Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 3409–3416

TETRAHEDRON: *ASYMMETRY*

Highly stereoselective synthesis of 1,3-aminoalcohols via Mannich reactions

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Received 26 July 1999; accepted 9 August 1999

Abstract

Diastereoselective synthesis of β-amino ketones by a one-pot Mannich reaction and their subsequent reduction afforded sterically congested enantiomerically pure 1,3-aminoalcohols in high diastereoselectivity: *dr* up to >98:<2 over two steps. The absolute configurations of the newly created stereogenic centers were assigned by NMR spectroscopy and chemical correlation.

1. Introduction

Considering the widespread interest in stereoselective organic chemistry towards the end of this century, the synthesis of optically active aminoalcohols still remains an attractive and challenging target.[1–3] Since these compounds have found enormous applications as chiral ligands in metal-mediated organic reactions, there has been a continual interest aimed at their structure modification. In particular, 1,2-aminoalcohols have received much attention, not least because they are generally readily accessible in enantiomerically pure form in a few steps from natural precursors, e.g. α-amino acids, carbohydrates, camphor, etc. With regard to 1,3- and 1,4-aminoalcohols as chiral auxiliaries, especially as ligands in enantioselective catalysis, publications focused on the design and application of these compounds are rather rare and only a few results are known.[4–6] This prompted us to prepare new sterically congested 1,3-aminoalcohols by highly diastereoselective reduction of β-amino ketones prepared before by Mannich reactions.[7]

In the context of our studies on the utilization of industrial waste materials we used the enantiomerically pure 2-azabicyclo[3.3.0]octane **2c** as the starting material for the synthesis of the new chiral auxiliaries.[8]

The chiral heterocyclic amine **2c** could be prepared by the cyclohexen-2-one catalyzed thermal decarboxylation of **2b**,[9] a derivative of the non-recyclable enantiomerically pure benzyl 2-

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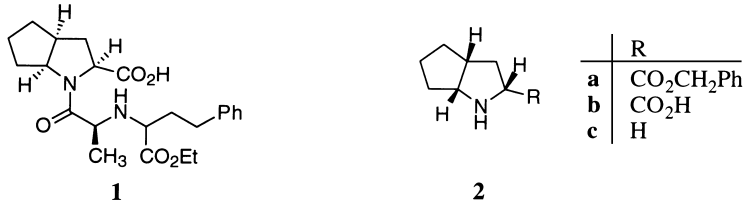
0957-4166/99/$ - see front matter
PII: S0957-4166(99)00342-0

azabicyclo[3.3.0]octane-3-carboxylate **2a**, which was obtained as a waste material in the process of synthesizing the angiotensin converting enzyme inhibitor Ramipril **1** by Hoechst AG (Scheme 1).[10]

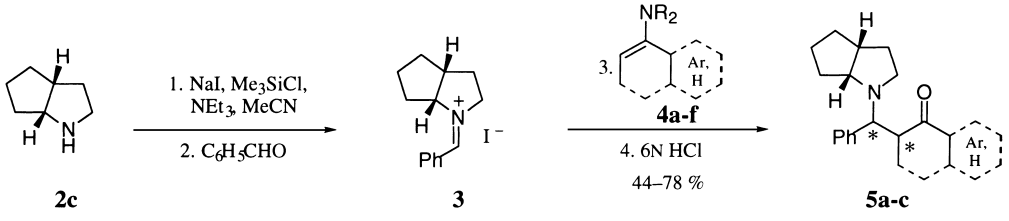


1 **2**

Scheme 1.

2. Results and discussion

The general synthesis of β-amino ketones **5a–c** by reaction of optically active amine **2c** with benzaldehyde and several enamines **4a–f** is shown in Scheme 2. In a one-pot procedure the secondary amine **2c** was first silylated by Me_3SiI (generated in situ from Me_3SiCl, NaI and NEt_3), followed by the addition of benzaldehyde to afford the corresponding iminium salt **3**, which was finally used without further purification for the aminoalkylation of enamines **4a–f**.[11]



2c **3** **5a-c**

Scheme 2.

