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An Unexpected Rearrangement of a β-Amino Sulfoxide under Pummerer Reaction Conditions†

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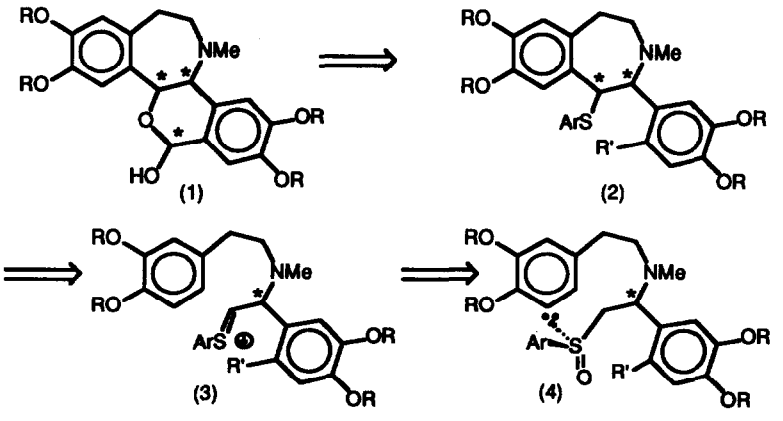
Abstract: Attempts to prepare the benzazepine ring system of the Rhoedine alkaloids using a Pummerer cyclization of the β-amino sulfoxide (16) gave instead the unexpected alcohol (19). The β-amino sulfoxide (16) was prepared via a diastereoselective reduction of the β-sulfinyl enamine (8) with sodium borohydride.

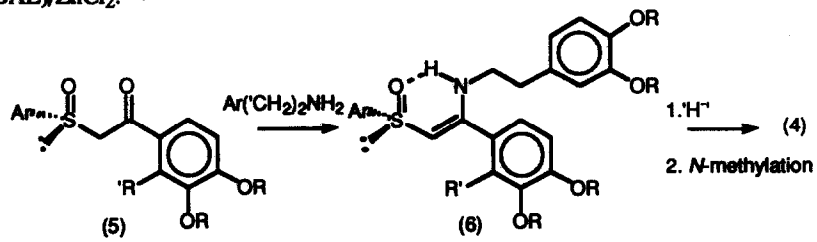
We have previously demonstrated that β-amino sulfoxides are useful compounds for the asymmetric synthesis of chiral alkaloids.[1-5] Cyclic β-amino and β-amido sulfoxides have also been successfully employed by Hua.[6] As an extension of our work in this area we have embarked on a project aimed at the asymmetric synthesis of the Rhoedine alkaloids .[7] Based on our previous experience we expected that the key benzazepine ring system of the general Rhoedine alkaloid structure (1) could be prepared via a Pummerer cyclization reaction of the β-amino sulfoxide (4).[2,4] While the Pummerer cyclization of β-amino sulfoxides has been used to prepare 5- and 6-membered ring compounds[2,4,8,9] only a few examples in the literature describe the synthesis of 7-membered ring compounds.[10,11] Nevertheless, the other alternative modes of cyclization of the sulfenium ion (3) that could result from the Pummerer reaction of the sulfoxide group of (4) seemed to us to be less likely.

Scheme 1



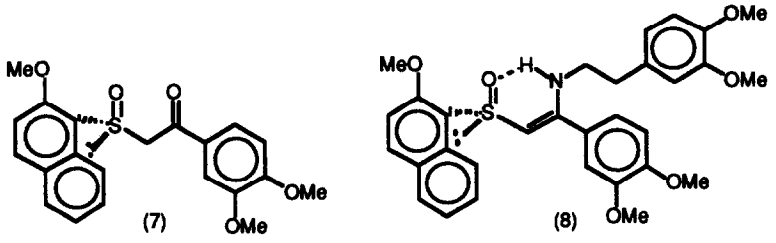
We decided to prepare (4) via a diastereoselective reduction of the β-sulfinyl enamine (6) which may be formed from the reaction of the β-sulfinyl ketone (5) and 2-(3,4-dimethoxyphenyl)ethylamine. The synthesis

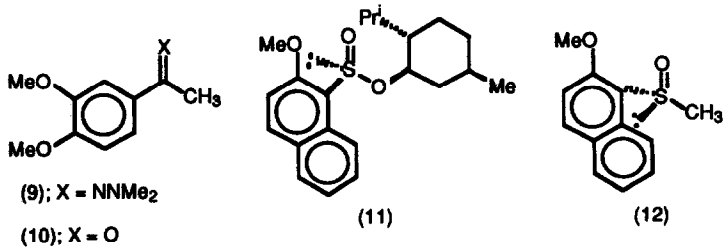
of β-amino *p*-tolyl sulfoxides via diastereoselective reduction of β-*p*-tolylsulfinyl enamines has been previously reported using lithium tri(*s*-butyl)borohydride (L-Selectride), borane·THF, or diisobutylaluminium hydride (DIBAL)/$ZnCl_2$.[12,13]



