

Asymmetric Intramolecular Oxa-Michael Reactions To Tetrahydrofurans/*2H*-pyrans Catalyzed by Primary-Secondary Diamines

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Supporting Information

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General Information:

Unless otherwise indicated, chemicals and solvents were purchased from commercial suppliers and purified by standard techniques.

Flash column chromatography was performed using silica gel. For thin-layer chromatography (TLC), and compounds were visualized by irradiation with UV light or by treatment with a solution of phosphomolybdic acid in ethanol followed by heating.

The ^1H NMR spectra were recorded on a Bruker DRX 400 MHz. All chemical shifts (δ) are given in ppm. Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR spectra were recorded on a Bruker DRX 400 MHz.

HPLC analysis was carried out on WATERS equipment using a chiral column.

Melting points were determined on a SGW X-4 and were uncorrected.

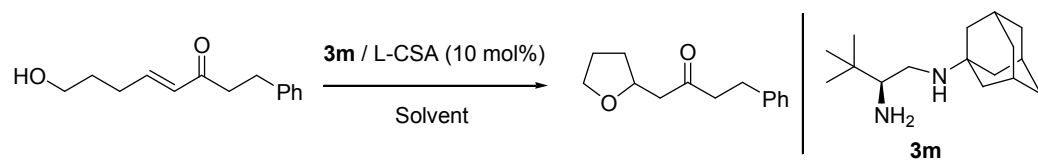
Optical rotations were measured on a JASCO-P1010 Polarimeter at $\lambda = 589$ nm.

IR spectra were recorded on a Perkin-Elmer 983G instrument.

Mass spectra analysis was performed on API 200 LC/MS system (Applied Biosystems Co. Ltd.).

Optimization of the reaction conditions

Table S1: Optimization of the reaction conditions^a



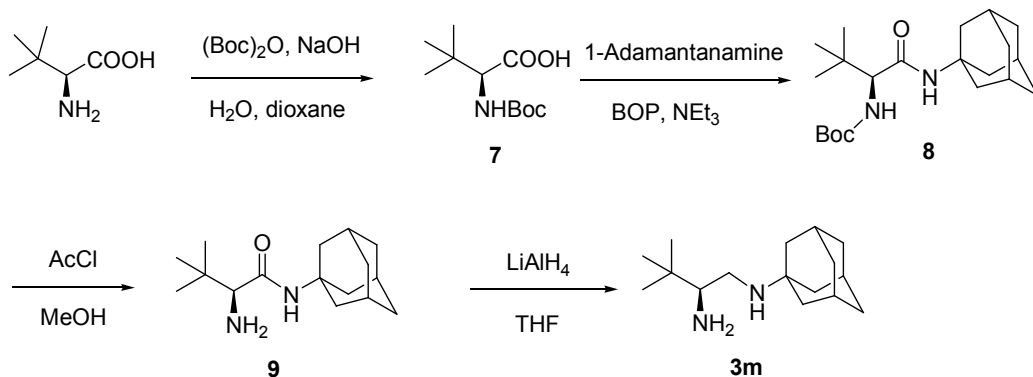
Entry	Solvent	Yield (%) ^b	Ee (%) ^c
1	CHCl₃	96	85
2	Hexane	42	35
3	CH ₂ Cl ₂	90	74
4	Toluene	92	72
5	THF	32	50
6	EtOAc	73	28
7	MeCN	62	31
8	DMF	n.d.	n.d.
9	MeOH	65	20
10	H ₂ O	36	0
11 ^d	CHCl ₃	54	70
12 ^e	CHCl ₃	96	80
13 ^f	CHCl ₃	60	71
14 ^g	CHCl ₃	75	74

^a Unless otherwise specified, the reaction was carried out with **1a** (0.1 mmol), **3m** (10 mol %), L-CSA (10 mol %) in solvent (1.0 mL) at room temperature for 48 h. ^b Isolated yields. ^c Determined by chiral HPLC analysis. The absolute configuration was determined by comparison of the specific optical rotation value with that of the literature reported¹. ^d The reaction was carried out at 10 °C. ^e **3m** (20 mol%) was used, **3m** : L-CSA = 2 : 1. ^f L-CSA (20 mol%) was used. **3m** : L-CSA = 1 : 2. ^g **3m** (5 mol%) and L-CSA (5 mol%) were used.

Preparation of Catalysts

Primary-tertiary diamine catalysts **3b-3c**², **3h**³, **3k-3l**⁴ and primary-secondary diamine catalysts **3d-3g**⁵, **3i-3j**⁶ were prepared following literature methods as specified.

Procedure for the preparation of catalyst **3m**



Preparation of **7**

To a suspension of *L*-*tert*-Leucine (6.55 g, 50 mmol) in 60 mL of 1,4-dioxane and NaOH (2.20 g, 55 mmol) in 60 mL of water, (Boc)₂O (13.08 g, 60 mmol) in 20 mL of 1,4-dioxane was added dropwise at 0 °C over 20 min. The reaction mixture was allowed to warm to room temperature and stirred for another 6 h. The mixture was rotaevaporated to remove the 1,4-dioxane, and then 1N HCl was added to adjust the pH of the mixture to 2-3. The mixture was extracted with ethyl acetate (40 mL × 3) and the combined organic phases were washed with water (30 mL), brine (30 mL), dried (Na₂SO₄) and concentrated to afford **7** as pale white solid 10.46 g (Yield: 90.6%). The product was used directly in next step without further purification.

Preparation of Amides **8**

To a solution of (*S*)-2-(*tert*-butoxycarbonylamino)-3,3-dimethylbutanoic acid (**7**) (4.62 g, 20 mmol) in THF (40 mL), 1-Adamantanamine (3.02 g, 20 mmol) and NEt₃ (4.04 g, 40 mmol) was added. Then BOP (11.49 g, 26 mmol) was added in one portion at 0 °C. The reaction mixture was stirred at 0 °C for 2 h, then allowed to warm to room temperature and stirred overnight. Water (20 mL) was added to quench the reaction. The mixture was rotaevaporated to remove THF. The residue was extracted with ethyl acetate (30 mL × 2). The combined organic phases were washed with water (10 mL), brine (10 mL), dried (Na₂SO₄) and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 8/1 as eluent to afford **8** as white solid 5.49 g. Yield: 75.4%.

Preparation of **9**

To a solution of (*S*)-*tert*-butyl-3,3-dimethyl-1-oxo-1-(adamantylamino)butan-2-ylcarbamate (**8**) (5.49 g, 15.1 mmol) in MeOH (30 mL), AcCl (3 mL) was added at 0 °C. The mixture was stirred at 0 °C for 2h, and was then rotaevaporated to remove MeOH. Ethyl acetate (30 mL) and saturated aqueous solution of Na₂CO₃ were added to adjust the pH of the mixture to 8-9. The organic phase was separated and washed with water (10 mL) and brine (10 mL), dried (Na₂SO₄) and

concentrated to give **9** as yellowish oil 3.90 g. The crude product was used directly in next step without further purification.

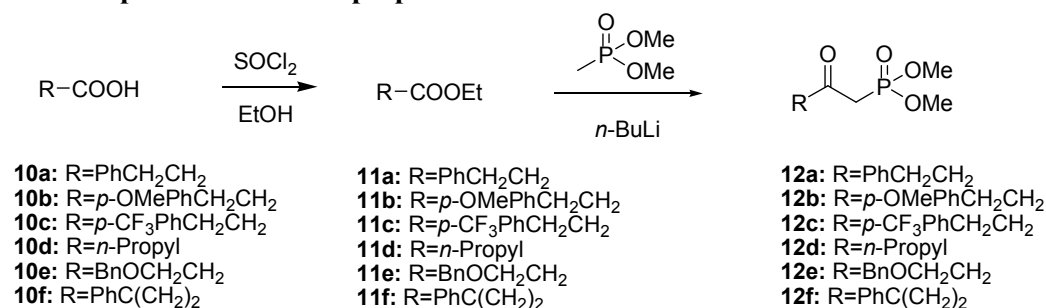
Preparation of Catalyst **3m**

To a suspension of LiAlH₄ (2.85 g, 75 mmol) in dry THF (40 mL), (*S*)-2-amino-3,3-dimethyl-*N*-adamantylbutanamide (**9**) (3.90 g) dissolved in THF (10 mL) was added at room temperature over 10 min. The reaction mixture was heated at reflux for 24 h. Na₂SO₄•10H₂O was added slowly at 0 °C to quench the reaction. The white-gray suspension was filtered and the filtrate was concentrated. The crude product was purified by silica gel chromatography using CH₂Cl₂/MeOH = 20/1 as eluent to give **3m** as white solid 2.25 g. Yield: 60.0% (2 steps).

Preparation of Substrates

Preparation of Substrates **1a-1g, 1j-1m**

General procedure for the preparation of intermediate **12**



The following procedure is general to **12b-12f**.

Ethyl 3-phenylpropanoate (**11a**)

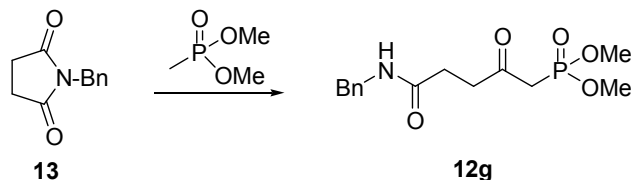
To a solution of 3-phenylpropanoic acid (**10a**) (7.5 g, 50 mmol) in EtOH (50 mL), SOCl₂ (5 mL) was added slowly. The reaction mixture was heated at reflux for 3 h and then evaporated to remove EtOH. Ethyl acetate (40 mL), water (20 mL) and saturated aqueous solution of NaOH were added to adjust the pH to 8-9. The organic phase was separated and washed with water (20 mL) and brine (20 mL), dried (Na₂SO₄) and concentrated to afford **11a** as colorless oil 8.50 g. Yield 95.5%. The product was used directly in next step without further purification.

Dimethyl 2-oxo-4-phenylbutylphosphonate (**12a**)

To 40 mL of dry THF at -78 °C under N₂ was added *n*-BuLi (12 mL, 30 mmol, 2.5 M in hexanes) followed by the dropwise addition of dimethyl methyl phosphonate (3.72 g, 30 mmol) with stirring over 0.5 h. The resulting white mixture was stirred at -78 °C for another 0.5 h, and then ethyl 3-phenylacetate (**11a**) (5.34 g, 30 mmol) was added dropwise. Stirring was continued for 0.5 h at -78 °C and for an additional hour while the mixture was warmed to room temperature. The resulting clear mixture was concentrated in vacuo, diluted with 50 mL of ethyl acetate, and washed with water (20 mL × 2), brine (20 mL), dried (Na₂SO₄) and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 3/1 as eluent to

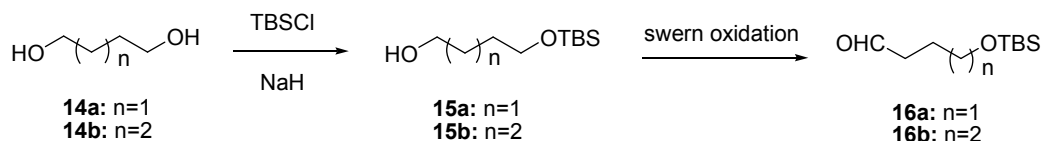
afford **12a** as colorless oil 4.80 g. Yield: 62.5%.

Preparation of intermediate **12g**



To 40 mL of dry THF at -78°C under N_2 was added *n*-BuLi (12 mL, 30 mmol, 2.5 M in hexanes) followed by the dropwise addition of dimethyl methyl phosphonate (3.72 g, 30 mmol) with stirring over 0.5 h. The resulting white mixture was stirred at -78°C for another 0.5 h, and then 1-benzylpyrrolidine-2,5-dione (**13**) (6.80 g, 36 mmol) in 20 mL dry THF was added dropwise. Stirring was continued for 1 h at -78°C and then for an additional 12 hour at room temperature. The resulting clear mixture was concentrated in vacuo, extracted with (50mL \times 2) ethyl acetate, and washed with water (20mL \times 2), brine (20 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by silica gel chromatography using $\text{CH}_2\text{Cl}_2/\text{MeOH} = 25/1$ as eluent to obtain **12g** as colorless oil 4.90 g. Yield: 52.2%.

General procedure for preparation of intermediate **16**



The following procedure is general to **16b**.

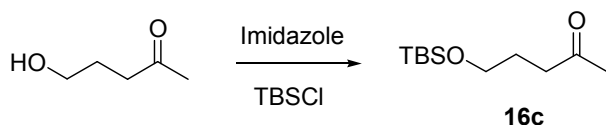
4-(*tert*-butyldimethylsilyloxy)butan-1-ol (**15a**)

To a solution of butane-1,4-diol (**14a**) (4.5 g, 50 mmol) in dry THF (90 mL), NaH (60%) (2.0 g, 50 mmol) was added slowly with stirring at 0°C . The mixture was kept at this temperature for 40 min, and then *tert*-butylchlorodimethylsilane (7.5g, 50mmol) was added. The reaction was stirred for 3 h and then evaporated to remove THF. The residue was extracted with (50mL \times 2) ethyl acetate, and washed with water (20mL), brine (20 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 20/1 as eluent to provide colorless oil 9.40 g. Yield: 92.2%.

4-(*tert*-butyldimethylsilyloxy)butanal (**16a**)

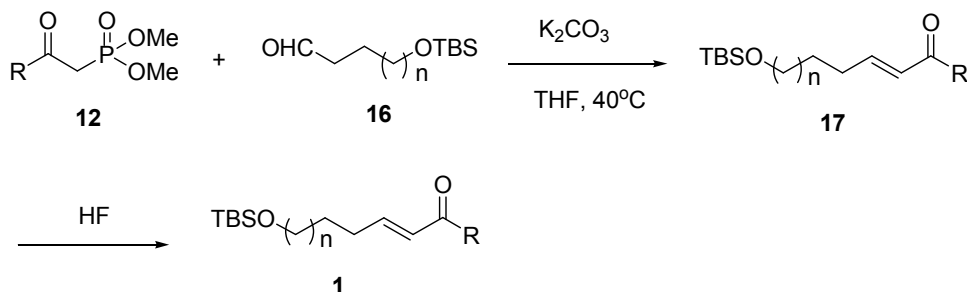
A flame-dried flask was charged with dry CH_2Cl_2 (50 mL) and cooled to -78°C with a dry ice/acetone bath. Oxalyl chloride (5.04g, 40 mmol) was then added followed by DMSO (4.25mL, 60 mmol). The mixture was kept at -78°C for 15 min, after which time 4-(*tert*-butyldimethylsilyloxy)butan-1-ol (**15a**) (4.08 g, 20 mmol, dissolved in 20 mL of dry CH_2Cl_2) was added. The reaction was kept at -78°C for 1 h, after which time triethylamine (14 mL, 0.1 mol) was added and the reaction was allowed to warm to room temperature over 30 min. The reaction mixture was then poured over ice-cold 1 M HCl and extracted with DCM. The combined extracts were dried by Na_2SO_4 and concentrated to give **16a** (3.47 g) as yellow oil, yield: 85.9%. The product was used directly in next step without further purification.

Preparation of intermediate 16c



To a solution of 5-hydroxypentan-2-one (2.0 g, 20 mmol) in dry CH_2Cl_2 (20 mL), imidazole (2.0g, 30 mmol) was added. The mixture was stirred at room temperature for 1 h, after which time *tert*-butylchlorodimethylsilane (3.3 g, 22 mmol) was added. The reaction was stirred at room temperature for 12 h. Water (20 mL) was added and the mixture was extracted with CH_2Cl_2 (20 mL \times 2). The combined extracts were dried with Na_2SO_4 and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 20/1 as eluent to give **16c** as colorless oil 3.14 g. Yield: 72.6%.

General procedure for preparation of substrates 1a-1g, 1j-1m



General procedure for the preparation of 17

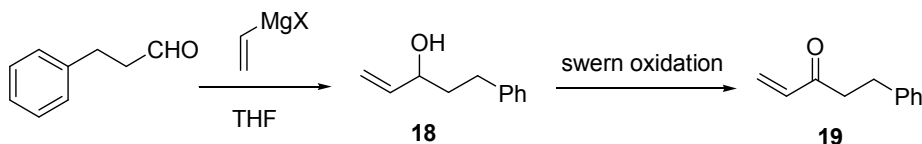
To a solution of phosphonate (**12**) (5 mmol) in dry THF (20 mL), K_2CO_3 (5.5 mmol) were added. The mixture was stirred at room temperature for 40 min, then aldehyde/ketone (**16**) (5 mmol) in THF (5 mL) was added dropwisely. The reaction mixture was heated and stirred at 40°C for 12h then cooled to room temperature. Water (20 mL) and ethyl acetate (20 mL) were added to quench the reaction. The organic phase was separated and washed by water (10 mL) and brine (10 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by silica gel chromatography using hexane and ethyl acetate as eluent to obtain **17** as colorless oil. Yields: 54-91%.

General procedure for the preparation of substrates 1

To a solution of enone (**17**) (2 mmol) in CH_3CN (20 mL), HF (30% water solution) (1 mL) was added. The reaction mixture was stirred at room temperature for 40 min. Saturated aqueous solution of NaHCO_3 (40 mL) were added to quench the reaction. The mixture was extracted with (20 mL \times 2) ethyl acetate, and washed with water (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated. The crude product was purified by silica gel chromatography using hexane and ethyl acetate as eluent to afford **1** with 65-74 % yield.

Preparation of substrates 1h and 1i

Preparation of intermediate 19



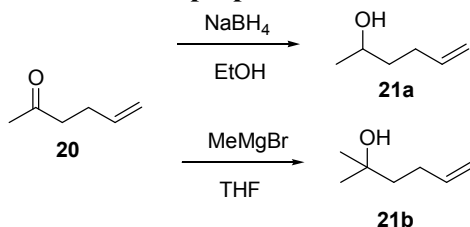
5-phenylpent-1-en-3-ol (**18**)

To a solution of 3-phenylpropanal (4.0 g, 30 mmol) in dry THF (40 mL), vinylmagnesium bromide solution in THF (1 mol/L, 33 mL, 33 mmol) was added dropwise by syringe at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. THF was removed by rotaevaporation and the residue was extracted with ethyl acetate (30 mL×2), washed with water (20 mL), brine (20 mL), dried (Na₂SO₄) and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 12/1 as eluent to give **18** as colorless oil 3.98 g. Yield: 81.9%.

5-phenylpent-1-en-3-one (**19**)

A flame-dried flask was charged with dry CH₂Cl₂ (60 mL) and cooled to -78 °C with a dry ice/acetone bath. Oxalyl chloride (6.30 g, 50 mmol) was then added followed by DMSO (5.31 mL, 75 mmol). The mixture was kept at -78 °C for 15 min, after which time 5-phenylpent-1-en-3-ol (**18**) (3.98 g, 24.6 mmol, dissolved in 20 mL of dry CH₂Cl₂) was added. The reaction was kept at -78 °C for 1 h, and then triethylamine (17.5 mL, 125 mmol) was added and the reaction was allowed to warm to room temperature over 30 min. The reaction mixture was then poured over ice-cold 1 M HCl and extracted with DCM. The combined organic extracts were washed with water (20 mL), brine (20 mL), dried with Na₂SO₄ and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 25/1 as eluent to give **19** as colorless oil 3.47 g. Yield: 88.2%.

Procedure for preparation of intermediate **21**



Hex-5-en-2-ol (**21a**)

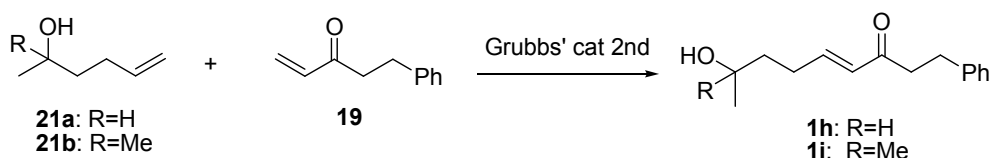
To a solution of hex-5-en-2-one (**20**) (1.0 g, 10 mmol) in EtOH (10 mL), NaBH₄ (0.57 g, 15 mmol) was added at 0 °C. The reaction mixture was stirred at this temperature for 2 h. EtOH was removed by rotaevaporation and the residue was extracted with (20 mL×2) ethyl acetate, washed with water (10 mL), brine (10 mL), dried (Na₂SO₄) and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 10/1 as eluent to give **21a** as colorless oil 0.76 g. Yield: 76.0%.

2-methylhex-5-en-2-ol (**21b**)

To a solution of hex-5-en-2-one (**20**) (1.0 g, 10 mmol) in dry THF (20 mL), methylmagnesium bromide solution in THF (3 mol/L, 4 mL, 12 mmol) was added dropwise by syringe at 0 °C. The

reaction mixture was allowed to warm to room temperature and stirred for 3 h. THF was removed by rotaevaporation and the residue was extracted with ethyl acetate (20 mL×2), washed with water (10 mL), brine (10 mL), dried (Na₂SO₄) and concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 8/1 as eluent to give **21b** as colorless oil 0.97 g. Yield: 85.1%.

Preparation of substrates **1h** and **1i**



The following procedure is general to **1i**.

(*E*)-8-hydroxy-1-phenylnon-4-en-3-one (**1h**)

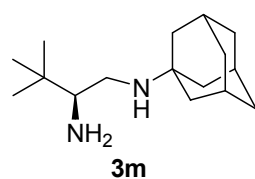
A flame-dried flask was charged with dry CH₂Cl₂ (20 mL), **21a** (400 mg, 4 mmol) and **19** (320 mg, 2 mmol) was added by syringe. Then the Grubbs catalyst 2nd generation (25 mg, 0.04 mmol) was added under protection of Argon. The reaction mixture was heated at reflux for 3 h. The mixture was filtered to recycle the catalyst and the filtrate was concentrated. The crude product was purified by silica gel chromatography using hexane/ethyl acetate = 8/1 as eluent to give **1h** as colorless oil 166 mg. Yield: 35.8%.

General procedure for the Oxa-Michael addition

Catalyst **3m** (5.0 mg, 0.02 mmol) was added to a solution of (L)-camphorsulfonic acid (4.6 mg, 0.02 mmol) in chloroform (1.5 mL). Then enone **1** (0.2 mmol) was added and the mixture was stirred at room temperature for 48-72 h. Water (3 mL) was added. The mixture was extracted with ethyl acetate (2×3 mL) and the combined organic phases were washed with brine, dried (Na₂SO₄), filtered and concentrated. Crude products were purified by silica gel column chromatography to afford the pure products **2**.

Data of catalysts

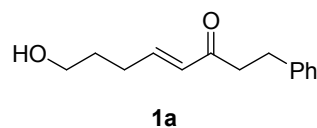
(S)-N¹-Adamantyl-3,3-dimethylbutane-1,2-diamine



White solid, mp: 120-126 °C; [α]_D²³ = 16.66 (*c* 0.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 2.77(dd, *J* = 2.4, 10.8 Hz, 1H), 2.37 (dd, *J* = 2.4, 10.8 Hz, 1H), 2.19 (t, *J* = 10.4 Hz, 1H), 2.06 (brs, 3H), 1.68-1.59 (m, 12H), 1.45 (brs, 3H), 0.89 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 61.08, 50.48, 42.92, 41.77, 36.81, 33.82, 29.64, 26.43; IR (Film): ν 3421, 3302, 2905, 2850, 1470, 1450, 1358, 1147, 1097, 735 cm⁻¹; ESI-MS (*m/z*): 251.2 (M+H⁺); HRMS Calc. C₁₆H₃₁N₂ (M+H⁺) 251.2842 Found: 251.2840.

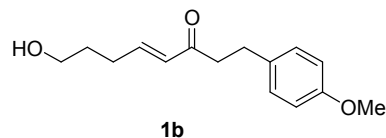
Data of substrates

(E)-8-Hydroxy-1-phenyloct-4-en-3-one



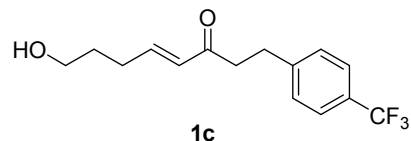
Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.26 (m, 2H), 7.20-7.17 (m, 3H), 6.84 (dt, *J* = 7.2, 15.6 Hz, 1H), 6.13 (dt, *J* = 1.6, 15.6 Hz, 1H), 3.67 (t, *J* = 6.4 Hz, 2H), 2.90-2.82 (m, 4H), 2.29-2.33 (m, 2H), 1.90-1.84 (m, 2H), 1.31 (brs, 1H).

(E)-8-Hydroxy-1-(4-methoxyphenyl)oct-4-en-3-one



Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 7.14 (d, *J* = 8.4 Hz, 2H), 6.87-6.83 (m, 3H), 6.14 (d, *J* = 15.6 Hz, 1H), 3.80 (s, 3H), 3.69 (t, *J* = 6.4 Hz, 2H), 2.91-2.85 (m, 4H), 2.33 (q, *J* = 3.6 Hz, 2H), 1.76-1.72 (m, 2H), 1.50 (brs, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 199.69, 158.00, 146.72, 133.31, 130.65, 129.31, 113.93, 61.98, 55.29, 42.02, 30.98, 29.29, 28.79; IR (Film): ν 3440, 2932, 1664, 1626, 1512, 1245, 1185, 1035, 825 cm⁻¹; ESI-MS (*m/z*): 271.1 (M+Na⁺); HRMS Calc. C₁₅H₂₀Na₁O₃ (M+Na⁺) 271.1304 Found: 271.1299.

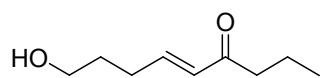
(E)-8-Hydroxy-1-(4-(trifluoromethyl)phenyl)oct-4-en-3-one



Colorless oil; ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 6.85 (dt, *J* = 6.8, 16.4 Hz, 1H), 6.13 (d, *J* = 15.6 Hz, 1H), 3.67 (t, *J* = 6.4 Hz, 2H), 3.00 (t, *J* = 6.4 Hz, 2H), 2.88 (t, *J* = 7.2 Hz, 2H),

2.32 (q, $J = 7.2$ Hz, 2H), 1.72 (m, $J = 7.2$ Hz, 2H), 1.64 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.67, 147.05, 145.44, 130.42, 128.76, 128.68, 128.36, 125.66, 125.45, 125.42, 125.38, 125.34, 122.96, 61.97, 41.17, 30.94, 29.70, 28.81; ν 3440, 2932, 1664, 1626, 1512, 1245, 1185, 1035, 825 cm^{-1} ; ESI-MS (m/z): 309.1 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{15}\text{H}_{17}\text{F}_3\text{Na}_1\text{O}_2$ ($\text{M}+\text{Na}^+$) 309.1073 Found: 309.1081.

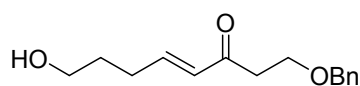
(E)-9-Hydroxynon-5-en-4-one



1d

Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 6.83 (dt, $J = 7.2$, 15.6 Hz, 1H) 6.11 (dt, $J = 1.6$, 15.6 Hz, 1H), 3.67 (t, $J = 6.4$ Hz, 2H), 2.50 (t, $J = 6.4$ Hz, 2H), 2.34-2.28 (m, 2H), 1.76-1.60 (m, 5H), 0.92 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 200.75, 146.25, 130.61, 61.96, 42.07, 30.96, 28.73, 17.67, 13.79; IR (Film): ν 3447, 2934, 2864, 1669, 1654, 1456, 1197, 1059, 978 cm^{-1} ; ESI-MS (m/z): 179.1 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_9\text{H}_{16}\text{Na}_1\text{O}_2$ ($\text{M}+\text{Na}^+$) 179.1043 Found: 179.1048.

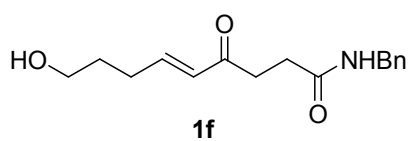
(E)-1-(Benzyloxy)-8-hydroxyoct-4-en-3-one



1e

Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.37-7.29 (m, 5H), 6.89 (dt, $J = 7.2$, 15.6 Hz, 1H) 6.19 (d, $J = 15.6$ Hz, 1H), 4.55 (s, 2H), 3.82 (t, $J = 6.4$ Hz, 2H), 3.70 (t, $J = 6.4$ Hz, 2H), 2.89 (t, $J = 6.4$ Hz, 2H), 2.36 (q, $J = 7.2$ Hz, 2H), 1.78-1.74 (m, 2H), 1.61 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.48, 147.21, 138.22, 130.91, 128.40, 127.73, 127.66, 73.27, 65.63, 62.01, 40.25, 30.97, 28.83; IR (Film): ν 3444, 2932, 2868, 1667, 1626, 1453, 1366, 1199, 1047, 740, 699 cm^{-1} ; ESI-MS (m/z): 271.1 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{15}\text{H}_{20}\text{Na}_1\text{O}_3$ ($\text{M}+\text{Na}^+$) 271.1304 Found: 271.1305.

