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SYNTHESIS OF FUSED TRICYCLIC HETEROCYCLES BY CONDENSATION, CYCLIZATION, DIPOLAR CYCLOADDITION CASCADE OF α-BENZENESULFONYL AND α-PHENYLTHIO SUBSTITUTED ALDEHYDES

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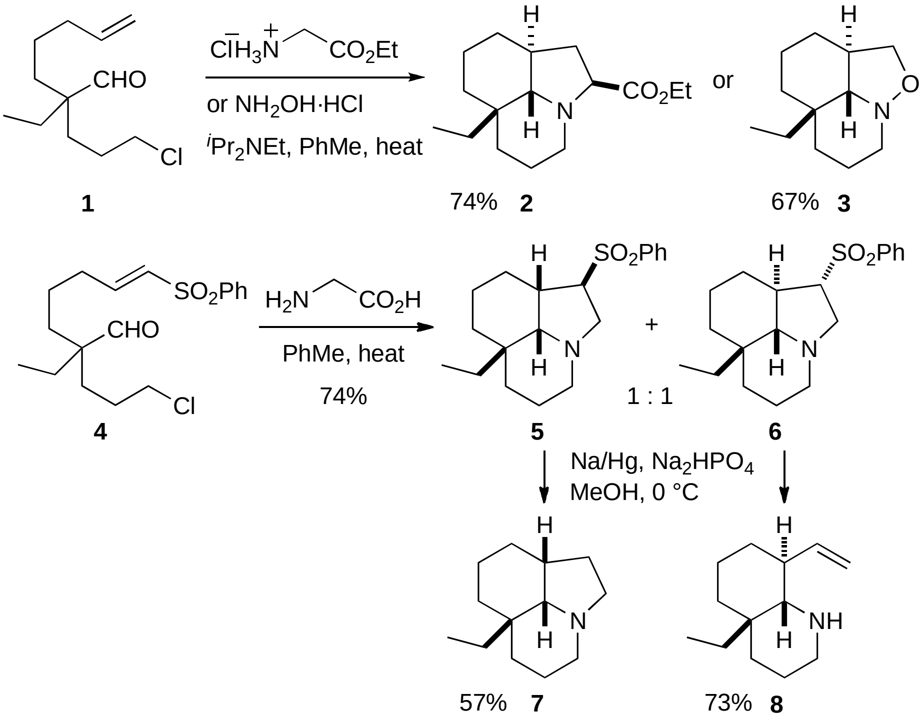
Dedicated to Professor Al Padwa on the occasion of his 75th birthday

Abstract – Heating α-benzenesulfonyl- or α-phenylthio-aldehydes that contain a tethered alkyl chloride and alkene originating from the α- position of the aldehyde with hydroxylamine sets up a cascade (tandem) reaction sequence involving condensation to an intermediate oxime, then cyclization to an intermediate nitrone, then intramolecular dipolar cycloaddition. The fused tricyclic products are formed with complete stereochemical control and were converted in two steps either to the natural product (±)-myrioxazine A or to a 1,3-oxazine that is present in some yuzurimine type *Daphniphyllum* alkaloids.

INTRODUCTION

Many natural products, particularly alkaloids, consist of polycyclic ring systems containing one nitrogen atom. A wide variety of approaches have been reported to such compounds and, in the interests of efficiency, cascade processes involving more than one ring formation in a single pot are desirable.[1] Methodology that uses the combination of a cyclization then an in situ intramolecular cycloaddition can provide a way to access three rings in one reaction sequence.[2–8] This chemistry provides, very rapidly, a high degree of molecular complexity often with high levels of stereocontrol and has found application for the preparation of several natural products. Of note are the impressive examples of the group of Padwa describing the synthesis of some indole alkaloids using a cascade involving cyclization of a metallocarbene (derived from a diazocarbonyl compound) with a tethered carbonyl of a carboxylic amide or lactam, followed by intramolecular dipolar cycloaddition of the resulting carbonyl ylide.[8]

Our work in this area stemmed from an interest in intramolecular dipolar cycloaddition reactions of azomethine ylides (for the synthesis of alkaloids containing a pyrrolidine ring).[9–16] We were interested in reports by Pearson and co-workers,[17,18] who showed that an imine could undergo cyclization onto a tethered alkyl halide to give an iminium ion which, after destannylation, provided an azomethine ylide that was amenable to dipolar cycloaddition with an activated dipolarophile. As a result, we prepared the aldehyde **1** that contains a tethered alkyl chloride (for initial cyclization of the intermediate imine) and a tethered (unactivated) dipolarophile. We were pleased to find that treatment of the aldehyde **1** with glycine ethyl ester or hydroxylamine resulted in the formation of the tricyclic products **2** or **3** respectively (Scheme 1).[19,20] In each case a single stereoisomer was formed and the stereochemistry was verified by single crystal X-ray analysis of derivatives of **2** and **3**. Formation of the intermediate azomethine ylide by decarboxylation using glycine followed by cycloaddition was possible using the activated substrate **4** and gave a mixture of diastereoisomers **5** and **6** (Scheme 1). Removal of the phenylsulfonyl group with sodium amalgam led to different outcomes, with the sulfone **5** providing the product **7**, and the sulfone **6** giving the elimination product **8**.[19]

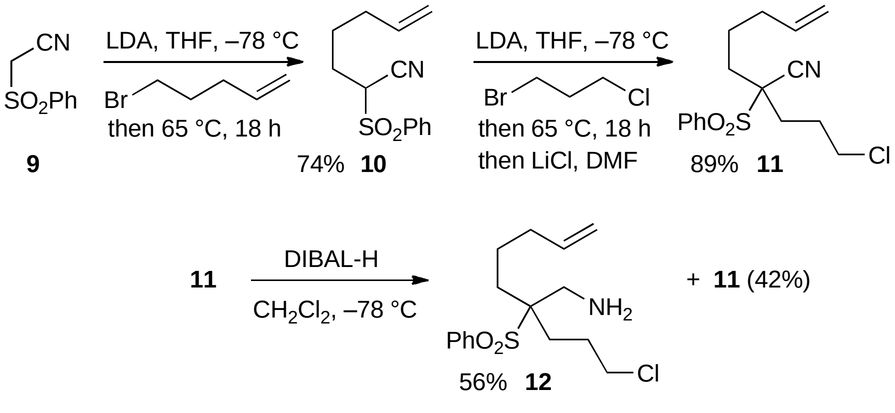


Scheme 1. Related syntheses of the fused tricyclic products

The successful demonstration of the cascade cyclization–cycloaddition chemistry with simple chloroaldehydes led to its subsequent application to a synthesis of some aspidosperma alkaloids and to the core of the stenine alkaloids.[19–21] In all these cases an ethyl substituent was located alpha to the aldehyde and this avoids any complications due to potential enolization or enamine formation. Indeed, the cascade chemistry was more difficult using an aldehyde with an α C–H.[22] Therefore, as a possible method to prepare tricyclic products that contain a hydrogen atom at all three ring junction carbon atoms, we decided to explore the use of aldehydes containing a phenylthio or benzenesulfonyl substituent at the alpha position that could potentially be removed after the cycloaddition reaction. Here we report the investigation of this chemistry and its application in synthesis.

