Preparation of β-amino-alcohol analogs by the addition of N-, O- and S-containing substituents to ferrocenyl-camphorsulfonamide – ligands for enantioselective addition of diethylzinc to benzaldehyde

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Abstract
The synthesis of 2-*exo*-hydroxy-3-ferrocenemethylidene-10-sulfonamido-camphane derivatives with 2-*endo*- positioned heterocyclic substituents was realized through addition reactions of N-, O-, and S- containing organolithium reagents. These chiral β-heteroatom- containing alcohols were found to catalyze effectively the addition Et_2Zn to benzaldehyde with up to 76% degree of enantioselectivity.

Keywords: Asymmetric synthesis, organolithium, ferrocene, enantioselectivity, diethylzinc, (+)-camphor-10-sulfonamide

Introduction

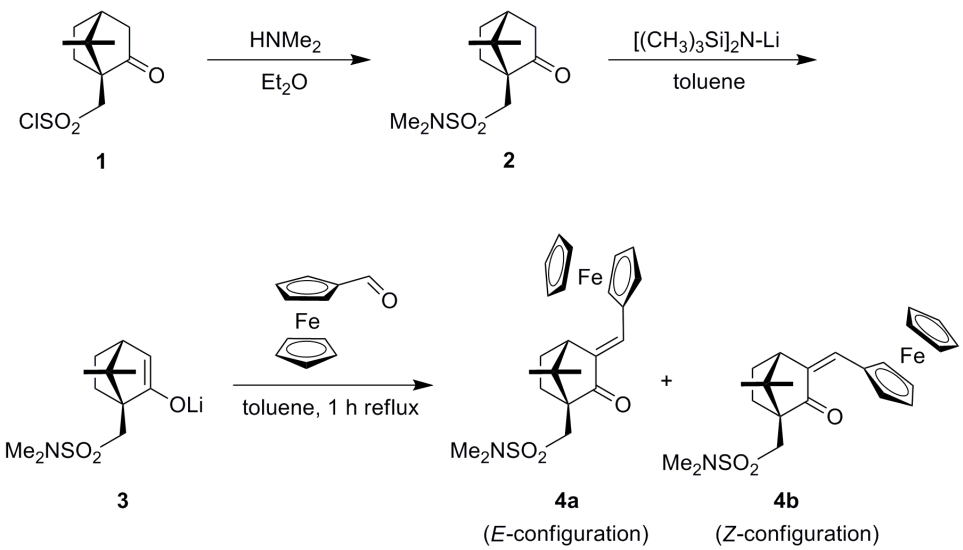
The synthesis of chiral amino-alcohols, first reported by Oguni and Omi,[1] to catalyze enantioselectively the addition of diorganozinc compounds to aldehydes, still attracts considerable interest due to the utility of the secondary alcohols formed by this reaction.[1,2] Over the past decades a large number of amino-alcohols has been synthesized and tested as ligands.[1-3] One of the most potent amino-alcohols used as a catalyst is the dimethylamino-isoborneol investigated by Noyori.[4] Therefore the large number of efforts for synthesis of ligands containing the bicyclic camphene core is highly justified. In recent years, a large variety of amino-alcohols starting from camphor,[5] fenchone,[5d-i, 6] camphor-10-sulfonamides[7] and similar chiral compounds[8] have been prepared and used as catalysts.

It is important to point out that chiral amino-alcohols have been applied as chiral catalysts in several different type of chemical reactions, *e.g.*, hydride reductions, nucleophile additions to carbonyl compounds, aldol reactions, Diels-Alder reactions, and also as auxiliaries for synthesis

of useful chiral building blocks and products.[9] However, in chiral catalysis there are no universal catalysts, and every process requires new ligand tuning. Therefore, there is a clear need to continue synthesis of chiral amino-alcohols with the purpose of obtaining "made-to-measure" catalysts for a given asymmetric process. We now describe the synthesis of β-heteroatom-containing hydroxy derivatives incorporating the ferrocene core, starting from (+)-camphor-10-sulfonamide as a readily available source of chirality.

Results and Discussion

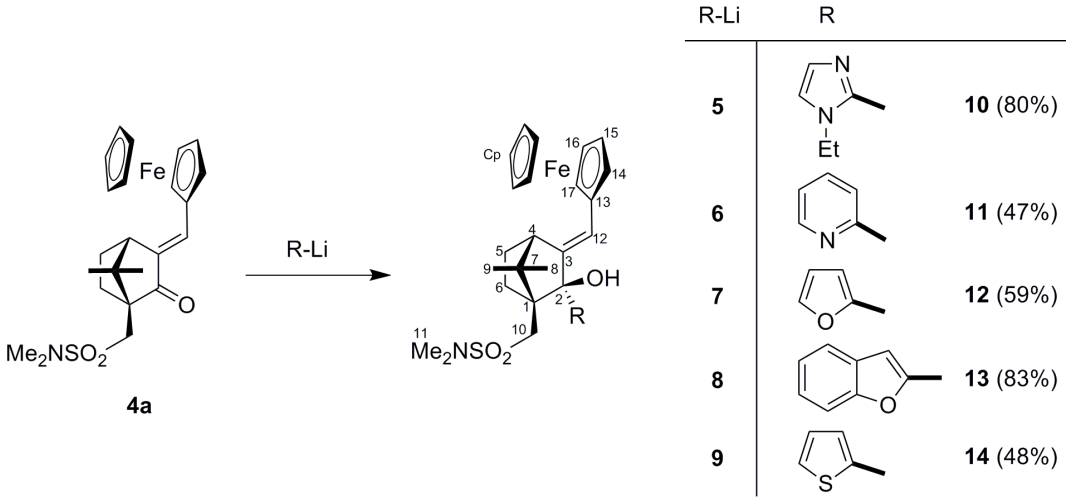
The commercially available (+)-camphor-10-sulfonamide was easily transformed into the dimethylsulfonamide **2** through reaction of the corresponding sulfochloride **1** with dimethylamine[10] (Scheme 1). By using **2** and Li-HMDS (lithium hexamethyldisilazide) the enolate **3** was generated *in situ*, which after reaction with ferrocene carboxaldehyde produced the ferrocene-substituted sulfonamides **4a** and **4b** (observed ratio **4a**/**4b**=97:3 by NMR spectroscopy). Compounds **4a** and **4b** were isolated as pure isomers in 59% and 5% yield after column chromatography (see Experimental).



