

## Supplementary Information

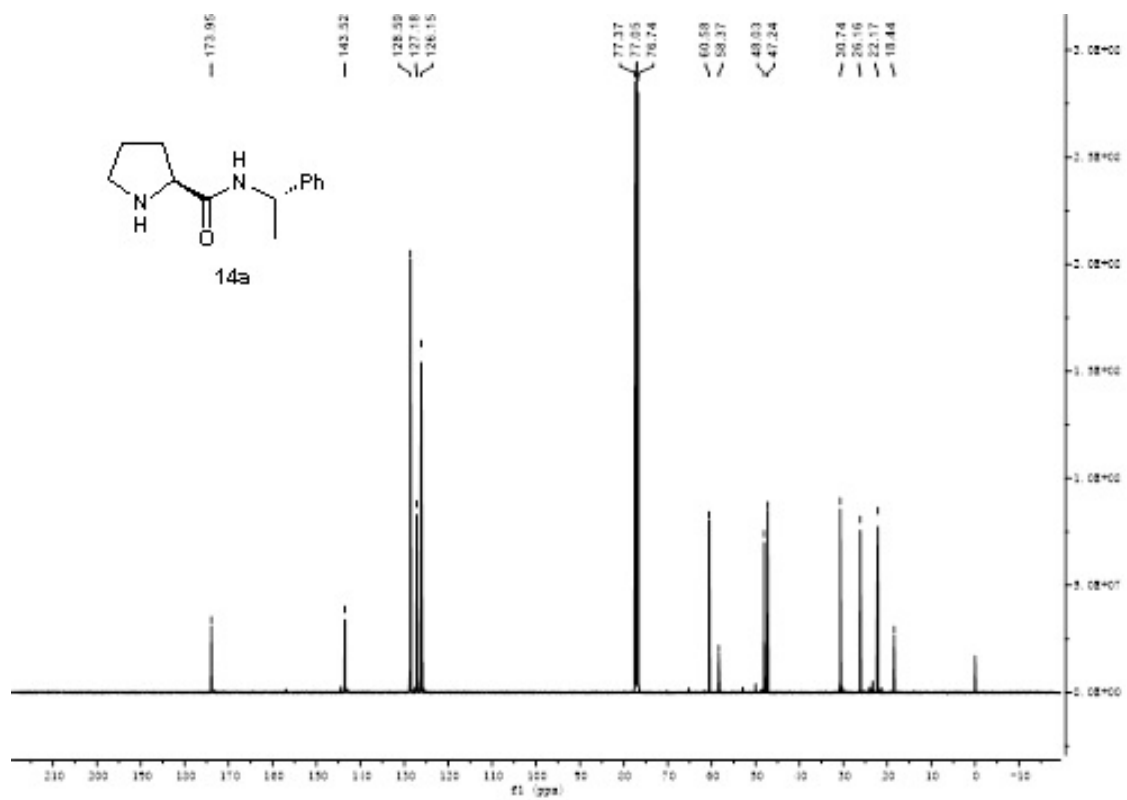
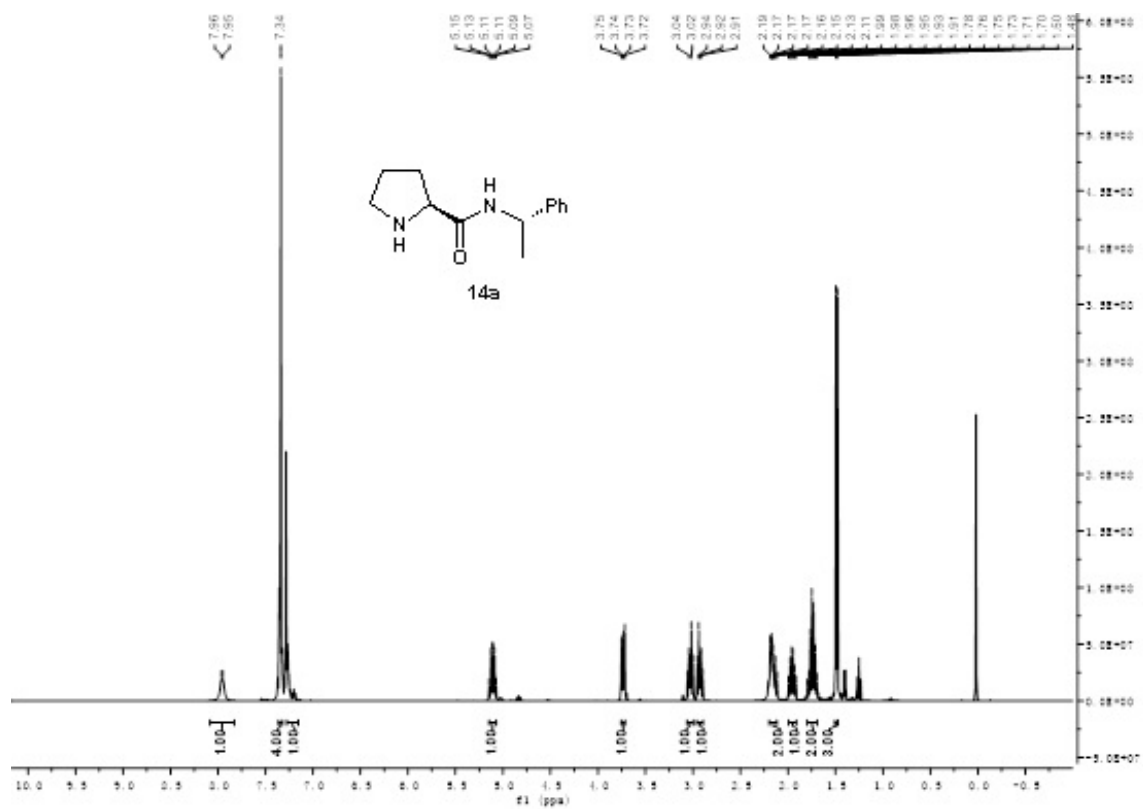
### Highly Modular Dipeptide-like Organocatalysts for Direct Asymmetric Aldol Reactions in Brine

Xiao-Mu Hu,<sup>a</sup> Dong-Xu Zhang,<sup>a</sup> Sheng-Yong Zhang<sup>\*a</sup> and Ping-An Wang<sup>\*a</sup>

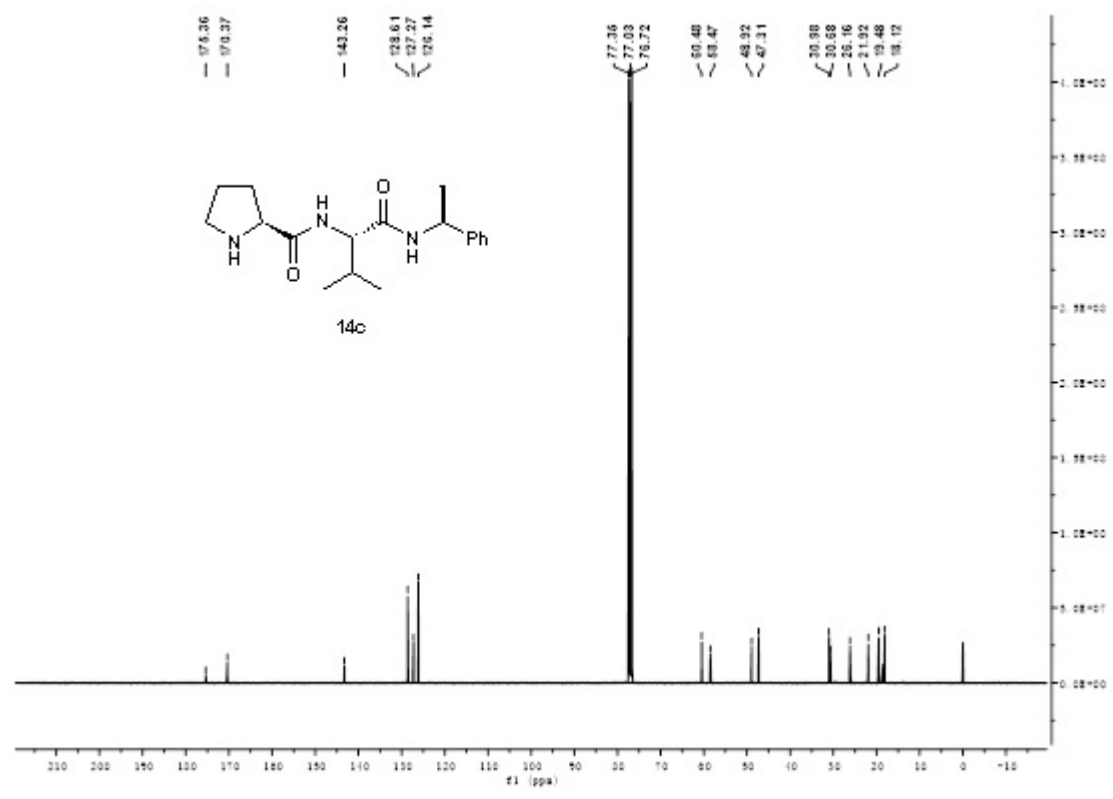
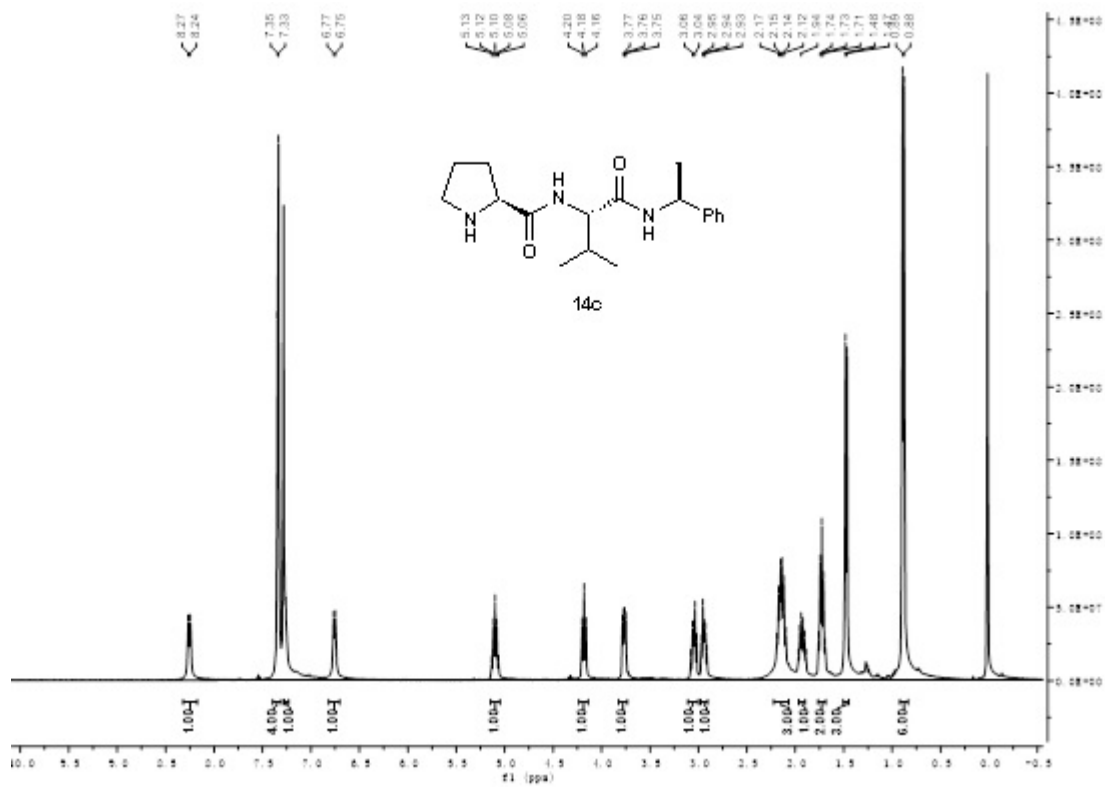
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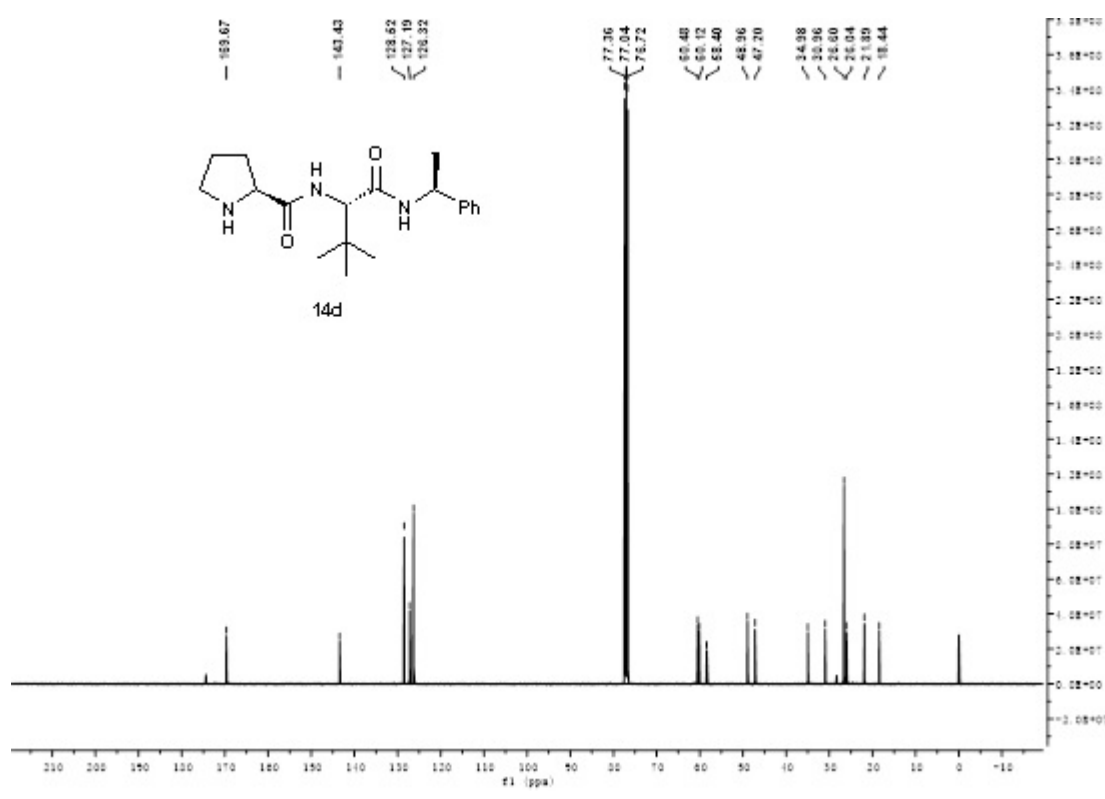
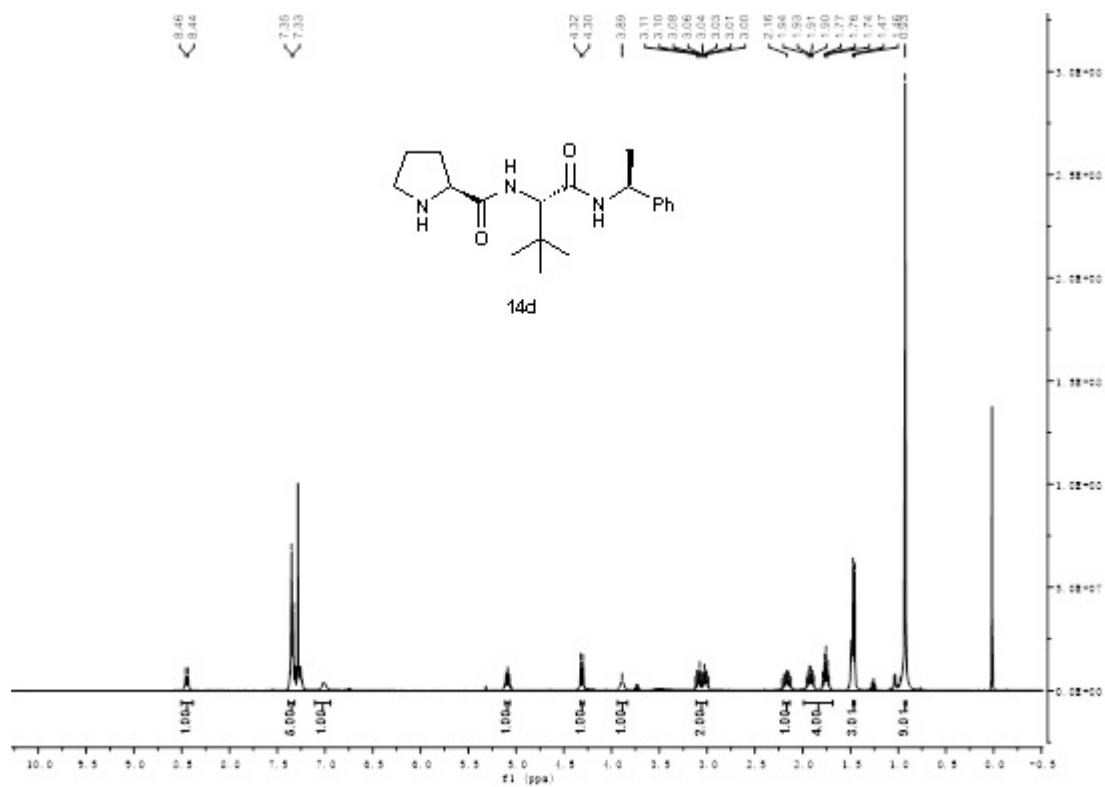
\*Corresponding author's E-mails: [ping\\_an1718@outlook.com](mailto:ping_an1718@outlook.com); [syzhang@fmmu.edu.cn](mailto:syzhang@fmmu.edu.cn)

