Aust. J. Chem., 1995, **48**, 1819–1825

New Macrocyclic Ligands. VI*
20- to 22-Membered Dibenzo-Substituted Rings Incorporating Mixed Nitrogen, Oxygen and/or Sulfur Donor Atoms

Carol A. Davis,[A,B] *Paul A. Duckworth,*[B] *Leonard F. Lindoy*[B,C] *and Wayne E. Moody*[B]

[A] Faculty of Science and Technology, Nathan Campus, Griffith University, Brisbane, Qld. 4111.
[B] Department of Molecular Science, James Cook University, Townsville, Qld. 4811.
[C] Author to whom correspondence should be addressed.

Abstract

The syntheses and characterization of 10 dibenzo-substituted macrocycles incorporating mixed nitrogen, oxygen and/or sulfur donor sets are reported. The new systems, which incorporate six potential donor sites, extend the range of related (potentially tetradentate and pentadentate) macrocyclic systems reported previously.

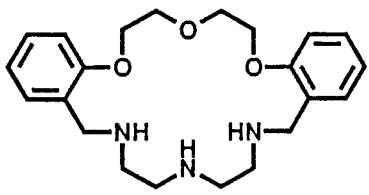
Introduction

The use of macrocyclic ligands for selective metal complex formation has received considerable attention over many years.[1,2] In past studies we have investigated the interaction of mixed donor macrocyclic ligands incorporating four,[3] five,[4] and eight[5] potential donor sites with a range of latter first-row transition and post-transition metal ions.[6] An overall aim of these studies was to achieve metal-ion discrimination within the respective ligand series and to understand the reasons for such discrimination when it was observed. One strategy employed in these studies has been to investigate metal-ion behaviour across a 'matrix' of ligands whose structures vary in a stepwise manner;[6,7] parameters

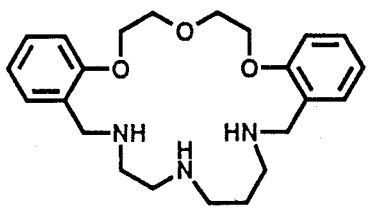
* Part V, *Aust. J. Chem.*, 1994, **47**, 1155.

[1] Lindoy, L. F., 'The Chemistry of Macrocyclic Ligand Complexes' (Cambridge University Press: Cambridge 1989).
[2] Izatt, R. M., Bradshaw, J. S., Nielsen, S. A., Lamb J. D., Christensen, J. J., and Sen, D., *Chem. Rev.*, 1985, **85**, 271; Izatt, R. M., Pawlak, K., Bradshaw, J. S., and Bruening, R. L., *Chem. Rev.*, 1991, **91**, 1721.
[3] Grimsley, P. G., Lindoy, L. F., Lip, H. C., Smith, R. J., and Baker, J. T., *Aust. J. Chem.*, 1977, **30**, 2095.
[4] Baldwin, D. S., Duckworth, P. A., Erickson, G. R., Lindoy, L. F., McPartlin, M., Mockler, G. M., Moody, W. E., and Tasker, P. A., *Aust. J. Chem.*, 1987, **40**, 1861.
[5] Adam, K. R., Anderegg, G., Henrick, K., Leong, A. J., Lindoy, L. F., Lip, H. C., McPartlin, M., Smith, R. J., and Tasker, P. A., *Inorg. Chem.*, 1981, **20**, 4048.
[6] Lindoy, L. F., *Prog. Macrocyclic Chem.*, 1987, **3**, 53.
[7] Adam, K. R., Leong, A. J., Lindoy, L. F., Lip, H. C., Skelton, B. W., and White, A. H., *J. Am. Chem. Soc.*, 1983, **105**, 4645; Adam, K. R., Dancey, K. P., Leong, A. J., Lindoy, L. F., McCool, B. J., McPartlin, M., and Tasker, P. A., *J. Am. Chem. Soc.*, 1988, **110**, 8471; Adam, K. R., Arshad, S. P. H., Baldwin, D. S., Duckworth, P. A., Leong, A. J., Lindoy, L. F., McCool, B. J., McPartlin, M., Tailor, B. A., and Tasker, P. A., *Inorg. Chem.*, 1994, **33**, 1194.

