Novel cryptands containing thiourea units as a part of the macrocyclic framework

Nikolay G. Lukyanenko,* Tatiana I. Kirichenko and Sergey V. Scherbakov

Department of Bioorganic Chemistry, A. V. Bogatsky Physico-Chemical Institute, National Academy of Sciences of Ukraine, Lustdorfskaya doroga 86, 65080 Odessa, Ukraine. E-mail: ngl@farlep.net.; Fax: +38-0482-652-012

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Alkylation of diaza-18-crown-6 by *N*-substituted phthalimides having a terminal halogen in the substituent, and subsequent product interaction with hydrazine hydrate and acid hydrolysis gave corresponding *N*,*N*′-disubstituted diaza-18-crown-6 compounds with terminal primary amino groups in the side chains. The reaction of these compounds with carbon disulfide or with appropriate bis[oligo(ethyleneoxy)]isothiocyanates afforded a series of novel cryptands with one or two thiourea units in one of the bridges.

Introduction

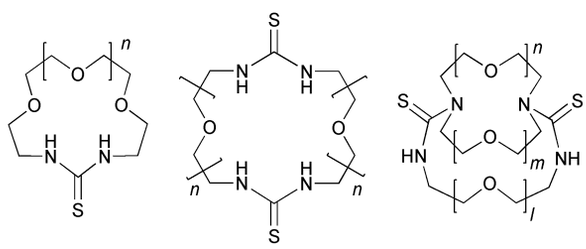
The synthesis and chemistry of crown ethers and cryptands that contain not only traditional ether oxygen and nitrogen atoms, but also other heteroatoms and/or functional groups have attracted considerable attention due to their unusual ability to act as hosts to both neutral and ionic species.[1] Such synthetic receptors provide a controlled means for studying the fundamentals of non-covalent intermolecular forces in nature and open new routes for the development of sensors, catalysts, switches and other molecular devices.[2] The binding power of a host is governed by the cavity size, the shape, the rigidity and the nature of the binding sites. Particularly important is the fact that highly flexible hosts often make binding entropically unfavorable. Therefore, structurally rigid cryptands have become an important area of investigation.[3]

The powerful binding abilities of macrocyclic receptors incorporating urea units are well documented.[3,4] However, cyclic receptors having thiourea groups as a part of the macrocyclic framework have received little attention, despite the fact that the binding ability and selectivity of such receptors is likely to be improved because of the expected preorganization of the binding sites.

The mesomeric π-character of the thiourea group restricts the C–N bond rotation. This makes *N*,*N*′-substituted thioureas rigid coplanar structures with the substituents in the sterically preferred *Z*,*Z*-conformations. The high polarizability of the thiourea group facilitates interactions with "soft" cations.[5] Moreover, since the thiourea groups are relatively strong hydrogen bond donors, they can exhibit anion-binding ability. Therefore, these compounds can be considered as bifunctional receptors in which the binding sites for anions and cations are linked covalently enabling them to exhibit allosteric or cooperative complexation where the binding affinity for anions (cations) is modified because of the cation (anion) complexation. Recently, such receptors have attracted much attention as a new class of reagent with possible application for a membrane transport, ion-selective electrodes and as catalysts.[6]

In most cases, bifunctional receptors are acyclic compounds; however, in our opinion, the best results can be achieved by integration of the binding sites for cations and anions in a combined macrocyclic system. However, to the best of our knowledge, no cryptands and only a few examples of crown ethers containing thiourea units in the macrocyclic framework, have been reported,[7] with the exception of our communications.[8]

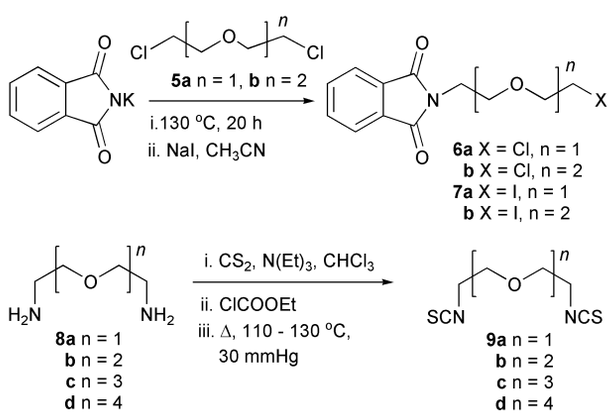
Earlier we described a series of crown ethers **1**, **2** and cryptands **3** incorporating thiourea moieties in the macrocyclic framework.[8] In all cases, the complexation selectivity of these compounds was unusual in comparison with ordinary crown ethers and cryptands.[8d,f] In cryptands **3**, one of the nitrogen atoms of the thiourea units simultaneously serves as a bridgehead. This decreases the basicity of this nitrogen and, as a result, the binding behavior of the cryptands. We were intrigued by cryptands containing thiourea units in one of the bridges at some distance from the nitrogen bridgeheads. Herein, we report an efficient and general approach to this type of cryptand.



