Asymmetric amination of tetralone and chromanone derivatives employing ω-transaminases

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Supporting Information

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S1. ω-Transaminases employed

Lyophilised *E. coli* cells containing overexpressed ω-transaminases were prepared as previously reported but with elongated induction time of the enzyme.[1]

Table S1. List of ω-transaminases (ω-TAs) employed.

Abbreviation	Original organism/Description	Internal Plasmid number	Selectivity
BM	*Bacillus megaterium* HisTag	pEG31	(*S*)
ArS	*Arthrobacter citreus* HisTag	pEG29	(*S*)
Cv	*Chromobacterium violaceum*	pEG20	(*S*)
Vf	*Vibrio fluvialis* HisTag	pEG27	(*S*)
PF	*Pseudomonas fluorescens*	pEG148	(*S*)
PD	*Paracoccus denitrificans* StrepTag	pEG24	(*S*)
ArR	*Arthrobacter sp.* (*R*)-selective	pEG23	(*R*)
ArRmut11	*Arthrobacter* (*R*) round 11 variant HisTag	pEG90	(*R*)
AT	*Aspergillus terreus* HisTag	pEG97	(*R*)
HN	*Hyphomonas neptunium* HisTag	pEG98	(*R*)

The activity of the cells was assayed employing the prochiral ketone 4-phenyl-2-butanone as model substrate. The obtained conversions were compared with available previous data collected by other operators following the same reaction conditions.

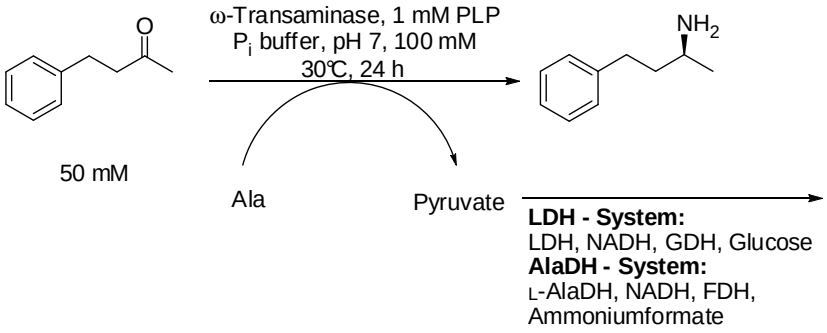


Table S2. Formal reductive amination for testing the activity of the employed ω-transaminases.

Enzyme	Product	c [%] [a]	c [%] [b]
Bacillus megaterium HisTag	(*S*)	92 [c]	76 [c]
Alcaligenes denitrificans HisTag	(*S*)	12 [c]	13 [c]
Arthrobacter citreus HisTag	(*S*)	48 [c]	58 [c]
Chromobacterium violaceum	(*S*)	>99 [c]	n.d. [f]
Vibrio fluvialis HisTag	(*S*)	97 [c]	99 [c]
Arthrobacter sp. (*R*)-selective	(*R*)	49 [d]	50 [d]
Arthrobacter(*R*) round 11 variant HisTag	(*R*)	66 [e]	67 [e]
Paracoccus denitrificans StrepTag	(*S*)	95 [c]	95 [c]
Aspergillus terreus HisTag	(*R*)	62 [d]	n.d. [f]
Hyphomonas neptunium HisTag	(*R*)	87 [d]	n.d. [f]

[a] Obtained conversion data for the activity tests of the employed ω-transaminases.
[b] Conversion data for the activity tests of the employed ω-transaminases obtained by other operators.
[c] LDH-system, reaction conditions: substrate (50 mM), L-alanine (250 mM), phosphate buffer (pH 7, 100 mM), PLP (1 mM), freeze dried *E. coli* cells containing overexpressed enzymes (20 mg), LDH (90 U), GDH (30 U), NAD^+ (1 mM), glucose (150 mM).
[d] LDH-system, reaction conditions: substrate (50 mM), D-alanine (250 mM), phosphate buffer (pH 7, 100 mM), PLP (1 mM), freeze dried *E. coli* cells containing overexpressed enzymes (20 mg), LDH (90 U), GDH (30 U), NAD^+ (1 mM), glucose (150 mM).
[e] 2-Propylamine-system, reaction conditions: substrate (50 mM), 2-propylamine (1 M), aqueous buffer (distilled water, pH 11 adjusted with 3 N HCl), DMSO (20%, v/v), PLP (0.5 mM), freeze dried *E. coli* cells containing overexpressed enzymes (20 mg).
[f] Not determined.

S2. Amination of ketones 1a-f employing (*S*) and (*R*)-selective ω-transaminases

The ω-transaminases were employed for the amination of ketones **1a-f**. The coproduct pyruvate was removed using either lactate dehydrogenase (LDH, system 1) or alanine dehydrogenase (AlaDH, system 2). L- or D- alanine were employed for the amination using (*S*)- or (*R*)- selective ω-TAs, respectively. The amination using the variant from *Arthrobacter sp.* (ArRmut11-ωTA) was conducted in aqueous system at pH 11 with DMSO as cosolvent (20% v v^{-1}) and 2-propylamine as amino donor.

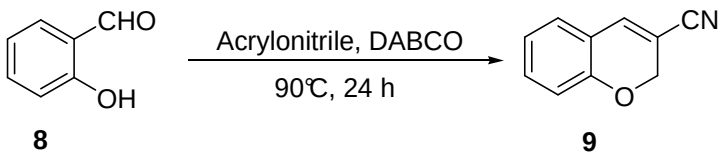
Table S3. Asymmetric amination of 1- and 2- tetralones and derivatives thereof as well as 3- and 4- chromanones employing (*S*)- and (*R*)- selective ω-transaminases.

ω-Transaminase	Substrate	LDH system		AlaDH system		2-propylamine system		LDH system – DMSO 15% v v^{-1}		AlaDH system – DMSO 15% v v^{-1}	
		c (%)	***ee* (%)**	**c (%)**	***ee* (%)**	**c (%)**	***ee* (%)**	**c (%)**	***ee* (%)**	**c (%)**	***ee* (%)**
VF	**1a**	82	54 (*S*)	>99	18 (*S*)						
PD	**1a**	>99	60 (*S*)	>99	48 (*S*)						
BM	**1a**	30	23 (*S*)	>99	24 (*S*)						
ArS	**1a**	>99	99 (*S*)	>99	98 (*S*)						
CV	**1a**	>99	74 (*S*)	>99	48 (*S*)						
PF	**1a**	>99	65 (*S*)	>99	67 (*S*)						
ArR	**1a**	<1	n.d.	14	76 (*R*)			15	34 (*R*)	56	54 (*R*)
AT	**1a**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
HN	**1a**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
ArRmut11	**1a**					>99	54 (*R*)				
VF	**1b**	78	76 (*S*)	82	76 (*S*)						
PD	**1b**	89	73 (*S*)	84	75 (*S*)						
BM	**1b**	80	>99 (*S*)	88	>99 (*S*)						
ArS	**1b**	68	>99 (*S*)	90	>99 (*S*)						
CV	**1b**	67	59 (*S*)	73	55 (*S*)						
PF	**1b**	>99	61 (*S*)	>99	57 (*S*)						
ArR	**1b**	<1	n.d.	23	70 (*R*)			18	>99 (*R*)	53	>99 (*R*)
AT	**1b**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
HN	**1b**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
ArRmut11	**1b**					>99	>99 (*R*)				
VF	**1c**	>99	>99 (*S*)	>99	>99 (*S*)						
PD	**1c**	>99	>99 (*S*)	>99	>99 (*S*)						
BM	**1c**	89	>99 (*S*)	97	>99 (*S*)						
ArS	**1c**	88	>99 (*S*)	61	90 (*S*)						
CV	**1c**	>99	>99 (*S*)	>99	>99 (*S*)						
PF	**1c**	91	>99 (*S*)	99	>99 (*S*)						

ArR	**1c**	<1	n.d.	<1	n.d.			17	>99 (*R*)	10	>99 (*R*)
AT	**1c**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
HN	**1c**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
ArRmut11	**1c**					>99	>99 (*R*)				
VF	**1d**	22	98 (*S*)	5	97 (*S*)						
PD	**1d**	8	>99 (*S*)	3	99 (*S*)						
BM	**1d**	<1	n.d.	<1	n.d.						
ArS	**1d**	2	93 (*S*)	3	98 (*S*)						
CV	**1d**	2	>99 (*S*)	2	>99 (*S*)						
PF	**1d**	3	81 (*S*)	3	>99 (*S*)						
ArR	**1d**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
AT	**1d**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
HN	**1d**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
ArRmut11	**1d**					26	>99 (*R*)				
VF	**1e**	56	>99 (*S*)	6	93 (*S*)						
PD	**1e**	45	>99 (*S*)	27	>99 (*S*)						
BM	**1e**	11	>99 (*S*)	11	>99 (*S*)						
ArS	**1e**	7	88 (*S*)	25	88 (*S*)						
CV	**1e**	41	98 (*S*)	26	79 (*S*)						
PF	**1e**	13	85 (*S*)	13	80 (*S*)						
ArR	**1e**	7	>99 (*R*)	6	>99 (*R*)			13	>99 (*R*)	19	>99 (*R*)
AT	**1e**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
HN	**1e**	<1	n.d.	<1	n.d.			<1	n.d.	<1	n.d.
ArRmut11	**1e**					54	>99 (*R*)				
VF	**1f**	>99	40 (*R*)	99	1 (*R*)						
PD	**1f**	>99	50 (*R*)	99	12 (*R*)						
BM	**1f**	>99	81 (*R*)	99	69 (*R*)						
ArS	**1f**	>99	>99 (*R*)	85	99 (*R*)						
CV	**1f**	>99	86 (*R*)	>99	48 (*R*)						
PF	**1f**	>99	93 (*R*)	99	83 (*R*)						
ArR	**1f**	97	31 (*S*)	22	4 (*S*)			74	racemic	85	racemic
AT	**1f**	99	16 (*S*)	97	19 (*S*)			94	56 (*S*)	94	55 (*S*)
HN	**1f**	20	>99 (*R*)	22	>99 (*R*)			47	78 (*R*)	37	75 (*R*)
ArRmut11	**1f**					>99	67 (*R*)				

S3. Chemo-enzymatic synthesis of 3-amino-chromane from *o*-hydroxy-benzaldehyde

1.Step: Synthesis of 2H-Chromene-3-carbonitrile (9):