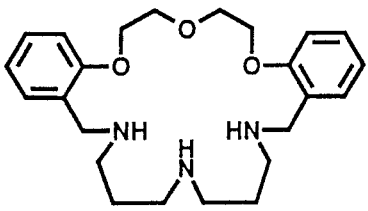
Manuscript received 14 June 1995 0004-9425/95/111819$05.00



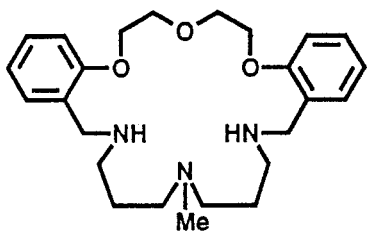
(1)



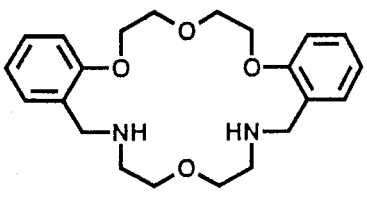
(2)



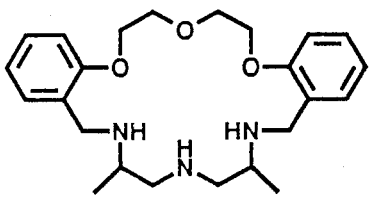
(3)



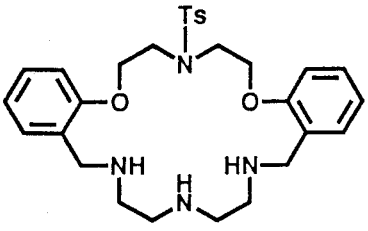
(4)



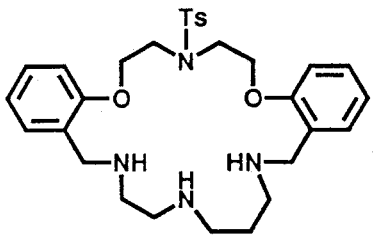
(5)



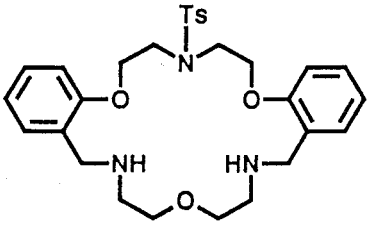
(6)



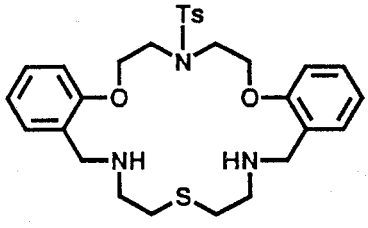
(7)



(8)

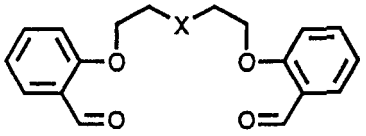


(9)



(10)

such as the macrocyclic ring size, donor atom set and the degree of ligand substitution have all been varied to form the required matrix. As an extension of these studies we now report the synthesis and characterization of a new series of related cyclic ligands (1)–(10) incorporating six potential (mixed) donor sites.



(11) X = O
(12) X = NTs

Results and Discussion

The synthesis of the macrocycles (1)–(10) was achieved by established procedures.[8] Schiff base condensation of the respective parent dialdehydes (11) and (12) and the appropriate linear di- or tri-amine derivative in methanol yields the corresponding cyclic products; these were not isolated but were reduced *in situ* by stepwise addition of sodium borohydride to the reaction solution. A similar non-template, reaction procedure was employed previously to obtain the related four-, five- and eight-donor macrocycles mentioned above.[3–5] As observed in the previous studies, it was not found necessary to carry out the respective ring-closing reactions under high-dilution conditions. It should be noted that previous attempts to use linear polyamines in Schiff base condensation reactions sometimes resulted in a non-terminal (secondary) amine reacting in concert with a primary amine and an aldehyde group to yield a 1,3-diazacyclopentane or a 1,3-diazacyclohexane (aminal) derivative.[9] Nevertheless, reduction of such derivatives has been documented[9] to give the required linear amine backbone incorporating only secondary amines. It is possible that similar diazacyclopentane or 1,3-diazacyclohexane derivatives also form as intermediates in the present reactions involving triamine reagents. However, in all cases the final reduced products were shown to be the required macrocyclic rings. It needs to be noted that reports of the use of (1) in metal-complex[6,10] and silica immobilization studies[11] have appeared; however, the detailed synthesis and characterization of this macrocycle have not been published.

