

Supplementary information

Beyond enzymatic promiscuity: Asymmetric induction by L-proline on lipase catalyzed synthesis of polyfunctionalized 4*H*-pyrans

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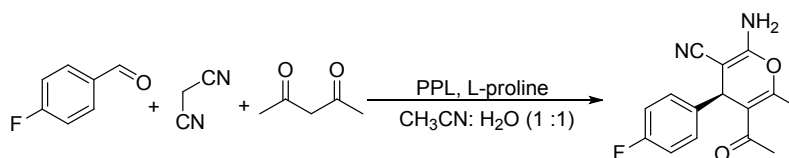
General remarks

All reagents were commercially available and used without further purification. All the compounds were characterized by ¹H NMR, ¹³C NMR and IR spectroscopy. The IR spectra were recorded on a Perkin Elmer spectrophotometer. ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were obtained on a Bruker AC-400 using CDCl₃ as solvent and TMS as internal standard, unless otherwise stated. Optical rotations were measured on a Perkin Elmer 341 polarimeter. HPLC analyses were performed on an Waters M515 series equipped with a chiral column (detailed for each compound below), using mixtures of *n*-hexane/isopropyl alcohol (IPA) as mobile phase, at 25 °C. For column chromatography, we employed Merck silica gel 60-120 mesh.

Table 1S Optimization of catalyst loading^a

Entry	PPL (mg)/mmol of aldehyde	Time (h)	% Yield ^b
1	5	48	42
2	10	48	65
3	20	48	78
4	25	36	90
5	30	36	88
6	40	36	93

^aReaction conditions: 4-Fluoro benzaldehyde (1 mmol), malononitrile (1 mmol) and acetylacetone (1.25 mmol) were stirred with PPL in aqueous acetonitrile (1: 1) (10 mL) at 30 °C. ^bYield of the pure product, purified by recrystallization from ethanol.

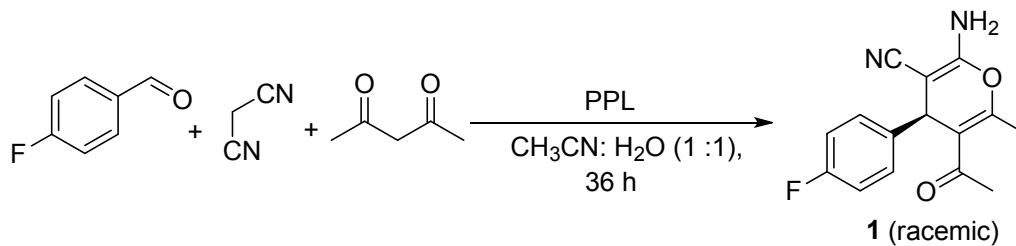
Table 2S Optimization of amount of catalyst for enantioselective synthesis of pyrans^a

Entry	PPL (mg)	L-proline (mol%)	Time (h)	% yield ^b	er ^c
1	10	10	36	52 ^d	-nd-
2	10	15	36	62 ^d	60: 40
3	20	10	30	90	60: 40
4	20	15	28	94	73: 27
5	25	15	28	95	70: 30

