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Functionalized organolithium reagents in the synthesis of chiral ligands for catalytic enantioselective addition of diethylzinc to aldehydes

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ABSTRACT

Series of functionalized organolithium compounds were prepared and added to chiral bicyclic ketones (1*R*-(+)-camphor analogue **2** and 1*R*-(−)-fenchone **3**), resulting in the preparation of a small "library" of chiral aminoalcohols able to serve as ligands in metal mediated asymmetric synthesis. The configuration of the chiral ligands was approved by applying advanced NMR experiments. The absolute configurations of 1,2-disubstituted planar chiral ferrocene-based aminoalcohols **15**, **18** and **19** were determined by means of NMR experiments and confirmed by X-ray crystallography. The new chiral ligands were tested as pre-catalysts for the addition of diethyl zinc to benzaldehyde. The reactions proceeded with excellent conversions and a moderate degree of enantioselectivity.

1. Introduction

The considerable interest in the synthesis and application of new enantiomerically pure β-, γ- and δ-aminoalcohols by utilizing different sources of chirality has been an obvious result of their efficiency as pre-catalysts for enantioselective addition of diorganozinc compounds to aldehydes, discovered first by Oguni and Omi [1]. The phenomenon of chirality amplification (the non-linear relationship between the enantiomeric purity of the ligand used and the enantiomeric excess of the product obtained) has attracted particular interest and has been studied in detail by Noyori [2] with the example of *N*,*N*-dimethylaminoisoborneol (DAIB). In recent years, a large number of aminoalcohols structurally based on the bicyclic camphane core have been synthesized using camphor [3], fenchone [3b,4], camphor-10-sulfonamide [5] and similar chiral sources [6] as the starting materials. The variation of the substituents attached to the camphane skeleton allows data collection to study the influence of the ligand structure on the degree and sense of enantioselectivity.

Over the few past years, we have been interested in the utilization of (+)-camphor and (−)-fenchone within the addition reactions of functionalized organometallic reagents, leading to various aminoalcohols [3a,3b,7] showing, in several cases, high efficiency as pre-catalysts to form *in situ* organozinc complexes that are able to provide enantioselective addition of diethylzinc to aldehydes.

In the present paper we are applying an organometallic approach to obtain *N*- and *S*-functionalized hydroxy-camphane derivatives of type **A** and **B** (Scheme 1) that possess a similar substitution at C-1 and C-3 of the bicyclic skeleton, but different stereochemistry at C-2, realized through the different *exo*/*endo*-selectivity of the addition of organolithiums to compounds **2** and **3**. Chiral compounds of type of **A** and **B** are versatile ligands for diverse metal catalyzed transformations and they could be employed in applications beyond the organozinc additions used to test them in the present work.

2. Results and discussion

2.1. Synthesis of chiral aminoalcohols and analogues by addition of functionalized organolithiums to bicyclic ketones

For the planned addition reactions, the commercially available 1*R*-(+)-camphor **1** was transformed into the ketone **2** applying a known procedure [8a,8c] (Scheme 1). Ketone **2** has been rarely used for transformations [8b–e]. To the best of our knowledge, addition reactions of organometallics to **2** have not been studied. Only the reduction with $LiAlH_4$ leading to the corresponding *iso*-borneol analogue has been described [8c]. A set of organolithium reagents was selected to perform addition reactions to these ketones, leading to dimethylaminoalcohols (with reagents **4**–**6**, **12**) and alcohols containing an *N*-heterocyclic moiety (with reagents **7**, **13**–**14**), which in the case of **13** and **14** possess an additional

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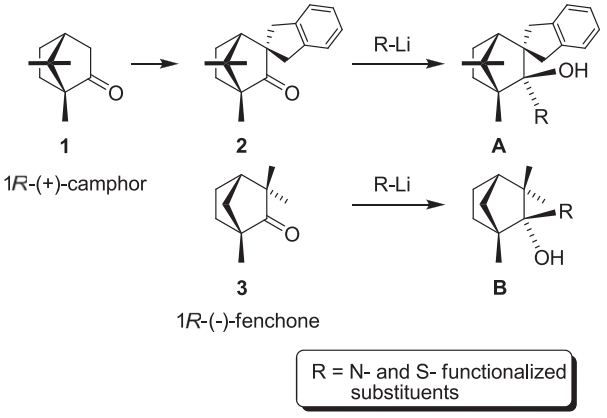
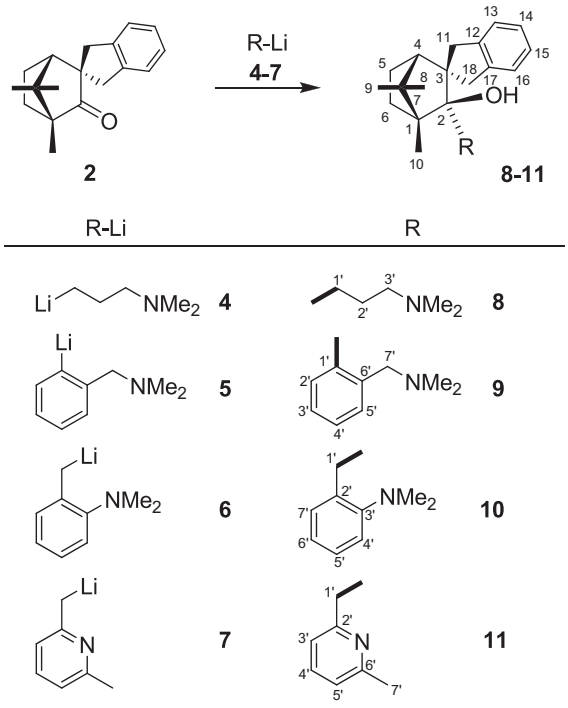


Scheme 1. The addition of organolithiums to **2** and **3** proceeds in a highly diastereoselective manner, leading to products of type **A** and **B** with defined stereochemistries.

Me_2N-group (Schemes 2 and 3). The organolithium reagents were prepared or generated *in situ* by using known or modified published procedures [9–17].[1]

Addition of organolithium **4** [9] occurred in hexane at room temperature leading to aminoalcohol **8**, isolated in excellent yield (Scheme 2). In this case the assistance of anhydrous $CeCl_3$ was not necessary compared with previously published results [3b]. The reaction of **5** [10] and **2** was performed in hexane/Et_2O at room temperature, with the formation of **9** in good yield. The addition of the *in situ* generated **6** [11] to **2** occurs in a low yield (in hexane/Et_2O). The similar addition of **6** to (−)-fenchone (**3**) was also low yielding and an inseparable mixture of the corresponding *endo*/*exo* fenchol isomers was formed in this case (the ratio of both diastereoisomers was determined by NMR as 8:1, without unambiguous identification). Organolithium reagent **7**, possessing low thermal stability, was generated *in situ* at −60 °C [12] and the addition was performed at the same temperature to obtain **11** in good yield. Similar results have been published for the addition of **7** to (+)-camphor [18].

The addition of reagents **12**–**14** to ketones **2** and **3** is presented in Scheme 3. The 1,2-disubstituted ferrocenyllithium compound **12** was formed and used as a racemate in respect of the chirality plane [13]. Therefore after addition of **12** to **2**, the formation of two diastereoisomers is to be expected, provided only *endo*-addition occurs. Remarkably, only one diastereoisomer, **15**, was observed and isolated. No experimental evidence for the formation of other diastereoisomers could be obtained. Compound **15** was identified as the *endo*-addition product (for the configuration determination see discussion below). Additionally, 60% of the *N*,*N*-dimethylaminomethyl-ferrocene used to generate **12** was recovered after performing the addition reaction, followed by aqueous work-up procedure (see Section 4). Therefore, these results indicate that only one of the planar chiral enantiomers of **12** took part in the addition reaction, probably due to steric reasons. This suggestion is strongly supported by the results of the addition reaction of **12** to **3** in respect of the lower steric hindrance in this case during the course of the nucleophilic attack. The reaction of **12** and **3** furnished the expected two diastereoisomers **18** and **19** in respect of the chirality plane and as a result of *exo*-addition (78% overall yield, ratio **18**:**19** = 1:2). It should be pointed out that in fact the normal addition of nucleophiles to bicyclo [2.2.1]-heptan-2-ones with respect to the stereoselectivity is *exo* due to the significant repulsion caused by the *endo*-protons. However, the presence of the methyl group at the C-7 position in the case of **2** executes additional hindrance, forcing reagent **12** to add against the repulsion of the



Scheme 2. Addition of organolithiums **4**–**7** to the camphor analogue **2**.

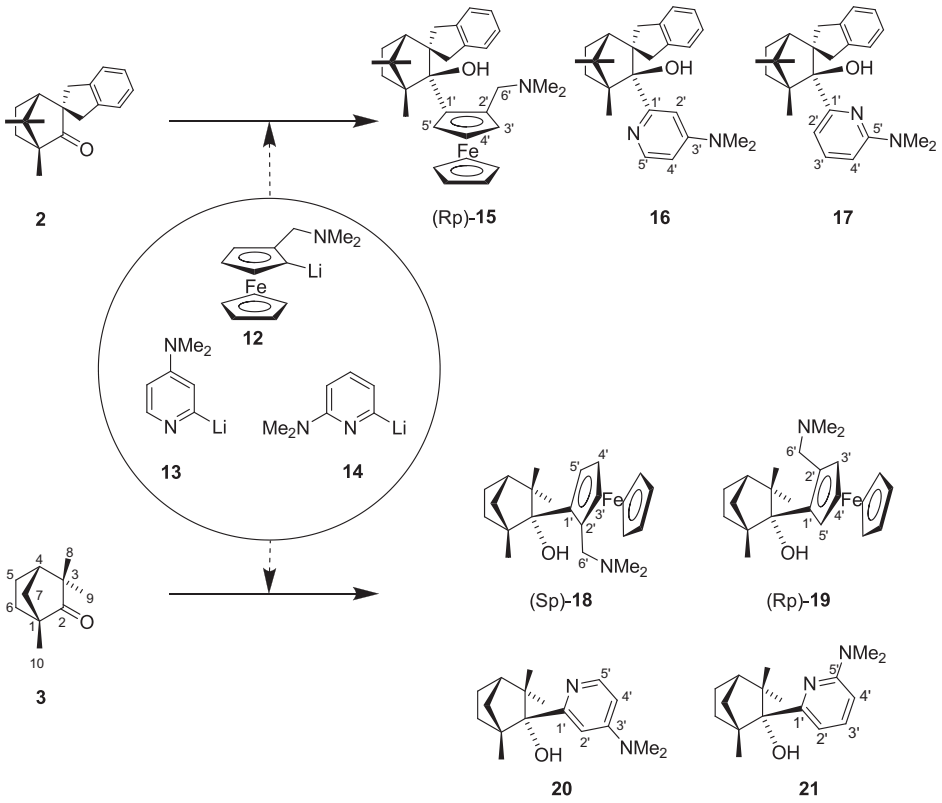
endo-protons. The application of organolithiums **13** [14] and **14**[1] provided, in the case of **2**, products **16** and **17**, and in case of **3**, compounds **20** and **21** respectively, isolated in moderate yields.

For the synthesis of β-heteroatom functionalized derivatives of type **B** (Scheme 1), the organolithium reagents **22a**–**d** [15], **23a**–**c** [15] and **24**–**27** [15–17] were prepared *in situ* from the corresponding heterocycles [19–21] and added to ketone **3** (Scheme 4). The products **28**–**34** were isolated in moderate to excellent yields as single diastereoisomers (see Section 4) as a consequence of the expected *exo*-addition selectivity. In the case of 2-lithio-thiophene (**26**), small amounts of the bis-substituted derivative **33** were isolated. This is obviously a result of the formation of 2,5-dilithio-thiophene during the lithiation of thiophene with *n*-BuLi. The addition reactions of reagents **22**–**27** to ketone **2** were abandoned because of the discouraging enantioselectivities, achieved with products **28**–**34** applied as ligands for the addition of Et_2Zn to benzaldehyde (see below).

For the synthesis of γ-aminoalcohols, the reagent $LiCH_2CN$ (generated *in situ* from *n*-BuLi and CH_3CN) was added to ketones **2** and **3** (Scheme 5). The addition reaction was performed at −78 °C in THF to give the compounds **35** and **36**, respectively, in excellent yields, which were then reduced quantitatively to the corresponding aminoalcohols **37** and **38** (the synthesis of **36** and **38** has been previously described [3a]). Compounds **37** and **38** were the starting materials for the preparation of the dialkylamino derivatives **39**–**43**, obtained in moderate to excellent yields using a standard procedure (RX/K_2CO_3 in refluxing THF/water). Surprisingly, an attempt to prepare the *N*,*N*-dimethyl substituted aminoalcohol from **37** using HCHO/HCOOH (Eschweiler–Clarke procedure) led, under the reaction conditions, to a new undesired product, assigned as the heterocyclic derivative **44**.

The structures of the new chiral compounds were established by NMR experiments and mass spectra. The unambiguous assignment

[1] To best of our knowledge there is no published procedure for the preparation of reagent **14**, so we have successfully used the *in-situ* procedure described for the preparation of **13**, starting from 2-(*N*,*N*-dimethylamino)-pyridine.



Scheme 3. Addition of organolithiums **12**–**14** to ketones **2** and **3**.

of the ^{1}H and ^{13}C NMR spectra was made on the basis of DEPT, COSY, HSQC, HMBC and NOESY experiments (see Section 4).

2.2. Configuration determination by NMR methods

In all cases the observed *endo*/*exo* diastereoselectivities of the addition reactions to the carbonyl C-atom of ketones **2** and **3** were excellent as a result of exclusive *endo*-attack of the organolithium reagents to **2** and *exo*-attack to **3**, respectively, proved by the NMR experiments.

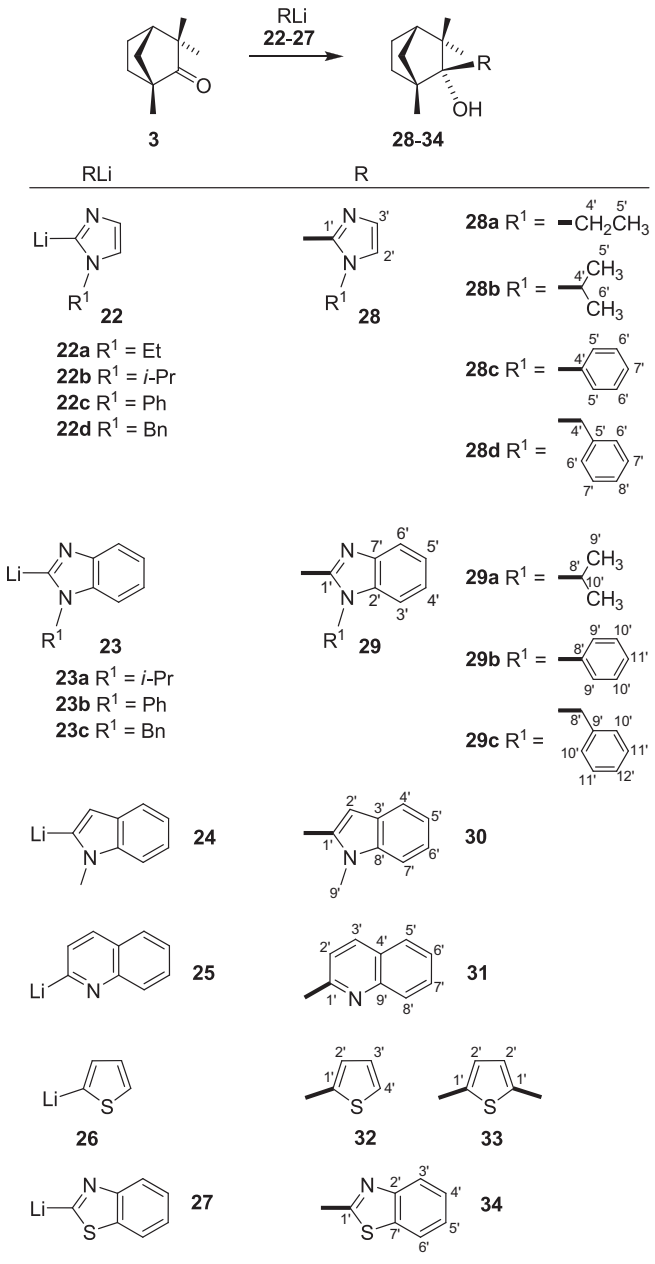
The *endo*-position of the substituents was confirmed by NOESY spectra through the observed proton proximities of H-atoms from the corresponding substituent in compounds **8**–**11**, **16**, **17**, **35** and **37** with the *endo*-positioned protons of the bicyclic core (Fig. 1). Furthermore, the H-atom proximities observed by the NOESY spectra have decisively contributed to the unambiguous assignment of the ^{1}H and ^{13}C signals within the structures synthesized.

The same approach has been applied to confirm the *exo*-position of the substituents in compounds **28**–**33**, **20** and **21** by means of the NOESY spectra. The most important H-atoms proximities observed and shown in Fig. 2 illustrate undoubtedly the *exo*-attack during the addition of the corresponding organolithium reagents (compare Schemes 3 and 4).

The determination of the configuration of the ferrocene derivatives **15**, **18** and **19** was of particular interest, since similar types of ferrocene compounds are important precursors for asymmetric catalysis. The NOESY experiments brought extensive information about the proton neighborhood within the ferrocene derivatives, allowing the determination of the locations of the protons and therefore of the individual parts of the molecules relative to each other. Consequently, the results of this approach also allow the determination of the absolute configuration of these three compounds in respect of the chirality plane within the ferrocene core, taking into account the known configuration of the corresponding bicyclic skeleton. For a successful determination of the configuration, it is sufficient to obtain information concerning the position of the dimethylamino-methyl-group relative to the C-C-bond connecting the substituted Cp-ring and C-2 of the bicyclic skeleton, and the relative position of the unsubstituted Cp-ring. In the case of compound **15**, the most important proton proximities (presented by means of arrows) undoubtedly show the location of the dimethylamino-methyl-group on the side of the spiro-indane-part of the structure. The unsubstituted Cp-ring lies below the plane of the substituted one (by the presented top view, Fig. 3) proved by the proton proximity of the 11a-proton and the protons of the Cp-ring. Consequently, the configuration of **15** is R_p with respect to the chirality plane.