We anticipated that reduction of the analogous (*R*)-2-methoxy-1-naphthylsulfinyl enamine (8) may be more diastereoselective and would be readily prepared from (*R*)-β-keto 2-methoxy-1-naphthyl sulfoxide (7). We now describe the synthesis of compounds (7) and (8) and our attempts to prepare a benzazepine compound of the type shown in structure (2) in Scheme 1 via a Pummerer cyclization reaction.

We have examined three methods for preparing the β-keto sulfoxide (7) as shown in Scheme 2. Addition of the lithiated *N*, *N*-dimethyl hydrazone of 3,4-dimethoxyacetophenone (9) to (*Ss*, 1*R*, 2*S*, 5*R*)-menthyl 2-methoxy-1-naphthyl sulfinate (11),[14] according to the method of Annunziata *et al.*[15] gave, after hydrolysis of the hydrazone moiety with aqueous copper (II) chloride at pH 7, the β-keto sulfoxide (7) in 43% yield overall yield. The enantiomeric purity of (7) was determined to be 80% from ^1H NMR analysis of a solution of (7) in the presence of 1 mole equivalent of (-) (*R*)-*N*-(3,5-dinitrobenzoyl)-α-phenylethylamine as a chiral shift reagent.[16] The ^1H NMR spectrum of pure (7) showed an AB quartet (δ 5.02 (d, J_{AB} = 13.2 Hz) and δ 4.85 (d, J_{AB} = 13.2 Hz)) for the two diastereotopic methylene protons of (7). In the presence of the chiral shift reagent peaks for these protons for the major (*R*)-enantiomer and the minor (*S*)-enantiomer could be detected in a ratio of 90 : 10. While the addition of the sodium salt of 3,4-dimethoxyacetophenone (10) to sulfinate (11) gave (7) in high yield (91%) the enantiomeric purity of this compound was disappointingly low (enantiomeric excess (e.e.) = 60%).[17] Compound (7) could be prepared in high enantiomeric purity (e.e. = 98%) via the reaction of the lithium salt of (+)-(*R*) methyl 2-methoxy-1-naphthyl sulfoxide (12) and methyl 3,4-dimethoxybenzoate (Scheme 2).[18]





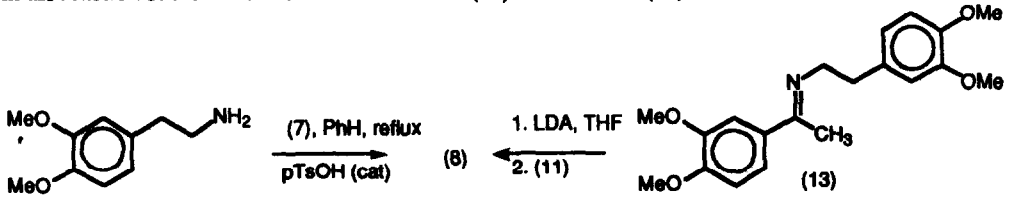
Scheme 2. Synthesis of β-keto sulfoxide (7).

(9) 1. LDA, THF; 2. (11); 3. $CuCl_2$ (aq) → (7) [yield 43%, e.e. 80%]

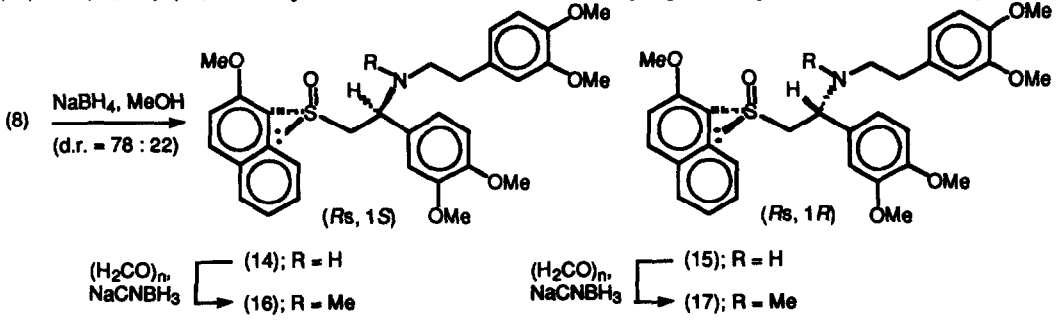
(10) 1. NaH, (11), THF, reflux → (7) [yield 91%, e.e. 60%]