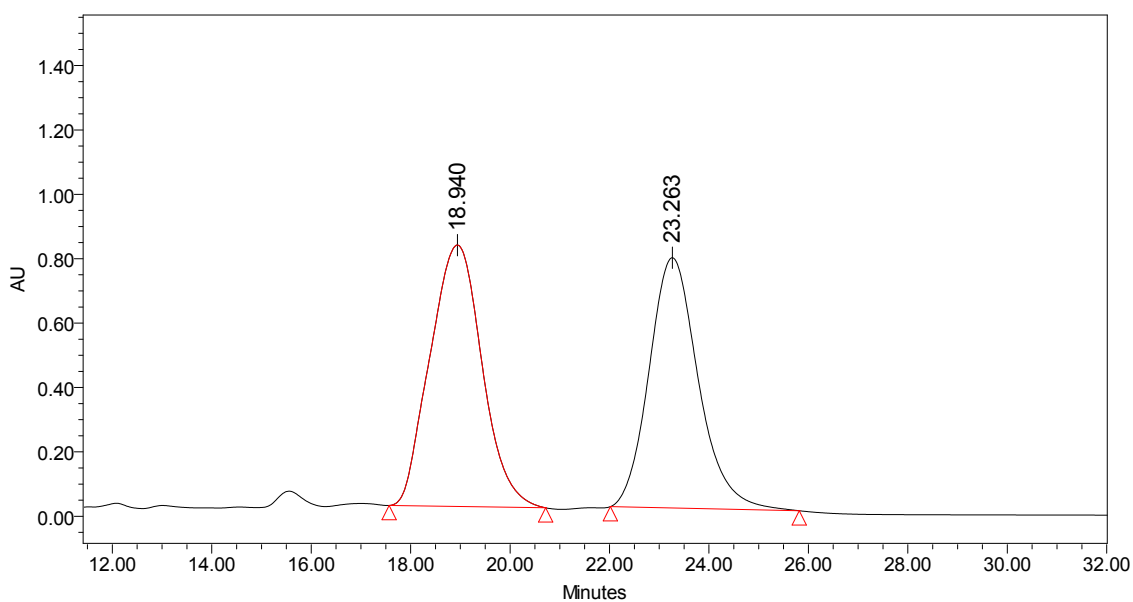
^aReaction conditions: 4-fluoro benzaldehyde (1 mmol), **2** (1 mmol) and **4** (1.25 mmol) were stirred with PPL and L-proline in aqueous acetonitrile (1: 1) at room temperature. ^bYield of the pure product, purified by recrystallization from ethanol. ^cEnantiomeric ratio (er) was determined by chiral HPLC analysis. ^dIncomplete conversion

HPLC analysis:

(a) PPL as a catalyst

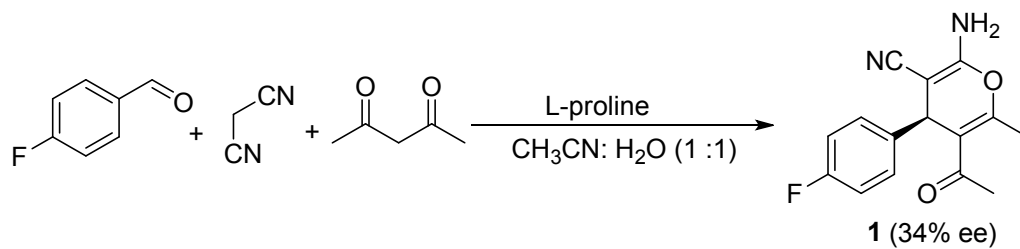


Enantiomeric ratio (50: 50) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (12: 88), flow 0.5 ml/min, UV 230 nm.

