Enantioselective Synthesis of 2-Phenyl-9-oxabispidines

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Abstract: A small selection of enantiomerically pure 2-phenyl-9-oxabispidines was synthesized in a three to five step procedure from commercially available starting materials. Ring opening of (*R*,*R*)-3-phenylglycidol with benzylamine, condensation with (*S*)-epichlorohydrin to the corresponding *cis*-2,6-bis(hydroxymethyl)-substituted morpholine intermediate, and final cyclization with a primary amine delivered the desired 2-phenyl-9-oxabispidines in good yields. The substituents at the nitrogen atoms were varied by debenzylation and subsequent alkylation.

Key words: 9-oxabispidines, stereoselective synthesis, bicyclic compounds, heterocycles, sparteine

The lupine alkaloid (–)-sparteine [(–)-**1**][1] (Figure 1) is the ligand of choice for many asymmetric transformations.[2] In combination with organolithium reagents, highly enantioselective deprotonation–electrophilic trapping reactions,[2,3] additions to C=C bonds,[4] and desymmetrizations of *meso*-epoxides[5] and anhydrides[6] have been achieved. The diamine (–)-**1** was also successfully used in Cu-mediated dynamic thermodynamic resolutions of racemic biaryl-2,2′-diols[7] and in Pd-catalyzed kinetic resolutions of secondary alcohols.[8] The breadth of its applicability, however, suffers from the non-availability of its enantiomer (+)-**1**.[9,10] The two known stereoselective syntheses of (–)-**1**[11] and (+)-**1**[12] are multi-step and, thus, not economical. The intensive search for simplified surrogates of (+)-**1** finally led to the diamine **2**, which is devoid of the axially annulated ring of **1**. It can be synthesized in three steps from the natural product (–)-cytisine and offers a comparably high potential in asymmetric transformations as (–)-**1** does.[13,14] The compounds **1** and **2** share the same three-dimensional architecture created by the chirally modified bispidine (3,7-diazabicyclo[3.3.1]nonane) skeleton **A**, which might be one of the privileged backbone structures for chiral ligands. Despite all synthetic efforts, efficient stereoselective routes to compounds of type **A** that are not based on a natural product precursor are still missing.[15]

On the contrary, no attention has yet been paid to chiral 9-oxabispidines of type **B**, in which the methylene bridge is replaced by an oxygen atom. These compounds should create a similar asymmetric environment and, thus, might provide versatile surrogates for the bispidines **A**. The additional heteroatom in the bridge, thereby, offers new options for a more convenient synthetic access. Herein we report on the first enantioselective preparation of a small collection of C_1-symmetric 2-phenyl-9-oxabispidines **B** (R = Ph) in just three to five steps from commercially available starting materials.

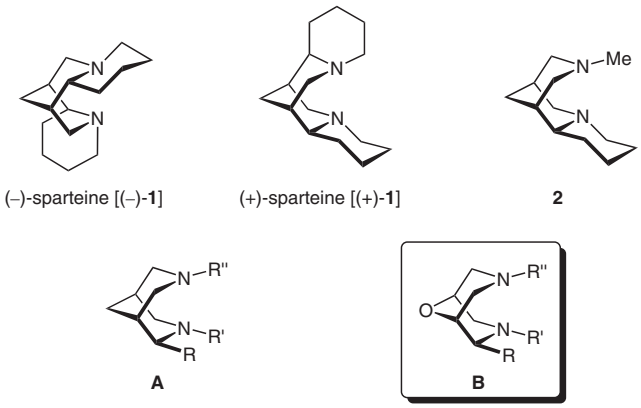
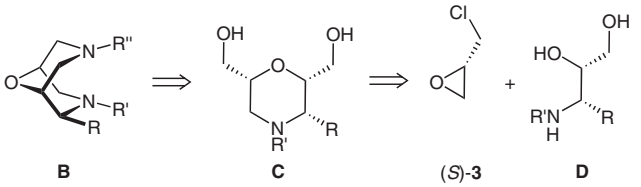


Figure 1 Chiral bispidines of the general formula **A** and the targeted 9-oxa analogues **B**

