Oxidation of 1-Aminopyridinium, 1-Aminoquinolinium, and 2-Aminoisoquinolinium Bromides with Lead(IV) Acetate

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The title reactions afford, respectively, 1-acetamido-2-pyridone, 1-acetamido-2-quinolone, and 2-acetamido-1-isoquinolone. In the case of 1-amino-2-methyl- and 1-amino-4-methyl-pyridinium bromides, ring bromination accompanies oxidation, suggesting the involvement of the bromide ion in the oxidation process.

OXIDATION of some 1-amino-4-alkylpyridinium salts with aqueous bromine has been reported [1] to yield 4,4'-dialkylpyridiniopyridinium salts (1). In a search for a more satisfactory route to these salts and also to obtain insight into the mechanism of their oxidative formation from 1-aminopyridinium salts, we are investigating the effect of other oxidants on 1-aminopyridinium and related salts.

A variety of 1,1'-disubstituted hydrazines have been oxidized by lead(IV) acetate,[2-6] and such hydrazines have been classified [2] according to the nature of the further reaction of the intermediate aminonitrenes. Thus, 1,1-dialkyl- and 1,1-diaryl-hydrazines [3] and *N*-amimophthalimide [4,5] undergo intermolecular reactions giving either tetrazenes or their decomposition products. Other aminonitrenes undergo extrusion of a neutral molecule and subsequent intramolecular reaction; thus the aminonitrene (3) derived from the 1-amino-2-pyridone (2) undergoes extrusion of carbon monoxide yielding the pyrazine (4).[6]

Treatment of the quaternary bromides (5), (18), and (21) with lead(IV) acetate in acetic acid solution afforded the respective acetylated cyclic hydrazides (10), (19), and (22), and subsequent hydrolysis gave the corresponding cyclic hydrazides (14), (20), and (23). The acetyl compound (10) was very hygroscopic and the hydrated form sublimed unchanged at either atmospheric or

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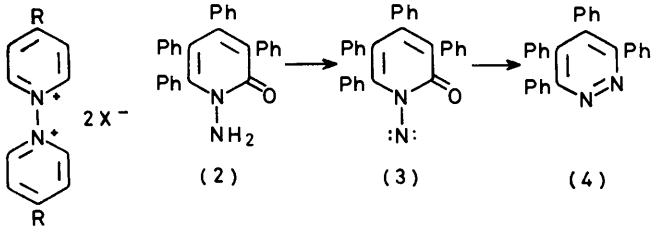


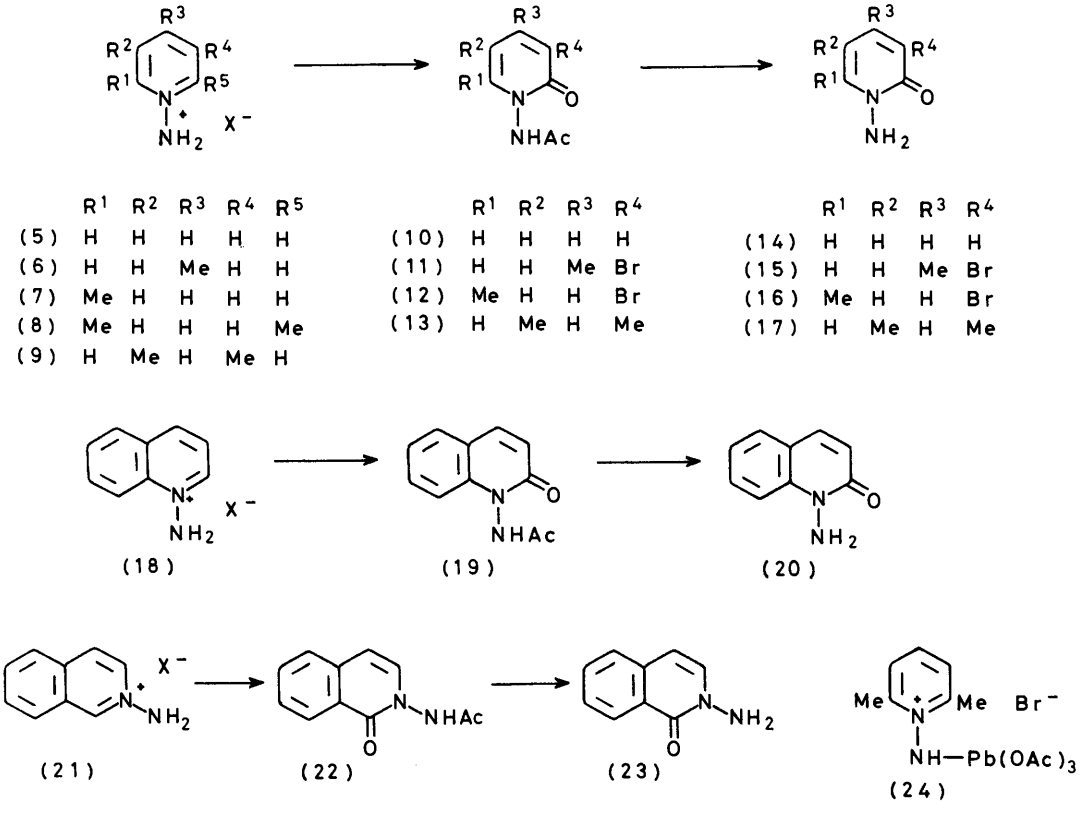
(1) (2) (3) (4)

