Electronic Supplementary Material (ESI) for Green Chemistry.

Supplementary Information

Construction of Biocatalytic Cascades for the Synthesis of Benzylisoquinoline Alkaloids from *p*-Coumaric Acid Derivatives and Dopamine

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1. Supporting Tables

Table S1. Plasmids used in this study

Plasmids	Descriptions	Sources
pET-28a(+)	Single T7 promoter, PBR322 ori, Kan^R	Novagen
pA7a-RFP	Single T7 promoter, P15A ori, Amp^R	BglBrick[1]
pA7a-BLPad	pA7a carrying *blpad*	[2]
pB7c-GFP	Single T7 promoter, pBBR1 ori, Cm^R	BglBrick[1]
pCas	repA101(Ts), kan, P_{cas}-cas9 P_{araB}-Red, $lacI^q$, Ptrc-sgRNA-pMB1	[3]
pTargetF	pBR322, Spec, P_{J23119}-sgRNA-*ldhA*	[3]
pT-FeaB	pTargetF carrying P_{J23119}-sgRNA-*feaB*	This study
pA7a-*Δ*29TfNCS	pA7a carrying *Δ29TfNCS*	This study
pB7c-*Δ*29TfNCS	pB7c carrying *Δ29TfNCS*	This study
pET28a-StyAB-RostyC-7-BLPad	pET28a carrying *styAB, RostyC* and *blpad*	[2]
pET28a-StyAB-RostyC	pET28a carrying *styAB* and *RostyC*	[2]
pA7a-BLPad-7-*Δ*29TfNCS	pA7a carrying *blpad* and *Δ29TfNCS*	This study
pB7c-BLPad-7-*Δ*29TfNCS	pB7c carrying *blpad* and *Δ29TfNCS*	This study
pET28a-StyAB-RostyC-7-AnPad	pET28a carrying *styAB, RostyC* and *AnPad*	This study

Table S2. Strains used in this study

Strains	Descriptions	Sources
E. coli DH5α	F^{-}, φ80d lacZΔM15, Δ(lacZYA-argF) U169, recA1, endA1, hsdR17(rk^{-}, mk^{+}), phoA, supE44λ^{-}, thi^{-1}, gyrA96, relA1	Novagen
E. coli BL21 (DE3)	F^{-}*ompT hsdS*$_B$ (*r*$_B^-$*m*$_B^-$) *gal dcm (DE3) ΔrecA*	Novagen
E. coli BL21 (DE3) RARE	*E. coli* BL21 (DE3) (*ΔdkgB*, *ΔyqhC*, *ΔyqhD*, *ΔyahK*, *ΔyeaE*, *ΔdkgA*, *ΔyjgB*, *ΔrecA*)	[4]
E. coli BL21 (DE3)RARE*ΔfeaB*	*E. coli* BL21 (DE3) (*ΔdkgB*, *ΔyqhC*, *ΔyqhD*, *ΔyahK*, *ΔyeaE*, *ΔdkgA*, *ΔyjgB*, *ΔrecA*, *ΔfeaB*)	This study
E.coli (BLPad)	*E. coli* BL21 (DE3) with pA7a-BLPad	This study
ZMTS 1	*E. coli* BL21 (DE3) RARE*ΔfeaB* with pA7a-*Δ*29TfNCS and pET28a-StyAB-RostyC-7-BLPad	This study
ZMTS 2	*E. coli* BL21 (DE3) RARE*ΔfeaB* with pB7c-*Δ*29TfNCS and pET28a-StyAB-RostyC-7-BLPad	This study
ZMTS 3	*E. coli* BL21 (DE3) RARE*ΔfeaB* with pA7a-BLPad-7-*Δ*29TfNCS and pET28a-StyAB-RostyC	This study
ZMTS 4	*E. coli* BL21 (DE3) RARE*ΔfeaB* with pB7c-BLPad-7-*Δ*29TfNCS and pET28a-StyAB-RostyC	This study
ZMTS 5	*E. coli* BL21 (DE3) RARE*ΔfeaB* with pA7a-*Δ*29TfNCS and pET28a-StyAB-RostyC-7-AnPad	This study
S*rac* 1	*E. coli* BL21 (DE3) RARE*ΔfeaB* with pET28a-StyAB-RostyC-7-BLPad	This study
S*rac* 2	*E. coli* BL21 (DE3) RARE*ΔfeaB* with pET28a-StyAB-RostyC-7-AnPad	This study

2. Supporting Figures

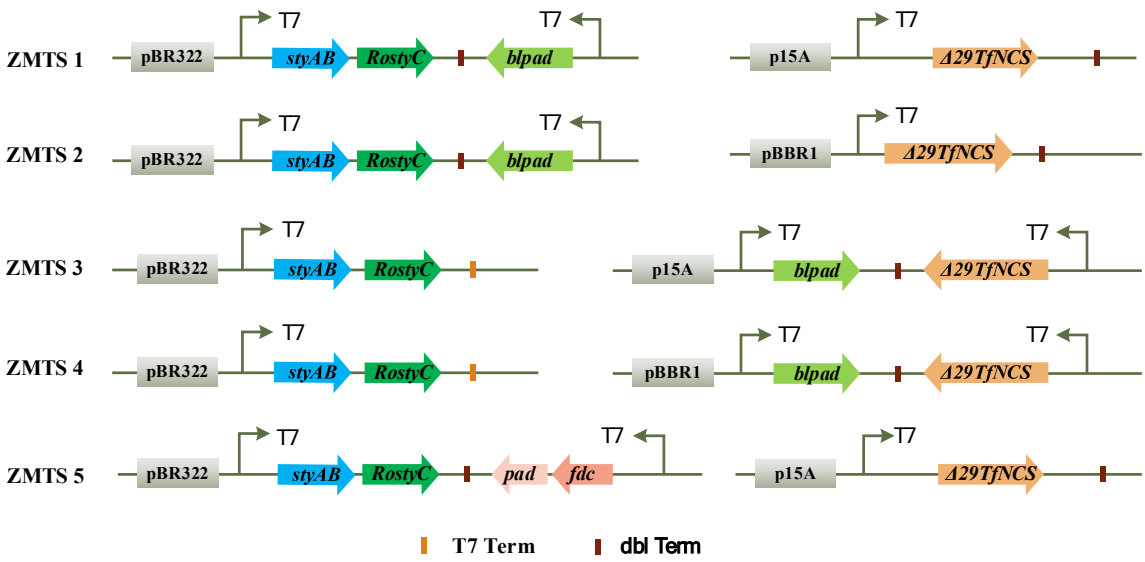

Fig. S1 Construction of strains coexpressing *blpad* or (*fdc* and *pad*), *styAB*, *RostyC* and *Δ29TfNCS* for the synthesis of BIAs.

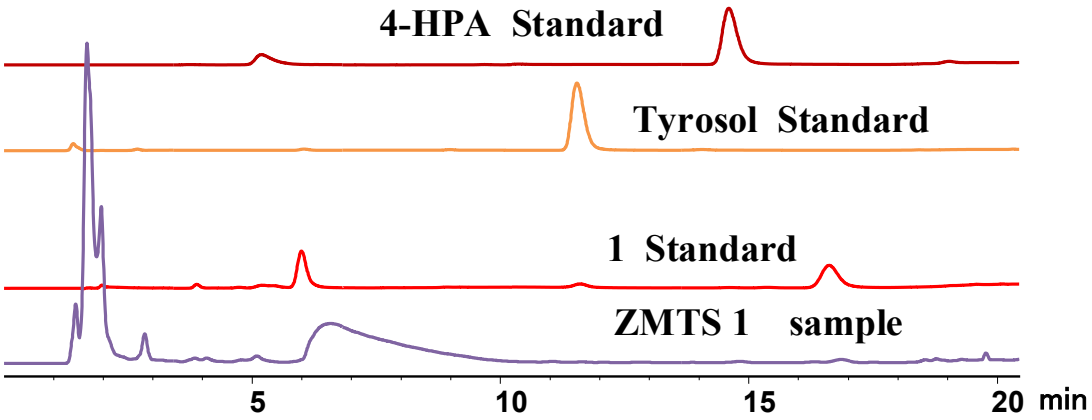

Fig. S2 HPLC analysis of the bioconversion samples from ZMTS 1. The bioconversion was performed in 50 mL HEPES buffer (50 mM, pH 7.0 and OD_{600} of 30) at 37 °C, 250 rpm, with adding 10 g L^{-1} of glucose, 7.5 mM *p*-coumaric acid **4**, 7.5 mM dopamine **2** and 7.5 mM sodium ascorbate for 1 h.

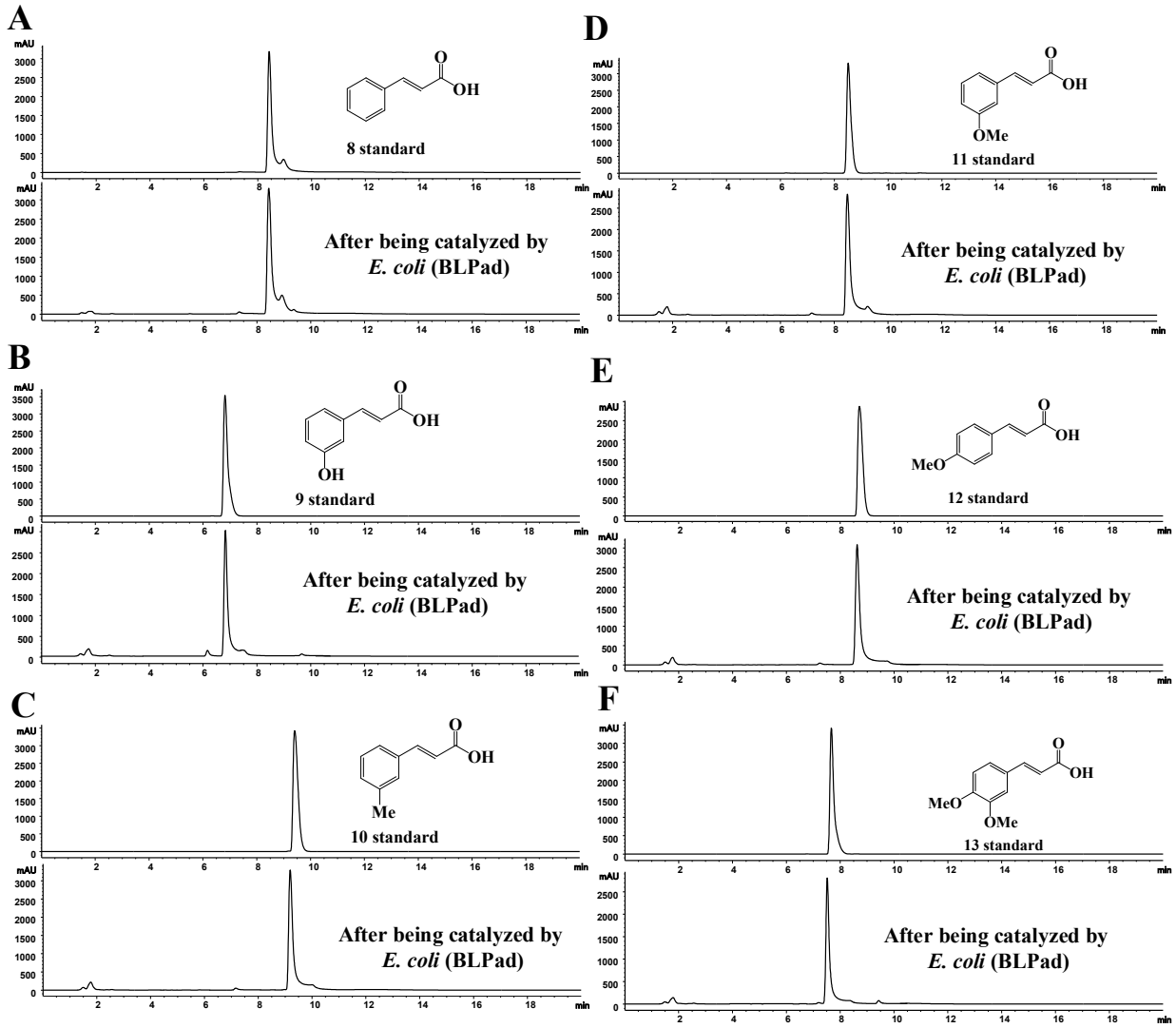

Fig. S3 Investigation of the catalytic activity of BLPad on *p*-coumaric acid derivatives, including cinnamic acid (**8**), 3-hydroxycinnamic acid (**9**), 3-methylcinnamic acid (**10**), 3-methoxycinnamic acid (**11**), 4-methoxycinnamic acid (**12**) and 3,4-dimethoxycinnamic acid (**13**), using strain *E. coli* (BLPad) carrying pA7a-BLPad. The bioconversions were performed in 5 mL HEPES buffer (50 mM, pH 7.0 and OD_{600} of 30) at 37 °C, 250 rpm, with adding 10 mM substrates for 1 h.

