

Supporting Information

Organocatalyzed Enantioselective Michael Additions of Nitroalkanes to Enones by Using Primary–Secondary Diamine Catalysts

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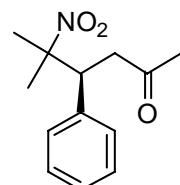
General Information: Unless otherwise indicated, all compounds and reagents were purchased from commercial suppliers and used without further purification. Proton nuclear magnetic resonance spectra are recorded at 300 MHz. All chemical shifts (δ) are given in ppm. NMR spectra were recorded on Varian EM-360A, Varian EM90 or Brucker AMX-300 NMR spectrometer. IR spectra were recorded on a Perkin-Elmer 983G instrument. MS or HRMS was recorded on a HP-5989A spectrometer. Melting points were determined on a METTLER-TOLEDO FP62 melting point apparatus and are uncorrected. HPLC analysis was carried out on WATERS equipment.

All Catalysts were prepared from our reported literature.¹⁻³

General procedure for the Michael reaction.

To a mixture of enone **2** (0.5 mmol), catalyst **3i** (0.1mmol) and 4-nitrophenol (0.1 mmol) in CH_2Cl_2 (1.0 mL) was added nitroalkne (1.0 mL) at ambient temperature. After 24 h of stirring, the reaction mixture was quenched with 1 M aqueous HCl solution, extracted with EtOAc. The combined organic layer was dried over Na_2SO_4 , filtered, and concentrated to afford the corresponding Michael adduct **4** after flash column chromatography on silica gel (petroleum ether/Et₂O as eluant).

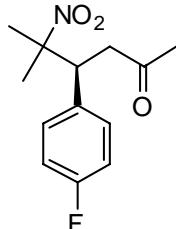
4aa: (S)-5-methyl-5-nitro-4-phenylhexan-2-one⁴



White solid; $[\alpha]_D^{22} -30.9$ (*c* 1.0, CHCl_3); m.p. 92-94°C; ^1H NMR (300MHz, CDCl_3) δ 1.45 (s, 3H), 1.53 (s, 3H), 1.99 (s, 3H), 2.68 (dd, $J = 3.6, 17.1$ Hz, 1H), 3.09 (dd, $J = 10.2, 17.1$ Hz, 1H), 3.92 (dd, $J =$

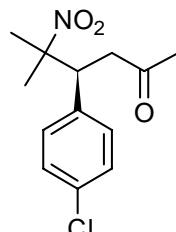
3.3, 10.5 Hz, 1H), 7.17-7.31 (m, 5H); Enantiomeric excess: 88%, determined by HPLC (Chiralpak OD column, hexane/*i*-PrOH 95:5, flow rate 0.7 mL/min, $t_{\text{major}} = 31.4$ min, $t_{\text{minor}} = 33.3$ min, $\lambda = 214$ nm).

4ab: (*S*)-4-(4-fluorophenyl)-5-methyl-5-nitrohexan-2-one



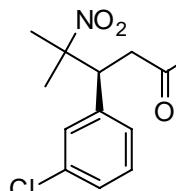
Colorless oil; $[\alpha]_D^{22} -32.7$ (*c* 1.0, CHCl₃); ¹H NMR (300MHz, CDCl₃) δ 1.44 (s, 3H), 1.51 (s, 3H), 2.00 (s, 3H), 2.70 (dd, *J* = 3.3, 17.1 Hz, 1H), 3.03 (dd, *J* = 10.5, 17.1 Hz, 1H), 3.89 (dd, *J* = 2.7, 10.2 Hz, 1H), 6.93-6.99 (m, 2H), 7.12-7.17 (m, 2H); ¹³C NMR (CDCl₃, 100MHz) δ 22.9, 25.5, 30.5, 44.2, 48.2, 91.1, 115.7 (d, ²J_{CF} = 21.0Hz), 130.9(d, ³J_{CF} = 8.1Hz), 133.7 (d, ⁴J_{CF} = 3.6Hz), 162.4 (d, ¹J_{CF} = 245.8Hz), 205.2; IR (neat): 3046, 2995, 2950, 1720, 1605, 1535, 1511, 1229, 1163, 848, 819 cm⁻¹; HRMS calc. C₁₃H₁₆O₃NF (M⁺): 253.1114. Found: 253.1115. Enantiomeric excess: 91%, determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 100:1, flow rate 1.00 mL/min, $t_{\text{major}} = 34.5$ min, $t_{\text{minor}} = 32.0$ min, $\lambda = 254$ nm).

4ac: (*S*)-4-(4-chlorophenyl)-5-methyl-5-nitrohexan-2-one⁴



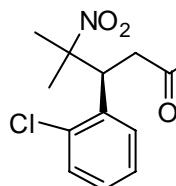
Colorless oil; $[\alpha]_D^{18} -35.2$ (*c* 1.0, CHCl₃); ¹H NMR (300MHz, CDCl₃) δ 1.48 (s, 3H), 1.54 (s, 3H), 2.05 (s, 3H), 2.74 (dd, *J* = 3.3, 17.1 Hz, 1H), 3.04 (dd, *J* = 10.5, 17.1 Hz, 1H), 3.90 (dd, *J* = 3.6, 10.8 Hz, 1H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 9.3 Hz, 2H); Enantiomeric excess: 90%, determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 90:10, flow rate 1.00 mL/min, $t_{\text{major}} = 11.8$ min, $t_{\text{minor}} = 10.7$ min, $\lambda = 254$ nm).

4ad: (*S*)-4-(3-chlorophenyl)-5-methyl-5-nitrohexan-2-one



Colorless oil; $[\alpha]_D^{18} -33.1$ (*c* 1.0, CHCl₃); ¹H NMR (300MHz, CDCl₃) δ 1.45 (s, 3H), 1.52 (s, 3H), 2.02 (s, 3H), 2.70 (dd, *J* = 3.3, 17.7 Hz, 1H), 3.05 (dd, *J* = 10.5, 17.4 Hz, 1H), 3.89 (dd, *J* = 2.7, 10.8 Hz, 1H), 7.05-7.08 (m, 1H), 7.16 (s, 1H), 7.20-7.22 (m, 2H); ¹³C NMR (CDCl₃, 100MHz) δ 22.9, 25.7, 30.6, 44.0, 48.5, 91.0, 127.7, 128.3, 129.4, 130.0, 134.5, 140.2, 204.9; IR (neat): 3651, 3422, 2994, 2951, 1715, 1596, 1537, 1471, 1373, 1164, 1084, 851, 780, 700 cm⁻¹; HRMS calc. C₁₃H₁₆O₃NCl (M⁺): 269.0819. Found: 269.0818. Enantiomeric excess: 87%, determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 100:1, flow rate 1.00 mL/min, $t_{\text{major}} = 24.8$ min, $t_{\text{minor}} = 22.2$ min, $\lambda = 254$ nm).

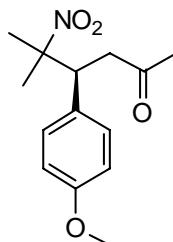
4ae: (*S*)-4-(2-chlorophenyl)-5-methyl-5-nitrohexan-2-one



Colorless oil; $[\alpha]_D^{22} -42.0$ (*c* 1.0, CHCl₃); ¹H NMR (300MHz,

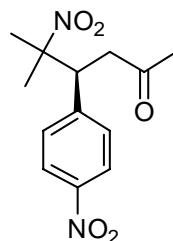
CDCl_3) δ 1.52 (s, 3H), 1.54 (s, 3H), 2.00 (s, 3H), 2.81 (dd, $J = 3.6, 17.1$ Hz, 1H), 3.02 (dd, $J = 10.8, 17.1$ Hz, 1H), 4.62 (dd, $J = 3.3, 10.5$ Hz, 1H), 7.08-7.11 (m, 1H), 7.16-7.20 (m, 2H), 7.37-7.40 (m, 1H); ^{13}C NMR (CDCl_3 , 100MHz) δ 22.2, 26.3, 30.2, 43.3, 44.9, 91.5, 127.3, 128.4, 129.1, 130.4, 136.2, 136.3, 205.2; IR (neat): 3067, 2994, 2950, 2870, 1714, 1571, 1536, 1472, 1438, 1164, 1036, 850, 757, 685 cm^{-1} ; HRMS calc. $\text{C}_{13}\text{H}_{16}\text{O}_3\text{NCl} (\text{M}^+)$: 269.0819. Found: 269.0824. Enantiomeric excess: 86%, determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 90:1 0, flow rate 1.00 mL/min, $t_{\text{major}} = 8.0$ min, $t_{\text{minor}} = 8.4$ min, $\lambda = 254$ nm).

4af: (S)-4-(4-methoxyphenyl)-5-methyl-5-nitrohexan-2-one



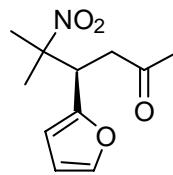
Colorless oil; $[\alpha]_D^{22} -22.7$ (c 1.0, CHCl_3); ^1H NMR (300MHz, CDCl_3) δ 1.43 (s, 3H), 1.51 (s, 3H), 1.98 (s, 3H), 2.63 (dd, $J = 3.3, 17.1$ Hz, 1H), 3.02 (dd, $J = 10.5, 16.5$ Hz, 1H), 3.73 (s, 3H), 3.85 (dd, $J = 3.6, 10.8$ Hz, 1H), 6.79 (d, $J = 8.4$ Hz, 2H), 7.08 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100MHz) δ 22.6, 25.7, 30.5, 44.2, 48.4, 55.4, 91.5, 114.1, 129.6, 130.4, 159.3, 205.7; IR (neat): 3668, 3647, 3420, 3038, 2996, 2955, 2839, 1705, 1612, 1583, 1538, 1515, 1470, 1241, 834 cm^{-1} ; HRMS calc. $\text{C}_{14}\text{H}_{19}\text{O}_4\text{N} (\text{M}^+)$: 265.1314. Found: 265.1311. Enantiomeric excess: 91%, determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 100:1, flow rate 1.00 mL/min, $t_{\text{major}} = 61.5$ min, $t_{\text{minor}} = 75.3$ min, $\lambda = 254$ nm).

4ag: (S)-5-methyl-5-nitro-4-(4-nitrophenyl)hexan-2-one⁴



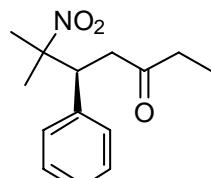
White solid; $[\alpha]_D^{22} -43.0$ (c 1.0, CHCl_3); m.p. 89-91°C; ^1H NMR (300MHz, CDCl_3) δ 1.48 (s, 3H), 1.55 (s, 3H), 2.05 (s, 3H), 2.84 (dd, $J = 3.0, 17.7$ Hz, 1H), 3.13 (dd, $J = 10.8, 18.0$ Hz, 1H), 4.01 (dd, $J = 3.0, 10.8$ Hz, 1H), 7.37 (d, $J = 9.0$ Hz, 2H), 8.12 (d, $J = 8.4$ Hz, 2H); Enantiomeric excess: 91%, determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 90:10, flow rate 1.00 mL/min, $t_{\text{major}} = 53.2$ min, $t_{\text{minor}} = 34.3$ min, $\lambda = 254$ nm).

4ah: (R)-4-(furan-2-yl)-5-methyl-5-nitrohexan-2-one⁴



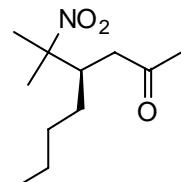
Colorless oil; $[\alpha]_D^{22} -28.3$ (c 1.0, CHCl_3); ^1H NMR (300MHz, CDCl_3) δ 1.47 (s, 3H), 1.54 (s, 3H), 2.05 (s, 3H), 2.50 (dd, $J = 2.7, 16.8$ Hz, 1H), 3.07 (dd, $J = 11.4, 17.1$ Hz, 1H), 4.09 (dd, $J = 3.0, 10.8$ Hz, 1H), 6.15 (d, $J = 3.0$ Hz, 1H), 6.26-6.27 (m, 1H), 7.29-7.30 (m, 1H); Enantiomeric excess: 88%, determined by HPLC (Chiralpak AD-H column, hexane/*i*-PrOH 80:20, flow rate 0.60 mL/min, $t_{\text{major}} = 9.1$ min, $t_{\text{minor}} = 8.8$ min, $\lambda = 254$ nm).

4ai: (S)-6-methyl-6-nitro-5-phenylheptan-3-one⁴



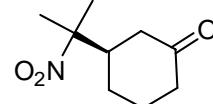
Colorless oil; $[\alpha]_D^{22} -17.7$ (*c* 1.0, CHCl₃); ¹H NMR (300MHz, CDCl₃) δ 0.87 (t, *J* = 7.2 Hz), 1.45 (s, 3H), 1.54 (s, 3H), 2.14-2.43 (m, 2H), 2.65 (dd, *J* = 2.4, 17.1 Hz, 1H), 3.08 (dd, *J* = 10.5, 16.5 Hz, 1H), 3.92-3.96 (m, 1H), 7.16-7.27 (m, 5H); Enantiomeric excess: 90%, determined by HPLC (Chiralpak AD-H column, hexane/*i*-PrOH 80:20, flow rate 0.60 mL/min, t_{major} = 8.6 min, t_{minor} = 9.1 min, λ = 220 nm).

4aj: (*R*)-4-(2-nitropropan-2-yl)octan-2-one⁴



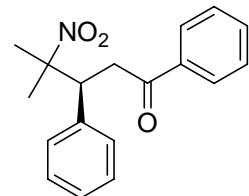
Colorless oil; $[\alpha]_D^{26} -20.7$ (*c* 1.0, CHCl₃); ¹H NMR (300MHz, CDCl₃) δ 0.82 (t, *J* = 6.9 Hz, 3H), 0.99-1.31 (m, 6H), 1.47 (s, 3H), 1.49 (s, 3H), 2.14 (s, 3H), 2.27-2.52 (m, 2H), 2.68-2.76 (m, 1H); Enantiomeric excess: 91%, determined by HPLC (Chiralpak AS-H column, hexane/*i*-PrOH 90:10, flow rate 0.70 mL/min, t_{major} = 9.5 min, t_{minor} = 8.8 min, λ = 220 nm).

4ak: (*R*)-3-(2-nitropropan-2-yl)cyclohexanone⁴



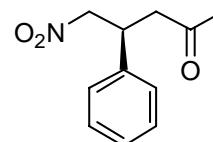
White solid; $[\alpha]_D^{26} -13.7$ (*c* 1.0, CHCl₃); m.p. 61-63°C; ¹H NMR (300MHz, CDCl₃) δ 1.30-1.45 (m, 1H), 1.50 (s, 3H), 1.52 (s, 3H), 1.55-1.64 (m, 1H), 1.72-1.77 (m, 1H), 2.02-2.40 (m, 6H); Enantiomeric excess: 60%, determined by GC (HP chiral 20% Permethylated B-Cyclodextrin, flow rate 2.0 mL/min, 10°C/min from 110°C to 200°C t_{major} = 149.9 min, t_{minor} = 154.6 min).

