Investigation of macrocyclisation routes to 1,4,7-triazacyclononanes: efficient syntheses from 1,2-ditosylamides†

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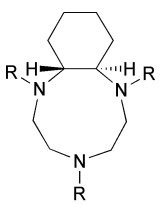
Two routes to the synthesis of a cyclohexyl-fused 1,4,7-triazacyclononane involving macrocyclisations of tosamides have been investigated. In the first approach, using a classic Richman–Atkins-type cyclisation of a cyclohexyl-substituted 1,4,7-tritosamide with ethylene glycol ditosylate, afforded the cyclohexyl-fused 1,4,7-triazacyclononane in 5.86% overall yield in four steps. The second, more concise, approach involving the macrocyclisation of *trans*-cyclohexane-1,2-ditosamide with the tritosyl derivative of diethanolamine initially gave poor yields (< 25%). The well-documented problems with efficiencies in macrocyclisations using 1,2-ditosamides led to the use of a wider range of 1,2-ditosamides including ethane-1,2-ditosamide and propane-1,2-ditosamide. These extended studies led to the development of an efficient macrocyclisation protocol using lithium hydride. This new method afforded 1,4,7-tritosyl-1,4,7-triazacyclononanes in good yield (57–90%) from 1,2-ditosamides in a single step. These efficient methods were then applied to the preparation of a chiral cyclohexyl-fused 1,4,7-tritosyl-1,4,7-triazacyclononane (65–70%). This key chiral intermediate was then converted into a copper(II) complex following detosylation and *N*-methylation. The resulting chiral copper(II) complex catalysed the aziridination of styrene but it did so in a racemic fashion.

Introduction

Polyazamacrocycles continue to stimulate considerable interest because of their varied coordination chemistry coupled with their biological properties and the synthetic utility of the derived metal ion complexes.[1] More specifically, the tridentate 1,4,7-triazacyclononanes are of particular interest because of their ability to stabilise both high and low oxidation states of various metal ions.[2] In this context, transition metal complexes of 1,4,7-triazacyclononane derivatives have been studied as biomimetics of manganese catalase,[3,4] Photosystem II[3,5] and hemocyanin.[6] These biological model systems studies led to the development of manganese complexes of 1,4,7-triazacyclononane derivatives as potent alkene epoxidation catalysts.[7] Indeed, stereoselective alkene epoxidation protocols have been developed while enantioselective epoxidations using manganese complexes of chiral 1,4,7-triazacyclononane derivatives have been described by Beller *et al.*,[8] Bolm *et al.*[9,10] and ourselves.[11] Manganese complexes of derivatives of 1,4,7-triazacyclononane have also been used in the oxidation of sulfides, alcohols and alkanes.[7] Recently, an iron(III) complex of 1,4,7-trimethyl-1,4,7-triazacyclononane was found to catalyse the atom transfer radical polymerisation of styrene.[12] In addition, hydrolytic catalysts have been developed from copper(II), zinc(II) and iron(III) complexes of derivatives of 1,4,7-triazacyclononane which have been used in the cleavage of RNA,[13] DNA[14,15] and peptides.[16] Intriguingly, the copper(II) trifluoroacetate complex of 1,4,7-triisopropyl-1,4,7-triazacyclononane was reported by Halfen *et al.* to be a remarkably efficient catalyst for the achiral aziridination of alkenes.[17]

Given the foregoing interest in 1,4,7-triazacyclononanes it is not surprising that chiral analogues have been prepared, including those with one,[11b,18] two [(C-2,3),[19] (C-2,5)[20] and (C-2,6)[11a,21,22]] and three[10] stereocentres on the carbon backbone of the macrocyclic ring. Despite this significant synthetic interest, the use of complexes of metal ions and chiral 1,4,7-triazacyclononanes, generated *in situ* or isolated entities, have been limited to enantioselective epoxidations.[8–11] However, a copper(II) complex of a chiral 4-oxa-1,7-diazonane has been used as a catalyst in the racemic hetero-Diels–Alder cycloaddition.[19c] Therefore, we were interested in trying to extend the catalytic repertoire of chiral 1,4,7-trizacyclononane-metal ion complexes in asymmetric transformations. We were particularly excited by the achiral alkene aziridination of Halfen *et al.* using copper(II) 1,4,7-triisopropyl-1,4,7-triazacyclononane (*vide supra*)[17] and wished to investigate chiral variants. Furthermore, we were keen to extend our investigations in asymmetric epoxidation studies using chiral manganese complexes.[11,23] Since high enantiomeric excess had been claimed



1 R = Me
2 R = H
3 R = Ts

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† Electronic supplementary information (ESI) available: Instrumentation, general synthetic methods and full experimental procedures for the synthesis *via* Route B, including compounds; (±)-**3**, (±)-**6** (±)-**10**, **12**, (±)-**13**. See DOI: 10.1039/b716938h

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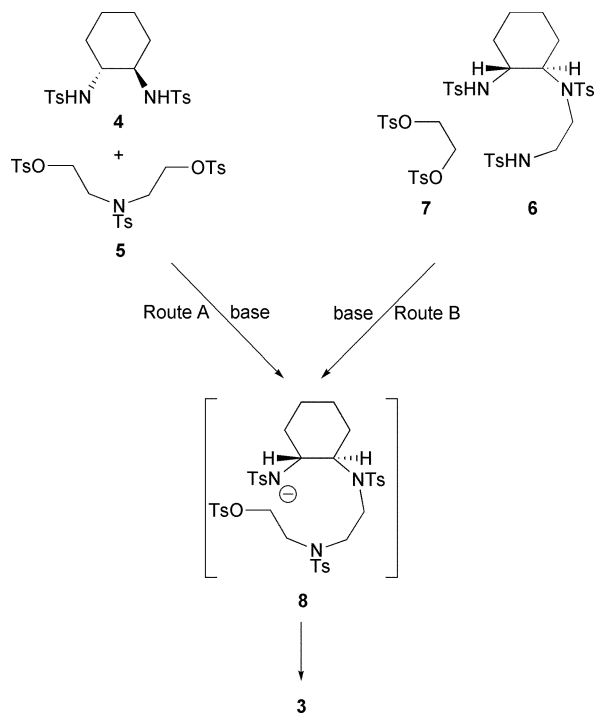
for alkene epoxidations using manganese complexes of cyclohexyl-fused azamacrocycle **1**,[8] we wished to prepare and investigate complexes of this conformationally constrained system.

The cyclohexyl-fused azamacrocycle **1** was prepared by Beller *et al.* from the corresponding non-methylated derivative **2**, which, in-turn, was accessed from the tritosamide **3**.[19a] At the outset of our work, Beller *et al.* had reported the preparation of cyclohexyl-fused tritosamide **3** by the macrocyclisation of the disodium salt of cyclohexyl ditosamide **4** with tosyl ester **5** in 68% yield (Scheme 1, Route A).[19a] In contrast, Lawrence and co-workers prepared the cyclohexyl-fused tritosamide **3** in only 28% yield using cyclohexyl ditosamide **4** with ditosyl ester **5** in DMF with potassium carbonate.[19b] After completion of our synthetic studies, Watkinson and co-workers also reported modest yields in the macrocyclisation of cyclohexyl ditosamide **4** and tosyl ester **5**.[19d] This latter group attributed the moderate macrocyclisation yield to geometric constraints as a result of ring strain. However, it had been previously documented that macrocyclisations of 1,2-ditosamides to provide tritosylamides of 1,4,7-triazacyclononanes do so in only modest yield.[18c,24] Searle and Geue concluded that these low yields were a consequence of inhibition of the first substitution step, that is the reaction of a bis-anion of a 1,2-ditosamide with ditosyl ester **5**. It was postulated that this inhibition may have been due to steric and/or electronic effects in the 1,2-ditosamide bis-anion.[24] Searle and Geue were, however, able to carry out successful macrocyclisations provided that 1,2-ditosamides were not used as the source of the nucleophilic component. Instead, an alternative disconnection involving classical Richman–Atkins cyclisations with ethylene glycol ditosylate and the tritosamide from diethylenetriamine provided good cyclisation yields.



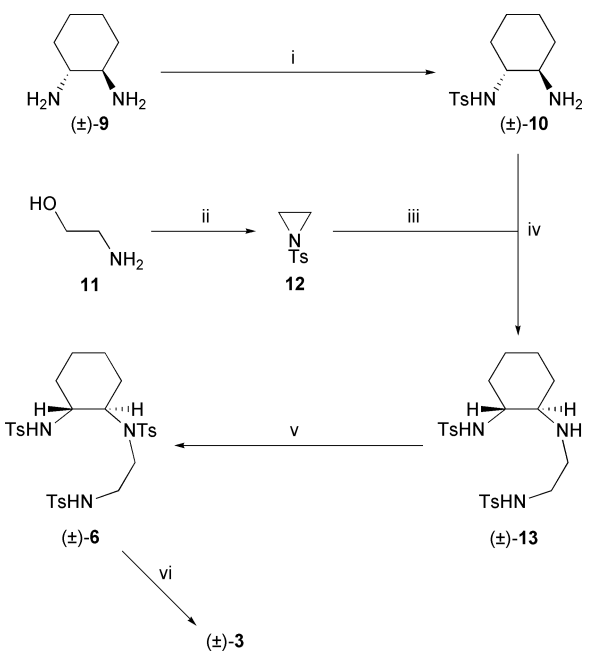
Scheme 1

The focus for this study was to investigate alternative cyclisation routes to the cyclohexyl-fused tritosamide **3** (Scheme 1). After developing efficient routes to tritosamide **3** we then planned to prepare the *N*-methyl derivative **1** and then prepare manganese and copper(II) complexes. These complexes were to be studied in catalytic asymmetric alkene epoxidations and aziridinations.

In order to develop efficient routes to the tritosamide **3** it was important to address the issues of the cyclisation chemistry. In view of the observations of Searle and Geue (*vide supra*) we envisiged an alternative disconnection of tritosamide **3** (Scheme 1, Route B). This route involved the classic Richman–Atkins cyclisation of the 1,4,7-tritosamide **6** with ethylene glycol ditosylate **7**. Since both Route A and Route B proceed *via* common intermediate **8**, then these studies may lead to an understanding of the moderate yields obtained in Route A (Scheme 1).