Enamine **4a** (Table 1) was aminoalkylated according to this general procedure providing β-amino ketone **5a** after acidic work-up. Based on the ^1H NMR data, on the integrals of a doublet originating from the single benzylic proton H1′, a diastereomeric ratio of *dr* (83:17) was determined.

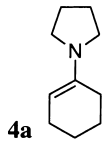
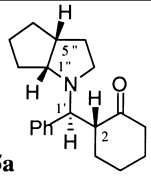
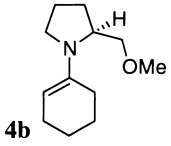
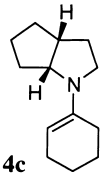
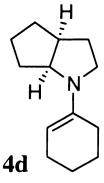
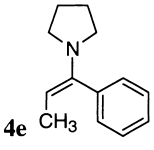
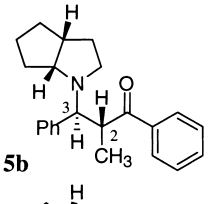
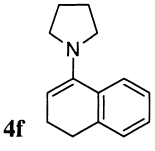
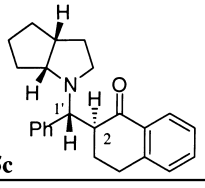
With the intention of improving the stereochemical outcome of this reaction, enantiomerically pure enamines **4b–d** were used for the synthesis of ketone **5a**. As can be seen from Table 1, the bicyclic pyrrolidine analog **4d** was aminoalkylated with higher diastereoselectivity compared to **4a** [entries 1 and 4 (matched situation)] whereas the optical antipode **4c** as well as SMP-enamine **4b** afforded **5a** only in moderate diastereomeric ratios [entries 2 and 3 (mismatched situation)]. However, as indicated by the coupling constant value between H1′ and H2, two *anti*-configured diastereomeric β-amino ketones were formed in all four cases ($J_{H1'H2}$=11.6 Hz for major diastereomer, $J_{H1'H2}$=9.4 Hz for minor diastereomer).

Using α-tetralone and propiophenone based optically inactive enamines **4e–f**, the corresponding β-amino ketones **5b** and **5c** were each produced as a single and *anti*-configured diastereomer (**5b**: J_{H3H2}=11.2 Hz, **5c**: $J_{H1'H2}$=9.4 Hz, entries 5 and 6).

Although it is known that β-amino ketones are generally sensitive towards heating or any purification method,[12] we were able to isolate the major diastereomers of **5a–c** by column chromatography on silica gel and store these Mannich bases in the refrigerator for several weeks without loss of chemical or enantiomeric purity.

The reduction of diastereomerically pure β-amino ketones **5a–c** by $LiAlH_4$ at −70°C afforded the corresponding 1,3-aminoalcohols **6a–c** in excellent chemical yields between 91 and 94% (Scheme 3).

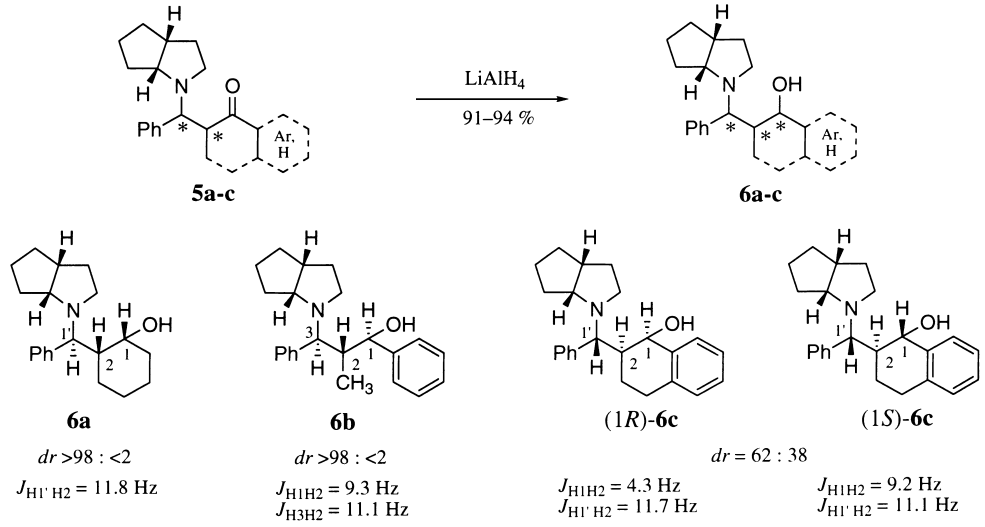
Table 1
Diastereoselective synthesis of β-amino ketones **5** via Mannich reaction