(12) 1. LDA, THF; 2. 3,4-$(MeO)_2C_6H_3CO_2Me$ → (7) [yield 50 %, e.e. 98%]

Treatment of a benzene solution of the ketone (7) with 2-(3,4-dimethoxyphenyl)ethyl amine and a catalytic amount of *p*-toluenesulfonic acid at reflux with the azeotropic removal of water (Dean-Stark apparatus) gave the β-sulfinyl enamine (8) in 86% yield. The enamine structure of (8) was clearly evident from ^{1}H NMR analysis (δ 4.60, s, 1H, ArSOC<u>H</u>=C(Ar')NH). The same enamine could be obtained in 65% yield directly from the reaction of the lithium carbanion of imine (13) and sulfinate (11).[19]

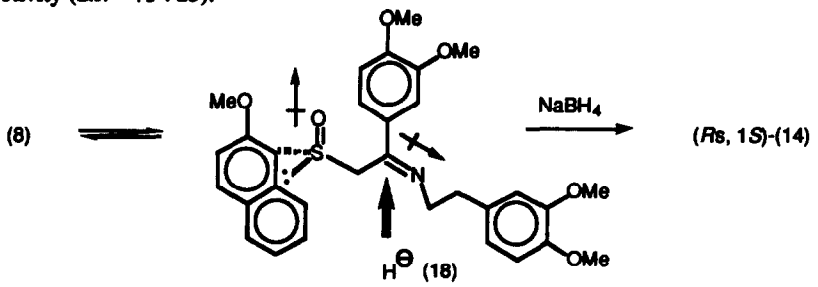


Attempts to reduce (8) with either DIBAL or L-Selectride in THF at -78°C to room temperature resulted in complete recovery of the starting enamine (8). In contrast, reduction of (8) with sodium borohydride in methanol at -78°C to room temperature gave a 78 : 22 mixture of the β-amino sulfoxides (*R*s, 1*S*)-(14) and (*R*s, 1*R*)-(15) in 95% yield. Reductive methylation of this mixture with formaldehyde and sodium cyanoborohydride[4] in acetonitrile at pH 7 gave a mixture of the *N*-methyl diastereomeric compounds (*R*s, 1*S*)-(16) and (*R*s, 1*R*)-(17) in 83% yield. This mixture could be readily separated by column chromatography.

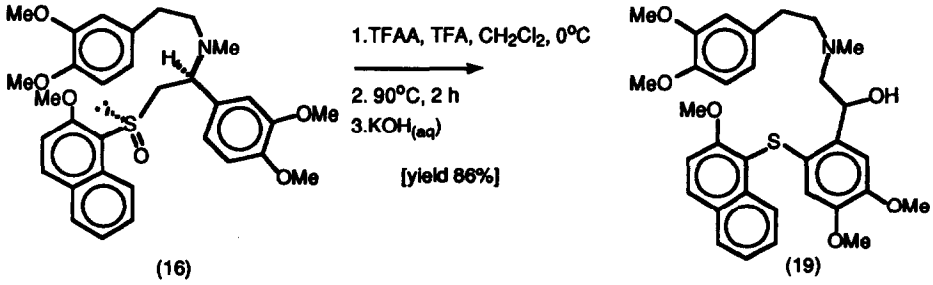


The successful reduction of enamine (8) requires it to be in equilibrium with its imine form (18) which can be reduced to the amines (14) and (15). The 2-methoxy-1-naphthyl substituent would be expected to enhance the basicity of the sulfoxide oxygen and hence further stabilize the internally H-bonded enamine form relative to the imine form (18). Thus in THF (like $CDCl_3$ in the ^{1}H NMR studies), only the enamine form exists in

solution and the reduction of (8) is not possible. In methanol solution, the intramolecular H-bonding in (8) is disrupted due to intermolecular H-bonding with the solvent and thus the free energy difference between the enamine and imine forms is less. The stereochemistry of (16) and (17) is based on a comparison of the ^{1}H NMR spectra of these compounds with those of related β-amino sulfoxides[3,4] and is that expected from reduction of the imine (18) on the conformation shown in which dipole-dipole interactions between the C=N and the S=O groups are minimized.[20] Hydride addition to (18) would be expected to occur from the least sterically demanding face of the imine moiety, that is the face *anti* to the *S*-2-methoxy-1-naphthyl group. Attempts to prepare amines (14) and (15) via reductive alkylation of (7) with 2-(3,4-dimethoxyphenyl)ethylamine and sodium cyanoborohydride suffered from poor yield (38%) and lower diastereoselectivity (d.r. = 75 : 25).



