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Asymmetric catalytic aziridination of dihydronaphthalenes for the preparation of substituted 2-aminotetralins

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ABSTRACT

An enantioselective synthesis of substituted 2-aminotetralins from dihydronaphthalenes in four steps is described. The key step is the Jacobsen's (diimine)copper-catalyzed asymmetric aziridination of dihydronaphthalenes to the respective aziridines in 33–82% yields and 60–87% enantiomeric excess. The enantioselectivity and the yield were dependent on the properties of the nitrene precursor. *p*Ts=NIPh appeared in general to give better results than *p*NsN=IPh. Aziridines were ring-opened in the benzylic position by catalytic hydrogenolysis in quantitative yields, and deprotected in two steps to the respective 2-aminotetralins in 66–85% yields. The synthesis of (*S*)-2-aminotetralin (>98% ee) and (*S*)-2-amino-7-methoxytetralin (56% ee) were accomplished in 30 and 52% overall yields, respectively.

1. Introduction

The pharmacological activity of 2-aminotetralin (2-amino-1,2,3,4-tetrahydronaphthalene, AT) was first described by Bamberger and Filehne in 1889.[1] Since then a large number of articles and patents, mostly describing studies of the physiological properties of this class of compounds, have appeared.[2] One of these compounds is the phenolic aminotetralin (*R*)-7-OH-DPAT (Fig. 1), which has been identified as a potent D3 dopamine receptor agonist.[3] Two other chiral examples are the central nervous system (CNS)-active 5-HT_{1B} (serotonin) receptor antagonist AR-A2,[4] and ST1214,[5] which is active in preventing and treating septic shock (Fig. 1).

The availability of substituted AT building blocks in high enantiomeric purity for synthesis and biological testing has been limited to less general methods and/or to non-cost-efficient methods. AT in enantiomeric pure form has been obtained by optical resolution[6] or bioconversion[7] of start materials to enantiopure precursors, and from optical resolution of racemic AT.[8] Naturally occuring α-amino acids like L-aspartic acid,[9] L-phenylalanine, and L-tyrosine[10] have been used as the chiral pool in multi-step reactions to construct optically pure AT. Other stereoselective synthetic methods of interest starting from substituted 2-tetralones, are enzymatic reduction,[11] bioconversion by (*S*)-aminotransferase,[12] reductive amination in the presence of a chiral amine,[13] reduction of chiral enamine,[14] and asymmetric catalytic hydrogenation of a prochiral enamide or ene carbamate.[15]

Here we report a short and stereoselective synthesis of substituted AT in accordance to the protocol shown in Scheme 1. The strategy applies known methods for enantioselective azirdination[16–18] of the corresponding dihydronapthalene **1** to form aziridine **2** (step i), which undergoes a regiospecific ring-opening in the benzylic position by hydrogenolysis to give the protected amine **3** (step ii). Removal of the *N*-protective group X (step iii) finally gives the substituted AT **4**.

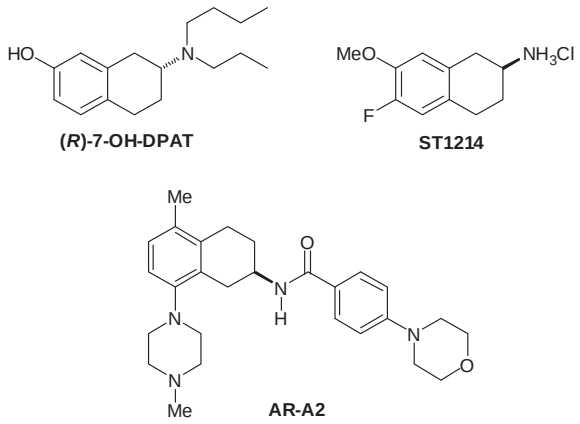

Fig. 1. Pharmacological active 2-aminotetralins.

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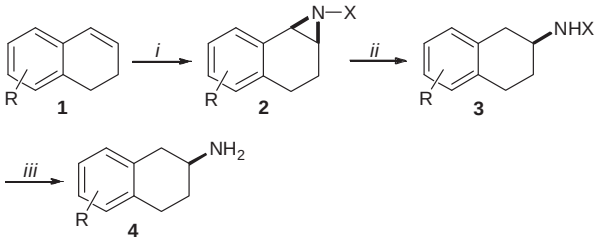
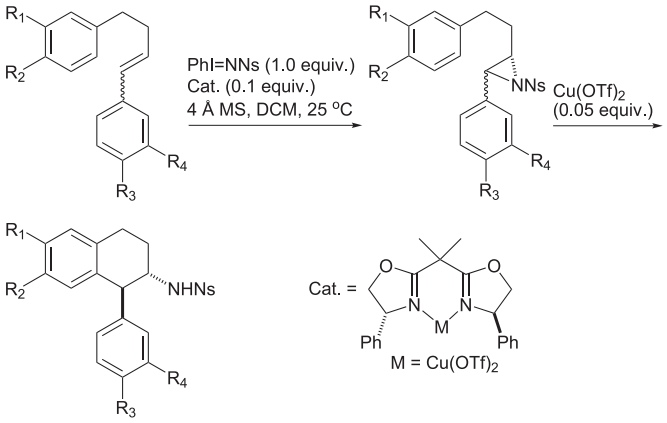


Scheme 1. General protocol for preparation of optically active 2-aminotetralins.

During our work a related enantioselective synthesis of *trans*-2-amino-1-aryltetralins was published (Scheme 2).[19] An enantioselective aziridination of aryl alkenes followed by an intramolecular Friedel–Crafts alkylation of the tethered and in situ generated aziridine provided a one-pot method synthesis of *trans*-2-amino-1-aryltetralins with excellent diastereo- (dr >99:1) and enantioselectivities (up to 92% ee).

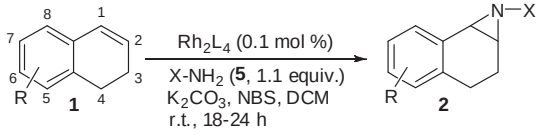


Scheme 2.

2. Results and discussion

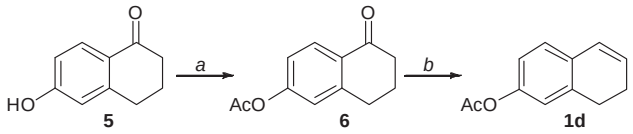
Substituted dihydronaphthalenes **1a**–**c** (see Table 1) were in general prepared from the respective α-tetralone in quantitative yields by following the work described by Hauser and Prasanna.[20] The less efficient preparation of 6-acetoxy-3,4-dihydronapthalene (**1d**) from tetralone **5** (36% overall yield, see Scheme 3) justifies a comment. Acetylation of **5** to **6** (Scheme 3, step a) and the following reduction to a benzylic alcohol (step b, part i) worked well.

Table 1
Preparation of racemic aziridines **2** (Doyle's method)[2]



Entry	Olefin (R)	X-NH$_2$ (X)	L[a]	Aziridine[b] (X)	Yield[c] %
1	**1a** (H)	**5a** (*p*Ts)	Cap	**2a** (*p*Ts)	92
2	**1a** (H)	**5a** (*p*Ts)	5*S*-MEPY	**2a** (*p*Ts)	90
3	**1a** (H)	**5b** (*p*Ns)	Cap	**2a** (*p*Ns)	30
4	**1a** (H)	**5b** (*p*Ns)	5*S*-MEPY	**2a** (*p*Ns)	60
5	**1a** (H)	**5c** (*p*MBs)	Cap	**2a** (*p*MBs)	76
6	**1b** (7-OMe)	**5a** (*p*Ts)	Cap	**2b** (*p*Ts)	54
7	**1c** (6-OMe)	**5a** (*p*Ts)	Cap	**2c** (*p*Ts)	4[d]
8	**1d** (6-OAc)	**5a** (*p*Ts)	Cap	**2d** (*p*Ts)	63

[a] Cap=caprolactamate and 5*S*-MEPY=methyl 2-oxopyrrolidine-5(*S*)-carboxylate.
[b] Racemic mixtures were confirmed by chiral HPLC (Daicels columns Chiralpak AD and Chiralcel OJ).
[c] Isolated yield after purification.
[d] Mixture of products.

