Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

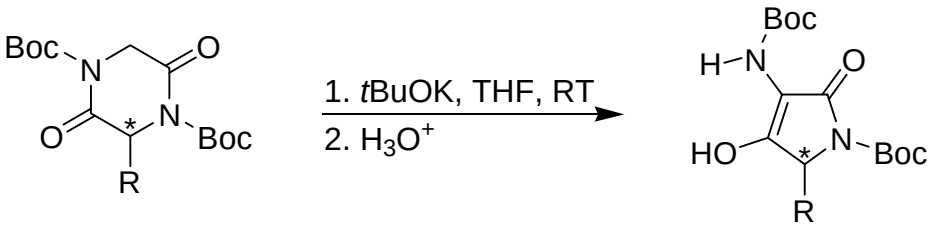
Transannular Rearrangement of Activated Lactams (TRAL): Stereocontrolled Synthesis of Substituted Pyrrolidine-2,4-diones Starting from Diketopiperazines

Daniel Farran, Isabelle Parrot, Jean Martinez* and Georges Dewynter*

[*] D. Farran, Dr. I. Parrot, Pr. J. Martinez, Pr. G. Dewynter
Institut des Biomolécules Max Mousseron (IBMM), UMR 5247 CNRS-Universités Montpellier 1 et 2
Bâtiment Chimie (17), Université Montpellier 2
Place Eugène Bataillon, 34095 Montpellier Cedex 5, France
Fax: (+33) 4-6714-4866
E-mail: Georges.Dewynter@univ-montp2.fr or martinez@univ-montp1.fr (equal contributors)

Complementary data for Table 1, Table 2 and Table 3

Table1. Stereocontrolled ring contraction of unsymmetrical DKPs into 3-aminotetramates.

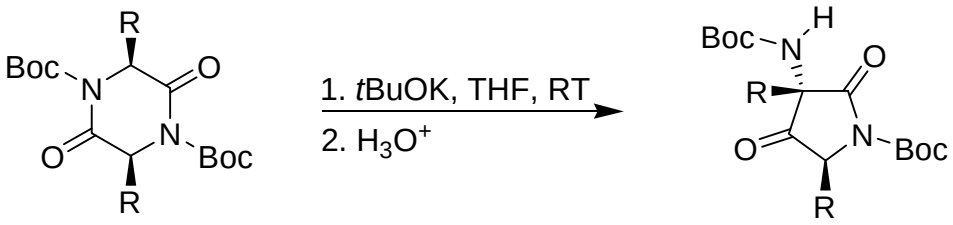


1 **2**

Entry	**1**	R	Product (ee)	Yield[c] [%]
1	**1a**	H	**2a**	72
2	**1b**	Me (*S*)	**2b** (>99%)[a]	60
3	**1c**	Me (*R*)	**2c** (>99%)[a]	64
4	**1d**	*i*Pr (*S*)	**2d** (>99%)[a]	82
5	**1e**	*i*Pr (*R*)	**2e** (>99%)[a]	84
6	**1f**	*s*Bu (*S*)	**2f** (>95%)[b]	71
7	**1g**	Bn (*S*)	**2g**	16[d]

[a] The diastereoisomeric excess was determined by chiral HPLC.
[b] The ^{13}C NMR spectrum gave only one set of peaks.
[c] Yield of isolated product after purification by flash chromatography.
[d] The product from thermodynamic enolate was obtained in 46% yield.

Table1. Stereocontrolled ring contraction of symmetrical DKPs into pyrrolidine-2,4-diones.



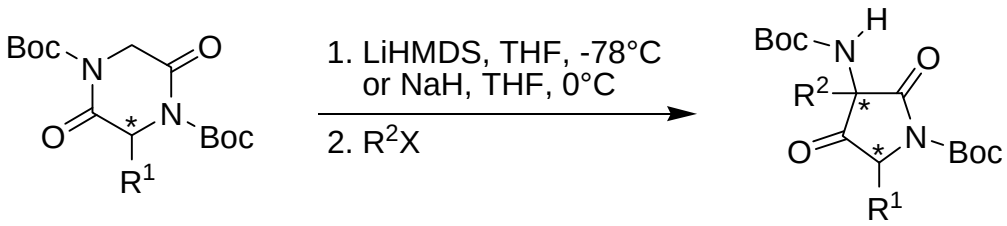
1 **3**

Entry	**1**	R	Product (de)	Yield[e] [%]
1	**1g**	Me (*S*)	**3h** (67%)[a,b]	66
2	**1h**	*i*Pr (*S*)	**3i**[c](>95%)[b,d]	68
3	**1i**	$MeO_2C(CH_2)_2$ (*S*)	**3j** (>95%)[d]	29[f]

[a] The diastereoisomeric excess was determined by HPLC of crude.
[b] The relative configuration was determined by nOe analysis (concerning **3h**: this determination occurred after separation of the two diastereoisomers)
[c] **1i** was not isolated because **3i** was obtained during the activation of *cyclo*-[L-Val-L-Val] in conventional conditions (Boc_2O, DMAP, DMF, r.t.).[#]
[d] The ^{13}C NMR spectrum gave only one set of peaks.
[e] Yield of isolated product after purification by flash chromatography.
[f] The product from retro-Michael reaction was obtained in 42% yield.

[#]M. Oba, T. Terauchi, Y. Owari, Y. Imai, I. Motoyama, K. Nishiyama, *J. Chem. Soc. Perkin Trans. 1* **1998**, 1275-1281.

Table 3. Tandem reaction: rearrangement-alkylation on bis-Boc *cyclo*-[Gly-Xaa].



1 e-f **5**

Entry	**1**	R^1	R^2X	Product	Base	Yield[b] [%] (de)
1	**1e**	*i*Pr (*R*)	MeI	**5a**[a]	LiHMDS	60 (>95%)[c]
					NaH	63 (>95%)[c]
					*t*BuOK	0
2	**1e**	*i*Pr (*R*)	BnBr	**5b**[a]	LiHMDS	72 (>95%)[c]
					NaH	62 (>95%)[c]
3	**1e**	*i*Pr (*R*)	EtO_2CCH_2I	**5c**	LiHMDS	69 (>95%)[c]
					NaH	0
4	**1e**	*i*Pr (*R*)	CH_2=$CHCH_2Br$	**5d**	LiHMDS	76 (>99%)[d]
					NaH	75 (>99%)[d]
5	**1e**	*i*Pr (*R*)	$(CH_3)_2C$=$CHCH_2Br$	**5e**	LiHMDS	84 (>95%)[c]
6	**1f**	*s*Bu (*S*)	CH_2=$CHCH_2Br$	**5f**	LiHMDS	68 (>95%)[c]

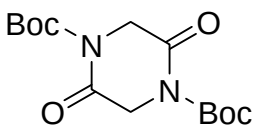
[a] The relative configuration was determined by nOe analysis.
[b] Yield of isolated product after purification by flash chromatography.
[c] The ^{13}C NMR spectrum gave only one set of peaks.
[d] The diastereoisomeric excess was determined by comparison of HPLC crude analysis between **5d** and **7**.

General Information and Materials

All solvents were dried and freshly distilled before use. Reactions were magnetically stirred and monitored by thin layer chromatography using Merck-Kieselgel 60 F_{254} plates. Visualisation was accomplished with UV light and exposure to ninhydrin solution followed by heating. Chromatography columns were performed using Merck-Kieselgel 60 (230-400 mesh). Melting points were recorded on a Buchi 510. Optical rotations were measured on a Perkin Elmer Polarimeter at 20°C with a sodium lamp (589 nm) and reported as follows: $[\alpha]_D^{20}$ (*c* g/100 mL, solvent). HPLC analysis were performed on a Waters-millenium (column 250 x 4.6 mm Nucleosil C18 5µ, detection UV). Mass spectra were obtained on a JEOL JMS-SX-102 high resolution magnetic sector mass spectrometer. ^{1}H NMR spectra were recorded at ambient temperature on Bruker 200 MHz, Bruker AC250 MHz, Bruker Advance 300 MHz or Bruker A DRX 400 MHz spectrometers. Chemicals shifts (δ) are reported from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ7.26, DMSO-*d6*: δ2.50). Data are reported as follows: chemical shift (δ), multiplicity (s = singulet, d = doublet, t = triplet, br = broad, m= multiplet), coupling constants (*J*/Hz), integration, and assignment. ^{13}C NMR spectra were recorded at ambient temperature on Bruker Advance 300 MHz or Bruker A DRX 400 MHz spectrometers. Chemicals shifts (δ) are reported from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ77.16, DMSO-*d6*: δ39.52). Data are reported as follows: chemical shift (δ) and assignment. The reported ^{1}H NMR signals were assigned using standard 2D NMR techniques or by direct comparison to the ^{1}H NMR spectra of corresponding starting materials. The reported ^{13}C NMR signals were assigned using DEPT-135 and HMQC techniques or by direct comparison to the ^{13}C NMR spectra of corresponding starting materials.

Activation of Diketopiperazines

General procedure: To a solution of DKP (35.00 mmol) and Di-*tert*-butyl dicarbonate Boc_2O (73.50 mmol) in dry DMF (30 mL) was added in three fractions DMAP (73.50 mmol). After stirring at r.t. under argon atmosphere for 1 hour, the solution was diluted with AcOEt (50 mL) and then washed with 1N aqueous solution of $KHSO_4$ (50 mL). After drying on $MgSO_4$, the solvent was removed *in vacuo*. Column chromatography (CH_2Cl_2/AcOEt) provided the activated DKP.



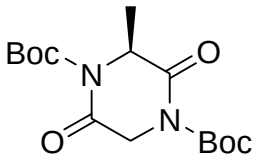
1,4-Di(*tert*-butoxycarbonyl)piperazine-2,5-dione (1a)

Yield = 82 %

White powder

Mp = 137 °C (litt: 135-137°C)[†]; t_r = 10.630 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.46 (s, 4H, C*H*$_2$), 1.57 (s, 18H, C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.6 (*C*O lactam), 149.5 (*C*O carbamate), 85.0 (*C* carbamate), 49.5 (*C*H$_2$), 27.9 (*C*H$_3$ carbamate); HRMS (FAB+) *m/z* calcd for $C_{14}H_{23}N_2O_6$ [M+H$^+$] 315.1556, found 315.1554.

[†] D. A. Peters, R. L. Beddoes, J. A. Joule, *J. Chem. Soc., Perkin Trans. 1* **1993**, 1217-1224.

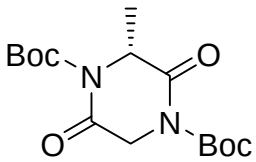


(*3S*)-1,4-Di(*tert*-butoxycarbonyl)-3-methylpiperazine-2,5-dione (1b)

Yield = 92 %

White powder

Mp = 106 °C; $[\alpha]_D^{20}$ = +87 (*c* = 1.83, CH_2Cl_2); t_r = 11.503 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.86 (d, *J* = 7.3 Hz, 1H, C*H**), 4.76 (d, J_{AB} = 18.2 Hz, 1H, C*H*$_2$), 4.10 (d, J_{AB} = 18.2 Hz, 1H, C*H*$_2$), 1.58-1.49 (s, 21H, C*H*$_3$CH* and C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.1 and 164.3 (*C*O lactam), 149.7 and 149.6 (*C*O carbamate), 85.1 and 84.9 (*C* carbamate), 56.4 (*C*H*), 48.6 (*C*H$_2$), 27.9 (*C*H$_3$ carbamate), 18.0 (*C*H$_3$CH*); HRMS (FAB+) *m/z* calcd for $C_{15}H_{25}N_2O_6$ [M+H$^+$] 329.1713, found 329.1712.

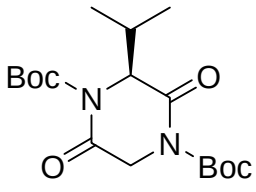


(*3R*)-1,4-Di(*tert*-butoxycarbonyl)-3-methylpiperazine-2,5-dione (1c)

Yield = 96 %

White powder

Mp = 106 °C; $[\alpha]_D^{20}$ = -86 (*c* = 1.26, CH_2Cl_2).



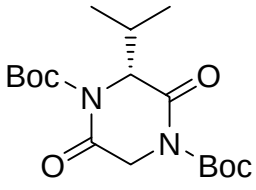
(*3S*)-1,4-Di(*tert*-butoxycarbonyl)-3-*iso*propylpiperazine-2,5-dione (1d)

Yield = 92 %

White powder

Mp = 130 °C (litt: 129-131°C)[#]; $[\alpha]_D^{20}$ = +76 (*c* = 1.93, CH_2Cl_2); t_r = 12.422 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.75 (d, J_{AB} = 18.6 Hz, 1H, CH_2), 4.60 (d, *J* = 9.6 Hz, 1H, CH^*), 4.16 (d, J_{AB} = 18.6 Hz, 1H, CH_2,), 2.14-1.98 (m, 1H, CHCH_3), 1.55 (s, 9H, CH_3 carbamate), 1.54 (s, 9H, CH_3 carbamate), 1.12 (d, *J* = 6.7 Hz, 3H, CH_3CH), 1.06 (d, *J* = 6.7 Hz, 3H, CH_3CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.7 and 164.8 (*C*O lactam), 150.0 and 149.9 (*C*O carbamate), 85.0 and 84.8 (*C* carbamate), 65.4 (*C*H*), 49.0 (*C*H_2), 31.7 (*C*H), 27.8 (*C*H_3 carbamate), 19.5 and 19.4 (*C*H_3CH); HRMS (FAB+) *m/z* calcd for $C_{17}H_{29}N_2O_6$ [M+H$^+$] 357.2026, found 357.2019.

[#]M. Oba, T. Terauchi, Y. Owari, Y. Imai, I. Motoyama, K. Nishiyama, *J. Chem. Soc. Perkin Trans. 1* **1998**, 1275-1281.

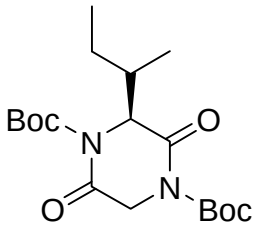


(*3R*)-1,4-Di(*tert*-butoxycarbonyl)-3-*iso*propylpiperazine-2,5-dione (1e)

Yield = 88 %

White powder

Mp = 130 °C (litt: 129-131°C); $[\alpha]_D^{20}$ = -77 (*c* = 2.04, CH_2Cl_2).



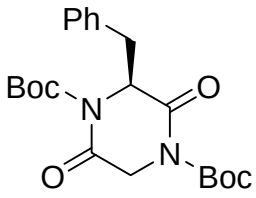
(*3S,6S*)-3-*sec*Butyl-1,4-di(*tert*-butoxycarbonyl)piperazine-2,5-dione (1f)

Yield = 77 %

Colorless oil

$[\alpha]_D^{20}$ = +51 (*c* = 1.05, CH_2Cl_2); t_r = 12.687 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.73 (d, *J* = 18.7 Hz, 1H, CH_2CO), 4.66 (d, *J* = 9.0 Hz, 1H, CH^*CO), 4.16 (d, *J* = 18.6 Hz, 1H, CH_2CO), 1.88-1.76 (m, 1H, CH^*CH_3), 1.63-1.47 (m, 1H, CH_2CH_3), 1.54 (s, 9H, CH_3 carbamate), 1.53 (s, 9H, CH_3 carbamate), 1.33-1.12 (m, 1H, CH_2CH_3), 1.05 (d, *J* = 6.7 Hz, 3H, CH_3CH*), 0.94 (t, *J* = 7.3 Hz, 3H, CH_3CH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.6 and 165.0 (*C*O lactam), 150.0 and 149.9 (*C*O carbamate), 84.9 and 84.8 (*C* carbamate), 64.4 (*C*H*CO), 49.1 (*C*H_2CO),

38.3 (*C*H*CH$_3$), 27.9 (*C*H$_3$ carbamate), 25.6 (*C*H$_2$CH$_3$), 15.6 and 11.3 (*C*H$_3$CH$_2$ and *C*H$_3$CH*); HRMS (FAB+) *m/z* calcd for $C_{18}H_{31}N_2O_6$ [M+H$^+$] 371.2182, found 371.2187.

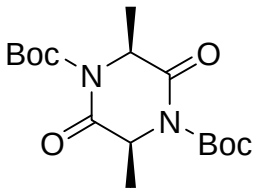


(*S*)-3-Benzyl-1,4-di(*tert*-butoxycarbonyl)piperazine-2,5-dione (1g)

Yield = 81 %

Colorless oil

[α]$_D^{20}$ = +10 (*c* = 1.38, CH_2Cl_2); t_r = 13.108 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.38-7.11 (m, 5H, *H$_{arom}$*), 5.11 (t, *J* = 5.4 Hz, 1H, C*H**), 4.29 (d, *J$_{AB}$* = 18.4 Hz, 1H, C*H$_2$*), 3.28 (d, *J* = 5.4 Hz, 2H, C*H$_2$*Ph), 2.82 (d, *J$_{AB}$* = 18.4 Hz, 1H, C*H$_2$*CO), 1.52 (s, 9H, C*H$_3$* carbamate), 1.48 (s, 9H, C*H$_3$* carbamate); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.6 and 162.5 (*C*O lactam), 147.6 (*C*O carbamate), 132.6 (*C$_{arom}$*), 128.1, 127.1 and 126.1 (*C*H$_{arom}$), 83.0 (*C* carbamate), 59.5 (*C*H*), 46.3 (*C*H$_2$CO), 37.2 (*C*H$_2$Ph), 25.9 (*C*H$_3$ carbamate); HRMS (FAB+) *m/z* calcd for $C_{21}H_{29}N_2O_6$ [M+H$^+$] 405.2026, found 405.2022.

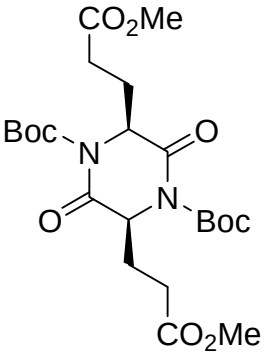


(*3S,6S*)-1,4-Di(*tert*-butoxycarbonyl)-3,6-dimethylpiperazine-2,5-dione (1h)

Yield = 83 %

Crystals

Mp = 101 °C; [α]$_D^{20}$ = +133 (*c* = 2.08, CH_2Cl_2); t_r = 11.809 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 4.76 (q, *J* = 7.3 Hz, 2H, C*H**), 1.54 (d, *J* = 7.3 Hz, 6H, C*H$_3$*CH*), 1.45 (s, 18H, C*H$_3$* carbamate); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.9 (*C*O lactam), 149.8 (*C*O carbamate), 84.6 (*C* carbamate), 55.9 (*C*H*), 27.8 (*C*H$_3$ carbamate), 20.3 (*C*H$_3$CH*); HRMS (FAB+) *m/z* calcd for $C_{16}H_{27}N_2O_6$ [M+H$^+$] 343.1883, found 343.1869.