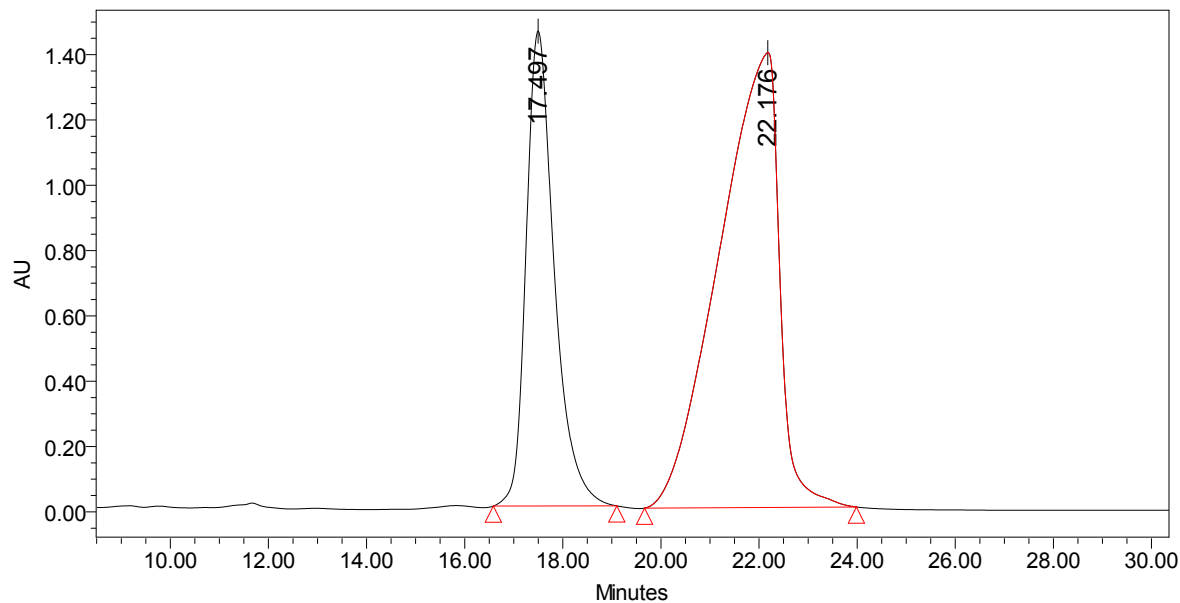


	Name	Retention Time	Area	% Area	Height
1		18.940	58707624	51.72	810390
2		23.263	54800065	48.28	782793

(2) L-PROLINE as a catalyst

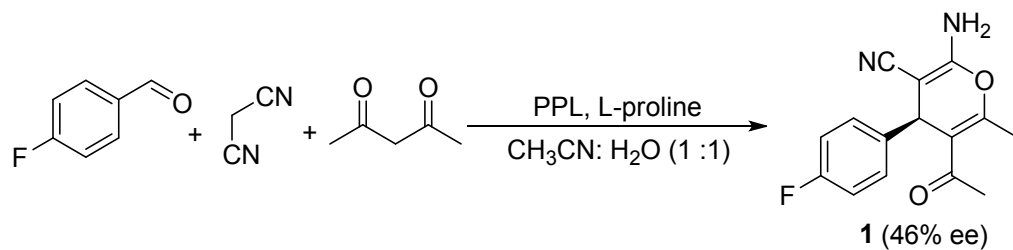


Enantiomeric ratio (33: 67) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (12: 88), flow 0.5 ml/min, UV 230 nm.