Treatment of (16) with trifluoroacetic anhydride (1.2 molar equiv.) in a solution of trifluoroacetic acid (3 molar equiv.) in dichloromethane at 0°C for 15 min and then at 90°C for 2 h gave, after an aqueous basic work up the unexpected alcohol (19) in 86 % yield. None of the expected benzazepine product could be detected in the crude reaction mixture. Treatment of (16) under other Pummerer reaction type conditions[9] also gave (19) plus other unidentifiable products. The structure of (19) was evident from ^{1}H and ^{13}C and 2D NMR analysis. The ^{1}H NMR spectrum of (19) revealed two aromatic proton singlets at δ 6.29 and δ 7.14 which indicated that substitution had occurred on one of the phenyl rings to give a 1,2,4,5 tetrasubstituted benzene. A doublet of doublets at δ 5.46 was consistent with the ArCH(OH)CH$_A$H$_B$NMe- structure. The DEPT NMR spectrum of (19) showed 2 CH_2 groups, 12 CH groups (1 aliphatic and 11 aromatic) and 6 Me groups. The HMBC and HMQC spectra were also consistent with the connectivity shown in structure (19).

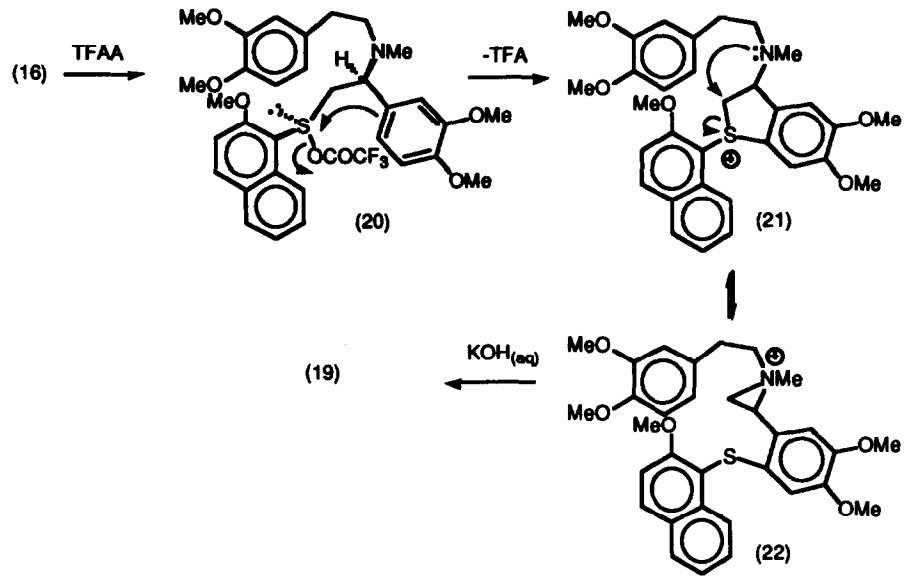


(16) (19)

A possible mechanism for the formation of the alcohol (19) is shown in Scheme 3. *O*-Acetylation of (16) gives the expected intermediate (20) which undergoes an electrophilic aromatic substitution reaction to give the five membered ring sulfonium salt (21). The salt (21) is in equilibrium with the aziridinium ion (22). Upon addition of aqueous base the aziridinium ion undergoes ring opening at the benzylic carbon to give the

observed alcohol (19). The alcohol (19) had no optical rotation and was therefore most likely racemic. This result suggested that ring opening and ring closure of the aziridinium ring of (22) must have occurred via a benzyl cation intermediate to give a racemic aziridinium ion. Alternatively, because the tertiary amino group of compound (21) would be protonated in the presence of trifluoroacetic acid, the aziridinium ion (22) may be formed during the work up of the Pummerer reaction with aqueous base.

Scheme 3



In conclusion we have discovered a useful method for preparing β-amino sulfoxides in good diastereomeric purity based on the reduction of β-(2-methoxy-1-naphthylsulfinyl)-enamines with sodium borohydride. Unfortunately compound (16) was not useful for the synthesis of benzazepine alkaloids since the Pummerer reaction of (16) did not proceed as proposed in Scheme 1. Instead of obtaining the desired 7-membered ring cyclization product, electrophilic attack at sulfur to give a 5-membered ring intermediate (21) was favoured. Further reaction of (21) lead to the unexpected alcohol (19).

Experimental

All NMR spectra were run in $CDCl_3$ solution at 400MHz (^{1}H NMR) or 100 MHz (^{13}C NMR).

(+)-*(R)* Methyl 2-methoxy-1-naphthyl sulfoxide (12).