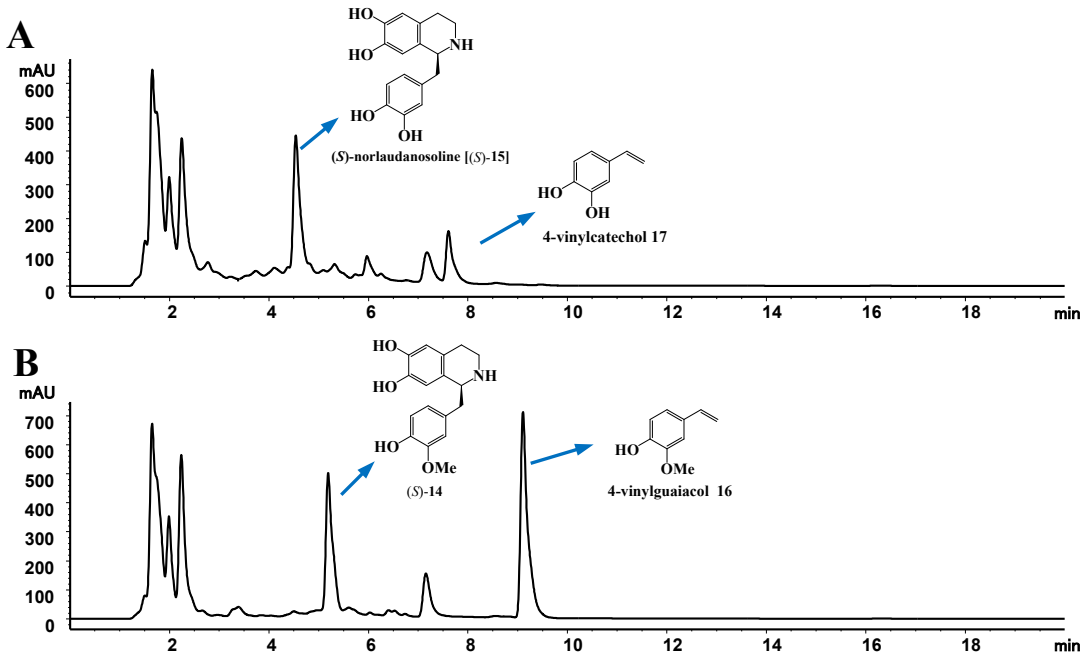

Fig. S4 Bioconversions for the synthesis of (*S*)-**14** and (*S*)-**15** using ZMTS 1 with adding 5 mM substrates (dopamine **2**, ferulic acid **6** or caffeic acid **7**). The bioconversions were performed in 5 mL HEPES buffer (50 mM, pH 7.0 and OD_{600} of 30) at 37 °C, 250 rpm, with adding 10 g L^{-1} of glucose and 10 mM sodium ascorbate for 2 h.

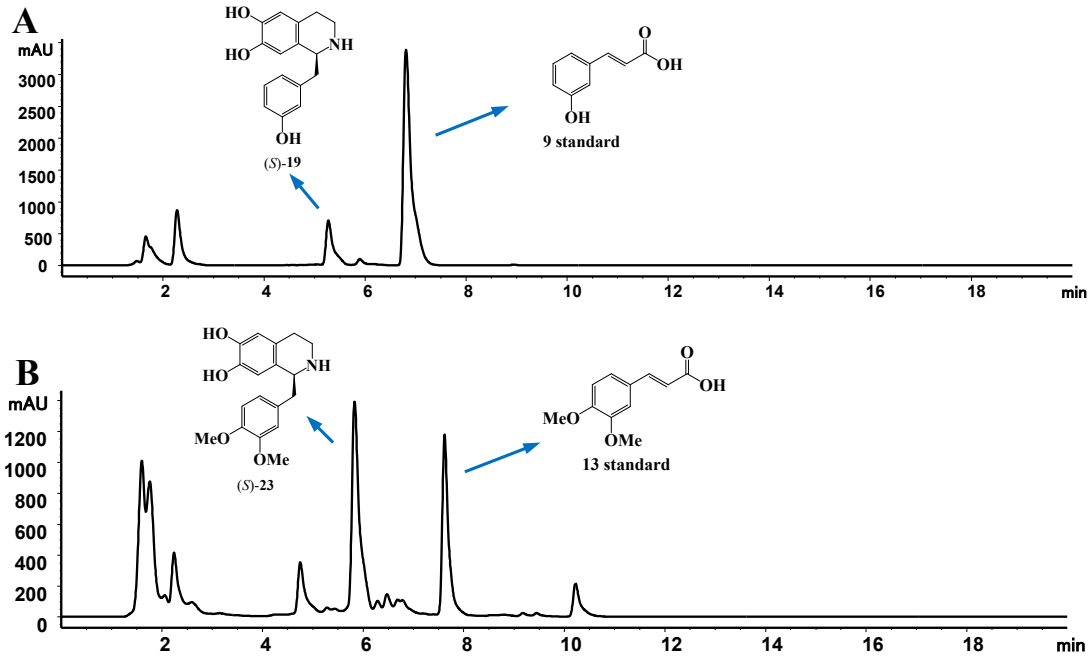

Fig. S5 Bioconversions for the synthesis of (*S*)-**19** and (*S*)-**23** using ZMTS 5 with adding 10 mM substrates (dopamine **2**, 3-hydroxycinnamic acid **9** or 3,4-dimethoxycinnamic acid **13**). The bioconversions were performed in 5 mL HEPES buffer (50 mM, pH 7.0 and OD_{600} of 30) at 37 °C, 250 rpm, with adding 10 g L^{-1} of glucose and 10 mM sodium ascorbate for 2 h.

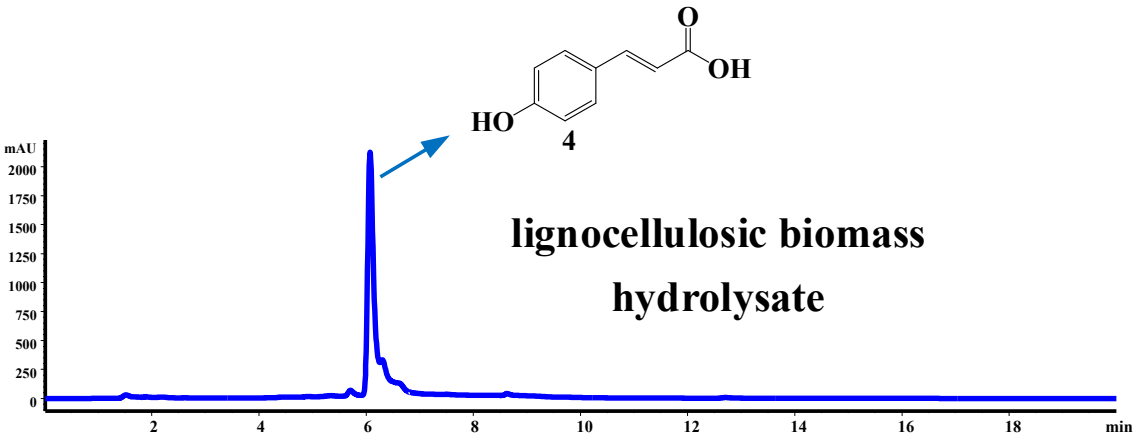

Fig. S6 HPLC analysis of lignocellulosic biomass hydrolysate from sorghum pith.

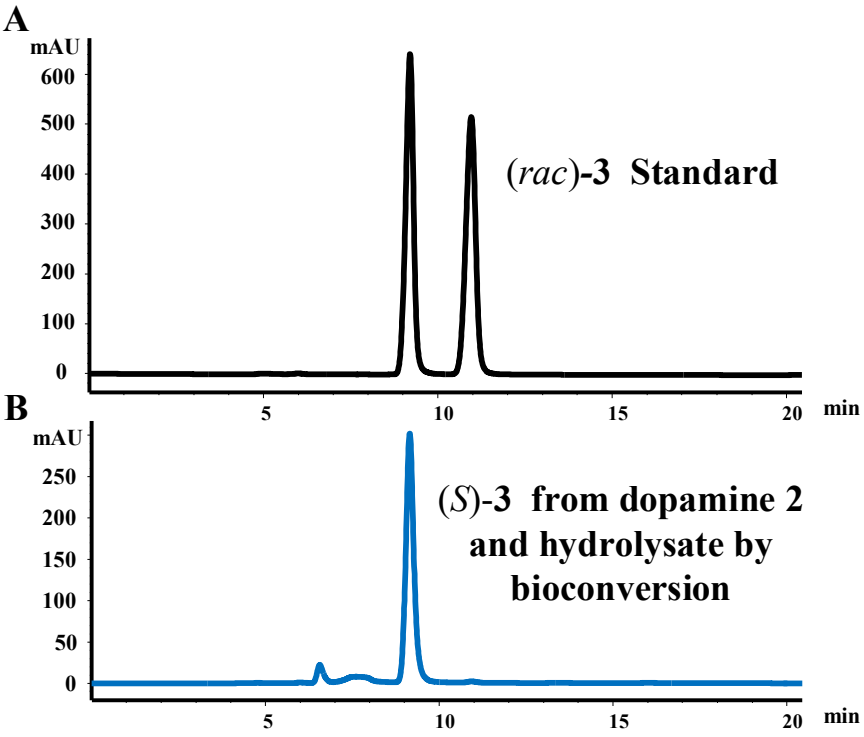

Fig. S7 Chiral HPLC analysis of the synthesis of (*rac*)-**3** (standard) and (*S*)-**3** from dopamine **2** and hydrolysate by bioconversion.

3. Experimental Section

3.1 Chemicals and reagents used in this study

All chemicals were purchased from commercial companies: *p*-coumaric acid (**4**), acetonitrile used for HPLC (Adamas Reagent Co., Ltd); ferulic acid (**6**) and 3-fluorocinnamic acid (**27**) (Macklin Biochemical Co., Ltd); 4-vinylphenol (**5**), 4-vinylguaiacol (**16**), 3-hydroxycinnamic acid (**9**) and 4-methoxycinnamic acid (**12**) (Ark Pharm); cinnamic acid (**8**) (Energy Chemical); tyrosol (Bidepharm); 4-hydroxyphenylacetaldehyde (**1**)

(APOLLO SCIENTIFIC); 4-hydroxyphenylacetic acid (4-HPA) (Energy Chemical); caffeic acid (**7**), 3-methoxycinnamic acid (**11**), 3-fluoro-4-hydroxycinnamic acid (**24**) and *trans*-3-bromocinnamic acid (**29**) (Aladdin); 3-chlorocinnamic acid (**28**) (H∧WN®); 3-methylcinnamic acid (**10**) (Alfa Aesar); 3-chloro-4-hydroxycinnamic acid (**25**), 3-bromo-4-hydroxycinnamic acid (**26**) and (*rac*)-norlaudanosoline [(*rac*)-**15**] (TRC Canada); (*rac*)-norcoclaurine [(*rac*)-**3**] (ANPEL).

Reagents: DNA gel extraction kit, plasmid purification kit, Phusion® High-Fidelity DNA Polymerase, and dNTP mix (10 mM each) were obtained from Thermo Fisher Scientific. Restriction endonucleases and T4 DNA ligase were obtained from New England Biolabs.

3.2 Genes used in this study

blpad from *Bacillus licheniformis* strain CGMCC 7172:[5]

> *blpad*

ATGAATCAAGATGTAAAAGAGTTTGTAGGAAGCCATATGATCTATACGTATGAAAACGGATGGG
AATATGAAATCTACATTAAAAATGACCATACCATCGATTACCGCATTCACAGCGGAATGGTTGGG
GGACGCTGGGTTCGCGATCAAAAAGCCGATATCGTCAAGCTGACTGAAGGCGTCTATAAAGTATC
CTGGACAGAACCGACAGGGACTGACGTTTCCTTGAACTTCATGCCGAATGAAAAGCGGATGCACG
GCATCATCTTCTTCCCTAAATGGGTTCATGAACGCCCTGATATTACAGTCTGCTATCAAAATGACC
ATATCGACTTAATGGAGGAATCGCGCGAAAAATATGAGACGTATCCAAAATATGTCGTACCGGAA
TTCGCCGATATCACATTTATTGAAAATGCCGGAATCGATAATGAAGATCTGATTTCAAAAGCCCCT
TATCCCGGAATGACGGATGACATCAGGGCAGGAAAGCGGGTATAA

styAB from *Pseudomonas* sp. strain VLB120 was codon optimized:[6]

>*styA*

ATGAAAAAGCGTATCGGTATTGTTGGTGCAGGCACTGCCGGCCTCCATCTTGGCCTCTTCCTTCGT
CAGCATGACGTCGACGTCACTGTGTACACTGATCGTAAGCCCGATGAGTACAGCGGACTGCGTCT
CCTGAATACCGTTGCTCACAACGCGGTGACGGTGCAGCGGGAGGTTGCCCTCGACGTCAATGAGT
GGCCGTCTGAGGAGTTTGGTTATTTCGGCCACTACTACTACGTAGGTGGGCCGCAGCCCATGCGTT
TCTACGGTGATCTCAAGGCTCCCAGCCGTGCAGTGGACTACCGTCTCTACCAGCCGATGCTGATGC
GTGCACTGGAAGCCAGGGGCGGCAAGTTCTGCTACGACGCGGTGTCTGCCGAAGATCTGGAAGG
GCTGTCGGAGCAGTACGATCTGCTGGTTGTGTGCACTGGTAAATACGCCCTCGGCAAGGTGTTCG
AGAAGCAGTCCGAAAACTCGCCCTTCGAGAAGCCGCAACGGGCACTGTGCGTTGGCCTCTTCAAG
GGCATCAAGGAAGCACCGATTCGCGCGGTGACTATGTCCTTCTCGCCAGGGCATGGCGAGCTGAT
TGAGATTCCAACCCTGTCGTTCAATGGCATGAGCACAGCGCTGGTGCTCGAAAACCATATTGGTA
GCGATCTGGAAGTTCTCGCCCACACCAAGTATGACGATGACCCGCGTGCGTTCCTCGATCTGATG
CTGGAGAAGCTGGGTAAGCATCATCCTTCCGTTGCCGAGCGCATCGATCCGGCTGAGTTCGACCT
TGCCAACAG

