Pergamon

Tetrahedron: *Asymmetry* 11 (2000) 4207–4219

TETRAHEDRON: *ASYMMETRY*

Synthesis of a new class of chiral aminoalcohols and their application in the enantioselective addition of diethylzinc to aldehydes

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Received 9 September 2000; accepted 19 September 2000

Abstract

Five new aminoalcohols containing a 2,2′-bridged binaphthyl entity were synthesised and applied as auxiliaries in the enantioselective addition of Et_2Zn to ten aldehydes. While reactivities were generally high and low concentrations of aminoalcohols were found sufficient to achieve complete conversions (<1 mol%), the observed enantioselectivities were highly dependent upon auxiliary and substrate structure. Up to 97% e.e.s have been observed in the case of aromatic substrates but significantly lower degrees of asymmetric induction were found for aliphatic substrates (up to ca. 60% e.e.). Suggestions concerning the structure of the transition states based on molecular mechanics calculations are presented to rationalise different enantiocontrol.

1. Introduction

Carbon–carbon bond-forming reactions conducted under 'asymmetric' conditions result in the formation of new stereogenic centres with defined configuration, and constitute a group of either stoichiometric or substoichiometric synthetic methods for the construction of a chiral carbon framework in an enantioselective and subsequently diastereoselective fashion. The stereoselective generation of the first asymmetric centre in a target molecule is most difficult to achieve and research in the wide and steadily growing field of catalytic asymmetric synthesis is devoted to this challenge.[1] This represents, in principle, some type of enantioface discrimination of

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0957-4166/00/$ - see front matter
PII: S0957-4166(00)00381-5

prochiral entities, present either in the substrate or generated during the course of the reaction and preceding the configuration determining step. The desired enantioselectivity is brought about by interaction with a chiral auxiliary, usually an enantiopure additive which acts either as a ligand in (transition) metal catalysed reactions, or as a modifier of a reagent. With few exceptions the latter type requires at least stoichiometric amounts of auxiliary to ensure complete formation of the chiral reagent.[2] Only in cases when the unmodified reagent is significantly less reactive do auxiliaries present in substoichiometric amounts give satisfying levels of asymmetric induction. To the latter group belong organozincs,[3] which add to aldehydes[4] or in 1,4-fashion to enones[5] if various chiral auxiliaries such as diols,[6] amino-alcohols,[7] diamides and diamines,[8] oxazoline derivatives,[9] diphosphines,[10] amidophosphines,[11] phosphorus amidites,[12] or aminophosphines[13] are added. In the case of conjugate addition Ni or Cu salts are necessary to promote the conversion. Except for some diol and diamide auxiliaries, which have been applied as orthotitanate complexes, typically no further additives are required in the alkylation of aldehydes. Mechanistic investigations point to dinuclear zinc intermediates and equilibria of diastereomeric dimers.[14] As a consequence dramatic 'chiral amplification' effects have been reported in several cases.[15]

However, in the overwhelming majority of applications at least 2 mol%, typically 5 mol%, of auxiliary has to be added for optimum stereocontrol. Since numerous auxiliaries, most of them with amino and hydroxy groups, have been developed which show excellent enantioselection for both aromatic and aliphatic substrates, further investigations in this field focus on varying the structure of the zinc reagents[16] and also on economic aspects such as lowering the concentration and/or recovery of ligands and facilitating work-up procedures by using polymeric or supported auxiliaries.[17] Moreover, a clearer relationship between ligand geometry and asymmetric induction is desired to enable a rational choice of properly designed ligands for specific applications.

2. Results and discussion

Chiral diols or aminoalcohols have often been derived either from natural sources, such as amino acids or carbohydrates,[18] or make use of structural motifs which have proven their high efficiency in other asymmetric transformations. 1,1′-Binaphthyl derivatives[19] and 1,2-disubstituted ferrocenes[20] belong to the latter group. In view of high enantioselectivities observed with ligands bearing the 2,2′-bridged binaphthyl fragment **1**, which represents a *tert* amino group with a C_2-symmetrical environment,[21] this chiral entity was chosen to prepare new amino-alcohols **2** and **3** with a rather rigid backbone. Since we were also interested in a combination of axial and planar chiral elements[22] the diastereomeric aminoalcohols **4** and **5** were also investigated to test for possible synergistic effects. While in **2** and **3** exclusively binaphthyl-originated effects will operate, the influence of the ferrocene unit in **4** and **5** might become evident with matched and mismatched pairs of stereogenic centres. For comparative studies compound **6** with primary alcohol functionality was also prepared (Fig. 1). All aminoalcohols were prepared by lithium/halogen exchange of the corresponding bromides at low temperature (**2**–**5**) or more conveniently via diastereoselective *ortho*-metallation (**4** and **6**) and subsequent treatment with benzophenone or paraformaldehyde, respectively.[22b] Isolated yields of enantiopure aminoalcohols range from 70 to 90% (Scheme 1).

