Synthesis of some substituted quinoxalines and polycyclic systems containing the quinoxaline nucleus

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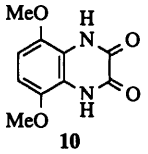
The synthesis is described of quinoxalines 11, 14, 15, 16, 20, 21, 23 and 25 of interest as intermediates. The preparation of 21 from 3 by the action of thiourea and the formation of the hexaazapentacycle 23 from sulfide 20 and butylamine are discussed. The methylation of the dione 10 is reinvestigated and the product found to be a mixture of 29 and 30. The preparation of dimethoxyquinoxaline podands, *e.g.* 32, 33, 34, 40 and 41, tricyclic crown ether 31 and pentacyclic crown ethers, *e.g.* 38, is described and the effects of metal ions on spectroscopic properties of 40 and 41 are reported.

Our objective was the synthesis of some 5,8- and 6,7-dimethoxyquinoxalines. These compounds are of interest as fluorophores[1] and the 5,8-dimethoxy series is a potential precursor of the corresponding *p*-quinones, useful as starting materials for the synthesis of tricyclic quinones through the Diels–Alder reaction. In the course of the work, we have uncovered some reactions leading to linear fused pentacyclic systems which may have interesting electronic or optoelectronic properties.[2]

A well-tried route to quinoxalines is the reaction of the appropriate *o*-phenylene diamine with a 1,2-dicarbonyl compound. Unfortunately, although the nitration of 1,4-dimethoxybenzene gives the required 2,3-dinitro derivative as the major product, it is accompanied by the isomeric 1,4-dimethoxy-2,5-dinitrobenzene,[3–5] and this unwanted product is difficult to remove when the nitration is performed on a large scale. In the present work, the mixture of dinitro isomers was hydrogenated over a palladium-on-carbon catalyst and the resulting mixture of diamines was quickly treated with the appropriate dicarbonyl compound whereupon only the *o*-diamine gave the quinoxaline. The products formed by the reaction of the *p*-diamine were easily removed. In this way, the known 5,8-dimethoxy-2,3-disubstituted quinoxalines, **1**,[5] **2**[6] and the quinoxalinedione **10**[6] were readily obtained and the last was converted to the dichloroquinoxaline, **3**.[6] This dichloro

1 R = Me
2 R = Ph
3 R = Cl
4 R = OMe
5 R = OEt
6 R = SEt
7 R = CN
8 R = CH_2Br
9 R = $NH(CH_2)_3CH_3$



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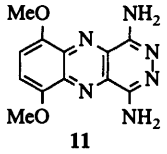

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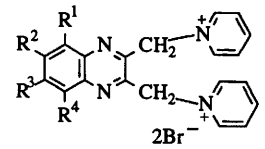
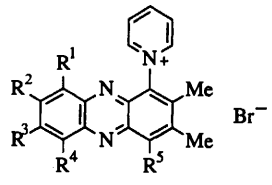
compound was then used to obtain the 2,3-dimethoxy, -diethoxy and -bis(ethylthio) derivatives, **4**, **5** and **6** respectively, all of which proved to be particularly interesting when the corresponding quinones were obtained (to be reported). The novel dimethoxy derivative **4** was also useful in the later work reported here. The dicyanoquinoxaline **7** was best obtained directly from the mixture of diamino-1,4-dimethoxybenzenes by treatment with diiminosuccinonitrile in trifluoroacetic acid.[7] The action of hydrazine on **7** gave the 1,4-diamino-6,9-dimethoxy derivative, **11**, of the pyridazino[4,5-*b*]quinoxaline nucleus prepared by Koksharova *et al.*[8]

An attempt to prepare a related diaminophenazine using the procedure described for 1,4-diamino-2,3-dimethylphenazine,[9] gave unsatisfactory results. The bis(bromomethyl)quinoxaline **8** (obtained from 1,4-dibromobutane-2,3-dione and the mixture of diaminodimethoxybenzenes) on treatment with pyridine gave the dipyridinium salt, **12**. The action of butane-2,3-dione in the presence of piperidine in methanol on **12** yielded both the phenazine **14** and the primary amine **15** (Scheme 1). Presumably, the latter was formed by attack on the α-position of the pyridinium ring by a nucleophile with subsequent ring opening and solvolysis of the Schiff's base in processes similar to those reported by Kröhnke.[10]



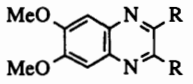
12 $R^1 = R^4 = OMe$, $R^2 = R^3 = H$
13 $R^1 = R^4 = H$, $R^2 = R^3 = OMe$



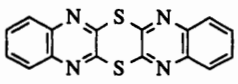
14 $R^1 = R^4 = OMe$, $R^2 = R^3 = H$, $R^5 = C_5H_4N^+Br^-$
15 $R^1 = R^4 = OMe$, $R^2 = R^3 = H$, $R^5 = NH_2$
16 $R^1 = R^4 = H$, $R^2 = R^3 = OMe$, $R^5 = NH_2$

Scheme 1

Similar reactions with the isomeric 2,3-bis(bromomethyl)-6,7-dimethoxyquinoxaline **17** and pyridine gave the dipyridinium salt **13** which, on treatment with butane-2,3-dione in methanolic solution in the presence of piperidine gave only the 1-aminophenazine derivative **16**. Attempts to cause further solvolysis of **16** to a diamine by treatment with piperidine[9] or methanolic or aqueous piperidine produced only intractable tars. The decreased reactivity of the pyridinium nucleus in **15** and **16** compared with **12** and **13** is thought to be due to electron release by the primary amino group in **15** and **16** with concomitant delocalisation of the charge.



