RESEARCH PAPERS

CHEMOTHERAPEUTIC PROPERTIES OF SOME NEW QUATERNARY AMMONIUM SALTS

PART I. CHEMISTRY

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The preparation of a large number of new heterocyclic quaternary ammonium salts for biological screening is described. Certain of the quaternary salts possess amoebicidal, antibacterial, antifilarial and trypanocidal activity.

SOME of the chemotherapeutic properties of certain heterocyclic bis-quaternary ammonium salts have already been described[1–5]. It appeared desirable to investigate the effect of introducing one or more amino groups into the nuclei, and the present paper records the preparation and physical properties of a large number of new quaternary salts which have been examined in these laboratories during the past few years. The antifilarial activity of selected compounds will be described by Dr. F. Hawking and Dr. R. J. Terry of the National Institute for Medical Research in Part II[6], and some of the antimicrobial properties and toxicities of certain of the compounds will be recorded by Dr. H. O. J. Collier and his colleagues in Part III[7] of this series. For ease of reference, the abbreviated nomenclature first employed by Barlow and Ing[8] will be used; thus, BQn, BIQn, BAIQn and BACn refer respectively to the bis-quinolinium, -*iso*quinolinium, -7-amino-*iso*quinolinium and -4-amino-cinnolinium series, where n is equal to the number of methylene groups in the chain.

The heterocyclic amines and amides used were prepared by standard methods. The nitration product of 2-ethylquinoline-*N*-oxide was assumed to be the 4-nitro derivative following the work of Ochiai[9] on the chemistry of *N*-oxides. According to John[10], acetylation of 4-amino-2-phenyl-quinoline with acetic anhydride yields the 4-acetamido derivative. We have found that acetylation under these conditions gives 4-diacetylamino-2-phenylquinoline, but that the monoacetyl derivative is obtained by acetylation of the amine with a mixture of acetic anhydride and acetic acid. The quaternary salts were generally prepared by refluxing an excess of the appropriate base with a polymethylene dihalide in an organic solvent, for example, benzene, ethanol or ethyl methyl ketone. Where the base contained a free primary amino group in addition to the nuclear nitrogen, the former was generally protected by acylation; the resulting amide was then quaternised, and the product hydrolysed to give the

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TABLE I

POLYMETHYLENE BISQUINOLINIUM AND BIS*iso*QUINOLINIUM DI-IODIDES

(BQ and BIQ series)

$R^+.(CH_2)_n.R^+ 2I^-$

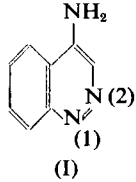
n	Reaction solvent and time (hr.)		m.p.	Cryst. form	Crystn. solvent	Found per cent				Formula	Required per cent			
						C	H	N	I		C	H	N	I
R^+ = *iso*Quinolinium														
22	EtOH	120	144°	Yellow granules or plates	EtOH	58·3	7·25	3·45	31·0	$C_{40}H_{58}N_2I_2$	58·5	7·1	3·4	31·0
23	MeCOEt	150	144–146°	Yellow microcrystals	EtOH	58·25	7·05	3·4	30·5	$C_{41}H_{60}N_2I_2$	59·0	7·25	3·4	30·5
24	MeCOEt	110	[1] 152–154°	Yellow plates	EtOH	59·7	7·7	3·0	29·5	$C_{42}H_{62}N_2I_2$	59·4	7·4	3·3	29·95
26	MeCOEt	100	114–117°	Yellow plates	EtOH	60·5	7·5	3·25	28·85	$C_{44}H_{66}N_2I_2$	60·3	7·6	3·2	29·0
30	MeCOEt	150	Sinters 100–104°, m.p. 120–124°	Yellow plates	EtOH	61·4	8·3	3·1	27·3	$C_{48}H_{74}N_2I_2$	61·8	8·0	3·0	27·25
32	MeCOEt	120	Sinters 122°, m.p. 144–146°	Yellow plates	MeOH	62·3	7·9	2·9	26·6	$C_{50}H_{78}N_2I_2$	62·5	8·2	2·9	26·5
36	MeCOEt	90	Melts to a glass at 126–128°, flows at 184°	Yellow plates	MeOH	64·4	8·6	2·6	24·6	$C_{54}H_{86}N_2I_2$	63·8	8·5	2·8	25·0
40	MeCOEt	90	Melts to a glass at 128–130°, flows at 210°	Yellow plates	MeOH	64·5	9·0	2·6	23·8	$C_{58}H_{94}N_2I_2$	64·9	8·8	2·6	23·7
R^+ = Quinolinium														
6	MeCOEt	140	228–229°	Orange-yellow needles	EtOH	48·5	4·5	4·6	42·6	$C_{24}H_{26}N_2I_2$	48·3	4·4	4·7	42·6
22	EtOH	100	166–168°	Yellow plates	MeOH-Et_2O	58·9	7·0	3·5	30·5	$C_{40}H_{58}N_2I_2$	58·5	7·1	3·4	31·0
24	MeCOEt	210	166–168°	Orange-yellow microcrystals	EtOH	59·5	7·5	3·1	29·85	$C_{42}H_{62}N_2I_2$	59·4	7·4	3·3	29·95
32	MeCOEt	210	165–166°	Yellow plates	MeOH	63·0	8·15	2·55	25·8	$C_{50}H_{78}N_2I_2$	62·5	8·2	2·9	26·5

[1] Also forms various solvated crystals of lower m.p.

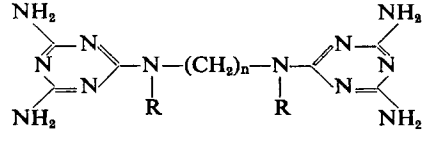
required quaternary salt. In some cases this precaution was found to be unneccessary; thus the products obtained by treating 4-aminoquinoline with either hexamethylene or decamethylene di-iodide were identical with those obtained by hydrolysis of the reaction product of 4-acetamidoquinoline with hexamethylene or decamethylene di-iodide respectively.

Attempts to quaternise the following were unsuccessful, possibly due to steric hindrance: 2-aminoquinoline, 8-acetamidoquinoline, 5:6- and 6:8-diacetamidoquinoline, 4-amino-6-acetamidoquinaldine and 3-acetamido-*iso*quinoline. Analysis of the reaction product of 5:7-diacetamidoquinoline with an alcoholic solution of decamethylene di-iodide corresponded reasonably with that of the hydriodide of the amide. This may be a solvent effect, since the amide was readily quaternised by, for example, *p*-xylylene di-iodide, when the reaction was carried out in ethyl methyl ketone solution. We have already reported numerous unsuccessful attempts to prepare decamethylene bisquaternary derivatives of 5-aminoacridine and related compounds[11].

