Diastereoselective Synthesis of 2,5-Disubstituted Decahydroquinolines via Ring-Rearrangement Metathesis and Zirconium-Mediated Cyclization

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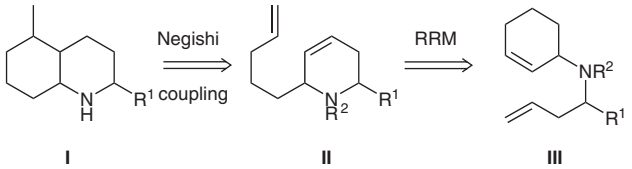
Abstract: A diastereoselective approach to 2,5-substituted decahydroquinolines by zirconium-mediated cyclization of unsaturated α,α′-disubstituted piperidines **II** is described. The required piperidines could be obtained from secondary sulfonamides **III** via ruthenium-catalyzed ring-rearrangement metathesis (RRM) in high yields. Racemic *trans*-195A and 2-epi-*trans*-195A were synthesized in 8 steps starting with butyraldehyde and cyclohex-2-enol.

Key words: metathesis, ruthenium, piperidines, zirconium, decahydroquinolines

Decahydroquinolines occur in nature in skin secretions of dendrobatid and mantelline frogs[1] as well as in bufonid toads,[2] ascidians,[3,4] marine flatworms[4] and myrmicine ants.[5] These relatively untoxic biologically active compounds have marked activity on ion channels.[6] They have proved to be noncompetitive blockers of nicotinic receptor channels and are thus interesting agents for biomedical research and molecular pharmacology.[7] Both *cis*- and *trans*-fused decahydroquinolines have been found since discovery of the first representative *cis*-195A, isolated from skin extracts of the panamanian frog *dendrobatus pumilio* in 1968.[8,9] Many of these compounds cannot be obtained from their natural sources in sufficient quantities for NMR- or X-ray-analysis and their structure and stereochemistry has been only tentatively assigned.[9] Synthesis is needed to confirm their structure by comparison with the natural material and to obtain these alkaloids, and derivatives thereof, in adequate amounts for biological screening.[10]

2,5-Disubstituted decahydroquinolines are the major class with nearly 30 different representatives.[11] In our work we tried to investigate an efficient and concise approach to these significant alkaloids. We focused on a strategy for synthesis of the 5-methyl substituted species by means of ring-rearrangement metathesis (RRM) and Negishi's zirconium-mediated olefin-coupling[12] as key steps (Scheme 1). Application of zirconium-mediated olefin-coupling to natural product synthesis has been succesfully established by Mori et al. for annulation of a 5,6-membered octahydroindole ring-system and subsequent carbonylation within the total synthesis of (–)-Dendrobine.[13] To the best of our knowledge an application to 6,6-membered rings has never been performed. We have tried now for the first time to investigate this versatile reaction for annulation of a 6,6-membered decahydroquinoline ring-system **I** by conversion of adequate unsaturated α,α′-disubstituted piperidines **II**. The required piperidines **II** were expected to be accessible through RRM of **III**. RRM-processes have already been proven to be a powerful tool in natural product synthesis[14] and in combination with a Negishi coupling reaction the desired decahydroquinolines **I** should readily be obtained in only a few steps.



Scheme 1 Retrosynthetic analysis

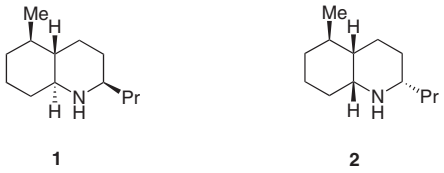


Figure 1 Structures of the decahydroquinolines *trans*-195A[15] and *cis*-195A

To explore our strategy we started with butyraldehyde as model compound (Scheme 2) in order to introduce a propyl chain in 2-position, which can be found in *trans*-195A (**1**) and *cis*-195A (**2**) (Figure 1).[9] Synthesis of **3** was performed in 84% yield by addition of the allylboron reagent derived from allylmagnesium bromide and triisopropoxy borate. The reaction of the homopropargylic alcohol **3** with methanesulfonyl chloride (MsCl) gave mesylate **4** in 80% yield. After treatment with sodium azide (NaN_3) **5** could be obtained in 93% yield. Subsequent $LiAlH_4$ reduction and in situ protection of the resulting amine with 2-nitrobenzenesulfonyl chloride (NsCl) gave **7** in 78% over 2 steps. The Ns-group was chosen in order to increase the acidity of the N-H bond, which is advantageous for subsequent Mitsunobu reaction.[16] In addition it prevents adverse interaction of the nitrogen lone pair with the metathesis-catalyst afterwards. A better result concerning the overall yield of **7** could be achieved in a two-step synthesis using the method of Fukuyama et al. who recently reported a concise approach to mono protected primary amines by conversion of alcohols with *N*-carboalkoxy-2-

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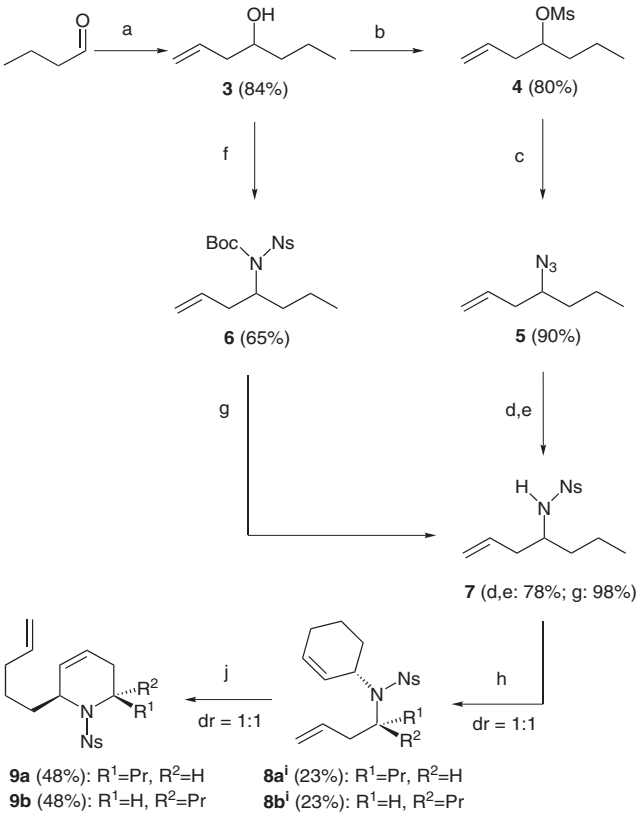
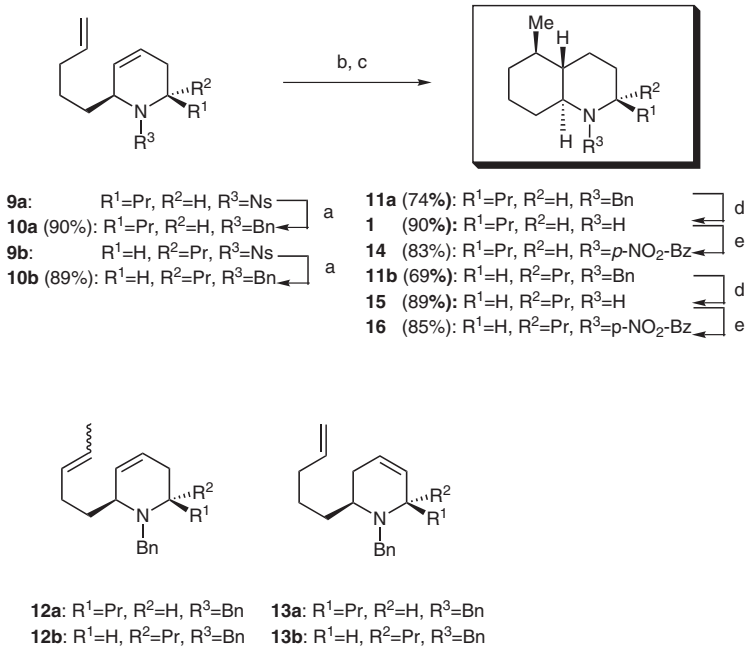


