Supporting Information

Highly Efficient Synthesis of Azabicyclo[*x*.*y*.0]alkane Amino Acids and Congeners by Means of Rh-Catalyzed Cyclohydrocarbonylation

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General Methods: NMR spectra, i.e., ^{1}H, ^{13}C, DEPT, COSY, HMQC, HMBC, ROESY, NOESY, NOE-difference, were recorded on a 300, 400, 500 or 600 MHz NMR spectrometers, which provided all necessary data for the full assignment of each compound. Specific rotations were measured on a polarimeter. Melting points were measured on a capillary melting point apparatus. High-resolution mass spectrometry (HRMS) analyses were conducted at the Mass Spectrometry Laboratory of the University of Illinois at Urbana-Champaign. GC-MS analyses were performed on a GC system equipped with a capillary column (50 m X 0.25 mm, 0.25 μm) and a mass selective detector. LC-MS analyses were carried out an on a liquid chromatograph mass spectrometer. IR spectra were measured on a FT-IR spectrophotometer. TLC analyses were performed on silica gel (230-400 mesh) and were visualized with UV light, iodine chamber, 10% sulfuric acid or 10% PMA solution. Purifications were performed by flash chromatography on silica gel (230-400 mesh).

Materials: Chemicals, reagents and solvents were commercially available. The reagents were used as received. Dichloromethane, pyridine, 1,4-dioxane, acetonitrile, 1,2-dichloroethane, DMSO and methanol were dried before use by distillation over calcium hydride under nitrogen or argon. Ether and THF were dried before use by distillation over sodium-benzophenone ketyl under nitrogen or argon. Toluene, benzene and dimethyl sulfide were dried by distillation over sodium metal under nitrogen or argon before use. Dry DMF was commercially available and used without further purification. A solvent drying and degassing apparatus provided an alternative source of dry toluene, THF, ether, and dichloromethane. The glasses were dried in a 110 ° C oven and allowed to cool to room temperature in a desiccator over calcium sulfate and assembled under inert gas nitrogen or argon atmosphere.

Charactrization data for the unsaturated dipeptide derivatives 1a-k

***N-tert*-Butoxycarbonyl-(*S*)-seryl-(*S*)-allylglycine methyl ester (*S,S*)-1a:**[1] 76% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.38(s, 9H), 2.05 (d, *J* = 6.8 Hz, 1H), 2.42-2.62(m, 2H), 3.61-3.69 (m, 1H), 3.72 (s, 3H), 3.91 (m, 1H), 4.16 (m, 1H), 4.57 (dd, *J* = 12.8, 6.8 Hz, 1H), 5.06 (m, 2H), 5.63 (m, 2H), 7.24 (br, 1H).^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.2, 35.9, 51.9, 52.4, 55.1, 62.7, 80.3, 119.1, 132.0, 155.9, 171.9, 174.2.

***N-tert*-Butoxycarbonyl-(*S*)-seryl-(*R*)-allylglycine methyl ester, (*S,R*)-1a:**[1] 66% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.38(s, 9H), 1.99 (d, *J* = 6.8 Hz, 1H), 2.48(m, 2H), 3.64 (m, 1H), 3.67 (s, 3H),

3.95 (m, 1H), 4.16 (m, 1H), 4.58 (dd, *J* = 12.8, 6.8 Hz, 1H), 5.08 (m, 2H), 5.62 (dddd, *J* = 17.2, 10, 7.2, 7.2 Hz, 1H), 5.73 (d, *J* = 6.0 Hz, 1H), 7.19 (br, 1H).^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.2, 36.0, 51.7, 52.4, 55.5, 62.7, 80.3, 119.2, 131.9, 155.9, 171.1, 172.0.

***N*-*tert*-Butoxycarbonyl-(*S*)-seryl-*O*-benzyl-(*S*)-allylglycinol, (*S*,*S*)-1b:**[2] 85% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.41, (s, 9H), 2.01 (d, *J* = 6.8 Hz, 1H), 2.23-2.38 (m, 2H), 3.43 (dd, *J* = 7.2, 4.8 Hz, 1H), 3.47 (dd, *J* = 7.2, 4.4 Hz, 1H), 3.55-3.60 (m, 1H), 3.99 (d, *J* = 11.0 Hz, 1H), 4.07-4.14 (m, 2H), 4.45 (d, *J* =12.4 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 5.01-5.06 (m, 2H), 5.62 (brs, 1H), 5.70 (dddd, *J* = 17.2, 10.0, 6.8, 6.8 Hz, 1H), 6.86(brs, 1H), 7.26-7.34(m, 5H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.5, 36.2, 48.9, 55.2, 63.1, 70.8, 73.4, 80.6, 118.1, 127.9, 128.0, 128.6, 134.3, 138.1, 156.3, 171.2.

***N'*-*tert*-Butoxycarbonyl-(*R*)-seryl-*O*-benzyl-(*S*)-allylglycinol, (*R*,*S*)-1b:**[3] 81% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.41 (s, 9H), 2.03 (d, *J* = 6.8 Hz, 1H), 2.26-2.39 (m, 2H), 3.42 (dd, *J* = 7.2, 4.4 Hz, 1H), 3.47 (dd, *J* = 7.2, 4.4 Hz, 1H), 3.61 (dd, *J* = 11.6, 4.8 Hz, 1H), 4.01 (d, *J* = 10.8 Hz, 1H), 4.07-4.16 (m, 2H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 5.03-5.09 (m, 2H), 5.62 (d, *J* = 7.2 Hz, 1H), 5.72 (dddd, *J* = 17.2, 10.8, 7.2, 7.2 Hz, 1H), 6.73 (brs, 1H), 7.24-7.35 (m, 5H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.5, 36.2, 48.8, 55.3, 63.3, 70.9, 73.4, 80.7, 118.2, 127.9, 128.0, 128.6, 134.3, 138.1, 156.3, 171.1.

***N*-*tert*-Butoxycarbonyl-(*S*)-homoseryl-(*S*)-allylglycine methyl ester, (*S*,*S*)-1c:**

First, *N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyldimethylsilyl)-(*S*)-homoseryl-(*S*)-allylglycine methyl ester, (*S*,*S*)-**1c'**, was prepared by coupling *N*-tert-butoxycarbonyl-(*S*)-homoserine with methyl (*S*)-allylglycinate hydrochloride under the standard conditions described in the Exprimental Section.

(*S*,*S*)-**1c'**: 272 mg, 90%; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ -0.04 (s, 6H), 0.80 (s, 9H), 1.33 (s, 9H), 1.85(m, 2H), 2.38 (m, 1H), 2.48 (m, 1H), 3.61 (s, 3H), 3.69 (m, 2H), 4.13 (m, 1H), 4.53 (dd, *J* = 13.2; 6.0 Hz, 1H), 5.06 (m, 2H), 5.63 (m, 1H), 5.95 (m, 1H); 6.94 (m, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ -5.7, 18.1, 25.9, 28.3, 33.6, 36.5, 51.8, 52.2, 53.7, 60.7, 79.7, 118.9, 132.3, 155.8, 171.7, 171.74.

Next, to a cooled solution of (*S*,*S*)-**1c'** (263 mg, 0.59 mmol) in pyridine (7.5 mL) and acetonitrile (7.5 mL) in an ice bath, hydrogen fluoride-pyridine (3 mL) was slowly added via a syringe. The reaction was exothermic. Ice bath was removed when the addition was completed. The reaction mixture was stirred at room temperature for 3 h. When the reaction was completed, saturated aqueous $NaHCO_3$ (100 mL) was

slowly added to the mixture. The reaction mixture was extracted with EtOAc (20 mL X 3). The combined organic layer was washed with saturated cupric sulfate solution (20 mL X 3), water (20 mL X 1), brine (20 mL X 1), and dried over $MgSO_4$. Then, the dried solution was concentrated under reduced pressure to give crude product. The crude product was purified by flash column chromatography on silica gel, using EtOAc/*n*-hexane as a eluant, to give (*S*,*S*)-**1c** (158 mg, 80% yield) as colorless liquid: ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.35 (s, 9H), 1.66 (m, 1H), 1.99 (m, 2H); 2.42 (m, 1H), 2.48 (m, 1H), 3.64 (m, 5H), 4.31 (m, 1H), 4.55 (dd, *J* = 12.8; 7.2 Hz, 1H), 5.02 (m, 2H), 5.63 (m, 2H), 7.24 (d, *J* = 7.2 Hz, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.3, 36.2, 36.2, 51.4, 52.0, 52.4, 58.5, 80.2, 119.0, 132.4, 156.5, 172.0, 172.2. MS (FAB) *m/z* calcd for $C_{15}H_{26}N_2O_6$•H^+, 331.1871; found, 331.08.

Methyl β-*tert*-butoxycarbonylamino-*N*-*tert*-butoxycarbonyl-(*S*)-alanyl-(*S*)-allylglycinate, (*S*,*S*-1d):[1] 82% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.45 (s, 9H), 2.44-2.65 (m, 2H), 3.49 (m, 2H), 3.74 (s, 3H), 4.18 (m, 1H), 4.62 (m, 1H), 5.10-5.14 (m, 3H), 5.61-5.75 (m, 2H), 7.11 (bs, 1H). HRMS (FAB) *m/z* calcd for $C_{19}H_{33}N_3O_7$•H^+ 416.2397; found, 416.2396 (Δ = - 0.1 ppm).

***N*-Benzyloxycarbonyl-*S*-trityl-(*R*)-cysteinyl-(*S*)-allylglycine methyl ester, (*R*,*S*)-1e**:[1] 81% yield; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.42 (m, 1H), 2.52 (m, 1H), 2.58 (dd, *J* = 13.0, 5.6 Hz, 1H), 2.74 (dd, *J* = 13.0, 7.6 Hz, 1H), 3.66 (s, 3H), 3.85 (m, 1H), 4.57 (dd, *J* = 13.0, 6.0 Hz, 1H), 5.05 (m, 4H), 5.34 (d, *J* = 7.6 Hz, 1H), 5.61 (m, 1H), 6.58 (d, *J* = 6.4 Hz, 1H), 7.30 (m, 20H).^{13}C-NMR (100 MHz, $CDCl_3$) δ 33.6, 36.1, 51.7, 52.1, 53.7, 66.8, 67.0, 119.0, 126.7, 127.8, 127.9, 127.9, 128.3, 129.4, 131.8, 136.0, 144.2, 155.7, 169.7, 171.3.

***N*-Benzyloxycarbonyl-*S*-trityl-(*S*)-homocysteinyl-(*S*)-allylglycine methyl ester, (*S*,*S*)-1f**:[2] 82% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.60 (m, 1H), 1.75 (m, 1H), 2.29 (m, 2H), 2.26 (m, 1H), 2.25 (m, 1H), 3.69 (s, 3H), 4.22 (ddd, *J* = 8.0; 8.0; 13.5 Hz, 1H); 4.58 (ddd, *J* = 6.6; 6.6; 13.0 Hz, 1H); 5.07 (m, 4H), 5.47 (d, *J* = 8.0 Hz, 1H), 5.63 (m, 1H), 6.80 (d, *J* = 8.0Hz, 1H), 7.20 (m, 20H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.0, 31.8, 36.3, 51.8, 52.3, 54.0, 66.9, 67.0, 119.2, 126.7, 127.9, 128.0, 128.1, 128.5, 129.6, 132.0, 136.3, 144.7, 156.1, 171.1, 171.7.

***N*-*tert*-Butoxycarbonyl-(2*S*,3*R*)-threonyl-(*S*)-allylglycine methyl ester, (*S*,*R*,*S*)-1g**:[3] 92% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.17 (d, *J* = 6.4 Hz, 3H), 1.44 (s, 9H), 1.45 (brs, 1H), 2.44-2.61 (m, 2H), 3.73 (s, 3H), 4.06 (d, *J* = 6.0 Hz, 1H), 4.32 (dddd, *J* = 6.8, 6.8, 6.8, 2.4 Hz, 1H), 4.61 (q, *J* = 6.8 Hz,

1H), 5.09-5.13 (m, 2H), 5.43 (d, *J* = 7.6 Hz, 1H), 5.65 (dddd, *J* = 17.2, 9.6, 7.2, 7.2 Hz, 1H), 7.00 (d, *J* = 6.0 Hz, 1H). ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 18.3, 28.5, 36.4, 52.0, 52.7, 58.0, 67.0, 80.6, 119.6, 132.2, 156.6, 171.6, 0.99.

