Electronic Supplementary Information

Asymmetric Friedel-Crafts reaction of N-heterocycles and nitroalkenes catalyzed by imidazoline-aminophenol-Cu complex

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General

Pyrrole was freshly distilled before using. Nitroalkenes were synthesized according to known procedure.[1] Dry solvent were purchased from commercial suppliers and used without further purification. Analytical thin-layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel containing a fluorescent indicator (Merck, #1.05715.0009). Silica gel column chromatography was performed on Kanto silica gel 60 (spherical, 100–210 μm). IR spectra were recorded on JASCO FT/IR-4100 using ATR. ^{1}H-NMR spectra were recorded on JEOL LA-400 (400MHz) or LA-500 (500MHz) spectrometers. Chemical shifts of ^{1}H-NMR spectra were reported relative to tetramethyl silane (δ 0). ^{13}C-NMR spectra were recorded on JEOL LA-400 (100MHz) or LA-500 (125MHz) spectrometers. Chemical shifts of ^{13}C-NMR spectra were reported relative to $CDCl_3$ (δ 77.0) or CD_3OD (49.86). Splitting patterns were reported as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

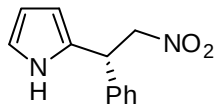
General procedure of asymmetric Friedel-Crafts Reaction using pyrrole

(CuOTf)•C_6H_6 (3.8 mg, 0.0075 mmol) was added to a two-necked round flask containing a stir bar under Ar. Ligand (0.0165 mmol) in toluene (0.375 ml) was added to the flask and the mixture was stirred for 2 hours. To the resulting green solution, the toluene solution (0.375 ml) of nitroalkene (0.15 mmol) and pyrrole (21 μl, 0.30 mmol) were added subsequently at 0 °C. After being stirred for appropriate time indicated in Table 2, the reaction mixture was purified by silica gel column chromatography to afford the adduct. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H, Chiralpak AD-H and Chiralpak AS-H column.

General procedure of asymmetric Friedel-Crafts Reaction using indole

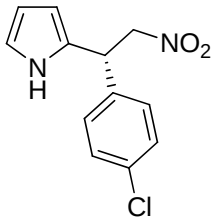
(CuOTf)•C_6H_6 (3.8 mg, 0.0075 mmol) was added to a two-necked round flask containing a stir bar under Ar. Ligand (0.0165 mmol) in toluene (0.375 ml) was added to the flask and the mixture was stirred for 2 hours. To the resulting green solution, 1,1,1,3,3,3-hexafluoro-2-propanol (31 μl, 0.30 mmol), the toluene solution (0.375 ml) of nitroalkene (0.30 mmol) and indole (0.15 mmol) were added at room temperature. After being stirred for appropriate time indicated in Table 3, the reaction mixture was purified by silica gel column chromatography to afford the adduct. The enantiomeric excesses of the products were determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H or Chiralpak AD-H column.

2-((*S*)-2-nitro-1-phenylethyl)-1*H*-pyrrole



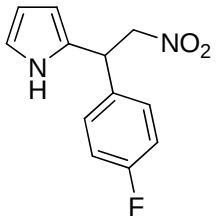
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane: AcOEt=5:1) give the product as a pale yellow oil (24 mg, 73% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.88 (br, 1H), 7.29-7.38 (m, 3H), 7.21-7.25 (m, 2H), 6.67-6.68 (m, 1H), 6.15-6.18 (m, 1H), 6.07-6.09 (m. 1H), 4.98 (dd, *J*=11.8, 7.2 Hz, 1H), 4.86-4.92 (m, 1H), 4.80 (dd, *J*=11.8, 7.6 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 137.9, 129.2, 128.9, 128.1, 127.9, 118.2, 108.6, 105.8, 79.2, 42.9; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.8 mL/min, 254 nm); minor enantiomer t_r = 9.6 min, major enantiomer t_r =11.0 min; 90% ee; $[\alpha]_D^{20}$= -67.6 (*c* =0.5, $CHCl_3$, 90% ee); IR (neat) 3419, 3029, 1548, 1369 cm^{-1}.

(*S*)-2-(1-(4-chlorophenyl)-2-nitroethyl)-1*H*-pyrrole



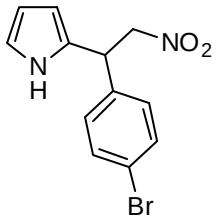
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane: AcOEt=4:1) give the product as a pale yellow solid (36 mg, 97% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.88 (br, 1H), 7.28-7.33 (d, *J*=11.8, 7.6 Hz, 2H), 7.13-7.17 (d, *J*=11.8, 7.6 Hz, 2H), 6.67-6.70 (m, 1H), 6.14-6.17 (m, 1H), 6.04-6.08 (m. 1H), 4.94 (dd, *J*=12.2, 7.1 Hz, 1H), 4.82-4.89 (m, 1H), 4.75 (dd, *J*=12.2, 8.0 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 136.5, 134.1, 129.4, 129.2, 128.3, 118.4, 108.8, 106.0, 79.0, 42.3; HRMS calcd for $C_{12}H_{12}ClN_2O_2$ (M+H): 251.0587, found: *m*/*z* 251.0593; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 28.7 min, major enantiomer t_r =31.1 min; 92% ee; $[\alpha]_D^{20}$= -65.7 (*c* =0.5, $CHCl_3$, 90% ee); IR (neat) 3423, 3027, 1548, 1492 cm^{-1}.

2-(1-(4-fluorophenyl)-2-nitroethyl)-1*H*-pyrrole



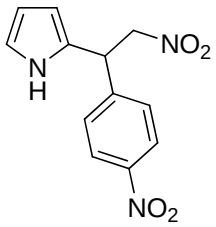
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow solid (28 mg, 81% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.86 (br, 1H), 7.14-7.22 (m, 2H), 7.00-7.06 (m, 2H), 6.69-6.71 (m, 1H), 6.15-6.18 (m, 1H), 6.05-6.08 (m. 1H), 4.97 (dd, *J*=12.3, 7.2, Hz, 1H), 4.85-4.91 (m, 1H), 4.77 (dd, *J*=12.3, 8.0 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 163.6, 161.1, 129.6, 129.5, 118.4, 116.3, 116.0, 108.7, 105.9, 79.2, 42.2; HRMS calcd for $C_{12}H_{12}FN_2O_2$ (M+H): 235.0883, found: *m*/*z* 235.0867; Enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 42.3 min, major enantiomer t_r =26.0 min; 91% ee; $[\alpha]_D^{20}$= -68.8 (*c* =0.5, $CHCl_3$, 72% ee); IR (neat) 3423, 3027, 1548, 1492 cm^{-1}.

2-(1-(4-bromophenyl)-2-nitroethyl)-1*H*-pyrrole



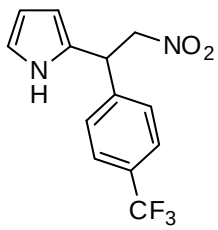
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=4:1) give the product as a pale yellow solid (44 mg, 99% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.86 (br, 1H), 7.46-7.51 (d, *J*=8.2 Hz, 2H), 7.09-7.13 (d, *J*=8.2 Hz, 2H), 6.69-6.72 (m, 1H), 6.16-6.19 (m, 1H), 6.05-6.09 (m. 1H), 4.97 (dd, *J*=12.0, 7.0 Hz, 1H), 4.83-4.89 (m, 1H), 4.78 (dd, *J*=12.0, 8.0 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 137.1, 132.3, 129.6, 128.2, 122.1, 118.4, 108.7, 105.9, 78.9, 42.3; HRMS calcd for $C_{12}H_{12}BrN_2O_2$ (M): 295.0082, found: *m*/*z* 295.0074; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 13.2 min, major enantiomer t_r =15.6 min; 91% ee; $[\alpha]_D^{20}$= -35.2 (*c* =1.0, $CHCl_3$, 91% ee); IR (neat) 3429, 3027, 1548, 1377 cm^{-1}.

2-(2-nitro-1-(4-nitrophenyl)ethyl)-1*H*-pyrrole



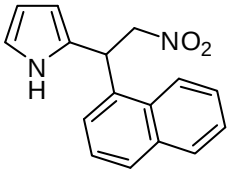
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale solid (26 mg, 67% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.17-8.23 (d, *J*=9.0 Hz, 2H), 7.97 (br, 1H), 7.39-7.45 (d, *J*=9.0 Hz, 2H), 6.72-6.77 (m, 1H), 6.17-6.21 (m, 1H), 6.08-6.12 (m. 1H), 4.98-5.06 (m, 2H), 4.85 (dd, *J*=12.2, 8.0 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 147.6, 145.4, 128.9, 127.1, 124.3, 119.0, 109.0, 106.5, 78.5, 42.6; HRMS calcd for $C_{12}H_{11}N_3O_4$ (M): 261.0750, found: *m*/*z* 261.0764; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 32.8 min, major enantiomer t_r =27.3 min; 92% ee; $[\alpha]_D^{20}$= -53.6 (*c* =0.5, $CHCl_3$, 86% ee); IR (neat) 3411, 2954, 1600, 1552, 1515, 1496 cm^{-1}.

2-(2-nitro-1-(4-(trifluoromethyl)phenyl)ethyl)-1*H*-pyrrole



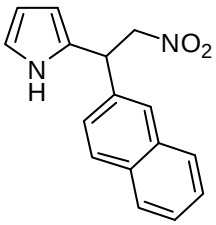
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale solid (39 mg, 91% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.88 (br, 1H), 7.6 (d, *J*=8.2 Hz, 2H), 7.36 (d, *J*=8.2 Hz, 2H), 6.69-6.72 (m, 1H), 6.16-6.19 (m, 1H), 6.07-6.10 (m. 1H), 4.93-5.02 (m, 2H), 4.82 (dd, *J*=11.9, 7.0 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 142.1, 130.6, 130.3, 128.3, 127.8, 126.1 (q, *J*=4.2 Hz, **C**F_3), 118.7, 108.8, 106.3, 78.8, 42.6; HRMS calcd for $C_{13}H_{12}F_3N_2O_2$ (M+H): 285.0851, found: *m*/*z* 285.0833; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (95:5 hexane: 2-propanol, 0.5 mL/min, 254 nm); minor enantiomer t_r = 37.4 min, major enantiomer t_r =39.4 min; 88% ee; $[\alpha]_D^{20}$= -56.3 (*c* =1.0, $CHCl_3$, 88% ee); IR (neat) 3392, 2921, 1551, 1324, 1112 cm^{-1}.

2-(1-(naphthalen-1-yl)-2-nitroethyl)-1*H*-pyrrole



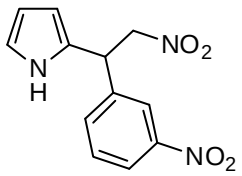
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow oil (28 mg, 70% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.10-8.14 (m, 1H), 7.88-7.92 (m, 1H), 7.74-7.84 (m, 2H), 7.50-7.59 (m, 2H), 7.40-7.45 (m, 1H), 7.25-7.29 (m, 1H), 6.63-6.66 (m, 1H), 6.17-6.23 (m. 2H), 5.77 (dd, *J*=8.9, 6.3 Hz, 1H) , 5.06 (dd, *J*=13.2, 8.9 Hz, 1H), 4.96 (dd, *J*=13.2, 6.3 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 134.6, 135.5, 131.0, 129.2, 128.9, 128.8, 127.2, 126.2, 125.47, 125,46, 122.4, 118.2, 108.8, 106.5, 78.5, 38.8; HRMS calcd for $C_{16}H_{15}N_2O_2$ (M+H): 267.1134, found: *m*/z 267.1124; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (20:1 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 19.9 min, major enantiomer t_r =21.3 min; 66% ee; $[\alpha]_D^{20}$ = -47.4 (*c* = 1.0, $CHCl_3$, 66% ee); IR (neat) 3429, 3054, 1549, 1375 cm^{-1}.

2-(1-(naphthalen-3-yl)-2-nitroethyl)-1*H*-pyrrole



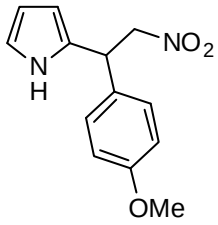
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow oil (32 mg, 81% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.75-7.91 (m, 3H), 7.68 (br, 1H), 7.45-7.52 (m, 2H), 7.27-7.31 (m, 1H), 7.40-7.45 (m, 1H), 6.63-6.68 (m, 1H), 6.16-6.19 (m. 1H), 6.10-6.14 (m, 1H), 5.00-5.07 (m, 2H), 4.85-4.92 (m, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 135.2, 133.3, 132.9, 129.1, 128.8, 127.8, 127.7, 126.9, 126.6, 126.4, 125.3, 118.2, 108.6, 105.8, 79.0, 43.0; HRMS calcd for $C_{16}H_{15}N_2O_2$ (M+H): 267.1134, found: *m*/z 267.1126; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 14.6 min, major enantiomer t_r =18.5 min; 81% ee; $[\alpha]_D^{20}$= -69.2 (*c* = 1.0, $CHCl_3$, 81% ee); IR (neat) 3430, 3025, 1549, 1375 cm^{-1}.

2-(2-nitro-1-(3-nitrophenyl)ethyl)-1*H*-pyrrole



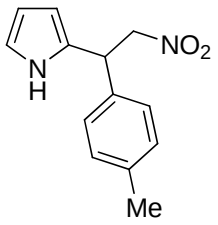
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=4:1) give the product as a pale yellow oil (32 mg, 81% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.14-8.18 (m, 1H), 8.12-8.13 (m, 1H), 8.06 (br, 1H), 7.58-7.61 (m, 1H), 7.52-7.56 (m, 1H), 6.73-6.76 (m, 1H), 6.17-6.21 (m. 1H), 6.10-6.12 (m, 1H), 4.99-5.06 (m, 2H), 4.85-4.91 (m, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 148.6, 140.4, 134.0, 130.2, 127.3, 123.2, 122.8, 119.0, 109.0, 106.5, 78.6, 42.5; HRMS calcd for $C_{12}H_{12}N_3O_4$ (M+H): 262.0828, found: *m*/*z* 262.0828; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 21.4 min, major enantiomer t_r =16.6 min; 80% ee; $[\alpha]_D^{20}$ = -40.4 (*c* = 0.5, $CHCl_3$, 80% ee); IR (neat) 3413, 3095, 1549, 1365 cm^{-1}.

2-(1-(4-methoxyphenyl)-2-nitroethyl)-1*H*-pyrrole



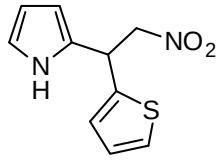
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=4:1) give the product as a pale yellow oil (20 mg, 55% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.83 (br, 1H), 7.08-7.17 (d, *J*=8.7 Hz, 2H), 6.84-6.89 (d, *J*=8.7 Hz, 2H), 6.66-6.69 (m, 1H), 6.13-6.18 (m. 1H), 6.04-6.08 (m, 1H), 4.95 (dd, *J*=12.0, 8.1 Hz, 1H), 4.81-4.87 (m, 1H), 4.76 (dd, *J*=12.0, 8.2 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 159.3, 129.8, 129.2, 129.0, 118.1, 114.5, 108.6, 105.5, 79.4, 55.3, 42.2; HRMS calcd for $C_{13}H_{15}N_2O_3$ (M+H): 247.1083, found: *m*/*z* 247.1096; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 36.2 min, major enantiomer t_r =46.2 min; 81% ee; $[\alpha]_D^{20}$ = -70.6 (*c* = 0.5, $CHCl_3$, 80% ee); IR (neat) 3413, 3095, 1549, 1365 cm^{-1}.

2-(2-nitro-1-*p*-tolylethyl)-1*H*-pyrrole



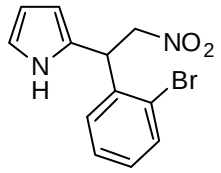
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow solid (27 mg, 78% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.81 (br, 1H), 7.08-7.16 (m, 4H), 6.64-6.67 (m, 1H), 6.13-6.17 (m. 1H), 6.04-6.07 (m, 1H), 4.95 (dd, *J*=11.8, 7.0 Hz, 1H), 4.81-4.87 (m, 1H), 4.77 (dd, *J*=11.8, 8.0 Hz, 1H,), 2.33 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 137.9, 134.9, 129.9, 127.8, 118.0, 108.6, 105.7, 79.3, 42.6, 21.0 ; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 28.8 min, major enantiomer t_r =33.2 min; 80% ee; $[\alpha]_D^{20}$ = -70.7 (*c* = 0.5, $CHCl_3$, 80% ee); IR (neat) 3419, 2921, 1549, 1377 cm^{-1}

2-(2-nitro-1-(thiophen-2-yl)ethyl)-1*H*-pyrrole



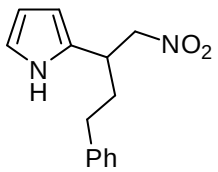
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow oil (22 mg, 66% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.02 (br, 1H), 7.23-7.26 (m,1H), 6.92-6.99 (m, 2H), 6.69-6.72 (m. 1H), 6.15-6.19 (m, 1H), 6.09-6.12 (m, 1H), 5.18-5.23 (m, 1H), 4.93 (dd, *J*=12.9, 7.6 Hz, 1H), 4.84 (dd, *J*=12.9, 8.1 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 141.0, 128.3, 127.2, 125.9, 125.6, 118.3, 108.9, 105.9, 79.7, 38.2 ; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 11.2 min, major enantiomer t_r =12.2 min; 80% ee; $[\alpha]_D^{20}$ = +35.8 (*c* = 0.5, $CHCl_3$, 83% ee); IR (neat) 3419, 2924, 1551, 1377 cm^{-1}.

2-(1-(2-bromophenyl)-2-nitroethyl)-1*H*-pyrrole



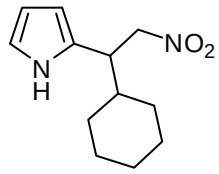
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=4:1) give the product as a pale yellow solid (42 mg, 96% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.01 (br, 1H), 7.58-7.62 (m, 1H), 7.23-7.28 (m, 1H),7.08-7.17 (m, 2H), 6.68-6.71 (m, 1H), 6.15-6.18 (m, 1H), 6.11-6.14 (m. 1H), 5.44 (dd, *J*=8.9, 6.6 Hz, 1H), 4.9 (dd, *J*=13.4, 8.9 Hz, 1H), 4.85 (dd, *J*=13.4, 6.6 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 137.3, 133.5, 129.1, 129.0, 128.2, 127.9, 124.6, 118.3, 108.8, 106.2, 77.3, 41.7; HRMS calcd for $C_{12}H_{12}BrN_2O_2$ (M+H): 295.0082, found: *m*/*z* 295.0074; Enantiomeric excess was determined by HPLC with a Chiralpak OD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 27.7 min, major enantiomer t_r =35.1 min; 56% ee; $[\alpha]_D^{20}$ = -57.7 (*c* = 1.0, $CHCl_3$, 56% ee); IR (neat) 3429, 3027, 1548, 1377 cm^{-1}.

2-(1-nitro-4-phenylbutan-2-yl)-1*H*-pyrrole



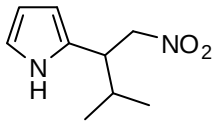
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow oil (30 mg, 81% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.08 (br, 1H), 7.25-7.31 (m, 2H), 7.18-7.22 (m, 1H), 7.08-7.13 (m, 2H), 6.68-6.71 (m, 1H), 6.17-6.20 (m. 1H), 6.03-6.07 (m, 1H), 4.45-4.54 (m, 2H), 3.44-3.52 (m, 1H), 2.62-2.69 (m, 1H), 2.49-2.56 (m, 1H), 1.96-2.02 (m, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ 140.7, 129.3, 128.5, 128.3, 126.2, 117.5, 108.8, 105.6, 80.3, 36.7, 33.7, 32.9; HRMS calcd for $C_{14}H_{17}N_2O_2$ (M+H): 245.1290, found: *m*/*z* 245.1271; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane:2-propanol, 0.8 mL/min, 254 nm); minor enantiomer t_r = 16.7 min, major enantiomer t_r =18.8 min; 83% ee; $[\alpha]_D^{20}$ = -7.6 (*c* = 0.5, $CHCl_3$, 83% ee); IR (neat) 3421, 2925, 1549, 1379 cm^{-1}.

2-(1-cyclohexyl-2-nitroethyl)-1*H*-pyrrole



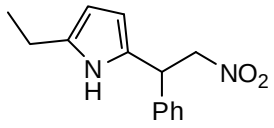
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=7:1) give the product as a pale yellow oil (26 mg, 71% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.03 (br, 1H), 6.66-6.68 (m, 1H), 6.13-6.16 (m. 1H), 5.95-5.97 (m, 1H), 4.68 (dd, *J*=12.5, 6.0 Hz, 1H), 4.58 (dd, *J*=12.5, 9.1 Hz, 1H), 3.31-3.36 (m, 1H), 1.50-1.80 (m, 6H), 0.88-1.30 (m, 5H); ^{13}C NMR (125MHz, $CDCl_3$) δ 128.9, 117.0, 108.6, 106.0, 78.1, 43.5, 40.6, 31.1, 30.0, 26.1, 26.0 (2C); HRMS calcd for $C_{12}H_{19}N_2O_2$ (M+H): 223.1447, found: *m*/*z* 223.1465; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 220 nm); minor enantiomer t_r = 28.1 min, major enantiomer t_r =25.5 min; 64% ee; $[\alpha]_D^{20}$ = +8.9 (*c* = 0.5, $CHCl_3$, 65% ee); IR (neat) 3415, 2925, 1550, 1379 cm^{-1}.

2-(3-methyl-1-nitrobutan-2-yl)-1*H*-pyrrole



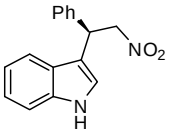
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=7:1) give the product as a pale yellow oil (17 mg, 61% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 8.04 (br, 1H), 6.67-6.69 (m, 1H), 6.13-6.16 (m. 1H), 5.96-5.98 (m, 1H), 4.66 (dd, *J*=12.5, 6.0 Hz, 1H), 4.58 (dd, *J*=12.5, 8.9 Hz, 1H), 3.32-3.37 (m, 1H), 1.92-1.99 (m, 1H), 0.97 (d, *J*=6.7 Hz, 3H), 0.90 (d, *J*=6.7 Hz, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 128.6, 117.1, 108.6, 106.1, 78.3, 44.1, 30.8, 20.6, 19.4; HRMS calcd for $C_9H_{15}N_2O_2$ (M+H): 183.1134, found: *m*/*z* 183.1141; Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 220 nm); minor enantiomer t_r = 20.8 min, major enantiomer t_r =23.2 min; 75% ee; $[\alpha]_D^{20}$ = +8.3 (*c* = 0.5, $CHCl_3$, 75% ee); IR (neat) 3423, 2962, 1550, 1379 cm^{-1}

2-ethyl-5-(2-nitro-1-phenylethyl)-1*H*-pyrrole



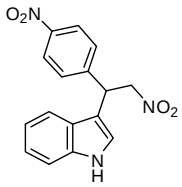
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow oil (-- mg, --% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.53 (br, 1H), 7.32-7.36 (m, 2H), 7.27-7.31 (m. 1H), 7.21-7.25 (m, 2H), 5.93-5.96 (m, 1H), 5.82-5.84 (m, 1H), 4.95 (dd, *J*=12.2, 7.4 Hz, 1H), 4.81-4.86 (m, 1H), 4.77 (dd, *J*=12.2, 7.9 Hz, 1H), 2.51 (q, *J*=7.4 Hz, 2H), 1.17 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 138.3, 134.8, 129.1, 128.0, 127.9, 127.2, 105.7, 104.3, 79.3, 50.0, 20.1, 13.3; HRMS calcd for $C_{14}H_{17}N_2O_2$ (M+H): 245.1290, found: *m*/*z* 245.1274; Enantiomeric excess was determined by HPLC with a Chiralcel AS-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 11.7 min, major enantiomer t_r =12.9 min; --% ee; $[\alpha]_D^{20}$ = -13.5 (*c* = 1.0, $CHCl_3$, 25% ee); IR (neat) 3423, 2967, 1550, 1376 cm^{-1}

3-((*R*)-2-nitro-1-phenylethyl)-1*H*-indole



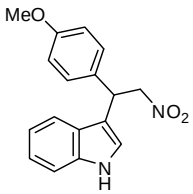
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=5:1) give the product as a pale yellow solid (39 mg, 98% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ 8.09 (br, 1H,), 7.02-7.46 (m, 10H), 5.17-5.21 (m, 1H), 5.07 (dd, *J*=12.4, 7.6 Hz, 1H), 4.94 (dd, *J*=12.4, 8.3 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 139.1, 136.4, 128.9, 127.7, 127.5, 126.0, 122.6, 121.6, 119.9, 118.8, 114.2, 111.4, 79.5, 41.5; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.7 mL/min, 254 nm); minor enantiomer t_r = 31.3 min, major enantiomer t_r = 36.4 min; 72% ee; $[\alpha]_D^{20}$ = -6.1 (*c* = 1.0, $CHCl_3$, 74% ee); IR (neat) 3420, 2987, 1546, 1455, 1378 cm^{-1}.

3-(2-nitro-1-(4-nitrophenyl)ethyl)-1*H*-indole



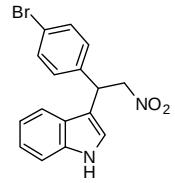
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=3:1) give the product as a pale yellow solid (46 mg, 99% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ 8.22 (br, 1H), 8.17 (d, *J*=8.7 Hz, 2H), 7.51 (d, *J*=8.7 Hz, 2H), 7.34-7.40 (m, 1H), 7.20-7.26 (m, 1H), 7.07-7.12 (m, 1H), 7.04-7.06 (m, 1H), 5.27-5.32 (m, 1H), 5.10 (dd, *J*=12.8, 7.0 Hz, 1H,), 4.99 (dd, *J*=12.8, 8.9 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 147.3, 146.7, 136.5, 128.7, 125.6, 124.2, 123.1, 121.6, 120.3, 118.5, 112.9, 111.6, 78.7, 41.2; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.7 mL/min, 254 nm); minor enantiomer t_r = 55.9min, major enantiomer t_r = 66.9 min; 81% ee; $[\alpha]_D^{20}$ = +8.7 (*c* = 1.0, $CHCl_3$, 81% ee); IR (neat) 3749, 2924, 2853, 1550, 1517, 1345 cm^{-1}.

3-(1-(4-methoxyphenyl)-2-nitroethyl)-1*H*-indole



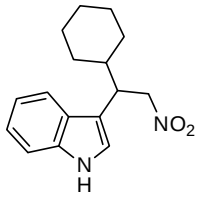
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=3:1) give the product as a pale yellow solid (44 mg, 99% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ 8.07 (br, 1H), 7.41-7.45 (m, 1H), 7.32-7.36 (m, 1H), 7.24 (d, *J*=8.2 Hz, 2H), 7.16-7.21 (m, 1H), 7.04-7.09 (m, 1H), 6.98-7.01 (m, 1H), 6.84 (d, *J*=8.2 Hz, 2H), 5.10-5.15 (m, 1H), 5.03 (dd, *J*=12.2, 7.7 Hz, 1H,), 4.89 (dd, *J*=12.2, 7.5 Hz, 1H,), 3.76 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 158.8, 131.1, 128.8, 122.6, 121.4, 119.9, 119.0, 114.7, 114.2, 111.3, 79.7, 55.2, 40.8; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.7 mL/min, 254 nm); minor enantiomer t_r = 23.8 min, major enantiomer t_r = 26.9 min; 54% ee; $[\alpha]_D^{20}$ = -3.9 (*c* = 1.0, $CHCl_3$, 54% ee); IR (neat) 3674, 3418, 2970, 1548, 1510, 1377, 1247 cm^{-1}.

3-(1-(4-bromophenyl)-2-nitroethyl)-1*H*-indole



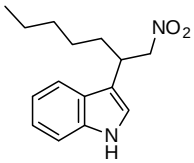
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=3:1) give the product as a white solid (51 mg, 99% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ 8.10 (br, 1H), 7.43 (d, J=8.4 Hz, 2H), 7.32-7.40 (m, 2H), 7.17-7.23 (m, 3H), 7.05-7.10 (m, 1H), 6.97-7.00 (m, 1H,), 5.11-5.16 (m, 1H), 5.03 (dd, *J*=12.5, 7.5Hz, 1H), 4.88 (dd, *J*=12.5, 8.4 Hz, 1H); ^{13}C NMR (100MHz, $CDCl_3$) δ 138.2, 136.4, 132.0, 129.5, 125.8, 122.8, 121.5 (2C), 120.1, 118.7, 113.8, 111.5, 79.1, 41.0; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.7 mL/min, 254 nm); minor enantiomer t_r = 26.8 min, major enantiomer t_r = 33.4 min; 76% ee; $[\alpha]_D^{20}$ = +9.0 (*c* = 1.0, $CHCl_3$, 76% ee); IR (neat) 3419, 2921, 1546, 1487, 1377 cm^{-1};.

3-(1-cyclohexyl-2-nitroethyl)-1*H*-indole



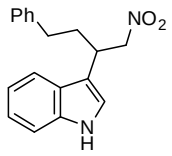
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=6:1) give the product as a yellow oil (33 mg, 80% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ 8.04 (br, 1H), 7.57-7.62 (m, 1H), 7.30-7.35 (m, 1H), 7.16-7.22 (m, 1H), 7.09-7.15 (m, 1H), 6.94-6.97 (m, 1H,), 4.81 (dd, *J*=12.0, 6.2Hz, 1H), 4.70 (dd, *J*=12.0, 9.4 Hz, 1H), 3.63-3.71 (m, 1H), 1.57-1.87 (m, 6H), 0.91-1.31 (m, 5H); ^{13}C NMR (100MHz, $CDCl_3$) δ 136.2, 126.8, 122.2 (2C), 119.6, 119.0, 113.2, 111.3, 78.4, 41.8, 40.4, 31.2, 30,4, 26.2, 26.13, 26.12; Enantiomeric excess was determined by HPLC with a Chiralcel AD-H column (90:10 hexane: 2-propanol, 0.7 mL/min, 254 nm); minor enantiomer t_r = 19.9 min, major enantiomer t_r = 12.8 min; 80% ee; $[\alpha]_D^{20}$ = +36.9 (*c* = 1.0, $CHCl_3$, 80% ee); IR (neat) 3420, 2987, 1546, 1455, 1378 cm^{-1}

3-(1-nitroheptan-2-yl)-1*H*-indole



According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=6:1) give the product as a yellow oil (36 mg, 92% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ 8.06 (br, 1H), 7.60-7.64 (m, 1H), 7.34-7.38 (m, 1H), 7.18-7.24 (m, 1H), 7.11-7.16 (m, 1H), 7.00-7.03 (m, 1H), 4.67 (dd, *J*=11.8, 7.5 Hz, 1H), 4.62 (dd, *J*=11.8, 7.7 Hz, 1H), 3.74-3.83 (m, 1H), 1.72-1.92 (m, 2H), 1.14-1.34 (m, 6H) 0.76 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 136.4, 126.1, 122.4, 121.9, 119.7, 118.7, 114.1, 111.5, 80.6, 36.3, 32.3, 31.6, 26.8, 22.4, 14.0; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.7 mL/min, 254 nm); minor enantiomer t_r = 41. 4min, major enantiomer t_r = 35.5 min; 79% ee; $[\alpha]_D^{20}$ = +13.7 (*c* = 1.0, $CHCl_3$, 79% ee); IR (neat) 3419, 2927, 1543, 1456, 1338 cm^{-1}.