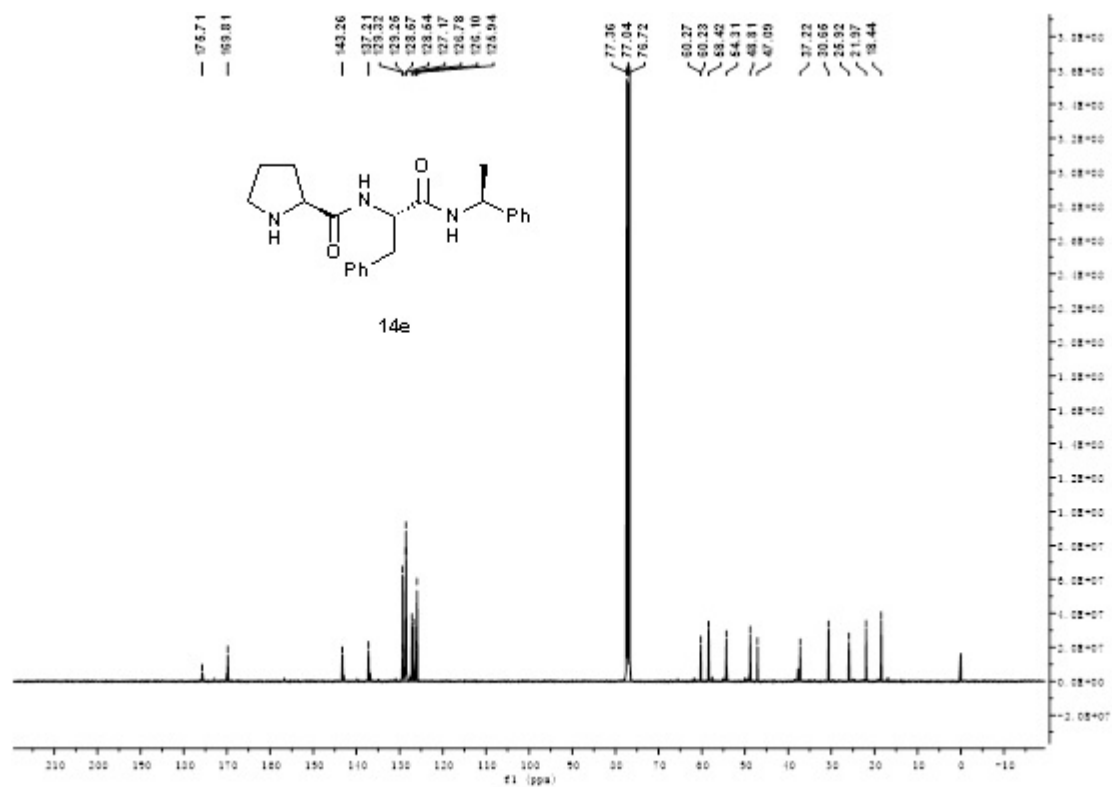
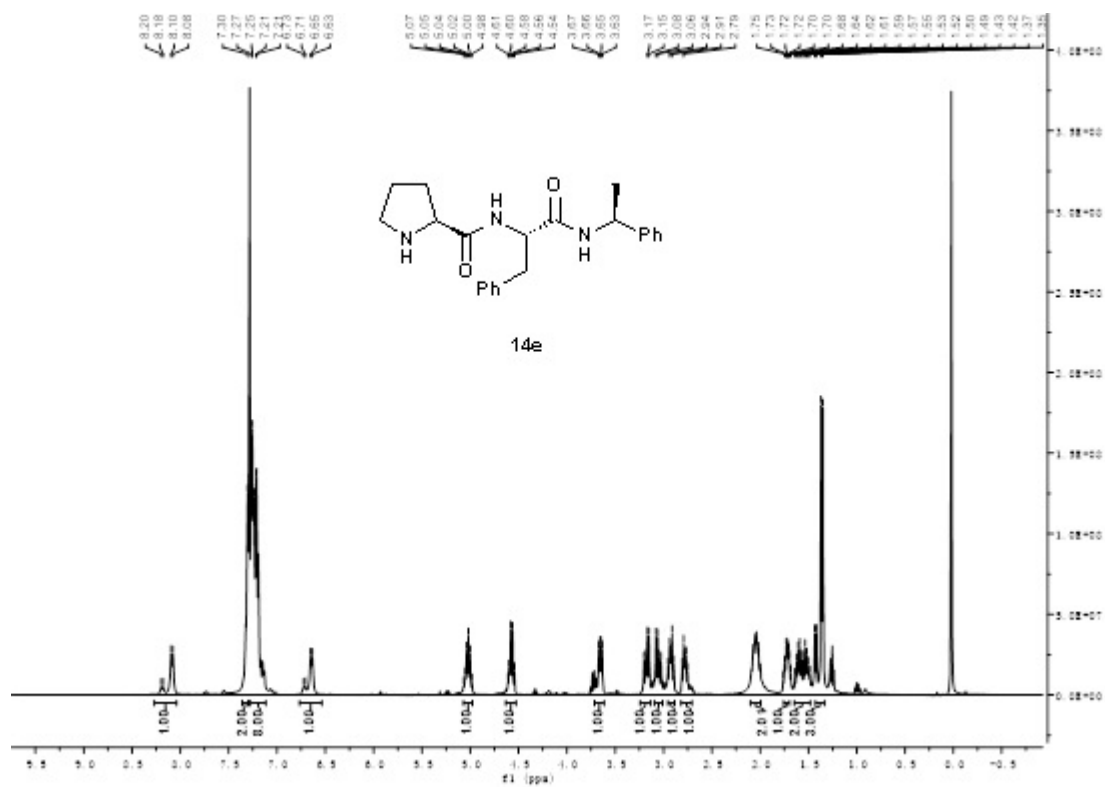
<sup>1</sup> H and <sup>13</sup> C NMR Spectra of <b>14a-i</b>	S2-S10
HRMS of <b>14a-i</b>	S11-S15
HPLC charts of aldol adducts <b>3a-j</b> , <b>15a-k</b> , <b>16</b>	S16-S36

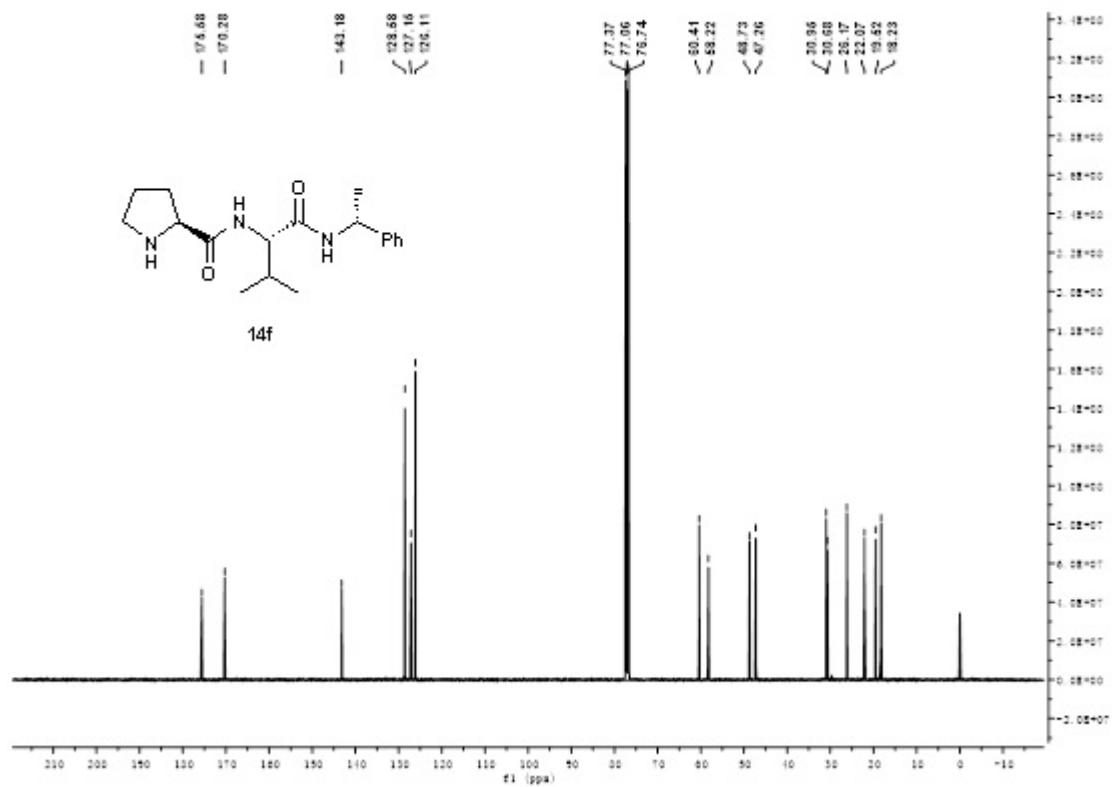
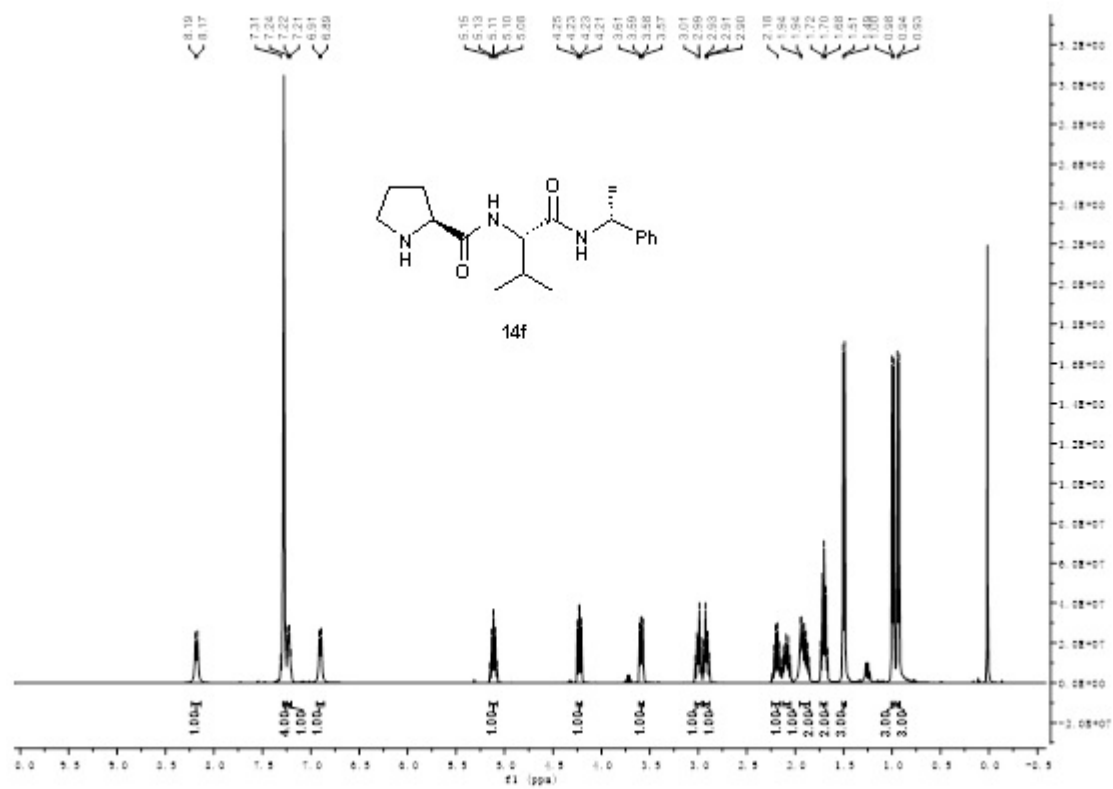


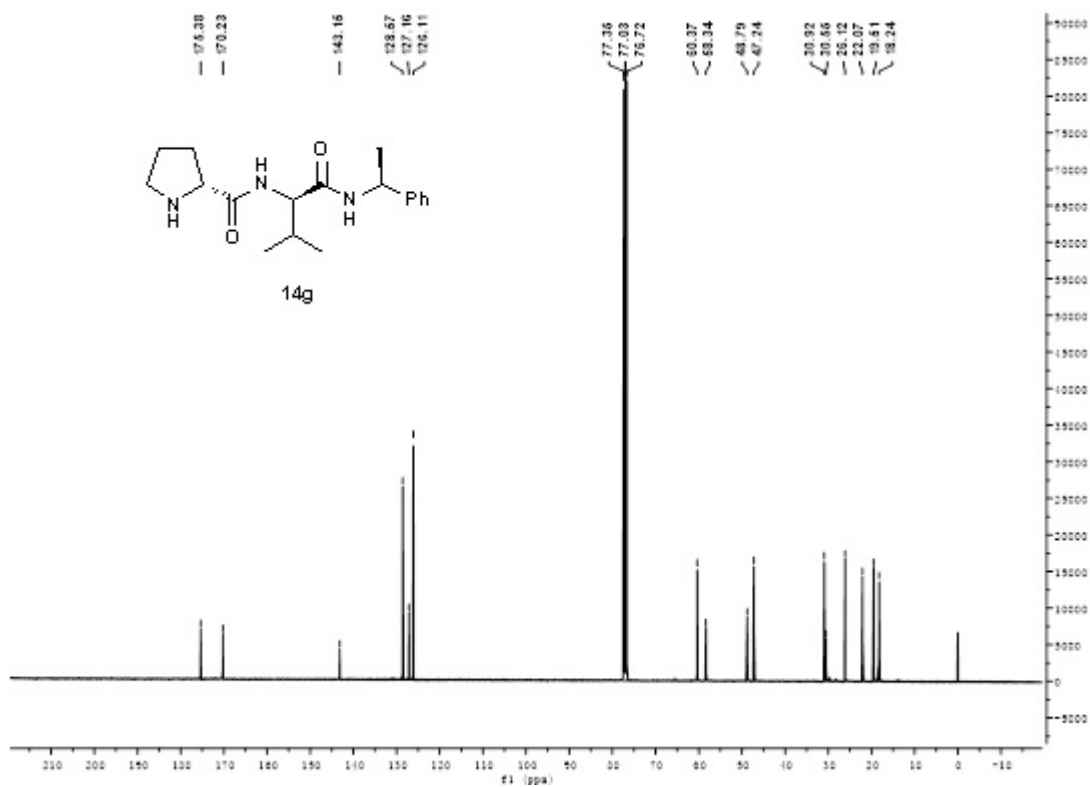
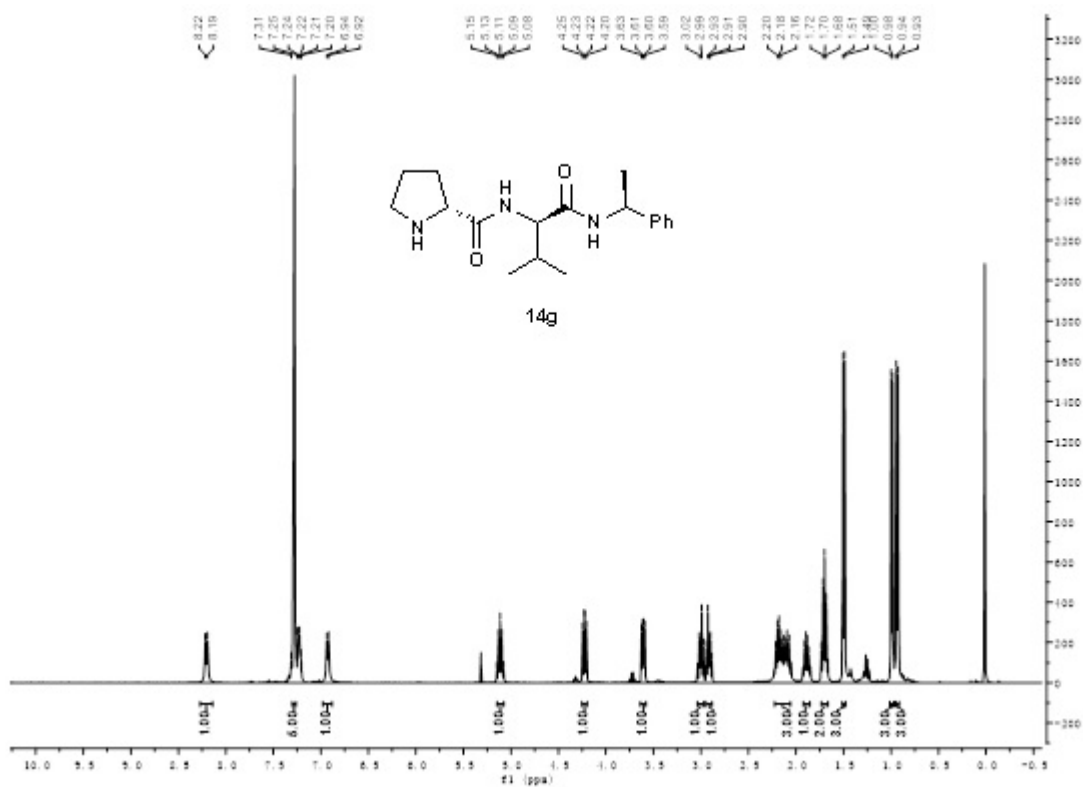




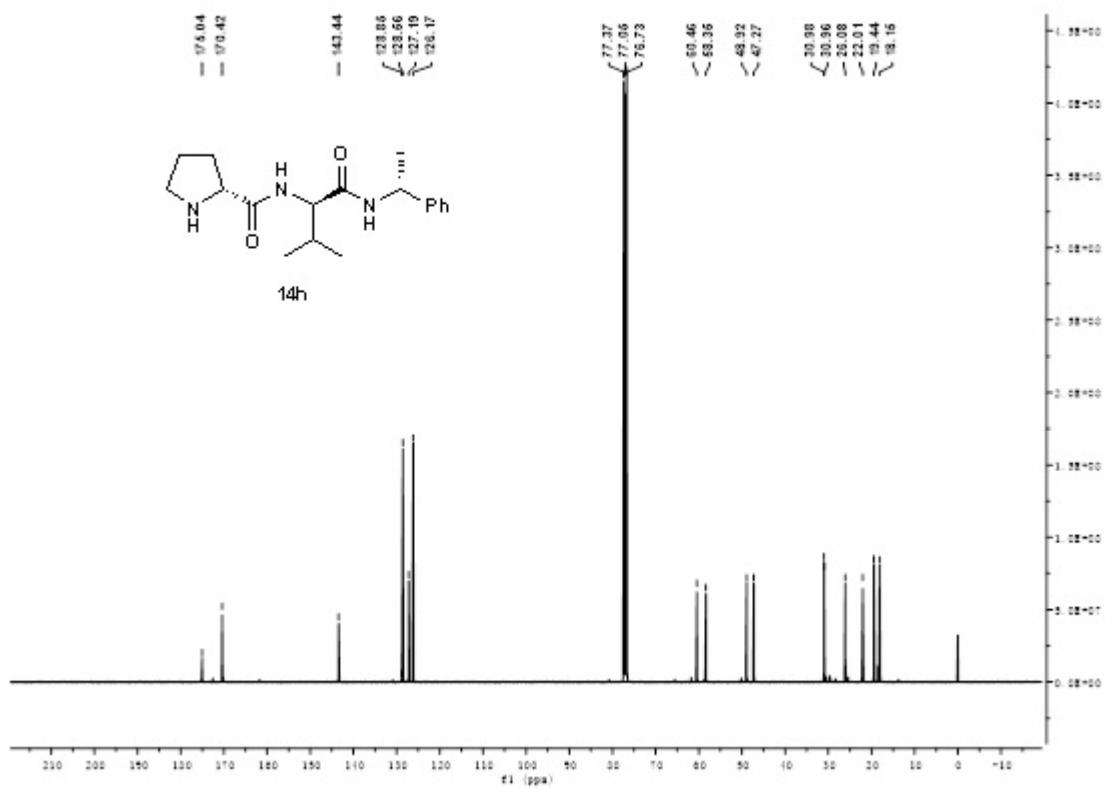
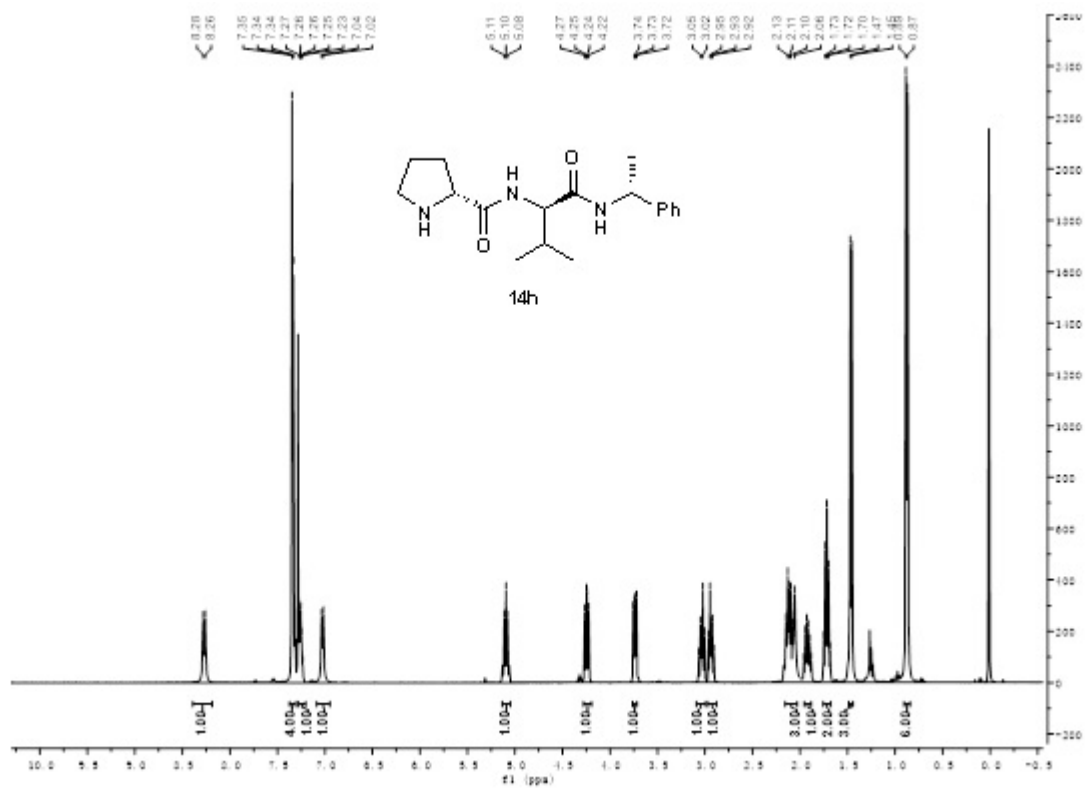