Scheme 2 Synthetic route to the tetrahydropyridines. *Reactions and conditions:* (a) AllylMgBr, B(O-*i*-Pr)$_3$, Et$_2$O; (b) MsCl, Et$_3$N, CH$_2$Cl$_2$; (c) NaN$_3$, DMSO; (d) LAH, Et$_2$O; (e) NsCl, K$_2$CO$_3$, CH$_2$Cl$_2$; (f) NsBocNH, DIAD, PPh$_3$, THF; (g) 5% TFA, THF; (h) cyclohex-2-enol, DIAD, PPh$_3$, THF; (i) isolated as diastereomeric mixture (1:1) in 46% yield; (j) 5 mol% Grubbs' catalyst, ethylene, CH$_2$Cl$_2$

nitrobenzenesulfonamides under Mitsunobu conditions and subsequent chemoselective cleavage either of the carbamate or the sulfonamide moiety.[17] Transformation of **3** with *N*-Boc-2-nitrobenzenesulfonamide, diisopropyl diazodicarboxylate (DIAD) and PPh$_3$ in THF yielded **6** in 65% and cleavage of the resulting carbamate was achieved with 5% TFA in THF to give **7** in 98% yield.

In this context we were next interested in investigating the possibility of a kinetic resolution or a kinetic transformation by employing a diastereomeric 1:1 mixture of the metathesis precursor to the desired RRM-process. Conversion of **7** with cyclohex-2-enol under Mitsunobu conditions gave **8a** and **8b** in a 1:1 ratio in 46% yield. Attempts to synthesize **8a** and **8b** by replacing the amine and alcohol functionality, employing cyclohex-2-enyl-2-nitrobenzenesulfonamide and hept-1-en-3-ol, respectively, under various conditions resulted in no conversion. Likewise, application of palladium-mediated allylic substitution, by treatment with cyclohex-2-enyl acetate or methylcarbonate, respectively, did not succeed. Subsequent metathesis was performed in CH$_2$Cl$_2$ under ethylene atmosphere, using 5 mol% benzylidene-bis(tricyclohexylphosphine)ruthenium dichloride (Grubbs catalyst). The transformation resulted in complete conversion to the desired tetrahydropyridine derivatives **9a** and **9b**, which could be separated by chromatographic purification in an overall yield of 96%. Employment of ethylene was essential in this reaction in order to suppress the formation of dimeric byproducts.[18] Contrary to our hopes both diastereomers were converted simultaneously as indicated by NMR-analysis of the reaction mixture.



Scheme 3 Synthetic route to the decahydroquinolines. *Reactions and conditions:* (a) PhSH, K$_2$CO$_3$, DMF, BnBr, TBAI; (b) Cp$_2$ZrCl$_2$, BuLi, THF; (HCl; (d) H$_2$, Pd/C, MeOH; (e) *p*-NO$_2$-BzCl, Et$_3$N, CH$_2$Cl$_2$

Whereas the cyclization of **9a** with BuLi and dicyclopentadienylzirconium dichloride (Cp_2ZrCl_2) resulted in dimerization by coupling of the aromatic nitro group, cyclization to the desired decahydroquinolines could be achieved after transformation of sulfonamide **9a** into the *N*-benzyl derivative **10a** (Scheme 3). The deprotection-protection sequence was performed with thiophenol (PhSH) and K_2CO_3 in DMF and subsequent treatment with benzyl bromide (BnBr) in a one-pot procedure to give **10a** in 90% yield. Subsequent zirconium mediated coupling afforded only decahydroquinoline **11a** along with isomerized starting material **12a**. The ratio of **11a** to **12a** was determined to be 7:2 by GC-analysis of the crude product. Compound **11a** could be isolated in 74% yield and final hydrogenation with 10% palladium on charcoal in MeOH gave **1** in 88% yield. Whereas determination of the product configuration was not clear by NMR analysis, structure of **1** could be established after transformation into its well crystallizing *N*-*p*-nitro-benzoyl derivative **14** and subsequent X-ray analysis (Figure 2). The found configuration was identical to the natural product *trans*-195A, isolated from skin extracts of the peruvian frog *epipedobates bassleri*.[9,19]

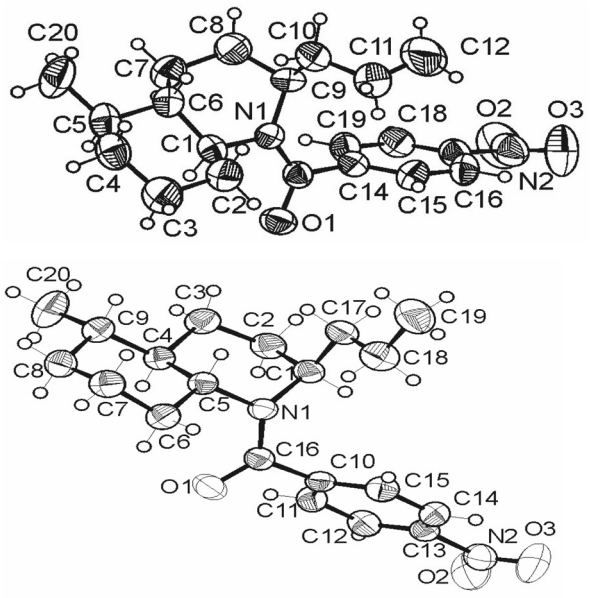


Figure 2 X-ray structures of **14** and **16**[20]

Taber et al. have shown that cyclozirconations are reversible processes in which the stereochemistry of the products can be influenced by stereogenic centers in the employed substrate, either through kinetic or thermodynamic control.[21] In our case, we assumed that the stereochemistry of the propyl group of **10a** could have a remarkable influence on the high diastereoselectivity observed within the cyclization to decahydroquinoline **11a**. To investigate the effect of a propyl group with contrary stereochemistry we transformed **9b** into the corresponding *N*-benzyl derivative **10b**. Surprisingly, cyclization of **10b** also resulted in only one diastereomer **11b**, which could be isolated with a negligible lower yield of 69% compared to **11a**. In addition a less polar fraction was isolated with 25% yield, which could be identified as a 2:1 mixture of **12b** with **13b**. Final hydrogenation of **11b** gave **15** in 89% yield. The configuration of **15** was established after transformation to the *N*-*p*-nitrobenzoyl derivative **16** and subsequent X-ray analysis (Figure 2). We presume that the observed lower rate of cyclization and the increased amount of isomerized starting material by employing **10b** could be caused by destabilization of the corresponding zirconacycle **B** due to adverse interaction of the propyl group, which is expected to be in unfavored axial position for **10b** and in an equatorial position for **10a** with the corresponding zirconacycle **A** (Figure 3).