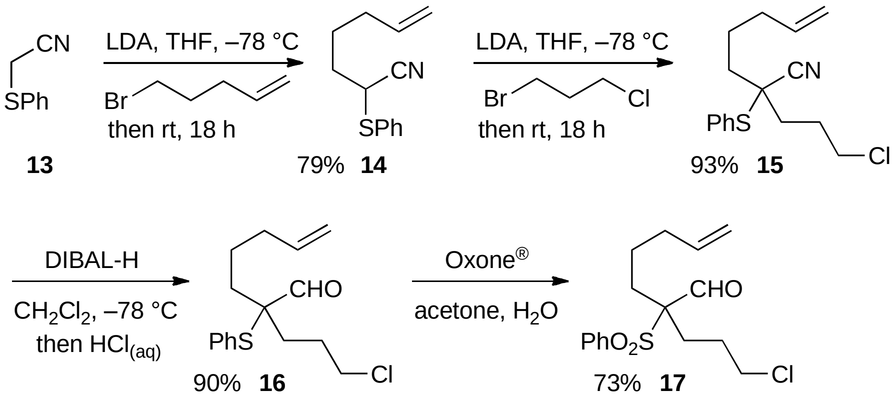
RESULTS AND DISCUSSION

Commercially available (phenylsulfonyl)acetonitrile **9** was treated with lithium diisopropylamide (LDA) and 5-bromopentene to give the nitrile **10** [which could be separated from a small amount (11%) of the dialkylated product by column chromatography] (Scheme 2). The mixture was heated to promote complete reaction in this step and in the subsequent alkylation to give the nitrile **11**. In this second step, in addition to the chloride **11**, some of the corresponding bromide product was obtained, due to the presence of bromide ions in solution; so the mixture was heated with lithium chloride to give solely the chloride **11**. We had anticipated that reduction of the nitrile with diisobutylaluminium hydride (DIBAL-H) would provide, after aqueous work-up, the desired aldehyde. However, we were disappointed to find that treatment with DIBAL-H in CH_2Cl_2, THF or toluene led to recovery of nitrile **11** together with over-reduction to amine **12**. None of the desired aldehyde was obtained.



Scheme 2. Initial attempt to prepare the desired substrate

We therefore turned to the alkylation of (phenylthio)acetonitrile **13** with 5-bromopentene, which gave the desired nitrile **14** (together with some dialkylated product) (Scheme 3). This step, and the second alkylation, with 1-bromo-3-chloropropane, took place at room temperature and the chloride **15** was isolated without contamination with the corresponding bromide. Reduction of nitrile **15** with DIBAL-H gave aldehyde **16** in excellent yield. Oxidation of the sulfide **16** using *m*CPBA was slow and attempted isolation of the sulfoxide intermediate resulted in decomposition. A better method was the use of Oxone® in acetone–water (0 °C to room temp., 5 h), which produced the aldehyde **17** in good yield.

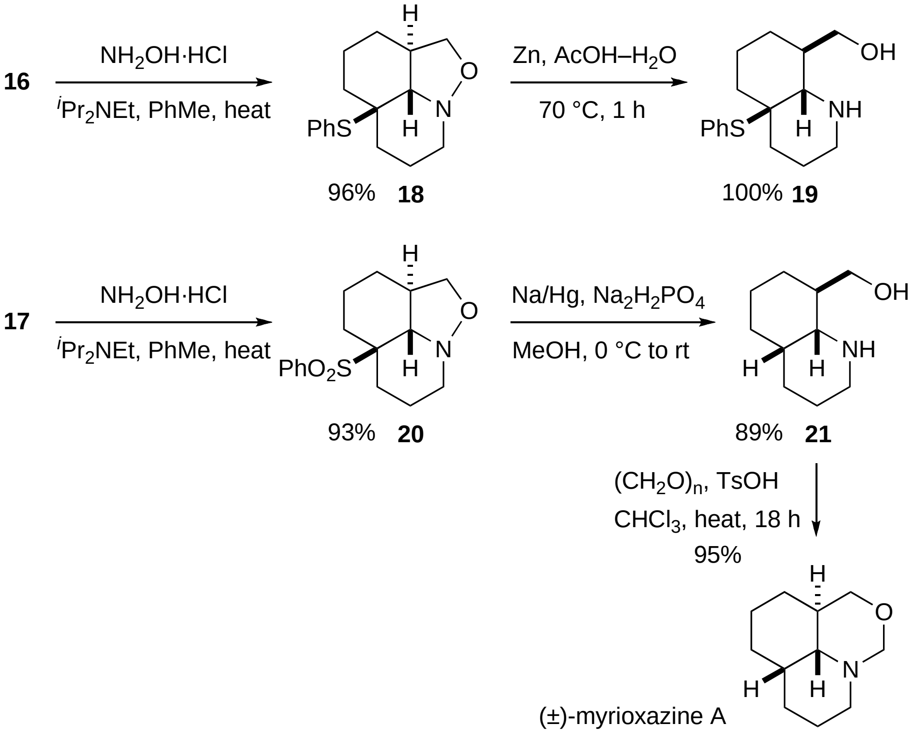


Scheme 3. Preparation of the aldehyde substrates

With the aldehydes **16** and **17** in hand, we attempted the cascade condensation, cyclization, cycloaddition chemistry. We were disappointed to find that heating either of these aldehydes with glycine or glycine ethyl ester in toluene (our standard conditions)[20] resulted only in decomposition or by-products (crude ^{1}H NMR spectroscopy showed a mixture of products and suggested that the alkene was still present). Therefore these substrates appear to be unsuitable for our cascade chemistry with cycloaddition using an intermediate azomethine ylide.

However, we were pleased to find that treatment of either aldehyde **16** or **17** with hydroxylamine resulted in successful reaction (Scheme 4). Remarkably, very high yields of a single stereoisomer were obtained using either aldehyde. The stereochemistry of cycloadduct **20** was confirmed by single crystal X-ray analysis (Figure 1). The stereochemistry of cycloadduct **18** is depicted as being in accord with that of **20** and that of the related product **3** (Scheme 1). In addition, the large coupling constant (J = 11.5 Hz) in the ^{1}H NMR spectrum across the ring junction protons is in agreement with the *trans* arrangement of these atoms.[20]

Treatment of cycloadduct **18** with Raney nickel led predominantly to decomposition, but reduction using zinc and acetic acid gave the product **19** in quantitative yield. The cycloadduct **20** was treated with sodium amalgam and this resulted (predominantly) in reduction of both the N–O and C–S bonds, with retention of configuration, to give the amino-alcohol **21** in high yield. This compound was heated with paraformaldehyde, as previously reported,[22,23] to give the natural product (±)–myrioxazine A. This route to the amino-alcohol **21** also completes a formal synthesis of myrionidine and schoberine, alkaloids with antimalarial activity.[24]



Scheme 4. Cascade chemistry and application to a synthesis of myrioxazine A

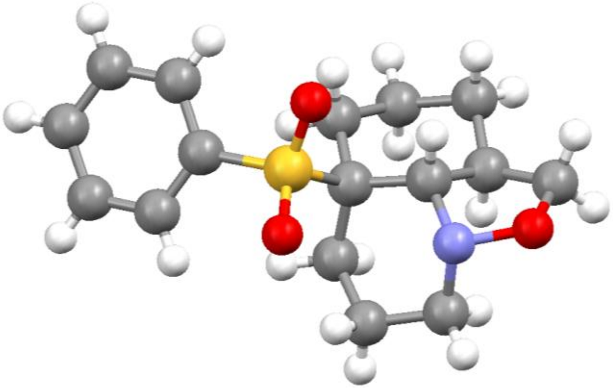
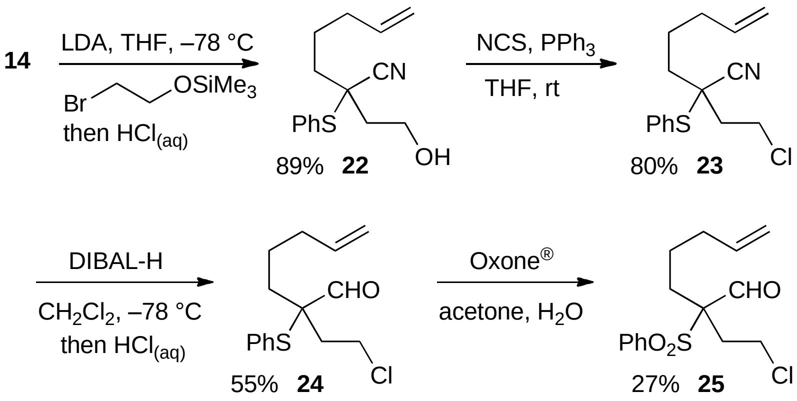


