Supporting information

An Enantioselective Synthetic Route to *cis*-2,4-Disubstituted and 2,4-Bridged Piperidines.

Mercedes Amat, Maria Pérez, Annamaria T. Minaglia, and*

*Joan Bosch**

Supporting information-1:

- Experimental procedures and full spectroscopic data for all compounds: pages S2-S29

- ^{1}H NMR and ^{13}C NMR spectra for compounds **3a**-**11b**: pages S30-S50

Supporting information-2:

- ^{1}H NMR and ^{13}C NMR spectra for compounds **12a**-**21:** pages S51-S71

General Procedures. All non-aqueous reactions were performed under an argon or nitrogen atmosphere with dry, freshly distilled solvents using standard procedures. Drying of organic extracts during the work-up of reactions was performed over anhydrous Na_2SO_4 or $MgSO_4$. Evaporation of solvents was accomplished with a rotatory evaporator. Thin-layer chromatography was done on SiO_2 (silica gel 60 F_{254}), and the spots were located by UV and either a 1% $KMnO_4$ solution or iodine. Chromatography refers to flash column chromatography and was carried out on SiO_2 (silica gel 60, 230-400 mesh). Melting points were determined in a capillary tube and are uncorrected. NMR spectra were recorded at 300 or 400 MHz (^{1}H) and 75.4 or 100.6 MHz (^{13}C), and chemical shifts are reported in δ values downfield from TMS or relative to residual chloroform (7.26 ppm, 77.0 ppm) as an internal standard. Data are reported in the following manner: chemical shift, multiplicity, coupling constant (*J*) in hertz (Hz), integrated intensity, and assignment (when possible). Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; ap, apparent. Only noteworthy IR absorptions (cm^{-1}) are listed. Mass spectra (MS) data are reported as *m*/*z* (%).

(3*R*,8a*S*)-6-(Benzyloxycarbonyl)-8a-methyl-5-oxo-3-phenyl-6-(phenylselenyl)-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (2a). Lithium bis(trimethylsilyl)amide (1 M in THF, 29.5 mL) was slowly added at –78 ºC to a solution of lactam **1a**[1] (3.1 g, 13.4 mmol) in anhydrous THF (172 ml), and the resulting mixture was stirred for 90 min. Then, benzyl chloroformate (1.89 mL, 13.4 mmol) and, after 60 min of continuous stirring at –78 ºC, PhSeCl (3.6 g, 18.8 mmol) were added to the solution. The resulting mixture was stirred for 1 h and poured into saturated aqueous NH_4Cl. The aqueous layer was extracted with EtOAc, and the combined organic extracts were dried and concentrated. Flash chromatography (1:9 to 3:7 EtOAc-hexane) of the resulting oil afforded **2a** as a mixture of

C-6 epimers (6.05 g, 88% overall yield). **2a** (higher R_f epimer): IR (NaCl) 1651, 1723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, COSY) δ 1.17 (s, 3H, CH_3), 1.81-2.28 (m, 4H, H-7, H-8), 3.49 (dd, *J* = 8.8, 7.8 Hz, 1H, H-2), 4.48 (t, *J* = 8.8 Hz, 1H, H-2), 5.18 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.33 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.39 (t, *J* = 8.8 Hz, 1H, H-3), 7.15-7.70 (m, 15H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 24.3 (CH_3), 28.1 (C-7), 32.2 (C-8), 54.9 (C-6), 58.8 (C-3), 67.8 (CH_2 benzyl), 69.4 (C-2), 93.7 (C-8a), 125.2-129.6, 138.3 (C-*o*, *m*, *p*), 135.0, 139.5 (C-*i*), 165.5 (NCO), 170.4 (COO); $[\alpha]^{22}_D$ –39.2 (*c* 0.75, $CHCl_3$). Anal. Calcd for $C_{28}H_{27}NO_4Se$: C, 64.61; H, 5.23; N, 2.69. Found: C, 64.21; H, 5.28; N, 2.69. **2a** (lower R_f epimer): IR (NaCl) 1654, 1731 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, COSY, HETCOR) δ 0.93 (s, 3H, CH_3), 1.89-2.49 (m, 4H, H-7, H-8), 3.89 (dd, *J* = 8.8, 8.0 Hz, 1H, H-2), 4.38 (t, *J* = 8.8 Hz, 1H, H-2), 5.20 (d, *J* = 12.6 Hz, 1H, CH_2 benzyl), 5.29 (d, *J* = 12.6 Hz, 1H, CH_2 benzyl), 5.30 (t, *J* = 8.4 Hz, 1H, H-3), 7.16-7.57 (m, 15H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 23.1 (CH_3), 30.4 (C-7), 33.8 (C-8), 55.1 (C-6), 60.0 (C-3), 67.9 (CH_2 benzyl), 69.4 (C-2), 93.6 (C-8a), 125.2-129.5, 138.7 (C-*o*, *m*, *p*), 135.1, 138.7 (C-*i*), 165.2 (NCO), 170.1 (COO); $[\alpha]^{22}_D$ –142.3 (*c* 0.9, $CHCl_3$). Anal. Calcd for $C_{28}H_{27}NO_4Se$: C, 64.61; H, 5.23; N, 2.69. Found: C, 64.33; H, 5.19; N, 2.79.

(3*R*,8a*R*)-6-(Benzyloxycarbonyl)-5-oxo-3,8a-diphenyl-6-(phenylselenyl)-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (2b). Operating as in the above preparation of **2a**, from lactam **1b**[2] (3.0 g, 10.2 mmol), lithium bis(trimethylsilyl)amide (1 M in THF, 22.5 mL), benzyl chloroformate (1.51 mL, 10.2 mmol), and PhSeCl (2.74 g, 14.3 mmol), lactam **2b** was obtained as a mixture of C-6 epimers (4.65 g, 78% overall yield) after column chromatography (1:9 to 3:7 EtOAc-hexane). **2b** (higher R_f epimer): IR (NaCl) 1651, 1728 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, COSY) δ 1.68-2.44 (4m, 4H, H-7, H-8), 3.62 (t, *J* = 9.3 Hz, 1H, H-2), 4.42 (dd, *J* = 9.3, 8.1 Hz, 1H, H-2), 5.17 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.28 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.35 (dd, *J* = 9.3, 8.1 Hz, 1H, H-3), 7.05-7.70 (m,

20H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 26.1 (C-7), 34.0 (C-8), 55.7 (C-6), 60.9 (C-3), 68.0 (CH_2 benzyl), 69.2 (C-2), 97.5 (C-8a), 126.7-129.7 (C-*o*, *m*, *p*), 135.1, 140.6 (C-*i*), 167.4 (NCO), 171.1 (COO); $[\alpha]^{22}_D$ –75.3 (*c* 0.76, EtOH). Anal. Calcd for $C_{33}H_{29}NO_4Se$: C, 68.04; H, 5.02; N, 2.40. Found: C, 67.68; H, 5.06; N, 2.45.

(3*R*,8a*S*)-6-(Benzyloxycarbonyl)-8a-methyl-5-oxo-3-phenyl-2,3,8,8a-tetrahydro-5*H*-oxazolo

[3,2-*a*]pyridine (3a). A stream of ozone gas was bubbled through a cooled (–78 °C) solution of selenides **2a** (400 mg, 1.1 mmol) in anhydrous CH_2Cl_2 (20 mL) until it turned pale blue. The solution was purged with O_2, and the temperature was slowly raised to 25 °C. After 30 min of stirring, the mixture was poured into brine (20 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were dried and concentrated under reduced pressure to give **3a** (350 mg) as an oil, which was used in the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$, HETCOR) δ 1.51 (s, 3H, CH_3), 2.74 (m, 2H, H-8), 4.13 (dd, *J* = 9.3, 6.0 Hz, 1H, H-2), 4.39 (dd, *J* = 9.0, 6.9 Hz, 1H, H-2), 5.22-5.32 (m, 2H, CH_2 benzyl), 5.36 (dd, *J* = 6.9, 6.0 Hz, 1H, H-3), 7.20-7.62 (m, 11H, ArH, H-7).

(3*R*,8a*R*)-6-(Benzyloxycarbonyl)-5-oxo-3,8a-diphenyl-2,3,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (3b). Operating as in the above preparation of **3a**, from selenides **2b** (370 mg, 0.86 mmol) and anhydrous CH_2Cl_2 (25 mL), unsaturated lactam **3b** (320 mg) was obtained as an oil, which was used in the next reaction without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.98 (dd, *J* = 17.6, 6.8 Hz, 1H, H-8), 3.11 (dd, *J* = 17.6, 2.4 Hz, 1H, H-8), 3.70 (t, *J* = 9.2 Hz, H-2), 4.47 (dd, *J* = 9.2, 7.6 Hz, 1H, H-2), 5.22 (d, *J* = 12.8 Hz, 1H, CH_2 benzyl), 5.28 (d, *J* = 12.8 Hz, 1H, CH_2 benzyl), 5.32 (t, *J* = 7.6 Hz, 1H, H-3), 7.13-7.62 (m, 16H, ArH, H-7).

(3*R*,7*R*,8a*S*)-6-(Benzyloxycarbonyl)-8a-methyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (4a). LiCl (189 mg, 4.5 mmol) was heated at 80 ºC for 1 h under vacuum (10-15 mm Hg) in a three-necked, 500 mL round-bottomed flask. Then, CuI (357 mg, 4.5 mmol) and THF (5 mL) were added at rt, and the mixture was stirred at rt for 5 min. The suspension was cooled at –78 ºC, and vinylmagnesium bromide (1 M in THF, 4.5 mL), TMSCl (0.57 mL, 4.5 mmol), and the crude of unsaturated lactam **3a** (1.8 mmol) in THF (8 mL) were successively added. The resulting mixture was stirred at –78 ºC for 20 h. The reaction was quenched with saturated aqueous NH_4Cl, and the organic layer was extracted with EtOAc. The combined organic extracts were dried and concentrated. Flash chromatography (1:4 EtOAc-hexane) gave lactams **4a** (major) and 7-*epi*-**4a** as mixtures of C-6 epimers (508 mg, 62% overall yield from **2a**). **4a** (major C-6 epimer): IR (NaCl) 1665, 1744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.54 (s, 3H, CH_3), 1.94 (dd, *J* = 14.4, 8.4 Hz, 1H, H-8), 2.38 (dd, *J* = 14.4, 7.2 Hz, 1H, H-8), 3.15 (m, 1H, H-7), 3.40 (d, *J* = 10.8 Hz, 1H, H-6), 4.03 (dd, *J* = 9.2, 6.8 Hz, 1H, H-2), 4.41 (t, *J* = 8.4 Hz, 1H, H-2), 5.09 (m, 2H, CH_2=), 5.17 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.24 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.42 (t, *J* = 7.2 Hz, 1H, H-3), 5.74 (ddd, *J* = 17.2, 10.4, 7.2 Hz, 1H, CH=), 7.25-7.36 (m, 10H ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.7 (CH_3), 36.0 (C-7), 39.5 (C-8), 53.7 (C-6), 59.1 (C-3), 67.0 (CH_2 benzyl), 69.2 (C-2), 93.2 (C-8a), 116.5 (CH_2=), 124.5-128.5 (C-*o*, *m*, *p*), 135.6, 139.7 (C-*i*), 138.1 (CH=), 166.7 (NCO), 168.7 (COO). Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.64; H, 6.44; N, 3.58. Found: C, 73.30; H, 6.58; N, 3.51.

(3*R*,7*R*,8a*R*)-6-(Benzyloxycarbonyl)-5-oxo-3,8a-diphenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (4b). Operating as described for the preparation of **4a**, from crude lactam **3b** (0.58 mmol), vinylmagnesium bromide (1 M solution in THF, 1.62 mL), CuI (308 g, 1.62 mmol), LiCl (69 mg, 1.62 mmol), and TMSCl (200 □L, 1.62 mmol) in THF (10.5 mL), lactams **4b** (major) and 7-*epi*-**4b** were obtained as mixtures of C-

6 epimers (160 mg, 61% overall yield from **2b**) after flash chromatography (1:4 to 1:2 EtOAc-hexane). **4b** (major C-6 epimer): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (s, 3H, CH_3), 2.02 (dd, *J* = 14.8, 10.4 Hz, 1H, H-8), 2.63 (dd, *J* = 14.8, 5.6 Hz, 1H, H-8), 3.19 (m, 1H, H-7), 3.40 (d, *J* = 11.6 Hz, 1H, H-6), 3.87 (t, *J* = 8.8 Hz, 1H, H-2), 4.39 (dd, *J* = 8.8, 8.4 Hz, 1H, H-2), 5.09 (m, 2H, CH_2=), 5.20 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.25 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.46 (m, 2H, H-3, CH=), 7.25-7.36 (m, 15H ArH); ^{13}C NMR ($CDCl_3$, 100.6) δ 37.3 (C-7), 42.4 (C-8), 55.0 (C-6), 60.7 (C-3), 67.1 (CH_2 benzyl), 68.5 (C-2), 96.3 (C-8a), 117.1 (CH_2=), 125.7-128.6 (C-*o*, *m*, *p*), 135.5, 138.0, 142.4 (C-*i*), 137.1 (CH=), 168.6 (NCO), 168.9 (COO).

(3*R*,7*S*,8a*S*)-7-Allyl-6-(benzyloxycarbonyl)-3-methyl-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (5a). Operating as in the preparation of **4a**, from crude lactam **3a** (0.54 mmol), allylmagnesium bromide (1 M solution in Et_2O, 2.15 mL), CuI (197 mg, 2.15 mmol), LiCl (91 mg, 2.15 mmol), and TMSCl (272 □L, 2.15 mmol) in THF (11 mL), lactams **5a** (major) and 7-*epi*-**5a** were obtained as mixtures of C-6 epimers (217 mg, 70% overall yield from **2a**) after flash chromatography (1:4 EtOAc-hexane). **5a** (major C-6 epimer): IR (NaCl) 1665, 1741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, COSY) δ 1.39 (2s, 3H, CH_3), 1.80 (dd, *J* = 14.7, 8.7 Hz, 1H, H-8), 2.11, 2.25 (2m, 2H, CH_2 allyl), 2.33 (dd, *J* = 14.1, 6.9 Hz, 1H, H-8), 2.57 (m, 1H, H-7), 3.25 (d, *J* = 11.4 Hz, 1H, H-6), 4.00 (dd, *J* = 8.7, 6.3 Hz, 1H, H-2), 4.38 (t, *J* = 8.7 Hz, 1H, H-2), 5.05 (m, 2H, CH_2=), 5.19 (d, *J* = 12.3 Hz, 1H, CH_2 benzyl), 5.26 (d, *J* = 12.3 Hz, 1H, CH_2 benzyl), 5.39 (t, *J* = 7.2 Hz, 1H, H-3), 5.69 (m, 1H, CH=), 7.20-7.40 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.0 (CH_3), 31.5 (C-7), 26.3 (C-8), 38.7 (CH_2 allyl), 54.1 (C-6), 59.1 (C-3), 67.0 (CH_2 benzyl), 69.1 (C-2), 93.2 (C-8a), 118.2 (CH_2=), 124.9-128.7 (C-*o*, *m*, *p*); 134.8 (CH=), 135.4, 139.7 (C-*i*), 167.2 (COO), 169.1 (NCO). Anal. Calcd for $C_{25}H_{27}NO_4$: C, 74.05; H, 6.71; N, 3.45. Found: C, 73.81; H, 6.82; N, 3.41.

(3*R*,7*S*,8a*R*)-7-Allyl-6-(benzyloxycarbonyl)-5-oxo-3,8a-diphenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (5b). Operating as in the preparation of **4a**, from crude lactam **3b** (0.63 mmol), allylmagnesium bromide (1 M solution in Et_2O, 1.76 mL), CuI (336 mg, 1.76 mmol), LiCl (65 mg, 1.76 mmol), and TMSCl (222 □L, 1.76 mmol) in THF (9 mL), lactams **5b** (major) and 7-*epi*-**5b** were obtained as mixtures of C-6 epimers (274 mg, 91% overall yield from **2b**) after column chromatography (1:5 to 1:2 EtOAc-hexane). **5b** (major C-6 epimer): IR (NaCl) 1667, 1743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, HETCOR) δ 1.75 (dt, *J* = 13.5, 7.2, 7.2 Hz, 1H, CH_2 allyl), 1.97 (dd, *J* = 14.4, 10.8 Hz, 1H, H-8), 1.99 (m, 1H, CH_2 allyl), 2.54 (dd, *J* = 14.4, 6.0 Hz, 1H, H-8), 2.60 (m, 1H, H-7), 3.28 (d, *J* = 10.8 Hz, 1H, H-6), 3.84 (t, *J* = 9.0 Hz, 1H, H-2), 4.36 (dd, *J* = 9.0, 8.4 Hz, 1H, H-2), 4.82 (dd, *J* = 17.1, 1.5 Hz, 1H, CH_2=), 4.93 (dm, *J* = 10.2 Hz, 1H, CH_2=), 5.22 (d, *J* = 12.3 Hz, 1H, CH_2 benzyl), 5.28 (d, *J* = 12.3 Hz, 1H, CH_2 benzyl), 5.41 (t, *J* = 8.1 Hz, 1H, H-3), 5.55 (m, 1H, CH=), 7.05-7.40 (m, 15H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 32.4 (C-7), 38.0 (CH_2 allyl), 41.4 (C-8), 55.1 (C-6), 60.8 (C-3), 67.2 (CH_2 benzyl), 68.6 (C-2), 96.0 (C-8a), 118.1 (CH_2=), 125.8-128.6 (C-*o*, *m*, *p*), 134.1, 135.4, 142.3 (C-*i*), 169.5 (COO), 170.0 (NCO).

(3*R*,7*S*,8a*S*)-6-(Benzyloxycarbonyl)-8a-methyl-5-oxo-3,7-diphenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (6a). Operating as in the preparation of **4a**, from crude lactam **3a** (0.46 mmol), phenylmagnesium bromide (1 M solution in THF, 1.12 mL), CuI (213 mg, 1.12 mmol), LiCl (47 mg, 1.12 mmol), and TMSCl (141 □L, 1.12 mmol) in THF (9 mL), lactams **6a** (major) and 7-*epi*-**6a** were obtained as mixtures of C-6 epimers (150 mg, 74% overall yield from **2a**) after column chromatography (1:4 EtOAc-hexane). Repurification by column chromatography (1:2 Et_2O-hexane) and then crystallization from Et_2O-hexane afforded pure **6a** (major C-6 epimer): IR (NaCl) 1663, 1744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.56 (s, 3H, CH_3), 2.15 (dd, *J* = 14.4, 12.0 Hz, 1H,

H-8), 2.64 (dd, *J* = 14.4, 5.6 Hz, 1H, H-8), 3.59 (td, *J* = 12.0, 12.0, 5.6 Hz, 1H, H-7), 3.82 (d, *J* = 12.0 Hz, 1H, H-6), 4.04 (dd, *J* = 8.4, 6.8 Hz, 1H, H-2), 4.53 (t, *J* = 8.4 Hz, 1H, H-2), 4.97 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.05 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.55 (t, *J* = 7.6 Hz, 1H, H-3), 7.25-7.36 (m, 15H ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.4 (CH_3), 38.8 (C-7), 42.8 (C-8), 55.3 (C-6), 59.0 (C-3), 66.8 (CH_2 benzyl), 69.0 (C-2), 93.2 (C-8a), 125.5-128.9 (C-*o*, *m*, *p*), 135.5, 140.2, 140.6 (C-*i*), 167.6 (NCO),168.2 (COO); mp 153-154 ºC; $[\alpha]^{22}_D$ – 87.1 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{28}H_{27}NO_4$: C, 76.17; H, 6.16; N, 3.17. Found: C, 75.97; H, 6.14; N, 3.14. **6a** (minor C-6 epimer): ^{1}H NMR (400 MHz, $CDCl_3$, selected resonances) δ 1.57 (s, 3H, CH_3), 3.65 (m, 1H, H-7), 4.04 (dd, *J* = 8.4, 6.8 Hz, 1H, H-2), 4.62 (t, *J* = 8.4 Hz, 1H, H-2), 5.44 (t, *J* = 7.6 Hz, 1H, H-3); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 27.4 (CH_3), 40.3 (C-8), 42.0 (C-7), 57.3 (C-6), 58.5 (C-3), 67.2 (CH_2 benzyl), 69.9 (C-2), 93.5 (C-8a), 135.4, 140.6, 140.9 (C-*i*); *m/z*: 442 (M+1, 8), 441 (M^+, 25), 427 (18), 426 (60), 350 (39), 306 (16), 162 (10), 160 (10), 120 (11), 104 (35), 91 (100); HMRS calcd for $C_{28}H_{27}NO_4$: 441.1940, found: 441.1920.

(3*R*,7*S*,8a*R*)-6-(Benzyloxycarbonyl)-5-oxo-3,7,8a-triphenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (6b). Operating as described for the preparation of **4a**, from crude lactam **3b** (0.27 mmol), phenylmagnesium bromide (1 M solution in THF, 0.75 mL), CuI (144 mg, 0.75 mmol), LiCl (32 mg, 0.75 mmol), and TMSCl (95 μL, 0.75 mmol) in THF (7 mL), lactams **6b** (major) and 7-*epi*-**6b** were obtained as mixtures of C-6 epimers (98 mg, 72% overall yield from **2b**) after column chromatography (1:4 to 1:2 EtOAc-hexane). **6b** (mixture of C-6 epimers): IR (NaCl) 1665, 1732 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, COSY) δ 2.17 (dd, *J* = 15.2, 12.8 Hz, 1H, H-8 isomer 1), 2.65 (ddd, *J* = 14.4, 4.0, 2.0 Hz, 1H, H-8 isomer 2), 2.80 (dd, *J* = 15.2, 4.8 Hz, 1H, H-8 isomer 1), 2.88 (t, *J* = 14.4 Hz, 1H, H-8 isomer 2), 3.68 (m, 2H, H-7), 3.90 (t, *J* = 8.8 Hz, 1H, H-2 isomer 1), 3.91 (d, *J* = 12.8 Hz, 1H, H-6 isomer 1), 3.97 (t, *J* = 8.8 Hz, 1H, H-2 isomer 2), 2.03 (dd, *J* = 4.8, 2.0 Hz, 1H, H-

6 isomer 2), 4.45 (td, *J* = 8.8, 2.0 Hz, 1H, H-2), 4.94 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl isomer 1), 4.98 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl isomer 1), 4.99 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl isomer 2), 5.06 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl isomer 2), 7.00-7.60 (20H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 36.5, 38.3 (C-7), 39.8, 45.7 (C-8), 56.3, 56.6 (C-6), 60.2, 61.0 (C-3), 67.2, 67.3 (CH_2 benzyl), 67.9, 68.6 (C-2), 96.5, 97.0 (C-8a), 125.4-128.7 (C-*o*, *m*, *p*), 135.1-143.1 (C-*i*), 168.2, 168.5 (COO), 169.3, 169.7 (NCO). Anal. Calcd for $C_{33}H_{29}NO_4 \cdot {}^1/_2H_2O$: C, 75.99; H, 5.99; N, 2.69. Found: C, 76.00; H, 5.60; N, 2.57.

(3*R*,7*S*,8a*S*)-7-Ethyl-8a-methyl-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (7a). A solution of **4a** containing minor amounts of 7-*epi*-**4a** (273 mg, 0.69 mmol) in MeOH (23 mL) containing 10% Pd/C (31 mg) was hydrogenated at rt for 48 h at atmospheric pressure. The catalyst was removed by filtration, and the solvent was evaporated. The resulting oil was dissolved in toluene (42 mL), and the solution was heated at reflux for 20 h, cooled, and poured into saturated aqueous NH_4Cl. The aqueous layer was extracted with EtOAc, and the combined organic extracts were dried and concentrated. The residue was chromatographed (1:1 EtOAc-hexane) to afford lactams **7a** and 7-*epi*-**7a** (ratio 93:7, 143 mg, 80% overall yield). **7a**: IR (NaCl) 1650 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 0.95 (t, *J* =7.2 Hz, 3H, CH_3 ethyl), 1.35 (s, 3H, CH_3 angular), 1.41 (q, *J* =7.2 Hz, 2H, CH_2 ethyl), 1.65 (dd, *J* = 14.0, 10.0 Hz, 1H, H-8), 1.84 (m, 1H, H-7), 2.05 (dd, *J* = 14.8, 12.0 Hz, 1H, H-6), 2.36 (ddd, *J* = 14.0, 5.2, 2.0 Hz, 1H, H-8), 2.55 (ddd, *J* = 14.8, 3.6, 2.4 Hz, 1H, H-6), 3.97 (dd, *J* = 8.8, 6.8 Hz, 1H, H-2), 4.57 (t, *J* = 8.8 Hz, 1H, H-2), 5.45 (t, *J* = 8.0 Hz, 1H, H-3), 7.20-7.34 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 11.3 (CH_3 ethyl), 27.3 (CH_3 angular), 28.6 (CH_2 ethyl), 31.5 (C-7), 38.7 (C-6), 41.2 (C-8), 58.4 (C-3), 69.0 (C-2), 93.7 (C-8a), 125.3-128.5 (C-*o*, *m*, *p*), 140.8 (C-*i*), 171.5 (NCO). Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 73.89; H, 8.14; N, 5.07.

