Supporting Information

Continuous-Flow Asymmetric Aldol Reactions Using Sawdust-Supported Cross-Linked L-Proline Catalysts

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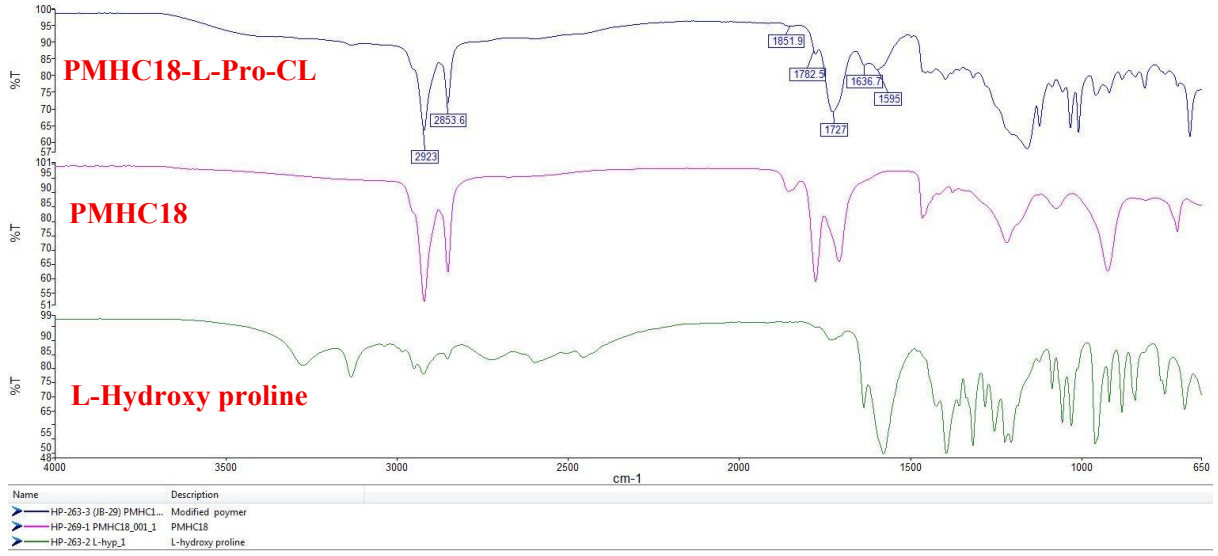


Fig. S1. FTIR Analysis of PMHC18-L-pro-CL and its comparison with PMHC18 and L-hydroxy proline

Table S1. Elemental analysis of PMHC18-L-pro-CL

SAMPLE	%N	%C	%H
4-Hydroxyl L-Proline	10.64	45.91	7.09
PMHC18	0.00	72.15	10.82
PMHC18-L-Pro-CL	4.93	57.13	8.80

*% Proline linkage in PMHC18-L-Pro-CL**: 46.16 %**

*(*Calculation on basis of %N present in the compound)*

Table S2. Acid Number Analysis of PMHC18-L-pro-CL

Polymer	Acid Number (KOH mg/g of sample)	% non-Cross linkage	Remarks
PMHC18	256	100	Soluble in $CHCl_3$
PMHC18-L-Pro-CL	63	24.61	cross-linked polymer, Insoluble in $CHCl_3$

*%Cross-linkage in PMHC18-L-Pro-CL = **75.39 %**

(Insoluble material in solvent considered as Cross-linking material)*

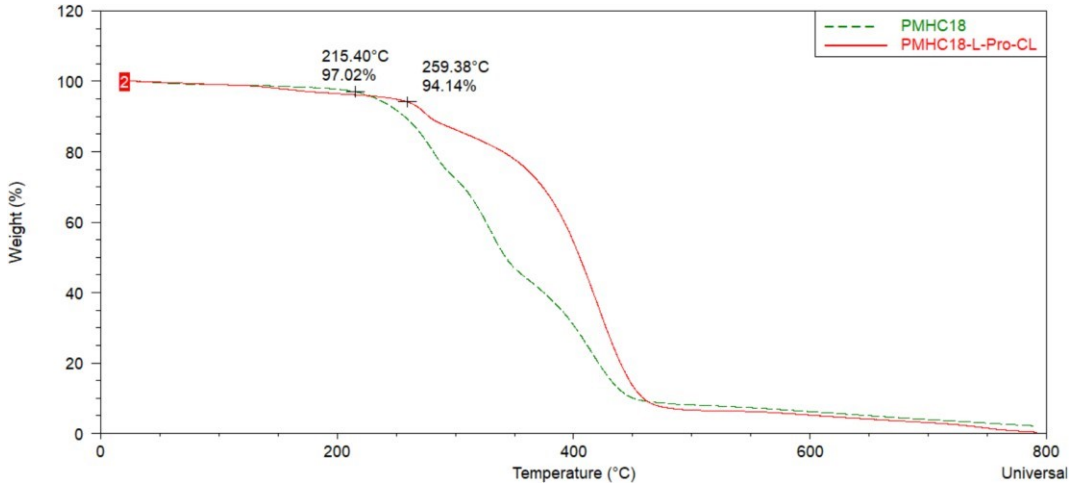


Fig. S2. TGA analysis of PMHC18-L-Pro-CL and PMHC18 (--- dash line)

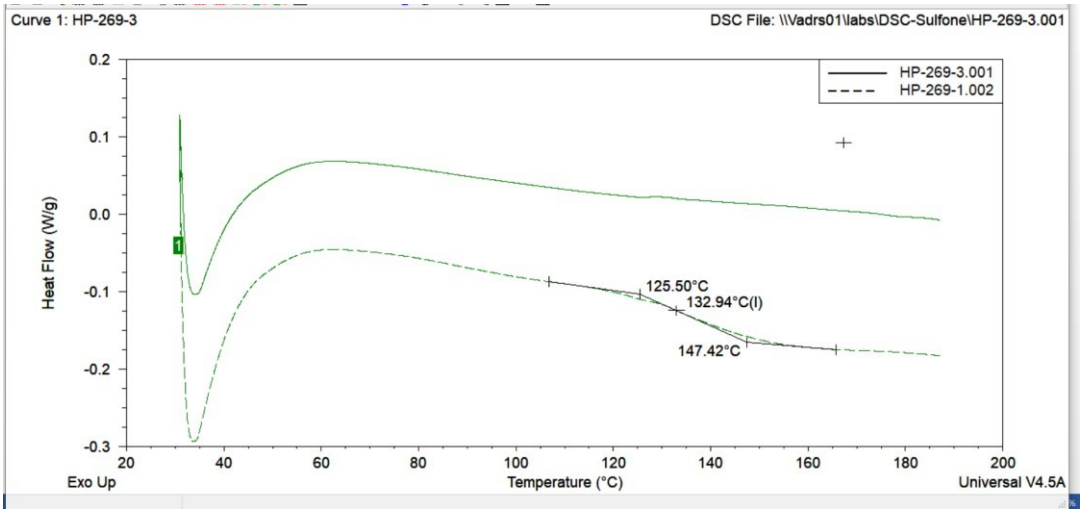


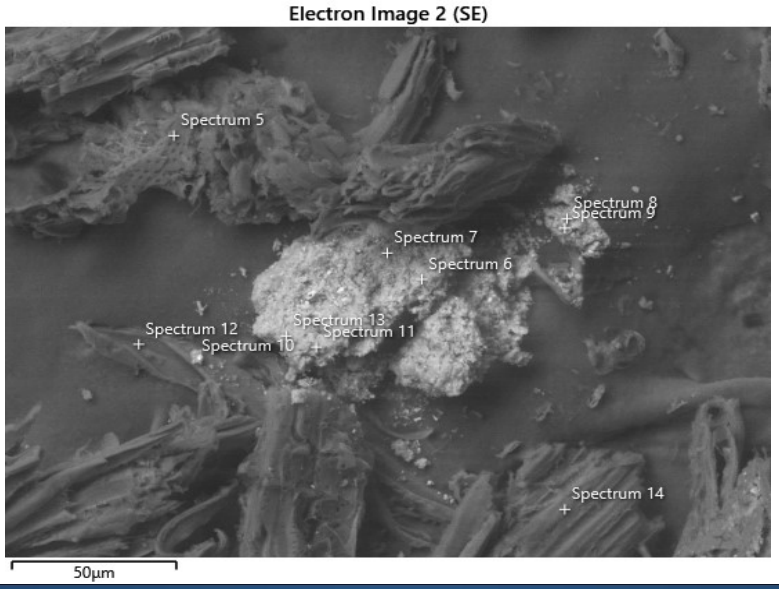
Fig. S3. DSC analysis of PMHC18-L-Pro-CL and PMHC18 (---dash line)

Table S3. SEM–EDX elemental composition of sawdust, polymer, and composite.

Element	Sawdust	Cross-linked Polymer (PMHC18-L-pro-CL)	Sawdust–Polymer Composite	Origin / Interpretation
C	High	Very High	High	Organic matrix (cellulose, polymer chains)
O	High	Medium	High	Oxygenated biopolymers and polymer functionalities
Si	High	Trace–ND	Medium–High	Naturally occurring silica/aluminosilicates in sawdust
Al	Medium	Low–Medium	Medium	Biomass minerals; minor silica/alumina residues in polymer
Ca	Medium	Trace	Low–Medium	Biomass inorganic mineral content
Mg	Low–Medium	Trace	Low	Natural wood mineral content
Fe	Low	Trace	Low	Soil-derived or biomass-bound iron
Ti	Trace	ND	Trace	Minor mineral inclusions (soil/clay)
Na	Trace	ND	Trace	Biogenic salts in sawdust
K	Trace	ND	Trace	Biogenic salts in sawdust
P	Trace	ND	Trace	Biomass phosphorus species
S	Low	Medium	Medium	Residual p-toluenesulfonate from polymer synthesis
Cl	Low	Low–Medium	Low–Medium	PTSA/trace solvent or reagent residuals

Notes:

1. "High / Medium / Low / Trace" refers to relative peak intensities normalized across samples.
2. ND = Not Detected in scanned regions.
3. Sawdust contains natural aluminosilicate and soil-derived mineral components; polymer shows only residual PTSA-derived species; composite reflects both.
4. These inorganic species are chemically inert under Aldol reaction conditions and do not influence catalytic activity.


Electron Image 2 (SE)
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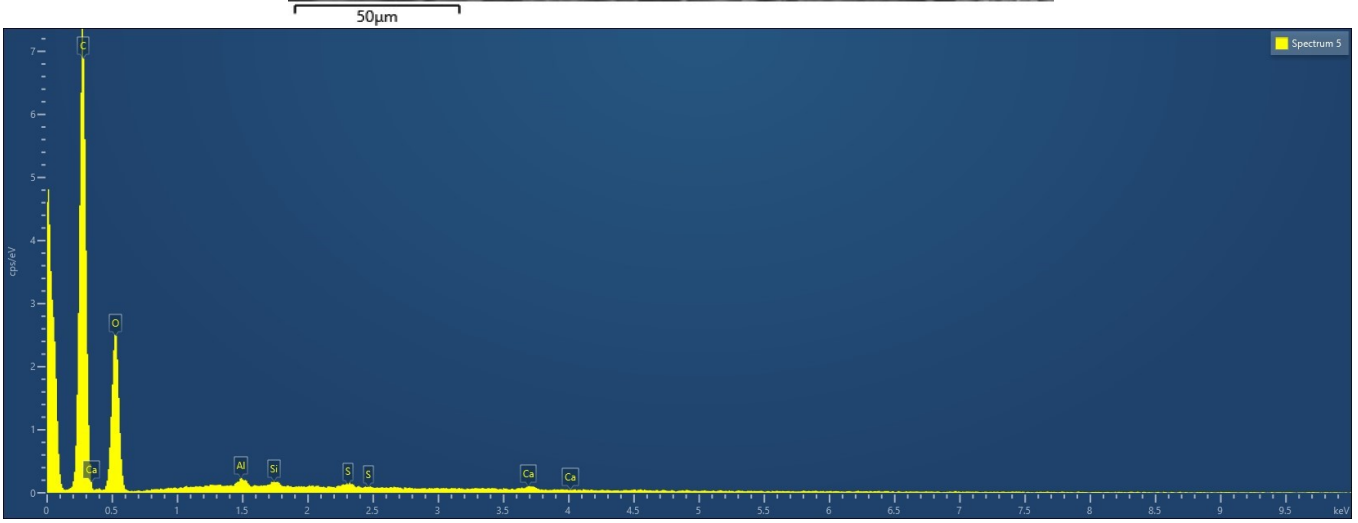
Spectrum 8
Spectrum 9
Spectrum 7
Spectrum 6
Spectrum 13
Spectrum 12
Spectrum 11
Spectrum 10
Spectrum 14
50µm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cps/eV
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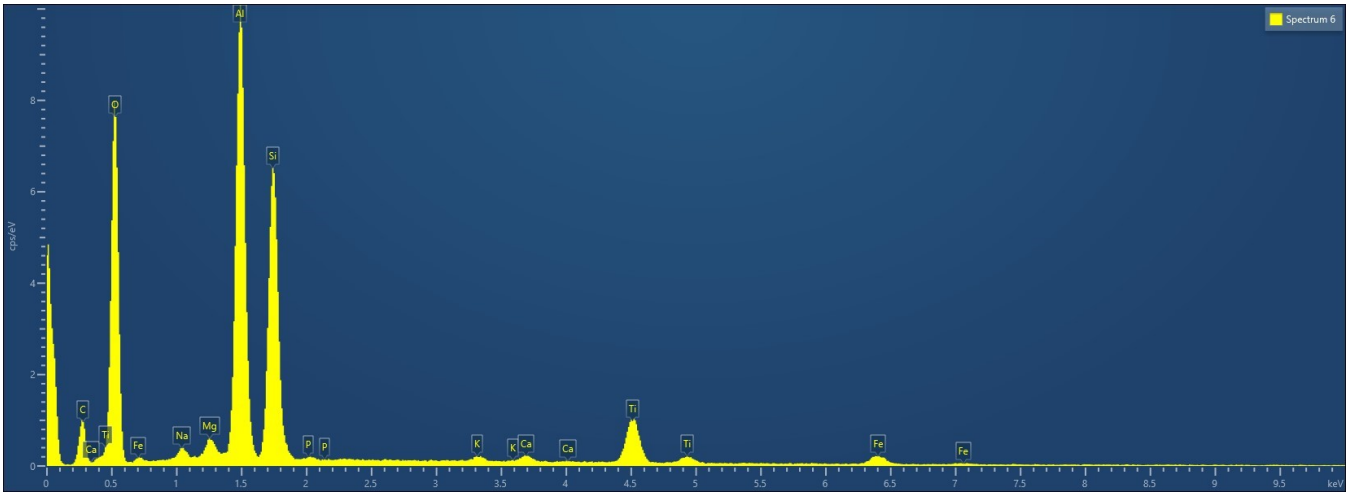
O
Ca
Al
Si
S
S
Ca
Ca
keV


Spectrum 6
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C
Ca
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Mg
P
P
K
K
Ca
Ca
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Ti
Fe
Fe
keV

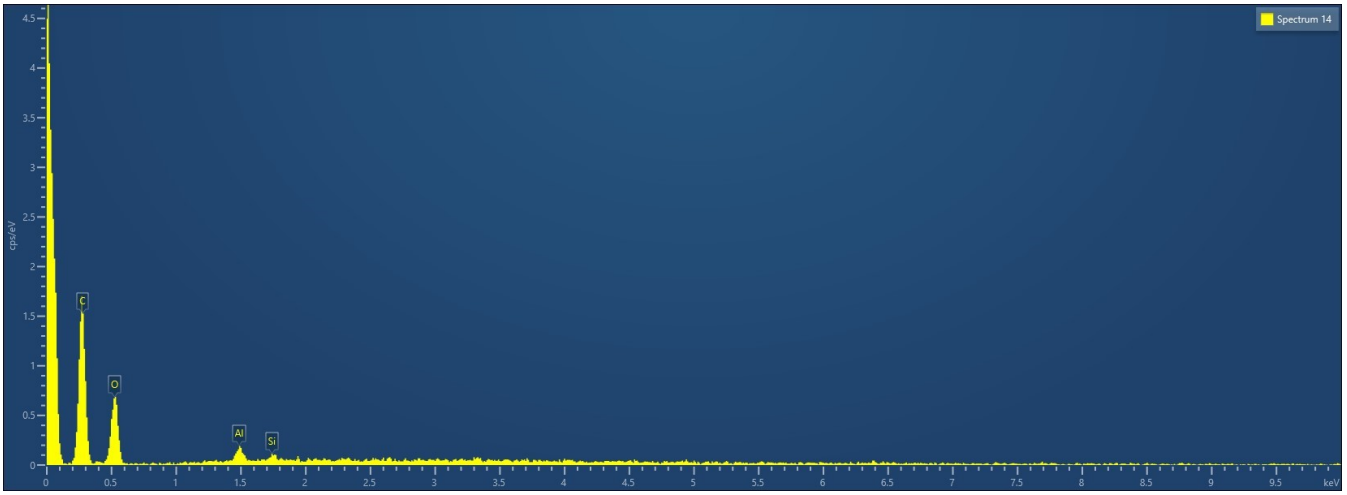
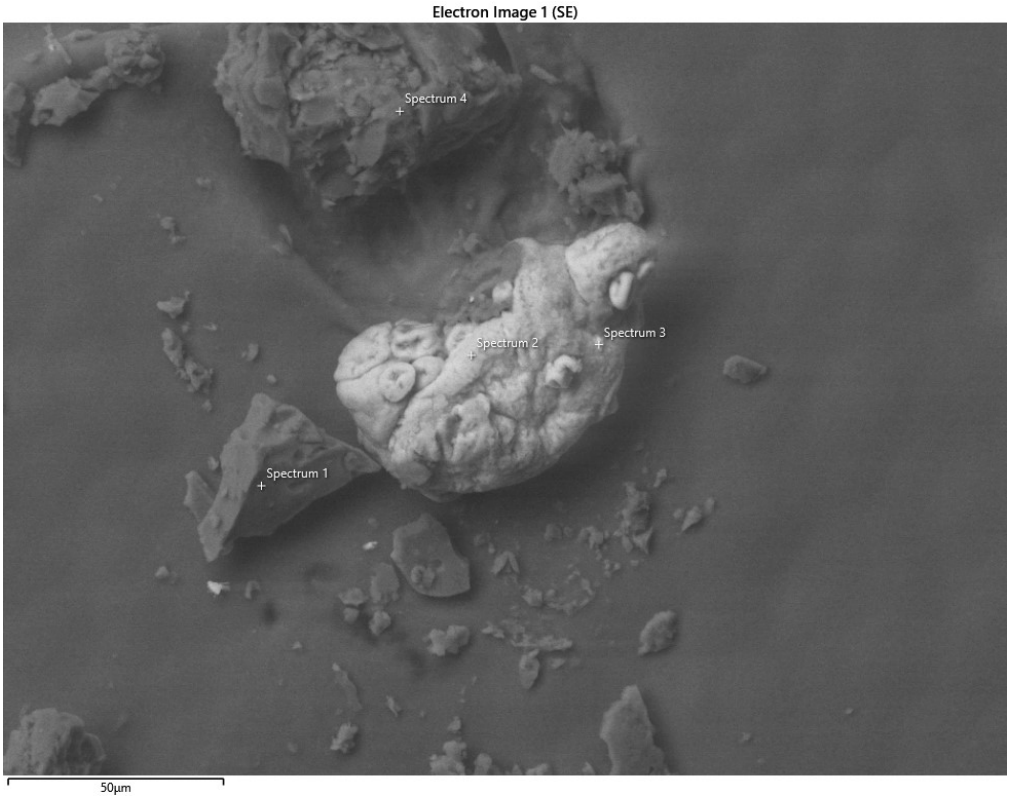


Fig. S3A. Semi-quantitative elemental composition of pristine sawdust, obtained from area-wise SEM–EDX analyses.