Figure 1. X-Ray crystal structure of cycloadduct **20**

The cascade chemistry using the substrates **16** and **17** involves a cyclization step to set up a piperidine ring, followed by an intramolecular cycloaddition that provides another six-membered ring together with a five-membered ring. To test the chemistry with a related substrate, we chose the aldehyde **24** that would lead, in the cyclization step, to a five-membered rather than six-membered ring. This was prepared by alkylation of the nitrile **14** to give the alcohol **22** followed by chlorination to give **23** and DIBAL-H reduction (Scheme 5). In the same way as the formation of the sulfone **17**, oxidation of the sulfide **24** gave the sulfone **25**. The low yield in this step was due to side reactions (possible elimination of the sulfone or intermediate sulfoxide).

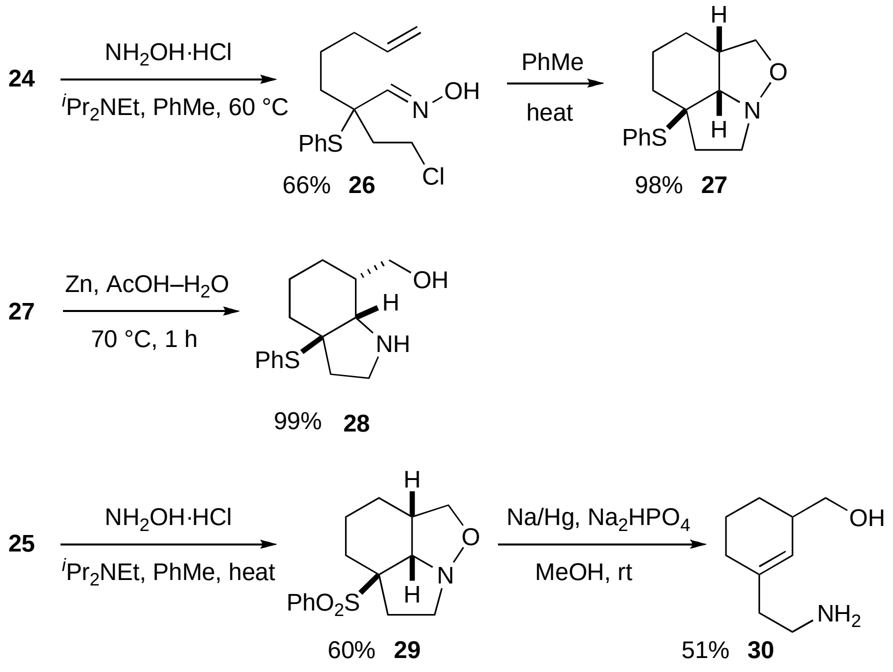


Scheme 5. Preparation of the homologous aldehyde substrates

Heating the aldehyde **24** with hydroxylamine at 60 °C gave the oxime **26** (Scheme 6). Using higher temperatures (heating under reflux in PhMe) resulted only in a lower yield of this oxime, rather than in situ tricycle formation. However, heating the isolated oxime alone in PhMe gave the desired tricyclic product **27** in excellent yield as a single stereoisomer. The all-*cis* stereochemistry was confirmed by single crystal X-ray structure analysis (Figure 2) of the amino-alcohol **28**, formed after treatment of the product **27** with zinc and acetic acid. This *cis* stereochemistry is in line with related cyclization–intramolecular cycloaddition reactions leading to the same ring sizes.[20] Treatment of the isoxazolidine **27** with sodium amalgam (Na/Hg, Na_2HPO_4, MeOH) did not remove the phenylthio group but gave the amino-alcohol **28** (80% yield). Other reductive conditions (lithium in liquid ammonia, Raney nickel or Bu_3SnH/AIBN) gave only recovered isoxazolidine **27**.

Heating the aldehyde **25** with hydroxylamine under reflux in PhMe promoted oxime formation then in situ cyclization and cycloaddition to give the tricyclic product **29**. This was formed as a single diastereoisomer and the stereochemistry was confirmed by ^{1}H NOESY studies. Treatment of the sulfone

29 with sodium amalgam gave the amino-alcohol **30**. This arises from reduction of the N–O bond together with the loss of the benzenesulfonyl group (the intermediate anion must undergo elimination rather than protonation).



Scheme 6. Cascade chemistry to an indole core

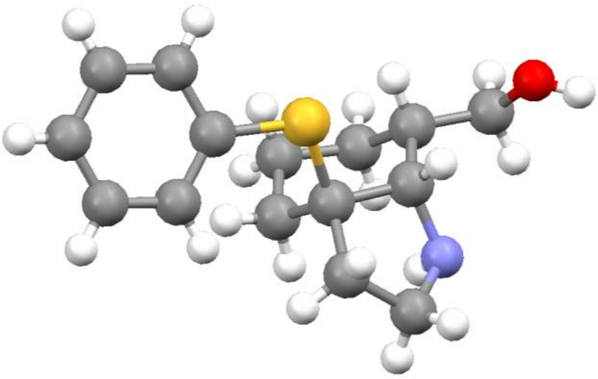
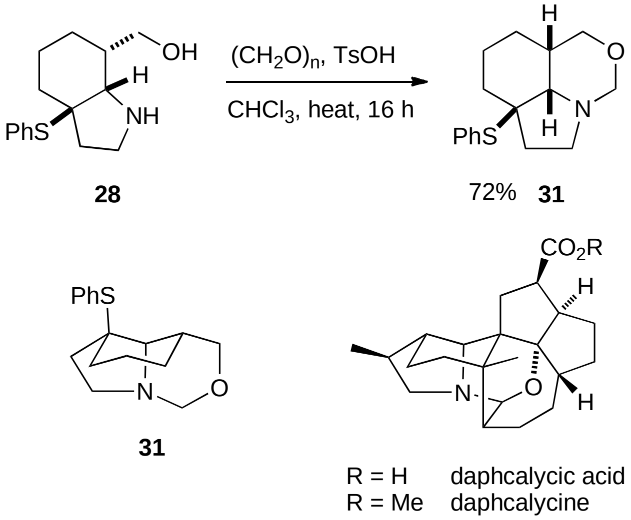


Figure 2. X-Ray crystal structure of cycloadduct **28**

Finally, we converted the amino-alcohol **28** to the 1,3-oxazine **31** using paraformaldehyde and acid. The 1,3-oxazine **31** has the same core structure as the yuzurimine type *Daphniphyllum* alkaloids daphcalycic acid, daphcalycine and daphcalycinosidine A.[25-29]



Scheme 7. Application to a synthesis of the core of some yuzurimine alkaloids

Hence, we have demonstrated that reaction of several different aldehydes (**16**, **17**, **24**, **25**) with hydroxylamine leads to tricyclic products by a cascade of condensation, cyclization and dipolar cycloaddition. The reaction is stereoselective, providing a single stereoisomer in each case. So far we have not been able to remove the phenylthio group from the products, however the benzenesulfonyl group can be removed using sodium amalgam. The chemistry has provided an efficient total synthesis of (±)-myrioxazine A and a synthesis of the tricyclic core of some yuzurimine type *Daphniphyllum* alkaloids.

