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Synthesis of New Chiral Monosulfonamides Prepared from (11*R*,12*R*)-11,12-Diamino-9,10-dihydro-9,10-ethanoanthracene and their Use as Ligands for Asymmetric Catalysis

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Abstract. New chiral monosulfonamides **6-16** containing (11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene as carbon skeleton were prepared. Compounds **6-12, 15** and **16** were used as optically active ligands in the enantioselective ethylation of benzaldehyde. Moreover, the monosulfonamides **6-10** were tested in the asymmetric transfer hydrogenation (ATH) of acetophenone with Rh(Cp*)L* complex.
Key words: Monosulfonamide, asymmetric catalysis, enantioselective addition.

Resumen. Nuevas monosulfonamidas quirales **6-16** teniendo a la (11*R*,12*R*)-diamino-9,10-dihidro-9,10-etanoantraceno como esqueleto carbonado fueron preparadas. Los compuestos **6-12**, **15** y **16** se utilizaron como ligantes ópticamente activos en la etilación enantioselectiva de benzaldehído. Además, las monosulfonamidas **6-10** se probaron en la reducción asimétrica por transferencia de hidrógeno (ATH) de acetofenona con Rh(Cp*)L* utilizándolos como catalizadores.
Palabras clave: Monosulfonamida, catálisis asimétrica, adición enantioselectiva.

Introduction

Chiral secondary alcohols are important structures present in natural products and in many pharmaceutical compounds, and are also precursors for many other complex organic molecules [1]. Hence, there is need to develop new methods for making chiral secondary alcohol. Asymmetric catalysis has been a powerful tool to obtain enantiomerically pure or enriched alcohols, mainly by nucleophilic additions to carbonyl compounds [2]. Several and efficient chiral ligands have been used, alone or in the presence of Lewis acids. These include amino alcohols [3-6], α-hydroxy acids [7], α-amino amides [8], α-hydroxy amides [9], and hydroxysulfonamides [10-14].

Our group has recently reported the preparation of bis(sulfonamide) **1**, containing (11*R*,12*R*)-11,12-diamino-9,10-dihydro-9,10-ethanoanthracene as carbon skeleton [15]. The bis(sulfonamide) **1** was used as ligand in the asymmetric alkylation of prochiral ketones with diethyl zinc in high yield and enantioselectivities up to 99% *ee* (Figure 1).

Subsequently, König *et al.* [16] described the synthesis of novel tetradentate sulfonamide ligands and used them in the catalytic asymmetric alkylation of aldehydes with diethylzinc. Quantitative yields of the corresponding secondary alcohol and good asymmetric induction (70% yield and 74% *ee*) were obtained with ligands **2a-b**.

Somanathan *et al.* [17-18] reported the use of monosulfonamide ligand **3a-b**, derived from *trans*-(1*R*,2*R*)-cyclohexane-1,2-diamine, in the asymmetric transfer hydrogenation of aromatic ketones. Enantioselectivities ranged from 70 to 99% and good yields for the synthesis of 1-phenylpropanol derivatives were achieved.

Recently Hirose [19] and co-workers described the synthesis of chiral 1,3-amino sulfonamides, **4, 5**.

They were prepared from (-)-*cis*-2-benzamidocyclohexanecarboxylic acid and studied by tested as ligands for catalytic enantioselective addition of diethyl zinc to aldehydes. They provided secondary alcohols in quantitative yields and in good to excellent enantioselectivities (up to 98% *ee*).

These reports prompted us to prepare the monosulfonamides **6-12, 15** and **16** and to test their catalytic activity. First,

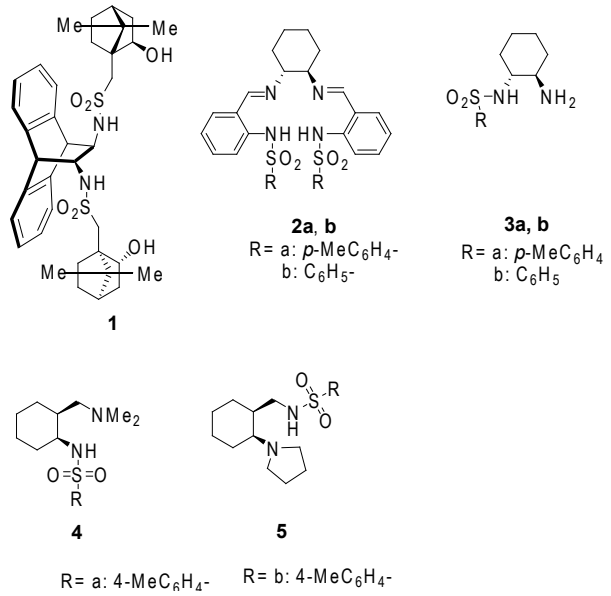


Fig. 1. Chiral sulfonamides used in asymmetric catalysis.

the ethylation of benzaldehyde was performed in the presence of diethylzinc. Second, monosulfonamides **6-10** were tested in the asymmetric induce hydrogenation (ATH) of acetophenone with Rh(Cp*)L* complex.