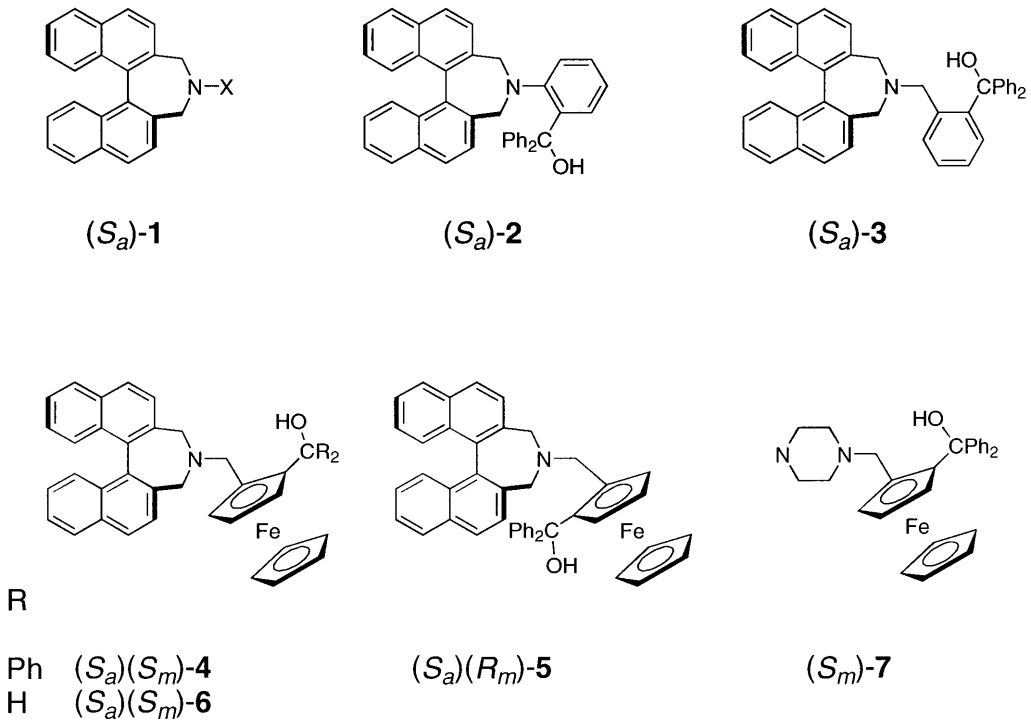
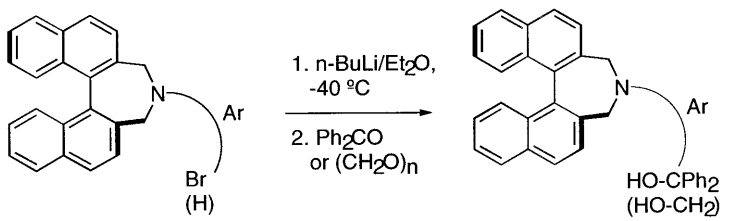


Figure 1. Chiral aminoalcohols



Scheme 1.

2.1. X-ray structures

To obtain reasonable starting geometries for molecular mechanics calculations (see below), crystal structure analyses of two aminoalcohols, (*S*)-**2** (orthorhombic space group $P2_12_12_1$, $Z=4$) and *rac*-**4** (monoclinic space group $P2_1/n$, $Z=4$) were performed (Figs. 2 and 3). Expectedly the structures show similar geometric features. In both structures the presence of a distinct hydrogen bond determines the overall geometry (O–N = 2.60 and 2.70 Å, respectively). Ph rings of the carbinol substituents adopt propeller arrangements. In *rac*-**4** one HOC(29)–C(36) lies in the Cp plane, while the second Ph ring points away from iron. Also the relative twist of Ph rings is nearly identical (75.5° in (*S*)-**2** and 77.4° in *rac*-**4**). A smaller biaryl angle of 55.5° was found in the ferrocene compound than for the *o*-phenylene-bridged analogue with 61.6°.