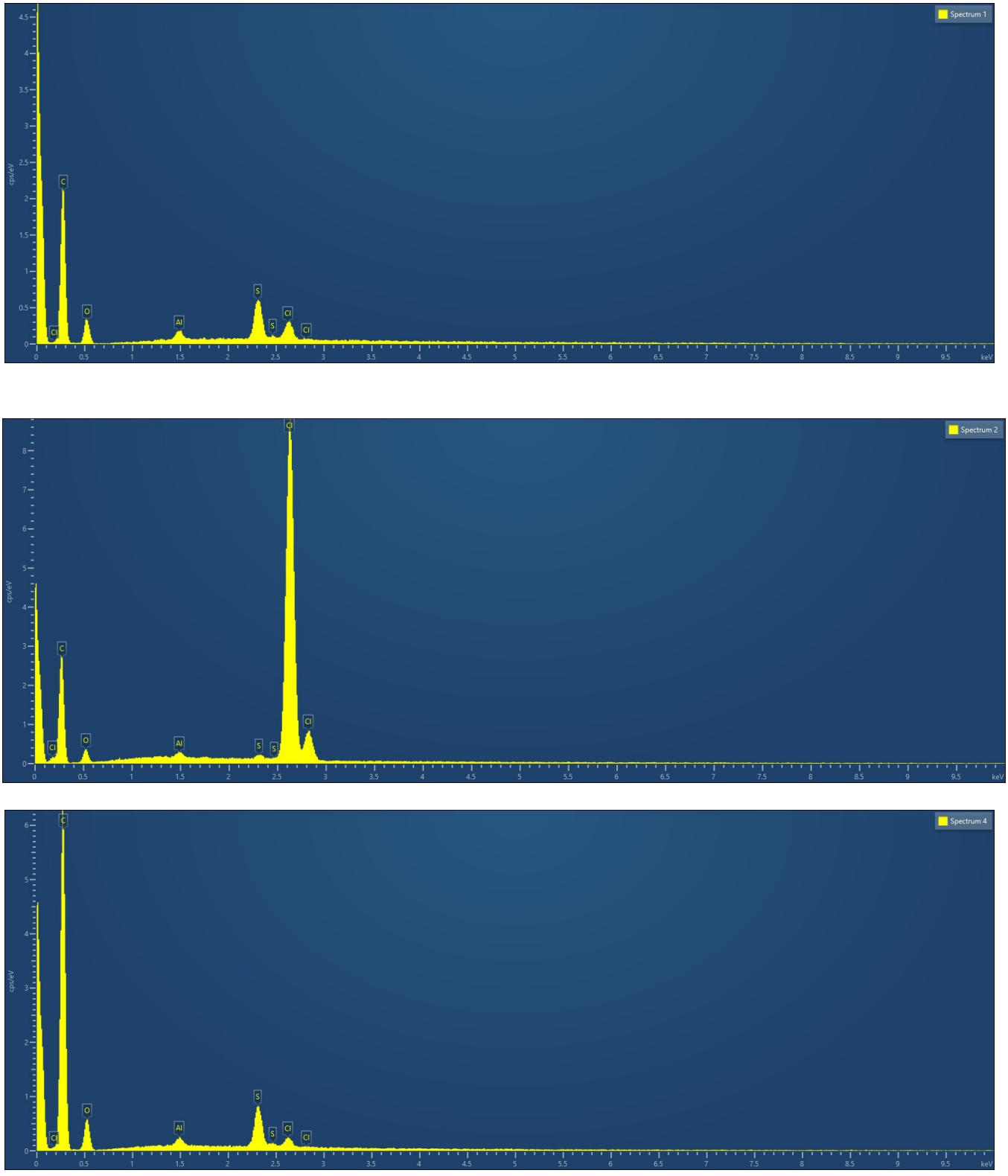
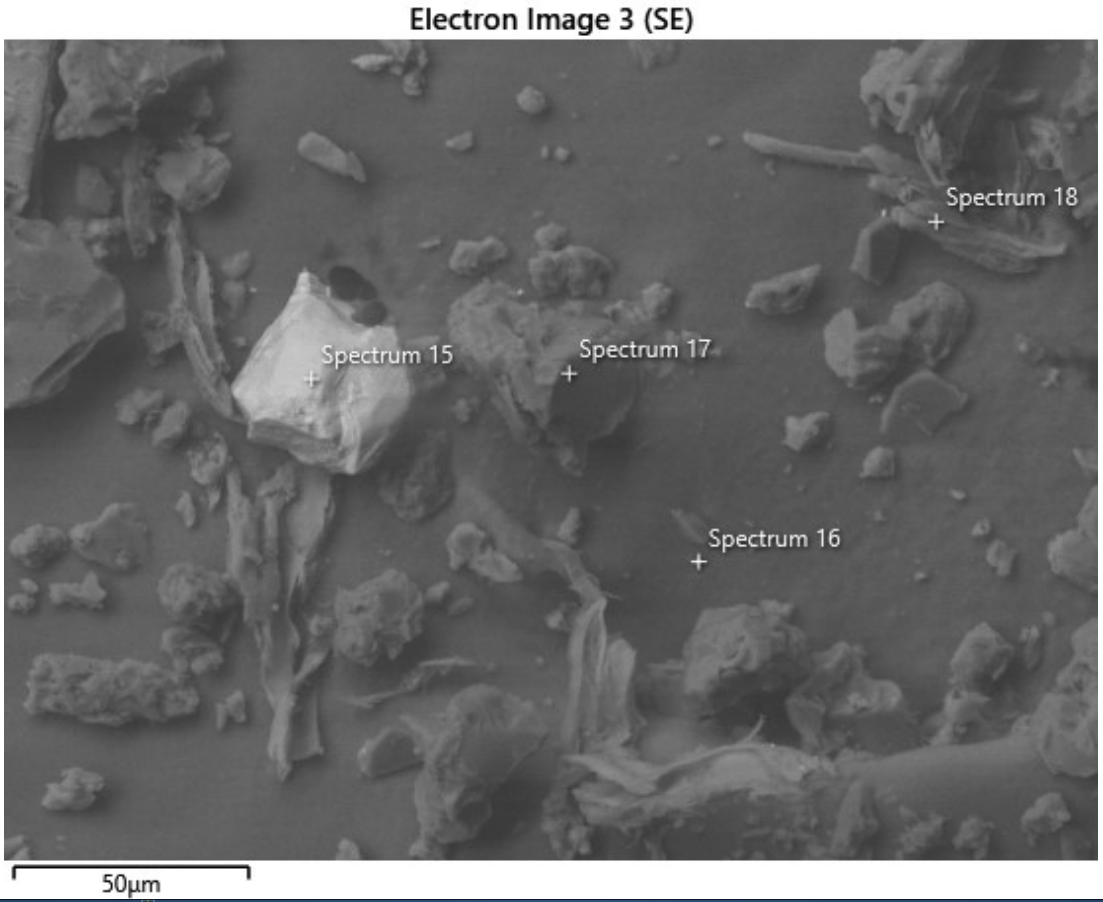
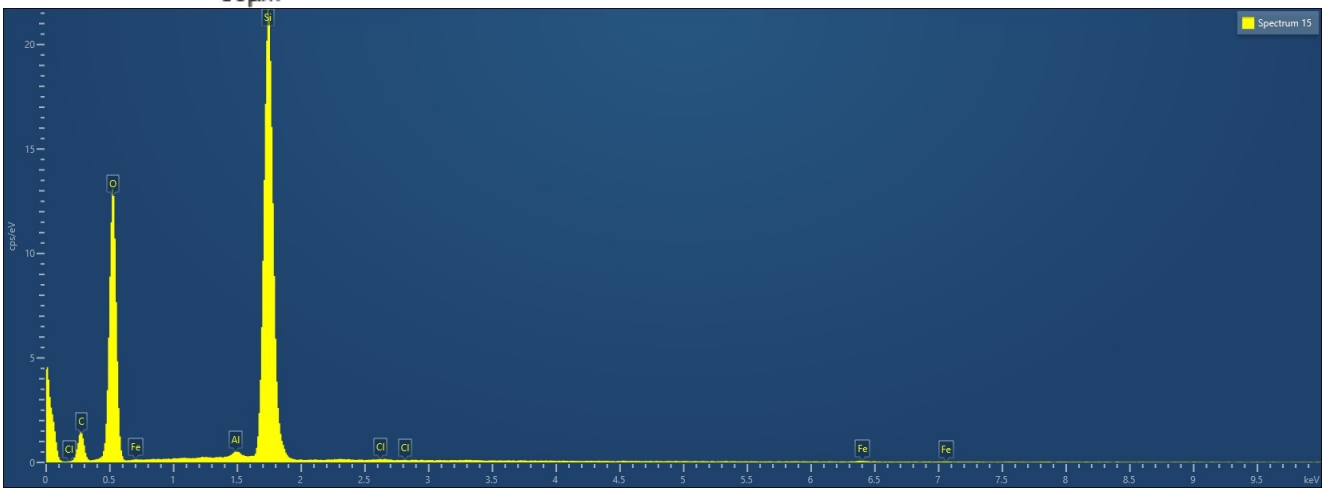


Fig. S3B. Semi-quantitative elemental composition of cross-linked polymer (PMHC18-L-pro-CL) obtained from area-wise SEM–EDX analyses.


Electron Image 3 (SE)
Spectrum 18
Spectrum 15
Spectrum 17
Spectrum 16
50µm


Spectrum 15
Si
O
C
Cl
Fe
Al
Cl
Cl
Fe
Fe
cps/eV
keV

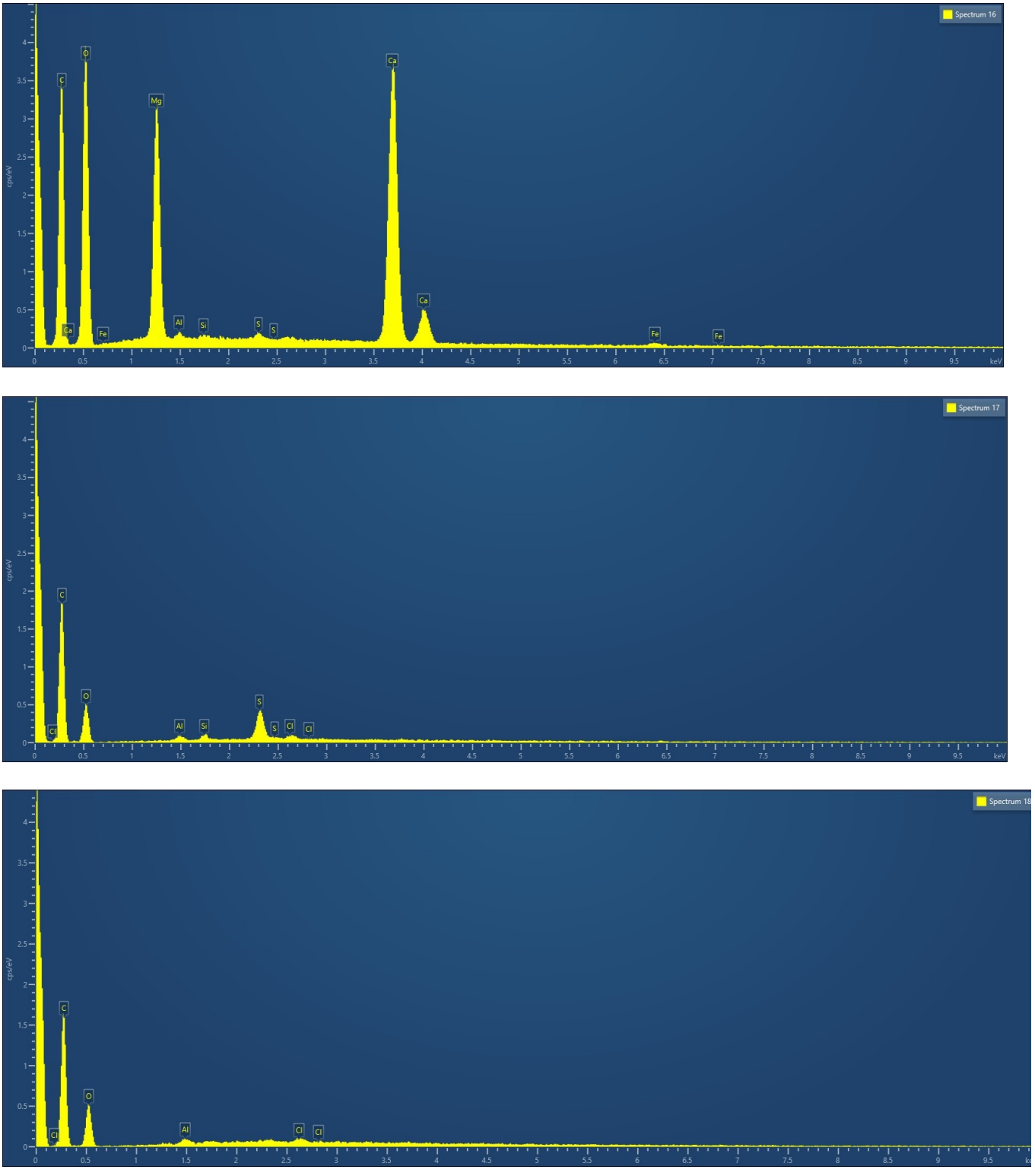


Fig. S3C. Semi-quantitative elemental composition of the sawdust–polymer composite obtained from area-wise SEM–EDX analyses.

Table S4. Turnover number (TON) and turnover frequency (TOF) data.

Mode of operation	Catalyst used (g)	Time or residence (h)	Conversion (%)	TON	TOF (h^{-1})	Notes
Batch (24 h)	0.050	24	60	3.4	0.14	Typical batch oxidation–aldol step
Flow (per run)	6.0	0.89 (h)	≈ 100	0.05	0.05	Gravity-driven packed bed
Flow (5 runs cumulative)	6.0	4.45 (h)	≈ 100	0.23	0.05	5 recycles, constant ee > 90 %

Table S5. Comparison of heterogeneous L-proline-based catalyst systems with reported TON/TOF values and operational characteristics.

Catalyst system	Mode of operation	TON	TOF (h^{-1})	Notes	Reference
PMHC18-L-pro-CL (this work)	Batch (24 h)	3.4	0.14	Standard batch aldol; partial gelation	–
PMHC18-L-pro-CL (this work)	Gravity-driven flow (per run)	0.05	0.05	Mass-normalized; pump-free system	–
PMHC18-L-pro-CL (this work)	Gravity-driven flow (5 runs cumulative)	0.23	0.05	Recyclable; ee > 90%	–
Immobilized diphenylprolinol ether (Hayashi et al.)	Pump-driven microflow	495	6–12	Highest reported TON/TOF in immobilized aldol catalysis	Hayashi *et al.*, *Chem. Asian J.*, 2022
PS-supported prolinamide (Pericàs group)	Batch/flow	n.r.	n.r.	High ee; excellent recyclability	Pericàs *et al.*, *Org. Lett.*, 2006
PS-supported L-proline (Gruttadauria & Noto)	Batch	n.r.	n.r.	High ee in water; long reaction time	Gruttadauria *et al.*, *Eur. J. Org. Chem.*, 2007
Gel-supported organocatalyst (Schmiegel et al.)	Flow	n.r.	n.r.	First gel-bound flow aldol catalyst	Schmiegel *et al.*, *Eur. J. Org. Chem.*, 2021
Ionic-liquid immobilized L-proline (Wu et al.)	Batch	n.r.	n.r.	Recyclable IL matrix	Wu *et al.*, *Org. Lett.*, 2006
Fe_3O_4-supported L-proline (Zhi et al.)	Batch	n.r.	n.r.	Magnetically recoverable catalyst	Zhi *et al.*, *RSC Adv.*, 2014

Notes:

- Only Hayashi et al. explicitly report TON/TOF values.
- "n.r." indicates TON/TOF not reported in the original publication.
- TON/TOF for this work are taken directly from Table S4 (mass-normalized).

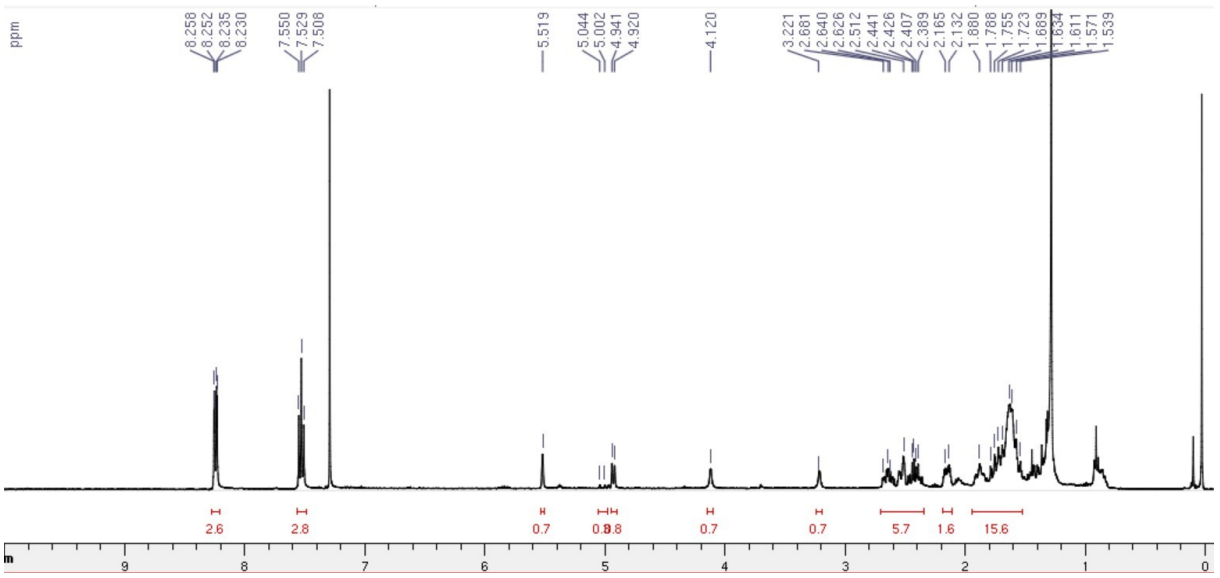


Fig. S4. [1]H NMR of the model Aldol product (Table 1, Entry 1) **3a**

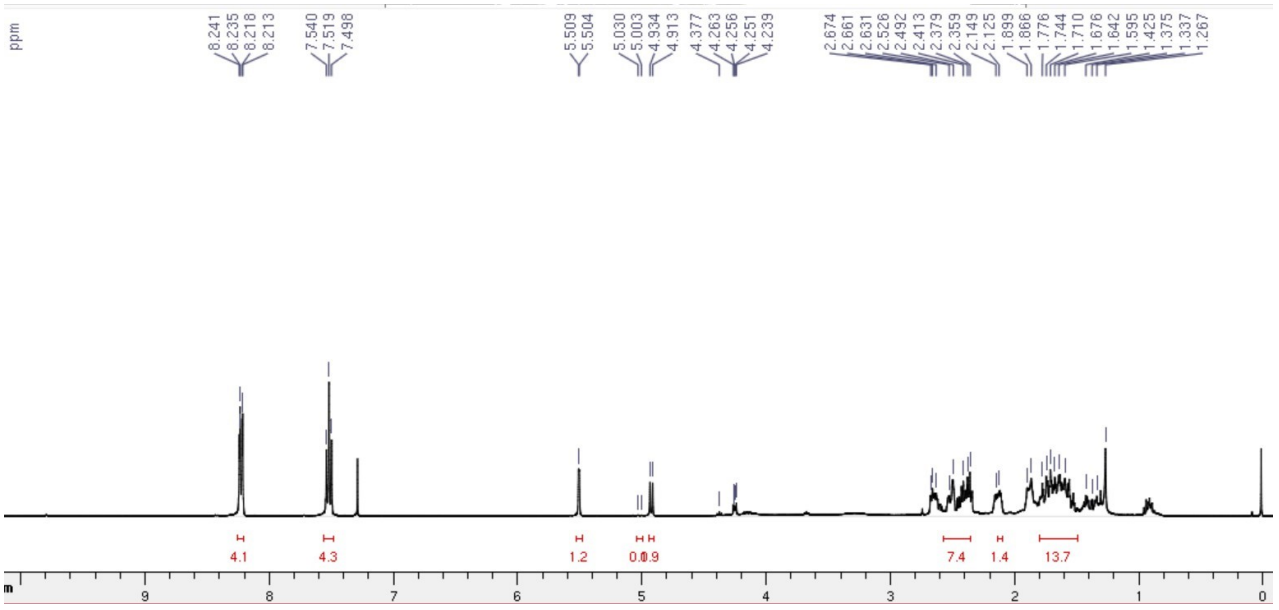


Fig. S5. 1H NMR of the model Aldol product (Table 2, Entry 1)**3a**

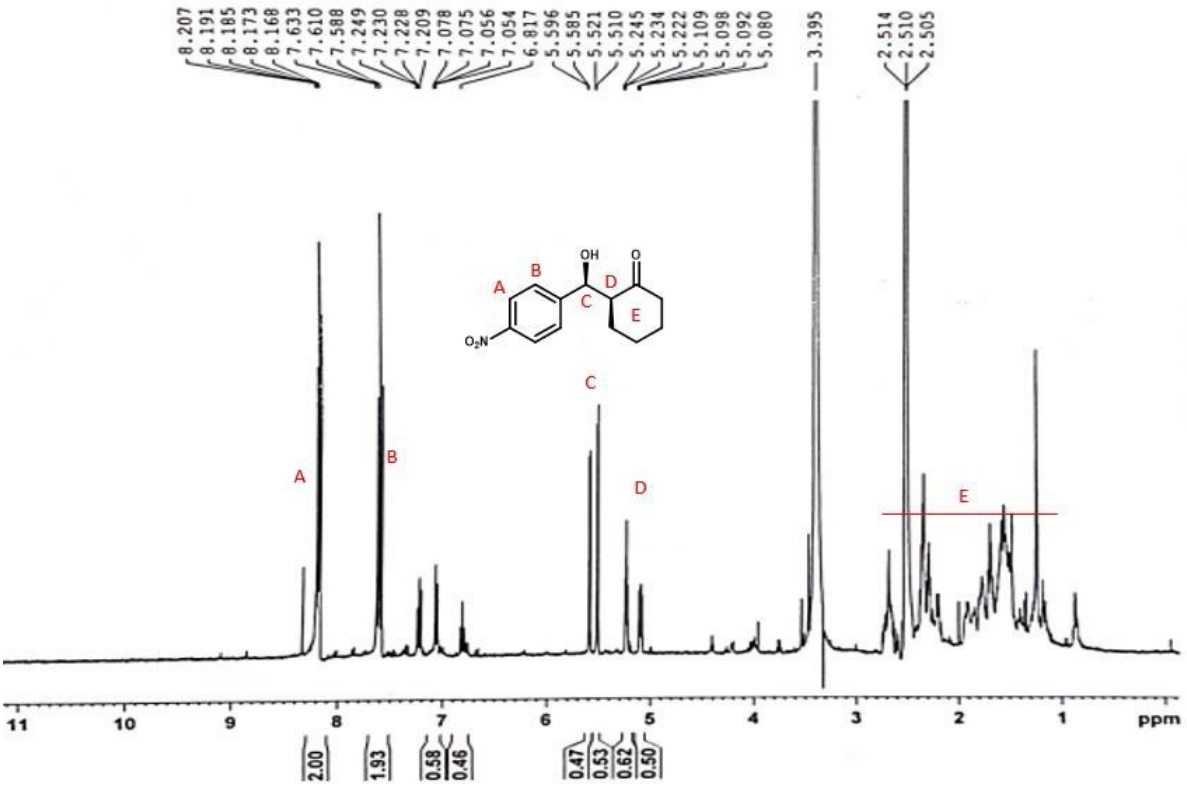


Fig. S6. ^{1}H NMR of the model Aldol product using DMSO-d6 (Table 2, Entry 5)

