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Synthesis of Tetrahydroisoquinolines *via* Intramolecular Electrophilic Aromatic Substitution Reactions of Pummerer-derived Substituted *N*-Benzyl-*N*-tosyl-α-aminothionium Ions

Donald Craig* and Kevin Daniels

Department of Chemistry, Imperial College of Science, Technology and Medicine, London SW7 2AY, U.K.

A. Roderick MacKenzie

Pfizer Central Research, Sandwich, Kent CT13 9NJ, U.K.

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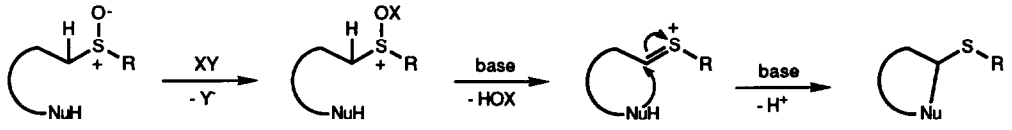
This paper is dedicated with respect and affection to Professor Charles W. Rees FRS on the occasion of his sixty-fifth birthday.

Abstract: Conjugate addition to (phenylsulfinyl)ethene **1** of substituted benzylic amines **2** followed by *N*-tosylation gives substituted *N*-benzyl-*N*-tosyl-2-amino-1-(phenylsulfinyl)ethanes **3**. Treatment of **3** with trimethylsilyl trifluoromethanesulfonate–Hünig's base gives 4-(phenylsulfenyl)-*N*-tosyl-1,2,3,4-tetrahydroisoquinolines **4** *via* presumed intramolecular trapping of Pummerer-derived substituted *N*-benzyl-*N*-tosyl-α-aminothionium ions **5**.

INTRODUCTION

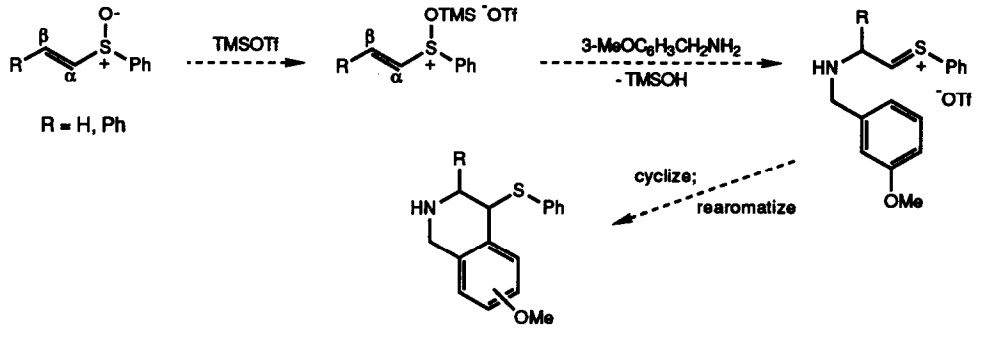
The Pummerer reaction continues to attract substantial research effort.[1] In particular, Pummerer-based transformations are finding widespread application in carbo- and heterocyclic synthesis, by reaction of the intermediate thionium ions (α-thiocarbocations) with internally-disposed nucleophiles (Scheme 1).



Scheme 1

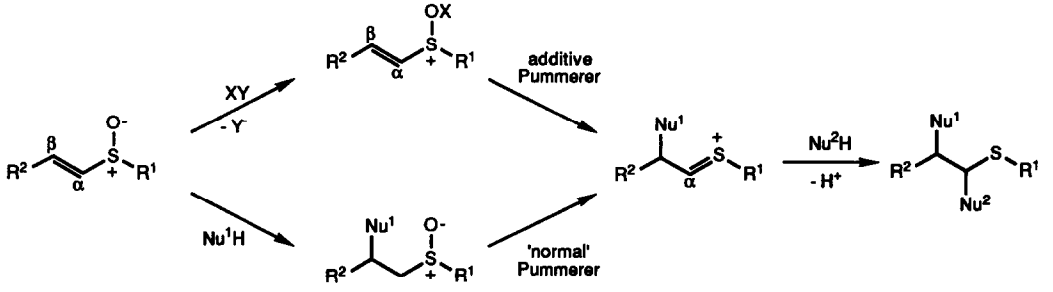
The related additive Pummerer reaction[2] of vinylic sulfoxides involves formation of the electrophilic thionium intermediate *via* nucleophilic attack at the β-position of the *O*-activated substrate. This then suffers attack by a second nucleophile at the newly electrophilic α-position to give an α,β-disubstituted thioether. In the additive mode, the Pummerer reaction confers thioether α,β-dication equivalence on the vinylic sulfoxide substrate.[3] In connection with our studies on carbon–heteroatom bond-forming reactions using additive

Pummerer processes,[4] we examined the trimethylsilyl trifluoromethanesulfonate (TMSOTf)-mediated reaction of *m*-methoxybenzylamine with vinylic sulfoxides. We anticipated that activation of the vinylic sulfoxide C-C double bond *via* sulfoxide *O*-silylation would be followed by intermolecular addition of the amine giving the intermediate thionium ion. This would then undergo intramolecular cyclization *via* nucleophilic addition of the aromatic nucleus to the electrophilic α-centre (Scheme 2). Disappointingly, all attempts to realize this plan met with failure: addition of *m*-methoxybenzylamine to equimolar mixtures of vinylic sulfoxide and TMSOTf in dichloromethane under a variety of reaction conditions resulted invariably in the recovery of starting materials.



Scheme 2

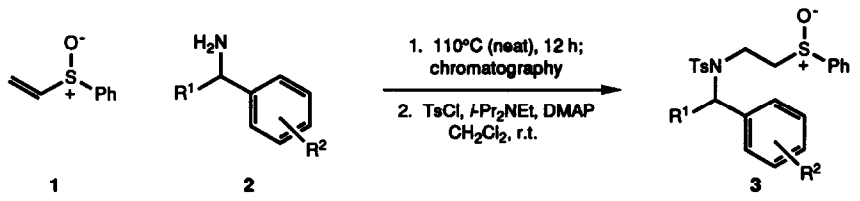
An alternative to the additive Pummerer strategy is sequential, uncatalyzed intermolecular nucleophilic addition to a vinylic sulfoxide, and intramolecular Pummerer reaction of the saturated sulfoxide so formed. Such a sequence would give the products of nucleophilic attack at the electrophilic α- and β-positions of a thioether dication synthon, in an overall formal additive Pummerer process (Scheme 3). It occurred to us that tetrahydroisoquinolines might be accessible *via* Pummerer-mediated cyclization reactions of vinylic sulfoxide–benzylic amine adducts. Applications of this general strategy have recently been reported in the context of isoquinolone[5] and furan[6] synthesis. We describe herein the results of our own investigations into the synthesis of *N*-tosyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinolines *via* a nucleophilic addition–Pummerer reaction sequence, starting from (phenylsulfinyl)ethene and benzylic amines.