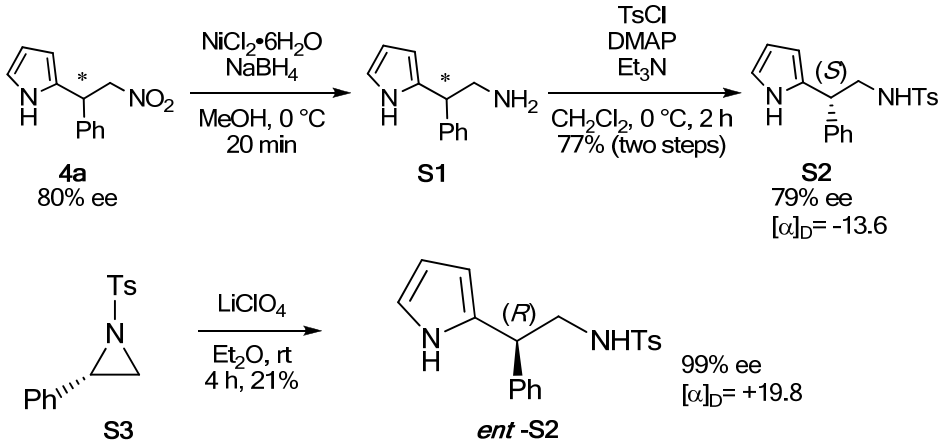
3-(1-nitro-4-phenylbutan-2-yl)-1*H*-indole



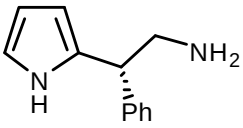
According to the General Procedure, the title compound was prepared. Silica gel column chromatography (Hexane:AcOEt=4:1) give the product as a yellow oil (44 mg, 99% yield). ^{1}H NMR (400MHz, $CDCl_3$) δ 8.06 (br, 1H), 7.58-7.63 (m, 1H), 7.34-7.38 (m, 1H), 7.10-7.30 (m, 5H), 7.04-7.10 (m, 2H), 6.98-7.03 (m, 1H), 4.58-4.69 (m, *2*H), 3.75-3.84 (m, 1H), 2.48-2.65 (m, 2H), 2.04-2.25 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) δ 141.2, 136.5, 128.4, 128.3, 126.0, 125.98, 122.4, 122.2, 119.8, 118.7, 113.3, 111.6, 80.4, 35.9, 33.9, 33.2; Enantiomeric excess was determined by HPLC with a Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.7 mL/min, 254 nm); minor enantiomer t_r = 27.8 min, major enantiomer t_r = 26.4 min; 81% ee; $[\alpha]_D^{20}$ = +14.3 (*c* = 1.0, $CHCl_3$, 81% ee); IR (neat) 3419, 2971, 1543, 1455, 1379 cm^{-1}.

Determination of absolute configuration of 4a obtained in the 1b-CuOTf catalyzed reaction (Table 2, Entry 1)

The absolute configration was determined by derivatization of FC adduct **4a** to the sulfonamide derivative **S2**. The sulfonamide **S2** was obtained by reduction of nitro group by nickel boride[2] at mild condition, followed by tosylation with TsCl gave the sulfonamide **S2** in 77%. From the comparison of its optical rotation and HPLC retention time with those of an authentic sample of *ent*-**S2**, which was prepared by the ring opening reaction of aziridine **S3** with pyrrole promoted by $LiClO_4$. Finally, we determined stereocenter was 2*S*.

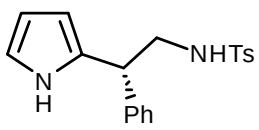


(*S*)-2-phenyl-2-(1*H*-pyrrol-2-yl)ethanamine S1



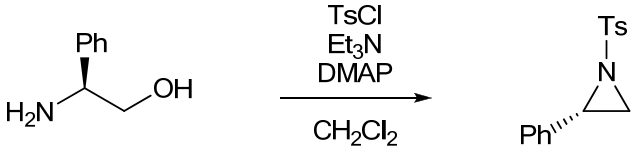
To a stirred solution of the **4a** (68 mg, 0.3 mmol) and $NiCl_2 \cdot 6H_2O$ (71mg, 0.3 mmol) in MeOH (3 ml), $NaBH_4$ (136 mg, 3.6 mmol) was added in portions at 0 ºC. After being stirred at 0 ºC for 20 min, the reaction mixture was quenched by an addition of NH_4Cl solution. The solution was filtered and MeOH was removed by evaporation under reduced pressure. The remaining aqueous phase was extracted with $CHCl_3$ (5 ml×5), and the combined organic layers were dried over anhydrous Na_2SO_4. After removed of Na_2SO_4 by a filtration, the solution was concentrated under reduced pressure. The crude product was used fruther reaction without purification. ^{1}H NMR (500MHz, CD_3OD) δ 7.15-7.29 (m, 5H), 6.61-6.64 (m, 1H), 6.02-6.04 (m, 1H), 5.96-5.99 (m, 1H), 3.96-4.01 (m, 1H), 3.18 (dd, *J*=12.8, 8.2 Hz, 1H), 3.05 (dd, *J*=12.8, 7.3 Hz, 1H). ^{13}C NMR (125MHz, CD_3OD) δ 144.7, 134.2, 130.3, 129.9, 128.5, 119.0, 109.2, 106.6, 48.4, 31.6; IR (neat) 3361, 3189, 3095, 2924, 2854, 1577, 1452 cm^{-1}.

(*S*)-4-methyl-*N*-(2-phenyl-2-(1*H*-pyrrol-2-yl)ethyl)benzenesulfonamide S2



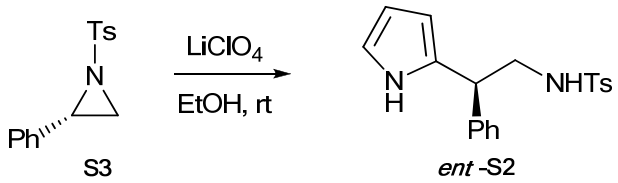
To a stirred solution of the **S1** (28mg, 0.15 mmol), Et_3N (28 μl, 0.2 mmol) and DMAP (2 mg, 0.015 mmol) in CH_2Cl_2 (1.5 ml), TsCl (29 mg, 0.15 mmol) was added in portions at 0 ºC. After being stirred at 0 ºC for 2 h, the reaction mixture was quenched by an addition of saturated $NaHCO_3$ solution. The solution was extracted with $CHCl_3$ (5 ml×3), and the combined organic layers were dried over anhydrous Na_2SO_4. After removed of Na_2SO_4 by a filtration, the solution was concentrated under reduced pressure. The crude product was purified by column chromatography (Hexane:AcOEt=4:1) to give **S2** (39 mg, 77%). ^{1}H NMR (500MHz, CD_3OD) δ 7.90 (br, 1H), 7.66-7.70 (m, 2H), 7.22-7.32 (m, 5H), 7.06-7.12 (m, 2H), 6.64-6.67 (m, 1H), 6.12-6.15 (m, 1H), 5.93-5.96 (m, 1H), 4.42-4.52 (m, 1H), 4.07-4.13 (m, 1H), 3.46-3.53 (m, 1H), 3.37-3.44 (m, 1H), 2.43 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 143.6, 139.8, 136.7, 130.7, 129.8, 129.0, 128.0, 127.5, 127.1, 117.7, 108.5, 105.7, 47.4, 44.5, 21.5; HRMS calcd for $C_{19}H_{21}N_2O_2S$ (M+H): 341.1324 found: *m*/*z* 341.1300; Enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (70:30 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 28.8 min, major enantiomer t_r =41.8 min; 79% ee. $[\alpha]_D^{20}$ = -13.6 (*c* = 1.0, $CHCl_3$, 79% ee); IR (neat) 3733, 3380, 2927, 1325, 1159 cm^{-1}.

(*S*)-2-phenyl-1-tosylaziridine S3[3]



To a solution of (*S*)-phenylglycinol (137 mg, 1 mmol), TsCl (477mg, 2.5 mmol) and DMAP (2 mg) in dry CH_2Cl_2 (4 ml) was added Et_3N (419 μl, 3 mmol) at 0 °C. The mixture was allowed to warm to r.t. and stirred for 17 h. After quenching by an addition of saturated NH_4Cl solution (10 ml), the mixture was extracted with $CHCl_3$ (10 ml×3). The combined organic layers were dried over Na_2SO_4. After removeal of Na_2SO_4, the solution was concentrated in vacuo. The crude product was purified by silica gel column chromatography (Hexane:AcOEt=5:1) to give the aziridine **S3** (169 mg, 62% yield). ^{1}H NMR (500MHz, CD_3OD) δ 7.85-7.89 (m, 2H), 7.18-7.37 (m, 7H), 3.77 (dd, *J*=7.0, 4.6 Hz, 1H), 2.98 (d, *J*=7.0 Hz, 1H), 2.43 (s, 3H), 2.38 (d, *J*=4.6 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 144.6, 135.0 (2C), 129.7, 128.5, 128.3, 127.9, 126.5, 41.0, 35.9, 21.6.

(*R*)-4-methyl-*N*-(2-phenyl-2-(1*H*-pyrrol-2-yl)ethyl)benzenesulfonamide *ent*-S2

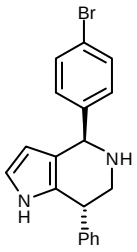


S3 *ent* -S2

To a solution of S3 (121 mg, 0.51 mmol), $LiClO_4$ (162 mg, 1.54 mmol) in dry Et_2O (0.3 ml) was added pyrrole (35 μl, 0.51 mmol) at r.t. The mixture was stirred for 17 h. After quenching by an addition of water (10 ml), the mixture was extracted with AcOEt (5 ml×3). The combined organic layers were dried over Na_2SO_4. After removeal of Na_2SO_4, the solution was concentrated in vacuo. The crude product was purified by silica gel column chromatography (Hexane:AcOEt=4:1) to give the aziridine *ent*-**S2** (29 mg, 21% yield). ^{1}H NMR (500MHz, CD_3OD) δ 7.85-7.89 (m, 2H), 7.18-7.37 (m, 7H), 3.77 (dd, *J*=7.0, 4.6 Hz, 1H), 2.98 (d, *J*=7.0 Hz, 1H), 2.43 (s, 3H), 2.38 (d, *J*=4.6 Hz, 1H); Enantiomeric excess was determined by HPLC with a Chiralpak AS-H column (70:30 hexane: 2-propanol, 1.0 mL/min, 254 nm); major enantiomer t_r = 28.8 min; 99% ee. $[\alpha]_D^{20}$ = +19.8 (*c* = 1.0, $CHCl_3$, 99% ee).

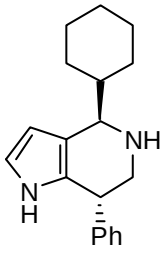
Pictet-Spengler Cyclization

(4*R*,7*S*)-4-(4-bromophenyl)-7-phenyl-4,5,6,7-tetrahydro-1*H*-pyrrolo[3,2-*c*]pyridine



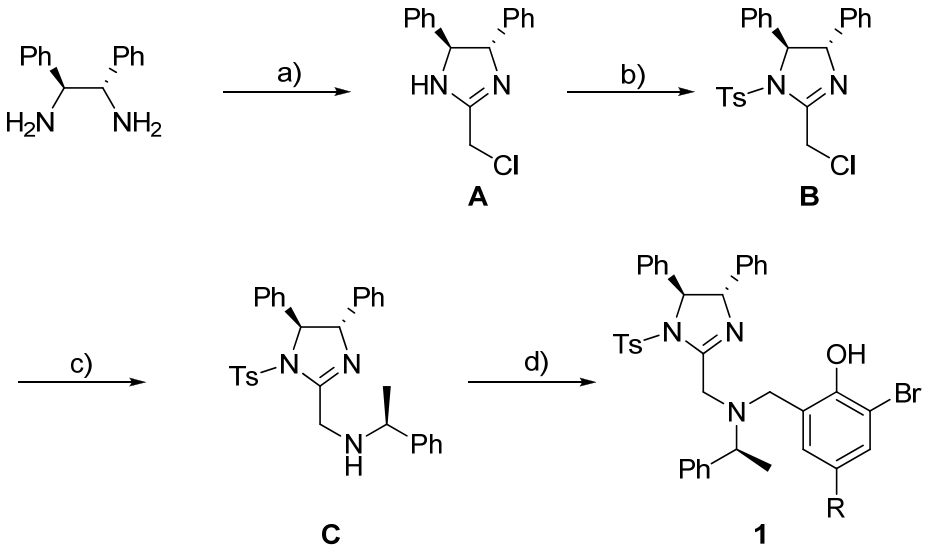
To suspension of **4a** (37mg, 0.08 mmol), 4-bromobenzaldehyde (37 mg, 0.12 mmol) and Na_2SO_4 (100 mg) in dry $ClCH_2CH_2Cl$ (0.8 ml) was added TFA (6 µl, 0.08 mmol). After being stirred for 1.5 h at 40 °C, a saturated $NaHCO_3$ solution (10 ml) was carefully added. The mixture was extracted with $CHCl_3$ (10 ml×3) and the organic layers were dried over Na_2SO_4. After removed of Na_2SO_4 by filtration, the solution was concentrated in vacuo. The crude product was purified by silica gel column chromatography (Hexane:AcOEt=2:1) to give an pale yellow solid (26 mg, 80% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.77 (br, 1H), 7.42-7.48 (m, 2H), 7.23-7.35 (m, 5H), 7.14-7.19 (m, 2H), 6.57-6.61 (m, 1H), 5.71-5.75 (m. 1H), 5.07-5.51 (s, 1H), 4.13-4.18 (m, 1H), 3.44 (dd, *J*=12.5, 5.2 Hz, 1H), 3.13 (br, 1H), 2.99 (dd, *J*=12.5, 9.2 Hz, 1H); ^{13}C NMR (125MHz, $CDCl_3$) δ 143.0, 141.8, 131.4, 130.1, 128.8, 128.3, 127.2, 121.2, 119.9, 116.8, 105.8, 58.1, 52.3, 42.0, 29.7; HRMS calcd for $C_{19}H_{18}BrN_2$ (M+H): 353.0653, found: *m*/*z* 353.0626; Enantiomeric excess was determined by HPLC with a Chiralpak OD-H column (90:10 hexane: 2-propanol, 0.8 mL/min, 254 nm); minor enantiomer t_r = 16.7 min, major enantiomer t_r = 25.8 min; 91% ee. $[\alpha]_D^{20}$= +12.1 (*c* =0.12, $CHCl_3$)

(4*R*,7*S*)-4-cyclohexyl-7-phenyl-4,5,6,7-tetrahydro-1*H*-pyrrolo[3,2-*c*]pyridine



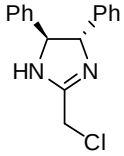
To suspension of **4a** (16mg, 0.088 mmol), cyclohexanecarboxyaldehyde (21 µl, 0.17 mmol) and Na_2SO_4 (100 mg) in dry $ClCH_2CH_2Cl$ (1 ml) was added TFA (7 µl, 0.1 mmol). After being stirred for 1 h at 40 °C, a saturated $NaHCO_3$ solution (10 ml) was carefully added. The mixture was extracted with $CHCl_3$ (10 ml×3) and the organic layers were dried over Na_2SO_4. After removed of Na_2SO_4 by filtration, the solution was concentrated in vacuo. The crude product was purified by silica gel column chromatography (AcOEt) to give an pale yellow solid (24 mg, 94% yield). ^{1}H NMR (500MHz, $CDCl_3$) δ 7.74(br, 1H), 7.24-7.33 (m, 3H), 7.12-7.16 (m, 2H), 6.61-6.64 (m, 1H), 6.16 (br, 1H), 6.03-6.06 (m. 1H), 4.18-4.23 (m, 1H), 4.15-4.17 (m, 1H), 3.56 (dd, *J*=12.6, 5.1 Hz, 1H), 2.91-2.97 (m, 1H), 1.60-2.00 (m, 6H), 1.08-1.41 (m, 5H); ^{13}C NMR (125MHz, $CDCl_3$) δ 140.7, 128.8, 128.4, 127.8, 127.4, 118.3, 117.1, 104.9, 58.9, 51.4, 42.3, 41.0, 29.8, 27.2, 26.7, 26.68, 26.5; HRMS calcd for $C19H_{25}N_2$ (M+H): 281.2018, found: *m*/*z* 281.2013; Enantiomeric excess was determined by HPLC with a Chiralpak AD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm); minor enantiomer t_r = 43.4 min, major enantiomer t_r = 10.6 min; 80% ee. $[\alpha]_D^{20}$= +19.3 (*c* =0.5, $CHCl_3$)

Synthesis of 1



a): chloroorthoaceticacidtriethylester, AcOH, r.t. 80%
b): *p*-toluenesulufonylchloride, DIPEA, MeCN, r.t. 89%
c): (*S*)-1-phenylethylamine, NaI, DMF, r.t. quant
d): corresponding salicylaldehyde, $NaBH_3CN$, MeOH

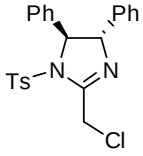
(4*S*,5*S*)-2-(chloromethly)-4,5-dihydro-4,5-diphenyl-1*H*-imidazole A



To the solution of (1*S*,2*S*)-1,2-diphenylehane-1,2-diamine (1 g, 4.71 mmol) in AcOH (23.5 ml) was added chloro orthoaceticacid thiethylester (1.17 ml, 6.12 mmol), and the mixture was stirred for 15 h at r.t. After diluting by adding $CHCl_3$ (100 ml), the reaction mixture was neutralized by 2N NaOH aq, and the aqueous layer was extracted with $CHCl_3$ (15 ml×3). The conbined organic extracts were dried over anhyd Na_2SO_4, and concentrated in vacuo after filtration. The residual crude product was purified by silica gel column chromatography to give the chloromethylated imidazoline **A** (1.01 g, 80% yield) as a colorless amorphous solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.38 (m, 10H, aromatic), 5.35 (br s, 1H, NH), 4.82 (s, 2H), 4.38 (s, 2H).

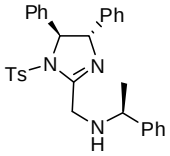
(4*S*,5*S*)-2-(chloromethly)-4,5-dihydro-4,5-diphenyl-1-tosyl-1*H*-imidazole B



To the solution of **A** (271 mg, 0.94 mmol), $^{i}Pr_2NEt$ (257 μl, 1.5 mmol) in dry MeCN (4.7 ml) was added TsCl (248 mg, 1.3 mmol) at 0 ˚C, and the mixture was stirred for 1 h at same temperature. The reaction was quenched by sat. $NaHCO_3$, and the aqueous layer was extracted by $CHCl_3$ (10 ml×3). The combined organic extracts was dried over anhyd Na_2SO_4, and concentrated in vacuo after filtration. The residual crude product was purified by silica gel column chromatography to give the tosylated imidazoline **B** (401 mg, 94% yield) as a white solid.

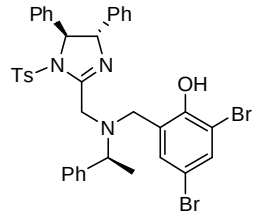
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88-7.50 (m, 14H, aromatic), 4.92-4.99 (m, 3H), 4.69 (d, *J*=12.5Hz, 1H), 2.32 (s, 3H, Ts-CH_3); ^{13}C NMR (100MHz, $CDCl_3$) δ 155.7, 144.6, 140.5, 140.5, 134.9, 129.4, 128.8, 128.6, 128.1, 127.7, 127.5, 126.3, 126.0, 77.7, 71.9, 38.6, 21.3,

(1*S*)-*N*-(((4*S*,5*S*)-4,5-dihydro-4,5-diphenyl-1-tosyl-1*H*—imidazol-2-yl)methyl)-1-phenylethanamine C



To the solution of **B** (543 mg, 1.28 mmol), KI (575mg, 3.8 mmol) in dry DMF (4.7 ml) was added (*S*)-1-phenylethylamine (0.82 ml, 6.4 mmol) at r.t., and the mixture was stirred for 14 h at same temperature. The reaction was quenched by sat. $NaHCO_3$, and the aqueous layer was extracted by Et_2O (10 ml×3). After washing the combined organic extracts with H_2O three times, the organic layer was dried over anhyd Na_2SO_4, and concentrated in vacuo after filtration. The residual crude product was purified by silica gel column chromatography to give the **C** (677 mg 97% yield) as a white amorphous oil. ^{1}H NMR(400 MHz, $CDCl_3$) δ 6.81-7.40 (m, 19H), 4.92 (d, J=8.7 Hz, 1H), 4.84 (d, *J*=8.7 Hz, 1H), 4.00 (q, *J*=6.5 Hz, 1H), 3.79-3.92 (m, 2H), 2.40 (s, 3H), 1.42 (d, *J*=6.5 Hz, 3H)

2-(((1*S*)-*N*-(((4*S*,5*S*)-4,5-dihydro-4,5-diphenyl-1-tosyl-1*H*—imidazol-2-yl)methyl)-1-phenylethanamino)methyl)4,6-dibromophenol 1a



To the solution of **C** (173 mg, 0.34 mmol) in dry MeOH (1.7 ml) was added 3,5-dibromosalicylaldehyde (476 mg, 1.7 mmol) at r.t. After stirring for 1 h at same temperature, the reaction mixture was added sodiumcyanoborohydride (1M in THF, 1 ml, 1 mmol) at 0 ˚C, then the reaction was stirred at r.t. for 24 h. The reaction was quenched by sat. $NaHCO_3$, and the aqueous layer was extracted by $CHCl_3$ (10 ml×3). The combined organic extracts was dried over anhyd Na_2SO_4, and concentrated in vacuo after filtration. The residual crude product was purified by silica gel column chromatography to give the **1a** (180 mg, 68% yield) as a yellow solid.

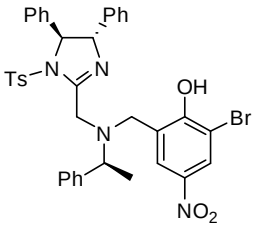
^{1}H NMR(500 MHz, $CDCl_3$) δ 11.26 (br, 1H), 6.66-7.55 (m, 21H), 5.04 (m, 1H), 4.67 (d, *J*=8.9 Hz, 1H), 4.08-4.11 (m, 2H), 3.77-3.95 (m, 3H), 2.35 (s, 3H), 1.50 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 164.1, 159.8, 153.8, 144.5, 142.3, 141.1, 141.0, 134.7, 134.3, 131.8, 129.9, 129.2, 128.5, 128.4, 128.35, 128.1, 127.3, 127.2, 126.7, 125.8, 125.5, 125.4, 111.6, 110.0, 76.1, 72.3, 55.7, 53.3, 47.8, 21.5.

HRMS (FAB+) calcd for $C_{38}H_{36}Br_2N_3O_3S$ (M+H) 772.0844: found 772.0831.

IR: 3028, 1647, 1365, 1163 cm^{-1}.

$[\alpha]_D^{20}$= +1.85 (*c* =1.0, $CHCl_3$).

4-bromo-2-(((((4*S*,5*S*)-4,5-diphenyl-1-tosyl-4,5-dihydro-1*H*-imidazol-2-yl)methyl)((*S*)-1-*p*henylethyl)amino)methyl)-6-nitrophenol 1b



To the solution of **C** (509 mg, 1 mmol) in dry MeOH (5 ml) was added 3-nitro-5-bromosalicylaldehyde (1.2 g, 5 mmol) at r.t. After stirring for 1 h at same temperature, the reaction mixture was added sodiumcyanoborohydride (1M in THF, 2 ml, 2 mmol) at 0 ˚C, then the reaction was stirred at r.t. for 5 h. The reaction was quenched by sat. $NaHCO_3$, and the aqueous layer was extracted by $CHCl_3$ (10 ml×3). The combined organic extracts was dried over anhyd Na_2SO_4, and concentrated in vacuo after filtration. The residual crude product was purified by silica gel column chromatography (Hexane:AcOEt=7:1) to give the **1b** (260 mg, 35% yield) as a yellow solid.

^{1}H NMR (500MHz, $CDCl_3$) δ 12.7 (br, 1H), 8.37-8.39 (m, 1H), 8.00-8.02 (m, 1H), 7.33-7.45 (m, 8H), 7.20-7.25 (m ,3H), 7.12-7.15 (m, 2H), 6.99-7.02 (m, 2H), 6.91-6.94 (m, 2H), 6.66-6.69 (m, 2H), 5.04-5.07 (m, 1H), 4.70-4.72 (m, 1H), 4.15 (d, *J*=13.8 Hz, 1H,), 4.01-4.05 (m, 1H), 3.93-3.99 (m, 2H), 3.79-3.85 (m, 1H), 2.36 (s, 3H), 1.54 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 160.1, 144.8, 142.0, 140.75, 140.7, 139.4, 134.2, 129.9, 129.4, 129.2, 129.0, 128.6, 128.5, 128.0, 127.5, 127.3, 126.8, 126.1, 125.8, 125.5, 125.3, 111.2, 75.8, 72.5, 55.6, 53.5, 47.9, 21.5.

$[\alpha]_D^{20}$ = -4.0 (*c* = 0.2, $CHCl_3$).

HRMS calcd for $C_{38}H_{36}BrN_4O_5S$ (M+H): 739.1590, found: *m*/*z* 739.1564.

IR (neat) 3466, 2952, 1671, 1599, 1454, 1334 cm^{-1}

Reference

1) D. M. Mampreian, A. H. Hoveyda, *Org*. *Lett*., **2004**, *6*, 2829.

2) F. Tur, J. M. Sa, *Org*. *Lett*., **2007**, *6*, 5079.

3) J. L. Vicario, D. Badia, L. Carrillo, *ARKIVOC* **2007**, 304.

Gaussian 03 (phenylethyl group was omitted for simplification)

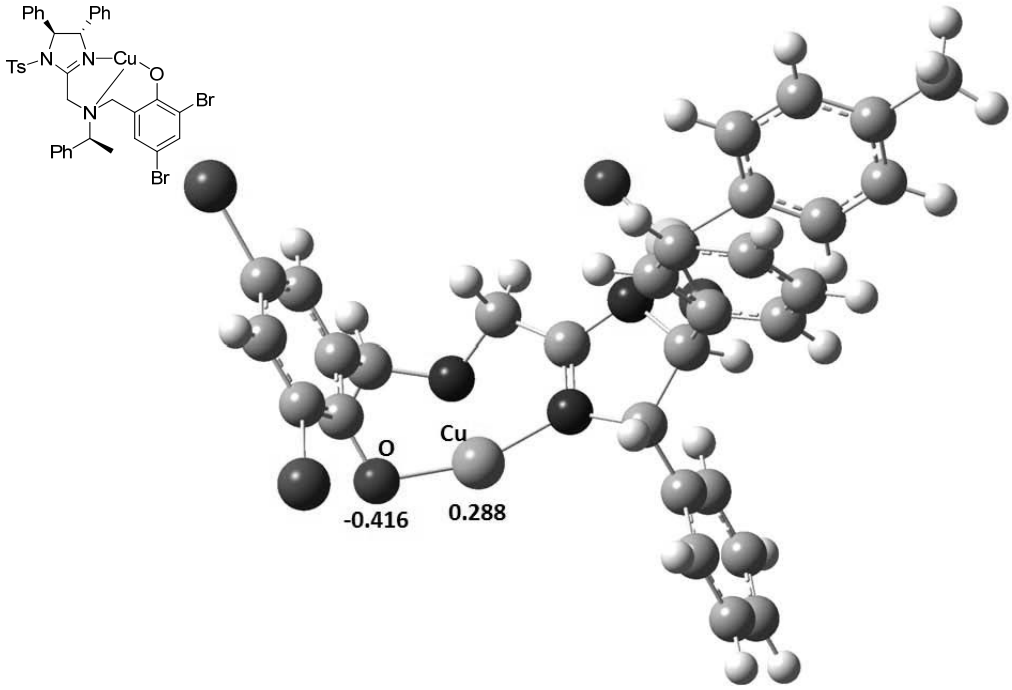


Fig S1a. DFT caluculation of **1a**-CuOTf. (DFT/B3LYP/SDD)

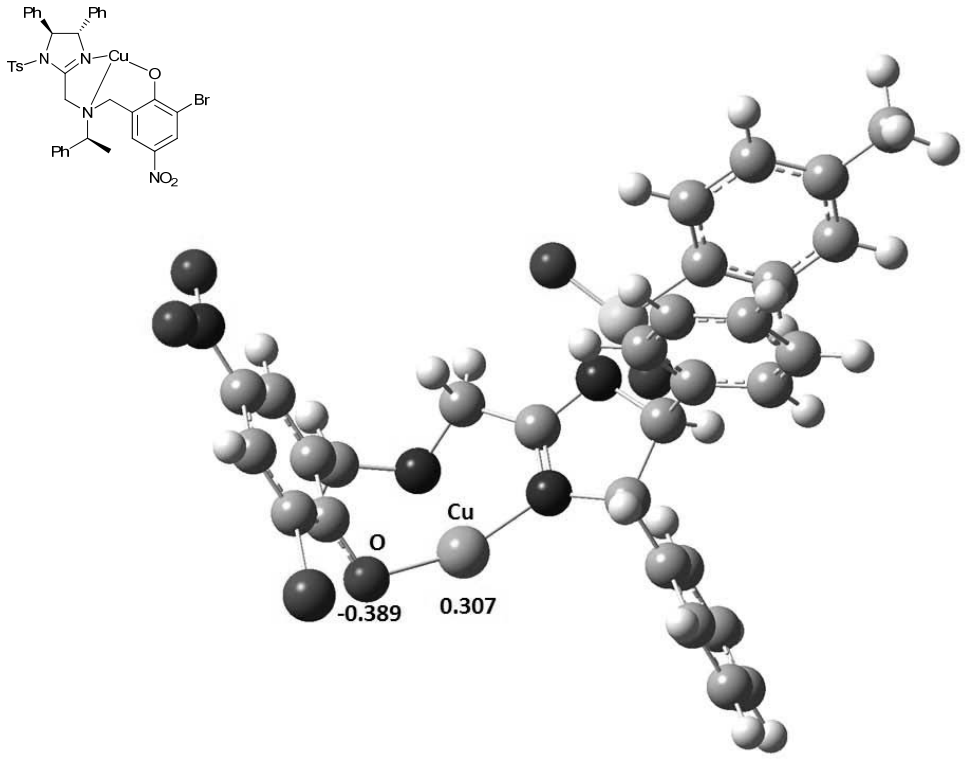
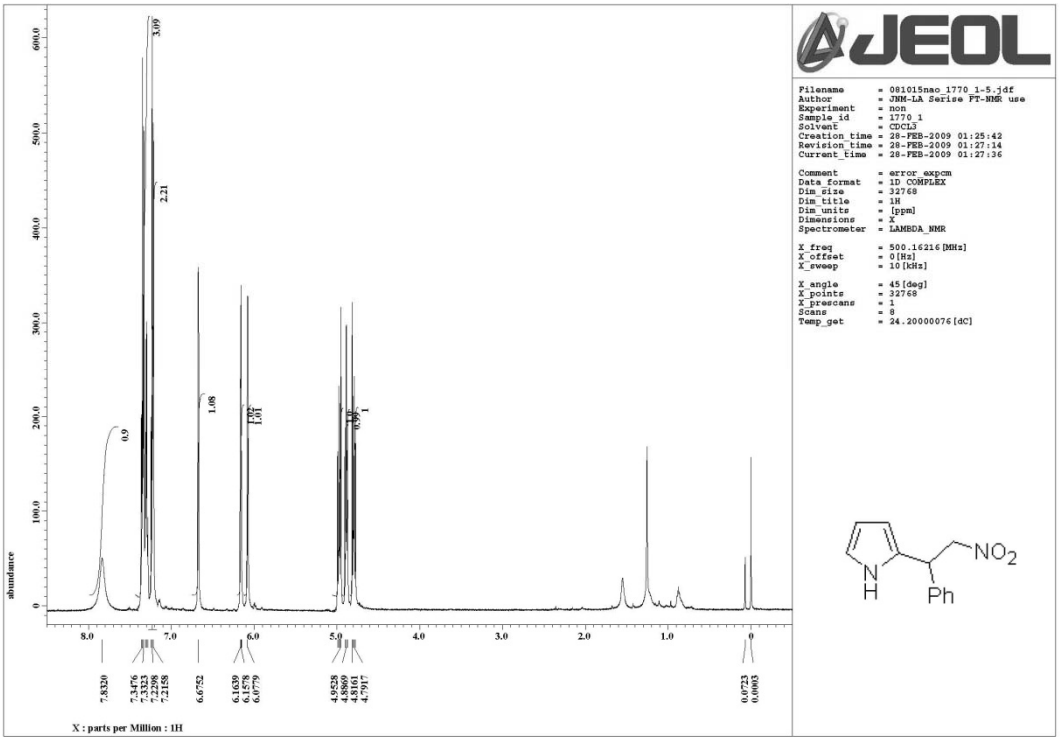
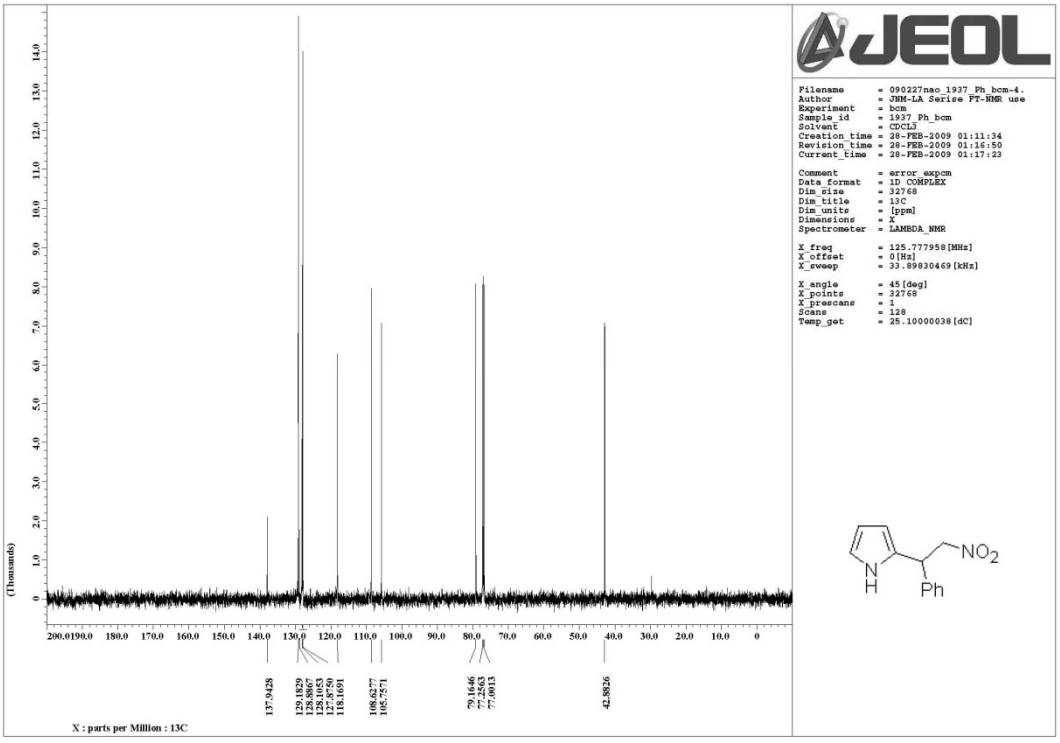


