SUPPORTING INFORMATION

One-pot Cross-coupling of *N*-Acyl *N*,*O*-Acetals with α,β-Unsaturated Compounds

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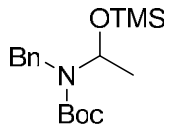
General Methods. Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$ (^1H at 400 MHz and ^{13}C at 100 MHz) with tertramethylsilane (TMS) as an internal standard. Chemical shifts are expressed in δ (ppm) units downfield from TMS. Mass spectra were recorded with a LC-MS apparatus (ESI, direct injection). Optical rotations were measured with an automatic polarimeter. Column chromatography separation was performed on silica gel. Tetrahydrofuran was distilled over sodium benzophenone ketyl under N_2. Dichloromethane was distilled from phosphorus pentoxide. Silica gel (300 ~ 400 mesh) was used for column chromatography, eluting (unless otherwise stated) with ethyl acetate/PE (60 ~ 90 °C) mixtures.

Preparation of Substrates

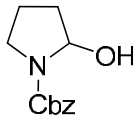
tert-Butyl Benzyl(1-(trimethylsilyloxy)ethyl)carbamate (5)



To a solution of *tert*-butyl acetyl(benzyl)carbamate (1.24 g, 5.0 mmol) in CH_2Cl_2 (25 mL) was dropwise added DIBAL-H (1.2 M solution in toluene, 6.3 mL, 7.5 mmol) at −78 °C. After 1 h, the reaction mixture was treated with pyridine (1.6 mL, 20 mmol) and TMSOTf (2.7 mL, 15 mmol). The mixture was stirred at −78 °C for 10 min, quenched with a 15% aqueous solution of sodium potassium tartrate (25 mL), and diluted with Et_2O (40 mL). The resultant mixture was warmed to rt and stirred vigorously until two layers were completely separated. The mixture was extracted with Et_2O (20 mL × 2) and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column flash chromatography (eluent: EtOAc/PE = 1/80) to afford **5**[1] (1.29 g, yield: 80%) as a colorless oil. IR (film): 2978, 1698, 1453, 1367 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.12 (s, 9H), 1.12-1.62 (m, 12H), 4.26-4.64 (m, 2H), 5.76-6.14 (m, 1H), 7.14-7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −0.2, 23.1, 28.3, 44.2, 75.7, 80.0, 126.3, 126.7, 128.0, 140.5, 154.8; MS (ESI, *m/z*): 346 (M +

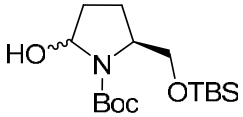
Na^+). Anal. Calcd for $C_{17}H_{29}NO_3Si$: C, 63.12; H, 9.04; N, 4.33. Found: C, 63.20; H, 8.91; N, 4.57.

1-(Benzyloxycarbonyl)-2-hydroxypyrrolidine (8)



To a stirring solution of *N*-benzyloxycarbonyl-L-proline (1.20 g, 4.76 mmol) in acetonitrile (24 mL) and water (24 mL) was added ceric ammonium nitrate (CAN) (5.22 g, 9.52 mmol) in one potion at rt. The reaction mixture was stirred for 30 min, and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column flash chromatography (eluent: EtOAc/PE 1:5) to afford the *N,O*-acetal **8**[2] (2.78 g, yield: 60%) as a white solid. Mp 55-56.5 °C (EtOAc/PE 1:5) (lit.[2b] 47-49 °C); IR (film): 3432, 2959, 2881, 1693, 1416, 1346 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.75-2.20 (m 4H), 3.28-3.44 (m, 1H), 3.51-3.68 (m, 1H), 4.68-4.80 (m, 1H), 5.10-5.20 (m, 2H), 5.46-5.57 (m, 1H), 7.25-7.45 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0 and 22.7, 32.7 and 33.6, 45.7 and 46.2, 66.8 and 67.1, 81.3 and 82.1, 127.8, 128.0, 128.5, 136.5, 154.1 and 155.4; MS (ESI, *m*/*z*): 244 ($M + Na^+$).

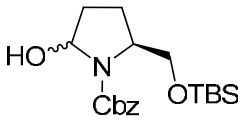
(5*S*)-1-(*tert*-Butyloxycarbonyl)-5-[(*tert*-butyldimethylsilyl)oxymethyl]-2-hydroxy-pyrrolidine (12a)



To a solution of (*S*)-1-(*tert*-butyloxycarbonyl)-[5-((*tert*-butyldimethylsilyl) oxymethyl)-2-pyrrolidinone (1.875 g, 5.70 mmol) in THF (57 mL) was dropwise added DIBAL-H (1.2 M in toluene, 6.7 mL, 7.98 mmol) at −78 °C under argon. The mixture was stirred for 30 min, then quenched with a saturated aqueous NH_4Cl (100 mL) and H_2O (100 mL). The resulting mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column flash chromatography (eluent: EtOAc/PE 1:10) to afford **12a**[3] (1.70 g,

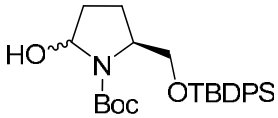
yield: 90%) as a colorless oil. IR (film): 3128, 2954, 1702, 1680, 1395 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.03, 0.07 (2s, 6H), 0.86, 0.90 (2s, 9H), 1.47 (s, 9H), 1.82-2.10 (m, 4H), 3.40-3.56 (2m, 1H), 3.58-3.86 (2m, 2H), 3.94-4.40 (m, 1H), 5.36-5.52 (2m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.5 and −5.4, 18.4, 23.6 and 24.9, 25.9, 28.4, 31.5 and 33.5, 58.1 and 58.4, 62.4 and 63.6, 80.1, 81.8 and 82.6, 153.2 and 154.4; MS (ESI, *m/z*): 354 ($M + Na^+$).

(5*S*)-1-(Benzyloxycarbonyl)-5-[(*tert*-butyldimethylsilyl)oxymethyl]-2-hydroxy-pyrrolidine (12b)



To a solution of (*S*)-1-(benzyloxycarbonyl)-5-[(*tert*-butyldimethylsilyl) oxymethyl] -2-pyrrolidinone (1.54 g, 4.24 mmol) in THF (42 mL) was dropwise added a solution of DIBAL-H (1.2 M in toluene, 4.95 mL, 5.94 mmol) at −78 °C under argon. The mixture was stirred for 30 min, then quenched with a saturated aqueous NH_4Cl (100 mL) and H_2O (100 mL). The resulting mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column flash chromatography (eluent: EtOAc/PE 1:10) to afford **12b**[4] (1.39 g, yield: 90%) as a colorless oil. IR (film): 3133, 3021, 1713, 1400 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −0.01-0.12 (2m, 6H), 0.82-0.94 (m, 9H), 1.82-2.13 (m, 4H), 3.44-4.12 (m, 4H), 5.08-5.26 (2m, 2H), 5.46-5.60 (m, 1H), 7.27-7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.5, 18.1 and 18.3, 23.6 and 24.9, 25.9, 29.7, 31.7, 33.7, 58.4 and 58.5, 62.4 and 63.7, 66.8 and 67.0, 81.6 and 83.0, 127.8, 127.9, 128.1, 128.4, 136.3, 153.6; MS (ESI, *m/z*): 388 ($M + Na^+$).

(5*S*)-1-(Benzyloxycarbonyl)-5-[(*tert*-butyldiphenylsilyl)oxymethyl]-2-hydroxy-pyrrolidine (12c)



To a solution of (*S*)-1-(*tert*-butyloxycarbonyl)-5-[(*tert*-butyldiphenylsilyl) oxymethyl] -2-pyrrolidinone (2.584 g, 5.70 mmol) in THF (57 mL) was dropwise added DIBAL-

H (1.2 M in toluene, 6.7 mL, 7.98 mmol) at −78 °C under argon. The mixture was stirred for 30 min, then quenched with a saturated aqueous NH_4Cl (100 mL) and H_2O (100 mL). The resulting mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was chromatographed (eluent: EtOAc/PE 1:10) to afford **12c**[5] (2.39 g, yield: 92%) as a colorless oil. IR (film): 3128, 2949, 2932, 1685, 1400 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.04 and 1.07 (br 2s, 9H), 1.34 and 1.52 (br 2s, 9H), 1.80-2.32 (m, 4H), 3.30-4.08 (m, 4H), 5.36-5.55 (m, 1H), 7.34-7.46 (m, 6H), 7.60-7.72 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 25.1, 26.8, 28.3 and 28.5, 30.5 and 31.2, 58.2 and 58.4, 63.2 and 64.3, 80.2 and 80.3, 82.2, 82.6, 82.9, 127.7, 129.7, 132.9, 133.2, 133.3, 135.5, 154.6; MS (ESI, *m/z*): 478 (M + Na^+).

Experimental Procedures

Preparation of the *t*-BuOH-containing SmI_2 solution in THF. To a slurry of Sm powder (flame dried under Ar, 826 mg, 5.5 mol) in THF (50 mL) was added I_2 (1,27 g, 5.0 mmol) at room temperature. The reaction mixture was stirred for 2 h at 45 °C to give a SmI_2 solution (0.1 M in THF). To the SmI_2 solution was added *t*-BuOH (0.43 mL, 5.0 mmol) at 45 °C and the mixture was stirred for 10 min to give the *t*-BuOH-containing SmI_2 solution in THF.

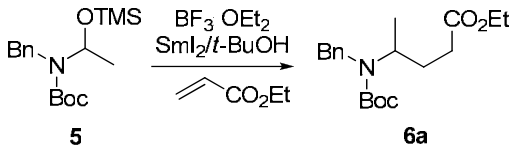
General procedure for the cross-coupling of *N*,*O*-acetals with α,β-unsaturated compounds: To a solution of a *N*,*O*-acetal (0.5 mmol), an α,β-unsaturated compound (1.0 mmol) and $BF_3{\cdot}Et_2O$ (1.0 mmol) in dry THF (10 mL) was dropwise added a freshly prepared *t*-BuOH-containing SmI_2 (0.1 M in THF, 20 mL, 2.0 mmol) at –40 °C. After being stirred for 10 min, the reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL). The mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified

by flash chromatography on silica gel to afford the desired cross-coupling product. In some cases, the reduced product was isolated as a side product.

Tabular Survey

Optimization of the conditions for the SmI_2-mediated cross-coupling of the *N,O*-acetal 5 and 8 with α,β-unsaturated compounds

SmI_2-mediated reductive coupling of *N,O*-acetal TMS ether **5** with ethyl acrylate.



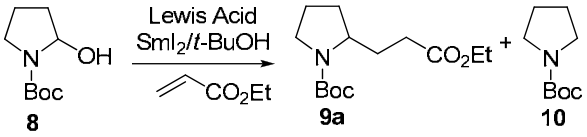
5 **6a**

Table 4.

entry	α,β-unsaturated compounds	product (% yield)	
1			(0)[a]
2	COOEt	Bn N Boc COOEt **6a**	(68)[b]
3			(72)

[a] $BF_3{\cdot}OEt_2$ was absent; [b] *t*-BuOH was absent.

The effects of both temperature and Lewis acid on the SmI_2-mediated cross-coupling of the *N,O*-acetal **8** with ethyl acrylate were tested, and the results were listed in Table 5 and Table 6.



8 **9a** **10**

Table 5

Entry	Temperature (°C)	Product **9a** [a] (% yield)	**10** (% yield)
1.	–40	76	-
2.	–60	70	-
3.	–78	43	-

[a] isolated yield.

Table 6

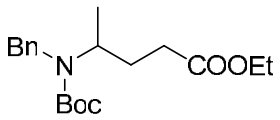
Entry	Lewis acid (2 equiv)	Product **9a**[a] (% yield)	**10** (% yield)
1.	$BF_3{\cdot}Et_2O$	76	-
2.	TBSOTf	52	-
3.	TMSI	50	-
4.	TMSOTf	36	-
5.	TMSCl	No reaction	
6.	Tf_2O	Complex results	

[a] isolated yield.

Analytical Data

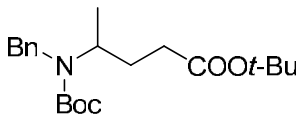
Samarium diiodide-mediated reductive coupling of the *tert*-butyl benzyl[1-(trimethylsilyloxy)ethyl]carbamate (5) with α,β-unsaturated compounds.

Ethyl 4-[Benzyl(*tert*-butoxycarbonyl)amino]pentanoate (6a)



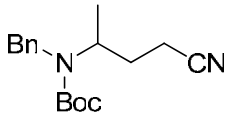
Following **the general procedure**, the SmI_2 mediated reaction of **5** with ethyl acrylate afforded **6a** in 72% yield as a colorless oil. IR (film): 2977, 1736, 1690, 1365 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.09 (d, J = 6.6 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H), 1.30-1.60 (m, 9H), 1.74 (br s, 1H), 1.88 (m, 1H), 2.19 (m, 2H), 3.70-3.98 and 4.16-4.50 (3m, 3H), 4.10 (q, J = 7.2 Hz, 2H), 7.18-7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 19.0, 28.4, 29.9, 31.4, 46.7 and 47.8, 51.1 and 52.4, 60.3, 79.8, 126.7, 127.5, 128.3, 140.0, 155.7, 173.3; MS (ESI, *m/z*): 358 ($M + Na^+$). Anal. calcd for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18. Found: C, 67.98; H, 8.96; N, 4.37.

***tert*-Butyl 4-[Benzyl(*tert*-butoxycarbonyl)amino]pentanoate (6b)**



Following **the general procedure**, the SmI_2 mediated reaction of **5** with *tert*-butyl acrylate afforded **6b** in 78% yield as a colorless oil. IR (film): 2976, 1729, 1691, 1365 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.08 (d, *J* = 6.2 Hz, 3H); 1.29-1.58 (3m, 18H), 1.63-1.95 (2m, 2H), 2.14 (m, 2H), 3.71-4.60 (m, 3H), 7.15-7.35 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.0 and 19.4, 28.0, 28.3, 29.9, 32.6, 46.5 and 48.0, 51.1 and 52.4, 79.6, 80.1, 126.6, 127.4, 128.2, 140.0, 155.7, 172.5; MS (ESI, *m/z*): 386 (M + Na^+). Anal. calcd for $C_{21}H_{33}NO_4$: C, 69.39; H, 9.15; N, 3.85. Found: C, 69.24; H, 9.17; N, 4.09.

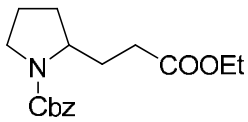
***tert*-Butyl Benzyl(4-cyanobutan-2-yl)carbamate (6c)**



Following **the general procedure**, the SmI_2 mediated reaction of **5** with acrylonitrile afforded **6c** in 73% yield as a colorless oil. IR (film): 2976, 2244, 1688, 1453, 1408, 1366 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.14 (d, *J* = 6.9 Hz, 3H), 1.30-1.60 (m, 9H), 1.63-1.80 (m, 1H), 1.84-2.34 (2m, 3H), 3.76-4.60 (m, 3H), 7.19-8.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 18.7, 28.3, 30.6, 48.0, 51.7, 80.3, 119.4, 127.1, 128.4, 139.2, 155.7; MS (ESI, *m/z*): 311 (M + Na^+). Anal. calcd for $C_{17}H_{24}N_2O_2$: C, 70.80; H, 8.39; N, 9.71. Found: C, 71.09; H, 8.24; N, 9.96.

Samarium diiodide-mediated reductive coupling of the *N*,*O*-acetal 8 with α,β-unsaturated compounds.

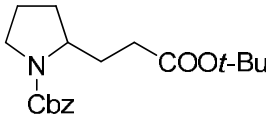
1-(Benzyloxycarbonyl)-2-[2-(ethyloxycarbonyl)ethyl]pyrrolidine (9a)



Following **the general procedure**, the SmI_2 mediated reaction of **8** with ethyl acrylate afforded **9a**[6] in 76% yield as a colorless oil. IR (film): 2917, 2865, 1734, 1698, 1449, 1412, 1355 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.11-1.22 (m, 3H), 1.52-1.70 (m, 2H), 1.70-2.02 (3m, 4H), 2.14-2.34 (2m, 2H), 3.24-3.48 (2m, 2H), 3.78-3.90 (m, 1H), 3.93-4.10 (m, 2H), 4.96-5.12 (m, 2H), 7.18-7.32 (m, 5H); ^{13}C NMR

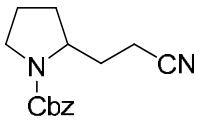
(100 MHz, $CDCl_3$): δ 14.1, 22.9 and 23.7, 29.4 and 29.7, 29.9 and 30.6, 31.1 and 31.3, 46.2 and 46.5, 56.5 and 57.2, 60.3, 66.5 and 66.7, 127.7, 127.8, 128.4, 136.8 and 137.0, 155.0, 173.1 and 173.3; MS (ESI, *m/z*): 328 ($M + Na^+$).

1-(Benzyloxycarbonyl)-2-[2-(*tert*-butyloxycarbonyl)ethyl]pyrrolidine (9b)



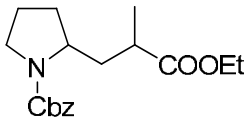
Following **the general procedure**, the SmI_2 mediated reaction of **8** with *tert*-butyl acrylate afforded **9b** in 67% yield as a colorless oil. IR (film): 2973, 2873, 1726, 1702, 1409, 1357 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 9H), 1.59-1.73 (m, 2H), 1.80-2.04 (m, 4H), 2.12-2.36 (m, 2H), 3.30-3.54 (m, 2H), 3.84-3.95 (m, 1H), 5.04-5.20 (m, 2H), 7.26-7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.9 and 23.7, 28.0, 29.4 and 29.9, 30.6, 32.5, 46.3 and 46.6, 56.7 and 57.3, 66.5 and 66.7, 80.1, 126.9, 127.8, 128.4, 155.0, 172.5; MS (ESI, *m/z*): 356 ($M + Na^+$). Anal. calcd for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20. Found: C, 68.17; H, 8.39; N, 4.58.

1-(Benzyloxycarbonyl)-2-(2-cyanoethyl)pyrrolidine (9c)



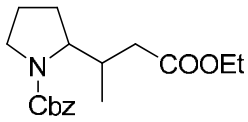
Following **the general procedure**, the SmI_2 mediated reaction of **8** with acrylonitrile afforded **9c**[6] in 79% yield as a colorless oil. IR (film): 2957, 2881, 2244, 1698, 1445, 1411, 1359, 1346 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.66-2.10 (m, 6H), 2.20-2.48 (2m, 2H), 3.27-3.64 (m, 2H), 3.92-4.00 (m, 1H), 5.08-5.22 (m, 2H), 7.26-7.44 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 22.9 and 23.7, 30.2 and 30.8, 30.4, 46.4 and 46.6, 56.0 and 56.8, 66.7 and 67.0, 119.2 and 119.6, 127.7, 127.9, 128.1, 128.4, 136.7, 154.9 and 155.3; MS (ESI, *m/z*): 281 ($M + Na^+$).

1-(Benzyloxycarbonyl)-2-[2-(ethyloxycarbonyl)propyl]pyrrolidine (9d)



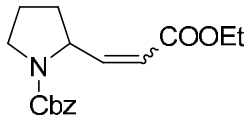
Following **the general procedure**, the SmI_2 mediated reaction of **8** with ethyl methacrylate afforded **9d** as an inseparable diastereomeric mixture (dr = 70: 30) in a combined yield of 84% as a colorless oil. **9d**: HPLC: Shim-pack CLC-SIL (150×4.6), hexane/EtOAc 90:10, 1.0 mL/min, λ= 254 nm, t_1 12.1 min (69.8%), t_2 12.7 min (30.2%). IR (film): 2974, 2878, 1731, 1454, 1411 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.04-1.30 (2m, 6H), 1.30-2.24 (m, 6H), 2.30-2.62 (m, 1H), 3.30-3.54 (m, 2H), 3.84-4.20 (m, 3H), 5.05-5.20 (m, 2H), 7.24-7.44 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 14.1, 17.3, 17.5, 17.7, 22.8, 23.6, 24.8, 25.6, 29.5, 29.8, 30.6, 30.8, 36.9, 37.1, 37.5, 38.3, 38.7, 45.6, 46.0, 46.1, 46.3, 55.2, 55.5, 55.7, 56.2, 60.07, 60.11, 66.3, 66.4, 66.6, 127.6, 127.7, 128.2, 136.7 and 136.9, 154.7, 176.1 and 176.3; MS (ESI, *m/z*): 342 ($M + Na^+$). HRMS (EI) calcd for $C_{18}H_{25}NO_4$: 319.1784. Found: 319.1786.