***N-tert*-Butoxycarbonyl-(2*R*,3*S*)-threonyl-(*S*)-allylglycine methyl ester, (*R*,*S*,*S*)-1g:**[3] 73% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.18 (d, *J* = 6.4 Hz, 3H), 1.44 (s, 9H), 1.45 (brs, 1H), 2.47-2.57 (m, 2H), 3.72 (s, 3H), 4.03 (d, *J* = 7.6 Hz, 1H), 4.34-4.40 (m, 1H), 4.60 (q, *J* = 6.8 Hz, 1H), 5.11-5.16 (m, 2H), 5.43 (d, *J* = 7.5 Hz, 1H), 5.66 (dddd, *J* = 16.8, 9.6, 7.2, 7.2 Hz, 1H), 6.99 (brs, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 18.6, 28.4, 36.2, 51.9, 52.6, 58.9, 67.1, 80.4, 119.5, 132.2, 156.5, 171.5, 172.2.

***N-tert*-Butoxycarbonyl-(2*S*,3*S*)-threonyl-(*S*)-allylglycine methyl ester, (*S*,*S*,*S*)-1g**:[3] 80% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.15 (d, *J* = 6.4 Hz, 3H), 1.34 (s, 9H), 2.37-2.53 (m, 2H), 3.64 (s, 3H), 3.85 (quintet, *J* = 6.0 Hz, 1H), 3.92 (brs, 1H), 4.00-4.06 (m, 1H), 4.53 (ddd, *J* = 7.2, 7.2, 12.8 Hz, 1H), 5.00-5.05 (m, 2H), 5.60 (dddd, *J* = 6.8, 6.8, 10.0, 17.2 Hz, 1H), 5.67 (d, *J* = 7.0 Hz, 1H), 7.20 (d, *J* = 6.4 Hz, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 19.5, 28.3, 35.9, 52.1, 52.5, 58.9, 69.2, 80.1, 119.2, 132.2, 156.1, 171.2, 172.1.

***N-tert*-Butoxycarbonyl-(2*R*,3*R*)-threonyl-(*S*)-allylglycine methyl ester, (*R*,*R*,*S*)-1g:**[3] 65% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.19 (d, *J* = 6.4 Hz, 3H), 1.38 (s, 9H), 2.41-2.57 (m, 2H), 3.68 (s, 3H), 3.86 (brs, 1H), 3.93 (quintet, *J* = 5.6 Hz, 1H), 4.09 (brs, 1H), 4.60 (ddd, *J* = 7.2, 7.2, 12.8 Hz, 1H), 5.05-5.10 (m, 2H), 5.64 (dddd, *J* = 6.8, 6.8, 10.0, 17.2 Hz, 1H), 5.68 (d, *J* = 7.2 Hz, 1H), 7.22 (brs, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 19.6, 28.4, 36.3, 51.9, 52.5, 58.9, 69.1, 80.4, 119.3, 132.3, 156.3, 171.0, 172.0.

***N-tert*-Butoxycarbonyl-(*S*)-seryl-(*S*)-vinylglycine methyl ester, (*S*,*S*)-1h**:[2] 80% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.35 (s, 9H), 3.60-3.70 (m, 1H), 3.67 (s, 3H), 3.81 (brs, 1H), 3.84-3.91 (m, 1H), 4.23 (brs, 1H), 5.03-5.07 (m, 1H), 5.16-5.32 (m, 2H), 5.80-5.89 (m, 2H), 7.50 (br, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.3, 52.8, 54.6, 55.5, 62.8, 80.3, 118.0, 131.6, 156.1, 170.6, 171.1.

***N-tert*-Butoxycarbonyl-(*R*)-seryl-(*S*)-vinylglycine methyl ester, (*R*,*S*)-1h:**[2] 86% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.36 (s, 9H), 3.60-3.70 (m, 2H), 3.67 (s, 3H), 3.89-3.96 (m, 1H), 4.22 (brs,

1H), 5.05-5.08 (m, 1H), 5.17-5.31 (m, 2H), 5.80-5.89(m, 2H), 7.42 (br, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.3, 52.8, 54.7, 55.8, 62.8, 80.5, 118.0, 131.6, 156.2, 170.8, 171.2.

***N*-*tert*-Butoxycarbonyl-(*S*)-seryl-*O*-benzyl-(*R*)-vinylglycinol, (*S,R*)-1i**:[2] 54% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.40 (s, 9H), 3.46 (dd, *J* = 5.2, 9.6 Hz, 1H), 3.48 (dd, *J* = 4.8, 10.0 Hz, 1H), 3.40-3.70 (brs, 1H), 3.62 (m, 1H), 3.94 (d, *J* = 8.8 Hz, 1H), 4.12 (m, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.65 (m, 1H), 5.14 (ddd, *J* = 1.2, 1.2, 10.2 Hz, 1H), 5.22 (ddd, *J* = 1.2, 1.2, 17.2 Hz, 1H), 5.71 (d, *J* = 6.4 Hz, 1H), 5.80 (ddd, *J* = 5.2; 10.8; 16.8 Hz, 1H), 7.04 (d, *J* = 4.8 Hz, 1H), 7.22-7.32 (m, 5H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.4, 51.2, 55.7, 62.9, 71.6, 73.3, 80.5, 116.4, 127.8, 127.9, 128.5, 135.2, 137.8, 156.2, 170.9.

***N*-*tert*-Butoxycarbonyl-(*R*)-seryl-*O*-benzyl-(*R*)-vinylglycinol, (*R,R*)-1i**:[2] 61% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.41 (s, 9H), 3.50 (d, *J* = 4.8 Hz, 2H), 3.62 (m, 2H), 3.96 (d, *J* = 8.8 Hz, 1H), 4.19 (m, 1H), 4.47 (d, *J* = 12.4 Hz, 1H), 4.53 (d, *J* = 12.4 Hz, 1H), 4.65 (m, 1H), 5.13 (d, *J* = 10.2 Hz, 1H), 5.22 (d, *J* = 17.2 Hz, 1H), 5.80 (ddd, *J* = 5.2; 10.4; 16.4 Hz, 2H), 7.14 (d, *J* = 7.2 Hz, 1H), 7.24-7.34 (m, 5H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.4, 51.2, 55.4, 62.9, 71.6, 73.3, 80.4, 116.3, 127.8, 127.9, 128.5, 135.3, 137.8, 156.2, 171.1.

***N*-[(*S*)-2-Aminobut-3-enyl]-(*N'*-*tert*-butoxycarbonyl)-(*S*)-serinamide, (*S,S*)-1j**:[2] ^{1}H-NMR (500 MHz, 25 ^{o}C, $CDCl_3$) δ 1.19 (d, *J* = 7.0 Hz, 3H), 1.41 (s, 9H), 3.01 (brs, 1H), 3.64 (m, 1H), 4.00 (d, *J* = 11 Hz, 1H), 4.12 (brs, 1H), 4.50 (m, 1H), 5.04 (d, *J* = 10.5 Hz, 1H), 5.13 (d, *J* = 17.5 Hz, 1H), 5.68 (d, *J* = 6.8 Hz, 1H), 5.78 (ddd, *J* = 5.0; 10.5; 17.5 Hz, 1H), 6.80 (m, 1H); ^{13}C-NMR (75 MHz, 25 ^{o}C, $CDCl_3$) δ 20.4, 28.5, 47.1, 55.2, 63.0, 80.7, 114.4, 139.2, 156.5, 170.7.

***N*-[(*S*)-2-Aminobut-3-enyl]-(*N'*-*tert*-butoxycarbonyl)-(*R*)-serinamide, (*R,S*)-1j**:[2] ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.19 (d, *J* = 6.9 Hz, 3H), 1.40 (s, 9H), 3.64 (brs, 2H), 4.00 (d, *J* = 8.0 Hz, 1H), 4.11 (m, 1H), 4.50 (m, 1H), 5.02 (d, *J* = 10.8 Hz, 1H), 5.10 (d, *J* = 17.2 Hz, 1H), 5.70 (d, *J* = 8.0 Hz, 1H), 5.78 (ddd, *J* = 4.8; 10.8; 16.8 Hz, 1H), 6.80 (m, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 20.5, 28.5, 47.0, 55.1, 62.9, 80.7, 114.3, 139.2, 156.5, 170.8.

***N*-Allyl-(*N'*-*tert*-butoxycarbonyl)-(*S*)-serinamide, (*S*)-1k**:[4] 69% yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.40 (s, 9H), 3.27 (brs, 1H), 3.58-3.70 (m, 1H), 3.79-3.94 (m, 2H), 4.08 (d, *J* = 10.4 Hz, 1H),

4.14 (brs, 1H), 5.11 (d, *J* = 10.4 Hz, 1H), 5.17 (d, *J* = 17.2 Hz, 1H), 5.62 (brs, 1H), 5.78 (dddd, *J* = 5.6, 5.6, 10.8, 10.8 Hz, 1H), 6.83 (brs, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 28.5, 41.9, 55.0, 63.1, 80.9, 116.5, 133.8, 156.6, 171.6.

Characterization data for (*S,S*)-**2a,** (*S,S*)-**6b,** (*R,S*)-**6b,** (*S*)-**7h** and (*R*)-**7h**

***N-tert*-Butoxycarbonyl-(*S*)-seryl-(*S*)-6-oxonorvaline methyl ester, (*S,S*)-2a:**[2] Colorless oil; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.41 (s, 9H), 1.56-1.73 (m, 3H), 1.82-1.91 (m, 1H), 2.43-2.47 (m, 2H), 3.62-3.66 (m, 1H), 3.71 (s, 3H), 3.70-3.73 (m, 1H), 4.00 (dd, *J* = 11.2, 3.6 Hz, 1H), 4.18 (brs, 1H), 4.52-4.58 (m, 1H), 5.64 (d, *J* = 6.4 Hz, 1H), 7.27 (d, *J* = 1.6 Hz, 1H), 9.70 (t, *J* = 1.2 Hz, 1H); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 17.7, 28.2, 31.2, 42.9, 52.0, 52.6, 55.1, 62.8, 80.4, 156.0, 171.3, 172.4, 201.7.

***N*-[*N-tert*-Butoxycarbonyl-(*R*)-seryl]-(*S*)-2-benzyloxymethyl-5,6-didehydropiperidine, (*R,S*)-6b:**[2] Colorless oil; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.28-1.41 (m, 2H), 1.41 (s, 9H), 1.54-1.61 (m, 1H), 1.69-1.79 (m, 1H), 3.44-3.48 (m, 2H), 3.64 (dd, *J* = 9.2, 3.6 Hz, 1H), 4.01-4.21 (m, 3H), 4.48 (d, *J* = 9.6 Hz, 1H), 4.49-4.61 (m, 1H), 4.54 (d, *J* = 9.6 Hz, 1H), 4.91-5.01 (m, 1H), 5.54 (brs, 1H), 6.66 (brs, 1H), 7.29-7.36 (m, 20H).

***N*-[*N-tert*-Butoxycarbonyl-(*S*)-seryl]-(*S*)-2-benzyloxymethyl-5,6-didehydropiperidine, (*S,S*)-6b:**[2] Colorless oil; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.27-1.41 (m, 2H), 1.41 (s, 9H), 1.53-1.61 (m, 1H), 1.69-1.76 (m, 1H), 3.42-3.46 (m, 2H), 3.66 (dd, *J* = 9.2, 3.6 Hz, 1H), 4.07-4.21 (m, 3H), 4.48 (d, *J* = 9.6 Hz, 1H), 4.49-4.61 (m, 1H), 4.54 (d, *J* = 9.6 Hz, 1H), 4.91-5.01 (m, 1H), 5.57 (brs, 1H), 6.65 (brs, 1H), 7.29-7.36 (m, 20H).

***N-tert*-Butoxylcarbonyl-(*S*)-seryl-2(*R/S*)-3(*R/S*)-4-oxovaline methyl ester, (*S*)-7h:**[2] Colorless oil, 21 % yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 0.95-1.20 (m, 3H), 1.39-1.51 (m, 9H), 2.92-3.28 (m, 1H), 3.60-3.80 (m, 4H), 4.00-4.62 (m, 3H), 4.92-5.10 (m, 1H), 5.56-5.74 (m, 1H), 7.26-7.46 (m, 1H), 9.55-9.72 (m, 1H); ^{13}C NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 6-8, 28-29, 47-48, 51-52, 53-54, 55-56, 62-63, 80-81, 155-156, 170-171, 171-172, 200-202.