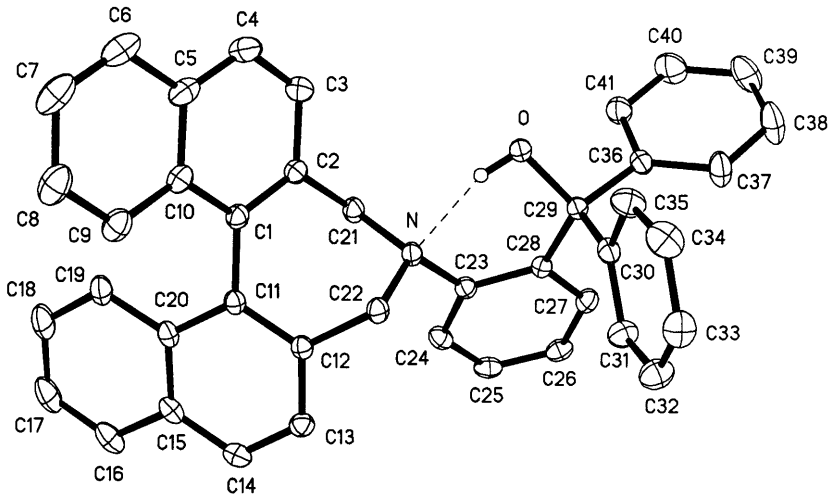


Figure 2. Crystal structure of (*S*)-**2**

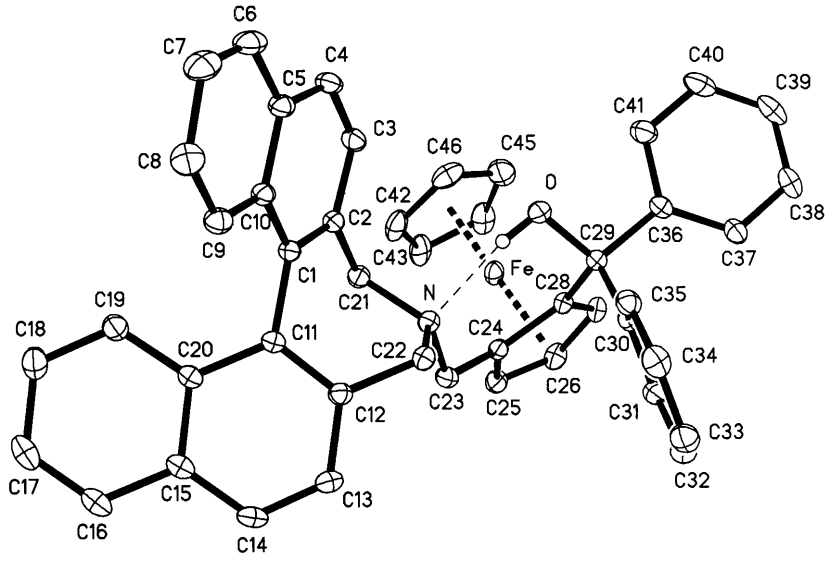


Figure 3. Crystal structure of *rac*-**2**; $(S_a)(S_m)$ configuration depicted

Asymmetric ethylations were routinely carried out on a 2 mmol scale in 5 mL of solvent at room temperature at reaction times of 24 h if not otherwise stated. After extractive work-up, the crude products were purified by Kugelrohr distillation and e.e. was determined on the basis of specific rotation and by chiral HPLC (see Section 4). To get a general view of ligand performance benzaldehyde was investigated first (Table 1). Ligands **2** and **3** showed moderate and low asymmetric induction reflecting the more efficient steric interaction in a five-membered than in a six-membered chelate ring. A significant improvement was achieved with the introduction of the ferrocene unit. Only with ligand **4** with an $(S_a)(S_m)$ configuration did the e.e. exceed 90%. In the second stereoisomer **5** the 'wrong' metallocene configuration had a deleterious effect with low e.e. Compound **5** obviously represents the stereoisomer with mismatched stereogenic centres. Also in terms of reactivity and stability **4** was outstanding; only

Table 1
Addition of diethylzinc to benzaldehyde in the presence of aminoalcohols **2**–**6**[a]

Entry	Solvent	Ligand	Temp.	Reaction time (h)	Ligand (mol%)	Isolated yield[b]	e.e.[c]
1	Toluene	**2**	rt	24	1	89	51 *S*
2	Toluene	**3**	rt	24	1	69	19 *R*
3	Toluene	**4**	rt	72	0.1	78[d]	72 *S*
4	Toluene	**4**	rt	48	0.3	77	95 *S*
5	Toluene	**4**	rt	24	1	84	96 *S*
6	Toluene	**4**	rt	24	3	81	96 *S*
7	Toluene	**4**	rt	24	5	84	95 *S*
8	Toluene	**4**	rt	24	10	75	96 *S*
9	Toluene	**4**	0°C	48	5	77	94 *S*
10	Toluene	**4**	−10°C	48	5	79	94 *S*
11	THF	**4**	rt	24	5	76	95 *S*
12	Hexane	**4**	rt	24	5	79	**97** *S*
13	Toluene	**5**	rt	24	1	79	2 *S*
14	Toluene	**6**	rt	24	5	79	78 *S*

[a] 2 mmol scale; for details see Section 4.
[b] After Kugelrohr distillation.
[c] By HPLC: Daicel® OD-H.
[d] Conversion (NMR).

0.3 mol% were required to effect complete conversion after 48 h at room temperature. At this concentration the enantioselectivity was nearly unchanged. Neither temperature nor the nature of solvent had a significant effect on the stereoselectivity of the reaction. The primary aminoalcohol **6** proved to be less selective with 78% e.e., which may be attributed to the absence of a screw-shaped arrangement of phenyl groups, a structural feature often considered favourable for efficient chirality transfer.