1-(Benzyloxycarbonyl)-2-[1-methyl-2-(ethyloxycarbonyl)ethyl]pyrrolidine (9e)



Following **the general procedure**, the SmI_2 mediated reaction of **8** with ethyl crotonate afforded **9e** as an inseparable diastereomeric mixture (dr = 51: 49) in a combined yield of 52% and **10** in 19% yield. **9e**: colorless oil. HPLC: Shim-pack CLC-SIL (150×4.6), Hexane/EtOAc 90:10, 1.0 mL/min, λ= 254 nm, t_1 11.3 min (49.7%), t_2 12.0 min (50.3%). IR (film): 2959, 2869, 1729, 1702, 1408 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.84-1.00 (m, 3H), 1.22-1.29 (m, 3H), 1.68-1.98 (m, 4H), 1.98-2.20 (m, 1H), 2.30-2.68 (m, 2H), 3.22-3.46 (2m, 1H), 3.47-3.75 (m, 1H), 3.75-3.94 (m, 1H), 4.04-4.20 (m, 2H), 5.04-5.24 (m, 2H), 7.29-7.47 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 15.6 and 15.9 and 16.8, 23.3 and 24.0 and 24.3, 26.5 and 27.2 and 27.6, 29.7, 33.0 and 33.5, 38.9 and 39.0, 46.7 and 47.0 and 47.2, 60.3 and 61.3 and 62.1, 66.7 and 66.9, 127.8, 128.4, 137.0, 155.5, 173.1; MS (ESI, *m/z*): 342 ($M + Na^+$). Anal. calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.52; H, 7.80; N, 4.69.

(*E*) and (*Z*)-1-(Benzyloxycarbonyl)-2-[2-(ethyloxycarbonyl)ethenyl]pyrrolidine (9f)

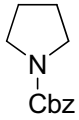


Following **the general procedure**, the SmI_2 mediated reaction of **8** with ethyl propiolate afforded **9f** in 88% yield (*E*-isomer: 51%, *Z*-isomer: 37%).

(*Z*)-1-(Benzyloxycarbonyl)-2-[2-(ethyloxycarbonyl)ethenyl]pyrrolidine: [7] colorless oil. IR (film): 2974, 2878, 1702, 1454, 1411 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.20-1.34 (m, 3H), 1.65-1.77 (m, 1H), 1.82-1.94 (m, 2H), 2.28-2.42 (m, 1H), 3.40-3.66 (m, 2H), 4.05-4.25 (m, 2H), 5.02-5.18 (m, 2H), 5.28-5.45 (m, 1H), 5.70 (d, *J* = 11.4 Hz, 0.5H), 5.90 (d, *J* = 11.4 Hz, 0.5H), 6.10-6.30 (2m, 1H), 7.22-7.40 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 24.0 and 24.6, 32.5 and 33.1, 46.8 and 47.1, 55.5 and 56.4, 60.0, 66.7, 118.7 and 119.1, 127.6, 127.9, 128.2, 128.4, 136.8, 151.7 and 152.0, 155.0, 165.8; MS (ESI, *m/z*): 326 ($M + Na^+$).

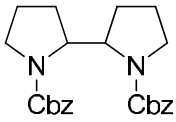
(*E*)-1-(Benzyloxycarbonyl)-2-[2-(ethyloxycarbonyl)ethenyl]pyrrolidine: colorless oil. IR (film): 2978, 2876, 1704, 1453, 1410, 1351, 1179 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, *J* = 7.1 Hz, 3H), 1.73-1.94 (2m, 3H), 2.01-2.18 (m, 1H), 3.38-3.57 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.45-4.62 (2m, 1H), 5.05-5.20 (m, 2H), 5.78 (d, *J* = 15.6 Hz, 0.5H), 5.86 (d, *J* = 15.6 Hz, 0.5H), 6.75-6.92 (m, 1H), 7.28-7.40 (m, 5H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.2, 22.7 and 23.5, 30.7 and 31.6, 46.4 and 46.8, 57.7 and 58.0, 60.3, 66.9, 120.9, 127.9, 128.4, 128.4, 136.6, 147.4 and 147.8, 154.7, 166.3; MS (ESI, *m/z*): 326 ($M + Na^+$). Anal. calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.17; H, 7.22; N, 4.88.

1-(Benzyloxycarbonyl)pyrrolidine (10)



10:[8] Colorless oil. IR (film): 2973, 2876, 1705, 1419, 1340 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.76-1.91 (m, 4H), 3.31-3.45 (m, 4H), 5.13 (s, 2H), 7.24-7.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9, 25.6, 45.7, 46.1, 66.5, 127.7, 128.3, 137.1, 154.8; MS (ESI, *m/z*): 228 ($M + Na^+$).

1,1'-(Dibenzyloxycarbonyl)-2,2'-bipyrrolidine (11)

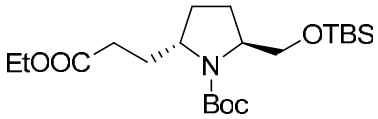


To a solution of *N*,*O*-acetal **8** (0.5 mmol) and $BF_3{\cdot}Et_2O$ (1.0 mmol) in dry THF (10 mL) was dropwise added a freshly prepared *t*-BuOH-containing SmI_2 (0.1 M in THF, 20 mL, 2.0 mmol) at –40 °C. After being stirred for 10 min, the reaction was quenched with a saturated aqueous solution of NH_4Cl (10 mL). The mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column flash chromatography on silica gel to afford **11** as a separable diastereomeric mixture (dr = 50: 50) in a combined yield of 24%, and **10** in 74% yield. **11-H** (less polar diastereomer): 12% yield: white solid; Mp 124.1-125.5 °C (EtOAc/PE 1:3); IR (film) 2964, 2888, 1697, 1406, 1351, 1356, 1332; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60-2.20 (m, 8H), 3.14-3.70 (m, 4H), 3.84-4.30 (2m, 2H), 4.90-5.22 (m, 4H), 7.20-7.24 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8 and 23.4, 27.0 and 27.7 and 28.1 and 28.9, 46.6, and 47.2, 60.0, 66.6 and 67.1, 127.7, 127.8, 128.4, 136.6 and 136.9, 155.7 and 156.0; MS (ESI, *m*/*z*): 431 ($M + Na^+$); Anal. calcd for $C_{24}H_{28}N_2O_4$: C, 70.57; H, 6.91; N, 6.86; Found: C, 70.19; H, 7.13; N, 7.02. **11-L** (more polar diastereomer): 12% yield: colorless oil. IR (film): 2963, 2882, 1702, 1414, 1359, 1207 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50-2.20 (m, 8H), 3.00-3.64 (m, 4H), 3.90-4.05 (m, 2H), 4.90-5.20 (m, 4H), 7.20-7.46 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.7 and 23.3, 28.0 and 28.4 and 28.7 and 28.9, 46.3 and 46.6 and 47.1, 59.2 and 59.4 and 59.6 and 60.0, 66.2 and 66.5 and 66.9 and 67.2, 127.4, 127.8, 128.2 and 128.3 and 128.4, 136.7 and 137.1 and 137.3, 155.0 and 155.1 and 155.3 and 155.4; MS (ESI, *m*/*z*): 431 ($M + Na^+$). Anal. calcd for $C_{24}H_{28}N_2O_4$: C, 70.57; H, 6.91; N, 6.86. Found: C, 70.18; H, 6.74; N, 7.02.

Samarium diiodide-mediated reductive coupling of *N*,*O*-acetals 12a, 12b, 12c with α, β-unsaturated compounds.

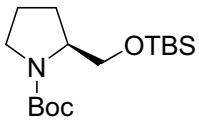
(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-[(*tert*-butyldimethylsilyl)oxymethyl]-2-[2-

(ethyloxycarbonyl)ethyl]pyrrolidine (13)



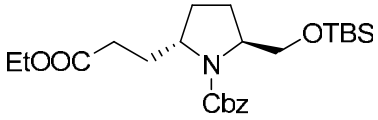
Following **the general procedure,** the reaction of **12a** with ethyl acrylate afforded **13** as an inseparable diastereomeric mixture [(2*S*,5*S*): (2*S*,5*R*) = 63: 31] in a combined yield of 67% and **14a** in 5% yield. **13**: colorless oil. IR (film): 2960, 2932, 2848, 1720, 1406, 1261 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.03 (br s, 6H), 0.87 (br s, 9H), 1.20-1.30 (m, 3H), 1.46 (br s, 9H), 1.52-1.64 (2m, 2H), 1.87-2.40 (m, 6H), 3.36-3.88 (m, 4H), 4.06-4.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.4 and −5.3, 14.2, 18.2, 25.7 and 25.9, 26.6, 28.1 and 28.2, 28.5 and 28.6, 29.5 and 29.7, 31.8, 57.6, 58.6 and 58.7, 60.3 and 60.4, 62.6 and 63.1, 79.2 and 79.3, 153.8, 173.3 and 173.4; MS (ESI, *m/z*): 438 ($M + Na^+$). Anal. calcd for $C_{21}H_{41}NO_5Si$: C, 60.68; H, 9.94; N, 3.37. Found: C, 60.70; H, 9.86; N, 3.63.

(*S*)-1-(*tert*-Butoxycarbonyl)-2-[(*tert*-butyldimethylsilyl)oxymethyl]pyrrolidine (14a)



14a[9]: $[\alpha]^{20}_D$ −42.2 (*c* 1.4, $CHCl_3$); IR (film): 2954, 1697, 1395 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.04 (s, 6H), 0.88 (s, 9H), 1.46 (m, 9H), 1.69-2.08 (m, 4H), 3.25-3.90 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ −5.4, 18.2, 22.8 and 23.9, 25.9, 27.5, 28.2 and 28.6, 46.7 and 47.1, 58.4, 63.7, 79.1, 154.5; MS (ESI, *m/z*): 338 ($M + Na^+$).

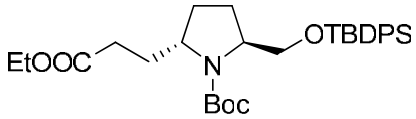
(2*S*,5*S*)-1-(Benzyloxycarbonyl)-5-[(*tert*-butyldimethylsilyl)oxymethyl]-2-[2-(ethyloxycarbonyl)ethyl]pyrrolidine (15)



Following **the general procedure,** the reaction of **12b** with ethyl acrylate afforded **15** as an inseparable diastereomeric mixture [(2*S*,5*S*): (2*S*,5*R*) = 87: 13] in a combined yield of 62% as a colorless oil. HPLC: Shim-pack VP-ODS (150×4.6), CH_3CN/H_2O 75:25, 1.0 mL/min, λ= 220 nm, t_1 25.1 min (9.6%), t_2 26.0 min (90.4%). IR (film): 3033, 2954, 2921, 2860, 1736, 1697, 1473, 1401, 1350 cm^{-1}; ^1H NMR (400 MHz,

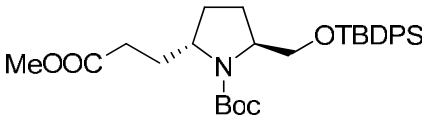
$CDCl_3$): δ –0.20 and 0.10 (br 2s, 6H), 0.80 and 0.90 (br 2s, 9H), 1.16-1.27 (m, 3H), 1.52-1.74 (2m, 2H), 1.90-2.39 (m, 6H), 3.34-3.65 (2m, 1H), 3.66-3.75 (m, 1H), 3.78-3.94 (2m, 2H), 4.02-4.14 (m, 2H), 5.01-5.20 (m, 2H), 7.27-7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ –5.6 and –5.5, 14.1, 18.1, 25.6 and 25.7 and 25.8, 26.1, 26.6, 27.9 and 28.0, 29.3, 31.5 and 31.6, 57.5, 58.0, 58.6, 59.1, 60.3, 62.3, 63.1, 66.5 and 66.6, 127.7, 127.8, 127.9, 128.2, 128.3, 128.4, 136.6 and 136.7, 154.1 and 154.2, 172.9 and 173.1; MS (ESI, *m/z*): 472 (M + Na^+). Anal. calcd for $C_{24}H_{39}NO_5Si$: C, 64.11; H, 8.74; N, 3.11. Found: C, 64.34; H, 8.95; N, 3.38.

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-[(*tert*-butyldiphenylsilyl)oxymethyl]-2-[2-(ethyloxycarbonyl)ethyl]pyrrolidine (16a)



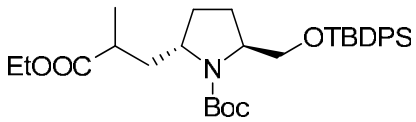
Following **the general procedure,** the reaction of **12c** with ethyl acrylate afforded **16a** as an inseparable diastereomeric mixture [(2*S*,5*S*): (2*S*,5*R*) = 91: 9] in a combined yield of 73% as a colorless oil. HPLC: Shim-pack VP-ODS (150×4.6), CH_3CN/H_2O 75:25, 1.5 mL/min, λ= 220 nm, t_1 37.1 min (8.8%), t_2 40.1 min (91.2%). IR (film): 3072, 2966, 2921, 2854, 1736, 1685, 1473, 1389 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.06 (s, 9H), 1.19-1.27 (m, 3H), 1.29 and 1.48 (br 2s, 9H), 1.54-1.75 (2m, 2H), 1.85-2.40 (m, 6H), 3.42-4.00 (4m, 4H), 4.05-4.18 (m, 2H), 7.33-7.46 (m, 6H), 7.61-7.71 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 19.2, 25.9 and 26.0, 26.7 and 26.8, 28.2, 28.3, 28.5, 29.5, 31.7, 57.5, 58.4 and 58.5, 60.2, 63.5 and 63.8, 79.2, 127.6, 127.7, 129.5 and 129.6, 133.4 and 133.5 and 133.7, 135.5, 153.6, 173.2 and 173.3; MS (ESI, *m/z*): 562 (M + Na^+). Anal. calcd for $C_{31}H_{45}NO_5Si$: C, 68.98; H, 8.40; N, 2.59. Found: C, 68.63; H, 8.18; N, 2.63.

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-[(*tert*-butyldiphenylsilyl)oxymethyl]-2-[2-(methyloxycarbonyl)ethyl]pyrrolidine (16b)



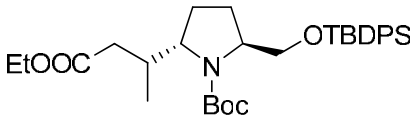
Following **the general procedure,** the reaction of **12c** with methyl acrylate afforded **16b** as an inseparable diastereomeric mixture [(2*S*,5*S*): (2*S*,5*R*) = 91: 9] in a combined yield of 74% as a colorless oil. HPLC: Shim-pack VP-ODS (150×4.6), CH_3CN/H_2O 75:25, 1.0 mL/min, λ= 220 nm, t_1 45.4 min (8.8%), t_2 49.0 min (91.2%). IR (film): 3072, 2954, 2927, 2854, 1736, 1691, 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.04 (br s, 9H), 1.30 and 1.48 (br 2s, 9H), 1.54-1.75 (m, 2H), 1.92-2.44 (m, 6H), 3.38-4.02 (m, 7H), 7.32-7.54 (m, 6H), 7.58-7.76 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 26.0, 26.7 and 26.8, 28.2, 28.3 and 28.5, 29.4, 31.4 and 31.5, 51.6, 57.5, 58.4 and 58.5, 63.5 and 63.7, 79.2, 127.6 and 127.7, 129.5 and 129.6, 133.5, 135.5, 153.7, 173.8; MS (ESI, *m/z*): 548 ($M + Na^+$). Anal. calcd for $C_{30}H_{43}NO_5Si$: C, 68.53; H, 8.24; N, 2.66. Found: C, 68.56; H, 8.15; N, 3.05.

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-[(*tert*-butyldiphenylsilyl)oxymethyl]-2-[2-(ethyloxycarbonyl)propyl]pyrrolidine (16c)



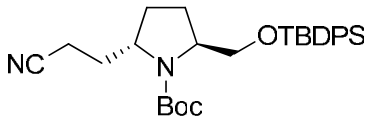
Following **the general procedure,** the reaction of **12c** with ethyl methacrylate afforded **16c** as an inseparable diastereomeric mixture (dr = 91: 6: 3) in a combined yield of 74% as a colorless oil. HPLC: Shim-pack VP-ODS (150×4.6), CH_3CN/H_2O 75:25, 1.5 mL/min, λ= 220 nm, t_1 49.9 min (2.9%), t_2 53.5 min (6.1%), t_3 55.5 min (91.0%). IR (film): 3072, 2965, 2921, 1736, 1697, 1389, 1373 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.07 (s, 9H), 1.16-1.29 (2m, 6H), 1.29 and 1.48 (br 2s, 9H), 1.53-2.58 (m, 7H), 3.40-4.01 (4m, 4H), 4.06-4.23 (m, 2H), 7.32-7.49 (m, 6H), 7.60-7.72 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 and 14.2, 16.6 and 16.9, 17.6 and 17.8, 19.2, 25.6 and 25.9, 26.6 and 26.8, 28.3, 28.5, 36.4, 36.9, 37.3, 37.5, 37.8, 38.3, 56.0 and 56.4, 58.3, 60.1 and 60.3, 63.5 and 63.8, 78.9 and 79.1 and 79.2, 127.6, 129.5 and 129.6, 133.4 and 133.6 and 133.7 , 135.5, 153.5, 175.9 and 176.1; MS (ESI, *m/z*): 576 ($M + Na^+$). Anal. calcd for $C_{32}H_{47}NO_5Si$: C, 69.40; H, 8.55; N, 2.53. Found: C, 69.17; H, 8.18; N, 2.73.

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-[(*tert*-butyldiphenylsilyl)oxymethyl]-2-[2-(ethyloxycarbonyl)-1-methylethyl]pyrrolidine (16d)



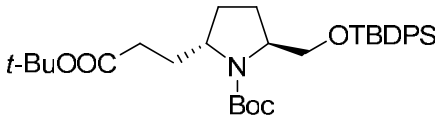
Following **the general procedure,** the reaction of **12c** with ethyl crotonate afforded **16d** as an inseparable diastereomeric mixture (dr: = 67: 33, determined by ^{1}H NMR at variant temperatures) in a combined yield of 48% and **14b** in 20% yield. **16d**: colorless oil. IR (film): 3078, 2966, 2921, 2859, 1736, 1691, 1473, 1384 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82-0.95 (2m, 3H), 1.05 (s, 9H), 1.16-1.35 (m, 3H), 1.28 and 1.48 (2s, 9H), 1.60-2.17 (m, 5H), 2.21-2.38 (m, 1H), 2.66-2.94 (m, 1H), 3.42-4.04 (m, 4H), 4.05-4.20 (m, 2H), 7.32-7.46 (m, 6H), 7.58-7.71 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2 and 14.4, 14.8, 19.2, 24.2, 25.2, 26.8, 27.2 and 27.4, 28.4 and 28.5, 32.1, 33.1, 39.1 and 39.5, 59.1 and 59.4, 60.1 and 60.2, 61.5 and 61.6, 63.6 and 64.0, 79.1 and 79.3, 127.6, 129.5 and 129.6, 133.5 and 133.7, 135.5, 153.8, 172.7 and 172.9; MS (ESI, *m/z*): 576 (M + Na^+). Anal. calcd for $C_{32}H_{47}NO_5Si$: C, 69.40; H, 8.55; N, 2.53. Found: C, 69.22; H, 8.69; N, 2.70.

