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Synthesis of phenazine derivatives for use as precursors to electrochemically generated bases

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1,6-Disubstituted phenazine derivatives for use as precursors to electrochemically generated bases have been synthesized from readily available starting materials. Reaction of 1,6-dihydroxyphenazine with 1,10-diododecane, 1,11-diiodo-3,6,9-trioxaundecane or (*R*,*R*)-(−)-1,2-bis(3-iodopropoxy)cyclohexane gave planar chiral phenazinophanes containing ether-linked bridges; molecular structures of all these compounds have been determined by X-ray crystallography. Substituted 1,6-diaminophenazines were prepared by palladium-mediated amination of 1,6-dichlorophenazine and acylation of 1,6-diaminophenazine followed by reduction. Reaction of 1,6-bis-(alkylamino)phenazines with sebacoyl chloride gave planar chiral phenazinophanes containing amide-linked bridges.

Introduction

Electrochemical reduction of neutral substrates ('probases'), including phenazine (**1**) (Fig. 1), generates radical anions and dianions which may act as bases.[1,2] In a recent communication we referred to some new C_2-symmetric homochiral phenazine derivatives, the radical-anions of which exhibited enantioselectivity in the rearrangement of the prochiral epoxide 3,4-epoxytetrahydrothiophene-1,1-dioxide (**2**) to the allylic alcohol (**3**).[3] Here, we describe in detail the synthesis of these chiral probases and some related phenazine derivatives.

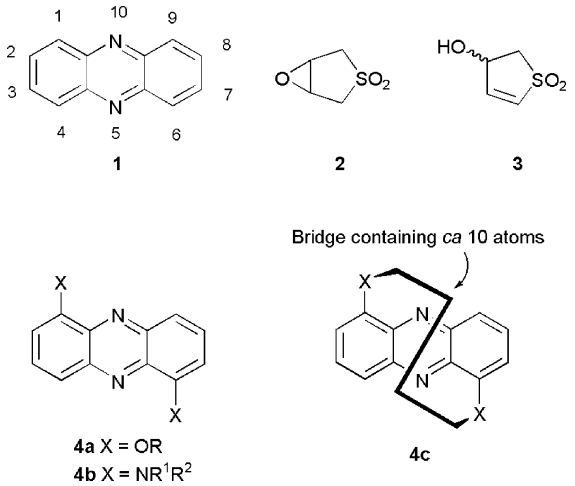


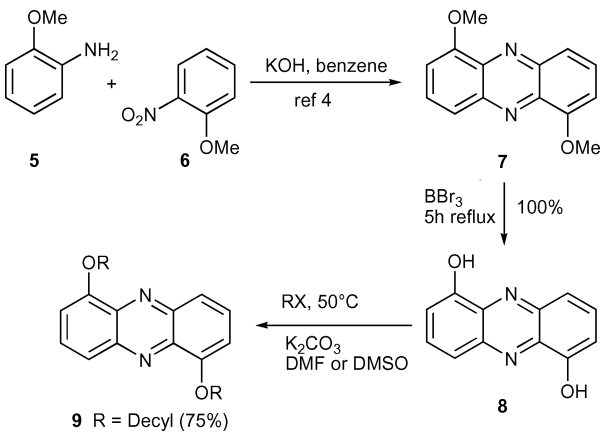
Fig. 1 Phenazine probases (**1** and **4**), substrate **2** and its rearrangement product (**3**).

In selecting target phenazine derivatives, we were guided by the need to produce single enantiomers that would be configurationally stable under basic and reducing conditions. We chose to make C_2-symmetric compounds of general structure (**4**) in which the 1- and 6-positions of phenazine carried identical substituents, thus maintaining the homotopic relationship between the two nitrogen atoms of the central phenazine ring. This should ensure that, following electrochemical reduction to form nitrogen-centred anionic species, the magnitude and direction of any asymmetric induction that occurs during deprotonation does not depend on which nitrogen atom acts as the base. The compounds studied fall into two main categories: firstly, ethers (**4a**) and secondly, nitrogen-containing systems (amides and amines, **4b**). In some cases the 1- and 6-positions are linked together to form bridges, thus giving rise to phenazinophanes (represented by general structure **4c**) that display the phenomenon of planar chirality.

Results and discussion

Synthesis of phenazine derivatives with oxygen substituents

The known 1,6-dimethoxyphenazine (**7**), prepared by the reaction of *o*-anisidine (**5**), *o*-nitroanisole (**6**) and potassium hydroxide in refluxing benzene,[4] was the precursor to the other phenazine ethers examined in this study (Scheme 1). Cleavage of both methoxyl groups in **7** by refluxing boron tribromide occurred in quantitative yield to give 1,6-dihydroxyphenazine (**8**). The diol **8** reacted smoothly with unbranched primary organic halides, potassium carbonate and DMF, leading to the isolation of *O*(1),*O*(6)-dialkylated products as exemplified by the di-*O*-decyl derivative **9**. However, we were unable to obtain useful quantities of chiral phenazine ethers through analogous reactions in which the electrophile was the secondary halide *rac*-1-phenylethyl bromide or the branched primary iodide (*S*)-**10**. In the latter case a ^{1}H NMR spectrum of the crude reaction mixture was consistent with quantitative elimination of HI from



Scheme 1 Synthesis of 1,6 dioxygenated phenazines.

† In part.

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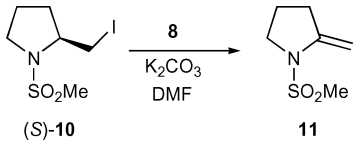
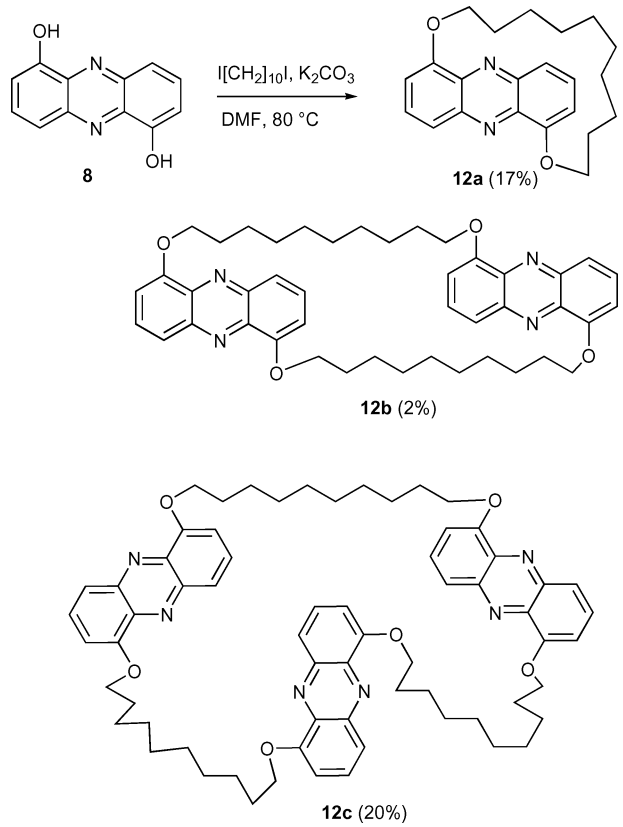
the iodide (*S*)-**10** to give the methylenepyrrolidine derivative **11** (Scheme 2).



(*S*)-**10** **11**

Scheme 2 Elimination of HI from chiral iodide (*S*)-**10**.

We reasoned that the construction of phenazinophanes of general structure **4c** (X = O) would place the phenazine ring in an asymmetric environment without requiring the use of hindered alkylating agents. Such structures resemble the chiral, but stereochemically labile, (1,5)-naphthalenophanes of Dougherty;[5] however, our use of shorter bridges in combination with the larger aromatic nucleus was expected to prevent racemization from occurring. Thus we investigated the reactions between 1,6-dihydroxyphenazine (**8**) and bis-electrophiles. 1,10-Diiododecane and potassium carbonate in dilute DMF solution (final concentration 0.003 M) gave a mixture of monomeric, dimeric and trimeric phenazinophanes **12a**–**c**, which could readily be separated on the basis of their solubility properties (Scheme 3). The analogous reaction of 1,11-diiodo-3,6,9-trioxaundecane (**13**) led to the isolation of the monomeric phenazinophane **14** in 14% yield (Scheme 4). Both the phenazinophanes **12a** and **14** possess planar chirality and

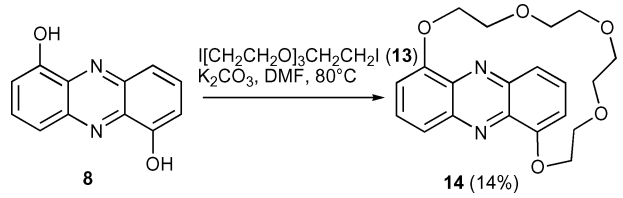


8 **12a** (17%)

12b (2%)

12c (20%)

Scheme 3 Preparation of cyclic ethers **12a**–**c**.

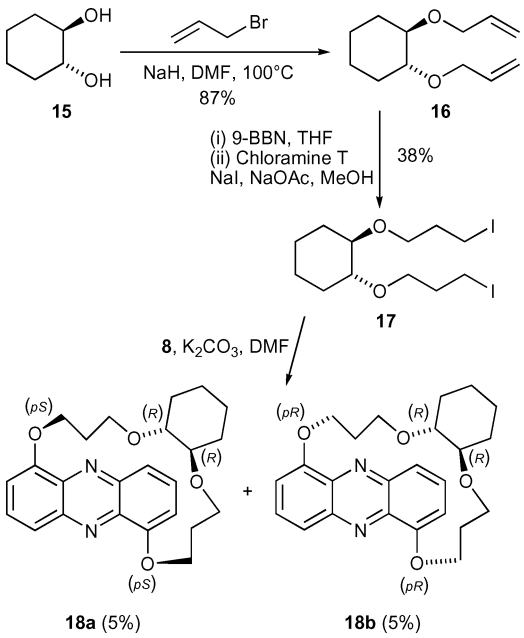


8 **14** (14%)

Scheme 4 Preparation of cyclic ether **14**.

were obtained as racemates: their resolution will be considered later in this article.

An alternative approach to enantiomerically pure planar-chiral phenazinophanes involves the use of a chiral bis-electrophile to form a bridge between the two phenazine oxygen substituents. Thus the diiodide **17**, prepared in two steps from (*R*,*R*)-cyclohexane-1,2-diol (**15**), reacted with 1,6-dihydroxyphenazine (**8**) under the usual cyclization conditions (Scheme 5) to afford 5% yields of each of two monomeric phenazinophane products **18a** and **18b**. These compounds could be separated by flash chromatography and were shown by single crystal X-ray diffraction to be a pair of diastereoisomers that differed from one another in their sense of planar chirality.



15 **16** **17**

18a (5%) **18b** (5%)

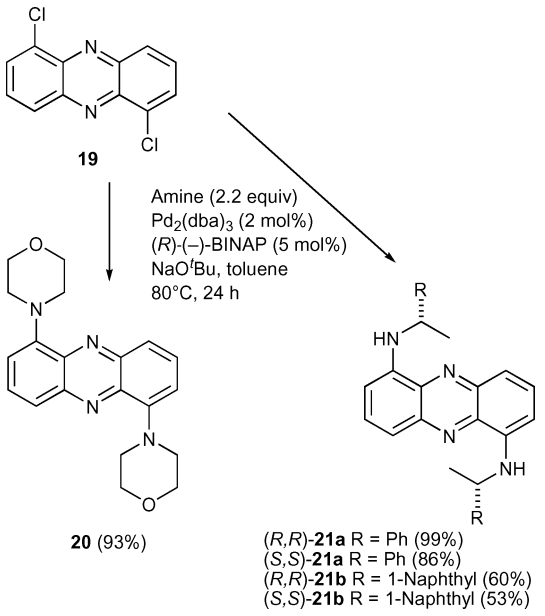
Scheme 5 Preparation of cyclic ethers **18a** and **18b**.