Table 2
Asymmetric induction in the addition of diethylzinc to aldehydes[a]

R =	Auxiliary (e.e. product configuration (isolated yield))			
	(S_a)-**2**	(S_a)-**3**	(S_a)(S_m)-**4**	(S_a)(R_m)-**5**
C_6H_5	51 *S* (86)	19 *R* (69)	96 *S* (84)	2 *S* (79)
p-CH_3O–C_6H_4	n.d.	22 *R* (85)	92 *S* (91)	6 *S* (90)
p-Cl–C_6H_4	n.d.	12 *R* (52)	93 *S* (80)	1 *R* (97)
2-Naphthyl	n.d.	24 *R* (71)	92 *S* (90)	9 *S* (79)
$C_5H_5FeC_5H_4$	74 *S* (87)	40 *R* (82)	94 *S* (82)	62 *R* (83)
C_6H_5–CH=CH	18 *S* (82)	9 *R* (74)	59 *S* (86)	7 *R* (90)
CH_3–CH=CH	n.d.	7 *R*[b] (53)	63 *S*[b] (77)	1 *S*[b] (62)
$(CH_3)_2CH$	n.d.	6 *R* (73)	47 *S* (72)	17 *R* (73)
c-C_6H_{11}	58 *S* (73)	7 *R* (46)	92 *S* (87)	22 *S* (80)
n-C_5H_{11}	55 *S* (80)	11 *S* (74)	56 *S* (76)	2 *R* (74)

[a] 2 mmol scale in toluene for aromatic substrates; in *n*-hexane for aliphatic substrates, with 1 mol% of aminoalcohol; reaction time: 24 h at room temperature; for details see Section 4.
[b] Tentative assignment.

Further application to other aromatic and aliphatic aldehydes showed similar trends (Table 2). Enantioselectivities with **4** ranging between 92 and 96% e.e. and for aromatic substrates were found to be close to the results obtained with solely planar chiral ferrocenyl aminoalcohols such as **7**.[23] In contrast aliphatic substrates showed generally moderate asymmetric induction (47–63% e.e.) with the exception of *c*-hexylcarbaldehyde (92% e.e.). With ligands **3** and **5** the degree of asymmetric induction is low with prevailing *R*-configuration of products in the case of **3**. Application of aminoalcohol **2** afforded exclusively products with opposite configuration and improved enantioselectivity, which can be attributed to increased conformational stability.

A rationalisation of our findings was attempted on the basis of reported mechanisms and suggested structures for transition states.[14,21c] Depending on the backbone of the auxiliary the ethylzinc alcoholate forms five- to seven-membered chelates and coordinates a second molecule of diethylzinc at the oxygen atom of the chelate. This arrangement might be well suited to form a chair-like transition state with the aldehyde substrate in which the substituent R adopts either a pseudo-equatorial or axial position (Fig. 4). To get some insight into relative stabilities of transition states molecular mechanics calculations were performed for **2**–**5** and the ferrocene ligand **7** with benzaldehyde as the substrate. We used the commercial program SYBYL with the Tripos force field[24] and introduced reasonable constraints for distances (Zn–O, Zn–N, Zn–CH_2–) and the bite angle (O–Zn–N) from X-ray structures.[14b,25] The distance constraints within the proposed six-membered transition state were set to reasonable values, while angles were fixed to 109° except for Zn–O–C, where 120° seemed a better approximation. This simple model for a more product-like transition state should be useful to give minimum geometries based solely on steric interactions and at least identify the more stable transition states. In the case of a seven-membered chelate ring (**I**) a chair-like conformation is found (**3**–**5** and **7**), while for **2**, with a six-membered chelate, an envelope geometry was found. For the six-membered transition state (**II**) a chair or half-chair geometry resulted, independent of the substrate (R = Ph) being in an axial or equatorial position. Expectedly, in all cases the equatorial Ph gives rise to the more stable species. Their configurations agree with the predominantly formed enantiomer (Fig. 5). Despite the simplicity of the model applied, the different degrees of asymmetric induction are well reflected by relative energy differences between axial and equatorial Ph in the