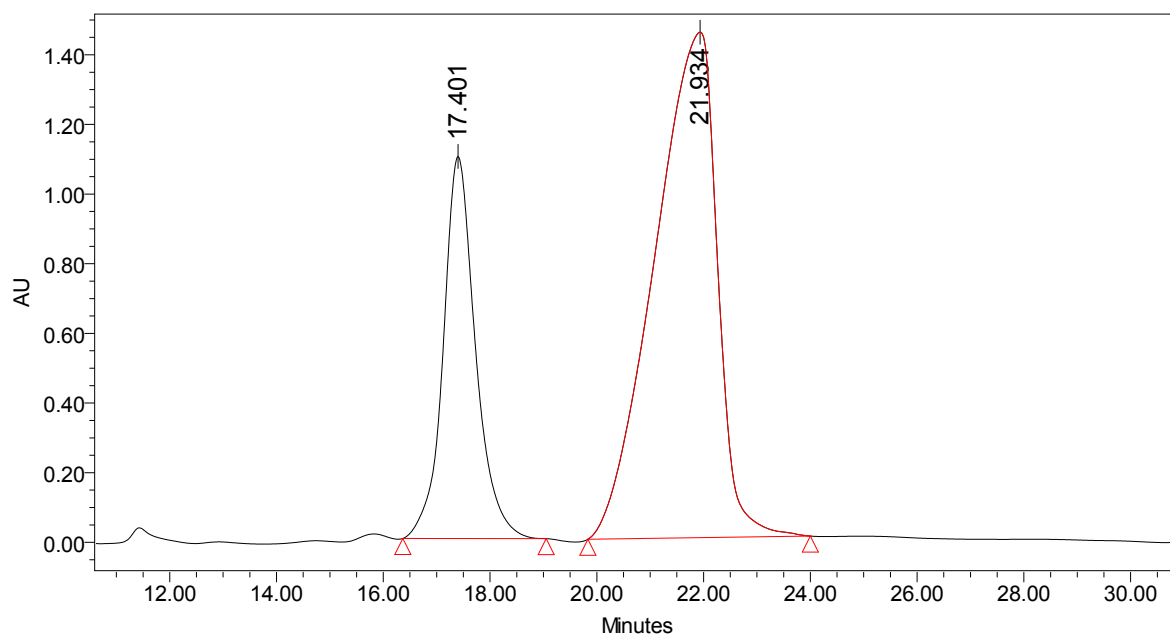


Name	Retention Time	Area	% Area	Height
1	17.497	58062980	32.84	1454637
2	22.176	118764520	67.16	1393032

(3) PLL and L-proline as catalysts

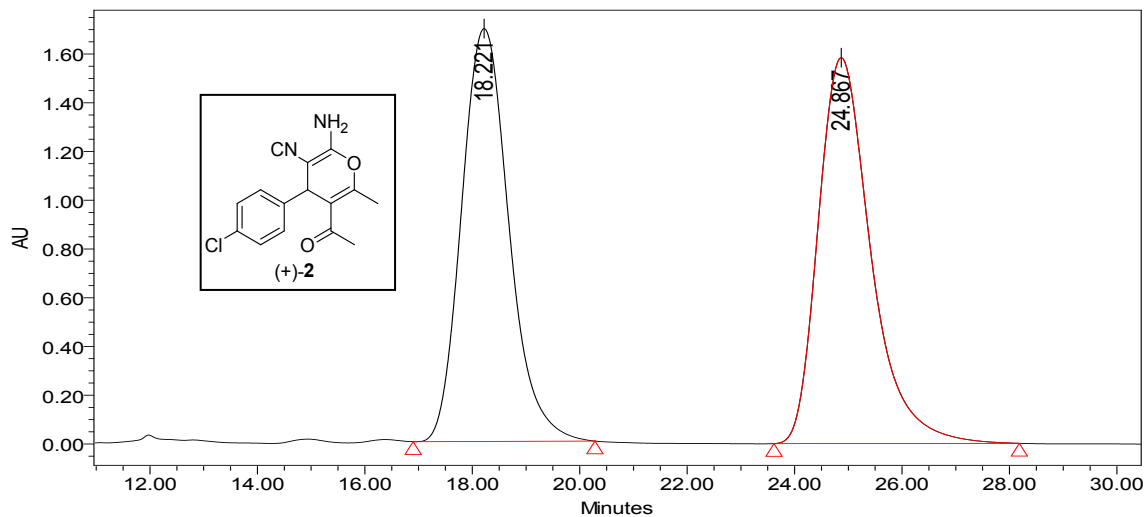


Enantiomeric ratio (27: 73) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (12: 88), flow 0.5 ml/min, UV 230 nm.