To a solution of (-) *(Ss, 1R, 2S, 5R)* menthyl 2-methoxy-1-naphthalenesulfinate (11)[14] (10.8 g, 30 mmol) in dry benzene (120 mL) at room temperature under nitrogen was added dropwise, via syringe over 30 min a solution of methylmagnesium iodide [prepared from magnesium (2 g) and methyl iodide (6.2 mL) in diethyl ether (70 mL)]. After the addition was complete, the reaction mixture was stirred at room temperature for 2 h and then quenched by the addition of saturated ammonium chloride solution (30 mL). The organic solvents were evaporated and the aqueous layer was extracted with hexane (50 mL) to remove menthol and

then four times with chloroform (50 mL). The combined chloroform extract was dried over MgSO4 and evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel, ethyl acetate). The second fraction was collected and evaporated to give 3.35 g (76 % yield) of compound (12) as white needles, m.p. 102-103° C, $[\alpha]_D^{26}$ +106.6 (c 1.2, $CHCl_3$). MS m/z, 221 (100 %, M^+). ^1H NMR δ 9.12 (dd, 1H, J_{ortho} 9.2, J_{meta} 1.6 Hz), 7.2-7.9 (m, 5 H), 4.01 (s, 3 H, OCH_3), 2.50 (s, 3 H, CH_3). Anal calcd. for $C_{12}H_{12}SO_2$: C, 65.43; H, 5.49; S, 14.55 %. Found: C, 65.44; H, 5.47; S, 14.56 %.

(+) (*R*)-2-(2'-Methoxynaphthyl-1'-sulfinyl)methyl (3',4'-dimethoxy)phenyl ketone (7).

Method 1: To a stirred suspension of the lithium salt of *N*, *N*-dimethylhydrazone (9) (15.24 mmol), (prepared according to the literature method[15] from lithium diisopropylamide (15.24 mmol) and *N*, *N*-dimethylhydrazone (9) (15.24 mmol, 2.9 g) in THF (25 mL)) at -78 °C was added a solution of (-) (*Ss*, 1*R*, 2*S*, 5*R*) menthyl 2-methoxynaphthyl-1-sulfinate (11)[14] (2.78 g, 7.62 mmol) in THF (35 mL) slowly dropwise over 20 min. After a further 30 min at -78 °C, the pale yellow, clear solution was quenched with saturated ammonium chloride solution (10 mL) and then extracted with dichloromethane (3x25 mL). The organic extract was dried over $MgSO_4$ and evaporated in vacuo. The crude product was purified by column chromatography using ethyl acetate containing 3% triethylamine as eluent to give the *N*, *N*-dimethylhydrazone of (7) as yellow crystals, m.p. 112-113 °C, in 53 % yield. ^1H NMR δ 8.95 (s, 1 H), 8.0-6.8 (m, 7 H), 4.38 and 4.31 (AB quartet, J=12 Hz, 2 H), 4.00 (s, 3 H, OMe), 3.95 (s, 3 H, OMe), 3.80 (s, 3 H, OMe), 2.34 (s, 6 H, $N(\underline{CH_3})_2$).

To a solution of the *N*, *N*-dimethylhydrazone of (7) (1 mmol, 0.395 g) in THF (20 mL) and phosphate buffer (8 mL, pH 7) was added copper(II) chloride (0.188 g, 1.1 mmol). The mixture was stirred at room temperature for 3 h, and was then worked up as described above. The crude product was purified by column chromatography on silica gel using ethyl acetate as eluent to give β-keto sulfoxide (7), 119-121 °C, in 63 % yield. ^1H NMR δ 8.95 (d, 1 H), 8.0-6.8 (m, 7 H), 5.02 and 4.85 (AB quartet, J=13.2 Hz, 2 H), 4.00 (s, 3 H, OMe), 3.95 (s, 3 H, OMe), 3.80 (s, 3 H, OMe). MS m/z, 385.1(50 %, M^+), 288.3 (25 %), 205 (100 %). Anal calcd for $C_{21}H_{20}O_5S$: C, 65.61; H, 5.24 %, Found: C, 65.70; 5.38 %.

Method 2: 3,4-Dimethoxyacetophenone (5 g, 28 mmol) in anhydrous THF (50 mL) was added over a 10 min period to a stirred refluxing suspension of 'oil free' sodium hydride (1.1 g, 42 mmol) in THF (50 mL) containing (-) (*Ss*, 1*R*, 2*S*, 5*R*) menthyl 2-methoxynaphthyl-1-sulfinate (11)[14] (10.22 g, 28 mmol) under a nitrogen atmosphere. The mixture was heated at reflux overnight, then cooled and treated with saturated aqueous ammonium chloride (30 mL) and finally extracted with dichloromethane (3x100 mL). The dichloromethane extracts were combined, washed with saturated sodium hydrogen carbonate (2x50 mL), dried over $MgSO_4$ and evaporated at reduced pressure to give a thick oil. Crystallisation from dichloromethane/hexane gave 9.79 g (91 %) of (7), m. p. 119-120 °C.