reduced pressure; an anhydrous sample was, however, obtained by repeated evaporation of solutions in dry benzene. The i.r. spectra of anhydrous and hydrated samples of (10) showed marked differences between the stretching frequencies of corresponding carbonyl groups, and spectra frequently showed samples to contain both anhydrous and hydrated forms.

Oxidation of *N*-aminopyridinium bromide (5) with lead(IV) acetate in methylene chloride solution likewise yielded 1-acetamido-2-pyridone (10) thereby indicating that both of the oxygen functions in (10) were derived from the lead(IV) acetate.

Previously the oxidation of benzoic acid hydrazide [7] and that of phenylhydrazine [8] have been suggested to proceed *via* an intermediate lead triacetate complex; the possibility of our oxidations involving similar intermediates and proceeding *via* the mechanism shown in the Scheme was, therefore, considered. An attempt to isolate the lead triacetate complex (24), further reaction of which in accordance with the Scheme is not possible, was, however, unsuccessful. Further, the formation of the brominated derivatives (11) and (12) when 1-amino-4-methyl- and 1-amino-2-methyl-pyridinium bromide, respectively, were treated with lead(IV) acetate suggested a more complex mechanism than that shown in the Scheme.

The structure of the brominated derivative (11) followed from its analytical figures and ^{1}H n.m.r. spectrum; the latter showed two methyl signals and an AX pattern for the ring protons with J 7 Hz, consistent with



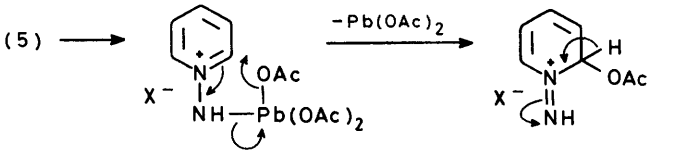
	R^1	R^2	R^3	R^4	R^5
(5)	H	H	H	H	H
(6)	H	H	Me	H	H
(7)	Me	H	H	H	H
(8)	Me	H	H	H	Me
(9)	H	Me	H	Me	H

	R^1	R^2	R^3	R^4
(10)	H	H	H	H
(11)	H	H	Me	Br
(12)	Me	H	H	Br
(13)	H	Me	H	Me

	R^1	R^2	R^3	R^4
(14)	H	H	H	H
(15)	H	H	Me	Br
(16)	Me	H	H	Br
(17)	H	Me	H	Me

(18) (19) (20)

(21) (22) (23) (24)



SCHEME

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[8] J. B. Ayward, *J. Chem. Soc.* (*C*), 1969, 1663.

Table 1

N-Amination reactions

Procedure. A solution of the base in chloroform was treated with a solution of *O*-*p*-tolylsulphonylhydroxylamine derived from a 1.1 molar proportion of ethyl *O*-*p*-tolylsulphonylacetohydroximate as described in ref. 10. The solution was then stirred for a further hour after which ether was added to complete the precipitation of the toluene-*p*-sulphonate salt which was filtered off and recrystallized from methanol–ether. The bromide was obtained by dissolving the corresponding toluene-*p*-sulphonate in the minimum volume of concentrated (48% w/v) hydrobromic acid followed by the addition of ethanol–ether. The solid which separated was filtered off and recrystallized from ethanol–ether.