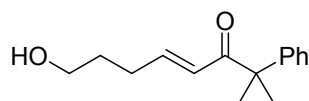
(E)-N-Benzyl-9-hydroxy-4-oxonon-5-enamide



1f

White solid; mp: 85-89 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.23 (m, 5H), 6.88 (dt, $J = 7.2$, 15.6 Hz, 1H), 6.20 (brs, 1H), 6.11 (d, $J = 16.0$ Hz, 1H), 4.39 (d, $J = 5.6$ Hz, 2H), 3.64 (t, $J = 6.4$ Hz, 2H), 2.93 (t, $J = 6.4$ Hz, 2H), 2.49 (t, $J = 6.4$ Hz, 2H), 2.33-2.27 (m, 2H), 1.89 (brs, 1H), 1.70 (m, $J = 7.2$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.22, 172.04, 147.52, 138.21, 130.25, 128.65, 127.69, 127.41, 61.84, 43.60, 35.08, 30.85, 29.99, 28.87; IR (Film): ν 3315, 2924, 1693, 1640, 1548, 1453, 1385, 1060, 695 cm^{-1} ; ESI-MS (m/z): 298.0 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{16}\text{H}_{21}\text{N}_1\text{Na}_1\text{O}_3$ ($\text{M}+\text{Na}^+$) 298.1414 Found: 298.1400.

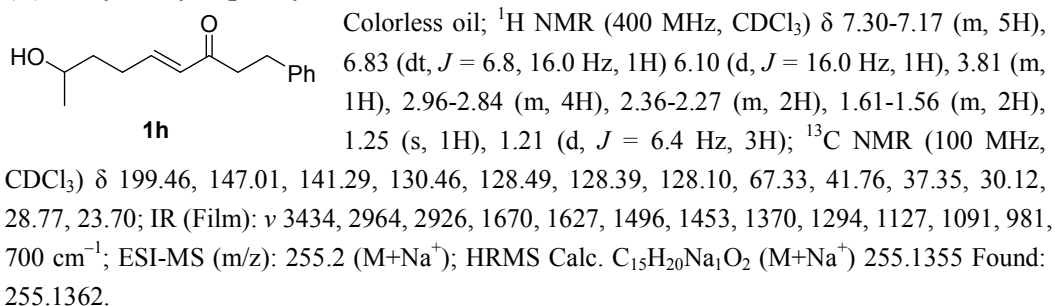
(E)-8-Hydroxy-2-methyl-2-phenyloct-4-en-3-one



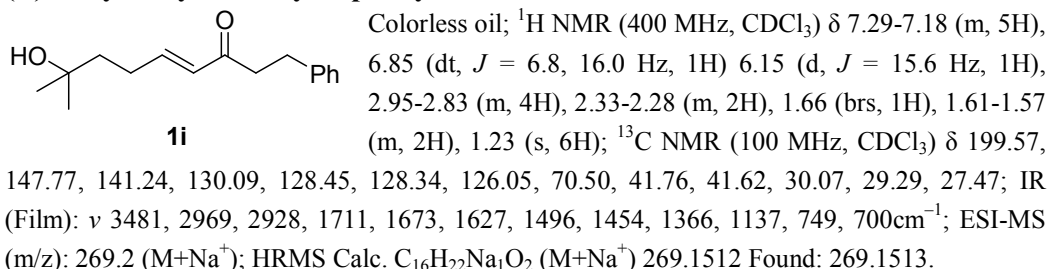
1g

Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.22 (m, 5H), 6.88 (dt, $J = 7.2$, 15.2 Hz, 1H), 5.96 (dt, $J = 1.6$, 15.2 Hz, 1H), 3.54 (t, $J = 6.4$ Hz, 2H), 2.17-2.15 (m, 2H), 1.63-1.59 (m, 3H), 1.47 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ 201.43, 146.11, 144.10, 128.69, 126.74, 126.33, 126.29, 61.94, 50.98, 30.93, 28.53, 25.19; IR (Film): ν 3448, 2973, 2933, 1691, 1625, 1496, 1360, 1381, 1063, 980, 700 cm^{-1} ; ESI-MS (m/z): 255.2 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{15}\text{H}_{20}\text{Na}_1\text{O}_2$ ($\text{M}+\text{Na}^+$) 255.1355 Found: 255.1347.

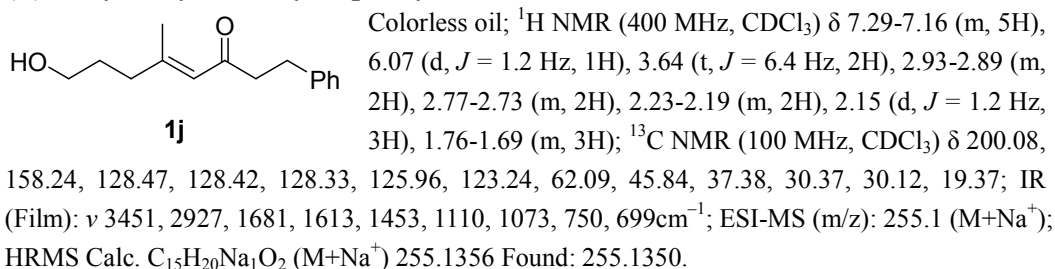
(E)-8-Hydroxy-1-phenylnon-4-en-3-one



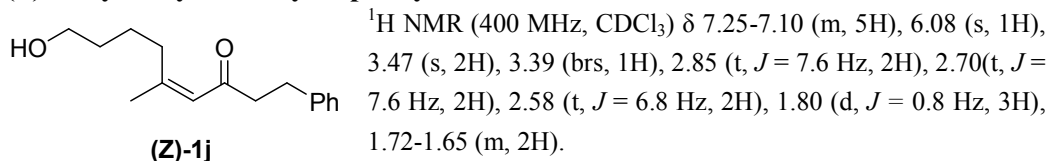
(E)-8-Hydroxy-8-methyl-1-phenylnon-4-en-3-one



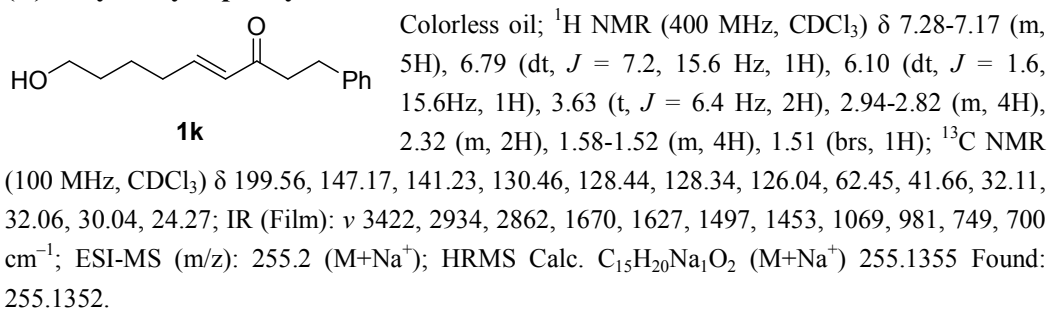
(E)-8-Hydroxy-5-methyl-1-phenyloct-4-en-3-one



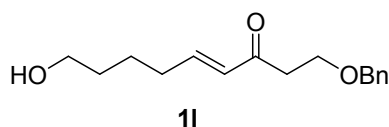
(Z)-8-Hydroxy-5-methyl-1-phenyloct-4-en-3-one



(E)-9-hydroxy-1-phenylnon-4-en-3-one

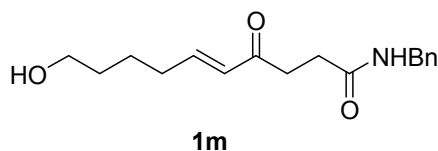


(E)-1-(benzyloxy)-9-hydroxynon-4-en-3-one



Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.26 (m, 5H), 6.84 (dt, $J = 7.2, 15.6$ Hz, 1H), 6.10 (dt, $J = 1.6, 16.0$ Hz, 1H), 4.51 (s, 2H), 3.78 (t, $J = 6.4$ Hz, 2H), 3.63 (t, $J = 6.0$ Hz, 2H), 2.84 (t, $J = 6.4$ Hz, 2H), 2.27-2.22 (m, 2H), 1.59-1.52 (m, 4H), 1.25 (brs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.54, 147.63, 138.15, 130.75, 128.35, 127.69, 127.62, 73.22, 65.56, 62.46, 40.11, 32.14, 32.08, 24.26; IR (Film): ν 3407, 2935, 2857, 1714, 1366, 1089, 738, 698cm^{-1} ; ESI-MS (m/z): 285.1 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{16}\text{H}_{22}\text{Na}_1\text{O}_3$ ($\text{M}+\text{Na}^+$) 285.1461 Found: 285.1450.

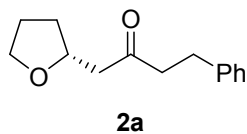
(E)-N-benzyl-10-hydroxy-4-oxodec-5-enamide



Colorless oil; ^1H NMR (400 MHz, CDCl_3) δ 7.33-7.24 (m, 5H), 6.87 (dt, $J = 6.8, 16.0$ Hz, 1H), 6.22 (brs, 1H), 6.10 (d, $J = 16.0$ Hz, 1H), 4.40 (d, $J = 6.0$ Hz, 2H), 3.63 (t, $J = 6.0$ Hz, 2H), 2.93 (t, $J = 6.4$ Hz, 2H), 2.50 (t, $J = 6.4$ Hz, 2H), 2.26-2.22 (m, 2H), 1.85 (brs, 1H), 1.59-1.53 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 199.22, 172.03, 147.80, 138.25, 130.21, 128.63, 127.69, 127.39, 62.36, 43.60, 35.09, 32.16, 32.07, 30.04, 24.24; IR (Film): ν 3306, 2924, 2852, 1638, 1543, 1457, 1377, 1186, 1156cm^{-1} ; ESI-MS (m/z): 290.2 ($\text{M}+\text{H}^+$); HRMS Calc. $\text{C}_{17}\text{H}_{23}\text{N}_1\text{O}_3$ ($\text{M}+\text{H}^+$) 290.1751 Found: 290.1754.

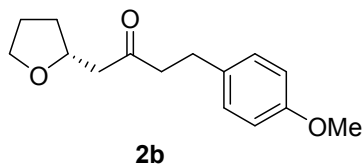
Data of products

(R)-4-Phenyl-1-(tetrahydrofuran-2-yl) butan-2-one



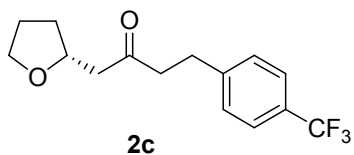
Colorless oil; $[\alpha]_{\text{D}}^{23} = -4.62$ (c 1.0, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.28-7.17 (m, 5H), 4.24-4.20 (m, 1H), 3.86-3.82 (m, 1H), 3.73-3.69 (m, 1H), 2.88 (t, $J = 8.0$ Hz, 2H), 2.77-2.80 (m, 2H), 2.72 (dd, $J = 6.8, 16.0$ Hz, 1H), 2.52 (dd, $J = 6.0, 16.0$ Hz, 1H), 2.11-2.04 (m, 1H), 1.90-1.86 (m, 2H), 1.41-1.48 (m, 1H); HPLC-separation conditions: Chiralcel OD-H, 20°C , 210 nm, 80 : 20 hexane/*i*-PrOH, 0.5 mL/min; $t_{\text{major}} = 14.6$ min, $t_{\text{minor}} = 18.6$ min; 85% ee.

(R)-4-(4-Methoxyphenyl)-1-(tetrahydrofuran-2-yl) butan-2-one



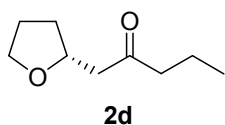
Colorless oil; $[\alpha]_{\text{D}}^{23} = -7.99$ (c 1.0, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.12 (d, $J = 8.8$ Hz, 2H), 6.86-6.83 (m, 2H), 4.26-4.21 (m, 1H), 3.88-3.71 (m, 2H), 3.81 (s, 3H), 2.89-2.71 (m, 5H), 2.53 (dd, $J = 5.6, 15.6$ Hz, 1H), 2.12-2.07 (m, 1H), 1.94-1.88 (m, 2H), 1.50-1.46 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 208.54, 157.99, 133.15, 129.27, 113.92, 75.05, 67.82, 55.28, 48.88, 45.32, 31.51, 28.70, 25.55; IR (Film): ν 2923, 2853, 1710, 1611, 1513, 1463, 1299, 1245, 1178, 1057, 1035, 825cm^{-1} ; ESI-MS (m/z): 271.1 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{15}\text{H}_{20}\text{Na}_1\text{O}_3$ ($\text{M}+\text{Na}^+$) 271.1305 Found: 271.1309; HPLC-separation conditions: Chiralcel AD-H, 20°C , 210 nm, 90 : 10 hexane/*i*-PrOH, 0.7 mL/min; $t_{\text{major}} = 14.7$ min, $t_{\text{minor}} = 14.0$ min; 90 % ee.

(R)-4-(4-(trifluoromethyl) phenyl)-1-(tetrahydrofuran-2-yl) butan-2-one



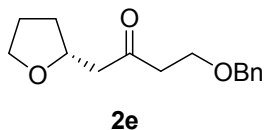
Colorless oil; $[\alpha]_D^{22} = -10.51$ (*c* 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 4.22-4.15 (m, 1H), 3.85-3.66 (m, 2H), 2.96-2.92 (m, 2H), 2.81-2.77 (m, 2H), 2.68 (dd, *J* = 8.0, 15.6 Hz, 1H), 2.50 (dd, *J* = 5.6, 15.6 Hz, 1H), 2.08 (m, 1H), 1.89-1.82 (m, 2H), 1.47-1.42 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 207.74, 145.27, 145.25, 128.69, 128.55, 128.22, 127.95, 125.60, 125.38, 125.34, 125.30, 125.26, 122.89, 120.19, 75.01, 67.85, 48.77, 44.44, 31.47, 29.13, 25.47; ν 2927, 2872, 1715, 1618, 1417, 1326, 1163, 1123, 1068, 1019, 834cm⁻¹; ESI-MS (*m/z*): 309.1 (M+Na⁺); HRMS Calc. C₁₅H₁₇F₃Na₁O₂ (M+Na⁺) 309.1073 Found: 309.1078; HPLC-separation conditions: Chiralcel PC-II, 20 °C, 210 nm, 80 : 20 hexane/*i*-PrOH, 0.4 mL/min; $t_{\text{major}} = 9.3$ min, $t_{\text{minor}} = 13.3$ min; 82 % ee.

(R)-1-(tetrahydrofuran-2-yl) pentan-2-one



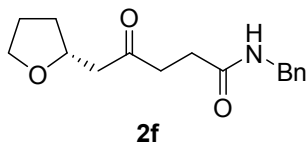
Colorless oil; $[\alpha]_D^{23} = -1.58$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 4.24-4.17 (m, 1H), 3.87-3.81 (m, 1H), 3.73-3.67 (m, 1H), 2.72 (dd, *J* = 6.8, 16.0 Hz, 1H), 2.49 (dd, *J* = 6.0, 16.0 Hz, 1H), 2.41 (t, *J* = 7.2 Hz, 2H), 2.11-2.04 (m, 1H), 1.91-1.64 (m, 2H), 1.61-1.56 (m, 2H), 1.47-1.42 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 209.64, 75.06, 67.77, 48.60, 45.64, 31.49, 25.53, 16.99, 13.66; IR (Film): ν 2922, 1708, 1680, 1649, 1179, 1093cm⁻¹; ESI-MS (*m/z*): 179.1 (M+Na⁺); HRMS Calc. C₉H₁₆Na₁O₂ (M+Na⁺) 179.1043 Found: 179.1044; HPLC-separation conditions: Chiralcel PC-II, 20 °C, 202 nm, 90 : 10 hexane/*i*-PrOH, 0.5 mL/min; $t_{\text{major}} = 13.5$ min, $t_{\text{minor}} = 17.3$ min; 87 % ee.

(R)-4-(benzyloxy)-1-(tetrahydrofuran-2-yl) butan-2-one



Colorless oil; $[\alpha]_D^{23} = -6.03$ (*c* 0.7, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.39-7.29 (m, 5H), 4.54 (s, 2H), 4.26 (m, 1H), 3.87 (q, *J* = 7.2 Hz, 1H), 3.79-3.74 (m, 3H), 2.83-2.77 (m, 3H), 2.61 (dd, *J* = 5.6, 16.0 Hz, 1H), 2.14-2.08 (m, 1H), 1.94-1.88 (m, 2H), 1.52-1.47 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 207.61, 138.16, 128.41, 127.73, 127.68, 74.90, 73.25, 67.83, 65.21, 49.23, 43.59, 31.51, 25.56; IR (Film): ν 2927, 2870, 1734, 1715, 1455, 1374, 1159, 1099, 1074, 740, 699 cm⁻¹; ESI-MS (*m/z*): 271.1 (M+Na⁺); HRMS Calc. C₁₅H₂₀Na₁O₃ (M+Na⁺) 271.1305 Found: 271.1301; HPLC-separation conditions: Chiralcel AS-H, 20 °C, 210 nm, 80 : 20 hexane/*i*-PrOH, 0.3 mL/min; $t_{\text{major}} = 31.3$ min, $t_{\text{minor}} = 33.1$ min; 86 % ee.

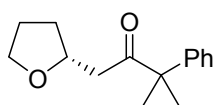
(R)-N-benzyl-4-oxo-5-(tetrahydrofuran-2-yl) pentanamide



Colorless oil; $[\alpha]_D^{26} = -12.89$ (*c* 0.6, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.28-7.17 (m, 5H), 6.09 (brs, 1H), 4.33 (d, *J* = 6.0 Hz, 2H), 4.17-4.10 (m, 1H), 3.78-3.73 (m, 1H), 3.64-3.58 (m, 1H), 2.80-2.76 (m, 2H), 2.66 (dd, *J* = 6.0, 15.6 Hz, 1H), 2.49 (dd, *J* = 4.8, 15.2 Hz, 1H), 2.43-2.38 (m, 2H), 2.03-1.95 (m, 1H), 1.82-1.78 (m, 2H), 1.44-1.37 (m, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 208.28, 171.78, 138.30, 128.62, 127.69, 127.37, 75.04, 67.83, 48.66, 43.60, 38.51, 31.46, 29.76, 25.50; IR (Film): ν 3310, 2927, 2855, 1710, 1652, 1546, 1436, 1356, 1087, 1045, 700cm⁻¹; ESI-MS (*m/z*): 298.0 (M+Na⁺); HRMS Calc. C₁₆H₂₁N₁Na₁O₃

(M+Na⁺) 298.1414 Found: 298.1402; HPLC-separation conditions: Chiralcel PC-II, 20 °C, 210 nm, 80 : 20 hexane/*i*-PrOH, 1.0 mL/min; $t_{\text{major}} = 38.4$ min, $t_{\text{minor}} = 43.3$ min; 88 % ee.

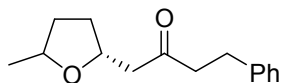
(*R*)-3-methyl-3-phenyl-1-(tetrahydrofuran-2-yl) butan-2-one



2g

Colorless oil; $[\alpha]_{\text{D}}^{23} = 6.31$ (c 0.3, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.34-7.22 (m, 5H), 4.16-4.13 (m, 1H), 3.69-3.61 (m, 2H), 2.61 (dd, $J = 6.0$, 16.8 Hz, 1H), 2.25 (dd, $J = 6.8$, 17.2 Hz, 1H), 2.02-2.97 (m, 1H), 1.79-1.73 (m, 2H), 1.48 (s, 3H), 1.46 (s, 3H), 1.24-1.17 (m, 1H); ESI-MS (m/z): 255.2 (M+Na⁺); ¹³C NMR (100 MHz, CDCl₃) δ 211.08, 143.64, 128.69, 126.86, 126.14, 75.20, 67.46, 52.28, 43.37, 31.22, 25.50, 25.26, 24.56; IR (Film): ν 2971, 2928, 2872, 1708, 1597, 1495, 1447, 1384, 1069, 1036, 701 cm⁻¹; HRMS Calc. C₁₅H₂₀Na₁O₂ (M+Na⁺) 255.1355 Found: 255.1348; HPLC-separation conditions: Chiralcel PC-II, 20 °C, 210 nm, 80 : 20 hexane/*i*-PrOH, 0.5 mL/min; $t_{\text{major}} = 28.1$ min, $t_{\text{minor}} = 25.5$ min; 38 % ee.

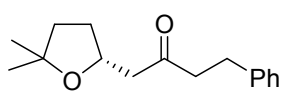
1-((*2R*)-5-methyl-tetrahydrofuran-2-yl)-4-phenylbutan-2-one



2h

Colorless oil; $[\alpha]_{\text{D}}^{27} = -10.17$ (c 0.7, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.17 (m, 10H), 4.40-4.36 (m, 1H), 4.22-4.18 (m, 1H), 4.09-4.04 (m, 1H), 3.96-3.91 (m, 1H), 2.92-2.87 (m, 4H), 2.80-2.69 (m, 6H), 2.50 (td, $J = 6.0$, 16.0 Hz, 2H), 2.17-1.94 (m, 4H), 1.54-1.42 (m, 4H), 1.22-1.18 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 208.49, 208.41, 141.09, 128.45, 128.33, 126.04, 75.46, 75.07, 74.81, 74.45, 49.39, 49.24, 45.11, 45.05, 33.64, 32.65, 32.41, 31.40, 29.51, 29.50, 21.38, 21.25; IR (Film): ν 3027, 2928, 1712, 1497, 1454, 1376, 1084, 749, 700cm⁻¹; ESI-MS (m/z): 255.2 (M+Na⁺); HRMS Calc. C₁₅H₂₀Na₁O₂ (M+Na⁺) 255.1355 Found: 255.1353; HPLC-separation conditions: Chiralcel PC-II, 20 °C, 210 nm, 80 : 20 hexane/*i*-PrOH, 0.5 mL/min; $t_{\text{major}} = 12.6$ min, $t_{\text{minor}} = 13.9$ min; 80 % ee; $t_{\text{major}} = 11.7$ min, $t_{\text{minor}} = 17.0$ min; 89 % ee.

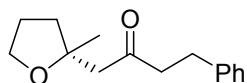
(*R*)-1-(5,5-dimethyl-tetrahydrofuran-2-yl)-4-phenylbutan-2-one



2i

Colorless oil; $[\alpha]_{\text{D}}^{27} = -2.86$ (c 0.5, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.29-7.17 (m, 5H), 4.35-4.29 (m, 1H), 2.91-2.76 (m, 4H), 2.73 (dd, $J = 6.8$, 15.6 Hz, 1H), 2.50 (dd, $J = 6.4$, 15.6 Hz, 1H), 2.15-2.07 (m, 1H), 1.74-1.70 (m, 2H), 1.62-1.54 (m, 1H), 1.22 (d, $J = 4.8$ Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 208.53, 141.11, 128.44, 128.32, 126.02, 80.81, 74.38, 49.70, 45.13, 38.31, 32.06, 29.52, 28.01; IR (Film): ν 3027, 2968, 2928, 1713, 1497, 1454, 1398, 1365, 1137, 1046, 748, 699cm⁻¹; ESI-MS (m/z): 269.2 (M+Na⁺); HRMS Calc. C₁₆H₂₂Na₁O₂ (M+Na⁺) 269.1512 Found: 269.1517; HPLC-separation conditions: Chiralcel PC-II, 20 °C, 210 nm, 90 : 10 hexane/*i*-PrOH, 0.4 mL/min; $t_{\text{major}} = 15.0$ min, $t_{\text{minor}} = 19.6$ min; 35 % ee.

(*R*)-1-(2-methyl-tetrahydrofuran-2-yl)-4-phenylbutan-2-one

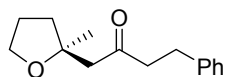


2j

Colorless oil; $[\alpha]_{\text{D}}^{25} = -5.84$ (c 0.3, MeOH); ¹H NMR (400 MHz, CDCl₃) δ 7.28-7.15 (m, 5H), 3.83-3.70 (m, 2H), 2.88-2.78 (m, 4H), 2.65-2.55 (m, 2H), 1.92-1.70 (m, 4H), 1.22 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 208.84, 141.18, 128.40, 128.35, 125.98, 81.80, 67.17, 53.22, 46.03, 36.68, 29.60, 26.44, 25.76; IR (Film): ν 2965, 2927, 2871, 1710, 1497, 1453, 1371, 1043, 746, 699cm⁻¹; ESI-MS (m/z): 255.1 (M+Na⁺); HRMS Calc. C₁₅H₂₀Na₁O₂ (M+Na⁺) 255.1356 Found:

255.1352; HPLC-separation conditions: Chiralcel PC-II, 20 °C, 210 nm, 90 : 10 hexane/*i*-PrOH, 0.4 mL/min; $t_{\text{major}} = 14.8$ min, $t_{\text{minor}} = 15.8$ min; 72 % ee.

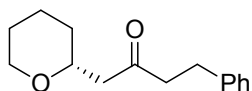
(S)-1-(2-methyl-tetrahydrofuran-2-yl)-4-phenylbutan-2-one



(S)-2j

HPLC-separation conditions: Chiralcel PC-II, 20 °C, 210 nm, 90 : 10 hexane/*i*-PrOH, 0.4 mL/min; $t_{\text{major}} = 14.5$ min, $t_{\text{minor}} = 13.7$ min; -36 % ee.

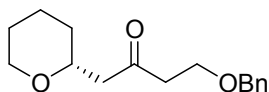
(R)-4-phenyl-1-(tetrahydro-2H-pyran-2-yl)butan-2-one



2k

Colorless oil; $[\alpha]_{\text{D}}^{24} = 2.72$ (c 1.1, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.28-7.16 (m, 5H), 3.93-3.90 (m, 1H), 3.76-3.73 (m, 1H), 3.44-3.38 (m, 1H), 2.92-2.87 (m, 2H), 2.80-2.75 (m, 2H), 2.64 (dd, $J = 8.0, 15.2$ Hz, 1H), 2.37 (dd, $J = 4.8, 15.6$ Hz, 1H), 1.81-1.79 (m, 1H), 1.64-1.47 (m, 4H), 1.30-1.26 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 208.44, 141.13, 128.43, 128.32, 126.01, 74.15, 68.51, 49.69, 45.25, 31.78, 29.44, 25.72, 23.32; IR (Film): ν 2928, 2853, 1715, 1453, 1377, 1089, 1044, 745, 699cm^{-1} ; ESI-MS (m/z): 255.2 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{15}\text{H}_{20}\text{Na}_1\text{O}_2$ ($\text{M}+\text{Na}^+$) 255.1355 Found: 255.1360; HPLC-separation conditions: Chiralcel AS-H, 20 °C, 210 nm, 90 : 10 hexane/*i*-PrOH, 0.8 mL/min; $t_{\text{major}} = 8.9$ min, $t_{\text{minor}} = 12.1$ min; 81 % ee.

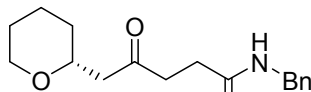
(R)-4-(benzyloxy)-1-(tetrahydro-2H-pyran-2-yl)butan-2-one



2l

Colorless oil; $[\alpha]_{\text{D}}^{24} = 2.61$ (c 0.5, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.34-7.25 (m, 5H), 4.48 (s, 2H), 3.92-3.88 (m, 1H), 3.76-3.70 (m, 3H), 3.44-3.37 (m, 1H), 2.73 (t, $J = 6.4$ Hz, 2H), 2.66 (dd, $J = 7.6, 16.0$ Hz, 1H), 2.42 (dd, $J = 5.2, 15.6$ Hz, 1H), 1.80-1.78 (m, 1H), 1.60-1.45 (m, 4H), 1.27-1.23 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 207.50, 138.13, 128.35, 127.67, 127.60, 73.94, 73.17, 68.48, 65.11, 50.00, 43.75, 31.75, 25.73, 23.30; IR (Film): ν 2926, 2854, 1716, 1454, 1365, 1089, 1047, 737, 698cm^{-1} ; ESI-MS (m/z): 285.1 ($\text{M}+\text{Na}^+$); HRMS Calc. $\text{C}_{16}\text{H}_{22}\text{Na}_1\text{O}_3$ ($\text{M}+\text{Na}^+$) 285.1461 Found: 285.1450; HPLC-separation conditions: Chiralcel (PC-II, 20 °C, 210 nm, 80 : 20 hexane/*i*-PrOH, 0.4 mL/min; $t_{\text{major}} = 16.9$ min, $t_{\text{minor}} = 19.9$ min; 90 % ee.

