Supporting Information

Kinetic resolution of (*RS*)-1-chloro-3-(4-(2-methoxyethyl)phenoxy) propan-2-ol : a metoprolol intermediate and its validation through homology model of *Pseudomonas fluorescens* lipase

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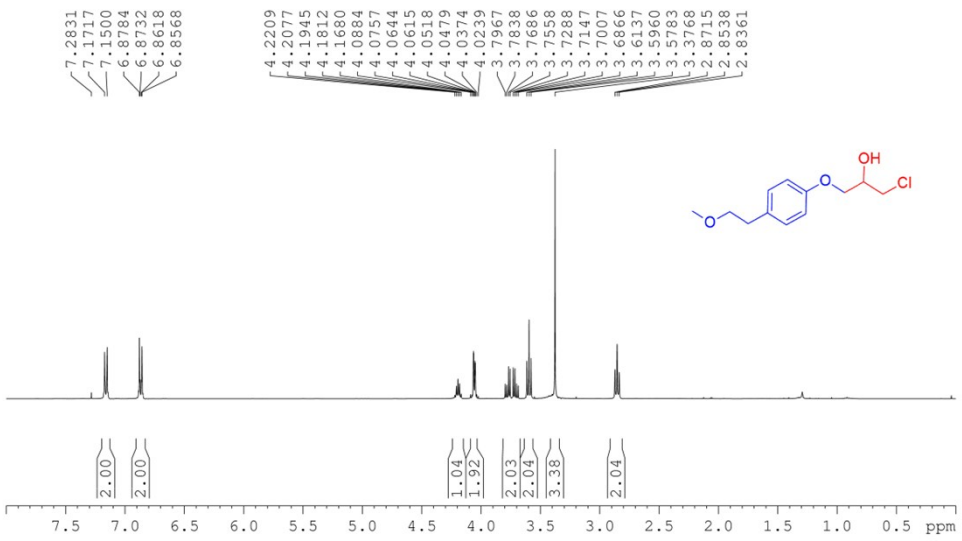
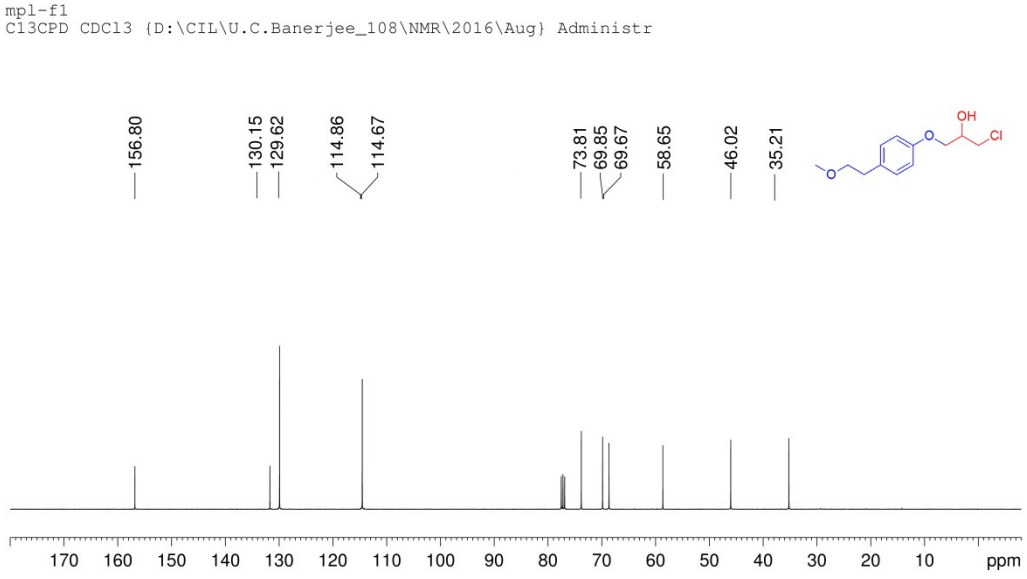
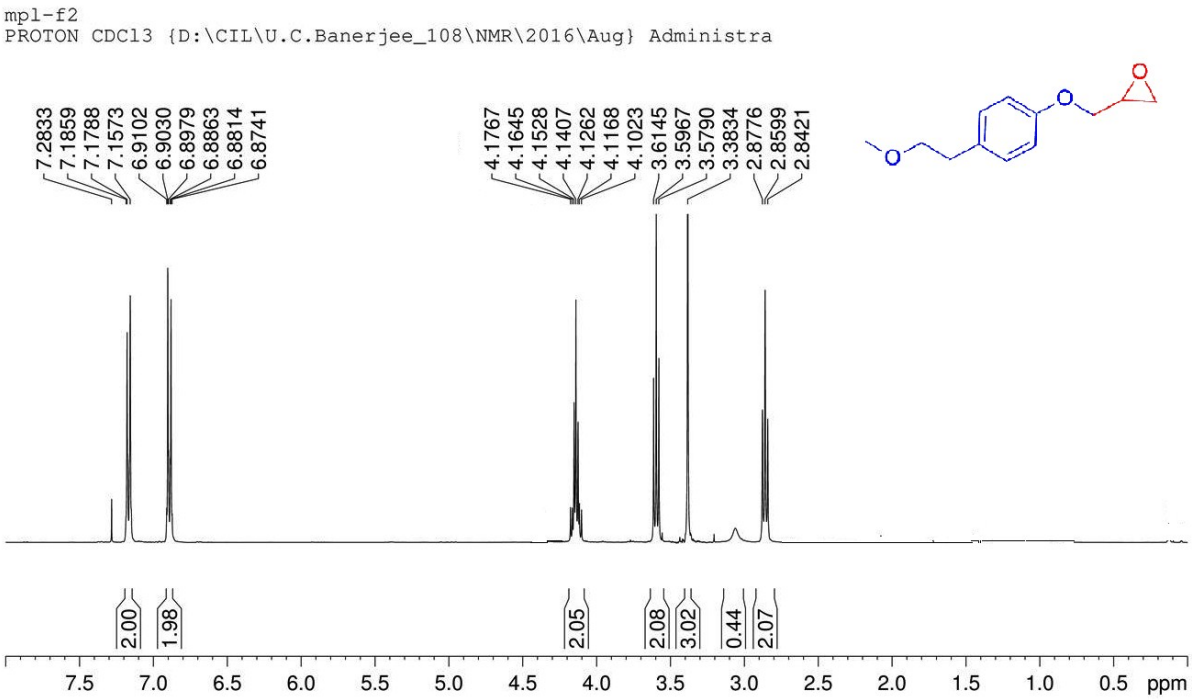
S1. ^{1}H NMR spectrum of [(*RS*)-4]