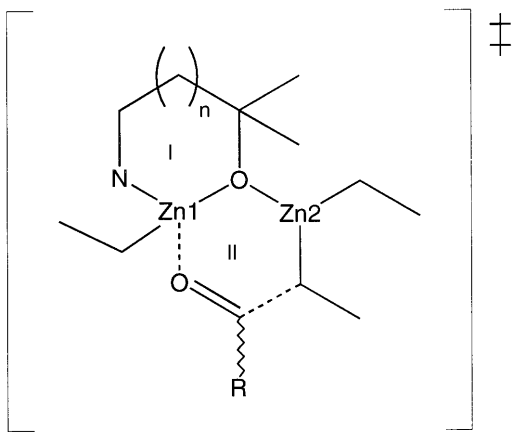
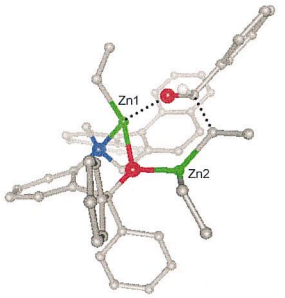
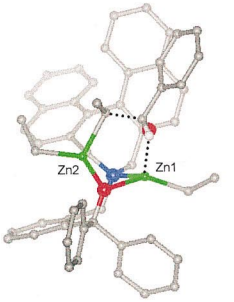
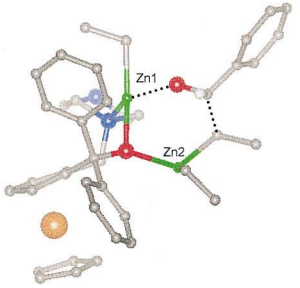


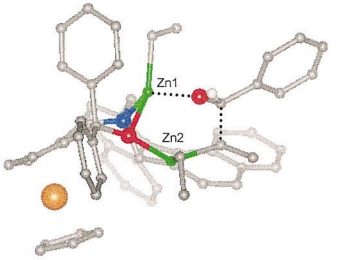
Figure 4. Proposed transition state

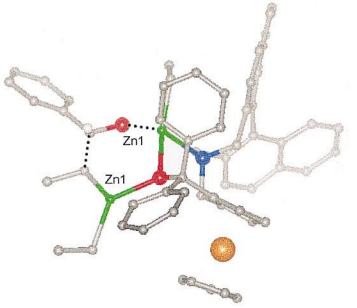




	A	*B*
auxiliary	(S_a)-**2**	(S_a)-**3**
product	*S*	*R*
$\Delta E_{ax\text{-}equ}$	1-2 kcal	3 kcal







	C	*D*	*E*
auxiliary	(S_m)-**7**	$(S_a)(S_m)$-**4**	$(S_a)(R_m)$-**5**
product	*S*	*S*	*R*
$\Delta E_{ax\text{-}equ}$	7-8 kcal	5 kcal	1-2 kcal

Figure 5. Proposed transition states for enantioselective addition of Et_2Zn to benzaldehyde (only the more stable arrangement with equatorial *Ph*-CHO depicted)

transition states. We therefore speculate that steric effects of this type will have the most dominating effect on the enantioselectivity. Nevertheless, in addition the conformational stability of the chelate may play an important role: tentatively we assume that particularly in the case of aminoalcohol **3** in addition to a 'most stable' chelate also one or more other conformers may be populated which eventually favour opposite product configurations (Fig. 6). It seems that conformationally more stable chelates generally afford higher degrees of enantioselectivity. This might be better met with five- or six-membered chelates but also through the incorporation of bulky substituents or condensed systems like ferrocene, which might slow down the interconversion of conformers, at least on the time-scale of the catalytic reaction.

Figure 6.

3. Conclusions

These results show once more that a combination of highly enantioselective entities with efficient chiral bias is not always sufficient to amplify asymmetric induction. It seems indeed just as important to arrange stereogenic centres relative to each other in a proper way to improve the enantioselectivity, a requirement not sufficiently fulfilled in the present case.

4. Experimental

4.1. General

Melting points: Kofler melting point apparatus, uncorrected. NMR: Bruker AM 400 spectrometer at 400.13 (^{1}H) and 100.61 MHz (^{13}C), respectively, in $CDCl_3$; chemical shifts δ are reported in ppm relative to $CHCl_3$ (7.24 or 77.00 ppm, respectively). Coupling patterns are designated as s (singlet), d (doublet), t (triplet), p (pseudo), and b (broad). $^{13}C\{^1H\}$ NMR spectra were recorded in a *J*-modulated mode; undesignated signals refer to CH-resonances. MS: MAT 900 EI (70 eV). Optical rotations were measured on a Perkin–Elmer polarimeter 241 in a 1 dm cell, thermostated. HPLC analyses were performed on an HP 1090 equipped with a diode array detector.

Petroleum ether (PE) and CH_2Cl_2 and ethyl acetate (EE) were distilled, absolute CH_2Cl_2 and toluene were distilled from CaH_2, THF from potassium benzophenone ketyl, Et_2O and *n*-hexane

from $LiAlH_4$. *n*-BuLi and *s*-BuLi were used as 1.6 and 1.3 M solutions, respectively, in hexane (Aldrich); the actual content of Li-organyl was determined prior to use by difference titration according to the method of Gilman et al.[26] Column chromatography was performed on silica gel Si 60, 25–40 μm (Merck). All the other chemicals were analytical grade and used without further purification.