4al: (*S*)-4-methyl-4-nitro-1,3-diphenylpentan-1-one⁵



White solid; $[\alpha]_D^{24} -77.5$ (*c* 1.0, CHCl₃); m.p. 147-149°C; ¹H NMR (400MHz, CDCl₃) δ 1.54 (s, 3H), 1.63 (s, 3H), 3.27 (dd, *J* = 3.2, 17.2 Hz, 1H), 3.68 (dd, *J* = 10.4, 17.6 Hz, 1H), 4.15 (dd, *J* = 3.2, 10.0 Hz, 1H), 7.22-7.27 (m, 5H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 2H); Enantiomeric excess: 92%, determined by HPLC (Chiralpak AD-H column, hexane/*i*-PrOH 90:10, flow rate 0.80 mL/min, t_{major} = 15.4 min, t_{minor} = 17.6 min, λ = 254 nm).

4ba: (*S*)-5-nitro-4-phenylpentan-2-one⁴



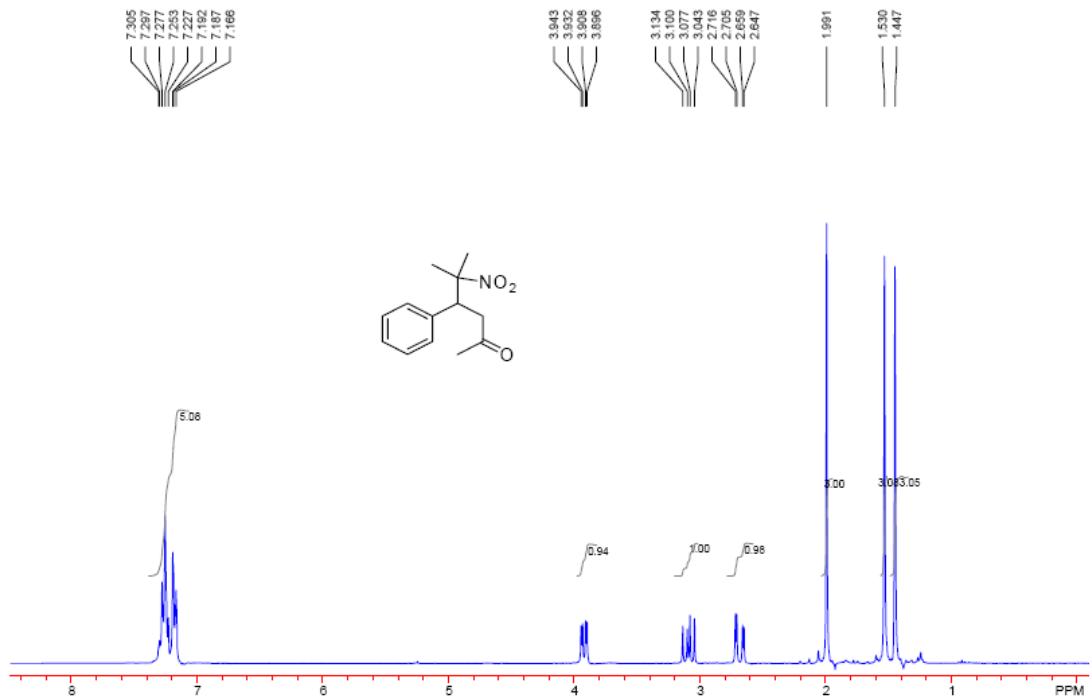
White solid; $[\alpha]_D^{18} 3.3$ (*c* 1.0, CHCl₃); m.p. 109-111°C; ¹H NMR (300MHz, CDCl₃) δ 3.14 (s, 3H), 2.92 (d, *J* = 6.9 Hz, 2H), 3.96-4.06 (m, 1H), 4.57-4.73 (m, 2H), 7.20-7.36 (m, 5H); Enantiomeric excess: 91%, determined by HPLC (Chiralpak AD column, hexane/*i*-PrOH 90:10, flow rate 1.0 mL/min, t_{major} = 13.7 min, t_{minor} = 14.5 min, λ = 254 nm).

References

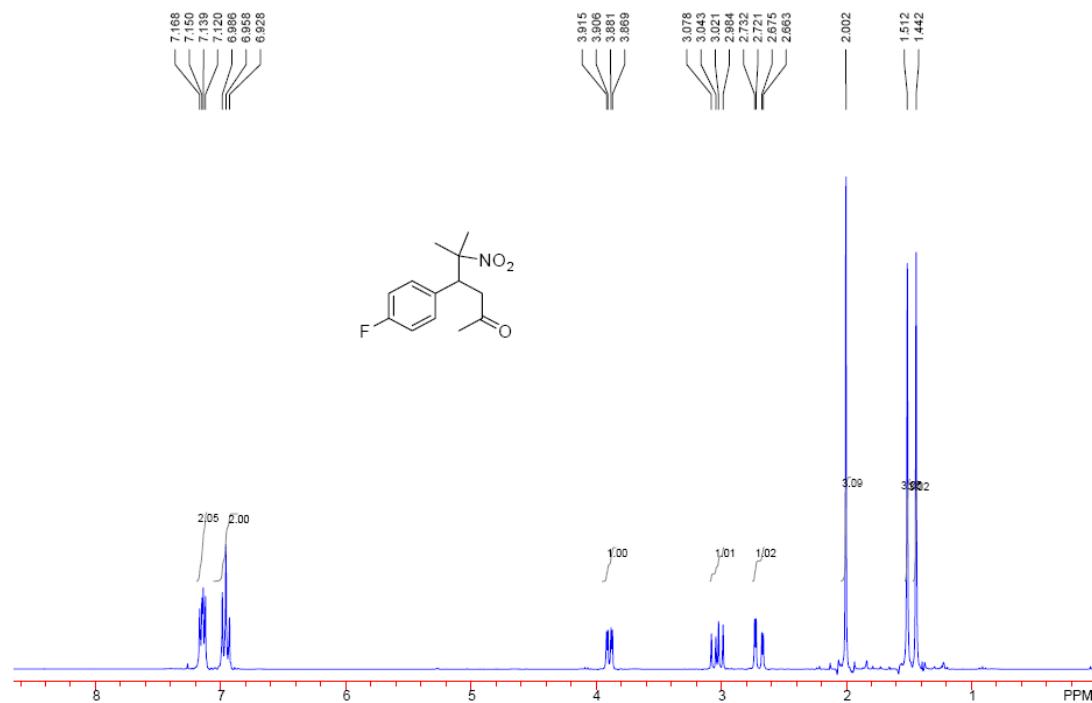
1. Y.-Q. Yang and G. Zhao, *Chem. Eur. J.* 2008, **14**, 10888.
2. Y.-Q. Yang, Z. Chai, H.-F. Wang, X.-K. Chen, H.-F. Cui, C.-W. Zheng, H. Xiao, P. Li and G. Zhao, *Chem. Eur. J.* 2009, **15**, 13295.
3. H.-F. Cui, Y.-Q. Yang, Z. Chai, P. Li, C.-W. Zheng, S.-Z. Zhu, and G. Zhao *J. Org. Chem.* 2010, **75**, 117.
4. N. Halland, R. G. Hazell and K. A. Jørgensen, *J. Org. Chem.* 2002, **67**, 8331.
5. D. Y. Kim and S. C. Huh, *Tetrahedron*. **2001**, *57*, 8933.

NMR spectra for compounds 4

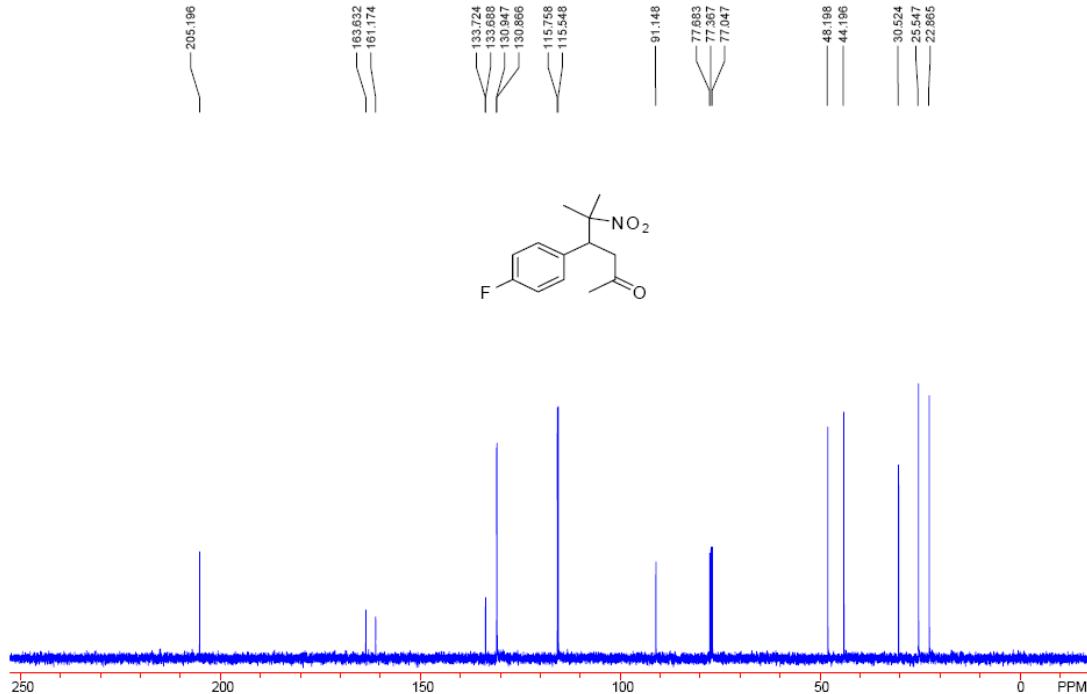
4aa (^1H NMR)