EXPERIMENTAL

2-Benzenesulfonylhept-6-enenitrile 10: *n*-Butyllithium (4.61 mL, 11.5 mmol, 2.5 M in hexanes) was added to diisopropylamine (1.78 mL, 12.6 mmol) in THF (10 mL) at –78 °C. After 10 min, phenylsulfonylacetonitrile **9** (1.99 g, 11 mmol) was added. After 10 min, 5-bromopentene (1.37 mL, 11 mmol) was added. After 30 min, the mixture was allowed to warm to room temperature and then was heated under reflux. After 18 h, saturated aqueous ammonium chloride solution (10 mL) was added and the mixture was extracted with Et_2O (3 × 20 mL). The organic layers were dried ($MgSO_4$) and evaporated. Purification by column chromatography, eluting with petrol–EtOAc (9:1), gave the nitrile **10** (2.02 g, 74%) as an oil [and the dialkylated nitrile (296 mg, 11%) as an oil]; R_f 0.24 [petrol–EtOAc (9:1)]; ν_{max}(film)/cm^{-1} 3075, 2940, 2235, 1640, 1445, 1440, 1320, 1315; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02–7.98 (2H, m, ArH), 7.79–7.74 (1H, m, ArH), 7.67–7.61 (2H, m, ArH), 5.73 (1H, ddt, *J* 17, 10.5, 6.5, C*H*=CH$_2$), 5.06–4.98 (2H, m, CH=C*H*$_2$), 3.92 (1H, dd, *J* 11, 4.5, CHCN), 2.24–2.07 (3H, m, 3 × CH), 1.90 (1H, dtd, *J* 13.5, 10.5, 5, CH), 1.80–1.68 (1H, m, CH), 1.63–1.51 (1H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.7, 135.6, 135.3, 129.7, 129.6, 116.2, 114.0, 57.4, 32.7, 26.1, 25.7; HRMS (ES) Found:

250.0909, $C_{13}H_{16}NO_2S$ requires MH^+, 250.0902; LRMS *m/z* (ES) 272 (100%), 250 (90). Data consistent with the literature.[30]

2-Benzenesulfonyl-2-(3-chloropropyl)hept-6-enenitrile 11: In the same way as the nitrile **10**, diisopropylamine (1.83 mL, 12.9 mmol), *n*-butyllithium (4.79 mL, 11.7 mmol, 2.45 M in hexanes), the nitrile **10** (1.95 g, 7.82 mmol) and 1-bromo-3-chloropropane (2.34 mL, 23.5 mmol) gave, after heating under reflux for 18 h and purification by column chromatography, eluting with petrol–EtOAc (9:1), a mixture of the chloride **11** and the corresponding bromide (ratio 4:1 by ^{1}H NMR spectroscopy). This mixture and LiCl (585 mg, 13.9 mmol) in DMF (15 mL) were heated to 80 °C. After 3 h, the mixture was allowed to cool to room temperature and EtOAc (10 mL) and ice-cold water (10 mL) were added. The organic layer was washed with water (2 × 10 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography, eluting with petrol–EtOAc (17:3), gave the nitrile **11** (2.26g, 89%) as an oil; R_f 0.43 [petrol–EtOAc (17:3)]; ν_{max}(film)/cm^{-1} 3075, 2940, 2240, 1640, 1445, 1440, 1325, 1310; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.93–7.98 (2H, m, ArH), 7.79–7.74 (1H, m, ArH), 7.67–7.61 (2H, m, ArH), 8.70 (1H, ddt, *J* 17, 10.5, 6.5, C*H*=CH$_2$), 5.03–4.96 (2H, m, CH=C*H*$_2$), 3.61–3.49 (2H, m, CH_2Cl), 2.20–1.90 (8H, m, 4 × CH_2), 1.71–1.52 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.7, 135.3, 134.3, 130.7, 129.4, 116.6, 116.2, 65.6, 44.0, 33.2, 31.5, 29.5, 27.8, 23.8; HRMS (ES) Found: 326.0992, $C_{16}H_{21}ClNO_2S$ requires MH^+, 326.0982; LRMS *m/z* (ES) 328 (20%), 326 (100).

2-Benzenesulfonyl-2-(3-chloropropyl)hept-6-enylamine 12: DIBAL-H (7.8 mL, 7.8 mmol, 1.0 M in hexanes) was added dropwise to the nitrile **11** (1.27 g, 3.89 mmol) in CH_2Cl_2 (20 mL) at –78 °C. After 1.5 h, aqueous HCl (10 mL, 2 M) was added. After 30 min, the mixture was allowed to warm to room temperature and was extracted with Et_2O (40 mL). The organic layer was washed with aqueous HCl (10 mL, 2 M) and the aqueous portions were extracted with Et_2O (5 × 75 mL). The organic layers were dried ($MgSO_4$) and evaporated. Purification by column chromatography, eluting with petrol–EtOAc (9:1), gave the nitrile **11** (532 mg, 42%) as an oil. Further elution with CH_2Cl_2–MeOH (19:1) gave the amine **12** (720 mg, 56%) as an oil; R_f 0.53 [CH_2Cl_2–MeOH (19:1)]; ν_{max}(film)/cm^{-1} 2945, 2860, 1640, 1445; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.02–7.97 (2H, m, ArH), 7.73–7.67 (1H, m, ArH), 7.63–7.57 (2H, m, ArH), 5.71 (1H, ddt, *J* 17, 10, 7, C*H*=CH$_2$), 5.01–4.91 (2H, m, CH=C*H*$_2$), 3.65–3.51 (2H, m, CH_2Cl), 3.21 (2H, br s, C*H*$_2$NH$_2$), 2.09–1.88 (6H, m, 3 × CH_2), 1.73–1.66 (2H, m, CH_2), 1.58–1.47 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.2, 134.9, 133.8, 130.4, 129.7, 116.0, 65.8, 44.7, 41.6, 33.6, 28.8, 26.2, 26.1, 22.0; HRMS (ES) Found: 330.1294, $C_{16}H_{25}ClNO_2S$ requires MH^+, 330.1295; LRMS *m/z* (ES) 332 (13%), 330 (100).

2-(Phenylthio)hept-6-enenitrile 14: *n*-Butyllithium (5.0 mL, 11.3 mmol, 2.24 M in hexanes) was added to diisopropylamine (1.80 mL, 12.1 mmol) in THF (10 mL) at –78 °C. After 10 min, phenylthioacetonitrile **13** (1.5 mL, 11.2 mmol) was added. After 10 min, 5-bromopentene (1.33 mL, 11.2 mmol) was added. After 30 min, the mixture was allowed to warm to room temperature. After 30 min, saturated aqueous ammonium chloride solution (10 mL) was added and the mixture was extracted with Et_2O (3 × 20 mL). The organic layers were dried ($MgSO_4$) and evaporated. Purification by column chromatography, eluting with petrol–EtOAc (97:3), gave the nitrile **14** (1.94 g, 79%) as an oil [and the dialkylated nitrile (243 mg, 15%) as an oil]; R_f 0.53 [petrol–EtOAc (9:1)]; ν_{max}(film)/cm^{-1} 3080, 2930, 2860, 2240, 1640, 1475, 1440; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61–7.58 (2H, m, ArH), 7.41–7.37 (3H, m, ArH), 5.76 (1H, ddt, *J* 17, 10.5, 6.5, C*H*=CH_2), 5.06–4.97 (2H, m, CH=CH_2), 3.69 (1H, t, *J* 7.5, CH), 2.10 (2H, qt, *J* 6.5, 1, CH_2), 1.88–1.81 (2H, m, CH_2), 1.72–1.63 (2H, m, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.3, 134.5, 129.55, 129.5, 129.4, 119.2, 115.7, 37.0, 32.8, 31.8, 26.1; HRMS (ES) Found: 218.0999, $C_{13}H_{16}NS$ requires MH$^+$, 218.1003; LRMS *m/z* (ES) 218 (100%).