1 **2** **3**

Results and discussion

The synthetic routes for preparing the starting phthalimides **7a**,**b** and bis[oligo(ethyleneoxy)]isothiocyanates **9a**–**d** are shown in Scheme 1. Heating of the potassium phthalimide in a tenfold excess of dichloride **5a** or **5b** at 130 °C for 20 h afforded the



Scheme 1

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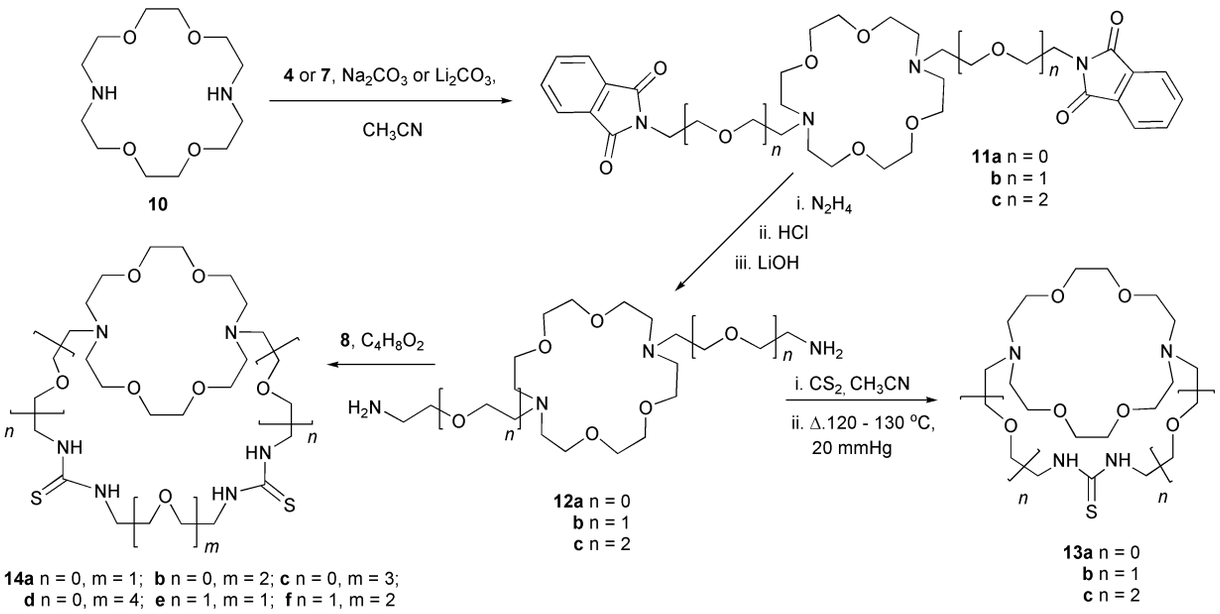

Scheme 2

chlorides **6a** and **6b** in yields of 91% and 89%, respectively. Reaction of chlorides **6a**,**b** with an excess of sodium iodide in acetonitrile give iodides **7a** and **7b** in yields of 97% and 96%, respectively. Bis[oligo(ethyleneoxy)]isothiocyanates **9** were prepared in good overall yields (65–85%) by the following reaction sequence. The diamines **8** reacted with carbon disulfide in the presence of triethylamine with formation of the corresponding dithiocarbamate salts, which were acylated with ethyl chloroformate in chloroform at 0 °C. Thermal decomposition of the acylation products under reduced pressure and subsequent distillation afforded the desired isothiocyanates **9**.

The key precursors of the cryptands **13** and **14** are diazacrown ethers **12** bearing terminal primary amine groups in the side chains (Scheme 2). Azacrown ethers with terminal amine groups are usually prepared by the reaction of azacrown ethers with derivatives of α-amino or α-halogen acids with the subsequent reduction of formed amides, or by alkylation of primary amines or secondary diamines with appropriate ditosylates or dihalides with following ring closure.[9] These multistage and time consuming methods are not common and afford desired products in only moderate yields. The alkylation of diazacrown ethers with *N*-substituted phthalimides bearing terminal halogen in the side chain, and deprotection of formed diphthalimides seems most rational and a more common pathway of deriving of the substituted azacrown ethers with terminal amine groups in the side chain.