For the diastereoisomer **18**, the observed NOEs indicate obviously short distances between the protons of the dimethylamino-groups and the C-10 methyl group, whereas the C-5′ proton lies in close proximity with one of the C-7 protons and the C-8 methyl-protons. The unsubstitute Cp-ring lies on the side of the C-8 and C-9 methyl groups. These observations are sufficient as a proof for the S_p configuration of **18** in respect of the chirality plane and by the known chirality of the bicyclic skeleton. In the case of diastereoisomer **19**, it was possible to determine the position of the dimethylamino group relative to the C–C-bond between C-2 of the bicyclic skeleton and the Cp-ring (the NOEs are shown with arrows in Fig. 4). However, no certain data could be obtained about the relative position of the unsubstituted Cp-group. Therefore, the R_p configuration of the diastereoisomer **19** was deduced from these observations and supported by the configuration determined for **18**.

The configurations of ferrocene derivatives **15** and **18** suggest a close proximity of the hydroxyl protons and the N-atoms, and thus existence of hydrogen bonding.



Scheme 4. Addition of organolithiums **22**–**27** to ketone **3**.

2.3. Crystal structure and configuration determination of ferrocene derivatives *15* and *18* by X-ray crystallography

Crystals of **15** were grown by recrystallization in a 6 ml $CHCl_3$/CH_3OH 1:1 v/v solution at room temperature. Compound **15** crystallizes in the non-centrosymmetric group $P2_12_12_1$ (SG 19) with one molecule per asymmetric unit (Table 1). The ORTEP plot with the atomic numbering system of **15** is shown in Fig. 5a and selected bond distances and bond angles are listed in Tables 2 and 3. The bond distance and angles of the camphane and spiro-indane moieties are comparable to those observed in other structures [22,8e,23–26]. The indane ring is almost planar (*rms* of 0.0348 Å) although it contains two sp^3 carbons (C23 and C30). The cyclopentadienyl rings are also nearly planar with *rms* values of 0.004 and 0.005 Å. The structure of **15** reveals a slightly distorted coordination geometry of the metal center (Fe) and the cyclopentadienyl ligands, with Fe–Cp distances of 1.652(4) and 1.665(4) Å for C4/C5/C6/C7/C8 and C9/C10/C11/C12/C13, respectively, and an angle between the mean planes of the cyclopentadienyl rings of 8.9(7)°. An intramolecular hydrogen bond, O1-H1···N1 (*D*···*A* distance of 2.831(4) Å), is probably responsible for the observed conformation. The lack of additional hydrogen bond donors and acceptors prevents the formation of intermolecular hydrogen bonds. However, a weak intermolecular interaction of the O·····π type (shortest distance O1·····C7 of the substituted Cp is 3.303 Å) can be detected (Fig. 6a). The absolute configuration of **15** has been determined independently as R_p, thus confirming the NMR analysis (see Fig. 3).

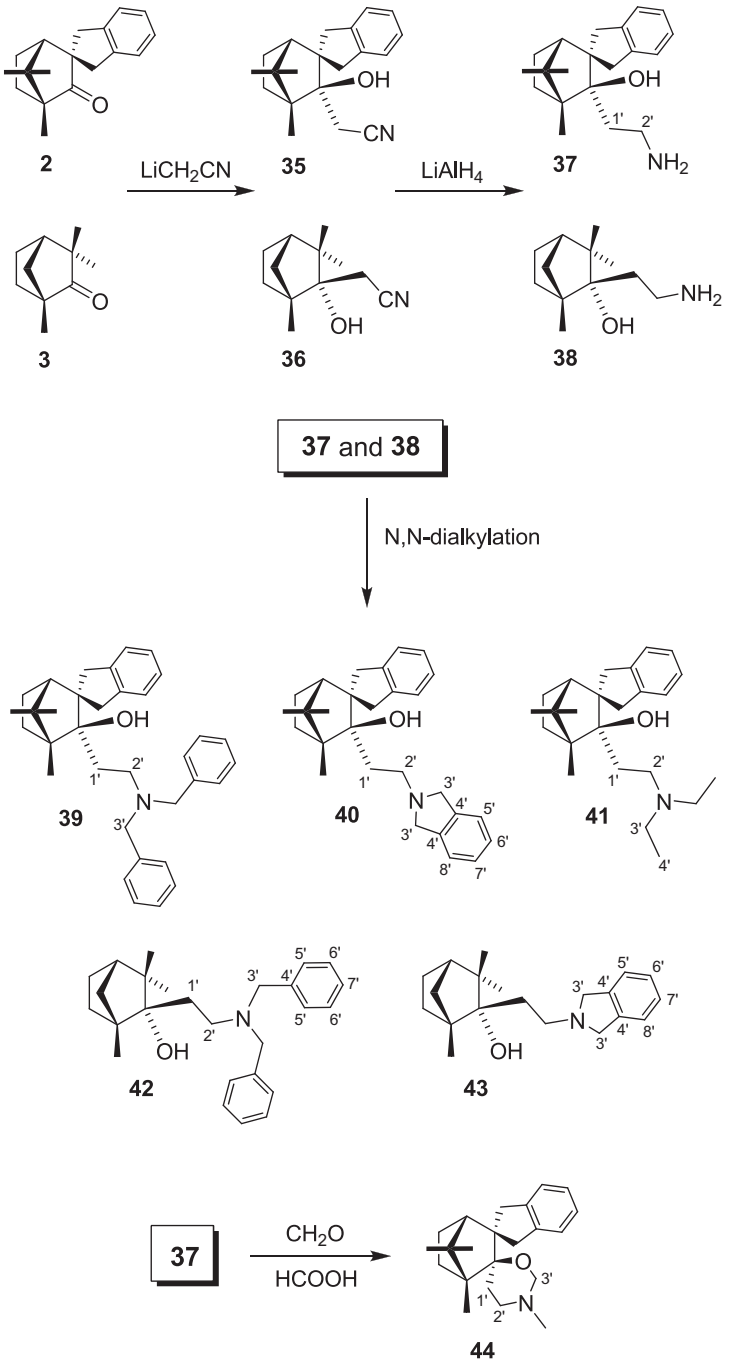
Suitable crystals of **18** for X-ray structural analysis were difficult to obtain. After several recrystallization attempts, crystals of **18** were grown by slow evaporation from CH_2Cl_2/DMSO solution (2/1.3 v/v) at room temperature. Compound **18** crystallizes in the non-centrosymmetric group $P2_12_12_1$ (SG 19) with one molecule per asymmetric unit (Table 1). An ORTEP view of a molecule of **18** is shown in Fig. 5b and selected bond distances and bond angles are given in Tables 2 and 3. The major structural features of **15** and **18** are comparable: similar bond lengths and angles, slightly distorted Cp–Fe–Cp coordination geometry (*rms* of 0.007 and 0.011 Å for C1/C2/C3/C4/C5 and C6/C7/C8/C9/C10 mean planes, respectively; the angle between the mean planes of the Cp rings is 4.0(6)°). Also in this case an intramolecular O1–H1···N1 (*D*···*A* distance of 2.822(3) Å) hydrogen bond is responsible for stabilizing the observed conformation. A weak intermolecular interaction of the O·····π type was also detected in **18** between O1 and the π-orbitals of the unsubstituted Cp ring (shortest O1·····C–Cp distance of 3.437 Å) (Fig. 6b). The absolute configuration of **18** has been determined independently as S_p, confirming the NMR analysis (see Fig. 4).

2.4. Enantioselective addition of Et_2Zn to benzaldehyde

The chiral aminoalcohols and analogues synthesized were tested as pre-catalysts (3 mol%) for the enantioselective addition of Et_2Zn to benzaldehyde (Table 4) by use of a standard procedure [28]. In all cases, the yields of the isolated 1-phenyl-1-propanol were excellent. However, the observed enantioselectivities were low to moderate, and in the case of **15**, **18** and **19** no asymmetric induction was realized. These latter results are surprising since 1,2-disubstituted ferrocene-based planar chiral aminoalcohols are very efficient pre-catalysts for enantioselective organo-zinc additions to aldehydes [1a]. The δ-aminoalcohols **8**–**11** afforded a similar degree of enantioselectivity as reported for their (+)-camphor derived analogues [3b]. Therefore the C-3 "fenchone-like" substitution realized within these compounds did not result in an enantioselectivity improvement. A comparison of the couples of compounds **16** and **20**, **17** and **21**, **39** and **42**, **40** and **43** leads to the conclusion that the position of the HO-group has a more significant influence on the enantioselectivity than the substituents in the 3- and 7-positions on the bicyclic skeleton – the *endo*-OH derivatives brought higher selectivity than the *exo*-one. The same trend was observed in the case of compound **41** and its fenchone derived analogue with a pyrrolidine group instead of an Et_2N-group – 26% ee for **41** and 79% ee for the *endo*-OH analogue (unpublished results; the synthesis was achieved by a different synthetic approach).

3. Conclusions

In conclusion, we have demonstrated a practicable application of functionalized organolithium reagents for the synthesis of chiral β-, γ- and δ-aminoalcohols and some analogues possessing the bicyclo-heptane skeleton as the central core. The use of cheap and readily available sources of chirality makes the presented synthetic strategies very advantageous. The series of compounds synthesized were isolated in the diastereoisomeric pure form and were characterized by spectroscopic methods. The configurations, in respect of



Scheme 5. Addition of cyanomethyl lithium to **2** and **3** and the consequent transformation into aminoalcohols **39**–**43**.

the newly induced chirality, within the compounds synthesized were determined by applying advanced NMR methods. In the case of the ferrocene-based derivatives, possessing a chirality plane, the configurations determined were proved by means of X-ray crystallography. The application of the compounds prepared as ligands for enantioselective addition of Et_2Zn to benzaldehyde brought in some cases an acceptable degree of enantioselectivity.

4. Experimental

4.1. Materials and instrumentation

The reactions with organolithiums were carried out in Schlenk flasks under an argon atmosphere. THF and Et_2O were distilled over Na/benzophenone. Hexane was distilled over Na[$AlEt_4$]. *N*,*N*-dimethylaminoethanol was dried over a molecular sieve (3 Å). Thin layer chromatography (TLC) was performed on aluminum sheets pre-coated with Merck Kieselgel 60 F_{254} 0.25 mm (Merck). Flash column chromatography was carried out using Silica Gel 60 230–400 mesh (Fluka). Melting temperatures 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. The NMR spectra were recorded at ambient temperature (300 K) on a Bruker Avance DRX-250 (250.13 MHz for ^1H and 62.90 MHz for ^{13}C) and Bruker Avance II + 600 (600.13 MHz for ^1H and 150.92 MHz and for ^{13}C NMR) spectrometers with TMS as internal standard for chemical shifts (δ, ppm). For the numbering of the C-atoms see

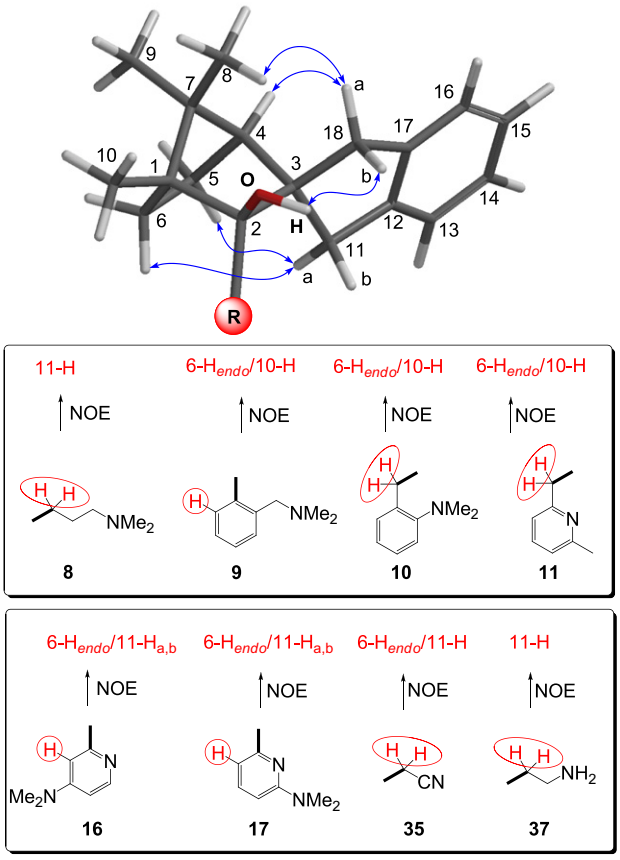


Fig. 1. Proton proximities of compounds **8**–**11**, **16**, **17**, **35** and **37**, obtained by means of NOESY spectra.

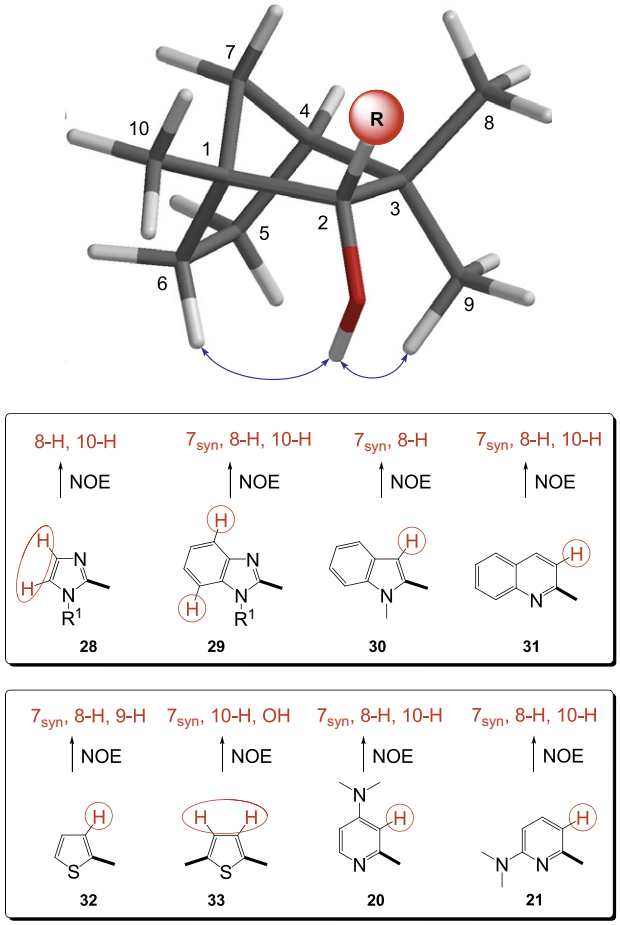


Fig. 2. Proton proximities of compounds **28**–**33**, **20** and **21**, obtained by means of NOESY spectra.

Schemes 2–5. ^{1}H and ^{13}C NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), integration, identification and coupling constants (Hz). The chemical shifts of the ambiguously assigned signals in NMR data are marked with an asterisk (Cp stands for cyclopentadienyl). Mass spectra (MS) were recorded on a Hewlett–Packard 5973A spectrometer at 70 eV EI and are reported as fragmentation in *m*/*z* with relative intensities (%) in parentheses. Enantiomeric excesses of 1-phenyl-1-propanol were determined by chiral GC using a Shimadzu 17-A chromatograph (chiral capillary column: Hydrodex-β-TBDAc, 25 m, 0.25 μm). Elemental analyses were performed by the Microanalytical service Laboratory of the Institute of Organic Chemistry, Bulgarian Academy of Science. X-ray crystallographic analysis: Crystals of (R_p)-**15** and (S_p)-**18** suitable for X-ray analyses were obtained after re-crystallization of the compounds. Subsequently a crystal of (R_p)-**15** or (S_p)-**18** was mounted on a glass capillary and all geometric and intensity data were taken from that crystal. Diffraction data were collected at room temperature by the ω-scan technique, on an Agilent Diffraction SuperNova Dual four-circle diffractometer equipped with an Atlas CCD detector using mirror-monochromatized Cu Kα (λ_{Cu} = 1.5418 Å) and Mo Kα (λ_{Mo} = 0.7107 Å) radiation from a micro-focus source. The determination of cell parameters, data integration, and scaling and absorption corrections were carried out using the CrysAlis Pro program package [29]. The structures were solved by direct methods [30] and refined by full-matrix least-square procedures on F2 [30]. The numbering of atoms in the X-ray structures (Figs. 5 and 6, Tables 2 and 3) is different from other numbering. The following starting materials were used (commercially available or prepared according to the literature): *n*-BuLi 1.6 and 2.5 M solutions in hexane (Aldrich), *t*-BuLi 1.7 M solution in pentane (Aldrich), (1*R*)-(+)-camphor (Fluka), (1*R*)-(−)-fenchone (Fluka), acetonitrile (Fluka), ethyliodide (Fluka), α,α′-dichloro-*o*-xylene (Aldrich), *N*,*N*-dimethylaminopropyl-lithium [9], benzylbromide (Fluka), *N*,*N*-dimethylbenzyl amine (Fluka),

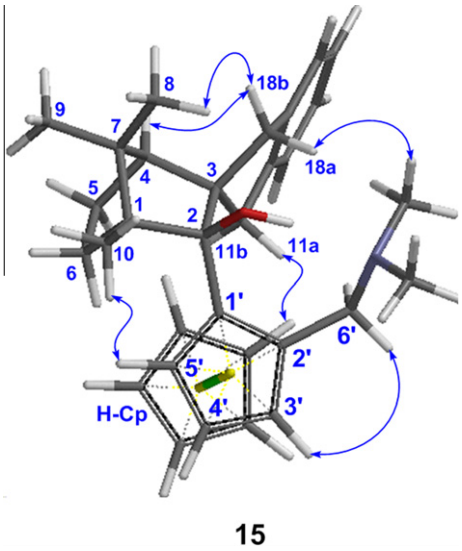


Fig. 3. Observed NOEs, allowing the determination of the absolute configuration of compound **15** (R_p) with respect to the chirality plane.

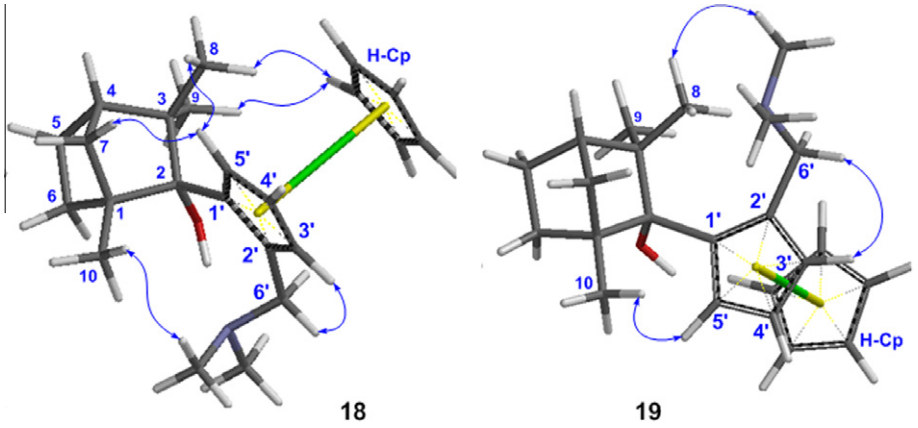


Fig. 4. Observed NOEs, allowing the determination of the absolute configuration of compounds **18** (S_p) and **19** (R_p) with respect to the chirality plane.