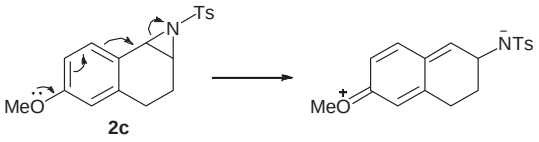


Scheme 3. (a) AcCl, pyr., DCM, 0 °C-rt, 97% yield; (b) (i) $NaBH_4$, 96% EtOH, rt; (ii) oxalic acid, benzene, Δ, 37% yield.

The final acid-catalyzed dehydration to **1d** (step b, part ii) appeared, however, to be more difficult. By applying the general method,[20] using catalytic *p*-toluenesulfonic acid (5 mol %) and azeotropic distillation in refluxing benzene, **1d** was prepared in maximum 10% yield (step b). Replacement of *p*-toluenesulfonic acid with the less acidic oxalic acid as catalyst improved the yield to 37% (best result).[21] In reactions applying higher concentrations of the substrate (step b, part ii) resulted in decreased yield of **1d**, indicating that intermolecular side reactions took place. Reversing the order of steps a and b shown in Scheme 3 to reduction/dehydration before the acetylation step did not give the desired product **1d** at all. The reaction failed at the reduction/dehydration step.

Racemic mixtures of *N*-arenesulfonyl aziridines **2** were prepared for chiral analysis purposes by applying Doyle's general and efficient dirhodium caprolactamate, $Rh_2(cap)_4$, catalyzed olefin aziridination procedure.[22] The results are presented in Table 1. The *N*-(*p*-toluenesulfonyl) (*p*Ts), *N*-(*p*-nitrobenzene-sulfonyl) (*p*Ns) and *N*-(*p*-methoxybenzenesulfonyl) (*p*Mbs) aziridines **2a** (R=H) were all prepared from olefin **1a** and the respective arenesulfonamide **5** in moderate to excellent yields (Table 1, entries 1, 3, and 5).

A substituent effect was observed in the aziridination of the two methoxy dihydronapthalenes **1b** (7-OMe) and **1c** (6-OMe). While the former substrate afforded aziridine **2b** (*p*Ts) in 54% yield (Table 1, entry 6), the latter substrate gave an inferior result (entry 7). According to TLC analysis, **1c** underwent full conversion, and ^{1}H NMR spectroscopic analysis of the reaction mixture (before work-up) showed that **2c** (*p*Ts) was the major product. However, attempts to purify **2c** (*p*Ts) by column chromatography were unsuccessful and afforded the target compound in ca. 4% yield together with other products (Table 1, entry 7). We assume the electron donating methoxy group in the *para* position makes the aziridine ring more labile (see Scheme 4), and more prone to nucleophilic ring opening in the benzylic position compared to the other aziridines described in this paper.



Scheme 4.

Since we were not able to prepare aziridine **2c** (*p*Ts) in pure form, a switch of the oxygen substituent from the electron donating MeO group to the electron withdrawing OAc group was considered and tested. Thus, aziridination of the dihydronapthalene **1d** worked rather well and afforded the 6-OAc aziridine **2d** (*p*Ts) in 63% yield (Table 1, entry 8).

Müller et al. have reported utilization of dirhodium tetrakis [methyl 2-oxopyrrolidine-5(*S*)-carboxylate], Rh_2(5*S*-MEPY)$_4$, as a chiral catalyst for the enantioselective aziridination of olefins with arylsulfonyl imino iodinanes ($ArSO_2N{=}IPh$).[23] Although the reported yields were quite good, the enantioselectivity was poor (up to 21% ee). Our attempts to induce enantioselectivity with Rh_2(5*S*-MEPY), applying Doyle's general protocol,[22] did not work at all. As the room temperature reactions afforded no enantiomeric excess (see entries 2 and 4, Table 1), reactions with **1a** and **5a** were tested at −20 °C [72 h reaction time, 56% yield of **2a** (*p*Ts)] and

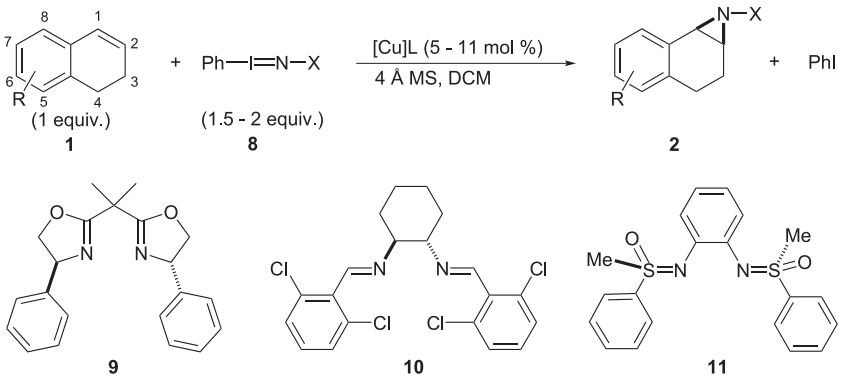
−78 °C [96 h reaction time, 50% yield of **2a** (*p*Ts)]. HPLC analysis (Daicel Chiralcel OJ) of the products showed that in all cases, the aziridine was formed as a racemate. It is not clear why no stereoselectivity was observed. The rhodium nitrene complex, that is, thought to be of mechanistic importance when sulfonyl imino iodinanes are used,[23] is probably not formed when arylsulfonamide **5** is used as nitrogen source. In their original work, Doyle suggested that an ionic mechanism is operative, as opposed to a nitrene process, with $Rh_2(cap)_4$ operating as a Lewis acid.[22]

Copper-catalyzed, enantioselective aziridination of olefins **1** to aziridines **2**, using $ArSO_2N{=}IPh$ (**8**, $ArSO_2{=}$*p*Ts, *p*Ns, and *p*Mbs) as the nitrene source, was performed according to procedures described by Evans et al.,[18] and by Jacobsen et al.,[17] applying the chiral ligands **9** and **10**, respectively. In addition, ligand **11**[24] and $[Cu(CH_3CN)_4]PF_6$ was tested following Jacobsen's procedure.[17] Representative results are presented in Table 2. In general, aziridination with the Jacobsen system provided aziridines **2a** (*p*Ts), **2a** (*p*Ns), and **2b** (*p*Ts) in better enantioselectivities (53–87% ee) and yields (33–82%) (Table 2, entries 3, 7, 11, and 12) compared to reactions with the Evans system (30–41% ee, and 0–26% yield) (Table 2, entries 1, 2, 9, and 10). This was expected since the Jacobsen system is complementary to the one developed by Evans in the sense that it affords high enantioselectivities with *cis*-olefins, while the latter method is more suited for the trans isomer.[16b] The best result was obtained for the unsubstituted olefin **1a** in reaction with **8a** (*p*Ts) affording aziridine **2a** (*p*Ts) in 87% ee and 82% yield (Table 2, entry 3), and ee value identical with Jacobsen's result published for the reaction.[17a] By a simple recrystallization, we were able to increase the enantiomeric excess of **2a** (*p*Ts) up to >98% ee and 47% yield. Asymmetric aziridination of **1a** with **8a** (*p*Ts) testing Bolm and Simić's ligand **11**[24] afforded **2a** (*p*Ts) in only 10% yield and 17% ee (Table 2, entry 4). For olefins **1b** and **1d**, the best results were obtained with imino iodinane **8a** (*p*Ts) and **10**-$[Cu(CH_3CN)_4PF_6]$ (the Jacobsen system) giving a 33% yield of **2b** (*p*Ts) (66% ee, entry 12) and 39% yield of **2d** (*p*Ts) (60% ee, entry 15), respectively. Similar experiments with nitrene precursor **8b** (*p*Ns) afforded aziridines **2b** (*p*Ns) and **2d** (*p*Ns) in low yields (21–24%) and low ee (35–45%, Table 2, entries 13 and 16). Attempts to increase the ee of aziridine **2b** (*p*Ns) by recrystallization (EtOAc/*n*-hexane) resulted in a reduction from 45 to 5% ee (13% yield, Table 2, entry 13). However, the filtrate provided enantiomerically enriched **2b** (*p*Ns) (91% ee, 10% yield).