Synthesis of phenazine derivatives with nitrogen substituents

We have employed two approaches for the preparation of phenazine derivatives with nitrogen substituents at positions 1 and 6: these are (i) transition-metal catalysed amination of 1,6-dichlorophenazine (**19**) and (ii) dinitration of phenazine followed by reduction and acylation.

1,6-Dichlorophenazine (**19**) was available in one step from *o*-chloroaniline and *o*-chloronitrobenzene, as previously described by Pacher and Kloetzel.[6] The dichloride **19** underwent Buchwald–Hartwig palladium-mediated amination with the amines morpholine, 1-phenylethylamine and 1-naphthylethylamine to give the corresponding 1,6-diaminophenazine derivatives **20**–**21** (Scheme 6). The stereoisomeric purity of the diamines (*R*,*R*)-**21a** and (*S*,*S*)-**21a** was confirmed by their identical NMR spectra but different retention times on chiral HPLC. Hindered amines such as *cis*-2,6-dimethylpiperidine were unreactive under the conditions used.

For the second approach phenazine was nitrated according to the literature,[7] using hot concentrated nitric and sulfuric acids (75 °C, 8 h). This gave a mixture of 1,6- and 1,9 dinitrophenazines, from which the desired 1,6-isomer **22** was isolated in 30% yield by exploiting its very low solubility in boiling glacial acetic acid. The reduction of 1,6-dinitrophenazine (**22**) to give 1,6-diaminophenazine (**23**) has been reported to occur in good yields using zinc in acetic acid.[4] However, we could not reproduce this last result, most probably because of the heterogeneous nature of the reaction mixture. Our preferred conditions for reduction involved brief catalytic hydrogenation (2 h, 1 atm, 10% Pd/C) of a solution of **22** in trifluoroacetic



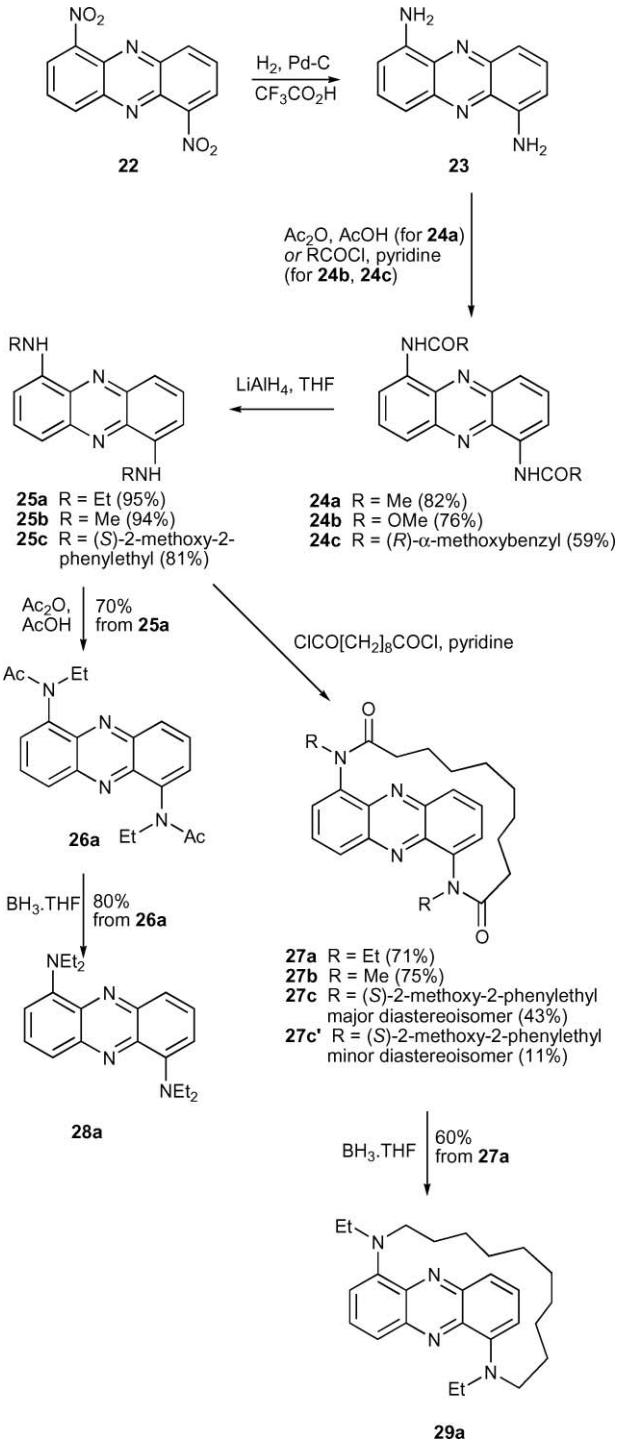
Scheme 6 Preparation of 1,6-diaminophenazine derivatives by catalytic amination.

acid, giving diamine **23** in 68% yield (Scheme 7). Longer reaction times led to over-reduction. *N*,*N*′-Diacylation, followed by $LiAlH_4$ or borane reduction proved to be a straightforward way of preparing 1,6-bis(alkylamino)phenazines **25**, including a chiral example **25c** derived from commercially available (*R*)-α-methoxyphenylacetic acid. Further *N*-acylation of the amines **25** occurred without difficulty to give amides **26a** and **27a**–**c**. We were particularly pleased by the ease with which the monomeric, planar chiral phenazinophanes **27a**–**c** formed when sebacoyl chloride was used as the electrophile. Final concentrations in these cyclizations were between 1 and 10 mM. It was notable that the presence of the chiral *N*-alkyl groups in diamine **25c** resulted in the production of unequal amounts of two diastereoisomeric phenazinophanes **27c** and **27c**′ (*ca.* 4 : 1 selectivity, based on the ^{1}H NMR spectrum of the crude product and the yields following separation of the isomers by flash chromatography). Treatment of the tertiary aromatic amides **26a** and **27** with $LiAlH_4$ or DIBALH led mainly to deacylation and hence reversion to the secondary amine precursors **25**, rather than providing the intended tertiary amines. On the other hand, borane reduction of the amides **26a** and **27a** was successful in forming the tertiary amines **28a** and **29a**.

Resolution of phenazinophanes

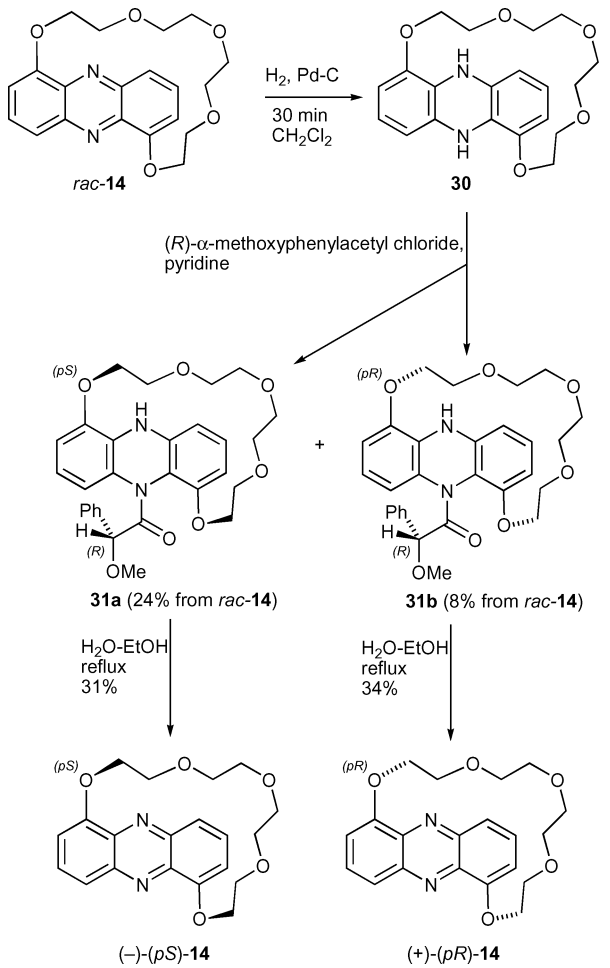
We have noted above how the presence of centres of chirality in the planar chiral phenazinophane derivatives **18a**–**b** and **27c**–**c**′ generated pairs of diastereoisomers that could be easily be separated by flash chromatography. These compounds could be obtained in both enantiomerically and diastereoisomerically pure forms, provided that a single enantiomer of the starting material was used. The other monomeric phenazinophanes **12a**, **14**, **27a**, **27b** and **29a** were formed as racemic mixtures. This was demonstrated by separation of the enantiomers of **12a**, **14**, **27a** and **29a** by analytical HPLC using a chiral stationary phase (ChiralPack OT).

We used the racemic phenazinophane **14** to exemplify an approach to resolution based on the following sequence (Scheme 8): reduction to the 5,10-dihydrophenazine **30**, preparation of a pair of diastereoisomeric derivatives by reaction of a chiral electrophile at one or both nitrogen atoms, separation of the diastereoisomers and regeneration of the aromatic phenazine system. The reduction step was conveniently achieved by hydrogenation over palladium on carbon. Completion of the reaction was indicated by the disappearance of the yellow colour from



Scheme 7 Preparation of 1,6-diaminophenazine derivatives from 1,6-dinitrophenazine.

the solution. Filtration to remove the catalyst gave a solution of the air-sensitive dihydrophenazine **30** which was used directly in reactions with chiral electrophilic reagents. NMR spectroscopy indicated the formation of *N*-monosubstituted derivatives upon treatment of **30** with menthyl chloroformate, camphor-10-sulfonyl chloride and 1-methoxyphenylacetyl chloride. However, the products formed with menthyl chloroformate and camphor-10-sulfonyl chloride decomposed during attempted chromatography on silica gel. Only when 1-methoxyphenylacetyl chloride was used were we able to perform flash chromatography on the diastereoisomeric derivatives. Following chromatography, the lower R_f product **31a** was obtained pure as judged by NMR, whereas the higher R_f product **31b** remained contaminated by *ca.* 10 mol% of the starting material **14**. However, recrystallisation



Scheme 8 Resolution of phenazinophane **14**.

of **31b** from heptane gave pure material and allowed the (*R*,*pR*) configuration to be established by X-ray diffraction. Conversion of the diastereoisomeric amides **31a** and **31b** into the enantiomeric phenazinophanes (−)-(*pS*)-**14** and (+)-(*pR*)-**14** was achieved by refluxing in aqueous ethanolic HCl under an atmosphere of air. Hydrolysis of **31a** readily gave (−)-(*pS*)-**14** as a single enantiomer, as indicated by chiral HPLC (Chiralpak OT(+), MeOH). The hydrolysis of the amide **31b** was found to be significantly slower than that of its diastereoisomer **31a** and the sample of (+)-(*pR*)-**14** as initially produced had 70% ee: partly, at least, this low ee resulted from the difficulty in obtaining a sample of **31b** which was free from racemic **14**, but it may also indicate that some racemisation occurred under the somewhat harsher conditions needed to hydrolyse **31b**. Following three recrystallisations from ethanol, however, (+)-(*pR*)-**14** was also obtained enantiomerically pure.