Results and Discussion

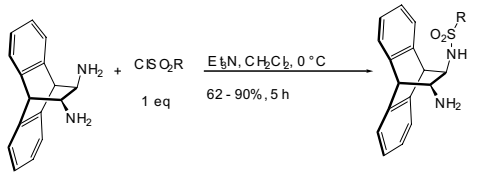
The synthesis of monosulfonamides **6-12** were achieved from enantiopure (11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene [20]. (11*R*,12*R*)-Diamine (1 equiv) was treated with sulfonyl chlorides (1 equiv) in DCM at 0 ºC in the presence of triethylamine. Monosulfonamides **6-12** were obtained in good yields (62-90%) after column chromatography purification on silica gel [Hexane:EtOAc; 1:5]. (Table 1).

Preparation of monosulfonamides 13-16

The reaction of (11*R*,12*R*)-diamine **17** with (*S*)-camphorsulfonyl chloride, under the same reaction conditions, afforded ketone **13** in 70% yield. The reduction of ketone **13** with $NaBH_4$, gave a mixture of two diastereomeric alcohols in a 5.3:1.0 ratio exo-exo:exo-endo in 69% yield. The major diastereomer **15** was isolated in 58% yield by flash chromatography purification (Scheme 1).

On the other hand, the preparation of ketone **14** was performed using (11*S*,12*S*)-diamine-**18** and (*S*)-camphorsulfonyl chloride. After purification by column chromatography, the desired ketone was obtained in 76% yield. Ketone **14** was reduced with $NaBH_4$ to provide a mixture of alcohols in a diastereomeric ratio of 8.0:1.0. The major exo-exo alcohol **16** was isolated in 67% yield, after flash chromatography purification (Scheme 2).

Table 1. Synthesis of the monosulfonamide ligands derived from (11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene.



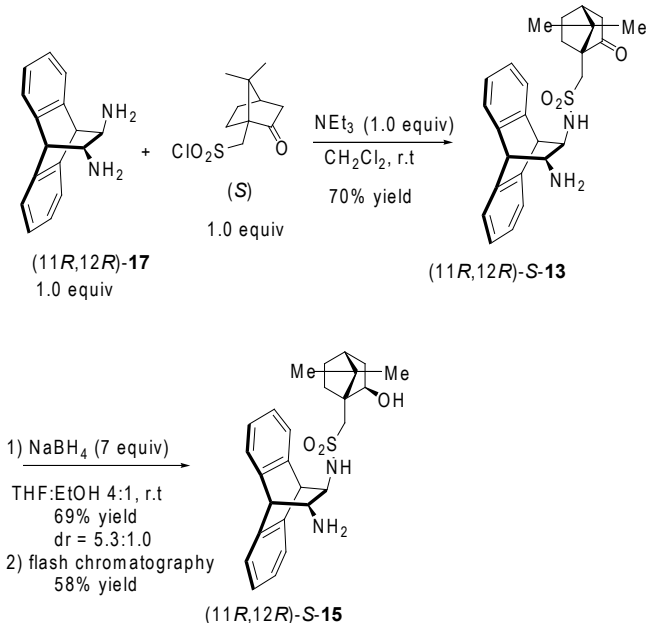
(11*R*,12*R*)-**17** **6 - 12**

Entry	Monosulfonamide	R	Yield (%)[a]
1	**6**	*p*-(*t*-Bu)-$C_6H_4^-$	85
2	**7**	C_6H_5-CH_2^-	75
3	**8**	2,4,6-(*i*-Pr)$_3^-C_6H_2^-$	90
4	**9**	*p*-$FC_6H_4^-$	81
5	**10**	CH_3	62
6	**11**	*p*-$CF_3C_6H_4^-$	66
7	**12**	*p*-$CH_3C_6H_4^-$	68