(3*R*,7*S*,8a*R*)-7-Ethyl-5-oxo-3,8a-diphenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (7b). Ammonium formate (134 mg, 1.74 mmol) and 10% Pd/C (55 mg) were added to a solution of **4b** containing minor amounts of 7-*epi*-**4b** (100 mg, 0.22 mmol) in anhydrous MeOH (4 mL). The resulting suspension was stirred at rt for 18 h, filtered (Celite®), and concentrated to give an oil, which was dissolved in toluene (27 mL). The solution was heated at reflux for 12 h, cooled, and poured into brine. The aqueous layer was extracted with EtOAc, and the combined organic layers were dried and concentrated. The residue was chromatographed (1:3 EtOAc-hexane) to afford lactams **7b** and 7-*epi*-**7b** (ratio 94:6, 51 mg, 73% overall yield). **7b**: IR (NaCl) 1668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, HETCOR) δ 0.89 (t, *J* = 7.6 Hz, 3H, CH_3), 1.24-1.34 (m, 2H, CH_2 ethyl), 1.71 (dd, *J* = 14.4, 11.2 Hz, 1H, H-8), 1.92 (m, 1H, H-7), 2.15 (dd, *J* = 14.8, 12.4 Hz, 1H, H-6), 2.60 (m, 2H, H-6, H-8), 3.82 (t, *J* = 8.8 Hz, 1H, H-2), 4.40 (t, *J* = 8.8 Hz, 1H, H-2), 5.45 (t, *J* = 8.8 Hz, 1 H, H-3), 6.98-7.38 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 11.1 (CH_3), 28.0 (CH_2 ethyl), 32.4 (C-7), 39.6 (C-6), 44.3 (C-8), 60.0 (C-3), 68.4 (C-2), 97.0 (C-8a), 125.6-128.4 (C-*o*, *m*, *p*), 138.9-143.6 (C-*i*), 173.3 (NCO). *m/z*: 322 (M+1, 8), 321 (M^+, 31), 264 (32), 244 (31), 225 (6), 224 (37), 223 (7), 222 (29), 203 (36), 193 (16), 175 (7), 146 (14), 120 (67), 119 (35), 105 (100), 104 (57), 103 (24), 91 (34). Anal. Calcd for $C_{21}H_{23}NO_2 \cdot {}^1/_2$hexane: C, 79.08; H, 8.30; N, 3.24. Found: C, 78.64; H, 8.30; N, 3.48.

(3*R*,7*S*,8a*S*)-8a-Methyl-5-oxo-3-phenyl-7-propyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (8a). Operating as above, from the above mixture of **5a** and 7-*epi*-**5a** (185 mg, 0.45 mmol), ammonium formate (560 mg, 9.0 mmol), and 10% Pd/C (86 mg) in MeOH (6.5 mL), lactams **8a** and 7-*epi*-**8a** were obtained (ratio 78:22, 89 mg, 72% overall yield) after column chromatography (1:2 EtOAc-hexane). **8a**: IR (NaCl) 1665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, HETCOR) δ 0.91-0.96 (m, 3H, CH_3 propyl), 1.36-1.44 (m, 7H, $2CH_2$ propyl, CH_3 angular), 1.65 (dd, *J* = 14.4, 10.4 Hz, 1H, H-8), 1.93 (m, 1H, H-7), 2.06 (dd, *J* = 14.8, 12.4 Hz, 1H, H-6), 2.35 (ddd, *J* = 14.4, 5.6, 2.4 Hz, 1H, H-8), 2.54 (ddd, *J* =

14.8, 3.2, 2.0 Hz, 1H, H-6), 3.97 (dd, *J* = 8.8, 6.8 Hz, 1H, H-2), 4.46 (t, *J* = 8.8 Hz, 1H, H-2), 5.45 (t, *J* = 8.0 Hz, 1H, H-3), 7.19-7.35 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.1 (CH_3 propyl), 19.8 (CH_2 propyl), 27.3 (CH_3 angular), 29.5 (C-7), 38.0 (CH_2 propyl), 39.0 (C-6), 41.6 (C-8), 58.4 (C-3), 69.0 (C-2), 93.8 (C-8a), 121.1-128.5 (C-*o*, *m*, *p*), 140.8 (C-*i*), 171.5 (NCO); *m/z*: 274 (M+1, 5), 273 (M^+, 25), 259 (6), 258 (36), 230 (5), 203 (4), 162 (23), 161 (21), 160 (24), 155 (4), 146 (8), 138 (4), 132 (6), 130 (8), 128 (9), 121 (8), 120 (100), 119 (31), 118 (31), 104 (45), 97 (26), 91 (21). 7-*epi*-**8a**: ^{1}H NMR (400 MHz, $CDCl_3$, selected resonances) δ 2.20 (dm, *J* = 12.0 Hz, 1H, H-6), 2.74 (dm, *J* = 12.0 Hz, 1H, H-6), 4.53 (t, *J* = 8.8 Hz, 1H, H-2), 5.35 (t, *J* = 8.0 Hz, 1H, H-3), 7.19-7.35 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 24.0 (CH_3), 29.5 (C-7), 38.5 (C-6), 31.3 (CH_2 propyl), 41.6 (C-8), 58.4 (C-3), 70.0 (C-2), 93.9 (C-8a), 140.1 (C-*i*), 170.0 (NCO); *m/z*: 274 (M+1, 5), 273 (M^+, 24), 259 (8), 258 (43), 230 (5), 203 (1), 162 (19), 161 (12), 160 (20), 155 (4), 146 (6), 138 (4), 132 (6), 130 (6), 128 (7), 121 (4), 120 (100), 119 (25), 118 (22), 104 (41), 97 (27), 91 (16). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.37; H, 8.60; N, 4.76.

(3*R*,7*S*,8a*R*)-5-Oxo-3,8a-diphenyl-7-propyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (8b). Operating as described for the preparation of **7b**, from the above mixture of **5b** and 7-*epi*-**5b** (75 mg, 0.16 mmol), ammonium formate (81 mg, 1.3 mmol), and 10% Pd/C (35 mg) in MeOH (2.3 mL), lactams **8b** and 7-*epi*-**8b** were obtained (ratio 85:15, 41 mg, 73% overall yield) after column chromatography (1:3 EtOAc-hexane). **8b**: IR (NaCl) 1667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.2 Hz, 3H, CH_3), 1.16-1.38 (m, 4H, $2CH_2$ propyl), 1.70 (dd, *J* = 14.4, 11.2 Hz, 1H, H-8), 1.96-2.10 (m, 1H, H-7), 2.35 (dd, *J* = 14.8, 12.8 Hz, 1H, H-6), 2.59 (m, 2H, H-6, H-8), 3.82 (t, *J* = 8.8 Hz, 1H, H-2), 4.40 (t, *J* = 8.4 Hz, 1H, H-2), 5.45 (t, *J* = 8.8 Hz, 1H, H-3), 6.98-7.48 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.0 (CH_3), 19.6 (CH_2 propyl), 30.4 (C-7), 37.4 (CH_2 propyl), 39.9 (C-6),

44.6 (C-8), 60.0 (C-3), 68.4 (C-2), 97.0 (C-8a), 125.6-128.5 (C-*o*, *m*, *p*), 138.9, 143.6 (C-*i*), 173.4 (NCO). 7-*epi*-**8b**: ^{1}H NMR (400 MHz, $CDCl_3$, selected resonances) δ 0.95 (t, *J* = 7.2 Hz, 3H, CH_3), 2.80 (m, 2H, H-6, H-8), 3.97 (t, *J* = 8.4 Hz, 1H, H-2), 4.45 (t, *J* = 8.8 Hz, 1H, H-2), 5.27 (t, *J* = 8.4 Hz, 1H, H-3); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 12.0 (CH_3), 19.6 (CH_2 propyl), 30.4 (C-7), 37.4 (CH_2 propyl), 39.9 (C-6), 44.6 (C-8), 60.0 (C-3), 68.4 (C-2), 97.2 (C-8a), 138.4, 142.0 (C-*i*), 171.8 (NCO). Anal. Calcd for $C_{22}H_{25}NO_2$: C, 78.77; H, 7.51; N, 4.18. Found: C, 78.39; H, 7.93; N, 3.91.

(3*R*,7*S*,8a*S*)-8a-Methyl-5-oxo-3,7-diphenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (9a). Operating as described for the preparation of **7b**, from pure lactam **6a** (major C-6 epimer, 200 mg, 0.45 mmol), ammonium formate (457 mg, 7.2 mmol), and 10% Pd/C (94 mg) in EtOAc-MeOH (5:7 mL), lactam **9a** was obtained as a white solid (94 mg, 68% overall yield) after column chromatography (1:2 EtOAc-hexane): IR (NaCl) 1664 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, HETCOR) δ 1.34 (s, 3H, CH_3), 2.15 (dd, *J* = 14.4, 12.0 Hz, 1H, H-8), 2.61 (ddd, *J* = 14.4, 4.8, 2.8 Hz, 1H, H-8), 2.66 (dd, *J* = 15.2, 12.0 Hz, 1H, H-6), 2.75 (ddd, *J* = 15.2, 3.6, 2.4 Hz, 1H, H-6), 3.21 (tt, *J* = 12.0, 4.4 Hz, 1H, H-7), 4.02 (dd, *J* = 8.8, 7.2 Hz, 1H, H-2), 4.55 (t, *J* = 8.8 Hz, 1H, H-2), 5.56 (t, *J* = 8.0 Hz, 1H, H-3), 7.06-7.42 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.2 (CH_3), 35.5 (C-7), 39.6 (C-6), 43.0 (C-8), 58.4 (C-3), 69.0 (C-2), 94.0 (C-8a), 125.3-128.9 (C-*o*, *m*, *p*), 140.8, 142.4 (C-*i*), 171.2 (NCO); mp 104-106 ºC; $[\alpha]^{22}_{D}$ – 11.6 (*c* 0.2, $CHCl_3$). Anal. Calcd for $C_{20}H_{21}NO_2 \cdot {}^{1}/_{4}H_2O$: C, 77.02; H, 6.95; N, 4.49. Found: C, 76.75; H, 7.31; N, 4.10. Operating as in the preparation of **7b**, from the above mixture of **6a** and 7-*epi*-**6a** (100 mg, 0.22 mmol), ammonium formate (220 mg, 3.5 mmol), and 10% Pd/C (47 mg) in EtOAc-MeOH (2.5:3.5 mL), lactams **9a** and 7-*epi*-**9a** were obtained (ratio 84:16, 60 mg, 69% overall yield) after column chromatography (1:2 EtOAc-hexane): 7-*epi*-**9a**: (400 MHz, $CDCl_3$, selected resonances) δ 1.25 (s, 3H, CH_3), 2.04 (*J* = 12.4 Hz, 1H, H-6), 2.39 (ddd, *J* = 12.4,

3.2, 2.0 Hz, 1H, H-6), 2.52 (dd, *J* = 18.4, 11.6 Hz, 1H, H-8), 2.96 (ddm, *J* = 18.2, 6.4 Hz, 1H, H-8), 3.33 (m, 1H, H-7), 4.03 (dd, *J* = 8.8, 8.0 Hz, 1H, H-2), 4.60 (t, *J* = 8.8 Hz, 1H, H-2), 5.43 (t, *J* = 8.4 Hz, 1 H, H-3), 7.06-7.42 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 24.0 (CH_3), 29.8 (C-6), 35.6 (C-7), 41.5 (C-8), 70.0 (C-2), 94.1 (C-8a), 125.3-128.9 (C-*o*, *m*, *p*), 140.2, 142.6 (C-*i*), 170.0 (NCO).

(3*R*,7*S*,8a*R*)-5-Oxo-3,7,8a-triphenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (9b). Operating as in the preparation of **7b**, from the above mixture of **6b** and 7-*epi*-**6b** (1.9 g, 3.77 mmol), ammonium formate (1.9 mg, 30.2 mmol), and 10% Pd/C (200 mg) in EtOAc (180 mL), lactams **9b** and 7-*epi*-**9b** were obtained (ratio 92:8). Flash chromatography (1:1 Et_2O-hexane) afforded pure **9b** (1.07 g, 83% overall yield): IR (NaCl) 1667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (dd, *J* = 14.8, 12.4 Hz, 1H, H-8), 2.70-2.84 (m, 3H, H-6, H-8), 3.28 (tt, *J* = 12.8, 3.6 Hz, 1H, H-7), 3.90 (t, *J* = 8.8 Hz, 1H, H-2), 4.47 (t, *J* = 8.8 Hz, 1H, H-2), 5.55 (t, *J* = 8.8 Hz, 1H, H-3), 7.00-7.40 (m, 15H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 36.4 (C-7), 40.7 (C-6), 46.0 (C-8), 60.1 (C-3), 68.4 (C-2), 97.0 (C-8a), 125.6-128.7 (C-*o*, *m*, *p*), 139.8, 141.9, 143.3 (C-*i*), 173.9 (NCO); *m/z*: 370 (M+1, 5), 369 (M^+, 16), 392 (13), 265 (18), 264 (47), 224 (25), 222 (34), 193 (20), 146 (23), 131 (54), 121 (21), 120 (91), 119 (26), 105 (98), 104 (100), 103 (59), 91 (40); HMRS calcd for $C_{25}H_{23}NO_2$: 370.1801, found: 370.1803. Anal. Calcd for $C_{25}H_{23}NO_2$: C, 81.27; H, 6.27; N, 3.79. Found: C, 81.05; H, 6.27; N, 3.60. 7-*epi*-**9b**: ^{1}H NMR (300 MHz, $CDCl_3$, selected resonances) δ 3.64 (t, *J* = 9.3 Hz, 1H, H-2), 4.41 (dd, *J* = 9.3, 8.4 Hz, 1H, H-2), 5.29 (t, *J* = 8.4 Hz, 1 H, H-3), 6.99-7.40 (m, 15H, ArH).

(2*R*,4*R*)-1-[(1*R*)-2-Hydroxy-1-phenylethyl]-2-methyl-4-phenylpiperidine (10a). $LiAlH_4$ (273 mg, 7.2 mmol) was slowly added to a solution of lactam **9a** (220 mg, 0.72 mmol) in anhydrous THF (20 mL) at 0 °C, and the mixture was stirred at room temperature for 20 h. The reaction was quenched by a slow addition of distillated water, and the aqueous layer

was extracted with EtOAc. The combined organic extracts were dried and concentrated, and the resulting residue was chromatographed (2:8 EtOAc-hexane) to give pure piperidine **10a** (149 mg, 70% yield): IR (NaCl) 3418 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, COSY) δ 1.35 (d, *J* = 6.0 Hz, 3H, CH_3), 1.52 (td, *J* = 12.3, 12.3, 10.8 Hz, 1H, H-3ax), 1.68 (td, *J* = 12.3, 12.3, 3.6 H, 1H, H-5ax), 1.85 (m, 3H, H-6ax, H-3eq, H-5eq), 2.41 (tt, *J* = 12.3, 3.6 Hz, 1H, H-4), 2.57 (ddddd, *J* = 10.8, 6.0, 6.0, 6.0, 2.4 Hz, 1H, H-2), 3.04 (dt, *J* = 11.4, 3.3, 3.3 Hz, 1H, H-6eq), 3.58 (dd, *J* = 10.2, 5.1 Hz, 1H, H-1'), 4.05 (t, *J* = 10.5 Hz, 1H, H-2'), 4.39 (dd, *J* = 10.8, 5.1 Hz, 1H, H-2'), 7.15-7.35 (m, 5H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 21.4 (CH_3), 33.6 (C-5), 42.6 (C-4), 43.7 (C-3), 45.4 (C-6), 53.5 (C-2), 59.0 (C-2'), 60.6 (C-1'), 126.1, 127.7 (C-*p*), 126.6, 128.1, 128.3, 128.8 (C-*o*, *m*), 135.1, 145.9 (C-*i*); $[\alpha]^{22}_D$ – 43.1 (*c* 1.1, $CHCl_3$); HMRS calcd for [$C_{20}H_{25}NO$ + H]: 296.2008, found: 296.2018.

(2*S*,4*S*)-1-[(1*R*)-2-Hydroxy-1-phenylethyl]-2,4-diphenylpiperidine (10b). Operating as in the preparation of **10a**, from lactam **9b** (70 mg, 0.19 mmol) in anhydrous THF (5 mL), and $LiAlH_4$ (72 mg, 1.9 mmol), pure piperidine **10b** was obtained (60 mg, 88% yield) after column chromatography (2:8 EtOAc-hexane): IR (NaCl) 3376 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, COSY, HETCOR) δ 1.81 (dt, *J* = 12.0, 12.0, 11.1 Hz, 1H, H-3ax), 1.87 (dddd, *J* = 12.6, 12.6, 12.6, 3.6 Hz, 1H, H-5ax), 1.95 (m, 2H, H-5eq, H-3eq), 2.12 (td *J* = 12.0, 12.0, 2.4 Hz, 1H, H-6ax), 2.52 (tt, *J* = 12.0, 3.9 Hz, 1H, H-4), 3.27 (dt, *J* = 12.0, 3.3, 3.3 Hz, 1H, H-6eq), 3.45 (m, 2H, H-2, H-2'), 4.09 (m, 2H, H-1', H-2'), 7.05-7.42 (m, 15H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 33.3 (C-5), 42.6 (C-4), 45.1 (C-3), 45.5 (C-6), 59.5 (C-2'), 61.7 (C-1'), 65.2 (C-2), 126.1-129.4 (C-*o*, *m*, *p*), 134.2, 143.4, 145.4 (C-*i*); $[\alpha]^{22}_D$ – 9.3 (*c* 1.5, $CHCl_3$). Anal. Calcd for $C_{25}H_{27}NO \cdot 1H_2O$: C, 79.99; H, 7.48; N, 3.66. Found: C, 79.96; H, 7.78; N, 3.73.

(2*R*,4*R*)-1-(*tert*-Butoxycarbonyl)-2-methyl-4-phenylpiperidine (11a). A solution of **10a** (120 mg, 0.41 mmol) and di-*tert*-butyl dicarbonate (178 mg, 0.81 mmol) in EtOAc (12 mL)

containing 20% $Pd(OH)_2$-C (20 mg) was hydrogenated at rt for 20 h at atmospheric pressure. The catalyst was removed by filtration, and the solvent was evaporated to give an oil, which was chromatographed (5:95 EtOAc-hexane) to afford **11a** (99 mg, 88% yield) as a white solid: IR (NaCl) 1692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, COSY) δ 1.20 (d, *J* = 6.6 Hz, 3H, CH_3), 1.49 [s, 9H, $(CH_3)_3C$], 1.52-1.68 (m, 2H, H-3ax, H-5ax), 1.90 (dddd, *J* = 13.5, 6.2, 3.3, 1.2 Hz, 1H, H-3eq), 2.15 (m, 1H, H-5eq), 2.75 (m, 1H, H-4), 3.25 (ddd, *J* = 13.8, 9.9, 6.6 Hz, 1H, H-6ax), 3.79 (ddd, *J* = 13.8, 7.5, 3.3 Hz, 1H, H-6eq), 3.95 (dddd, *J* = 9.3, 6.0, 6.0, 6.0 Hz, 1H, H-2), 7.15-7.35 (m, 5H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 19.8 (CH_3), 28.5 [$(CH_3)_3C$], 31.2 (C-5), 37.1 (C-3), 37.6 (C-6), 38.0 (C-4), 50.0 (C-2), 79.8 [$(CH_3)_3C$], 126.0 (C-*p*), 126.7, 128.4 (C-*o*, *m*), 146.0 (C-*i*), 155.3 (COO); mp 54-55 ºC; $[\alpha]^{22}_D$ – 72.1 (*c* 0.6, $CHCl_3$). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.00; H, 9.24; N, 4.97.

(2*S*,4*R*)-1-(*tert*-Butoxycarbonyl)-2,4-diphenylpiperidine (11b). Operating as described above in the preparation of **11a**, from **10b** (190 mg, 0.53 mmol), di-*tert*-butyl dicarbonate (232 mg, 1.06 mmol) in EtOAc (15 mL), and 20% $Pd(OH)_2$-C (48 mg), compound **11b** was obtained (134 mg, 75% yield) after flash chromatrography (5:95 EtOAc-hexane) as a white solid: IR (NaCl) 1692 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, COSY, HETCOR) δ 1.28 [s, 9H, $(CH_3)_3C$], 1.70 (dddd, *J* = 16.5, 9.6, 6.6, 3.3 Hz, 1H, H-5), 1.96 (dt, *J* = 13.5, 13.5, 11.7 Hz, 1H, H-3ax), 2.18 (dddd, *J* = 13.5, 6.6, 3.3, 1.5 Hz, 1H, H-3eq), 2.31 (m, 1H, H-5), 2.91 (m, 1H, H-4), 3.52 (ddd, *J* = 13.8, 9.9, 6.3 Hz, 1H, H-6ax), 4.11 (ddd, *J* = 13.8, 7.5, 3.0 Hz, 1H, H-6eq), 4.88 (dd, *J* = 11.7, 6.3 Hz, 1H, H-2), 7.18-7.28 (m, 10H, ArH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 26.2 [$(CH_3)_3C$], 31.2 (C-5), 38.1, 39.2 (C-3, C-6), 38.2 (C-4), 58.0 (C-2), 79.5 [$(CH_3)_3C$], 125.0, 126.7, 128.3, 128.5 (C-*o*, *m*), 126.2, 126.5 (C-*p*), 144.6, 146.0 (C-*i*), 155.8 (COO); mp 70-72 ºC; $[\alpha]^{22}_D$ – 45.6 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{22}H_{27}NO_2$: C, 78.30; H, 8.06; N, 4.15. Found: C, 78.17; H, 8.13; N, 4.03.

(3*R*,8a*R*)-8a-(3-Hydroxypropyl)-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine. A solution **(3*R*)-8a-(3-benzyloxypropyl)-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine**[3] (4:1 mixture of C-8a epimers; 286 mg, 0.78 mmol) in MeOH (25 mL) containing 10% Pd/C (40 mg) was hydrogenated at rt for 48 h at atmospheric pressure. The catalyst was removed by filtration, and the solvent was concentrated. The residue was chromatographed (pure EtOAc to 95:5 EtOAc-MeOH) to afford the title alcohol (141 mg, 66% yield) and its 8a-epimer (55 mg, 26% yield). **3*R*,8a*R*-isomer** (higher R_f): IR (NaCl) 3415, 1660 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.57 (m, 3H, $CH_2CH_2CH_2O$, H-8), 1.80 (m, 3H, H-7, $CH_2CH_2CH_2O$), 1.92 (m, 1H, H-7), 2.10 (br, 1H, OH), 2.35 (m, 1H, H-8), 2.43 (dd, *J* = 18.1, 9.2 Hz, 1H, H-6), 2.58 (dd, *J* = 18.4, 6.0 Hz, 1H, H-6), 3.53 (m, 2H, $CH_2CH_2CH_2O$), 3.88 (t, *J* = 8.4 Hz, 1H, H-2), 4.48 (t, *J* = 9.2 Hz, 1H, H-2), 5.34 (t, *J* = 8.4 Hz, 1H, H-3), 7.05-7.20 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 16.6 (C-7), 27.2 ($CH_2CH_2CH_2O$), 30.6 (C-6), 30.8 (C-8), 31.2 ($CH_2CH_2CH_2O$), 58.6 (C-3), 62.2 ($CH_2CH_2CH_2O$), 69.3 (C-2), 95.9 (C-8a), 125.4, 128.5 (C-*o*, *m*), 127.1 (C-*p*), 139.6 (C-*i*), 169.9 (COO); $[\alpha]^{22}_D$ – 131.7 (*c* 1.0, $CHCl_3$); HMRS calcd for [$C_{16}H_{21}NO_3$ + H]: 276.1594, found: 276.1603. Anal. Calcd for $C_{16}H_{21}NO_3 \cdot {}^1/_2H_2O$: C, 67.58; H, 7.80; N, 4.93. Found: C, 67.24; H, 7.77; N, 4.62. **3*R*,8a*S*-isomer** (lower R_f): IR (NaCl) 3450, 1650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.52-1.96 (m, 7H, H-8, 2H-7, $2CH_2$), 2.20-2.50 (m, 3H, 2H-6, H-8), 2.94 (br, 1H, OH), 3.57 (m, 2H, $CH_2CH_2CH_2O$), 3.88 (dd, *J* = 8.8, 1.6 Hz, 1H, H-2), 4.40 (t, *J* = 8.8, 7.2 Hz, 1H, H-2), 4.93 (dd, *J* = 7.2, 1.6 Hz, 1H, H-3), 7.10-7.20 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 16.7 (C-7), 27.0 ($CH_2CH_2CH_2O$), 29.7 (C-6), 30.1 (C-8), 30.7 ($CH_2CH_2CH_2O$), 58.8 (C-3), 61.8 ($CH_2CH_2CH_2O$), 71.1 (C-2), 95.1 (C-8a), 126.1, 128.4 (C-*o*, *m*), 127.2 (C-*p*), 141.5 (C-*i*), 167.5 (COO); $[\alpha]^{22}_D$ – 15.3 (*c* 1.5, $CHCl_3$); HMRS calcd for [$C_{16}H_{21}NO_3$ + H]: 276.1594, found: 276.1601.