Structures of phenazinophanes

The molecular structures of the following phenazinophanes have been established by single crystal X-ray diffraction: *rac*-**12a**, *rac*-**14**, (−)-(*pS*)-**14**, **18a**, **18b** and **31b** (Figs. 2–7).‡ These data revealed that the aromatic phenazine systems were somewhat twisted by the presence of the bridges between positions 1 and 6. A quantitative measure of this deformation was obtained by calculating the torsion angle between the two planes generated by least squares fitting of the positions of the carbon atoms in the two carbocyclic rings (Table 1). The conformations of the saturated bridges present in **12** and **14** do not maintain the

‡ CCDC reference numbers 266538 and 269351. See http://dx.doi.org/10.1039/b506295k for crystallographic data in CIF or other electronic format.

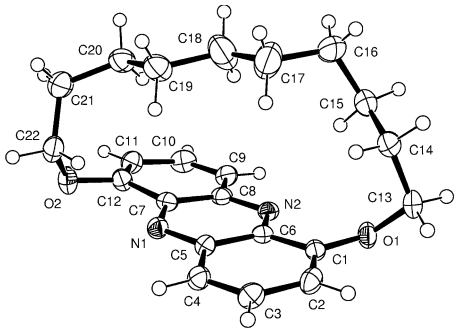


Fig. 2 Molecular structure of *rac*-**12a**.

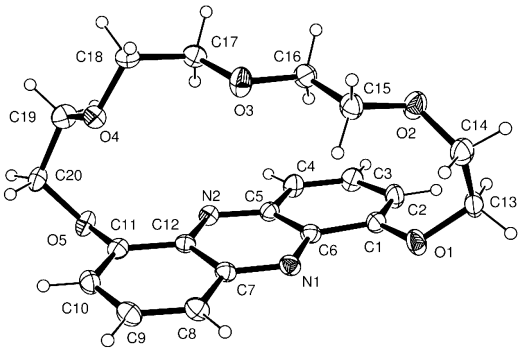


Fig. 3 Molecular structure of *rac*-**14**.

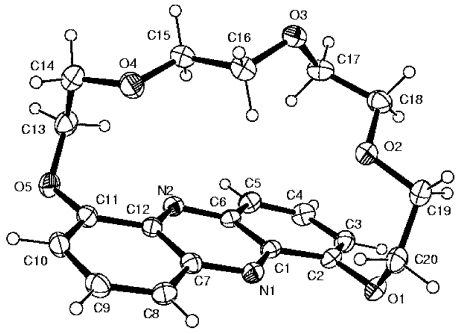


Fig. 4 Molecular structure of (−)-(*pS*)-**14**.

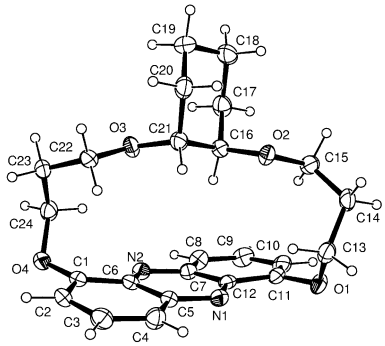


Fig. 5 Molecular structure of **18a**.

C_2-symmetry of these molecules in the solid state. There are conformational differences between the structures of *rac*-**14** and (−)-(*pS*)-**14**, whilst **18b** gives rise to two independent molecules within the unit cell of the crystal, implying that these molecules are somewhat flexible. Of the structures examined, compound **18b**, with a cyclohexane unit in the bridge, is closest to having C_2 symmetry in the solid state and also shows the greatest twisting of the phenazine ring system, suggesting a relatively strained structure.

The ^{1}H and ^{13}C NMR spectra of the monomeric aromatic phenazinophanes were consistent with the presence of C_2

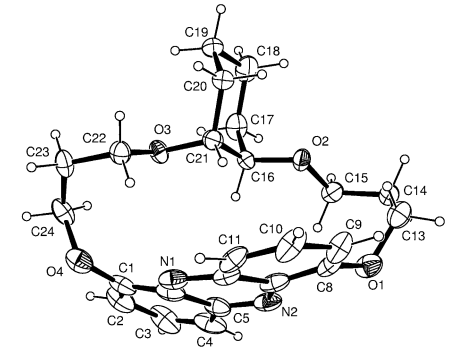


Fig. 6 Molecular structure of **18b**.

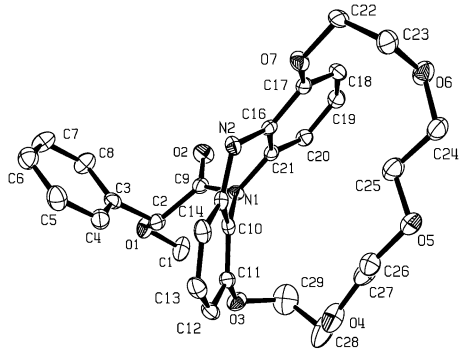


Fig. 7 Molecular structure of **31b**.

Table 1 Torsion angles between the planes which best fit the positions of the carbon atoms in the two outer rings of phenazinophanes

Phenazinophane	Number of C and O atoms in the bridge	Torsion angle(s)/deg
rac-**12a**	12	9
rac-**14**	13	7
(−)-(*pS*)-**14**	13	9
18a	12	10
18b	12	15 and 21[a]

[a] The two values reported relate to the two independent molecules within the unit cell.

symmetry on the NMR timescale. Some of the phenazine derivatives, notably **31a**, showed line broadening, which is attributable to restricted rotation at amide bonds. The pairs of protons in the bridging CH_2 groups occupied diastereotopic environments and differed from one another in their chemical shift values. ^{1}H NMR spectra of the phenazinophane **12a** were recorded in $CDCl_2CDCl_2$ at a range of temperatures between 30 and 110 °C: even at the highest temperatures studied the CH_2 protons did not become equivalent to each other on the NMR timescale. The NMR spectra exhibited upfield shifts associated with the central regions of the bridging groups, for example two of the four central CH_2 protons of **12a** resonate at $\delta + 0.1$ and the other two at $\delta - 0.4$. Similar observations have been made for other cyclophane systems: they are attributable to ring current effects combined with the chirality inherent in these systems.[5]

Conclusions

Routes have been devised to 1,6-disubstituted phenazine ethers and amines, including C_2-symmetric chiral phenazinophanes. The planar chirality associated with bridges of 12 or 13 atoms between the 1- and 6-positions leads to distinct, isolable stereoisomers that are accessible from inexpensive starting materials in a few steps. The formation of amide bridges gives good yields, whereas cyclization to form ether-bridged phenazinophanes appears to be much less efficient. The use of these compounds as precursors to electrogenerated bases will be examined in the following article.[12]

Experimental

'Petrol' or 'petroleum spirit' refers to the fraction of bp 40–60 °C. Toluene was distilled from sodium benzophenone ketyl before use. Flash chromatography was performed on BDH silica gel (33–70 μm). All new compounds were homogeneous as assessed by TLC and high field NMR. Melting points were determined using a Reichert hot stage microscope. Specific rotations were determined on an Optical Activity Ltd AA-1000 polarimeter with a path length of 0.5 or 2 dm. IR spectra were recorded using a Shimadzu FTIR 8300; samples were prepared either as films by evaporation of CH_2Cl_2 solutions on NaCl plates (indicated as 'film') or pellets formed by grinding with KBr followed by pressing (indicated as 'KBr'). NMR spectra were recorded on Jeol EX270 and Bruker AM250, AMX400 or AMX600 spectrometers. FAB mass spectra were recorded on a ZAB-SE4F machine at the School of Pharmacy, University of London; other mass spectra were obtained by the EPSRC National Service in Swansea using a Finnigan MAT 900. All HPLC experiments were performed using a Hewlett-Packard 1100 series liquid chromatography system equipped with Daicel Chiralpak OT(+) chiral columns (0.46 cm × 5 cm guard column and 0.46 cm × 25 cm main column) and a UV absorbance detector.

1,6-Dihydroxyphenazine (8)

Boron tribromide (17 ml, 0.18 mol) was added to 1,6-dimethoxyphenazine[4] (**7**) (1.12 g, 4.66 mmol) under nitrogen. The mixture was refluxed for 5 h, then cooled to room temperature, poured onto ice (200 g) and left overnight. The pH of the mixture was adjusted to **7** using NaOH. The yellow precipitate was filtered off, washed with water and dried *in vacuo* to give 1,6-dihydroxyphenazine (**8**) (0.97 g, 100%), mp 278–279 °C (lit.[4] 278 °C). δ_H (270 MHz, DMSO-d_6) 10.5 (s, 2H, exch D_2O, OH), 7.8–7.7 (m, 4H, Ar), 7.19 (2H, dd, *J* 6.4 and 2.0 Hz).

1,6-Bis(decan-1-oxy)phenazine (9)

1,6-Dihydroxyphenazine (**8**) (150 mg, 0.71 mmol), 1-iododecane (0.3 ml, 1.4 mmol) and K_2CO_3 (0.98 g, 7.0 mmol) were stirred together in DMF (11 ml) at 50 °C for 3 h. Water was added and the solution was twice extracted with Et_2O. The Et_2O extracts were washed several times with water and dried ($MgSO_4$). The solvent was evaporated and the residue was purified by flash chromatography (petrol–CH_2Cl_2, 1 : 1) yielding 1,6-bis(decan-1-oxy)phenazine (**9**) (260 mg, 75%) as a yellow solid, mp 77–79 °C. (Found: C, 77.6; H, 9.6; N, 5.6. $C_{32}H_{48}N_2O_2$ requires C, 78.0; H, 9.8; N, 5.7%); δ_H (270 MHz, $CDCl_3$) 7.89 (d, 2H, *J* 8.8 Hz, Ar H-4,9), 7.63 (dd, 2H, *J* 8.8, 7.7 Hz, Ar H-3,8), 6.98 (d, 2H, *J* 7.7 Hz, Ar H-2,7), 4.23 (t, 2H, *J* 7.1 Hz, C*H*$_2$OAr), 2.0 (quint, 2H, *J* 7.1 Hz, C*H*$_2$CH$_2$OAr), 1.6–1.0 (m, 14H, 7 × CH_2), 0.81 (t, 2H, *J* 7.1 Hz, CH_3); δ_C (68 MHz, $CDCl_3$) 154.2, 142.9, 136.9, 129.7, 121.8, 107.5, 69.3, 31.7, 29.4, 29.3, 29.2, 28.6, 25.8, 22.5, 14.0; ν_{max}/cm^{-1} (KBr) 2920, 2850, 1624, 1533, 1485, 1470, 1271, 1153, 797; *m*/*z* (FAB) 493.3800 (M + H$^+$, $C_{32}H_{49}N_2O_2$ requires 493.3794).

