298. *Potential Trypanocides. The Action of Polymethylene Dihalides on 4-Aminoquinaldine.*

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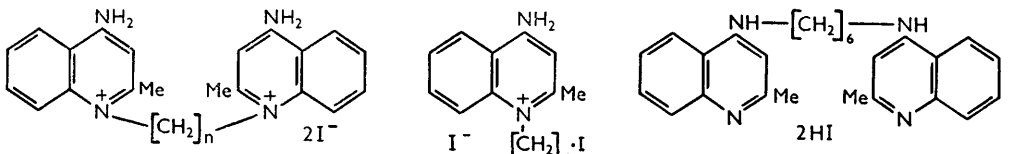
In an attempt to obtain a synthetic trypanocide, a series of polymethylene-bis-(4-aminoquinaldinium salts) was prepared. The decamethylene member was found to be a potent antibacterial agent, and is now commercially available. During the preparation of the hexamethylene homologue, the presence of a highly trypanocidal impurity was demonstrated. This was identified as 4-amino-1-(6-4′-quinaldinylaminohexyl)quinaldinium iodide hydriodide, and a practicable synthesis of it has been developed.

Our recent investigations have shown that heterocyclic polymethylenebis(quaternary ammonium salts) exhibit a wide range of biological activity.[1,2] These compounds have symmetrical molecules with relatively large end-groups, a feature which is also present in many compounds active against trypanosomiasis (the so-called " butterfly "[3] or " dumb-bell-shaped "[4] structure). Consequently, the possible therapeutic action of a simple series, the polymethylenebis(*iso*quinolinium salts), was examined in mice infected with *Trypanosoma congolense*. Slight activity was demonstrated, highest in the hexamethylene compound.

Since the decamethylene chain was the most readily available, we next prepared a series of basically substituted heterocyclic decamethylenebis(quaternary ammonium salts), with the intention of later shortening the chain length of the most promising compounds. One of the first compounds made was decamethylenebis-(4-aminoquinaldinium iodide) (I), since several synthetic trypanocides are derivatives of 4-aminoquinaldine.[5] This was



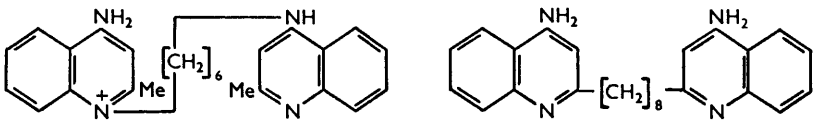
appreciably active against *T. congolense*; it also possessed high antibacterial and antifungal activity,[6] and the chloride, given the approved name of " dequalinium chloride " by the General Medical Council, is commercially available under the name " Dequadin ". Reduction of the chain length increased the trypanocidal activity in infected mice. The octamethylene homologue (II), at a dose of 10 mg./kg., was approximately as active against *T. rhodesiense* in mice as was suramin and stilbamidine, although it was less effective at a dose of 1 mg./kg. The product from the reaction of 4-aminoquinaldine with hexamethylene di-iodide, on recrystallisation from ethanol–ether, gave satisfactory analyses for the expected hexamethylene bis-(4-aminoquinaldinium iodide) (III) and appeared particularly active against *T. congolense* in mice. It was therefore prepared on a larger scale, but the product, after recrystallisation from ethanol or ethanol–methanol, while still giving satisfactory analyses, had a slightly higher melting point but an unexpectedly low trypanocidal activity (less than the crude material before recrystallisation). The original high activity might thus have been due to impurities.

Fractional crystallisation of the crude reaction mixture was difficult but, although

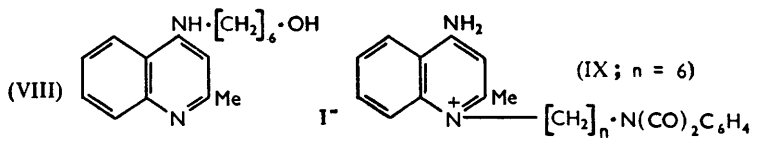
[1] Taylor, *J.*, (*a*) 1951, 1150; (*b*) 1952, 142; (*c*) 1952, 1309.
[2] Collier, Potter, and Taylor, *Brit. J. Pharmacol.*, (*a*) 1953, **8**, 34; (*b*) 1955, **10**, 343.
[3] Goble, *J. Pharmacol.*, 1950, **98**, 49.
[4] Walls, *Chem. and Ind.*, 1951, 606.
[5] Jensch, *Angew. Chem.*, 1937, **50**, 891.
[6] Babbs, Collier, Austin, Potter, and Taylor, *J. Pharm. Pharmacol.*, 1956, **8**, 110.

complete separation was not originally achieved, pharmacological testing of different fractions indicated that at least three substances were present. Since the second fraction was most active against *T. congolense* (and had low toxicity), it was considered to contain the active impurity, which we provisionally called " Substance II."

Paper-chromatographic separation of the crude mixture obtained by reaction in 4-methylpentan-2-ol, yielded 4 spots of approximate R_F values 0·35 (A), 0·56 (B), 0·63 (C), and 0·72 (D). When the reaction was carried out in ethyl methyl ketone, the crude product gave the same 4 spots and an additional spot of approximate R_F value 0·8 (E). The first spot A, which rapidly faded, was due to the iodide ion (cf. Marini-Bettolo and Miranda [7]). An aqueous extract of the crude product from the reaction in 4-methylpentan-2-ol, when made alkaline, yielded 4-aminoquinaldine, indicating that one of the fractions might be 4-aminoquinaldine hydriodide. This was confirmed, the chromatogram being identical with spot D.



Repeated recrystallisation (from methanol–ethanol) of the water-insoluble residue yielded the pure product corresponding to spot B, whose analysis and reactions (*e.g.*, reprecipitation by the addition of sodium iodide to an alkaline solution) showed it to be the originally required hexamethylenebis-(4-aminoquinaldinium iodide) (III). This compound was also prepared, although in exceedingly small yield, by the action of hexamethylene di-iodide on 4-acetamidoquinaldine, followed by acid hydrolysis and addition of potassium iodide. Very laborious fractional crystallisation of the alcoholic mother-liquors from the bisquaternary salt eventually yielded a very small quantity of pure " Substance II " corresponding to spot C, which analysis showed to be isomeric with the bisquaternary salt. A very approximate composition of the crude reaction mixture was: 4-aminoquinaldine hydriodide, 15%; hexamethylenebis-(4-aminoquinaldinium iodide), 70—75%; and " Substance II ", 15—10%.