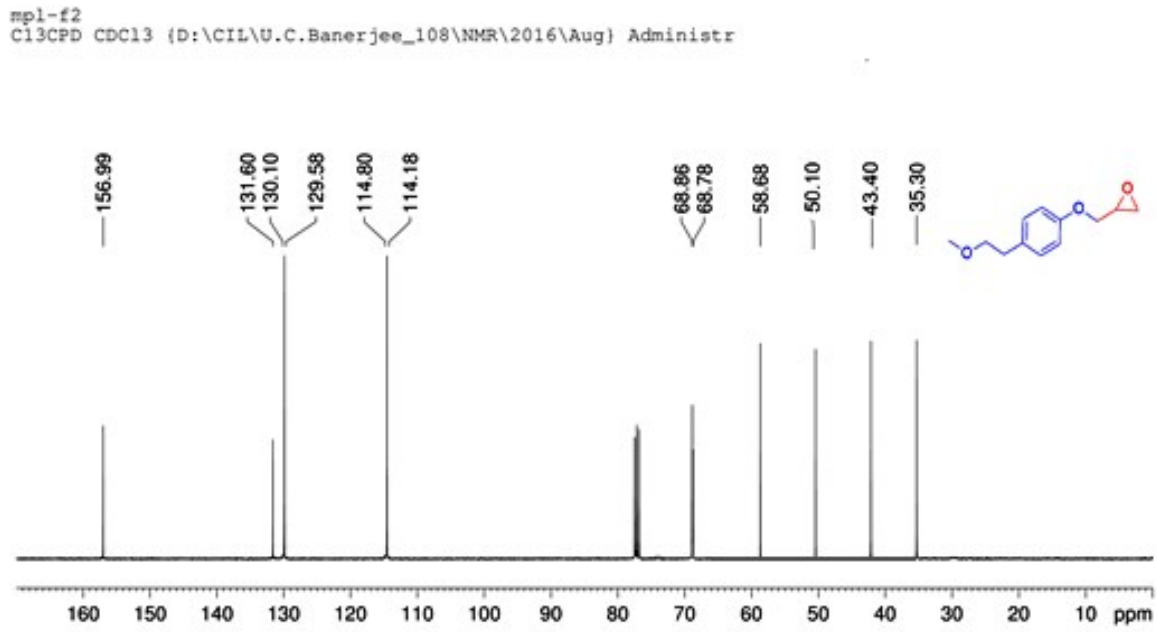
S2. ^{13}C NMR spectroscopy of [(*RS*)-4]