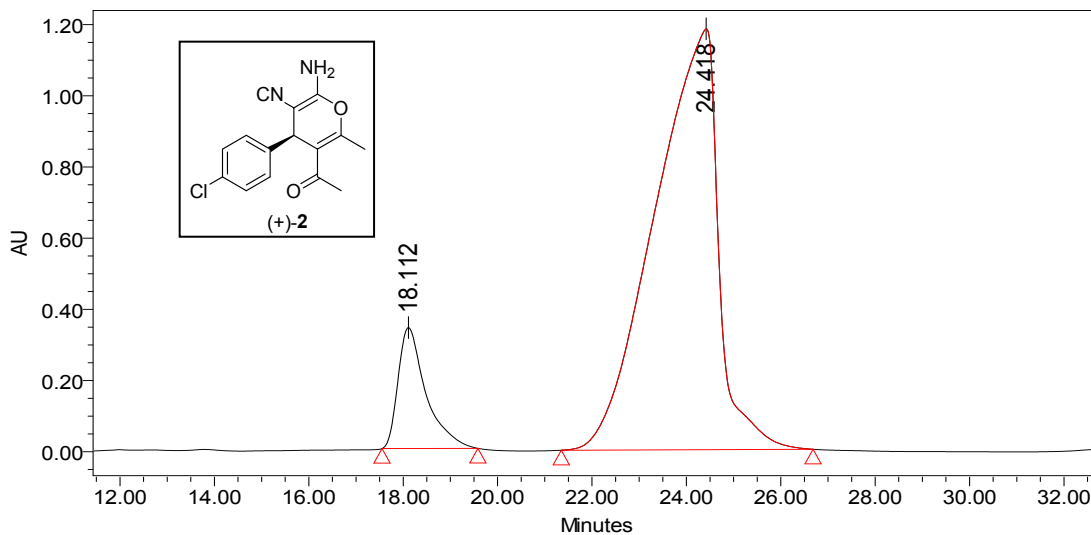


Name	Retention Time	Area	% Area	Height
1	17.401	44246848	27.05	1082125
2	21.934	119315883	72.95	1454701

Enantiomeric ratio (89: 11) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (12: 88), flow 0.5 ml/min, UV 230 nm.

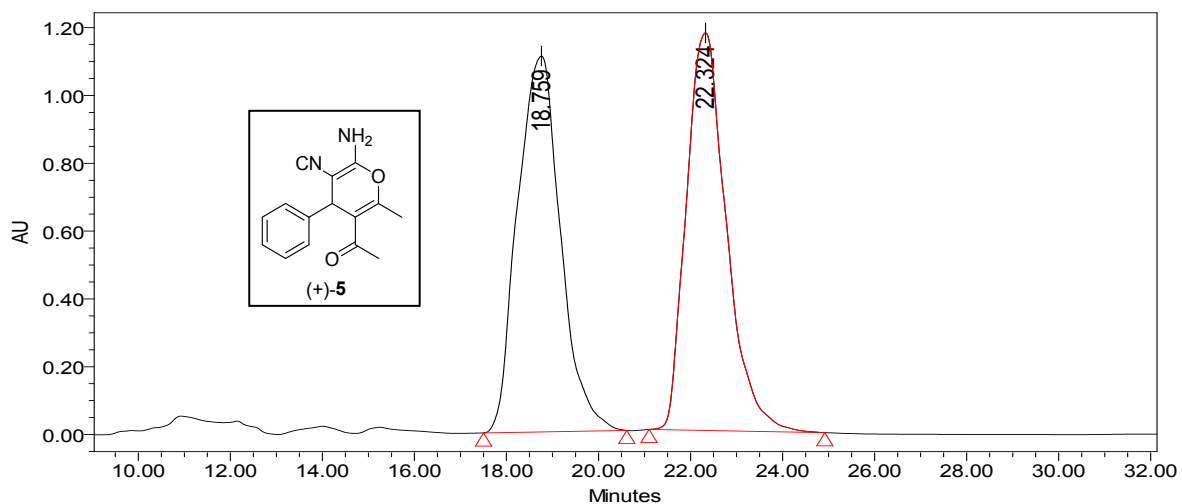


	Name	Retention Time	Area	% Area	Height	Int Type
1		18.221	103642509	49.04	1694159	bb
2		24.867	107690129	50.96	1583028	bb