Method 3: (+) (*R*)-Methyl 2-methoxy-1-naphthyl sulfoxide (12) (4.0 mmol, 0.88 g) in anhydrous THF (5 mL) was added dropwise to a cooled (-78° C), stirred solution of lithium diisopropylamide (4 mmol). The mixture was allowed to reach -20°C, and was then cooled again to -78°C and treated with a solution of methyl 3,4-dimethoxybenzoate (2 mmol) in THF (15 mL). The mixture was stirred for 30 min at -78°C and then warmed to room temperature and stirred at this temperature overnight. The mixture was quenched with

saturated aqueous ammonium chloride and then extracted with dichloromethane (2 x 20 mL). The combined extracts were washed with water, dried ($MgSO_4$) and then evaporated to dryness. The crude product was then purified by column chromatography on silica gel using ethyl acetate/hexane (1:1) as the eluent to give (+) (*R*)-(7) in 50 % yield, $[\alpha]_D^{28}$ +90.37 (c 0.12, CH_2Cl_2).

(*R*)-*N*-[2-(2'-methoxy-1'-naphthylsulfinyl)-1-(3',4'-dimethoxyphenyl)]ethenyl-*N*-[2-(3',4'-dimethoxyphenyl)]ethylamine (8)

Method 1: To the β-keto sulfoxide (7) (0.6 mmol, 0.23 g) in benzene (10 mL) and 2-(3,4-dimethoxyphenyl)ethylamine (0.9 mmol, 164 mg) was added *p*-toluenesulfonic acid (3 mg). The mixture was heated to reflux and a Dean-Stark apparatus was used to separate the theoretical amount of water. After 20 hr refluxing the mixture was concentrated by evaporated, treated with 2 M aqueous potassium hydroxide (2 mL) and then extracted with chloroform (3x15 mL). The combined extracts were dried ($MgSO_4$) and evaporated. The crude product was purified by crystallisation from dichloromethane/hexane (4:1) to give compound (8) as yellow pale crystals, m.p. 68-69 °C, in 86 % yield (281 mg). ^{1}H NMR δ 8.65 (d, J=8.4 Hz, 1 H), 8.0-6.6 (m, 11 H), 4.60 (s, 1 H, C<u>H</u>=C-N), 3.99 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 3.78 (s, 6 H, OMe), 3.72 (s, 3 H, OMe), 2.80 (t, 4 H). ^{13}C NMR δ, 35.63, 38.85, 54.93, 55.65, 55.87, 55.99, 58.22, 68.53 110.98, 112.19, 113.85, 120.51, 120.78, 132.74, 124.44, 127.69, 128.64, 129.206, 129.46, 132.67, 133.16, 133.79, 147.23, 148.44, 148.72, 156.24. MS m/z, 547 (100 %, M^+). Anal. calcd. for $C_{31}H_{33}NO_6S$: C, 67.99; H, 6.07; N, 2.56 %, Found: C, 68.26; H, 5.98; N, 2.62 %.

Method 2: To a solution of 3,4-dimethoxyacetophenone (18.0 g, 0.1 mol) in benzene (150 mL) was added 2-(3,4-dimethoxyphenyl)ethylamine (27.3 g, 0.15 mol) and *p*-toluenesulfonic acid (0.01 g). The mixture was heated to reflux and a Dean-Stark apparatus was used to separate the theoretical amount of water. Evaporated of the solvent, and crystallisation the residue from ethanol gave the imine (13) in 75 % yield (25.9 g), m.p. 86-87 °C. ^{1}H NMR δ 2.05 (s, 3 H), 3.01 (t, 4 H), 3.79 (2 x s, 6H), 6.8-7.4 (m, 6 H).

