Supplementary material

for

pH-controlled regioselective nucleophilic ring opening of epoxide: Improved process for the preparation of (*R*)-(−)- or (*S*)-(+)-3-hydroxytetrahydrofuran.

Ankita Chakraborty,[‡a,b] Avula Shiva Krishna,[‡a,b] Gurrala Sheelu,[a] Subhash Ghosh,[a,b] and Thenkrishnan Kumaraguru[*a,b]

[a]Department of Organic Synthesis and Process Chemistry, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India.

[b]Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201 002, India.

Corresponding author:

kumaraguru@iict.res.in

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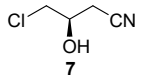
1. General information

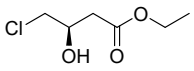
^{1}H NMR spectra were determined in $CDCl_3$ using a Bruker AC 400 spectrometer at operating at 400 MHz, using TMS as an internal standard. Splitting patterns are as follows: *s*, singlet; *d*, doublet; *m*, multiplet; *br*, broad signal. The ^{13}C NMR spectrum was obtained using the same apparatus described above at 100 MHz. Epichlorohydrin was purchased from Sigma-Aldrich and was utilized as the chromatographic standard in TLC analysis. The progress of the reactions was monitored by TLC and GC. The chromatograms were visualized using a solution of $KMnO_4$ in water.

2. Characterisation data of synthesized compounds



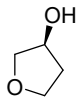
7

4-chloro-3-hydroxybutanenitrile (7): Pale yellowish oil, IR (neat): ν 3422, 2963, 2257, 1632, 1419, 1302, 1088 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): δ 4.24-4.17 (m, 1H), 3.71- 3.63 (m, 2H), 3.10 (d, *J*= 4Hz, 1H), 2.78-2.67 (m, 2H), ^{13}C NMR (100MHz, $CDCl_3$): δ 117.1, 67.4, 47.3, 23.3.



1

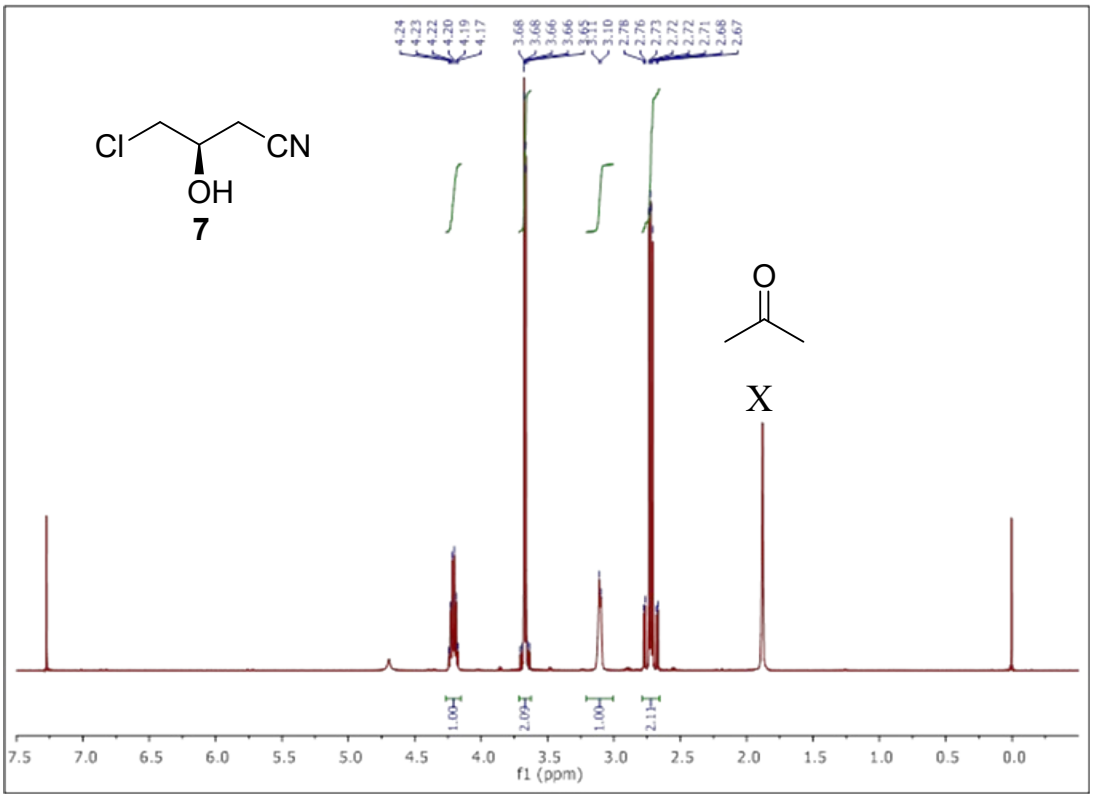
Ethyl- (*R*)-4-chloro-3-hydroxybutanoate (1) Yellowish oil, IR (neat): ν 3449, 2983, 1725, 1637, 1380, 1192, 1031 cm^{-1}; ^{1}H NMR (400MHz, $CDCl_3$): *δ* 4.27-4.22 (m, 1H), 4.17 (q, *J*= 8Hz, 2H), 3.63-3.56 (m, 2H), 3.17 (d, *J*=4 Hz, 1H), 2.66-2.57 (m, 2H), 1.26 (t, *J*= 4Hz, 3H), ^{13}C NMR (100MHz, $CDCl_3$): δ 171.8, 68.0, 61.1, 48.2, 38.6, 14.2, MS (ESI) m/z $(M+Na)^+$ calculated for $C_6H_{11}ClO_3Na$: 189, observed: 189.