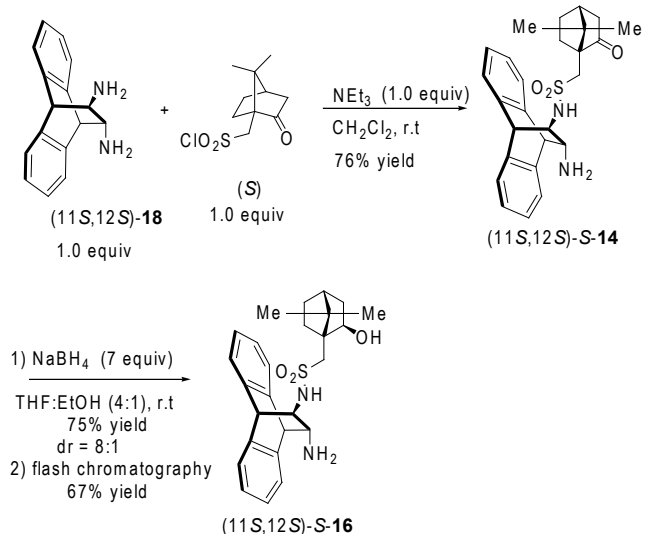
[a] Yields were measured after column chromatography on silica gel (Et_3N/SiO_2 = 2.5% v/w, (hexane/EtOAc; 15:1 as eluent).

Enantioselective addition of diethylzinc to benzaldehyde

Chiral monosulfonamides **6-12**, **15** and **16** were tested as ligands in the enantioselective addition of diethylzinc to benzaldehyde. The reaction was performed using 5 mol% of the corresponding optically active ligands in the presence of toluene as solvent and under solvent-free conditions. The chiral zinc catalyst was generated *in situ* upon the addition of 2.0 equivalents of diethylzinc to the corresponding chiral monosulfonamide. 1-Phenylpropan-1-ol was obtained in moderate to good yields (in toluene 55-95%, under solvent free conditions 47-92%) and low to moderate enantioselectivities (in toluene 4-52%, under solvent free conditions 8-56%). We found that the presence or



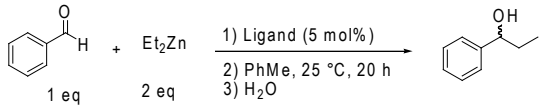
Scheme 1. Synthesis of ligand **15**.



Scheme 2. Synthesis of the ligand **16**.

absence of solvent did not lead to significant improvements. Monosulfonamide **8** (Table 2) gave the best yields and enantioselectivities (entries 5 and 6) (Table 2). Monosulfonamides **6-12** provided (*R*)-1-phenylpropan-1-ol as major enantiomer; however monosulfonamides **15** and **16** afforded the alcohol with the opposite configuration (Table 2). The transition state for alkylation of benzaldehyde with diethylzinc is show in (Figure 2) [23].

Table 2. Diethylzinc addition of benzaldehyde catalyzed by monosulfonamides **6** - **12** and **15** - **16** under different reaction conditions.



Entry	Ligand	Solvent	Yield (%)[a]	*ee* (%)[b]
1	**6**	Toluene	75	18 (*R*)
2		Solvent-free	47	22 (*R*)
3	**7**	Toluene	95	4 (*R*)
4		Solvent-free	53	8 (*R*)
5	**8**	Toluene	94	52 (*R*)
6		Solvent-free	92	56 (*R*)
7	**9**	Toluene	55	8 (*R*)
8		Solvent-free	51	26 (*R*)
9	**10**	Toluene	85	12 (*R*)
10		Solvent-free	54	19 (*R*)
11	**11**	Toluene	56	28 (*R*)
12		Solvent-free	63	24 (*R*)
13	**12**	Toluene	72	28 (*R*)
14		Solvent-free	68	24 (*R*)
15	**15**	Toluene	81	44 (*S*)
16		Solvent-free	55	18 (*S*)
17	**16**	Toluene	85	18 (*S*)
18		Solvent-free	69	26 (*S*)

[a] Yields were measured after column chromatography on silica gel (Et_3N/SiO_2 = 2.5% v/w, (hexane/EtOAc; 15:1 as eluent).
[b] The enantiomeric excess was determined by HPLC on a chiral OD column. Absolute configuration was assigned by comparing the specific rotation with literature values.

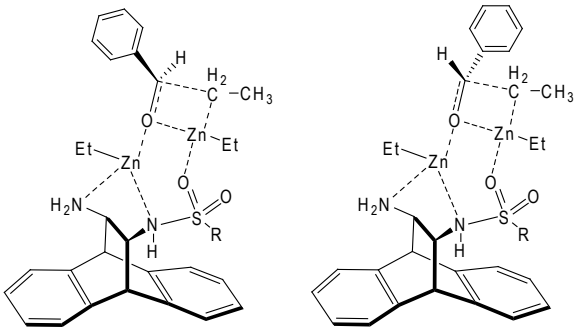


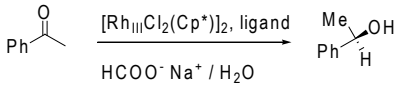
Fig. 2. Transition states for alkylation of benzaldehyde with diethylzinc.