Results and discussion

Our alternative approach to the synthesis of cyclohexyl-fused tritosamide **3**, *via* route B (Scheme 1), started from the racemic cyclohexyl diamine (±)-**9** which was monotosylated using 0.31 equivalents of tosyl chloride which gave the amino tosyl amide (±)-**10** [83% based on limiting tosyl chloride, 27% based on (±)-**9**] (Scheme 2).[25] A two-step conversion of ethanolamine **11** into tosyl aziridine **12** (70% over two steps) was carried out using a modification of the method of Bulkowski and co-workers.[26] Bulkowski and co-workers had reported the effective ring opening of aziridine **12** with 1,2-amino tosamides.[26] Analogous ring opening of the aziridine **12** with amino tosyl amide (±)-**10** in toluene at reflux afforded the ditosamide amine (±)-**13** (45%). This ring opening was sluggish (60 h) and may reflect the hindered nature of the amino functionality in amino tosyl amide (±)-**10**. *N*-Tosylation of ditosamide amine (±)-**13** with tosyl chloride in pyridine smoothly afforded the tritosamide (±)-**6** (72%). Ritchman-Atkins

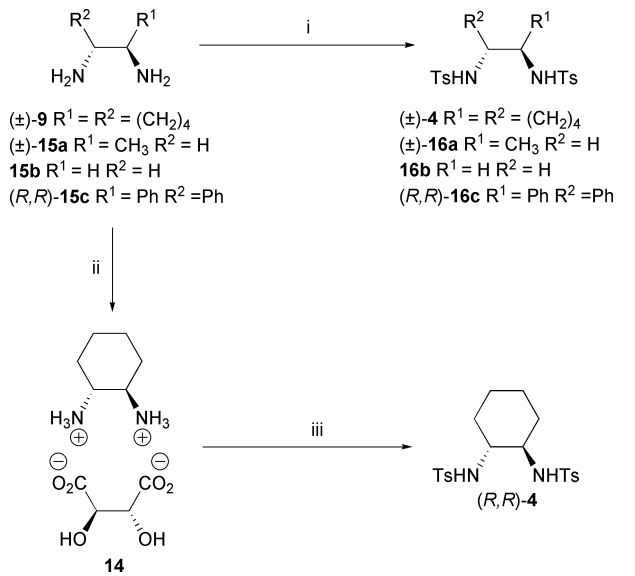


Scheme 2 *Reagents and conditions*: i, 0.31 equiv. TsCl, CH_2Cl_2, 3 N NaOH, 0 °C, 83% [27% based on (±)-**9**]; ii, 2 equiv. TsCl, Py, 73%; iii, NaH, THF, 96%; iv, toluene, Δ, 45%; v, TsCl, Py, 72%; vi, (a) NaH, DMF, 25 °C, (b) $(CH_2OTs)_2$, 80 °C, 67%.

macrocyclisation by treatment of tritosamide (±)-**6** with two equivalents of sodium hydride together with ethylene glycol ditosylate readily gave the target macrocycle tritosamide (±)-**3** (67%).

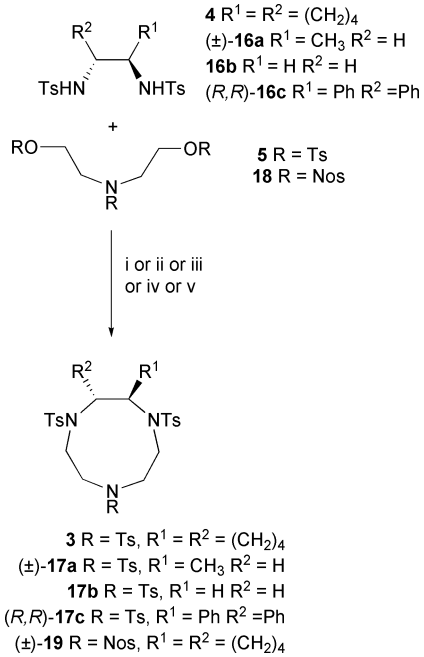
The yield obtained in the macrocyclisation of tritosamide (±)-**6** (67%) (Scheme 1, Route B) is very much in line with the yields of other Richman–Atkins cyclisations (53–83%) using tritosamides and ethylene glycol ditosylate to give 1,4,7-triazacyclonane derivatives.[11,18e,21,22,24,27] This observation does not appear to support the conclusions of Watkinson *et al.* that the poor yields in the macrocyclisation of ditosamide **4** with ditosyl ester **5** to give macrocycle **3** (Scheme 1, Route A) are a consequence of geometric constraints from ring strain. Both Routes A and B (Scheme 1) proced *via* the common intermediate **8**, and our results, therefore, indicate that cyclisation of anion **8** is not particularly hindered. However, the sluggish reaction between aziridine **12** with amino tosyl amide (±)-**10** may suggest that the first substitution step of the dianion of ditosamide **4** by ditosyl ester **5** is hindered.

Although Richman–Atkins macrocyclisation of cyclohexyl tritosamide (±)-**6** efficiently gave the cyclohexyl-fused macrocycle tritosamide (±)-**3**, the overall yield was unacceptably low (5.86%) over four steps. This is a consequence of the low yield in two steps: firstly, in the monotosylation of diamine (±)-**9** [83% based on limiting tosyl chloride, 27% based on (±)-**9**]; and secondly, in the ring opening of aziridine **12** with amino tosyl amide (±)-**10** (45%) (Scheme 2). Consequently, we decided to re-investigate the reactions of 1,2-ditosamides with tosyl ester **5** (Scheme 1, Route A). Thus, the 1,2-diamines (±)-**9** and **15a**–**c** were converted into the corresponding 1,2-ditosamides (±)-**4** and **16a**–**c** (68–79%) using tosyl chloride and base (Et_3N or $^iPrNEt_2$) (Scheme 3). Additionally, the enantiopure (*R*,*R*)-**4** was prepared by resolution of 1,2-diamine (±)-**9** *via* the tartrate salt **14** (85%).[28] Subsequent ditosylation of the salt **14**, using a modification of the monotosylation conditions of Walsh and co-workers,[29] afforded the enantiopure cyclohexyl ditosamide (*R*,*R*)-**4** (85%).[19b,c]



Scheme 3 *Reagents and conditions*: i, TsCl, Et_3N or $^iPrNEt_2$, CH_2Cl_2, 68–79%; ii, (a) L-(+)-(2*R*,3*R*) tartaric acid, 70 °C, (b) AcOH, 90 °C, 85%; iii, TsCl, 1.2 N NaOH, CH_2Cl_2, 85%.

With access to the 1,2-ditosamides **4** and **16a**–**c** in hand, we investigated the macrocyclisation with tosyl ester **5** (Scheme 4, Table 1). In the first instance, we repeated the macrocyclisation of cyclohexyl ditosamide (±)-**4** and tosyl ester **5** as previously reported by Golding *et al.*[19b] In this case, a yield of 18% was achieved for macrocycle (±)-**3**, in broad agreement with the yields observed by Golding *et al.* (28%)[19b] and Watkinson and co-workers (20%)[19c] (Table 1, entry 1, method A). In contrast, Beller *et al.* had used the sodium salt of cyclohexyl (*R*,*R*)-**4** with tosyl ester **5**, which cyclised to provide cyclohexyl-fused macrocycle (*R*,*R*)-**3** in 68%.[19a] In our hands, this cyclisation gave cyclohexyl-fused (*R*,*R*)-**3** in a disappointing 23%, identical to that observed by Watkinson and co-workers[19c] (Table 1, entry 2, method B).



Scheme 4 *Reagents and conditions*: i, (method A) K_2CO_3, DMF, 50 °C, 7 d; ii, (method B) (a) NaOEt, EtOH (b) **5**, DMF, 100 °C; iii, (method C) (a) 2 equiv. NaH, DMF, (b) **5**, DMF, 70 °C; iv (method D) disodium salt of **16a**, **5**, DMSO, 100 °C; v, (method E) (a) 2 equiv. LiH, DMF, 70 °C, (b) **5** or **18**, DMF, 50 °C, 7 d.

The low yields observed in the macrocyclisation of 1,2-ditosamide **4** and ditosyl ester **5** taken together with the inefficient formation of cyclohexyl ditosamide amine (±)-**13** from amino tosyl amide (±)-**10** and aziridine **12** (Scheme 2) initially suggested that steric hindrance in both cyclohexyl 1,2-ditosamide **4** and amino tosyl amide (±)-**10** may have been a problem. In order to understand these issues we chose to investigate the less sterically demanding propane-1,2-ditosamide (±)-**16a** as the source of the nucleophile in macrocyclisation. Given the previous success of the macrocyclisation conditions using two equivalents of sodium hydride in the formation of cyclohexyl-fused azamacrocycle (±)-**3** from 1,4,7-tritotosamide (±)-**13** (Scheme 1, Route B), we decided to use sodium hydride in DMF with propane-1,2-ditosamide (±)-**16a**.[24] Thus, cyclisation of propane-1,2-ditosamide (±)-**16a** under these conditions (conditions C, Table 1) with ditosyl ester **5** gave the mono-substituted macrocycle (±)-**17a** in a meagre 10% (entry 3, Table 1). This observation was in line with the results

Table 1 Investigation of macrocyclisation methods using 1,2-ditosamides **4** and **16a**–**c** with sulfonates **5** and **18** (Scheme 4)

Entry	Ditosamide (R^1, R^2)	Electrophile (P)	Method[a]	Macrocyclic product (R^1, R^2)	Yield (%) (Lit. Yield (%))
1	(±)-**4** ($R^1 = R^2 = (CH_2)_4$)	**5** ($R = SO_2C_6H_4CH_3$)	A	(±)-**3** ($R^1 = R^2 = (CH_2)_4$)	18 (28,[19b] 20[19c])
2	(±)- or (*R*,*R*)-**4** ($R^1 = R^2 = (CH_2)_4$)	**5** ($R = SO_2C_6H_4CH_3$)	B	(±)- or (*R*,*R*)-**3** ($R^1 = R^2 = (CH_2)_4$)	23 (68,[19a] 23[19c])
3	(±)-**16a** ($R^1 = CH_3$, $R^2 = H$)	**5** ($R = SO_2C_6H_4CH_3$)	C	(±)-**17a** ($R^1 = CH_3$, $R^2 = H$)	10
4	(±)-**16a** ($R^1 = CH_3$, $R^2 = H$)	**5** ($R = SO_2C_6H_4CH_3$)	D	(±)-**17a** ($R^1 = CH_3$, $R^2 = H$)	(20[18d])
5	(±)-**16a** ($R^1 = CH_3$, $R^2 = H$)	**5** ($R = SO_2C_6H_4CH_3$)	B	(±)-**17a** ($R^1 = CH_3$, $R^2 = H$)	(60[18a])
6	**16b** ($R^1 = R^2 = H$)	**5** ($R = SO_2C_6H_4CH_3$)	C[b]	**17b** ($R^1 = R^2 = H$)	(25[24])
7	**16b** ($R^1 = R^2 = H$)	**5** ($R = SO_2C_6H_4CH_3$)	E	**17b** ($R^1 = R^2 = H$)	91
8	(±)-**16a** ($R^1 = CH_3$, $R^2 = H$)	**5** ($R = SO_2C_6H_4CH_3$)	E	(±)-**17a** ($R^1 = CH_3$, $R^2 = H$)	60
9	(*R*,*R*)-**16c** ($R^1 = R^2 = Ph$)	**5** ($R = SO_2C_6H_4CH_3$)	E	(*R*,*R*)-**17c** ($R^1 = R^2 = Ph$)	0
10	(*R*,*R*)-**4** ($R^1 = R^2 = (CH_2)_4$)	**5** ($R = SO_2C_6H_4CH_3$)	E	(*R*,*R*)-**3** ($R^1 = R^2 = (CH_2)_4$)	65–70
11	(*R*,*R*)-**4** ($R^1 = R^2 = (CH_2)_4$)	**18** ($R = SO_2C_6H_4NO_2$)	E	(±)-**19** ($R^1 = R^2 = (CH_2)_4$)	57