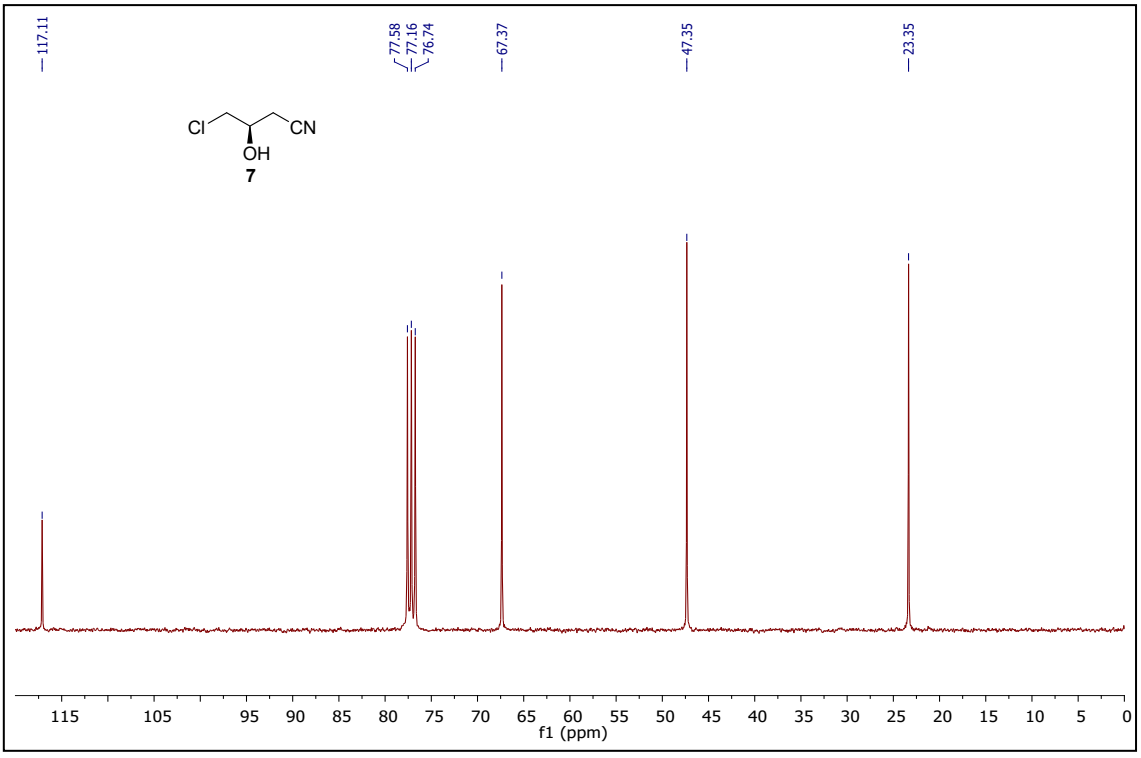
2

(*R*)-3-hydroxytetrahydrofuran (2): Colourless oil, IR (neat): ν 3410, 2952, 2882, 1764, 1647, 1054cm^{-1}, ^{1}H NMR (400MHz, $CDCl_3$): 4.52-4.49 (m, 1H), 4.0- 3.95(m, 1H), 3.87-3.74 (m, 3H), 2.16-2.04 (m, 1H), 1.95-1.87 (m, 1H), ^{13}C NMR (100MHz, $CDCl_3$): 75.8, 72.3, 66.8, 35.8. $[\alpha]_D^{23.9}$ = -16.99 (c= 2.45, CH_3OH), lit[18] $[\alpha]_D^{23}$ = -17.3 (c= 2.4, CH_3OH).

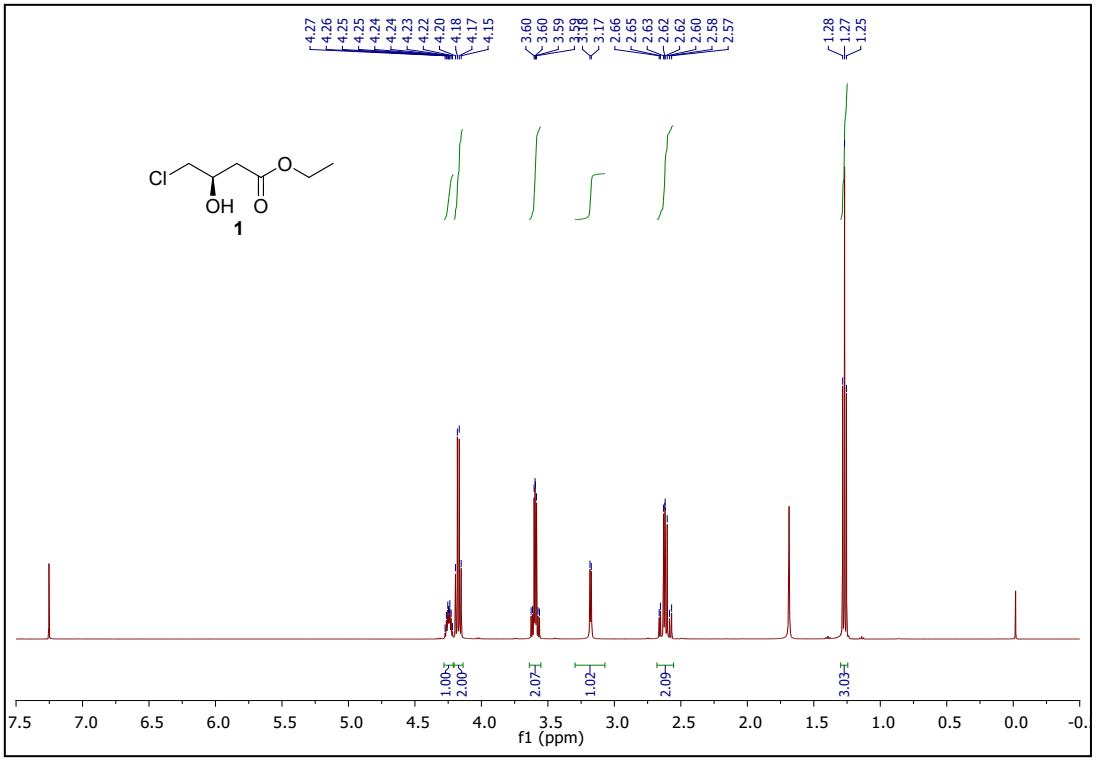
^{1}H NMR of 7 (400 MHz, $CDCl_3$)