Fractional crystallisation of the crude product from the reaction in ethyl methyl ketone yielded the fourth product, corresponding to spot E, which was identified by synthesis, mixed melting point, and chromatography as the monoquaternary salt, 4-amino-1-6′-iodohexylquinaldinium iodide (IV).

From the analysis of " Substance II ", several structures were possible, *e.g.* (V), (VI), and (VII).

The hydrochloride corresponding to the salt (V) was readily synthesised by interaction of hexamethylenediamine and 4-chloroquinaldine, but the corresponding dihydriodide differed from " Substance II." Since chromatography indicated the total absence of product (V) from the crude reaction mixture, it was originally considered unlikely that " Substance II " would possess the related structure (VI), and considerable work on the synthesis of the isomer (VII) was therefore carried out. This proved extremely difficult and has not yet been accomplished, although work continues.

Consequently the synthesis of the asymmetrical compound (VI) was investigated.

[7] Marini-Bettolo and Miranda, *Rend. Ist. sup. San.*, 1954, **17**, 463.

6-Aminohexanol reacted with 4-chloroquinaldine to give 4-6′-hydroxyhexylaminoquinaldine (VIII), which with hydriodic acid gave the hydriodide of the corresponding 6-iodo-compound. Refluxing this with 4-aminoquinaldine in 4-methylpentan-2-ol and fractionating the product gave " Substance II " (m. p., mixed m. p., chromatography, and biological activity), although in poor yield. This proved the presence of a 4-[substituted hexylamino]quinaldine structure, but was obviously not a practicable synthesis of the trypanocide.

Such a synthesis was finally effected as follows: *N*-6-iodohexylphthalimide and 4-aminoquinaldine in boiling ethyl methyl ketone gave the phthalimido-quaternary salt (IX). With hydrazine and hydrochloric acid this yielded the amino-compound, which with 4-chloroquinaldine (alone or in phenol) gave " Substance II " (VI) in excellent yield. The last reaction was also carried out satisfactorily by using 4-phenoxy- or 4-methoxy- in place of 4-chloro-quinaldine, as is to be expected since 4-phenoxyquinolines are intermediates in reactions of 4-chloroquinolines with aliphatic amines in the presence of phenol.[8]

The two synthetic products and " Substance II " were identical in m. p., mixed m. p., chromatography, infrared absorption spectrum, and biological activity. The structure of " Substance II " was confirmed when addition of sodium iodide to its alkaline solution gave the quaternary monoiodide corresponding to (VI). This with alkyl halides yielded the corresponding quaternary salts.

Of several salts of " Substance II " prepared, preliminary field trials in Africa indicate that the chloride (registered name Tozocide) possesses high therapeutic activity against trypanosomiasis in cattle. Other salts are being investigated for prophylactic activity.

NN′-Di-4-quinaldinylhexamethylenediamine dihydriodide (V) had little activity against *T. congolense* or *T. rhodesiense*, although Schock and his collaborators [9] have recently reported that this and some closely related compounds possess curative activity against *T. gambiense* in mice.

In view of the recently reported [10] neuromuscular blocking activity of some quaternary *N*-ω-piperidinoalkylphthalimides, the corresponding activity of some of the 4-amino-1-ω-phthalimidoalkylquinaldinium iodides was investigated. 4-Amino-1-(6-phthalimidohexyl)quinaldinium iodide was approximately half as potent as (+)-tubocurarine chloride in the frog's rectus preparation.

A preliminary report of our work has been published,[11] and full pharmacological details will be described elsewhere by Collier and Smith.

Experimental

Unless otherwise stated, analyses of quaternary ammonium salts were of materials dried at 100° *in vacuo*.

Most of the polymethylenebis(*iso*quinolinium iodides) have been previously described, but the following appear to be new: *Trimethylene*, yellow plates (from methanol–ethanol), m. p. 251—253° (decomp.) (Found: C, 45·6; H, 3·7; N, 5·25; I, 45·5. $C_{21}H_{20}N_2I_2$ requires C, 45·5; H, 3·6; N, 5·05; I, 45·85%). *Tetramethylene*, yellow needles (from methanol), m. p. 247—249° (decomp.) (Found: C, 46·65; H, 3·9; N, 4·8; I, 44·35. $C_{22}H_{22}N_2I_2$ requires C, 46·5; H, 3·9; N, 4·9; I, 44·7%). *Pentamethylene*, yellow plates (from ethanol), m. p. 190—191° (Found: C, 47·4; H, 4·4; N, 4·9; I, 43·6. $C_{23}H_{24}N_2I_2$ requires C, 47·4; H, 4·2; N, 4·8; I, 43·6%). *Hexamethylene*, yellow needles or plates (from methanol–ethanol), m. p. 233—234° (Found: C, 48·5; H, 4·4; N, 4·5; I, 42·3. $C_{24}H_{26}N_2I_2$ requires C, 48·3; H, 4·4; N, 4·7; I, 42·6%). *Heptamethylene*, yellow plates (from 95% ethanol), m. p. 216—217° (Found: C, 49·1, H, 4·65; N, 4·55; I, 41·3. $C_{25}H_{28}N_2I_2$ requires C, 49·2; H, 4·6; N, 4·6; I, 41·6%). These compounds were prepared by refluxing the appropriate polymethylene dihalide with *iso*quinoline (50% excess) in benzene.

[8] Surrey and Cutler, *J. Amer. Chem. Soc.*, 1951, **73**, 2623.
[9] Schock, *J. Amer. Chem. Soc.*, 1957, **79**, 1672; Otto, Moetsch, and Schock, *Amer. J. Trop. Med. Hyg.*, 1957, **6**, 393.
[10] Donahoe, Seiwald, Neumann, and Kimura, *J. Org. Chem.*, 1957, **22**, 68.
[11] Austin, Collier, Potter, Smith, and Taylor, *Nature*, 1957, **179**, 143.

The following 4-aminoquinaldine salts appear to be new: *Hydrochloride*, needles (from ethanol), m. p. 346—347° (decomp.) (Found: C, 61·1; H, 6·2; N, 14·05; Cl, 18·1. $C_{10}H_{11}N_2Cl$ requires C, 61·7; H, 5·7; N, 14·4; Cl, 18·25%). *Hydrobromide*, needles (from methanol–ethanol), m. p. 335—336° (decomp.) (Found: C, 50·2; H, 5·0; N, 11·7, Br, 33·25. $C_{10}H_{11}N_2Br$ requires C, 50·2; H, 4·6; N, 11·7; Br, 33·5%). *Hydriodide*, needles (from ethanol), m. p. 282—283° (decomp.) (Found: C, 41·7; H, 4·05; N, 9·9; I, 44·25. $C_{10}H_{11}N_2I$ requires C, 42·0; H, 3·9; N, 9·8; I, 44·4%).