A solution of the imine (13) (8 mmol, 2.76 g) in anhydrous THF (12 mL) was added dropwise over 30 min via a syringe under nitrogen to a solution of lithium diisopropylamide (8 mmol) in THF (20 mL) at -40°C. The mixture was then stirred at -10 °C for 1 hr, then cooled to -78 °C. A solution of (-) (*Ss, 1R, 2S, 5R)* menthyl 2-methoxynaphthyl-1-sulfinate (11)[14] (1.45 g, 4 mmol) in THF (10 mL) was then added dropwise over 10 min. After being stirred for 2 hr at -78 °C, the reaction mixture was quenched with methanol (5 mL) and the mixture was brought to room temperature and the solvents were evaporated under reduced pressure. The residue was dissolved in dichloromethane (50 mL) and the organic phase was washed with water, and then dried ($MgSO_4$). The solvent was evaporated under reduced pressure at room temperature and the residue was crystallised from dichloromethane and hexane (5:1) to give compound (8) as yellow pale crystals, m.p 68-69 °C, 1.34 g (65 % yield).

***N*-[1-(3,4-Dimethoxyphenyl)-2-(2'-methoxynaphthyl-1'-sulfinyl)]ethyl-*N*-[2-(3',4'-dimethoxyphenyl)]ethylamine (14) and (15).**

To a solution of (8) (0.6 mmol, 0.33 g), in dry methanol (10 mL) at -78°C was added sodium borohydride (1.2 mmol , 0.046 g). The reaction mixture was stirred at -78°C for 2 h and then the mixture was slowly warmed to room temperature. The methanol was then evaporated and the residue was treated with 2 M aqueous

potassium hydroxide (2 mL) and extracted with chloroform (3 x 15 mL). The combined extracts were dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography on silica gel using ethyl acetate/methanol (95:5) as eluent, to give a mixture of compounds (14) and (15) as semi-solid (315 mg, 95 % yield).

(*Rs*,1*S*) *N*-[1-(3,4-Dimethoxyphenyl)-2-(2'-methoxynaphthyl-1'-sulfinyl)]ethyl-*N*-[2-(3',4'-dimethoxyphenyl)]ethylamine (14).

Semi-solid, ^1H NMR δ 8.93 (d, J=8.8 Hz, 1 H), 8.0-6.6 (m, 11 H), 4.32 (dd, 1 H, J=3.2 and 10.4 Hz), 3.98 (s, 3 H, OMe), 3.86 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 3.80 (s, 3H, OMe), 3.18 (dd, J=10.2, 13.2 Hz, 1 H), 2.80 (t, 4 H). ^{13}C NMR δ 35.76 (CH_2), 37.59 (CH_2), 54.83 (OMe), 55.65 (OMe), 55.84 (OMe), 55.90 (OMe), 56.99 (OMe), 63.43 (Ar<u>C</u>HNH-Ar), 66.3 (<u>C</u>H_2S(O)), 110.58, 111.144, 113.05, 120.51, 120.78, 132.74, 124.44, 127.69, 128.64, 129.21, 129.46, 132.67, 133.16, 133.79, 147.23, 148.44, 148.72, 156.24. DEPT, 12 CH, 3 CH_2, 5 CH_3. MS m/z, 550.3 (100 %, M+H$^+$). Anal. calcd. for $C_{31}H_{35}NO_6S$: C, 67.74; H, 6.42; N, 2.55 %; Found: C, 67.85; H, 6.48; N, 2.50 %.

(*Rs*,1*R*) *N*-[1-(3,4-Dimethoxyphenyl)-2-(2'-methoxynaphthyl-1'-sulfinyl)]ethyl-*N*-[2-(3',4'-dimethoxyphenyl)]ethylamine (15).

^1H NMR (in part), δ 8.95, (d, J=8.8 Hz, 1 H), 4.15 (dd, J=5.6, 8.4 Hz. 1 H), 3.94 (s,3 H, OMe), 3.87 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.25 (dd, J=5.6, 13.2 Hz, 1 H).

***N*-Methyl-*N*-[1-(3',4'-dimethoxyphenyl)-2-(2'-methoxynaphthyl-1'-sulfinyl)ethyl-*N*-[2-(3',4'-dimethoxyphenylethyl)]amine (16) and (17).**

To a solution of the crude mixture (124 mg, 0.22 mmol) of (14) and (15) in acetonitrile (4 mL) and aqueous formaldehyde (37 %, 0.5 mL) was added sodium cyanoborohydride (50 mg, 0.8 mmol). After 20 min. the pH of the solution was adjusted to neutral on wet pH paper by the addition of glacial acetic acid. After 6 hr the mixture was concentrated by evaporation under reduced pressure. The mixture was treated with 2 M aqueous potassium hydroxide (2 mL) and extracted with chloroform (3x15 mL). The combined extracts were dried ($MgSO_4$) and evaporated. The crude product was purified by filtration through a short column of silica gel using ethyl acetate/methanol (95:5) as eluent, to give a 78 : 22 mixture of (16) and (17) as semi-solid in 86 % yield (110 mg). Careful column chromatography on silica gel using ethyl acetate/methanol (95:5) as eluent, gave diastereomerically pure (16).