Fig S1b. DFT caluculation of **1b**-CuOTf. (DFT/B3LYP/SDD)

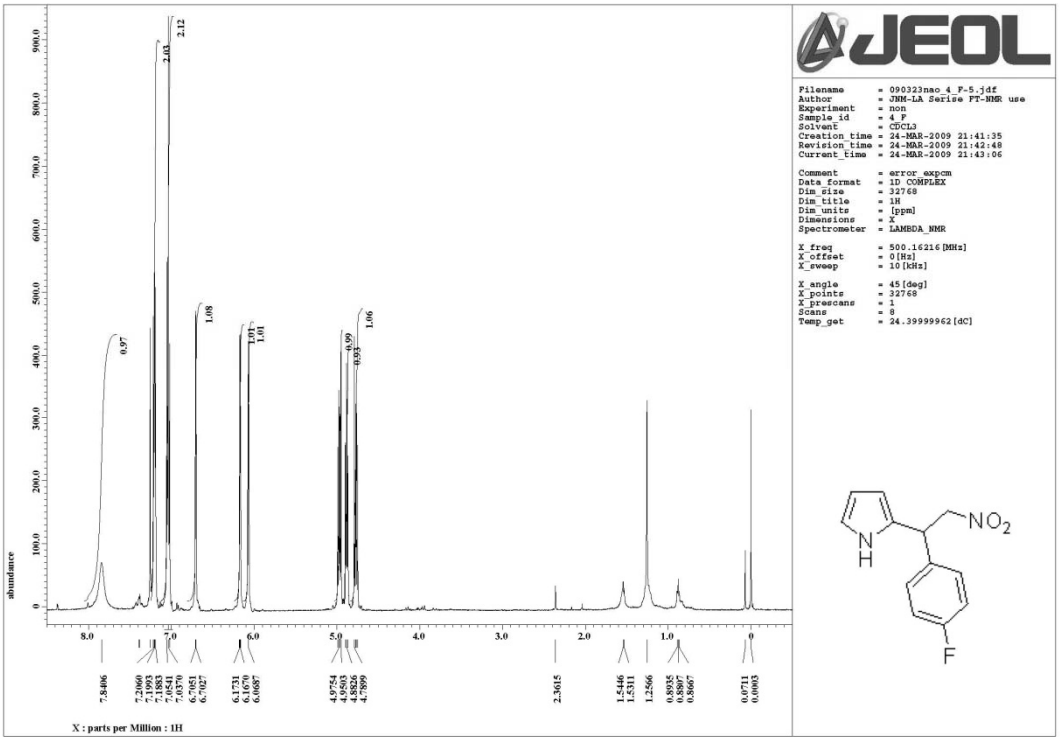
^{1}H-NMR of the product obtained in entry 1, Table 2



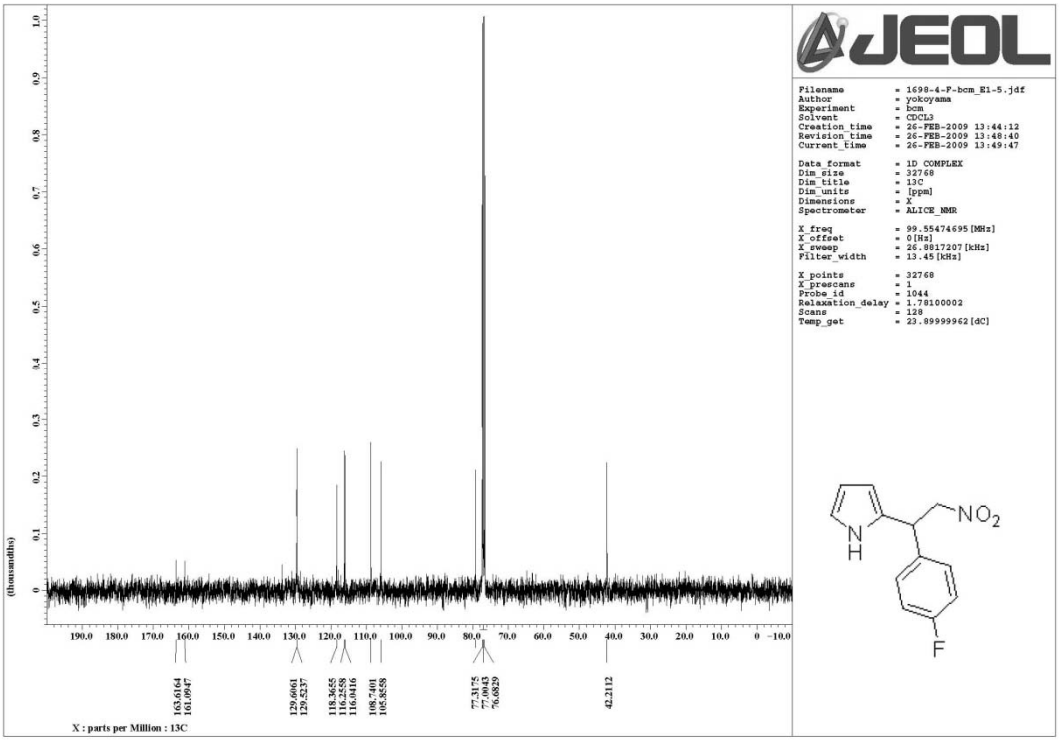
^{13}C-NMR of the product obtained in entry 1, Table 2



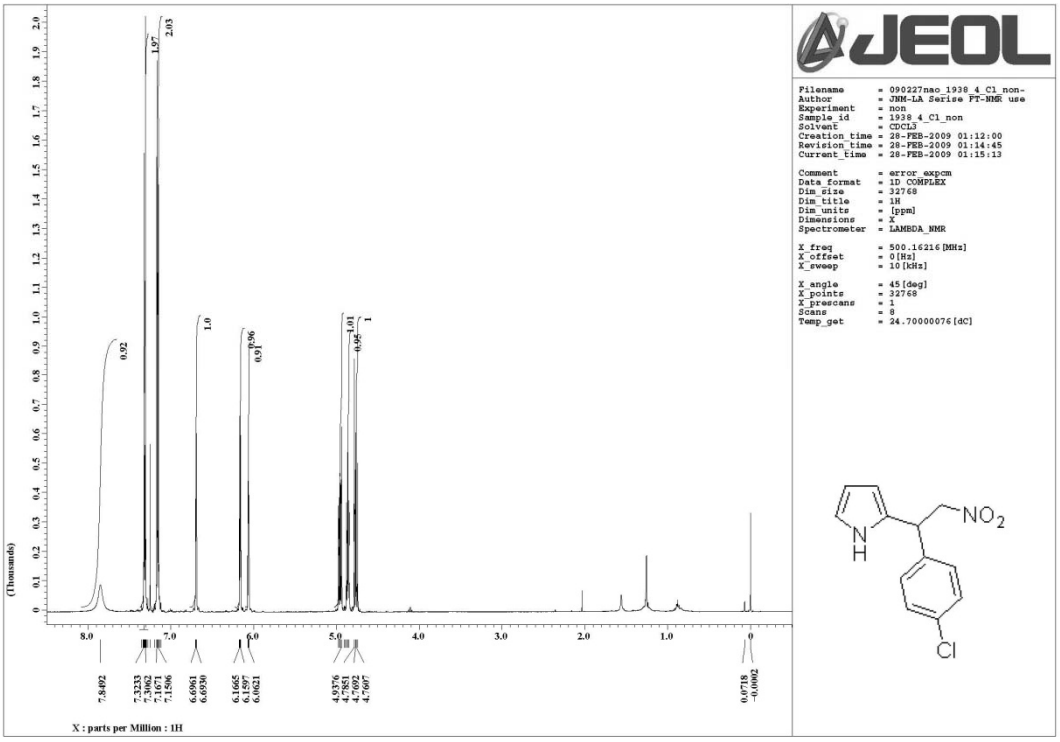
^{1}H-NMR of the product obtained in entry 2, Table 2



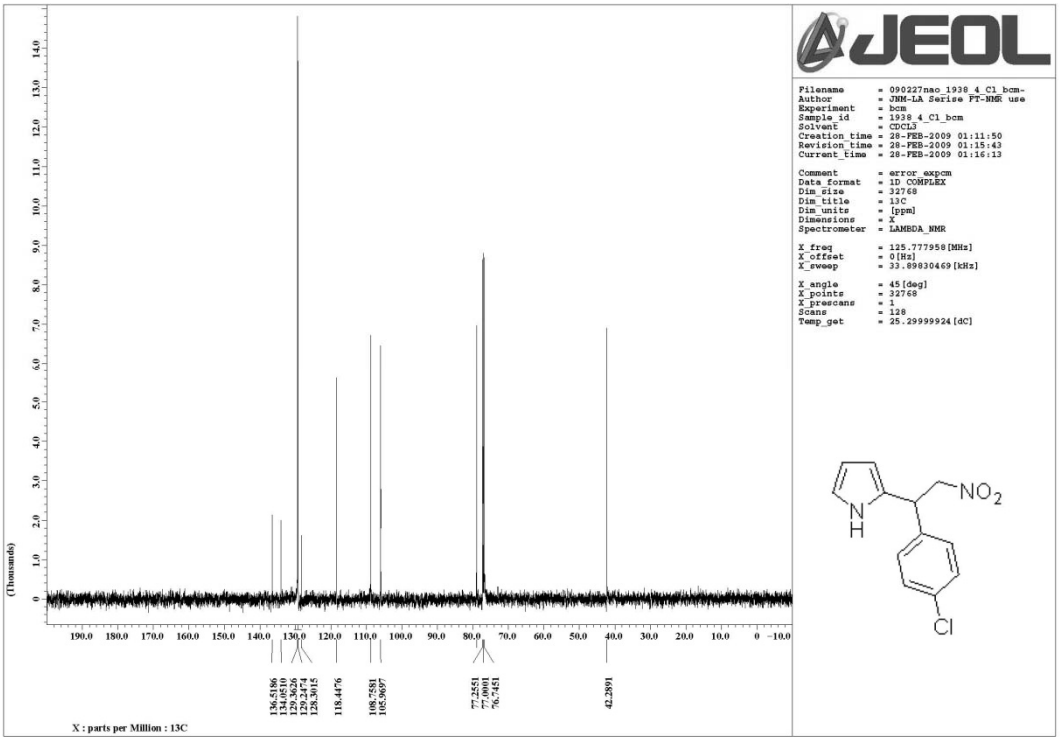
^{13}C-NMR of the product obtained in entry 2, Table 2



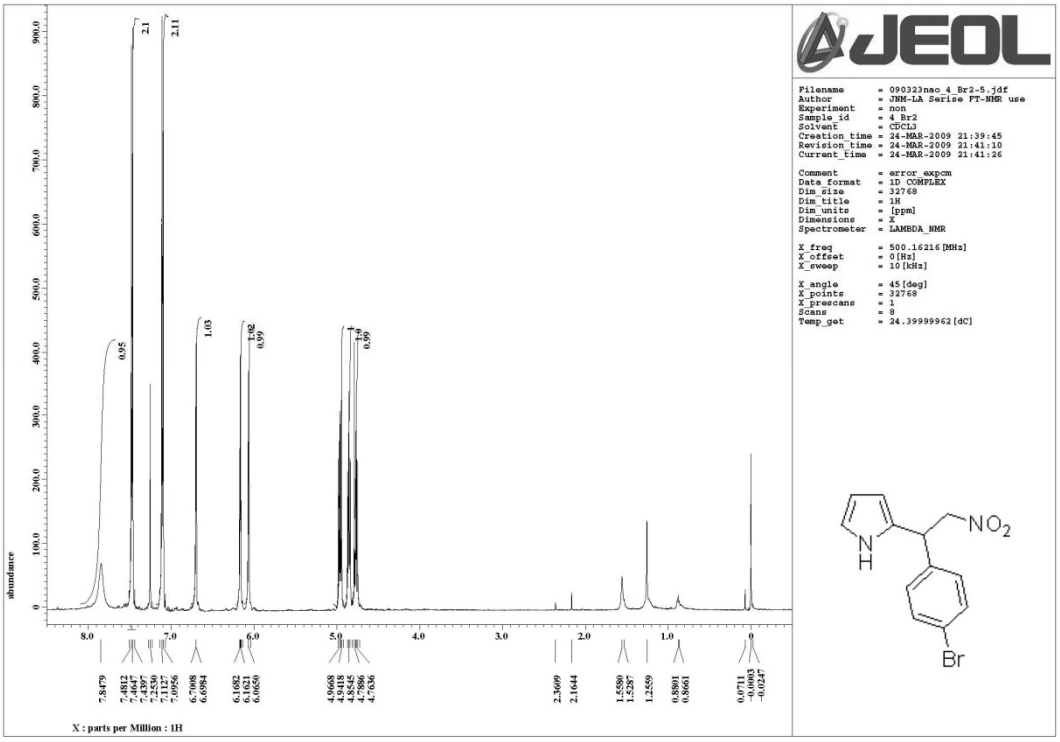
^{1}H-NMR of the product obtained in entry 3, Table 2



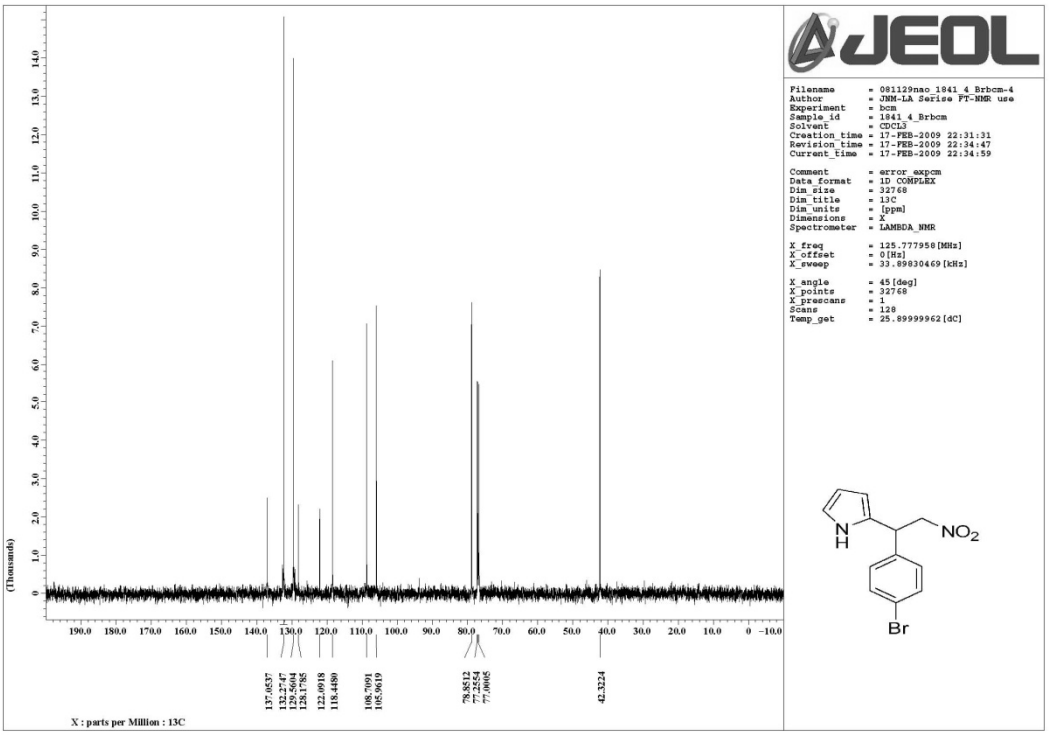
^{13}C-NMR of the product obtained in entry 3, Table 2



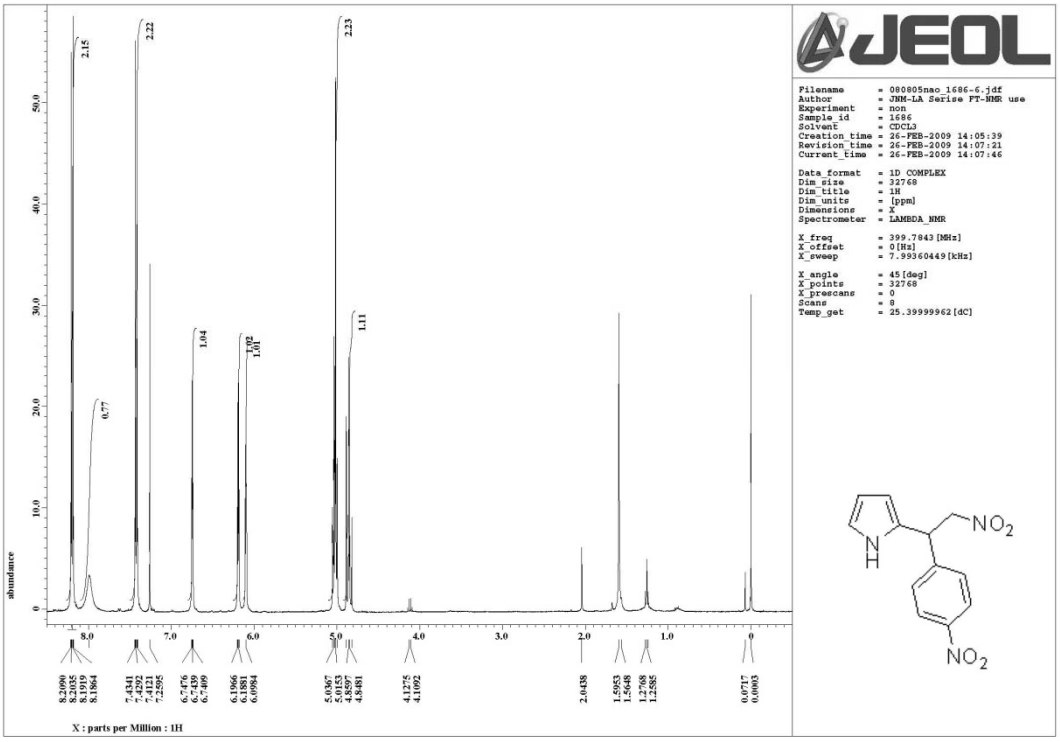
^{1}H-NMR of the product obtained in entry 4, Table 2



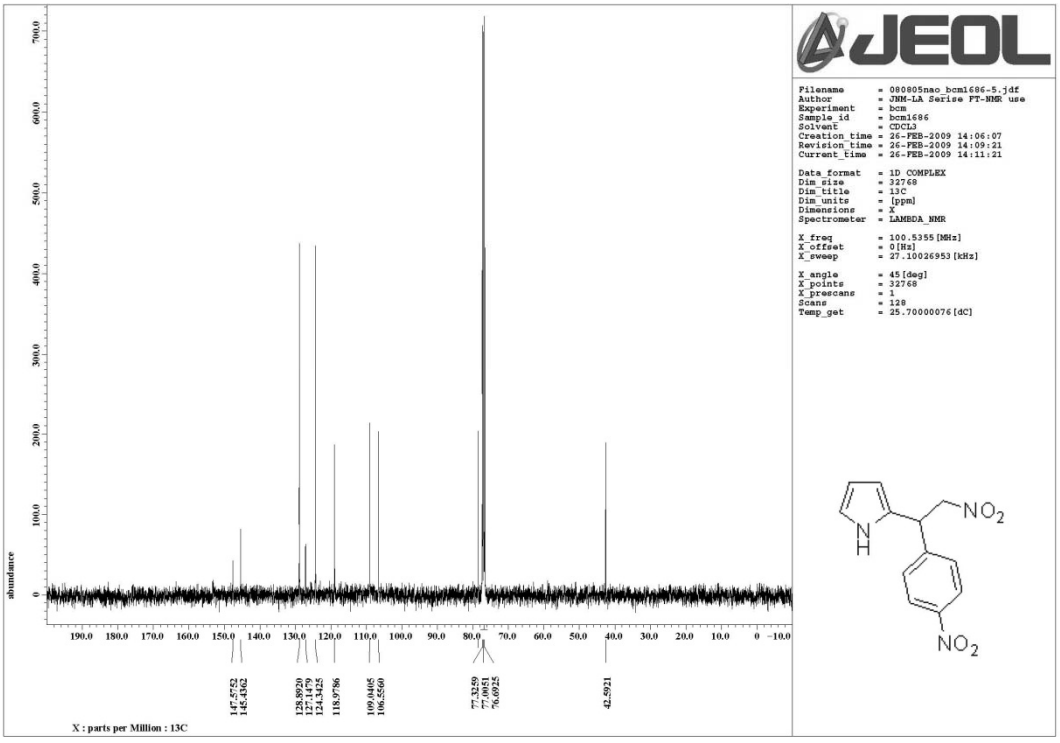
^{13}C-NMR of the product obtained in entry 4, Table 2



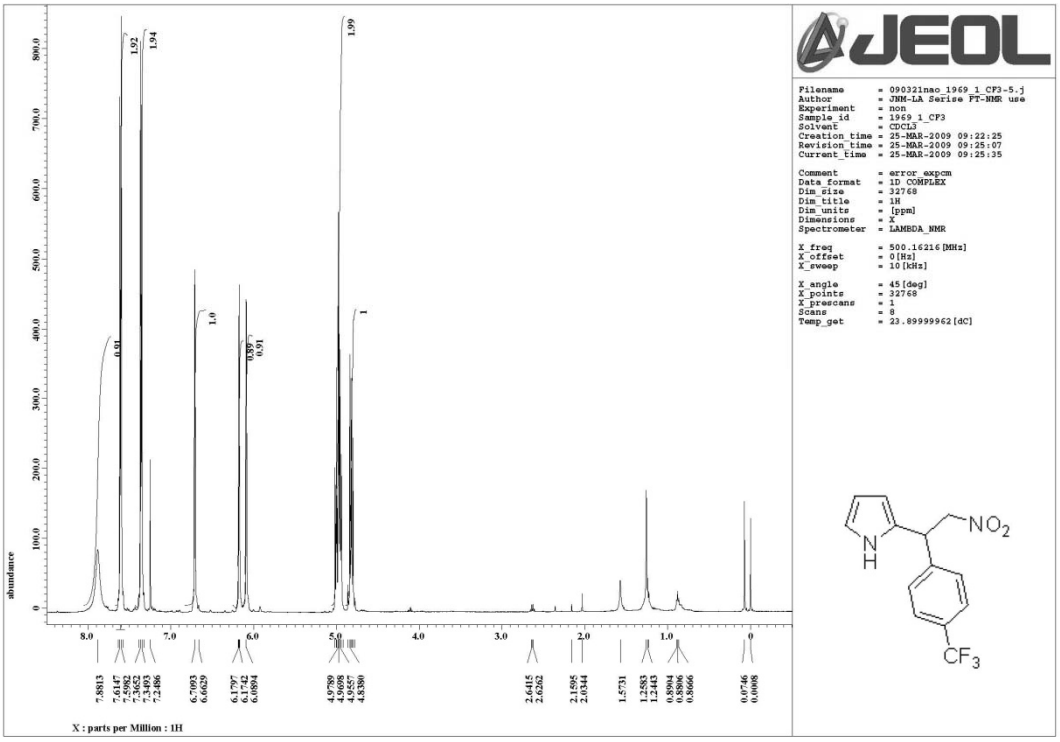
^{1}H-NMR of the product obtained in entry 5, Table 2



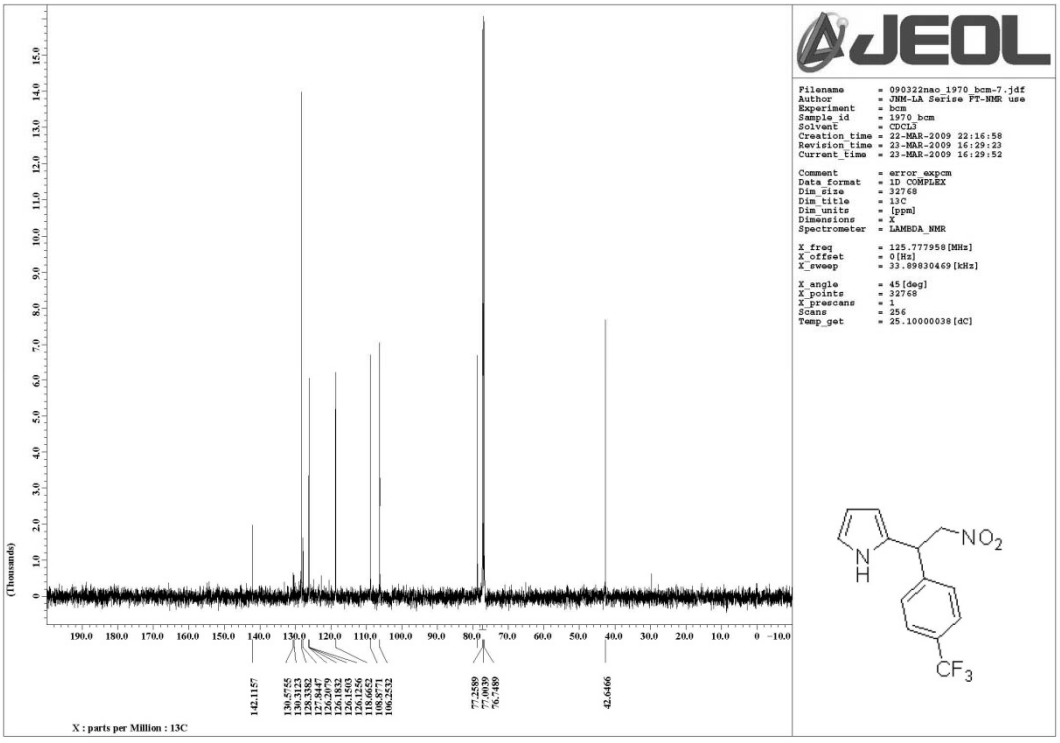
^{13}C-NMR of the product obtained in entry 5, Table 2



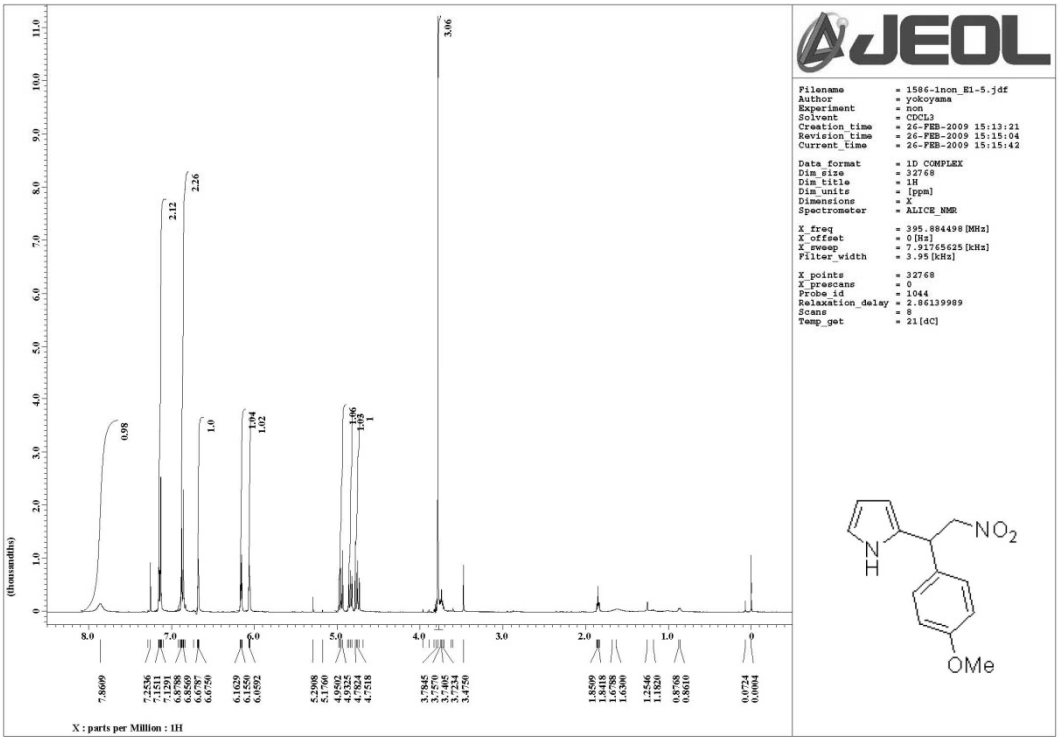
^{1}H-NMR of the product obtained in entry 6, Table 2



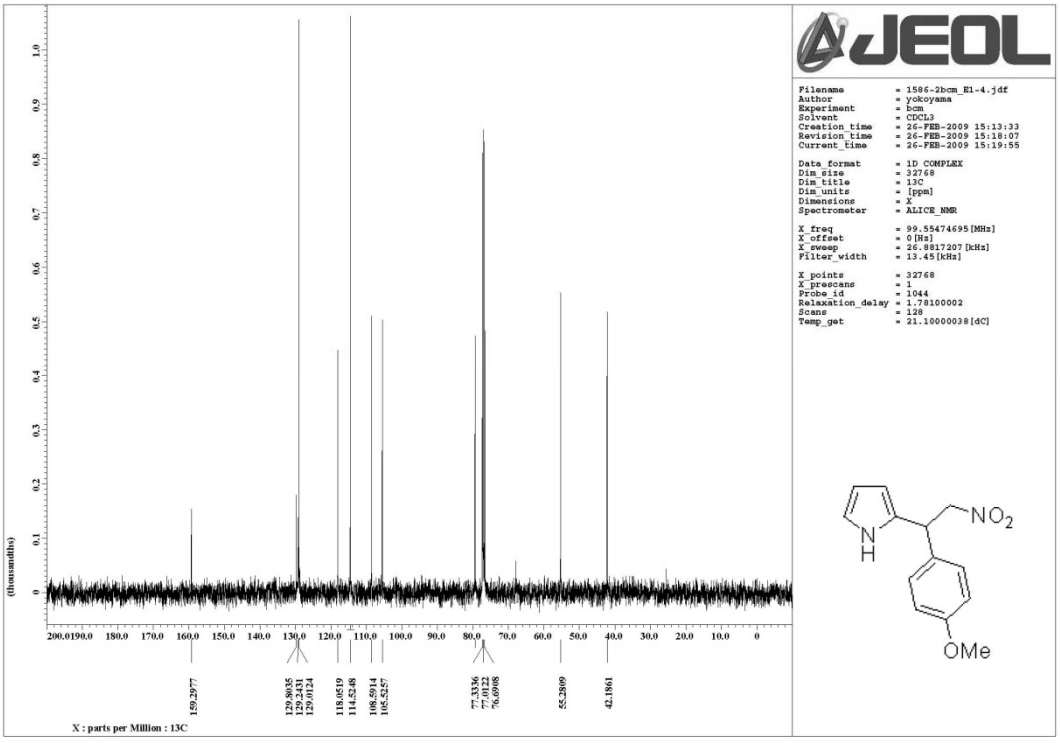
^{13}C-NMR of the product obtained in entry 6, Table 2