In most instances the reduced cyclic products were isolated as oils, with final purification involving generation of their protonated salts (see Experimental).

The infrared spectra of the respective reduced products confirmed the presence of secondary amine N–H stretching bands in the region 3100–3300 cm^{-1} (and contained no bands at 1650–1700 cm^{-1} where imine stretches are expected). The ^{1}H and ^{13}C n.m.r. spectra of the respective products in each case were consistent

[8] Bradshaw, J. S., Krakowiak, K. R., and Izatt, R. M., 'Aza-Crown Macrocycles' (John Wiley: New York 1993).

[9] Menif, R., Martell, A. E., Squattrito, P. J., and Clearfield, A., *Inorg. Chem.*, 1990, **29**, 4723; Pietraszkiewicz, M., and Gasiorowski, R., *Chem. Ber.*, 1990, **123**, 405; Guerriero, P., Vigato, P. A., Fenton, D. E., and Hellier, P. C., *Acta Chem. Scand.*, 1992, **46**, 1025; Lindoy, L. F., Mahendran, S., Krakowiak, K. E., An, H., and Bradshaw, J. S., *J. Heterocycl. Chem.*, 1992, **29**, 141.

[10] Cho, M.-H., Jung, H.-J., Lee, S.-I., Kim, J.-H., and Kim, S.-J., *J. Korean Chem. Soc.*, 1994, **38**, 122.

[11] Davis, C. A., Graves, P. R., Healy, P. C., and Myhra, S., *Appl. Surf. Sci.*, 1993, **72**, 419.

with the assigned structures; once again, there was no evidence for the presence of imine groups. Positive-ion fast atom bombardment (f.a.b.) mass spectra were obtained for the respective products. In each case no peaks were present at higher m/z values than that expected for the corresponding parent ion, LH^+—providing strong evidence that the macrocycles were 1 : 1 condensation products.

Macrocycles (1)–(10), taken together with the structurally related mixed-donor dibenzo macrocycles described previously, represent a *very extensive* set of related rings available for comparative metal-ion binding studies. Further studies in this area, with continuing emphasis on the factors influencing metal-ion recognition, are planned for the future.

Experimental

^1H and ^{13}C n.m.r. spectra were determined at 298 K on a Bruker AM300 spectrometer at 300 and 75 MHz, respectively. For particular samples, decoupling experiments were conducted to aid in making the peak assignments. Infrared spectra were recorded on a Perkin Elmer 197 spectrophotometer. Positive-ion f.a.b. mass spectra were determined on a JEOL JMS-DX300 instrument by Dr I. Liepa, Division of Coal and Energy Technology, CSIRO, at the Coal and Energy Division, CSIRO. Where microanalysis indicated the presence of solvates, the existence of corresponding signals was confirmed in the respective n.m.r. and infrared spectra.

2,2'-[Oxybis(ethyleneoxy)]dibenzaldehyde (11)

This (parent) dialdehyde was synthesized as reported previously[12]* (Found: C, 69·2; H, 5·8. Calc. for $C_{18}H_{18}O_5$: C, 68·8; H 5·8%). ^1H n.m.r. ($CDCl_3/SiMe_4$) δ 3·98, m, $ArOCH_2C\mathbf{H}_2$; 4·28, m, $ArOC\mathbf{H}_2$; 6·9–7·9, m, C_6H_4; 10·5, s, CHO. ^{13}C n.m.r. ($CDCl_3/SiMe_4$) δ 68·3, 69·9, OCH_2; 112·9, 121·1, 128·4, 135·8, Ar; 189·5, CHO. Mass spectral parent ion (f.a.b.) m/z 315.