(*3S,6S*)-1,4-Di(*tert*-butoxycarbonyl)-3,6-di[2-(methoxycarbonyl)ethyl]piperazine-2,5-dione (1j)

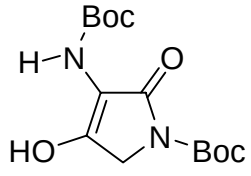
Yield = 77 %

Yellow oil

$[\alpha]_D^{20}$ = +68 (*c* = 1.59, CH_2Cl_2); t_r = 11.903 min; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.83 (t, *J* = 7.9 Hz, 2H, C*H**), 3.69 (s, 6H, OC*H*$_3$), 2.75-2.00 (m, 8H, C*H*$_2$), 1.58 (s, 18H, C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.5 and 166.5 (*C*O lactam and *C*O ester), 150.2 (*C*O carbamate), 85.1 (*C* carbamate), 62.6 (*C*H*), 51.8 (O*C*H$_3$), 30.8 (*C*H$_2$), 27.9 (*C*H$_3$ carbamate); HRMS (FAB+) *m/z* calcd for $C_{22}H_{35}N_2O_{10}$ [M+H$^+$] 487.2292, found 487.2294.

Rearrangement

General procedure: To a solution of activated DKP (2.50 mmol) in dry THF (10 mL) was added at *r.t.* *t*BuOK (2.75 mmol). The solution was stirred for 12 hours under argon atmosphere. The medium was then diluted with AcOEt (20 mL), washed with a solution HCl 0.1N (20 mL), and dried on anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude residue was purified by column chromatography (CH_2Cl_2/MeOH) to obtain the desired compound.

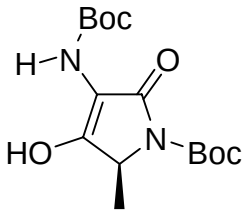


1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-3-pyrrolin-2-one (2a)

Yield = 72 %

White powder

Mp = 65 °C; t_r = 11.463 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.65 (br s, 1H, N*H*), 4.16 (s, 2H, C*H*$_2$), 1.55 (s, 9H, C*H*$_3$ carbamate), 1.51 (s, 9H, C*H*$_3$ carbamate); ^{1}H NMR (DMSO-*d*6, 200 MHz): δ 11.96 (m, 1H, O*H*), 7.84 (br s, 1H, N*H*), 4.12 (s, 2H, C*H*$_2$), 1.46 (s, 9H, C*H*$_3$ carbamate), 1.40 (s, 9H, C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.1 (*C*O lactam), 155.7 and 148.9 (*C*O carbamate), 150.8 (*C*OH), 104.1 (*C*NH), 83.3 and 83.1 (*C* carbamate), 47.0 (*C*H$_2$), 28.0 (*C*H$_3$ carbamate).

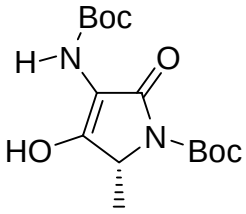


(*5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-methyl-3-pyrrolin-2-one (2b)

Yield = 60 %

Colorless oil

$[\alpha]_D^{20}$ = +33 (*c* = 2.06, CH_2Cl_2); t_r = 12.559 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 11.30 (m, 1H, O*H*), 6.56 (br s, 1H, N*H*), 4.34-4.21 (m, 1H, C*H**), 1.66-1.41 (m, 21H, CH_3CH* and CH_3 carbamate); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.8 (*C*O lactam), 155.2 (*C*OH), 155.7 and 148.8 (*C*O carbamate), 102.7 (*C*NH), 83.1 and 82.8 (*C* carbamate), 54.0 (*C*H*), 28.1 (*C*H_3 carbamate), 17.5 (*C*H_3CH*); HRMS (FAB+) *m/z* calcd for $C_{15}H_{25}N_2O_6$ [M+H$^+$] 329.1713, found 329.1722.

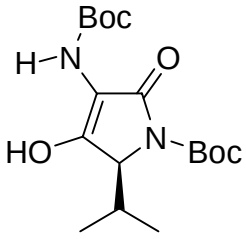


(*5R*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-methyl-3-pyrrolin-2-one (2c)

Yield = 60 %

Colorless oil

$[\alpha]_D^{20}$ = -32 (*c* = 1.76, CH_2Cl_2).



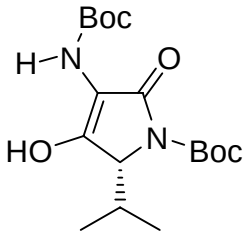
(*5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-*iso*propyl-3-pyrrolin-2-one (2d)

Yield = 82 %

Colorless oil

$[\alpha]_D^{20}$ = +53 (*c* = 1.39, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 11.87 (m, 1H, O*H*), 7.93 (br s, 1H, N*H*), 4.23 (br s, 1H, C*H**), 2.46-2.29 (m, 1H, C*H*CH_3), 1.46 (s, 9H, CH_3 carbamate), 1.41 (s, 9H, CH_3 carbamate), 1.03 (d, *J* = 7.1 Hz, 3H, CH_3CH), 0.79 (d, *J* = 6.9 Hz, 3H, CH_3CH); ^{1}H NMR (DMSO-*d*6, 200 MHz): δ 11.25 (m, 1H, O*H*), 6.59 (br s, 1H, N*H*), 4.26 (d, *J* = 2.5 Hz, 1H, C*H**), 2.53-2.37 (m, 1H, C*H*CH_3), 1.49 (s, 9H, CH_3 carbamate), 1.45 (s, 9H, CH_3 carbamate), 1.11 (d, *J* = 7.2 Hz, 3H, CH_3CH) ,0.81 (d, *J* = 6.9 Hz, 3H, CH_3CH); ^{13}C

NMR ($CDCl_3$, 100 MHz): δ 18.4 and 15.4 (*C*H_3CH), 27.9 (*C*H_3 carbamate), 29.6 (*C*H), 62.1 (*C*H*), 83.1 and 82.8 (*C* carbamate), 103.4 (*C*NH), 154.5 and 149.0 (*C*O carbamate), 155.7 (*C*OH), 165.3 (*C*O lactam); HRMS (FAB+) *m/z* calcd for $C_{17}H_{29}N_2O_6$ [M+H^+] 357.2026, found 357.2031.



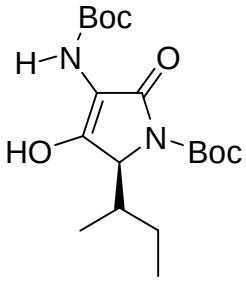
(5*R*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-*iso*propyl-3-pyrrolin-2-one (2e)

Yield = 84 %

Colorless oil

$[\alpha]_D^{20}$ = -53 (*c* = 1.15, CH_2Cl_2).

Chiral HPLC analyses of **2b, 2c, 2d** and **2e** were performed on a Chiralcel OD-RH column (Solvents: acetonitrile/water in a 70/30 ratio with 0.1% of trifluoroacetic acid; flow: 1 mL/min).

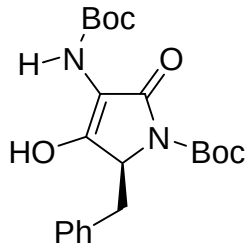


(5*S*,6*S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-*sec*butyl-3-pyrrolin-2-one (2f)

Yield = 71 %

Colorless oil

$[\alpha]_D^{20}$ = +46 (*c* = 1.02, CH_2Cl_2); t_r = 14.180 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 11.26 (m, 1H, O*H*), 6.55 (br s, 1H, N*H*), 4.39 (d, *J* = 2.5 Hz, 1H, C*H**CO), 2.30-2.16 (m, 1H, C*H**CH_3), 1.72-1.60 (m, 1H, C*H*$_2$$CH_3$), 1.56 (s, 9H, C*H*$_3$ carbamate), 1.60-1.42 (m, 1H, C*H*$_2$$CH_3$), 1.50 (s, 9H, C*H*$_3$ carbamate), 1.10-0.85 (m, 3H, C*H*$_3$$CH_2$), 0.80 (d, *J* = 6.9 Hz 3H, C*H*$_3$CH*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.5 (*C*O lactam), 155.7 and 154.4 (*C*O carbamate and *C*OH), 148.9 (*C*O carbamate), 104.1 (*C*NH),12.4 (*C*$H_3$$CH_2$), 83.2 and 82.9 (*C* carbamate), 60.7 (*C*H*CO), 36.4 (*C*H*CH_3), 28.1 and 27.9 (*C*H_3 carbamate), 25.9 (*C*$H_2$$CH_3$), 15.6 (*C*$H_3$CH*); HRMS (FAB+) *m/z* calcd for $C_{18}H_{31}N_2O_6$ [M+H^+] 371.2182, found 371.2189.

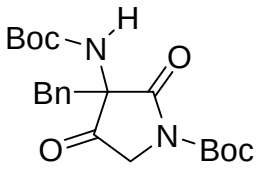


(*5S*)-5-Benzyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-3-pyrrolin-2-one (2g)

Yield = 16 %

Colorless oil

t_r = 14.040 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 11.20 (m, 1H, O*H*), 7.29-6.95 (m, 5H, H_{arom}), 6.23 (br s, 1H, N*H*), 4.50 (br s, 1H, C*H**), 3.36 (dd, J_{AB} = 16.5 Hz, J_{AX} = 5.3 Hz, 1H, CH_2Ph), 3.15 (dd, J_{AB} = 16.5 Hz, J_{BX} = 2.6 Hz, 1H, CH_2Ph), 1.53 (s, 9H, CH_3 carbamate), 1.37 (s, 9H, CH_3 carbamate).

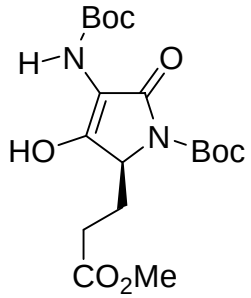


3-Benzyl-1-(*tert*-butoxycarbonyl)-3-[*tert*-butoxycarbonyl)amino]pyrrolidine-2,4-dione (3g)

Yield = 46 %

White powder

Mp = 164°C; t_r = 12.759 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.32-7.11 (m, 5H, H_{arom}), 5.45 (br s, 1H, N*H*), 4.02 (d, J_{AB} = 18.3 Hz, 1H, CH_2CO), 3.17 (d, J_{AB} = 12.1 Hz, 1H, CH_2Ph), 3.00 (d, J_{AB} = 18.4 Hz, 1H, CH_2CO), 2.99 (d, J_{AB} = 12.0 Hz, 1H, CH_2Ph), 1.44 (s, 9H, CH_3 carbamate), 1.40 (s, 9H, CH_3 carbamate); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 203.9 (*C*O ketone), 170.9 (*C*O lactam), 154.8 and 148.3 (*C*O carbamate), 130.9 (C_{arom}), 130.0, 128.8 and 128.3 (CH_{arom}), 83.6 and 81.8 (*C* carbamate), 65.2 (*C*CH_2Ph), 54.6 (*C*H_2CO), 40.5 (*C*H_2Ph), 28.2 and 28.0 (*C*H_3 carbamate); HRMS (FAB+) *m/z* calcd for $C_{21}H_{29}N_2O_6$ [M+H$^+$] 405.2026, found 405.2022.



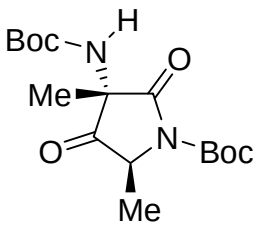
(*5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-[2-(methoxycarbonyl)ethyl]-3-pyrrolin-2-one (2j)

Yield = 42 %

Yellow oil

$[\alpha]_D^{20}$ = -4 (*c* = 1.89, CH_2Cl_2); t_r = 11.667 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.66 (s, 1H, N*H*), 4.46 (dd, *J* = 5.3 Hz, *J* = 2.6 Hz, 1H, C*H**), 3.79-3.60 (m, 3H, OCH_3), 2.64-2.11 (m, 4H,

C*H*$_2$), 1.53 (s, 9H, C*H*$_3$ carbamate), 1.48 (s, 9H, C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.0 (*C*O lactam), 164.9 (*C*O ester), 155.7, 152.9 and 148.6 (*C*O carbamate and *C*OH), 103.9 (*C*NH), 83.2 (*C* carbamate), 56.6 (*C*H*), 51.7 (O*C*H$_3$), 27.8 (*C*H$_3$ carbamate), 27.3 (CH**C*H$_2$), 24.7 (*C*H$_2$CO).

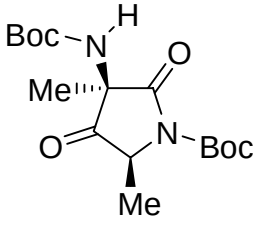


(*3S,5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3,5-dimethylpyrrolidine-2,4-dione (*3S,5S*)-(3h)

Yield = 55 %

White powder

Mp = 104 °C; $[\alpha]_D^{20}$ = -9 (*c* = 2.12, CH_2Cl_2); t_r = 11.153 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.54 (br s, 1H, N*H*), 4.52 (q, *J* = 7.1 Hz, 1H, C*H**), 1.54 (s, 9H, C*H*$_3$ carbamate), 1.52 (s, 3H, C*H*$_3$), 1.40 (s, 3H, C*H*$_3$), 1.35 (s, 9H, C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 207.1 (*C*O ketone), 172.0 (*C*O lactam), 154.9 and 149.0 (*C*O carbamate), 84.0 and 81.5 (*C* carbamate), 60.6 (*C*H*), 59.5 (*C**), 28.1 and 28.0 (*C*H$_3$ carbamate), 20.2 and 17.9 (*C*H$_3$); HRMS (FAB+) *m/z* calcd for $C_{16}H_{27}N_2O_6$ [M+H$^+$] 343.1869, found 343.1870. Medium range nOe coupling is observed between the C$_5$*H* (4.52 ppm) and the N*H* (5.54 ppm).

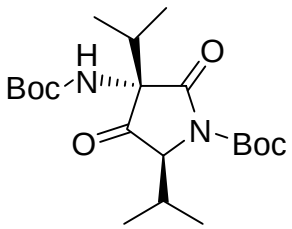


(*3R,5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3,5-dimethylpyrrolidine-2,4-dione (*3R,5S*)-(3h)

Yield = 11 %

Crystals

Mp = 159 °C; $[\alpha]_D^{20}$ = -101 (*c* = 1.57, CH_2Cl_2); t_r = 11.602 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.23 (br s, 1H, N*H*), 4.47 (q, *J* = 6.7 Hz, 1H, C*H**), 1.69 (d, *J* = 6.6 Hz, 3H, C*H*$_3$CH*), 1.59 (s, 9H, C*H*$_3$ carbamate), 1.43 (s, 3H, C*H*$_3$), 1.41 (s, 9H, C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 207.2 (*C*O ketone), 171.6 (*C*O lactam), 154.4 and 149.1 (*C*O carbamate), 84.0 and 81.4 (*C* carbamate), 60.0 (*C**), 59.9 (*C*H*), 28.1 and 28.0 (*C*H$_3$ carbamate), 19.8 (*C*H$_3$), 16.4 (*C*H$_3$CH*); HRMS (FAB+) *m/z* calcd for $C_{16}H_{27}N_2O_6$ [M+H$^+$] 343.1869, found 343.1870. Medium range nOe coupling is observed between the methyl group bearing by the stereogenic center in C$_5$ position, C*H*$_3$CH* (1.69 ppm) and the N*H* (5.23 ppm), and between the methyl group in C$_3$ position, C*H*$_3$ (1.43 ppm) and the C$_5$*H* (4.47 ppm).

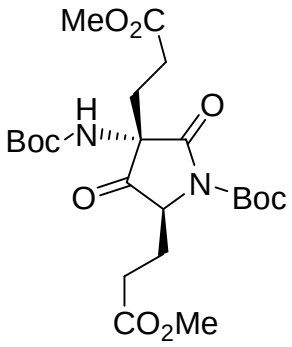


(*3S,5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3,5-di(*iso*propyl)pyrrolidine-2,4-dione (3i)

Yield = 68 %

Crystals

Mp = 88 °C; $[\alpha]_D^{20}$ = -18 (*c* = 0.40, MeOH); t_r = 13.309 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.08 (br s, 1H, N*H*), 4.32 (d, *J* = 5.7 Hz, 1H, C*H**), 2.30-2.08 (m, 2H, C*H*CH_3), 1.49 (s, 9H, CH_3 carbamate), 1.32 (s, 6H, CH_3 carbamate), 1.27 (s, 3H, CH_3 carbamate), 1.12-1.04 (m, 6H, CH_3CH), 1.01-0.83 (m, 6H, CH_3CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 205.3 (*C*O ketone), 171.4 (*C*O lactam), 155.3 and 150.0 (*C*O carbamate), 83.9 and 81.2 (*C* carbamate), 69.3 (*C*H*), 65.1 (*C**), 30.5 and 29.8 (*C*H), 28.1 and 27.9 (*C*H_3 carbamate), 19.4, 18.8, 16.5 and 16.0 (*C*H_3CH); HRMS (FAB+) *m/z* calcd for $C_{20}H_{35}N_2O_6$ [M+H$^+$] 399.2495, found 399.2484.



(*3S,5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]- 3,5-di[2-(methoxycarbonyl)ethyl]pyrrolidine-2,4-dione (3i)

Yield = 29 %

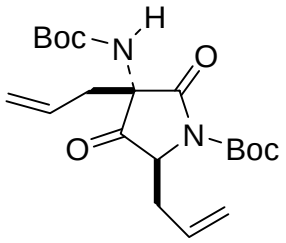
Yellow oil

t_r = 11.832 min; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.39 (s, 9H, CH_3 carbamate), 1.59 (s, 9H, CH_3 carbamate), 2.75-2.05 (m, 8H, CH_2), 3.71 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 4.48 (dd, *J* = 3.8 Hz, *J* = 9.9 Hz, 1H, C*H**), 6.25 (br s, 1H, N*H*); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.6 (*C*O ketone), 173.1, 172.6 and 171.2 (*C*O lactam and *C*O ester), 155.3 and 149.1 (*C*O carbamate), 84.5 and 81.5 (*C* carbamate), 63.3 (*C*H*), 61.7 (*C**), 52.4 and 51.9 (O*C*H_3), 29.8, 27.3 and 26.8 (*C*H_2), 28.2 and 28.0 (*C*H_3 carbamate); HRMS (FAB+) *m/z* calcd for $C_{22}H_{35}N_2O_{10}$ [M+H$^+$] 487.2292, found 487.2300.

Rearrangement-Alkylation

General procedure with LiHMDS: To a stirred solution of activated DKP (0.75 mmol) in dry THF (4 mL), cooled at -78°C under argon, was added drop by drop a solution of LiHMDS 1.06 M in THF (for **2a-b**: 1.5 mmol; for **5c-d**: 0.75 mmol). After 45 min., the alkylating agent (for **2a-b**: 1.5 mmol; for **5c-d**: 0.75 mmol) was added. The reaction was leaved at r.t. for 12 hrs. The mixture was then diluted by AcOEt (10 mL) and washed by HCl 0.1N (10 mL). The organic layer was then dried on $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by column chromatography (CH_2Cl_2/AcOEt), providing the desired compound.

General procedure with NaH: A suspension of 60% NaH in mineral oil (2.00 mmol) was diluted in dry THF (50 mL). A solution of activated DKP (2.00 mmol), dissolved in dry THF was added dropwise at 0°C under argon atmosphere. The reaction was allowed to stir for 1 hr, and the alkylating agent (2.00 mmol) was added. After 12 hrs stirring, AcOEt (100 mL) was added. The organic layer was washed with 0.1N HCl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by column chromatography (CH_2Cl_2/AcOEt), providing the desired compound.