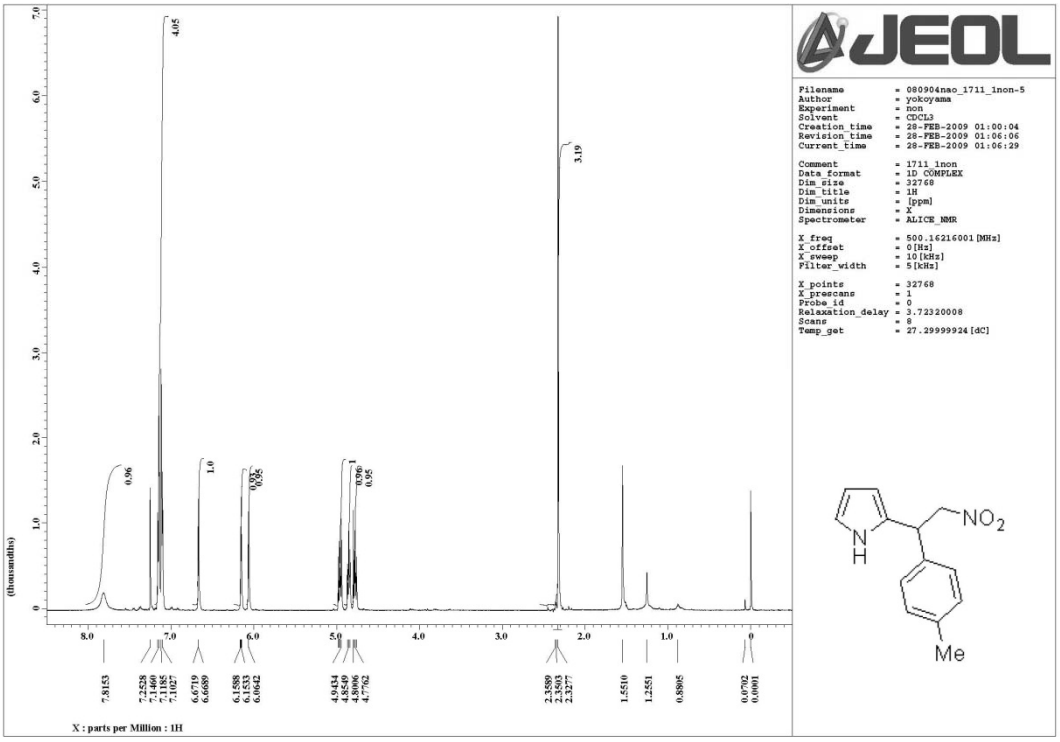
^{1}H-NMR of the product obtained in entry 7, Table 2



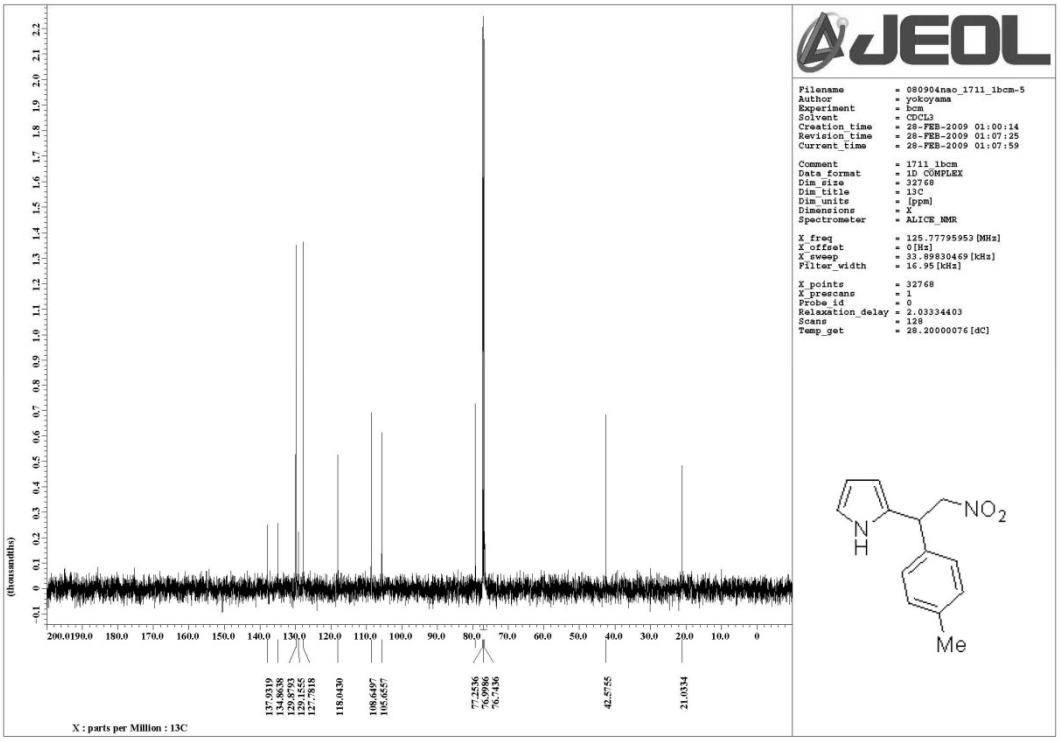
^{13}C-NMR of the product obtained in entry 7, Table 2



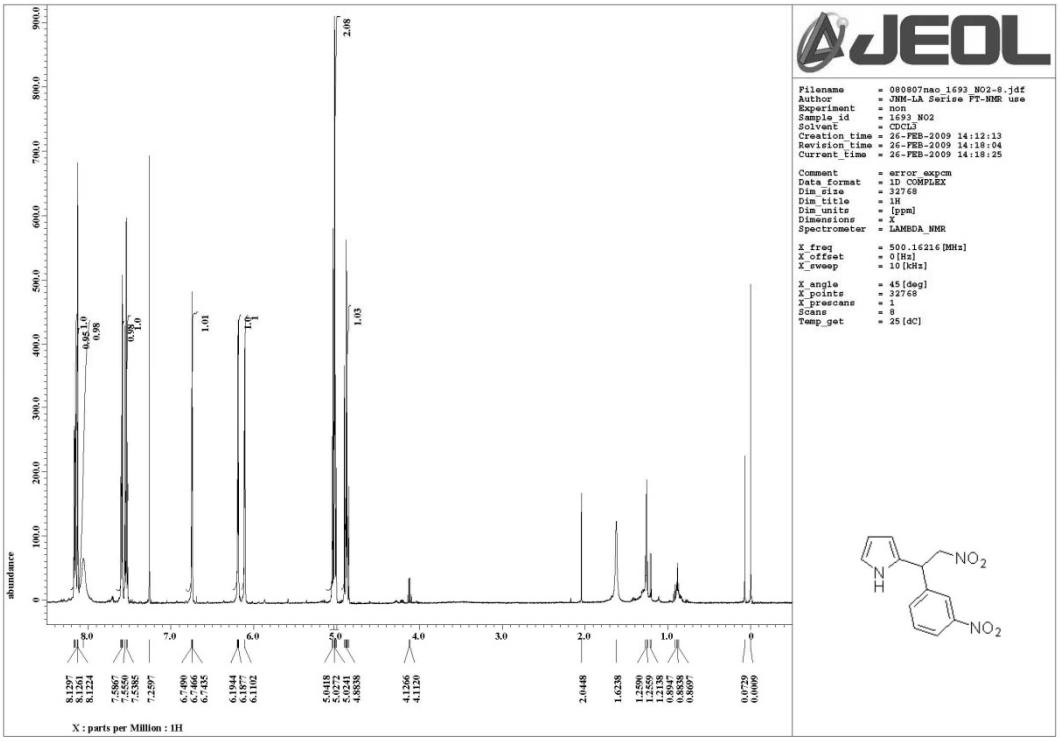
^{1}H-NMR of the product obtained in entry 8, Table 2



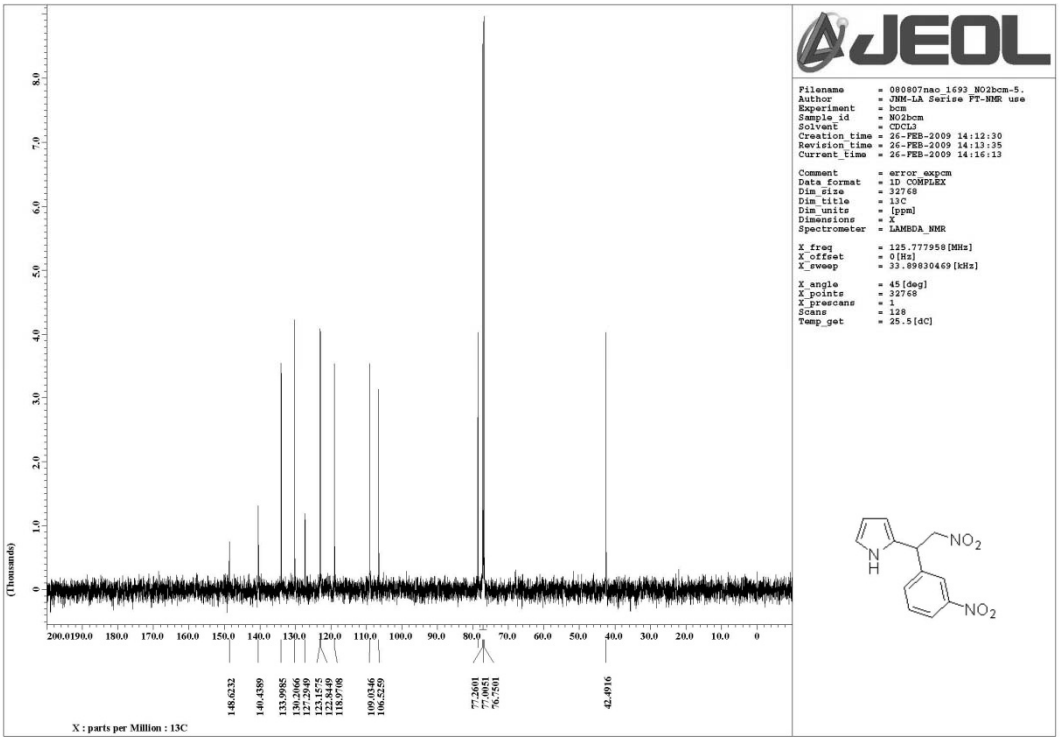
^{13}C-NMR of the product obtained in entry 8, Table 2



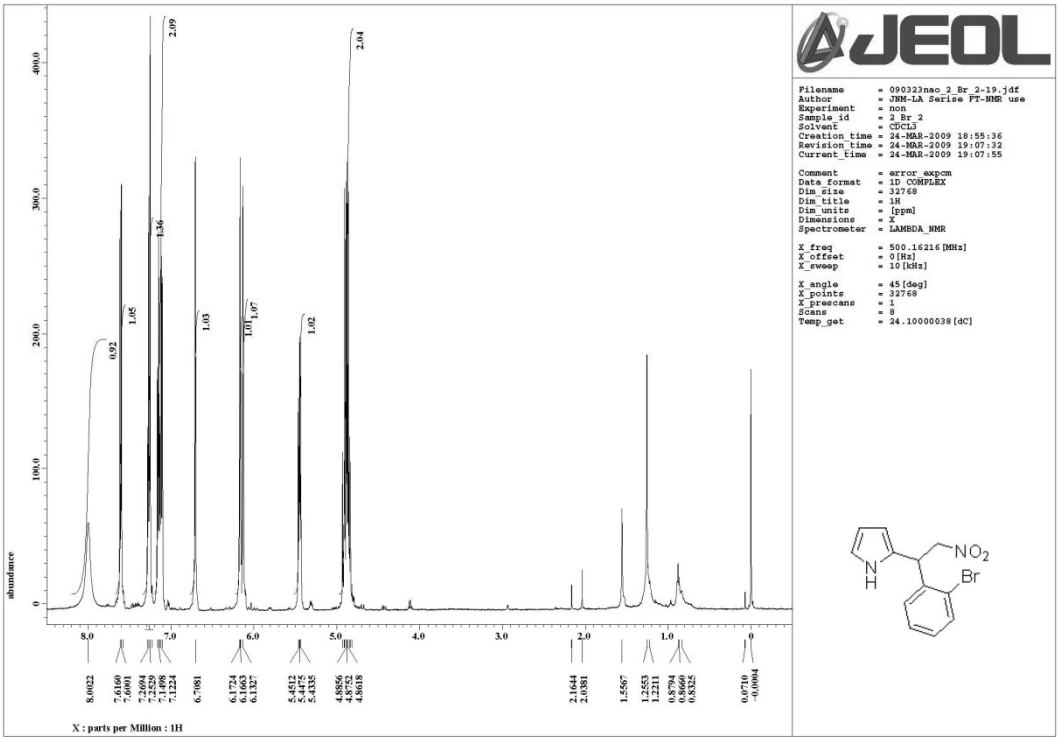
^{1}H-NMR of the product obtained in entry 9, Table 2



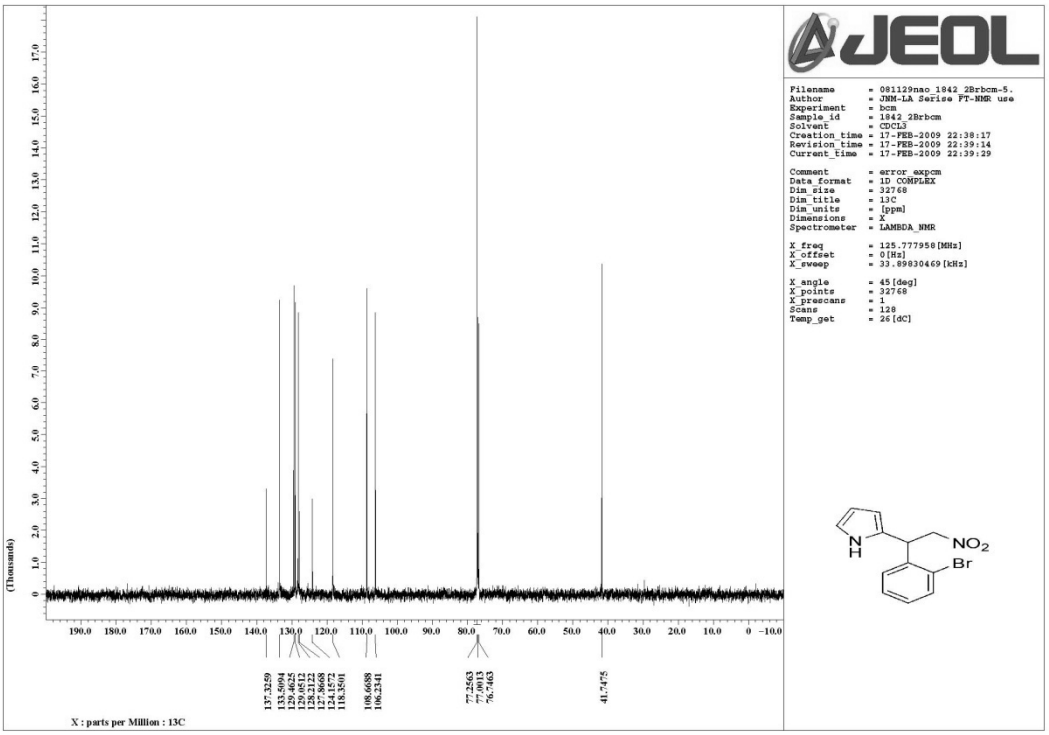
^{13}C-NMR of the product obtained in entry 9, Table 2



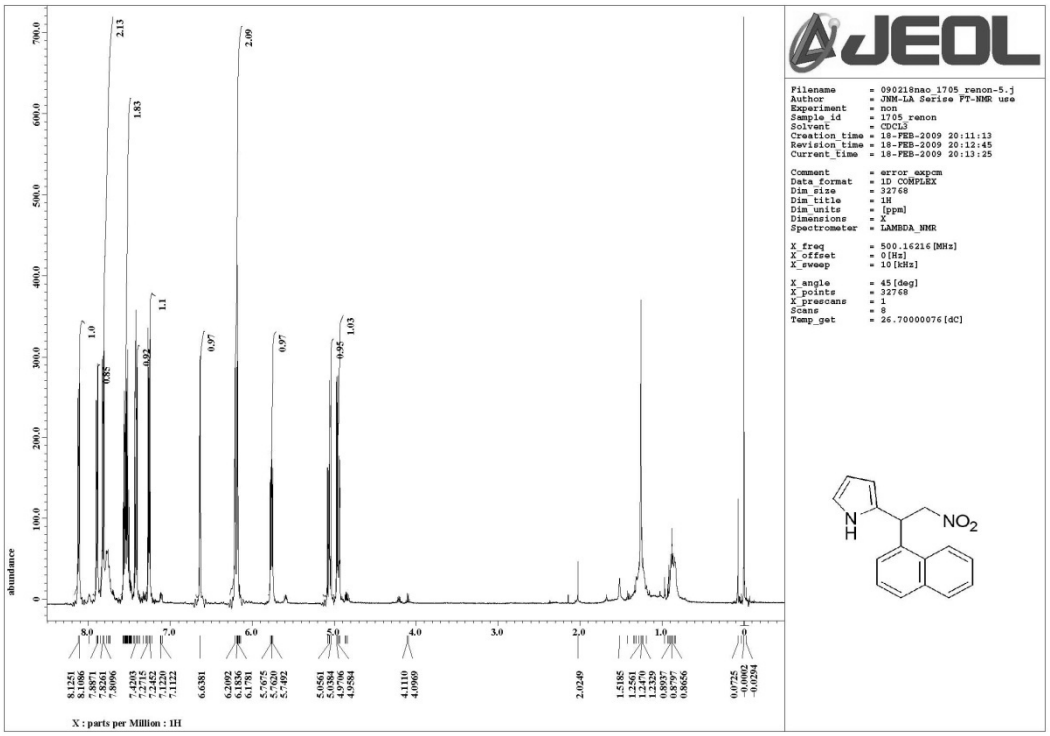
^{1}H-NMR of the product obtained in entry 10, Table 2



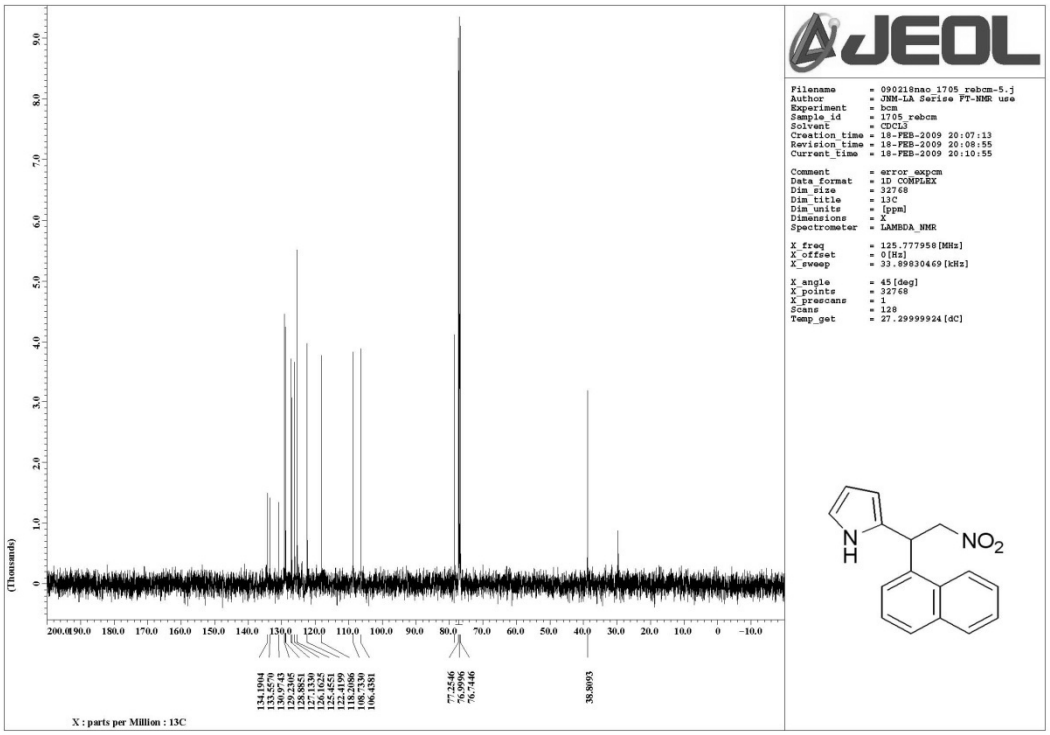
^{13}C-NMR of the product obtained in entry 10, Table 2



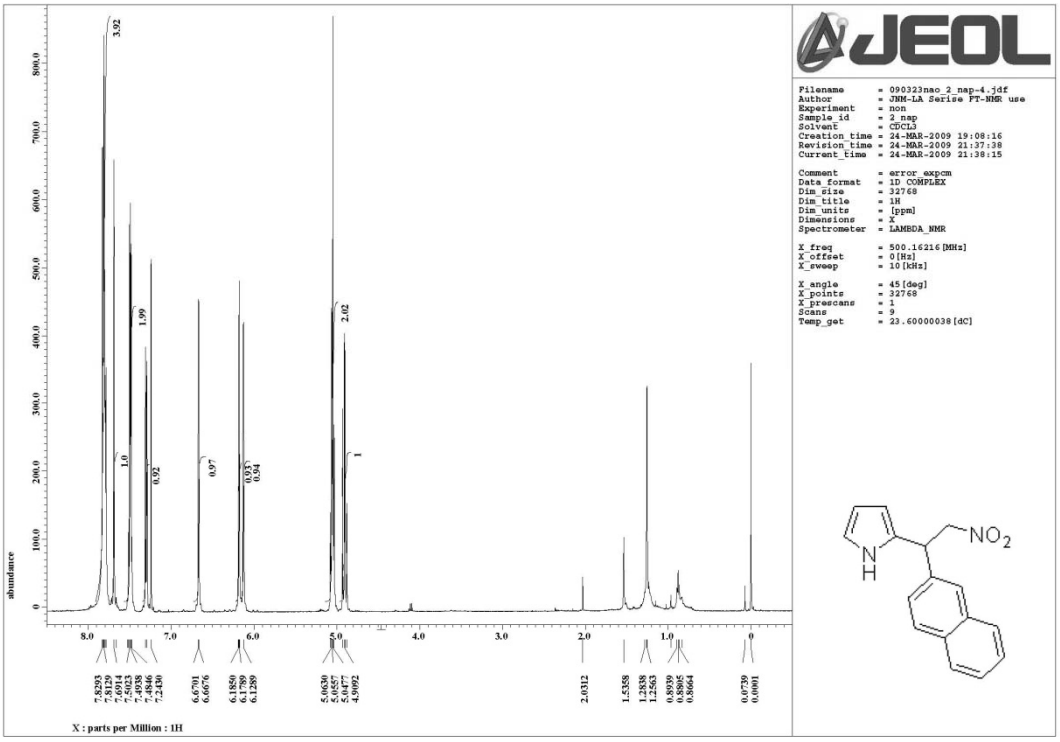
^{1}H-NMR of the product obtained in entry 11, Table 2



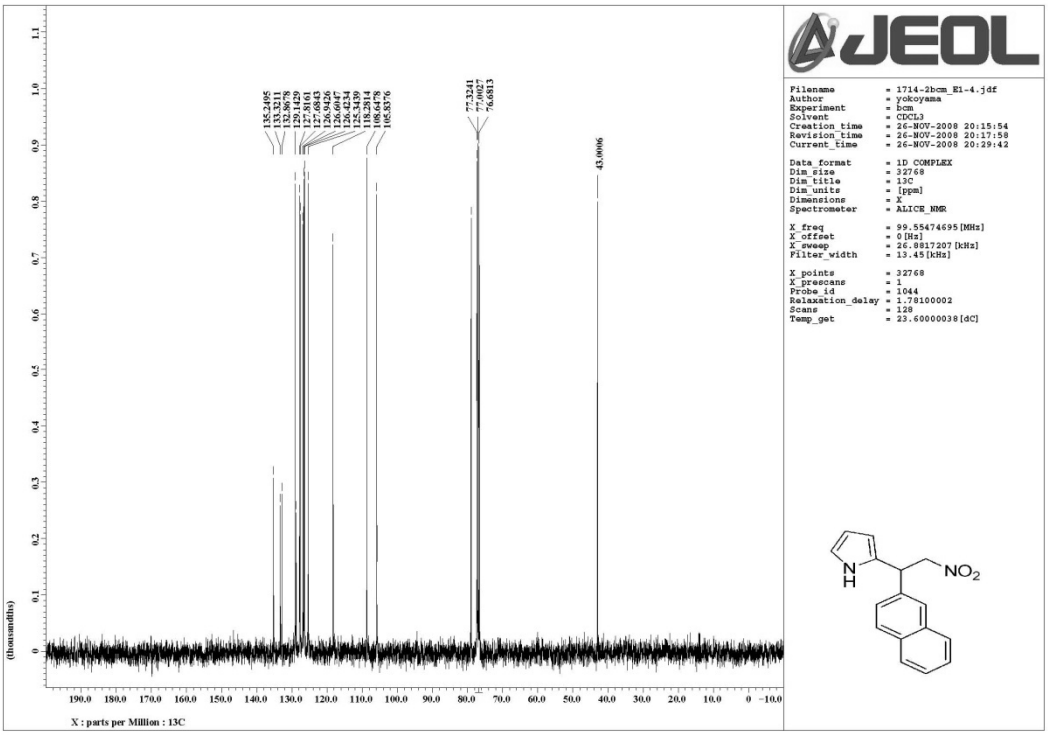
^{13}C-NMR of the product obtained in entry 11, Table 2



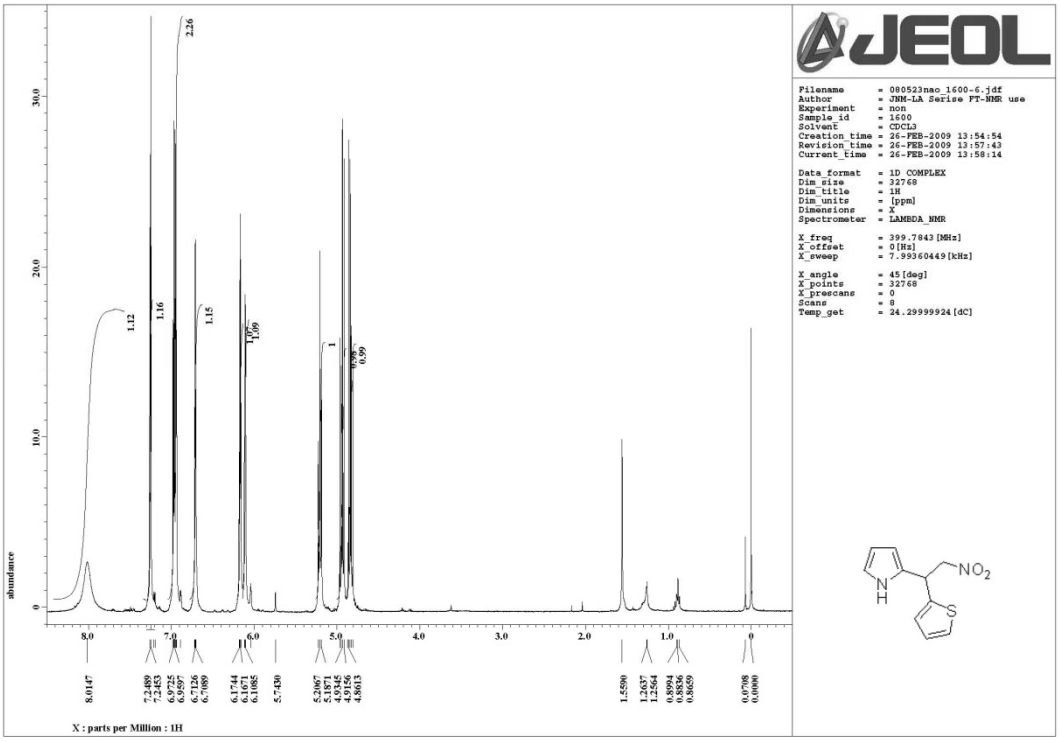
^{1}H-NMR of the product obtained in entry 12, Table 2



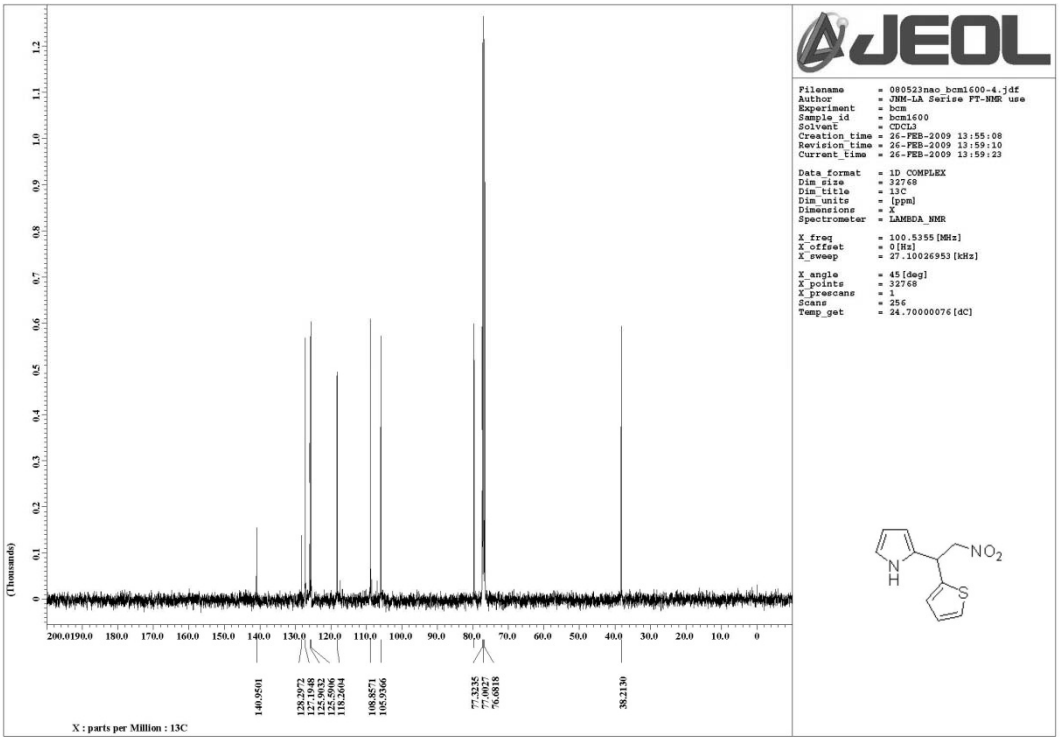
^{13}C-NMR of the product obtained in entry 12, Table 2