Asymmetric induced hydrogenation with rhodium complex as ligands 6-10

Next, we performed the catalytic enantioselective reduction reaction using ligands **6-10**, in the asymmetric induced hydrogenation of acetophenone with a rhodium complex (Table 3). A mixture of the metal precursor $[RhCl_2(Cp^*)]_2$ and the monosulfonamide was heated in water to form the Rh(Cp*)L* complex. Then sodium formate and acetophenone were added to form the 1-phenyl-1-ethanol. The reaction proceeded with low to moderate results (10-34% yield and 3-42% *ee*). Best enantioselectivity was achieved with ligand **10** (42% *ee*, entry 5) (Table 3). The transition state for ATH of aromatic ketones is show in (Figure 3).

In our previous study [21, 22] we found that the dihedral angle N-C-C-N is critical in obtaining maximum overlap, in order to get good yields and enantioselectivities. The dihedral angle calculations were carried out by B3LYP density functional level of theory, using a cc-pVDZ basis set calculations. The angles N-C-C-N of ligands **6**, **7**, **8, 9**, and **10** were found to be in the range of 114.16 to 116.96°, compared to 59° observed for monosulfonamide of 1,2-cyclohexane diamine.

Table 3. Asymmetric transfer hydrogenation of acetophenone catalyzed by Rh(Cp*)L* complexes with ligands **6-10**.



Entry	Ligand	Yield (%)[a]	ee (%)[b]
1	**6**	26	31 (*R*)
2	**7**	21	18 (*R*)
3	**8**	18	3 (*R*)
4	**9**	34	30 (*R*)
5	**10**	10	42 (*R*)

[a] Yields were measured after column chromatography on silica gel (Et_3N/SiO_2 = 2.5% v/w, (hexane/EtOAc; 15:1 as eluent).
[b] The enantiomeric excess was determined by GC analysis of the acetylated alcohol with chiral capillary column β-DEX 120.

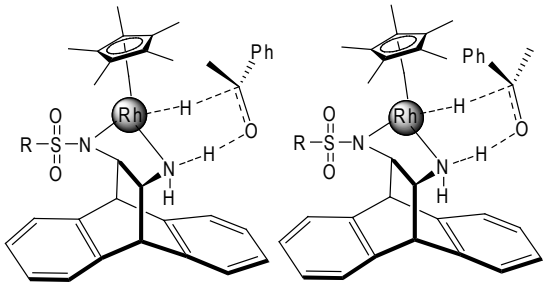


Fig. 3. Transition states for ATH of acetophenone.

Conclusion

In conclusion, we have described an easy and simple synthesis of different chiral monosulfonamides from (11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene in good yields (62-90%). They have been used as zinc-based catalysts in the enantioselective addition of diethylzinc to benzaldehyde with high yield (94%) and moderate *ee* (56%).

We also evaluated the potential of these ligands as catalysts in the asymmetric enantioselective reduction in the ATH of acetophenone with Rh(Cp*)L* complex. We observed low conversion (10-34%) and low enantioselectivities (3-42%).

These results clearly indicate that the monosulfonamides derived from (1*R*,2*R*)-cyclohexane-1,2-diamine are more stereoselective than those prepared with (11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene. Based on these results, we are working on the design of new chiral sulfonamides based ligands that display better stereoinduction.

Experimental

All manipulations involving diethylzinc were carried out under argon atmosphere. Benzaldehyde was distilled prior to use. NMR spectra were obtained on a Varian 200 MHz. Fourier transform spectrometer. ^{1}H NMR spectra were referenced to tetramethylsilane; ^{13}C{^{1}H} NMR spectra were referenced to residual solvent.

General procedure for synthesis of monosulfonamides 6-14

To a solution of enantiopure 11,12-diamino-9,10-dihydro-9,10-ethanoanthracene (300 mg, 1.3 mmol) in CH_2Cl_2 (10 mL) and triethylamine (0.5 mL, 1.3 mmol) at 0 °C a sulfonyl chloride solution was added dropwise (300 mg, 1.3 mmol) in CH_2Cl_2 (10 mL) over 60 min. After the addition was completed, the mixture was allowed to warm to room temperature. After being stirred for 5 h, the mixture was washed with water (3 x 50 mL). The organic phase was separated and dried over $NaSO_4$. The solution was filtered and the solvent was removed under vacuum, the crude product was purified by flash chromatography on silica gel, (Hexane/EtOAc 1:5 as eluent).