(*S*)-2-(Iodomethyl)-*N*-methanesulfonylpyrrolidine (10)

(*S*)-*N*-Methanesulfonyl-*O*-methanesulfonylprolinol[8] (274 mg, 1.07 mmol) and NaI (260 mg, 1.70 mmol) were refluxed in acetone (10 ml) for 6 d. The solvent was evaporated and the solid residue was partitioned between Et_2O and H_2O. The organic layer was washed with saturated aqueous sodium metabisulfite, then with brine, and dried ($MgSO_4$). The solvent was evaporated to yield the iodide **10** (262 mg, 85%), $[a]_D^{27}$ −61.2 (*c* 0.93, CH_2Cl_2),

mp 96–98 °C; δ_H (270 MHz, $CDCl_3$) 3.9–3.7 (m, 1H, H-1); 3.6–3.3 (m, 3H, CH_2N + CHI); 3.24 (t, 1H, *J* 9.4 Hz, CHI); 2.86 (s, 3H, CH_3); 2.2–1.7 (m, 4H, CCH_2CH_2C); δ_C (68 MHz, $CDCl_3$): 60.5, 49.9, 36.0, 32.4, 24.0, 11.6; ν_{max}/cm^{-1} (film) 3022, 2935, 1425, 1321, 1145; *m/z* (FAB) 289.9705 (M + H^+, $C_6H_{13}INO_2S$ requires 289.9712).

rac-2,13-Dioxa-1(1,6)-phenazinacyclotridecaphane (*rac*-12a)

1,6-Dihydroxyphenazine (**8**) (0.80 g, 3.8 mmol) and K_2CO_3 (5.25 g, 38 mmol) in DMF (625 ml) were heated at 80 °C under nitrogen. A solution of 1,10-diiododecane (1.57 g, 3.8 mmol) in DMF (625 ml) was then added over a period of 30 h using a dropping funnel. Once the addition was complete, the mixture was stirred at 80 °C for further 3 h. DMF was removed by evaporation under vacuum. The residue was dissolved in $CHCl_3$, washed with brine and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography ($CHCl_3$) gave a mixture containing the cyclic monomer **12a**, dimer **12b** and trimer **12c**. The monomer *rac*-**12a** was soluble in cold petrol, whereas the dimer **12b** was only soluble in the hot solvent, and the trimer **12c** was completely insoluble. The mixture was added to petrol, which was boiled for 5 min. The insoluble material was filtered off and on the basis of mass spectrometry and NMR was considered to comprise mainly the trimer 2,12,14,25,27,38-hexoxa-1(1,6),13(1,6),26(1,6)-(triphenazina)cyclononatriacontaphane (**12c**) (264 mg, 20%) as a yellow solid, mp 157–163 °C; δ_H (270 MHz, $CDCl_3$) 7.95 (d, 6H, *J* 9.0 Hz, Ar), 7.67 (t, 6H, *J* 9.0 Hz, Ar), 7.03 (d, 6H, *J* 9.0 Hz, Ar), 4.29 (t, 12H, *J* 6.5 Hz, OCH_2), 2.06 (quint, 12H, *J* 6.5 Hz, OCH_2CH_2), 1.8–1.2 (m, 36H, 18 × CH_2); δ_C (68 MHz, $CDCl_3$) 155.0, 143.0, 137.0, 129.9, 122.0, 107.8, 69.5, 29.5, 28.8, 26.1; *m/z* (FAB) 1051.6048 (M + H^+, $C_{66}H_{79}N_6O_6$ requires 1051.6060).

The petrol extract was cooled down to room temperature and half of the solvent evaporated at room temperature overnight. Then the dimer 1(1,6),13(1,6)-diphenazina-2,12,14,24-(tetroxa)cyclohexadocosaphane (**12b**) (33 mg, 2%) precipitated as a yellow solid, mp 205–210 °C; δ_H (270 MHz, $CDCl_3$) 7.82 (dd, 4H, *J* 8.9 and 1 Hz, Ar), 7.57 (dd, 4H, *J* 8.9 and 7.4 Hz, Ar), 6.88 (d, 4H, *J* 7.4 and 1 Hz, Ar), 4.18 (t, 8H, *J* 6.4 Hz, OCH_2), 1.87 (quint, 8H, *J* 6.4 Hz, OCH_2CH_2), 1.5–1.2 (m, 24H, 12 × CH_2) *m/z* (FAB) 701.4091 (M + H^+, $C_{44}H_{53}N_4O_4$ requires 701.4067).

The mother liquor was evaporated and the residue was recrystallised from EtOH to yield 2,13-dioxa-1(1,6)-(phenazina)cyclotridecaphane (*rac*-**12a**) (227 mg, 17%) as orange crystals, mp 162–164 °C. (Found C 75.1; H 7.6; N 8.0. $C_{22}H_{26}N_2O_2$ requires C 75.4; H 7.5; N 8.0%); δ_H (400 MHz, $CDCl_2CDCl_2$, assignment by COSY) 8.07 (dd, 2H, *J* 8.9 and 0.9 Hz, Ar H-4,9) 7.77 (dd, 2H, *J* 8.9 and 7.8 Hz, Ar H-3,8), 7.38 (dd, 2H, *J* 7.8 and 0.9 Hz, Ar H-2,7), 4.9–4.7 (m, 2H, ArOC*H*), 4.5–4.4 (m, 2H, ArOC*H*), 1.5–1.4 (m, 4H, $ArOCH_2CH_2$), 1.0–0.8 (m, 2H, OCH_2CH_2CH), 0.6–0.5 (m, 4H, OCH_2CH_2CHCH), 0.50–0.35 (m, 2H, $OCH_2CH_2CH_2CH$), 0.15–0.02 (m, 2H, $OCH_2CH_2CH_2CH_2CH$), −0.3–−0.5 (m, 2H, $OCH_2CH_2CH_2CH_2CH$); δ_C (101 MHz, $CDCl_2CDCl_2$, assignment by HSQC) 154.9, 142.7, 138.2, 130.3 (Ar C-3,8), 123.7 (Ar C-4,9), 117.5 (Ar C-2,7), 72.8 (CH_2O), 28.2 (OCH_2CH_2), 28.1 ($OCH_2CH_2CH_2CH_2$), 27.9 ($OCH_2CH_2CH_2CH_2CH_2$), 25.0 ($OCH_2CH_2CH_2$); ν_{max}/cm^{-1} (film) 2924, 2852, 1732, 1622, 1526, 1481, 1464, 1346, 1252, 1132, 1115, 816; *m/z* (FAB) 351.2055 (M + H^+, $C_{22}H_{27}N_2O_2$ requires 351.2077); HPLC t_R/min [Chiralpak OT(+); hexane–propan-2-ol, 99 : 1; 0.7 ml min^{-1}; λ 276 nm; 30 °C] 18.5 (50%), 20.9 (50%).

1,11-Diiodo-3,6,9-trioxaundecane (13)

Our procedure is similar to that of Marquis *et al.*[9] Tetra(ethylene glycol) di-*p*-tosylate (0.50 g, 0.96 mmol) and sodium iodide (0.23 g, 1.54 mmol) were refluxed together in acetone (5 ml) for 3 h. The solvent was evaporated and the residue was distributed between Et_2O and saturated aqueous sodium metabisulfite. The ether phase was washed with water, dried ($MgSO_4$) and the solvent was evaporated to leave 1,11-diiodo-3,6,9-trioxaundecane (**13**) (332 mg, 84%) as a pale yellow oil, δ_H (270 MHz, $CDCl_3$) δ 3.70 (t, 4H, *J* 6.9 Hz, ICH_2CH_2O), 3.61 (s, 8H, OCH_2CH_2O) and 3.20 (t, 4H, *J* 6.9 Hz, ICH_2CH_2O); δ_C (68 MHz, $CDCl_3$) 71.75, 70.47, 70.02; ν_{max}/cm^{-1} (film) 2866, 1458, 1413, 1350, 1263, 1169, 1105, 1034, 995, 976; *m/z* (FAB) 414.9248 (M + H^+, $C_8H_{17}I_2O_3$ requires 414.9267).

2,5,8,11,14-Pentaoxa-1(1,6)-(phenazina)cyclotetradecaphane (14)

A mixture of 1,6-dihydroxyphenazine (**8**) (1.00 g, 4.7 mmol) and K_2CO_3 (6.55 g, 47 mmol) in DMF (700 ml) was heated to 80 °C under N_2. A solution of 1,11-diiodo-3,6,9-trioxaundecane (1.95 g, 4.7 mmol) in DMF (700 ml) was added over 27 h by HPLC pump. The mixture was stirred at 80 °C for an additional 3 h after the addition was complete. DMF was removed by evaporation under reduced pressure. The residue was dissolved in dichloromethane and washed with water and brine. The organic phase was dried ($MgSO_4$) and the solvent was evaporated. The residue was purified by flash chromatography ($CHCl_3$) and recrystallization from EtOH to yield *rac*-2,5,8,11,14-pentaoxa-1(1,6)-(phenazina)cyclotetradecaphane (**14**) (240 mg, 14%) as orange crystals, mp 184–185 °C (Found: C, 64.7; H, 6.1; N, 7.4. $C_{20}H_{22}N_2O_5$ requires C, 64.85; H, 6.0; N 7.6%). ν_{max}/cm^{-1} (film) 3067, 2924, 2862, 1624, 1525, 1483, 1254, 1138, 1119; δ_H (270 MHz, $CDCl_3$, assignment by COSY) 8.06 (dd, 2H, *J* 8.8, 1.0 Hz, Ar H-4,9), 7.73 (dd, 2H, *J* 8.8, 7.4 Hz, Ar H-3,8), 7.39 (dd, 2H, *J* 7.4 and 1 Hz, Ar H-2,7), 4.90 (ddd, 2H, *J* 12.9, 3.7, 1.5 Hz, ArOC*H*), 4.48 (ddd, 2H, *J* 12.9, 8.7, 1.2 Hz, ArOC*H*), 4.03 (ddd, 2H, *J* 11.1, 8.7, 1.5 Hz, $ArOCH_2CH$), 3.69 (ddd, 2H, *J* 11.1, 3.7, 1.2 Hz, $ArOCH_2CH$), 3.00–2.88 (m, 4H, $ArOCH_2CH_2OCH_2$), 2.63 (dt, 2H, *J* 10.6, 4.2 Hz, $ArOCH_2CH_2OCH_2CH$), 2.37 (ddd, 2H, *J* 10.9, 6.4, 4.7 Hz, $ArOCH_2CH_2OCH_2CH$); δ_C (101 MHz, $CDCl_3$, assignment by HSQC) 156.3, 143.3, 139.2, 129.9 (Ar C-3,8), 124.2 (Ar C-4,9), 117.2 (Ar C-2,7), 74.2 (ArO*C*), 72.1 ($ArOCH_2C$), 69.7 ($ArOCH_2CH_2OC$), 69.2 ($ArOCH_2CH_2OCH_2C$); *m/z* (FAB) 371.1613 (M + H^+, $C_{20}H_{23}N_2O_5$ requires 371.1607); HPLC t_R/min [Chiralpak OT(+), MeOH, 0.1 ml min^{-1}; λ 271 nm; 0 °C] 63.1 (50%), 66.8 (50%).

(*R*,*R*)-(−)-1,2-Bis(allyloxy)cyclohexane (16)

The ether **16** was prepared according to the literature[10] except that the starting material (*R*,*R*)-(−)-cyclohexane-1,2-diol (**15**) had been obtained by catalytic desymmetrisation of cyclohexane oxide by Jacobsen's procedure,[11] then hydrolysis of the resulting benzoate ester. (*R*,*R*)-(−)-1,2-Bis(allyloxy)cyclohexane (**16**) was obtained as a pale yellow oil (87% yield from **15**), $[\alpha]_D^{25}$ −46 (*c* 1.25, CH_2Cl_2). δ_H (270 MHz, $CDCl_3$) 6.00–5.85 (m, 2H, =CH), 5.27 (dq, 2H, *J* 17.1, 1.7 Hz, =CH), 5.12 (dd, 2H, *J* 10.1, 1.5 Hz, =CH), 4.12 (dt, 4H, *J* 5.7, 1.5 Hz, CH_2O), 3.22 (t, 2H, 4.0 Hz, OCH), 2.00–1.15 (m, 8H, $[CH_2]_4$).