Scheme 1

The ferrocene-substituted camphor derivative **4a** was used as starting compound for addition reactions of heteroatom-substituted organolithiums (Scheme 2). The organolithium compounds **5** and **7-9** were generated *in situ* by known procedures,[11] and the ketone **4a** was added at appropriate temperature. The desired hydroxy derivatives **10** and **12–14** were isolated in moderate to very good yields after column chromatography. Compound **11** was synthesized by a published procedure.[12] This procedure (addition of n-BuLi to a mixture of **4a** and 2-

bromopyridine at -80°C) is expected to give better yields than that in which 2-lithiopyridine is generated *in situ* prior to the addition reaction.[5d] In the present case we could obtain **11** in 47% yield (after column chromatography) together with unchanged **4a** (18%) and 5% of the addition product of *n*-BuLi to **4a**.[13]



Scheme 2

The *endo*-position of the substituents was proved by NOESY spectra through the observed proximities of H-atoms from the heterocyclic moiety in compounds **10**–**14** with the *endo*-positioned protons of the bicyclic core (Figure 1). Besides, the observed proximity of the other protons indicates the rigid structure of the compounds. The position of the unsubstituted Cp-ring is arbitrary, since there are no Cp-proton proximities observed.

The ^{13}C- signals of compounds **2**, **4** and **10**-**14** are listed in Table 2. The assignments for quaternary C-atoms C(2)–C(13), C(3)–C(2') and for C(14)–C(17) are tentative, due to a significant overlap of signals in the latter case.

The compounds **10**–**14** were applied as ligands (3 mol. %) for the enantioselective addition of Et_2Zn to benzaldehyde (Table 1) according to the published procedure.[5,6]

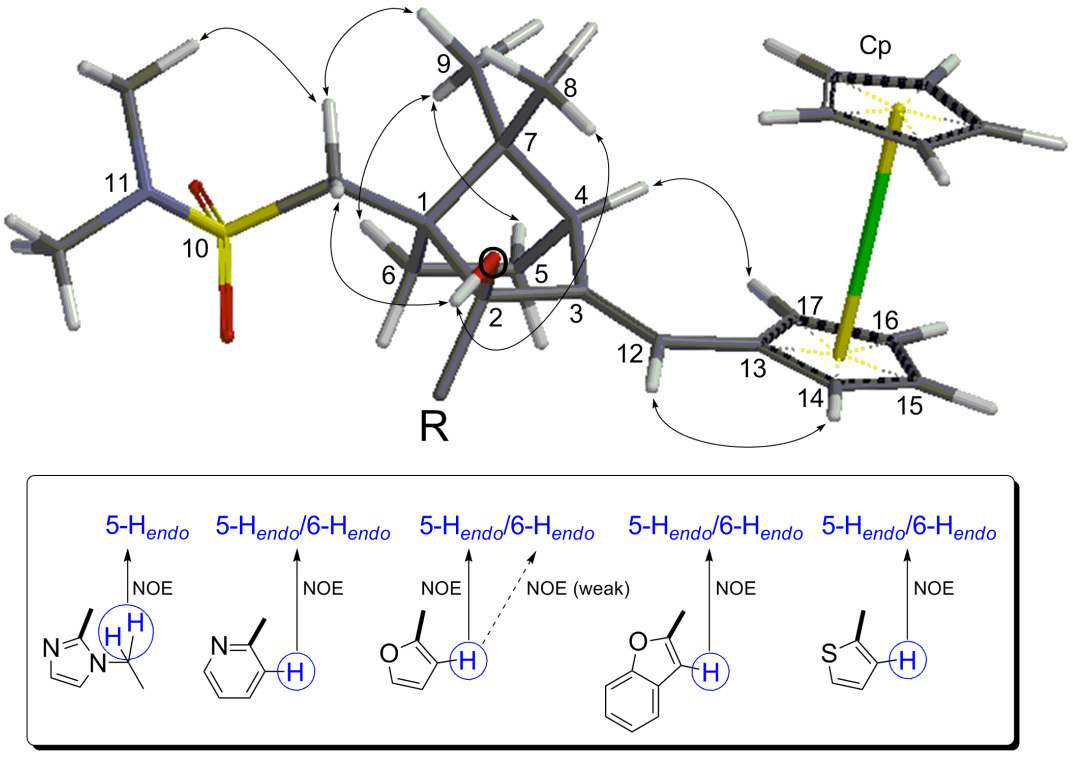
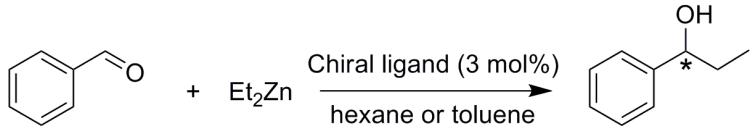