Interestingly, reactions with dihydronaphthalene **1b** (7-OMe) and **8a** (*p*Ts), with the Evans system, yielded no aziridine product at all. Instead the substrate was aromatized to form 2-methoxynaphthalene in moderate to excellent yield (52–90%, entries 9 and 10). Similar attempts with the Jacobsen system afforded, however, **2b** (*p*Ts) in low yields (33–53%) and moderate enantiomeric excess (64–66%, entries 11 and 12).

Aziridines **2a** (*p*Ts), **2b** (*p*Ts), and **2d** (*p*Ts) were all ring-opened in the benzylic position by catalytic hydrogenolysis (10% Pd/C, 1 atm H_2)[25] in quantitative yields (see Scheme 5). The *N*-tosyl groups in **3a** and **3b** were deprotected by adopting a recent procedure described

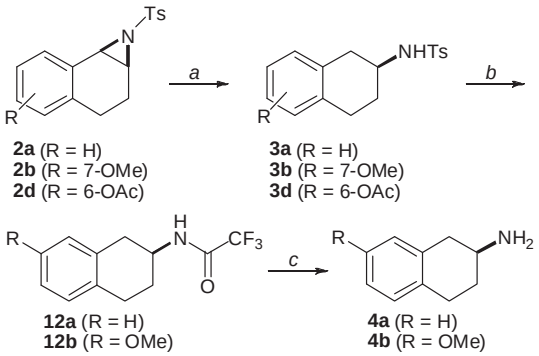
Table 2
Asymmetric aziridination of dihydronaphthalenes (**1**)



Entry	Olefin (R)	X–N=I-Ph (X)	[Cu]	L	Temp., °C (time, h)	Aziridine	Yield[a] %	ee[b] %	Config.
1	**1a** (H)	**8a** (*p*Ts)	$Cu(OTf)_2$	**9**	20 (36)	**2a** (*p*Ts)	16	30	(1*R*,2*S*)
2	**1a** (H)	**8a** (*p*Ts)	$Cu(OTf)_2$	**9**	−20 (72)	**2a** (*p*Ts)	22	36	(1*R*,2*S*)
3	**1a** (H)	**8a** (*p*Ts)	$[Cu(CH_3CN)_4]PF_6$	**10**	−40 (48)	**2a** (*p*Ts)	82[c]	87[c]	(1*R*,2*S*)[17a]
4	**1a** (H)	**8a** (*p*Ts)	$[Cu(CH_3CN)_4]PF_6$	**11**	−40 (24)	**2a** (*p*Ts)	10	17	(1*S*,2*R*)
5	**1a** (H)	**8b** (*p*Ns)	$Cu(OTf)_2$	**9**	20 (36)	**2a** (*p*Ns)	26	37	(1*R*,2*S*)[d]
6	**1a** (H)	**8b** (*p*Ns)	$Cu(OTf)_2$	**9**	−78 (96)	**2a** (*p*Ns)	16	41	(1*R*,2*S*)[d]
7	**1a** (H)	**8b** (*p*Ns)	$[Cu(CH_3CN)_4]PF_6$	**10**	−40 (24)	**2a** (*p*Ns)	33	53	(1*R*,2*S*)[d]
8	**1a** (H)	**8c** (*p*Mbs)	$Cu(OTf)_2$	**9**	20 (36)	**2a** (*p*Mbs)	22	36	(1*R*,2*S*)[d]
9	**1b** (7-OMe)	**8a** (*p*Ts)	$Cu(OTf)_2$	**9**	20 (36)	**2b** (*p*Ts)	0[e]		
10	**1b** (7-OMe)	**8a** (*p*Ts)	$Cu(OTf)_2$	**9**	−20 (72)	**2b** (*p*Ts)	0[f]		
11	**1b** (7-OMe)	**8a** (*p*Ts)	$[Cu(CH_3CN)_4]PF_6$	**10**	−20 (48)	**2b** (*p*Ts)	53	64	(1*R*,2*S*)
12	**1b** (7-OMe)	**8a** (*p*Ts)	$[Cu(CH_3CN)_4]PF_6$	**10**	−40 (48)	**2b** (*p*Ts)	33	66	(1*R*,2*S*)
13	**1b** (7-OMe)	**8b** (*p*Ns)	$[Cu(CH_3CN)_4]PF_6$	**10**	−20 (48)	**2b** (*p*Ns)	24[g]	45[g]	(1*R*,2*S*)[d]
14	**1d** (6-OAc)	**8a** (*p*Ts)	$[Cu(CH_3CN)_4]PF_6$	**10**	−20 (24)	**2d** (*p*Ts)	56	55	(1*R*,2*S*)[d]
15	**1d** (6-OAc)	**8a** (*p*Ts)	$[Cu(CH_3CN)_4]PF_6$	**10**	−40 (48)	**2d** (*p*Ts)	39	60	(1*R*,2*S*)[d]
16	**1d** (6-OAc)	**8b** (*p*Ns)	$[Cu(CH_3CN)_4]PF_6$	**10**	−40 (48)	**2d** (*p*Ns)	21	35	(1*R*,2*S*)[d]

[a] Isolated yield after purification.
[b] Determined by HPLC analysis (Daicels columns Chiralpak AD, Chiralcel OJ and Chiralcel OD-H, see the Experimental section for details).
[c] Recrystallization from 96% EtOAc afforded **2a** (*p*Ts) in 47% yield and ee >98%.
[d] The configuration is based on analysis of the applied catalyst, and by comparing the stereochemical results obtained with substrates **1a** (H) and **1b** (7-OMe) affording azirdines **2a** (*p*Ts)[17a] and **2b** (*p*Ts) with known configuration. Absolute configuration of the latter compound was established by chemical correlation with the known trifluoroacetylaminotetralin **12b** (see Scheme 5).[9d]
[e] 2-Methoxynaphthalene was isolated in 90% yield.
[f] 2-Methoxynaphthalene was isolated in 52% yield.
[g] Recrystallization from EtOAc/*n*-hexane afforded **2b** (*p*Ns) in 13% yield and 5% ee. Concentration of the filtrate yielded enantiomerically enriched **2b** (Ns) (91% ee) in 10% yield.

by Moussa and Romo[26] forming trifluoroacetylamino compounds **12a** and **12b** in 82 and 85% yields, respectively. Chiral HPLC analysis of the products showed that no racemization had taken place during this and the previous reaction. Comparison of the optical rotation of **12b** with literature data established the absolute configuration of the compound.[9d] Finally, basic hydrolysis of **12a** and **12b** provided AT compounds **4a** and **4b** in 81 and 100% yields, respectively. Comparison of our data for optical rotation of **4a** with the literature data confirmed the absolute configuration of the compound and verified that the basic hydrolysis proceeded without notable racemization.[7]



Scheme 5. (a) 10% Pd/C, 1 atm H_2, 96% EtOH, rt, 1 h, 95–100% yield; (b) (i) $(CF_3CO)_2O$, NEt_3, DCM, rt, 1 h; (ii) SmI_2, THF, −78 °C, 1.0–1.5 h, **12a** (82% yield), **12b** (85% yield); (c) K_2CO_3, MeOH, rt, 20–22 h, **4a** (81% yield), **4b** (100% yield).

3. Conclusions

In conclusion, we have developed a four step, enantioselective approach towards the pharmacologically interesting (*S*)-2-amino-tetralin (**4a**) (30% overall yield, >98% ee) and (*S*)-2-amino-7-methoxytetralin (**4b**) (52% overall yield, 56% ee) starting from the respective dihydronaphthalenes. The key step is the asymmetric catalytic aziridination of dihydronapthalenes **1** to aziridines **2**. Three different substituted dihydronapthalenes **1a** (H), **1b** (7-OMe), and **1d** (6-OAc), and two nitrene precursors [$ArSO_2N{=}IPh$, $ArSO_2{=}$*p*Ts (**8a**) and *p*Ns (**8b**)] were evaluated applying known methods for enantioselective aziridination. The best results were obtained with the Jacobsen system[17] applying catalyst **10**-$[Cu(CH_3CN)_4PF_6]$ and **8a** (*p*Ts) affording aziridines with enantioselectivities in the range of 60–87%, and yields of 39–82%. The synthetic protocol outlined in Scheme 1 appears to be promising for the preparation of various substituted AT compounds.