Acetylation of 4-Aminoquinaldine.—This was difficult but was carried out by refluxing 4-aminoquinaldine (2 g.), acetic anhydride (4 ml.), and pyridine (8 ml.) for 4 hr., distilling off the bulk of the solvent *in vacuo*, treating the residue with ice-water (20 ml.), and making the whole alkaline with ammonia. After further cooling, the precipitate was filtered off, washed with cold water, and recrystallised from benzene, *4-acetamidoquinaldine* being obtained as needles (2·25 g.), m. p. 162—164° (Found: loss at 100°, 15·4. $C_{12}H_{12}ON_2,2H_2O$ requires 15·25%. Found, in anhydrous material: C, 71·8; H, 6·0; N, 14·4. $C_{12}H_{12}ON_2$ requires C, 72·0; H, 6·05; N, 14·0%).

Preparation of Polymethylenebis-(4-aminoquinaldinium Salts).—Decamethylenebis-(4-aminoquinaldinium iodide) (I). Decamethylene di-iodide (17·4 g., 1 mol.), 4-aminoquinaldine (16 g., 2·3 mol.), and 4-methylpentan-2-ol (150 ml.) were refluxed for 72 hr., then cooled and filtered, and the solid was washed successively with 4-methylpentan-2-ol, acetone, water, and acetone and dried. The residue was treated in methanol with charcoal, and the solution filtered, concentrated to small bulk, and allowed to crystallise; *decamethylenebis-(4-aminoquinaldinium iodide)* (14·3 g.) was obtained as a cream-coloured microcrystalline powder, m. p. 308—309° (decomp.) (Found: C, 50·6; H, 5·5; N, 7·9; I, 35·6. $C_{30}H_{40}N_4I_2$ requires C, 50·7; H, 5·7; N, 7·9; I, 35·8%). Use of decamethylene dibromide and the same solvent gave the corresponding but colourless *bromide* (from methanol–ethanol), m. p. 326—327° (decomp.) (Found: C, 58·3; H, 6·65; N, 8·95; Br, 26·4. $C_{30}H_{40}N_4Br_2$ requires C, 58·4; H, 6·55; N, 9·1; Br, 26·0%). Reaction in ethanol gave as the only product 4-aminoquinaldine hydrobromide. The following decamethylenebis-(4-aminoquinaldinium salts) were prepared by double decomposition: *Nitrate*, needles (from ethanol–ether), m. p. 299—301° (decomp.) (Found: C, 62·5; H, 7·3; N, 13·9. $C_{30}H_{40}O_6N_6$ requires C, 62·1; H, 6·95; N, 14·5). *Chloride* (from ethanol), m. p. 326° (decomp.) (Found, on material dried at 180° *in vacuo*: C, 68·3; H, 7·8; N, 10·4; Cl, 13·25. $C_{30}H_{40}N_4Cl_2$ requires C, 68·3; H, 7·65; N, 10·6; Cl, 13·5). *Perchlorate* (from methanol–ethanol), m. p. 282—284° (decomp.) (Found: C, 55·0; H, 6·3; N, 8·7; Cl, 10·9. $C_{30}H_{40}O_8N_4Cl_2$ requires C, 55·0; H, 6·2; N, 8·55; Cl, 10·8%).

The salts in Table 1 were prepared in boiling ethyl methyl ketone, the reaction time varying from 100 to 450 hr.

TABLE 1. *Polymethylenebis-(4-aminoquinaldinium iodides)* (cf. I—III).

			Found (%)					Required (%)			
n	Solvent	M. p.*	C	H	N	I	Formula	C	H	N	I
4	M–E †	340—341°	45·7	5·0	8·9	40·0	$C_{24}H_{28}N_4I_2$	46·0	4·5	8·95	40·6
5	M–E	293—294	46·9	4·9	8·6	39·4	$C_{25}H_{30}N_4I_2$	46·9	4·7	8·75	39·7
7	EtOH	297	48·25	5·2	8·5	37·9	$C_{27}H_{34}N_4I_2$	48·5	5·1	8·4	38·0
‡	EtOH	317—318	46·8	4·85	8·0	37·3	$C_{26}H_{32}ON_4I_2$	46·6	4·8	8·4	37·9
8	EtOH	294—295	48·9	5·5	8·1	37·8	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
9	EtOH	288—289	49·8	5·7	8·1	36·6	$C_{29}H_{38}N_4I_2$	50·0	5·5	8·05	36·5
12	M–E	291—292	52·3	5·9	7·5	34·4	$C_{32}H_{44}N_4I_2$	52·0	6·0	7·6	34·4
14	E–Et ¶	266—267	53·5	6·5	7·4	32·7	$C_{34}H_{48}N_4I_2$	53·3	6·3	7·3	33·2
16	EtOH	253—255	54·45	6·3	6·8	31·65	$C_{36}H_{52}N_4I_2$	54·4	6·6	7·05	32·0
18	E–Et	253—254	55·75	6·9	6·8	30·7	$C_{38}H_{56}N_4I_2$	55·5	6·9	6·8	30·9
20	EtOH	241—242	56·0	7·3	6·8	29·5	$C_{40}H_{60}N_4I_2$	56·5	7·1	6·6	29·9

* With decomp. † M–E = MeOH–EtOH. ‡ 4-Oxaheptamethylene, $-[CH_2]_3\cdot O\cdot[CH_2]_3-$. ¶ E–Et = EtOH–$Et_2O$. The *dinitrate* corresponding to the tetradecamethylene compound had m. p. 239—241° (decomp.) (from EtOH–Et_2O) (Found: C, 63·5; H, 7·7; N, 13·2. $C_{34}H_{48}O_6N_6$ requires C, 64·15; H, 7·6; N, 13·2%).

4-Amino-1-6′-iodohexyl- (IV), yellow rosettes (from ethanol–methanol), m. p. 202° (Found: C, 39·1; H, 4·5; N, 5·8; I, 51·0. $C_{16}H_{22}N_2I_2$ requires C, 38·7; H, 4·5; N, 5·65; I, 51·2%) and *4-amino-1-3′-iodopropyl-quinaldinium iodide*, yellow prisms (from ethanol), m. p. 230—231° (Found: C, 34·7; H, 3·6; N, 6·2; I, 55·9. $C_{13}H_{16}N_2I_2$ requires C, 34·4; H, 3·55; N, 6·2; I, 55·95%), were prepared by refluxing 4-aminoquinaldine with 3 mols. of the appropriate

polymethylene di-iodide in ethyl methyl ketone. Treating the latter product with methylamine (0·5 mol.) in methanol for 6 weeks at room temperature yielded a small quantity of *4-methyl-azaheptamethylenebis-(4-aminoquinaldinium iodide)*, m. p. 282° (decomp.) (from methanol) (Found: C, 47·2; H, 5·35; N, 10·4; I, 36·8. $C_{27}H_{35}N_5I_2$ requires C, 47·4; H, 5·2; N, 10·25; I, 37·2%).