(R)-N-benzyl-4-oxo-5-(tetrahydro-2H-pyran-2-yl)pentanamide



2m

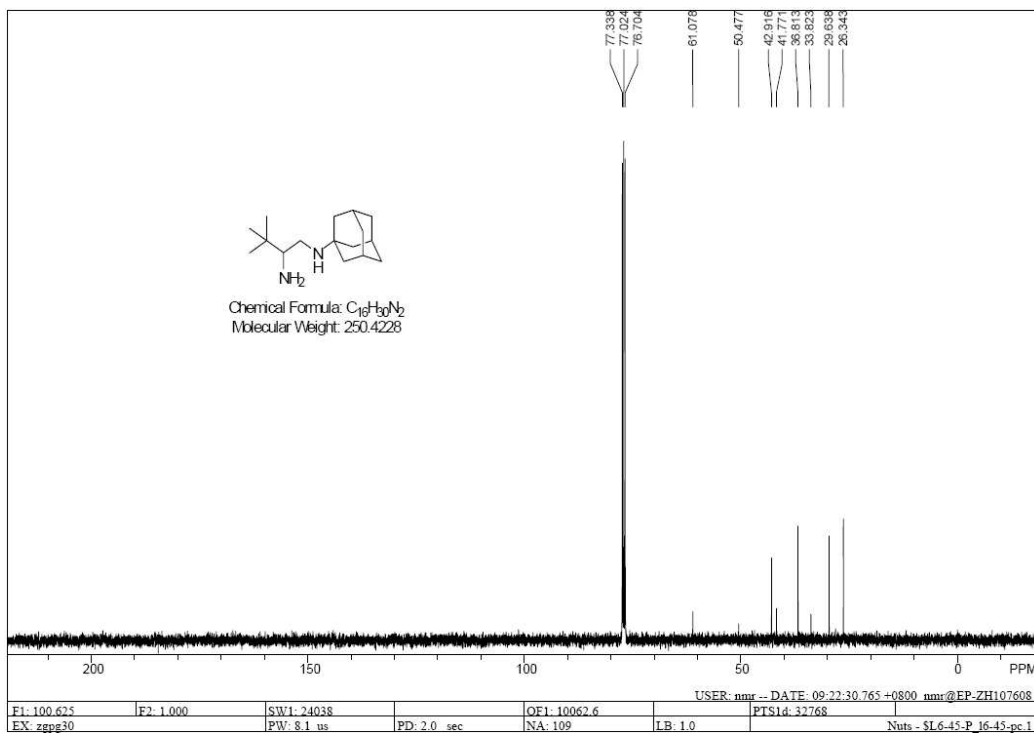
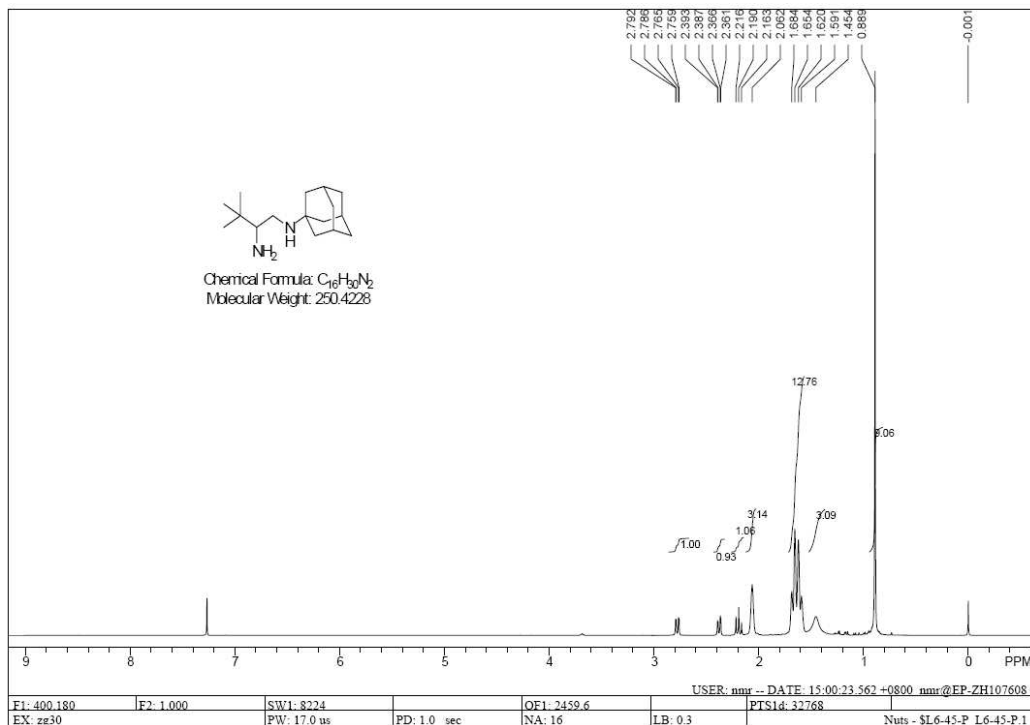
Colorless oil; $[\alpha]_{\text{D}}^{24} = 24.11$ (c 0.5, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.31-7.23 (m, 5H), 6.50 (brs, 1H), 4.36 (d, $J = 5.6$ Hz, 2H), 3.89-3.85 (m, 1H), 3.74-3.71 (m, 1H), 3.40-3.34 (m, 1H), 2.82-2.76 (m, 2H), 2.66-2.60 (m, 1H), 2.47-2.38 (m, 3H), 1.80-1.78 (m, 1H), 1.59-1.45 (m, 4H), 1.27-1.21 (m, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 208.37, 171.92, 138.45, 128.53, 127.59, 127.23, 74.06, 68.38, 49.47, 43.43, 38.66, 31.70, 29.65, 25.66, 23.25; IR (Film): ν 3312, 2933, 2855, 1710, 1651, 1545, 1439, 1356, 1087, 1045, 699cm^{-1} ; ESI-MS (m/z): 290.2 ($\text{M}+\text{H}^+$); HRMS Calc. $\text{C}_{17}\text{H}_{23}\text{N}_1\text{O}_3$ ($\text{M}+\text{H}^+$) 290.1751 Found: 290.1761; HPLC-separation conditions: Chiralcel (PC-II, 20 °C, 210 nm, 80 : 20 hexane/*i*-PrOH, 0.7 mL/min; $t_{\text{major}} = 35.8$ min, $t_{\text{minor}} = 49.0$ min; 83 % ee.

Reference:

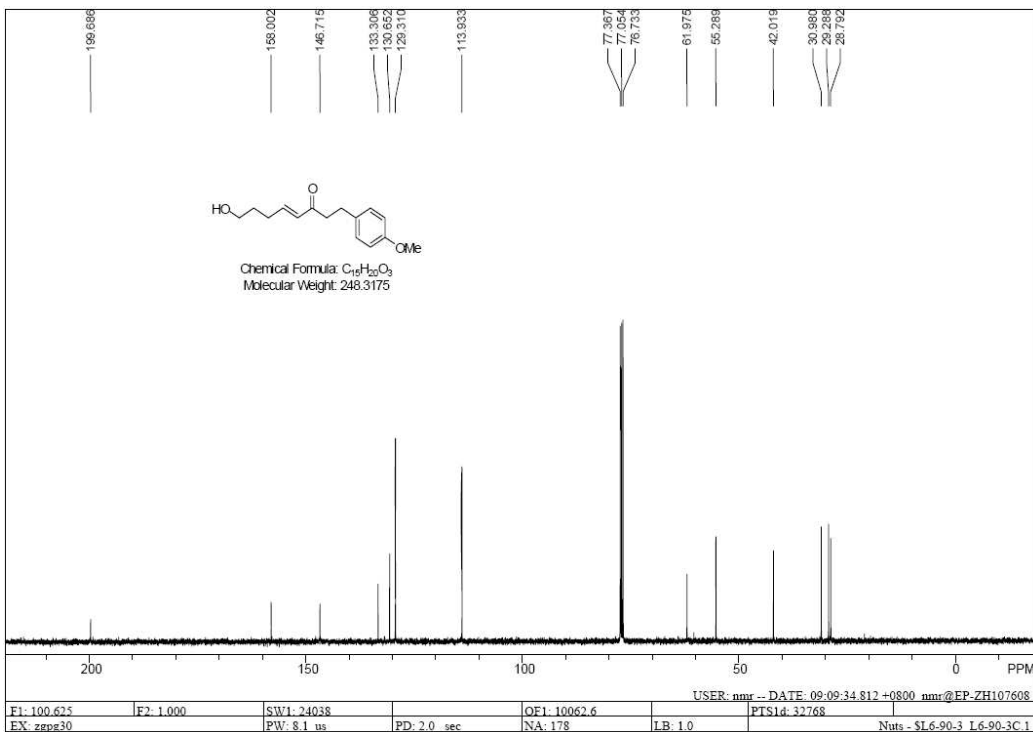
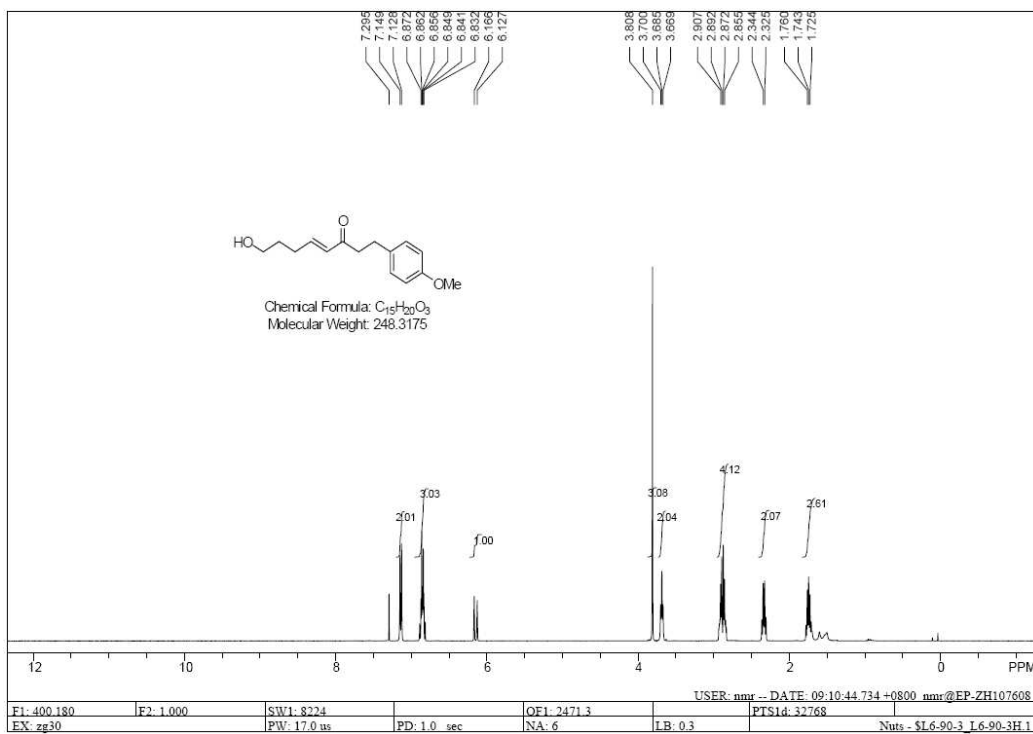
- [1] Asano, K.; Matsubara, S. *J. Am. Chem. Soc.* **2011**, 133, 16711-16713.
- [2] Li, J. Y.; S Luo, S. Z.; Cheng, J. P. *J. Org. Chem.*, **2009**, 74, 1747-1750.
- [3] Li, P.; Zhao, G.; Zhu, S. Z. *Chin. J. Org. Chem.*, **2011**, 29, 2749-2758.
- [4] Gao, Y.; Ren, Q.; Wang, L.; Wang, J. *Chem. Eur. J.*, **2010**, 16, 13068.
- [5] Lu, Y. P.; Zheng, C. W.; Zhao, G.; Zou, G. *Adv. Synth. Catal.* **2011**, 353, 3129-3133.
- [6] Yang, Y. Q.; Chen, X. K.; Xiao, H.; Liu, W.; Zhao, G. *Chem. Commun.* **2010**, 46, 4130.

Copies of NMR spectra and HPLC traces

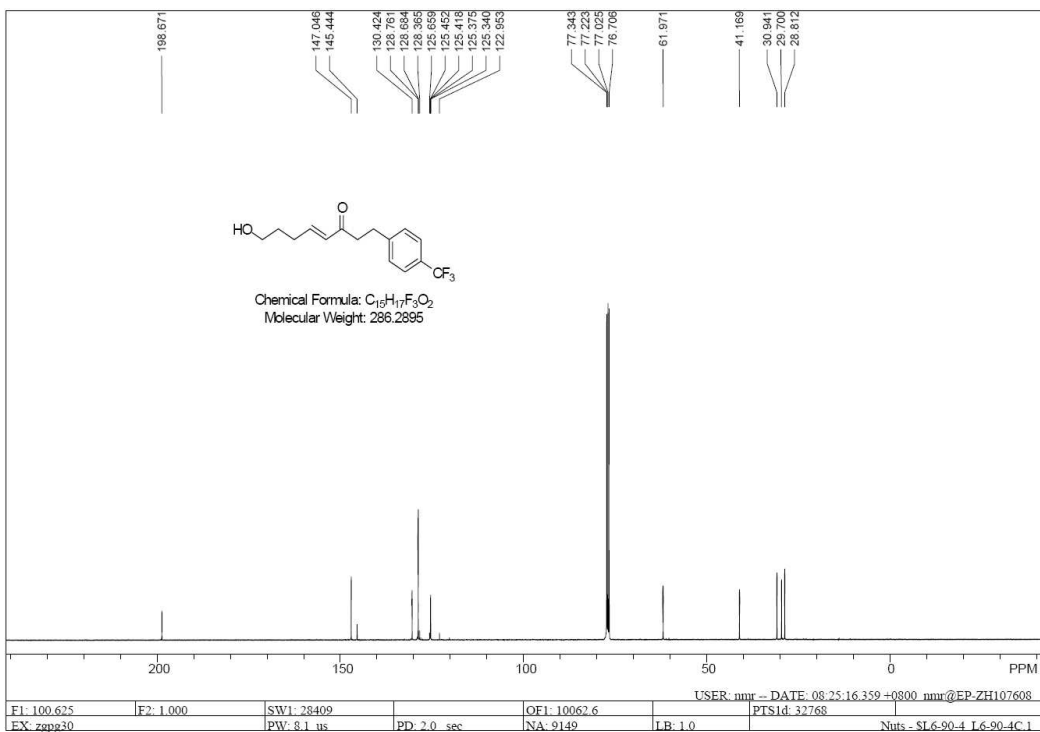
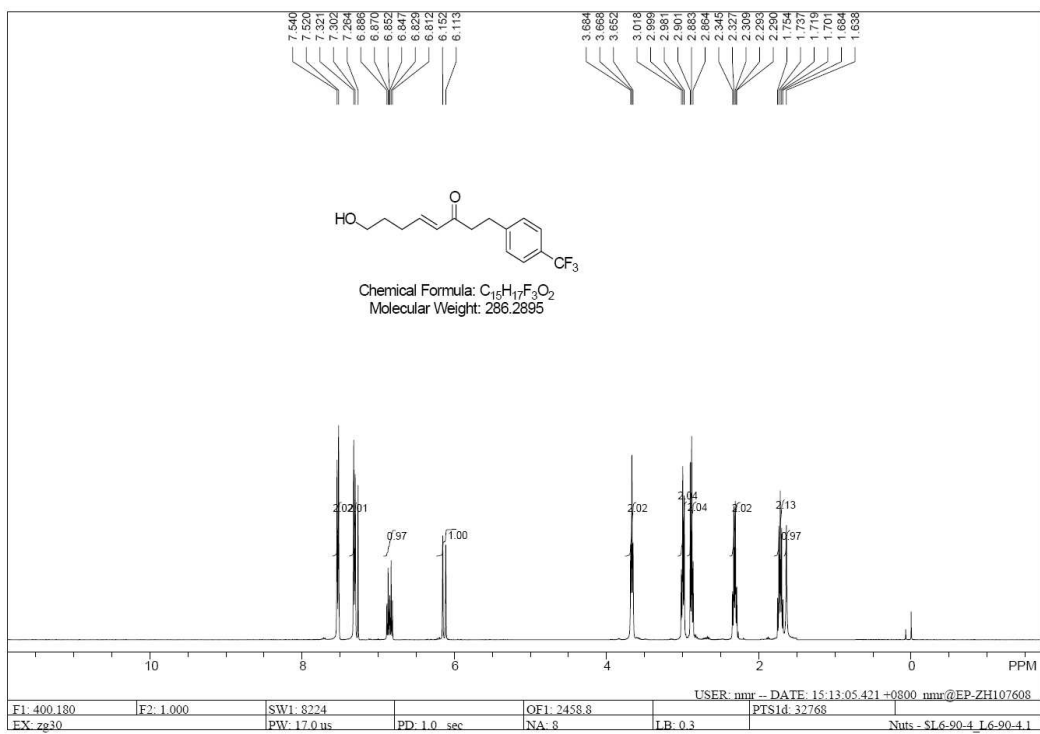
3m:



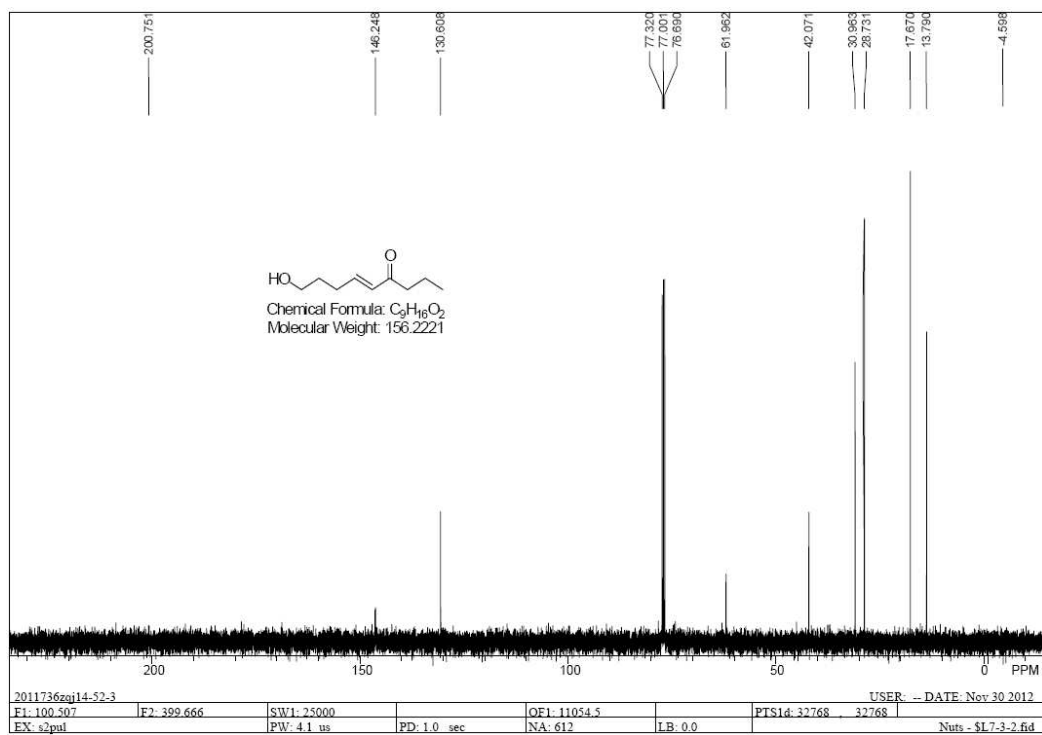
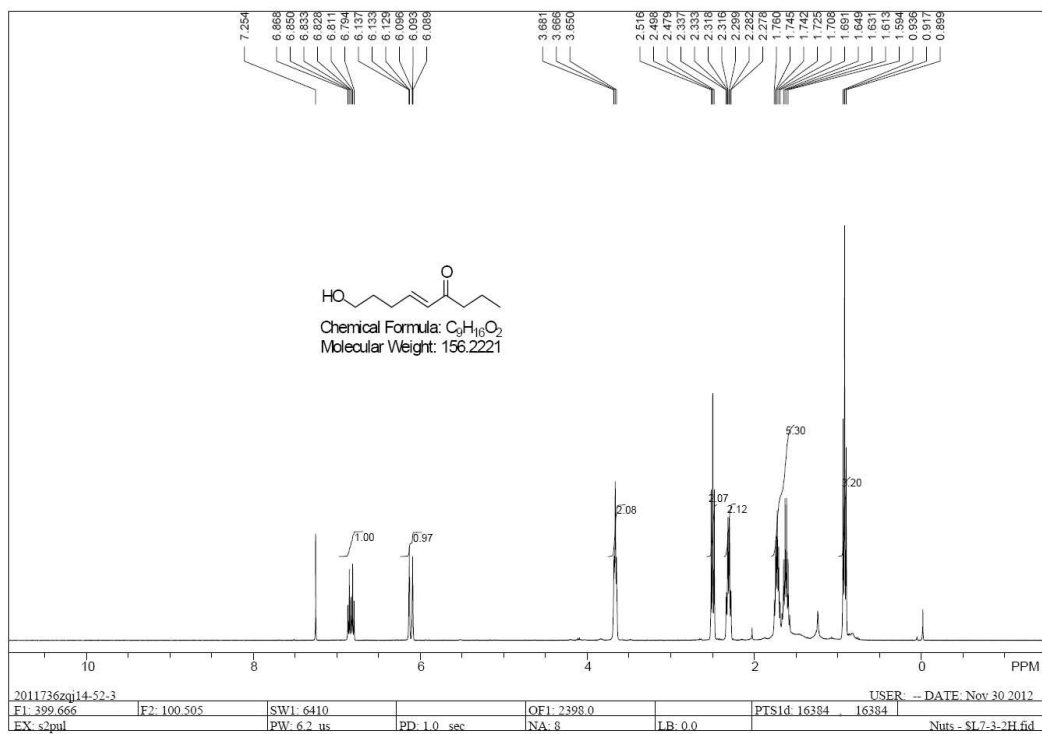
1b



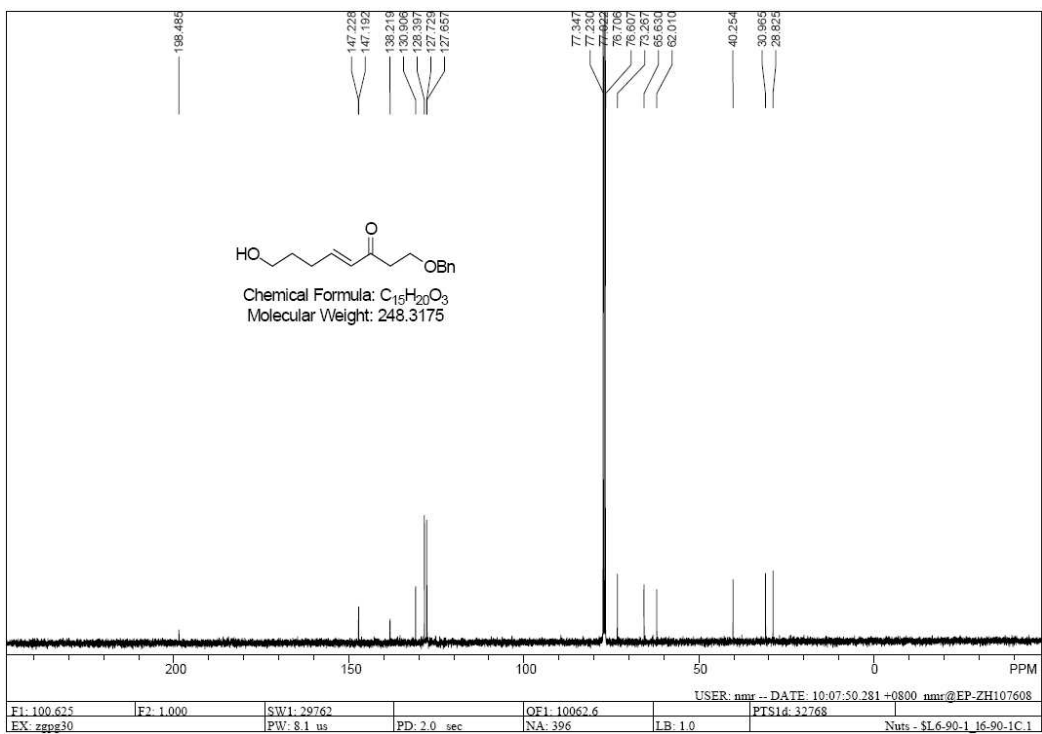
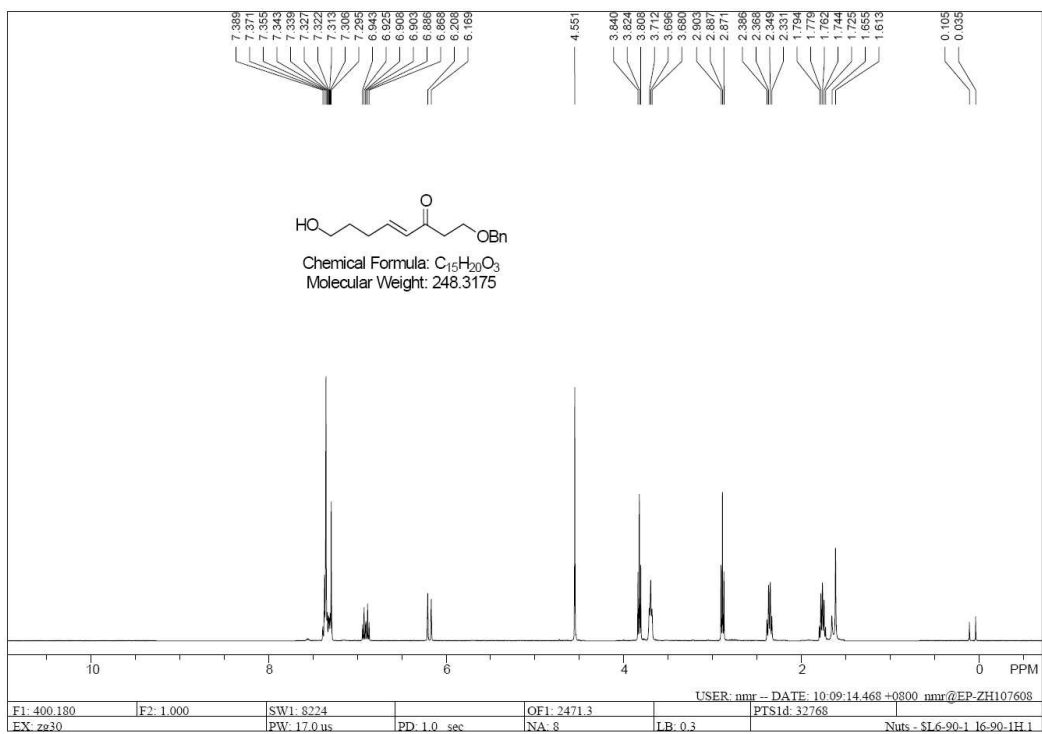
1c



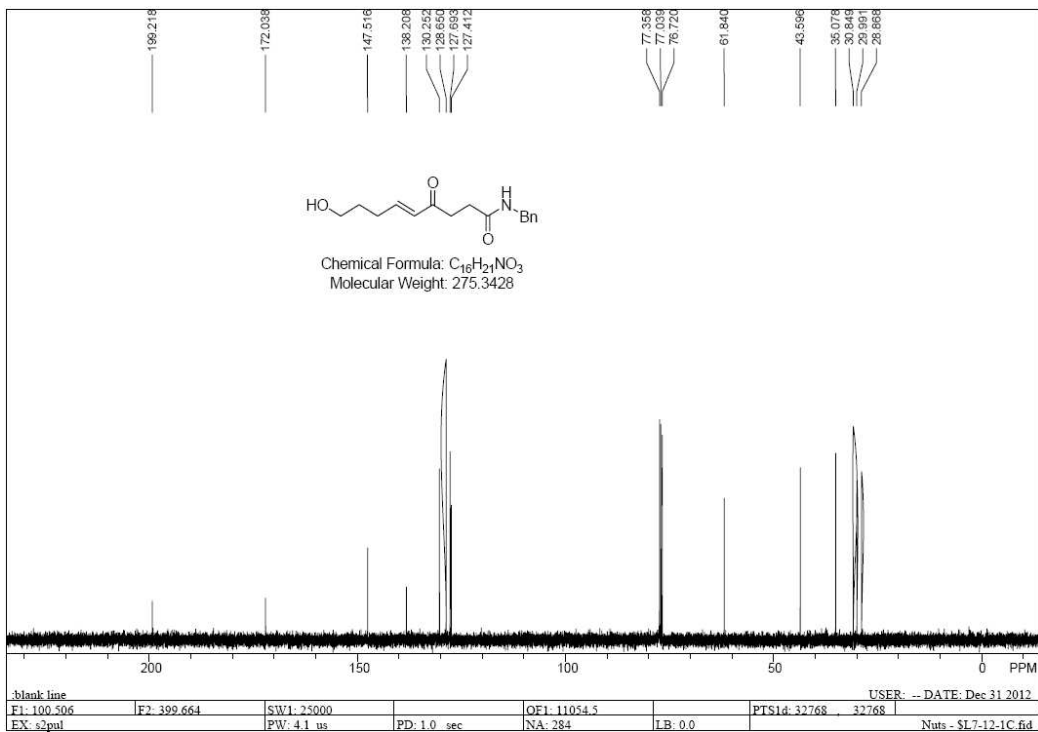
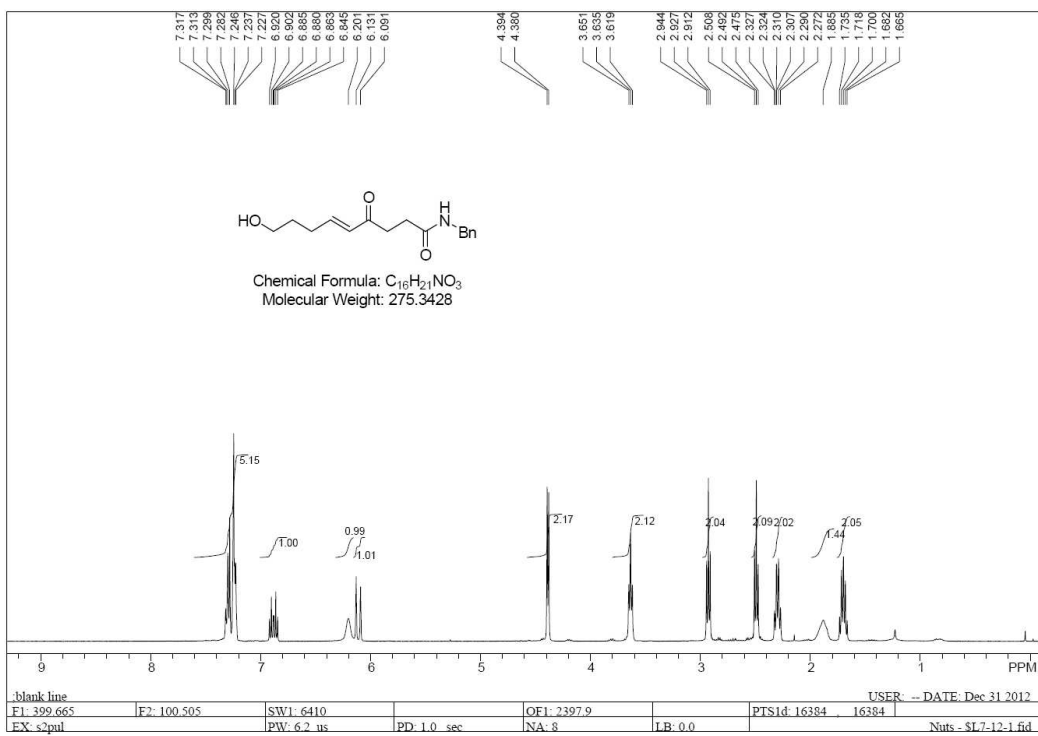
1d