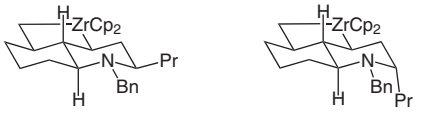


Figure 3 Postulated zirconacycle intermediates

In conclusion, we have presented a concise and highly diastereoselective approach to *trans*-fused 2,5-disubstituted decahydroquinolines. Racemic *trans*-195A (**1**) and 2-epi-*trans*-195A (**15**) were synthesized in 8 steps starting with butyraldehyde and cyclohex-2-enol. Enantioselective synthesis in order to determine the absolute configuration of *trans*-195A, which still remains unknown, is currently under investigation in our laboratory.

^{1}H NMR spectra (500 MHz) and ^{13}C NMR spectra (125 MHz) were recorded on a Bruker DRX 500 spectrometer using the indicated solvents. NMR chemical shifts are expressed in ppm upfield, relative to the internal solvent peak. HRMS were recorded on a Finnigan MAT 95 SQ spectrometer. IR spectra were measured on a Nicolet FT-IR 750 spectrometer. Melting points were determined on a Leica Galen III heater table microscope and are uncorrected. Elemental analyses were recorded on an Elementar Vario El Fa. (Analytik Jena). Analytical TLC was performed on Merck silica gel 60 (0.040–0.063 mm) or Fluka alumina (type H, neutral) and preparative chromatography was performed on ICN silica gel 60 (0.040–0.063 mm) or Fluka alumina (type 5016A basic, Brockmann activity grade 3) using the indicated solvents. Anhyd Et_2O, anhyd DMSO and all chemicals were purchased from Aldrich and were used without further purification. THF was freshly distilled under N_2 from sodium/benzophenone and CH_2Cl_2 was distilled from CaH_2. All reactions were carried out under N_2 using flame dried glassware with the exception of Negishi coupling which was carried out under Ar. Metathesis reactions were performed in a Braun MB 150B-G glove box under N_2.

Hept-1-en-4-ol (3)

A stirred solution of allylmagnesium bromide in hexane (90.0 mL, 1.0 M) was diluted with anhyd Et_2O (150 mL) and cooled in an ice bath. Triisopropoxy borate (20.8 mL, 90.0 mmol) was added dropwise at 0 °C over 15 min. After stirring for 2 h at r.t. *n*-butanal (5.41 mL, 60.0 mmol) was added dropwise via a syringe and stirring was continued for 3 h. An aq solution of NaOH (30 mL, 3 M) was added and the mixture was refluxed for 3 h. The organic layer was washed with water (50 mL), brine (50 mL) and dried ($MgSO_4$). The solvent was removed by distillation over a 10 cm Vigreux column at atmospheric pressure. Fractional distillation of the crude product at re-

duced pressure yielded **3** (5.76 g, 84%) as colorless liquid; bp 67–68 °C (24 mbar).

IR (film): 3453 (m), 2960 (m), 2932 (m), 1710 (s), 1435 (m), 1419 (m), 1362 (s), 1221 (s), 1018 (m), 998 (m), 912 (m) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 5.88–5.76 (m, 1 H), 5.12 (d, *J* = 15.2 Hz, 1 H), 5.12 (d, *J* = 11.0 Hz, 1 H), 3.65 (br s, 1 H), 2.33–2.25 (m, 1 H), 2.17–2.08 (m, 1 H), 1.65 (s, 1 H), 1.56–1.40 (m, 3 H), 1.40–1.30 (m, 1 H), 0.92 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 135.0 (CH), 118.0 (CH_2), 70.5 (CH), 42.0 (CH_2), 39.0 (CH_2), 18.9 (CH_2), 14.1 (CH_3).

MS (EI): *m*/*z* (%) = 97 (1) $[M – OH]^+$, 73 (72), 71 (11), 55 (100).

HRMS: *m*/*z* $[M]^+$ calcd for $C_7H_{14}O$: 114.1044; found: 114.1047.

Methanesulfonic Acid 1-Propyl-but-3-enyl Ester (4)

To an ice-cold stirred solution of **3** (9.50 g, 83.2 mmol) and Et_3N (17.4 mL, 125 mmol) in CH_2Cl_2 (60 mL) was added dropwise MsCl (7.73 mL, 99.8 mmol) over 15 min. The resulting mixture was allowed to warm to r.t. and stirred for 3 h. After diluting with CH_2Cl_2 (400 mL) the reaction mixture was washed with H_2O (3 × 100 mL), brine (100 mL) and dried ($MgSO_4$). The solvent was removed in vacuo and the crude product was purified by flash chromatography on silica gel (cyclohexane–MTBE, 3:1) to give **4** (12.8 g, 80%) as pale yellow oil; R_f 0.40.

IR (film): 2960 (m), 2925 (m), 2875 (w), 2850 (w), 1355 (m), 1336 (m), 1175 (s), 972 (w), 913 (s), 802 (w) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 5.87–5.78 (m, 1 H), 5.12 (d, *J* = 16.5 Hz, 1 H), 5.11 (d, *J* = 10.6 Hz, 1 H), 4.73 (quint, *J* = 6.0 Hz, 1 H), 2.98 (s, 3 H), 2.52–2.41 (m, 2 H), 1.73–1.59 (m, 2 H), 1.53–1.32 (m, 2 H), 0.92 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 132.6 (CH), 119.0 (CH_2), 82.7 (CH), 39.2 (CH_2), 38.8 (CH_3), 36.3 (CH_2), 18.4 (CH_2), 13.8 (CH_3).

MS (EI): *m*/*z* (%) = 191 (1) $[M – 1]^+$, 151 (33), 105 (22), 97 (13), 96 (26), 81 (22), 79 (18), 67 (22), 55 (100), 54 (34).

HRMS: *m*/*z* $[M – C_3H_5]^+$ calcd for $C_5H_{11}O_3S$: 151.0429; found: 151.0421

4-Azido-hept-1-ene (5)

To a stirred solution of **4** (12.8 g, 66.4 mmol) in DMSO (70 mL) at r.t. was added NaN_3 (8.68 g, 134 mmol) and the resulting suspension was stirred at 50 °C for 24 h. After cooling to r.t. and diluting with Et_2O (500 mL) the mixture was washed with H_2O (3 × 100 mL), brine (100 mL) and dried ($MgSO_4$). The solvent was removed by distillation over a 10 cm Vigreux column at atmospheric pressure to give **5** (8.58 g, 93%) as a yellowish oil, which was spectroscopically pure and subsequently used without further purification.

IR (film): 3081 (w), 2960 (s), 2935 (s), 2875 (m), 2100 (ss), 1340 (m), 1258 (s), 993 (m), 918 (s) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 5.90–5.79 (m, 1 H), 5.15 (d, *J* = 16.5 Hz, 1 H), 5.12 (d, *J* = 9.8 Hz, 1 H), 3.34 (quint, *J* = 6.3 Hz, 1 H), 2.30 (t, *J* = 6.3 Hz, 2 H), 1.56–1.44 (m, 3 H), 1.44–1.33 (m, 1 H), 0.94 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 134.1 (CH), 118.1 (CH_2), 62.1 (CH), 38.9 (CH_2), 36.1 (CH_2), 19.4 (CH_2), 13.9 (CH_3).

MS (EI): *m*/*z* (%) = 110 (1) $[M – C_2H_5]^+$, 98 (12), 97 (10), 96 (8), 83 (12), 82 (12), 70 (24), 68 (26), 55 (100).

HRMS: *m*/*z* $[M]^+$ calcd for $C_7H_{13}N_3$: 139.1109; found: 139.1124.