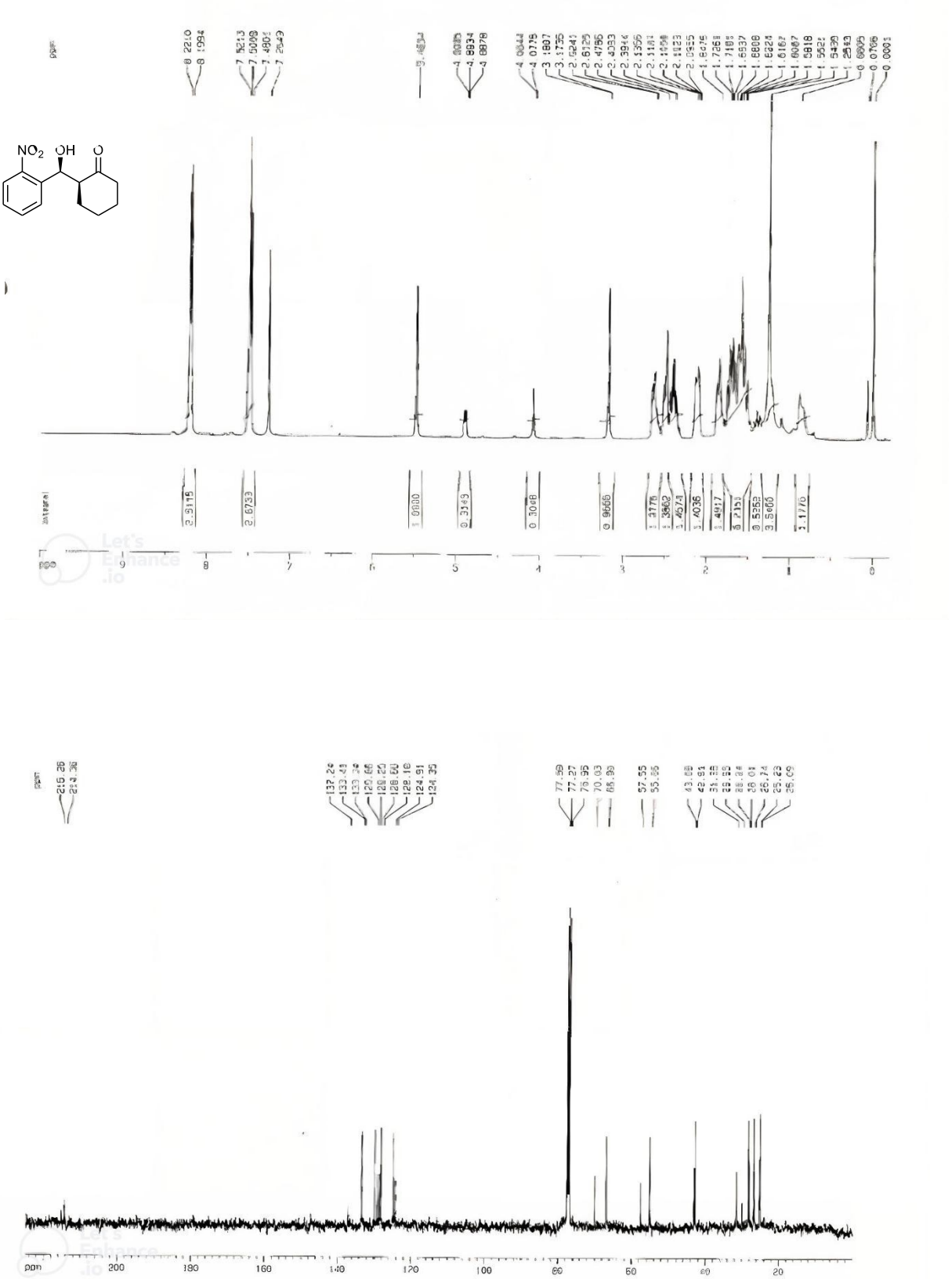


Fig. S7. ^{1}H & ^{13}C NMR Spectra of (S)-2-((S)-hydroxy(2-nitrophenyl)methyl)cyclohexan-1- one **(3b)**.

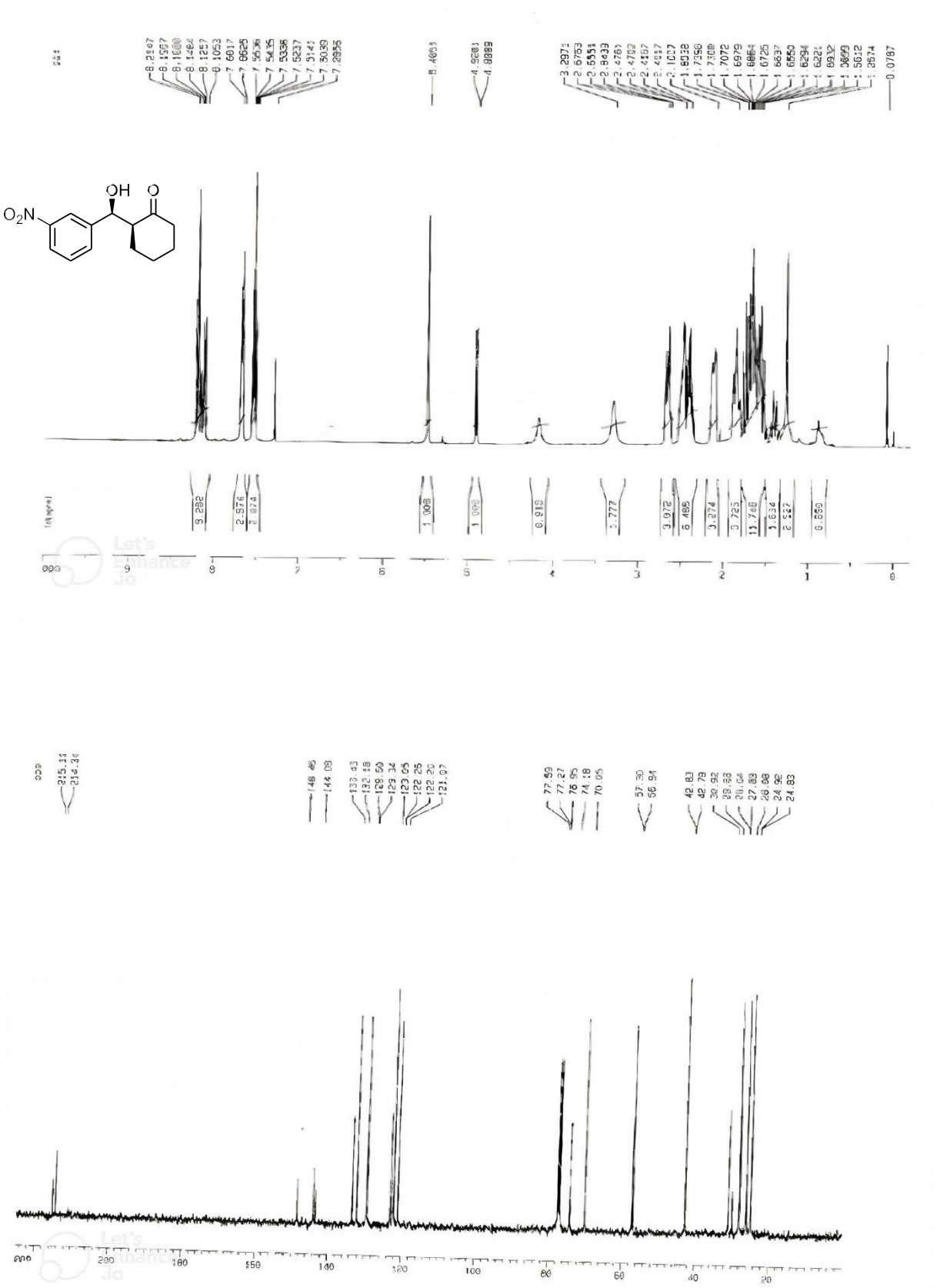


Fig. S8. ^{1}H & ^{13}C NMR Spectra of ((S)-2-((S)-hydroxy(3-nitrophenyl)methyl)cyclohexan-1-one. **(3c)**

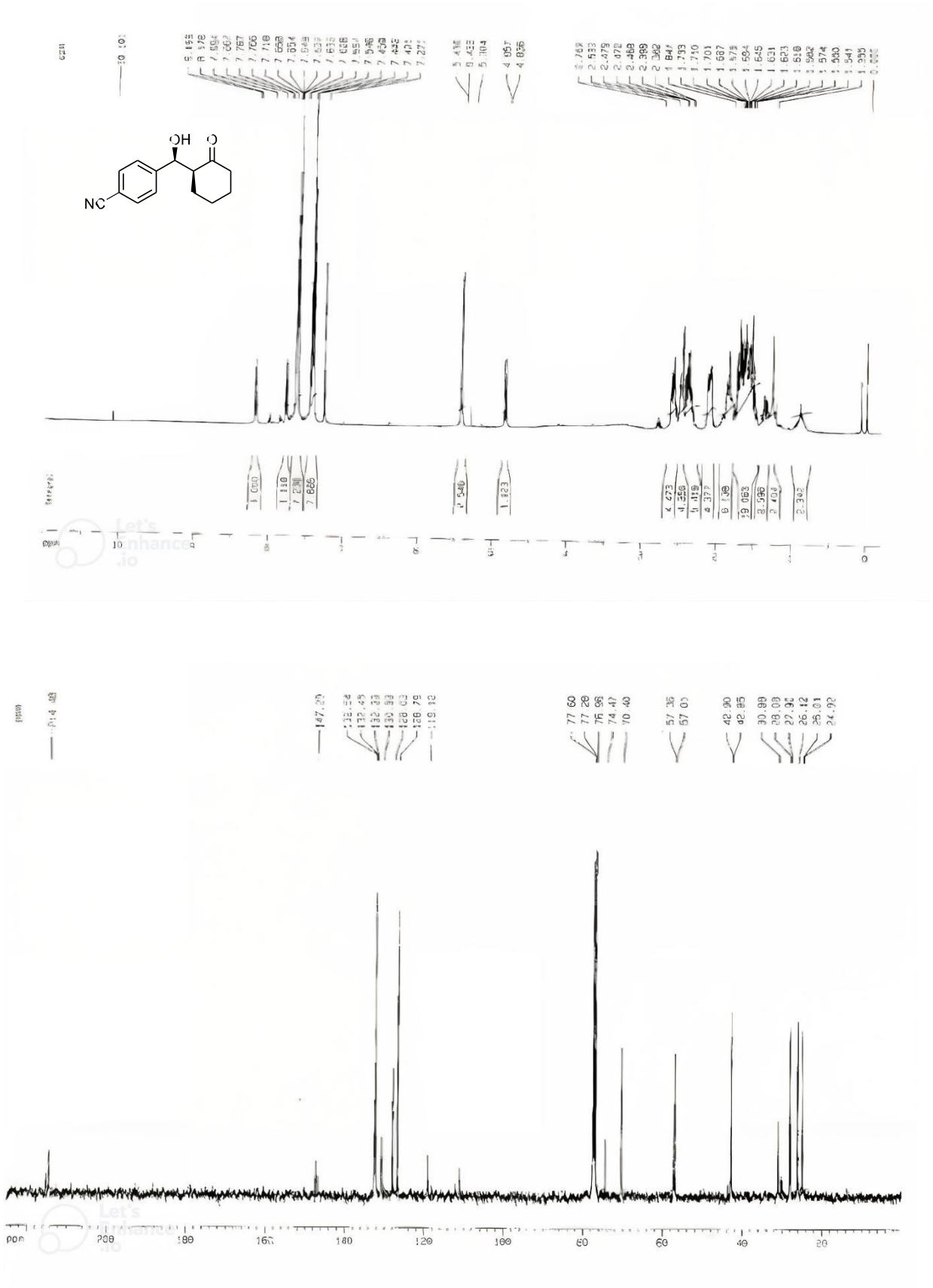


Fig. S9. ^{1}H & ^{13}C NMR Spectra of 4-((S)-hydroxy((S)-2-oxocyclohexyl)methyl)benzonitrile **(3d)**.

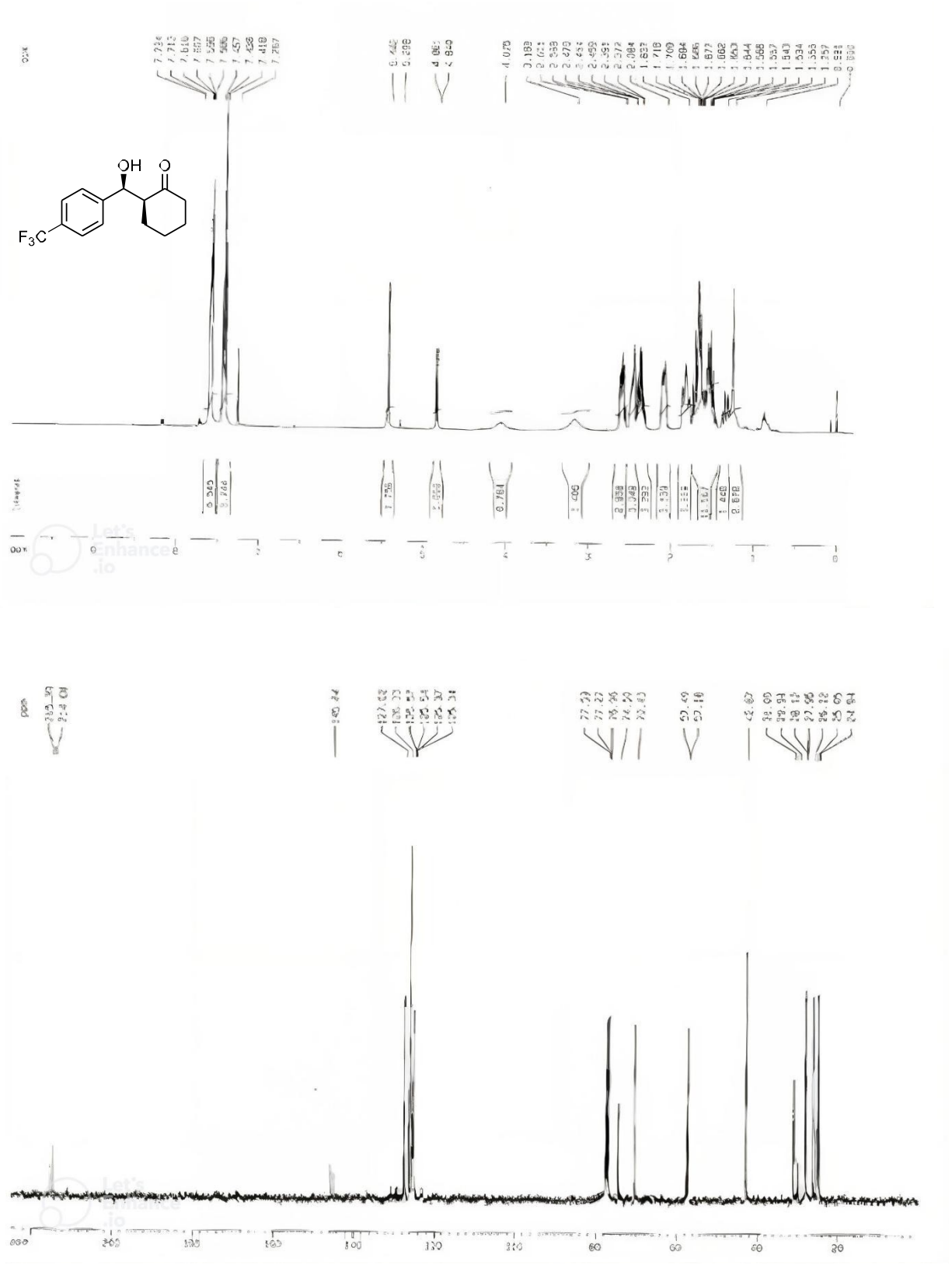


Fig. S10. ^{1}H & ^{13}C NMR Spectra of (S)-2-((S)-hydroxy(4-(trifluoromethyl)phenyl)methyl) cyclohexan-1-one **(3e).**

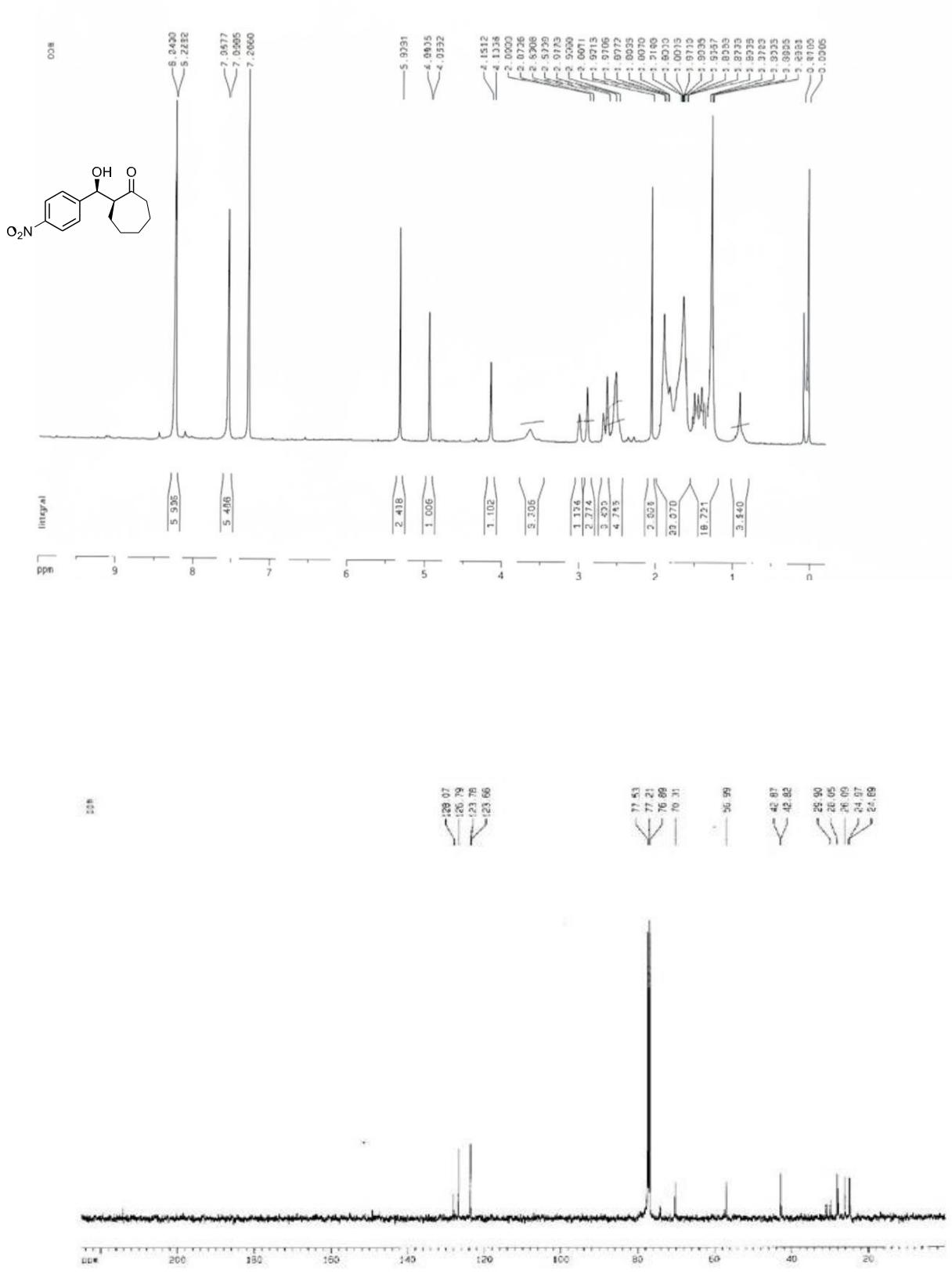


Fig. S11. ^{1}H & ^{13}C NMR Spectra of (S)-2-((S)-hydroxy(4-nitrophenyl)methyl)cycloheptan-1-one **(3f).**

Fig. S12. ^{1}H & ^{13}C NMR Spectra of (S)-4-(4-chlorophenyl)-4-hydroxybutan-2-one **(3g).**

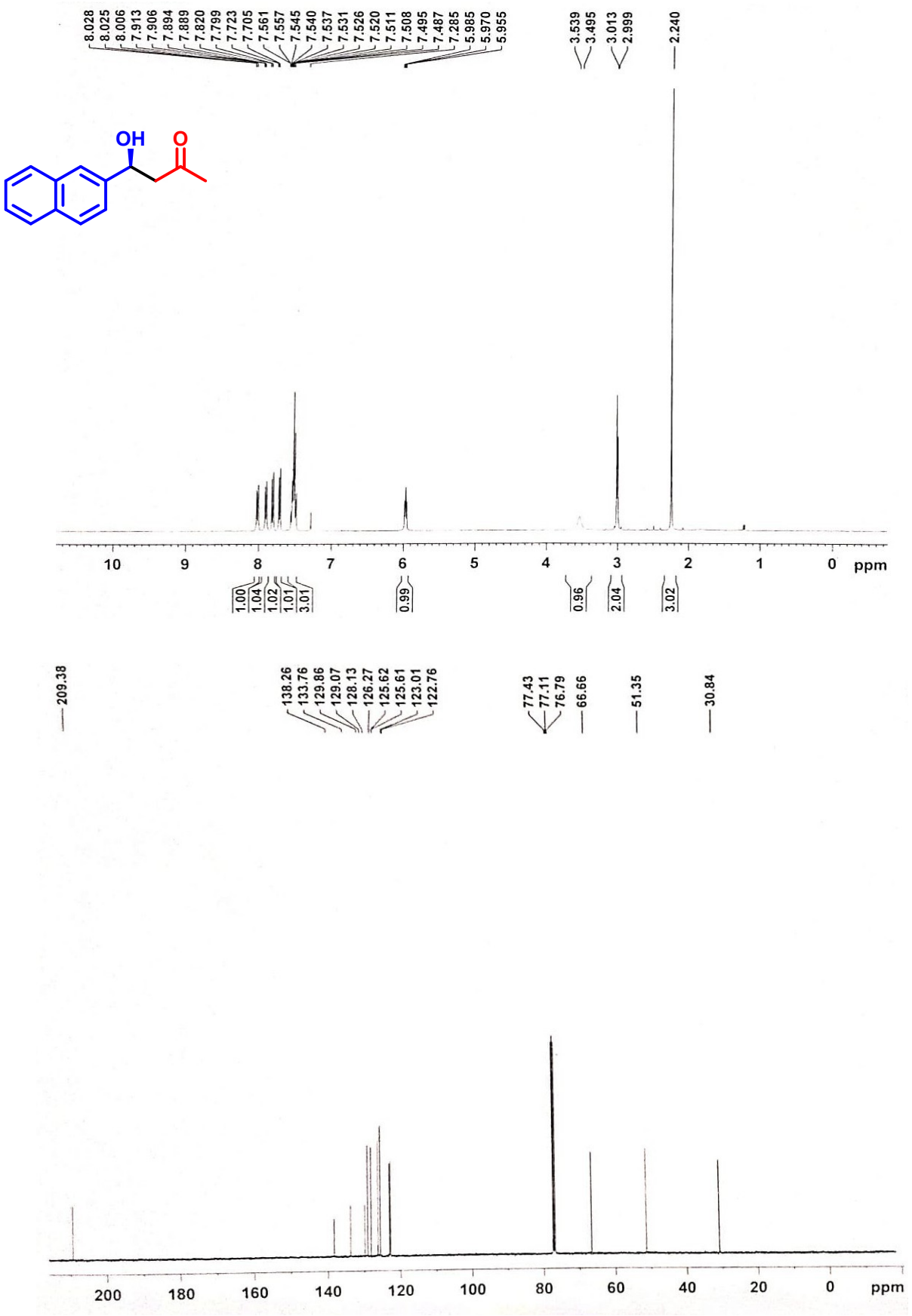


Fig. S13. ^{1}H & ^{13}C NMR Spectra of (S)-4-hydroxy-4-(naphthalen-2-yl)butan-2-one **(3h)**.