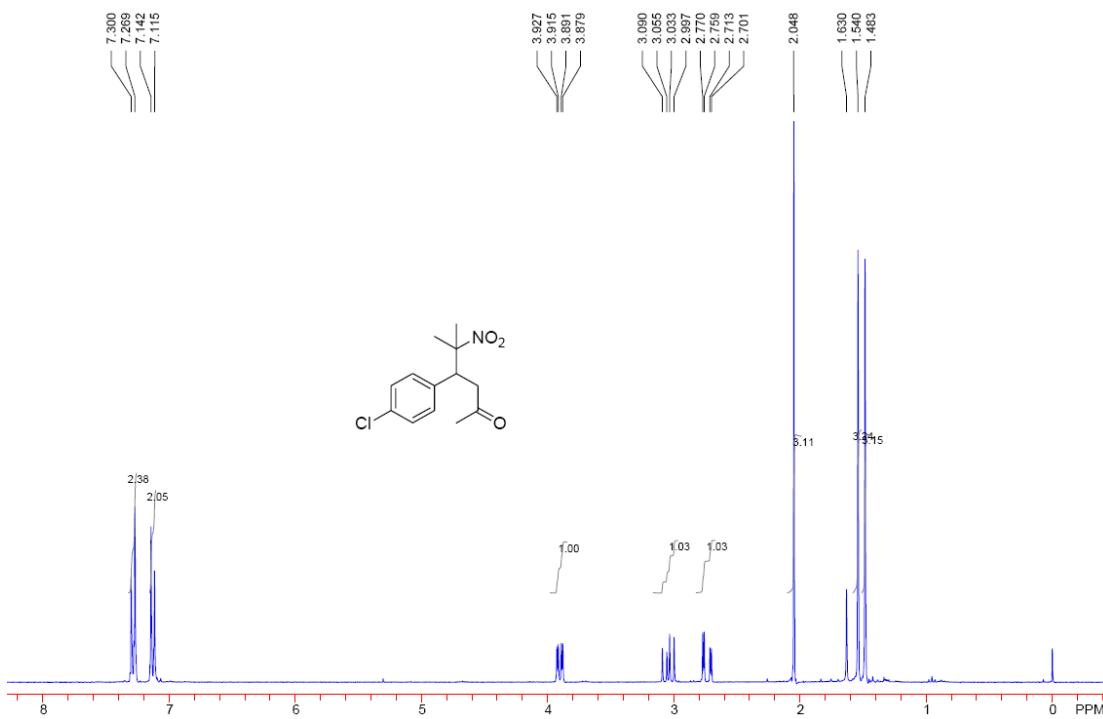
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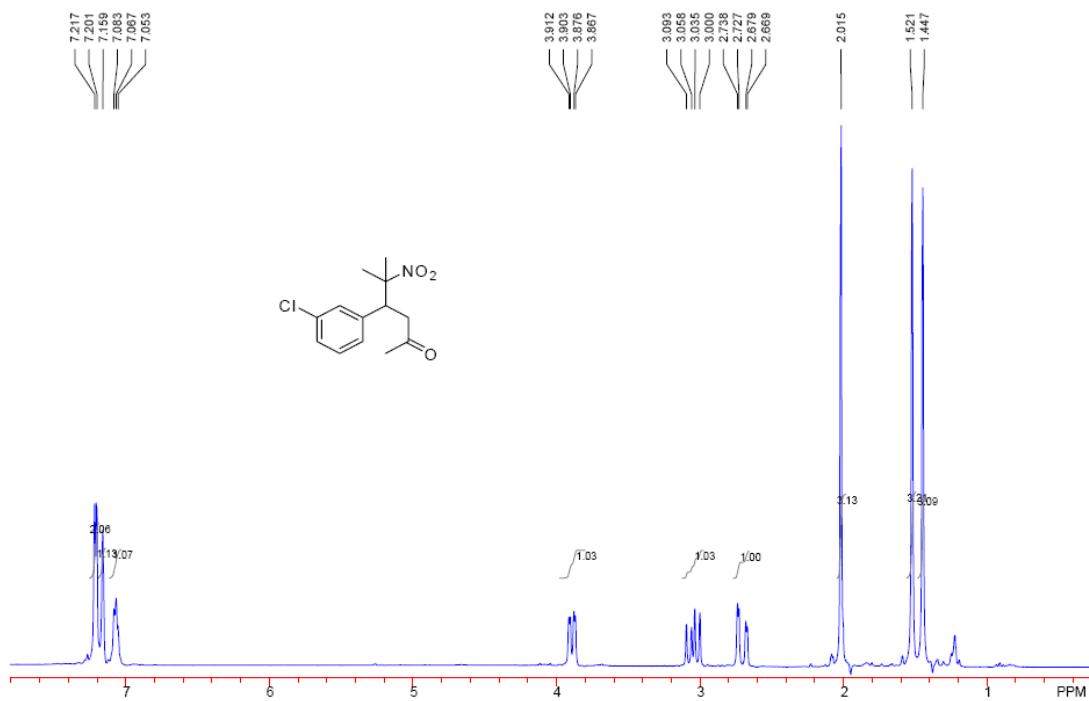
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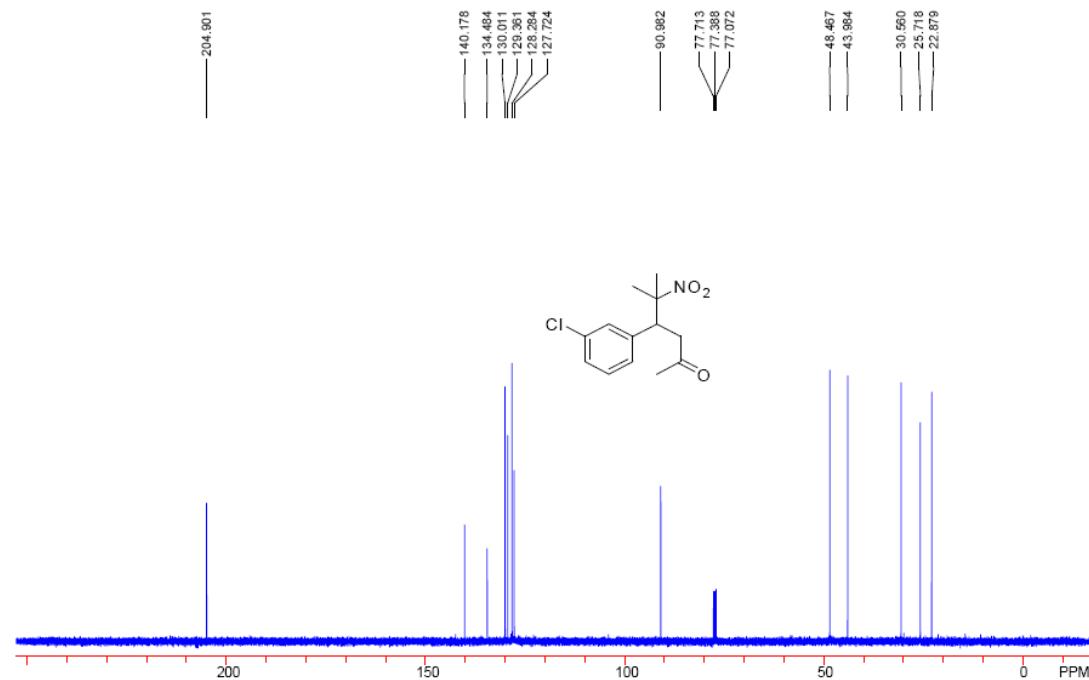
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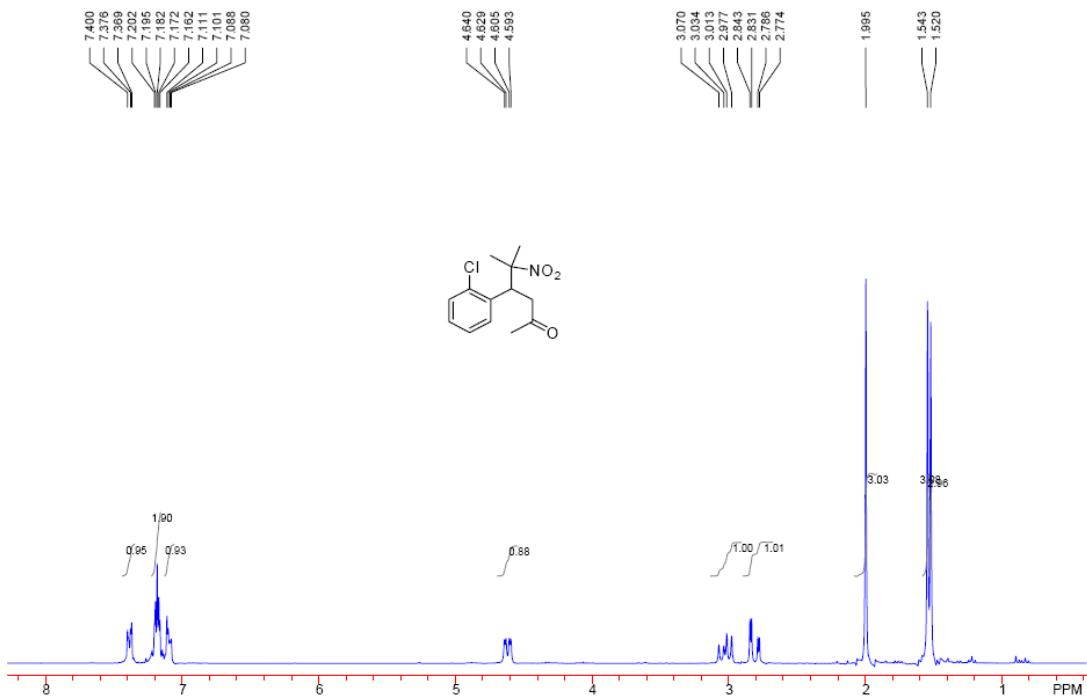
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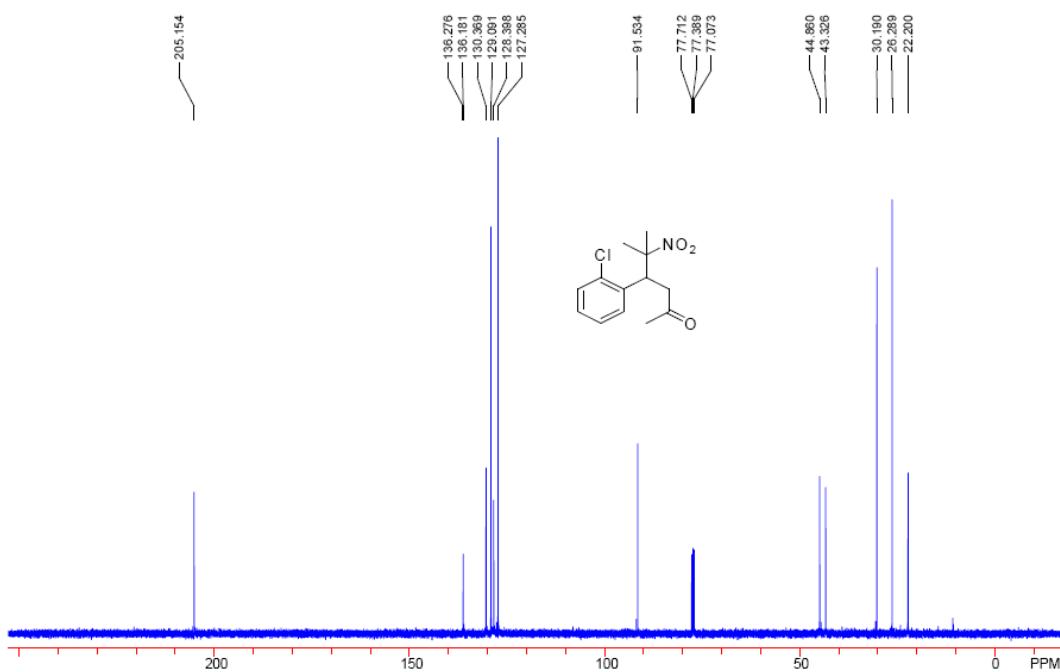
4ad (^{13}C NMR)



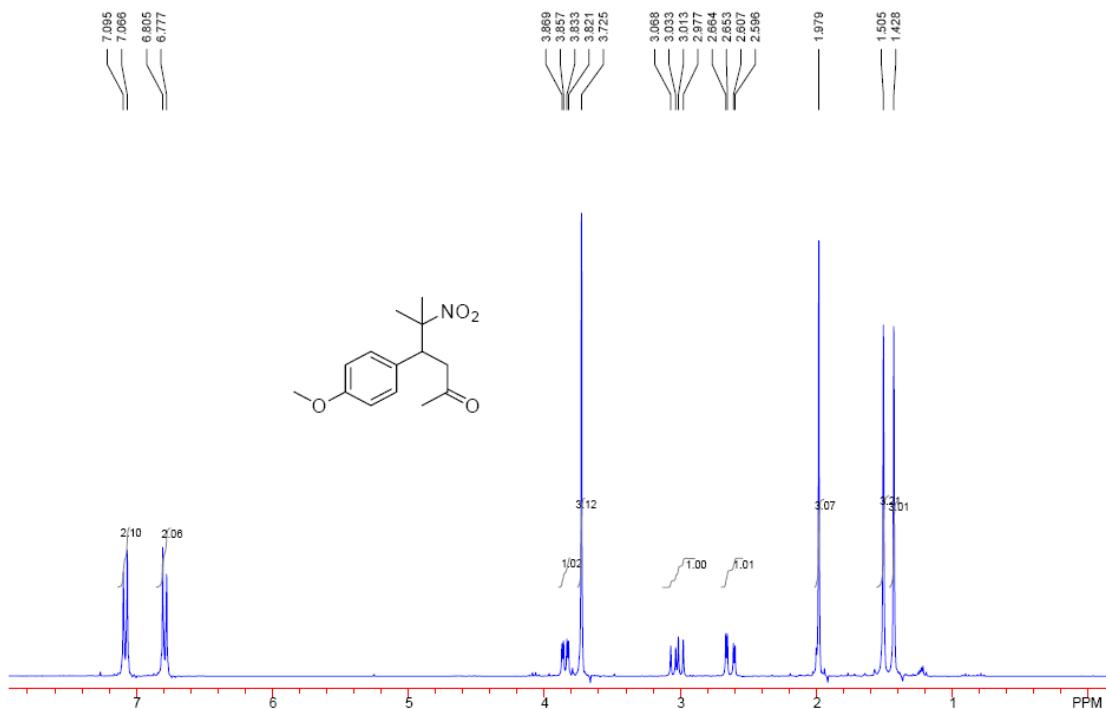
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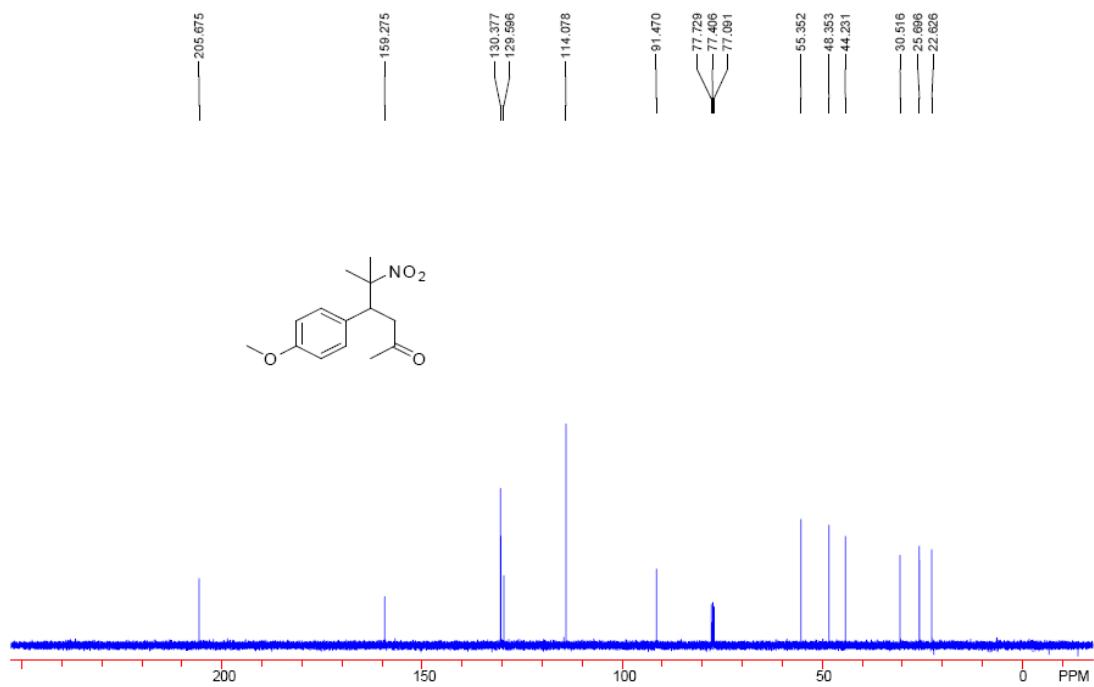
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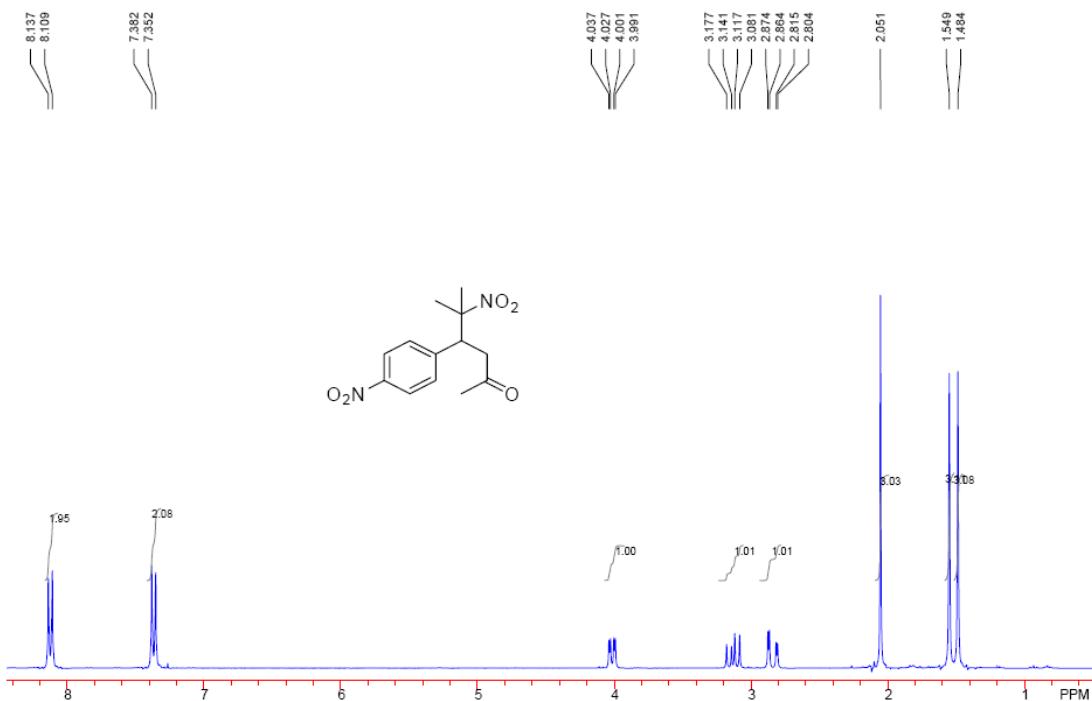
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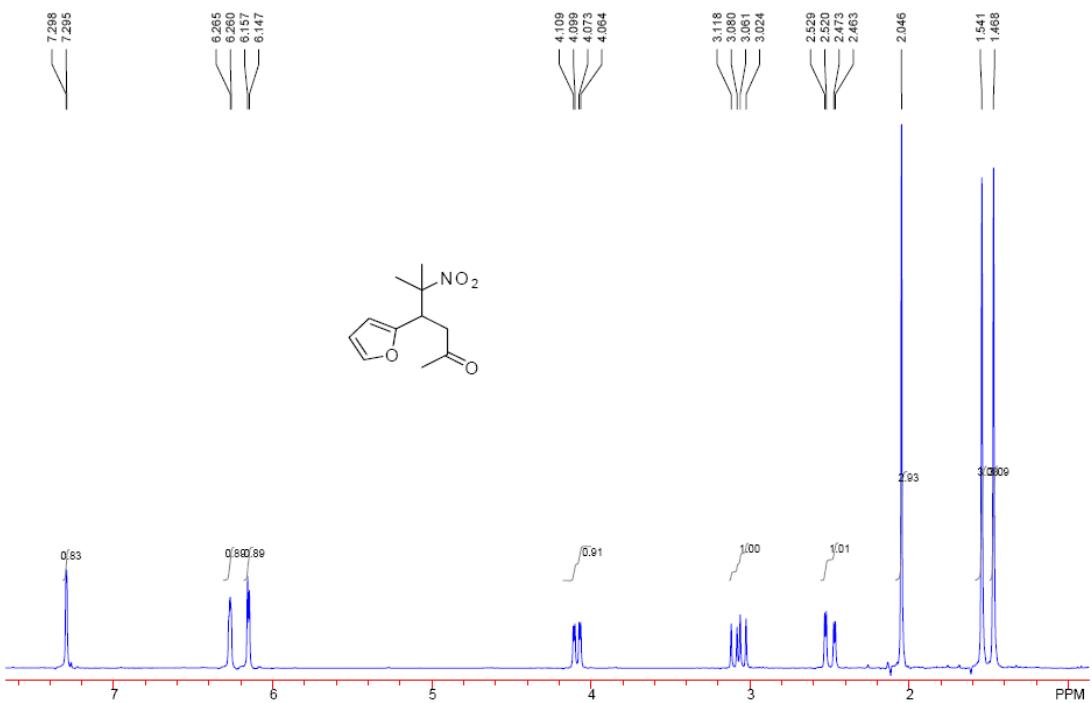
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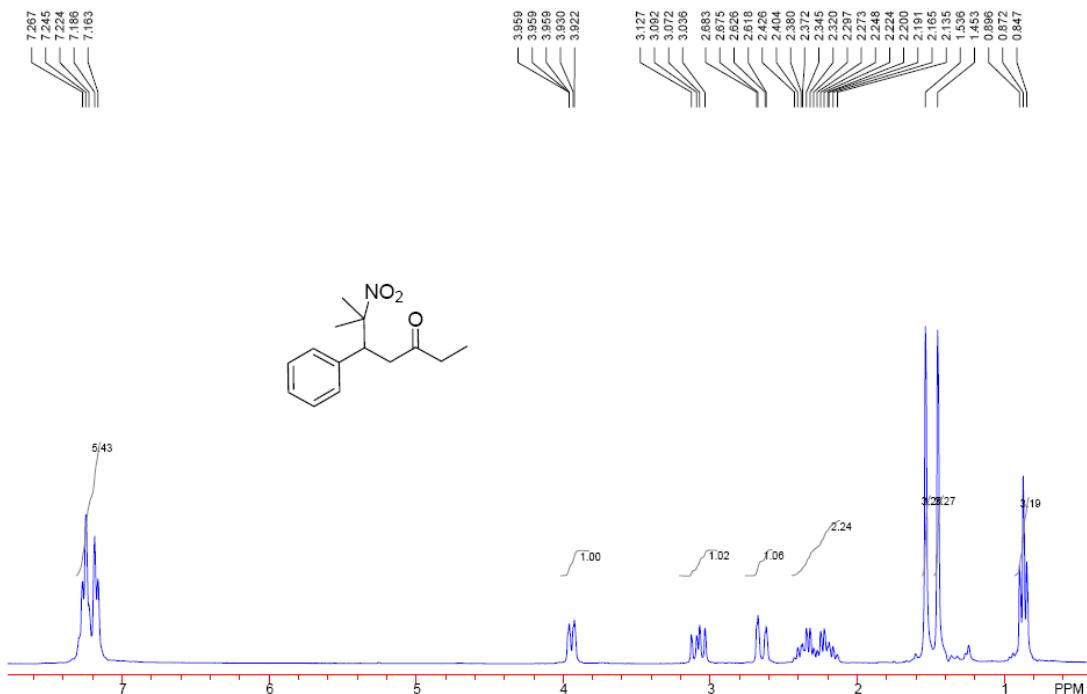
4ag (^1H NMR)