Scheme 3

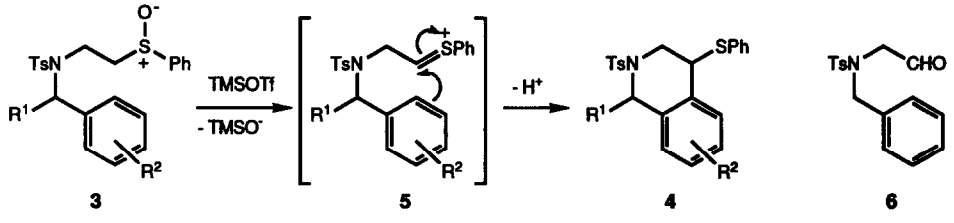
RESULTS AND DISCUSSION

Our investigations began with an examination of the addition reaction to (phenylsulfinyl)ethene **1** of benzylamine **2a**. Primary[5] and secondary[7,8] amines have been reported to add readily to α,β-unsaturated sulfoxides. In contrast with these apparently facile additions, in our hands the yield of the desired adduct was maximized by heating an equimolar mixture of the reactants *in the absence of solvent* at 110°C overnight. *N*-Tosylation of the resultant secondary amine followed by chromatography to remove traces of the addition product of **2a** to two equivalents of **1** gave cyclization substrate **3a** in good overall yield for the two-step sequence from **1** and **2a**. Substrates **3b** - **3h** were similarly prepared in good yield (Scheme 4, Table).



Scheme 4

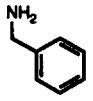
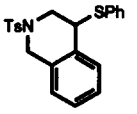
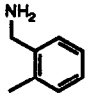
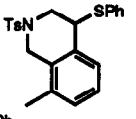
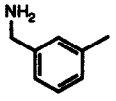
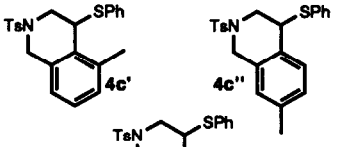
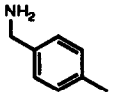
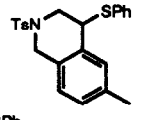
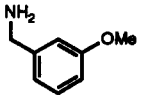
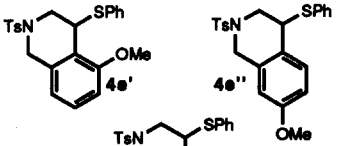
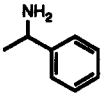
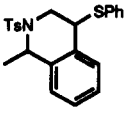
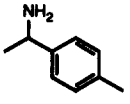
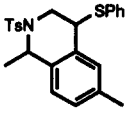
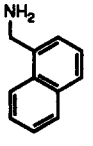
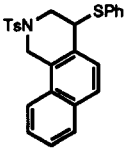
With a convenient route established to the Pummerer substrates **3**, attention was turned to their cyclization reactions. Extensive experimentation established that the best yields of bicyclic products **4** were obtained by using 2.2 equivalents each of TMSOTf and Hünig's base.[9] The use of smaller quantities of TMSOTf resulted in incomplete reaction; this may be rationalized in terms of reaction with unconsumed TMSOTf of the $TMSO^-$ group generated subsequent to *O*-silylation during formation of the electrophilic thionium species **5** (Scheme 5). The use of trifluoroacetic anhydride (TFAA) in place of TMSOTf for the cyclization reaction of **3a** gave the Pummerer-derived aldehyde **6** in 86% yield. Attempted Pummerer-mediated cyclization reactions of the *N*-unprotected analogue of **3e** gave a lower yield of the corresponding 4-(phenylsulfenyl)tetrahydroisoquinoline.



Scheme 5

For substrates **3c** and **3e**, the cyclization reactions showed modest selectivity for the products **4** corresponding to intramolecular electrophilic aromatic substitution *para*- to the electron-releasing methyl or methoxy substituent. In examples **f** and **g**, highly diastereoselective cyclization was observed.[10] Exposure to

Table. Preparation and Pummerer-mediated Cyclization of Substituted *N*-Benzyl-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethanes.

Entry	Amine 2	Yield of 3[a,b]	Products 4	Yield of 4	Ratio of 4':4''[c]
a		69		37	-
b		69		79	-
c		60		97	1 : 4
d		62		71	-
e		72		92	1 : 2.9
f		53		81	10 : 1[d]
g		59		88	>20 : 1[d]
h		59		86	-

[a] All yields cited herein are for isolated, pure materials, characterized by ^{1}H nmr, ir and ms analysis, and by elemental combustion analysis.

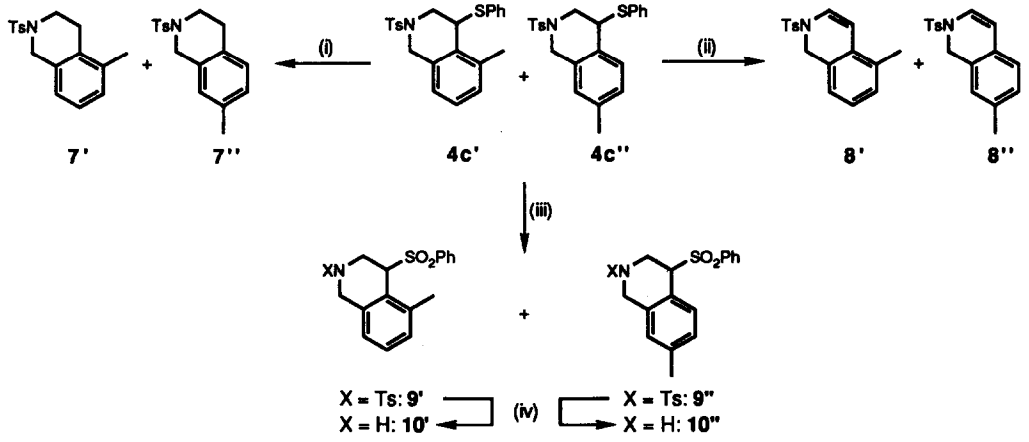
[b] Yields of 3 are for the two steps from 1 and 2.

[c] Where applicable; determined by ^{1}H nmr.

[d] Ratio of diastereomers.

the reaction conditions of substrates **3** possessing methoxy substituents *ortho-* or *para-* to the nitrogen-containing side-chain , or a *meta-* chlorine atom gave complex product mixtures. The cyclization reactions of **3** are summarized in the Table.