Reaction of 4-Aminoquinaldine with Hexamethylene Di-iodide.—Hexamethylene di-iodide (3·5 g., 1 mol.), 4-aminoquinaldine (4·2 g., 2·6 mol.), and 4-methylpentan-2-ol (35 ml.) were refluxed for 156 hr., cooled, and filtered, and the residue was washed three times with 4-methylpentan-2-ol, then repeatedly with acetone, and dried, giving a purplish solid (6·4 g.). This was boiled with water (100 ml.), then cooled. The solid material was collected, and extracted with water (2 × 100 ml.), the mixture being cooled before filtration. The combined aqueous extracts were concentrated to 150 ml., made alkaline with sodium hydroxide solution, kept overnight, and filtered, and the precipitate was washed with cold water and dried, giving crude 4-aminoquinaldine (0·67 g.), m. p. 152—154°. This was dissolved as far as possible in hot benzene (0·07 g. of insoluble material), and the filtrate was concentrated to small bulk and allowed to crystallise; fairly pure 4-aminoquinaldine (0·5 g.), m. p. and mixed m. p. 163°, was obtained.

The dark, water-insoluble residue obtained above was dried (4·15 g.), dissolved in methanol (450 ml.), treated with charcoal, and the whole filtered hot. To the filtrate ethanol (600 ml.) was added, the solution concentrated to 250 ml., a further 350 ml. of ethanol were added, and the solution was concentrated to 40 ml. This was allowed to cool and filtered (and the filtrate *A* retained), and the residue washed with a little ethanol and dried (2·9 g.). This material (m. p. 287—291°) gave little more than single chromatogram spot, corresponding to spot B. Repeated recrystallisation from methanol–ethanol gave cream-coloured *hexamethylenebis-(4-aminoquinaldinium iodide)* (III), m. p. 296—297° (decomp.) (Found: C, 47·5; H, 5·3; N, 8·55; I, 38·4. $C_{26}H_{32}N_4I_2$ requires C, 47·7; H, 4·9; N, 8·6; I, 38·8%). The corresponding *perchlorate* (from methanol–ethanol) had m. p. 263—265° (decomp.) (Found: C, 51·7; H, 5·5; N, 9·1; Cl, 12·1. $C_{26}H_{32}O_8N_4Cl_2$ requires C, 52·1; H, 5·4; N, 9·35; Cl, 11·85%), and the *picrate* (from aqueous acetone) had m. p. 266—268° (Found: C, 53·65; H, 4·5; N, 16·2. $C_{38}H_{36}O_{14}N_{10}$ requires C, 53·3; H, 4·2; N, 16·4%).

The alcoholic filtrate *A* was warmed and treated with warm ether (80 ml.); an oil separated. Next morning the solvent was decanted and rejected. The residual gum was dissolved as far as possible in hot ethanol (30 ml.) and kept overnight. The insoluble residue (0·11 g.; m. p. 265—270°), mainly crude hexamethylenebis-(4-aminoquinaldinium iodide), was rejected. The filtrate was concentrated to 15 ml., and warm ether (30 ml.) added, an oil separating which partly crystallised. The solvent was decanted, and a solution of the residue in the minimum quantity of boiling ethanol treated with warm acetone to turbidity, allowed to crystallise, and filtered. The residue was washed with acetone–ethanol, then with acetone, and dried, giving 0·2 g. of product, m. p. 276—278° (decomp.). Repeated recrystallisation of this from ethanol–acetone gave *Substance II*, m. p. 287—289° (decomp.) (Found: C, 47·7; H, 5·1; N, 8·4; I, 38·2%), giving a chromatogram corresponding to spot C.

Paper Chromatography.—This was carried out with Whatman No. 1 paper, by the descending technique. The most satisfactory mobile phase found was the upper layer of butanol–ethanol–water (30 : 9 : 25); development was best by iodine in chloroform; after drying, the background colour faded, leaving the fractions marked by brown spots.

NN′-Di-4′-quinaldinylhexamethylenediamine Dihydriodide (V).—4-Chloroquinaldine (2·2 g.) and hexamethylenediamine (0·66 g.) were heated on a steam-bath for 3 hr., then at 165° for 8 hr. After cooling, the solid was washed with dry ether, then dissolved in water containing a little hydrogen chloride. The solution was saturated with salt, and the tan-coloured precipitate of the dihydrochloride filtered off. This was re-dissolved in hot water, reprecipitated by 5N-ammonia, collected, and recrystallised from aqueous ethanol. *NN′-Di-4′-quinaldinylhexamethylenediamine* was obtained as needles, m. p. 210—211° (Found: C, 78·0; H, 7·7; N, 14·0. $C_{26}H_{30}N_4$ requires C, 78·4; H, 7·6; N, 14·1%). Addition of sodium iodide to a solution of this base in dilute hydrochloric acid yielded the corresponding tan-coloured *dihydriodide*, m. p. 338—340° (from methanol–ethanol) (Found: C, 47·6; H, 5·05; N, 8·75; I, 38·3. $C_{26}H_{32}N_4I_2$ requires C, 47·7; H, 4·9; N, 8·6; I, 38·8%).

The pale yellow *tetramethylene homologue*, crystallised from methanol–ethanol, had m. p. 305—306° (Found: C, 45·8; H, 4·8; N, 9·1; I, 40·2. $C_{24}H_{28}N_4I_2$ requires C, 46·0; H, 4·5;

N, 8·95; I, 40·6%), and the buff *decamethylene homologue* (from methanol–ether) m. p. 258—260° (Found: C, 50·5; H, 5·3; N, 8·0; I, 36·0. $C_{30}H_{40}N_4I_2$ requires C, 50·7; H, 5·7; N, 7·9; I, 35·8%); the *base* from the latter formed prisms (from aqueous ethanol), m. p. 178—179° (Found: C, 79·2; H, 8·6; N, 12·2. $C_{30}H_{38}N_4$ requires C, 79·3; H, 8·4; N, 12·3%).