[a] Method A: K_2CO_3, DMF, 50 °C; method B: (a) NaOEt, EtOH, (b) **5**, DMF, 100 °C; method C: (a) 2 equiv. NaH, DMF, (b) **5**, DMF, 70 °C; method D: disodium salt of **16a**, **5**, DMSO, 100 °C; method E: (a) 2 equiv. LiH, DMF, 70 °C (b) **5** or **18**, DMF, 50 °C. [b] Cyclisation step carried out at 105 °C.

of Graham and Weatherburn[18d] who cyclised the disodium salt of propane ditosamide(±)-**16a** with ditosyl ester **5** in DMSO at 100 °C which gave the macrocycle (±)-**17a** in 20% yield (entry 4, Table 1, method D). This is in contrast to the findings of Mason and Peacock who claimed a 60% yield of macrocycle (*R*)-**17a** by reaction of the disodium salt of (*R*)-**16a** and ditosyl ester **16a** using DMF at 100 °C (entry 5, Table 1).[18a] However, even with the less sterically demanding ethane-1,2-ditosamide **16b** Searle and Geue formed the parent 1,4,7-tritosyl-1,4,7-triazacyclononane **17b** in only 25% using two equivalents of sodium hydride in DMF at 105 °C (entry 6, Table 1).[24] Indeed, it was Searle and Geue who first delineated the problems in the formation of 1,4,7-tritosyl-1,4,7-triazacycloalkanes using dianions of 1,2-ditosamides. These workers postulated that steric and/or electronic effects inhibit the first nucleophilic substitution step in the reaction of 1,2-ditosamide dianions with bis-electrophiles (*cf.* Route A, Scheme 1). The lack of a clear correlation of yield of macrocycle with the anticipated steric encumbrance of 1,2-ditosamides **4** and **16a** in our results (entries 1–3, Table 1) argues against just steric effects. However, electronic effects, solubility and nucleophilicity of 1,2-ditosamide dianions remained as possible causes for low yields in macrocyclisations.

In the context of the above issues of cyclisation of dianions of 1,2-ditosamides we wondered if alternatives to the sodium counterion might be helpful in developing efficient routes to cyclohexyl-fused macrocycle **3** *via* 1,2-ditosamides (Route A, Scheme 1). In this context, caesium carbonate has been found to be beneficial in Richman–Atkins cyclisations[30] and in macrolactonisations.[31] These observations were rationalised in terms of the basicity of caesium bicarbonate[30] and in terms of ion-paring properties of caesium salts[31] rather than a templating effect of the caesium cation. However, in related macrocyclisations of cyclohexyl ditosamide **4** using caesium carbonate we had observed poor yields of macrocycles.[32] This suggested that ion-pairing properties of salts of cyclohexyl ditosamide **4** may not be the source of low macrocyclisation yields. We wondered, from our experimental observations, if solubility of dianions of 1,2-ditosamides might be an issue with low macrocyclisation yields.

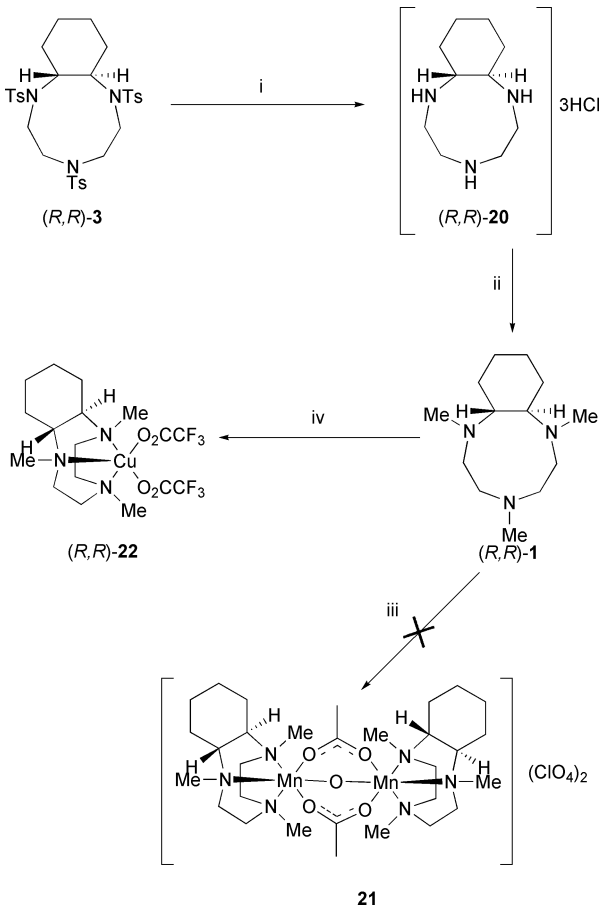
Lithium salts are markedly different from the other alkali metal salts.[33] Unlike the latter, the salts lithium chloride and lithium bromide are somewhat soluble in polar organic solvents such as alcohols and ethers. The solubility of these salts can be attributed to the relatively strong coordination of solvent molecules around the small lithium cation that has a large surface to charge density (Li^+ 0.13 Z $Å^{-3}$).[33] Therefore, we hoped that the use of lithium counterions in dianions of 1,2-ditosamides would provide for a more effective macrocyclisation. Unfortunately, lithium carbonate is not basic enough to deprotonate secondary tosamides[30] but we anticipated that lithium hydride might result in effective macrocyclisations of 1,2-ditosamides. Accordingly, treatment of ethylene 1,2-ditosamide **16b** with two equivalents of lithium hydride in DMF at 70 °C followed by addition of ditosyl ester **5** at 50 °C gave the parent 1,4,7-tritosyl-1,4,7-triazacyclononane **17b** in an unprecedented 91% yield (entry 7, Table 1). To explore the scope of this process we investigated the use of propyl 1,2-ditosamide (±)-**16a** and diphenyl 1,2-ditosamide (*R*,*R*)-**16c** (entries 8 and 9, Table 1). The former provided the methyl-substituted macrocycle **17a** in 60% yield while the latter failed to afford the diphenyl macrocycle **17c**. Clearly, there is a complex interplay of steric and counterion effects at work in these macrocyclisations. The use of lithium as the cation enables some of these cyclisations to proceed efficiently. However, the decrease in yield on increasing the steric requirements of the 1,2-ditosamide (entries 7 and 8, Table 1) indicates that the macrocyclisation is subject to some steric hindrance factors. With these observations in mind we then investigated the key macrocyclisation of cyclohexyl ditosamide (*R*,*R*)-**4** with ditosyl ester **5**. Satisfyingly, the cyclohexyl macrocycle (*R*,*R*)-**3** was obtained in consistently good yields (65–70%) (entry 10, Table 1).§ Since 4-nitrosulfonamides (nosyl; Nos) have been used in heterocyclic cyclisations[34] and the nosyl group can be removed under mild conditions we investigated our cyclisation protocol with cyclohexyl ditosamide (±)-**4** and bisnosyl ester **18**. This macrocyclisation gave the ditosamide nosyl amide **19** in 57% yield (entry 11, Table 1).

The efficient macrocyclisation of **4** with **5** (Scheme 4) suggests, in contrast to the observations of Watkinson and co-workers,[19c,d] that the cyclohexyl macrocycle **3** is not subject to undue ring strain to prevent macrocyclisation. Indeed, this approach presents a much more effective synthesis of **3** (two steps from salt **14**, 55% overall) in contrast to Route A (Scheme 1) (four steps, 5.86% overall)

Having established an effective route to the chiral macrocycle (*R*,*R*)-**3** (Schemes 3 and 4) we wished to prepare metal complexes

§ Three separate workers in these laboratories have achieved consistent yields in the synthesis of (*R*,*R*)-**3**.

of the corresponding *N*-alkyl derivatives. Thus, deprotection of the chiral macrocyclic tritosylamide (*R*,*R*)-**3** was accomplished *via* using lithium in ammonia,[18e] which afforded the hydrochloride salt (*R*,*R*)-**20** (73%) (Scheme 5). The macrocyclic amine hydrochloride (*R*,*R*)-**20** was converted into its free base (*R*,*R*)-**2** with aqueous NaOH. Methylation of the free base (*R*,*R*)-**2** was conveniently achieved using the Eschweiler–Clarke *N*-methylation procedure which afforded the *N*-methyl macrocycle (*R*,*R*)-**1** (79%).[35]



Scheme 5 *Reagents and conditions*: i, (a) Li, NH_3, EtOH, (b) aq. HCl (73%); ii, (a) aq. NaOH, (b) HCO_2H, HCHO, Δ, 24 h (79%); iii, $Mn(OAc)_3$, MeOH–H_2O (9 : 1), $NaClO_4$; iv, (a) $CuCl_2$, CH_3CN (b) AgO_2CCF_3.