***N*-Boc-2-nitro-*N*-(1-propyl-but-3-enyl)-benzenesulfonamide (6)**

To an ice-cold stirred solution of **3** (1.14 g, 10.0 mmol), PPh_3 (7.86 g, 30.0 mmol) and *N*-Boc-2-nitrobenzene-sulfonamide[17] (7.56 g, 25.0 mmol) in THF (30 mL) was added dropwise DIAD (4.92 mL, 25.0 mmol) over 30 min. After warming to r.t. the mixture was stirred for 72 h. The solvent was removed in vacuo and the remaining oil was purified by flash chromatography on silica gel (2:1 CH_2Cl_2–cyclohexane) to give **6** (2.58 g, 65%) as a pale yellow oil; R_f 0.30.

IR (film): 2978 (w), 2961 (w), 2934 (w), 2874 (w), 1731 (s), 1546 (s), 1368 (s), 1272 (m), 1256 (m), 1178 (m), 1150 (s), 1124 (m), 772 (w), 742 (w), 734 (w), 722 (w) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.34–8.28 (m, 1 H), 7.75–7.67 (m, 3 H), 5.95–5.85 (m, 1 H), 5.12 (d, *J* = 17.1 Hz, 1 H), 5.09 (d, *J* = 10.0 Hz, 1 H), 4.31 (quint, *J* = 7.0 Hz, 1 H), 2.73–2.60 (m, 1 H), 2.62–2.53 (m, 1 H), 1.93–1.84 (m, 1 H), 1.83–1.73 (m, 1 H), 1.53–1.40 (m, 2 H), 1.38 (s, 9 H), 0.94 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 150.6 (C_q), 148.0 (C_q), 135.7 (CH), 134.3 (C_q), 133.8 (CH), 132.9 (CH), 131.6 (CH), 124.3 (CH), 117.7 (CH_2), 84.8 (C_q), 60.0 (CH), 38.8 (CH_2), 35.9 (CH_2), 28.0 (CH), 20.4 (CH_2), 14.2 (CH_3).

MS (EI): *m*/*z* (%) = 325 (1) $[M – C_4H_9O]^+$, 278 (9), 277 (24), 258 (26), 257 (100), 255 (10), 187 (10), 186 (88), 97 (12), 77 (8), 57 (96), 55 (18).

HRMS: *m*/*z* $[M – C_4H_9O]^+$ calcd for $C_{14}H_{17}N_2O_5S$: 325.0858; found: 325.0851.

Anal Calcd for $C_{18}H_{26}N_2O_6S$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.28; H, 6.54; N, 7.16.

2-Nitro-*N*-(1-propyl-3-en-1-yl)-benzenesulfonamide (7)

From 5: To an ice-cold stirred suspension of $LiAlH_4$ (4.68 g, 123 mmol) in Et_2O (60 mL) was added dropwise **5** (8.58 g, 61.6 mmol) in Et_2O (60 mL) over 30 min. The mixture was allowed to warm to r.t. and stirred for 3 h. After dropwise addition of NaOH (30 mL, 2.5 M) at 0 °C the resulting suspension was vigorously stirred at r.t. for 30 min. The solvent was decanted off, the remaining solid was washed with Et_2O (5 × 50 mL) and the combined extracts were dried ($MgSO_4$). The solvent was removed by distillation over a 10 cm Vigreux column at atmospheric pressure and the remaining liquid was diluted with CH_2Cl_2 (40 mL). After addition of K_2CO_3 (17.4 g, 123 mmol) the mixture was cooled to 0 °C and NsCl (16.4 g, 74.0 mmol) was added portionwise over 15 min. The ice bath was removed and the suspension was stirred at r.t. for 24 h. After diluting with CH_2Cl_2 (500 mL) the mixture was washed with H_2O (100 mL), brine (100 mL) and dried ($MgSO_4$). The solvent was evaporated and the crude product was purified by flash chromatography on silica gel (CH_2Cl_2–cyclohexane, 3:1) to give **7** (14.4 g, 78%) as pale yellow solid; R_f 0.38, mp 30–32 °C.

From 6: To an ice-cold stirred solution of **6** (2.00 g, 5.02 mmol) in THF (500 mL) was added dropwise TFA (25.0 mL, 324 mmol) over 10 min. The mixture was allowed to warm to r.t., stirred for 1 h and cooled to 0 °C. Aq sat. $NaHCO_3$ (350 mL) was added until the aqueous phase showed pH 8. After separation of the organic layer, the aqueous layer was extracted with CH_2Cl_2 (3 × 300 mL) and the combined organic layers were dried ($MgSO_4$). The solvent was removed in vacuo and the remaining solid was purified by flash chromatography on silica gel (CH_2Cl_2–cyclohexane, 3:1) to give **7** as pale yellow solid (1.47 g, 98%); R_f 0.38; mp 30–32 °C.

IR (film): 3338 (m), 3098 (w), 3077 (w), 2959 (m), 2931 (m), 2873 (m), 1539 (s), 1442 (m), 1413 (m), 1360 (s), 1168 (s), 1124 (m), 854 (m), 783 (m), 742 (m), 730 (m), 655 (m) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.17–8.10 (m, 1 H), 7.89–7.83 (m, 1 H), 7.77–7.69 (m, 2 H), 5.63–5.53 (m, 1 H), 5.19 (d, *J* = 7.9 Hz, 1 H, NH), 4.93 (d, *J* = 16.0 Hz, 1 H), 4.93 (d, *J* = 11.0 Hz, 1 H), 3.58–3.49 (m, 1 H), 2.25–2.13 (m, 2 H), 1.52–1.39 (m, 2 H), 1.39–1.29 (m, 1 H), 1.29–1.18 (m, 1 H), 0.82 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.8 (C_q), 135.4 (C_q), 133.3 (CH), 133.1 (CH), 132.9 (CH), 130.5 (CH), 125.4 (CH), 118.8 (CH_2), 54.8 (CH), 39.6 (CH_2), 37.0 (CH_2), 18.7 (CH_2), 13.8 (CH_3).

MS (EI): *m*/*z* (%) = 259 (60) [M – C_3H_7]$^+$, 258 (8), 257 (60), 188 (6), 187 (8), 186 (100), 92 (8).

HRMS: *m*/*z* [M – C_3H_5]$^+$ calcd for $C_{10}H_{13}N_2O_4S$: 257.0596; found: 257.0592.

Anal. Calcd for $C_{13}H_{18}N_2O_4S$: C, 52.33; H, 6.08; N, 9.38. Found: C, 52.47; H, 6.11; N, 9.24.

N-Cyclohex-2-enyl-2-nitro-*N*-(1-propyl-but-3-enyl)-benzenesulfonamide (8a with 8b)

DIAD (3.41 mL, 17.3 mmol) was added dropwise over 15 min to an ice-cold stirred solution of **7** (3.97 g, 13.3 mmol), PPh_3 (5.24 g, 20.0 mmol) and cyclohex-2-en-1-ol (1.70 mL, 17.3 mmol) in THF (60 mL). The mixture was stirred at r.t. for 72 h and the solvent was removed in vacuo. Flash chromatography of the remaining oil on silica gel (CH_2Cl_2–cyclohexane, 3:2) yielded a 1:1 diastereomeric mixture of **8a** with **8b** (2.30 g, 46%) as a pale yellow oil; R_f 0.24.