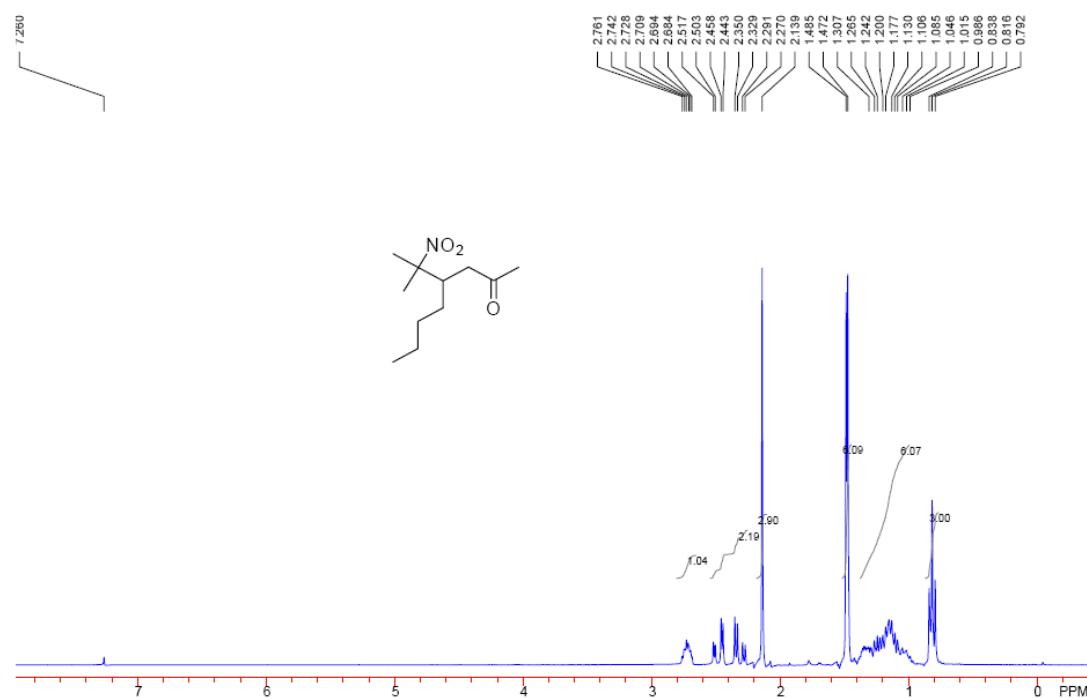
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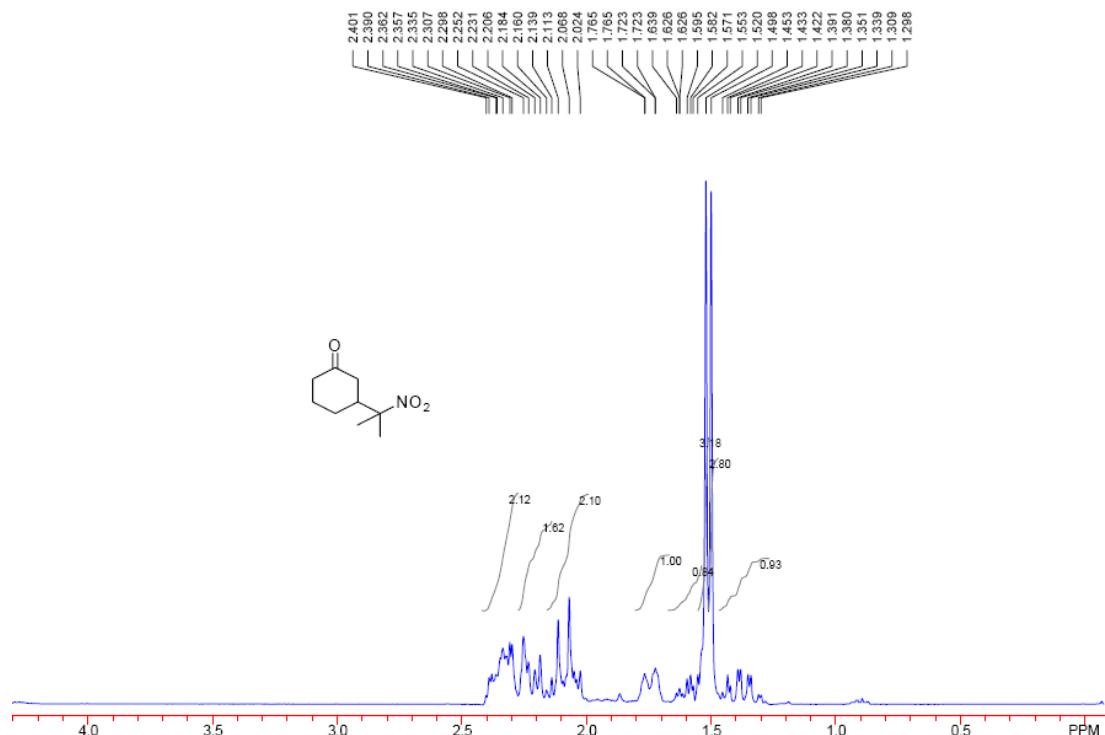
4ai (^1H NMR)



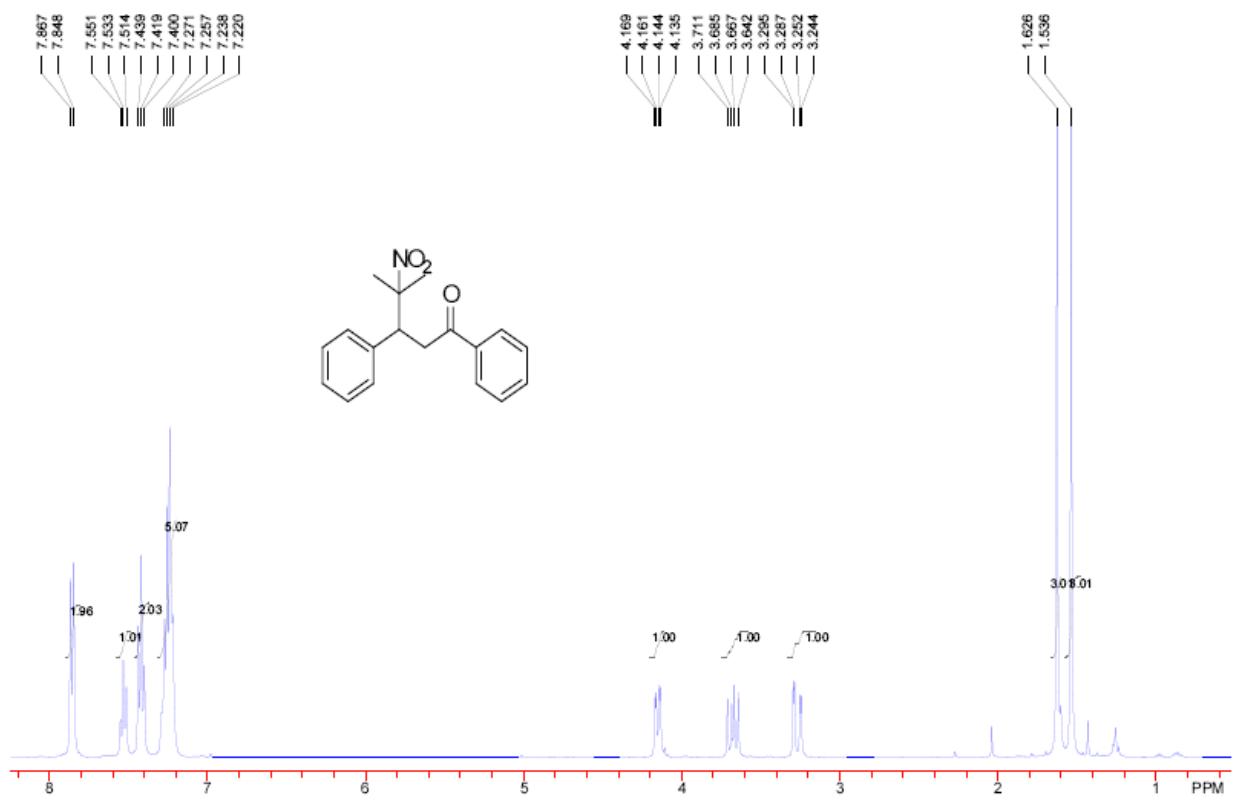
4aj (^1H NMR)



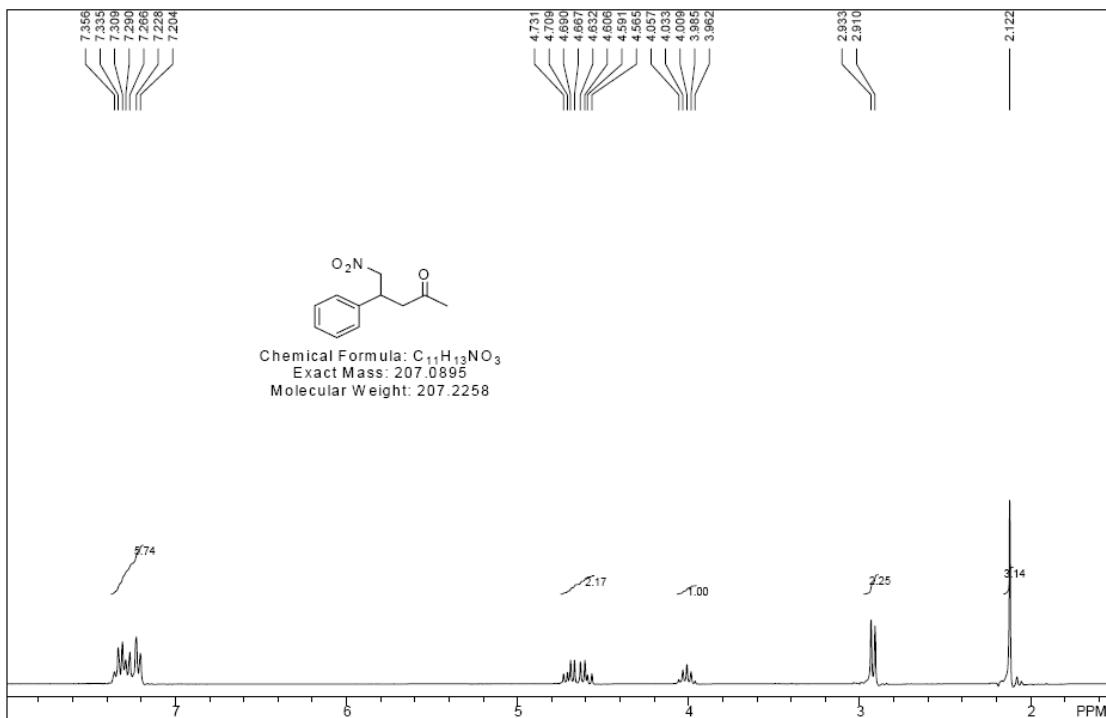
4ak (^1H NMR)



4al (^1H NMR)



4ba (^1H NMR)

