Synthesis of 2-Unsubstituted Pyrrolidines and Piperidines from Donor-Acceptor Cyclopropanes and Cyclobutanes: 1,3,5-Triazinanes as Surrogates for Formylimines

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Dimethyl 1,5-diphenylpyrrolidine-3,3-dicarboxylate (5aa)

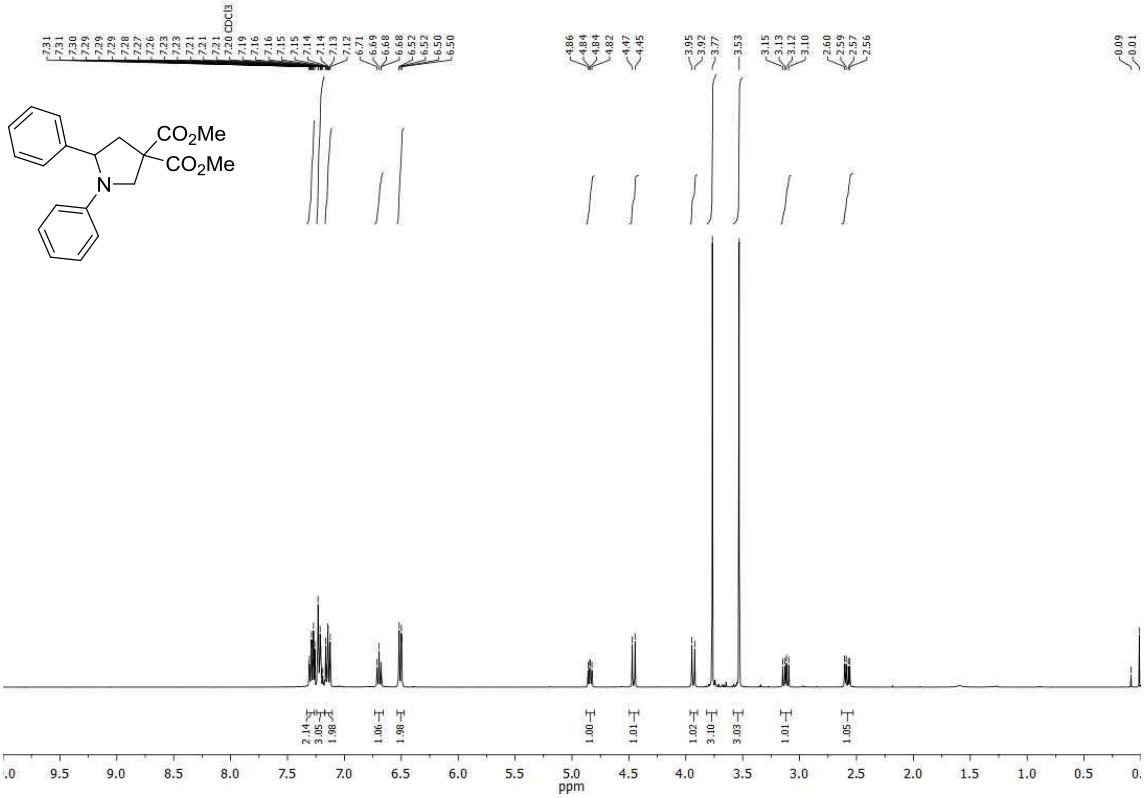


Figure S1: ^{1}H-NMR (400 MHz, $CDCl_3$).

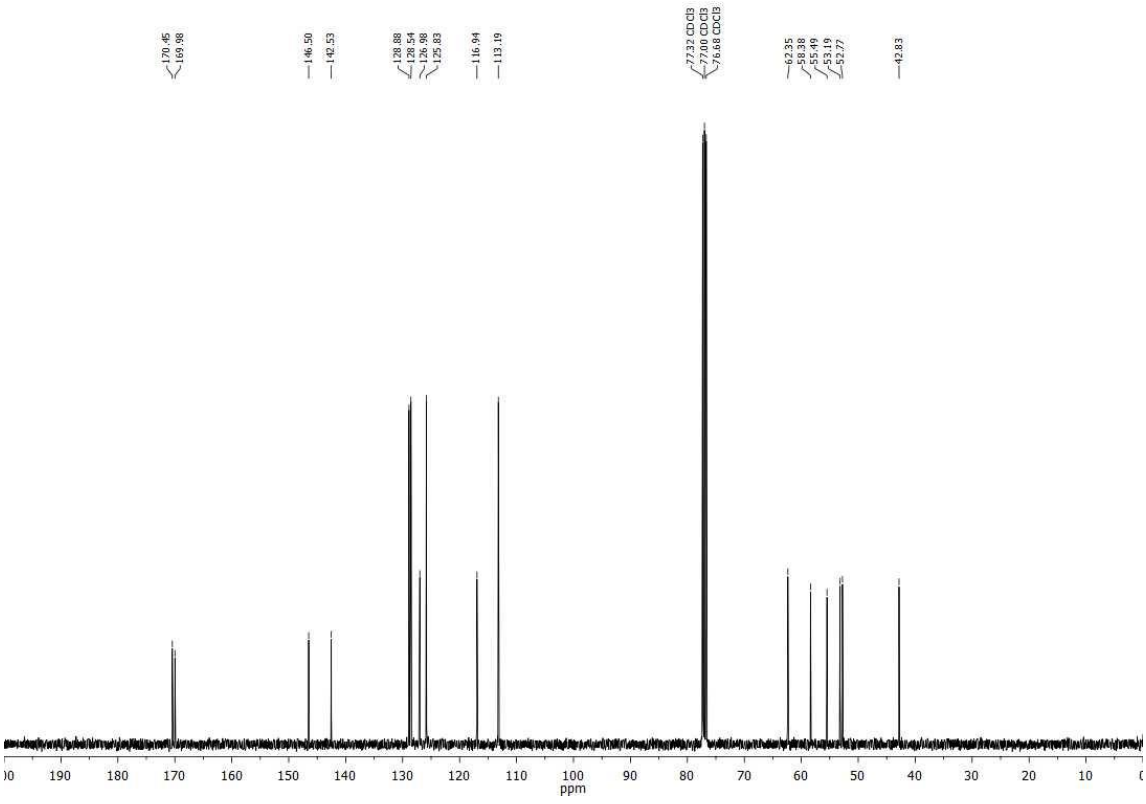


Figure S2: ^{13}C-NMR (100 MHz, $CDCl_3$).

Diethyl 1-(4-methoxyphenyl)-5-(*p*-tolyl)pyrrolidine-3,3-dicarboxylate (5bb)

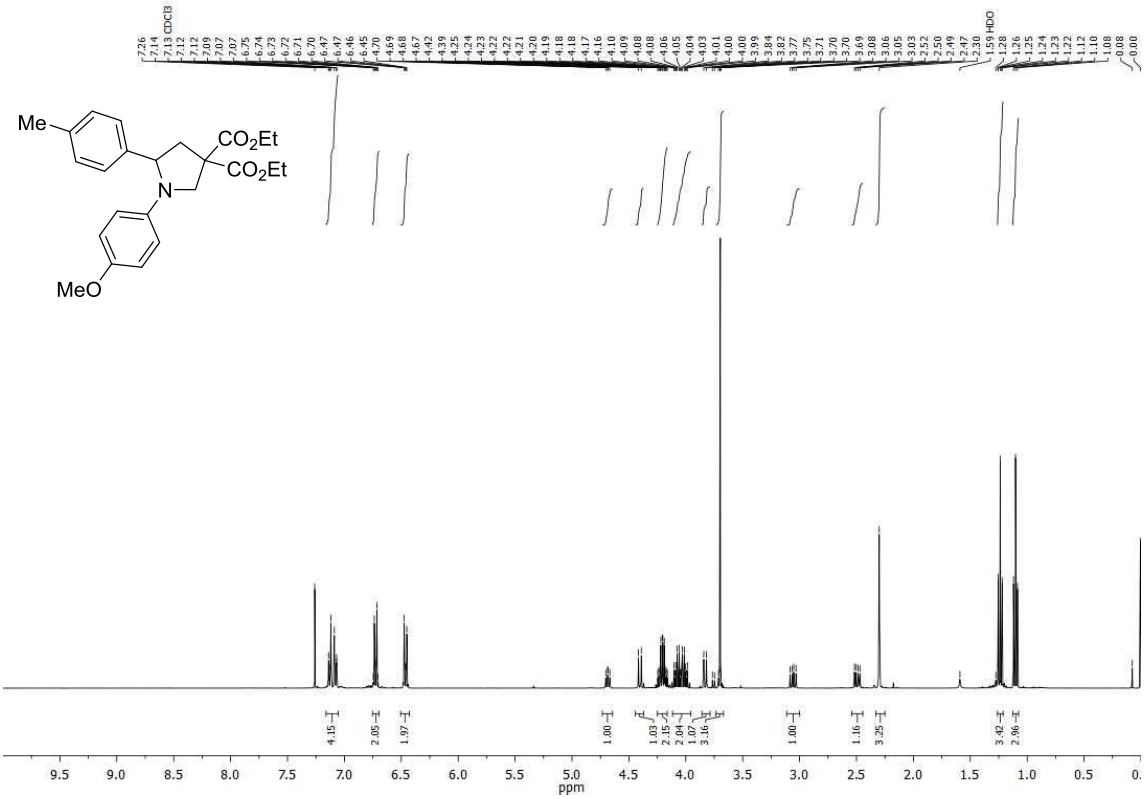


Figure S3: ^{1}H-NMR (400 MHz, $CDCl_3$).

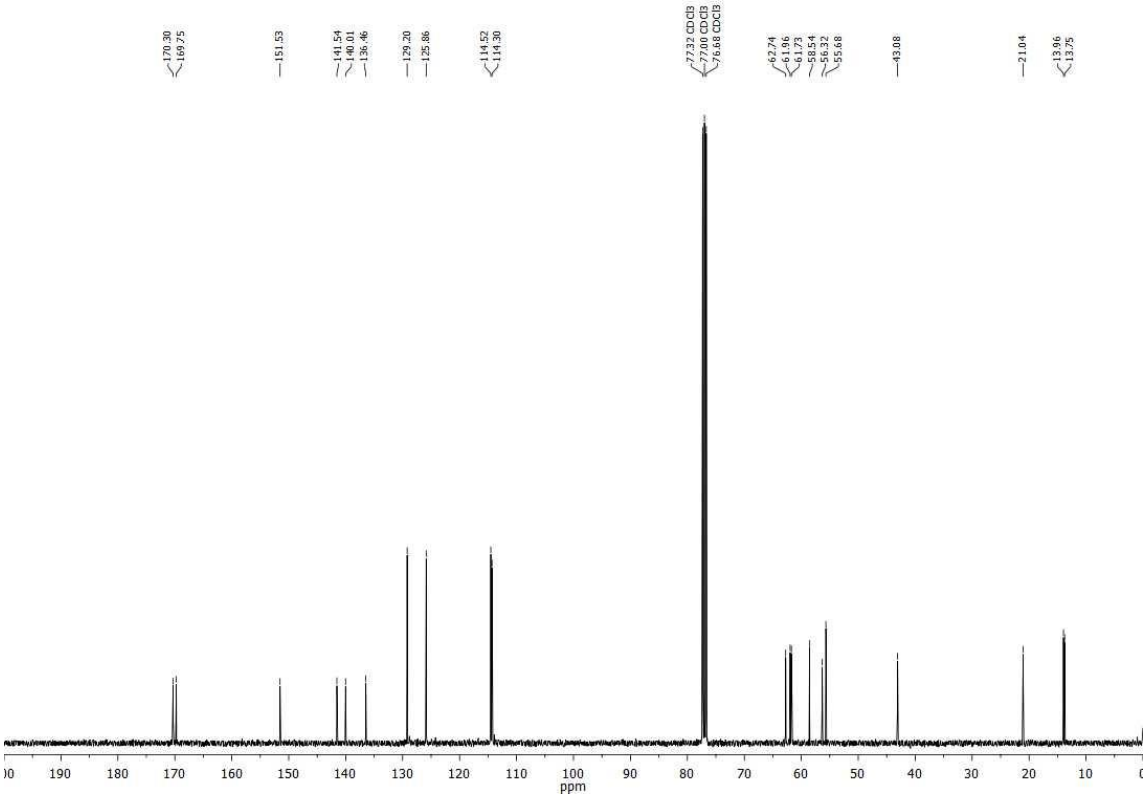


Figure S4: ^{13}C-NMR (100 MHz, $CDCl_3$).

Diethyl 1-(4-methoxyphenyl)-5-(*m*-tolyl)pyrrolidine-3,3-dicarboxylate (5cb)

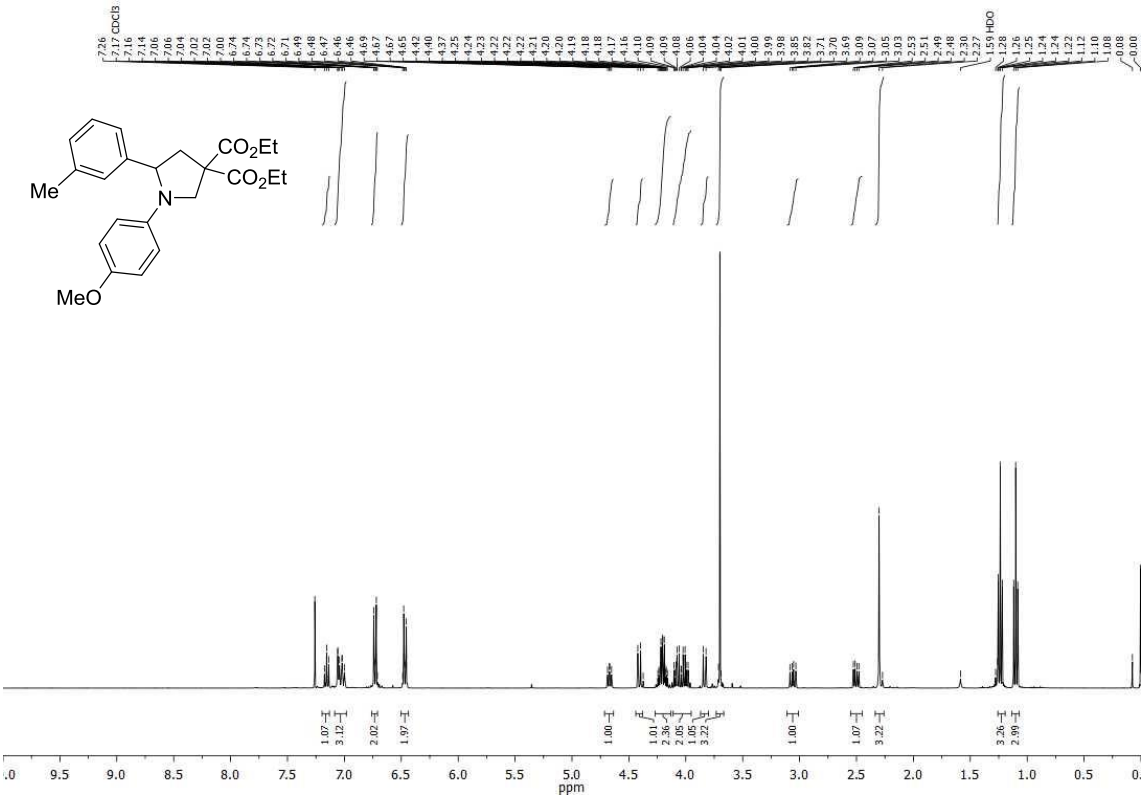


Figure S5: ^{1}H-NMR (400 MHz, $CDCl_3$).

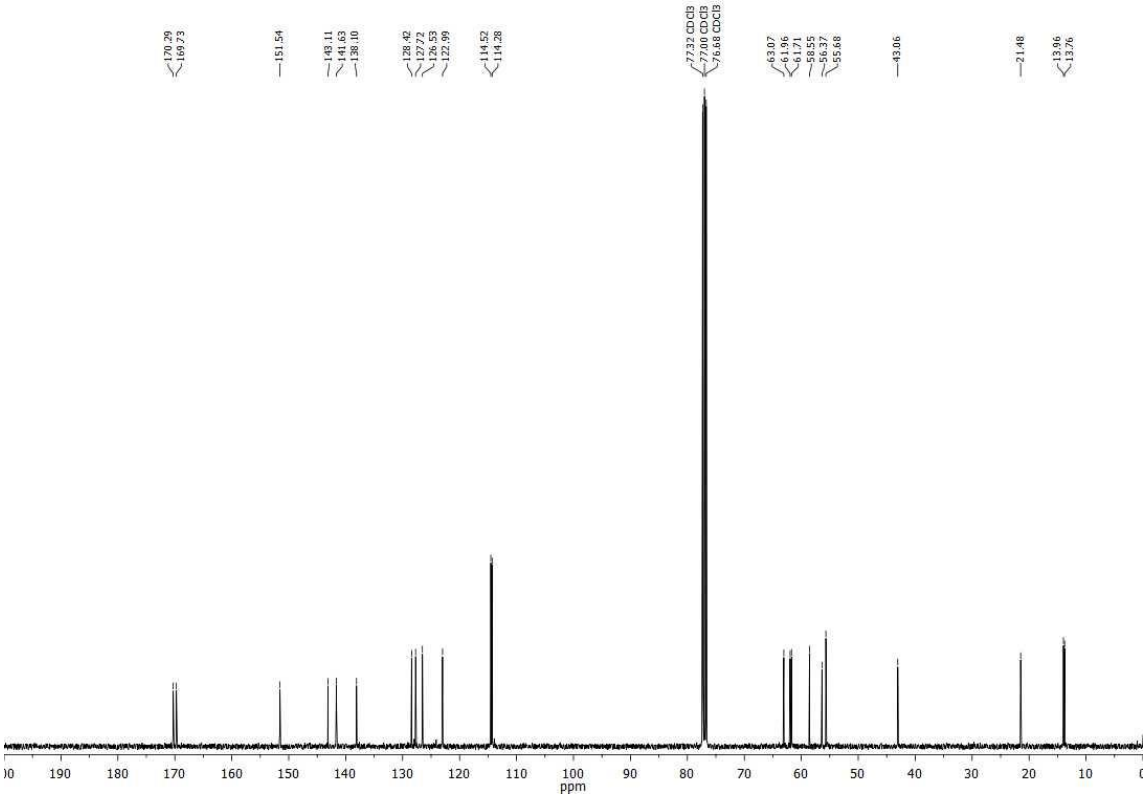


Figure S6: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 1-(4-methoxyphenyl)-5-(*o*-tolyl)pyrrolidine-3,3-dicarboxylate (5db)

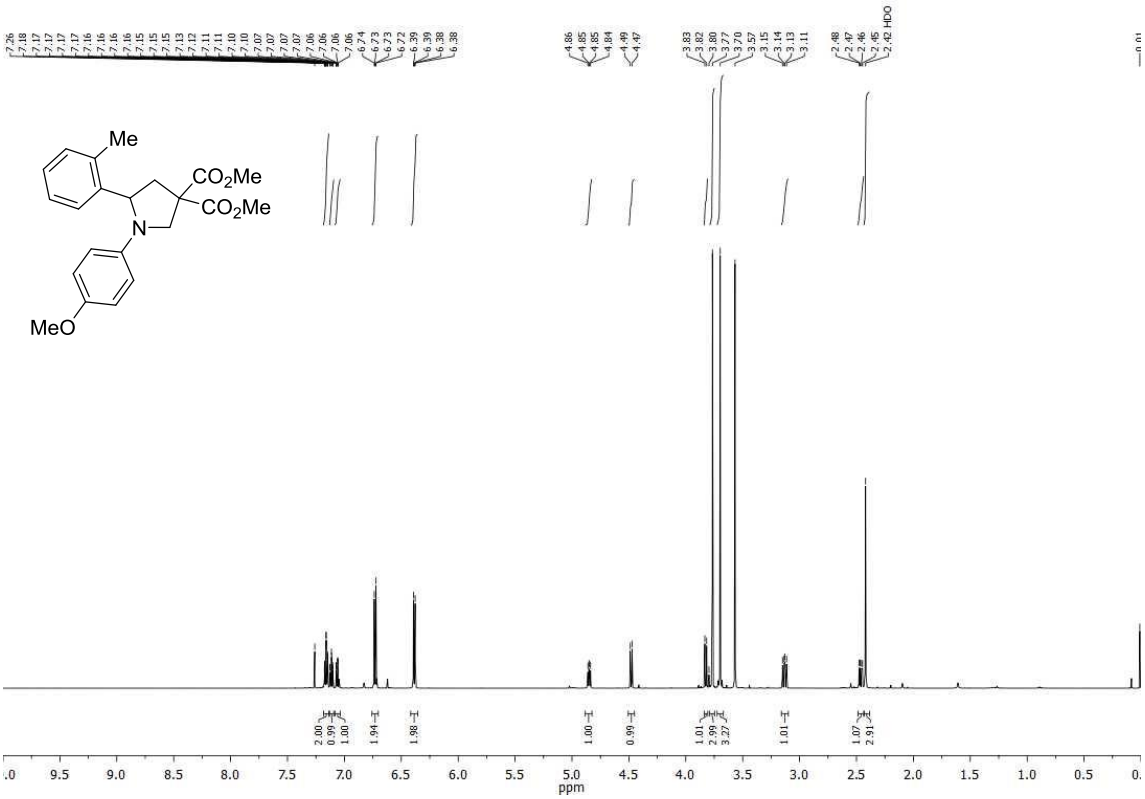


Figure S7: ^{1}H-NMR (600 MHz, $CDCl_3$).