Figure 1

Table 1. Addition of Et_2Zn to benzaldehyde catalyzed by ligands **10-14**



Entry	Ligand	Yield (%)		*ee* (%)	
		In hexane	In toluene	In hexane	In toluene
1.	**10**	97	95	10 (*S*)	21 (*S*)
2.	**11**	97	98	9 (*S*)	12 (*S*)
3.	**12**	97	99	63 (*R*)	76 (*R*)
4.	**13**	99	99	63 (*R*)	76 (*R*)
5	**14**	96	99	41 (*R*)	56 (*R*)

The yields of the isolated 1-phenyl-1-propanol were in all cases excellent. The observed enantioselectivities were low to moderate. Comparison of **11** with the published results for 2-*endo*-pyridyl-isoborneol (observed 41% *ee R*) [5d] shows, however, that there is a lowering of the enantioselectivity with formation of the *S*-enantiomer. In all cases, the use of toluene as solvent

provided better results, owing to the higher solubility of the catalyst formed *in situ* by reaction of Et_2Zn and the corresponding ligand. The best enantioselectivities were realized with ligands **12** and **13** possessing the furan heterocyclic moiety (Entry 3 and 4).

In conclusion, a practical synthesis of new chiral β-heteroatom-containing hydroxy camphene derivatives has been realized. These compounds used as ligands catalyzed the addition of Et_2Zn to benzaldehyde with moderate enantioselectivity.

Experimental Section

General. Reactions were carried out in flame-dried Schlenk flasks under an argon atmosphere. THF and Et_2O were distilled over sodium–benzophenone. Hexane and toluene were distilled over $Na(Et_4Al)$. Thin layer chromatography (TLC) used aluminum sheets pre-coated with silica gel 60 F_{254} (Merck). Column chromatography was carried out at normal pressure, using silica gel 60 (0.040–0.063 mm, 230-400 mesh ASTM, Merck). Melting points were determined in capillary tubes on an Electrothermal MEL-TEMP 1102D-230 VAC apparatus without corrections. Optical rotation $[\alpha]_D^{20}$ measurements were obtained using a Perkin–Elmer 241 polarimeter. Enantiomeric excesses were measured on a Shimadzu GC-17A gas chromatograph equipped with a chiral capillary column Cyclodex-β-I/P (L = 30 m, Ø = 0.38 mm, film thickness 0.25 μm) and flame ionization detector (FID). Mass spectra (MS) were recorded on a Hewlett Packard Mass Selective Detector 5973, and are reported as fragmentation in *m/z* with relative intensities (%). NMR spectra were recorded on Bruker Avance DRX-250 (^{1}H at 250.13 MHz; ^{13}C at 62.90 MHz) and Bruker Avance II+ 600 (^{1}H at 600.13 MHz; ^{13}C at 150.92 MHz) instruments with TMS as internal standard; samples for NOE difference experiments were prepared by blowing argon through the $CDCl_3$ solution of the corresponding compound. Elemental analyses were performed by the Microanalytical Laboratory for Elemental Analysis of the Institute of Organic Chemistry, Bulgarian Academy of Sciences. The following starting materials were commercially available: thiophene, furan, (+)-camphor-10-sulfonyl chloride, *n*-BuLi, benzofuran, diethylzinc (1 *M* solution in hexane), and gaseous Me_2NH (from 40% aqueous solution) were obtained from Fluka probably; 1-ethylimidazole was from Merck and ferrocenecarboxaldehyde from Acros.

1-((1*S*,4*R*)-7,7–dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-*N*,*N*-dimethyl methanesulfonamide (2). The Me_2NH in gaseous form was passed through a solution of **1** (4.00 g, 15.95 mmol) in 100 ml dry Et_2O. The ammonium salt formed during the reaction was filtered off and washed with Et_2O (2×30 ml). The combined organic phases were washed with water (2×20 ml), dried (Na_2SO_4), and evaporated to dryness. The remaining crude product was chromatographed (Ø = 30 mm, *h* = 320 mm, 80 g silica gel, Et_2O) to give **2** (3.90 g, 94%) as colorless crystals; mp 61-62°C. $[\alpha]_D^{20}$ = +31.7 (c 1.00, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K): δ = 3.30 (d, 1H, 10-H_a, J = 14.6 Hz), 2.88 (s, 6H, 11-H), 2.72 (d, 1H, 10-H_b, J = 14.6 Hz), 2.59-2.44 (m, 1H, 6-H_{exo}),