Recently, we developed a one-pot procedure to chiral 2-hydroxymethyl-substituted morpholines by nucleophilic ring opening of enantiomerically pure epichlorohydrin with 1,2-amino alcohols.[16] It seemed feasible to extend this method to the synthesis of 2-substituted 9-oxabispidines **B** as depicted in the retrosynthetic analysis in Scheme 1. The bicyclic framework of **B** should be constructible from the heterocycle **C** by ring closure with a primary amine. This reduces the synthetic problem to the stereoselective preparation of a *cis*-2,6-bis(hydroxymethyl)-substituted morpholine **C**, which should be accessible according to our method[16] by condensation of (*S*)-epichlorohydrin [(*S*)-**3**] with an appropriately substituted 3-amino-1,2-diol **D**. The latter compound can be synthesized in enantiomerically pure form by ring opening of a chiral epoxy alcohol with a primary amine.

The commercially available epoxy alcohol (*R*,*R*)-3-phenylglycidol [(*R*,*R*)-**4**] was chosen as the starting material for validating our synthetic concept (Scheme 2). Treatment of (*R*,*R*)-**4** with benzylamine in MeOH at 70 °C af-



Scheme 1 Retrosynthetic analysis of **B**

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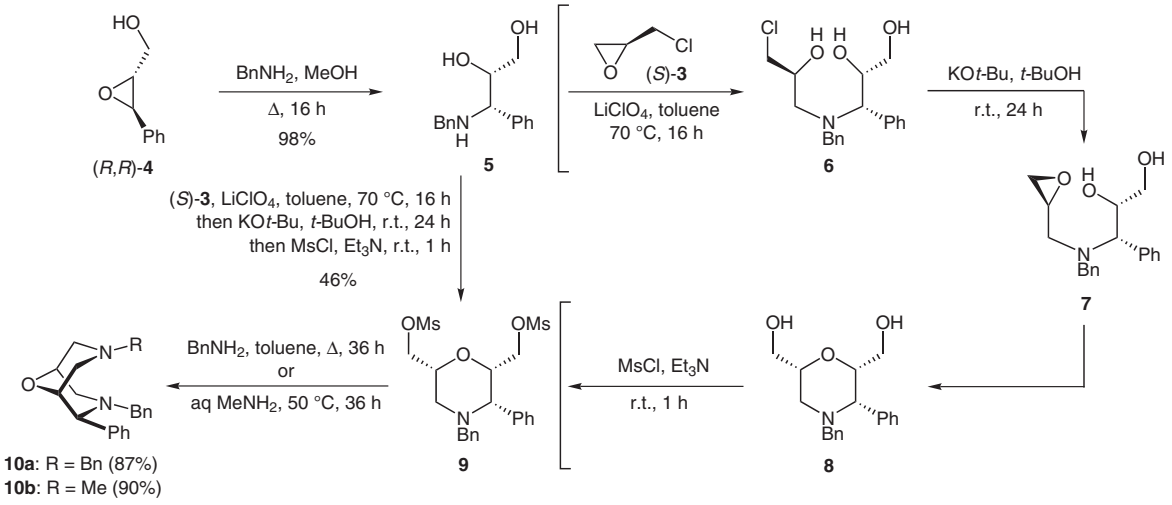
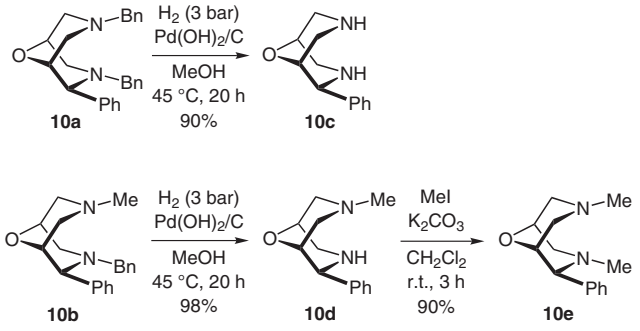