(*R*,*R*)-(−)-1,2-Bis-(3-iodopropoxy)cyclohexane (17)

(*R*,*R*)-(−)-1,2-Bis(allyloxy)cyclohexane (**16**) (1.00 g, 5.09 mmol) was stirred in THF (50 ml) at 0 °C under nitrogen. 0.5 M 9-BBN in THF (41 ml, 20.4 mmol) was added slowly and the solution was stirred at 0 °C for 1 h and then at room temperature for 5 h. Anhydrous methanol (33 ml) was added. Then a solution of sodium acetate (4.11 g, 50.1 mmol) in methanol (50 ml) was added followed by a solution of sodium iodide (7.51 g, 50.1 mmol) in water (50 ml). Subsequently a solution of chloramine T trihydrate (14.11 g, 50.1 mmol) in methanol (50 ml) was added. The mixture was stirred overnight at room temperature, then it was extracted with petroleum ether, which

was washed with a saturated aqueous sodium metabisulfite. The organic phase was washed with water, dried ($MgSO_4$) and the solvent was evaporated. The crude mixture was purified by flash chromatography (petroleum ether–ethyl acetate, 50 : 2) to yield (*R*,*R*)-(−)-1,2-bis-(3-iodopropoxy)cyclohexane (**17**) (859 mg, 38%) as a colourless liquid, $[a]_D^{24}$ −27 (*c* 1, CH_2Cl_2). δ_H (270 MHz, $CDCl_3$) 3.7–3.5 (m, 4H, OCH_2), 3.30 (t, 4H, *J* 6.7 Hz, ICH_2), 3.2–3.0 (m, 2H, OC*H* cyclohexane), 2.2–1.8 (m, 4H, $OCH_2CH_2CH_2I$), 1.7–1.5 (m, 4H, 2 × CH_2), 1.3–1.0 (m, 4H, 2 × CH_2); *m*/*z* (FAB) 452.9775 (*M* + H^+, $C_{12}H_{23}I_2O_2$ requires 452.9788).

(*R*,*R*,*pS*)-(+)-/(*R*,*R*,*pR*)-(−)-7(1,2)-Cyclohexana-1(1,6)-phenazina-2,6,8,12-tetraoxacyclododecaphanes (18a and 18b)

1,6-Dihydroxyphenazine (1.03 g, 4.89 mmol) and potassium carbonate (6.75 g, 48.9 mmol) in DMF (700 ml) were degassed by bubbling nitrogen for 90 min and then heated to 80 °C under nitrogen. A solution of (*R*,*R*)-(−)-1,2-bis(3-iodopropoxy)cyclohexane (**17**) (2.21 g, 4.89 mmol) in DMF (700 ml) was added over 27 h by HPLC pump. The solution was then stirred at 80 °C for an additional 3 h. DMF was removed by rotary evaporation. The residue was extracted with $CHCl_3$ and filtered. The filtrate was washed with brine, dried ($MgSO_4$) and the solvent evaporated. The crude residue was purified by flash chromatography ($CHCl_3$–petrol–Et_2O, 7 : 2 : 1) yielding first (*R*,*R*,*pS*)-(+)- and then (*R*,*R*,*pR*)-(−)-7(1,2)-cyclohexana-1(1,6)phenazina-2,6,8,12-tetraoxacyclododecaphanes (**18a** and **18b**).

The (*R*,*R*,*pS*)-(+)-diastereosomer **18a** was recrystallized from MeOH to yield orange crystals (106 mg, 5%). R_f 0.42 ($CHCl_3$–petrol–Et_2O 7 : 2 : 1), mp 143–145 °C, $[a]_D^{26}$ +486 (*c* 1, $CHCl_3$). (Found: C, 70.1%; H, 7.0%; N, 7.0%. $C_{24}H_{28}N_2O_4$ requires C, 70.6%; H, 6.9%; N, 6.9%).δ_H (600 MHz, $CDCl_3$, assignment by COSY) 8.06 (dd, 2H, *J* 8.8, 1.2 Hz, Ar H-4,9), 7.71 (dd, 2H, *J* 8.8, 7.4 Hz, Ar H-3,8), 7.48 (dd, 2H, *J* 7.4, 1.2 Hz, Ar H-2,7), 5.46 (ddd, 2H, *J* 12.5, 10.2, 1.8 Hz, ArOC*H*), 4.39 (ddd, 2H, *J* 12.5, 5.2, 2.9 Hz, ArOC*H*), 3.12 (ddd, 2H, *J* 9.5, 5.8, 3.7 Hz, CyOC*H*), 2.13 (td, 2H, *J* 10.8, 6.8, CyOC*H*), 1.98–1.91 (m, 2H, $ArOCH_2CHHCH_2OCy$), 1.84–1.77 (m, 2H, $ArOCH_2CHHCH_2OCy$), 1.2–0.9 (m, 10H, Cy); δ_C (151 MHz, $CDCl_3$, assignment by HSQC and DEPT, quaternary carbons not reported due to unfavourable signal/noise) 130.2 (Ar C-3,8), 124.6 (Ar C-4,9), 119.5 (Ar C-2,7), 75.4 (Cy C-1,2), 69.0 ($ArOCH_2$), 63.9 ($CyOCH_2$), 31.9 ($ArOCH_2C$), 23.6, 19.3; ν_{max}/cm^{-1} (film) 2933, 1623, 1527, 1481, 1254, 1163, 1128; *m*/*z* (FAB) 409.2129 (M + H^+, $C_{24}H_{29}N_2O_4$ requires 409.2127).

The (*R*,*R*,*pR*)-(−)-diastereosomer **18b** was recrystallized from EtOH to yield orange crystals (102 mg, 5%). R_f 0.28 ($CHCl_3$–petrol–Et_2O, 7 : 2 : 1), mp 157–159 °C, $[a]_D^{26}$ −452 (*c* 1, $CHCl_3$). (Found: C, 70.5%; H, 7.0%; N, 7.1%. $C_{24}H_{28}N_2O_4$ requires C, 70.6%; H, 6.9%; N, 6.9%). δ_H (600 MHz, $CDCl_3$, assignment by COSY) 8.06 (dd, 2H, *J* 8.8 Hz and 1.1 Hz, Ar H-4,9), 7.78 (dd, 2H, *J* 8.8 and 7.4 Hz, Ar H-3,8), 7.37 (dd, 2H, *J* 7.4 and 1.1 Hz, Ar H-2,7), 4.79 (ddd, *J* 11.5, 6.7, 3.4 Hz, 2H, ArOC*H*), 4.28 (ddd, 2H, *J* 11.5, 8.4, 2.8 Hz ArOC*H*), 3.10–3.04 (m, 2H, CyOC*H*), 2.63–2.58 (m, 2H, CyOC*H*), 2.02–1.95 (m, 2H, $ArOCH_2CHHCH_2OCy$), 1.67–1.59 (m, 2H, $ArOCH_2CHHCH_2OCy$), 1.2–0.7 (m, 10H, Cy); δ_C (151 MHz, $CDCl_3$, assignment by HSQC and DEPT, quaternary carbons not reported due to unfavourable signal/noise) 130.5 (Ar C-3,8), 123.9 (Ar C-4,9), 117.9 (Ar C-2,7), 75.1 (Cy C-1,2), 72.1 ($ArOCH_2$), 64.7 ($CyOCH_2$), 30.5 ($ArOCH_2C$), 24.8, 19.6; ν_{max}/cm^{-1} (film) 2933, 1621, 1525, 1481, 1263, 1112, 1069; *m*/*z* (FAB) 409.21251 (M + H^+, $C_{24}H_{29}N_2O_4$ requires 409.21272).

1,6-Bis(morpholino)phenazine (20)

1,6-Dichlorophenazine (**19**) (125 mg, 0.5 mmol), $Pd_2(dba)_3$ (10.7 mg, 0.012 mmol), (*R*)-(−)-BINAP (17.2 mg, 0.028 mmol), and ^{t}BuONa (139 mg, 1.45 mmol) were dissolved under nitrogen in dry toluene (1 ml). Morpholine (96 µl, 1.1 mmol) was added and the mixture was heated at 80 °C for 24 h, then cooled and filtered through Celite. Evaporation of the solvent gave a red residue, which after flash chromatography (CH_2Cl_2–EtOAc, 9 : 1) gave 1,6-bis(morpholino)phenazine (**20**) (162 mg, 93%) as an orange solid, mp 276–277 °C. δ_H (270 MHz, $CDCl_3$) 7.85 (d, 2H, *J* 8.6 Hz, Ar), 7.69 (dd, 2H, *J* 8.6, 7.4 Hz, Ar), 7.11 (d, 2H, *J* 7.4 Hz, Ar), 4.10 (t, 8H, *J* 4.4 Hz, CH_2O), 3.53 (t, 8H, *J* 4.4 Hz, CH_2N); δ_C (68 MHz, $CDCl_3$) 148.8 (Ar), 142.6 (Ar), 138.2 (Ar), 130.3 (Ar), 123.9 (Ar), 115.1 (Ar), 67.3 (CH_2), 52.7 (CH_2); ν_{max}/cm^{-1} (KBr) 2943, 2851, 1612, 1528, 1481, 1119; *m*/*z* (EI) 350.17399 (M^+, $C_{20}H_{22}O_2N_4$ requires 350.17488).

1,6-Bis(1-phenylethylamino)phenazine (21a)

1,6-Bis(1-phenylethylamino)phenazine (**21a**) was prepared by analogy with 1,6-bis(morpholino)phenazine (**20**), by using (*R*,*R*)- or (*S*,*S*)-1-phenylethylamine in place of morpholine. Flash chromatography (petrol–CH_2Cl_2, 7 : 3) gave enantiomerically pure (*R*,*R*)- or (*S*,*S*)-1,6-bis(1-phenylethylamino)-phenazine (99% yield for (*R*,*R*)-**21a**; 86% yield for (*S*,*S*)-**21a**) as a red solid, mp 155–157 °C. δ_H (270 MHz, $CDCl_3$) 7.48–7.24 (m, 14H, Ar–H); 6.79 (d, 2H, *J* 6 Hz, NH); 6.35 (dd, 2H, *J* 6.4, 2.2 Hz); 4.72 (quintet, 2H, *J* 6 Hz, C*H*Me); 1.74 (d, 6H, *J* 6.8 Hz, Me); δ_C (68 MHz, $CDCl_3$) 144.9, 143.5, 141.7, 135.4, 131.4, 128.9, 127.2, 126.1, 115.4, 104.3, 53.6 (*C*Me), 25.2 (Me); ν_{max}/cm^{-1} (KBr): 3404, 3061, 2966, 1618, 1541, 1491, 1354; *m*/*z* (FAB) 419.2236 (M + H^+, $C_{28}H_{27}N_4$ requires 419.2236); λ_{max} (MeOH) 250 (ε 7200), 296 (56300) and 522 (4400); HPLC, t_R/min [Daicel Chiralpak OT (+), propan-2-ol, 0.5 ml min^{-1}] 13.4 (*R*,*R*)-enantiomer, 15.3 (*S*,*S*)-enantiomer.