4. Experimental

4.1. General

All reactions were performed under an argon or nitrogen atmosphere. Tetrahydrofuran (THF) was distilled under nitrogen atmosphere from Na/benzophenone. Dichloromethane was distilled under nitrogen from calicium hydride. The nitrene precursors **8a**–**c** were all prepared according to the procedure described for preparation of **8a**.[27] Melting points were determined on a Buchi 535 apparatus. TLC was performed on Merck silica gel 60 F_{254} plates, using UV light at 312 nm and a 5% alcoholic molybdophosphoric acid for detection. Silica gel for flash chromatography was purchased from Merck. Optical rotations were measured with a Perkin–Elmer 241 Polarimeter. Enantiomeric excesses were determined by HPLC analysis, using Daicels columns Chiralcel OD-H, OJ or Chiralpak AD (250×4.6 mm). ^1H and ^{13}C NMR spectra (Bruker Advance DPX instruments 300/75 MHz and 400/100 MHz) were obtained from solutions of $CDCl_3$, and chemical shifts are in parts per million and referenced to TMS via the lock signal of the solvent. ^1H and ^{13}C NMR signals were assigned by 2D correlation techniques (COSY, HSQC). IR spectra were run on a Thermo Nicolet FTIR NEXUS instrument, and only the strongest/structurally most important peaks are listed. The mass spectra were recorded on a Finnigan MAT 95XL mass spectrometer. The electron-impact mass spectra, MS (EI), were recorded at 50 eV with a direct inlet, and the electron spray ionization mass spectra, MS (ESI), at 4.7 kV for low resolution spectra and 10 kV for high resolution spectra. The high resolution mass spectra, HRMS (EI) and (ESI), were obtained by using perfluorokerosene (PFK) and polyethyleneimine (PEI) as standards, respectively, to provide the reference masses. The elemental analyses were performed at the Mikroanalytisches labor Beller, Göttingen, Germany.

4.2. Preparation of dihydronapthalenes

The dihydronaphthalenes **1a**–**c** were prepared from the respective α-tetralones according to the work described by Hauser and Prasanna.[20]

*4.2.1. 6-Acetoxy-α-tetralone (**6**).* The title compound was prepared according to an adopted procedure described by Bolchi et al.[28] Acetyl chloride (2.90 mL, 40.7 mmol) was added dropwise to a cooled solution of 6-hydroxy-α-tetralone (**5**, 6.00 g, 37 mmol) and pyridine (3.59 mL, 44.4 mmol) in DCM (35 mL), keeping the temperature below 5 °C. The reaction mixture was then stirred at room temperature for 2 h (TLC showed complete acetylation of **5**). The mixture was treated with 10% aqueous HCl (15 mL), washed with water (2×8 mL), dried ($MgSO_4$), and concentrated to afford **6** (7.33 g, 97% yield) as an orange solid. The product was used for the subsequent step without further purification. A sample of the crude product was recrystallized (*i*-PrOH/*n*-hexane) for spectroscopic analysis. Data for **6**: White solid: R_f (Et_2O)=0.5. Mp=60.5–61.0 °C (from *i*-PrOH/*n*-hexane) {lit. mp=61–62 °C (from diluted ethanol)}.[29] ^1H NMR (400 MHz): δ 8.06 (app d, 1H, *J* 8.3 Hz, H-8), 7.04–7.00 (m, 2H, H-5/H-7), 2.96 (t, 2H, *J* 6.2 Hz, H-4), 2.64 (t, 2H, *J* 6.2 Hz, H-2), 2.30 (s, 3H, Me), 2.14 (app p, 2H, *J* 6.2 Hz, H-3). ^{13}C NMR (100 MHz): δ 197.9 (C-1), 169.0 ($COCH_3$), 154.4 (C-6), 146.3, 130.5, 129.2 (C-8), 121.5 (C-5), 120.2 (C-7), 39.0 (C-4), 29.8 (C-2), 23.2 (C-3), 21.2 ($COCH_3$). IR (KBr tablet): 2944 (w), 2875 (w), 1757 (s), 1684 (s), 1604 (m), 1278 (m), 1237 (s), 1212 (s), 1189 (s) cm^{-1}.

*4.2.2. 6-Acetoxy-3,4-dihydronaphthalene (**1d**).* Sodium borohydride (20.8 mg, 0.55 mmol) was added to a stirred solution of **6** (225 mg, 1.1 mmol) in 96% EtOH (5 mL). The mixture was heated under reflux for 15 min and then cooled to room temperature. The resultant suspension was filtered through a silica plug, and the filtrate concentrated under reduced pressure. The EtOH residue was removed by dissolving the resultant red oil twice in benzene (5 mL) followed by an azeotropic evaporation under reduced pressure. The remainder was dissolved in benzene (15 mL), added oxalic acid (14.9 mg, 0.165 mmol), and heated to reflux with azeotrope removal of water (Dean–Stark apparatus) until TLC analysis showed complete dehydration of the alcohol to the olefinic product (ca. 2 h). The reaction mixture was cooled to room temperature, washed with brine (2×10 mL), dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (EtOAc/*n*-hexane, 5:95) to afford **1d** (76.6 mg, 37% yield) as a colorless oil. Data for **1d**: R_f (EtOAc/*n*-hexane, 1:1)=0.56. ^1H NMR (400 MHz): δ 7.01 (d, 1H, *J* 8.0 Hz, H-8), 6.85–6.82 (m, 2H, H-5/H-7), 6.44 (dt, 1H, *J* 9.6, 1.8 Hz, H-1), 6.01 (app p, 1H, *J* 4.6 Hz, H-2), 2.78 (t, 2H, *J* 8.1 Hz, H-4), 2.30–2.20 (m, 2H, H-3), 2.29 (s, 3H, Me). ^{13}C NMR (100 MHz): δ 169.7 (CO), 149.2 (C-6), 137.0, 132.0, 128.4 (C-2), 127.0 (C-1), 126.6 (C-8), 120.8 (C-5),

119.2 (C-7), 27.5 (C-4), 22.8 (C-3), 21.1 (Me). IR (thin film, NaCl): 3033 (w), 2935 (w), 2885 (w), 2830 (w), 1761 (s), 1608 (w), 1575 (w), 1493 (m), 1369 (m), 1209 (s), 1196 (s), 1142 (m), 1016 (m) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 188 (M^+, 16), 147 (11), 146 (100), 145 (38), 144 (12), 131 (18), 127 (11), 117 (12), 116 (13), 115 (25), 91 (25), 83 (13), 81 (18), 69 (13), 67 (13). HRMS (EI) calcd for $C_{12}H_{12}O_2$ 188.0837 (M^+), found 188.0836.

4.3. Aziridination of dihydronaphthalenes

General procedure for aziridination of dihydronaphthalenes under achiral conditions (Doyle's method)[22] *references for HPLC analysis.* To a stirred suspension of the olefin **1** (2.72 mmol, 100 mol %), arylsulfonamide (**5**, 2.99 mmol, 110 mol %), K_2CO_3 (5.71 mmol, 210 mol %) ,and dirhodium catalyst [Rh_2(cap)$_4$ or Rh_2(5S-MEPY)$_4$, 0.0027 mmol, 0.1 mol %] in dry CH_2Cl_2 (10 mL), at ambient temperature under a nitrogen atmosphere, was added NBS (2.99 mmol, 110 mol %) in one portion. The color of the stirred suspension immediately turned from pink to red. After the appropriate reaction time (see Table 1), silica gel was added to the reaction mixture and the solvent was evaporated. The silica phase containing the product was added directly to a pre-packed silica column, and then eluted (EtOAc/*n*-hexane, 1:4) to afford the racemic (shown by HPLC) and analytical pure aziridine **2**. Isolated yields are shown in Table 1.