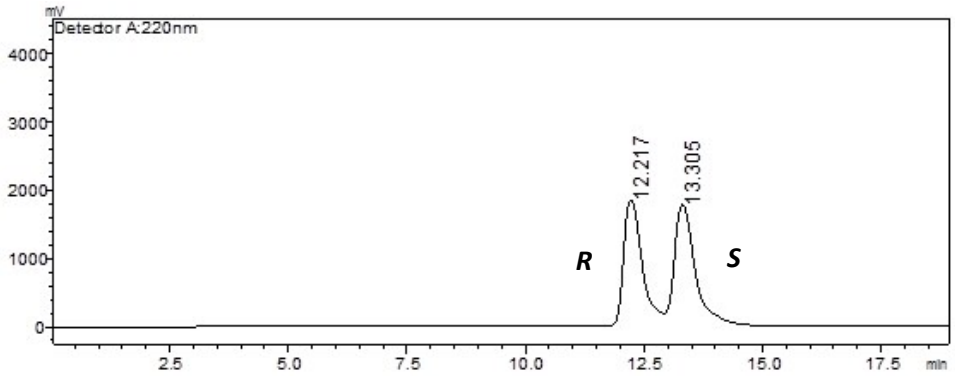
S3. ^{1}H NMR spectrum of [(*RS*)-3]



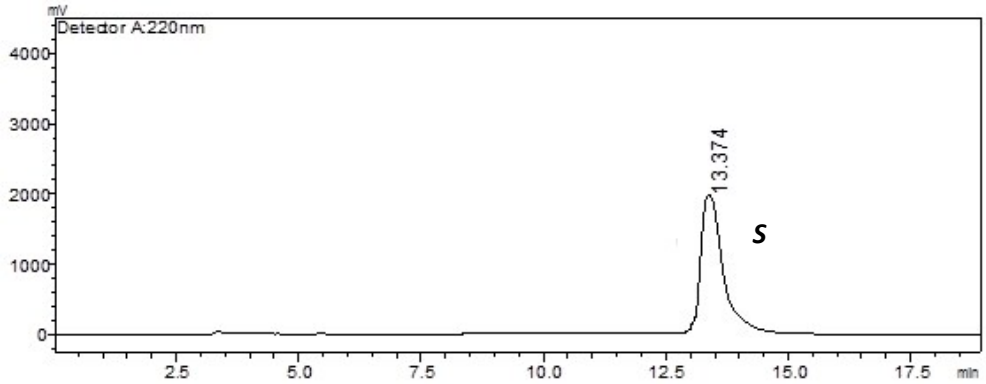
S4. ^{13}C NMR spectroscopy of [(*RS*)-3]



S5. HPLC chromatogram of (*RS*)-**4**



S6. HPLC chromatogram of (*S*)-**4**



S7. Optimization of process parameters for the kinetic resolution of (*RS*)-4

(a) Effect of organic solvents: Toluene was selected as a suitable solvent for the PFL catalyzed kinetic resolution of (*RS*)-**4.** The effect of different organic solvents on PFL mediated kinetic resolution of (*RS*)-**4** are presented in **Table S1**.