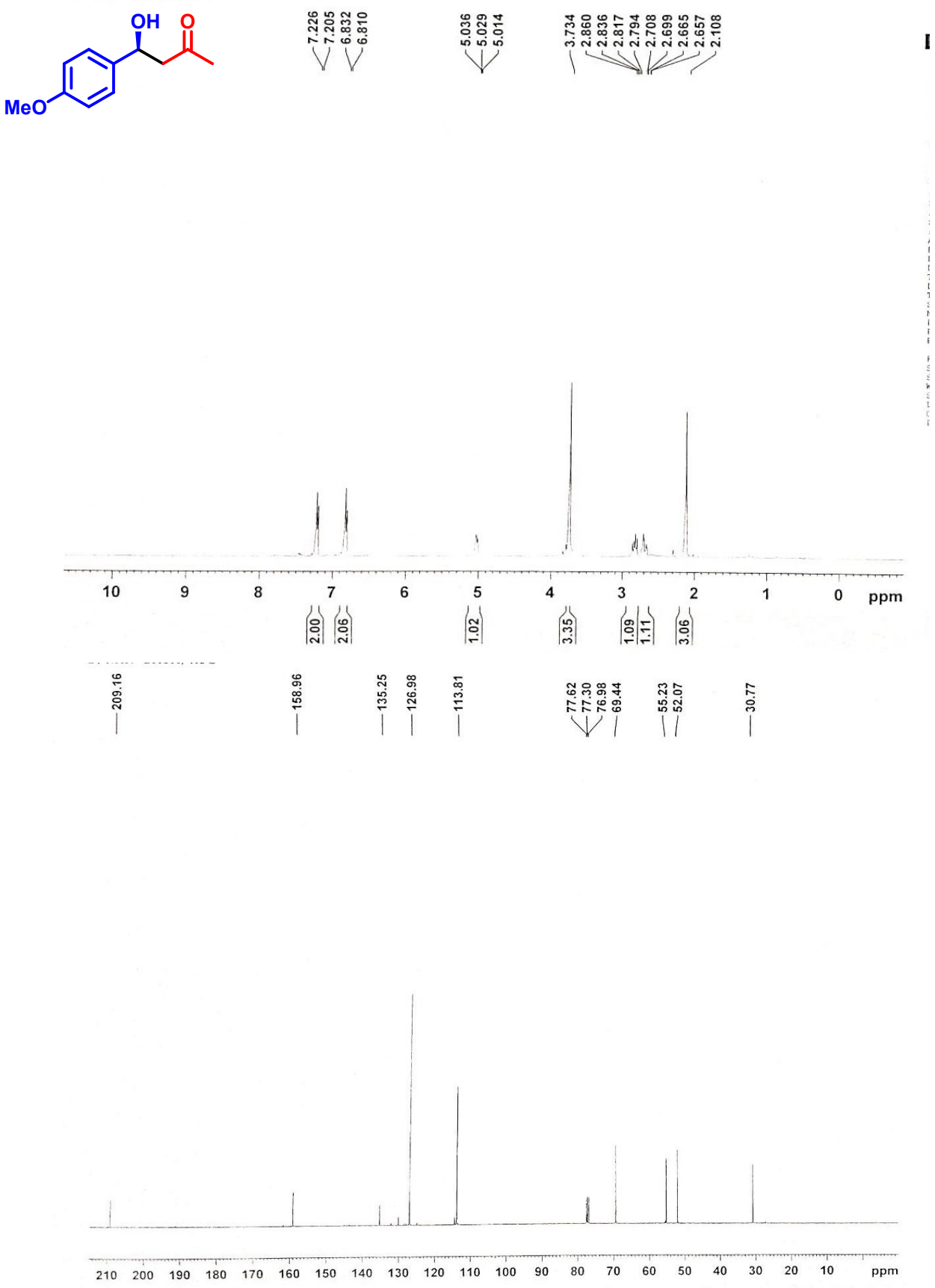


Fig. S14. ^{1}H & ^{13}C NMR Spectra of (S)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one **(3i)**.

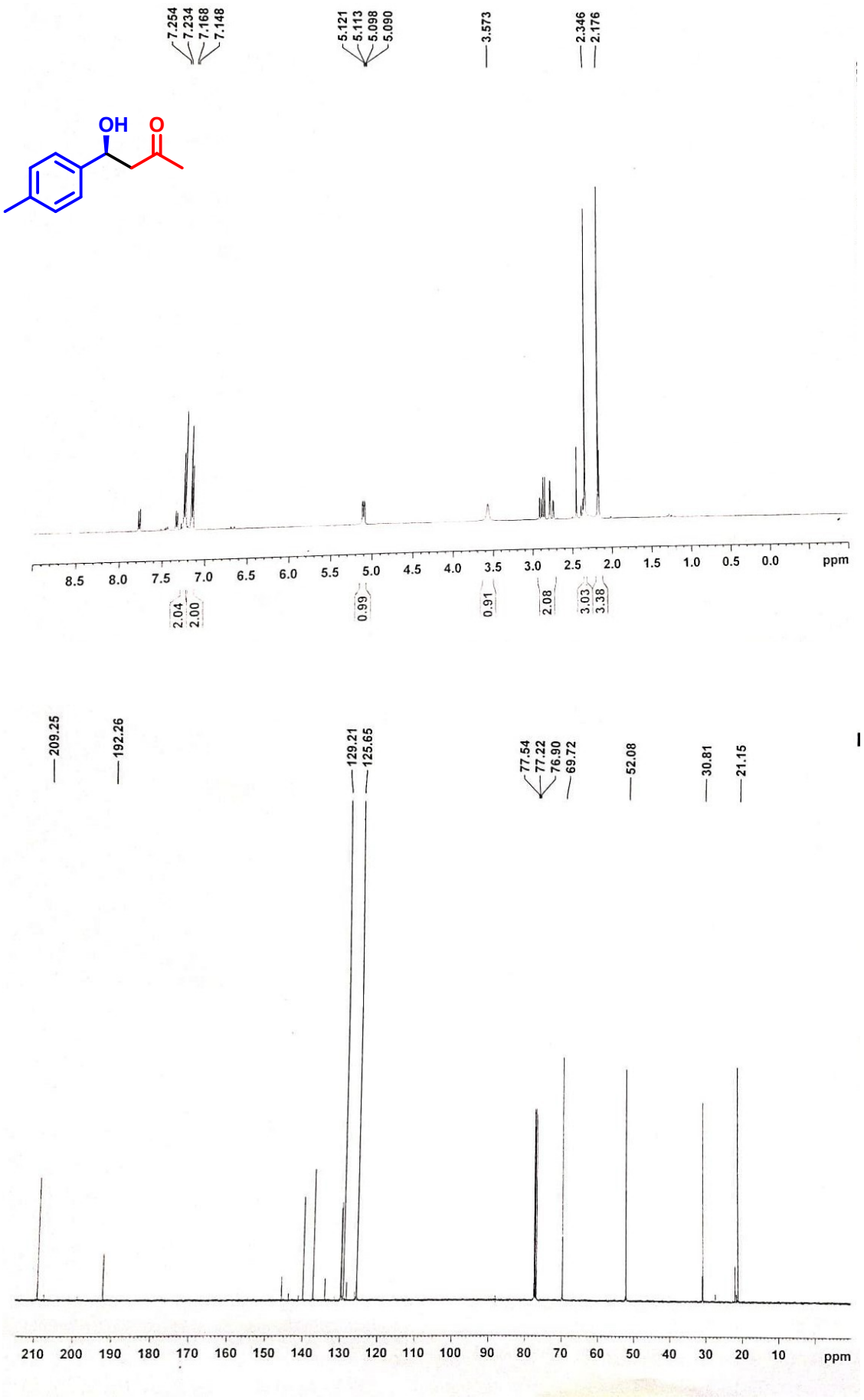


Fig. S15. ^{1}H & ^{13}C NMR Spectra of (S)-4-hydroxy-4-(p-tolyl)butan-2-one **(3j)**.

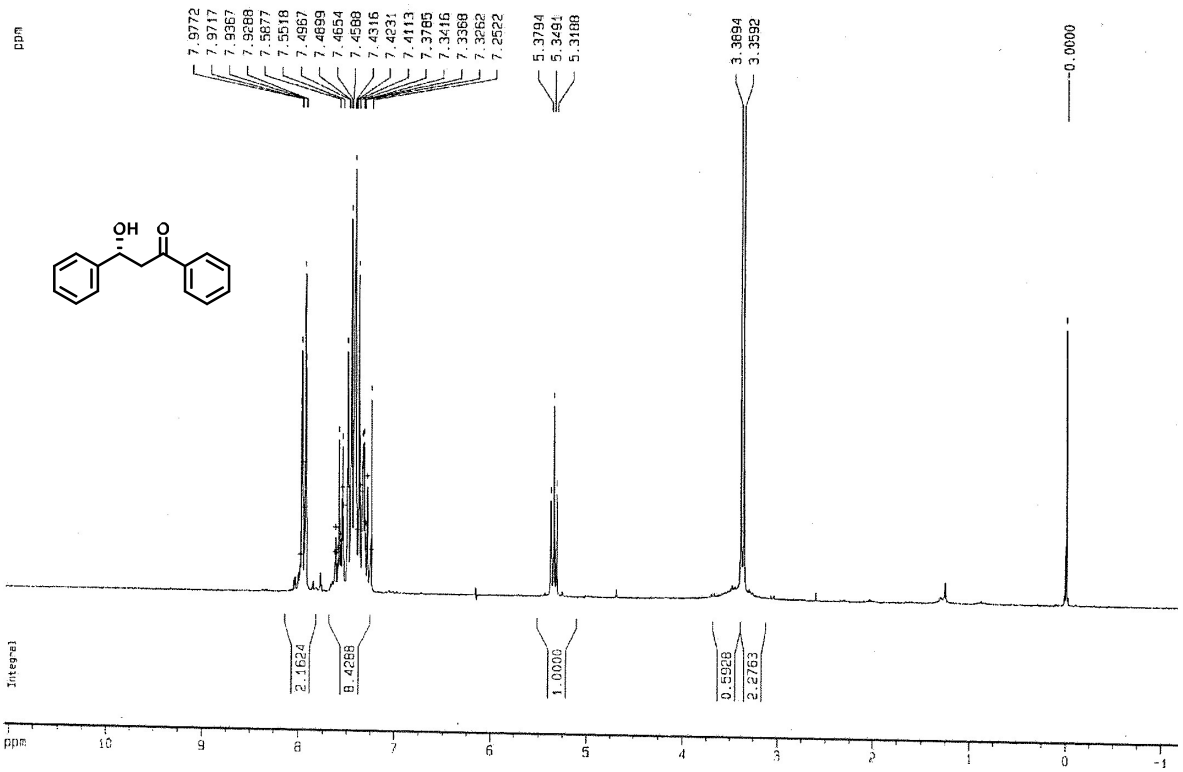


Fig. S16. ^{1}**H** NMR (R)-3-hydroxy-1,3-diphenylpropan-1-one **(3k)**.

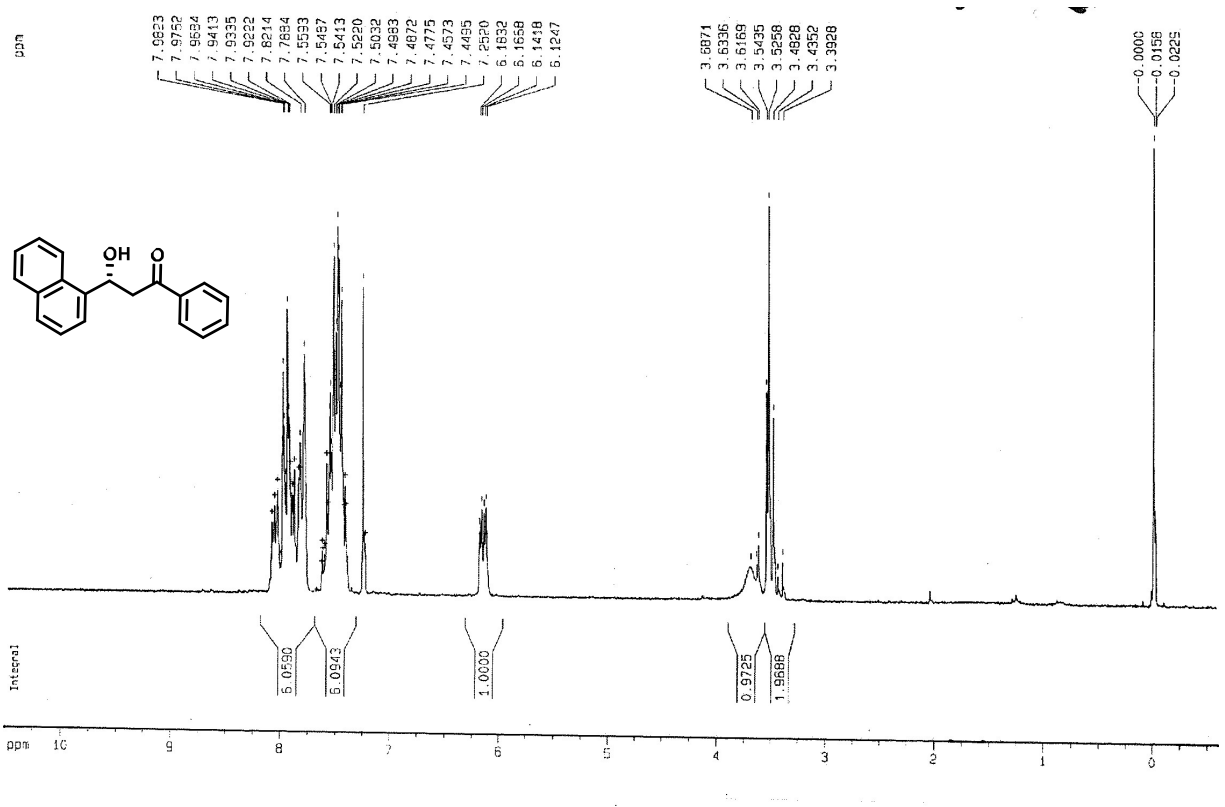


Fig. S17. ^{1}**H** NMR (R)-3-hydroxy-3-(naphthalen-1-yl)-1-phenylpropan-1-one **(3l)**.

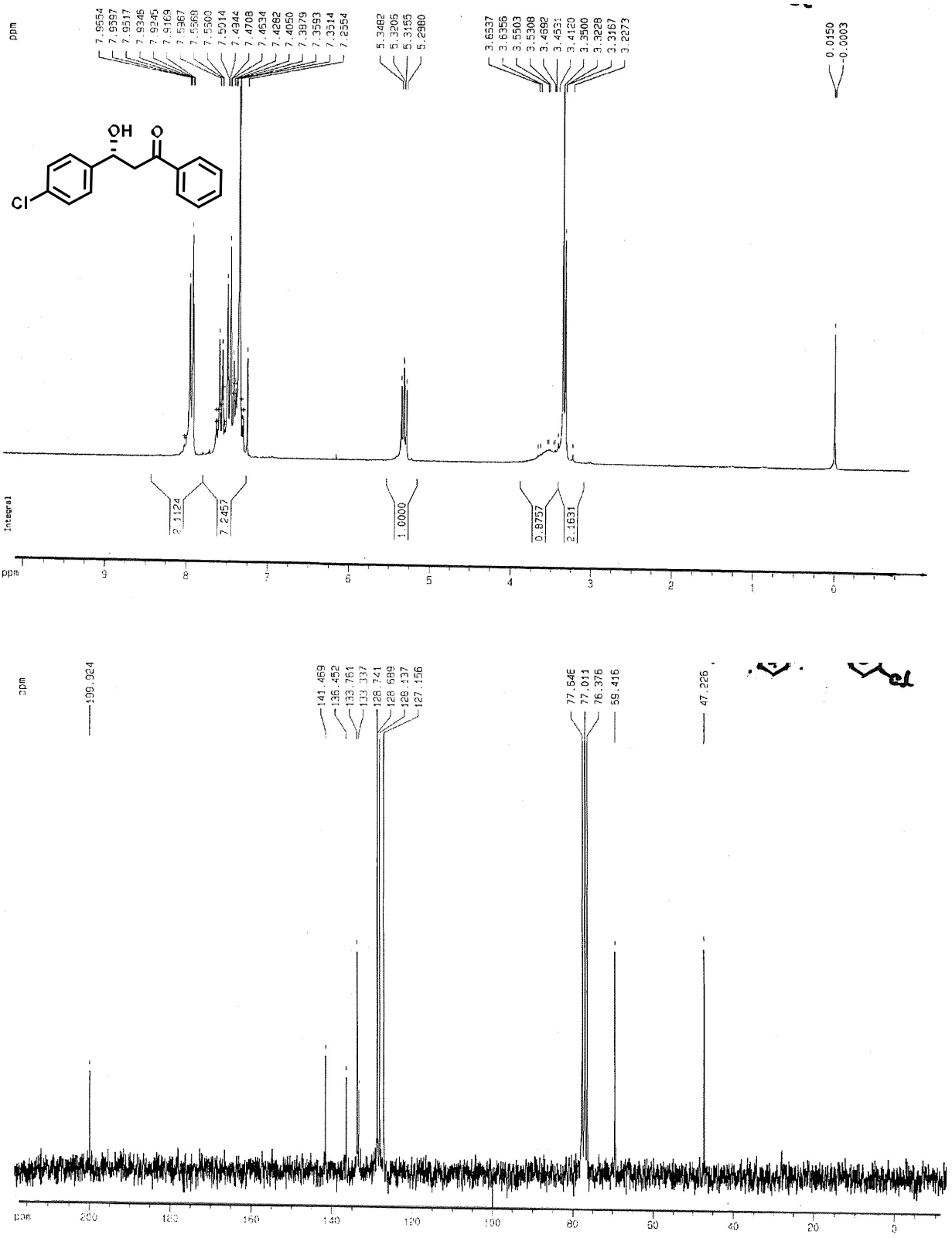


Fig. S18. ^{1}**H** NMR and ^{13}**C** NMR (R)-3-(4-chlorophenyl)-3-hydroxy-1-phenylpropan-1-one **(3m)**.