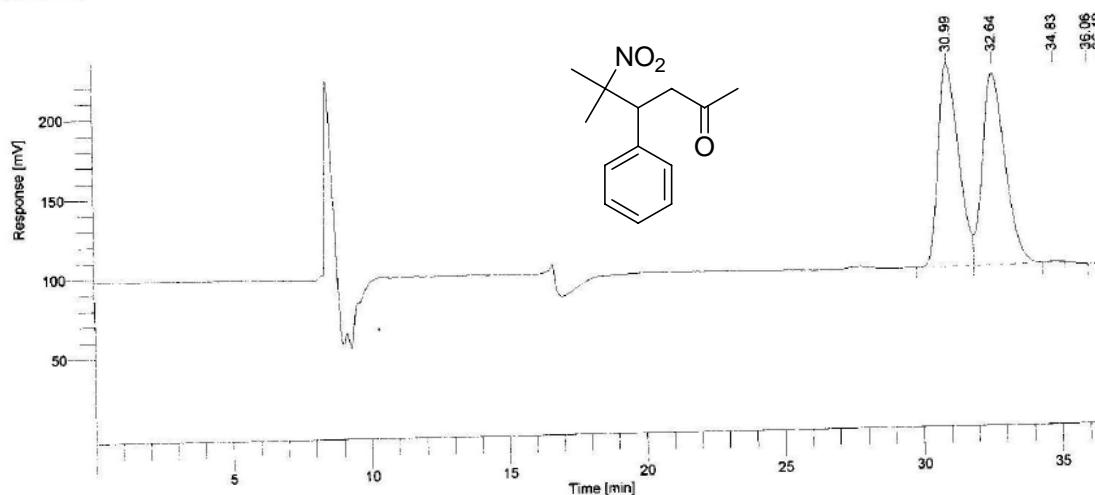


HPLC spectra for compounds 4

4aa

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Instrument Name	:	NCI901	Channel	:	A
Rack/Vial	:	0/0	Operator	:	manager
Sample Amount	:	1.000000	Dilution Factor	:	1.000000
Cycle	:	1			

Result File :
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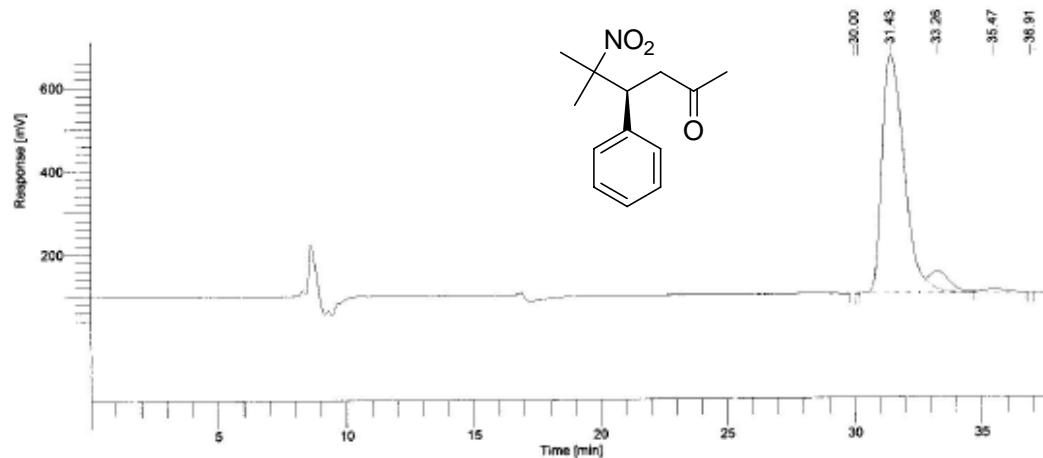


HPLC REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
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2		32.636	6825369.73	120799.93	50.849	VV
3		34.833	20332.42	715.36	0.151	VB
4		36.061	801.18	91.63	0.006	BB
5		36.493	673.59	103.14	0.005	BB

Software Version	:	6.3.1.0504	Date	:	2009-6-1 14:58:23
Sample Name	:	Y6-22-A	Data Acquisition Time	:	2009-6-1 14:19:26
Instrument Name	:	NCI901	Channel	:	A
Rack/Vial	:	0/0	Operator	:	manager
Sample Amount	:	1.000000	Dilution Factor	:	1.000000
Cycle	:	1			

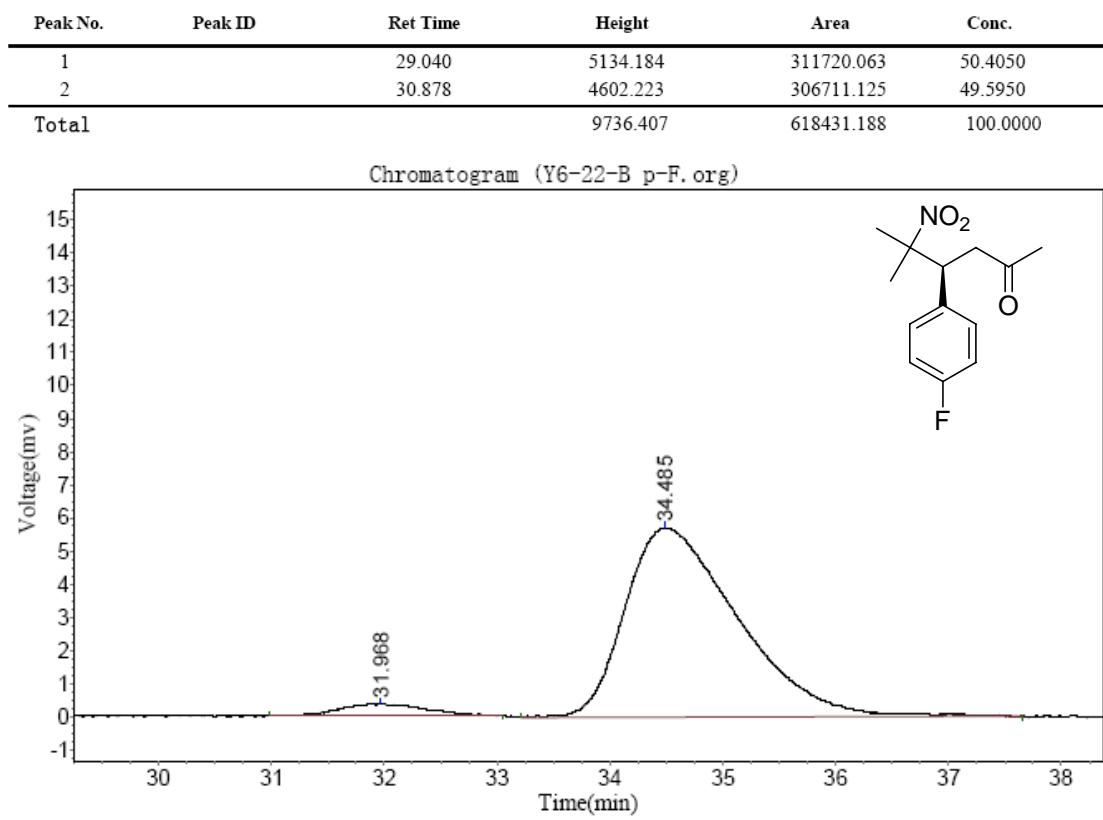
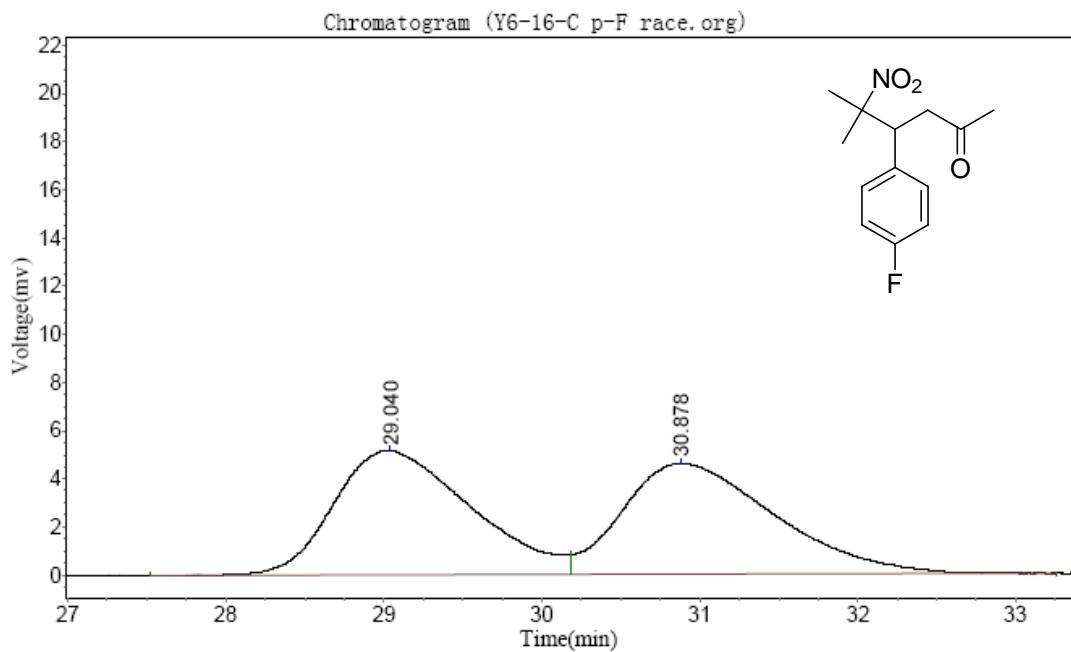
Result File :
Sequence File : D:\200090601-.seq



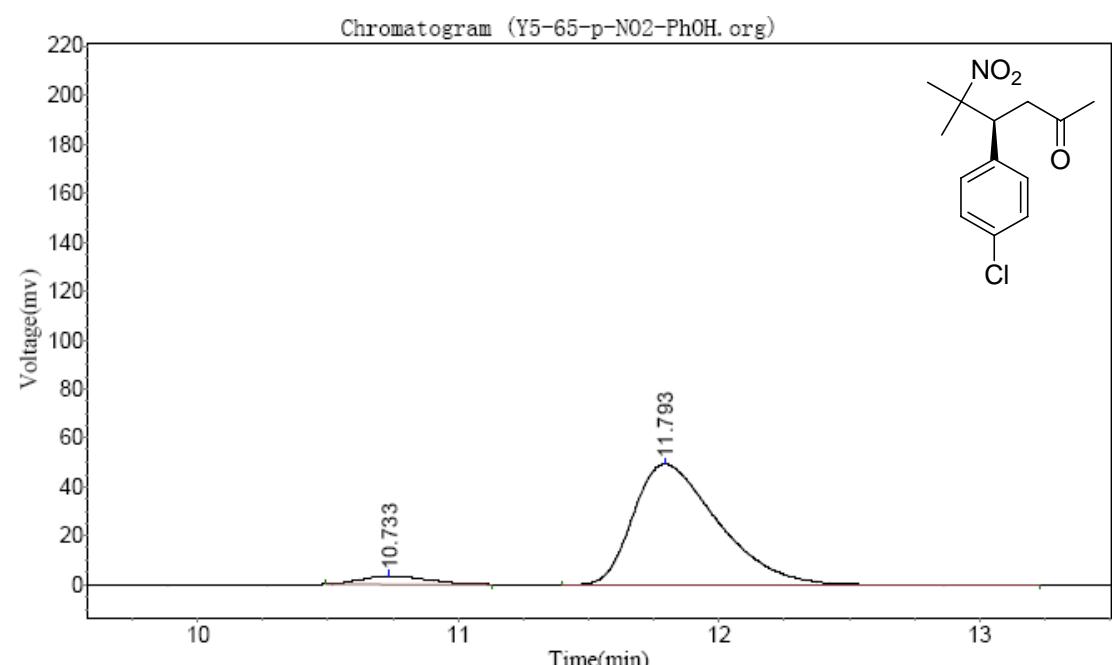
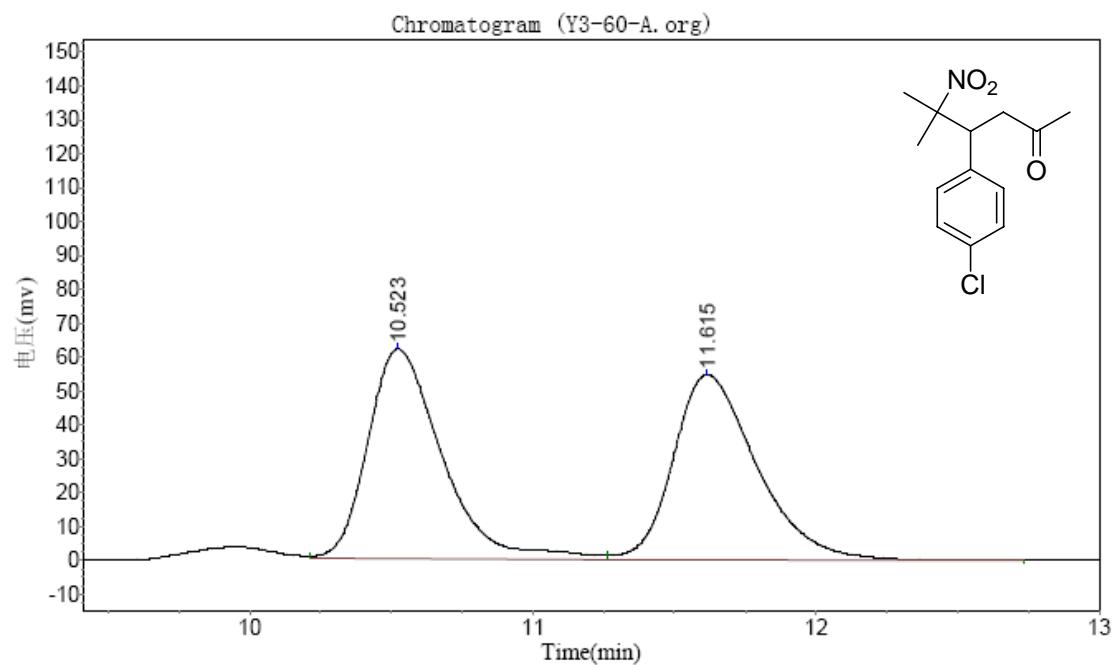
HPLC REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	BL
1		30.001	515.56	46.47	0.001	BV
2		30.145	129.89	32.73	3e-04	VV
3		31.430	3.50e+07	571868.10	92.751	VE
4		33.264	2247075.10	41892.25	5.946	EV
5		35.470	490786.92	8289.21	1.299	VB
6		36.908	562.31	64.67	0.001	BB
7		37.101	356.44	55.24	9e-04	BB
			3.78e+07	622248.67	1e+02	