We have investigated a number of derivatization reactions of the bicyclic products **4** of these Pummerer-mediated cyclization reactions. The regioisomeric mixture **4c** was smoothly desulfurized using Raney nickel[11] to give the *N*-tosyl-1,2,3,4-tetrahydroisoquinolines **7**. Alternatively, *S*-oxidation followed by thermally-induced *syn*-elimination[12] of the resultant crude sulfoxides gave *N*-tosyl-1,2-dihydroisoquinolines **8** in good overall yield for the two-step sequence from **4c**. Oxidation of **4c** with an excess of peracetic acid gave the disulfonyl compounds **9**, which were efficiently converted into the corresponding free 4-(phenylsulfonyl)-1,2,3,4-tetrahydroisoquinolines **10** by the action of HBr–phenol in acetic acid[13] (Scheme 6).



Reagents and conditions: (i) Ni(R), EtOH, reflux, 1 h; (ii) CH_3CO_3H (1 eq.), NaOAc (1 eq.), CH_2Cl_2, 0°C, 5 min, then PhMe, reflux, 15 min; (iii) CH_3CO_3H (2.2 eq.), NaOAc (2.2 eq.), CH_2Cl_2, r.t., 12 h; (iv) PhOH (3 eq.), 30 wt. % HBr–AcOH (30 eq.), 70°C, 8 h (92% yield).

Scheme 6

CONCLUSIONS

The work described herein demonstrates that the conjugate addition–intramolecular Pummerer strategy is an efficient, versatile and convenient method for the synthesis of sulphur-substituted tetrahydro- and dihydroisoquinolines with varying degrees of substitution in the aromatic nucleus. We are currently exploring modified sequences using α- and β-branched vinylic sulfoxides in conjunction with more reactive nitrogen nucleophiles for the preparation of more highly substituted isoquinoline derivatives. The results of these studies will be reported in due course.

ACKNOWLEDGEMENTS

We thank the SERC and Pfizer Central Research (CASE award to K. D.) for financial support of this research.

EXPERIMENTAL

^{1}H Nmr spectra were recorded in $CDCl_3$ using a Jeol QX-270 nmr spectrometer. Infra-red spectra were recorded on a Perkin-Elmer 881 spectrophotometer. Mass spectra were obtained using VG-7070B or Jeol SX-102 instruments. Elemental combustion analyses were performed in the Imperial College Chemistry Department microanalytical laboratory. Melting points were measured on a Reichert hot stage apparatus and are uncorrected. Chromatography refers to column chromatography on Merck Kieselgel 60 (230-400 mesh) under pressure unless otherwise stated. DCM Refers to dichloromethane, ether to diethyl ether and petrol to redistilled petroleum ether, bp 40-60°C. (Phenylsulfinyl)ethene **1**, amines **2a-f** and **2h** and 4-methylacetophenone were purchased from Aldrich Chemical Co. Where appropriate all solvents and reagents were purified before use according to standard procedures.[14]

Preparation of (±)-α,4-dimethylbenzylamine (2g). To a solution of 4-methylacetophenone (2g, 14.9 mmol) in dry methanol (75 ml; 0.2M) containing flame-dried powdered 3Å molecular sieves (4 g) was added ammonium acetate (freshly sublimed, 11.5 g, 149 mmol, 10 eq.) followed by sodium cyanoborohydride (937 mg, 14.9 mmol, 1 eq.). The reaction was stirred at r.t. for 72 h and then quenched by the addition of water (20 ml). The reaction mixture was filtered through Celite, washing thoroughly with methanol (200 ml). The solvents were removed under reduced pressure and DCM (250 ml) was added, followed by 15% aqueous sodium hydroxide solution (100 ml). The aqueous layer was separated and further extracted with DCM (2 x 100 ml). The combined organic layers were dried ($MgSO_4$) and concentrated to give the crude product as a yellow oil. Purification by chromatography (DCM/MeOH/0.88 NH_3: 95/4/1) gave (±)-α,4-dimethylbenzylamine **2g** (882 mg, 44%) as a colourless oil; ν_{max} (film) 3359, 2963, 1586, 1514, 1451, 1369, 1183, 1100, 1020, 817, 723, 704 cm^{-1}; δ (270 MHz) 7.22 (2H, d, J 4.5 Hz, *o*-protons), 7.16 (2H, d, J 4.5 Hz, *m*-protons), 4.09 (1H, q, J 4 Hz, benzylic CH), 2.53 (3H, s, 4-Me), 1.38 (3H, d, J 4 Hz, α-Me); *m/z* (EI) 134 (M^+ - H), 120 (M^+ - NH_2), 91 ($PhCH_2$).

Preparation of (±)$_S$-*N*-(3-methylbenzyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3c). A mixture of (phenylsulfinyl)ethene (5 ml, 37 mmol) and 3-methylbenzylamine (4.70 ml, 37 mmol, 1 eq.) was heated at 110°C for 20 h. Purification by chromatography (DCM/MeOH/0.88 NH_3: 95/4/1) gave the crude secondary amine (8.54 g). This was dissolved in DCM (62.5 ml; 0.5M) at r.t. under argon and *p*-toluenesulphonyl chloride (5.96 g, 31.2 mmol, 1 eq. with respect to crude amine), *N*,*N*-dimethyl-4-aminopyridine (382 mg, 3.1 mmol, 0.1 eq.) and *N*,*N*-diisopropylethylamine (5.44 ml, 31.2 mmol, 1 eq.) were added successively. The reaction was stirred at r.t. for 30 min and then DCM (200 ml) was added. The organic layer was washed successively with saturated aqueous ammonium chloride (100 ml), water (100 ml) and saturated aqueous sodium hydrogencarbonate (100 ml), dried ($MgSO_4$) and the solvents were removed

under reduced pressure to give the crude product as a brown oil. Purification by chromatography (80% - 100% ether-petrol) gave **3c** (9.54 g, 60%) as a white solid, mp 67-68°C; ν_{max} (Nujol) 2923, 2854, 1597, 1463, 1378, 1337, 1259, 1223, 1194, 1158, 1089, 1056, 1031, 997, 967, 917, 821, 767, 748, 706, 690, 655, 611 cm^{-1}; δ (270 MHz) 7.62 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.52-7.39 (5H, m, PhS(O)), 7.30 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 7.18 (1H, t, J 4.5 Hz, H-5 on 3-MeAr), 7.08 (1H, br. d, J 4.5 Hz, H-4 or H-6 on 3-MeAr), 7.02 (2H, br. s, H-2 and (H-4 or H-6 on 3-MeAr)), 4.26 and 4.20 (2H, AB quartet, J 7 Hz, benzylic CH_2), 3.50 (1H, m, H-1 or H-2), 3.18 (1H, m, H-1 or H-2), 2.96 (1H, m, H-1 or H-2), 2.71 (1H, m, H-1 or H-2), 2.43 (3H, s, tolyl Me), 2.29 (3H, s, Me on 3-MeAr); *m/z* (EI) 302 (M^+ - PhS(O)), 288 (M^+ - $PhS(O)CH_2$), 146, 135, 118, 105, 91 (Found: C, 64.37; H, 5.86; N, 3.26. $C_{23}H_{25}NO_3S_2$ requires C, 64.61; H, 5.89; N, 3.28%).