(4-*tert*-Butylbenzenesulfonamido)-(11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (6)

Affording a white solid (85% yield): mp 188-190 °C; $[\alpha]_D^{20}$ = –6.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.36 (s, 9H), 1.42 (s, 3H), 2.81-2.84 (m, 1H), 3.07-3.10 (m, 1H), 3.95 (d, 1H, *J* = 2.6 Hz), 4.04 (d, 1H, *J* = 3.0 Hz), 7.07-7.27 (m, 8H), 7.54 (d, 2H, *J* = 8.8 Hz), 7.80 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ 31.8, 50.0, 52.2, 61.1, 63.6, 124.1, 124.2, 125.6, 125.9, 126.2, 126.3, 126.7, 126.8, 137.2, 137.5, 138.6, 139.6, 141.5, 156.2. IR-FT (KBr) ν_{max}/ cm^{-1}: 3344, 3277, 3072, 2958, 2874, 2799, 2754, 1595, 1575, 1464, 1398, 1368, 1335, 1268, 1228, 1199, 1162, 1109, 1088, 1021, 930, 902, 836, 792, 757, 641, 582, 555, 525, 406. HRMS-FAB$^+$: m/z [M+H]$^+$ calcd. for $C_{26}H_{29}O_2N_2S$: 433.1950; found: 433.1942.

(Phenylmethanesulfonamido)-(11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (7)

Affording a white solid (75% yield): mp 185-186 °C; $[\alpha]_D^{20}$ = –26.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.25 (broad, 2H), 2.74-2.76 (m, 1H), 2.91 (broad, 1H), 4.00-4.01 (m, 1H), 4.04-4.10 (m, 2H), 4.28 (s, 2H), 7.06-7.42 (m, 13H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 51.0, 52.8, 60.2, 61.4, 64.0, 124.1, 124.2, 125.7, 125.9, 126.2, 126.4, 126.7, 128.5, 129.1, 130.5, 137.2, 138.3, 139.6, 141.4. IR-FT (KBr) ν_{max}/cm^{-1}: 3341, 3278, 3066, 3041, 2951, 2924, 2880, 2753, 1947, 1800, 1603, 1578, 1487, 1459, 1410, 1378, 1322, 1257, 1228, 1200, 1149, 1123, 1099, 1069, 1030, 960, 935, 909, 872, 847, 824, 782, 758, 696, 635, 603, 564, 543, 509, 462, 347. HRMS-FAB$^+$: m/z [M+H]$^+$ calcd. for $C_{23}H_{23}O_2N_2S$: 391.1480; found: 391.1478.

(2,4,6-Triisopropylbenzenesulfonamido)-(11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (8)

Affording a white solid (90% yield): mp 183-184 °C; $[\alpha]_D^{20}$ = –8.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.19-1.27 (m, 18H), 2.80-2.93 (m, 3H), 3.17-3.24 (m, 1H), 4.01-4.27 (m, 6H), 7.08-7.31 (m, 10H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.3, 25.5, 30.2, 34.7, 50.3, 52.1, 61.0, 63.7, 123.5, 124.2, 125.6, 125.9, 126.2, 126.3, 126.7, 132.9, 137.4, 138.6, 139.7, 141.6, 149.5, 152.4. IR-FT (KBr) ν_{max}/ cm^{-1}: 3343, 3275, 3074, 2958, 2873, 1599, 1572, 1462, 1420, 1361, 1324, 1256, 1227, 1195, 1158, 1104, 1066, 1037, 932, 903, 881, 788, 757, 660, 546. HRMS-FAB$^+$: m/z [M+H]$^+$ calcd. for $C_{31}H_{39}O_2N_2S$: 503.2732; found: 503.2737.

(4-Fluorobenzenesulfonamido)-(11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (9)

Affording a white solid (81% yield): mp 178-179 °C; $[\alpha]_D^{20}$ = –13.5 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.72-2.74 (m, 1H), 2.98-3.0 (m, 1H), 3.87 (d, 1H, *J* = 3.0 Hz), 3.94 (d, 1H, *J* = 2.6 Hz), 5.18 (s, 3H), 6.97-7.21 (m, 10H), 7.82 (dd, 2H, *J* = 5.2, 5.2 Hz).. ^{13}C NMR (50 MHz, $CDCl_3$) δ 50.1, 52.4, 60.9, 63.5, 116.0, 116.5, 124.2, 125.6, 126.0 126.2, 126.4, 126.7, 129.5, 129.7, 136.7, 136.7, 137.1, 138.4, 139.4, 141.5, 161.9, 166.9. IR-FT (KBr) ν_{max}/cm^{-1} 3359, 3298, 3070, 3029, 2948, 2867, 2746, 1591, 1491, 1463, 1407, 1330, 1291, 1233, 1158, 1091, 1020, 980, 925, 892, 840, 788, 758, 669, 635, 579, 551. HRMS-FAB$^+$: m/z [M+H]$^+$ calcd. for $C_{22}H_{20}O_2N_2F_1S$: 395.1230; found: 395.1234.

