

**Supporting Information for  
Highly Enantioselective Direct Aldol Reaction Catalyzed By Cinchona  
Derived Primary Amines**

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## Experimental Section

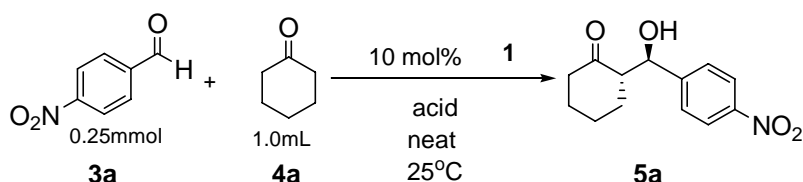
**General Information:** Unless otherwise noted, material were purchased from commercial suppliers and used without further purification. cyclohexanone and cyclopentanone were freshly distilled. Hexane and ethyl acetate for flash column chromatography were distilled before use. Flash column chromatography was performed using 200-300 mesh silica gel. <sup>1</sup>H NMR spectra were recorded on a Bruker-300 (300 MHz) spectrophotometer. Chemical shifts are reported in ppm from the solvent resonance as the internal standard (CDCl<sub>3</sub>: 7.26 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. Chiral HPLC was performed on Waters 2996 series with chiral columns (Chirapak AD-H, AS-H, OD-H columns, Daicel Chemical Ind., Ltd.). Catalysts **1** and **2** were prepared according to literature procedure<sup>1</sup>

### General procedure for the Aldol reaction

To a mixture of catalyst **1** (0.025 mmol) and TfOH (0.0375 mmol) was added Cyclohexanone (1 mL), cyclopentanone (1 mL), tetrahydro-4H-puran-4-one (1.25 mmol) or tetrahydrothiopuran-4-one (0.50 mmol). The reaction mixture was stirred for 5 min in a closed system and then aldehyde (0.25 mmol) was added. The reaction mixture was stirred for 9-166 h (monitored by TLC). the reaction was quenched with saturated ammonium chloride solution (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated in vacuo. The crude product was purified by flash column chromatography to give pure aldol adduct. Diastereoselectivity was determined by <sup>1</sup>H NMR analysis of the crude aldol product.

### Optimization of Conditions:

#### Acid and Acid loading screening:

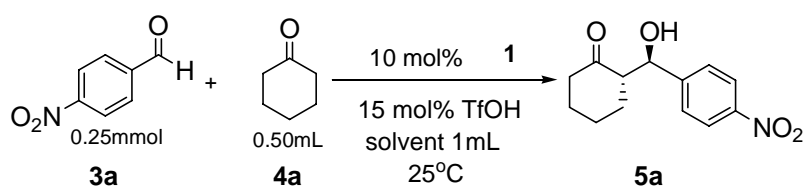


entry	acid	Time(h)	Acid(%)	Yield(%) <sup>a</sup>	Ee(%)	dr
1	TFA	19	15	54.8	95	6.8:1
2	No acid	39	0	74	87	1.6:1
3	TfOH	18	5	99	98	6.3:1
4	TfOH	12	10	97	98	6.9:1
5	TfOH	9	15	99	99	9.2:1
6	TfOH	15	20	77	98	9.0:1
7 <sup>b</sup>	TfOH	18	15	76	-94	10:1

<sup>a</sup> isolated yields. <sup>b</sup> 10% **2** used as catalyst

<sup>1</sup> Brunner, H.; Biigler, J.; Nuber, B. *Tetrahedron: Asymmetry*, **1995**, *6*, 1699-1702.

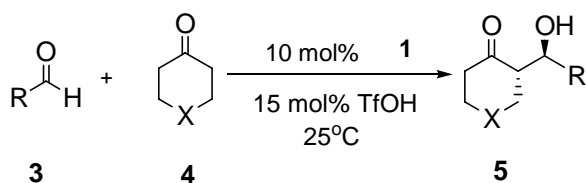
### Solvent screening:



entry	solvent	Time(h)	Yield(%) <sup>a</sup>	Ee(%)	dr
1	neat	9	99	99	9.2:1
2	THF	17	98	99	9.8:1
3	DMSO	45	77	97	3.5:1
4	DMF	44	74	97	5.0:1
5	Toluene	23	94	98	8.6:1
6	H <sub>2</sub> O	4	97	97	4.8:1
7	CHCl <sub>3</sub>	22	84	98	7.0:1
8	EtOH	20	79	98	6.6:1
9	CH <sub>2</sub> Cl <sub>2</sub>	12	82	98	7.5:1
10	Et <sub>2</sub> O	19	98	98	8.1:1
11 <sup>b</sup>	DMF-H <sub>2</sub> O	24	94	97	4.1:1
12 <sup>c</sup>	neat	96	11	91	2.4:1
13 <sup>d</sup>	neat	38	90	98	5.0:1
14 <sup>e</sup>	neat	18	86	92	2.0:1
15 <sup>f</sup>	neat	18	73	86	1.7:1

<sup>a</sup> isolated yields. <sup>b</sup> volume ratio 1:1. <sup>c</sup> the reaction was carried out at -16°C. <sup>d</sup> the reaction was carried out at 0°C. <sup>e</sup> the reaction was carried out at 40°C. <sup>f</sup> the reaction was carried out at 60°C.

### Full list of substrates



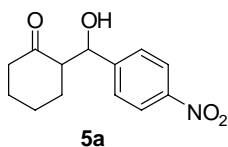
entry	R	X	Time(h)	Yield(%) <sup>a</sup>	Ee(%)	dr
1	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub>	9	99	99	9.2:1
2	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	-- <sup>c</sup>	24	70	86	5.0:1
3	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	O	87	92	91	5.4:1
4	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	S	117	38	94	3.0:1
5	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub>	34	74	97	3.2:1
6	2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub>	35	98	97	7.5:1
7	2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	-- <sup>c</sup>	20	99	84	2.4:1
8	2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	O	140	44	87	3.2:1
9	4-CF <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub>	71	99	98	2.3:1
10	4-FC <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub>	90	58	94	1.7:1
11	C <sub>6</sub> H <sub>5</sub>	CH <sub>2</sub>	100	31	86	1.0:1
12	2-furanyl	CH <sub>2</sub>	47	39	94	1:2.5
13	1-naphthyl	CH <sub>2</sub>	166	55	93	4.9:1

14 <sup>b</sup>	4-ClC <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub>	69	70	91	4.1:1
15 <sup>b</sup>	4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub>	100	19	89	3.7:1
16 <sup>d</sup>	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>		52	25	56	--

<sup>a</sup> isolated yields. <sup>b</sup> 0.5 mL H<sub>2</sub>O was added. <sup>c</sup> cyclopentanone used <sup>d</sup> neat acetone used instead of cyclic ketone in the presence of 10% of catalyst and 15% of triflic acid.<sup>e</sup>

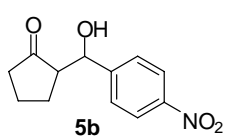
## Spectra data for all the Aldol products

### 2-(Hydroxy-(4-nitrophenyl)methyl)cyclohexan-1-one 5a: <sup>[5]</sup>



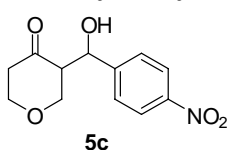
Reaction time: 9 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 5:1) to give pure aldol adduct. yield: 99%; ee: 99%; *Anti/Syn*= 9.2:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 8.19-8.23 (m, 2H), 7.48-7.53 (m, 2H), 4.89 (dd, *J* = 8.4, 3.1 Hz, 1H), 4.08 (d, *J* = 3.1 Hz, 1H), 2.46-2.59 (m, 2H), 2.35-2.40 (m, 1H), 2.08-2.14 (m, 1H), 1.81-1.85 (m, 1H), 1.52-1.69 (m, 3H), 1.34-1.43 (m, 1H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C) *t<sub>R</sub>* (major)= 55.6 min and *t<sub>R</sub>* (minor)= 75.9 min.

### 2-(Hydroxy-(4-nitrophenyl)methyl)cyclopentan-1-one 5b <sup>[3]</sup>



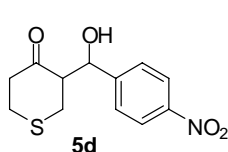
Reaction time: 24 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 4:1) to give pure aldol adduct. yield: 70%; 86%ee; *Anti/Syn*= 5.0:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 8.19-8.23 (m, 2H), 7.50-7.55 (m, 2H), 4.84 (d, *J* = 9.2 Hz, 1H), 4.76 (s, 1H), 2.27-2.45 (m, 3H), 1.54-2.02 (m, 4H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C) *t<sub>R</sub>* (major)= 97.2 min and *t<sub>R</sub>* (minor)= 101.5 min.

### 3-((1-hydroxy-1-(4-nitrophenyl))methyl)-tetrahydropyran-4-one 5c <sup>[3]</sup>



Reaction time: 87 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 3:1) to give pure aldol adduct. yield: 92%; 91%ee; *Anti/Syn*= 5.4:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 8.21-8.26 (m, 2H), 7.50-7.53 (m, 2H), 4.99 (d, *J* = 8.0 Hz, 1H), 4.19-4.25 (m, 1H), 3.70-3.85 (m, 3H), 3.42-3.49 (m, 1H), 2.88-2.94 (m, 1H), 2.64-2.70 (m, 1H), 2.50-2.57 (m, 1H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C) *t<sub>R</sub>* (major)= 22.7 min and *t<sub>R</sub>* (minor)= 26.8 min

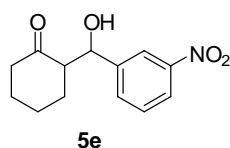
### 3-((1-hydroxy-1-(4-nitrophenyl))methyl)-tetrahydrothiopyran-4-one 5d <sup>[3]</sup>



Reaction time: 117 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 4:1) to give pure aldol adduct. yield: 38%; 94%ee; *Anti/Syn*= 3.0:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 8.24 (dd, *J* = 8.7, 1.8 Hz, 2H), 7.51-7.56 (dd, *J* = 8.7, 1.8 Hz, 2H), 5.05 (d, *J* = 8.0 Hz, 1H), 3.61 (br, 1H), 2.94-3.09 (m, 3H), 2.75-2.89 (m, 2H), 2.64-2.72 (m, 1H), 2.48-2.55 (m, 1H). HPLC analysis Chiralcel

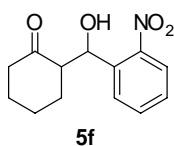
AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C)  $t_R$  (major)= 44.3 min and  $t_R$  (minor)= 81.5 min.

### 2-(Hydroxy-(3-nitrophenyl)methyl)cyclohexan-1-one **5e** <sup>[5]</sup>



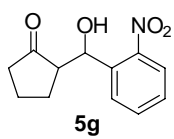
Reaction time: 34 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 5:1) to give pure aldol adduct. yield: 74%; 97%ee; *Anti/Syn*= 3.2:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 8.21 (m, 1H), 8.14-8.18 (m, 1H), 7.67(d, *J* = 7.7 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 4.89 (dd, *J* = 8.5, 3.0 Hz, 1H), 4.12 (d, *J* = 3.0 Hz, 1H), 2.36-2.62 (m, 3H), 2.10-2.11 (m, 1H), 1.80-1.82 (m, 1H), 1.55-1.63 (m, 3H), 1.23-1.25 (m, 1H), HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C)  $t_R$  (minor)= 39.1 min and  $t_R$  (major)= 51.5 min.

### 2-(Hydroxy-(2-nitrophenyl)methyl)cyclohexan-1-one **5f** <sup>[2]</sup>



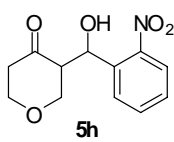
Reaction time: 35 h. The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 7:1) to give pure aldol adduct. yield: 98%; 97%ee; *Anti/Syn*= 7.5:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 7.84 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 5.44 (d, *J* = 7.1 Hz, 1H), 3.80 (br, 1H), 2.71-2.79 (m, 1H), 2.28-2.47 (m, 2H), 2.06-2.12 (m, 1H), 1.82-1.86 (m, 1H), 1.52-1.79 (m, 4H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 90/10, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C)  $t_R$  (minor)= 45.6 min and  $t_R$  (major)= 50.4 min.

### 2-(Hydroxy-(2-nitrophenyl)methyl)cyclopentan-1-one **5g**



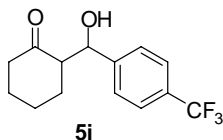
Reaction time: 20 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 7:1) to give pure aldol adduct. yield: 99%; 84%ee; *Anti/Syn*= 2.4:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 7.98 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.88 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.62-7.68 (m, 1H), 7.40-7.46 (m, 1H), 5.91 (d, *J* = 3.0 Hz, 1H), 2.70-2.74 (m, 1H), 2.34-2.37 (m, 2H), 2.16-2.19 (m, 1H), 2.01-2.07 (m, 2H), 1.71-1.75 (m, 2H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C)  $t_R$  (minor)= 35.5 min and  $t_R$  (major)= 38.5 min.

