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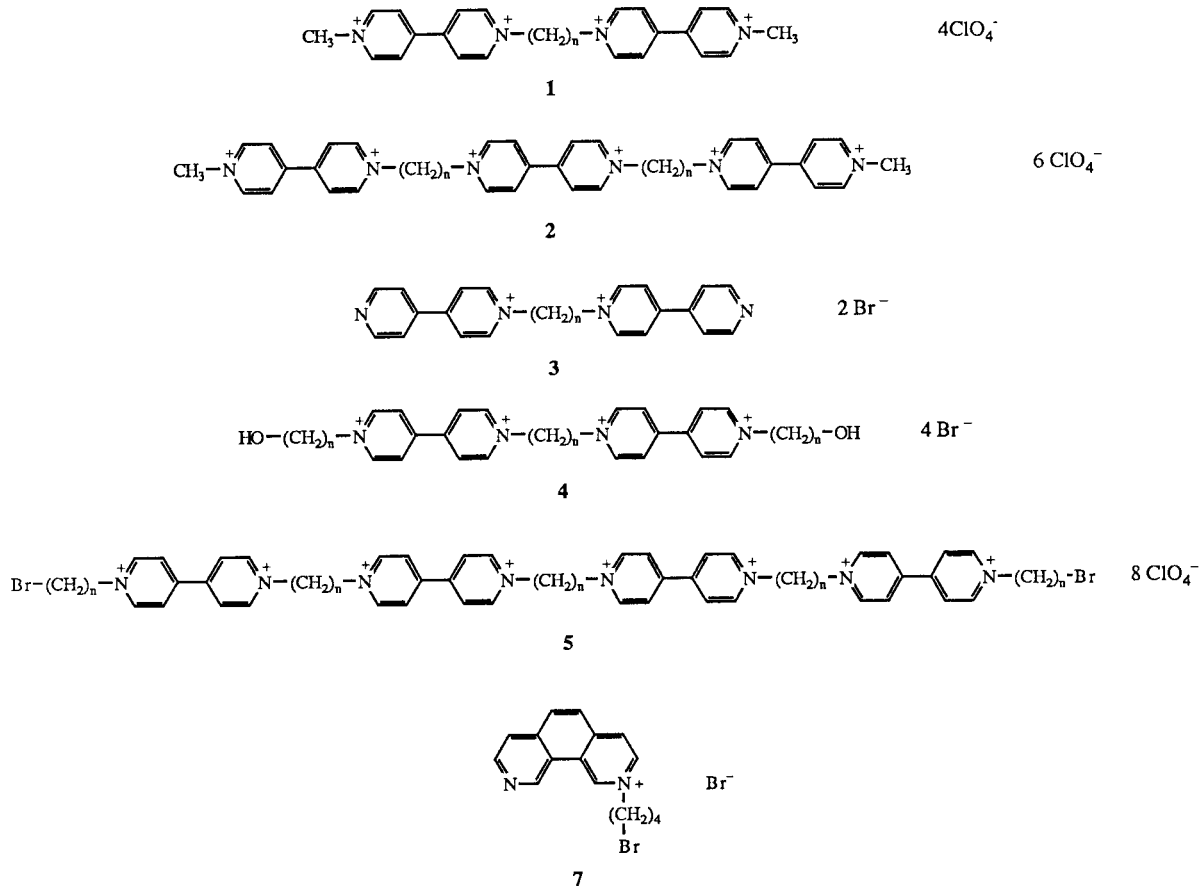
1,1''-(1,3-Propanediyl)bis-4,4'-bipyridinium dibromide is converted to 1,1''-(1,3-propanediyl)bis[1'-(3-hydroxypropyl)-4,4'-bipyridinium] tetrabromide by reaction with 1,3-dibromopropane in hot aqueous dimethylformamide. The tetraquaternary salt participates in a dequaternization and coupling reaction on treatment with hot aqueous hydrobromic acid to afford an octaquaternary salt, which is readily converted to decaquaternary and dodecaquaternary derivatives. The 1,4-butanediyl analogue participates in a similar sequence of reactions.