Preparation of (±)$_S$-*N*-benzyl-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3a). Prepared according to the standard procedure decsribed for **3c**. Purification by chromatography (80% - 100% ether-petrol) gave **3a** (69%) as a white solid, mp 108-109°C; ν_{max} (Nujol) 2924, 2854, 1597, 1494, 1454, 1379, 1334, 1196, 1158, 1121, 1090, 1057, 1041, 999, 931, 907, 866, 833, 806, 767, 748, 723, 693, 656 cm^{-1}; δ (270 MHz) 7.60 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.47-7.18 (12H, m, PhS(O), Ph and *m*-protons on tolyl), 4.31 and 4.22 (2H, AB quartet, J 7 Hz, benzylic CH_2), 3.49 (1H, m, H-1 or H-2), 3.18 (1H, m, H-1 or H-2), 2.95 (1H, m, H-1 or H-2), 2.67 (1H, m, H-1 or H-2), 2.39 (3H, s, tolyl Me); *m/z* (EI) 397 (M^+ - O), 288 (M^+ - PhS(O)), 274 (M^+ - $PhS(O)CH_2$), 242, 132, 110, 106, 91 (Found: C, 63.66; H, 5.59; N, 3.36. $C_{22}H_{23}NO_3S_2$ requires C, 63.90; H, 5.61; N, 3.39%).

Preparation of (±)$_S$-*N*-(2-methylbenzyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3b). Prepared according to the standard procedure described for **3c**. Purification by chromatography (30% - 40% ethyl acetate-petrol) gave **3b** (69%) as a white solid, mp 113-114°C; ν_{max} (Nujol) 2924, 2854, 1596, 1461, 1377, 1337, 1310, 1165, 1111, 1090, 1048, 1032, 921, 865, 809, 747, 693, 654 cm^{-1}; δ (270 MHz) 7.62 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.51-7.03 (9H, m, PhS(O), H-3, H-4, H-5 and H-6 on 2-MeAr), 7.32 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 4.31 and 4.22 (2H, AB quartet, J 7 Hz, benzylic CH_2), 3.42 (1H, m, H-1 or H-2), 3.08 (1H, m, H-1 or H-2), 2.80 (1H, m, H-1 or H-2), 2.57 (1H, m, H-1 or H-2), 2.43 (3H, s, tolyl Me), 2.37 (3H, s, Me on 2-MeAr); *m/z* (EI) 411 (M^+ - O), 302 (M^+ - PhS(O)), 288 (M^+ - $PhS(O)CH_2$), 146, 135, 117, 105, 91 (Found: C, 64.38; H, 5.92; N, 3.25. $C_{23}H_{25}NO_3S_2$ requires C, 64.61; H, 5.89; N, 3.28%).

Preparation of (±)$_S$-*N*-(4-methylbenzyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3d). Prepared according to the standard procedure described for **3c**. Purification by chromatography (50% - 100% ethyl acetate-petrol) gave **3d** (62%) as a white solid, mp 126-128°C; ν_{max} (Nujol) 2924, 2854, 1598, 1515, 1461, 1399, 1377, 1340, 1292, 1203, 1186, 1157, 1116, 1089, 1056, 1039, 996, 922, 848, 827, 809, 778, 746, 709, 691, 653 cm^{-1}; δ (270 MHz) 7.60 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.52-7.37 (5H, m, PhS(O)), 7.30 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 7.12 (4H, br. s, H-2, H-3, H-5 and H-6 on 4-MeAr), 4.26 and 4.08 (2H, AB quartet, J 6 Hz, benzylic CH_2), 3.48 (1H, m, H-1 or H-2), 3.18 (1H, m, H-1 or H-2), 2.93 (1H, m, H-1 or H-2), 2.69 (1H, m, H-1 or H-2), 2.46 (3H, s, tolyl Me), 2.35 (3H, s, Me on 4-MeAr); *m/z* (EI) 411 (M^+ - O), 302 (M^+ - PhS(O)), 288 (M^+ - $PhS(O)CH_2$), 146, 135, 117, 105, 91 (Found: C, 64.22; H, 5.87; N, 3.24. $C_{23}H_{25}NO_3S_2$ requires C, 64.61; H, 5.89; N, 3.28%).

Preparation of (±)$_S$-*N*-(3-methoxybenzyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3e). Prepared according to the standard procedure described for **3c**. Purification by chromatography (80% - 100% ether-petrol) gave **3e** (72%) as a white solid, mp 97-98°C; ν_{max} (Nujol) 2924, 2855, 1584, 1462, 1377, 1339, 1308, 1293, 1274, 1246, 1157, 1122, 1087, 1043, 941, 898, 818, 802, 772, 749, 732, 692, 658 cm^{-1}; δ (270 MHz) 7.63 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.50-7.40 (5H, m, PhS(O)), 7.30 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 7.21 (1H, t, J 4.5 Hz, H-5 on 3-MeOAr), 6.81 (3H, m, H-2, H-4 and H-6 on 3-MeOAr), 4.25 (2H, br. s, benzylic CH_2), 3.77 (3H, s, MeO), 3.51 (1H, m, H-1 or H-2), 3.19 (1H, m, H-1 or H-2), 2.98 (1H, m, H-1 or H-2), 2.74 (1H, m, H-1 or H-2), 2.42 (3H, s, tolyl Me); *m/z* (EI) 427 (M^+ - O), 318 (M^+ - PhS(O)), 304 (M^+ - PhS(O)CH_2), 162, 146, 121, 110, 91 (Found: C, 61.97; H, 5.63; N, 3.11. $C_{23}H_{25}NO_4S_2$ requires C, 62.28; H, 5.68; N, 3.16%).