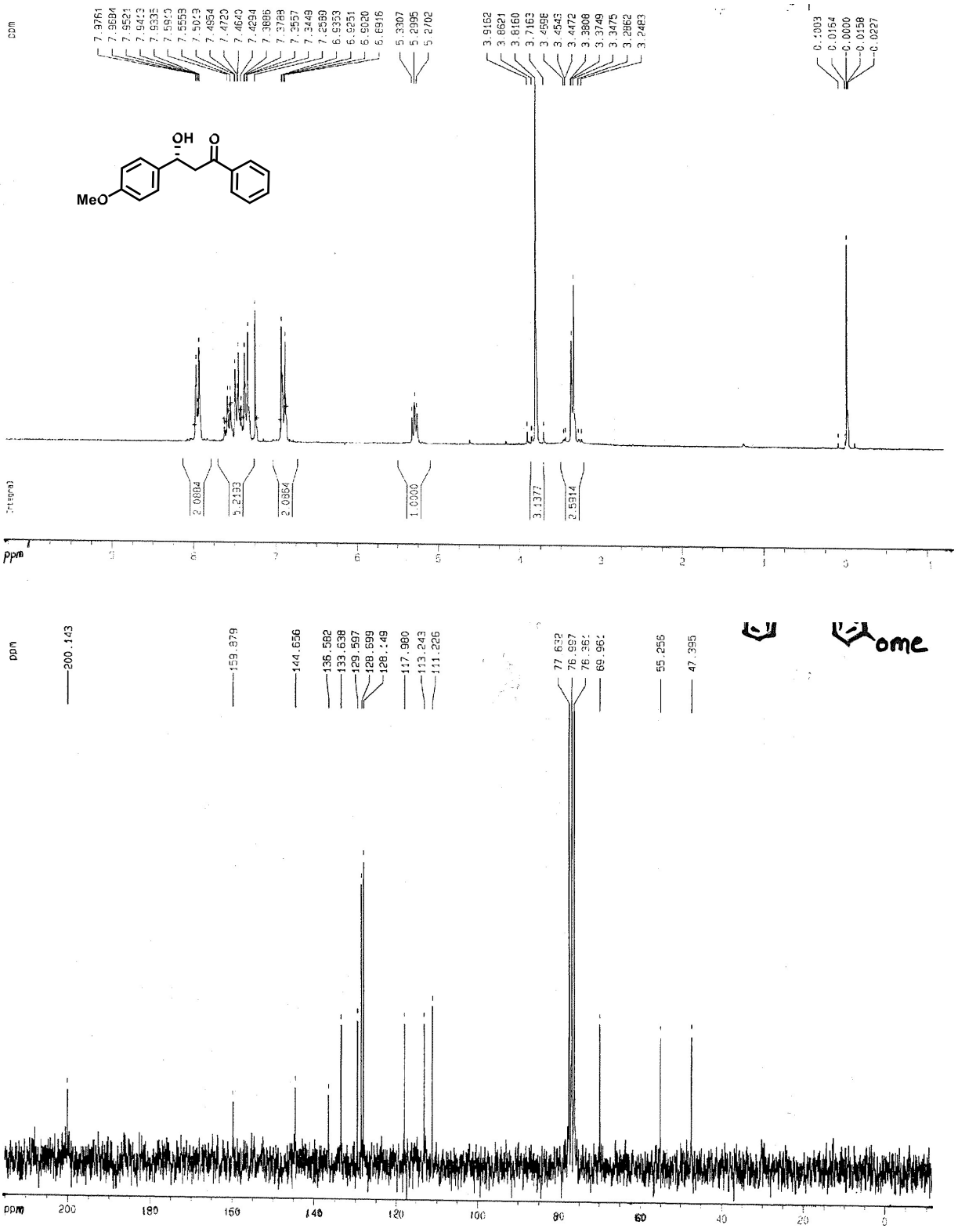
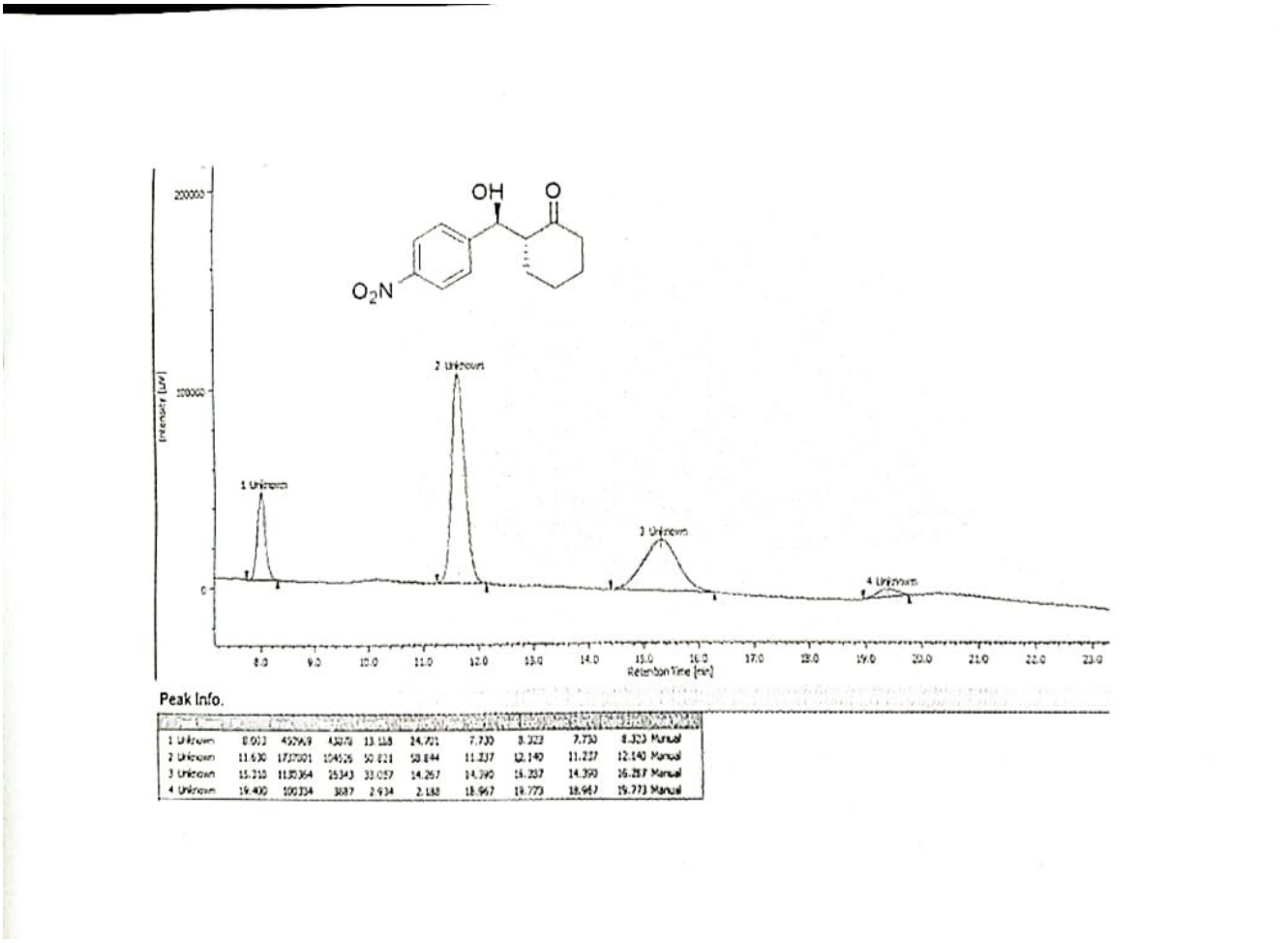
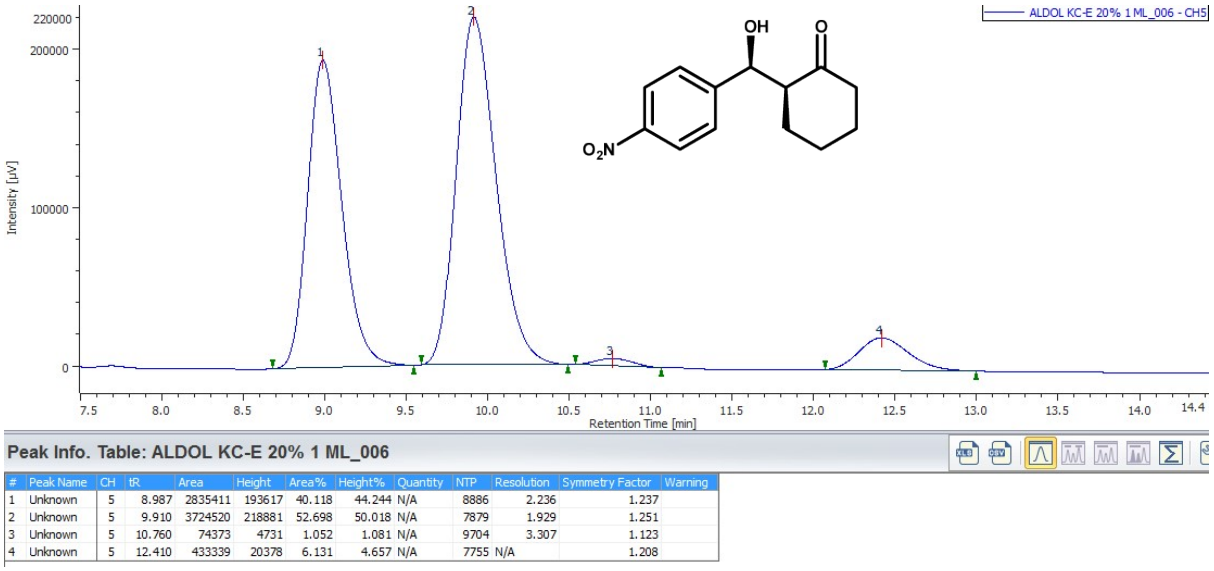


Fig. S19. **^{1}H** NMR and **^{13}C** NMR (R)-3-hydroxy-3-(4-methoxyphenyl)-1-phenylpropan-1-one **(3n)**.



1 Unknown	8.003	492949	43078	13.118	24.701	7.730	8.323	7.730	8.323 Manual
2 Unknown	11.630	1737001	104526	50.821	58.844	11.237	12.140	11.237	12.140 Manual
3 Unknown	15.210	1130364	25343	33.057	14.267	14.390	16.257	14.390	16.257 Manual
4 Unknown	19.400	100334	3887	2.934	2.188	18.967	19.773	18.967	19.773 Manual

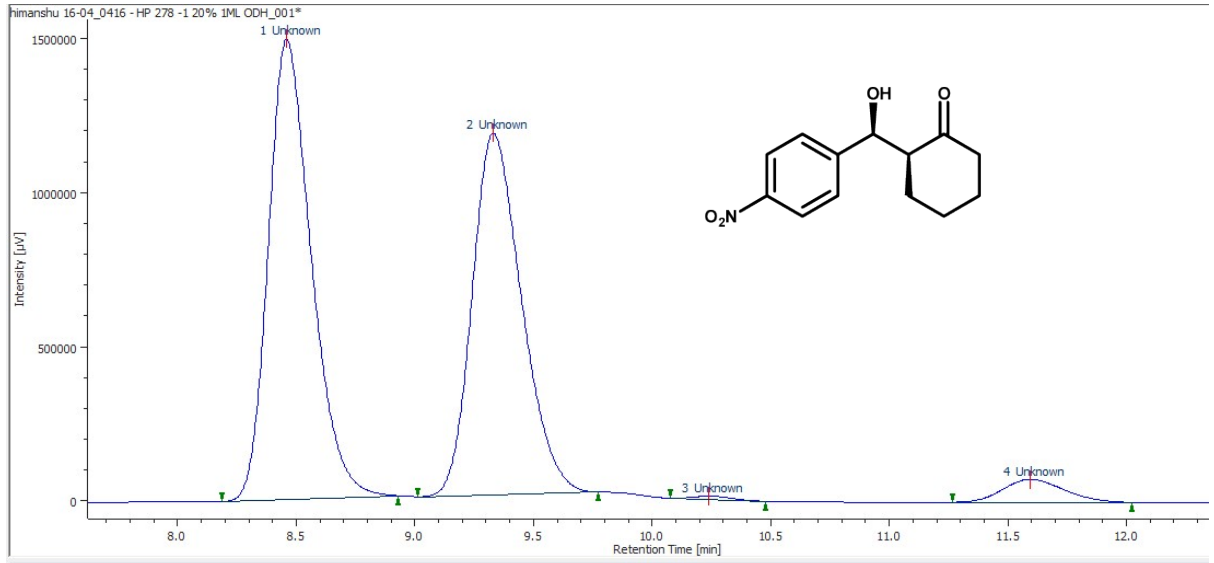
Fig. S20. Chiral HPLC of the model Aldol product (Table 1, Entry 1)



Peak Info. Table: ALDOL KC-E 20% 1 ML_006

#	Peak Name	CH	tR	Area	Height	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	5	8.987	2835411	193617	40.118	44.244	N/A	8886	2.236	1.237	
2	Unknown	5	9.910	3724520	218881	52.698	50.018	N/A	7879	1.929	1.251	
3	Unknown	5	10.760	74373	4731	1.052	1.081	N/A	9704	3.307	1.123	
4	Unknown	5	12.410	433339	20378	6.131	4.657	N/A	7755	N/A	1.208	

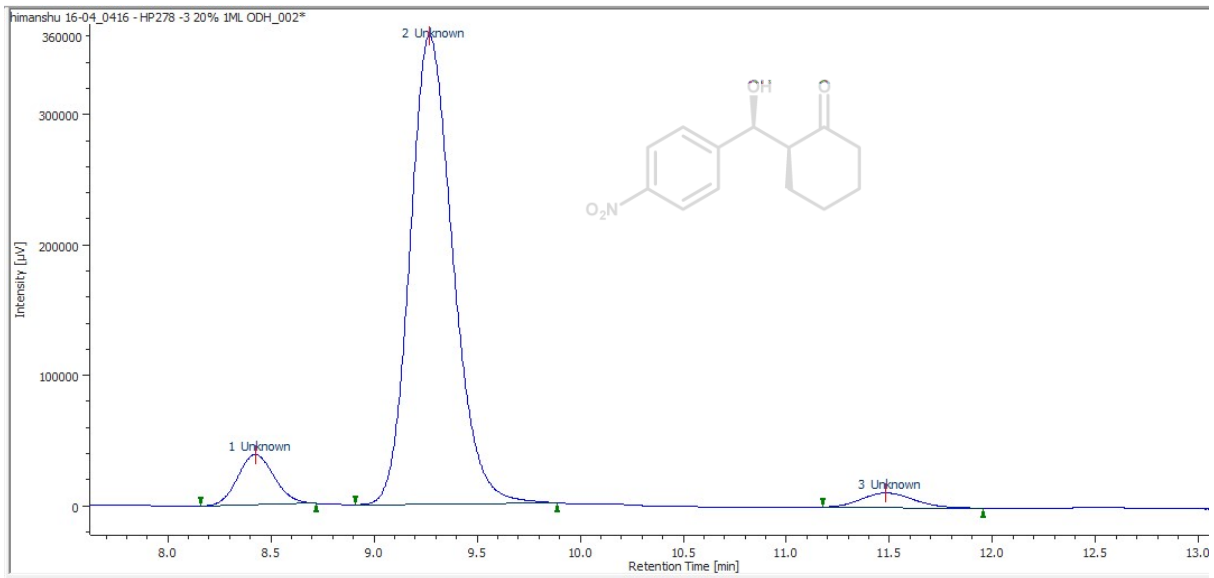
Fig. S21. Chiral HPLC of the model Aldol product (Table 1, Entry 4)



Peak Info. Table: himanshu 16-04_0416 - HP 278 -1 20% 1ML ODH_001*

#	Peak Name	tR	Area	Height	Area%	Height%	Peak Start	Peak End	Base Start	Base End	Peak Mark
1	Unknown	8.460	18717421	1489597	50.493	54.269	8.187	8.927	8.187	8.927	Manual
2	Unknown	9.330	16903596	1170576	45.600	42.646	9.010	9.770	9.010	9.770	Manual
3	Unknown	10.237	116796	10543	0.315	0.384	10.073	10.477	10.073	10.477	Manual
4	Unknown	11.590	1331792	74148	3.593	2.701	11.263	12.020	11.263	12.020	Manual

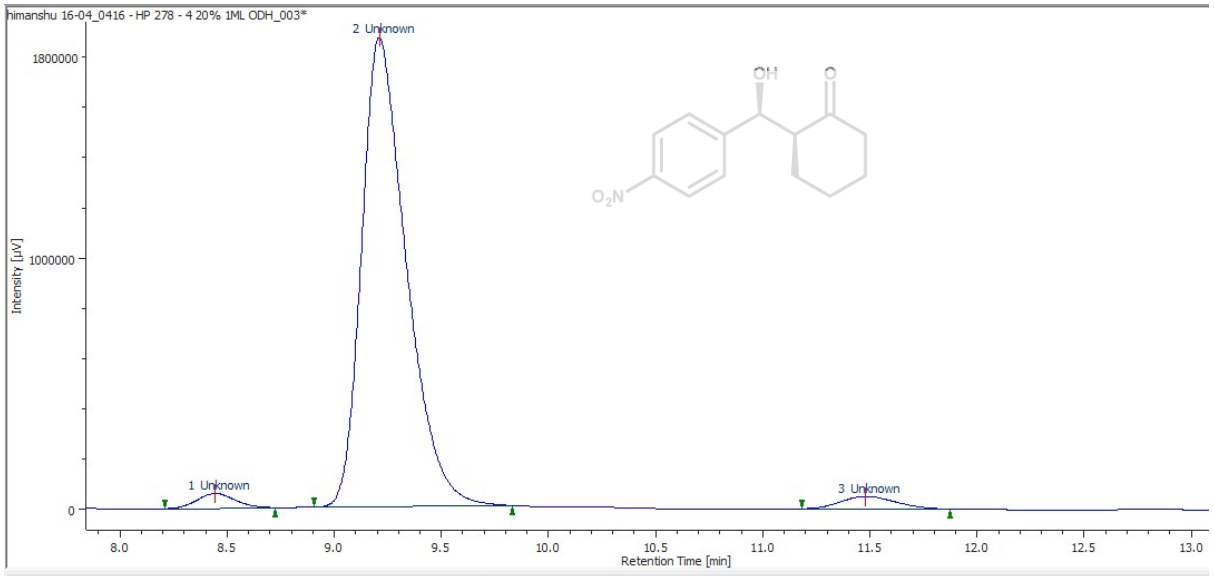
Fig. S22. Chiral HPLC of the model Aldol product (Table 2, Entry 5)



Peak Info. Table: himanshu 16-04_0416 - HP278 -3 20% 1ML ODH_002*

#	Peak Name	tR	Area	Height	Area%	Height%	Peak Start	Peak End	Base Start	Base End	Peak Mark
1	Unknown	8.423	470941	38488	8.046	9.427	8.160	8.720	8.160	8.720	Manual
2	Unknown	9.267	5186602	358674	88.615	87.851	8.910	9.887	8.910	9.887	Manual
3	Unknown	11.477	195428	11111	3.339	2.722	11.173	11.950	11.173	11.950	Manual

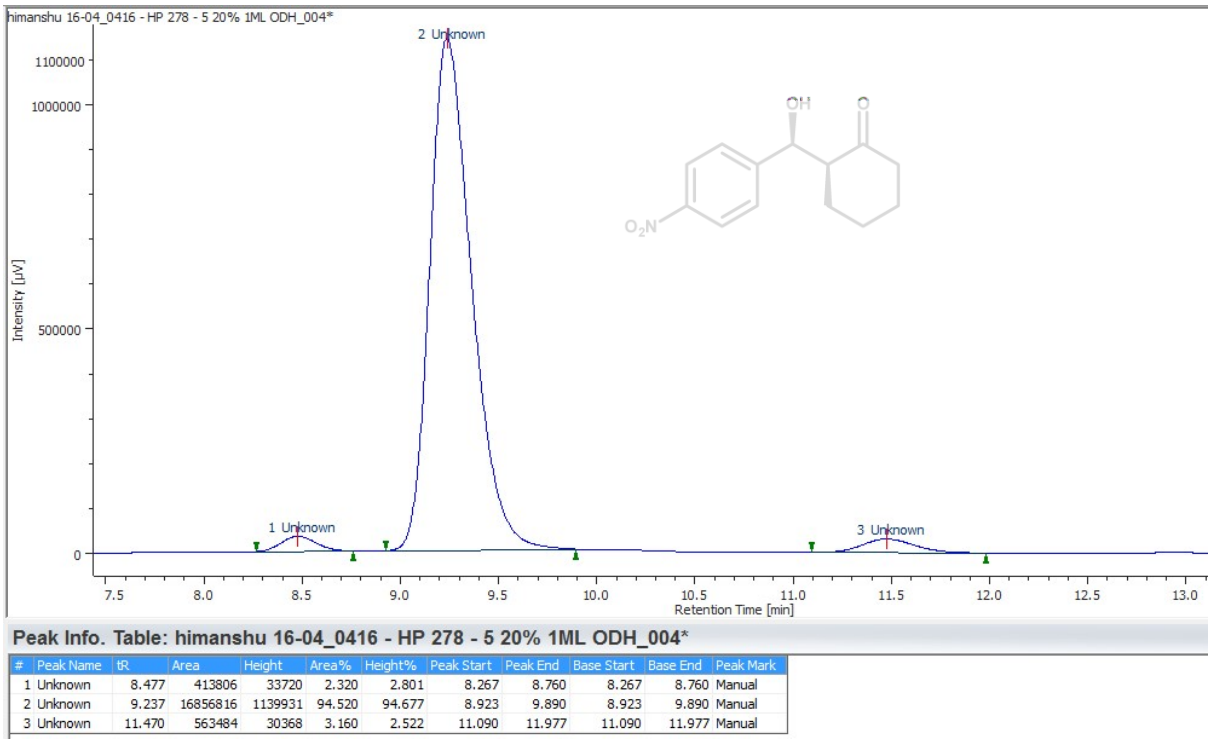
Fig. S23. Chiral HPLC of the model Aldol product (Table 2, Entry 3)



Peak Info. Table: himanshu 16-04_0416 - HP 278 - 4 20% 1ML ODH_003*

#	Peak Name	tR	Area	Height	Area%	Height%	Peak Start	Peak End	Base Start	Base End	Peak Mark
1	Unknown	8.443	716989	57988	2.505	2.941	8.210	8.723	8.210	8.723	Manual
2	Unknown	9.210	27024196	1864441	94.413	94.549	8.907	9.830	8.907	9.830	Manual
3	Unknown	11.477	882199	49496	3.082	2.510	11.180	11.870	11.180	11.870	Manual