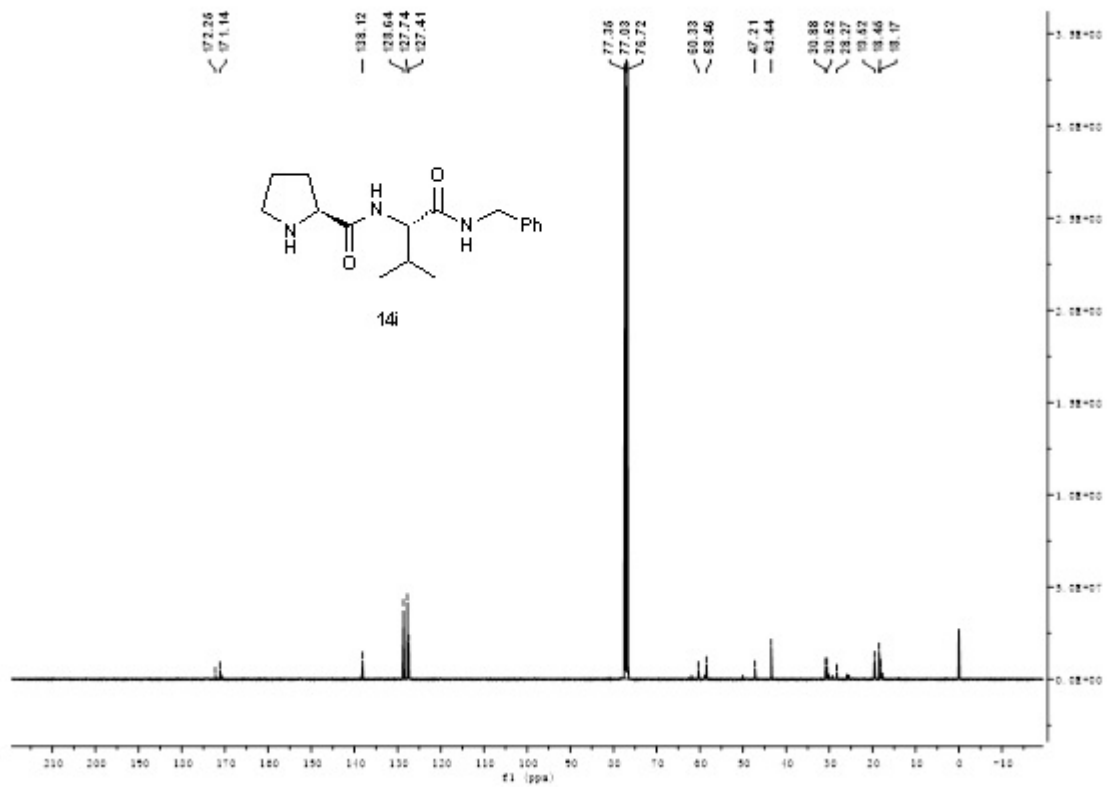
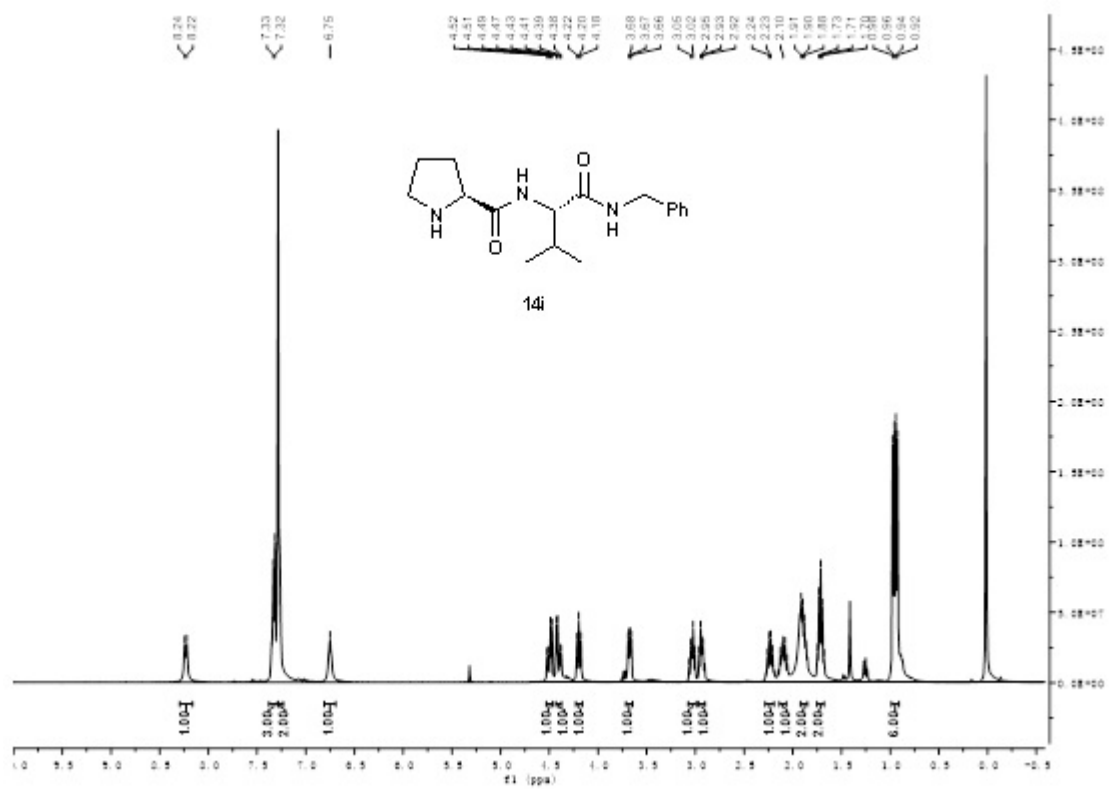






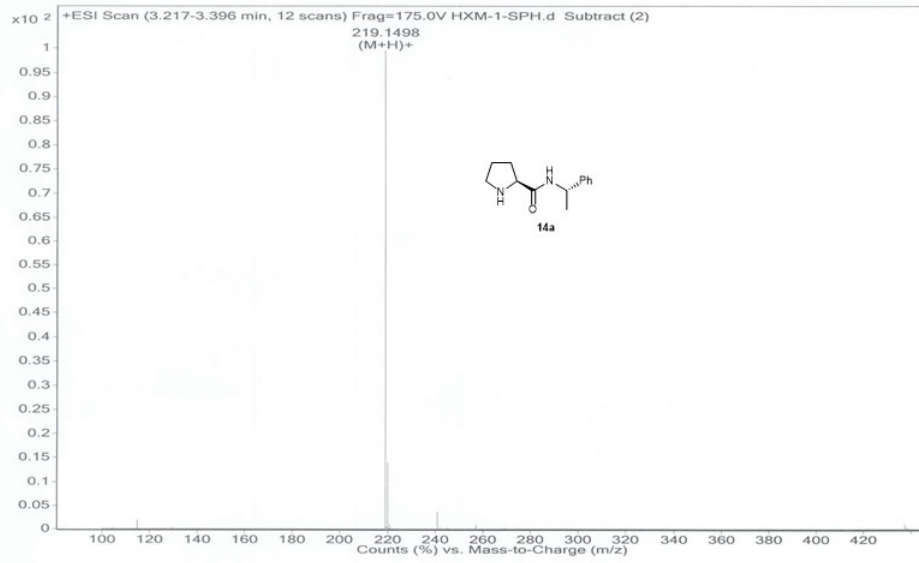






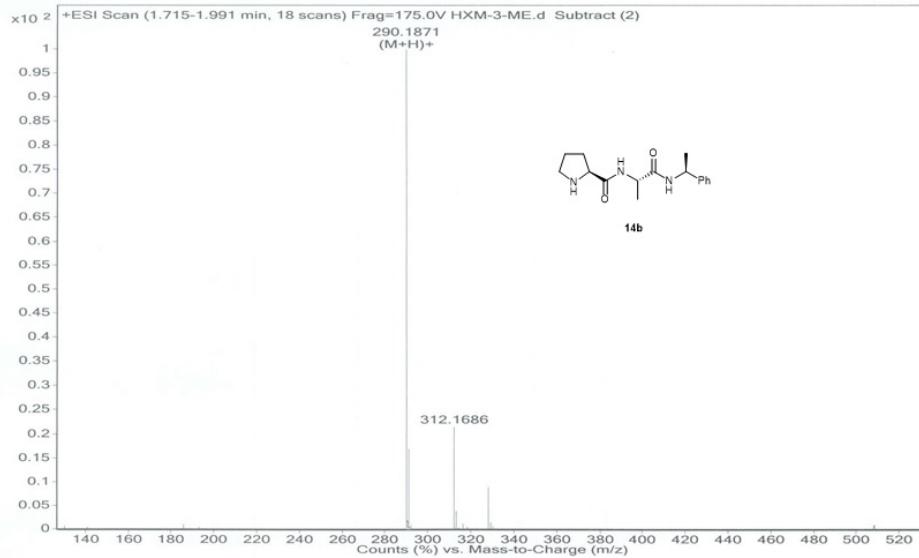
18

Sample Name	lc/ms	Position	P1-A3	Instrument Name	Instrument 1	User Name
Inj Vol	1	InjPosition		SampleType	Sample	IRM Calibration Status
Data Filename	HXM-1-SPH.d	ACQ Method	chen-ms.m	Comment		Acquired Time



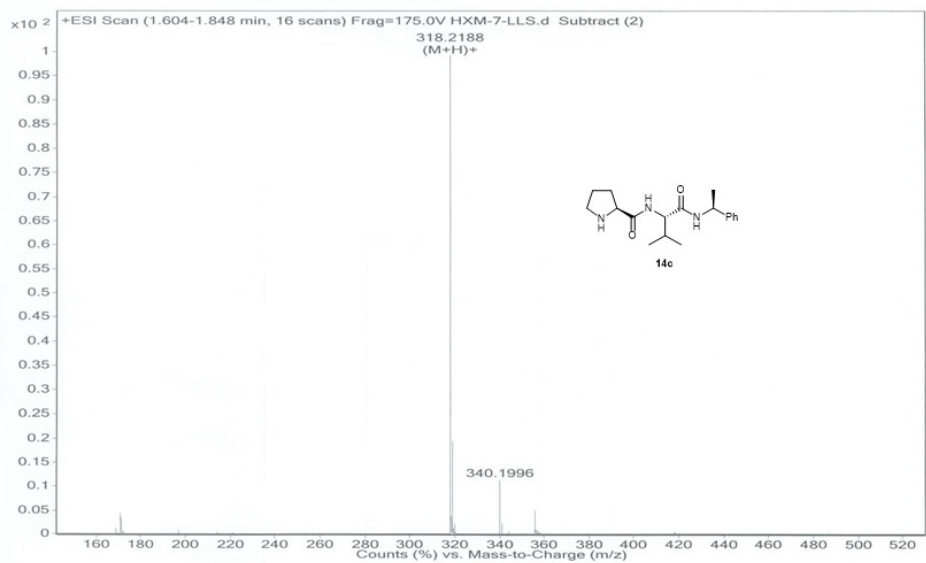
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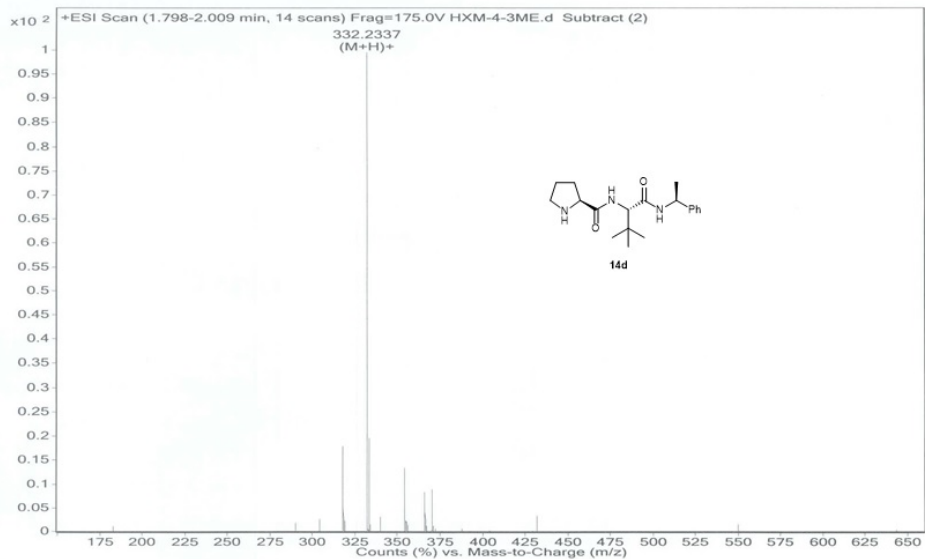
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Sample Name	lc/ms	Position	P1-A9	Instrument Name	Instrument 1	User Name	IRM Calibration Status	Some Ions Missed
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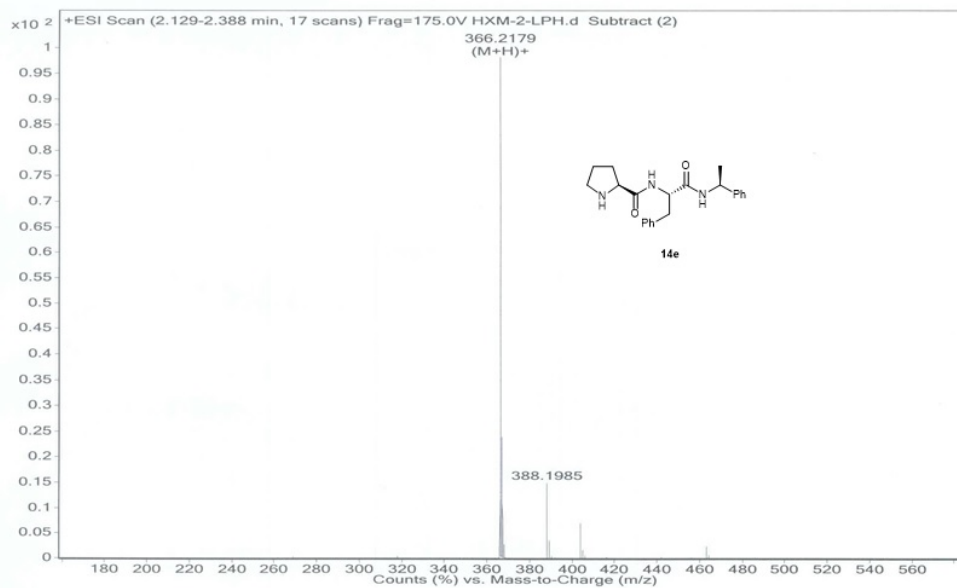
16

Sample Name	lc/ms	Position	P1-A6	Instrument Name	Instrument 1	User Name	IRM Calibration Status	Some Ions Missed
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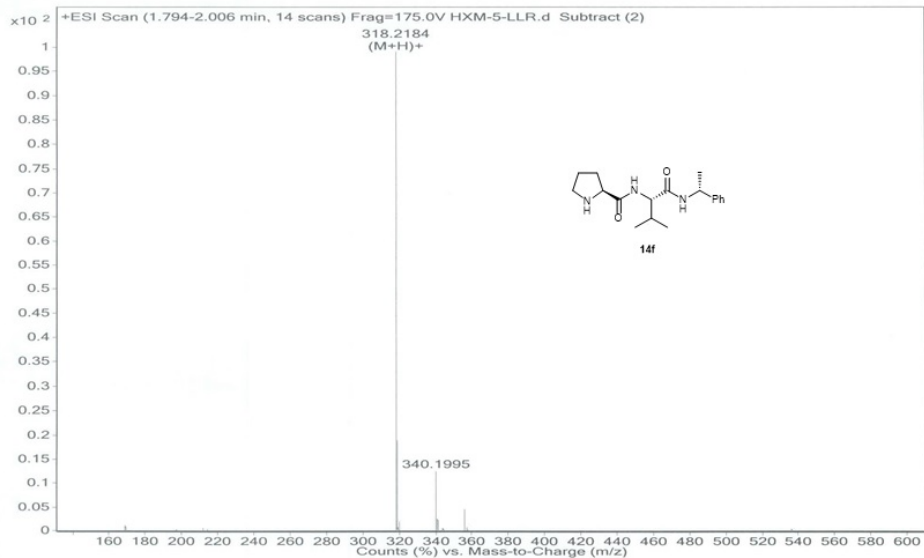
14

Sample Name	lc/ms	Position	P1-A4	Instrument Name	Instrument 1	User Name	IRM Calibration Status	Some Ions Missed
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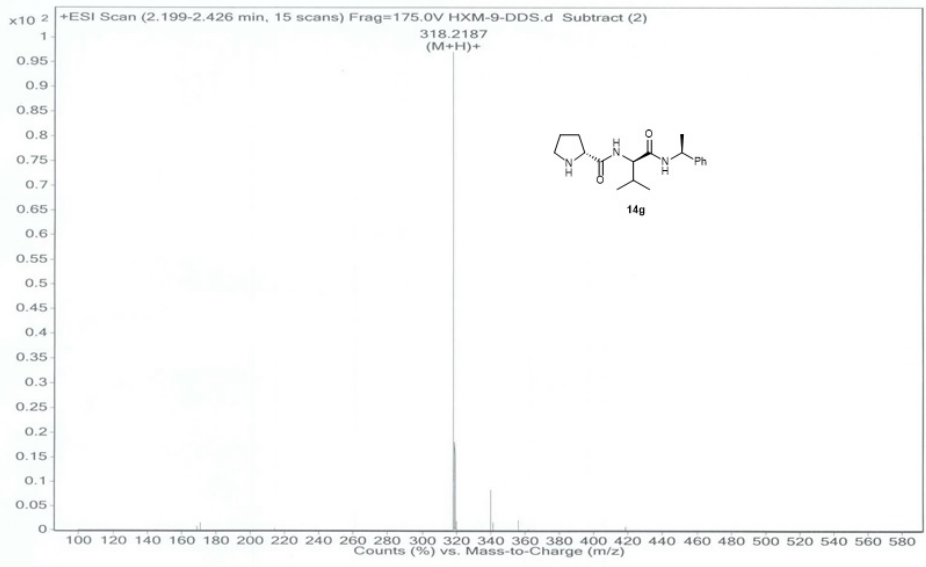
19

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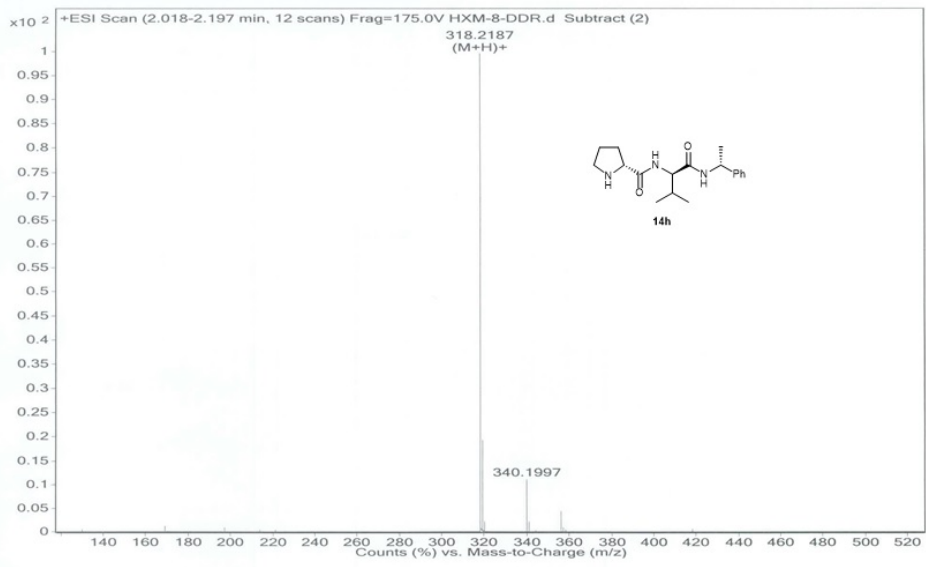
22