2.35 (ddd, 1H, 3-H$_{exo}$, J = 3.3, 4.5, 18.3 Hz), 2.09-2.06 (m, 1H, 4-H), 2.04-1.96 (m, 1H, 5-H$_{exo}$), 1.91 (d, 1H, 3-H$_{endo}$, J = 18.3 Hz), 1.65-1.54 (m, 1H, 6-H$_{endo}$), 1.44-1.34 (m, 1H, 5-H$_{endo}$), 1.11 (s, 3H, 9-H), 0.86 (s, 3H, 8-H). MS (EI) *m/z* (rel. int.): 259 ($M^{+\bullet}$, 1), 195 (22), 180 (10), 167 (18), 152 (36), 151 (22), 133 (8), 110 (11), 109 (100), 108 (39), 106 (8), 95 (24), 93 (35), 92 (15), 91 (23), 87 (84), 82 (10), 81 (97), 79 (33), 77 (20), 69 (19), 65 (10), 55 (28), 53 (21), 46 (12), 45 (31). Anal. Calcd. for $C_{12}H_{21}NO_3S$ (259.37): C, 55.57; H, 8.16; N, 5.40; S, 12.36. Found: C, 55.80; H, 8.25; N, 5.60; S, 12.18%.

1-((1*S*-, 4*S*-, *E*-)-3-Ferrocenylmethylene-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-*N*,*N*-dimethylmethanesulfonamide (4a), and 1-((1*S*,4*S*,*Z*)-3-ferrocenylmethylene-7,7-dimethyl-2-oxobicyclo[2.2.1] heptan-1-yl)-*N*,*N*- dimethylmethanesulfonamide (4b). To a solution of **2** (3.50 g, 13.49 mmol) in 70 ml dry toluene, Li-HMDS (16.19 ml of 1 M solution in THF) was added dropwise at R.T.. After stirring for 15 min, ferrocenecarboxaldehyde (2.89 g, 13.49 mmol) was added. The mixture was heated under reflux for 1h, and monitored by TLC (petroleum/Et_2O, 2:1) until the ferrocenecarboxaldehyde was consumed. The deep red mixture was cooled and quenched with water (30 ml). The water phase was extracted with Et_2O (2×50 ml). The combined organic phases were dried (Na_2SO_4) and evaporated to dryness. The remaining crude product was chromatographed (Ø = 55 mm, h = 390 mm, 500 g silica gel, petroleum/Et_2O = 5:1 to 2:1) to give **4b** (0.33 g, 5%) as deep red crystals, and **4a** (3.60 g, 59%) as dark red crystals.

Data for 4a: mp 140-143°C. $[\alpha]_D^{20}$ = -35.3 (*c* 0.02, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K): δ = 7.09 (s, 1H, 12-H), 4.51-4.48 (m, 2H, 17-H, 14-H), 4.43-4.39 (m, 2H, 15-H, 16-H), 4.13 (s, 5H, Cp), 3.45 (d, 1H, 10-H$_a$, J = 14.6 Hz), 2.93 (s, 6H, 11-H), 2.90 (d, 1H, 4-H, J = 3.9 Hz), 2.83 (d, 1H, 10-H$_b$, J = 14.6 Hz), 2.65-2.53 (m, 1H, 6-H$_{exo}$), 2.24-2.12 (m, 1H, 5-H$_{exo}$), 1.73-1.62 (m, 1H, 6-H$_{endo}$), 1.57-1.47 (m, 1H, 5-H$_{endo}$), 1.15 (s, 3H, 9-H), 0.85 (s, 3H, 8-H). MS (EI) *m/z* (rel. int.): 455 ($M^{+\bullet}$, 100), 453 (8), 348 (5), 347 (15), 319 (8), 304 (9), 283 (16), 282 (7), 281 (31), 279 (6), 276 (6), 265 (6), 251 (7), 239 (8), 238 (6), 237 (6), 210 (6), 199 (6), 186 (6), 165 (5), 153 (6), 121 (21), 115 (6). Anal. Calcd. for $C_{23}H_{29}FeNO_3S$ (455.39): C, 60.66; H, 6.42; Fe, 12.26; N, 3.08; S, 7.04. Found C, 60.55, H, 6.75, Fe, 12.06, N, 3.28, S, 6.90%.

Data for 4b. mp 133-136°C. $[\alpha]_D^{20}$ = 0 (the measurement failed because no light penetrates the deep colored solution even at *c* = 0.02, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K): δ = 6.41 (s, 1H, 12-H), 5.05-5.03* (m, 1H, 17-H), 4.94-4.92* (m, 1H, 14-H), 4.40-4.36 (m, 2H, 15-H, 16-H), 4.11 (s, 5H, Cp), 3.48 (d, 1H, 10-H$_a$, J = 14.7 Hz), 2.95 (s, 6H, 11-H), 2.82 (d, 1H, 10-H$_b$, J = 14.7 Hz), 2.67-2.51 (m, 1H, 6-H$_{exo}$), 2.5 (d, 1H, 4-H, J = 4 Hz), 2.21-2.09 (m, 1H, 5-H$_{exo}$), 1.68-1.57 (m, 1H, 6-H$_{endo}$), 1.56-1.46 (m, 1H, 5-H$_{endo}$), 1.13 (s, 3H, 9-H), 0.93 (s, 3H, 8-H). MS (EI) *m/z* (rel. int.): 455 ($M^{+\bullet}$, 100), 453 (7), 347 (13), 304 (8), 283 (19), 282 (8), 281 (34), 279 (6), 276 (5), 265 (5), 253 (5), 251 (6), 239 (8), 238 (6), 237 (5), 236 (5), 210 (5), 199 (5), 186 (6), 153 (5), 121 (18), 115 (5). Anal. Calcd. for $C_{23}H_{29}FeNO_3S$ (455.39): C, 60.66; H, 6.42; Fe, 12.26; N, 3.08; S, 7.04. Found C, 60.71, H, 6.70, Fe, 12.11, N, 2.90, S, 7.20%.