### 3-((1-hydroxy-1-(2-nitrophenyl))methyl)-tetrahydropyran-4-one **5h** <sup>[3]</sup>



Reaction time: 140 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 3:1) to give pure aldol adduct. yield: 46%; 87%ee; *Anti/Syn*= 3.2:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 7.92 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.78-7.83(m, 1H), 7.65-7.70 (m, 1H), 7.44-7.49 (m, 1H), 5.48 (d, *J* = 6.6 Hz, 1H), 4.22-4.28 (m, 1H), 3.89-3.95 (m, 2H), 3.71-3.85 (m, 2H), 3.04-3.08 (m, 1H), 2.65-2.68 (m, 1H), 2.47-2.54 (m, 1H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C)  $t_R$  (minor)= 35.1 min and  $t_R$  (major)= 37.1 min.

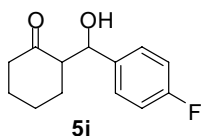
### 2-(Hydroxy-(4-(trifluoromethyl)phenyl)methyl)cyclohexan-1-one **5i** <sup>[2]</sup>



Reaction time: 71 h; The crude product was purified by flash column

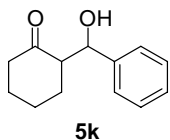
chromatography (hexane/ ethyl acetate= 15:1) to give pure aldol adduct. yield: 99%; 98%*ee*; *Anti/Syn*= 2.3:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ(ppm) 7.61 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 4.84 (d, *J* = 8.6 Hz, 1H), 4.05 (s, 1H), 2.57-2.64 (m, 1H), 2.46-2.51 (m, 1H), 2.35-2.39 (m, 1H), 2.07-2.14 (m, 1H), 1.79-1.83 (m, 1H), 1.48-1.73 (m, 3H), 1.25-1.39 (m, 1H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 90/10, 0.5 mL/min, λ = 220 nm, 20°C) *t<sub>R</sub>* (major)= 22.6 min and *t<sub>R</sub>* (minor)= 28.3 min.

### 2-(Hydroxy-(4-fluorophenyl)methyl)cyclohexan-1-one **5j** <sup>[2]</sup>



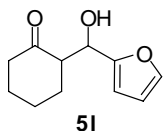
Reaction time: 90 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 15:1) to give pure aldol adduct. yield: 58%; 94%*ee*; *Anti/Syn*= 1.7:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ(ppm) 7.26-7.32 (m, 2H), 7.00-7.07 (m, 2H), 4.77 (d, *J* = 8.8 Hz, 1H), 3.99 (br, 1H), 2.45-2.56 (m, 2H), 2.34-2.48 (m, 1H), 2.06-2.11 (m, 1H), 1.77-1.82 (m, 1H), 1.51-1.68 (m, 3H), 1.25-1.30 (m, 1H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min, λ = 220 nm, 20°C) *t<sub>R</sub>* (major)= 27.9 min and *t<sub>R</sub>* (minor)= 30.6 min.

### 2-(Hydroxy(phenyl)methyl)cyclohexan-1-one **5k** <sup>[2]</sup>



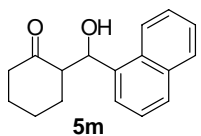
Reaction time: 100 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 10:1) to give pure aldol adduct. yield: 31%; 86%*ee*; *Anti/Syn*= 1.0:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ(ppm) 7.22-7.37 (m, 5H), 4.79 (d, *J* = 8.8 Hz, 1H), 3.97 (br, 1H), 2.57-2.64 (m, 1H), 2.05-2.12 (m, 1H), 1.51-1.70 (m, 4H), 1.25-1.32 (m, 1H). HPLC analysis Chiralcel OD-H (Hexane/ i-PrOH = 90/10, 0.5 mL/min, λ = 220 nm, 20°C) *t<sub>R</sub>* (minor)= 16.8 min and *t<sub>R</sub>* (major)= 23.9 min.

### 2-(Hydroxy-(furan-2-yl)propyl)cyclohexan-1-one **5l** <sup>[2]</sup>



Reaction time: 47 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 5:1) to give pure aldol adduct. yield: 39%; 94%*ee*; *Anti/Syn*= 1:2.5, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ(ppm) 7.34 (s, 1H), 6.34 (s, 1H), 6.23 (s, 1H), 5.28 (s, 1H), 3.03 (s, 1H), 2.80-2.84 (m, 1H), 2.31-2.48 (m, 2H), 2.08-2.09 (m, 1H), 1.67-1.98 (m, 5H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 0.5 mL/min, λ = 220 nm, 20°C) *t<sub>R</sub>* (major)= 33.1 min and *t<sub>R</sub>* (minor)= 36.3 min.

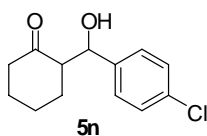
### 2-(Hydroxy(naphthalen-1-yl)methyl)cyclohexan-1-one **5m** <sup>[2]</sup>



Reaction time: 166 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 15:1) to give pure aldol adduct. yield: 55%; 93%*ee*; *Anti/Syn*= 4.9:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>) δ(ppm) 8.24-8.27 (m, 1H), 7.84-7.89 (m, 1H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.57 (d, *J* = 6.3 Hz, 1H), 7.45-7.53 (m, 3H), 5.58 (dd, *J* = 8.7, 2.9 Hz, 1H), 4.15 (d, *J* = 2.9 Hz, 1H), 2.95-3.04 (m, 1H), 2.49-2.54 (m, 1H), 2.35-2.45 (m, 1H), 2.05-2.12 (m, 1H), 1.61-1.74 (m, 2H), 1.33-1.51 (m, 3H). HPLC analysis Chiralcel AD-H (Hexane/ i-PrOH = 95/5, 1.0 mL/min, λ = 254 nm, 20°C) *t<sub>R</sub>*(major)= 25.6 min

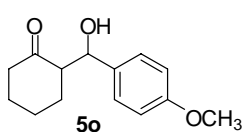
and  $t_R$  (minor) = 31.2 min.

### 2-(Hydroxy-(4-chlorophenyl)methyl)cyclohexan-1-one **5n** <sup>[2]</sup>



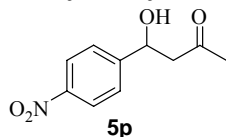
Reaction time: 69 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 10:1) to give pure aldol adduct. yield: 70%; 91%ee; *Anti/Syn*= 4.1:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 7.31-7.33 (m, 2H), 7.24-7.27 (m, 2H), 4.76 (dd, *J* = 8.7, 2.8 Hz, 1H), 3.98 (d, *J* = 2.8 Hz, 1H), 2.45-2.58 (m, 2H), 2.30-2.40 (m, 1H), 2.06-2.13 (m, 1H), 1.77-1.83 (m, 1H), 1.51-1.69 (m, 3H), 1.26-1.36 (m, 1H). HPLC analysis Chiralcel AD-H (Hexane/ *i*-PrOH = 90/10, 0.5 mL/min,  $\lambda$  = 220 nm, 20°C)  $t_R$  (major)= 25.9 min and  $t_R$  (minor)= 30.0 min.

### 2-(Hydroxy-(4-methoxyphenyl)methyl)cyclohexan-1-one **5o** <sup>[2]</sup>



Reaction time: 100 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 10:1) to give pure aldol adduct. yield: 19%; 89%ee; *Anti/Syn*= 3.7:1, <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 7.21-7.26 (m, 2H), 6.85-6.91 (m, 2H), 4.74 (dd, *J* = 8.7, 2.0 Hz, 1H), 3.91 (d, *J* = 2.0 Hz, 1H), 3.80 (s, 3H), 2.57-2.60 (m, 1H), 2.44-2.50 (m, 1H), 2.34-2.41 (m, 1H), 2.05-2.11 (m, 1H), 1.76-1.81 (m, 1H), 1.52-1.69 (m, 3H), 1.23-1.33 (m, 1H). HPLC analysis Chiralcel AD-H (Hexane/ *i*-PrOH = 95/5, 0.5 mL/min,  $\lambda$  = 220 nm, 20°C)  $t_R$  (major)= 78.1 min and  $t_R$  (minor)= 81.8 min.

### 2-(Hydroxy-(4-nitrophenyl)methyl)butan-2-one **5p** <sup>[4]</sup>



Reaction time: 52 h; The crude product was purified by flash column chromatography (hexane/ ethyl acetate= 3:1) to give pure aldol adduct. yield: 25%; 56%ee; <sup>1</sup>HNMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ (ppm) 8.21 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.7 Hz, 2H), 5.26 (dd, *J* = 7.3, 4.9 Hz, 1H), 3.61 (br, 1H), 2.84-2.86 (m, 2H), 2.22 (s, 3H). HPLC analysis Chiralcel AS-H (Hexane/ *i*-PrOH = 70/30, 1.0 mL/min,  $\lambda$  = 254 nm, 20°C)  $t_R$  (minor)= 22.2 min and  $t_R$  (major)= 27.4 min.

<sup>2</sup> Wu, Y.-Y.; Zhang, Y.-Z.; Yu, M.-L.; Zhao, G.; Wang, S.-W. *Org. Lett.* **2006**, *8*, 4417-4420.

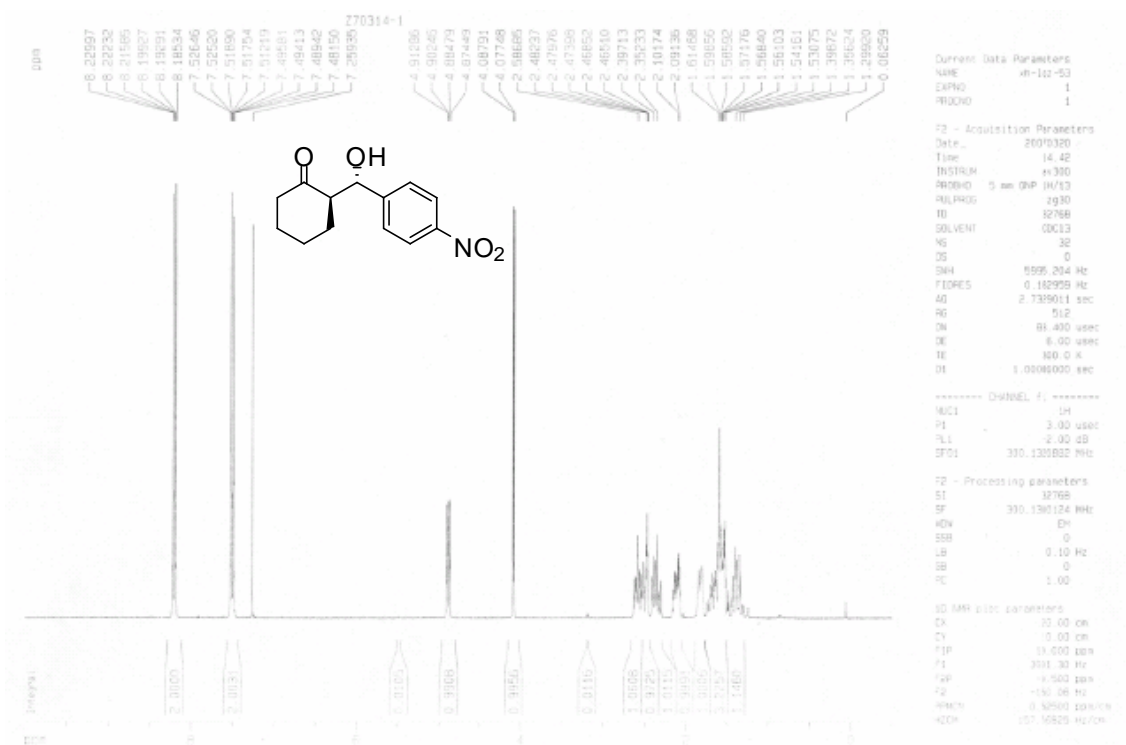
<sup>3</sup> Chen, J.-R.; Li, X.-Y.; Xing, X.-N.; Xiao, W.-J. *J. Org. Chem.* **2006**, *71*, 8198-8202

<sup>4</sup> Tang, Z.; Yang, Z.-H.; Chen, X.-H.; Cun, L.-F.; Mi, A.-Q.; Jiang, Y.-Z.; Gong, L.-Z. *J. Am. Chem. Soc.*; **2005**; *127*; 9285-9289

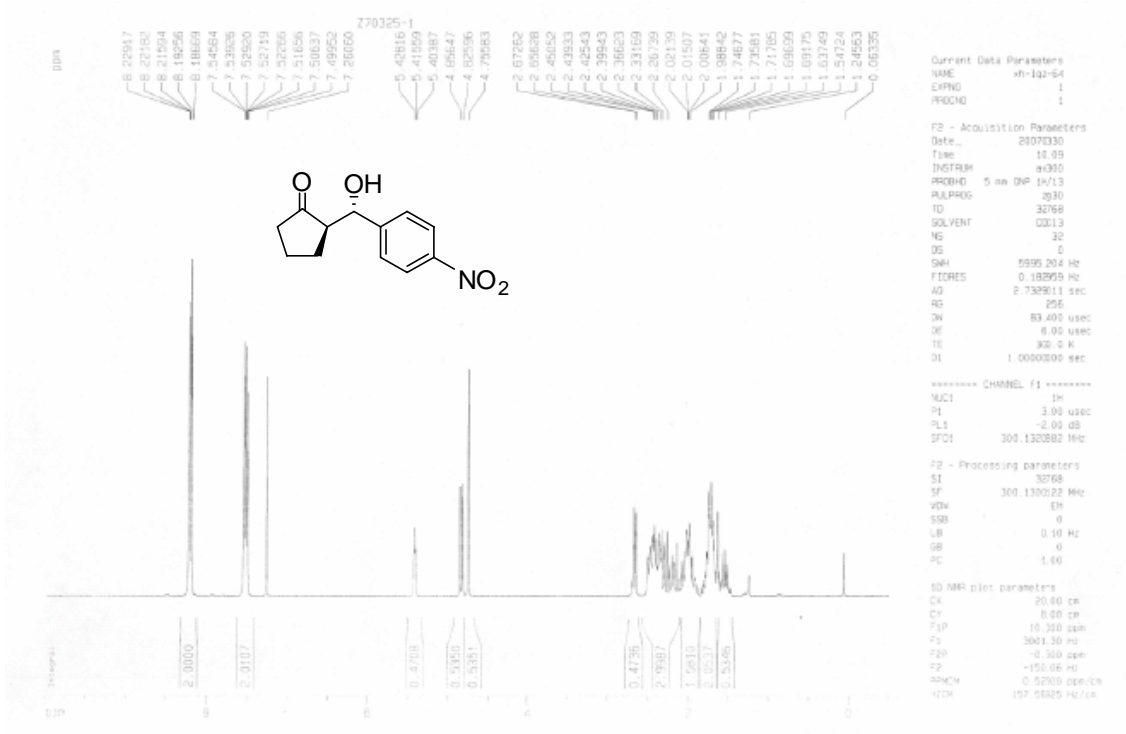
<sup>5</sup> Chen, J.-R.; Lu, H.-H.; Li, X.-Y.; Cheng, L.; Wan, J.; Xiao, W.-J. *Org. Lett.* **2005**, *7*, 4543-4545.