IR (film): 3076 (w), 3031 (w), 2958 (m), 2934 (m), 2839 (w), 1545 (s), 1373 (m), 1347 (m), 1164 (m), 1141 (m), 1126 (m), 852 (w), 772 (w), 741 (w), 728 (w) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–8.02 (m, 2 H), 7.69–7.60 (m, 4 H), 7.56–7.47 (m, 2 H), 5.88–5.79 (m, 2 H), 5.77–5.63 (m, 2 H), 5.55 (d, *J* = 10.0 Hz, 2 H), 5.05 (d, *J* = 17.0 Hz, 1 H), 4.99 (d, *J* = 8.0 Hz, 1 H), 4.98 (d, *J* = 17.5 Hz, 1 H), 4.95 (d, *J* = 9.9 Hz, 1 H), 4.38 (br s, 1 H), 4.27 (br s, 1 H), 3.55 (bs, 1 H), 3.44 (br s, 1 H), 2.57–2.44 (m, 3 H), 2.43–2.34 (m, 1 H), 2.10–1.80 (m, 10 H), 1.78–1.55 (m, 6 H), 1.41–1.18 (m, 4 H), 0.86 (t, *J* = 7.3 Hz, 3 H), 0.76 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.7 (C_q), 148.6 (C_q), 135.8 (CH), 135.2 (C_q), 134.9 (C_q), 133.3 (CH), 133.3 (CH), 131.3 (CH), 131.2 (CH), 130.9 (CH), 130.8 (CH), 128.9 (CH), 128.7 (CH), 123.8 (CH), 123.6 (CH), 117.3 (CH_2), 117.2 (CH_2), 59.1 (CH), 58.9 (CH), 56.4 (CH), 55.9 (CH), 39.5 (CH_2), 35.9 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 24.5 (CH_2), 24.5 (CH_2), 22.5 (CH_2), 22.4 (CH_2), 20.6 (CH_2), 20.5 (CH_2), 14.0 (CH_3), 13.9 (CH_3).

MS (EI): *m*/*z* (%) = 337 (8) [M – C_3H_5]$^+$, 257 (83), 186 (65), 81 (100), 79 (13), 55 (15).

HRMS: *m*/*z* [M – C_3H_5]$^+$ calcd for $C_{16}H_{21}N_2O_4S$: 337.1222; found: 337.1226.

Anal. Calcd for $C_{19}H_{26}N_2O_4S$: C, 60.30; H, 6.92; N, 7.40. Found: C, 60.16; H, 6.91; N, 7.41.

(*rac*)-(2*R*,6*S*)-1-(2-Nitro-benzenesulfonyl)-6-pent-4-enyl-2-propyl-1,2,3,6-tetrahydropyridine (9a) and (*rac*)-(2*S*,6*S*)-1-(2-Nitro-benzenesulfonyl)-6-pent-4-enyl-2-propyl-1,2,3,6-tetrahydropyridine (9b)

To a stirred solution of **8a** and **8b** (575 mg, 1.52 mmol) in CH_2Cl_2 (75 mL) at r.t. was added Grubbs catalyst (63.0 mg, 0.08 mmol). The mixture was saturated with ethylene via a syringe and stirred for 24 h under ethylene atmosphere at 50 °C in a sealed vial. After evaporation of the solvent and flash chromatography on silica gel (MTBE–cyclohexane, 1:3) **9a** (274 mg, 48%) and **9b** (276 mg, 48%) were obtained.

9a

Pale yellow solid; mp 67–68 °C; R_f 0.27.

IR (film): 3076 (w), 3040 (w), 2957 (m), 2933 (m), 2872 (m), 1544 (s), 1373 (s), 1347 (s), 1174 (s), 1139 (m), 1126 (m), 852 (m), 776 (m), 750 (m), 744 (m), 730 (m), 711 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.97–7.89 (m, 1 H), 7.68–7.60 (m, 2 H), 7.60–7.53 (m, 1 H), 5.86–5.73 (m, 2 H), 5.68–5.60 (m, 1 H), 5.02 (dd, *J* = 17.1, 1.7 Hz, 1 H), 4.96 (dd, *J* = 10.1, 0.9 Hz, 1 H), 4.32–4.23 (m, 1 H), 4.06–3.97 (m, 1 H), 2.15–2.04 (m, 2 H), 2.02–1.92 (m, 1 H), 1.89–1.79 (m, 2 H), 1.73–1.35 (m, 7 H), 0.92 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.3 (C_q), 138.5 (CH), 134.2 (C_q), 133.2 (CH), 131.5 (CH), 130.4 (CH), 126.0 (CH), 124.1 (CH), 122.1 (CH), 114.9 (CH_2), 54.1 (CH), 50.9 (CH), 37.3 (CH_2), 37.2 (CH_2), 33.6 (CH_2), 27.1 (CH_2), 26.2 (CH_2), 20.1 (CH_2), 13.8 (CH_3).

MS (EI): *m*/*z* (%) = 337 (3) [M – C_3H_7]$^+$, 310 (14), 309 (100), 186 (56), 94 (14), 80 (23).

HRMS: *m*/*z* [M – C_3H_5]$^+$ calcd for $C_{16}H_{21}N_2O_4S$: 378.1613; found: 378.1622.

Anal. Calcd for $C_{19}H_{26}N_2O_4S$: C, 60.30; H, 6.92; N, 7.40. Found: C, 60.09; H, 6.91; N, 7.39.

9b

Yellowish oil; R_f 0.34.

IR (film): 3077 (w), 3034 (w), 2960 (m), 2933 (m), 2872 (m), 1544 (s), 1372 (s), 1342 (s), 1335 (s), 1161 (s), 1123 (m), 852 (m), 778 (m), 743 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09–7.99 (m, 1 H), 7.69–7.60 (m, 3 H), 5.75–5.68 (m, 1 H), 5.68–5.63 (m, 1 H), 5.63–5.54 (m, 1 H), 4.86 (d, *J* = 9.5 Hz, 1 H), 4.85 (d, *J* = 17.5 Hz, 1 H), 4.36 (br s, 1 H), 3.92–3.84 (m, 1 H), 2.35–2.25 (m, 1 H), 2.20–2.11 (m, 1 H), 1.90–1.68 (m, 4 H), 1.66–1.56 (m, 1 H), 1.55–1.45 (m, 1 H), 1.41–1.23 (m, 3 H), 1.23–1.11 (m, 1 H), 4.85 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.9 (C_q), 138.2 (CH), 136.5 (C_q), 133.2 (CH), 131.7 (CH), 130.5 (CH), 128.2 (CH), 124.4 (CH), 124.2 (CH), 114.8 (CH_2), 55.7 (CH), 55.4 (CH), 34.9 (CH_2), 33.5 (CH_2), 33.1 (CH_2), 28.7 (CH_2), 24.2 (CH_2), 20.5 (CH_2), 14.0 (CH_3).

MS (EI): *m*/*z* (%) = 335 (13) [M – C_3H_7]$^+$, 310 (14), 309 (100), 257 (14), 186 (40), 81 (16), 55 (8).

HRMS: *m*/*z* [M]$^+$ calcd for $C_{19}H_{26}N_2O_4S$: 378.1613; found: 378.1627.

Anal. Calcd for $C_{19}H_{26}N_2O_4S$: C, 60.30; H, 6.92; N, 7.40. Found: C, 60.22; H, 6.88; N, 7.46.