Table S1. Effect of organic solvents on the enantioselectivity in the resolution of (*RS*)-4 with lipase[a]

S.No	Solvent	%*C*[d]	ee_S (%)[b]	ee_P (%)[c]	E[e]
1.	Isooctane	50.3 ± 1.72	99.9 ± 1.93	98.7 ± 1.77	1102 ± 4.58
2.	Hexane	50.8 ± 2.15	99.9 ± 2.42	96.8 ± 1.30	443 ± 4.58
3.	Heptane	50.0 ± 2.00	98.6 ± 2.12	98.6 ± 2.21	713 ± 4.16
4.	DEE	50.1 ± 1.54	99.0 ± 2.08	98.6 ± 1.89	761 ± 2.08
5.	n-Butanol	50.3 ± 3.06	99.7 ± 1.67	98.6 ± 1.97	919 ± 3.51
6.	**Toluene**	**50.5 ± 1.48**	**97.4 ± 2.40**	**95.5 ± 2.34**	**188 ± 4.00**

[a]Conditions: (*RS*)-**4** (20 mM) in toluene (1 mL) was treated with vinyl acetate (5.4 mmol) at 30 °C in the presence of different lipases (300 IU/mL).

[b]Enantiomeric excess of (*S*)-**4** was determined by HPLC analysis (Daicel Chiralcel OD-H column) 90:10; Hexane: IPA, flow rate of 1.0 mL/min, detected at 254 nm.

[c]Enantiomeric excess of (*R*)-**5** was determined by HPLC analysis (Daicel Chiralcel OD-H column) 90:10; Hexane: IPA, flow rate of 1.0 mL/min, detected at 254 nm.

[d]% Conversion were calculated from the enantiomeric excess (*ee*) of (*S*)-**4** and (*R*)-**5** as follows: Conversion (C) = $ee_s/(ee_s + ee_p)$.

[e]E value were calculated using the formula:

$E = \ln [(ee_p (1 - ee_s)/(ee_p + ee_s)]/\ln[(ee_p (1+ ee_s)/(ee_p + ee_s)]$

*The values presented in the table are the average of three repetitive experiments

(b) Effect of reaction time: PFL showed the best result for the kinetic resolution of (*RS*)-**4** in 3 h using h toluene as solvent. The effect of reaction time on PFL mediated kinetic resolution of (*RS*)-**4** are presented in **Table S2**.

Table S2. Effect of reaction time on the enantioselectivity in the resolution of (*RS*)-4 with lipase[a≠]

S.No.	Reaction time (h)	%*C*	ee_S (%)	ee_P (%)	E
1.	0.5	32.5 ± 1.05	47.4 ± 1.27	98.3 ± 2.08	185 ± 3.51
2.	1	42.7 ± 2.30	73.3 ± 2.76	98.6 ± 2.43	303 ± 2.65
3.	1.5	48.7 ± 2.56	91.8 ± 1.76	96.7 ± 3.99	195 ± 2.65
4.	2	49.6 ± 2.39	95.6 ± 2.76	97.2 ± 3.08	270 ± 3.79
5.	2.5	49.7 ± 1.59	95.6 ± 2.95	96.9 ± 2.75	245 ± 3.21
6.	**3**	**49.9 ± 2.25**	**95.5 ± 3.03**	**95.9 ± 2.71**	**184 ± 3.61**
7.	4	50.8 ± 1.91	98.9 ± 2.04	95.8 ± 3.66	244 ± 4.00
8.	6	50.2 ± 3.04	99.7 ± 2.81	99.0 ± 1.12	1316 ± 3.21
9.	12	50.1 ± 3.66	99.7 ± 3.33	99.5 ± 2.52	2545 ± 4.04

[a]Conditions: (*RS*)-**4** (20 mM) in toluene (1 mL) was treated with vinyl acetate (5.4 mmol) at 30 °C in the presence of the PFL (300 IU/mL) for different time intervals.

[≠]The reaction conditions and formulas are same as mentioned in **Table S1**.

*The values presented in the table are the average of three repetitive experiments.