## NMR spectra for all the Aldol products

### <sup>1</sup>H NMR spectra of **5a**



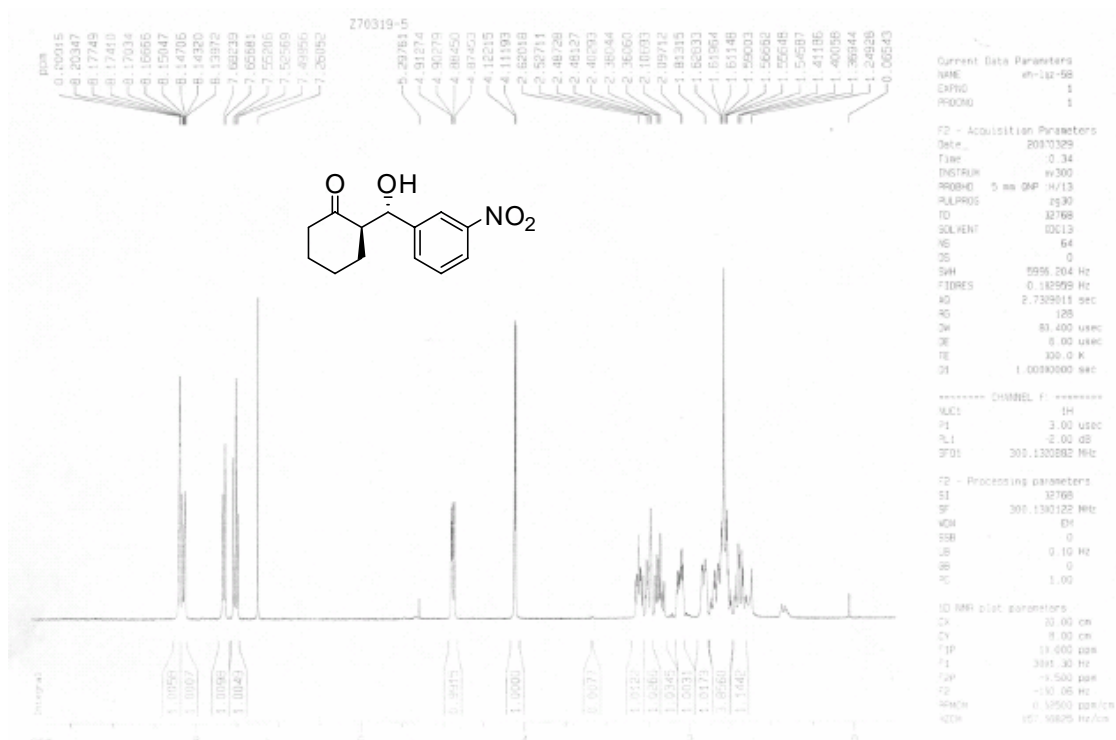
### <sup>1</sup>H NMR spectra of **5b**



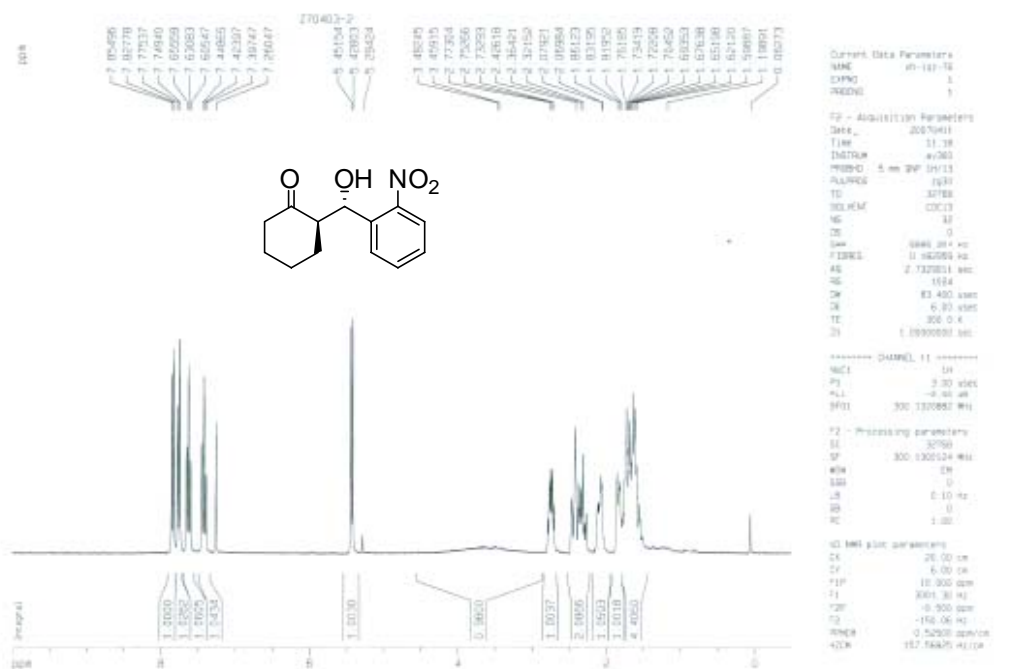




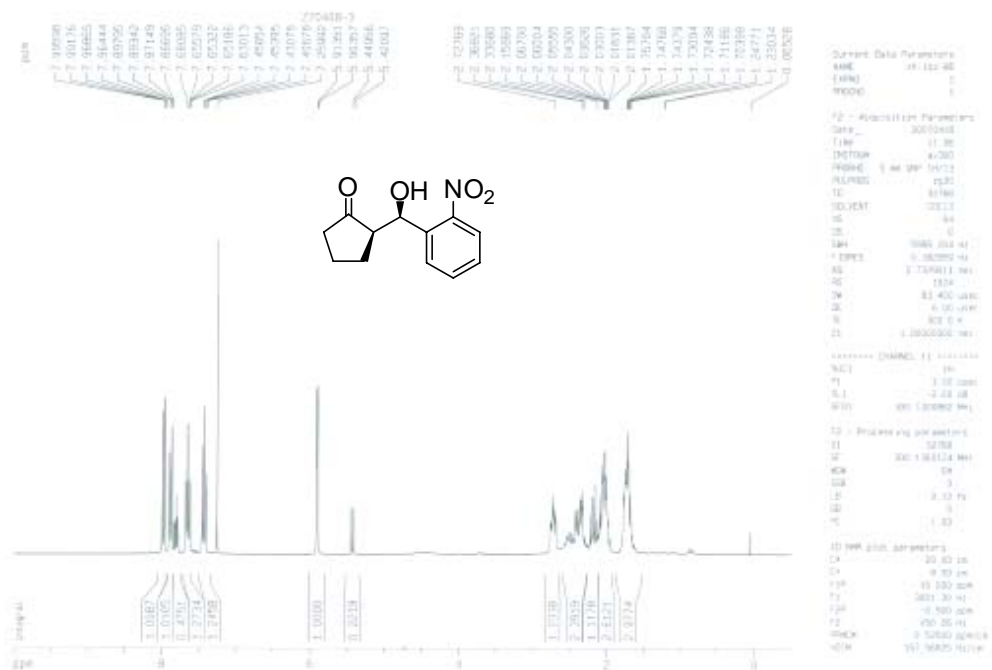
<sup>1</sup>H NMR spectra of **5e**



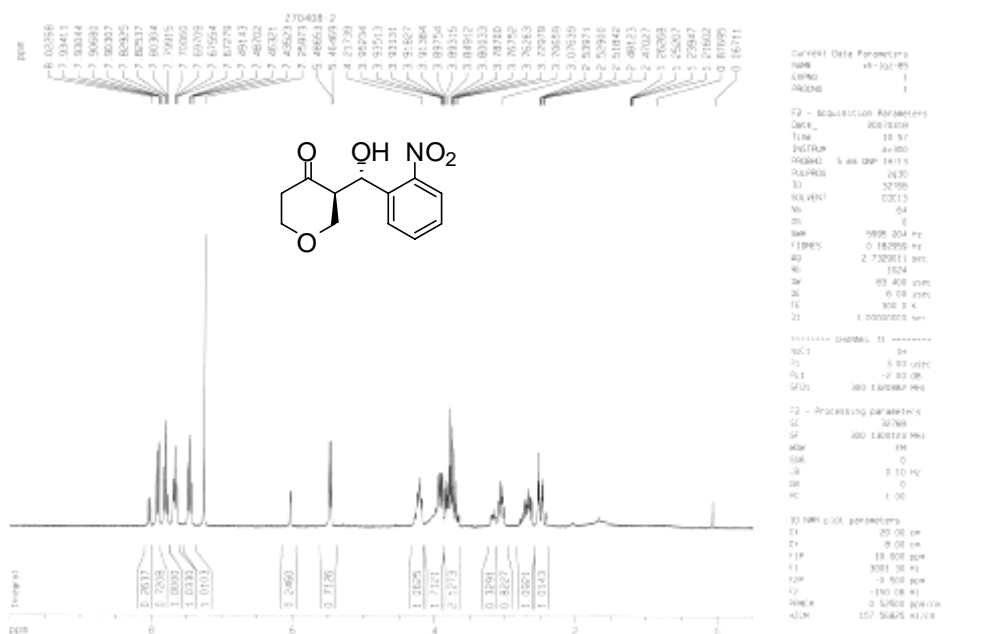
<sup>1</sup>H NMR spectra of **5f**



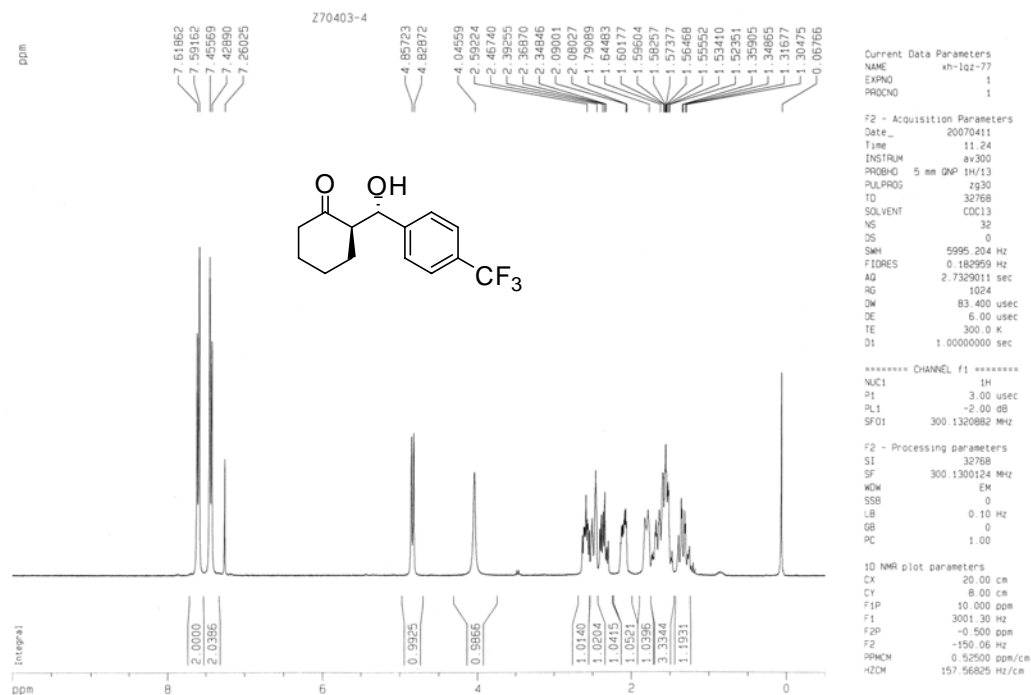
<sup>1</sup>H NMR spectra of **5g**



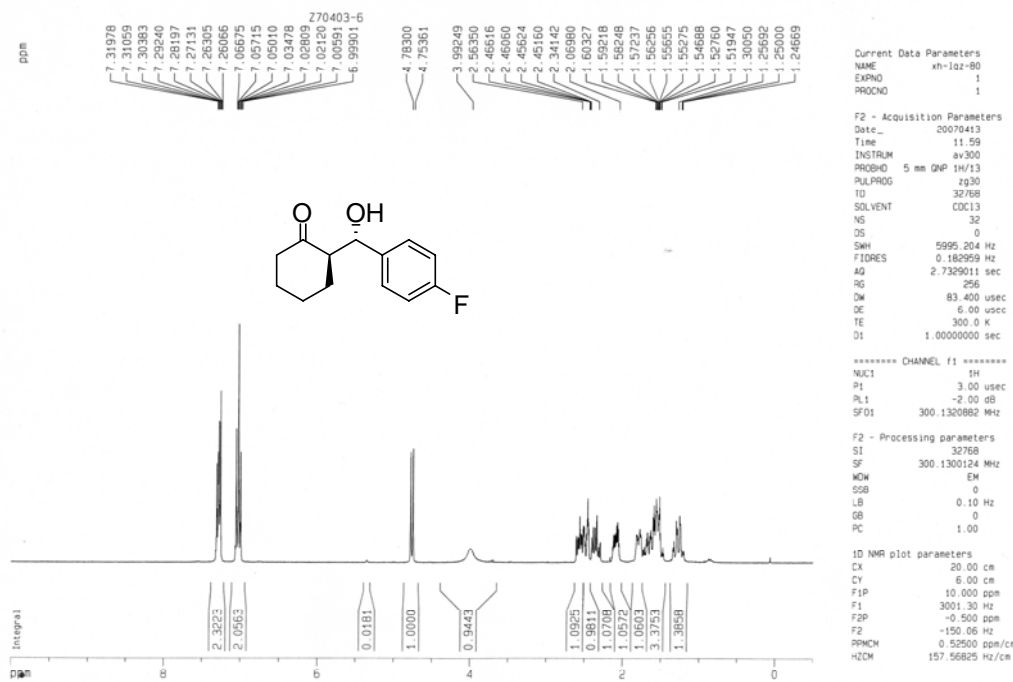
<sup>1</sup>H NMR spectra of **5h**