1-((1-*S*-, 2-*R*-,4-*S*-,*E*-)-3-Ferrocenylmethylene-2-(1-ethyl-1H-imidazole-2-yl)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl)-*N*,*N*-dimethyl methanesulfonamide (10). To a solution of 1-ethylimidazole (0.19 g, 1.98 mmol) in 5 ml hexane and 5 ml THF was added dropwise *n*-BuLi

(1.36 ml, 2.18 mmol of 1.6 *M* solution in hexane) at -90°C. The temperature was allowed to rise to -20°C within 1 h. Then it was cooled to –60°C, and **4a** (0.30 g, 0.66 mmol) was added at this temperature. The mixture was warmed slowly (1 h) to -20°C and during this time **4a** was consumed (monitored by TLC, Et_2O: aq. NH_3 = 300:1). The mixture was quenched with water (10 ml). The water phase was extracted with Et_2O (3×20 ml). The organic phase was dried (Na_2SO_4) and evaporated to dryness. The remaining crude product was chromatographed (Ø = 30 mm, *h* = 320 mm, 80 g silica gel, Et_2O: aq. NH_3 = 300:1) to give **10** (0.290 g, 80%) as a pale orange solid; mp 135-137°C. $[\alpha]_D^{20}$ = +276.5 (c 0.52, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K): δ = 7.00 (d, 1H, 4'-H, J = 1.3 Hz), 6.92 (d, 1H, 5'-H, J = 1.3 Hz), 6.28 (s, 1H, 12-H), 5.05 (s, 1H, OH), 4.41 (s, br, 1H, 17*-H), 4.25 (m, 3H, 14-H, 15-H, 16-H), 4.15 (s, 5H, Cp), 4.08 (q, 2H, 6'-H, J = 14.4, 7.2 Hz), 3.73 (d, 1H, 10-H_b, J = 14.8 Hz), 3.06 (d, 1H, 10-H_a, J = 14.8 Hz), 3.00 (d, 1H, 4-H, J = 4.1 Hz), 2.84 (s, 6H, 11-H), 2.4 (ddd, 1H, 6-H_{exo}, J = 14.2, 12.1, 3.8 Hz), 2.09-1.96 (m, 1H, 5-H_{exo}), 1.63-1.53 (m, 1H, 5-H_{endo}), 1.34 (t, 3H, 7'-H, J = 7.2 Hz), 1.24 (s, 3H, 8-H), 1.24-1.12 (m, 1H, 6-H_{endo}), 1.18 (s, 3H, 9-H). MS (EI) *m/z* (rel. int.): 551 ($M^{+\bullet}$, 1), 457 (12), 456 (35), 455 (100), 453 (7), 347 (13), 319 (8), 304 (8), 383 (15), 281 (29), 121 (19). Anal. Calcd. for $C_{28}H_{37}FeN_3O_3S$ (551.52): C, 60.98; H, 6.76; Fe, 10.13; N, 7.62; O, 8.70; S, 5.81. Found C, 61.23, H, 6.87, Fe, 9.83, N, 7.44, S, 6.00%.

1-((1-S-, 2-R-,*4-S-*,*E*--)-3-Ferrocenylmethylene-2-hydroxy-7,7-dimethyl-2-(pyridin-2-yl)-bicyclo-[2.2.1]-heptan-1-yl)-*N,N*-dimethyl methanesulfonamide (11). To a solution of **4a** (0.25 g, 0.55 mmol) and 2-bromopyridine (0.087 g, 0.55 mmol) in 3 ml THF was added at –80°C *n*-BuLi (0.33 ml, 0.83 mmol of 2.5 *M* solution in hexane). After stirring for 2 h at –80°C the mixture was quenched with dilute aq. NH_4Cl (10 ml) and extracted with Et_2O (3×20 ml). The organic phase was dried (Na_2SO_4) and evaporated to dryness. The remaining crude product was chromatographed (Ø = 23 mm, *h* = 580 mm, 90 g silica gel, petroleum/Et_2O = 2:1) to give **11** (0.139 g, 47%) as a pale orange solid; mp 192-195°C with decomp. $[\alpha]_D^{20}$ = –107.6 (c 1.00, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$, 300K): δ = 8.54 (*ddd*, 1H, 6'-H, J = 4.9, 1.7, 0.9 Hz), 7.68 (*ddd*, 1H, 4'-H, J = 7.8, 1.7, 0.3 Hz), 7.42-7.36 (m, 1H, 3'-H), 7.27 (*ddd*, 1H, 5'-H, J = 7.8, 4.9, 1.1 Hz), 6.23 (s, 1H, OH), 5.97 (s, 1H, 12-H), 4.39–4.37* (m, 1H, 17-H), 4.33-4.30* (m, 1H, 14-H), 4.26–4.24* (m, 1H, 16-H), 4.22–4.20* (m, 1H, 15-H), 4.13 (s, 5H, Cp), 3.57 (d, 1H, 10-H_a, *J* = 14.9 Hz), 2.94 (d, 1H, 10-H_b, *J* = 14.9 Hz), 2.95 (d, 1H, 4-H, *J* = 4.2 Hz), 2.82 (s, 6H, 11-H), 2.36, (ddd, 1H, 6-H_{exo}, J = 13.5, 12.1, 4.2 Hz), 2.12-2.08 (m, 1H, 5-H_{exo}), 1.66–1.56 (m, 1H, 5-H_{endo}), 1.48-1.37 (m, 1H, 6-H_{endo}), 1.21 (s, 3H, 8-H), 1.14 (s, 3H, 9-H). MS (EI) *m/z* (rel. int.): 534 ($M^{+\bullet}$, 100), 469 (11), 455 (14), 427 (15), 426 (45), 425 (14), 408 (24), 361 (13), 360 (47), 342 (15), 332 (10), 321 (11), 320 (43), 318 (10), 317 (14), 252 (12), 224 (12), 204 (10), 199 (38), 167 (10), 121 (28), 78 (17). Anal. Calcd. for $C_{28}H_{34}FeN_2O_3S$ (534.49): C, 62.92; H, 6.41; Fe, 10.45; N, 5.24; S, 6.00. Found C, 62.72, H, 6.69, Fe, 10.66, N, 5.01, S, 6.22%.