(3*R*,8a*R*)-8a-[3-(2-Nitrophenylselenyl)propyl]-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine. To a stirred solution of the above 8a*R*-epimer (145 mg, 0.53 mmol) and *o*-nitrophenylselenocyanate (157 mg, 0.69 mmol) in anhydrous THF (3 mL) was added *n*-tributylphosphine (170 μL, 0.69 mmol) at rt. After 2 h, the solvent was removed under reduced pressure. Flash chromatography of the residue (1:9 to 7:3 EtOAc-hexane) gave the title ***o*-nitrophenylselenide** (180 mg, 73% yield): IR (NaCl) 1650 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.58 (td, *J* = 13.3, 13.3, 4.0 Hz, 1H, H-8), 1.76-1.99 (m, 6H, 2H-7, $2CH_2$), 2.30 (dt, *J* = 13.3, 3.7 Hz, 1H, H-8), 2.45 (dd, *J* = 18.2, 8.6 Hz, 1H, H-6), 2.61 (dd, *J* = 18.2, 6.1 Hz, 1H, H-6), 2.79-2.96 (2m, 2H, $CH_2CH_2CH_2Se$), 3.91 (t, *J* = 8.2 Hz, 1H, H-2), 4.48 (t, *J* = 8.8 Hz, 1H, H-2), 5.39 (t, *J* = 8.0 Hz, 1H, H-3), 7.20-7.52 (2m, 9H, ArH), 8.26-8.28 (d, *J* = 8.4 Hz, 1H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 16.6 (C-7), 22.9 ($CH_2CH_2CH_2Se$), 25.7 ($CH_2CH_2CH_2Se$), 30.6 (C-6), 30.9 (C-8), 34.8 ($CH_2CH_2CH_2Se$), 58.4 (C-3), 69.3 (C-2), 95.5 (C-8a), 125.4-130.7 (C-*o*, *m*, *p*), 126.4 (C-*o*-PhSe), 132.9, 138.7 (C-*i*), 146.8 (CNO_2), 169.8 (NCO); $[\alpha]^{22}_D$ – 16.9 (*c* 1.0, $CHCl_3$); HMRS calcd for [$C_{22}H_{24}N_2O_4Se$ + H]: 461.0974, found: 461.0978.

(3*R*,8a*R*)-8a-Allyl-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (12a). 30% aqueous H_2O_2 (40 μL, 1.3 mmol) and pyridine (12 μL, 0.14 mmol) were added to a solution of the above *o*-nitrophenylselenide (60 mg, 0.13 mmol) in CH_2Cl_2 (20 mL), and the resulting mixture was stirred at rt for 2 h. The resulting solution was washed with water (10 x 5 mL), dried, and concentrated to give an oil. The residue was chromatographed (1:4 to 1:1 EtOAc-hexane) to afford compound **12a** (20 mg, 70% yield) as a trasparent oil: IR (NaCl) 1656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.51 (tdd, *J* = 13.6, 13.6, 5.2, 1.6 Hz, 1H, H-8), 1.89 (m, 2H, H-7), 2.38 (m, 2H, CH_2 allyl, H-8), 2.44 (dd, *J* = 18.4, 7.6 Hz, 1H, H-6), 2.51 (m, 1H, CH_2 allyl), 2.62 (ddd, *J* = 18.4, 10.0, 2.8 Hz, 1H, H-6),

3.94 (t, *J* = 7.2 Hz, 1H, H-2), 4.53 (t, *J* = 9.2 Hz, 1H H-2), 5.11 (m, 2H, CH_2=), 5.39 (t, *J* = 8.0 Hz, 1H, H-3), 5.72 (dddd, *J* = 16.0, 10.0, 8.4, 5.6 Hz, 1H, CH=), 7.10-7.35 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 16.4 (C-7), 30.6 (C-6), 30.9 (C-8), 39.4 (CH_2 allyl), 58.4 (C-3), 69.3 (C-2), 95.2 (C-8a), 118.8 (CH_2=), 125.3, 128.5 (C-*o*, *m*), 127.1 (C-*p*), 139.8 (C-*i*), 169.8 (NCO); $[\alpha]^{22}_D$ – 118.5 (*c* 2.0, $CHCl_3$). Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.468; H, 7.44; N, 5.44. Found: C, 74.58; H, 7.20; N, 5.32.

(3*R*,8a*R*)-8a-(3-Butenyl)-5-oxo-3-phenyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (12b). A stirred solution of (-)-(*R*)-phenylglycinol (350 mg, 2.56 mmol) and 5-oxo-8-nonenoic acid[4] (435 mg, 2.56 mmol) in toluene (6 mL), containing molecular sieves (4 Å, 5 g), was heated at reflux for 24 h, with azeotropic elimination of water produced. The resulting solution was filtered (Celite®) and concentrated, and the residue was taken up with EtOAc. The organic solution was washed with 5% aqueous $NaHCO_3$, dried, and concentrated to give an orange oil. Column chromatography (1:2 EtOAc-hexane to EtOAc) afforded a mixture of lactams **12b** and 8a-*epi*-**12b** (ratio 8:2, 489 mg, 71% overall yield). **12b**: IR (NaCl) 1654 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.57 (td, *J* = 13.3, 13.3, 4.4 Hz, 1H, H-8), 1.83 (m, 3H, H-7, CH_2), 1.96 (m, 1H, H-7), 2.12 (m, 2H, CH_2), 2.35 (dt, *J* = 13.3, 8.8, 8.8 Hz, 1H, H-8), 2.48 (ddd, *J* = 18.1, 9.6, 8.2 Hz, 1H, H-6), 2.64 (ddd, *J* = 18.0, 7.4, 2.1 Hz, 1H, H-6), 3.88 (t, *J* = 8.4 Hz, 1H, H-2), 4.52 (t, *J* = 8.8 Hz, 1H, H-2), 4.95 (m, 2H, CH_2=), 5.38 (t, *J* = 8.2 Hz, 1H, H-3), 5.75 (tt, *J* = 10.1, 6.5 Hz, 1H, CH=), 7.20-7.36 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 16.8 (C-7), 28.4 (C-8), 30.6 (C-6), 30.9 (*C*$H_2$$CH_2$CH=), 33.8 ($CH_2$*C*$H_2$CH=), 58.7 (C-3), 69.5 (C-2), 95.9 (C-8a), 115.1 (CH_2=), 125.4-128.6 (C-*o*, *m*, *p*), 137.4 (CH=), 139.9 (C-*i*), 169.9 (COO). 8a-*epi*-**12b**: ^{1}H NMR (400 MHz, $CDCl_3$, selected resonances) δ 3.95 (dd, *J* = 9.1, 1.8 Hz, 1H, H-2), 4.42 (dd, *J* = 9.1, 7.4 Hz, 1H, H-2), 5.05 (m, 2H, CH_2=), 5.87 (tt, *J* = 10.4, 6.9 Hz, 1H, CH=); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 16.9 (C-7), 28.4 (C-8), 29.9 (C-6),

30.4 (*C*H_2CH_2CH=), 33.6 (CH_2*C*H_2CH=), 59.1 (C-3), 71.3 (C-2); HMRS calcd for [$C_{17}H_{21}NO_2$ + H]: 272.1645, found: 272.1650.

(3*R*,8a*R*)-8a-Allyl-6-(benzyloxycarbonyl)-5-oxo-3-phenyl-6-(phenylselenyl)-6-2,3,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (13a). Operating as described for the preparation of **2a**, from lactam **12a** (294 mg, 1.14 mmol), lithium bis(trimethylsilyl)amide (1 M in THF, 2.5 mL), benzyl chloroformate (161 μL, 1.14 mmol), and PhSeCl (307 mg, 1.6 mmol) in anhydrous THF (23 mL), lactam **13a** was obtained as a mixture of C-6 epimers (437 mg, 70% overall yield) after column chromatography (1:5 EtOAc-hexane). **13a** (major, higher R_f): IR (NaCl) 1658, 1726 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.85-2.16 (m, 5H, 2H-8, 2H-7, CH_2 allyl), 2.51 (dd, *J* = 14.4, 5.6 Hz, 1H, CH_2 allyl), 3.93 (t, *J* = 8.0 Hz, 1H, H-2), 4.53 (t, *J* = 8.8 Hz, 1H H-2), 4.87 (d, *J* = 17.2 Hz, 1H, CH_2=), 4.99 (d, *J* = 10.4 Hz, 1H, CH_2=), 5.20 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.34 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.47 (t, *J* = 8.0 Hz, 1H, H-3), 5.53 (m, 1H, CH=), 7.11-7.64 (m, 15H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.6, 28.5 (C-7, C-8), 40.5 (CH_2 allyl), 54.8 (C-6), 58.8 (C-3), 67.9 (CH_2 benzyl), 69.2 (C-2), 95.1 (C-8a), 119.3 (CH_2=), 125.3-138.5 (C-*o*, *m*, *p*), 135.1 (CH=), 139.6 (C-*ipso*), 166.2 (COO), 169.8 (NCO); $[\alpha]^{22}_D$ – 115.6 (*c* 1.6, $CHCl_3$). HMRS calcd for [$C_{30}H_{29}NO_4Se$ + H]: 548.1326, found: 548.1330. **13a** (minor, lower R_f): IR (NaCl) 1659, 1738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.41 (dd, *J* = 15.6, 9.6 Hz, 1H, CH_2 allyl), 1.79 (tdd, *J* = 13.2, 13.2, 6.4, 1.6 Hz, 1H, H-8), 2.12 (dt, *J* = 13.2, 3.2, 3.2 Hz, 1H, H-8), 2.21 (m, 2H, H-7, CH_2 allyl), 2.34 (dt, *J* = 14.8, 4.0, 4.0 Hz, 1H, H-7), 3.89 (t, *J* = 8.4 Hz, 1H, H-2), 4.40 (t, *J* = 8.8 Hz, 1H, H-2), 4.86 (d, *J* = 17.2 Hz, 1H, CH_2=), 5.02 (d, *J* = 10.0 Hz, 1H, CH_2=), 5.20 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.27 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.33 (t, *J* = 8.4 Hz, 1H, H-3), 5.52 (dddd, *J* = 17.2, 10.0, 10.0, 5.2 Hz, 1H, CH=), 7.20-7.60 (m, 15H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 29.5, 29.6 (C-7, C-8), 38.9 (CH_2 allyl), 55.1 (C-6), 60.1 (C-3), 68.1 (CH_2 benzyl),

69.4 (C-2), 94.9 (C-8a), 118.8 (CH_2=), 125.3-138.7 (C-*o*, *m*, *p*), 135.2 (CH=), 138.9 (C-*i*), 166.6 (COO), 170.2 (NCO). HMRS calcd for [$C_{30}H_{29}NO_4Se$ + H]: 548.1326, found: 548.1331.

(3*R*,8a*S*)-6-(Benzyloxycarbonyl)-8a-(3-butenyl)-5-oxo-3-phenyl-6-(phenylselenyl)-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (13b). Operating as in the preparation of **2a**, from the above mixture of lactam **12b** and its C-8a epimer (440 mg, 1.62 mmol), lithium bis(trimethylsilyl)amide (1 M in THF, 3.6 mL), benzyl chloroformate (50% in toluene, 3.2 mL, 1.62 mmol), and PhSeCl (435 mg, 2.27 mmol) in THF (33 mL), followed by column chromatography (1:5 EtOAc-hexane), lactam **13b** was obtained as a mixture of C-6 epimers (785 mg, 88% overall yield), which were separated after an additional column chromatography (1:9 EtOAc-hexane). **13b** (major, higher R_f): IR (NaCl) 1659, 1731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.25-1.37 (m, 2H, CH_2), 1.81-2.16 (m, 6H, H-7, H-8, CH_2), 3.84 (t, *J* = 8.4 Hz, 1H, H-2), 4.48 (t, *J* = 8.4 Hz, 1H, H-2), 4.78-4.84 (m, 2H, CH_2=), 5.17 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.32 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.43 (t, *J* = 8.4 Hz, 1H, H-3), 5.48-5.57 (m, 1H, CH=), 7.07-7.41 (m, 15H, ArH), 7.62 (d, *J* = 7.6 Hz, 1H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.8, 29.4, 29.9 (C-7, C-8, CH_2), 32.8 (CH_2), 55.1 (C-6), 60.2 (C-3), 68.0 (CH_2 benzyl), 69.3 (C-2), 95.4 (C-8a), 114.9 (CH_2=), 126.6-129.0, 138.8 (C-*o, m, p*), 135.2, 137.2, 138.7 (C-*i*), 166.5 (COO), 170.3 (NCO); $[\alpha]^{22}_D$ – 113.7 (*c* 0.35, $CHCl_3$); HMRS calcd for [$C_{31}H_{31}NO_4Se$ + H]: 562.1491, found: 562.1492. **13b** (minor, lower R_f): ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.25-1.37 (m, 1H, CH_2), 1.60 (m, 1H, CH_2), 2.79-2.20 (m, 6H, H-7, H-8, CH_2), 3.84 (t, *J* = 8.4 Hz, 1H, H-2), 4.48 (t, *J* = 9.2 Hz, 1H, H-2), 4.80 (d, *J* = 13.6 Hz, 1H, CH_2=), 4.83 (d, *J* = 5.6 Hz, 1H, CH_2=), 5.17 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.32 (d, *J* = 12.0 Hz, 1H, CH_2 benzyl), 5.43 (t, *J* = 8.4 Hz, 1H, H-3), 5.47-5.57 (m, 1H, CH=), 7.05-7.41 (m, 15H, ArH), 7.62 (d, *J* = 7.6 Hz, 1H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.7, 27.8, 28.6 (C-7, C-8,

CH_2), 34.9 (CH_2), 54.7 (C-6), 58.9 (C-3), 67.9 (CH_2 benzyl), 69.0 (C-2), 95.7 (C-8a), 115.0 (CH_2=), 125.2-129.7, 138.5 (C-*o, m*, *p*), 135.0, 137.0, 139.5 (C-*i*), 166.1 (COO), 170.3 (NCO); $[\alpha]^{22}_{D}$ + 36.9 (*c* 0.35, $CHCl_3$).

(3*R*,8a*S*)-8a-Allyl-6-(benzyloxycarbonyl)-5-oxo-3-phenyl-2,3,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (14a). 30% aqueous H_2O_2 (25 μL, 0.83 mmol) and pyridine (11 μL, 0.14 mmol) were added to a solution of selenides **13a** (71 mg, 0.12 mmol) in CH_2Cl_2 (9 mL), and the resulting mixture was stirred at rt for 30 minutes. The reaction was quenched with distilled water, the two phases were separated, and the organic layer was washed with water, dried, and concentrated to give crude **14a** (70 mg) as an yellow oil, which was used in the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44-2.60 (m, 3H, CH_2 allyl, H-8), 2.96 (dd, *J* = 18.0, 7.2 Hz, 1H, H-8), 4.13 (dd, *J* = 9.2, 6.4 Hz, 1H, H-2), 4.43 (dd, *J* = 9.2, 7.6 Hz, 1H, H-2), 5.08 (dd, *J* = 17.2, 1.2 Hz, 1H, CH_2=), 5.13 (d, *J* = 10.0 Hz, 1H, CH_2=), 5.27 (d, *J* = 13.2 Hz, 1H, CH_2 benzyl), 5.29 (d, *J* = 13.2 Hz, 1H, CH_2 benzyl), 5.41 (t, *J* = 6.8 Hz, 1H, H-3), 5.73 (dddd, *J* = 17.2, 10.0, 8.8, 6.4 Hz, 1H, CH=), 7.25-7.40 (m, 11H, ArH, H-7).

(3*R*,8a*S*)-6-(Benzyloxycarbonyl)-8a-(3-butenyl)-5-oxo-3-phenyl-2,3,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (14b). Operating as described for the preparation of **14a**, from selenides **13b** (190 mg, 0.34 mmol), 30% aqueous H_2O_2 (70 μL, 2.3 mmol), and pyridine (30 μL, 0.37 mmol) in CH_2Cl_2 (23 mL), crude unsaturated lactam **14b** was obtained and used in the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.77 (m, 1H, CH_2), 1.95 (m, 1H, CH_2), 2.07 (m, 1H, CH_2), 2.62 (br, *J* = 13.5 Hz, 1H, H-8), 2.93 (dd, *J* = 13.5, 4.8 Hz, 1H, H-8), 4.07 (dd, *J* = 6.9, 4.8 Hz, 1H, H-2), 4.42 (dd, *J* = 6.9, 5.7 Hz, 1H, H-2), 4.97 (m, 2H, CH_2=), 5.27 (s, 1H, CH_2 benzyl), 5.30 (s, 1H, CH_2 benzyl), 5.38

(t, *J* = 5.1 Hz, 1H, H-3), 5.72 (dddd, *J* = 12.6, 7.5, 4.5, 4.5 Hz, 1H, CH=), 7.26-7.34 (m, 11H, ArH, H-7).

(3*R*,7*R*,8a*S*)-8a-Allyl-6-(benzyloxycarbonyl)-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (15a). Operating as described for the preparation of **4a**, from crude lactam **14a** (0.12 mmol), vinylmagnesium bromide (1.7 M solution in THF, 0.3 mL), CuI (93 mg, 0.49 mmol), LiCl (21 mg, 0.49 mmol), and TMSCl (62 μL, 0.49 mmol) in THF (4 mL), lactam **15a** was obtained as a mixture of C-6 epimers (ratio 75:25, 33 mg, 60% overall yield from **13a**) after column chromatography (hexane). **15a** (major): IR (NaCl) 1667, 1743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, HETCOR) δ 2.01 (dd, *J* = 14.8, 10.8 Hz, 1H, H-8), 2.25 (dd, *J* = 14.8 Hz, 1H, H-8), 2.27 (m, 1H, CH_2 allyl), 2.35 (td, *J* = 14.0, 7.2, 7.2 Hz, 1H, CH_2 allyl), 3.05 (m, 1H, H-7), 3.34 (d, *J* = 12.0 Hz, 1H, H-6), 4.06 (dd, *J* = 9.2, 7.2 Hz, 1H, H-2), 4.90 (t, *J* = 8.8 Hz, 1H, H-2), 5.05-5.17 (m, 4H, $2CH_2$=), 5.18 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.23 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.51 (t, *J* = 8.0 Hz, 1H, H-3), 5.61-5.73 (m, 2H, 2CH=), 7.20-7.40 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 36.3 (C-8), 36.4 (C-7), 42.6 (CH_2 allyl), 54.3 (C-6), 59.1 (C-3), 67.1 (CH_2 benzyl), 68.6 (C-2), 94.5 (C-8a), 117.0, 120.2 (CH_2=), 125.6-128.6 (C-*o*, *m*, *p*), 131.6, 137.5 (CH=), 135.5, 139.8 (C-*i*), 167.7, 168.6 (COO, NCO). **15a** (minor): ^{1}H NMR (400 MHz, $CDCl_3$, selected resonances) δ 2.11 (dd, *J* = 14.4, 8.4 Hz, 1H, H-8), 2.84 (m, 1H, H-7), 3.68 (dd, *J* = 4.0, 0.8 Hz, 1H, H-6), 3.94 (dd, *J* = 8.8, 7.6 Hz, 1H, H-2), 4.55 (t, *J* = 9.2 Hz, 1H, H-2), 5.53 (t, *J* = 8.0 Hz, 1H, H-3), 5.91 (ddd, *J* = 17.6, 10.4, 7.2 Hz, 1H, CH=), 7.20-7.40 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 33.1 (C-8), 36.8 (C-7), 42.0 (CH_2 allyl), 54.0 (C-6), 58.2 (C-3), 67.3 (CH_2 benzyl), 68.5 (C-2), 94.8 (C-8a), 116.6, 119.2 (CH_2=), 131.6, 136.6 (CH=), 135.1, 140.4 (C-*i*), 166.8, 168.0 (COO, NCO); HMRS calcd for [$C_{26}H_{27}NO_4$ + H]: 418.2012, found: 418.2018.

(3*R*,7*R*,8a*S*)-6-(Benzyloxycarbonyl)-8a-(3-butenyl)-5-oxo-3-phenyl-7-vinyl-2,3,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (15b). Operating as in the preparation of **4a**, from crude lactam **14b** (0.34 mmol), vinylmagnesium bromide (1.7 M solution in THF, 0.86 mL), CuI (280 mg, 1.47 mmol), LiCl (62 mg, 1.47 mmol), and TMSCl (186 μL, 1.47 mmol) in THF (5 mL), lactam **15b** was obtained as a mixture of C-6 epimers (ratio 77:23, 123 mg, 68% overall yield from **13b**) after column chromatography (1:6 to 3:7 EtOAc-hexane). **15b** (major): IR (NaCl) 1666, 1744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.55 (ddd, *J* = 14.0, 10.8, 5.6 Hz, 1H, CH_2), 1.75 (ddd, *J* = 14.0, 11.2, 6.0 Hz, 1H, CH_2), 1.96 (dd, *J* = 14.8, 10.4 Hz, 1H, H-8), 2.06 (m, 2H, CH_2), 2.30 (dd, *J* = 14.8, 6.0 Hz, 1H, H-8), 3.09 (m, 1H, H-7), 3.36 (d, *J* = 11.6 Hz, 1H, H-6), 4.00 (dd, *J* = 8.4, 7.2 Hz, 1H, H-2), 4.43 (t, *J* = 8.4 Hz, 1H, H-2), 4.87-4.92 (m, 2H, CH_2=), 5.06-5.25 (m, 4H, CH_2 benzyl, CH_2=), 5.46 (t, *J* = 7.6 Hz, 1H, H-3), 5.73-5.75 (m, 2H, CH=), 7.21-7.40 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.1 (*C*$H_2CH_2CH_2$=CH_2), 36.3 (C-7), 36.6 (C-8), 37.3 (CH_2*C*H_2CH_2=CH_2), 54.1 (C-6), 59.1 (C-3), 67.1 (CH_2 benzyl), 68.5 (C-2), 95.5 (C-8a), 115.2 (CH_2=), 116.9 (*C*H_2=), 125.6-128.6 (C-*o*, *m*, *p*), 135.5 (C-*i*), 136.8, 137.6 (CH=), 139.7 (C-*i*), 167.5 (COO), 168.5 (NCO). **15b** (minor): ^1H NMR (400 MHz, $CDCl_3$, selected resonances) δ 2.84 (dt, *J* = 11.6, 11.6, 4.4 Hz, 1H, H-7), 3.68 (d, *J* = 2.8 Hz, 1H, H-6), 3.85 (t, *J* = 8.0 Hz, 1H, H-2), 4.50 (t, *J* = 8.4 Hz, 1H, H-2), 4.83 (m, 2H, CH_2=), 5.06-5.25 (m, 5H, CH_2 benzyl, CH_2=, H-3), 5.93 (m, 1H, CH=); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 28.0 (*C*$H_2CH_2CH_2$=CH_2), 36.3 (C-7), 36.5 (C-8), 37.0 (CH_2*C*H_2CH_2=CH_2), 53.9 (C-6), 58.3 (C-3), 67.1 (CH_2 benzyl), 68.3 (C-2), 95.7 (C-8a), 114.7 (CH_2=), 116.6 (CH_2=), 135.0 (C-*i*), 136.9, 137.3 (CH=), 140.4 (C-*i*), 166.7 (COO), 168.0 (NCO); HMRS calcd for [$C_{27}H_{29}NO_4$ + H]: 432.2169, found: 432.2173.

(3*R*,7*R*,11*S*)-6-(Benzyloxycarbonyl)-7,11-methano-5-oxo-3-phenyl-2,3,6,7,10,11-hexahydro-5*H*-oxazolo[3,2-*a*]azocine (16a). Second-generation Grubbs catalyst (3 mg)

was added to a solution of lactams **15a** (20 mg, 0.05 mmol) in CH_2Cl_2 (7 ml). The mixture was stirred at rt for 2 h, concentrated, and purified by flash column chromatography (1:9 to 1:4 EtOAc-hexane) to yield tricyclic lactam **16a** as a mixture of C-6 epimers (ratio 2:1, 16 mg, 80% yield). **16a** (major): IR (NaCl) 1659, 1734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, HETCOR) δ 2.30-2.45 (m, 3H, 2H-10, CH_2), 2.35 (dd, *J* = 12.0, 4.0 Hz, 1H, CH_2), 3.24 (d, *J* = 4.0 Hz, 1H, H-7), 3.67 (d, *J* = 6.4 Hz, 1H, H-6), 4.00 (t, *J* = 8.8 Hz, 1H, H-2), 4.61 (t, *J* = 8.4 Hz, 1H, H-2), 5.18 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.22 (d, *J* = 12.4 Hz, 1H, CH_2 benzyl), 5.48 (t, *J* = 8.0 Hz, 1H, H-3), 5.64 (m, 1H, CH=), 5.76 (m, 1H, CH=), 7.05-7.20 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 31.8 (C-10), 34.4 (C-7), 36.1 (CH_2), 52.0 (C-6), 58.7 (C-3), 67.2 (CH_2 benzyl), 70.1 (C-2), 92.3 (C-11), 125.0-129.9 (C-*o*, *m*, *p*, CH=), 135.4, 139.2 (C-*i*), 164.2 (NCO), 169.7 (COO). **16a** (minor): ^1H NMR (400 MHz, $CDCl_3$, selected resonances) δ 2.19 (ddd, *J* = 12.4, 4.4, 1.6 Hz, 1H, H-10), 3.05 (br, 1H, H-7), 3.53 (s, 1H, H-6), 4.02 (dd, *J* = 9.2, 7.6 Hz, 1H, H-2), 4.57 (t, *J* = 8.8 Hz, 1H, H-2), 5.45 (t, *J* = 7.6 Hz, 1H, H-3), 5.76 (m, 1H, CH=), 5.90 (m, 1H, CH=); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 30.9 (C-10), 33.3 (C-7), 36.2 (CH_2), 53.5 (C-6), 57.9 (C-3), 67.0 (CH_2 benzyl), 70.1 (C-2), 92.4 (C-11), 164.5 (NCO), 168.9 (COO); HMRS calcd for [$C_{24}H_{23}NO_4$ + H]: 390.1699, found: 390.1704.