TTCTCTGGACATCCTCCAGGGTGGTGTTGTGCCGGCATTCCGCGACGGTCATGCGACCCTCAATAA
CGGCAAAACCATCATTGGGCTGGGCGACATCCAGGCAACTGTCGATCCGGTCTTGGGCCAGGGCG
CGAACATGGCGTCCTATGCGGCATGGATTCTGGGCGAGGAAATCCTTGCGCACTCTGTCTACGAC
CTGCGCTTCAGCGAACACCTGGAGCGTCGCCGCCAGGATCGCGTGCTGTGTGCCACGCGATGGAC
CAACTTCACTCTGAGCGCTCTCTCGGCACTTCCGCCGGAGTTCCTCGCCTTCCTTCAGATCCTGAG
CCAGAGCCGTGAAATGGCTGATGAGTTCACGGACAACTTCAACTACCCGGAACGTCAGTGGGATC
GCTTCTCCAGCCCGGAACGTATCGGACAGTGGTGCAGTCAGTTCGCACCCACTATCGCGGCCTGA

>*styB*

ATGACGTTAAAAAAAGATATGGCGGTGGATATCGACTCCACCAACTTCCGCCAGGCGGTTGCATT
GTTCGCGACGGGAATTGCGGTTCTCAGCGCGGAGACTGAAGAGGGCGATGTGCACGGCATGACC
GTGAACAGTTTCACCTCCATCAGTCTGGATCCGCCGACTGTGATGGTTTCCCTGAAATCGGGCCGT
ATGCATGAGTTGCTGACTCAAGGCGGACGCTTCGGAGTTAGCCTCTTGGGTGAAAGCCAGAAGGT
GTTCTCGGCATTCTTCAGCAAGCGCGCGATGGATGACACGCCTCCCCCCGCCTTCACCATTCAGGC
CGGCCTTCCCACTCTGCAGGGCGCCATGGCCTGGTTCGAATGCGAGGTGGAGAGCACGGTTCAAG
TACACGACCACACGCTCTTCATTGCGCGCGTTAGCGCCTGTGGAACGCCTGAGGCGAATACCCCC
CAGCCGCTGCTGTTCTTTGCCAGCCGTTATCACGGCAACCCGTTGCCACTGAATTGA

RostyC from *Rhodococcus opacus* 1CP was codon optimized:[7]

>*RostyC*

ATGAAAACGCTGGAACGCAAAATCTACGGCCACGGCGTGCTGATGATTCTGAGCACGCTGATCTT
CGGTCTGTTTCTGTGGATGAATCTGGTTGGCGGCTTCGAGATCGTGCCGGGCTACATCATCAACTT
CAACATCCCGGGTACGGCGGAAGGTTGGGCGAAAGCCCATGTTGGCCCGGCGCTGAATGGCATG
ATGGTTATCGCGATCGGTCTGGTTCTGCCAAAACTGGCGTTCCCGCTGAAGACGGCCAAGAAACT
GGGCTATATCATCGTGCTGGACGGCTGGGGCAATGTGTGCTTCTACTTCTTCAGCAACTTCGCGCC
GAGCCGTGGTCTGAGTTTCGGCAGCAATCGTCTGGGCGAAACCAACATCTTCGGCGTTCTGGCGC
TGGCCCCGGCCTATGTTTTTGGCGTGCTGGCGATTGGCGCGCTGGCGATCATCGGCTTTAAAGCGC
TGCGCCAGACGGATGCCGAAGATCGCGCCATCGAAAGCGCGAACGCCTAA

Δ29TfNCS from *Thalictrum flavum* was codon optimized:[8]

>*Δ29TfNCS*

ATGTTGCATCACCAGGGTATCATCAATCAAGTTAGCACCGTCACGAAAGTAATTCATCACGAGCT
GGAAGTTGCGGCATCCGCTGACGACATTTGGACCGTGTACAGCTGGCCGGGTCTGGCGAAGCACT
TGCCGGATCTGCTGCCTGGCGCGTTCGAAAAACTGGAGATTATCGGCGATGGCGGTGTTGGTACG
ATTCTGGACATGACCTTTGTCCCGGGTGAATTCCCGCACGAGTATAAAGAGAAATTCATCCTGGTT
GATAACGAACATCGTCTGAAGAAGGTGCAGATGATCGAAGGCGGCTATCTGGACCTGGGTGTGA

CGTATTACATGGACACGATTCACGTTGTGCCGACCGGTAAAGACAGCTGCGTCATCAAGAGCAGC
ACTGAGTACCACGTCAAGCCGGAGTTTGTGAAGATTGTTGAGCCGCTGATCACCACCGGTCCACT
GGCAGCCATGGCAGATGCCATTAGCAAGTTGGTCCTGGAACATAAATCTAAAAGCAACTCCGATG
AAATTGAGGCGGCGATCATCACCGTGTGA

AnPad (*pad* and *fcd*) from *Aspergillus niger* was codon optimized[9]:

> *pad*

ATGTTTAACAGCCTGCTGAGCGGCACCACCACACCTAATAGCGGCCGCGCGAGCCCGCCGGCGAG
CGAAATGCCGATCGACAATGACCACGTTGCTGTCGCCAGGCCAGCACCGCGACGTAGACGTATAG
TCGTTGCAATGACCGGCGCGACCGGCGCGATGCTGGGCATTAAAGTGCTGATTGCGCTGCGCCGC
CTGAACGTGGAAACCCATCTGGTGATGAGCAAATGGGCGGAAGCGACCATTAAATATGAAACCG
ATTATCATCCGAGCAACGTGCGCGCGCTGGCGGATTATGTGCATAACATTAACGATATGGCGGCG
CCGGTGAGCAGCGGCAGCTTTCGCGCGGATGGCATGATTGTGGTGCCGTGCAGCATGAAGACTTT
GGCGGCGATTCATAGCGGCTTCTGTGACGATCTGATTAGCCGCACCGCGGATGTGATGCTGAAAG
AACGCCGCCGCCTGGTGCTGGTGGCGCGCGAAACGCCTCTTAGCGAAATTCATCTGCGCAACATG
CTGGAAGTGACCCGCGCGGGCGCGGTGATATTCCCACCTGTTCCGGCGTTCTACATCAAAGCGGG
CAGCATTGAAGATCTGATTGATCAGAGCGTGGGCCGCATGCTGGATCTGTTTGATCTGGATACCG
GCGATTTCGAGCGATGGAACGGCTGGGAGAAGTAA

> *fcd*

ATGAGCGCGCAGCCGGCGCATCTGTGCTTTCGCAGCTTTGTGGAAGCGCTGAAAGTGGATAACGA
TCTGGTGGAAATTAACACACCAATCGATCCGAACCTGGAAGCCGCTGCCATCACTAGGCGCGTGT
GCGAAACCAACGATAAAGCGCCGCTGTTTAACAACCTGATTGGCATGAAGAATGGGCTGTTTCGC
ATTCTGGGCGCGCCGGGCAGCCTGCGCAAGTCTAGTGCGGATCGCTATGGCCGCCTGGCGCGCCA
TCTGGCGCTGCCGCCGACCGCGAGCATGCGCGAAATTCTGGATAAGATGTTGAGCGCGAGCGATA
TGCCGCCGATTCCGCCGACCATTGTGCCGACCGGCCCGTGCAAAGAGAATAGTCTGGATGATAGC
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GACCTATGGCATGCATATTGTGCAGAGCCCGGATGGCACCTGGACCAACTGGAGCATTGCGCGCG
CGATGGTGCATGATAAGAATCACCTGACCGGCCTGGTGATTCCGCCGCAGCATATTTGGCAGATT
CATCAGATGTGGAAGAAGGAGGGACGCAGCGATGTGCCGTGGGCGCTGGCGTTTGGCGTGCCGC
CCGCAGCCATAATGGCCAGCAGCATGCCGATTCCGGATGGCGTGACCGAAGCGGGCTATGTGGGC
GCGATGACCGGCAGCAGCCTGGAACTGGTGAAATGCGATACCAACGATCTGTATGTGCCGGCGAC
CAGCGAAATTGTGCTGGAAGGCACCCTGAGCATTAGCGAAACCGGCCCGGAAGGCCCGTTTGGC
GAAATGCATGGCTATATATTCCCAGGAGATACCCATCTGGGCGCGAAATATAAAGTGAACCGCAT
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CCATGATTGGCAGCCTGG

CGGCGGCGGAAATTCGCAAACTGTGCCAGCAGAACGATCTGCCGATTACCGATGCGTTTGCGCCG
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GATTCCGTATATGGGCCATGGCAACGGCCCGGCGCATCGCGGCGGCAAAGTGGTGAGCGATGCG
CTGATGCCGACCGAATATACCACCGGCCGCAACTGGGAAGCGGCGGATTTCAATCAAAGCTATCC
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4. Analytical HPLC and MS results

4.1 Achiral HPLC and MS analysis

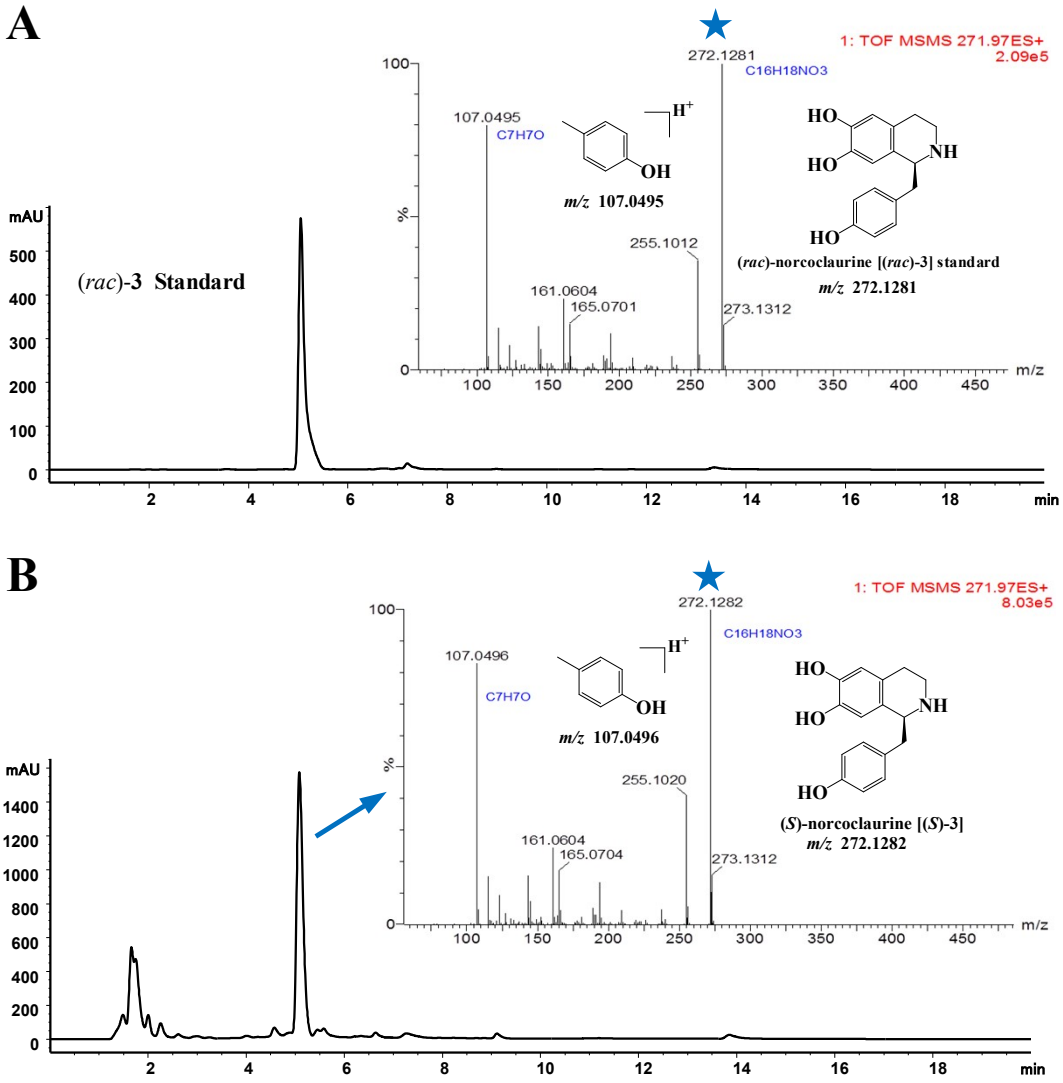

Fig. S8 (A) HPLC and MS analysis of the standard of (*rac*)-**3**. (B) HPLC and MS analysis of the synthesis of (*S*)-**3** from dopamine **2** and *p*-CA **4** with strain ZMTS 1.