We have not proved the constitution of the bisquaternary ammonium salts derived from 4-aminocinnoline derivatives, but have assumed that quaternisation has occurred at N (1) and not at N (2) (I), since Simpson[12] has already advanced evidence of quaternary salt formation at N (1) for 4-amino-6-chlorocinnoline. Although Atkinson and Taylor[13] have shown that quaternisation of 4-amino-6-nitrocinnoline occurred at each of the ring nitrogens, they found that only the N (1) quaternary salt was formed when 4-acetamido-6-nitrocinnoline was used. All our cinnolinium salts have been prepared from 4-acetamidocinnoline derivatives; moreover, paper chromatographic investigation of a random selection indicated that the final products were single substances.



(I)



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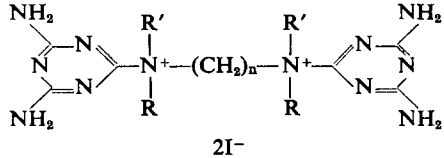


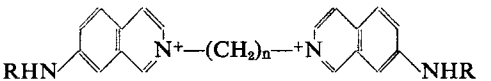
(III)

Melamine derivatives were prepared by reacting 2-chloro-4:6-diamino-*s*-triazine with the requisite *NN'*-dialkylpolymethylene diamine, and treating the product (II) with an alkyl iodide. Here again, we have not established the final identity of the quaternary products, but have assumed the structure shown by III. Attempts to prove this by reacting 2-chloro-4:6-diamino-*s*-triazine with *NNN'N'*-tetra-alkylpolymethylene diamines

TABLE II

POLYMETHYLENE BIS[(7-ACYLAMIDO-) AND (7-AMINO-)*iso*QUINOLINIUM IODIDES]

(BAIQ series)



Reaction solvent = ethyl methyl ketone

R	n	Reaction time (hr.)	m.p.	Cryst. form	Crystn. solvent	Found per cent C	H	N	I	Formula	Required per cent C	H	N	I
Ac	3	24	321–323°	Yellow microcrystals	$EtOH/H_2O$	45·1	4·2	8·7	38·2	$C_{35}H_{36}O_2N_4I_2$	44·9	3·9	8·4	38·0
H	3	—	290–292° after softening at 165°	Yellow needles	$MeOH/Et_2O$	43·3	3·8	9·45	43·2	$C_{31}H_{32}N_4I_2$	43·15	3·8	9·6	43·5
Bz	4	40	335–337°	Yellow microcrystals	$EtOH/H_2O$	54·2	4·3	6·75	30·8	$C_{36}H_{32}O_2N_4I_2$	53·6	4·0	6·95	31·5
Ac	5	24	313–314°	Yellow microcrystals	$MeOH/Et_2O$	46·6	4·5	7·8	36·3	$C_{27}H_{30}O_2N_4I_2$	46·55	4·3	8·05	36·5
H	5	—	192–194°	Yellow needles	MeOH/EtOH	42·9	4·8	8·85	39·6[1]	$C_{23}H_{26}N_4I_2.1\frac{1}{2}H_2O$	43·2	4·6	8·8	39·75
Ac	6	24	320–321°	Yellow microcrystals	$MeOH/Et_2O$	46·9	4·6	8·1	36·1	$C_{28}H_{32}O_2N_4I_2$	47·3	4·5	7·9	35·8
H	6	—	Softens at 90°, m.p. 224–226°	Yellow micro-needles	$EtOH/Et_2O$	43·1	4·85	8·7	38·5[2]	$C_{24}H_{28}N_4I_2.2H_2O$	43·5	4·9	8·5	38·4
Ac	8	24	278–279°	Yellow nodules	$MeOH/Et_2O$	48·7	5·0	7·7	34·25	$C_{30}H_{36}O_2N_4I_2$	48·8	4·9	7·6	34·4
H	8	—	226–228°	Tan platelets	$MeOH/Et_2O$	48·0	4·9	8·2	34·4	$C_{26}H_{32}N_4I_2$	47·7	4·9	8·6	38·8
Ac[3]	9	24	—	—	—	—	—	—	—	—	—	—	—	—
H	9	—	226—228°	Yellow granules	$MeOH/Et_2O$	48·5	5·0	8·5	38·0	$C_{27}H_{34}N_4I_2$	48·5	5·1	8·4	38·0
Ac	10	24	[4]206–208° with efferves-cence	Pale pink microcrystals	$MeOH/EtOH/Et_2O$	50·1	5·5	7·2	33·0	$C_{32}H_{40}O_2N_4I_2$	50·1	5·3	7·3	33·2
H	10	—	239–240°	Yellow microcrystals	$MeOH/Et_2O$	48·9	5·5	8·3	37·3	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
Ac	12	24	204–206°	Yellow microcrystals	$MeOH/Et_2O$	51·5	5·7	7·05	31·85	$C_{34}H_{44}O_2N_4I_2$	51·4	5·6	7·05	32·0
H	12	—	267–268°	Yellow microcrystals	$MeOH/Et_2O$	50·7	5·65	7·8	35·7	$C_{30}H_{40}N_4I_2$	50·7	5·7	7·9	35·8
Ac	16	24	199–201°	Yellow needles	EtOH	53·95	6·3	6·8	30·7	$C_{38}H_{52}O_2N_4I_2$	53·65	6·2	6·6	29·9
H	16	—	230–232°	Yellow microcrystals	$EtOH/Et_2O$	54·0	6·25	6·9	32·5	$C_{34}H_{48}N_4I_2$	53·3	6·3	7·3	33·2
Ac[3]	19	43	—	—	—	—	—	—	—	—	—	—	—	—
H	19	—	225–227°	Yellow microcrystals	$EtOH/Et_2O$	54·4	6·6	7·2	31·6	$C_{37}H_{54}N_4I_2$	54·95	6·7	6·9	31·4
Ac	$(CH_2)n$ = But-2-ene	18	289–290°	Pink microcrystals	$EtOH/H_2O$	53·1	4·5	9·8	27·3[5]	[6]$C_{36}H_{36}O_2N_4Br_2$	53·2	4·5	9·6	27·3[5]
H			249–250°	Yellow microcrystals	$MeOH/H_2O/Et_2O$	44·4	3·95	9·4	42·4	$C_{28}H_{32}N_4I_2$	44·3	3·7	9·4	42·6

[1] Sample lost $\frac{1}{2}H_2O$ when dried at 100° *in vacuo*, and as analysis then corresponded to crystals containing $1\frac{1}{2}H_2O$, the original material must have been a di-hydrate.
[2] Analysis of material dried *in vacuo* at room temperature.
[3] Hydrolysed directly to the amino quaternary without purification.
[4] Monohydrate.
[5] Bromine.
[6] Bromide.

were unsuccessful, unidentifiable products containing no halogen being obtained. However, the fact that the compounds (assumed to be III) are reprecipitated unaltered by the addition of excess potassium iodide to an alkaline aqueous solution indicates that they are definitely quaternary salts and that methylation at the primary amino groups has not occurred.