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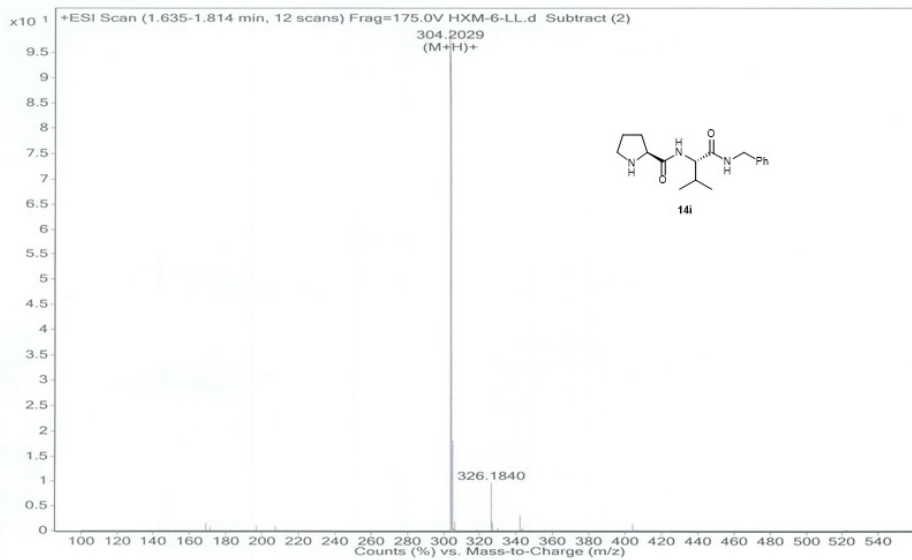
21

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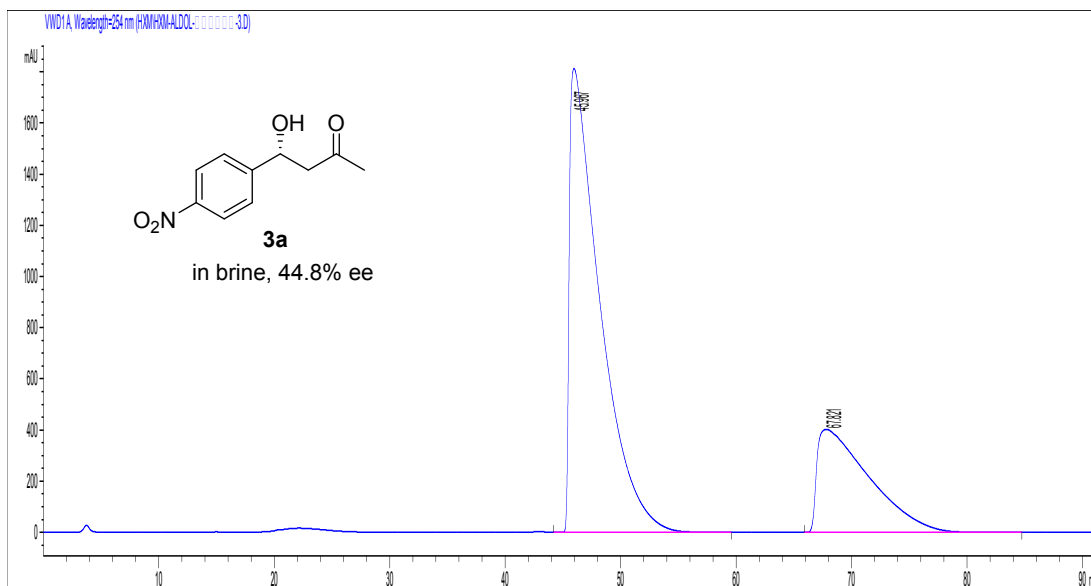
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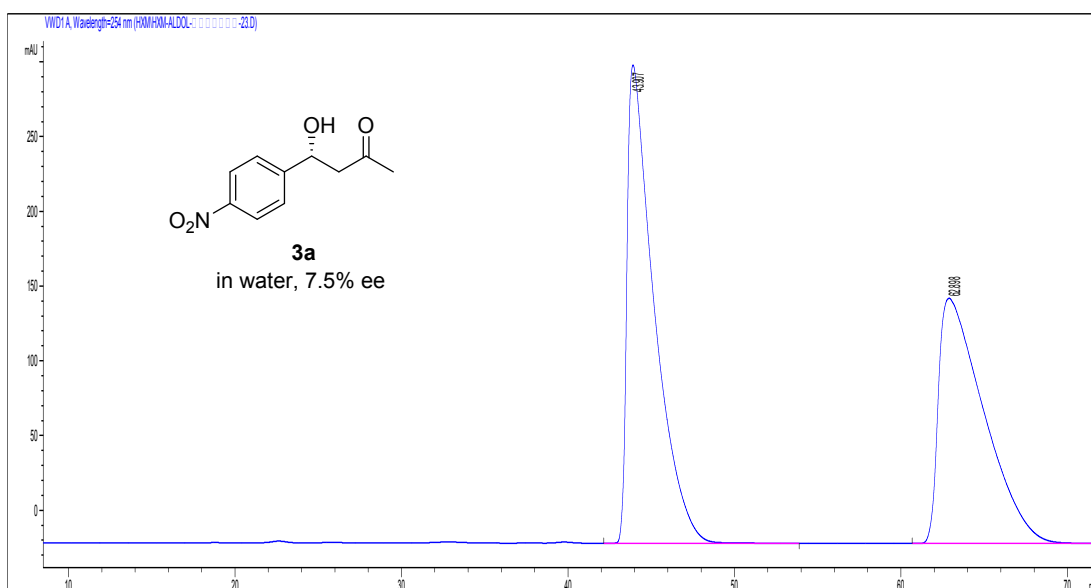
## HPLC charts for aldol adducts 3a-j, 15a-k

### (*R*)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (**3a**)

80% yield, 44.8% e.e. in brine, 77% yield, 7.5% e.e. in water at r.t. for 24 h, determined by HPLC analysis (Chiralcel AS-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	45.967	332276	1813.4	2.5217	0.165	72.409
2	67.821	126610.8	402	4.122	0.199	27.591

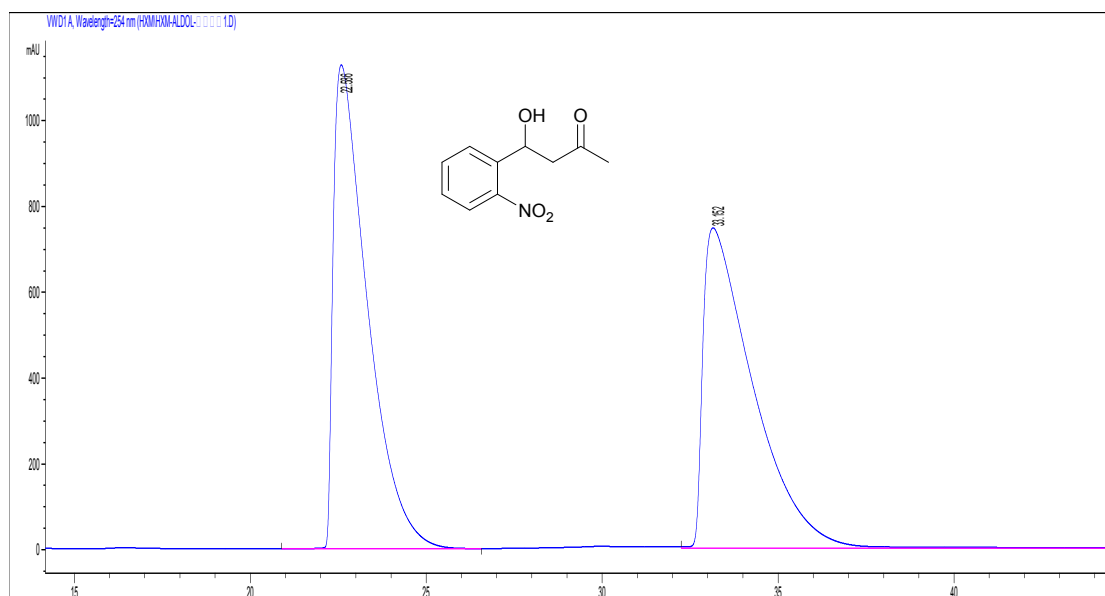


#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	43.907	36065.9	319.8	1.5756	0.261	53.775
2	62.898	31002.6	164	2.4736	0.287	46.225

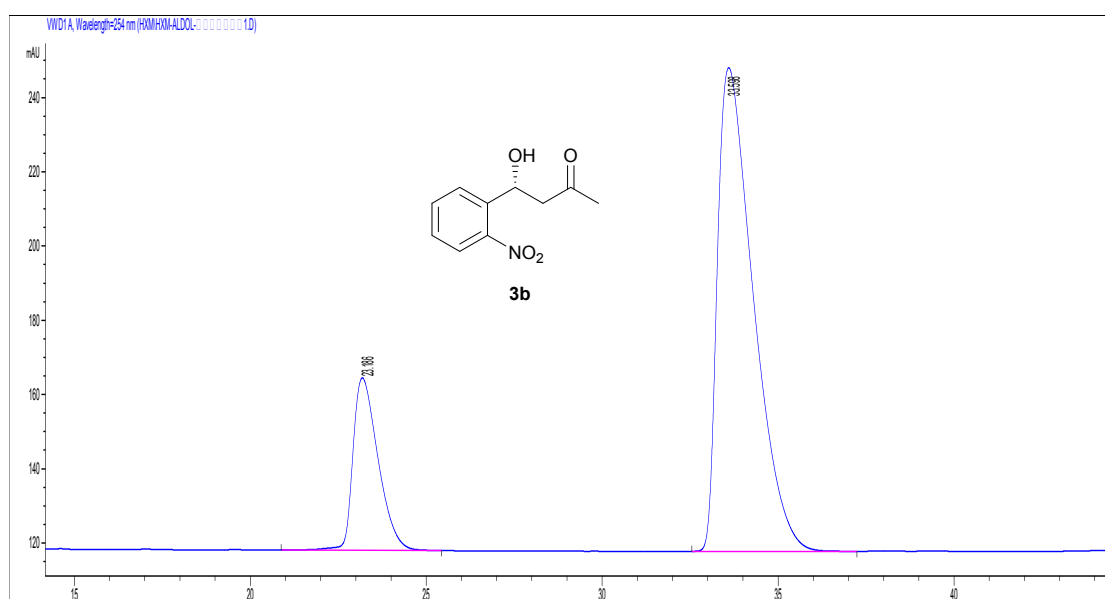


*(R)*-4-hydroxy-4-(2-nitrophenyl)butan-2-one (**3b**)

82% yield, 59.9% e.e. determined by HPLC analysis (Chiralcel AS-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



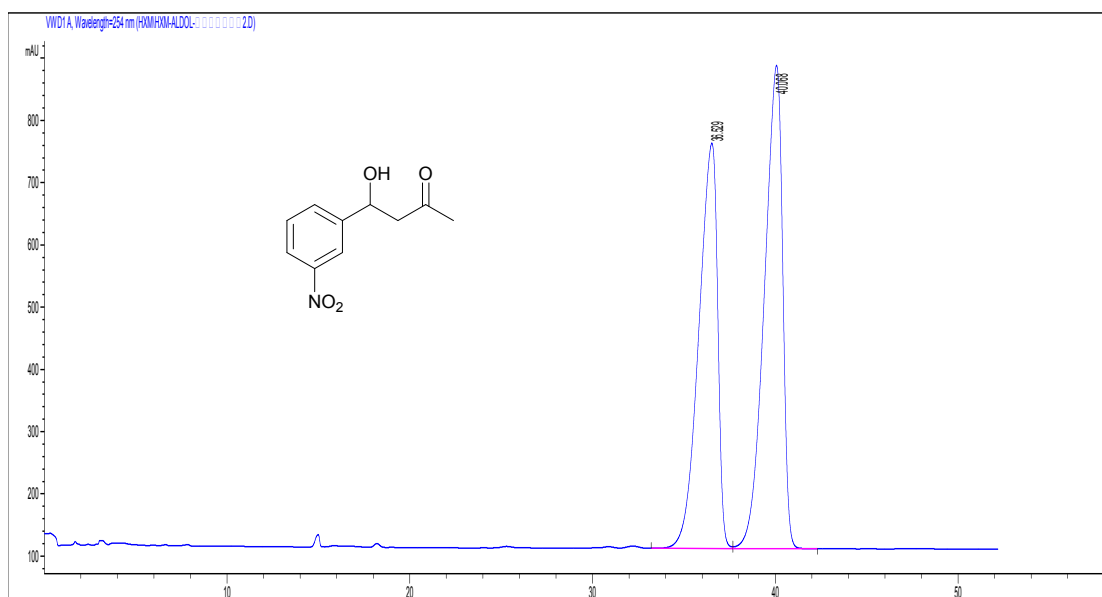
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	22.586	75853.8	1127.4	1.0169	0.281	50.430
2	33.152	74559.2	747	1.4365	0.23	49.570



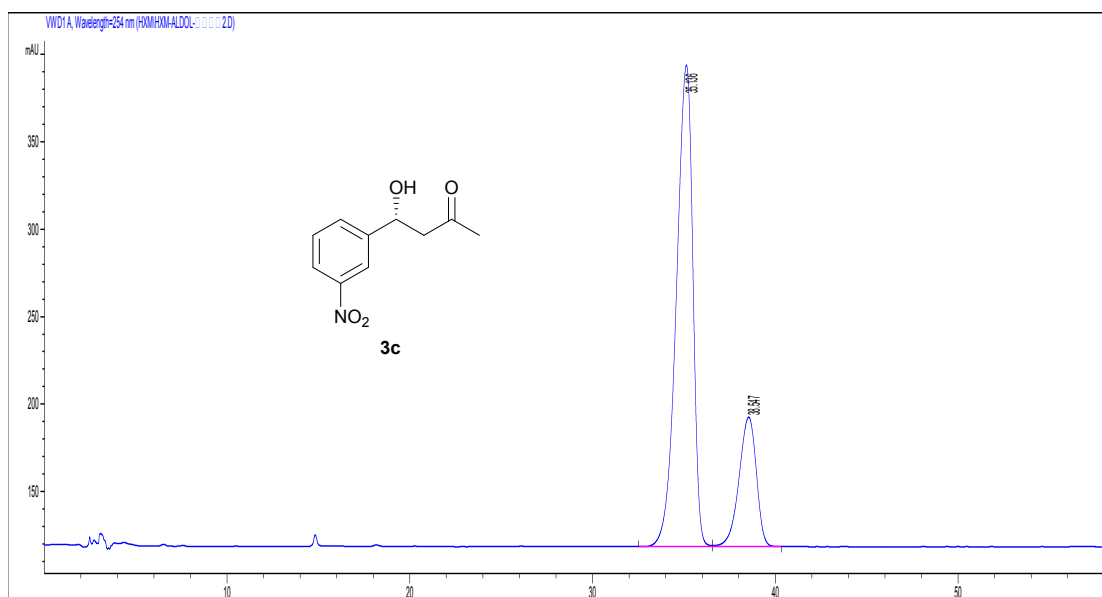
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	23.186	2308	46.5	0.7676	0.573	20.038
2	33.598	9210.1	130.3	1.0727	0.426	79.962

*(R)*-4-hydroxy-4-(3-nitrophenyl)butan-2-one (**3c**)

80% yield, 55.6% e.e. determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=98/2, Flow rate: 1.0 mL/min, UV detection at 254 nm).



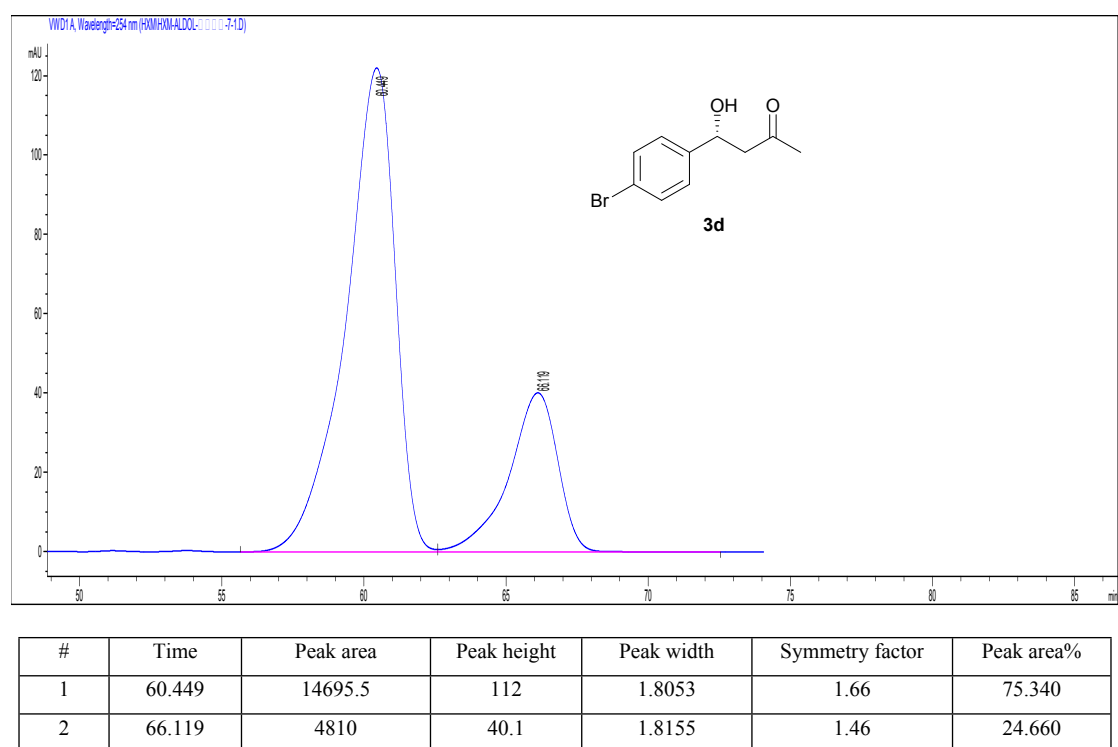
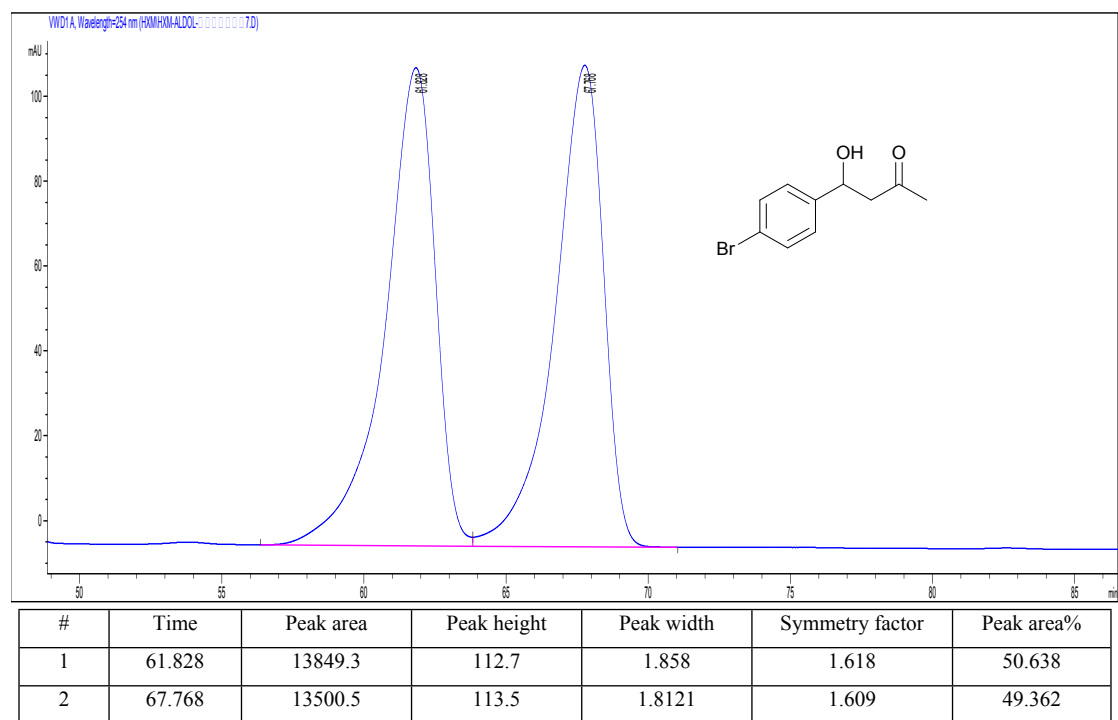
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	36.529	46499.6	651.3	1.143	2.178	46.371
2	40.068	53777.6	776.5	1.06	1.937	53.629