(Methansulfonamido)-(11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (10)

Affording a white solid (62% yield): mp 112-113 °C; $[\alpha]_D^{20}$ = –8.7 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.02 (s, 3H), 2.94 (broad, 1H), 3.10 (s, 3H), 3.26 (broad, 1H), 4.10 (broad, 1H), 4.28 (d, 1H, *J* = 2.6 Hz), 7.14-7.40 (m, 8H). ^{13}C

NMR ($CDCl_3$, 50 MHz) δ 42.1, 50.8, 53.0, 61.0, 62.8, 124.0, 124.3, 125.8, 126.0, 126.3, 126.4, 126.5, 126.6, 137.3, 138.1, 139.8, 141.3. IR-FT (KBr) ν_{max}/cm^{-1}: 3349, 3281, 3070, 3042, 3023, 2954, 2930, 2872, 1629, 1588, 1463, 1411, 1323, 1227, 1149, 1116, 1068, 1023, 982, 868, 845, 823, 762, 718, 671, 636, 603, 563, 519, 459. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd. for $C_{17}H_{19}O_2N_2S$: 315.1167; found: 315.1171.

(4-Trifluoromethanbenzenesulfonamido)-(11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (11)

Affording a white solid (66% yield): mp 190-191 °C; $[\alpha]_D^{20}$ = –10 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.33 (broad, 3H), 2.71-2.74 (m, 1H), 3.04 (s, 1H), 3.94-3.95 (m, 2H), 6.96-7.21 (m, 8 H), 7.71 (d, 2H, *J* = 8.4 Hz), 7.94 (d, 2H, *J* = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 50.2, 52.5, 60.8, 63.5, 98.2, 124.0, 124.1, 125.6, 126.0, 126.2, 126.5, 126.7 127.3, 137.2, 138.1, 138.3, 139.4, 141.4, 144.3. IR-FT (KBr) ν_{max}/cm^{-1}: 3349, 3281, 3065, 3033, 2950, 2929, 2872, 2750, 1583, 1491, 1460, 1415, 1323, 1226, 1203, 1152, 1124, 1068, 1026, 951, 901, 849, 785, 758, 728, 698, 636, 604, 543, 508, 450. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd. for $C_{23}H_{20}O_2N_2F_3S$: 445.1198; found: 445.1202.

(4-Methylbenzenesulfonamido)-(11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (12)

Affording a white solid (68% yield): mp 166-168 °C; $[\alpha]_D^{20}$ = –23.5 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.3 (broad, 3H), 2.44 (s, 3H), 2.79 (t, 1H, *J* = 2.6 Hz), 4.03 (d, 1H, *J* = 2.6 Hz), 3.92 (d, 1H, *J*= 2.6 Hz), 4.03 (d, 1H, *J* = 2.6 Hz), 7.06-7.35 (m, 10 H), 7.76 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.3, 50.0, 52.1, 61.0, 63.6, 124.1, 124.1, 125.6, 125.9, 126.2, 126.3, 126.7, 126.9, 129.5, 137.2, 137.6, 138.5, 139.6, 141.5, 143.2. IR-FT (KBr) ν_{max}/cm^{-1}: 3339, 3262, 3069, 3023, 2959, 2878, 1739, 1593, 1492, 1460, 1327, 1295, 1224, 1154, 1091, 1022, 975, 923, 889, 842, 818, 791, 760, 710, 666, 636, 601, 578, 552, 532. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd. for $C_{23}H_{23}O_2N_2S$: 391.1480; found 391.1485.

[7,7-Dimethyl-2-oxobicyclo[2.2.1]heptan-1-methylsulfonamido](11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (13)

Affording a white solid (70% yield): mp 218-219 °C; $[\alpha]_D^{20}$ = +13.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.91 (s, 3H), 1.02 (s, 3H), 1.36-1.48 (m, 2H), 1.74-2.47 (m, 7H), 2.94 (d, 1H, *J* = 15 Hz) 2.99-3.01 (m, 1H), 3.25-3.29 (m, 1H), 3.57 (d, 1H, *J* = 15 Hz), 4.11 (d, 1H, *J* = 2.6 Hz), 4.30 (d, 1H, *J* = 2.6 Hz), 4.80 (d, 1H, *J* = 8 Hz), 7.08-7.36 (m, 8H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.3, 20.6, 26.5, 27.6, 43.2, 43.3, 48.9, 50.4, 51.0, 52.5, 59.3, 61.4, 63.9, 124.2, 125.5, 125.9, 126.2, 126.3, 126.7, 137.3, 138.7, 139.8, 141.6, 215.0. IR-FT (KBr) ν_{max}/cm^{-1}: 3354, 3297, 3073, 3029, 2950, 2929, 2911, 2884, 2807, 2764, 1742, 1593, 1456, 1414, 1389, 1330, 1279, 1235, 1202, 1149, 1098, 1067, 1051, 1026, 975, 937, 913, 888, 850, 785, 765, 748, 637, 602, 571, 527, 500. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd. for $C_{26}H_{31}O_3N_2S$: 451.2055; found: 451.2059.