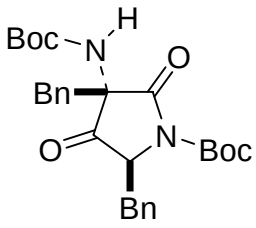


3,5-*trans*-Diallyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidine-2,4-dione (4a)

Yield = 62 %

Colorless oil

t_r = 13.078 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.14-5.53 (m, 2H, C*H*=CH_2), 5.35-5.04 (m, 5H, N*H* and CH_2=CH), 4.66-4.56 (m, 1H, C*H**), 3.05-2.61 (m, 2H, CH*CH_2CH=CH_2), 2.61-2.31 (m, 2H, CCH_2CH=CH_2), 1.64 (s, 9H, CH_3 carbamate), 1.39 (s, 9H, CH_3 carbamate).

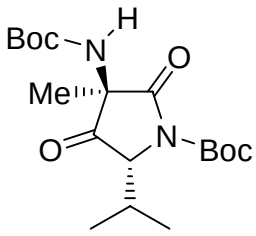


3,5-*trans*-Dibenzyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidine-2,4-dione (4b)

Yield = 57 %

White powder

Mp = 147 °C; t_r = 14.504 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.39-7.01 (m, 5H, H_{arom}), 5.05 (br s, 1H, N*H*), 4.87-4.82 (m, 1H, C*H**), 3.04-2.79 (m, 2H, CH*C*H*$_2$Ph), 2.25 (d, J_{AB} = 13.8 Hz, 1H, CC*H*$_2$Ph), 2.03 (d, J_{AB} = 13.8 Hz, 1H, CC*H*$_2$Ph), 1.64 (s, 9H, C*H*$_3$ carbamate), 1.34 (s, 9H, C*H*$_3$ carbamate); ^{1}H NMR (DMSO-*d*6, 200 MHz): δ 8.31 (s, 1H, N*H*), 7.44-6.98 (m, 5H, H_{arom}), 4.42 (dd, J_{AX} = 8.7 Hz, J_{BX} = 4.3 Hz, 1H, C*H**), 2.97 (d, $J_{A'B'}$ = 13.3 Hz, 1H, CC*H*$_2$Ph), 2.62 (d, $J_{A'B'}$ = 13.3 Hz, 1H, CC*H*$_2$Ph), 2.30 (dd, J_{AB} = 13.9 Hz, J_{AX} = 8.8 Hz, J_{BX} = 4.3 Hz, 1H, CH*C*H*$_2$Ph), 1.65 (dd, J_{AB} = 13.9 Hz, J_{AX} = 8.8 Hz, J_{BX} = 4.3 Hz, 1H, CH*C*H*$_2$Ph), 1.45 (s, 9H, C*H*$_3$ carbamate), 1.32 (s, 9H, C*H*$_3$ carbamate); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.4 (*C*O ketone), 171.4 (*C*O lactam), 154.9 and 149.3 (*C*O carbamate), 130.8-128.3 (C_{arom}), 81.6 and 84.3 (*C* carbamate), 66.1 (*C*H*CH$_2$Ph), 61.8 (*C*CH$_2$Ph), 37.7 (C*C*H$_2$Ph), 34.9 (CH**C*H$_2$Ph), 28.1 (*C*H$_3$ carbamate); HRMS (FAB+) *m/z* calcd for $C_{28}H_{35}N_2O_6$ [M+H$^+$] 495.2495, found 495.2528.

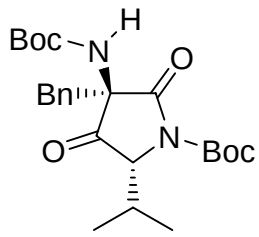


(*3R,5R*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3-methyl-5-*iso*propylpyrrolidine-2,4-dione (5a)

Yield = 63 %

White powder

Mp = 111 °C; $[\alpha]_D^{20}$ = +11 (*c* = 2.10, CH_2Cl_2); t_r = 12.454 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.36 (br s, 1H, N*H*), 4.53 (d, *J* = 4.2 Hz, 1H, C*H**), 2.50-2.32 (m, 1H, C*H*CH$_3$), 1.56 (s, 9H, C*H*$_3$ carbamate), 1.38 (s, 3H, C*H*$_3$C*), 1.36 (s, 9H, C*H*$_3$ carbamate), 1.20 (d, *J* = 7.1 Hz, 3H, C*H*$_3$CH), 0.93 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 206.7 (*C*O ketone), 172.4 (*C*O lactam), 154.7 and 149.6 (*C*O carbamate), 83.8 and 81.3 (*C* carbamate), 69.9 (*C*H*), 59.3 (*C**), 29.7 (*C*H), 28.0 (*C*H$_3$ carbamate), 18.7 (*C*H$_3$C*), 17.8 and 16.5 (*C*H$_3$CH); HRMS (FAB+) *m/z* calcd for $C_{18}H_{31}N_2O_6$ [M+H$^+$] 371.2182, found 371.2167.

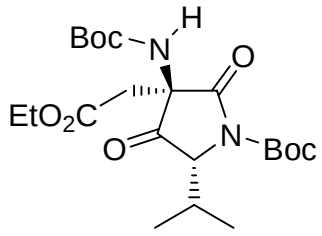


(*3R,5R*)-3-Benzyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*iso*propylpyrrolidine-2,4-dione (5b)

Yield = 72 %

Crystals

Mp = 114 °C; $[\alpha]_D^{20}$ = +20 (*c* = 2.01, CH_2Cl_2); t_r = 14.324 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.40-7.15 (m, 5H, H_{arom}), 5.11 (br s, 1H, N*H*), 4.47 (d, *J* = 5.6 Hz, 1H, C*H**), 3.03 (br s, 2H, CH_2), 2.16-1.92 (m, 1H, C*H*CH_3), 1.56 (s, 9H, CH_3 carbamate), 1.32 (s, 9H, CH_3 carbamate), 1.08 (d, *J* = 7.0 Hz, 3H, CH_3CH), 1.01 (d, *J* = 6.8 Hz, 3H, CH_3CH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 206.1 (*C*O ketone), 171.7 (*C*O lactam), 154.8 and 149.8 (*C*O carbamate), 131.8-128.2 (C_{arom}), 84.0 and 81.4 (*C* carbamate), 69.7 (*C*H*), 61.8 (*C*CH_2Ph), 38.0 (CH_2), 30.1 (*C*H), 28.0 (*C*H_3 carbamate), 19.3 and 18.7 (*C*H_3CH); HRMS (FAB+) *m/z* calcd for $C_{24}H_{35}N_2O_6$ [M+H$^+$] 447.2495, found 447.2521.

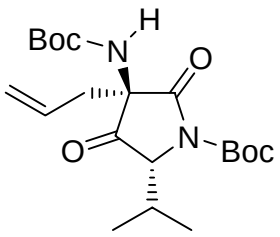


(*3R,5R*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3-[(ethoxycarbonyl)methyl]-5-*iso*propylpyrrolidine-2,4-dione (5c)

Yield = 69 %

Yellow oil

$[\alpha]_D^{20}$ = +21 (*c* = 1.31, CH_2Cl_2); t_r = 13.694 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.61 (br s, 1H, N*H*), 4.54 (d, *J* = 4.3 Hz, 1H, C*H**), 4.28-4.05 (m, 2H, C$H_2$$CH_3$), 2.62-2.49 (m, 2H, *C*$H_2$*C**), 2.49-2.36 (m, 1H, C*H*CH_3), 1.56 (s, 9H, CH_3 carbamate), 1.37 (s, 9H, CH_3 carbamate), 1.29 (t, *J* = 7.0 Hz, 3H, C$H_3$$CH_2$), 1.20 (d, *J* = 7.1 Hz, 3H, CH_3CH), 0.98 (d, *J* = 7.0 Hz, 3H, CH_3CH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 204.6 (*C*O ketone), 170.0 and 168.4 (*C*O lactam and *C*O ester), 155.0 and 149.5 (*C*O carbamate), 84.3 and 81.4 (*C* carbamate), 69.9 (*C*H*), 61.9 (*C*$H_2$$CH_3$), 59.8 (*C**), 34.8 (*C*H_2*C**), 30.1 (*C*H), 28.1 and 27.9 (*C*H_3 carbamate), 19.1 and 17.7 (*C*H_3CH), 14.0 (*C*$H_3$$CH_2$); HRMS (FAB+) *m/z* calcd for $C_{21}H_{35}N_2O_8$ [M+H$^+$] 443.2393, found 443.2411.

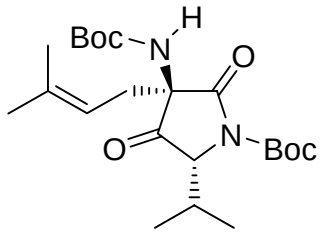


(*3R,5R*)-3-Allyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*iso*propylpyrrolidine-2,4-dione (5d)

Yield = 76 %

White powder

Mp = 83 °C; $[\alpha]_D^{20}$ = +15 (*c* = 1.92, CH_2Cl_2); t_r = 13.338 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.03-5.82 (m, 1H, C*H*=CH_2), 5.37-5.21 (m, 3H, N*H* and CH_2=CH), 4.52 (d, *J* = 4.4 Hz, 1H, C*H**), 2.61-2.34 (m, 3H, C*H*CH_3 and CH_2CH=CH_2), 1.58 (s, 9H, CH_3 carbamate), 1.38 (s, 9H, CH_3 carbamate), 1.22 (d, *J* = 7.1 Hz, 3H, CH_3CH), 0.98 (d, *J* = 7.0 Hz, 3H, CH_3CH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.9 (*C*O ketone), 171.6 (*C*O lactam), 154.8 and 149.6 (*C*O carbamate), 129.1 (*C*H=CH_2), 122.1 (*C*H_2=CH), 84.2 and 81.5 (*C* carbamate), 69.8 (*C*H*), 60.9 (*C**), 36.1 (*C*H_2CH=CH_2), 30.2 (*C*HCH_3), 28.0 (*C*H_3 carbamate), 19.3 and 18.0 (*C*H_3CH); HRMS (FAB+) *m/z* calcd for $C_{20}H_{33}N_2O_6$ [M+H$^+$] 397.2339, found 397.2349.

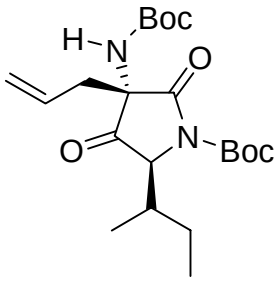


(*3R,5R*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3-[3,3-(dimethyl)allyl]-5-*iso*propylpyrrolidine-2,4-dione (5e)

Yield = 84 %

Colorless oil

$[\alpha]_D^{20}$ = +17 (*c* = 1.16, CH_2Cl_2); t_r = 14.109 min; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.22-5.15 (m, 1H, C*H*=C$(CH_3)_2$), 5.05 (br s, 1H, N*H*), 4.42 (d, *J* = 4.6 Hz, 1H, C*H**), 2.48-2.29 (m, 3H, C*H*CH_3 and CH_2CH=C$(CH_3)_2$), 1.71 (s, 3H, (CH_3)$_2$C=CH), 1.58 (s, 3H, (CH_3)$_2$C=CH), 1.50 (s, 9H, CH_3 carbamate), 1.31 (s, 9H, CH_3 carbamate), 1.13 (d, *J* = 7.1 Hz, 3H, CH_3CH), 0.90 (d, *J* = 7.0 Hz, 3H, CH_3CH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 206.3 (*C*O ketone), 171.9 (*C*O lactam), 154.9 and 149.8 (*C*O carbamate), 139.2 ((CH_3)$_2$*C*=CH), 113.8 (*C*H=C$(CH_3)_2$), 84.1 and 81.4 (*C* carbamate), 69.7 (*C*H*), 61.6 (*C**), 30.8 (*C*H_2CH=C$(CH_3)_2$), 30.2 (*C*HCH_3), 28.2 and 28.0 (*C*H_3 carbamate), 26.1 ((*C*H_3)$_2$C=CH), 19.3, 18.2 and 18.0 (*C*H_3CH and (*C*H_3)$_2$C=CH); HRMS (FAB+) *m/z* calcd for $C_{22}H_{37}N_2O_6$ [M+H$^+$] 425.2652, found 425.2668.



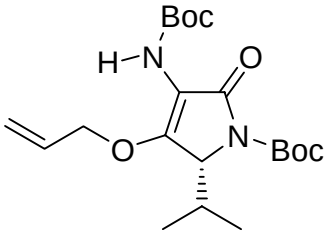
(*3S,5S,6S*)-3-Allyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*sec*butylpyrrolidine-2,4-dione (5f)

Yield = 68 %

White powder

Mp = 101 °C ; $[\alpha]_D^{20}$ = -10 (*c* = 1.07, CH_2Cl_2); t_r = 13.805 min; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 6.00-5.82 (m, 1H, C*H*=CH_2), 5.40-5.18 (m, 3H, N*H* and CH_2=CH), 4.62 (d, *J* = 3.9 Hz, 1H, C*H**), 2.55 (dd, 1H, J_{AB} = 14.6 Hz, *J* = 7.0 Hz, CH_2CH=CH_2), 2.40 (dd, 1H, J_{AB} = 14.6 Hz, *J* = 7.8 Hz, CH_2CH=CH_2), 2.30-2.11 (m, 1H, C*H**CH_3), 1.85-1.70 (m, 1H, C$H_2$$CH_3$), 1.58 (s, 10H, C$H_3$ carbamate and C$H_2$$CH_3$), 1.38 (s, 9H, C$H_3$ carbamate), 1.02 (t, *J* = 7.4 Hz, 3H, C$H_3$$CH_2$), 0.92 (d, *J* = 7.0 Hz, 3H, CH_3CH*); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 206.0 (*C*O ketone), 171.7 (*C*O lactam), 154.7 and 149.4 (*C*O carbamate), 129.1 (*C*H=CH_2), 122.1 (*C*H_2=CH), 84.8 and 84.2 (*C* carbamate), 68.8 (*C*H*), 60.8 (*C**), 36.6 (*C*H*CH_3), 36.0 (*C*H_2CH=CH_2), 28.0 (*C*H_3 carbamate), 26.1 (*C*$H_2$$CH_3$), 15.4 and 12.2 (*C*$H_3$$CH_2$ and *C*H_3CH*); HRMS (FAB+) *m/z* calcd for $C_{21}H_{35}N_2O_6$ [M+H^+] 411.2495, found 411.2486.

Claisen-like Rearrangement



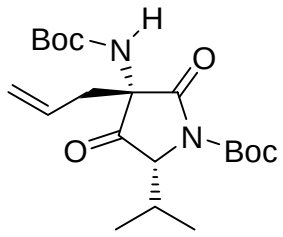
(*5R*)-4-Allyloxy-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*iso*propyl-3-pyrrolin-2-one (6)

Yield = 60 %

Colorless oil

To a solution of the enol **6c** (0.521 g, 1.46 mmol) in dry DMSO (5.5 mL) was added KOH in powder (0.074 g, 1.32 mmol) under magnetic stirring. A gentle warming is necessary for dissolution. The mixture became coloured from pink to deep violet. The allyl bromide (0.11 mL, 1.32 mmol) was then added and the medium was stirred under argon atmosphere for 6 hrs. Then, AcOEt (11mL) was added. The organic layer was washed by 0.1N HCl (11 mL), dried on $MgSO_4$ and concentrated *in vacuo*. The crude residue was purified by column chromatography (CH_2Cl_2/AcOEt 100/0→80/20), providing the derivative **10** (0.347 g) as a colorless oil in a 60% yield.

$[\alpha]_D^{20}$ = -23 (*c* = 0.24, MeOH); t_r = 13.220 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 6.02-5.93 (m, 1H, C*H*=CH_2), 5.65 (br s , 1H, N*H*), 5.29 (d, *J* = 1.4 Hz, 2H, CH_2=CH), 4.90 (m, 2H, CH_2O), 4.20 (d, *J* = 3.2 Hz, 1H, C*H**), 2.53-2.45 (m, 1H, C*H*CH_3), 1.56 (s, 9H, CH_3 carbamate), 1.48 (s, 9H, CH_3 carbamate), 1.14 (d, *J* = 7.2 Hz, 3H, CH_3CH), 0.90 (d, *J* = 7.0 Hz, 3H, CH_3CH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 167.6 and 165.5 (*C*OCH_2 and *C*O lactam), 155.2 and 149.2 (*C*O carbamate), 132.1 (*C*H=CH_2), 118.9 (*C*H_2=CH), 104.7 (*C*NH), 82.8 and 81.1 (*C* carbamate), 71.3 (*C*H_2O), 62.6 (*C*H*), 29.8 (*C*HCH_3), 28.1 (*C*H_3 carbamate), 18.6 and 15.9 (*C*H_3CH); HRMS (FAB+) *m/z* calcd for $C_{20}H_{33}N_2O_6$ [M+H$^+$] 397.2339, found 397.2326.



(*3S,5R*)-3-Allyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*iso*propylpyrrolidine-2,4-dione (7)

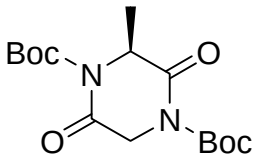
Yield = 69 %

Crystals

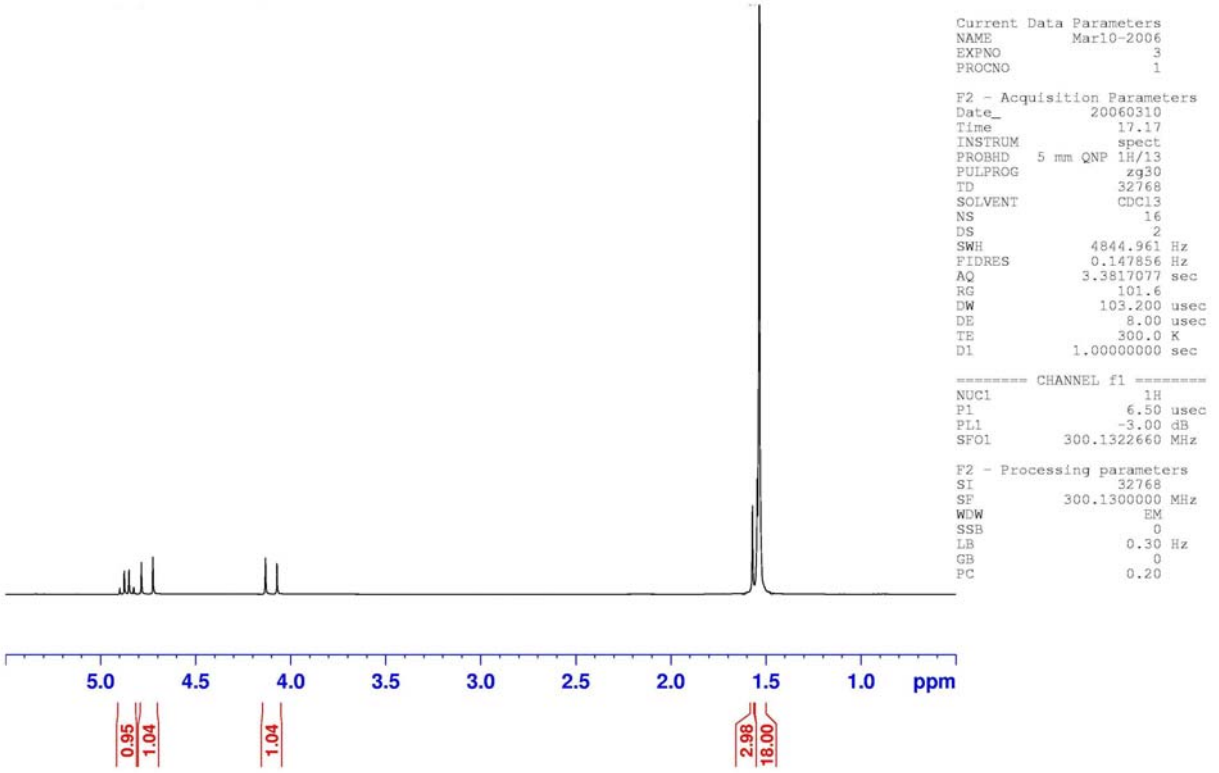
A solution of **10** (0.180 g, 0.45 mmol) in toluene (3 mL) with some drops of DMSO, was irradiated for 30 min at 170°C (Biotage Initiator apparatus). The medium was then concentrated *in vacuo* and the crude residue was purified by column chromatography (CH_2Cl_2/AcOEt 100/0→95/5), providing **11** in 69% yield (0.124 g) as colorless crystals after evaporation.