Entry	Enamine	β-Amino ketone[a)]	*dr* (anti / syn)[b)]	*dr* (anti / anti)[b)]
1	 **4a**	 **5a**	>98 : <2	83 : 17
2	 **4b**	**5a**	>98 : <2	74 : 26
3	 **4c**	**5a**	>98 : <2	57 : 43
4	 **4d**	**5a**	>98 : <2	92 : 8
5	 **4e**	 **5b**	>98 : <2	>98 : <2
6	 **4f**	 **5c**	>98 : <2	>98 : <2

a) The major diastereomer is illustrated. b) The diastereomeric ratios were determined for the crude products by ^{1}H- and ^{13}C-NMR.

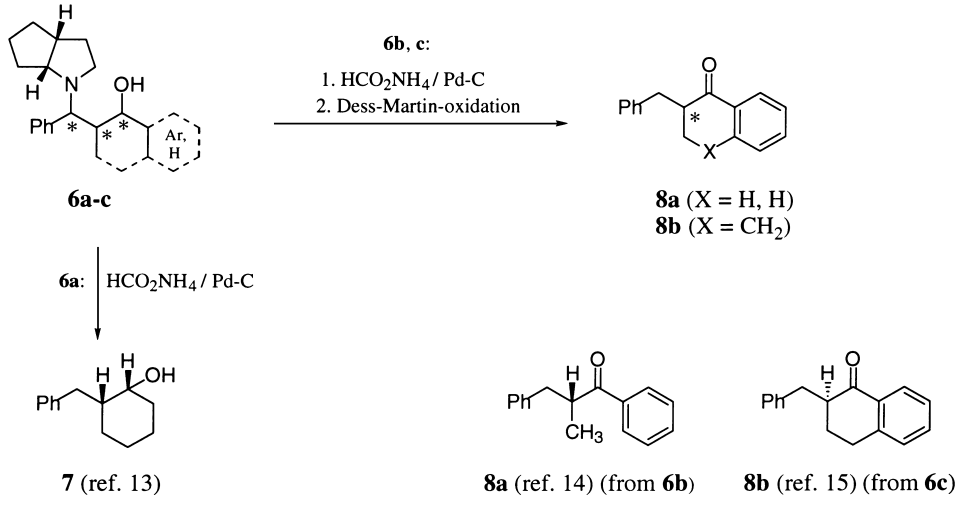
Concerning the stereoselectivity, the formation of only one diastereomer was observed for aminoalcohol **6a** as well as for **6b** (*dr* >98:<2). In contrast, the reduction of **5c** provided two stereoisomers, namely (1*R*)-**6c** and (1*S*)-**6c** in a ratio of *dr* (62:38). By using DIBAH instead of $LiAlH_4$ at −70°C, 1,3-aminoalcohol (1*R*)-**6c** was obtained completely diastereoselectively.

Based on the value of vicinal coupling constants between H1 and H2 as well as H1′ and H2, respectively, H3 and H2 the relative configurations of compounds **6b–c** were assigned, but determination of the absolute stereochemistry was not possible by NMR spectroscopy. Concerning aminoalcohol **6a**, neither the complete relative nor the absolute configuration could be established by this method. Therefore, we decided to pursue the chemical correlation by converting aminoalcohols **6a–c** to the well-



Scheme 3.

known optically active α-substituted cyclohexanol, respectively, propanone and indanone derivatives **7**, **8a** and **8b** (Scheme 4).



Scheme 4.