(*rac*)-(2*R*,6*S*)-1-Benzyl-6-pent-4-enyl-2-propyl-1,2,3,6-tetrahydropyridine (10a)

To a stirred solution of **9a** (2.88 g, 7.61 mmol) and K_2CO_3 (8.41 g, 60.9 mmol) in DMF (65 mL) at 80 °C was added dropwise PhSH (0.86 mL, 8.37 mmol). The mixture was stirred at 80 °C for 2 h before TBAI (140 mg, 0.38 mmol) was added. To this solution was added dropwise BnBr (4.51 mL, 38.0 mmol) and the resulting bright yellow mixture was stirred for 1 h at 80 °C. After cooling to r.t. it was diluted with MTBE (800 mL) and extracted with H_2O (500 mL). The aq layer was extracted with MTBE (2 × 200 mL) and the combined organic layers were washed with brine (200 mL). After evaporation of the solvent the residue was dissolved in cyclohexane (50 mL) and extracted with aq HCl (3 × 50 mL, 1 M). To the combined aq layers was added MTBE (50 mL) and the mixture was saturated with K_2CO_3 under vigorously stirring. After separation of the organic layer, the aq layer was extracted with MTBE (2 × 50 mL) and the combined organic layers were dried ($MgSO_4$). Evaporation of the solvent and flash chromatographic purification of the crude product on alumina (cyclohexane–CH_2Cl_2, 10:1) gave **10a** (1.94 g, 90%) as colorless oil.

IR (film): 3075 (w), 3063 (w), 3024 (m), 2956 (s), 2929 (ss), 2861 (m), 2836 (m), 1640 (w), 1494 (m), 1453 (m), 909 (m), 728 (m), 697 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 7.4 Hz, 2 H), 7.29 (t, *J* = 7.4 Hz, 2 H), 7.20 (t, *J* = 7.4 Hz, 1 H), 5.80–5.61 (m, 3 H), 4.93 (dd, *J* = 17.3, 1.7 Hz, 1 H), 4.89 (dd, *J* = 11.2, 0.8 Hz, 1 H), 3.73 (d,

J = 14.7 Hz, 1 H), 3.71 (d, *J* = 14.7 Hz, 1 H), 3.11–3.03 (m, 1 H), 2.83–2.75 (m, 1 H), 2.28–2.19 (m, 1 H), 1.95–1.87 (m, 2 H), 1.84–1.76 (m, 1 H), 1.63–1.47 (m, 3 H), 1.47–1.22 (m, 5 H), 0.82 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.0 (C_q), 139.1 (CH), 129.5 (CH), 128.5 (CH), 128.0 (CH), 126.4 (CH), 123.9 (CH), 114.2 (CH_2), 59.6 (CH), 56.9 (CH_2), 56.2 (CH), 37.0 (CH_2), 34.8 (CH_2), 33.9 (CH_2), 26.3 (CH_2), 26.1 (CH_2), 20.2 (CH_2), 14.3 (CH_3).

MS (EI): *m*/*z* (%) = 283 (1) $[M]^+$, 240 (15), 215 (12), 214 (100), 91 (66).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{20}H_{29}N$: 283.2300; found: 283.2301.

Anal. Calcd for $C_{20}H_{29}N$: C, 84.75; H, 10.31; N, 4.94. Found: C, 84.35; H, 9.93; N, 5.02.

(*rac*)-(2*S*,6*S*)-1-Benzyl-6-pent-4-enyl-2-propyl-1,2,3,6-tetrahydropyridine (10b)

The preparation of **10b** was similar to the procedure described for **10a**. After conversion of **9b** (3.75 g, 9.91 mmol) and chromatographic purification of the crude product on alumina (cyclohexane–CH_2Cl_2, 10:1) **10b** (2.50 g, 89%) was isolated as a colorless oil.

IR (film): 3074 (w), 3063 (w), 3022 (m), 2655 (s), 2930 (ss), 2871 (m), 2860 (m), 2832 (m), 2804 (w), 1640 (m), 1494 (m), 1466 (m), 1454 (m), 908 (s), 739 (m), 729 (m), 697 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 7.4 Hz, 2 H), 7.30 (t, *J* = 7.4 Hz, 2 H), 7.23 (t, *J* = 7.4 Hz, 1 H), 5.85–5.79 (m, 1 H), 5.78–5.67 (m, 1 H), 5.62–5.51 (m, 1 H), 4.91 (d, *J* = 17.3 Hz, 1 H), 4.89 (d, *J* = 9.9 Hz, 1 H), 3.78 (d, *J* = 13.7 Hz, 1 H), 3.34 (d, *J* = 13.7 Hz, 1 H), 3.07–2.99 (m, 1 H), 2.87 (br s, 1 H), 2.01–1.92 (m, 1 H), 1.90–1.81 (m, 3 H), 1.65–1.30 (m, 7 H), 1.30–1.17 (m, 1 H), 0.95 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.3 (Cq), 139.3 (CH), 129.8 (CH), 129.0 (CH), 128.0 (CH), 126.5 (CH), 125.5 (CH), 114.1 (CH_2), 56.7 (CH), 50.6 (CH), 49.6 (CH_2), 34.8 (CH_2), 33.7 (CH_2), 33.4 (CH_2), 27.0 (CH_2), 25.6 (CH_2), 19.8 (CH_2), 14.3 (CH_3).

MS (EI): *m*/*z* (%) = 283 (4) $[M]^+$, 240 (20), 215 (16), 214 (100), 91 (57).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{20}H_{29}N$: 283.2300; found: 283.2306.

Anal. Calcd for $C_{20}H_{29}N$: C, 84.75; H, 10.31; N, 4.94. Found: C, 84.84; H, 10.32; N, 4.90.

(*rac*)-(2*R*,4a*S*,5*R*,8a*S*)-1-Benzyl-5-methyl-2-propyl-decahydroquinoline (11a)

BuLi (6.17 mL, 1.6 M in hexane) was added dropwise over 10 min to a stirred solution of Cp_2ZrCl_2 (1.44 g, 4.94 mmol) in THF (150 mL) at –78 °C and the mixture was stirred for 30 min. Compound **10a** (1.40 g, 4.94 mmol) in THF (50 mL) was added dropwise over 15 min and stirring was continued for 1 h. The cooling bath was removed and the yellow solution was allowed to warm to r.t. and stirred for 5 h. The resulting clear bright orange solution was quenched dropwise with aq HCl (50 mL, 1 M) and stirred for 30 min. The aqueous layer was basified and saturated with K_2CO_3 under vigorously stirring. The organic layer was separated and the aqueous layer was extracted with MTBE (3 × 100 mL). The combined organic layers were washed with brine (50 mL) and dried ($MgSO_4$). Evaporation of the solvent and chromatographic purification of the crude product on alumina (cyclohexane–CH_2Cl_2, 20:1) yielded **11a** (1.04 g, 74%) and **12a** (279 mg, 20%).

11a

Polar fraction; colorless solid; mp 29–30 °C.

IR (film): 3084 (w), 3061 (w), 3025 (w), 2954 (s), 2926 (ss), 2859 (s), 1493 (w), 1452 (m), 1440 (w), 1356 (w), 951 (w), 727 (m), 696 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 7.4 Hz, 2 H), 7.27 (t, *J* = 7.4 Hz, 2 H), 7.17 (t, *J* = 7.4 Hz, 1 H), 3.75 (d, *J* = 17.1 Hz, 1 H), 3.67 (d, *J* = 17.1 Hz, 1 H), 2.55–2.47 (m, 1 H), 2.29–2.23 (m, 1 H), 2.05–1.96 (m, 1 H), 1.79–1.70 (m, 1 H), 1.70–1.58 (m, 2 H), 1.58–1.48 (m, 1 H), 1.48–1.43 (m, 1 H), 1.38–1.15 (m, 5 H), 1.10–0.90 (m, 5 H), 0.90 (d, *J* = 6.4 Hz, 3 H), 0.79 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.2 (C_q), 127.9 (CH), 127.5 (CH), 125.8 (CH), 68.3 (CH), 63.3 (CH), 51.3 (CH_2), 44.1 (CH), 37.8 (CH_2), 37.3 (CH), 35.6 (CH_2), 32.9 (CH_2), 29.5 (CH_2), 28.8 (CH_2), 25.4 (CH_2), 19.8 (CH_2), 19.6 (CH_3), 14.4 (CH_3).