2-(3-Chloropropyl)-2-(phenylthio)hept-6-enenitrile 15: In the same way as the nitrile **14**, diisopropylamine (1.14 mL, 8.06 mmol), *n*-butyllithium (3.5 mL, 7.6 mmol, 2.15 M in hexanes), the nitrile **14** (1.095 g, 5.04 mmol) and 1-bromo-3-chloropropane (1.49 mL, 15.1 mmol) gave, after purification by column chromatography, eluting with petrol–EtOAc (24:1), the nitrile **15** (1.38 g, 93%) as an oil; R_f 0.53 [petrol–EtOAc (9:1)]; ν_{max}(film)/cm^{-1} 3075, 2950, 2855, 2240, 1640, 1475, 1440; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.68–7.63 (2H, m, ArH), 7.49–7.37 (3H, m, ArH), 5.75 (1H, ddt, *J* 17, 10.5, 6.5, C*H*=CH_2), 5.06–4.96 (2H, m, CH=CH_2), 3.58–3.52 (2H, m, CH_2Cl), 2.15–1.82 (6H, m, 3 × CH_2), 1.78–1.59 (4H, m, 2 × CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.3, 137.1, 130.4, 129.3, 129.0, 120.8, 115.7, 48.8, 44.2, 36.2, 34.2, 33.2, 27.7, 23.7; HRMS (ES) Found: 294.1081, $C_{16}H_{21}ClNS$ requires MH$^+$, 294.1083; LRMS *m/z* (ES) 296 (20%), 294 (100).

2-(3-Chloropropyl)-2-(phenylthio)hept-6-enal 16: In the same way as the amine **12**, the nitrile **15** (3.43 g, 11.7 mmol) and DIBAL-H (18.7 mL, 18.7 mmol, 1.0 M in hexanes) gave, after purification by column chromatography, eluting with petrol–EtOAc (49:1), the aldehyde **16** (3.12 g, 90%) as an oil; R_f 0.53 [petrol–EtOAc (9:1)]; ν_{max}(film)/cm^{-1} 3075, 2940, 2860, 1715, 1640, 1475, 1440; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.32 (1H, s, CHO), 7.39–7.25 (5H, m, ArH), 5.75 (1H, ddt, *J* 17, 10.5, 6.5, C*H*=CH_2), 5.05–4.96 (2H, m, CH=CH_2), 3.51 (2H, t, *J* 6, CH_2Cl), 2.10–2.00 (3H, m, CH_2 and CH), 1.31–1.51 (6H, m, 3 × CH_2), 1.34–1.23 (1H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 194.9, 137.6, 136.9, 129.8, 129.1, 128.8, 115.5, 63.0, 44.7, 33.7, 29.5, 26.9, 26.6, 23.2; HRMS (ES) Found: 297.1088, $C_{16}H_{22}ClOS$ requires MH$^+$, 297.1080; LRMS *m/z* (ES) 299 (20%), 297 (100).

2-Benzenesulfonyl-2-(3-chloropropyl)hept-6-enal 17: To the aldehyde **16** (2.25 g, 7.59 mmol) in acetone (30 mL) at room temperature was added Oxone® (11.7 g, 19.0 mmol) in water (54 mL). After 5 h, water (30 mL) and CH_2Cl_2 (50 mL) were added. The mixture was extracted with CH_2Cl_2 (2 × 20 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography, eluting with petrol–EtOAc (9:1), gave the aldehyde **17** (1.82 g, 73%) as an oil; R_f 0.47 [petrol–EtOAc (17:3)]; ν_{max}(film)/cm^{-1} 3070, 2955, 2870, 1725, 1640, 1445, 1305, 1140; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.66 (1H, s, CHO), 7.74–7.66 (3H, m, ArH), 7.58–7.52 (2H, m, ArH), 5.72 (1H, ddt, *J* 17, 10, 7, C*H*=CH_2), 5.05–4.96 (2H, m, CH=C*H*$_2$), 3.52 (2H, t, *J* 6, CH_2Cl), 2.15–1.93 (7H, m, 3 × CH_2 and CH), 1.79–1.68 (1H, m, CH), 1.61–1.48 (1H, m, CH), 1.32–1.19 (1H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 196.5, 137.0, 135.5, 134.6, 129.6, 129.3, 116.0, 76.3, 44.7, 33.8, 26.2, 25.7, 24.2, 22.3; HRMS (ES) Found: 351.0801, $C_{16}H_{21}ClNaO_3S$ requires MNa^+, 351.0798; LRMS *m/z* (ES) 353 (6%), 351 (100).

(2aR*,5aR*,8bS*)-5a-(Phenylthio)octahydro-1-oxa-8a-azaacenaphthylene 18: The aldehyde **16** (302 mg, 1.02 mmol), hydroxylamine hydrochloride (108 mg, 1.53 mmol) and *N*,*N*-diisopropylethylamine (0.53 mL, 3.05 mmol) in PhMe (10 mL) were heated under reflux. After 2 h, the solvent was evaporated. Purification by column chromatography, eluting with petrol–EtOAc (3:2), gave the cycloadduct **18** (269 mg, 96%) as an oil, which solidified on standing; mp 97–99 °C; R_f 0.44 [petrol–EtOAc (1:1)]; ν_{max}(film)/cm^{-1} 3080, 2930, 2860, 1470; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.57–7.53 (2H, m, ArH), 7.38–7.29 (3H, m, ArH), 4.21 (1H, dd, *J* 8, 6.5, CH), 3.38 (1H, dd, *J* 10, 6.5, CH), 3.27–3.23 (1H, m, CH), 2.76 (1H, d, *J* 11.5, CH), 2.67 (1H, ddd, *J* 14, 10.5, 3.5, CH), 2.62–2.46 (2H, m, 2 × CH), 1.96–1.90 (1H, m, CH), 1.82–1.71 (3H, m, 3 × CH), 1.68–1.61 (2H, m, 2 × CH), 1.38–1.28 (2H, m, 2 × CH), 0.98 (1H, qd, *J* 12.5, 3.5, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 137.9, 130.8, 130.0, 128.6, 71.2, 69.8, 53.2, 51.4, 39.3, 38.7, 26.6, 26.0, 23.4, 21.8; HRMS (ES) Found: 276.1427, $C_{16}H_{22}NOS$ requires MH^+, 276.1422; LRMS *m/z* (ES) 276 (100%); Anal. Calcd for $C_{16}H_{21}NOS$: C, 69.78; H, 7.69; N, 5.09; S, 11.64. Found: C, 69.73; H, 7.93; N, 5.04; S, 11.71%.