In the case of aminoalcohol **6a**, the benzylic carbon–nitrogen bond was cleaved by treatment with HCO_2NH_4/Pd–C resulting in the formation of the enantiomer of the known (1*S*,2*S*)-configured α-benzylcyclohexanol **7**,[13] which now allowed the absolute stereochemistry at position C1′ to be assigned based on the coupling constant between the benzylic proton H1′ and H2 of **6a** (Scheme 4).

Aminoalcohols **6b** and (1*R*)-**6c** [or (1*S*)-**6d**] were then subjected to the same procedure (Scheme 4) as described for **6a**, but the corresponding propanol and indanol derivatives were subsequently oxidized to the known chiral ketones **8a** and **8b**. Due to the agreement of the obtained analytical data for **8a**,**b** with those described for these compounds in the literature,[14,15] the absolute configuration of **8a** was assigned as *R* and of **8b** as *S*. Consequently, based on these results the stereochemical assignment for aminoalcohols **6b**,**c** and amino ketones **5b**,**c**, respectively, was carried out in the same manner as described above.

In summary, we have shown that 1,3-aminoalcohols **6** may be obtained in high stereoselectivity by Mannich reactions and successive reductions of the amino ketones **5**. Nevertheless, the application of 1,3-aminoalcohols **6a–c** as chiral auxiliaries in the enantioselective addition of diethylzinc to benzaldehyde is under investigation at present.

3. Experimental

All reactions were carried out in oven dried glassware, under argon atmosphere using anhydrous solvents. Optical rotations were measured on a Perkin–Elmer polarimeter 241 MC. IR spectra were recorded on a Philips PU 9706 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AM 300 (300 MHz) spectrometer using TMS as internal standard. Mass spectra were measured with a Finnigan-MAT 212 (data system SS 300; CI, isobutane). Elemental analyses (CHN) were performed by using a Carlo Erba Stumentalione (MOD 1104) analyzer. The enamines **4** were either purchased, or synthesized according to literature procedures: **4a** (Aldrich), **4b–f**.[16]

*3.1. General procedure for the synthesis of β-amino ketones **5a–d** (GP 1)*

To a solution of 1.65 g (11 mmol) anhydrous NaI in 11 mL dry acetonitrile were added 0.56 g (5 mmol) amine **2c**, 0.51 g (5 mmol) NEt_3 and 1.19 g (11 mmol) Me_3SiCl. After stirring for 1 h, 0.53 g (5 mmol) freshly distilled benzaldehyde was added and stirring was continued for a further 1 h 30 min. Subsequently, 5 mmol of enamine **4** were added and the reaction mixture was stirred for 2 h at ambient temperature. The mixture was acidified with 20 mL 6N HCl and stirred for 30 min, then basified with aqueous NaOH (20%) and extracted with Et_2O (3×10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. The major diastereomer was isolated by column chromatography on silica gel 60.

*3.1.1. (1′S,1′′R,2R,5′′R)-2-[Phenyl-(1′-(2′′-azabicyclo[3.3.0]octane-2′′-yl)methyl]cyclohexanone **5a***

Synthesis according to GP 1; diastereomeric ratio: see Table 1. Eluent: *n*-hexane:NEt_3 (7:3), R_f-value: 0.74, yield: 1.08 g (73%). $[\alpha]_D^{20}$ −45.1 (*c*=1.11, CH_2Cl_2). IR (NaCl): ν=1700 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): δ=1.24–2.37 (2m, 17H, 2×H3, 2×H4, 2×H5, 2×H6, 2×H4′′, H5′′, 2×H6′′, 2×H7′′, 2×H8′′); 2.69 (m, 2H, 2×H2′′); 3.03 (m, 1H, H1′′); 3.12 (m, H, H2); 4.31 (d, *J*=11.69 Hz, 1H, CHN); 7.16–7.42 (2m, 5H, aromatic-H). ^{13}C NMR ($CDCl_3$, 75.47 MHz): δ=20.62, 23.97, 28.01, 29.31, 31.21, 31.52, 33.14, 38.99 (C3, C4, C5, C6, C4′′, C6′′, C7′′, C8′′); 40.91 (C5′′); 45.92 (C2); 53.02 (C2′′); 62.35, 64.21 (C1′, C1′′); 127.31, 127.88, 129.59 (aromatic-C); 134.09 (q.-aromatic-C); 212.93 (CO). MS (CI, isobutane): m/z (%)=298 (95) [MH^+]; 200 (100) [$M^+-C_6H_9O$]. $C_{20}H_{27}NO$ (297.4): calcd C 80.76, H 9.15, N 4.71; found C 80.39, H 9.02, N 4.50.