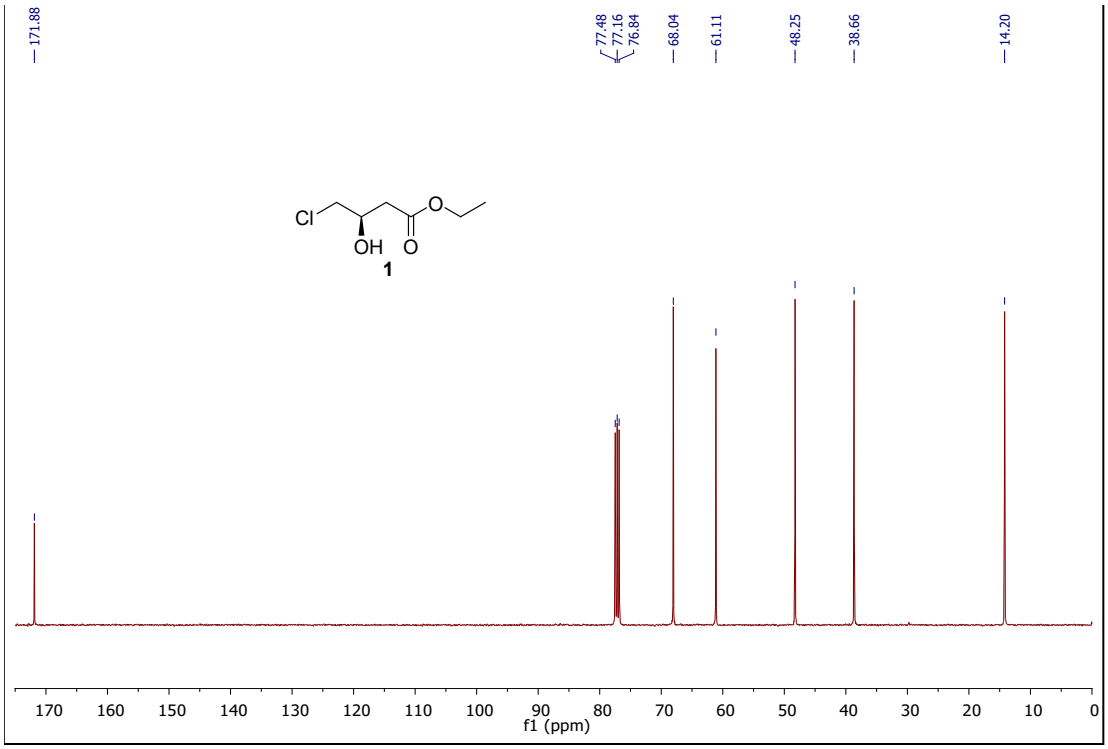
^{13} C NMR of 7 (100 MHz, $CDCl_3$)



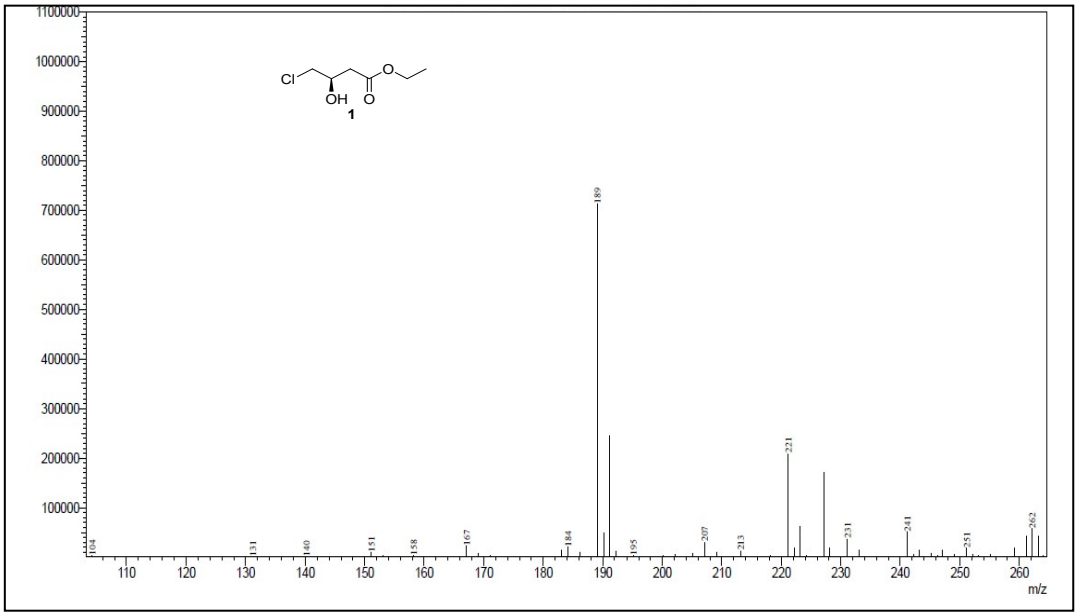
^{1}H NMR of 1 (400MHz, $CDCl_3$)