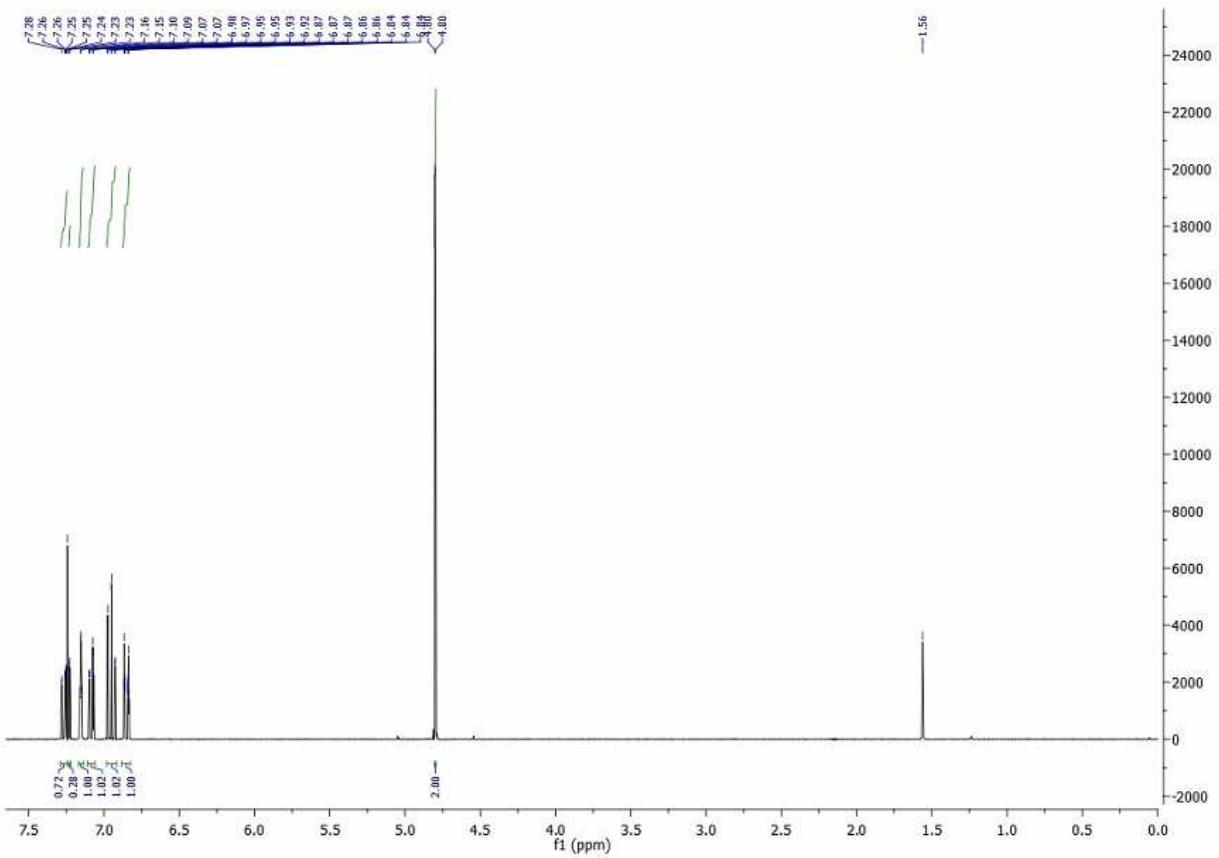


8 **9**

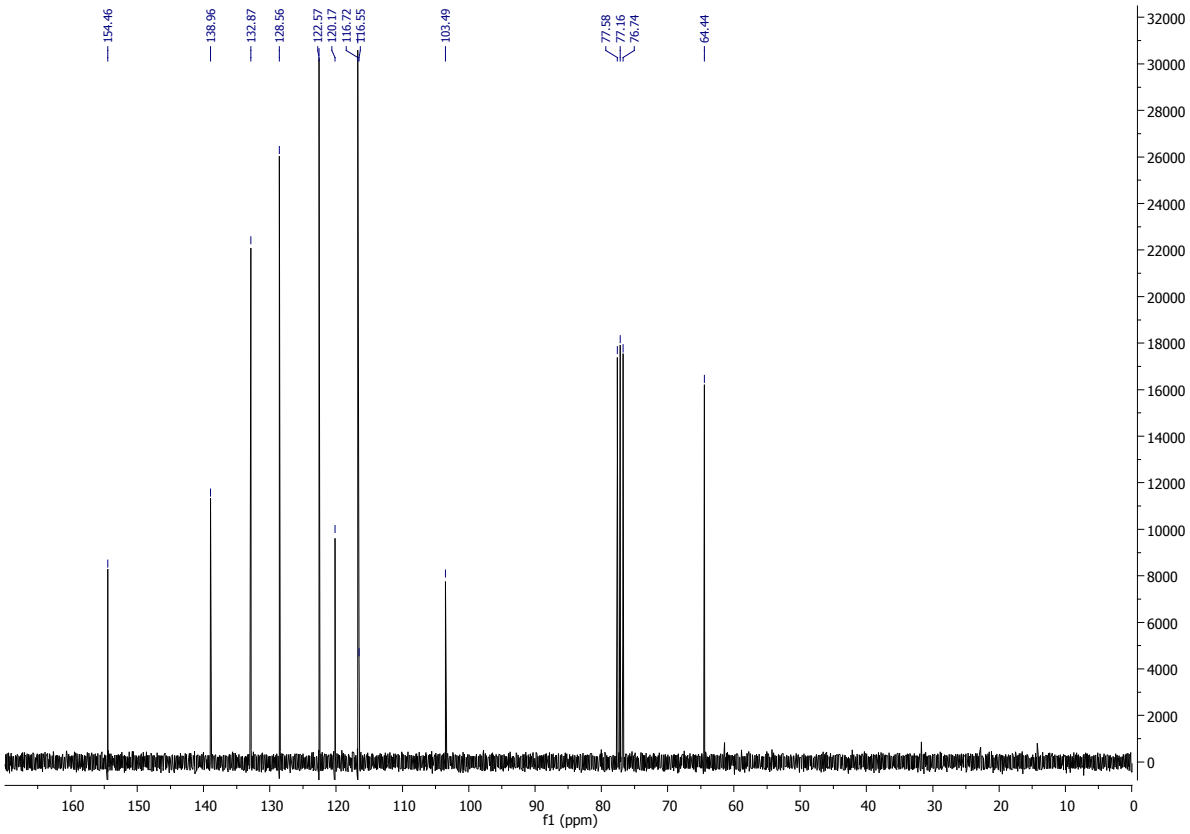
Scheme S.1 Synthesis of 2*H*-Chromene-3-carbonitrile (2).

Salicylaldehyde **8** (20.00 g, 17.45 mL, 164 mmol), acrylonitrile (43.45 g, 819 mmol) and DABCO (4.10 g, 37 mmol) were stirred for 24 h at 90 °C. The course of the reaction was followed by TLC on silica (eluent: petroleum ether/CH_2Cl_2, 7:3 v v^{-1}; R_f (2*H*-chromene-3-carbonitrile) = 0.21; R_f (salicylaldehyde) = 0.40). The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The crude mixture was dissolved in CH_2Cl_2 (300 mL) and washed with a saturated solution of $NaHCO_3$ and brine. The organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The product was purified by column chromatography on silica gel and eluted with a gradient (pure petroleum ether – petroleum ether/CH_2Cl_2 7:3, v v^{-1}). The product **9** was obtained as a white solid (22.0 g, 140 mmol, yield 86%).

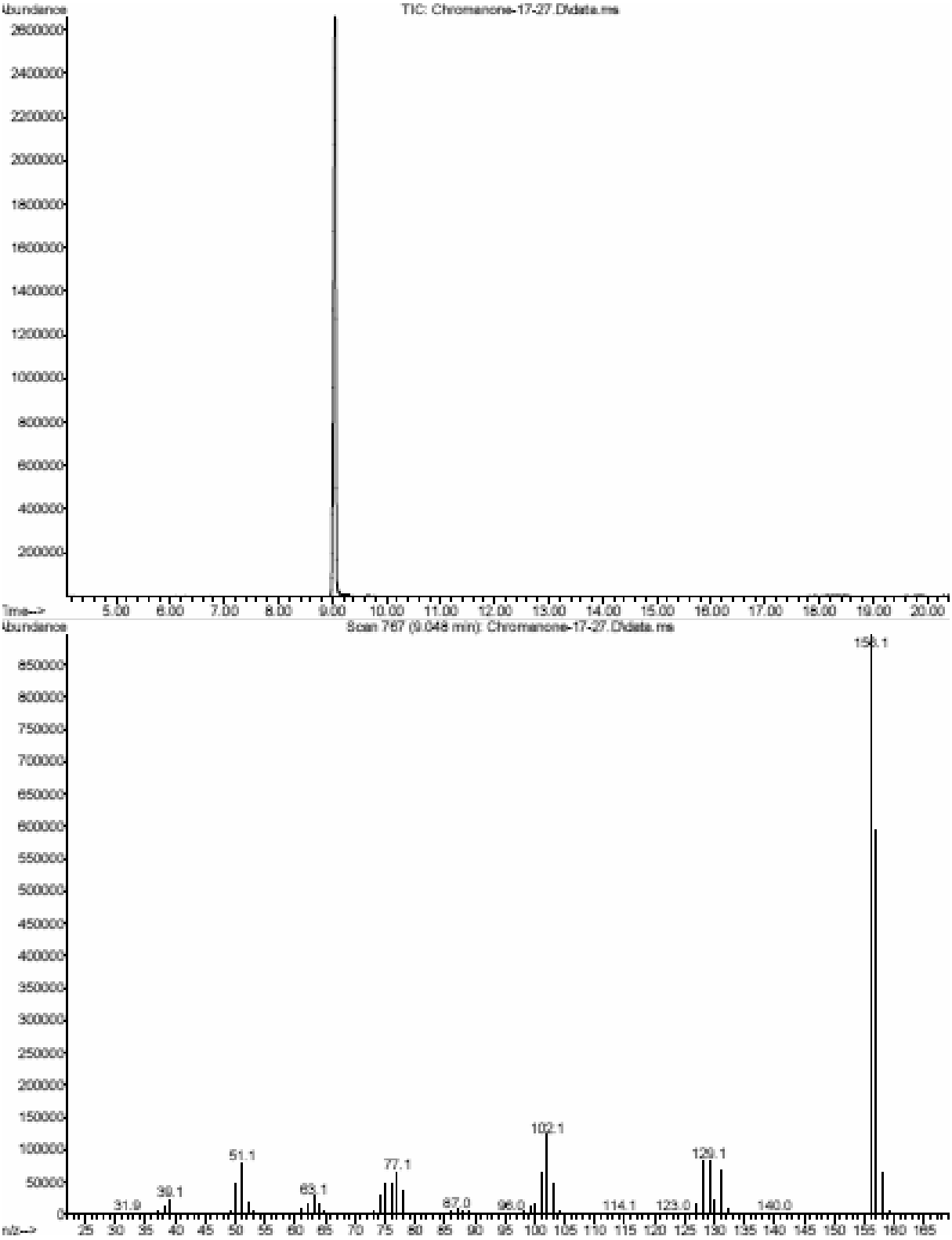
^{1}H-NMR ($CDCl_3$, 300 MHz, δ [ppm]): 4.82 (2H, d, J = 1.5 Hz, CH_2), 6.88 (1H, dd, ^{3}J = 8.4 Hz, ^{4}J = 1.8 Hz, Ph), 6.97 (1H, dt, ^{3}J = 7.5 Hz, ^{4}J = 1.0 Hz, Ph), 7.10 (1H, dd, ^{3}J = 7.5 Hz, ^{4}J = 1.8 Hz, Ph), 7.17 (1H, s, CH), 7.28 (1H, dt, ^{3}J = 7.5 Hz, ^{4}J = 1.8 Hz, Ph).