Scheme 2 Enantioselective synthesis of the 2-phenyl-9-oxabispidines **10a** and **10b** from (*R*,*R*)-3-phenylglycidol [(*R*,*R*)-**4**] and (*S*)-epichlorohydrin [(*S*)-**3**]

forded the 3-amino-1,2-diol **5** as a single regioisomer in excellent 98% yield.[17] The transformation of **5** into the morpholine **8** and its activation as the dimesylate **9** was accomplished in a three-step one-pot reaction sequence: $LiClO_4$-mediated addition of **5** to (*S*)-epichlorohydrin [(*S*)-**3**] in toluene at 70 °C delivered the chloroalcohol **6**, which, upon treatment with KO*t*-Bu/*t*-BuOH, cyclized to give the epoxide **7** and, subsequently, the morpholine **8**. Mesylation of the two alcohol functions with $MsCl/Et_3N$ delivered **9** in 46% overall yield. An isolation of the intermediates **6**–**8** is possible, but time-consuming and results in a significantly reduced yield. The final ring closure of **9** to **10a** and **10b** was achieved with benzylamine in refluxing toluene (87% yield) and aqueous methylamine at 50 °C (90% yield), respectively. Thus, starting from commercially available (*R*,*R*)-**4** and (*S*)-**3**, an efficient three-step route to the enantiomerically pure 2-phenyl-9-oxabispidines **10a** and **10b** in 39 and 41% overall yield was established.

The *N*-benzyl groups in **10a** and **10b** allow further modifications of the substituents at the nitrogen atoms (Scheme 3). Hydrogenolytic debenzylation of **10a** with Pearlman's catalyst liberated the free diamine **10c** in 90% yield, while deprotection of **10b** led to the monoamine **10d**, which was methylated to give the 9-oxabispidine **10e** possessing two *N*-methyl functionalities (87% overall yield from **10b**).



Scheme 3 Derivatization of **10a** and **10b**

In conclusion, a small collection of enantiomerically pure 2-phenyl-9-oxabispidines with different substituents at the nitrogen atoms were conveniently synthesized in three to five steps (35–41% yield) from commercially available (*R*,*R*)-3-phenylglycidol [(*R*,*R*)-**4**] and (*S*)-epichlorohydrin [(*S*)-**3**]. A variation of the substituent in position 2 should be possible by starting from the respective chiral epoxy alcohols easily available by Sharpless asymmetric epoxidation of allylic alcohols.[18] Investigations on the preparation of the latter compounds and on the application of the 2-phenyl-9-oxabispidines as chiral auxiliaries and ligands in asymmetric synthesis are in progress.

Optical rotations (10 cm cell) were measured on a Jasco P-1020 polarimeter. All NMR spectra were acquired at 20 °C on a Bruker AV 400 instrument using $CDCl_3$ as the internal reference. IR spectra were recorded on a Jasco FT-IR-410 spectrometer. High-resolution mass spectra were measured on a Bruker Daltonics micrOTOF focus. R_f values refer to TLC on aluminum foil-backed silica gel plates. Column chromatography was performed on silica gel (63–200 mesh). Microanalyses were performed at the Institute of Inorganic Chemistry, University of Würzburg. All reactions were performed under argon in anhyd solvents. (*S*)-Epichlorohydrin [(*S*)-**3**, 97% ee] and (*R*,*R*)-3-phenylglycidol [(*R*,*R*)-**4**, >96% ee] are commercially available and were used as received.

(+)-(2*S*,3*S*)-3-(Benzylamino)-3-phenylpropane-1,2-diol (5)

A solution of (*R*,*R*)-3-phenylglycidol [(*R*,*R*)-**4**, 10.0 g, 66.6 mmol] and benzylamine (8.00 mL, 7.85 g, 73.3 mmol) in MeOH (100 mL) was refluxed for 24 h. The solvent was removed in vacuo and the resulting oil was crystallized from Et_2O–*n*-pentane to give **5** (16.8 g, 98%) as a white solid; mp 87–89 °C (Lit.[17] mp 89–90 °C); $[\alpha]_D^{20}$ +61.6 (*c* = 0.89, EtOH) {Lit.[17] $[\alpha]_D^{20}$ +68.0 (*c* = 1.00, EtOH)}; R_f = 0.24 (CH_2Cl_2–MeOH, 95:5).