Asymmetric aziridination of dihydronaphthales adopting Evans general procedure[18a]. $Cu(OTf)_2$ (0.04 mmol, 5.2 mol %) was added a solution of the PhBOX ligand **9** (0.04 mmol, 5.2 mol %) in dry CH_2Cl_2 (2 mL), and stirred at room temperature for 3 h under an argon atmosphere. The resulting mixture was then transferred via cannula to a stirred suspension (cooled or at room temperature, see Table 2) of the olefin **1** (0.77 mmol, 100 mol %), PhI=N–SO_2Ar (**8**, 1.54 mmol, 200 mol %) and activated 4 Å molecular sieves (powder, 770 mg). Transfer was assisted with 0.5 mL CH_2Cl_2. After the specified reaction time (36–96 h, see Table 2), the reaction was quenched by diluting with 50% *n*-hexane/EtOAc (10 mL) and filtering through a short plug of silica gel. The silica was washed with additional portions of 50% *n*-hexane/EtOAc (2×10 mL) and the filtrate was concentrated by rotary evaporation. The crude product was purified by flash chromatography (EtOAc/*n*-hexane, 1:4). All ee's were determined by HPLC analysis. Isolated yields of **2** are shown in Table 2.

Asymmetric aziridinantion of dihydronaphthalenes adopting Jacobsen's general procedure[17]. A solution of [$Cu(CH_3CN)_4$] (0.081 mmol, 10.6 mol %) and diimine ligand (**10** or **11**, 0.088 mmol, 11 mol %) in dry CH_2Cl_2 (2 mL) was stirred under an argon atmosphere for 30 min at room temperature. The olefin **1** (0.766 mmol, 100 mol %) was added via syringe and the resultant mixture stirred for additional 15 min, and then cannulated to a stirred and cooled (−40−−20 °C, see Table 2 for the temperature given for the specific reaction) suspension of PhI=N–SO_2Ar (**8**, 1.17 mmol, 153 mol %) and activated 4 Å molecular sieves (powder, 827 mg) in dry CH_2Cl_2 (1 mL). After the specified reaction time (24–48 h, see Table 2), the reaction was allowed to warm to room temperature and filtered through a silica plug washed with EtOAc. The resultant solution was concentrated and the crude product purified by flash chromatography (EtOAc/*n*-hexane, 1:4). All ee's were determined by HPLC analysis. Isolated yields of **2** are shown in Table 2.

4.3.1. (1R,2S)-N-(p-Methylbenzenesulfonyl)amino-1,2,3,4-tetrahydro-naphthalene-1,2-imine, ***2a*** *(pTs).* Data for **2a** (*p*Ts): White solid: R_f (EtOAc/*n*-hexane, 1:4)=0.21. Mp=120–135 °C (from EtOAc). $[\alpha]_D^{22}$ +67.5 (*c* 1.0, CH_2Cl_2). HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): 97% ee, t_R 31.3 (1*R*,2*S*) and 37.1 (1*S*,2*R*) min. The ^1H and ^{13}C NMR spectra were comparable with data reported for racemic **2a** (*p*Ts).[30]

4.3.2. (1R,2S)-N-(p-Nitrobenzenesulfonyl)amino-1,2,3,4-tetrahydro-naphthalene-1,2-imine, ***2a*** *(pNs).* Data for **2a** (*p*Ns): Pale yellow solid: R_f (EtOAc/*n*-hexane, 1:4)=0.12. Mp=155–163 °C (EtOAc/*n*-hexane). $[\alpha]_D^{23}$ +37.6 (*c* 1.0, CH_2Cl_2). HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 35/65, 1.0 mL min^{-1}, 230 nm): 34% ee, t_R 43.2 (major) and 56.7 min. The ^1H and ^{13}C NMR spectra were comparable with data reported for racemic **2a** (*p*Ns).[31]

4.3.3. (1R,2S)-N-(p-Methoxybenzenesulfonyl)amino-1,2,3,4-tetrahydronaphthalene-1,2-imine, ***2a*** *(pMbs).* Data for **2a** (*p*Mbs): White solid: R_f (EtOAc/*n*-hexane, 1:4)=0.11. $[\alpha]_D^{23}$ +55.7 (*c* 1.0, CH_2Cl_2). HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 35/65, 1.0 mL min^{-1}, 230 nm): 36% ee, t_R 19.2 (major) and 24.6 min. ^1H NMR (400 MHz): δ 7.87 (app d, 2H, *J* 8.0 Hz, Mbs H-2/H-6), 7.30 (dd, 1H, *J* 7.3, 1.3 Hz, H-8), 7.24–7.12 (m, 2H, H-6/H-7), 7.05 (br d, 1H, *J* 7.4 Hz, H-5), 6.98 (app d, 2H, *J* 8.0 Hz, Mbs H-3/H-5), 3.86 (s, 3H, OCH_3), 3.79 (d, 1H, *J* 7.0 Hz, H-1), 3.54 (br d, 1H, *J* 7.0 Hz, H-2), 2.76 (app dt, 1H, *J* 13.4, 6.3 Hz, H-4), 2.54 (dd, 1H, *J* 15.6, 5.4 Hz, H-4), 2.26 (ddt, 1H, *J* 14.3, 6.3, 1.9 Hz, H-3), 1.72–1.62 (m, 1H, H-3). ^{13}C NMR (100 MHz): 163.4 (*p*-$MeOC_6H_4$ C-4), 136.6, 130.14, 130.07, 129.8 (*p*-$MeOC_6H_4$ C-2/C-6), 129.4 (C-8), 128.5 (C-5), 128.4 (C-6), 126.3 (C-7), 114.2 (*p*-$MeOC_6H_4$ C-3/C-5), 55.6 (OCH_3), 42.0 (C-1), 41.7 (C-2), 24.7 (C-4), 20.0 (C-3). IR (KBr tablet): 3097 (w), 3014 (w), 2934 (m), 2912 (m), 2855 (m), 1596 (s), 1577 (s), 1498 (s), 1449 (s), 1325 (s), 1264 (s), 1152 (s), 1092 (s) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 315 (M^+, 19), 251 (4), 171 (7), 145 (30), 144 (100), 143 (14), 128 (17), 118 (15), 117 (94), 116 (40), 115 (73), 92 (13), 91 (16), 77 (17). HRMS (EI) calcd for $C_{17}H_{17}NO_3S$: 315.0929 (M^+), found 315.0925.

4.3.4. (1R,2S)-N-(p-Methylbenzenesulfonyl)amino-1,2,3,4-tetrahydro-7-methoxynaphthalene-1,2-imine, ***2b*** *(pTs).* Data for **2b** (*p*Ts): White solid: R_f (EtOAc/*n*-hexane, 1:4)=0.18. Mp=131–133 °C (from *i*-PrOH/*n*-hexane). $[\alpha]_D^{22}$ +80.6 (*c* 0.84, CH_2Cl_2). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): 56% ee, t_R 20.7 (major) and 25.7 min. ^1H NMR (400 MHz): δ 7.81 (app d, 2H, *J* 8.3 Hz, Ts H-2/H-6), 7.30 (app d, 2H, *J* 8.0 Hz, Ts H-3/H-5), 6.95 (d, 2H, *J* 8.3 Hz, H-5), 6.86 (d, 1H, *J* 2.7 Hz, H-8), 6.77 (dd, 1H, *J* 8.3, 2.7 Hz, H-6), 3.78 (s, 3H, OCH_3), 3.77 (d, 1H, hidden, H-1), 3.52 (app d, 1H, *J* 7.0 Hz, H-2), 2.65 (app dt, 1H, *J* 14.9, 6.2 Hz, H-4), 2.46 (app dd, 1H, *J* 15.4, 5.4 Hz, H-4), 2.42 (s, 3H, Ts CH_3), 2.28–1.80 (m, 1H, H-3), 1.70–1.58 (m, 1H, H-3). ^{13}C NMR (100 MHz): δ 157.9 (C-7), 144.2, 135.6, 130.9, 129.6 (Ts C-3/C-5), 129.4 (C-5), 128.6, 127.6 (Ts C-2/C-6), 115.0 (C-8), 113.8 (C-6), 55.4 (OCH_3), 42.1 (C-1), 41.7 (C-2), 23.8 (C-4), 21.6 (Ts CH_3, 20.3 C-3). IR (KBr tablet): 3068 (w), 3048 (w), 3019 (w), 2936 (m), 2854 (w), 2835 (w), 1618 (m), 1596 (m), 1580 (m), 1500 (s), 1454 (m), 1320 (s), 1267 (s), 1157 (s), 1091 (s), 1042 (s) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 329 (M^+, 12), 175 (16), 174 (100), 173 (8), 160 (7), 159 (16), 158 (32), 148 (6), 147 (45), 146 (10), 145 (19), 131 (11), 130 (10), 115 (9), 103 (6), 92 (5), 91 (21). HRMS (EI) calcd for $C_{18}H_{19}NO_3S$: 329.1086 (M^+), found 329.1088.