1-((1*S*,2*R*,4*S*,*E*-)-3-Ferrocenylmethylene-2-(furan-2-yl)-2-hydroxy-7,7-dimethylbicyclo-[2.2.1]heptan-1-yl)-*N,N*-dimethylmethanesulfonamide (12). To a solution of furan (0.158 g, 2.32 mmol) in 3 ml hexane and 3 ml Et_2O was added dropwise at 10°C *n*-BuLi (1.22 ml, 1.94 mmol of 1.6 *M* solution in hexane). The mixture was stirred for 30 min at R.T. and, after cooling

to 0°C, **4a** (0.30 g, 0.66 mmol) was added. The reaction was monitored by TLC (petroleum/Et_2O = 2:1). After stirring for 24 h at R.T. the reaction was quenched with water (5 ml) and extracted with Et_2O (3×20 ml). The organic phase was dried (Na_2SO_4) and evaporated to dryness. The remaining crude product was chromatographed (Ø = 30 mm, *h* = 320 mm, 80 g silica gel, petroleum/Et_2O = 2:1 to 1:1), to give **12** (0.203 g, 59%) as a yellow solid; mp 160-163°C with decomp. $[\alpha]_D^{20}$ = –138 (c 0.35, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K): δ 7.43 (dd, 1H, 5'-H, *J* = 1.8, 0.8 Hz), 6.36 (dd, 1H, 3'-H, J = 3.2, 1.8 Hz), 6.31 (dd, 1H, 4'-H, *J* = 3.2, 0.8 Hz), 6.19 (s, 1H, 12-H), 4.39 (s, br, 1H, 17-H), 4.32 (s, br, 1H, 14-H), 4.27* (s, br, 1H, 16-H), 4.24* (s, br, 1H, 15-H), 4.16 (s, 5H, Cp), 3.59 (d, 1H, 10-H_b, J = 14.9 Hz), 3.20 (d, 1H, 10-H_a, J = 14.9 Hz), 2.9 (s, 6H,11-H), 2.85 (d, 1H, 4-H, J = 4.8 Hz), 2.67 (s, 1H, OH), 2.23 (ddd, 1H, 6-H_{exo}, J = 13.2, 12.1, 4.5 Hz), 2.1-1.9 (m, 1H, 5-H_{exo}), 1.42 (ddd, 1H, 5-H_{endo}, J = 12.1, 9.2, 4.5 Hz), 1.26-1.16 (m, 1H, 6-H_{endo}), 1.20 (s, 3H, 8-H), 1.16 (s, 3H, 9-H). MS (EI) *m/z* (rel. int.): 523 ($M^{+\bullet}$, 100), 521 (7), 416 (5), 415 (18), 414(20), 397 (11), 350 (18), 349 (71), 347 (13), 277 (19), 261 (12), 165 (12), 121 (18). Anal. Calcd. for $C_{27}H_{33}FeNO_4S$ (523.47): C, 61.95; H, 6.35; Fe, 10.67; N, 2.68; S, 6.13. Found C, 62.70, H 6.41, Fe, 10.50, N, 2.38, S, 5.91%.

