Cyclic Quaternary Ammonium Salts. Part VIII.[1] Imidazo[1,2-*a*]pyrazinium Salts

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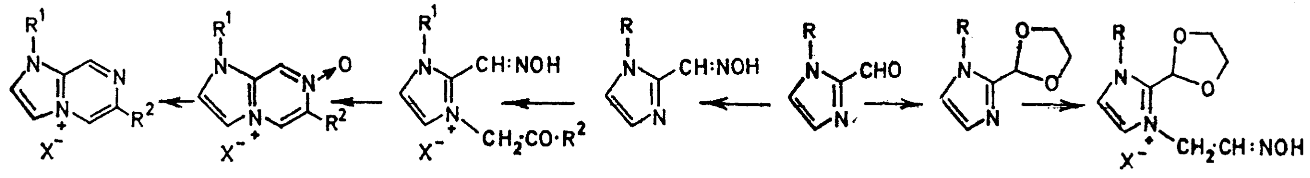
The synthesis of imidazo[1,2-*a*]pyrazinium 7-oxide salts and their deoxygenation to the title compounds is described.

THE synthesis of imidazo[1,2-*a*]pyrazine hydroperchlorate has been previously described[2] but to date no quaternary salts in which the 1-nitrogen atom is alkylated, have been recorded. We now report the synthesis of such compounds [(19)—(22)], by the deoxygenation of the corresponding *N*-oxides [(15)—(18)]. The starting materials for the preparation of the *N*-oxides were *N*-methyl- (2) and *N*-benzyl-imidazole-2-carbaldehyde



	R^1	R^2
(19)	Me	H
(20)	Me	Me
(21)	Me	Ph
(22)	$PhCH_2$	H

	R^1	R^2
(14)	H	H
(15)	Me	H
(16)	Me	Me
(17)	Me	Ph
(18)	$PhCH_2$	H

	R^1	R^2
(11)	Me	Me
(12)	Me	Ph
(13)	$PhCH_2$	H

	R
(9)	Me
(10)	$PhCH_2$

	R
(1)	H
(2)	Me
(3)	$PhCH_2$

	R
(4)	H
(5)	Me
(6)	$PhCH_2$

	R
(7)	H
(8)	Me

TABLE 1

2-(1,2-Dioxolan-2-yl)imidazoles

Precursor	Product	Yield %	Cryst. solvent	M.p.	Found C	Found H	Found N	Calc. C	Calc. H	Calc. N
(2)	(5)[a]	62		98—99°/ 0·1mm[b]	54·15	6·7	17·8	54·5	6·5	18·2
	(5) (picrate)		H_2O	126—127	40·7	3·1	18·6	40·7	3·4	18·3
(3)	(6)[a]	80	Light petroleum (b.p. 40—60°)–Et_2O	79—80	68·0	6·0	12·2	67·8	6·1	12·2
(6)	(4)[c]	77	Light petroleum (b.p. 40—60°)	127—128	51·7	5·7	20·2	51·4	5·75	20·0

[a] The procedure used was that described by Bradsher and Parham[4] for the preparation of 2-(1,3-dioxolan-2-yl)pyridine. [b] Liquid b.p. [c] The procedure used was that described by Iversen and Lund[3] for the preparation of the corresponding diethyl acetal.

TABLE 2

Imidazole quaternary salts

Precursors Wt(g)	Precursors Wt(g)	Solvent	Reaction Time(h)	Reaction Temp	Product X	Cryst. solvent	Yield[a] (%)	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Calc. (%) C	Calc. (%) H	Calc. (%) N
(5) 1·0	(23) 0·95	Tetra-methylene sulphone (1 ml)	264[b]	Room	(8)[c] Br	EtOH–$Pr^i{}_2O$	39	193—195[d]						
					(8) $C_6H_2N_3O_7$	EtOH		140—142	41·2	3·7	18·9	40·9	3·7	19·1
(4) 1·0	(23) 1·05	None	336[e]	Room	(7)[c] Br	EtOH–$Pr^i{}_2O$	18	132—135						
					(7) $C_6H_2N_3O_7$	H_2O		149—150	39·0	3·3		39·4	3·3	
(9)[i] 0·5	(25) 0·58	MeCN (1 ml)	1[f]	Reflux	(11) Br	EtOH–$Pr^i{}_2O$	60	126—128	35·8	4·7	15·05	35·4	4·8	15·5[g]
					(11) $C_6H_2N_3O_7$	EtOH–$Pr^i{}_2O$		156—158	41·2	3·5	20·6	41·0	3·4	20·5
(9)[i] 1·0	(26) 1·65	MeCN (2 ml)	1·5[h]	Reflux	(12) Br	EtOH–$MeNO_2$	68	205—207	48·2	4·4	12·8	48·2	4·35	13·0
					(12) $C_6H_2N_3O_7$	MeOH–H_2O		167—170	48·55	3·7	17·75	48·3	3·4	17·8