***N-tert*-Butoxylcarbonyl-(*R*)-seryl-2(*R/S*)-3(*R/S*)-4-oxovaline methyl ester, (*R*)-7h:**[2] Colorless oil, 23 % yield; ^{1}H-NMR (400 MHz, 25 ^{o}C, $CDCl_3$) δ 1.04-1.26 (m, 3H), 1.40-1.51 (m, 9H), 2.20-2.80 (m, 1H), 2.92-3.26 (m, 1H), 3.62-3.80 (m, 4H), 3.98-4.24 (m, 2H), 4.90-5.12 (m, 1H), 5.55-5.72 (m, 1H), 7.24-7.48 (m, 1H), 9.58-9.74 (m, 1H); ^{13}C NMR (100 MHz, 25 ^{o}C, $CDCl_3$) δ 9-10, 28-29, 48-49, 52-53, 53-54, 55-57, 62-64, 80-81, 155-157, 170-171, 171-172, 200-202.

Full assignments of NMR data for 1-azabicyclic products 5a-k and determination of stereochemistry by NMR spectroscopy

The structure determination of **5a-k** and assignment of ^{1}H and ^{13}C were performed by using various NMR techniques, including ^{1}H, ^{13}C, DEPT, H-H COSY, HMQC, ROESY, and nOe difference spectroscopy by double pulse field gradient spin echo (DPFGSE) or CYCLENOE. Only critical nOe relationships are indicated by arrows in the figures shown below. A detailed description for these NMR advanced NMR spectroscopic analyses is provided for the case of (3*R*,4*S*,6*R*,10*S*)-**5g.** All measurements were carried out in $CDCl_3$ at 25^{o}C unless otherwise noted.

(3*S*,6*S*,10*S*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-5-oxa-2-oxobicyclo[4.4.0]-decane, (3*S*,6*S*,10*S*)-5a:

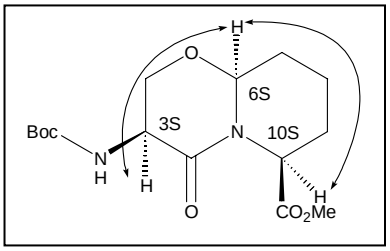


Table 1. ^{1}H and ^{13}C NMR data for (3*S*,6*S*,10*S*)-**5a**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	168.4	---	---
3	49.8	4.39-4.44, m	---
4	67.0	4.16, dd 10.2; 6.2	3.75, dd 10.2; 7.0
6	82.7	4.93, dd 8.4; 4.4	
7	28.0	1.84-2.01, m	1.65-1.79, m
8	16.5	1.65-1.79, m	1.47-1.57, m
9	24.4	1.84-2.01, m	1.84-2.01, m

10	54.0	4.39-4.44, m	---
11	171.5	---	---
$CO_2\underline{C}H_3$	52.4	3.68, s	---
N-H	---	5.36, d 6.0	---
O(O)$\underline{C}$N	155.4	---	---
$\underline{C}(CH_3)_3$	80.0	---	---
$C(\underline{C}H_3)_3$	28.2	1.38, s	---

(3*S*,6*R*,10*R*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-5-oxa-2-oxobicyclo[4.4.0]-decane, (3*S*,6*R*,10*R*)-5a:

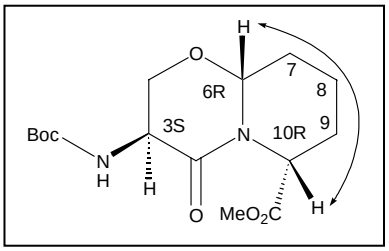


Table 2. ^{1}H and ^{13}C NMR data for (3*S*,6*R*,10*S*)-**5a**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	166.5	---	---
3	50.9	4.25, brs	---
4	68.2	3.98-4.02, m	3.98-4.02, m
6	85.1	---	4.90, dd 10.2; 3.4
7	31.4	1.39-1.49, m	1.92-1.99, m
8	19.1	1.31-1.41, m	1.71-1.77, m
9	26.1	1.57-1.67, m	2.16-2.23, m
10	52.5	---	5.33, d 5.2
11	171.1	---	---
$CO_2\underline{C}H_3$	52.2	3.69, s	---
N-H	---	5.23, d 7.2	---
O(O)$\underline{C}$N	155.2	---	---
$\underline{C}(CH_3)_3$	80.1	---	---
$C(\underline{C}H_3)_3$	28.3	1.40, s	---

(3*S*,6*R*,10*S*)-1-Aza-10-benyloxymethyl-3-*tert*-butoxycarbonylamino-5-oxa-2-oxobicyclo[4.4.0]-decane, (3*S*,6*R*,10*S*)-5b:

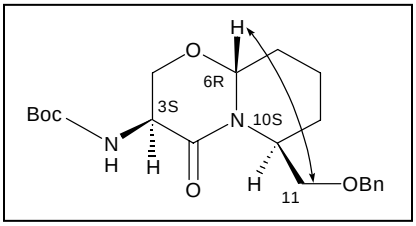


Table 3. ^{1}H and ^{13}C NMR data for (3*S*,6*R*,10*S*)-**5b**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	167.1	-----	-----
3	48.9	4.14, quintet, 6.0	-----
4	67.0	4.37-4.43, m	3.45-3.46, m.
6	85.7	-----	4.80, dd, 10.8; 3.0
7	32.5	1.39-1.45, m	1.93, dt, 12.6, 1.8, 1.8
8	18.3	1.66-1.68, m	1.66-1.68, m
9	25.4	1.54-1.60, m	1.84, d, 13.8
10	50.5	4.86, quartet, 6.0	-----
11	69.2	3.55, t, 7.8 and 3.48-3.51, m	
NH	-----	5.24, br s	-----
O<u>C</u>(O)-N	156.1	-----	-----
<u>C</u>$(CH_3)_3$	80.1	-----	-----
C(<u>C</u>$H_3)_3$	28.5	1.42, s	-----
O-CH_2-Ph	73.2	4.50, s	-----
ipso-C_6H_5	138.4	-------	-----
ortho-C_6H_5	127.8	7.25-7.34, m	-----
meta-C_6H_5	128.6	7.25-7.34, m	-----
para-C_6H_5	127.9	7.25-7.34, m	-----

(3*R*,6*R*,10*S*)-1-Aza-10-benyloxymethyl-3-*tert*-butoxycarbonylamino-5-oxa-2-oxobicyclo[4.4.0]-decane, (3*R*,6*R*,10*S*)-5b:

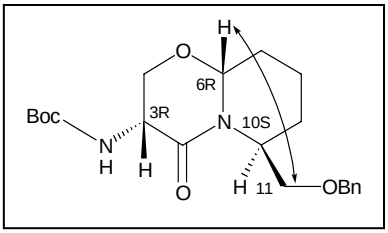


Table 4. ^{1}H and ^{13}C NMR data for (3*R*,6*R*,10*S*)-**5b**

Position	^{13}C, δ, ppm	$^{1}H(\alpha)$, δ, ppm, Hz	$^{1}H(\beta)$, δ, ppm, Hz
2	165.7	-----	-----
3	48.4	-----	4.18, br, s
4	67.5	3.95, d, 12.0	3.86, dd, 12.0, 3.6
6	84.7	-----	4.79, dd, 10.8; 3.0
7	32.1	1.42-1.49, m	1.92, dd, 12.6, 3.0
8	18.5	1.66-1.72, m	1.66-1.72, m
9	25.5	1.54-1.60, m	1.80, d, 13.8
10	51.2	4.98, quartet, 6.0	-----
11	69.6	3.55, t, 7.8 and 3.48-3.51, m	
NH	-----	5.27, br s	-----
O<u>C</u>(O)-N	155.7	-----	-----
<u>C</u>$(CH_3)_3$	80.2	-----	-----
C(<u>C</u>$H_3)_3$	28.5	1.42, s	-----
O-CH_2-Ph	73.2	4.48, and 4.46, d, 12.0	-----
ipso-C_6H_5	138.2	-------	-----
ortho-C_6H_5	127.8	7.25-7.33, m	-----
meta-C_6H_5	128.6	7.25-7.33, m	-----
para-C_6H_5	127.9	7.25-7.33, m	-----

(3*S*,7*S*,11*S*)-1-Aza-3-*tert*-butoxycarbonylamino-11-methoxycarbonyl-2-oxo-6-oxabicyclo[5.4.0]undecane, (3*S*,7*S*,11*S*)-5c:

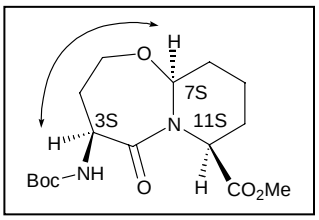


Table 5. ^{1}H and ^{13}C NMR data for (3*S*,7*S*,11*S*)-**5c,** 25 ^{o}C in d_6-benzene.

Position	^{13}C, δ, ppm	$^{1}H(\alpha)$, δ, ppm, Hz	$^{1}H(\beta)$, δ, ppm, Hz
2	175.1	-----	-----
3	53.5	4.73, ddd, 2.0; 6.3; 11.5	-----
4	33.8	1.80, dd, 14.0; 2.0	2.09-2.17, m

5	70.4	3.50, ddd, 1.5; 12.0; 12.0	3.77, ddd, 3.5; 7.0; 12.0
7	82.9	4.36, brs	-----
8	30.9	1.45-1.55, m	1.06, dddd, 4.5; 4.5; 12.5; 12.5
9	15.9	1.35-1.45, m	0.95, ddddd, 4.8; 4.8; 4.8; 9.6; 13.2
10	25.6	2.09-2.17, m	1.17, dddd, 4.0; 7.0; 13.0; 15.0
11	52.8	5.15, dd, 7.5; 2.0	-----
NH	-----	6.20, d, 5.5	-----
$\underline{C}O_2CH_3$	171.9	------	-----
$CO_2\underline{C}H_3$	52.1	3.27, s	-----
O$\underline{C}$(O)-N	155.7	-----	-----
$\underline{C}(CH_3)_3$	79.4	-----	-----
$C(\underline{C}H_3)_3$	28.8	1.46, s	-----

(3*S*,6*S*,10*S*)-1,5-Diaza-3-*tert*-butoxycarbonylamino-5-*tert*-butoxycarbonyl-10-methoxycarbonyl-2-oxobicyclo[4.4.0]decane, (3*S*,6*S*,10*S*)-5d (see the X-ray crystal structure for the determination of stereochemistry)**:**

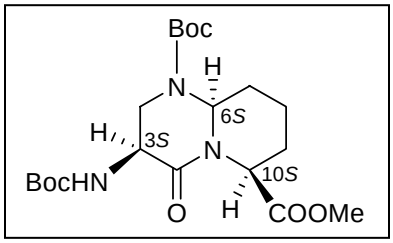


Table 6. ^{1}H and ^{13}C NMR data for (3*S*,6*S*,10*S*)-**5d**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	167.8	---	---
3	50.3	4.01, ddd, 10.8, 4.8, 4.8	---
4	68.5	3.03, t, 12.0	3.74, m
6	81.8	5.30, brs	
7	41.7	1.65-2.02, m	1.65-2.02, m
8	21.5	1.65-2.02, m	1.65-2.02, m
9	29.6	1.65-2.02, m	1.65-2.02, m
10	59.8	4.06, brs	---
11	169.5	---	---

$CO_2\underline{C}H_3$	52.2	3.71, s	---
N-H	---	5.47, brs	---
O(O)$\underline{C}$N	155.4, 153.2	---	---
$\underline{C}(CH_3)_3$	79.8 (2C)	---	---
$C(\underline{C}H_3)_3$	28.3, 24.5	1.41, 1.49	---

(3*R*,6*S*,10*S*)-1-Aza-3-benzyloxycarbonylamino-10-methoxycarbonyl-2-oxo-6-thiabicyclo[4.4.0]-decane, (3*R*,6*S*,10*S*)-5e:

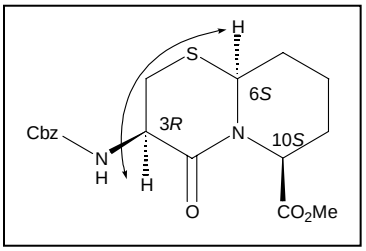


Table 7. ^{1}H and ^{13}C NMR data for (3*R*,6*S*,10*S*)-**5e**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	170.9	-----	-----
3	51.5	4.69, ddd, 12.0, 6.0, 6.0	-----
4	29.0	2.69, dd, 12.0, 10.5	3.55, dd, 10.5, 6.0
6	53.1	5.04-5.14, m	-----
7	27.8	1.94-2.04, m	1.70-1.80, m
8	17.2	1.62-1.82, m	1.50-1.60, m
9	24.6	2.16-2.26, m	1.84-1.90, m
10	53.5	4.88, dd, 7.2, 3.6	-----
NH	-----	6.13, d, 6.0	-----
$\underline{C}O_2CH_3$	171.5	------	-----
$CO_2\underline{C}H_3$	52.4	3.70, s	-----
O$\underline{C}$(O)-N	155.5	-----	-----
Ph-$\underline{C}H_2$	66.9	5.09, s, 2H	-----
C_6H_5, *ortho*	127.9	7.25-7.35, m	-----
C_6H_5, *meta*	128.4	7.25-7.35, m	-----
C_6H_5, *para*	128.0	7.25-7.35, m	-----
C_6H_5, *ipso*	136.2	-----	-----

(3*S*,7*S*,11*S*)-1-Aza-3-benzyloxycarbonylamino-11-methoxycarbonyl-2-oxo-6-thiabicyclo[5.4.0]-undecane, (3*S*,7*S*,11*S*)-5f:

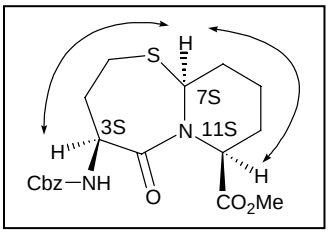


Table 8. ^{1}H and ^{13}C NMR data for (3*S*,7*S*,11*S*)-**5f**, $CDCl_3$, 50 ^{o}C for ^{1}H-NMR.