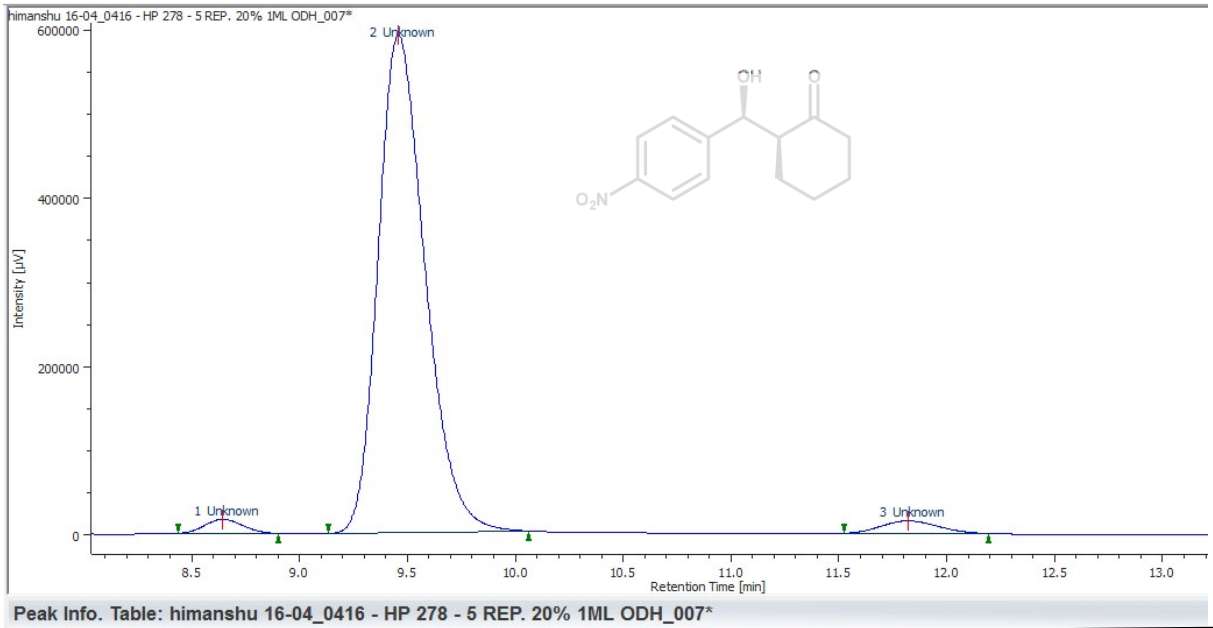
Fig. S24. Chiral HPLC of the model Aldol product (Table 2, Entry 4)



Peak Info. Table: himanshu 16-04_0416 - HP 278 - 5 20% 1ML ODH_004*

#	Peak Name	tR	Area	Height	Area%	Height%	Peak Start	Peak End	Base Start	Base End	Peak Mark
1	Unknown	8.477	413806	33720	2.320	2.801	8.267	8.760	8.267	8.760	Manual
2	Unknown	9.237	16856816	1139931	94.520	94.677	8.923	9.890	8.923	9.890	Manual
3	Unknown	11.470	563484	30368	3.160	2.522	11.090	11.977	11.090	11.977	Manual

Fig. S25. Chiral HPLC of the model Aldol product (Table 4, Entry 2)



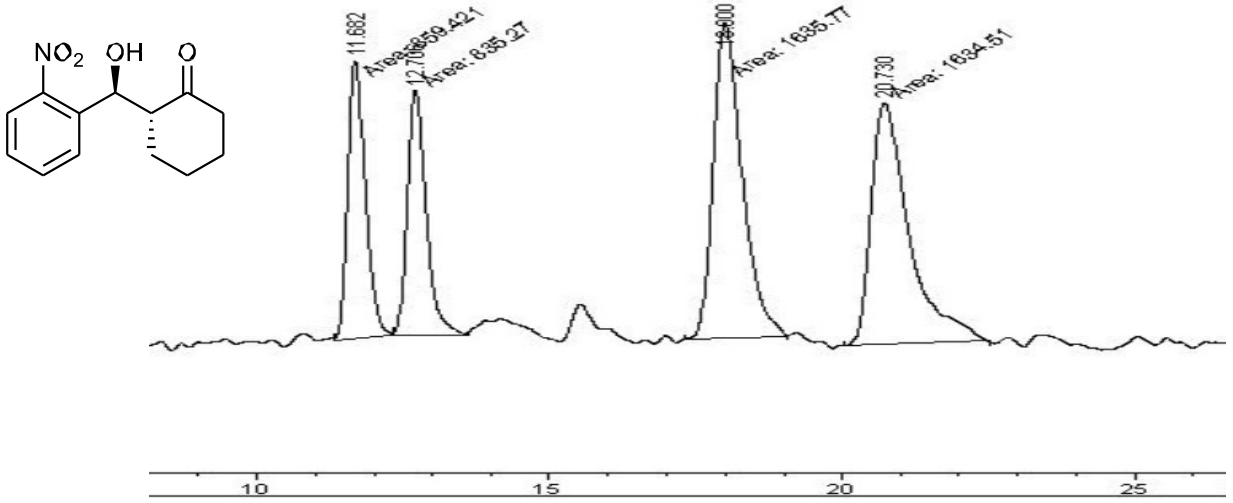
Peak Info. Table: himanshu 16-04_0416 - HP 278 - 5 REP. 20% 1ML ODH_007*

#	Peak Name	tR	Area	Height	Area%	Height%	Peak Start	Peak End	Base Start	Base End	Peak Mark
1	Unknown	8.643	203186	16682	2.159	2.682	8.437	8.900	8.437	8.900	Manual
2	Unknown	9.457	8933990	590372	94.946	94.921	9.133	10.060	9.133	10.060	Manual
3	Unknown	11.817	272342	14906	2.894	2.397	11.520	12.190	11.520	12.190	Manual

Fig. S26. Chiral HPLC of the model Aldol product (Table 4, Entry 5)

HPLC data for aldol products (3b-f)

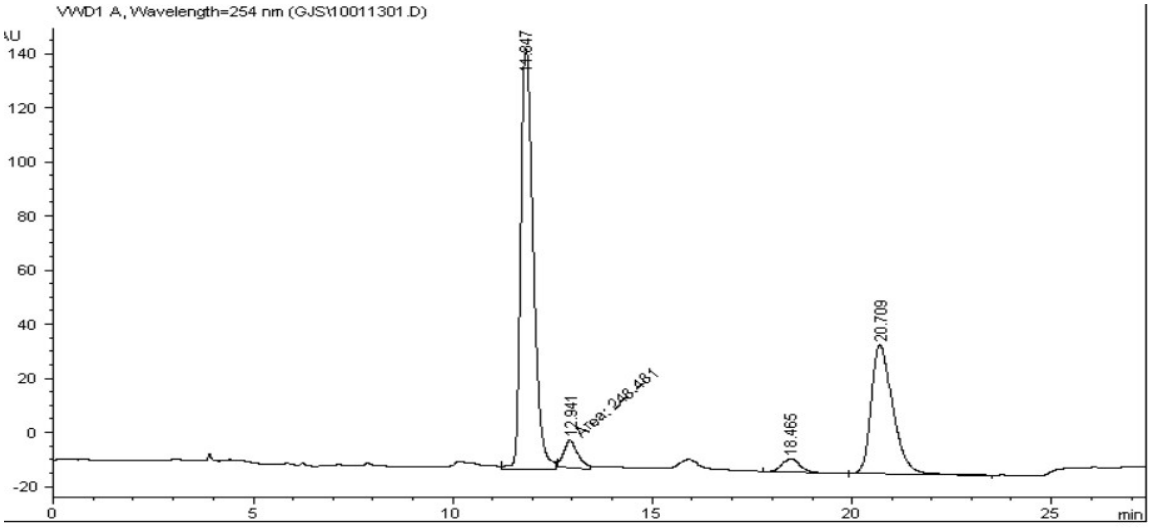
Racemic:



RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
11.682	-	859.42133	41.82713	0.92	0.3106	7836	-	-
12.706	-	835.27014	36.78238	0.91	0.3397	7749	1.85	1.09
18.000	-	1635.76807	47.28149	0.71	0.5145	6782	7.28	1.42
20.730	-	1634.50732	36.29799	0.57	0.6261	6073	2.81	1.15

*** End of Report ***

Chiral

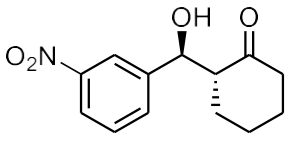


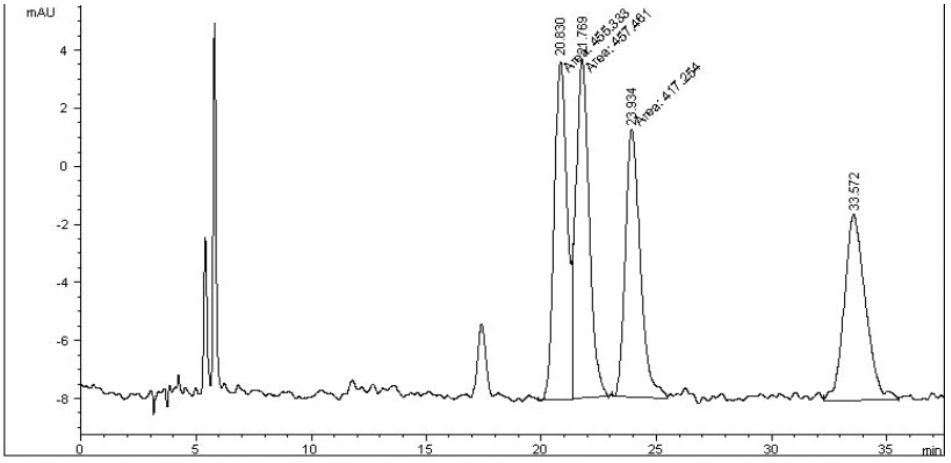
RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
11.847	-	3297.36548	152.74306	0.72	0.3203	7578	-	-
12.941	-	248.48138	10.05526	0.83	0.3689	6819	1.86	1.09
18.465	-	167.84442	5.01066	0.88	0.4902	7861	7.56	1.43
20.709	-	1799.42102	47.35897	0.65	0.5678	7369	2.49	1.12

*** End of Report ***

Fig. S27. (R)-2-((S)-hydroxy(2-nitrophenyl)methyl)cyclohexan-1-one **(3b).**

Racemic:

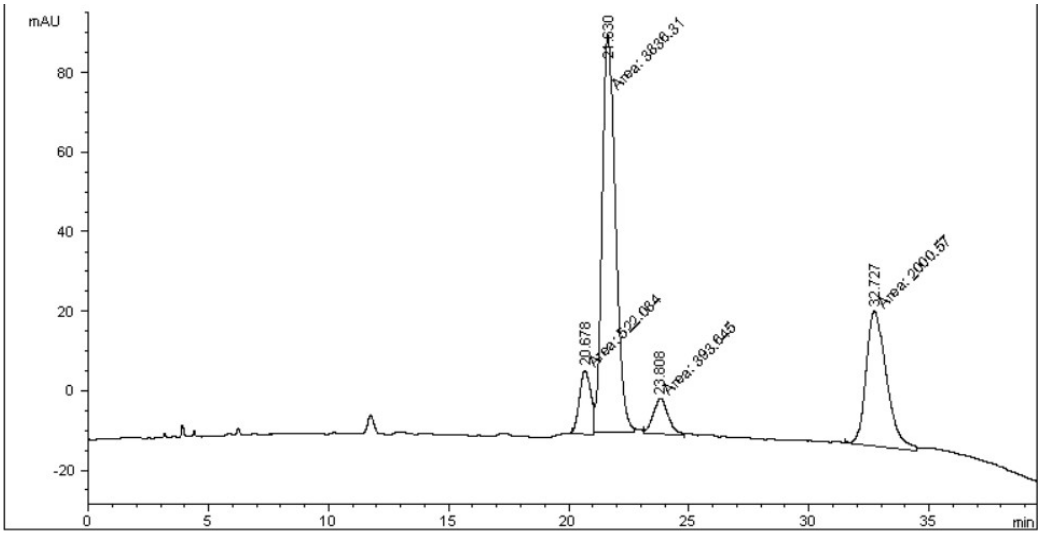




RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
20.830	-	455.33347	11.72084	0.68	0.6212	6229	-	-
21.769	-	457.46088	11.69538	0.83	0.6625	5982	0.86	1.05
23.934	-	417.25424	9.25202	0.85	0.6601	7284	1.92	1.10
33.572	-	415.25781	6.40810	0.76	0.9610	6762	6.99	1.40

*** End of Report ***

Chiral

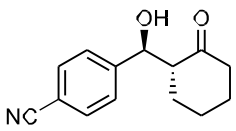


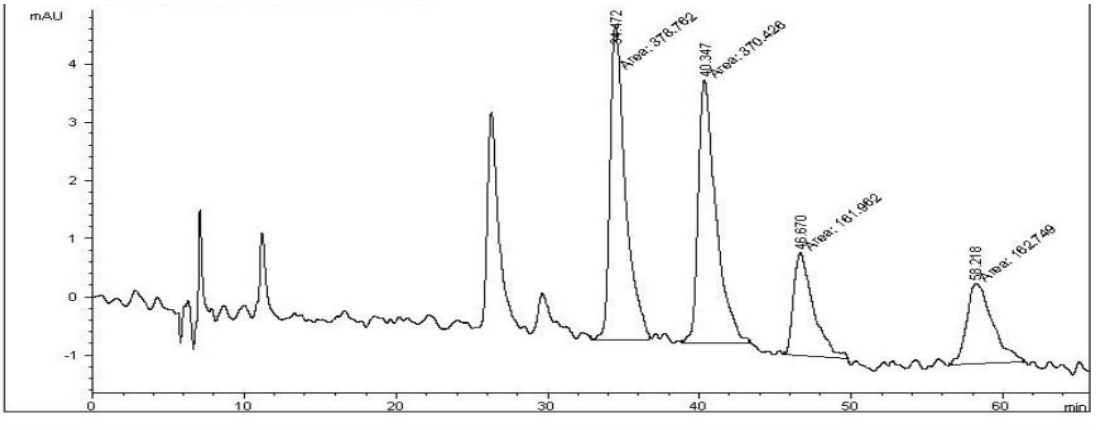
RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
20.678	-	522.08411	16.14416	0.91	0.5654	7409	-	-
21.630	-	3836.30811	100.04895	0.92	0.5824	7641	0.97	1.05
23.808	-	393.64481	8.98480	0.81	0.6455	7537	2.08	1.10
32.727	-	2000.57141	33.91225	0.79	0.8882	7522	6.83	1.37

*** End of Report ***

Fig. S28. (R)-2-((S)-hydroxy(3-nitrophenyl)methyl)cyclohexan-1-one **(3c).**

Racemic:

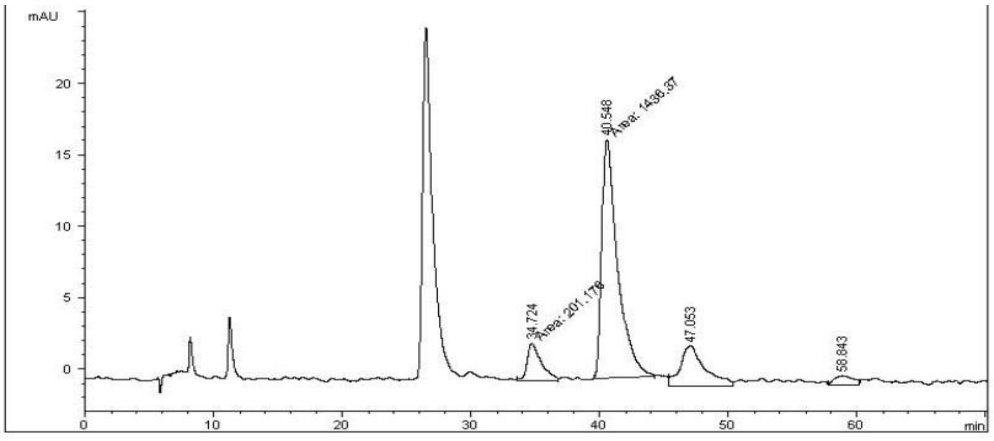




RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
34.472	-	378.76221	5.39652	0.51	0.9707	6987	-	-
40.347	-	370.42554	4.51371	0.58	1.1891	6379	3.20	1.17
46.670	-	161.96198	1.77071	0.55	1.2958	7186	2.99	1.16
58.218	-	162.74921	1.37424	0.56	1.7666	6017	4.43	1.25

*** End of Report ***

Chiral

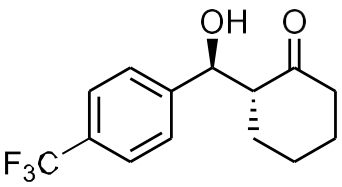


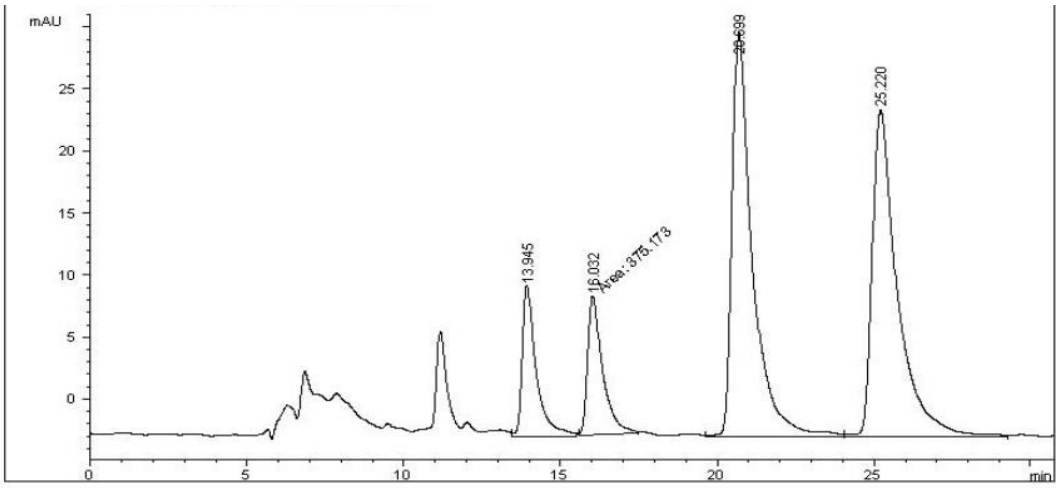
RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
34.724	-	201.17650	2.62804	0.49	1.0629	5913	-	-
40.548	-	1436.37097	16.76122	0.47	1.2036	6287	3.02	1.17
47.053	-	377.32501	2.84129	0.66	1.6841	4325	2.65	1.16
58.843	-	65.69677	6.41719e-1	0.67	2.1194	4271	3.64	1.25

*** End of Report ***

Fig. S29. 4-((S)-hydroxy((R)-2-oxocyclohexyl)methyl)benzonitrile **(3d).**

Racemic

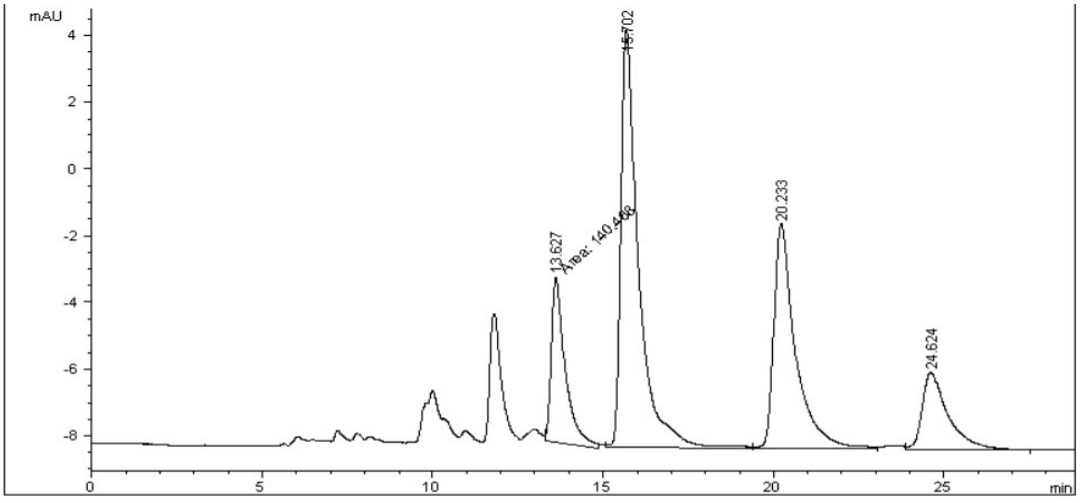




RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
13.945	-	373.12479	12.05669	0.49	0.4028	6639	-	-
16.032	-	375.17255	11.21222	0.67	0.4514	6990	2.87	1.15
20.699	-	1476.72656	32.36541	0.46	0.6018	6554	5.21	1.29
25.220	-	1472.10364	26.29125	0.45	0.7474	6308	3.94	1.22