4.3.5. (1R,2S)-N-(p-Nitrobenzenesulfonyl)amino-1,2,3,4-tetrahydro-7-methoxynaphthalene-1,2-imine, ***2b*** *(pNs).* Data for **2b** (*p*Ns): Pale yellow solid: R_f (EtOAc/*n*-hexane, 1:4)=0.18. Mp=140.5–141.0 °C (from EtOAc/*n*-hexane). $[\alpha]_D^{22}$ +11 (*c* 0.45, CH_2Cl_2). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 35/65, 1.0 mL min^{-1}, 230 nm): 11% ee, t_R 14.1 (major) and 34.0 min. ^1H NMR (400 MHz): δ 8.36 (app d, 2H, *J* 9.0 Hz, Ns H-3/H-5), 8.14 (app d, 2H, *J* 9.0 Hz, Ns H-2/H-6), 6.99 (d, 1H, *J* 8.3 Hz, H-5), 6.87 (d, 1H, *J* 2.7 Hz, H-8), 6.79 (dd, 1H, *J* 8.3, 2.7 Hz, H-6), 3.89 (d, 1H, *J* 7.1 Hz, H-1), 3.79 (s, 3H, OCH_3), 3.69 (app d, 1H, *J* 7.1 Hz, H-2), 2.69–2.49 (m, 2H, H-4), 2.32–2.24 (m, 1H, H-3), 1.77–1.67 (m, 1H, H-3). ^{13}C NMR (100 MHz): δ 158.4 (C-7), 150.7 (Ns C-4), 144.8 (Ns C-1), 130.3 (C-9), 129.9 (C-5), 129.1 (Ns C-2/C-6),

128.6 (C-10), 115.4 (C-8), 114.3 (C-6), 55.6 (OCH_3), 43.5 (C-1), 42.9 (C-2), 23.9 (C-4), 20.6 (C-3). IR (thin film, NaCl): 3108 (w), 2964 (w), 1604 (m), 1558 (m), 1530 (s), 1350 (s), 1315 (s), 1265 (s), 1087 (s), 1156 (s) cm^{-1}. Anal. Calcd for $C_{17}H_{16}N_2O_5S$: C, 56.66; H, 4.47; N, 7.77; S, 8.90, found: C, 56.35; H, 4.30; N, 7.55; S, 8.87.

4.3.6. (1R,2S)-N-(p-Methylbenzenesulfonyl)amino-1,2,3,4-tetrahydro-6-acetoxynaphthalene-1,2-imine, ***2d*** *(pTs).* Data for **2d** (*p*Ts): White solidified foam: R_f(EtOAc/*n*-hexane, 1:4)=0.06. $[\alpha]_D^{22}$ +27.9 (*c* 1.0, CH_2Cl_2). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): 60% ee, t_R 26.2 (major) and 30.3 min. ^1H NMR (400 MHz): δ 7.81 (app d, 2H, *J* 8.3 Hz, Ts H-2/H-6), 7.31 (app dd, 3H, *J* 8.2, 2.7 Hz, H-8 and Ts H-3/H-5), 6.88 (app dd, 1H, *J* 8.1, 1.8 Hz, H-7), 6.80 (br s, 1H, H-5), 3.81 (d, 1H, *J* 7.1 Hz, H-1), 3.56 (app d, 1H, *J* 7.1 Hz, H-2), 2.76 (app dt, 1H, *J* 14.4, 6.2 Hz, H-4), 2.52 (app dd, 1H, *J* 15.6, 5.3 Hz, H-4), 2.43 (s, 3H, Ts CH_3), 2.28 (s, 3H, Ac), 2.34–2.19 (m, 1H, H-3), 1.76–1.61 (m, 1H, H-3). ^{13}C NMR (100 MHz): δ 169.5 (C=O), 150.6 (C-6), 144.4, 138.2, 135.5, 130.4, 129.6 (Ts C-3/C-5), 127.7 (Ts C-2/C-6), 126.4, 121.8 (C-5), 119.4 (C-7), 41.6 (C-1), 41.5 (C-2), 24.8 (C-4), 21.6 (Ts CH_3), 21.1 ($COCH_3$), 19.7 (C-3). IR (KBr tablet): 3029 (m), 2938 (m), 2853 (m), 1758 (s), 1617 (m), 1597 (s), 1499 (s), 1432 (m), 1370 (s), 1208 (s), 1158 (s), 1091 (s), 1044 (m), 1015 (s), 998 (m) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 357 (M^+, 1), 188 (5), 171 (69), 162 (47), 160 (12), 155 (88), 146 (61), 147 (13), 145 (28), 13 (14), 120 (12), 108 (12), 107 (24), 91 (100), 79 (16), 77 (14), 65 (44), 63 (10), 43 (59). HRMS (EI) calcd for $C_{19}H_{19}NO_4S$: 357.1035 (M^+), found 357.1040.

4.3.7. (1R,2S)-N-(p-Nitrobenzenesulfonyl)amino-1,2,3,4-tetrahydro-6-acetoxynaphthalene-1,2-imine, ***2d*** *(pNs).* Data for **2d** (*p*Ns): White solid: R_f (EtOAc/*n*-hexane, 1:4)=0.04. Mp=150–156 °C (from EtOAc/*n*-hexane). $[\alpha]_D^{23}$ +47.2 (*c* 0.69, CH_2Cl_2). HPLC (Chiralcel OD-H, *i*-PrOH/*n*-hexane, 35/65, 1.0 mL min^{-1}, 230 nm): 35% ee, t_R 21.4 and 28.6 (major) min. ^1H NMR (400 MHz): δ 8.37 (app d, 2H, *J* 9.0 Hz, Ns), 8.13 (app d, 2H, *J* 9.0 Hz, Ns), 7.32 (d, 1H, *J* 8.2 Hz, H-8), 6.90 (app ddd, 1H, *J* 8.2, 2.4, 0.8 Hz, H-7), 6.83 (br s, 1H, H-5), 3.93 (d, 1H, *J* 7.1 Hz, H-1), 3.71 (app d, 1H, *J* 7.1 Hz, H-2), 2.73 (app dt, 1H, *J* 14.5, 6.5 Hz, H-4), 2.56 (app dd, 1H, *J* 15.8, 5.5 Hz, H-4), 2.36–2.25 (m, 1H, H-3), 2.28 (3H, s, Ac), 1.83–1.68 (m, 1H, H-3). ^{13}C NMR (100 MHz): δ 169.4 (C=O), 150.9 (C-6 or Ns C-4), 150.5 (C-6 or Ns C-4), 144.5 (Ns C-1), 138.1 (C-10), 130.4 (C-8), 128.8 (Ns C-2/C-6), 126.8 (C-9), 124.4 (Ns C-3/C-5), 122.0 (C-5), 119.7 (C-7), 42.6 (C-1), 42.4 (C-2), 24.6 (C-4) 21.0 ($COCH_3$), 19.7 (C-3). IR (KBr tablet): 3110 (w), 2940 (w), 1763 (s), 1608 (m), 1525 (s), 1500 (m), 1351 (s), 1309 (s), 1207 (s), 1160 (s) cm^{-1}. HRMS (EI) calcd for $C_{18}H_{16}N_2O_6S$: 388.0729 (M^+), found 388.0723.