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-[(*tert*-butyldiphenylsilyl)oxymethyl]-2-[2-cyanoethyl]pyrrolidine (16e)



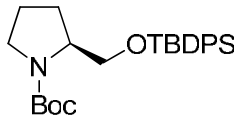
Following **the general procedure,** the reaction of **12c** with acrylonitrile afforded **16e** as a colorless oil in 73% yield. $[\alpha]^{20}_{D}$ –40 (*c* 1.0, $CHCl_3$); IR (film): 3078, 2960, 2932, 2854, 2239, 1686, 1378 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (s, 9H), 1.29 and 1.49 (br 2s, 9H), 1.54-1.76 (m, 2H), 1.92-2.43 (m, 6H), 3.40-4.00 (4m, 4H), 7.35-7.47 (m, 6H), 7.60-7.68 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.5, 19.2, 25.9, 26.3, 26.8, 27.2, 28.3 and 28.5, 29.2, 29.8, 57.2, 58.6, 63.5 and 63.8, 79.7 and 79.8, 119.6, 127.7, 129.6, 129.7, 133.3 and 133.5, 135.5, 153.8; MS (ESI, *m/z*): 515 (M + Na^+). Anal. calcd for $C_{29}H_{40}N_2O_3Si$: C, 70.69; H, 8.18; N, 5.69. Found: C, 70.59; H, 8.43; N, 6.02.

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-2-[2-(*tert*-butyloxycarbonyl)ethyl]-5-[(*tert*-butyldiphenylsilyl)oxymethyl]-pyrrolidine (16f)



Following **the general procedure,** the reaction of **12c** with *tert*-butyl acrylate afforded **16f** as an inseparable diastereomeric mixture [(2*S*,5*S*): (2*S*,5*R*) = 92: 8] in a combined yield of 53% and **14c** in 12% yield as a colorless oil. HPLC: Shim-pack VP-ODS (150×4.6), CH_3CN/H_2O 75:25, 1.5 mL/min, λ= 220 nm, t_1 73.0 min (7.7%), t_2 80.9 min (92.3%). IR (film): 3072, 2966, 2927, 2848, 1730, 1686, 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.05 (s, 9H), 1.29 (s, 5H), 1.40-1.49 (m, 13H), 1.52-1.70 (m, 2H), 1.92-2.32 (m, 6H), 3.39-4.01 (4m, 4H), 7.32-7.46 (m, 6H), 7.60-7.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 25.9 and 26.0, 26.7 and 26.8, 28.1, 28.2, 28.4, 28.5, 29.7, 33.0, 57.6 and 57.7, 58.3 and 58.4 and 58.6, 63.6 and 63.9, 79.1, 80.1 and 80.2, 127.6, 129.5 and 129.6, 133.5 and 133.6 and 133.8, 135.5, 153.6 and 153.8, 172.6 and 172.7; MS (ESI, *m/z*): 590 ($M + Na^+$). Anal. calcd for $C_{33}H_{49}NO_5Si$: C, 69.80; H, 8.70; N, 2.47. Found: C, 69.52; H, 9.02; N, 2.82.

(*S*)-1-(*tert*-Butoxycarbonyl)-2-[(*tert*-butyldiphenylsilyl)oxymethyl]pyrrolidine (14c)

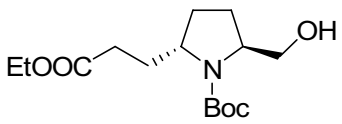


14c:[10] $[\alpha]^{20}_D$ –33.8 (*c* 1.8, $CHCl_3$); IR (film): 3072, 2971, 2932, 2859, 1691, 1383 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.06 (s, 9H), 1.35 and 1.47 (br 2s, 9H), 1.70-2.20 (m, 4H), 3.30-4.05 (m, 5H), 7.30-7.48 (m, 6H), 7.60-7.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2, 23.0, 26.8, 27.7, 28.4, 46.6 and 47.1, 58.3, 64.2 and 64.6, 79.1, 127.6, 129.6, 133.5 and 133.7, 135.5, 154.5; MS (ESI, *m/z*): 462 ($M + Na^+$).

Determination of the diastereomeric ratios of compounds 13 and 16d

The diastereomeric ratio of compound **13** was determined via desilylation.

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-(hydroxymethyl)-2-[2-(ethyloxycarbonyl)-ethyl] pyrrolidine (23)

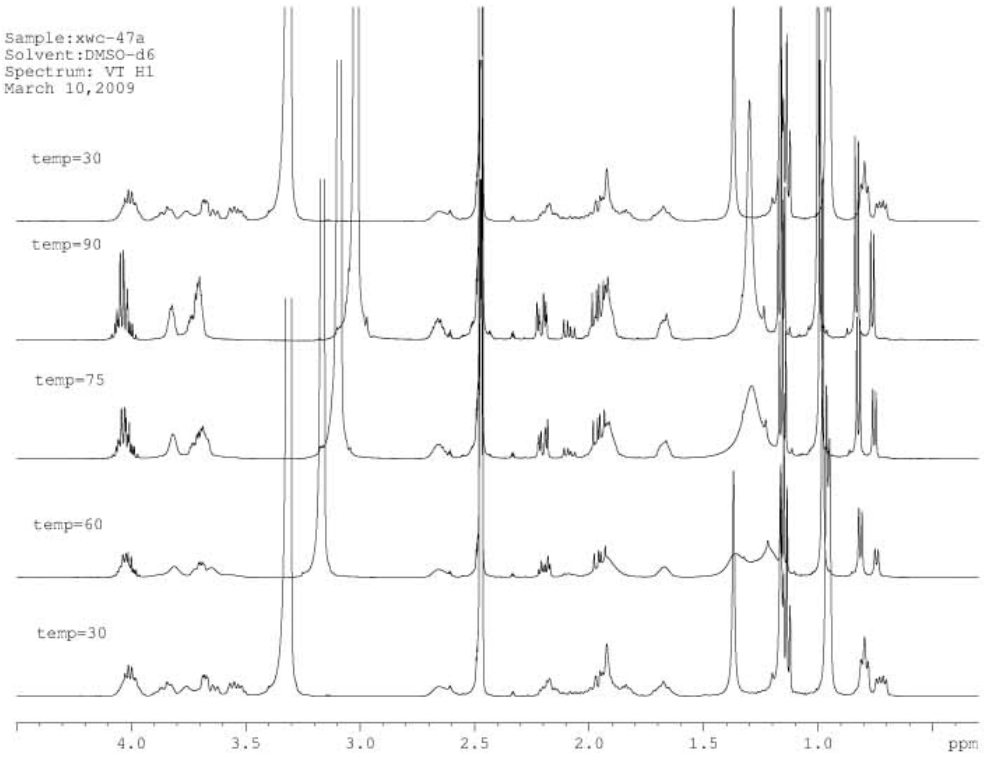


To a solution of compound **13** (92 mg, 0.22 mmol) in THF (6 mL) was added a 1M THF solution of Bu_4NF (0.24 mL, 0.24 mmol), and the resulting solution was stirred at room temperature for 3h. After removing the solvent, the residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE 1:3) to afford (2*S*,5*R*)-**23** and (2*S*,5*S*)-**23** (31:69) in a combined yield of 82%. (2*S*,5*S*)-**23** (Less polar diastereomer), 25.4% yield: Colorless oil: $[\alpha]^{20}_D$ –5.5 (*c* 0.8, $CHCl_3$); IR (film): 3435, 2971, 2927, 1736, 1686, 1389 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.25 (t, *J* = 7.1 Hz, 3H), 1.47 (s, 9H), 1.61-1.65 (m, 3H), 1.82-2.06 (m, 3H), 2.25-2.44 (m, 2H), 3.45-3.54 (m, 1H), 3.66-3.80 (m, 1H), 3.84-4.03 (m, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 4.80 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 26.6, 28.4, 29.5, 30.4, 31.5, 58.7, 60.4, 61.3, 68.1, 80.7, 157.3, 173.3; MS (ESI, *m/z*): 324 (M + Na^+). (2*S*,5*S*)-**23** (More polar diastereomer), 56.6% yield: $[\alpha]^{20}_D$ –44.9 (*c* 1.3, $CHCl_3$); IR (film): 3441, 2966, 2927, 1730, 1686, 1395 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.24 (t, *J* = 7.1 Hz, 3H), 1.44 (s, 9H), 1.55-1.68 (m, 3H), 1.89-2.12 (m, 3H), 2.17-2.35 (m, 2H), 3.44-3.62 (m, 1H), 3.63-3.83 (m, 2H), 3.92-4.05 (m, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 4.27-4.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 26.6, 28.1, 28.4, 28.9, 31.6, 58.2, 59.9, 60.4, 67.4, 80.5, 156.2, 173.0; MS (ESI, *m/z*): 324 (M + Na^+).

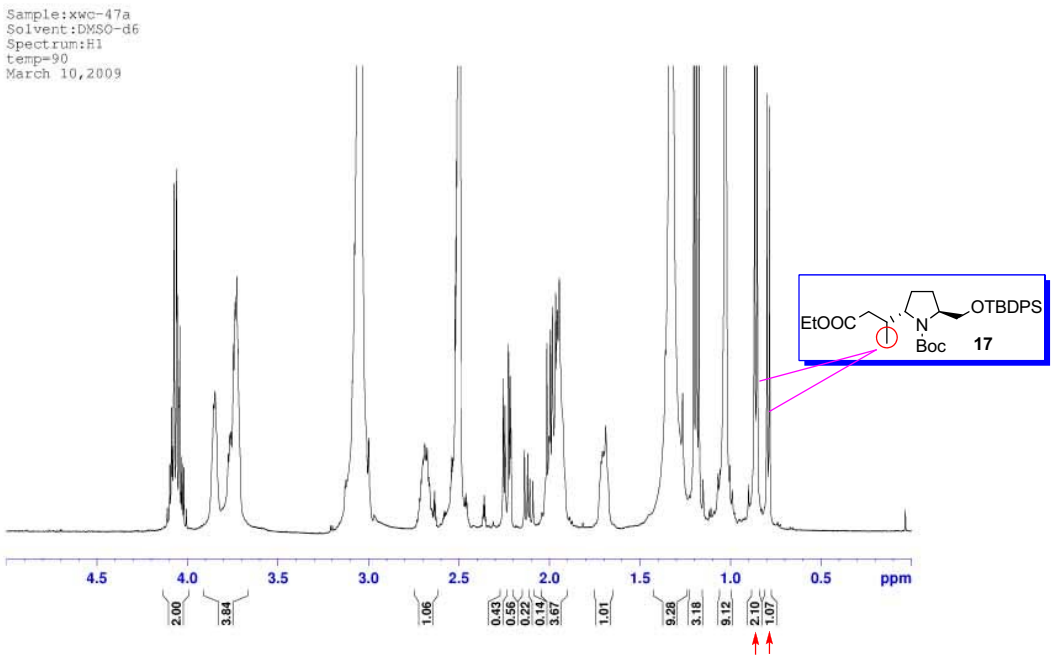
Determination of the diastereomeric ratio of compound 16d:

^1H NMR experiments of **16d** were performed in deuterated DMSO at variant temperatures. At 90 °C, the ^1H NMR spectra of **16d** in deuterated DMSO simplified and two isomers were observed. According to the integration of the β-aminomethyl proton, compound **16d** is a mixture of two diastereomers in a ratio of 2:1.

The overlaped ^{1}H NMR spectra of 16d in DMSO-d_6 under the different temperatures.

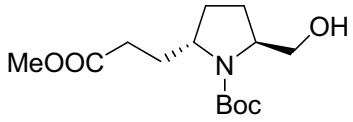


The ^{1}H NMR spectra of compound 16d in DMSO-d_6 at 90 ^{o}C.



Synthesis of (+)-Xenovenine

(2*S*,5*S*)-1-(*tert*-Butyloxycarbonyl)-5-(hydroxymethyl)-2-[2-(methyloxycarbonyl)ethyl]pyrrolidine (17)

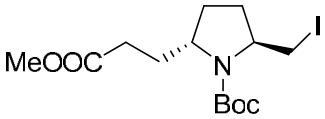


To a solution of compound **16b** (674 mg, 1.28 mmol) in THF (5 mL) was added a 1M solution of Bu_4NF in THF (1.93 mL, 1.93 mmol). The resulting solution was stirred at room temperature for 2 h. After concentration, the residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE 1:4) to afford (2*S*,5*R*)-**17** and (2*S*,5*S*)-**17** (1:10) in a combined yield of 85%.

(2*S*,5*R*)-**17** (Less polar diastereomer): 8% yield. Colorless oil: $[\alpha]^{20}_D$ –8.0 (*c* 1.3, $CHCl_3$); IR (film): 3418, 2971, 1736, 1686, 1663, 1395 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 9H), 1.49-1.68 (m, 3H), 1.78-2.10 (m, 3H), 2.18-2.50 (m, 2H), 3.40-3.50 (m, 1H), 3.63 (s, 3H), 3.66-3.80 (m, 1H), 3.82-4.00 (m, 2H), 4.82 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.4, 28.3, 29.4, 30.3, 31.1, 51.6, 58.5, 61.2, 68.0, 80.6, 157.3, 173.7; MS (ESI, *m/z*): 310 (M+ Na^+). Anal. calcd for $C_{14}H_{25}NO_5$: C, 58.52; H, 8.77; N, 4.87. Found: C, 58.75; H, 8.88; N, 5.04.

(2*S*,5*S*)-**17** (More polar diastereomer): 77% yield. Colorless oil: $[\alpha]^{20}_D$ –46.7 (*c* 1.3, $CHCl_3$); IR (film): 3402, 2960, 1747, 1680, 1669, 1389 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.43 (s, 9H), 1.52-1.66 (m, 3H), 1.84-2.05 (m, 3H), 2.05-2.50 (m, 2H), 3.39-3.57 (2m, 1H), 3.63 (s, 3H), 3.64-3.79 (m, 2H), 3.91-3.99 (m, 1H), 4.39 (br s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.5, 27.9, 28.4, 28.7, 31.2, 51.6, 58.0, 59.8, 67.1, 80.4, 156.0, 173.4; MS (ESI, *m/z*): 310 (M + Na^+). Anal. calcd for $C_{14}H_{25}NO_5$: C, 58.52; H, 8.77; N, 4.87. Found: C, 58.75; H, 8.88; N, 5.04.

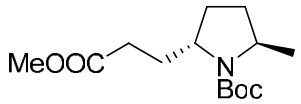
(2*S*,5*S*)-1-(*tert*-Butyloxylcarbonyl)-2-iodomethyl-5-[2-(methyloxylcarbonyl)ethyl] pyrrolidine (18)



To a suspension of imidazole (82 mg, 1.21 mmol) and triphenylphosphine (237 mg, 0.91 mmol) in THF (5 mL) at 0 °C under N_2 was added iodine (230 mg, 0.91 mmol)

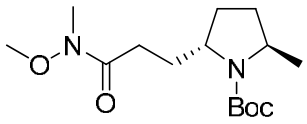
in three portions over 30 min. A red-brownish solid was formed. After stirring for an additional 10 min at rt, a solution of **17** (173 mg, 0.60 mmol) in THF (2 mL) was added. The red-brownish solid become yellowish after about 1 h. The pale yellow reaction mixture was filtered through Celite, and the filtrate concentrated under reduced pressure. The residue was purified by flash chromatography (eluent: EtOAc/PE 1:10) to yield iodide **18** (206 mg, yield: 86%) as a pale yellow oil. $[\alpha]^{20}_{D}$ –24.3 (*c* 0.9, $CHCl_3$); IR (film): 1736, 1697, 1395 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.40 (s, 9H), 1.50-1.63 (m, 2H), 1.85-2.12 (m, 4H), 2.14-2.34 (m, 2H), 2.88-3.11 (2m, 1H), 3.33-3.60 (2m, 1H), 3.60 (br s, 3H), 3.67-3.83 (2m, 1H), 3.87-4.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.7 and 8.9, 26.2, 27.0, 27.8, 28.3, 28.9, 29.5, 31.1 and 31.3, 51.4 and 51.5, 57.8, 58.4, 58.8, 79.8, 153.2 and 153.5, 173.2 and 173.4; MS (ESI, *m/z*): 420 (M+ Na^+). Anal. calcd for $C_{14}H_{24}INO_4$: C, 42.33; H, 6.09; N, 3.53. Found: C, 42.69; H, 6.40; N, 3.53.

(2*S*,5*R*)-1-(*tert*-Butyloxylcarbonyl)-5-methyl-2-[2-(methyloxylcarbonyl)ethyl]-pyrrolidine (19)



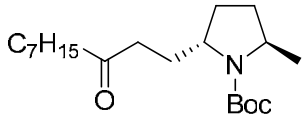
The mixture of **18** (206 mg, 0.52 mmol), triethylamine (0.07 mL, 0.52 mmol) and 10% palladium on carbon (20.6 mg) in methanol (5 mL) was allowed to react at room temperature under a blanket of hydrogen gas overnight (MS indicated that all the starting material was consumed). The reaction mixture was filtered through Celite and the residue was washed with methanol. The combined organic layers were concentrated. The residue was purified by flash chromatography (eluent : EtOAc/PE 1:6) to afford **19** (136 mg, yield: 97%) as a colorless oil . $[\alpha]^{20}_{D}$ –42.5 (*c* 1.3, $CHCl_3$); IR (film): 1741, 1691, 1406 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.05-1.15 (m, 3H), 1.43 (s, 9H), 1.45-1.65 (2m, 3H), 1.90-2.13 (m, 3H), 2.16-2.38 (m, 2H), 3.63 (br s, 3H), 3.65-3.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.2 and 20.3, 26.6 and 27.4, 28.5, 29.4 and 29.7, 30.5, 31.4, 51.5, 53.0, 56.9, 78.9 and 79.0, 153.7 and 154.0, 173.6 and 173.8; MS (ESI, *m/z*): 294 (M + Na^+). HRMS calcd for $[C_{14}H_{25}NO_4+H]^+$: 272.1862; found: 272.1852.

(2*S*,5*R*)-1-(*tert*-Butyloxylcarbonyl)-5-methyl-2-[2-(*N*-methyl-*N*-methyloxylamine carbonyl)ethyl]pyrrolidine (20)



To a solution of *N*,*O*-dimethylhydroxylamine hydrochloride salt (65 mg, 0.66 mmol) in CH_2Cl_2 (2 mL) at 0 °C was dropwise added $AlMe_3$ (0.66 mL of a 1M solution in toluene, 0.66 mmol). After being stirred for 30 min, a solution of ester **19** (60 mg, 0.22 mmol) in CH_2Cl_2 (1 mL) was added. The mixture was stirred for 3 h at rt, then quenched with a saturate aqueous solution of $KHSO_4$, and filtered through Celite. The filtrate was extracted with EtOAc, dried over Na_2SO_4, and filtered. And concentrated. The residue was purified by flash chromatography (eluent: EtOAc/PE 1:4) to afford **20** (54 mg, yield: 81%) as a colorless oil. $[\alpha]^{20}_D$ –45.2 (*c* 2.7, $CHCl_3$); IR (film): 2966, 2921, 1686, 1596, 1384, 1361 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.08-1.20 (2m, 3H), 1.44 (s, 9H), 1.46-2.55 (m, 8H), 3.10-3.20 (m, 3H), 3.66 (s, 3H), 3.68-3.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.3 and 20.4, 26.7, 27.5, 28.5, 29.2, 29.5, 29.7, 30.5, 32.1, 52.85 and 52.91, 57.2, 61.2, 78.8 and 78.9, 153.7 and 154.0, 174.3; MS (ESI, *m/z*): 323 (M+ Na^+). HRMS calcd for $[C_{15}H_{28}N_2O_4+H]^+$: 301.2127; found: 301.2116.

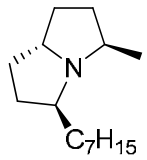
(2*S*,5*R*)-1-(*tert*-Butyloxycarbonyl)-5-methyl-2-(3-oxodecyl)pyrrolidine (21)



A solution of 1-bromoheptane (0.91 mL, 5.79 mmol) in THF (5 mL) was dropwise added to magnesium (135 mg, 5.62 mmol) at rt under argon, initiated by a little heating. After 1 h, the Grignard reagent was added to a solution of **20** (541 mg, 1.80 mmol) in THF (2 mL) at rt. The reaction mixture was stirred at 50 °C for 3 h, cooled and quenched with saturated aqueous NH_4Cl, extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (eluent: EtOAc/PE 1:25) to afford **21** (489 mg, yield: 80%) as a colorless oil. $[\alpha]^{20}_D$ –44.3 (*c* 1.0, $CHCl_3$); IR (film): 2921, 2854, 1697, 1400 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (t, *J* = 6.5 Hz, 3H), 1.06-1.18

(2m, 3H), 1.21-1.34 (m, 9H), 1.45 (s, 9H), 1.50-1.65 (m, 5H), 1.88-2.14 (m, 3H), 2.30-2.45 (m, 3H), 3.60-4.02 (4m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 20.4, 22.6, 23.9, 26.8, 27.5 and 27.6, 28.3 and 28.6, 29.1 and 29.2, 29.7, 30.6, 31.7, 40.0 and 40.2, 42.7 and 42.8, 53.0, 57.1, 78.9, 153.7 and 154.1, 210.6 and 211.0; MS (ESI, *m/z*): 362 (M+ Na^+). HRMS calcd for $[C_{20}H_{37}NO_3+Na]^+$: 362.2671; found: 362.2673.