Preparation of Macrocycle (1).3HNO$_3$

Diethylenetriamine (0·66 g, 6 mmol) in methanol (30 ml) was added to a boiling solution of the product from (11) (2·0 g, 6 mmol) in methanol (200 ml). The solution was heated and stirred for 25 min, then sodium borohydride (1·0 g) was added in small portions over 10 min. The solution was concentrated to approximately 50 ml, cooled, and the volume was increased twofold by addition of crushed ice. Stirring was continued at room temperature overnight in an open beaker. The pH of the solution was adjusted to approximately 12 and the mixture was extracted with chloroform (3×50 ml). The combined extracts were dried over anhydrous sodium sulfate and then taken to dryness on a rotary evaporator. The crude product was obtained as a light brown oil; yield 1·5 g. The trihydronitrate *salt* was obtained by slow crystallization of the oil dissolved in aqueous nitric acid/ethanol solution (Found: C, 45·9; H, 6·1; N, 14·2. $C_{22}H_{34}N_6O_{12}$ requires C, 46·0; H, 6·0; N, 14·6%). ^1H n.m.r. (D_2O/dioxan) δ 3·56, m, $NC\mathbf{H}_2C\mathbf{H}_2N$; 4·11, m, $ArOCH_2C\mathbf{H}_2$; 4·29, m, OCH_2; 4·36, s, $ArCH_2$; 6·9–7·6, m, C_6H_4. ^{13}C n.m.r. (D_2O/dioxan) δ 43·2, 44·1, NCH_2CH_2N; 47·7, $ArCH_2$; 68·5, 70·4, $ArOCH_2CH_2O$; 113·3, 119·1, 122·5, 132·7, 132·8, 157·8, C_6H_4. Mass spectral parent ion (f.a.b.) m/z 386.

Preparation of Macrocycle (2).3HNO$_3$.$\frac{1}{2}$H$_2$O.$\frac{1}{2}$EtOH

In a manner similar to that described for (1) above, *N*-(2-aminoethyl)propane-1,3-diamine and (11) yielded the macrocycle as a light yellow oil. ^1H n.m.r. ($CDCl_3/SiMe_4$) δ 1·65, q, $NCH_2C\mathbf{H}_2CH_2N$; 2·00, br, NH; 2·4–2·7, m, NCH_2; 3·78, s, $ArCH_2$; 3·97, m, $ArOCH_2C\mathbf{H}_2$; 4·11, m, OCH_2; 6·7–7·9, m, aromatic. ^{13}C n.m.r. ($CDCl_3/SiMe_4$) δ 29·7, $NCH_2\mathbf{C}H_2CH_2N$; 47·2, 47·4, 47·9, 48·8, NCH_2; 49·8, 50·0, $ArCH_2$; 67·2, 67·4, $ArOCH_2\mathbf{C}H_2O$; 69·8, OCH_2;

* See also Adam *et al.* (1983).[7]

[12] Battaglia, L. P., Corradi, A. B., and Mangia, A., *Inorg. Chim. Acta*, 1980, **42**, 191.

111·2, 120·6, 128·1, 128·7, 130·4, 156·8, aromatic. Mass spectral parent ion (f.a.b.) *m/z* 400. The trihydronitrate *salt* was obtained by crystallization of the above product from an aqueous nitric acid/ethanol solution (Found: C, 46·1; H, 6·2; N, 13·3. $C_{24}H_{40}N_6O_{13}$ requires C, 46·5; H, 6·5; N, 13·5%). ^{1}H n.m.r. (D_2O/dioxan) δ 2·05 quin, $NCH_2C\mathbf{H}_2CH_2N$; 3·36, dd, NCH_2CH_2N; 3·58, dt, $NC\mathbf{H}_2CH_2C\mathbf{H}_2N$; 3·90, t, $ArOCH_2C\mathbf{H}_2O$; 4·14, 4·19, s, $ArCH_2$; 4·16, t, $ArOCH_2$; 6·8–7·4, m, C_6H_4. ^{13}C n.m.r. (D_2O/dioxan) δ 22·6, $NCH_2\mathbf{C}H_2CH_2N$; 42·9, 43·3, 44·1, 45·3, NCH_2; 46·9, 47·6, $ArCH_2$; 67·9, $ArOCH_2\mathbf{C}H_2O$; 69·70, $ArOCH_2$; 113·3, 119·2, 119·6, 122·5, 132·7, 132·9, 157·7, aromatic.