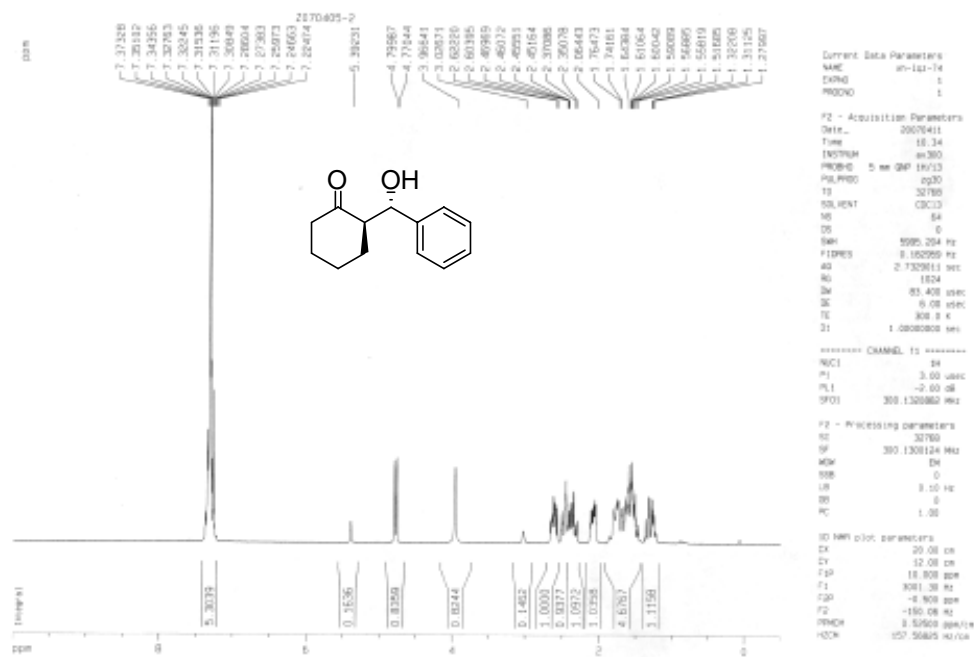
<sup>1</sup>H NMR spectra of **5i**



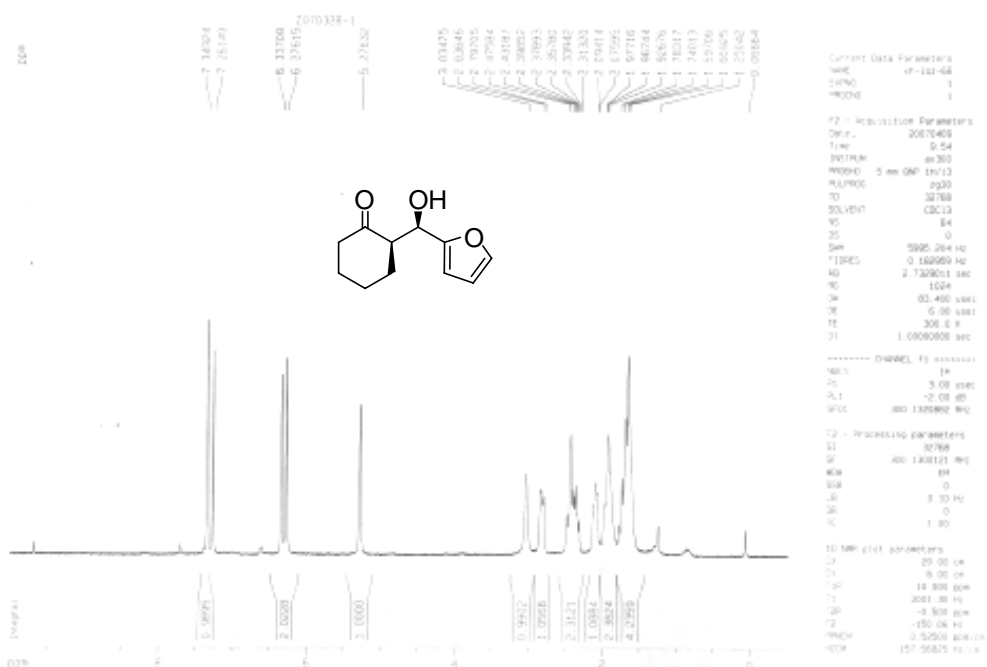
<sup>1</sup>H NMR spectra of **5j**



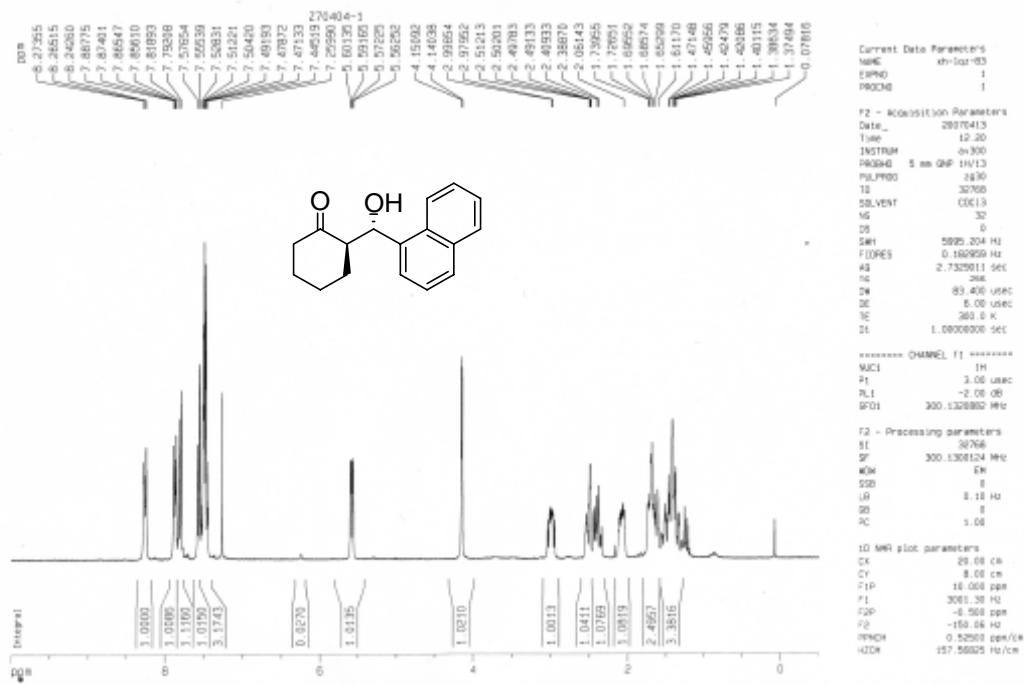
<sup>1</sup>H NMR spectra of **5k**



<sup>1</sup>H NMR spectra of **5l**



<sup>1</sup>H NMR spectra of **5m**



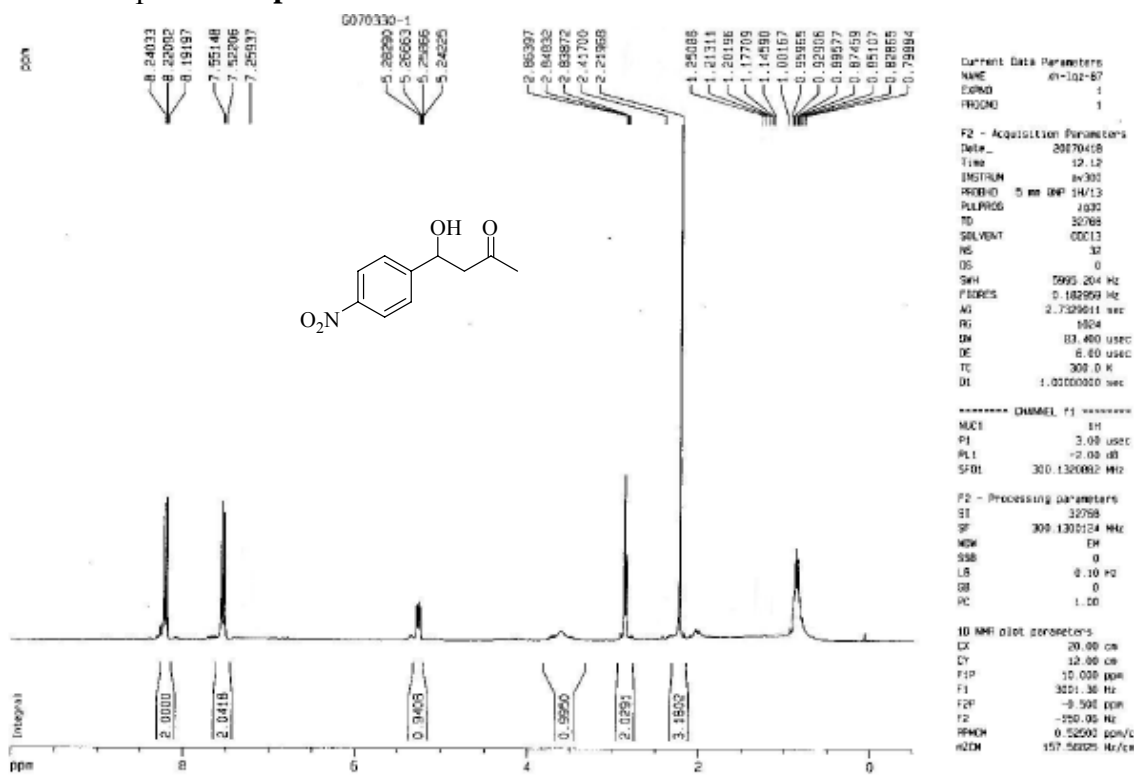
<sup>1</sup>H NMR spectra of **5n**



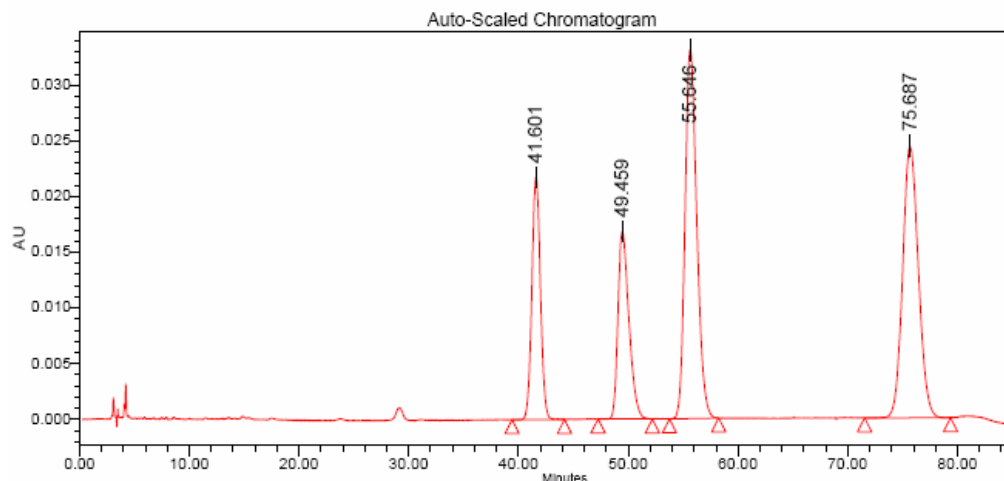
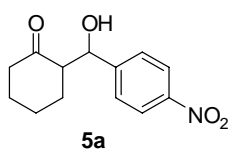
<sup>1</sup>H NMR spectra of **5o**