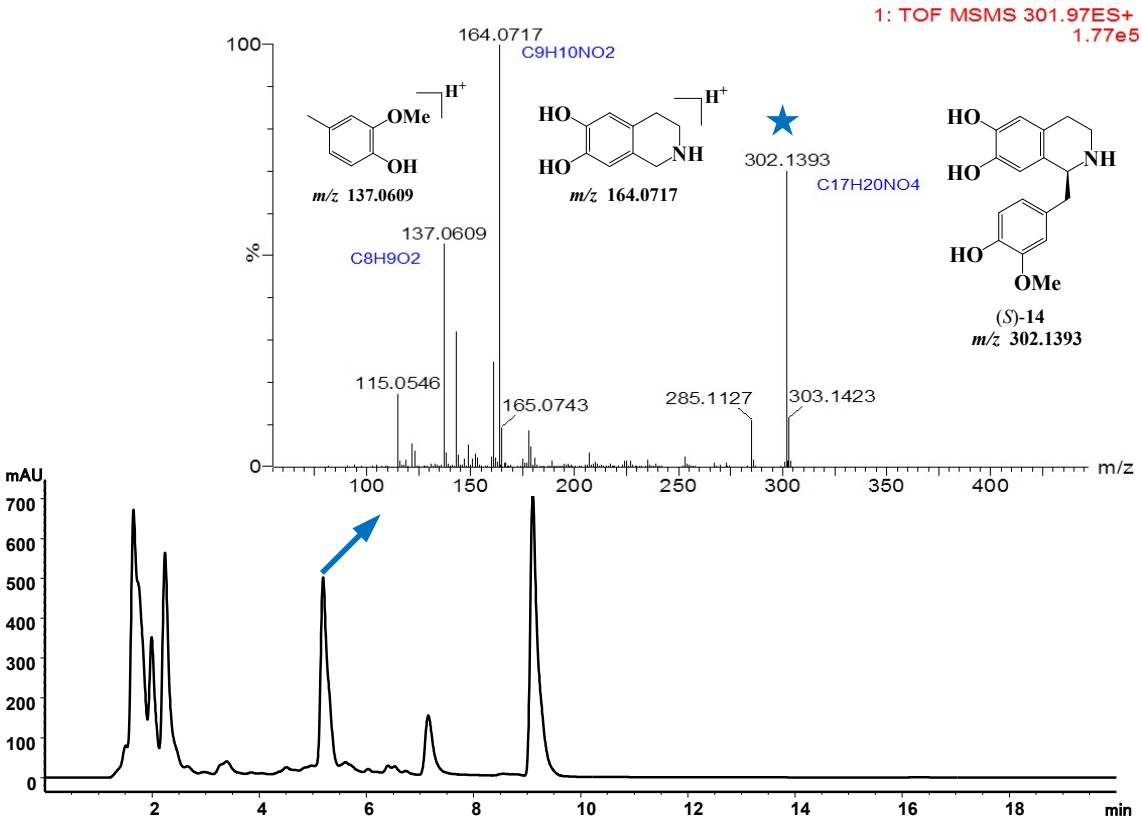

Fig. S9 HPLC analysis of the synthesis of (*S*)-**14** from dopamine **2** and ferulic acid **6** with strain ZMTS 1.

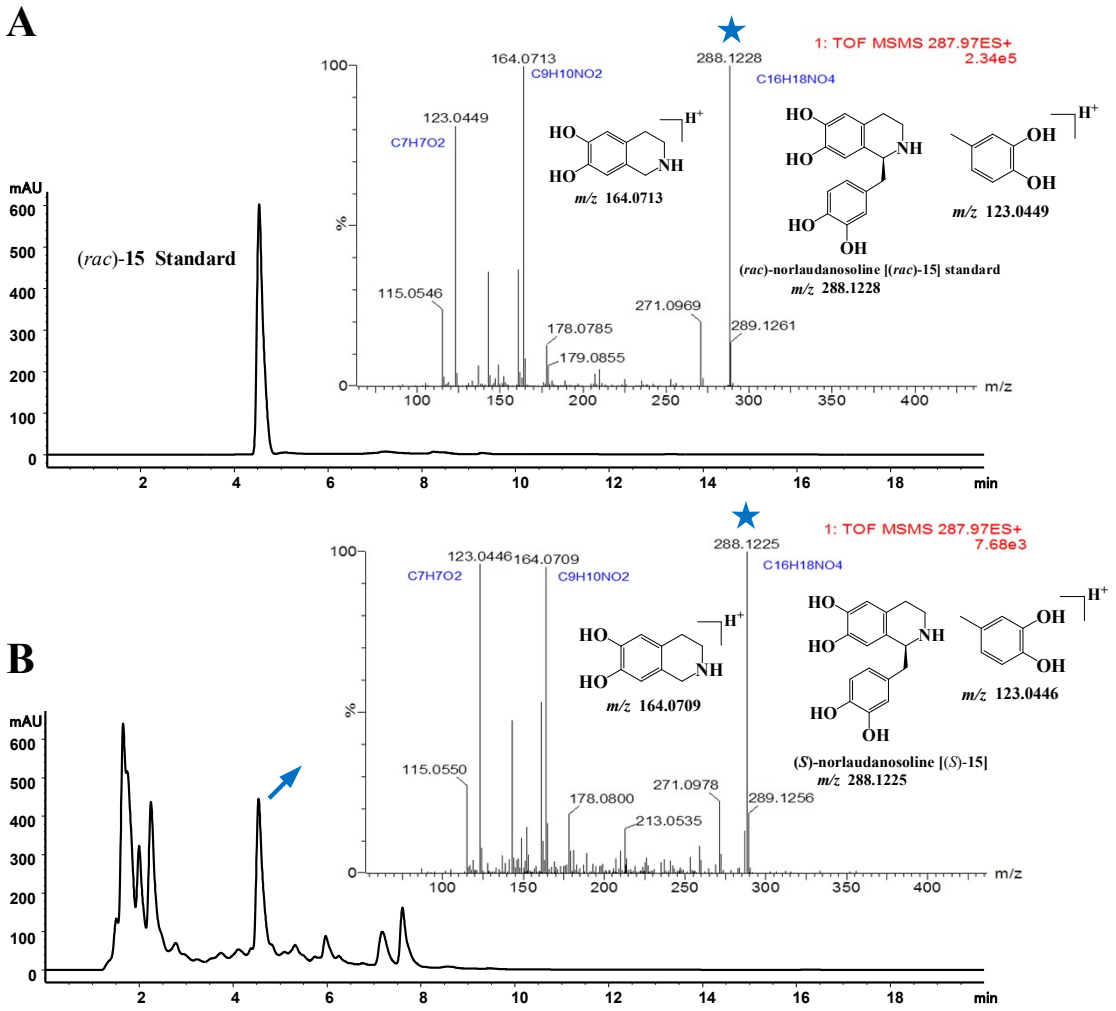

Fig. S10 (A) HPLC and MS analysis of (*rac*)-**15** standard. (B) HPLC and MS analysis of the synthesis of (*S*)-**15** from dopamine **2** and caffeic acid **7** with strain ZMTS 1.

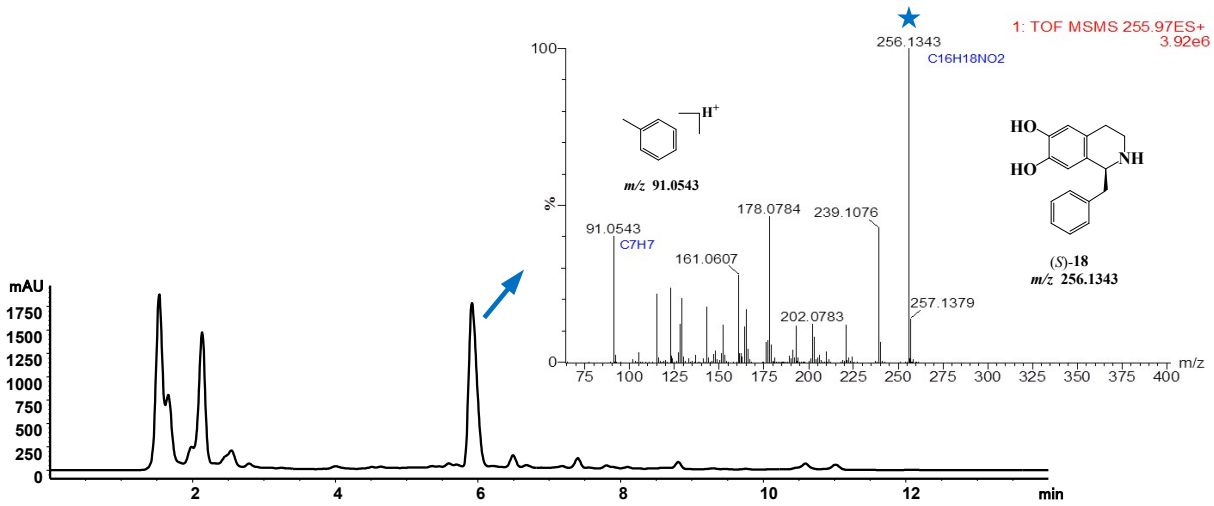

Fig. S11 HPLC analysis of the synthesis of (*S*)-**18** from **2** and cinnamic acid **8** with strain ZMTS 5.

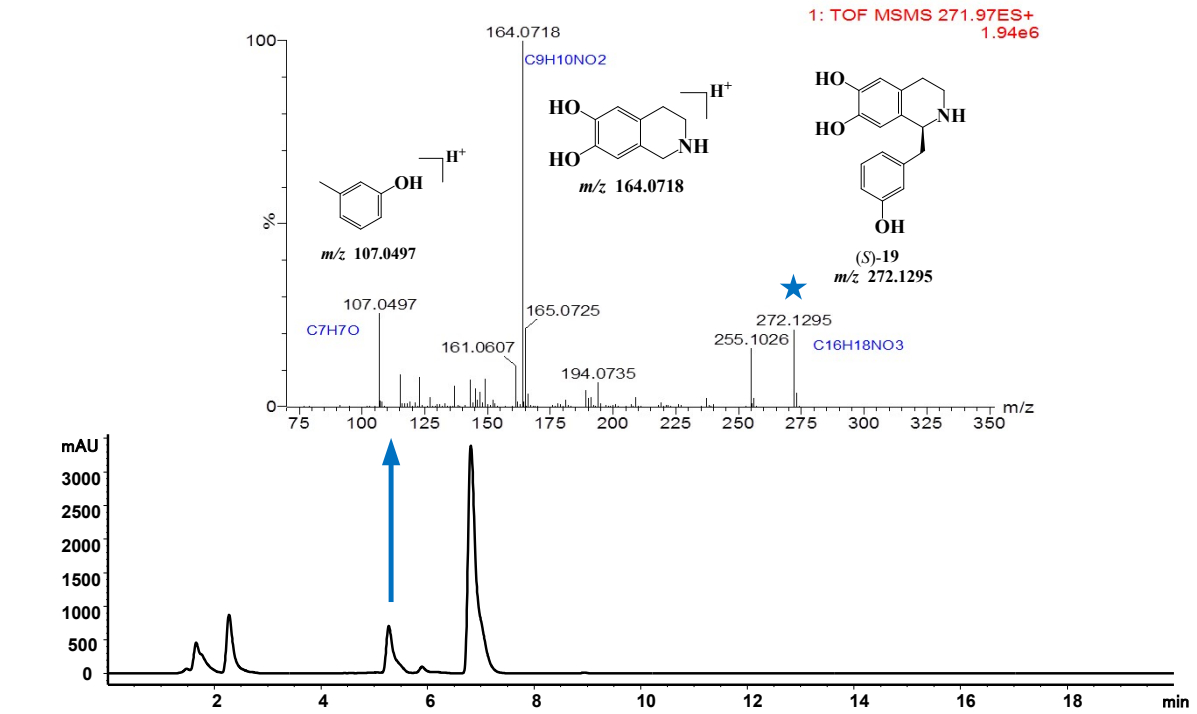

Fig. S12 HPLC and MS analysis of the synthesis of (*S*)-**19** from dopamine **2** and 3-hydroxycinnamic acid **9** with strain ZMTS 5.

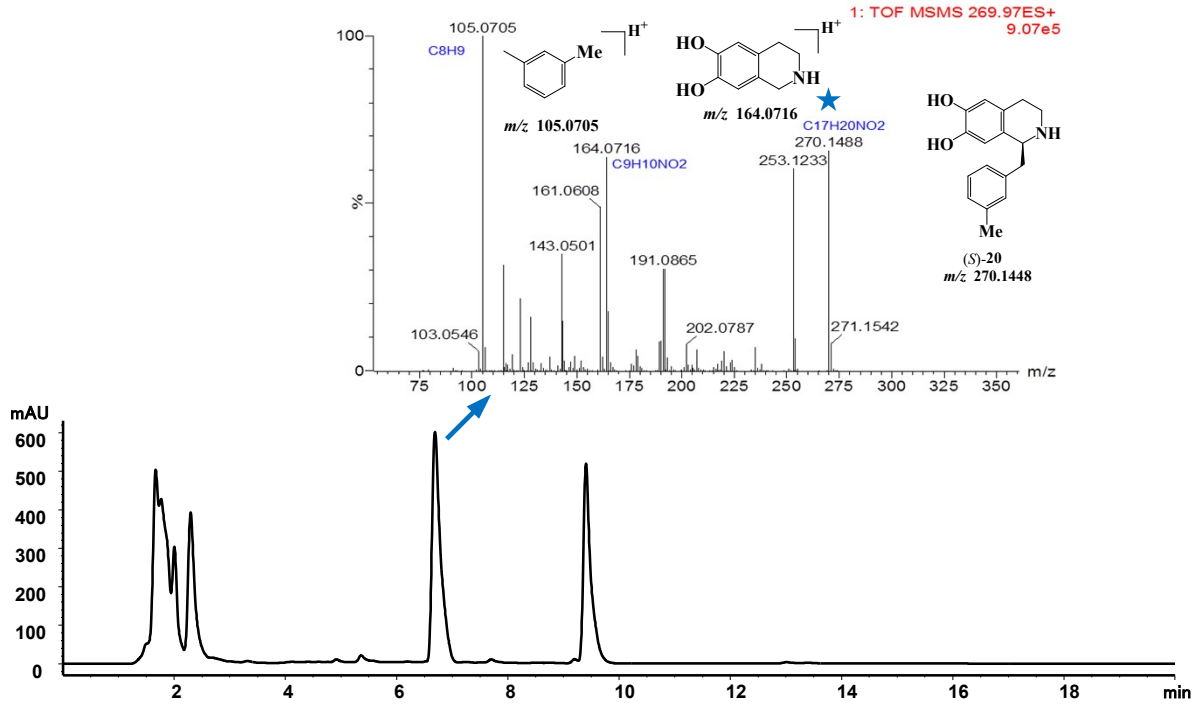

Fig. S13 HPLC and MS analysis of the synthesis of (*S*)-**20** from dopamine **2** and 3-methylcinnamic acid **10** with strain ZMTS 5.