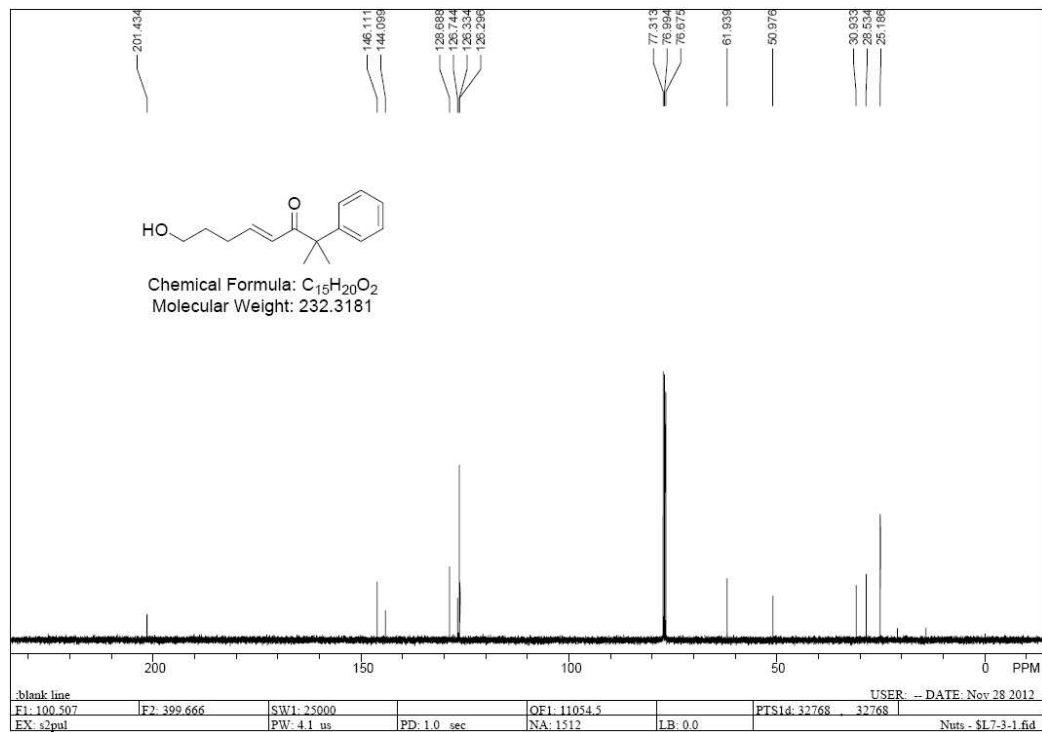
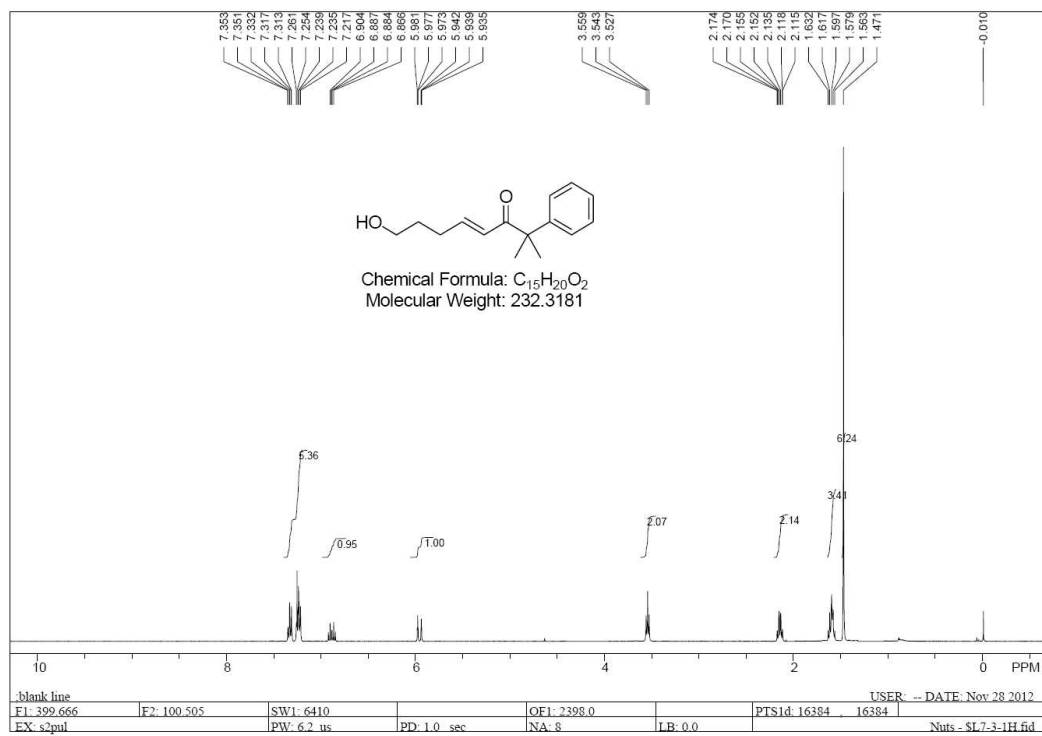
1e



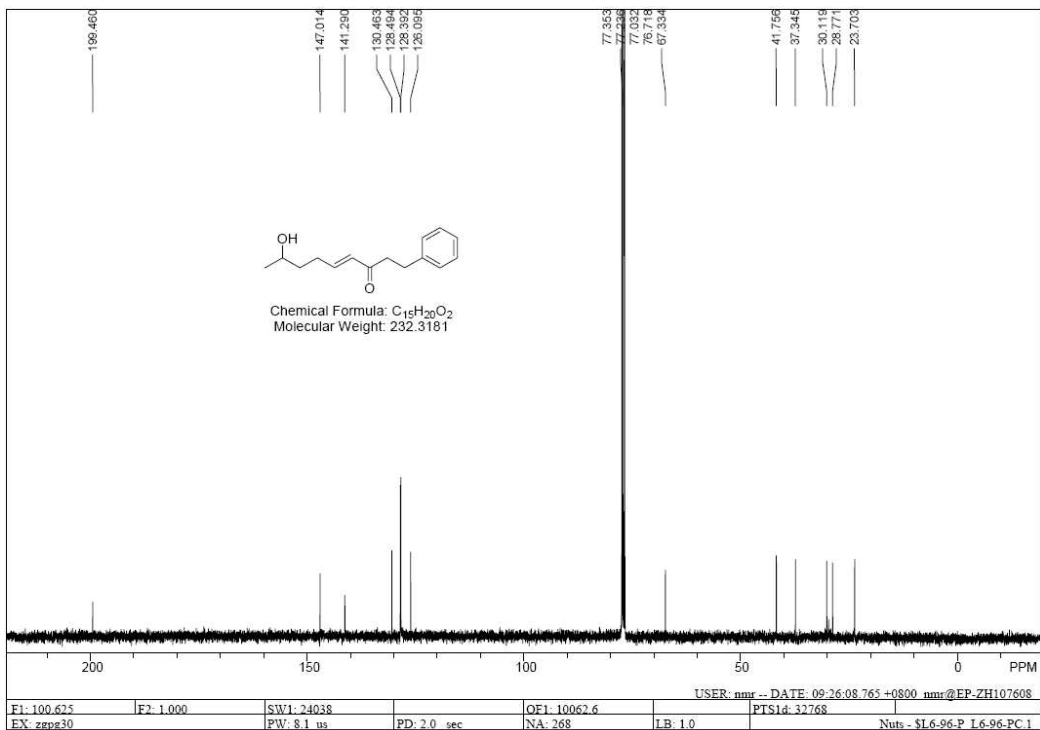
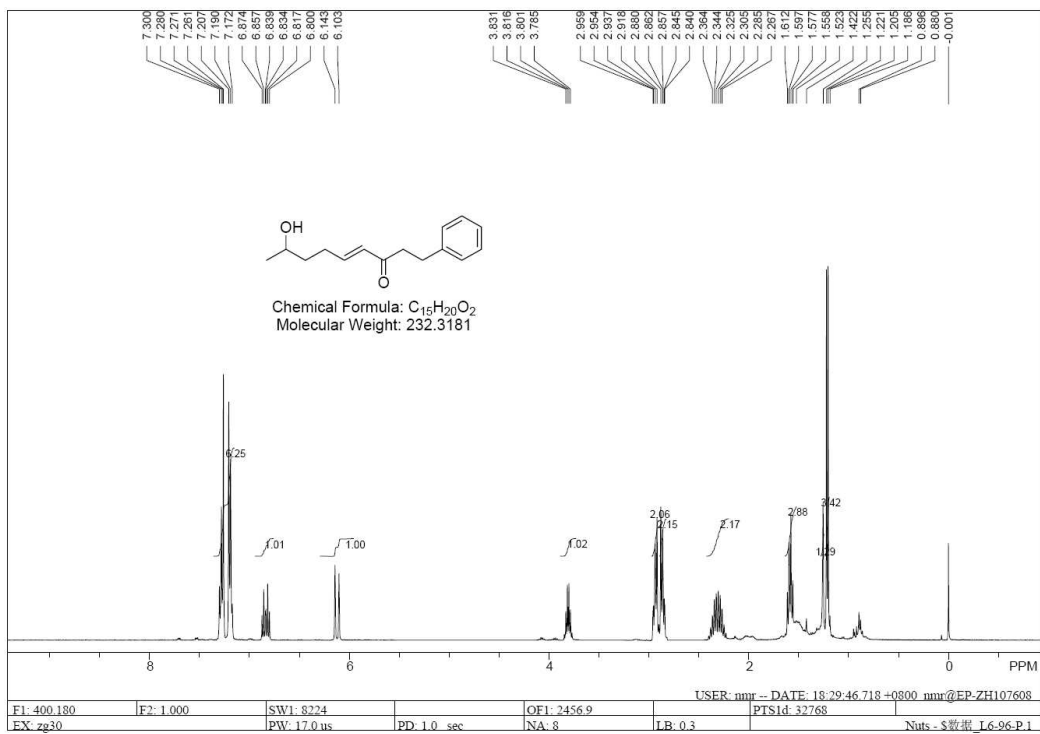
1f



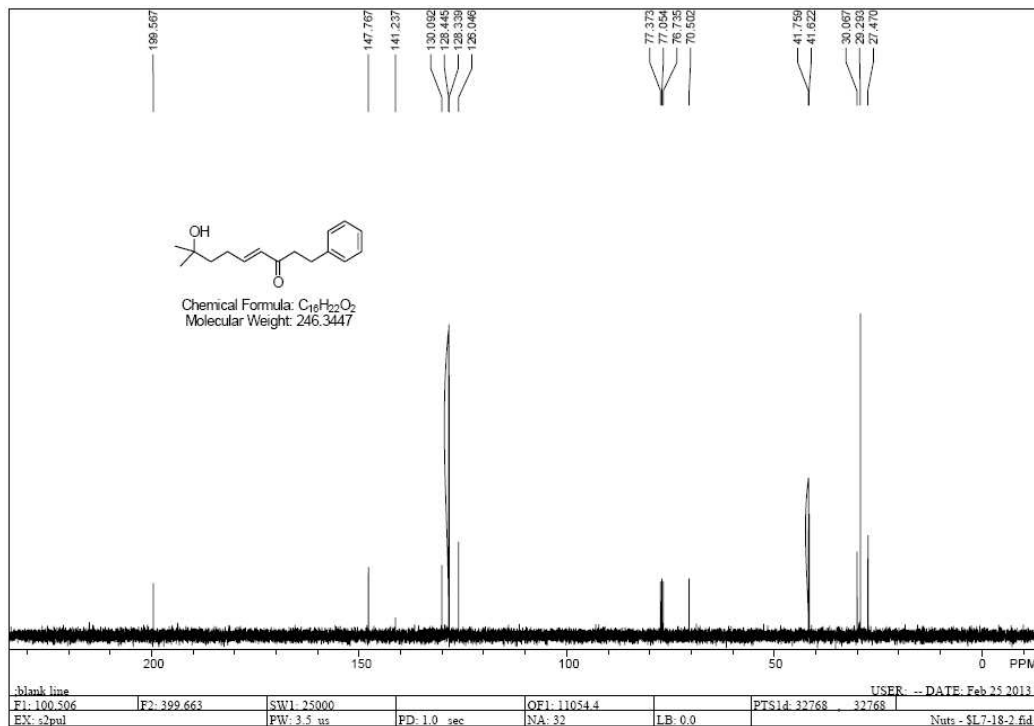
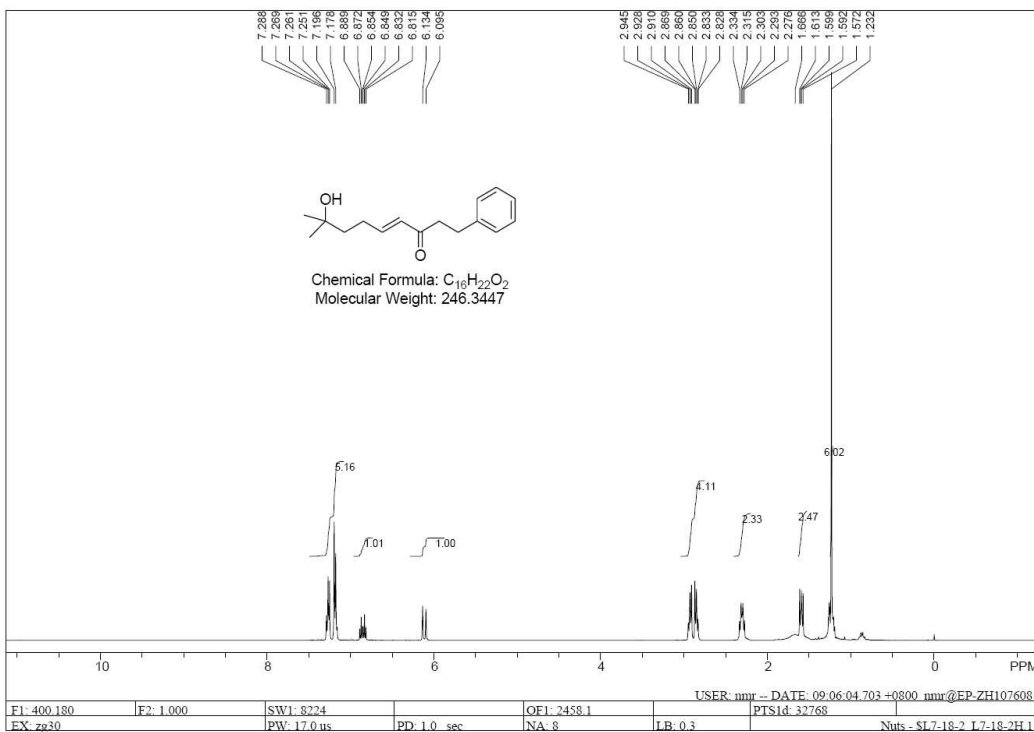
1g



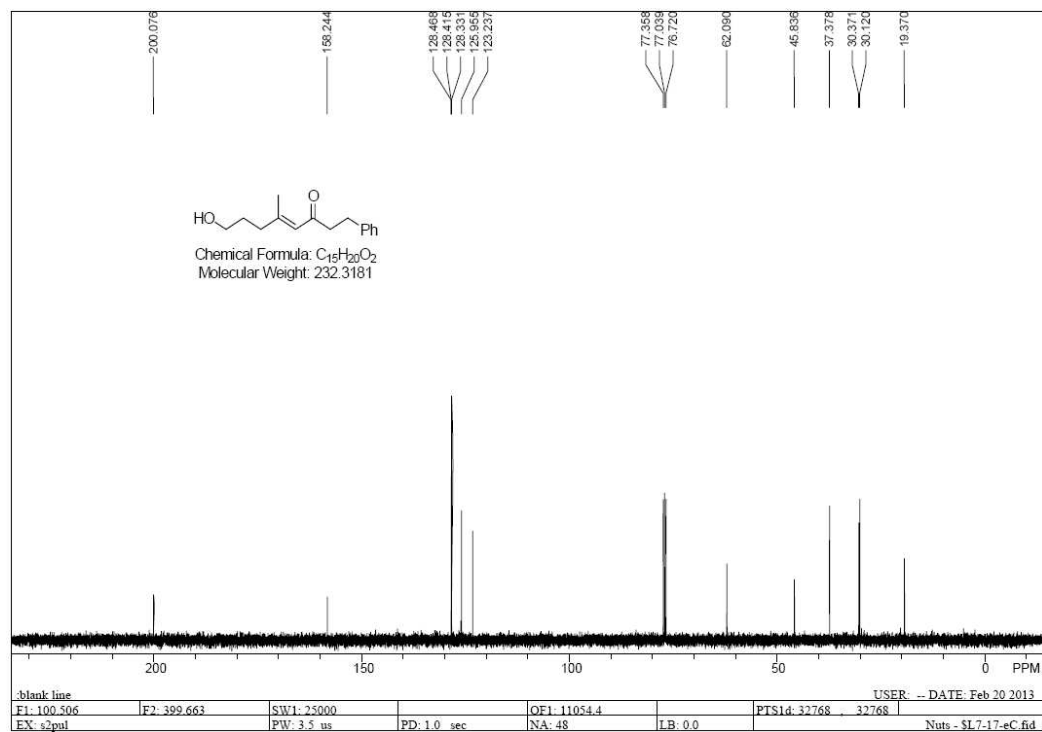
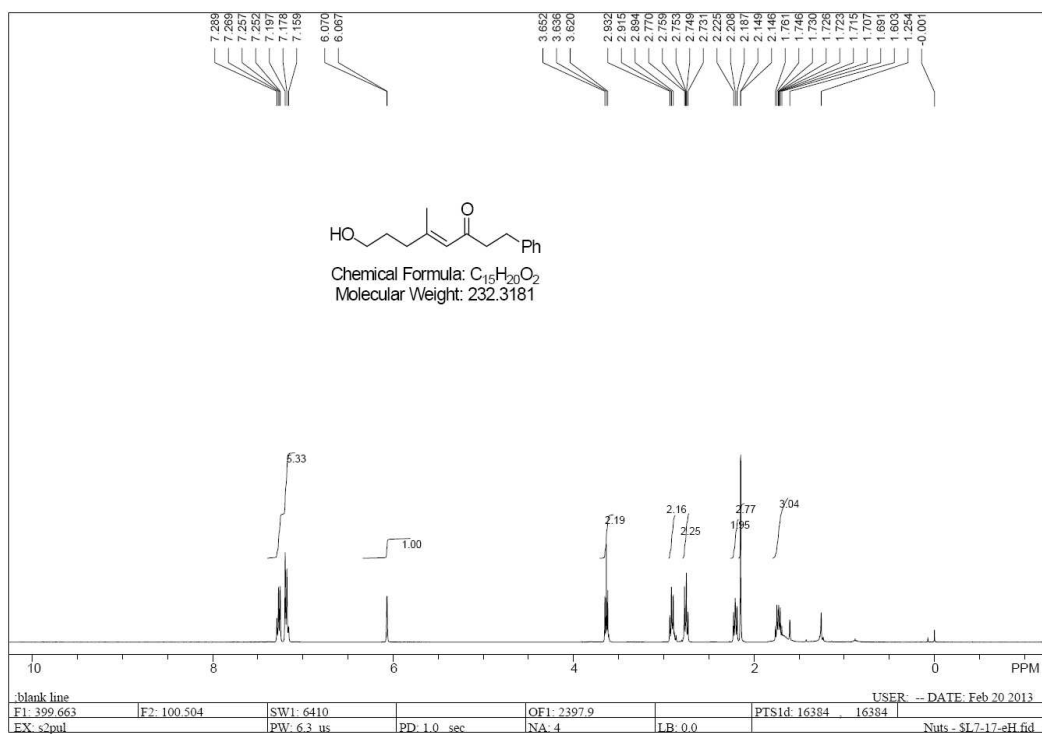
1h



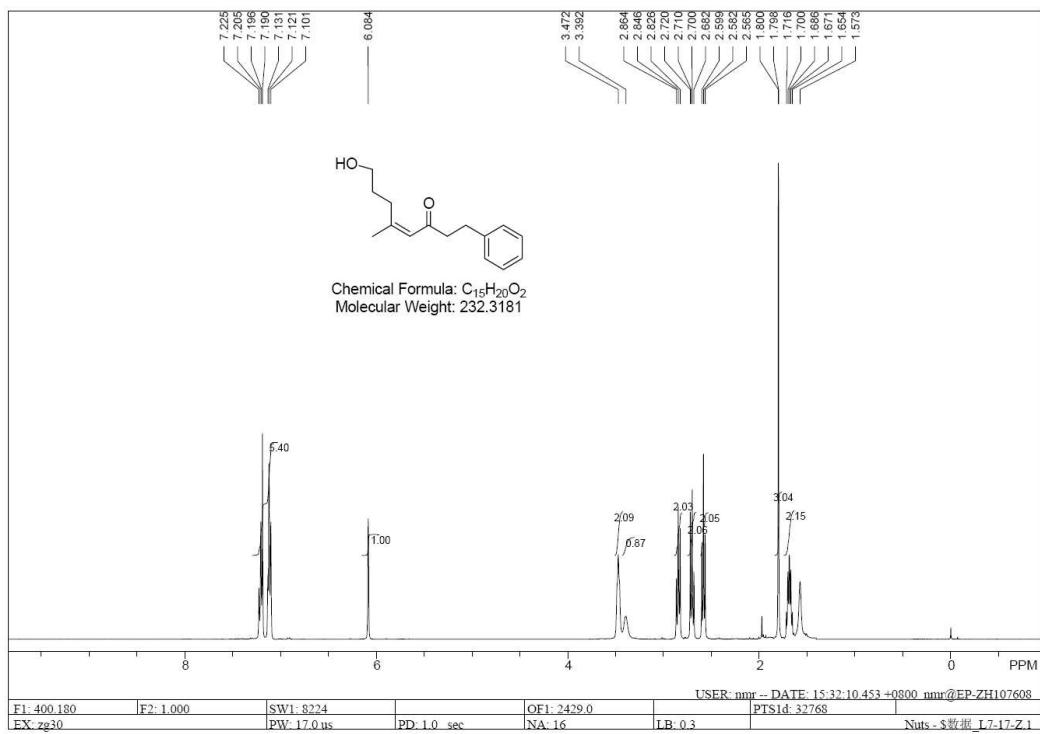
ii

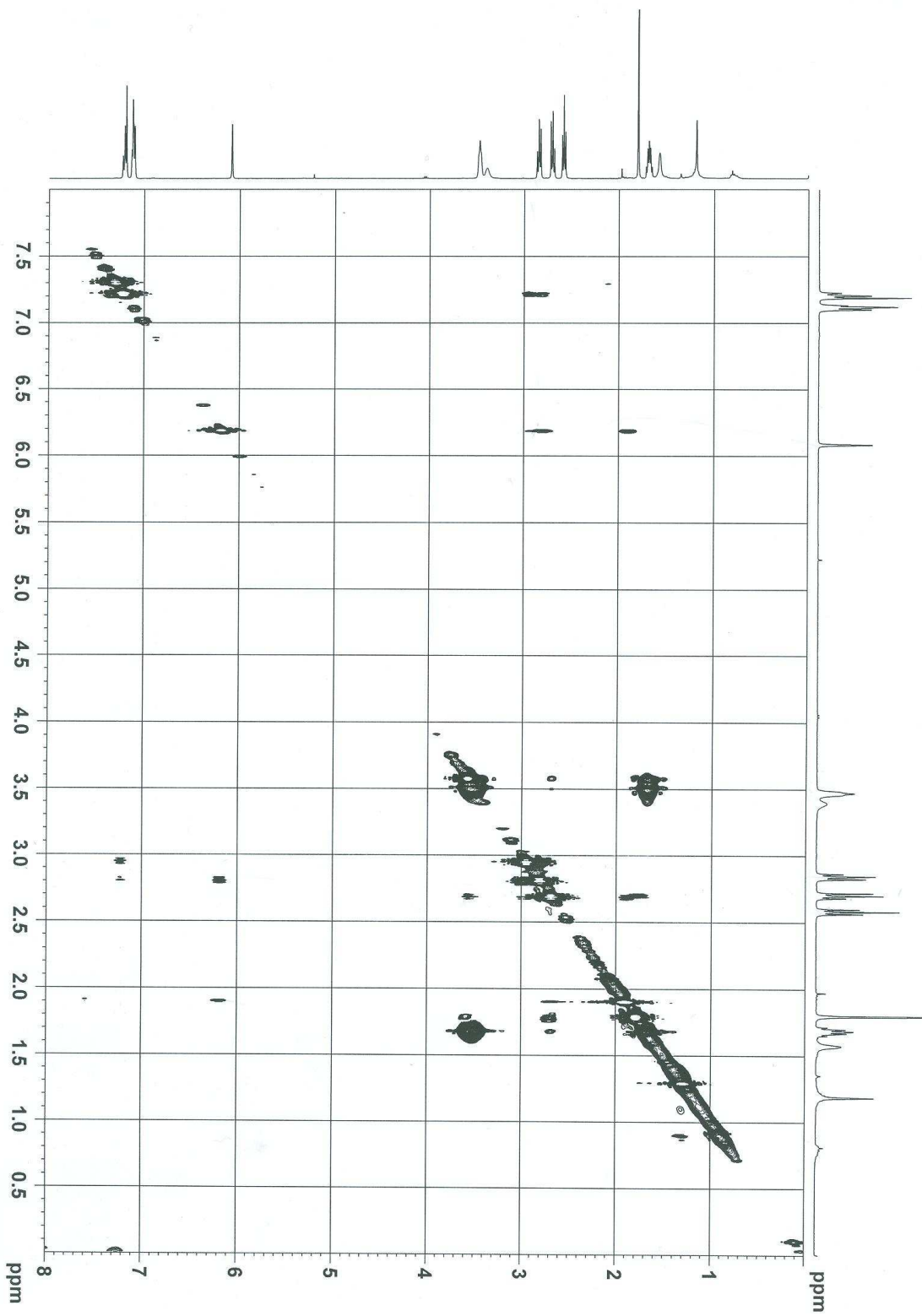


(E)-1j

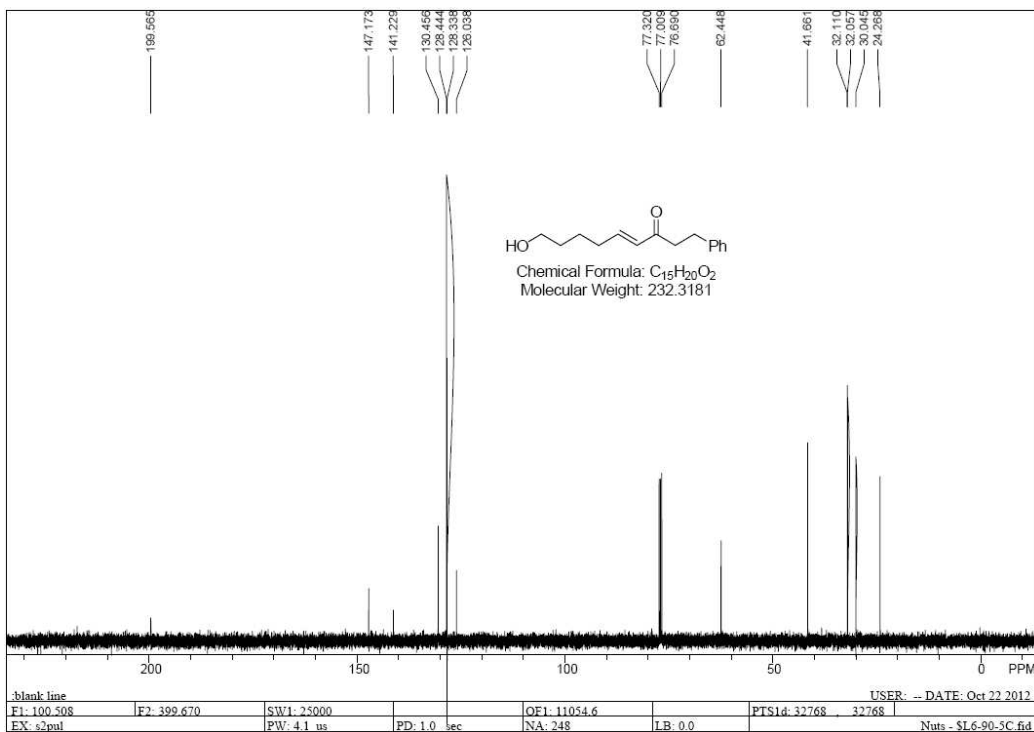
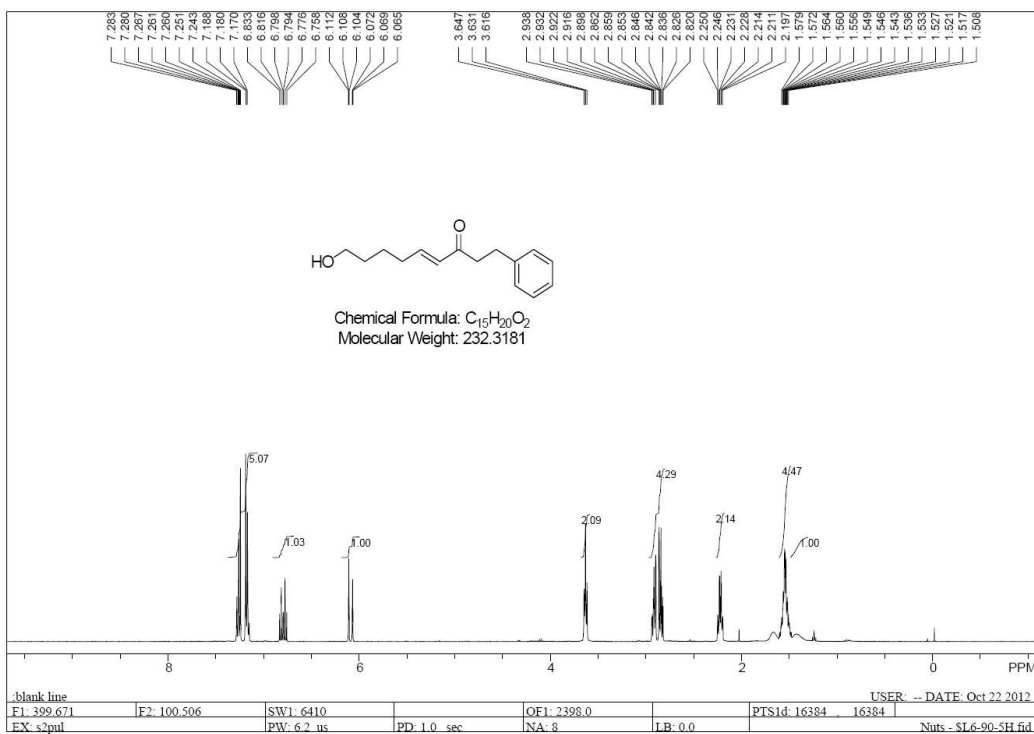