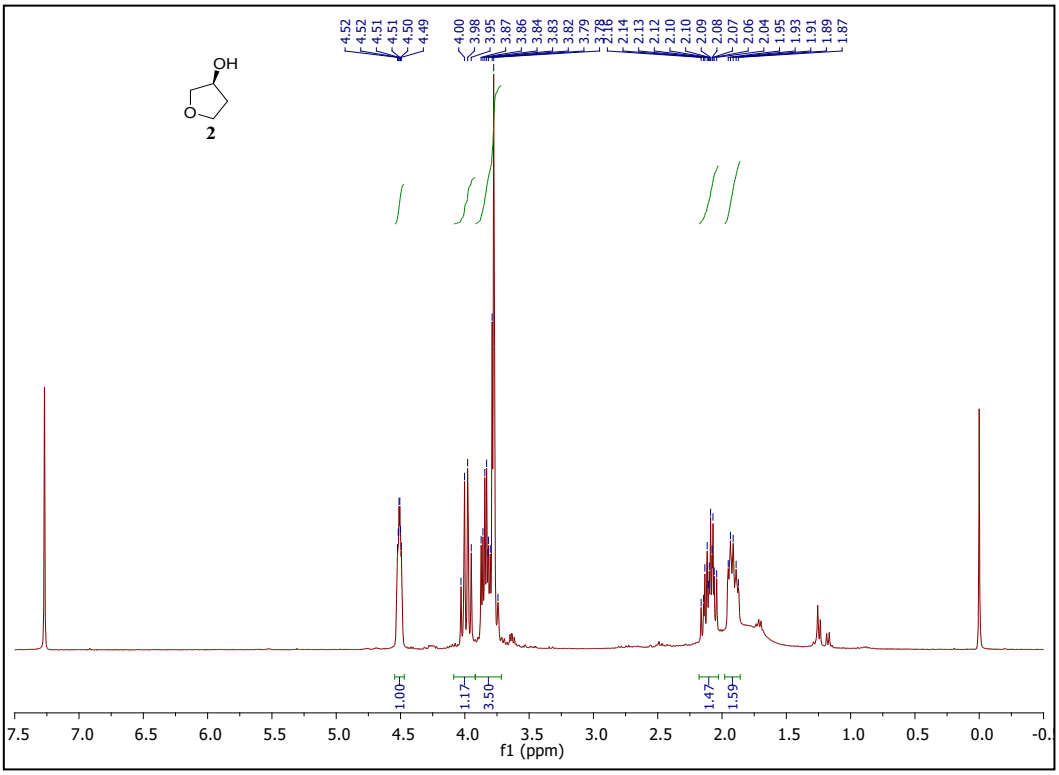
^{13}C NMR of 1 (100 MHz, $CDCl_3$)