17 R = CH_2Br
18 R = Cl



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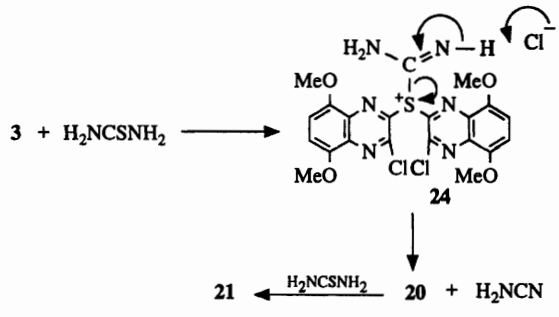
Recently, Matsuoka *et al.* reported[2] the reaction of 2,3-dichloroquinoxaline to give the dithiine **19**, a compound of interest for its electronic properties. The compound has been reported previously but was then given an incorrect structure.[11] When **3** was treated with an equimolecular quantity of thiourea in dimethylformamide (DMF), two products were obtained. The spectroscopic and elemental analysis evidence for these products is in line with the structures **20** and **21** (Scheme 2), in agreement with Matsuoka's proposal for the pentacyclic formula for the products from similar reactions. The dichloro compound **20** was an intermediate in the formation of **21**, and **20** was thought to be formed from the isothiouronium salt **24** (Scheme 3). A similar reaction of **20** with thiourea was then expected to give **21**. It was thought that the reaction of **20** with butylamine would give **22** (Scheme 2), an analogue of **21** but with both sulfur and nitrogen atoms in the middle ring. However, the reaction yielded one product which had an even number of nitrogen atoms (mass spectral data) and two butyl groups per molecule (NMR data). The compound appeared to be **23**. An attempt was made to synthesise **23** by an independent route. The 2,3-bis(butylamino)quinoxaline **9** was obtained by reaction of **3** with an excess of butylamine, but the expected reaction of **9** with **3** to give **23** did not proceed and starting materials were recovered even when the mixture was refluxed in DMF for 24 h. Presumably, this is due to the weak nucleophilicity of the exocyclic nitrogen atoms in **9** and possibly because of steric factors. The conversion of **20** to **23** was thought to go through the intermediate **22** (Scheme 4) which undergoes intermolecular attack by butylamine at the very electron deficient bridgehead atom followed by intramolecular cyclisation with elimination of hydrogen sulfide. When 2,3-dichloro-6,7-dimethoxyquinoxaline **18**[6] was treated with an excess of thiourea the only product was **25** (Scheme 5). We were interested in the preparation of crown ethers having a fused dimethoxyquinoxaline nucleus, *e.g.* **26**, as precursors of the corresponding quinones **27**, which were expected to be readily obtainable from the *p*-dimethoxy compounds. Initial attempts to obtain these compounds by *O*-alkylation of the dilactam **10** failed and caused us to survey the literature for the alkylation of **10**. Oguchi has reported[6] that methylation using dimethyl sulfate and alkali gave only the *N,N*-dimethylated product **28**, mp 180 °C. Unfortunately, only an elemental analysis (Found: N, 10.58. Calc. N, 11.20%) was given in support of the proposed structure. In our hands, repetition of Oguchi's experiment gave a product, mp 180–181 °C, which was separated into two compounds by column chromatography. Neither of these compounds was **28**. The first compound eluted, mp 202–203 °C, showed a strong absorption at 1670 cm^{-1} in the IR spectrum (therefore the compound was not **30**, an authentic



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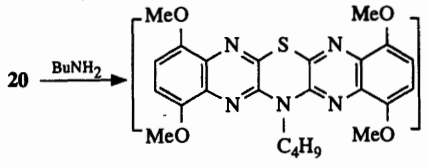
Scheme 3



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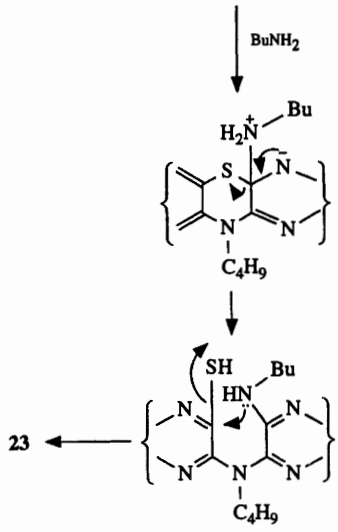
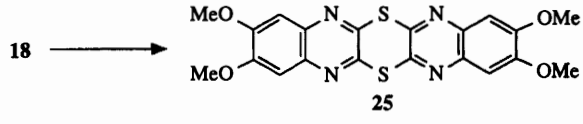


Scheme 4



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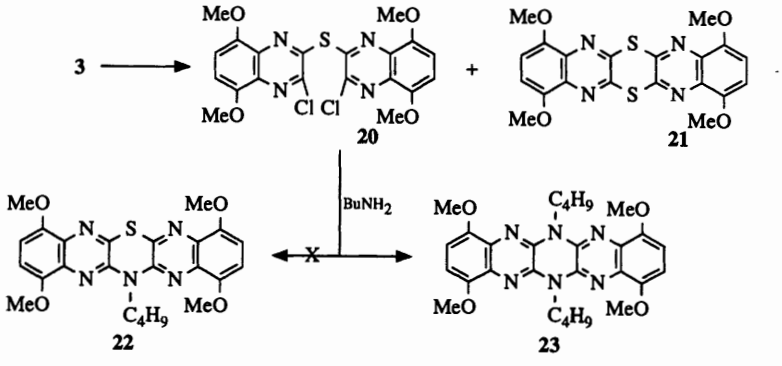
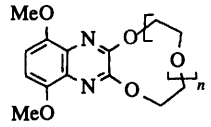
Scheme 5

sample of which was available) and no peak characteristic of the OH group. The ^1H NMR spectrum showed the compound to be unsymmetrical and to contain two different methyl groups in addition to the two methoxy groups on the carbocyclic system. This compound was assigned the structure **29**. The second compound eluted showed strong signals for the OH and lactam CO groups in the IR spectrum. The ^1H NMR spectrum showed only one methyl group in addition to the two methoxy groups



20 **21** **22** **23**

Scheme 2



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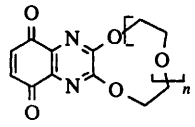

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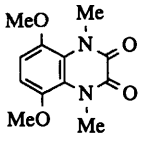

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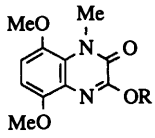
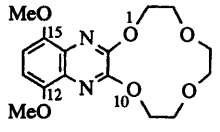


29 R = Me
30 R = H

but an exchangeable proton was present. The compound, mp 176–177 °C was assigned the structure **30**. These findings encouraged us to adopt a different route to structures of type **26**.

The 2,3-dichloroquinoxaline **3** reacted readily with alkoxides and the reaction with the disodium salt of triethylene glycol gave the crown ether **31**. Under similar reaction conditions, but with two molar equivalents of the sodium salts of ethylene glycol, diethylene glycol and triethylene glycol, the podands **32**, **33** and **34**, respectively, were formed. In case of ethylene glycol, a second product **35** was isolated (11%). Interestingly, the same product **35** (in 59% yield) was obtained on treatment of **32** with sodium hydride in DMF and dimethyl sulfoxide (DMSO). The diols **33** and **36** were obtained in high yield and as the only isolated product when **3** and **18**, respectively, were reacted with an excess of the disodium salt of ethylene glycol. However, an attempt to utilise the same procedure with the disodium salt of triethylene glycol and **3** showed that the reaction was much slower as both **34** and **37** were isolated. Treatment of the disodium salt of **33** with **3** yielded **38**. The 24-crown-8, **39**, was obtained in a similar way from **34** using a high dilution technique.