Certain of the compounds described herein possess interesting amoebicidal (e.g., BAIQ 4), antibacterial (BIQ series in general), antifilarial (e.g., BIQ 20, BAC 20) or trypanocidal activity (e.g., melamine derivatives); these properties will be described in detail in Parts II and III.

EXPERIMENTAL

All m.p.s are uncorrected. Unless otherwise stated, the microanalyses of all quaternary salts were carried out on materials dried at 100° *in vacuo*.

The polymethylene dihalides employed were prepared from the diols by standard methods. 1:23-*di-iodotricosane*, colourless plates from acetone, m.p. 71·5–72°. Found: C, 48·2; H, 8·0; I, 43·1. $C_{23}H_{46}I_2$ requires C, 47·9; H, 8·05; I, 44·1 per cent; 1:26-*di-iodohexacosane*, colourless plates from acetone-ethanol, m.p. 77·5–78°. Found: C, 50·5; H, 8·8; I, 40·6. $C_{26}H_{52}I_2$ requires C, 50·5; H, 8·5; I, 41·1 per cent; and 1:36-*di-iodohexatriacontane*, colourless plates from acetone-benzene, m.p. 89–91°. Found: C, 56·5; H, 9·3; I, 34·0. $C_{36}H_{72}I_2$ requires C, 57·0; H, 9·6; I, 33·5 per cent.

1:23-*Dihydroxytricosane*, colourless plates from benzene, m.p. 106–106·5°. Found: C, 77·4; H, 13·85. $C_{23}H_{48}O_2$ requires C, 77·5; H, 13·6 per cent; and *hexatriacontane*-1:36-*bis*(p-*methoxyphenyl ether*), colourless plates from benzene, m.p. 122°. Found: C, 79·6; H, 11·3. $C_{50}H_{86}O_4$ requires C, 80·0; H, 11·6 per cent.

1:21-Dibromoheneicosane was prepared from heneicosa-1:20-dien-11-one[14] by Huang-Minlon reduction to *heneicosa*-1:20-*diene* (colourless oil, b.p. 166°/0·5 mm. Found: C, 86·0; H, 13·45. $C_{21}H_{40}$ requires C, 86·3; H, 13·8 per cent), and subsequent addition of hydrogen bromide in the presence of air.

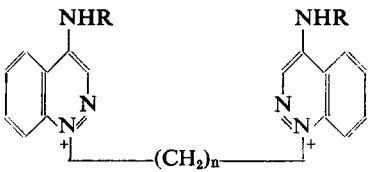
3-*Acetamido*isoquinoline, colourless needles from water, m.p. 122–123°. Found: C, 71·0; H, 5·65; N, 14·75. $C_{11}H_{10}ON_2$ requires C, 71·0; H. 5·4; N, 15·05 per cent; 7-*benzamido*isoquinoline, colourless needles from benzene, m.p. 177–179°. Found: C, 77·5; H, 4·9; N, 11·1. $C_{16}H_{12}ON_2$ requires C, 77·4; H, 4·9; N, 11·3 per cent; 5:8-*diacetamido*-isoquinoline, colourless needles from water, m.p. 295–296°. Found: C, 64·0; H, 5·2; N, 17·2. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·4; N, 17·3 per cent.

4-*Iodoquinaldine*, cream coloured needles from aqueous ethanol, m.p. 109–110·5°. Found: C, 44·2; H, 3·0; N, 5·2; I, 47·5. $C_{10}H_8NI$ requires C, 44·6; H, 3·0; N, 5·2; I, 47·2 per cent; 4-*acetamidoquinaldine hydrochloride*, colourless needles from ethanol, m.p. 280–282° (decomp.). Found: C, 60·0; H, 5·7; N, 11·9; Cl, 15·0. $C_{12}H_{13}ON_2Cl$ requires C, 60·9; H, 5·5; N, 11·8; Cl, 15·0 per cent; 4-*acetamido*-6-*methylquinaldine*, colourless needles from aqueous ethanol, m.p. 191–192°. Found: C, 72·75; H, 6·75; N, 12·9. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·6; N, 13·1 per cent; 4-*acetamido*-5-*methylquinaldine*, colourless needles from benzene,

TABLE III

POLYMETHYLENE BIS[(4-ACYLAMIDO-) AND (4-AMINO)CINNOLINIUM IODIDES]

(BAC series)



Reaction solvent = ethyl methyl ketone

R	n	Reaction time (hr.)	m.p.	Cryst. form	Crystn. solvent	Found per cent C	H	N	I	Formula	Required per cent C	H	N	I
Ac	4	75	262–263°	Orange microcrystals	MeOH/EtOH	42·7	4·2	11·9	36·2	$C_{24}H_{26}O_2N_6I_2$	42·1	3·8	12·3	37·1
H	4	—	277–279°	Yellow microcrystals	MeOH/EtOH	40·2	3·9	14·1	41·7	$C_{20}H_{22}N_6I_2$	40·0	3·7	14·0	42·3
H	4	—	253–254°	Colourless microcrystals	MeOH/EtOH	44·6	4·3	15·2	12·7[1]	[5]$C_{20}H_{22}O_2N_6Cl_2$	44·0	4·1	15·4	13·0[1]
Ac	6	205	223°	Orange-red microcrystals	MeOH/EtOH	43·7	4·7	11·7	35·2	$C_{26}H_{30}O_2N_6I_2$	43·8	4·25	11·8	35·7
H	6	—	281–282°	Yellow prisms	EtOH/H_2O	42·2	3·9	13·2	40·2	$C_{22}H_{26}N_6I_2$	42·0	4·2	13·4	40·45
Ac	7	204	236–238°	Orange-red prisms	MeOH/EtOH	44·1	4·65	11·7	34·8	$C_{27}H_{32}O_2N_6I_2$	44·6	4·4	11·6	35·0
H	7	—	222–224°	Yellow granules	EtOH	43·2	4·6	13·0	39·35	$C_{23}H_{28}N_6I_2$	43·0	4·4	13·1	39·6
Ac	8	232	223–224°	Orange granules	MeOH/EtOH	45·4	4·95	11·4	34·0	$C_{28}H_{34}O_2N_6I_2$	45·4	4·6	11·35	34·3
H	8	—	252°	Dark yellow rosettes	MeOH/EtOH	43·95	4·8	12·7	38·5	$C_{24}H_{30}N_6I_2$	43·9	4·6	12·8	38·7
Bz	10	53	160–162°	Orange plates	EtOH	53·7	4·8	9·3	28·45	$C_{40}H_{42}O_2N_6I_2$	53·8	4·75	9·4	28·5
H	10	—	209–210°	Yellow plates	EtOH/Et_2O	45·65	5·4	11·9	37·05	$C_{26}H_{34}N_6I_2$	45·6	5·0	12·3	37·1
H	10	—	195–197°	Cream needles	EtOH	56·3	6·1	19·9	—	[3]$C_{26}H_{34}O_6N_6$	56·3	6·2	20·2	—
Ac	16	210	156–158°	Buff plates	EtOH/Et_2O	50·8	6·3	9·65	29·8	$C_{36}H_{50}O_2N_6I_2$	50·7	5·9	9·9	29·8
H	16	—	[4]181–183°	Yellow-brown nodules	EtOH	50·3	5·7	10·8	32·7	$C_{32}H_{46}N_6I_2$	50·0	6·0	10·9	33·1
Ac[5]	18	280[6]	—	—	—	—	—	—	—	—	—	—	—	—
H	18	—	164–166°	Yellow needle clusters	EtOH	52·0	6·3	10·45	31·2	$C_{34}H_{50}N_6I_2$	51·3	6·3	10·55	31·9
Ac[5]	20	286[6]	—	—	—	—	—	—	—	—	—	—	—	—
H	20	—	186–188°	Yellow granules	EtOH/Et_2O	52·45	6·7	10·2	30·6	$C_{36}H_{54}N_6I_2$	52·4	6·6	10·2	30·8
H	20	—	198–199°	Cream microcrystals	EtOH/Et_2O	67·3	8·4	12·9	11·2[1]	[7]$C_{36}H_{54}N_6Cl_2$	67·4	8·5	13·1	11·1[1]
Ac	22	158	171°	Red plates	EtOH	53·6	6·7	9·1	27·4	$C_{42}H_{62}O_2N_6I_2$	53·85	6·7	9·0	27·1
H	22	—	162–163°	Yellow needles	EtOH	53·8	6·9	10·0	29·7	$C_{38}H_{58}N_6I_2$	53·5	6·9	9·9	29·8