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	168.2	-----	-----
3	58.1	5.02, d, 6.5	-----
4	36.8	2.05-2.25, m	2.05-2.25, m
5	20.3	2.61-2.70[a], m	2.50-2.58[a], m
7	69.8	5.10-5.20, m	-----
8	32.8	2.38-2.46[b], m	1.14-1.22[b], m
9	19.4	1.76-1.84, m	1.50-1.60, m
10	26.5	1.55-1.65, m	2.05-2.25, m
11	51.4	4.37, dd, 5.0; 5.0	-----
NH	-----	5.15-5.25, m	-----
$\underline{C}O_2CH_3$	170.6	------	-----
$CO_2\underline{C}H_3$	52.9	3.77, s	-----
O$\underline{C}$(O)-N	154.7	-----	-----
Ph-$\underline{C}H_2$	67.9	5.23, d 12.5; 5.19 d, 12.5	-----
C_6H_5, *ortho*	128.4	7.25-7.35, m	-----
C_6H_5, *meta*	128.7	7.25-7.35, m	-----
C_6H_5, *para*	128.89	7.25-7.35, m	-----
C_6H_5, *ipso*	135.92	-----	-----

a, b: interchangeable

(3*S*,4*R*,6*S*,10*S*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-4-methyl-5-oxa-2-oxobicyclo[4.4.0]decane, (3*S*,4*R*,6*S*,10*S*)-5g:

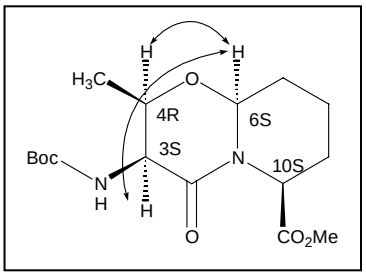


Table 9. ^{1}H and ^{13}C NMR data for (3*S*,4*R*,6*S*,10*S*)-**5g**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	168.1	---	---
3	53.4	4.45, dd 8.0, 5.0	---
4	72.6	4.27, dq 6.0, 5.0	---
6	82.7	4.92, dd 10; 4.5	---
7	28.4	1.95-2.00, m	1.66-1.72, m
8	17.0	1.74-1.81, m	1.52-1.58, m
9	24.7	1.95-2.00, m	1.97-2.03, m
10	53.8	4.41, t, 7.0	---
11	171.7	---	---
$CO_2\underline{C}H_3$	52.4	3.72, s	---
4-CH_3	16.5	---	1.21, d 6.0
N-H	---	5.25, d 8.0	---
O(O)$\underline{C}$-N	155.6	---	---
$\underline{C}(CH_3)_3$	80.0	---	---
$C(\underline{C}H_3)_3$	28.3	1.44, s	---

(3*S*,4*S*,6*S*,10*S*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-4-methyl-5-oxa-2-oxobicyclo[4.4.0]decane, (3*S*,4*S*,6*S*,10*S*)-5g:

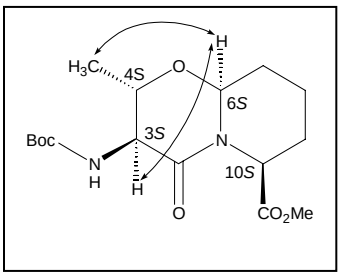


Table 10. ^{1}H and ^{13}C NMR data for (3*S*,4*S*,6*S*,10*S*)-**5g**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	170.2	---	---
3	55.1	4.31, t, 8.5	---
4	72.5	---	3.78,qd, 6.0,10.0
6	79.1	5.12, dd, 5.5, 7.0	---
7	28.3	1.85-1.94, m	1.67-1.78, m
8	16.7	1.46-1.53, m	1.67-1.78, m
9	24.7	1.85-1.94, m	1.99-2.06, m
10	52.5	4.48, t, 6.0	---
11	171.8	---	---
$CO_2\underline{C}H_3$	52.5	3.70, s	---
4-CH_3	19.2	1.34, d, 5.5	---
N-H	---	5.15, d 6.5	---
O(O)$\underline{C}$-N	156.2	---	---
$\underline{C}(CH_3)_3$	80.1	---	---
$C(\underline{C}H_3)_3$	28.3	1.41, s	---

(3*S*,4*S*,6*R*,10*S*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-4-methyl-5-oxa-2-oxobicyclo[4.4.0]decane, (3*S*,4*S*,6*R*,10*S*)-5g:

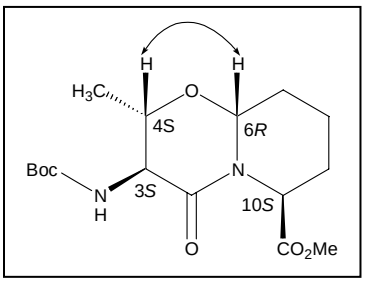


Table 11. ^{1}H and ^{13}C NMR data for (3*S*,4*S*,6*R*,10*S*)-**5g**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	169.1	---	---
3	56.1	4.04-4.11, m	---
4	74.7	---	3.77,dddd, 6.0,6.0,6.0,10.0
6	85.4	---	4.98, dd, 3.0, 11.0

7	31.8	1.39-1.47, m	1.94,dddd, 13.0,10.0,3.5,1.5
8	19.5	1.75,qnt/d, 3.0, 13.0	1.30-1.36, m
9	26.3	2.19,qnt/d, 1.5, 14.0,	1.65,dddd, 13.5,13.5,6.5,4.0
10	53.1	5.18, d, 6.0	---
11	171.6	---	---
$CO_2\underline{C}H_3$	52.6	3.70, s	---
4-CH_3	19.1	1.33, d, 6.0	---
N-H	---	4.87, brs	---
O(O)$\underline{C}$-N	156.6	---	---
$\underline{C}(CH_3)_3$	80.1	---	---
$C(\underline{C}H_3)_3$	28.5	1.42, s	---

(3*R*,4*R*,6*R*,10*S*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-4-methyl-5-oxa-2-oxo-bicyclo[4.4.0]decane, (3*R*,4*R*,6*R*,10*S*)-5g:

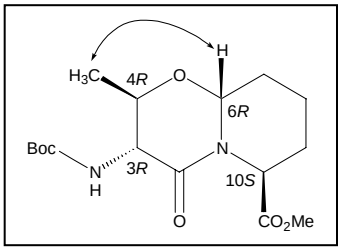


Table 12. ^{1}H and ^{13}C NMR data for (3*R*,4*R*,6*R*,10*S*)-**5g**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	167.0	---	---
3	55.6	---	4.01-4.08, m
4	71.4	4.12, quintet, 6.0	---
6	80.7	---	5.08, dd, 3.0, 10.5
7	31.3	1.59, qd, 13.0; 3.0	1.90-1.94, m
8	19.7	1.82-1.86, m	1.43-1.50, m
9	26.2	2.23-2.26, m	1.66,dddd, 14.0,14.0,6.0,4.0
10	52.6	5.43, d, 6.0	---
11	171.3	---	---
$CO_2\underline{C}H_3$	52.6	3.75, s	---
4-CH_3	17.1	---	1.43, d, 7.0

N-H	------	5.17, d, 7.0	---
O(O)<u>C</u>-N	155.8	------	---
<u>C</u>$(CH_3)_3$	80.1	------	---
C(<u>C</u>$H_3)_3$	28.4	1.46, s	---

(3*R*,4*S*,6*S*,10*S*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-4-methyl-5-oxa-2-oxobicyclo[4.4.0]decane, (3*R*,4*S*,6*S*,10*S*)-5g:

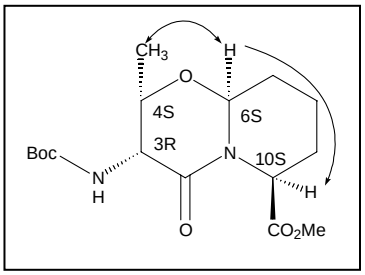
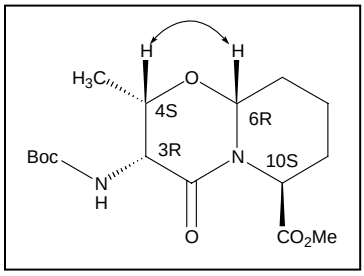


Table 13. ^{1}H and ^{13}C NMR data for (3*R*,4*S*,6*S*,10*S*)-**5g**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	169.3	---	---
3	54.2	---	4.46, brs
4	70.5	---	4.71-4.78, m
6	81.3	4.72, dd, 3.0, 11.0	---
7	30.5	1.83-1.91, m	1.67-1.77, m
8	20.0	1.46-1.55, m	1.83-1.91, m
9	27.5	1.67-1.77, m	1.90-1.97, m
10	56.7	5.34, dd , 11.0, 4.0	---
11	171.5	---	---
CO_2<u>C</u>H_3	52.5	3.72, s	---
4-CH_3	12.9	1.18, d 7.0	
N-H	---	5.45, brs	---
O(O)<u>C</u>-N	155.8	---	---
<u>C</u>$(CH_3)_3$	80.1	---	---
C(<u>C</u>$H_3)_3$	28.5	1.40, s	---

(3*R*,4*S*,6*R*,10*S*)-1-Aza-3-*tert*-butoxycarbonylamino-10-methoxycarbonyl-4-methyl-5-oxa-2-oxobicyclo[4.4.0]decane, (3*R*,4*S*,6*R*,10*S*)-5g:



The full structure determination of (3*R*,4*S*,6*R*,10*S*)-**5g** was carried out using advanced NMR techniques. HMQC experiment afforded the direct proton-carbon connectivity, which helped to distinguished H-6 and H-10 because the chemical shift of C-6 should be more downfield than that of C-10. H-H-COSY clearly indicated two independent coupling systems, which were used to identify H-3, H-4, H-6 H-10, NH. It should be noted that the chemical shift of H-10 (δ 5.34) was quite large (in downfield) beyond the normal range. It should be attributed to the magnetic anisotropy effect from the 2-oxo group. Double pulse field gradient spin echo transient NOE experiment, a kind of NOE difference technique, provided the sensitive information about the spatial arrangement. Irradiation of the δ 4.95 peak resulted in the enhancement of H-4 and two protons, which were assigned to H-7β and H-8β, whereas irradiation of H-4 enhanced only H-6. Irradiation of the δ 5.34 peak only gave a week enhancement on H-9α. These results have provided the strong supporting evidence that the angular proton, H-6, is *cis* to the 10-methoxycarbonyl group.