((4aR*,8R*,8aS*)-4a-(Phenylthio)decahydroquinolin-8-yl)-methanol 19: Zn powder (135 mg, 2.07 mmol) was added to the cycloadduct **18** (95 mg, 0.35 mmol) in AcOH–H_2O (1:2, 3 mL) and the mixture was heated at 70 °C. After 1.5 h, the mixture was allowed to cool to room temperature, filtered, washed with CH_2Cl_2 and the solvent was evaporated. The residue was partioned between ammonia solution (5 mL) and CH_2Cl_2 (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), and the organic fractions were dried ($MgSO_4$), filtered and evaporated to give the amino-alcohol **19** (96 mg, 100%) as an oil which solidified on standing; mp 50–52 °C; R_f 0.13 [CH_2Cl_2–MeOH (19:1)]; ν_{max}(film)/cm^{-1} 3385, 2925, 2850, 1475; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48–7.44 (2H, m, ArH), 7.40–7.31 (3H, m, ArH), 3.57 (1H, dd, *J* 10.5, 3.5, CH), 3.39 (1H, t, *J* 10.5, CH), 2.91–2.85 (2H, m, 2 × CH), 2.59 (1H, d, *J* 11, CH), 2.26–2.08 (3H, m, 3 × CH), 1.65–1.53 (2H, m, 2 × CH), 1.52–1.36 (5H, m, 5 × CH), 0.66 (1H, qd, *J* 12.5, 4.5, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 137.8, 130.6, 129.1, 128.7, 70.6, 63.2, 54.7, 39.2, 39.1, 35.3, 28.1 (2 × CH_2), 22.2, 21.2; HRMS (ES) Found: 278.1565, $C_{16}H_{24}NOS$ requires MH^+, 278.1579; LRMS *m/z* (ES) 278 (100%).

(2aR*,5aR*,8bS*)-5a-Benzenesulfonyloctahydro-1-oxa-8a-azaacenaphthylene 20: The aldehyde **17** (260 mg, 0.79 mmol), hydroxylamine hydrochloride (73 mg, 1.03 mmol) and *N*,*N*-diisopropylethylamine (0.36 mL, 2.06 mmol) in PhMe (10 mL) were heated under reflux. After 1 h, the solvent was evaporated. Purification by column chromatography, eluting with petrol–EtOAc (1:1), gave the cycloadduct **20** (226 mg, 93%) as a solid, which recrystallised from CH_2Cl_2–Et_2O–petrol as cubes; mp 192–193 °C (dec); R_f 0.41 [petrol–EtOAc (1:1)]; ν_{max}(film)/cm^{-1} 2935, 2870, 1445, 1305, 1280; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.98–7.95 (2H, m, ArH), 7.67–7.62 (1H, m, ArH), 7.57–7.53 (2H, m, ArH), 4.18 (1H, dd, *J* 8.5, 6.5, CH), 3.37 (1H, dd, *J* 10.5, 6.5, CH), 3.20 (1H, d, *J* 11.5, CH), 3.18–3.14 (1H, m, CH), 2.65–2.53 (2H, m, 2 × CH), 2.36 (1H, qt, *J* 14, 5, CH), 2.03–1.93 (2H, m, 2 × CH), 1.87 (1H, td, *J* 13.5, 4.5, CH), 1.83–1.72 (2H, m, 2 × CH), 1.69–1.72 (1H, m, CH), 1.59–1.53 (1H, m, CH), 1.36 (1H, qt, *J* 13.5, 3.5, CH), 1.02 (1H, qd, *J* 12.5, 3.5, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 136.1, 133.8, 130.7, 128.8, 69.8, 67.8, 63.8, 49.7, 38.9, 31.4, 25.7, 22.6, 21.9, 21.1; HRMS (EI) Found: 307.1247, $C_{16}H_{21}NO_3S$ requires M^+, 307.1242; LRMS *m/z* (EI) 307 (21%), 165 (100); Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56; S, 10.43. Found: C, 62.25; H, 6.93; N, 4.26; S, 10.61%. X-Ray data deposited at CCDC 827991.

(4aS*,8R*,8aR*)-1-(Decahydroquinolin-8-yl)methanol 21: Freshly crushed sodium mercury amalgam (3.58 g) was added to cycloadduct **20** (161 mg, 0.52 mmol) and Na_2HPO_4 (595 mg, 4.2 mmol) in MeOH (10 mL) at –15 °C, then the mixture was allowed to warm to 0 °C. After 2 h, the mixture was allowed to warm to room temperature. After 2 h, aqueous ammonium hydroxide solution (10%, 10 mL) and CH_2Cl_2 (20 mL) were added and the mixture was extracted with CH_2Cl_2 (2 × 15 mL). The organic portions were dried ($MgSO_4$) and evaporated. Purification by chromatography, eluting with CH_2Cl_2–MeOH–NH_3 (8:2:0.1), gave a small amount of the desulfonylated cycloadduct (10 mg, 11%) and the amino-alcohol **21** (79 mg, 89%) as a solid; mp 84–86 °C; Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.28. Found: C, 70.62; H, 11.74; N, 8.15%; data as reported.[22]

Myrioxazine A: The amino-alcohol **21** (78 mg, 0.46 mmol), paraformaldehyde (55 mg, 1.84 mmol) and TsOH·H_2O (5 mg, 0.02 mmol) in $CHCl_3$ (3 mL) were heated under reflux. After 12 h, the mixture was allowed to cool to room temperature and H_2O (5 mL) and potassium carbonate (0.5 g) were added. The mixture was extracted with CH_2Cl_2 (2 × 10 mL) and the organic layer was dried ($MgSO_4$) and evaporated. Purification by column chromatography, eluting with EtOAc–MeOH (9:1), gave myrioxazine A (79 mg, 95%) as an oil; R_f 0.43 [EtOAc–MeOH (9:1)]; HRMS (ES) Found: 182.1550, $C_{11}H_{20}NO$ requires MH^+, 182.1545; data as reported.[22,23]

2-(2-Hydroxyethyl)-2-(phenylthio)hept-6-enenitrile 22: *n*-Butyllithium (3.00 mL, 7.5 mmol, 2.5 M in hexanes) was added to diisopropylamine (1.15 mL, 8.20 mmol) in THF (10 mL) at –78 °C. After 10 min, the nitrile **14** (1.55 g, 7.13 mmol) was added. After 10 min, the 2-bromoethyl trimethylsilyl ether (1.55 g, 7.85 mmol) was added and the mixture was allowed to warm to room temperature. After 1 h, HCl (10 mL, 2 M) was added. After 1 h, the mixture was extracted with Et_2O (3 × 30 mL). The organic layers were dried ($MgSO_4$) and evaporated. Purification by column chromatography, eluting with petrol–EtOAc (4:1), gave the nitrile **22** (1.99 g, 89%) as an oil; R_f 0.30 [petrol–EtOAc (4:1)]; ν_{max}(film)/cm^{-1} 3450, 2935, 2250, 1475, 1440; ^1H NMR (400 MHz, $CDCl_3$) δ = 7.73–7.67 (2H, m, ArH), 7.53–7.41 (3H, m, ArH), 5.78 (1H, ddt, *J* 17, 10, 6.5, $HC=CH_2$), 5.09–4.98 (2H, m, $HC=CH_2$), 3.96 (2H, t, *J* 6.5, CH_2), 2.17–1.98 (4H, m, 2 × CH_2), 1.91–1.62 (4H, m, 2 × CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.4, 137.1, 130.4, 129.3, 128.9, 120.8, 115.6, 59.1, 47.6, 39.1, 36.8, 33.2, 23.9; HRMS (EI) Found: 261.1196, $C_{15}H_{19}NOS$ requires M^+, 261.1187; LRMS *m/z* (EI) 261 (10%), 110 (100).