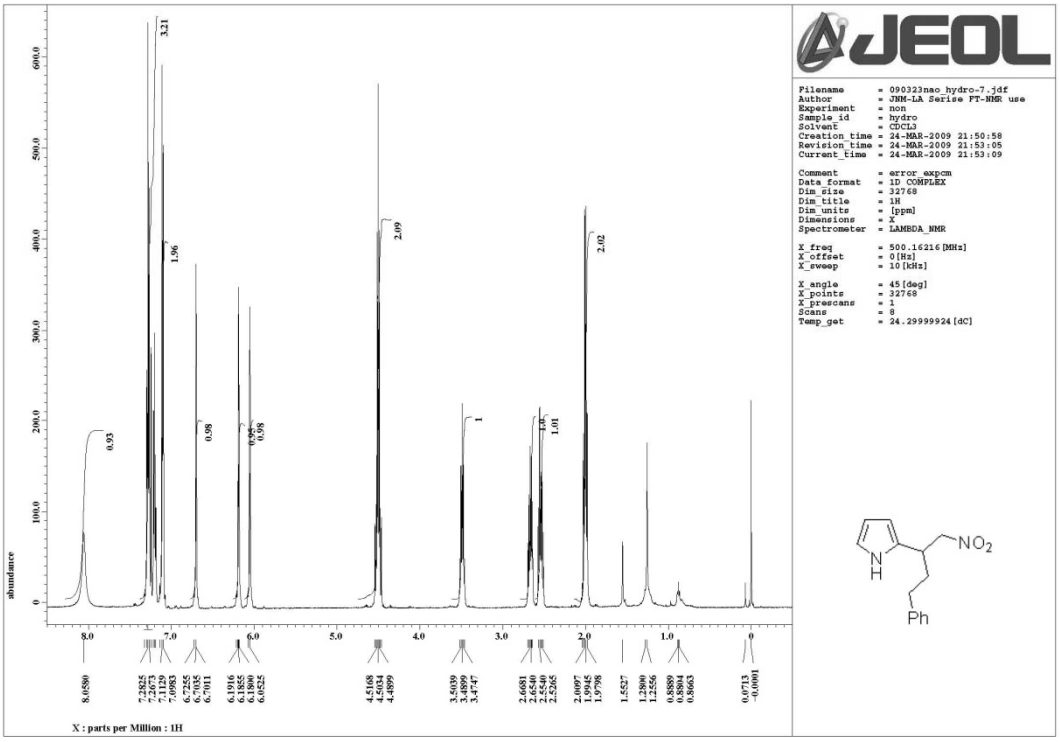
^{1}H-NMR of the product obtained in entry 13, Table 2



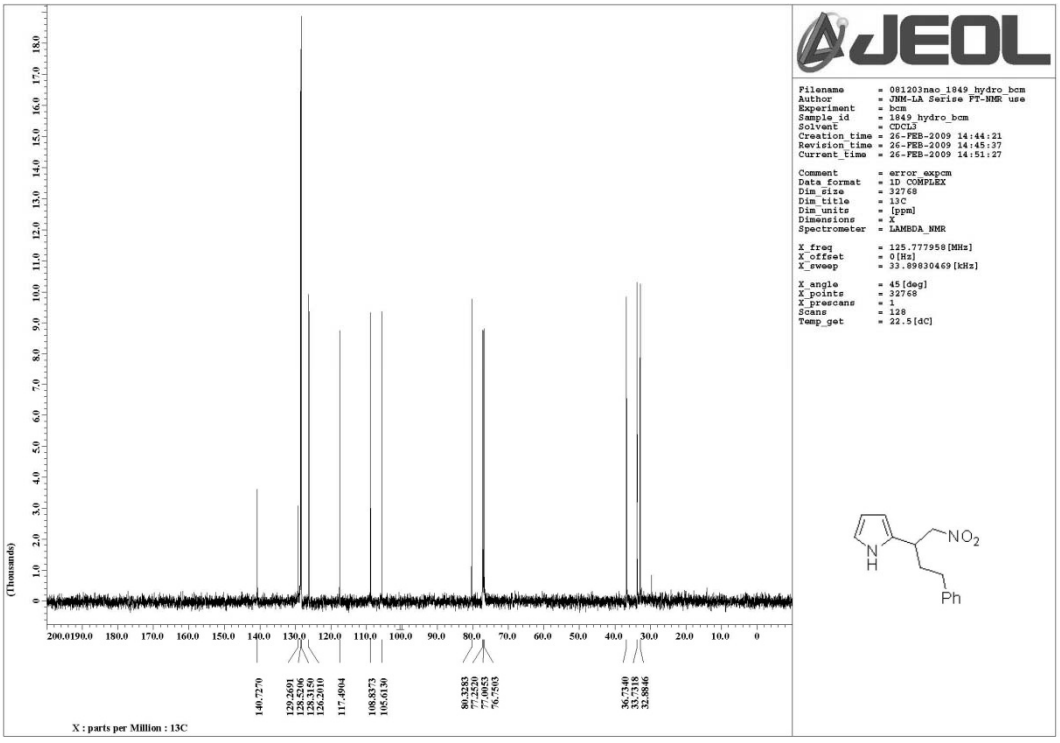
^{13}C-NMR of the product obtained in entry 13, Table 2



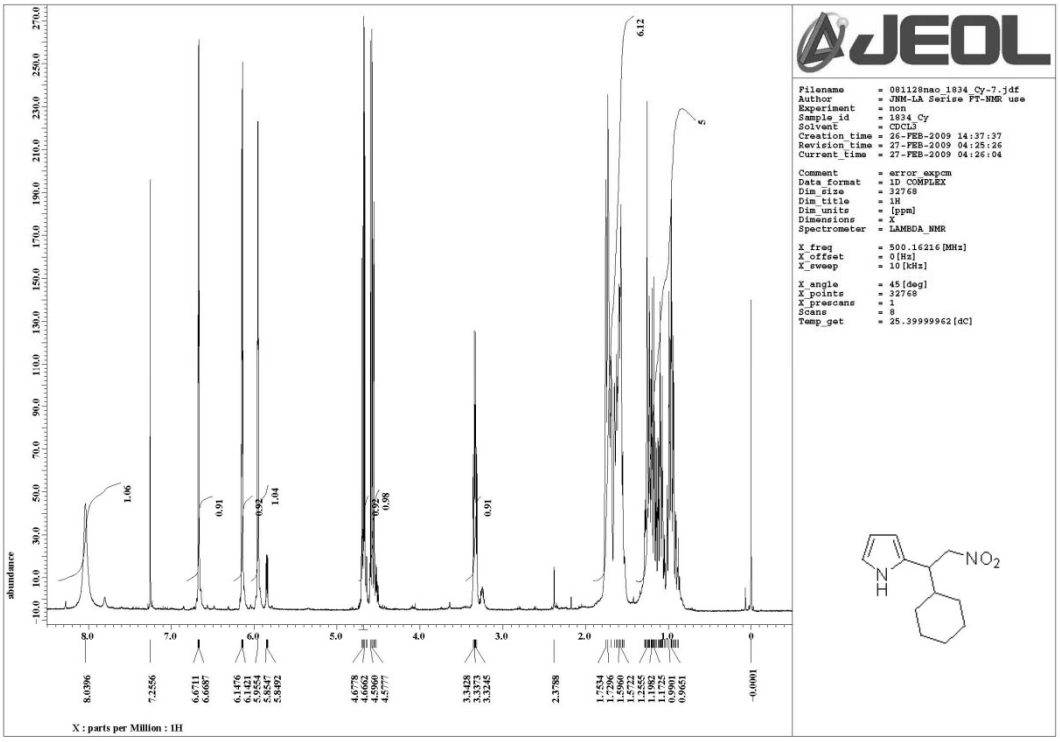
^{1}H-NMR of the product obtained in entry 14, Table 2



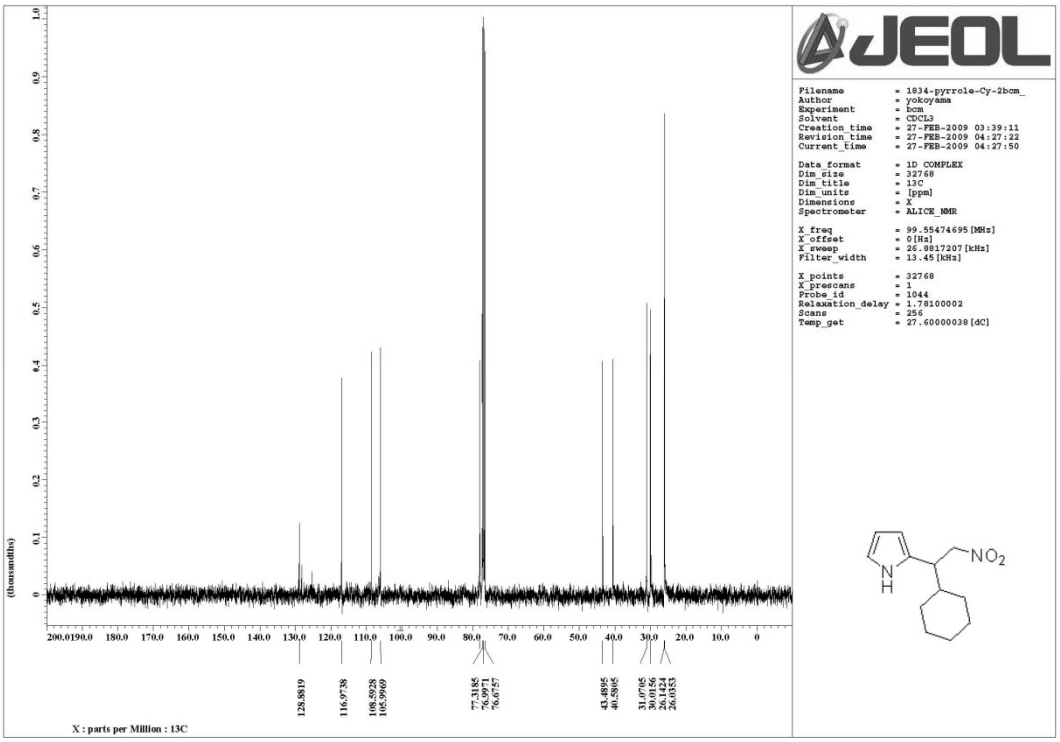
^{13}C-NMR of the product obtained in entry 14, Table 2



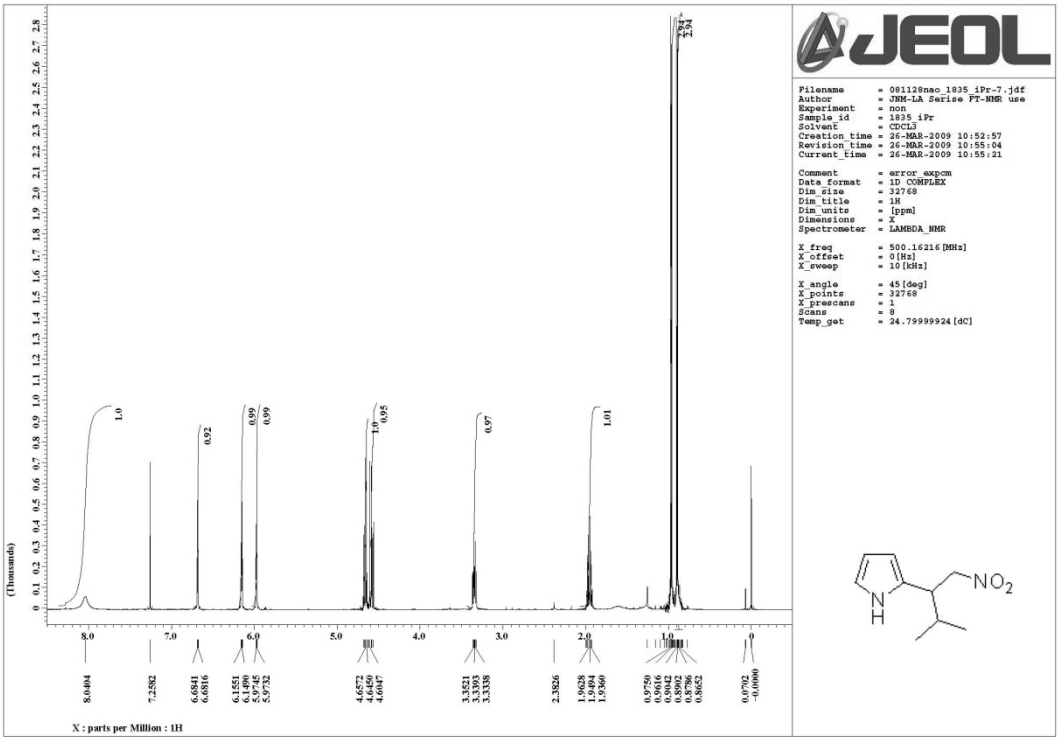
^{1}H-NMR of the product obtained in entry 15, Table 2



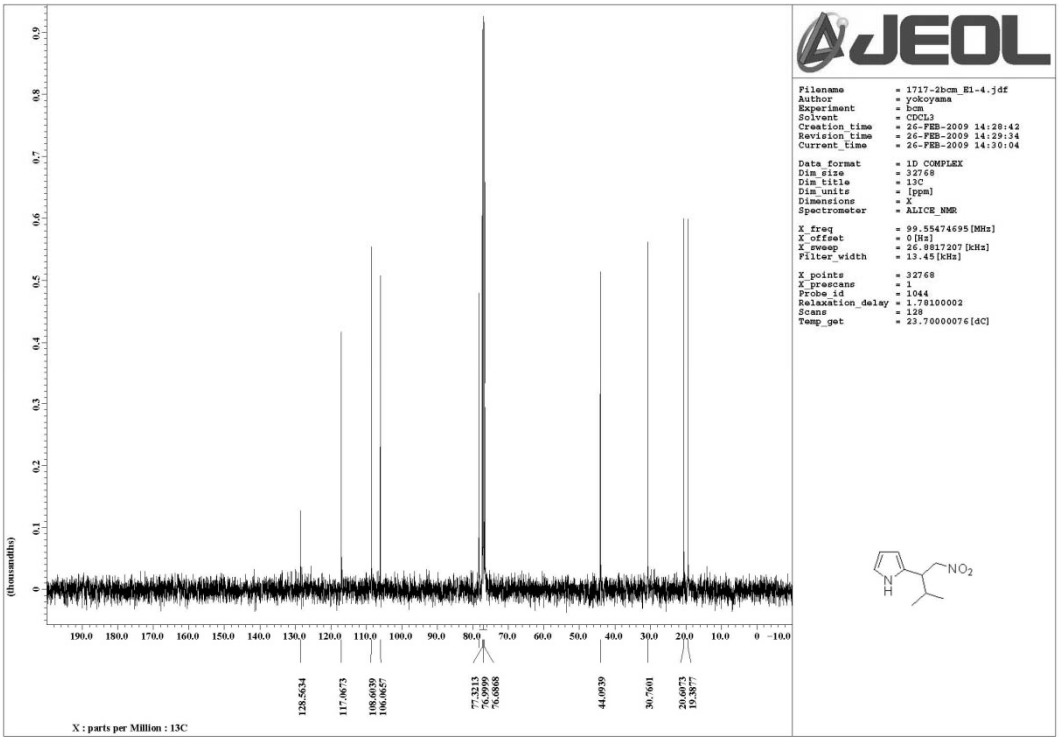
^{13}C-NMR of the product obtained in entry 15, Table 2



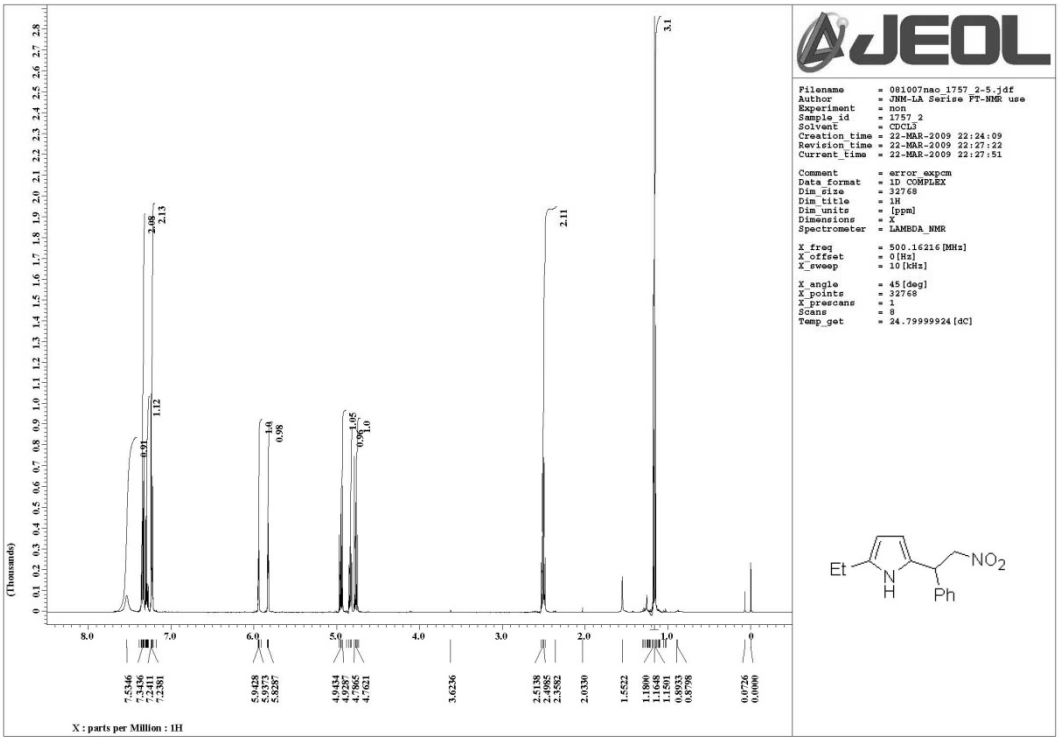
^{1}H-NMR of the product obtained in entry 16, Table 2



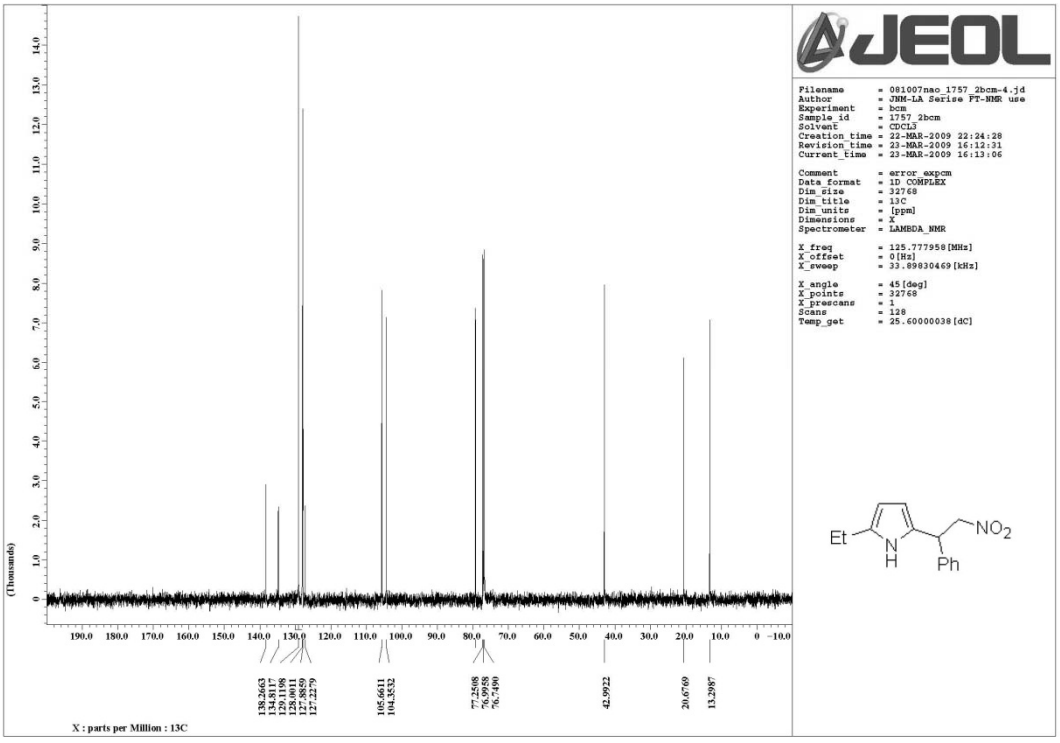
^{13}C-NMR of the product obtained in entry 16, Table 2



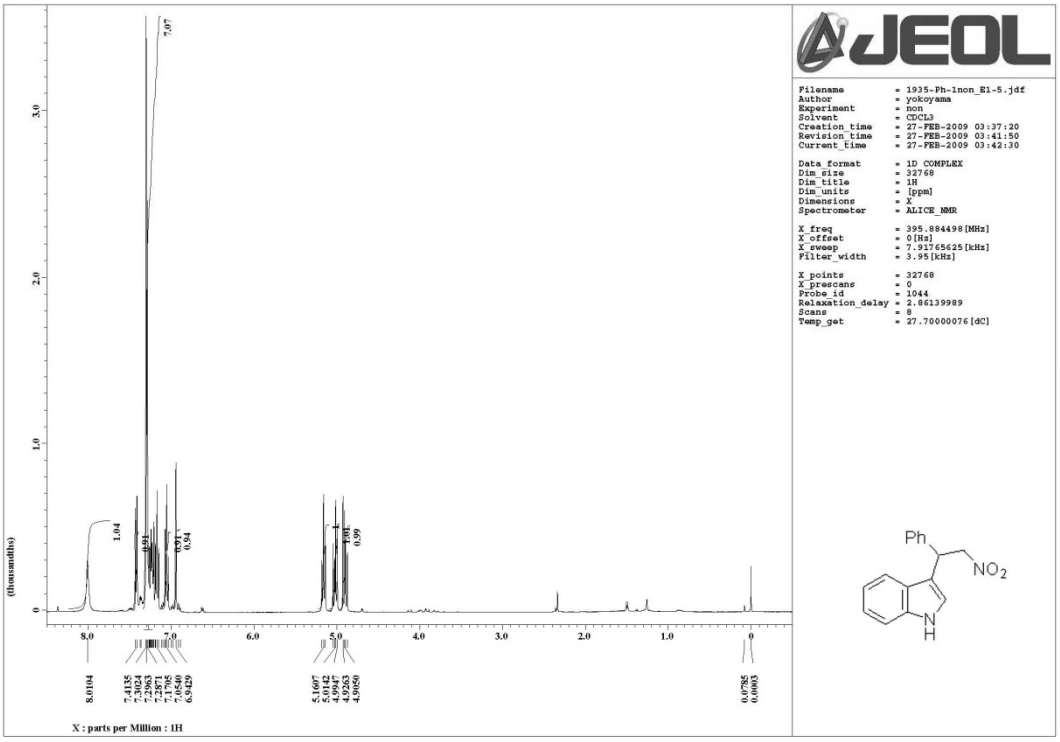
^{1}H-NMR of the product obtained in ref 11



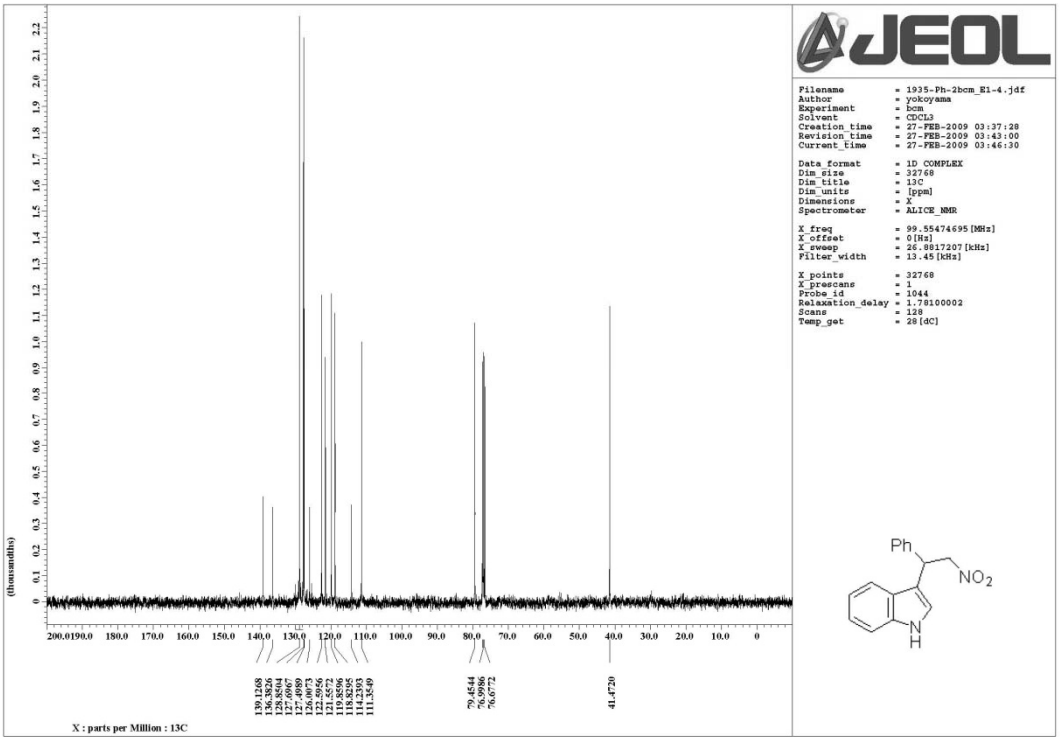
^{13}C-NMR of the product obtained in ref 11



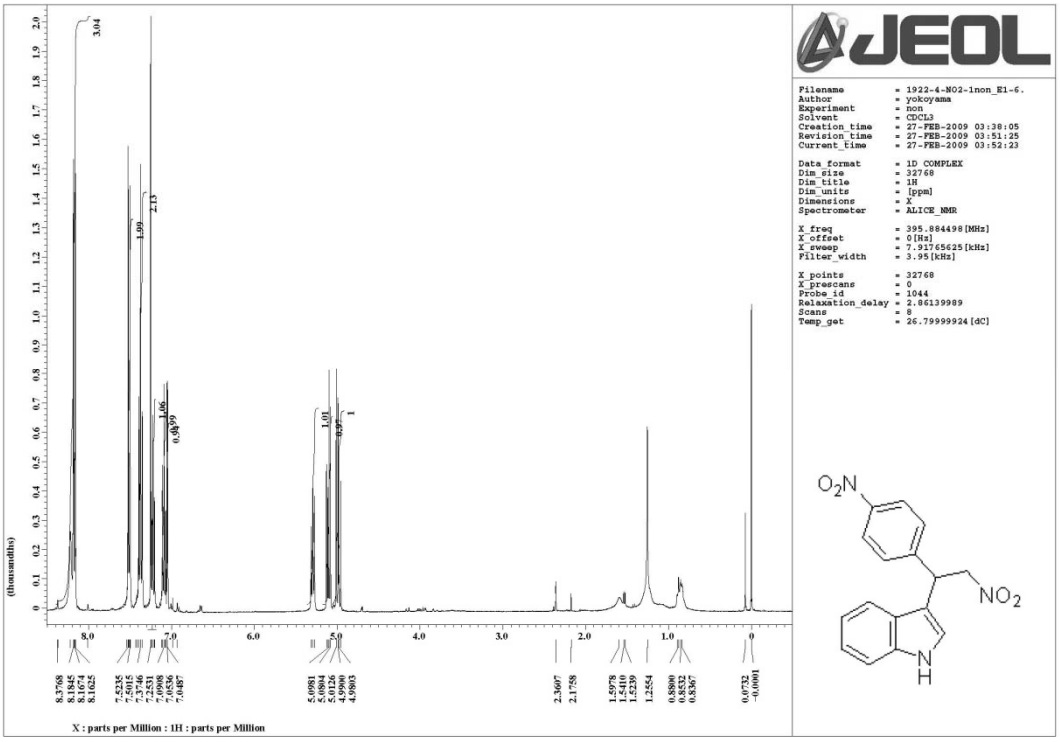
^{1}H-NMR of the product obtained in entry 1, Table 3



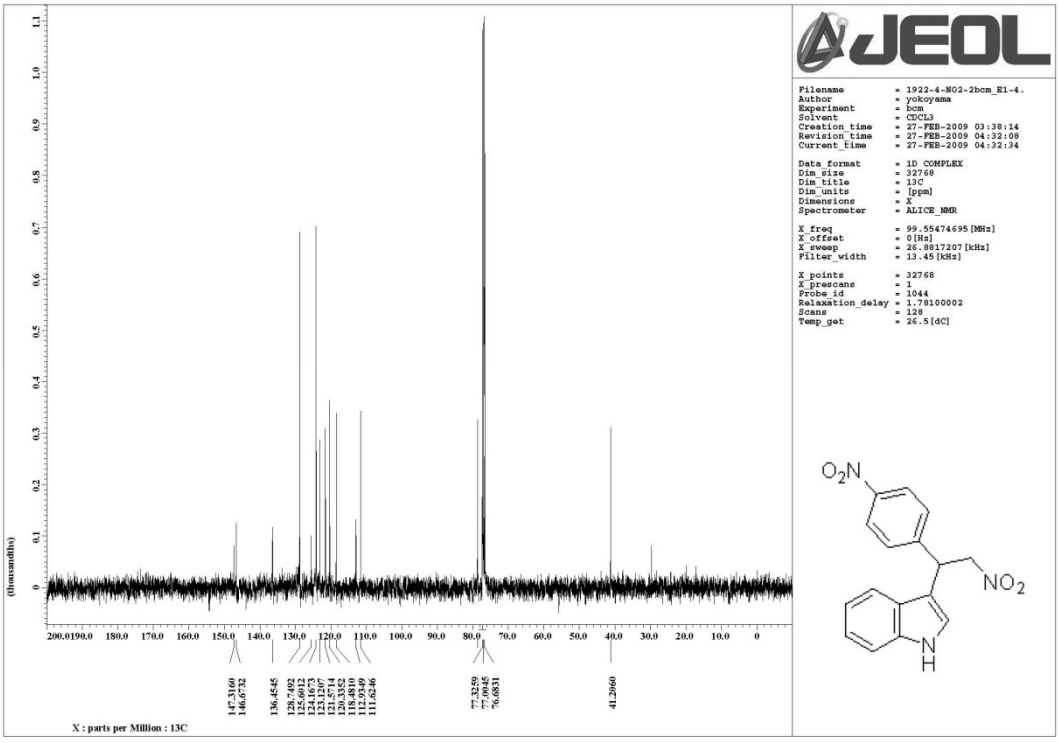
^{13}C-NMR of the product obtained in entry 1, Table 3



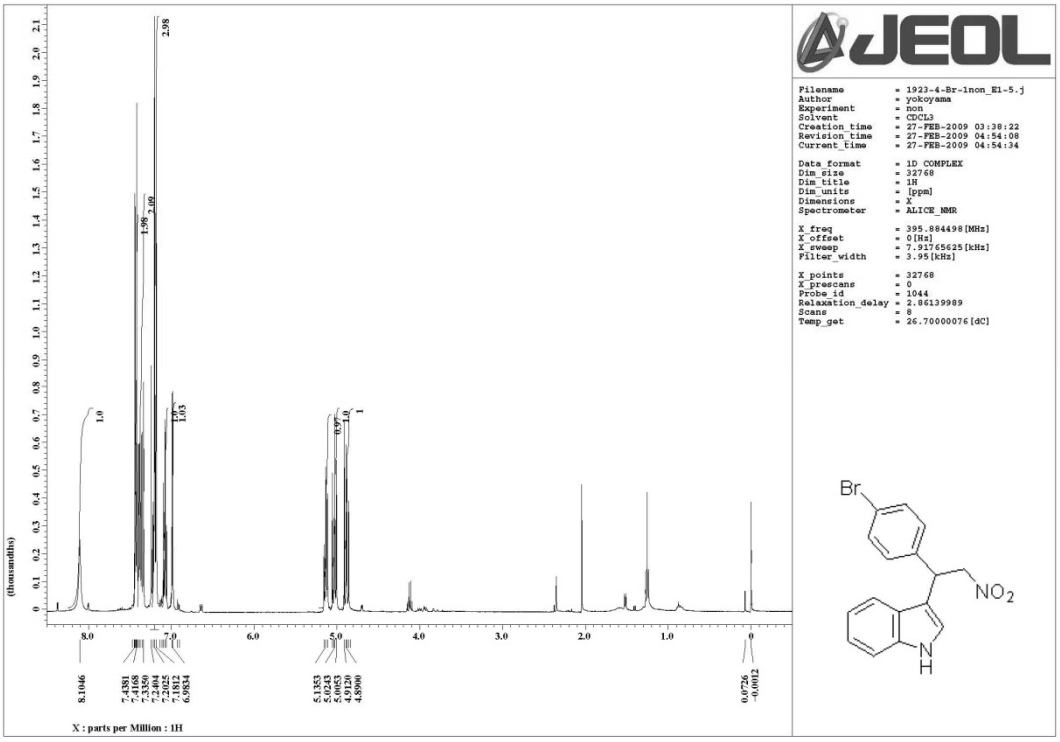
^{1}H-NMR of the product obtained in entry 3, Table 3