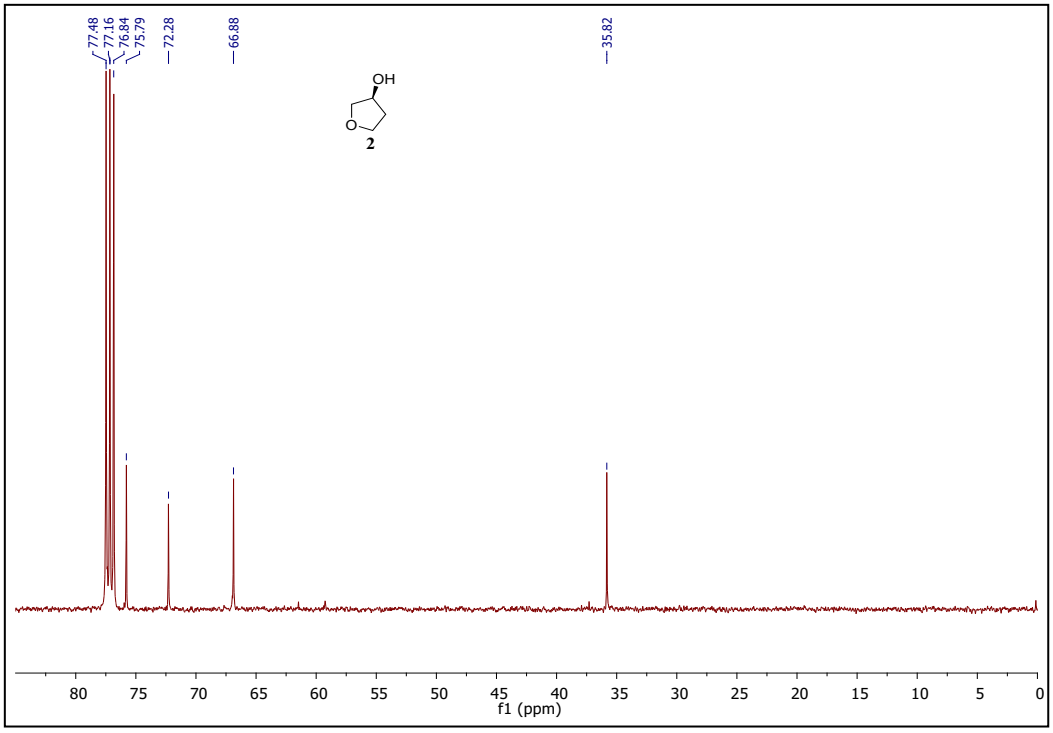
Mass spectra (ESI) of 1



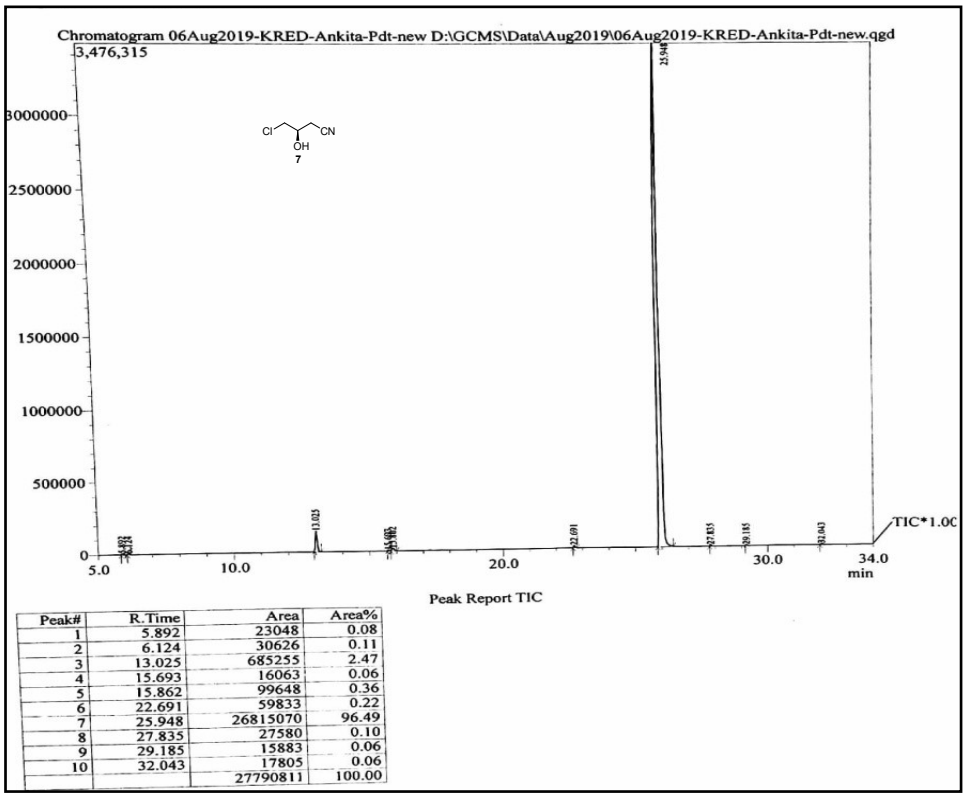
^{1}H NMR of 2 (400MHz, $CDCl_3$)



^{13}C NMR of 2 (100 MHz, $CDCl_3$)