Table 14. ^{1}H and ^{13}C NMR data for (3*R*,4*S*,6*R*,10*S*)-**5g**

No	^{13}C δ, ppm	^{1}H-NMR, ppm, α	^{1}H-NMR, ppm, β
2	167.2	---	---
3	54.3	---	4.21, d, 10.0
4	73.6	---	3.96-4.02, m
6	85.1	---	4.87, d, 6.0
7	31.8	1.27-1.33, m	1.88-1.94, m
8	19.4	1.32-1.40, m	1.66-1.72, m
9	26.3	1.54-1.60, m	2.14-2.18, m
10	52.1	5.24, d, 5.0	---
11	171.3	---	---
$CO_2\underline{C}H_3$	52.6	3.64, s	---
4-CH_3	15.8	1.15, d, 6.0	---
N-H	------	4.97, d, 10.0	---
O(O)$\underline{C}$-N	155.8	---	---
$\underline{C}(CH_3)_3$	80.1	---	---

$C(\underline{C}H_3)_3$	28.4	1.36, s	---

(3*S*,6*S*,9*R*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methoxycarbonyl-5-oxa-2-oxobicyclo[4.3.0]-nonane, (3*S*,6*S*,9*R*)-5h (see X-ray crystal structure as well)**:**

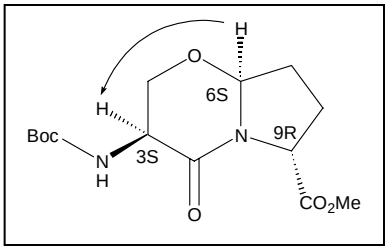


Table 15. ^{1}H and ^{13}C NMR data for (3*S*,6*S*,9*R*)-**5h**

Position	^{13}C, δ, ppm	$^{1}H(\alpha)$, δ, ppm, Hz	$^{1}H(\beta)$, δ, ppm, Hz
2	166.8	---	---
3	49.3	4.41-4.46, m	---
4	68.9	4.36, t, 10.0	3.64, dd, 10.0, 7.0
6	87.6	5.21, dd, 4.5, 5.5	---
7	31.7	2.23-2.33, m, [a]	1.88-1.98, m [a]
8	26.3	2.23-2.33, m [b]	1.88-1.98, m [b]
9	58.2	---	4.72, dd, 5.0, 8.0
10	171.6	---	---
$CO_2\underline{C}H_3$	52.8	3.70, s	---
NH	-----	5.49, brs	---
$O\underline{C}(O)$-N	155.9	---	---
$\underline{C}(CH_3)_3$	80.4	---	---
$C(\underline{C}H_3)_3$	28.5	1.41, s	---

a,b: interchangeable

(3*S*,6*S*,9*S*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methoxycarbonyl-5-oxa-2-oxobicyclo[4.3.0]-nonane, (3*S*,6*S*,9*S*)-5h:

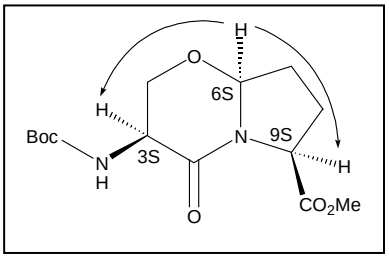


Table 16. ^{1}H and ^{13}C NMR data for (3*S*,6*S*,9*S*)-**5h**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	166.8	---	---
3	49.4	4.32-4.37, m	---
4	69.3	4.29, dd, 9.0, 8.0	3.81, dd, 9.0, 6.5
6	88.0	5.17, dd, 6.0, 7.0	---
7	30.9	2.23-2.28, m	1.93-2.01, m
8	26.46	2.06-2.17, m	2.04-2.12, m
9	57.9	4.40, dd, 8.0,1.0	---
10	171.3	---	---
$CO_2\underline{C}H_3$	52.7	3.70, s	---
NH	-----	5.49, brs	---
O$\underline{C}$(O)-N	156.0	---	---
$\underline{C}(CH_3)_3$	80.3	---	---
$C(\underline{C}H_3)_3$	28.4	1.39, s	---

(3*R*,6*R*,9*S*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methoxycarbonyl-5-oxa-2-oxobicyclo[4.3.0]-nonane, (3*R*,6*R*,9*S*)-5h (see X-ray crystal structure as well):

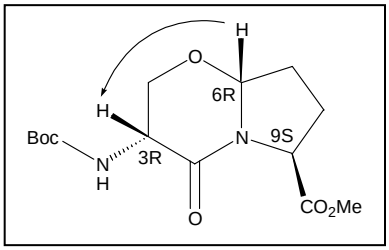


Table 17. ^{1}H and ^{13}C NMR data for (3*R*,6*R*,9*S*)-**5h**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	166.8	---	---
3	49.3	---	4.41-4.46, m
4	68.9	4.36, t, 10	3.64, dd, 10.0, 7.0
6	87.6	---	5.21, dd, 4.5, 5.5
7	31.7	2.23-2.33, m, [a]	1.88-1.98, m [a]
8	26.3	2.23-2.33, m, [b]	1.88-1.98, m [b]
9	58.2	4.72, dd, 5.0, 8.0	---
10	171.6	---	---

$CO_2\underline{C}H_3$	52.8	3.70, s	---
NH	-----	5.49, brs	---
O$\underline{C}$(O)-N	155.9	---	---
$\underline{C}(CH_3)_3$	80.4	---	---
$C(\underline{C}H_3)_3$	28.5	1.41, s	---

a,b: interchangeable

(3*R*,6*R*,9*R*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methoxycarbonyl-5-oxa-2-oxobicyclo[4.3.0]-nonane, (3*R*,6*R*,9*R*)-5h:

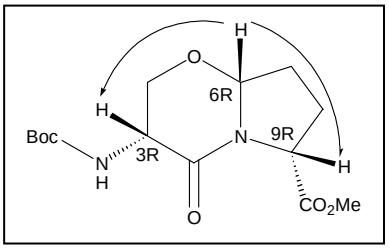


Table 18. ^{1}H and ^{13}C NMR data for (3*R*,6*R*,9*R*)-**5h**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	166.8	---	---
3	49.4	---	4.32-4.37, m
4	69.3	4.29, dd, 9.0, 8.0	3.81, dd, 9.0, 6.5
6	88.0	---	5.17, dd, 6.0, 7.0
7	30.9	1.93-2.01, m	2.23-2.28, m
8	26.5	2.04-2.12, m	2.06-2.17, m
9	57.9	---	4.40, dd, 8.0,1.0
10	171.3	---	---
$CO_2\underline{C}H_3$	52.7	3.70, s	---
NH	-----	5.49, brs	---
O$\underline{C}$(O)-N	156.0	---	---
$\underline{C}(CH_3)_3$	80.3	---	---
$C(\underline{C}H_3)_3$	28.4	1.39, s	---

(3*S*,6*S*,9*R*)-1-Aza-9-benyloxymethyl-3-*tert*-butoxycarbonylamino-5-oxa-2-oxobicyclo[4.3.0]nonane, (3*S*,6*S*,9*R*)-5i:

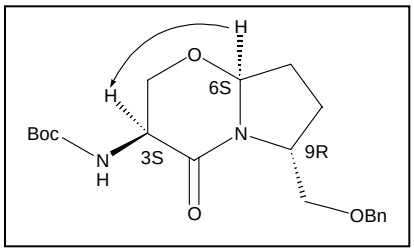


Table 19. ^{1}H and ^{13}C NMR data for (3*S*,6*S*,9*R*)-**5i**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	166.8	-----	-----
3	49.5	4.31-4.38, m	-----
4	68.7	4.30, t, 8.0	3.61, dd, 9.5; 6.0
6	87.9	5.06, dd, 3.5; 6.0	-----
7	31.8	2.27-2.34, m	1.79-1.85, m
8	24.6	1.83-1.91, m	2.02-2.10, m
9	57.3	-----	4.38-4.43, m
10	71.0	3.56, dd, 9.5; 5.0 and 3.52, dd, 9.5; 3.0	
NH	-----	5.45, brs	-----
O<u>C</u>(O)-N	156.1	-----	-----
<u>C</u>$(CH_3)_3$	80.4	-----	-----
C(<u>C</u>$H_3)_3$	28.5	1.43, s	-----
O-CH_2-Ph	73.5	4.49, d, 12.0; 4.46, d, 12.0	-----
Ipso-C_6H_5	138.4	-------	-----
ortho-C_6H_5	127.8	7.24-7.29, m	-----
meta-C_6H_5	128.6	7.30-7.34, m	-----
Para-C_6H_5	127.9	7.24-7.29, m	-----

(3*R*,6*R*,9*R*)-1-Aza-9-benyloxymethyl-3-*tert*-butoxycarbonylamino-5-oxa-2-oxobicyclo[4.3.0]-nonane, (3*R*,6*R*,9*R*)-5i:

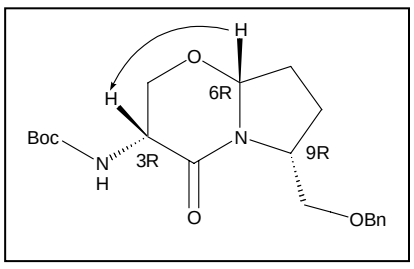


Table 20. ^{1}H and ^{13}C NMR data for (3*R*,6*R*,9*R*)-**5i**

Position	^{13}C, δ, ppm	$^{1}H(\alpha)$, δ, ppm, Hz	$^{1}H(\beta)$, δ, ppm, Hz
2	166.6	---	---
3	49.4	---	4.36-4.44, m
4	68.4	3.58, t, 8.5	4.36-4.44, m
6	87.2	---	5.16, t; 6.5
7	30.6	1.98-2.07, m	2.21, quintet, 6.0
8	25.5	2.13, dd, 12.0, 1.5	1.94, dddd, 12.0,12.0,7.0,7.0
9	56.7	-----	4.38-4.43, m
10	68.6	3.56, dd, 9.5; 5.0 and 3.52, dd, 9.5; 3.0	
NH	-----	5.45, brs	-----
O<u>C</u>(O)-N	156.0	-----	-----
<u>C</u>$(CH_3)_3$	80.3	-----	-----
C(<u>C</u>$H_3)_3$	28.5	1.43, s	-----
O-CH_2-Ph	73.5	4.49, d, 12.0; 4.46, d, 12.0	-----
ipso-C_6H_5	138.4	-------	-----
ortho-C_6H_5	127.7	7.24-7.36, m	-----
meta-C_6H_5	128.6	7.24-7.36, m	-----
para-C_6H_5	127.8	7.24-7.36, m	-----

(3*R*,6*S*,9*R*)-1-Aza-9-benyloxymethyl-3-*tert*-butoxycarbonylamino-5-oxa-2-oxobicyclo[4.3.0]nonane, (3*R*,6*S*,9*R*)-5i:

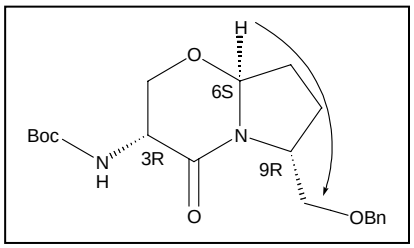


Table 21. ^{1}H and ^{13}C NMR data for (3*R*,6*S*,9*R*)-**5i**

Position	^{13}C, δ, ppm	$^{1}H(\alpha)$, δ, ppm, Hz	$^{1}H(\beta)$, δ, ppm, Hz
2	166.7	---	---
3	49.9	---	4.04, brs
4	69.2	3.64, t, 10.8	4.43, brs

6	90.1	5.03, dd; 8.4, 6.5	---
7	31.4	2.17-2.21, m	1.66-1.73, m
8	22.7	1.84-1.90, m	1.99-2.04, m
9	56.0	---	4.27, brs
10	70.7	3.74, dd, 9.6; 4.2 and	3.53, dd, 9.6; 2.4
NH	-----	5.11, d, 6.0	---
O<u>C</u>(O)-N	156.1	---	---
<u>C</u>$(CH_3)_3$	80.2	---	---
C(<u>C</u>$H_3)_3$	28.5	1.41, s	---
O-CH_2-Ph	73.4	4.49, d, 12.6; 4.46, d, 12.0	---
ipso-C_6H_5	138.5	-------	---
ortho-C_6H_5	127.8	7.24-7.36, m	---
meta-C_6H_5	128.6	7.24-7.36, m	---
para-C_6H_5	127.7	7.24-7.36, m	---

(3*S*,6*S*,9*S*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methyl-5-oxa-2-oxobicyclo[4.3.0]nonane, (3*S*,6*S*,9*S*)-5j (see X-ray crystal structure as well)**:**

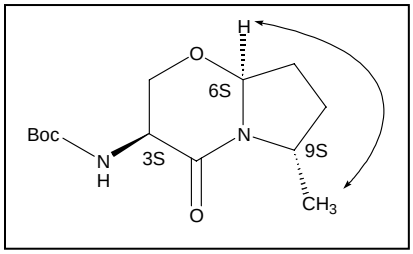


Table 22. ^{1}H and ^{13}C NMR data for (3*S*,6*S*,9*S*)-**5j**

Position	^{13}C, δ, ppm	$^{1}H(\alpha)$, δ, ppm, Hz	$^{1}H(\beta)$, δ, ppm, Hz
2	166.6	---	---
3	49.5	4.30, m	---
4	68.9	4.30, m	3.61, dd, 9.0; 6.0
6	87.4	5.05, dd, 5.5; 5.0	---
7	31.2	2.22, dddd, 6.5,7.0,7.0, 13.5	1.80, dddd, 4.5,7.5,7.5,15.0
8	29.4	1.44, m	2.10, dddd, 7.5,7.5,7.5, 14.0
9	53.7	---	4.23, sextet, 6.5Hz
10	20.7	1.21, d, 6.0 Hz	---