[7,7-Dimethyl-2-oxobicyclo[2.2.1]heptan-1-methylsulfonamido](11*S*,12*S*)-diamino-9,10-dihydro-9,10-ethanoanthracene (14)

Affording a white solid (76% yield): mp 225-226 °C; $[\alpha]_D^{20}$ = +32.1 (*c* 9.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.92 (s, 3H), 0.98 (s, 3H), 1.31-1.44 (m, 2H), 1.80-2.39 (m, 7H), 2.91-2.94 (m, 1H), 3.04 (d, 1H, *J* = 15.0 Hz), 3.26-3.30 (m, 1H), 3.76 (d, 1H, *J* = 15.4 Hz), 4.02 (d, 1H, *J* = 2.6 Hz), 4.32 (d, 1H, *J* = 2.6 Hz), 4.90 (d, 1H, *J* = 8.6 Hz), 7.10-7.38 (m, 8H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.2, 20.6, 27.3, 27.7, 43.1, 43.4, 49.2, 51.5, 51.8, 53.9, 59.7, 61.0, 63.5, 123.9, 124.4, 126.0, 126.3, 126.5, 126.6, 137.4, 138.3, 140.4, 141.5, 215.6. IR-FT (KBr) ν_{max}/cm^{-1}: 3363, 3264, 3070, 3021, 2952, 2899, 1732, 1585, 1442, 1390, 1326, 1276, 1209, 1135, 1060, 1032, 1020, 989, 941, 900, 864, 821, 781, 752, 710, 663, 606, 555, 519, 503, 423, 387, 353, 329, 297. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd. for $C_{26}H_{31}O_3N_2S$: 451.2055; found: 451.2051

General procedure for synthesis of ligands 15 and 16

In a 100 mL flask ketone (300 mg, 0.67 mmol) was dissolved in a mixture solvent (40 mL, MeOH/ THF = 4:1). Next $NaBH_4$ (180 mg, 4.6 mmol, 7 equiv) was added slowly. The mixture was stirred for another 4 h. The reaction mixture was quenched with saturated aqueous ammonium chloride, and the solid was filtered. The filtrate was extracted with CH_2Cl_2 (3 × 50 mL). The organic phase was washed with water and was dried over $NaSO_4$. The solvent was removed under vacuum; the crude product was purified by flash chromatography on silica gel (Hexane/EtOAc 7:3 as eluent).

[2-(*S*)-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-methylsulfonamido](11*R*,12*R*)-diamino-9,10-dihydro-9,10-ethanoanthracene (15)

Affording a white solid (58% yield): mp 128-129 °C; $[\alpha]_D^{20}$ = +6.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.81 (s, 3H), 0.96 (s, 3H), 1.61-1.89 (m, 5H), 2.21-2.27 (m, 5H), 2.79-2.82 (m, 1H), 2.93 (d, 2H, *J* = 14.4 Hz), 3.13-3.20 (m, 1H), 3.72 (d, 1H, *J* = 14.6 Hz), 3.92-4.00 (m, 2H), 4.50 (d, 1H, *J* = 2.6 Hz), 7.11-7.42 (m, 8H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.6, 21.3, 28.0, 29.9, 41.3, 44.6, 49.4, 50.3, 51.3, 51.7, 54.0, 60.9, 62.6, 74.6, 123.9, 124.7, 126.0, 126.3, 126.5, 126.6, 126.8, 136.9, 137.5, 140.1, 141.1. IR-FT (KBr) ν_{max}/cm^{-1}: 3459, 3377, 3304, 3146, 3072, 3043, 3021, 2954, 2931, 2892, 1585, 1460, 1415, 1392, 1320, 1280, 1207, 1139, 1062, 1027, 988, 955, 887, 848, 817, 789, 753, 713, 638, 582, 560, 506, 450, 347. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd. for $C_{26}H_{33}O_3N_2S$: 453.2212; found: 453.2218.