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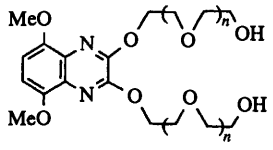
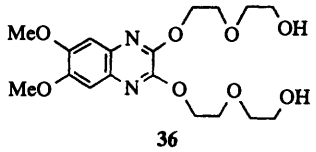


32 $n = 0$
33 $n = 1$
34 $n = 2$

35



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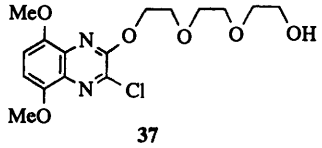

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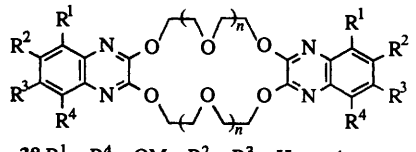
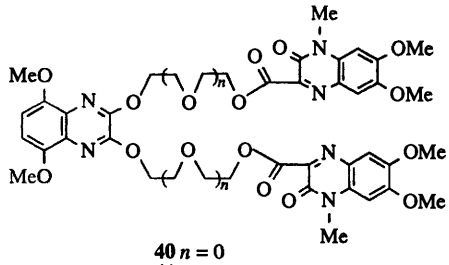
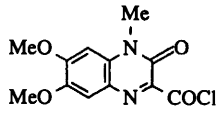


38 $R^1 = R^4 = OMe$, $R^2 = R^3 = H$, $n = 1$
39 $R^1 = R^4 = OMe$, $R^2 = R^3 = H$, $n = 2$

Potential fluoroionophores, **40** and **41**, were formed by the reaction of **32** and **33**, respectively, with the acid chloride **42**. The excitation spectrum of **40** (λex_{max} 400 nm) showed a



40 $n = 0$
41 $n = 1$



42

significant bathochromic shift in dichloromethane in the presence of lithium (λex_{max} 424 nm) and barium ions (λex_{max} 430 nm) but with a hypsochromic effect. Other alkali metal and alkaline earth ions (*e.g.* Na^+, K^+, Mg^{2+} and Ca^{2+}) produced weaker bathochromic shifts and sodium and potassium ions gave a hypsochromic effect. Compound **41** showed a hypsochromic effect in the presence of each of the ions mentioned above and gave a weaker red-shift in the excitation spectrum. Unfortunately, neither **40** or **41** showed significant shifts in their fluorescence spectra (λem_{max} 485 nm, φ_f 0.07 and λem_{max} 485 nm, φ_f 0.06, respectively) in the presence of the metal ions.

Interestingly, the FAB mass spectrum of **40** in *p*-nitrobenzyl alcohol (NOBA) matrix showed the base peak to be the molecular ion with a complexed sodium ion, whereas the molecular ion had a relative abundance of only 10%.

The synthesis of the corresponding quinones, their reactions and complexation properties will be reported.

Experimental

Infrared, ultraviolet, fluorescence and ^1H NMR spectroscopy data, low resolution mass spectra, elemental analyses and melting points were obtained by the procedures reported.[1]

Solvents were distilled before use in chromatography. Thin layer chromatography was carried out on silica gel plates (0.25 mm with fluorescent indicator UV_{254}) obtained from Camlab. Chromatography columns were packed dry with Kieselgel 60 (230–400 mesh ASTM) and developed under slight positive pressure. Ether refers to diethyl ether.

1,2-Diamino-4,5-dimethoxybenzene hydrochloride,[12] 2,3-dimethyl- **1**,[3] 2,3-diphenyl- **2**,[6] 2,3-diethoxy- **5**[6] and 2,3-bis(ethylthio)-5,8-dimethoxyquinoxaline **6**,[6] were obtained by known methods, as were 5,8-dimethoxy-1*H*,4*H*-quinoxaline-2,3-dione **10**,[6] 2,3-dichloro-6,7-dimethoxyquinoxaline **18**[4] and 6,7-dimethoxy-1-methyl-2-oxo-1*H*-quinoxaline-3-carbonyl chloride **42**.[1]

The mixture of 2,3- and 2,5-diamino-1,4-dimethoxybenzene, used as the source of the *o*-diamine, was obtained by hydrogenation of an ethanolic solution of the corresponding nitro compounds[5] in the presence of palladium on carbon (10%) at room temperature and 3 atm† pressure. After removal of the catalyst and solvent, the residue was assumed to contain 80% (w/w) of 2,3-diamino-1,4-dimethoxybenzene.[4] A fresh batch of amines was prepared for each cyclisation to give a quinoxaline.

2,3,5,8-Tetramethoxyquinoxaline 4

A solution of 2,3-dichloro-5,8-dimethoxyquinoxaline **3** (2.58 g,

† 1 atm = 101 325 Pa.

10 mmol) in methanol (25 cm^3) was added to a freshly prepared solution of sodium methoxide [obtained by adding sodium hydride (0.92 g, 40 mmol) to methanol (50 cm^3)]. The reaction mixture was refluxed for 3 h and then poured into ice–water (100 cm^3). The resultant precipitate was filtered off, washed with water and crystallised from methanol to give 2,3,5,8-*tetramethoxyquinoxaline* **4** (2.2 g, 87%), mp 174–175 °C; δ_H(80 MHz, $CDCl_3$) 3.97 (6 H, s, 5- and 8-OCH_3), 4.18 (6 H, s, 2- and 3-OCH_3), 6.82 (2 H, s, 6- and 7-H); *m/z* 251 (12%), 250 (M^+, 100), 235 (96) (Found: C, 57.52; H, 5.61; N, 11.18. $C_{12}H_{14}N_2O_4$ requires C, 57.60; H, 5.60; N, 11.20%).

2,3-Dicyano-5,8-dimethoxyquinoxaline 7

A powdered mixture of diiminosuccinonitrile[6] (3 g) and a mixture of 2,3-diamino- and 2,5-diamino-1,4-dimethoxybenzene hydrochloride (3.2 g) [prepared by the addition of conc. hydrochloric acid (5 cm^3) to the mixture of 2,3- and 2,5-diamino-1,4-dimethoxybenzene followed by the evaporation of the solvent] was added in 15 min to trifluoroacetic acid (60 cm^3) while the temperature was maintained at 20 °C with occasional cooling. The reaction mixture was stirred overnight at room temperature and then poured on to ice-cold water (200 cm^3). The resultant precipitate was filtered off, washed thoroughly with water and finally with cold methanol and crystallised from a mixture of methanol and dichloromethane (7:3) to yield bright red 2,3-*dicyano*-5,8-*dimethoxyquinoxaline* **7** (1.88 g, 77%), mp 281–282 °C; ν_{max}/cm^{-1} 3450 (OH), 2260 (CN); δ_H(80 MHz, $CDCl_3$) 4.09 (6 H, s, 5- and 8-OCH_3), 7.30 (2 H, s, 6- and 7-H); *m/z* 241 (14%), 240 (M^+, 87), 225 (100), 211 (50) (Found: C, 59.70; H, 3.49; N, 23.06. $C_{12}H_8N_4O_2$ requires C, 60.00; H, 3.36; N, 23.31).