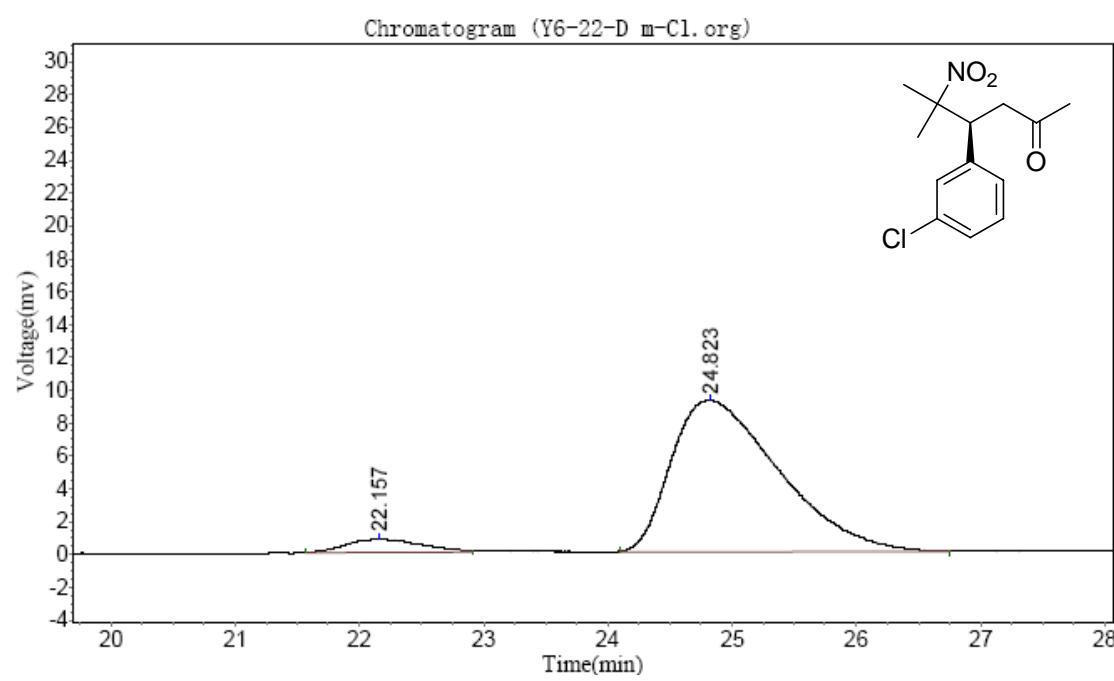
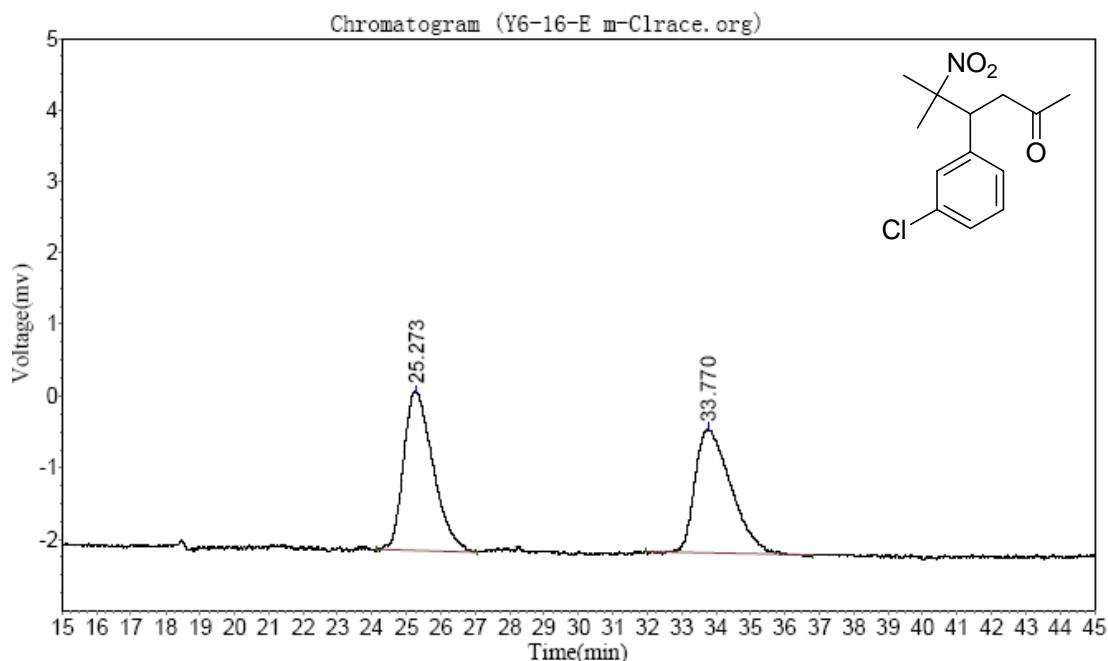
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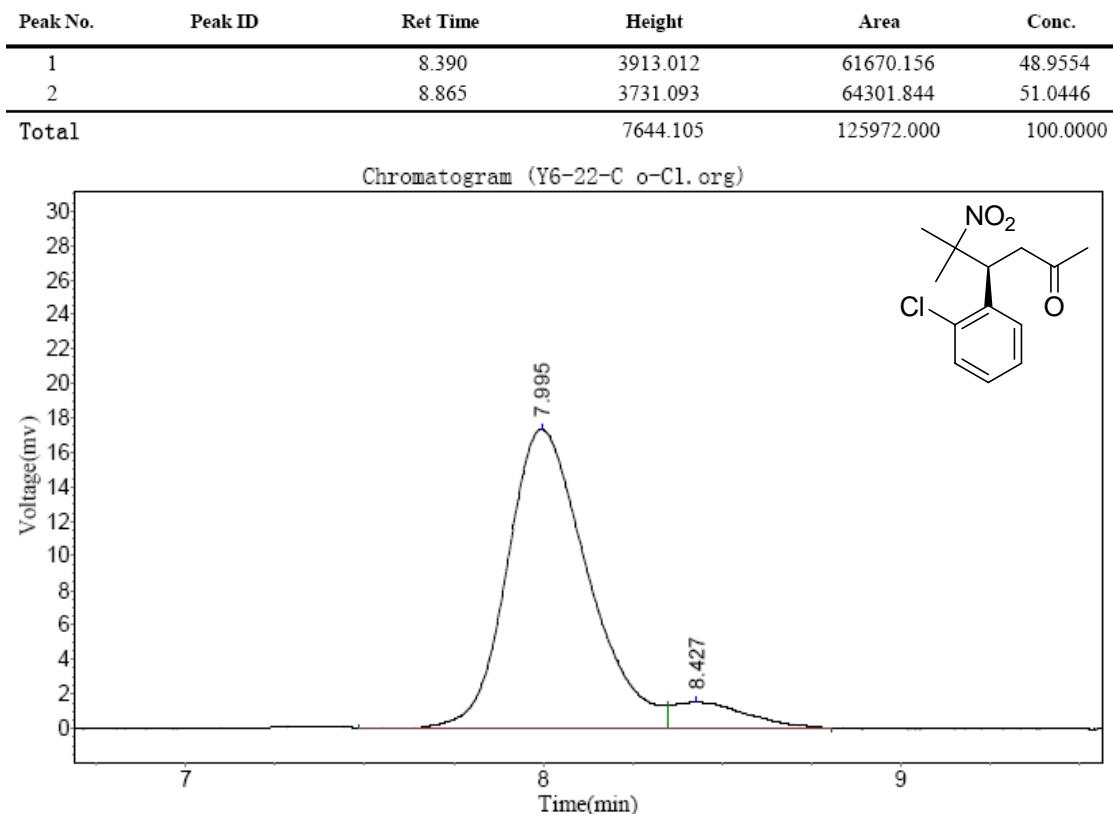
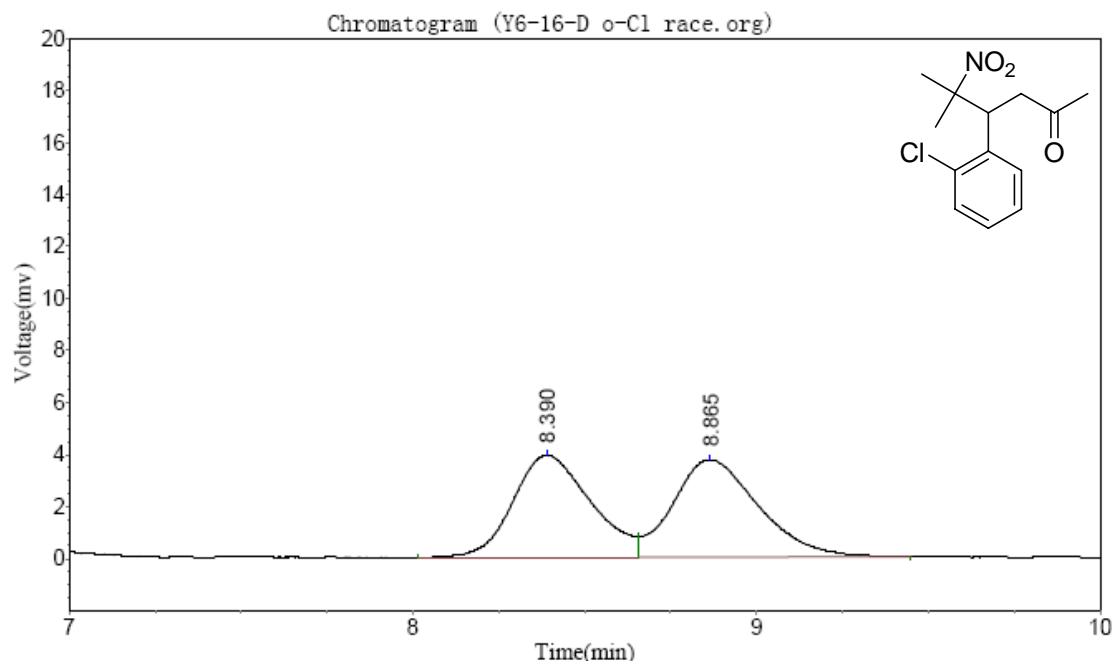
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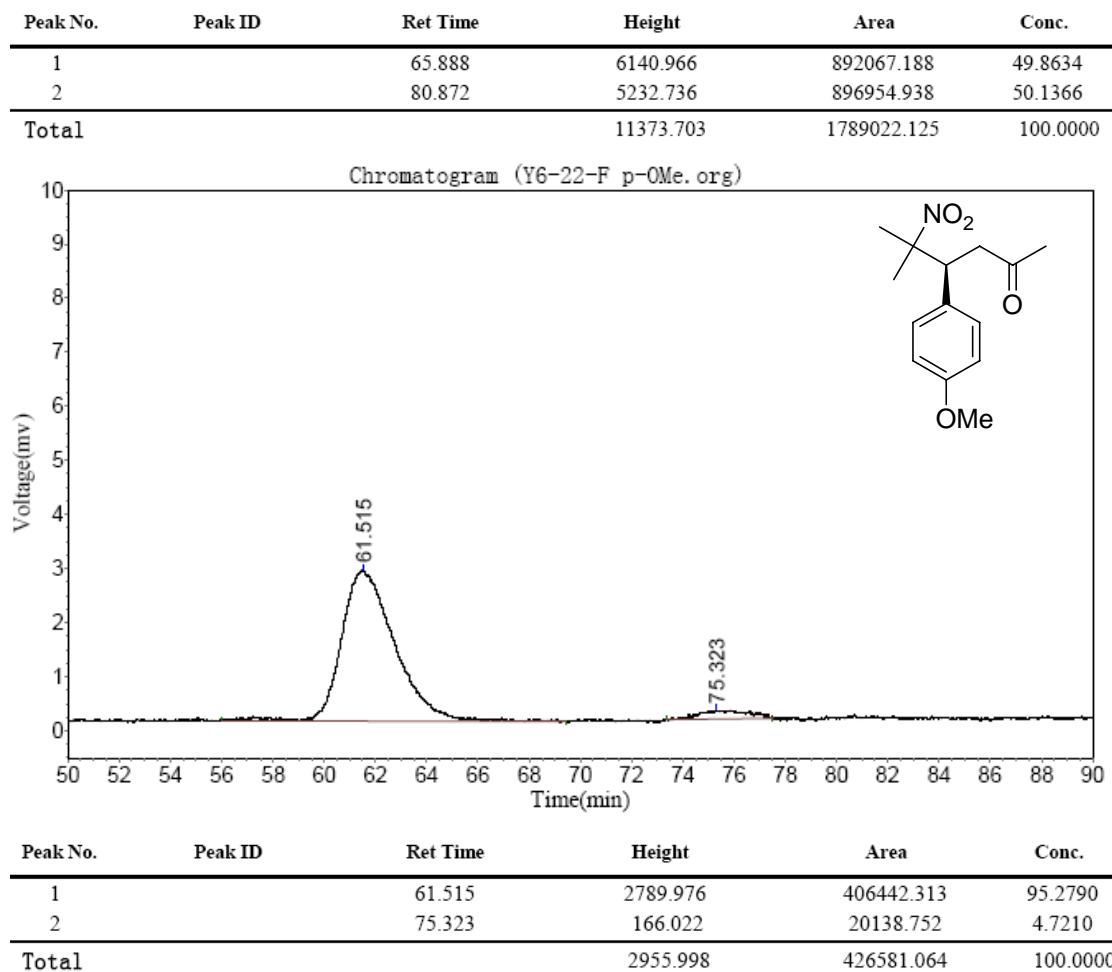
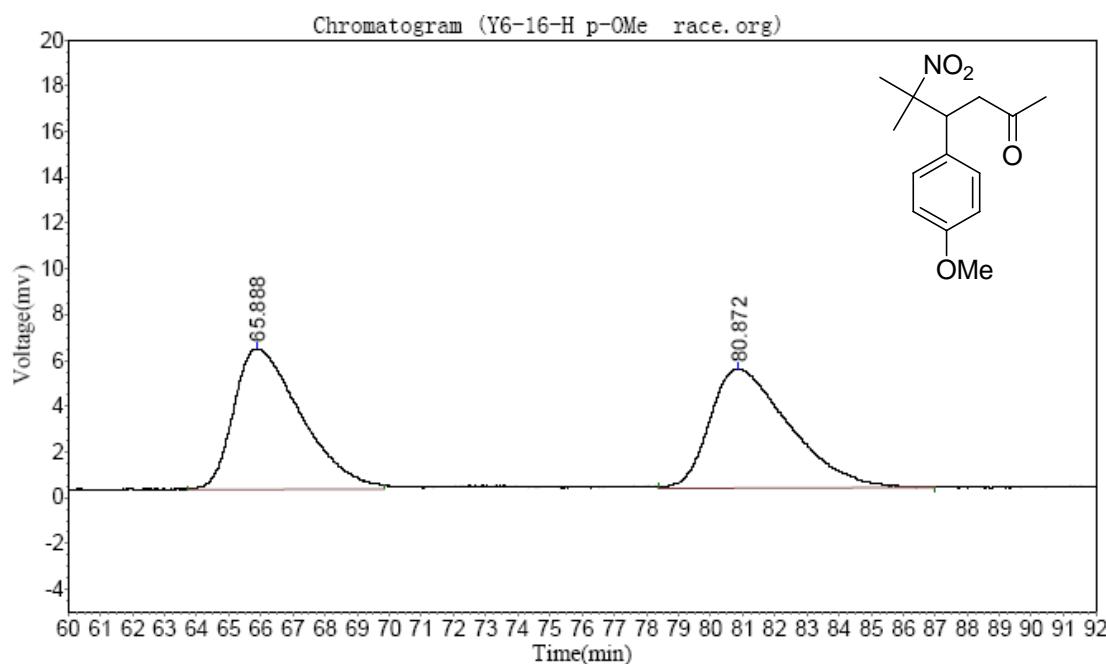
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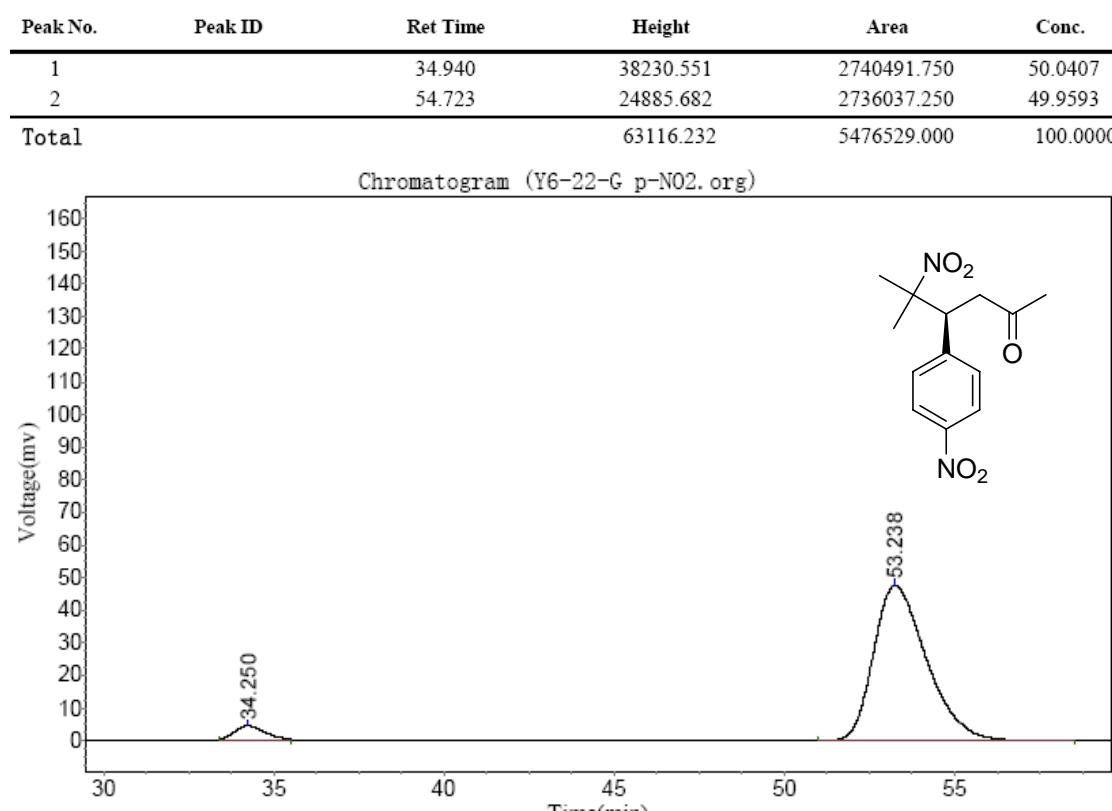
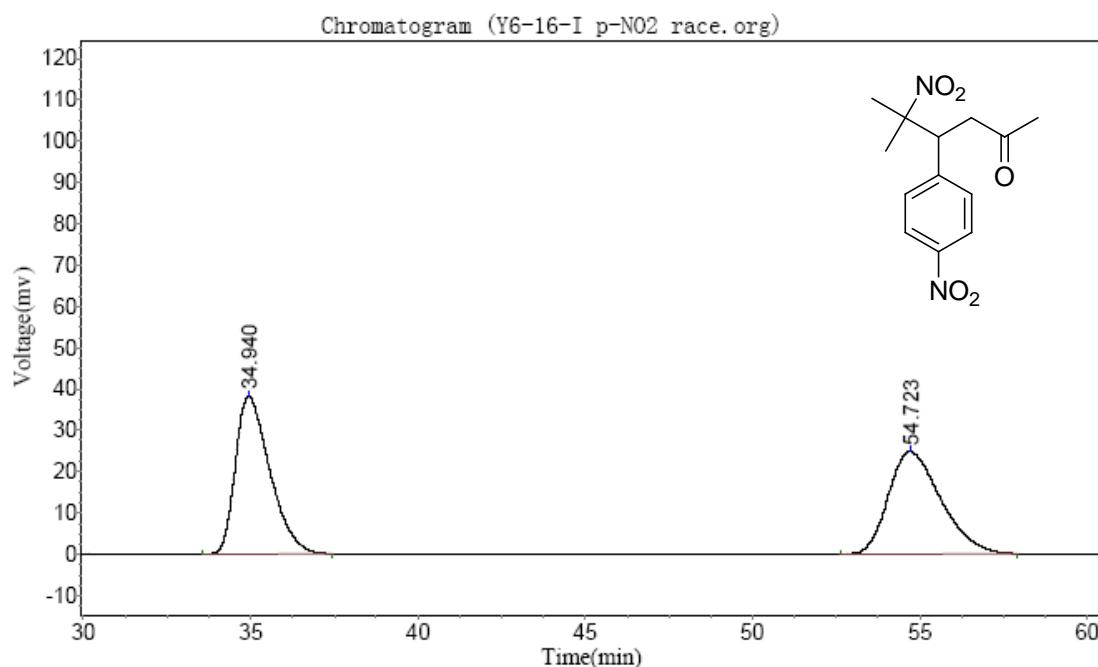