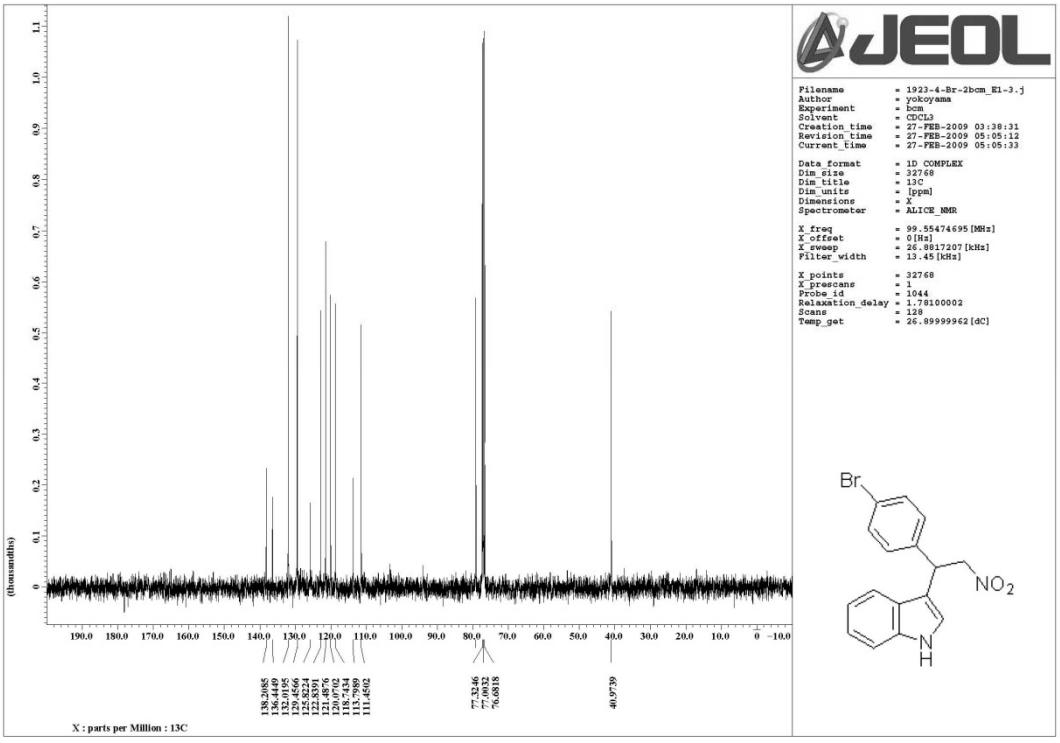
^{13}C-NMR of the product obtained in entry 3, Table 3



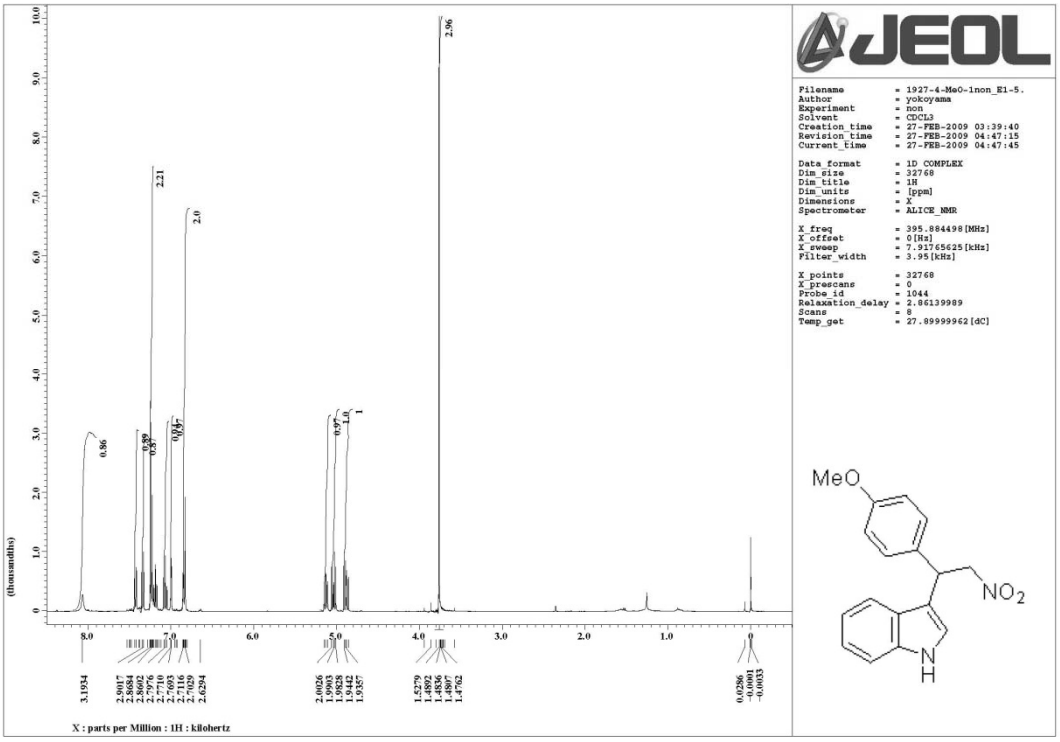
^{1}H-NMR of the product obtained in entry 4, Table 3



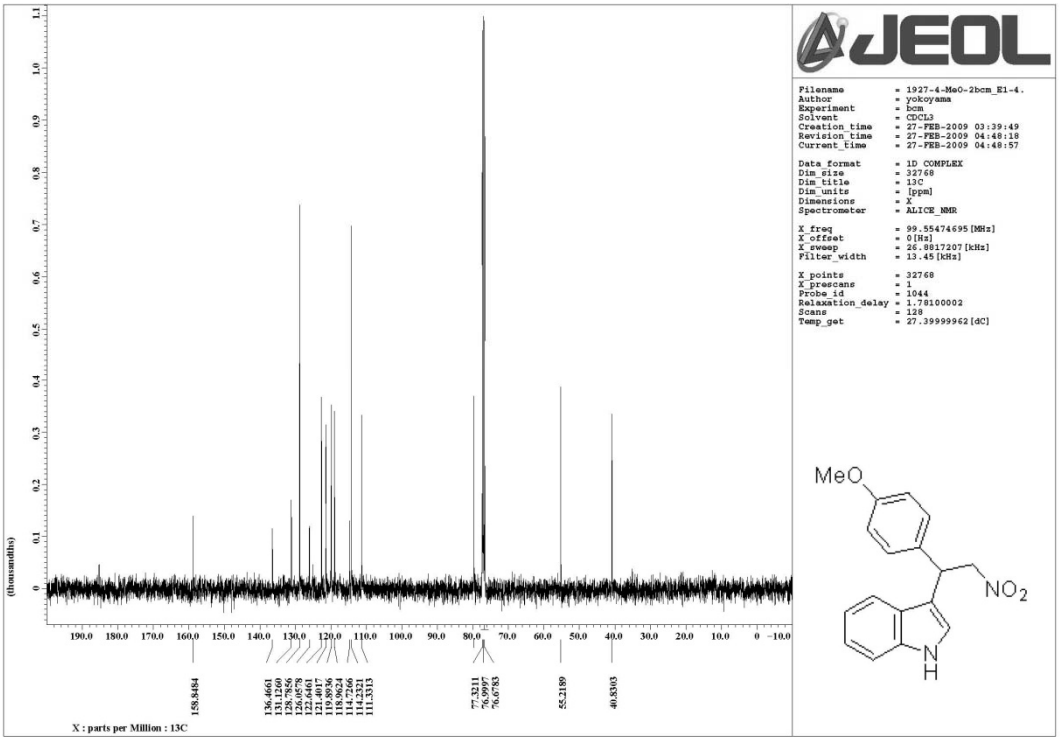
^{13}C-NMR of the product obtained in entry 4, Table 3



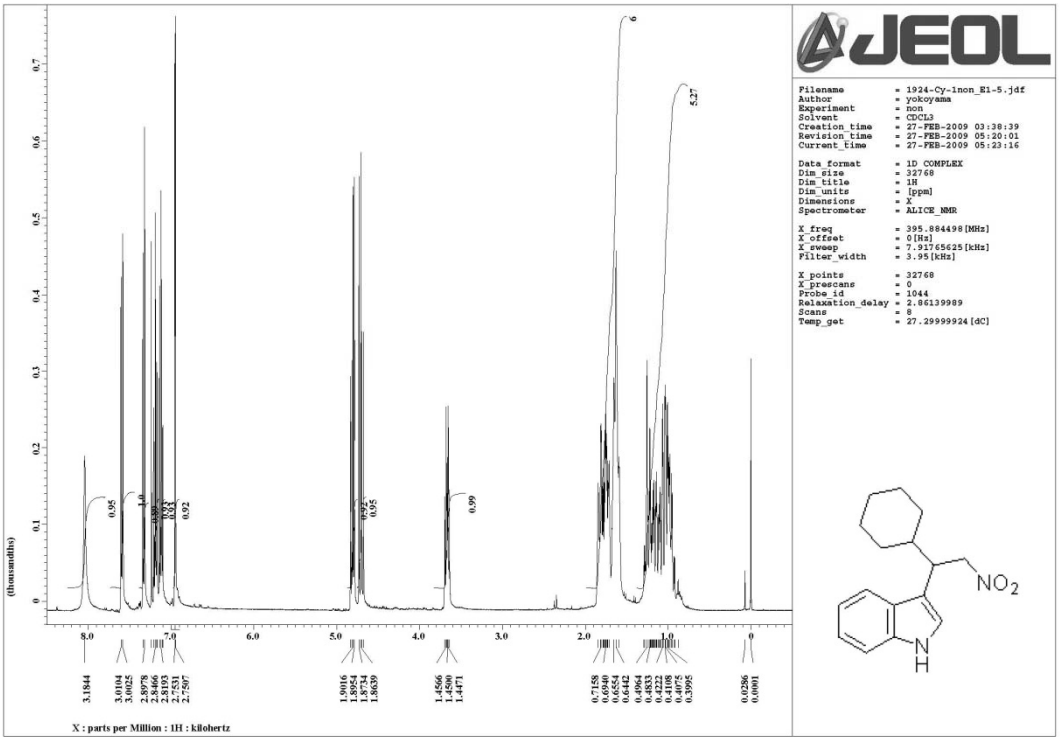
^{1}H-NMR of the product obtained in entry 5, Table 3



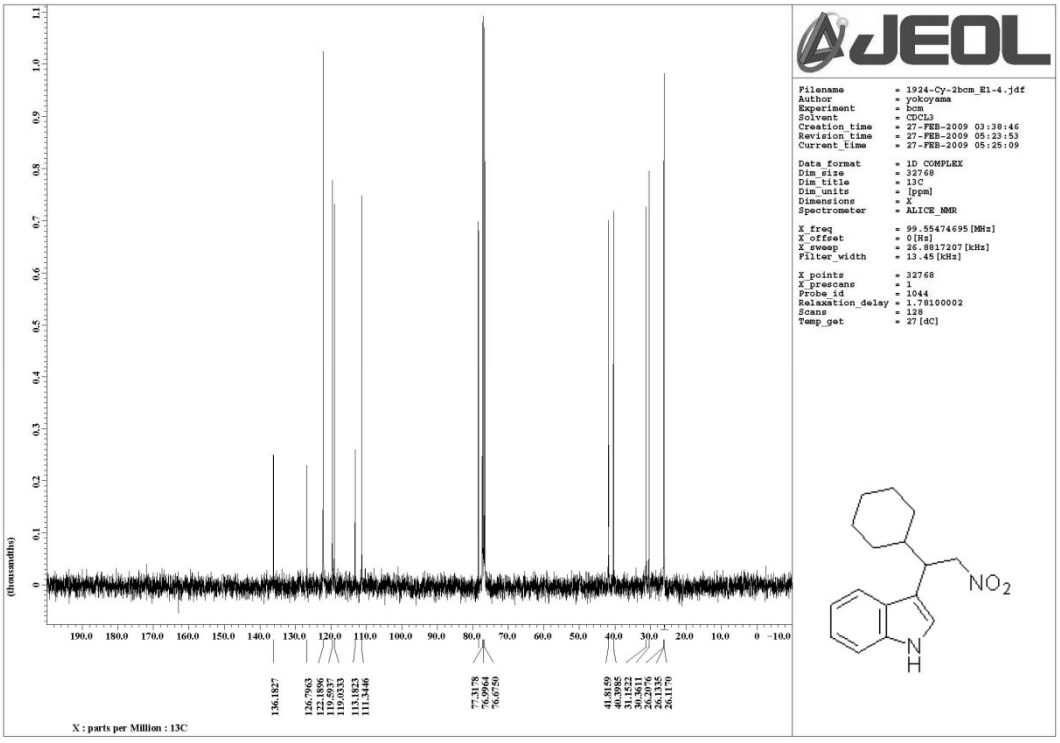
^{13}C-NMR of the product obtained in entry 5, Table 3



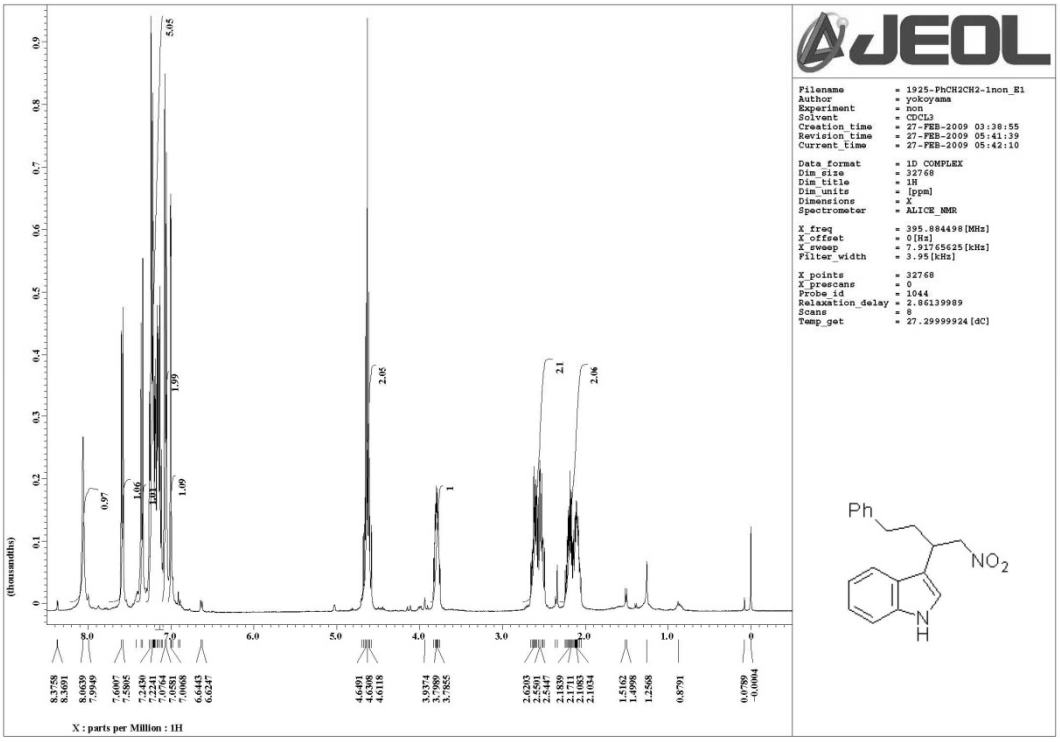
^{1}H-NMR of the product obtained in entry 6, Table 3



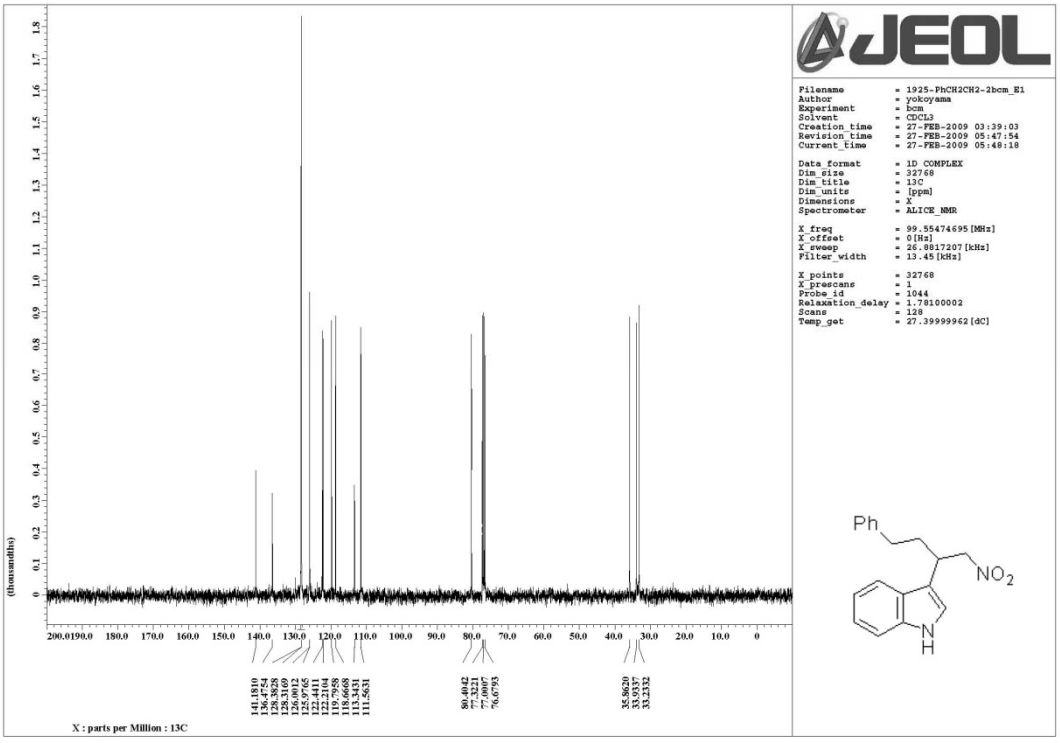
^{13}C-NMR of the product obtained in entry 6, Table 3



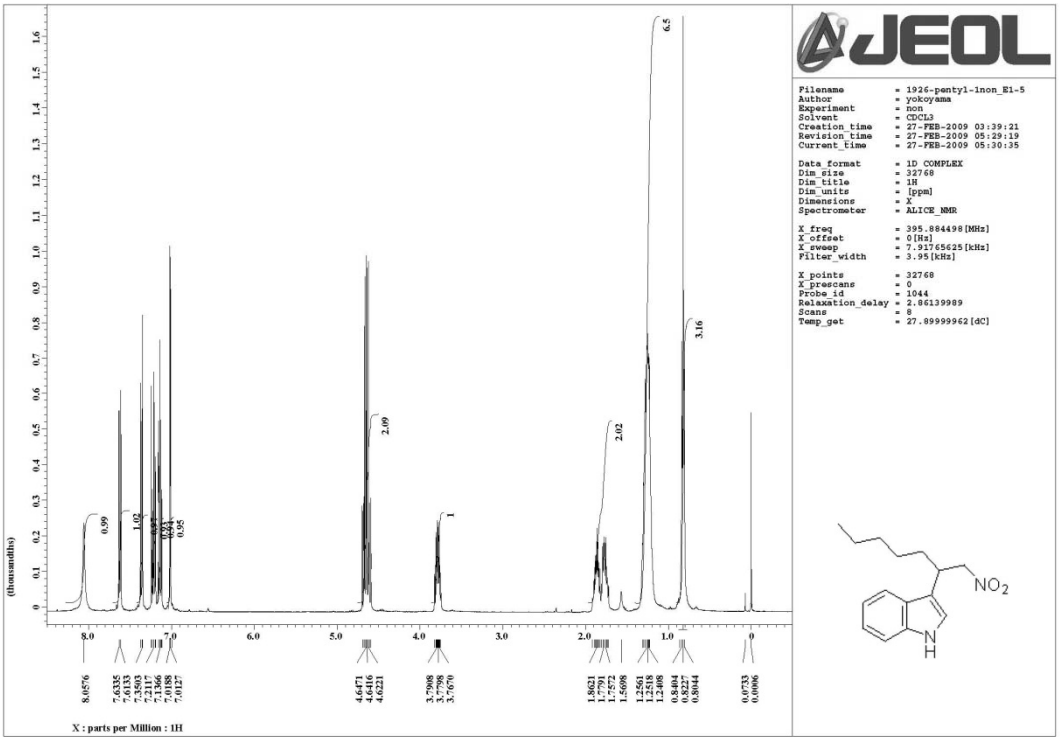
^{1}H-NMR of the product obtained in entry 7, Table 3



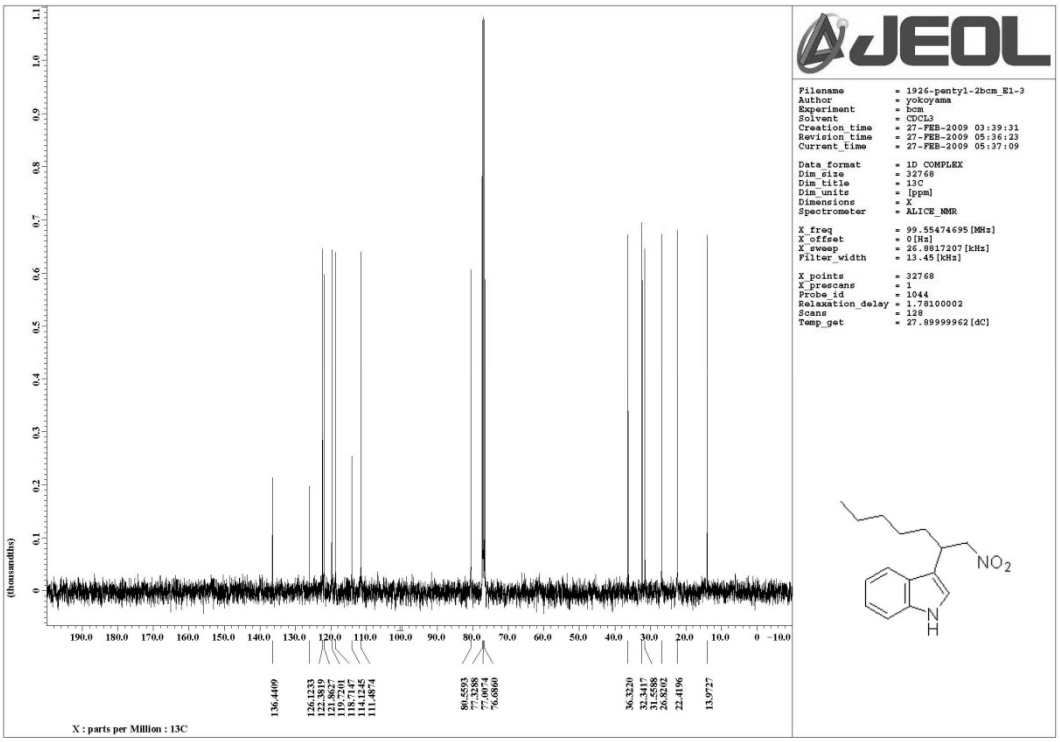
^{13}C-NMR of the product obtained in entry 7, Table 3



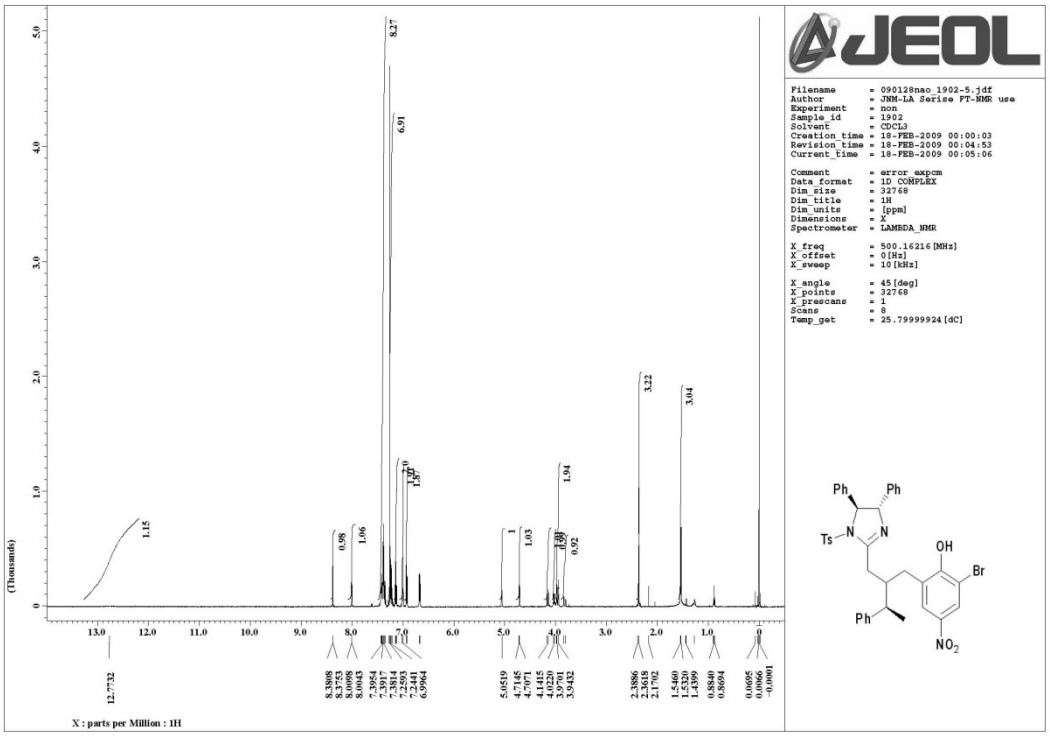
^{1}H-NMR of the product obtained in entry 8, Table 3



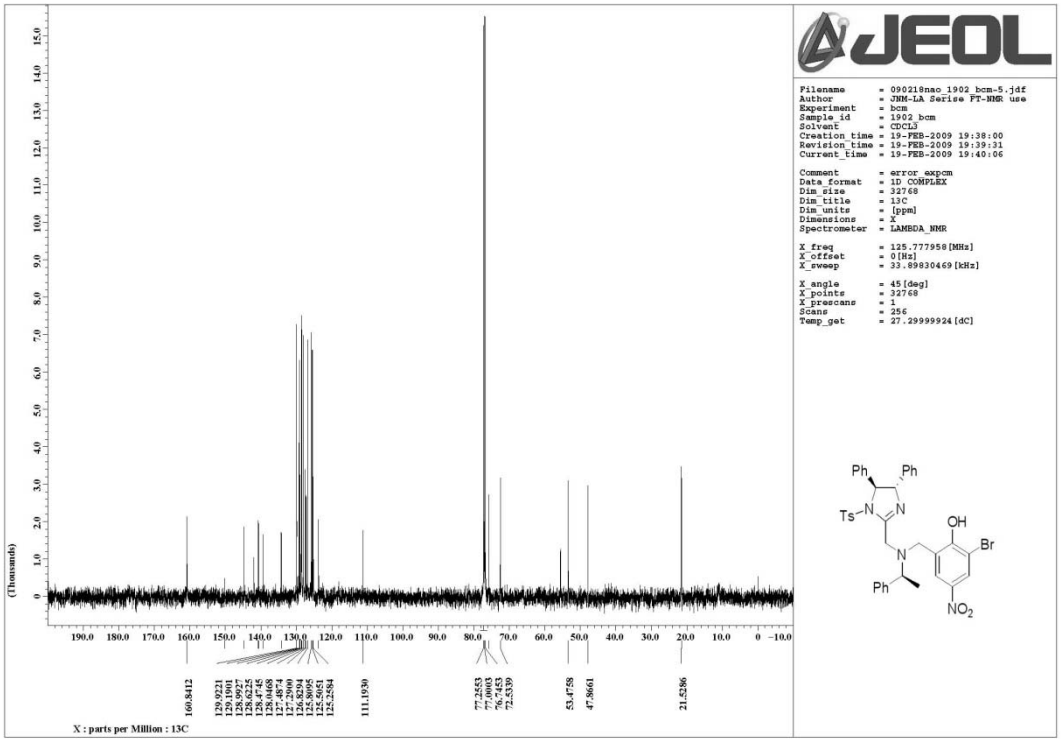
^{13}C-NMR of the product obtained in entry 8, Table 3