(+)-Xenovenine (22)



To a solution of **21** (97 mg, 0.29 mmol) in EtOAc was added 2 mL of a 2*N* HCl/EtOAc solution, and the mixture was stirred at rt for 6 h. The solvent was removed and the residue was dissolved in MeOH and neutralized with a 2*N* MeONa/MeOH solution. The mixture was hydrogenated with H_2 from a balloon in the presence of 10% Pd/C (28 mg) for 6 h. After filtration through Celite, the residue was washed with methanol. The combined organic layers were concentrated and the residue was purified by column chromatography (eluent: CH_2Cl_2/MeOH/$NH_3 \cdot H_2O$ 200:1:2) to afford (+)-xenovenine (**22**) (27 mg, yield: 42%) as a colorless oil. $[\alpha]^{20}_D$ +7.5 (*c* 2.0, $CHCl_3$) {lit.[11a] $[\alpha]^{20}_D$ +9 (*c* 2.13, $CHCl_3$); lit.[11b] $[\alpha]^{22}_D$ +6.6 (*c* 2.35, $CHCl_3$); lit.[11c] $[\alpha]_D^{24}$ +11.3 (*c* 2.255 , $CHCl_3$)}; IR (film): 2954, 2921, 2584, 1406 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (t, *J* = 7.1 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 3H), 1.15-1.60 (m, 16H), 1.85-2.05 (m, 4H), 2.55-2.65 (m, 1H), 2.70-2.82 (m, 1H), 3.55-3.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 21.9, 22.6, 27.2, 29.3, 29.9, 31.7, 31.8, 32.1, 32.4, 34.5, 37.1, 61.7, 65.0, 66.6; MS (ESI, *m/z*) : 224 (M + H^+).

Reference

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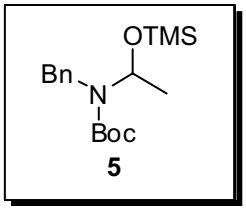
OTMS
Bn
N
Boc

5

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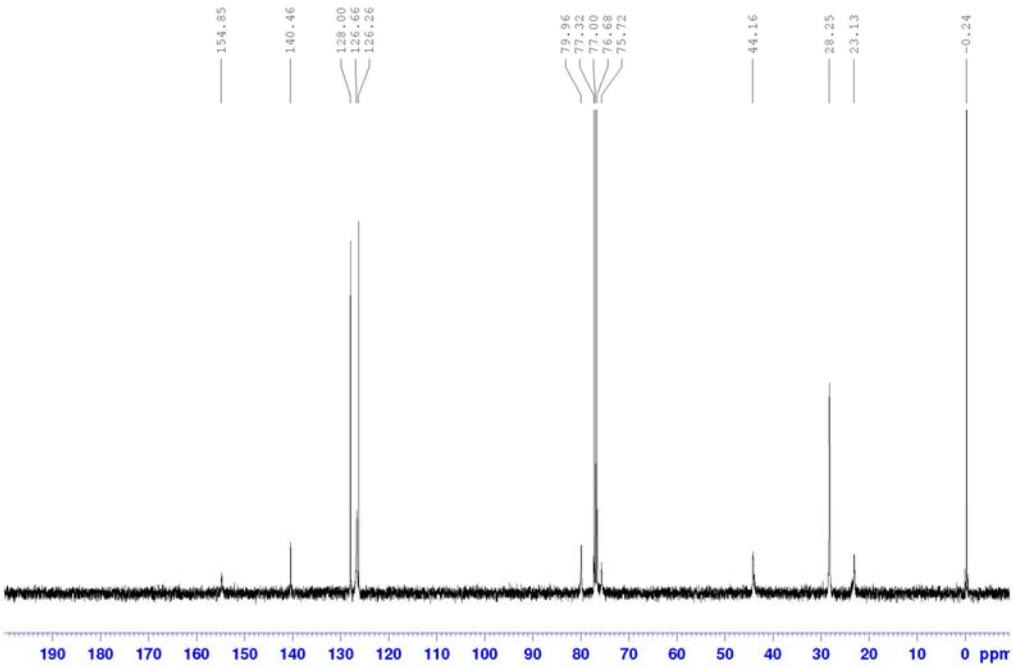
0.92
1.98
12.27
8.95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140.46
128.00
126.66
126.26
79.96
77.32
77.00
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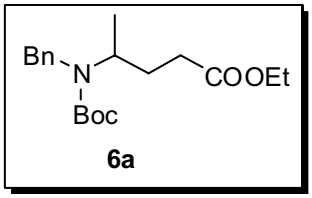
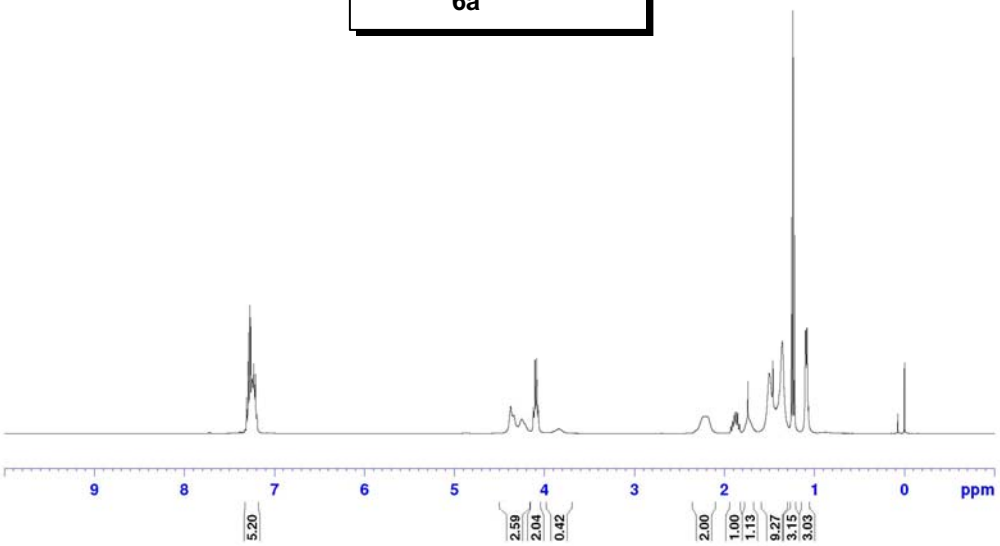
75.72
44.16
28.25
23.13
-0.24
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


Bn
N
Boc
COOEt

6a


9
8
7
6
5
4
3
2
1
0
ppm
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2.04
0.42
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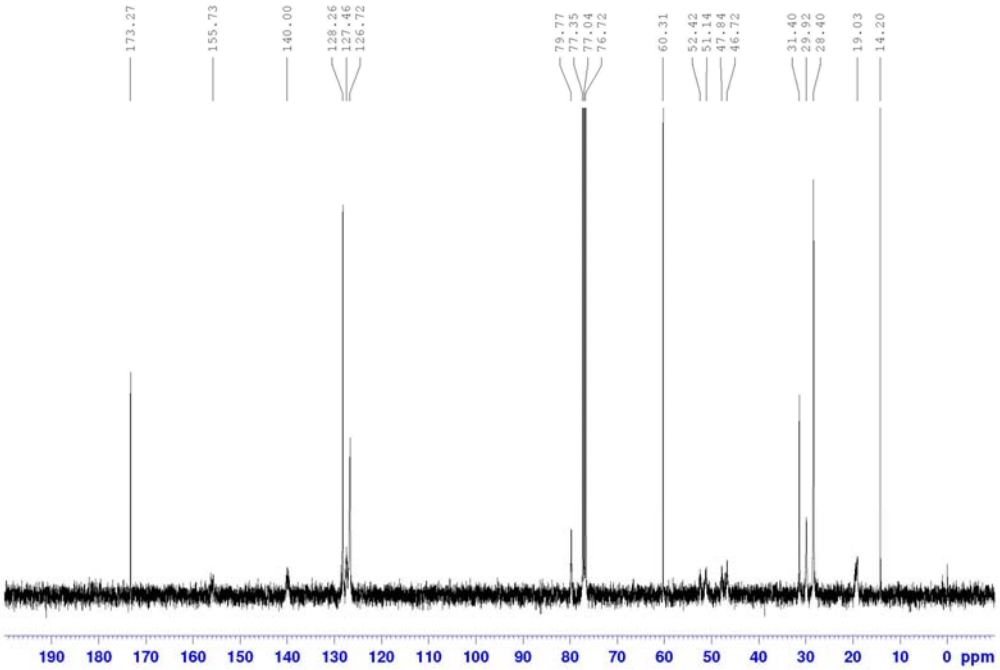
1.00
1.13
9.27
3.15
3.03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77.35
77.04
76.72
60.31
52.42
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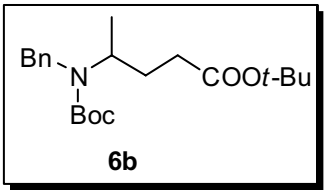
47.84
46.72
31.40
29.92
28.40
19.03
14.20
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


Bn
N
Boc
COO*t*-Bu

6b

9
8
7
6
5
4
3
2
1
0
ppm
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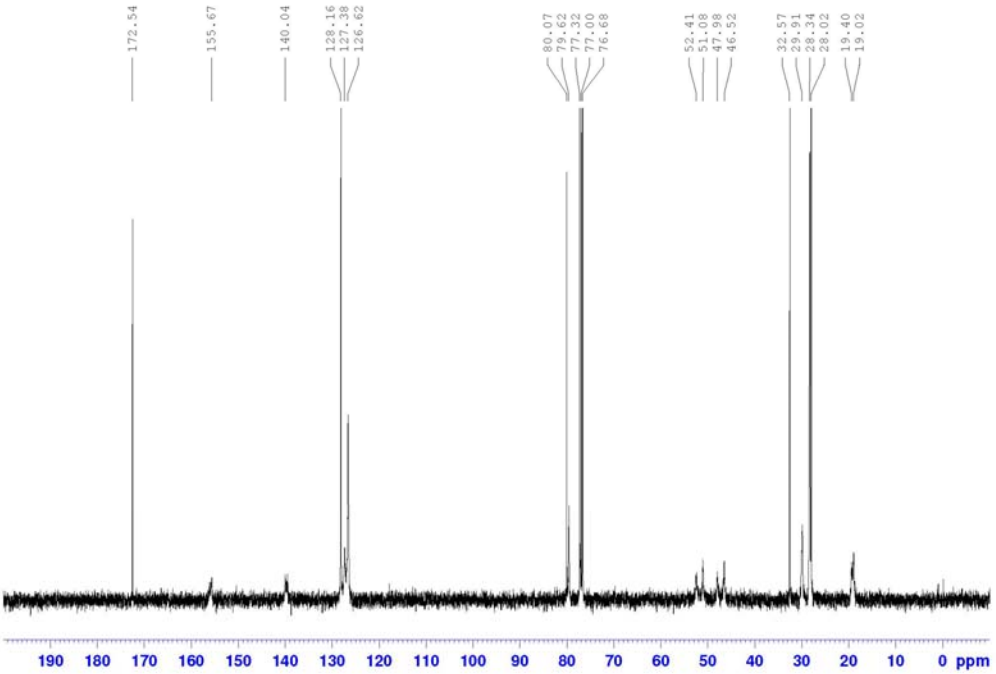
2.96
2.00
2.19
18.30
3.04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77.00
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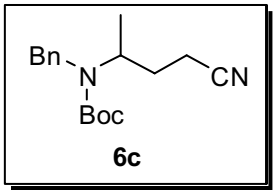
52.41
51.08
47.98
46.52
32.57
29.91
28.34
28.02
19.40
19.02
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


Bn
N
Boc
CN

6c

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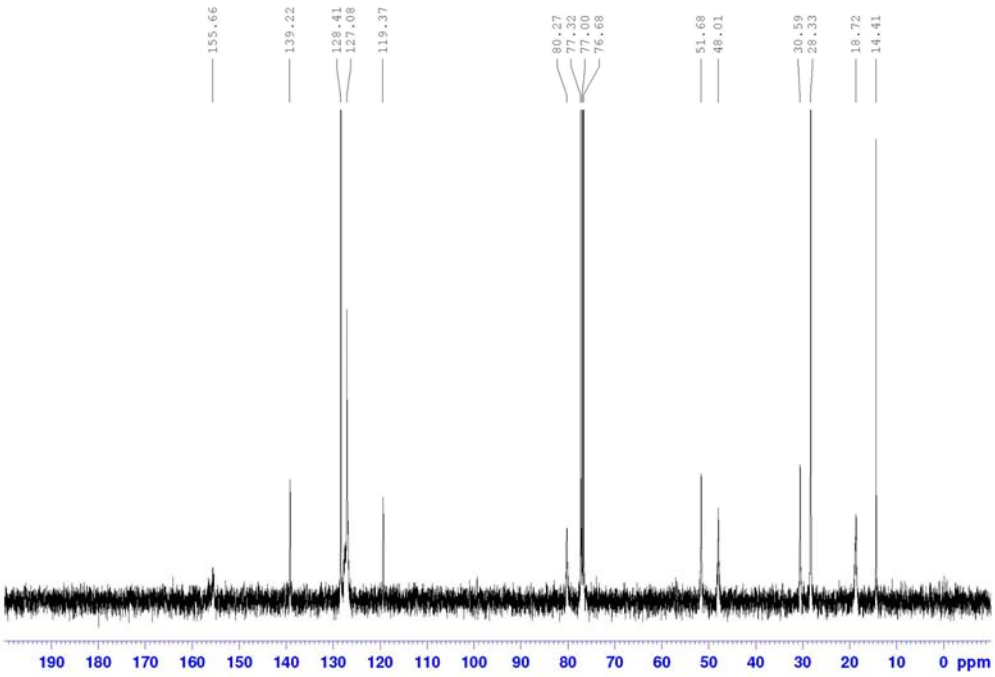
3.06
3.07
1.17
9.02
3.00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14.41
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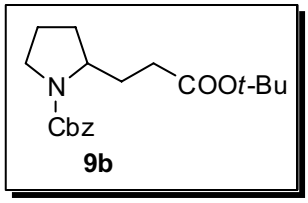
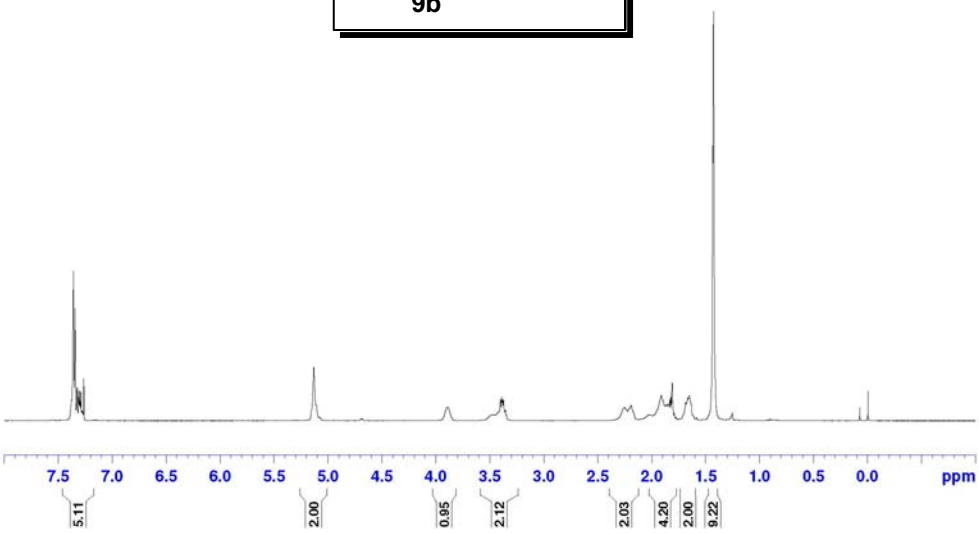

N
Cbz
COO*t*-Bu

9b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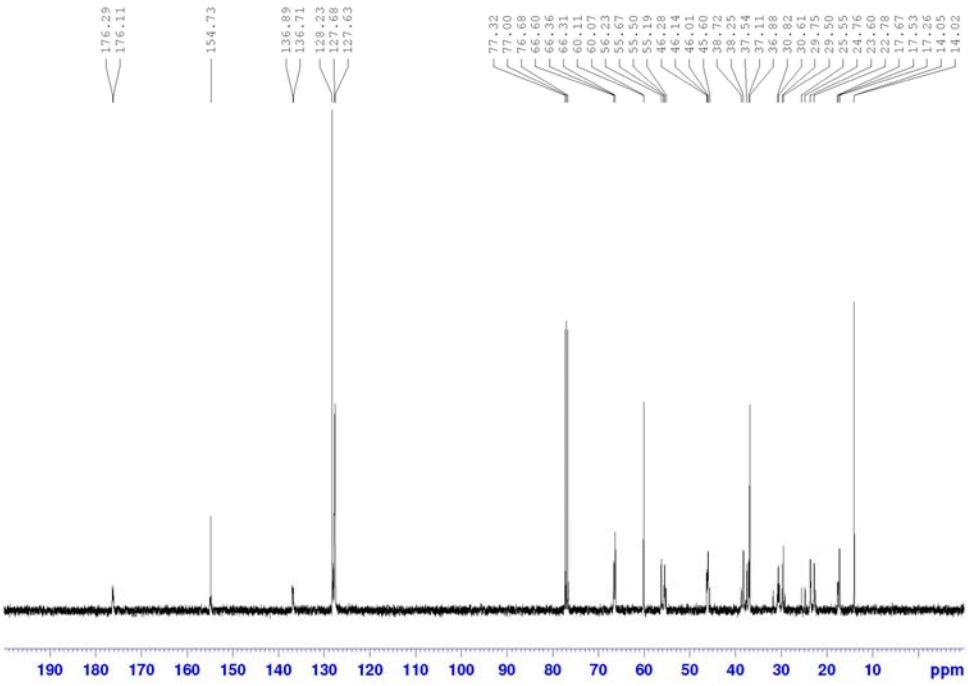
2.00
0.95
2.12
2.03
4.20
2.00
9.22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176.11
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136.71
128.23
127.68
127.63
77.32
77.00
76.68
66.60
66.36
66.31
60.11
60.07
56.23
55.67
55.50
55.19
46.28
46.14
46.01
45.60
38.72
38.25
37.54
37.11
36.88
30.82
30.61
29.75
29.50
25.55
24.76
23.60
22.78
17.67
17.53
17.26
14.05
14.02
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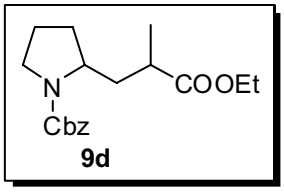
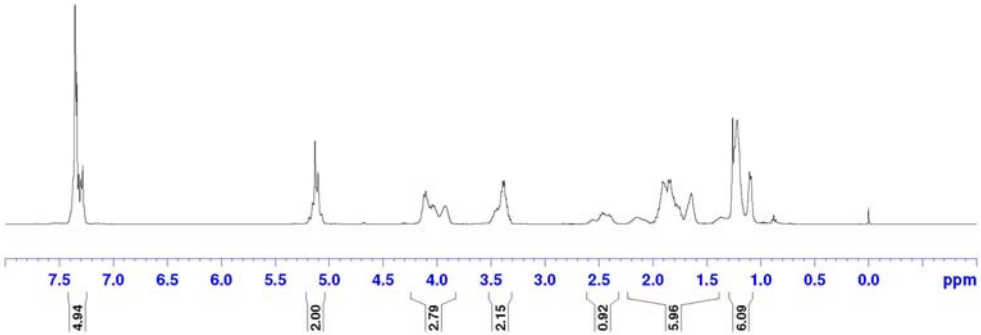