Table 1
Important crystallographic and refinement details for compounds **15** and **18**.

Compound	**15**	**18**
Chemical formula	$C_{31}H_{39}FeNO$	$C_{23}H_{33}FeNO$
MW	497.48	395.35
Crystal system, SG	orthorhombic, $P2_12_12_1$	orthorhombic, $P2_12_12_1$
a (Å)	10.1616(4)	8.7060(6)
b (Å)	11.1554(5)	12.8582(8)
c (Å)	23.0979(10)	18.3465(9)
V (Å^3)	2618.30(19)	2053.8(2)
Z	4	4
$F(000)$	1064	848
D_{calc} (Mg m^{-3})	1.262	1.279
Radiation/λ (Å)	Cu Kα/1.5418	Mo Kα/0.7107
μ (mm^{-1})	4.78	0.75
T (K)	290(2)	290(2)
Crystal habit, color	prism, yellow	prism, yellow
Crystal size (mm)	0.24 × 0.23 × 0.22	0.16 × 0.12 × 0.12
Diffractometer	SuperNova, Dual, Cu at zero, Atlas	SuperNova, Dual, Cu at zero, Atlas
Radiation source	SuperNova (Cu) X-ray Source	SuperNova (Mo) X-ray Source
Monochromator	mirror	mirror
Detector resolution,pixels (mm^{-1})	10.3974	10.3974
Measurement method	ω scans	ω scans
Measured reflections/reflections with $I > 2\sigma(I)$	9344/2775	9157/1914
R_{int}	0.066	0.184
$\theta_{min}/\theta_{max}$ (°)	3.8/71.6	3.2/28.2
Refinement	on F^2	on F^2
Least-squares matrix	full	full
$R[F^2 > 2\sigma(F^2)]$	0.078	0.088
$wR(F^2)$	0.185	0.248
S	1.07	1.02
Independent reflections	4561	4224
Parameters	313	236
Constraints	0	0
Primary atom site location	structure-invariant direct methods	structure-invariant direct methods
Secondary atom site location	difference Fourier map	difference Fourier map
Hydrogen site location	inferred from neighboring sites	inferred from neighboring sites
H-atom parameters	constrained	constrained
Weighing scheme w	$1/[\sigma^2(F_o^2) + (0.0549P)^2 + 3.6227P]$where $P = (F_o^2 + 2F_c^2)/3$	$1/[\sigma^2(F_o^2) + (0.1038P)^2]$where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$	0.001	0.001
$\Delta\rho_{min}/\Delta\rho_{max}$ (e Å^{-3})	−0.37/0.30	−0.55/0.7
Extinction correction	0.00171 (18)	none
Absolute structure	Flack H.D. [27]	Flack H.D. [27]
Flack parameter	−0.011 (10)	−0.09 (6)

N,*N*-dimethyl-*o*-toluidine (Aldrich), 2,6-dimethylpyridine (Aldrich), *N*,*N*-dimethylaminomethylferrocene (Alfa-Aeser), 2-dimethylaminopyridine (Fluka), 4-dimethylaminopyridine (Fluka), imidazole (Fluka), *N*-ethylimidazole (Merck), *N*-benzylimidazole (Aldrich), *N*-phenyl-imidazole (Alfa-Aesar), benzimidazole (Acros), *N*-methylindole (Aldrich), quinoline (Fluka), thiophene (Fluka), benzothiazole (Aldrich), *N*,*N*-dimethylaminoethanol (Fluka).

*4.2. (3R,4R)-3-(3-(dimethylamino)propyl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]-heptane-2,2′-inden]-3-ol (**8**)*

To a stirred solution of *N*,*N*-dimethylaminopropyl-lithium **4** (0.137 g, 1.47 mmol) in 10 ml hexane, ketone **2** (0.250 g, 0.98 mmol) was added at room temperature and the reaction mixture was stirred for 4 h (the reaction progress was monitored by

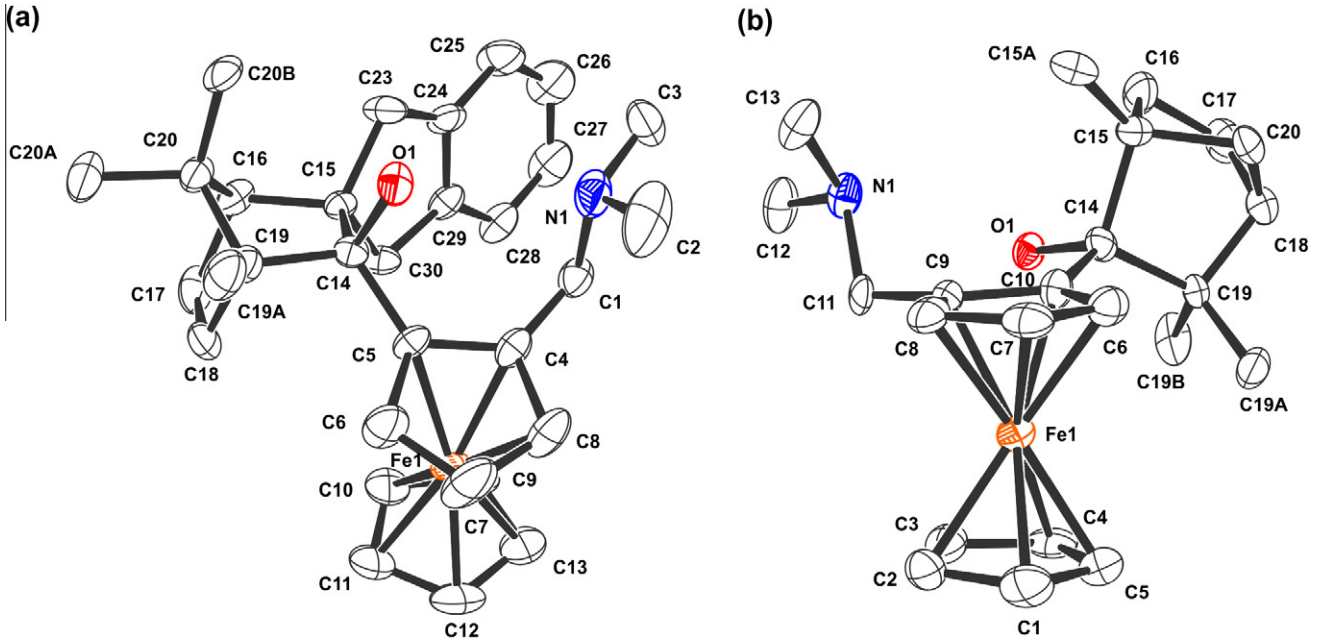


Fig. 5. ORTEP view of compounds (R_p)-**15** (a) and (S_p)-**18** (b) with the atomic numbering scheme; ellipsoids are drawn at 50% probability, hydrogen atoms have been omitted for clarity.

Table 2
Selected bond lengths for compounds **15** and **18**.

Compound **15**	Bond lengths (Å)	Compound **18**	Bond lengths(Å)
N1—C1	1.486(8)	N1—C11	1.464(13)
N1—C2	1.462(11)	N1—C12	1.471(14)
N1—C3	1.477(11)	N1—C13	1.467(13)
O1—C14	1.439(7)	C14—O1	1.442(10)
Fe1—C11	2.050(10)	Fe1—C1	2.052(10)
Fe1—C12	2.023(8)	Fe1—C2	2.057(10)
Fe1—C13	2.033(9)	Fe1—C3	2.043(10)
Fe1—C4	2.068(7)	Fe1—C4	2.047(9)
Fe1—C5	2.106(6)	Fe1—C5	2.007(10)
Fe1—C6	2.051(8)	Fe1—C6	2.031(10)
Fe1—C7	2.031(10)	Fe1—C7	2.032(10)
Fe1—C8	2.036(9)	Fe1—C8	2.018(10)
Fe1—C9	2.039(9)	Fe1—C9	2.025(9)
Fe1—C10	2.040(10)	Fe1—C10	2.073(10)
C18—C19	1.516(13)	C15—C14	1.627(8)
C19—C19A	1.521(14)	C15—C23	1.565(8)
C19—C19B	1.558(13)	C15—C30	1.564(8)
C14—C19	1.594(13)	C19—C14	1.548(8)
C15—C16	1.540(15)	C19—C18	1.566(9)
C15—C20	1.562(13)	C19—C19A	1.517(9)
C15—C14	1.603(14)	C19—C20	1.566(9)

TLC). The reaction was carefully quenched with 2 ml H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 20 mm, h = 280 mm, 20 g silica gel, Et_2O:Et_3N = 100:1), to give 0.270 g, (80%) of **8** as colorless crystals. Mp 93–94 °C. $[\alpha]_D^{20}$ = +33.0 (c 0.57, $CHCl_3$). *Anal.* Calc. for $C_{23}H_{35}NO$ (341.27): C, 80.88; H, 10.33; N, 4.10. Found: C, 80.60; H, 10.14; N, 4.11%. MS (EI) *m/z* (rel. int.): 341 (M^+., 100), 230 (37), 198 (35), 185 (16), 156 (35). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 7.13–7.04 (m, 4H, Ar), 4.00 (d, 1H, 18-H_a, J = 16.4 Hz), 3.14 and 3.02 (AB-system, 2H, 11-H, J = 16.4 Hz), 2.77 (d, 1H, 18-H_b, J = 16.4 Hz), 2.12–1.99 (m, 2H, 3′-H_a, 1′-H_a), 1.94 (s, 6H, $N(CH_3)_2$), 1.95–1.87 (m, 1H, 3′-H_b), 1.66–1.43 (m, 5H, 4-H, 2′-H, 6-H_{exo}, 1′-H_b), 1.35 (s, 3H, 8-H), 1.36–1.16 (m, 2H, 5-H_{exo}, 6-H_{endo}), 0.93–0.80 (m, 1H, 5-H_{endo}), 0.88 (s, 3H, 9-H), 0.85 (s, 3H, 10-H).^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 145.00 (s, 1 arom. C), 143.16 (s, 1 arom. C), 125.78 (d, 1 arom. C), 125.63 (d, 1 arom. C), 123.81 (d, 1 arom. C), 122.94 (d, 1 arom. C), 82.75 (s, C-2), 61.73 (t, C-3′), 60.43 (s, C-3), 59.04 (d, C-4), 50.09 (s, C-1), 48.78 (s, C-7), 45.17 (q, 2C, $N(CH_3)_2$), 43.29 (t, C-11), 42.99 (t, C-18), 35.23 (t, C-1′), 30.44 (t, C-6), 24.03 (t, C-2′), 23.28 (q, C-8), 23.06 (q, C-9), 22.33 (t, C-5), 12.00 (q, C-10).

*4.3. (3R,4R)-3-(2-((dimethylamino)methyl)phenyl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]-heptane-2,2′-inden]-3-ol (**9**)*

To a stirred solution of *N,N*-dimethylbenzylamine (0.390 g, 2.9 mmol) in hexane/Et_2O (5 ml/2 ml) 2.5 M *n*-BuLi in hexane (0.8 ml, 2.00 mmol) was added at room temperature and the solution was refluxed for 3 h. Then **2** (0.350 g, 1.40 mmol) was added at room temperature and the reaction mixture was stirred for 22 h (the reaction progress was monitored by TLC). The reaction was carefully quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 20 mm, h = 280 mm, 40 g silica gel, hexane:Et_2O = 4:1), to give 0.383 g, (64%) of **9** as colorless crystals. Mp 58–60 °C. $[\alpha]_D^{20}$ = 0 (c 0.62, $CHCl_3$). *Anal.* Calc. for $C_{27}H_{35}NO$ (389.57): C, 83.24; H, 9.06; N, 3.60. Found: C, 83.18; H, 9.07; N, 3.62%. MS (EI) *m/z* (rel. int.): 389 (M^+., 73), 344 (97), 246 (47), 233 (39), 163 (100). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 7.72 (d, 1H, 2′-H, J = 8.1 Hz), 7.30–7.69 (m, 7H, Ar), 4.01 (d, 1H, 18-H_a, J = 18.0 Hz), 3.53 (d, 1H, 7′-H, J = 12.3 Hz), 3.27 (d, 1H, 18-H_b, J = 18.0 Hz), 3.03 (d, 1H, 11-H_a, J = 18.2 Hz), 2.76 (d, 1H, 11-H_b, J = 18.2 Hz), 2.50 (d, 1H, 7′-H, J = 12.3 Hz), 2.51–2.36 (m, 1H, 6-H_{endo}), 1.97 (s, 6H, $N(CH_3)_2$), 1.69–1.57 (m, 4H, 4-H, 5-H, 6-H_{exo}), 1.54 (s, 3H, 8-H), 1.30 (s, 3H, 10-H), 1.01 (s, 3H, 9-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 144.79 (s, 1 arom. C), 143.86 (s, 1 arom. C), 142.19 (s, 1 arom. C), 137.42 (s, 1 arom. C), 134.13 (d, 1 arom. C), 130.87 (d, 1 arom. C), 126.59 (d, 1 arom. C), 126.16 (d, 1 arom. C), 126.09 (d, 1 arom. C), 125.70 (d, 1 arom. C), 124.47 (d, 1 arom. C), 123.83 (d, 1 arom. C), 90.93 (s, C-2), 63.84 (t, C-7′), 59.69 (s, C-3), 58.52 (d, C-4), 54.75 (s, C-1), 51.23 (s, C-7), 46.13 (t, C-18), 44.24 (q, 2C, $N(CH_3)_2$), 41.67 (t, C-11), 31.54 (t, C-6), 24.84 (q, C-9), 24.60 (q, C-8), 23.69 (t, C-5), 14.62 (q, C-10).

Table 3
Selected bond angles for compounds **15** and **18**.

Compound **15**	Bond angles (°)	Compound **18**	Bond angles (°)
C1–C2–C3	106.6(9)	C6–C5–C4	105.6(6)
C1–C5–C4	110.9(10)	C6–C7–C8	107.4(7)
C5–C4–C3	106.1(11)	C7–C6–C5	110.5(7)
C4–C3–C2	108.4(11)	C7–C8–C4	108.8(7)
C8–C7–C6	109.0(10)	C9–C10–C11	108.8(10)
C7–C8–C9	109.2(9)	C11–C12–C13	108.7(11)
C7–C6–C10	108.8(9)	O1–C14–C15	110.3(4)
C8–C9–C10	107.6(8)	O1–C14–C19	106.3(4)
O1–C14–C10	107.0(6)	O1–C14–C5	102.9(5)
O1–C14–C15	110.1(8)	C8–C4–C5	107.7(6)
O1–C14–C19	106.3(8)	O1–C14–C5	102.9(5)
C20–C15–C14	99.7(8)	C19–C14–C15	102.1(5)
C15A–C15–C14	114.5(8)	C19–C14–C15	102.1(5)
C15A–C15–C16	116.9(10)	C5–C14–C15	121.1(5)
C15A–C15–C20	116.9(9)	C5–C14–C19	113.4(5)
C16–C15–C14	106.6(9)	C29–C30–C15	107.1(5)
C16–C15–C20	99.9(8)	C29–C24–C23	111.9(6)
C19A–C19–C14	117.1(8)	C20B–C20–C20A	104.2(5)
C19A–C19–C19B	105.5(9)	C29–C24–C23	111.9(6)
C19B–C19–C14	112.5(7)	C16–C15–C23	110.5(5)
C18–C19–C19A	107.1(8)	C29–C30–C15	107.1(5)
C18–C19–C19B	111.6(9)	C24–C29–C30	110.1(6)
N1–C11–C9	112.5(8)	N1–C1–C4	110.4(6)
C11–N1–C12	111.0(8)	C2–N1–C1	111.4(7)
C11–N1–C13	109.1(8)	C2–N1–C3	110.8(8)
C13–N1–C12	110.1(9)	C3–N1–C1	109.4(6)
Compound **15**	Torsion angles (°)	Compound **18**	Torsion angles (°)
C1–C2–C3–C4	−0.4(12)	C1–C4–C5–C14	−14.0(10)
C2–C1–C5–C4	−1.8(13)	C1–C4–C5–C6	−172.5(7)
C2–C3–C4–C5	−0.6(12)	C1–C4–C8–C7	173.2(7)
C3–C4–C5–C1	1.5(12)	C4–C5–C6–C7	0.5(9)
C5–C1–C2–C3	1.3(13)	C4–C8–C7–C6	−0.9(11)
C6–C7–C8–C9	−0.3(12)	C10–C9–C13–C12	−0.2(10)
C11–C9–C10–C14	20.7(18)	C10–C11–C12–C13	−1.0(13)
C10–C6–C7–C8	1.8(12)	C11–C12–C13–C9	0.7(12)
C11–C9–C10–C6	−175.4(10)	C12–C11–C10–C9	0.9(11)
O1–C14–C15–C16	−41.7(10)	O1–C14–C5–C4	−55.0(7)
O1–C14–C15–C20	−145.2(8)	O1–C14–C5–C6	99.5(7)

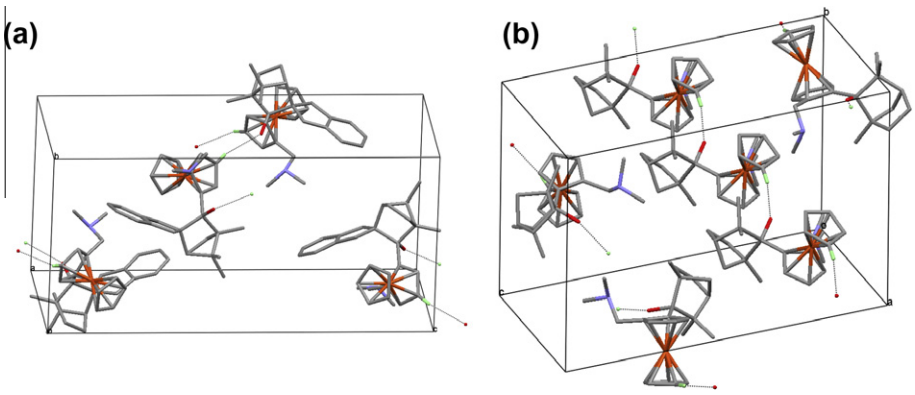


Fig. 6. Three-dimensional arrangement of the molecules in the crystal structures of compounds (R_p)-**15** (a) and (S_p)-**18** (b). The weak O···*Cp* (O···π type) interaction is shown as a dashed line. Hydrogen atoms not involved in interactions have been omitted for clarity.