<sup>1</sup>H NMR spectra of **5p**

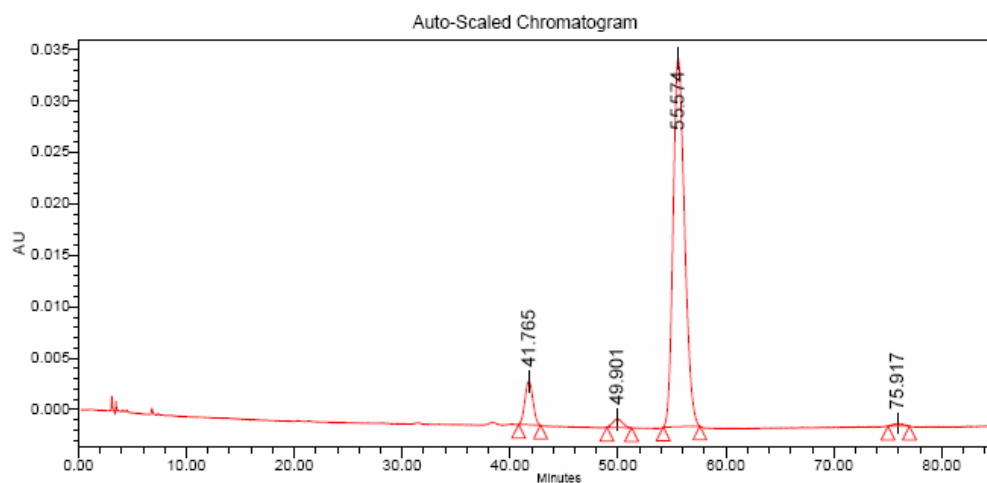


## HPLC spectra for compounds 5a-p



Peak Results

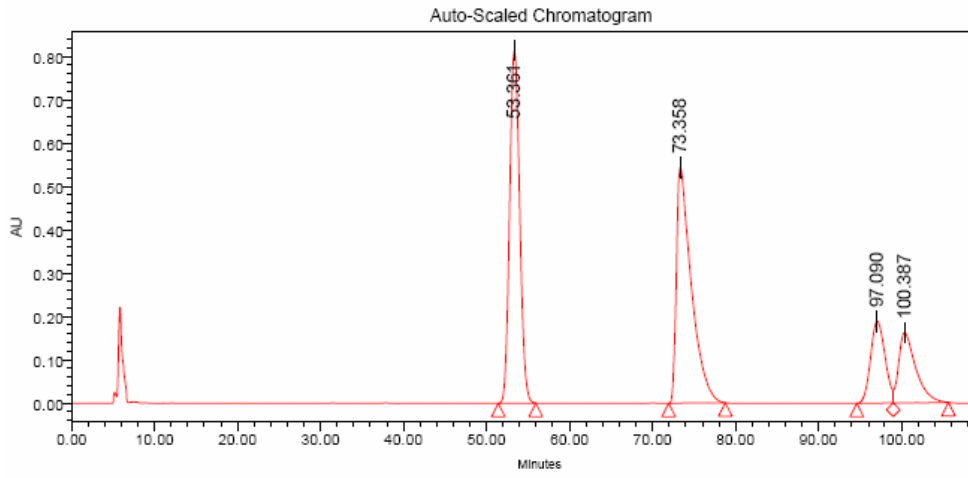
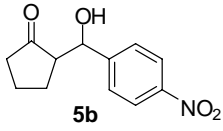
	Name	Retention Time	Area	Total	Area Percent
1		41.601	1175951	7239378	16.24
2		49.459	1171700	7239378	16.19
3		55.646	2461099	7239378	34.00
4		75.687	2430627	7239378	33.58



Peak Results

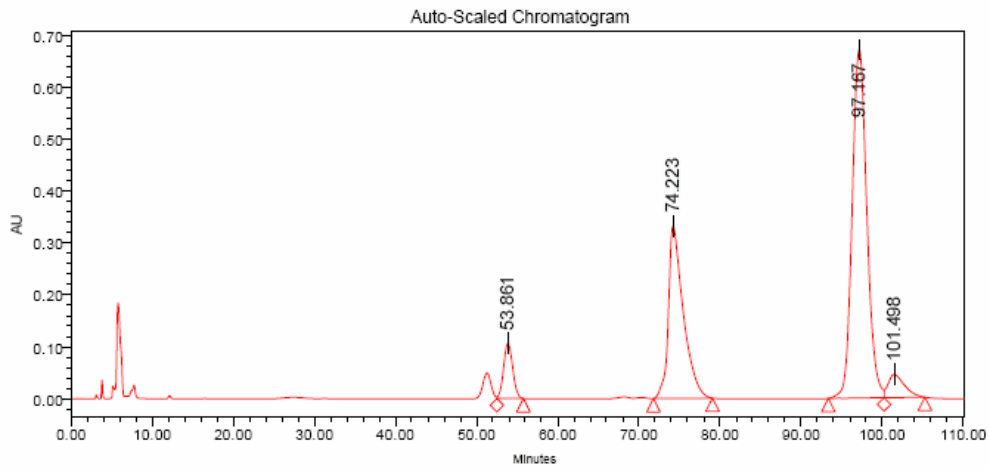
	Name	Retention Time	Area	Area Percent	Totals
1		41.765	217327	7.44	2922071
2		49.901	51583	1.77	2922071
3		55.574	2634486	90.16	2922071
4		75.917	18674	0.64	2922071





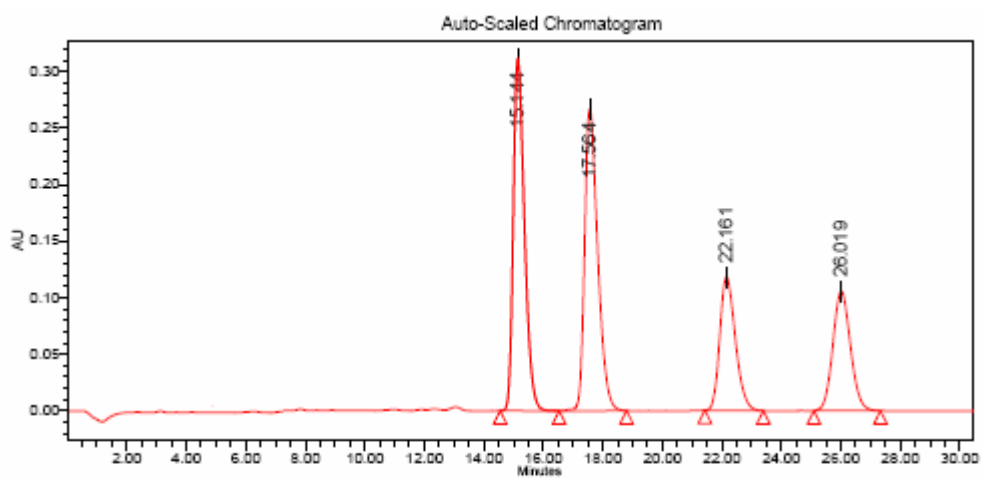
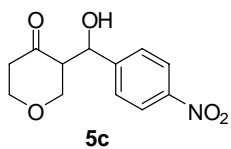
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	53.361	68676779	18286048	37.56
2	73.358	68065101	18286048	37.22
3	97.090	22860786	18286048	12.50
4	100.387	23273379	18286048	12.73



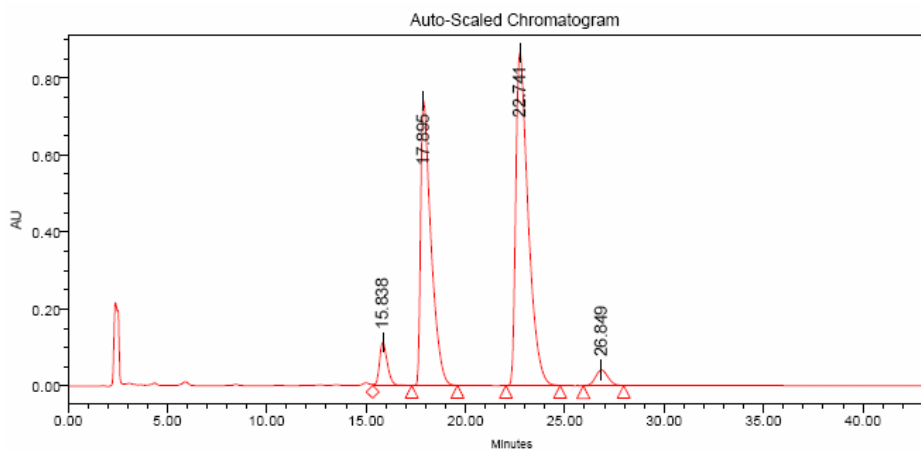
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	53.861	8303914	141464451	5.87
2	74.223	42481783	141464451	30.03
3	97.167	84428561	141464451	59.68
4	101.498	6252192	141464451	4.42



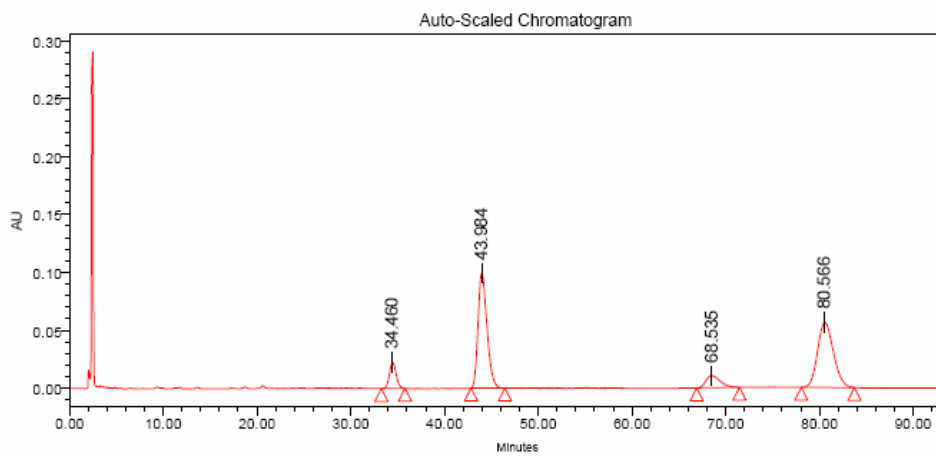
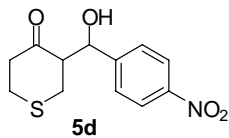
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	15.144	8118935	24932715	32.56
2	17.564	8170841	24932715	32.77
3	22.161	4315222	24932715	17.31
4	26.019	4327717	24932715	17.35



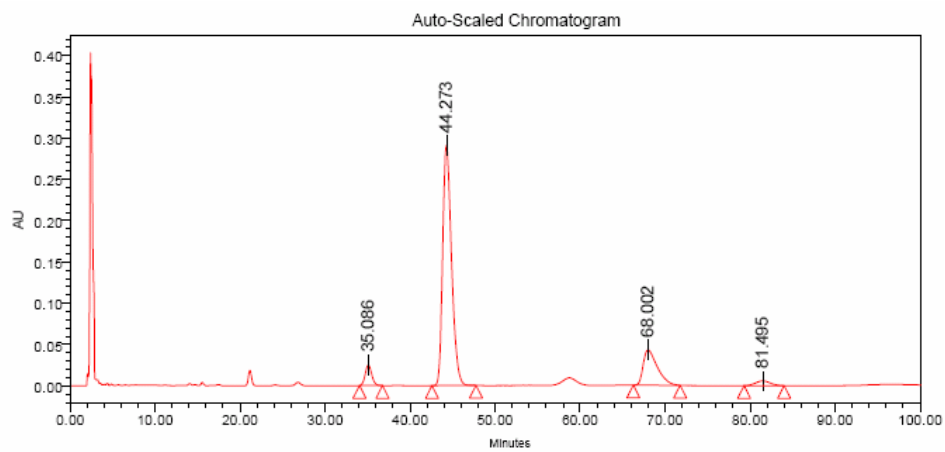
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	15.838	3044920	89115858	4.41
2	17.895	26882502	89115858	38.99
3	22.741	37444575	89115858	54.18
4	26.849	1743861	89115858	2.52



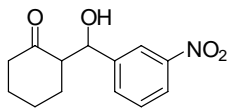
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	34.480	1116382	15378217	7.28
2	43.984	6584691	15378217	42.82
3	68.535	1085772	15378217	7.08
4	80.588	6591373	15378217	42.86