4.4. Aziridine ring-opening by catalytic hydrogenolysis

The ring-opening of aziridines **2a** (*p*Ts), **2b** (*p*Ts), and **2d** (*p*Ts) were performed by adaption of a literature procedure.[25] The ring opening of **2a** (Ts) is shown as a general example. Aziridine **2a** (*p*Ts) (0.107 g, 0.358 mmol, >98% ee) was dissolved with stirring in 96% ethanol (7 mL). Catalyst 10% Pd/C (13.1 mg) was added, the flask was evacuated and an atmosphere of hydrogen was secured. The mixture was stirred under balloon pressure of hydrogen for 1 h (reaction complete according to TLC). The mixture was filtered through a plug of silica, which was washed with ethyl acetate. The combined filtrate and washings were evaporated to dryness to give **3a** as a white solid (0.107 g, 99% yield, >98% ee according to HPLC). Catalytic hydrogenolysis of **2b** (*p*Ts) and **2c** (*p*Ts) afforded **3b** and **3d** in 95–100% yields, and without racemization.

*4.4.1. (S)-2-(p-Methylbenzenesulfonyl)amino-1,2,3,4-tetrahydronaphthalene (****3a****).* Data for **3a**: White solid: R_f (EtOAc/*n*-hexane, 1:4)=0.23. Mp=105–106 °C (from 96% EtOH). $[\alpha]_D^{23}$ −64.6 (*c* 1.1, CH_2Cl_2). HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): >98% ee, t_R 36.0 (*S*) and 59.9 (*R*) min. ^1H NMR (300 MHz): 7.78 (app d, 2H, *J* 8.3 Hz, Ts H-2/H-6), 7.31 (app d, 2H, *J* 8.3 Hz, Ts H-3/H-5), 7.15–7.10 (m, 3H, H-6/H-7/H-8), 6.96–6.89 (m, 1H, H-5), 4.49 (br d, 1H, *J* 7.7 Hz, NH), 3.68–3.54 (m, 1H, H-2), 2.95 (dd, 1H, *J* 16.4, 5.1 Hz, H-1), 2.87–2.69 (m, 2H, H-4), 2.59 (dd, 1H, *J* 16.4, 8.0 Hz, H-1), 2.45 (s, 3H, Ts CH_3), 2.02–1.88 (m, 1H, H-3), 1.80–1.65 (m, 1H, H-3). ^{13}C NMR (100 MHz): δ 143.3 (Ts C-1), 138.0 (Ts C-4), 135.1 (C-10), 133.4 (C-9), 129.7 (Ts C-3/C-5), 129.3 (C-5), 128.7 (C-8), 127.0 (Ts C-2/C-6), 126.3 (C-6), 125.9 (C-7), 49.5 (C-2), 36.4 (C-1), 29.6 (C-3), 26.9 (C-4), 21.5 (Ts CH_3). IR (KBr tablet): 3243 (s), 3075 (w), 3040 (w), 2923 (m), 1735 (w), 1596 (m), 1578 (w), 1494 (m), 1451 (s), 1327 (s), 1302 (m), 1287 (m), 1236 (m), 1161 (s), 1074 (s), 946 (s), 893 (s) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 302 (20), 301 (M^+, 100), 279 (12), 130 (21), 104 (6). HRMS (EI) calcd for $C_{17}H_{17}NO_3S$: 301.1136 (M^+), found 301.1129. Data for racemic **3a**: mp=124–125 °C (from 96% EtOH).

*4.4.2. (S)-2-(p-Methylbenzenesulfonyl)amino-7-methoxy-1,2,3,4-tetrahydronaphthalene (****3b****).* Data for **3b**: White solid: R_f (Al_2O_3, EtOAc/*n*-hexane, 1:4)=0.23. Mp=122–123 °C (from 96% EtOH) $[\alpha]_D^{23}$ −44.5 (*c* 1.01, CH_2Cl_2). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): 60% ee, t_R 28.7 (major) and 30.3 min. ^1H NMR (400 MHz): δ 7.77 (app d, 2H, *J* 8.3 Hz, Ts H-2/H-6), 7.31 (app d, 2H, *J* 8.3 Hz, Ts H-3/H-5), 6.96 (d, 1H, *J* 8.4 Hz, H-5), 6.69 (dd, 1H, *J* 8.4, 2.7 Hz, H-6), 6.47 (d, 1H, *J* 2.7 Hz, H-8), 4.44 (br d, 1H, *J* 8.1 Hz, N*H*), 3.74 (s, 3H, OCH_3), 3.70–3.60 (m, 1H, H-2), 2.92 (dd, 1H, *J* 16.2, 5.0 Hz, H-1), 2.81–2.66 (m, 2H, H-4), 2.57 (dd, 1H, *J* 16.2, 7.5 Hz, H-1), 2.44 (s, 3H, Ts CH_3), 1.96–1.87 (m, 1H, H-3), 1.77–1.66 (m, 1H, H-3). ^{13}C NMR (100 MHz): δ 157.7 (C-7), 143.4 (Ts C-4), 138.0 (C-9), 134.4 (Ts C-1), 129.7 (C-5 and Ts C-2/C-6), 127.0 (C-10 and Ts C-3/C-5), 113.8 (C-8), 112.8 (C-6), 55.2 (OCH_3), 49.2 (C-2), 36.7 (C-1), 29.7 (C-3), 25.9 (C-4), 21.5 (Ts CH_3). IR (KBr tablet): 3318 (br s), 3052 (w), 3009 (w), 2938 (m), 2836 (m), 1609 (s), 1505 (s), 1456 (m), 1422 (m), 1322 (s), 1251 (s), 1161 (s), 1062 8 (m), 811 (m) cm^{-1}. Anal. Calcd for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23; S, 9.67, found: C, 64.83; H, 6.35; N, 4.18; S, 9.78. Data for racemic **3b**: mp=106–107 °C (from 96% EtOH).

*4.4.3. (S)-2-(p-Methylbenzenesulfonyl)amino-6-acetoxy-1,2,3,4-tetrahydronaphthalene (****3d****).* Data for **3d**: White solid. Mp=114–116 °C (from 96% EtOH). $[\alpha]_D^{23}$ −30.4 (*c* 1.0, CH_2Cl_2). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): 45% ee, t_R 38.1 and 42.2 (major) min. ^1H NMR (400 MHz): δ 7.76 (app d, 2H, *J* 8.2 Hz, Ts H-2/H-6), 7.29 (app d, 2H, *J* 8.2 Hz, Ts H-3/H-5), 6.94 (app d, 1H, *J* 8.2 Hz, H-8), 6.81–6.76 (m, 2H, H-5/H-7), 4.68 (d, 1H, *J* 7.5 Hz, NH), 3.66–3.56 (m, 1H, H-2), 2.91 (dd, 1H, *J* 16.4, 4.6 Hz, H-1), 2.85–2.72 (m, 2H, H-4), 2.57 (dd, 1H, *J* 16.4, 8.0 Hz, H-1), 2.43 (s, 3H, Ts CH_3), 2.26 (s, 3H, $COCH_3$), 1.97–1.87 (m, 1H, H-3), 1.76–1.65 (m, 1H, H-3). ^{13}C NMR (100 MHz): δ 169.8 ($COCH_3$), 148.9 (C-6), 143.5, 137.9, 136.5, 131.1, 130.3 (C-8), 129.8 (Ts C-3/C-5), 127.0 (Ts C-2/C-6), 121.5 (C-7), 119.4 (C-5), 49.4 (C-2), 36.0 (C-1), 29.3 (C-3), 27.0 (C-4), 21.6 (Ts CH_3), 21.1 ($COCH_3$). IR (CCl_4): 3273 (s), 2927 (s), 2360 (s), 1959 (m), 1763 (s), 1600 (w), 1498 (m), 1438 (m), 1368 (m), 1329 (m), 1210 (s), 1162 (s), 1096 (m), 1015 (m) 909 (m) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 359 (M^+, 4), 356 (12), 314 (11), 188 (28), 160 (18), 147 (17), 146 (100), 145 (54), 133 (17), 131 (14), 117 (18), 91 (19), 65 (11). HRMS (EI) calcd for $C_{19}H_{21}NO_4S$: 359.1191 (M^+), found 359.1190.