1-((1*S*,2*R*,4*S*,*E*)-2-(Benzofuran-2-yl)-3-ferrocenylmethylene-2-hydroxy-7,7-dimethylbicyclo-[2.2.1]-heptan-1-yl)-*N*,*N*-dimethyl methanesulfonamide (13). To a solution of benzofuran (0.28 g, 2.38 mmol) in 8 ml THF was added dropwise at 0°C *n*-BuLi (1.24 ml, 1.98 mmol of 1.6 *M* solution in hexane). The mixture was stirred for 1 h at R.T. and then **4a** (0.30 g, 0.66 mmol) was added. The reaction was monitored by TLC (petroleum:Et_2O = 2:1) until **4a** was consumed (1 h). The mixture was quenched with water (5 ml) and extracted with Et_2O (3×20 ml). The organic phase was dried (Na_2SO_4) and evaporated to dryness. The remaining crude product was chromatographed (Ø = 30 mm, *h* = 320 mm, 80 g silica gel, petroleum:Et_2O = 5:1), to give **13** (0.313 g, 83%) as a yellow solid; mp 107-110°C. $[\alpha]_D^{20}$ = –198.1 (*c* 1.005, $CHCl_3$). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K): δ = 7.57-7.56 (m, 1H, 5'-H), 7.46-7.42 (m, 1H, 8'-H), 7.28-7.19 (m, 2H, 6'-H, 7'-H), 6.73 (d, 1H, 3'-H, J = 0.7 Hz), 6.25 (s, 1H, 12-H), 4.44 (s, br, 1H, 17-H), 4.33 (s, br, 1H, 14-H), 4.30* (s, br, 1H, 16-H), 4.26* (s, br, 1H, 15-H), 4.19 (s, 5H, Cp), 3.68 (d, 1H, 10-H_a, J = 14.9 Hz), 3.29 (d, 1H, 10-H_b, J = 14.9 Hz), 2.92 (s, 6H, 11-H), 2.90 (d, br, 1H, 4-H), 2.8 (s, 1H, OH), 2.24-2.21 (m, 1H, 6-H_{exo}), 2.11-1.98 (m, 1H, 5-H_{exo}), 1.64-1.49 (m ,1H, 5-H_{endo}), 1.43-1.30 (m, 1H, 6-H_{endo}), 1.26 (s, 3H, 8-H), 1.20 (s, 3H, 9-H). MS (EI) *m/z* (rel. int.): 573 ($M^{+\bullet}$, 100), 571 (7), 465 (18), 464 (18), 447 (11), 353 (15), 352 (50), 397 (10), 327 (23), 283 (14), 199 (11), 189 (9), 186 (10), 145 (10), 121 (20). Anal. Calcd. for $C_{31}H_{35}FeNO_4S$ (573.52): C, 64.92; H, 6.15; Fe, 9.74; N, 2.44; S, 5.59. Found C, 64.75, H 6.38, Fe, 9.97, N, 2.61, S, 5.34%.

1-((*1S,2R,4S,E*)-3-Ferrocenylmethylene)-2-hydroxy-7,7-dimethyl-2-(thiophene-2-yl)-bicyclo-[2.2.1]heptan-1-yl)-*N*,*N*-dimethyl methanesulfonamide (14). To a solution of *n*-BuLi (1.04 ml, 1.66 mmol of 1.6 *M* solution in hexane) in 2 ml hexane and 2 ml THF was added within 10 min. at 0 °C thiophene (0.17 ml, 1.99 mmol). The mixture was stirred for 1 h at R.T. and then **4a** (0.25 g, 0.55 mmol) was added. The reaction was monitored by TLC (petroleum:Et_2O = 2:1). After stirring for 1 h at R.T., the reaction was quenched with water (5

ml) and extracted with Et_2O (3×20 ml). The organic phase was dried (Na_2SO_4) and evaporated to dryness. The remaining crude product was chromatographed (Ø = 17 mm, h = 550 mm, 50 g silica gel, petroleum/Et_2O = 2:1), to give **14** (0.142 g, 48%) as a yellow solid; mp 157–160°C with decomp. $[\alpha]_D^{20}$ = -208.7 (c 1.002, $CHCl_3$). ^1H NMR (250 MHz, $CDCl_3$, 300 K): δ = 7.3 (dd, 1H, 5'-H, J = 4.1, 2.2 Hz), 7.03-6.99 (m, 2H, 3'-H, 4'-H), 6.22 (s, 1H, 12-H), 4.40-4.39 (m, 1H, 17-H), 4.31-4.30 (m, 1H, 14-H), 4.29-4.23 (m, 2H, 15-H, 16-H), 4.18 (s, 5H, Cp), 3.46 (d, 1H, 10-H_b, J = 14.9 Hz), 3.22 (d, 10-H_a, J = 14.9 Hz), 2.90 (s, 6H, 11-H), 2.90 (s, br, 1H, 4-H), 2.63 (s, 1H, OH), 2.36-2.25 (m, 1H, 6-H_{exo}), 2.11-1.99 (m, 1H, 5-H_{exo}), 1.54-1.44 (m, 1H, 5-H_{endo}), 1.40-1.30 (m, 1H, 6-H_{endo}), 1.21 (s, br, 6H, 8-H, 9-H). MS (EI) *m/z* (rel. int.): 539 ($M^{+\bullet}$, 82), 537 (6), 431 (22), 430 (24), 366 (28), 365 (100), 363 (12), 320 (9), 293 (35), 281 (10), 251 (10), 217 (10), 199 (10), 186 (11), 165 (11), 121 (20), 111 (15). Anal. Calcd. for $C_{27}H_{33}FeNO_3S_2$ (539.53): C, 60.11; H, 6.16; Fe, 10.35; N, 2.60; S, 11.89. Found C, 60.38, H 6.10, Fe, 10.21, N, 2.72, S, 11.67%.