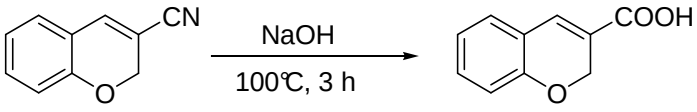
^{13}C-NMR ($CDCl_3$, 300 MHz, δ [ppm]): 64.4, 103.5, 116.5, 116.7, 120.2, 122.6, 128.6, 132.9, 139.0, 154.5. The chemical shifts were in accordance with literature data.[2]



GC-MS: *m/z* (rel. int.): 157 [M^+] (65), 156 (100), 128 (12), 102 (20), 77 (11), 63 (6), 51 (15), 39 (6).



2. Step: Synthesis of 2H-Chromene-3-carboxylic acid (10):

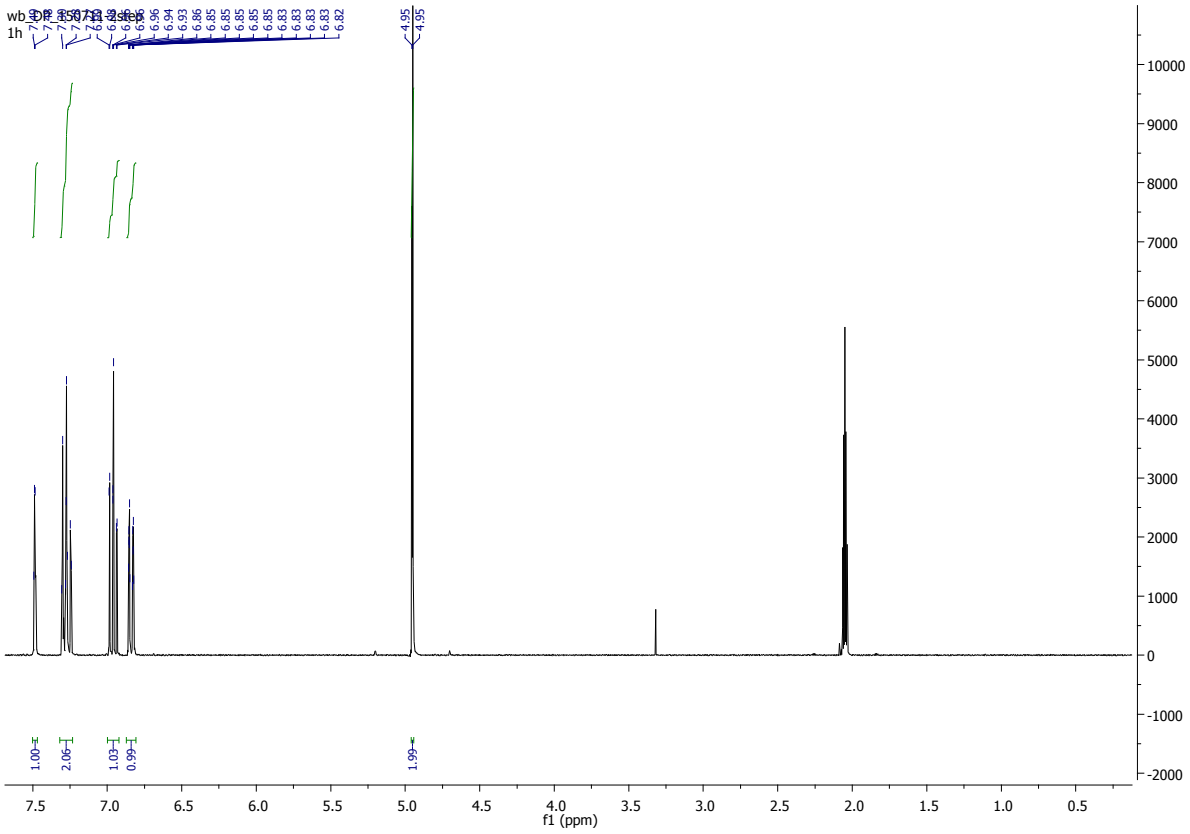


9 **10**

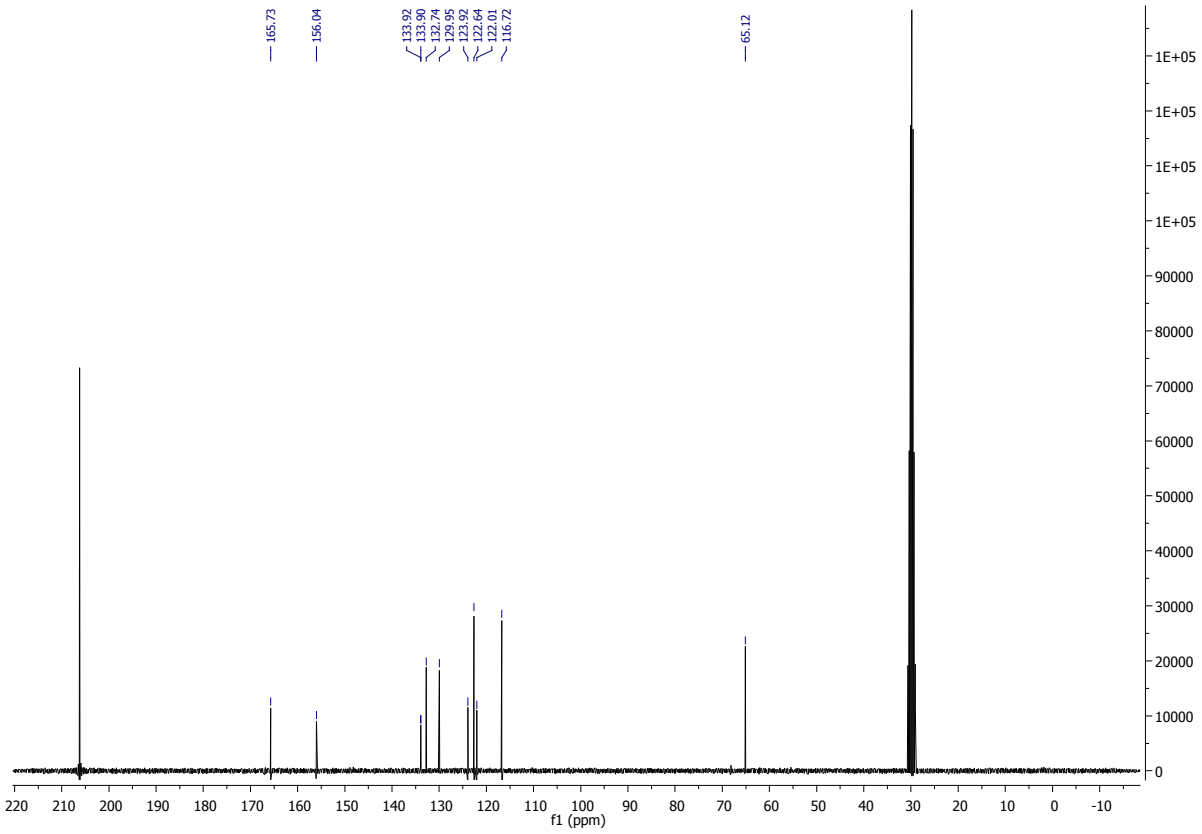
Scheme S.2 Synthesis of 2*H*-Chromene-3-carboxylic acid (3).

An aqueous solution of NaOH (10%, 350 mL) was added to the 2H-chromenecarbonitrile **9** (19.90 g, 127 mmol). The reaction mixture was heated to 100°C for 3 h. The course of the reaction was followed by TLC on silica (eluent: petroleum ether/CH_2Cl_2, 1:1 v v^{-1}; R_f (2*H*-chromene-3-carboxylic acid) = 0.0; R_f (2*H*-chromene-3-carbonitrile) = 0.52). The reaction mixture was cooled to room temperature and an aqueous solution of HCl (3 N) was carefully added dropwise until pH 3 was reached. The product precipitated as a pale yellow solid. The product was filtered, recrystallized in MeOH (200 mL) and dried over night over $CaCl_2$ in an essicator. The product **10** was obtained as a pale yellow solid (20.74 g, 118 mmol, yield 93%).