(Z)-1j

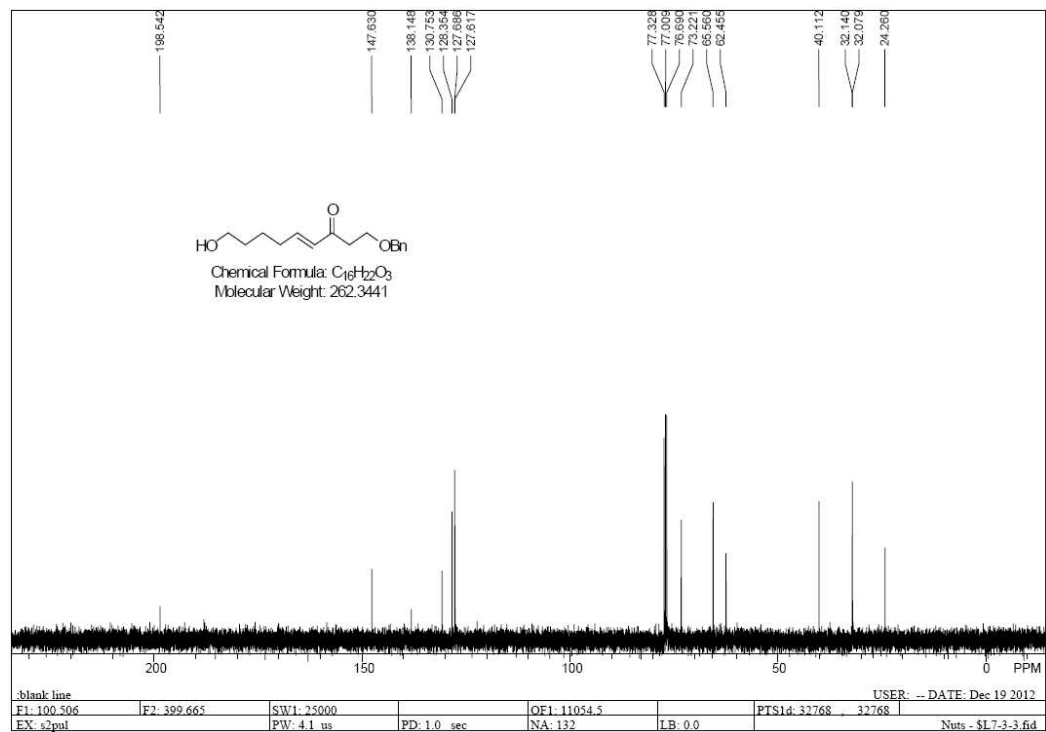
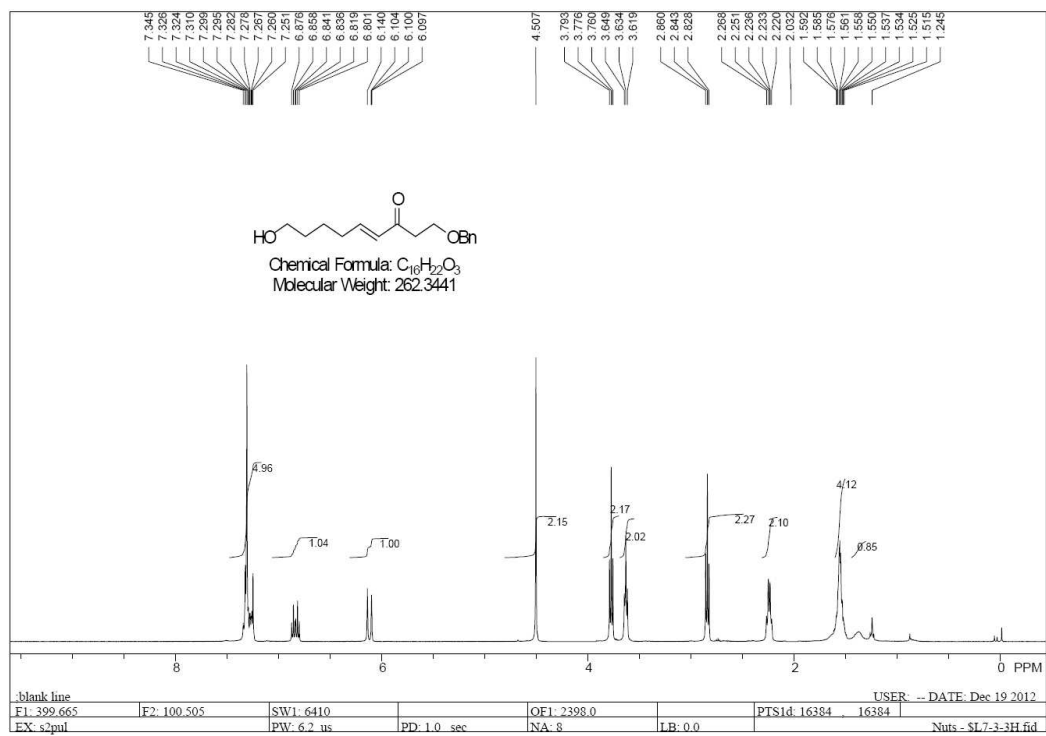




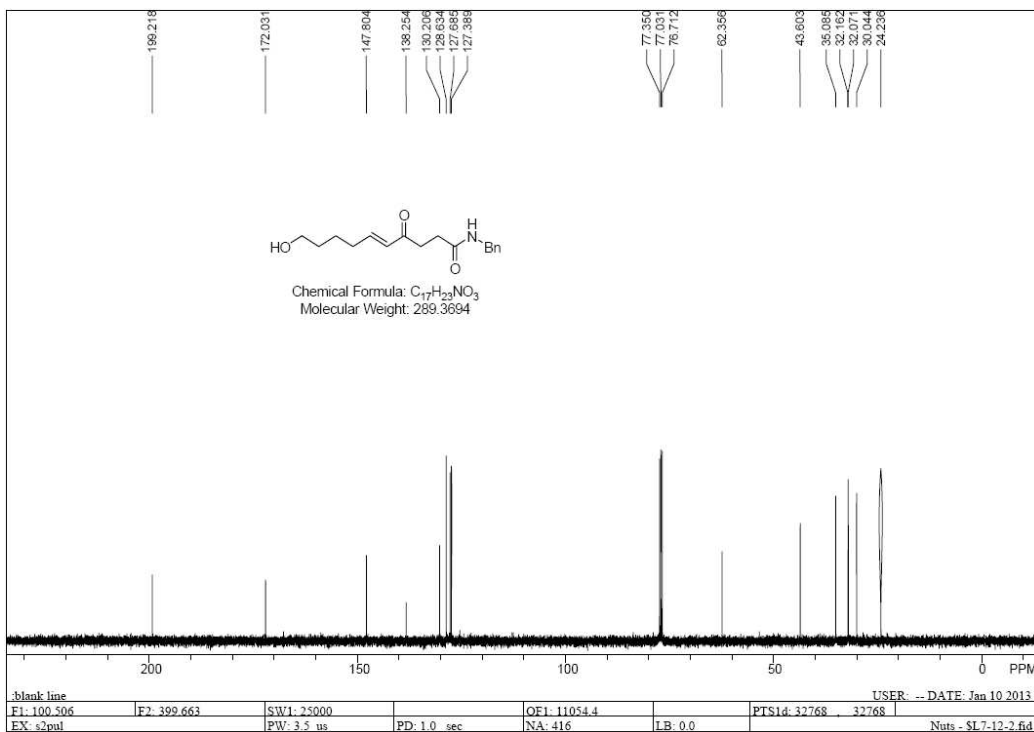
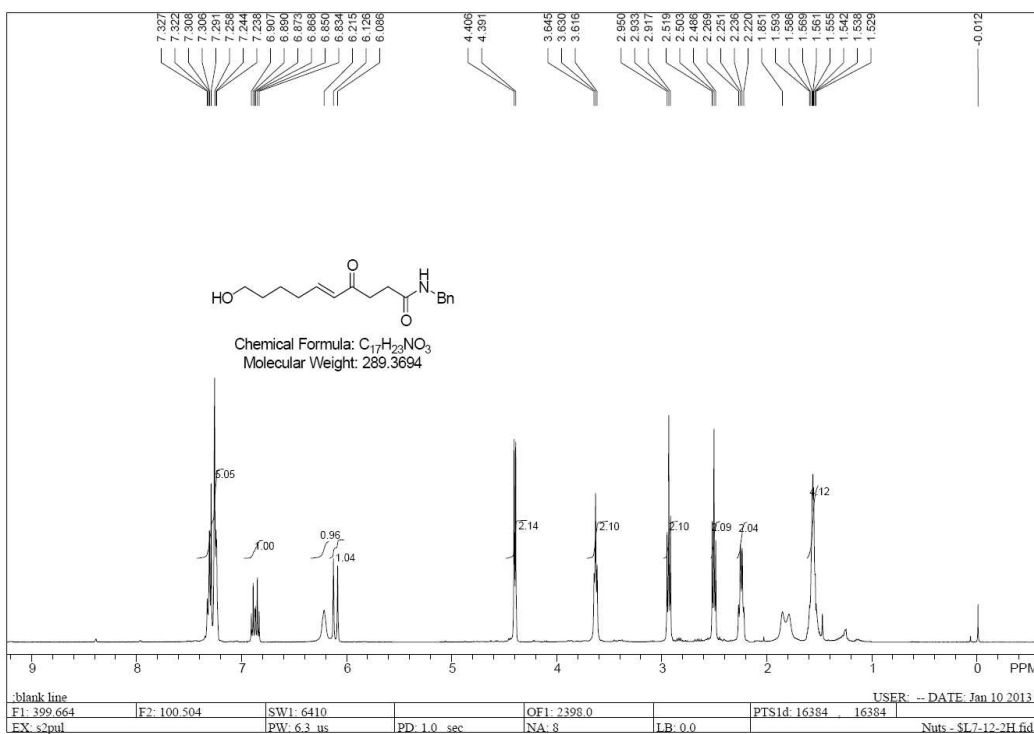
1k



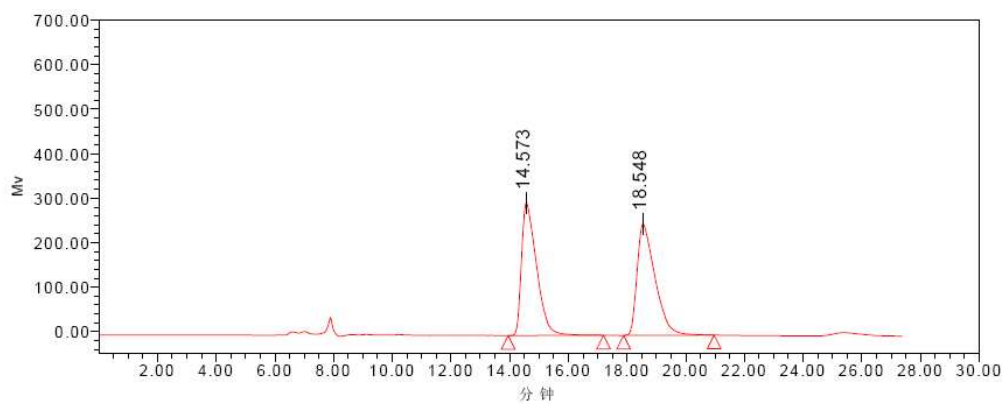
11



1m



2a

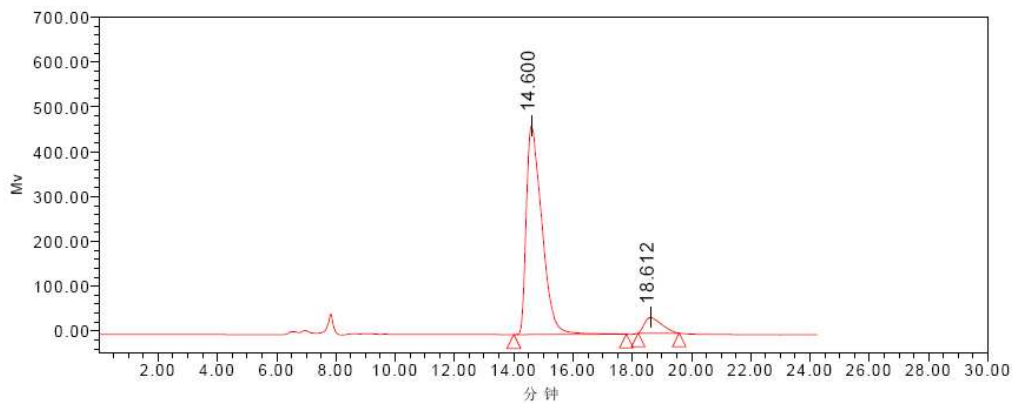


SampleName L6-47-rac(ODH,1/4,210, 0.5); Vial 1; Injection 72; Channel Satin Ch 1;
Date Acquired 2013-3-11 11:36:39 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	14.573	10588183	49.92	297731
2	18.548	10624062	50.08	250279



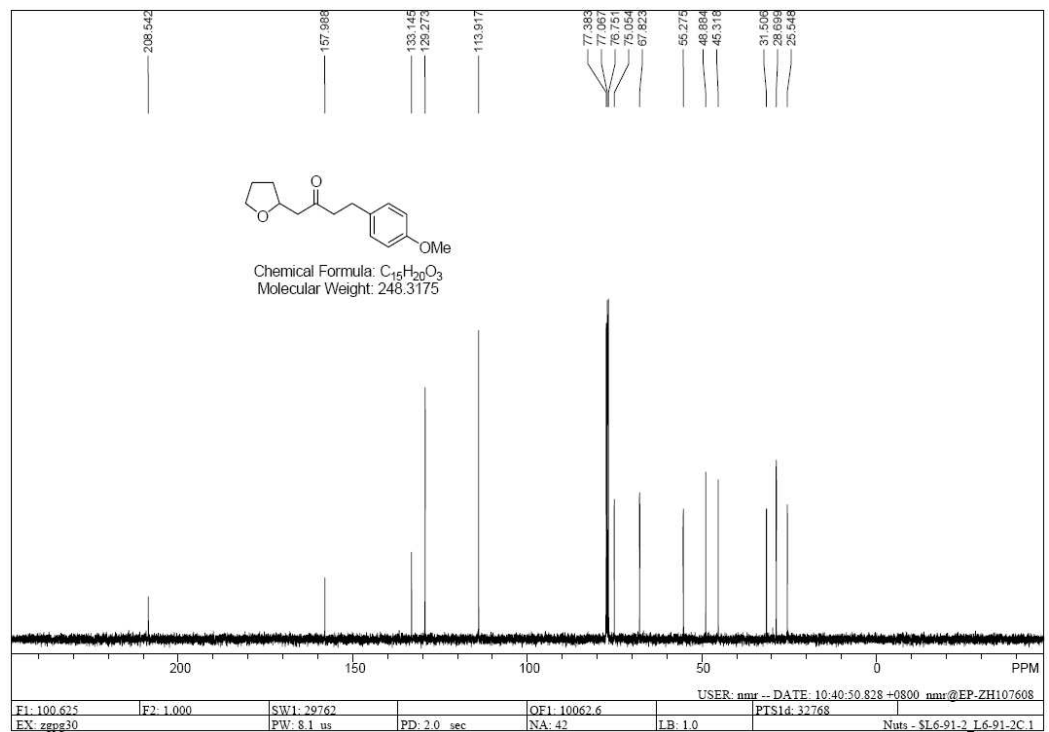
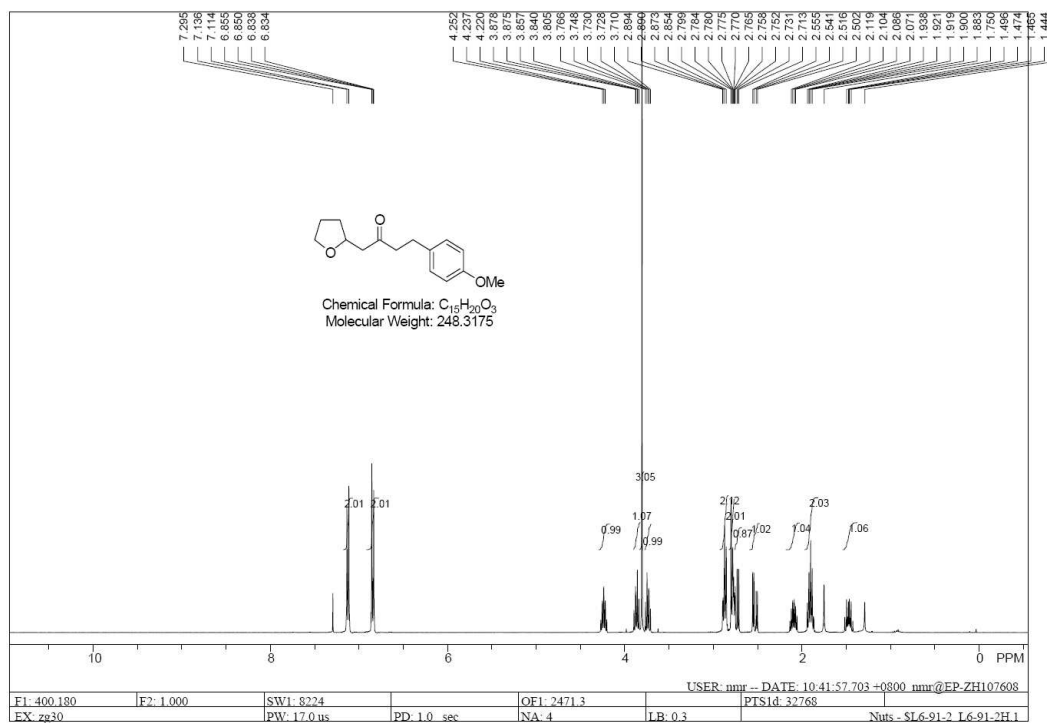
SampleName L6-47-6(ODH,1/4,210, 0.5); Vial 1; Injection 74; Channel Satin Ch 1;
Date Acquired 2013-3-11 12:27:01 CST

Peak Results

处理通道:

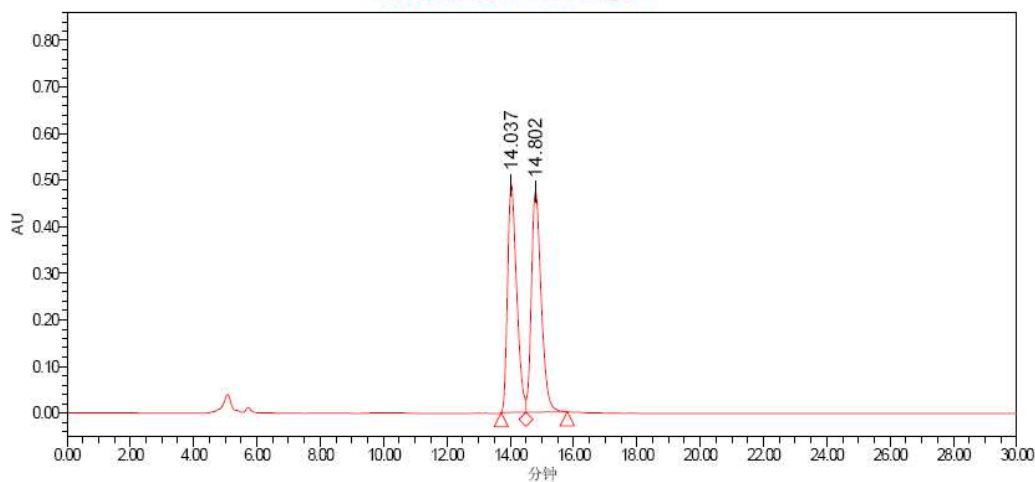
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1	14.600	17027367	92.43	465999
2	18.612	1394034	7.57	35049

2b



2b

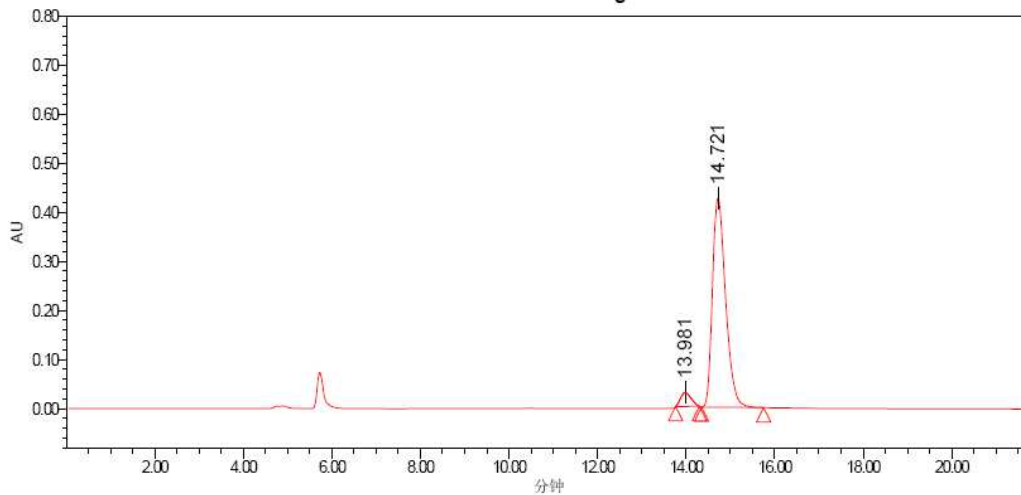
Auto-Scaled Chromatogram



Peak Results

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1	14.037	9792648	489616	49.05
2	14.802	10171680	473746	50.95

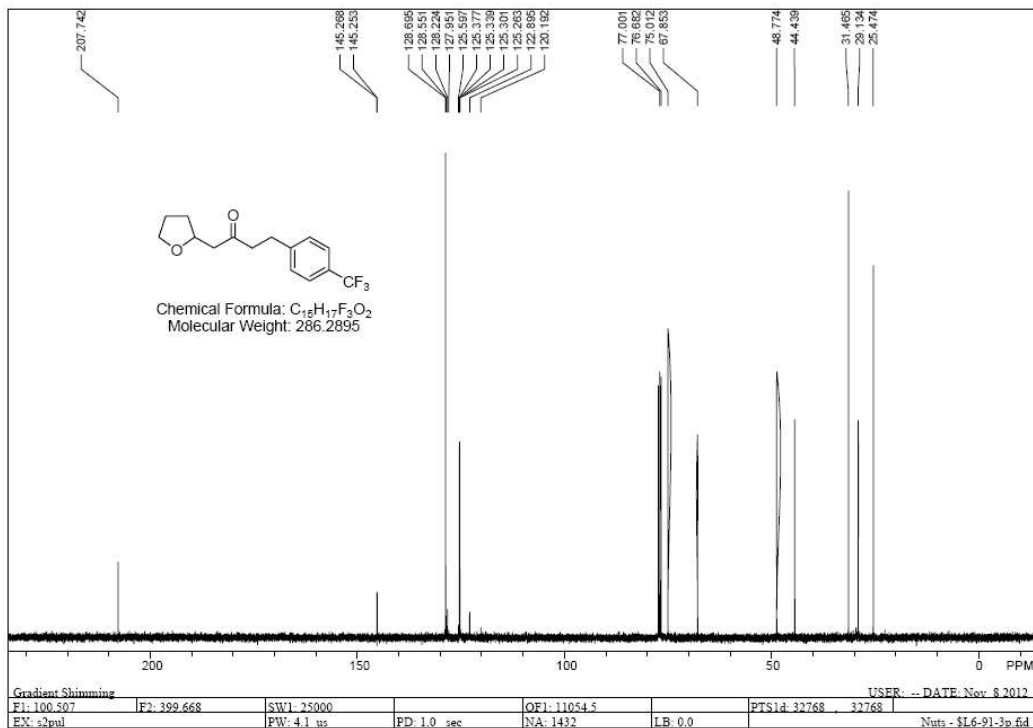
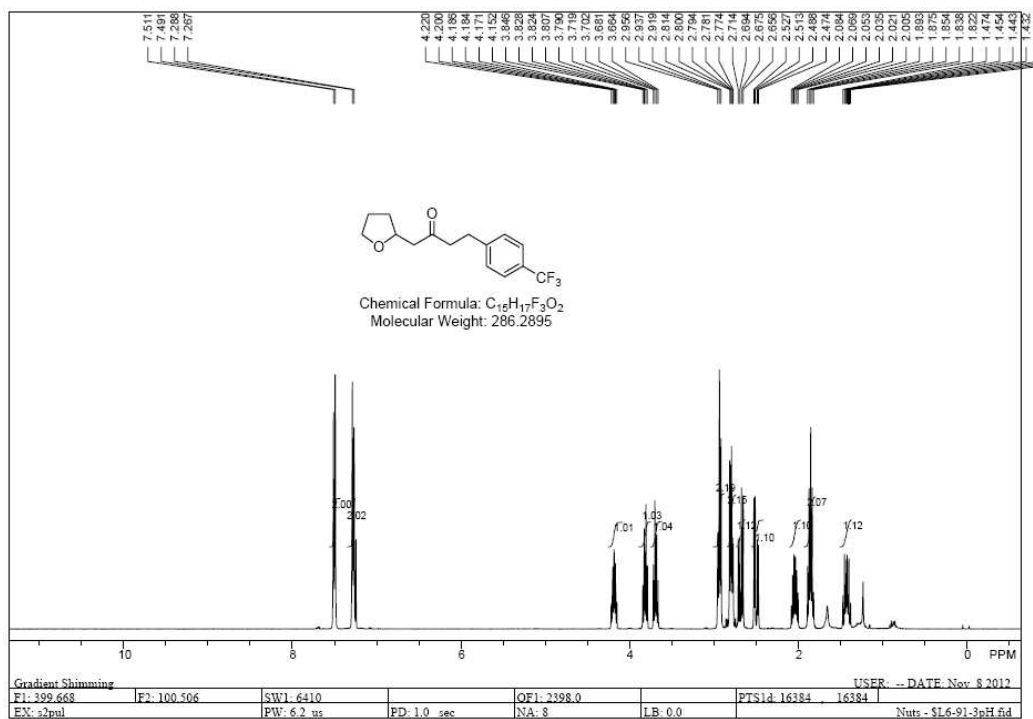
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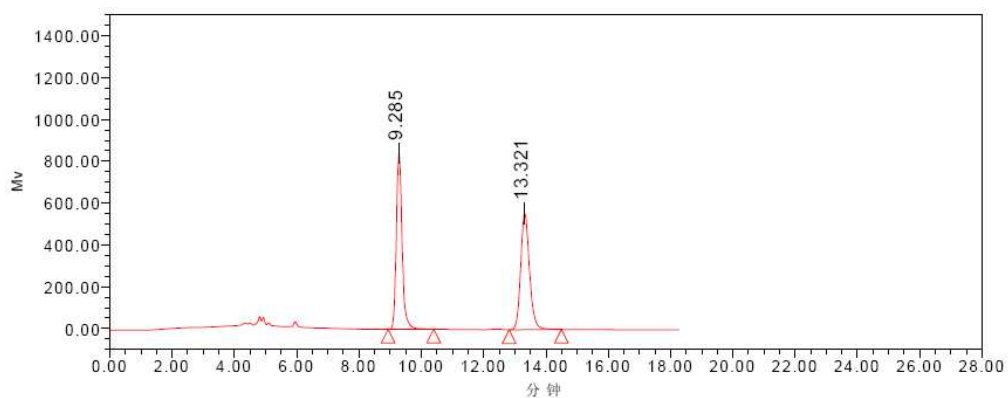
Integration Results

