Synthesis of 1,1'-Dimethyl-4,4'-azo-1,2,4-triazolium and 3,3'-Dimethyl-1,1'-azobenzotriazolium Salts

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The synthesis of 1,1'-dimethyl-4,4'-azo-1,2,4-triazolium salts, by oxidation of 4-amino-1,2,4-triazoles followed by quaternisation of the derived tetrazenes with methyl fluorosulphonate, is described. The azotriazolium salts were also obtained by oxidising the methobromides of 4-amino-1,2,4-triazoles with saturated aqueous bromine. No 1,1'-azobenzotriazole was isolated when 1-aminobenzotriazole was oxidised with acidified potassium bromate but the required title salts were obtained by oxidation of 1-aminobenzotriazole methobromide with saturated aqueous bromine.

THE diquaternary tetrazenes (1) [1] and (2) [2] exhibit non-depolarising neuromuscular blocking activity. In a continued search for compounds of this type having potential medicinal value, the synthesis of the title compounds (10), (11), and (17) was undertaken.

The necessary precursors for the synthesis of the azo-1,2,4-triazolum salts (10) and (11) were the 4-amino-1,2,4-triazoles (3) and (4), which were obtained by heating commercially available acetohydrazide [3] and by treating benzonitrile with hydrazine hydrate,[4] respectively. Oxidation of the aminotriazoles (3) and (4) with acidified potassium bromate gave the corresponding tetrazenes (5) and (6) in moderate yield, but treatment of the tetramethyltetrazene (5) with methyl iodide did not yield the required diquaternary salt (10); the product was 1,3,4,5-tetramethyl-1,2,4-triazolium tri-iodide (7), identified from its analytical figures and n.m.r. spectrum [δ ($CF_3 \cdot CO_2H$) 2·12, 2·32, 2·35, and 3·58 (4 × Me)]. The required diquaternary tetrazenes (10) and (11) were subsequently obtained by treating the respective tetrazene bases (5) and (6) with methyl fluorosulphonate. They were also obtained by oxidation of the corresponding 4-amino-1-methyltriazolium salts (8) and (9) with saturated aqueous bromine.

The starting material for the preparation of 1,1'-azobenzotriazolium salts (17) was 1-aminobenzotriazole (12),[5] the oxidation of which by a variety of reagents has been shown [6] to yield the amino-nitrene (13) which subsequently loses nitrogen with the formation of benzyne. It was anticipated that formation of the amino-nitrene (13) in mildly acidic solution would be followed by formation of the conjugate acid (14). Coupling between the amino-nitrene and its conjugate acid would then be expected to give the tetrazene (15), *via* a mechanism previously established.[7]

Treatment of 1-aminobenzotriazole with acidified potassium bromate, however, resulted in a vigorous reaction from which none of the expected tetrazene (15)

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TABLE 1
Monoquaternary salts

Precursor	Reagent	Heating time and temp.	Product	X	Cryst. solvent	Yield (%)	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Rqd. (%) C	Rqd. (%) H	Rqd. (%) N
(3)[3] (2·2 g)	MeI (10 ml) in MeOH (5 ml)	20 h, reflux	(8)[a]	$C_6H_2N_3O_7$	EtOH	95	137·5—138·5	37·1	3·7	27·6	37·2	3·7	27·6
(4)[4] (2·0 g)	MeI (5 ml) in MeOH (20 ml)	20 h, reflux	(9)[b]	I	H_2O–MeOH	51	95—97	45·3	4·2	14·0	45·5	4·3	14·1[c]
			(9)[d]	Br	MeOH–Et_2O		144—146	54·5	4·6	16·9	54·4	4·6	16·9
(5) (0·1 g)	MeI (5 ml)	72 h, reflux	(7)[e]	I_3	EtOH	62	146—147	14·0	2·3	8·1	14·2	2·4	8·3
			(7)[f]	ClO_4	EtOH–Et_2O		138—140	31·9	5·3	18·7	31·9	5·4	18·6
(12)[5] (2·0 g)	MeI (20 ml) in MeOH (20 ml)	20 h, reflux	(16)[g]	I	Pr^nOH	76	173—174	30·4	3·3	20·4	30·45	3·3	20·3
			(16)[d]	Br	MeOH–Et_2O		214—215[h]	36·4	4·0	24·4	36·7	4·0	24·5