*4.4. (3R,4R)-3-(2-(dimethylamino)benzyl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]heptane-2,2′-inden]-3-ol (**10**)*

To a stirred solution of *N*,*N*-dimethyl-*o*-toluidine (0.178 g, 1.32 mmol) in hexane/Et_2O (5 ml/0.3 ml), 2.5 M *n*-BuLi in hexane (0.44 ml, 1.10 mmol) was added at room temperature and the solution was refluxed for 72 h. Then **2** (0.280 g, 1.10 mmol) was added at room temperature and the reaction mixture was stirred for 6 h (the reaction progress was monitored by TLC). The reaction was carefully quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 17 mm, *h* = 380 mm, 20 g silica gel, hexane:CH_2Cl_2 = 10:1), to give 0.090 g, (22%) of **10** as an oil. $[\alpha]_D^{20}$ = +72.7 (c 1.08, $CHCl_3$). *Anal.* Calc. for $C_{27}H_{35}NO$ (389.57): C, 83.24; H, 9.06; N, 3.60. Found: C, 83.22; H, 9.08; N, 3.59%. MS (EI) *m/z* (rel. int.): 389 ($M^{+\cdot}$, 33), 278 (31), 246 (20), 204 (19), 164 (19), 135 (100). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.26 (s, OH), 7.22–7.19 (m, 2H, Ar), 7.14–7.12 (m, 2H, Ar), 7.00 (m, 4H, Ar), 4.00 (d, 1H, 18-H_a, *J* = 15.3 Hz), 3.30 (d, 1H, 11-H_b, *J* = 15.7 Hz),

Table 4
Enantioselective addition of Et_2Zn to benzaldehyde using the ligands synthesized.

Ligand	Yield[a] (%)	ee[b] (%)	Ligand	Yield[a] (%)	ee[b] (%)
8	99	58 (*S*)	**28d**	99	30 (*S*)
9	84	14 (*S*)	**29a**	97	50 (*S*)
10	96	58 (*S*)	**29b**	99	44 (*S*)
11	99	12 (*R*)	**29c**	97	52 (*S*)
15	55	2 (*R*)	**30**	92	18 (*R*)
16	96	6 (*S*)	**31**	96	34 (*S*)
17	84	11 (*R*)	**32**	59	4 (*R*)
18	93	0	**33**	85	16 (*R*)
19	91	4 (*S*)	**34**	92	46 (*S*)
20	97	46 (*S*)	**39**	92	10 (*S*)
21	99	42 (*R*)	**40**	99	3 (*R*)
28a	96	42 (*S*)	**41**	99	26 (*S*)
28b	88	26 (*S*)	**42**	96	60 (*R*)
28c	97	36 (*S*)	**43**	99	22 (*R*)

[a] Yields of the isolated compounds after column chromatography.
[b] Enantiomeric excess of the reaction product (1-phenyl-1-propanol) determined by GC (chiral capillary column Hydrodex-β-TBDAc).

3.17 (d, 1H, 1′-H_a, *J* = 14.4 Hz), 3.01 (d, 1H, 11-H_a, *J* = 15.7 Hz), 2.87 (d, 1H, 1′-H_b, *J* = 14.4 Hz), 2.76 (d, 1H, 18-H_b, *J* = 15.3 Hz), 2.23 (s, 6H, $N(CH_3)_2$), 1.93–1.88 (m, 1H, 6-H_{endo}), 1.68–1.62 (m, 3H, 4-H, 5-H), 1.45–1.40 (m, 1H, 6-H_{exo}), 1.29 (s, 3H, 8-H), 0.81 (s, 3H, 9-H), 0.36 (s, 3H, 10-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) *δ*: 152.14 (s, 1 arom. C), 145.99 (s, 1 arom. C), 143.14 (s, 1 arom. C), 135.93 (s, 1 arom. C), 133.07 (d, 1 arom. C), 127.30 (d, 1 arom. C), 125.77 (d, 1 arom. C), 125.55 (d, 1 arom. C), 124.79 (d, 1 arom. C), 123.55 (d, 1 arom. C), 122.78 (d, 1 arom. C), 120.04 (d, 1 arom. C), 84.30 (s, C-2), 63.28 (s, C-3), 56.28 (d, C-4), 54.57 (s, C-1), 49.13 (s, C-7), 43.82 (q, 2C, $N(CH_3)_2$), 43.00 (t, C-11), 42.92 (t, C-18), 39.36 (t, C-1′), 31.03 (t, C-6), 24.57 (t, C-5), 23.19 (q, C-8), 23.12 (q, C-9), 11.98 (q, C-10).

*4.5. (3R,4R)-4,7,7-trimethyl-3-((6-methylpyridin-2-yl)methyl)-1′,3′-dihydrospiro[bicyclo[2.2.1]-heptane-2,2′-inden]-3-ol (**11**)*

To a stirred solution of 2,6-dimethylpyridine (0.192 g, 1.79 mmol) in 10 ml THF, 2.5 M *n*-BuLi in hexane (0.72 ml, 1.79 mmol) was added at −60 °C and the solution was stirred for 1 h. Then **2** (0.350 g 1.40 mmol) was added and the reaction mixture was stirred for 1.5 h at −60 °C (the reaction progress was monitored by TLC). The reaction was carefully quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (*Φ* = 17 mm, *h* = 380 mm, 25 g silica gel, hexane/EtOAc = 250:1), to give 0.375 g, (75%) of **11** as colorless crystals. Mp 118–119 °C. $[\alpha]_D^{20}$ = +60.9 (c 1.02, $CHCl_3$). *Anal.* Calc. for $C_{25}H_{31}NO$ (361.24): C, 83.06; H, 8.64; N, 3.87. Found: C, 83.04; H, 8.65; N, 3.73%. MS (EI) *m/z* (rel. int.): 361 (M^+., 100), 250 (48), 245 (17), 218(40), 176 (43), 163 (30), 107 (89). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) *δ*: 7.98 (brs, OH), 7.31 (m, 1H, Ar), 7.05 (d, 1H, Ar, *J* = 7.3 Hz), 6.91 (m, 2H, Ar), 6.74 (t, 1H, Ar, *J* = 7.3 Hz), 6.65 (d, 1H, Ar, *J* = 7.7 Hz), 6.57 (d, 1H, Ar, *J* = 7.3 Hz), 4.03 (d, 1H, 18-H_a, *J* = 16.4 Hz), 3.11 (d, 1H, 1′-H_a, *J* = 15.3 Hz), 3.05 (d, 1H, 11-H_b, *J* = 16.4 Hz), 3.01 (d, 1H, 1′-H_b, *J* = 15.3 Hz), 2. 92 (d, 1H, 11-H_a, *J* = 16.4 Hz), 2.77 (d, 1H, 18_b-H, *J* = 16.4 Hz), 2.09 (s, 3H, 7′-H), 1.69–168 (m, 1H, 4-H), 1.67–1.56 (m, 3H, 5-H, 6-H_{exo}), 1.39–1.35 (m, 1H, 6-H_{endo}), 1.40 (s, 3H, 8-H), 0.89 (s, 3H, 9-H), 0.70 (s, 3H, 10-H).^{13}C NMR (600 MHz, $CDCl_3$, 300 K) *δ*: 159.78 (s, 1 arom. C), 155.89 (s, 1 arom. C), 144.56 (s, 1 arom. C), 142.09 (s, 1 arom. C), 136.67 (d, 1 arom. C), 125.36 (d, 1 arom. C), 125.04 (d, 1 arom. C), 123.11 (d, 1 arom. C), 122.66 (d, 1 arom. C), 121.59 (d, 1 arom. C), 120.58 (d, 1 arom. C), 85.30 (s, C-2), 60.88 (s, C-3), 58.58 (d, C-4), 55.19 (s, C-1), 48.78 (s, C-7), 43.46 (t, C-11), 43.15 (t, C-18), 39.92 (t, C-1′), 30.36 (t, C-6), 241 (t, C-5), 23.79 (q, C-7′), 23.07 (q, C-8), 23.04 (q, C-9), 12.20 (q, C-10).

*4.6. (3R,4R,pS)-3-(2-(N,N-dimethylaminomethyl)ferrocen-yl)-4,7,7-trimethyl-1′,3′-dihydrospiro-[bicyclo[2.2.1]heptane-2,2′-inden]-3-ol (**15**)*

To a stirred solution of *N*,*N*-dimethylaminomethylferrocene (0.46 g, 1.89 mmol) in 10 ml hexane, 2.5 M *n*-BuLi in hexane (0.76 ml, 1.89 mmol) was added at room temperature and the solution was stirred for 24 h. Then **2** (0.40 g, 1.57 mmol) was added at room temperature and the reaction mixture was stirred for 24 h (the reaction progress was monitored by TLC). The reaction was carefully quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product (0.964 g) was purified by column chromatography (*Φ* = 17 mm, *h* = 380 mm, 30 g silica gel, CH_2Cl_2/CH_3OH = 50:1), to give 0.225 g, (30%) of **15** as colorless crystals and 0.277 g (60%) of the starting *N*,*N*-dimethylaminomethylferrocene.

Data of 15: Mp 83–85 °C. $[\alpha]_D^{20}$ = −90.6 (c 0.60, $CHCl_3$). *Anal.* Calc. for $C_{31}H_{39}FeNO$ (497.49): C, 74.84; H, 7.90; Fe, 11.23; N, 2.82. Found: C, 74.58; H, 7.84; Fe, 11.53; N, 2.93%. MS (EI) *m/z* (rel. int.): 497 (M^+., 27), 452 (100), 386 (27), 308 (19), 188 (19). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) *δ*: 7.23–7.19 (m, 2H, arom.), 7.17–7.12 (m, 2H, arom.), 5.27 (br s, 1H, 11-H_b), 4.21 (s, 1H, 4′-H,), 4.14 (s, 6H, 5′-H, 5H-Cp), 4.00 (s, 1H, 3′-H), 3.86 (d, 1H, 18-H_b, *J* = 17.6 Hz), 3.36 (d, 1H, 11-H_a, *J* = 17.6 Hz), 3.37–3.34 (m, 1H, 6′-H_a), 3.16 (d, 1H, 18-H_a, *J* = 17.6 Hz), 2.44 (br s, 1H, 6-H_{endo}), 2.35 (d, 1H, 6′-H_b, *J* = 12.5 Hz), 1.91 (s, 6H, $N(CH_3)_2$), 1.86–1.82 (m, 1H, 5-H_{endo}), 1.66–1.61 (m, 2H, 4-H, 5-H_{exo}), 1.40 (s, 3H, 8-H), 1.37–1.33 (m, 1H, 6-H_{exo}), 0.94 (s, 3H, 10-H), 0.93 (s, 3H, 9-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) *δ*: 143.37 (s, 1 arom. C), 142.93 (s, 1 arom. C), 125.96 (d, 1 arom. C), 125.86 (d, 1 arom. C), 124.19 (d, 1 arom. C), 123.47 (d, 1 arom. C), 95.18 (s, C-1′), 87.20 (s, C-2′), 81.22 (s, C-2), 71.18 (d, C-5′), 71.08 (d, C-3′), 70.06 (d, Cp5), 65.68 (d, C-4′), 59.78 (s, C-3), 56.76 (d, C-4), 55.68 (s, C-1), 50.06 (s, C-7), 44.57 (q, 2C, $N(CH_3)_2$), 44.27 (t, C-18), 42.76 (t, C-11), 30.46 (t, C-6), 24.42 (q, C-9), 24.05 (t, C-5), 23.93 (q, C-8), 13.50 (q, C-10).

*4.7. (3R,4R)-3-(4-(dimethylamino)pyridin-2-yl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]-heptane-2,2′-inden]-3-ol (**16**)*

To a stirred solution of *N*,*N*-dimethylaminoethanol (0.250 g, 2.80 mmol) in 8 ml hexane 2.5 M *n*-BuLi in hexane (2.24 ml, 5.60 mmol) was added at −10 °C and the solution was stirred for 0.5 h. Then 4-dimethylaminopyridine (0.173 g, 1.18 mmol) was added. The mixture was stirred for 1 h at −5 °C, **2** (0.300 g, 1.18 mmol) was added at −40 °C and the reaction was stirred for 4 h (the reaction progress was monitored by TLC). The reaction was carefully quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (*Φ* = 17 mm, *h* = 380 mm, 20 g silica gel, Et_2O:hexane = 3:1), to give 0.090 g, (20%) of **16** as colorless crystals. Mp 139–140 °C. $[\alpha]_D^{20}$ = −87.9 (c 0.59, $CHCl_3$). *Anal.* Calc. for $C_{25}H_{32}N_2O$ (376.53): C, 79.75; H, 8.57; N, 7.44. Found: C, 79.80; H, 8.53; N, 7.50%. MS (EI) *m/z* (rel. int.): 376 (M^+., 79), 267 (100), 233 (16), 191 (29), 152 (17), 122 (96). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) *δ*: 8.07 (d, 1H, 5′-H, *J* = 6.0 Hz), 7.15 (d, 1H, Ar, *J* = 6.9 Hz), 7.02 (m, 3H, Ar), 6.57 (d, 1H, 2′-H, *J* = 2.4 Hz), 6.40 (dd, 1H, 4′-H, *J* = 6.0, 2.4 Hz), 3.77 (d, 1H, 18-H_b), *J* = 16.5 Hz), 3.19 (dd, 2H, 18-H_a, 11-H_a, *J* = 16.5, 15.7 Hz), 3.00 (s, 6H, $N(CH_3)_2$), 2.83 (d, 1H, 11-H_b, *J* = 15.7 Hz), 2.19–2.08 (m, 1H, 6-H_{endo}), 1.79–1.63 (m, 3H, 4-H, 5-H), 1.56 (s, 3H, 8-H), 1.46–1.36 (m, 1H, 6-H_{exo}), 0.96 (s, 3H, 9-H), 0.73 (s, 3H, 10-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) *δ*: 160.64 (s, 1 arom. C), 153.41 (s, 1 arom. C), 145.92 (d, 1 arom. C), 143.86 (s, 1 arom. C), 142.46 (s, 1 arom. C), 125.73 (d, 1 arom. C),

125.39 (d, 1 arom. C), 123.71 (d, 1 arom. C), 122.97 (d, 1 arom. C), 108.03 (d, 1 arom. C), 105.40 (d, 1 arom. C), 86.91 (s, C-2), 62.05 (s, C-3), 54.95 (s, C-1), 53.74 (d, C-4), 50.32 (s, C-7), 42.88 (t, C-18), 42.79 (t, C-11), 39.24 (q, 2C, $N(CH_3)_2$), 30.24 (t, C-6), 24.09 (q, C-8), 24.01 (s, C-9), 23.37 (t, C-5), 11.59 (q, C-10).

4.8. (3R,4R)-3-(6-(dimethylamino)pyridin-2-yl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]-heptane-2,2′-inden]-3-ol (**17**)

To a stirred solution of dry *N*,*N*-dimethylaminoethanol (0.316 g, 3.54 mmol) in 2 ml hexane 2.5 M *n*-BuLi in hexane (2.84 ml, 7.08 mmol) was added at −10 °C and the solution was stirred for 0.5 h. Then 2-dimethylaminopyridine (0.220 g, 1.18 mmol) was added. The mixture was stirred for 1 h at −5 °C and ketone **2** (0.300 g, 1.18 mmol) was added at −40 °C. The reaction mixture was stirred for 20 h (the reaction progress was monitored by TLC). The reaction was carefully quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 17 mm, *h* = 380 mm, 20 g silica gel, hexane:Et_2O = 50:1), to give 0.180 g, (40%) of **17** as colorless crystals. Mp 75–77 °C. $[\alpha]_D^{20}$ = +89.3 (c 0.27, $CHCl_3$). *Anal.* Calc. for $C_{25}H_{32}N_2O$ (376.53): C, 79.75; H, 8.57; N, 7.44. Found: C, 79.83; H, 8.55; N, 7.49%. MS (EI) *m/z* (rel. int.): 376 (M^+., 76), 348 (95), 267 (51), 237 (50), 205 (60), 192 (43), 122 (100). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 7.45 (t, 1H, 3′-H, *J* = 8.0 Hz), 7.15 (d, 1H, 16-H, *J* = 7.0 Hz), 7.06 (dd, 1H, 15-H, *J* = 7.2, 7.3 Hz), 7.00 (t, 1H, 14-H, *J* = 7.2 Hz), 6.97 (d, 1H, 13-H, *J* = 7.2 Hz), 6.74 (d, 1H, 2′-H, *J* = 7.6 Hz), 6.60 (s, 1H, OH), 6.37 (d, 1H, 4′-H, *J* = 8.4 Hz), 3.77 (d, 1H, 18-H_b, *J* = 16.3 Hz), 3.22 (d, 1H, 11-H_a, *J* = 15.7 Hz), 3.18 (d, 1H, 18-H_a, *J* = 16.3 Hz), 2.95 (s, 6H, $N(CH_3)_2$), 2.83 (d, 1H, 11-H_b, *J* = 15.7 Hz), 2.05–2.01 (m, 1H, 6-H_{endo}), 1.80–1.75 (m, 1H, 5-H_{endo}), 1.73–1.72 (m, 1H, 4-H), 1.70–1.65 (m, 1H, 5-H_{exo}), 1.57 (s, 3H, 8-H), 1.42–1.37 (m, 1H, 6-H_{exo}), 0.98 (s, 3H, 9-H), 0.76 (s, 3H, 10-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 158.54 (s, 1 arom. C), 156.54 (s, 1 arom. C), 143.79 (s, 1 arom. C), 142.62 (s, 1 arom. C), 136.21 (d, 1 arom. C), 125.62 (d, 1 arom. C), 125.34 (d, 1 arom. C), 123.60 (d, 1 arom. C), 112.96 (d, 1 arom. C), 112.62 (d, 1 arom. C), 103.60 (d, 1 arom. C), 87.03 (s, C-2), 62.06 (s, C-3), 54.81 (s, C-1), 53.94 (d, C-4), 50.40 (s, C-7), 43.04 (t, C-18), 42.62 (t, C-11), 37.94 (q, 2C, $N(CH_3)_2$), 30.11 (t, C-6), 24.01 (q, C-8), 23.97 (q, C-9), 23.34 (t, C-5), 11.61 (q, C-10).