(3*R*,7*R*,12*S*)-6-(Benzyloxycarbonyl)-3-phenyl-7,12-methano-5-oxo-2,3,5,6,7,10,11,12-octahydrooxazolo[3,2-*a*]azonine (16b). Operating as described for the preparation of **16a**, from lactams **15b** (90 mg, 0.21 mmol) and second-generation Grubbs catalyst (14 mg) in CH_2Cl_2 (30 mL), tricyclic lactam **16b** was obtained as a mixture of C-6 epimers (ratio 2:1, 70 mg, 83% overall yield) after column chromatography (1:9 to 1:4 EtOAc-hexane). **16b** (major): IR (NaCl) 1658, 1738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.71 (ddd, *J* = 14.0, 12.0, 3.2 Hz, 1H, H-11), 2.05 (dm, *J* = 14.0 Hz, 1H, H-11), 2.13-2.20 (m, 4H, H-13, H-10), 3.09 (m, 1H, H-7), 3.47 (d, *J* = 1.6 Hz, 1H, H-6), 4.04 (dd, *J* = 9.2, 8.4

Hz, 1H, H-2), 4.46 (dd, *J* = 9.2, 8.4 Hz, 1H, H-2), 5.19 (s, 2H, CH_2 benzyl), 5.39 (t, *J* = 8.4 Hz, 1H, H-3), 5.85 (m, 1H, CH=), 6.06 (ddd, *J* = 11.6, 9.2, 2.8 Hz, 1H, CH=), 7.25-7.40 (m, 10H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 22.5 (CH_2), 31.9 (C-7), 35.6 (C-11), 37.8 (CH_2), 53.0 (C-6), 60.2 (C-3), 67.2 (CH_2 benzyl), 69.3 (C-2), 96.6 (C-12), 125.4-128.6 (C-*o*, *m*, *p*), 131.7, 135.0 (CH=), 135.5, 139.0 (C-*i*), 167.0 (NCO), 170.7 (COO). **16b** (minor): ^{1}H NMR (400 MHz, $CDCl_3$, selected resonances) δ 1.75 (dt, *J* = 13.6, 13.6, 3.6 Hz, 1H, H-11), 1.85 (dm, *J* = 13.6 Hz, 1H, H-11), 1.97 (dm, *J* = 13.6 Hz, 1H, H-10), 2.27 (m, 1H, H-10), 3.32 (m, 1H, H-7), 3.82 (d, *J* = 9.6 Hz, 1H, H-6), 4.04 (t, *J* = 7.6 Hz, 1H, H-2), 4.54 (dt, *J* = 8.8 Hz, 1H, H-2), 5.13 (s, 2H, CH_2 benzyl), 5.50 (t, *J* = 8.0 Hz, 1H, H-3), 5.71 (ddd, *J* = 11.6, 9.2, 2.8 Hz, 1H, CH=), 5.85 (m, 1H, CH=); ^{13}C NMR (100.6 MHz, $CDCl_3$, selected resonances) δ 22.3 (CH_2), 30.8 (C-7), 33.9 (CH_2), 39.2 (C-10), 51.9 (C-6), 58.9 (C-3), 67.1 (CH_2 benzyl), 68.8 (C-2), 96.2 (C-12), 130.7, 134.3 (CH=), 135.2, 139.2 (C-*i*), 166.3 (NCO), 169.2 (COO); HMRS calcd for [$C_{25}H_{25}NO_4$ + H]: 404.1856, found: 404.1860.

(3*R*,7*S*,11*S*)-7,11-Methano-5-oxo-3-phenyl-2,3,6,7,8,9,10,11-octahydro-5*H*-oxazolo[3,2-*a*]azocine (17a). Operating as in the preparation of **7a**, from lactams **16a** (110 mg, 0.28 mmol) and 10% Pd/C (20 mg) in MeOH (15 mL) for 48 h, pure lactam **17a** was obtained (56 mg, 78% overall yield) after column chromatography (1:1.5 EtOAc-hexane): ^{1}H NMR (400 MHz, $CDCl_3$, HETCOR) δ 1.50-1.70 (m, 3H, H-10, 2H-12), 1.72 (m, 1H, H-9), 1.72 (dm, *J* = 12.0 Hz, 1H, H-8), 1.83-1.93 (m, 2H, H-9, H-10), 2.04 (ddd, *J* = 12.0, 3.3, 1.5 Hz, 1H, H-8), 2.32 (d, *J* = 18.6 Hz, 1H, H-6), 2.54 (m, 1H, H-7), 2.67 (dd, *J* = 18.6, 7.8 Hz, 1H, H-6), 3.95 (dd, *J* = 9.0, 7.8 Hz, 1H, H-2), 4.42 (dd, *J* = 9.0, 7.8 Hz, 1H, H-2), 5.24 (t, *J* = 7.8 Hz, 1H, H-3), 7.20-7.43 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 19.7 (C-9), 28.1 (C-7), 31.3, 34.3 (C-10, C-12), 36.8 (C-6), 38.3 (C-8), 59.6 (C-3), 69.8 (C-2), 93.3 (C-11), 125.5, 128.7 (C-*o*, *m*), 127.3 (C-*p*), 139.4 (C-*i*), 170.1 (NCO); $[\alpha]^{22}_D$ – 137.8 (*c* 0.4, $CHCl_3$); HMRS calcd for [$C_{16}H_{19}NO_2$ + H]: 258.1488, found: 258.1490.

(3*R*,7*S*,12*S*)-7,12-Methano-5-oxo-3-phenyl-2,3,5,6,7,8,9,10,10,11,12-decahydrooxazolo-[3,2-*a*]azonine (17b). Operating as described for the preparation of **7a**, from lactams **16b** (60 mg, 0.13 mmol) and 10% Pd/C (27 mg) in MeOH (3 mL) for 48 h, pure lactam **17b** was obtained (28 mg, 83% overall yield) after column chromatography (1:1.5 EtOAc-hexane): ^{1}H NMR (400 MHz, $CDCl_3$, HETCOR) δ 1.55-1.76 (m, 6H, CH_2), 1.85-2.00 (m, 3H, CH_2), 2.35 (m, 1H, CH_2), 2.39 (d, *J* = 18.0 Hz, 1H, H-6), 2.48 (m, 1H, H-7), 2.65 (dd, *J* = 18.0, 8.0 Hz, 1H, H-6), 3.98 (dd, *J* = 8.4, 7.2 Hz, 1H, H-2), 4.48 (t, *J* = 8.8 Hz, 1H, H-2), 5.47 (t, *J* = 8.4 Hz, 1H, H-3), 7.20-7.35 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.5 (CH_2), 23.9 (CH_2), 26.1 (C-7), 35.7 (C-11), 37.2, 37.3 (CH_2), 38.2 (C-6), 58.5 (C-3), 69.2 (C-2), 96.0 (C-12), 125.4-128.5 (C-*o*, *m*), 127.0 (C-*p*), 140.4 (C-*i*), 170.8 (NCO).

(1*R*,5*R*)-2-[(1*R*)-2-Hydroxy-1-phenylethyl]-2-azabicylo[3.3.1]nonane (18a). $LiAlH_4$ (68 mg, 1.8 mmol) was slowly added to a suspension of $AlCl_3$ (80 mg, 0.58 mmol) in THF (8 mL) at 0 ºC. After the mixture was stirred at 25 ºC for 30 min and cooled to –78 ºC, lactam **17a** (60 mg, 0.23 mmol) in THF (2 mL) was slowly added. The stirring was continued at –78 ºC for 90 min and at rt for 18 h. The reaction was quenched with water, the aqueous layer was extracted with EtOAc, and the combined organic extracts were dried and concentrated. The resulting oil was dissolved in CH_2Cl_2 (7 mL), and then $TiCl_4$ (0.11 mL, 0.98 mmol) and Et_3SiH (97 μL, 0.61 mmol) were added. The resulting mixture was heated at reflux for 48 h, poured into saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated, and the resulting residue was chromatographed (EtOAc) to give **18a** (24 mg, 48% overall yield): IR (NaCl) 3306 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$,) δ 1.20-2.00 (m, 10H, H-4, H-6, H-7, H-8, H-9), 1.94 (m, 1H, H-5), 2.82 (m, 2H, H-3), 3.00 (m, 1H, H-1), 3.24 (br, 1H, OH), 3.73 (dd, *J* = 9.6, 4.8 Hz, 1H, H-2'), 3.75 (dd, *J* = 12.4, 4.8 Hz, 1H, H-2'), 3.86 (ddd, *J* = 12.4, 9.6, 4.8 Hz, 1H, H-1'),

7.20-7.40 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 19.2 (C-7), 24.5 (C-5), 28.4 (CH_2), 29.3 (CH_2), 31.4 (CH_2), 31.6 (CH_2), 42.3 (C-3), 50.1 (C-1), 61.2 (C-2'), 68.8 (C-1'), 128.3, 128,6 (C-*o*, *m*), 127.7 (C-*p*), 138.0 (C-*i*); HMRS calcd for [$C_{16}H_{23}NO$ + H]: 246.1852, found: 246.1846.

(1*R*,6*R*)-7-[(1*R*)-2-Hydroxy-1-phenylethyl]-7-azabicyclo[4.3.1]decane (18b). $LiAlH_4$ (75 mg, 1.9 mmol) was slowly added to a suspension of $AlCl_3$ (76 mg, 0.55 mmol) in THF (8 mL) at 0 ºC. After the mixture was stirred at rt for 30 min and cooled to –78 ºC, lactam **17b** (60 mg, 0.22 mmol) in THF (2 mL) was slowly added. The stirring was continued at –78 ºC for 90 min and at rt for 3 h. The mixture was cooled to 0 ºC, and the reaction was quenched with water. The aqueous layer was extracted with EtOAc, and the combined organic extracts were dried and concentrated to give an oil, which was chromatographed (1:1.5 EtOAc-hexane) to afford **18b** (46 mg, 80% yield): IR (NaCl) 3193 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.28-2.23 (m, 10H, CH_2), 2.03 (m, 1H, H-1), 2.65 (m, 1H, H-8), 2.75 (ddd, *J* = 18.4, 8.4, 4.8 Hz, 1H, H-8), 3.11 (m, 1H, H-6), 3.25 (br, 1H, OH), 3.70 (dd, *J* = 6.4, 5.6 Hz, 1H, H-1'), 3.77 (dd, *J* = 10.4, 5.6 Hz, 1H, H-2'), 3.83 (dd, *J* = 10.4, 6.4 Hz, 1H, H-2'), 7.28-7.35 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.4 (CH_2), 26.9 (CH_2), 28.0 (C-1), 29.7 (CH_2), 31.0 (CH_2), 31.4 (CH_2), 36.5 (CH_2), 41.2 (C-8), 52.1 (C-6), 61.8 (C-2'), 66.1 (C-1'), 127.6-128.4 (C-*o*, *m*), 127.6 (C-*p*), 138.7 (C-*i*); $[\alpha]^{22}_D$ – 2.8 (*c* 0.25, $CHCl_3$); HMRS calcd for [$C_{17}H_{25}NO$ + H]: 260.2008, found: 260.2010.

(1*R*,5*R*)-2-(*tert*-Butoxycarbonyl)-2-azabicyclo[3.3.1]nonane (19a). Operating as described in the preparation of **11a**, from **18a** (20 mg, 0.08 mmol), di-*tert*-butyl dicarbonate (27 mg, 0.12 mmol) and 20% $Pd(OH)_2$-C (10 mg) in MeOH (5 mL) for 48 h, compound **19a** was obtained (11 mg, 61% yield) after flash chromatrography (1:99 to 5:95 EtOAc-hexane): IR (NaCl) 1693 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, HETCOR) δ 1.20-1.90 (m,

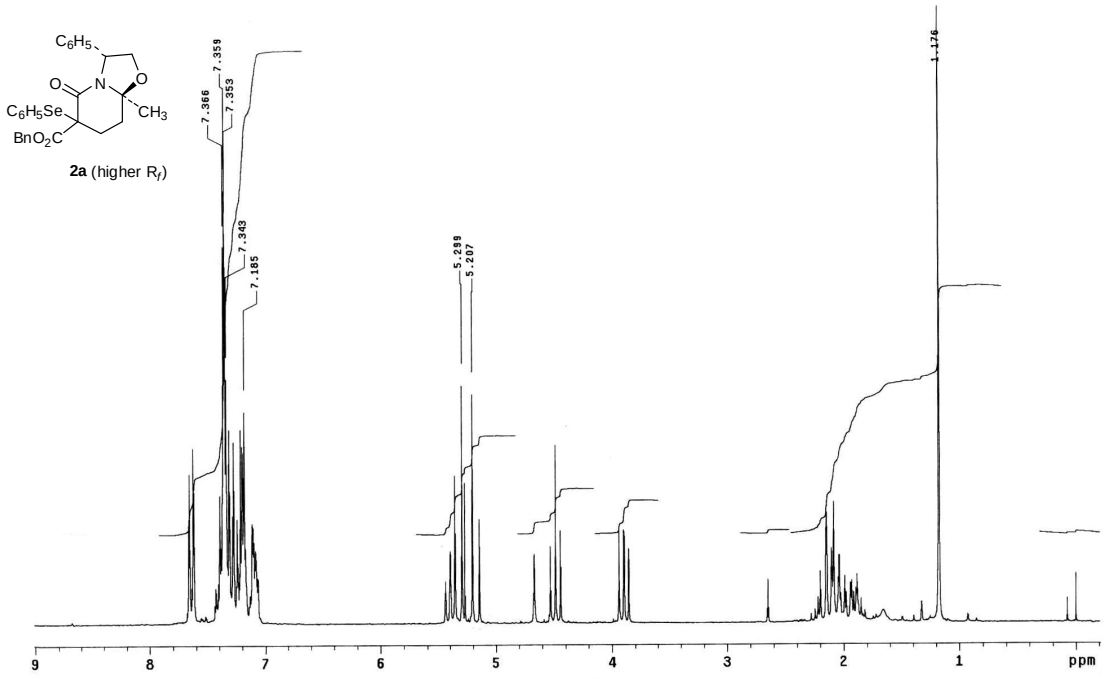
10H, H-4, H-6, H-7, H-8, H-9), 1.46 [s, 9H, $(CH_3)_3C$], 2.00 (m, 1H, H-5), 3.50 (m, 2H, H-3), 4.00, 4.18 (2m, 1H, H-1); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 19.1, 19.7 (C-7), 24.5, 24.8 (C-5), 28.4, 28.8 (CH_2), 28.5 [$C(CH_3)_3$], 30.3, 31.0 (CH_2), 31.1, 31.3 (CH_2), 31.9, 32.2 (CH_2), 39.7, 40.8 (C-3), 46.2, 47.2 (C-1), 78.9 [$C(CH_3)_3$], 155.9 (COO); $[\alpha]^{22}_D$ – 14.6 (*c* 0.9, $CHCl_3$); HMRS calcd for [$C_{13}H_{23}NO_2$ + H]: 226.1788, found: 226.1794.

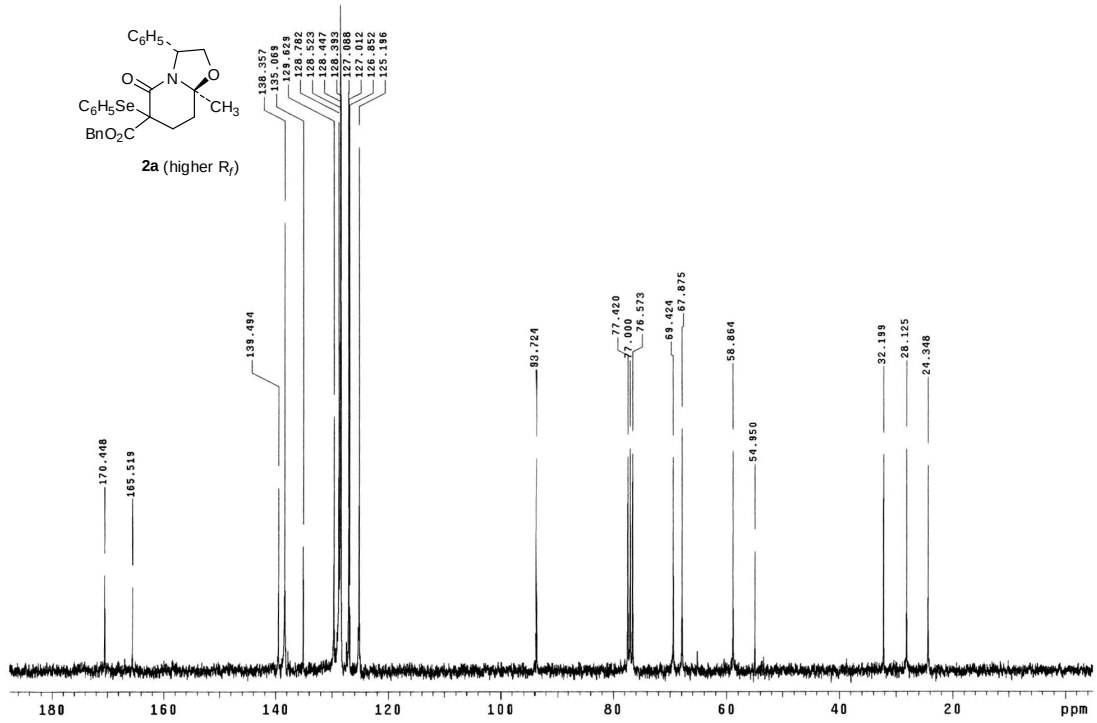
(1*R*,6*R*)-2-(*tert*-Butoxycarbonyl)-7-azabicyclo[4.3.1]decane (19b). Operating as described in the preparation of **11a**, from **18b** (45 mg, 0.17 mmol), di-*tert*-butyl dicarbonate (66 mg, 0.3 mmol) and 20% $Pd(OH)_2$-C (17 mg) in EtOAc (10 mL) for 48 h, compound **19b** was obtained (129 mg, 73% yield) after flash chromatrography (1:99 to 5:95 EtOAc-hexane): IR (NaCl) 1692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.40-1.80 (m, 9H, CH_2), 1.45 [s, 9H, $(CH_3)_3C$], 1.86 (m, 1H, CH_2), 2.14 (m, 1H, H-1), 3.13, 3.19 (2d, *J* = 12.0 Hz, 1H, H-8), 3.78, 3.84 (2dm, *J* = 12.0 Hz, 1H, H-8), 4.24, 4.39 (2s, 1H, H-6); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 27.2 (C-1), 28.5 [$(CH_3)_3C$], 30.8 (CH_2), 30.9, 31.3 (CH_2), 32.8, 33.3 (CH_2), 34.9, 35.8 (CH_2), 37.5, 38.5 (C-8), 48.3, 49.5 (C-6), 78.9 [$(CH_3)_3C$], 155.5, 155.8 (COO); HMRS calcd for [$C_{14}H_{25}NO_2$ + H]: 240.1958, found: 240.1958.

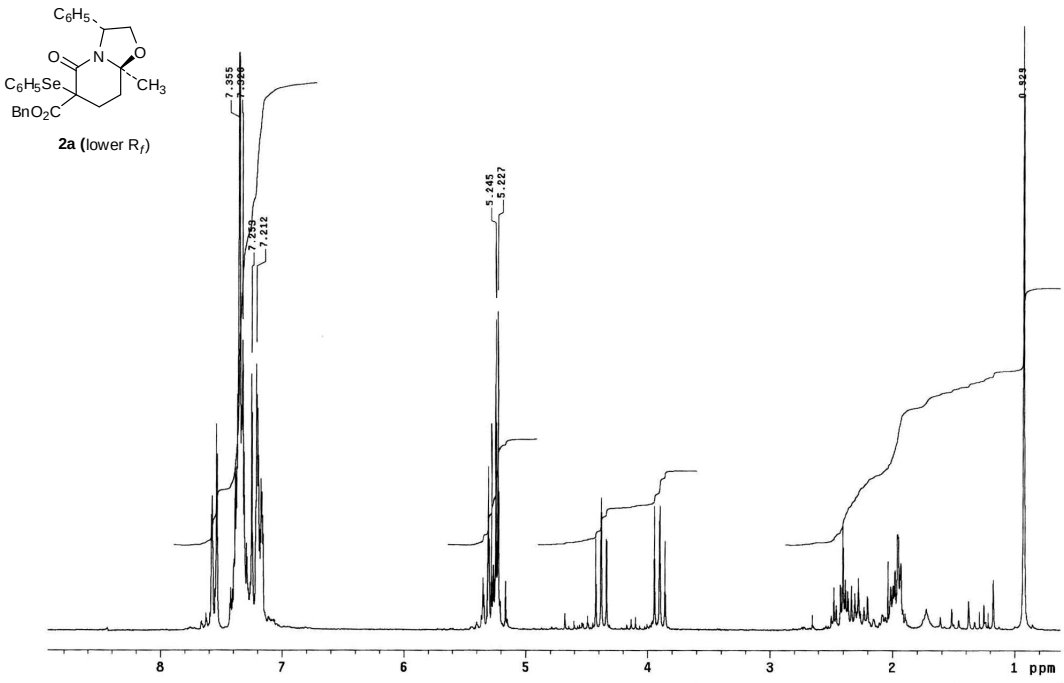
(1*S*,6*R*)-7-[(1*R*)-2-Hydroxy-1-phenylethyl]-7-azabicyclo[4.3.1]decan-8-one (20). $TiCl_4$ (166 μL, 0.88 mmol) and Et_3SiH (88 μL, 0.55 mmol) were added to a solution of lactam **17b** (60 mg, 0.22 mmol) in CH_2Cl_2 (4 mL), and the resulting mixture was heated at reflux for 20 h. The mixture was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated, and the resulting residue was chromatographed (1:9 EtOAc-hexane to EtOAc) to give recovered compound **17b** (20 mg) and alcohol **20** (29 mg; 73% yield based on consumed **17b**): IR (NaCl) 3400, 1615 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.60 (m, 5H, CH_2), 1.84 (m, 3H, CH_2), 2.03 (dt, *J* = 12.3, 6.0, 6.0 Hz, 1H, H-10), 2.36 (d, *J* = 17.7 Hz, 1H, H-9), 2.42

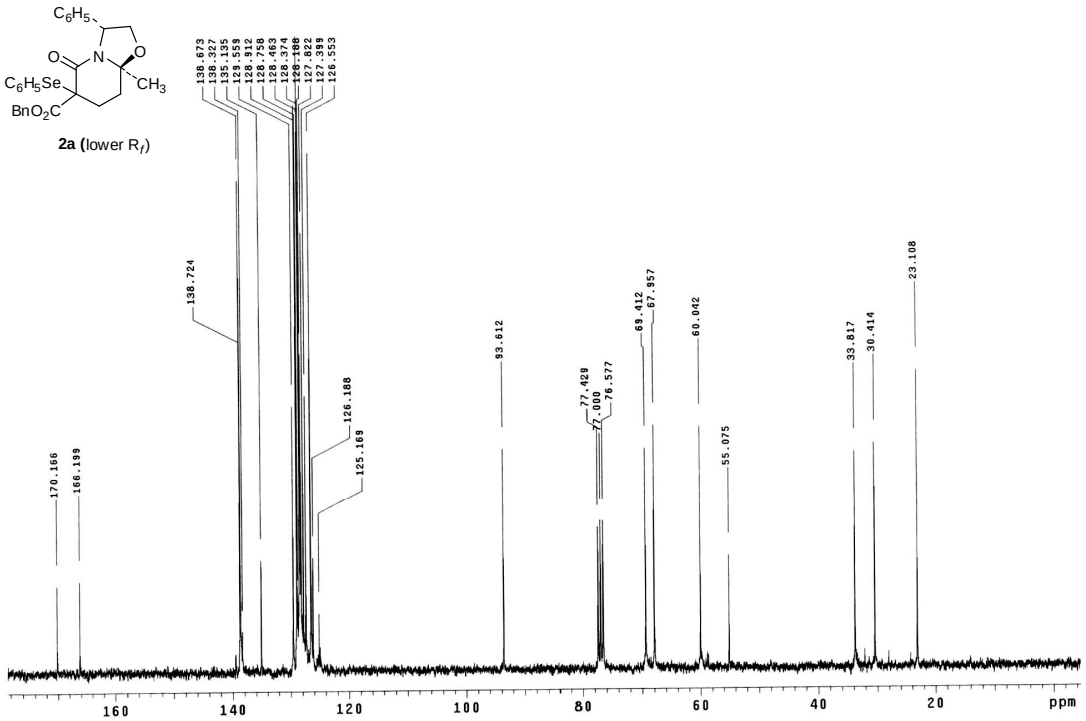
(m, 1H, H-1), 2.68 (dd, *J* = 17.7, 7.8 Hz, 1H, H-9), 3.64 (d, *J* = 4.8 Hz, 1H, H-6), 4.07 (ddd, *J* = 12.0, 6.9, 2.4 Hz, 1H, H-2'), 4.30 (dd, *J* = 12.0, 6.9 Hz, 1H, H-2'), 4.64 (dd, *J* = 6.9, 2.4 Hz, 1H, H-1'), 7.27-7.31 (m, 5H, ArH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 24.3, 24.9 (CH_2), 28.3 (C-1), 32.1 (C-10), 33.0, 34.8 (CH_2), 39.2 (C-7), 56.7 (C-6), 64.5 (C-2'), 65.6 (C-1'), 127.4, 128.6 (C-*o*, *m*), 127.4 (C-*p*), 137.2 (C-*i*), 172.6 (NCO); $[\alpha]^{22}_D$ + 53.7 (*c* 0.2, $CHCl_3$); *m/z*: 275 (M+2, 22), 274 (M+1, 100), 272 (1), 258 (2), 256 (4), 255 (2), 243 (1), 242 (3); HMRS calcd for [$C_{17}H_{23}NO_2$ + H]: 274.1790, found: 274.1801.