[1] Chlorine. [2] Perchlorate. [3] Nitrate. [4] Monohydrate. [5] Reaction solvent = ethanol. [6] Hydrolysed directly to the amino quaternary without purification. [7] Chloride.

m.p. 173–174°. Found: C, 72·5; H, 6·5; N, 12·9. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·6; N, 13·1 per cent.

2-*Ethylquinoline*-N-*oxide*, yellow oil, b.p. 192–194°/14 mm. Found: C, 75·6; H, 6·2; N, 8·35. $C_{11}H_{11}ON$ requires C, 76·3; H, 6·4; N, 8·1 per cent; 4-*nitro*-2-*ethylquinoline*-N-*oxide*, yellow needles from ethanol, m.p. 123–124°. Found: C, 60·4; H, 4·6; N, 12·95. $C_{11}H_{10}O_3N_2$ requires C, 60·55; H, 4·6; N, 12·8 per cent; 4-*amino*-2-*ethylquinoline*, colourless needles from benzene-light petroleum (b.p. 40–60°), m.p. 153–155°. Found: C, 76·65; H, 7·1; N, 15·9. $C_{11}H_{12}N_2$ requires C, 76·7; H, 7·0; N, 16·3 per cent; 4-*hydroxy*-2-*ethylquinoline*, colourless needles from water, m.p. 180–181°. Found: C, 76·05; H, 6·4; N, 7·9. $C_{11}H_{11}ON$ requires C, 76·3; H, 6·4; N, 8·1 per cent.

2-n-*Propylcinchoninamide*, colourless needles from benzene, m.p. 193–194°. Found: C, 72·75; H, 6·7; N, 12·85. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·6; N, 13·1 per cent; 4-*amino*-2-n-*propylquinoline*, cream coloured needles from benzene, m.p. 141–142°. Found: C, 77·1; H, 7·6; N, 14·8. $C_{12}H_{14}N_2$ requires C, 77·4; H, 7·6; N, 15·05 per cent; 4-*acetamido*-2-n-*propylquinoline*, colourless needles from benzene-light petroleum (b.p. 40–60°), m.p. 135–137°. Found: C, 73·6; H, 6·9; N, 11·9. $C_{14}H_{16}ON_2$ requires C, 73·7; H, 7·1; N, 12·3 per cent; 4-*chloro*-2-n-*propylquinoline*, colourless liquid, b.p. 88–90°/0·1 mm. Found: C, 70·1; H, 5·8; N, 6·8; Cl, 16·9. $C_{12}H_{12}NCl$ requires C, 70·1; H, 5·9; N, 6·8; Cl, 17·3 per cent.

4-*Amino*-2-*phenylquinoline hydriodide*, colourless needles from ethanol, m.p. 249–250° (decomp.). Found: C, 51·9; H, 3·65; N, 7·85; I, 36·65. $C_{15}H_{13}N_2I$ requires C, 51·7; H, 3·8; N, 8·05; I, 36·5 per cent; 4-diacetylamino-2-phenylquinoline, colourless needles from ethanol, m.p. 108–110° (recorded[10] 117°). Found: C, 75·6; H, 5·25; N, 8·7. Calc. for $C_{19}H_{16}O_2N_2$, C, 75·0; H, 5·3; N, 9·2 per cent; 4-acetamido-2-phenylquinoline, colourless needles from ethanol, m.p. 193–194° (recorded[10] 108°). Found, C, 77·6; H, 5·5; N, 10·7. Calc. for $C_{17}H_{14}ON_2$, C, 77·9; H, 5·4; N, 10·7 per cent; *hydriodide*, colourless needles from ethanol, m.p. 279–281° (decomp.). Found: C, 51·75; H, 4·1; N, 6·8; I, 31·7. $C_{17}H_{15}ON_2I$ requires C, 52·3; H, 3·9; N, 7·2; I, 32·6 per cent.

5-*Acetamido*-6-*methylquinaldine*, colourless needles from benzene, m.p. 206–207°. Found: C, 72·4; H, 6·6; N, 13·0. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·6; N, 13·1 per cent; 5:6-*diacetamidoquinoline*, cream coloured needles from aqueous ethanol, m.p. 257–258°. Found: C, 64·4; H, 5·15; N, 17·1. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·4; N, 17·3 per cent; 5:7-*diacetamidoquinoline*, colourless needles from aqueous ethanol, m.p. 283°. Found: C, 64·1; H, 5·25; N, 17·1. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·4; N, 17·3 per cent; 6:8-*diacetamidoquinoline*, colourless needles from aqueous ethanol, m.p. 243–244°. Found: C, 64·3; H, 5·4; N, 17·5. $C_{13}H_{13}O_2N_3$ requires C, 64·2; H, 5·4; N, 17·3 per cent.