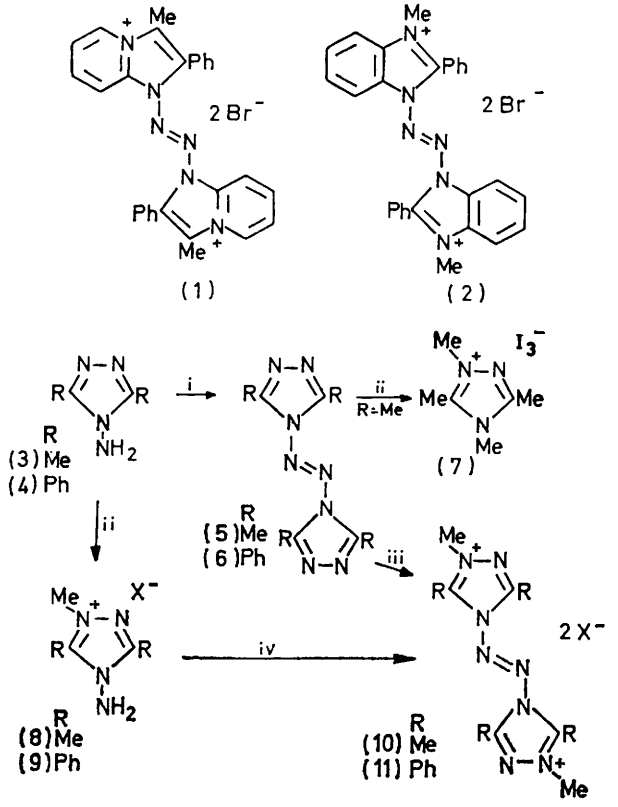
[a] The solution was evaporated under reduced pressure and the residue treated with saturated alcoholic picric acid, giving the picrate. [b] The solution was evaporated under reduced pressure and the residue treated with water giving the iodide. [c] For the monohydrate. [d] Obtained from the iodide by ion exchange on Amberlite IRA 400 (Br^-). [e] The reaction mixture was cooled and the product precipitated with ether. [f] Obtained by dissolving the tri-iodide in warm 70% perchloric acid followed by addition of ethanol–ether. [g] The solution was evaporated and the residue treated with ether giving the iodide. [h] With decomposition.

TABLE 2
Tetrazenes and their diquaternary salts

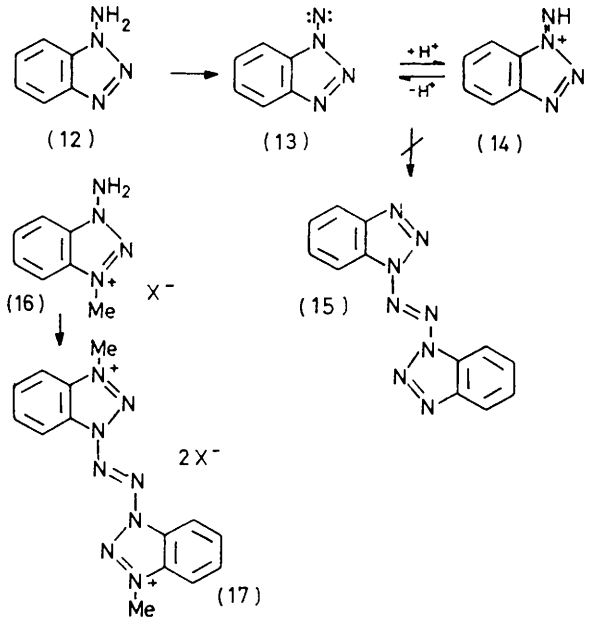
Reactants	Heating time and temp.	Product	X	Cryst. solvent	Yield (%)	M.p. (°C)	Found (%) C	Found (%) H	Found (%) N	Rqd. (%) C	Rqd. (%) H	Rqd. (%) N
(3)[3] (2·0 g) + $KBrO_3$ (4·0 g) in H_2O (30 ml) + 3M-HCl[a]	18 h, ambient	(5)		H_2O	29	261	37·1	6·2	44·2	37·5	6·3	43·7[b]
(5) (0·1 g) + $MeOSO_2F$ (0·15 g) in CH_2Cl_2 (10 ml)	2 h[c]	(10)	SO_3F	MeOH–Et_2O	69	210—211	26·5	4·2	24·7	26·8	4·0	25·0
		(10)[d]	ClO_4	EtOH–Et_2O		274—275	27·0	4·2	24·9	26·7	4·0	24·9
		(10)[e]	$C_6H_2N_3O_7$	$MeNO_2$		205	37·0	3·2	27·7	37·4	3·1	27·8
(8)[f] (1·0 g) in H_2O (sat. soln.) + sat. aq. Br_2 (190 ml)[g]	Ambient	(10)[h]	ClO_4	EtOH–Et_2O	27	274—275						
(4)[4] (2·0 g) + $KBrO_3$ (6·0 g) in H_2O (50 ml) + 3M-HCl[i]	Ambient	(6)[j]		MeCN–Et_2O	27	206—208	68·1	4·3	22·3	67·9	4·7	22·6[k]
(6) (0·77 g) + $MeOSO_2F$ (0·7 g) in $CHCl_3$ (30 ml)[l]	0·5 h,	(11)[m]	SO_3F	MeCN–Et_2O	70	170	48·3	4·0	14·8	48·0	4·3	14·9[n]
		(11)[d]	ClO_4	MeCN–Et_2O		254	50·7	3·7	15·7	50·4	3·9	15·7[o]
(9)[p] (0·2 g) in H_2O (sat. soln.)[q] + sat. aq. Br_2 (40 ml)[g]		(11)	ClO_4	MeCN–Et_2O	46	254						
(16)[p] (0·3 g) in H_2O (sat. soln.)[q] + sat. aq. Br_2 (30 ml)[g]		(17)[r]	Br	MeOH–Et_2O	57	156	36·7	3·1	24·6	37·0	3·1	24·7
		(17)[s]	ClO_4	$HClO_4$ (60%)–Me_2CO		259	32·9	3·1	22·7	33·5	3·0	22·3[t]