Preparation of Macrocycle (3).HNO_3

This macrocycle was prepared from bis(3-aminopropyl)amine and (11) by using the general method described for (1). ^{1}H n.m.r. ($CDCl_3$/$SiMe_4$) δ 1·69, quin, $NCH_2C\mathbf{H}_2CH_2N$; 2·44, br, NH; 2·64, 2·69, t, NCH_2; 3·81, s, $ArCH_2$; 3·9, m, $ArOCH_2C\mathbf{H}_2O$; 4·2, m, $ArOCH_2$; 6·7–7·35, m, C_6H_4. ^{13}C n.m.r. ($CDCl_3$/$SiMe_4$) δ 29·6, $NCH_2\mathbf{C}H_2CH_2N$; 47·7, 48·6, $NHCH_2$; 50·4, $ArCH_2$; 67·7, $ArOCH_2\mathbf{C}H_2O$; 70·4, $ArOCH_2$; 111·8, 121·1, 128·6, 129·0, 130·9, 157·3, C_6H_4. Mass spectral parent ion (f.a.b.) *m/z* 414. The monohydronitrate *salt* was obtained by slow crystallization of the above product from an aqueous nitric acid/ethanol solution (Found: C, 60·2; H, 7·7; N, 11·5. $C_{24}H_{36}N_4O_6$ requires C, 60·5; H, 7·6; N, 11·8%). ^{1}H n.m.r. (D_2O/dioxan) δ 2·03, quin, $NCH_2C\mathbf{H}_2CH_2N$; 3·06, dd, NCH_2; 3·89, m, $ArOCH_2C\mathbf{H}_2$; 4·14, s, $ArCH_2$; 4·17, m, OCH_2; 6·85–7·4, m, C_6H_4. ^{13}C n.m.r. (D_2O/dioxan) δ 25·8, $NCH_2\mathbf{C}H_2CH_2N$; 46·9, 46·4, NCH_2; 48·1, $ArCH_2$; 68·0, $ArOCH_2\mathbf{C}H_2O$; 70·0, $ArOCH_2$; 113·3, 120·0, 125·8, 130·5, 131·7, 157·3, C_6H_4.

Preparation of Macrocycle (4).2H_2O

By using the general method reported for (1), *N*-methylbis(3-aminopropyl)amine and (11) yielded the required *macrocycle*. The brown oil obtained on evaporation of the chloroform extracts was dried under vacuum whereupon it slowly crystallized (Found: C, 65·0; H, 7·8; N, 9·3. $C_{25}H_{41}N_3O_5$ requires C, 64·8; H, 8·9; N, 9·1%). ^{1}H n.m.r. ($CDCl_3$/$SiMe_4$) δ 1·74, quin, $NCH_2C\mathbf{H}_2CH_2N$; 2·03, s, NCH_3; 2·33, 2·77, t, NCH_2; 3·93, s, $ArCH_2$; 4·00, m, $OCH_2C\mathbf{H}_2O$; 4·30, m, $ArOCH_2$; 6·8–7·5, m, C_6H_4. ^{13}C n.m.r. ($CDCl_3$/$SiMe_4$) δ 26·6, $NCH_2\mathbf{C}H_2CH_2N$; 42·1, NCH_3; 47·7, 49·5, NCH_2; 55·9, $ArCH_2$; 67·5, $ArOCH_2\mathbf{C}H_2O$; 69·9, $ArOCH_2$; 111·5, 120·7, 128·0, 128·3, 130·3, 156·8, C_6H_4. Mass spectral parent ion (f.a.b.) *m/z* 428.