(c) Effect of acyl donors: PFL showed the best result for kinetic resolution of (*RS*)-**4** using vinyl acetate as acyl donor and toluene as solvent in 3 h. The effect of different acyl donors on PFL mediated kinetic resolution of (*RS*)-**4** are presented in **Table S3**.

Table S3. Effect of acyl donors on the (PFL) catalyzed transesterification of (*RS*)-6 in toluene [a≠]

S.No.	Acyl donors[a]	C (%)	ee_s (%)	ee_p (%)	E
1.	Benzyl acetate	9.3 ± 1.72	54.2 ± 2.81	5.6 ± 2.06	0.30 ± 0.36
2.	Ethyl acetate	1.0 ± 4.51	64.9 ± 3.67	0.6 ± 2.89	4.70 ± 1.53
3.	Isopropyl acetate	48.3 ± 2.61	96.0 ± 2.40	89.6 ± 4.89	150 ± 3.54
4.	**Vinyl acetate**	**50.1 ± 2.57**	**96.4 ± 2.36**	**96.1 ± 1.45**	**205 ± 3.78**

[a]Conditions: (*RS*)-**4** (20 mM) in toluene (1 mL) was treated with different acyl donors (5.4 mmol) at 30 °C in the presence of the PFL (300 IU/mL) for different time intervals.

≠The reaction conditions and formulas are same as mentioned in **Table S1**.

*The values presented in the table are the average of three repetitive experiments.

(d) Effect of concentration of acyl donor: PFL showed the best result for kinetic resolution of (*RS*)-**4** using vinyl acetate as acyl donor and toluene as solvent in 3 h. The effect of concentration of vinyl acetate on PFL mediated kinetic resolution of (*RS*)-**4** are presented in **Table S4**.

Table S4. Effect of concentration of vinyl acetate on the (PFL) catalyzed transesterification of (*RS*)-4 in toluene [a≠]

S.No.	Concentration of acyl donors[a] (mmol)	C[b] (%)	ee_s (%)	ee_p[d] (%)	E[e]
1.	1.25	49.6 ± 2.47	94.6 ± 2.15	96.2 ± 3.65	189 ± 3.61
2.	2.5	46.2 ± 2.46	83.3 ± 2.63	97.1 ± 5.05	178 ± 4.36
3.	**5.0**	**48.3** ± 3.30	**91.0** ± 2.36	**97.0** ± 1.35	**200** ± 3.06
4.	10.0	47.0 ± 3.14	85.4 ± 5.66	96.5 ± 4.79	152 ± 4.58
5.	12.5	46.4 ± 2.82	83.6 ± 2.50	96.6 ± 2.56	154 ± 5.03

[a]Conditions: (*RS*)-**4** (20 mM) in toluene (1 mL) was treated with different concentration of vinyl acetate (5.4 mmol) at 30 °C in the presence of the PFL (300 IU/mL) for different time intervals.

≠The reaction conditions and formulas are same as mentioned in **Table S1**.

*The values presented in the table are the average of three repetitive experiments.

(e) Optimization of substrate concentration: PFL showed the best result for kinetic resolution of (*RS*)-**4** using toluene and vinyl acetate at a substrate concentration of 20 mM in 3 h. The effect of different substrate concentration on PFL mediated kinetic resolution of (*RS*)-**4** are presented in **Table S5.**

Table S5. Effect of substrate concentration on the enantioselectivity in the resolution of (*RS*)-4 in toluene [a≠]

S.No.	Substrate concentration (mM)	%C[b]	ee_S (%)[c]	ee_P (%)[d]	E[e]
1.	1	48.7 ± 2.79	92.0 ± 1.59	97.0 ± 1.80	217 ± 3.51
2.	5	48.9 ± 3.06	93.2 ± 1.75	97.3 ± 2.75	248 ± 3.61
3.	**10**	**49.2** ± 1.78	**93.4** ± 1.71	**96.3** ± 1.15	**187** ± **2.00**
4.	20	50.0 ± 1.20	97.0 ± 2.55	96.9 ± 2.50	273 ± 2.65
5.	30	48.4 ± 3.40	91.2 ± 2.25	97.4 ± 2.46	242 ± 2.52

[a]Conditions: Different concentration of (*RS*)-**4** in toluene (1 mL) was treated with vinyl acetate (5.4 mmol) at 30 °C in the presence of the PFL (300 IU/mL) for 3 h.