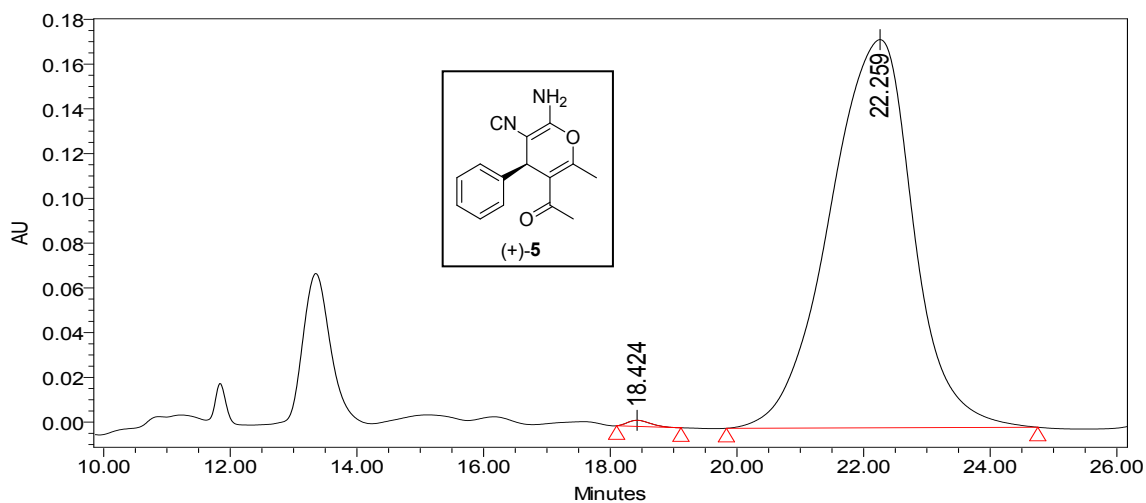


	Name	Retention Time	Area	% Area	Height	Int Type
1		18.112	13316462	10.66	335221	bb
2		24.418	111567842	89.34	1183913	bb

Enantiomeric ratio (99.6: 0.4) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (12: 88), flow 0.5 ml/min, UV 230 nm.

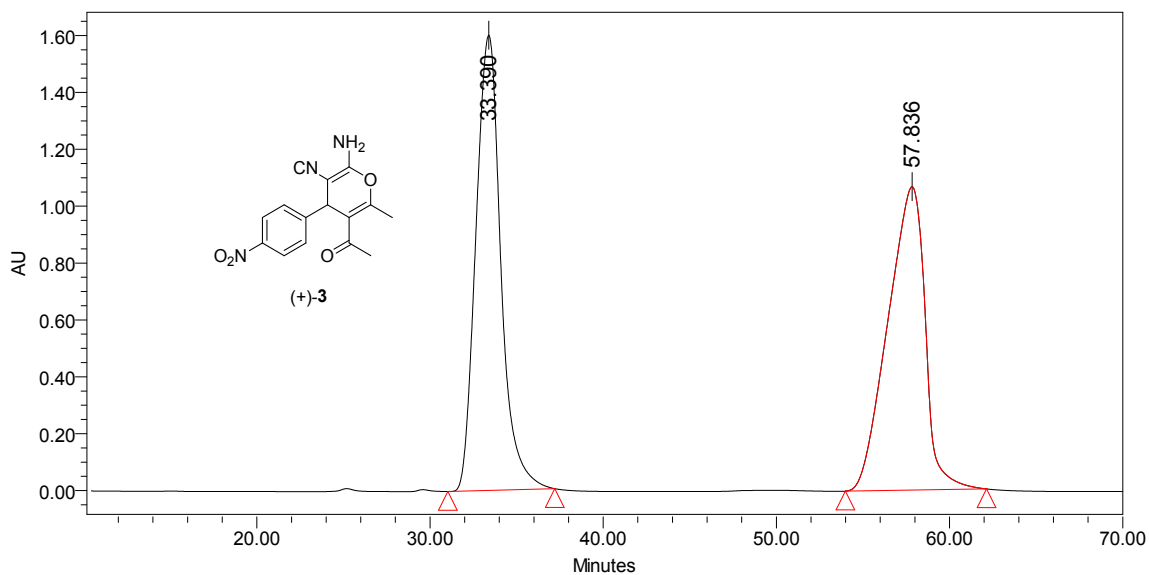


	Name	Retention Time	Area	% Area	Height
1		18.759	71962650	50.34	1108804
2		22.324	70989379	49.66	1172817