The reaction of diaza-18-crown-6 **10** with *N*-(2-bromoethyl)-phthalimide **4** in boiling acetonitrile in the presence of sodium carbonate resulted in **11a** in moderate yield (65%). The execution of the same reaction without solvent at 100 °C increased the yield of **11a** to 91%. In contrast to this, the alkylation of diazacrown ether **10** by iodides **7a** and **7b** under similar conditions did not yield satisfactory results, while the reaction carried out in acetonitrile in the presence of lithium carbonate with heating under reflux for 30 h gave the target products **11b** and **11c** in yields of 65% and 48%, respectively. Increasing the reaction time reduced the yield of main products, apparently because of partial quaternization.

The reaction of diphthalimides **11a**–**c** with hydrazine hydrate in ethanol at reflux for 7 h, with subsequent hydrolysis with 6 M HCl, gave the hydrochlorides of diamines **12a**–**c**. Treatment of these hydrochlorides with saturated aqueous lithium hydroxide afforded the corresponding azacrown ethers **12a**–**c**. Use of sodium or potassium hydroxides led to the formation of complexes of **12a**–**c** with the chlorides of sodium or potassium.

The synthesis of the cryptands **13** and **14** was accomplished under high dilution conditions. The low concentration of reactants was maintained by their simultaneous addition to the reaction vessel by calibrated pumps. Azacrown ethers **12** react with carbon disulfide in acetonitrile with the formation of dithiocarbamate salts, the thermal decomposition of which under reduced pressure at 120–130 °C afforded cryptands **13** in 37–66% yields. The reaction of **13** with diisothiocyanates **8** in boiling dioxane gave the corresponding cryptands **14** in 48–69% yields.

In summary, reaction of the azacrown ethers bearing terminal amino groups in the side chains with carbon disulfide or diisothiocyanates constitutes an efficient and common approach to cryptands containing thiourea units in the macrocyclic framework. Such ligands may be employed as either monofunctional receptors for cations or bifunctional receptors for cations and anions. Now we are evaluating their complexation properties. These will be reported elsewhere.

Experimental

N-(2-Bromoethyl)phthalimide **4**, dichlorides **5**, diamines **8** and diaza-18-crown-6 **10** were commercially available and used without purification. All other reagents and solvents were used as supplied unless otherwise stated. Mps were determined in open capillaries and are uncorrected. ^{1}H NMR spectra at 250 MHz were recorded with a Bruker AM-250 spectrometer for solutions in $CDCl_3$ unless otherwise specified, with TMS as internal standard. *J* values are given in Hz. EI mass spectra were obtained on Varian MAT 112 and MX 1321 spectrometers (70 eV). UV spectra were recorded on a Specord M-40 spectrophotometer and are given in nm with log ε in parentheses. IR spectra were measured on a Perkin Elmer 580B spectrometer.

2-[2-(2-Chloroethoxy)ethyl]isoindole-1,3-dione 6a

A mixture of dichloride **5a** (152.20 g, 1.06 mol) and potassium phthalimide (20.37g, 0.11 mol) was stirred at 130 °C for 20 h. After concentration, *in vacuo*, the residue was treated with benzene (700 cm^3) and solid material was removed by filtration. The filtrate was concentrated under reduced pressure and the residue was extracted with pentane using a Soxhlet extractor for 50 h. The extract was evaporated to give compound **6a** (25.39 g, 91%) as a white solid, mp 71–72 °C (Found: C, 56.78; H, 4.78; N, 5.49; M$^+$, 253. $C_{12}H_{12}ClNO_3$ requires C, 56.81; H, 4.77; N,

5.52; *M*, 253.68); δ_H 3.60–3.68 (4 H, m, CH_2O), 3.82 (2 H, t, *J* 6.6, CH_2Cl), 3.96 (2 H, t, *J* 5.8, CH_2N), 7.55–7.72 (4 H, m, Ph).

2-{2-[2-(2-Chloroethoxy)ethoxy]ethyl}isoindole-1,3-dione 6b

Compound **6b** was prepared analogously to **6a** from **5b** (187.06 g, 1.00 mol) and potassium phthalimide (18.52 g, 0.10 mol). Colourless oil (26.50 g, 89%); (Found: C, 56.41; H, 5.45; N, 4.68; M^+, 297. $C_{14}H_{16}ClNO_4$ requires C, 56.48; H, 5.42; N, 4.70; *M*, 297.74); δ_H 3.47–3.64 (8 H, m, CH_2O), 3.82–3.93 (4 H, m, CH_2Cl, CH_2N), 7.55–7.70 (4 H, m, Ph).