Proof of the Presence of a 4-(*Substituted Hexylamino*)*quinaldine Structure in "Substance II".*—*5-Cyanopentyl acetate.* 5-Chloropentyl acetate [12] (159 g.), sodium iodide (151 g.), and acetone (1100 ml.) were refluxed for 34 hr., the mixture was then filtered, the acetone distilled off, the residue dissolved as far as possible in ether, and after filtration the ether was removed. The resulting crude 5-iodopentyl acetate was dissolved in ethanol (300 ml.), potassium cyanide (70 g.) in water (90 ml.) added, and the stirred mixture heated under reflux for 5 hr. The ethanol was then distilled off and the black liquid residue extracted four times with benzene, each benzene extract being washed successively with the same N-sodium hydroxide solution (50 ml.), and then with water. The combined benzene extracts were shaken with sodium sulphate, filtered, and evaporated, and the residue was distilled *in vacuo*. The fraction boiling at 134—142°/12 mm. (100 g.) was redistilled, giving *5-cyanopentyl acetate* (88 g.), b. p. 135—137°/12 mm. (Found: C, 61·9; H, 8·8; N, 8·65. $C_8H_{13}O_2N$ requires C, 61·9; H, 8·45; N, 9·0%).

6-Aminohexanol. 5-Cyanopentyl acetate (25·6 g.) and liquid ammonia (25 ml.) were heated in a rotating bomb with hydrogen (initial pressure 75 atm.) and Raney nickel. The temperature was raised as rapidly as possible to 140° (pressure rose to 130 atm.), and the bomb then allowed to cool, rotation being continued (pressure dropped to 65 atm.). After filtration and washing of the residue with ether, ethanolic hydrogen chloride was added to the combined filtrate and washings until no more heavy oil separated. Water was then added, the aqueous layer separated, 20% sodium hydroxide solution (200 ml.) added, and the mixture refluxed for 1 hr. After cooling, the clear solution was saturated with potassium carbonate, the oil extracted with chloroform, the extract shaken with anhydrous potassium carbonate, the solvent recovered, and the residue distilled *in vacuo*, giving 6-aminohexanol (15·8 g.), b. p. 126—127°/14 mm. (lit.,[13] 126°/15·3 mm.), needles, m. p. 52—54° (Found: N, 12·0. Calc. for $C_6H_{15}ON$: N, 12·0%). Distillation of the crude hydrogenation product of 5-cyanopentyl acetate without hydrolysis yielded a mixture of 6-aminohexanol and *6-aminohexyl acetate*, b. p. 111—113°/11 mm. (Found: C, 60·7; H, 11·1; N, 9·05. $C_8H_{17}O_2N$ requires C, 60·4; H, 10·8; N, 8·8%). Hydrolysis of this with hydriodic acid (*d* 1·94), followed by neutralisation and acidification with ethanolic hydrogen chloride, gave the hydrochloride of *6-aminohexyl iodide*, plates (from acetone–ether), m. p. 118—119° (Found: C, 27·45; H, 5·7; N, 5·4; Hal, 61·6. $C_6H_{15}NClI$ requires C, 27·3; H, 5·7; N, 5·3; Hal, 61·7%).

4-6′-Hydroxyhexylaminoquinaldine (VIII). 6-Aminohexanol (2 g.) and 4-chloroquinaldine (3 g.) were mixed and heated at 165—170°. When the internal temperature reached 167°, the bath was removed, but the internal temperature rose to 260°, and then fell. The mixture was then heated for a further 30 min. at 165—170°. After cooling, the reddish-orange residue was dissolved in hot ethanol and poured into excess of 2N-sodium hydroxide. The precipitated oil crystallised and was filtered off, washed with water, and dried. On recrystallisation from benzene, *4-6′-hydroxyhexylaminoquinaldine* (3·3 g.) separated as needles, m. p. 134—136° (Found: C, 74·2; H, 8·4; N, 10·9. $C_{16}H_{22}ON_2$ requires C, 74·4; H, 8·6; N, 10·85%). This reaction was more easily controlled in boiling *p*-cymene (10 ml.) but the yield was lower (2·5 g.). 4-Chloroquinaldine, heated with excess of *n*-hexylamine in a sealed tube at 160° for 3 hr. (cf. general method of Fulton and his collaborators [14]), gave *4-hexylaminoquinaldine*, needles [from light petroleum, (b. p. 100—120°)], m. p. 119—121° (Found: C, 79·0; H, 9·0; N, 11·8. $C_{16}H_{22}N_2$ requires C, 79·3; H, 9·2; N, 11·6%).

4-6′-Iodohexylaminoquinaldine hydriodide. 4-6′-Hydroxyhexylaminoquinaldine (4 g.) and hydriodic acid (8 ml.; *d* 1·94) were refluxed with stirring for 2 hr., cooled, and diluted with water, the aqueous layer was decanted and rejected, and the gummy residue washed by decantation with water. It was then dissolved in warm acetone (30 ml.), and ether added to turbidity. After crystallisation, filtration and washing with acetone–ether gave a yellowish residue which, recrystallised from ethanol, gave the required *hydriodide* (5 g.), m. p. 132—134° (Found: C, 38·75; H, 4·6; N, 5·85; I, 50·7. $C_{16}H_{22}N_2I_2$ requires C, 38·7; H, 4·5; N, 5·65; I, 51·2%).

[12] Cason, Wallcave, and Whiteside, *J. Org. Chem.*, 1949, **14**, 37.
[13] Takamoto, *J. Pharm. Soc. Japan*, 1928, **48**, 366.
[14] Fulton, Joyner, King, Osbond, and Wright, *Proc. Roy. Soc.*, 1950, *B*, **137**, 339.