(*S*)-*N*-(2-Bromobenzyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine, (*S*)-*N*-(2-bromophenyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine, $(S_a)(R_m)$-*N*-(1-bromo-2-ferrocenyl-methyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine, $(S_a)(S_m)$-*N*-(1-hydroxymethyl-2-ferro-cenylmethyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine **6**, and $(S_a)(S_m)$-*N*-(1-diphenylhydroxymethyl-2-ferrocenylmethyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine **4** were prepared according to reported procedures.[21h,22b]

4.2. (S)-N-(2-Diphenylhydroxymethylphenyl)-3,5-dihydro-4H-dinaphth[2,1-c:1′,2′-e]azepine **2**

(*S*)-*N*-(2-Bromophenyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine (450 mg, 1 mmol) was dissolved in 20 mL of dry ether, cooled to −40°C and *n*-BuLi solution (1.5 mmol) was added. After stirring for 3 h the temperature was lowered to −78°C and solid benzophenone (364 mg, 2 mmol) was introduced in one portion. Stirring was continued overnight, while the mixture reached room temperature. The reaction was quenched with water; extractive work-up with EtOAc and evaporation of solvent left the crude aminoalcohol which was purified by column chromatography (70×2 cm, EtOAc/PE, 5:95) to give (*S*)-**2** (498 mg, 90%) as a white solid. Crystallisation from Et_2O/*n*-hexane gave a crystalline sample which softened above 200°C. During melting between 250 and 300°C reformation of crystals took place which decomposed at ca. 311°C. ^{1}H NMR δ: 3.37 (1H, d, $J=14.3$ Hz), 3.68 (1H, d, $J=10.9$ Hz), 3.69 (1H, d, $J=14.3$ Hz), 3.76 (1H, d, $J=10.9$ Hz), 6.82 (1H, dd, $J=7.8$, 1.7 Hz), 7.00 (1H, dd, $J=7.8$, 1.3 Hz), 7.13 (1H, ptd, $J=7.3$, 1.3 Hz), 7.21 (1H, ptd, $J=7.6$, 1.5 Hz), 7.24–7.57 (18H, m), 7.99–8.05 (4H, m), 9.55 (1H, s). ^{13}C NMR δ: 55.64 (CH_2), 56.06 (CH_2), 82.98 (C), 125.59, 125.66, 125.79, 125.83, 125.99, 126.83, 127.08, 127.30, 127.36, 127.49, 127.53, 127.74‡, 127.76‡, 127.99, 128.05‡, 128.23, 128.36‡, 128.56‡, 128.63, 129.24, 130.53, 131.26 (C), 131.38 (C), 132.36 (C), 133.24 (C), 133.25 (C), 133.35 (C), 135.05 (C), 135.12 (C), 143.82 (C), 147.54 (C), 147.57 (C), 150.80 (C). MS (150°C) *m*/*z*: 535 (8%, M^+). HRMS: calcd for $C_{41}H_{31}NO$: 553.2406; found: 553.2411. $[\alpha]_D^{22}$ +135.0 (*c* 0.739, CH_2Cl_2).

4.3. (S)-N-(2-Diphenylhydroxymethylbenzyl)-3,5-dihydro-4H-dinaphth[2,1-c:1′,2′-e]azepine **3**

The preparation was conducted essentially the same way as described for (*S*)-**2** but with (*S*)-*N*-(2-bromobenzyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine as the educt to give (*S*)-**3** as white foam (89%). ^{1}H NMR δ: 3.08 (1H, d, $J=12.9$ Hz), ~3.15 (2H, bs), 3.22 (1H, d, $J=12.9$ Hz), 3.41 (2H, d, $J=12.5$ Hz), 6.74 (1H, d, $J=8.0$ Hz), 7.16 (1H, m), 7.22–7.56 (20H, m), 7.93 (2H, d, $J=8.0$ Hz), 7.95 (2H, d, $J=8.0$ Hz), 10.02 (1H, s). ^{13}C NMR δ: 58.70 (CH_2), 81.93 (C), 125.64, 125.89, 126.72, 126.85, 127.26, 126.40, 127.62, 127.76 (2×CH), 127.80, 127.86, 128.09, 128.31, 128.64 (b), 130.64, 131.38 (C), 133.23, 133.28 (C), 135.14 (C), 136.16 (C), 147.48 (C), 147.89 (C), 149.32 (C) (signals due to one C and one CH_2 were missing). MS (220°C) *m*/*z*:

‡ One of these five signals corresponds accidentally to two chemically different CH_{ar}, the remaining four resonances arise from *ortho* and *meta* CH of phenyl groups.

567 (60%, M^+), 549 (7%), 490 (19%), 465 (5%), 385 (5%), 294 (100%). HRMS: calcd for $C_{42}H_{33}NO$: 567.2562; found: 567.2573. $[\alpha]_D^{20}$ +76.7 (*c* 0.788, CH_2Cl_2).