*3.1.2. (1′R,2R,3S,5′R)-3-(-2′-Azabicyclo[3.3.0]octane-2′-yl)-2-methylpropanone **5b***

Synthesis according to GP 1. Diastereomeric ratio: *dr* >95:5. Eluent: *n*-hexane:ethyl acetate (8:2), addition of 2% NEt_3. R_f-value: 0.68, yield: 1.16 g (70%). $[\alpha]_D^{20}$ −81.0 (*c*=0.75, CH_2Cl_2). IR (KBr): ν=1740 cm^{-1} (CO). ^{1}H NMR ($CDCl_3$): δ=0.98 (d, *J*=6.58 Hz, 3H, CH_3); 1.11–1.58 (m, 7H, H4′, 2×H6′, 2×H7′, 2×H8′); 1.74–1.92 (m, 2H, H4′, H5′); 2.04 (m, 1H, H2′); 2.67–2.76 (2m, 2H, H2′, H1′); 4.15 (d, *J*=11.21 Hz, 1H, CHN); 4.30 (m, 1H, H2); 7.25–7.57, 8.01 (2m, 10H, aromatic-H). ^{13}C NMR ($CDCl_3$): δ=15.50 (CH_3); 24.04, 30.65, 31.24, 33.24 (C4′, C6′, C7′, C8′); 40.83, 41.96 (C2, C5′); 46.81 (C2′); 64.58, 67.69 (C1′, C3); 127.10, 127.57, 127.79, 127.94, 128.32, 129.73, 132.11 (aromatic-

C); 134.47, 138.89 (aromatic-C); 205.20 (CO). MS (CI, isobutane): m/z (%)=334 (64) [MH^+]; 200 (100) [$M^+-C_9H_9O$]. $C_{23}H_{27}NO$ (333.47): calcd C 82.84, H 8.16, N 4.20; found C 82.64, H 8.11, N 4.17.

*3.1.3. (1′*R*,1′′*R*,2*S*,5′′*R*)-2-[Phenyl-(1′-(2′′-azabicyclo[3.3.0]octane-2′′-yl)methyl]1,2,3,4-tetrahydro-1-naphthalinone* ***5c***

Synthesis according to GP 1. Diastereomeric ratio: *dr* >95:5. Eluent: *n*-hexane:NEt_3 (8:2). R_f-value: 0.71, yield: 1.34 g (78%). $[\alpha]_D^{20}$ −5.6 (*c*=0.85, CH_2Cl_2). IR (KBr): ν=1710 cm^{-1} (CO). ^1H NMR ($CDCl_3$): δ=1.18–1.84 (m, 9H, 2×H4′′, H5′′, 2×H6′′, 2×H7′′, 2×H8′′); 2.03 (m, 1H, H3); 2.25 (m, 2H, H3, H4); 2.82 (m, 2H, H4, H2′′); 3.05 (m, 2H, H1′′, H2′′); 3.42 (m, 1H, H2); 4.25 (d, *J*=9.43 Hz, 1H, CHN); 7.21–7.47, 7.97 (2m, 9H, aromatic-H). ^{13}C NMR ($CDCl_3$): δ=24.06, 25.71, 31.68, 33.09 (C3, C4, C4′′, C6′′, C7′′, C8′′); 41.44 (C5′′); 48.14, 49.76 (C2, C2′′); 62.67, 65.04 (C1′, C1′′); 126.37, 127.13, 127.39, 127.77, 128.54, 129.58, 132.62 (aromatic-C); 133.61, 135.74, 142.44 (aromatic-C); 199.61 (CO). MS (CI, isobutane): m/z (%)=346 (66) [MH^+]; 200 (100) [$MH^+-C_{10}H_9O$]. $C_{24}H_{27}NO$ (345.48): calcd C 83.44, H 7.88, N 4.05; found C 82.98, H 7.90, N 3.99.