(*Rs*,1*S*) *N*-Methyl-*N*-[1-(3,4-dimethoxyphenyl)-2-(2'-methoxy-1'-naphthylsulfinyl)]ethyl-*N*-[2-(3',4'-dimethoxyphenyl)]ethylamine (16).

^1H NMR δ 8.87 (d, J=8.8 Hz, 1 H), 8.0-6.6 (m, 11 H, aromatic), 4.31 (dd, 1 H, J = 5.3, 10.4 Hz), 3.99 (s, 3 H, OMe), 3.95 (s, 6 H, OMe), 3.91 (s, 3 H, OMe), 3.89 (s, 3 H, OMe), 3.88 (dd, J=3.2, 14 Hz, 1 H), 2.70 (m, 5 H), 2.30 (s, 3 H, Me). ^{13}C NMR δ 30.92 (CH_2), 34.10 (CH_2), 37.59 (N-Me), 54.83(OMe), 55.65 (OMe), 55.84 (OMe), 55.90 (OMe), 56.99 (OMe), 61.43 (Ar<u>C</u>HNMe), 66.4 (<u>C</u>H_2S(O)) 110.58, 111.144, 113.05, 120.51, 120.78, 132.74, 124.44, 127.69, 128.64, 129.21, 129.46, 132.67, 133.16, 133.79, 147.23,

148.44, 148.72, 156.24. DEPT, 12 CH, 3 CH_2, 6 CH_3. MS m/z, 564.3 (100 %, $M+H^+$). Anal. calcd. for $C_{32}H_{37}NO_6S$: C, 68.18; H, 6.62; N, 2.48 %, Found: C, 64.22 ; H, 6.68; N, 2.50 %.

(*Rs*,1*R*) *N*-Methyl-*N*-[1-(3',4'-dimethoxyphenyl)-2-(2'-methoxy-1'-naphthylsulfinyl)]ethyl-*N*-[2-(3',4'-dimethoxyphenyl)]ethylamine (17)

^1H NMR (in part), δ 8.84 (d, J=8.4 Hz, 1 H) , 3.87 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.76 (s, 3 H, OMe), 3.72 (dd, J=3.6, 12.4 Hz, 1 H), 2.23 (s, 3 H, NMe).

1-[2-(2'-Methoxy-1'-naphthyl)thio-4,5-dimethoxy]phenyl-2-[*N*-methyl-2-(3,4-dimethoxy)phenyl]ethylaminoethanol (19)

To a solution of β-amino sulfoxide (16) (0.563 g, 1 mmol) in dichloromethane (2 mL) and trifluoroacetic acid (1 mL) at 0 °C was added trifluoroacetic anhydride (1.2 eq., 0.23 g) in one portion and then the reaction was heated at 90 °C for 30 min in a sealed tube under argon. The reaction mixture was cooled and then made basic with 10 % aqueous potassium hydroxide (10 mL). The reaction mixture was extracted with chloroform (3x20 mL) and the extracts were dried over K_2CO_3. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (silica gel, ethyl acetate). The last fraction was collected as a semi-solid to give (19), (0.470 g, 86 % yield). ^1H NMR δ 8.45 (d, J=8.8 Hz, 1 H), 6.8-8 (m, 9 H, aromatic), 7.14 (s, 1 H), 6.29 (s,1 H), 5.46 (dd, 1 H, J=2 , 10.8 Hz), 3.99 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 3.78 (s, 6 H, OMe), 3.72 (s, 3 H, OMe), 3.40 (s, 3 H, OMe) 2.95 (dd, J=10.2, 14 Hz, 1 H), 2.80 (t, 4 H), 2.75 (dd, 1 H, J=2, 14 Hz) 2.35 (s, 3 H, Me). ^{13}C NMR δ 33.1 (CH_2), 41.7 (NMe), 55.5 (OMe), 55.6 (OMe), 55.7 (2 x OMe), 56.6 (OMe), 59.1 (CH_2), 64.2 (CH_2), 66.4 (CH), 108.7, 111.1, 111.8, 112.0, 113.3, 114.9, 120.4, 123.9, 125.1, 125.3, 127.5, 128.1, 129.3, 131.3, 132.6, 133.3, 135.7, 147.2, 147.7, 147.9, 148.7, 158.7. DEPT NMR, 12 CH, 3 CH_2, 6 CH3. MS m/z 564.3 (100 %, M^+). Anal. calcd. for $C_{32}H_{37}NO_6S$: C, 68.18; H, 6.62; N, 2.48 %, Found: C. 68.22; H, 6.68; N, 2.50 %.

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