IR (KBr): 3269, 3065, 2849, 2421, 1453, 1047 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.23–3.18 (br s, 3 H, NH, 2 × OH), 3.55 (d, 1 H, *J* = 12.8 Hz, NC*H*HPh), 3.23 (dd, 1 H, *J* = 11.4, 4.8 Hz, C*H*HOH), 3.56 (dd, 1 H, *J* = 11.5, 4.9 Hz, C*H*HOH), 3.75 (d, 1 H, *J* = 13.0 Hz, NC*H*HPh), 3.82 (m, 1 H,

C*H*OH), 3.88 (d, 1 H, *J* = 5.9 Hz, NCHPh), 7.25 (m, 3 H, ArH), 7.32 (m, 5 H, ArH), 7.40 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 51.40, 64.59, 65.91, 73.47, 127.2, 127.6, 127.9, 128.2, 128.5, 128.8, 139.3, 139.5.

MS (ESI, +): *m*/*z* (%) = 258.1488 ([M + H]$^+$, 100).

HRMS (ESI, +): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{20}NO_2$: 258.1494; found: 258.1488.

(–)-(2*S*,3*S*,6*R*)-4-Benzyl-2,6-bis(methanesulfonyloxymethyl)-3-phenylmorpholine (9)

$LiClO_4$ (4.96 g, 46.6 mmol) was added to a solution of **5** (10.0 g, 38.9 mmol) in toluene (700 mL). (*S*)-Epichlorohydrin [(*S*)-**3**; 3.66 mL, 4.31 g, 46.6 mmol] was introduced and the mixture was heated at 70 °C for 16 h. *t*-BuOH (700 mL) and KO*t*-Bu (10.9 g, 97.2 mmol) were added at r.t. and stirring was continued for 24 h. Et_3N (32.5 mL, 23.6 g, 233 mmol) and MsCl (12.0 mL, 17.8 g, 155 mmol) were added slowly. After 1 h at r.t., the mixture was diluted with H_2O (1 L) and extracted with CH_2Cl_2 (3 × 500 mL). The combined organic layers were washed with sat. aq $NaHCO_3$ (1 L) and brine (1 L), dried ($MgSO_4$), and concentrated in vacuo. Purification by flash chromatography [1. silica gel, CH_2Cl_2–MeOH (100:0 → 10:1); 2. silica gel, *n*-pentane–Et_2O (1:2 → 0:100)] afforded **9** (8.38 g, 46%) as a white foamy solid; mp 53–58 °C; $[\alpha]_D^{20}$ –10.7 (*c* = 0.11, $CHCl_3$); R_f = 0.53 (*n*-pentane–Et_2O, 1:3).

IR (KBr): 3025, 1363, 1181, 999, 969 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.49 (dd, 1 H, *J* = 12.0, 3.2 Hz, NC*H*H), 2.70 (pseudo-t, 1 H, *J* = 11.6 Hz, NC*H*H), 2.89 (s, 3 H, CH_3SO_2), 3.09 (s, 3 H, CH_3SO_2), 3.13 (d, 1 H, *J* = 13.6 Hz, C*H*HPh), 3.54 (d, 1 H, *J* = 13.6 Hz, C*H*HPh), 3.72 (d, 1 H, *J* = 3.2 Hz, NCH), 3.88 (dd, 1 H, *J* = 11.2, 3.7 Hz, C*H*HOMs), 4.02 (dd, 1 H, *J* = 11.2, 8.0 Hz, C*H*HOMs), 4.13 (m, 1 H, OCH), 4.33 (dd, 1 H, *J* = 11.2, 3.5 Hz, C*H*HOMs), 4.33 (dd, 1 H, *J* = 11.2, 5.4 Hz, C*H*HOMs), 4.42 (m, 1 H, OCH), 7.25–7.40 (m, 10 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 37.50, 37.94, 46.20, 58.68, 61.19, 70.00, 70.39, 74.63, 77.65, 127.5, 128.5, 128.56, 128.64, 128.9, 137.9.