1,6-Bis(1-naphthylethylamino)phenazine (21b)

1,6-Bis(1-naphthylethylamino)phenazine (**21b**) was prepared by analogy with 1,6-bis(morpholino)phenazine (**22**), by using (*R*,*R*)- or (*S*,*S*)-1-naphthylethylamine in place of morpholine. Flash chromatography (petroleum spirit–CH_2Cl_2, 7 : 3), followed by recrystallization from MeOH gave 1,6-bis(1-naphthylethylamino)phenazine (**21b**) (60% yield for (*R*,*R*)-**21b**; 53% yield for (*S*,*S*)-**21b**) as a red solid, mp 199–200 °C (from MeOH). δ_H (270 MHz, $CDCl_3$) 8.25 (d, 2H, *J* 8 Hz), 7.94 (t, 2H, *J* 8 Hz), 7.76 (d, 2H, *J* 8 Hz), 7.51–7.69 (m, 5H), 7.33–7.49 (m, 7H), 6.93 (d, 2H, *J* 6 Hz, NH), 6.21 (d, 2H, *J* 7 Hz), 5.48–5.57 (m, 2H, CH), 1.89 (d, 6H, *J* 6.6 Hz, CH_3); δ_C (68 MHz, $CDCl_3$): 143.3, 141.7, 139.5, 135.4, 134.3, 131.5, 131.0, 129.4, 127.8, 126.4, 126.1, 125.7, 122.7, 122.4, 115.4, 104.4, 49.7 (*C*Me), 23.8 (Me); ν_{max}/cm^{-1} (KBr) 3394, 3049, 2962, 1618, 1541, 1490, 1353; *m*/*z* (EI) 518.2460 (M^+, $C_{36}H_{30}N_4$ requires 518.2470).

1,6-Diaminophenazine (23)

A mixture of 1,6-dinitrophenazine (**22**) (1 g, 3.7 mmol), trifluoroacetic acid (5 ml) and 10% palladium on charcoal (250 mg) stirred under a balloon of hydrogen gas for 2 h. The solution was then basified with concentrated aqueous ammonia. The red suspension was extracted into chloroform, dried ($MgSO_4$) and evaporated to give **23** as a lustrous red solid (528 mg, 68%), mp 242 °C (lit.[4] 245 °C). δ_H (270 MHz, $CDCl_3$) 7.51 (t, 2H, *J* 7.7 Hz, Ar H-3,8), 7.32 (d, 2H, *J* 7.7 Hz, Ar), 6.86 (d, 2H, *J* 7.7 Hz, Ar), 6.29 (s, 4H, NH_2).

1,6-Bis(acetamido)phenazine (24a)

1,6-Diaminophenazine (**23**) (325 mg, 1.54 mmol) was dissolved in a mixture of acetic acid (20 ml) and acetic anhydride (5 ml). The mixture was allowed to stir for 4 h at room temperature. Water (10 ml) was added, and the resultant yellow precipitate was filtered off and dried to give 1,6-bis(acetamido)phenazine (**24a**) (352 mg) as a yellow solid. Evaporation of the filtrate, then flash chromatography (CH_2Cl_2–EtOAc, 85 : 15) gave 20 mg more of the title compound (**24a**) (combined yield 372 mg, 82%), mp

224 °C (sublimes). δ_H (270 MHz, $CDCl_3$,) 9.8 (br s, 2H, NH), 8.87 (d, 2H, *J* 8.8 Hz, Ar), 8.0–7.8 (m, 4H, Ar), 2.46 (s, 6H, CH_3CO); ν_{max}/cm^{-1} (KBr) 3348, 1670, 1535, 1516, 1402, 1288, 1118, 806; *m/z* (FAB) 295.1192 (M + H^+, $C_{16}H_{15}N_4O_2$ requires 295.1195).

1,6-Bis(methoxycarbamido)phenazine (24b)

A mixture of 1,6-diaminophenazine (**23**) (223 mg, 1.02 mmol), dry dichloromethane (50 ml) and dry pyridine (157 µl, 1.94 mmol) was treated with methyl chloroformate (156 µl, 2.02 mmol). The mixture was stirred at room temperature for 1 h, and then the golden yellow precipitate was filtered off to give 1,6-bis(methoxycarbamido)phenazine (**24b**) (254 mg, 76%), mp 210–220 °C (sublimes). δ_H (270 MHz, $CDCl_3$,) 9.23 (br s, 2H, NH), 8.49 (d, 2H, *J* 8.4 Hz, Ar), 7.8–7.9 (4H, m, Ar), 3.92 (6H, s, OCH_3); ν_{max}/cm^{-1} (KBr) 3368, 1747, 1545, 1518, 1429, 1406, 1306, 1227, 1038, 800; *m/z* (FAB) 327.1096 (M + H^+, $C_{16}H_{15}N_4O_4$ requires 327.1093).

(*R*,*R*)-1,6-Bis(α-methoxyphenylacetamido)phenazine (24c)

1,6-Diaminophenazine (**23**) (200 mg, 0.95 mmol) was dissolved in dry dichloromethane (5 ml) and pyridine (162 µl, 2.00 mmol) was added to the solution. (*R*)-α-methoxyphenylacetyl chloride (332 mg, 1.80 mmol), dissolved in dried dichloromethane (2 ml), was then added. After 24 h, the solvent was removed and unreacted 1,6-diaminophenazine was removed by stirring for 30 min with acetic acid (25 ml) and acetic anhydride (10 ml). Water (10 ml) was then added to the system to destroy excess acetic anhydride and after evaporation of the acetic acid, (*R*,*R*)-1,6-bis(α-methoxyphenylacetamido)phenazine (**24c**) was isolated by flash chromatography (CH_2Cl_2) and obtained as a bright yellow solid (267 mg, 59% from the acid chloride), mp 203–205 °C. δ_H (270 MHz, $CDCl_3$) 11.09 (s, 2H, NH), 8.85 (d, 2H, *J* 7, Ar), 8.03 (d, 2H, *J* 7 Hz, Ar), 7.85 (t, 2H, *J* 7 Hz, Ar), 7.3–7.7 (m, 10H, Ph), 4.94 (s, 2H, CH), 3.64 (s, 6H, OCH_3); ν_{max}/cm^{-1} (KBr) 3329, 1686, 1541, 1508, 1406, 1097; *m/z* (FAB) 507.2036 (M + H^+, $C_{30}H_{27}N_4O_4$ requires 507.2032).

1,6-Bis(ethylamino)phenazine (25a)

1,6-Bis(acetamido)phenazine **24a** (210 mg, 0.71 mmol) was refluxed with $LiAlH_4$ (107 mg, 2.82 mmol) in dry THF (20 ml) until the colour of the mixture changed from red to green (2 h). Aqueous 5% NaOH (5 ml) was added and the mixture was filtered through Celite®. The filtrate was washed with distilled water and the THF was evaporated to give 1,6-bis(ethylamino)phenazine (**25a**) (179 mg, 95%) as a red solid, mp 152 °C (sublimes); δ_H (270 MHz, $CDCl_3$) 7.58 (t, 2H, *J* 8.5 Hz, Ar–H), 7.38 (d, 2H, *J* 8.5 Hz, Ar–H), 6.60 (d, 2H, *J* 8.5 Hz, Ar–H), 6.27 (br s, 2H, N–H), 3.34–4.49 (m, 4H, CH_2), 1.54 (t, 6H, *J* 7.3 Hz, CH_3), δ_C (68 MHz, $CDCl_3$,) 145.8 (Ar), 142.1 (Ar), 136.6 (Ar), 131.8 (Ar), 113.6 (Ar), 102.4 (Ar), 38.8 (CH_2), 14.5 (CH_3); ν_{max}/cm^{-1} (KBr) 3384, 2964, 1618, 1543, 1485, 1396, 1342, 1294, 1188, 794; *m/z* (FAB) 266.1543 (M^+, $C_{16}H_{18}N_4$ requires 266.1531).

1,6-Bis(methylamino)phenazine (25b)

1,6-Bis(methoxycarbamido)phenazine (**24b**) (95 mg, 0.291 mmol) was refluxed with $LiAlH_4$ (65.9 mg, 1.74 mmol) in dry THF (20 ml) under nitrogen. After 3 h the mixture, which had become green, was cooled to 0 °C and treated with 5% aqueous NaOH (5 ml). The mixture was filtered through Celite®, then the filtrate was washed with water and the THF evaporated to give 1,6-bis(methylamino)phenazine (**25b**) (65 mg, 94%) as a red solid, mp 169 °C. δ_H (270 MHz, $CDCl_3$) 7.62 (2H, t, *J* 7.5 Hz, Ar), 7.39 (2H, d, *J* 7.5 Hz, Ar), 6.53 (2H, d, *J* 7.5 Hz, Ar), 6.3–6.4 (2H, m, NH), 3.51 (6H, d, *J* 5.2 Hz, Me); ν_{max}/cm^{-1} (KBr) 3418, 2924, 1618, 1553, 1495, 1391, 1354, 799, 741; *m/z* (FAB) 238.1214 (M^+, $C_{14}H_{14}N_4$ requires 238.1218).

(*R*,*R*)-1,6-Bis[(2-methoxy-2-phenyl)ethylamino)]phenazine (25c)

A 1 M solution of borane in THF (5 ml, 5 mmol) was added at room temperature under nitrogen to (*R*,*R*)-1,6-bis(α-methoxyphenylacetamido)phenazine (**24c**) (143 mg, 0.282 mmol); the mixture was then refluxed for 1 h. The unreacted borane was then destroyed by addition of methanol (20 ml), followed by reflux for 30 min. After evaporation of the solvent and purification by flash chromatography (CH_2Cl_2) (*R*,*R*)-1,6-bis[(2-methoxy-2-phenyl)ethylamino)]phenazine (**25c**) (109 mg, 81%) was obtained as a red solid, mp 153–155 °C. δ_H (270 MHz, $CDCl_3$) 7.69 (dd, 2H, *J* 8.7, 7.4 Hz, Ar), 7.6–7.4 (m, 12H, Ar and Ph), 6.89 (br t, 2H, *J* 6 Hz, NH), 6.72 (d, 2H, *J* 7.4 Hz, Ar), 4.71 (dd, 2H, *J* 7.5, 5.0 Hz, CH), 3.8–3.6 (m, 4H, CH_2), 3.47 (s, 6H, OCH_3); δ_C (68 MHz, $CDCl_3$,) 144.6 (Ar), 141.8 (Ar), 140.1 (Ar), 135.6 (Ar), 131.3 (Ar), 128.9 (Ar), 128.4 (Ar), 127.0 (Ar), 115.7 (Ar), 102.9 (Ar), 82.3 (CH), 57.3 (CH_3O), 50.5 (CH_2N); ν_{max}/cm^{-1} (KBr) 3412, 2924, 2853, 1618, 1541, 1458, 1111; *m/z* (FAB) 479.2462 (M + H^+, $C_{30}H_{31}N_4O_2$ requires 479.2447).

1,6-Bis(*N*-ethylacetamido)phenazine (26a)

A mixture of 1,6-bis(ethylamino)phenazine (**25a**) (179 mg, 0.67 mmol), acetic acid (10 ml) and acetic anhydride (2 ml) was refluxed for 24 h, then water (10 ml) was added. After evaporation of the solvent and flash chromatography (EtOAc–petrol, 3 : 1), 1,6-bis(*N*-ethylacetamido)phenazine (**26a**) (149 mg, 63%) was obtained as a yellow solid, mp 199 °C (decomp); δ_H (270 MHz, $CDCl_3$) 8.33 (d, 2H, *J* 8.8 Hz, Ar), 7.92 (dd, 2H, *J* 8.7, 7.2 Hz, Ar), 7.78 (d, 2H, *J* 7.2 Hz, Ar), 4.4–4.2 (br m, 2H, NCH_2), 3.9–3.6 (br m, 2H, NCH_2), 1.9–1.7 (br m, 6H, CH_3), 1.4–1.1 (br m, 6H, CH_3); δ_C (68 MHz, $CDCl_3$) 171.1 (CO), 144.2 (Ar), 140.7 (Ar), 140.4 (Ar), 131.0 (Ar), 130.8 (Ar), 130.5 (Ar), 44.4 (Ac), 23.0 (CH_2), 13.6 (CH_3); ν_{max}/cm^{-1} (KBr) 2928, 1659, 1624, 1531, 1485, 1393, 1288, 1130, 1061; *m/z* (FAB) 351.1814 (M + H^+, $C_{20}H_{23}N_4O_2$ requires 351.1821).