4.4. (S_a)(R_m)-N-*(1-Diphenylhydroxymethyl-2-ferrocenylmethyl)-3,5-dihydro-4*H*-dinaphth-[2,1-*c*:1′,2′-*e*]azepine **5**

A similar procedure was applied as given for the preparation of (*S*)-**2**, except that (S_a)(R_m)-*N*-(1-bromo-2-ferrocenylmethyl)-3,5-dihydro-4*H*-dinaphth[2,1-*c*:1′,2′-*e*]azepine was used as starting material and the lithiation was performed at room temperature with *s*-BuLi; yield: 66%, yellow foam. ^{1}H NMR δ: 2.82 (1H, d, J=13.4 Hz), 3.00 (2H, bd, J=11.0 Hz), 3.52 (2H, bd, J=11.0 Hz), 3.87 (1H, m), 3.91 (1H, d, J=13.4 Hz), 4.00 (1H, m), 4.05 (5H, s), 4.07 (1H, pt, J=2.5 Hz), 7.01 (2H, bd, J=7.5 Hz), 7.19–7.45 (14H, m), 7.55 (2H, bd, J=7.5 Hz), 7.83 (2H, d, J=8.5 Hz), 7.90 (2H, d, J=8.0 Hz), 8.48 (1H, s). ^{13}C NMR δ: 54.22 (CH_2), 54.43 (CH_2), 65.42, 69.85 (Cp), 70.57, 71.20, 77.59 (C), 81.91 (C), 96.09 (C), 125.52, 125.77, 126.23, 126.70, 127.08, 127.22, 127.36, 127.66, 127.80, 127.82, 128.23, 128.34, 131.30 (C), 132.87 (C), 133.19 (C), 135.05 (C), 147.44 (C), 150.26 (C). MS (230°C) m/z: 675 (100%, M^+), 610 (25%), 537 (5%), 493 (6%), 366 (42%). HRMS: calcd for $C_{46}H_{37}FeNO$: 675.2225; found: 675.2227. $[\alpha]_D^{20}$ +38.6 (*c* 1.04, CH_2Cl_2).

4.5. Enantioselective addition of Et_2Zn to aldehydes (general procedure)

A degassed solution of aminoalcohol in 2 mL of the specified solvent was prepared in a 10 mL Schlenk tube. The substrate (2 mmol) was added at room temperature, followed by addition of Et_2Zn (3.2 mmol) via syringe at the intended reaction temperature. The reaction was kept under Ar with stirring routinely for 24–72 h. Et_2O (20 mL) and saturated NH_4Cl solution (10 mL) were added carefully and the organic layer was separated. The aqueous layer was extracted twice with Et_2O (5 mL). The combined extracts were again washed with NH_4Cl and dried with $MgSO_4$. After careful evaporation of solvent under vacuum without heating to avoid loss of low boiling products, the carbinols were purified by bulb-to-bulb distillation or chromatography (1-ferrocenylpropan-1-ol). Chemical integrity was checked by ^{1}H NMR, the enantiomeric excess was determined directly by enantioselective HPLC and specific rotation, or of the corresponding benzoate in the case of aliphatic products (see below).

4.6. Derivatisation of carbinols with benzoyl chloride (gereral procedure)

To 20–25 μL of carbinol in a vial was added subsequently 0.2 mL of CCl_4 p.a., 25 μL of freshly distilled benzoyl chloride and three drops of pyridine. The vial was stoppered and kept overnight at room temperature. Water (1 mL) and Et_2O (2 mL) were added. After shaking the aqueous layer was removed and the organic phase was dried with a small amount of $MgSO_4$. The solvent was evaporated and the sample was evacuated at an oil pump to remove traces of pyridine (10–20 min). If side products are present (DC) the benzoate may be filtered over a short column of SiO_2 (Pasteur pipette) in Et_2O.

4.7. Enantioselective HPLC of products

HPLC: Chiralcel OD-H (Daicel) 250×4.6 mm, room temperature, flow rate: 0.5 mL min^{-1},

detection at 230 and 254 nm, samples: 1 mg mL^{-1} dissolved in 2-PrOH/*n*-hexane (5:95), 5 μL injected. For specific rotations highest reported values are given, if necessary corrected for enantiomerically pure compounds.

1-Phenyl-1-propanol: MW 136.19, Kp: 103°C (14 mm), $[\alpha]_D^{22}$ −48.5 (*c* 4, $CHCl_3$),[23] HPLC in 3.8% 2-PrOH, 0.2% HOAc, 96% *n*-hexane, 16.63 min (+)-(*R*), 17.86 min (−)-(*S*).

1-(4-Chlorophenyl)-1-propanol: MW 170.64, Kp: 91°C (1 mm), $[\alpha]_D^{21}$ −28.6 (*c* 5.1, benzene),[27] HPLC in 3.8% 2-PrOH, 0.2% HOAc, 96% *n*-hexane, 15.04 min (−)-(*S*), 16.08 min (+)-(*R*).

1-(4-Methoxyphenyl)-1-propanol: MW 166.22, Kp: 102°C (0.7 mm), $[\alpha]_D^{21}$ −36.5 (*c* 5.1, benzene),[27] HPLC in 3.8% 2-PrOH, 0.2% HOAc, 96% *n*-hexane, 21.21 min (+)-(*R*), 24.13 min (−)-(*S*).