NH	-----	5.50, brs	---
O<u>C</u>(O)-N	156.1	---	---
<u>C</u>$(CH_3)_3$	80.2	---	---
C(<u>C</u>$H_3)_3$	28.5	1.40, s	---

(3*R*,6*R*,9*S*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methyl-5-oxa-2-oxobicyclo[4.3.0]nonane, (3*R*,6*R*,9*S*)-5j:

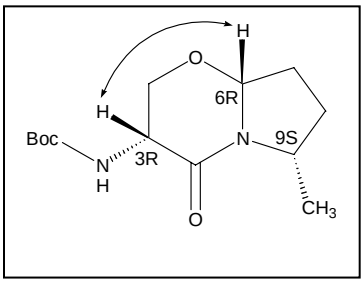


Table 23. ^{1}H and ^{13}C NMR data for (3*R*,6*R*,9*S*)-**5j**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	166.2	---	---
3	49.3	---	4.32, q, 7.8
4	68.5	3.54, t, 9.0	4.40, t, 9.0
6	87.2	---	5.10, t, 6.3
7	30.3	1.92-2.01, m	2.19-2.22, m
8	29.5	1.65-1.70, m	1.92-2.01, m
9	53.2	---	4.09, quintet, 6.6
10	19.2	1.31, d, 6.6 Hz	---
NH	-----	5.49, brs	---
O<u>C</u>(O)-N	156.1	---	---
<u>C</u>$(CH_3)_3$	80.3	---	---
C(<u>C</u>$H_3)_3$	28.5	1.41, s	---

(3*R*,6*S*,9*S*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methyl-5-oxa-2-oxobicyclo[4.3.0]nonane, (3*R*,6*S*,9*S*)-5j:

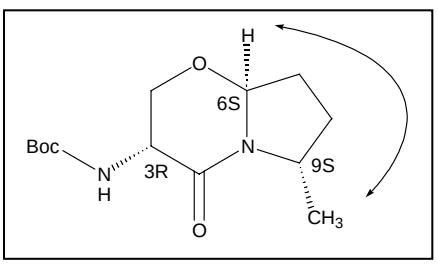


Table 24. ^{1}H and ^{13}C NMR data for (3*R*,6*S*,9*S*)-**5j**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	165.7	---	---
3	50.0	---	4.02, brs
4	69.3	3.67, t, 10.8	4.45, brs
6	89.2	5.03, dd, 8.8, 5.2	---
7	31.4	2.16-2.21, m	1.69-1.76, m
8	21.7	1.39-1.45, m	2.16-2.21, m
9	52.6	---	4.15, sixtet, 7.0
10	21.7	1.28, d, 6.4 Hz	---
NH	-----	5.49, brs	---
O<u>C</u>(O)-N	156.2	---	---
<u>C</u>$(CH_3)_3$	80.3	---	---
C(<u>C</u>$H_3)_3$	28.5	1.41, s	---

(3*S*,6*S*)-1-Aza-3-*tert*-butoxycarbonylamino-5-oxa-2-oxobicyclo[4.3.0]nonane, (3*S*,6*S*)-5k:

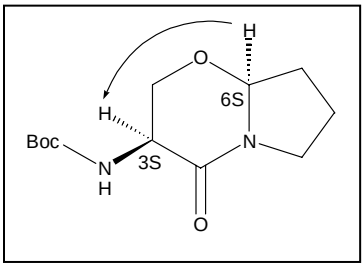


Table 25. ^{1}H and ^{13}C NMR data for (3*S*,6*S*)-**5k**

Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	166.2	---	---
3	49.4	4.22-4.34, m	---
4	68.5	4.22-4.34, m	3.55, dd, 9.0, 6.0
6	86.4	5.01, t, 5.5	---
7	32.4	2.15, dddd, 12.0,6.0,6.0,6.0	1.82-1.88, m
8	21.4	1.70-1.77, m	1.89-1.96, m
9	44.8	3.26, ddd, 12.0, 7.5, 5.5	3.73, ddd, 11.5, 7.0, 7.0

NH	-----	5.54, d, 4.5	---
O<u>C</u>(O)-N	156.0	---	---
<u>C</u>$(CH_3)_3$	79.3	---	---
C(<u>C</u>$H_3)_3$	28.2	1.41, s	---

(3*S*,6*R*)-1-Aza-3-*tert*-butoxycarbonylamino-5-oxa-2-oxobicyclo[4.3.0]nonane, (3*S*,6*R*)-5k:

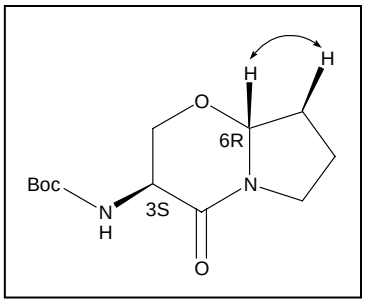
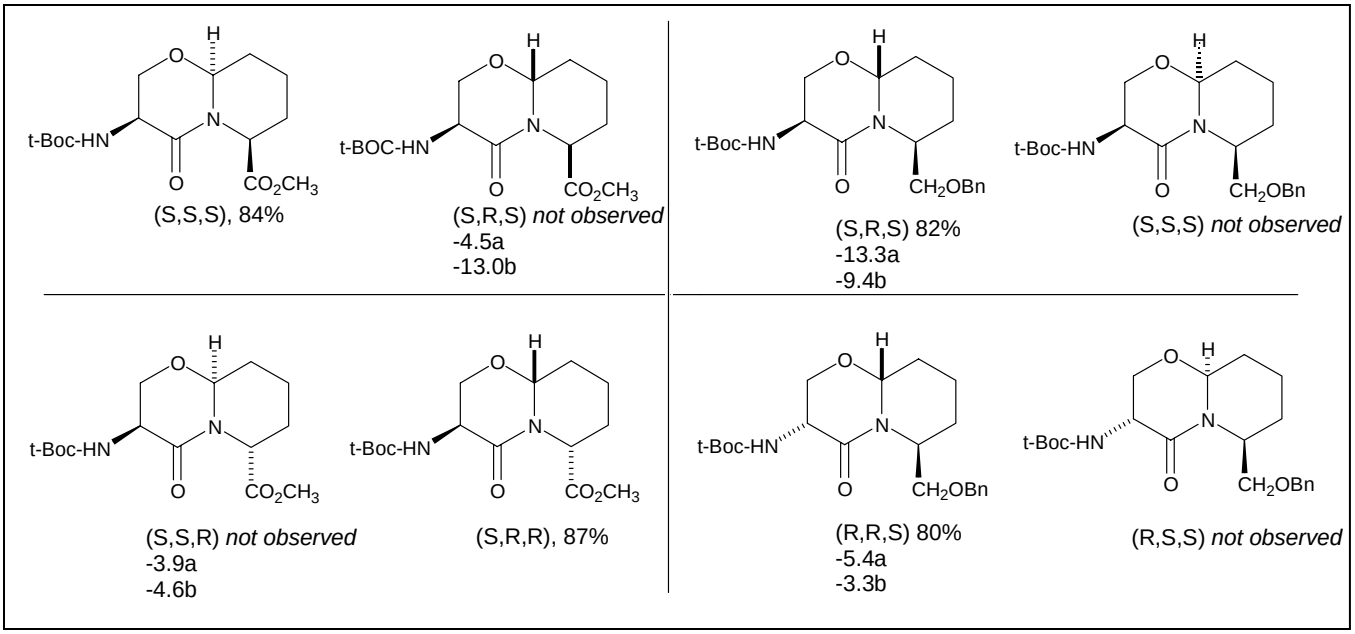


Table 26. ^{1}H and ^{13}C NMR data for (3*S*,6*R*)-**5k**

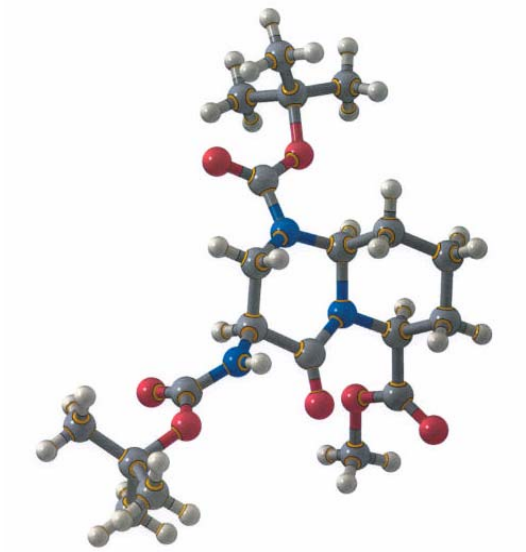
Position	^{13}C, δ, ppm	^{1}H(α), δ, ppm, Hz	^{1}H(β), δ, ppm, Hz
2	166.0	---	---
3	49.8	3.93-4.01, m	---
4	69.3	3.74, t, 11.0	4.38-4.48, m
6	90.0	---	5.00-5.05, m
7	31.8	1.73-1.85, m	2.16-2.23, m
8	19.7	1.73-1.85, m[a]	1.94-2.00, m[a]
9	43.6	3.41-3.46, m[b]	3.68, ddd, 12.0, 8.5, 8.5[b]
NH	-----	5.14, brs	---
O<u>C</u>(O)-N	156.1	---	---
<u>C</u>$(CH_3)_3$	80.5	---	---
C(<u>C</u>$H_3)_3$	28.5	1.41, s	---

Molecular mechanics data for the stability of diasteromer pairs, 5a and 5b



a: by MMFF, b: by Hartree-Fock. Unit: kcal/mole

Figure S1. Single crystal X-ray structure of (3*S*,6*S*,10*S*)-**5d**



(Adapted from the Supporting Information of Reference 1)

Figure S2. X-ray structure of (3*S*,6*S*,*9R*)-**5h**

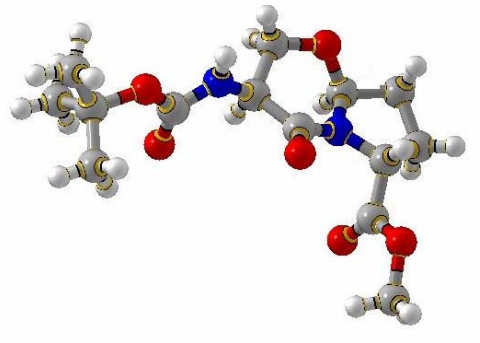


Figure S3. X-ray structure of (*R*,*R*,*S*)-**5h**

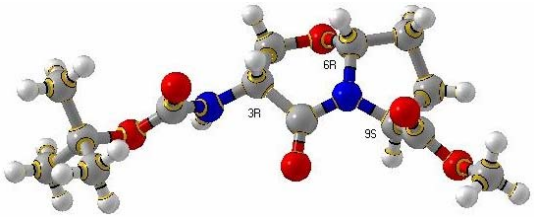
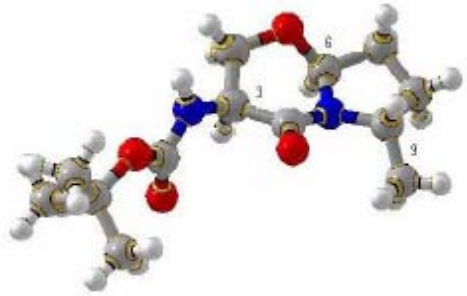


Figure S4. X-ray structure of (*S*,*S*,*S*)-**5j**



X-ray Crystallography Data

(3*S*,6*S*,9*R*)-1-Aza-3-*tert*-butoxycarbonylamino-9-methoxycarbonyl-5-oxa-2-oxobicyclo[4.3.0]-nonane, (3*S*,6*S*,9*R*)-5h:

Table 1. Crystal data and structure refinement for (3*S*,6*S*,9*R*)-**5h**:.