With adequate quantities of chiral macrocycle (*R*,*R*)-**1** in hand, we wished to prepare the (μ-oxo)-bis(μ-acetoxy) perchlorate salt **21** and derivatives. The corresponding hexafluorophosphate salt of **21** had been prepared by Beller *et al.*,[19a] albeit in 18% yield. Beller *et al.* used the hexafluorophosphate salt of **21** as well as the corresponding tris(μ-oxo) complex in the impressive enantioselective epoxidation of alkenes (8–92% ee).[8]

Wieghardt *et al.* had originally developed the synthesis of (μ-oxo)-bis(μ-acetoxy)-dimanganese complexes of the parent macrocycle 1,4,7-trimethyl-1,4,7-triazacyclononane.[36] However, using the modified method of Wieghardt and Weyhermüller[37] with (*R*,*R*)-**1** failed to give any of complex **21**.¶ The difficulty in preparing complex **21** is perhaps reflected in the meagre yield (18%) reported for the preparation of the hexafluorophosphate salt of **21**.[19a]

Undeterred by our experiences in preparing (μ-oxo)-bis(μ-acetoxy)-dimanganese complexes we then explored the preparation of copper(II) complexes of (*R*,*R*)-**1**. Thus, treatment of (*R*,*R*)-**1** with copper(II) chloride in acetonitrile followed by addition of silver trifluoroacetate afforded blue crystals of **22** (53%) (Scheme 5).[17] The crystalline nature of copper(II) complex **22** allowed an X-ray analysis to be carried out: this enabled both the stereochemistry and the absolute structure to be confirmed unequivocally by single crystal diffraction (Fig. 1).‖

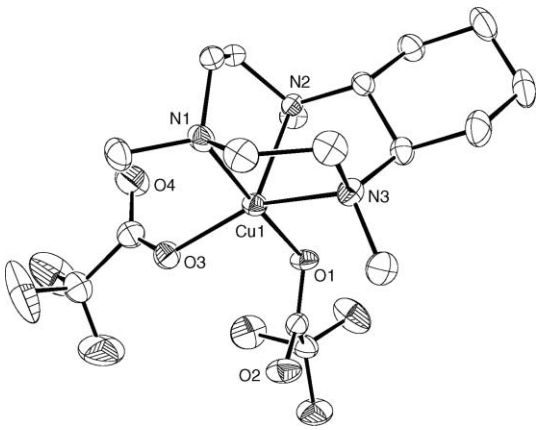
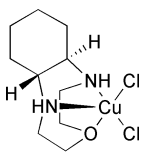


Fig. 1 ORTEP representation of complex **22**. Hydrogen atoms are omitted for clarity.

The closest known structure to complex **22** is that of a copper complex of an analogous 4-oxa-1,7-diazonane (N,N,O) ligand, $[CuCl_2(C_{10}H_{18}N_2O)]$ **23**.[19c]



23

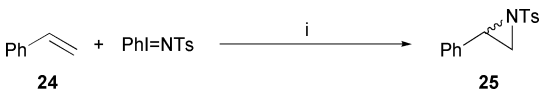
The complex **23** adopts a square planar structure (all angles about Cu are within 10° of ideal 90 and 180° values) with a longer contact to O (average Cu ··· O distance 2.335 Å) giving a pseudo square pyramidal geometry. In **22**, although one Cu–N distance is longer than the others [compare 2.195(2) with 2.033(3) and 2.094(2) Å] the difference is not so marked as in **23**. In **22** there is also some distortion away from square pyramidal and towards trigonal bipyramidal geometry, with O1 and N1 axial. Complete

¶ We are indebtited to Dr Thomas Weyhermüller (Max Planck Institute for Bioorganic chemistry, Mulheim, Germany) for providing the details of these modified conditions.[37] In our hands, this process worked extremely well for (μ-oxo)-bis(μ-acetoxy)-dimanganese complexes of 1,4,7-trimethyl-1,4,7-triazacyclononane (58%). However, using (*R*,*R*)-**1**, material with a low carbon, hydrogen and nitrogen content was isolated.

‖ Crystal data for **22**: $C_{17}H_{27}CuF_6N_3O_4$, $M_r = 514.96$, orthorhombic, space group $P2_12_12_1$, $a = 8.3666(2)$, $b = 15.4945(3)$, $c = 16.3029(4)$ Å, $V = 2133.45(8)$ Å^3, $Z = 4$, $\rho_{calc} = 1.618$ g cm^{-3}, Mo-Kα radiation, $\lambda = 0.71073$ Å, $\mu = 1.115$ mm^{-1}, $T = 173$ K; 30 600 reflections were collected, 4836 were unique, R_{int} 0.077; final refinement to convergence on F^2 with all non-H atoms anisotropic gave $R = 0.0405$ (F, 3771 obs. data only) and $R_w = 0.0719$ (F^2, all data), GOF = 1.033, for 283 refined parameters. Residual electron density max. and min. 0.331 and −0.301 e Å^{-3}. Flack parameter refined to −0.001(1) indicating the correct assignment of absolute configuration.

adoption of trigonal bipyramidal geometry is hindered by the polydentate ligand imposing small (< 90°) NCuN angles. The N3CuO3, N2CuO3 and N2CuN3 angles, 152.36(9), 124.75(9) and 82.87(9)° respectively, emphasise the distorted nature of the resulting structure.

With an efficient synthesis of (*R*,*R*)-cyclohexyl macrocycle **1** developed and the preparation of the corresponding copper(II) complex **22** in hand we turned our attention to the use of the latter in the aziridination of styrene. Thus, catalyst **22** (5 mol%) and PhNITs (1 equivalent) sluggishly catalysed the aziridination of styrene **24** (10 equiv.) to afford the aziridine **25** (49%) (Scheme 6). Disappointingly, analysis of the aziridine **25** by chiral HPLC indicated that racemic material had been obtained. The sluggish catalysis by **22** together with the production of racemic aziridine **25** suggests that C-substitution of the azamacrocycle ring inhibits the catalysis without establishing an effective chiral pocket. This observation is supported by our experiences in the use of chiral azamacrocycles in epoxidation processes.[11,32]



Scheme 6 *Reagents and conditions*: i, 5 mol% **22**, CH_3CN, RT.

Conclusions

Classical Richman–Atkins macrocyclisation of tritosamide **6** with ethylene glycol ditosylate **7**, efficiently gave the cyclohexyl-fused macrocycle **3**. In contrast to published views, this indicated that macrocycle **3** was not unduly strained. Inefficiencies in the preparation of tritosamide **6** led to a re-investigation of a more direct macrocyclisation using 1,2-ditosamides. In agreement with long-standing literature precedence, initially, these cyclisations were inefficient. However, a new protocol was developed that used lithium salts of 1,2-ditosamides, generated *in situ*, to improve the solubility of these nucleophilic components. The improved solubility of these lithium salts of 1,2-ditosamides over their sodium salt counterparts led to dramatic improvements in the macrocyclisation yields. These improved yields were still subject to a degree of steric effects depending on the nature of the α-substituents in the 1,2-ditosamides **4** and **16a**–**c**. The 1,2-ditosamide **16b**, lacking an α-substituent, gave the unsubstituted 1,4,7-triazacyclononane **17b** in exceptional 91% yield using our modified macrocyclisation procedure. A single methyl α-substituent in 1,2-ditosamide **16a** led to a drop in the macrocyclisation efficiency, with methyl 1,4,7-triazacyclononane **17a** being produced in 60% yield. However, an α,α′-disubstitution pattern in the 1,2-ditosamide was as efficient provided that the α,α′-substituents were not too sterically demanding. So, *trans*-cyclohexyl-1,2-ditosamide (*R*,*R*)-**4** gave the cyclohexyl-fused 1,4,7-triazacyclonanone (*R*,*R*)-**3** in 65–70% yield. In contrast, the sterically demanding α,α′-diphenyl 1,2-ditosamide **16** failed to give any macrocycle. The efficiency of this macrocyclisation protocol allowed the synthesis of useful quantities of chiral cyclohexyl-fused azamacrocycle **3**. Subsequent deprotection, *N*-methylation of the chiral cyclohexyl-fused azamacrocycle **3** followed by copper(II) complex formation led to the preparation of the new chiral copper(II) complex **22**. Although complex **22** sluggishly catalysed the aziridination of stryrene, it did so in a racemic fashion.

Experimental

Synthetic studies *via* Route A

(±)-4-Methyl-*N*-(2-{[(4-methylphenyl)sulfonyl]amino}cyclohexyl) benzenesulfonamide 4. To a solution of (±)-1,2-diaminocyclohexane **9** (1.20 g, 10.5 mmol), diisopropylethylamine (7.3 cm^3, 67 mmol, 6.4 equiv.) in DCM (10 cm^3) was added *p*-toluenesulfonyl chloride (4.0 g, 21 mmol, 2 equiv.) in batches over 30 min at 0 °C. The reaction was continued for an additional 12 h at room temperature. On completion, the reaction was quenched with 2 M HCl (20 cm^3). The aqueous mixture was extracted with diethyl ether (×3, 20 cm^3) and the combined organic extracts were dried (Na_2SO_4), filtered and evaporated to form the crude dark brown oil. Purification by column chromatography on silica (hexane–EtOAc–CH_2Cl_2 4 : 1 : 5) afforded a white solid (3.0 g, 7.1 mmol, 68%); mp 180–181 °C. Found: C, 56.7; H, 6.1; N, 6.6; S, 15.2%; MH^+ 423.1427. Calculated for $C_{20}H_{26}O_4S_2N_2$: C, 56.9; H, 6.2; N, 6.6; S, 15.2%; MH^+ 423.1412. ν_{max} (KBr, cm^{-1}) 3256 (s, NHTs), 3055 (w, C_6H_4), 2925 (m, CH), 2856 (m, CH), 1333 (s, SO_2NH), 1161 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$), 1.09 (m, 4H, 2 × CH_2), 1.53 (m, 2H, CH_2), 1.81 (m, 2H, CH_2), 2.75 (m, 2H, 2 × C*H*NHTs), 4.98 (m, 2H, 2 × N*H*Ts), 7.31 (d, *J* 8.3 Hz, 4H, $C_6H_4CH_3$), 7.76 (d, *J* 8.3, 4H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$) 21.7 ($C_6H_4CH_3$), 21.9 ($C_6H_4CH_3$), 24.0 (CH_2), 26.5 (CH_2), 31.0 (CH_2), 35.3 (CH_2), 54.9 (*C*H), 66.3 (*C*H), 127.3 (4 × Ar*C*H), 129.7 (4 × Ar*C*H), 139.6 (2 × Ar*C*), 143.3 (2 × Ar*C*).