4.9. (1R,2R,pR)-2-(2-((dimethylamino)methyl)ferrocenyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (18) and (1R,2R,pS)-2-(2-((dimethylamino)methyl)ferrocenyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**19**)

To 0.60 g (2.47 mmol) *N*,*N*-dimethylaminomethylferrocene were added at room temperature 2.50 ml (3.00 mmol) 1.2 M solution of *n*-BuLi in hexane. After stirring for 24 h at room temperature the resulting solution was cooled to 0 °C and 0.45 ml (2.85 mmol) (−)-fenchone (**3**) was added dropwise. The reaction was monitored by TLC (hexane:Et_2O:Et_3N = 80:40:1). After stirring for 18 h at room temperature, the reaction was quenched with 5% aqueous H_3PO_4 (pH 4) and the resulting mixture was washed with Et_2O. The aqueous phase was treated immediately with excess of solid K_2CO_3 (pH 10) and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 23 mm, *h* = 580 mm, 100 g silica gel, hexane:Et_2O:E_3N = 300:100:1) to give 0.23 g (26%) **18** as an orange solid and 0.46 g (52%) **19** as an orange solid. Overall yield 78%.

Data of 18: Mp 122–124 °C. $[\alpha]_D^{20}$ = −43.9 (c 1.02, $CHCl_3$). *Anal.* Calc. for $C_{23}H_{33}FeNO$ (395.19): C, 69.87; H, 8.41; Fe, 14.13; N, 3.54. Found: C, 69.92; H, 8.47; Fe, 14.17; N, 3.60%. MS (EI) *m/z* (rel. int.): 395 (M^+., 5), 350 (100), 227 (19), 199 (21), 121 (14). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 5.42 (s, 1H, OH), 4.11–4.16 (m, 2H, 15-H, 16-H_a), 4.09 (s, 5H, 5H-Cp), 4.01 (dd, 1H, 14-H, *J* = 2.3, 1.6 Hz), 3.87 (dd, 1H, 13-H, *J* = 2.3, 1.6 Hz), 2.49 (d, 1H, 16-H_b, *J* = 12.2 Hz), 2.17 (s, 6H, $N(CH_3)_2$), 2.03 (m, 1H, 6-H_{endo}), 1.71–1.88 (m, 2H, 7-H_{syn}, 5-H_{endo}), 1.62–1.66 (m, 1H, 4-H), 1.58 (s, 3H, 8-H), 1.37 (m, 1H, 5-H_{exo}), 1.21 (s, 3H, 9-H), 0.95–1.03 (m, 1H, 6-H_{exo}), 0.85–1.00 (m, 1H, 7-H_{anti}), 0.34 (s, 3H, 10-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 96.47 (s, 1C, 2-C), 83.15* (s, 1C, 12-C), 79.81* (s, 1C, 11-C), 70.94 (d, 1C, 14-C), 70.78 (d, 1C, 15-C), 70.02 (d, 5C, Cp5), 66.37 (d, 1C, 13-C), 61.70 (t, 1C, 16-C), 57.37 (s, 1C, 1-C), 49.89 (d, 1C, 4-C), 47.16 (s, 1C, 3-C), 44.87 (q, 2C, $N(CH_3)_2$), 41.78 (t, 1C, 7-C), 32.15 (t, 1C, 6-C), 28.52 (q, 1C, 8-C), 24.27 (t, 1C, 5-C), 23.34 (q, 1C, 9-C), 18.03 (q, 1C, 10-C).

Data of 19: Mp 83–85 °C. $[\alpha]_D^{20}$ = −25.0 (c 1.00, $CHCl_3$). *Anal.* Calc. for $C_{23}H_{33}FeNO$ (395.19): C, 69.87; H, 8.41; Fe, 14.13; N, 3.54. Found: C, 69.84; H, 8.40; Fe, 14.14; N, 3.59%. MS (EI) *m/z* (rel. int.): 395 (M^+., 10), 350 (100), 227 (28), 199 (27), 121 (18). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 4.18 (d, 2H, 13-H, 14-H), 4.11 (s, 5H, 5H-Cp), 4.03 (t, 1H, 15-H, *J* = 2.1 Hz), 3.59 (d, 1H, 16-H_a, *J* = 13.8 Hz), 3.11 (d, 1H, 16-H_b, *J* = 13.8 Hz), 2.30–2.45 (m, 1H, 6-H_{endo}), 2.29 (s, 6H, $N(CH_3)_2$), 1.94 (dq, 1H, 7-H_{syn}, *J* = 10.2, 2.5 Hz), 1.72 (m, 1H, 5-H_{endo}), 1.58 (s, 3H, 10-H), 1.55–1.58 (m, 1H, 4-H), 1.35 (tdd, 1H, 5-H_{exo}, *J* = 12.2, 5.3, 4.1 Hz), 1.00–1.14 (m, 1H, 7-H_{anti}), 1.00–1.13 (m, 1H, 6-H_{exo}), 1.00 (s, 3H, 9-H), 0.41 (s, 3H, 8-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 95.25 (s, 1C, C-2), 81.91* (s, 1C, 11-C), 81.87* (s, 1C, 12-C), 71.06 (d, 1C, 15-C), 69.87 (d, 5C, Cp5), 69.52* (d, 1C, 13-C), 65.53* (d, 1C, 14-C), 60.15 (t, 1C, 16-C), 53.49 (s, 1C, 1-C), 50.37 (d, 1C, 4-C), 45.87 (q, 2C, $N(CH_3)_2$), 45.87 (s, 1C, 3-C), 41.35 (t, 1C, 7-C), 32.17 (t, 1C, 6-C), 28.68 (q, 1C, 8-C), 25.25 (t, 1C, 5-C), 22.39 (q, 1C, 9-C), 20.49 (q, 1C, 10-C).

4.10. (1R,2R)-2-(4-(dimethylamino)pyridin-2-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**20**)

To a solution of 1.79 ml (17.80 mmol) *N*,*N*-dimethylaminoethanol in 20 ml hexane was added dropwise at −5 °C 12.61 ml (31.50 mmol) 2.5 M solution of *n*-BuLi in hexane. After stirring for 30 min at 0 °C was added 0.96 g (7.88 mmol) 4-dimethylaminopyridine, and the resulting mixture was stirred for an additional 1 h. The mixture was cooled to −40 °C and 1.00 g (6.57 mmol) (−)-fenchone (**3**) was added. The reaction was monitored by TLC (hexane:Et_2O:Et_3N = 30:30:1). The resulting orange mixture was stirred and allowed to warm to −20 °C for 2.5 h. The reaction was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 70 g silica gel, (a) hexane:Et_2O = 2:1, (b) Et_2O to give 0.39 g (22%) of **20** as white crystals. Mp 140–141 °C. $[\alpha]_D^{20}$ = +15.1 (c 0.36, $CHCl_3$). *Anal.* Calc. for $C_{17}H_{26}N_2O$ (274.40): C, 74.41; H, 9.55; N, 10.21. Found: C, 74.46; H, 9.59; N, 10.18%. MS (EI) *m/z* (rel. int.): 274 (M^+., 33), 246 (43), 205 (92), 193 (97), 191 (41), 177 (49), 163 (22), 136 (32), 122 (100). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 8.10 (d, 1H, 5`-H, *J* = 5.9 Hz), 6.70 (d, 1H, 2`-H, *J* = 2.4 Hz), 6.39 (dd, 1H, 4`-H, *J* = 5.9, 2.4 Hz), 6.10 (br s, 1H, OH), 3.02 (s, 6H, 6`-H), 2.35 (m, 1H, 6-H_{endo}), 2.22 (br d, 1H, 7-H_{syn}, *J* = 10.3 Hz), 1.85 (m, 1H, 5-H_{endo}), 1.77 (m, 1H, 4-H), 1.47 (dddd, 1H, 5-H_{exo}, *J* = 12.4, 12.4, 4.6, 4.6 Hz), 1.34 (dd, 1H, 7-H_{anti}, *J* = 10.3, 1.5 Hz), 1.12 (dt, 1H, 6-H_{exo}, *J* = 12.5, 4.6 Hz), 1.05 (s, 3H, 10-H), 0.99 (s, 3H, 9-H), 0.52 (s, 3H, 8-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 153.75 (s, 1C, 1`-C), 146.48 (d, 1C, 5`-C), 105.83 (d, 1C, 2`-C), 105.10 (s, 1C, 3`-C), 105.10 (d, 1C, 4`-C), 83.44 (s, 1C, 2-C), 51.63 (s, 1C, 1-C), 48.92 (d, 1C, 4-C), 45.67 (s, 1C, 3-C), 42.20 (t, 1C, 7-C), 39.30 (q, 2C, 6`-C), 32.74 (t, 1C, 6-C), 29.35 (q, 1C, 8-C), 24.45 (t, 1C, 5-C), 22.33 (q, 1C, 9-C), 17.56 (q, 1C, 10-C).

4.11. (1R,2R)-2-(6-(dimethylamino)pyridin-2-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**21**)

To a solution of 1.60 ml (15.76 mmol) dry *N*,*N*-dimethylaminoethanol in 10 ml hexane was added dropwise at −5 °C 12.60 ml (31.52 mmol) 2.5 M solution of *n*-BuLi in hexane. After stirring for 30 min at 0 °C 0.96 g (7.88 mmol) 2-dimethylaminopyridine was added, and the resulting mixture was stirred at 0 °C for 1.5 h. The formed dark red solution was cooled to −30 °C and 1.00 g (6.57 mmol) (−)-fenchone (**3**) was added. The reaction was monitored by TLC (hexane:Et_2O = 20:1) and stirred for 4 h at −30 °C. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, (a) hexane:CH_2Cl_2 = 40:1, (b) hexane:Et_2O = 40:1) to give 0.43 g (24%) of **21** as a white solid. Mp 49–50 °C. $[\alpha]_D^{20}$ = −85.9 (c 0.77, $CHCl_3$). *Anal.* Calc. for $C_{17}H_{26}N_2O$ (274.40): C, 74.41; H, 9.55; N, 10.21%. Found: C, 74.40; H, 9.52; N, 10.24%. MS (EI) *m/z* (rel. int.): 274 (M^+**.**, 9), 246 (29), 205 (21), 193 (25), 177 (100), 164 (20), 150 (14), 136 (30). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.42 (m, 1H, 3`-H), 6.74 (d, 1H, 2`-H, *J* = 7.5 Hz), 6.34 (d, 1H, 4`-H, *J* = 8.2 Hz), 6.12 (br s, 1H, OH), 3.06 (br s, 6H, 6`-H), 2.25–2.34 (m, 1H, 6-H_{endo}), 2.15–2.25 (m, 1H, 7-H_{syn}), 1.84 (m, 1H, 5-H_{endo}), 1.76 (m, 1H, 4-H), 1.46 (dddd, 1H, 5-H_{exo}, *J* = 12.5, 12.5, 4.6, 4.6 Hz), 1.29 (dd, 1H, 7-H_{anti}, *J* = 10.4, 1.0 Hz), 1.13 (dt, 1H, 6-H_{exo}, *J* = 12.5, 4.6 Hz), 1.03 (s, 3H, 10-H), 0.98 (s, 3H, 9-H), 0.51 (s, 3H, 8-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 156.80* (s, 1C, 1`-C), 156.80* (s, 1C, 5`-C), 136.58 (d, 1C, 3`-C), 110.84 (d, 1C, 2`-C), 103.03 (d, 1C, 4`-C), 83.49 (s, 1C, 2-C), 51.56 (s, 1C, 1-C), 48.87 (d, 1C, 4-C), 45.71 (s, 1C, 3-C), 41.84 (t, 1C, 7-C), 38.01 (q, 1C, 6`-C), 32.63 (t, 1C, 6-C), 29.00 (q, 1C, 8-C), 24.46 (t, 1C, 5-C), 22.42 (q, 1C, 9-C), 17.28 (q, 1C, 10-C).

4.12. (1R,2R)-2-(1-ethyl-1H-imidazol-2-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**28a**)

To a solution of 0.76 g (7.88 mmol) *N*-ethylimidazole in 15 ml hexane and 15 ml THF was added at −80 °C 3.45 ml (8.70 mmol) 2.5 M solution of *n*-BuLi in hexane, and the resulting mixture was stirred for 2 h at −65 °C. To the formed yellow solution was added 1.00 g (6.57 mmol) (−)-fenchone (**3**) and the mixture was stirred at −50 °C. The reaction was monitored by TLC (hexane:Et_2O = 1:1) and after 1.5 h was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 24 mm, *h* = 520 mm, 70 g silica gel, hexane:Et_2O = 1:1) to give 1.58 g (97%) **28a** as white crystals. Mp 133–134 °C. $[\alpha]_D^{20}$ = −56.0 (c 0.88, $CHCl_3$). *Anal.* Calc. for $C_{15}H_{24}N_2O$ (248.36): C, 72.54; H, 9.74; N, 11.28. Found: C, 72.45; H, 9.70; N, 11.29%. MS (EI) *m/z* (rel. int.): 248 (M^+**.**, 59), 233 (51), 219 (33), 205 (25), 191 (28), 177 (27), 167 (100), 151 (31), 137 (17), 123 (30), 110 (19). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 6.91 (d, 1H, 3`-H, *J* = 1.2 Hz), 6.78 (d, 1H, 2`-H, *J* = 1.2 Hz), 4.42 (dq, 1H, 4`-$H_a$, *J* = 14.4, 7.1 Hz), 3.95 (dq, 1H, 4`-H_b, *J* = 14.4, 7.1 Hz), 2.81 (dq, 1H, 7-H_{syn}, *J* = 10.3, 4.4, 2.5 Hz), 1.86 (s, 1H, OH), 1.84–1.97 (m, 1H, 6-H_{endo}), 1.63–1.75 (m, 1H, 5-H_{endo}), 1.68–1.74 (m, 1H, 4-H), 1.38 (t, 3H, 5`-H, *J* = 7.1 Hz), 1.36–1.50 (m, 1H, 5-$H_{exo}$), 1.33 (s, 3H, 10-H), 1.27 (dd, 1H, 7-$H_{anti}$, *J* = 10.3, 1.5 Hz), 1.18 (dt, 1H, 6-$H_{exo}$, *J* = 12.7, 3.7 Hz), 1.08 (s, 3H, 9-H), 0.49 (s, 3H, 8-H). $^{13}$C NMR (250 MHz, $CDCl_3$, 300 K) $\delta$: 149.52 (s, 1C, 1`-C), 125.76 (d, 1C, 3`-C), 118.75 (d, 1C, 2`-C), 84.01 (s, 1C, 2-C), 54.27 (s, 1C, 1-C), 49.52 (d, 1C, 4-C), 45.74 (s, 1C, 3-C), 42.64 (t, 1C, 4`-C), 40.62 (t, 1C, 7-C), 30.93 (t, 1C, 6-C), 27.49 (q, 1C, 8-C), 25.15 (t, 1C, 5-C), 22.60 (q, 1C, 9-C), 17.58 (q, 1C, 10-C), 17.10 (q, 1C, 5`-C).

4.13. (1R,2R)-2-(1-isopropyl-1H-imidazol-2-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**28b**)

To a solution of 0.87 g (7.88 mmol) *N*-isopropylimidazole in 15 ml hexane and 15 ml THF was added at −80 °C 3.45 ml (8.70 mmol) 2.5 M solution of *n*-BuLi in hexane, and the resulting mixture was stirred for 2 h at −65 °C. To the formed yellow solution was added 1.00 g (6.57 mmol) (−)-fenchone (**3**) and the mixture was stirred at −50 °C. The reaction was monitored by TLC (hexane:Et_2O = 1:1) and after 2 h was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, hexane:Et_2O = 2:1) to give 1.49 g (86%) **28b** as white crystals. Mp 102–103 °C. $[\alpha]_D^{20}$ = −58.3 (c 0.74, $CHCl_3$). *Anal.* Calc. for $C_{16}H_{26}N_2O$ (262.39): C, 73.24; H, 9.99; N, 10.68. Found: C, 73.21; H, 9.95; N, 10.69%. MS (EI) *m/z* (rel. int.): 262 (M^+**.**, 51), 247 (33), 219 (84), 205 (26), 191 (21), 181 (100), 165 (29), 149 (44), 139 (42), 95 (37). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 6.93 (d, 1H, 3`-H, *J* = 1.3 Hz), 6.87 (d, 1H, 2`-H, *J* = 1.3 Hz), 5.15 (septet, 1H, 4`-H, *J* = 6.6 Hz), 2.80 (dq, 1H, 7-$H_{syn}$, *J* = 10.4, 4.3, 2.4 Hz), 1.91 (m, 1H, 6-$H_{endo}$), 1.81 (s, 1H, OH), 1.72 (m, 1H, 4-H), 1.69 (m, 1H, 5-$H_{endo}$), 1.43 (m, 1H, 5-$H_{exo}$), 1.42 (d, 3H, 6`-H, *J* = 6.6 Hz), 1.36 (d, 3H, 5`-H, *J* = 6.6 Hz), 1.34 (s, 3H, 8-H), 1.27 (dd, 1H, 7-$H_{anti}$, *J* = 10.4, 1.5 Hz), 1.19 (dt, 1H, 6-$H_{exo}$, *J* = 13.1, 4.0 Hz), 1.08 (s, 3H, 9-H), 0.52 (s, 3H, 10-H). $^{13}$C NMR (250 MHz, $CDCl_3$, 300 K) $\delta$: 148.97 (s, 1C, 1`-C), 125.90 (d, 1C, 3`-C), 115.09 (d, 1C, 2`-C), 84.17 (s, 1C, 2-C), 54.56 (s, 1C, 1-C), 49.64 (d, 1C, 4-C), 48.29 (d, 1C, 4`-C), 45.62 (s, 1C, 3-C), 40.67 (t, 1C, 7-C), 31.23 (t, 1C, 6-C), 27.90 (q, 1C, 8-C), 25.57 (q, 1C, 5`-C), 24.94 (t, 1C, 5-C), 23.60 (q, 1C, 6`-C), 22.34 (q, 1C, 9-C), 17.66 (q, 1C, 10-C).