General method for the preparation of 2,3-bis(bromomethyl)-dimethoxyquinoxalines 8 and 17

A mixture of the appropriate diamine [obtained by reduction of the corresponding dinitro compound (5 g)], 1,4-dibromobutane-2,3-dione (5.37 g) and carbon tetrachloride (100 cm^3) was refluxed for 4 h. The solid was removed, the solution treated with decolourising charcoal, and the solvent evaporated.

2,3-Bis(bromomethyl)-5,8-dimethoxyquinoxaline 8. Crystallised from a mixture of chloroform and petroleum spirit (bp 40–60 °C) to give yellow needles (2.4 g), mp 225–227 °C; δ_H(80 MHz, $CDCl_3$) 4.03 (6 H, s, 5- and 8-OCH_3), 4.98 (4 H, s, 2- and 3-CH_2Br), 7.01 (2 H, s, 6- and 7-H); *m/z* 378 (M^+ for ^{81}Br, 35%), 376 (M^+ for ^{81}Br and ^{79}Br, 72), 374 (M^+ for ^{79}Br, 38), 295 (M^+ – Br, 100) (Found: C, 38.24; H, 3.23; N, 7.20. $C_{12}H_{12}N_2O_2Br_2$ requires C, 38.33; H, 3.22; N, 7.45%).

2,3-Bis(bromomethyl)-6,7-dimethoxyquinoxaline 17. Obtained as a light brown solid from benzene (3.2 g), mp 182–183 °C; δ_H(80 MHz, $CDCl_3$) 4.03 (6 H, s, 6- and 7-OCH_3), 4.90 (4 H, d, *J* 9, 2- and 3-CH_2Br), 7.29 (2 H, s, 5- and 8-H); *m/z* 378 (M^+ for ^{81}Br, 11%), 376 (M^+ for ^{81}Br and ^{79}Br, 22), 374 (M^+ for ^{79}Br, 11) (Found: C, 38.23; H, 3.01; N, 7.62. $C_{12}H_{12}N_2O_2Br_2$ requires C, 38.33; H, 3.22; N, 7.45%).

1,4-Diamino-6,9-dimethoxypyridazino[4,5-*b*]quinoxaline 11

Hydrazine hydrate (3 cm^3, 98%) was added with stirring to a solution of 2,3-dicyano-5,8-dimethoxyquinoxaline **7** (0.5 g) in methanol (100 cm^3) at room temperature. The reaction mixture was stirred for 24 h. The resultant precipitate was filtered off, washed with water and recrystallised from aqueous dimethylformamide to give bright purple 1,4-*diamino*-6,9-*dimethoxypyridazino*[4,5-b]*quinoxaline* **11** (0.38 g, 74%), mp >325 °C; ν_{max}/cm^{-1} 3340 (OH), 3300 (NH_2), 3180 (NH_2); δ_H[80 MHz, $(CD_3)_2SO$] 4.02 (6 H, s, 6- and 9-OCH_3), 6.14 (4 H, br s, exchanged with D_2O, 1- and 4-NH_2), 7.33 (2 H, s, 7- and 8-H); *m/z* 273 (14%), 272 (M^+, 82), 257 (M^+ – CH_3, 10), 242 (M^+ – $2CH_3$, 11), 121 (100) (Found: C, 49.98; H, 4.76; N, 28.69. $C_{12}H_{12}N_6O_2 \cdot H_2O$ requires C, 49.65; H, 4.82; N, 28.96%).

General method for the preparation of 2,3-bis(pyridiniomethyl)-quinoxaline dibromide 12 and 13

The appropriate 2,3-bis(bromomethyl)quinoxaline (2 g, 5.3 mmol) was added to dry pyridine (40 cm^3) and stirred for 30 min at room temperature. The solid was filtered off and crystallised from a mixture of methanol and diethyl ether.

5,8-Dimethoxy-2,3-bis(pyridiniomethyl)quinoxaline dibromide 12. The *title compound* was obtained as a yellow solid (2.25g, 79%), mp >350 °C; ν_{max}/cm^{-1} 3400 (OH); δ_H[80 MHz, $(CD_3)_2SO$] 3.69 (6 H, s, 5- and 8-OCH_3), 6.64 (2 H, s, 2- and 3-CH_2), 7.13 (2 H, s, 6- and 7-H), 8.29 (4 H, t, 2- and 3-py-H-3, -5), 8.77 (2 H, t, 2- and 3-py-H-4), 9.27 (4 H, d, *J* 5.3, 2- and 3-py-H-2, -6); *m/z* 376 (2%), 374 (M^+ – 2Br, 4), 295 (8), 216 (4), 79 (100) (Found: C, 47.73; H, 4.56; N, 10.11. $C_{22}H_{22}N_4O_2Br_2 \cdot H_2O$ requires C, 47.82; H, 4.34; N, 10.14%).

6,7-Dimethoxy-2,3-bis(pyridiniomethyl)quinoxaline dibromide 13. The *title compound* was a cream solid (1.78 g, 64%), mp >300 °C; δ_H[80 MHz, $(CD_3)_2SO$] 3.86 (6 H, s, 6- and 7-OCH_3), 6.65 (4 H, s, 2- and 3-CH_2), 7.02 (2 H, s, 5- and 8-H), 8.22–8.39 (4 H, m, 2- and 3-py-H-3, -5), 8.73 (2 H, m, 2- and 3-py-H-4), 9.34 (4 H, d, *J* 5.6, 2- and 3-py-H-2, -6); *m/z* 376 (9%), 374 (M^+ – 2Br, 5.3), 295 (4), 94 (34) (Found: C, 49.74; H, 4.55; N, 10.44. $C_{22}H_{22}N_4O_2Br_2$ requires C, 49.46; H, 4.15; N, 10.49%).