MS (EI): *m*/*z* (%) = 285 (3) $[M]^+$, 243 (16), 242 (100), 91 (25).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{20}H_{31}N$: 285.2456; found: 285.2455.

Anal. Calcd for $C_{20}H_{31}N$: C, 84.15; H, 10.95; N, 4.91. Found: C, 84.15; H, 10.86; N, 4.91.

12a

Apolar fraction; pale yellow oil.

IR (film): 3085 (w), 3062 (w), 3024 (m), 2957 (ss), 2930 (ss), 2871 (m), 2861 (m), 1494 (m), 1453 (m), 965 (m), 728 (m), 697 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 7.4 Hz, 2 H), 7.29 (t, *J* = 7.4 Hz, 2 H), 7.21 (t, *J* = 7.4 Hz, 1 H), 5.80–5.73 (m, 1 H), 5.70–5.63 (m, 1 H), 5.43–5.24 (m, 2 H), 3.76 (d, *J* = 14.7 Hz, 1 H), 3.71 (d, *J* = 14.7 Hz, 1 H), 3.10–3.03 (m, 1 H), 2.84–2.75 (m, 1 H), 2.30–2.19 (m, 1 H), 2.05–1.94 (m, 2 H), 1.84–1.75 (m, 1 H), 1.65–1.52 (m, 1 H), 1.59 (d, *J* = 4.6 Hz, 3 H), 1.40–1.20 (m, 5 H), 0.82 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.9 (C_q), 131.5 (CH), 129.4 (CH), 128.5 (CH), 128.0 (CH), 126.5 (CH), 124.8 (CH), 123.8 (CH), 59.0 (CH), 57.2 (CH_2), 55.8 (CH), 37.0 (CH_2), 35.2 (CH_2), 29.8 (CH_2), 22.6 (CH_2), 20.2 (CH_2), 18.0 (CH_3), 14.3 (CH_3).

MS (EI): *m*/*z* (%) = 283 (1) $[M]^+$, 240 (14), 215 (16), 214 (100), 91 (62).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{20}H_{29}N$: 283.2300; found: 283.2304.

(*rac*)-(2*S*,4a*S*,5*R*,8a*S*)-1-Benzyl-5-methyl-2-propyl-decahydroquinoline (11b)

The preparation of **11b** was similar to the procedure described for **11a**. Conversion of **10b** (500 mg, 1.76 mmol) and chromatographic purification of the crude product on alumina (cyclohexane–CH_2Cl_2, 20:1) gave **11b** (347 mg, 69%) as colorless oil and an inseparable mixture of **12a** with **13a** (124 mg, 25%). Polar fraction (**11b**); apolar fraction (**12a** with **13a**).

11b

IR (film): 3084 (w), 3062 (w), 3025 (w), 2951 (s), 2926 (ss), 2868 (s), 2857 (s), 2801 (w), 2728 (w), 1493 (m), 1452 (s), 1374 (m), 1356 (m), 1161 (m), 1147 (m), 1139 (m), 1086 (m), 1072 (m), 1027 (m), 730 (s), 697 (s) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 7.4 Hz, 2 H), 7.28 (t, *J* = 7.4 Hz, 2 H), 7.18 (t, *J* = 7.4 Hz, 1 H), 3.77 (d, *J* = 14.7 Hz, 1 H), 3.73 (d, *J* = 14.7 Hz, 1 H), 2.66–2.59 (m, 1 H), 2.62–2.48 (m, 1 H), 1.88–1.76 (m, 2 H), 1.75–1.67 (m, 2 H), 1.64–1.55 (m, 2 H), 1.45–1.28 (m, 3 H), 1.28–1.03 (m, 5 H), 1.03–0.91 (m, 2 H), 0.88 (d, *J* = 6.4 Hz, 3 H), 0.83 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.9 (C_q), 128.2 (CH), 128.0 (CH), 126.2 (CH), 58.5 (CH), 56.1 (CH), 52.7 (CH_2), 44.6 (CH), 37.4 (CH), 35.7 (CH_2), 32.0 (CH_2), 29.6 (CH_2), 25.7 (CH_2), 24.8 (CH_2), 24.6 (CH_2), 20.4 (CH_2), 19.5 (CH_3), 14.4 (CH_2).

MS (EI): *m*/*z* (%) = 285 (3) $[M]^+$, 243 (16), 242 (100), 91 (25).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{20}H_{31}N$: 285.2456; found: 285.2456.

Anal. Calcd for $C_{20}H_{31}N$: C, 84.15; H, 10.95; N, 4.91. Found: C, 83.99; H, 10.73; N, 4.98.

12a with 13a

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.3 (C_q), 141.3 (C_q), 133.0 (CH), 131.1 (CH), 129.7 (CH), 129.4 (CH), 129.1 (CH), 129.0 (CH), 128.7 (CH), 128.0 (CH), 127.2 (CH), 126.5 (CH), 125.7 (CH), 125.6 (CH), 124.5 (CH), 105.4 (CH_2), 57.8 (CH), 56.5 (CH), 50.8 (CH), 50.7 (CH), 49.7 (CH_2), 49.6 (CH_2), 37.6 (CH_2), 35.1 (CH_2), 34.7 (CH_2), 34.5 (CH_2), 29.5 (CH_2), 27.1 (CH_2), 25.7 (CH_2), 19.9 (CH_2), 19.8 (CH_2), 18.0 (CH_3, CH), 14.3 (CH_3), 14.3 (CH), 13.8 (CH), 12.8 (CH_3).

MS (EI): *m*/*z* (%) = 283 (4) $[M]^+$, 240 (16), 238 (5), 215 (17), 214 (100), 91 (48).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{20}H_{29}N$: 283.2300; found: 283.2302.

(*rac*)-(2*R*,4a*S*,5*R*,8a*S*)-5-Methyl-2-propyl-decahydroquinoline (1)

Compound **11a** (500 mg, 1.75 mmol) was added to a stirred suspension of palladium on charcoal (94 mg, 10% Pd/C) in MeOH (35 mL). The mixture was flushed with hydrogen and stirred under ballon pressure at r.t. for 16 h. After filtration through celite and washing with MeOH (2 × 20 mL) the combined filtrates were dried ($MgSO_4$). The solvent was removed by distillation over a 10 cm Vigreux column at atmospheric pressure and the remaining liquid was purified by bulb to bulb distillation (0.05 mbar, 150 °C) to give **1** (302 mg, 88%) as colorless solid; mp 27–28 °C.

IR (film): 3274 (w), 2954 (s), 2923 (ss), 2869 (s), 2855 (s), 2793 (m), 2729 (w), 2671 (w), 2623 (w), 1450 (s), 752 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.52–2.44 (m, 1 H), 2.35–0.80 (m, 1 H, NH), 2.20–2.13 (m, 1 H), 2.00–1.93 (m, 1 H), 1.74–1.72 (m, 2 H), 1.66–1.58 (m, 2 H), 1.42–1.20 (m, 6 H), 1.23–0.93 (m, 3 H), 0.93–0.83 (m, 1 H), 0.90 (t, *J* = 6.8 Hz, 3 H), 0.87 (d, *J* = 6.3 Hz, 3 H), 0.70 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 61.4 (CH), 56.7 (CH), 48.5 (CH), 39.3 (CH_2), 36.3 (CH), 35.6 (CH_2), 33.8 (CH_2), 32.9 (CH_2), 29.0 (CH_2), 24.8 (CH_2), 19.2 (CH_3), 14.3 (CH_3).