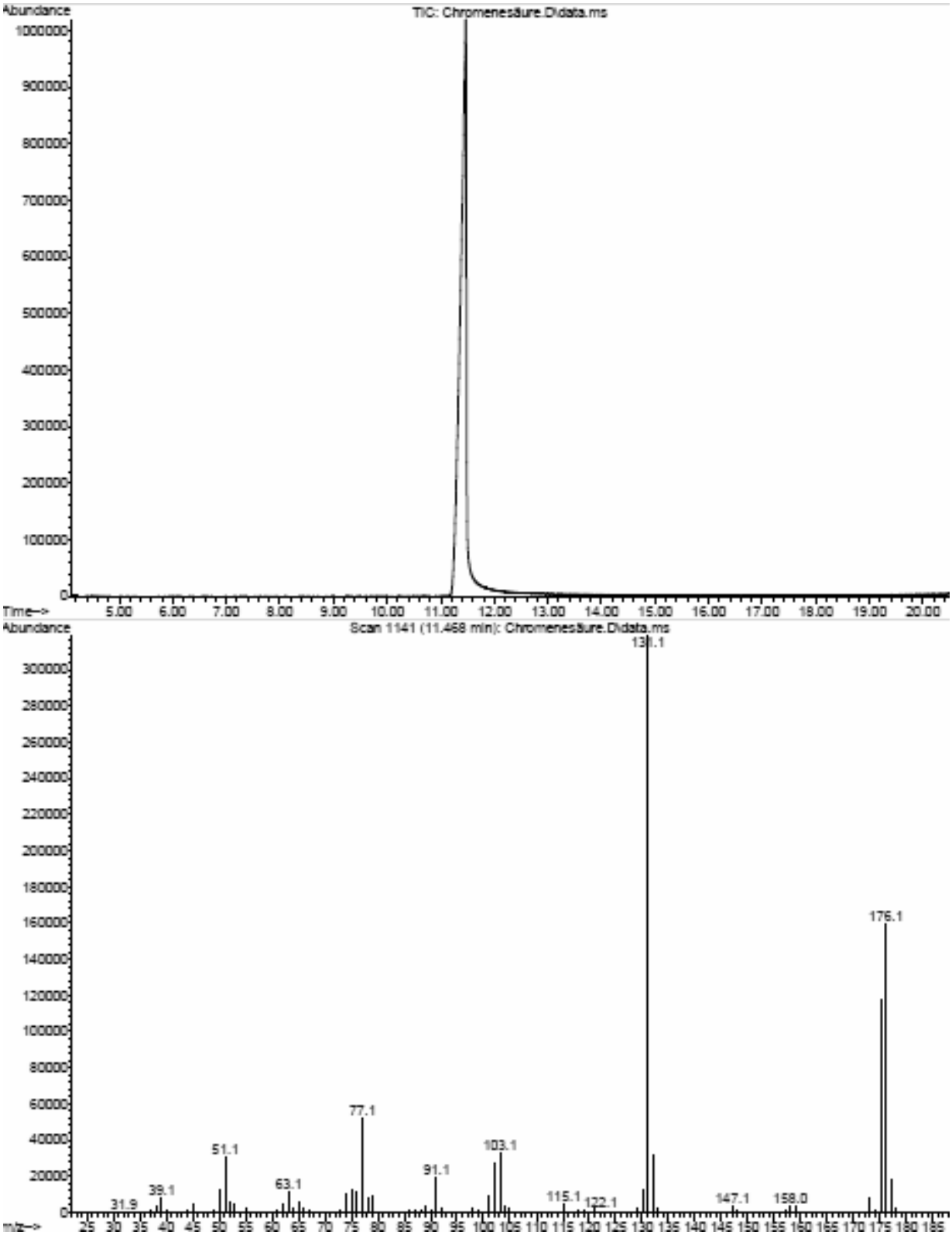
^{1}H-NMR (Acetone-d6, 300 MHz, δ [ppm]): 4.95 (2H, d, J = 1.46 Hz, CH_2), 6.84 (1H, dd, ^{3}J = 7.8 Hz, ^{4}J = 1.0 Hz, Ph), 6.96 (1H, dt, ^{3}J = 7.5 Hz, ^{4}J = 1.8 Hz, Ph), 7.24 – 7.31 (2H, m, Ph), 7.48 - 7.49 (1H, m, CH).



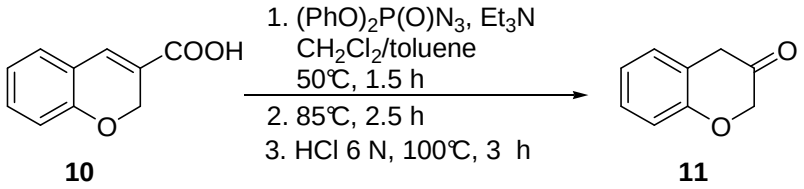
^{13}C-NMR (Acetone-d6, 300 MHz, δ [ppm]): 65.1, 116.7, 122.0, 122.6, 123.9, 129.9, 132.7, 133.9, 156.0, 165.7. The chemical shifts were in accordance with literature data.[2]



GC-MS: *m/z* (rel. int.): 176 [M^+] (46), 131 (100), 103 (11), 91 (6), 77 (18), 63 (4), 51 (11), 39 (3).



3. Step: Synthesis of Chroman-3-one (4):

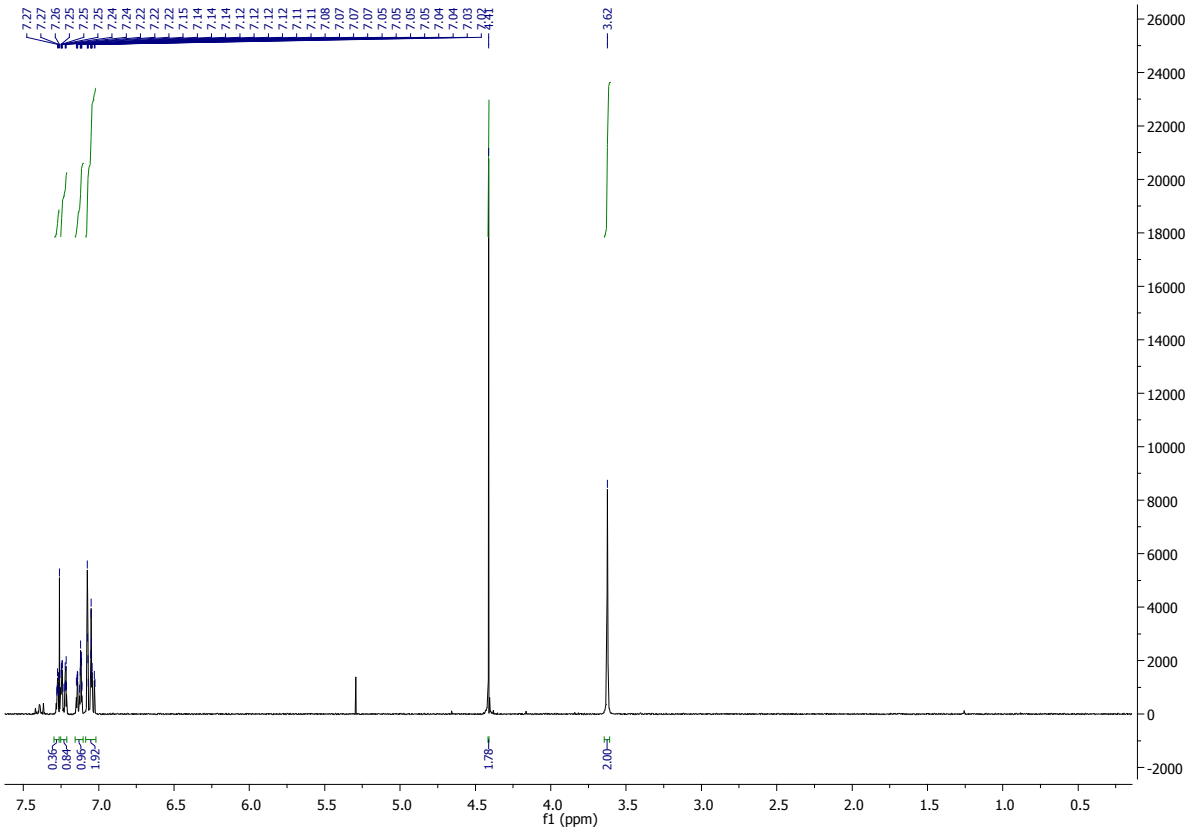


10 **11**

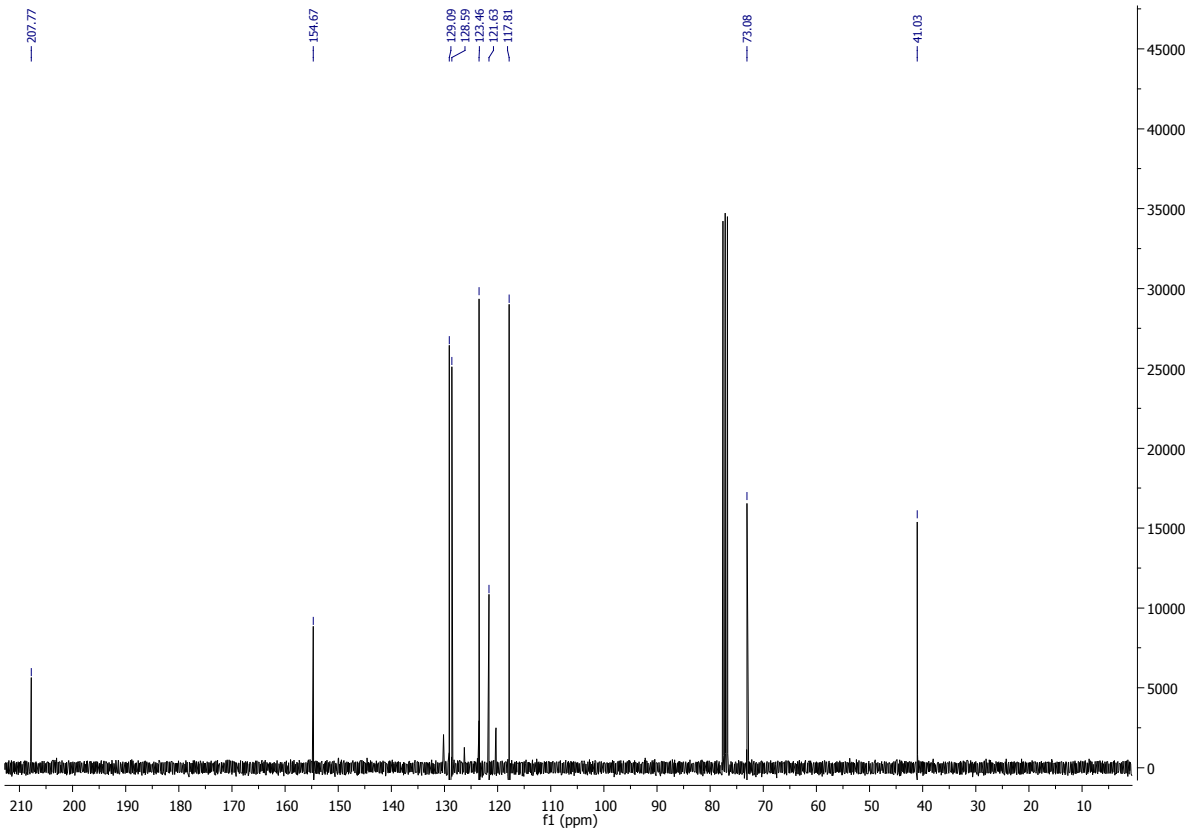
Scheme 4.4 Synthesis of chroman-3one (4).

The reaction was performed under argon atmosphere. 2*H*-Chromenecarboxylic acid **10** (1.00 g, 5.68 mmol) was suspended in CH_2Cl_2 (13 mL). After addition of Et_3N (1 mL), a homogeneous solution was obtained. Then, a solution of $(PhO)_2P(O)N_3$ (1.72 g, 1.35 mL, 6.24 mmol) in toluene (5 mL) was added dropwise to the reaction mixture over a period of 15 minutes. Afterwards, the solution was heated to 50°C for 1.5 h. Another aliquot of toluene (13 mL) was added and the solution was heated subsequently to 85°C for 2.5 h. The quantitative formation of the isocyanate intermediate was followed by TLC on silica (eluent: petroleum ether/CH_2Cl_2, 1:4 v v^{-1}; R_f (2*H*-chromene-3-carboxylic acid) = 0.0; R_f $(PhO)_2P(O)N_3$ = 0.61; R_f (isocyanate intermediate) = 0.79) and GC-MS (isocyanate intermediate, *m/z* (rel. int.): 173 [M^+] (95), 172 (100), 144 (5), 131 (86), 116 (16), 103 (4), 89 (14), 77 (7), 63 (8), 51 (10), 39 (5). Finally, the reaction mixture was cooled down and an aqueous solution of HCl (6 N, 50 mL) was added. The biphasic system was heated under reflux for 16 h. The course of the reaction was controlled by TLC on silica gel (eluent: petroleum ether/CH_2Cl_2, 1:4 v v^{-1}; R_f (isocyanate intermediate) = 0.79; R_f (chroman-3-one) = 0.71). Then, the layers were separated; the organic phase was washed with a saturated solution of $NaHCO_3$ and brine, dried with Na_2SO_4 and concentrated under reduced pressure. The product was purified by column purification on silica gel and eluting with a gradient (pure petroleum ether – EtOAc/petroleum ether, 1:4 v v^{-1}). The product **11** was isolated as yellow oil (739 mg, 4.99 mmol, yield 88%).