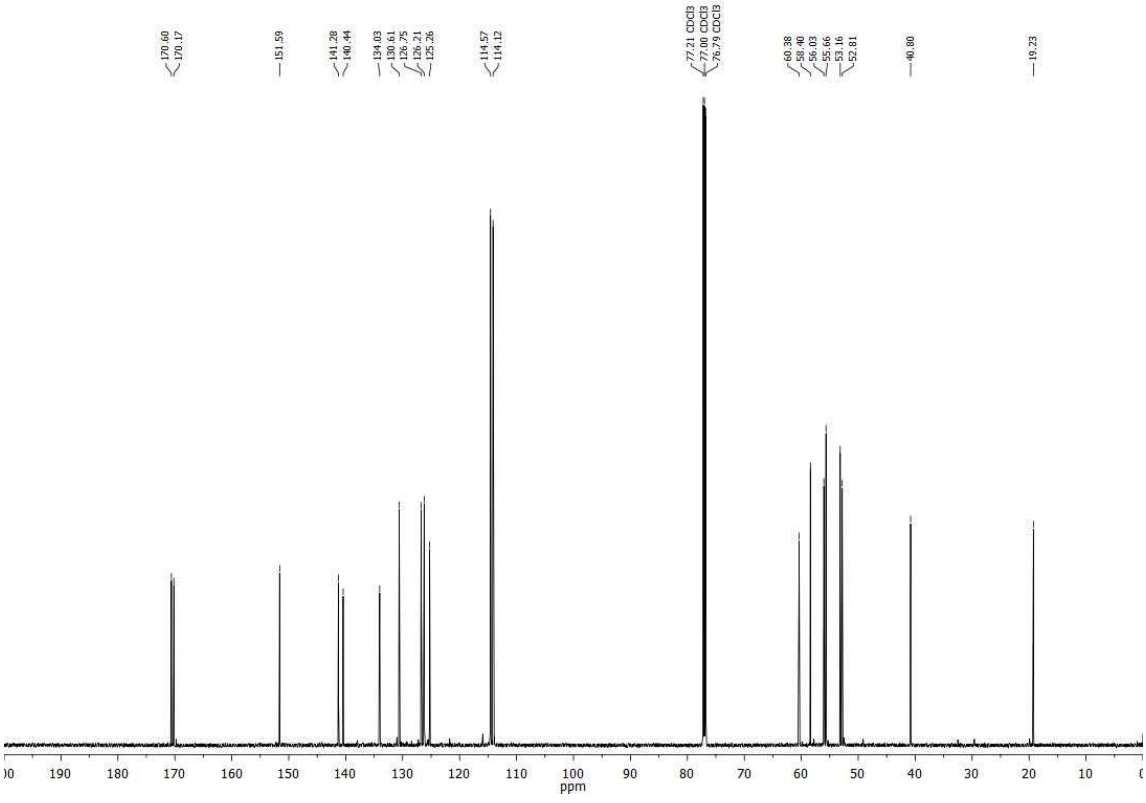


Figure S8: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 5-(4-methoxyphenyl)-1-phenylpyrrolidine-3,3-dicarboxylate (5ea)

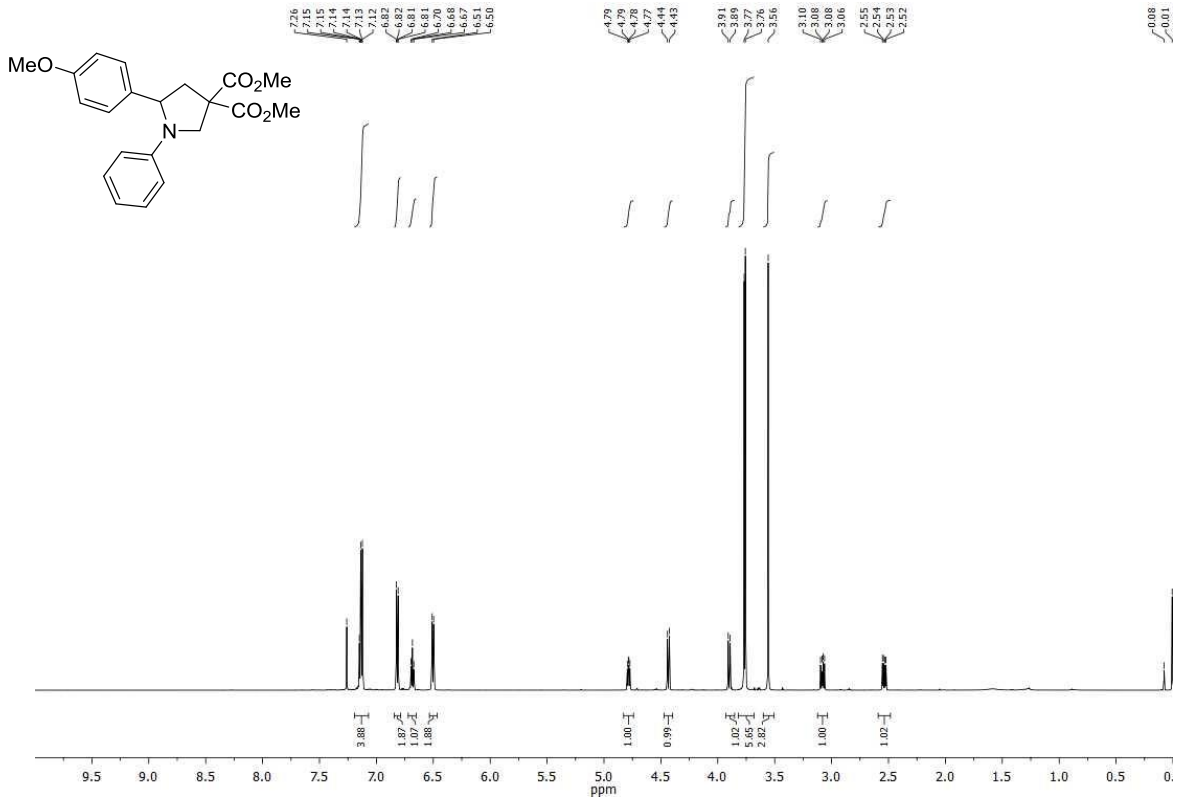


Figure S9: ^{1}H-NMR (600 MHz, $CDCl_3$).

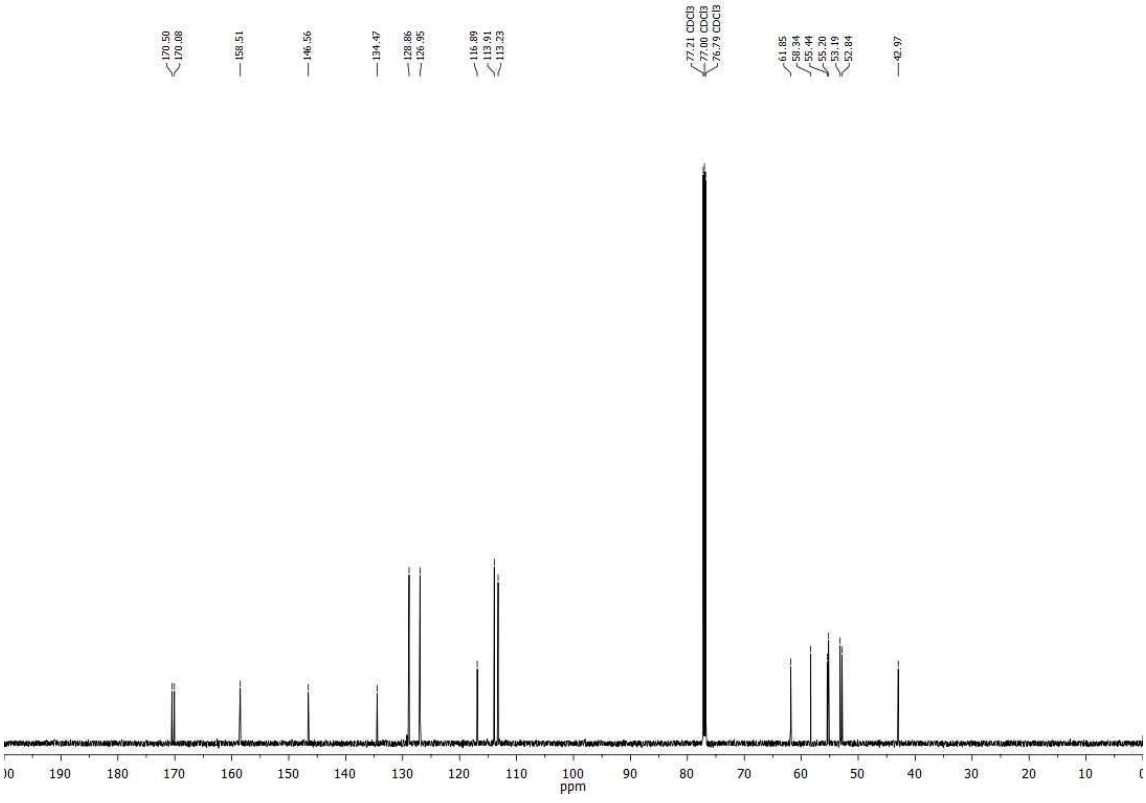


Figure S10: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 1-(4-methoxyphenyl)-5-(naphthalen-2-yl)pyrrolidine-3,3-dicarboxylate (5fb)

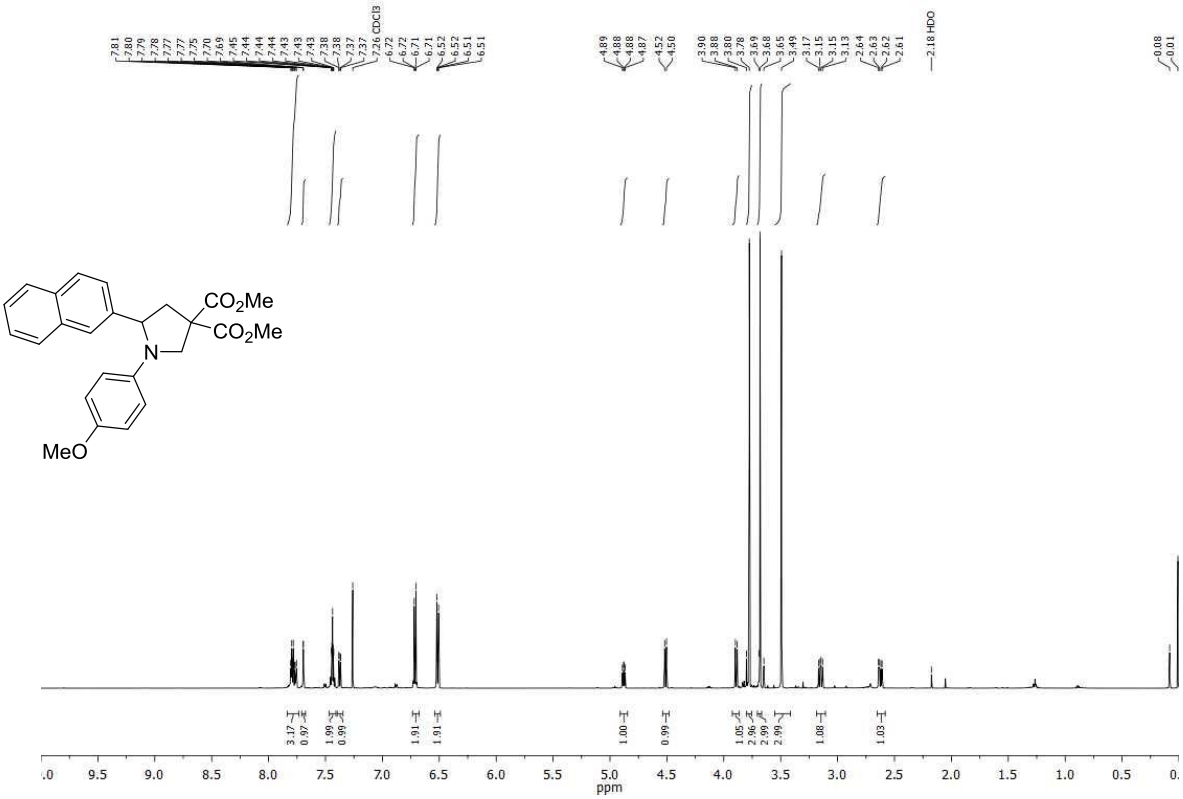


Figure S11: ^{1}H-NMR (600 MHz, $CDCl_3$).

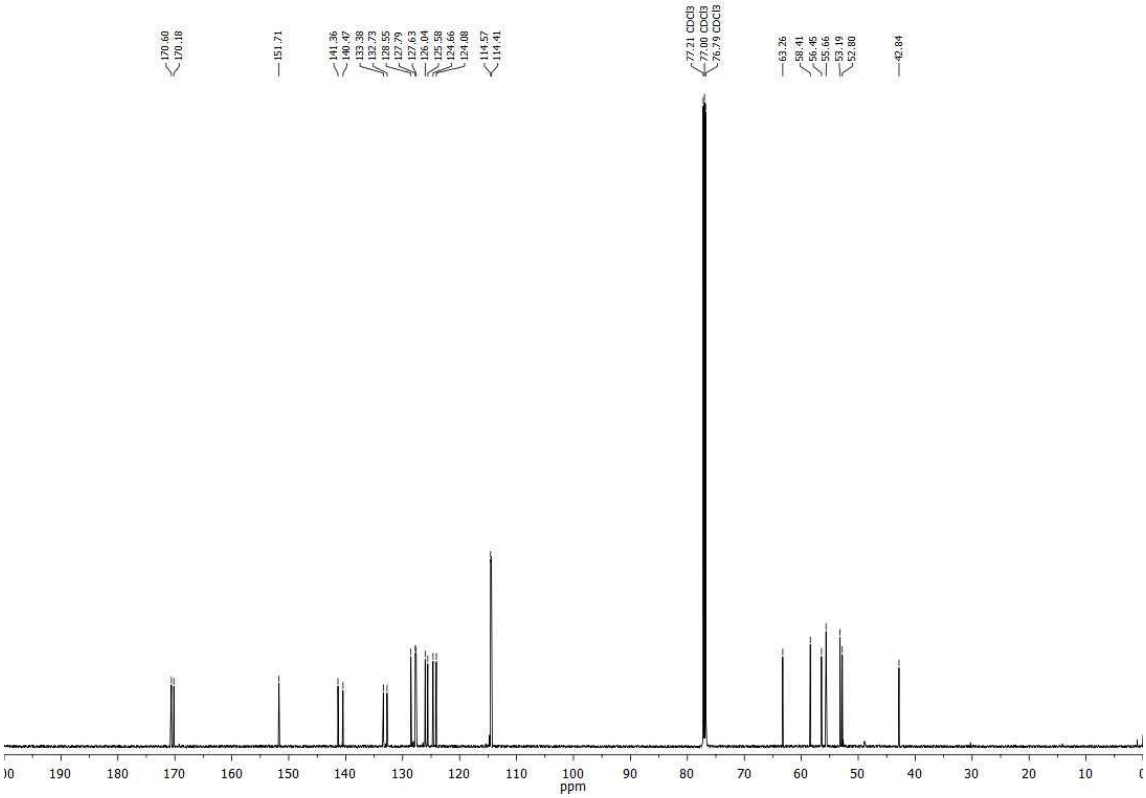


Figure S12: ^{13}C-NMR (150 MHz, $CDCl_3$).

Diethyl 5-(4-acetamidophenyl)-1-(4-methoxyphenyl)pyrrolidine-3,3-dicarboxylate (5gb)

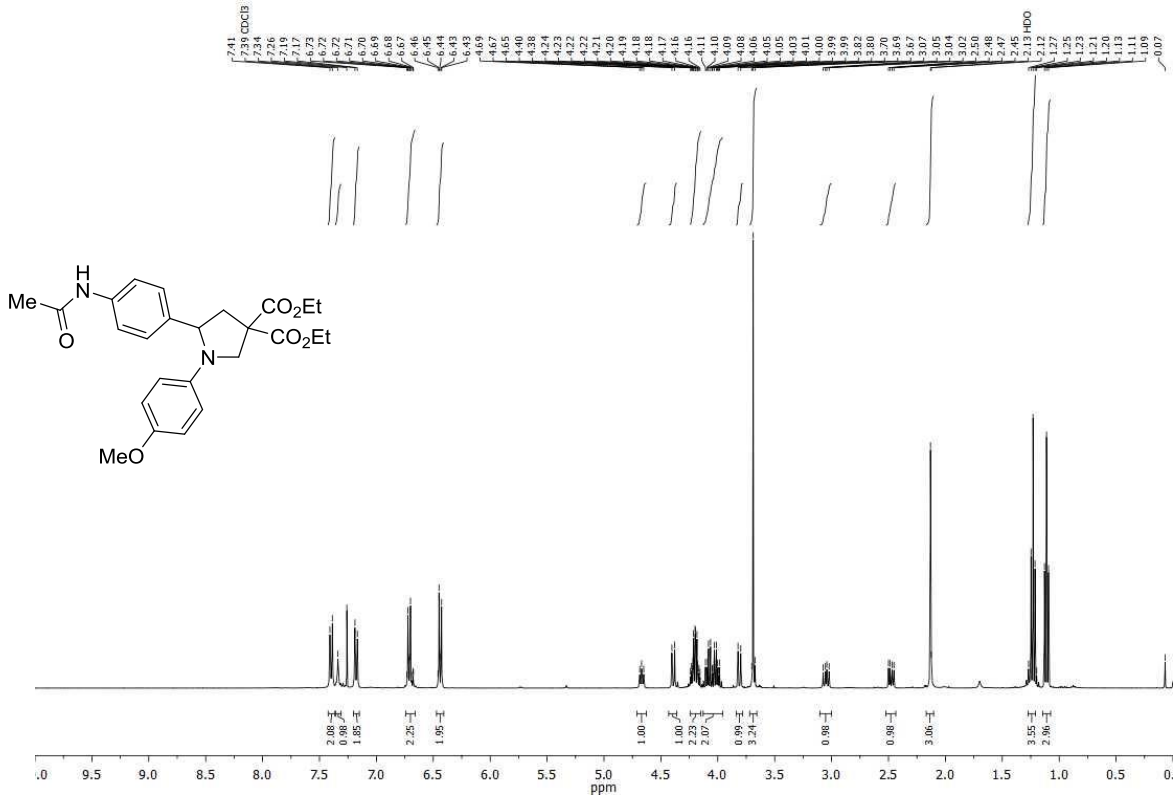


Figure S13: ^{1}H-NMR (400 MHz, $CDCl_3$).

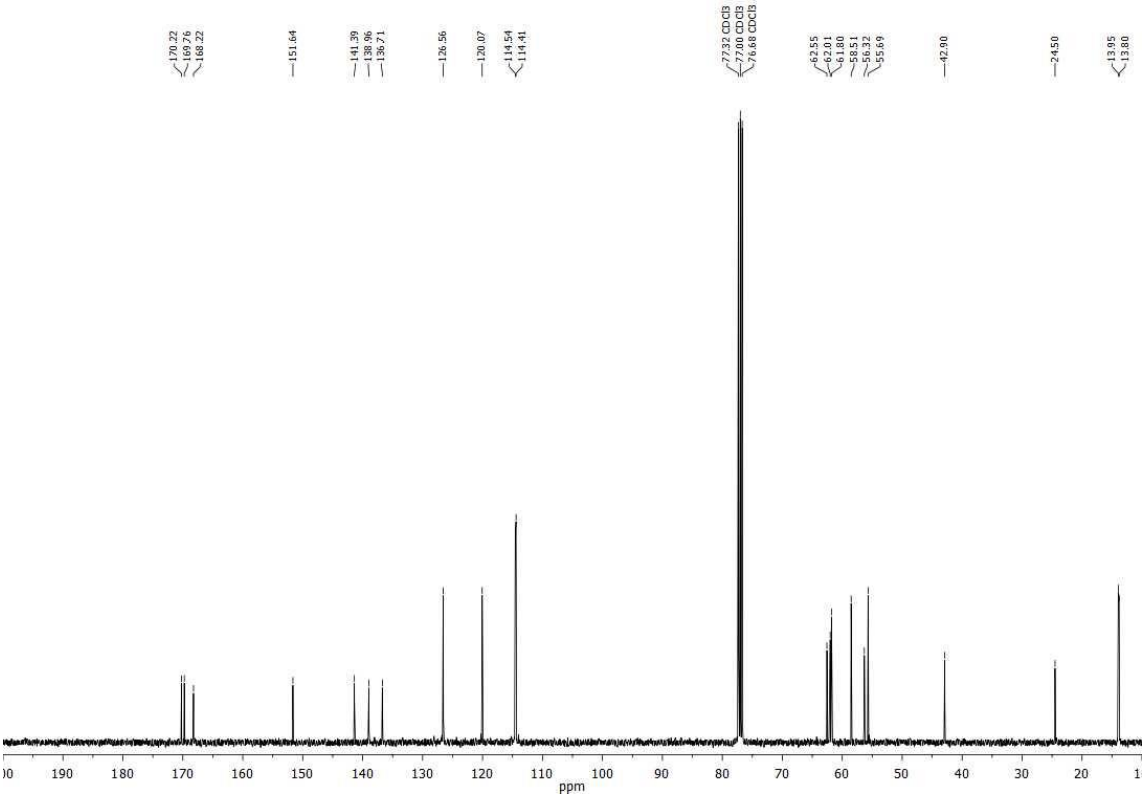


Figure S14: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 1-phenyl-5-(thiophen-2-yl)pyrrolidine-3,3-dicarboxylate (5ha)

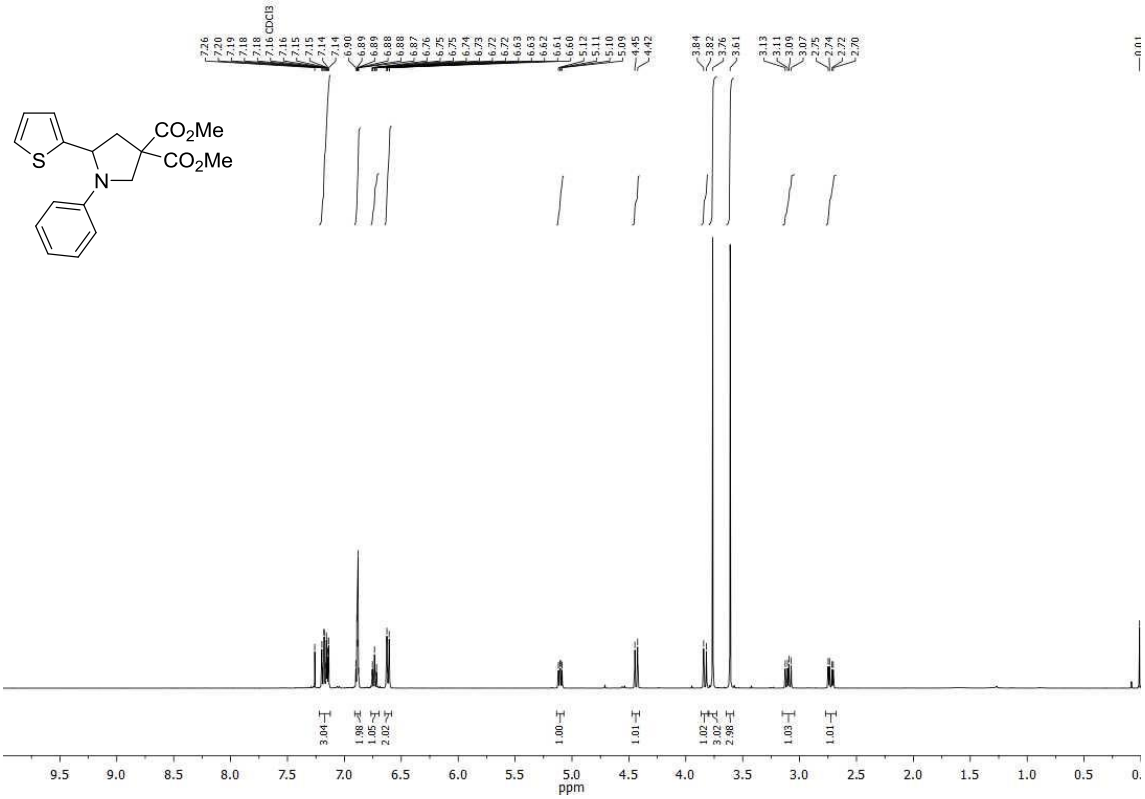


Figure S15: ^{1}H-NMR (400 MHz, $CDCl_3$).

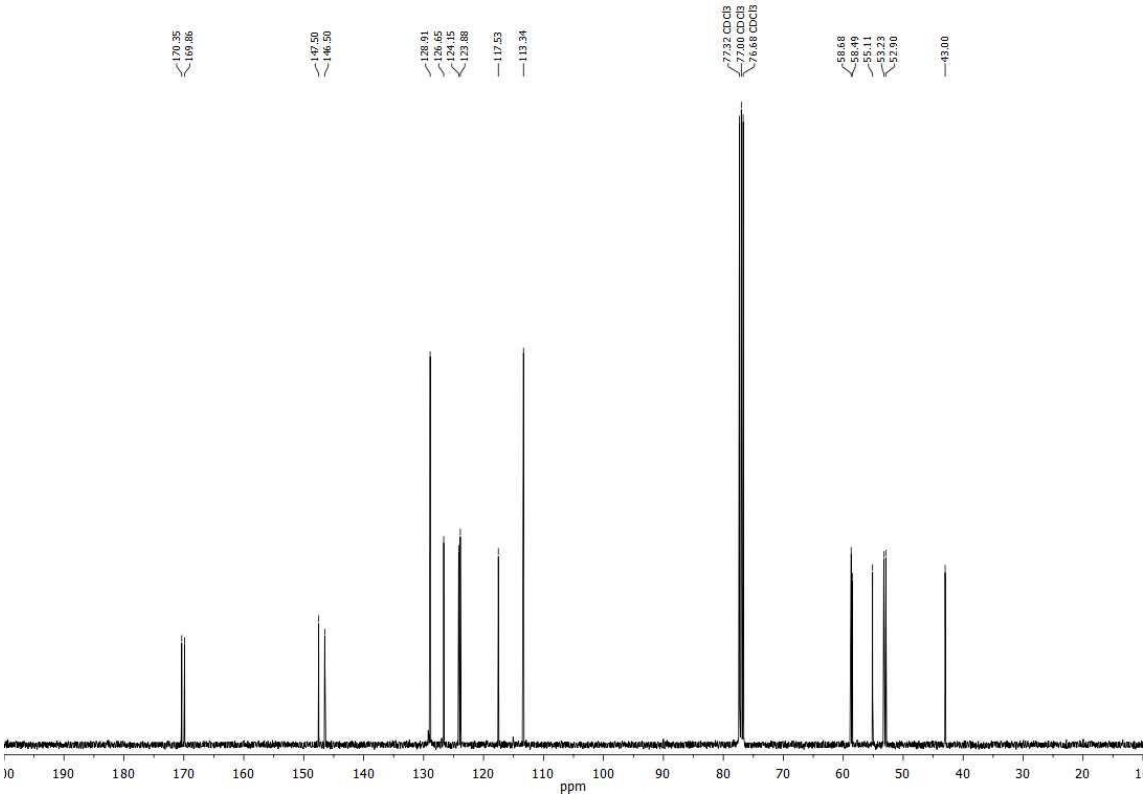


Figure S16: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 5-(furan-2-yl)-1-(4-methoxyphenyl)pyrrolidine-3,3-dicarboxylate (5ib)

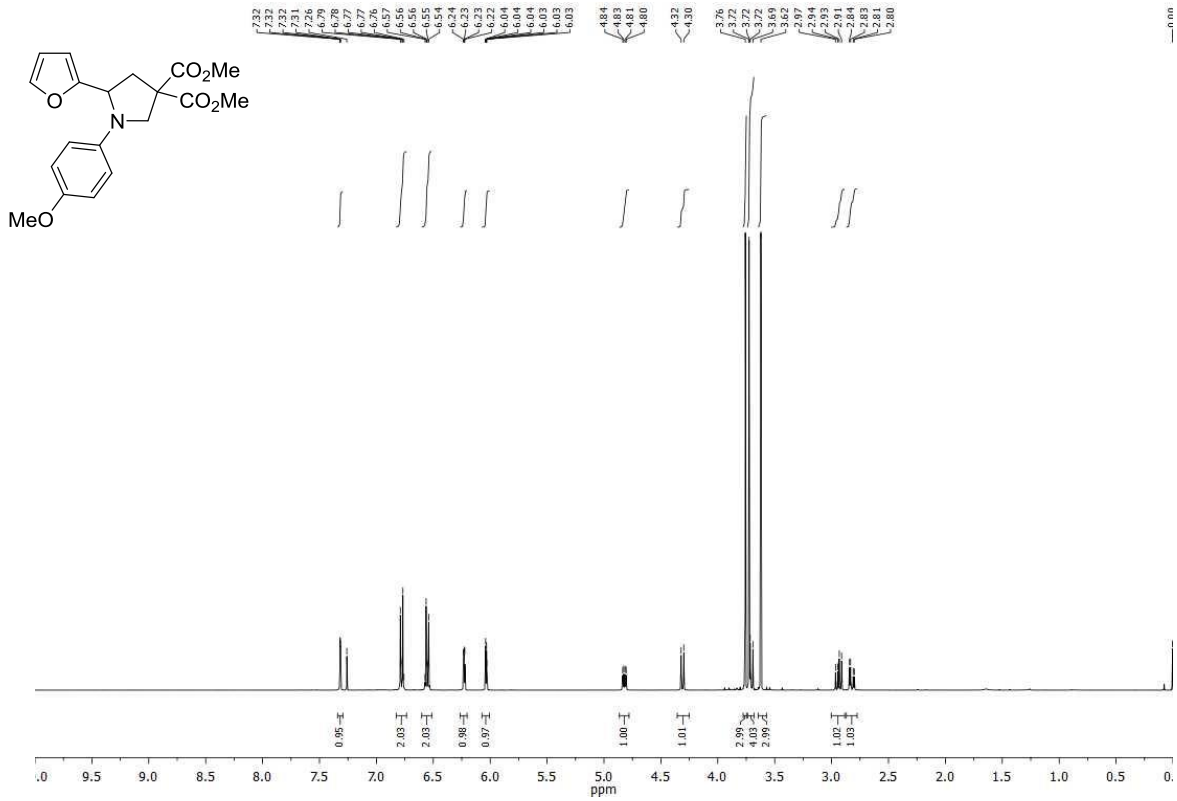


Figure S17: ^{1}H-NMR (400 MHz, $CDCl_3$).

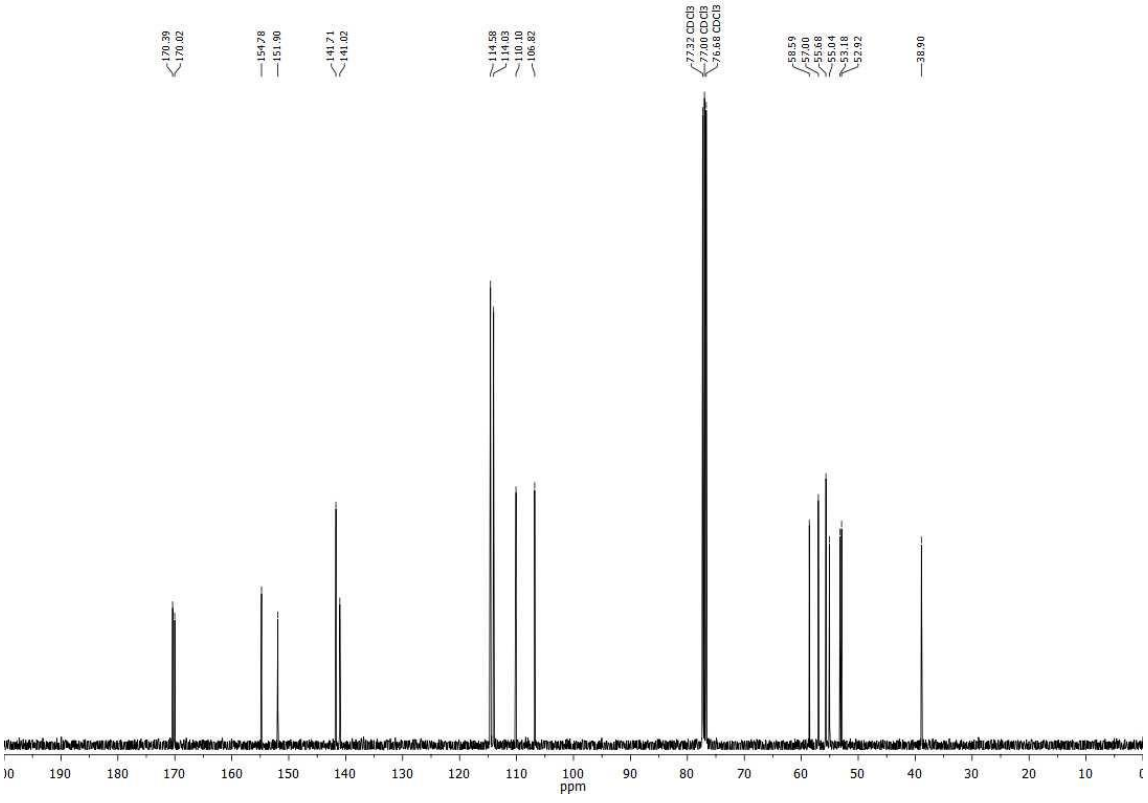


Figure S18: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 5-(4-chlorophenyl)-1-(4-methoxyphenyl)pyrrolidine-3,3-dicarboxylate (5jb)

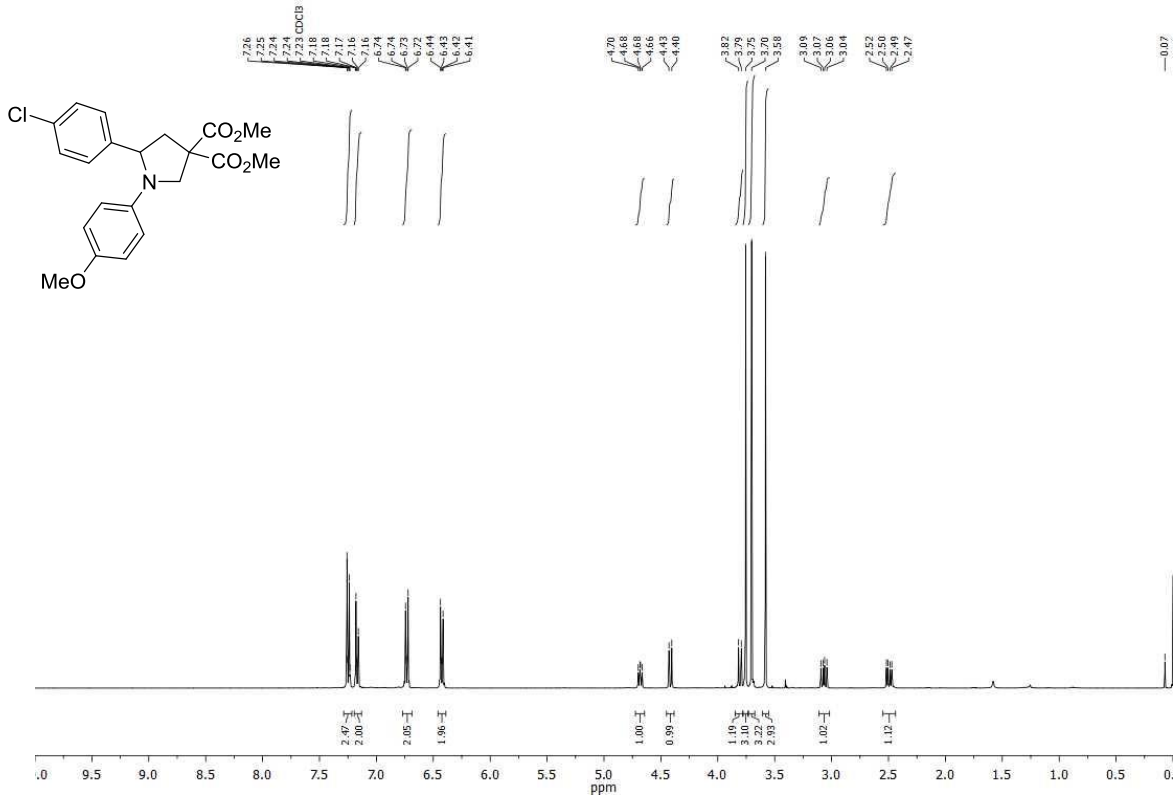


Figure S19: ^{1}H-NMR (400 MHz, $CDCl_3$).

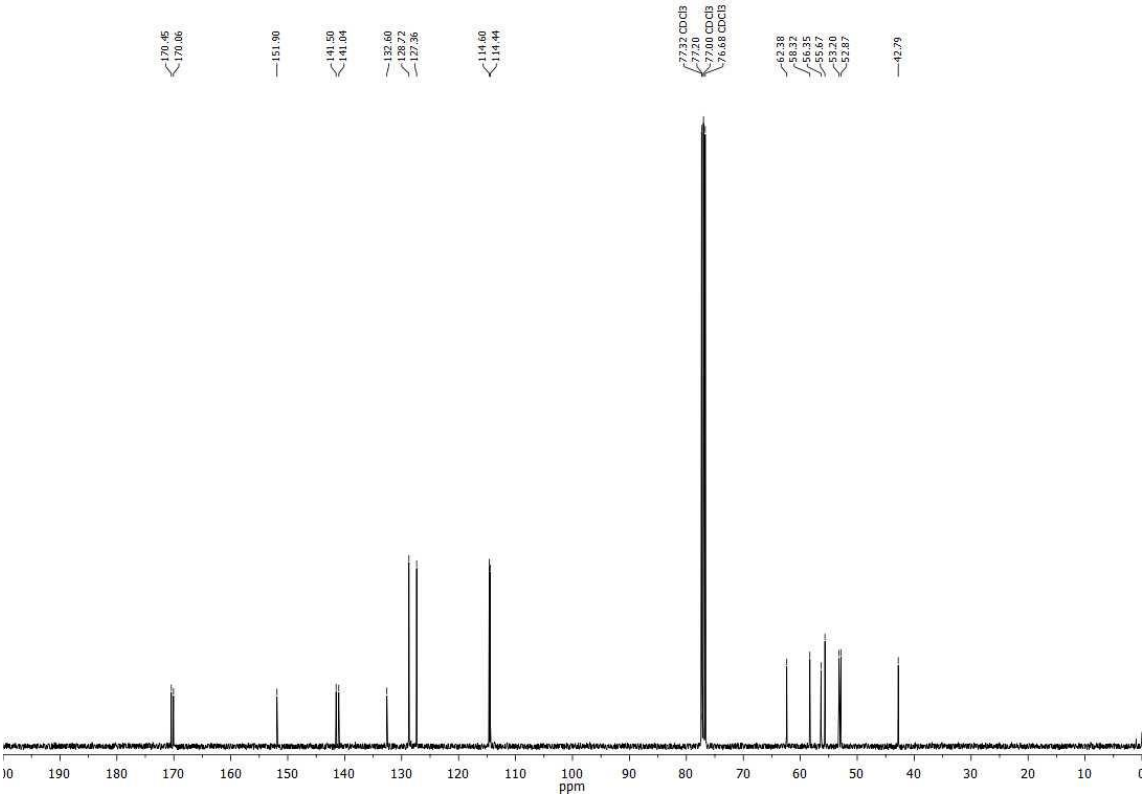


Figure S20: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 5-(4-bromophenyl)-1-(4-methoxyphenyl)pyrrolidine-3,3-dicarboxylate (5kb)

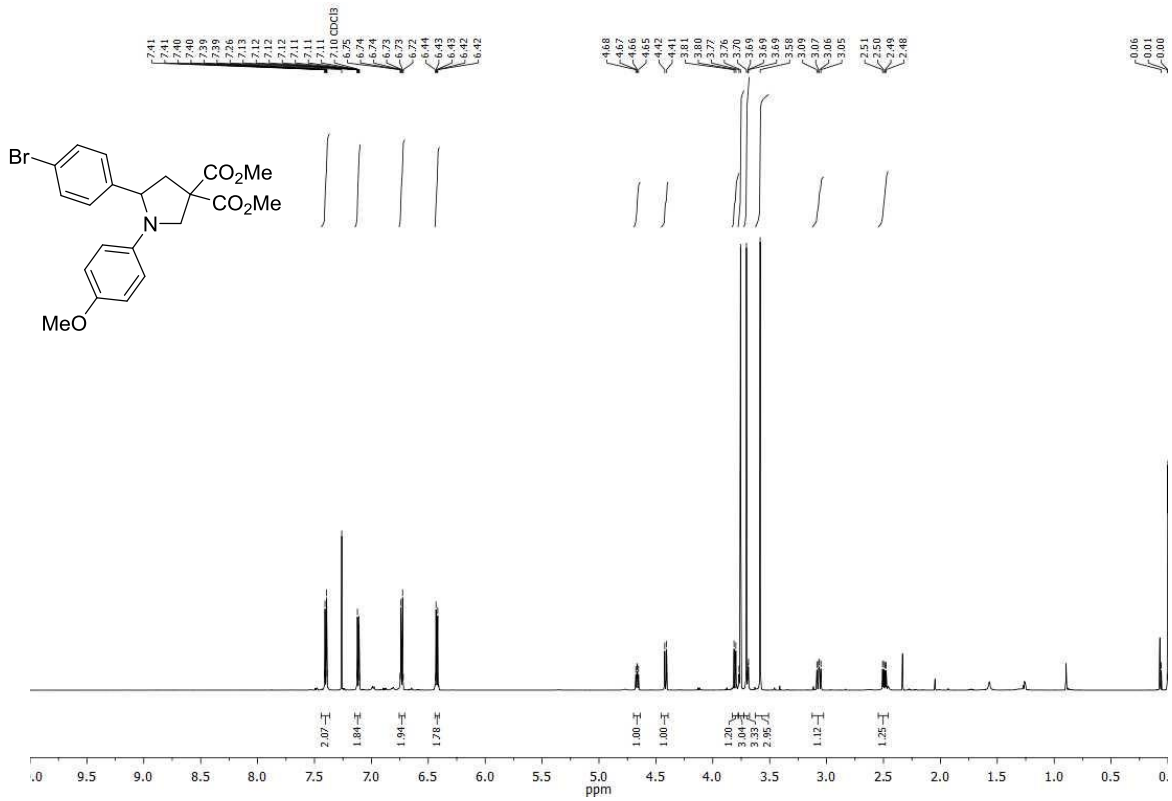


Figure S21: ^{1}H-NMR (600 MHz, $CDCl_3$).

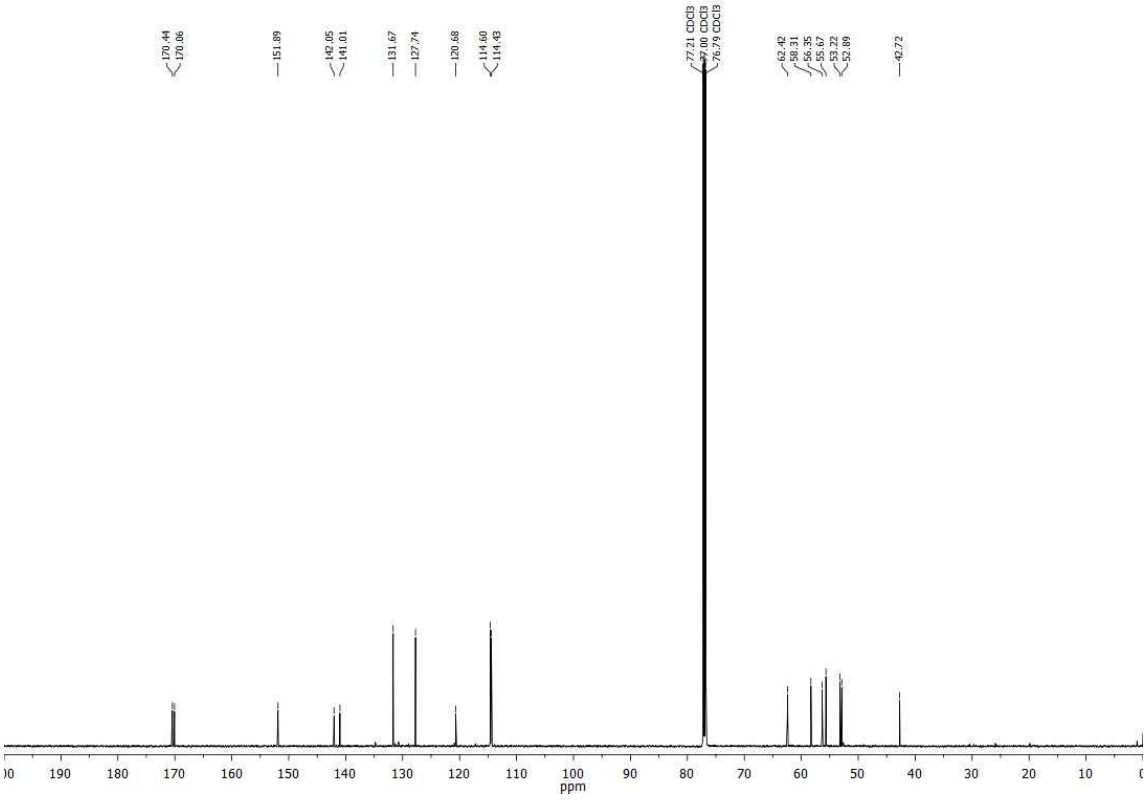


Figure S22: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 1-phenyl-5-(4-(trifluoromethyl)phenyl)pyrrolidine-3,3-dicarboxylate (5la)

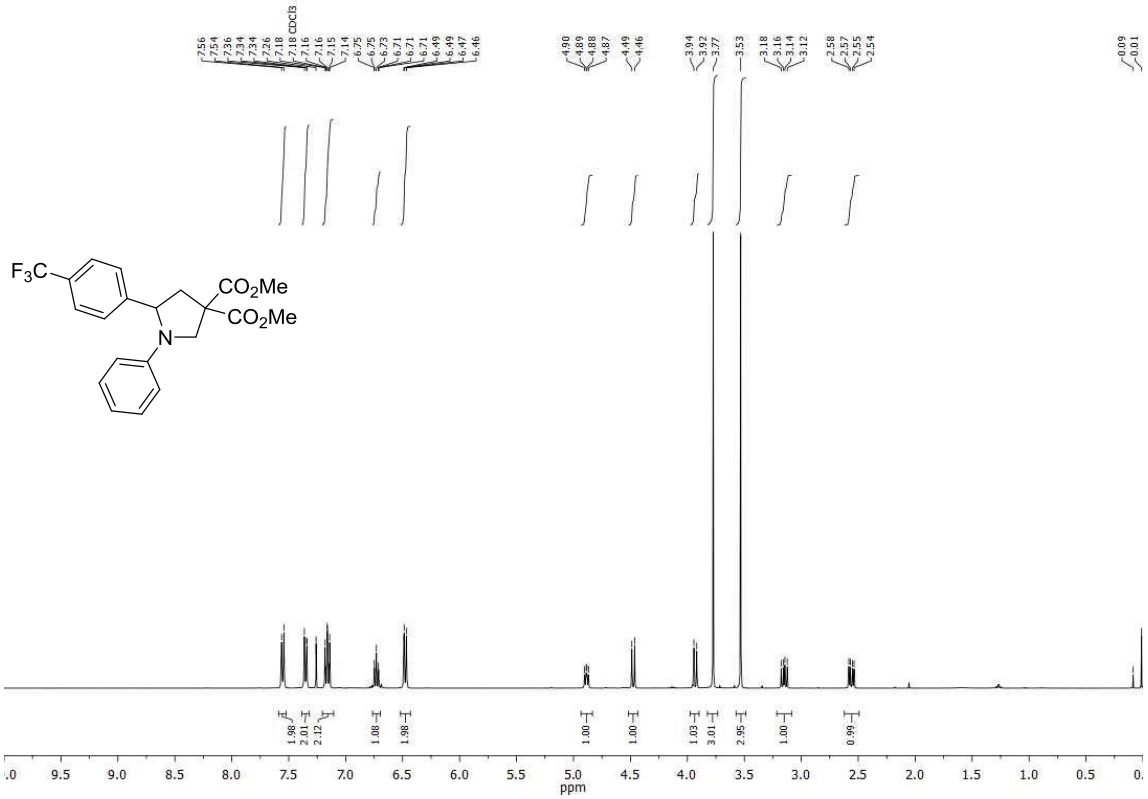


Figure S23: ^{1}H-NMR (400 MHz, $CDCl_3$).

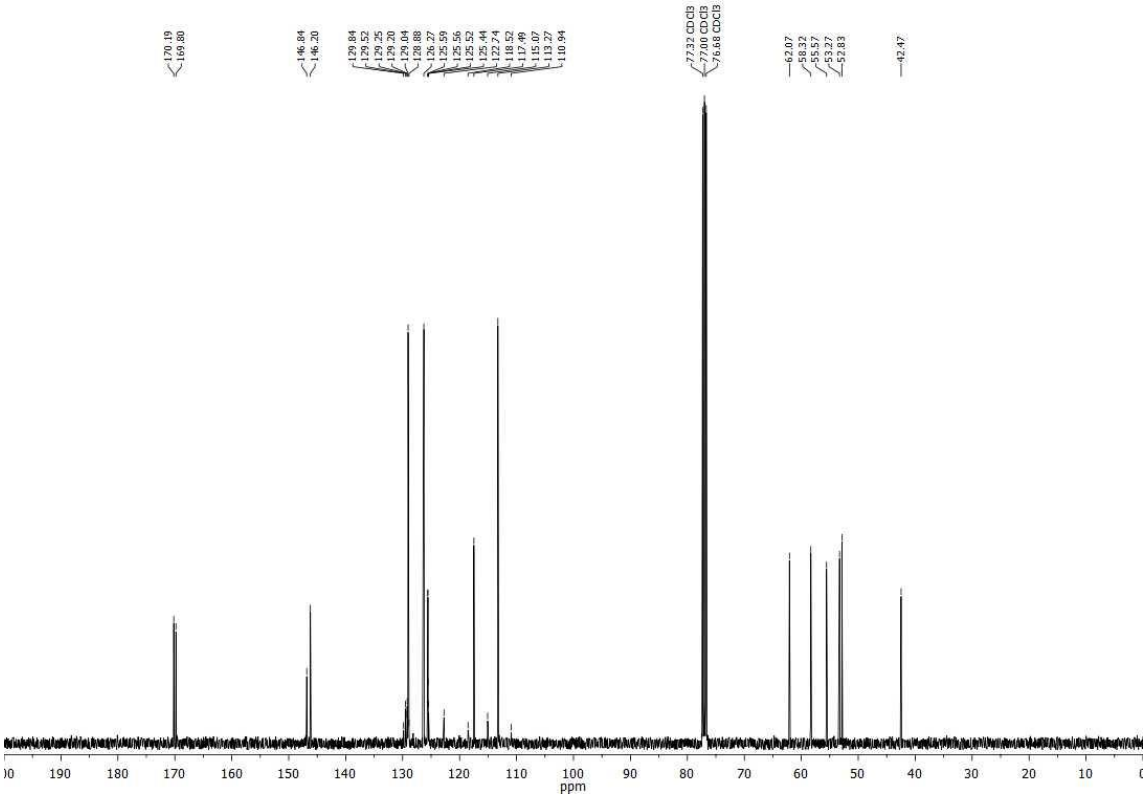


Figure S24: ^{13}C-NMR (100 MHz, $CDCl_3$).

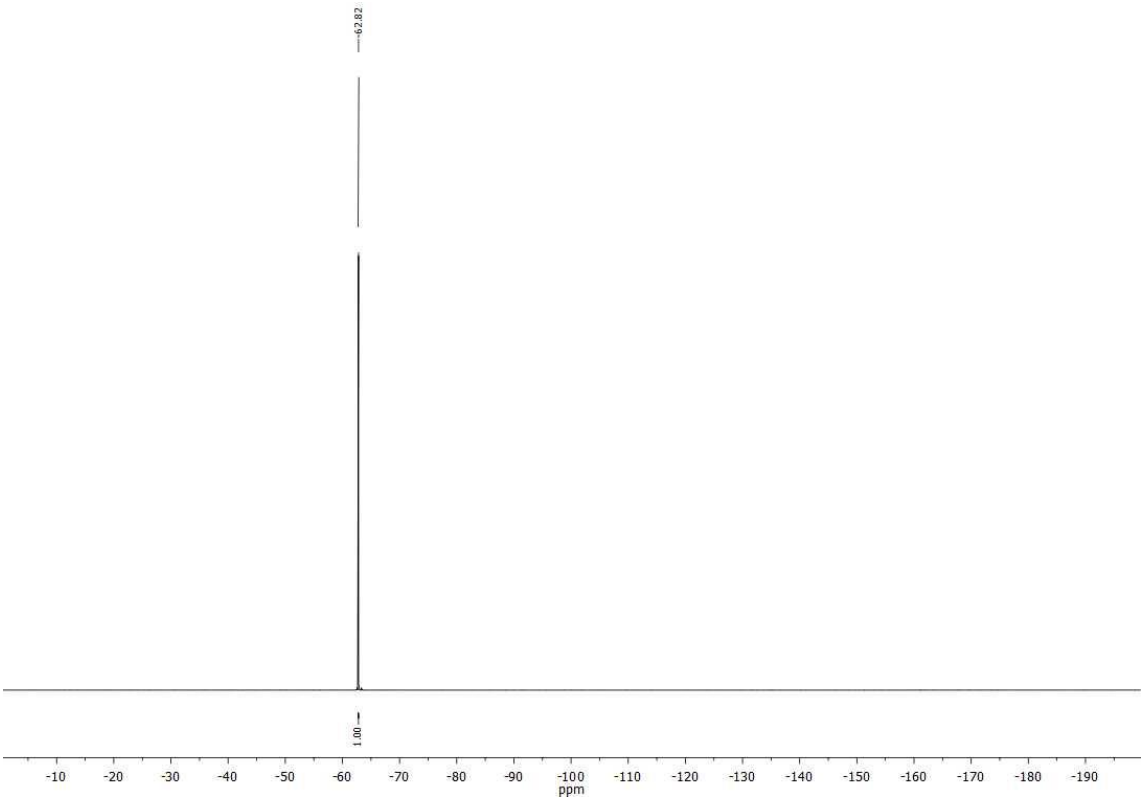


Figure S25: ^{19}F-NMR (400 MHz, $CDCl_3$).

Dimethyl 5-(1,3-dioxoisoindolin-2-yl)-1-phenylpyrrolidine-3,3-dicarboxylate (5ma)

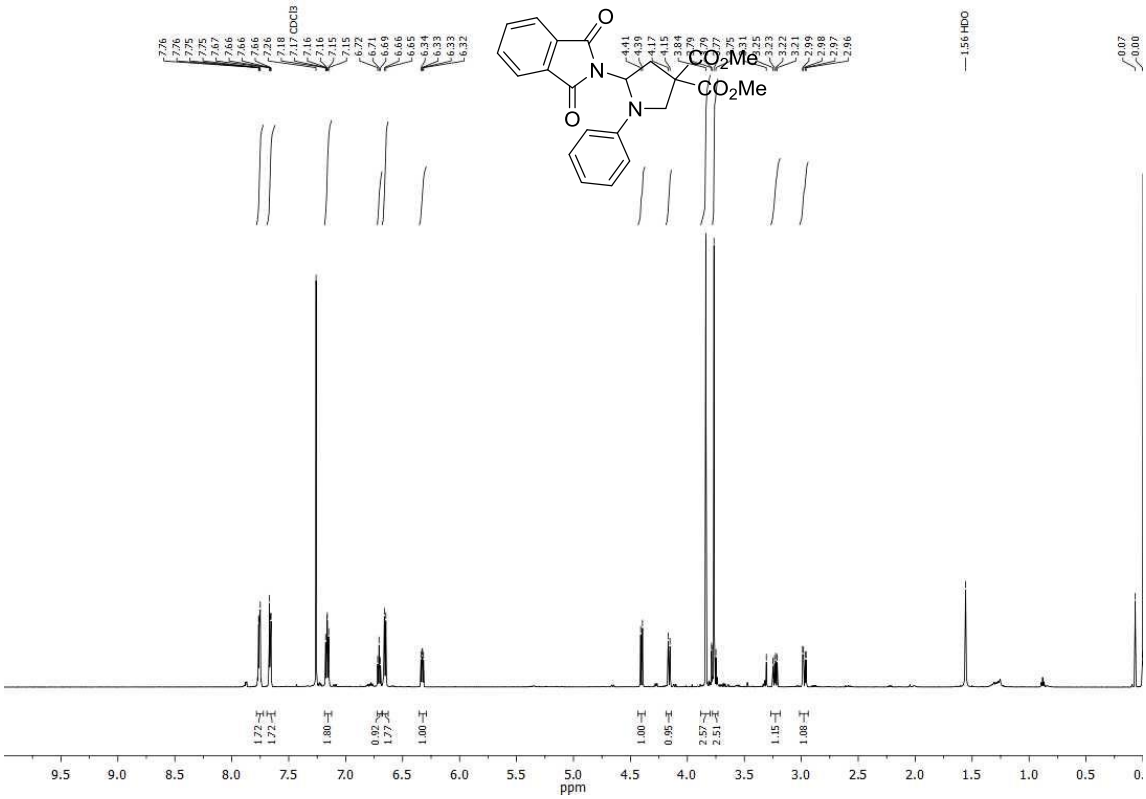


Figure S26: ^{1}H-NMR (600 MHz, $CDCl_3$).

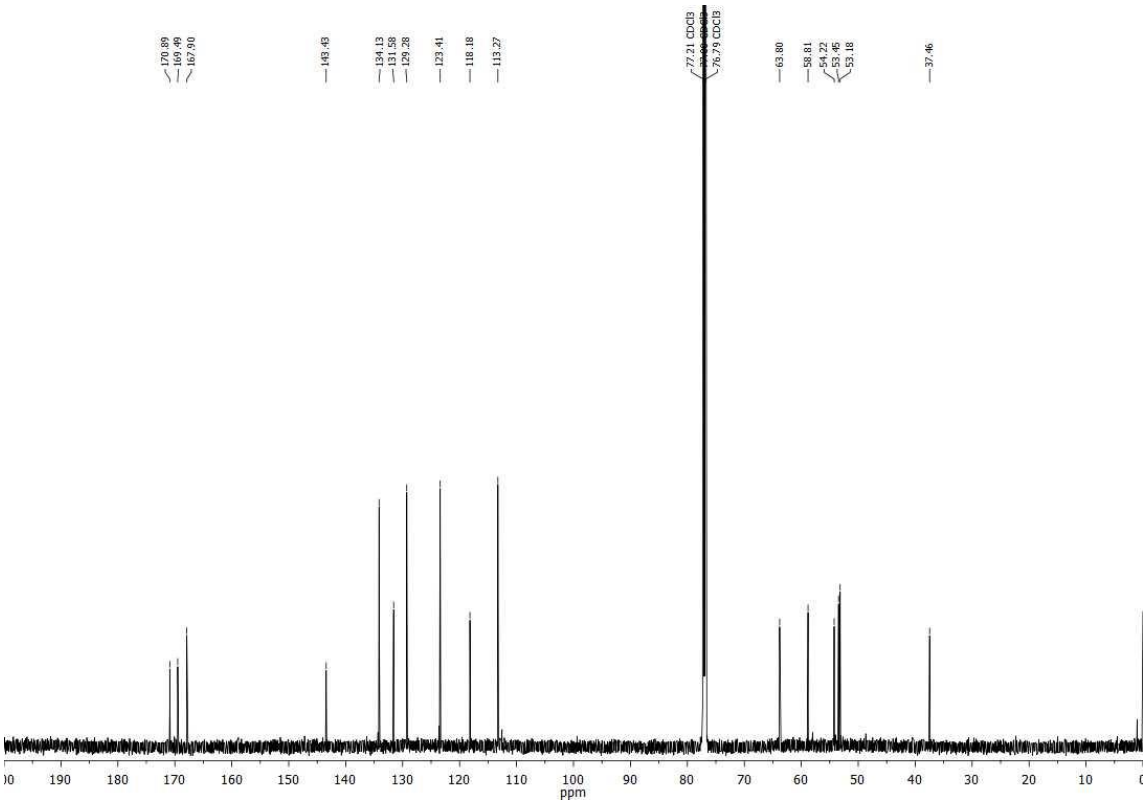


Figure S27: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 5-phenoxy-1-phenylpyrrolidine-3,3-dicarboxylate (5na)

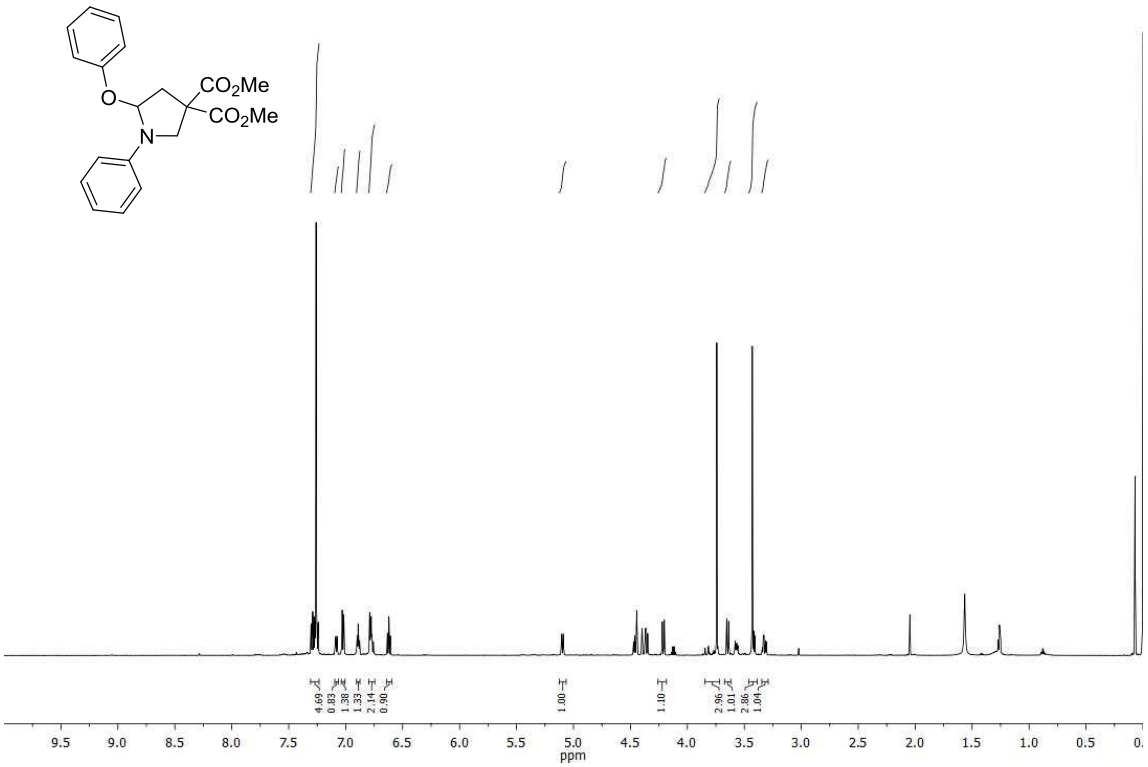


Figure S28: ^{1}H-NMR (600 MHz, $CDCl_3$).

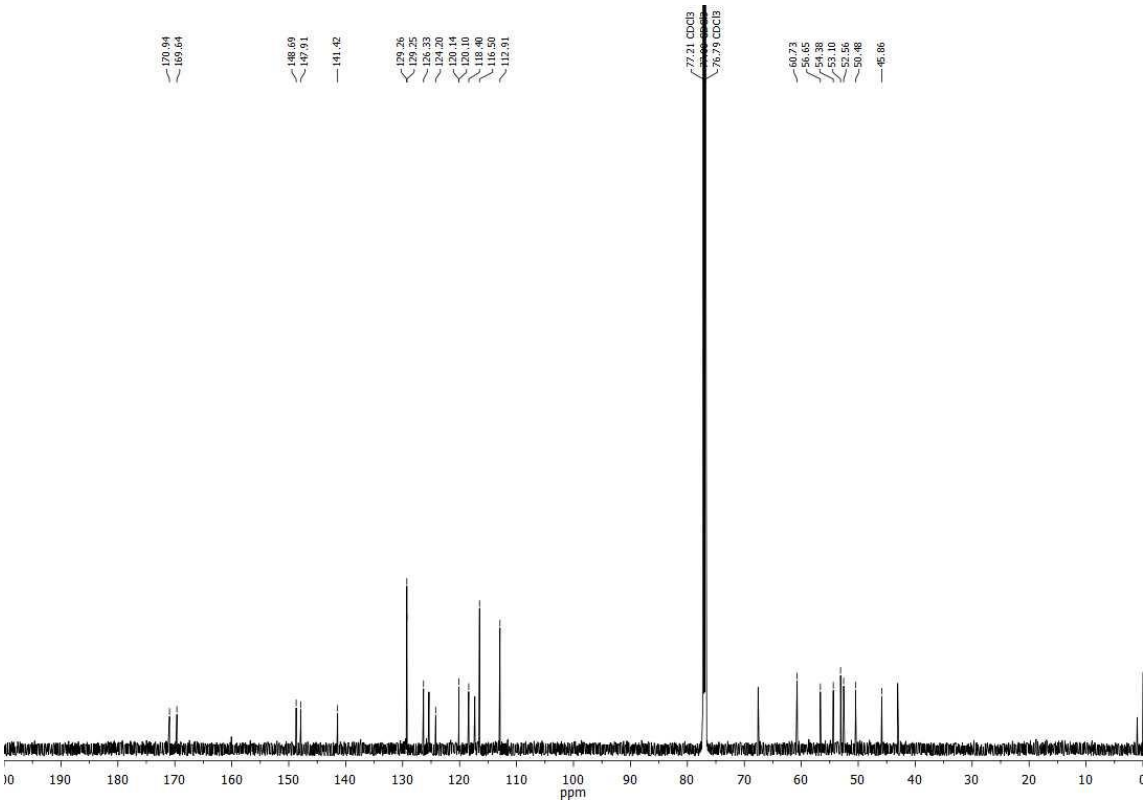


Figure S29: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 1-(4-methoxyphenyl)-5-vinylpyrrolidine-3,3-dicarboxylate (5ob)

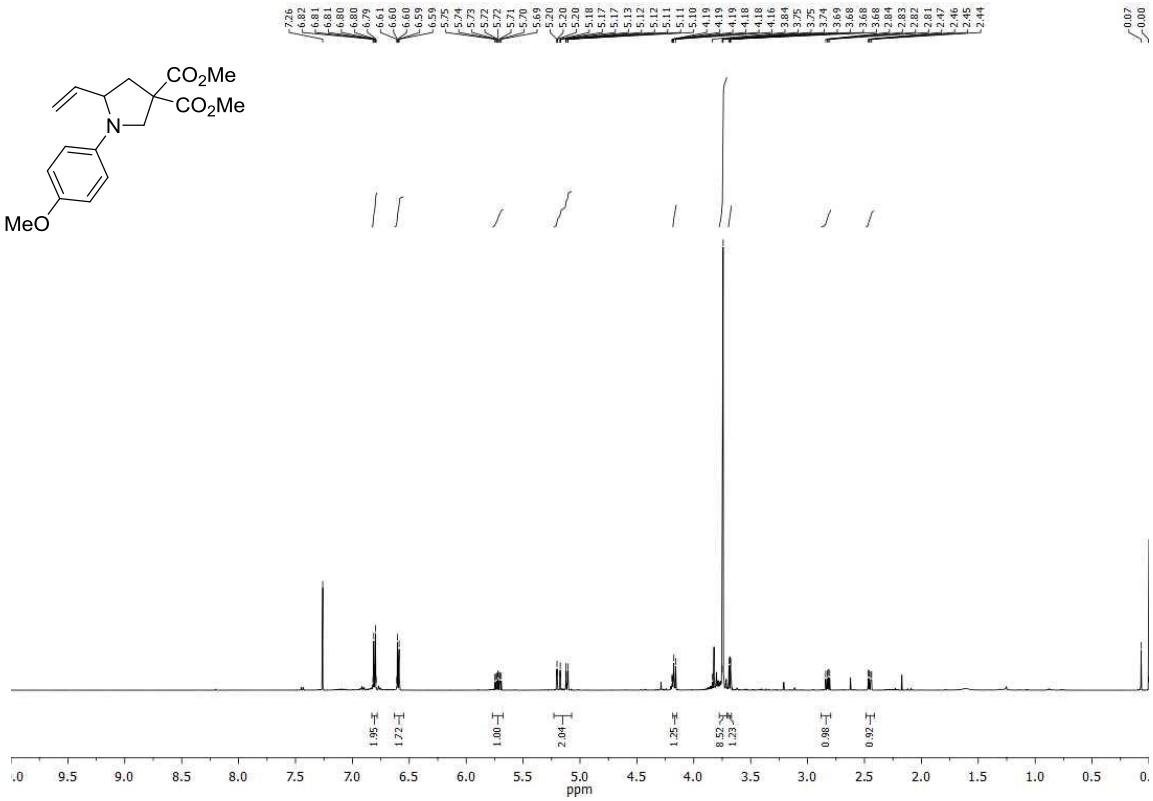


Figure S30: ^{1}H-NMR (600 MHz, $CDCl_3$).

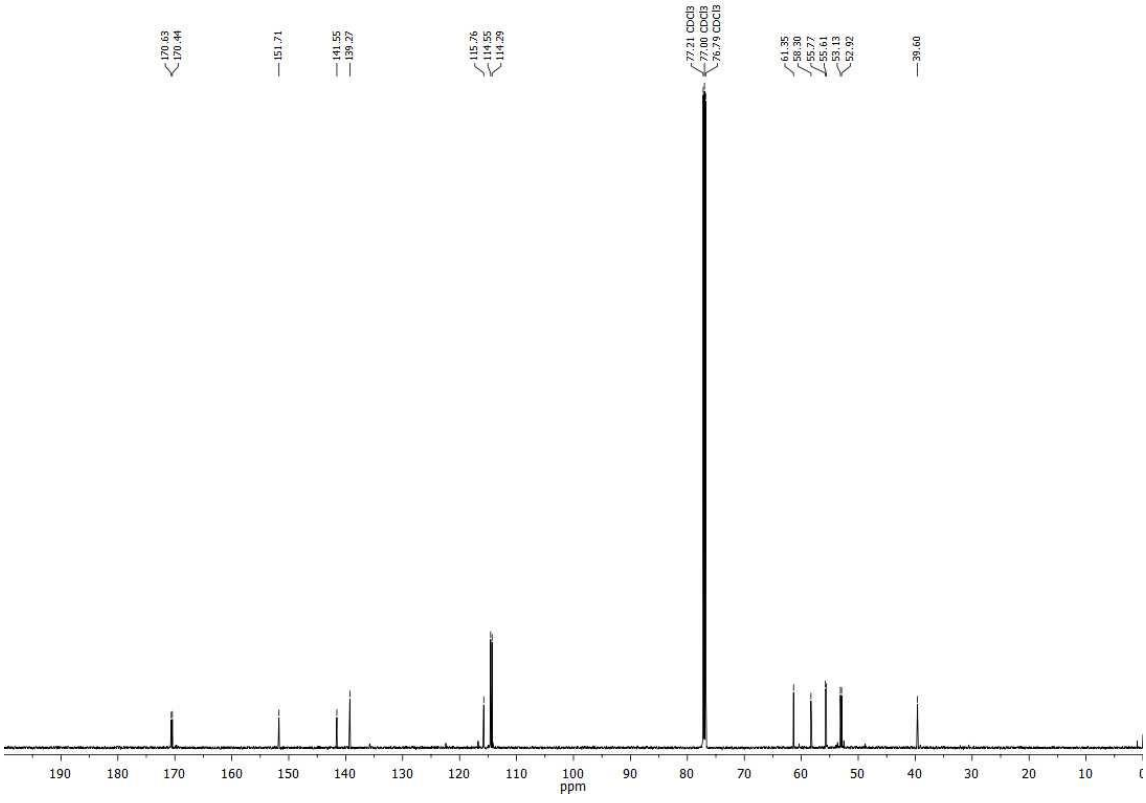


Figure S31: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 1-(4-methoxyphenyl)-5-phenylpyrrolidine-3,3-dicarboxylate (5ab)

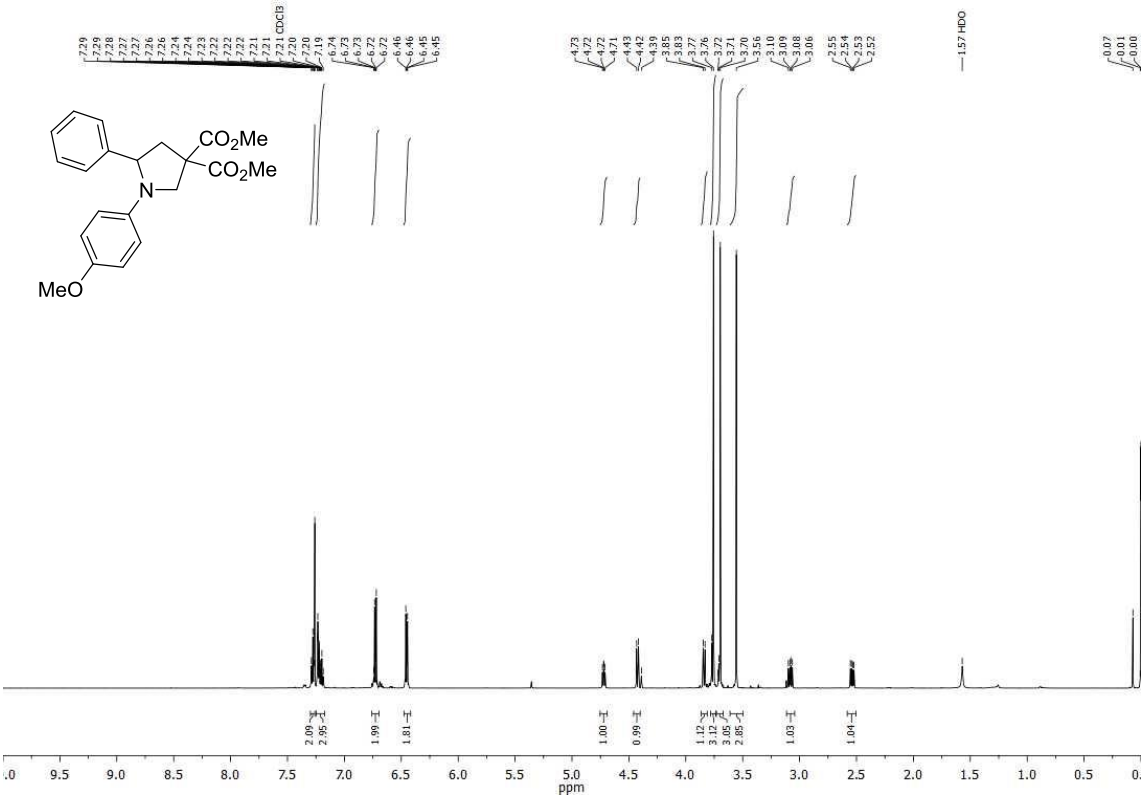


Figure S32: ^{1}H-NMR (600 MHz, $CDCl_3$).

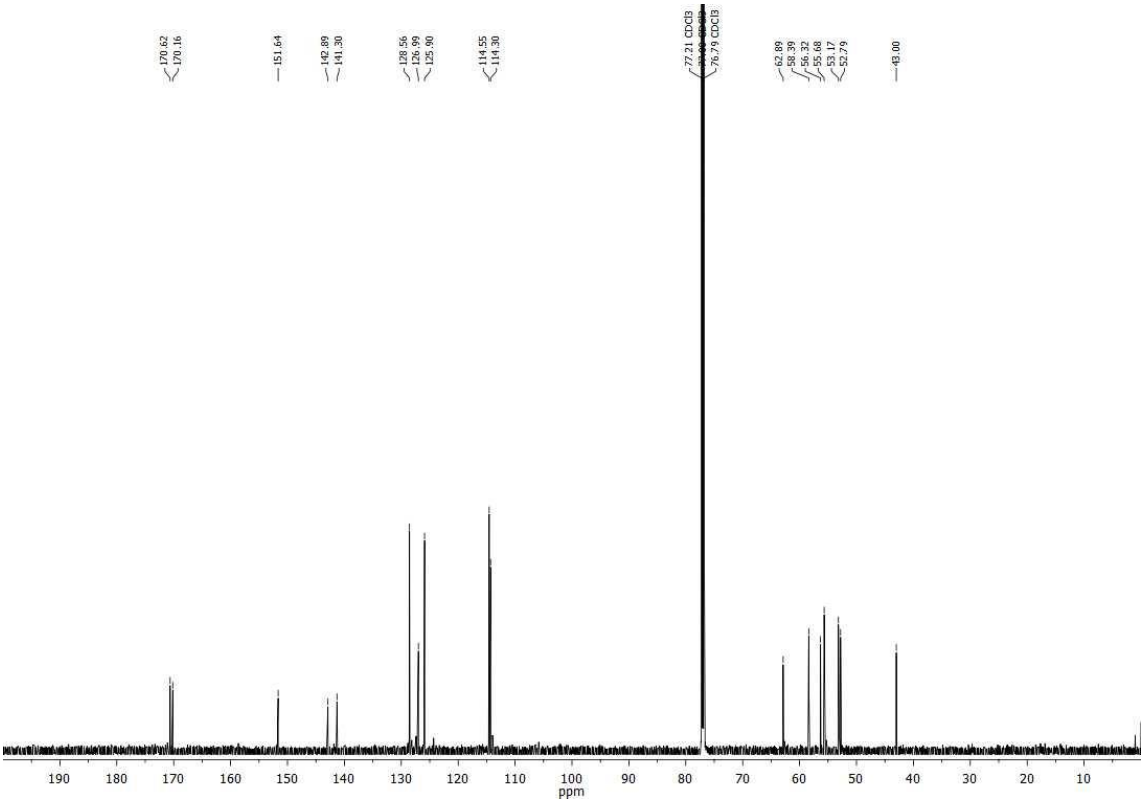


Figure S33: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 1-(2-methoxyphenyl)-5-phenylpyrrolidine-3,3-dicarboxylate (5ac)

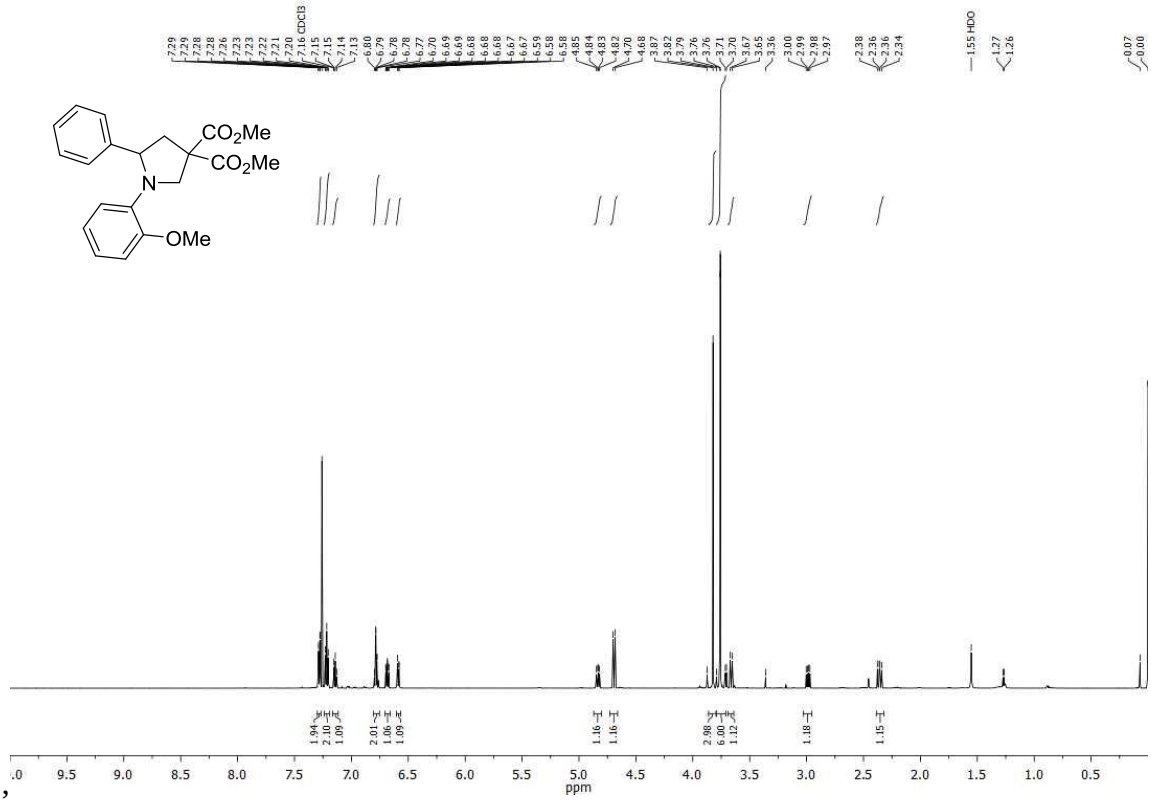


Figure S34: ^{1}H-NMR (600 MHz, $CDCl_3$).

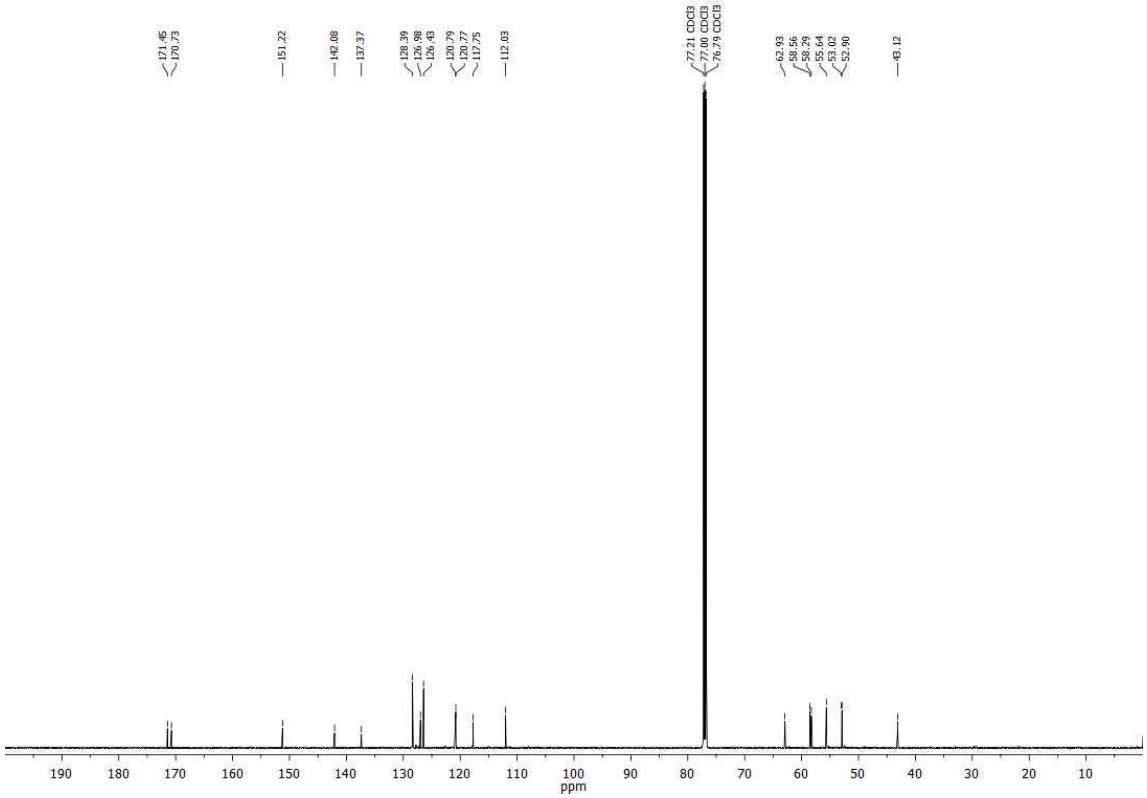


Figure S35: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 5-phenyl-1-(*p*-tolyl)pyrrolidine-3,3-dicarboxylate (5ad)

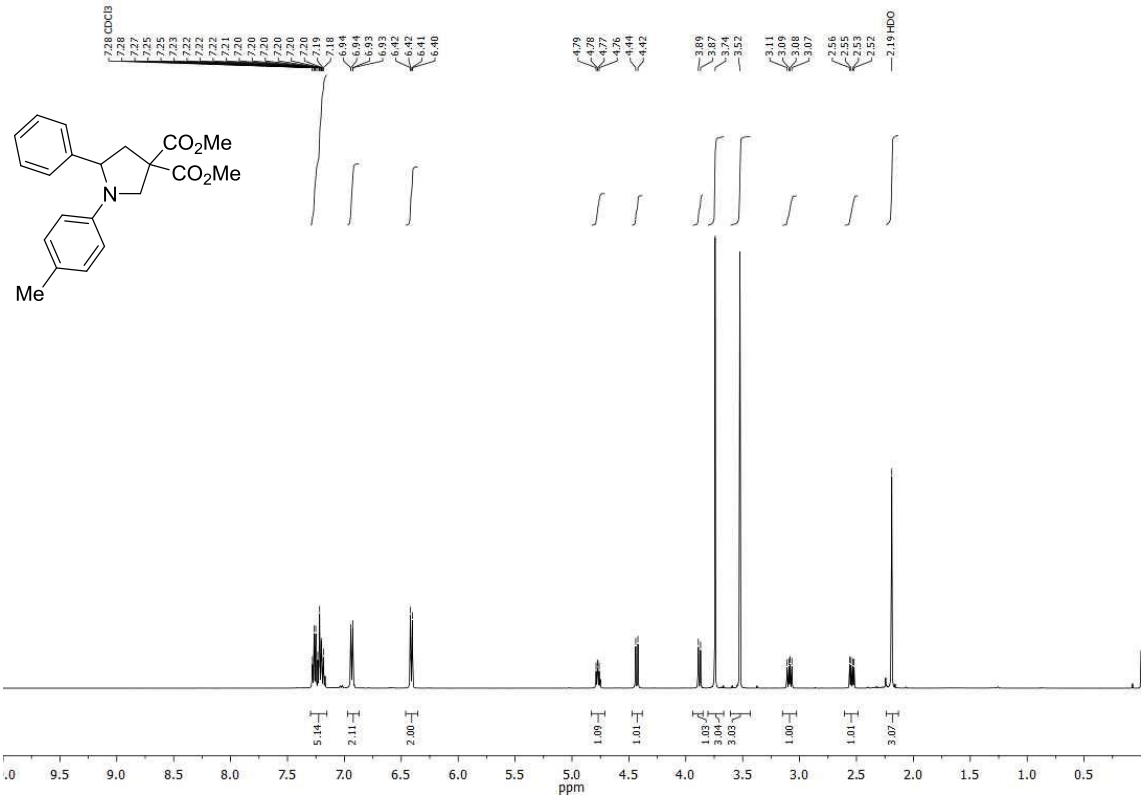


Figure S36: ^{1}H-NMR (500 MHz, $CDCl_3$).

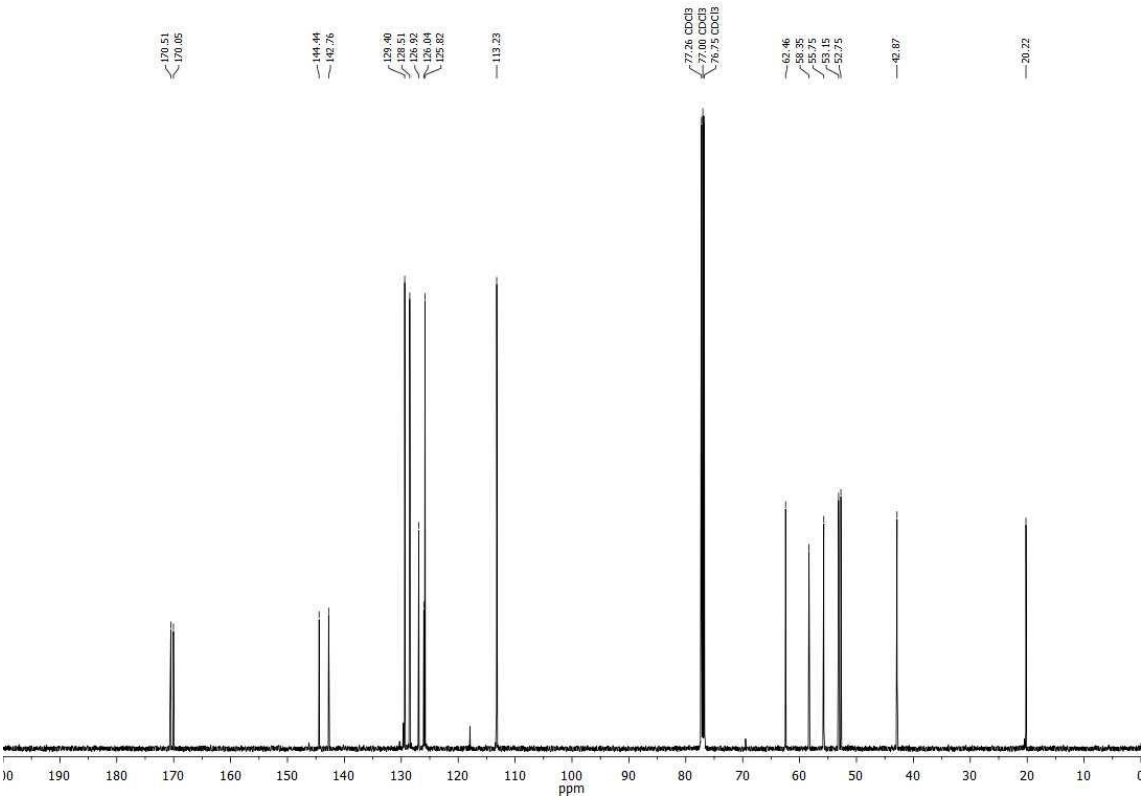


Figure S37: ^{13}C-NMR (125 MHz, $CDCl_3$).

Dimethyl 1-(4-fluorophenyl)-5-phenylpyrrolidine-3,3-dicarboxylate (5ae)

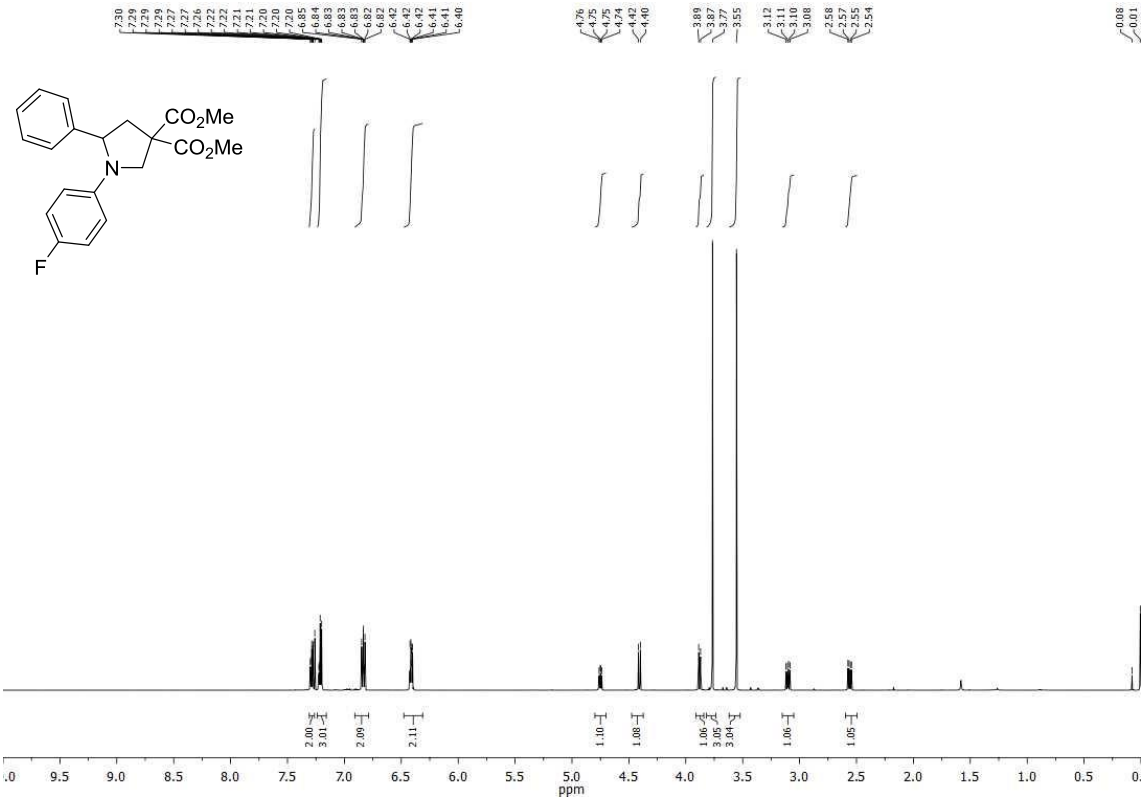


Figure S38: ^{1}H-NMR (500 MHz, $CDCl_3$).

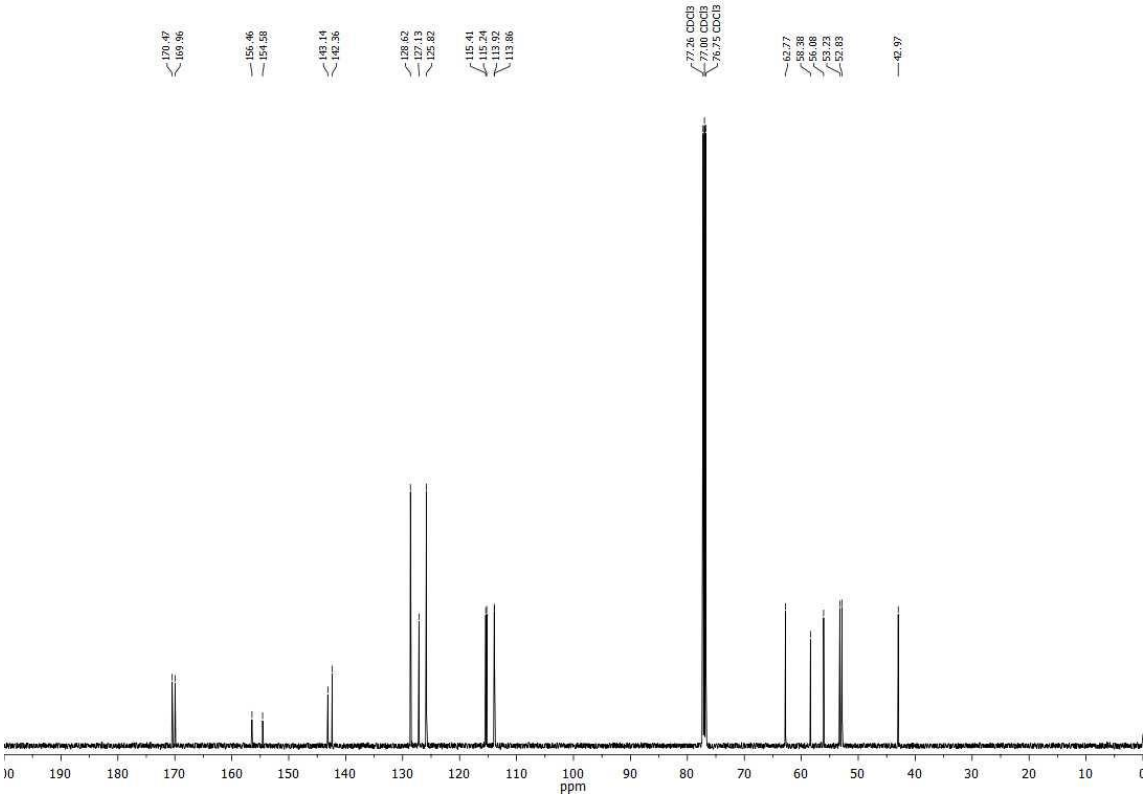


Figure S39: ^{13}C-NMR (125 MHz, $CDCl_3$).

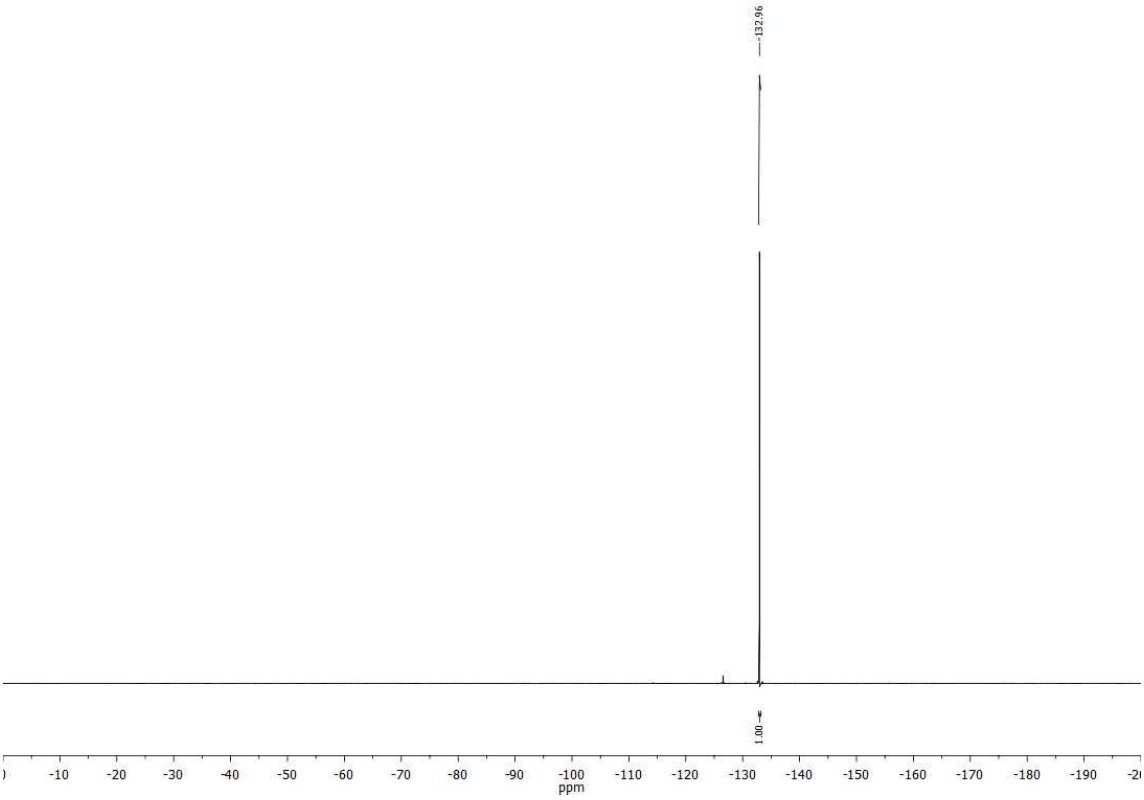


Figure S40: ^{19}F-NMR (283 MHz, $CDCl_3$).

Dimethyl 1-(4-chlorophenyl)-5-phenylpyrrolidine-3,3-dicarboxylate (5af)

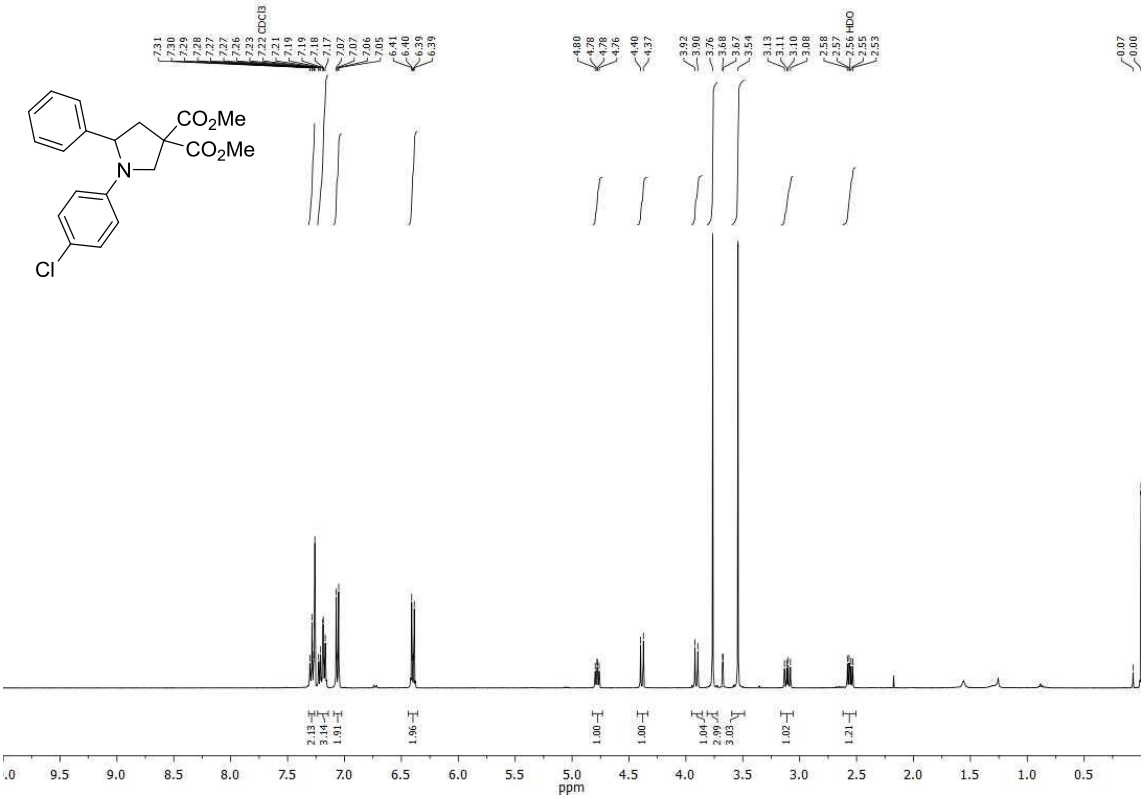


Figure S41: ^{1}H-NMR (400 MHz, $CDCl_3$).

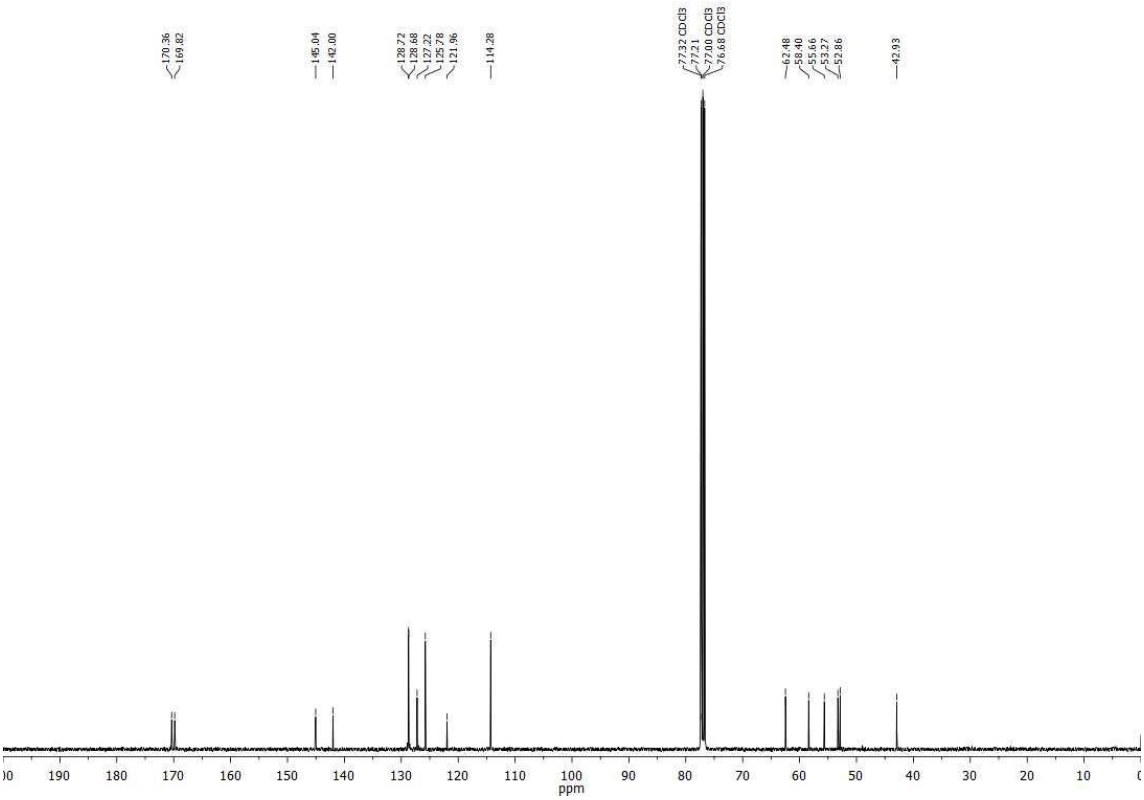


Figure S42: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 1-(4-bromophenyl)-5-(4-methoxyphenyl)pyrrolidine-3,3-dicarboxylate (5eg)

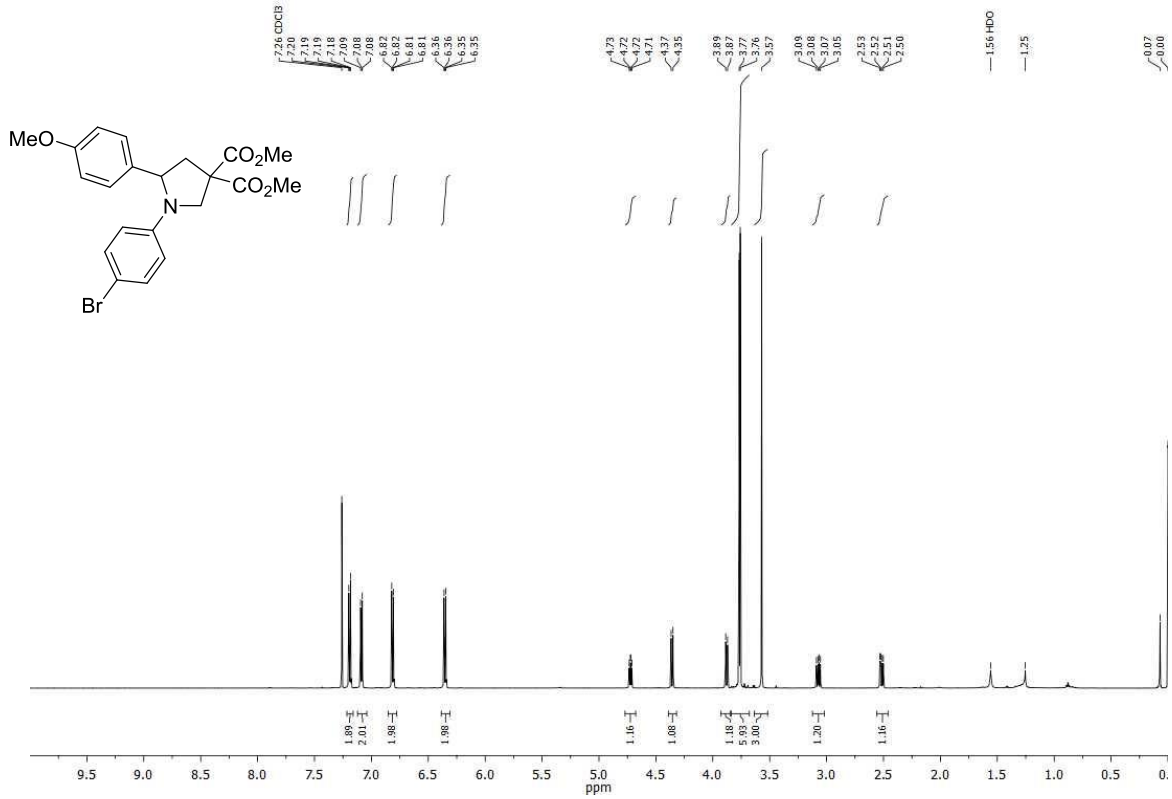


Figure S43: ^{1}H-NMR (600 MHz, $CDCl_3$).

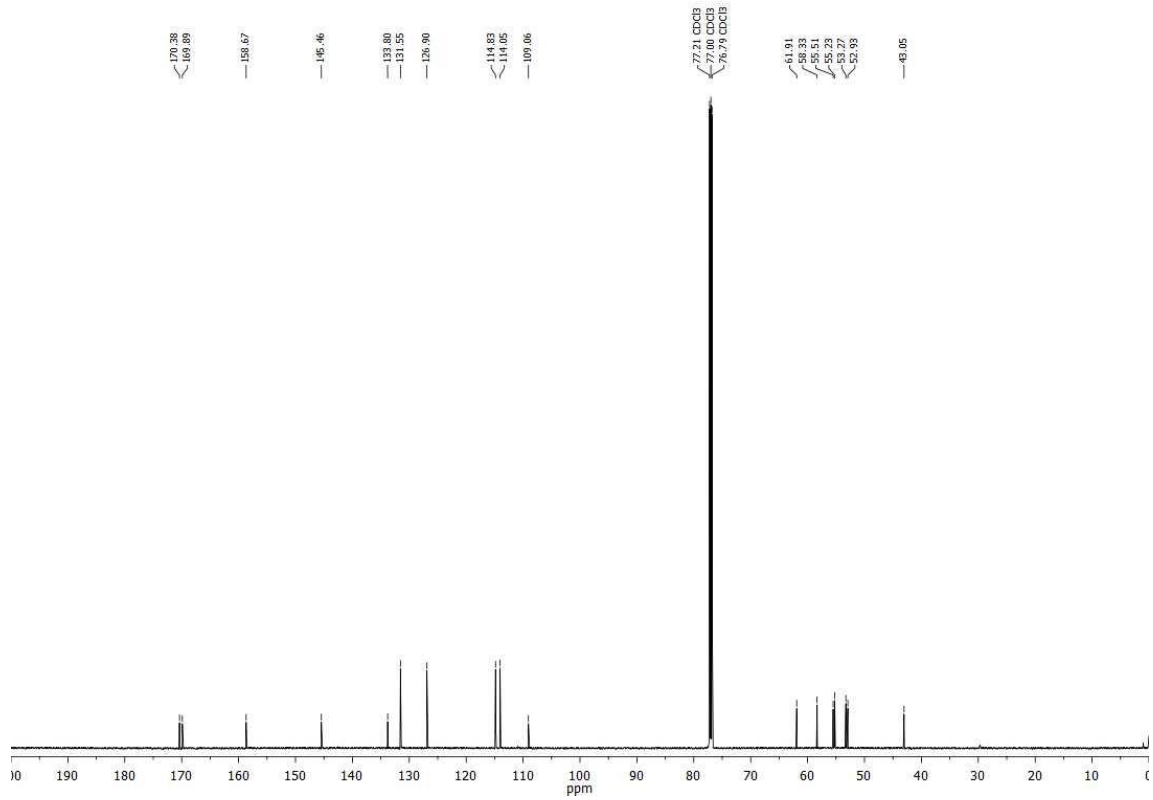


Figure S44: ^{13}C-NMR (150 MHz, $CDCl_3$).

Dimethyl 5-phenyl-1-(3-(trifluoromethyl)phenyl)pyrrolidine-3,3-dicarboxylate (5ah)

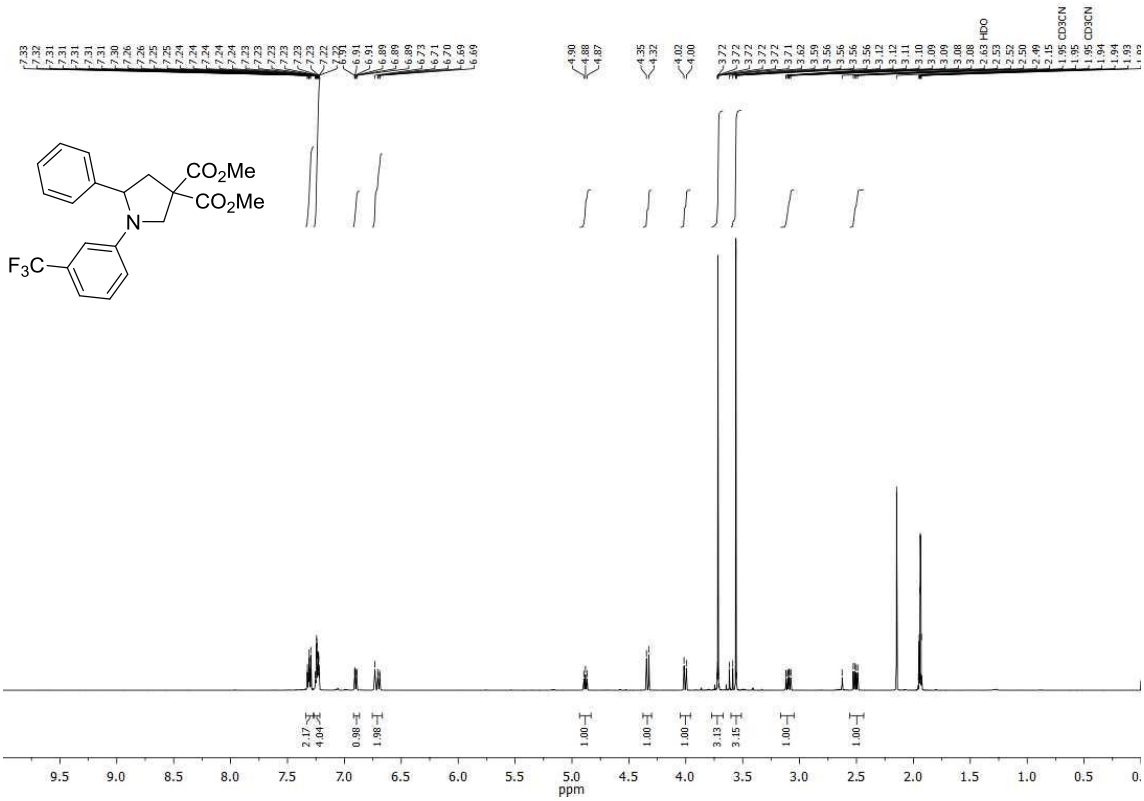


Figure S45: ^{1}H-NMR (500 MHz, CD_3CN).

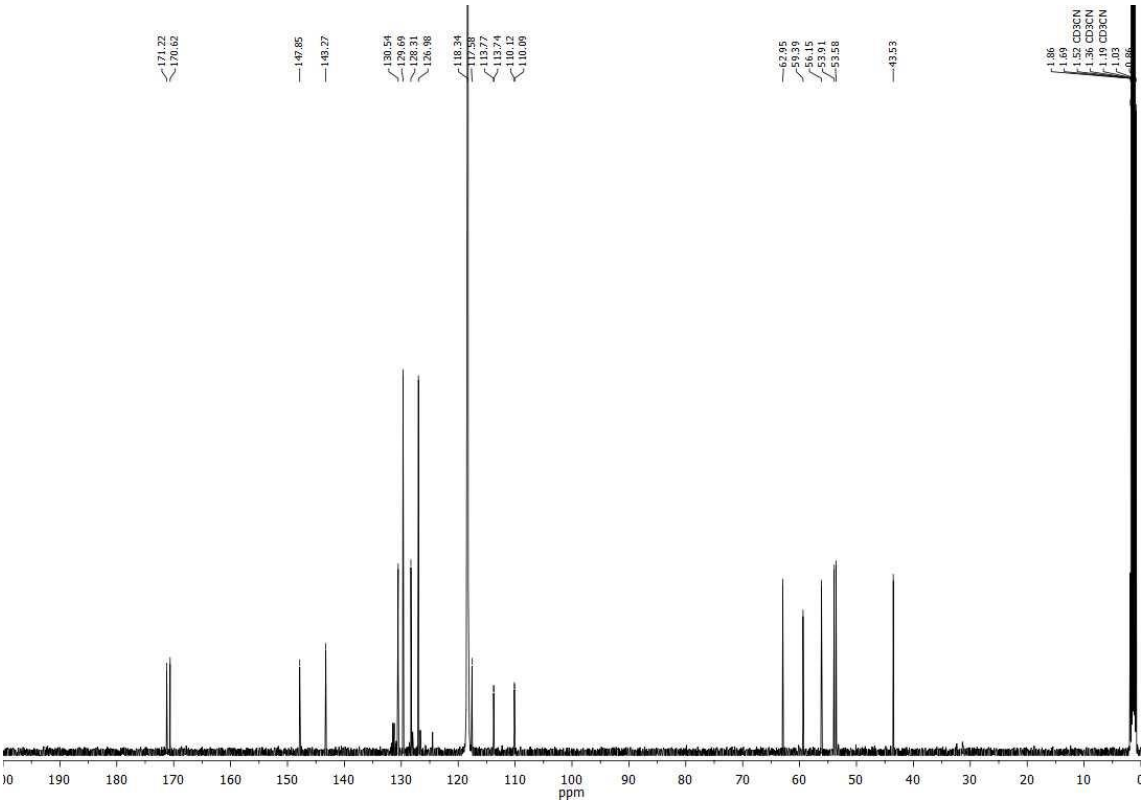


Figure S46: ^{13}C-NMR (125 MHz, CD_3CN).

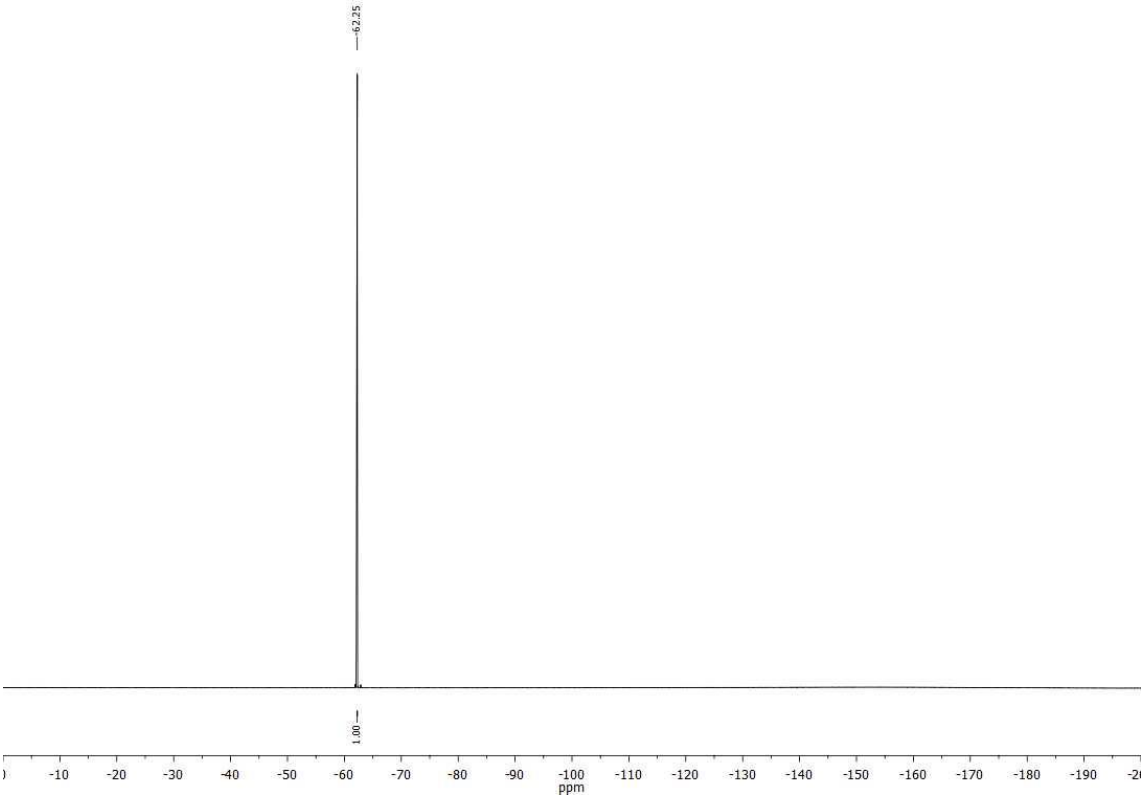


Figure S47: ^{19}F-NMR (283 MHz, CD_3CN).

Dimethyl 1,6-diphenylpiperidine-3,3-dicarboxylate (7aa)

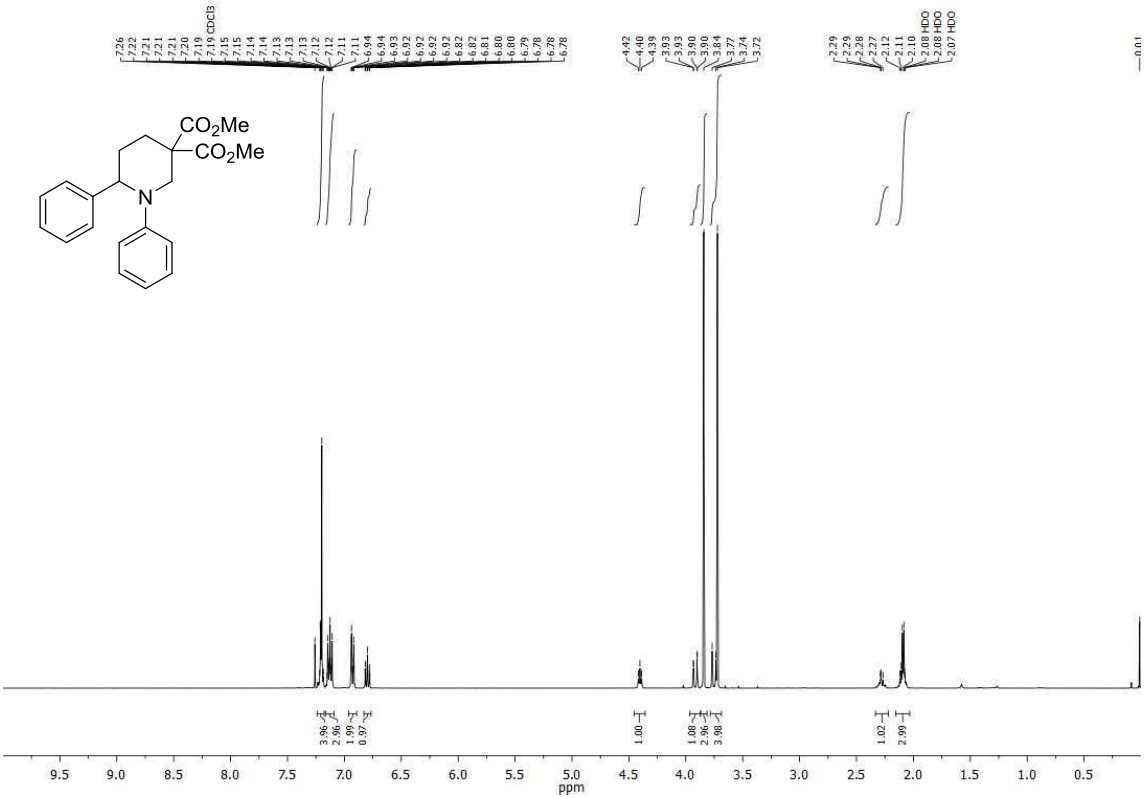


Figure S48: ^{1}H-NMR (400 MHz, $CDCl_3$).

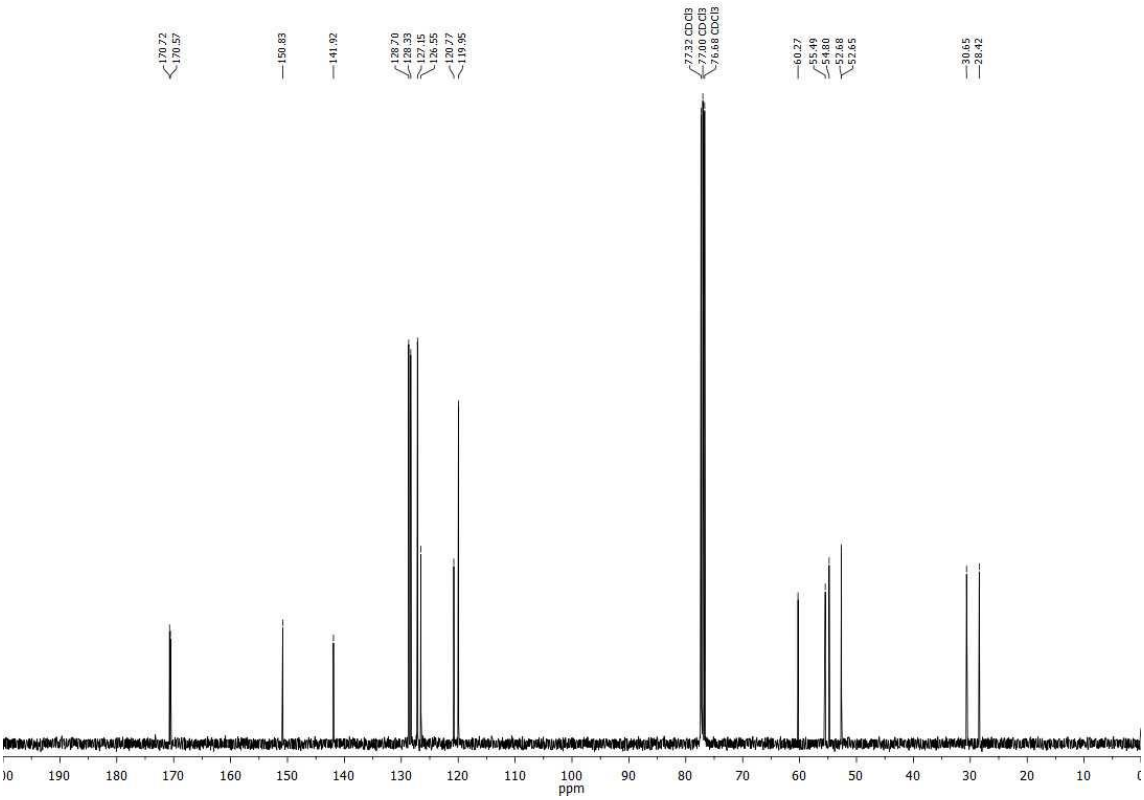


Figure S49: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 6-(3,4-dimethoxyphenyl)-1-phenylpiperidine-3,3-dicarboxylate (7ba)

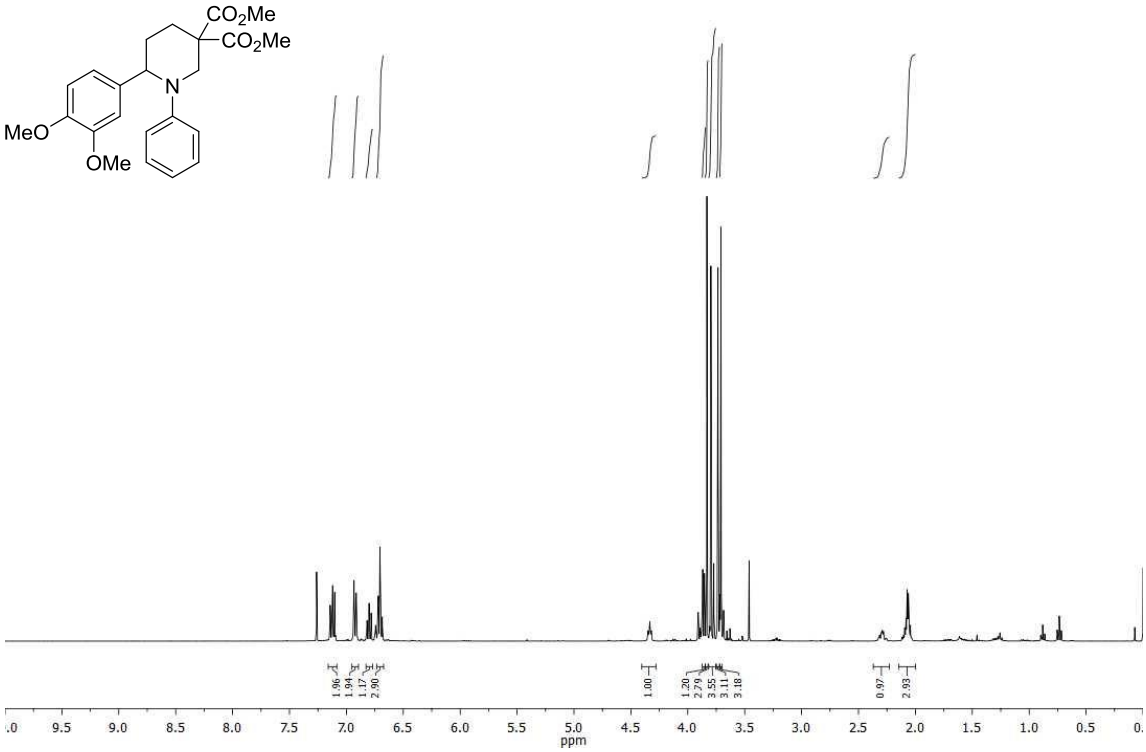


Figure S50: ^{1}H-NMR (400 MHz, $CDCl_3$).

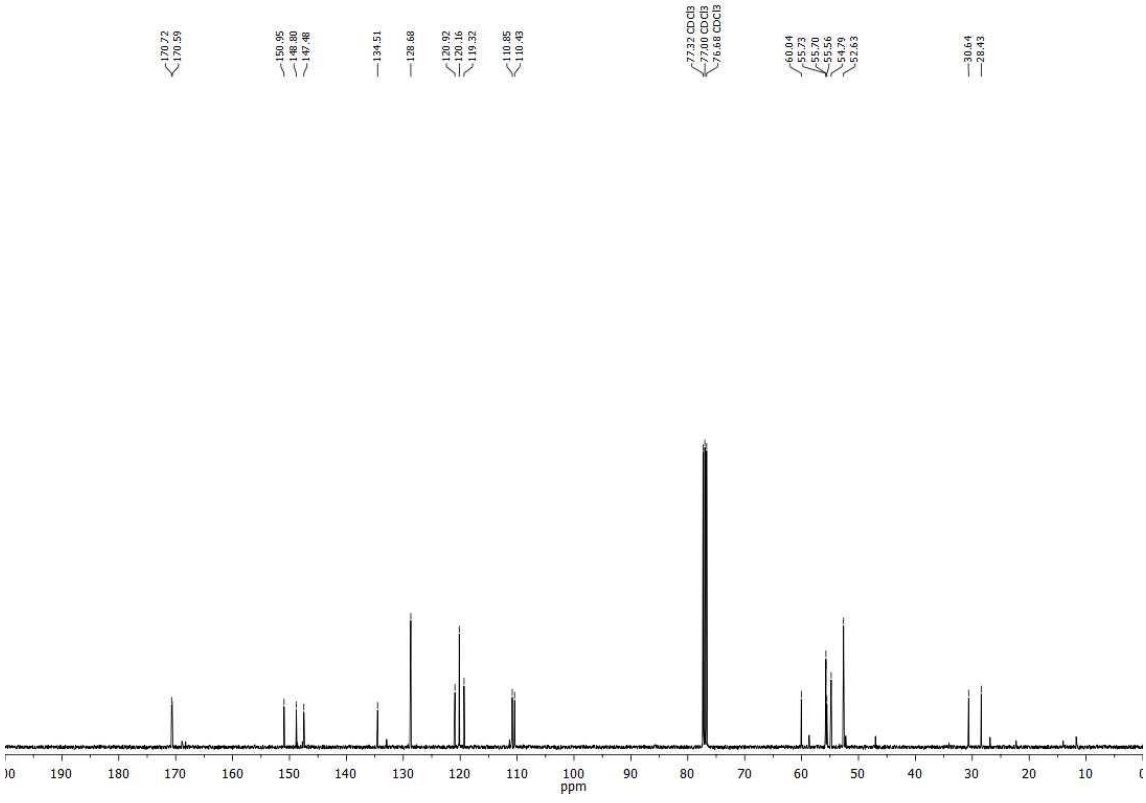


Figure S51: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 6-(4-methoxyphenyl)-1-phenylpiperidine-3,3-dicarboxylate (7ca)

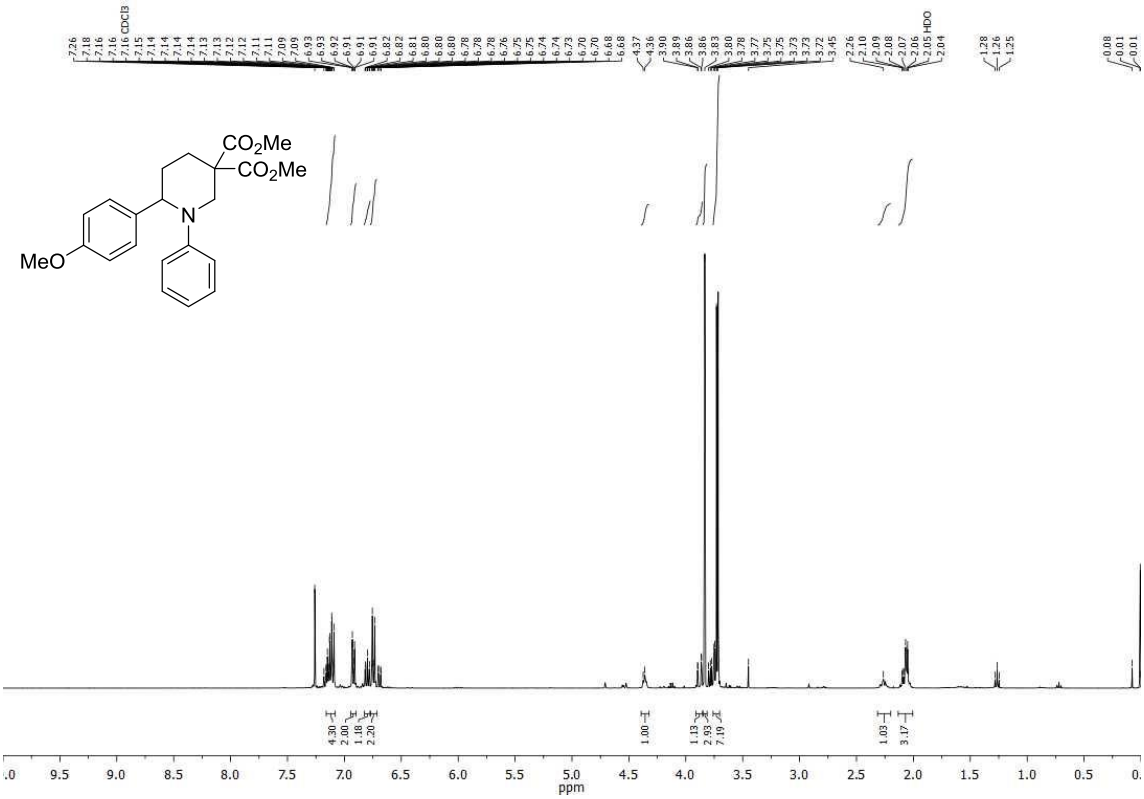


Figure S52: ^{1}H-NMR (400 MHz, $CDCl_3$).

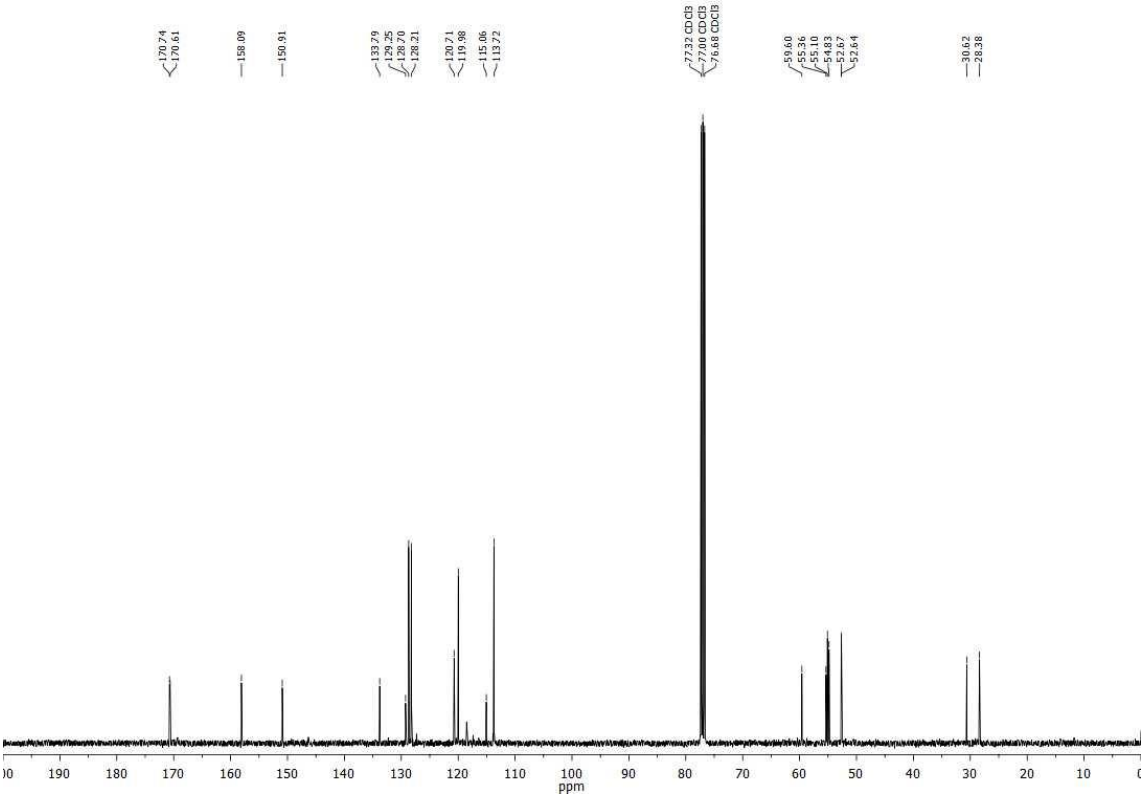


Figure S53: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 1-(4-chlorophenyl)-6-(4-methoxyphenyl)piperidine-3,3-dicarboxylate (7cb)

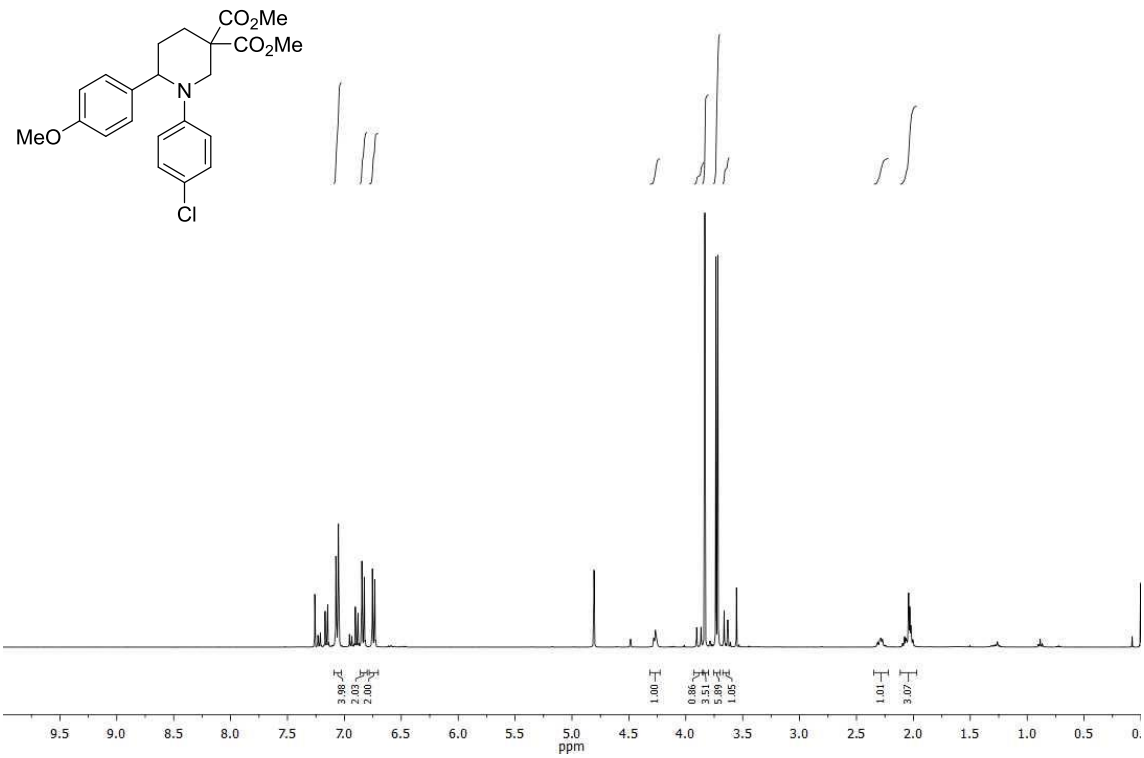


Figure S54: ^{1}H-NMR (400 MHz, $CDCl_3$).

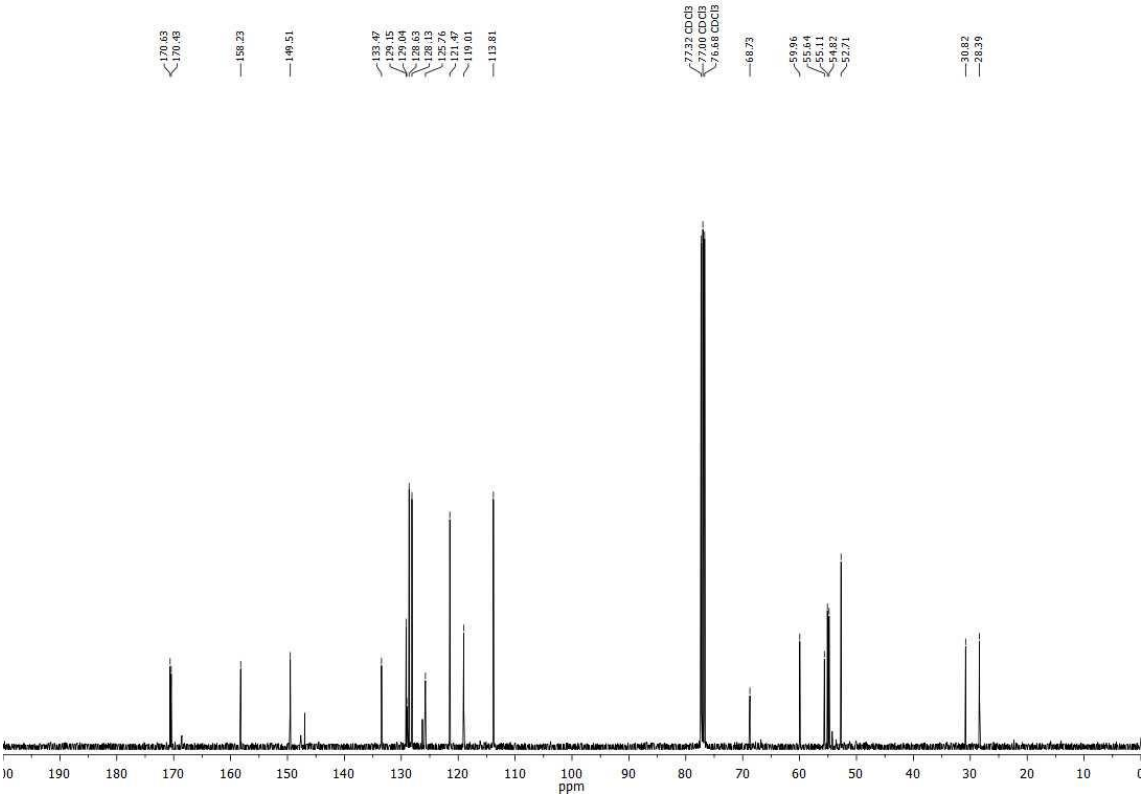


Figure S55: ^{13}C-NMR (100 MHz, $CDCl_3$).

Dimethyl 1,6-bis(4-methoxyphenyl)piperidine-3,3-dicarboxylate (7cc)

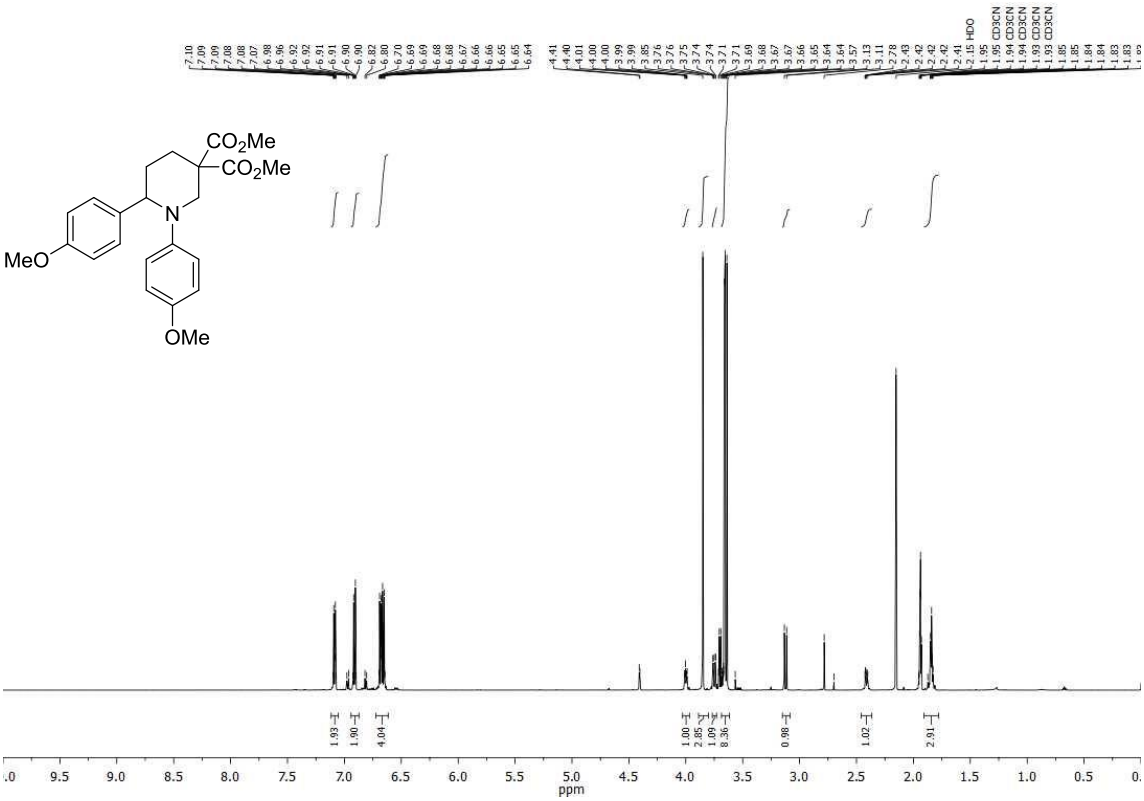


Figure S56: ^{1}H-NMR (500 MHz, CD_3CN).

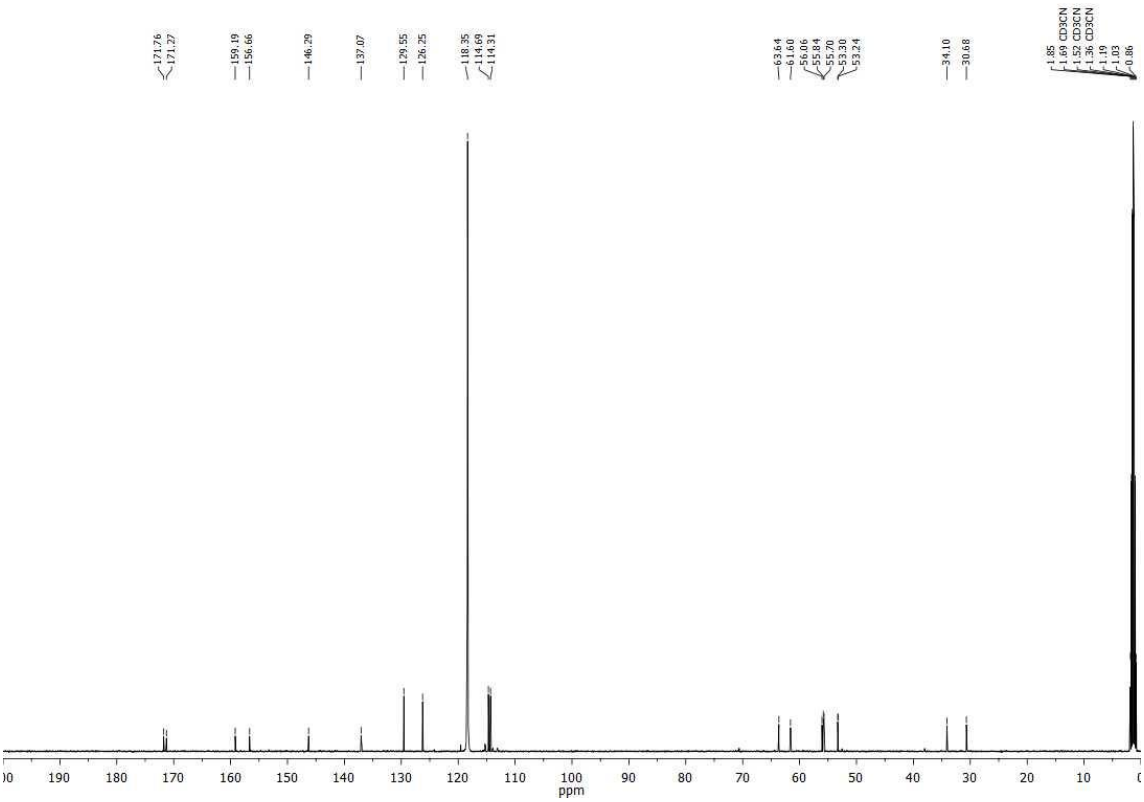


Figure S57: ^{13}C-NMR (125 MHz, CD_3CN).

Dimethyl 6-(4-methoxyphenyl)-1-(p-tolyl)piperidine-3,3-dicarboxylate (7cd)

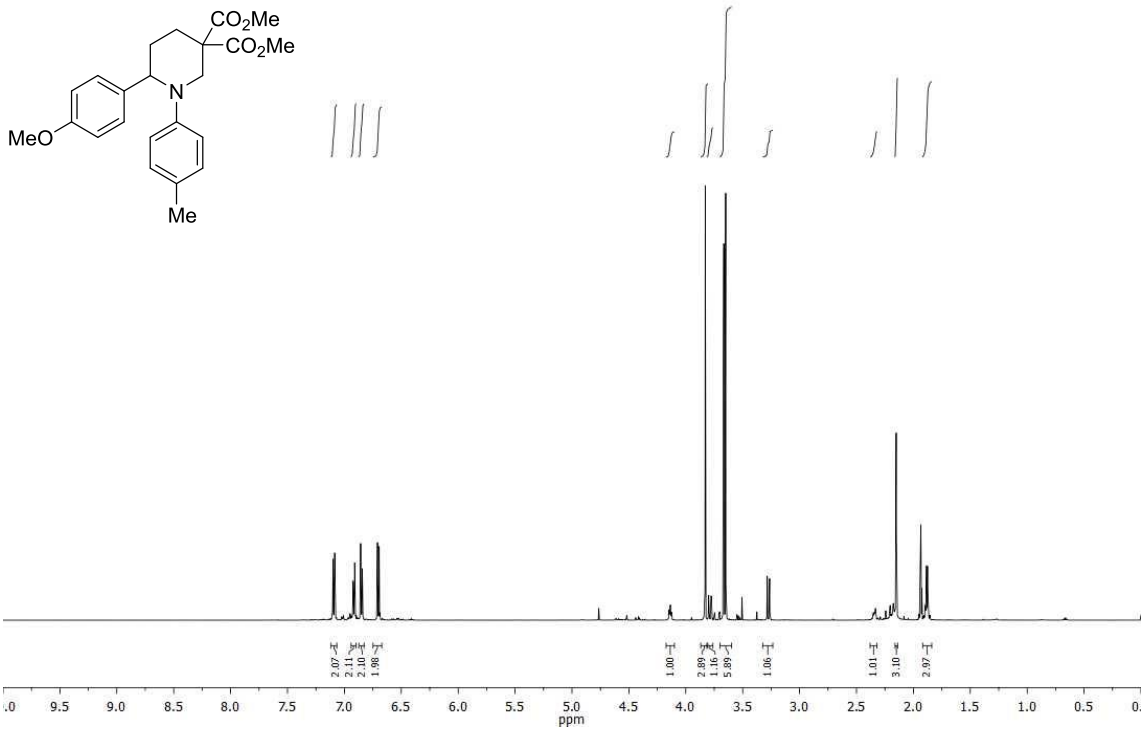


Figure S58: ^{1}H-NMR (500 MHz, CD_3CN).

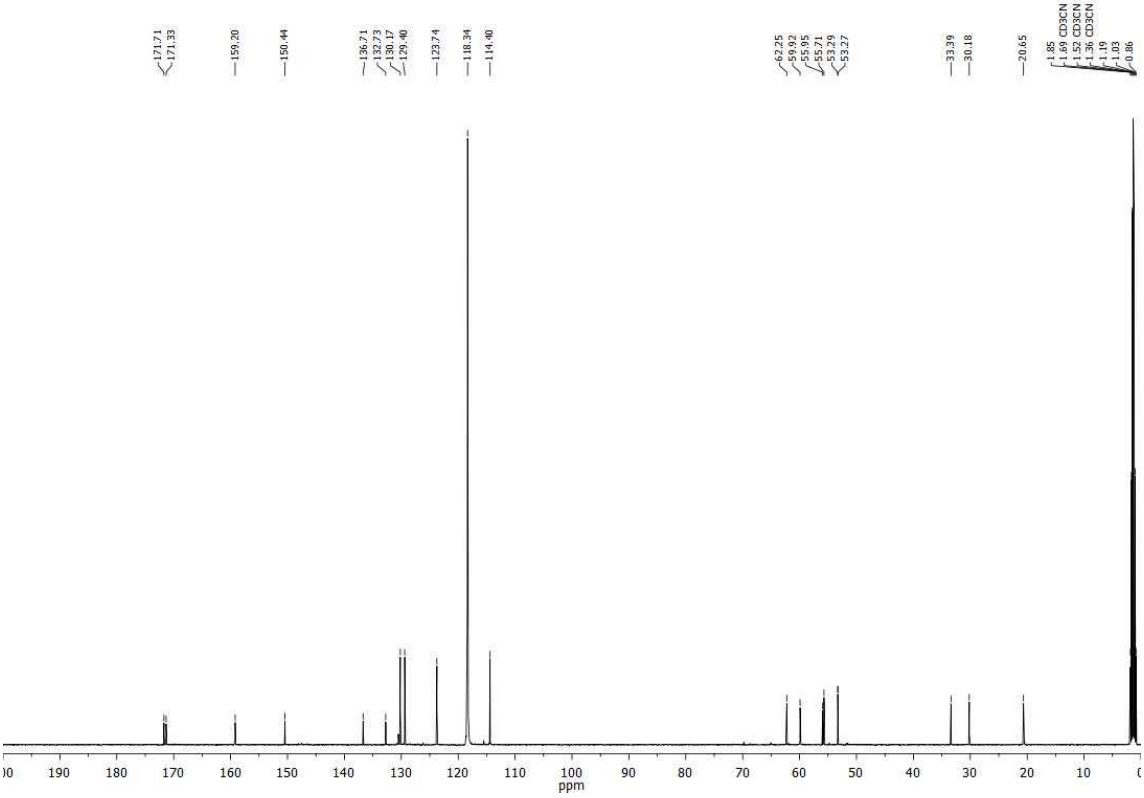


Figure S59: ^{13}C-NMR (125 MHz, CD_3CN).

X-Ray Structure Determination of Compound 5eg

The crystal was mounted in inert oil on a glass fibre and transferred to the cold gas stream of the diffractometer (Oxford Diffraction Xcalibur E using monochromated Mo K_α radiation). Absorption corrections were implemented on the basis of multi-scans. The structures were refined anisotropically on F^2 using the program SHELXL-97.[1] Hydrogens were refined using rigid methyl groups or a riding model starting from calculated positions. *Special features*: The compound crystallizes from dichloromethane/hexane as a dichloromethane solvate; the solvent is well ordered. The sample was not enantiomerically pure and crystallized only by chance in a chiral (Sohncke) space group. The structure was refined as an enantiomeric twin, with a corresponding Flack parameter of 0.37(3).

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-1543675 (**5eg**). Copies of the data can be obtained free of charge from www.ccdc.cam.ac.uk/data_request/cif.

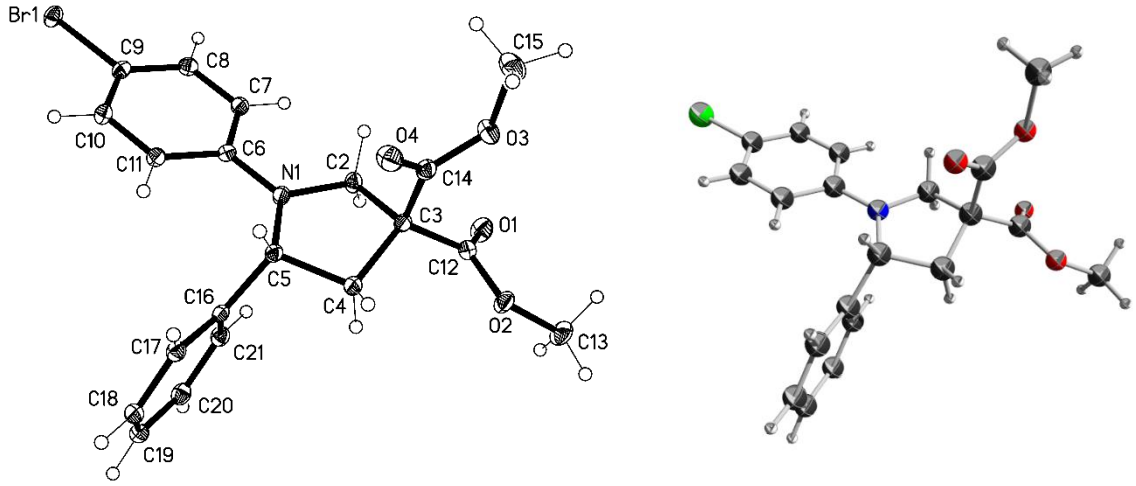


Figure S60: The molecule of compound **5eg** in the crystal. Ellipsoids correspond to 50% probability levels. The dichloromethane molecule, which is connected to **5eg** via a hydrogen bond H···O1 of 2.31 Å, is omitted for clarity. The oxygen atoms are shown in red, nitrogen in blue and bromine in green.

Table S1: Crystal data and structure refinement.

Empirical formula	$C_{20}H_{20}BrNO_4$	
Formula weight	418.28	
Temperature	100(2) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 13.3569(2) Å	α= 90°
	b = 8.15707(12) Å	β= 107.1564(9)°
	c = 17.6178(3) Å	γ = 90°
Volume	1834.10(5) $Å^3$	
Z	4	
Density (calculated)	1.515 Mg/m^3	
Absorption coefficient	3.271 mm^{-1}	
F(000)	856	
Crystal size	0.20 x 0.10 x 0.04 mm^3	
Theta range for data collection	3.46 to 76.20°	
Index ranges	-16<=h<=16, -10<=k<=10, -22<=l<=21	
Reflections collected	54952	
Independent reflections	3838 [R(int) = 0.0589]	
Completeness to theta = 75.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.63491	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3838 / 0 / 237	
Goodness-of-fit on F^2	1.046	
Final R indices [I>2sigma(I)]	R1 = 0.0286, wR2 = 0.0709	
R indices (all data)	R1 = 0.0333, wR2 = 0.0746	
Largest diff. peak and hole	0.539 and -0.621 e.$Å^{-3}$	

Table S2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3). U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	7370.1(12)	3912(2)	4220.2(9)	23.5(3)
C(2)	8335.7(14)	4830(2)	4516.1(11)	23.5(4)
C(3)	8410.8(14)	5848(2)	3795.9(11)	20.8(4)
C(4)	7256.0(14)	6050(2)	3304.5(11)	22.6(4)
C(5)	6704.7(13)	4463(2)	3441.0(10)	19.9(3)
C(6)	7188.4(14)	2532(2)	4608.4(11)	19.7(3)
C(7)	7855.1(14)	2138(2)	5369.8(11)	21.3(4)
C(8)	7673.0(14)	762(2)	5771.7(11)	23.3(4)
C(9)	6830.0(14)	-245(2)	5424.5(11)	21.9(4)
C(10)	6162.5(15)	108(2)	4674.7(11)	22.1(4)
C(11)	6334.3(14)	1489(2)	4271.4(11)	20.6(3)
C(12)	8942.8(14)	7480(2)	4089.7(12)	23.2(4)
C(13)	9197.7(18)	10186(3)	3736.7(15)	36.0(5)
C(14)	9016.4(14)	4866(2)	3347.3(11)	23.3(4)
C(15)	10705.7(17)	4096(3)	3310.7(15)	38.5(5)
C(16)	5583.0(13)	4871(2)	3407.5(11)	19.3(3)
C(17)	4777.0(14)	4553(2)	2717.0(11)	21.4(4)
C(18)	3761.9(14)	5114(2)	2643.7(11)	24.4(4)
C(19)	3556.1(15)	5977(2)	3257.9(12)	26.2(4)
C(20)	4352.4(16)	6262(2)	3953.4(12)	26.6(4)

C(21)	5360.2(15)	5700(2)	4029.2(11)	23.7(4)
O(1)	9427.1(12)	7773.3(18)	4766.8(9)	33.0(3)
O(2)	8782.9(11)	8557.3(16)	3498.6(8)	27.6(3)
O(3)	10045.3(10)	5156.9(18)	3621.6(9)	29.5(3)
O(4)	8625.1(11)	3888.0(19)	2833.6(9)	34.2(3)
Br(1)	6584.0(2)	-2118.1(2)	5988.0(1)	27.0(1)

Table S3: Bond lengths [Å] and angles [°].

N(1)-C(6)	1.376(2)	C(9)-Br(1)	1.9031(18)
N(1)-C(2)	1.449(2)	C(10)-C(11)	1.387(3)
N(1)-C(5)	1.468(2)	C(12)-O(1)	1.201(2)
C(2)-C(3)	1.544(3)	C(12)-O(2)	1.331(2)
C(3)-C(14)	1.516(3)	C(13)-O(2)	1.453(2)
C(3)-C(12)	1.526(2)	C(14)-O(4)	1.204(2)
C(3)-C(4)	1.539(2)	C(14)-O(3)	1.337(2)
C(4)-C(5)	1.543(2)	C(15)-O(3)	1.453(3)
C(5)-C(16)	1.519(2)	C(16)-C(17)	1.391(2)
C(6)-C(11)	1.406(2)	C(16)-C(21)	1.392(3)
C(6)-C(7)	1.411(2)	C(17)-C(18)	1.400(3)
C(7)-C(8)	1.387(3)	C(18)-C(19)	1.385(3)
C(8)-C(9)	1.382(3)	C(19)-C(20)	1.385(3)
C(9)-C(10)	1.388(3)	C(20)-C(21)	1.390(3)

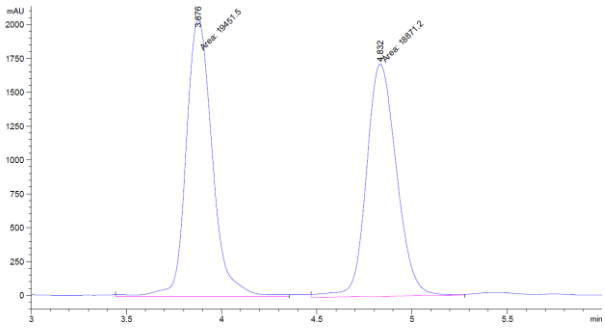
C(6)-N(1)-C(2)	120.85(15)	C(8)-C(9)-Br(1)	119.31(14)
C(6)-N(1)-C(5)	124.63(15)	C(10)-C(9)-Br(1)	120.09(14)
C(2)-N(1)-C(5)	114.05(14)	C(11)-C(10)-C(9)	119.91(17)
N(1)-C(2)-C(3)	104.41(14)	C(10)-C(11)-C(6)	120.76(16)
C(14)-C(3)-C(12)	111.77(15)	O(1)-C(12)-O(2)	124.07(18)
C(14)-C(3)-C(4)	111.32(15)	O(1)-C(12)-C(3)	124.84(18)
C(12)-C(3)-C(4)	112.76(15)	O(2)-C(12)-C(3)	111.07(16)
C(14)-C(3)-C(2)	108.56(15)	O(4)-C(14)-O(3)	124.14(19)
C(12)-C(3)-C(2)	109.10(15)	O(4)-C(14)-C(3)	124.19(17)
C(4)-C(3)-C(2)	102.86(14)	O(3)-C(14)-C(3)	111.58(16)
C(3)-C(4)-C(5)	105.54(14)	C(17)-C(16)-C(21)	119.28(17)
N(1)-C(5)-C(16)	114.93(15)	C(17)-C(16)-C(5)	119.56(16)
N(1)-C(5)-C(4)	102.55(14)	C(21)-C(16)-C(5)	120.88(16)
C(16)-C(5)-C(4)	108.70(14)	C(16)-C(17)-C(18)	119.89(17)
N(1)-C(6)-C(11)	121.69(16)	C(19)-C(18)-C(17)	120.27(17)
N(1)-C(6)-C(7)	120.32(16)	C(20)-C(19)-C(18)	119.93(18)
C(11)-C(6)-C(7)	117.99(17)	C(19)-C(20)-C(21)	119.93(18)
C(8)-C(7)-C(6)	120.90(17)	C(20)-C(21)-C(16)	120.66(17)
C(9)-C(8)-C(7)	119.84(17)	C(12)-O(2)-C(13)	114.74(16)
C(8)-C(9)-C(10)	120.60(17)	C(14)-O(3)-C(15)	115.58(16)

Table S4: Torsion angles [°].

C(6)-N(1)-C(2)-C(3)	160.73(17)	C(8)-C(9)-C(10)-C(11)	-0.6(3)
C(5)-N(1)-C(2)-C(3)	-11.8(2)	Br(1)-C(9)-C(10)-C(11)	178.93(14)
N(1)-C(2)-C(3)-C(14)	-90.98(17)	C(9)-C(10)-C(11)-C(6)	0.9(3)
N(1)-C(2)-C(3)-C(12)	146.99(15)	N(1)-C(6)-C(11)-C(10)	-179.70(17)
N(1)-C(2)-C(3)-C(4)	27.06(19)	C(7)-C(6)-C(11)-C(10)	-0.6(3)
C(14)-C(3)-C(4)-C(5)	83.18(18)	C(14)-C(3)-C(12)-O(1)	-105.0(2)
C(12)-C(3)-C(4)-C(5)	-150.27(16)	C(4)-C(3)-C(12)-O(1)	128.7(2)
C(2)-C(3)-C(4)-C(5)	-32.90(19)	C(2)-C(3)-C(12)-O(1)	15.1(3)
C(6)-N(1)-C(5)-C(16)	61.4(2)	C(14)-C(3)-C(12)-O(2)	76.29(19)
C(2)-N(1)-C(5)-C(16)	-126.47(17)	C(4)-C(3)-C(12)-O(2)	-50.0(2)
C(6)-N(1)-C(5)-C(4)	179.13(17)	C(2)-C(3)-C(12)-O(2)	-163.64(15)
C(2)-N(1)-C(5)-C(4)	-8.7(2)	C(12)-C(3)-C(14)-O(4)	-152.32(19)
C(3)-C(4)-C(5)-N(1)	25.80(19)	C(4)-C(3)-C(14)-O(4)	-25.2(3)
C(3)-C(4)-C(5)-C(16)	147.89(15)	C(2)-C(3)-C(14)-O(4)	87.3(2)
C(2)-N(1)-C(6)-C(11)	-170.36(18)	C(12)-C(3)-C(14)-O(3)	31.0(2)
C(5)-N(1)-C(6)-C(11)	1.3(3)	C(4)-C(3)-C(14)-O(3)	158.11(15)
C(2)-N(1)-C(6)-C(7)	10.6(3)	C(2)-C(3)-C(14)-O(3)	-89.37(18)
C(5)-N(1)-C(6)-C(7)	-177.75(17)	N(1)-C(5)-C(16)-C(17)	-145.69(16)
N(1)-C(6)-C(7)-C(8)	179.19(17)	C(4)-C(5)-C(16)-C(17)	100.08(19)
C(11)-C(6)-C(7)-C(8)	0.1(3)	N(1)-C(5)-C(16)-C(21)	40.4(2)
C(6)-C(7)-C(8)-C(9)	0.2(3)	C(4)-C(5)-C(16)-C(21)	-73.8(2)
C(7)-C(8)-C(9)-C(10)	0.1(3)	C(21)-C(16)-C(17)-C(18)	2.1(3)
C(7)-C(8)-C(9)-Br(1)	-179.45(14)	C(5)-C(16)-C(17)-C(18)	-171.84(16)

C(16)-C(17)-C(18)-C(19)	-0.4(3)	C(5)-C(16)-C(21)-C(20)	171.47(17)
C(17)-C(18)-C(19)-C(20)	-1.2(3)	O(1)-C(12)-O(2)-C(13)	-3.0(3)
C(18)-C(19)-C(20)-C(21)	0.9(3)	C(3)-C(12)-O(2)-C(13)	175.67(16)
C(19)-C(20)-C(21)-C(16)	0.9(3)	O(4)-C(14)-O(3)-C(15)	-5.5(3)
C(17)-C(16)-C(21)-C(20)	-2.4(3)	C(3)-C(14)-O(3)-C(15)	171.22(17)

HPLC Separation



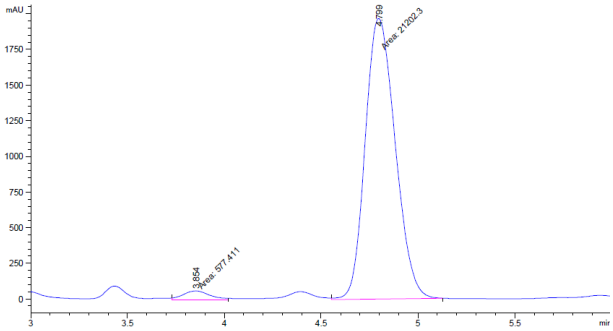
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.876	MM	0.1588	1.94515e4	2040.96497	50.7571
2	4.832	MM	0.1832	1.88712e4	1716.86584	49.2429
Totals :				3.83227e4	3757.83081	

Figure S61: Chromatogram of compound **5aa** (rac).

Column: Chiralpak IG Detection: 254 nm

Mobile Phase: H_2O/MeCN = 70:30 Temperature: 25 °C

Flow Rate: 4.5 ml/min



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.854	MM	0.1589	577.41107	60.54892	2.6511
2	4.799	MM	0.1794	2.12023e4	1969.20410	97.3489
Totals :				2.17797e4	2029.75302	

Figure S62: Chromatogram of compound (*S*)-**5aa**.

Column: Chiralpak IG Detection: 254 nm

Mobile Phase: H_2O/MeCN = 70:30 Temperature: 25 °C

Flow Rate: 4.5 ml/min

References

(1) G. M. Sheldrick, *Acta Cryst*. **2008**, *A64*, 112 and **2015**, *C71*, 3.