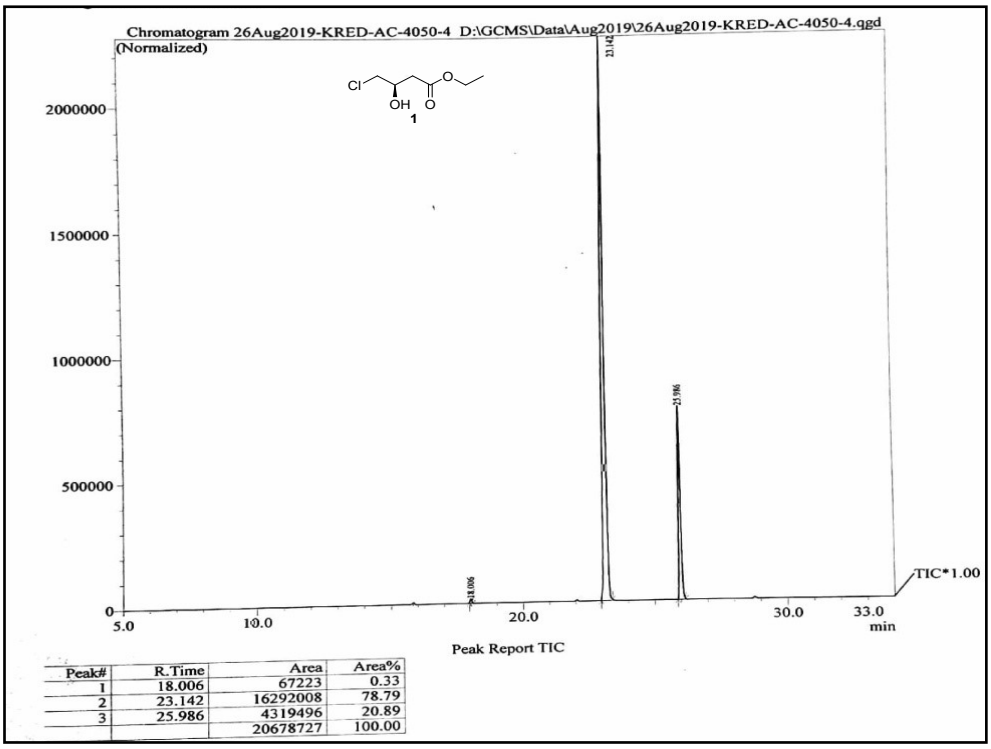


GC CHROMATOGRAMS

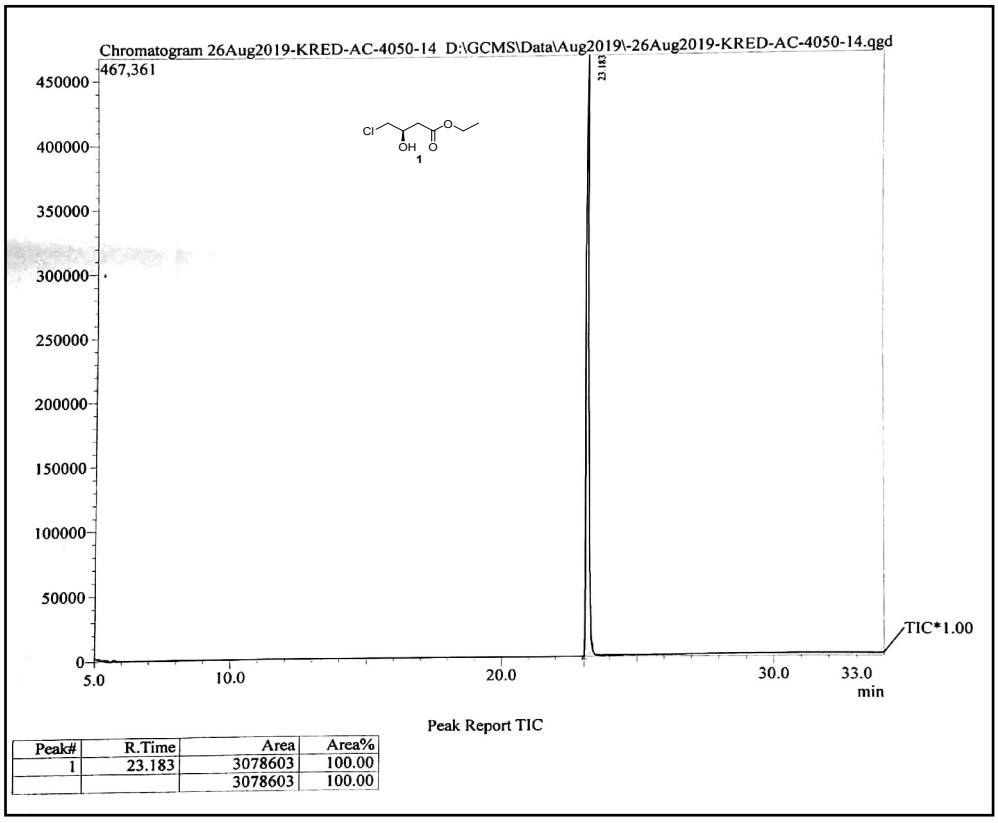


Peak Report TIC

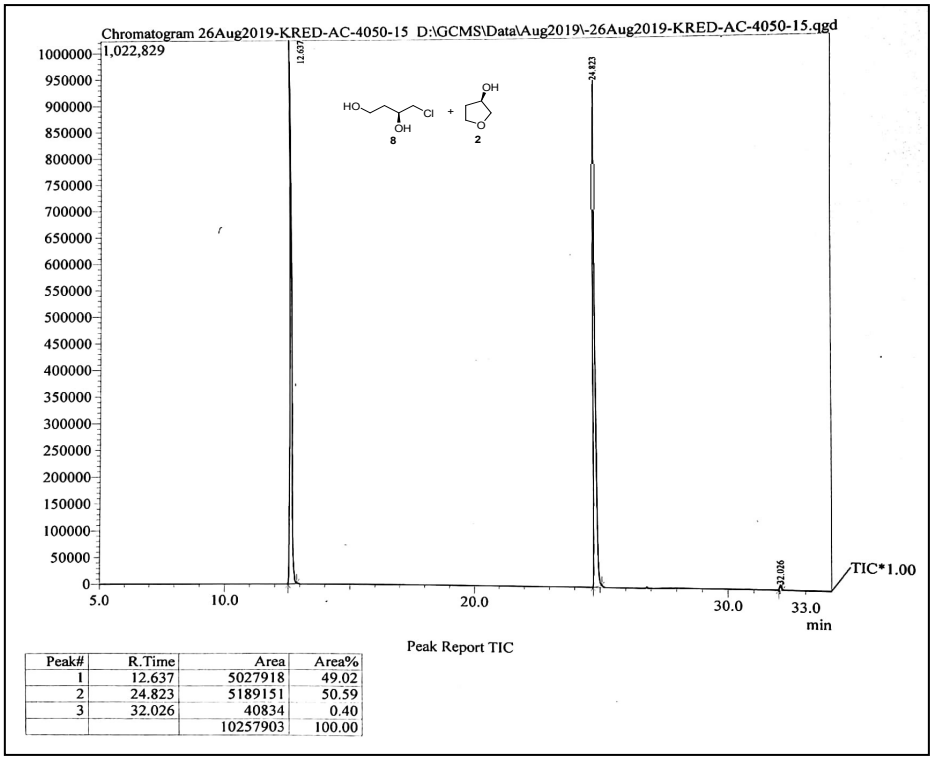
Peak#	R.Time	Area	Area%
1	5.892	23048	0.08
2	6.124	30626	0.11
3	13.025	685255	2.47
4	15.693	16063	0.06
5	15.862	99648	0.36
6	22.691	59833	0.22
7	25.948	26815070	96.49
8	27.835	27580	0.10
9	29.185	15883	0.06
10	32.043	17805	0.06
		27790811	100.00