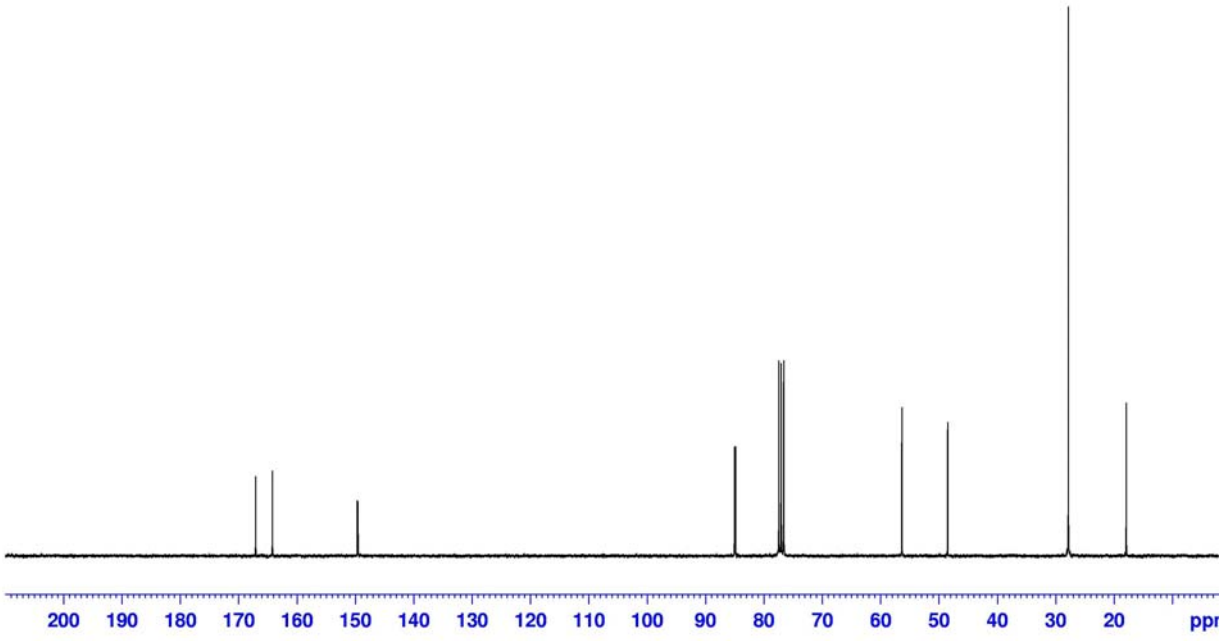
Mp = 117 °C; $[\alpha]_D^{20}$ = -88 (*c* = 1.34, CH_2Cl_2); t_r = 13.411 min; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.80-5.59 (m, 1H, C*H*=CH_2), 5.33-5.23 (m, 2H, CH_2=CH), 5.04 (br s, 1H, N*H*), 4.21 (d, *J* = 4.9 Hz, 1H, C*H**), 2.59-2.48 (m, 1H, C*H*CH_3), 2.47 (d, *J* = 7.5 Hz, 2H, CH_2CH=CH_2), 1.58 (s, 9H, CH_3 carbamate), 1.39 (s, 9H, CH_3 carbamate), 1.17 (d, *J* = 7.5 Hz, 3H, CH_3CH), 1.13 (d, *J* = 7.2 Hz, 3H, CH_3CH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 205.9 (*C*O ketone), 170.5 (*C*O lactam), 153.9 and 149.8 (*C*O carbamate), 128.3 (*C*H=CH_2), 122.6 (*C*H_2=CH), 84.0 and 81.1 (*C* carbamate), 68.1 (*C*H*), 63.6 (*C**), 39.2 (*C*H_2CH=CH_2), 31.0 (*C*HCH_3), 28.1 and 28.0 (*C*H_3 carbamate), 19.2 and 19.0 (*C*H_3CH); HRMS (FAB+) *m/z* calcd for $C_{20}H_{33}N_2O_6$ [M+H$^+$] 397.2339, found 397.2318.

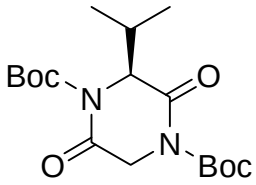
^{1}H NMR and ^{13}C NMR spectra



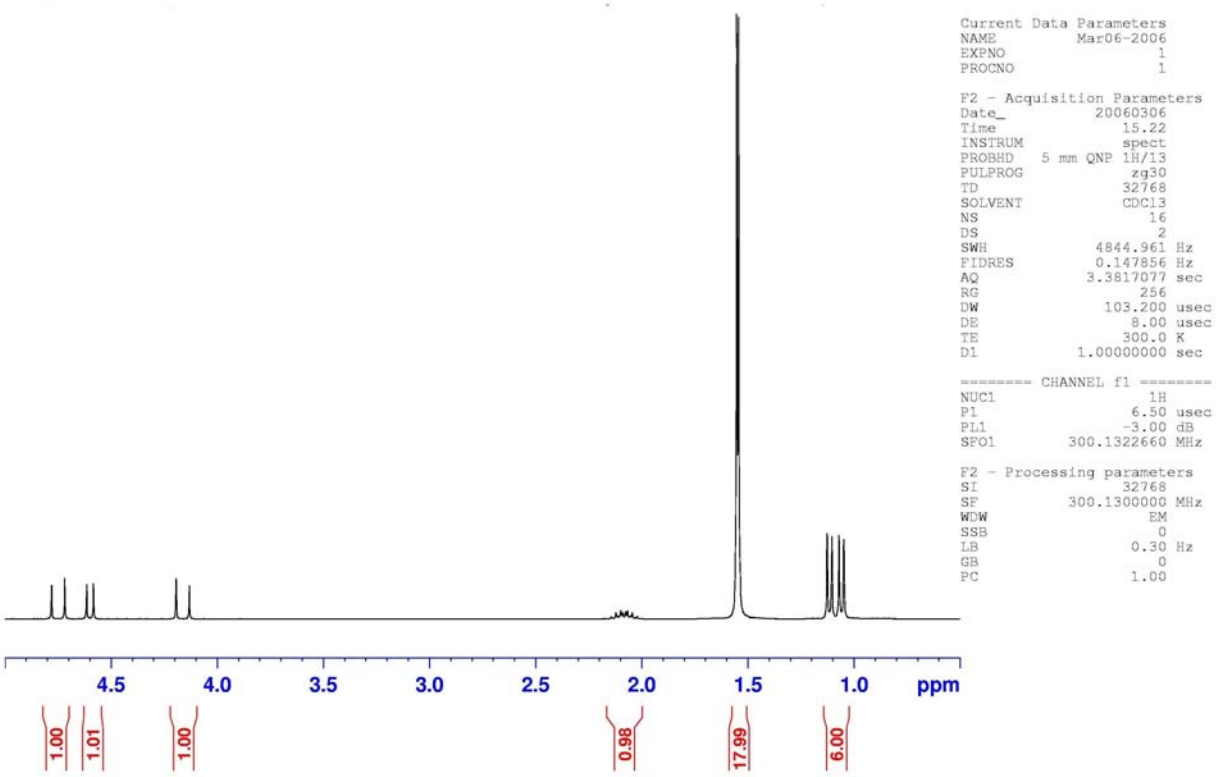
(*3S*)-1,4-Di(*tert*-butoxycarbonyl)-3-methylpiperazine-2,5-dione (1b)

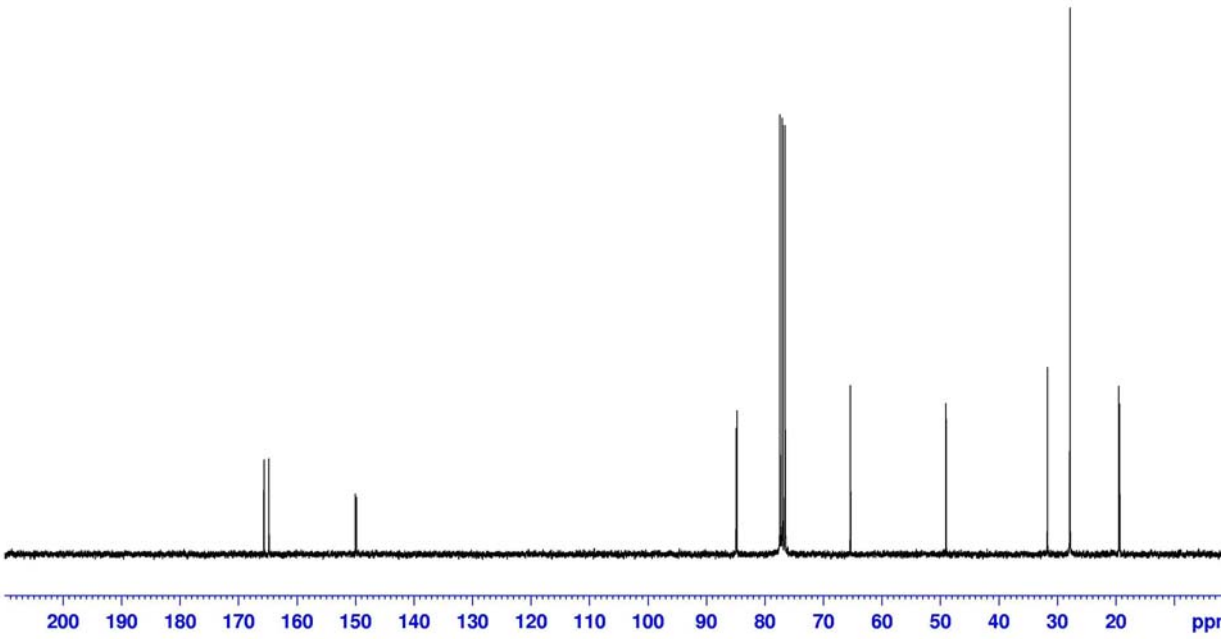


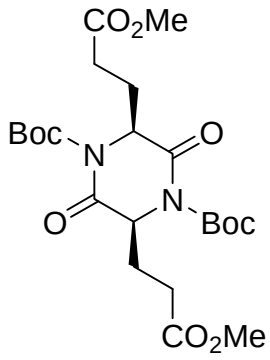




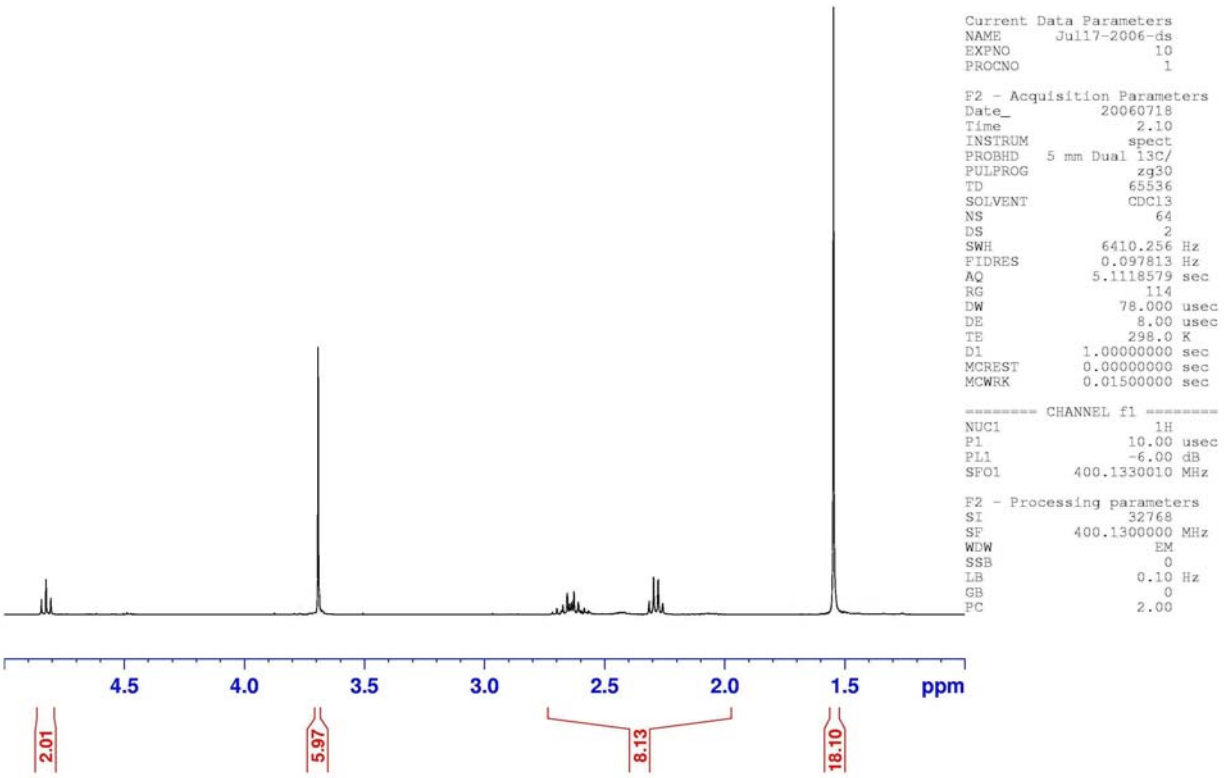
(*3S*)-1,4-Di(*tert*-butoxycarbonyl)-3-*iso*propylpiperazine-2,5-dione (1d)

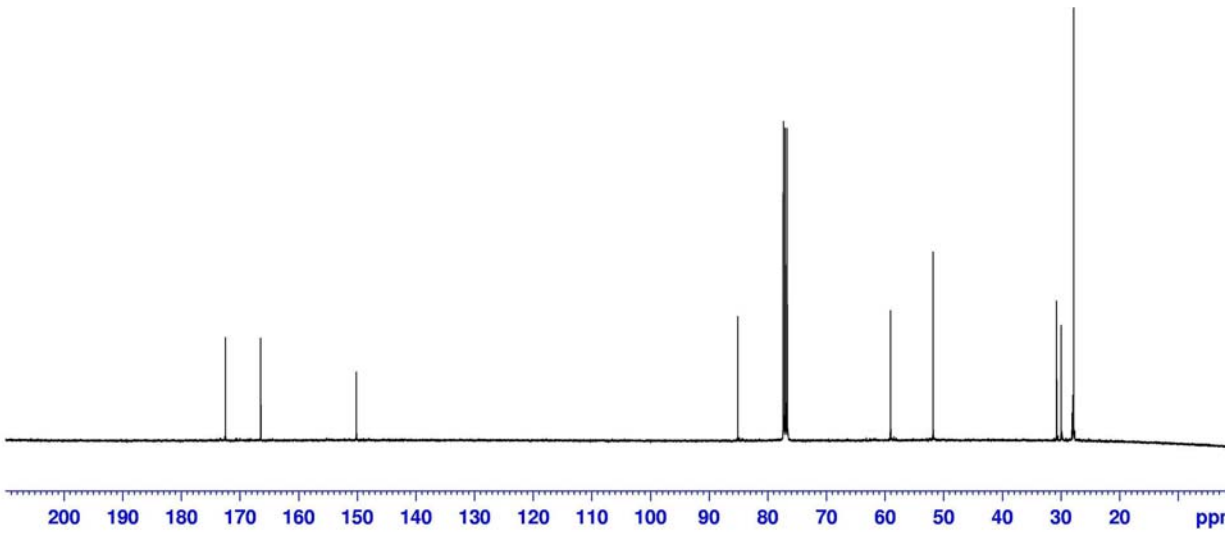


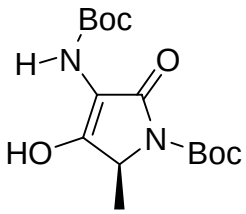




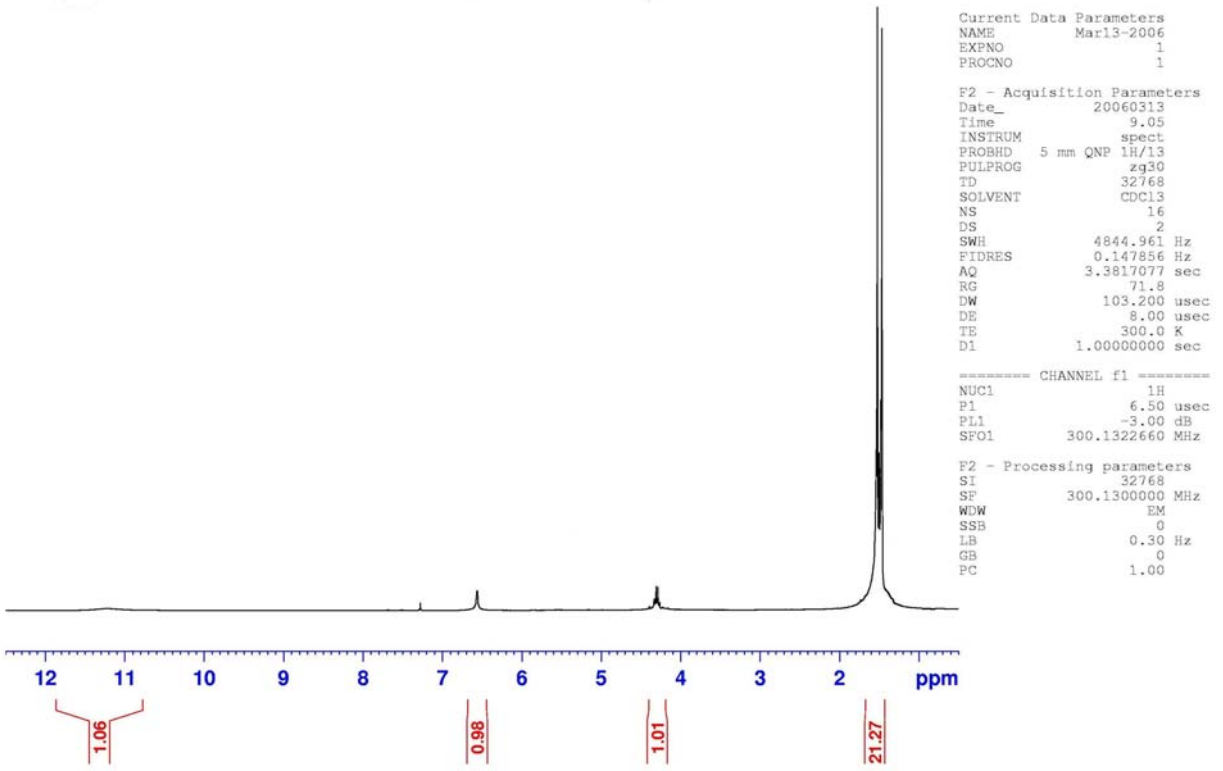
(*3S,6S*)-1,4-Di(*tert*-butoxycarbonyl)-3,6-di[2-(methoxycarbonyl)ethyl]piperazine-2,5-dione (1j)