2-(2-Chloroethyl)-2-(phenylthio)hept-6-enenitrile 23: The alcohol **22** (1.65 g, 6.30 mmol) was added to PPh_3 (2.48 g, 9.50 mmol) and freshly recrystallised *N*-chlorosuccinimide (0.93 g, 6.90 mmol) in THF (12 mL) at 0 °C and the mixture was allowed to warm to room temperature. After 16 h, the solvent was evaporated, the residue was partitioned between Et_2O and water, and the mixture was extracted with Et_2O (3 × 30 mL). The organic layers were dried ($MgSO_4$) and evaporated. Petrol was added, the mixture was filtered over Celite® and the solvent was evaporated. Purification by column chromatography, eluting with petrol–EtOAc (99:1), gave the chloride **23** (1.41 g, 80%) as an oil; R_f 0.20 [petrol–EtOAc (99:1)]; ν_{max}(film)/cm^{-1} 2935, 2230, 1475, 1440; ^1H NMR (250 MHz, $CDCl_3$) δ = 7.77–7.58 (2H, m, ArH), 7.57–7.37 (3H, m, ArH), 5.79 (1H, ddt, *J* 17, 10, 6.5, $HC=CH_2$), 5.11–4.97 (2H, m, $HC=CH_2$), 3.82–3.63 (2H, m, CH_2Cl), 2.30–2.19 (2H, m, CH_2), 2.17–2.04 (2H, m, CH_2), 1.85–1.61 (4H, m, 2 × CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.2, 137.1, 130.7, 129.5, 129.3, 120.0, 115.8, 48.1, 39.5, 38.9, 36.5, 33.1, 23.9; HRMS (ES) Found: 279.0861, $C_{15}H_{18}ClNS$ requires MH^+, 279.0848; LRMS *m/z* (ES) 304 (10%), 302 (100), 301 (40).

2-(2-Chloroethyl)-2-(phenylthio)hept-6-enal 24: In the same way as the amine **12**, the nitrile **23** (1.40 g, 5.04 mmol) and DIBAL-H (11.4 mL, 11.4 mmol, 1.0 M in hexanes) gave, after purification by column chromatography, eluting with petrol–EtOAc (99:1), the aldehyde **24** (0.78 g, 55%) as an oil; *R_f* 0.20 [petrol–EtOAc (99:1)]; ν_{max}(film)/cm^{-1} 2935, 1715, 1560, 1475, 1440; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.32 (1H, s, CHO), 7.44–7.33 (5H, m, ArCH), 5.80 (1H, ddt, *J* 17, 10, 6.5, *H*C=CH_2), 5.09–5.01 (2H, m, HC=CH_2), 3.79 (1H, td, *J* 10.5, 5.5, CH), 3.58 (1H, td, *J* 10.5, 5.5, CH), 2.20–1.99 (4H, m, 2 × CH_2), 1.73–1.60 (3H, m, 3 × CH), 1.38–1.32 (1H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 193.9, 137.4, 137.0, 130.0, 129.3, 128.2, 115.7, 62.4, 39.5, 33.6, 32.3, 29.6, 23.4; HRMS (EI) Found: 282.0845, $C_{15}H_{19}ClOS$ requires M$^+$, 282.0845; LRMS *m/z* (ES) 307 (20%), 305 (100), 283 (10).

2-(2-Chloroethyl)-2-(phenylsulfonyl)hept-6-enal 25: In the same way as the sulfone **17**, the aldehyde **24** (3.46 g, 12.30 mmol) and Oxone® (18.0 g, 29.4 mmol) gave, after purification by column chromatography, eluting with petrol–EtOAc (49:1), the aldehyde **25** (1.03 g, 27%) as an oil; R_f 0.20 [petrol–EtOAc (49:1)]; ν_{max}(film)/cm^{-1} 2920, 2850, 1725, 1445, 1305; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 9.68 (1H, s, CHO), 7.80–7.71 (3H, m, ArCH), 7.66–7.57 (2H, m, ArCH), 5.76 (1H, ddt, *J* 17, 10, 6.5, *H*C=CH_2), 5.12–5.00 (2H, m, HC=CH_2), 3.94–3.81 (1H, m, CHCl), 3.64–3.50 (1H, m, CHCl), 2.42–2.32 (2H, m, CH_2), 2.22–1.96 (4H, m, 2 × CH_2), 1.68–1.48 (1H, m, CH), 1.40–1.20 (1H, m, CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ =195.4, 136.8, 135.2, 134.8, 129.6, 129.4, 116.2, 76.3, 38.5, 33.6, 30.3, 26.0, 22.5; HRMS (ES) Found: 315.0817, $C_{15}H_{20}ClO_3S$ requires MH$^+$, 315.0822; LRMS *m/z* (ES) 315 (100%).

2-(2-Chloroethyl)-2-(phenylthio)hept-6-enal oxime 26: The aldehyde **24** (0.50 g, 1.80 mmol), hydroxylamine hydrochloride (0.18 g, 2.70 mmol) and $^iPr_2NEt$ (0.92 mL, 5.30 mmol) in PhMe (17 mL) were heated under reflux. After 16 h, the mixture was adsorbed onto silica. Purification by column chromatography, eluting with CH_2Cl_2–MeOH (49:1), gave the oxime **26** (0.34 g, 66%) as a mixture of isomers [(*E*):(*Z*) ratio 1:1] as an oil; R_f 0.3 [CH_2Cl_2–MeOH (49:1)]; ν_{max}(film)/cm^{-1} 3385, 2935, 1570, 1460; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.60–7.53 (2H, m, ArH), 7.49–7.38 (3H, m, ArH), 6.83 (0.5H, d, *J* 1.5, HC=N), 6.83 (0.5H, d, *J* 1.5, HC=N), 5.80 (1H, ddt, *J* 17, 10, 7, *H*C=CH_2), 5.09–4.98 (2H, m, HC=CH_2), 3.73–3.60 (1H, m, CHCl), 3.18–3.06 (1H, m, CHCl), 2.44–2.36 (2H, m, CH_2), 2.15–2.09 (2H, m, CH_2), 1.88–1.43 (4H, m, 2 × CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 138.3, 137.6, 137.3, 130.0, 129.9, 129.3, 115.6, 61.8, 61.4, 38.1, 33.5, 32.8, 24.2; *m/z* could not be obtained.

(4aR*,7aS*,7bS*)-4a-Phenylthio-octahydro-2-oxa-2a-aza-cyclopenta[cd]indene 27: The oxime **26** (470 mg, 1.56 mmol) in PhMe (16 mL) was heated under reflux. After 16 h, the mixture was adsorbed onto silica. Purification by column chromatography, eluting with CH_2Cl_2–MeOH (99:1), gave the cycloadduct **27** (400 mg, 98%) as an oil; R_f 0.30 [CH_2Cl_2–MeOH (99:1)]; ν_{max}(film)/cm^{-1} 2935, 1440, 1250; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.52–7.49 (2H, m, ArH), 7.37–7.30 (3H, m, ArH), 3.84 (1H, t, *J* 8, CH), 3.60–3.53 (3H, m, 3 × CH), 3.34 (1H, ddd, *J* 13.5, 6.5, 2, CH), 2.84 (1H, tq, *J* 10, 3.5, CH), 2.08 (1H, ddd, *J* 13.5, 11, 6.5, CH), 1.95–1.87 (2H, m, CH_2), 1.80 (1H, ddd, *J* 13.5, 6.5, 2, CH), 1.66–1.54 (2H, m, CH_2), 1.53–1.46 (1H, m, CH), 1.44–1.36 (1H, m, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 137.0, 132.0, 129.0, 128.7, 72.2, 70.7, 57.7, 56.4, 41.7, 37.7, 35.6, 25.0, 17.4; HRMS (ES) Found: 262.1270, $C_{15}H_{20}NOS$ requires MH^+, 262.1266; LRMS *m/z* (ES) 262 (100%).