4-Methyl-*N*-(1-methyl-2-{[(4-methylphenyl)sulfonyl]amino}ethyl)benzenesulfonamide 16a. The title compound **16a** was prepared in a similar manner to **4** using (±)-1,2-propanediamine **15a** (2 cm^3, 1.74 g, 23.5 mmol), triethylamine (17 cm^3, 12.34 g, 122 mmol, 5.2 equiv.) and *p*-toluenesulfonyl chloride (10.00 g, 52.6 mmol mmol). The crude product was filtered through silica (6 × 5 cm^3) which gave a gum that was precipitated from ethanol using diethyl ether. Recrystallisation from ethanol gave the title compound **16a** as large long needles (7.73 g, 20.2 mmol, 86%); mp 106–108 °C (lit.[38] 103–104 °C). Found: C, 53.4; H, 5.8; N, 7.2; S, 16.7%; MH^+ 383.1099. Calculated for $C_{17}H_{22}N_2O_4S_2$: C, 53.4; H, 5.8; N, 7.3; S, 16.8%; MH^+ 383.1099. ν_{max} (KBr, cm^{-1}) 3303 (s, NHTs), 2925 (m, CH), 2978 (w, CH), 1598 (w, C_6H_4), 1322 (s, SO_2NH), 1159 (s, SO_2NH), 814 (s, C_6H_4); δ_H (400 MHz, $CDCl_3$) 0.97 (d, *J* 6.4 Hz, 3H, CH_3), 2.40 (s, 6H, 2 × H CH_3), 2.82–2.88 (m, 1H, C*H*H), 2.91–2.98 (m, 1H, CH*H*), 3.27–3.36 (m, 1H, C*H*), 5.23 (d, *J* 7.6, 1H, N*H*), 5.36 (d, *J* 6.4, 1H, N*H*), 7.25–7.28 (m, 4H, $C_6H_4CH_3$), 7.65–7.74 (m, 4H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$) 18.8 (CH_3), 21.6 (CH_3), 21.7 (CH_3), 48.5 (CH_2N), 49.7 (*C*HN), 127.2, 127.3, 129.9, 130.0 (all 2 × $C_6H_4CH_3$), 136.9 and 137.4 (both Ar*C*), 143.6 and 143.8 (both Ar*C*).

4-Methyl-*N*-(2-{[(4-methylphenyl)sulfonyl]amino}ethyl)benzenesulfonamide 16b. The title compound **16b** was prepared in a similar manner to **4** using ethylenediamine **15b** (3 cm^3, 44 mmol), triethylamine (32 cm^3, 0.224 mol) and *p*-toluenesulfonyl chloride (18.8 g, 98 mmol). Addition of diethyl ether gave a precipitate that was collected by filtration and washed with hexane. The crude product **16b** (12.60 g, 0.034 mol, 76%) was pure enough for the next step; mp 163–164 °C (lit.[24] 162–164 °C). Found: C, 52.1; H, 5.5; N, 7.8; S, 17.4%. Calculated for $C_{16}H_{20}N_2O_4S_2$: C, 52.2; H, 5.5; N, 7.6; S, 17.4%. ν_{max} (KBr, cm^{-1}) 3289 (s, TsNH), 3076

(w, C_6H_4), 2928, (m, CH), 2884 (m, CH), 1333, (s, SO_2NH), 1156 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$) 2.37 (s, 6H, $C_6H_4CH_3$), 2.70 (s, 4H, CH_2), 7.37 (d, *J* 8.0 Hz, 4H, C_6H_4), 7.60 (d, *J* 8.0, 4H, C_6H_4); ^{13}C NMR (CD_3SOCD_3) δ_C 21.4 ($C_6H_4CH_3$), 42.6 (CH_2N), 126.8, 130.1 (all $C_6H_4CH_3$), 137.7, 143.2 (both Ar*C*).

4-Methyl-*N*-((1*R*,2*R*)-2-{[(4-methylphenyl)sulfonyl]amino}-1,2-diphenylethyl)benzenesulfonamide 16c. The title compound **16c** was prepared according to the method of Corey *et al.*[39] using (1*R*,2*R*)-1,2-diphenyl-1,2-ethanediamine **15c** (1.08 g, 5.07 mmol), triethylamine (3.5 cm^3, 25.1 mmol), *N*,*N*-dimethylaminopyridine (25 mg, 0.2 mmol) and *p*-toluenesulfonyl chloride (2.18 g, 11.4 mmol). Recrystallisation from ethanol gave the title compound **16c** as fine white needles (2.35 g, 4.5 mmol, 89%); mp 209–210 °C (lit.[40] 202 °C); $[\alpha]_D = 40.5$ ($c = 1.76$, $CHCl_3$) (lit.[39] $[\alpha]_D = 43.9$ ($c = 1.74$, $CHCl_3$). Found: C, 64.8; H, 5.3; N, 5.6; S, 13.4%. Calculated for $C_{28}H_{28}N_2O_4S_2$: C, 64.6; H, 5.4; N, 5.4; S, 12.3%. δ_H (400 MHz, $CDCl_3$) 2.31 (s, 6H, 2 × $C_6H_4CH_3$), 4.51–4.56 (ABX m, 2H, 2 × C*H*NH), 5.89–5.95 (ABX m 2H, 2 × N*H*), 6.71 (d, *J* 8.0 Hz, 4H, $C_6H_4CH_3$), 6.99–7.05 (m, 10H, C_6H_5), 7.47 (d, *J* 8.0, 4H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$) 21.6 (2 × $C_6H_4CH_3$), 62.5 (2 × *C*HNH), 127.3 (4 × Ar*C*H), 127.7 (2 × Ar*C*H), 127.8 (4 × Ar*C*H), 128.2 (4 × Ar*C*H), 129.0 (4 × Ar*C*H), 136.5 (2 × Ar*C*), 137.2 (2 × Ar*C*), 143.3 (2 × Ar*C*). Using the chiral shift reagent Eu(hfc)$_2$ indicated an ee ⩾ 99%.

(1*R*,2*R*)-1,2-Cyclohexanediaminium (2*R*,3*R*)-2,3-dihydroxybutanedioate 14. The title compound **14** was prepared according to the method of Jacobsen and co-workers.[28] Thus, using (±)-1,2-cyclohexanediamine **9** (24 cm^3, 0.2 mol), L-tartaric acid (15.00 g, 0.1 mol) and glacial acetic acid (10 cm^3, 0.175 mol) gave the title compound **14** as a white solid (21.73 g, 82 mmol, 85%). An analytical sample was obtained by recrystallisation from water, which afforded colourless plates; mp 252.5–256 °C (lit.[40] 252–255 °C); $[\alpha]_D = +12.2$ ($c = 1$, H_2O) [lit.[23] $[\alpha]_D = +12.4$ ($c = 2$, H_2O)]. Found: C, 45.5; H, 7.6; N, 10.4%. Calculated for $C_{10}H_{20}N_2O_6$: C, 45.5; H, 7.6; N, 10.6%.

4-Methyl-*N*-((1*R*,2*R*)-2-{[(4-methylphenyl)sulfonyl]amino}cyclohexyl)benzenesulfonamide (*R*,*R*)-4. To a stirred solution of (1*R*,2*R*)-1,2-cyclohexanediaminium (2*R*,3*R*)-2,3-dihydroxybutanedioate **14** (11.20 g, 42.4 mmol) in distilled water (150 cm^3) and sodium hydroxide (7.10 g, 177.7 mmol) at 0 °C under a nitrogen atmosphere was added dropwise a solution of *p*-toluenesulfonyl chloride (16.99 g, 89.1 mmol) in dichloromethane (100 cm^3) over a 1 h period. The reaction mixture was allowed to warm to room temperature and then stirred for 18 h. At the completion of this period the phases were separated and the aqueous phase was extracted with dichloromethane (2 × 100 cm^3). The combined organic extracts were washed with brine (5 cm^3), dried (Na_2SO_4), filtered and evaporated to afford a white foam (20.54 g). Recrystallisation from methanol gave the title compound (15.30 g, 36.14 mmol, 85%) as a colourless microcrystalline solid; mp 172–184 °C (lit.[41] 167–168 °C); $[\alpha]_D = 12.2$ ($c = 2.04$, $CHCl_3$) [lit.[40] $[\alpha]_D = 9.76$ ($c = 2.06$, $CHCl_3$)]. Found: C, 57.0; H, 6.1; N, 6.8; S, 15.1%. Calculated for $C_{20}H_{26}N_2O_4S_2$: C, 56.9; H, 6.2; N, 6.6; S, 15.2%. ν_{max} (KBr, cm^{-1}) 3286 (s, TsNH), 3065 (w, C_6H_4), 2928 (m, CH), 2870 (m, CH), 1326 (s, SO_2NH), 1162 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$) 1.05–1.14 (m, 4H, 2 × CH_2), 1.53–1.55 (m, 2H, CH_2), 1.81–1.84 (m, 2H, CH_2), 2.42 (s, 6H, 2 × $C_6H_4CH_3$), 2.75–2.77 (m, 2H, 2 × ArSO$_2$NHC*H*), 4.95–5.00 (m, 2H, 2 × ArSO$_2$N*H*CH), 7.30 (d, *J* 8.3 Hz, 4H, 2 × $C_6H_4CH_3$), 7.75 (d, *J* 8.3, 4H, 2 × $C_6H_4CH_3$); δ_C (400 MHz, $CDCl_3$) 21.7 (2 × $C_6H_4CH_3$), 24.3 (2 × CCH_2C), 33.3 (2 × CCH_2C), 56.7 (2 × NH*C*H), 127.4 (4 × $C_6H_4CH_3$), 129.9 (4 × $C_6H_4CH_3$), 137.2 (2 × Ar*C*), 143.7 (2 × Ar*C*).

2-[[(4-Methylphenyl)sulfonyl](3-{[(4-methylphenyl)sulfonyl]oxy}propyl)amino]ethyl-4-methylbenzenesulfonate 5. The title compound was prepared according to the method of Searle and Geue[24] using diethanolamine (1.00 g, 9.5 mmol) and *p*-toluenesulfonyl chloride (4.00 g, 21 mmol) which gave a crude dark brown oil. Purification by column chromatography on silica (hexane–EtOAc–CH_2Cl_2 4 : 1 : 5) afforded a white solid (3.20 g, 5.7 mmol, 60%); mp 94–96 °C (lit.[24] 96–98 °C). Found: C, 53.1; H, 5.2; N, 2.5; S, 16.7%; MH^+ 568.1144. Calculated for $C_{25}H_{30}O_8S_3N$: C, 52.9; H, 5.2; N, 2.5; S, 16.9%; MH^+ 568.1134. ν_{max} (KBr, cm^{-1}) 3062 (w, C_6H_4), 2952 (m, CH), 1357 (s, SO_2NH), 1174 (s, SO_2OR), 1158 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$) 2.42 (s, 3H, $C_6H_4CH_3$), 2.47 (s, 6H, $C_6H_4CH_3$), 3.38 (t, *J* 5.9 Hz, 4H, CH_2NTs), 4.12 (t, *J* 5.9, 4H, CH_2OTs), 7.29 (d, *J* 8.0, 2H, $C_6H_4CH_3$); 7.35 (d, *J* 8.0, 4H, $C_6H_4CH_3$); 7.63 (d, *J* 8.0, 2H, $C_6H_4CH_3$); 7.78 (d, *J* 8.0, 4H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$) 21.7 ($C_6H_4CH_3$), 21.8 (2 × $C_6H_4CH_3$), 48.7 (2 × CH_2NTs), 68.5 (2 × CH_2OTs), 127.5 (2 × Ar*C*H), 128.2 (4 × Ar*C*H), 130.1 (4 × Ar*C*H), 130.2 (2 × Ar*C*H), 132.7 (2 × Ar*C*), 135.5 (Ar*C*), 144.4 (Ar*C*), 145.4 (2 × Ar*C*).