Quinoline-7-*carboxamide*, cream coloured needles from chloroform-light petroleum (b.p. 40–60°), m.p. 178–179°. Found: C, 69·65; H, 4·7; N, 16·0. $C_{10}H_8O_2N$ requires C, 69·8; H, 4·7; N, 16·3 per cent; 7-*acetamido*-4-*aminoquinoline*, colourless needles from water, m.p. 287–288°.

TABLE IV

MISCELLANEOUS DECAMETHYLENE BIS(QUATERNARY AMMONIUM IODIDES)

$[R^+.(CH_2)_{10}.R^+]2I^-$

Reaction solvent = ethyl methyl ketone

R	Reaction time (hr.)	m.p.	Cryst. form	Crystn. solvent	Found per cent C	H	N	I	Formula	Required per cent C	H	N	I
3 AcNH Q	580	206–207°	Yellow nodules	MeOH/EtOH	50·0	5·3	7·2	33·2	$C_{32}H_{40}O_2N_4I_2$	50·1	5·3	7·3	33·2
3 NH_2 Q	—	159–161°	Yellow microcrystals	EtOH	48·5	5·6	8·2	36·9	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
4 AcNH Q[1]	260	—	—	—	—	—	—	—	—	—	—	—	—
4 NH_2 Q[2]	40	238–239°	Cream microcrystals	EtOH	48·65	5·5	8·2	37·1	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
4 AcNH.6MeO Q	600	215–216°	Yellow needles	EtOH	49·0	5·7	6·7	30·75	$C_{34}H_{44}O_4N_4I_2$	49·4	5·4	6·8	30·75
4 NH_2.6MeO Q	—	253–254°	Yellow needles	EtOH/Et_2O	48·5	5·8	7·5	34·1	$C_{30}H_{40}O_2N_4I_2$	48·5	5·4	7·55	34·2
5 AcNH Q[1]	400	—	—	—	—	—	—	—	—	—	—	—	—
5 NH_2 Q	—	281°	Red microcrystals	MeOH/EtOH	49·2	5·5	8·4	36·9	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
5 Cl Q	400	218–220°	Orange-red needles	MeOH/Et_2O	46·2	4·4	3·8	45·1[3]	$C_{28}H_{32}N_2Cl_2I_2$	46·6	4·5	3·9	45·1[3]
6 AcNH Q[4]	980	238–240°	Yellow needles or nodules	MeOH	49·7	5·0	7·3	33·5	$C_{32}H_{40}O_2N_4I_2$	50·1	5·3	7·3	33·2
6 NH_2 Q	—	242–243°	Orange prisms	MeOH/EtOH	48·7	5·3	8·3	37·1	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
7 AcNH Q	135	[5]Sinters at 120° m.p. 216–218°	Orange nodules	MeOH/EtOH	49·7	5·1	7·3	33·2	$C_{32}H_{40}O_2N_4I_2$	50·1	5·3	7·3	33·2
7 NH_2 Q	—	249–251°	Orange needles	MeOH/EtOH	49·8	5·4	8·2	36·8	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
4 AcNH iQ	125	214–215°	Yellow needles	EtOH/Et_2O	50·0	5·4	7·4	32·9	$C_{32}H_{40}O_2N_4I_2$	50·1	5·3	7·3	33·2
4 NH_2 iQ	—	194–195°	Yellow needles	EtOH/light petroleum b.p. 40–60°	49·4	5·4	8·2	37·05	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
5 AcNH iQ[6]	440	186–188°	Yellow granules	EtOH	50·5	5·0	7·1	32·85	$C_{32}H_{40}O_2N_4I_2$	50·1	5·3	7·3	33·2
5 NH_2 iQ	—	208°	Yellow microcrystals	MeOH/EtOH	49·4	5·3	7·9	36·9	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
5:8 diAcNH iQ[1]	300	—	—	—	—	—	—	—	—	—	—	—	—
5:8 diNH_2 iQ	—	155–156°	Red needles	EtOH/Et_2O	46·8	5·7	11·85	35·35	$C_{28}H_{38}N_6I_2$	47·2	5·4	11·8	35·7
4:6 diAcNH C	130	223–225°	Orange granules	MeOH/EtOH	46·4	5·25	12·6	28·45	$C_{34}H_{44}O_4N_8I_2$	46·3	5·0	12·7	28·8
4:6 diNH_2 C	—	209–211°	Yellow microcrystals	MeOH/EtOH	44·0	5·2	15·65	35·3	$C_{26}H_{36}N_6I_2$	43·7	5·1	15·7	35·6
3 AcNH P[4]	96	Sinters 95–97°[5] then melts over a range	Cream coloured granules	EtOH	43·5	5·35	8·5	37·85	$C_{24}H_{36}O_2N_4I_2$	43·2	5·45	8·4	38·1
3 NH_2 P	—	177–178°	Cream coloured microcrystals	EtOH	41·35	5·7	9·8	43·2	$C_{20}H_{32}N_4I_2$	41·2	5·5	9·6	43·6
3 $CONH_2$ P	70	206–208°	Colourless microcrystals	EtOH	48·4	5·85	9·9	29·2[7]	$[8]C_{22}H_{32}O_2N_4Br_2$	48·5	5·9	10·3	29·4[7]
4 AcNH P	115	173–174°	Cream coloured clusters	EtOH	43·4	5·5	8·7	37·8	$C_{24}H_{36}O_2N_4I_2$	43·2	5·45	8·4	38·1
4 NH_2 P	—	243–244°	Colourless needles	EtOH	41·6	5·3	9·5	43·5	$C_{20}H_{32}N_4I_2$	41·2	5·5	9·6	43·6
4 AcNH.NH.CO P	340	179–181°	Yellow granules	EtOH	42·0	5·4	11·4	33·8	$C_{26}H_{38}O_4N_6I_2$	41·5	5·1	11·2	33·8

Q = Quinolinium. iQ = *iso*Quinolinium. C = Cinnolinium. P = Pyridinium.

[1] Hydrolysed directly to the amino quaternary without purification. [2] Also prepared by acid hydrolysis of the 4-acetamidoquaternary salt. [3] Total halogen. [4] Reaction solvent benzene. [5] Dihydrate. [6] Reaction solvent ethanol. [7] Bromine. [8] Bromide.

Found: C, 65·1; H, 5·7; N, 20·85. $C_{11}H_{11}ON_3$ requires C, 65·7; H, 5·5; N, 20·9 per cent.

Baker[15] has prepared 4-aminocinnoline in 39 per cent yield from 4-hydroxycinnoline by conversion to the 4-chloro compound and treatment of this with alcoholic ammonia in the presence of copper acetate. We have obtained the amine in 70·5 per cent yield (calculated on the hydroxy compound) by the action of gaseous ammonia on a phenolic solution of 4-chlorocinnoline. The acetyl derivative, cream coloured needles from water, had m.p. 272–273° (as recorded[16]). Found: C, 64·1; H, 4·9; N, 22·35. Calc. for $C_{10}H_9ON_3$, C, 64·2; H, 4·85; N, 22·5 per cent. 4-*Benzamidocinnoline*, cream coloured needles from ethanol, m.p. 222–224°. Found: C, 72·15; H, 4·4; N, 16·75. $C_{15}H_{11}ON_3$ requires C, 72·3; H, 4·45; N, 16·9 per cent.