	Name	RT	Area	Height	% Area
1		13.981	469995	28549	5.09
2		14.721	8768862	426830	94.91

2c



2c

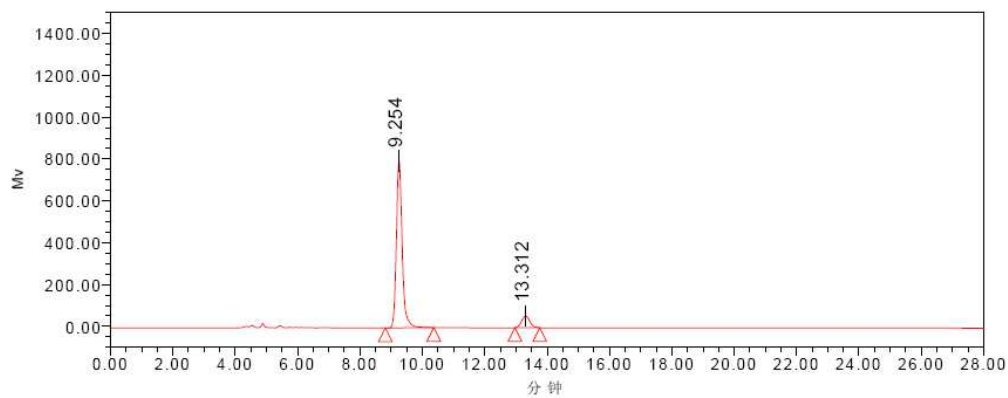


SampleName L6-91-3rac (PC-2,1/4,0.4,210); Vial 1; Injection 36; Channel Satin Ch 1; Date Acquired 2012-11-17 10:17:31 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	9.285	10924914	50.00	842248
2	13.321	10924931	50.00	554791



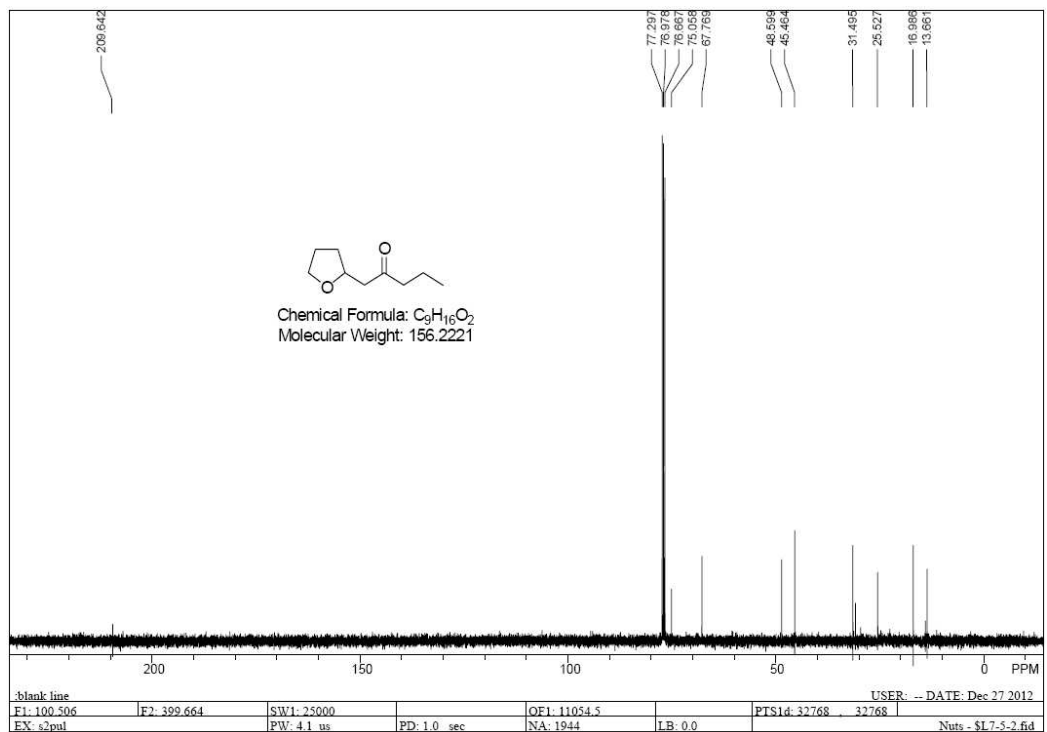
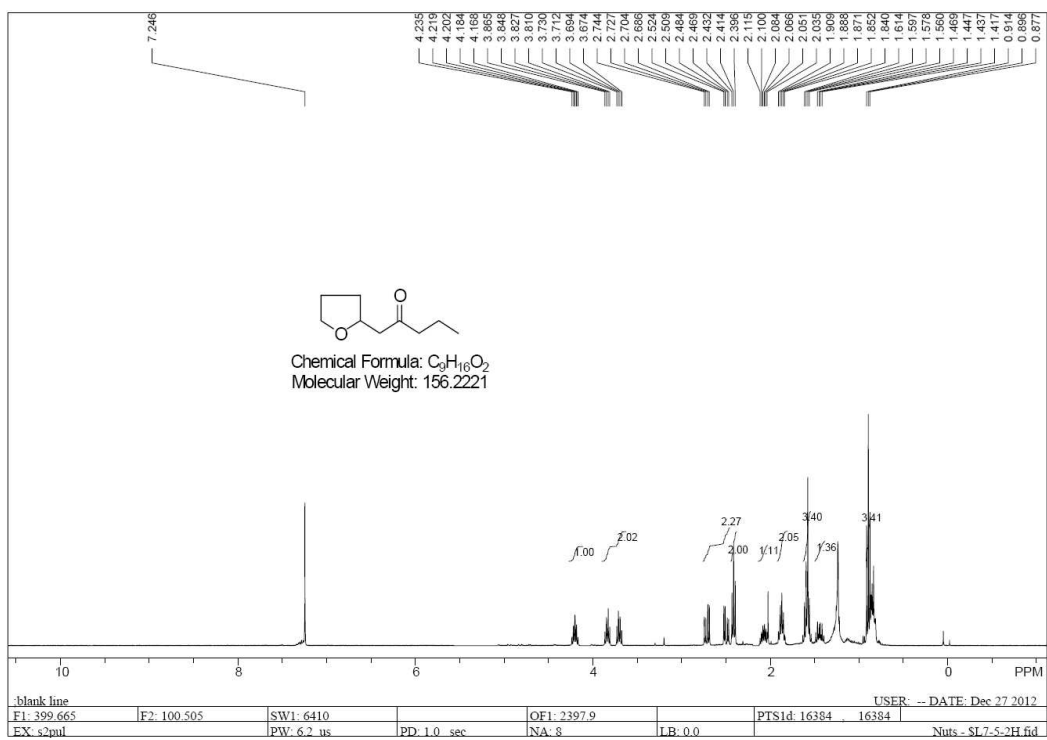
SampleName L6-91-3P (PC-2,1/4,0.4,210); Vial 1; Injection 39; Channel Satin Ch 1; Date Acquired 2012-11-17 11:09:25 CST

Peak Results

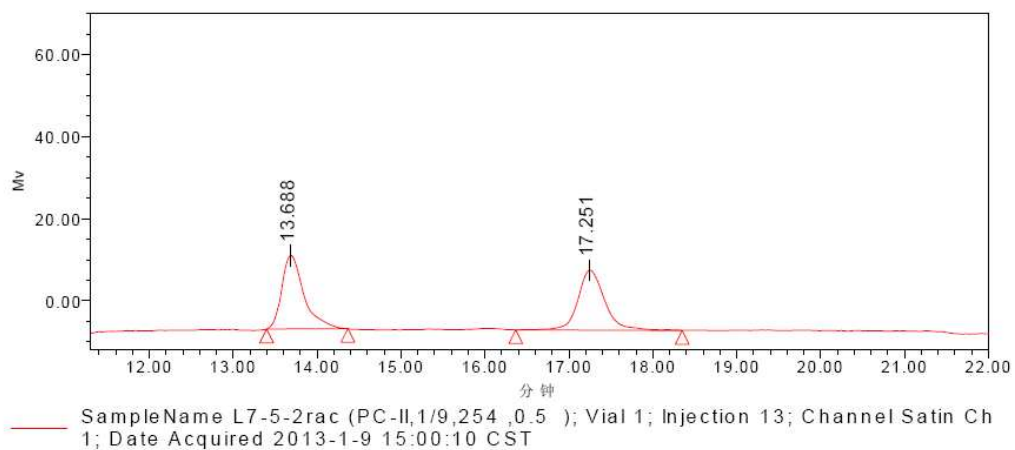
处理通道:

	RT	Area	% Area	Height
1	9.254	10335858	91.05	801026
2	13.312	1016561	8.95	55472

2d



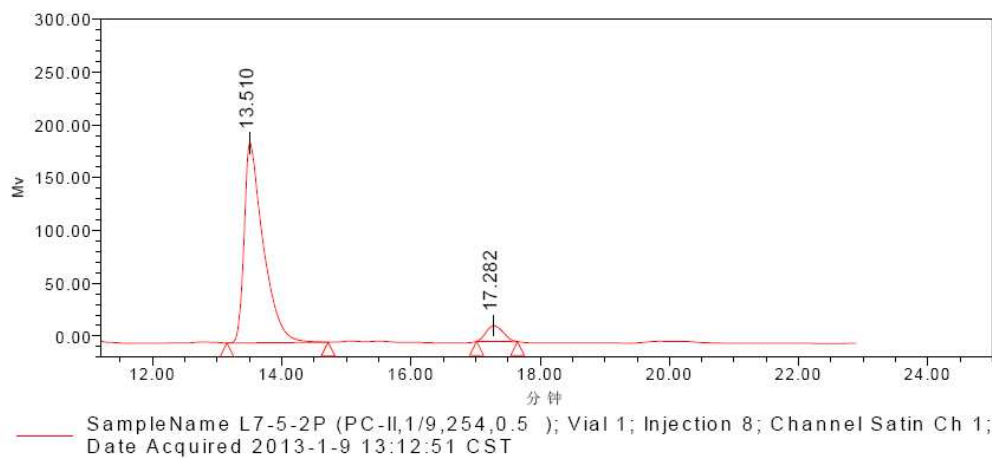
2d



Peak Results

处理通道:

	RT	Area	% Area	Height
1	13.688	328309	50.38	17970
2	17.251	323334	49.62	14580

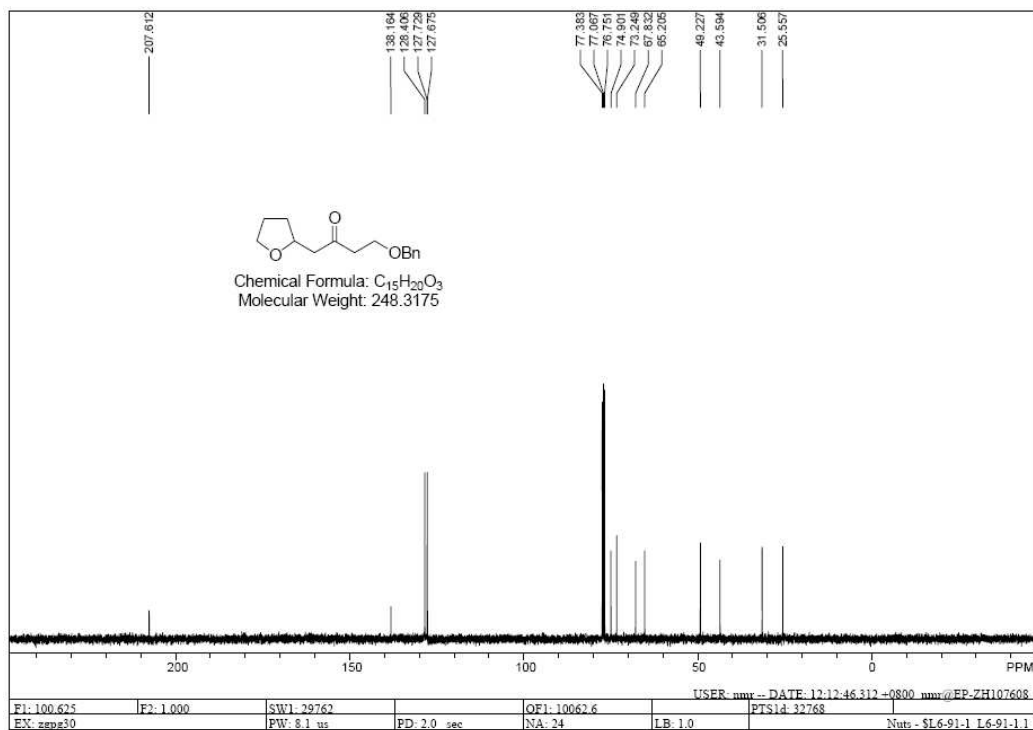
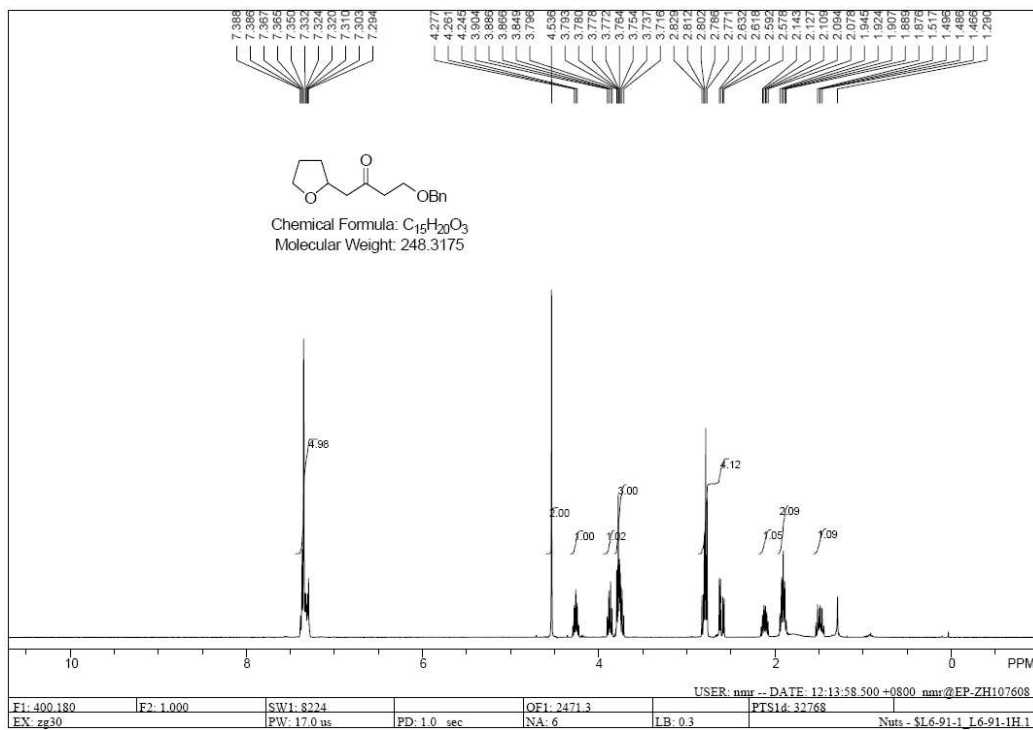


Peak Results

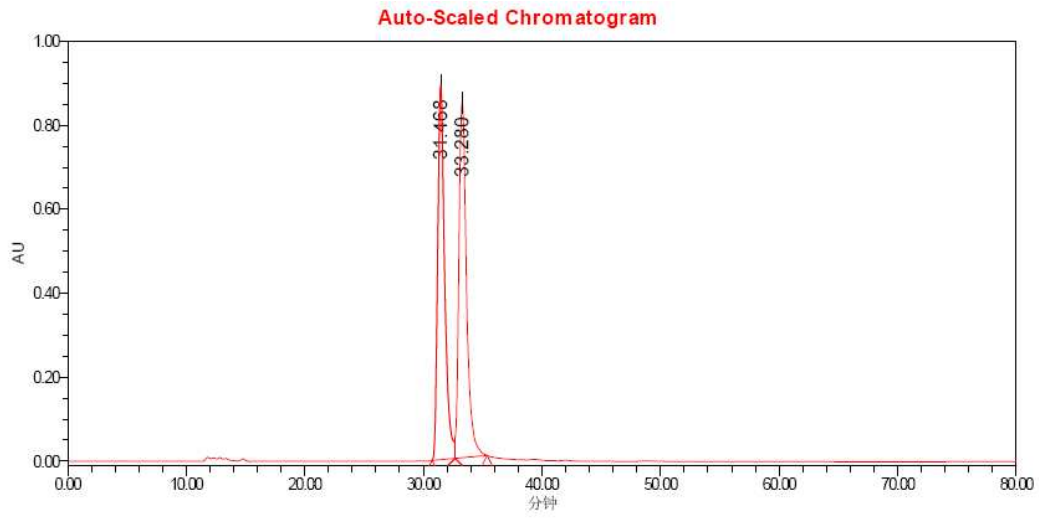
处理通道:

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1	13.510	3885801	93.40	190163
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2e

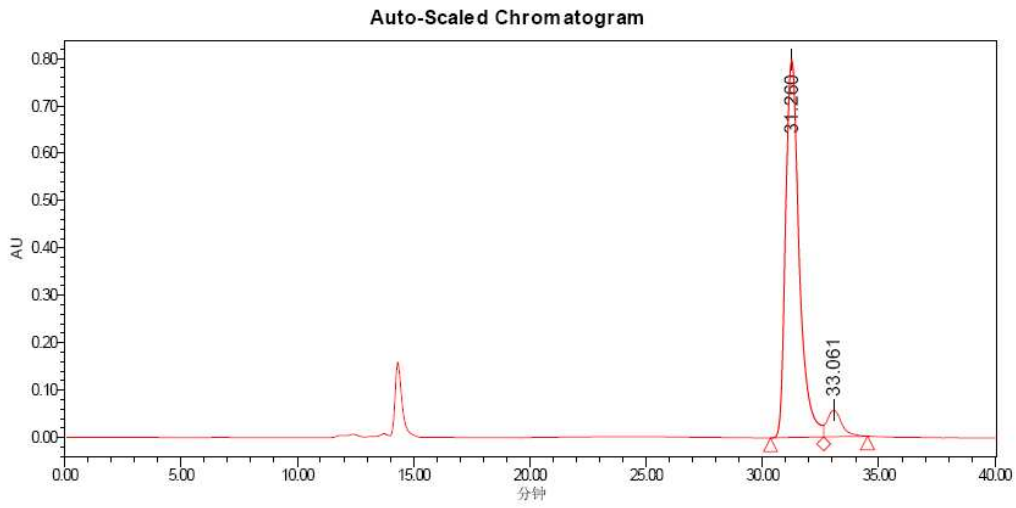


2e



Peak Results

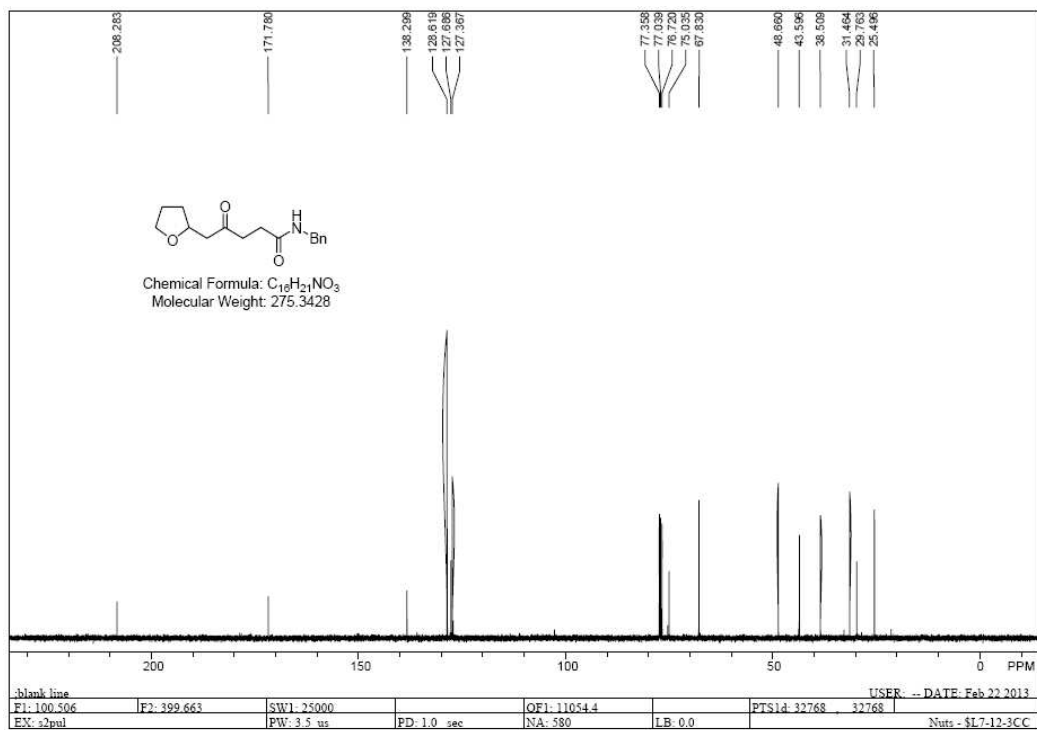
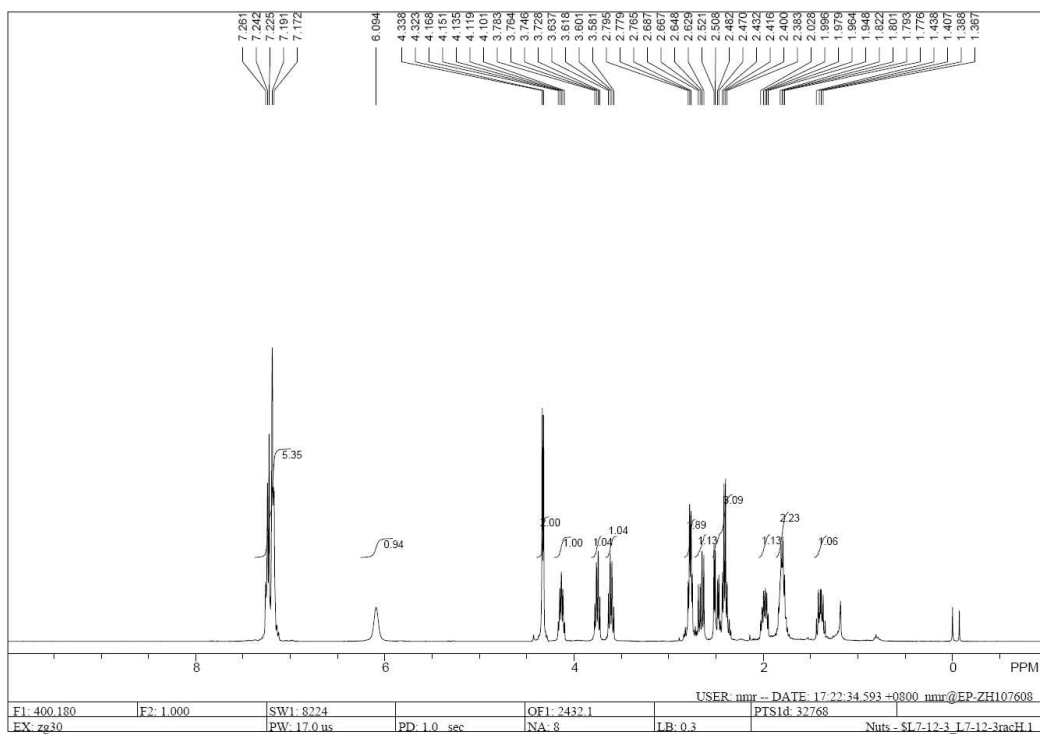
	RT	Area	Height	% Area
1	31.468	36442259	891678	49.02
2	33.280	37904779	846542	50.98



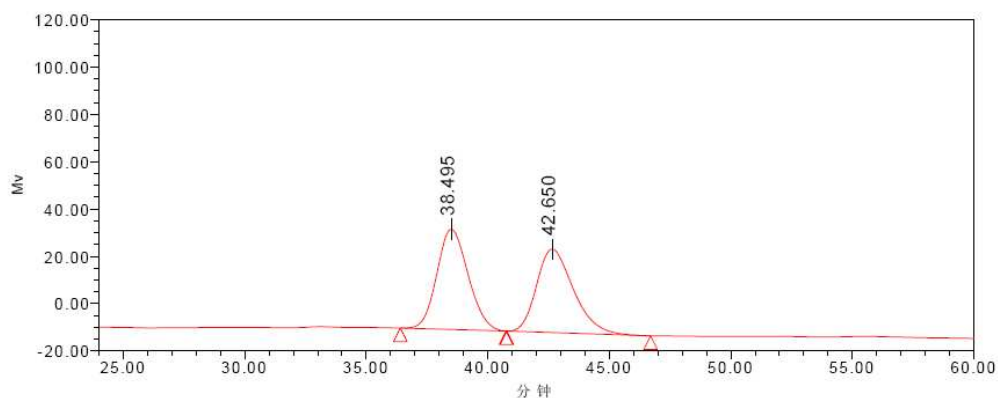
Integration Results

	Name	RT	Area	Height	% Area
1		31.260	32497445	797475	93.03
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2f



2f

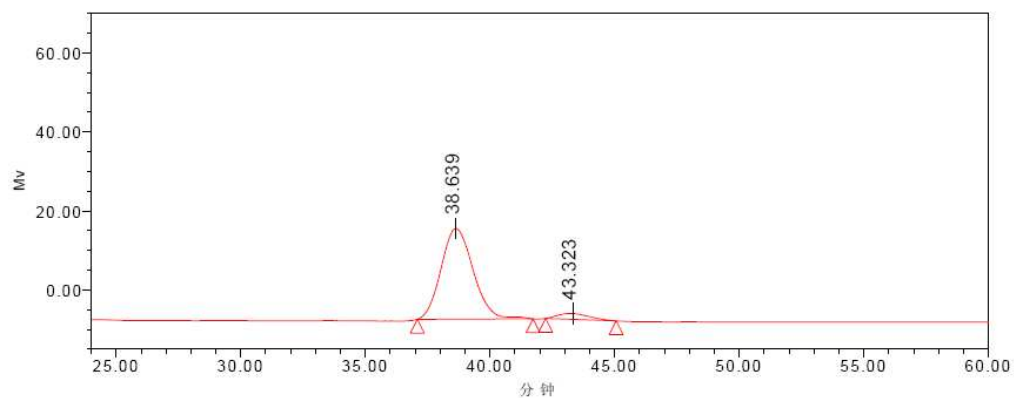


SampleName L7-12-3rac (PC-II,210,1.0,1/4); Vial 1; Injection 17; Channel Satin Ch 1; Date Acquired 2013-1-24 15:34:55 CST

Peak Results

处理通道:

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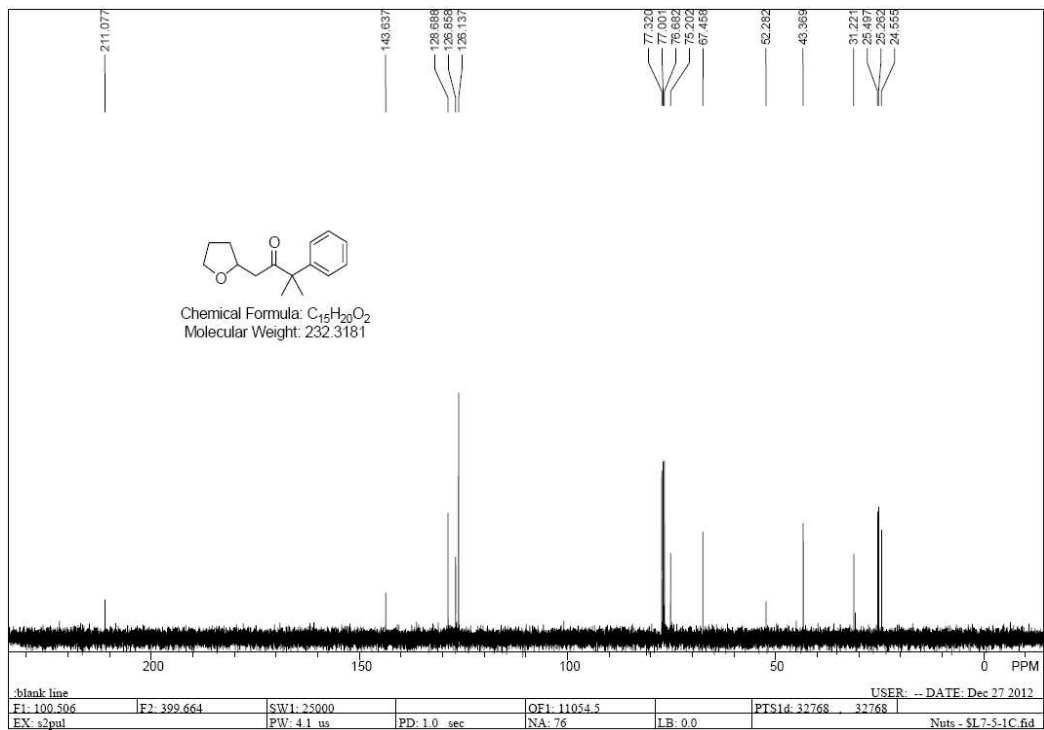
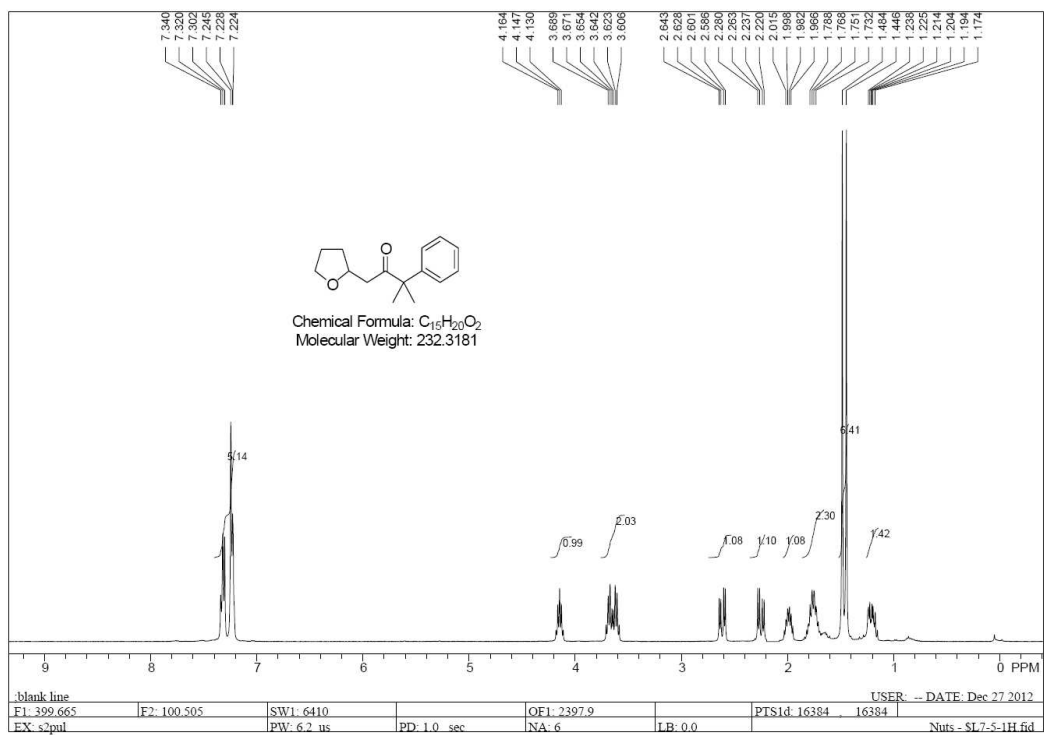
SampleName L7-12-3P (PC-II,210,1.0,1/4); Vial 1; Injection 20; Channel Satin Ch 1; Date Acquired 2013-1-24 18:21:28 CST

Peak Results

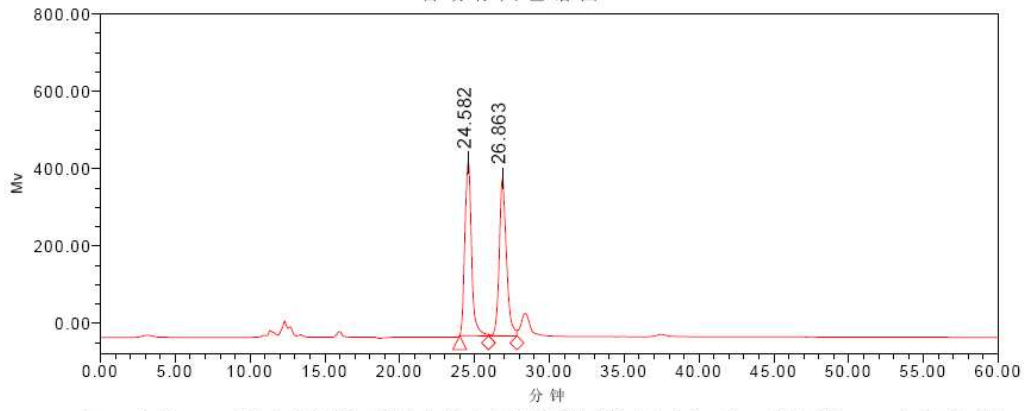
处理通道:

	RT	Area	% Area	Height
1	38.639	2056494	94.13	22965
2	43.323	128183	5.87	1493

2g



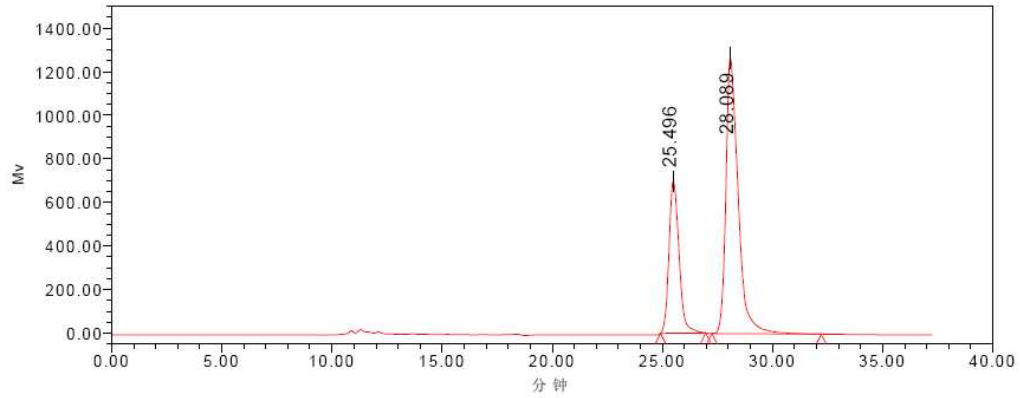
2g



SampleName L7-5-1RAC (PC-II,0.5,1/4,210); Vial 1; Injection 84; Channel Satin Ch 1; Date Acquired 2012-12-7 16:14:05 CST

Peak Results
处理通道:

	RT	Area	% Area	Height
1	24.582	13960460	50.71	448538
2	26.863	13571755	49.29	407499

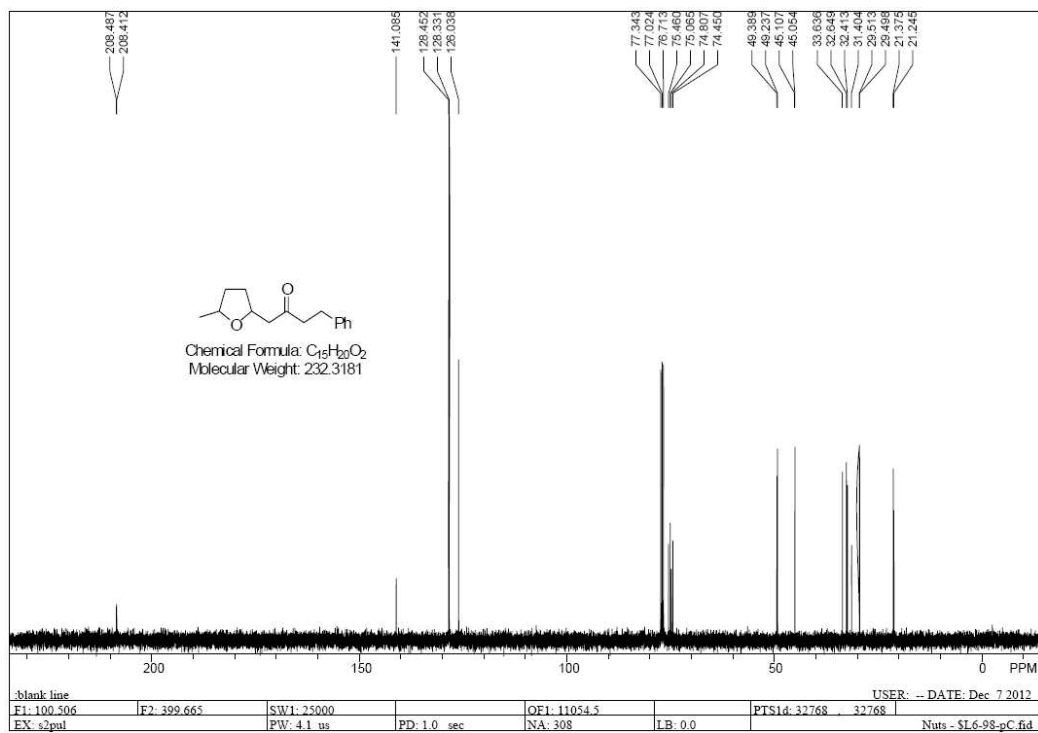
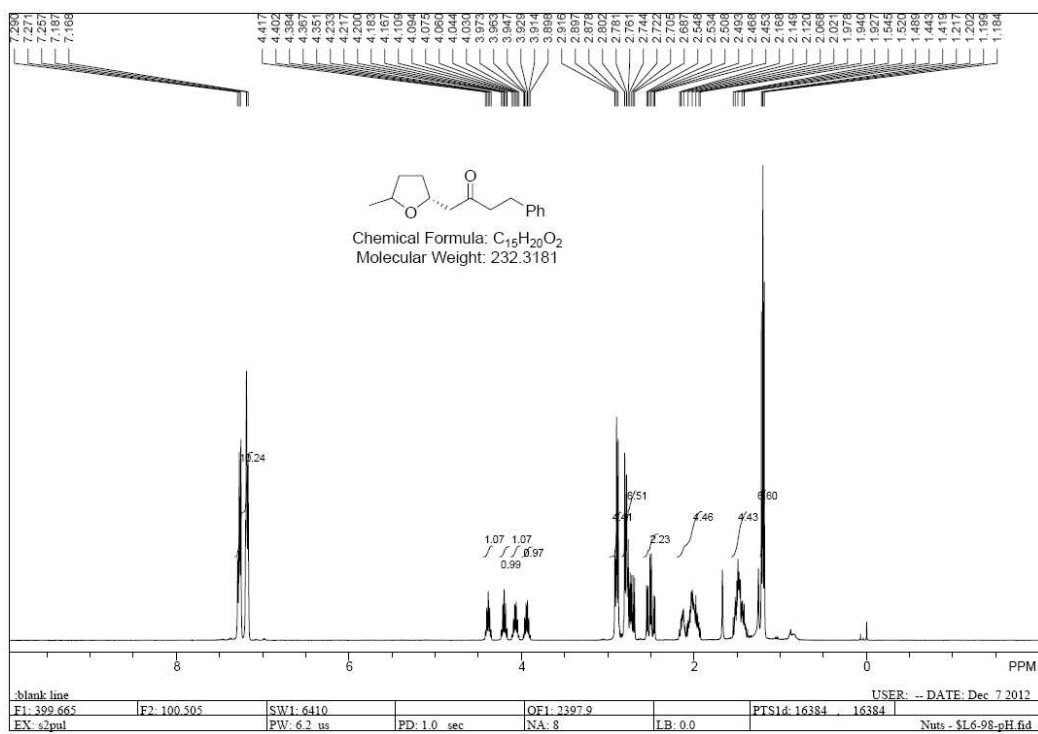


SampleName L7-5-1 (PC-II,0.5,1/4,210); Vial 1; Injection 87; Channel Satin Ch 1; Date Acquired 2012-12-7 18:39:23 CST

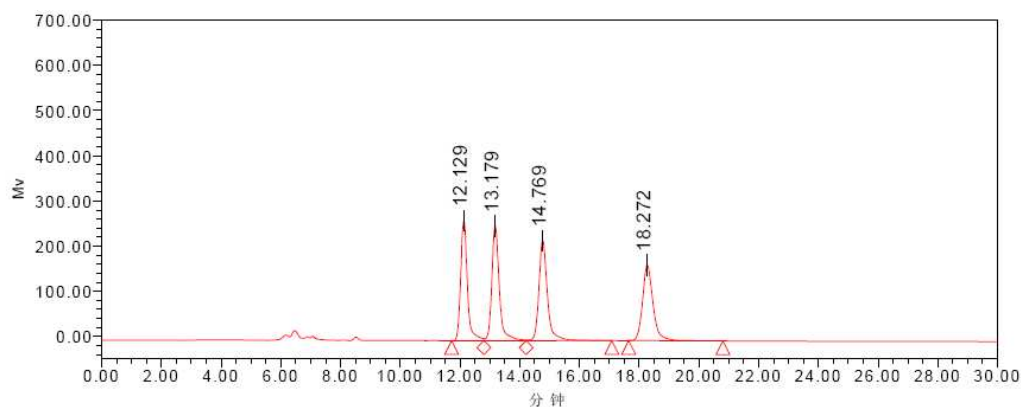
Peak Results
处理通道:

	RT	Area	% Area	Height
1	25.496	22069848	31.14	697939
2	28.089	48811984	68.86	1263920

2h



2h

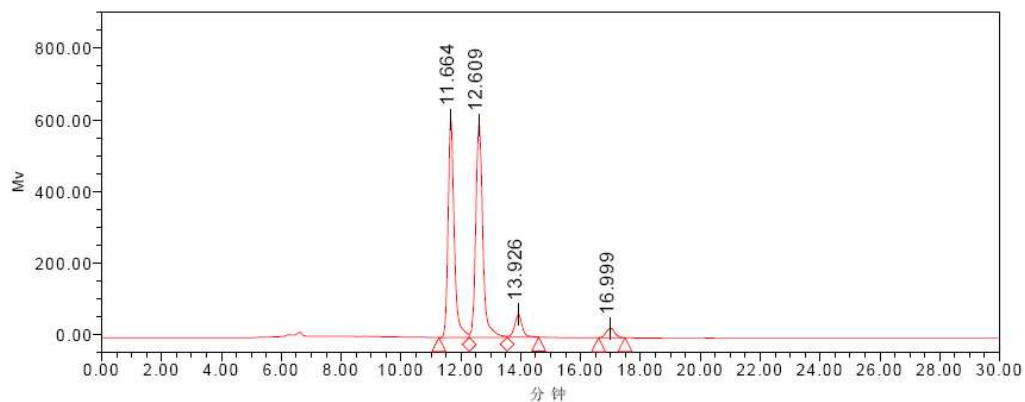


SampleName L6-98-rac(PC-II,0.5,1/4,210); Vial 1; Injection 63; Channel Satin Ch 1;
Date Acquired 2012-12-6 9:37:19 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	12.129	4167622	24.41	267158
2	13.179	4422805	25.90	254074
3	14.769	4393665	25.73	221636
4	18.272	4092487	23.97	167795



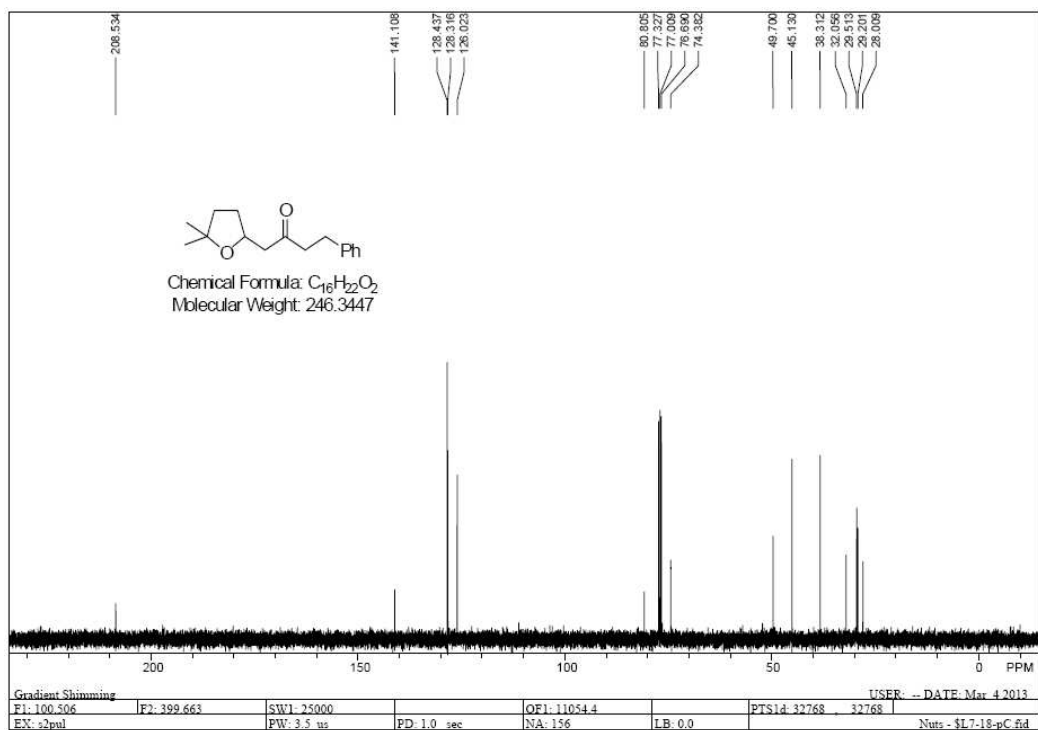
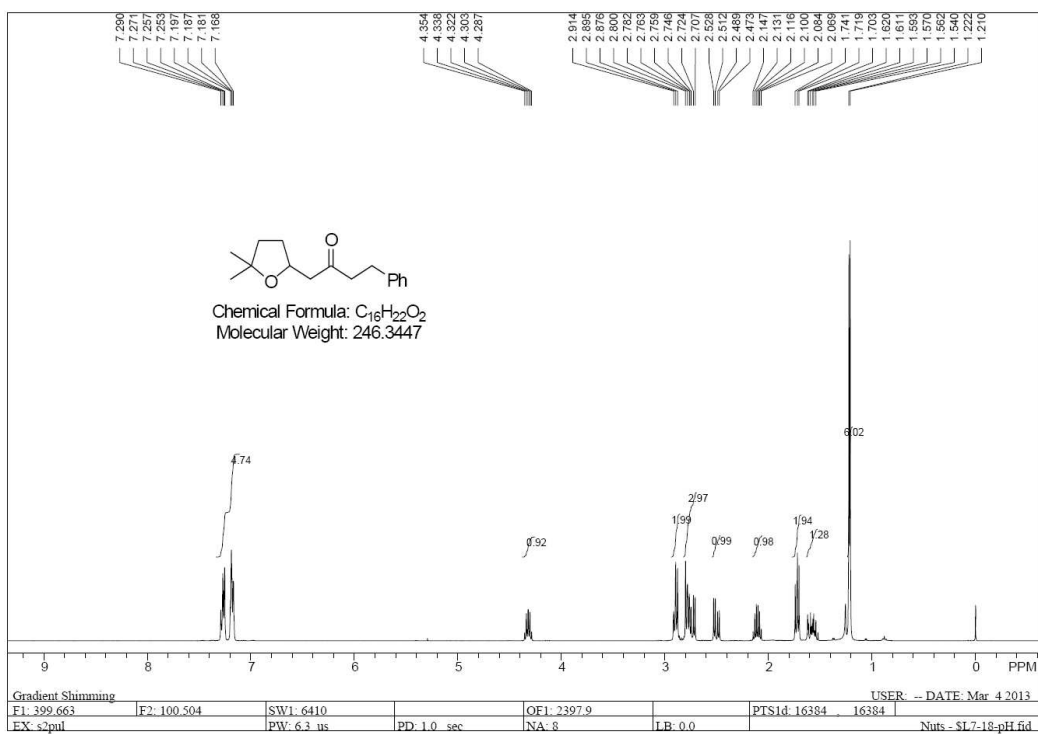
SampleName L6-98-P(PC-II,0.5,1/4,210); Vial 1; Injection 68; Channel Satin Ch 1;
Date Acquired 2012-12-6 13:28:07 CST

Peak Results

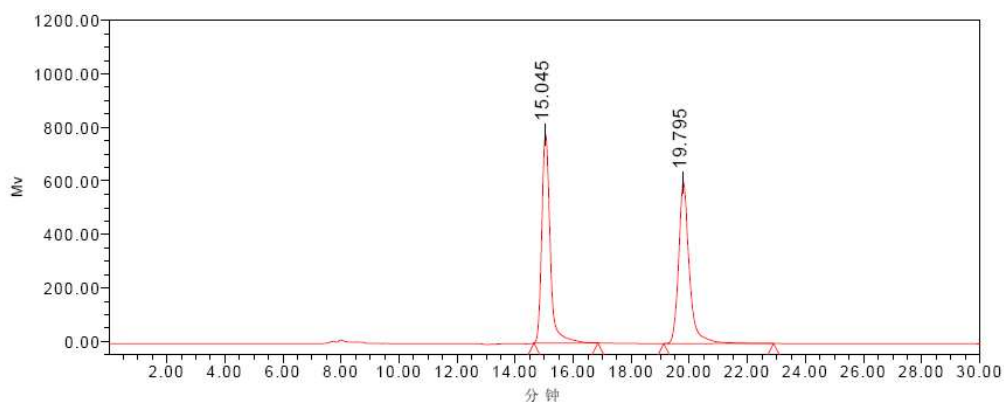
处理通道:

	RT	Area	% Area	Height
1	11.664	8691307	43.35	608825
2	12.609	9715052	48.45	594505
3	13.926	1112462	5.55	63559
4	16.999	532163	2.65	26554

2i



2i

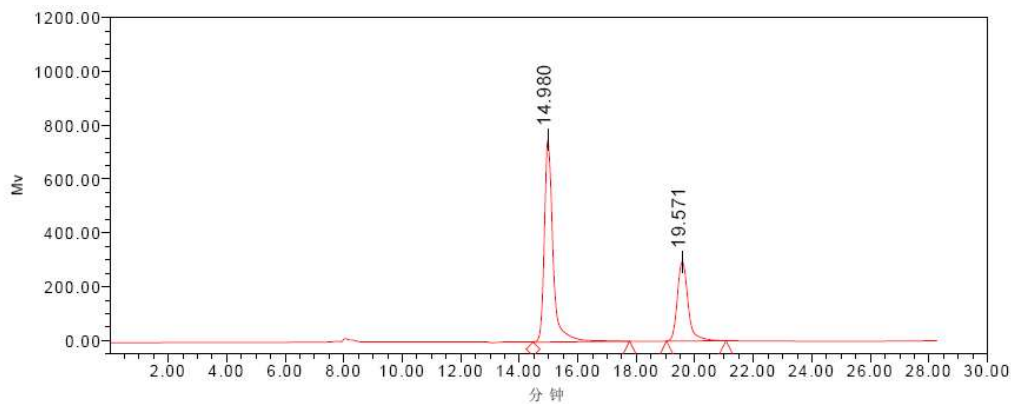


SampleName L7-18-rac (PC-II,1/9,210,0.4); Vial 1; Injection 17; Channel Satin Ch 1;
Date Acquired 2013-2-27 14:31:20 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	15.045	15733944	50.46	780017
2	19.795	15445549	49.54	601806



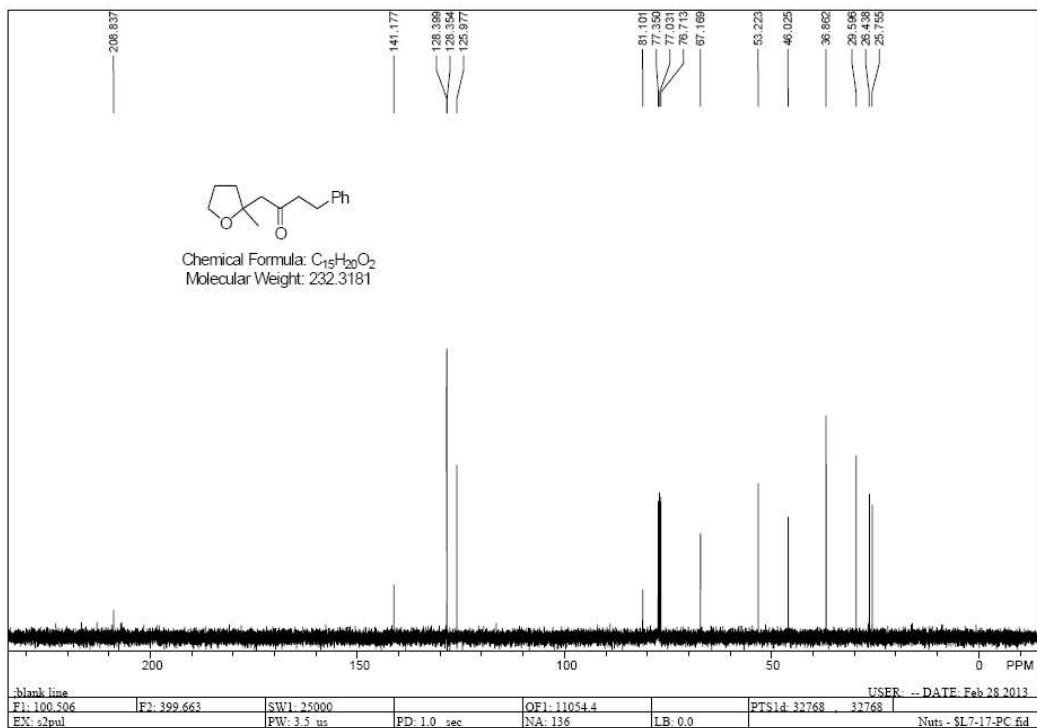
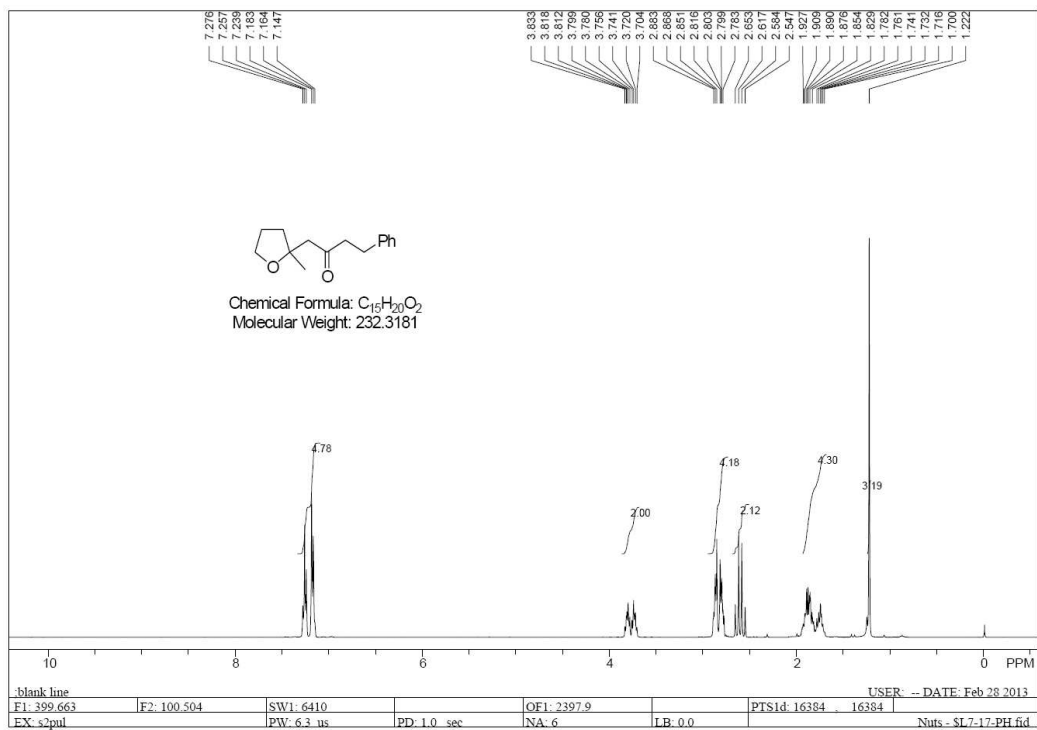
SampleName L7-18-P(PC-II,210,1/9,0.4); Vial 1; Injection 2; Channel Satin Ch 1;
Date Acquired 2013-3-4 9:52:51 CST

Peak Results

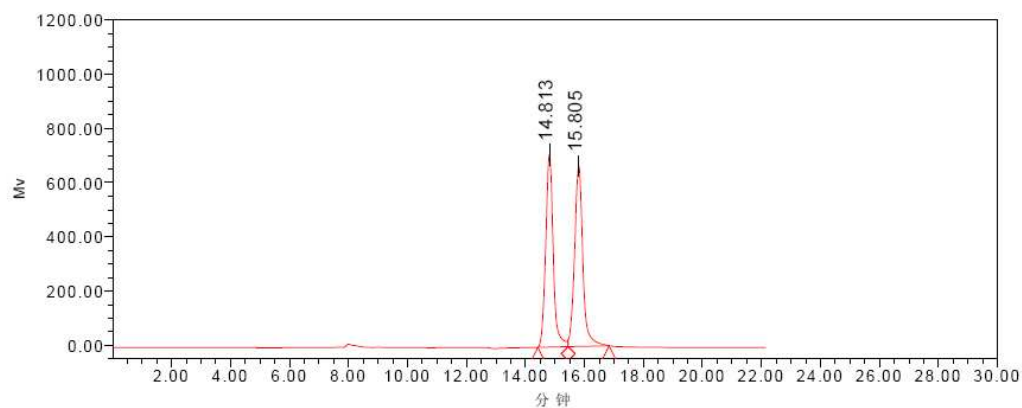
处理通道:

	RT	Area	% Area	Height
1	14.980	15549256	67.43	753373
2	19.571	7509322	32.57	293871