Preparation of (±)-*N*-(α-methylbenzyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3f). Prepared according to the standard procedure described for **3c**. Purification by chromatography (50% ethyl acetate-petrol) gave **3f** (1:1 mixture of diastereomers; 53%) as a white solid; ν_{max} (Nujol) 2924, 2854, 1595, 1494, 1464, 1378, 1323, 1214, 1157, 1090, 1046, 932, 819, 784, 736, 693, 654, 610 cm^{-1}; δ (270 MHz) 7.69-7.13 (28H, m, PhS(O), Ph and protons on tolyl), 5.20 (2H, m, J 7 Hz, benzylic CH), 3.59 (1H, m, H-1 or H-2), 3.35 (1H, m, H-1 or H-2), 3.23-2.98 (3H, m, three H-1 and H-2 protons), 2.87 (1H, m, H-1 or H-2), 2.77 (1H, m, H-1 or H-2), 2.38 (3H, s, tolyl Me), 2.36 (3H, s, tolyl Me), 2.26 (1H, m, H-1 or H-2), 1.30 (3H, d, J 1.5 Hz, α-Me), 1.27 (3H, d, J 1.5 Hz, α-Me); *m/z* (EI) 411 (M^+ - O), 302 (M^+ - PhS(O)), 288 (M^+ - PhS(O)CH_2), 135, 105, 91, 78 (Found: C, 64.36; H, 5.89; N, 3.26. $C_{23}H_{25}NO_3S_2$ requires C, 64.61; H, 5.89; N, 3.28%).

Preparation of (±)-*N*-(α,4-dimethylbenzyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3g). Prepared according to the standard procedure described for **3c**. Purification by chromatography (40% ethyl acetate-petrol) gave **3g** (1:1 mixture of diastereomers; 59%) as a white solid; ν_{max} (Nujol) 2924, 2854, 1596, 1512, 1458, 1443, 1378, 1356, 1330, 1288, 1214, 1192, 1163, 1141, 1092, 1046, 1022, 998, 969, 932, 874, 842, 824, 752, 735, 690, 655, 632 cm^{-1}; δ (270 MHz) 7.65 (2H, d, J 4.5 Hz, *o*-protons on tolyl (one diastereomer)), 7.61-7.29 (16H, m, *o*-protons on tolyl (one diastereomer), *m*-protons on tolyl (both diastereomers), and PhS(O)), 7.05 (8H, d, J 7 Hz, 4-MeAr protons), 5.18 (2H, m, benzylic CH), 3.57 (1H, m, H-1 or H-2), 3.35 (1H, m, H-1 or H-2), 3.23-2.98 (3H, m, three H-1 and H-2 protons), 2.89 (1H, m, H-1 or H-2), 2.56 (1H, m, H-1 or H-2), 2.40 (3H, s, tolyl Me), 2.39 (3H, s, tolyl Me), 2.37-2.22 (1H, m, H-1 or H-2), 2.33 (3H, s, Me on 4-MeAr), 2.29 (3H, s, Me on 4-MeAr), 1.23 (3H, d, J 2 Hz, α-Me), 1.20 (3H, d, J 2 Hz, α-Me); *m/z* (EI) 441(M^+), 425 (M^+ - O), 317 (MH^+ - PhS(O)), 302 (M^+ - PhS(O)CH_2), 286, 198, 160, 119, 110, 91 (Found: C, 64.98; H, 6.23; N, 3.22. $C_{24}H_{27}NO_3S_2$ requires C, 65.28; H, 6.16; N, 3.17%).

Preparation of (±)$_S$-*N*-(1-naphthylmethyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane (3h). Prepared according to the standard procedure described for **3c**. Purification by chromatography (50% ethyl acetate-petrol) gave **3h** (59%) as a white solid, mp 107-110°C; ν_{max} (Nujol) 2924, 2854, 1596, 1463, 1377, 1337, 1159, 1089, 1045, 927, 782, 724, 691, 661 cm^{-1}; δ (270 MHz) 8.40 (1H, d, J 4 Hz), 7.87 (1H, dd, J 4, 1 Hz), 7.84 (1H, d, J 4.5 Hz), 7.70 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.59

(2H, m), 7.44-7.33 (7H, m, PhS(O) and *m*-protons on tolyl), 7.20 (1H, br. d, J 3.5 Hz), 7.15 (1H, dd, J 4, 1 Hz), 4.70 and 4.64 (2H, AB quartet, J 7 Hz, benzylic CH_2), 3.50 (1H, m, H-1 or H-2), 3.08 (1H, m, H-1 or H-2), 2.57-2.33 (2H, m, two H-1 and H-2 protons), 2.45 (3H, s, tolyl Me); *m/z* (EI) 447 (M^+ - O), 337 (M+ - PhSOH), 324 (M^+ - $PhS(O)CH_2$), 308, 292, 218, 182, 166, 153, 141, 110 (Found: C, 67.58; H, 5.20; N, 3.23. $C_{26}H_{25}NO_3S_2$ requires C, 67.36; H, 5.44; N, 3.02%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-5-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroiso-quinoline (4c') and (±)-*N*-(*p*-tolylsulfonyl)-7-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydro-isoquinoline (4c"). To a solution of $(\pm)_S$-*N*-(3-methylbenzyl)-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane **3c** (147.4 mg, 0.34 mmol) in DCM (689 µl; 0.5M) at r.t. under argon was added TMSOTf (147 µl, 0.75 mmol, 2.2 eq.) followed by *N,N*-diisopropylethylamine (132 µl, 0.75 mmol, 2.2 eq.). The reaction was stirred at r.t. for 5 min and then quenched by the addition of saturated aqueous sodium hydrogencarbonate (5 ml). The organic layer was separated, washed with 2M HCl (10 ml), dried ($MgSO_4$) and the solvents were removed under reduced pressure to give the crude product as a yellow foam. Purification by chromatography (20% ether-petrol) gave **4c'** and **4c"** (1:4 ratio by ^1H nmr; 127.8 mg, 91%) as a white solid; ν_{max} (Nujol) 2955, 2925, 2854, 1457, 1376, 1348, 1337, 1306, 1245, 1169, 1137, 1088, 1056, 956, 929, 864, 817, 750, 734, 683, 656, 634 cm^{-1}; δ (270 MHz) (**4c'**) 7.76 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.63 (2H, m, *m*-protons on PhS), 7.41-7.26 (5H, m, *o*- and *p*-protons on PhS and *m*-protons on tolyl), 7.14 (1H, t, J 4 Hz, H-7), 7.10-7.00 (2H, m, H-6 and H-8), 4.65 and 3.86 (2H, AB quartet, J 7.5 Hz, H-1), 4.28 (1H, t, J 1 Hz, H-4), 4.10 and 2.86 (2H, ABX, J 8, 1 Hz, H-3), 2.57 (3H, s, 5-Me), 2.42 (3H, s, tolyl Me); (**4c"**) 7.72 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.54 (2H, m, *m*-protons on PhS), 7.41-7.26 (5H, m, *o*- and *p*-protons on PhS and *m*-protons on tolyl), 7.10-7.00 (1H, m, H-5), 6.89 (1H, d, J 4 Hz, H-6), 6.86 (1H, s, H-8), 4.40 (1H, t, J 2.5 Hz, H-4), 4.08 and 3.64 (2H, AB quartet, J 8 Hz, H-1), 3.64 and 3.30 (2H, ABX, J 6, 2.5 Hz, H-3), 2.42 (3H, s, tolyl Me), 2.29 (3H, s, 7-Me); *m/z* (EI) 409 (M^+), 300 (M^+ - PhS), 299 (M^+ - PhSH), 144 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 67.44; H, 5.73; N, 3.35. $C_{23}H_{23}NO_2S_2$ requires C, 67.45; H, 5.66; N, 3.42%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-4-(phenylsulfenyl)-1,2,3,4-tetrahydroiso-quinoline (4a). Prepared according to the standard procedure described for **4c**. Purification by chromatography (5% - 20% ether-petrol) gave **4a** (37%) as a white solid, mp 175-177°C; ν_{max} (Nujol) 2924, 2854, 1595, 1458, 1376, 1348, 1238, 1159, 1057, 951, 814, 757, 722 cm^{-1}; δ (270 MHz) 7.72 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.53 (2H, m, *m*-protons on PhS), 7.40-7.18 (8H, m), 7.03 (1H, m), 4.43 (1H, t, J 3 Hz, H-4), 4.40 and 4.12 (2H, AB quartet, J 8 Hz, H-1), 3.64 and 3.37 (2H, ABX, J 6, 3 Hz, H-3), 2.43 (3H, s, tolyl Me); *m/z* (EI) 395 (M^+), 286 (M^+ - PhS), 285 (M^+ - PhSH), 130 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 66.58; H, 5.31; N, 3.36. $C_{22}H_{21}NO_2S_2$ requires C, 66.81; H, 5.35; N, 3.54%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-8-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline (4b). Prepared according to the standard procedure described for **4c**. Purification by chromatography (20% ether-petrol) gave **4b** (79%) as a white solid, mp 132-133°C; ν_{max} (Nujol) 2924, 2854, 1597, 1464, 1376, 1350, 1334, 1161, 1105, 1019, 971, 927, 836, 815, 789, 753, 722, 705, 682, 662 cm^{-1}; δ (270 MHz) 7.76 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.55 (2H, m, *m*-protons on PhS), 7.38-7.25 (6H, m,