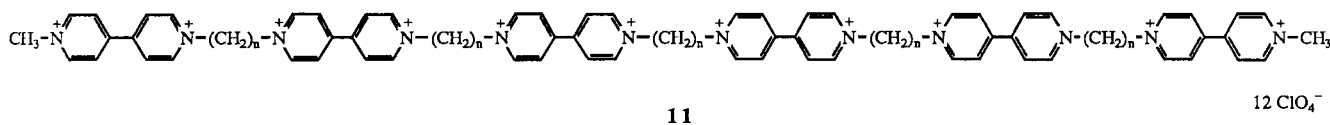
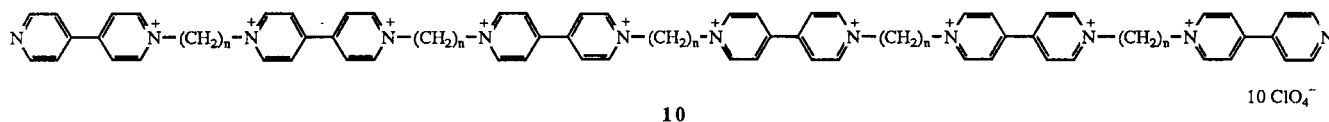
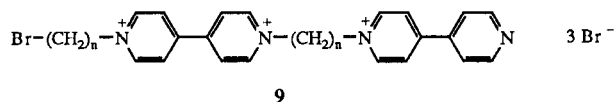
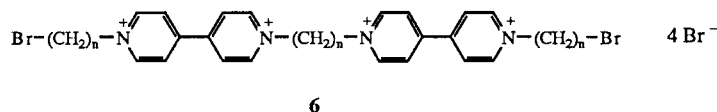
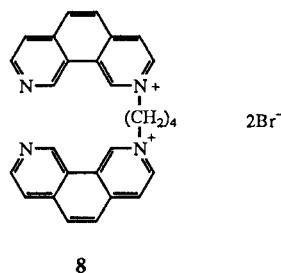
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Tetraquaternary salts derived from 4,4'-bipyridine of type **1** ($n = 2-4$) have attracted much attention as reversible redox systems [1,2] of interest as electrochromic memory display devices [3-6], as bioelectronic mediators [7,8] and as components of redox active membranes [9]. Related hexaquaternary salts of type **2** ($n = 2,3$) have also recently been prepared [10] and have been found to be potent inhibitors of the uptake of polyamines by melanoma cells [11]. Because of the diversity of interest in these tetraquaternary and hexaquaternary salts we have explored ways of preparing linear quaternary salts derived from 4,4'-bipyridine with greater numbers of quaternary centres. We

now report the synthesis of some octaquaternary, decaquaternary and dodecaquaternary salts. The synthetic routes are of general application.

The diquaternary salts **3** ($n = 3$) and **3** ($n = 4$) were each allowed to react with a large excess of 1,3-dibromopropane and 1,4-dibromobutane respectively in hot aqueous dimethylformamide. This reaction afforded the corresponding bishydroxyalkyl tetraquaternary salts **4** ($n = 3$) and **4** ($n = 4$), hydrolysis of the bromine groups accompanying quaternization. Reaction of the bishydroxyalkyl tetraquaternary salts **4** ($n = 3$) and **4** ($n = 4$) with concentrated aqueous hydrobromic acid under reflux afforded





the bisbromoalkyl octaquaternary salts **5** ($n = 3$) and **5** ($n = 4$) respectively, which were characterized as their octoperchlorates, instead of the expected bisbromoalkyl tetraquaternary salts **6** ($n = 3$) and **6** ($n = 4$). This displacement and coupling reaction has ample analogy, for example, in the thermal conversion of 4-(bromoalkyl)-4,7-phenanthroline bromides such as **7** to 4,4'-(1,4-butane-diyl)bis-4,7-phenanthroline salts **8** [12]. It presumably occurs by way of replacement of the hydroxyl groups in salts of type **4** by bromine followed by partial dequaternization of the resulting bisbromoalkyl tetraquaternary salts **6** ($n = 3$) and **6** ($n = 4$) to the triquaternary quaternary salts **9** ($n = 3$) and **9** ($n = 4$) respectively under the influence of the hot hydrobromic acid. This dequaternization reaction is then followed *in situ* by quaternization of the triquaternary salts by remaining bisbromoalkyl tetraquaternary salt to afford the bisbromoalkyl octaquaternary salts.

The bisbromoalkyl octaquaternary salts **5** ($n = 3$) and **5** ($n = 4$) were readily converted to the decaquaternary salts **10** ($n = 3$) and **10** ($n = 4$) respectively by reaction with excess 4,4'-bipyridine in dimethyl sulfoxide. The decaquaternary salts **10** ($n = 3$) and **10** ($n = 4$) were further quaternized to the dodecaquaternary salts **11** ($n = 3$) and **11** ($n = 4$) with methyl iodide in dimethyl sulfoxide and were

purified as the dodecaperchlorates.

The structures of all of the salts were in accord with their elemental analyses and nmr spectra. Their biological and redox properties are under investigation.

EXPERIMENTAL

The nmr spectra refer to proton nmr spectra (90 MHz) with tetramethylsilane as internal standard. Sometimes the spectra were run at 80° because of the poor solubility of the salts at room temperature. Microanalyses were performed by the staff of the Australian National University microanalytical laboratory.

1,1''-(1,3-Propanediyl)bis[1'-(3-hydroxypropyl)-4,4'-bipyridinium]-Tetrabromide (**4**, $n = 3$).