1,4-Dimethoxy-7,8-dimethyl-6,9-dipyridiniophenazine dibromide 14 and 1-amino-2,3-dimethyl-6,9-dimethoxy-4-pyridiniophenazine bromide 15

Piperidine (1 cm^3) was added to a solution of 5,8-dimethoxy-2,3-bis(pyridiniomethyl)quinoxaline dibromide **12** (1 g, 1.87 mmol) and butane-2,3-dione (0.241 g, 2.8 mmol) in methanol (50 cm^3) and refluxed for 1 h. The reaction mixture was then poured into ethyl acetate (100 cm^3), and the resultant precipitate filtered off and washed with chloroform. This crude mixture of two components was separated by column chromatography [methanol and chloroform (1:1)]. The first eluted component was characterised as 1-*amino*-2,3-*dimethyl*-6,9-*dimethoxy*-4-*pyridiniophenazine bromide* **15** (0.49 g, 59%), mp 271 °C (decomp.); ν_{max}/cm^{-1} 3400 (NH_2), 3300 (NH_2); δ_H(200 MHz, CD_3OD) 2.23 (3 H, s, 2-CH_3), 2.31 (3 H, s, 3-CH_3), 3.85 (3 H, s, 9-OCH_3), 4.11 (3 H, s, 6-OCH_3), 7.09 (2 H, s, 7- and 8-H), 8.35 (2 H, t, 4-py-H-3, -5), 8.89 (1 H, t, 4-py-H-4), 9.11 (2 H, d, *J* 8, 4-py-H-2, -6); *m/z* 362 (MH^+ – Br, 9%), 360 (8), 359 (26), 358 (100), 344 (40), 329 (43), 313 (12), 298 (68), 283 (44), 268 (86) (Found: C, 55.33; H, 4.86; N, 11.95; Br, 18.01%; M^+ – Br, 361.1685. $C_{21}H_{21}N_4O_2Br \cdot \frac{3}{4}H_2O$ requires C, 55.44; H, 4.62; N, 12.32; Br, 17.60%; M^+ – Br, 361.1664).

The second component was 1,4-*dimethoxy*-7,8-*dimethyl*-6,9-*dipyridiniophenazine dibromide* **14** (0.32 g, 34%), mp 150–153 °C (decomp.); ν_{max}/cm^{-1} 3440 (OH); δ_H(200 MHz, D_2O) 2.46 (6 H, s, 7- and 8-CH_3), 3.98 (6 H, s, 1- and 4-OCH_3), 7.40 (2 H, s, 2- and 3-H), 8.54 (4 H, t, 6- and 9-py-H-3, -5), 9.10 (2 H, t, 6- and 9-py-H-4), 9.16 (4 H, d, *J* 5.5, 6- and 9-py-H-2, -6); *m/z* 424 (M^+ – 2Br, 2%), 343 (15), 329 (34), 315 (84), 95, (88), 79 (100) (Found: C, 50.23; H, 4.35; N, 8.99; Br, 25.29. $C_{26}H_{24}N_4O_2Br_2 \cdot 2H_2O$ requires C, 50.32; H, 4.51; N, 9.03; Br, 25.48%).

1-Amino-2,3-dimethyl-7,8-dimethoxy-4-pyridiniophenazine bromide 16

A mixture of piperidine (0.2 cm^3), 6,7-dimethoxy-2,3-bis(pyridiniomethyl)quinoxaline dibromide **13** (0.2 g, 0.38 mmol), butane-2,3-dione (0.06 g) and methanol (10 cm^3) was refluxed for 18 h. The reaction mixture was poured into ethyl acetate, the red solid filtered off and crystallised from a mixture of methanol and ether to give the *title compound* (0.085 g, 50%), mp 235–237 °C (decomp.); ν_{max}/cm^{-1} 3400–3300 (NH_2); δ_H[200 MHz, $(CD_3)_2SO$] 2.16 (3 H, s, 2-CH_3), 2.33 (3 H, s, 3-CH_3), 3.91 (3 H, s, 8-OCH_3), 3.99 (3 H, s, 7-OCH_3), 6.98 (1 H, s, 9-H), 7.40 (1 H, s, 6-H), 8.29–8.47 (2 H, m, 4-py-H-3, -5), 8.90 (1 H,

m, 4-py-H-4), 9.16 (2 H, d, *J* 6, 4-py-H-2, -6); *m/z* 360 (M^+ − Br, 4.5%), 358 (55), 83 (100) (Found: C, 54.64; H, 4.94; N, 12.07. $C_{21}H_{21}N_4O_2Br·H_2O$ requires C, 54.91; H, 5.05; N, 12.20%).

Reactions of 2,3-dichloro-5,8-dimethoxyquinoxaline 3 with thiourea to give compounds 21 and 20

2,3-Dichloro-5,8-dimethoxyquinoxaline **3** (2.27 g, 8.8 mmol) and thiourea (0.688 g, 8.8 mmol) was dissolved in DMF (30 cm^3) and triethylamine (1.8 g) were added with stirring. The reaction mixture was refluxed for 5 h. The yellow product precipitated out during the reaction. After cooling the reaction mixture, the product was collected by filtration and washed with water and methanol. The solid was recrystallized from aqueous formaldehyde to yield bright yellow needles of 1,4,8,11-*tetramethoxy*-6,13-*dithia*-5,7,12,14-*tetraazapentacene* **21** (2.01 g, 52%), mp > 330 °C; δ_H(200 MHz, [^{2}H]TFA) 4.14 (12 H, s, 1-, 4-, 8- and 11-OCH_3), 7.38 (4 H, s, 2-, 3-, 9- and 10-H); *m/z* 440 (M^+, 100%), 425 ($M^+ - CH_3$, 37), 227 (68) (Found: C, 54.47; H, 3.92; N, 12.39; S, 14.44. $C_{20}H_{16}N_4O_4S_2$ requires C, 54.53; H, 3.66; N, 12.72; S, 14.54%).

Water (50 cm^3) was added to the initial filtrate from the above reaction to produce a yellow precipitate. The solid was collected and crystallised from a mixture of ethyl acetate and dichloromethane (3:1). The yellow *bis*(3-*chloro*-5,8-*dimethoxyquinoxalin*-2-*yl*) *sulfide* **20** (0.95 g, 22.5%) had mp 221–222 °C; δ_H(80 MHz, $CDCl_3$) 3.76 (6 H, s, 5- or 8-OCH_3), 4.01 (6 H, s, 5- or 8-OCH_3), 7.21 (4 H, s, 6- and 7-H); *m/z* 482 (2%), 480 (M^+ for ^{37}Cl, 3), 478 (M^+ for ^{35}Cl, 5), 447 (12), 445 (42), 443 (100) (Found: C, 49.99; H, 3.36; N, 11.41; S, 6.67; Cl, 14.46. $C_{20}H_{16}N_4O_4SCl_2$ requires C, 50.12; H, 3.36; N, 11.69; S, 6.69; Cl, 14.79%).