Identification code	(3*S*,6*S*,9*R*)-**5h**	
Empirical formula	C14 H22 N2 O6	
Formula weight	314.34	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.8560(18) Å	α= 90°.
	b = 10.534(2) Å	β= 90°.
	c = 17.443(4) Å	γ = 90°.
Volume	1627.2(6) $Å^3$	
Z	4	
Density (calculated)	1.283 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	
F(000)	672	
Theta range for data collection	2.26 to 28.36°.	
Index ranges	-10<=h<=11, -13<=k<=11, -16<=l<=22	
Reflections collected	10015	
Independent reflections	3657 [R(int) = 0.1565]	
Completeness to theta = 28.36°	93.0 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3657 / 0 / 212	
Goodness-of-fit on F^2	0.676	
Final R indices [I>2sigma(I)]	R1 = 0.0522, wR2 = 0.0997	
R indices (all data)	R1 = 0.2408, wR2 = 0.1337	
Absolute structure parameter	-2(2)	
Largest diff. peak and hole	0.205 and -0.250 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (3*S*,6*S*,9*R*)-**5h**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(4)	4978(4)	9333(3)	-988(2)	66(1)
O(1)	5504(4)	3893(4)	-1025(2)	81(1)
O(6)	5633(4)	8746(3)	2297(2)	68(1)
N(1)	4774(4)	7138(3)	-790(2)	53(1)
O(3)	5937(4)	6431(3)	266(2)	66(1)
N(2)	5339(4)	8710(4)	1045(2)	59(1)
C(10)	4724(7)	8398(5)	1714(3)	53(1)
O(5)	3516(5)	7859(3)	1783(2)	72(1)
C(4)	4614(6)	6456(5)	-2071(2)	61(2)
C(6)	4203(7)	8236(5)	-1231(3)	58(2)
C(3)	5265(6)	6070(5)	-1275(3)	52(2)
C(2)	4525(8)	4846(6)	-986(3)	58(2)
O(2)	3244(5)	4744(3)	-750(2)	78(1)
C(9)	5187(6)	7251(5)	-57(3)	53(2)
C(8)	4593(6)	8457(5)	324(3)	53(2)
C(11)	5144(6)	8626(5)	3104(3)	62(2)
C(12)	5025(8)	7221(5)	3310(3)	112(2)
C(5)	4645(6)	7919(5)	-2043(2)	68(2)
C(1)	4886(8)	2670(5)	-783(3)	120(3)
C(7)	4726(7)	9625(4)	-205(3)	80(2)
C(14)	6416(6)	9268(6)	3533(3)	93(2)
C(13)	3708(6)	9335(5)	3234(3)	91(2)

Table 3. Bond lengths [Å] and angles [°] for (3*S*,6*S*,9*R*)-**5h**.

O(4)-C(6)	1.410(6)
O(4)-C(7)	1.417(5)
O(1)-C(2)	1.328(6)
O(1)-C(1)	1.463(6)
O(6)-C(10)	1.347(5)
O(6)-C(11)	1.478(5)
N(1)-C(9)	1.335(5)
N(1)-C(3)	1.474(5)
N(1)-C(6)	1.479(5)
O(3)-C(9)	1.227(5)
N(2)-C(10)	1.329(6)
N(2)-C(8)	1.446(6)
C(10)-O(5)	1.217(5)
C(4)-C(5)	1.542(6)
C(4)-C(3)	1.557(6)
C(6)-C(5)	1.507(6)
C(3)-C(2)	1.532(7)
C(2)-O(2)	1.212(6)
C(9)-C(8)	1.527(7)
C(8)-C(7)	1.542(6)
C(11)-C(13)	1.492(6)
C(11)-C(14)	1.512(6)
C(11)-C(12)	1.527(6)

C(6)-O(4)-C(7)	113.0(4)
C(2)-O(1)-C(1)	114.0(5)
C(10)-O(6)-C(11)	121.3(4)
C(9)-N(1)-C(3)	122.5(4)
C(9)-N(1)-C(6)	121.5(4)
C(3)-N(1)-C(6)	113.5(4)
C(10)-N(2)-C(8)	122.1(4)
O(5)-C(10)-N(2)	124.3(5)
O(5)-C(10)-O(6)	125.2(5)
N(2)-C(10)-O(6)	110.5(5)
C(5)-C(4)-C(3)	103.1(4)
O(4)-C(6)-N(1)	108.5(4)
O(4)-C(6)-C(5)	109.7(5)

N(1)-C(6)-C(5)	103.2(4)
N(1)-C(3)-C(2)	109.1(4)
N(1)-C(3)-C(4)	101.8(4)
C(2)-C(3)-C(4)	110.8(4)
O(2)-C(2)-O(1)	124.2(6)
O(2)-C(2)-C(3)	125.9(6)
O(1)-C(2)-C(3)	109.9(5)
O(3)-C(9)-N(1)	121.6(5)
O(3)-C(9)-C(8)	125.0(5)
N(1)-C(9)-C(8)	113.3(5)
N(2)-C(8)-C(9)	112.0(4)
N(2)-C(8)-C(7)	109.8(4)
C(9)-C(8)-C(7)	112.2(4)
O(6)-C(11)-C(13)	110.7(4)
O(6)-C(11)-C(14)	102.5(4)
C(13)-C(11)-C(14)	109.6(4)
O(6)-C(11)-C(12)	109.1(4)
C(13)-C(11)-C(12)	112.9(5)
C(14)-C(11)-C(12)	111.6(5)
C(6)-C(5)-C(4)	104.3(4)
O(4)-C(7)-C(8)	114.6(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (3*S*,6*S*,9*R*)-**5h**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(4)	94(3)	45(2)	59(2)	10(2)	-3(2)	-19(2)
O(1)	106(3)	53(2)	83(3)	4(2)	17(2)	22(3)
O(6)	79(3)	88(3)	38(2)	-10(2)	0(2)	-4(2)
N(1)	67(3)	46(3)	46(3)	-2(2)	0(2)	5(3)
O(3)	83(3)	63(3)	51(2)	1(2)	-7(2)	11(2)
N(2)	70(3)	69(3)	36(3)	-4(2)	-3(2)	-10(3)
C(10)	65(5)	55(3)	37(3)	-1(3)	0(4)	-2(3)
O(5)	71(3)	80(3)	64(2)	5(2)	4(2)	-12(2)
C(4)	72(4)	78(4)	34(3)	-2(3)	1(3)	0(3)
C(6)	86(5)	46(4)	42(3)	19(3)	-3(3)	9(4)
C(3)	60(4)	44(3)	52(3)	-1(3)	4(3)	-1(4)
C(2)	66(5)	69(4)	39(3)	2(3)	1(3)	3(4)
O(2)	88(4)	54(2)	92(3)	7(2)	11(3)	-3(3)
C(9)	59(4)	47(4)	53(4)	11(3)	-4(3)	1(3)
C(8)	65(4)	49(3)	44(3)	2(3)	-5(3)	0(4)
C(11)	74(5)	72(4)	41(3)	-4(3)	7(3)	8(4)
C(12)	186(8)	73(4)	77(4)	15(4)	-3(5)	0(5)
C(5)	90(5)	74(4)	39(3)	13(3)	2(3)	-6(4)
C(1)	207(8)	28(3)	124(5)	17(4)	48(5)	13(5)
C(7)	136(6)	50(4)	54(4)	8(3)	-18(4)	-10(4)
C(14)	94(5)	122(6)	62(4)	-14(4)	-10(4)	-6(4)
C(13)	84(5)	105(5)	83(4)	-14(4)	5(4)	24(4)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (3*S*,6*S*,9*R*)-**5h**.

	x	y	z	U(eq)
H(2)	6208	9074	1041	70
H(4A)	5239	6136	-2485	73
H(4B)	3592	6142	-2136	73
H(6)	3110(50)	8330(40)	-1180(20)	70
H(3)	6370(50)	6000(40)	-1290(20)	63
H(8)	3520(40)	8330(40)	430(20)	63
H(12A)	5972	6810	3208	168
H(12B)	4246	6833	3008	168
H(12C)	4784	7137	3844	168
H(5A)	5647	8238	-2159	81
H(5B)	3932	8277	-2405	81
H(1A)	4140	2394	-1146	180
H(1B)	4429	2757	-287	180
H(1C)	5684	2054	-757	180
H(7A)	3806	10119	-165	96
H(7B)	5551	10152	-24	96
H(14A)	6610	10085	3311	139
H(14B)	7310	8755	3501	139
H(14C)	6136	9370	4061	139
H(13A)	2903	8929	2959	136
H(13B)	3819	10192	3057	136
H(13C)	3476	9338	3772	136

(3*R*,6*R*,9*S*)-1-Aza-3-tert-butoxycarbonylamino-9-methoxycarbonyl-5-oxa-2-oxobicyclo[4.3.0]-nonane, (3*R*,6*R*,9*S*)-5h:

Table 1. Crystal data and structure refinement for (3*R*,6*R*,9*S*)-**5h**:

Identification code	(3*R*,6*R*,9*S*)-**5h**	
Empirical formula	C14 H22 N2 O6	
Formula weight	314.34	
Temperature	273(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 9.474(4) Å	α= 90°.
	b = 11.504(5) Å	β= 90°.
	c = 16.118(7) Å	γ = 90°.
Volume	1756.8(13) $Å^3$	
Z	4	
Density (calculated)	1.188 Mg/m^3	
Absorption coefficient	0.093 mm^{-1}	
F(000)	672	
Theta range for data collection	2.17 to 28.12°.	
Index ranges	-12<=h<=12, -10<=k<=14, -20<=l<=20	
Reflections collected	8718	
Independent reflections	3709 [R(int) = 0.2158]	
Completeness to theta = 28.12°	90.7 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3709 / 0 / 212	
Goodness-of-fit on F^2	0.678	
Final R indices [I>2sigma(I)]	R1 = 0.0786, wR2 = 0.1768	
R indices (all data)	R1 = 0.3102, wR2 = 0.2326	
Absolute structure parameter	5(4)	
Largest diff. peak and hole	0.227 and -0.320 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (3*R*,6*R*,9*S*)-**5h**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(3)	4877(6)	8213(4)	11659(3)	77(2)
N(1)	4847(7)	6644(5)	10732(4)	57(2)
O(4)	6191(6)	6925(5)	9578(3)	78(2)
O(6)	5716(6)	10312(4)	8364(3)	80(2)
O(5)	3655(7)	9358(6)	8629(4)	89(2)
C(3)	5358(10)	5449(8)	10940(5)	70(3)
N(2)	5488(7)	9304(5)	9536(4)	77(2)
C(11)	5263(10)	10842(7)	7572(4)	74(3)
C(9)	5367(10)	7284(7)	10119(5)	65(2)
C(8)	4838(9)	8538(7)	10136(4)	59(2)
C(5)	4065(9)	6307(7)	12109(5)	82(3)
C(6)	4100(9)	7189(8)	11417(5)	68(3)
C(2)	4561(14)	4523(9)	10527(6)	90(3)
C(7)	4954(10)	9038(6)	11001(4)	82(3)
O(1)	5193(9)	3504(6)	10616(4)	145(3)
O(2)	3409(8)	4628(5)	10183(5)	103(2)
C(4)	5308(9)	5462(7)	11887(4)	83(3)
C(10)	4843(12)	9619(7)	8816(6)	76(3)
C(14)	4948(14)	9929(7)	6948(4)	140(5)
C(13)	4012(9)	11654(7)	7739(5)	101(3)
C(1)	4439(16)	2474(8)	10300(7)	194(7)
C(12)	6548(10)	11582(8)	7350(6)	129(4)

Table 3. Bond lengths [Å] and angles [°] for (3*R*,6*R*,9*S*)-**5h**.

O(3)-C(7)	1.426(7)
O(3)-C(6)	1.442(9)
N(1)-C(9)	1.328(9)
N(1)-C(6)	1.453(9)
N(1)-C(3)	1.495(10)
O(4)-C(9)	1.240(8)
O(6)-C(10)	1.360(9)
O(6)-C(11)	1.479(7)
O(5)-C(10)	1.203(10)
C(3)-C(2)	1.466(13)
C(3)-C(4)	1.526(9)
N(2)-C(10)	1.362(11)
N(2)-C(8)	1.445(9)
C(11)-C(14)	1.485(9)
C(11)-C(12)	1.528(10)
C(11)-C(13)	1.533(10)
C(9)-C(8)	1.527(10)
C(8)-C(7)	1.512(9)
C(5)-C(6)	1.509(9)
C(5)-C(4)	1.568(10)
C(2)-O(2)	1.230(11)
C(2)-O(1)	1.325(11)
O(1)-C(1)	1.474(12)

C(7)-O(3)-C(6)	111.6(5)
C(9)-N(1)-C(6)	120.4(6)
C(9)-N(1)-C(3)	123.8(7)
C(6)-N(1)-C(3)	112.6(6)
C(10)-O(6)-C(11)	121.8(7)
C(2)-C(3)-N(1)	113.5(7)
C(2)-C(3)-C(4)	116.5(8)
N(1)-C(3)-C(4)	101.8(6)
C(10)-N(2)-C(8)	122.8(8)
O(6)-C(11)-C(14)	110.5(6)
O(6)-C(11)-C(12)	101.6(7)
C(14)-C(11)-C(12)	113.3(8)
O(6)-C(11)-C(13)	109.0(6)