N
Cbz
COOEt

9d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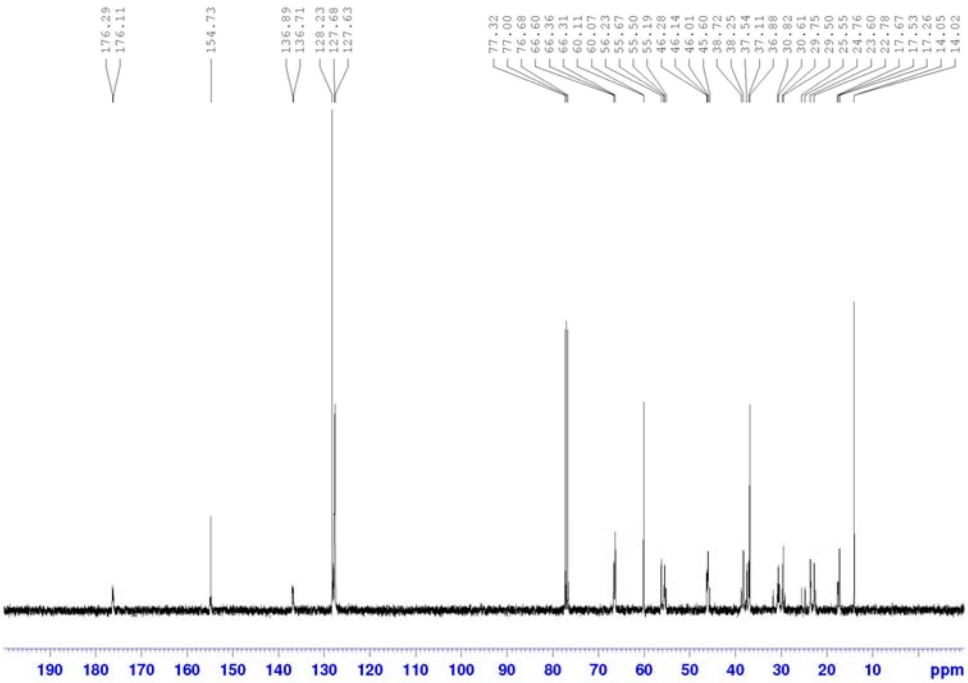
2.79
2.15
0.92
5.96
6.09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176.11
154.73
136.89
136.71
128.23
127.68
127.63
77.32
77.00
76.68
66.60
66.36
66.31
60.11
60.07
56.23
55.67
55.50
55.19
46.28
46.14
46.01
45.60
38.72
38.25
37.54
37.11
36.88
30.82
30.61
29.75
29.50
25.55
24.76
23.60
22.78
17.67
17.53
17.26
14.05
14.02
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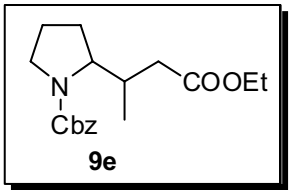
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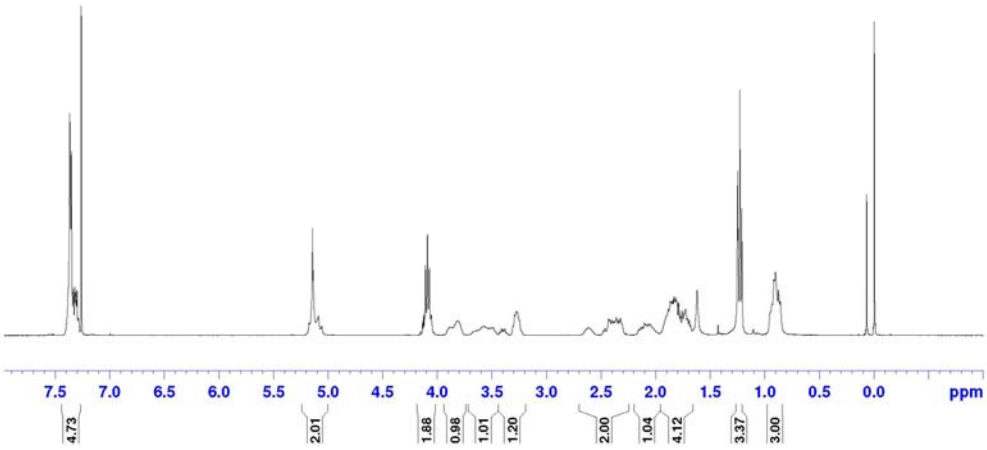
Cbz
COOEt

9e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1.88
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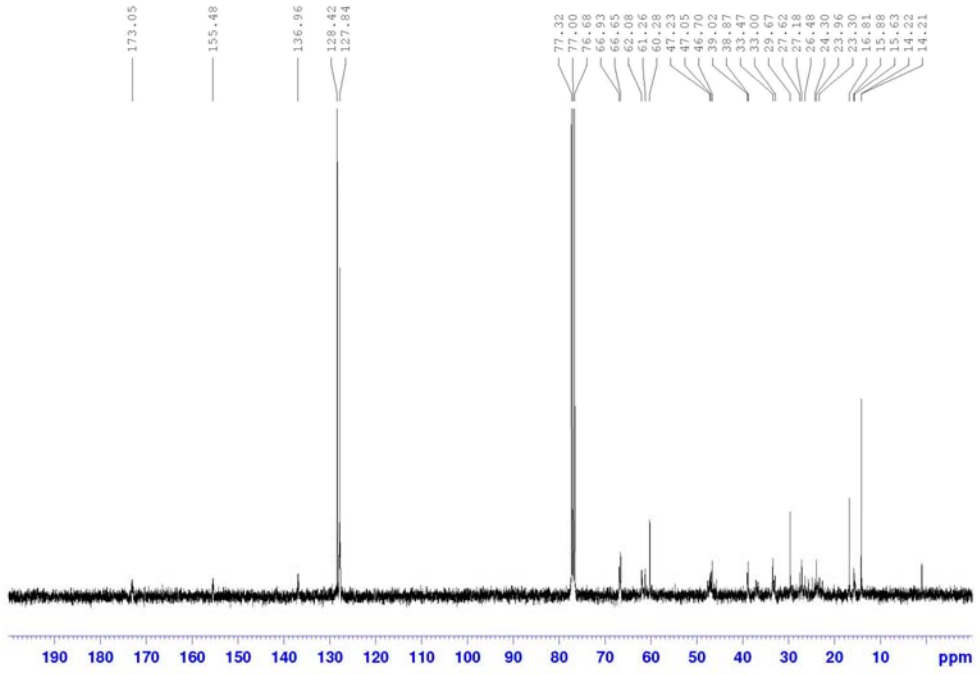
1.01
1.20
2.00
1.04
4.12
3.37
3.00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76.68
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66.65
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60.28
47.23
47.05
46.70
39.02
38.87
33.47
33.00
29.67
27.62
27.18
26.48
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16.81
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15.63
14.22
14.21
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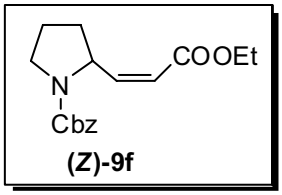
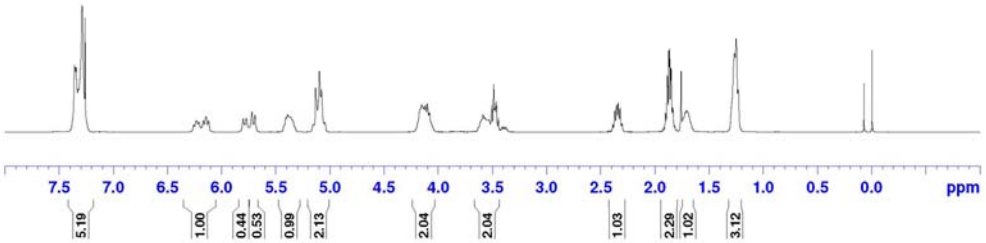

COOEt
N
Cbz

(*Z*)-9f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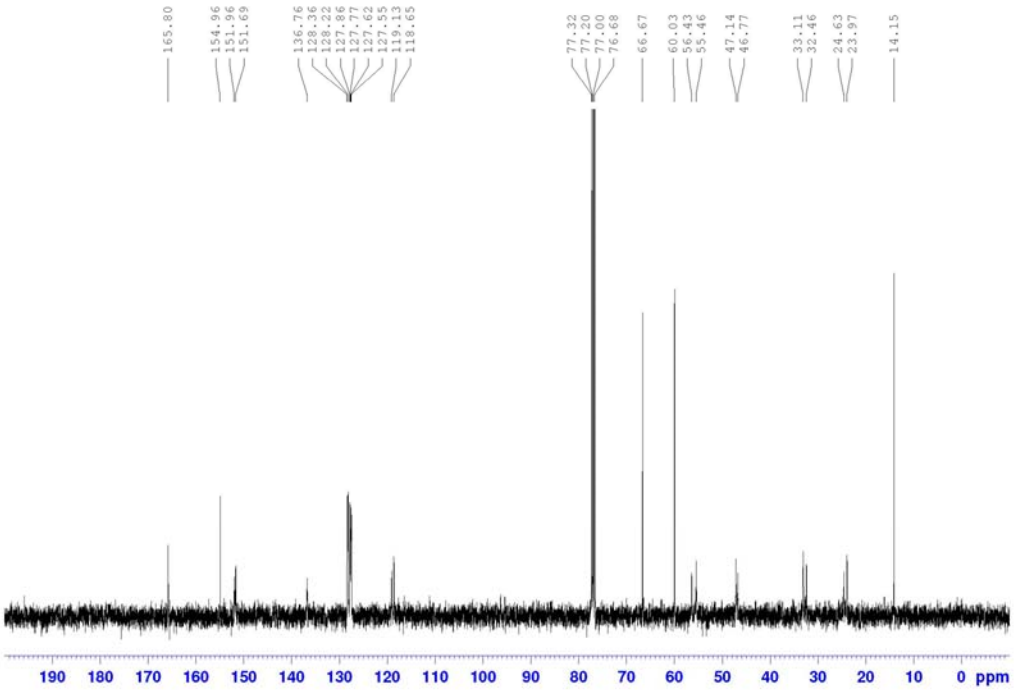
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151.96
151.69
136.76
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128.22
127.86
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127.62
127.55
119.13
118.65
77.32
77.20
77.00
76.68
66.67
60.03
56.43
55.46
47.14
46.77
33.11
32.46
24.63
23.97
14.15
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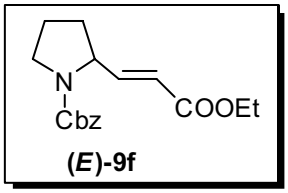
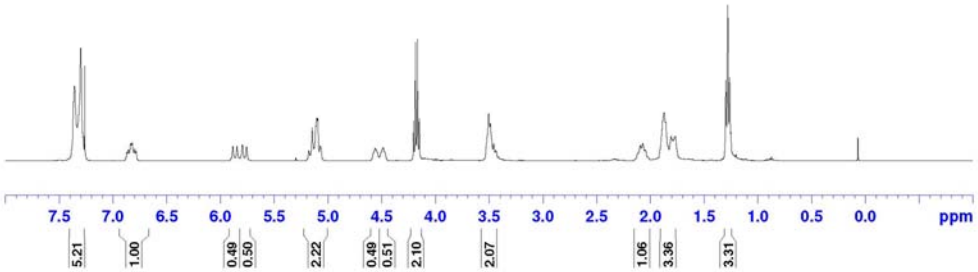

N
Cbz
COOEt

(*E*)-9f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0.49
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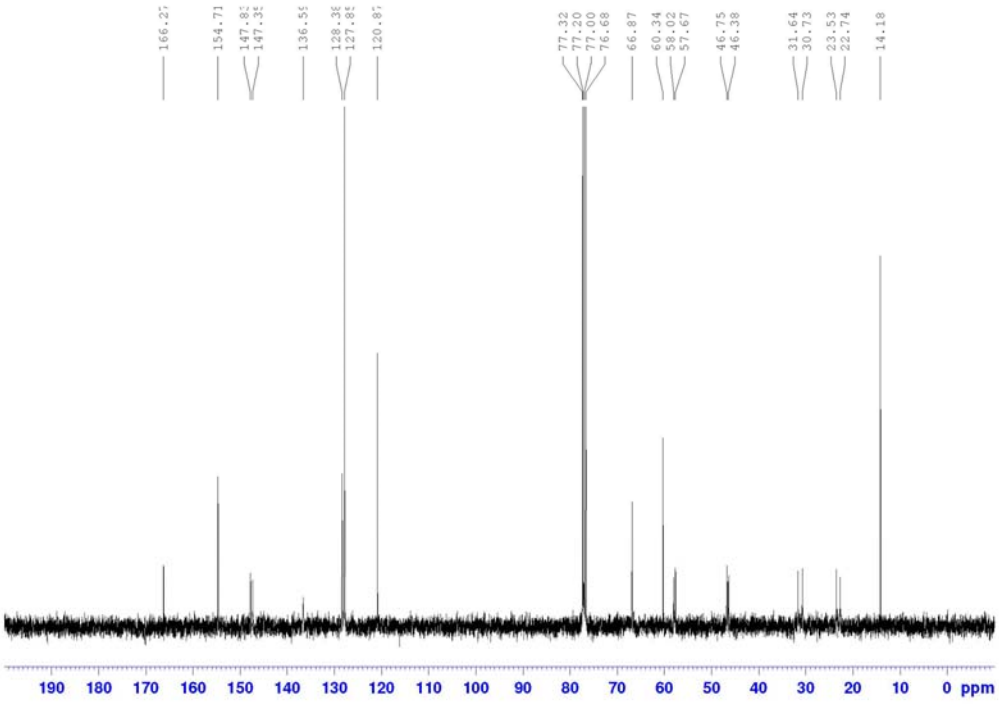
0.51
2.10
2.07
1.06
3.36
3.31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77.20
77.00
76.68
66.87
60.34
58.02
57.67
46.75
46.38
31.64
30.73
23.53
22.74
14.18
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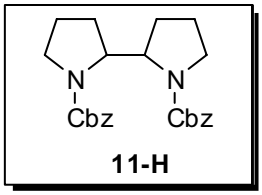
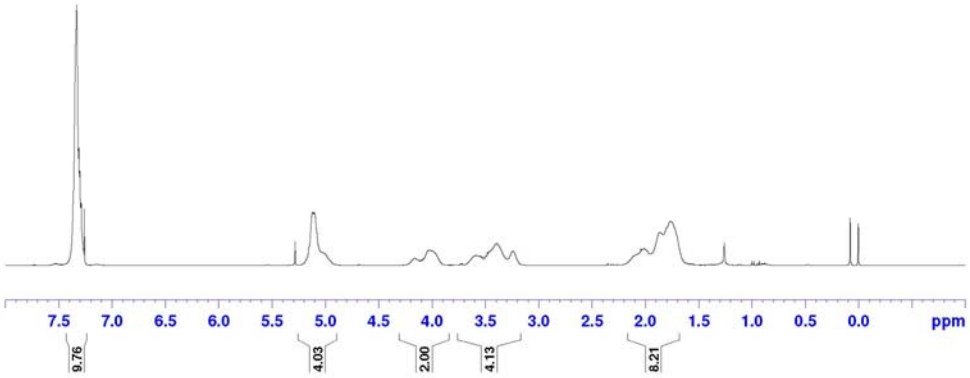

N
Cbz
N
Cbz

11-H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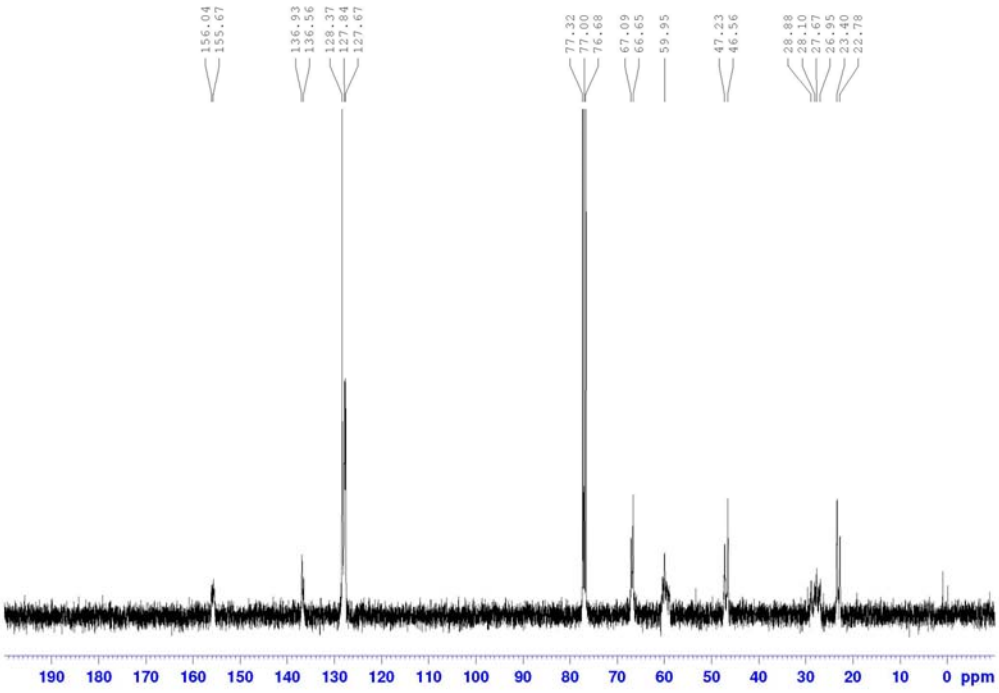
2.00
4.13
8.21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76.68
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66.65
59.95
47.23
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28.10
27.67
26.95
23.40
22.78
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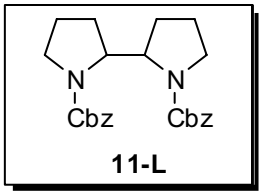
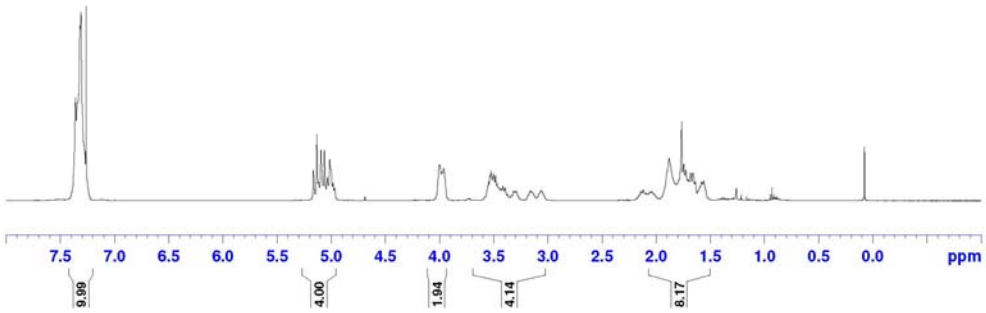