o- and *p*-protons on PhS, *m*-protons on tolyl and H-5 or H-7), 7.14 (1H, t, J 3.5 Hz, H-6), 7.04 (1H, d, J 3.5 Hz, H-5 or H-7), 4.43 (1H, t, J 2.5 Hz, H-4), 4.37 and 3.95 (2H, AB quartet, J 7.5 Hz, H-1), 3.75 and 3.24 (2H, ABX, J 6, 2.5 Hz, H-3), 2.43 (3H, s, tolyl Me), 2.20 (3H, s, 8-Me); *m/z* (EI) 409 (M^+), 300 (M^+ - PhS), 299 (M^+ - PhSH), 144 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 67.28; H, 5.62; N, 3.43. $C_{23}H_{23}NO_2S_2$ requires C, 67.45; H, 5.66; N, 3.42%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-6-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline (4d). Prepared according to the standard procedure described for **4c**. Purification by chromatography (10% ethyl acetate-petrol) gave **4d** (71%) as a white solid, mp 146-147°C; ν_{max} (Nujol) 2923, 2854, 1597, 1457, 1377, 1353, 1242, 1165, 1091, 1060, 960, 919, 852, 814, 754, 681, 661 cm^{-1}; δ (270 MHz) 7.72 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.58 (2H, m, *m*-protons on PhS), 7.40-7.25 (6H, m, *o*- and *p*-protons on PhS, *m*-protons on tolyl and H-5), 7.02 (1H, d, J 4.5 Hz, H-7 or H-8), 6.94 (1H, d, J 4.5 Hz, H-7 or H-8), 4.39 (1H, t, J 2.5 Hz, H-4), 4.38 and 4.05 (2H, AB quartet, J 8 Hz, H-1), 3.64 and 3.26 (2H, ABX, J 6.5, 2.5 Hz, H-3), 2.42 (3H, s, tolyl Me), 2.30 (3H, s, 6-Me); *m/z* (EI) 409 (M^+), 300 (M^+ - PhS), 299 (M^+ - PhSH), 144 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 67.28; H, 5.59; N, 3.41. $C_{23}H_{23}NO_2S_2$ requires C, 67.45; H, 5.66; N, 3.42%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-5-methoxy-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline (4e') and (±)-*N*-(*p*-tolylsulfonyl)-7-methoxy-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline (4e''). Prepared according to the standard procedure described for **4c**. Purification by chromatography (20% ether-petrol) gave **4e'** and **4e''** (1:2.9 ratio by ^1H nmr; 92%) as a white solid; ν_{max} (Nujol) 2925, 2853, 1611, 1502, 1456, 1376, 1352, 1278, 1242, 1166, 1121, 1090, 1060, 1033, 957, 931, 864, 815, 741, 682, 659, 633 cm^{-1}; δ (270 MHz) (**4e'**) 7.76 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.59 (2H, m, *m*-protons on PhS), 7.41 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 7.38-7.29 (3H, m, *o*- and *p*-protons on PhS), 7.08 (1H, t, J 4 Hz, H-7), 6.74 (1H, d, J 4 Hz, H-6 or H-8), 6.63 (1H, d, J 4 Hz, H-6 or H-8), 4.62 and 3.87 (2H, AB quartet, J 8 Hz, H-1), 4.55 (1H, br. t, J 1 Hz, H-4), 4.07 and 2.86 (2H, ABX, J 5.5, 1 Hz, H-3), 3.88 (3H, s, MeO), 2.42 (3H, s, tolyl Me); (**4e''**) 7.73 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.53 (2H, m, *m*-protons on PhS), 7.38-7.29 (4H, m, *o*- and *p*-protons on PhS and H-5), 7.32 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 6.79 (1H, dd, J 4.5, 1 Hz, H-6), 6.57 (1H, d, J 1 Hz, H-8), 4.20 (1H, t, J 2.5 Hz, H-4), 4.18 and 4.09 (2H, AB quartet, J 8 Hz, H-1), 3.78 (3H, s, MeO), 3.64 and 3.30 (2H, ABX, J 7, 2.5 Hz, H-3), 2.42 (3H, s, tolyl Me); *m/z* (EI) 425 (M^+), 316 (M^+ - PhS), 315 (M^+ - PhSH), 160 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 64.83; H, 5.35; N, 3.21. $C_{23}H_{23}NO_3S_2$ requires C, 64.92; H, 5.45; N, 3.29%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-1-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline (4f). Prepared according to the standard procedure described for **4c**. Purification by chromatography (10% ethyl acetate-petrol) gave **4f** (10:1 mixture of diastereomers by ^1H nmr; 81%) as a white solid; ν_{max} (Nujol) 2923, 2854, 1598, 1460, 1377, 1337, 1159, 1092, 1059, 973, 922, 813, 746, 689, 657 cm^{-1}; δ (270 MHz) (major diastereomer) 7.83 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.43-7.17 (11H, m), 5.14 (1H, br. q, J 3.5 Hz, H-1), 4.41 (1H, br. s, H-4), 3.97 and 3.59 (2H, ABX, J 7, 1 Hz, H-3), 2.40 (3H, s, tolyl Me), 1.42 (3H, d, J 3.5 Hz, 1-Me); *m/z* (EI) 409 (M^+), 300 (M^+ - PhS), 299 (M^+ - PhSH), 144 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 67.55; H, 5.84; N, 3.20. $C_{23}H_{23}NO_2S_2$ requires C, 67.45; H, 5.66; N,