1-Phenylpent-1-en-3-ol: MW 162.23, Kp: 121–123°C (1.5 mm), $[\alpha]_D^{21}$ −6.53 (*c* 3.2, $CHCl_3$),[27] HPLC in 10% 2-PrOH, 0.5% HOAc, 89.5% *n*-hexane, 10.22 min (+)-(*R*), 13.31 min (−)-(*S*).

1-(2-Naphthyl)-1-propanol: MW 186.25, $[\alpha]_D$ −28.2 (*c* 3.4, benzene),[28] HPLC in 10% 2-PrOH, 90% *n*-hexane, 18.37 min (−)-(*S*), 20.61 min (+)-(*R*).

1-Ferrocenylpropan-1-ol: MW 244.12, $[\alpha]_D^{20}$ +56 (*c* 1.40, benzene), HPLC: Daicel OD-H, 2% 2-PrOH, 0.1% HOAc, 97.9% *n*-hexane, 16.67 min (−)-(*R*), 17.64 min (+)-(*S*).

3-Octanol: MW 130.23, Kp: 175–177°C, $[\alpha]_D^{20}$ +12.5 (*c* 1.29, $CHCl_3$),[29] HPLC (benzoate) in 0.06% 2-PrOH, 99.94% *n*-hexane, 13.66 min (*S*), 14.35 min (*R*).

5-Methyl-3-hexanol: MW 116.20, Kp: 146–148°C, $[\alpha]_D^{22}$ +20.3 (*c* 3.7, EtOH),[23] HPLC (benzoate) in 0.06% 2-PrOH, 99.94% *n*-hexane, 11.81 min (*S*), 12.51 min (*R*).

1-Cyclohexyl-1-propanol: MW 142.29, Kp: 85–86°C (9 mm), $[\alpha]_D$ −8.1 (*c* 7, Et_2O),[23] HPLC (benzoate) in 0.1% 2-PrOH, 99.9% *n*-hexane, 12.80 min (*R*), 13.33 min (*S*).

Hex-4-en-3-ol: MW 100.16, Kp: 133–135°C, $[\alpha]_D$ −2.8 (*c* 1.3, $CHCl_3$),[6d] HPLC (benzoate): in 0.07% 2-PrOH, 99.93% *n*-hexane, 14.40 min (*R*), 15.14 min (*S*).

4.8. X-ray structure analyses

4.8.1. Crystal data for (S)-**2**

$C_{41}H_{31}NO$, $M=553.67$, orthorhombic, space group $P2_12_12_1$, $a=8.987(4)$, $b=14.493(6)$, $c=23.238(9)$ Å, $\alpha=90$, $\beta=90$, $\gamma=90°$, $U=3027(2)$ Å^3, $Z=4$, $D_c=1.215$ g cm^{-3}, $T=297(2)$ K, $\mu=0.072$ mm^{-1}, $\lambda=0.71073$ Å, $F(000)=1168$, colourless block (0.76×0.60×0.42 mm). Data were collected on a Siemens SMART 3-circle diffractometer with a CCD area detector and graphite monochromatised Mo Kα radiation by recording 4×606 ω-scan frames ($\Delta\omega=0.3°$, $t=15$ s) covering a complete sphere of the reciprocal space, $\theta_{max}=30°$. Corrections for absorption applied. Structure solution by direct methods, refinement by full-matrix least-squares on F^2, absolute structure known from chemistry, data/restraints/parameters=8722/0/393; final $R_1=0.0465$, $wR_2=0.1031$ (all data). CCDC 182/151223.

4.8.2. Crystal data for (±)-**4**

$C_{46}H_{37}FeNO$, $M=675.62$, monoclinic, space group $P2_1/n$, $a=8.750(8)$, $b=25.89(2)$, $c=15.354(14)$ Å, $\alpha=90$, $\beta=98.57(2)$, $\gamma=90°$, $U=3440(5)$ Å^3, $Z=4$, $D_c=1.304$ g cm^{-3}, $T=297(2)$ K, $\mu=0.476$ mm^{-1}, $\lambda=0.71073$ Å, $F(000)=1416$, orange block (0.70×0.55×0.35 mm). Data collected on a Siemens SMART diffractometer (see above), $\theta_{max}=27.5°$. Corrections for

absorption applied. Structure solution by direct methods, refinement by full-matrix least-squares on F^2 (SHELX-97).[30] Data/restraints/parameters = 7890/0/446; final $R_1 = 0.0523$, $wR_2 = 0.1063$ (all data). CCDC 182/151224.

Acknowledgements

This work was generously supported by the *Fonds zur Förderung der Wissenschaftlichen Forschung in Österreich* (P11990-CHE). N.A. thanks the European Union for a grant within the SOKRATES program.

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