Preparation of Macrocycle (5).H_2O

By using the general method described for (1), bis(2-aminoethyl) ether[13] and (11) yielded a white solid after addition of ice. The mixture was stirred overnight; the white *solid* was then collected and washed with water (Found C, 65·1; H, 7·5; N, 6·6. $C_{22}H_{32}N_2O_5$ requires C, 65·4; H, 8·0; N, 6·9%). ^{1}H n.m.r. ($CDCl_3$/$SiMe_4$) δ 2·33, br, NH; 2·75, t, $OCH_2C\mathbf{H}_2N$; 3·50, t, $OCH_2C\mathbf{H}_2N$; 3·78, s, $ArCH_2$; 4·11, m, $ArOCH_2C\mathbf{H}_2$; 4·13, m, $ArOCH_2$; 6·8–7·5, m, aromatic. ^{13}C n.m.r. ($CDCl_3$/$SiMe_4$) δ 49·3, NCH_2; 51·0, $ArCH_2$; 68·7, $O\mathbf{C}H_2CH_2N$; 71·1, 70·4, OCH_2CH_2O; 111·3, 120·8, 128·1, 128·6, 130·8, 157·2, aromatic. Mass spectral parent ion (f.a.b.) *m/z* 343.

Preparation of Macrocycle (6).2HNO_3.1$\frac{1}{2}H_2O$

The crude macrocycle was obtained from bis(2-aminopropyl)amine and (11) by using the general method described for (1). Its hydronitrate *salt* was obtained by (slow) crystallization of the above product from an aqueous nitric acid/acetonitrile solution (Found: C, 50·5; H. 6·8; N, 13·3. $C_{24}H_{40}N_5O_{10\cdot5}$ requires, C, 50·9; H, 7·1; N, 12·4%). ^{1}H n.m.r. (D_2O/dioxan) δ 1·3, d, $NCH_2CH(\mathbf{Me})N$; 1·8, m, $NCH_2C\mathbf{H}(Me)N$; 2·9, m, $NC\mathbf{H}_2CH(Me)N$; 4·0, 4·3, m, OCH_2, $ArCH_2$; 6·9–7·6, m, C_6H_4. ^{13}C n.m.r. (D_2O/dioxan) δ 15·4, m, $NCH_2CH(\mathbf{Me})N$; 45·4, m, $NCH_2\mathbf{C}H(Me)N$; 50·6, m, $N\mathbf{C}H_2CH(Me)N$; 51·8, $ArCH_2$; 67·7, 69·0, OCH_2; 113·3, 119·6, 122·5, 132·5, 132·8, 157·6, C_6H_4. *m/z* 414.

[13] Kulstad, S., and Malmsten, L. A., *Acta. Chem. Scand., Ser. B*, 1979, **33**, 469.

N,N-*Bis[2-(p-tolylsulfonyloxy)ethyl]*-p-*toluenesulfonamide*

This precursor was prepared by means of a modification of the literature method.[14] Tosyl chloride (141 g, 0·74 mol) in diethyl ether (850 ml) was slowly added to a mixture of diethanolamine (22·3 g, 0·21 mol) and triethylamine (150 ml). The solution was stirred for 1·5 h and water (300 ml) was then added to dissolve the $Et_3N.HCl$ precipitate which had formed. The layers were separated and the ether fraction was washed with water (3×200 ml). Following its separation, the ether phase was then taken to dryness on a rotary evaporator. The residue which remained was recrystallized from ethanol/water to yield white crystals of the product; yield 148 g (Found: C, 52·9; H, 5·2; N, 2·5. Calc. for $C_{25}H_{29}NO_8S_3$: C, 53·0; H, 5·3; N, 2·5%). ^{1}H n.m.r. ($CDCl_3$) δ 2·43, s, CH_3ArSO_2N; 2·46, s, CH_3ArSO_3; 3·37, t, NCH_2; 4·12, t, OCH_2; 7·2–7·8, m, C_6H_4. ^{13}C n.m.r. ($CDCl_3$) δ 21·5, CH_3ArSO_2N; 21·6, CH_3ArSO_3; 48·4, NCH_2; 68·2, OCH_2; 127·2, 127·9, 129·95, 130·0, 132·4, 135·2, 144·1, 145·2, C_6H_4. Mass spectral parent ion (f.a.b.) *m/z* 568.