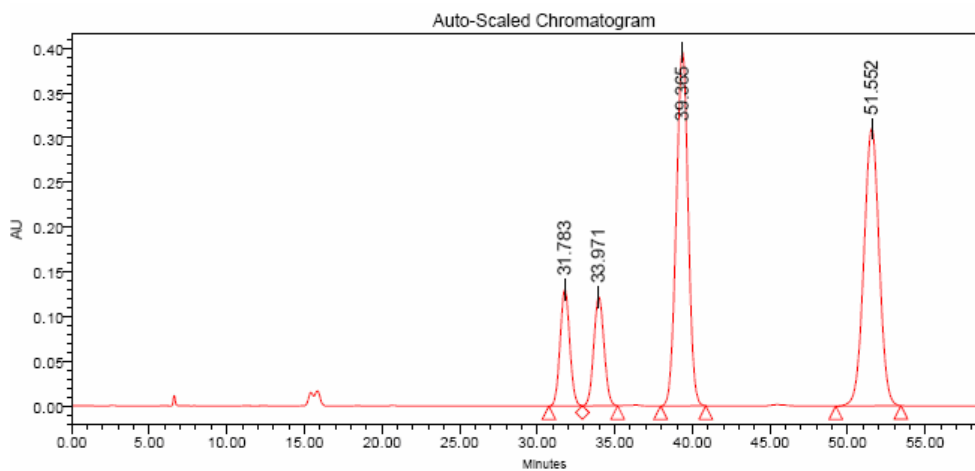


Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	35.086	1336464	27863315	4.80
2	44.273	20972541	27863315	75.27
3	68.002	4880365	27863315	17.52
4	81.495	873956	27863315	2.42

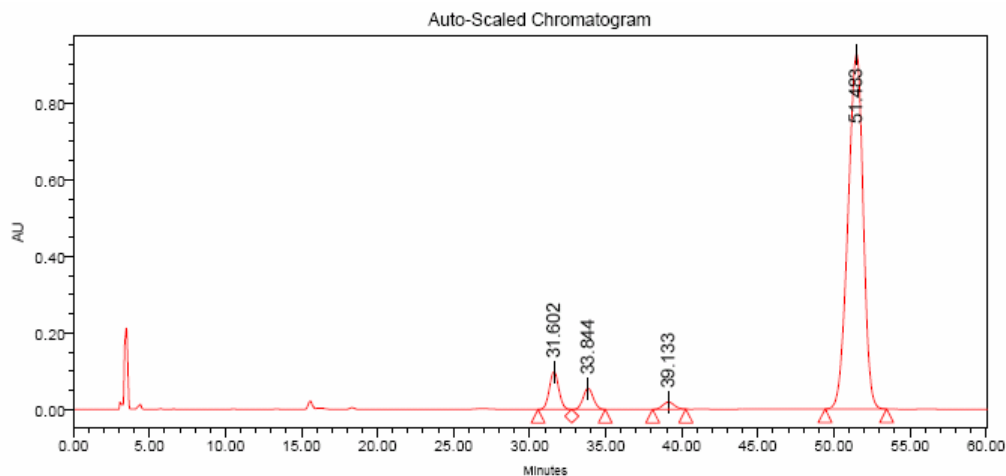


5e



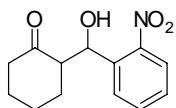
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	31.783	5632934	53577892	10.51
2	33.971	5638854	53577892	10.52
3	39.365	21023818	53577892	39.24
4	51.552	21284286	53577892	39.73

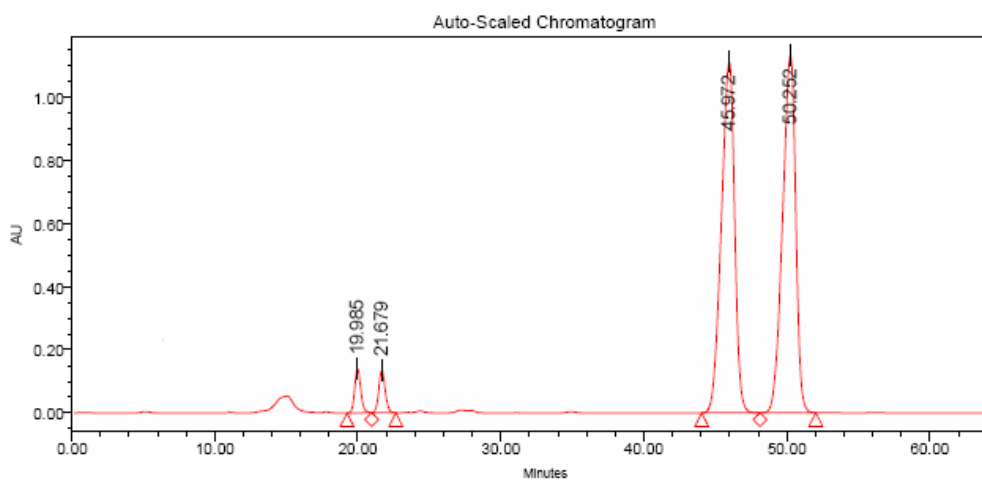


Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	31.602	4214708	72202576	5.84
2	33.844	2532438	72202576	3.51
3	39.133	964180	72202576	1.34
4	51.483	64491250	72202576	89.32

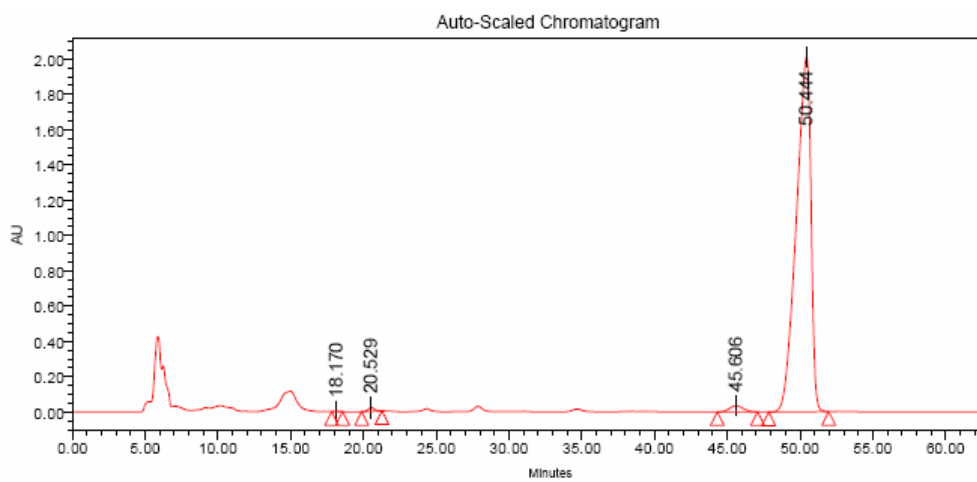


5f



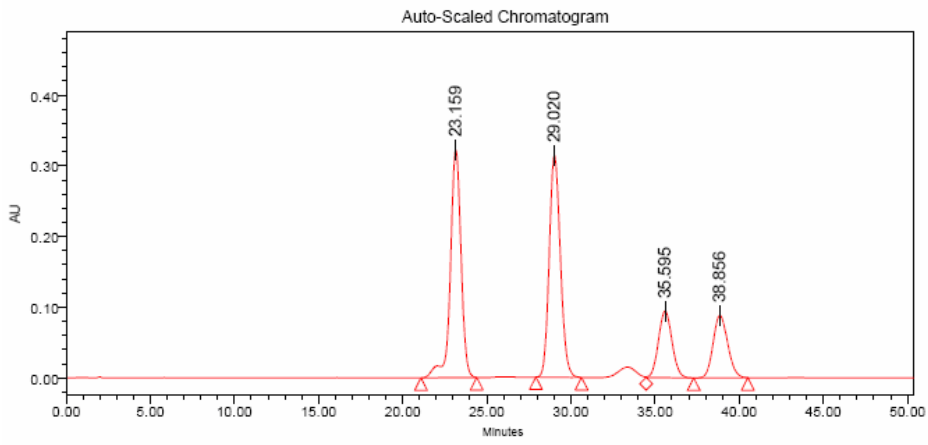
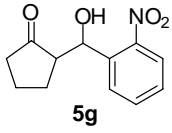
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	19.985	4174324	151830456	2.75
2	21.679	4208380	151830456	2.77
3	45.972	71550841	151830456	47.13
4	50.252	71898911	151830456	47.35



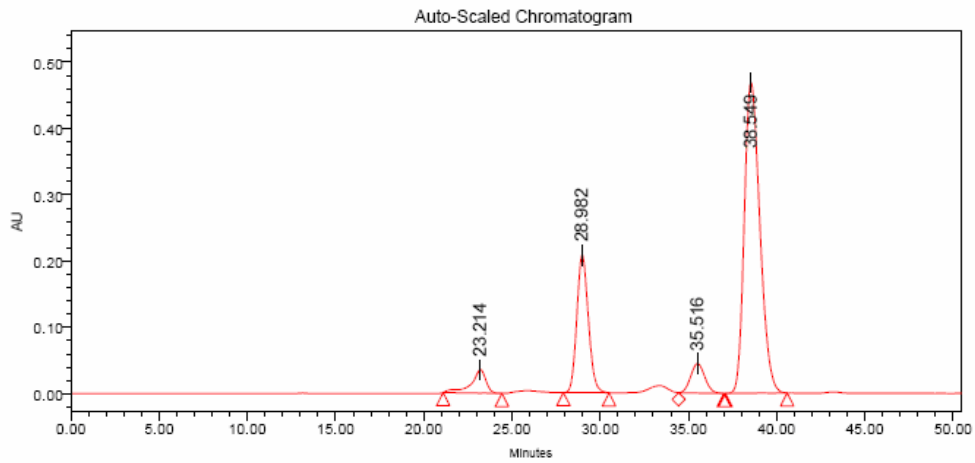
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	18.170	35037	143944123	0.02
2	20.529	634556	143944123	0.44
3	45.606	2238084	143944123	1.55
4	50.444	141036446	143944123	97.98



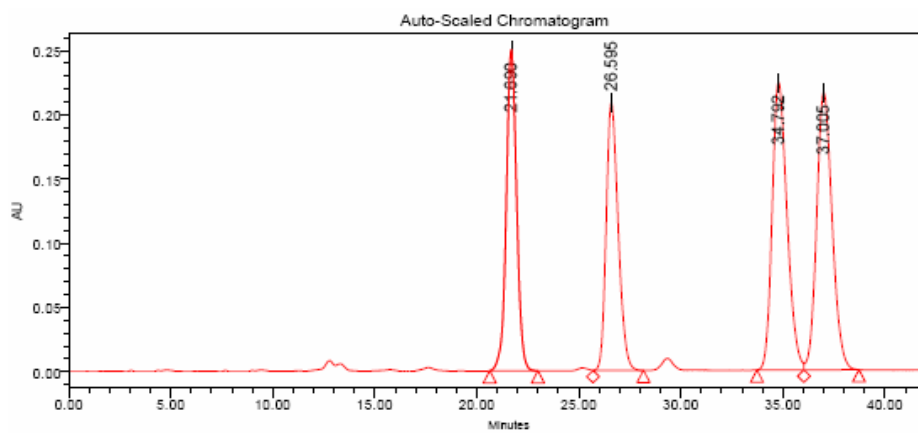
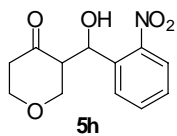
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	23.159	14279817	39254553	36.38
2	29.020	14407887	39254553	36.70
3	35.595	5258088	39254553	13.39
4	38.856	5310982	39254553	13.53



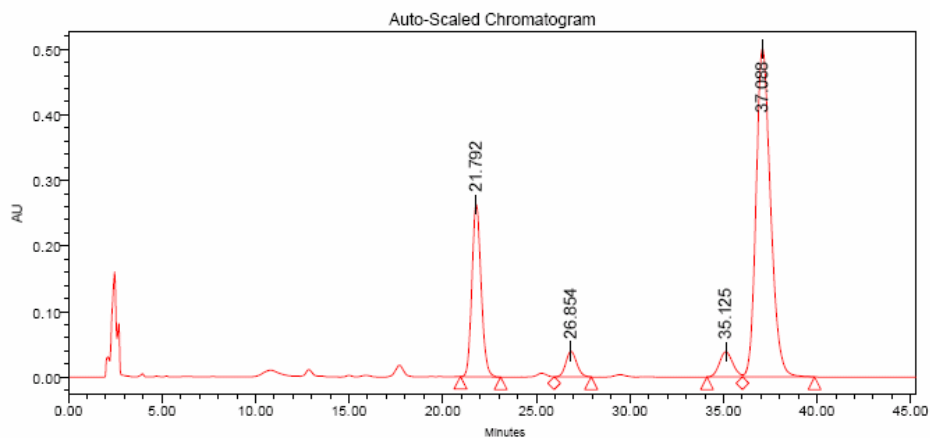
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	23.214	2051324	42742869	4.80
2	28.982	9492631	42742869	22.21
3	35.516	2455310	42742869	5.74
4	38.549	28743804	42742869	67.25