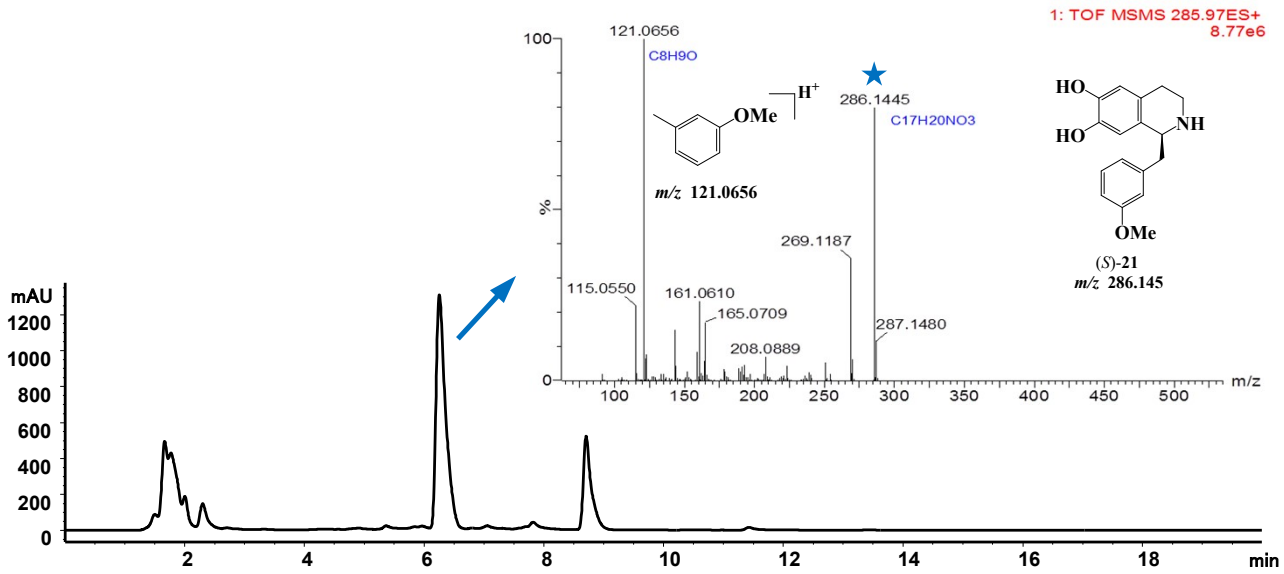

Fig. S14 HPLC and MS analysis of the synthesis of (*S*)-**21** from dopamine **2** and 3-methoxycinnamic acid **11** with strain ZMTS 5.

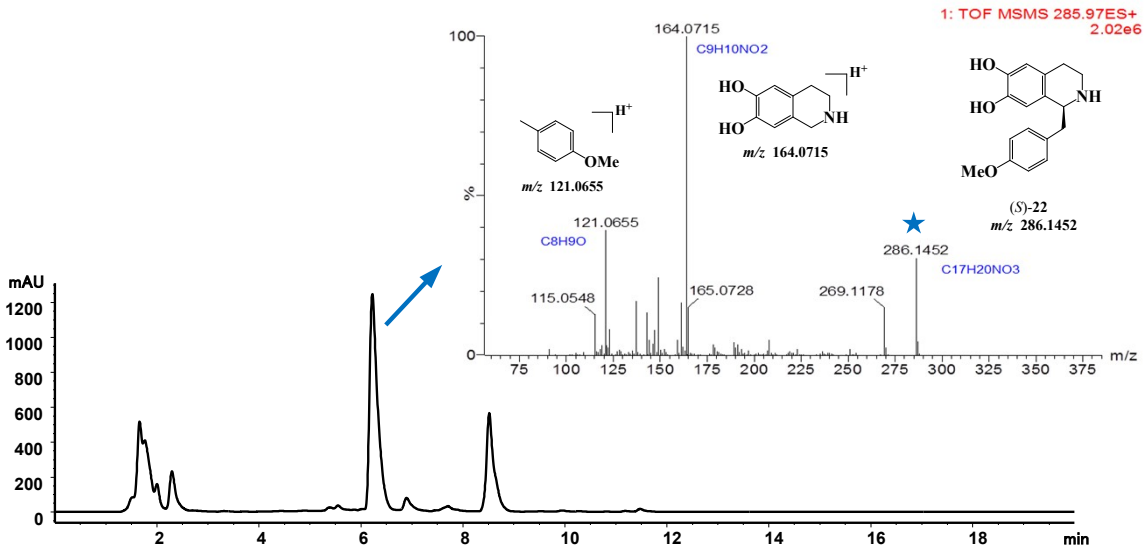

Fig. S15 HPLC and MS analysis of the synthesis of (*S*)-**22** from dopamine **2** and 4-methoxycinnamic acid **12** with strain ZMTS 5.

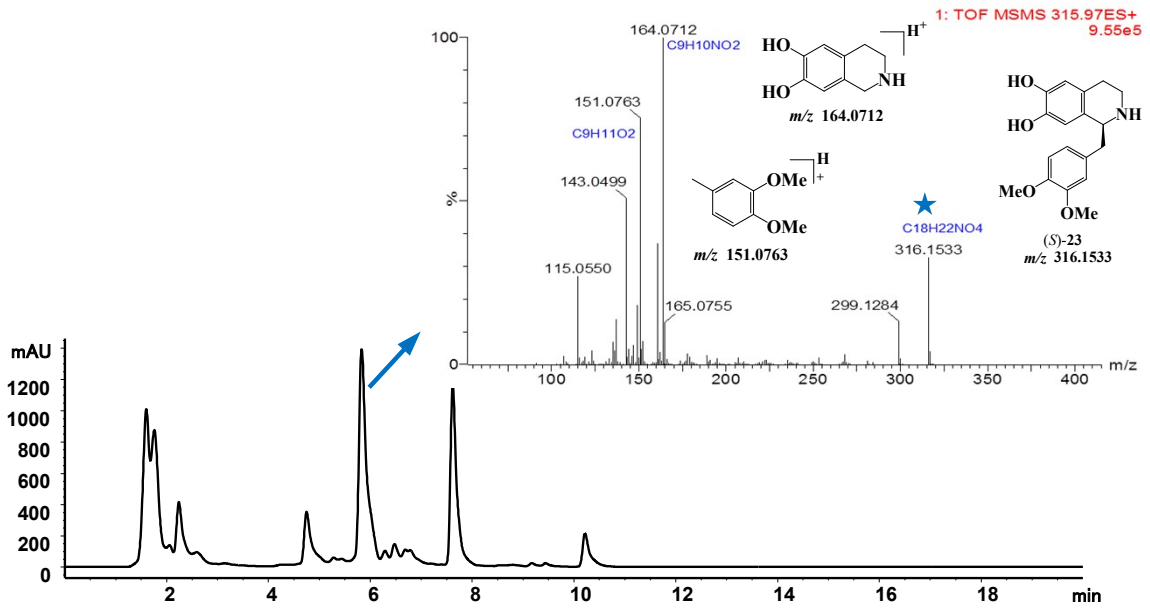

Fig. S16 HPLC and MS analysis of the synthesis of (*S*)-**23** from dopamine **2** and 3,4-dimethoxycinnamic acid **13** with strain ZMTS 5.

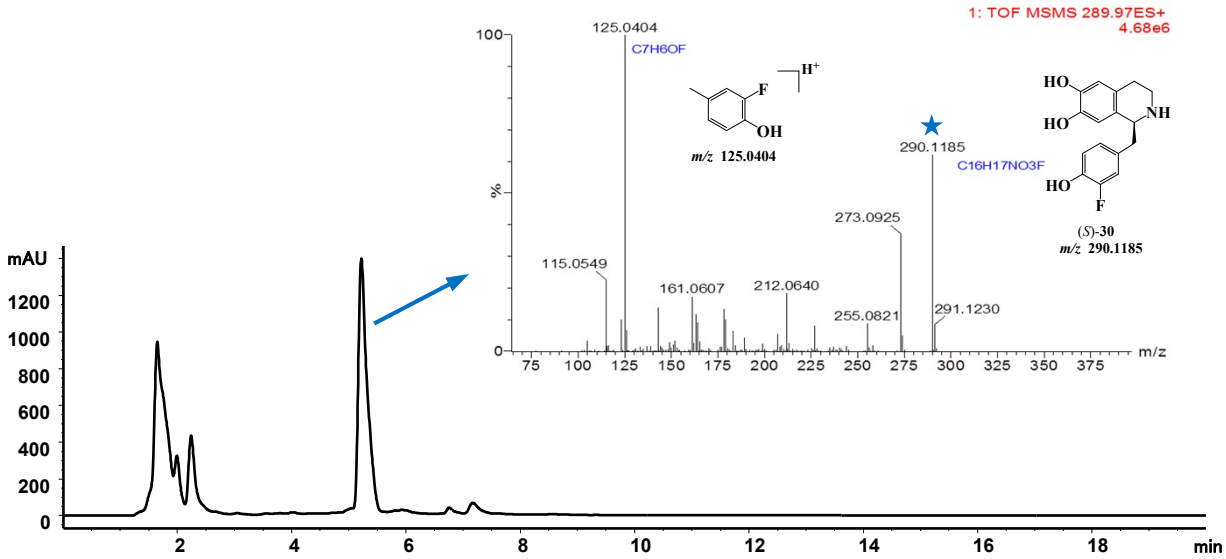

Fig. S17 HPLC and MS analysis of the synthesis of (*S*)-**30** from dopamine **2** and 3-fluoro-4-hydroxycinnamic acid **24** with strain ZMTS 1.

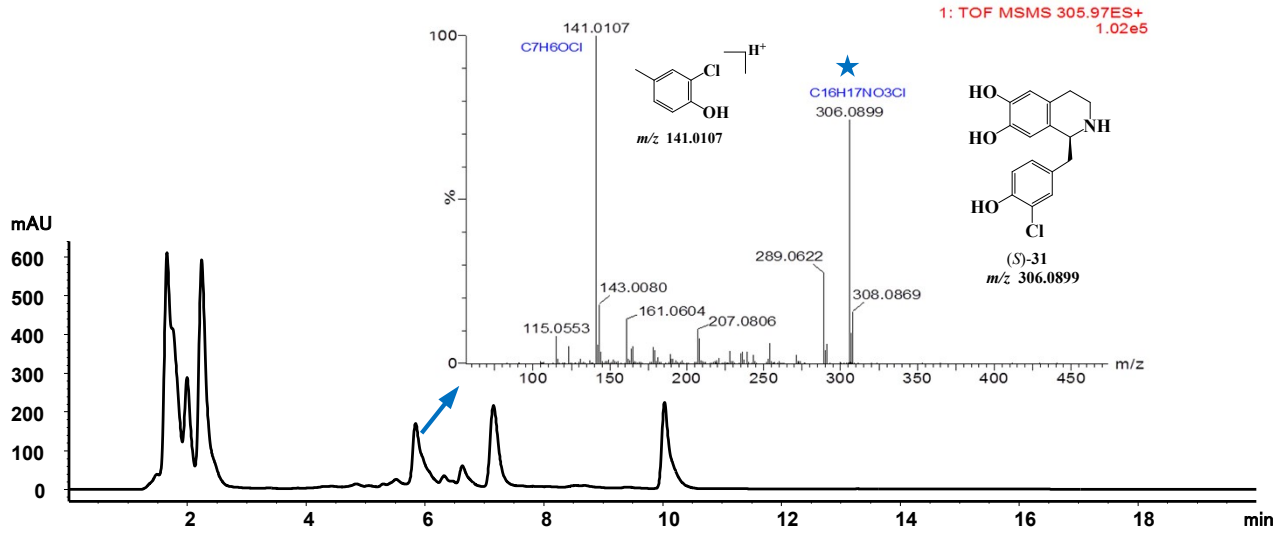

Fig. S18 HPLC and MS analysis of the synthesis of (*S*)-**31** from dopamine **2** and 3-chloro-4-hydroxycinnamic acid **25** with strain ZMTS 1.