2-[2-(2-Iodoethoxy)ethyl]isoindole-1,3-dione 7a

A mixture of chloride **6a** (9.13 g, 36 mmol) and sodium iodide (11.99 g, 80 mmol) in dry acetonitrile (50 cm^3) was stirred with heating under reflux for 10 h. After cooling, it was filtered and concentrated to dryness under reduced pressure. The residue was dissolved in chloroform (30 cm^3), the solution was washed with aqueous sodium thiosulfate (5%, 2 × 10 cm^3) and dried over $CaCl_2$, and the solvent was evaporated off under reduced pressure. The residue was purified by recrystallization from hexane–benzene (10:3) to give the iodide **7a** (12.05 g, 97%) as a white solid, mp 84–86 °C (Found: C, 41.62; H, 3.49; N, 4.07; M^+, 345. $C_{12}H_{12}INO_3$ requires C, 41.76; H, 3.50; N, 4.06; *M*, 345.13); δ_H 3.22 (2 H, t, *J* 7.0, CH_2I), 3.58 (2 H, t, *J* 5.8, CH_2O), 3.76 (2 H, t, *J* 7.0, CH_2O), 3.91 (2 H, t, *J* 5.8, CH_2N) 7.54–7.71 (4 H, m, Ph).

2-{2-[2-(2-Iodoethoxy)ethoxy]ethyl}isoindole-1,3-dione 7b

Compound **7b** was prepared analogously to **7a** from **6b** (8.93 g, 30 mmol) and sodium iodide (10.49 g, 70 mmol). After evaporation of acetonitrile, the residue was extracted with boiling hexane (100 cm^3). The solvent was removed under reduced pressure to give the iodide **7b** (11.59 g, 96%) as pale yellow oil (Found: C, 43.15; H, 4.15; N, 3.61; M^+, 386. $C_{14}H_{16}INO_4$ requires C, 43.21; H, 4.14; N, 3.60; *M*, 386.19); δ_H 3.25 (2 H, t, *J* 6.9, CH_2I), 3.40–3.53 (4 H, m, CH_2O), 3.61 (2 H, t, *J* 5.8, CH_2O), 3.74 (2 H, t, *J* 6.9, CH_2O), 3.90 (2 H, t, *J* 5.8, CH_2N) 7.56–7.73 (4 H, m, Ph).

General procedure for the synthesis of isothiocyanates 9

To a solution of appropriate diamine **8** (0.5 mol) and triethylamine (1.0 mol) in chloroform (750 cm^3) was added carbon disulfide (1.0 mol). The mixture was stirred for 2 h at room temperature then cooled to 0 °C. Ethyl chloroformate (1.0 mol) was added dropwise. The mixture was stirred at 0 °C for 0.5 h, then at room temperature for 2 h, whereupon it was washed with water (3 × 250 cm^3), dried over Na_2SO_4 and evaporated. The residue was heated at 110–130 °C under reduced pressure (~30 mmHg) until gas evolution ceased. The crude material was purified by distillation *in vacuo* to give the desired isothiocyanates **9** as colourless or pale yellow oils.

1,9-Dithioxo-5-oxa-2,8-diazanonane 9a. Colourless oil (78%), bp 150–154 °C/0.2 mmHg; (Found: C, 38.16; H, 4.30; N, 14.84; M^+, 188. $C_6H_8N_2OS_2$ requires C, 38.28; H, 4.28; N, 14.88; *M*, 188.27); δ_H 3.73–3.79 (4 H, m, CH_2N), 3.84–3.90 (4 H, m, CH_2O).

1,12-Dithioxo-5,8-dioxa-2,11-diazadodecane 9b. Colourless oil (85%), bp 165–163 °C/0.08 mmHg; (Found: C, 41.26; H, 5.23; N, 12.08; M^+, 232. $C_8H_{12}N_2O_2S_2$ requires C, 41.36; H, 5.21; N, 12.06; *M*, 232.32); δ_H 3.46 (4 H, s, CH_2O), 3.75–3.90 (8 H, m, CH_2N, CH_2O).

1,15-Dithioxo-5,8,11-trioxa-2,14-diazapentadecane 9c. Colourless oil (80%), bp 177–180 °C/0.05 mmHg; (Found: C, 43.33; H, 5.85; N, 10.15; M^+, 276. $C_{10}H_{16}N_2O_3S_2$ requires C, 43.46; H, 5.84; N, 10.14; *M*, 276.38); δ_H 3.47 (8 H, t, *J* 6.9, CH_2O), 3.75–3.90 (8 H, m, CH_2N, CH_2O).

1,18-Dithioxo-5,8,11,14-tetraoxa-2,17-diazaoctadecane 9d. Pale yellow oil (65%), bp 205–208 °C/0.05 mmHg; (Found: C, 45.16; H, 6.30; N, 8.76; M^+, 320. $C_{12}H_{20}N_2O_4S_2$ requires C, 44.98; H, 6.29; N, 8.74; *M*, 320.43); δ_H 3.47 (8 H, t, *J* 6.9, CH_2O), 3.57 (4 H, t, *J* 6.9, CH_2O), 3.75–3.90 (8 H, m, CH_2N, CH_2O).