Preparation of "Substance II." 4-6′-Iodohexylaminoquinaldine hydriodide (3 g.) was added to a solution of 4-aminoquinaldine (3 g.) in hot 4-methylpentan-2-ol (60 ml.), and the mixture heated at 110—120° for 48 hr. After cooling, the purplish-brown precipitate was filtered, washed with ethyl methyl ketone, and dried, then washed three times with hot water (the aqueous washings being rejected) in order to remove 4-aminoquinaldine hydriodide. The insoluble residue, which had become gummy, was dissolved in methanol (150 ml.) (charcoal), ethanol (100 ml.) was added to the filtrate, and the whole concentrated to approximately half-bulk. After cooling, a resinous non-crystallisable gum separated, which was rejected. The solution was then concentrated to small bulk, acetone added until cloudy, and left to crystallise. The small quantity (*ca.* 0·2 g.) of material which separated was filtered off and rejected. The filtrate was again concentrated to half-bulk, excess of ether added, and the mixture set aside overnight. The resinous solid (1·7 g.; sinters at 110°) which separated was filtered off and dried. Paper chromatography showed this to be rich in "Substance II". It was dissolved as far as possible in hot ethanol (45 ml.), and the mixture filtered and kept overnight. The small amount of gum which separated was removed, and excess of ether added to the solution. A gum separated which solidified in a few days. This was washed with ether, dried, and dissolved in methanol (30 ml.), ethanol (60 ml.) was added, and the solution concentrated to half-bulk, treated with a further 30 ml. of ethanol and allowed to cool. A small quantity of gum separated, and was removed; acetone was then added until crystals slowly separated. These were filtered off, washed with acetone–alcohol, and dried. The product [0·6 g.; m. p. 276—278° (decomp.)], recrystallised from methanol–ethanol–acetone, gave almost pure "Substance II" (0·2 g.), m. p. 284—286° (decomp.), mixed m. p. 286—288° (decomp.) (Found: C, 48·0; H, 5·1; N, 8·45; I, 38·5%). Further recrystallisation raised the m. p. to 287—289° (decomp.).

Synthesis of "Substance II."—N-6-*Iodohexylphthalimide.* Potassium phthalimide (11·1 g., 1 mol.) and hexamethylene di-iodide (81 g., 4 mol.) were heated at 140—150° for 24 hr., ether (600 ml.) was added, inorganic material filtered off, and the bulk of the solvent recovered. The residue, on cooling, deposited a small quantity (0·3 g.) of phthalimide, which was removed. The excess of hexamethylene di-iodide was then distilled off *in vacuo*, and the residue triturated with light petroleum (b. p. 40—60°) (75 ml.), a solid slowly crystallising. This was filtered, off washed with light petroleum (b. p. 40—60°), dried, and recrystallised from ethanol, giving N-6-*iodohexylphthalimide* as needles, m. p. 76° (14·5 g.) (Found: C, 47·6; H, 4·5; N, 3·8; I, 36·2. $C_{14}H_{16}O_2NI$ requires C, 47·1; H, 4·5; N, 3·9; I, 35·6%).

The following N-ω-*iodoalkylphthalimides* were prepared similarly: butyl, m. p. 87—89° (lit.,[15] 88—89°), *pentyl*, m. p. 73—75° (Found: N, 4·0; I, 36·2. $C_{13}H_{14}O_2NI$ requires N, 4·1; I, 37·0%), *heptyl*, m. p. 42—43° (Found: N, 3·8; I, 34·5. $C_{15}H_{18}O_2NI$ requires N, 3·8; I, 34·2%), *octyl*, m. p. 63—64° (Found: N, 3·7; I, 32·8. $C_{16}H_{20}O_2NI$ requires N, 3·6; I, 33·0%), *nonyl*, m. p. 48—50° (Found: N, 3·6; I, 32·5. $C_{17}H_{22}O_2NI$ requires N, 3·5; I, 31·8%), *decyl*, m. p. 64—65° (Found: N, 3·1; I, 30·0. $C_{18}H_{24}O_2NI$ requires N, 3·4; I, 30·75%), *tridecyl*, m. p. 60—62° (Found: N, 3·1; I, 27·7. $C_{21}H_{30}O_2NI$ requires N, 3·1; I, 27·9%). All formed needles from ethanol.

Owing to the difficulty of removing excess of the higher-boiling polymethylene di-iodides, certain *N*-ω-iodoalkylphthalimides were prepared by heating potassium phthalimide with an equimolecular quantity of di-iodide. Considerable quantities of the αω-diphthalimidoalkanes resulted, the bulk of which separated on cooling of the filtered ethereal solution of the reaction mixture. However it proved extremely difficult to remove the last traces of these compounds from the required products, which were therefore used in the rather crude state in the next reaction, since the diphthalimidoalkanes did not interfere and could be easily removed at this stage. *N*-14-Iodotetradecylphthalimide, m. p. *ca.* 71—73°, and the hexadecyl, m. p. *ca.* 68—70°, octadecyl, m. p. *ca.* 74—76°, and eicosyl, m. p. *ca.* 74—76°, homologues were then prepared.

The following are new: 1 : 16-*diphthalimidohexadecane*, plates (from ethanol), m. p. 116—117° (Found: C, 74·7; H, 8·0; N, 5·35. $C_{32}H_{40}O_4N_2$ requires C, 74·4; H, 7·8; N, 5·4%), and *octadecane*, needles (from ethanol), m. p. 117—118° (Found: C, 74·6; H, 7·8; N, 5·0. $C_{34}H_{44}O_4N_2$ requires C, 75·0; H, 8·15; N, 5·15%), and *eicosane homologues*, needles (from ethanol), m. p. 114—116° (Found: C, 75·4; H, 8·1; N, 4·7. $C_{36}H_{48}O_4N_2$ requires C, 75·5; H, 8·5; N, 4·9%).

[15] Arnstein, Hunter, Muir, and Neuberger, *J.*, 1952, 1329.

4-Amino-1-6′-phthalimidohexylquinaldinium Iodide (IX).—4-Aminoquinaldine (5·18 g.), *N*-(6-iodohexyl)phthalimide (11·7 g.) and ethyl methyl ketone (50 ml.) were refluxed for 300 hr. After cooling, the precipitate was filtered off, washed with ethyl methyl ketone, and recrystallised from ethanol–methanol, *4-amino-1-6′-phthalimidohexylquinaldinium iodide* (9·8 g.) being obtained as thick needles, m. p. 229—230° (Found: C, 55·9; H, 4·9; N, 8·15; I, 24·55. $C_{24}H_{26}O_2N_3I$ requires C, 55·9; H, 5·1; N, 8·2; I, 24·7%). This compound was also prepared by heating a solution of 4-amino-1-6′-iodohexylquinaldinium iodide (IV) and potassium phthalimide in dimethylformamide for 1 hr. on a steam-bath. The corresponding *perchlorate* crystallised from methanol as needles, m. p. 223—225° (Found: C, 59·0; H, 5·7; N, 8·45; Cl, 7·5. $C_{24}H_{26}O_6N_3Cl$ requires C, 59·1; H, 5·4; N, 8·6; Cl, 7·3%).

4-Amino-1-ω-phthalimidoalkylquinaldinium iodides, prepared by refluxing ethyl methyl ketone solutions of the appropriate *N*-ω-iodoalkylphthalimides and 4-aminoquinaldine for varying times (100—450 hr.), are recorded in Table 2. All formed needles from ethanol (unless otherwise stated).