#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	35.136	17178.5	275.2	0.9763	1.51	77.891
2	38.547	4876.1	74	1.0449	1.262	22.109

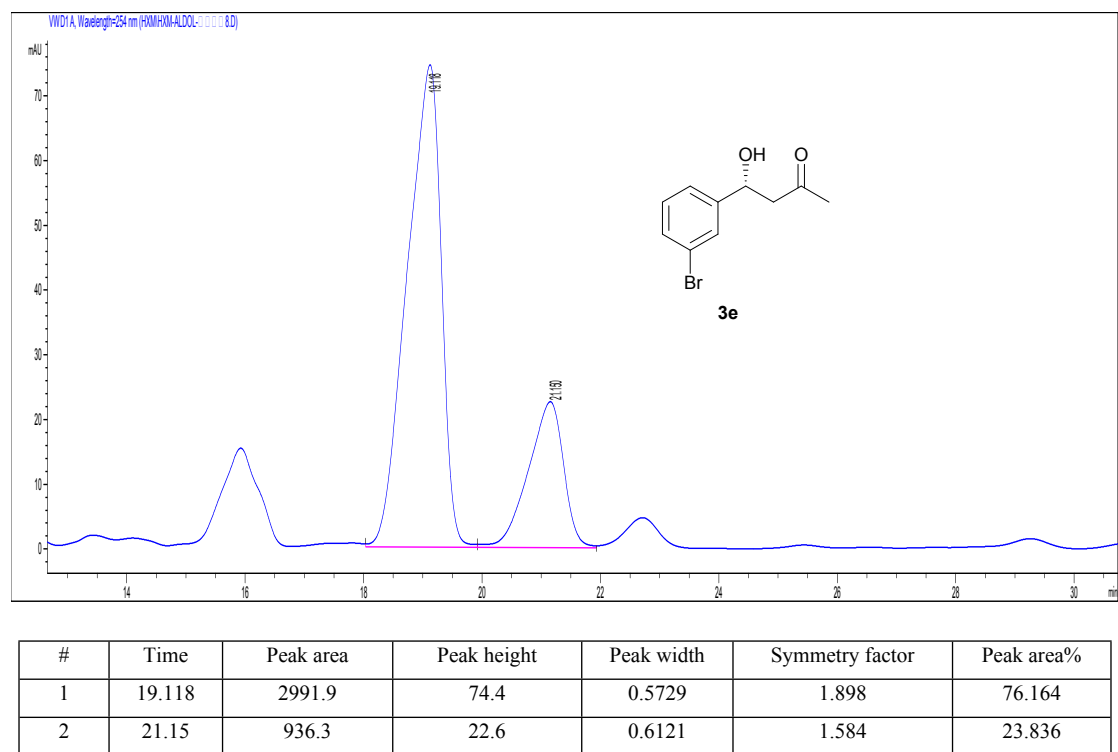
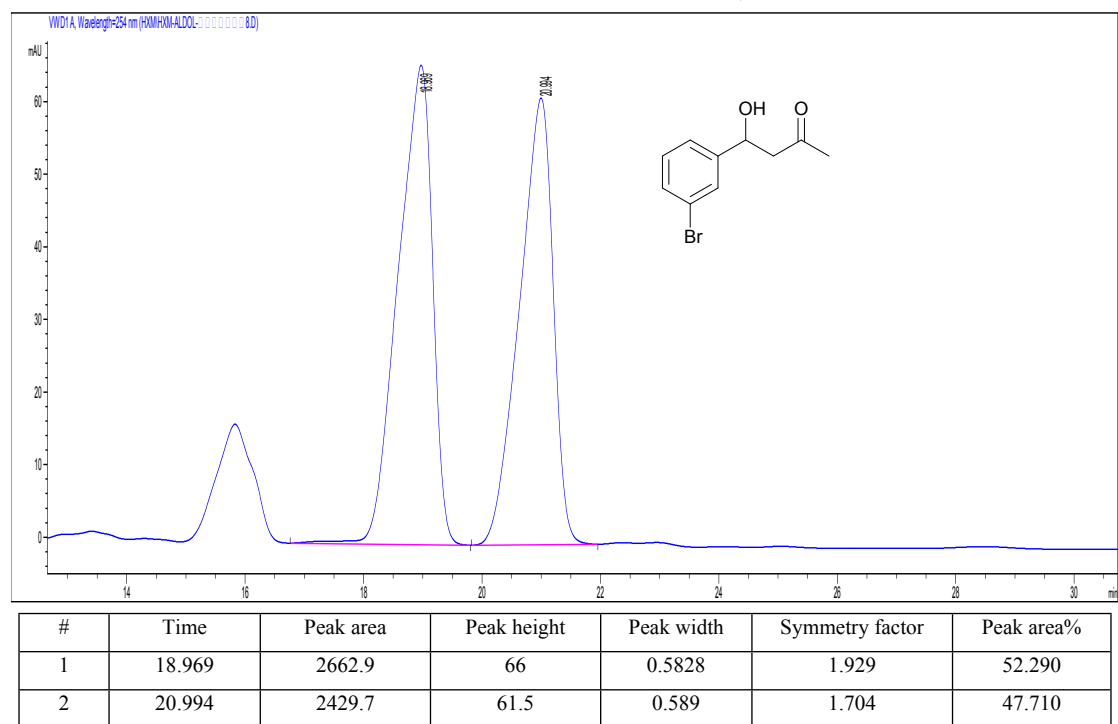
(*R*)-4-hydroxy-4-(4-bromophenyl)butan-2-one (**3d**)

75% yield, 50.7% e.e. determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=95/5, Flow rate: 0.25 mL/min, UV detection at 254 nm).



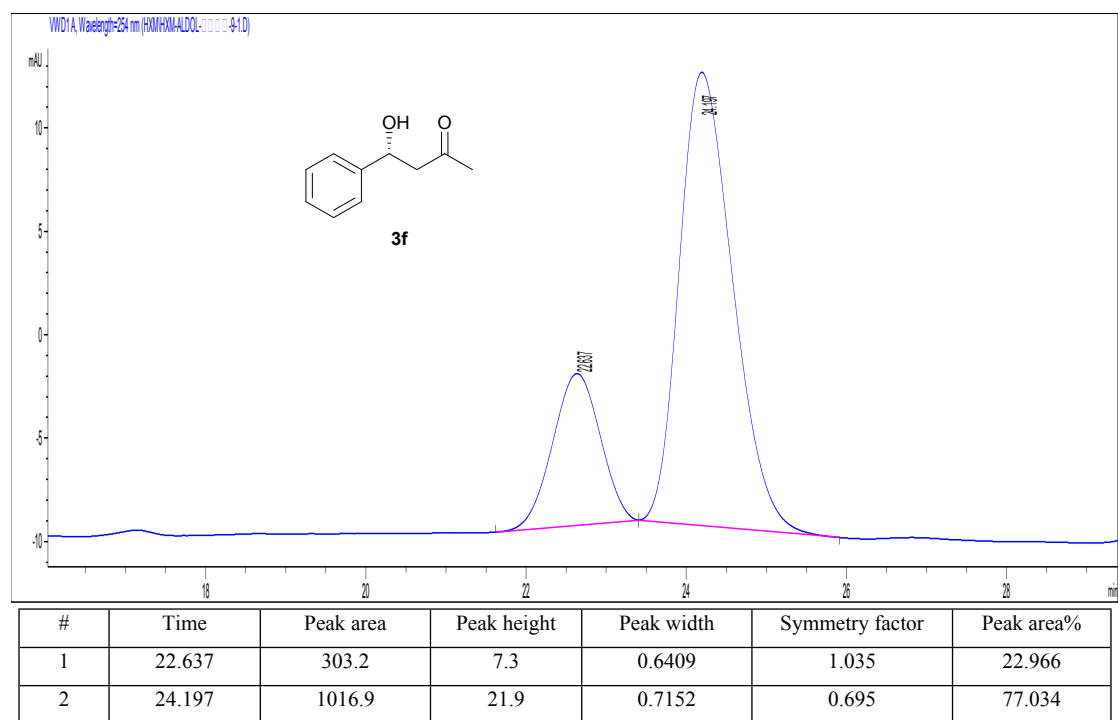
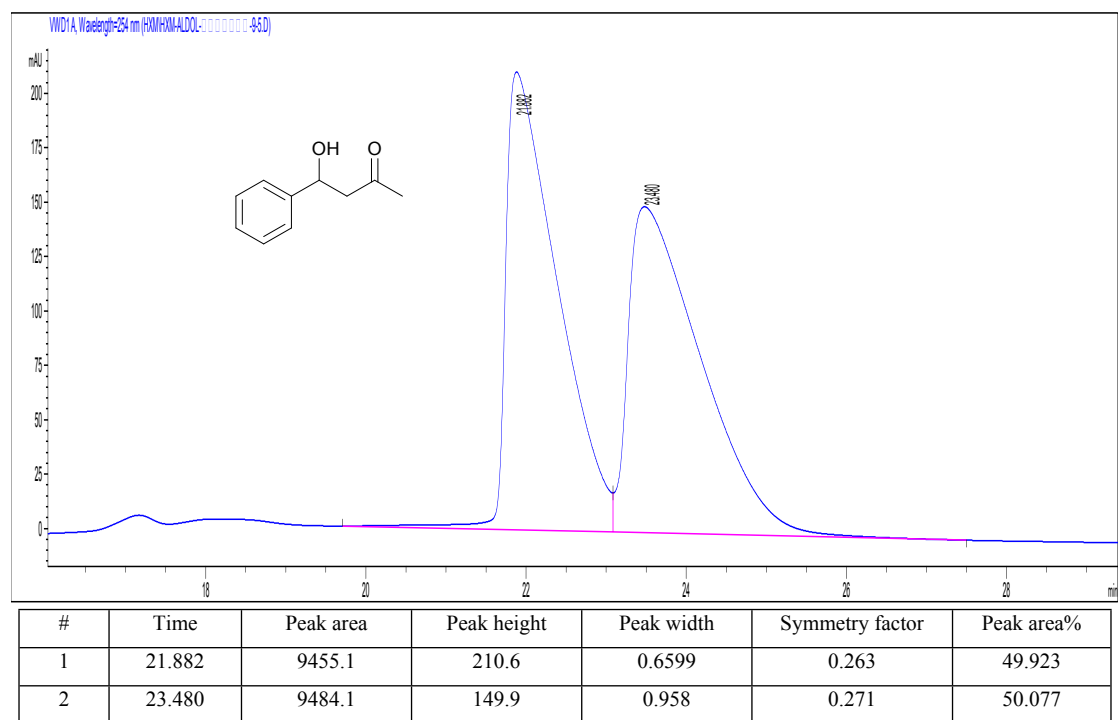
*(R)*-4-hydroxy-4-(3-bromophenyl)butan-2-one (**3e**)

78% yield, 52.3% e.e. determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=95/5, Flow rate: 0.25 mL/min, UV detection at 254 nm).



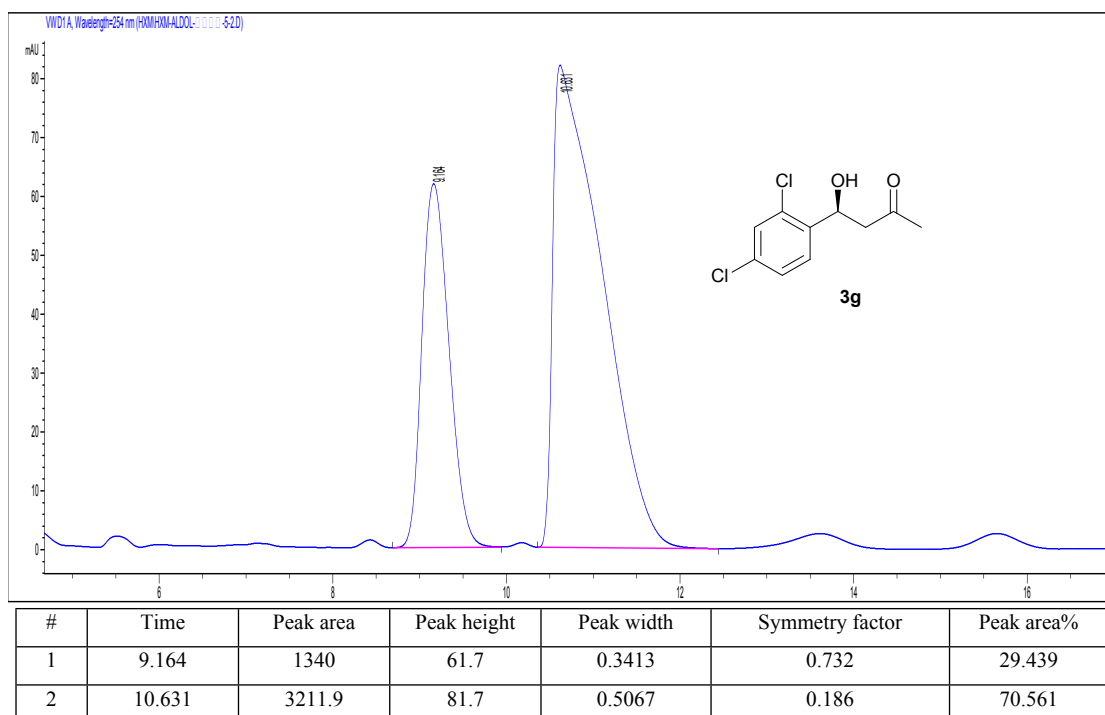
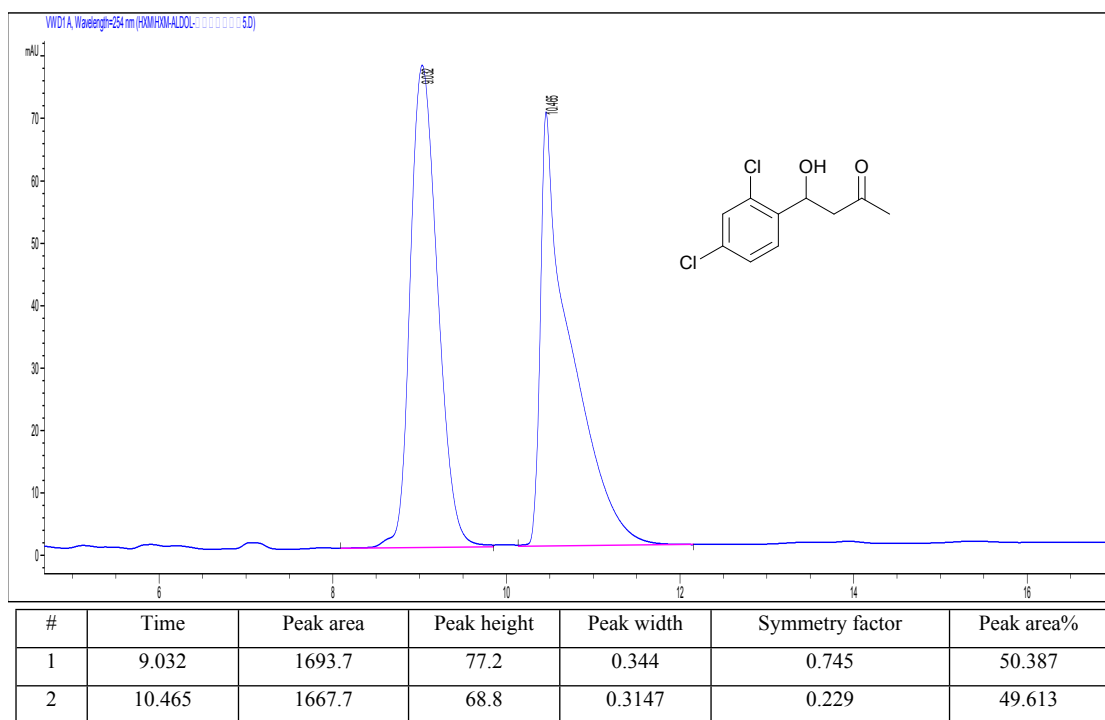
*(R)*-4-hydroxy-4-phenylbutan-2-one (**3f**)

60% yield, 54.1% e.e. determined by HPLC analysis (Chiralcel OD-H column, Hexane/*i*-PrOH=92/8, Flow rate: 0.50 mL/min, UV detection at 254 nm).