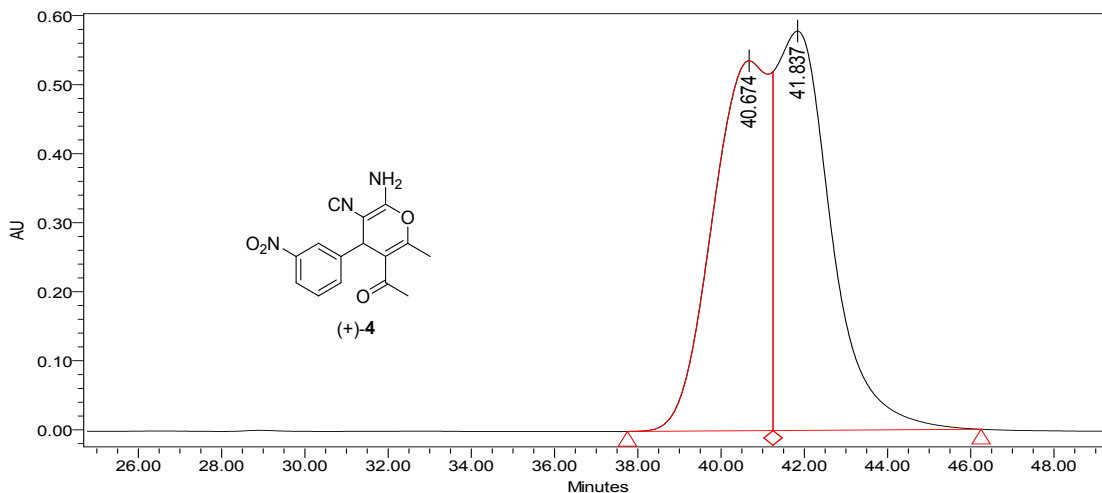
	Name	Retention Time	Area	% Area	Height
1		18.424	68222	0.43	2723
2		22.259	15898443	99.57	173466

Enantiomeric ratio (50: 50) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (14: 86), flow 0.5 ml/min, UV 230 nm.



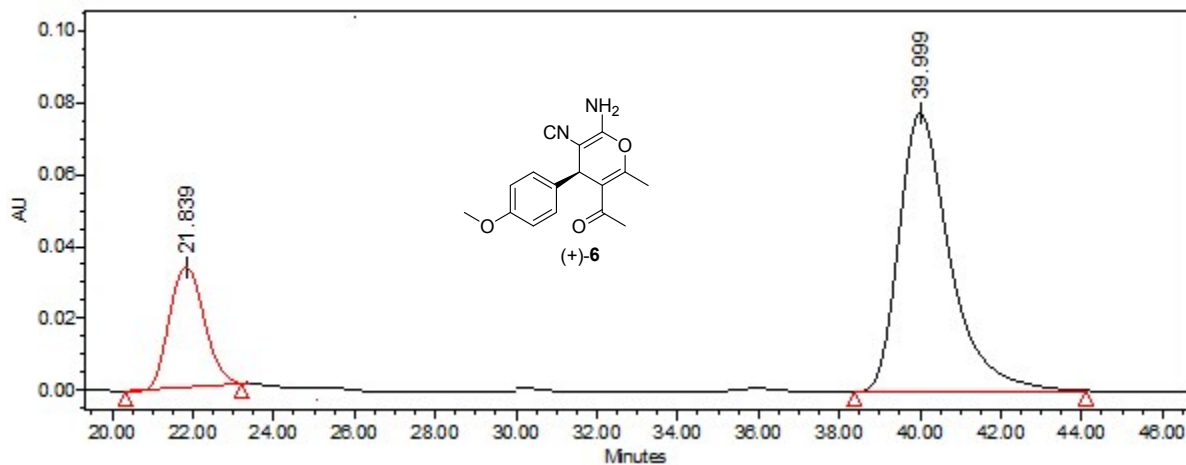
	Name	Retention Time	Area	% Area	Height
1		33.390	160202664	50.13	1600833
2		57.836	159388240	49.87	1067091

Enantiomeric ratio (50: 50) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (14: 86), flow 0.5 ml/min, UV 230 nm.



Name	Retention Time	Area	% Area	Height
1	40.674	50309772	48.73	535860
2	41.837	52931775	51.27	578462

Enantiomeric ratio (79: 21) was determined by chiral HPLC analysis on DIACEL CHIRALPAK AD-H column, isopropanol: n- hexane (12: 88), flow 0.5 ml/min, UV 230 nm.



Name	Retention Time	Area	% Area	Height
1	21.839	1787428	20.87	33265
2	39.999	6777154	79.13	77310