TABLE 2. *4-Amino-1-ω-phthalimidoalkylquinaldinium iodides* (IX).

		Found (%)					Required (%)			
n	M. p.	C	H	N	I	Formula	C	H	N	I
3	260—262° *	53·05	4·35	8·85	26·7	$C_{21}H_{20}O_2N_3I$	53·3	4·3	8·9	26·85
4	263—264	54·4	4·9	8·8	25·6	$C_{22}H_{22}O_2N_3I$	54·2	4·55	8·6	26·1
5	236—238	55·4	4·8	8·45	25·4	$C_{23}H_{24}O_2N_3I$	55·1	4·8	8·4	25·35
7	170—172	56·0	5·6	7·9	24·25	$C_{25}H_{28}O_2N_3I$	56·7	5·3	7·9	24·0
8	238—240	57·9	6·0	7·9	24·0	$C_{26}H_{30}O_2N_3I$	57·5	5·6	7·7	23·4
9	174—176	57·7	5·45	7·5	23·2	$C_{27}H_{32}O_2N_3I$	58·2	5·8	7·5	22·8
10	189—191 †	58·4	6·1	7·3	22·6	$C_{28}H_{34}O_2N_3I$	58·8	6·0	7·35	22·2
13	142—144	60·5	6·7	7·1	20·6	$C_{31}H_{40}O_2N_3I$	60·7	6·6	6·85	20·7
14	155—156	60·9	6·6	7·2	20·8	$C_{32}H_{42}O_2N_3I$	61·2	6·75	6·7	20·3
16	155—157 ‡	62·5	7·05	6·15	18·9	$C_{34}H_{46}O_2N_3I$	62·3	7·1	6·4	19·4
18	151—152 §	63·25	7·5	6·15	18·6	$C_{36}H_{50}O_2N_3I$	63·25	7·4	6·15	18·6
20	144—146 §	64·0	7·5	5·7	17·7	$C_{38}H_{54}O_2N_3I$	64·1	7·7	5·9	17·9

* Microcryst., from MeOH–EtOH. † The corresponding *bromide* formed needles (from EtOH), m. p. 205—207° (Found: C, 63·6; H, 6·75; N, 7·8; Br, 15·1. $C_{28}H_{34}O_2N_3Br$ requires C, 64·1; H, 6·5; N, 8·0; Br, 15·3%), and the *nitrate* needles (from EtOH), m. p. 170—172° (Found: C, 65·8; H, 6·7; N, 11·3. $C_{28}H_{34}O_5N_4$ requires C, 66·4; H, 6·8; N, 11·1%). ‡ Nodules. § Prisms.

4-Amino-1-(6-4′-quinaldinylaminohexyl)quinaldinium iodide hydriodide (VI) (*"Substance II"*). 4-Amino-6-phthalimidohexylquinaldinium iodide (6·18 g.), methanol (60 ml.), and 90% aqueous hydrazine hydrate (0·66 g.) were heated on a steam-bath under reflux for 1 hr., water (15 ml.) added, and the bulk of the methanol distilled off under reduced pressure. Concentrated hydrochloric acid (15 ml.) was then added, and the mixture heated on a steam-bath for a further 1 hr. After cooling in ice water, the precipitated phthalhydrazide was filtered off, washed with a little ice-water, and rejected. The combined filtrate and washing were evaporated to dryness *in vacuo*, the residue dissolved in the minimum quantity of water, and concentrated sodium hydroxide solution added until no more oil separated. The aqueous layer was decanted and rejected. Saturated aqueous sodium iodide solution (6 ml.) was added to the residual oil, which was converted into a pink upper layer. After 1 hr. in a separator, the lower aqueous layer was run off and rejected. The oil was washed with aqueous sodium iodide solution (3 ml.), and the aqueous layer again rejected. After drying, the residue, which had partly solidified, was extracted with the minimum quantity of cool ethanol, the extract evaporated *in vacuo*, and the residue dried *in vacuo*, treated with 4-chloroquinaldine (1·95 g.) in methanol (7·5 ml.), and heated slowly to 160°, by which time the methanol had distilled off. The temperature of the bath was then kept at 160—170° for 1 hr. After cooling, the reddish-brown residue was triturated with a warm mixture of sodium iodide (15 g.), concentrated hydrochloric acid (7·5 ml.), and water (22·5 ml.). The mixture was then cooled and filtered (filtrate rejected), and the residue washed with water, sucked dry, dissolved in methanol (300 ml.), treated with sodium iodide (7·5 g.), refluxed for 10 min., then treated with charcoal and filtered. Ethanol (300 ml.) was added to the filtrate, and the mixture concentrated to 75 ml. Warm acetone (225 ml.) was added, the volume reduced to 75 ml., an equal volume of warm acetone added, and the mixture allowed to crystallise. The product was filtered off, washed with acetone–ethanol, then acetone and water, and dried. It was then dissolved in methanol (225 ml.), ethanol (225 ml.) added,

the solution concentrated to half-bulk, an equal volume of ethanol added, and the whole concentrated to 150 ml. and allowed to crystallise. The precipitate was filtered off, washed with ethanol, then with acetone, and dried, giving 4-*amino*-1-(6-4′-*quinaldinylaminohexyl*)*quinaldinium iodide hydriodide* (4·3 g.), m. p. 288—289° (decomp.) (Found: C, 47·5; H, 4·95; N, 8·5; I, 38·7. $C_{26}H_{32}N_4I_2$ requires C, 47·7; H, 4·9; N, 8·6; I, 38·8%).

In a further experiment, crude 4-amino-*N*-6′-aminohexylquinaldinium iodide and 4-chloroquinaldine were refluxed in phenol for 1½ hr., then poured into acetone containing sodium iodide. The reaction was also carried out by using 4-methoxy-, 4-phenoxy-, 4-*o*-tolyloxy-, or 4-(2 : 4-xylyloxy)-quinaldine (in either phenol or *o*-cresol) in place of 4-chloroquinaldine. 4-o-*Tolyloxyquinaldine* formed needles (from aqueous ethanol), m. p. 71—72° (Found: C, 81·2; H, 6·1; N, 5·85. $C_{17}H_{15}ON$ requires C, 81·9; H, 6·1; N, 5·6%) and 4-(2 : 4-*xylyloxy*)*quinaldine*, needles (from aqueous alcohol), m. p. 86—87°, b. p. 138°/0·1 mm. (Found: C, 82·1; H, 6·5; N, 5·1. $C_{18}H_{17}ON$ requires C, 82·1; H, 6·5; N, 5·3%).