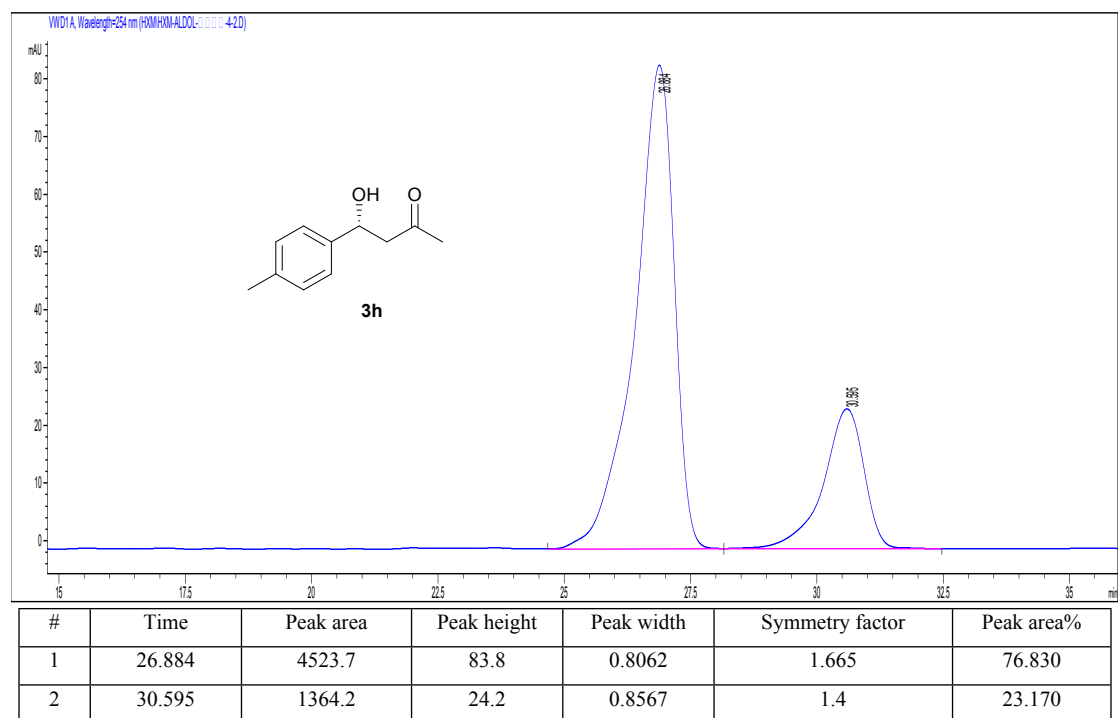
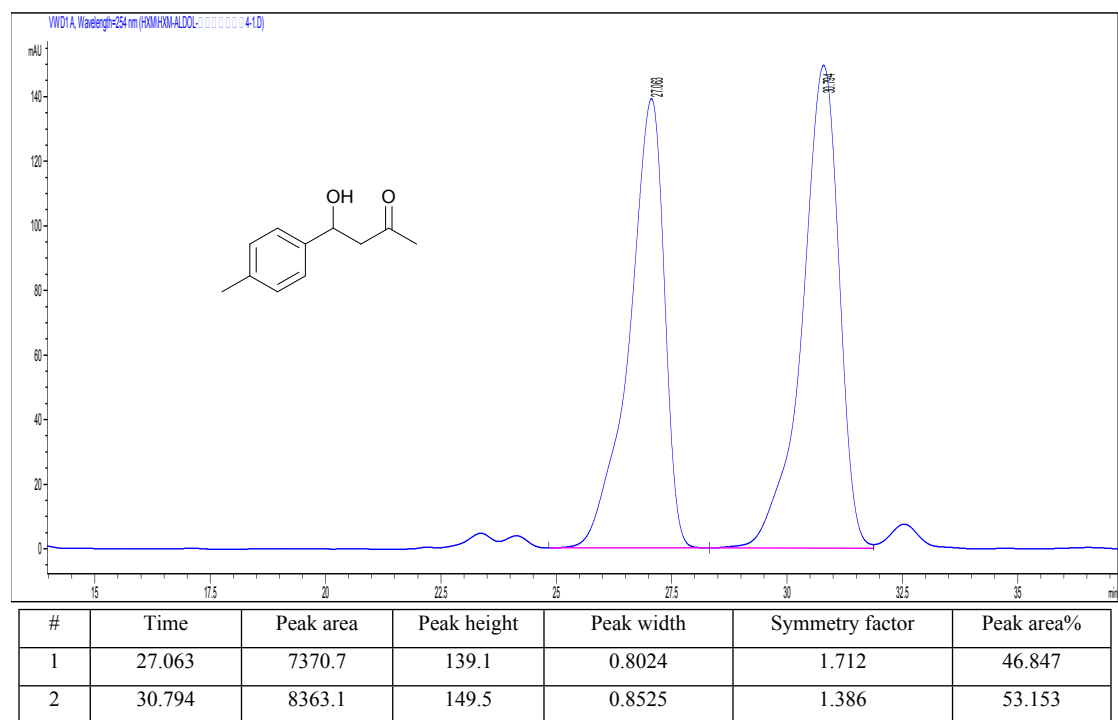
(S)-4-(2,4-dichlorophenyl)-4-hydroxybutan-2-one (**3g**)

67% yield, 41.1% e.e. determined by HPLC analysis (Chiralcel AS-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



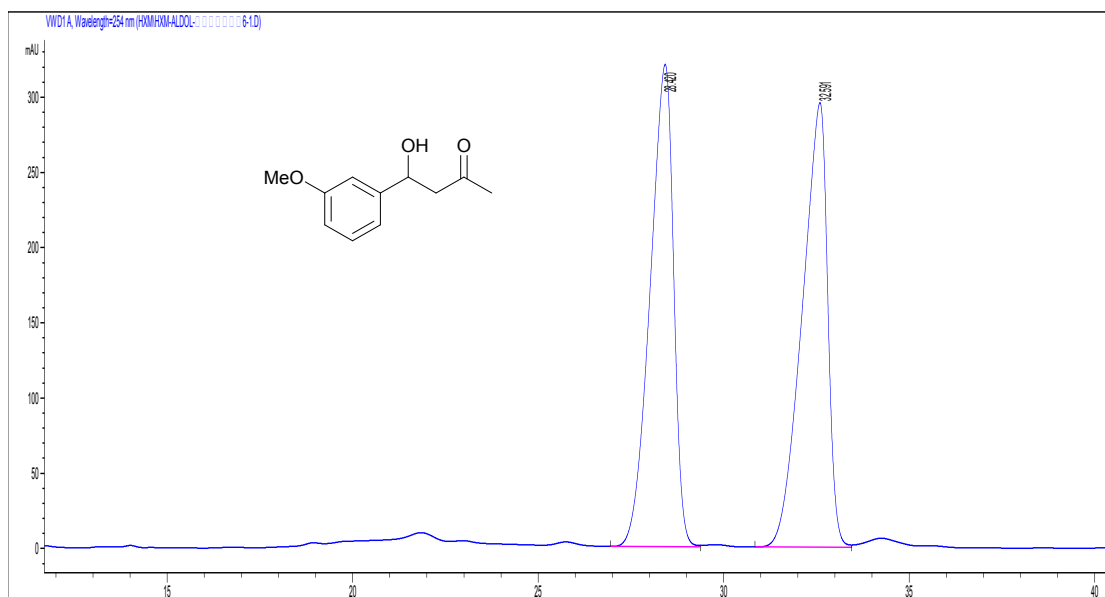
*(R)*-4-hydroxy-4-(*p*-tolyl)butan-2-one (**3h**)

61% yield, 53.7% e.e. determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=95/5, Flow rate: 0.5 mL/min, UV detection at 254 nm).

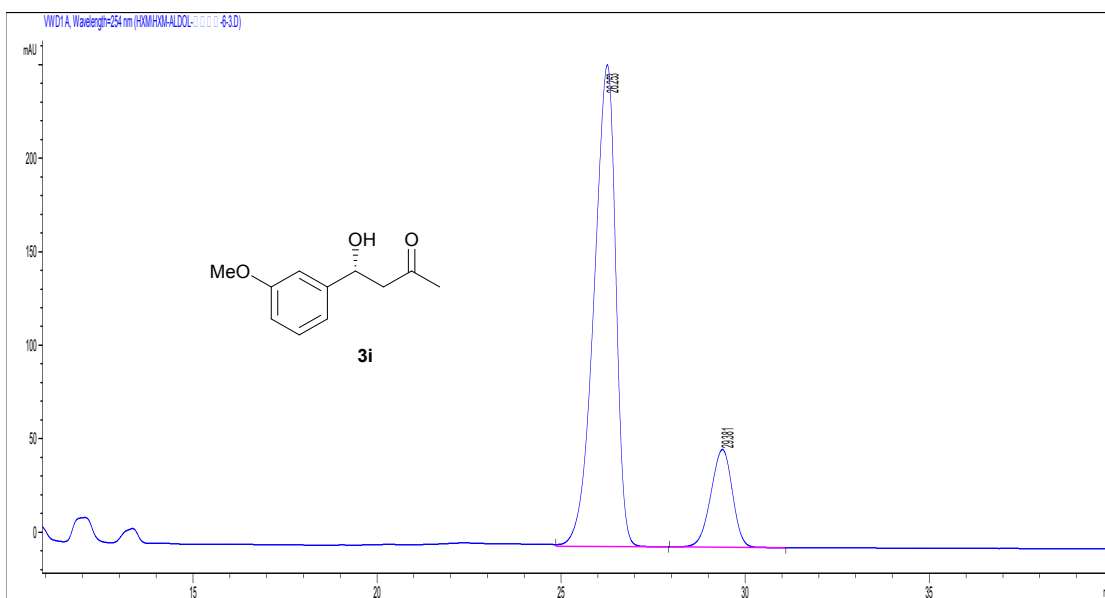


*(R)*-4-hydroxy-4-(3-methoxyphenyl)butan-2-one (**3i**)

65% yield, 66.3% e.e. determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 0.5 mL/min, UV detection at 254 nm).



#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	28.42	14064.6	320.5	0.68	1.692	50.040
2	32.591	14041.8	295.5	0.7223	2.151	49.960

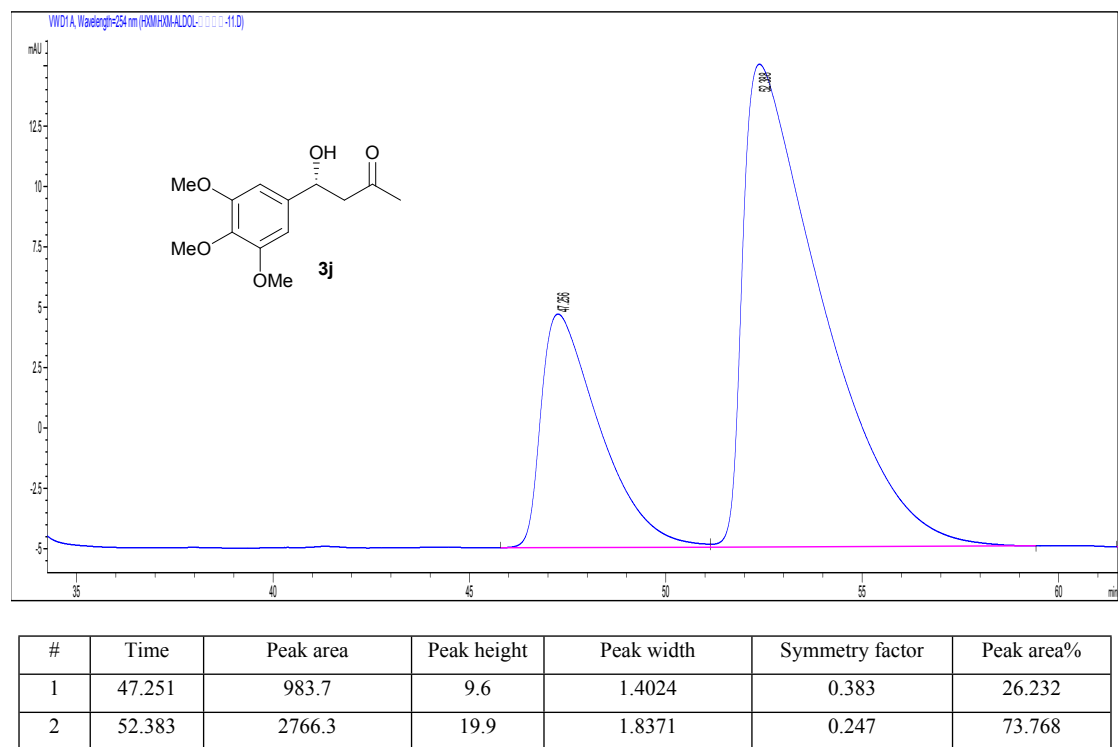
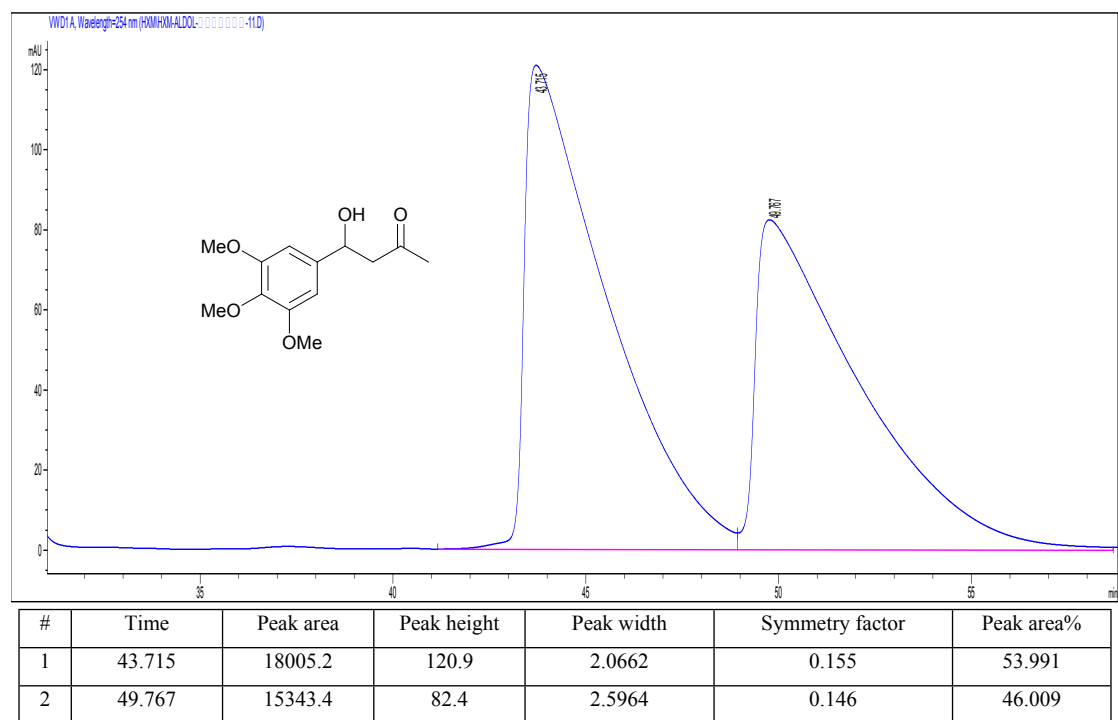


#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	26.253	10563.5	257.6	0.6384	1.511	83.165
2	29.381	2138.4	52.3	0.6453	1.127	16.835



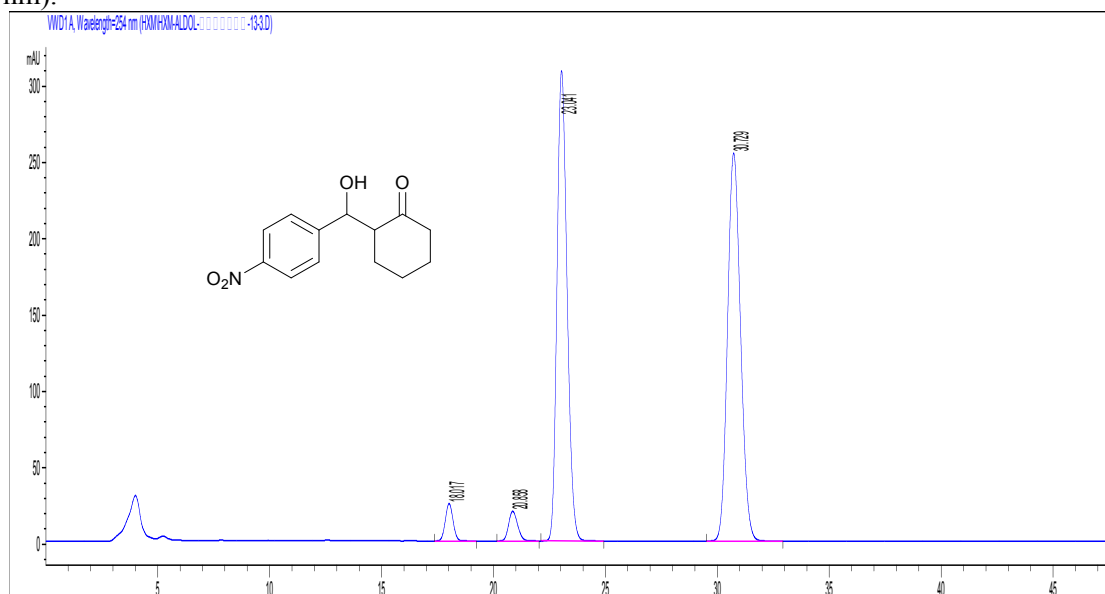
*(R)*-4-hydroxy-4-(3,4,5-trimethoxyphenyl)butan-2-one (**3j**)

78% yield, 47.5% e.e. determined by HPLC analysis (Chiralcel OD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 0.5 mL/min, UV detection at 254 nm).

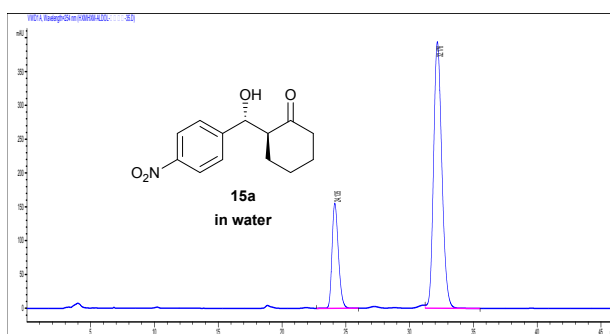


**(S)-2-((R)-hydroxy(4-nitrophenyl)methyl)cyclohexan-1-one (15a)**

82% yield, anti/syn=96/4, anti-product 87.7 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	18.017	588.7	24.5	0.3767	0.936	2.802
2	20.858	545.3	19.5	0.436	0.803	2.596
3	23.041	9610.6	308.1	0.486	0.783	45.744
4	30.729	10264.9	254.2	0.6292	0.852	48.858



**In water, 53.6% ee**

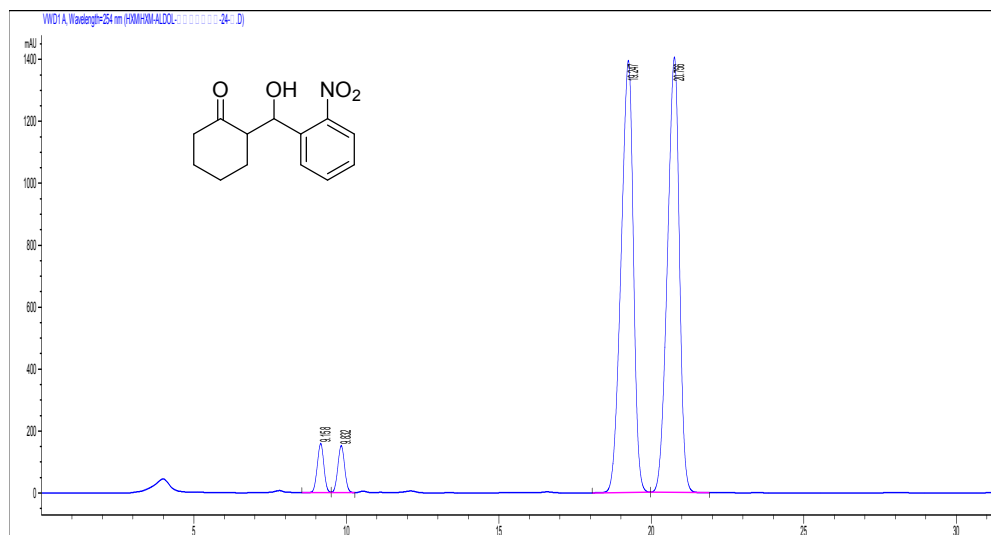
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	24.135	5370.5	155.3	0.5355	0.729	23.173
2	32.176	17805.4	393.9	0.7033	0.801	76.827

**In brine, 87.7% ee**

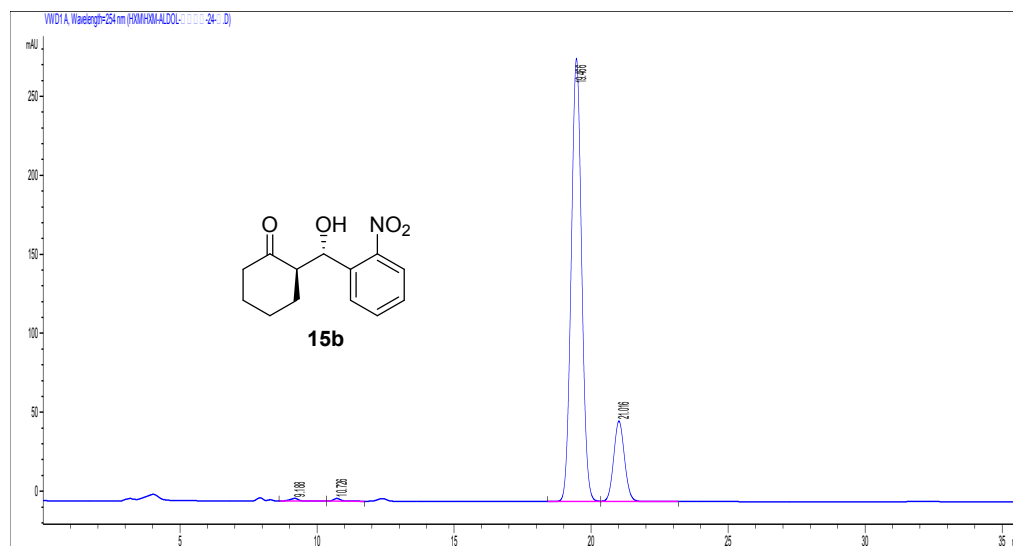
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	18.372	1075.4	42.8	0.3914	0.897	1.511
2	20.971	1608.1	55.1	0.4523	0.696	2.259
3	23.321	4204.8	131.9	0.4958	0.806	5.906
4	31.228	64302.7	1465	0.6671	1.375	90.324