4.14. (1R,2R)-1,3,3-trimethyl-2-(1-phenyl-1H-imidazol-2-yl)bicyclo[2.2.1]heptan-2-ol (**28c**)

To a solution of 1.04 g (7.21 mmol) *N*-phenylimidazole in 20 ml THF was added at −70 °C 2.90 ml (7.21 mmol) 2.5 M solution of *n*-BuLi in hexane, and the resulting mixture was stirred for 1 h at −70 °C. To the formed yellow solution was added 1.00 g (6.57 mmol) (−)-fenchone (**3**) and the mixture was stirred at −70 °C. The reaction was monitored by TLC (hexane:Et_2O = 2:1) and after 2 h was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, hexane:Et_2O = 10:1) to give 1.34 g (69%) **28c** as white crystals. Mp 83–84 °C. $[\alpha]_D^{20}$ = −36.7 (c 0.75, $CHCl_3$). *Anal.* Calc. for $C_{19}H_{24}N_2O$ (296.41): C, 76.99; H, 8.16; N, 9.45. Found: C, 77.02; H, 8.18; N, 9.47%. MS (EI) *m/z* (rel. int.): 296 (M^+**.**, 91), 281 (50), 215 (100), 199 (25), 171 (27), 145 (48). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.38–7.44 (m, 3H, 7`-H, 6`-H), 7.26–7.35 (m, 2H, 5`-H), 7.06 (d, 1H, 3`-H, *J* = 1.3 Hz), 6.78 (d, 1H, 2`-H, *J* = 1.3 Hz), 2.98 (dq, 1H, 7-H_{syn}, *J* = 10.2, 4.0, 2.1 Hz), 1.77–1.90 (m, 1H, 6-H_{endo}), 1.72–1.76 (m, 1H, 4-H), 1.51–1.64 (m, 1H, 5-H_{endo}), 1.40 (dddd, 1H, 5-H_{exo}, *J* = 12.5, 12.5, 4.2, 4.2 Hz), 1.28 (dd, 1H, 7-H_{anti}, *J* = 10.2, 1.5 Hz), 1.23 (s, 1H, OH), 1.20 (s, 3H, 10-H), 1.09 (dt, 1H, 6-H_{exo}, *J* = 12.5, 4.2 Hz), 0.78 (s, 3H, 9-H), 0.77 (s, 3H, 8-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 150.63 (s, 1C, 1`-C), 141.12 (s, 1C, 4`-C), 128.47 (d, 2C, 6`-C), 128.23 (d, 1C, 7`-C), 127.05 (d, 2C, 5`-C), 126.03 (d, 1C, 3`-C), 122.22 (d, 1C, 2`-C), 85.15 (s, 1C, 2-C), 54.63 (s, 1C, 1-C), 48.95 (d, 1C, 4-C), 46.30 (s, 1C, 3-C), 40.89 (t, 1C, 7-C), 30.46 (t, 1C, 6-C), 28.45 (q, 1C, 8-C), 24.83 (t, 1C, 5-C), 21.22 (q, 1C, 9-C), 17.50 (q, 1C, 10-C).

4.15. (1R,2R)-2-(1-benzyl-1H-imidazol-2-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**28d**)

To a solution of 1.25 g (7.87 mmol) *N*-benzylimidazole in 20 ml THF was added at −70 °C 3.15 ml (7.87 mmol) 2.5 M solution of *n*-BuLi in hexane, and the resulting mixture was stirred for 1 h at −70 °C (with the formation of an orange-red solution). To this solution was added 1.00 g (6.57 mmol) (−)-fenchone (**3**) and the mixture was stirred at −70 °C. The reaction was monitored by TLC (hexane:Et_2O = 2:1) and after 2 h was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, (a) hexane, (b) hexane:Et_2O = 5:1) to give 1.56 g (76%) **28d** as white crystals. Mp 74–75 °C. $[\alpha]_D^{20}$ = −70.5 (c 0.67, $CHCl_3$). *Anal.* Calc. for $C_{20}H_{26}N_2O$ (310.43): C, 77.38; H, 8.44; N, 9.02. Found: C, 77.34; H, 8.45; N, 9.04%. MS (EI) *m/z* (rel. int.): 310 (M^+**.**, 34), 229 (59), 219 (100), 91 (86). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.23–7.37 (m, 3H, 6'-H, 8'-H), 7.07–7.11 (m, 2H, 7'-H), 7.00 (d, 1H, 3'-H, *J* = 1.2 Hz), 6.72 (d, 1H, 2'-H, *J* = 1.2 Hz), 5.73 (d, 1H, 4'-H_a, *J* = 15.4 Hz), 5.05 (d, 1H, 4'-H_b, *J* = 15.4 Hz), 2.89 (dq, 1H, 7-H_{syn}, *J* = 10.3, 4.0, 2.2 Hz), 1.79–1.93 (m, 1H, 6-H_{endo}), 1.70–1.78 (m, 1H, 4-H), 1.62–1.70 m, 1H, 5-H_{endo}), 1.37–1.51 (m, 1H, 5-H_{exo}), 1.27–1.33 (m, 1H, 7-H_{anti}), 1.29 (s, 3H, 10-H), 1.15 (dt, 1H, 6-H_{exo}, *J* = 12.7, 3.6 Hz), 1.06 (s, 3H, 9-H), 0.59 (s, 3H, 8-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 149.86 (s, 1C, 1'-C), 138.84 (s, 1C, 5'-C), 128.75 (d, 2C, 6'-C), 127.40 (d, 1C, 8'-C), 126.41 (d, 2C, 7'-C), 126.03 (d, 1C, 3'-C), 120.53 (d, 1C, 2'-C), 84.31 (s, 1C, 2-C), 54.33 (s, 1C, 1-C), 51.70 (t, 1C, 4'-C), 49.35 (d, 1C, 4-C), 46.11 (s, 1C, 3-C), 40.77 (t, 1C, 7-C), 30.80 (t, 1C, 6-C), 27.80 (q, 1C, 8-C), 25.09 (t, 1C, 5-C), 22.55 (q, 1C, 9-C), 17.45 (q, 1C, 10-C).

4.16. (1R,2R)-2-(1-isopropyl-1H-benzo[d]imidazol-2-yl)-1,3,3-trimethylbicyclo[2.2.1] heptan-2-ol (**29a**)

To a solution of 1.16 g (7.23 mmol) *N*-isopropylbenzimidazole in 15 ml hexane and 15 ml THF was added at −80 °C 2.90 ml (7.23 mmol) 2.5 M solution of *n*-BuLi in hexane, and the resulting mixture was stirred for 2 h at −65 °C. To the formed yellow solution was added 1.00 g (6.57 mmol) (−)-fenchone (**3**) and the mixture was stirred at −40 °C. The reaction was monitored by TLC (Et_2O) and after 3.5 h was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 20 mm, *h* = 280 mm, 34 g silica gel, (a) hexane:Et_2O = 50:1, (b) hexane:Et_2O = 2:1) to give 0.54 g (26%) **29a** as white crystals. Mp 135–136 °C. $[\alpha]_D^{20}$ = −41.1 (c 0.83, $CHCl_3$). *Anal.* Calc. for $C_{20}H_{28}N_2O$ (312.45): C, 76.88; H, 9.03; N, 8.97. Found: C, 76.82; H, 9.00; N, 8.99%. MS (EI) *m/z* (rel. int.): 312 (M^+**.**, 54), 269 (98), 231 (100), 215 (33), 189 (53), 118 (43). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 7.76 (m, 1H, 6'-H), 7.56 (m, 1H, 3'-H), 7.15–7.23 (m, 2H, 4'-H, 5'-H), 5.58 (septet, 1H, 8'-H, *J* = 7.0 Hz), 3.01 (dq, 1H, 7-H_{syn}, *J* = 10.4, 4.3, 2.3 Hz), 1.98 (s, 1H, OH), 1.92–2.04 (m, 1H, 6-H_{endo}), 1.70–1.80 (m, 2H, 4-H, 5-H_{endo}), 1.67 (d, 3H, 10'-H, *J* = 7.0 Hz), 1.62 (d, 3H, 9'-H, *J* = 7.0 Hz), 1.43–1.57 (m, 1H, 5-H_{exo}), 1.41 (s, 3H, 10-H), 1.38 (dd, 7-H_{anti}, *J* = 10.4, 1.5 Hz), 1.26 (dt, 1H, 6-H_{exo}, *J* = 12.7, 3.9 Hz), 1.17 (s, 3H, 9-H), 0.65 (s, 3H, 8-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 155.70 (s, 1C, 1'-C), 142.66* (s, 1C, 2'-C), 133.08* (s, 1C, 7'-C), 121.30* (d, 1C, 4'-C), 120.89* (d, 1C, 5'-C), 120.07 (d, 1C, 6'-C), 112.63 (d, 1C, 3'-C), 84.69 (s, 1C, 2-C), 55.40 (s, 1C, 1-C), 49.89 (d, 1C, 4-C), 48.66 (d, 1C, 8'-C), 45.09 (s, 1C, 3-C), 40.91 (t, 1C, 7-C), 31.62 (t, 1C, 6-C), 28.31 (q, 1C, 8-C), 24.83 (t, 1C, 5-C), 22.17 (q, 1C, 9-C), 21.98 (q, 1C, 9'-C), 20.87 (q, 1C, 10'-C), 17.80 (q, 1C, 10-C).

4.17. (1R,2R)-1,3,3-trimethyl-2-(1-phenyl-1H-benzo[d]imidazol-2-yl)bicyclo[2.2.1]heptan-2-ol (**29b**)

To a solution of 0.95 g (4.89 mmol) *N*-phenylbenzimidazole in 20 ml THF was added at −70 °C 1.95 ml (4.89 mmol) 2.5 M solution of *n*-BuLi in hexane, and the resulting mixture was stirred for 1.5 h at −70 °C. To the formed yellow solution was added 0.67 g (4.37 mmol) (−)-fenchone (**3**) and the mixture was stirred at −70 °C. The reaction was monitored by TLC (hexane:Et_2O = 10:1) and after 3 h was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, (a) hexane, (b) hexane:Et_2O = 10:1) to give 0.66 g (39%) **29b** as white crystals. Mp 129–130 °C. $[\alpha]_D^{20}$ = −29.8 (c 0.80, $CHCl_3$). *Anal.* Calc. for $C_{23}H_{26}N_2O$ (346.47): C, 79.73; H, 7.56; N, 8.09. Found: C, 79.75; H, 7.57; N, 8.11%. MS (EI) *m/z* (rel. int.): 346 (M^+**.**, 53), 331 (30), 265 (100), 249 (24), 195 (47). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.80 (d, 1H, 3'-H, J = 8.1 Hz), 7.47–7.54 (m, 3H, 10'-H, 11'-H), 7.35–7.39 (m, 1H, 9'-H_a), 7.28–7.31 (m, 1H, 9'-H_b), 7.25 (m, 1H, 4'-H), 7.14 (m, 1H, 5'-H), 6.77 (d, 1H, 6'-H, *J* = 8.1 Hz), 3.20 (dq, 1H, 7-H_{syn}, *J* = 10.3, 4.1, 2.2 Hz), 1.88 (m, 1H, 6-H_{endo}), 1.80 (m, 1H, 4-H), 1.61 (m, 1H, 5-H_{endo}), 1.44 (m, 1H, 5-H_{exo}), 1.40 (s, 1H, OH), 1.36 (dd, 1H, 7-H_{anti}, *J* = 10.3, 1.5 Hz), 1.27 (s, 3H, 10-H), 1.15 (dt, 1H, 6-H_{exo}, *J* = 13.1, 4.1 Hz), 0.83 (s, 3H, 9-H), 0.82 (s, 3H, 8-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 156.35 (s, 1C, 1'-C), 141.53 (s, 1C, 2'-C), 139.36* (s, 1C, 8'-C), 137.54* (s, 1C, 7'-C), 129.36* (d, 1C, 9'-C_b), 129.00* (d, 1C, 10'-C_a), 128.91* (d, 1C, 10'-C_b), 127.15 (d, 1C, 9'-C_a), 128.57 (d, 1C, 11'-C), 122.32 (d, 1C, 5'-C), 121.95 (d, 1C, 4'-C), 119.34 (d, 1C, 3'-C), 110.28 (d, 1C, 6'-C), 85.58 (s, 1C, 2-C), 55.06 (s, 1C, 1-C), 49.04 (d, 1C, 4-C), 46.11 (s, 1C, 3-C), 41.05 (t, 1C, 7-C), 30.60 (t, 1C, 6-C), 28.64 (q, 1C, 8-C), 24.87 (t, 1C, 5-C), 21.23 (q, 1C, 9-C), 17.53 (q, 1C, 10-C).

4.18. (1R,2R)-2-(1-benzyl-1H-benzo[d]imidazol-2-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**29c**)

To a solution of 0.91 g (4.37 mmol) *N*-benzylbenzimidazole in 20 ml THF was added at −70 °C 1.75 ml (4.37 mmol) 2.5 M solution of *n*-BuLi in hexane, and the resulting mixture was stirred for 1 h at −70 °C. To the formed yellow solution was added 0.67 g (4.37 mmol) (−)-fenchone (**3**) and the mixture was stirred at −70 °C. The reaction was monitored by TLC (hexane:Et_2O = 5:1) and after 3.5 h was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, hexane:CH_2Cl_2 = 2:1). The obtained product was purified again by column chromatography (Φ = 20 mm, *h* = 280 mm, 40 g silica gel, hexane:Et_2O = 5:1) to give 1.02 g (65%) **29c** as white crystals. Mp 135–136 °C. $[\alpha]_D^{20}$ = −6.4 (c 0.43, $CHCl_3$). *Anal.* Calc. for $C_{24}H_{28}N_2O$ (360.49): C, 79.96; H, 7.83; N, 7.77. Found: C, 79.99; H, 7.80; N, 7.75%. MS (EI) *m/z* (rel. int.): 360 (M^+**.**, 54), 279 (94), 269 (100), 207 (25), 119 (24), 91 (97). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.79 (m, 1H, 3'-H), 7.17–7.32 (m, 4H, 10'-H, 2 arom. H), 7.10–7.16 (m, 2H, arom. H), 7.00–7.07 (m, 2H, 11'-H), 6.03 (d, 1H, 8'-H_a, *J* = 16.2 Hz), 5.24 (d, 1H, 8'-H_b, *J* = 16.2 Hz), 3.13 (dq, 1H, 7-H_{syn}, *J* = 10.4, 4.0, 2.3 Hz), 1.82–1.94 (m, 1H, 6-H_{endo}), 1.77–1.83 (m, 1H, 4-H), 1.80 (s, 1H, OH), 1.67–1.78 (m, 1H, 5-H_{endo}), 1.40–1.55 (m, 1H, 5-H_{exo}), 1.37–1.42 (m, 1H, 7-H_{anti}), 1.37 (s, 3H, 10-H), 1.21 (dt, 1H, 6-H_{exo}, *J* = 12.9, 3.8 Hz), 1.12 (s, 3H, 9-H), 0.62 (s, 3H, 8-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 156.29 (s, 1C, 1'-C), 141.91* (s, 1C, 2'-C), 138.33* (s, 1C, 9'-C), 135.47* (s, 1C, 7'-C), 128.72 (d, 2C, 10'-C), 127.11* (d, 1C, 12'-C), 125.61 (d, 2C, 11'-C), 122.28* (d, 1C, 6'-C), 121.74* (d,

1C, 5'-C), 119.70 (d, 1C, 3'-C), 109.88* (d, 1C, 4'-C), 84.73 (s, 1C, 2-C), 54.76 (s, 1C, 1-C), 49.47 (t, 1C, 8'-C), 49.40 (d, 1C, 4-C), 45.77 (s, 1C, 3-C), 40.91 (t, 1C, 7-C), 30.87 (t, 1C, 6-C), 27.98 (q, 1C, 8-C), 25.14 (t, 1C, 5-C), 22.64 (q, 1C, 9-C), 17.48 (q, 1C, 10-C).

4.19. (1R,2R)-1,3,3-trimethyl-2-(1-methyl-1H-indol-2-yl)bicyclo[2.2.1]heptan-2-ol (**30**)

To a solution of 0.52 g (3.96 mmol) *N*-methylindole in 10 ml THF was added dropwise at room temperature 2.35 ml (3.96 mmol) 1.7 M solution of *t*-BuLi in pentane. After stirring for 1 h, the formed yellow precipitate was cooled to 0 °C and 0.50 g (3.28 mmol) (−)-fenchone (**3**) was added. The reaction was monitored by TLC (hexane:Et_2O = 10:1) and stirred for 30 min. The formed clear dark yellow mixture was quenched with water and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, (a) hexane:Et_2O = 50:1, (b) hexane:Et_2O = 20:1) to give 0.85 g (91%) of **30** as white crystals. Mp 119–120 °C. $[\alpha]_D^{20}$ = −63.1 (c 0.75, $CHCl_3$). *Anal.* Calc. for $C_{19}H_{25}NO$ (283.41): C, 80.52; H, 8.89; N, 4.94. Found: C, 80.55; H, 8.92; N, 4.91%. MS (EI) *m/z* (rel. int.): 283 (M^+., 100), 202 (32), 158 (76), 131 (22). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 7.54 (ddd, 1H, 4'-H, *J* = 7.6, 1.3, 0.7 Hz), 7.28 (ddd, 1H, 7'-H, *J* = 8.2, 2.0, 0.7 Hz), 7.17 (m, 1H, 6'-H), 7.07 (m, 1H, 5'-H), 6.52 (d, 1H, 2'-H, *J* = 0.8 Hz), 3.94 (s, 3H, 9'-H), 2.56 (dq, 1H, 7-H_{syn}, *J* = 10.4, 4.5, 2.3 Hz), 2.17 (m, 1H, 6-H_{endo}), 1.70–1.82 (m, 2H, 4-H, 5-H_{endo}), 1.72 (s, 1H, OH), 1.45 (m, 1H, 5-H_{exo}), 1.36 (m, 1H, 7-H_{anti}), 1.34 (s, 3H, 8-H), 1.22 (dt, 1H, 6-H_{exo}, *J* = 12.6, 3.8 Hz), 1.20 (s, 3H, 9-H), 0.56 (s, 3H, 10-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 142.28 (s, 1C, 1'-C), 137.21 (s, 1C, 8'-C), 126.76 (s, 1C, 3'-C), 121.07 (d, 1C, 6'-C), 120.12 (d, 1C, 4'-C), 119.31 (d, 1C, 5'-C), 109.11 (d, 1C, 7'-C), 102.20 (d, 1C, 2'-C), 83.94 (s, 1C, 2-C), 53.94 (s, 1C, 1-C), 50.47 (d, 1C, 4-C), 44.64 (s, 1C, 3-C), 40.67 (t, 1C, 7-C), 33.20 (q, 1C, 9'-C), 32.00 (t, 1C, 6-C), 28.61 (q, 1C, 8-C), 25.14 (t, 1C, 5-C), 22.60 (q, 1C, 9-C), 18.30 (q, 1C, 10-C).