	Product		Average yield	M.p.	Found (%)			Reqd. (%)		
Starting base	No.	X	(%)	(°C)	C	H	N	C	H	N
Pyridine	(5)	$C_7H_7SO_3$ [a]	83	105—106	53.9	5.4	10.4	54.1	5.3	10.5
	(5)	Br	96	152	34.5	4.2	16.0	34.3	4.0	16.0
2-Methylpyridine	(7)	$C_7H_7SO_3$ [a]	95	130	56.0	5.75	9.7	55.7	5.75	10.0
	(7)	Br	93	176	38.1	4.8	14.9	38.1	4.8	14.8
2,6-Dimethylpyridine	(8)	$C_7H_7SO_3$ [a]	92	147	55.75	5.9	9.2	55.4	6.3	9.2 [b]
	(8)	Br	87	235 [c]	41.25	5.6	13.45	41.4	5.5	13.8
3,5-Dimethylpyridine	(9)	$C_7H_7SO_3$ [a]	89	106	57.15	6.15	9.4	57.1	6.2	9.5
	(9)	Br	89	189	41.3	5.5	13.8	41.4	5.5	13.8
Quinoline	(18)	$C_7H_7SO_3$ [a]	99	179	61.0	5.1	8.6	60.8	5.1	8.9
	(18)	Br	97	180	48.0	3.85	12.3	48.0	4.0	12.45
Isoquinoline	(21)	$C_7H_7SO_3$ [a]	99	134.5	60.9	5.1	8.5	60.8	5.1	8.9
	(21)	Br	89	159	44.5	4.6	11.5	44.5	4.6	11.5 [d]
2-Acetoxypyridine [9]	(25)		39	160	53.55	5.0	5.4	53.9	4.9	5.2

[a] Toluene-*p*-sulphonate. [b] Hemihydrate. [c] Lit.,[11] m.p. 228 °C. [d] Monohydrate.

Table 2

Oxidations with lead(IV) acetate

Procedure. A stirred solution of the *N*-amino-bromide (2 mmol) in acetic acid (50 cm³) was treated dropwise with a solution of lead(IV) acetate (2 mmol) in acetic acid (50 cm³) during 2 h. After being stirred for a further 1 h the mixture was filtered to remove lead bromide and then saturated with hydrogen sulphide. The precipitated lead sulphide was filtered off and the filtrate again evaporated; the residue was worked up as indicated.

Starting *N*-amino-bromide	Product	Average yield (%)	M.p. (°C)	Cryst. solvent	Found (%) C	H	N	Reqd. (%) C	H	N
(5) [a]	(10) [b]	40	159—161 [c,d]	C_6H_6 [e]	55.1	5.3	18.4	55.3	5.3	18.4
(6) [f,g]	(11) [h]	22	220	C_6H_6–Et_2O	39.5	3.9	11.4	39.2	3.7	11.4
(7) [i]	(12) [j]	15	202	C_6H_6–Et_2O	39.6	3.7	11.0	39.2	3.7	11.4
(9) [k]	(13)	29	169	C_6H_6–light pet. (b.p. 40—60 °C)	57.3	6.4	14.1	57.1	6.9	14.8 [m]
(18) [k]	(19)	91	214	H_2O or C_6H_6 [e]	65.2	4.9	13.6	65.3	5.0	13.85
(20) [l]	(22)	61	241	H_2O or C_6H_6 [e]	65.4	4.9	14.1	65.3	5.0	13.85

[a] The residue referred to in the general procedure was dissolved in alcohol and the solution re-evaporated under reduced pressure. The residue was then recrystallized from benzene. [b] An anhydrous sample showed ν(C=O) bands at 1 712 and 1 655 cm^{-1}. The *hemihydrate* (Found: C, 52.3; H, 5.6; N, 17.8. $C_7H_8N_2O_2,0.5H_2O$ requires C, 52.2; H, 5.6; N, 17.4%) showed ν(C=O) bands at 1 690 and 1 652 cm^{-1} and a ν(O–H) band at 3 370 cm^{-1}. [c] The sample softened between 126 and 130 °C and changed into fine needles which melted at the temperature shown. [d] Lit.,[12] m.p. 157—158°. [e] An anhydrous sample was obtained by evaporating a solution in dry benzene followed by recrystallization from dry benzene. [f] The bromide, which was too hygroscopic for satisfactory micro-analysis, was obtained from the toluene-*p*-sulphonate salt [1] by ion exchange on Amberlite IRA 400 (Br^-). [g] The residue referred to in the general procedure was dissolved in alcohol and the solution re-evaporated under reduced pressure. The residue was then extracted with benzene and the extract decolourised with charcoal. The solution was then evaporated under reduced pressure and the residue recrystallized. [h] δ 1.96 (s, ring Me), 2.1 (s, Ac), and 7.3 and 6.2 (each 1 H, AXd, J 7 Hz). [i] The residue referred to in the general procedure was dissolved in alcohol and the solution re-evaporated under reduced pressure. The residue was then extracted with benzene and the extract decolourised with charcoal. The solution was then evaporated and the residue sublimed under reduced pressure. A solution of the sublimate in chloroform was then passed through a short alumina column and evaporated. The residue was then recrystallized. [j] δ 2.18 (s, ring Me), 2.45 (s, Ac), and 6.42 and 7.48 (each 1 H, AXd, J 9 Hz). [k] The residue referred to in the general procedure was dissolved in alcohol and the solution re-evaporated. The residue was then extracted with benzene and the solution decolourised with charcoal and evaporated. The residue was sublimed under reduced pressure and the sublimate recrystallized. [l] The residue referred to in the general procedure was extracted with boiling water and the extract decolourised with charcoal before cooling. The product which separated was filtered off and recrystallized. [m] Hemihydrate.