N,N-*Bis[2-(2′-formylphenoxy)ethyl]*-p-*toluenesulfonamide (12)*

The product (29 g, 0·05 mol) from the above preparation was added to a mixture of salicylaldehyde (12·2 g, 0·12 mol) in ethanol (100 ml). This solution was warmed and sodium hydroxide (3 g) in water was added. The solution was then refluxed for approximately 36 h, then allowed to cool (with stirring), and the crystalline *product* which separated was isolated and washed with water; yield 14·0 g (Found: C, 63·8; H, 5·4; N, 2·9. $C_{25}H_{25}NO_6S$ requires C, 64·2; H, 5·4; N, 3·0%). ^{1}H n.m.r. ($CDCl_3$) δ 2·36, s, $ArCH_3$; 3·78, t, NCH_2; 4·31, t, OCH_2; 6·8–7·85, m, C_6H_4; 10·28, s, CHO. ^{13}C n.m.r. ($CDCl_3$) δ 21·5, s, $ArCH_3$; 49·1, NCH_2; 67·6, OCH_2; 189·1, CHO; 112·4, 121·3, 124·8, 126·9, 129·2, 129·9, 136·0, 144·0, 160·2, C_6H_4. Mass spectral parent ion (f.a.b.) *m/z* 468.

Preparation of Macrocycle (7).H_2O

Diethylenetriamine (0·44 g, 4 mmol) in methanol (40 ml) was added to a boiling solution of (12) (2·0 g, 4 mmol) in methanol (200 ml). The solution was heated and stirred for 25 min. Sodium borohydride (1·0 g) was added in small portions over 10 min. The solution was then concentrated to approximately 50 ml, cooled, and the volume was increased twofold by addition of crushed ice. Stirring was continued overnight at room temperature in an open beaker. The pH of the solution was then adjusted to approximately 12 before extracting it with chloroform (3×50 ml). The combined extracts were dried over anhydrous sodium sulfate, and the solution was then taken to dryness on a rotary evaporator to yield the crude *product* as a light brown oil; yield 1·5 g (Found: C, 62·8; H, 6·9; N, 10·1. $C_{29}H_{40}N_4O_5S$ requires C, 62·6; H, 7·2; N, 10·1%). ^{1}H n.m.r. ($CDCl_3$) δ 2·28, s, CH_3ArSO_2N; 2·66, 2·63, m, NCH_2; 3·67, t, $OCH_2C\mathbf{H}_2NTs$; 3·88, s, $ArCH_2$; 4·20, t, OCH_2; 6·70–7·7, m, aromatic. ^{13}C n.m.r. ($CDCl_3$); δ 21·4, $ArCH_3$; 49·0, 50·0, NCH_2CH_2; 50·3, $ArCH_2$; 67·8, OCH_2; 111·5, 121·0, 128·5, 128·8, 129·7, 137·5, 143·4, 156·6, aromatic. Mass spectral parent ion (f.a.b.) *m/z* 539. The product was converted into its trihydronitrate *salt* by crystallization from aqueous nitric acid/ethanol solution (Found: C, 47·6; H, 5·8; N, 13·3. $C_{29}H_{41}N_7O_{13}S$ requires C, 47·9; H, 5·7; N, 13·5%).

Preparation of Macrocycle (8).$1\frac{1}{2}H_2O$

In a manner similar to that described for (7), *N*-(2-aminoethyl)propane-1,3-diamine and (12) yielded a light-coloured *oil* which crystallized on standing (Found: C, 62·4; H, 7·1; N, 9·5. $C_{30}H_{43}N_4O_{5\cdot5}S$ requires C, 62·2; H, 7·5; N, 9·7%). ^{1}H n.m.r. ($CDCl_3$) δ 1·61, quin, $NCH_2C\mathbf{H}_2CH_2N$; 2·28, s, CH_3ArSO_2N; 2·63, m, $NC\mathbf{H}_2C\mathbf{H}_2N$; 3·66, 3·69, s, $ArCH_2$; 3·83, m, $OCH_2C\mathbf{H}_2NTs$; 4·20, m, OCH_2; 6·6–7·15, m, aromatic. ^{13}C n.m.r. ($CDCl_3$) δ 21·32, CH_3ArSO_2N; 29·2, $NCH_2\mathbf{C}H_2CH_2N$; 48·1, 48·2, 48·5, 49·2, 49·4, 49·9, $ArCH_2$, NCH_2; 111·2, 111·3, 120·8; 120·9; 126·9; 127·0; 128·3; 128·4; 128·5; 129·7; 129·8, 130·45, 130·47, 137·1, 143·5, 156·6, 156·7, aromatic. The trihydronitrate *salt* was obtained by crystallization

[14] Peacock, D. H., and Dutta, U. C., *J. Chem. Soc.*, 1934, 1303; Richman, J. E., and Atkins, T. J., *J. Am. Chem. Soc.*, 1974, **96**, 2268.

of the above product from an aqueous nitric acid/ethanol solution (Found: C, 48·2; H, 5·7; N, 13·2. $C_{30}H_{43}N_7O_{13}S$ requires C, 48·8; H, 5·8; N, 13·2%). Mass spectral parent ion (f.a.b.) *m/z* 553.