*** End of Report ***

Chiral

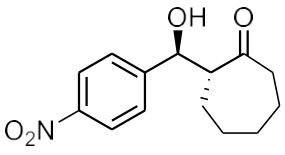


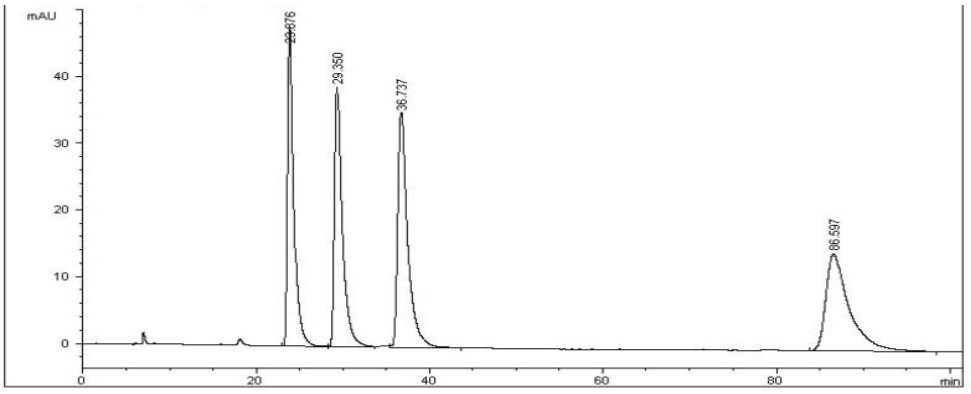
RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
13.627	-	140.46758	4.97499	0.53	0.3786	7179	-	-
15.702	-	453.92279	12.29983	0.46	0.4805	5916	2.84	1.15
20.233	-	295.81152	6.69252	0.47	0.5824	6686	5.01	1.29
24.624	-	119.95596	2.27647	0.49	0.7183	6511	3.97	1.22

*** End of Report ***

Fig. S30. (R)-2-((S)-hydroxy(4-(trifluoromethyl)phenyl)methyl)cyclohexan-1-one **(3e).**

Racemate:

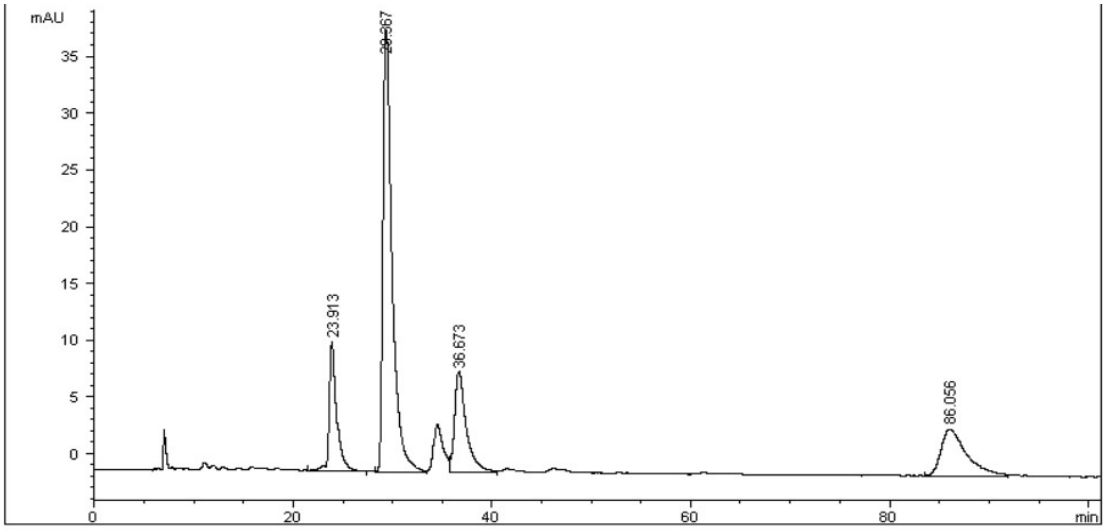




RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
23.876	-	2412.09595	47.82505	0.48	0.6843	6744	-	-
29.350	-	2422.04297	38.95824	0.47	0.8445	6692	4.21	1.23
36.737	-	2760.76855	35.12834	0.48	1.0629	6618	4.55	1.25
86.597	-	2732.67114	14.56970	0.46	2.5529	6375	16.20	2.36

*** End of Report ***

Chiral

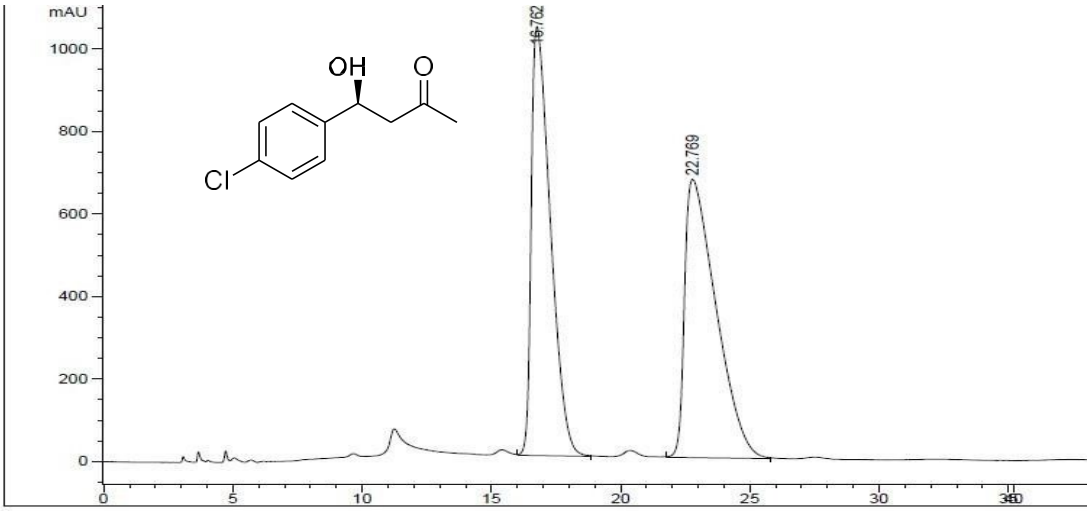


RetTime [min]	k'	Area mAU *s	Height [mAU]	Symm.	Width [min]	Plates	Resol ution	Select ivity
23.913	-	606.09351	11.37281	0.57	0.6843	6765	-	-
29.367	-	2417.83057	38.72247	0.47	0.8445	6699	4.19	1.23
36.673	-	717.26404	8.83688	0.52	1.0774	6418	4.47	1.25
86.056	-	759.01685	4.16856	0.49	2.5189	6466	16.13	2.35

*** End of Report ***

Fig. S31. (R)-2-((S)-hydroxy(4-nitrophenyl)methyl)cycloheptan-1-one **(3f).**

Racemic



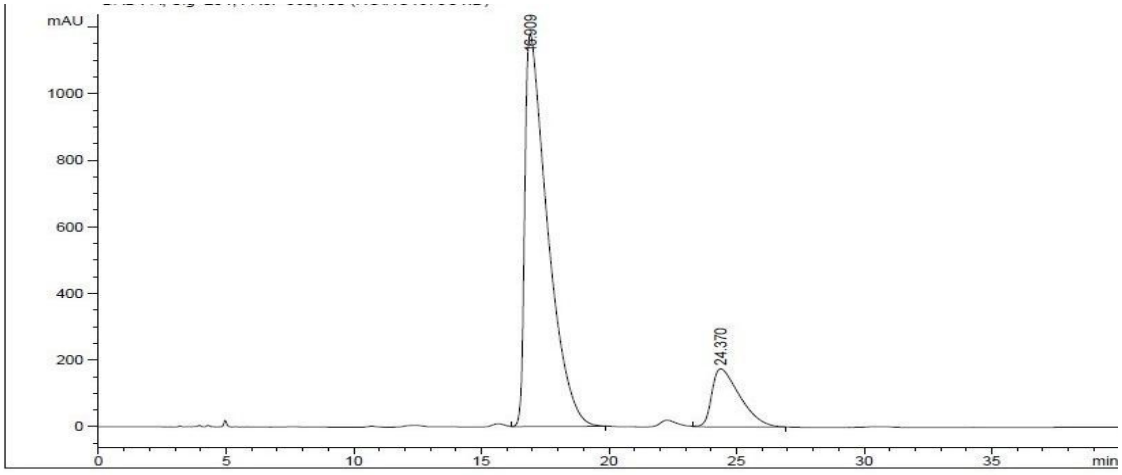

```
=====================================================================
                      Area Percent Report
=====================================================================

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

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #    [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  16.762 VV     0.6946 5.35379e4  1040.03723  48.4599
   2  22.769 BB     0.9978 5.69409e4   675.26349  51.5401
```

Chiral

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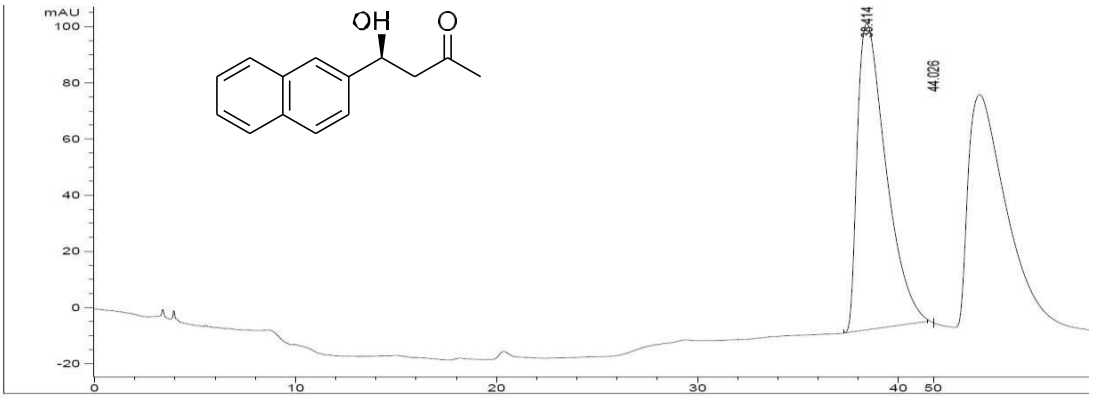
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #    [min]        [min]    [mAU*s]     [mAU]      %
----|-------|----|-------|----------|----------|--------|
   1  16.909 VB     0.8582 7.29671e4  1178.66638  84.5605
   2  24.370 VB     1.0943 1.33227e4   174.59250  15.4395
```

Fig. S32. (S)-4-(4-chlorophenyl)-4-hydroxybutan-2-one **(3g)**.

Racemic

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                            Area Percent Report
================================================================================

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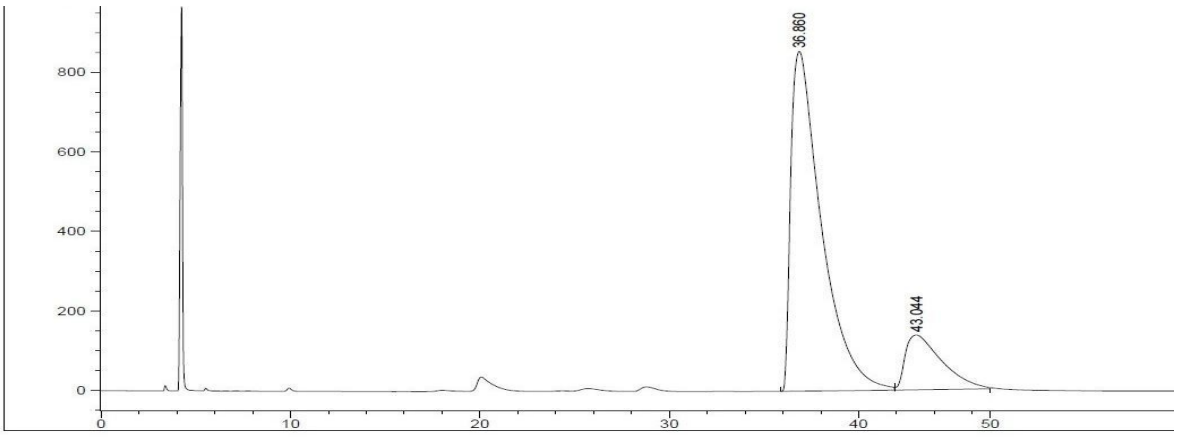
Multiplier               :       1.0000
Dilution                 :       1.0000
Sample Amount            :       1.00000   [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=240,16 Ref=360,100

Peak RetTime Type  Width      Area       Height      Area
   #    [min]     [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  38.414 PB     1.4302 1.08117e4   109.09745  50.9591
   2  44.026 PB     1.5452 1.04047e4    82.28828  49.0409
```

Chiral

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================================================================================
                            Area Percent Report
================================================================================

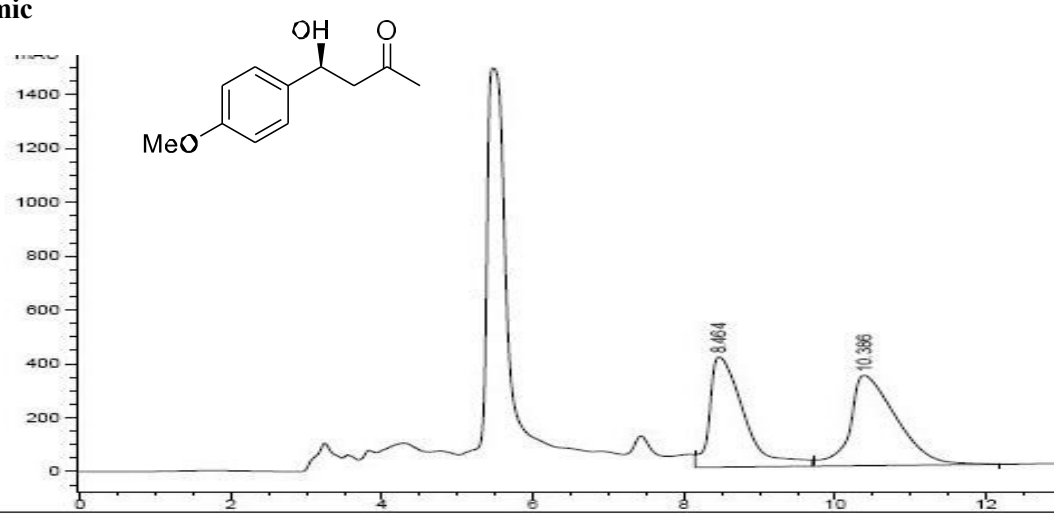
Sorted By                :       Signal
Multiplier               :       1.0000
Dilution                 :       1.0000
Sample Amount            :       1.00000   [ng/ul]    (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=240,16 Ref=360,100

Peak RetTime Type  Width      Area       Height      Area
   #    [min]     [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  36.860 PB     1.5239 9.61367e4   854.92126  83.7728
   2  43.044 BB     1.8415 1.86222e4   138.07594  16.2272
```

Fig. S33. (S)-4-hydroxy-4-(naphthalen-2-yl)butan-2-one **(3h)**.

Racemic

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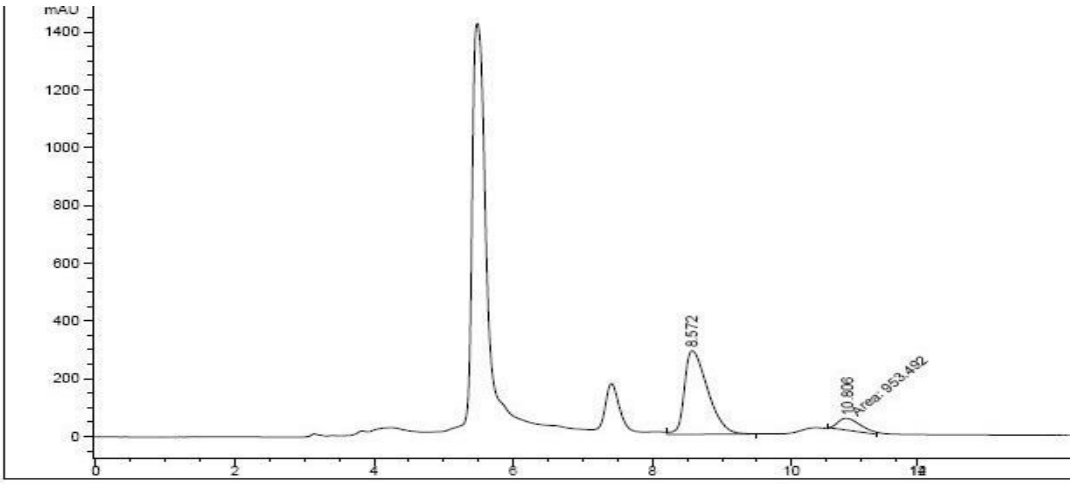
================================================================================
                          Area Percent Report
================================================================================

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

Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.464 VV     0.4901 1.28705e4  410.17987  47.3647
   2  10.386 VB     0.5589 1.43026e4  335.82611  52.6353
```

Chiral

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================================================================================
                          Area Percent Report
================================================================================