≠The reaction conditions and formulas are same as mentioned in **Table S1**.

* The values presented in the table are the average of three repetitive experiments.

(f) Optimization of enzyme concentration: PFL showed the best result for kinetic resolution of (*RS*)-**4** at the concentration of 400 IU/mL, using toluene and vinyl acetate and substrate concentration of 10 mM in 3 h. The effect of different concentration of PFL on kinetic resolution of (*RS*)-**4** are presented in **Table S6**.

Table S6. Effect of enzyme concentration on the enantioselectivity in the resolution of (*RS*)-4 in toluene [a≠]

S.No.	Enzyme concentration (IU)	%C[b]	ee_S (%)[c]	ee_P (%)[d]	E[e]
1.	20	9.8 ± 1.46	10.0 ± 1.80	92.9 ± 1.22	29.9 ± 2.70
2.	100	33.8 ± 2.95	48.9 ± 1.11	95.9 ± 2.97	77.3 ± 3.24
3.	200	44.0 ± 1.57	76.0 ± 1.80	96.6 ± 1.97	133 ± 2.75
4.	**400**	**50.6** ± **2.01**	**97.4** ± **1.85**	**95.1** ± **2.39**	**173** ± 2.91
5.	500	49.7 ± 3.31	95.4 ± 3.15	96.7 ± 2.46	229 ± 4.15
6.	600	49.8 ± 2.55	97.5 ± 2.51	98.3 ± 3.04	522 ± 3.21

[a]Conditions: (*RS*)-**4** (10 mM) in toluene (1 mL) was treated with vinyl acetate (5.4 mmol) at 30 °C in the presence of different concentration of PFL for 3 h.

≠The reaction conditions and formulas are same as mentioned in **Table S1**.

* The values presented in the table are the average of three repetitive experiments.

(g) Effect of temperature : PFL showed the best result for kinetic resolution of (*RS*)-**4** at 30 °C using toluene and vinyl acetate at a substrate concentration of 10 mM in 3 h. The effect of different temperature on PFL mediated kinetic resolution of (*RS*)-**4** are presented in **Table S7.**

Table S7. Effect of temperature on the enantioselectivity in the resolution of (*RS*)-4 in toluene [a≠]

S.No.	Temperature (°C)	%C	ee_S (%)	ee_P (%)	E
1.	4	50.5 ± 1.05	97.9 ± 2.05	95.8 ± 2.33	214 ± 3.79
2.	20	48.6 ± 2.72	92.0 ± 2.75	97.2 ± 2.75	233 ± 2.52
3.	25	46.3 ± 2.31	82.8 ± 2.41	96.3 ± 1.85	137 ± 2.08
4.	**30**	**49.3** ± **1.86**	**93.8** ± **2.48**	**96.5** ± **1.04**	**201** ± **1.53**
5.	40	45.9 ± 1.91	82.1 ± 2.73	96.9 ± 1.42	163 ± 2.52
6.	50	50.3 ± 2.73	97.8 ± 4.98	96.8 ± 2.50	274 ± 4.51
7.	60	50.4 ± 3.01	99.3 ± 1.54	97.6 ± 3.40	459 ± 4.93

[a]Conditions: (*RS*)-**4** (10 mM) in toluene (1 mL) was treated with vinyl acetate (5.4 mmol) at different temperature in the presence of the PFL (300 IU/mL) for 3 h.

≠The reaction conditions and formulas are same as mentioned in **Table S1**.

*The values presented in the table are the average of three repetitive experiments.

S8. HPLC chromatogram for PFL-catalyzed transesterification of (*RS*)-4 at optimized conditions

Lipase	***Pseudomomas fluorescens* lipase (PFL)**
Solvent	Toluene

Reaction time	3 h
Enzyme concentration	400 IU/mL
Substrate concentration	10 mM
Acyl donor	Vinyl acetate
Temperature	30 °C

S9. HPLC chromatogram for PFL-catalyzed transesterification of (*RS*)-4 at optimized condition