2,13-Diethyl-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane-3,12-dione (27a)

Sebacoyl chloride (202 µl, 0.95 mmol) in dry dichloromethane (80 ml) was added dropwise at room temperature over 24 h to a stirred mixture of 1,6-bis(ethylamino)phenazine (**25a**) (253 mg, 0.95 mmol), dry dichloromethane (80 ml) and pyridine (144 µl, 1.78 mmol). Evaporation of the solvent and flash chromatography (CH_2Cl_2–EtOAc, 4 : 1) gave 2,13-diethyl-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane-3,12-dione (**27a**) (293 mg, 71%) as a yellow solid, mp 159 °C. δ_H (270 MHz, $CDCl_3$) 8.30 (d, 2H, *J* 9 Hz), 7.92 (dd, 2H, *J* 9, 7 Hz), 7.77 (d, 2H, *J* 7 Hz), 4.37 (dq, 2H, *J* 14, 7 Hz, NC*H*HCH$_3$), 3.91 (dq, 2H, *J* 14, 7 Hz, NCH*H*CH$_3$), 1.8–0.6 (m, 22 H, 8 × CH_2 + 2 × CH_3); δ_C (68 MHz, $CDCl_3$) 174.2 (CO), 143.7 (Ar), 141.0 (Ar), 140.2 (Ar), 130.5 (Ar), 130.44 (Ar), 130.37 (Ar), 43.8 (CH_2), 33.6 (CH_2), 27.8 (CH_2), 26.4 (CH_2), 24.8 (CH_2), 13.6 (CH_3); ν_{max}/cm^{-1} (KBr) 2931, 1670, 1647, 1625, 1527, 1327, 1308, 1265, 1076, 884; *m/z* (FAB) 433.2592 (M + H^+, $C_{26}H_{33}N_4O_2$ requires 433.2604; HPLC, t_r/min (methanol, column OT(+), detector 255 nm, flow 0.5 ml min^{-1}) 14.2 (50%), 16.0 (50%).

2,13-Dimethyl-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane-3,12-dione (27b)

Sebacoyl chloride (55 µl, 0.257 mmol) in dry dichloromethane (100 ml) was added dropwise at room temperature over 24 h to a stirred mixture of 1,6-bis(methylamino)phenazine (**25b**) (61.2 mg, 0.257 mmol), dichloromethane (100 ml) and pyridine (42 µl, 0.52 mmol). Evaporation of the solvent and flash chromatography (CH_2Cl_2–EtOAc, 1 : 1) gave 2,13-dimethyl-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane-3,12-dione (**27b**)

(78 mg, 75%) as a yellow solid, mp 222–223 °C. δ_H (270 MHz, $CDCl_3$) 8.30 (d, 2H, *J* 9 Hz), 7.92 (dd, 2H, *J* 9, 8 Hz), 7.82 (d, 2H, *J* 8 Hz), 3.62 (s, 6H, Me), 1.9–0.5 (m, 16 H, 8 × CH_2); δ_C (68 MHz, $CDCl_3$) 174.9 (CO), 143.8 (Ar), 142.1 (Ar), 140.8 (Ar), 130.8 (Ar), 130.6 (Ar), 129.7 (Ar), 37.6, 33.1, 27.9, 26.7, 25.0; ν_{max}/cm^{-1} (KBr) 2928, 1661, 1641, 1529, 1483, 1448, 1412, 1379; *m/z* (FAB) 405.2272 (M + H^+, $C_{24}H_{29}N_4O_2$ requires 405.2291).

(*R*,*R*)-2,13-Bis[(2-methoxy-2-phenyl)ethyl]-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane-3,12-diones (27c and 27c′)

A solution of sebacoyl chloride (54 μl, 0.253 mmol) in dichloromethane (15 ml) was added dropwise at room temperature over 12 h to a stirred mixture of (*R*,*R*)-1,6-bis[(2-methoxy-2-phenyl)ethylamino)]phenazine (**25c**) (120 mg, 0.251 mmol), dichloromethane (10 ml), and pyridine (40 μl, 0.508 mmol). Evaporation of the solvent and separation by flash chromatography (40% ethyl acetate in petroleum ether) gave first **27c** (69 mg, 43%) and then **27c′** (18 mg, 11%), both as yellow solids.

The major product **27c** had the following properties. mp 74–76 °C, $[\alpha]_D^{27}$ +127 (*c* 0.5, CH_2Cl_2). δ_H (270 MHz, $CDCl_3$) 8.19 (dd, 2H, *J* 8.8, 1.2 Hz, Ar), 8.04 (dd, 2H, *J* 7.0, 1.2 Hz, Ar), 7.91 (dd, 2H, *J* 8.8, 7.0 Hz, Ar H-3,8), 7.45–7.25 (m, 10H, m, Ph), 4.93 (dd, 2H, *J* 9.8, 2.4 Hz, OCH), 4.73 (dd, 2H, *J* 14.0, 2.4 Hz, NCH_2), 3.52 (dd, 2H, *J* 14.3, 9.8 Hz, NCH_2), 3.35 (s, 6H, OCH_3), 1.9–1.7 (m, 4H, chain), 1.5–1.3 (m, 2H, chain), 1.2–1.0 (m, 2H, chain), 0.85–0.55 (m, 4H, chain), 0.1–0.0 (m, 2H, chain), −0.6–(−0.8) (m, 2H, chain), δ_C (68 MHz, $CDCl_3$) 175.3 (CO), 143.7 (Ar), 141.9 (Ar), 140.0 (Ar), 131.2 (Ar), 130.9 (Ar), 130.4 (Ar), 128.7 (Ar), 128.0 (Ar), 126.9 (Ar), 112.5 (Ar), 82.9 (CH), 57.7, 57.3, 33.4, 27.9, 27.1, 24.9; ν_{max}/cm^{-1} (KBr) 2924, 1660, 1529, 1107, 750; *m/z* (FAB) 667.3245 (M + Na^+, $C_{40}H_{44}N_4O_4Na$ requires 667.3260).

The minor product, **27c′** had δ_H (270 MHz, $CDCl_3$) 8.22 (dd, 2H, *J* 9, 1 Hz, Ar), 7.75 (dd, 2H, *J* 9,7 Hz, Ar), 7.33–7.45 (10H, m, Ph), 6.11 (dd, 2H, *J* 7, 1 Hz, Ar), 4.80 (dd, 2H, *J* 8.5, 6 Hz, PhCH), 4.57 (dd, 2H, *J* 14, 8 Hz, NCH_2), 3.94 (dd, 2H, *J* 14, 5 Hz, CH_2), 3.04 (s, 6H, OMe), 1.9–1.7 (m, 4H), 1.5–0.5 (m, 10H), 0.1–(−0.1) (m, 2H), −0.6–(−0.8) (m, 2H).

1,6-Bis(diethylamino)phenazine (28a)

Borane solution (1 M in THF; 5 ml, 5 mmol) was added under nitrogen to 1,6-bis(*N*-ethylacetamido)phenazine (**26a**) (149 mg, 0.425 mmol). The mixture was refluxed for 2 h, then methanol (10 ml) was added and the mixture was refluxed for a further 5 min. Evaporation of the solvent followed by flash chromatography (CH_2Cl_2–EtOAc, 9 : 1) gave 1,6-bis(diethylamino)phenazine (**28a**) (113 mg, 82%) as a red solid, mp 55–56 °C. δ_H (270 MHz, $CDCl_3$) 7.76 (dd, 2H, *J* 8.7, 1.2 Hz, Ar), 7.61 (dd, 2H, *J* 8.7, 7.7 Hz, Ar), 7.01 (dd, 2H, *J* 7.7, 1.2 Hz, Ar), 3.67 (q, 8H, *J* 7.1 Hz, CH_2), 1.25 (t, 12H, *J* 7.1 Hz, CH_3); δ_C (68 MHz, $CDCl_3$) 147.2 (Ar), 142.5 (Ar), 138.8 (Ar), 129.7 (Ar), 121.6 (Ar), 115.3 (Ar), 47.2 (CH_2), 12.4 (CH_3); ν_{max}/cm^{-1} (KBr) 2970, 2928, 1607, 1530, 1484, 1265, 1209, 1094, 801; *m/z* (FAB) 323.2250 (M + H^+, $C_{20}H_{27}N_4$ requires 323.2236).

2,13-Diethyl-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane (29a)

Borane solution (1 M in THF; 10 ml, 10 mmol) was added to 2,13-diethyl-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane-3,12-dione (**27a**) (184 mg, 0.425 mmol) under nitrogen. The mixture was refluxed for 5 h, then methanol (20 ml) was added and the mixture was refluxed for a further 15 min. Evaporation of the solvent followed by flash chromatography ($CHCl_3$) gave 2,13-diethyl-2,13-diaza-1(1,6)-(phenazina)cyclotridecaphane (**29a**) (103 mg, 60%) as a red solid, mp 123–125 °C, δ_H (400 MHz, $CDCl_3$, assignments supported by COSY) 7.82 (d, 2H, *J* 8.5 Hz, Ar H-4,9), 7.63 (dd, 2H, *J* 8.5, 7.5 Hz, Ar H-3,8), 7.01 (d, 2H, *J* 7.6 Hz, Ar H-2,7), 4.92–4.84 (m, 2H, $NCH\mathit{H}CH_2$), 3.57 (dq, 2H, *J* 14, 7 Hz, $NCH\mathit{H}CH_3$), 3.31 (m, 4H, $NC\mathit{H}HCH_2$ and $NC\mathit{H}HCH_3$), 1.43 (t, 6H, *J* 7.0 Hz, CH_3), 1.37–1.12 (m, 4H, $NCH_2C\mathit{H}_2$), 0.99–0.76 (m, 4H, $NCH_2CH_2C\mathit{H}_2$), 0.58–0.48 (m, 2H, $NCH_2CH_2CH_2C\mathit{H}$), 0.48–0.39 (m, 2H, $NCH_2CH_2CH_2CH_2C\mathit{H}$), 0.27–0.16 (m, 2H, $NCH_2CH_2CH_2C\mathit{H}$), −0.24–(−0.35) (m, 2H, $NCH_2CH_2CH_2$-$CH_2C\mathit{H}$); δ_C (101 MHz, $CDCl_3$, assignments supported by DEPT and ^1H–^{13}C correlation) 147.2 (Ar quaternary), 141.4 (Ar quaternary), 137.3 (Ar quaternary), 129.7 (Ar CH), 121.2 (Ar CH), 115.9 (Ar CH), 51.0 ($CH_2\mathit{C}H_2N$), 45.3 ($CH_3\mathit{C}H_2N$), 28.6 ($NCH_2CH_2CH_2CH_2\mathit{C}$), 26.8 ($NCH_2CH_2CH_2\mathit{C}$), 25.3 ($NCH_2CH_2\mathit{C}H_2$), 23.3 ($NCH_2\mathit{C}H_2$), 12.8 ($\mathit{C}H_3CH_2$); ν_{max}/cm^{-1} (KBr) 2924, 2851, 1528, 1477, 1458, 1321, 1267, 1101, 800, 739; *m/z* (FAB) 404.2925 (M^+, $C_{26}H_{36}N_4$ requires 404.2940); HPLC, t_R/min [Daicel Chiralpak OT (+), hexane–propan-2-ol (9 : 1), 1.0 ml min^{-1}, detector 297 nm, T = 12 °C] 5.9 and 6.5.