7,16-(2-Phthalimidoethyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane 11a

A mixture of diaza-18-crown-6 **10** (2.62 g, 10 mmol), phthalimide **4** (12.70 g, 50 mmol) and powdered Na_2CO_3 (5.30 g, 50 mmol) was stirred at 100 °C for 10 h. To the hot solution was added dropwise chloroform (30 cm^3). After cooling, solid material was removed by filtration and the solvent was evaporated under reduced pressure. The residue was dissolved in benzene-1 M HCl (1:1, 100 cm^3) at 40–60 °C. The organic layer was separated and discarded. The aqueous layer was basified with Na_2CO_3 to pH 9–10 and extracted with benzene (2 × 50 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by recrystallization from heptane-benzene (1:1) to give diazacrown ether **11a** (5.29 g, 87%) as a white solid, mp 116–117 °C (Found: C, 62.97; H, 6.63; N, 9.18; M^+, 608. $C_{32}H_{40}N_4O_8$ requires C, 63.14; H, 6.62; N, 9.20; *M*, 608.68); δ_H 2.69 (8 H, t, *J* 6.1, CH_2N), 2.93 (4 H, t, *J* 6.9, CH_2N), 3.35 (8 H, t, *J* 6.1, CH_2O), 3.53 (8 H, s, CH_2O), 3.75 (8 H, t, *J* 6.9, CH_2N), 7.65–7.80 (8 H, m, Ph).

7,16-Bis(5-phthalimido-3-oxapentyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane 11b

A stirred mixture of diaza-18-crown-6 **10** (1.05 g, 4 mmol), phthalimide **7a** (3.45 g, 10 mmol) and powdered Li_2CO_3 (3.32 g, 45 mmol) in dry acetonitrile (20 cm^3) was heated under reflux for 30 h. After cooling, the mixture was filtered and concentrated to dryness under reduced pressure. The residue was dissolved in benzene-1 M HCl (1:1, 40 cm^3) at 50–60 °C. The organic layer was separated and discarded. The aqueous layer was basified with Na_2CO_3 to pH 9–10 and extracted with warm benzene (50–60 °C, 2 × 20 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by recrystallization from heptane-benzene (9:5) to give diazacrown ether **11b** (1.78 g, 64%) as a white solid, mp 96–97 °C (Found: C, 61.89; H, 6.95; N, 8.06; M^+, 696. $C_{36}H_{48}N_4O_{10}$ requires C, 62.05; H, 6.94; N, 8.04; *M*, 696.79); δ_H 2.48–2.64 (12 H, m, CH_2N), 3.29–3.61 (24 H, m, CH_2O), 3.85 (4 H, t, *J* 5.8, CH_2N), 7.67–7.78 (8 H, m, Ph).

7,16-Bis(8-phthalimido-3,6-dioxaoctyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane 11c

This compound was prepared by the reaction of diaza-18-crown-6 **10** (1.05 g, 4 mmol) with phthalimide **7b** (3.86 g, 10 mmol) as described for diazacrown ether **11b**. After evaporation of benzene diazacrown ether **11c** (1.51 g, 48%) was obtained as a pale yellow oil (Found: C, 61.12; H, 7.21; N, 7.12; M^+, 784. $C_{40}H_{56}N_4O_{12}$ requires C, 61.21; H, 7.19; N, 7.14; *M*, 784.89); δ_H 2.48–2.62 (12 H, m, CH_2N), 3.35–3.61 (32 H, m, CH_2O), 3.78 (4 H, t, *J* 5.8, CH_2N), 7.63–7.78 (8 H, m, Ph).

General procedure for the synthesis of diazacrown ethers 12

Hydrazine hydrate (67 mmol) was added dropwise to a boiling solution of compound **11** (33 mmol) in ethanol (100 cm^3) with intensive stirring. The mixture was heated under reflux for 7 h whereupon it was acidified with 6 M HCl (22 cm^3), filtered and

evaporated under reduced pressure. Water (120 cm^3) was added to the residue and the precipitate was removed by filtration. The filtrate was basified with saturated aqueous LiOH to pH 10–11 and extracted with chloroform using a liquid–liquid extractor for 10 h. The chloroform was evaporated off *in vacuo* to give the desired products **12**.

2-[16-(2-Aminoethyl)-1,4,10,13-tetraoxa-7,16-diazacyclooctadecan-7-yl]ethylamine 12a. Pale yellow oil (75%); (Found: C, 55.01; H, 10.42; N, 16.12; M^+, 348. $C_{16}H_{36}N_4O_4$ requires C, 55.15; H, 10.41; N, 16.08; *M*, 348.48); δ_H 1.67 (4 H, br s, NH_2), 2.49–2.67 (16 H, m, CH_2N, CH_2NH_2), 3.37 (8 H, t, *J* 6.2, CH_2O), 3.53 (8 H, s, CH_2O).