2j



(R)-2j

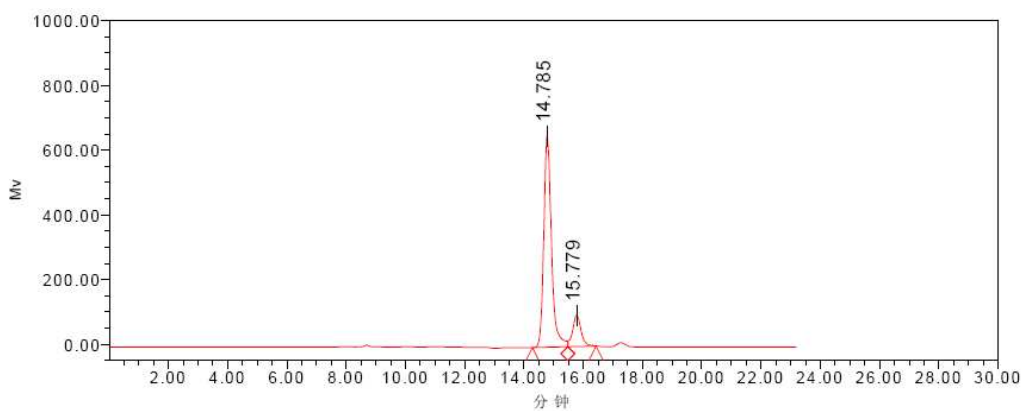


SampleName L7-17-rac(PC-II,1/9,210,0.4); Vial 1; Injection 12; Channel Satin Ch 1;
Date Acquired 2013-2-27 12:11:05 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	14.813	12605622	49.34	710514
2	15.805	12944511	50.66	666638



SampleName L7-17-P (PC-II,1/9,210,0.4); Vial 1; Injection 15; Channel Satin Ch 1;
Date Acquired 2013-2-27 13:31:20 CST

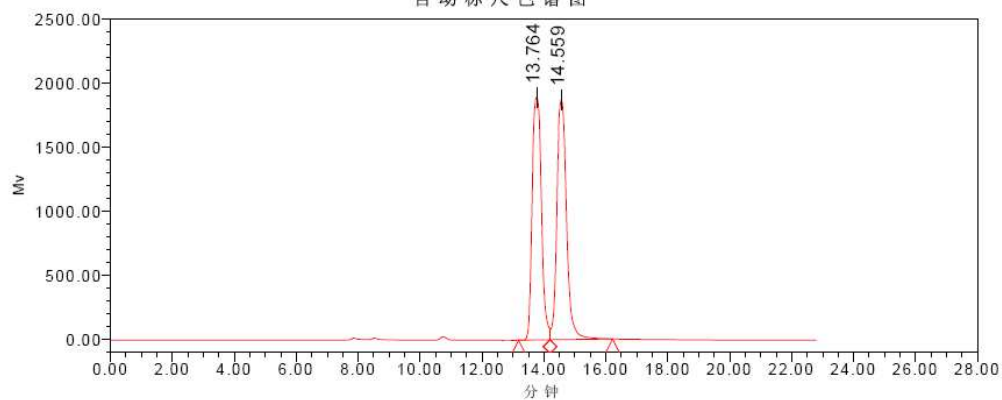
Peak Results

处理通道:

	RT	Area	% Area	Height
1	14.785	11771771	86.07	652688
2	15.779	1904846	13.93	96251

(S)-2j

自动标尺色谱图

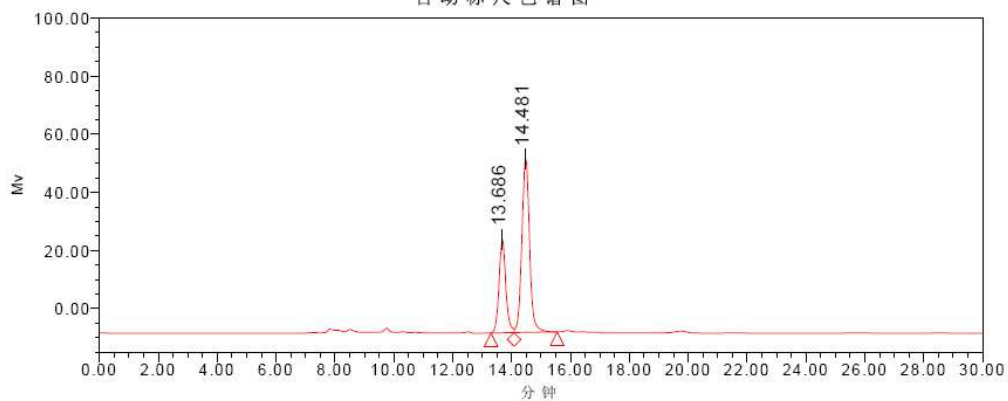


SampleName L7-17-rac(PC-II,1/9,0.4,210); Vial 1; Injection 31; Channel Satin Ch 1;
Date Acquired 2013-5-11 16:10:12 CST

Peak Results
处理通道:

	RT	Area	% Area	Height
1	13.764	39379491	49.25	1897253
2	14.559	40570802	50.75	1874638

自动标尺色谱图

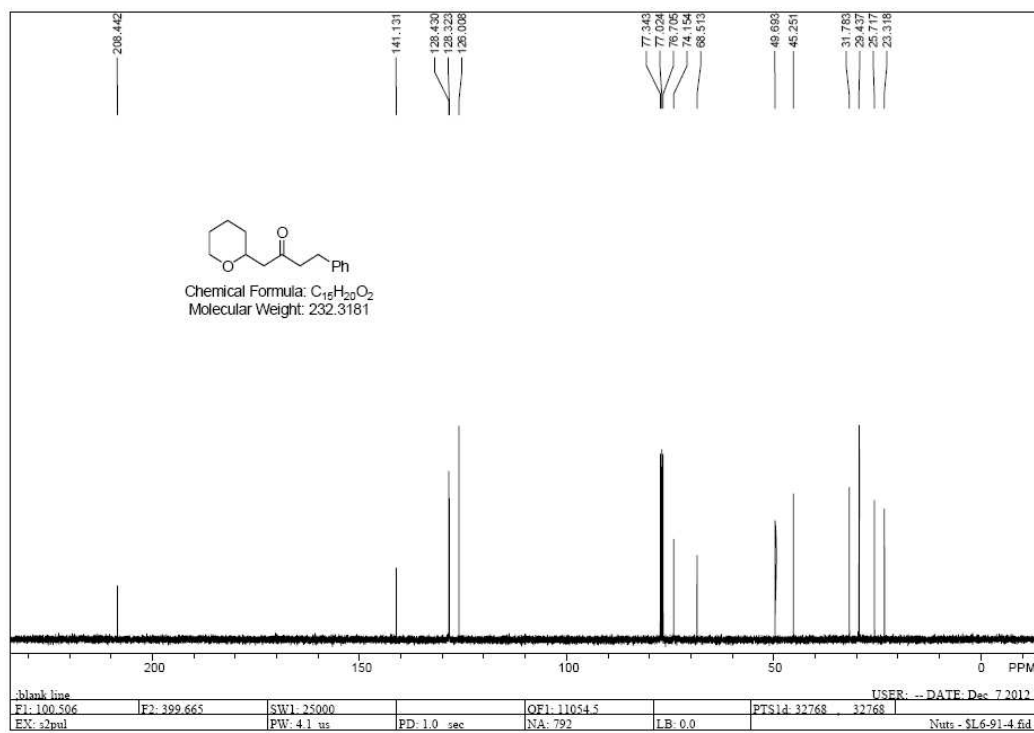
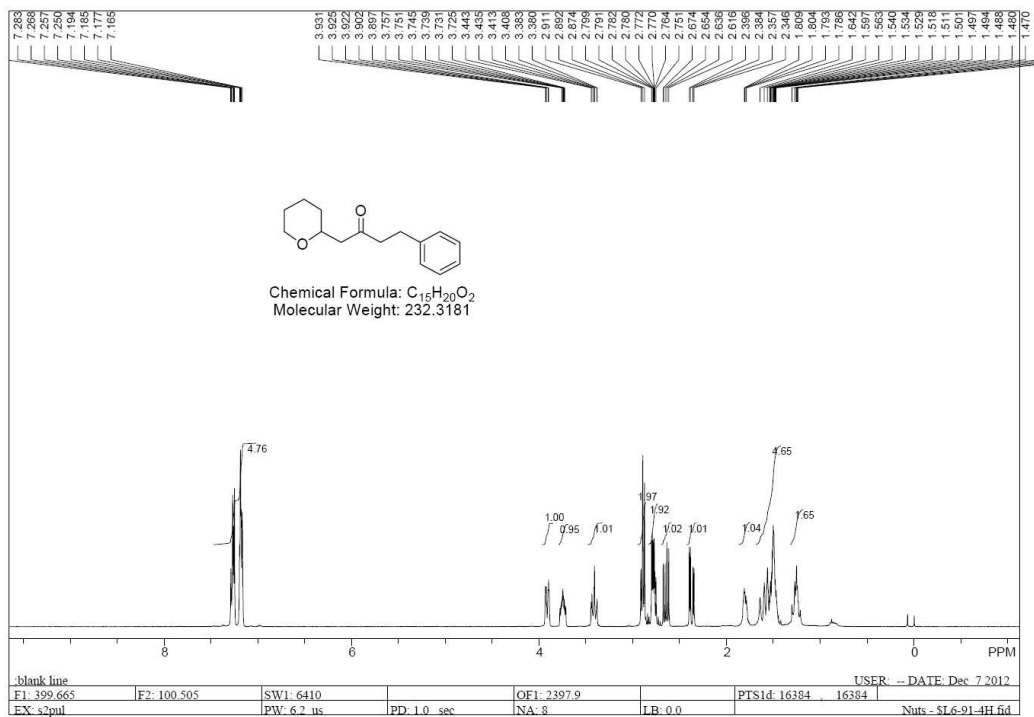


SampleName L7-17-ZP(PC-II,1/9,0.4,210); Vial 1; Injection 34; Channel Satin Ch 1;
Date Acquired 2013-5-11 17:28:34 CST

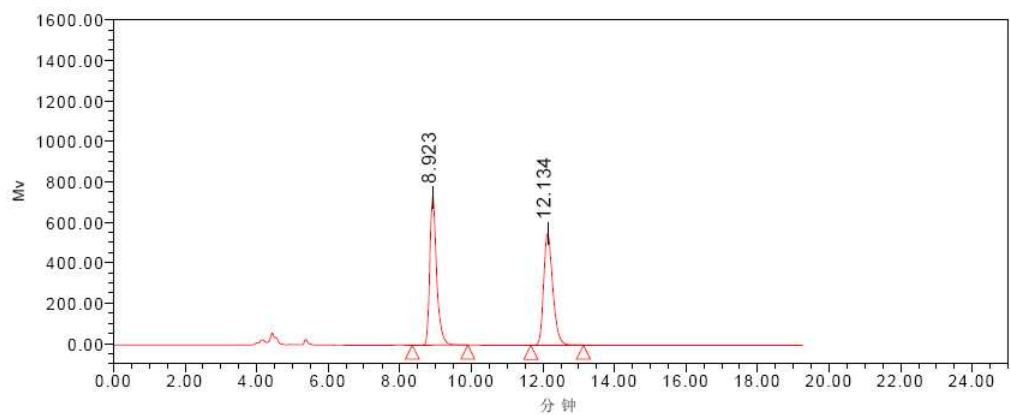
Peak Results
处理通道:

	RT	Area	% Area	Height
1	13.686	515679	32.02	32099
2	14.481	1094711	67.98	59696

2k



2k

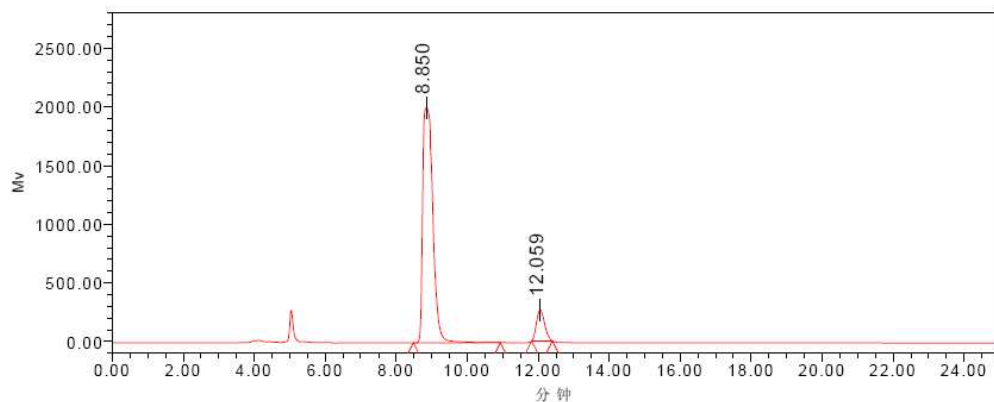


SampleName L6-91-4rac (AS-H,1/9,210,0.8); Vial 1; Injection 45; Channel Satin Ch 1; Date Acquired 2013-1-7 16:05:32 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	8.923	9758547	49.85	732946
2	12.134	9818528	50.15	551990



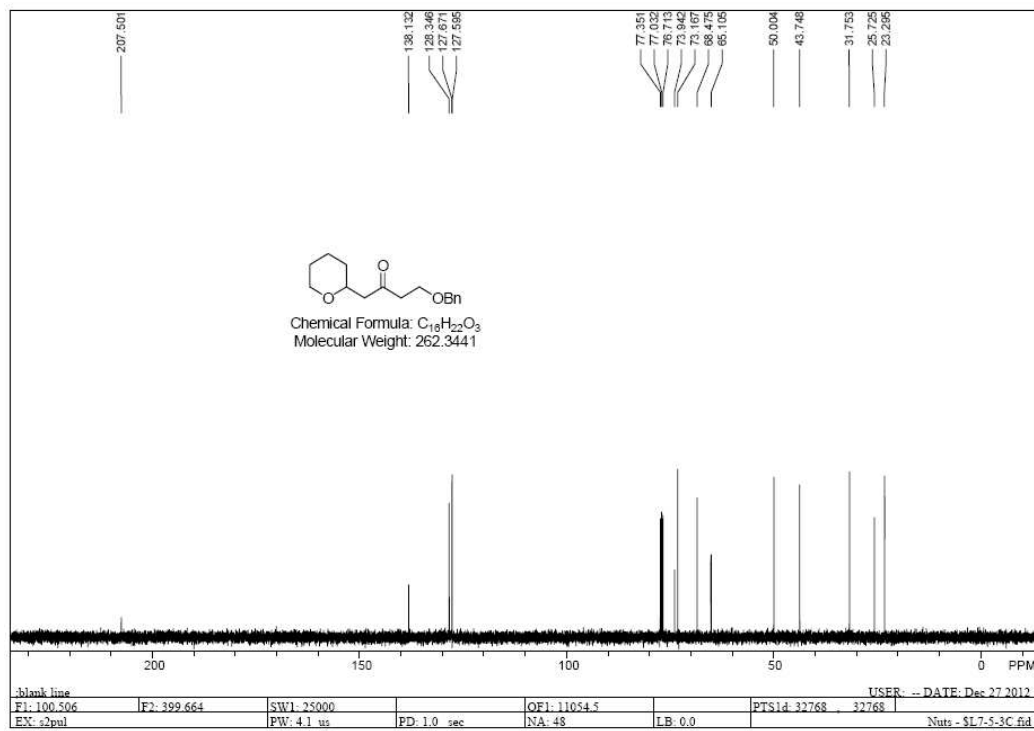
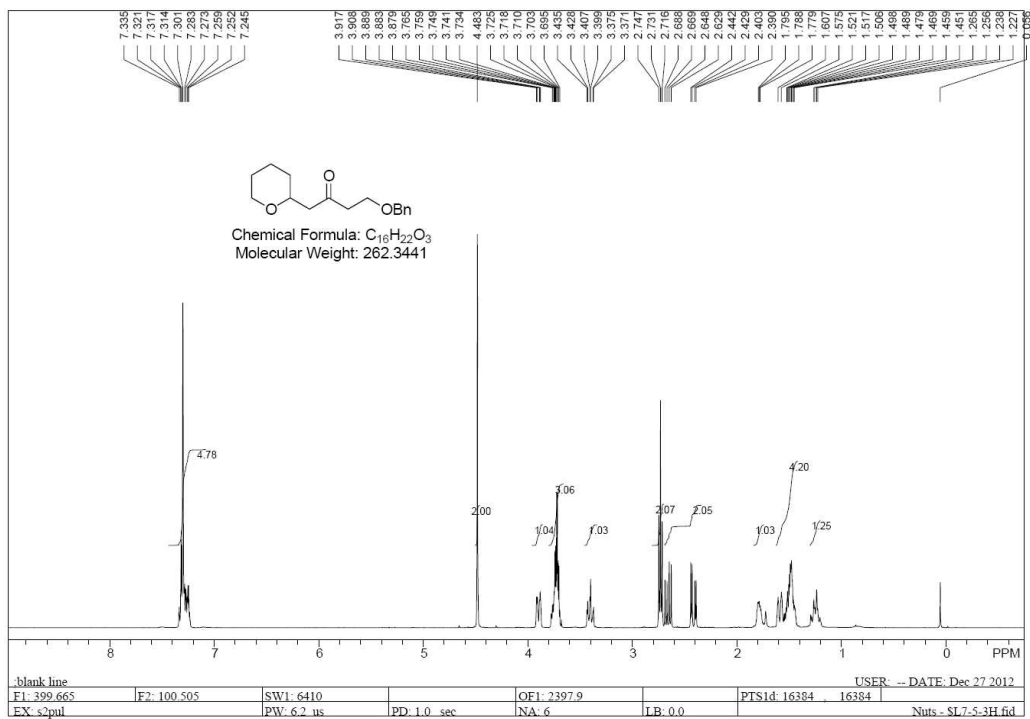
SampleName L6-91-4P (AS-H,1/9,210,0.8); Vial 1; Injection 48; Channel Satin Ch 1; Date Acquired 2013-1-7 17:02:15 CST

Peak Results

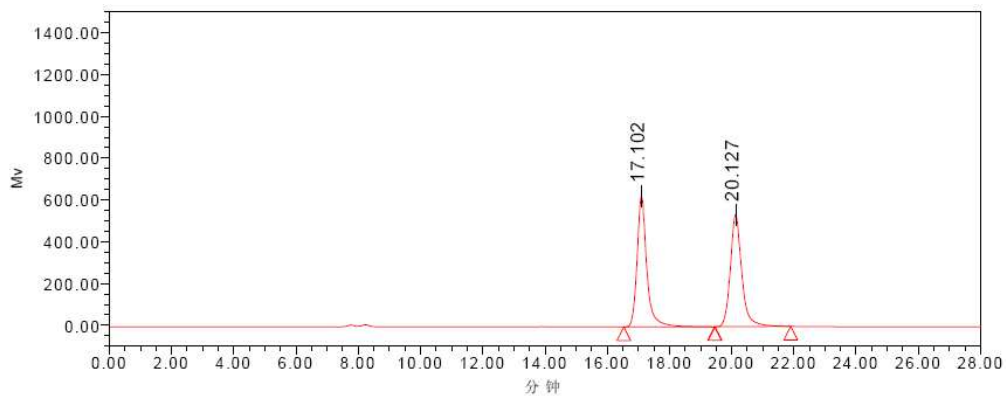
处理通道:

	RT	Area	% Area	Height
1	8.850	39750082	90.46	2001261
2	12.059	4192732	9.54	265399

21



21

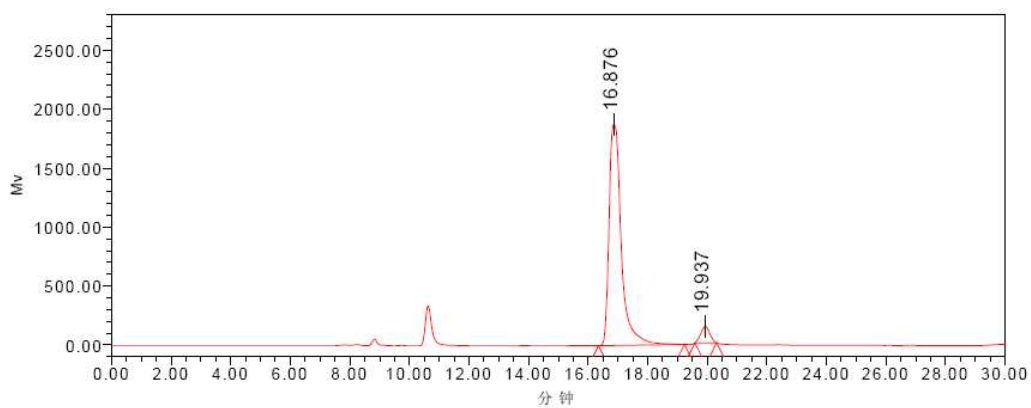


SampleName L7-5-3rac(pc-2,0.4,1/4,210); Vial 1; Injection 66; Channel Satin Ch 1;
Date Acquired 2012-12-27 11:58:36 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	17.102	13604085	49.91	625027
2	20.127	13654303	50.09	535576



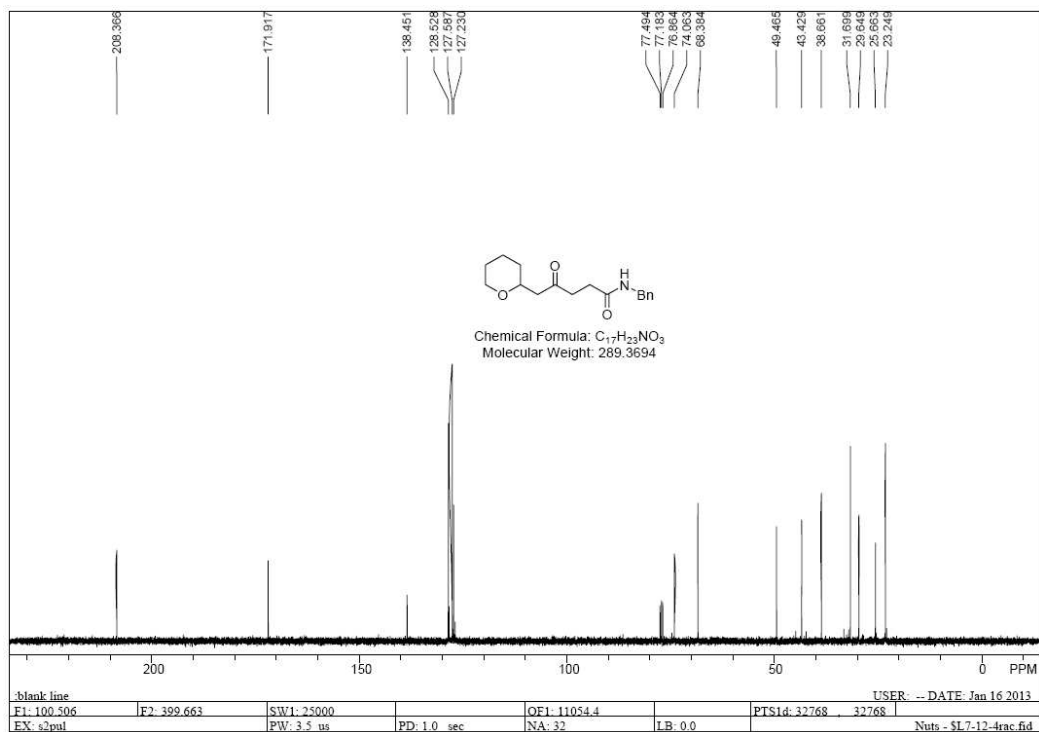
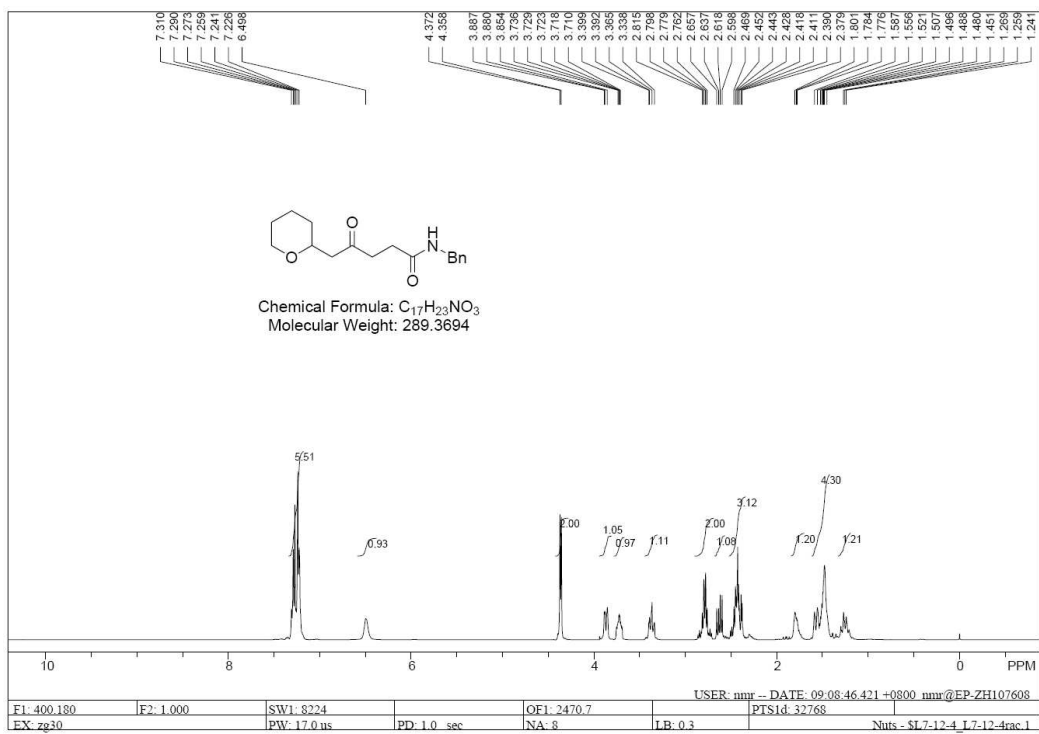
SampleName L7-5-3P(pc-2,0.4,1/4,210); Vial 1; Injection 69; Channel Satin Ch 1;
Date Acquired 2012-12-27 14:04:31 CST

Peak Results

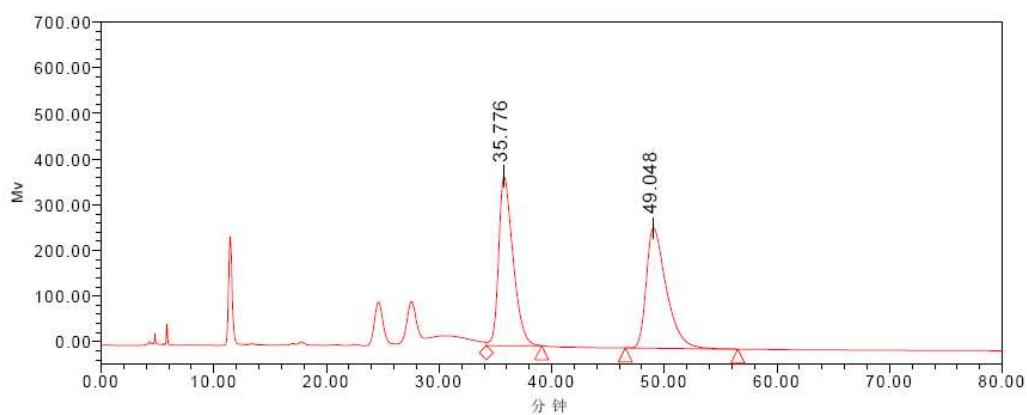
处理通道:

	RT	Area	% Area	Height
1	16.876	53522249	94.90	1876868
2	19.937	2876469	5.10	138880

2m



2m

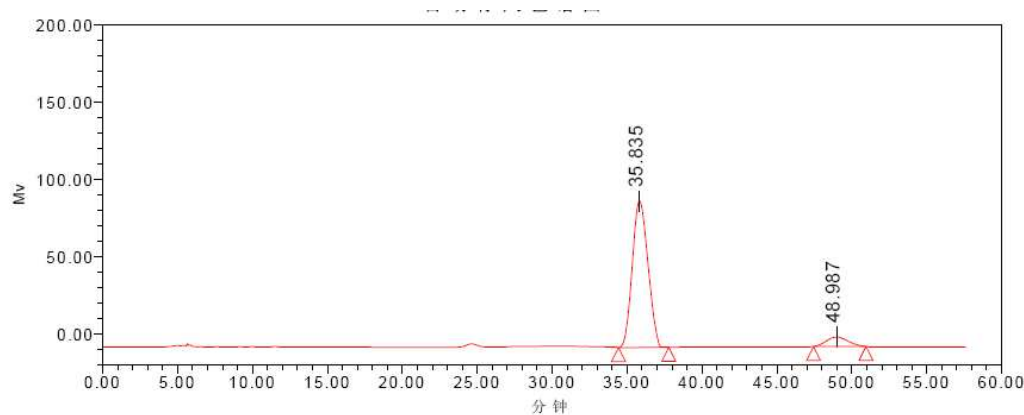


SampleName L7-12-4rac (PC-II,0.7,210,1/4); Vial 1; Injection 15; Channel Satin Ch 1; Date Acquired 2013-1-21 20:16:51 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	35.776	32881169	50.20	371746
2	49.048	32625062	49.80	263569



SampleName L7-12-4P(PC-II,0.7,210,1/4); Vial 1; Injection 11; Channel Satin Ch 1; Date Acquired 2013-1-21 15:23:31 CST

Peak Results

处理通道:

	RT	Area	% Area	Height
1	35.835	6883176	91.83	94603
2	48.987	612317	8.17	6100