the protons being on adjacent ring carbon atoms. The ^{1}H n.m.r. spectrum of (12) likewise showed an AX pattern for the ring protons with J 9 Hz, again consistent with their being on adjacent ring carbon atoms; by analogy with (11) the bromine atom in (12) is suggested to be α to the carbonyl group. Additional evidence for the position of the bromine atom in (11) and (12) came from the observation that oxidation of 1-amino-3,5-dimethylpyridinium bromide (9) afforded the unbrominated acetylated cyclic hydrazide (13).

The formation of the brominated derivatives (11) and (12) suggested the involvement of the bromide ion in the oxidation process. This was confirmed by our failure to obtain 1-acetamido-2-pyridone (10) when 1-aminopyridinium toluene-*p*-sulphonate, acetate, chloride, or iodide was treated with lead(IV) acetate in acetic acid solution. Further, treatment of saturated solutions in acetic acid of potassium chloride, bromide, or iodine, with lead(IV) acetate at room temperature was without effect in the case of the chloride but rapidly liberated the corresponding free halogen from the bromide and iodide solutions. Thus our failure to obtain (10) from the treatment of 1-aminopyridinium chloride with lead(IV) acetate may be due to the inability of the latter to oxidize chlorides to chlorine under the reaction conditions used. The failure of the reaction in the case of 1-aminopyridinium iodide is, however, more difficult to explain, and the detailed mechanism of the oxidation is the subject of our further investigations.

TABLE 3

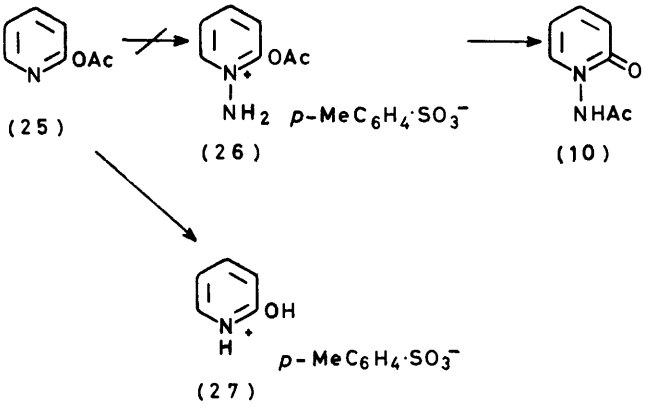
Acidic hydrolyses

Procedure. A solution of the acetyl compound (0.1 g) in 48% hydrobromic acid (2 cm^3) was boiled for 0.5 min then evaporated to dryness under reduced pressure. The residue was dissolved in water and basified with aqueous sodium hydroxide, and the liberated base was extracted into chloroform. Evaporation of the dried extract gave the base, which was purified by vacuum sublimation.

Starting acetyl compound	Product	Average yield (%)	M.p. (°C)	Found (%)			Reqd. (%)		
				C	H	N	C	H	N
(10)	(14)	69	62—64 [a]	54.3	5.5	25.6	54.5	5.5	25.4
(11)	(15)	90	92	35.2	3.5	13.8	35.5	3.5	13.8
(12)	(16)	73	134	35.3	3.4	13.5	35.5	3.5	13.8
(13)	(17)	78	146	61.0	7.3	20.2	60.85	7.3	20.3
(19)	(20)	87	128 [b]	67.25	5.0	17.7	67.5	5.0	17.5
(22)	(23)	91	102	67.5	5.0	17.5	67.5	5.0	17.5

[a] Lit.,[12] m.p. 64—66 °C. [b] Lit.,[13] m.p. 127 °C.

An attempt to confirm the feasibility of the suggested acetyl group migration shown in the Scheme failed. Treatment of 2-acetoxypyridine [9] (25) with *O*-*p*-tolylsulphonylhydroxylamine gave 2-hydroxypyridinium toluene-*p*-sulphonate (27) instead of the hoped for *N*-amino-salt (26) or the rearrangement product (10).



EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were determined with a Perkin-Elmer 377 spectrometer; ^{1}H n.m.r. spectra were determined with a Perkin-Elmer R12A spectrometer for solutions in deuteriochloroform and an internal Me_4Si standard.

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