2-(2-{16-[2-(2-Aminoethoxy)ethyl]-1,4,10,13-tetraoxa-7,16-diazacyclooctadecan-7-yl}ethoxy)ethylamine 12b. Pale yellow oil (71%); (Found: C, 55.11; H, 10.19; N, 12.79; M^+, 436. $C_{20}H_{44}N_4O_6$ requires C, 55.02; H, 10.16; N, 12.83; *M*, 436.59); δ_H 1.78 (4 H, br s, NH_2), 2.48 (8 H, t, *J* 6.2 CH_2N), 2.60 (4 H, t, *J* 5.8, CH_2N), 2.74 (4 H, t, *J* 5.8, CH_2NH_2), 3.31 (8 H, t, *J* 6.2, CH_2O), 3.43–3.55 (16 H, m, CH_2O).

2-{2-[2-(16-{2-[2-(2-Aminoethoxy)ethoxy]ethyl}-1,4,10,13-tetraoxa-7,16-diazacyclooctadecan-7-yl)ethoxy]ethoxy}ethylamine 12c. Pale yellow oil (79%); (Found: C, 54.79; H, 9.97; N, 10.71; M^+, 524. $C_{24}H_{52}N_4O_8$ requires C, 54.94; H, 9.99; N, 10.68; *M*, 524.69); δ_H 1.95 (4 H, br s, NH_2), 2.50 (8 H, t, *J* 6.2 CH_2N), 2.62 (4 H, t, *J* 5.8, CH_2N), 2.77 (4 H, t, *J* 5.8, CH_2NH_2), 3.29 (8 H, t, *J* 6.2, CH_2O), 3.39–3.53 (24 H, m, CH_2O).

4,7,13,16-Tetraoxa-1,10,21,23-tetraazabicyclo[8.8.7]pentacosane-22-thione 13a

Solutions of diazacrown ether **12a** (1.0 g, 2.87 mmol) in dry acetonitrile (250 cm^3) and of carbon disulfide (0.22 g, 2.87 mmol) in dry acetonitrile (250 cm^3) were added dropwise simultaneously over 2.5 h to dry acetonitrile (250 cm^3) under reflux using calibrated pumps. The mixture was refluxed and stirred for a further 7.5 h and the solvent was evaporated off. The residue was heated under reduced pressure (~20 mmHg) at 120–130 °C until gas evolution ceased (~0.5 h). The crude product was purified by column chromatography on basic alumina using chloroform–hexane (3:4) as the eluent. The main fraction was evaporated and the residue was washed successively with water (10 cm^3) and ethanol (2 × 10 cm^3), and dried *in vacuo* to give the cryptand **13a** (0.61 g, 54%) as a white solid, mp 198–199 °C (Found: C, 52.15; H, 8.79; N, 14.32; M^+, 390. $C_{17}H_{34}N_4O_4S$ requires C, 52.28; H, 8.77; N, 14.35; *M*, 390.54); ν_{max}(KBr)/cm^{-1} 3450, 3295, 3240, 1565, 1540 and 1110; λ_{max}(MeOH)/nm 209 and 235 (log ε 4.26 and 4.25); δ_H 2.43 (4 H, t, *J* 5.0, NCH_2), 2.50 (8 H, t, *J* 4.5, NCH_2), 3.32 (8 H, t, *J* 4.5, OCH_2), 3.50 (8 H, s, OCH_2), 3.56 (4 H, q, *J* 5.0, NCH_2), 6.98 (2 H, br s, NH).

4,12,18,21,26,29-Hexaoxa-1,7,9,15-tetraazabicyclo[13.8.8]hentriacontane-8-thione 13b

This compound was prepared by the reaction of diazacrown ether **12b** (2.0 g, 4.58 mmol) with carbon disulfide (0.35 g, 4.58 mmol) as described for cryptand **13a**. The crude product was purified by column chromatography on basic alumina using chloroform–hexane (1:1) as the eluent to give cryptand **13b** (1.45 g, 66%) as a white solid, mp 74–75 °C (Found: C, 52.83; H, 8.82; N, 11.68; M^+, 478. $C_{21}H_{42}N_4O_6S$ requires C, 52.70; H, 8.84; N, 11.71; *M*, 478.65); ν_{max} (KBr)/cm^{-1} 3450, 3260, 3080, 1555, 1540 and 1105; λ_{max}(MeOH)/nm 207 and 241 (log ε 4.15 and 4.11); δ_H 2.57 (4 H, t, *J* 5.0, NCH_2), 2.65 (8 H, t, *J* 4.5, NCH_2), 3.42 (16 H, t, *J* 4.5, OCH_2), 3.52 (8 H, s, OCH_2), 3.65 (4 H, q, *J* 5.0, NCH_2), 7.43 (2 H, br s, NH).