4.20. (1R,2R)-1,3,3-trimethyl-2-(quinolin-2-yl)bicyclo[2.2.1]heptan-2-ol (**31**)

To a solution of 3.6 ml (31.50 mmol) dry *N*,*N*-dimethylaminoethanol in 10 ml hexane was added dropwise at −5 °C 25.2 ml (62.80 mmol) 2.5 M solution of *n*-BuLi in hexane. After stirring for 30 min at 0 °C, the mixture was cooled to −78 °C and 0.93 ml (7.88 mmol) quinoline was added dropwise. After stirring for 30 min, 5 ml Et_2O and 1.00 g (6.57 mmol) (−)-fenchone (**3**) were added and the mixture was stirred at −78 °C for additional 1 h. The reaction was monitored by TLC (hexane:Et_2O = 10:1), quenched with 10% HCl and warmed to room temperature (pH 4). The resulting mixture was washed with Et_2O and aqueous phase was treated with solid K_2CO_3 (pH 10–11) and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 33 mm, *h* = 400 mm, 110 g silica gel, (a) hexane, (b) hexane:Et_2O = 40:1) to give 0.31 g (17%) of **31** as white crystals. Mp 125–126 °C. $[\alpha]_D^{20}$ = −55.8 (c 0.45, $CHCl_3$). *Anal.* Calc. for $C_{19}H_{23}NO$ (281.39): C, 81.10; H, 8.24; N, 4.98. Found: C, 81.14; H, 8.22; N, 4.95%. MS (EI) *m/z* (rel. int.): 281 (M^+., 4), 200 (83), 184 (100), 170 (28), 129 (68). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 8.09 (m, 1H, 6'-H), 8.03 (m, 1H, 8'-H), 7.81 (m, 1H, 3'-H), 7.66–7.73 (2H, 2'-H, 7'-H), 7.53 (m, 1H, 5'-H), 6.42 (br s, 1H, OH), 2.32–2.47 (m, 2H, 6-H_{endo}, 7-H_{syn}), 1.87–1.98 (m, 1H, 5-H_{endo}), 1.86 (m, 1H, 4-H), 1.49–1.61 (m, 1H, 5-H_{exo}), 1.44 (dd, 1H, 7-H_{anti}, *J* = 10.5, 1.4 Hz), 1.17 (dt, 1H, 6-H_{exo}, *J* = 12.6, 4.7 Hz), 1.03 (s, 3H, 9-H), 0.97 (s, 3H, 10-H), 0.53 (s, 3H, 8-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 162.88* (s, 1C, 1'-C), 145.41* (s, 1C, 9'-C), 129.39* (d, 1C, 7'-C), 129.38 (d, 1C, 6'-C), 128.82 (d, 1C, 8'-C), 127.11 (d, 1C, 3'-C), 126.82 (s, 1C, 4'-C), 126.33 (d, 1C, 5'-C), 121.63* (d, 1C, 2'-C), 83.93 (s, 1C, 2-C), 52.13 (s, 1C, 1-C), 48.76 (d, 1C, 4-C), 46.56 (s, 1C, 3-C), 42.31 (t, 1C, 7-C), 32.66 (t, 1C, 6-C), 29.21 (q, 1C, 8-C), 24.26 (t, 1C, 5-C), 22.48 (q, 1C, 9-C), 17.18 (q, 1C, 10-C).

4.21. (1R,2R)-1,3,3-trimethyl-2-(thiophen-2-yl)bicyclo[2.2.1]heptan-2-ol (**32**) and (1R,1′R,2R,2′R)-2,2′-(thiophen-2,5-diyl)bis(trimethylbicyclo[2.2.1]heptan-2-ol) (**33**)

To 0.63 ml (7.88 mmol) thiophene was added at 0 °C 7.23 ml (8.67 mmol) 1.2 M solution of *n*-BuLi in hexane. To this solution was added dropwise 7 ml THF and the mixture was allowed to warm to room temperature for 15 min. The resulting mixture was cooled again to 0 °C and 1.06 ml (6.57 mmol) (−)-fenchone (**3**) was added dropwise. The reaction was monitored by TLC (hexane:Et_2O = 10:1) and after stirring for 20 min was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 335 mm, 80 g silica gel, hexane:Et_2O = 50:1) to give 0.12 g (3%) pure **33** as white crystals and a fraction containing **32** and (−)-fenchone. After evaporation of the solvent the crude **32** was dissolved in 100 ml Et_2O and treated with 2.65 g (70 mmol) of $LiAlH_4$ for 1 h at room temperature. The mixture was carefully quenched with 40 ml water and filtered through Celite. The organic layer was separated, washed with water and dried over anhydrous Na_2SO_4. After evaporation of solvent, the crude product was purified by column chromatography (Φ = 32 mm, *h* = 580 mm, 150 g silica gel, (a) hexane and (b) hexane:Et_2O = 50:1) to give 1.19 g (77%) **32** as white crystals.

Data of 32: Mp 49–50 °C. $[\alpha]_D^{20}$ = −59.4 (c 1.05, $CHCl_3$). *Anal.* Calc. for $C_{14}H_{20}OS$ (236.37): C, 71.14; H, 8.53; S, 13.57. Found: C, 71.12; H, 8.50; S, 13.59%. MS (EI) *m/z* (rel. int.): 236 (M^+., 41), 153 (100), 140 (31), 123 (32), 111 (60). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 7.13 (dd, 1H, 4'-H, *J* = 4.9, 1.5 Hz), 6.94–7.00 (m, 2H, 2'-H, 3'-H), 2.21 (dq, 1H, 7-H_{syn}, *J* = 10.5, 4.4, 2.4 Hz), 2.00–2.13 (m, 1H, 6-H_{endo}), 2.05 (s, 1H, OH), 1.71–1.83 (m, 2H, 4-H, 5-H_{endo}), 1.48 (m, 1H, 5-H_{exo}), 1.34 (dd, 1H, 7-H_{anti}, *J* = 10.5, 1.7 Hz), 1.21 (dt, 1H, 6-H_{exo}, *J* = 12.5, 4.2 Hz), 1.05 (s, 3H, 10-H), 1.04 (s, 3H, 9-H), 0.66 (s, 3H, 8-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 151.07 (s, 1C, 1'-C), 126.34* (d, 1C, 3'-C), 123.95* (d, 1C, 2'-C), 122.38 (d, 1C, 4'-C), 85.22 (s, 1C, 2-C), 53.46 (s, 1C, 1-C), 48.89 (d, 1C, 4-C), 45.81 (s, 1C, 3-C), 41.34 (t, 1C, 7-C), 31.51 (t, 1C, 6-C), 29.16 (q, 1C, 8-C), 24.75 (t, 1C, 5-C), 21.28 (q, 1C, 9-C), 17.64 (q, 1C, 10-C).

Data of 33: Mp 102–104 °C. $[\alpha]_D^{20}$ = −71.9 (c 0.99, $CHCl_3$). *Anal.* Calc. for $C_{24}H_{36}O_2S$ (388.61): C, 74.18; H, 9.34; S, 8.25. Found: C, 74.26; H, 9.45; S, 8.31%. MS (EI) *m/z* (rel. int.): 388 (M^+., 76), 305 (62), 265 (64), 235 (99), 181 (47), 153 (52), 123 (91), 111 (26), 81 (100). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 6.79 (s, 2H, 2'-H), 2.18 (dq, 2H, 7-H_{syn}, *J* = 10.5, 4.2, 2.3 Hz), 2.07 (m, 2H, 6-H_{endo}), 1.95 (s, 2H, OH), 1.69–1.80 (m, 4H, 4-H, 5-H_{endo}), 1.45 (m, 2H, 5-H_{exo}), 1.30 (dd, 2H, 7-H_{anti}, *J* = 10.5, 1.5 Hz), 1.17 (dt, 2H, 6-H_{exo}, *J* = 12.6, 4.1 Hz), 1.05 (s, 6H, 10-H), 1.01 (s, 6H, 9-H), 0.68 (s, 6H, 8-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 147.21 (s, 2C, 1'-C), 123.31 (d, 2C, 2'-C), 85.05 (s, 2C, 2-C), 53.36 (s, 2C, 1-C), 48.90 (d, 2C, 4-C), 45.71 (s, 2C, 3-C), 41.31 (t, 2C, 7-C), 31.41 (t, 2C, 6-C), 29.19 (q, 2C, 8-C), 24.80 (t, 2C, 5-C), 21.40 (q, 2C, 9-C), 17.71 (q, 2C, 10-C).

4.22. (1R,2R)-2-(benzo[d]thiazol-2-yl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**34**)

To a solution of 1.06 g (7.88 mmol) benzothiazole in 10 ml THF was added dropwise at −85 °C 3.15 ml (7.88 mmol) 2.5 M solution

of *n*-BuLi in hexane. The resulting orange mixture was stirred for 1 h at −85 °C and (−)-fenchone (**3**) was added. The reaction was monitored by TLC (hexane/Et_2O = 20:1) and after additional stirring for 1 h at −85 °C the resulting brown mixture was quenched with water, warmed to room temperature and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 340 mm, 80 g silica gel, (a) hexane, (b) hexane/Et_2O = 80:1) to give 1.55 g (82%) **34** as white crystals. Mp 73–74 °C. $[\alpha]_D^{20}$ = −39.4 (c 0.83, $CHCl_3$). *Anal.* Calc. for $C_{17}H_{21}NOS$ (287.42): C, 71.04; H, 7.36; N, 4.87; S, 11.16. Found: C, 71.08; H, 7.32; N, 4.90; S, 11.18%. MS (EI) *m/z* (rel. int.): 287 (M^+., 22), 206 (100), 190 (42), 176 (37), 136 (67). ^{1}H NMR (250 MHz, $CDCl_3$, 300 K) δ: 8.00 (dq, 1H, 6`-H, *J* = 8.0, 1.2, 0.6 Hz), 7.87 (dq, 1H, 3`-H, *J* = 8.0, 1.2, 0.6 Hz), 7.45 (dt, 1H, 5`-H, *J* = 7.1, 1.2 Hz), 7.35 (dt, 1H, 4`-H, *J* = 7.1, 1.2 Hz), 3.08 (br s, 1H, OH), 2.86 (dd, 1H, 7-H_{syn}, *J* = 10.5, 1.2 Hz), 2.00 (m, 1H, 6-H_{endo}), 1.76–1.88 (m, 1H, 5-H_{endo}), 1.83–1.87 (m, 1H, 4-H), 1.54 (dddd, 1H, 5-H_{exo}, *J* = 12.7, 12.7, 4.4, 4.4 Hz), 1.36 (dd, 1H, 7-H_{anti}, *J* = 10.5, 1.6 Hz), 1.25 (dt, 1H, 6-H_{exo}, *J* = 12.7, 3.9 Hz), 1.09 (s, 3H, 9-H), 1.04 (s, 3H, 10-H), 0.81 (s, 3H, 8-H). ^{13}C NMR (250 MHz, $CDCl_3$, 300 K) δ: 177.65 (s, 1C, 1`-C), 152.91 (s, 1C, 7`-C), 134.77 (s, 1C, 2`-C), 125.51 (d, 1C, 4`-C), 124.47 (d, 1C, 5`-C), 122.91 (d, 1C, 6`-C), 121.28 (d, 1C, 3`-C), 86.59 (s, 1C, 2-C), 54.02 (s, 1C, 1-C), 48.75 (d, 1C, 4-C), 46.22 (s, 1C, 3-C), 40.91 (t, 1C, 7-C), 30.72 (t, 1C, 6-C), 28.56 (q, 1C, 8-C), 25.25 (t, 1C, 5-C), 21.92 (q, 1C, 9-C), 17.03 (q, 1C, 10-C).

4.23. 2-((3R,4R)-3-hydroxy-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]heptane-2,2′-indene]-3-yl)acetonitrile (**35**)

To a stirred solution of acetonitrile (0.174 g, 4.25 mmol) in 4 ml THF 2.5 M *n*-BuLi in hexane (1.42 ml, 3.54 mmol) was added at −78 °C. After stirring for 45 min at −78 °C, to the formed white precipitate was added **2** (0.300 g, 1.18 mmol) and the reaction was stirred for 3 h at −78 °C (the reaction progress was monitored by TLC). The reaction was carefully quenched with saturated aqueous NH_4Cl, warmed to room temperature and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 17 mm, *h* = 380 mm, 20 g silica gel, hexane:Et_2O = 4:1), to give 0.330 g, (95%) of **35** as colorless crystals. Mp 93–94 °C. $[\alpha]_D^{20}$ = +80.6 (c 0.56, $CHCl_3$). *Anal.* Calc. for $C_{20}H_{25}NO$ (295.42): C, 81.31; H, 8.53; N, 4.74. Found: C, 81.39; H, 8.55; N, 4.78%. MS (EI) *m/z* (rel. int.): 295 (M^+., 5), 277 (40), 185 (18), 145 (60), 142 (100), 95 (28). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.18–7.12 (m, 4H, Ar), 3.75 (d, 1H, 18-H_a, *J* = 15.8 Hz), 3.02 and 2.96 (AB-system, 2H, 11-H, *J* = 16.7 Hz), 2.88 (dd, 2H, 1′-H_a, 18-H_b, *J* = 16.8, 15.8 Hz), 2.40 (d, 1H, 1′-H_b, *J* = 16.8 Hz), 1.89 (s, 1H, OH), 1.78 (d, 1H, 4-H, *J* = 4.1 Hz), 1.79–1.66 (m, 1H, 5-H_{exo}), 1.56–1.51 (m, 2H, 6-H_{exo}, 5-H_{endo}), 1.38–1.32 (m, 1H, 6-H_{endo}), 1.35 (s, 3H, 8-H), 1.06 (s, 1H, 10-H), 0.92 (s, 3H, 9-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 143.62 (s, 1 arom. C), 141.06 (s, 1 arom. C), 126.82 (d, 1 arom. C), 126.60 (d, 1 arom. C), 123.83 (d, 1 arom. C), 123.24 (d, 1 arom. C), 118.34 (s, CN), 81.87 (s, C-2), 61.19 (s, C-3), 56.26 (d, C-4), 54.98 (s, C-1), 49.03 (s, C-7), 42.64 (t, C-11), 42.15 (t, C-18), 31.12 (t, C-6), 26.38 (t, C-1′), 24.03 (t, C-5), 23.00 (q, C-8), 22.82 (q, C-9), 11.22 (q, C-10).

4.24. 2-((1R,2R)-2-hydroxy-1,3,3-trimethylbicyclo[2.2.1]heptan-2-yl)acetonitrile (**36**)

To a solution of 1.94 g (47.30 mmol) dry CH_3CN in 50 ml THF was added at −80 °C 15.75 ml (39.40 mmol) 2.5 M solution of *n*-BuLi in hexane (after stirring for 45 min at this temperature, a white precipitate was formed). To the mixture was added 3.00 g (19.70 mmol) (−)-fenchone (**3**). The reaction was monitored by TLC (hexane:Et_2O = 2:1) and stirred for 30 min at −80 °C. The resulting clear yellow mixture was quenched with saturated aqueous NH_4Cl, warmed to room temperature and extracted with Et_2O. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 30 mm, *h* = 320 mm, 80 g silica gel, hexane:Et_2O = 2:1) to give 3.78 g (99%) of **36** as white crystals. The analytical data for **36** are identically to that presented in the literature [3a].

4.25. (3R,4R)-3-(2-aminoethyl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]heptane-2,2′-inden]-3-ol (**37**)

To a suspension of $LiAlH_4$ (0.34 g, 8.88 mmol) in 30 ml Et_2O was added dropwise a solution of **35** (0.328 g, 1.11 mmol) in 10 ml Et_2O at room temperature, and the resulting mixture was stirred for 1 h. The reaction mixture was carefully quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 20 mm, *h* = 280 mm, 20 g silica gel, Et_2O:CH_3OH:Et_3N = 100:1:1), to give 0.330 g, (99%) of **37** as a waxy solid. $[\alpha]_D^{20}$ = +57.6 (c 0.60, $CHCl_3$). *Anal.* Calc. for $C_{20}H_{29}NO$ (295.42): C, 80.22; H, 9.76; N, 4.68. Found: C, 80.29; H, 9.73; N, 4.70%. MS (EI) *m/z* (rel. int.): 299 (M^+., 64), 252 (24), 188 (100), 171 (24), 159 (61), 156 (60), 142 (87), 128 (47), 115 (56). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.09–7.08 (m, 1H, Ar), 7.04–6.99 (m, 3H, Ar), 3.97 (d, 1H, 18-H_a, *J* = 16.1 Hz), 3.02 and 2.95 (AB-system, 2H, 11-H, *J* = 16.4 Hz), 2.75–2.71 (m, 1H, 2′-H_a), 2.70 (d, 1H, 18-H_b, *J* = 16.1 Hz), 2.24–2.20 (m, 1H, 2′-H_b), 1.70–1.66 (m, 1H, 1′-H_a), 1.62–1.57 (m, 1H, 1′-H_b), 1.58 (d, 1H, 4-H, *J* = 4.3 Hz), 1.54–1.49 (m, 1H, 5-H_{exo}), 1.44–1.40 (m, 1H, 5-H_{endo}), 1.37–1.33 (m, 1H, 6-H_{endo}), 1.26–1.21 (m, 1H, 6-H_{exo}), 1.25 (s, 3H, 8-H), 0.83 (s, 3H, 10-H), 0.80 (s, 3H, 9-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 145.27 (s, 1 arom. C), 142.87 (s, 1 arom. C), 125.94 (d, 1 arom. C), 125.66 (d, 1 arom. C), 123.97 (d, 1 arom. C), 122.83 (d, 1 arom. C), 85.59 (s, C-2), 60.84 (s, C-3), 58.68 (d, C-4), 55.08 (s, C-1), 48.71 (s, C-7), 43.25 (t, C-11), 42.89 (t, C-18), 38.68 (t, C-2′), 34.27 (t, C-1′), 29.89 (t, C-6), 24.20 (t, C-5), 23.10 (q, C-9), 22.96 (q, C-8), 12.25 (q, C-10).

4.26. (1R,2R,4S)-2-(2-aminoethyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**38**)

This compound was prepared in quantitative yield according to the previous published literature [3a] (the analytical and spectroscopic data were identical).