[2-(*S*)-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-methylsulfonamido](11*S*,12*S*)-diamino-9,10-dihydro-9,10-ethanoanthracene (16)

Affording a white solid (68% yield): mp 217-219 °C; $[\alpha]_D^{20}$ = +19.7 (*c* 9.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.81 (s, 3H), 0.96 (s, 3H), 1.15-1.28 (m, 2H), 1.68-1.87 (m, 6H), 2.78-2.81 (m, 1H), 2.93 (d, 2H, *J* = 14.4 Hz), 3.16-3.19 (m, 1H), 3.71 (d, 1H, *J* = 14.4 Hz), 3.90-4.00 (m, 4H), 4.50 (d,

1H, *J* = 2.6 Hz), 7.12-7.42 (m, 8H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.9, 21.5, 28.2, 30.2, 41.5, 44.8, 49.6, 50.6, 51.5, 52.0, 54.2, 61.0, 62.9, 74.8, 124.1, 124.9, 126.3, 126.6, 126.7, 126.8, 127.0, 127.1, 137.2, 137.7, 140.3, 141.4. IR-FT (KBr) ν_{max}/cm^{-1}: 3457, 3377, 3136, 2954, 2927, 2890, 1459, 1414, 1398, 1356, 1317, 1272, 1137, 1061, 1024, 986, 954, 885, 848, 814, 790, 748, 710, 638, 602, 581, 557, 529, 502, 447, 421, 394, 344, 317. HRMS-FAB$^+$: m/z $[M+H]^+$ calcd. for $C_{26}H_{33}O_3N_2S$: 453.2212; found: 453.2220.

General procedure for the asymmetric diethylzinc addition to benzaldehyde

The ligands **6-12, 15** and **16** (5 mol %) were weighed into the reaction vessel that was then purged with nitrogen, and dissolved in toluene (3 mL). Diethylzinc (1.0 M in hexane, 2.0 equiv, 0.94 mL) was then added at rt. After 10 min, benzaldehyde (1.0 equiv, 0.47 mmol) was added. The homogeneous reaction mixture was stirred at rt, after 20 h the reaction was quenched with water (5 mL), extracted with EtOAc (2 × 40 mL) and the combined organic layers were washed with brine, dried over $NaSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography on deactivated silica gel (Et_3N/SiO_2 = 2.5% v/w, Hexane/EtOAc 95:5) to afford 1-phenyl-1-propanol. The enantiomeric excess of the product was determined by HPLC analysis using a Chiracel OD column, 254 nm UV detector, 95:5 Hexane/*i*-propanol, flow rate 0.5 mL min, retention time (*R*): 14 min, retention time (*S*): 15 min. Specific rotations of the secondary alcohols were measured and compared with those reported on the literature to assign configuration [23].

General procedure for the asymmetric diethylzinc addition to benzaldehyde under solvent-free conditions

The ligands **6-12, 15** and **16** (5 mol %) were weighed into the reaction vessel and diethylzinc (1.0 M in hexane, 2.0 equiv, 0.94 mL) was then added at rt. After 10 min, benzaldehyde (1.0 equiv, 0.47mmol) was added. The homogeneous reaction mixture was stirred at rt. After 20 h the reaction was quenched with water (5 mL), extracted with EtOAc (2 × 40 mL) and the combined organic layers were washed with brine, dried over $NaSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography on deactivated silica gel (Et_3N/SiO_2 = 2.5% v/w, Hexane/EtOAc 95:5) to afford 1-phenyl-1-propanol.

The enantiomeric excess of the product was determined by HPLC analysis using a Chiracel OD column, 254 nm UV detector, 95:5 Hexane/*i*-propanol, flow rate 0.5 mL min, retention time (*R*): 14 min, retention time (*S*): 15 min. Specific rotations of the secondary alcohols were measured and compared with those reported on the literature to assign configuration [24].

General procedure for the asymmetric transfer hydrogenation of acetophenone in water

A mixture of the metal precursor $[RhCl_2(Cp^*)]_2$ (0.0039 mmol) and chiral ligand (0.00075 mmol) was heated in water (2 mL) at 40 °C for 1 h in air. HCOONa (5.7 mmol) and the substrate were subsequently added (1.14 mmol). The reaction mixture was stirred at 40 °C in air. The reaction mixture was extracted with ether (3 × 10 mL). The ether layers were combined, dried over anhydrous $NaSO_4$, filtered and concentrated under vacuum. The residue containing the alcohol was acetylated using acetic anhydride. The enantiomeric excess of the product was determined by GC analysis of the acetylated alcohol with chiral capillary column β-DEX 120.

Specific rotations of the secondary alcohols were measured and compared with those reported on the literature to assign configuration [23].

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