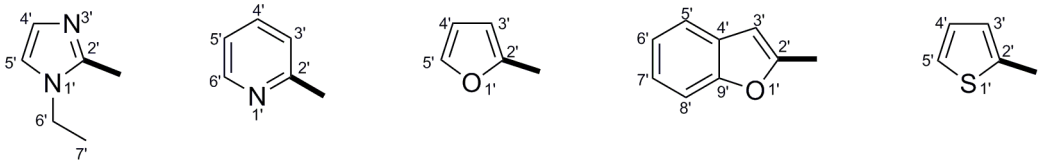
Enantioselective addition of dialkylzinc to aldehyde in presence of ligands 11–14. General procedure

To a solution of 6 ml hexane or toluene and ligand **11**–**14** (3 mol. %) Et_2Zn (5.67 mmol of 1 *M* solution in hexane) was added dropwise at -10°C. The mixture was stirred for 30 min at –10°C and then PhCHO (2.83 mmol) was added at -20°C. The reaction was stirred at R.T. and monitored by TLC (petroleum: Et_2O = 4:1) until the PhCHO was consumed. The mixture was quenched (aq. NH_4Cl), extracted with Et_2O (3×20 ml) and dried. After evaporation of the solvent the crude 1-phenyl-1-propanol was purified by column chromatography (petroleum/Et_2O = 5:1).

Table 2. ^{13}C NMR chemical shifts of compounds **2**, **4** and **10**–**14** ($CDCl_3$, 300 K, δ in ppm from TMS); assignments marked with asterisks are tentative[a]

No. C-atom	Compound							
	2	**4a**	**4b**	**10**	**11**	**12**	**13**	**14**
C(1)	58.06*	57.40*	59.55*	55.39*	53.87*	54.90*	55.02*	54.85*
C(2)	215.42	203.81	202.50	81.53*	82.45*	82.16	81.87*	82.03*
C(3)	42.52	136.39	135.81	144.92*	149.26*	147.59*	147.11*	149.59*
C(4)	42.74	49.06	54.22	51.15	50.82	50.89	51.09	51.11
C(5)	26.83	25.50	27.36	24.19	24.93	24.53	24.55	22.44
C(6)	25.09	26.05	25.03	25.68	26.37	27.45	27.83	27.30
C(7)	47.86*	47.57*	47.28*	49.62*	51.28*	49.57*	49.75*	49.82*
C(8)	19.68	20.55	20.54	22.28	22.34	22.12	22.20	22.41*
C(9)	19.92	19.31	19.59	21.51	20.96	21.29	21.25	21.80*
C(10)	43.49	43.78	43.56	42.82	42.86	44.15	44.36	43.09
C(11)	37.41	37.46	37.55	37.61	37.61	37.59	37.59	37.68
C(12)	-	129.91	134.50	124.68	123.37	121.65	122.28	122.21
C(13)	-	78.18	78.22	83.12*	84.36*	82.20*	82.61*	84.75*
C(14)	-	69.01*	72.21*	68.34*	69.38*	69.34*	69.43*	69.33*
C(15)	-	70.83	70.79*	68.92*	68.71*	68.76	68.86	68.73
C(16)	-	70.83	70.88*	69.28*	68.60*	68.76	68.86	68.73
C(17)	-	71.49*	71.79*	68.29*	68.05*	68.05*	68.07*	67.88*
Cp	-	69.36	69.19	68.87	68.63	68.88	68.90	68.73
C(2`)	-	-	-	149.64	162.37	157.39	159.96	150.22
C(3`)	-	-	-	-	122.78	109.92	105.78	126.19
C(4`)	-	-	-	126.50	135.84	108.82	127.60	126.28
C(5`)	-	-	-	120.20	122.72	142.25	121.16	125.22
C(6`)	-	-	-	42.15	146.88	-	122.89	-
C(7`)	-	-	-	16.11	-	-	124.39	-
C(8`)	-	-	-	-	-	-	111.15	-
C(9`)	-	-	-	-	-	-	154.95	-

[a] For the numbering of the bicyclic moiety see Scheme 2 and the following fragments:



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13. Data for: 1-((1*S*,2*R*,4*S*,*E*)-2-butyl-3-ferrocenylmethylene-2-hydroxy-7,7-dimethyl-bicyclo[2.2.1]heptan-1-yl)-*N,N*-dimethylmethanesulfonamide: ^{1}H NMR (600 MHz, $CDCl_3$, 300 K): δ = 6.22 (s, 1H), 4.30-4.28 (m, 2H), 4.20-4.17 (m, 2H), 4.10 (s, 5H, Cp), 3.33 (d, 1H), 2.90 (s, 6H), 2.74 (d, 1H), 2.70 (d, 1H), 2.46 (s, 1H), 2.29-2.09 (m, 2H), 2.05-1.81 (m, 2H), 1.71-1.56 (m, 4H), 1.54-1.33 (m, 2H), 1.03 (s, 3H,), 0.96 (t, 3H,), 0.95 (s, 3H,). ^{13}C NMR ($CDCl_3$) δ = 150.07, 117.61, 83.15, 80.39, 69.20, 68.89, 68.36, 68.25, 68.04, 54.45, 50.72, 50.65, 45.52, 39.51, 37.61, 27.43, 25.89, 25.16, 23.53, 21.90, 20.42, 14.18. MS (EI) *m/z* (rel. int.): 513 ($M^{+\bullet}$, 24), 497 (9), 496 (29), 495 (100), 493 (5).