4.27. (3R,4R)-3-(2-(dibenzylamino)ethyl)-4,7,7-trimethyl-1′,3′-dihydrospiro[heptane[2.2.1]heptanes-2,2′-inden]-3-ol (**39**)

To a stirred solution of **37** (0.050 g, 0.17 mmol) in THF/H_2O (3 ml/0.5 ml) were added K_2CO_3 (0.07 g, 0.50 mmol) and benzylbromide (0.086 g, 0.5 mmol) at room temperature. The reaction mixture was refluxed for 1.5 h. The reaction was quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 13 mm, *h* = 220 mm, 8 g silica gel, hexane:Et_2O = 50:1) to give 0.068 g, (85%) of **39** as a colorless oil. $[\alpha]_D^{20}$ = +19.7 (c 1.46, $CHCl_3$). *Anal.* Calc. for $C_{34}H_{41}NO$ (479.70): C, 85.13; H, 8.61; N, 2.92. Found: C, 85.17; H, 8.59; N, 2.95%. MS (EI) *m/z* (rel. int.): 479 (M^+., 36), 210 (100), 198 (16), 106 (20), 81 (87). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.19–7.13 (m, 5H, Ar), 7.09–7.01 (m, 4H, Ar), 6.95–6.91 (m, 5H, Ar), 4.06 (d, 1H, 18-H_a, *J* = 16.2 Hz), 3.10 (d, 2H, 3`-H, *J* = 13.8 Hz), 3.01 (s, 2H, 11-H), 2.99 (d, 2H, 3`-H, *J* = 13.8 Hz), 2.70 (d, 1H, 18-

H_b, J = 16.2 Hz), 2.24–2.21 (m, 1H, 2′-H_a), 2.18–2.14 (m, 1H, 2′-H_b), 1.79–1.74 (m, 1H, 1′-H_a), 1.70–1.67 (m, 1H, 1′-H_b), 1.60 (d, 1H, 4-H, J = 4.3 Hz), 1.53–1.48 (m, 1H, 5-H_{exo}), 1.43–1.39 (m, 1H, 5-H_{endo}), 1.31–1.36 (m, 1H, 6-H_{endo}), 1.29 (s, 3H, 8-H), 1.22–1.17 (m, 1H, 6-H_{exo}), 0.80 (s, 3H, 9-H), 0.75 (s, 3H, 10-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 145.41 (s, 1 arom. C), 143.14 (s, 1 arom. C), 136.34 (s, 1 arom. C), 129.75 (d, 1 arom. C), 128.13 (d, 1 arom. C), 127.10 (d, 1 arom. C), 126.22 (d, 1 arom. C), 125.79 (d, 1 arom. C), 124.19 (d, 1 arom. C), 122.92 (d, 1 arom. C), 85.96 (s, C-2), 60.65 (s, C-3), 59.33 (d, C-4), 55.42 (s, C-1), 55.23 (t, C-3‵), 51.39 (t, C-2′), 48.56 (s, C-7), 43.56 (t, C-11), 43.06 (t, C-18), 29.67 (t, C-6), 27.89 (t, C-1′), 24.16 (t, C-5), 23.02 (q, C-8), 23.00 (q, C-9), 12.01 (q, C-10).

4.28. (3R,4R)-3-(2-(isoindolin-2-yl)ethyl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]heptane-2,2′-inden]-3-ol (**40**)

To a stirred solution of **37** (0.098 g, 0.33 mmol) in THF/H_2O (6 ml/1 ml) were added K_2CO_3 (0.137 g, 0.99 mmol) and α, α′-dichloro-*o*-xylene (0.075 g, 0.43 mmol) at room temperature. The reaction mixture was refluxed for 10 h (the reaction progress was monitored by TLC). The reaction was quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 12 mm, h = 280 mm, 13 g silica gel, hexane/Et_2O = 5:1), to give 0.114 g, (86%) of **40** as a waxy solid. $[\alpha]_D^{20}$ = 0 (c 1.28, $CHCl_3$). *Anal.* Calc. for $C_{28}H_{35}NO$ (401.58): C, 83.74; H, 8.78; N, 3.49. Found: C, 83.79; H, 8.74; N, 3.53%. MS (EI) *m/z* (rel. int.): 401 (M^+., 53), 132 (100), 118 (46), 105 (29). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.19–7.13 (m, 4H, arom. H), 7.11–7.10 (m, 2H, arom. H), 7.05–7.03 (m, 2H, arom. H), 4.07 (d, 1H, 18-H_a, J = 16.1 Hz), 3.64 (d, 1H, 3′-H, J = 11.9 Hz), 3.29 (d, 1H, 3′-H, J = 11.9 Hz), 3.12 and 3.09 (d, AB-system, 2H, 11-H, J = 16.6 Hz), 2.75 (d, 1H, 18-H_b, J = 16.1 Hz), 2.53 (dt, 1H, 2′-H_a, J = 12.9, 4.1 Hz), 2.40–2.36 (m, 1H, 2′-H_b), 1.89–1.82 (m, 2H, 1′-H), 1.69 (d, 1H, 4-H, J = 4.3 Hz), 1.63–1.57 (m, 1H, 5-H_{exo}), 1.53–1.44 (m, 2H, 5-H_{endo}, 6-H_{endo}), 1.34–1.28 (m, 1H, 6-H_{exo}), 1.28 (s, 3H, 8-H), 0.92 (s, 3H, 10-H), 0.87 (s, 3H, 9-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 145.48 (s, 1 arom. C), 143.28 (s, 1 arom. C), 139.35 (s, 1 arom. C), 126.66 (d, 1 arom. C), 126.06 (d, 1 arom. C), 125.88 (d, 1 arom. C), 124.05 (d, 1 arom. C), 123.04 (d, 1 arom. C), 122.12 (d, 1 arom. C), 86.01 (s, C-2), 60.98 (s, C-3), 59.22 (d, C-4), 58.23 (t, C-3′), 55.43 (s, C-1), 53.05 (t, C-2′), 48.62 (s, C-7), 43.64 (C-11), 43.13 (t, C-18), 29.79 (t, C-6), 29.36 (t, C-1′), 24.24 (t, C-5), 23.05 (q, C-9), 22.87 (q, C-8), 12.07 (q, C-10).

4.29. (3R,4R)-3-(2-(diethylamino)ethyl)-4,7,7-trimethyl-1′,3′-dihydrospiro[bicyclo[2.2.1]heptane-2,2′-inden]-3-ol (**41**)

To a stirred solution of **37** (0.170 g, 0.57 mmol) in THF/H_2O (10 ml/1 ml) were added K_2CO_3 (0.240 g, 1.70 mmol) and ethyliodide (0.265 g, 1.70 mmol) at room temperature. The reaction mixture was refluxed for 12 h (the reaction progress was monitored by TLC). The reaction was quenched with H_2O and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 20 mm, h = 280 mm, 15 g silica gel, hexane/Et_2O = 2:1), to give 0.079 g, (40%) of **41** as a colorless oil. $[\alpha]_D^{20}$ = +41.1 (c 0.48, $CHCl_3$). *Anal.* Calc. for $C_{24}H_{37}NO$ (355.56): C, 81.07; H, 10.49; N, 3.94. Found: C, 81.09; H, 10.53; N, 3.97%. MS (EI) *m/z* (rel. int.): 355 (M^+., 10), 281 (23), 207 (67), 91 (42), 86 (100), 73 (51). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.14–7.10 (m, 2H, Ar), 7.08–7.05 (m, 2H, arom. H), 4.13 (d, 1H, 18-H_a, J = 16.3 Hz), 3.11 and 3.07 (AB-system, 2H, 11-H, J = 16.4 Hz), 2.76 (d, 1H, 18H_b, J = 16.3 Hz), 2.26–2.20 (m, 3H, 2′-H_a, 3′-H), 2.05–1.96 (m, 3H, 2′-H_b, 3′-H), 1.81–1.76 (m, 1H, 1′-H_a), 1.71–1.68 (m, 1H, 1′-H_b), 1.66 (d, 1H, 4-H, J = 4.4 Hz), 1.60–1.55 (m, 1H, 5-H_{exo}), 1.50–1.42 (m, 2H, 5-H_{endo}, 6-H_{endo}), 1.30 (s, 3H, 8-H), 1.29–1.25 (m, 1H, 6-H_{exo}), 0.873 (s, 3H, 10-H), 0.867 (s, 3H, 9-H), 0.66 (t, 6H, 4′-H, J = 7.2 Hz). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 145.41 (s, 1 arom. C), 143.06 (s, 1 arom. C), 125.97 (d, 1 arom. C), 125.71 (d, 1 arom. C), 124.17 (d, 1 arom. C), 122.87 (d, 1 arom. C), 85.89 (s, C-2), 60.46 (s, C-3), 59.59 (d, C-4), 55.45 (s, C-1), 50.32 (t, C-3′), 48.51 (s, C-7), 45.28 (t, C-2′), 43.63 (t, C-11), 43.20 (t, C-18), 29.65 (t, C-6), 27.73 (t, C-1′), 24.08 (t, C-5), 22.96 (q, C-8, C-9), 11.95 (q, C-10), 10.41 (q, C-4′).

4.30. (1R,2R)-2-(2-(dibenzylamino)ethyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**42**)

To a solution of 0.48 g (2.41 mmol) **38** in 40 ml THF and 4 ml water were added 1.03 g (7.50 mmol) K_2CO_3 and 2.48 g (14.50 mmol) benzylbromide. The resulting mixture was refluxed for 3 h and the reaction was monitored by TLC (hexane:Et_2O = 20:1). After cooling, the solvent was evaporated *in vacuo*. The residue was diluted with 150 ml water and extracted with Et_2O. The organic phase was washed 2 times with water, dried over anhydrous K_2CO_3 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 20 mm, h = 280 mm, 40 g silica gel, (a) hexane, (b) hexane:Et_2O = 50:1) to give 0.74 g (81%) **42** as white crystals. Mp 49–50 °C. $[\alpha]_D^{20}$ = −28.6 (c 0.44, $CHCl_3$). *Anal.* Calc. for $C_{26}H_{35}NO$ (377.56): C, 82.71; H, 9.34; N, 3.71. Found: C, 82.69; H, 9.34; N, 3.73%. MS (EI) *m/z* (rel. int.): 377 (M^+., 5), 308 (23), 295 (40), 286 (55), 210 (100), 197 (39), 181 (25), 106 (57), 91 (95). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.29–7.35 (m, 8H, 5‵-H, 6‵-H), 7.24–7.28 (m, 2H, 7‵-H), 6.07 (s, 1H, OH), 3.84 (d, 2H, 3‵-H_a, J = 13.1 Hz), 3.19 (d, 2H, 3‵-H_b, J = 13.1 Hz), 2.91 (m, 1H, 2‵-H_b), 2.53 (ddd, 1H, 2‵-H_a J = 13.0, 5.9, 2.4 Hz), 2.07 (m, 1H, 6-H_{endo}), 1.93 (ddd, 1H, 1‵-H_b, J = 15.1, 11.1, 2.4 Hz), 1.59–1.67 (2H, 1‵-H_a, 5-H_{endo}), 1.47 (m, 1H, 4-H), 1.43 (m, 1H, 7-H_{syn}), 1.30 (dddd, 1H, 5-H_{exo}, J = 12.5, 4.7 Hz), 0.98 (dd, 1H, 7-H_{anti}, J = 10.1, 1.6 Hz), 0.93 (s, 3H, 10-H), 0.86 (dt, 1H, 6-H_{exo}, J = 12.5, 4.3 Hz), 0.83 (s, 3H, 8-H), 0.43 (s, 3H, 9-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 137.73 (s, 2C, 4‵-C), 129.66* (d, 4C, 5‵-C), 128.44* (d, 4C, 6‵-C), 127.33 (d, 2C, 7‵-C), 82.10 (s, 1C, 2-C), 58.25 (t, 2C, 3‵-C), 52.71 (s, 1C, 1-C), 51.49 (t, 1C, 2‵-C), 50.37 (d, 1C, 4-C), 44.04 (s, 1C, 3-C), 40.62 (t, 1C, 7-C), 30.01 (t, 1C, 6-C), 28.94 (t, 1C, 1‵-C), 27.88 (q, 1C, 8-C), 25.11 (t, 1C, 5-C), 22.49 (q, 1C, 9-C), 18.13 (q, 1C, 10-C).

4.31. (1R,2R)-2-(2-(isoindolin-2-yl)ethyl)-1,3,3-trimethylbicyclo[2.2.1]heptan-2-ol (**43**)

To a solution of 0.50 g (2.53 mmol) **38** in 40 ml dioxane and 10 ml water were added 0.73 g (5.31 mmol) K_2CO_3 and 0.89 g (5.07 mmol) α, α′-dichloro-*o*-xylene. The resulting mixture was refluxed for 7 h and the reaction was monitored by TLC (hexane:Et_2O = 2:1). After cooling the mixture was diluted with 150 ml water and extracted with Et_2O. The organic phase was washed 2 times with water, dried over anhydrous K_2CO_3 and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 20 mm, h = 280 mm, 40 g silica gel, hexane:Et_2O = 3:1) to give 0.28 g (37%) **43** as white crystals. Mp 101–102 °C. $[\alpha]_D^{20}$ = −26.7 (c 0.33, $CHCl_3$). *Anal.* Calc. for $C_{20}H_{29}NO$ (299.45): C, 80.22; H, 9.76; N, 4.68. Found: C, 80.19; H, 9.71; N, 4.69%. MS (EI) *m/z* (rel. int.): 299 (M^+., 6), 217 (24), 132 (100), 118 (52), 105 (22). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.17 (m, 4H, 5‵-H, 6‵-H, 7‵-H, 8‵-H), 6.67 (br s, 1H, OH), 4.06 (d, 2H, 3‵-H_a, J = 11.3 Hz), 3.90 (d, 2H, 3‵-H_b, J = 11.3 Hz), 3.19 (m, 1H, 2‵-H_b), 2.94 (dddd, 1H, 2‵-H_a, J = 12.5, 8.4, 5.4, 2.9 Hz), 2.09 (dddd, 1H, 6-H_{endo}, J = 12.3, 7.3, 4.9, 2.3 Hz), 1.85 (m, 1H, 1‵-H_b), 1.66–1.73 (m, 2H, 1‵-H_a, 5-H_{endo}), 1.59 (m, 1H, 4-H), 1.53 (dq, 1H, 7-H_{syn},

J = 10.1, 4.0, 2.3 Hz), 1.36 (ddt, 1H, 5-H_{exo}, J = 12.6, 9.4, 4.4 Hz), 1.10 (s, 3H, 8-H), 1.07 (s, 3H, 10-H), 1.06 (m, 1H, 1H, 7-H_{anti}), 1.02 (s, 3H, 9-H), 0.90 (dt, 1H, 6-H_{exo}, J = 12.3, 4.4 Hz). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 139.39 (s, 2C, 4`-C), 126.79 (d, 2C, 5`-C, 8`-C), 122.19 (d, 2C, 6`-C, 7`-C), 81.88 (s, 1C, 2-C), 58.92 (t, 2C, 3`-C), 54.46 (t, 1C, 2`-C), 52.77 (s, 1C, 1-C), 50.49 (d, 1C, 4-C), 44.50 (s, 1C, 3-C), 40.81 (t, 1C, 7-C), 30.83 (t, 1C, 1`-C), 30.08 (t, 1C, 6-C), 28.14 (q, 1C, 8-C), 25.05 (t, 1C, 5-C), 23.44 (q, 1C, 9-C), 18.15 (q, 1C, 10-C).

*4.32. (8R,10R)-7,13,13-trimethyldispiro[1,3-oxazaperhydroine-6,2′-bicyclo[2.2.1]heptane-3′,2″-indane] (**44**)*

To a stirred solution of **37** (0.166 g, 0.56 mmol) in 0.5 ml formic acid, 0.3 ml 40% aqueous solution of formaldehyde was added at room temperature and the mixture was refluxed for 1.5 h (the reaction progress was monitored by TLC). The reaction was quenched with 10% aqueous solution of NaOH and extracted with Et_2O. The organic extract was dried over anhydrous Na_2SO_4 and the solvent evaporated *in vacuo*. The crude product was purified by column chromatography (Φ = 17 mm, h = 380 mm, 20 g silica gel, CH_2Cl_2/CH_3OH = 100:1), to give 0.120 g, (67%) of **44** as colorless crystals. Mp 75–76 °C $[\alpha]_D^{20}$ = −23.7 (c 0.27, $CHCl_3$). *Anal.* Calc. for $C_{22}H_{31}NO$ (325.49): C, 81.18; H, 9.60; N, 4.30. Found: C, 81.09; H, 9.53; N, 4.27%. MS (EI) *m/z* (rel. int.): 325 (M^{+}., 100), 216 (30), 142 (35), 129 (24), 115 (23), 71 (69). ^{1}H NMR (600 MHz, $CDCl_3$, 300 K) δ: 7.15–7.10 (m, 4H, arom. H), 4.00 (dd, 1H, 3′-H_a, J = 9.2, 2.2 Hz), 3.58 (d, 1H, 18-H_a, J = 17.0 Hz), 3.43 (d, 1H, 3′-H_b, J = 9.2 Hz), 3.17 and 3.04 (AB-system, 2H, 11-H, J = 16.9 Hz), 2.88 (d, 1H, 18-H_b, J = 17.0 Hz), 2.54–2.52 (m, 1H, 2′-H_a), 2.07 (s, 3H, N-CH_3), 2.02–1.94 (m, 2H, 2′-H_b, 1′-H_a), 1.69 (d, 1H, 4-H, J = 4.7 Hz), 1.66–1.57 (m, 2H, 1′-H_b, 5-H_{exo}), 1.53–1.43 (m, 2H, 5-H_{endo}, 6-H_{endo}), 1.29 (s, 3H, 8-H), 1.25–1.20 (m, 1H, 6-H_{exo}), 0.93 (s, 3H, 10-H), 0.89 (s, 3H, 9-H). ^{13}C NMR (600 MHz, $CDCl_3$, 300 K) δ: 144.66 (s, 1 arom. C), 142.25 (s, 1 arom. C), 126.51 (d, 1 arom. C), 126.28 (d, 1 arom. C), 123.81 (d, 1 arom. C), 123.36 (d, 1 arom. C), 86.30 (s, C-2), 82.01 (t, C-3′), 61.37 (d, C-4), 59.80 (s, C-3), 56.83 (s, C-1), 49.10 (t, C-2′), 48.16 (s, C-7), 44.52 (t, C-18), 42.97 (t, C-11), 38.87 (q, C-4′), 29.08 (t, C-6), 24.78 (t, C-1′), 23.89 (t, C-5), 22.92 (q, C-8, C-9), 11.72 (q, C-10).

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Appendix A. Supplementary data

CCDC 871586 and 871585 contains the supplementary crystallographic data for *R*p-**15** and *S*p-**18**, respectively. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033 or e-mail: deposit@ccdc.cam.ac.uk.

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