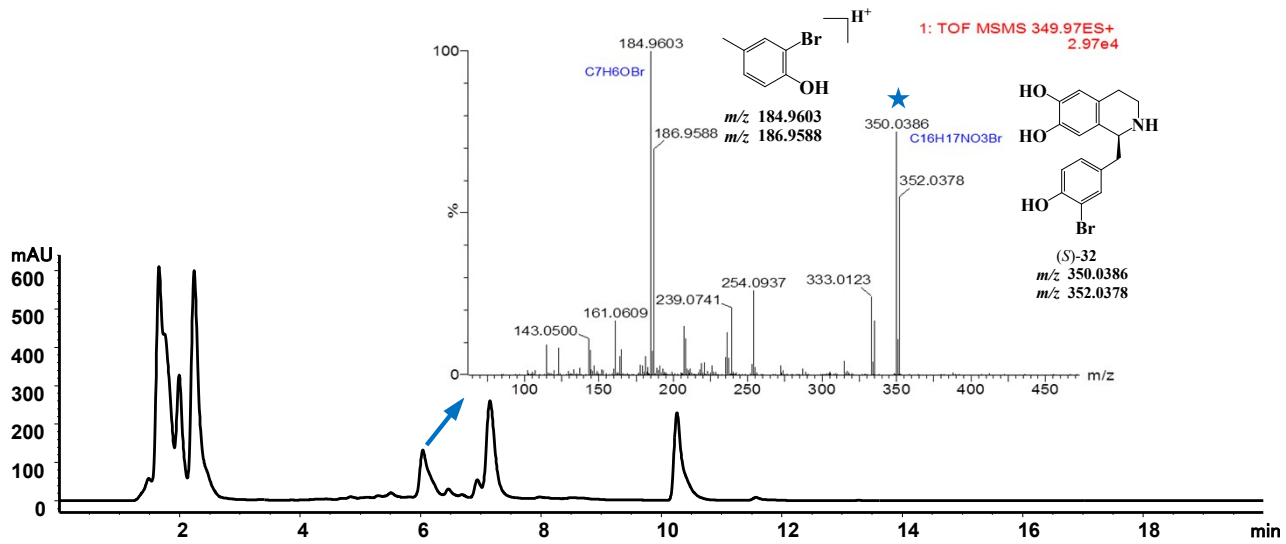

Fig. S19 HPLC and MS analysis of the synthesis of (*S*)-**32** from dopamine **2** and (*E*)-3-bromo-4-hydroxycinnamic acid **26** with strain ZMTS 1.

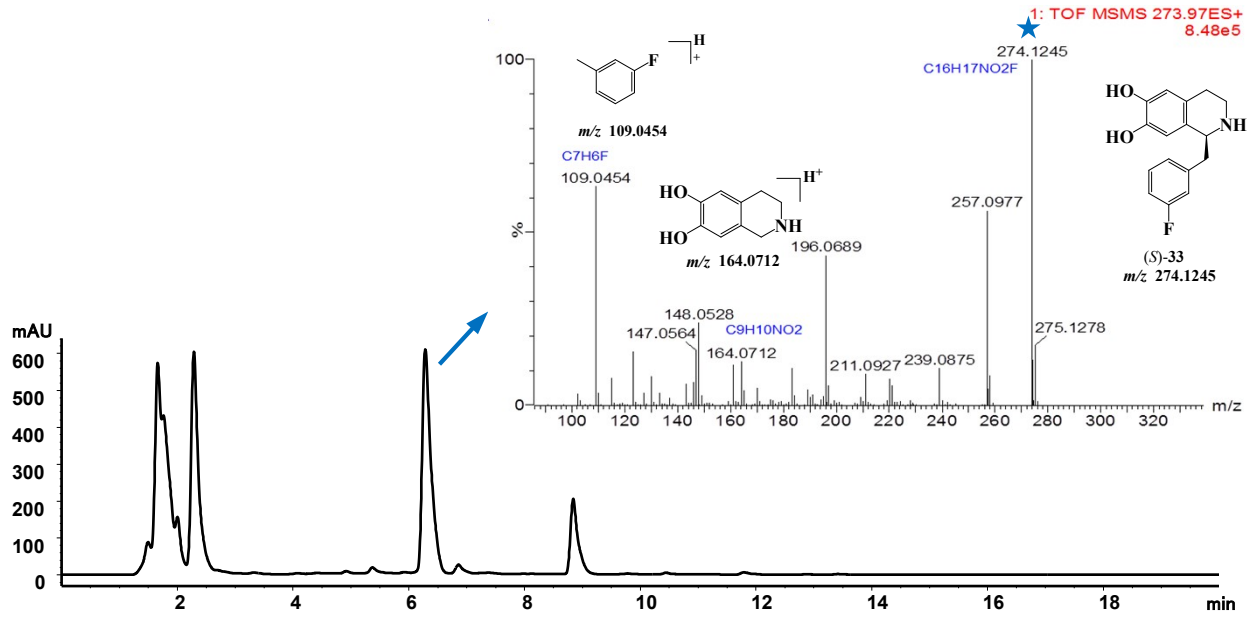

Fig. S20 HPLC and MS analysis of the synthesis of (*S*)-**33** from dopamine **2** and 3-fluorocinnamic acid **27** with strain ZMTS 5.

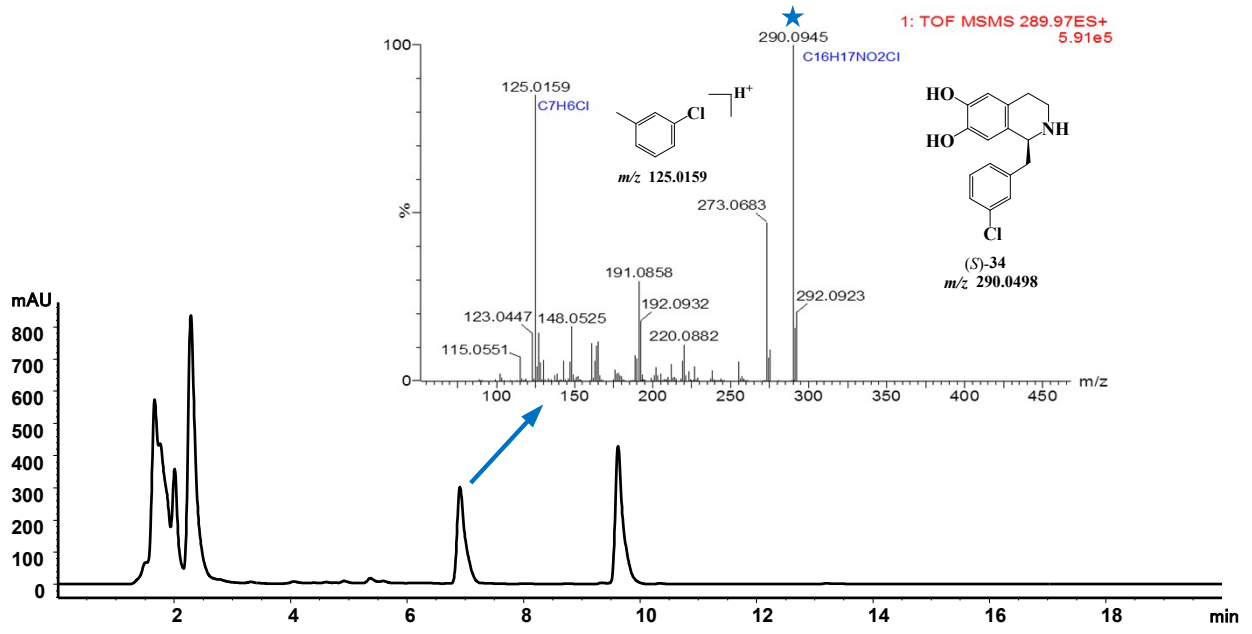

Fig. S21 HPLC and MS analysis of the synthesis of (*S*)-**34** from dopamine **2** and 3-chlorocinnamic acid **28** with strain ZMTS 5.

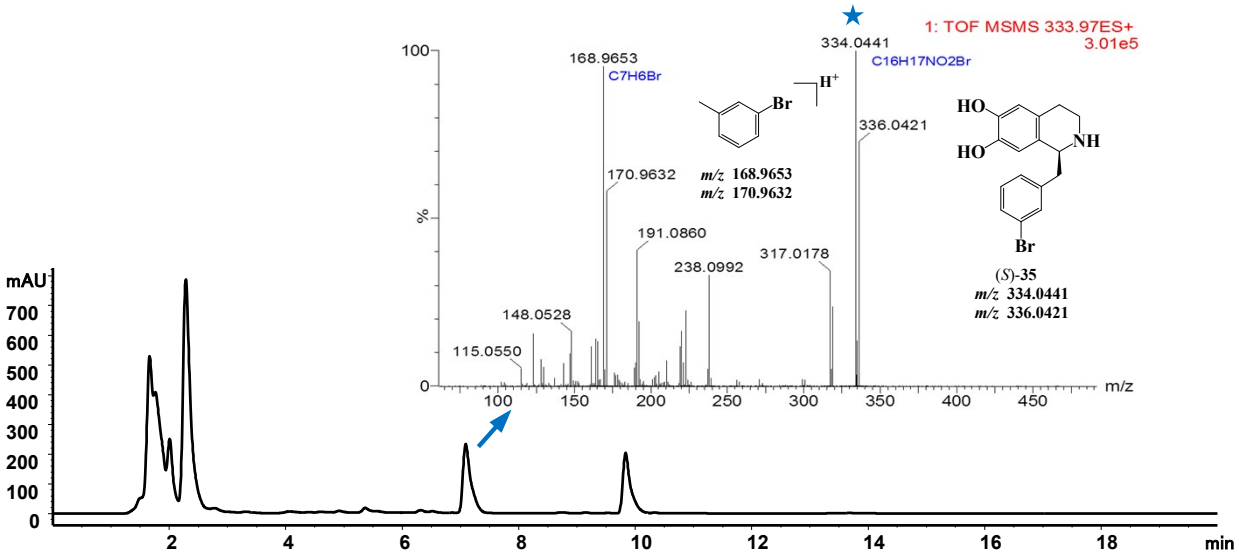

Fig. S22 HPLC and MS analysis of the synthesis of (*S*)-**35** from dopamine **2** and *trans*-3-bromocinnamic acid **29** with strain ZMTS 5.

4.2 Chiral HPLC analysis

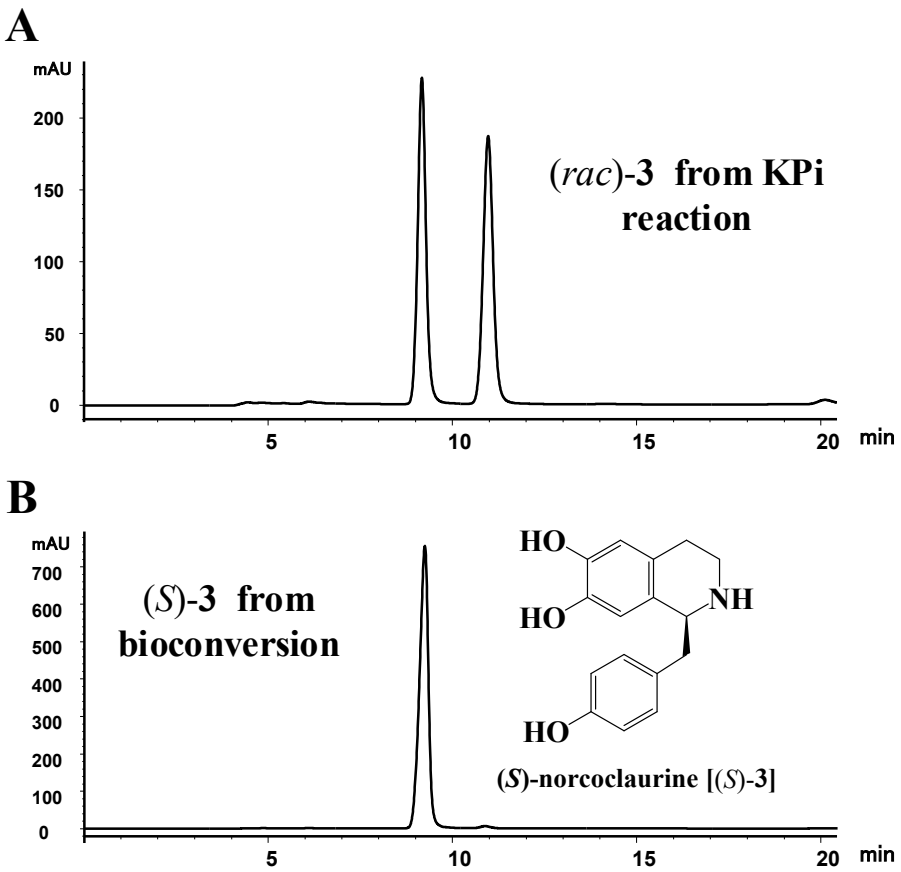

Fig. S23 Chiral HPLC analysis of the synthesis of (*rac*)-**3** and (*S*)-**3**.

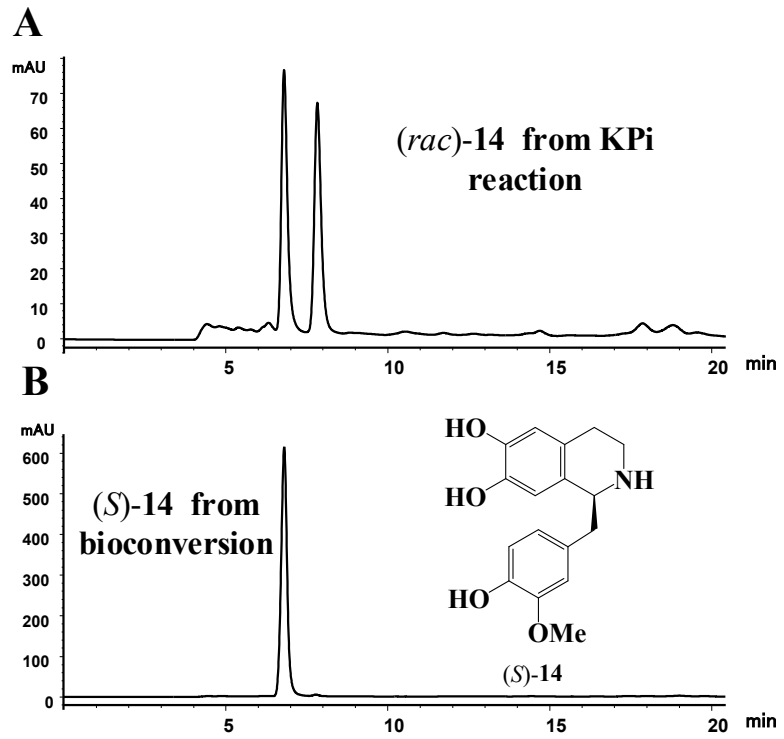

Fig. S24 Chiral HPLC analysis of the synthesis of (*rac*)-**14** and (*S*)-**14**.