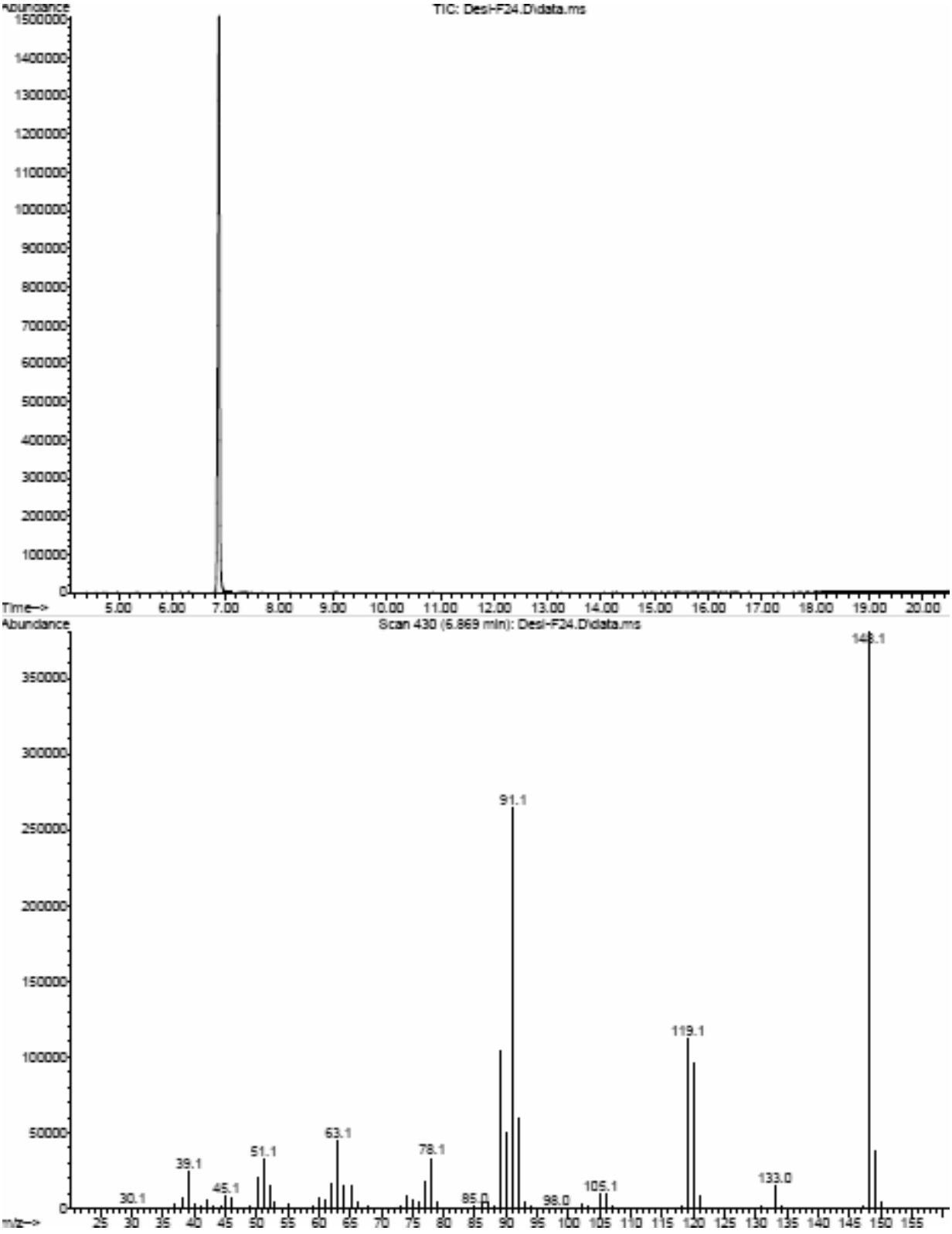
^{1}H-NMR ($CDCl_3$, 300 MHz, δ [ppm]): 3.62 (2H, s, CH_2), 4.41 (2H, s, CH_2), 7.02 – 7.08 (2H, m, Ph), 7.11 – 7.15 (1H, m, Ph), 7.21 – 7-28 (1H, m, Ph).



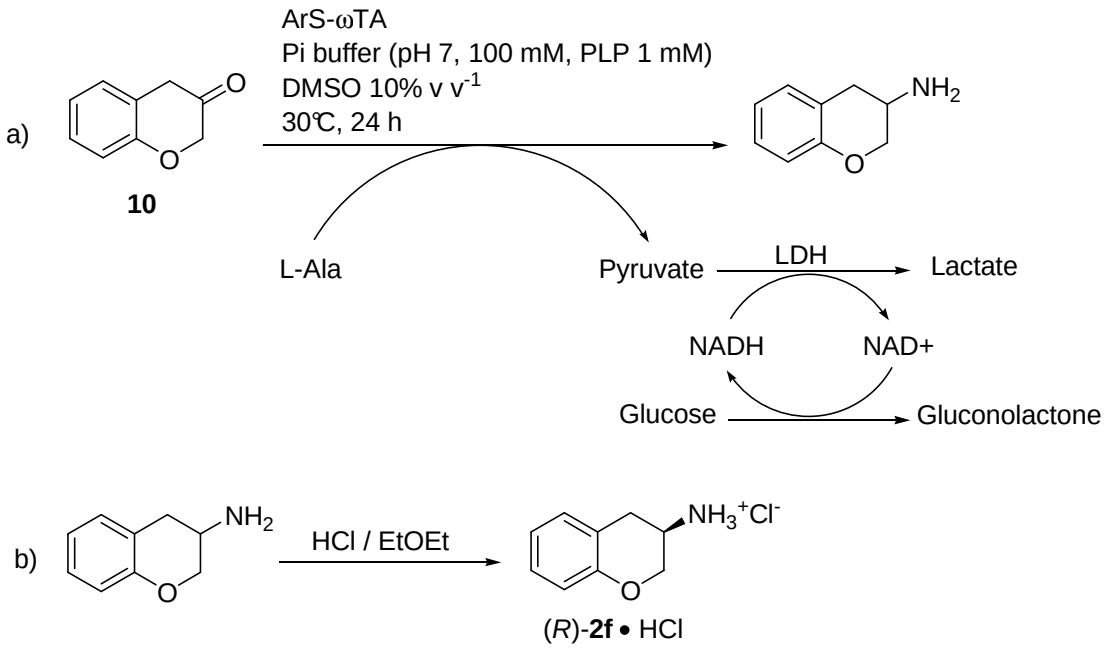
^{13}C-NMR ($CDCl_3$, 300 MHz, δ [ppm]): 41.3, 73.1, 117.8, 121.6, 123.5, 128.6, 129.1, 154.7, 207.8. The chemical shifts were in accordance with literature data.[2]



GC-MS *m/z* (rel. int.): 148 [M^+] (100), 133 (4), 119 (35), 91 (97), 78 (15), 63 (22), 51 (17), 39 (13).



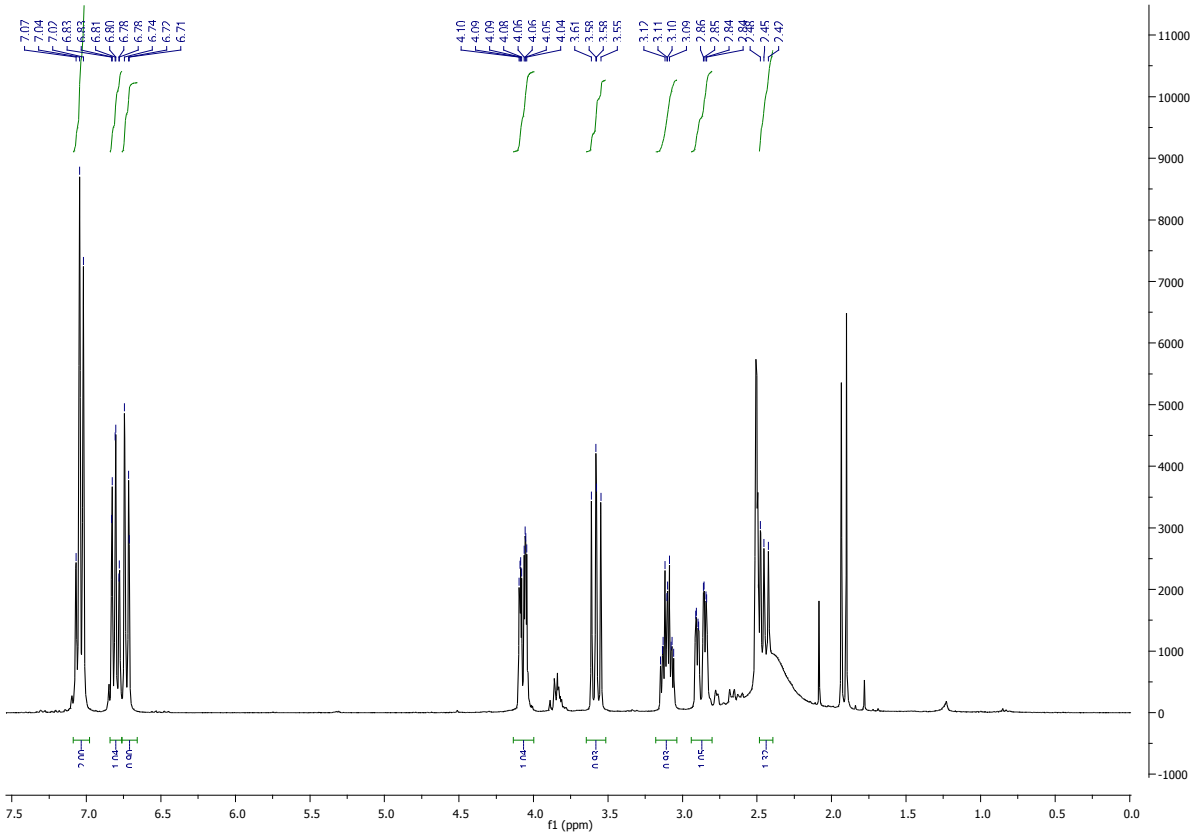
4. Step: Enzymatic synthesis of enantiopure (R)-3-aminochromane employing Arthrobacter citreus (S)-selective ω-transaminase:



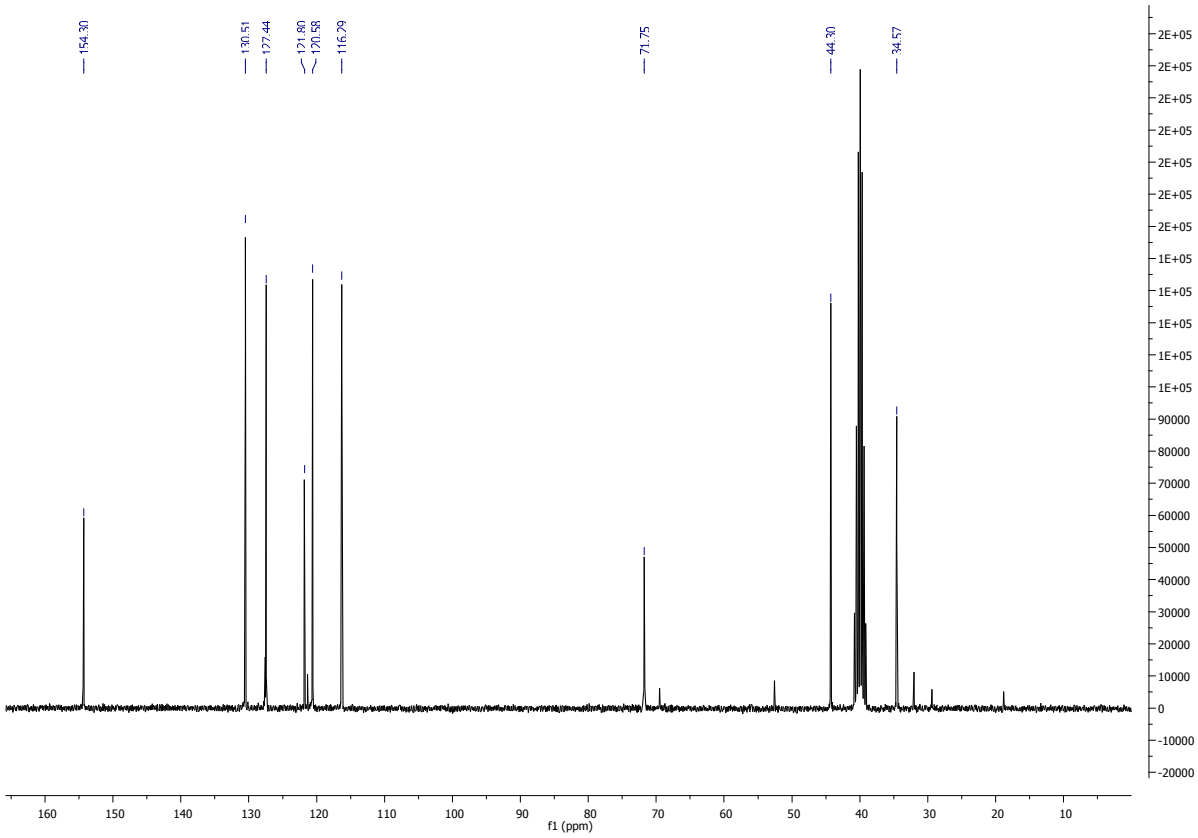
Lyophilised cells of *E. coli* containing the overexpressed ArS-ωTA (1.00 g) were disrupted in a lysis buffer [16 mL of lysis buffer per gram of lyophilised cells, phosphate buffer pH 7, 100 mM, 1 mM EDTA, 1 mM PLP, lysozyme from chicken egg white (1.06 mg mL^{-1} >40000 U mg^{-1}) and 1 mM phenylmethanesulfonyl fluoride]. The preparation was shaken on an orbital shaker at 150 rpm, 22 °C, for 3 h. The suspension was centrifuged (18000 rpm, 15 min, 4 °C) and the supernatant was lyophilised yielding a crude powder extract. In a round-bottom flask, an aliquot of the crude powder extract of ArS-ωTA (270 mg, 1.26 U $mg^{-1}_{\text{crude preparation}}$) was dissolved in phosphate buffer (13.5 mL, pH 7, 100 mM, PLP 1 mM). L-alanine (301 mg, 3.375 mmol), lactate dehydrogenase (90 U mL^{-1}), glucose dehydrogenase (30 U mL^{-1}) and NADH (1 mM) were added. Finally, the ketone substrate **10** (100 mg, 0.675 mmol) was dissolved in DMSO (135 μL) and added to the aqueous solution. The flask was shaken on an orbital shaker at 150 rpm, for 24 h and at 30 °C. A small aliquot (500 μL) was taken, basified with NaOH 10 N (100 μL), extracted with EtOAc (2 × 300 μL) and dried with Na_2SO_4 anhydrous. Quantitative conversion of 3-chromanone to the amine product was detected by

GC-MS. Thus, the reaction mixture was basified with aqueous NaOH 10 N (2.7 mL), extracted with EtOAc (3 × 5 mL) and dried with Na_2SO_4 anhydrous. The organic phase was evaporated to a small volume (2 mL). After cooling to 4 °C, an ethereal solution of hydrogen chloride (2 N, 1 mL) was added. The solution became cloudy due to formation of (*R*)-**2f**·HCl. The organic solvent was then completely evaporated and the residual oil was dried under vacuum. The crude product was recrystallised in anhydrous Et_2O (2 mL), yielding a yellow solid (98.2 mg, 0.529 mmol, yield 78%). An aliquot of (*R*)-**2f** was derivatised as previously described and the *ee* was determined to be >99% by chiral GC. The absolute configuration was determined to be (*R*) by measuring the $[\alpha]_D$ and comparing the value with literature data. Measured: $[\alpha]_D$ = +46.4 (c 1.00 as hydrochloride salt in methanol; *ee* >99%). Literature: $[\alpha]_D$ = +61.3 (c 0.5, as hydrochloride salt in methanol, *R* enantiomer, *ee* 99.5%).[3]

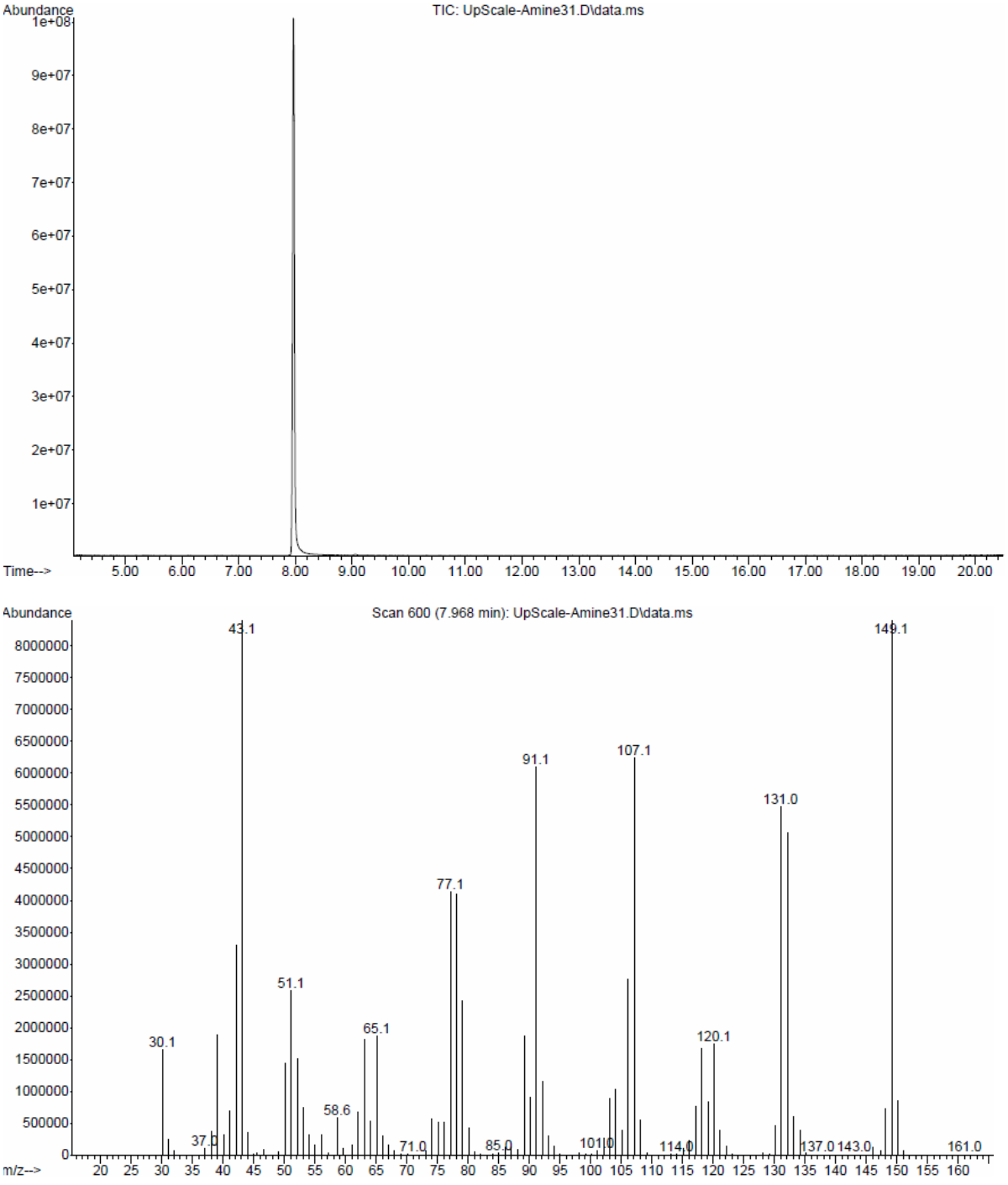
^{1}H-NMR (DMSO-d6, 300 MHz, δ [ppm]): 2.42-2.45 (1H, m) 2.87 (1H, dd, ^{2}J = 16 Hz, ^{3}J = 5.0 Hz), 3.06–3.15 (1H, m), 3.58 (1H, q, ^{2}J = 10 Hz, ^{3}J = 3.4 Hz, ^{4}J = 1.9 Hz), 4.07 (1H, qd, ^{2}J = 10 Hz, ^{3}J = 3.4 Hz, ^{4}J = 1.9 Hz), 6.73 (1H, dd, Ar, ^{3}J = 8.3 Hz, ^{4}J = 1.3 Hz, 6.81 (1H, dt, Ar, ^{3}J = 7.5 Hz, ^{3}J = 7.3 Hz, ^{4}J = 1.3 Hz), 7.02-7.07 (2H, m, Ar).



^{13}C-NMR (DMSO-d6, 300 MHz, δ [ppm]): 34.6, 44.3, 71.8, 116.3, 120.6, 121.8, 127.4, 130.5, 154.3.