1,1''-(1,3-Propanediyl)bis-4,4'-bipyridinium dibromide (**3**, $n = 3$) [1] (1 g) was dissolved in dimethylformamide (20 ml) and water (10 ml) and 1,3-dibromopropane (3.9 g) was added. The mixture was heated for six hours at 90° and cooled. On dilution with acetone a yellow precipitate was obtained which was crystallised twice from aqueous ethanol to give the product, mp > 300° (yield 0.6 g). The nmr spectrum (deuterium oxide) consisted of a triplet at δ 2.38 (2H, central CH₂ protons), a broad quintet at 3.0 (4H, side chain central CH₂ protons), a triplet at 3.7 (4H, CH₂ protons adjacent to hydroxyl groups), a triplet at 4.99 (8H, CH₂ protons adjacent to quaternized nitrogens), a doublet at 8.68 (8H, aromatic protons *meta* to ring nitrogens) and a doublet at 9.30 ppm (8H, aromatic protons *ortho* to ring nitrogens).

Anal. Calcd. for $C_{29}H_{36}Br_4N_4O_2$: C, 43.9; H, 4.5; N, 7.1; Br, 40.4. Found: C, 43.6; H, 4.75; N, 7.3; Br (total) 40.7; Br (ionic) 40.3.

1,1''-(1,4-Butanediyl)bis[1'-(4-hydroxybutyl)-4,4'-bipyridinium]-Tetrabromide (**4**, $n = 4$).

1,1''-(1,4-Butanediyl)bis-4,4'-bipyridinium dibromide (**3**, $n = 4$) [1] (1 g) was dissolved in dimethylformamide (20 ml) and water (10 ml) and 1,4-dibromobutane (4.1 g) was added. The mixture was heated for six hours at 90° and cooled. On dilution with acetone a yellow precipitate was obtained which was crystallised twice from aqueous ethanol to give the product as the dihydrate mp > 300° (yield 0.8 g). The nmr spectrum (deuterium oxide) consisted of a multiplet at $\delta \sim 1.6$ -2.4 (12H, four central CH₂ protons and eight side chain central CH₂ protons), a triplet at 3.7 (4H, CH₂ protons adjacent to hydroxyl groups), a multiplet at ~ 4.6 -4.9 (8H, CH₂ protons adjacent to quaternized nitrogens), a doublet at 8.55 (8H, aromatic protons *meta* to ring nitrogens) and a doublet at 9.15 ppm (8H, aromatic protons *ortho* to ring nitrogens).

Anal. Calcd. for $C_{32}H_{42}Br_4N_4O_2 \cdot 2H_2O$: C, 44.1; H, 5.3; N, 6.4. Found: C, 44.15; H, 5.0; N, 6.6.

Octaquaternary Salt **5** ($n = 3$).

The tetraquaternary salt **4** ($n = 3$) (0.4 g) was dissolved in 48% aqueous hydrobromic acid (20 ml) and the solution was refluxed for three hours. After cooling, concentrated aqueous lithium perchlorate was added to precipitate the product as a pale brown powder which was crystallised twice from water, mp > 320° (yield 46%). The nmr spectrum (deuterium oxide) consisted of a multiplet at $\delta \sim 2.6$ -3.15 (10H, six central CH₂ protons and four side chain central CH₂ protons), a triplet at 3.6 (4H, CH₂Br protons), a multiplet at ~ 4.85 -5.10 (16H, CH₂ protons adjacent to quaternized nitrogens), a doublet at 8.60 (16H, aromatic protons *meta* to ring nitrogens) and a doublet at 9.20 ppm (16H, aromatic protons *ortho* to ring nitrogens).

Anal. Calcd. for $C_{55}H_{62}Br_2Cl_8N_8O_{32}$: C, 36.9; H, 3.5; N, 6.25. Found: C, 37.0; H, 3.5; N, 6.4.

Octaquaternary Salt **5** ($n = 4$).

The tetraquaternary salt **4** ($n = 4$) (0.4 g) was dissolved in 48% aqueous hydrobromic acid (20 ml) and the solution was refluxed for three hours. After cooling concentrated aqueous lithium perchlorate was added to precipitate the product as a white powder which was crystallised twice from water, mp > 320° (yield 53%). The nmr spectrum (deuterium oxide) consisted of a multiplet at $\delta \sim 1.9$ -2.4 (20H, twelve central CH₂ protons and eight side chain central CH₂ protons), a triplet at 3.6 (4H, CH₂Br protons), a multiplet at ~ 4.7 -4.95 (16H, CH₂ protons adjacent to quaternized nitrogens), a doublet at 8.55 (16H, aromatic protons *meta* to ring nitrogens) and a doublet at 9.15 ppm (16H, aromatic protons *ortho* to ring nitrogens).