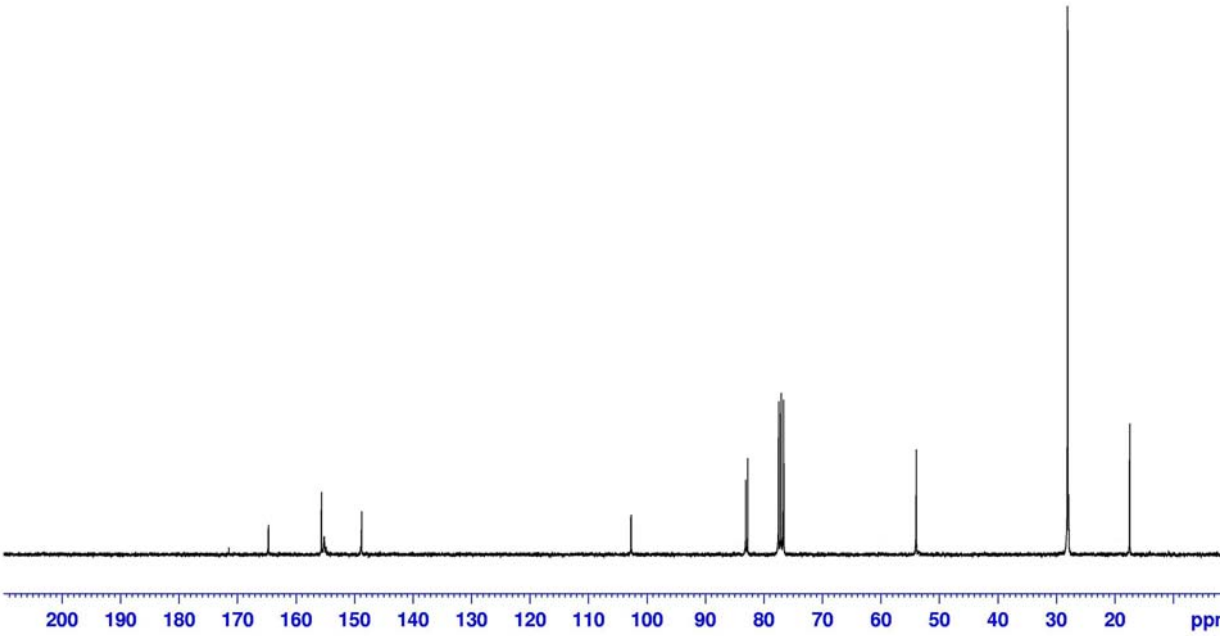


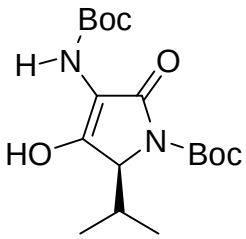




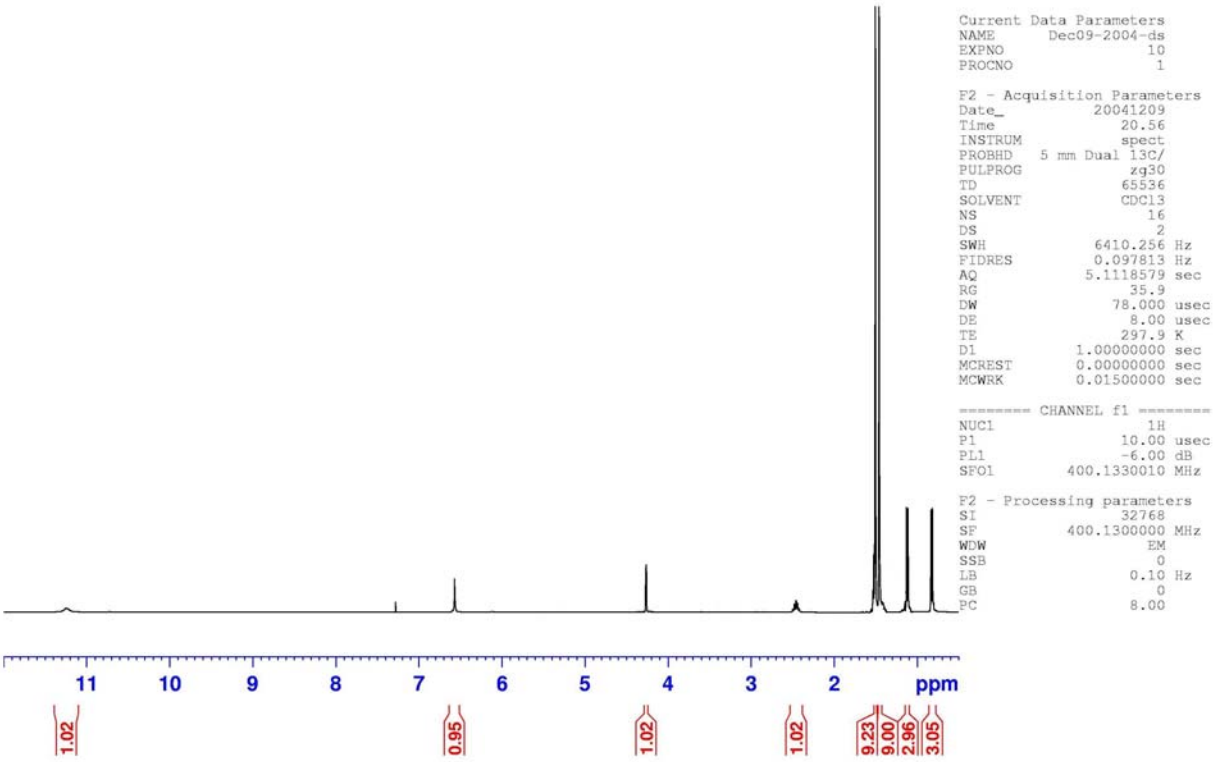
(*5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-methyl-3-pyrrolin-2-one (2b)

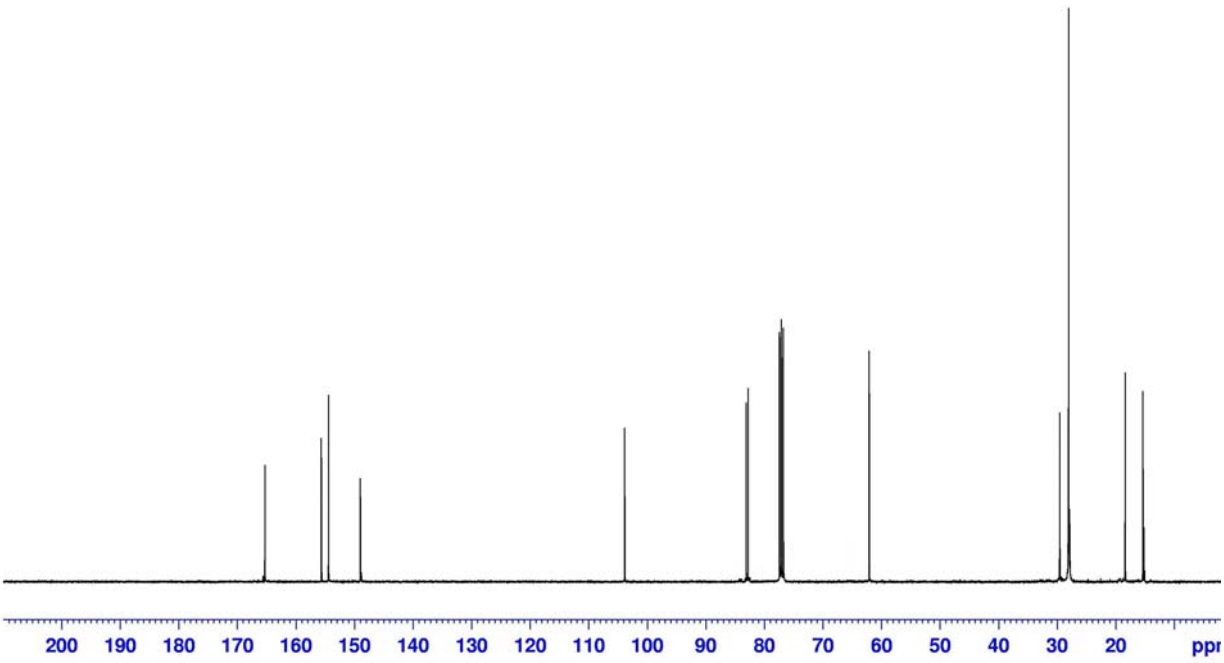


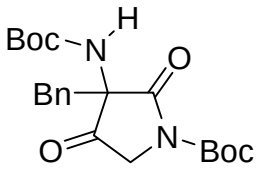




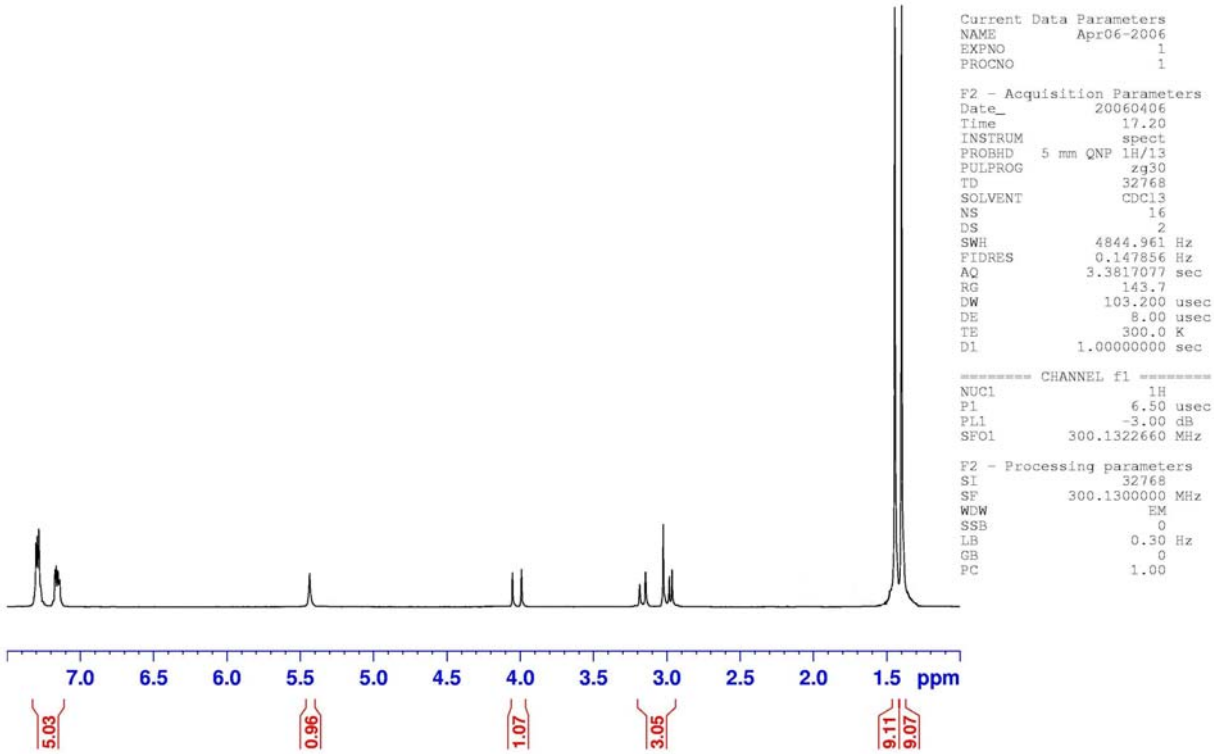
(*5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-4-hydroxy-5-*iso*propyl-3-pyrrolin-2-one (2d)

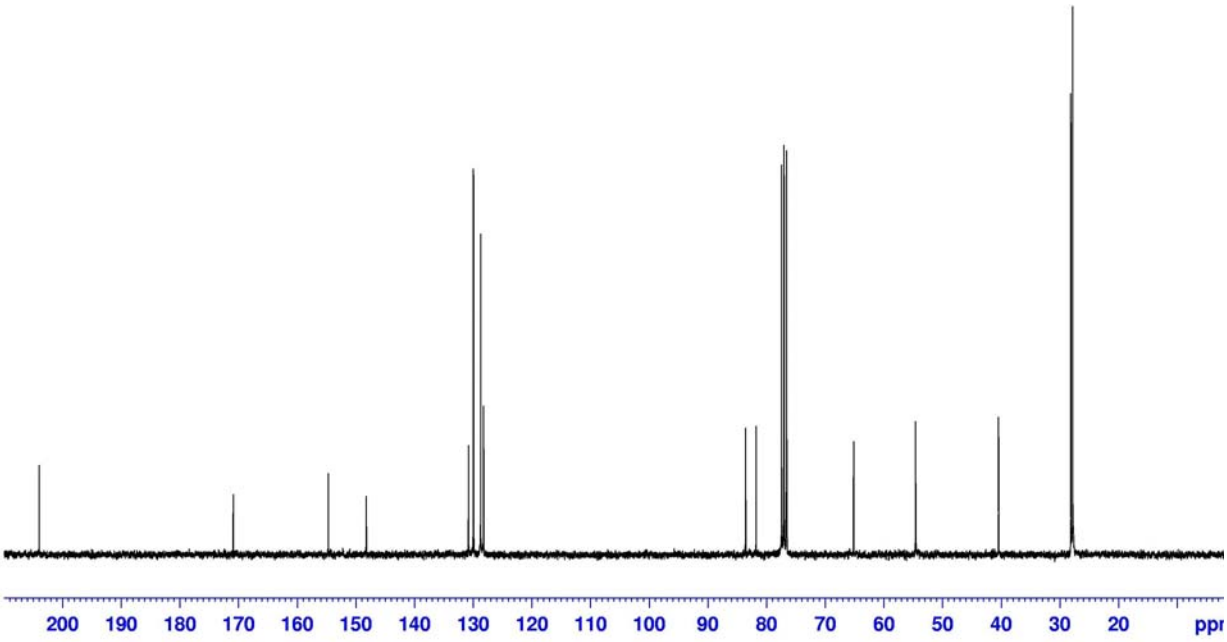


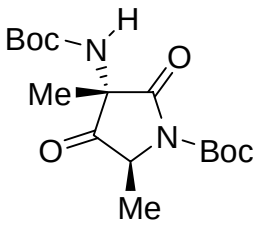




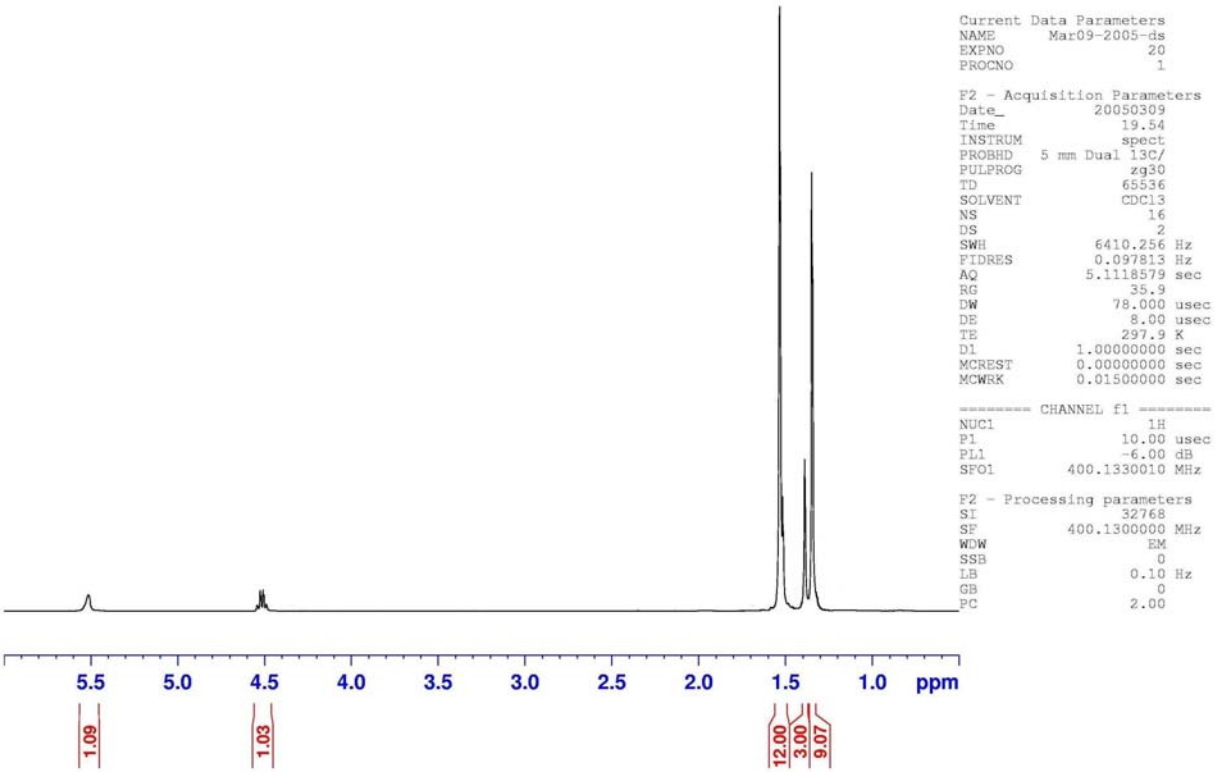
3-Benzyl-1-(*tert*-butoxycarbonyl)-3-[*tert*-butoxycarbonyl)amino]pyrrolidine-2,4-dione (3g)