MS (ESI, +): *m*/*z* (%) = 492.1133 ([M + Na]$^+$, 100), 374.1414 ([M – OMs – H]$^+$, 40).

HRMS (ESI, +): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{27}NO_7S_2$ + Na: 492.1127; found: 492.1133.

Anal. Calcd for $C_{21}H_{27}NO_7S$: C, 53.71; H, 5.80; N, 2.98; S, 13.66. Found: C, 53.94; H, 5.81; N, 2.96; S, 13.35.

(+)-(1*R*,2*S*,5*S*)-3,7-Dibenzyl-2-phenyl-9-oxa-3,7-diazabicyclo[3.3.1]nonane (10a)

A solution of **9** (4.62 g, 9.85 mmol) and benzylamine (16.6 mL, 16.3 g, 152 mmol) in toluene (100 mL) was refluxed for 24 h. The mixture was diluted with H_2O (100 mL) and extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by column chromatography [silica gel, deactivated with concd NH_3 (7.5 wt%), *n*-pentane–Et_2O (10:1 → 1:1)] afforded **10a** (3.33 g, 87%) as a yellowish solid, which can be crystallized from *i*-PrOH to give colorless needles; mp 92–94 °C; $[\alpha]_D^{20}$ +34.6 (*c* = 0.10, $CHCl_3$); R_f = 0.74 [*n*-pentane–Et_2O (3:1), deactivated with NH_3].

IR (KBr): 3025, 2926, 1463, 1099, 1091, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.25 (dd, 1 H, *J* = 11.6, 3.5 Hz, NC*H*H), 2.44 (ddd, 1 H, *J* = 11.2, 3.9, 1.5 Hz, NC*H*H), 2.55 (ddd, 1 H, *J* = 11.6, 4.2, 1.6 Hz, NC*H*H), 2.75 (d, 1 H, *J* = 13.6 Hz, NC*H*HPh), 2.77 (d, 1 H, *J* = 11.6 Hz, NC*H*H), 2.82 (d, 1 H, *J* = 11.2 Hz, NC*H*H), 2.91 (d, 1 H, *J* = 11.6 Hz, NC*H*H), 3.28 (d, 1 H, *J* = 12.9 Hz, NC*H*HPh), 3.50 (d, 1 H, *J* = 12.9 Hz, NC*H*HPh), 3.76 (m, 1 H, OCH), 3.86 (d, 1 H, NC*H*Ph), 3.88 (m, 1 H, OCH), 3.97 (d, 1 H, *J* = 13.6 Hz, NC*H*HPh), 7.16–7.41 (m, 10 H, ArH), 7.45 (m, 2 H, ArH), 7.52 (m, 2 H, ArH), 7.95 (br s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 52.68, 55.70, 56.35, 61.03, 63.90, 69.90, 69.52, 70.10, 73.83, 126.8, 127.1, 127.5, 128.31, 128.33, 128.7, 129.4, 138.8, 139.5, 140.9.

MS (ESI, +): *m*/*z* (%) = 385.2264 ([M + H]$^+$, 100).

HRMS (ESI, +): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{29}N_2O$: 385.2280; found: 385.2264.

Anal. Calcd for $C_{26}H_{28}N_2O$: C, 81.21; H, 7.34; N, 7.29. Found: C, 81.37; H, 7.28; N, 7.02.

(+)-(1*R*,2*S*,5*S*)-3-Benzyl-7-methyl-2-phenyl-9-oxa-3,7-diazabicyclo[3.3.1]nonane (10b)

A solution of aqueous methylamine (40%, 48 mL, 556 mmol) and **9** (3.44 g, 7.34 mmol) was stirred for 36 h at 50 °C. The mixture was diluted with H_2O (150 mL) and extracted with Et_2O (3 × 300 mL). The combined organic layers were washed with brine (200 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by column chromatography [silica gel, deactivated with concd NH_3 (7.5 wt%), *n*-pentane–Et_2O (3:1 → 1:3)] afforded **10b** (2.05 g, 90%) as a slightly yellow oil; $[\alpha]_D^{22}$ +26.8 (*c* = 0.16, $CHCl_3$); R_f = 0.90 (Et_2O, deactivated with NH_3).