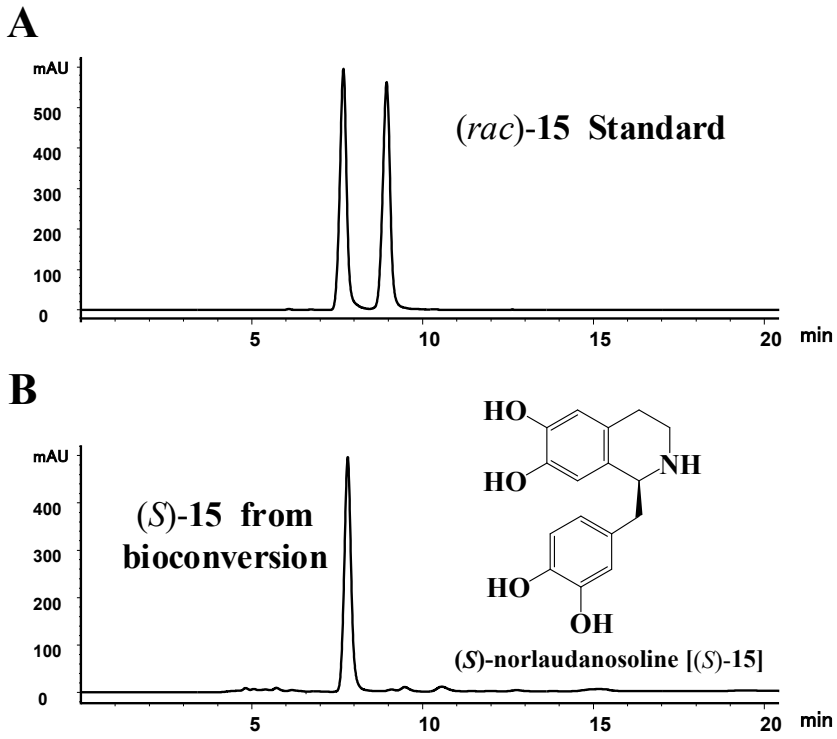

Fig. S25 Chiral HPLC analysis of the synthesis of (*rac*)-**15** and (*S*)-**15**.

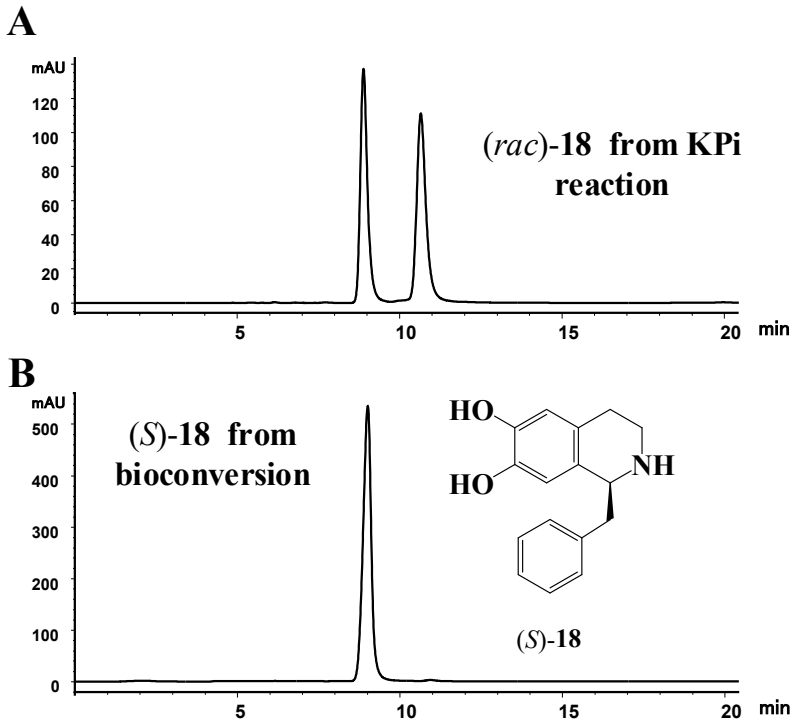

Fig. S26 Chiral HPLC analysis of the synthesis of (*rac*)-**15** and (*S*)-**18**.

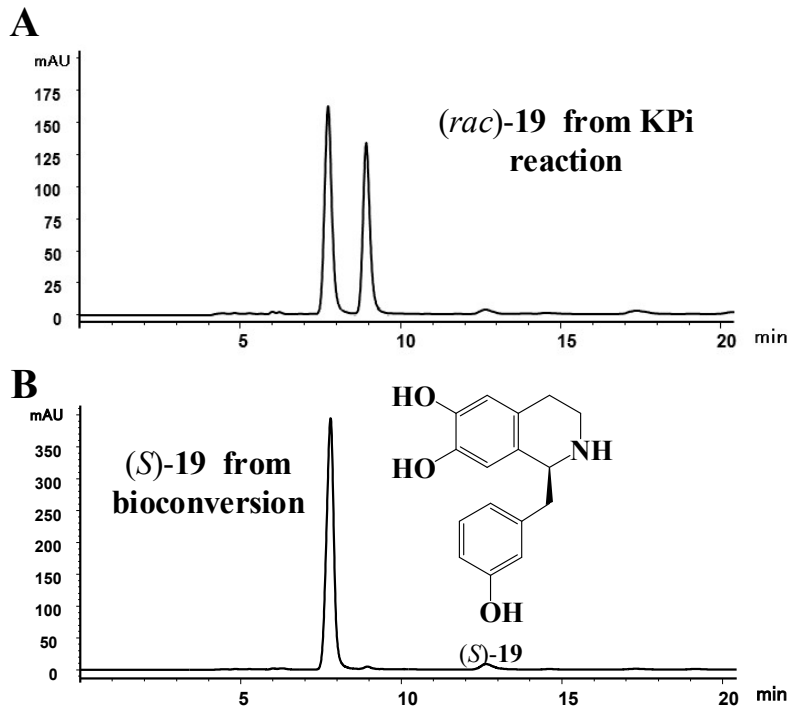

Fig. S27 Chiral HPLC analysis of the synthesis of (*rac*)-**19** and (*S*)-**19**.

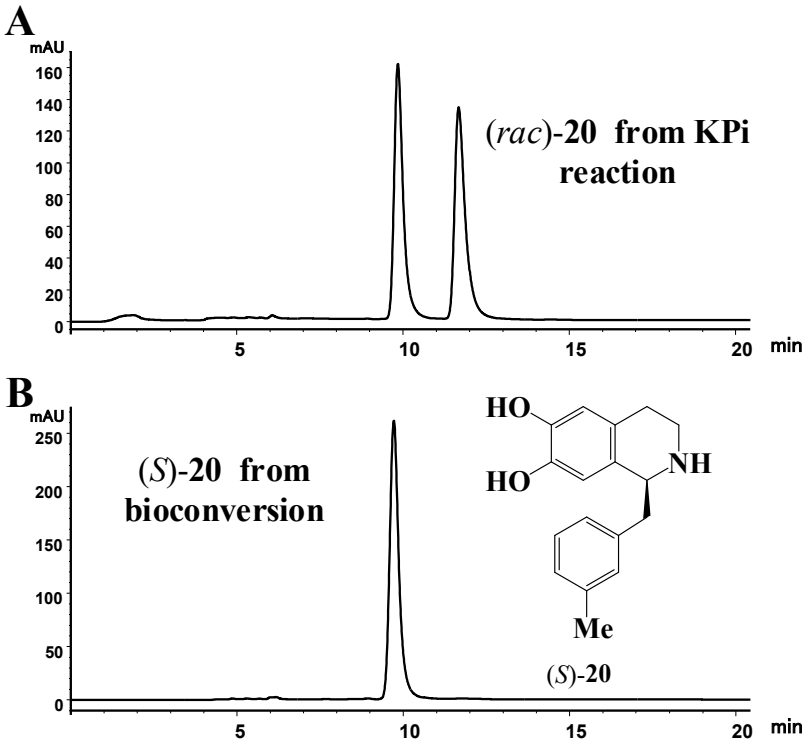

Fig. S28 Chiral HPLC analysis of the synthesis of (*rac*)-**20** and (*S*)-**20**.

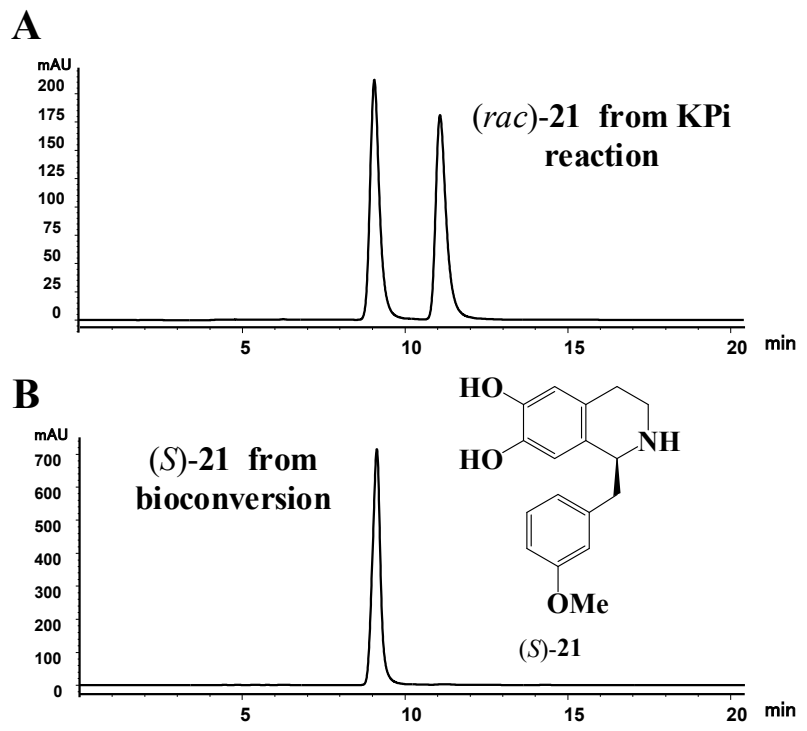

Fig. S29 Chiral HPLC analysis of the synthesis of (*rac*)-**21** and (*S*)-**21**.

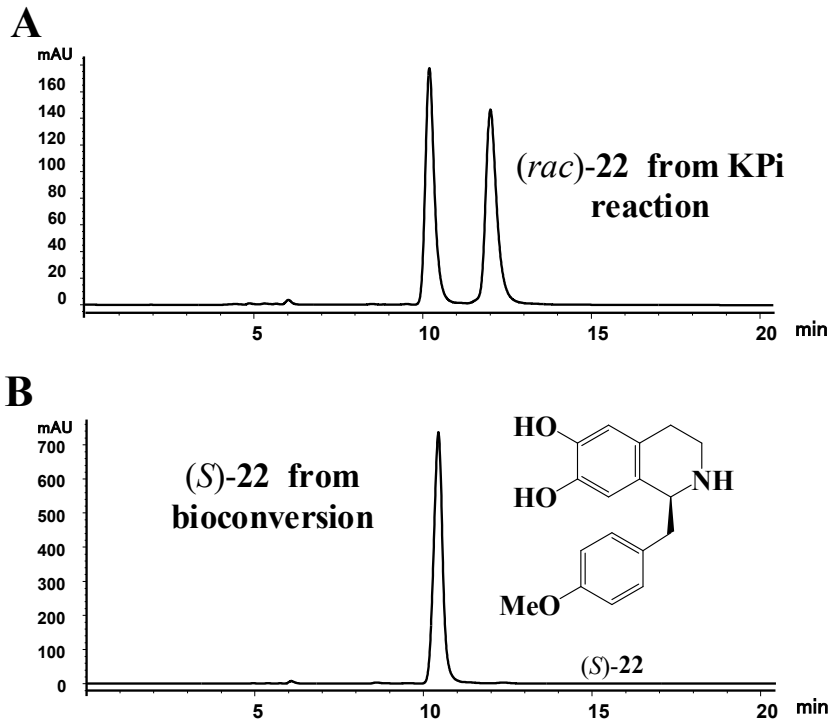

Fig. S30 Chiral HPLC analysis of the synthesis of (*rac*)-**22** and (*S*)-**22**.