Preparation of Quaternary Salts

Method (*a*). By refluxing excess of the tertiary base with a dihalide in an appropriate solvent, for example: *Heneicosylenebis*(iso*quinolinium bromide*). 1:21-Dibromoheneicosane (1·0 g.) and *iso*quinoline (1·0 g.) in ethyl methyl ketone (25 ml.) were refluxed for 90 hr. The oil which separated solidified on scratching, and was filtered off, washed with ethyl methyl ketone, then water, and dried. After recrystallisation from methanol-acetone, *heneicosylenebis*(iso*quinolinium bromide*) was obtained as a cream coloured microcrystalline powder, m.p. 147–148°. Found: C, 65·8; H, 7·8; N, 3·9; Br, 22·4. $C_{39}H_{56}N_2Br_2$ requires C, 65·7; H, 7·9; N, 3·9; Br, 22·5 per cent. The properties of related polymethylenebis (-quinolinium and -*iso*quinolinium iodides) are listed in Table I. Other salts listed below were prepared by conventional double decomposition methods: *Dotriacontylenebis*(iso*quinolinium perchlorate*) colourless microcrystalline solid from ethanol, m.p. 124°. Found: C, 65·9; H, 8·6; N, 2·9; Cl, 8·05. $C_{50}H_{78}O_8N_2Cl_2$ requires C, 66·3; H, 8·7; N, 3·1; Cl, 7·85 per cent. *Dotriacontylenebis*(iso*quinolinium methosulphate*), colourless needle clusters from ethanol-acetone, melting over the range 96–120°. Found: N, 3·0; S, 6·7. $C_{52}H_{84}O_8N_2S_2$ requires N, 3·0; S, 6·9 per cent. *Dotriacontylenebis*(iso*quinolinium nitrate*), pale pink microcrystalline solid from ethanol, sinters at 104°, m.p. 138–140°. Found: N, 6·4. $C_{50}H_{78}O_6N_4$ requires N, 6·75 per cent. With suramin, very sparingly soluble products separated, which could not be recrystallised, e.g., *Eicosylenebis*(iso*quinolinium suramin salt*), colourless microcrystalline powder, sintering at 158° and becoming homogeneous at 168–170°. Found: N, 5·8; S, 6·75. $C_{165}H_{196}O_{23}N_{12}S_6$ requires N, 5·8; S, 6·6 per cent and *Docosylenebis*(iso*quinolinium suramin salt*) colourless microcrystalline powder, sintering at 153–155° and becoming homogeneous at 173–175°. Found: N, 6·0; S, 6·55. $C_{171}H_{208}O_{23}N_{12}S_6$ requires N, 5·6; S, 6·4 per cent.

Method (*b*). By refluxing excess of the amide with a dihalide in an appropriate solvent, followed by acid hydrolysis of the resultant quaternary amide, for example: *Tetramethylenebis*(7-*amino*iso*quinolinium iodide*). 7-Acetamido*iso*quinoline (0·4 g.), and tetramethylene di-iodide (0·22 g.) in ethyl methyl ketone (10 ml.) were refluxed for 40 hr. After cooling,

TABLE V

MISCELLANEOUS POLYMETHYLENE BIS(QUATERNARY AMMONIUM IODIDES)