2-[[(4-Nitrophenyl)sulfonyl](2-{[(4-nitrophenyl)sulfonyl]oxy}ethyl)amino]ethyl 3-nitrobenzenesulfonate 18. To a stirred solution of diethanolamine (587 mg, 5.69 mmol) and triethylamine (2.8 cm^3, 20 mmol) in anhydrous THF (14 cm^3) at 0 °C under a nitrogen atmosphere was added portionwise, 4-nitrobenzenesulfonyl chloride (4.10 g, 18.7 mmol). This mixture was stirred at 0 °C for 1 h then at room temperature for 18 h. At the conclusion of this period the reaction mixture was concentrated at reduced pressure (20 mm Hg). The residue was dissolved in dichloromethane (20 cm^3), washed with water (25 cm^3), dried (Na_2SO_4), filtered and evaporated to afford an orange solid. Recrystallisation from methanol–THF gave the title compound **18** (2.42 g, 3.66 mmol, 65%) as colourless needles; mp 131–134 °C. Found: C, 40.1; H, 2.9; N, 8.3%; MNH_4^+ 678.0482. $C_{22}H_{20}N_4O_{14}S_3$ requires: C, 40.0; H, 3.0; N, 8.5%; MNH_4^+ 678.0476. ν_{max} (KBr, cm^{-1}) 3108 and 3041 (w, C_6H_4), 2936 (w, CH), 1530 (s, $C_6H_4NO_2$), 1366 (s, SO_2N), 1352 (s, OSO_2), 1312 (s), 1184 (s, SO_2); δ_H (400 MHz, CD_3NO_2) 3.54–3.62 (m, 4H, 2 × CH_2OSO_2), 4.23–4.31 (m, 4H, 2 × CH_2NSO_2), 8.01 (d, *J* 8.0 Hz, 2H, $C_6H_4SO_2N$), 8.13 (d, *J* 8.0, 4H, $NO_2C_6H_4SO_2O$), 8.34 (d, *J* 8.0, 2H, $NO_2C_6H_4SO_2N$), 8.44 (d, *J* 8.0, 4H, $NO_2C_6H_4SO_2O$); δ_C (100 MHz, CD_3NO_2) 49.1 (2 × CH_2NSO_2), 70.5 (4 × CH_2OSO_2), 125.9 (2 × C_6H_4), 126.0 (4 × C_6H_4), 130 (2 × C_6H_4), 130.8 (2 × C_6H_4), 142.1 (2 × Ar*C*), 145.5, 152 and 152.7 (all Ar*C*).

(±)-1,4,7-Tris[(4-methylphenyl)sulfonyl]dodecahydro-1*H*-1,4,7-benzotriazonine 3.

(a) Method A (potassium carbonate in DMF) (Table 1, entry 1). To (±)-4-methyl-*N*-(2-{[(4-methylphenyl)sulfonyl]amino}cyclohexyl) benzenesulfonamide **4** (600 mg, 1.4 mmol) in DMF (19 cm^3) was added potassium carbonate (461 mg, 3.3 mmol). The resulting suspension was heated to 50 °C for 1 h. On completion

of this period a solution of 2-[[(4-methylphenyl)sulfonyl]-(3-{[(4-methylphenyl)sulfonyl]oxy}propyl)amino]ethyl-4-methylbenzenesulfonate **5** (990 mg, 1.7 mmol) in DMF (10 cm^3) was added dropwise over 24 h. The DMF was removed under reduced pressure (12 mm Hg) and the residue was dissolved in dichloromethane (15 cm^3). The organic layer was washed with water (×2, 20 cm^3), dried (Na_2SO_4), filtered and evaporated to give a off-white solid (520 mg). The off-white solid was dissolved in ethanol (10 cm^3) and heated to reflux for 2 h. The white precipitate that formed was removed by filtration, washed with ethanol (10 cm^3) and dried under reduced pressure (0.1 mm Hg) to give the title macrocycle (±)-**3** as a white solid (162 mg, 0.25 mmol, 18%); mp 260–262 °C. Found: C, 57.7; H, 5.9; N, 6.2; S, 14.9%; MH^+ 646.2093. $C_{31}H_{39}O_6S_3N_3$ requires: C, 57.7; H, 6.1; N, 6.5; S, 14.9%; MH^+ 646.2079. ν_{max} (KBr, cm^{-1}) 3065 (w, C_6H_4), 2928 (m, CH), 2865 (m, CH), 1326 (s, SO_2NH), 1153 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$) 1.14 (m, 2H, CH_2), 1.27 (m, 2H, CH_2), 1.58 (m, 2H, CH_2), 1.79 (m, 1H, CH_2), 2.17 (m, 1H, CH_2), 2.35 (s, 3H, $C_6H_4CH_3$), 2.42 (s, 6H, $C_6H_4CH_3$), 2.62 (m, 1H, CH_2NTs), 3.07 (m, 1H, CH_2NTs), 3.28 (m, 3H, CH_2NTs), 3.48 (m, 3H, CH_2NTs), 3.75 (m, 1H, CHNTs), 4.89 (m, 1H, CHNTs), 7.29 (m, 6H, $C_6H_4CH_3$), 7.61 (d, *J* 8.3 Hz, 2H, $C_6H_4CH_3$), 7.76 (m, 2H, $C_6H_4CH_3$), 8.00 (m, 2H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$) 21.7 (3 × $C_6H_4CH_3$), 24.7 (CH_2), 26.1 (CH_2), 29.0 (CH_2), 30.3 (CH_2), 47.1 (CH_2NTs), 52.4 (CH_2NTs), 55.0 (CH_2NTs), 55.8 (CH_2NTs), 60.2 (CHNTs), 68.2 (CHNTs), 127.3 (2 × ArCH), 127.9 (2 × ArCH), 128.7 (2 × ArCH), 129.7 (2 × ArCH), 129.9 (4 × ArCH), 130.1 (2 × ArC), 135.1 (ArC), 137.5 (ArC), 143.6 (ArC), 144.2 (ArC).

(b) Method B (sodium ethoxide in ethanol then DMF) (Table 1, entry 2)[19a]. To a stirred suspension of (±)-4-methyl-*N*-(2-{[(4-methylphenyl)sulfonyl]amino}cyclohexyl)benzenesulfonamide **4** (500 mg, 1.2 mmol) in anhydrous ethanol (2 cm^3) at reflux under nitrogen was added a solution of sodium ethoxide (170 mg, 2.6 mmol) in ethanol (1 cm^3). The mixture became homogenous then a white precipitate formed which was diluted with a further portion of ethanol (10 cm^3). The resulting suspension was boiled for 30 min and then cooled to room temperature. The precipitate was collected by filtration and dried under high vacuum (0.1 mm Hg) which gave the crude disodium salt (491 mg, 1.05 mmol, 89%) a white papery solid.

The above disodium salt (491 mg, 1.05 mmol) was suspended in anhydrous DMF (7 cm^3) under a nitrogen atmosphere and heated to 100 °C. To this suspension was added a solution of 2-[[(4-methylphenyl)sulfonyl](3-{[(4-methylphenyl)sulfonyl]oxy}-propyl)amino]ethyl-4-methylbenzenesulfonate **5** (719 mg, 1.27 mmol) in DMF (3.5 cm^3) over a 4 h period. The resulting solution was stirred at 100 °C for 7 days, whereupon, the volatiles were removed (0.1 mm Hg). The residue was partitioned between dichloromethane (10 cm^3) and dilute hydrochloric acid (0.23 M, 13 cm^3) and the layers were separated. The aqueous phase was extracted with dichloromethane (2 × 10 cm^3) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated to afford an oil. This oil was dissolved in ethanol (10 cm^3) under a nitrogen atmosphere and this solution was heated under reflux for 2 h to afford a white solid. Filtration afforded the title macrocycle (±)-**3** as a white microcrystalline solid (153 mg, 0.24 mmol, 23%). The physical and spectroscopic properties were identical to those reported above.

(±)-2-Methyl-1,4,7-tris[(4-methylphenyl)sulfonyl]-1,4,7-triazacyclononane 17a.

(a) Method C (sodium hydride in DMF) (Table 1, entry 3). To a stirred solution of the 4-methyl-*N*-(1-methyl-2-{[(4-methylphenyl)sulfonyl]amino}ethyl)benzenesulfonamide **16a** (300 mg, 0.79 mmol) and 2-[[(4-methylphenyl)sulfonyl](3-{[(4-methylphenyl)sulfonyl]oxy}propyl)amino]ethyl-4-methylbenzenesulfonate **5** (443 mg, 0.78 mmol) in DMF (7 cm^3) at 60 °C was added a suspension of hexane washed sodium hydride (60% in oil, 65 mg, 1.63 mmol) in DMF (2 cm^3) over a 3 h period. The reaction mixture was then brought to 80 °C and maintained at that temperature for a further 2 days. At the completion of this period the volatiles were removed (12 mm Hg) and the residue was dissolved in ethyl acetate (15 cm^3). This solution was washed with water (2 × 15 cm^3), dried (Na_2SO_4), filtered and evaporated to afford an oil. Purification by column chromatography using ethyl aceate–hexane (2 : 3) as the eluant afforded an oil that precipated the title macrocycle from hot ethanol as a white solid (47 mg, 0.08 mmol, 10%). The physical and spectroscopic data were identical to those reported below using method E.