[a] Based on the imidazole. [b] The reaction mixture was triturated with ether, allowed to stand for a further day, the product filtered off and washed with ice-cold n-propanol. [c] Satisfactory analyses could not be obtained. [d] Decomp. [e] The gum was dissolved in n-propanol (2 ml), $Pr^i{}_2O$ added to initiate precipitation and the reaction mixture set aside for a further 4 days. [f] Ether was added to the cooled reaction mixture, the precipitated gum washed with ether and triturated with ethanol–acetone until solid. [g] Hemihydrate. [h] The bromide was filtered off and washed with ice-cold acetonitrile. [i] Prepared from the aldehyde[3] (2) in 62% yield, the oxime crystallized from aqueous methanol as needles, m.p. 172—174° (lit.,[5] m.p. 176°) (Found: C, 48·0; H, 5·9; N, 33·8. Calc. for $C_5H_7N_3O$: C, 48·0; H, 5·6; N, 33·6%).

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[4] C. K. Bradsher and J. C. Parham, *J. Org. Chem.*, 1963, **28**, 83.

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TABLE 3

Imidazo[1,2-*a*]pyrazinium 7-oxide salts

Precursor(s)	Reagent	Reaction Time (min)	Reaction Temp. (°C)	Product X	Cryst. solvent	Yield (%)	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Calc. (%) C	Calc. (%) H	Calc. (%) N
(7) (0·2 g)	Conc. H_2SO_4 (1·5 ml)	5 [a]	100	(14) [b] Br	EtOH–Pr^i_2O	84	168—172 [c]						
				(14) ClO_4	MeOH–Pr^i_2O		204—206 [c]	30·4	2·6	18·0	30·6	2·6	17·8
(8) (0·31 g)	Conc. H_2SO_4 (2 ml)	5 [a]	100	(15) Br	MeOH	81	>330 [d]	36·3	3·4	18·2	36·5	3·5	18·3
				(15) $C_6H_2N_3O_7$	H_2O		218—221	40·95	2·65	22·2	41·3	2·7	22·2
(12) (0·4 g)	Conc. H_2SO_4 (2 ml)	5 [a]	100	(17) [e] ClO_4	H_2O	79	225—228 [c]	47·7	3·6	13·1	47·9	3·7	12·9
				(17) $C_6H_2N_3O_7$	H_2O		153—155	49·7	3·5	18·0	50·2	3·1	18·5
(9) (1·0 g) + (25) (1·15 g)	MeCN (2 ml)–48% HBr (0·2 ml)	150 [g]	Reflux	(16) Br	EtOH–MeOH	71	264—267 [c]	36·5	4·1	16·0	36·7	4·6	16·0 [h]
(11) (0·51 g)	Conc. H_2SO_4 (2 ml)	5 [a]	100	(16) Br	EtOH–MeOH	81	264—267 [c]						
				(16) ClO_4	EtOH		252—255 [c]	36·6	3·8	16·1	36·4	3·8	15·9
(10) (1·0 g) + (24) (0·65 g)	MeCN (2 ml)–48% HBr (0·2 ml)	180 [g]	Reflux	(18) [e] ClO_4	MeOH–H_2O	53 [f]	214—217	47·85	3·7	12·5	47·9	3·7	12·9

[a] The cooled reaction mixture was treated with ether, the precipitated gum dissolved in 48% hydrobromic acid and the product precipitated with ethanol–ether. [b] Satisfactory analyses could not be obtained. [c] Decomp. [d] Decomposed without melting below 330°. [e] The hygroscopic bromide was converted to the perchlorate. [f] Based on the crude bromide. [g] The cooled reaction mixture was treated with ether and the precipitated gum was triturated with ether until solid. [h] Monohydrate.