6,13-Dibutyl-6,13-dihydro-1,4,8,11-tetramethoxy-5,6,7,12,13,14-hexaazapentacene 23

The dichloro compound **20** (0.526 g, 1.1 mmol) and butylamine (0.321 g, 4.4 mmol) were dissolved in anhydrous THF (50 cm^3) containing anhydrous potassium carbonate (1 g) and refluxed for 6 h. After the completion of the reaction, the solvent was evaporated *in vacuo* and the residue was dissolved in water. The product was extracted with dichloromethane, dried (anhydrous sodium sulfate) and purified by TLC [light petroleum (bp 40–60 °C) and ethyl acetate (2:1)] to give the *hexaazapentacene* **23** (0.381 g, 67%), mp 301–302 °C; δ_H(200 MHz, $CDCl_3$) 1.03 [6 H, m, 2 × $N(CH_2)_3CH_3$], 1.62 [4 H, m, 2 × $N(CH_2)_2CH_2CH_3$], 1.83 (4 H, m, 2 × $NCH_2CH_2CH_2CH_3$), 3.95 (12 H, s, 1-, 4-, 8- and 11-OCH_3), 4.47 (4 H, m, 2 × $NCH_2CH_2CH_2CH_3$), 6.73 (4 H, s, 2-, 3-, 9- and 10-H); *m/z* 519 (M^+, 100%), 462 ($M^+ - CH_3$, 43), 447 ($M^+ - 2CH_3$, 42), 433 (15), 405 (22) (Found: C, 63.58; H, 6.48; N, 15.89. $C_{28}H_{34}N_6O_4·\frac{1}{2}H_2O$ requires C, 63.57; H, 6.64; N, 15.93%).

2,3,9,10-Tetramethoxy-6,13-dithia-5,7,12,14-tetraazapentacene 25

This compound was prepared from **18** by the method used for **21**. The yellow solid obtained was crystallized from dimethylformamide to give the *title compound* **25** (2.4 g, 68%), mp > 330 °C; δ_H(200 MHz, [^{2}H]TFA) 4.24 (12 H, s, 2-, 3-, 9- and 10-OCH_3), 7.65 (4 H, s, 1-, 4-, 8- and 11-H); *m/z* 440 (M^+, 100%), 425 ($M^+ - CH_3$, 5), 410 ($M^+ - 2CH_3$, 33) (Found: MH^+, 441.0691. $C_{20}H_{17}N_4S_2$ requires MH^+, 441.0682).

Methylation of 1,4-dihydro-5,8-dimethoxyquinoxaline-2,3-dione 10

The compound **10** (0.25 g, 1.1 mmol) was dissolved in aqueous sodium hydroxide (2 M, 20 cm^3) and then dimethyl sulfate (6 cm^3) was added. The reaction mixture was stirred for 2 h at room temperature, then diluted with water (100 cm^3) and extracted with chloroform. The extract was dried (anhydrous sodium sulfate) and the solvent removed *in vacuo*. The crude mixture (mp 180–181 °C) was separated by preparative TLC [ethyl acetate–dichloromethane (4:1)]. The component of higher R_f was crystallised from ethyl acetate to yield 3,5,8-*trimethoxy*-1-*methylquinoxalin*-2(1*H*)-one **29** (0.037 g, 13%), mp 176–177 °C; ν_{max}/cm^{-1} 1670 (CO); δ_H(80 MHz, $CDCl_3$) 3.83 (3 H, s, N-CH_3), 3.92 (3 H, s, 5-OCH_3), 3.95 (3 H, s, 8-OCH_3), 4.10 (2 H, s, 3-OCH_3), 6.73 (1 H, d, *J* 9, 7-H), 6.80 (1 H, d, *J* 8.8, 6-H); *m/z* 250 (M^+, 24%), 222 (68), 207 (100) (Found: C, 57.39; H, 5.52; N, 11.14. $C_{12}H_{14}N_2$ requires C, 57.59; H, 5.64; N, 11.19%). The component of lower R_f was crystallised from ethyl acetate as colourless needles of 3-*hydroxy*-1-*methyl*-5,8-*dimethoxyquinoxalin*-2(1*H*)-one **30** (0.127 g, 47%), mp 202–203 °C; ν_{max}/cm^{-1} 1700 (CO), 1680 (CO); δ_H(80 MHz, $CDCl_3$) 3.82 (3 H, s, N-CH_3), 3.85 (3 H, s, 8-OCH_3), 3.88 (3 H, s, 5-OCH_3), 6.64 (2 H, s, 6- and 7-H), 8.91 (1 H, br s, 3-OH exchanged with D_2O); *m/z* 237 (14%), 236 (M^+, 100), 221 (28), 207 (5), 193 (68) (Found: C, 55.87; H, 5.13; N, 11.77. $C_{11}H_{12}N_2O_4$ requires C, 55.93; H, 5.12; N, 11.86%).

2,3,5,6,8,9-Hexahydro-12,15-dimethoxy-1,4,7,10-tetraoxacyclododecino[2,3-*b*]quinoxaline 31

To 2,3-dichloro-5,8-dimethoxyquinoxaline **3** (0.258 g, 1 mmol) in anhydrous THF (100 cm^3), a solution of the disodium salt of triethylene glycol in THF [prepared by treating triethylene glycol (0.15 g, 11 mmol) with sodium metal (0.05 g, 22 mmol)] was added dropwise during 30 min and stirred for 12 h at 40–45 °C. The solid was filtered off, washed with water and then with acetone. The compound was insoluble in all the common solvents and further purification was achieved by dissolution of the solid in a minimum quantity of trichloroacetic acid and subsequent precipitation by the addition of water. The colourless solid was filtered off and washed thoroughly with water to yield the *title compound* **31** (0.151 g, 45%), mp 158–159 °C; δ_H(200 MHz, [^{2}H]TFA) 4.19 (10 H, s, 3- and 8-CH_2 and 12- and 15-OCH_3), 4.30 (4 H, s, 5- and 6-CH_2), 5.01 (4 H, br s, 2- and 9-CH_2), 7.38 (2 H, s, 13- and 14-H); *m/z* 337 (18%), 336 (M^+, 100), 421 ($M^+ - CH_3$, 41), 307 (25) (Found: C, 53.96; H, 5.80; N, 7.78. $C_{16}H_{20}N_2O_6·H_2O$ requires C, 54.23; H, 5.64; N, 7.90%).

2,3-Bis(2-hydroxyethoxy)-5,8-dimethoxyquinoxaline 32

To a solution of **3** (2.58 g, 10 mmol) in dry THF (30 cm^3), a freshly prepared solution of the disodium salt of ethane-1,2-diol [prepared by treating sodium metal (1 g, 44 mmol) with ethane-1,2-diol (2.5 g, 40 mmol)] in dry THF (20 cm^3) was added and the mixture refluxed for 4 h. The solid was filtered off, washed with water and crystallised from methanol to give 2,3-*bis*(2-*hydroxyethoxy*)-5,8-*dimethoxyquinoxaline* **32** (2.51 g, 81%), mp 222–223 °C; ν_{max}/cm^{-1} 3350 (OH); δ_H[200 MHz, $(CD_3)_2SO$] 3.77 (4 H, q, 2- and 3-OCH_2CH_2OH), 3.88 (6 H, s, 5- and 8-OCH_3), 4.50 (4 H, t, 2- and 3-OCH_2CH_2OH), 4.80 (2 H, t, 2- and 3-OCH_2CH_2OH exchanged with D_2O), 6.95 (2 H, s, 6- and 7-H); *m/z* 310 (M^+, 25%), 222 (74), 45 (66), 44 (100) (Found: C, 53.82; H, 5.92; N, 8.92. $C_{14}H_{18}N_2O_6$ requires C, 54.19; H, 5.85; N, 9.03%).