N
Cbz
N
Cbz

11-L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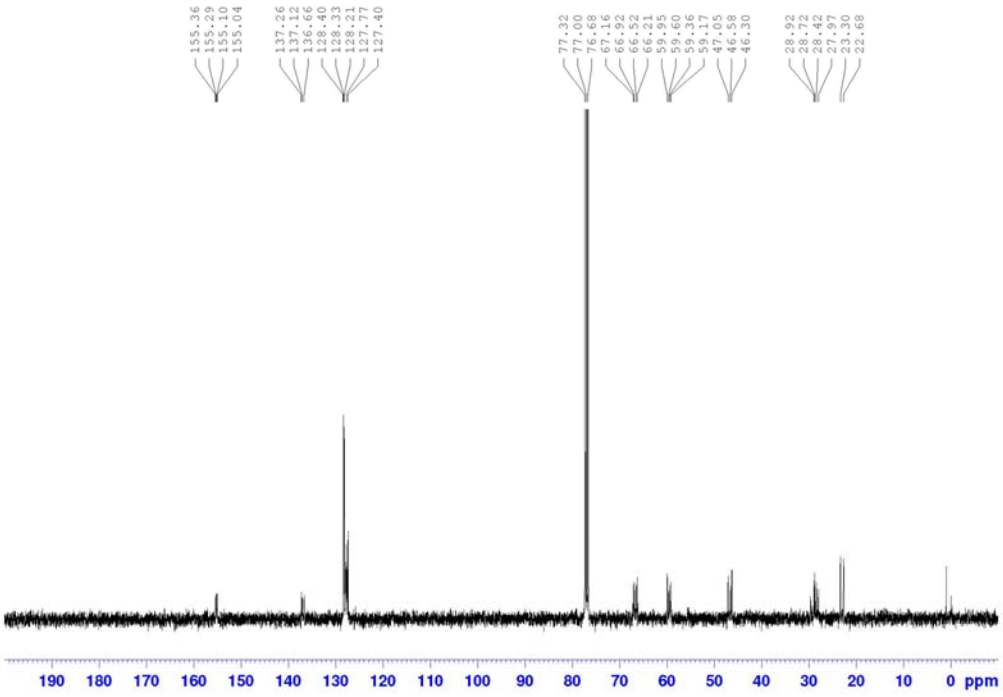
4.00
1.94
4.14
8.17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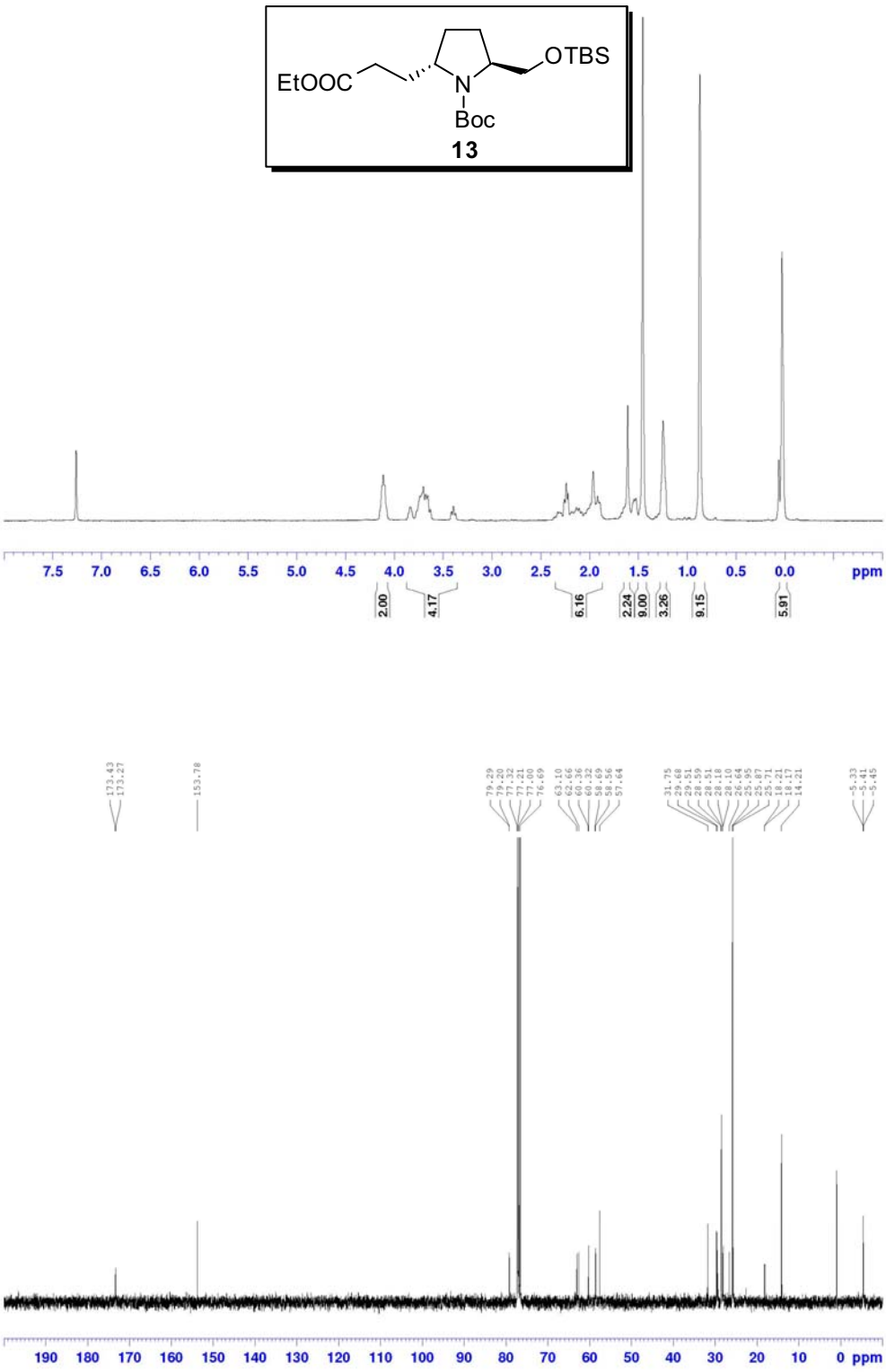
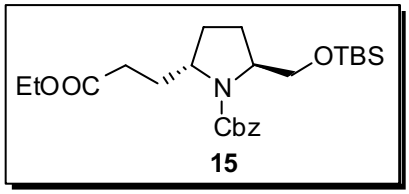
128.21
127.77
127.40
77.32
77.00
76.68
67.16
66.92
66.52
66.21
59.95
59.60
59.36
59.17
47.05
46.58
46.30
28.92
28.72
28.42
27.97
23.30
22.68
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

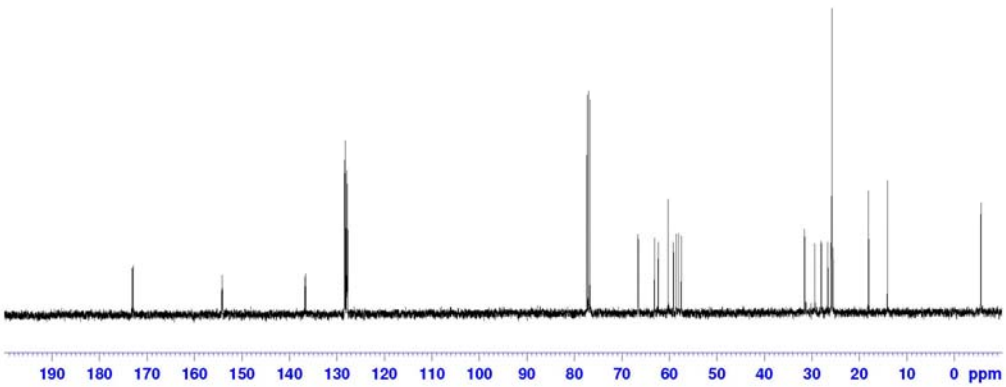

EtOOC
OTBS
N
Boc
13
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00 4.17 6.16 2.24 9.00 3.26 9.15 5.91
173.43
173.27
153.78
79.29
79.20
77.32
77.21
77.00
76.69
63.10
62.66
62.36
60.32
58.69
58.56
57.64
31.75
29.68
29.51
28.59
28.51
28.18
28.10
26.64
25.95
25.87
25.71
18.21
18.17
14.21
-5.33
-5.41
-5.45
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

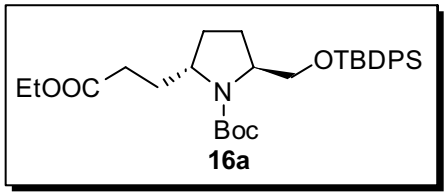

EtOOC
OTBS
N
Cbz

15

9
8
7
6
5
4
3
2
1
0
ppm
4.90
1.97
1.94
1.99
0.96
0.50
0.47
6.21
1.95
2.94
9.00
5.87


173.14
172.94
154.20
154.12
136.74
136.59
128.39
128.33
128.16
127.92
127.83
127.76
77.32
77.00
76.68
66.60
66.51
63.11
62.32
60.27
59.11
58.55
58.04
57.47
31.58
31.49
29.34
28.02
27.95
26.63
26.05
25.77
25.74
25.56
18.07
14.13
-5.54
-5.57

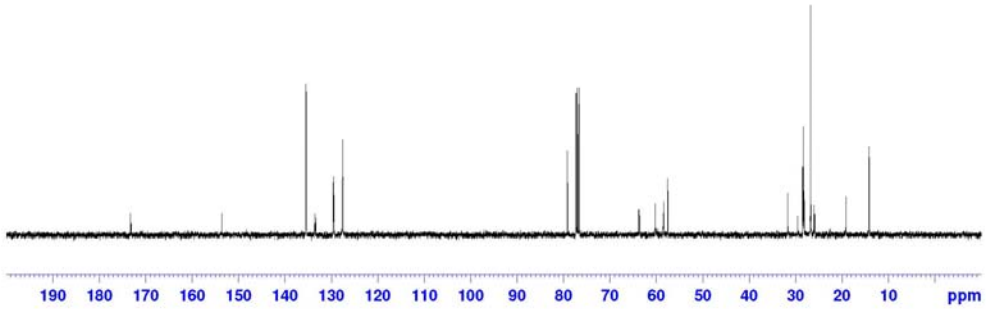

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

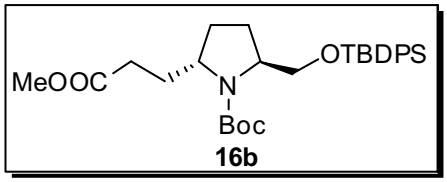

EtOOC
OTBDPS
N
Boc

16a

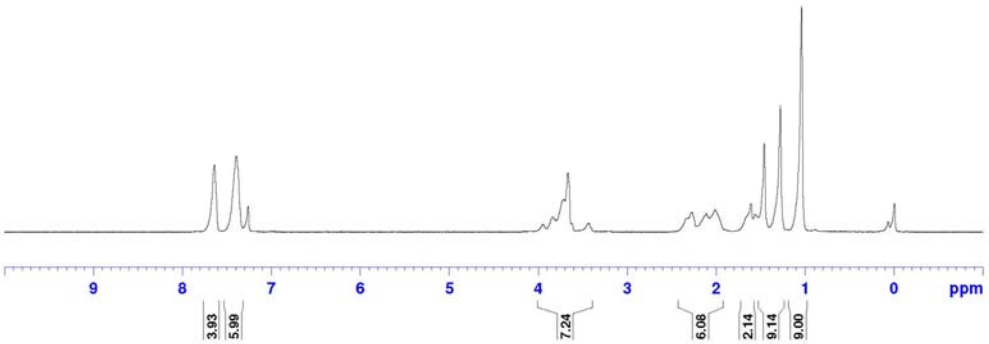
9
8
7
6
5
4
3
2
1
0
ppm
4.00
5.99
2.01
0.42
2.99
0.52
5.97
2.09
3.82
5.06
3.14
9.07

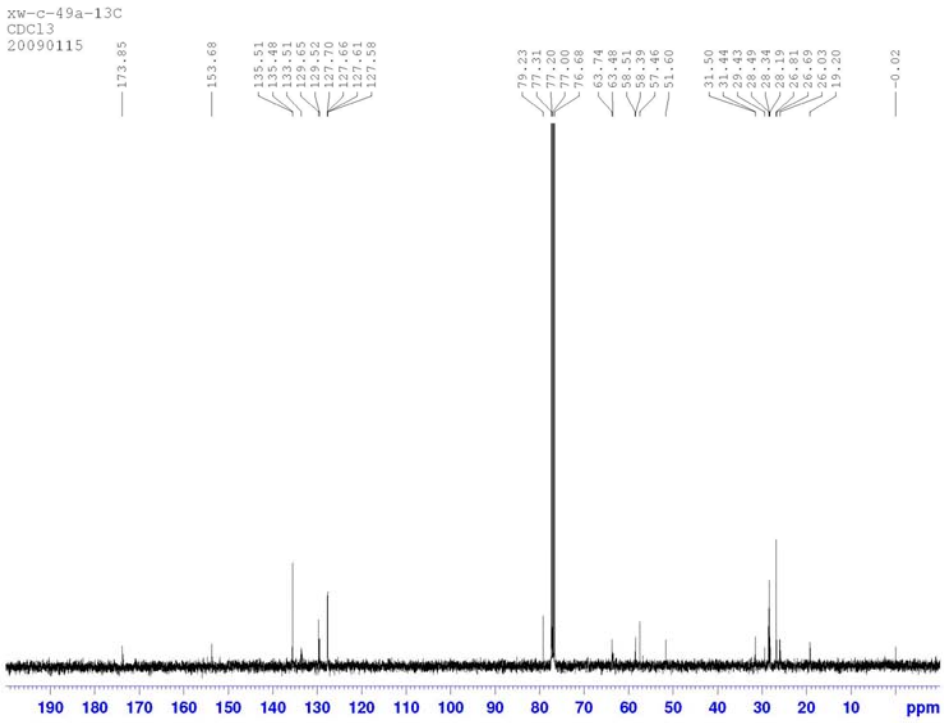

173.32
173.16
153.63
135.48
133.70
133.54
133.38
129.61
129.48
127.66
127.62
127.57
79.16
77.32
77.00
76.68
63.81
63.53
60.24
58.52
58.41
57.53
31.71
29.51
28.47
28.31
28.18
28.00
26.71
26.03
25.88
19.17
14.16

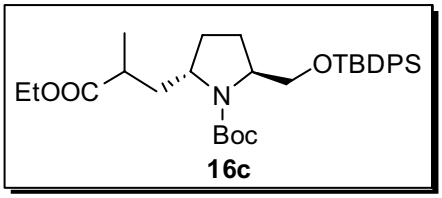

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


MeOOC
N
Boc
OTBDPS

16b

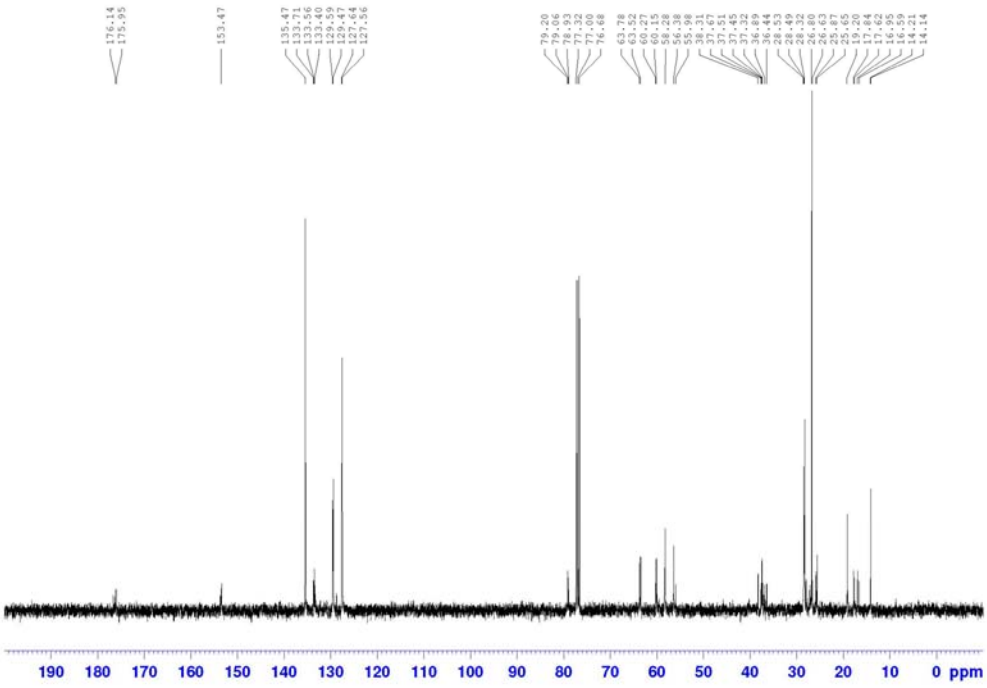

9
8
7
6
5
4
3
2
1
0
ppm
3.93
5.99
7.24
6.08
2.14
9.14
9.00

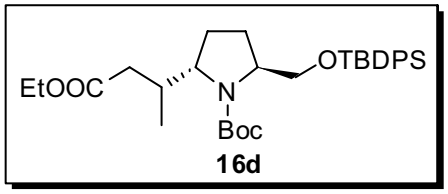

xw-c-49a-13C
CDCl3
20090115
173.85
153.68
135.51
135.48
133.51
129.65
129.52
127.70
127.66
127.61
127.58
79.23
77.31
77.20
77.00
76.68
63.74
63.48
58.51
58.39
57.46
51.60
31.50
31.44
29.43
28.49
28.34
28.19
26.81
26.69
26.03
19.20
-0.02
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


EtOOC
OTBDPS
N
Boc

16c

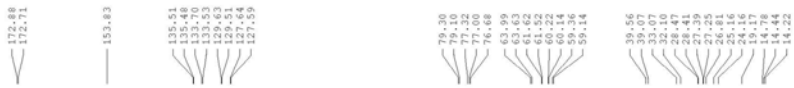
9
8
7
6
5
4
3
2
1
0
ppm
3.86
5.87
2.03
4.00
7.00
9.20
6.00
9.10

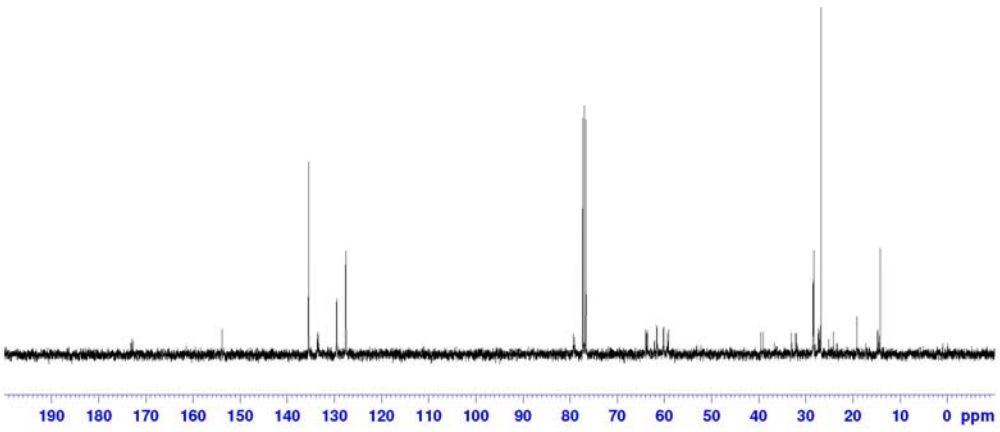

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

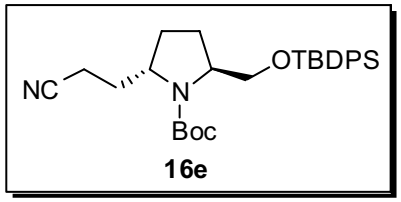

EtOOC
OTBDPS
N
Boc

16d

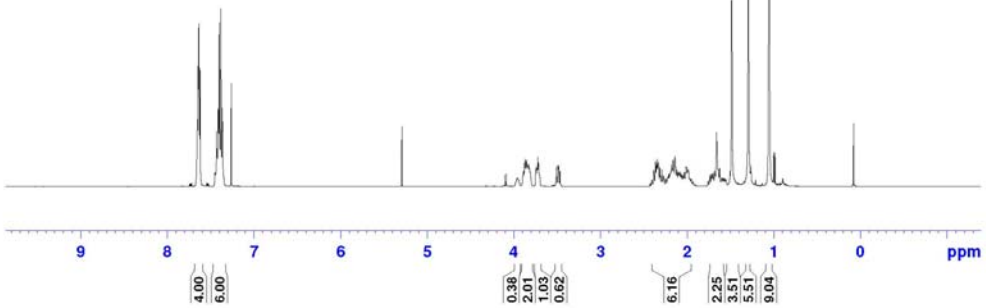
9
8
7
6
5
4
3
2
1
0
ppm
4.02
6.01
1.82
4.01
0.85
0.96
5.28
12.28
9.00
2.87