(b) Method E (lithium hydride in DMF) (Table 1, entry 8). To a stirred suspension of lithium hydride (17 mg, 2.2 mmol) in anhydrous DMF (10 cm^3) at 0 °C was added a solution of 4-methyl-*N*-(1-methyl-2-{[(4-methylphenyl)sulfonyl]amino}ethyl)-benzenesulfonamide **16a** (820 mg, 2.15 mmol) in DMF (2 cm^3) over a 20 min period. The resulting mixture was warmed to room temperature, whereupon, a solution of 2-[[(4-methylphenyl)-sulfonyl](3-{[(4-methylphenyl)sulfonyl]oxy}propyl)amino]ethyl-4-methylbenzenesulfonate **5** (1.217 g, 2.1 mmol) in DMF (2 cm^3) was added dropwise over 1 h. The cloudy suspension was then heated to 80 °C and the final aliquot of lithium hydride (17 mg, 2.2 mmol) was added to the now homogeneous solution. The reaction was stirred at 80 °C for 5 days and at the completion of this period was cooled to room temperature and quenched by addition of water (15 cm^3). The volatiles were removed under reduced pressure (0.5 mm Hg) and the residue was dissolved in dichloromethane (25 cm^3). The organic layer was washed with water (15 cm^3) then brine (15 cm^3) and dried (Na_2SO_4), filtered and evaporated. The resulting yellow oil was dissolved in ethanol (8 cm^3) and heated to reflux for 2 h. Slow crystallisation from this solution over several days gave the title macrocycle as a white microcrystalline solid (784 mg, 1.3 mmol, 60%). An analytically pure sample was obtained by recrystallisation from $CHCl_3$–MeOH which gave microcrystalline white pellets; mp 203–205 °C (lit.[18d] 193–194 °C). Found: C, 55.3; H, 5.8; N, 6.8; S, 15.6%; MH^+ 606.1766. $C_{28}H_{35}N_3O_6S_3$ requires: C, 55.5; H, 5.8; N, 6.9; S, 15.9%; MH^+ 606.1766. ν_{max} (KBr, cm^{-1}) 3029 (w, C_6H_4), 2928 (w, CH), 1339 (s, SO_2NH), 1158 (s, SO_2NH), 816 (w, C_6H_4); δ_H (400 MHz, $CDCl_3$) 0.78 (d, *J* 5.2 Hz, 3H, CH_3CH), 2.43 (s, 9H, 3 × $C_6H_4CH_3$), 3.09–3.19 (m, 3H, CH_2), 3.31–3.39 (m, 3H, CH_2), 3.49–3.53 (m, 1H, CH_2), 3.62–3.68 (m, 3H, CH_2), 4.40–4.53 (m, 1H, CH_2CH), 7.29–7.37 (m, 6H, $C_6H_4CH_3$), 7.62 (d, *J* 8.4, 2H, $C_6H_4CH_3$), 7.75 (d, *J* 8.0, 2H, $C_6H_4CH_3$), 7.78 (d, *J* 8.4, 2H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$) 14.6 (CH_3CH), 21.7 (3 × $C_6H_4CH_3$), 45.8 (NCH_2), 50.8 (NCH_2), 53.3 (NCH_2), 54.0 (NCH_2), 54.3 (NCH_2), 55.3 (NCH), 127.5 (2 × $C_6H_4CH_3$), 127.6 (2 × $C_6H_4CH_3$), 127.8 (2 × $C_6H_4CH_3$), 130.0 (4 × $C_6H_4CH_3$), 130.1 (2 × $C_6H_4CH_3$), 134.5, 135.2, 136.8 (all ArC), 143.8 (2 × ArC), 144.3 (ArC).

1,4,7-Tris[(4-methylphenyl)sulfonyl]-1,4,7-triazacyclononane 17b.

Method E (lithium hydride in DMF) (Table 1, entry 7). To a stirred suspension of lithium hydride (33 mg, 4.18 mmol) in anhydrous DMF (15 cm^3) was added 4-methyl-*N*-(2-{[(4-methylphenyl)sulfonyl]amino}ethyl)benzenesulfonamide **16b** (731 mg, 1.98 mmol) under a nitrogen atmosphere. The resulting mixture was heated to 70 °C for 2 h, whereupon, it was cooled to 50 °C. A solution of 2-[[(4-methylphenyl)sulfonyl](3-{[(4-methylphenyl)sulfonyl]oxy}propyl)amino]ethyl-4-methylbenzenesulfonate **5** (1.24 g, 2.18 mmol) in DMF (3.6 cm^3) was added dropwise over a 2.5 h period. The reaction mixture was maintained at 50 °C for 5 days, whereupon, it was cooled to room temperature. Water (5 cm^3) was added and the volatiles were removed *in vacuo* (0.5 mm Hg). The resulting residue was dissolved in dichloromethane (25 cm^3). and washed with water (15 cm^3) then brine (15 cm^3) and dried (Na_2SO_4), filtered and evaporated. The resulting oil was suspended in ethanol (15 cm^3) and heated to reflux for 2 h under a nitrogen atmosphere which afforded the title compound **17b** as a white solid (1.07 g, 1.8 mmol, 91%). An analytical sample was obtained by recrystallisation from $CHCl_3$–MeOH which gave fine white needles; mp 222–223 °C (lit.[24] 218–220 °C). Found: C, 54.5; H, 5.6, N, 7.0; S, 16.0%; MH^+ 592.1609. $C_{27}H_{33}N_3O_6S_3$ requires: C, 54.8; H, 5.6; N, 7.1; S, 16.3%; MH^+ 592.1609. ν_{max} (KBr, cm^{-1}) 2927 (w, CH), 1336 (s, SO_2NH), 1322 (m), 1161 (s, SO_2NH), 817 (w, C6H4); δ_H (400 MHz, $CDCl_3$) 2.41 (s, 9H, 3 × $C_6H_4CH_3$), 3.46 (s, 12H, 6 × NCH_2), 7.31 (d, *J* 8.0 Hz, 6H, $C_6H_4CH_3$), 7.69 (d, *J* 8.0, 6H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$), 21.7 (3 × $C_6H_4CH_3$), 52.0 (6 × NCH_2), 127.6 (6 × $C_6H_4CH_3$), 130.0 (6 × $C_6H_4CH_3$), 134.8 (3 × Ar*C*), 144.0 (3 × Ar*C*).

(7a*R*,11a*R*)-1,4,7-Tris[(4-methylphenyl)sulfonyl]dodecahydro-1*H*-1,4,7-benzotriazonine 3.

Method E (lithium hydride in DMF) (Table 1, entry 10). The title compound (1*R*,2*R*)-**3** was prepared in a similar manner to **17b** *via* method E using (1*R*,2*R*)-4-methyl-*N*-(2-{[(4-methylphenyl)sulfonyl]amino}cyclohexyl)benzenesulfonamide **4** (2.70 g, 6.4 mmol) and 2-[[(4-methylphenyl)sulfonyl](3-{[(4-methylphenyl)sulfonyl] oxy}propyl)amino]ethyl-4-methylbenzenesulfonate **5** (4.00 g, 7 mmol) which afforded the title macrocycle as a white solid (2.81 g, 0.25 mmol, 68%); mp 301–302 °C (lit.[19c] 294–295 °C); Found: C, 57.7; H, 6.1; N, 6.5; S, 14.9%; MH^+ 646.2086. $C_{31}H_{39}O_6S_3N3$ requires: C, 57.7; H, 6.1; N, 6.5; S, 14.9%; MH^+ 646.2079; $[\alpha]_D = -63.4$ (*c* = 1, $CHCl_3$) [lit.[19c] $[\alpha]_D = -53.9$ (*c* = 1, CH_2Cl_2)]. ν_{max} (KBr, cm^{-1}) 3065 (w, C_6H_4), 2928 (m, CH), 2865 (m, CH), 1326 (s, SO_2NH), 1153 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$) 1.11 (m, 2H, CH_2), 1.26 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), 1.76 (m, 1H, CH_2), 2.16 (m, 1H, CH_2), 2.35 (s, 3H, $C_6H_4CH_3$), 2.41 (s, 6H, $C_6H_4CH_3$), 2.59 (m, 1H, CH_2NTs), 3.11 (m, 1H, CH_2NTs), 3.27 (m, 3H, CH_2NTs), 3.49 (m, 3H, CH_2NTs), 3.75 (m, 1H, C*H*NTs), 4.89 (m, 1H, C*H*NTs), 7.29 (m, 6H, $C_6H_4CH_3$), 7.61 (d, *J* 8.3 Hz, 2H, $C_6H_4CH_3$), 7.76 (m, 2H, $C_6H_4CH_3$), 8.00 (m, 2H, $C_6H_4CH_3$); δ_C (100 MHz, $CDCl_3$) 21.7 (3 × $C_6H_4CH_3$), 24.7 (CH_2), 26.1 (CH_2), 29.0 (CH_2), 30.3 (CH_2), 47.1 (CH_2NTs), 52.4 (CH_2NTs), 55.0 (CH_2NTs), 55.8 (CH_2NTs), 60.2 (*C*HNTs), 68.2 (*C*HNTs), 127.3 (2 × Ar*C*H), 127.9 (2 × Ar*C*H), 128.7 (2 × Ar*C*H), 129.7 (2 × Ar*C*H), 129.9 (4 × Ar*C*H), 130.1 (2 × Ar*C*), 135.1 (Ar*C*), 137.5 (Ar*C*), 143.6 (Ar*C*), 144.2 (Ar*C*).

(±)-1,7-Bis[(4-methylphenyl)sulfonyl]-4-[(4-nitrophenyl)-sulfonyl]dodecahydro-1*H*-1,4,7-benzotriazonine 19.