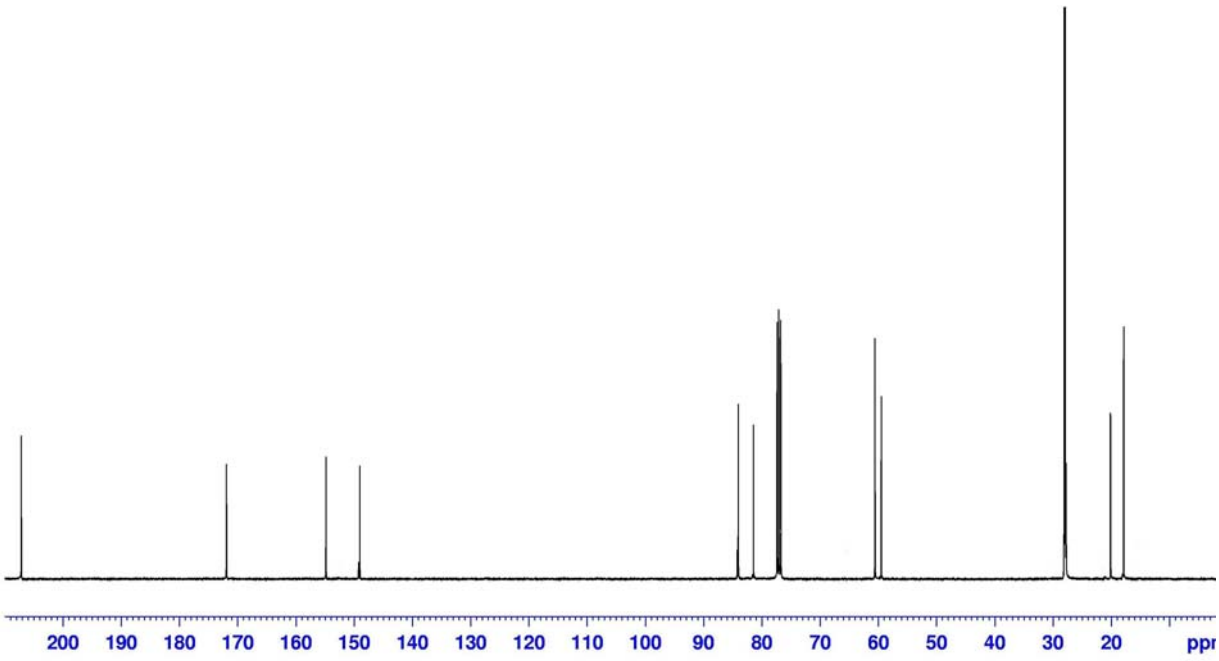


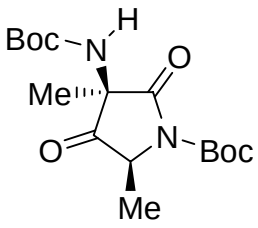




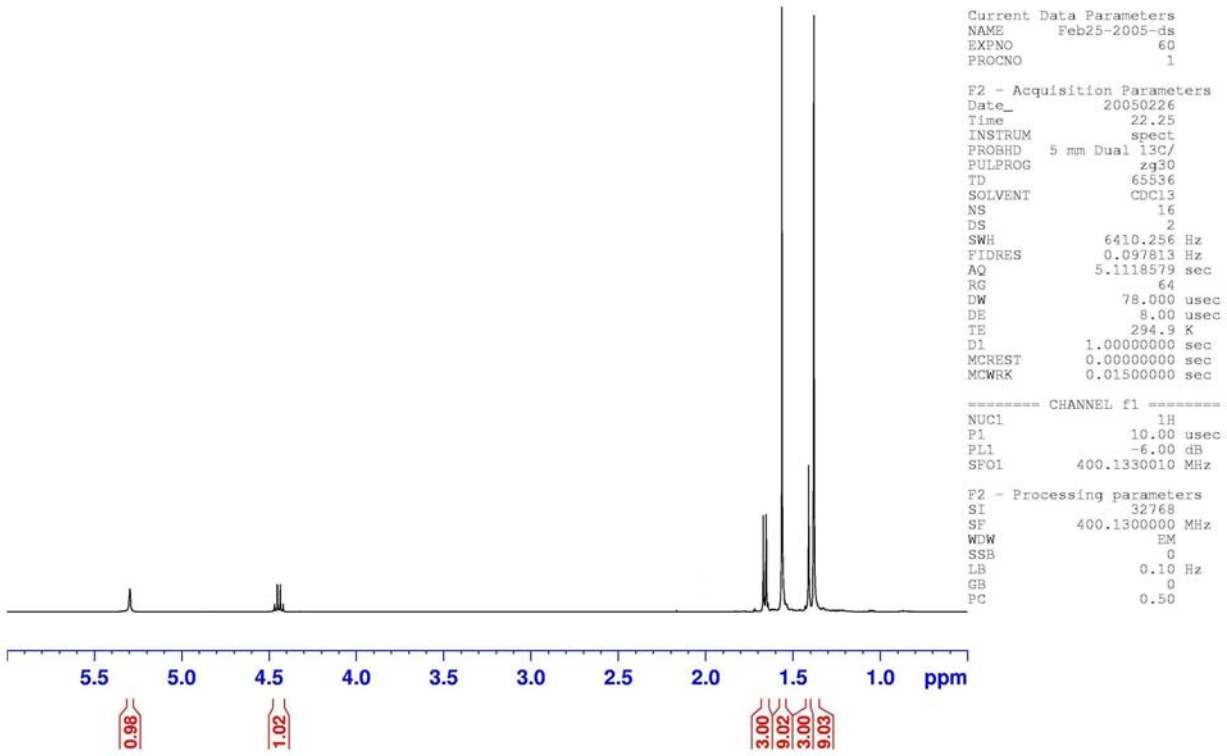
(*3S,5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3,5-dimethylpyrrolidine-2,4-dione (3h)

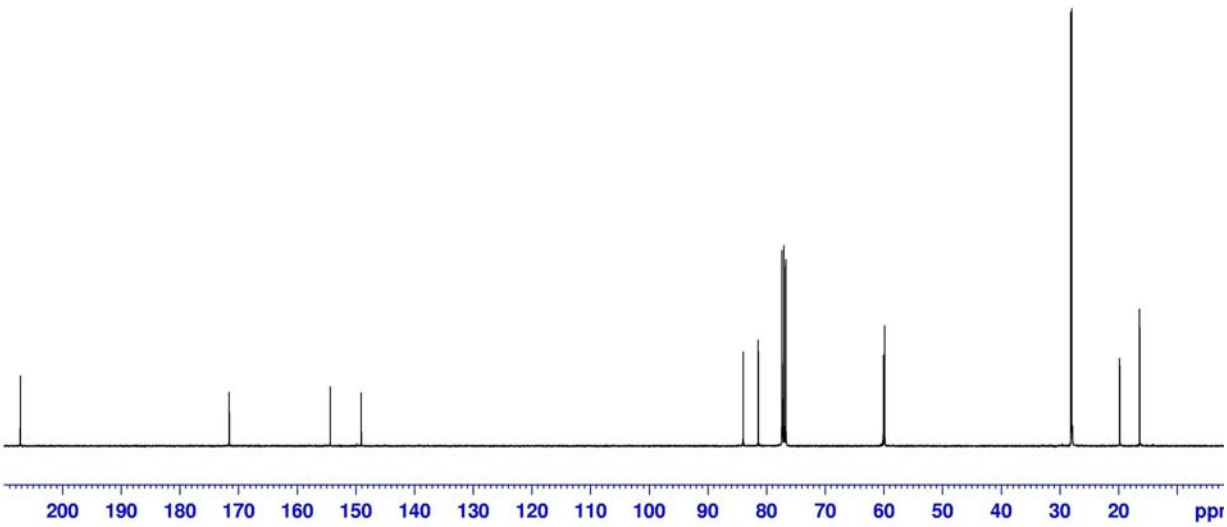


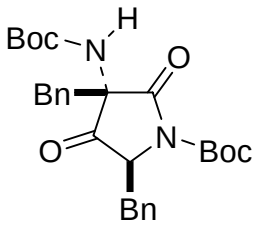




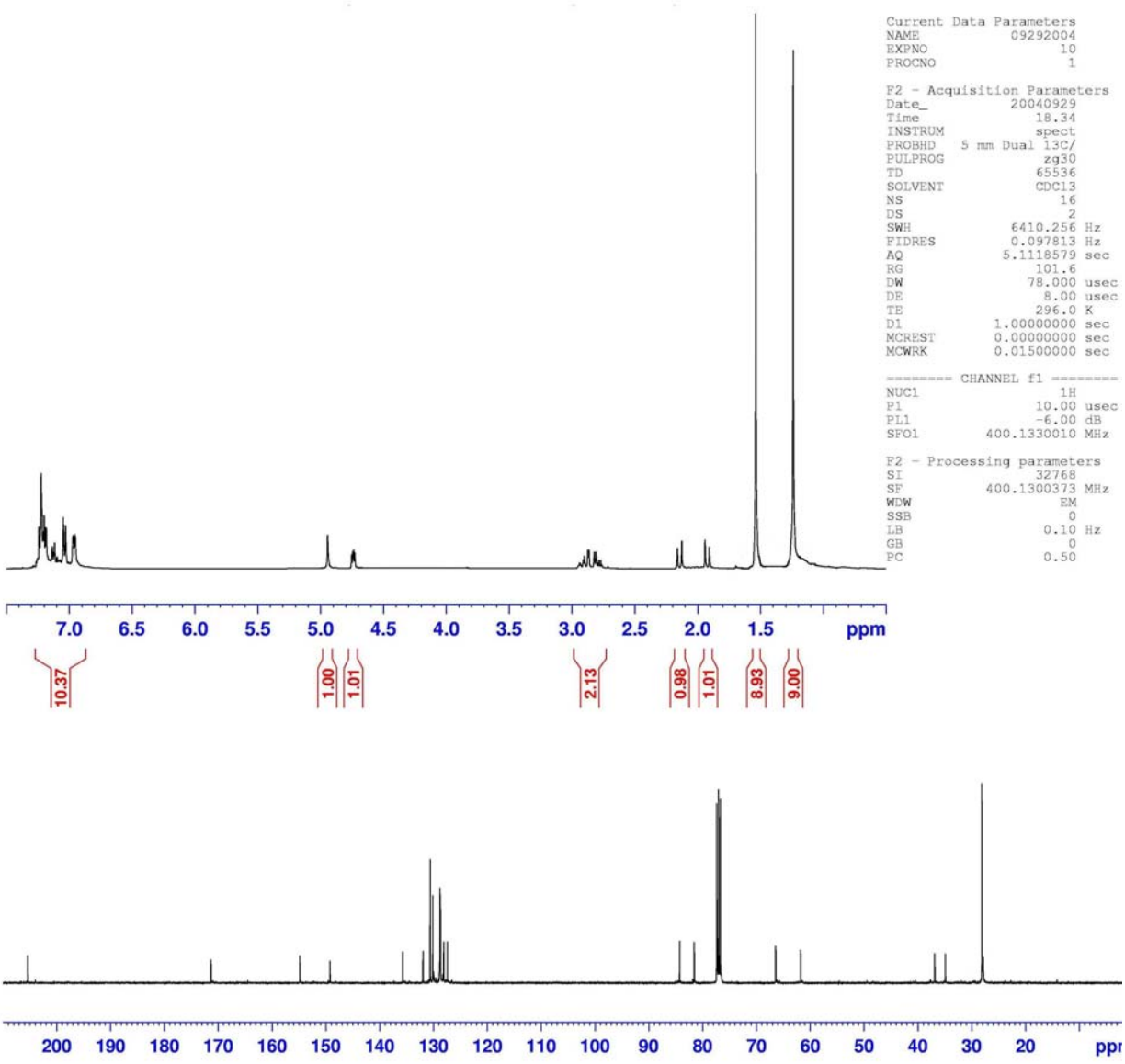
(*3R,5S*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3,5-dimethylpyrrolidine-2,4-dione (3h)

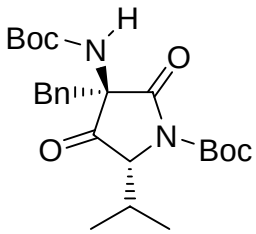




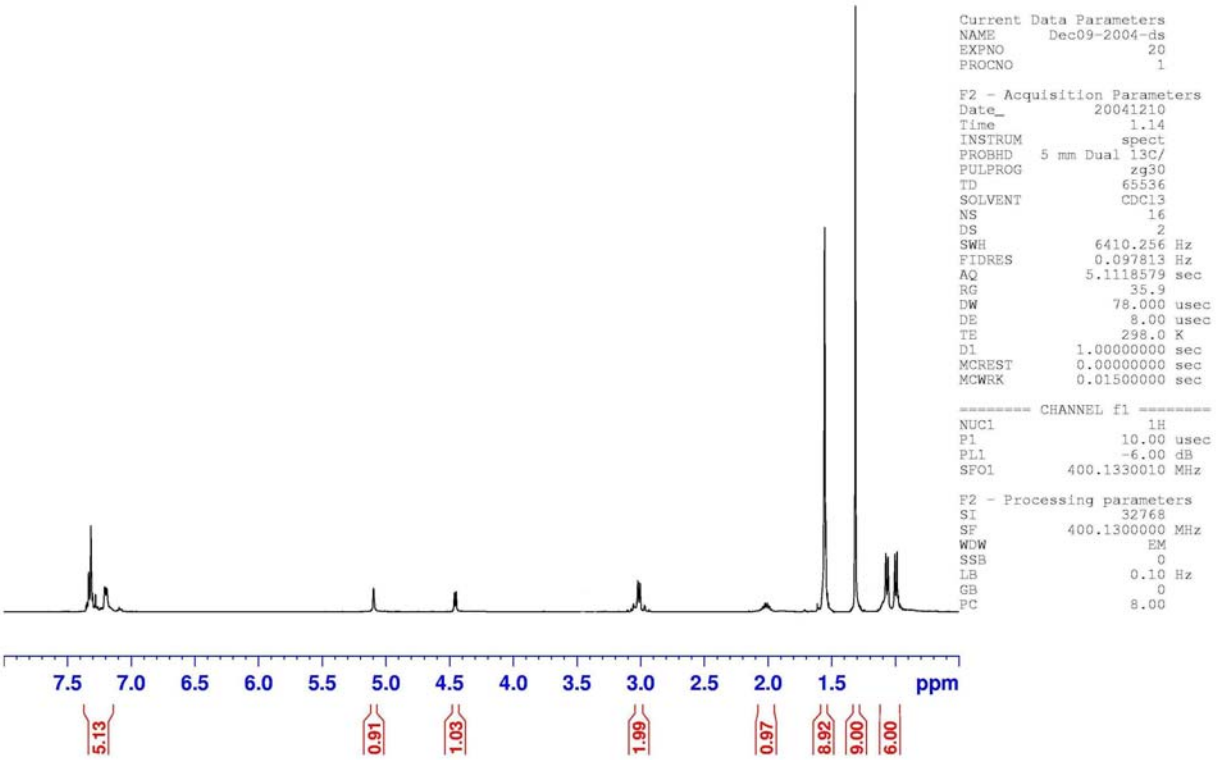


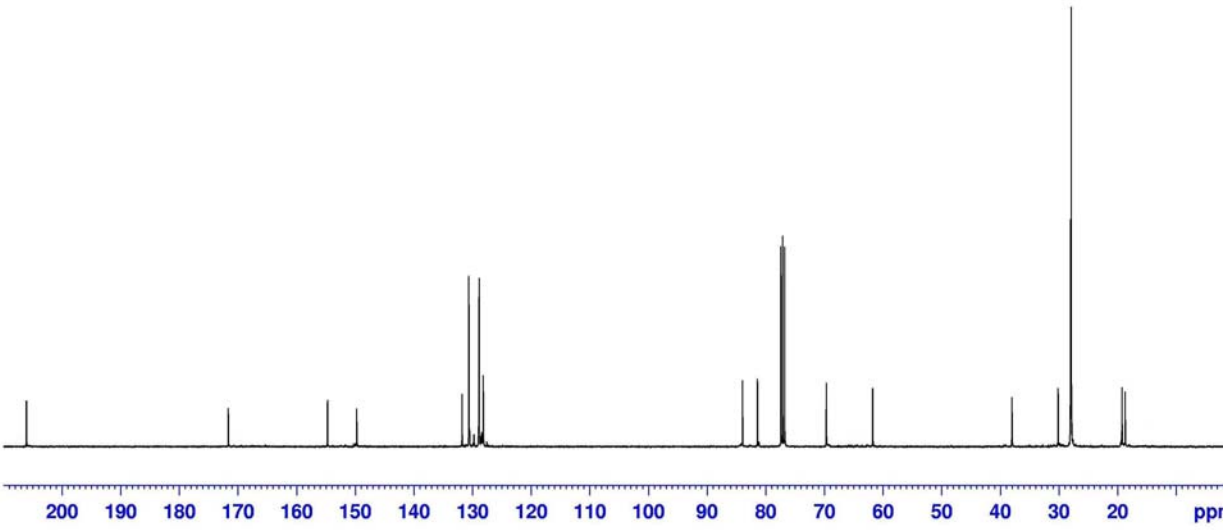
3,5-*trans*-Dibenzyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidine-2,4-dione (4b)

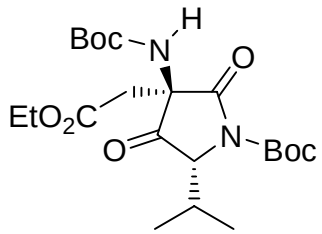




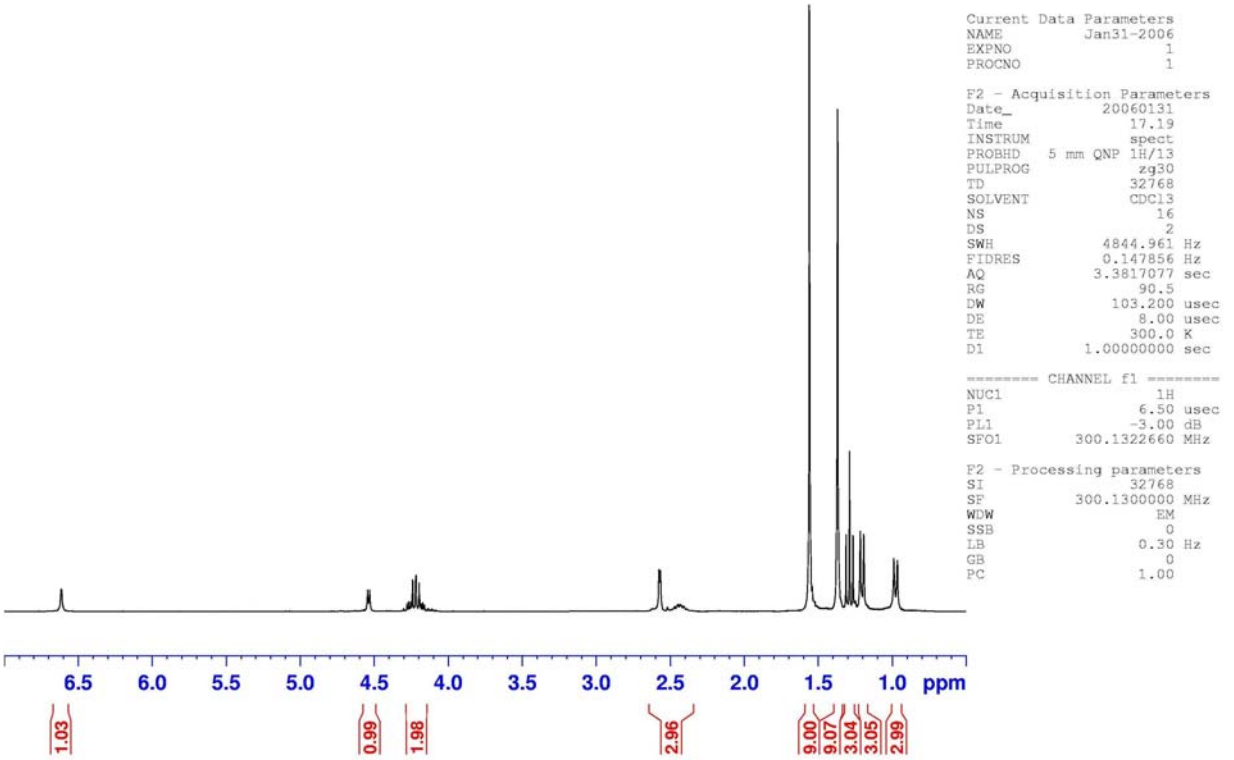
(*3R,5R*)-3-Benzyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*iso*propylpyrrolidine-2,4-dione (5b)