GC-MS *m/z* (rel. int.): 149 [M^+] (100), 131 (54), 120 (17), 107 (52), 91 (42), 77 (28), 65 (12), 51 (17), 43 (99), 30 (14).



S4. Analytics

Methods for determination of conversion

Method 1. Column: Agilent J&W DB-1701 (30 m, 250 μm, 0.25 μm); GC program parameters: injector 250°C; constant pressure 1 bar; temperature program 80 °C/hold 6.5 min; 160 °C/rate 10 °C per min/hold 5 min; 200 °C/rate 20 °C per min/hold 2 min.

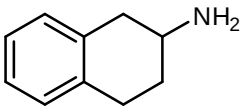
Method 2. Column: Agilent J&W DB-1701 (30 m, 250 μm, 0.25 μm); GC program parameters: injector 250°C; constant pressure 1 bar; temperature program 80 °C/hold 6.5 min; 160 °C/rate 10 °C per min/hold 5 min; 240 °C/rate 20 °C per min/hold 3 min.

Methods for determination of enantiomeric excess

The enantiomeric excess of the amines was analysed by GC on a chiral phase after derivatisation to acetamides. For the procedure see experimental section in the paper.

Method A. Column: Varian Chrompack Chirasil Dex-CB (25 m, 320 μm, 0.25 μm); GC program parameters: injector 200 °C; constant flow 1.7 mL/min; temperature program 100 °C/hold 2 min; 130 °C/rate 2 °C per min/hold 5 min; 180 °C/rate 10 °C per min/hold 9 min.

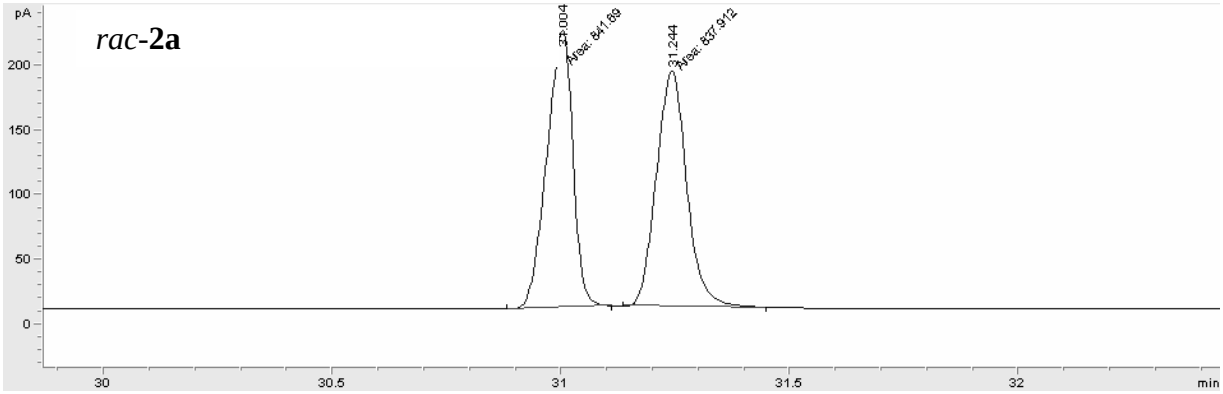
Method B. Column: Varian Chrompack Chirasil Dex-CB (25 m, 320 μm, 0.25 μm); GC program parameters: injector 200°C; constant flow 1.7 mL/min; temperature program 100 °C/hold 2 min; 130 °C/rate 2 °C per min/hold 5 min; 180 °C/rate 10 °C per min/hold 9 min; 200 °C/rate 10 °C per min/hold 10 min

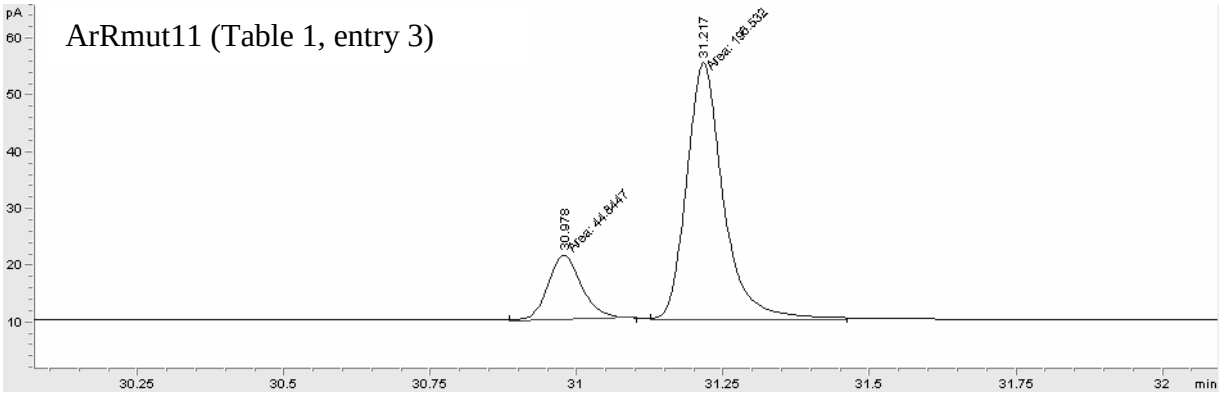


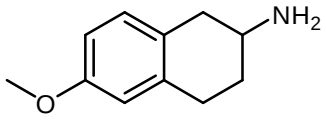
2a

Conversion: method 1, ketone **1a** 19.9 min; amine **2a** 18.8 min.

ee: method A, (*S*)-**2a** 30.9 min; (*R*)-**2a** 31.2 min (derivatised as acetamides). Racemic amine was a gift from BASF. Then, the absolute configuration was assigned by comparison of elution order on chiral phase on GC with data from literature.[4]



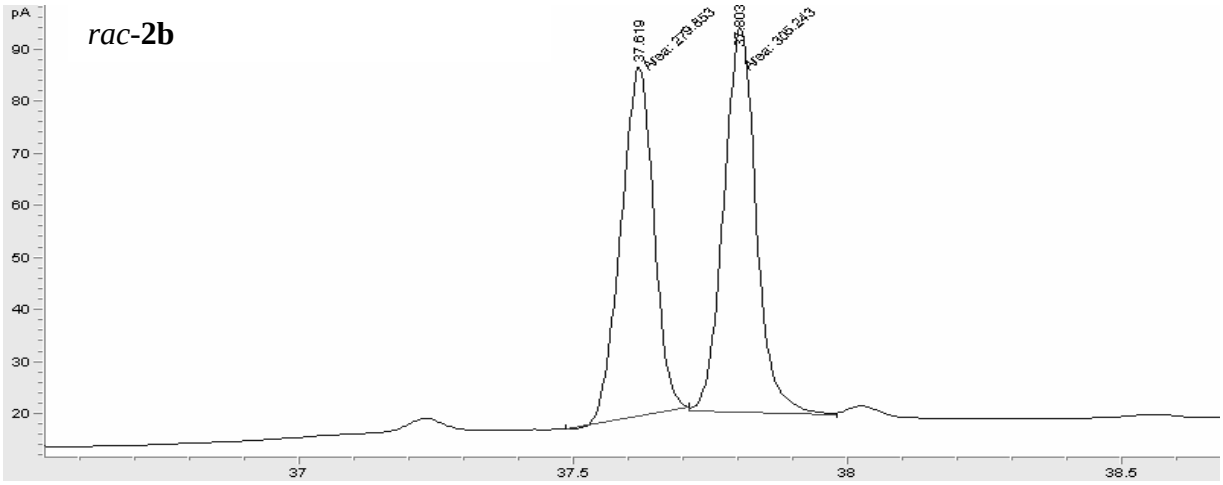


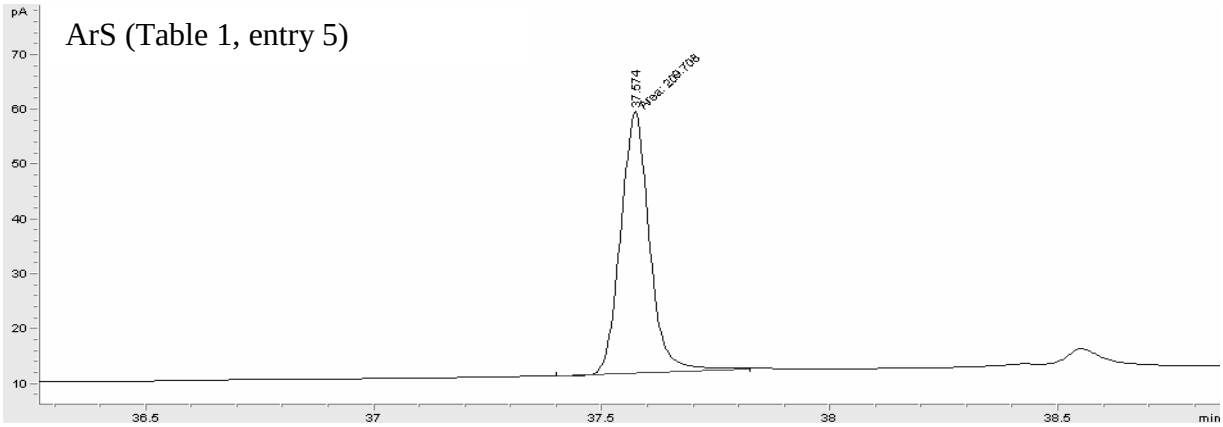


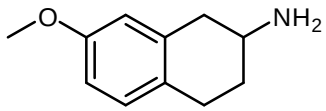
2b

Conversion: method 2, ketone **1b** 24.6 min; amine **2b** 24.0 min.

ee: method B, (*S*)-**2b** 37.6 min; (*R*)-**2b** 37.8 min (derivatised as acetamides). Racemic amine was synthesised according to literature.[1] The absolute configuration was assigned by comparison of elution order on chiral phase on GC with literature.[4]