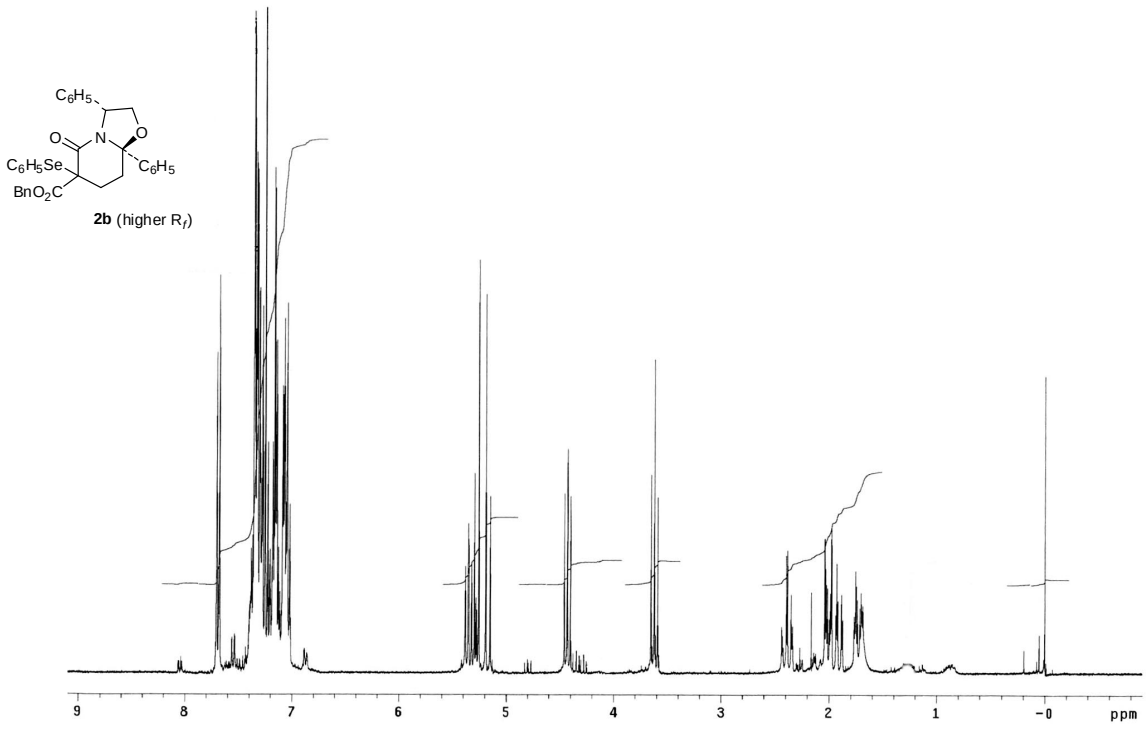
(1*S*,6*R*)-7-Azabicyclo[4.3.1]decan-8-one (21). Into a three-necked, 100 mL round-bottomed flask equipped with a coldfinger condenser charged with dry ice-acetone were condensed 10 mL of NH_3 at –78 ºC, and a solution of **20** (30 mg, 0.11 mmol) in THF (3 mL) was added. The temperature was raised to –33 ºC, and then sodium metal was added in small portions until the blue color persisted. The mixture was stirred at –33 ºC for 1 min. The reaction was quenched by addition of solid NH_4Cl until the blue color disappeared, and then the mixture was stirred at rt for 4 h. The resulting residue was digested at rt with CH_2Cl_2, and the suspension was filtered throw Celite® and concentrated. Flash chromatography (1:9 EtOAc-hexane to 95:5 EtOAc-MeOH) afforded **21** (19 mg, 90% yield): IR (NaCl) 1664, 3190 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, COSY, HETCOR) δ 1.20-1.77 (m, 7H, CH_2), 1.84 (br, *J* = 14.4 Hz, 1H, CH_2), 1.98 (m, 2H, CH_2), 2.17 (d, *J* = 16.8 Hz, 1H, H-9), 2.35 (m, 1H, H-1), 2.43 (dd, *J* = 16.8, 6.0 Hz, 1H, H-9), 3.86 (d, *J* = 4.0 Hz, 1H, H-6), 6.15 (br,1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 24.3 (CH_2), 26.3 (CH_2), 27.7 (C-1), 28.9 (CH_2), 35.3 (CH_2), 35.6 (CH_2), 39.4 (C-9), 50.8 (C-6), 172.6 (NCO); $[\alpha]^{22}_D$ + 46.9 (*c* 0.8, $CHCl_3$); HMRS calcd for [$C_9H_{15}NO$ + H]: 154.1225, found: 154.1226.

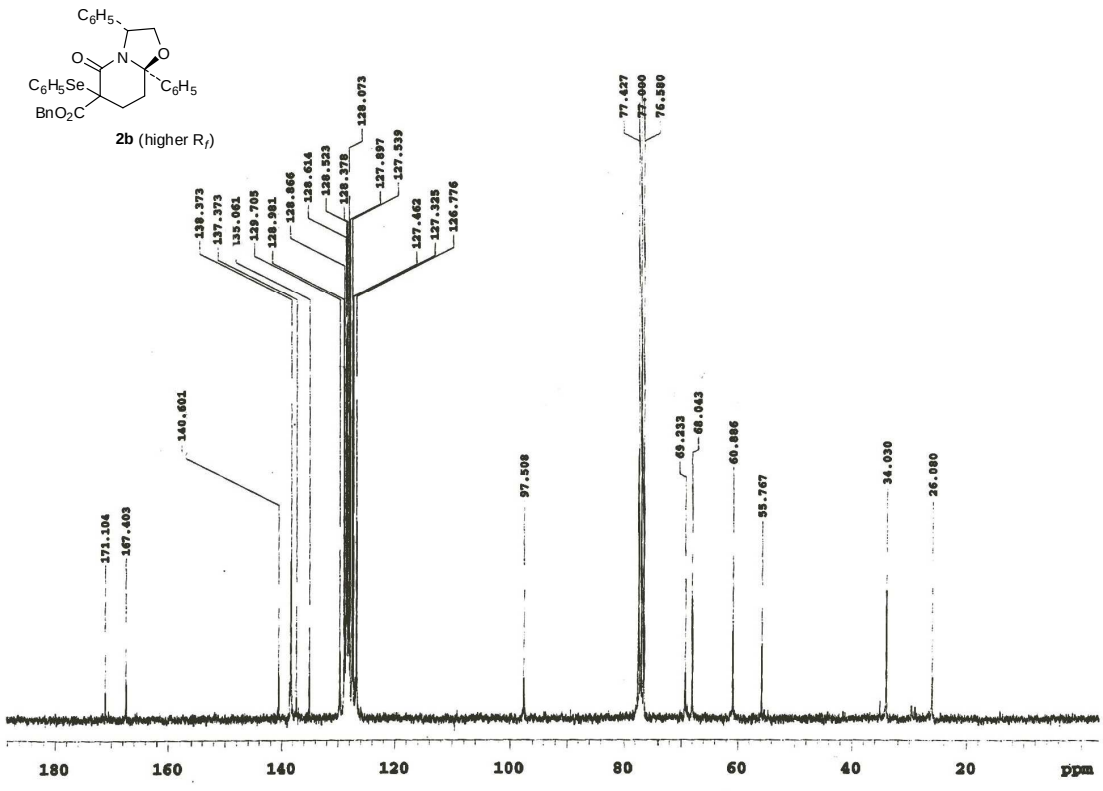

C6H5
O
N
O
C6H5Se
CH3
BnO2C
2a (higher Rf)
7.366
7.359
7.353
7.343
7.165
5.299
5.287
1.176
9
8
7
6
5
4
3
2
1
ppm

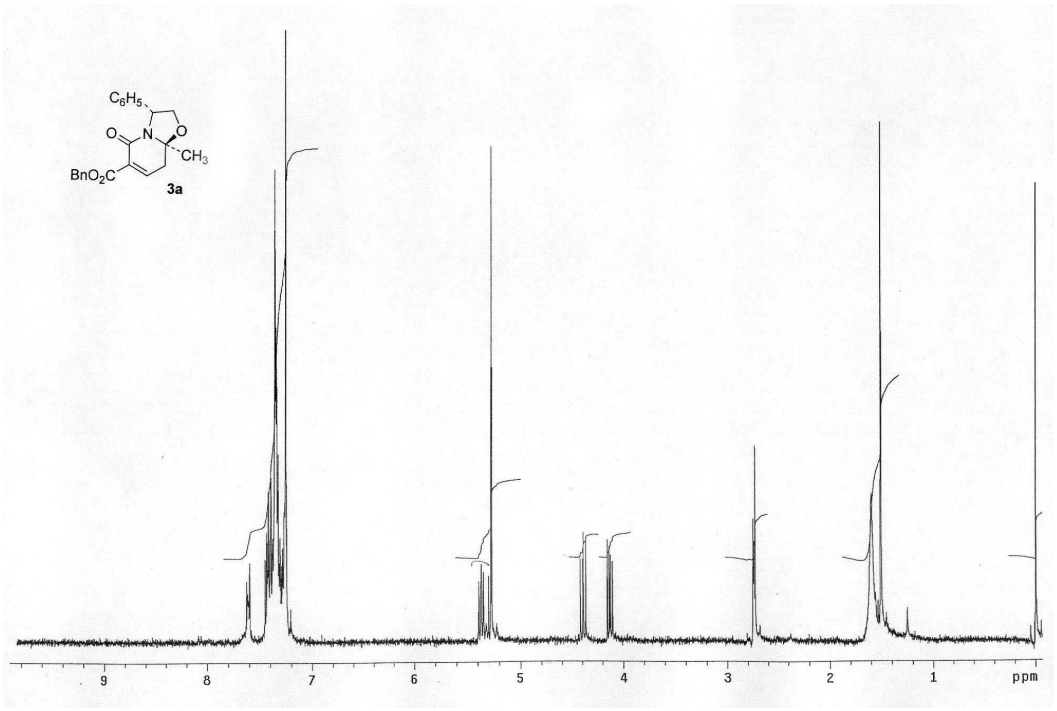

C6H5
O
N
O
C6H5Se
CH3
BnO2C
2a (higher Rf)
138.357
135.069
128.623
128.522
128.447
128.393
127.088
127.012
126.852
125.196
139.494
93.724
77.420
77.000
76.573
69.424
67.875
58.864
54.950
32.199
28.125
24.348
170.448
165.519
180
160
140
120
100
80
60
40
20
ppm

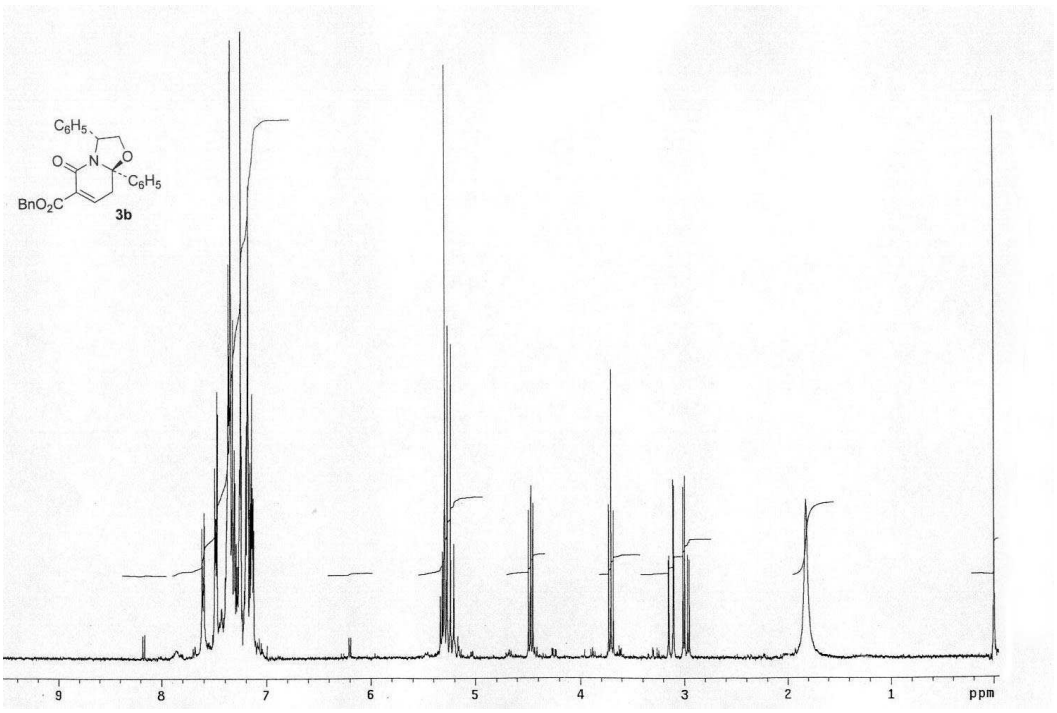

C6H5
O
N
O
CH3
C6H5Se
BnO2C
2a (lower Rf)
7.355
7.320
7.299
7.212
5.245
5.227
0.928
8
7
6
5
4
3
2
1 ppm

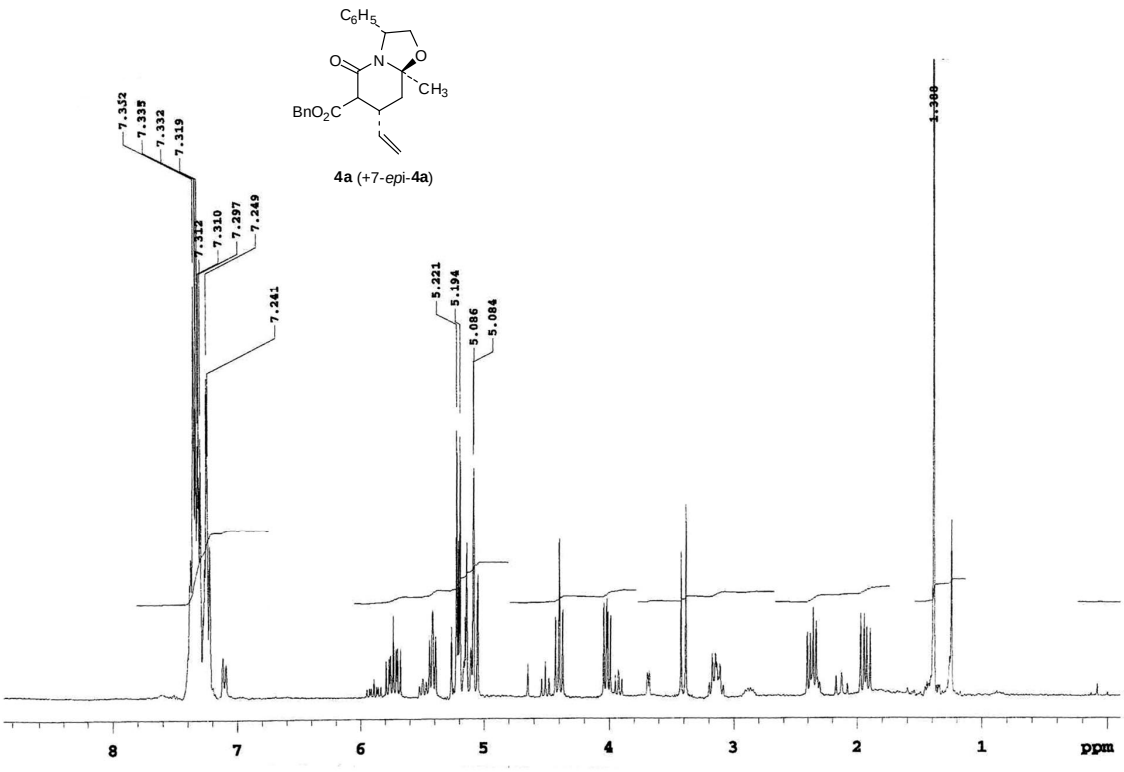

C6H5
O
N
O
CH3
C6H5Se
BnO2C
2a (lower Rf)
138.673
138.327
135.135
129.559
128.912
128.758
128.463
128.374
128.188
127.822
127.399
126.553
138.724
170.166
166.199
126.188
125.169
93.612
77.428
77.000
76.577
69.412
67.957
60.042
55.075
33.817
30.414
23.108
160
140
120
100
80
60
40
20
ppm

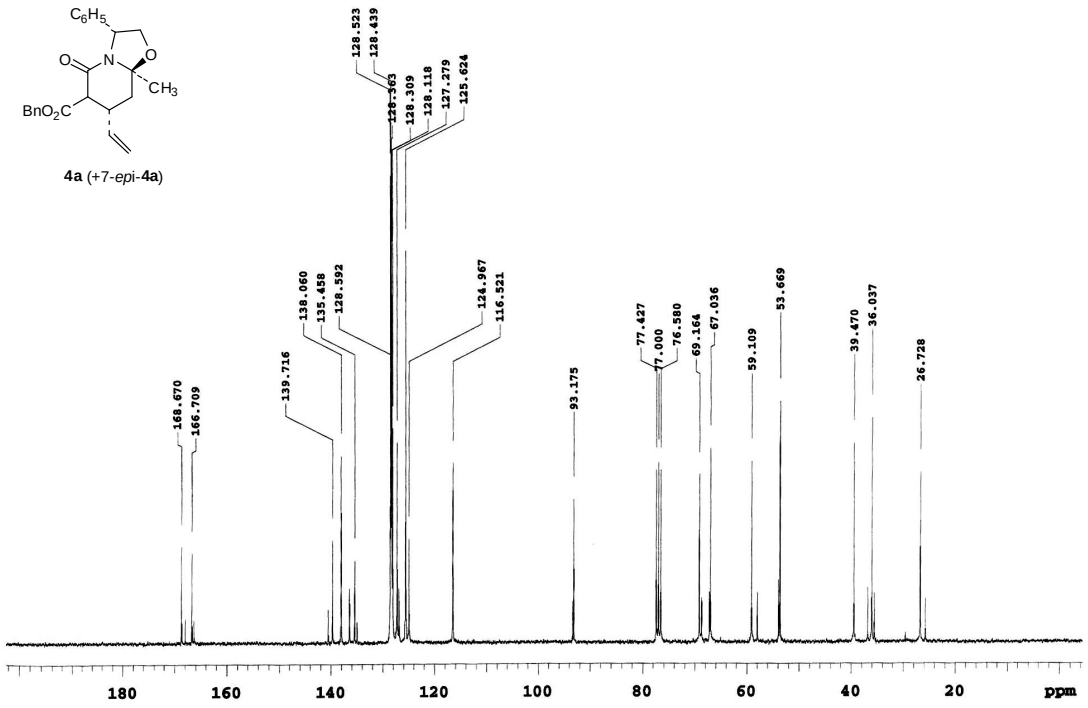

C6H5
O
N
O
C6H5Se
C6H5
BnO2C
2b (higher Rf)
9
8
7
6
5
4
3
2
1
−0
ppm

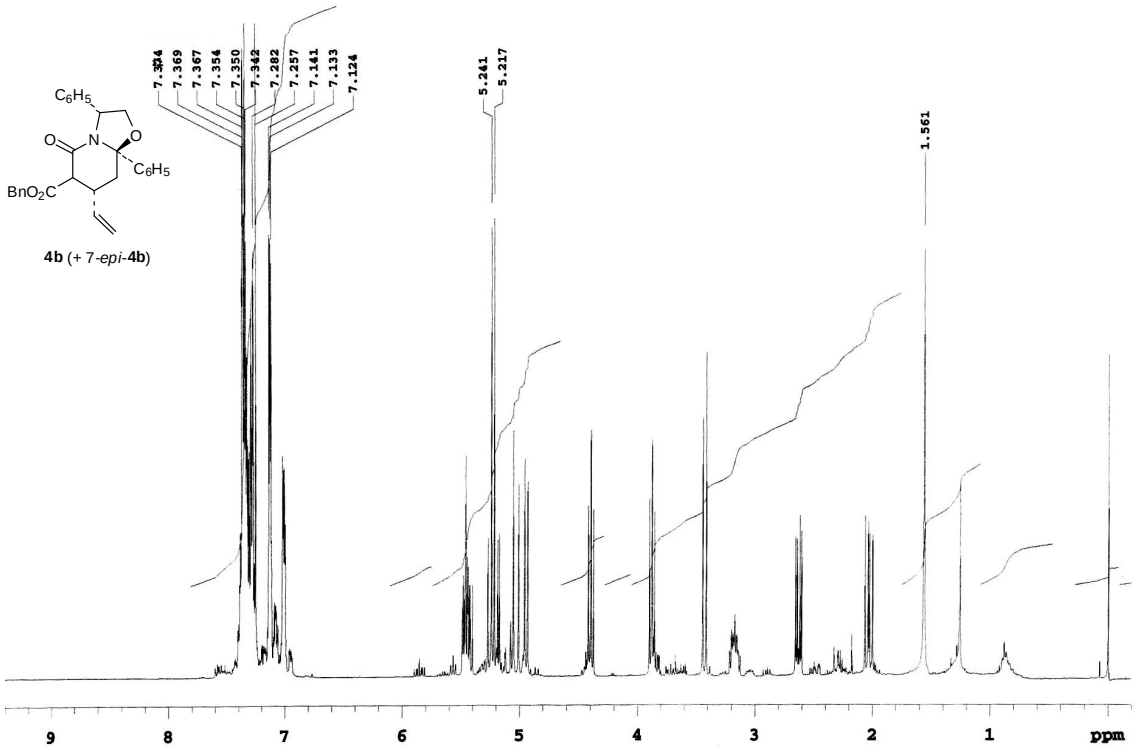

C6H5
O
N
O
C6H5Se
C6H5
BnO2C
2b (higher Rf)
130.373
137.373
135.061
129.705
128.981
128.666
128.614
128.523
128.378
128.073
127.897
127.539
127.462
127.325
126.776
140.601
171.104
167.403
97.508
77.427
77.000
76.580
69.233
68.043
60.886
55.767
34.030
26.080
180
160
140
120
100
80
60
40
20
ppm


C6H5
O
N
O
CH3
BnO2C
3a
9
8
7
6
5
4
3
2
1
ppm

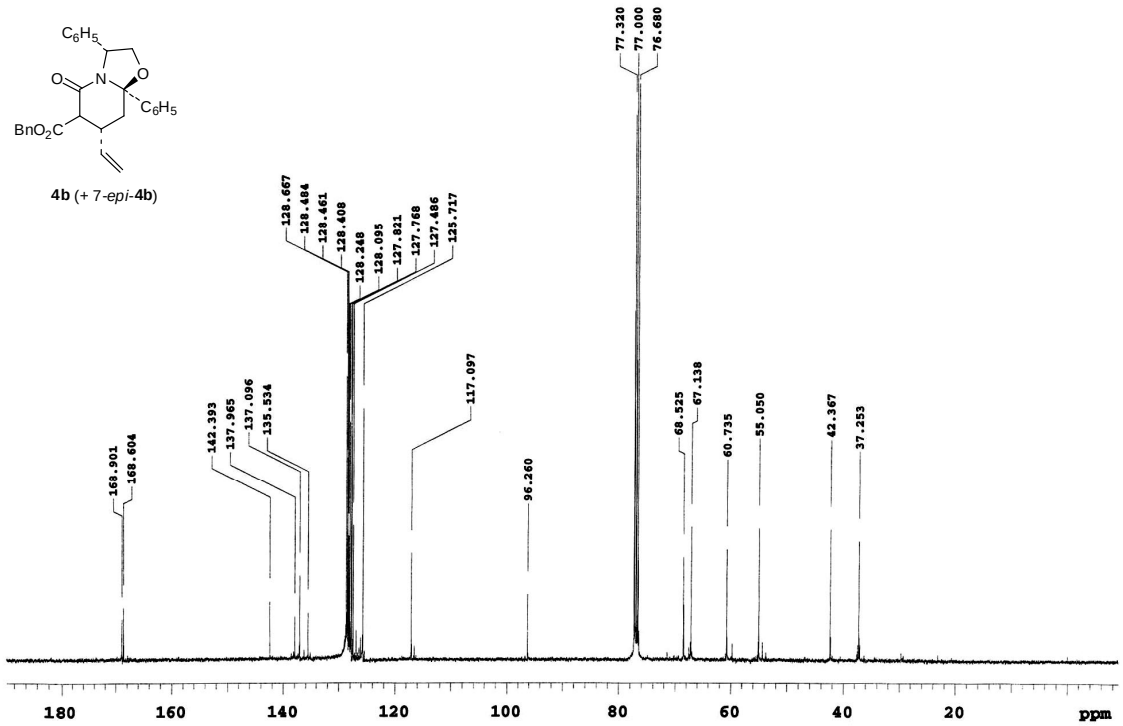

C6H5
O
N
O
C6H5
BnO2C
3b
9
8
7
6
5
4
3
2
1
ppm


C6H5
O
N
O
CH3
BnO2C
4a (+7-epi-4a)
7.352
7.335
7.332
7.319
7.312
7.310
7.297
7.249
7.241
5.221
5.194
5.086
5.084
1.300
8
7
6
5
4
3
2
1
ppm