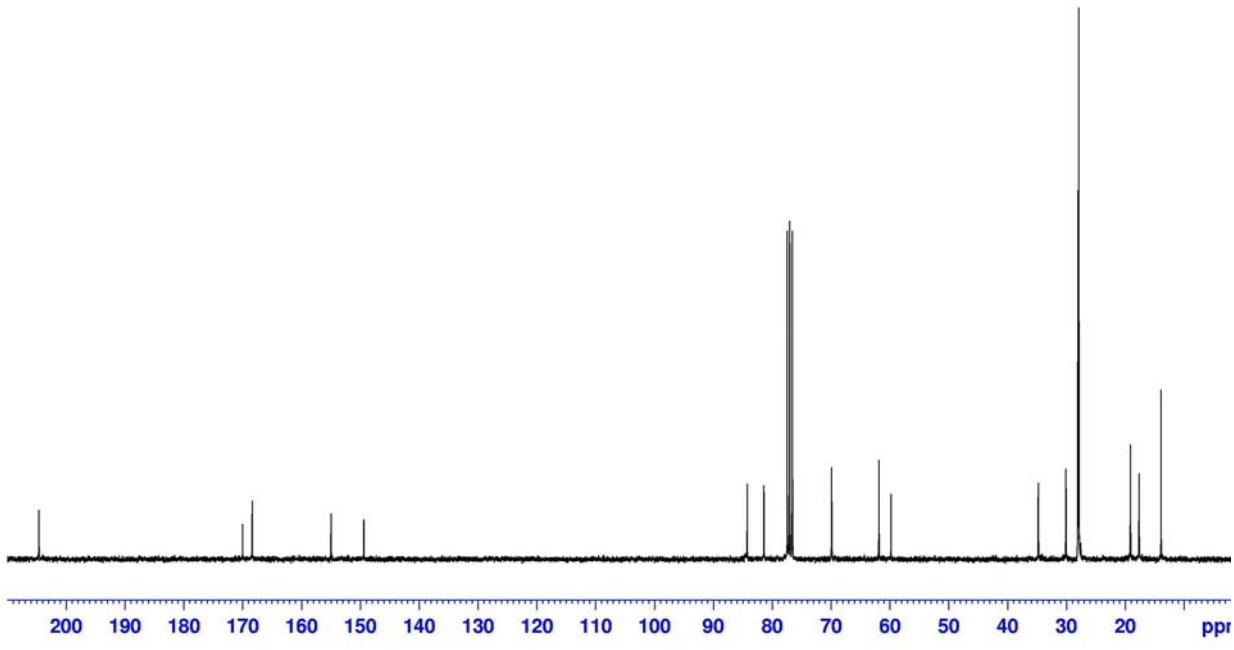


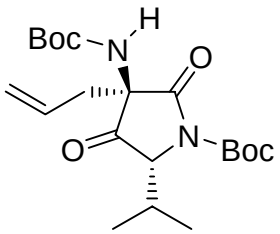




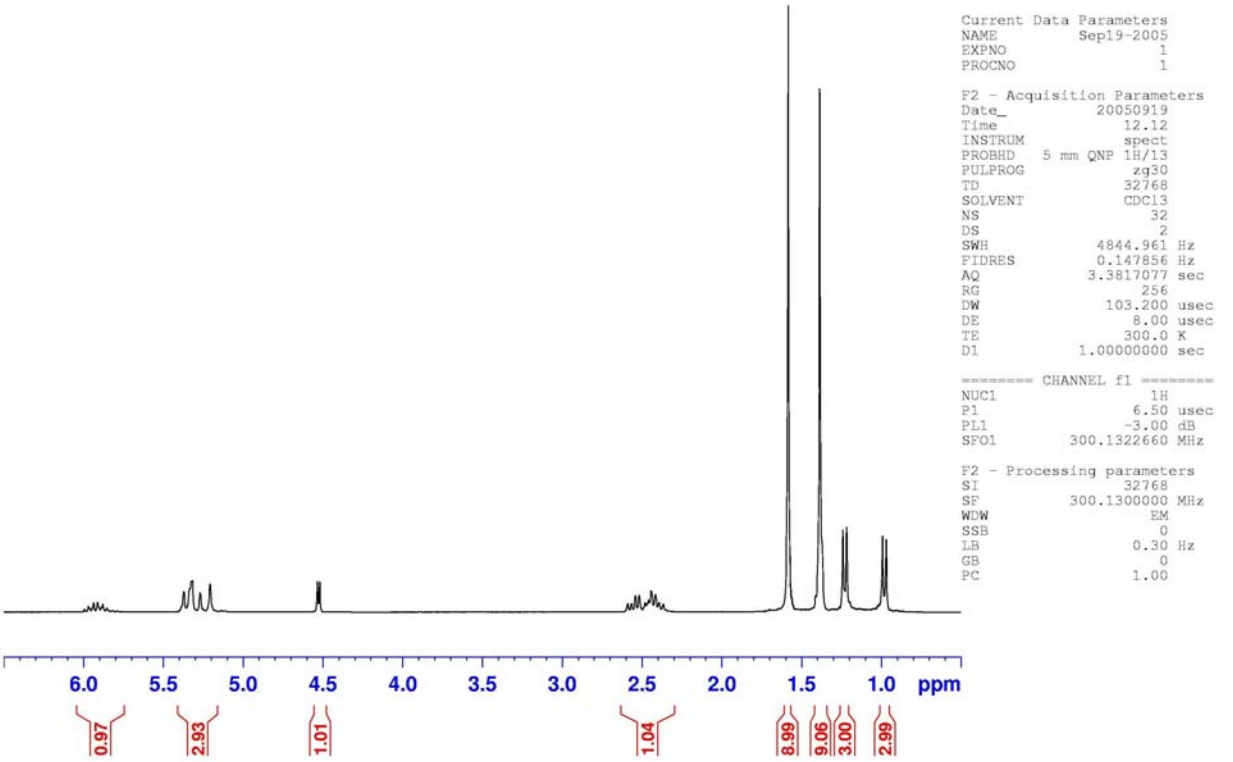
(*3R,5R*)-1-(*tert*-butoxycarbonyl)-3-[(*tert*-*b*utoxycarbonyl)amino]-3-[(ethoxycarbonyl)methyl]-5-*iso*propylpyrrolidine-2,4-dione (5c)

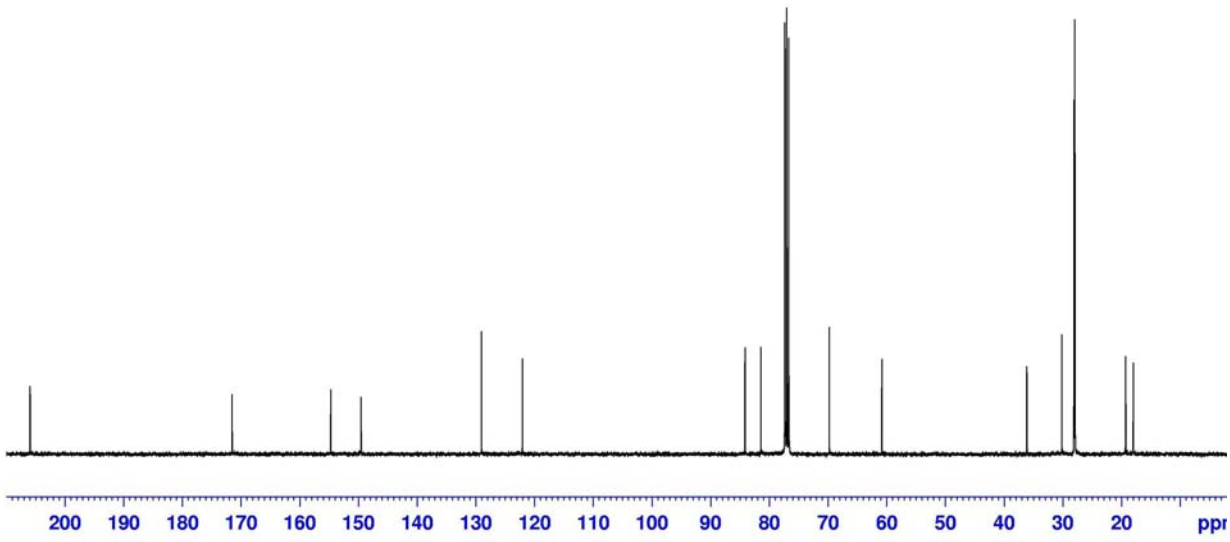


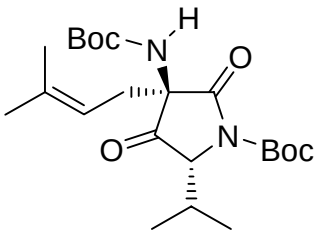




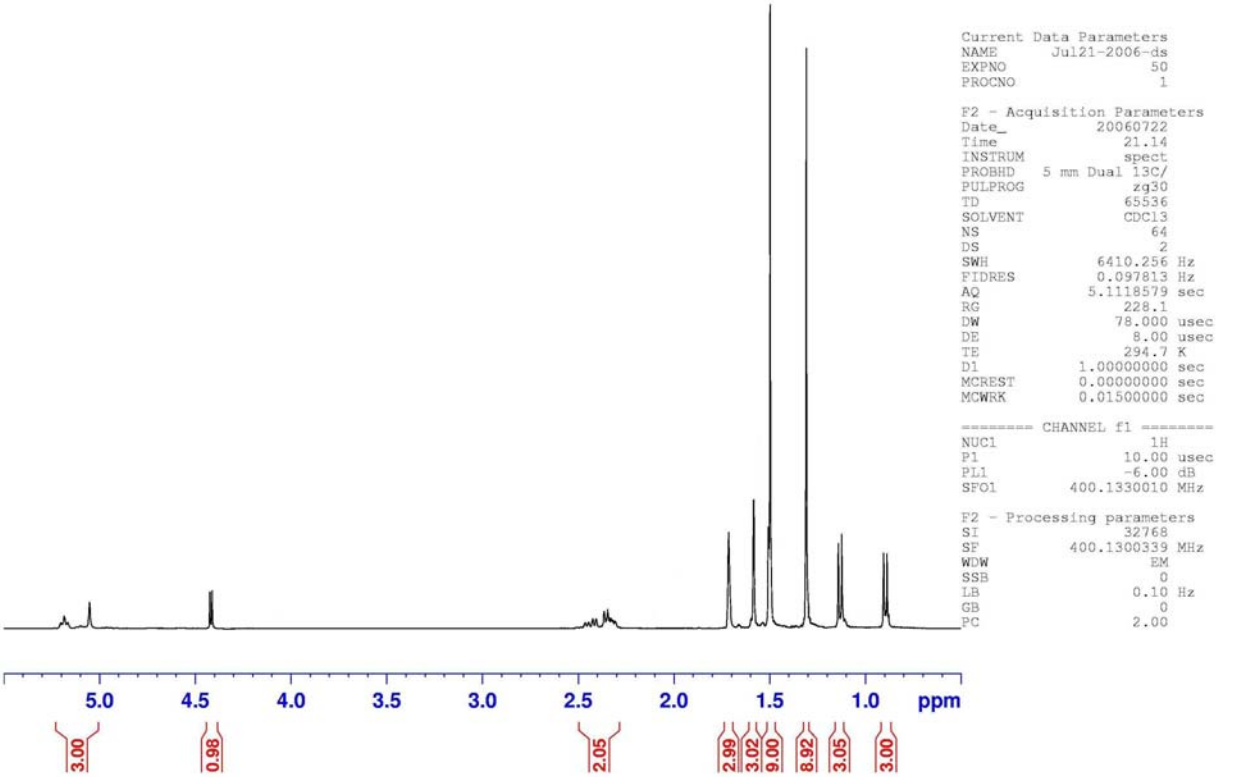
(*3R,5R*)-3-Allyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*iso*propylpyrrolidine-2,4-dione (5d)

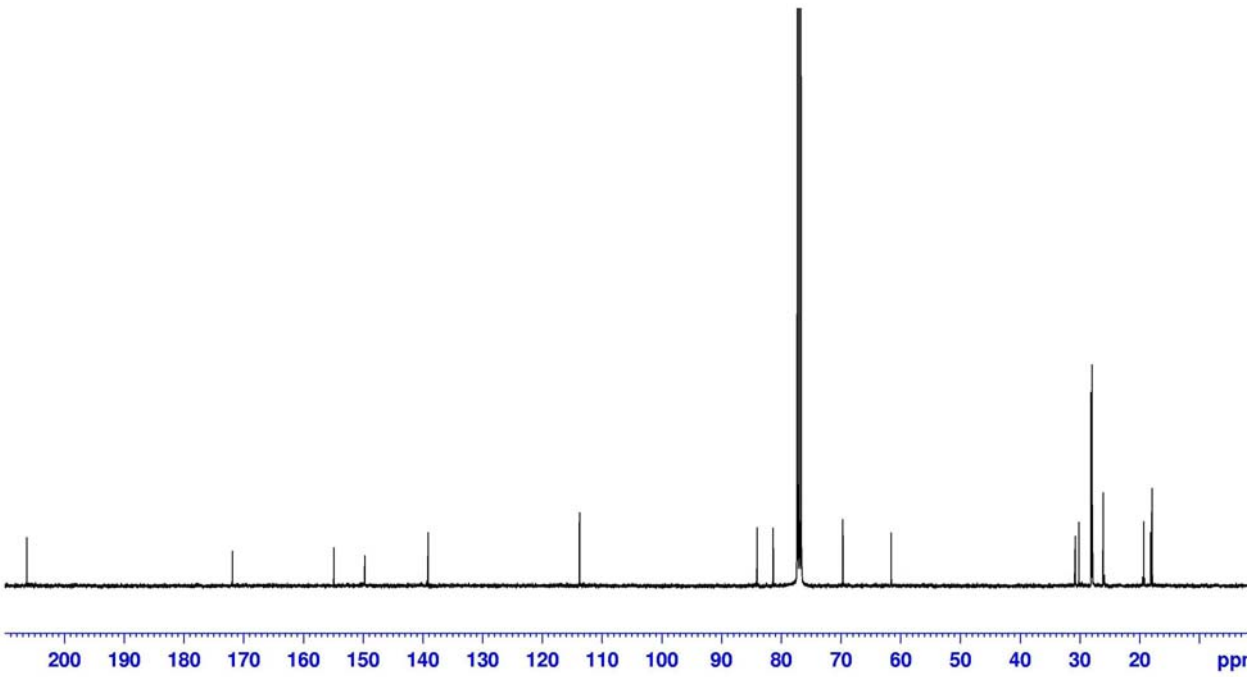


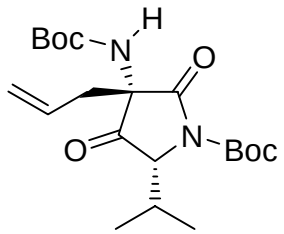




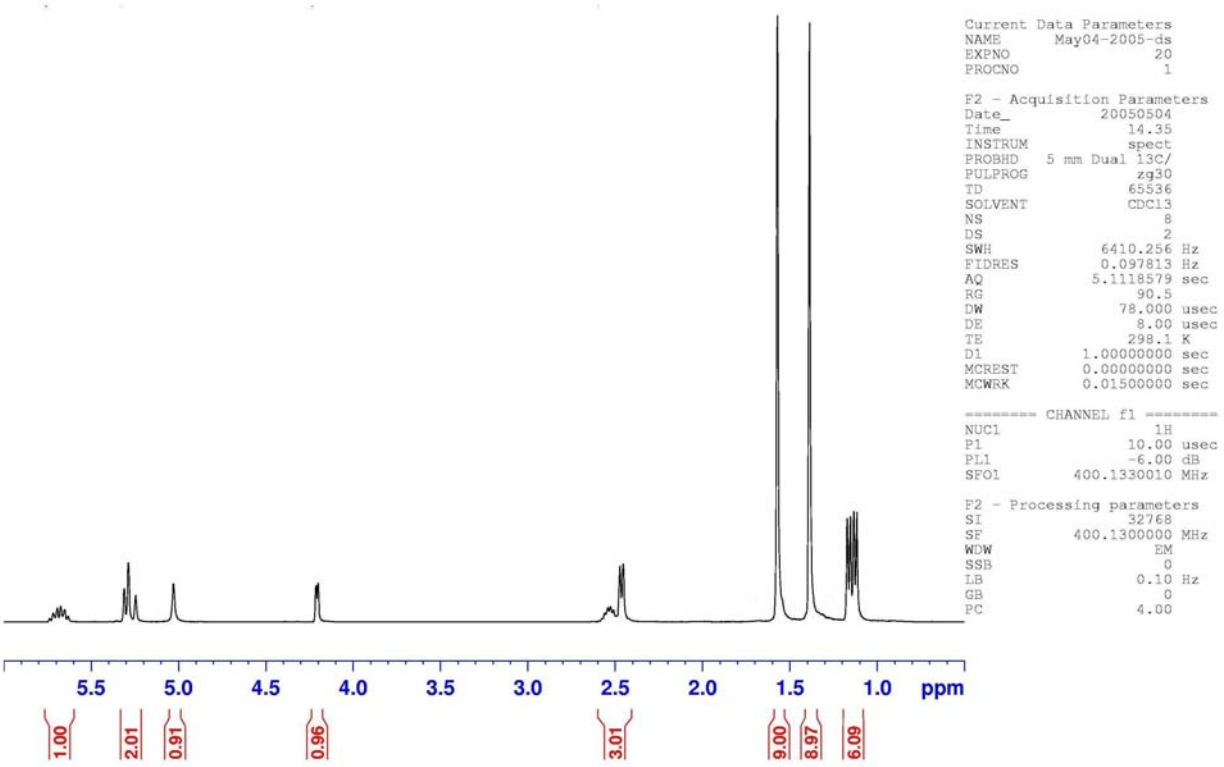
(*3R,5R*)-1-(*tert*-Butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-3-[3,3-(dimethyl)allyl]-5-*iso*propylpyrrolidine-2,4-dione (5e)