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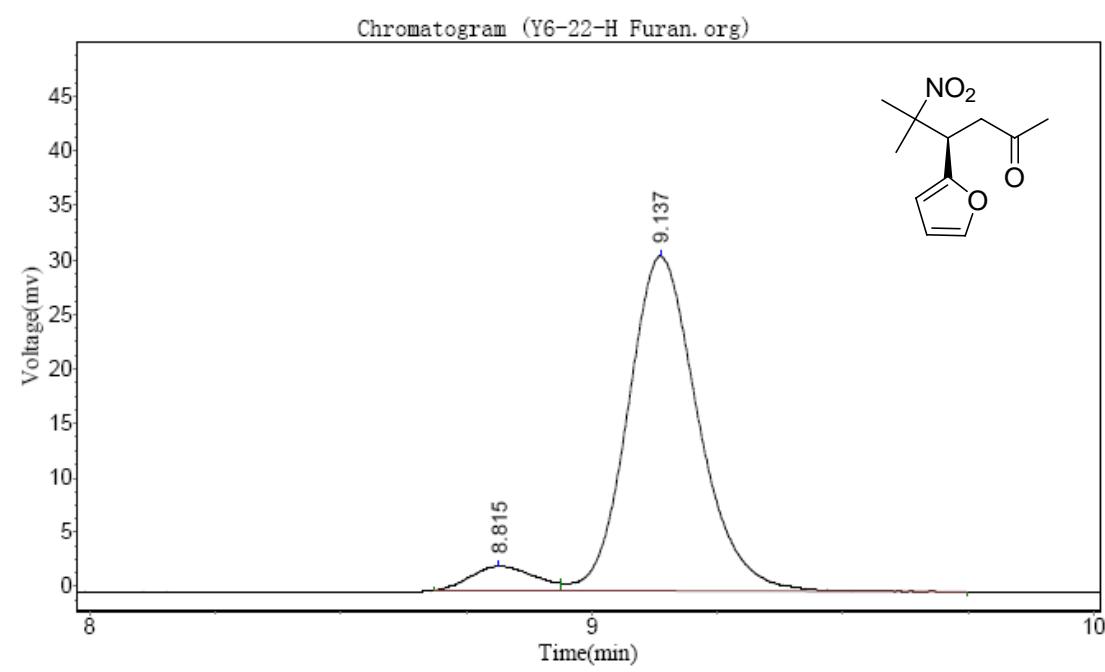
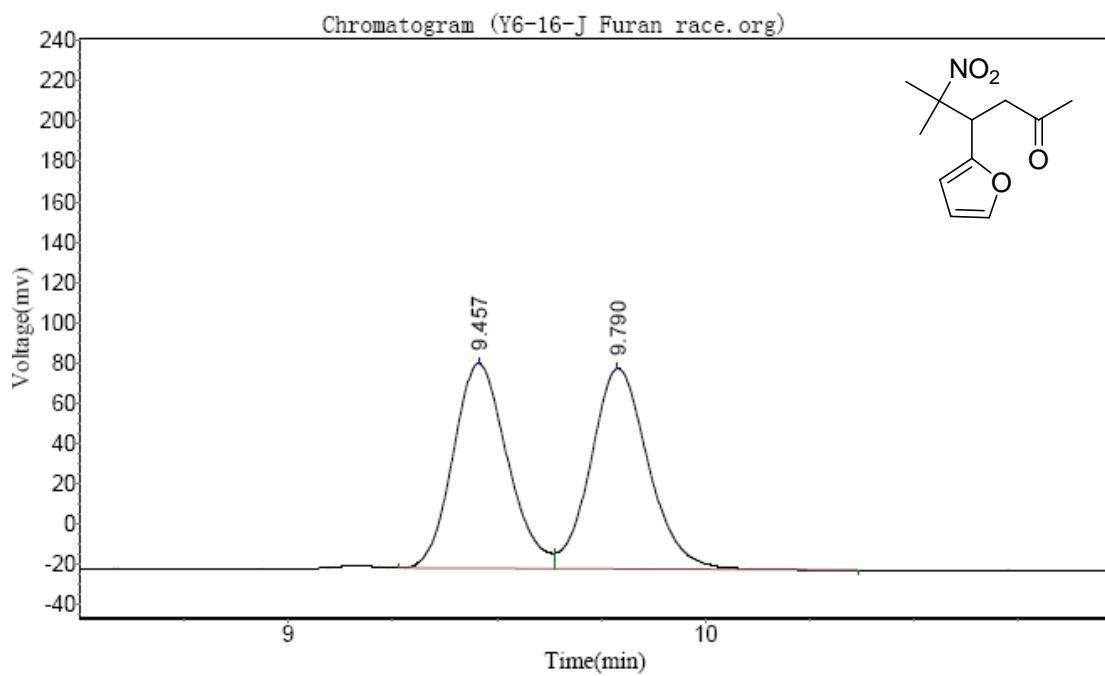
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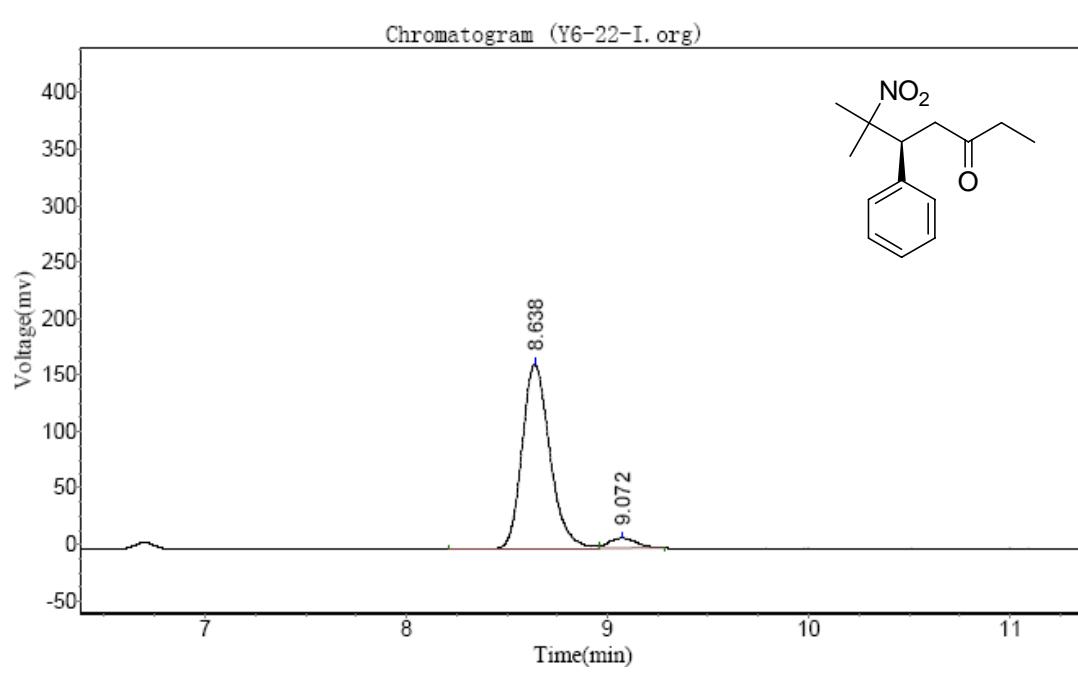
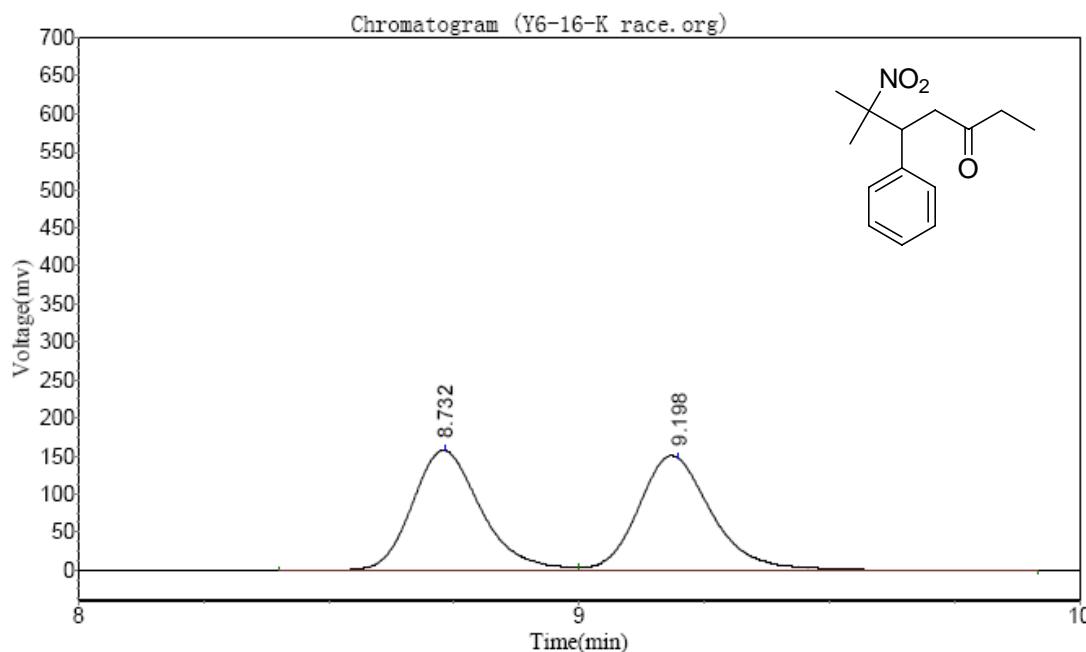
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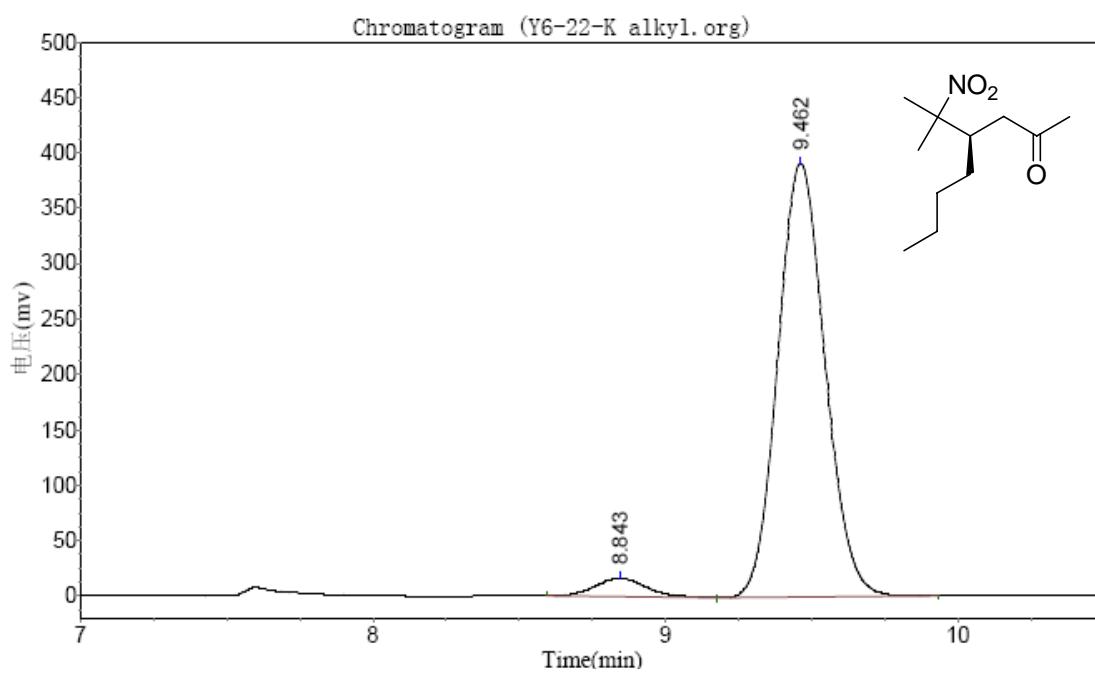
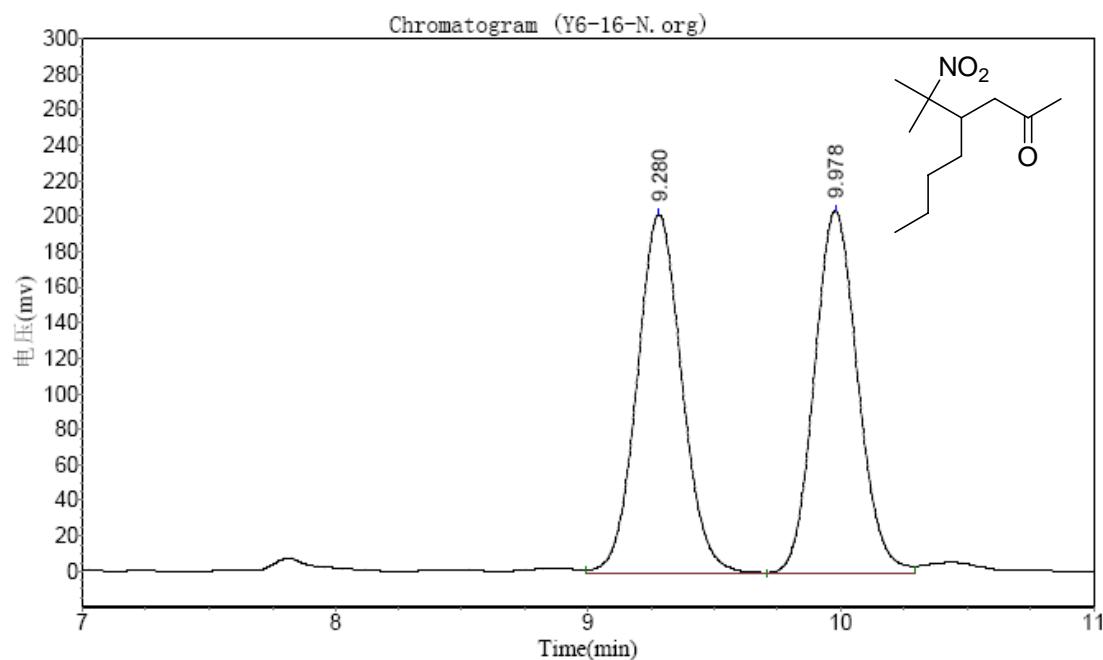
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4ai