*(R)*-2-((*S*)-hydroxy(2-nitrophenyl)methyl)cyclohexan-1-one (**15b**)

89% yield, anti/syn=99/1, anti-product 68.0 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



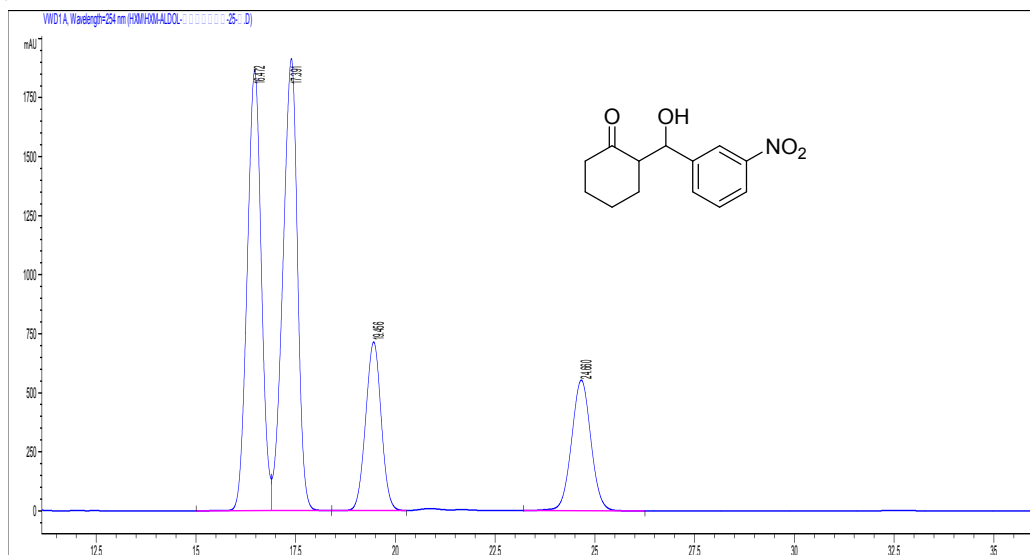
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	9.158	2410.1	158.9	0.236	1.057	2.936
2	9.832	2368.9	152.1	0.2427	0.972	2.886
3	19.247	39030.3	1394.9	0.4355	1.404	47.560
4	20.756	38266.6	1405.6	0.4226	1.336	46.618



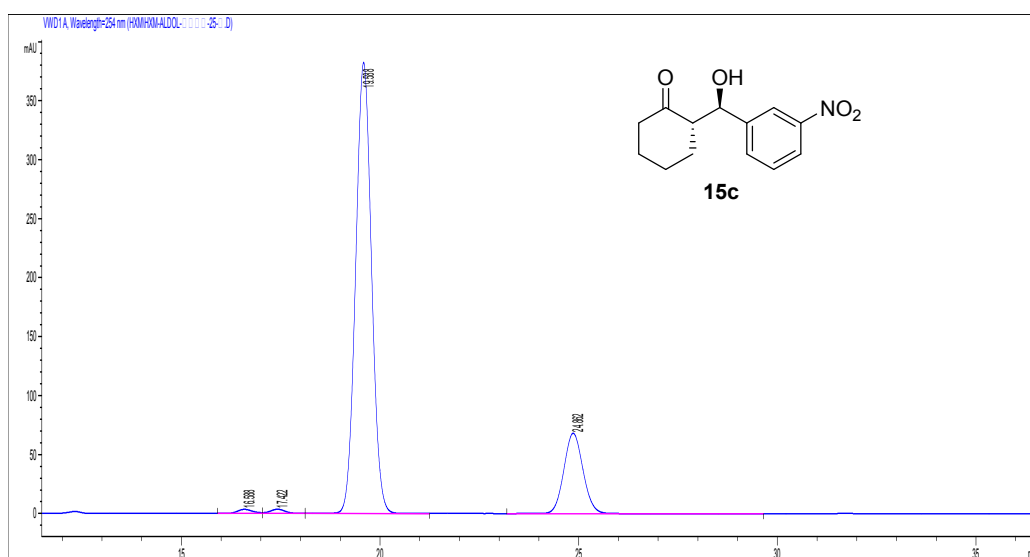
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	9.188	43.4	1.7	0.3632	0.959	2.936
2	10.726	33.4	1.7	0.292	0.806	2.886
3	19.247	7383.2	280.4	0.4112	0.966	83.266
4	20.756	1406.9	51	0.4258	0.911	15.867

*(S)*-2-((*R*)-hydroxy(3-nitrophenyl)methyl)cyclohexan-1-one (**15c**)

91% yield, anti/syn=99/1, anti-product 64.6 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



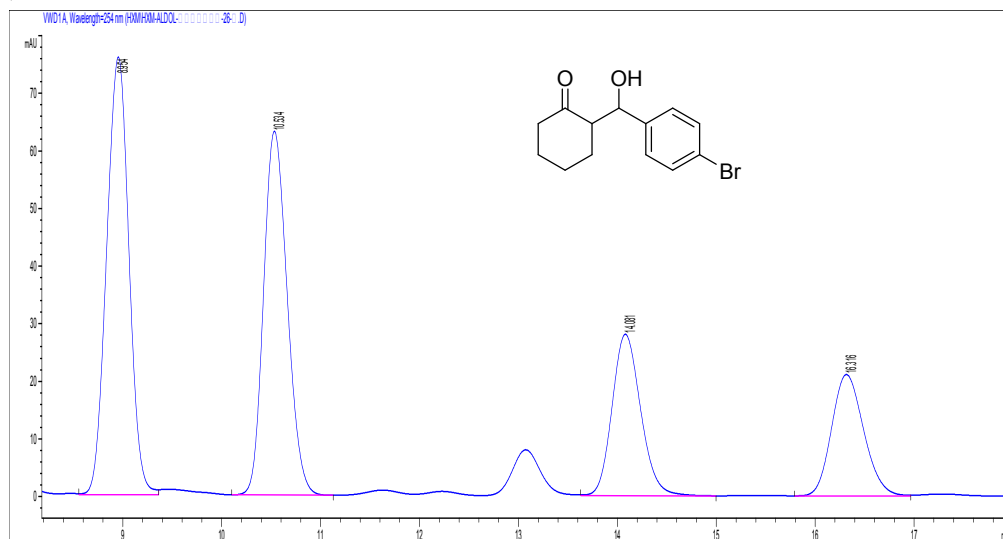
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	16.472	45738.7	1862.4	0.3865	1.064	34.559
2	17.391	48624.8	1913.4	0.3965	1.297	36.740
3	19.456	19306.1	713.8	0.4235	1.026	14.587
4	24.66	18678.2	553.1	0.5299	0.991	14.113



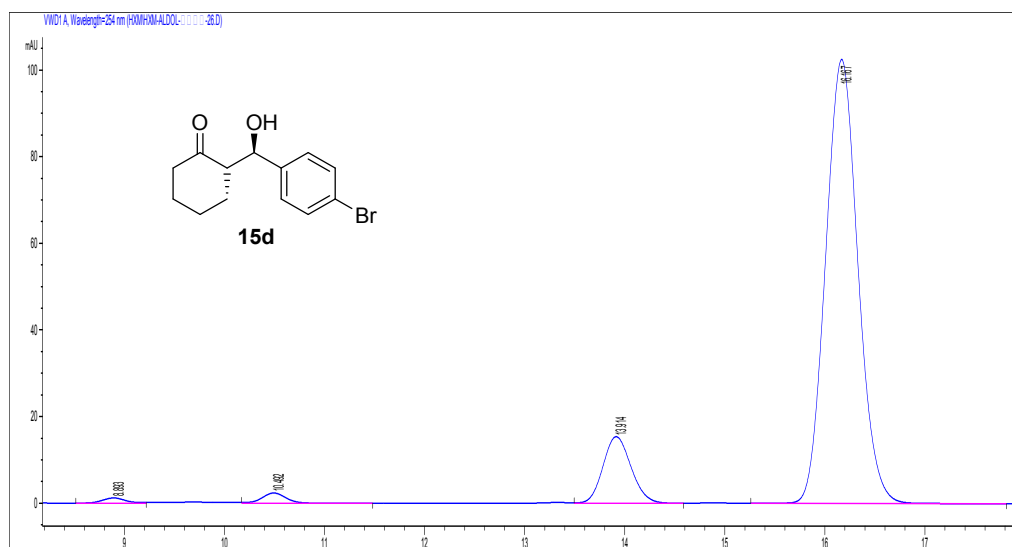
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	16.588	95.9	3.6	0.4101	0.795	0.734
2	17.422	96.7	3.7	0.4041	0.952	0.740
3	19.588	10594.6	382.4	0.4313	0.971	81.074
4	24.862	2280.6	68.1	0.5186	0.906	17.452

(S)-2-((R)-hydroxy(4-bromophenyl)methyl)cyclohexan-1-one (**15d**)

85% yield, anti/syn=98/2, anti-product 76.8 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



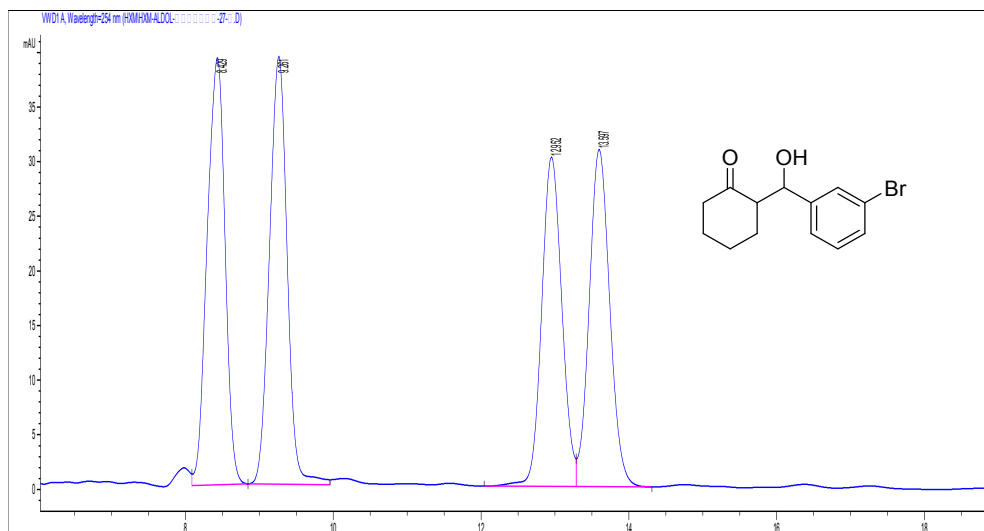
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	8.954	1190.9	75.9	0.2469	1.027	36.366
2	10.534	1046.7	63.1	0.2616	0.808	31.963
3	14.081	562.7	28	0.3143	0.83	17.183
4	16.316	474.4	21.1	0.3509	0.821	14.487



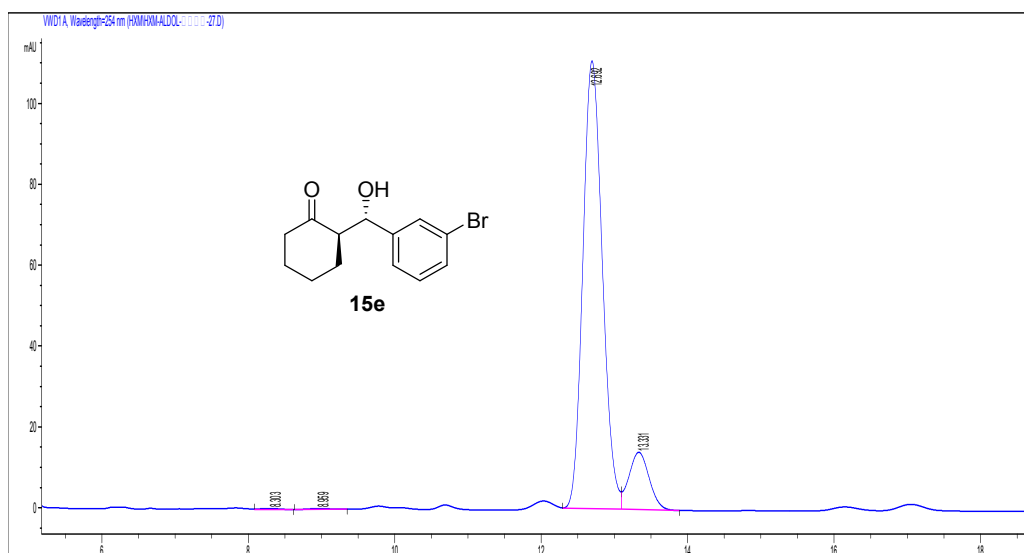
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	8.893	19.7	1.2	0.2505	0.898	0.741
2	10.492	40.3	2.4	0.2618	0.927	1.515
3	13.914	301.1	15.4	0.3043	0.858	11.330
4	16.167	2296.4	102.4	0.3496	0.935	86.414

*(R)*-2-((*S*)-hydroxy(3-bromophenyl)methyl)cyclohexan-1-one (**15e**)

86% yield, anti/syn=99/1, anti-product 76.4 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



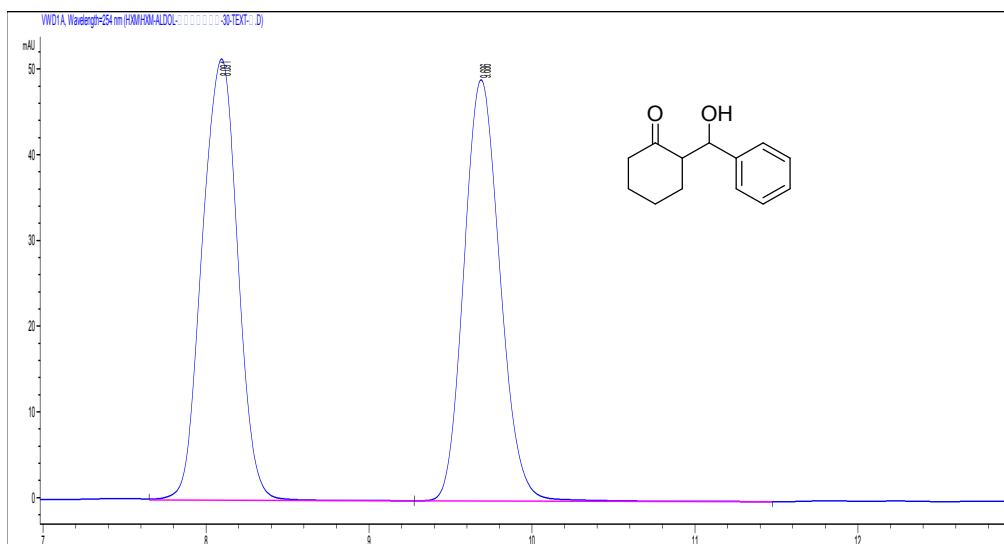
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	8.429	657	39.1	0.2761	1.217	26.523
2	9.261	651.5	39.1	0.2583	1.021	26.299
3	12.952	572.3	30.1	0.2975	0.925	23.101
4	13.597	596.4	30.8	0.3016	0.898	24.077



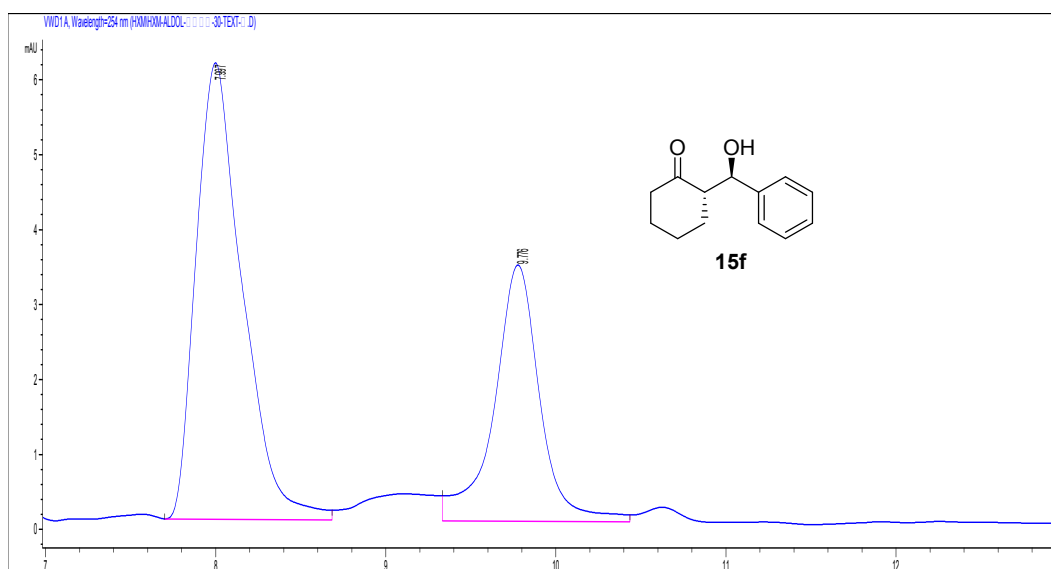
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	8.303	3.9	2.3E-1	0.265	1.244	0.166
2	8.959	4.3	2.4E-1	0.2762	0.816	0.184
3	12.692	2044.8	110.7	0.2876	0.839	87.892
4	13.331	273.4	14.2	0.2967	0.904	11.758

*(S)*-2-((*R*)-hydroxy(phenyl)methyl)cyclohexan-1-one (**15f**)

72% yield, anti/syn=98/2, anti-product 27.6 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



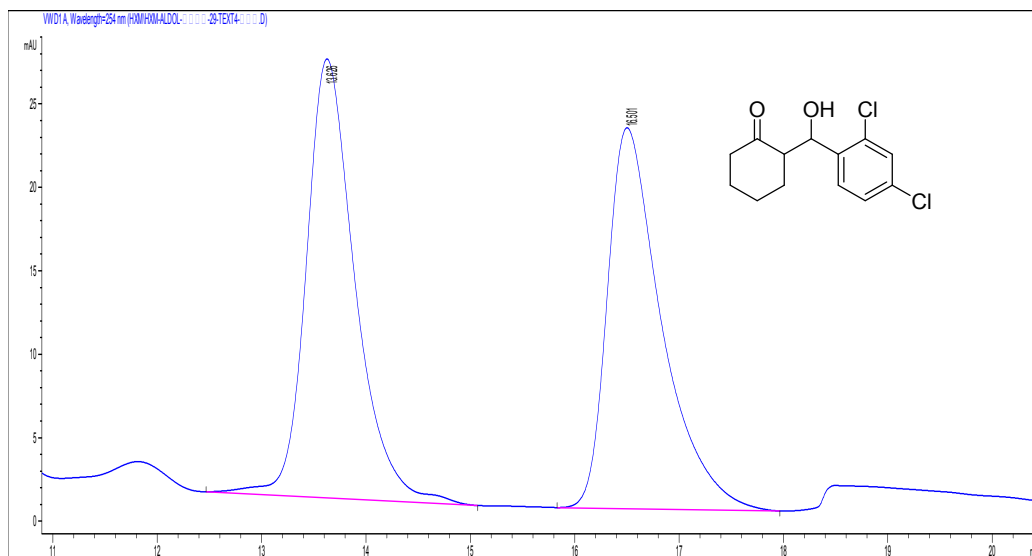
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	8.091	779.5	51.4	0.245	1.086	50.785
2	9.686	755.4	49.1	0.2435	0.855	49.215



