture was set aside for a further 3 h, after which the perbromide was filtered off and boiled with acetone (7.5 ml) and methanol (7.5 ml). Ether was then added, the solution cooled, and the bromide which separated filtered off and recrystallized. [q] $\lambda_{max.}$(H_2O) 256, 285sh, and 424 nm ($\log_{10}\varepsilon$ 4.14, 3.97, and 4.67). [r] The bromide was orange when dried *in vacuo* at 60 °C but turned yellow on exposure to the atmosphere. [s] Prepared by ion exchange on Amberlite IRA 400 (ClO_4^-).

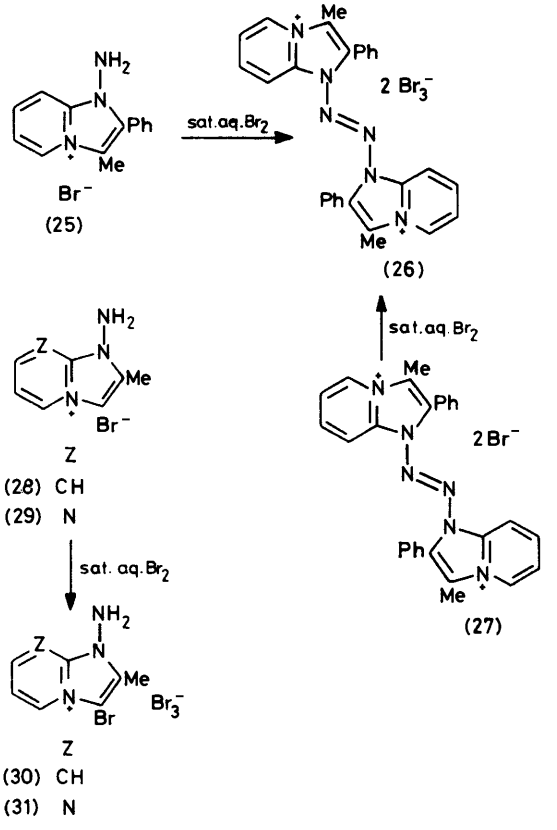
4-amino-derivatives (14) and (15) with saturated aqueous bromine precipitated the respective perbromide salts



Reagents: i, O-*p*-tolylsulphonylhydroxylamine; ii, sat. aq. Br_2; iii, H_2/Pt, iv, Na/$Me(CH_2)_3OH$; v, HBr; vi, $PhNH_2$; vii, 2,4-$(NO_2)_2C_6H_3Cl$.

(16)—(19), which were converted into the bromides by boiling acetone. Confirmation that tetrazene formation occurred in the saturated aqueous bromine and not subsequently in the boiling acetone was again obtained by showing the perbromide salt obtained by addition of bromine to the *N*-amino-bromide (15) to be identical with a sample obtained by similar treatment of the tetrazene dibromide (19).

Treatment of the 4-methyl and 4-t-butyl compounds (10) and (11) with saturated aqueous bromine did not



yield tetrazenes, giving instead the corresponding 1-pyridiniopyridinium salts (20) and (21). Similar treat-

TABLE 3

1,1′-Pyridiniopyridinium salts

Reactants	Product	X	Yield (%)	M.p. (°C)	Cryst. solvent	Found (%) C	H	N	Reqd (%) C	H	N
(10) [a] (2.0 g) in H_2O (20 ml) + sat.aq.Br_2 (100 ml) [b,c]	(20) [d]	ClO_4	10	140	MeOH–Et_2O	37.2	3.5	7.1	37.4	3.7	7.3
(11) [a,e] (2.0 g) in H_2O (20 ml) + sat.aq.Br_2 (80 ml) [b,f]	(21) [g,h,i]	Br	13.5	310 [j,k]	MeOH–Et_2O	50.0	6.2	6.5	50.25	6.1	6.5