Peak#	R.Time	Area	Area%
1	18.006	67223	0.33
2	23.142	16292008	78.79
3	25.986	4319496	20.89
		20678727	100.00

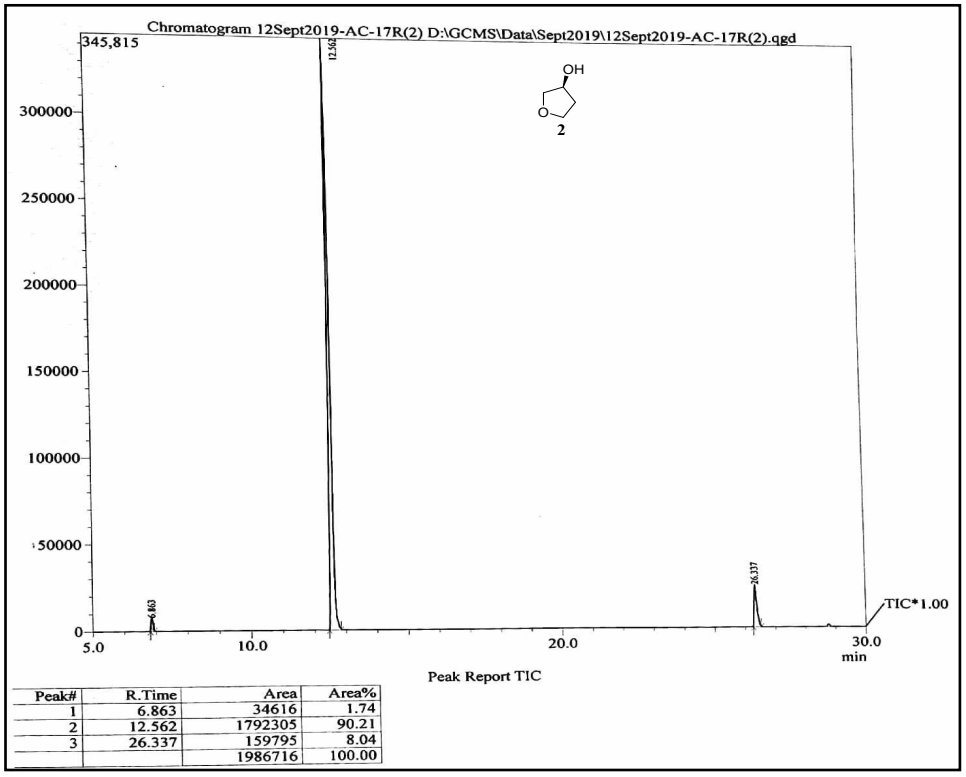


Peak#	R.Time	Area	Area%
1	23.183	3078603	100.00
		3078603	100.00



Peak Report TIC

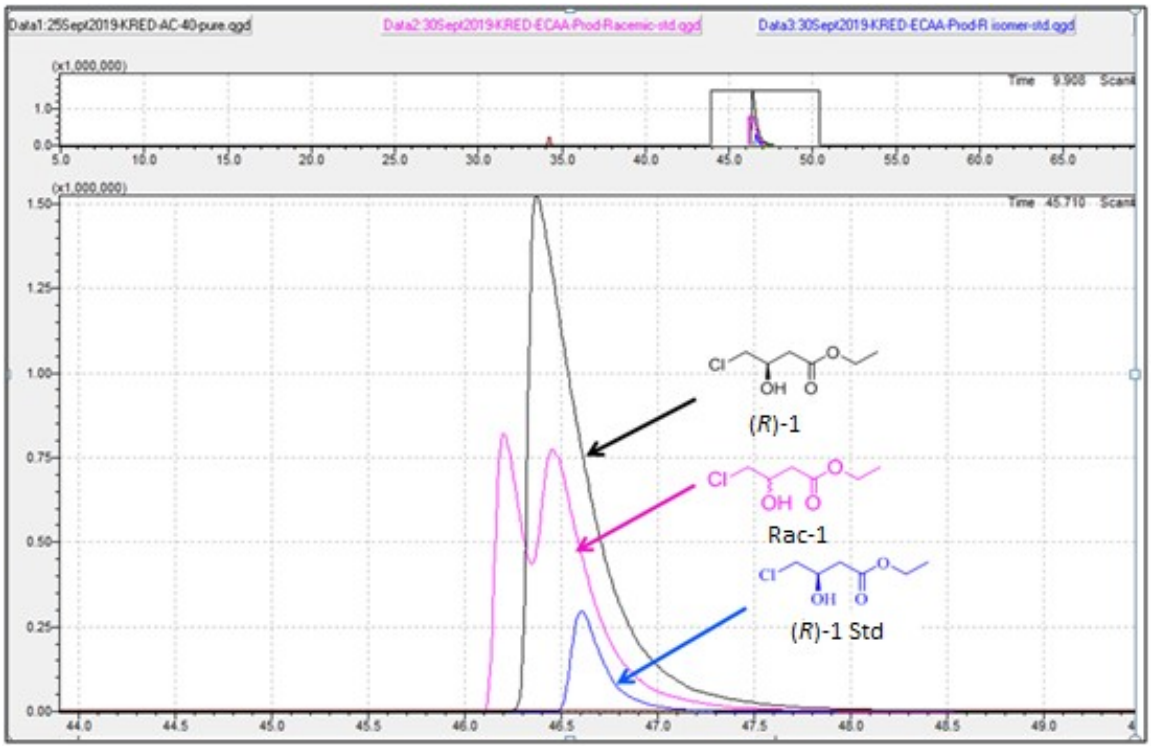
Peak#	R.Time	Area	Area%
1	12.637	5027918	49.02
2	24.823	5189151	50.59
3	32.026	40834	0.40
		10257903	100.00



Peak Report TIC

Peak#	R.Time	Area	Area%
1	6.863	34616	1.74
2	12.562	1792305	90.21
3	26.337	159795	8.04
		1986716	100.00

Comparison of (*R*)-Ethyl-4-chloro-3-hydroxybutanoate (1) with standard sample.