$[R^+.(CH_2)_n.R^+]2I^-$

Reaction solvent = ethyl methyl ketone

R	Reaction time (hr.)	m.p.	Cryst. form	Crystn. solvent	Found per cent C	H	N	I	Formula	Required per cent C	H	N	I
n = 4													
5 AcNH Q	250	290–291°	Yellow microcrystals	H_2O/EtOH/Et_2O	45·4	4·3	8·15	37·3	$C_{26}H_{28}O_2N_4I_2$	45·75	4·1	8·2	37·2
5 NH_2 Q	—	287–288°	Red needles	MeOH/EtOH	44·2	4·35	9·2	41·9	$C_{22}H_{24}N_4I_2$	44·15	4·05	9·4	42·5
7 AcNH Q	100	303–304°	Orange-yellow needles	MeOH/EtOH	45·9	4·2	8·2	36·85	$C_{26}H_{28}O_2N_4I_2$	45·75	4·1	8·2	37·2
7 NH_2 Q	—	321–322°	Yellow microcrystals	MeOH/EtOH	44·3	4·15	9·6	42·05	$C_{22}H_{24}N_4I_2$	44·15	4·05	9·4	42·5
5 AcNH iQ	40	285°	Yellow microcrystals	MeOH/EtOH	45·5	4·0	8·2	37·1	$C_{26}H_{28}O_2N_4I_2$	45·75	4·1	8·2	37·2
5 NH_2 iQ	—	290–291°	Yellow microcrystals	MeOH/EtOH	43·9	4·2	9·05	42·35	$C_{22}H_{24}N_4I_2$	44·15	4·05	9·4	42·5
7 Cl iQ	24	242–243°	Yellow needles	MeOH/Et_2O	41·1	3·2	4·4	50·8[1]	$C_{22}H_{20}N_2Cl_2I_2$	41·4	3·2	4·4	51·0[1]
3 Br P[2]	24	[2]247°	Yellow needles	H_2O/MeOH	27·0	2·6	4·4	66·1[1]	$C_{14}H_{16}N_2Br_2I_2$	26·8	2·6	4·5	66·1[1]
n = 5													
3 Br P[2]	24	243°	Yellow needles	H_2O/MeOH	28·2	3·0	4·4	64·45[1]	$C_{15}H_{18}N_2Br_2I_2$	28·1	2·8	4·4	64·7[1]
n = 6													
3 Br P[2]	24	218°	Yellow rosettes	MeOH	29·4	3·3	4·3	63·5[1]	$C_{16}H_{20}N_2Br_2I_2$	29·4	3·1	4·3	63·3[1]
4 AcNH Q	400	249–250°	Yellow microcrystals	MeOH/EtOH	47·0	4·7	7·6	35·2	$C_{28}H_{32}O_2N_4I_2$	47·3	4·5	7·9	35·8
4 NH_2 Q[4]	50	274–275°	Cream microcrystals	EtOH	46·0	4·4	8·7	40·6	$C_{24}H_{28}N_4I_2$	46·0	4·5	8·95	40·6
4 PrNH 2 Me Q	380	281–282°	Tan prisms	MeOH/EtOH	51·7	6·1	7·6	34·2	$C_{32}H_{44}N_4I_2$	52·0	6·0	7·6	34·4
4-n-Heptyl-amino 2 Me Q	336	208–209°	Pink prisms	MeOH/Et_2O	56·4	7·0	6·4	29·7	$C_{40}H_{60}N_4I_2$	56·5	7·1	6·6	29·9
4 AcNH.2:6 di-Me Q	1030	275°	Cream microcrystals	EtOH/MeOH	49·6	5·5	7·2	33·3	$C_{32}H_{40}O_2N_4I_2$	50·1	5·3	7·3	33·2
4 NH_2 2:6 di-Me Q-4	260	332°	Cream granules	MeOH/EtOH	49·3	5·6	8·0	36·9	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
5 AcNHQ	350	334–336°	Orange needles	MeOH/Et_2O	47·2	4·7	7·5	35·0	$C_{28}H_{32}O_2N_4I_2$	47·3	4·5	7·9	35·8
5 NH_2 Q	—	298–299°	Red needles	H_2O/MeOH	46·2	4·8	8·55	40·3	$C_{24}H_{28}N_4I_2$	46·0	4·5	8·95	40·6
5 AcNH 6 Me Q	260	256°	Orange-red microcrystals	EtOH	48·8	4·95	7·2	34·4	$C_{30}H_{36}O_2N_4I_2$	48·8	4·9	7·6	34·4
5 NH_2 6 Me Q	—	288°	Red microcrystals	MeOH/EtOH	47·9	5·05	8·55	38·55	$C_{26}H_{32}N_4I_2$	47·7	4·9	8·6	38·8
7 AcNH Q	96	283–284°	Yellow microcrystals	MeOH/EtOH	47·4	4·7	7·7	35·5	$C_{28}H_{32}O_2N_4I_2$	47·3	4·5	7·9	35·8
7 NH_2 Q	—	257–259°	Yellow needles	MeOH/EtOH	45·75	4·55	8·8	40·4	$C_{24}H_{28}N_4I_2$	46·0	4·5	8·95	40·6
4:6 diAcNH C[5]	260	—	—	—	—	—	—	—	—	—	—	—	—
4:6 diNH_2 C	—	291°	Yellow granules	MeOH/EtOH	40·2	4·4	17·3	38·6	$C_{22}H_{28}N_8I_2$	40·1	4·3	17·0	38·6
n = 8													
4:6 diAcNH C	280	[3]Slow 267–269° rapid 276°	Yellow granules	MeOH/EtOH	45·0	5·2	12·9	29·8	$C_{32}H_{40}O_4N_8I_2$	45·0	4·7	13·1	29·7
4:6 diNH_2 C	—	[6]Sintered 155–157° m.p. 205–207°	Yellow granules	MeOH/EtOH	41·7	5·05	16·6	36·7	$C_{24}H_{32}N_8I_2$	42·0	4·7	16·3	37·0
5 AcNH Q	200	231–233°	Orange microcrystals	MeOH/Et_2O	48·6	5·0	7·8	34·3	$C_{30}H_{36}O_2N_4I_2$	48·8	4·9	7·6	34·4
5 NH_2 Q	—	290–292°	Red microneedles	MeOH/EtOH	48·3	4·8	8·3	38·4	$C_{26}H_{32}N_4I_2$	47·7	4·9	8·6	38·8
7 AcNH Q	100	277°	Orange needles	MeOH/EtOH	49·4	5·2	7·7	34·5	$C_{30}H_{36}O_2N_4I_2$	48·8	4·9	7·6	34·4
7 NH_2 Q	—	215–216°	Orange needles	EtOH/Et_2O	47·5	4·95	8·7	38·6	$C_{26}H_{32}N_4I_2$	47·7	4·9	8·6	38·8

[1] Total halogen. [2] Reaction solvent benzene. [3] Monohydrate. [4] Also prepared by acid hydrolysis of the 4-acetamido quaternary salt. [5] Hydrolysed directly to the aminoquaternary without purification. [6] Trihydrate.

the solid was filtered off, washed with ethyl methyl ketone, dried and recrystallised from water, giving *tetramethylenebis*(*7-acetamido*-iso*quinolinium iodide*) as a pale yellow microcrystalline powder, m.p. 309–310°. Found: C, 45·6; H, 4·1; N, 8·25; I, 37·2. $C_{26}H_{28}O_2N_4I_2$ requires C, 45·75; H, 4·1; N, 8·2; I, 37·2 per cent. 0·45 g. of this was heated on the steam bath with hydrochloric acid (3 ml.) for 10 minutes, the mixture diluted with water, filtered hot, made alkaline with ammonium hydroxide, boiled, and solid potassium iodide (8 g.) added. After cooling, the precipitate was filtered off, washed with water, dried, and recrystallised from aqueous acetone, giving *tetramethylenebis*(*7-amino*iso*quinolinium iodide*) as a bright yellow microcrystalline powder, m.p. 300–301°. Found: C, 43·9; H, 4·1; N, 9·4; I, 42·15. $C_{22}H_{24}N_4I_2$ requires C, 44·15; H, 4·05; N, 9·4; I, 42·5 per cent. The following salts were prepared by double decomposition: *chloride*, yellow microcrystalline powder, from methanol-ethanol, m.p. 306–307° (decomp.). Found: C, 63·3; H, 6·2; N, 13·7; Cl, 17·3. $C_{22}H_{24}N_4Cl_2$ requires C, 63·6; H, 5·8; N, 13·5; Cl, 17·1 per cent; *nitrate*, yellow needles from aqueous acetone, m.p. 289–290°. Found: C, 56·65; H, 4·9; N, 18·0. $C_{22}H_{24}O_6N_6$ requires C, 56·4; H, 5·2; N, 17·95 per cent; *perchlorate*, yellow needles from aqueous acetone, m.p. 271–272°. Found: C, 48·4; H, 4·4; N, 10·3; Cl, 13·25. $C_{22}H_{24}O_8N_4Cl_2$ requires C, 48·6; H, 4·5; N, 10·3; Cl, 13·1 per cent.

The majority of the quaternary salts were prepared by method (*b*) and their properties are listed in Tables II–VI.

Preparation of Melamine Derivatives (BM series)

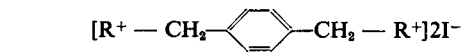
The *NN'*-dialkyl- and *NNN'N'*-tetra-alkyl polymethylene diamines employed have all been reported in the literature[17–21]. We found that the most convenient preparation (but not necessarily the best) was to treat an ethereal solution of a polymethylene dihalide with an excess of the appropriate amine at room temperature for 1–2 weeks. With primary amines, the yields were poor, large quantities of high boiling fractions being formed, but with secondary amines, e.g., diethylamine, excellent yields of the order of 80–85 per cent resulted.