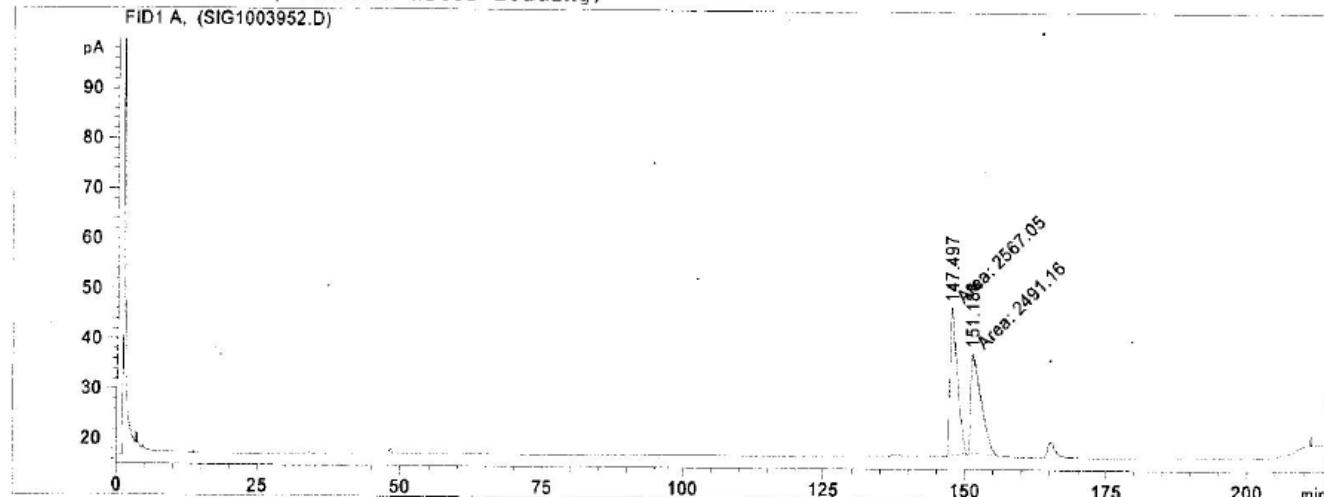


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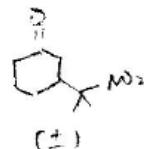
4ak

=====
Acq. Operator : LXI
Acq. Instrument : Instrument 2 Location : Vial 1
Injection Date : 3/31/2009 10:07:14 AM Inj : 1
Inj Volume : External
Acq. Method : C:\CHEM32\2\DATA\TEST.M
Last changed : 3/31/2009 10:07:39 AM by LXI
(modified after loading)
Analysis Method : C:\CHEM32\2\DATA\TEST.M
Last changed : 3/31/2009 2:11:07 PM by LXI
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

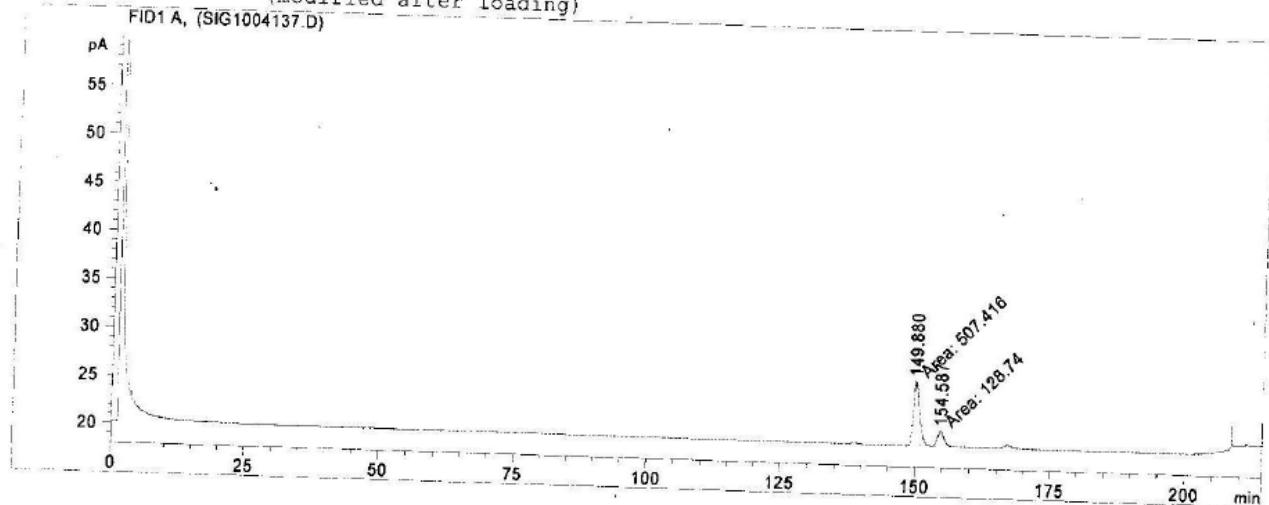


Signal 1: FID1 A,

Peak #	RetTime {min}	Type	Width [min]	Area [pA*s]	Height [pA]	Area %
1	147.497	MM	1.4455	2567.05200	29.59840	50.75023
2	151.187	MM	2.0829	2491.15527	19.93313	49.24977
Totals :					5058.20728	49.53153

=====
*** End of Report ***

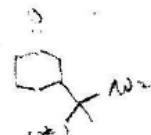
=====
Acq. Operator : 1x1
Acq. Instrument : Instrument 2
Injection Date : 4/30/2009 2:01:07 PM Location : Vial 1
Inj : 1
Inj Volume : External
Acq. Method : C:\CHEM32\2\DATA\TEST.M
Last changed : 4/30/2009 1:37:55 PM by 1x1
(modified after loading)
Analysis Method : C:\CHEM32\2\DATA\TEST.M
Last changed : 4/30/2009 5:55:37 PM by 1x1
(modified after loading)



=====
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

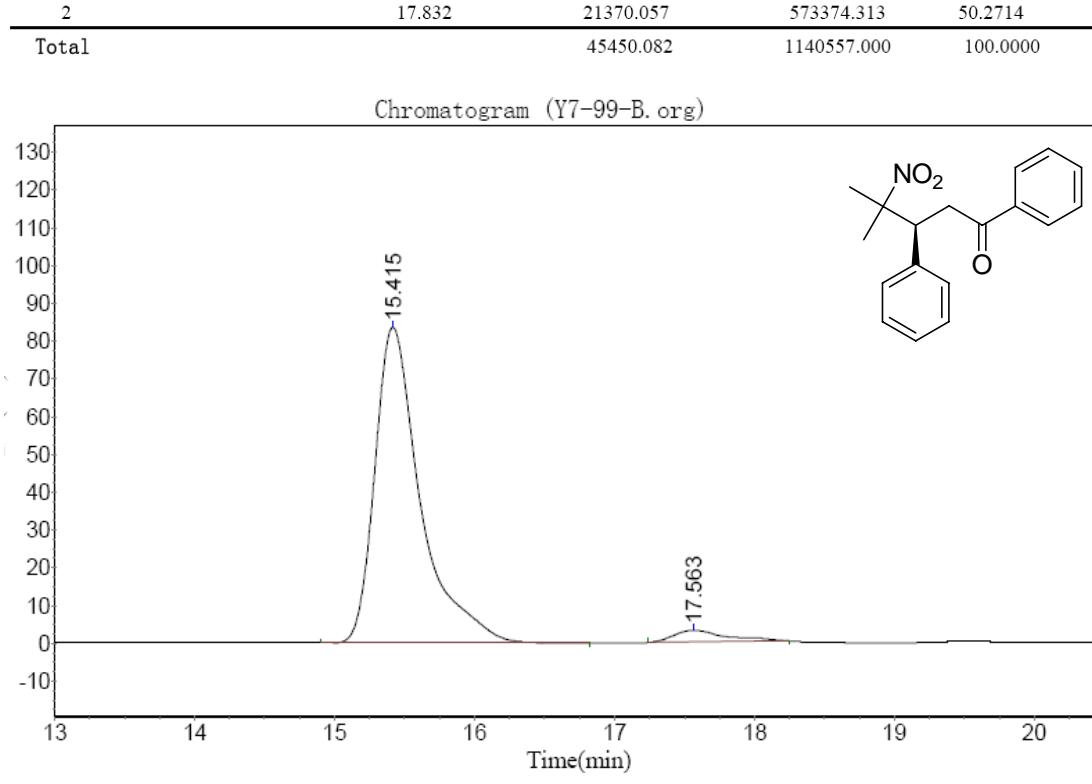
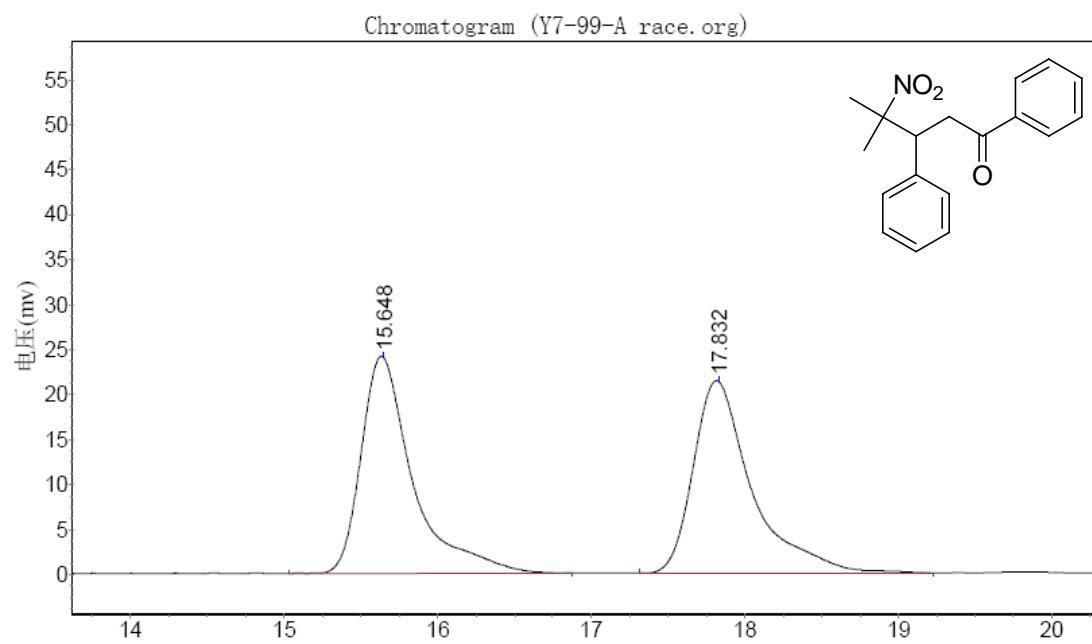
Signal 1: FID1 A,



Peak #	RetTime [min]	Type	Width [min]	Area [pA*s]	Height (pA)	Area %
1	149.880	MM	1.2830	507.41629	6.59174	79.76288
2	154.587	MM	1.3706	128.73961	1.56551	20.23712
Totals :					636.15590	8.15725

=====
*** End of Report ***

4al



4ba