3.2. General procedure for the synthesis of 1,3-aminoalcohols ***6a–c*** *by reduction of amino ketones* ***5a–c*** *(GP 2)*

A solution of 3 mmol of the respective β-amino ketone **5** in 10 mL anhydrous THF was cooled down to −70°C. $LiAlH_4$ (0.15 g, 4 mmol) was cautiously added in three portions and the reaction mixture was stirred for 1 h 30 min at this temperature. Excess reducing reagent was destroyed by adding 2 mL of aqueous KOH (10%). The resulting white precipitate was filtered off and washed twice with a small amount of ethyl acetate. The combined organic layers were dried ($MgSO_4$) and the solvent was removed under reduced pressure. The obtained residue was finally purified by column chromatography on silica gel 60.

*3.2.1. (1*R*,1′*S*,1′′*R*,2*R*,5′′*R*)-2-[Phenyl-(1′-(2′′-azabicyclo[3.3.0]octane-2′′-yl)methyl]cyclohexanol* ***6a***

Synthesis according to GP 2. Diastereomeric ratio: *dr* >98:<2. Eluent: *n*-hexane:ethyl acetate (6:4). R_f-value: 0.36, yield: 0.82 g (92%). Mp: 97°C. $[\alpha]_D^{20}$ −24.9 (*c*=1.0, CH_2Cl_2). IR (KBr): ν=3000–3500, 1450 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.10–2.07 (m, 17H, 2×H3, 2×H4, 2×H5, 2×H6, 2×H4′′, H5′′, 2×H6′′, 2×H7′′, 2×H8′′); 2.18 (m, 1H, H3′′); 2.64, 2.82, 3.10 (3m, 3H, H1′′, H3′′, H2); 3.94 (m, 1H, H1); 4.22 (d, *J*=11.77 Hz; 1H, CHN); 6.79 (bs, 1H, OH); 7.13, 7.27–7.40 (2m, 5H, aromatic-H). ^{13}C NMR ($CDCl_3$): δ=20.76, 24.35, 24.52, 27.67, 30.99, 31.25, 31.93, 33.03 (C3, C4, C5, C6, C4′′, C6′′, C7′, C8′′); 37.89 (C2); 40.83 (C5′′); 46.78 (C2′′); 62.35, 64.43 (CHN, C1′′); 72.63 (C1); 127.20, 127.75, 130.14 (aromatic-C); 133.27 (aromatic-C). MS (CI, isobutane): m/z (%)=300 (100) [MH^+]. $C_{20}H_{29}NO$ (299.4): calcd C 80.22, H 9.76, N 4.68; found C 80.49, H 9.61, N 4.60.

*3.2.2. (1*R*,1′*R*,2*R*,3*S*,5′*R*)-3-(-2′-Azabicyclo[3.3.0]octane-2′-yl)-2-methylpropanol* ***6b***

Synthesis according to GP 2. Diastereomeric ratio: *dr* >98:<2. Eluent: *n*-hexane:ethyl acetate (8:2), addition of 1% NEt_3. R_f-value: 0.36, yield: 94 g (94%) colorless oil. $[\alpha]_D^{20}$ −47.6 (*c*=0.63, CH_2Cl_2). IR (KBr): ν=3500–3100, 1520, 1410 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.33 (d, *J*=6.68 Hz, 3H, CH_3); 1.29–1.94 (m, 7H, H4′, 2×H6′, 2×H7′, 2×H8′); 2.95 (m, 2H, H4′, H5′); 2.27 (m, 1H, H2′); 2.48 (m, 1H, H2); 2.99 (m, 1H, H1′); 3.24 (m, H2); 3.91 (d, *J*=11.04 Hz, 1H, CHN); 4.58 (d, *J*=9.17 Hz, 1H, C*H*OH); 7.28–7.45 (m, 10H, aromatic-H); 9.02 (bs, 1H, OH). ^{13}C NMR ($CDCl_3$): δ=15.82 (CH_3); 24.32, 30.94, 31.48, 33.07 (C4′, C6′, C7′, C8′); 38.61 (C2); 40.95 (C5′); 47.18 (C2′); 64.72, 70.61 (CHN, C1′); 82.88 (C1); 125.92, 127.31, 127.39, 127.83, 128.08, 12.32 (aromatic-C); 133.81, 144.14 (aromatic-C). MS (CI,