The following salts of " Substance II " were prepared: *Chloride hydrochloride* (from ethanol–acetone), m. p. 297—298° (decomp.) (Found: C, 66·1; H, 6·85; N, 11·8; Cl, 15·25. $C_{26}H_{32}N_4Cl_2$ requires C, 66·2; H, 6·85; N, 11·9; Cl, 15·1%). *Nitrate hydrogen nitrate* (from methanol–ethanol), m. p. 263—264° (decomp.) (Found: C, 59·2; H, 6·2; N, 16·15. $C_{26}H_{32}O_6N_6$ requires C, 59·5; H, 6·2; N, 16·0%). *Perchlorate hydrogen perchlorate* (from ethanol–methanol), m. p. 224—226° (decomp.) (Found: C, 52·2; H, 5·3; N, 9·2; Cl, 11·85. $C_{26}H_{32}O_8N_4Cl_2$ requires C, 52·1; H, 5·4; N, 9·35; Cl, 11·85%).

When an alcoholic solution of the iodide hydriodide was mixed with an aqueous solution of the sodium or ammonium derivatives of the following compounds, very sparingly soluble precipitates of the corresponding *salts* were obtained (these did not readily crystallise, and the analyses were determined on the freshly precipitated materials): 2 : 2′-dihydroxy-1 : 1′-dinaphthylmethane-3 : 3′-dicarboxylic acid, m. p. >300° (Found: C, 74·5; H, 6·1; N, 7·1. $C_{49}H_{46}O_6N_4$ requires C, 74·8; H, 5·9; N, 7·1%); 4 : 4′-diaminostilbene-2 : 2′-disulphonic acid, m. p. >300° (Found: N, 10·8; S, 7·9. $C_{40}H_{44}O_6N_6S_2$ requires N, 10·9; S, 8·3%); *Suramin*, sinters at 270° and slowly decomposes (Found: N, 10·0; S, 7·6. $C_{129}H_{130}O_{23}N_{18}S_6$ requires N, 10·1; S, 7·7%).

4-*Amino*-1-(ω-4′-*quinaldinylaminoalkyl*)*quinaldinium iodides hydriodides* were prepared as recorded in Table 3.

TABLE 3. 4-*Amino*-1-(ω-4′-*quinaldinylaminoalkyl*)*quinaldinium iodides hydriodides.*

n in alkyl $[CH_2]_n$	Solvent *	M. p.†	Found (%) C	H	N	I	Formula	Required (%) C	H	N	I
4	M–E	311—312°	46·5	4·9	8·75	39·9	$C_{24}H_{28}N_4I_2$	46·0	4·5	8·95	40·6
5	,,	264—266	46·5	5·0	8·75	39·4	$C_{25}H_{30}N_4I_2$	46·9	4·7	8·75	39·7
7	E–A–Et	155—157	48·9	5·35	8·3	37·4	$C_{27}H_{34}N_4I_2$	48·5	5·1	8·4	38·0
8	E–A	251—253	49·35	5·4	8·2	36·9	$C_{28}H_{36}N_4I_2$	49·3	5·3	8·2	37·2
9	E–A–Et	190—192	49·8	5·45	7·6	35·8	$C_{29}H_{38}N_4I_2$	50·0	5·5	8·05	36·5
10	E–A	208—210	50·7	6·0	7·9	35·7	$C_{30}H_{40}N_4I_2$	50·7	5·7	7·9	35·8
14	E–A–Et	220—222	52·8	6·3	7·1	33·6	$C_{34}H_{48}N_4I_2$	53·3	6·3	7·3	33·2
16	,,	194—195	54·3	6·8	6·8	31·6	$C_{36}H_{52}N_4I_2$	54·4	6·6	7·05	32·0
18	M–A–Et	186—188	55·5	6·8	6·9	30·6	$C_{38}H_{56}N_4I_2$	55·5	6·9	6·8	30·9
20	E–A–Et	172—174	56·0	7·35	6·3	29·5	$C_{40}H_{60}N_4I_2$	56·5	7·1	6·6	29·9

* M = MeOH. E = EtOH. A = Acetone. Et = Et_2O. † With decomp.

Basification of " Substance II."—4-Amino-1-(6-4′-quinaldinylaminohexyl)quinaldinium iodide hydriodide (5 g.) was refluxed with potassium carbonate (5 g.) in methanol (200 ml.) and water (200 ml.) for 3 hr. on the steam-bath. Sodium iodide (50 g.) was then added, the mixture refluxed for a further 5 min., and the clear solution concentrated to half-bulk. An oil separated. Next morning the gum was filtered off, triturated several times with water, and dried, giving 4·4 g. of a friable mass. This was dissolved in ethanol (60 ml.) and after filtration concentrated to 20 ml.; warm acetone (40 ml.) was added. The following day the solvent was decanted from a small quantity of gum (which was rejected), an equal volume of acetone added, and the mixture set aside for several days with occasional scratching; crystals slowly separated. These were filtered off, washed with acetone, and recrystallised twice from ethanol–acetone, giving 4-*amino*-1-(6-4′-*quinaldinylaminohexyl*)*quinaldinium iodide*, decomp. from 132—134° (Found: C, 59·2; H, 6·15; N, 10·5; I, 24·0. $C_{26}H_{31}N_4I$ requires C, 59·3; H, 5·9; N, 10·65; I, 24·1%).

With alkyl halides this yielded the *methiodide* (from methanol–ethanol), m. p. 282—284° (decomp.) [mixed m. p. with the hydriodide, 265—270° (decomp.)] (Found: C, 48·2; H, 5·0; N, 8·3; I, 37·6. $C_{27}H_{34}N_4I_2$ requires C, 48·5; H, 5·1; N, 8·4; I, 38·0%), *ethiodide* (from methanol), m. p. 219—221° (decomp.) (Found: C, 48·9; H, 5·3; N, 8·1; I, 37·1. $C_{28}H_{36}N_4I_2$ requires C, 49·3; H, 5·3; N, 8·2; I, 37·2%), and *butiodide* (from ethanol–ether), m. p. 252—254° (decomp.) (Found: C, 50·2; H, 5·8; N, 8·2; I, 35·6. $C_{30}H_{40}N_4I_2$ requires C, 50·7; H, 5·7; N, 7·9; I, 35·8%).

When hexamethylenebis-(4-aminoquinaldinium iodide) (0·4 g.) was treated with potassium carbonate and sodium iodide in a similar manner it was recovered unchanged (0·38 g.).

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