Overlap of all products in GC:

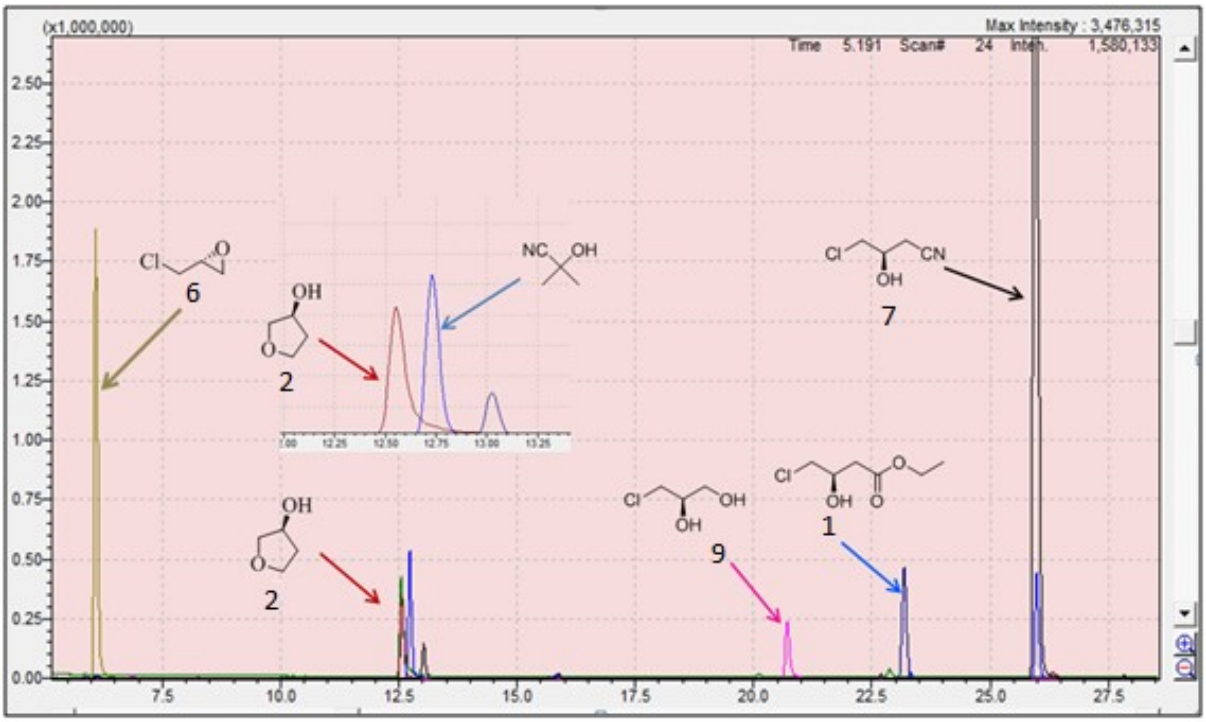


Table S1. Comparison of present work with reported methods

S.No	Reaction conditions	Remarks	References
1.	HCN	HCN is toxic.	1
2.	NaCN, Acetic acid, pH 8 – 10.	Using salts.	2
3.	Cyanide salt, inorganic acid. pH 8-10.	Simultaneous adjustment of pH. Racemization issues.	3
4.	NaCN, inorganic acid, pH 7 – 8.	No simultaneous pH adjustment	4
5.	NaCN, Citric acid, pH 7.8 – 8.3	Replaced H_2SO_4.	5
6.	HCN (aq. solution), H_2SO_4, pH 8-10 & enzymatic resolution of ester.	Process for *L*-Carnitine and acetyl *L*-Carnitine Hydrochloride.	6
7.	Liq. HCN, several days in sealed container.	Highly toxic to handle	7
8.	HCN, KCN (cat).	Highly toxic to handle	8
9.	Aq. solution of HCN, KCN, Acetic acid.	-	9
10	$Ce(OTf)_4$, 10 mole% NaCN, Neat	6h, 85 % yield.	10
11	$Ce(OTf)_4$, NaCN, Micellar media, rt	7 h, 85 % yield.	11
12	i). KCN, cat. TBAB, 1N KOH/DCE. ii). Actone cyanohydrin, Et_3N, reflux.	Product extraction issues in the biphasic system. 4 h, 67 % yield.	12
13	i). Acetone cyanohydrin, 0.1 M KPB, pH 7.5–8.5 ii). Water: DCM (1:1), TBAB (0.1% w/w). iii). Acetone cyanohydrins, 0.1 eq K_2CO_3.	12h, 93% yield & 94.5% GC purity. 24h, 88% yield & 83.28% GC purity 24h, 90% yield & > 99% GC purity	Present study

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