[a] Toluene-*p*-sulphonate salt. [b] The saturated aqueous bromine was added in bulk. [c] The mixture was set aside for 2 h, then the aqueous phase was decanted from the red oil which had separated. The oil was kept under reduced pressure over anhydrous $CaCl_2$ overnight and the resulting solid boiled with acetone (40 ml) and ethanol (10 ml). The solid which separated was filtered off and dissolved in the minimum volume of methanol. Addition of 70% perchloric acid (2 drops) followed by ether precipitated the perchlorate, which was filtered off and recrystallized. [d] The ^1H n.m.r. spectrum in D_2O (1 ml) containing 48% DBr in D_2O (1 drop) showed a methyl singlet δ 2.97 and the AA′XX′ signal expected of a 4-substituted pyridinium system, the centres of the distorted doublets being at δ 9.51 and 8.42. [e] An attempt to oxidise (11) with bromine in acetic acid gave, after decomposition of an initially formed perbromide, 1-acetamido-4-t-butylpyridinium bromide, m.p. 203—205 °C (from $CHCl_3$–Et_2O) (Found: C, 48.7; H, 6.2; N, 9.9. $C_{11}H_{17}BrN_2O$ requires C, 48.4, H, 6.3; N, 10.3%). [f] The mixture was set aside for 1 h and then the aqueous phase was decanted from the red gum which was dried in the atmosphere. Absolute acetone (40 ml) was then added and the mixture boiled. After cooling the product was filtered off and recrystallized. [g] $\lambda_{max.}$ (H_2O) 254 nm ($\log_{10}\varepsilon$ 4.37). [h] The ^1H n.m.r. spectrum in D_2O showed a t-butyl singlet at δ 1.55 and the AA′XX′ signal expected of a 4-substituted pyridinium system, the centres of the distorted doublets being at δ 9.52 and 8.58. [i] A solution of (21) (0.116 g) in methanol (100 ml) was hydrogenated to completion over Adams catalyst. Work-up in the usual way gave *4-t-butylpiperidine hydrobromide*, m.p. 288—290 °C (from ethanol–ether) (0.078 g, 65%) (Found: C, 49.0; H, 9.1; N, 6.3. $C_9H_{19}N$,HBr requires C, 48.7; H, 9.1; N, 6.3%), identical with a sample obtained by slow reduction of 4-t-butylpyridine with an excess of sodium in butanol, with subsequent conversion into the hydrobromide. [j] With decomp. [k] In capillary.

ment of *N*-aminopyridinium bromide, however, did not yield any solid products.

The structure of the 1-pyridiniopyridinium salts was confirmed by hydrogenation of the 4,4′-di-t-butyl diquaternary salt (21), which yielded 4-t-butylpiperidine hydrobromide (22), identical with a sample obtained by reduction of 4-t-butylpyridine with sodium in butanol with subsequent conversion into the hydrobromide. Further, boiling the diquaternary dibromide (21) with aniline afforded the 1-phenyl-4-t-butylpyridinium ion, isolated as the perchlorate salt (24), identical with a sample obtained by similar treatment of the 2,4-dinitrophenyl quaternary salt (23). This last reaction is similar to that used by Zincke [8] for the preparation of 1-phenylpyridinium salts, and that recorded by Katritzky and Sammes [9] for the authentication of the 1-pyridinio-4-pyridone ion and hence of 4-chloropyridiniopyridinium salts, hitherto the only other recorded pyridiniopyridinium salts.

On the basis of the above observations we suggest that the degree of charge distribution in quaternary *N*-amino-salts necessary for tetrazene formation is that which results from mesomeric electron release by a heteroatom conjugated with the quaternary centre.

The mechanism of formation of our pyridiniopyridinium salts remains obscure but it seems improbable that they could be formed by nitrogen loss from an initially formed tetrazene with subsequent coupling of a pair of the resulting radical cations.

TABLE 4

1-Aryl-4-t-butylpyridinium salts

Reactants	Product	Yield (%)	M.p. (°C)	Cryst. solvent	Found (%) C	H	N	Reqd. (%) C	H	N
(5) (1.35 g) + 2,4-$(NO_2)_2C_6H_3Cl$ (2.1 g) in EtOH (10 ml) [a]	(23)	92	177	EtOH–Et_2O	50.2	5.5	11.6	50.6	5.1	11.8 [b]
(21) [c] (0.22 g) + $PhNH_2$ (0.3 g) in EtOH (20 ml) [d]	(24)	29	203—205	MeOH–Et_2O	58.0	5.8	4.6	57.8	5.8	4.5
(23) (1.0 g) + $PhNH_2$ (10 ml) [e]	(24)	20	203—204	MeOH–Et_2O						

[a] The solution was boiled under reflux for 3 h after which it was cooled and ether added. The solid which separated was then filtered off and recrystallized. [b] Monohydrate. [c] Bromide salt. [d] The solution was boiled under reflux for 5 h, then evaporated. The residual gum was washed thoroughly with ether and then boiled with chloroform (10 ml). On cooling aniline hydrobromide (0.041 g) separated and was filtered off. The filtrate was treated with ether (60 ml) and stored at −10 °C for 48 h. The liquid was then decanted and the residue dissolved in water (10 ml). Addition of 70% perchloric acid (2 ml) and cooling resulted in separation of the perchlorate salt, which was filtered off and recrystallized. [e] The mixture was boiled under gentle reflux for 1 h; it was then cooled, treated with ether (50 ml), and stored at −10 °C for 18 h. The liquid was then decanted off and the residue boiled with water (20 ml). After cooling in ice the aqueous layer was separated and treated with 70% perchloric acid (1 ml). The product which separated was washed with water followed by ether and then recrystallized.

EXPERIMENTAL

Except where otherwise stated, m.p.s were determined with a Kofler hot-stage apparatus. U.v. spectra were determined with a Perkin-Elmer 137 spectrophotometer and ^1H n.m.r. spectra with a Perkin-Elmer R12A spectrometer (external Me_4Si standard).

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[8] T. Zincke, *Annalen*, 1904, **330**, 361.
[9] A. R. Katritzky and M. P. Sammes, *J.C.S. Chem. Comm.*, 1975, 247.