NN'-*Dimethyl*-NN'-*bis*(4:6-*diamino*-s-*triazino*)-*decamethylene diamine* (II, R = Me, n = 10)

A mixture of 2-chloro-4:6-diamino-*s*-triazine[22] (1·455 g., 2 mol.), *NN'*-dimethyldecamethylene diamine (1·0 g., 1 mol.), anhydrous potassium carbonate (0·69 g., 1 mol.) and dimethylformamide (30 ml.) was heated under reflux on a steam bath for 36 hr. (the observed slight ammoniacal smell may have been due to some decomposition of the amide by the potassium carbonate). After cooling, the colourless crystals which separated were filtered, washed with dimethylformamide, then with cold water and dried. The product (2·05 g.) was then recrystallised from dimethylformamide, giving the required *base* as colourless microcrystals, m.p. 232–234°. This lost 25·6 per cent by weight at 100° *in vacuo*. $C_{18}H_{34}N_{12}\cdot 2HCON(CH_3)_2$ requires 25·9 per cent. Found for the dried material: C, 51·6; H, 8·2; N, 40·3. $C_{18}H_{34}N_{12}$ requires C, 51·7; H, 8·2; N, 40·2

TABLE VI

p-XYLYLENE BIS(QUATERNARY AMMONIUM IODIDES)



Reaction solvent = ethyl methyl ketone

R	Reaction time (hr.)	m.p.	Cryst. form	Crystn. solvent	Found per cent C	H	N	I	Formula	Required per cent C	H	N	I
5:7 diAcNH Q[1]	250	—	—	—	—	—	—	—	—	—	—	—	—
5:7 diNH$_2$ Q	—	>320°	Orange-red microcrystals	EtOH/H$_2$O	46·0	4·2	12·0	36·9	$C_{26}H_{28}N_6I_2$	46·15	3·9	12·4	37·6
7 AcNH iQ	20	327–328°	Yellow microcrystals	MeOH/H$_2$O/Et$_2$O	49·1	4·2	7·6	34·7	$C_{30}H_{32}O_2N_4I_2$	49·3	3·9	7·7	34·8
7 NH$_2$ iQ	—	278–279°	Yellow microcrystals	MeOH/H$_2$O/Et$_2$O	48·5	3·8	8·7	39·0	$C_{26}H_{24}N_4I_2$	48·3	3·7	8·7	39·3
4 AcNH C[1]	24	—	—	—	—	—	—	—	—	—	—	—	—
4 NH$_2$ C	—	278–279°	Yellow nodules	MeOH/EtOH	44·5	3·4	12·7	39·15	$C_{24}H_{22}N_6I_2$	44·4	3·4	13·0	39·2

Q = Quinolinium. iQ = *iso*Quinolinium. C = Cinnolinium.

[1] Hydrolysed directly to the aminoquaternary without purification.

per cent. Treatment of this with methyl iodide (2·1 mol.) in dimethylformamide at room temperature for 4 weeks gave the *methiodide* (III, R = R′ = Me, n = 10) as cream coloured granules from ethanol-ether, m.p. 252–253°. Found: C, 34·4; H, 5·7; N, 23·5; I, 36·3. $C_{20}H_{40}N_{12}I_2$ requires C, 34·2; H, 5·7; N, 23·9; I, 36·2 per cent; *perchlorate*, colourless granules from ethanol-ether, m.p. 226–228°. Found: C, 37·7; H, 6·4; N, 26·1; Cl, 10·9. $C_{20}H_{40}O_8N_{12}Cl_2$ requires C, 37·1; H, 6·2; N, 26·0; Cl, 11·0 per cent.

NN′-dimethyl-NN′-*bis*(4:6-*diamino*-s-*triazino*)*octamethylene diamine*, colourless granules from dimethylformamide, m.p. 216–218°. This lost 27·0 per cent by weight at 100° *in vacuo*. $C_{16}H_{30}N_{12}2HCON(CH_3)_2$ requires 27·2 per cent. Despite repeated recrystallisations and drying at 100° *in vacuo*, it was impossible to obtain a satisfactory nitrogen analysis. Found: C, 49·2; H, 8·1; N, 41·3. $C_{16}H_{30}N_{12}$ requires C, 49·2; H, 7·75; N, 43·1 per cent; the corresponding *methiodide*, cream coloured granules from ethanol-ether, m.p. 252–254° was also difficult to analyse. Found: C, 33·35; H, 5·7; N, 25·2; I, 35·5. $C_{18}H_{36}N_{12}I_2$ requires C, 32·05; H, 5·4; N, 24·9; I, 37·7 per cent, although the *perchlorate* obtained from it by double decomposition as colourless microcrystals from ethanol-ether, m.p. 202–204°, analysed satisfactorily. Found: C, 35·0; H, 6·0; N, 27·35; Cl, 11·3. $C_{18}H_{36}O_8N_{12}Cl_2$ requires C, 34·9; H, 5·9; N, 27·1; Cl, 11·5 per cent; NN′-*dimethyl*-NN′-*bis*(4:6-*diamino*-s-*triazino*)*hexamethylene diamine*, cream coloured microcrystalline powder from dimethylformamide-ether, m.p. 124–126°. It was not possible to drive off all the solvent of crystallisation, and this material was therefore analysed after drying at room temperature. Found: C, 46·2; H, 7·5; N, 38·8. $C_{14}H_{26}N_{12}.2HCON(CH_3)_2$ requires C, 47·2; H, 7·9; N, 38·6 per cent; *methiodide*, cream coloured microcrystals from ethanol-ether, m.p. 272°. Found: C, 29·85; H, 5·3; N, 25·7; I, 38·8. $C_{16}H_{32}N_{12}I_2$ requires C, 29·7; H, 5·0; N, 26·0; I, 39·3 per cent.

Attempt to Prepare the Di-ethochloride of NN′-*Diethyl*-NN′-*bis*(4:6-*diamino*-s-*triazino*)*decamethylene diamine* (III, R = R′ = Et, n = 10) *by an Unambiguous Route*

A mixture of 2-chloro-4:6-diamino-*s*-triazine (1·5 g., 2 mol.) and *NNN′N′*-tetraethyl decamethylene diamine (1·46 g., 1 mol.) in dimethylformamide (80 ml.) was refluxed for 260 hr. The solvent was then distilled off *in vacuo*, the residue treated with ether and left overnight, when the brown oily product had become almost solid. The solvent was then decanted off, the residue dissolved as far as possible in ethanol, filtered, concentrated to small bulk and cooled. After filtering, the resultant brownish product was recrystallised from ethanol (after charcoal), giving 0·4 g. of unidentified colourless needles or octahedra, m.p. 305–307°, which contained no halogen. Found: C, 39·2; H, 6·4; N, 54·5; Cl, 0 per cent. When *NNN′N′*-tetramethyl hexamethylene diamine was used, the unidentified crude product again contained no halogen.

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