((3aR*,7S*,7aS*)-3a-(Phenylthio)octahydro-1*H*-indol-7-yl)methanol 28: In the same way as the alcohol **19**, Zn powder (200 mg, 3.04 mmol) and the cycloadduct **27** (450 mg, 1.71 mmol) in AcOH–H_2O (1:2, 9 mL) gave, after heating at 70 °C for 5 h, the amino-alcohol **28** (400 mg, 98%) as needles; mp 135–137 °C; R_f 0.1 [CH_2Cl_2–MeOH (1:1)]; ν_{max}(film)/cm^{-1} 3280, 3055, 2940, 1445, 1435, 1260; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.54–7.45 (2H, m, ArH), 7.37–7.27 (3H, m, ArH), 3.70 (1H, dd, *J* 11, 5, CH), 3.59 (1H, dd, *J* 11, 5, CH), 3.04–2.97 (2H, m, 2 × CH), 2.91 (1H, td, *J* 10, 3.5, CH), 2.35 (2H, bs, OH, NH), 2.20–2.09 (2H, m, 2 × CH), 1.84 (1H, qt, *J* 13.5, 4, CH), 1.76–1.70 (1H, m, CH), 1.59–1.48 (3H, m, 3 × CH), 1.42 – 1.32 (2H, m, 2 × CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 136.6, 131.9, 128.7, 128.7, 66.5, 63.3, 56.0, 43.3, 41.0, 37.0, 30.9, 22.6, 21.4; HRMS (ES) Found: 264.1418, $C_{15}H_{22}NOS$ requires MH^+, 264.1422; LRMS *m/z* (ES) 264 (100%); Anal. Calcd for $C_{15}H_{21}NOS$: C, 68.40; H, 8.04; N, 5.32; S, 12.17. Found: C, 68.40; H, 7.97; N, 5.45; S, 12.09%. X-Ray data deposited at CCDC 827990.

(5aR*,8aS*,8bS*)-5a-(Phenylsulfonyl)heptahydro-2*H*-isoxazolo[4,3,2-hi]indole 29: The aldehyde **25** (0.58 g, 1.84 mmol), hydroxylamine hydrochloride (0.19 g, 2.76 mmol) and *N*,*N*-diisopropylethylamine (0.96 mL, 5.53 mmol) in PhMe (18 mL) were heated under reflux. After 16 h, the mixture was adsorbed onto silica. Purification by column chromatography, eluting with CH_2Cl_2–MeOH (99:1), gave the cycloadduct **29** (0.32 g, 60%) as an oil; R_f 0.3 [CH_2Cl_2–MeOH (99:1)]; ν_{max}(film)/cm^{-1} 2935, 1440, 1305, 1250; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.95–7.90 (2H, m, ArH), 7.71–7.66 (1H, m, ArH), 7.61–7.55 (2H, m, ArH), 4.35 (1H, d, *J* 8, CH), 3.97 (1H, t, *J* 8, CH), 3.56 (1H, dd, *J* 8, 3, CH), 3.36–3.29 (1H, m, CH), 3.25–3.14 (1H, m, CH), 3.07–2.98 (1H, m, CH), 2.41 (1H, ddd, *J* 14, 6, 2, CH), 2.27–2.16 (1H, m, CH), 2.12–2.01 (1H, m, CH), 1.71–1.60 (2H, m, 2 × CH), 1.60–1.30 (3H, m, 3 × CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 135.8, 134.0, 130.5, 129.1, 73.2, 71.9, 64.6, 54.4, 41.0, 35.6, 30.3, 26.8, 16.4; HRMS (ES) Found: 294.1167, $C_{15}H_{20}NO_3S$ requires MH^+, 294.1164; LRMS *m/z* (ES) 294 (100%).

(3-(2-Aminoethyl)cyclohex-2-enyl)methanol 30: Freshly crushed sodium mercury amalgam (5 g) was added to cycloadduct **29** (200 mg, 0.68 mmol) and Na_2HPO_4 (0.75 g, 5.28 mmol) in MeOH (11 mL) at 0 °C. The mixture was allowed to warm slowly to room temperature over 16 h, then was filtered, washed with MeOH and the solvent was evaporated. Purification by column chromatography, eluting with

CH_2Cl_2–MeOH (4:1), gave the amino-alcohol **30** (50 mg, 51%) as an oil; R_f 0.2 [CH_2Cl_2–MeOH (4:1)]; ν_{max}(film)/cm^{-1} 3300, 2935, 1440; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.41–5.37 (1H, m, CH), 3.52–3.44 (2H, m, CH_2), 2.76 (2H, t, *J* 6.5, CH_2), 2.30 (1H, bs, OH), 2.11 (2H, t, *J* 6.5, CH_2), 1.95–1.88 (2H, m, 2 × CH), 1.85–1.68 (3H, m, 3 × CH), 1.61–1.47 (1H, m, CH), 1.39–1.28 (1H, m, CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ =124.1, 123.5, 66.7, 41.5, 39.4, 38.0, 28.4, 25.2, 21.4; HRMS (EI) Found: 155.1306, $C_9H_{17}NO$ requires M$^+$, 155.1310; LRMS *m/z* (EI) 155 (10%), 125 (76), 108 (63), 95 (100).

(6aR*,9aS*,9bS*)-6a-(Phenylthio)decahydro-[1,3]oxazino[5,4,3-hi]indole 31: Paraformaldehyde (0.09 g, 3.04 mmol) was added to the amino-alcohol **28** (200 mg, 0.76 mmol) and TsOH·H_2O (8 mg, 0.04 mmol) in $CHCl_3$ (15 mL) and the mixture was heated under reflux. After 16 h, the mixture was allowed to cool to room temperature and was adsorbed onto silica. Purification by column chromatography, eluting with CH_2Cl_2–MeOH–NH_3 (99.5:0.5:0.05), gave the acetal **31** (150 mg, 72%) as an oil; R_f 0.3 [CH_2Cl_2–MeOH–NH_3 (99.5:0.5:0.05)]; ν_{max}(film)/cm^{-1} 2935, 2855, 1475, 1440, 1275; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54–7.50 (2H, m, ArH), 7.38–7.31 (3H, m, ArH), 4.60 (1H, d, *J* 7, CH), 3.85 (1H, d, *J* 11.5, CH), 3.58 (1H, d, *J* 7, CH), 3.54 (1H, dd, *J* 11.5, 2.5, CH), 3.00 (1H, td, *J* 8.5, 2.5 Hz, CH), 2.25 (1H, td, 11.5, 2.5, CH), 2.18–2.11 (2H, m, 2 × CH), 2.00–1.73 (4H, m, 4 × CH), 1.69 (1H, td, *J* 13, 3, CH), 1.62–1.48 (3H, m, 3 × CH); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 136.0, 132.1, 128.7, 128.4, 85.8, 71.4, 67.3, 55.3, 46.6, 38.5, 33.4, 33.0, 24.4, 22.1; HRMS (ES) Found: 276.1419, $C_{16}H_{22}NOS$ requires MH$^+$, 276.1422. LRMS *m/z* (ES) 276 (100%).

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