IR (film): 3038, 2791, 1496, 1453, 996 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.02 (dd, 1 H, *J* = 11.8, 3.7 Hz, NC*H*H), 2.19 (s, 3 H, NCH_3), 2.43 (ddd, 1 H, *J* = 11.2, 4.0, 1.7 Hz, NC*H*H), 2.65 (m, 2 H, NCH_2), 2.84 (d, 1 H, *J* = 11.2 Hz, NC*H*H), 2.95 (dd, 1 H, *J* = 11.5, 0.8 Hz, NC*H*H), 2.97 (d, 1 H, *J* = 14.1 Hz, NC*H*HPh), 3.71 (m, 1 H, OCH), 3.87 (m, 3 H, NC*H*HPh, NCHPh, OCH), 7.15–7.40 (m, 9 H, ArH), 7.80–8.20 (br s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.86, 54.17, 55.30, 58.30, 58.56, 60.28, 69.08, 69.29, 73.59, 126.8, 127.5, 128.3, 128.7, 128.9, 138.7, 140.9.

MS (ESI, +): *m*/*z* (%) = 309.1956 ([M + H]$^+$, 100), 217.1323 ([M – CH_2Ph]$^+$, 2).

HRMS (ESI, +): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{25}N_2O$: 309.1967; found: 309.1956.

Anal. Calcd for $C_{20}H_{24}N_2O$: C, 77.89; H, 7.84; N, 9.08. Found: C, 77.88; H, 7.62; N, 8.91.

(+)-(1*R*,2*S*,5*S*)-2-Phenyl-9-oxa-3,7-diazabicyclo[3.3.1]nonane (10c)

A solution of **10a** (103 mg, 226 μmol) in MeOH (5 mL) was hydrogenated over $Pd(OH)_2$/C (20%, 50 mg) under 3.5 bar H_2 pressure for 20 h at 45 °C. The mixture was filtered through a pad of Celite and washed with MeOH (3 × 10 mL). Removal of the solvent under reduced pressure delivered **10c** (48.9 mg, 90%) as a white solid; mp 85 °C; $[\alpha]_D^{20}$ +27.4 (*c* = 0.18, MeOH); R_f = 0.50 [CH_2Cl_2–MeOH (9:1), deactivated with NH_3].

IR (KBr): 3419, 2955, 2827, 1452, 1070, 859 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.59 (br s, 1 H, 2 × NH), 2.82 (d, 1 H, *J* = 13.7 Hz, NC*H*H), 3.02 (ddd, 1 H, *J* = 13.7, 3.7, 1.3 Hz, NC*H*H), 3.14 (d, 1 H, *J* = 13.3 Hz, NC*H*H), 3.34 (d, 1 H, *J* = 11.6 Hz, NC*H*H), 3.39 (dt, 1 H, *J* = 13.3, 2.9 Hz, NC*H*H), 3.59 (m, 1 H, OCH), 3.64 (dt, 1 H, *J* = 11.7, 2.9 Hz, NC*H*H), 3.67 (m, 1 H, OCH), 4.58 (d, 1 H, *J* = 2.3 Hz, NCHPh), 7.26–7.29 (m, 1 H, ArH), 7.34–7.41 (m, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.23, 50.44, 51.16, 63.92, 66.92, 72.23, 126.5, 127.4, 128.7, 140.9.

MS (ESI, +): *m*/*z* (%) = 205.1336 ([M + H]$^+$, 100).

HRMS (ESI, +): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{17}N_2O$: 205.1341; found: 205.1336.

(+)-(1*R*,2*S*,5*S*)-7-Methyl-2-phenyl-9-oxa-3,7-diazabicyclo[3.3.1]nonane (10d)

Compound **10b** (1.38 g, 4.47 mmol) in MeOH (60 mL) was hydrogenated over $Pd(OH)_2/C$ (20%, 500 mg) under 3 bar H_2 pressure for 20 h at 45 °C. The crude product was sucked through a pad of Celite and washed with MeOH (300 mL). Removal of the solvent in vacuo delivered **10d** (955 mg, 98%) as a white solid; mp 35 °C; $[\alpha]_D^{20}$ +42.3 (*c* = 0.17, MeOH); R_f = 0.43 [Et_2O–MeOH (10:1), deactivated with NH_3].