4,7,15,18,24,27,32,35-Octaoxa-1,10,12,21-tetraazabicyclo[19.8.8]heptatriacontane-11-thione 13c

This compound was prepared by the reaction of diazacrown ether **12c** (2.0 g, 3.81 mmol) with carbon disulfide (0.29 g, 3.81 mmol) as described for cryptand **13a**. The crude product was purified by column chromatography on basic alumina using chloroform–dioxane (1:3) as the eluent to give cryptand **13c** (0.799 g, 37%) as a pale yellow oil (Found: C, 52.85; H, 8.91; N, 9.87; M^+, 566. $C_{25}H_{50}N_4O_8S$ requires C, 52.98; H, 8.89; N, 9.89; *M*, 566.75); ν_{max} (KBr)/cm^{-1} 3440, 3260, 3080, 1560, 1540 and 1110; λ_{max}(MeOH)/nm 207 and 241 (log ε 4.16 and 4.11); δ_H 2.62 (4 H, t, *J* 5.0, NCH_2), 2.70 (8 H, t, *J* 5.0, NCH_2), 3.46–3.58 (36 H, m, NCH_2, OCH_2), 7.12 (2 H, br s, NH).

9,20,23,28,31-Pentaoxa-1,4,6,12,14,17-hexaazabicyclo[15.8.8]tritriacontane-5,13-dithione 14a

Solutions of diazacrown ether **12a** (2.50 g, 7.18 mmol) in dry dioxane (500 cm^3) and of diisothiocyanate **9a** (1.35 g, 7.18 mmol) in dry dioxane (500 cm^3) were added dropwise and simultaneously over 5 h to dry dioxane (500 cm^3) under reflux using calibrated pumps. The mixture was refluxed and stirred for a further 1 h and the solvent was evaporated off under reduced pressure. The residue was purified by column chromatography on basic alumina using chloroform as the eluent to give the cryptand **14a** (2.1 g, 55%) as a white solid, mp 139–140 °C (Found: C, 49.11; H, 8.24; N, 15.68; M^+, 536. $C_{22}H_{44}N_6O_5S_2$ requires C, 49.23; H, 8.26; N, 15.66; *M*, 536.75); ν_{max}(KBr)/cm^{-1} 3240, 1555 and 1120; λ_{max}(MeOH)/nm 206 (log ε 4.39); δ_H 2.44 (4 H, t, *J* 4.5, NCH_2), 2.56 (8 H, t, *J* 5.2, NCH_2), 3.30 (8 H, t, *J* 5.2, OCH_2), 3.37 (4 H, t, *J* 4.5, NCH_2), 3.44–3.58 (16H, m, OCH_2, NCH_2), 7.31 (4 H, br s, NH).

9,12,23,26,31,34-Hexaoxa-1,4,6,15,17,20-hexaazabicyclo[18.8.8]hexatriacontane-5,16-dithione 14b

This compound was prepared by the reaction of diazacrown ether **12a** (1.74 g, 5.0 mmol) with diisothiocyanate **9b** (1.16 g, 5.0 mmol) as described for cryptand **14a**. The crude product was purified by column chromatography on basic alumina using chloroform as the eluent to give cryptand **14b** (2.03 g, 70%) as a white solid, mp 169–170 °C (Found: C, 49.75; H, 8.35; N, 14.43; M^+, 580. $C_{24}H_{48}N_6O_6S_2$ requires C, 49.63; H, 8.33; N, 14.47; *M*, 580.81); ν_{max}(KBr)/cm^{-1} 3450, 3240, 3070, 1560 and 1110; λ_{max}(MeOH)/nm 207 (log ε 4.38); δ_H 2.48 (4 H, t, *J* 5.2, NCH_2), 2.65 (8 H, t, *J* 4.8, NCH_2), 3.29 (8 H, t, *J* 4.8, OCH_2), 3.37 (4 H, t, *J* 5.2, NCH_2), 3.46–3.50 (8 H, m, OCH_2, NCH_2), 3.53 (8 H, s, OCH_2), 3.65 (4 H, t, *J* 5.8, OCH_2), 7.18 (4 H, br s, NH).