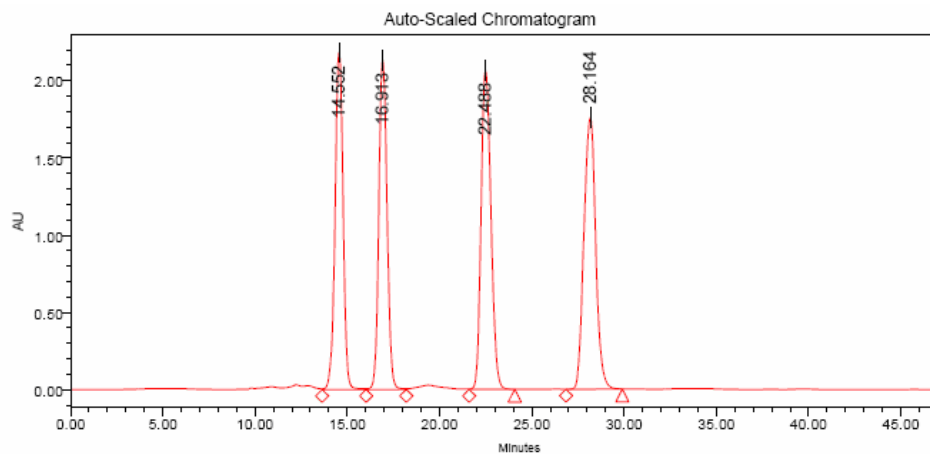
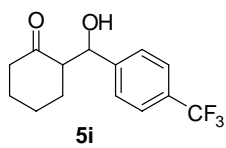
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	21.690	8806320	40046701	21.99
2	26.595	8491156	40046701	21.20
3	34.792	11350246	40046701	28.34
4	37.005	11398979	40046701	28.46



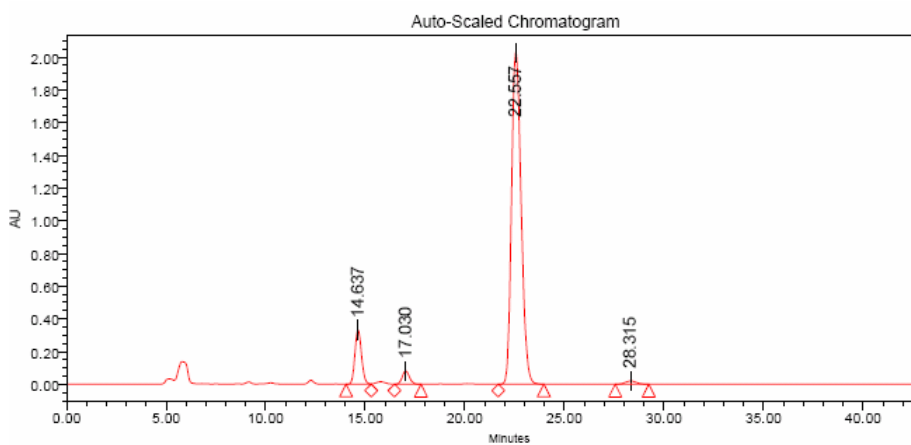
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	21.792	8997134	39348790	22.87
2	26.854	1575373	39348790	4.00
3	35.125	1891348	39348790	4.81
4	37.068	26884924	39348790	68.32



Peak Results

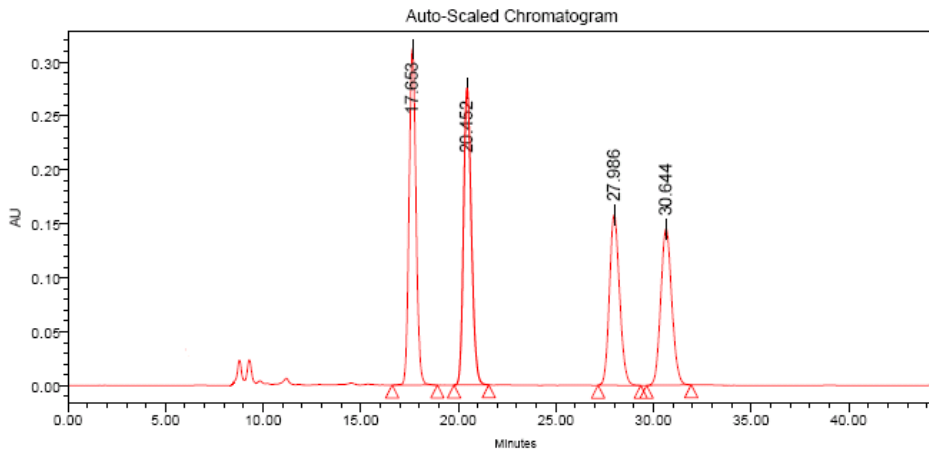
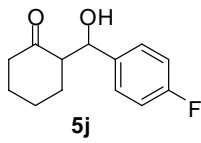
Name	Retention Time	Area	Totals	Area Percent
1	14.552	65969344	288559547	23.02
2	16.913	65983868	288559547	23.03
3	22.488	78558195	288559547	26.72
4	28.164	78048342	288559547	27.24



Peak Results

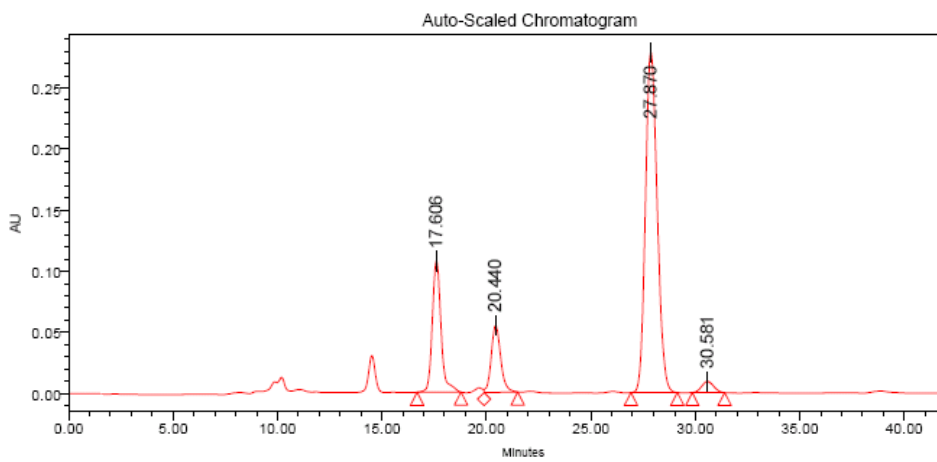
Name	Retention Time	Area	Totals	Area Percent
1	14.637	7685087	78124504	9.81
2	17.030	2049370	78124504	2.62
3	22.557	67845841	78124504	86.59
4	28.315	764206	78124504	0.98





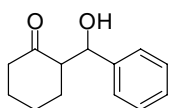
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	17.653	7682717	28794417	28.67
2	20.452	7680029	28794417	28.66
3	27.986	5717704	28794417	21.34
4	30.644	5713966	28794417	21.33

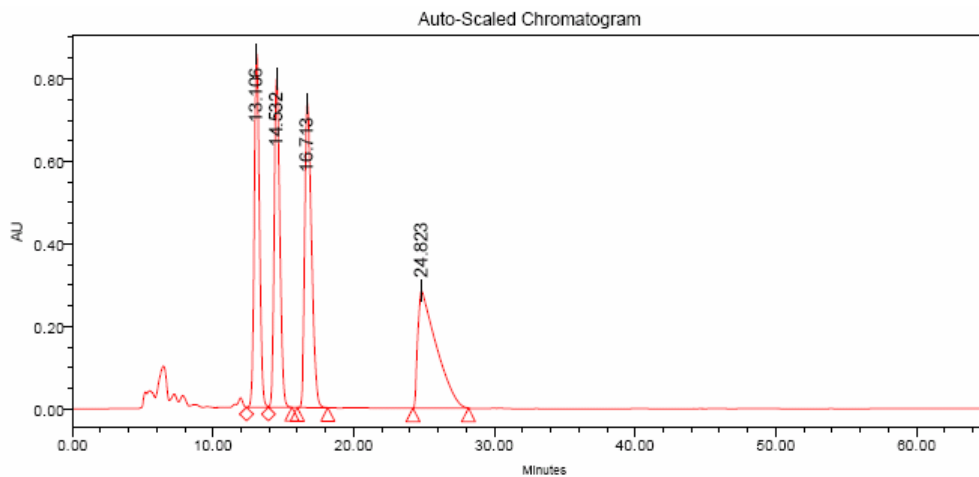


Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	17.606	3126580	16101738	19.42
2	20.440	1724573	16101738	10.71
3	27.870	10889493	16101738	67.63
4	30.581	361093	16101738	2.24

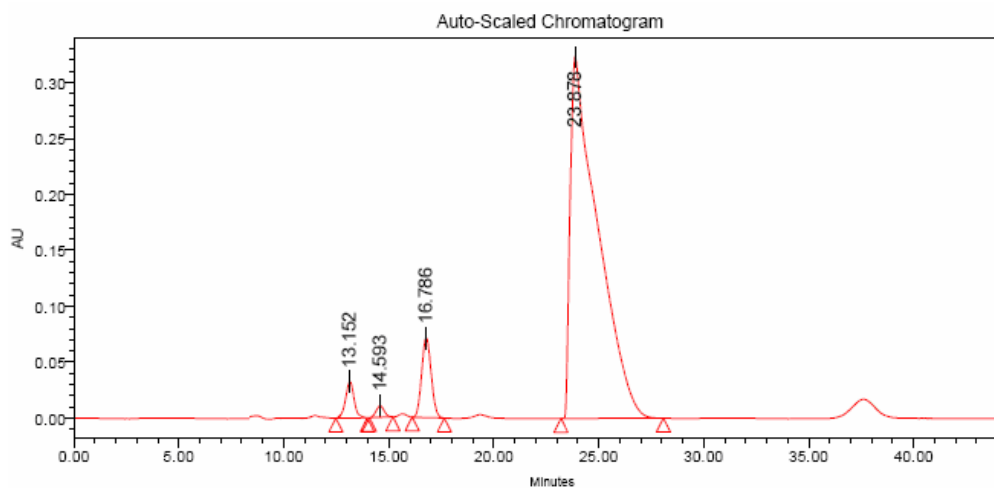


5k



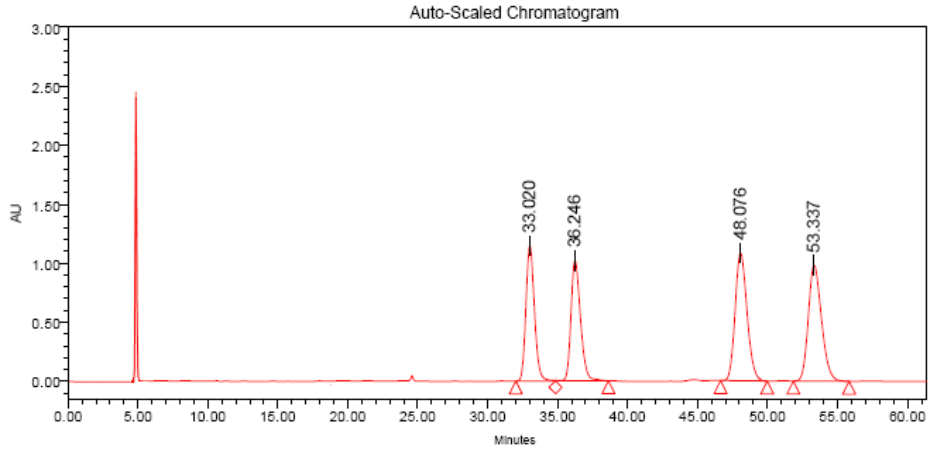
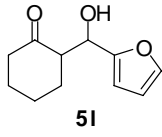
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	13.106	21959298	94896842	23.14
2	14.532	22010867	94896842	23.19
3	16.713	24843506	94896842	26.18
4	24.823	26082172	94896842	27.49



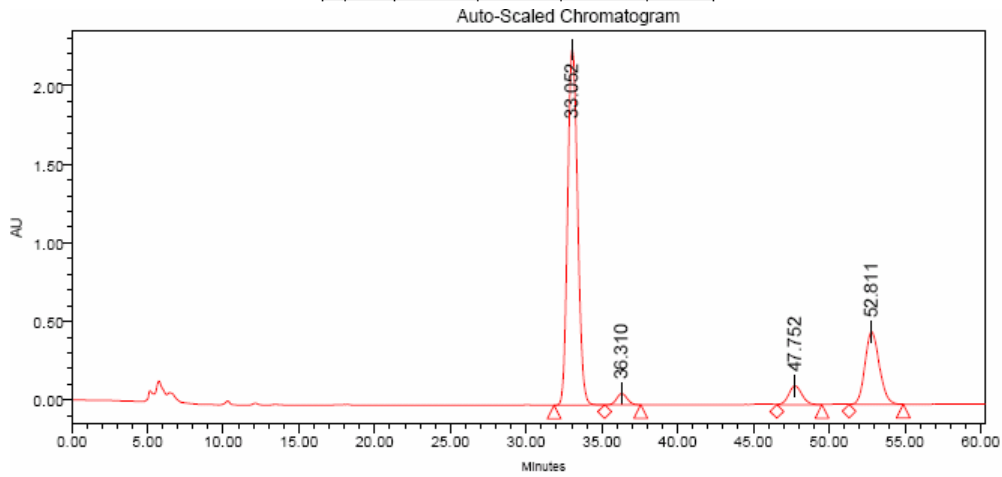
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	13.152	918366	32959514	2.78
2	14.593	275671	32959514	0.84
3	16.786	2253980	32959514	6.84
4	23.878	29513497	32959514	89.54