isobutane): m/z (%)=336 (100) [MH^+]. $C_{23}H_{29}NO$ (335.49): calcd C 82.34, H 8.71, N 4.18; found C 82.01, H 8.68, N 4.20.

*3.2.3. (1*R,*1′*R,*1″*R,*2*S,*5″*R*)-2-[Phenyl-(1′-(2″-azabicyclo[3.3.0]octane-2″-yl)methyl]1,2,3,4-tetrahydro-1-naphthalinol (major diastereomer) (1*R*)-**6c***

Synthesis according to GP 2. Diastereomeric ratio: *dr* (1*R*)-**6c**:(1*S*)-**6c** (62:38). Eluent: *n*-hexane:ethyl acetate (8:2). R_f-value: 0.10, yield: 0.57 g (55%) slightly yellow oil. $[\alpha]_D^{20}$ +8.4 (*c*=0.5, CH_2Cl_2). IR (NaCl): ν=3400–3200, 1520 cm^{-1}. ^1H NMR ($CDCl_3$): δ=0.87–2.06 (m, 12H, 2×H3, 2×H4, 2×H4″, 2×H6″, 2×H7″, 2×H8″); 2.17 (m, 1H, H5″); 2.55 (m, 1H, H2″); 2.74 (m, 1H, H2″); 2.94 (m, 1H, H1″); 3.16 (m, 1H, H2); 3.95 (d, *J*=11.72 Hz, 1H, CHN); 5.04 (d, *J*=4.3 Hz, 1H, H1); 7.07–7.41, 7.82 (2m, 9H, aromatic-H). ^{13}C NMR ($CDCl_3$): δ=23.94, 24.26, 25.27, 30.64, 31.14, 33.04, 36.45 (C3, C4, C5, C6, 2×*cyclo*-CH_2); 40.67 (C3a); 46.79 (C2); 62.56, 64.52 (C6a, CHN); 72.23 (COH); 125.92, 126.45, 127.43, 127.78, 127.89, 130.14 (aromatic-C); 133.24, 135.49, 140.35 (aromatic-C). MS (CI, isobutane): m/z (%)=348 (100) [MH^+]; 200 (28) [$M^+-C_{10}H_{12}O$]. $C_{24}H_{29}NO$ (347.5): calcd C 82.95, H 8.41, N 4.03; found C 83.06, H 8.43, N 3.99.

*3.2.4. (1*S,*1′*R,*1″*R,*2*S,*5″*R*)-2-[Phenyl-(1′-(2″-azabicyclo[3.3.0]octane-2″-yl)methyl]1,2,3,4-tetrahydro-1-naphthalinol (minor diastereomer) (1*S*)-**6c***