MS (EI): *m*/*z* (%) = 196 (3) $[M+1]^+$, 195 (3), 153 (15), 152 (100), 109 (5).

HRMS: *m*/*z* $[M]^+$ calcd for $C_{13}H_{25}N$: 195.1987; found: 195.1988.

Anal. Calcd for $C_{13}H_{25}N$: C, 79.93; H, 12.90; N, 7.17. Found: C, 79.98; H, 12.92; N, 7.08.

(*rac*)-(2*S*,4a*S*,5*R*,8a*S*)-5-Methyl-2-propyl-decahydroquinoline (15)

The preparation of **15** was similar to the procedure described for **1**. Conversion of **11b** (235 mg, 0.82 mmol) and purification of the crude product by bulb-to-bulb distillation (0.05 mbar, 150 °C) yielded **15** (146 mg, 91%) as a colorless liquid.

IR (film): 3283 (w), 2952 (s), 2922 (ss), 2855 (s), 2783 (w), 2666 (w), 2636 (w), 2598 (w), 1457 (m), 1444 (m), 735 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.00–2.93 (m, 1 H), 2.39–2.30 (m, 1 H), 2.00–0.70 (m, 1 H, NH), 1.82–1.65 (m, 3 H), 1.65–1.48 (m, 4 H), 1.48–1.19 (m, 4 H), 1.19–0.94 (m, 4 H), 0.92 (t, *J* = 7.3 Hz, 3 H), 0.85 (d, *J* = 6.4 Hz, 3 H), 0.68 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 53.5 (CH), 52.0 (CH), 49.6 (CH), 36.2 (CH), 35.8 (CH_2), 34.6 (CH_2), 33.4 (CH_2), 29.8 (CH_2), 24.9 (CH_2), 23.8 (CH_2), 20.1 (CH_2), 19.0 (CH_3), 14.3 (CH_3).

MS (EI): *m*/*z* (%) = 195 (2) $[M]^+$, 153 (14), 152 (100), 109 (5), 55 (5), 41 (5).

HRMS: *m*/*z* calcd for $C_{13}H_{25}N$: 152.1439; found: 152.1433.

Anal. Calcd for $C_{13}H_{25}N$: C, 79.93; H, 12.90; N, 7.17. Found: C, 79.57; H, 12.79; N, 7.05.

(*rac*)-[(2*R*,4a*S*,5*R*,8a*S*)-5-Methyl-2-propyl-octahydroquinoline-1-yl]-(4-nitro-phenyl)-methanone (14)

p-Nitrobenzoyl chloride (114 mg, 614 μmol) was added to an ice-cold stirred suspension of **1** (100 mg, 512 μmol) and Et_3N (340 μL, 2.56 mmol) in CH_2Cl_2 (3 mL). The mixture was allowed to warm to r.t. and stirred for 3 h. After diluting with MTBE (50 mL) the mixture was washed with H_2O (2 × 10 mL), brine (10 mL) and dried ($MgSO_4$). Evaporation of the solvent and flash chromatographic purification of the crude product on silica gel (EtOAc–cyclohexane, 1:4) afforded **14** (146 mg, 83%) as a pale yellow solid; R_f 0.26; mp 134–136 °C (after recrystallization from Et_2O).

IR (film): 3104 (w), 3077 (w), 2954 (m), 2930 (m), 2870 (m), 1626 (ss), 1600 (m), 1522 (s), 1423 (m), 1346 (s), 862 (m), 851 (m), 705 (m) cm^{-1}.

^{1}H NMR (500 MHz, C_6D_6): δ = 7.73 (d, *J* = 8.5 Hz, 2 H), 6.94 (d, *J* = 8.5 Hz, 2 H), 3.83–3.72 (m, 1 H), 3.37 (br s, 1 H), 2.58 (br s, 1 H), 1.66–1.57 (m, 3 H), 1.55–1.40 (m, 3 H), 1.42–0.98 (m, 6 H), 0.92–0.73 (m, 3 H), 0.77 (d, *J* = 6.4 Hz, 3 H), 0.68 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.6 (C_q), 147.8 (C_q), 144.5 (C_q), 127.3 (CH), 123.9 (CH), 77.3 (CH), 60.5 (CH), 44.5 (CH), 41.9 (CH_2), 37.7 (CH), 35.9 (CH_2), 27.6 (CH_2), 25.3 (CH_2), 22.3 (CH_2), 20.2 (CH_2), 19.4 (CH_3), 14.7 (CH_2), 13.9 (CH_3).

MS (EI): *m*/*z* (%) = 195 (5) $[M+1]^+$, 303 (20), 302 (17), 301 (100), 275 (23), 150 (67).

HRMS: *m*/*z* calcd for $C_{20}H_{28}N_2O_3$: 344.2100; found: 344.2098.

Anal. Calcd for $C_{20}H_{28}N_2O_3$: C, 69.74; H, 7.92; N, 8.19. Found: C, 69.73; H, 8.04; N, 8.21

X-ray analysis in ref.[20]

(*rac*)-[(2*S*,4a*S*,5*R*,8a*S*)-5-Methyl-2-propyl-octahydroquinoline-1-yl]-(4-nitro-phenyl)-methanone (16)

The preparation of **16** was similar to the procedure described for **14**. Conversion of **15** (100 mg, 0.82 mmol) and purification of the crude product by flash chromatography on silica gel (cyclohexane–EtOAc, 1:4) gave **16** (154 mg, 87%) as a pale yellow solid; R_f 0.38, mp 122–124 °C (after recrystallization from Et_2O).

IR (film): 3106 (w), 3077 (w), 2955 (m), 2930 (m), 1645 (ss), 1602 (m), 1522 (s), 1458 (m), 1442 (m), 1420 (m), 1341 (ss), 1312 (m), 1293 (m), 863 (m), 853 (m), 726 (m) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 7.4 Hz, 2 H), 7.56 (d, *J* = 7.4 Hz, 2 H), 3.69–3.58 (m, 1 H), 2.99 (dt, *J* = 11.3 Hz, 3.6 Hz, 1 H), 2.68–2.50 (m, 1 H), 1.99–1.88 (m, 2 H), 1.87–1.79 (m, 1 H), 1.79–1.69 (m, 1 H), 1.65–1.52 (m, 4 H), 1.50–1.40 (m, 1 H), 1.33–1.18 (m, 4 H), 1.18–1.03 (m, 2 H), 1.26 (d, *J* = 6.0 Hz, 3 H), 0.90 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (500 MHz, $CDCl_3$): δ = 171.4 (C_q), 148.2 (C_q), 145.2 (C_q), 127.8 (CH), 123.9 (CH), 58.7 (CH), 57.3 (CH), 44.9 (CH), 38.4 (CH), 34.9 (CH_2), 32.2 (CH_2), 30.0 (CH_2), 29.4 (CH_2), 26.1 (CH_2), 25.3 (CH_2), 20.0 (CH_2), 19.4 (CH_3), 14.2 (CH_3).

MS (EI): *m*/*z* (%) = 344 (2) $[M]^+$, 302 (20), 301 (100), 150 (52), 104 (12), 69 (8).

HRMS: *m*/*z* calcd for $C_{20}H_{28}N_2O_3$: 344.2100; found: 344.2100.

Anal. Calcd for $C_{20}H_{28}N_2O_3$: C, 69.74; H, 7.92; N, 8.19. Found: C, 69.72; H, 8.28; N, 7.97.

X-ray analysis in ref.[20]

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