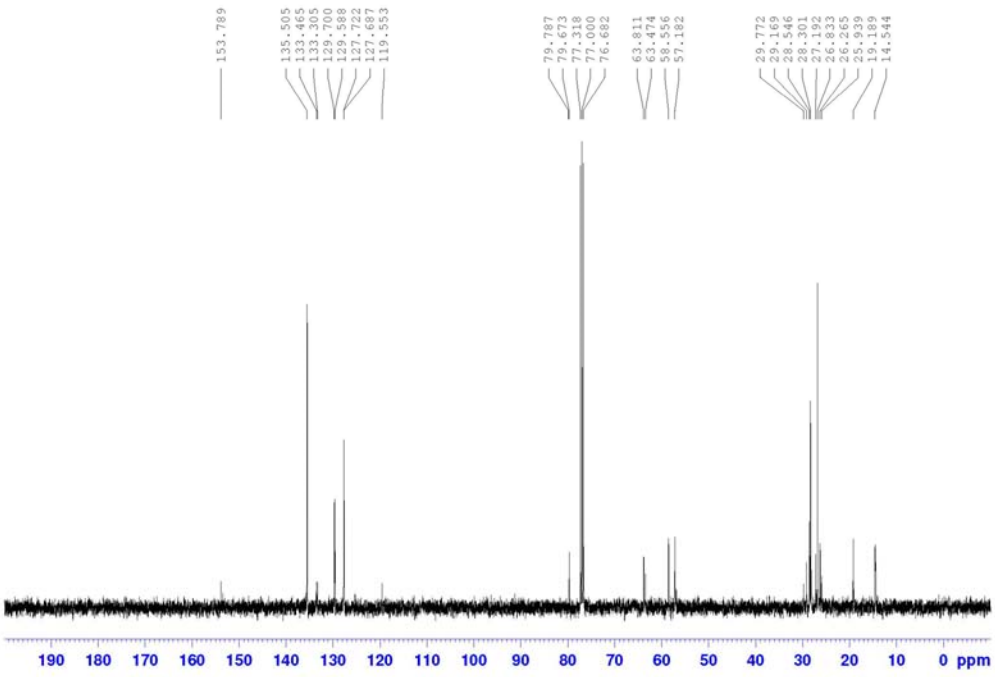


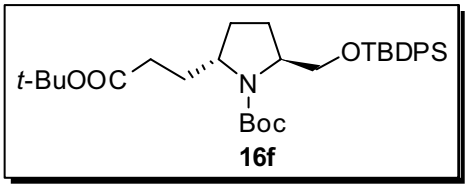

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


NC
N
Boc
OTBDPS

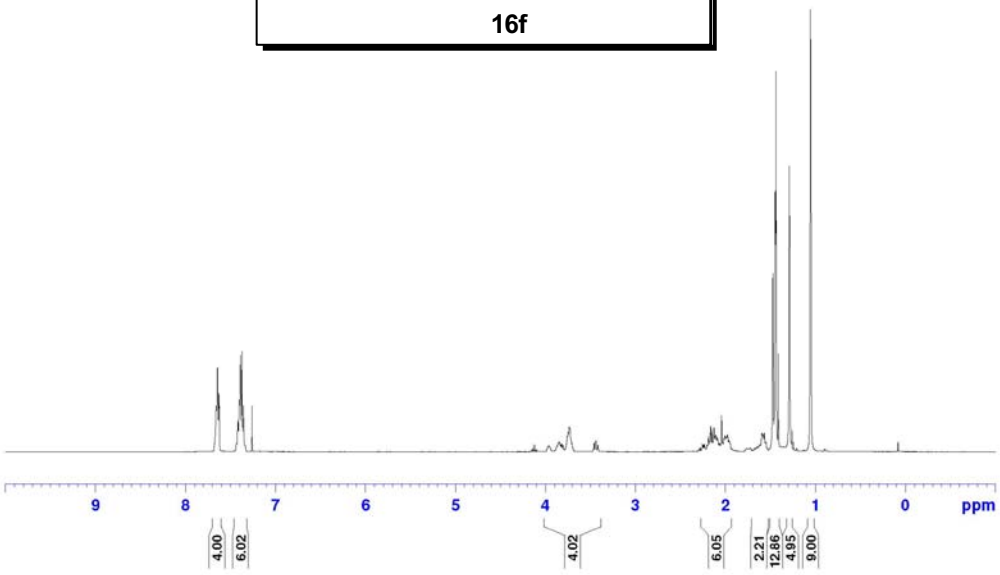
16e


9
8
7
6
5
4
3
2
1
0
ppm
4.00
6.00
0.38
2.01
1.03
0.62
6.16
2.25
3.51
5.51
9.04


153.789
135.505
133.465
133.305
129.700
129.588
127.722
127.687
119.553
79.787
79.673
77.318
77.000
76.682
63.811
63.474
58.556
57.182
29.772
29.169
28.546
28.301
27.192
26.833
26.265
25.939
19.189
14.544
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm


t-BuOOC
OTBDPS
N
Boc

16f


9
8
7
6
5
4
3
2
1
0
ppm
4.00
6.02
4.02
6.05
2.21
12.86
4.95
9.00


172.72
172.57
153.75
153.65
135.52
133.77
133.62
133.47
129.63
129.51
127.65
80.15
80.07
79.14
77.32
77.00
76.69
63.87
63.61
58.57
58.43
58.27
57.72
57.63
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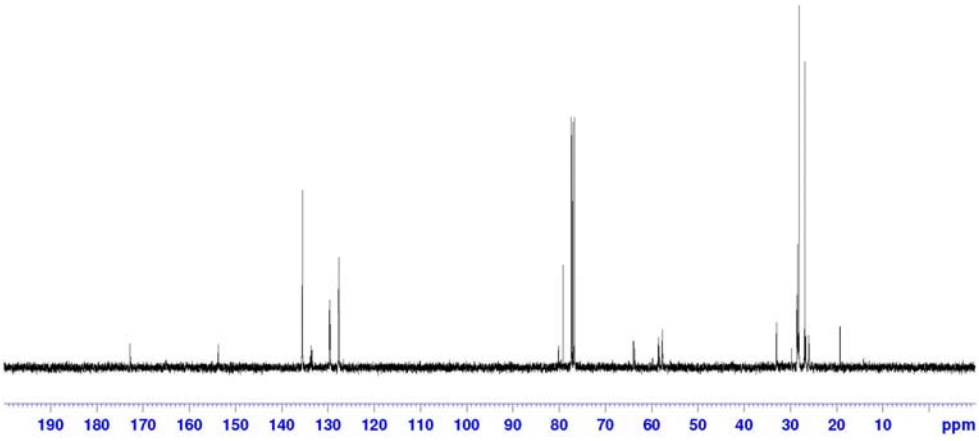
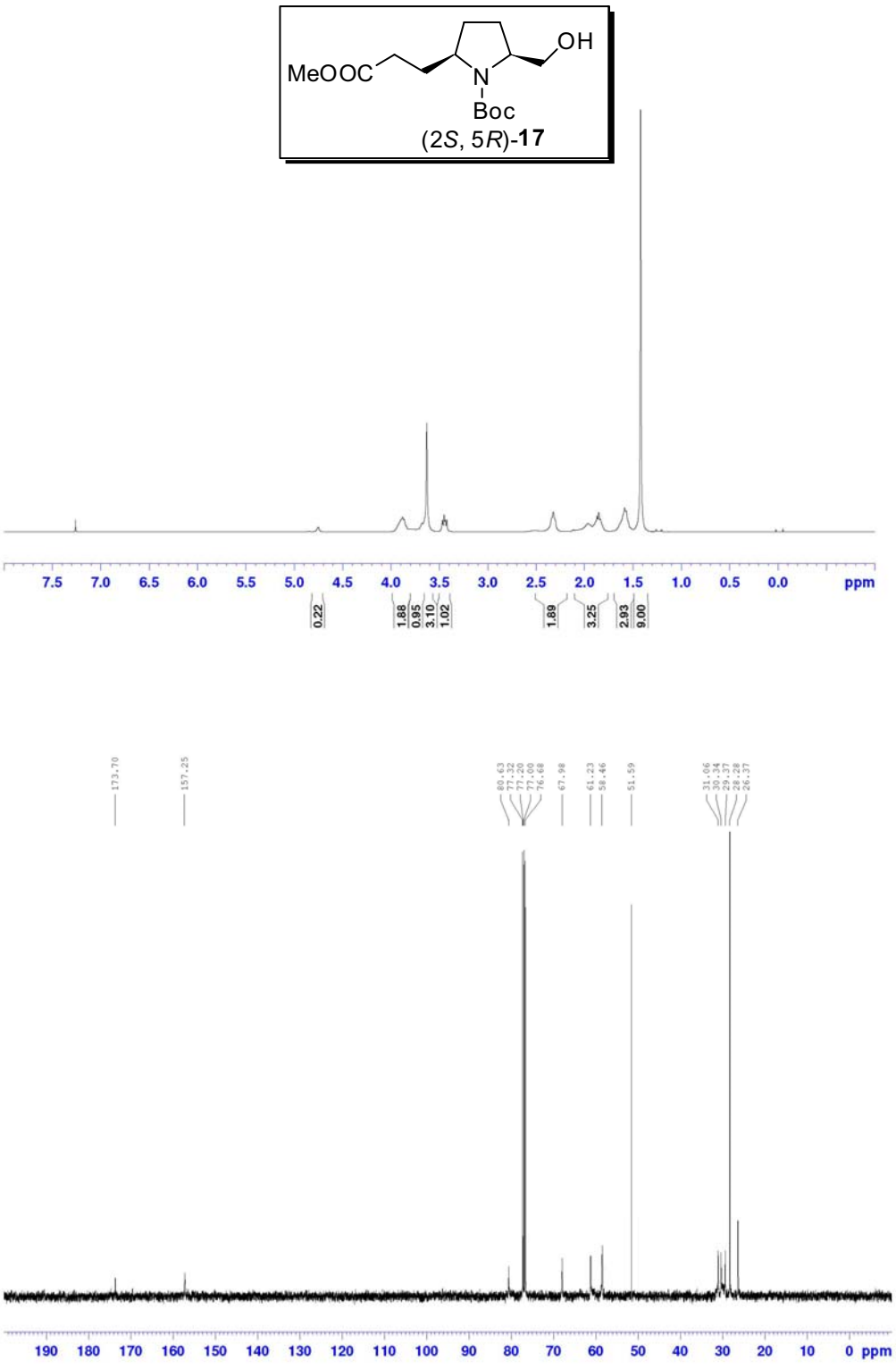
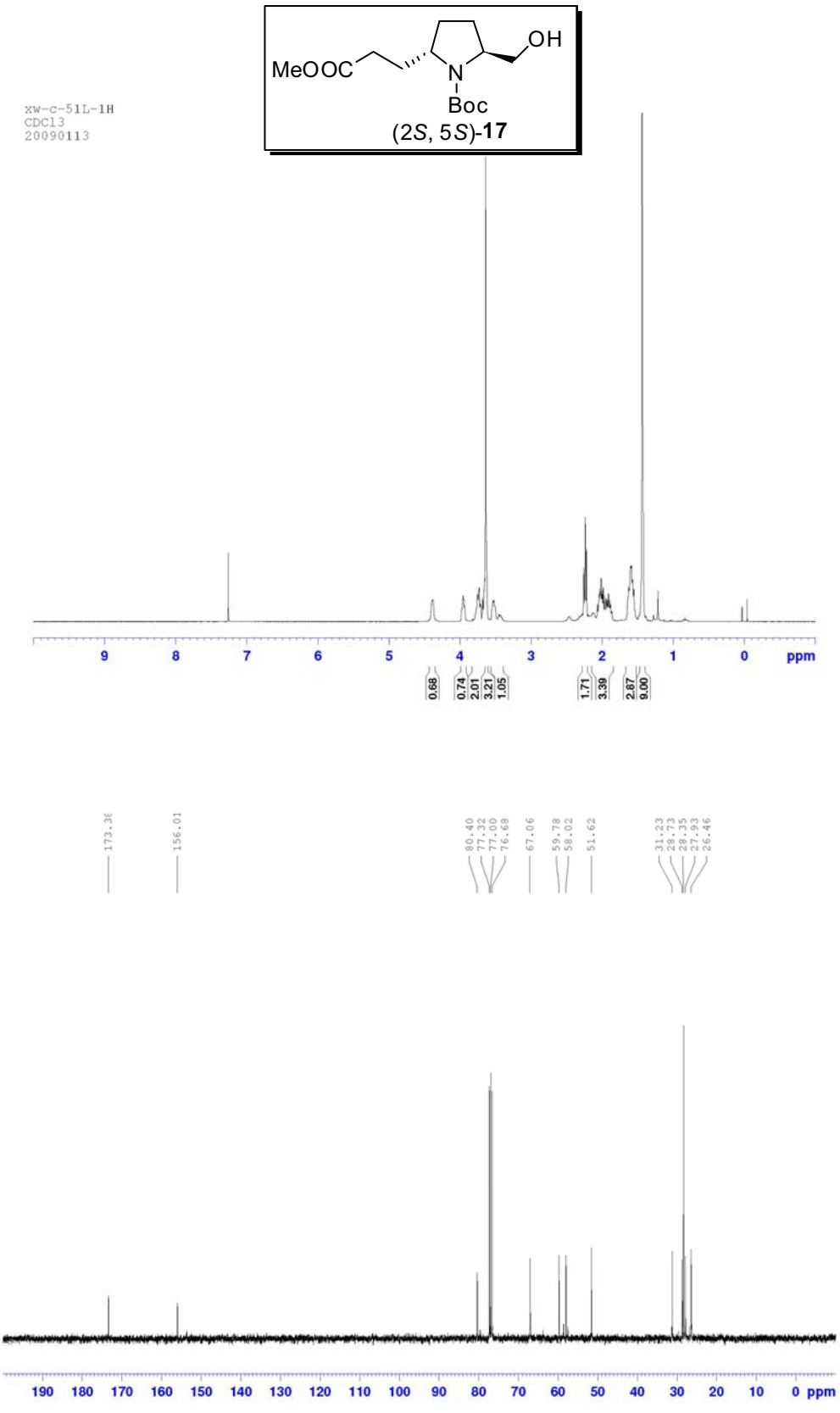
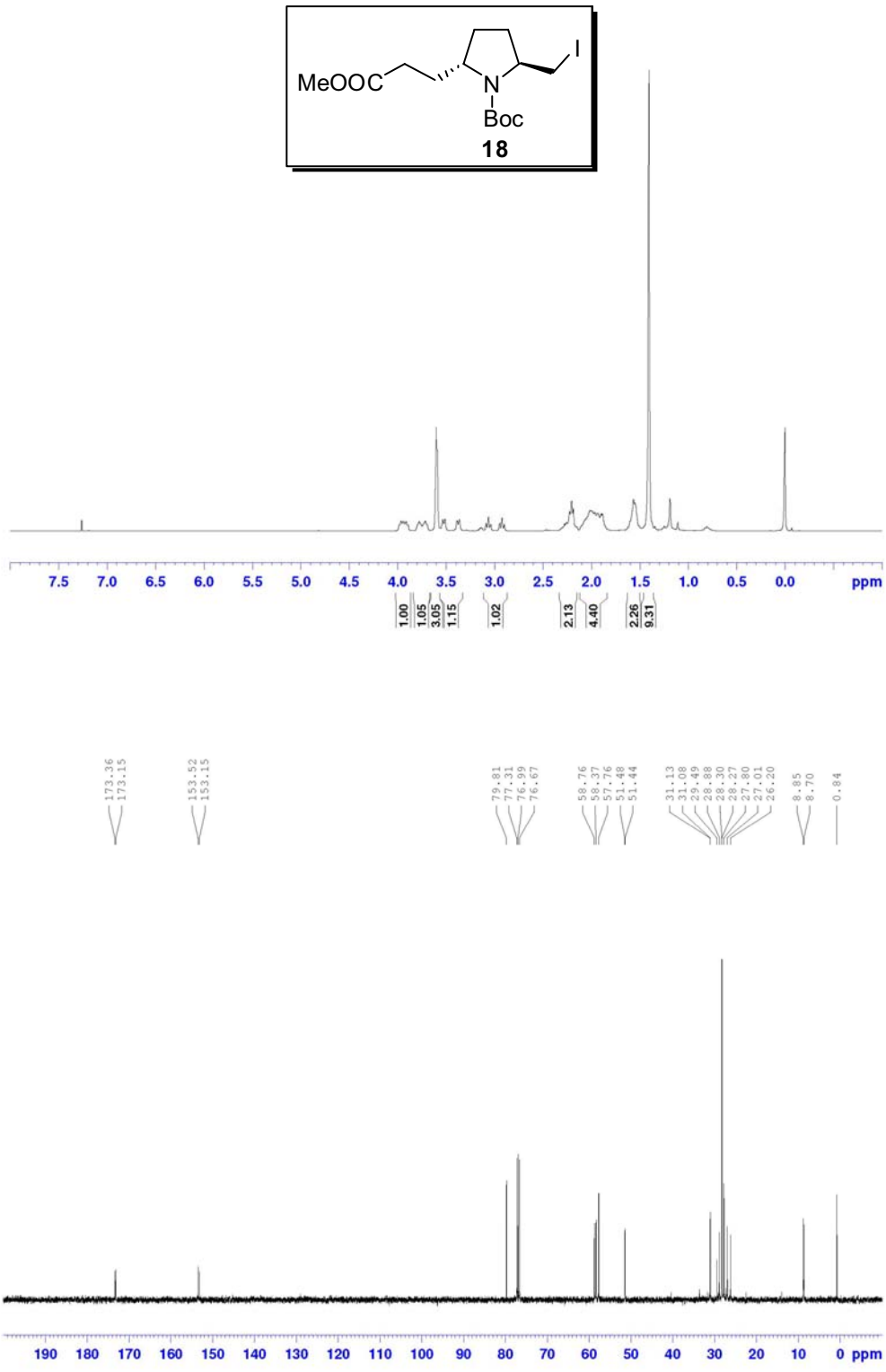
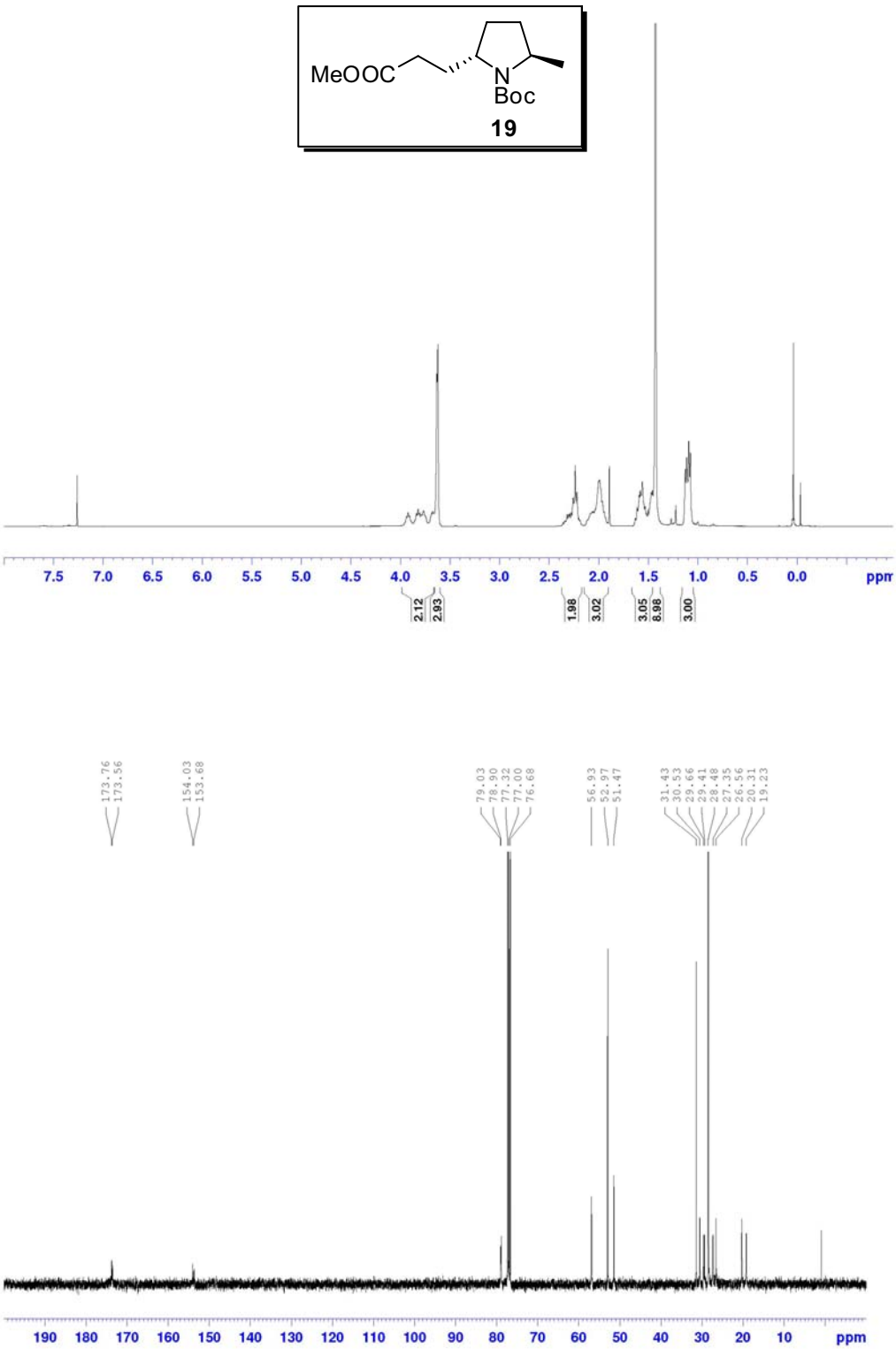
28.07
26.84
26.66
26.03
25.92
19.22