TABLE 4

Imidazo[1,2-*a*]pyrazinium salts

Starting *N*-oxide (X = Br)	Reagent	Heating time (min)	Product [a] X	Cryst. solvent	Yield (%)	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Calc. (%) C	Calc. (%) H	Calc. (%) N
(15)	PBr_3	25	(19) Br	MeOH–Pr^i_2O	69	>330 [b]	39·1	3·8	19·2	39·3	3·8	19·6
(16)	PCl_3	120	(20) Br	EtOH–Pr^i_2O	89	>330 [b]	41·7	4·4	17·9	42·1	4·4	18·4
			(20) ClO_4	EtOH		201—204			16·7			17·0
			(20) $C_6H_2N_3O_7$	$MeNO_2$–Pr^i_2O		162—164	44·7	3·2	22·1	44·2	3·2	22·3
(17)	PBr_3	4	(21) [c] ClO_4	EtOH	66	209—211	50·3	3·85	13·3	50·4	3·9	13·6
			(21) $C_6H_2N_3O_7$	EtOH–H_2O		214—217	52·6	3·4		52·1	3·2	
(18)	PCl_3	4	(22) [c] ClO_4	EtOH–Pr^i_2O	21	118—121	50·15	4·0	13·6	50·4	3·9	13·6

[a] A suspension of the *N*-oxide in the phosphorus trihalide was boiled under reflux for the time indicated, the reaction mixture cooled and the product filtered off. [b] Decomposed without melting below 330°. [c] The crude product was washed with ether, dissolved in ethanol and treated with 60% perchloric acid followed by ether.

TABLE 5

U.v. spectra

Compound X	$\lambda_{max.}$ (nm)	log ε
(14) ClO_4	211, 251, 292sh, 306sh, 337	4·18, 4·2, 3·65, 3·7, 3·88
(15) Br	206, 228sh, 238, 249, 317, 331sh	3·97, 3·77, 3·87, 3·85, 3·92, 3·89
(16) Br	200, 229, 237, 250, 319, 334sh	4·3, 3·99, 3·99, 3·94, 3·97, 3·92
(17) ClO_4	203, 245, 324, 333sh	4·27, 4·22, 4·0, 3·97
(18) ClO_4	193, 206, 238, 252, 317, 331sh	4·34, 4·29, 3·91, 3·91, 3·98, 3·96
(19) Br	202, 217, 300	4·25, 4·18, 3·84
(20) Br	208, 255, 310, 321sh	4·25, 3·45, 3·87, 3·8
(21) ClO_4	206, 256, 325	4·36, 4·39, 3·82
(22) ClO_4	193, 204, 297	4·39, 4·31, 3·91

(3), the synthesis of which in good yield, has been described by Iversen and Lund.[3] The aldehydes (1), (2), and (3) were then converted into either the 1,3-dioxolan-2-yl derivatives (4)—(6) or the oximes (9) and (10); the resulting bases were quaternized with bromoacetaldehyde oxime (23), bromoacetaldehyde (24), bromoacetone (25), or phenacyl bromide (26). The most satisfactory combination of base and quaternizing agent is shown in Tables 2 and 3.

The monoquaternary salts (7), (8), and (11)—(13) were cyclized by acid and the resulting *N*-oxides (15)—(18) were deoxygenated with either boiling phosphorus tribromide or trichloride (see Table 4). In the cases where phosphorus trichloride was used, the use of the higher boiling tribromide gave rise to extensive decomposition. The unsubstituted *N*-oxide was recovered unchanged from boiling phosphorus trichloride and the use of boiling phosphorus tribromide gave only an intractable gum.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus; u.v. spectra were obtained with a Perkin-Elmer 137 spectrometer and are for aqueous solutions.

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