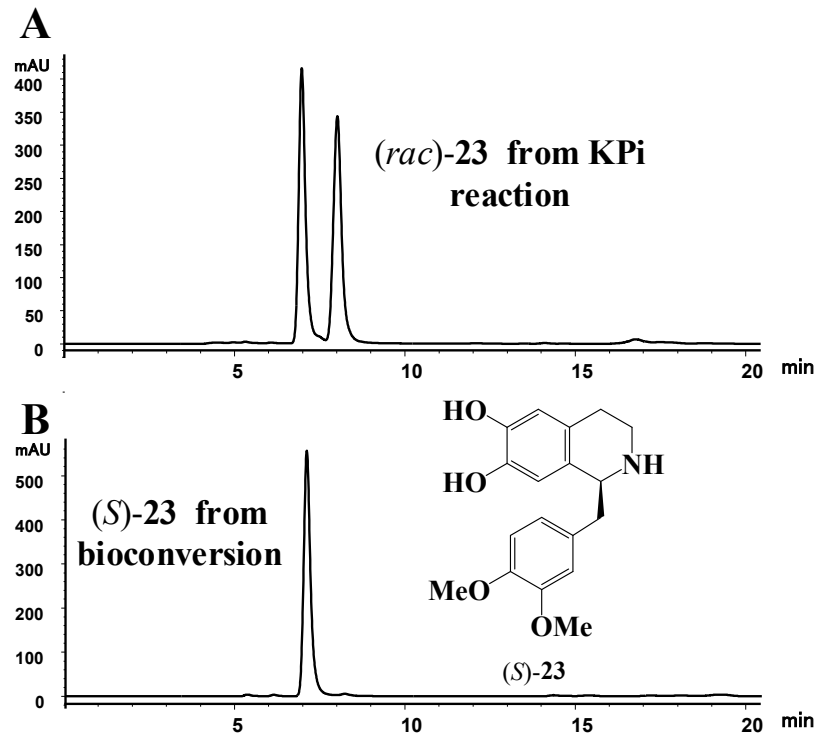

Fig. S31 Chiral HPLC analysis of the synthesis of (*rac*)-**23** and (*S*)-**23**.

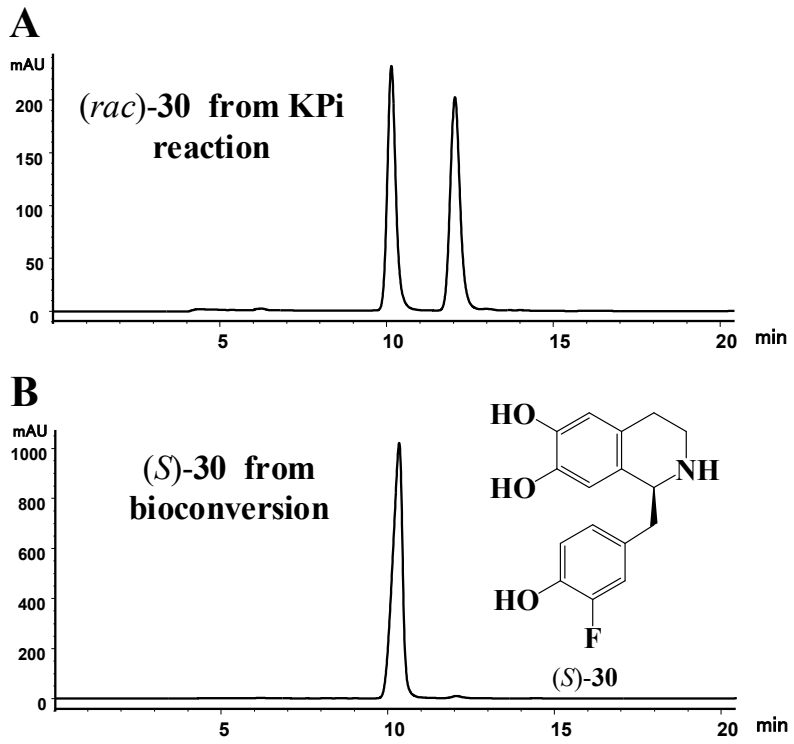

Fig. S32 Chiral HPLC analysis of the synthesis of (*rac*)-**30** and (*S*)-**30**.

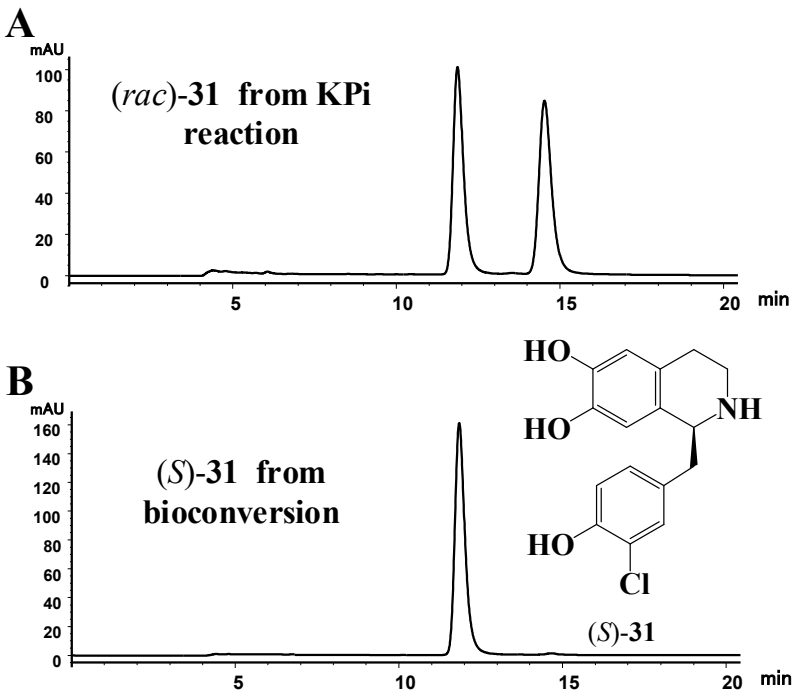

Fig. S33 Chiral HPLC analysis of the synthesis of (*rac*)-**31** and (*S*)-**31**.

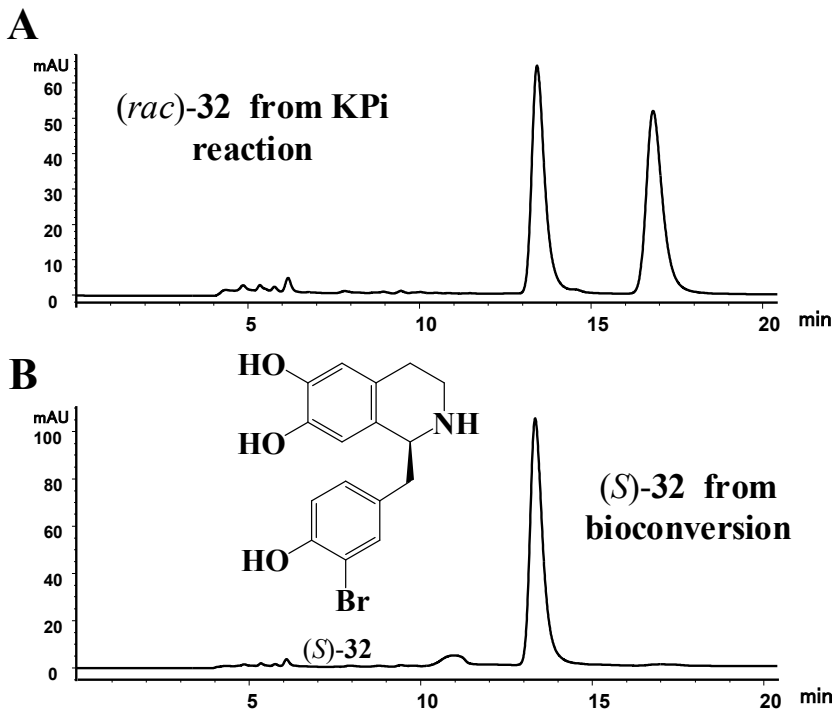

Fig. S34 Chiral HPLC analysis of the synthesis of (*rac*)-**32** and (*S*)-**32**.

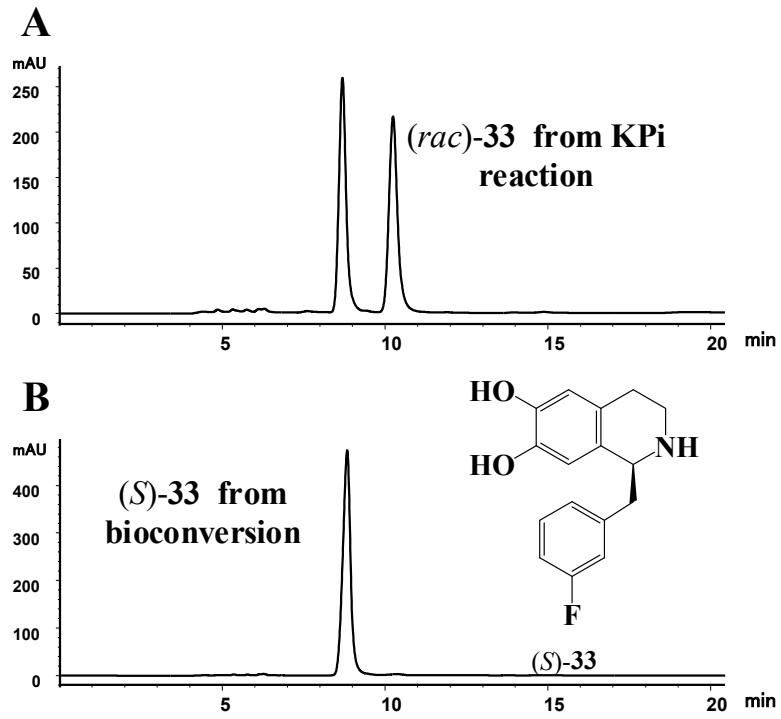

Fig. S35 Chiral HPLC analysis of the synthesis of (*rac*)-**33** and (*S*)-**33**.

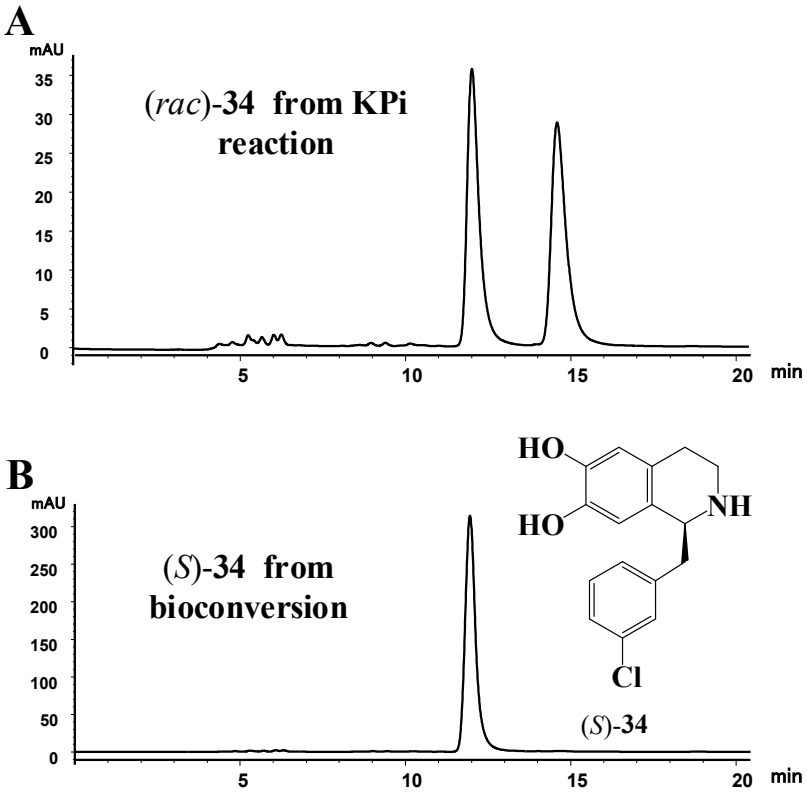

Fig. S36 Chiral HPLC analysis of the synthesis of (*rac*)-**34** and (*S*)-**34**.

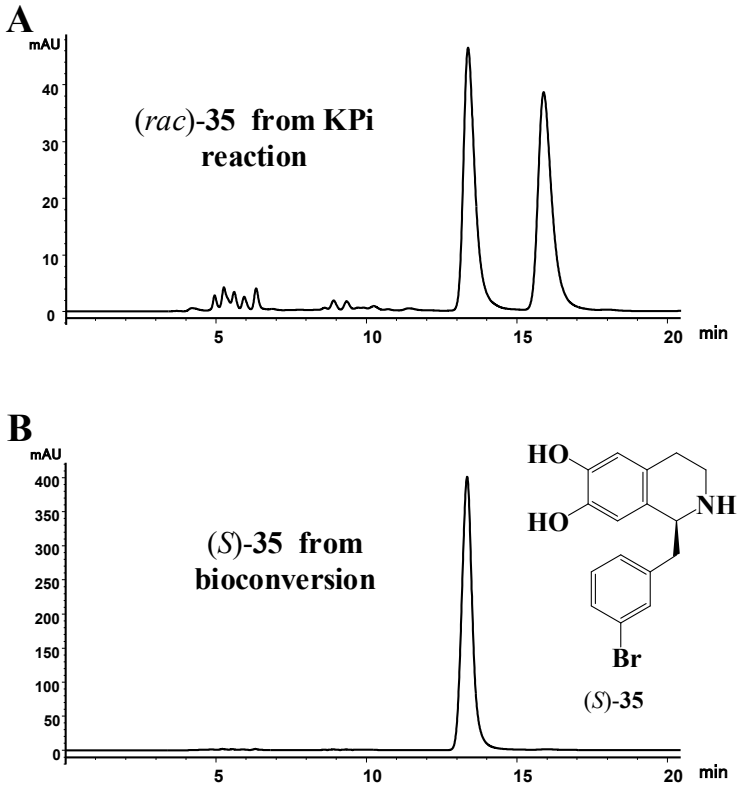

Fig. S37 Chiral HPLC analysis of the synthesis of (*rac*)-**35** and (*S*)-**35**.

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