General method for the preparation of 2,3-bis(6-hydroxy-1,4-dioxahexyl)-5,8-dimethoxyquinoxaline 33 and 2,3-bis(6-hydroxy-1,4-dioxahexyl)-6,7-dimethoxyquinoxaline 36

The appropriate 2,3-dichloroquinoxaline (2.58 g, 10 mmol) in dry THF (30 cm^3) was added to the disodium salt of diethylene glycol in THF (10 cm^3) [prepared by treating diethylene glycol (4.15 g, 40 mmol) with sodium metal (1 g, 44 mmol)] and boiled under reflux for 5 h. At the end of the reaction (TLC) the volume of the mixture was reduced to 5 cm^3, water (100 cm^3) was added and the mixture extracted with dichloromethane. The extract was washed with water, dried (anhydrous sodium sulfate), evaporated *in vacuo*, and the residue crystallised from a mixture of ethyl acetate and dichloromethane (3:2).

2,3-Bis(6-hydroxy-1,4-dioxahexyl)-5,8-dimethoxyquinoxaline 33. The *title compound* (2.62 g, 66%) had mp 145–146 °C; ν_{max}/cm^{-1} 3400 (OH); δ_H[80 MHz, $(CD_3)_2SO$] 3.48 (2 H, s, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$ exchanged with D_2O), 3.52 (8 H, s, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$), 3.85 (10 H, br s, 5- and 8-OCH_3, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$), 4.56 (4 H, t, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$), 6.92 (2 H, s, 6- and 7-H); *m/z* 399 (8%), 398 (M^+, 38), 222 (82), 207 (70), 193 (31), 45 (100) (Found: C, 54.19; H, 6.72; N, 7.04. $C_{18}H_{26}N_2O_8$ requires C, 54.26; H, 6.58; N, 7.03%).

2,3-Bis(6-hydroxy-1,4-dioxahexyl)-6,7-dimethoxyquinoxaline 36. The *title compound* (2.81 g, 71%) had mp 101–102 °C; ν_{max}/cm^{-1} 3400 (OH); δ_H(80 MHz, $CDCl_3$) 3.52 (2 H, s, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$ exchanged with D_2O), 3.70 (8 H, s, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$), 3.91 (4 H, t, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$), 3.96 (6 H, s, 6- and 7-OCH_3), 4.62 (4 H, t, 2- and 3-$OCH_2CH_2OCH_2CH_2OH$), 7.09 (2 H, s, 5- and 8-H); *m/z* 399 (8%), 398 (M^+, 33), 222 (100) (Found: C, 54.08; H, 6.51; N, 6.95. $C_{18}H_{26}N_2O_8$ requires C, 54.26; H, 6.58; N, 7.03%).

2,3-Bis(9-hydroxy-1,4,7-trioxanonyl)-5,8-dimethoxyquinoxaline 34 and 2-chloro-3-(9-hydroxy-1,4,7-trioxanonyl)-5,8-dimethoxyquinoxaline 37

2,3-Dichloro-5,8-dimethoxyquinoxaline **3** (1.29 g, 5 mmol) in dry THF (30 cm^3) was added to the disodium salt of triethylene glycol in THF (10 cm^3) [prepared by treating triethylene glycol (2.65 g, 25 mmol) with sodium metal (0.5 g, 22 mmol)] and the mixture boiled under reflux for 12 h. The volume was reduced, water (100 cm^3) added and the mixture extracted with dichloromethane. The extract was washed with water, dried (anhydrous sodium sulfate), the solvent evaporated *in vacuo* and the products separated by preparative TLC [ethyl acetate, light petroleum bp 40–60 °C (1:1)]. The compound having the higher R_f value was crystallized from the same solvent and characterised as *2-chloro-3-(9-hydroxy-1,4,7-trioxanonyl)-5,8-dimethoxyquinoxaline* **37** (1.13g, 61%), mp 163–165 °C; ν_{max}/cm^{-1} 3390 (OH); δ_H(80 MHz, $CDCl_3$) 3.53 (1 H, br s, 9-OH exchanged with D_2O), 3.60–3.79 (8 H, m, 3-, 5-, 6- and 8-CH_2), 3.95 (2 H, t, 9-CH_2), 3.96 (3 H, s, 5-OCH_3), 3.98 (3 H, s, 8-OCH_3), 4.75 (2 H, t, 2-CH_2), 6.86 (1 H, d, *J* 8.7, 7-H), 6.93 (1 H, d, *J* 8.7, 6-H); *m/z* 374 (M^+ for ^{37}Cl, 11%), 372 (M^+ for ^{35}Cl, 33), 242 (25), 240 (74), 227 (23), 225 (68), 45 (100) (Found: C, 51.46; H, 5.72; N, 7.58; Cl, 9.57. $C_{16}H_{21}N_2O_6Cl$ requires C, 51.55; H, 5.68; N, 7.51; Cl, 9.51%). The second component was crystallised from a mixture of ethyl acetate and dichloromethane (4:1) to give *2,3-bis(9-hydroxy-1,4,7-trioxanonyl)-5,8-dimethoxyquinoxaline* **34** as a waxy solid (0.925 g, 38%), mp 89–90 °C; ν_{max}/cm^{-1} 3300 (OH); δ_H(80 MHz, $CDCl_3$) 3.45–3.98 (20 H, m, 2- and 3-$OCH_2CH_2OCH_2CH_2OCH_2CH_2OH$), 3.94 (6 H, s, 5- and 8-OCH_3), 4.74 (4 H, t, 2- and 3-$OCH_2CH_2OCH_2CH_2OCH_2CH_2OH$), 6.81 (2 H, s, 6- and 7-H); *m/z* 487 (3%), 486 (M^+, 8), 442 (3), 354 (20), 222 (100) (Found: C, 53.06; H, 6.95; N, 5.77. $C_{22}H_{34}N_2O_{10}\cdot\frac{1}{2}H_2O$ requires C, 53.33; H, 7.07; N, 5.65%).