C(14)-C(11)-C(13)	113.2(8)
C(12)-C(11)-C(13)	108.5(7)
O(4)-C(9)-N(1)	124.9(7)
O(4)-C(9)-C(8)	122.2(8)
N(1)-C(9)-C(8)	112.9(7)
N(2)-C(8)-C(7)	110.7(6)
N(2)-C(8)-C(9)	115.1(7)
C(7)-C(8)-C(9)	110.6(6)
C(6)-C(5)-C(4)	103.4(6)
O(3)-C(6)-N(1)	108.1(7)
O(3)-C(6)-C(5)	111.1(6)
N(1)-C(6)-C(5)	106.3(7)
O(2)-C(2)-O(1)	122.5(10)
O(2)-C(2)-C(3)	126.2(10)
O(1)-C(2)-C(3)	111.2(10)
O(3)-C(7)-C(8)	115.4(5)
C(2)-O(1)-C(1)	117.1(9)
C(3)-C(4)-C(5)	104.9(6)
O(5)-C(10)-O(6)	125.5(10)
O(5)-C(10)-N(2)	124.5(9)
O(6)-C(10)-N(2)	109.9(10)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (3*R*,6*R*,9*S*)-**5h**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(3)	85(5)	77(4)	68(3)	-2(3)	-1(3)	-8(4)
N(1)	63(5)	57(4)	50(4)	8(3)	13(4)	-6(4)
O(4)	79(5)	82(4)	71(4)	-1(3)	12(3)	-10(4)
O(6)	65(4)	85(4)	89(4)	36(3)	2(3)	9(4)
O(5)	57(4)	117(5)	92(4)	17(4)	-7(4)	2(5)
C(3)	71(7)	61(5)	78(6)	9(5)	0(6)	10(6)
N(2)	61(5)	80(4)	90(5)	24(4)	-17(4)	-9(4)
C(11)	72(7)	92(6)	57(5)	32(5)	2(5)	19(6)
C(9)	67(7)	73(6)	54(5)	-4(5)	2(5)	-12(5)
C(8)	66(6)	58(5)	52(5)	19(4)	7(5)	5(5)
C(5)	80(7)	99(6)	67(6)	10(5)	-2(5)	9(6)
C(6)	74(7)	77(6)	53(5)	7(5)	-6(5)	-5(6)
C(2)	101(10)	62(7)	108(8)	-1(6)	10(7)	9(8)
C(7)	108(9)	60(5)	79(6)	5(4)	12(6)	-9(6)
O(1)	167(8)	57(4)	210(7)	-18(4)	-50(7)	38(5)
O(2)	85(6)	77(4)	147(6)	-15(4)	10(5)	-9(4)
C(4)	75(7)	91(6)	83(6)	13(5)	-2(5)	9(6)
C(10)	79(9)	61(6)	88(7)	10(5)	16(7)	16(7)
C(14)	255(15)	106(7)	58(5)	5(5)	6(8)	35(9)
C(13)	79(8)	92(6)	132(8)	24(6)	7(6)	32(6)
C(1)	280(20)	59(6)	242(13)	-27(7)	-46(14)	4(10)
C(12)	77(8)	137(9)	174(10)	62(8)	22(7)	-6(7)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (3*R*,6*R*,9*S*)-**5h**.

	x	y	z	U(eq)
H(3)	6350(80)	5390(60)	10770(40)	84
H(2)	6317	9572	9639	92
H(8)	3830(70)	8510(60)	10000(40)	70
H(5A)	3170	5897	12120	99
H(5B)	4219	6674	12643	99
H(6)	3140(80)	7400(60)	11250(40)	82
H(7A)	5844	9450	11045	99
H(7B)	4204	9603	11076	99
H(4A)	6192	5744	12114	99
H(4B)	5129	4689	12103	99
H(14A)	5779	9471	6852	209
H(14B)	4657	10288	6439	209
H(14C)	4205	9438	7151	209
H(13A)	3227	11209	7941	152
H(13B)	3749	12040	7234	152
H(13C)	4276	12223	8146	152
H(1A)	3477	2493	10487	291
H(1B)	4888	1782	10503	291
H(1C)	4460	2476	9705	291
H(12A)	6746	12112	7795	194
H(12B)	6357	12014	6852	194
H(12C)	7349	11086	7262	194

(3*S*,6*S*,9*S*)-1-Aza-3-tert-butoxycarbonylamino-9-methyl-5-oxa-2-oxobicyclo [4.3.0]nonane, (3*S*,6*S*,9*S*)-5j:

Table 1. Crystal data and structure refinement for (3*S*,6*S*,9*S*)-**5j**

Identification code	(3*S*,6*S*,9*S*)-**5j**	
Empirical formula	C13 H21 N2 O4	
Formula weight	269.32	
Temperature	273(2) K	
Wavelength	0.71073 Å	
Crystal system		
Space group	P(2)1	
Unit cell dimensions	a = 10.050(8) Å	α= 90°.
	b = 6.229(5) Å	β= 101.780(13)°.
	c = 12.106(9) Å	γ = 90°.
Volume	741.9(10) $Å^3$	
Z	2	
Density (calculated)	1.206 Mg/m^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	290	
Theta range for data collection	1.72 to 23.28°.	
Index ranges	-10<=h<=11, -6<=k<=6, -11<=l<=13	
Reflections collected	2813	
Independent reflections	1926 [R(int) = 0.0696]	
Completeness to theta = 23.28°	99.6 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1926 / 1 / 90	
Goodness-of-fit on F^2	1.171	
Final R indices [I>2sigma(I)]	R1 = 0.1406, wR2 = 0.3364	
R indices (all data)	R1 = 0.1890, wR2 = 0.3720	
Absolute structure parameter	2(6)	
Largest diff. peak and hole	0.622 and -0.456 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (3*S*,6*S*,9*S*)-**5j**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(7)	2139(9)	3062(16)	1094(8)	59(2)
C(8)	2567(9)	4342(16)	142(9)	60(2)
O(2)	971(6)	993(10)	-534(6)	73(2)
O(4)	1772(7)	6997(12)	3139(6)	79(2)
N(1)	2839(7)	3160(12)	-684(7)	62(2)
O(3)	3622(7)	4920(11)	3105(7)	84(2)
N(2)	1613(8)	4441(13)	1860(7)	69(2)
C(5)	2271(10)	1032(17)	-886(9)	69(3)
O(1)	2691(7)	6305(13)	210(7)	92(2)
C(6)	1152(10)	1280(20)	677(10)	83(3)
C(2)	3170(11)	4150(19)	-1721(10)	75(3)
C(4)	2070(11)	640(20)	-2153(10)	90(4)
C(9)	2456(10)	5408(17)	2743(9)	70(3)
C(10)	2339(9)	8135(18)	4210(9)	72(3)
C(1)	4474(12)	5250(20)	-1557(12)	100(4)
C(12)	1201(14)	9700(20)	4329(13)	112(4)
C(3)	3095(14)	2100(20)	-2482(12)	106(4)
C(11)	2600(14)	6510(30)	5204(13)	115(4)
C(13)	3582(13)	9340(20)	4096(13)	109(4)

Table 3. Bond lengths [Å] and angles [°] for (3*S*,6*S*,9*S*)-**5j**.

C(7)-N(2)	1.442(12)
C(7)-C(6)	1.506(14)
C(7)-C(8)	1.534(14)
C(8)-O(1)	1.230(12)
C(8)-N(1)	1.314(13)
O(2)-C(6)	1.451(13)
O(2)-C(5)	1.454(11)
O(4)-C(9)	1.348(12)
O(4)-C(10)	1.486(13)
N(1)-C(5)	1.444(13)
N(1)-C(2)	1.496(14)
O(3)-C(9)	1.203(10)
N(2)-C(9)	1.361(12)
C(5)-C(4)	1.526(16)
C(2)-C(1)	1.456(16)
C(2)-C(3)	1.569(19)
C(4)-C(3)	1.488(17)
C(10)-C(13)	1.486(15)
C(10)-C(12)	1.532(17)
C(10)-C(11)	1.555(18)

N(2)-C(7)-C(6)	110.6(7)
N(2)-C(7)-C(8)	111.7(7)
C(6)-C(7)-C(8)	113.4(8)
O(1)-C(8)-N(1)	125.0(10)
O(1)-C(8)-C(7)	120.4(10)
N(1)-C(8)-C(7)	114.5(8)
C(6)-O(2)-C(5)	111.1(8)
C(9)-O(4)-C(10)	121.9(8)
C(8)-N(1)-C(5)	120.4(8)
C(8)-N(1)-C(2)	121.6(8)
C(5)-N(1)-C(2)	112.6(8)
C(9)-N(2)-C(7)	121.2(8)
N(1)-C(5)-O(2)	108.3(8)
N(1)-C(5)-C(4)	106.6(9)
O(2)-C(5)-C(4)	110.5(9)
O(2)-C(6)-C(7)	111.6(9)

C(1)-C(2)-N(1)	115.3(10)
C(1)-C(2)-C(3)	113.4(10)
N(1)-C(2)-C(3)	99.5(9)
C(3)-C(4)-C(5)	102.3(11)
O(3)-C(9)-O(4)	125.9(10)
O(3)-C(9)-N(2)	125.3(9)
O(4)-C(9)-N(2)	108.9(8)
O(4)-C(10)-C(13)	109.9(9)
O(4)-C(10)-C(12)	103.0(9)
C(13)-C(10)-C(12)	110.2(10)
O(4)-C(10)-C(11)	109.8(9)
C(13)-C(10)-C(11)	112.8(11)
C(12)-C(10)-C(11)	110.7(10)
C(4)-C(3)-C(2)	107.1(10)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (3*S*,6*S*,9*S*)-**5j**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	68(5)	54(5)	65(5)	-1(5)	7(4)	3(4)
O(4)	75(3)	110(4)	69(3)	28(3)	-3(3)	-14(3)
O(1)	76(3)	102(4)	57(3)	10(3)	15(3)	16(3)
O(3)	65(3)	131(5)	71(3)	13(4)	-11(3)	-15(3)
N(2)	54(3)	110(5)	58(4)	10(4)	0(3)	-9(3)
N(1)	68(3)	76(4)	49(4)	5(4)	13(3)	8(4)
C(2)	85(6)	84(7)	59(5)	-1(5)	28(4)	0(5)
C(3)	59(4)	85(5)	55(4)	0(5)	8(4)	-13(4)
O(2)	125(5)	75(5)	79(4)	1(4)	31(3)	6(3)
C(4)	99(6)	100(6)	63(5)	7(5)	26(4)	13(5)
C(5)	125(7)	101(6)	72(6)	20(6)	38(5)	22(6)
C(6)	76(5)	95(6)	70(5)	2(6)	21(4)	13(4)
C(7)	73(5)	91(5)	53(4)	0(5)	-4(4)	3(5)
C(8)	98(6)	139(8)	77(6)	-10(6)	19(5)	42(6)
C(9)	92(6)	91(6)	56(5)	11(5)	22(4)	18(5)
C(10)	128(7)	132(9)	92(7)	32(7)	12(6)	-38(7)
C(11)	117(7)	115(7)	82(6)	2(7)	36(6)	17(6)
C(12)	134(9)	169(11)	72(6)	-21(7)	32(6)	-20(8)
C(13)	113(7)	126(8)	106(7)	10(8)	39(6)	25(7)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (3*S*,6*S*,9*S*)-**5j**.

	x	y	z	U(eq)
H(2)	4234	5750	3216	90
H(2A)	2110(80)	1090(140)	5460(70)	89
H(3)	2040(70)	3460(130)	3480(70)	80
H(4A)	3583	1102	3947	103
H(4B)	4747	2821	4180	103
H(5A)	3851	2137	7525	116
H(5B)	2765	267	7296	116
H(6)	2570(90)	6240(150)	7070(80)	96
H(8A)	478	7488	6014	157
H(8B)	349	6921	7249	157
H(8C)	-210	5330	6260	157
H(10A)	4027	11665	1336	178
H(10B)	3509	11700	24	178
H(10C)	4590	9998	577	178
H(11A)	2151	3599	8272	123
H(11B)	1007	2536	7349	123
H(12A)	3221	6843	-191	185
H(12B)	2111	8363	-880	185
H(12C)	1703	6632	-70	185
H(13A)	783	9520	1152	169
H(13B)	992	11041	170	169
H(13C)	1659	11610	1422	169

References

(1) Mizutani, N.; Chiou, W.-H.; Ojima, I. *Org. Lett.* 2002, *4*, 4575-4578.

(2) Chiou, W.-H.; Ojima, I. *Abstracts of Papers, 228th ACS National Meeting, August 22-26, 2004* 2004, ORGN-144.

(3) Chiou, W.-H.; Mizutani, N.; Ojima, I. *Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003*, ORGN-112.

(4) Warshawsky, A. M.; Patel, M. V.; Chen, T.-M. *J. Org. Chem.* 1997, *62*, 6439-6440.