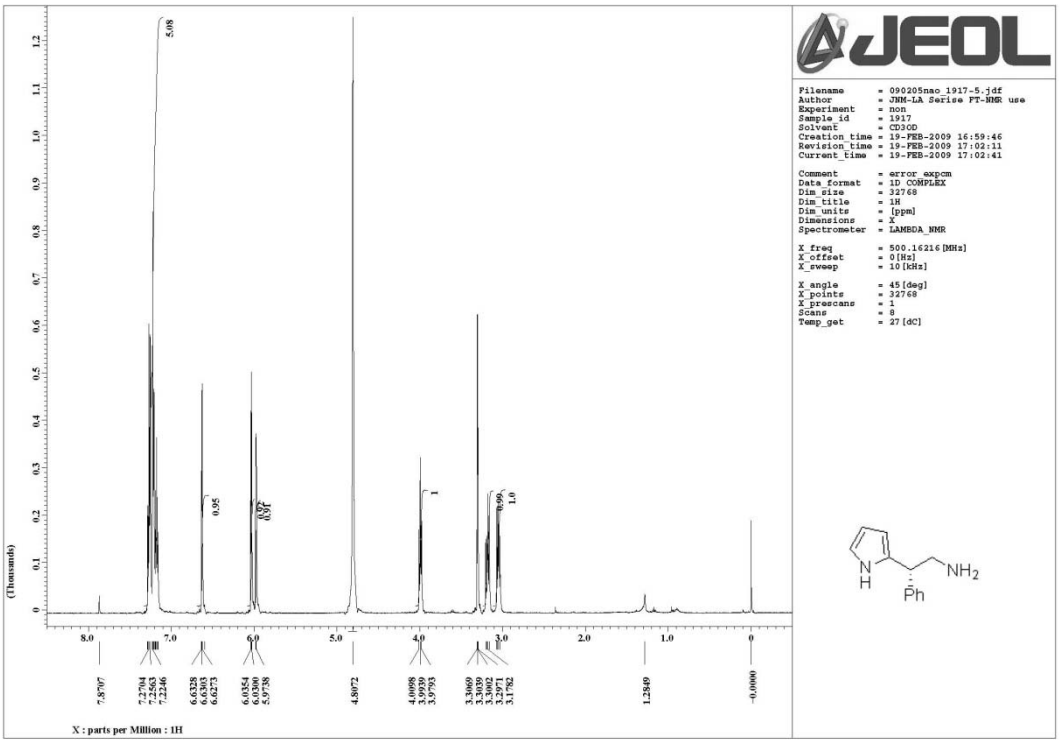
^{1}H-NMR of **1b**



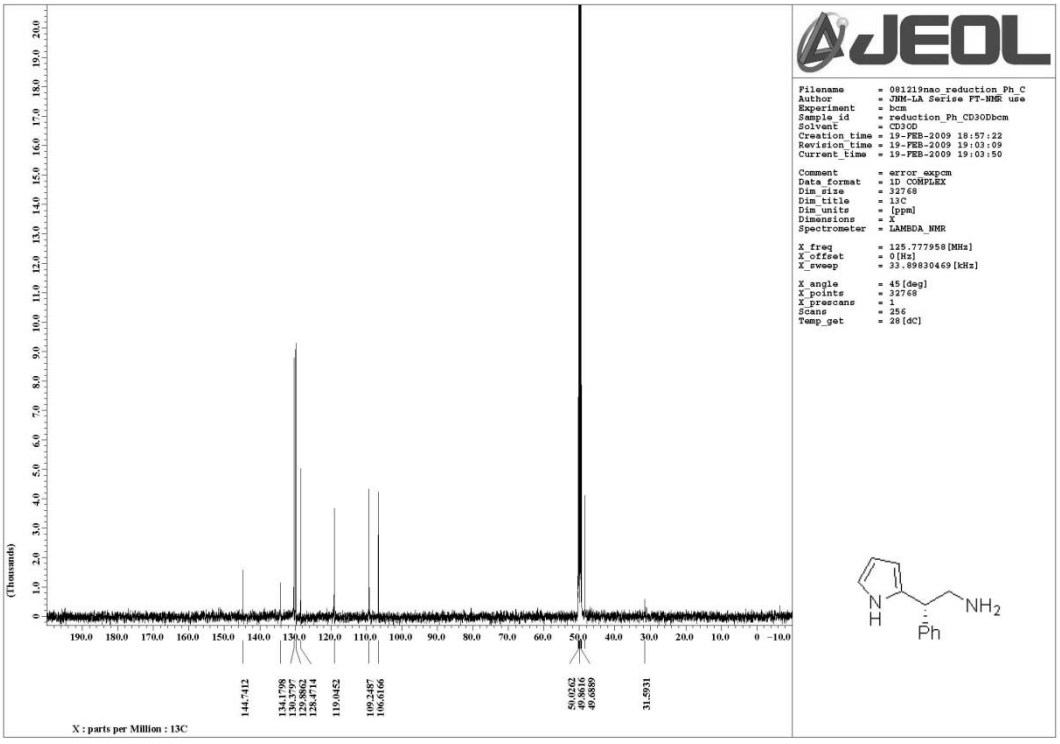
^{13}C-NMR of **1b**



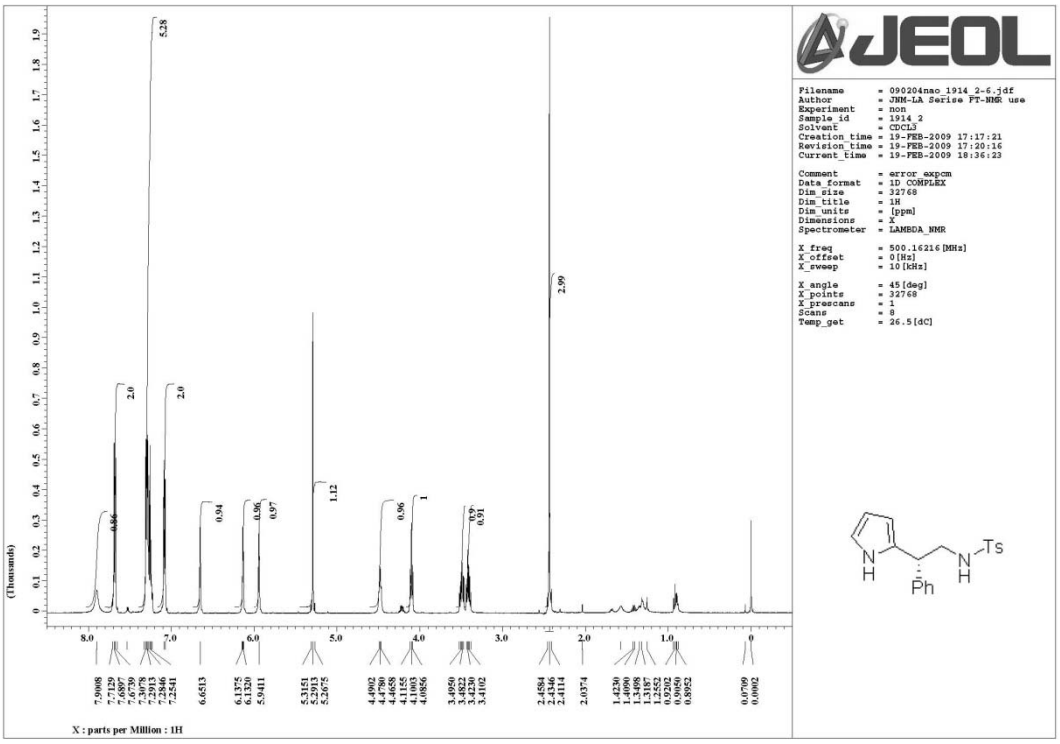
^{1}H-NMR of crude **S1**



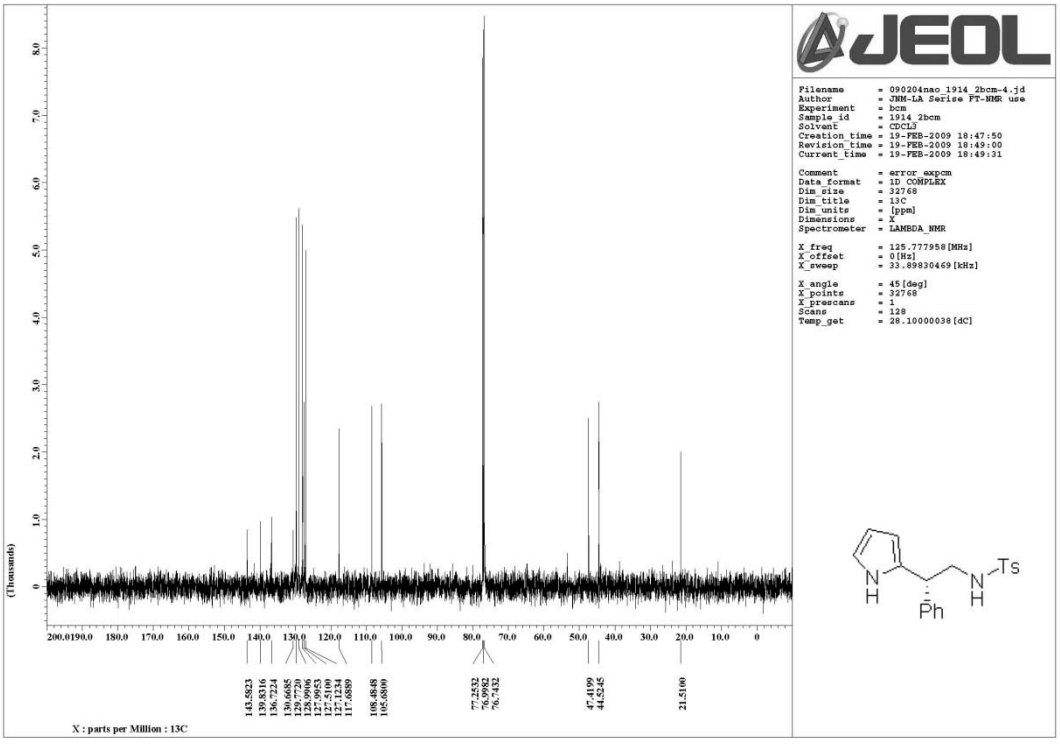
^{13}C-NMR of crude **S1**



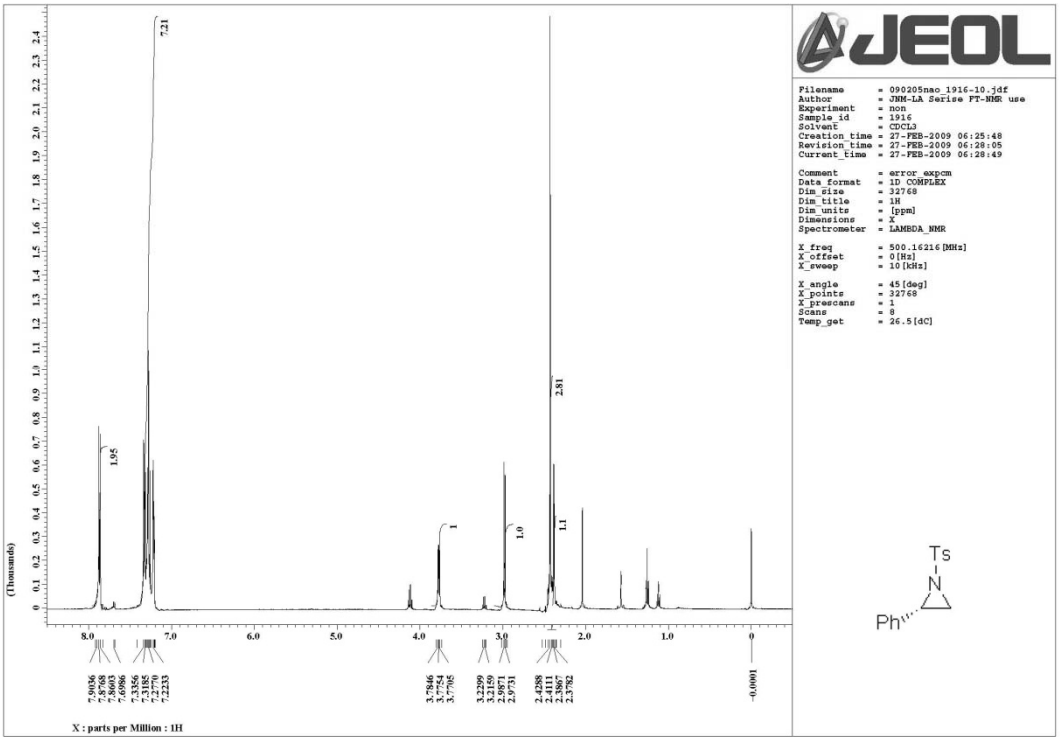
^{1}H-NMR of **S2**



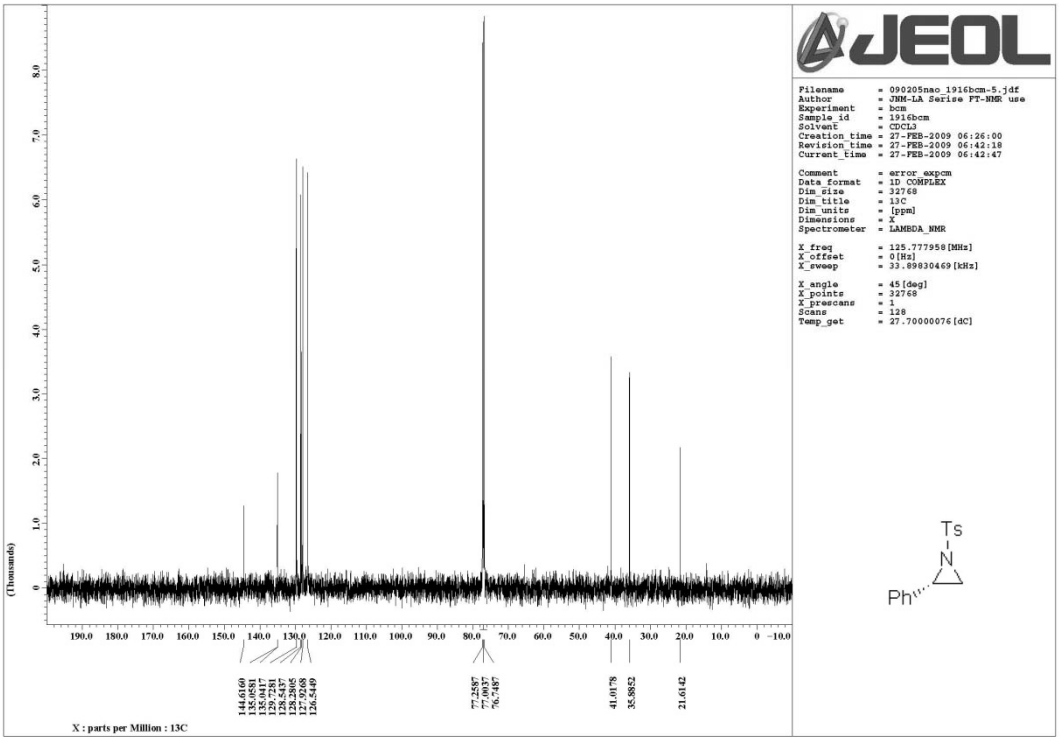
^{13}C-NMR of **S2**



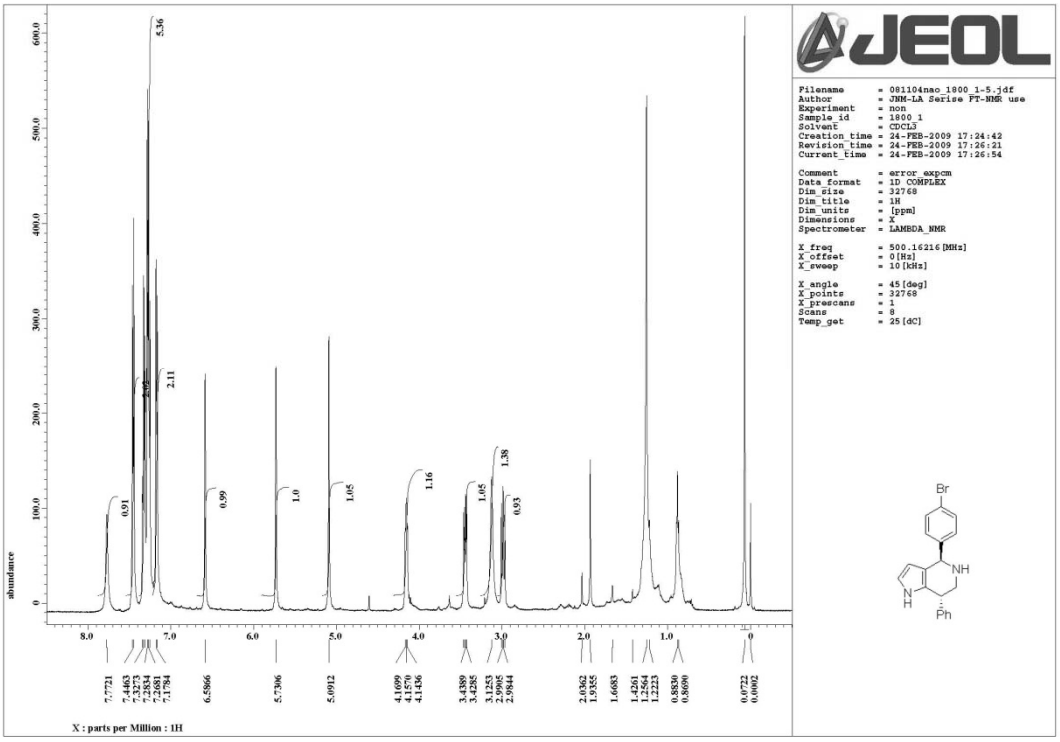
^{1}H-NMR of **S3**



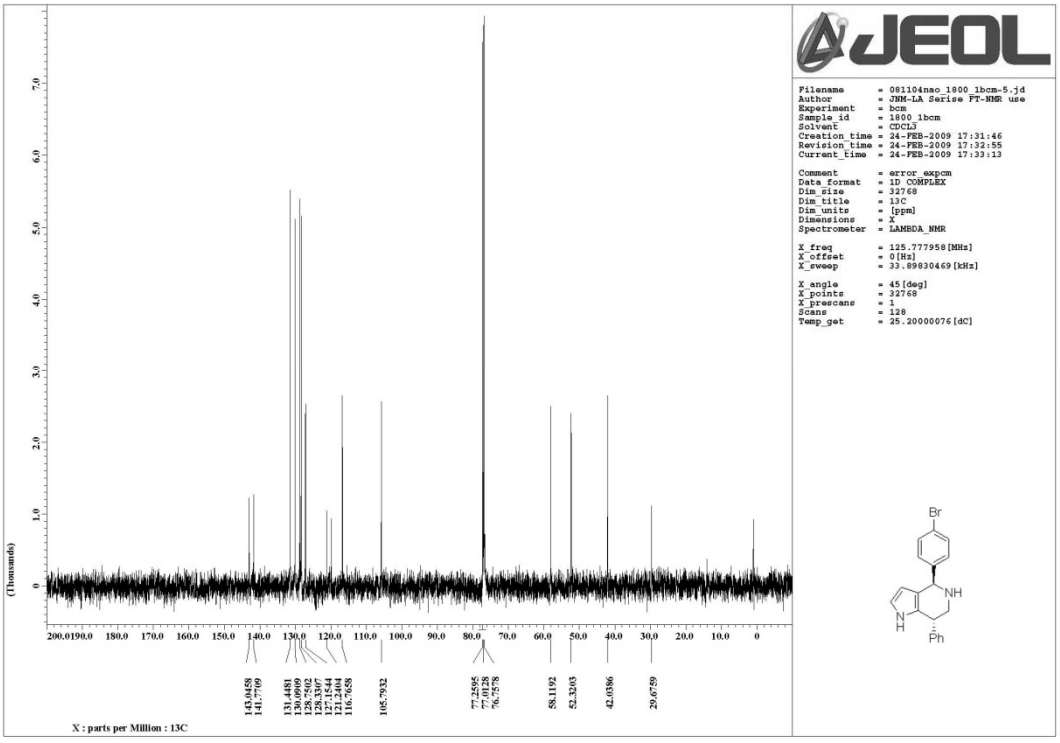
^{13}C-NMR of **S2**



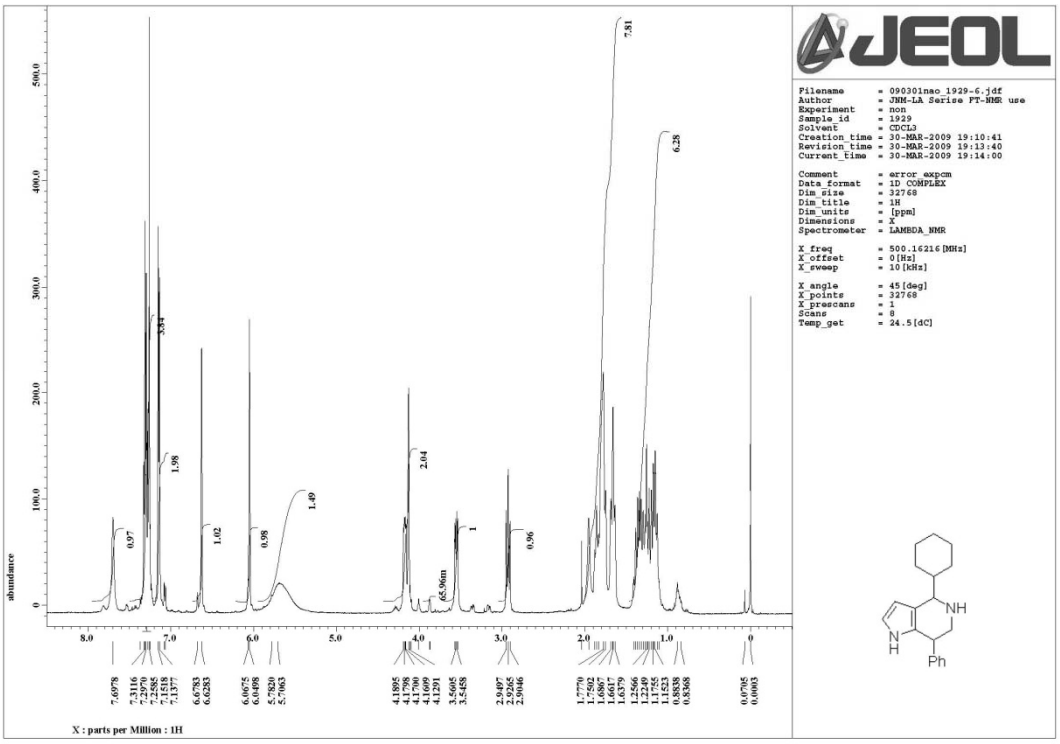
^{1}H-NMR of Pictet-Spengler adduct **8a**



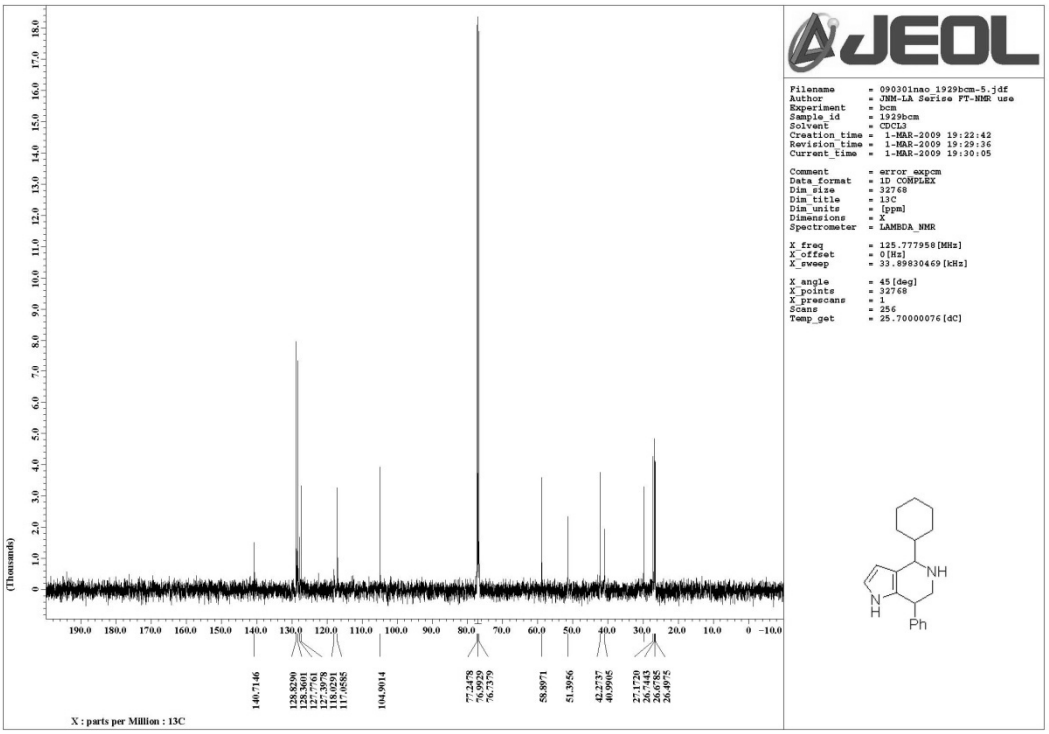
^{13}C-NMR of Pictet-Spengler adduct **8a**



^{1}H-NMR of Pictet-Spengler adduct **8b** (diastereo mixture)

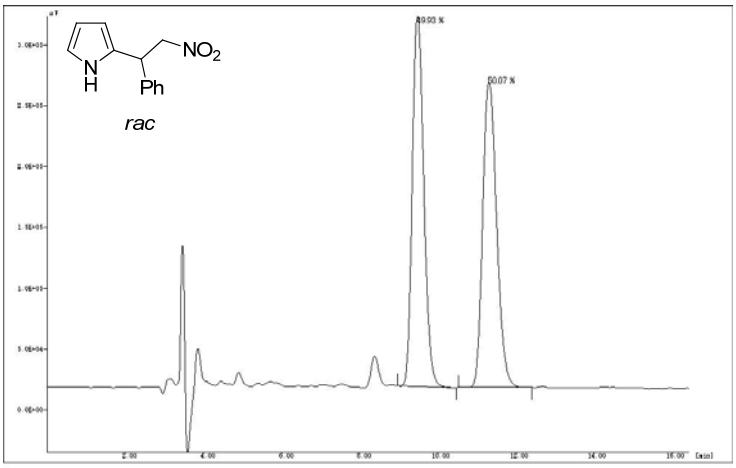


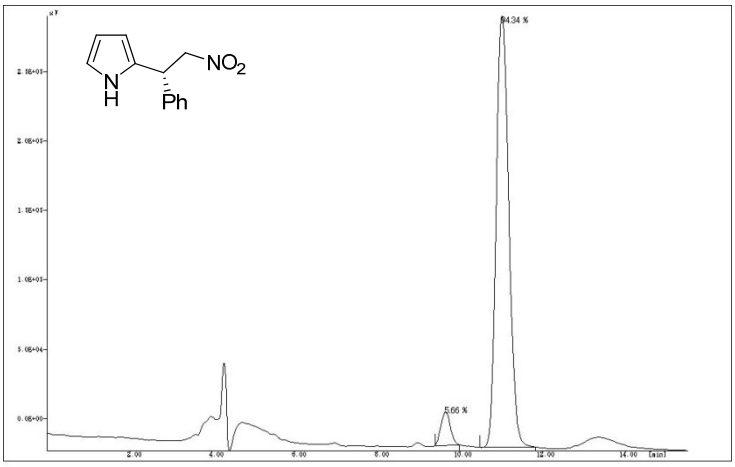
^{13}C-NMR of Pictet-Spengler adduct **8b** (diastereo mixture)



HPLC data

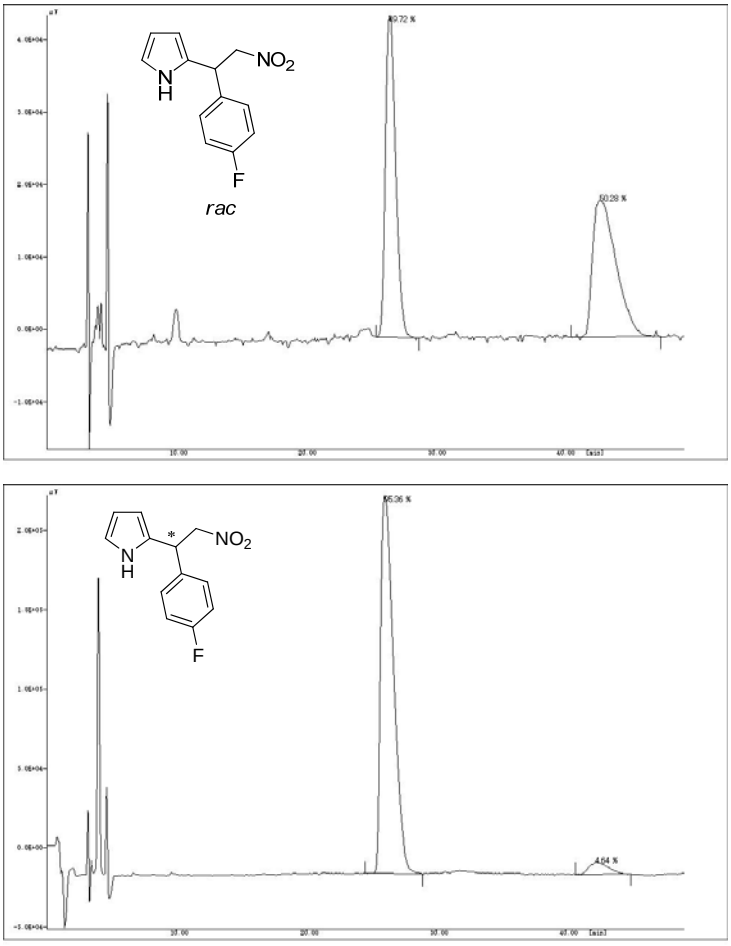
Table 2, entry 1





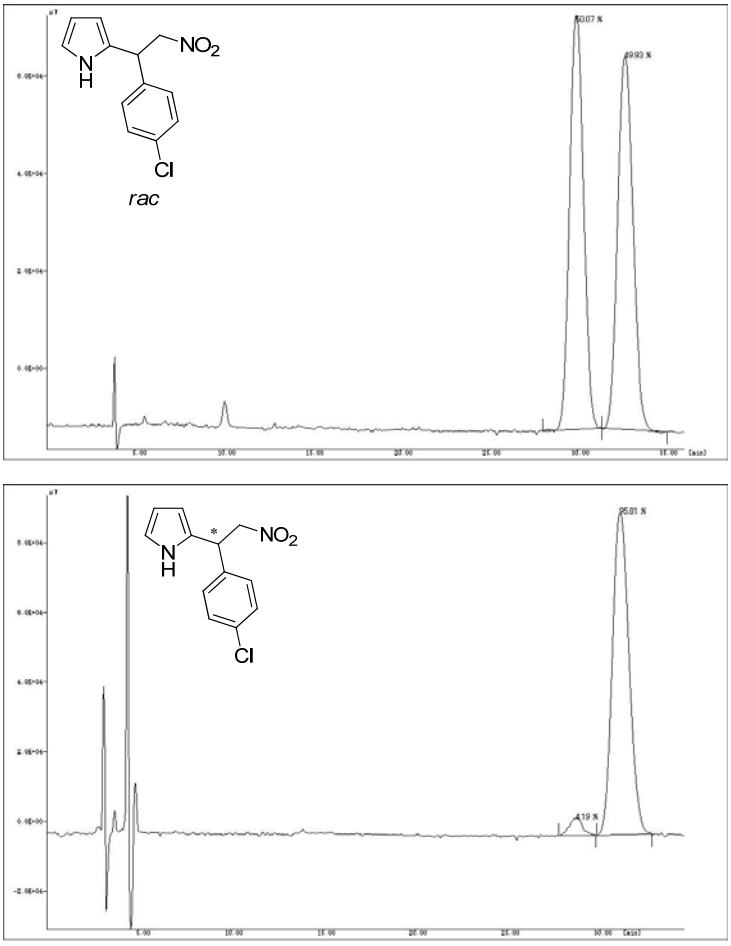
Chiralcel OD-H column (70:30 hexane: 2-propanol, 0.7 mL/min, 254 nm)

Table 2, entry 2



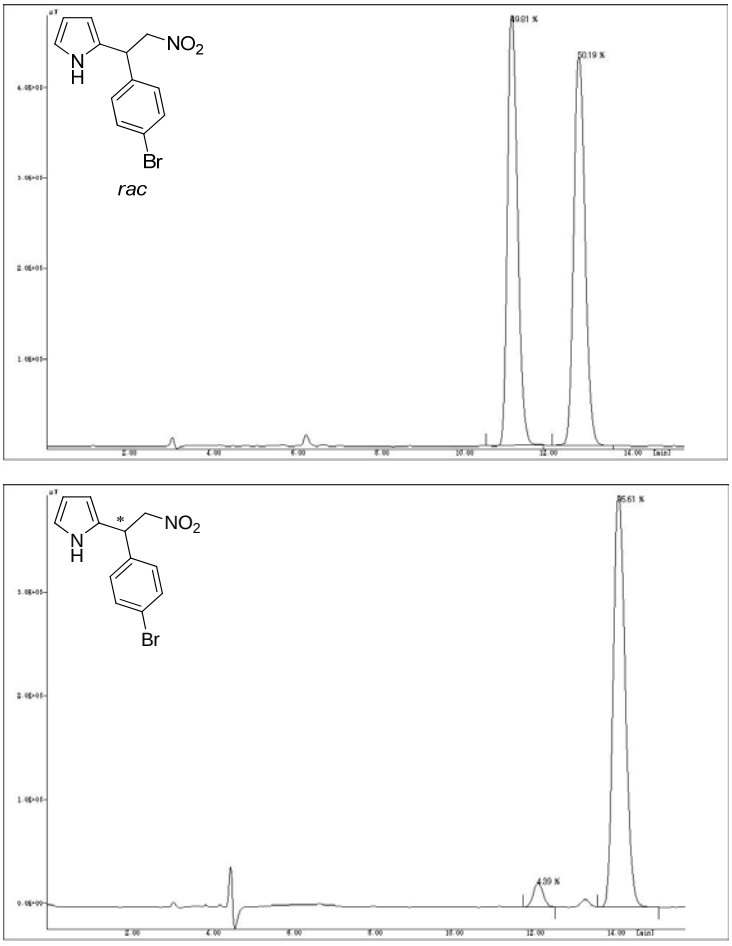
Chiralpak AS-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 3



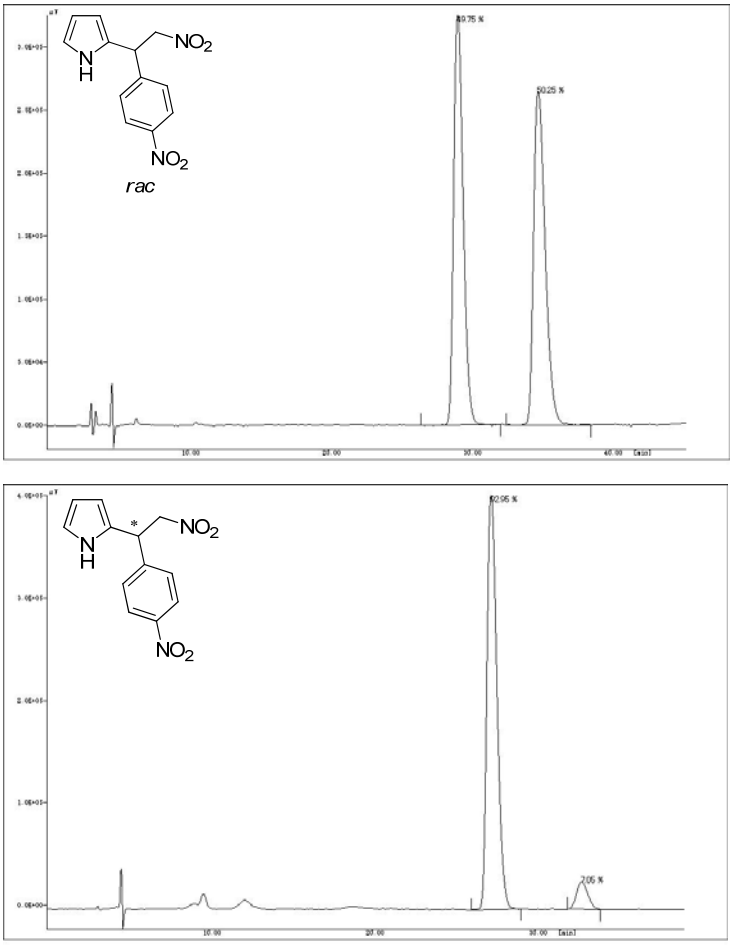
Chiralcel OD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 4