3.42%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-1,6-dimethyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline (4g). Prepared according to the standard procedure described for **4c**. Purification by chromatography (10% ethyl acetate-petrol) gave **4g** (>20:1 mixture of diastereomers by ^{1}H nmr; 88%) as a white solid; ν_{max} (Nujol) 2977, 2924, 1735, 1598, 1584, 1500, 1479, 1440, 1377, 1337, 1275, 1215, 1161, 1094, 1056, 1024, 980, 924, 815, 739, 678, 636 cm^{-1}; δ (270 MHz) (major diastereomer) 7.82 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.40-7.20 (8H, m, PhS, *m*-protons on tolyl and H-5), 5.10 (1H, br. q, J 3.5 Hz, H-1), 4.37 (1H, br. s, H-4), 3.98 and 3.58 (2H, ABX, J 7, 2 Hz, H-3), 2.40 (3H, s, tolyl Me), 2.29 (3H, s, 6-Me), 1.40 (3H, d, J 3.5 Hz, 1-Me); *m/z* (EI) 423 (M^+), 314 (M^+ - PhS), 313 (M^+ - PhSH), 158 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 67.89; H, 6.12; N, 3.11. $C_{24}H_{25}NO_2S_2$ requires C, 68.05; H, 5.95; N, 3.31%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-4-(phenylsulfenyl)-7,8-benzo-1,2,3,4-tetrahydroisoquinoline (4h). Prepared according to the standard procedure described for **4c**. Purification by chromatography (10% ethyl acetate-petrol) gave **4h** (86%) as a white solid, mp 77-79°C; ν_{max} (Nujol) 2924, 2854, 2317, 1596, 1458, 1377, 1342, 1248, 1162, 1113, 1088, 970, 927, 812, 734, 691, 663 cm^{-1}; δ (270 MHz) 7.82 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.75 (2H, m), 7.63-7.47 (4H, m), 7.40-7.18 (7H, m), 4.93 and 4.40 (2H, AB quartet, J 7.5 Hz, H-1), 4.50 (1H, t, J 2.5 Hz, H-4), 3.91 and 3.29 (2H, ABX, J 7, 2.5 Hz, H-3), 2.41 (3H, s, tolyl Me); *m/z* (EI) 445 (M^+), 336 (M^+ - PhS), 335 (M^+ - PhSH), 180 (M^+ - PhSH, Ts), 91 ($PhCH_2$) (Found: C, 69.96; H, 5.38; N, 2.99. $C_{26}H_{23}NO_2S_2$ requires C, 70.08; H, 5.20; N, 3.14%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-5-methyl-1,2,3,4-tetrahydroisoquinoline (7') and (±)-*N*-(*p*-tolylsulfonyl)-7-methyl-1,2,3,4-tetrahydroisoquinoline (7''). To a solution of (±)-*N*-(*p*-tolylsulfonyl)-5-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline **4c'** and (±)-*N*-(*p*-tolylsulfonyl)-7-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline **4c''** (1:4 ratio by ^{1}H nmr, 107.4 mg, 0.26 mmol) in absolute ethanol (13.1 ml; 0.02M) at r.t. under argon was added Raney nickel (0.9 ml of a 50% dispersion in water). The reaction was heated under reflux for 1 h, cooled and the reaction mixture was filtered through Celite, washing thoroughly with ethyl acetate (200 ml). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a white solid. Purification by chromatography (5% ethyl acetate-petrol) gave **7'** and **7''** (1:4 ratio by ^{1}H nmr; 64.4 mg, 81%) as a white crystalline solid; ν_{max} (Nujol) 2926, 1598, 1463, 1377, 1348, 1335, 1289, 1235, 1165, 1095, 1071, 1025, 957, 929, 914, 881, 814, 759, 722, 662, 631 cm^{-1}; δ (270 MHz) (7') 7.74 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.35 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 7.07-6.87 (3H, m, H-6, H-7 and H-8), 4.21 (2H, s, H-1), 3.37 (2H, t, J 3 Hz, H-4), 2.80 (2H, t, J 3 Hz, H-3), 2.43 (3H, s, tolyl Me), 2.29 (3H, s, 5-Me); (7'') 7.74 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.35 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 6.96 (2H, s, H-5 and H-6), 6.85 (1H, s, H-8), 4.21 (2H, s, H-1), 3.33 (2H, t, J 3 Hz, H-4), 2.89 (2H, t, J 3 Hz, H-3), 2.43 (3H, s, tolyl Me), 2.29 (3H, s, 7-Me); *m/z* (EI) 301 (M^+), 300 (M^+ - H), 146 (M^+ - Ts), 91 ($PhCH_2$) (Found: C, 67.45; H, 6.22; N, 4.64. $C_{17}H_{19}NO_2S$ requires C, 67.75; H, 6.35; N, 4.65%).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-5-methyl-1,2-dihydroisoquinoline (8') and (±)-*N*-(*p*-tolylsulfonyl)-7-methyl-1,2-dihydroisoquinoline (8''). To a solution of (±)-*N*-(*p*-tolylsulfonyl)-5-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline **4c'** and (±)-*N*-(*p*-tolylsulfonyl)-7-methyl-4-(phenylsulfenyl)-1,2,3,4-tetrahydroisoquinoline **4c''** (1:4 ratio by ^{1}H nmr, 187.2 mg, 0.42 mmol) and sodium acetate (35 mg, 0.42 mmol, 1 eq.) in DCM (2.12 ml; 0.2M) at 0°C under argon was added peracetic acid (90 µl of a 36% wt. solution in dilute acetic acid, 1.0 eq.). The reaction was stirred at 0°C for 5 min and then quenched with 10% aqueous sodium thiosulfate (5 ml). The organic layer was separated, washed with saturated aqueous sodium hydrogencarbonate (2 x 10 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a white solid. The crude sulfoxides were then dissolved in toluene (4.2 ml, 0.1M) and the reaction mixture was heated to reflux for 15 min. Concentration of the mixture under reduced pressure gave the crude products as a white foam. Purification by chromatography (40% DCM-petrol) gave **8'** and **8''** (1:4 ratio by ^{1}H nmr; 120 mg, 81%) as a white solid; ν_{max} (Nujol) 2925, 2854, 1627, 1594, 1458, 1404, 1377, 1355, 1340, 1308, 1292, 1253, 1234, 1187, 1168, 1114, 1089, 1043, 976, 932, 896, 874, 830, 819, 754, 726, 668, 636 cm^{-1}; δ (270 MHz) (**8'**) 7.71 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.29 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 6.99 (1H, t, J 3 Hz, H-7), 6.98 (1H, d, J 4 Hz, H-4), 6.82 (2H, m, H-6 and H-8), 6.01 (1H, d, J 4 Hz, H-3), 4.55 (2H, s, H-1), 2.39 (3H, s, tolyl Me), 2.24 (3H, s, 5-Me); (**8''**) 7.71 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.29 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 6.96 (1H, d, J 4 Hz, H-5 or H-6), 6.83 (1H, d, J 4 Hz, H-5 or H-6), 6.81 (1H, s, H-8), 6.73 (1H, d, J 4 Hz, H-4), 5.82 (1H, d, J 4 Hz, H-3), 4.56 (2H, s, H-1), 2.39 (3H, s, tolyl Me), 2.27 (3H, s, 7-Me); *m/z* (EI) 299 (M^+), 144 (M^+ - Ts) (Found: (M^+), 299.0980. $C_{17}H_{17}NO_2S$ requires (M^+), 299.0980).