[a] The HCl was added to an ice-cold stirred suspension of the reactants until the solution became deep red. After stirring, the precipitated yellow solid was filtered off, boiled with acetone, and then recrystallised. [b] For $2H_2O$. [c] The reaction mixture was stirred at room temperature for 1·5 h and then boiled under reflux for 0·5 h. The solid which separated was filtered off and recrystallised. [d] Obtained by dissolving the bisfluorosulphonate salt in 60% perchloric acid followed by addition of acetone–ether. [e] Prepared by treating an ethanolic solution of the perchlorate salt with sat. alcoholic picric acid. [f] The crude bromide salt, obtained from the crude iodide salt by ion exchange on Amberlite IRA 400 (Br^-), was used. [g] Added in bulk. [h] Trituration yielded a dark red solid which was filtered off and boiled in acetone. Ether was added to the cooled solution and the precipitated oil separated off and dissolved in ethanol. Addition of 60% perchloric acid precipitated the diperchlorate. [i] The HCl was added to a stirred suspension of the reactants until a brown gummy solid precipitated. [j] The liquor was decanted from the brown solid which was then boiled in acetone; the resulting yellow solid was then filtered off and recrystallised. [k] For $1·5H_2O$. [l] With stirring. [m] The precipitated yellow solid was filtered off and recrystallised. [n] For $3H_2O$. [o] For $1H_2O$. [p] As the bromide salt. [q] At 60 °C. [r] The reaction mixture was triturated and cooled and the red solid which separated dissolved in boiling acetone. Addition of ether precipitated a green solid which was dissolved in 60% perchloric acid; the diperchlorate salt was then precipitated by addition of acetone–ether. [s] The reaction mixture was triturated and cooled yielding a red solid which was filtered off and boiled in acetone (30 ml). The resulting yellow solid was then filtered off and recrystallised. [t] With decomposition. [u] Obtained by dissolving the dibromide salt in 60% perchloric acid followed by addition of acetone. [v] For $0·5H_2O$.

was isolated. The required 1,1′-azobenzotriazolium salt (17) was subsequently obtained by oxidising the methobromide of 1-aminobenzotriazole (16) with saturated aqueous bromine.



Reagents: i, $KBrO_3$–HCl; ii, MeI; iii, $MeOSO_2F$; iv, sat. aq. Br_2



EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus and n.m.r. spectra on a Perkin-Elmer R12A spectrometer.

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