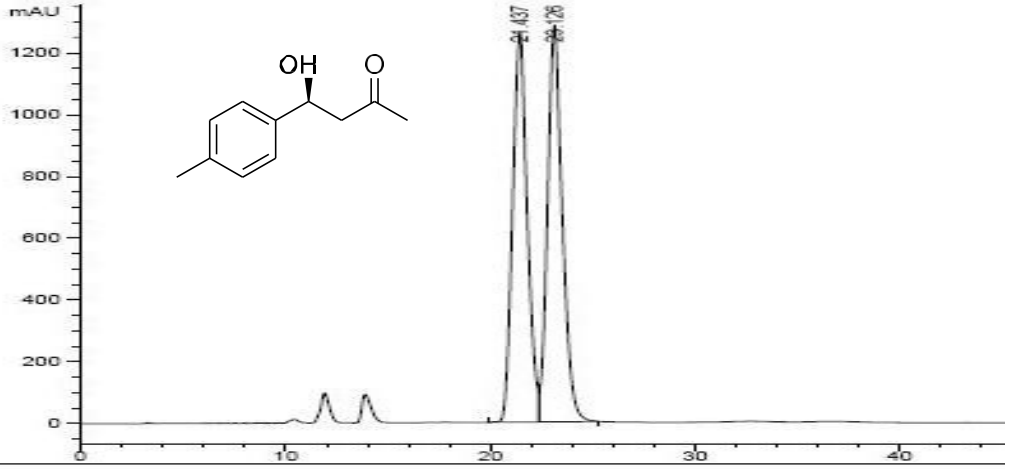
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=230,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]      [min]    [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.572 VB     0.3595 6739.86865  289.59125  87.6063
   2  10.806 MM     0.3857  953.49225   41.20644  12.3937
```

Fig. S34. (S)-4-hydroxy-4-(4-methoxyphenyl)butan-2-one **(3i)**.

Racemic



Area Percent Report

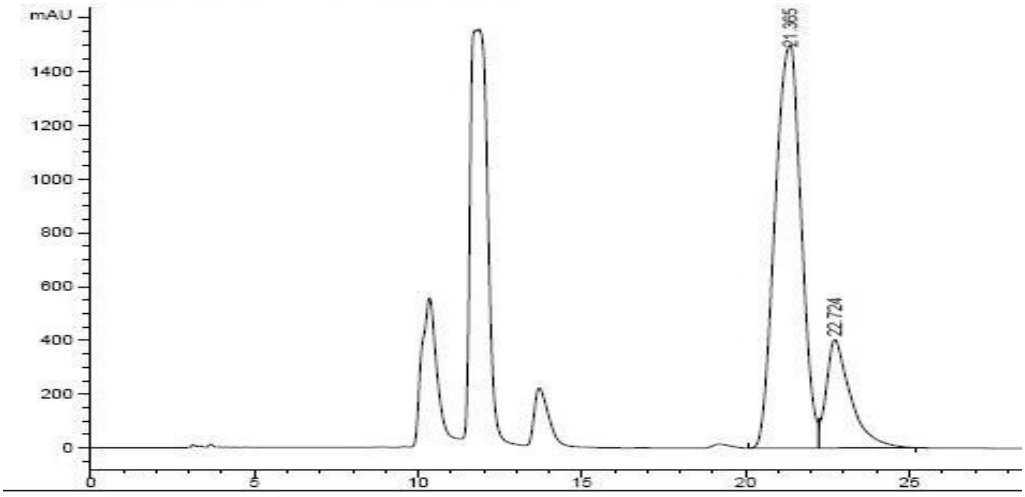
Sorted By	: Signal
Multiplier	: 1.0000
Dilution	: 1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.437	PV	0.7369	6.24765e4	1263.40625	49.2414
2	23.126	VB	0.6448	6.44013e4	1284.89001	50.7586

Chiral



Area Percent Report

Sorted By	: Signal
Multiplier	: 1.0000
Dilution	: 1.0000

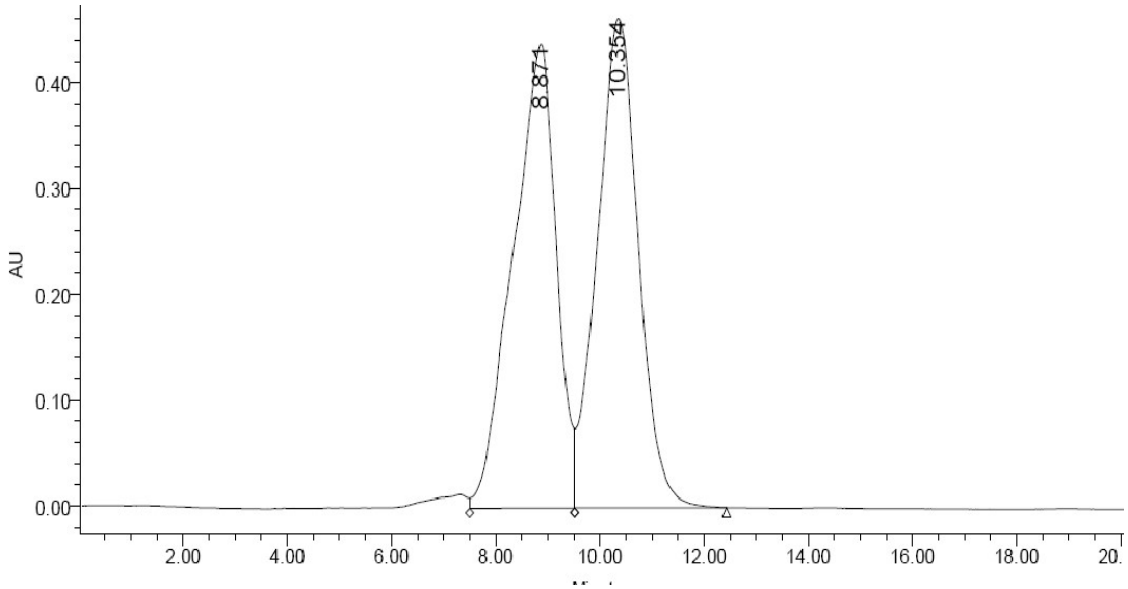
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.365	VV	0.7080	8.34426e4	1502.34717	79.9436
2	22.724	VB	0.7256	2.09342e4	403.30258	20.0564

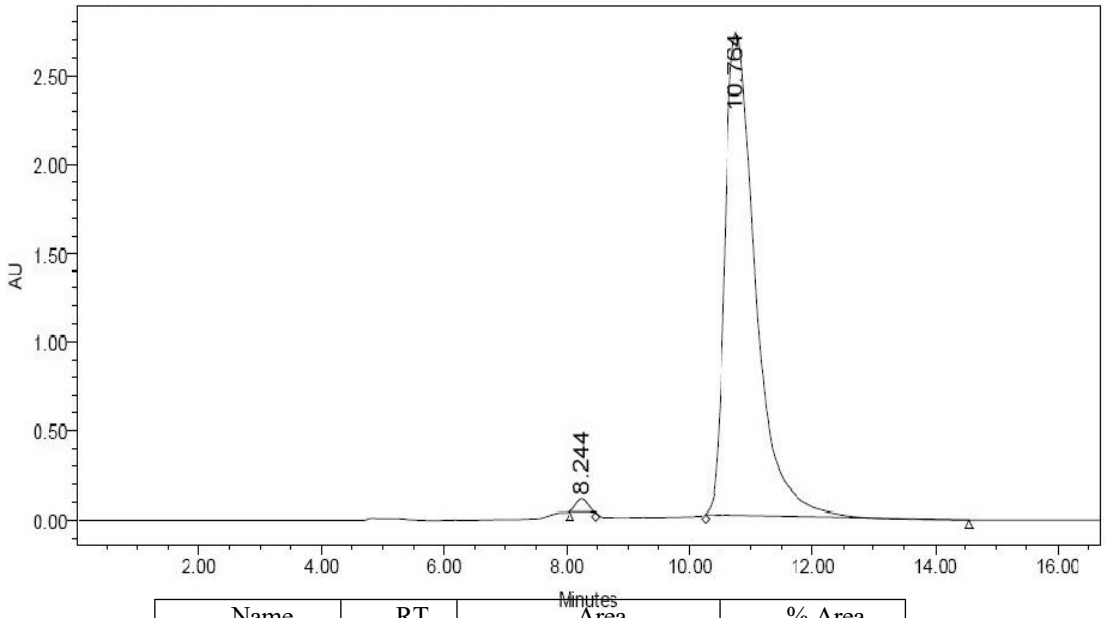
Fig. S35. (S)-4-hydroxy-4-(p-tolyl)butan-2-one **(3j)**.

Racemic)



Name	RT	Area	% Area
Peak1	8.87	25287268	49.87
Peak2	10.35	25421753	50.13

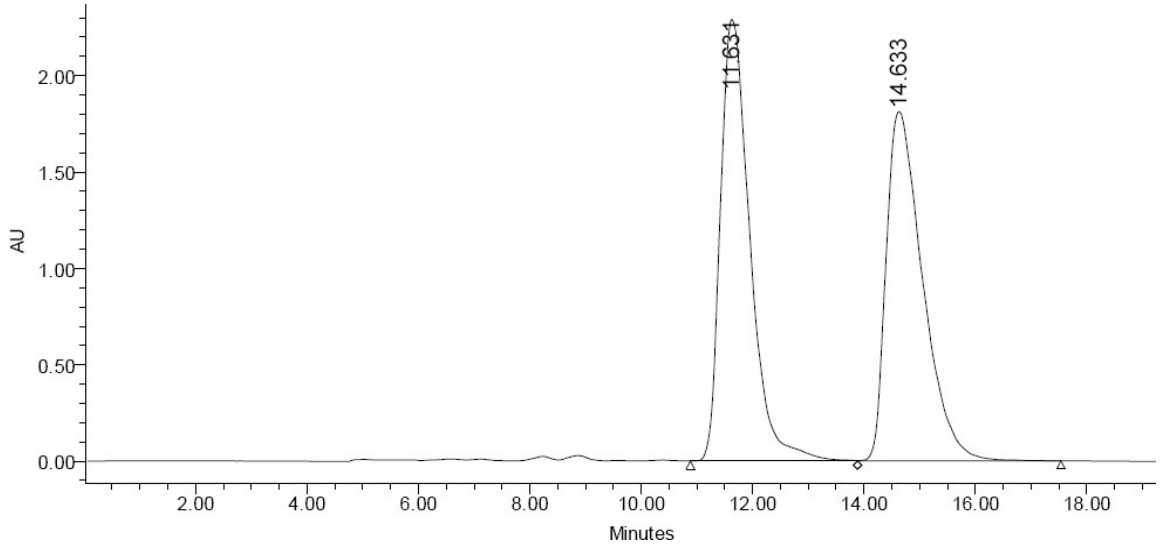
(Chiral)



Name	RT	Area	% Area
Peak1	8.24	556703	6.38
Peak2	10.76	8722704	96.81

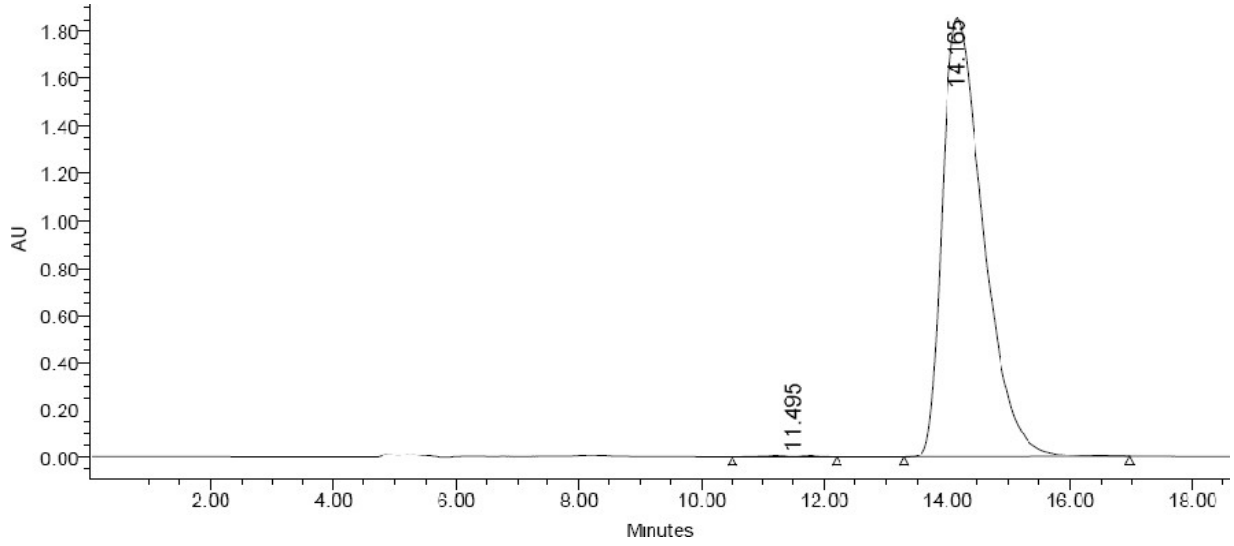
Fig. S36. HPLC Chromatogram of (R)-3-hydroxy-1,3-diphenylpropan-1-one. **(3k).**

(Racemic)



Name	RT	Area	% Area
Peak1	11.63	8430448	50.57
Peak2	14.63	8240889	49.43

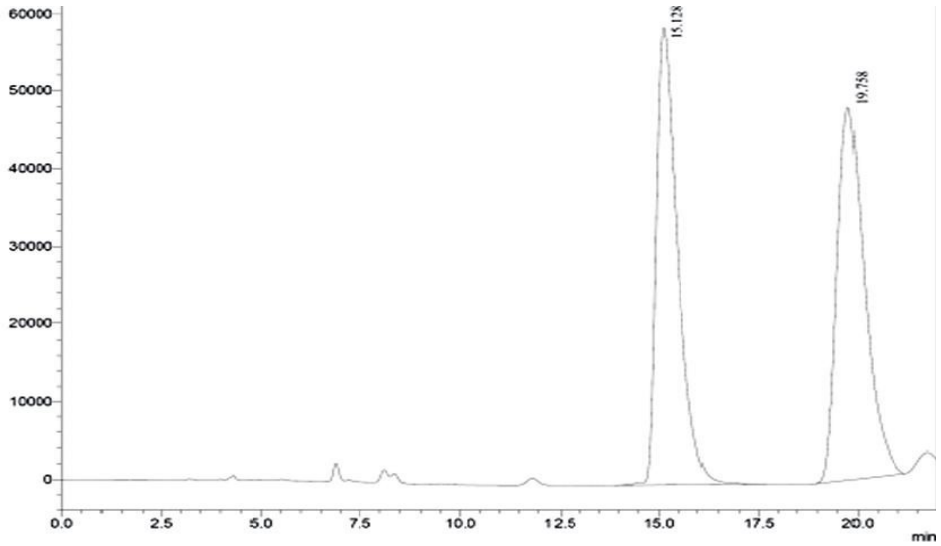
(Chiral)



Name	RT	Area	% Area
Peak1	11.49	355262	1
Peak2	14.16	86034911	99

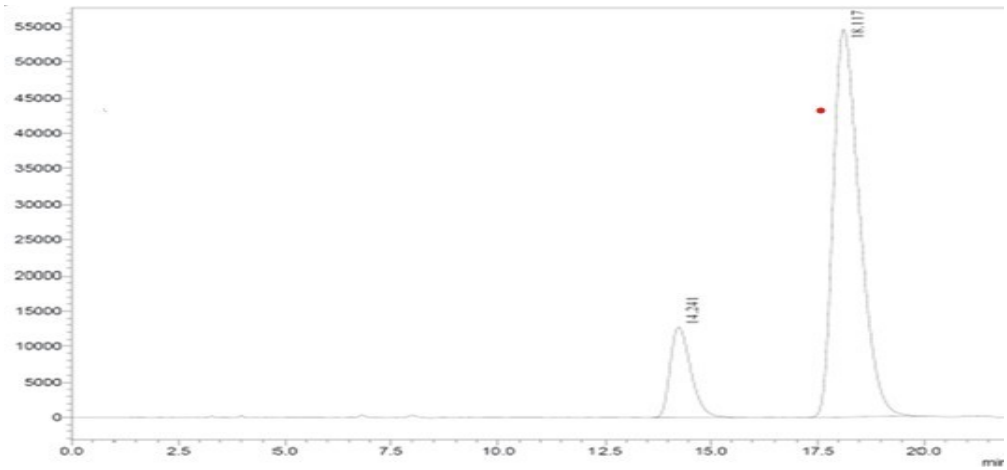
Fig. S37. HPLC Chromatogram of (R)-3-hydroxy-3-(naphthalen-1-yl)-1-phenylpropan-1-one **(3l).**

(Racemic)



Name	RT	Area	% Area
Peak1	15.12	596301	50.35
Peak2	19.75	587955	49.64

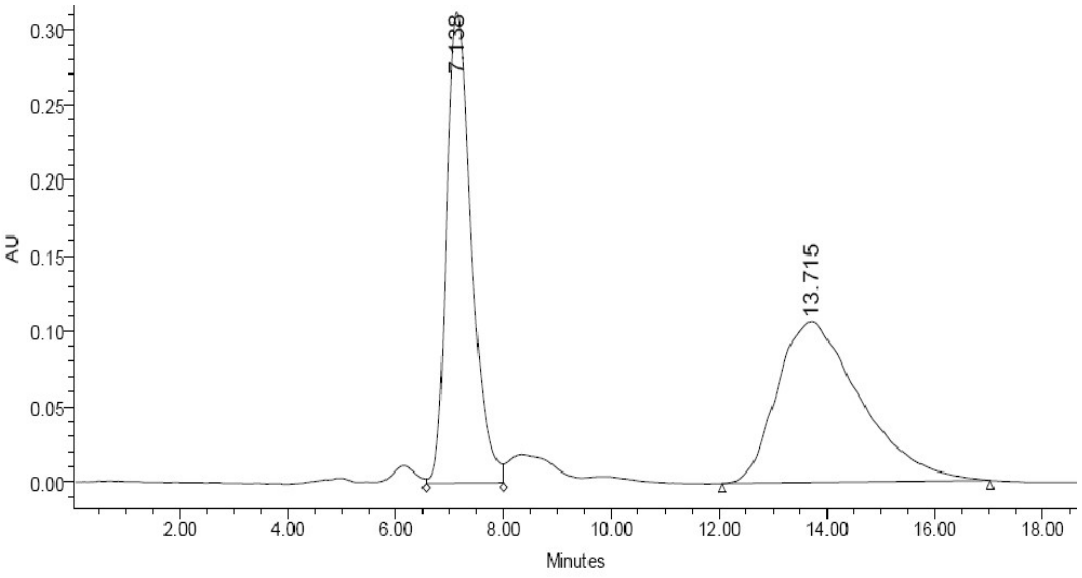
(Chiral)



Name	RT	Area	% Area
Peak1	14.24	82898	7.15
Peak2	18.11	1101358	96.85

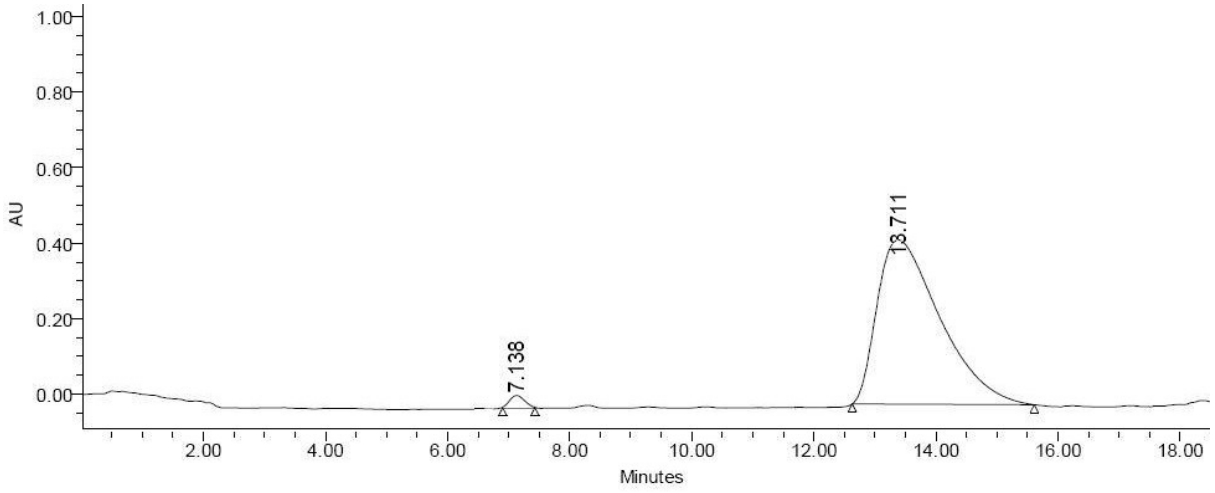
Fig. S38. HPLC Chromatogram of (R)-3-(4-chlorophenyl)-3-hydroxy-1-phenylpropan-1-one **(3m).**

(Racemic)



Peak1	7.13	1002225	46.70
Peak2	13.71	1143932	53.30

(Chiral)



Peak1	7.13	367686	10.12
Peak2	13.71	3309171	89.88

Fig. S39. HPLC Chromatogram of (R)-3-hydroxy-3-(4-methoxyphenyl)-1- phenylpropan-1-one. **(3n).**

E-factor and PMI Calculations:

E-factor was defined as

$$\text{E} = \frac{Mass\ of\ waste}{Mass\ of\ isolated\ product}$$

where *waste* excludes recovered reagents/solvents.

Process Mass Intensity (PMI) was calculated as:

$$\text{PMI} = \frac{Total\ Mass\ Input}{Mass\ of\ Isolated\ product} = E + 1$$

Basis: As per experimental procedure (per run, 0.25 g Aldol product):

- *p*-Nitrobenzaldehyde: 75.0 mg (1.0 mmol)
- Cyclohexanone: 5.0 mmol (~0.49 g)
- DMSO: 40 mL (~43.8 g)
- Water: 5.0 mL (5.0 g)
- DMSO wash: 5.0 mL (~5.5 g)

(simple E-factor, sEF = excludes water; and complete E-factor, cEF = includes water.)

Scenario A — Literal lab run (no solvent recycle, wash every run):

- Product: 0.249 g
- Waste (excl. water): DMSO feed (43.8 g), wash (5.5 g), excess cyclohexanone (~0.34 g) → ~50 g waste
- sEF = ~22.7; cEF = ~25.0 (including water)

Scenario B — Industrial campaign (95% solvent recovery, wash every 10 runs, 90% wash recovery):

- Product: 0.249 g
- Waste (excl. water): feed DMSO loss (~2.2 g), wash loss (~0.55 g), cyclohexanone loss (~0.02 g) → **~2.8 g waste**
- sEF = ~2.6; PMI_excl = ~3.6
- Normalized per kg product: sEF ≈ 0.6–0.8, cEF ≈ 3.0–3.2

Multi-Tubular Packed Bed Reactor: Estimation for Industrial Scale [1-4]

Lab Experiment Parameter:

- Bulk Volume Occupied by catalyst Bed; 37 cm^3
- Flow rate: 0.3 mL/min
- Hold up Volume: 16 mL
- Porosity of bed; 16/37 = 0.432
- Residence Time: Volume / Flow rate = 16/0.3 = 53.33 min (Considering 100% conversion)
- Density of catalyst: mass/volume = 11/37 = 0.297 g/mL

Considering, Scale up Capacity: 500 Ton/Annum (For working days = 330 days)

Production Rate: (500*1000)/ (330*24) = 63.13 kg / h

Assuming Production Rate: 70 kg/ h

Reactant Mass Flow rate from Stoichiometry = Mol. wt. of limiting Reactant* Production rate / Mol.wt. of Product

= (151.12*70000)/ 249.27 = 42437.51 gm/h = 43 kg/h

As per the Laboratory experiment, the value of kg of limiting reactant (4-Nitro Benzaldehyde) in kg/h as per 0.3 mL/min Flow rate =

2.7* 10^{-5} kg limiting reactant in 18 mL for 1 hour.

Catalyst 5 g = 0.005 kg

Proportionality Constant Mw/ Mf = C_p = (kg of catalyst/ kg of limiting reactant in kg/h)

= 0.005/ 2.7*10^{-5} = 185.18

Mass of catalyst required for commercial scale = C_p * 43 kg/h = 185.18* 43= 7962 kg

The volume of catalyst based on density = mass/ density = 7962/297 = 26.8 m^3

Calculate total Cross section Area= we have volume of catalyst for scale up

$V_1 = \pi/4 * D^2 * h$

Considering, Height 7 m, Diameter will be 2.21 m

Total cross sectional area (A_1) will be = $\pi/4 * D^2 = \pi r^2 = 3.83$ m^2

Considering 10 cm = 0.1 m diameter for each Tube, Cross section area of each Tube will be

$A_2 = \pi/4 * D^2 = 0.00785$ m^2

Number of Tubes required = A_1/A_2 = 3.83 / 0.00785 = **488 Tubes**

Table S6. Summary of E-factor calculations for continuous-flow Aldol reaction

Scenario	Inputs per run (≈0.25 g product)	Assumptions on recovery	Waste considered (excl. water)	sEF	cEF (incl. water)	PMI_{excl}	PMI_{incl}
A. Lab run (literal)	75.0 mg *p*-nitrobenzaldehyde, 0.49 g cyclohexanone, 40 mL DMSO (43.8 g), 5.0 mL H_2O (5.0 g), 5.0 mL DMSO wash (5.5 g)	No solvent recovery; wash every run	DMSO feed (43.8 g), wash (5.5 g), cyclohexanone excess (~0.34 g), aldehyde loss (~0.002 g) → ~50 g	22.7	25.0	23.7	26.0
B. Industrial campaign (optimized)	Same feed as above	95% DMSO & cyclohexanone recovery; wash every 10 runs, 90% wash recovery	Feed DMSO loss (~2.2 g), wash loss (~0.55 g), cyclohexanone loss (~0.02 g), aldehyde loss (~0.002 g) → ~2.8 g	2.6	5.0	3.6	6.0
Normalized per kg product (Scenario B)		same as above	–	0.6–0.8	3.0–3.2	1.6–1.8	4.0–4.2

References

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3. Moustafa T. M.; Elreesh, M. A.; Fateen, S. –E, K. Modeling, Simulation, and Optimization of the Catalytic Reactor for Methanol Oxidative Dehydrogenation. *COMSOL Conference Boston,* **2007**.
4. Zhu, J.; Araya, S. S.; Cui, X.; Sahlin, S. L.; Kær, S. K. Modeling and Design of a Multi-Tubular Packed-Bed Reactor for Methanol Steam Reforming over a Cu/ZnO/Al2O3 Catalyst. *Energies* **2020**, *13*, 610.