Anal. Calcd. for $C_{60}H_{72}Br_2Cl_8N_8O_{32}$: C, 38.7; H, 3.9; N, 6.0. Found: C, 38.9; H, 3.7; N, 6.2.

Decaquaternary Salt **10** ($n = 3$).

The octaquaternary salt **5** ($n = 3$) (1 g) and a fourfold excess of 4,4'-bipyridine (0.7 g) were dissolved in dimethyl sulfoxide (15 ml) and the mixture heated at 80° for eight hours. The cooled mixture was diluted with concentrated aqueous lithium perchlorate whereupon a light brown precipitate of the product formed. It was crystallised twice from water as the pentahydrate mp > 300° (yield 61%). The nmr spectrum (deuterium oxide) consisted of a

multiplet at $\delta \sim 2.8$ -3.15 (10H, central CH₂ protons), a triplet at 5.0 (20H, CH₂ protons adjacent to quaternized nitrogens) a doublet at 7.9 (4H, aromatic protons *meta* to nitrogen in unquaternized pyridine rings), and a multiplet at 8.45-9.3 ppm (44H, remaining aromatic protons).

Anal. Calcd. for $C_{75}H_{78}Cl_{10}N_{12}O_{40} \cdot 5H_2O$: C, 40.3; H, 3.9; N, 7.5. Found: C, 40.4; H, 3.5; N, 7.3.

Decaquaternary Salt **10** ($n = 4$).

The octaquaternary salt **5** ($n = 4$) (1 g) and a fourfold excess of 4,4'-bipyridine (0.67 g) were dissolved in dimethyl sulfoxide (15 ml) and the mixture heated at 80° for eight hours. The cooled mixture was diluted with concentrated aqueous lithium perchlorate. A white precipitate formed which was crystallised twice from water as the pentahydrate mp > 300° (yield 69%). The nmr spectrum (deuterium oxide) consisted of a multiplet at $\delta \sim 2.1$ -2.4 (20H, central CH₂ protons), a multiplet at ~ 4.7 -5.0 (20H, CH₂ protons adjacent to quaternized nitrogens), a doublet at 7.9 (4H, aromatic protons *meta* to nitrogen in unquaternized pyridine rings) and a multiplet at 8.4-9.2 ppm (44H, remaining aromatic protons).

Anal. Calcd. for $C_{80}H_{88}Cl_{10}N_{12}O_{40} \cdot 5H_2O$: C, 41.7; H, 4.25; N, 7.3. Found: C, 41.7; H, 4.0; N, 7.0.

Dodecaquaternary Salt **11** ($n = 3$).

The decaquaternary salt **10** ($n = 3$) (0.5 g) and methyl iodide (1.0 g) were heated in dimethyl sulfoxide (8 ml) for six hours at 80°. On cooling the mixture was diluted with concentrated aqueous lithium perchlorate whereupon a yellow precipitate of the product formed. It was crystallised twice from water as the dihydrate mp > 300° (yield 55%). The nmr spectrum (deuterium oxide) consisted of a multiplet at $\delta \sim 2.75$ -3.15 (10H, central CH₂ protons), a singlet at 4.55 (6H, CH₃ protons), a triplet at 5.0 (20H, CH₂ protons adjacent to quaternized nitrogens), a doublet at 8.6 (24H, aromatic protons *meta* to nitrogen) and a doublet at 9.2 ppm (24H, aromatic protons *ortho* to nitrogen).

Anal. Calcd. for $C_{77}H_{84}Cl_{12}N_{12}O_{48} \cdot 2H_2O$: C, 38.4; H, 3.7; N, 7.0. Found: C, 38.35; H, 3.6; N, 7.1.

Dodecaquaternary Salt **11** ($n = 4$).

The decaquaternary salt **10** ($n = 4$) (0.5 g) and methyl iodide (1.0 g) were heated in dimethyl sulfoxide (8 ml) for six hours at 80°. The cooled mixture was diluted with concentrated aqueous lithium perchlorate. A pale brown precipitate formed which was crystallised twice from water, mp > 300° (yield 48%). The nmr spectrum (deuterium oxide) consisted of a multiplet at $\delta \sim 2.0$ -2.4 (20H, central CH₂ protons), a singlet at 4.5 (6H, CH₃ protons), multiplet at ~ 4.7 -5.0 (20H, CH₂ protons adjacent to quaternized nitrogens), a doublet at 8.5 (24H, aromatic protons *meta* to nitrogen) and a doublet at 9.1 ppm (24H, aromatic protons *ortho* to nitrogen).

Anal. Calcd. for $C_{82}H_{94}Cl_{12}N_{12}O_{48}$: C, 40.3; H, 3.85; N, 6.9. Found: C, 40.3; H, 3.9; N, 6.8.

Acknowledgements.

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