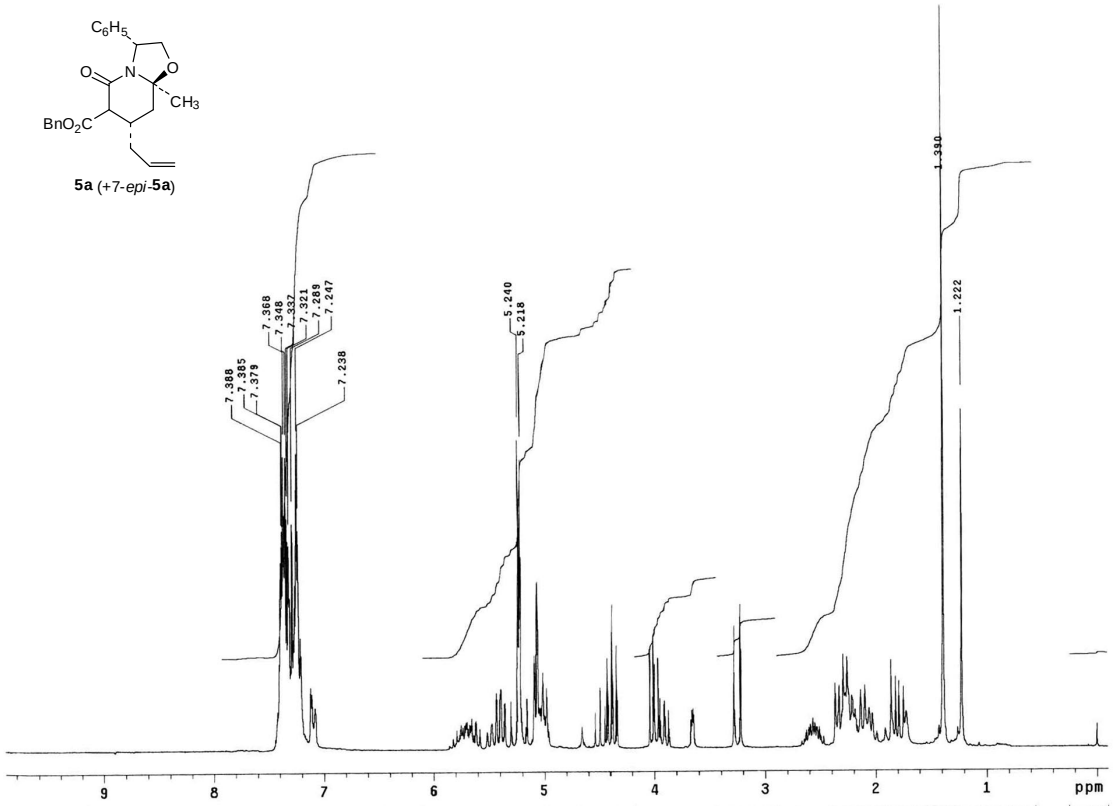

C6H5
O
N
O
CH3
BnO2C
4a (+7-epi-4a)
128.523
128.439
128.363
128.309
128.118
127.279
125.624
138.060
135.458
128.592
124.967
116.521
139.716
168.670
166.709
93.175
77.427
77.000
76.580
69.164
67.036
59.109
53.669
39.470
36.037
26.728
180
160
140
120
100
80
60
40
20
ppm

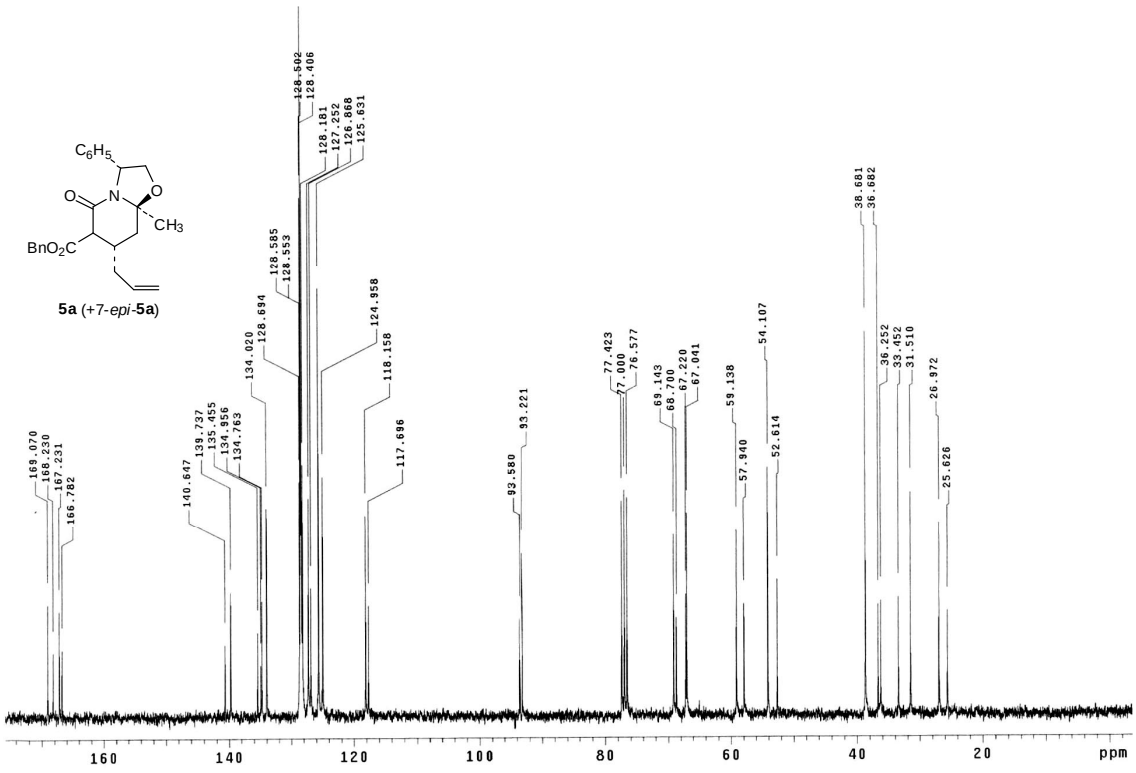


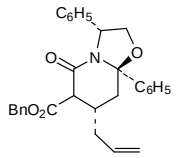
4b (+ 7-*epi*-**4b**)



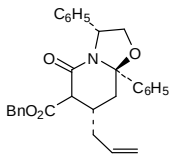
4b (+ 7-*epi*-**4b**)


C6H5
O
N
O
CH3
BnO2C
5a (+7-epi-5a)
7.388
7.385
7.379
7.368
7.348
7.332
7.321
7.289
7.247
7.238
5.240
5.218
1.390
1.222
9
8
7
6
5
4
3
2
1
ppm

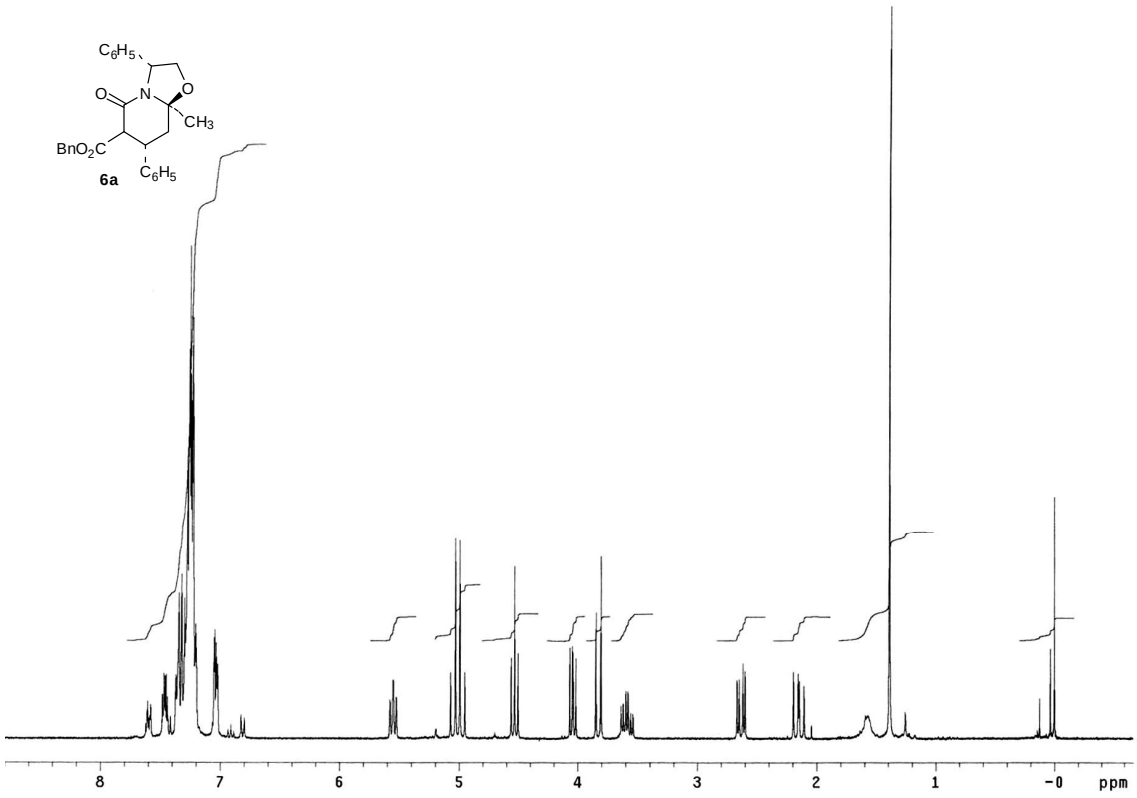

C6H5
O
N
O
CH3
BnO2C
5a (+7-epi-5a)
169.070
168.230
167.231
166.782
140.647
139.737
135.455
134.956
134.763
134.020
128.694
128.585
128.553
128.502
128.406
128.181
127.252
126.868
125.631
124.958
118.158
117.696
93.580
93.221
77.423
77.000
76.577
69.143
68.700
67.220
67.041
59.138
57.940
54.107
52.614
38.681
36.682
36.252
33.452
31.510
26.972
25.626
160
140
120
100
80
60
40
20
ppm

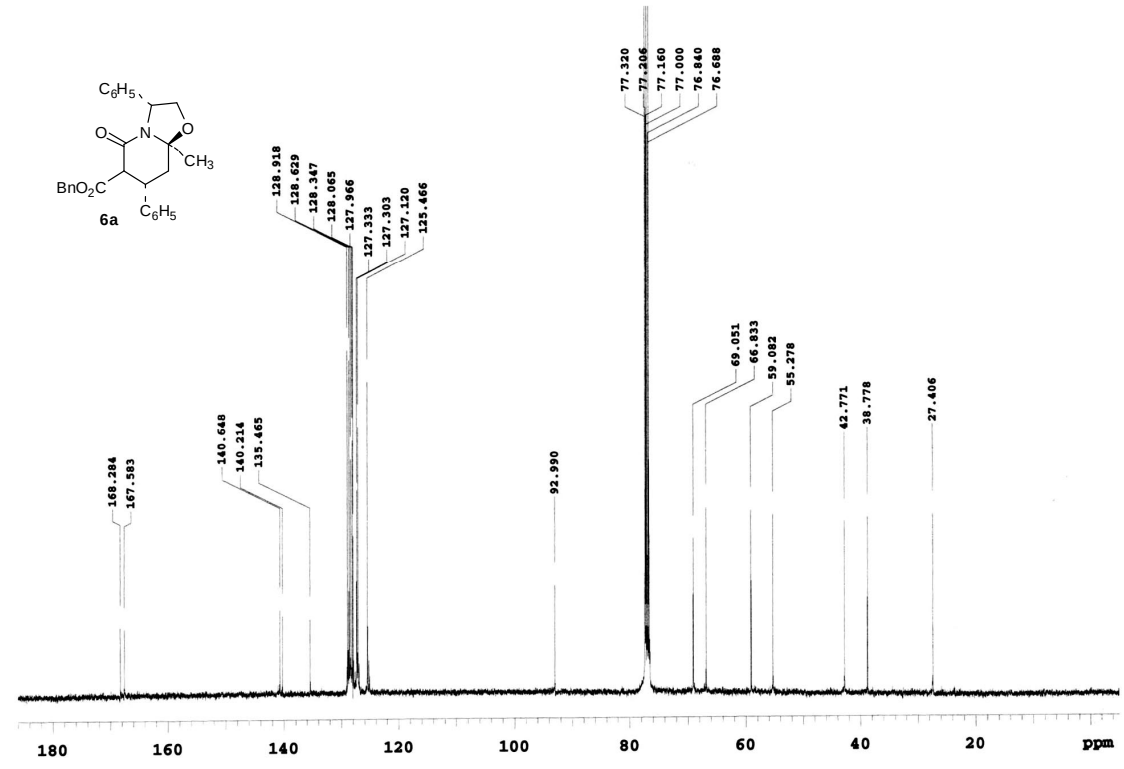


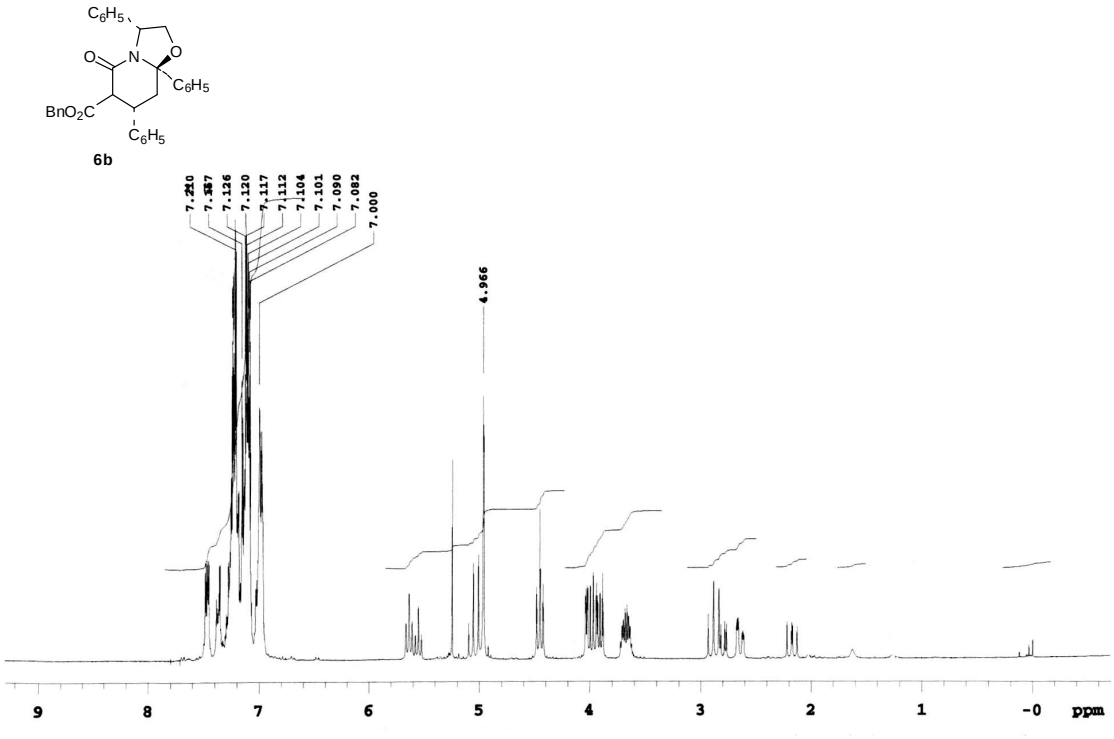
5b (+7-*epi*-**5b**)

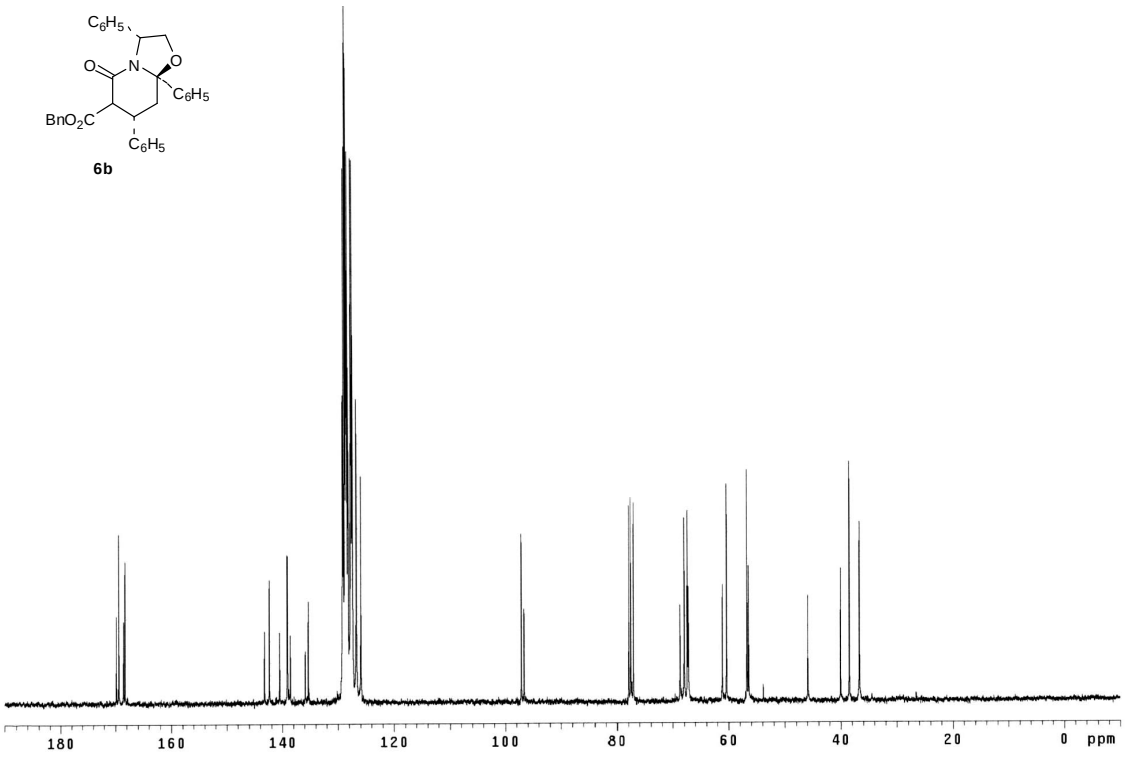


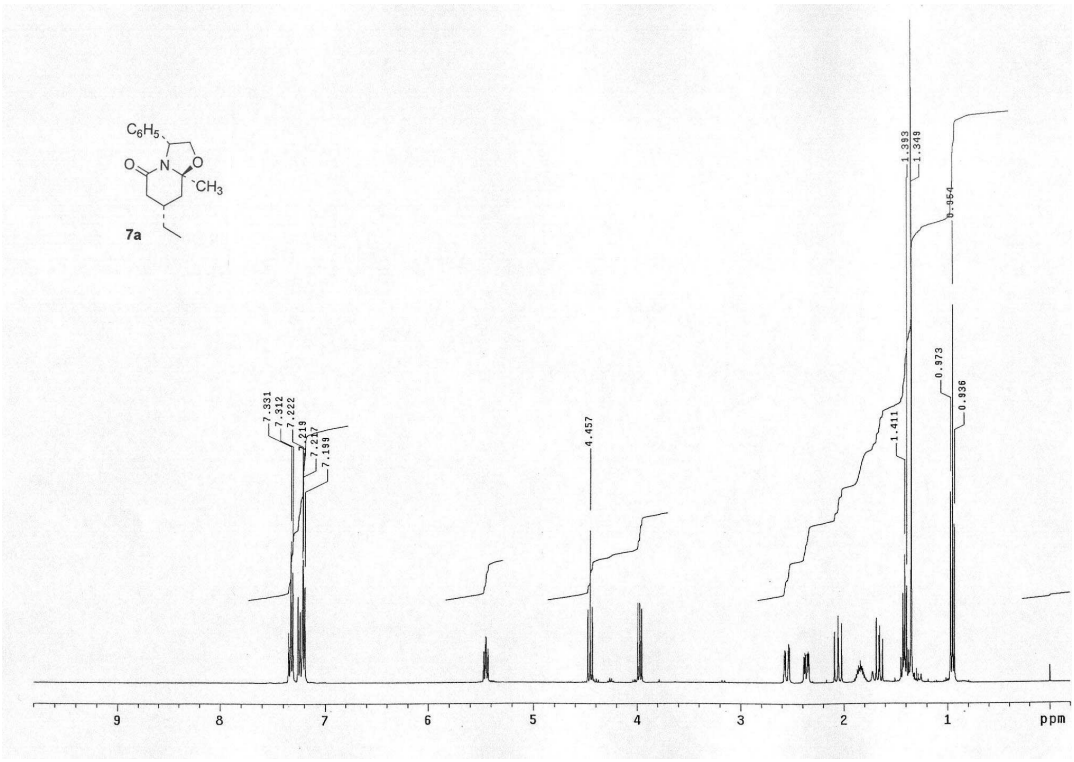
5b (+7-*epi*-**5b**)

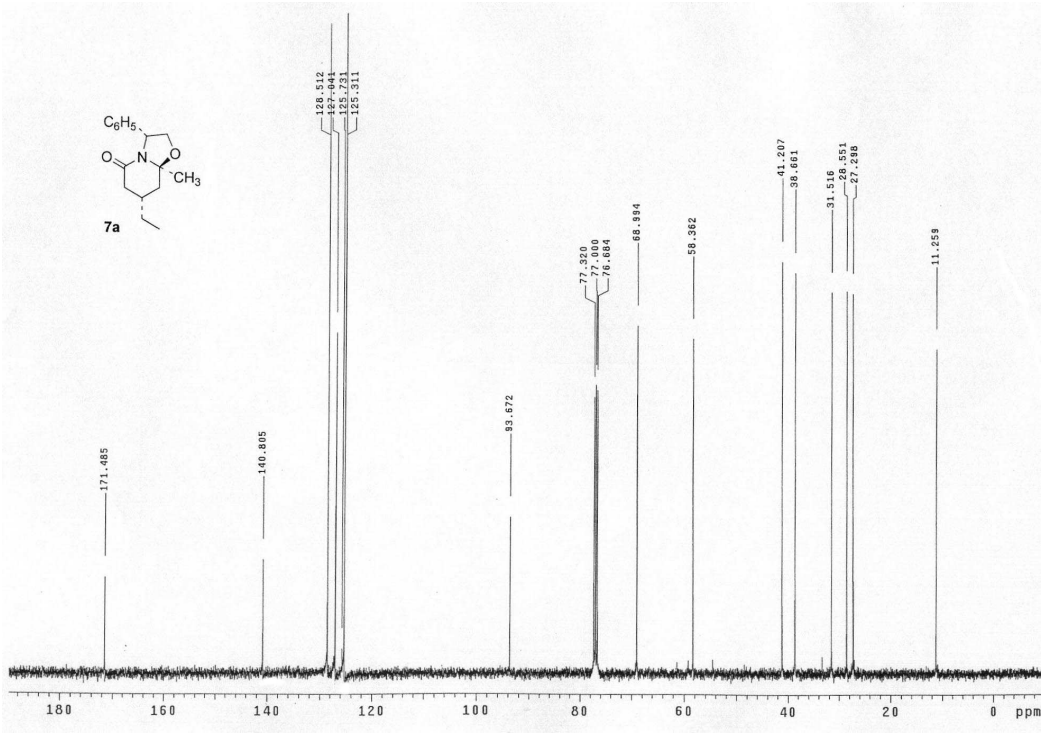

C6H5
O
N
O
CH3
BnO2C
C6H5
6a
8
7
6
5
4
3
2
1
-0
ppm

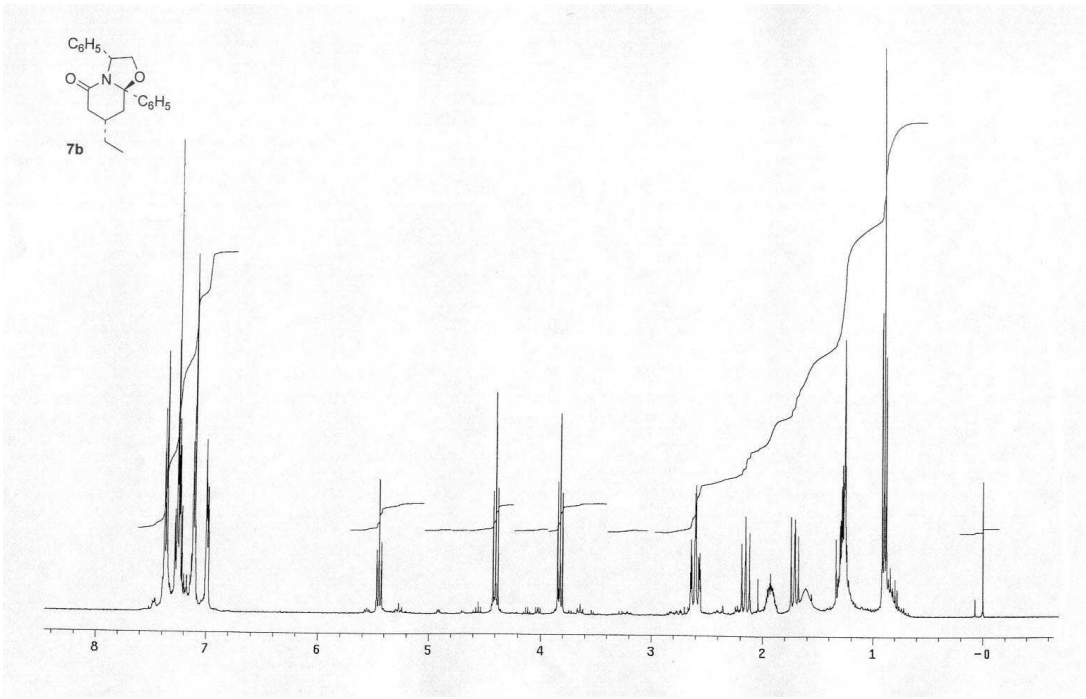

C6H5
O
N
O
CH3
BnO2C
C6H5
6a
168.284
167.583
140.648
140.214
135.465
128.918
128.629
128.347
128.065
127.966
127.333
127.303
127.120
125.466
92.990
77.320
77.206
77.160
77.000
76.840
76.688
69.051
66.833
59.082
55.278
42.771
38.778
27.406
180
160
140
120
100
80
60
40
20
ppm