Preparation of (±)-*N*-(*p*-tolylsulfonyl)-5-methyl-4-(phenylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (9') and (±)-*N*-(*p*-tolylsulfonyl)-7-methyl-4-(phenylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (9''). To a solution of (±)-*N*-(*p*-tolylsulfonyl)-5-methyl-4-(phenyl-sulfenyl)-1,2,3,4-tetrahydroisoquinoline **4c'** and (±)-*N*-(*p*-tolylsulfonyl)-7-methyl-4-(phenylsulphenyl)-1,2,3,4-tetrahydroisoquinoline **4c''** (1:4 ratio by ^{1}H nmr, 440.9 mg, 1.1 mmol) and sodium acetate (194 mg, 2.4 mmol, 2.2 eq.) in DCM (5.4 ml; 0.2M) at r.t. under argon was added peracetic acid (500 µl of a 36% wt. solution in dilute acetic acid, 2.4 mmol, 2.2 eq.). The reaction was stirred at r.t. for 12 h and then quenched with 10% aqueous sodium thiosulfate (20 ml). The organic layer was separated, washed with saturated aqueous sodium hydrogencarbonate (2 x 25 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a white solid. Purification by chromatography (50% ether-petrol) gave **9'** and **9''** (1:4 ratio by ^{1}H nmr; 404.9 mg, 85%) as a white solid; ν_{max} (Nujol) 2926, 2854, 1689, 1596, 1458, 1377, 1355, 1339, 1304, 1210, 1189, 1167, 1130, 1081, 1058, 955, 927, 867, 816, 758, 731, 681, 654, 622 cm^{-1}; δ (270 MHz) (**9'**) 7.62 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.58-7.49 (3H, m, *o*- and *p*-protons on $PhSO_2$), 7.40-7.27 (5H, m, *m*-protons on $PhSO_2$, *m*-protons on tolyl and H-6 or H-8), 7.10 (1H, m, H-7), 6.69 (1H, m, H-6 or H-8), 4.67 (1H, t, J 2 Hz, H-4), 3.90 and 2.88 (2H, ABX, J 7, 2 Hz, H-3), 3.77 and 3.59 (2H, AB quartet, J 8 Hz, H-1), 2.40 (3H, s, tolyl Me), 2.38 (3H, s, 5-Me); (**9''**) 7.62 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.58-7.49 (3H, m, *o*- and *p*-protons on $PhSO_2$), 7.40-7.27 (5H, m, *m*-protons on $PhSO_2$, *m*-protons on tolyl and H-5 or H-6), 7.10 (1H, m, H-5 or H-6), 6.69 (1H, m, H-8), 4.74 and 2.81 (2H, ABX, J 7, 2.5 Hz, H-3), 4.32 (1H, t, J 2.5 Hz, H-4), 3.90 and 3.44 (2H, AB quartet, J 8 Hz, H-1), 2.40 (3H, s, tolyl Me), 2.26

(3H, s, 7-Me); *m/z* (EI) 300 (M^+ - $PhSO_2$), 144 (M^+ - H, Ts) (Found: C, 62.15; H, 5.00; N, 3.35. $C_{23}H_{23}NO_4S_2$ requires C, 62.56; H, 5.25; N, 3.17%).

Preparation of *N*-benzyl-*N*-(*p*-tolylsulfonyl)-2-aminoethanal (6). To a solution of $(\pm)_S$-*N*-benzyl-*N*-(*p*-tolylsulfonyl)-2-amino-1-(phenylsulfinyl)ethane **3a** (88.5 mg, 0.21 mmol) in DCM (428 µl; 0.5M) at r.t. under argon was added TFAA (33 µl, 0.23 mmol, 1.1 eq.) followed by triethylamine (66 µl, 0.46 mmol, 2.2 eq.). The reaction was stirred at r.t. for 5 h and then quenched with saturated aqueous sodium hydrogencarbonate (5 ml). The organic layer was separated and washed with 2M HCl (5 ml), water (5 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product as a pale yellow oil. Purification by chromatography (50% ether-petrol) gave **6** (55.9 mg, 86%) as a colourless oil, ν_{max} (film) 3032, 2922, 1735, 1598, 1495, 1454, 1404, 1345, 1207, 1161, 1108, 996, 945, 912, 869, 816, 784, 746, 699, 657 cm^{-1}; δ (270 MHz) 9.30 (1H, d, J 0.5 Hz, CHO), 7.76 (2H, d, J 4.5 Hz, *o*-protons on tolyl), 7.37 (2H, d, J 4.5 Hz, *m*-protons on tolyl), 7.34-7.25 (5H, m, Ph), 4.33 (2H, s, benzylic CH_2), 3.70 (2H, d, J 0.5 Hz, H-2), 2.44 (3H, s, tolyl Me; *m/z* (EI) 303 (M^+), 274 (M^+ - CHO), 91 ($PhCH_2$) (Found: (M^+), 303.0930. $C_{16}H_{17}NO_3S$ requires (M^+), 303.0929).

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