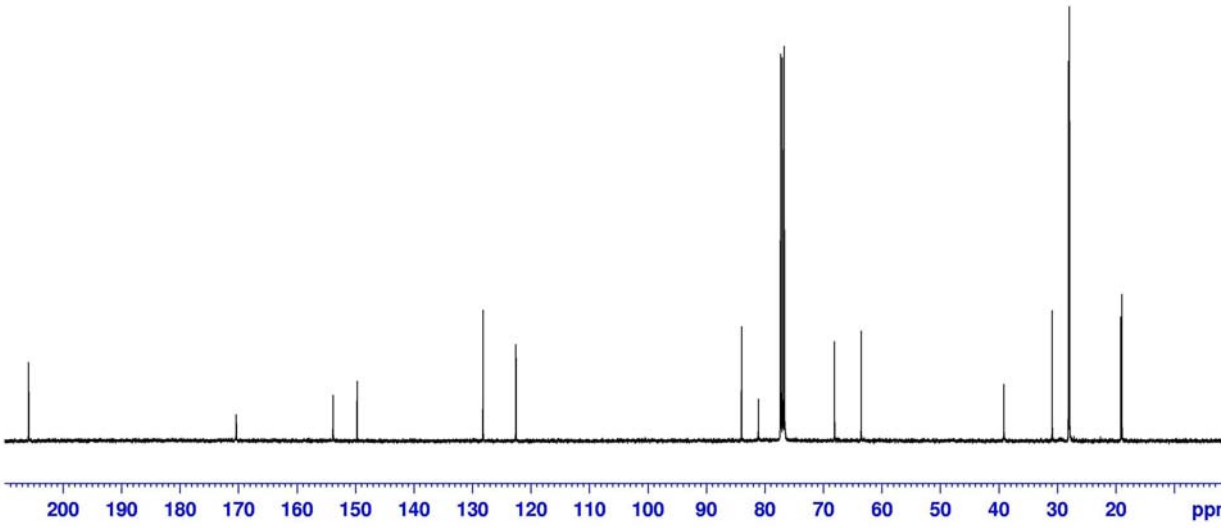






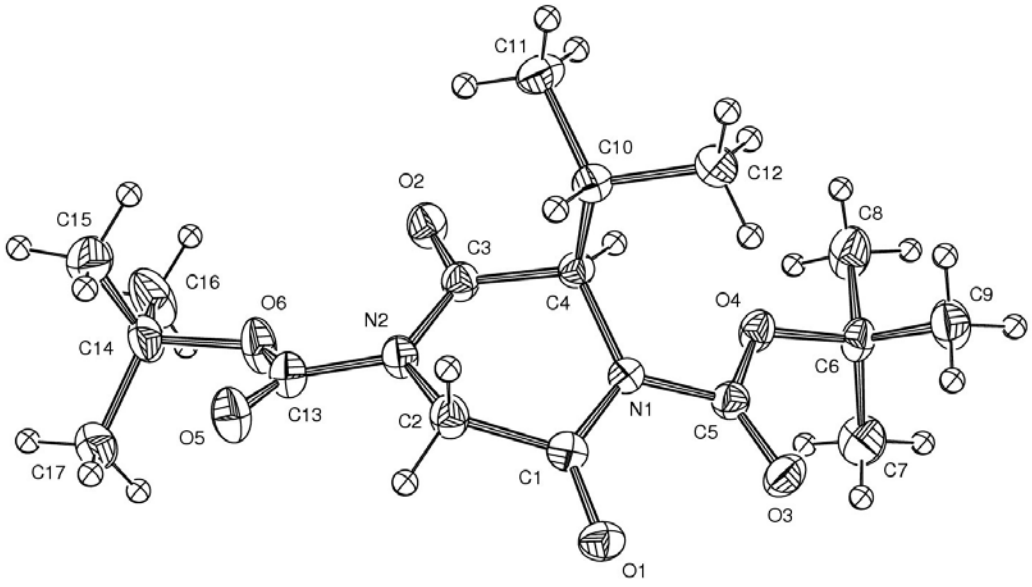
(*3S,5R*)-3-Allyl-1-(*tert*-butoxycarbonyl)-3-[(*tert*-butoxycarbonyl)amino]-5-*iso*propylpyrrolidine-2,4-dione (7)





X-Ray crystallographic analysis of 1e

We wanted to explore the reaction mechanism, in order to determine how the reaction proceeds (i) to strictly conserve the stereoselectivity during the rearrangement and (ii) to permit a highly stereoselective alkylation. X-ray analysis of bis-Boc *cyclo*-[Gly-D-Val] **1e** (Scheme 4) indicates that the DKP ring adopt a boat conformation with the *iso*-propyl group and the H-pro*S* of Gly located in *flagpole* position, and with the αH of Val and H-pro*R* of Gly positioned in *bowsprit*. Moreover, it appears that the αH and the βH of Val are in *anti* position, consistent to the high value of ^3J = 11.3 Hz observed in the ^{1}H-NMR spectrum. It is also relevant to notice that both carboxylic groups included in the Boc protecting moiety present two different orientations relative to their adjacent carbonyl group: a position *anti* for *N*-Boc-Gly and *syn* for *N*-Boc-Val. In this last case, the bulky *tert*-butoxy group was located spatially under the side chain of the Val.



Scheme 4. ORTEP representation of bis-Boc *cyclo*-[Gly-D-Val] **1e.**

$C_{17}H_{28}N_2O_6$, M_r = 356.41, 0.40*0.10*0.10 mm^3, orthorhombic, P $2_12_12_1$, a = 6.0501(1), b = 17.4171(2), c = 17.9984(3) Å, V = 1896.58(5) Å^3, Z = 4, D_x = 1.248 Mg.m-3, λ(MoKα) = 0.71073Å, μ = 0.94 cm-1, F(000) = 768, T = 120(1) K. The sample was studied on a NONIUS Kappa CCD with graphite monochromatized MoKα radiation. The cell parameters were obtained with 10 frames (psi rotation: 1° per frame). The data collection[$] (2θmax = 54°, 300 frames via 2.0° omega rotation and 60 s per frame, range HKL: H 0.7 K 0.22 L 0.23) gives 51742 reflections. The data reduction with *Denzo* and *Scalepack* led to 2507 independent reflections from which 2364 with I>2.0σ(I). The structure was solved with SIR-97[*] that revealed the non-hydrogen atoms of the molecule. After anisotropic refinement, several hydrogen atoms were found with a Fourier Difference. The whole structure was refined with *SHELXL97*[¤] by the full-matrix least-square techniques (use of F square magnitude; x, y, z, βij for C, N and O atoms, x, y, z in riding mode for H atoms; 227 variables and 2364 observations with I > 2.0σ(I); Calc w = 1/[σ^2(Fo^2) +(0.06P)^2+0.37P] where P = (Fo^2+2Fc^2)/3 with the resulting R = 0.037, Rw = 0.099 and Sw = 1.071, Δρ < 0.23 eÅ^{-3}.

Atomic scattering factors were reported from International Tables for X-ray Crystallography[±] and Ortep views realized with *PLATON-98*.[Ó] CCDC 274800 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk./data_request/cif.

[$]Bruker SMART (version 5.611) and SAINT+(version 6.45). Bruker AXS inc., Madison, Wisconsin, (USA), **2003**.

[*]A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, G. Polidori, R. Spagna, *J. App. Cryst.* **1998**, *31*, 74-77.

[¤]G.M. Sheldrick, SHELX97, Program for the Refinement of Crystal Structures, University of Göttingen, Göttingen (Germany), **1997**.

[±]*International Tables for X-ray Crystallography. Vol.F*, Kluwer Academic, Dordrecht, **1992**.

[Ó]A. L. Spek, *PLATON. A multipurpose crystallographic tool,* Utrecht University, Utrecht, (The Netherlands), **1998**.

Table 3. Crystal data and structure refinement for **1e.**

Identification code,df157
Empirical formula,C17 H28 N2 O6
Formula weight,356.41
Temperature,120(1) K
Wavelength,0.71069 Agst
Crystal system,Orthorhombic
Space group,p212121
Unit cell dimensions
a = 6.05010(10)Agst alpha = 90deg
, b = 17.4171(2)Agst beta = 90deg
, c = 17.9984(3)Agst gamma = 90deg
Volume, 1896.58(5) Agst@3
Z, 4
Density (calculated), 1.248 Mg/m@3
Absorption coefficient, 0.094 mm@-1
F(000), 768
Crystal size, 0.40 x 0.10 x 0.10 mm
Theta range for data collection, 2.26 to 27.48 deg.
Index ranges,0<=h<=7; 0<=k<=22; 0<=l<=23
Reflections collected, 2507
Independent reflections, 2507 [R(int) = 0.0000]
Reflections observed (>2sigma), 2364
Data Completeness, 1.000
Absorption correction, None
Refinement method, Full-matrix least-squares on F@2
Data / restraints / parameters, 2507 / 0 / 227
Goodness-of-fit on F@2, 1.071
Final R indices [I>2sigma(I)],R~1 = 0.0379 wR~2 = 0.0992
R indices (all data), R~1 = 0.0414 wR~2 = 0.1043

Absolute structure parameter, 0.8(11)
Largest diff. peak and hole, 0.238 and -0.174 e.Agst@-3
calc w=1/[\s^2^(Fo^2^)+(0.0655P)^2^+0.3797P] where P=(Fo^2^+2Fc^2^)/3

Table 4. Atomic coordinates (x 10@4) and equivalent isotropic displacement parameters Agst@2 x 10@3) for **1e**.U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Atom, x, y, z, U(eq)

O(1),5263(2),7253(1),10187(1),28(1)
O(2),7934(3),8738(1),7811(1),32(1)
O(3),5493(3),8605(1),10867(1),33(1)
O(4),6514(2),9567(1),10093(1),26(1)
O(5),6935(3),6433(1),7735(1),35(1)
O(6),9441(3),7358(1),7455(1),37(1)
N(1),5617(3),8425(1),9597(1),21(1)
N(2),6797(3),7590(1),8323(1),25(1)
C(1),5396(3),7632(1),9624(1),23(1)
C(2),5320(3),7241(1),8874(1),27(1)
C(3),6935(3),8382(1),8282(1),25(1)
C(4),5563(3),8809(1),8861(1),22(1)
C(5),5842(3),8854(1),10257(1),24(1)
C(6),6874(4),10136(1),10694(1),27(1)
C(7),8702(4),9860(1),11203(1),41(1)
C(8),7628(5),10835(1),10257(1),42(1)
C(9),4745(4),10294(1),11101(1),37(1)
C(10),3169(3),8961(1),8599(1),24(1)
C(11),3147(4),9362(1),7842(1),32(1)
C(12),1926(3),9449(1),9167(1),29(1)
C(13),7710(3),7063(1),7809(1),29(1)
C(14),10336(4),6952(1),6796(1),36(1)
C(15),8520(5),6869(2),6219(1),51(1)
C(16),12117(5),7502(1),6536(2),54(1)
C(17),11343(4),6192(1),7019(1),37(1)

Table 5. Bond lengths [Agst] and angles [deg] for **1e.**

O(1)-C(1),1.211(2),O(2)-C(3),1.213(2)
O(3)-C(5),1.199(2),O(4)-C(5),1.339(2)
O(4)-C(6),1.483(2),O(5)-C(13),1.201(2)
O(6)-C(13),1.330(2),O(6)-C(14),1.483(2)
N(1)-C(1),1.389(2),N(1)-C(5),1.410(2)
N(1)-C(4),1.485(2),N(2)-C(3),1.384(2)
N(2)-C(13),1.415(2),N(2)-C(2),1.467(2)
C(1)-C(2),1.513(2),C(2)-H(2A),0.9700
C(2)-H(2B),0.9700,C(3)-C(4),1.526(2)
C(4)-C(10),1.546(3),C(4)-H(4),0.9800
C(6)-C(9),1.507(3),C(6)-C(7),1.515(3)
C(6)-C(8),1.519(3),C(7)-H(7A),0.9600

C(7)-H(7B),0.9600,C(7)-H(7C),0.9600
C(8)-H(8A),0.9600,C(8)-H(8B),0.9600
C(8)-H(8C),0.9600,C(9)-H(9A),0.9600
C(9)-H(9B),0.9600,C(9)-H(9C),0.9600
C(10)-C(12),1.527(2),C(10)-C(11),1.532(2)
C(10)-H(10),0.9800,C(11)-H(11A),0.9600
C(11)-H(11B),0.9600,C(11)-H(11C),0.9600
C(12)-H(12A),0.9600,C(12)-H(12B),0.9600
C(12)-H(12C),0.9600,C(14)-C(17),1.513(3)
C(14)-C(16),1.515(4),C(14)-C(15),1.519(4)
C(15)-H(15A),0.9600,C(15)-H(15B),0.9600
C(15)-H(15C),0.9600,C(16)-H(16A),0.9600
C(16)-H(16B),0.9600,C(16)-H(16C),0.9600
C(17)-H(17A),0.9600,C(17)-H(17B),0.9600
C(17)-H(17C),0.9600

C(5)-O(4)-C(6),120.29(13),C(13)-O(6)-C(14),119.12(15)
C(1)-N(1)-C(5),120.46(14),C(1)-N(1)-C(4),118.54(14)
C(5)-N(1)-C(4),120.99(13),C(3)-N(2)-C(13),126.00(16)
C(3)-N(2)-C(2),119.06(15),C(13)-N(2)-C(2),114.27(14)
O(1)-C(1)-N(1),125.33(17),O(1)-C(1)-C(2),119.88(15)
N(1)-C(1)-C(2),114.79(15),N(2)-C(2)-C(1),113.45(15)
N(2)-C(2)-H(2A),108.9,C(1)-C(2)-H(2A),108.9
N(2)-C(2)-H(2B),108.9,C(1)-C(2)-H(2B),108.9
H(2A)-C(2)-H(2B),107.7,O(2)-C(3)-N(2),125.27(17)
O(2)-C(3)-C(4),119.94(15),N(2)-C(3)-C(4),114.66(15)
N(1)-C(4)-C(3),112.17(14),N(1)-C(4)-C(10),111.68(14)
C(3)-C(4)-C(10),112.64(14),N(1)-C(4)-H(4),106.6
C(3)-C(4)-H(4),106.6,C(10)-C(4)-H(4),106.6
O(3)-C(5)-O(4),126.21(16),O(3)-C(5)-N(1),124.17(16)
O(4)-C(5)-N(1),109.61(14),O(4)-C(6)-C(9),110.51(16)
O(4)-C(6)-C(7),109.63(15),C(9)-C(6)-C(7),112.79(17)
O(4)-C(6)-C(8),101.67(14),C(9)-C(6)-C(8),111.26(17)
C(7)-C(6)-C(8),110.4(2),C(6)-C(7)-H(7A),109.5
C(6)-C(7)-H(7B),109.5,H(7A)-C(7)-H(7B),109.5
C(6)-C(7)-H(7C),109.5,H(7A)-C(7)-H(7C),109.5
H(7B)-C(7)-H(7C),109.5,C(6)-C(8)-H(8A),109.5
C(6)-C(8)-H(8B),109.5,H(8A)-C(8)-H(8B),109.5
C(6)-C(8)-H(8C),109.5,H(8A)-C(8)-H(8C),109.5
H(8B)-C(8)-H(8C),109.5,C(6)-C(9)-H(9A),109.5
C(6)-C(9)-H(9B),109.5,H(9A)-C(9)-H(9B),109.5
C(6)-C(9)-H(9C),109.5,H(9A)-C(9)-H(9C),109.5
H(9B)-C(9)-H(9C),109.5,C(12)-C(10)-C(11),109.68(15)
C(12)-C(10)-C(4),110.64(14),C(11)-C(10)-C(4),110.91(15)
C(12)-C(10)-H(10),108.5,C(11)-C(10)-H(10),108.5
C(4)-C(10)-H(10),108.5,C(10)-C(11)-H(11A),109.5
C(10)-C(11)-H(11B),109.5,H(11A)-C(11)-H(11B),109.5
C(10)-C(11)-H(11C),109.5,H(11A)-C(11)-H(11C),109.5
H(11B)-C(11)-H(11C),109.5,C(10)-C(12)-H(12A),109.5
C(10)-C(12)-H(12B),109.5,H(12A)-C(12)-H(12B),109.5

C(10)-C(12)-H(12C),109.5,H(12A)-C(12)-H(12C),109.5
H(12B)-C(12)-H(12C),109.5,O(5)-C(13)-O(6),127.40(17)
O(5)-C(13)-N(2),120.85(18),O(6)-C(13)-N(2),111.74(15)
O(6)-C(14)-C(17),110.63(16),O(6)-C(14)-C(16),101.83(16)
C(17)-C(14)-C(16),110.4(2),O(6)-C(14)-C(15),109.16(18)
C(17)-C(14)-C(15),112.92(19),C(16)-C(14)-C(15),111.3(2)
C(14)-C(15)-H(15A),109.5,C(14)-C(15)-H(15B),109.5
H(15A)-C(15)-H(15B),109.5,C(14)-C(15)-H(15C),109.5
H(15A)-C(15)-H(15C),109.5,H(15B)-C(15)-H(15C),109.5
C(14)-C(16)-H(16A),109.5,C(14)-C(16)-H(16B),109.5
H(16A)-C(16)-H(16B),109.5,C(14)-C(16)-H(16C),109.5
H(16A)-C(16)-H(16C),109.5,H(16B)-C(16)-H(16C),109.5
C(14)-C(17)-H(17A),109.5,C(14)-C(17)-H(17B),109.5
H(17A)-C(17)-H(17B),109.5,C(14)-C(17)-H(17C),109.5
H(17A)-C(17)-H(17C),109.5,H(17B)-C(17)-H(17C),109.5

Symmetry transformations used to generate equivalent atoms:

Table 6. Anisotropic displacement parameters (Agst@2 x 10@3) for **1e**. The anisotropic displacement factor exponent takes the form: -2 gpi@2 [h@2 a*@2 U11 + .. + 2 h k a* b* U.

Atom, U11, U22, U33, U23, U13, U12

O(1),29(1),28(1),28(1),6(1),1(1),-1(1)
O(2),36(1),28(1),31(1),1(1),12(1),-2(1)
O(3),46(1),31(1),21(1),2(1),2(1),-3(1)
O(4),33(1),24(1),22(1),-3(1),2(1),-6(1)
O(5),37(1),29(1),39(1),-11(1),5(1),-5(1)
O(6),40(1),31(1),39(1),-10(1),18(1),-3(1)
N(1),23(1),22(1),20(1),0(1),0(1),1(1)
N(2),28(1),22(1),26(1),-3(1),5(1),-1(1)
C(1),19(1),24(1),26(1),2(1),1(1),-1(1)
C(2),30(1),23(1),27(1),-2(1),5(1),-3(1)
C(3),26(1),24(1),24(1),0(1),2(1),-1(1)
C(4),23(1),22(1),20(1),1(1),1(1),-1(1)
C(5),23(1),25(1),23(1),0(1),0(1),1(1)
C(6),33(1),27(1),23(1),-6(1),2(1),-4(1)
C(7),41(1),43(1),40(1),-10(1),-14(1),-4(1)
C(8),63(2),28(1),37(1),-6(1),10(1),-12(1)
C(9),40(1),34(1),38(1),-4(1),11(1),3(1)
C(10),23(1),26(1),23(1),1(1),-1(1),-1(1)
C(11),34(1),38(1),25(1),7(1),-2(1),2(1)
C(12),27(1),31(1),30(1),0(1),0(1),6(1)
C(13),30(1),29(1),28(1),-5(1),4(1),0(1)
C(14),45(1),31(1),32(1),-5(1),11(1),10(1)
C(15),61(2),59(1),33(1),-4(1),0(1),26(1)
C(16),66(2),35(1),62(2),1(1),38(1),7(1)
C(17),41(1),33(1),39(1),-4(1),5(1),7(1)

Table 7. Hydrogen coordinates (x 10@4) and isotropic displacement parameters (Agst@2 x 10@3) for **1e**.

Atom, x, y, z, U(eq)

H(2A),5721,6705,8936,32
H(2B),3817,7258,8687,32
H(4),6258,9313,8927,26
H(7A),10015,9767,10918,62
H(7B),8251,9393,11443,62
H(7C),8999,10244,11572,62
H(8A),8974,10716,9999,63
H(8B),7877,11255,10591,63
H(8C),6507,10974,9904,63
H(9A),3646,10466,10754,56
H(9B),4989,10683,11469,56
H(9C),4246,9832,11338,56
H(10),2408,8466,8550,29
H(11A),3938,9056,7487,48
H(11B),3842,9856,7885,48
H(11C),1648,9427,7679,48
H(12A),1946,9196,9641,44
H(12B),424,9515,9007,44
H(12C),2626,9941,9209,44
H(15A),7421,6517,6397,76
H(15B),9140,6677,5764,76
H(15C),7852,7361,6130,76
H(16A),13243,7541,6910,82
H(16B),11480,7998,6450,82
H(16C),12758,7313,6084,82
H(17A),10195,5847,7176,56
H(17B),12363,6271,7420,56
H(17C),12111,5974,6602,56