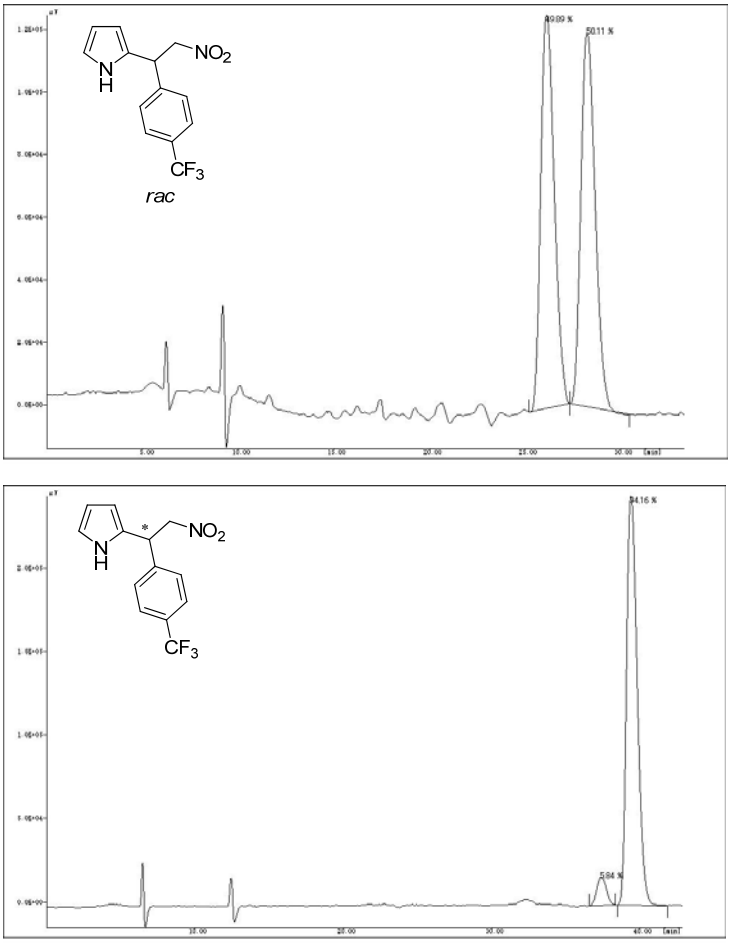
Chiralpak AD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 5



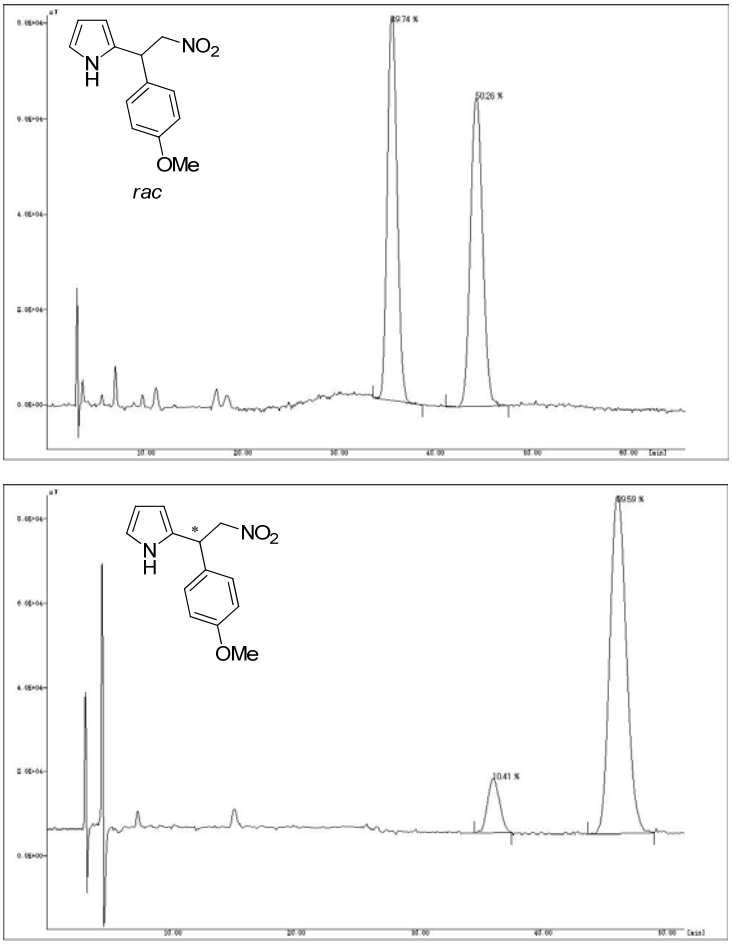
AD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 6



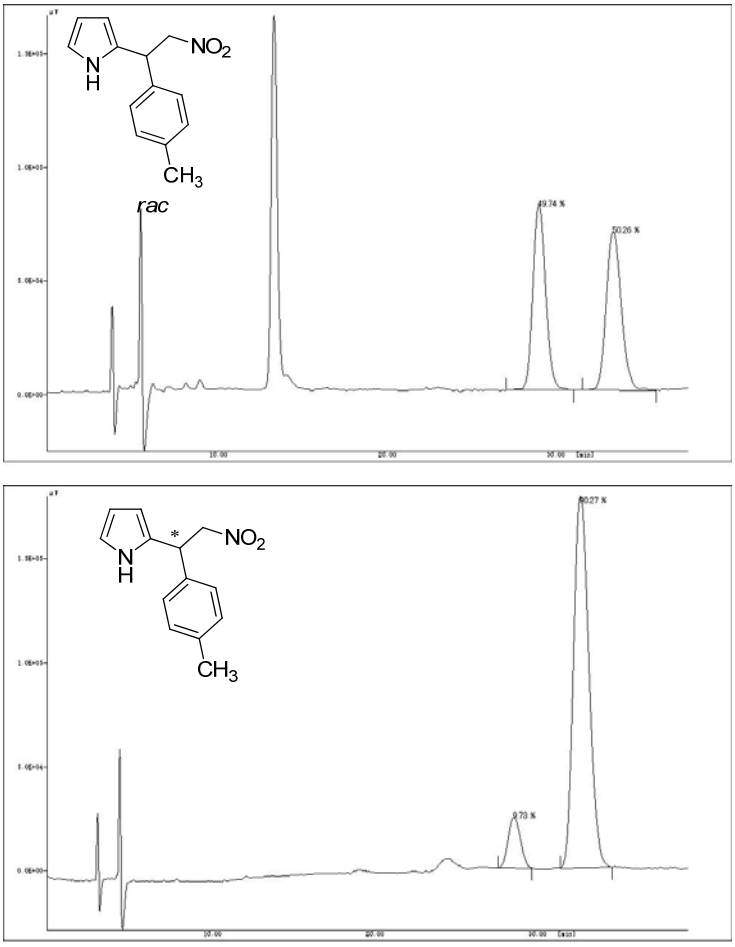
AD-H column (95:5 hexane: 2-propanol, 0.5 mL/min, 254 nm)

Table2, entry 7



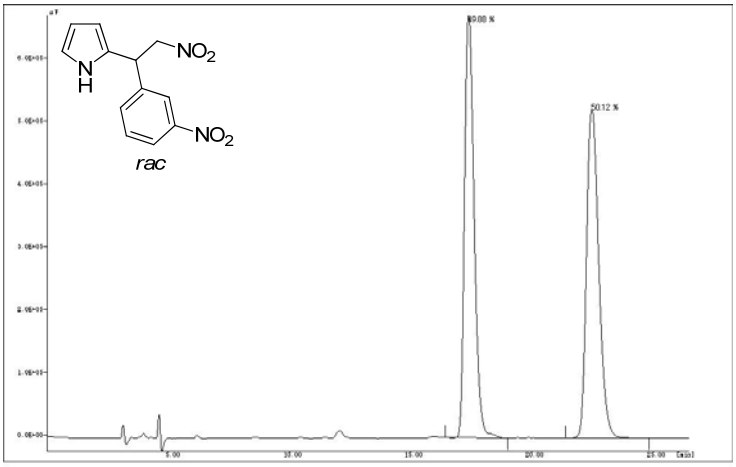
Chiralcel OD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm)

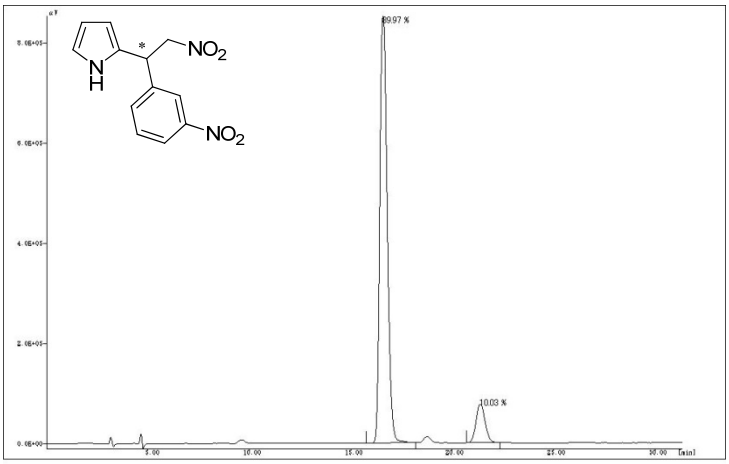
Table 2, entry 8



Chiralcel OD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm)

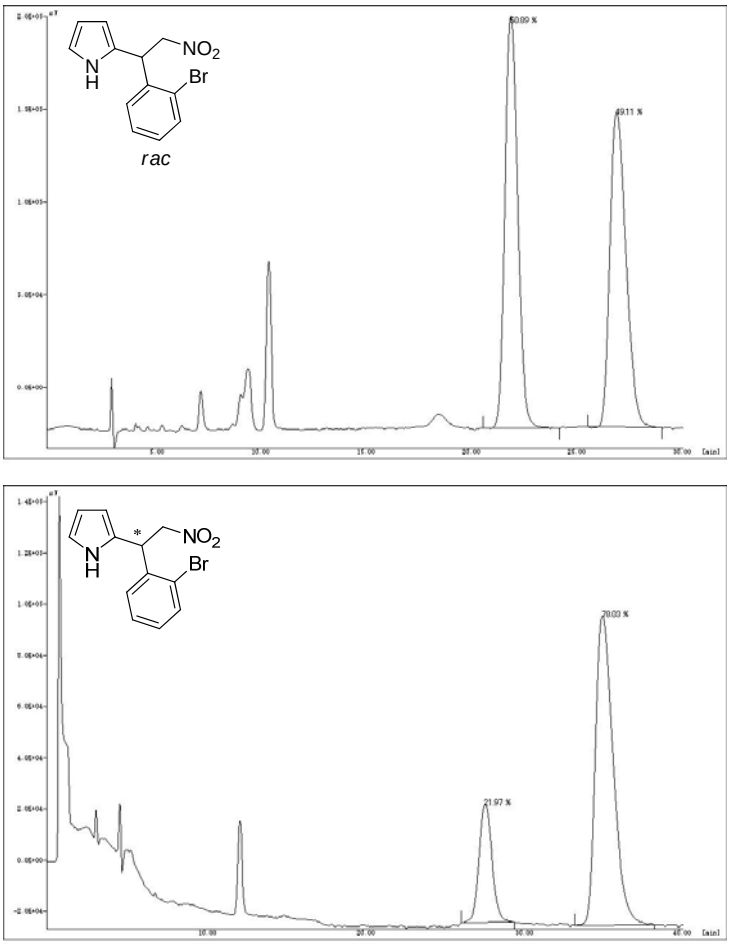
Table 2, entry 9





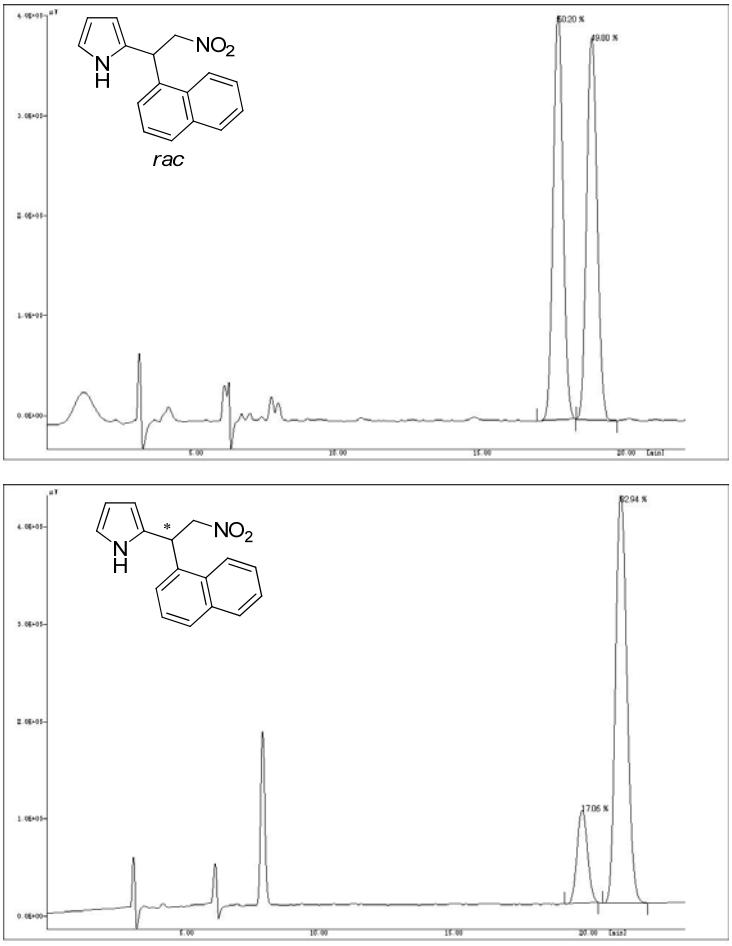
Chiralpak AD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 10



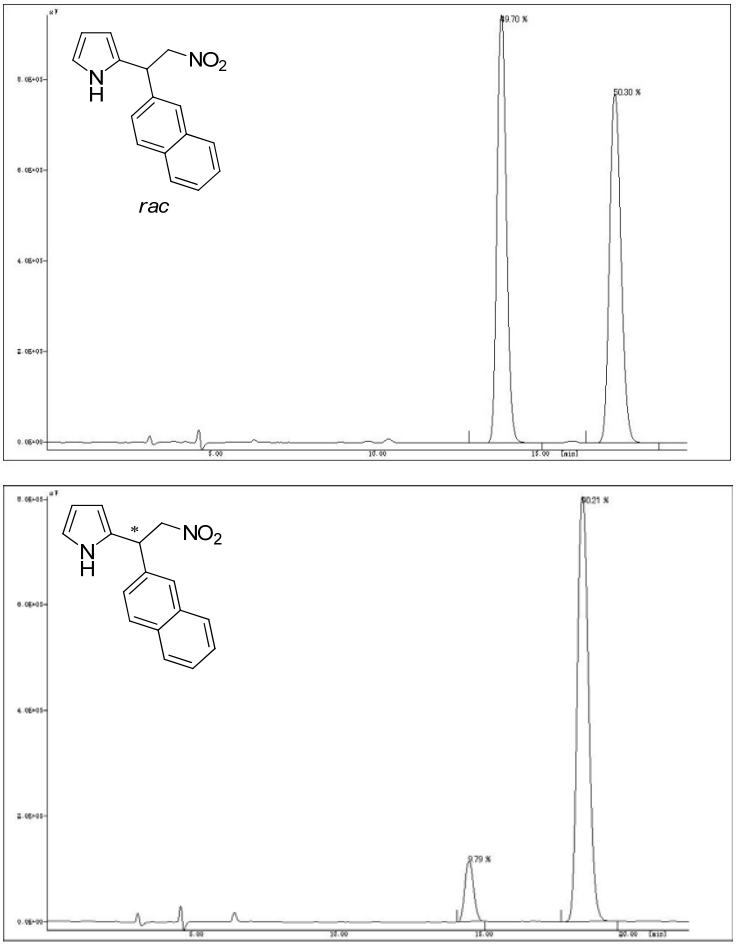
Chiralpak OD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 11



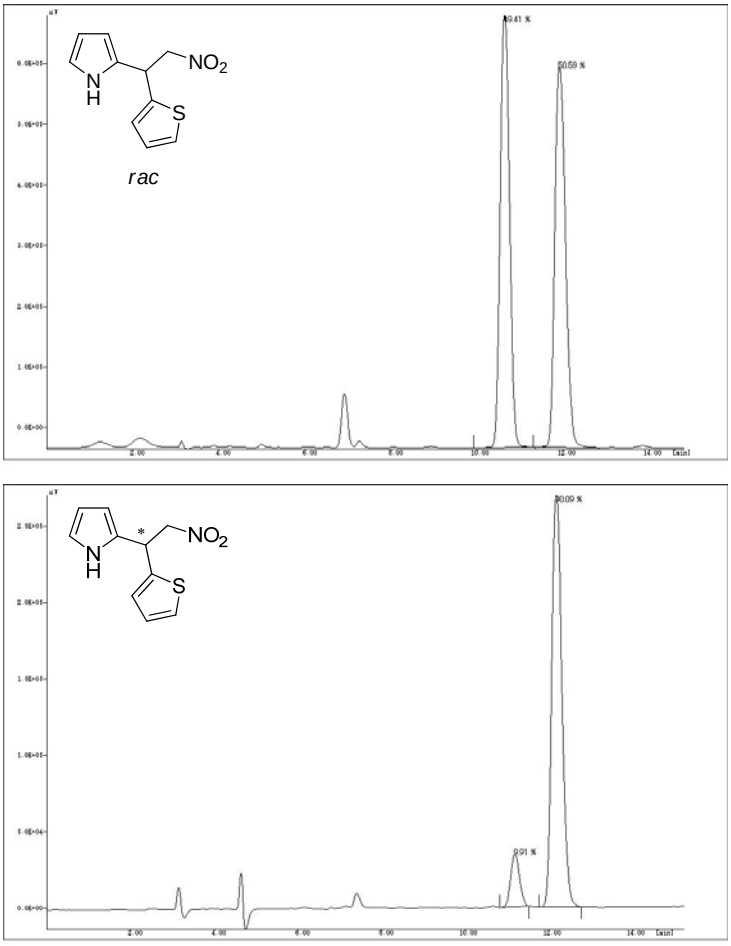
Chiralpak AD-H column (20:1 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 12



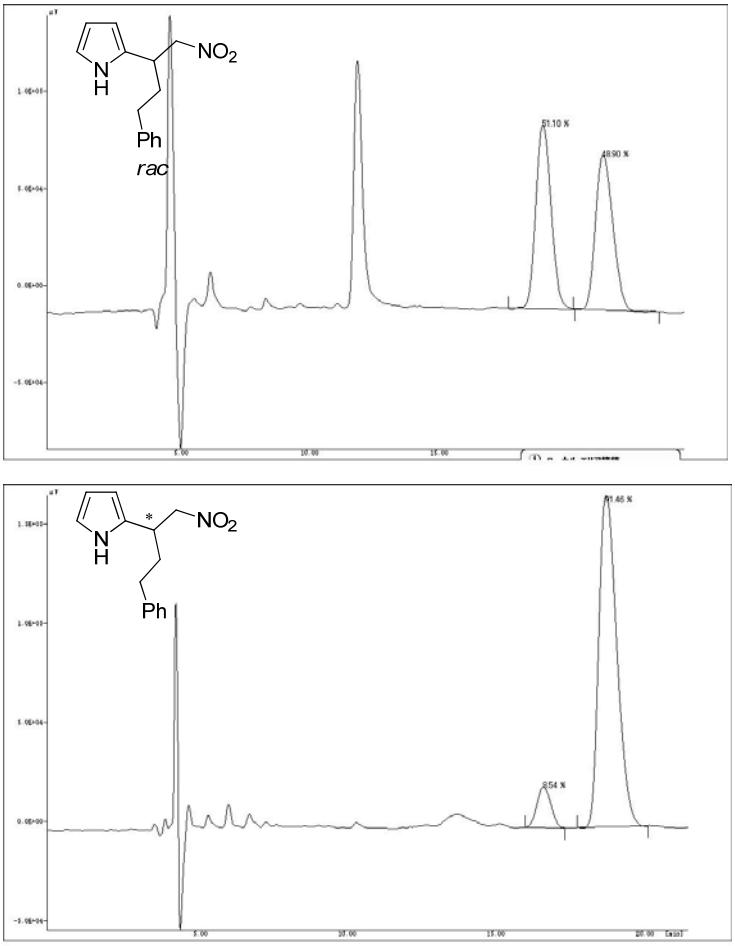
AD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 13



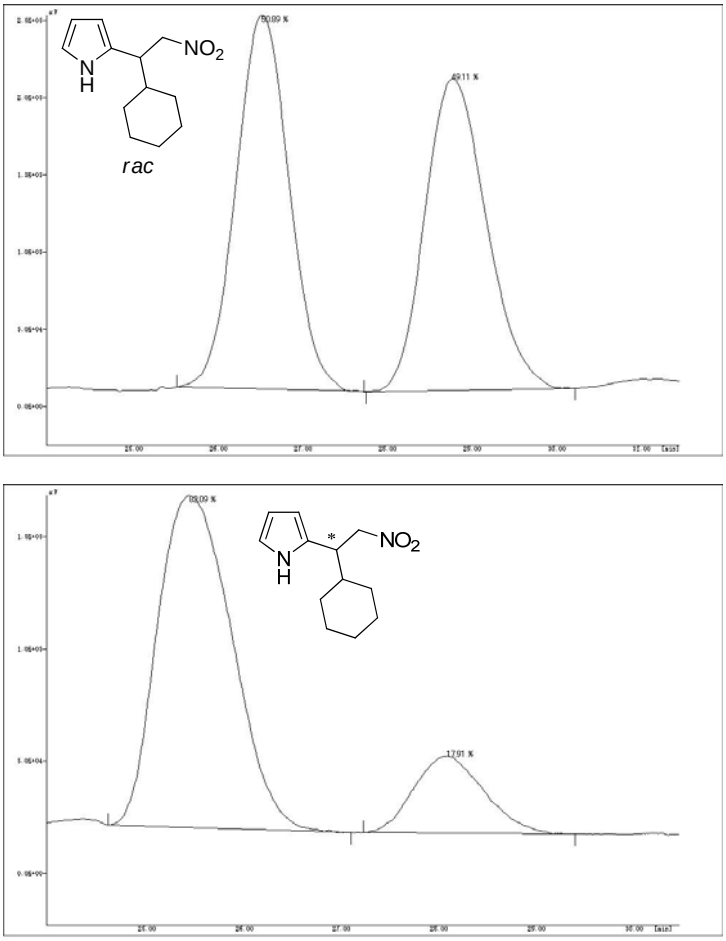
Chiralpak AD-H column (9:1 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Table 2, entry 14



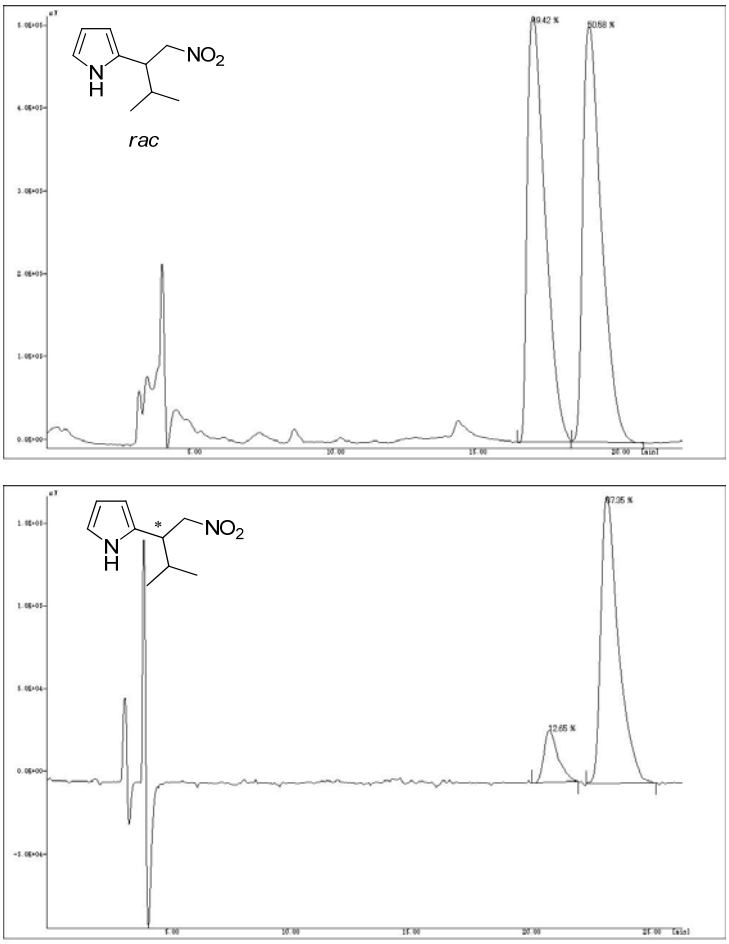
Chiralcel OD-H column (70:30 hexane:2-propanol, 0.8 mL/min, 254 nm)

Table 2, entry 15



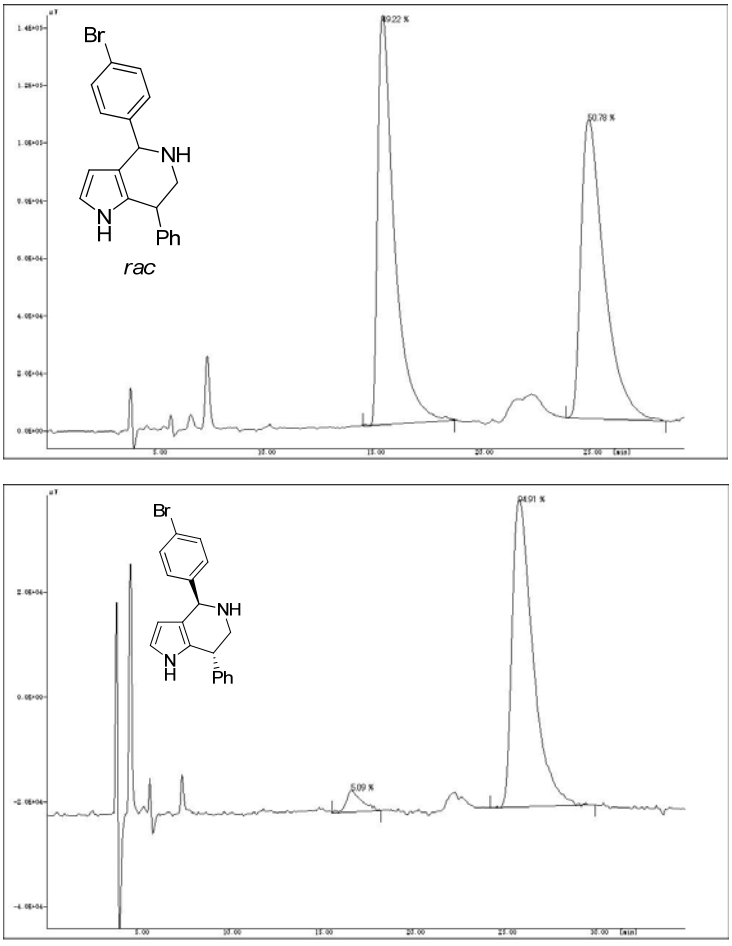
OD-H column (95:5 hexane: 2-propanol, 1.0 mL/min, 220 nm)

Table 2, entry 16



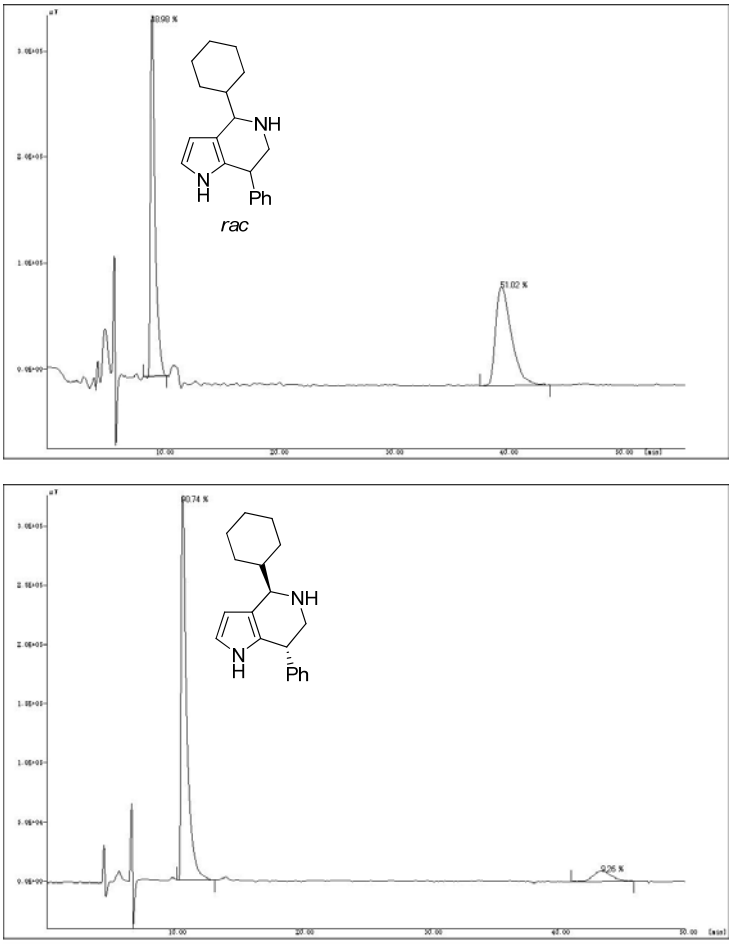
OJ-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 220 nm)

Scheme 2, R=4-Br-C_6H_4



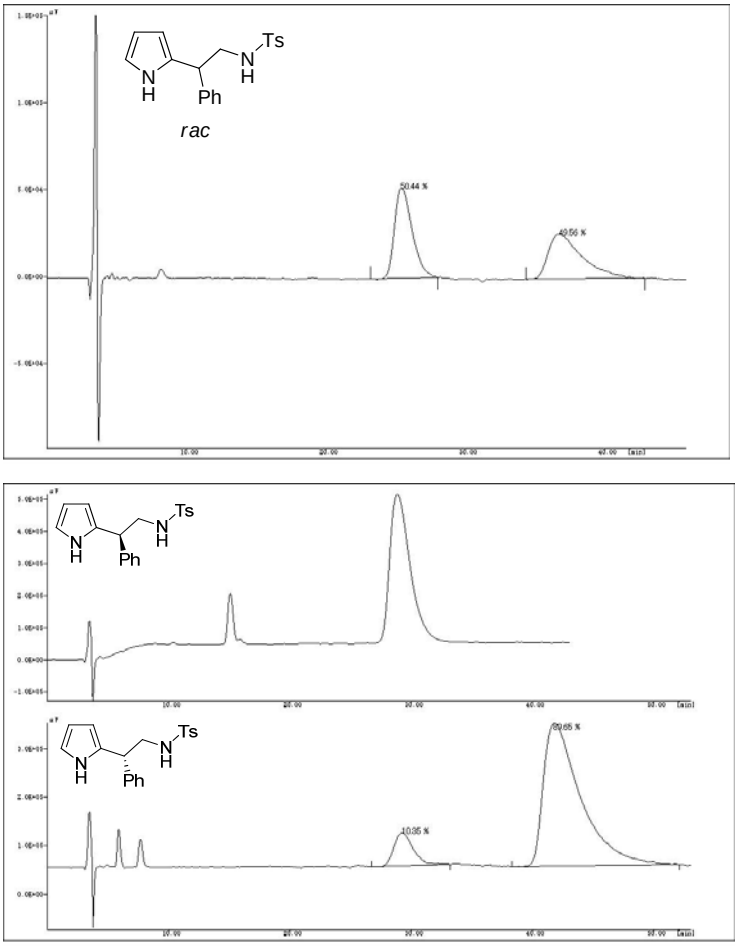
Chiralpak OD-H column (90:10 hexane: 2-propanol, 0.8 mL/min, 254 nm)

Scheme 2, R=*c*-C_6H_{11}



Chiralpak AD-H column (90:10 hexane: 2-propanol, 1.0 mL/min, 254 nm)

Scheme 2, Ts-amide



AS-H column (70:30 hexane: 2-propanol, 1.0 mL/min, 254 nm)