IR (KBr): 3296, 2931, 2793, 1484, 1458, 1066 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.10 (s, 3 H, NCH_3), 2.24 (ddd, 1 H, *J* = 11.8, 3.8, 1.6 Hz, NC*H*H), 2.57 (ddd, 1 H, *J* = 11.3, 3.4, 2.8 Hz, NC*H*H), 2.65 (d, 1 H, *J* = 11.7 Hz, NC*H*H), 2.94 (d, 1 H, *J* = 11.3 Hz, NC*H*H), 3.24 (d, 1 H, *J* = 13.8 Hz, NC*H*H), 3.48 (ddd, 1 H, *J* = 13.8, 3.9, 2.5 Hz, NC*H*H), 3.72 (br t, 1 H, *J* = 3.7 Hz, OCH), 3.79 (br t, 1 H, *J* = 3.6 Hz, OCH), 4.43 (br d, 1 H, *J* = 8.5 Hz, NCHPh), 7.23–7.29 (m, 3 H, ArH), 7.33–7.37 (m, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.92, 51.08, 54.70, 59.70, 62.64, 67.19, 72.31, 126.3, 127.0, 128.6, 140.2.

MS (ESI, +): *m*/*z* (%) = 219.1488 ($[M + H]^+$, 100).

HRMS (ESI, +): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{19}N_2SO$: 219.1497; found: 219.1488.

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 70.87; H, 8.27; N, 12.78.

(+)-(1*R*,2*S*,5*S*)-3,7-Dimethyl-2-phenyl-9-oxa-3,7-diazabicyclo[3.3.1]nonane (10e)

K_2CO_3 (778 mg, 5.63 mmol) and MeI (351 μL, 799 mg, 5.63 mmol) were added to a solution of **10d** (878 mg, 4.02 mmol) in CH_2Cl_2 (12 mL). After 3 h at r.t., H_2O (50 mL) was added and the mixture was extracted with CH_2Cl_2 (4 × 30 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo to give **10e** (859 mg, 92%) as white needles; mp 65 °C; $[\alpha]_D^{20}$ +154.4 (*c* = 1.15, MeOH); R_f = 0.48 (Et_2O, deactivated with NH_3).

IR (KBr): 2937, 2780, 1451, 1266, 1088, 1062 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.01 (dd, 1 H, *J* = 11.9, 3.8 Hz, NC*H*H), 2.08 (s, 3 H, NCH_3), 2.20 (s, 3 H, NCH_3), 2.45 (ddd, 1 H, *J* = 11.4, 3.9, 1.6 Hz, NC*H*H), 2.70 (ddd, 1 H, *J* = 11.8, 4.5, 1.7 Hz, NC*H*H), 2.72 (br d, 1 H, *J* = 11.8 Hz, NC*H*H), 3.03 (d, 1 H, *J* = 11.4 Hz, NC*H*H), 3.14 (d, 1 H, *J* = 11.7 Hz, NC*H*H), 3.46 (d, 1 H, *J* = 4.0 Hz, NCHPh), 3.67 (br t, 1 H, *J* = 3.7 Hz, OCH), 3.95 (br t, 1 H, *J* = 4.1 Hz, OCH), 7.23–7.41 (m, 4 H, ArH), 7.44 (br s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.89, 45.88, 47.32, 53.93, 58.51, 58.95, 68.89, 72.31, 73.19, 127.3, 128.4, 129.4.

MS (ESI, +): *m*/*z* (%) = 233.1648 ($[M + H]^+$, 100).

HRMS (ESI, +): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{21}N_2O$: 233.1654; found: 233.1648.

Anal. Calcd for $C_{14}H_{20}N_2O$: C, 72.38; H, 8.68; N, 12.06. Found: C, 71.75; H, 8.61; N, 11.88.

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