9,12,15,26,29,34,37-Heptaoxa-1,4,6,18,20,23-hexaazabicyclo[21.8.8]nonatriacontane-5,19-dithione 14c

This compound was prepared by the reaction of diazacrown ether **12a** (1.74 g, 5.0 mmol) with diisothiocyanate **9c** (1.38 g, 5.0 mmol) as described for cryptand **14a**. The crude product was purified by column chromatography on basic alumina using chloroform as the eluent to give cryptand **14c** (1.91 g, 61%) as a white solid, mp 80–81 °C (Found: C, 49.86; H, 8.41; N, 13.42; M^+, 624. $C_{26}H_{52}N_6O_7S_2$ requires C, 49.98; H, 8.39; N, 13.45; *M*, 624.86); ν_{max}(KBr)/cm^{-1} 3450, 3230, 3070, 1555 and 1115; λ_{max}(MeOH)/nm 207 and 241 (log ε 4.39 and 4.38); δ_H 2.45 (4 H, t, *J* 5.2, NCH_2), 2.68 (8 H, t, *J* 4.8, NCH_2), 3.30–3.39 (12 H, m, NCH_2, OCH_2), 3.44–3.49 (12 H, m, NCH_2, OCH_2), 3.55 (8 H, s, OCH_2), 3.67 (4 H, t, *J* 5.8, OCH_2), 7.41 (4 H, br s, NH).

9,12,15,18,29,32,37,40-Octaoxa-1,4,6,21,23,26-hexaazabicyclo[24.8.8]dotetracontane-5,22-dithione 14d

This compound was prepared by the reaction of diazacrown ether **12a** (1.74 g, 5.0 mmol) with diisothiocyanate **9d** (1.60 g,

5.0 mmol) as described for cryptand **14a**. The crude product was purified by column chromatography on basic alumina using chloroform–dioxane (1:1) as the eluent to give cryptand **14d** (1.61 g, 48%) as a white solid, mp 68–69 °C (Found: C, 50.39; H, 8.42; N, 12.59; M^+, 668. $C_{28}H_{56}N_6O_8S_2$ requires C, 50.28; H, 8.44; N, 12.56; *M*, 668.91); ν_{max}(KBr)/cm^{-1} 3450, 3300, 3070, 1555 and 1115; λ_{max}(MeOH)/nm 208 and 242 (log ε 4.39 and 4.38); δ_H 2.44 (4 H, t, *J* 5.2, NCH_2), 2.72 (8 H, t, *J* 4.8, NCH_2), 3.29–3.41 (12 H, m, NCH_2, OCH_2), 3.44–3.49 (16 H, m, NCH_2, OCH_2), 3.54 (8 H, s, OCH_2), 3.65 (4 H, t, *J* 5.8, OCH_2), 7.35 (4 H, br s, NH).

4,12,20,26,29,34,37-Heptaoxa-1,7,9,15,17,23-hexaazabicyclo-[21.8.8]nonatriacontane-8,16-dithione 14e

This compound was prepared by the reaction of diazacrown ether **12b** (2.50 g, 5.73 mmol) with diisothiocyanate **9a** (1.08 g, 5.73 mmol) as described for cryptand **14a**. The crude product was purified by column chromatography on basic alumina using chloroform–methanol (100:1) as the eluent to give cryptand **14e** (2.11 g, 59%) as a white solid, mp 72–73 °C (Found: C, 50.11; H, 8.41; N, 13.48; M^+, 624. $C_{26}H_{52}N_6O_7S_2$ requires C, 49.98; H, 8.39; N, 13.45; *M*, 624.86); ν_{max}(KBr)/cm^{-1} 3440, 3260, 3080, 1560 and 1110; λ_{max}(MeOH)/nm 207 and 241 (log ε 4.40 and 4.41); δ_H 2.47–2.54 (12 H, m, NCH_2), 3.20–3.32 (12 H, m, NCH_2, OCH_2), 3.43–3.48 (8 H, m, NCH_2), 3.53–3.58 (16 H, m, OCH_2), 7.10 (4 H, br s, NH).

4,12,15,23,29,32,37,40-Octaoxa-1,7,9,18,20,26-hexaazabicyclo-[24.8.8]dotetracontane-8,19-dithione 14f

This compound was prepared by the reaction of diazacrown ether **12b** (2.18 g, 5.00 mmol) with diisothiocyanate **9b** (1.16 g, 5.00 mmol) as described for cryptand **14a**. The crude product was purified by column chromatography on basic alumina using chloroform–dioxane–isopropyl alcohol (5:5:1) as the eluent to give cryptand **14f** (1.71 g, 51%) as pale yellow oil (Found: C, 50.15; H, 8.46; N, 12.59; M^+, 668. $C_{28}H_{56}N_6O_8S_2$ requires C, 50.28; H, 8.44; N, 12.56; *M*, 668.91); ν_{max}(KBr)/cm^{-1} 3450, 3250, 3065, 1560 and 1105; λ_{max}(MeOH)/nm 207 and 241 (log ε 4.34 and 4.33); δ_H 2.47–2.54 (12 H, m, NCH_2), 3.23–3.29 (12 H, m, NCH_2, OCH_2), 3.44–3.49 (12 H, m, NCH_2, OCH_2), 3.53–3.61 (16 H, m, OCH_2), 7.47 (4 H, br s, NH).

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