Method E (lithium hydride in DMF) (Table 1, entry 11). The title compound **19** was prepared in a similar manner to **17b** *via* method E using (±)-4-methyl-*N*-(2-{[(4-methylphenyl)-sulfonyl]amino}cyclohexyl)benzenesulfonamide **4** (306 mg, 0.72 mmol) and 2-[[(4-nitrophenyl)sulfonyl](2-{[(4-nitrophenyl)-sulfonyl]oxy}ethyl)amino]ethyl 3-nitrobenzenesulfonate **18** (521 mg, 0.79 mmol) which afforded the title compound **19** as a white solid (279 mg, 0.41 mmol, 57%). An analytical sample was obtained by column chromatography using alumina (grade III) using dichloromethane as the eluant which gave a white microcrystalline solid; mp 262–264 °C. Found: C, 53.5; H, 5.4; N, 7.9%; MH^+677.1767. Calculated for $C_{30}H_{36}N_4O_8S_3$: C, 53.2; H, 5.4; N, 8.3%; MH^+ 677.1773. ν_{max} (KBr, cm^{-1}) 2930 (w, CH), 1599 (w, Ar), 1531 (s, $ArNO_2$), 1352 (s, $ArNO_2$), 1331 (s, SO_2NH), 1158 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$) 1.09–1.19 (m, 2H, CH_2), 1.21–1.42 (m, 3H, CH_2), 1.52–1.56 (m, 1H, CH_2), 1.72–1.80 (m, 1H, CH_2), 2.04–2.14 (m, 1H, CH_2), 2.39 (s, 3H, $C_6H_4CH_3$), 2.42 (s, 3H, $C_6H_4CH_3$), 2.73–2.85 (m, 1H, CH_2NTs), 3.18–3.35 (m, 4H, CH_2NTs), 3.44–3.59 (m, 3H, CH_2NTs 3.72–3.75 (m, 1H, C*H*NTs), 4.79–4.80 (m, 1H, C*H*NTs), 7.23–7.36 (m, 4H, $C_6H_4SO_2$), 7.23–7.36 (m, 4H, $C_6H_4CH_3$), 7.75 (d, *J* 6.0 Hz, 2H, $C_6H_4SO_2$), 7.92–8.01 (m, 2H, $C_6H_4SO_2$) 7.91 (d, *J* 8.4, 2H, $C_6H_4SO_2$), 8.29 (d, *J* 8.4, 2H, $C_6H_4NO_2$); δ_C (100 MHz, $CDCl_3$) 21.6 (2 × $C_6H_4CH_3$), 24.6 (CH_2) 26.0 (CH_2), 28.9 (CH_2), 30.2 (CH_2), 46.9 (NCH_2), 52.5 (NCH_2), 55.4 (NCH_2), 55.7 (NCH_2), 60.3 (N*C*H), 68.2 (N*C*H), 124.7 (4 × $C_6H_4SO_2$), 127.7 ($C_6H_4SO_2$), 128.5 ($C_6H_4SO_2$) 128.6 (4 × $C_6H_4SO_2$), 129.7 ($C_6H_4SO_2$), 129.9 ($C_6H_4SO_2$), 137.2 (Ar*C*), 138.2 (Ar*C*), 143.4 (2 × Ar*C*), 143.8 (Ar*C*), 150.4 (Ar*C*).

Deprotection and *N*-methylation

(7a*R*,11a*R*)-Dodecahydro-1*H*-1,4,7-benzotriazonine trihydrochloride 20. To a solution of 1,4,7-tris[(4-methylphenyl)-sulfonyl]dodecahydro-1*H*-1,4,7-benzotriazonine (*R*,*R*)-**3** (1.00 g, 1.5 mmol) in THF (25 cm^3) and EtOH (4.8 cm^3, 84 mmol) was condensed dry NH_3 (200 cm^3) at −78 °C. To this solution was added lithium metal (542 mg, 77 mmol) in small portions to give an intense blue colour. The reaction mixture was allowed to warm to room temperature overnight. Water was added (10 cm^3) and the solution was acidified (pH 1) with conc. HCl (1 cm^3). The aqueous solution was extracted with dichloromethane (×2, 10 cm^3). The aqueous phase was made basic (pH 14) by addition of solid NaOH (*ca.* 500 mg). The basic solution was extracted with dichloromethane (×4, 10 cm^3) and the combined organic phases were dried (Na_2SO_4), filtered and evaporated to give a crude dark yellow oil (310 mg). The yellow oil was dissolved in methanol (2 cm^3) and conc. HCl (0.08 cm^3) was added dropwise at room temperature with rapid stirring. To this solution was added diethyl ether (8 cm^3) and the white precipitate that formed was removed by filtration and dried under reduced pressure to give the crude hydrochloride salt (297 mg, 1.1 mmol, 73%); mp 176–178 °C (lit.[19c] 240 °C (decomp.). Found: C, 40.6; H, 8.6; N, 13.1%; $(MH - 3HCl)^+$ 184.1815. $C_{10}H_{21}N_3{\cdot}MeOH$ requires: C, 40.7; H, 8.7; N, 12.9%; $(MH - 3HCl)^+$ 184.1813; $[\alpha]_D$ −122 (*c* = 0.135, H_2O) (lit.[19c] $[\alpha]_D = -55.6$ (*c* = 0.4, H_2O). ν_{max} (KBr, cm^{-1}) 3419 (w, NH); 2943 (s, CH), 2862 (s, CH), 2778

(s, CH); δ_H (400 MHz, D_2O) 1.31 (m, 2H, CH_2), 1.50 (m, 2H, CH_2), 1.82 (m, 2H, CH_2), 2.10 (m, 2H, CH_2), 3.13 (m, 2H, $NHCH_2$), 3.31 (m, 6H, $NHCH_2$), 3.41 (m, 2H, NHCH); δ_C (100 MHz, CD_3OD) 24.3 (2 × CH_2), 29.7 (2 × CH_2), 39.7 (2 × $NHCH_2$), 43.2 (2 × $NHCH_2$), 57.7 (2 × NHCH).

(7a*R*,11a*R*)-1,4,7-Trimethyldodecahydro-1*H*-1,4,7-benzotriazonine 1. (7a*R*,11a*R*)-Dodecahydro-1*H*-1,4,7-benzotriazonine trihydrochloride (*R*,*R*)-**20** (305 mg, 1.04 mmol) was dissolved in water (20 cm^3) and the solution was made basic (pH 14) by the addition of solid NaOH (*ca.* 250 mg). The basic solution was extracted with dichloromethane (×4, 10 cm^3) and the combined organic phases were dried (Na_2SO_4), filtered and evaporated to give a pale yellow oil. To this oil was added formaldehyde (38%, 0.8 cm^3) and formic acid (90%, 0.9 cm^3) and the solution was heated to reflux (bath temp. 90 °C) under a nitrogen atmosphere for 20 h. After cooling to room temperature the reaction was acidified (pH 1) with conc. HCl (1 cm^3) and the volatiles were removed under reduced pressure. The aqueous solution was extracted with dichloromethane (×2, 10 cm^3). The aqueous phase was made basic (pH 14) by addition of solid NaOH (*ca.* 250 mg). The basic solution was extracted with dichloromethane (×4, 10 cm^3), and the combined organic phases were dried (Na_2SO_4), filtered and evaporated to give a pale yellow oil (185 mg, 0.82 mmol, 79%). Found: MH^+ 226.2280. Calculated for $C_{13}H_{27}N_3$ MH^+: 226.2283; $[a]_D$ −48.8 (c = 0.5, $CHCl_3$). ν_{max} (liq. film, cm^{-1}) 2933 (m, CH), 2857 (m, CH), 2791 (m, CH), 1666 (s), 1451 (s, CH), 732 (s, CH_2); δ_H (400 MHz, $CDCl_3$) 1.05 (m, 4H, CH_2), 1.63 (m, 2H, CH_2), 1.73 (m, 2H, CH_2), 2.29 (s, 9H, NCH_3), 2.48 (m, 6H, NCH_2), 2.60 (m, 2H, NCH_2) 2.95 (m, 2H, NCH); δ_C (100 MHz, $CDCl_3$) 25.2 (2× CH_2), 27.0 (2× CH_2), 40.2 (2 × NCH_3), 46.8 (NCH_3), 54.4 (2× NCH_2), 54.8 (2× NCH_2), 63.6 (2 × NCH).

Copper(II) complex formation

To a solution of copper(II) chloride (162 mg, 1.2 mmol) in anhydrous acetonitrile (20 cm^3) under a nitrogen atmosphere was added a solution of (7a*R*,11a*R*)-1,4,7-trimethyldodecahydro-1*H*-1,4,7-benzotriazonine **1** (271 mg, 1.2 mmol) in acetonitrile (5 cm^3). The resulting green solution was stirred under nitrogen for 90 min, whereupon, it was diluted with acetonitrile (50 cm^3), and a solution of silver trifluoroacetate (530 mg, 2.4 mmol) in acetonitrile (10 cm^3) was added. The now bright blue solution was stirred for 1 h giving a precipitate of silver(II) chloride. The reaction mixture was filtered through Celite and the solvent was evaporated to afford a blue solid. Recystallisation from acetone–diethyl ether gave the title compound as blue rhomboid crystals (328 mg, 0.64 mmol, 53%) that were suitable for X-ray crystallography. Mp 211 °C (decomp.) Found: C, 39.4; H, 5.3; N, 8.1%. Calculated for $C_{17}H_{27}CuF_6N_3O_4$: C, 39.6; H, 5.3; N, 8.2%. ν_{max} (KBr, cm^{-1}) 2943 (m, CH), 2859 (w, CH), 1705 (s), 1690 (s), 1422 (s), 1204 (s), 1180 (s), 1126 (s), 723 (s); λ_{max} [CH_3CN, nm (ε)] 284 (4806), 548 (28), 652 (88).

Aziridination of styrene 24

A mixture of [*N*-(4-tolylsulfonyl)imino]phenyliodinane[42] (112 mg, 0.3 mmol) and complex **22** (8 mg, 15 μmol, 5 mol%) in acetonitrile (2 cm^3) under a nitrogen atmosphere was stirred for 2 h until a homogeneous solution resulted. Styrene (0.35 cm^3, 3 mmol) was added and the reaction mixture was stirred for 72 h. The resulting mixture was filtered through alumina using ethyl acetate as the eluant. Evaporation of the solvent and recrystallisation from diethyl ether–hexane at −20 °C afforded 1-[(4-methylphenyl)sulfonyl]-2-phenylaziridine **25** as an off-white solid (40 mg, 0.15 mmol, 49%) mp 86–88 °C (lit.[17] 88–90 °C). Found: MH^+ 274.0903. $C_{15}H_{15}NO_2S$ requires:MH^+ 274.0902. ν_{max} (KBr, cm^{-1}) 3359 (w, NHTs), 3042 (m, NH), 2977 (w, CH), 1316 (s, SO_2NH), 1154 (s, SO_2NH); δ_H (400 MHz, $CDCl_3$) 2.43 (d, J 4.5 Hz, 1H, CHH), 2,47 (s, 3H, $C_6H_4CH_3$), 3.02 (d, J 7.2, 1H, CHH), 3.82 (dd, J 7.2, 4.5, 1H, CHPh), 7.25–7.38 (m, 7H, ArCH), 7.91 (d, J 8.3, 2H, C_6H_4); δ_C (100 MHz, $CDCl_3$) 21.9 ($C_6H_4CH_3$) 36.1 (CH_2), 41.3 (CH), 126.8 (2 × ArCH), 128.2 (2 × ArCH), 128.5 (ArC), 128.8 (ArCH), 130.0 (2 × ArCH), 135.3 (ArC), 144.8 (ArC). Chiral HPLC indicated that the two enatiomeric products were formed in a 1 : 1 ratio; t_R = 11.45 min and 13.98 min

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