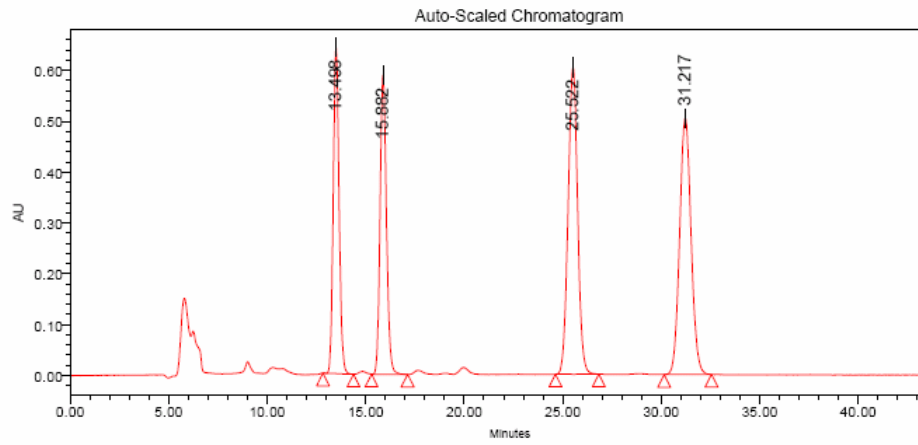
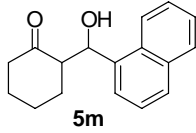
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	33.020	48489244	225358994	21.52
2	36.246	48336675	225358994	21.45
3	48.076	64042388	225358994	28.42
4	53.337	64488686	225358994	28.62



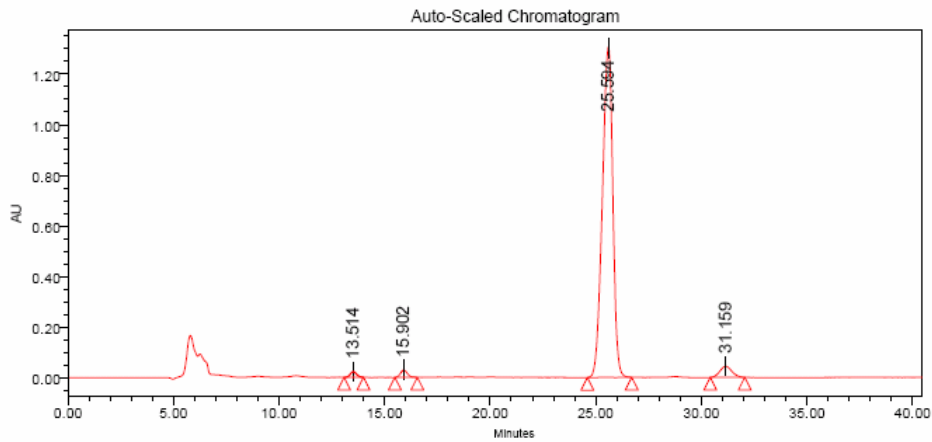
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	33.052	103370680	144432580	71.57
2	36.310	3457452	144432580	2.39
3	47.752	7165786	144432580	4.96
4	52.811	30438662	144432580	21.07



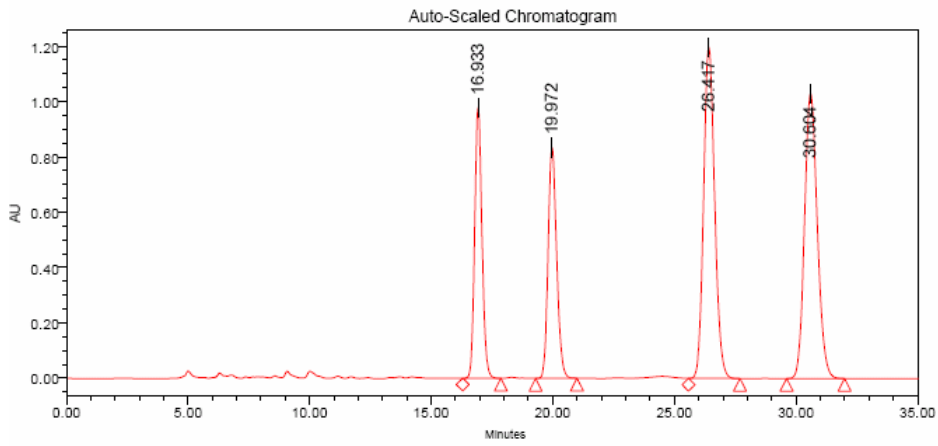
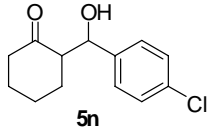
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	13.498	13161418	67036965	19.63
2	15.882	13312514	67036965	19.86
3	25.522	20249230	67036965	30.21
4	31.217	20313802	67036965	30.30



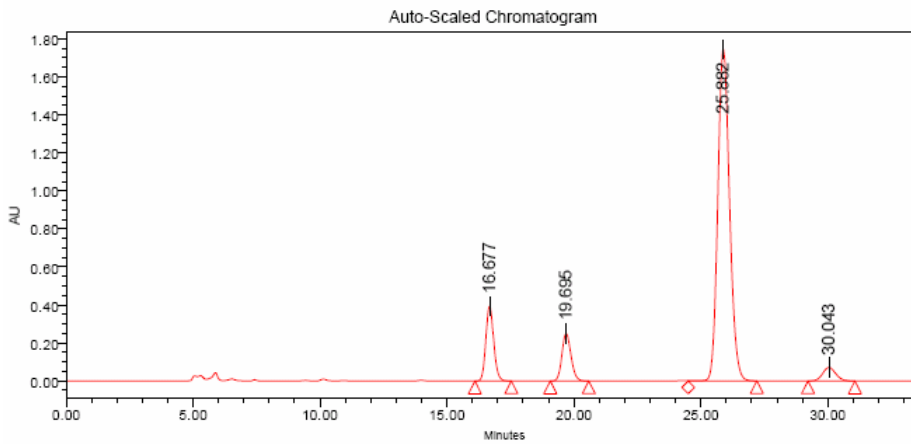
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	13.514	473697	47744785	0.99
2	15.902	657204	47744785	1.38
3	25.564	44909553	47744785	94.06
4	31.159	1704331	47744785	3.57



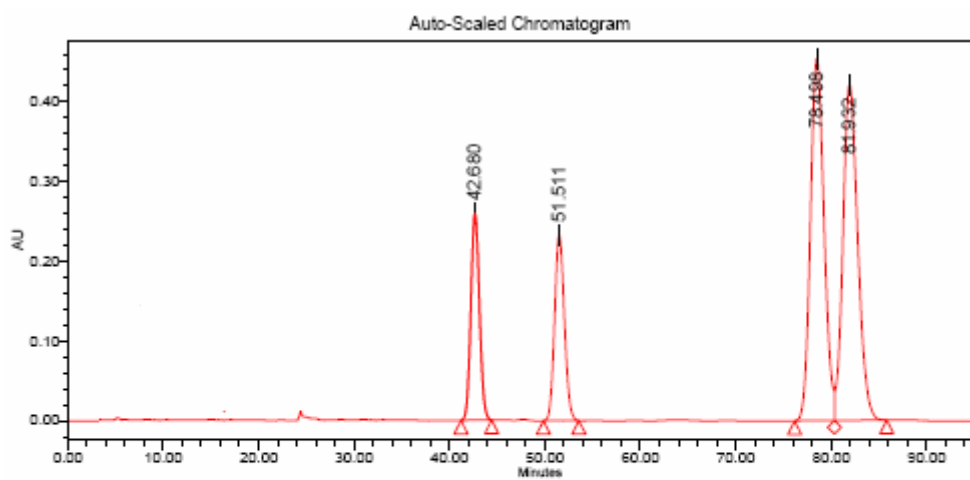
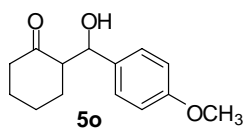
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	16.933	20407955	116218174	17.58
2	19.972	20341445	116218174	17.50
3	26.417	37827956	116218174	32.55
4	30.604	37640819	116218174	32.39



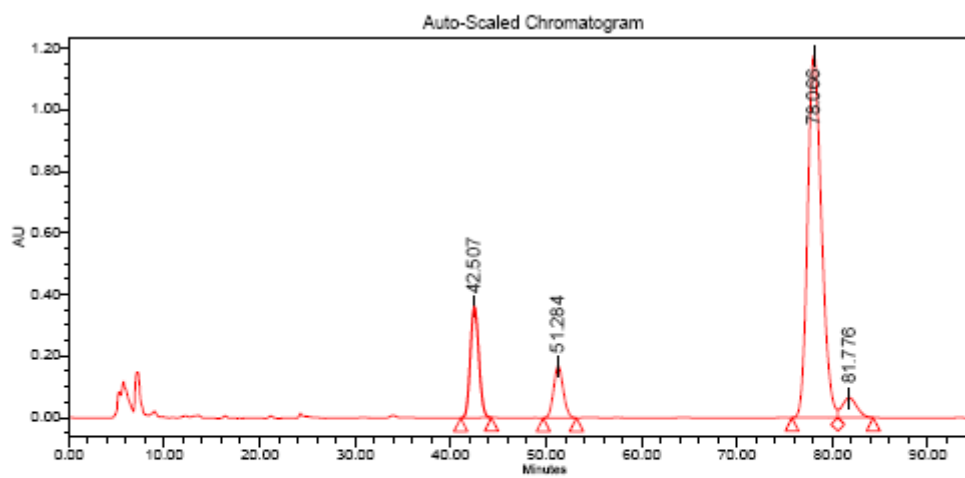
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	16.677	8504871	73302435	11.80
2	19.695	6168142	73302435	8.41
3	25.882	56078915	73302435	76.50
4	30.043	2552507	73302435	3.48



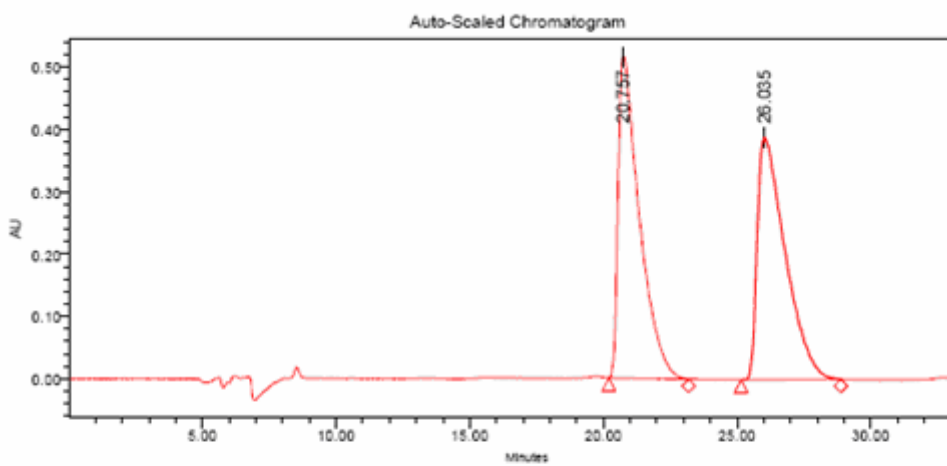
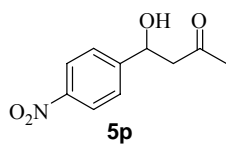
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	42.680	16275625	123455828	13.18
2	51.511	16641384	123455828	13.48
3	78.488	45052942	123455828	36.49
4	81.932	45485668	123455828	36.84



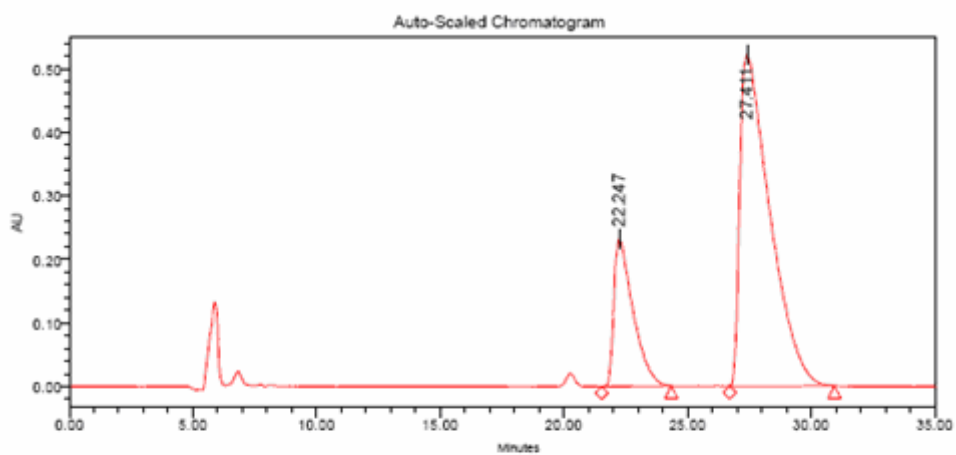
Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	42.507	22408286	160129827	13.99
2	51.284	11851164	160129827	7.40
3	78.066	118967193	160129827	74.29
4	81.776	6903184	160129827	4.31



Peak Results

Name	Retention Time	Area	Totals	Area Percent
1	20.757	28475568	56673053	50.33
2	26.035	28097495	56673053	49.67



Peak Results

Name	Retention Time	Area	Area Percent	Totals
1	22.247	12455410	22.04	56500871
2	27.411	44045461	77.96	56500871