2,3-Dihydro-5,8-dimethoxy-1,4-dioxa-9,10-diazaanthracene 35

2,3-Bis(2-hydroxyethoxy)-5,8-dimethoxyquinoxaline **32** (0.31 g, 1 mmol) was dissolved in dry dimethyl sulfoxide (20 cm^3) followed by the addition of sodium hydride (0.05 g, 2.2 mmol). The reaction mixture was stirred at room temperature for 4 h under nitrogen, then diluted with water (100 cm^3) and extracted with dichloromethane. The combined extracts were washed several times with water, dried (anhydrous sodium sulfate) and, after evaporation of the solvent *in vacuo*, the residue was crystallised from ethyl acetate to yield yellow needles of the *title compound* **35** (0.146 g, 59%), mp 176–177 °C; δ_H(80 MHz, $CDCl_3$) 3.95 (6 H, s, 5- and 8-OCH_3), 4.55 (4 H, s, 2- and 3-CH_2), 6.82 (2 H, s, 6- and 7-H); *m/z* 249 (16%), 248 (M^+, 100), 233 ($M^+ - CH_3$, 64), 219 (43) (Found: C, 57.98; H, 5.04; N, 11.28. $C_{12}H_{12}N_2O_4$ requires C, 58.06; H, 4.87; N, 11.28%).

General method for the preparation of crown ethers containing two dimethoxyquinoxaline groups 38 and 39

A mixture of the appropriate dihydroxy compound (**33** or **34**) (1 mmol), dry THF (75 cm^3) and sodium hydride (1.2 mmol) was stirred for 15 min at room temperature. Then the appropriate 2,3-dichloroquinoxaline (1 mmol) in dry THF (10 cm^3) was added dropwise during 1 h. The stirred reaction mixture was refluxed for 6 h. After cooling the mixture, the resultant white solid was filtered off, washed with water and crystallised from dichloromethane to give the colourless product.

7,8,10,11,20,21,23,24-Octahydro-1,4,14,17-tetramethoxy-[1,4,7,10,13,16]hexaoxacyclooctadecino[2,3-*b*:11,12-*b*']diquinoxaline 38. 0.421 g (72%), Mp 321–322 °C; δ_H(200 MHz, [^{2}H]TFA) 4.15 (12 H, s, 1-, 4-, 14- and 17-OCH_3), 4.32 (8 H, s, 8-, 10-, 21- and 23-CH_2), 5.07 (8 H, s, 7-, 11-, 20- and 24-CH_2), 7.19 (4 H, s, 2-, 3-, 15- and 16-H); *m/z* 584 (M^+, 35%) (Found: MH^+, 585.2197. $C_{28}H_{33}N_4O_{10}$ requires MH^+, 585.2194).

7,8,10,11,13,14,23,24,26,27,29,30-Dodecahydro-1,4,17,20-tetramethoxy[1,4,7,10,13,16,19,22]octaoxacyclotetracosino-[2,3-*b*:14,15-*b*']diquinoxaline 39. 0.215 g (32%), Mp 218–219 °C; δ_H(200 MHz, $CDCl_3$) 3.77 (8 H, t, 10-, 11-, 26- and 27-CH_2), 3.95 (20 H, m, 1-, 4-, 17- and 20-OCH_3, 8-, 13-, 24- and 29-CH_2), 4.67 (8 H, t, 7-, 14-, 23- and 30-CH_2), 6.79 (4 H, s, 2-, 3-, 18- and 19-H); *m/z* 672 (M^+, 10%), 628 ($M^+ - C_2H_4O$, 100), 457 (73), 325 (45), 310 (77), 296 (38), 249 (46), 222 (46) (Found: M^+, 672.2640. $C_{32}H_{40}N_4O_{12}$ requires M^+, 672.2642).

General procedure for the diesters 40 and 41

A mixture of the appropriate dihydroxy compound (**32** or **33**) (0.5 mmol), sodium hydride (1.2 mmol) and dry benzene (30 cm^3) was stirred for 15 min followed by the addition of the acid chloride (**42**) (1.1 mmol). The mixture was refluxed for 6 h and then washed thoroughly with water. The dried organic solution was evaporated and the residue crystallised from a mixture of methanol and dichloromethane (4:1) to give the diester.

2,3-Bis{2-[(3',4'-dihydro-6',7'-dimethoxy-4'-methyl-3'-oxoquinoxalin-2'-yl)carbonyloxy]ethoxy}-5,8-dimethoxyquinoxaline 40. 0.284 g (71%), Mp 226–227 °C; ν_{max}/cm^{-1} 3450 (OH), 1735 (CO), 1655 (CO); δ_H(200 MHz, $CDCl_3$) 3.69 (6 H, s, 2 × N'-CH_3), 3.92 (6 H, s, 2 × 7'-OCH_3), 3.93 (6 H, s, 5- and 8-OCH_3), 4.03 (6 H, s, 2 × 6'-OCH_3), 4.87 (4 H, t, 2 × α'-CH_2), 4.96 (4 H, t, 2 × β'-CH_2), 6.62 (2 H, s, 2 × 5'-H), 6.77 (2 H, s, 6- and 7-H), 7.24 (2 H, s, 2 × 8'-H); *m/z* (FAB, NOBA) 825 (M^+ + Na, 100%), 802 (M^+, 10), 579 (12), 308 (38), 291 (64) (Found: C, 55.40; H, 4.85; N, 10.11. $C_{38}H_{38}N_6O_{14}\cdot H_2O$ requires C, 55.60; H, 4.87; N, 10.24%) (Found: M^+ + Na, 825.2324. $C_{38}H_{38}N_6O_{14}Na$ requires M^+ + Na, 825.2344).

2,3-Bis{6-[(3',4'-dihydro-6',7'-dimethoxy-4'-methyl-3'-oxoquinoxalin-2'-yl)carbonyloxy]-1,4-dioxahexyl}quinoxaline 41. 0.343 g (77%), Mp 177–179 °C; ν_{max}/cm^{-1} 1730 (CO), 1650 (CO); δ_H(200 MHz, $CDCl_3$) 3.69 (6 H, s, 2 × N'-CH_3), 3.92 (6 H, s, 2 × 7'-OCH_3), 3.99 (6 H, s, 5- and 8-OCH_3), 3.97–4.02 (8 H, m, 2 × β'- and 2 × γ'-CH_2), 4.03 (6 H, s, 2 × 6'-OCH_3), 4.59 (4 H, t, 2 × α'-CH_2), 4.73 (4 H, t, 2 × δ'-CH_2), 6.63 (2 H, s, 2 × 5'-H), 6.77 (2 H, s, 6- and 7-H), 7.31 (2 H, s, 2 × 8'-H); *m/z* 890 (M^+, 30%), 278 (55), 220 (100) (Found: C, 56.42; H, 5.28; N, 9.10. $C_{42}H_{46}N_6O_{16}$ requires C, 56.63; H, 5.20; N, 9.43%).

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