Synthesis according to GP 2. Diastereomeric ratio: *dr* (1*R*)-**6c**:(1*S*)-**6c** (62:38). Eluent: *n*-hexane:ethyl acetate (8:2). R_f-value: 0.27, yield: 0.33 g (32%) colorless crystals. Mp: 88°C. $[\alpha]_D^{20}$ −78.1 (*c*=0.5, CH_2Cl_2). IR (KBr): ν=3400–3200, 1490 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.21–2.05 (m, 11H, 2×H3, 2×H4, H4″, 2×H6″, 2×H7″, 2×H8″); 2.23–2.45 (m, 2H, H4″, H5″); 2.66–2.87 (m, 2H, 2×H2″); 2.98–3.12 (m, 2H, H1″, H2); 3.89 (d, *J*=11.13 Hz, 1H, CHN); 4.90 (d, *J*=9.19 Hz, H1); 7.04–7.48, 7.72 (2m, 9H, aromatic-H); 7.98 (bs, 1H, OH). ^{13}C NMR ($CDCl_3$): δ=24.52, 25.29, 29.02, 31.01, 31.79, 33.10 (C3, C4, C4″, C6″, C7″, C8″); 40.94 (C5″); 47.27 (C2″); 64.83, 70.05 (C1′, C1″); 75.96 (C1); 126.10, 126.22, 126.52, 127.44, 127.89, 127.98 (aromatic-C), 133.52, 135.57, 139.77 (aromatic-C). MS (CI, isobutane): m/z (%)=348 (100) [MH^+]; 200 (75) [$M^+-C_{10}H_{12}O$]. $C_{24}H_{29}NO$ (347.5): calcd C 82.95, H 8.41, N 4.03; found C 82.71, H 8.36, N 4.10.

*3.3. Hydrogenolysis of aminoalcohols **5a–c***

A solution of 1 mmol of the respective aminoalcohol **5**, 16 mmol $NH_4HCO_2 \cdot 5H_2O$ and 0.5 g Pd–C in 20 mL EtOH was stirred at 40°C for 4 h. After filtration, the heterogeneous catalyst was washed twice with methanol and the combined solvents were evaporated under reduced pressure. The resulting residue was purified by micro column chromatography on silica gel.

*3.4. (1*R,*2*R)-2-Phenylmethyl-cyclohexanol **7***

Eluent: *n*-hexane:diethyl ether (8:2). R_f-value: 0.49, yield: 0.15 g (80%). $[\alpha]_D^{20}$ −24.8 (*c*=1.0, $CHCl_3$); lit.[13] $[\alpha]_D^{20}$ +28.2 (*c*=1.0, $CHCl_3$) for (1*S*,2*S*)-**7**. *op*: 88%. Mp: 67–68°C; lit.[13] mp: 67–69°C. The spectral data are in accord with those described in the literature.[13]

*3.5. Synthesis of ketones **8a**,**b** according to the procedure of Dess and Martin[17]*

A solution of the corresponding secondary alcohol (0.75 mmol) in 3 mL CH_2Cl_2 was added with stirring to a suspension of 0.86 mmol Dess–Martin periodinane in 3 mL dry CH_2Cl_2. Two drops of

CF_3CO_2H were added and the reaction mixture was stirred for 30 min. The homogeneous reaction mixture was diluted with 20 mL Et_2O and 20 mL 1 N NaOH and stirred for a further 20 min. The separated organic layer was washed twice with water, dried over $MgSO_4$ and concentrated in vacuo. Final purification was performed by micro column chromatography (silica gel 69) to afford the optical active products.

*3.6. (2*R*)-1,3-Diphenyl-2-methyl-propan-1-one **8a***

Eluent: *n*-hexane:ethyl acetate (8:2). R_f-value: 0.60, yield: 0.15 g (66% referred to **6b**). $[\alpha]_D^{20}$ −70.2 (*c*=0.84, $CHCl_3$); lit.[14] $[\alpha]_D^{20}$ −71.7 (*c*=0.84, $CHCl_3$). The spectral data are in accord with those in the literature.[14]

*3.7. (2*S*)-2-Phenylmethyl-1,2-tetrahydro-2*H*-naphthalin-1-one **8b***

Eluent: *n*-hexane:ethyl acetate (8:2). R_f-value: 0.68, yield: 0.13 g (55% referred to **6c**). $[\alpha]_D^{20}$ −16.7 (*c*=1.80, MeOH); lit.[15] $[\alpha]_D^{20}$ +17.8 (*c*=1.89, MeOH) for (1*R*)-**8b** (92% *ee*). The spectral data are in accord with those in the literature.[15]

Acknowledgements

We express our thanks to HMR Deutschland GmbH for the generous provision of chemicals and the Heinz Neumüller Stiftung as well as the Fond der Chemischen Industrie for financial support. We thank Professor Fuganti for a sample of enantiopure (1*S*,2*S*)-**6**.

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