Preparation of Macrocycle (9).2½H₂O

By using the procedure described above for (7), reaction of bis(2-aminoethyl) ether[13] with (12) yielded the required product which precipitated as a solid on the slow addition of crushed ice to the reaction solution. The cream *solid* was isolated and washed with water (Found: C, 59·7; H, 6·8; N, 7·3. $C_{29}H_{42}N_3O_{7\cdot5}S$ requires C, 59·6; H, 7·2; N, 7·2%). ^{1}H n.m.r. ($CDCl_3$); δ 2·20, CH_3ArSO_2N; 2·26, t, NH; 2·71, t, $OCH_2C\mathbf{H}_2NH$; 3·52, t, $OC\mathbf{H}_2CH_2NH$; 3·65, s, $ArCH_2$; 3·91, t, $C\mathbf{H}_2NTs$; 4·28, t, $OC\mathbf{H}_2CH_2NTs$; 6·6–7·25, m, aromatic. ^{13}C n.m.r. ($CDCl_3$) δ 21·3, CH_3ArSO_2N; 49·5, $OCH_2\mathbf{C}H_2NTs$; 50·4, $NHCH_2O$; 51·1, $ArCH_2$; 68·0, $O\mathbf{C}H_2CH_2NTs$; 70·5, $NHCH_2\mathbf{C}H_2O$; 113·3, 121·1, 126·7, 128·2, 128·6, 129·6, 130·6, 138·0, 143·3, 156·6, aromatic. Mass spectral parent ion (f.a.b.) *m/z* 540.

Preparation of Macrocycle (10).2HNO₃

This macrocycle was prepared from (12) and bis(2-aminoethyl) thioether[15] by using the general method described above to yield a light-coloured oil. ^{1}H n.m.r. ($CDCl_3$) δ 2·35, s, CH_3ArSO_2N; 2·66, t, $NCH_2C\mathbf{H}_2S$; 2·75, t, $NC\mathbf{H}_2CH_2S$; 3·72, s, $ArCH_2$; 3·80, t, $TsNCH_2$; 4·24, t, OCH_2; 6·70–7·75, m, aromatic. ^{13}C n.m.r. ($CDCl_3$) δ 21·4, CH_3ArSO_2N; 33·0, SCH_2; 48·3, $NHCH_2$; 49·3, $TsNCH_2$; 50·1, $ArCH_2$; 67·7, OCH_2; 111·4, 111·7, 121·2, 127·1, 128·6, 129·9, 130·5, 137·0, 143·7, 158·6, aromatic. The dihydronitrate *salt* was obtained by crystallization of the product from aqueous nitric acid/ethanol solution (Found: C, 50·7; H, 5·6; N, 10·6. $C_{29}H_{39}N_5O_{10}S_2$ requires C, 51·1; H, 5·8; N, 10·3%). Mass spectral parent ion (f.a.b.) *m/z* 556.

Attempted Detosylation of (7)–(10)

Attempts to detosylate these species by using sodium naphthalenide in dry tetrahydrofuran[16] were unsuccessful and resulted in a complex mixture of products.

Acknowledgment

We thank the Australian Research Council for support.

[15] Nathan, A. H., and Bogert, M. T., *J. Am. Chem. Soc.*, 1941, **63**, 2361.
[16] Ji, S., Gortler, L. B., Waring, A., Battisti, A., Bank, S., Closson, W. D., and Wriede, P., *J. Am. Chem. Soc.*, 1967, **89**, 5311; Glosson, W. D., Ji, S., and Schulenberg, S., *J. Am. Chem. Soc.*, 1970, **92**, 650.