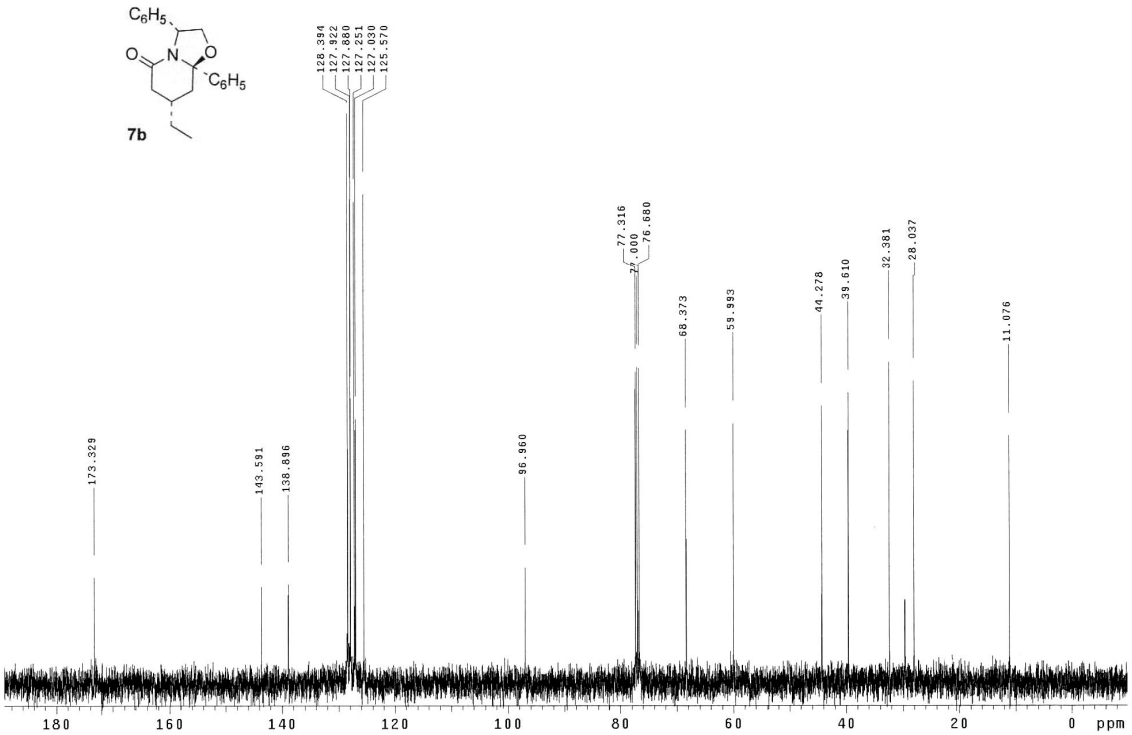

6b
7.126
7.120
7.117
7.112
7.104
7.101
7.090
7.082
7.000
4.966
9
8
7
6
5
4
3
2
1
-0
ppm

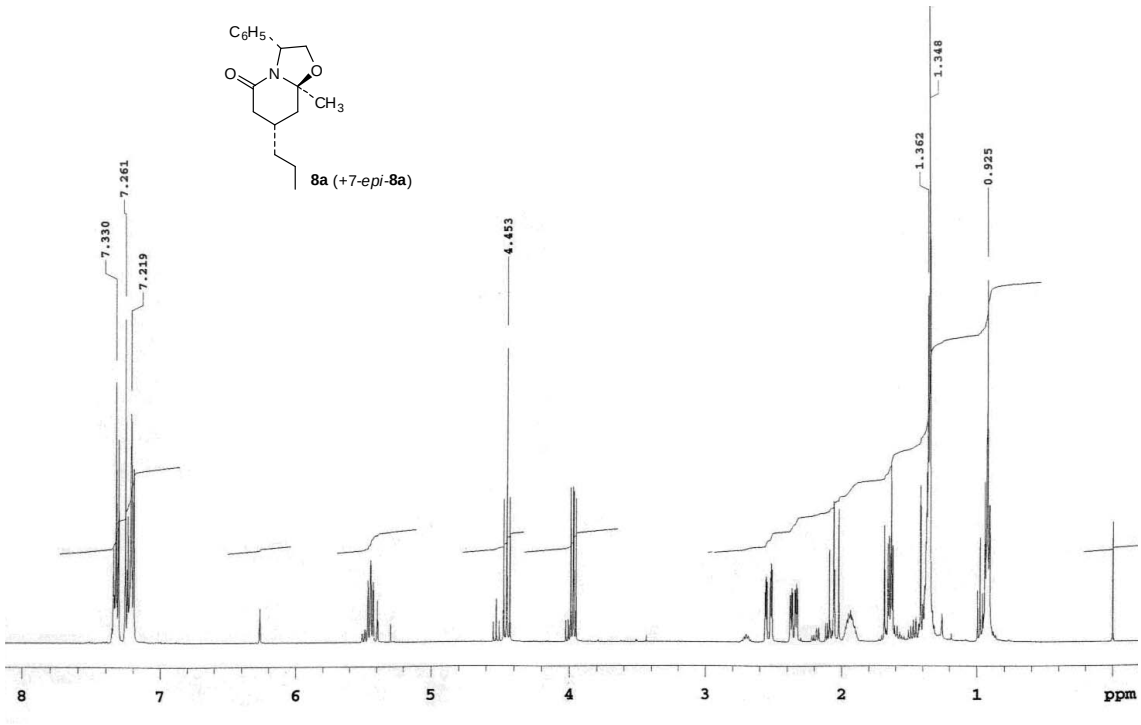

6b
180
160
140
120
100
80
60
40
20
0
ppm

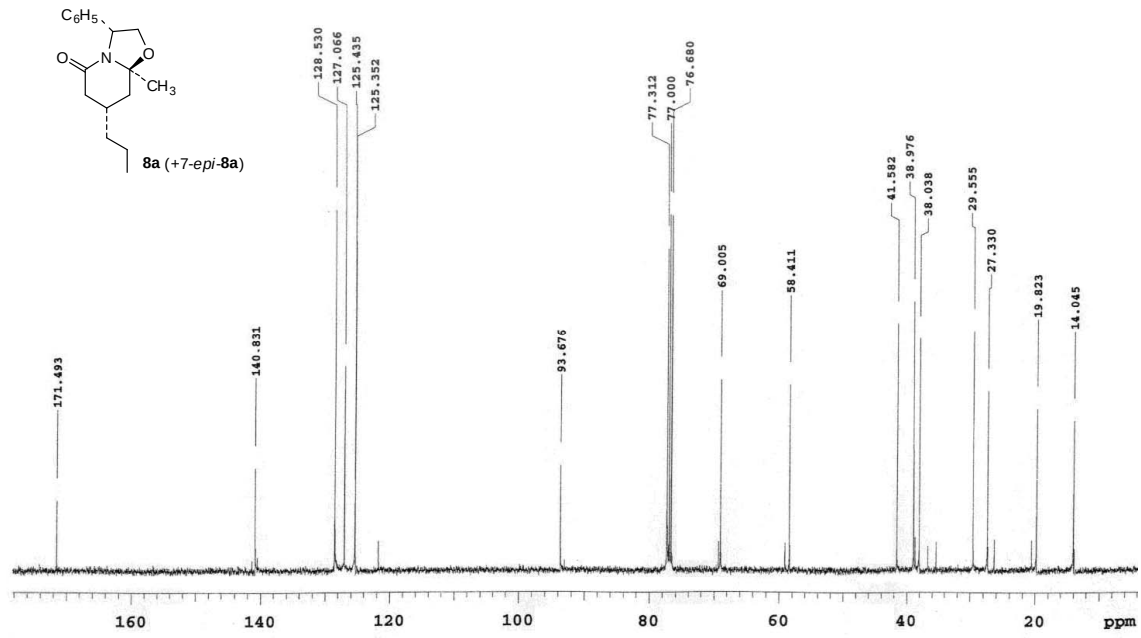

7a
7.331
7.312
7.222
7.219
7.217
7.199
4.457
1.393
1.349
0.964
0.973
0.936
1.411
9
8
7
6
5
4
3
2
1
ppm

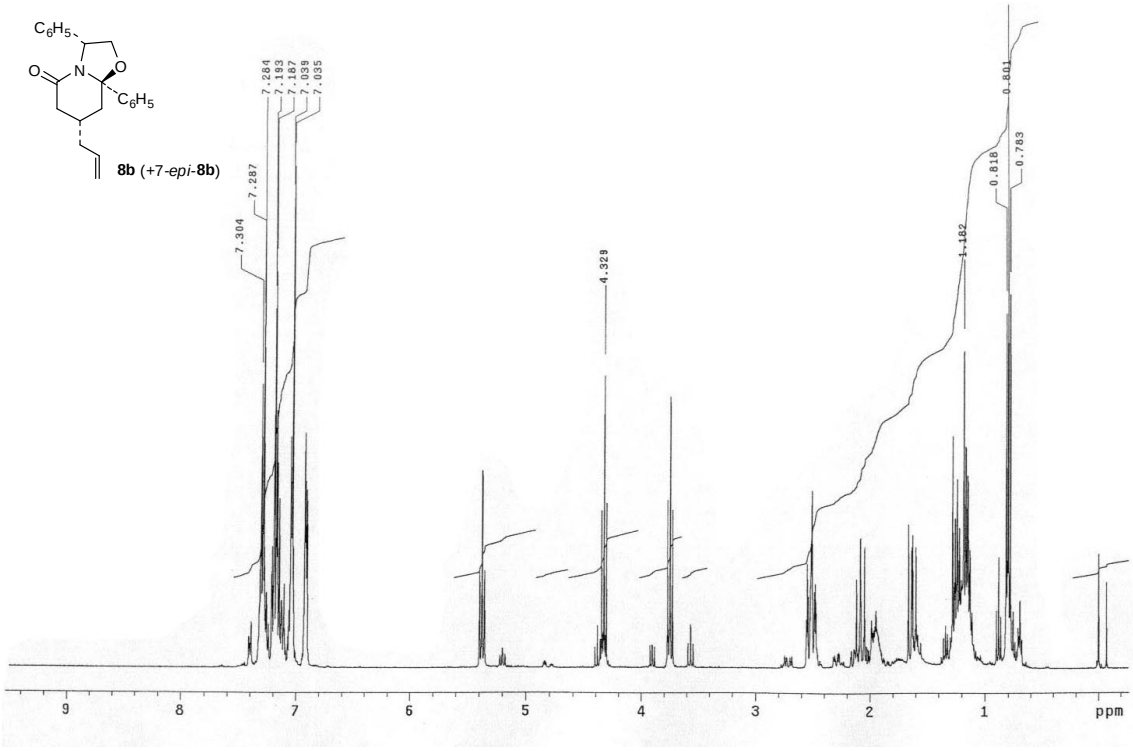

7a
171.485
140.805
128.512
127.941
127.731
125.311
93.672
77.320
77.000
76.684
68.994
58.362
41.207
38.661
31.516
28.551
27.298
11.259
180
160
140
120
100
80
60
40
20
0
ppm

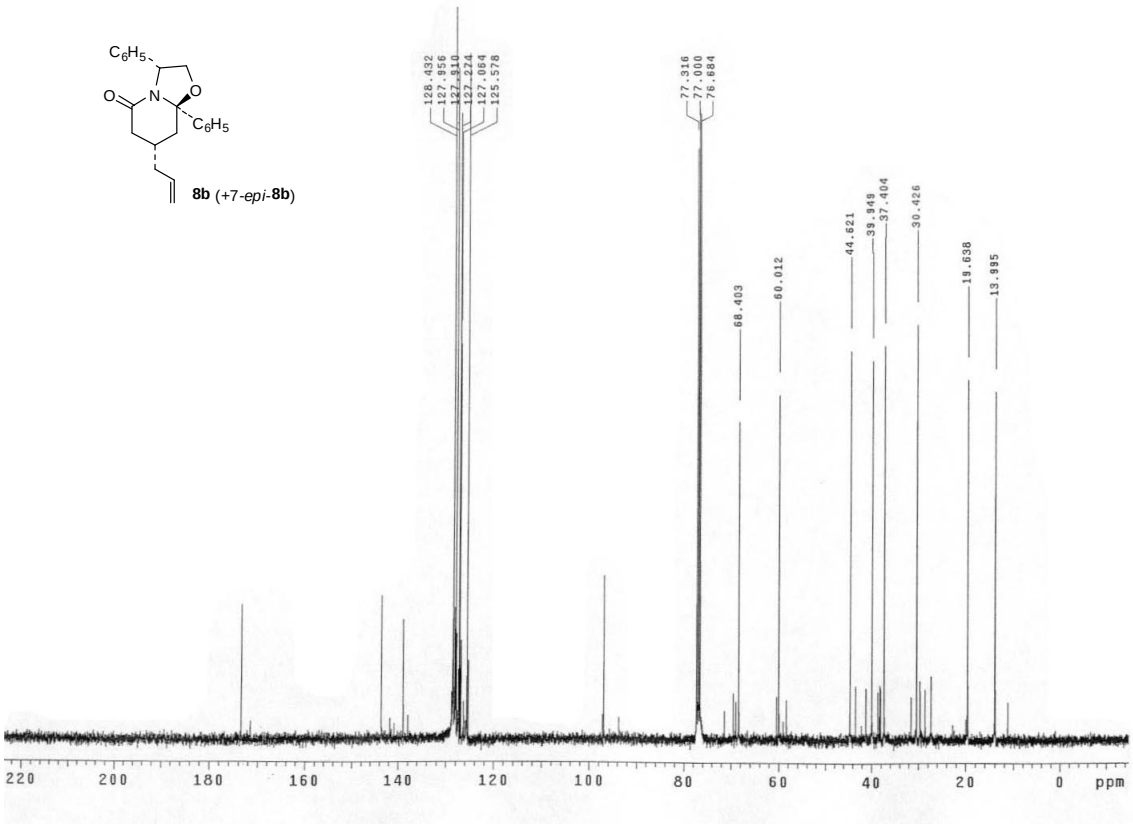

C6H5
O
N
O
C6H5
7b
8
7
6
5
4
3
2
1
-0

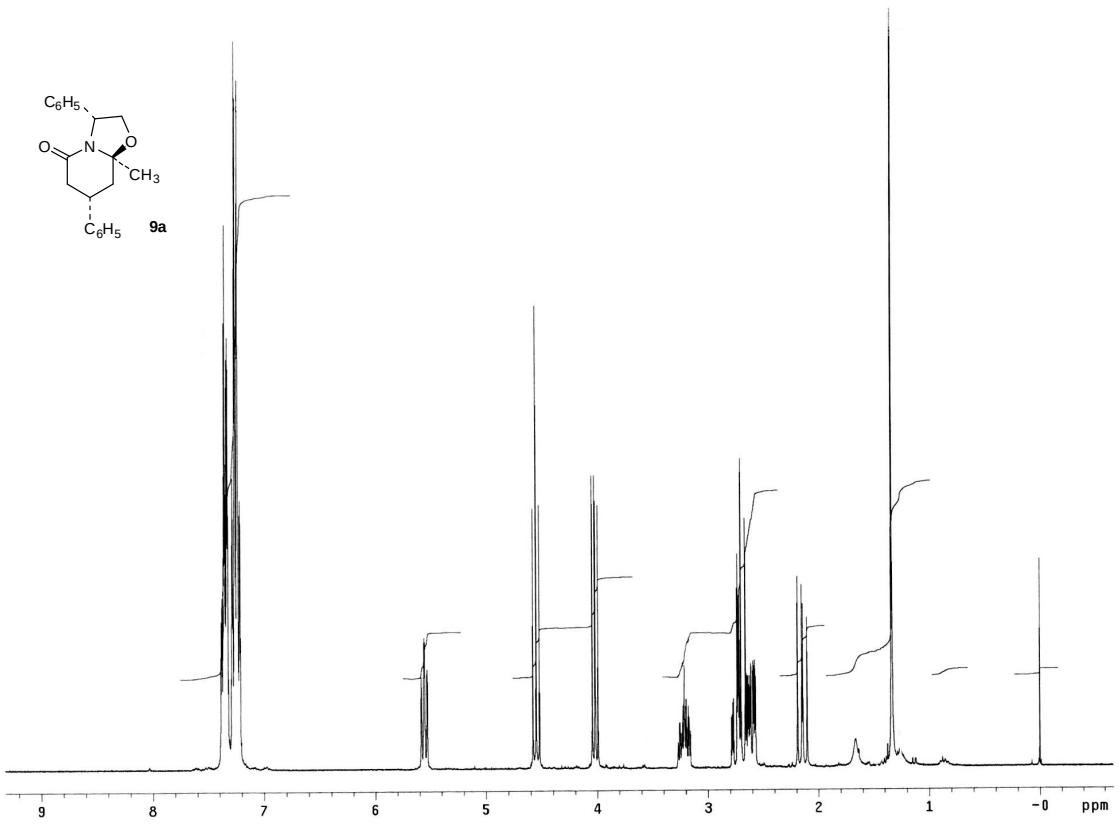

C6H5
O
N
O
C6H5
7b
128.394
127.922
127.860
127.251
127.090
125.570
77.316
77.000
76.680
68.373
59.993
44.278
39.610
32.381
28.037
11.076
173.329
143.591
138.896
96.960
180
160
140
120
100
80
60
40
20
0 ppm

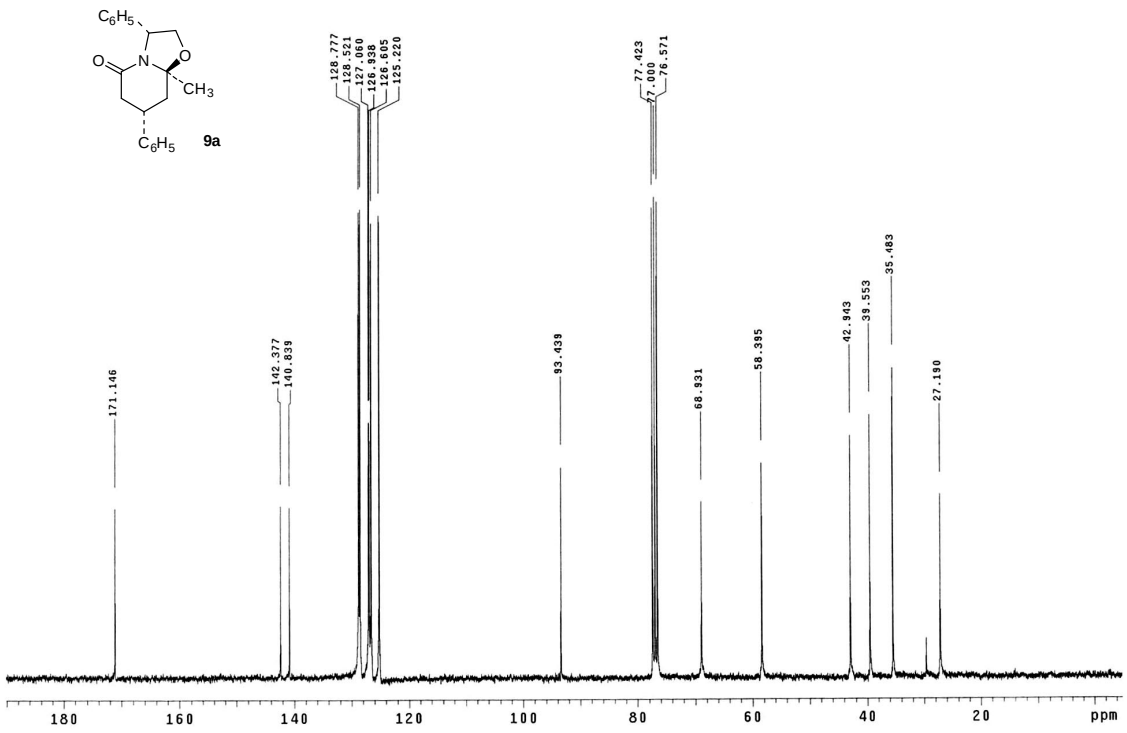

C6H5
O
N
O
CH3
8a (+7-epi-8a)
7.330
7.261
7.219
4.453
1.362
1.348
0.925
8
7
6
5
4
3
2
1
ppm

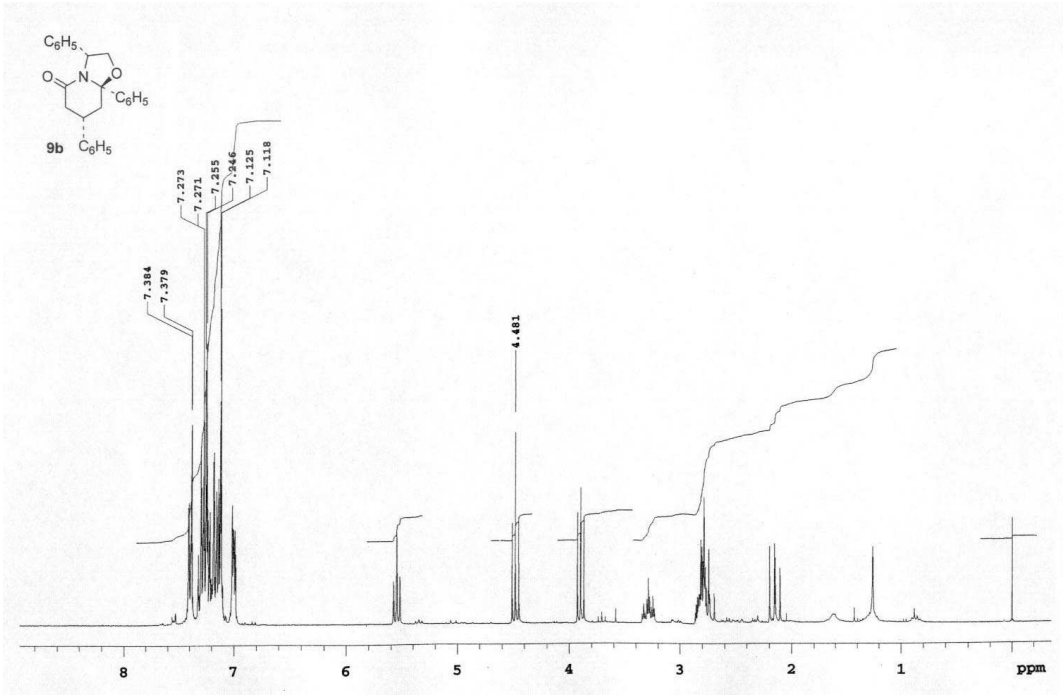

C6H5
O
N
O
CH3
8a (+7-epi-8a)
171.493
140.831
128.530
127.066
125.435
125.352
93.676
77.312
77.000
76.680
69.005
58.411
41.582
38.976
38.038
29.555
27.330
19.823
14.045
160
140
120
100
80
60
40
20
ppm