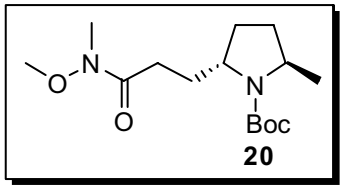

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


MeOOC
OH
N
Boc
(2S, 5R)-17
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.22 1.88 0.95 3.10 1.02 1.89 3.25 2.93 9.00
173.70 157.25 80.63 77.32 77.20 77.00 76.68 67.98 61.23 58.46 51.59 31.06 30.34 28.37 28.28 26.37
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

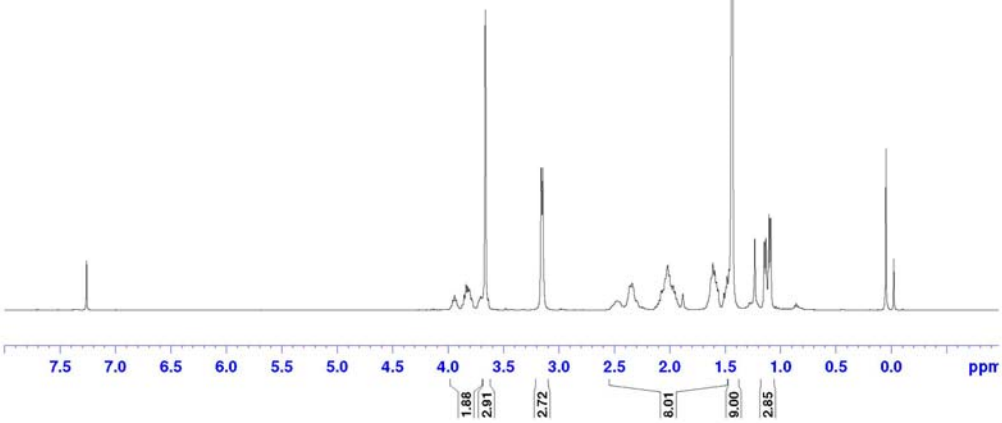

MeOOC
OH
N
Boc
(2S, 5S)-17
xw-c-51L-1H
CDCl3
20090113
9
8
7
6
5
4
3
2
1
0
ppm
0.68
0.74
2.01
3.21
1.05
1.71
3.39
2.87
9.00
173.3
156.01
80.40
77.32
77.00
76.68
67.06
59.78
58.02
51.62
31.23
28.73
28.35
27.93
26.46
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

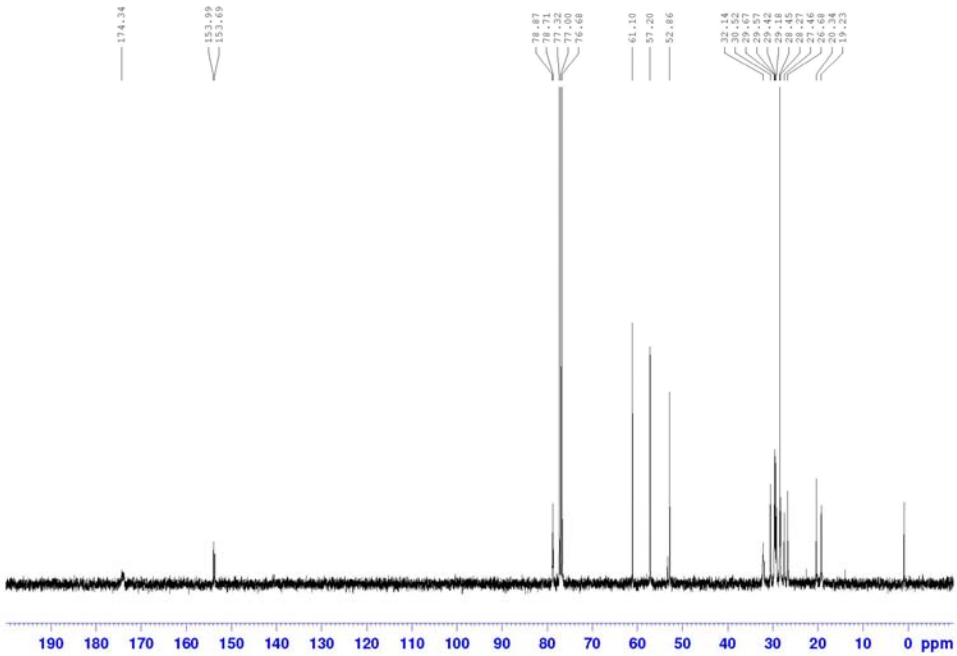

MeOOC
N
Boc
I
18
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00 1.05 3.05 1.15 1.02 2.13 4.40 2.26 9.31
173.36 173.15 153.52 153.15 79.81 77.31 76.99 76.67 58.76 58.37 57.76 51.48 51.44 31.13 31.08 29.49 28.88 28.30 28.27 27.80 27.01 26.20 8.85 8.70 0.84
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

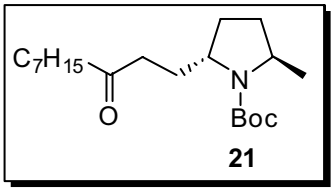

MeOOC
N
Boc
19
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.12
2.93
1.98
3.02
3.05
8.98
3.00
173.76
173.56
154.03
153.68
79.03
78.90
77.32
77.00
76.68
56.93
52.97
51.47
31.43
30.53
29.66
29.41
28.48
27.35
26.56
20.31
19.23
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


O
N
O
N
Boc

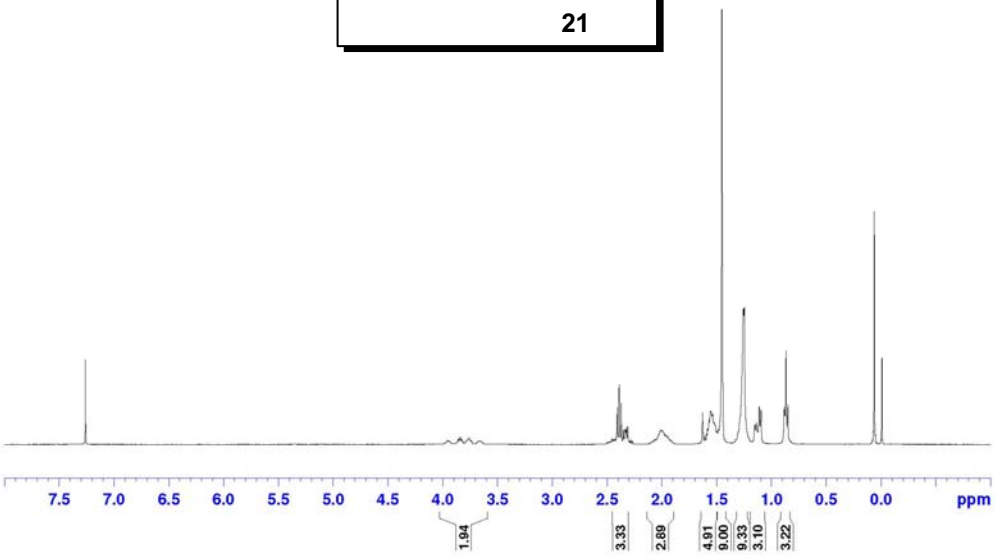
20

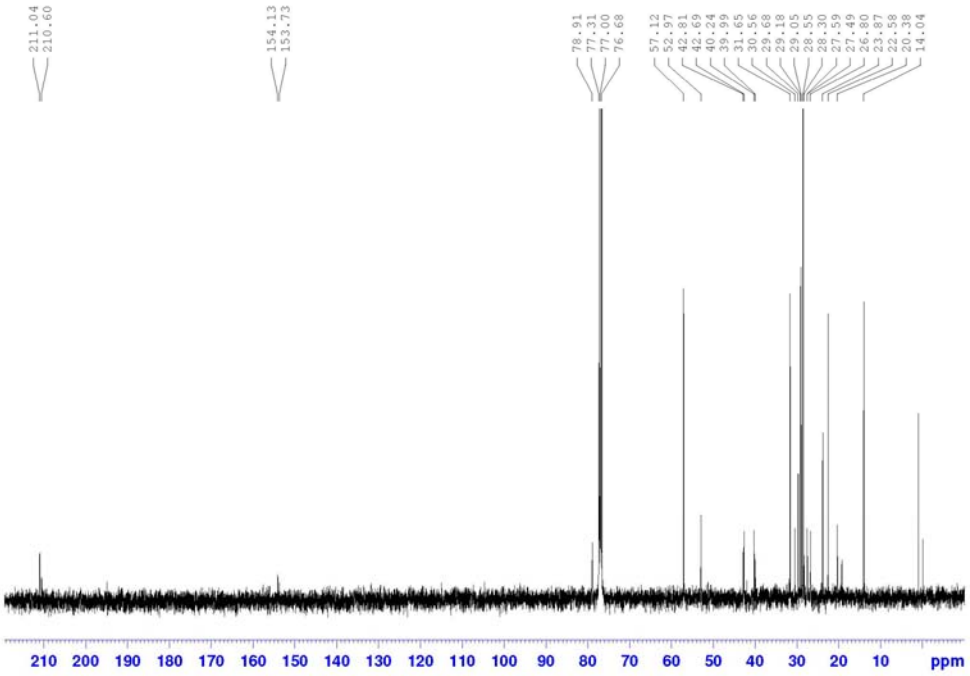

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.88
2.91
2.72
8.01
9.00
2.85

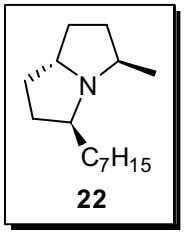

174.34
153.99
153.69
79.87
79.71
79.32
77.00
76.68
61.10
57.20
52.86
32.14
30.52
29.67
29.53
29.42
29.18
28.45
28.27
28.06
26.68
20.34
19.23
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


C7H15
O
N
Boc

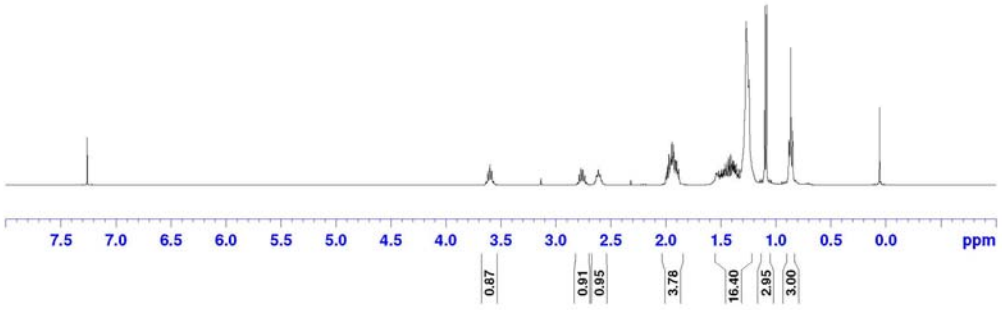
21

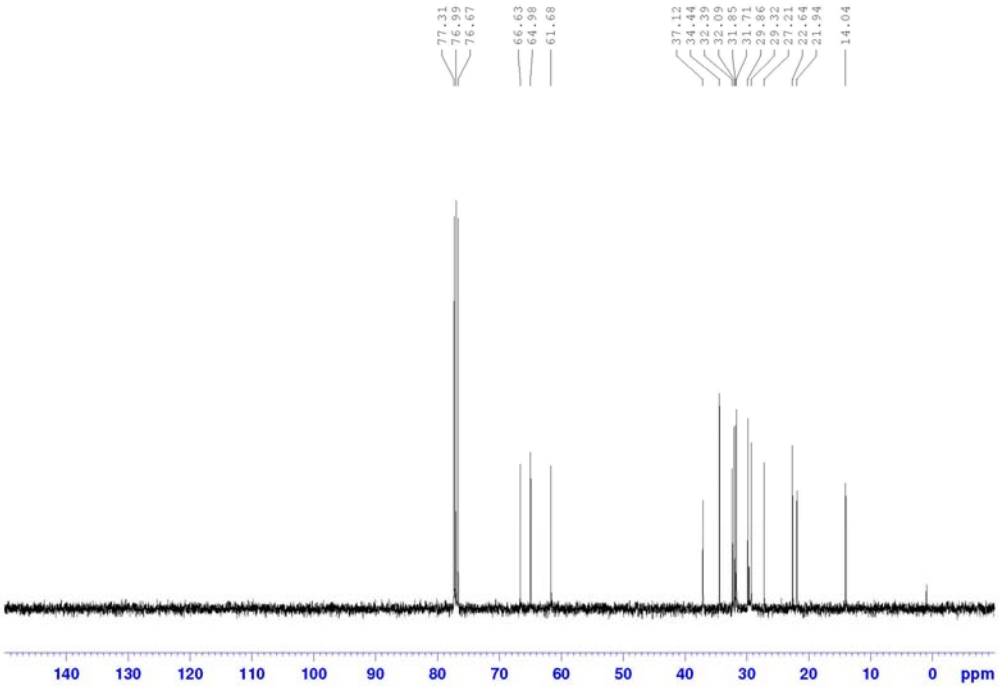

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.94
3.33
2.89
4.91
9.00
9.33
3.10
3.22

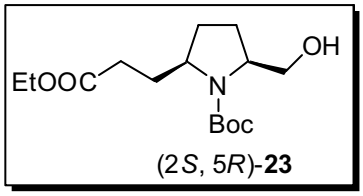

211.04
210.60
154.13
153.73
78.91
77.31
77.00
76.68
57.12
52.97
42.81
42.69
40.24
39.99
31.65
30.56
29.68
29.18
29.05
28.55
28.30
27.59
27.49
26.80
23.87
22.58
20.38
14.04
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


N
C7H15

22

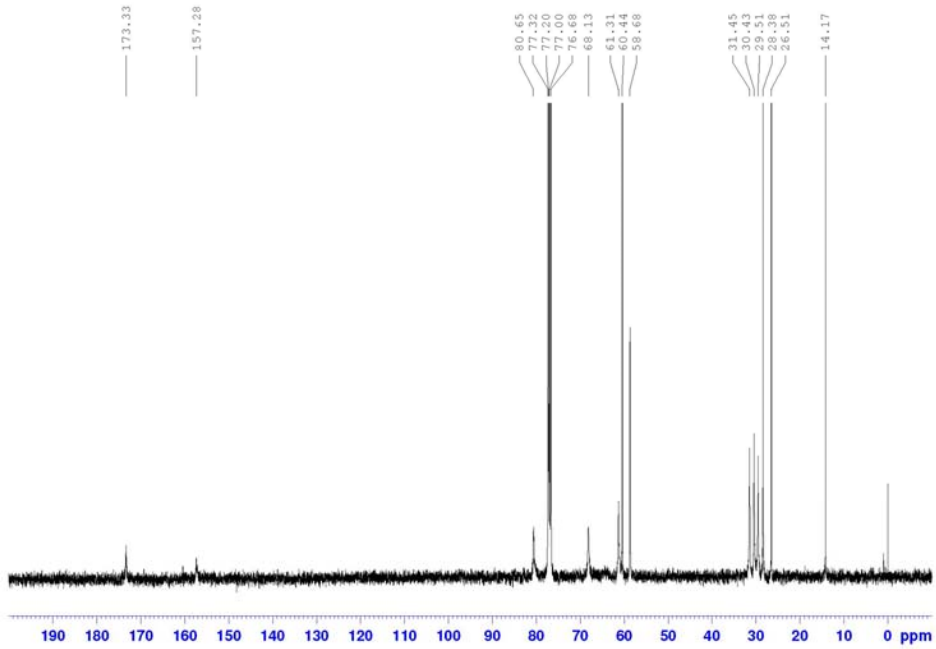

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.87
0.91
0.95
3.78
16.40
2.95
3.00

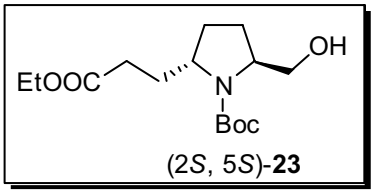

77.31
76.99
76.67
66.63
64.98
61.68
37.12
34.44
32.39
32.09
31.85
31.71
29.86
29.32
27.21
22.64
21.94
14.04
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


EtOOC
OH
N
Boc

(2*S*, 5*R*)-**23**

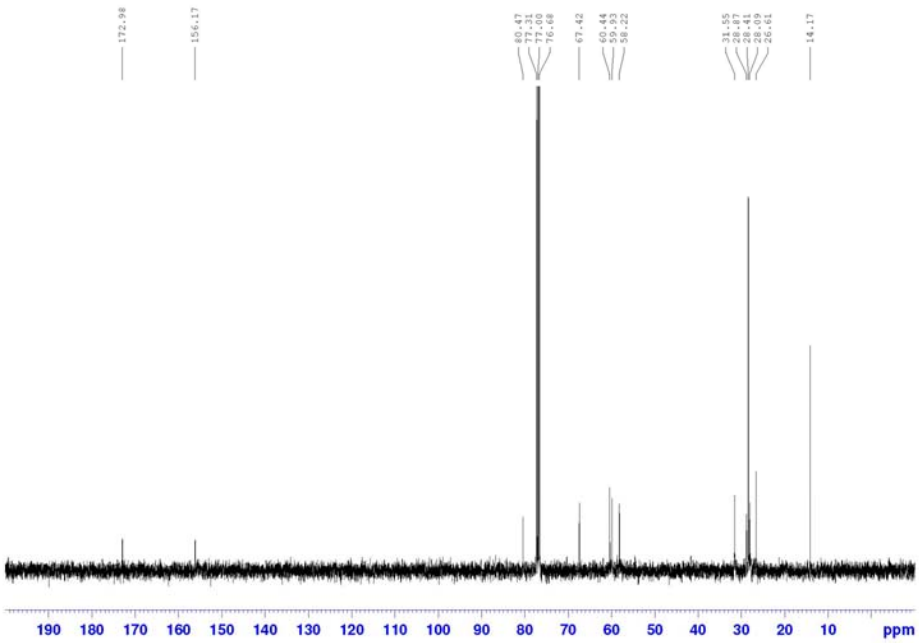
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.59
1.91
1.96
1.02
1.00
1.74
3.03
3.27
9.00
3.05


173.33
157.28
80.65
77.32
77.20
77.00
76.68
68.13
61.31
60.44
58.68
31.45
30.43
29.51
28.38
26.51
14.17
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


EtOOC
OH
N
Boc

(2*S*, 5*S*)-**23**

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.74 1.99 0.81 2.22 1.02 2.11 3.14 2.89 9.00 3.14


172.98
156.17
80.47
77.31
77.00
76.68
67.42
60.44
59.03
58.22
31.55
28.87
28.41
28.09
26.61
14.17
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm