Supporting Information

Unusual *anti*-Selective Asymmetric Conjugate Addition of Aldehydes to Nitroalkenes Catalyzed by a Biphenyl-based Chiral Secondary Amine

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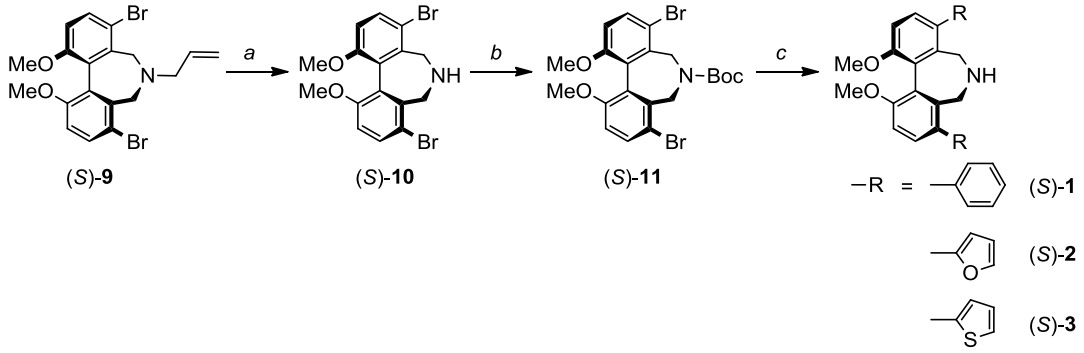
General information

Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer or a Thermo SCIENTIFIC NICOLET iS5. ^{1}H NMR spectra were measured on a JEOL JNM-FX500 spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, m = multiplet, br = broad, and app = apparent), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on a JEOL JNM-FX500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High performance liquid chromatography (HPLC) was performed on Shimadzu 20A instruments using Daicel Chiralpak AD-H, AD-3, IB, IC-3 and Chiralcel OJ-3 4.6 mm x 25 cm column. High-resolution mass spectra (HRMS) were performed on Brucker microTOF. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel 60 (Merck 1.09386.9025, 230-400 mesh).

Dry DMSO was prepared by distillation from CaH_2 under reduced pressure after standing over CaH_2 and stored under molecular sieves 4A. The commercially available aldehydes were distilled and stored under argon atmosphere at –17 °C.

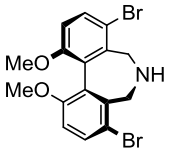
Catalyst (*S*)-**4**[1], (*S*)-**5**[2], allylamine **9**[3] and nitroalkenes[4] were synthesized according to the literature procedures.

Synthesis of catalysts (*S*)-1, (*S*)-2 and (*S*)-3



[a] $Pd(OAc)_2$, PPh_3, NDMBA, CH_2Cl_2, [b] $(Boc)_2O$, Et_3N, DMAP, CH_2Cl_2, [c] $RB(OH)_2$, $Pd(OAc)_2$, $P(oTol)_3$, K_3PO_4, DMF/H_2O; 6N HCl aq, *i*PrOH/EtOAc

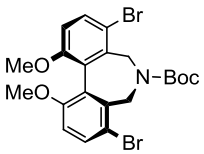
Amine (*S*)-10



(*S*)-**10**

A mixture of (*S*)-**9** (500 mg, 1.10 mmol), 1,3-dimethylbarbituric acid (NDMBA) (515 mg, 3.30 mmol), $Pd(OAc)_2$ (24.7 mg, 0.110 mmol) and PPh_3 (72.0 mg, 0.275 mmol) in CH_2Cl_2 (5 mL) was stirred at 30 °C for 18 h under argon atmosphere. After cooling to room temperature, the reaction mixture was poured into 1N NaOH aq. and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 2.5/1) to afford (*S*)-**10** (400 mg, 0.968 mmol, 88% yield); $[\alpha]_D^{31}$ 185.6 (*c* = 0.30, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.8 Hz, Ar-H), 6.84 (2H, d, *J* = 8.8 Hz, Ar-H), 4.26 (2H, d, *J* = 12.8 Hz, -CHH-), 3.79 (6H, s, -OCH_3), 3.16 (2H, d, *J* = 12.8 Hz, -CHH-); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6, 136.3, 133.1, 127.0, 114.3, 111.7, 55.9, 47.3; IR (neat) 3319, 2933, 2834, 1560, 1464, 1276, 1083, 923, 804, 735, 695 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{16}H_{16}Br_2NO_2$: 411.9548 ($[M + H]^+$), Found: 411.9550 ($[M + H]^+$)

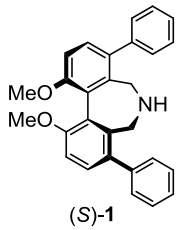
***N*-Boc-amine (*S*)-11**



(*S*)-**11**

To a solution of (*S*)-**10** (400 mg, 0.968 mmol) and triethylamine (337 μL, 2.42 mmol) in CH_2Cl_2 (10 mL) were added $(Boc)_2O$ (528 μL, 2.42 mmol) and DMAP (11.8 mg, 0.0968 mmol) at room temperature. The mixture was stirred at room temperature for 22 h under argon atmosphere. The reaction mixture was poured into brine and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 5/1) to afford (*S*)-**11** (415 mg, 0.809 mmol, 84% yield); $[\alpha]_D^{30}$ −127.0 (*c* = 1.50, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (2H, d, *J* = 9.0 Hz, Ar-H), 6.85, (2H, d, *J* = 9.0 Hz, Ar-H), 5.46 (2H, app dd, *J* = 26.5, 13.0 Hz, -C<u>H</u>H-), 3.80 (6H, s, -OCH_3), 3.33 (2H, app dd, *J* = 35.4, 13.0 Hz, -CH<u>H</u>-), 1.53 (9H, s, -$C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 153.6, 134.8, 133.3, 127.2, 114.8, 112.2, 80.1, 56.0 , 46.2 , 28.4; IR 2974, 2934, 2836, 1685, 1463, 1402, 1268, 1161, 1103, 932, 805, 735, 602 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{21}H_{23}Br_2NNaO_4$: 533.9886 ([M + Na]$^+$), Found: 533.9847 ([M + Na]$^+$)

Amine (*S*)-1



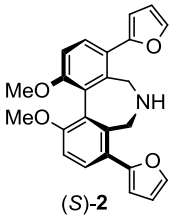
(*S*)-**1**

A mixture of (*S*)-**11** (50.0 mg, 0.0974 mmol), phenylboronic acid (47.5 mg, 0.390 mmol), $Pd(OAc)_2$ (2.2 mg, 0.00974 mmol), P(*o*Tol)$_3$ (11.9 mg, 0.0390 mmol) and K_3PO_4 (83.0 mg, 0.390 mmol) in DMF (910 μL) and H_2O (90 μL) was degassed and stirred at 100 °C for 9 h under argon atmosphere. The reaction mixture was poured into brine and extracted with EtOAc. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was roughly purified by flash column chromatography on silica gel (hexane/EtOAc = 6/1), which was used for the next step without further purification.

To a solution of the roughly purified product in isopropyl alcohol (1.5 mL) and EtOAc (1.5 mL) was added 6N HCl aq. (1 mL) at room temperature. The mixture was stirred at 70 °C for 30 min. The reaction mixture was poured into saturated $NaHCO_3$ aq. and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (hexane/EtOAc = 3/1) to afford (*S*)-**1** (39.7 mg, 0.0974 mmol, quantitative yield (two steps)) ; $[\alpha]_D^{27}$ 249.1 (*c* = 0.95, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.42 (4H, m, Ar-H), 7.42-7.35 (6H, m, Ar-H), 7.34-7.30 (2H, m, Ar-H), 7.04 (2H, d, *J* = 8.5 Hz, Ar-H), 3.90 (6H, s, -OCH_3), 3.85 (2H, d, *J* = 12.5 Hz, -C<u>H</u>H-), 3.31 (2H, d, *J* = 12.5 Hz, -CH<u>H</u>-), 1.83 (1H, br s, -NH-); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 141.3, 135.4, 134.0, 130.1, 129.6, 128.0, 126.6, 126.0, 109.8, 55.9, 44.7; IR (neat) 3321, 2931, 2833, 2245, 1583, 1475, 1269, 1083, 908, 813,

763, 731, 704 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{28}H_{26}NO_2$: 408.1958 ($[M + H]^+$), Found: 408.1932 ($[M + H]^+$)

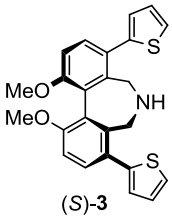
Amine (*S*)-2



(*S*)-**2**

The same procedure described for the preparation of (*S*)-**1** with 2-furylboronic acid (43.6 mg, 0.390 mmol) was applied to the synthesis of (*S*)-**2** (33.3 mg, 0.0859 mmol, 88% yield (two steps)); $[\alpha]_D^{30}$ 363.5 (*c* = 0.30, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.8 Hz, Ar-H), 7.48 (2H, dd, *J* = 1.8, 0.6 Hz, Ar-H), 7.01 (2H, d, *J* = 8.8 Hz, Ar-H), 6.51 (2H, dd, *J* = 3.3, 0.6 Hz, Ar-H), 6.47 (2H, dd, *J* = 3.3, 1.8 Hz, Ar-H), 4.15 (2H, d, *J* = 12.5 Hz, -CHH-), 3.86 (6H, s, $-OCH_3$), 3.28 (2H, d, *J* = 12.5 Hz, -CHH-), 2.09 (1H, br s, -NH-); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 153.9, 141.9, 135.5, 130.0, 126.2, 123.0, 111.1, 110.1, 107.6, 55.8, 44.9; IR (neat) 2930, 2835, 1597, 1580, 1504, 1472, 1437, 1271, 1084, 1009, 908, 808, 729, 700 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{24}H_{22}NO_4$: 388.1543 ($[M + H]^+$), Found: 388.1545 ($[M + H]^+$)

Amine (*S*)-3



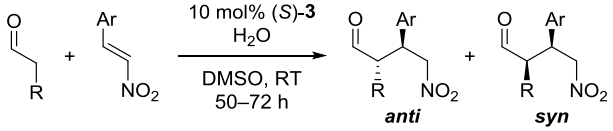
(*S*)-**3**

The same procedure described for the preparation of (*S*)-**1** with 2-thienylboronic acid (49.9 mg, 0.390 mmol) was applied to the synthesis of (*S*)-**3** (40.4 mg, 0.0964 mmol, 99% yield (two steps)); $[\alpha]_D^{31}$ 182.7 (*c* = 1.78, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (2H, d, *J* = 8.5 Hz, Ar-H), 7.31 (2H, dd, *J* = 5.1, 1.0 Hz, Ar-H), 7.13 (2H, dd, *J* = 3.4, 1.0 Hz, Ar-H), 7.07 (2H, dd, *J* = 5.1, 3.4 Hz, Ar-H), 7.00 (2H, d, *J* = 8.5 Hz, Ar-H), 4.06 (2H, d, *J* = 12.5 Hz, -CHH-), 3.88 (6H, s, $-OCH_3$), 3.27 (2H, d, *J* = 12.5 Hz, -CHH-); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.1, 142.3, 136.0, 131.9, 127.1, 126.7, 126.2, 126.0, 125.0, 109.9, 55.8 , 44.6; IR (neat) 2934, 2833, 1584, 1481, 1462, 1269, 1084, 908, 812, 731, 696 cm^{-1}; HRMS (ESI-TOF) Calcd. for $C_{24}H_{22}NO_2S_2$: 420.1086 ($[M + H]^+$), Found: 420.1083 ($[M + H]^+$)

Typical procedure for conjugate addition of propanal to β-nitrostyrenes

A frame-dried two-neck round-bottom flask equipped with a magnetic stirrer bar was charged with β-nitrostyrene (14.9 mg, 0.1 mmol), (*S*)-**3** (4.2 mg, 0.01 mmol), DMSO (200 μL), H_2O (1.8 μL) and propanal (72 μL, 1 mmol) under argon atmosphere, which was capped with a glass-stopper. After stirring for 72 h, the reaction mixture was directly purified by column chromatography on silica gel (hexane/EtOAc =4/1) to afford 2-methyl-4-nitro-3-phenylbutanal (17.1 mg, 0.826 mmol, 83% yield).

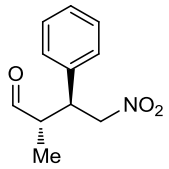
Table 3. Conjugate addition to various nitrostyrenes catalyzed by (*S*)-**3**.[a]



Entry	R, Ar	Time [h]	Yield [%][b]	*anti*/*syn*[c]	ee (*anti*/*syn*) [%][d]
1	Me, Ph	72	83	3.3/1	96/64
2	Me, 4-Me-C_6H_4	64	86	4.1/1	96/46
3	Me, 4-MeO-C_6H_4	72	88	2.8/1	93/45
4	Me, 4-Br-C_6H_4	50	73	3.9/1	97/73
5	Me, 4-F-C_6H_4	72	95	3.3/1	96/72
6	Me, 3-F-C_6H_4	54	95	2.5/1	91/75
7	Me, 2-F-C_6H_4	54	99	2.4/1	99/77
8	Me, 3-furanyl	72	93	3.2/1	86/39
9	Me, 2-thiophenyl	60	84	3.1/1	86/63
10[e]	Et, Ph	72	85	1.4/1	91/38
11	*i*-Pr, Ph	72	n.r.	-	-

[a] The reaction of propanal (1.0 mmol) with nitrostyrene (0.1 mmol) was carried out in the presence of a catalyst (0.01 mmol) and H_2O (0.1 mmol) in DMSO (0.2 mL) at room temperature. [b] Isolated yield. [c] Determined by ^{1}H-NMR. [d] Determined by HPLC using chiral column. [e] Use of 20 mol% of (*S*)-**3**.

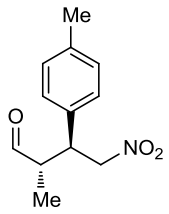
(2*S*,3*S*)-2-Methyl-3-phenyl-4-nitrobutanal (Table 3, entry 1)



Spectroscopic data of the title compound were in agreement with the reported data.[5]

HPLC analysis: Daicel Chiralpak IB, hexane/*i*-PrOH = 10/1, flow rate = 1.0 mL/min, λ = 210 nm, retention time; t_R(*syn* minor) = 15.2 min, t_R(*anti* minor) = 17.9 min, t_R(*syn* major) = 20.1 min, t_R(*anti* major) = 23.1 min.

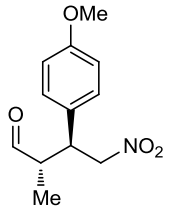
(2*S*,3*S*)-2-Methyl-3-(4-methylphenyl)-4-nitrobutanal (Table 3, entry 2)



Spectroscopic data of the title compound were in agreement with the reported data.[5]

HPLC analysis: Daicel Chiralcel OJ-3, hexane/*i*-PrOH = 10/1, flow rate = 0.7 mL/min, λ = 210 nm, retention time; t_R(*syn* minor) = 40.8 min, t_R(*syn* major) = 44.5 min, t_R(*anti* minor) = 53.0 min, t_R(*anti* major) = 55.7 min.

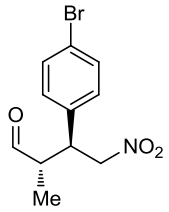
(2*S*,3*S*)-3-(4-Methoxylphenyl)-2-methyl-4-nitrobutanal (Table 3, entry 3)



Spectroscopic data of the title compound were in agreement with the reported data.[5]

HPLC analysis: Daicel Chiralcel OJ-3, hexane/*i*-PrOH = 4/1, flow rate = 0.75 mL/min, λ = 210 nm, retention time; t_R(*syn* minor) = 50.9 min, t_R(*syn* major) = 53.3 min, t_R(*anti* major) = 59.4 min, t_R(*anti* minor) = 62.8 min.

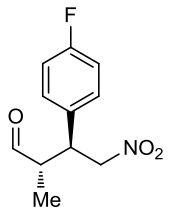
(2*S*,3*S*)-3-(4-Bromophenyl)-2-methyl-4-nitrobutanal (Table 3, entry 4)



Spectroscopic data of the title compound were in agreement with the reported data.[5]

HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 50/1, flow rate = 0.75 mL/min, λ = 210 nm, retention time; t_R(*syn* major) = 67.8 min, t_R(*anti* minor) = 80.6 min, t_R(*anti* major) = 85.8 min, t_R(*syn* minor) = 96.1 min.

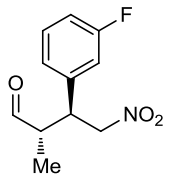
(2*S*,3*S*)-3-(4-Fluorophenyl)-2-methyl-4-nitrobutanal (Table 3, entry 5)



Spectroscopic data of the title compound were in agreement with the reported data.[5]

HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 50/1, flow rate = 0.75 mL/min, λ = 210 nm, retention time; t_R(*syn* major) = 49.8 min, t_R(*anti* major) = 62.1 min, t_R(*anti* minor) = 70.0 min, t_R(*syn* minor) = 73.7 min.

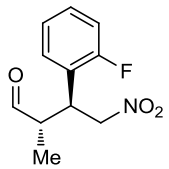
(2*S*,3*S*)-3-(3-Fluorophenyl)-2-methyl-4-nitrobutanal (Table 3, entry 6)



The title compound was obtained as inseparable mixture of two diastreomers.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (1H, d, J = 1.0 Hz, -CHO), 7.35-7.28 (1H, m, Ar-H), 7.02-6.88 (3H, m, Ar-H), 4.82-4.63 (2H, m, -CH_2NO_2), 3.89-3.78 (1H, m, -CHAr-), 2.85-2.73 (1H, m, -C<u>H</u>(CHO)-), 1.23 (3H, d, J = 7.4 Hz, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8 , 163.0 (d, $J_{C\text{-}F}$ = 248 Hz), 139.2 (d, $J_{C\text{-}F}$ = 6.0 Hz), 130.7, 123.8, 115.3 (d, $J_{C\text{-}F}$ = 21.5 Hz), 115.2 (d, $J_{C\text{-}F}$ = 20.4 Hz), 77.8, 48.6, 44.3, 11.6**;** HRMS (ESI-TOF) Calcd. for $C_{12}H_{16}FNNaO_4$: 280.0956 ([M + MeOH + Na]$^+$), Found: 280.0950 ([M + MeOH + Na]$^+$) (observed as hemiacetal form); HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 10/1, flow rate = 0.5 mL/min, λ = 210 nm, retention time; t_R(*anti* major) = 47.4 min, t_R(*syn* minor) = 71.5 min, t_R(*syn* major) = 78.5 min, t_R(*anti* minor) = 114.8 min.

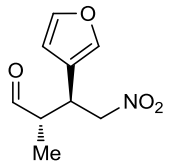
(2*S*,3*S*)-3-(2-Fluorophenyl)-2-methyl-4-nitrobutanal (Table 3, entry 7)



Spectroscopic data of the title compound were in agreement with the reported data.[5]

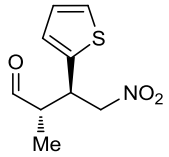
HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 80/1, flow rate = 0.85 mL/min, λ = 210 nm, retention time; t_R(*syn* major) = 38.6 min, t_R(*syn* minor) = 45.4 min, t_R(*anti* major) = 47.6 min, t_R(*anti* minor) = 61.1 min.

(2*S*,3*S*)-3-Furan-3-yl-2-methyl-4-nitrobutanal (Table 3, entry 8)



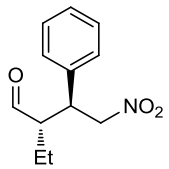
The title compound was obtained as inseparable mixture of two diastreomers.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (1H, d, J = 1.5 Hz, -CHO), 7.40 (1H, app s, Ar-H), 7.34 (1H, app s, Ar-H), 6.29 (1H, app s, Ar-H), 4.73 (1H, dd, J = 12.8, 6.0 Hz, -C<u>H</u>HNO$_2$), 4.66 (1H, dd, J =12.8, 9.6 Hz, -CH<u>H</u>NO$_2$), 3.79-3.74 (1H, m, -CHAr-), 2.77-2.67 (1H, m, -C<u>H</u>(CHO)-), 1.23 (3H, d, J = 7.4 Hz, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 143.9, 140.6, 120.8, 109.6, 77.4, 47.7, 36.0, 11.8; HRMS (ESI-TOF) Calcd. for $C_{10}H_{15}NNaO_5$: 252.0842 ([M + MeOH + Na]$^+$), Found: 252.0842 ([M + MeOH + Na]$^+$) (observed as hemiacetal form); HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 40/1, flow rate = 0.75 mL/min, λ = 210 nm, retention time; t_R(*syn* major) = 30.3 min, t_R(*anti* minor) = 32.6 min, t_R(*anti* major) = 34.5 min, t_R(*syn* minor) = 38.4 min.

(2*S*,3*S*)-2-Methyl-4-nitro-3-thiophen-2-ylbutanal (Table 3, entry 9)



The title compound was obtained as inseparable mixture of two diastreomers.
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62 (1H, d, J = 1.5 Hz, -CHO), 7.24 (1H, d, J = 5.1 Hz, Ar-H), 6.95 (1H, dd, J = 5.1, 3.1 Hz, Ar-H), 6.92 (1H, d, J = 3.1 Hz, Ar-H), 4.80 (1H, dd, J = 13.0, 6.0 Hz, -C<u>H</u>HNO$_2$), 4.74 (1H, dd, J = 13.0, 8.8 Hz, -CH<u>H</u>NO$_2$), 4.20-4.14 (1H, m, -CHAr-), 2.87-2.75 (1H, m, -C<u>H</u>(CHO)-), 1.26 (3H, d, J = 7.4 Hz, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.0, 139.2, 127.2, 126.8, 125.4, 78.0, 48.9, 40.1, 11.8; HRMS (ESI-TOF) Calcd. for $C_{10}H_{15}NNaO_4S$: 268.0614 ([M + MeOH + Na]$^+$), Found: 268.0601 ([M + MeOH + Na]$^+$) (observed as hemiacetal form); HPLC analysis: Daicel Chiralpak AD-3, hexane/*i*-PrOH = 100/1, flow rate = 0.85 mL/min, λ = 210 nm, retention time; t_R(*syn* major) = 63.4 min, t_R(*anti* major) = 69.2 min, t_R(*anti* minor) = 80.6 min, t_R(*syn* minor) = 87.4 min.

(2*S*,3*S*)-2-Ethyl-4-nitro-3-phenylbutanal (Table 3, entry 10)



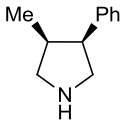
Spectroscopic data of the title compound were in agreement with the reported data.[5]

HPLC analysis: Daicel Chiralpak AD-H, hexane/*i*-PrOH = 200/1, flow rate = 0.9 mL/min, λ = 210 nm, retention time; t_R(*syn* major) = 44.5 min, t_R(*anti* major) = 52.4 min, t_R(*anti* minor) = 63.4 min, t_R(*syn* minor) = 66.2 min.

Synthesis of (3*S*,4*R*)-3-methyl-4-phenylpyrrolidine 8[6]

A round-bottom flask equipped with a magnetic stirrer bar was charged with 2-methyl-4-nitro-3-phenylbutanal **7** (11.0 mg, 0.0531 mmol, *anti*/*syn* = 3.3:1), AcOH (500 μL) and H_2O (500 μL). To the mixture was slowly added Zn (104 mg, 1.59 mmol) at 0 °C. After stirring for 21 h at room temperature, the reaction mixture was poured into 1N NaOH aq. and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated to afford pure 3-methyl-4-phenylpyrrolidine **8** (8.5 mg, 0.0525 mmol, 99% yield, *cis*/*trans* = 3.0:1). The enantiomeric excess was determined after *N*-tosylation. HPLC analysis: Daicel Chiralpak AD-3, hexane/EtOH = 10/1, flow rate = 0.70 mL/min, λ = 210 nm, retention time; t_R(*trans* major) = 21.8 min, t_R(*cis* minor) = 27.7 min, t_R(*trans* minor) = 29.5 min, t_R(*cis* major) = 37.1 min.

(3*S*,4*R*)-3-Methyl-4-phenylpyrrolidine 8



The title compound was obtained as inseparable mixture of two diastereomers.

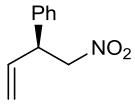
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.28 (2H, m, Ar-H), 7.24-7.21 (1H, m, Ar-H), 7.21-7.17 (2H, m, Ar-H), 3.40 (1H, dd, *J* = 10.5, 7.5 Hz, -CHHNH-), 3.32 (1H, dd, *J* = 15.0, 7.5 Hz, -CHHNH-), 3.26 (1H, dd, *J* = 11.2, 7.5 Hz, -NHCHH-), 3.22 (1H, dd, *J* = 10.3, 7.5 Hz, -NHCHH-), 2.71-2.64 (1H, m, -CHPh-), 2.49-2.40 (1H, m, -CHMe-), 0.65 (3H, d, *J* = 7.1 Hz, $-CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.2, 128.5, 128.1, 126.1, 54.1, 51.3, 48.9, 38.2, 14.8; HRMS (ESI-TOF) Calcd. for $C_{11}H_{16}N$: 162.1283 ($[M + H]^+$), Found: 162.1239 ($[M + H]^+$)

Synthesis of (*S*)-4-nitro-3-phenyl-1-butene 12[7]

A round-bottom flask equipped with a magnetic stirrer bar was charged with 2-methyl-4-nitro-3-phenylbutanal **7** (40.3 mg, 0.195 mmol), cyclohexane (2 mL), activated molecular sieves 4A (57 mg) and $Pd(OAc)_2$ (11.0 mg, 0.0488 mmol) under argon atmosphere at room temperature. After stirring for 24 h at 130 °C, the reaction mixture was filtered through short silicagel-pad and concentrated. The residue was purified by flash column chromatography on silica gel

(hexane/EtOAc = 40/1) to afford (*S*)-4-nitro-3-phenyl-1-butene **12** (30.0 mg, 0.169 mmol, 87% yield).

(*S*)-4-Nitro-3-phenyl-1-butene 12

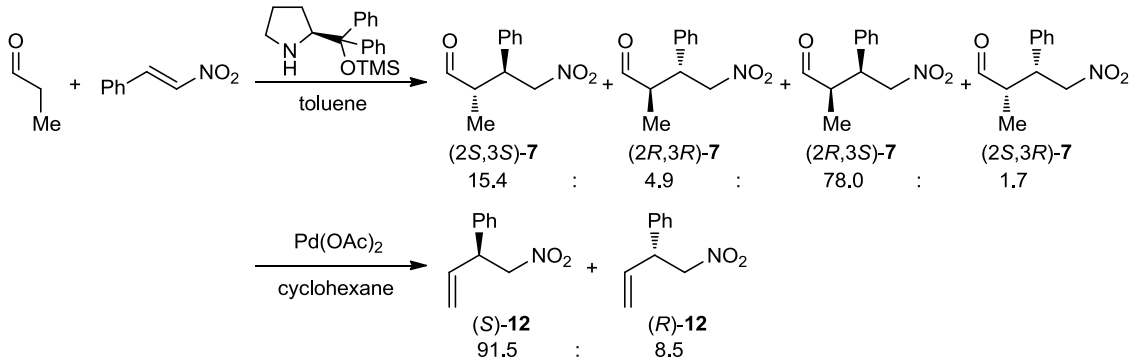


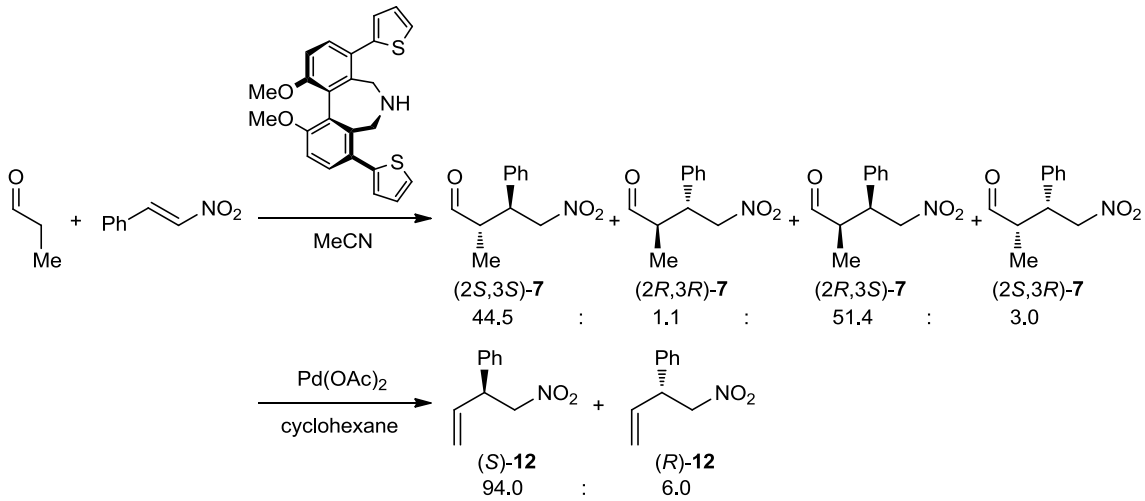
$[\alpha]_D^{25}$ –0.85 (*c* = 0.50, $CHCl_3$, 88% ee); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (2H, app t, *J* = 7.4 Hz, Ar-H), 7.29 (1H, d, *J* = 7.4 Hz, Ar-H), 7.22 (2H, app t, *J* = 7.4 Hz, Ar-H), 5.99 (1H, ddd, *J* = 17.0, 10.5, 7.7 Hz, H_2C=C<u>H</u>-), 5.23 (1H, d, *J* = 10.5 Hz, <u>H</u>HC=CH-), 5.19 (1H, d, *J* = 17.0 Hz, H<u>H</u>C=CH-), 4.69 (1H, dd, *J* = 12.2, 8.8 Hz, -C<u>H</u>HNO_2), 4.63 (1H, dd, *J* = 12.2, 7.4 Hz, -CH<u>H</u>NO_2), 4.21 (1H, app q, *J* = 7.7 Hz, -CHPh-); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 135.8, 129.1, 127.8, 127.6, 117.8, 79.5, 47.8; IR (neat) 2365, 1635, 1506, 1376, 1260, 926, 699, 580 cm^{-1}; HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 50/1, flow rate = 0.75 mL/min, λ = 210 nm, retention time; t_R(major) = 13.8 min, t_R(minor) = 14.6 min.

Determination of absolute configuration

The absolute configuration of the *syn*-conjugate adduct, which was obtained from (*S*)-**3** catalyzed reaction between propanal and β-nitrostyrene, was determined to be (2*R*,3*S*) by comparison of the HPLC retention times with those obtained from the (*S*)-diphenylprolinol silyl ether catalyzed reaction.[8]

The absolute configuration of the *anti*-conjugate adduct, which was obtained from (*S*)-**3** catalyzed reaction between propanal and β-nitrostyrene, was determined to be (2*S*,3*S*) by converting to nitroethene **12**[7] and determining the absolute configuration at the phenyl-bearing stereocenter to be *S*.





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7 A. Modak, A. Deb, T. Patra, S. Rana, S. Maity and D. Maiti, *Chem. Commun.*, 2012, **48**, 4253-4255.
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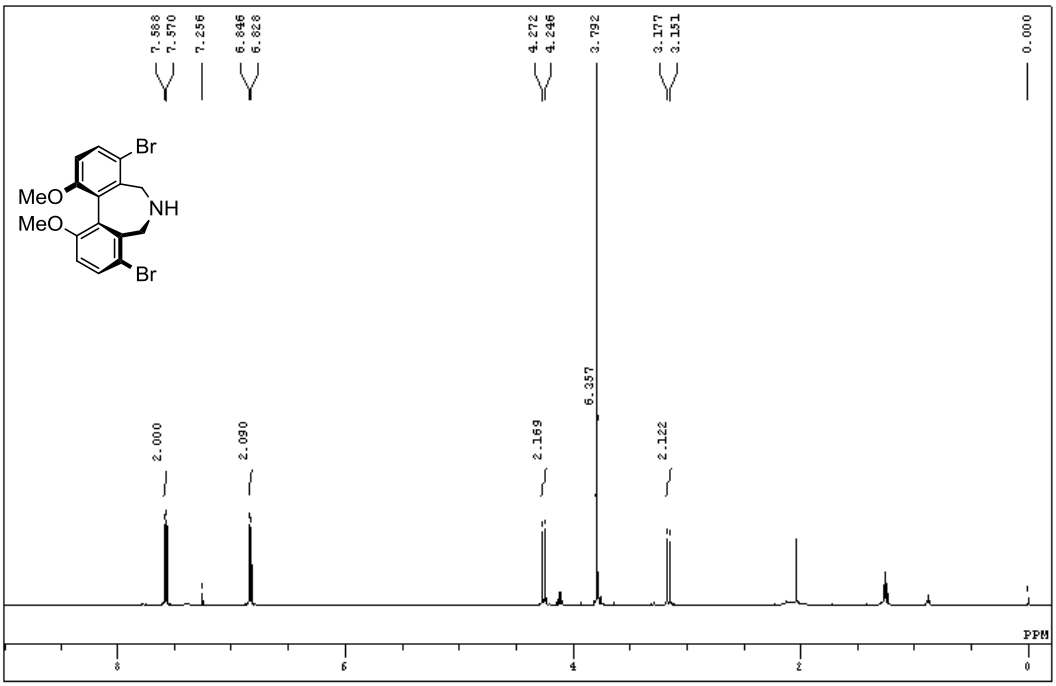
Amine (*S*)-10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6.828
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4.246
3.792
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3.151
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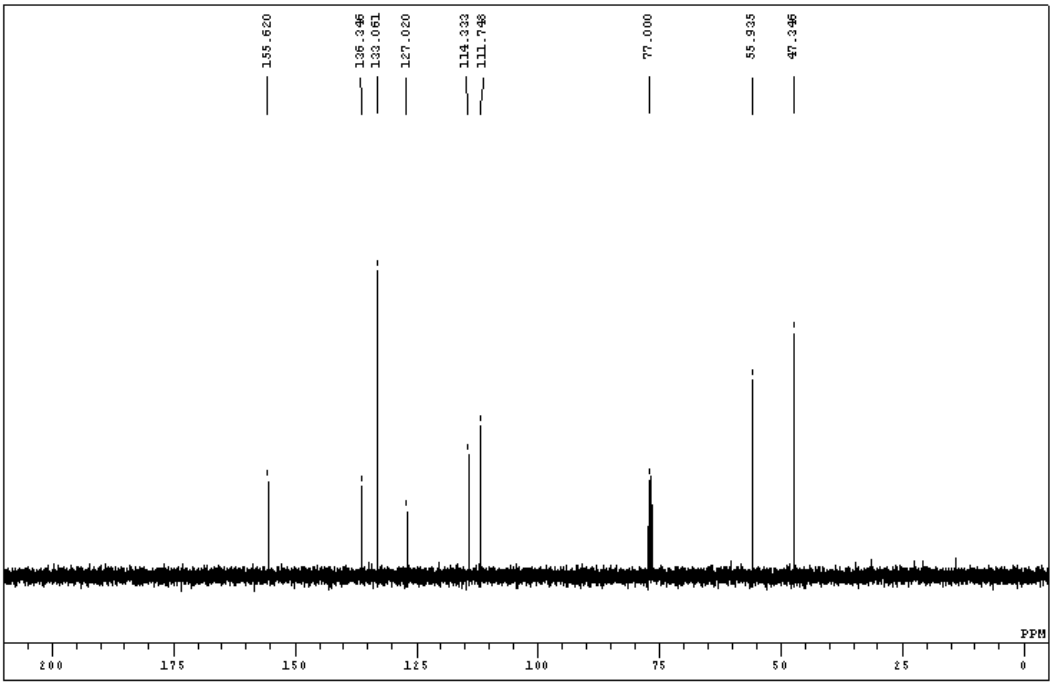
MeO
MeO
NH
Br
6.357
2.000
2.090
2.169
2.122
PPM
8
6
4
2
0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127.020
114.333
111.748
77.000
55.935
47.346
PPM
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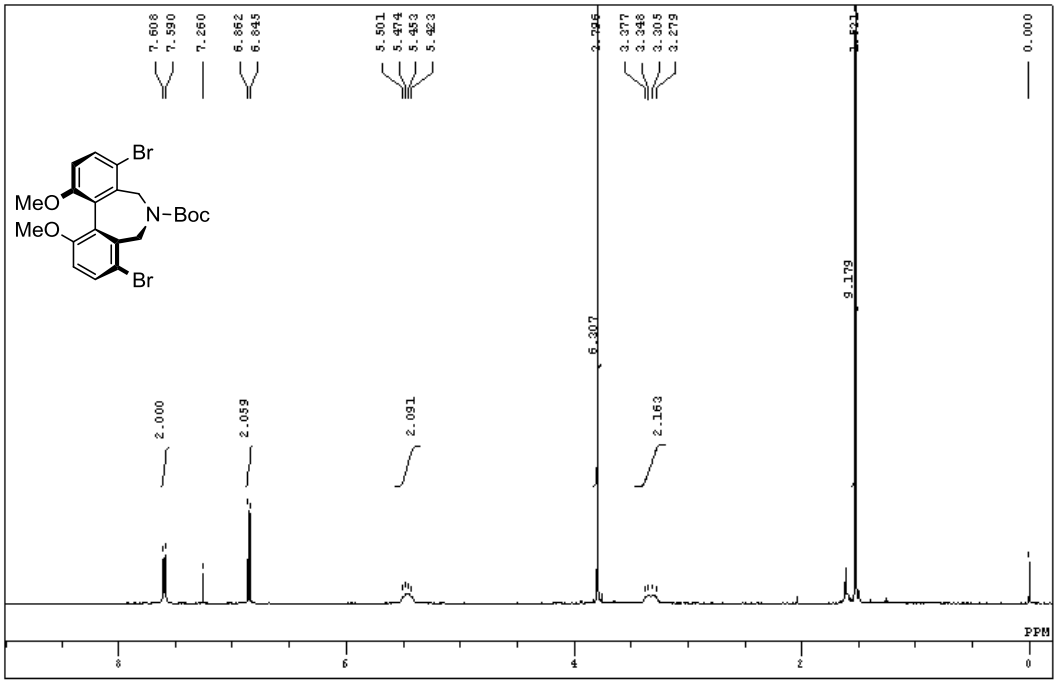
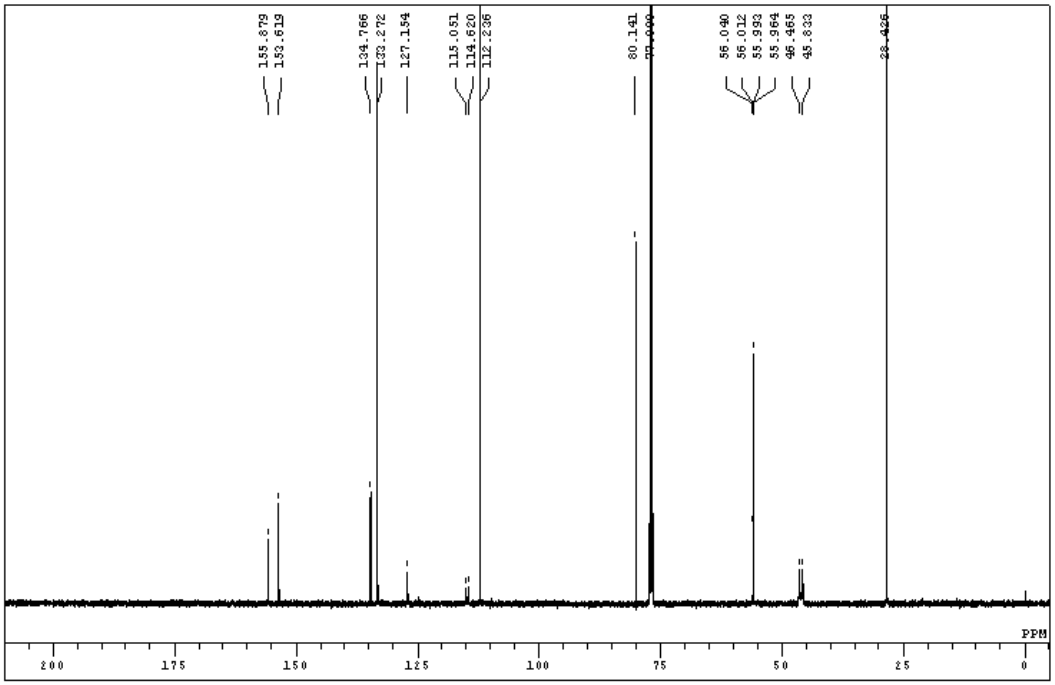
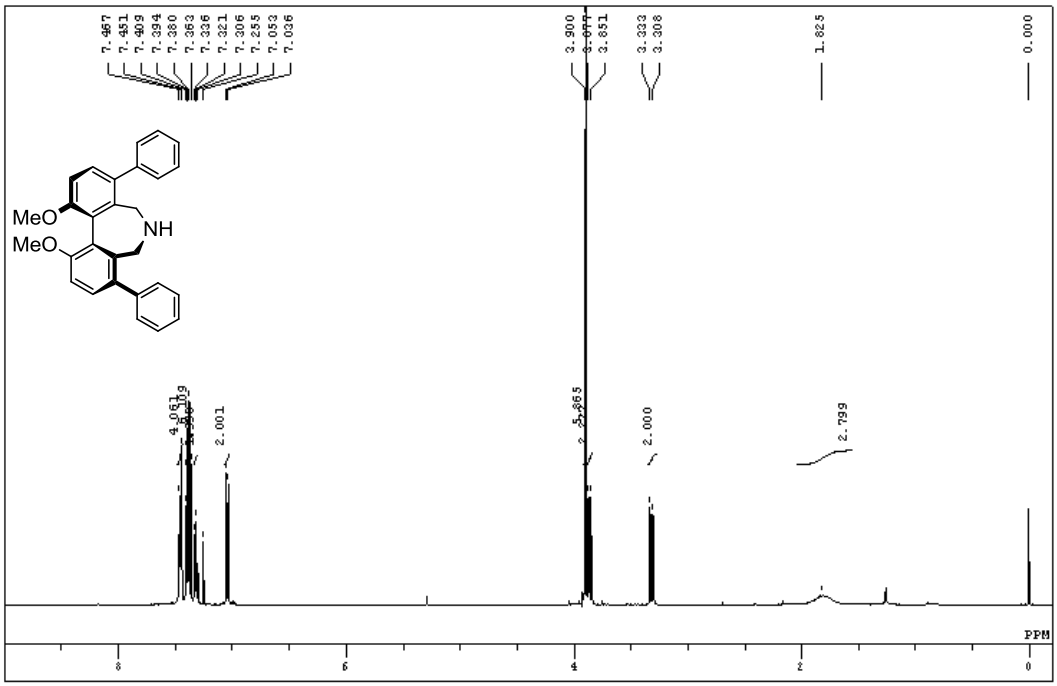
175
150
125
100
75
50
25
0

***N*-Boc-amine (*S*)-11**





Amine (*S*)-1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7.255
7.053
7.036
3.900
3.877
3.851
3.333
3.308
1.825
0.000
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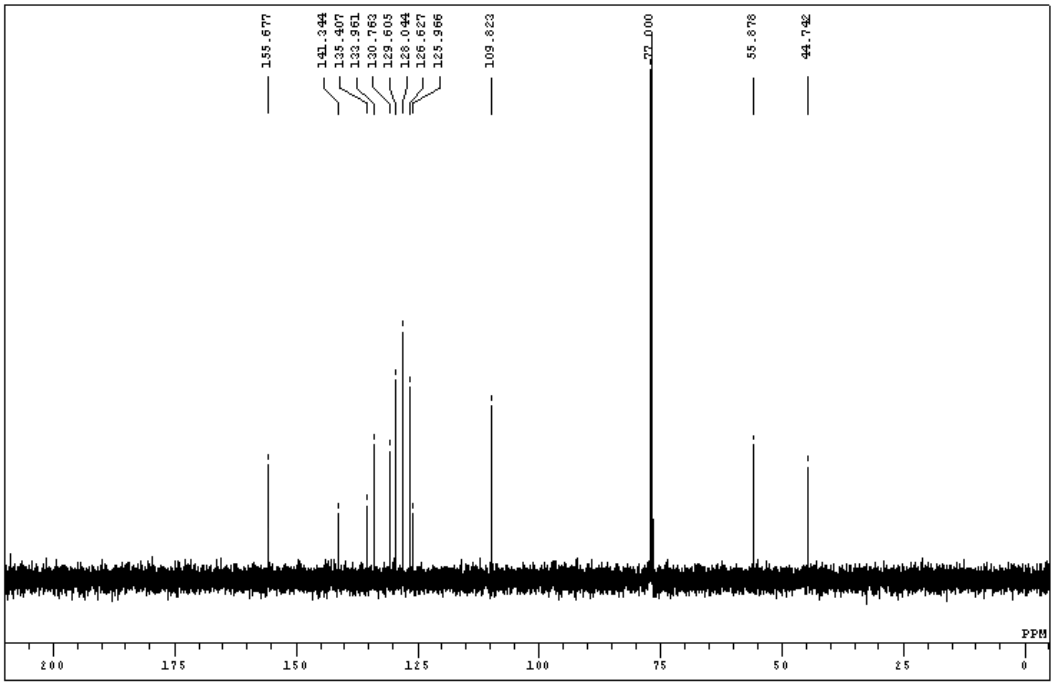
MeO
NH
2.001
5.865
2.000
2.799
PPM
8
6
4
2
0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129.605
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126.627
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44.742
PPM
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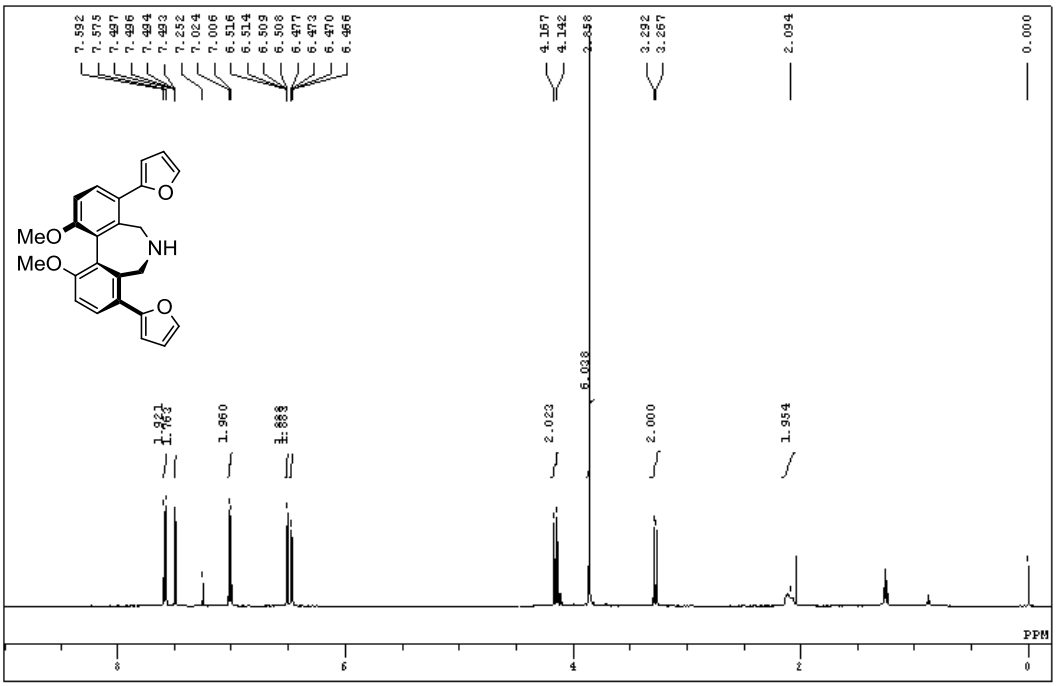
150
125
100
75
50
25
0

Amine (*S*)-2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6.514
6.509
6.508
6.477
6.473
6.470
6.466
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4.142
3.258
3.232
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NH
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O
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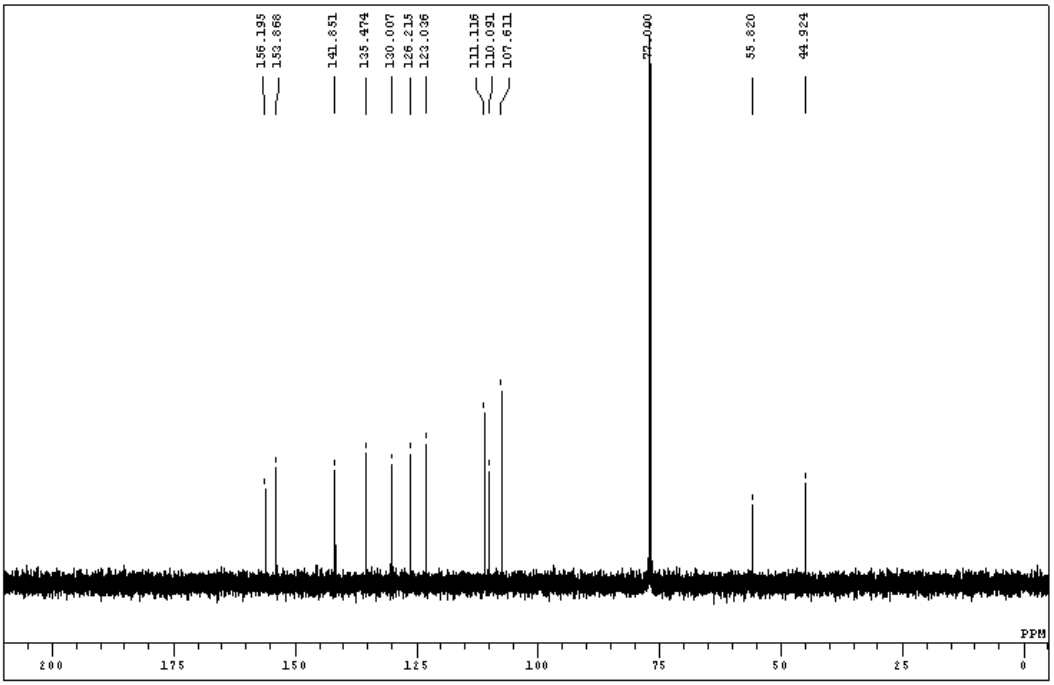
2.000
1.954
PPM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130.007
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77.000
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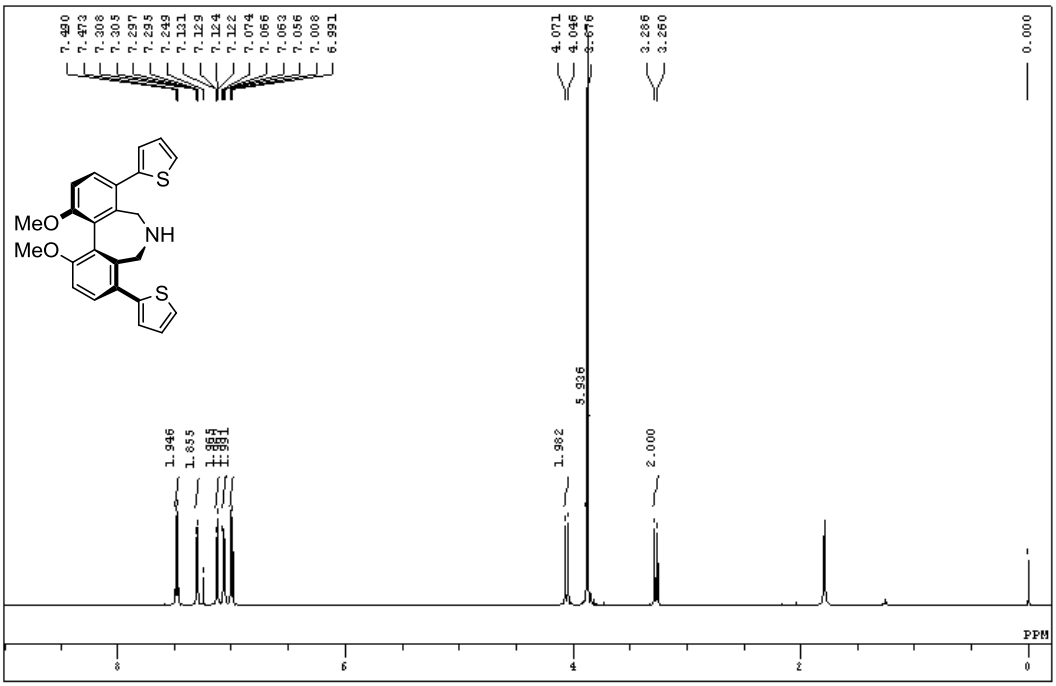
44.924
PPM

Amine (*S*)-3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7.305
7.297
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7.131
7.129
7.124
7.122
7.074
7.066
7.063
7.056
7.008
6.991
4.071
4.046
3.676
3.286
3.260
0.000
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S
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4
2
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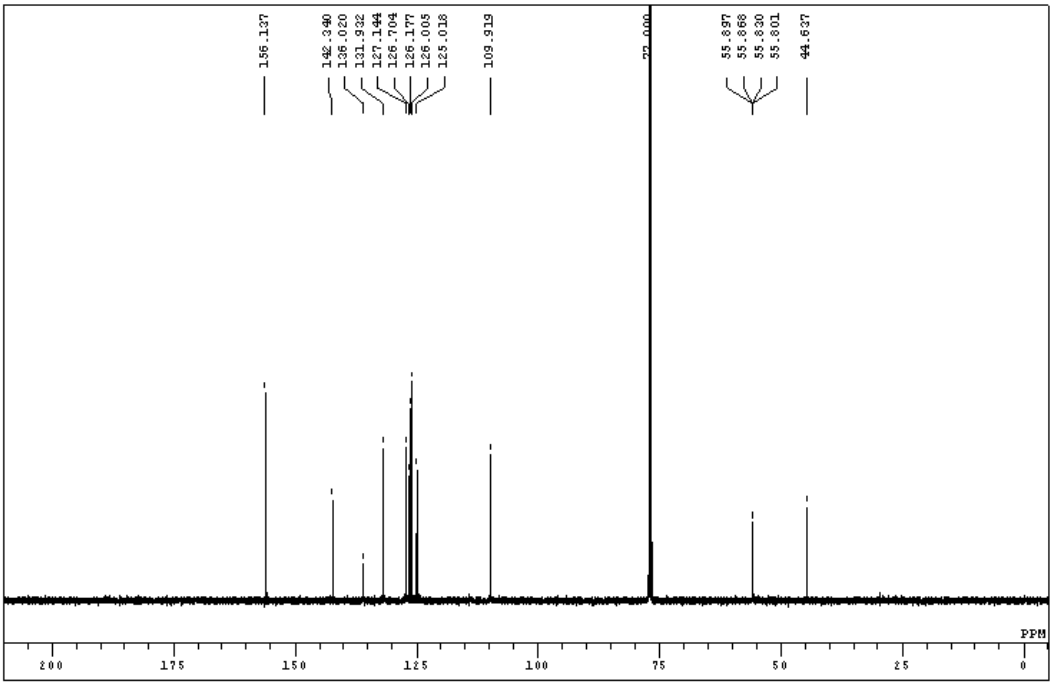
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55.830
55.801
44.637
PPM
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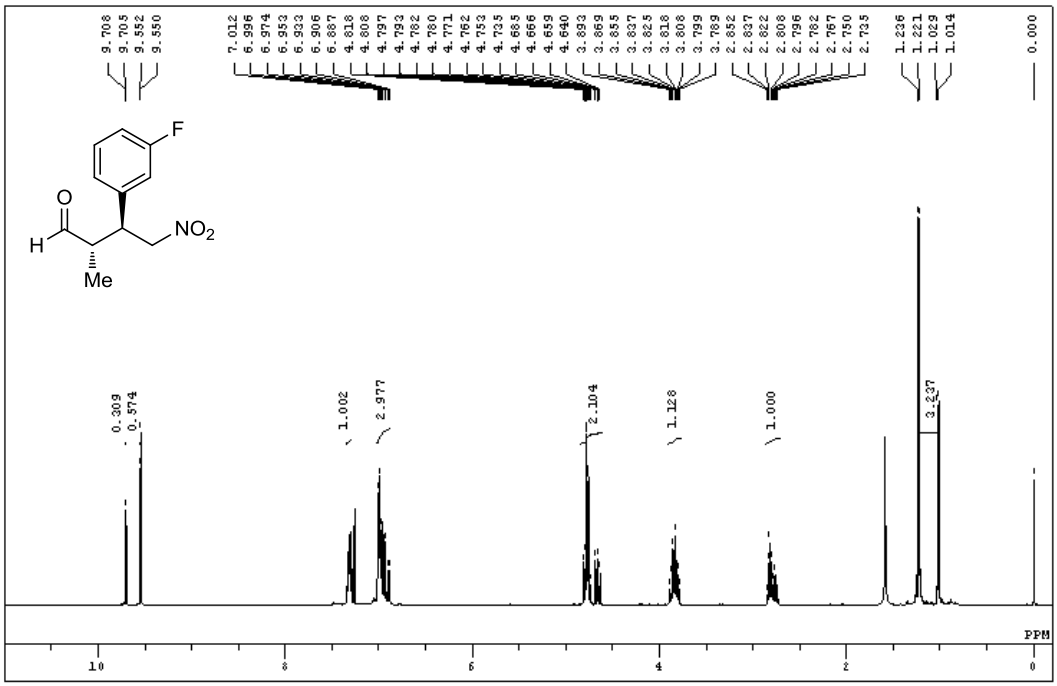
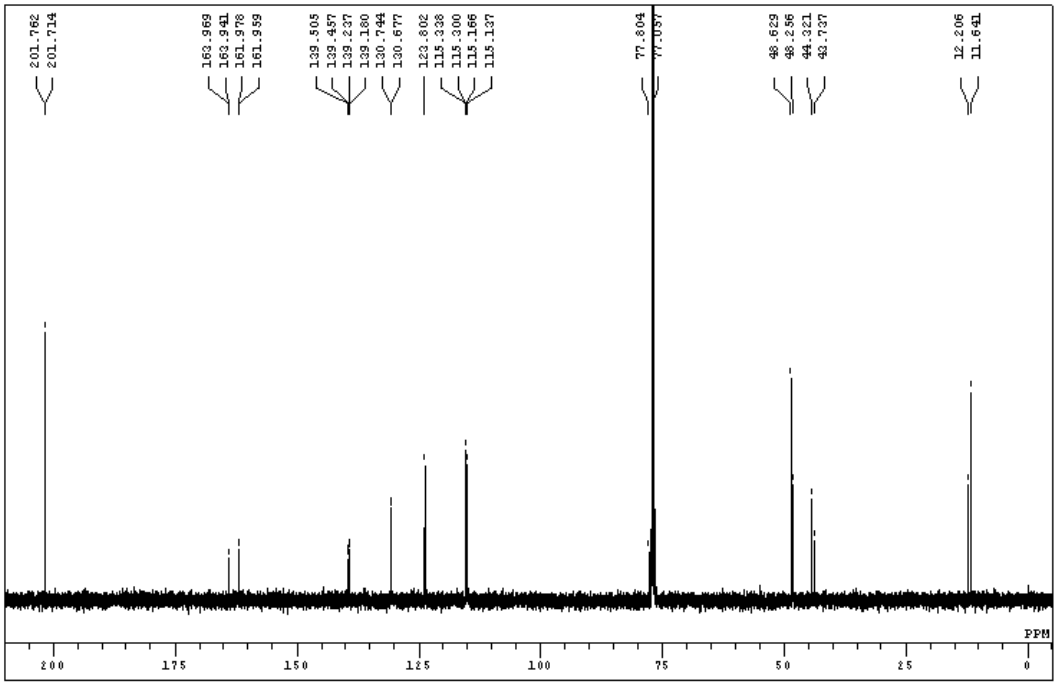
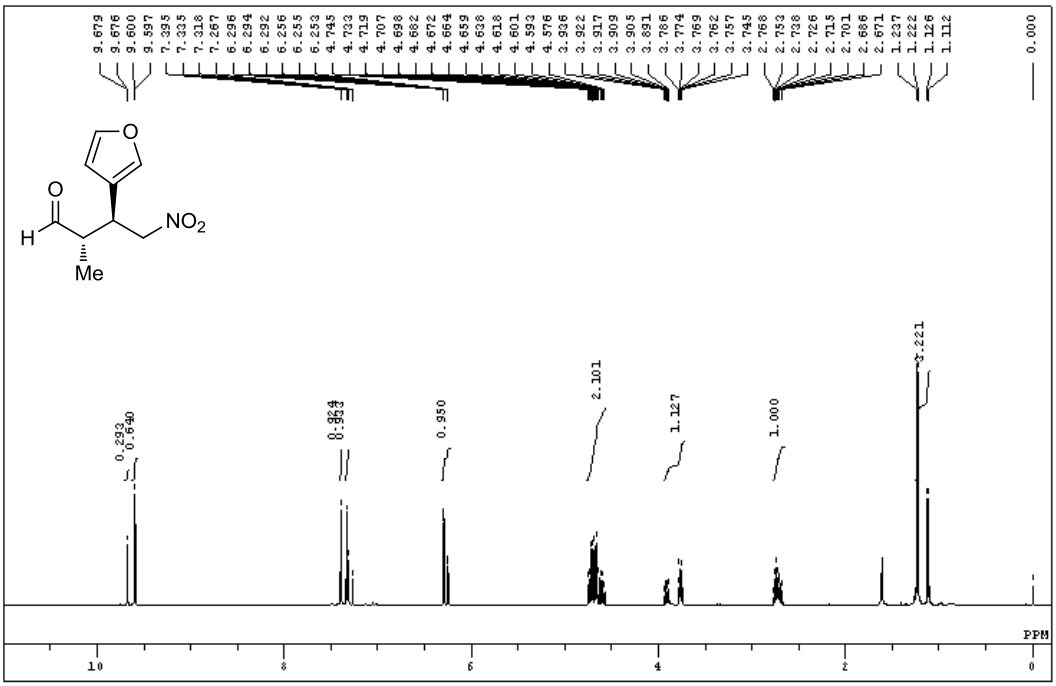
150
125
100
75
50
25
0

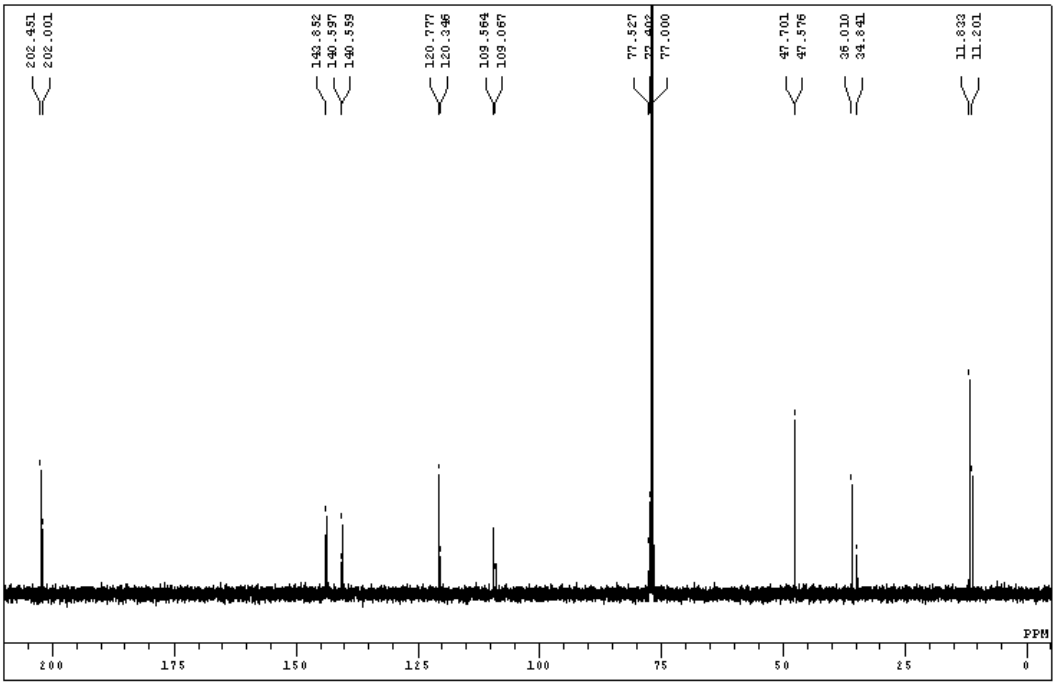
(2*S*,3*S*)-3-(3-fluorophenyl)-2-methyl-4-nitrobutanal



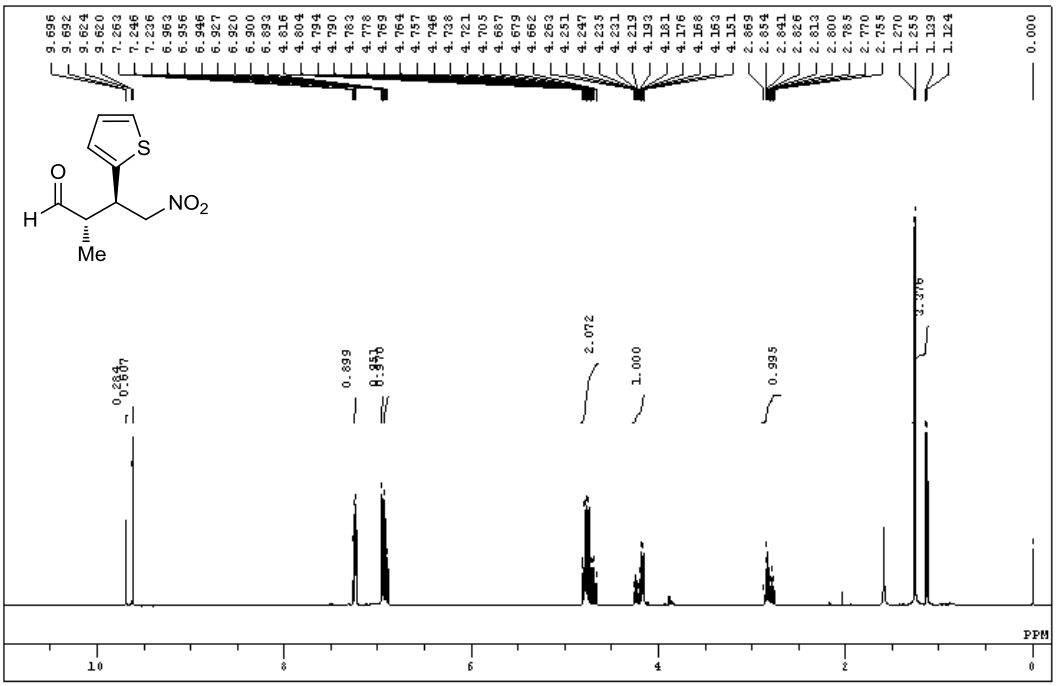


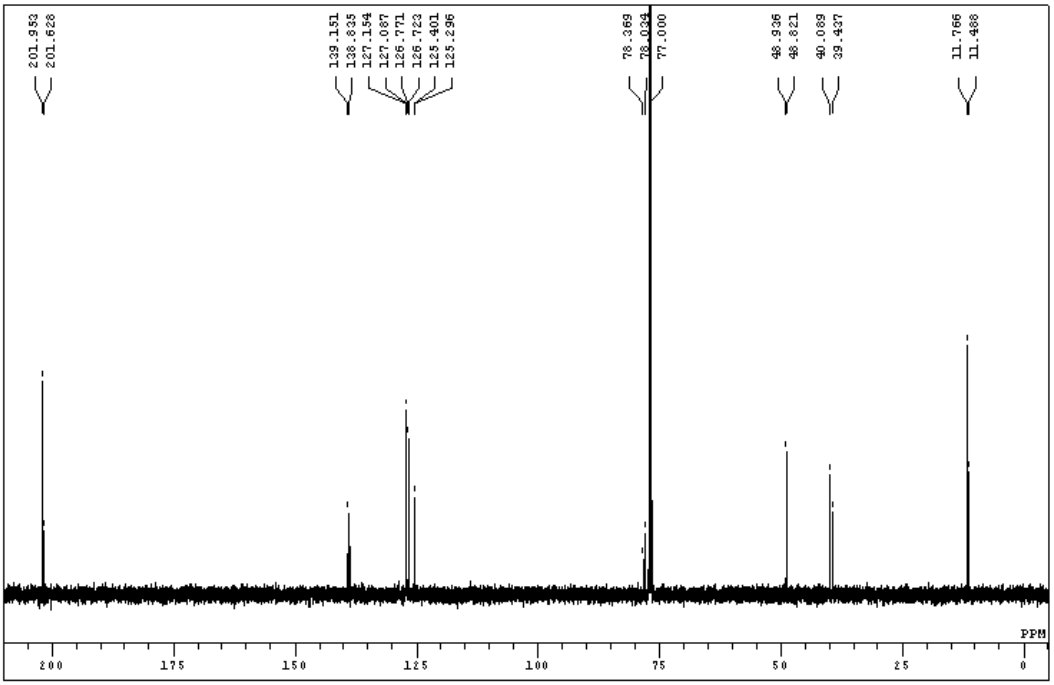
(2*S*,3*S*)-3-furan-3-yl-2-methyl-4-nitrobutanal



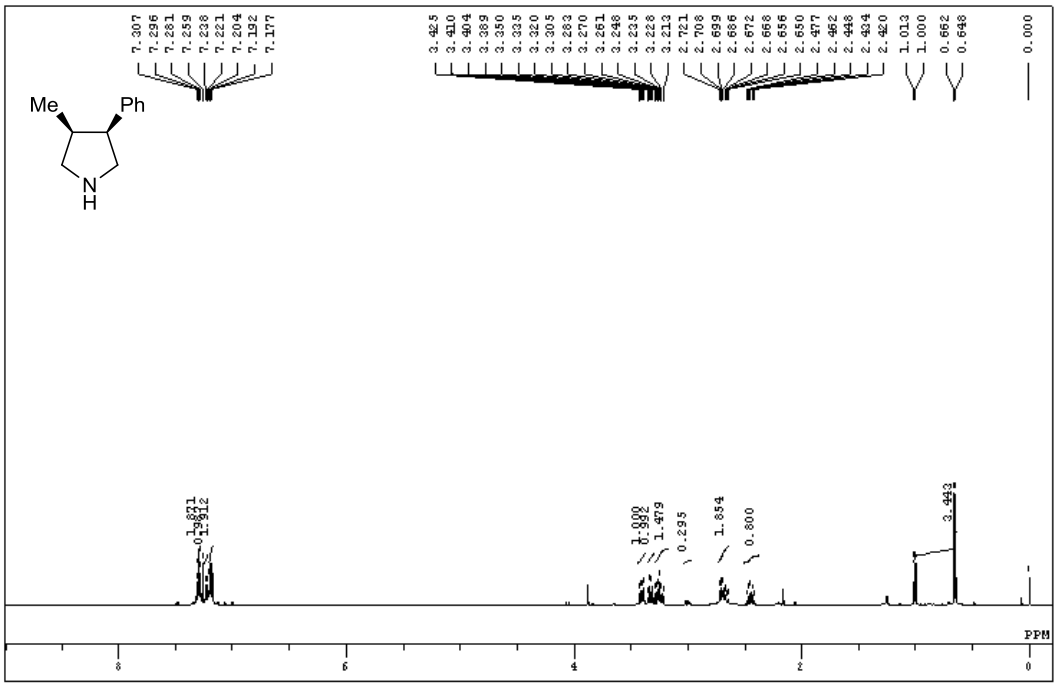


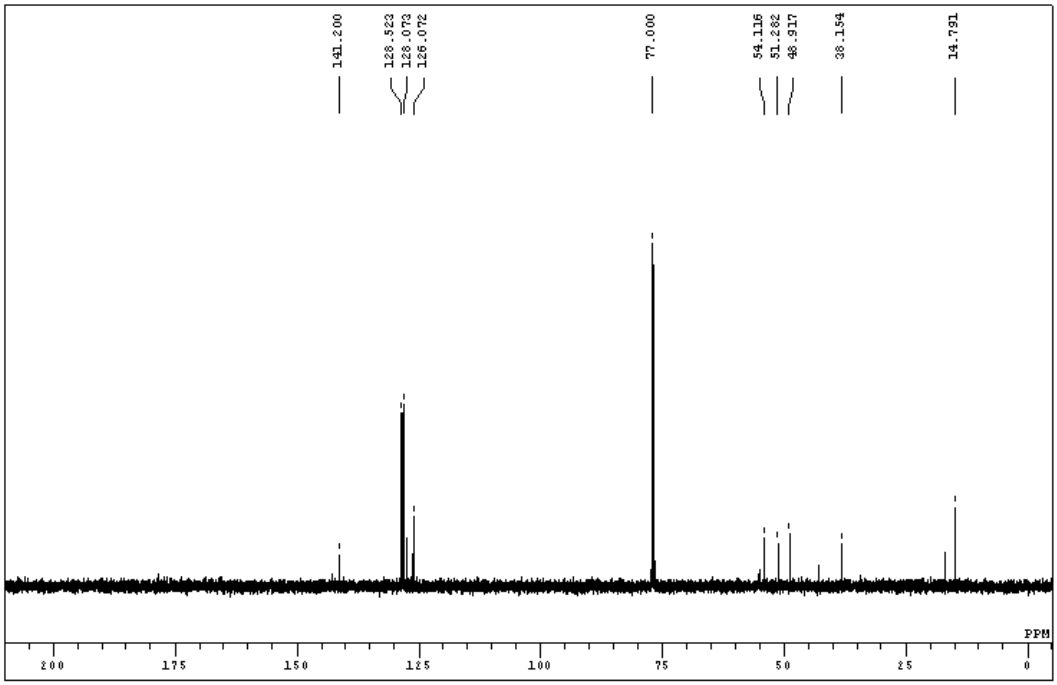
(2*S*,3*S*)-2-methyl-4-nitro-3-thiophen-2-ylbutanal





(3*S*,4*R*)-3-methyl-4-phenylpyrrolidine 8





(*S*)-4-nitro-3-phenyl-1-butene 12