(*R*,*pS*)-(−)-/(*R*,*pR*)-(+)-2,5,8,11,14-Pentaoxa-1(1,6)-[5-(α-methoxyphenylacetyl)-5,10-dihydrophenazina]-cyclotetradecaphanes (31a and 31b)

rac-2,5,8,11,14-Pentaoxa-1(1,6)-(phenazina)cyclotetradecaphane (**14**) (124 mg, 0.336 mmol) and 10% Pd/C (240 mg) were stirred in dry, oxygen-free CH_2Cl_2 (2 ml) under a hydrogen balloon at room temperature until the yellow solution had become colourless (30 min). Then the mixture was filtered through celite under nitrogen and the celite was rinsed with CH_2Cl_2 (4 ml). The solvent was evaporated under vacuum and CH_2Cl_2 (1 ml) was added to the residue under nitrogen. (*R*)-α-Methoxyphenylacetyl chloride (155 mg, 0.84 mmol) and anhydrous pyridine (68 μl, 0.84 mmol) were added and the mixture was heated overnight at 40 °C. The solvent was evaporated and the crude mixture was purified by flash chromatography on silica which had previously been washed with 10% Et_3N in hexane. Elution with $CHCl_3$–Et_2O (9 : 1) gave (*R*,*pS*)-(−)-2,5,8,11,14-pentaoxa-1(1,6)-[5-(α-methoxyphenylacetyl)-5,10-dihydrophenazina]cyclotetradecaphane (**31a**) (42 mg, 24%) and (*R*,*pR*)-(+)-2,5,8,11,14-pentaoxa-1(1,6)-[5-(α-methoxyphenylacetyl)-5,10-dihydrophenazina]cyclotetradecaphane (**31b**) (51 mg; contaminated with 10 mol% of **14** as judged by ^1H NMR) as pale yellow solids. Recrystallisation from heptane gave spectroscopically pure **31b** (14 mg, 8%).

The (*R*,*pS*)-(−)-diastereoisomer **31a** had the following properties. R_f 0.04 ($CHCl_3$–Et_2O, 9 : 1), mp >230 °C, $[\alpha]_D^{20}$ −114 (*c* 1, CH_2Cl_2); δ_H (400 MHz, $CDCl_3$) 7.5–6.2 (m, 12H, Ar + NH), 5.29 (br s, 1H, MeOC*H*), 4.5–4.2 (m, 4H, $ArOC\mathit{H}_2$), 3.7–2.5 (m, 15H); δ_C (101 MHz, $CDCl_3$, assignment by DEPT) 171.1 (br, C=O), 153.6 (Ar C quat), 146.7 (Ar C quat), 146.2 (Ar C quat), 144.1 (Ar C quat), 143.4 (Ar C quat), 136.2 (Ar C quat), 131.8 (Ar C quat), 128.4 (Ar CH), 128.0 (Ar), 127.9 (Ar), 127.7 (Ar), 127.4 (Ar), 127.1 (Ar CH), 120.0 (Ar CH), 119.3 (Ar CH), 114.6 (Ar CH), 112.3 (Ar CH), 108.5 (Ar CH), 80.3 (OCH), 72.7 (CH_2), 72.65 (CH_2), 71.8 (CH_2), 71.2 (CH_2), 70.8 (CH_2), 70.7 (CH_2), 70.1 (CH_2), 57.1 (CH_3); ν_{max}/cm^{-1} (film) 3400 (br, N–H), 1679 (C=O); *m/z* (ESI) 521.2287 (M + H^+, $C_{29}H_{33}N_2O_7$ requires 521.2282).

The (*R*,*pR*)-(+)-diastereoisomer **31b** had the following properties. R_f 0.14 ($CHCl_3$–Et_2O, 9 : 1), mp 182–184 °C (heptane), $[\alpha]_D^{26}$ +42 (*c* 0.25, CH_2Cl_2). δ_H (400 MHz, $CDCl_3$) 7.39 (m, 1H, Ar), 7.2–7.0 (m, 4H, Ar), 6.9–6.7 (m, 5H, Ar), 6.31 (m, 2H, Ar and NH), 5.28 (s, 1H, MeOC*H*), 4.5–4.2 (m, 4H, $ArOC\mathit{H}_2$), 3.8–3.5 (m, 4H, $ArOCH_2C\mathit{H}_2$), 3.47 (s, 3H, $C\mathit{H}_3O$), 3.2–2.5 (m, 8H, $ArOCH_2CH_2OC\mathit{H}_2C\mathit{H}_2O$); δ_C (101 MHz, $CDCl_3$, assignment by DEPT) 171.1 (C=O), 153.6 (Ar C quat), 146.2 (Ar C quat), 144.1 (Ar C quat), 136.2 (Ar C quat), 131.9 (Ar C quat), 128.1 (Ar), 127.9 (Ar), 127.8 (Ar), 127.5 (Ar), 127.3 (Ar), 120.0 (Ar CH), 119.6 (Ar CH), 117.7 (Ar CH), 114.4 (Ar CH), 112.6 (Ar

CH), 108.7 (Ar CH), 81.5 (OCH), 72.6 (CH_2), 71.8 (CH_2), 71.6 (CH_2), 71.5 (CH_2), 71.1 (CH_2), 70.7 (CH_2), 70.14 (CH_2), 70.08 (CH_2), 57.1 (CH_3); ν_{max}/cm^{-1} (film) 3435 (br, N–H), 1679 (C=O); *m*/*z* (ESI) 521.2287 (M + H$^+$, $C_{29}H_{33}N_2O_7$ requires 521.2282).

(*pS*)-(−)-2,5,8,11,14-Pentaoxa-1(1,6)-(phenazina)cyclotetradecaphane (*pS*-14)

(*R*,*pS*)-(−)-2,5,8,11,14-Pentaoxa-1(1,6)-[5-(α-methoxyphenylacetyl)-5,10-dihydrophenazina]cyclotetradecaphane **31a** (91 mg, 0.245 mmol) was refluxed in a mixture of EtOH (5 ml) and 0.1 M hydrochloric acid (10 ml) for 3 d. Water was added and the solution was extracted twice with dichloromethane. The organic phase was washed with saturated aqueous $NaHCO_3$ and with brine. Then it was dried ($MgSO_4$) and the solvent was evaporated at reduced pressure. The crude mixture was purified by flash chromatography (chloroform) then recrystallisation from EtOH to yield the title compound (*pS*)-**14** (20 mg, 31%) as yellow crystals, mp 170–174 °C, $[\alpha]_D^{28}$ −325 (*c* 0.4, CH_2Cl_2). The ^{1}H NMR spectrum of (*pR*)-**14** was identical to that of *rac*-**14** described above. HPLC t_R/min [Chiralpak OT(+), MeOH, 0.1 ml min^{-1}, λ 271 nm, 0 °C] 63.1.

(*pR*)-(+)-2,5,8,11,14-Pentaoxa-1(1,6)-(phenazina)cyclotetradecaphane (*pR*)-14

(*R*,*pR*)-(+)-2,5,8,11,14-Pentaoxa-1(1,6)-[5-(α-methoxyphenylacetyl)-5,10-dihydrophenazina]cyclotetradecaphane **31b** (128 mg, 0.345 mmol) was refluxed in a mixture of EtOH (5 ml) and 0.3 M hydrochloric acid (10 ml) for 7 d. Product isolation as for (*pS*)-**14** above, but with three recrystallisations from ethanol yielded (*pR*)-**14** (31 mg, 34%) as yellow crystals, mp 170–173 °C, $[\alpha]_D^{28}$ +346 (*c* 0.4, CH_2Cl_2). The ^{1}H NMR spectrum of (*pR*)-**14** (400 MHz, $CDCl_3$) was identical to that of *rac*-**14** described above; HPLC t_R/min [Chiralpak OT(+), MeOH, 0.1 ml min^{-1}, λ 271 nm, 0 °C] 66.8.

Crystallography

Crystal data for (−)-(*pS*)-**14**, **18a**, **18b** and **31b** were reported in our preliminary communication.[3]

Crystal data for *rac*-**12a**.‡ $C_{22}H_{26}N_2O_2$, M = 350.45, Monoclinic, a = 21.854(12), b = 10.992(5), c = 7.770(10) Å, α = 90.00, β = 90.01(7), γ = 90.00°, V = 1867(3) Å^3, space group $P2_1/a$, Z = 4, D_c = 1.247 Mg m^{-3}, μ = 0.080 mm^{-1}, reflections measured 3265, reflections unique 3298 with R_{int} = 0.0227, T = 160(2) K, final R indices [$I > 2\sigma(I)$] $R1$ = 0.0660, $wR2$ = 0.1564 and for all data $R1$ = 0.1357, $wR2$ = 0.1887. CCDC reference number 269351.

Crystal data for *rac*-**14**.‡ $C_{20}H_{22}N_2O_5$, M = 370.40, Monoclinic, a = 14.5548(2), b = 7.2083 (1), c = 17.2662(4) Å, α = 90.00, β = 103.938(1), γ = 90.00°, V = 1758.15(5) Å^3, space group $P2_1/c$, Z = 4, D_c = 1.399 Mg m^{-3}, μ = 0.101 mm^{-1}, reflections measured 23675, reflections unique 4011 with Rint = 0.0573, T = 120(2) K, final R indices [$I > 2\sigma(I)$] $R1$ = 0.0432, w$R2$ = 0.1058 and for all data $R1$ = 0.0670, $wR2$ = 0.1167. CCDC reference number 266538.

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References

1 J. H. P. Utley and M. F. Nielsen, in *Organic Electrochemistry—Electrogenerated Bases*, ed H. Lund and O. Hammerich, Marcel Dekker Inc., New York, 2001, ch. 30.
2 A.-P. Bettencourt, A. M. Freitas, M. I. Montenegro, M. F. Nielsen and J. H. P. Utley, *J. Chem. Soc., Perkin Trans. 2*, 1998, 515–522.
3 A. Mateo-Alonso, R. Horcajada, H. J. Groombridge, R. Mandalia, M. Motevalli, J. H. P. Utley and P. B. Wyatt, *Chem. Commun.*, 2004, 412–413.
4 E. Breitmaier and U. Hollstein, *J. Org. Chem.*, 1976, **41**, 2104–2108.
5 M. H. Chang, B. B. Masek and D. A. Dougherty, *J. Am. Chem. Soc.*, 1985, **107**, 1124–1133.
6 I. J. Pacher and M. C. Kloetzel, *J. Am. Chem. Soc.*, 1951, **73**, 4958–4961.
7 P. Huszthy, E. Samu, B. Vermes, G. Mezey-Vandor, M. Nógrádi, J. S. Bradshaw and R. M. Izatt, *Tetrahedron*, 1999, **58**, 1491–1504.
8 G. F. Cooper, *Synthesis*, 1991, 859–860.
9 D. Marquis, J.-P. Desvergne and H. Bouas-Laurent, *J. Org. Chem.*, 1995, **60**, 7984–7996.
10 R. C. Hayward, C. H. Overton and G. H. Whitham, *J. Chem. Soc., Perkin Trans. 1*, 1976, 2413–2415.
11 E. N. Jacobsen, F. Kakiuchi, R. G. Konsler, J. F. Larrow and M. Tokunaga, *Tetrahedron Lett.*, 1997, **38**, 773–776.
12 A. Mateo-Alonso, R. Horcajada, M. Motevalli, J. H. P. Utley and P. B. Wyatt, *Org. Biomol. Chem.*, 2005, **3**, DOI: 10.1039/b506309d.