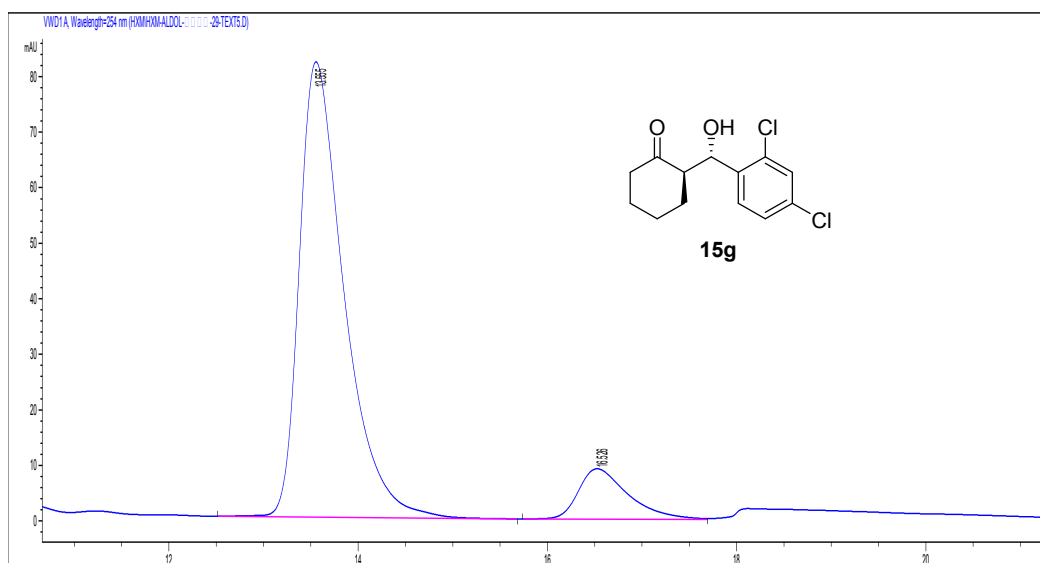
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	7.997	115.2	6.1	0.2849	0.658	64.286
2	9.776	64	3.4	0.2786	1.041	35.714

*(R)*-2-((*S*)-(2,4-dichlorophenyl)(hydroxy)methyl)cyclohexan-1-one (**15g**)

87% yield, anti/syn=99/1, anti-product 78.4 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	13.626	856.1	26.3	0.4918	0.717	50.942
2	16.501	824.5	22.8	0.5375	0.539	49.058

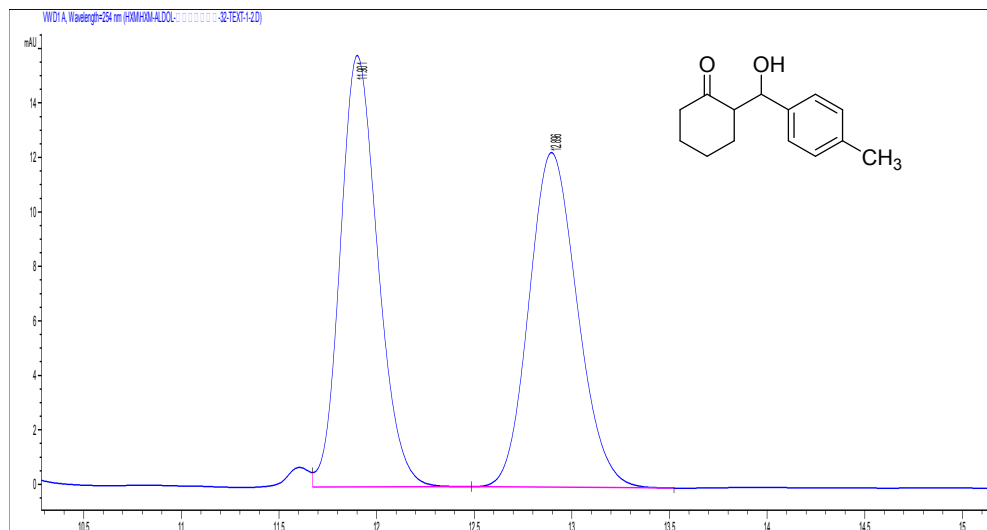


#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	13.555	2687.7	81.9	0.4946	0.558	89.020
2	16.526	331.5	9.1	0.5422	0.574	10.980

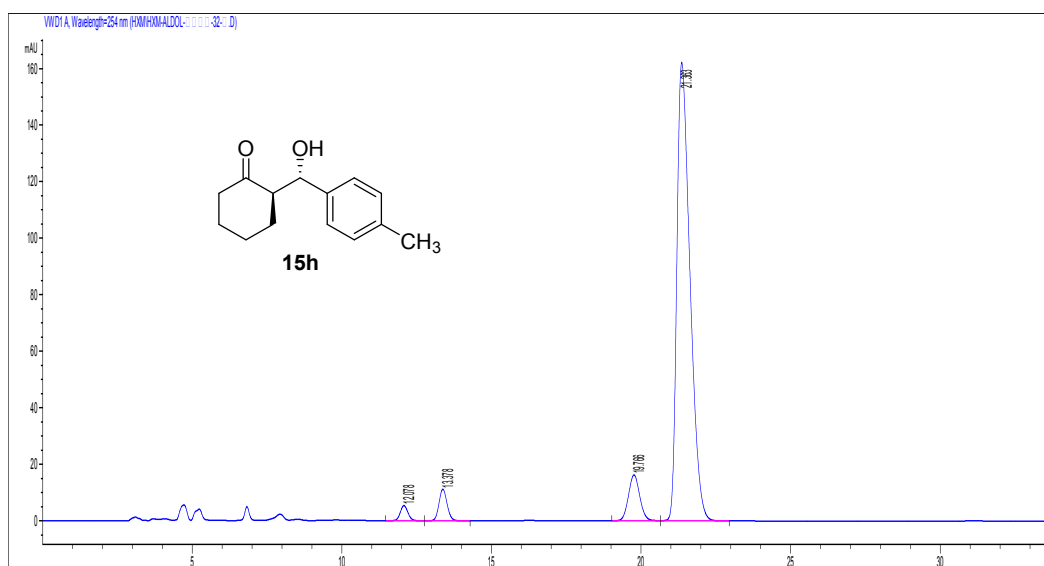


*(R)*-2-((*S*)-hydroxy(*p*-tolyl)methyl)cyclohexan-1-one (**15h**)

76% yield, anti/syn=95/5, anti-product 84.1 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



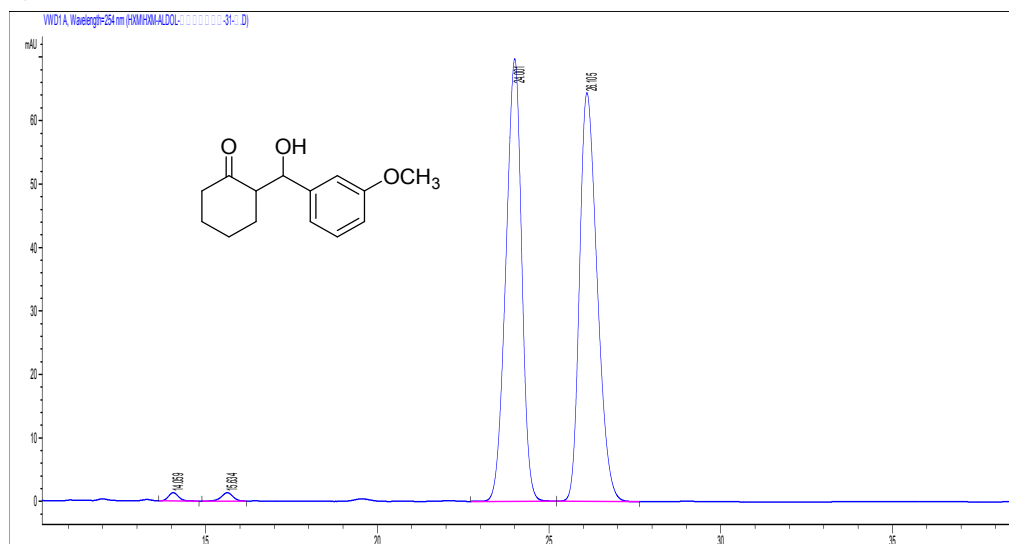
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	11.901	211.6	15.8	0.2058	0.792	50.010
2	12.896	211.5	12.3	0.2679	0.84	49.990



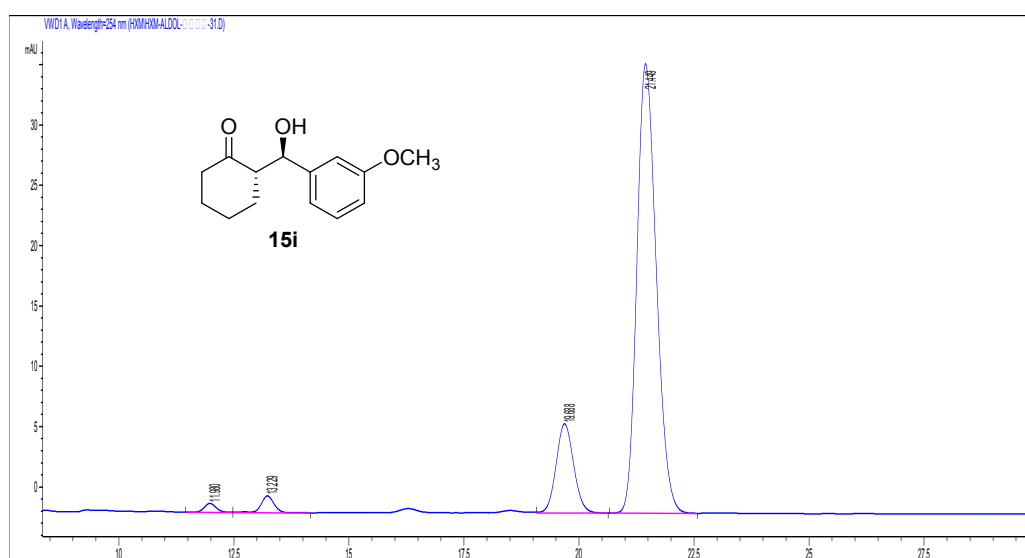
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	12.078	94.4	5.3	0.2767	0.903	1.670
2	13.378	210.3	11.2	0.2937	0.88	3.717
3	19.766	423.9	16.2	0.4074	0.918	7.493
4	21.363	4928.3	162.2	0.4665	0.56	87.121

*(S)*-2-((*R*)-hydroxy(3-methoxyphenyl)methyl)cyclohexan-1-one (**15i**)

81% yield, anti/syn=97/3, anti-product 67.5 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



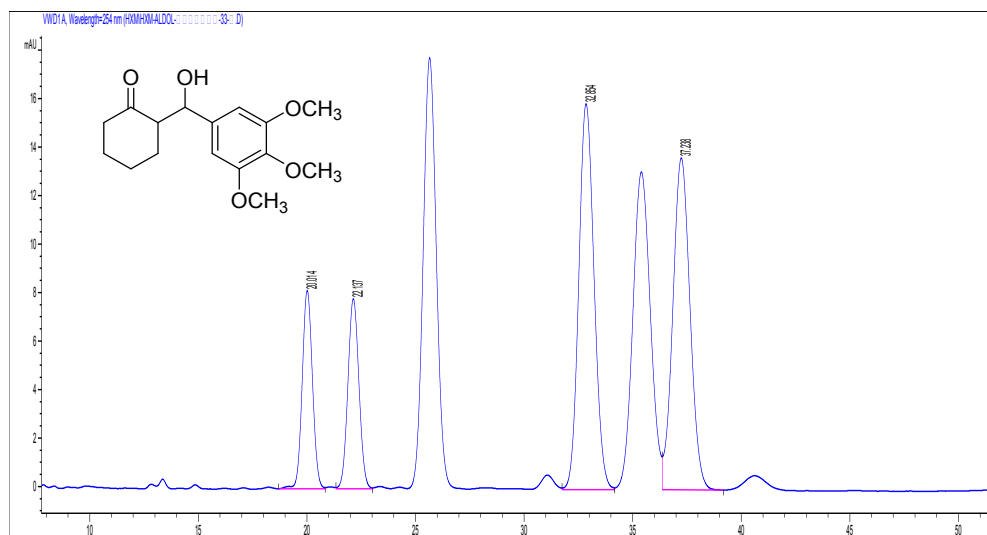
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	14.059	26.6	1.3	0.3177	0.871	0.580
2	15.634	30.5	1.3	0.3591	1.075	0.666
3	24.001	2229.7	69.7	0.4971	1.214	48.674
4	26.105	2294.1	64.4	0.5558	0.683	50.081



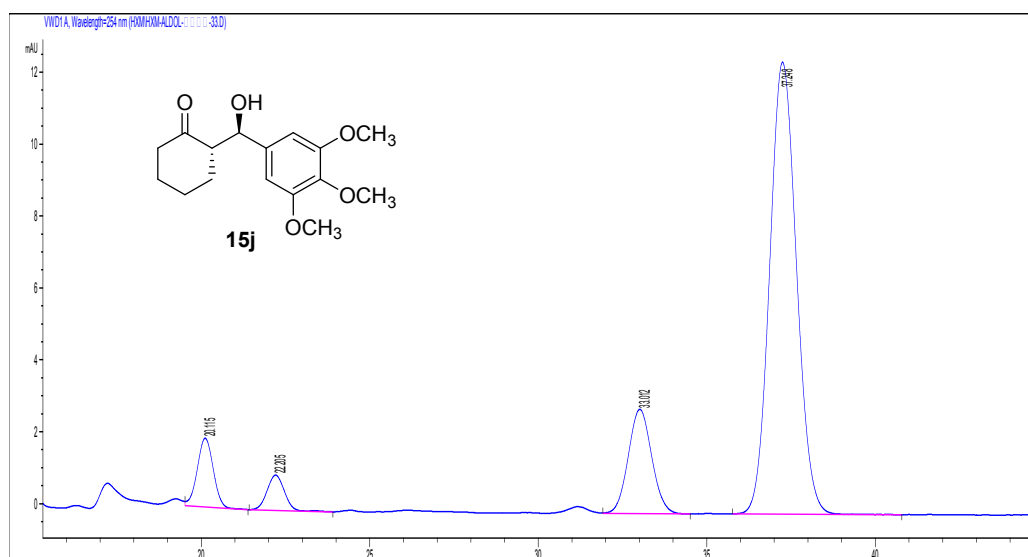
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	11.98	13.2	7.3E-1	0.2784	0.897	1.000
2	13.229	27.2	1.4	0.3008	0.955	2.055
3	19.688	195.3	7.4	0.4083	0.904	14.748
4	21.449	1088.3	37.2	0.4529	0.777	82.196

*(S)*-2-((*R*)-hydroxy(3,4,5-trimethoxyphenyl)methyl)cyclohexan-1-one (**15j**)

80% yield, anti/syn=89/11, anti-product 66.3 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



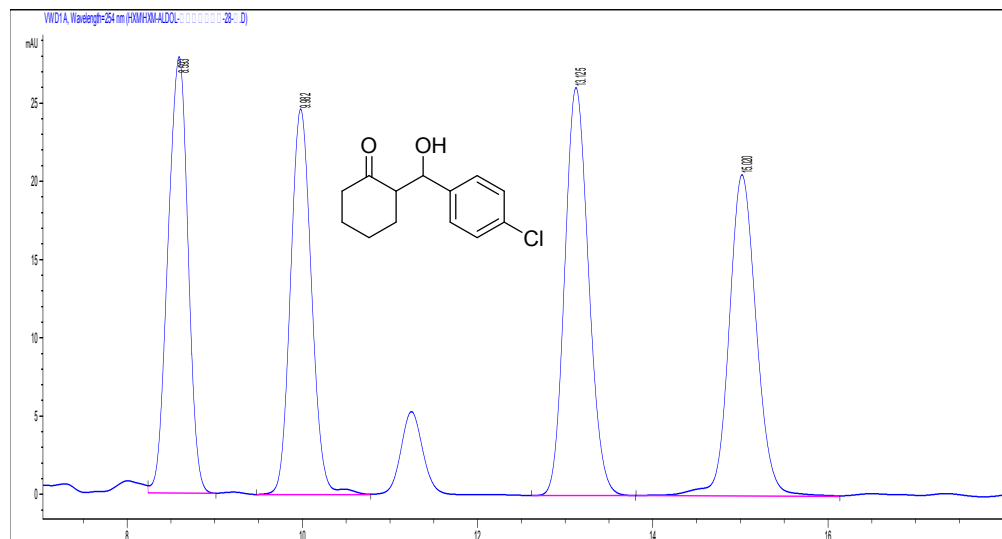
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	20.014	268.5	8.2	0.5111	0.942	12.926
2	22.137	276.4	7.8	0.5518	0.939	13.307
3	32.854	777.6	15.6	0.7624	0.875	37.434
4	37.238	754.8	13.7	0.8593	0.928	36.336



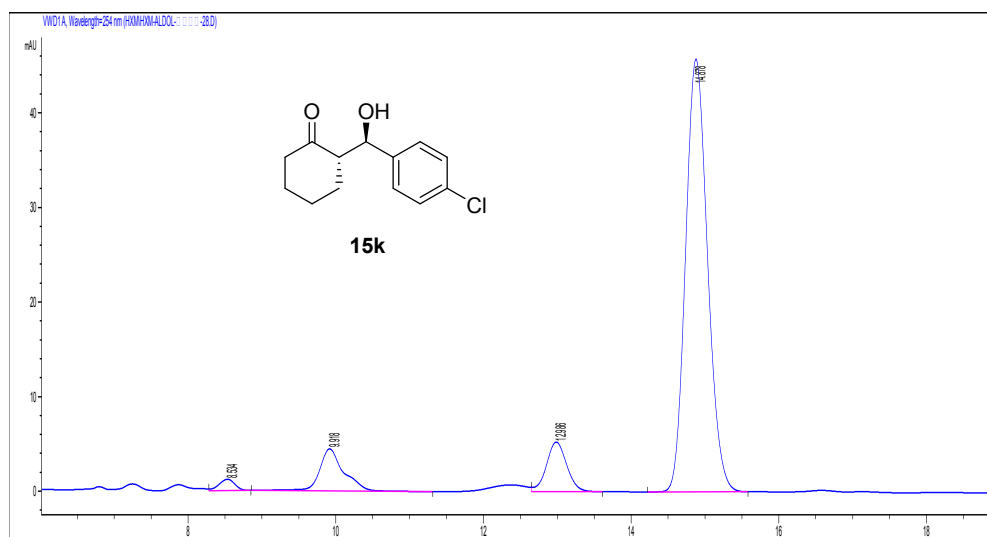
#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	20.115	63.3	1.9	0.5221	0.951	6.783
2	22.205	35.1	9.8E-1	0.5693	0.925	3.762
3	33.012	140.7	2.9	0.7574	0.937	15.090
4	37.248	693.5	12.6	0.8678	0.889	74.364

(S)-2-((R)-hydroxy(4-chlorophenyl)methyl)cyclohexan-1-one (**15k**)

91% yield, anti/syn=91/9, anti-product 80.8 % e.e. E.e. and dr determined by HPLC analysis (Chiralcel AD-H column, Hexane/*i*-PrOH=90/10, Flow rate: 1.0 mL/min, UV detection at 254 nm).



#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	8.593	443.8	27.9	0.2578	1.151	24.798
2	9.982	409.9	24.6	0.2623	0.877	22.906
3	13.125	492	26	0.2964	0.849	27.492
4	15.02	443.9	20.5	0.3365	0.883	24.805



#	Time	Peak area	Peak height	Peak width	Symmetry factor	Peak area%
1	8.534	17.8	1.2	0.2331	1.138	1.528
2	9.918	102.9	4.5	0.3335	0.683	8.843
3	12.986	100.1	5.2	0.2949	0.923	8.602
4	14.878	942.8	45.7	0.3205	0.852	81.027