4.5. Deprotecting the *N*-Ts group

The *N*-tosyl protecting groups in **3a** and **3b** were cleaved with SmI_2 and by initial activation of the nitrogen with a trifluoroacetyl group in accordance with a general procedure recently described by Moussa and Romo.[26] Basic hydrolysis[32] of respective *N*-trifluoroacetyl products **12a** and **12b** provided target compounds **4a**

and **4b**, respectively. The deprotection of **3a** to **12a**, and **12a** to aminotetralin **4a** is shown as a general example.

*4.5.1. (S)-2-Trifluoroacetylamino-1,2,3,4-tetrahydro-naphthalene (**12a**).* To a stirred solution of sulfonamide **3a** (0.1039 g, 0.335 mmol, >98% ee) and triethylamine (104 μL, 0.746 mmol) in dry CH_2Cl_2 (5 mL) was added TFAA (98 μL, 0.705 mmol) dropwise via syringe under a nitrogen atmosphere. After stirring for 1 h at room temperature, the reaction mixture was concentrated in vacuo and the residue diluted with dry THF (1.7 mL), cooled to −78 °C and subsequently treated dropwise with SmI_2 in THF (17.3 mL, 0.1 M, 1.73 mmol). The resulting mixture was stirred for 1.5 h at −78 °C, warmed to room temperature and then quenched by filtering through a compressed pad of silica gel. The filter pad was washed with EtOAc and the combined filtrate and washings were evaporated under reduced pressure. The residue was purified by flash chromatography (EtOAc/*n*-hexane, 1:9) to afford **12a** (68.75 mg, 82% yield) as a white solid. Data for **12a**: R_f (EtOAc/*n*-hexane, 1:4)=0.35. Mp=112–113 °C (from EtOAc/*n*-hexane).$[\alpha]_D^{22}$ −41.6 (*c* 1.06, CH_2Cl_2). HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): >98% ee, t_R 11.4 (*S*) and 15.9 (*R*) min. ^{1}H NMR (400 MHz): *δ* 7.19–7.05 (m, 4H, H-5/H-6/H-7/H-8), 6.33 (br s, 1H, NH), 4.39–4.28 (m, 1H, H-2), 3.18 (dd, 1H, *J* 16.3, 5.1 Hz, H-1), 3.00–2.84 (m, 2H, H-4), 2.75 (dd, 1H, *J* 16.3, 8.4 Hz, H-1), 2.17–2.08 (m, 1H, H-3), 1.93–1.82 (m, 1H, H-3). ^{13}C NMR (100 MHz): *δ* 156.7 (app d, *J* 37 Hz, C=O), 134.9 (C-10), 132.8 (C-9), 129.4, 128.9, 126.6, 126.2 (C-5/C-6/C-7/C-8), 115.8 (q, *J* 288 Hz, *C*F_3), 46.3 (C-2), 34.9 (C-1), 28.1 (C-3), 26.8 (C-4). ^{19}F NMR (376 MHz, ref C_6F_6=−162.3): *δ* −76.5 (s, C*F*$_3$). IR (KBr tablet): 3307 (br s), 3097 (w), 2938 (m), 2904 (w), 1698 (s), 1558 (s), 1455 (m), 1184 (s), 746 (s) cm^{-1}. Anal. Calcd for $C_{12}H_{12}F_3NO$: C, 59.26; H, 4.97; F, 23.43; N, 5.76, found: C, 59.27; H, 5.05; F, 23.15; N, 5.65. Data for racemic **12a**: mp=87–88 °C (from EtOAc/*n*-hexane).

*4.5.2. (2S)-1,2,3,4-Tetrahydro-2-naphthalenamine (**4a**).* To a solution of trifluoracetamide **12a** (60.3 mg, 0.248 mmol, >98% ee) in MeOH/H_2O (7:3, 7 mL) was added K_2CO_3 (172 mg, 1.244 mol) and the mixture was stirred for 22.5 h at room temperature. The solvent was removed under reduced pressure, and the residue was suspended in an aqueous solution of K_2CO_3 (15 mL, 20 wt%), and extracted with $CHCl_3$ (5×15 mL). The organic phase was dried ($MgSO_4$), filtrated, and concentrated under reduced pressure affording **4a** (29.6 mg, 81% yield) as pale yellow oil. Data for **4a**: $[\alpha]_D^{22}$ −84.5 (*c* 0.54, $CHCl_3$) {lit. for (*R*)-**4a**: $[\alpha]_D$ +85.4 (*c* 5 mg/mL, CH_2Cl_2)}.[7] The ^{1}H and ^{13}C NMR spectra were comparable with data reported for (*R*)-**4a**.[7]

*4.5.3. (2S)-7-Methoxy-2-(trifluoroacetylamino)-1,2,3,4-tetrahydronaphthalene (**12b**).* The title compound was prepared from sulfonamide **3b** (56% ee) in accordance with the procedure described for preparation of **12a**. The crude product was purified by flash chromatography (EtOAc/*n*-hexane, 1:4) affording **12b** (85% yield) as a white solid. Data for **12b**: R_f (EtOAc/*n*-hexane, 1:4)=0.28. Mp=107–108 °C (from EtOAc/*n*-hexane) (lit. mp=113–118 °C).[9d] $[\alpha]_D^{23}$ −50.9 (*c* 0.57, MeOH) {lit. for the (*S*)-enantiomer: $[\alpha]_D^{20}$ −90.8 (*c* 0.5, MeOH)}.[9d] HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 10/90, 1.0 mL min^{-1}, 230 nm): 56% ee, t_R 18.7 (*S*) and 38.2 (*R*) min. ^{1}H NMR (300 MHz): *δ* 7.04 (d, 1H, *J* 8.4 Hz, H-5), 6.74 (dd, 1H, *J* 8.4, 2.7 Hz, H-6), 6.60 (d, 1H, *J* 2.7 Hz, H-8), 6.23 (br s, 1H, NH), 4.40–4.27 (m, 1H, H-2), 3.78 (s, 3H, OC*H*$_3$), 3.16 (dd, 1H, *J* 16.4, 5.1 Hz, H-1), 2.95–2.76 (m, 2H, H-4), 2.72 (dd, 1H, *J* 16.4, 8.0 Hz, H-1), 2.16–2.04 (m, 1H, H-3), 1.94–1.80 (m, 1H, H-3). ^{13}C NMR (100 MHz): *δ* 157.9 (C-7), 156.7 (q, *J* 36.9 Hz, *C*OCF$_3$), 133.9 (C-9), 129.8 (C-5), 126.8 (C-10), 115.8 (q, *J* 228 Hz, *C*F$_3$), 113.9 (C-8), 113.0 (C-6), 55.2 (O*C*H$_3$), 46.2 (C-2), 35.2 (C-1), 28.2 (C-3), 25.8 (C-4). ^{19}F NMR (376 MHz, ref C_6F_6=−162.3): *δ* −76.5 (C*F*$_3$). Anal. Calcd for $C_{13}H_{14}F_3NO_2$: C, 57.14; H, 5.16; F, 20.86; N, 5.13, found: C, 57.14; H, 5.30; F, 20.45; N, 5.12. Data for racemic **12b**: mp=102–103 °C (from EtOAc/*n*-hexane).

4.5.4. (2R)-1,2,3,4-Tetrahydro-7-methoxy-2-naphthalenamine (**4b**).* The title compound was prepared from racemic trifluoroacetamide **12b** in accordance to the procedure described for preparation of **4a**. The racemic **4b** (100% yield) was obtained as a pale yellow oil. The ^{1}H NMR spectra of the compound was in accordance with reported data.[33]

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.11.010.

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