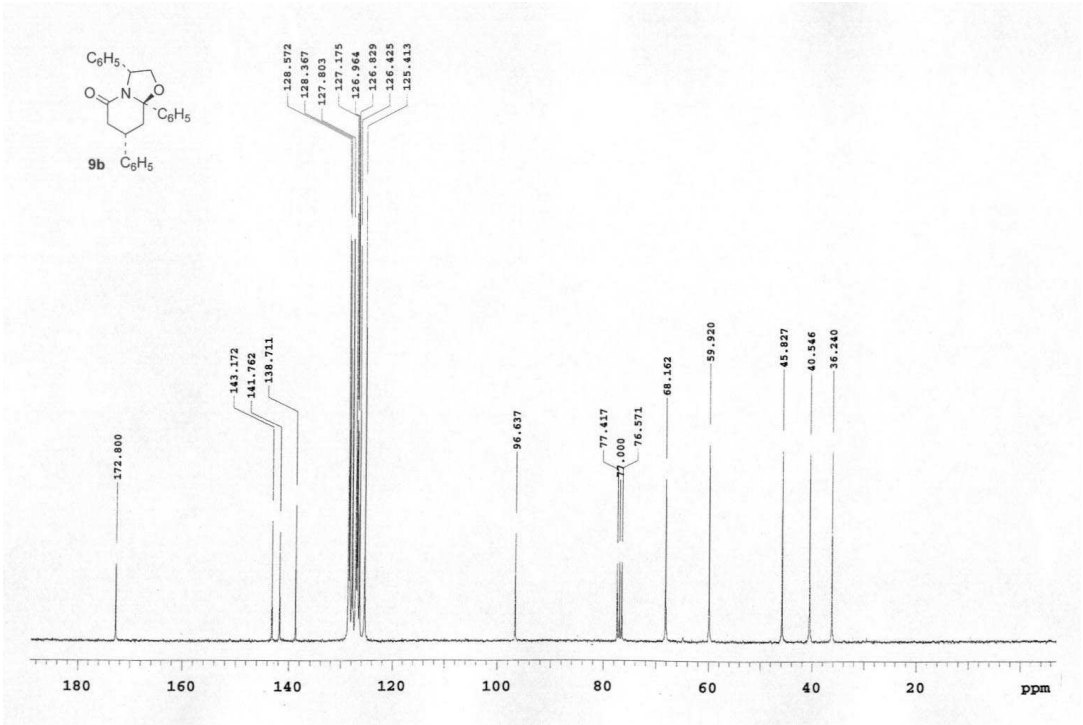

C6H5
O
N
O
C6H5
8b (+7-epi-8b)
7.304
7.287
7.284
7.183
7.167
7.039
7.035
4.329
1.182
0.801
0.818
0.783
9
8
7
6
5
4
3
2
1
ppm

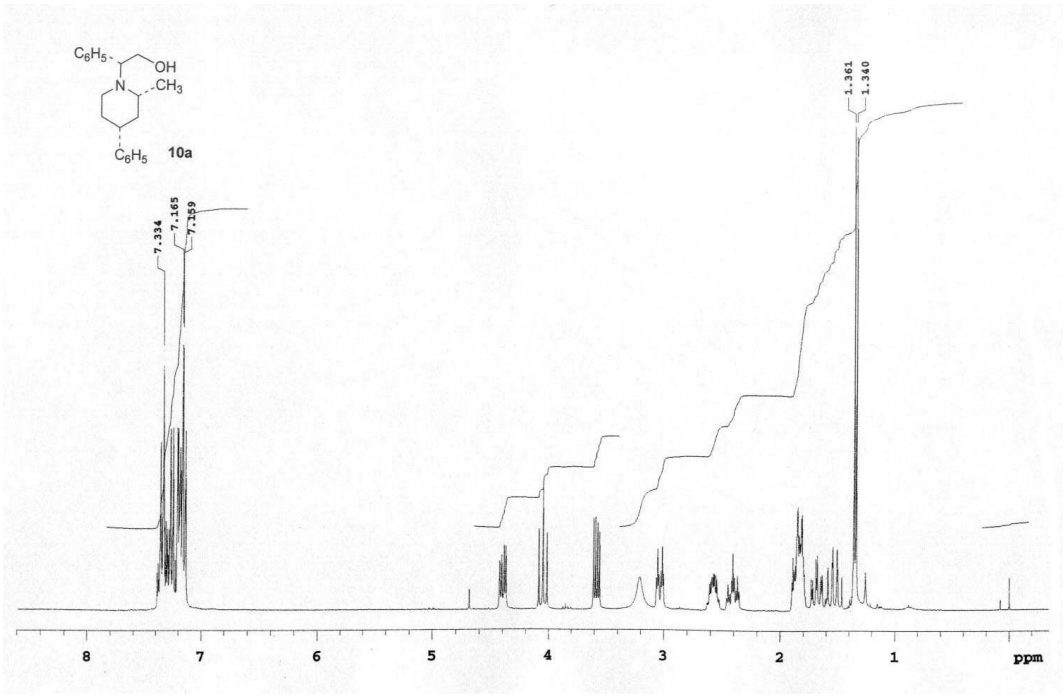

C6H5
O
N
O
C6H5
8b (+7-epi-8b)
128.432
127.956
127.810
127.274
127.064
125.578
77.316
77.000
76.684
68.403
60.012
44.621
39.949
37.404
30.426
19.638
13.995
220
200
180
160
140
120
100
80
60
40
20
0
ppm

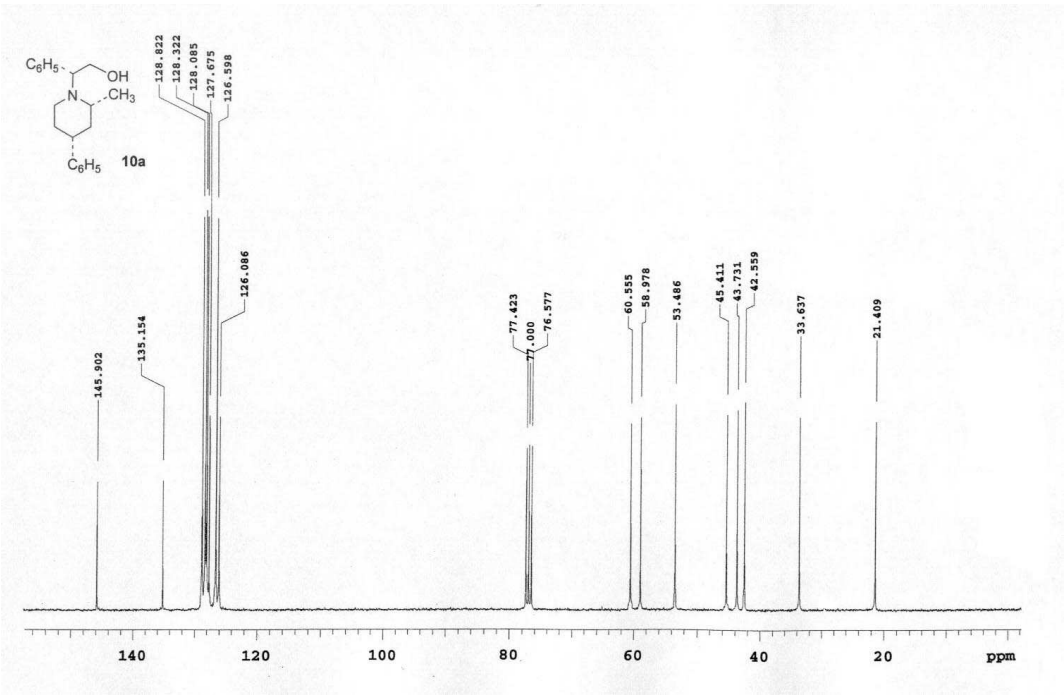

C6H5
O
N
O
CH3
C6H5
9a
9
8
7
6
5
4
3
2
1
-0
ppm

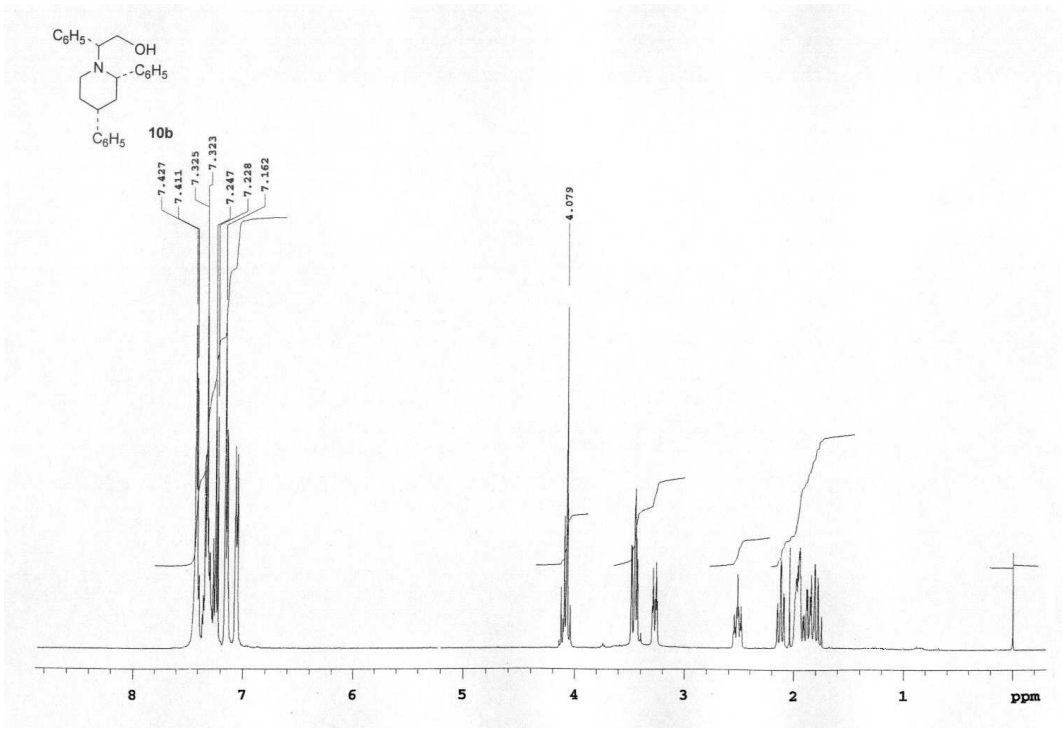

C6H5
O
N
O
CH3
C6H5
9a
128.777
128.521
127.060
126.938
126.605
125.220
77.423
77.000
76.571
171.146
142.377
140.639
93.439
68.931
58.385
42.943
39.553
35.483
27.190
180
160
140
120
100
80
60
40
20
ppm

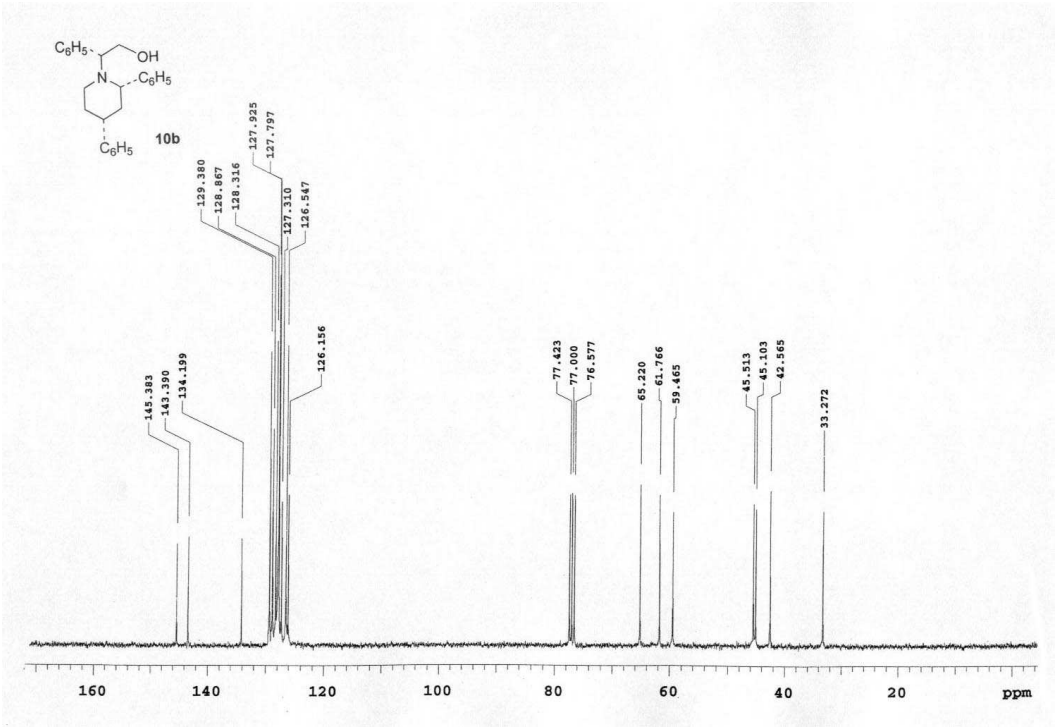

9b
7.384
7.379
7.273
7.271
7.255
7.246
7.125
7.118
4.481
8
7
6
5
4
3
2
1
ppm

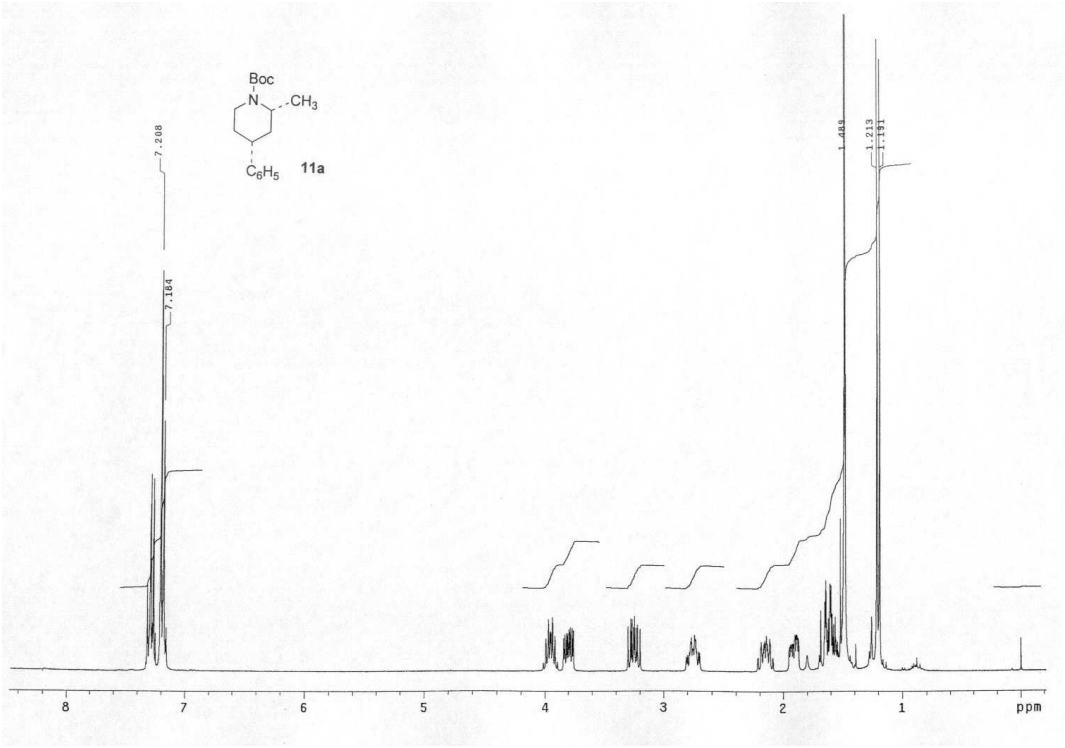

9b
172.800
143.172
141.762
138.711
128.572
128.367
127.803
127.175
126.964
126.829
126.425
125.413
96.637
77.417
77.000
76.571
68.162
59.920
45.827
40.546
36.240
180
160
140
120
100
80
60
40
20
ppm

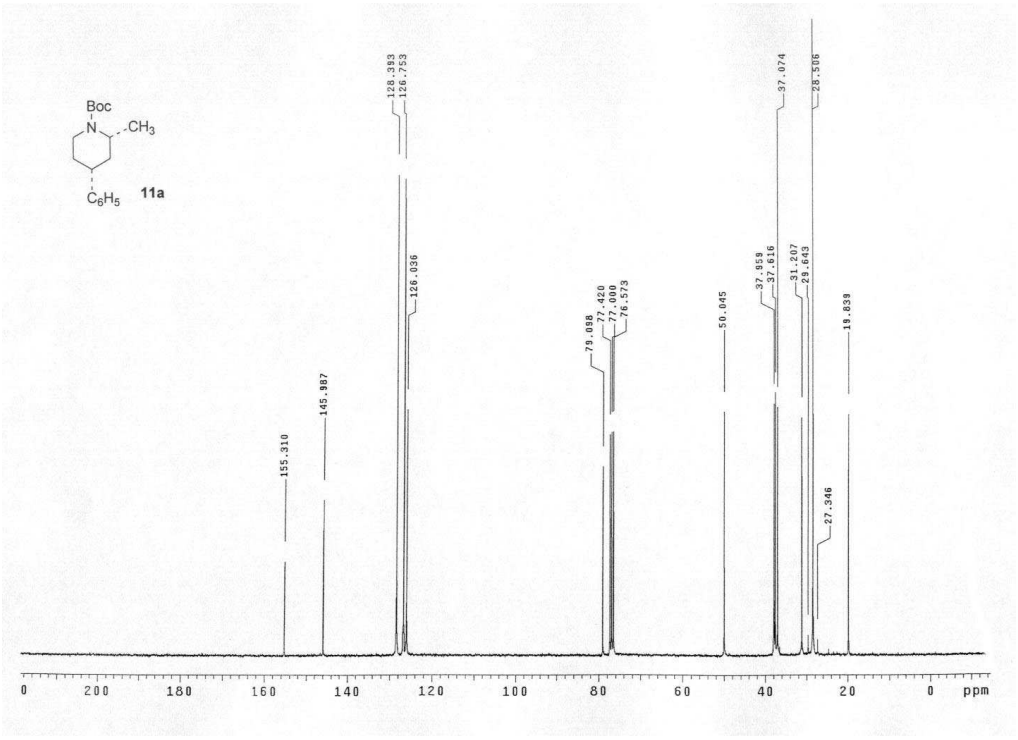

C6H5
OH
N
CH3
C6H5
10a
7.334
7.165
7.159
1.361
1.340
8
7
6
5
4
3
2
1
ppm

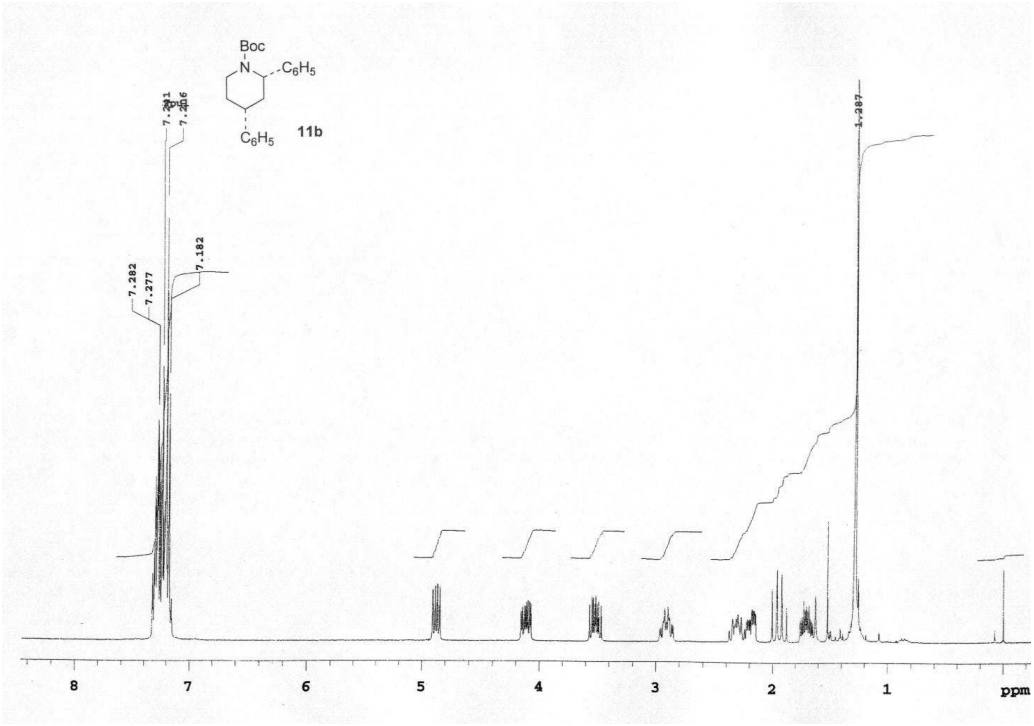

C6H5
OH
N
CH3
C6H5
10a
128.822
128.322
128.085
127.675
126.598
126.086
145.902
135.154
77.423
77.000
76.577
60.555
58.978
53.486
45.411
43.731
42.559
33.637
21.409
140
120
100
80
60
40
20
ppm

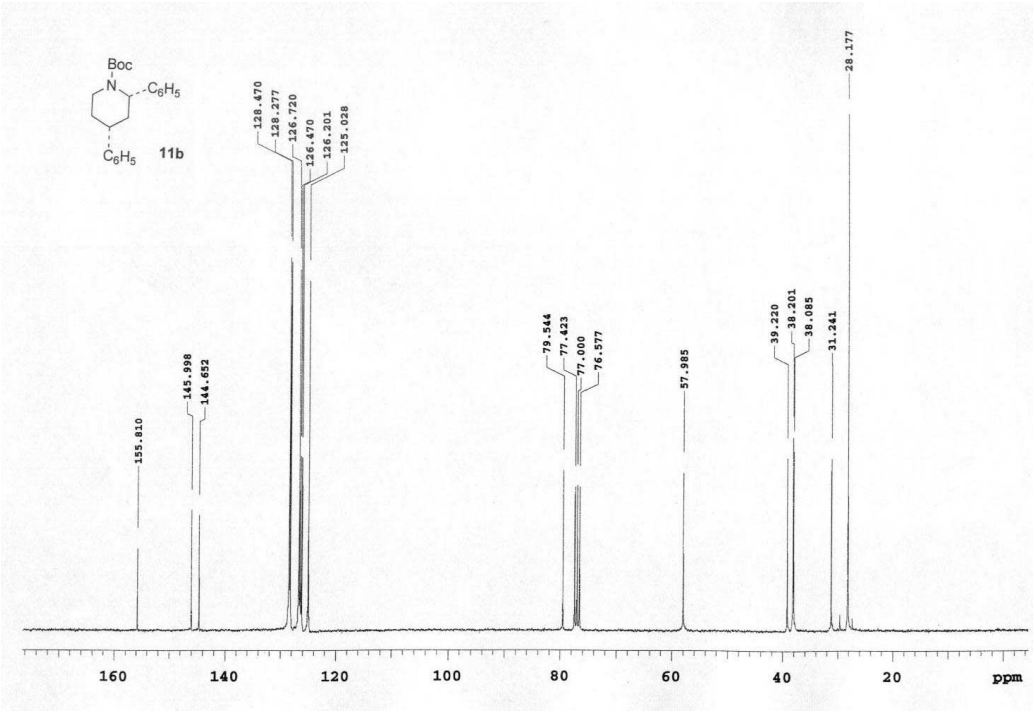

C6H5
OH
N
C6H5
C6H5
10b
7.427
7.411
7.325
7.323
7.247
7.228
7.162
4.079
8
7
6
5
4
3
2
1
ppm


C6H5
OH
N
C6H5
C6H5
10b
129.380
128.867
128.316
127.925
127.797
127.310
126.547
126.156
145.383
143.390
134.199
77.423
77.000
76.577
65.220
61.766
59.465
45.513
45.103
42.565
33.272
160
140
120
100
80
60
40
20
ppm


Boc
N
CH3
C6H5
11a
7.208
7.184
1.483
1.213
1.191
8
7
6
5
4
3
2
1
ppm


Boc
N
CH3
C6H5
11a
128.393
126.753
126.036
155.310
145.987
79.098
77.420
77.000
76.579
50.045
37.959
37.616
37.074
31.207
29.643
28.306
27.346
19.839
0
200
180
160
140
120
100
80
60
40
20
0
ppm


Boc
N
C_6H_5
C_6H_5
11b
7.282
7.277
7.182
1.287
8
7
6
5
4
3
2
1
ppm


Boc
N
C_6H_5
C_6H_5
11b
155.810
145.998
144.652
128.470
128.277
126.720
126.470
126.201
125.028
79.544
77.423
77.000
76.577
57.985
39.220
38.201
38.085
31.241
28.177
160
140
120
100
80
60
40
20
ppm

[1] Munchhof, M. J.; Meyers, A. I. *J. Org. Chem.* **1995**, 60, 7084–7085
[2] Amat, M.; Bassas, O.; Llor, N.; Cantó, M.; Pérez, M.; Molins, E.; Bosch, J. *Chem. Eur. J.* **2006**, *12*, 7872–7881.
[3] Munchhof, M. J.; Meyers, A. I. *J. Org. Chem.* **1995**, 60, 7084–7085.
[4] Mazur, P.; Nakanishi, K. *J. Org. Chem.* **1992**, *57*, 1047–1051