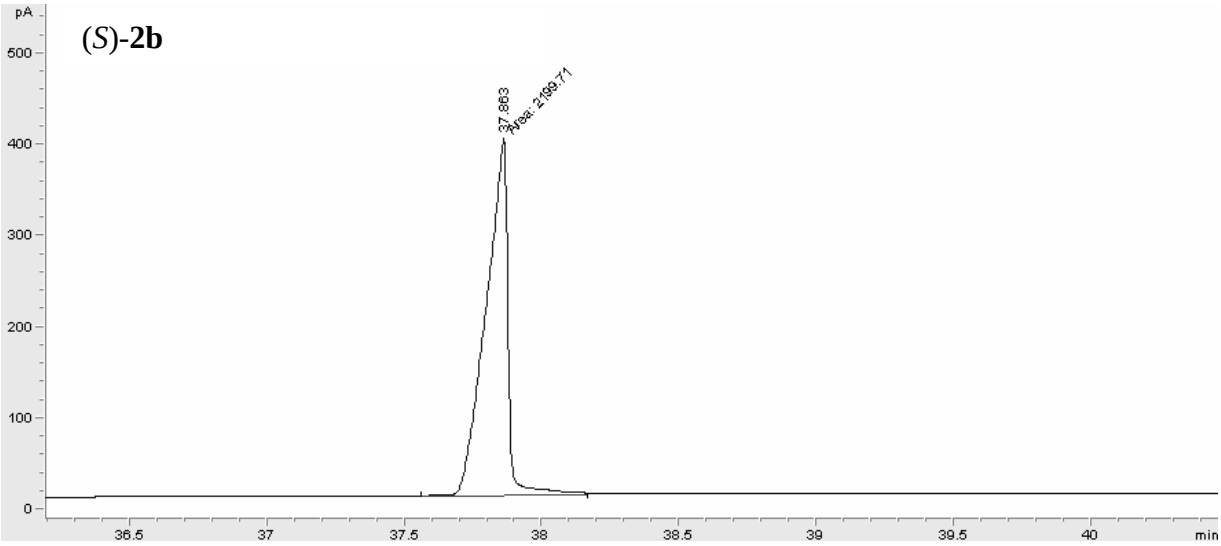


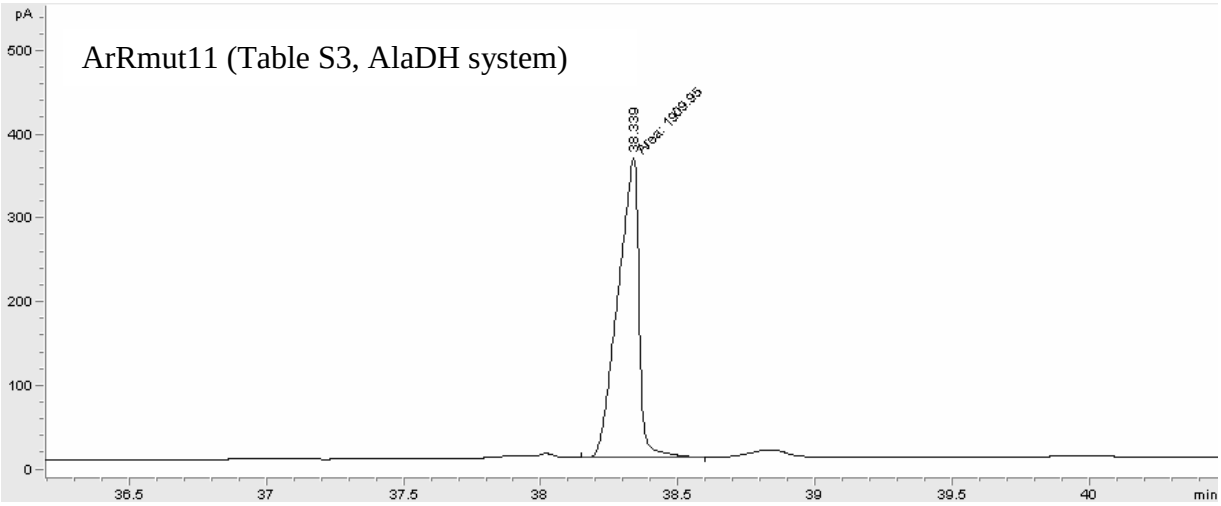


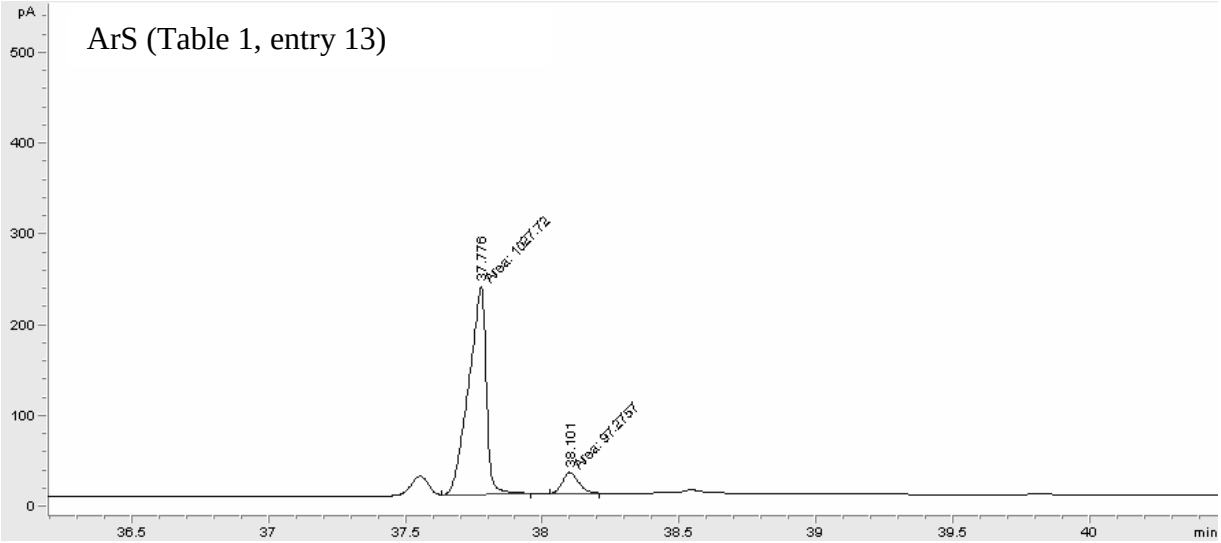
2c

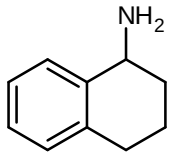
Conversion: method 2, ketone **1c** 24.6 min; amine **2c** 24.1 min.

ee: method B, (*S*)-**2c** 37.8 min; (*R*)-**2c** 38.3 min (derivatised as acetamides). The absolute configuration was assigned by comparison of elution order on GC and coinjection with optically pure amines, which were a gift from BASF.





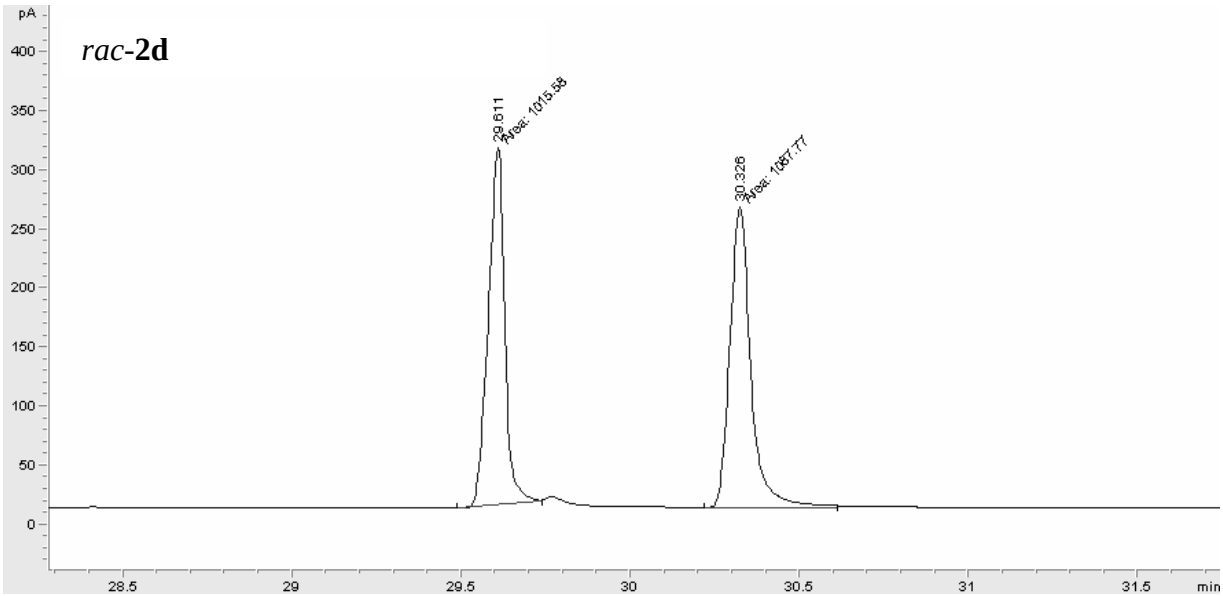

ArS (Table 1, entry 13)
pA
500
400
300
200
100
0
37.776
Area: 1027.72
38.101
Area: 97.2757
36.5
37
37.5
38
38.5
39
39.5
40
min

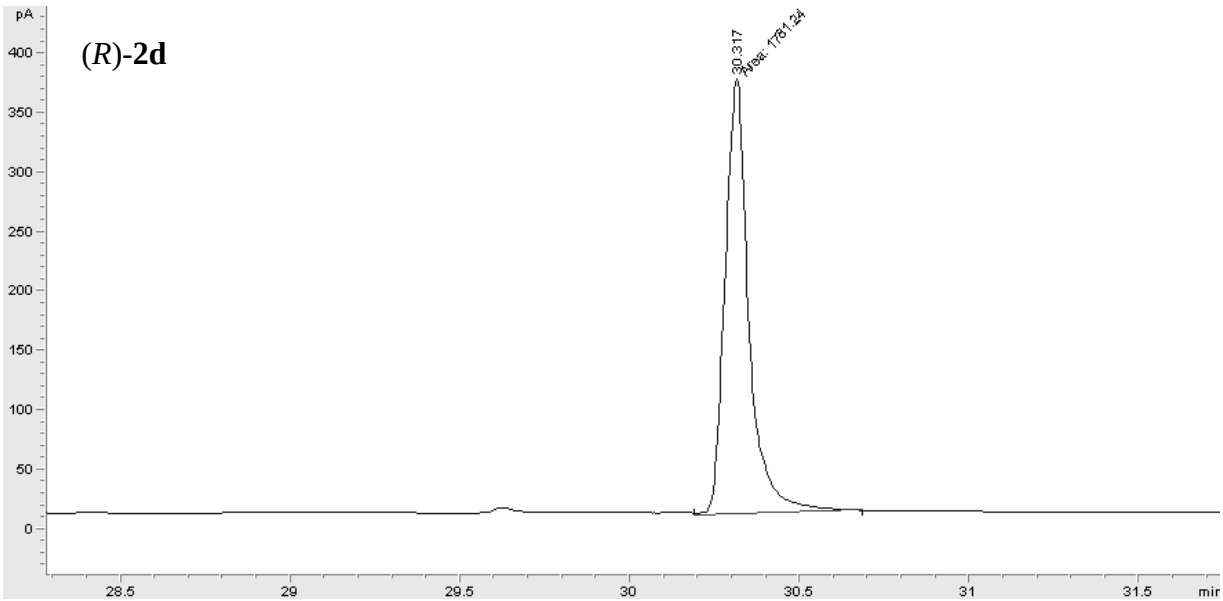


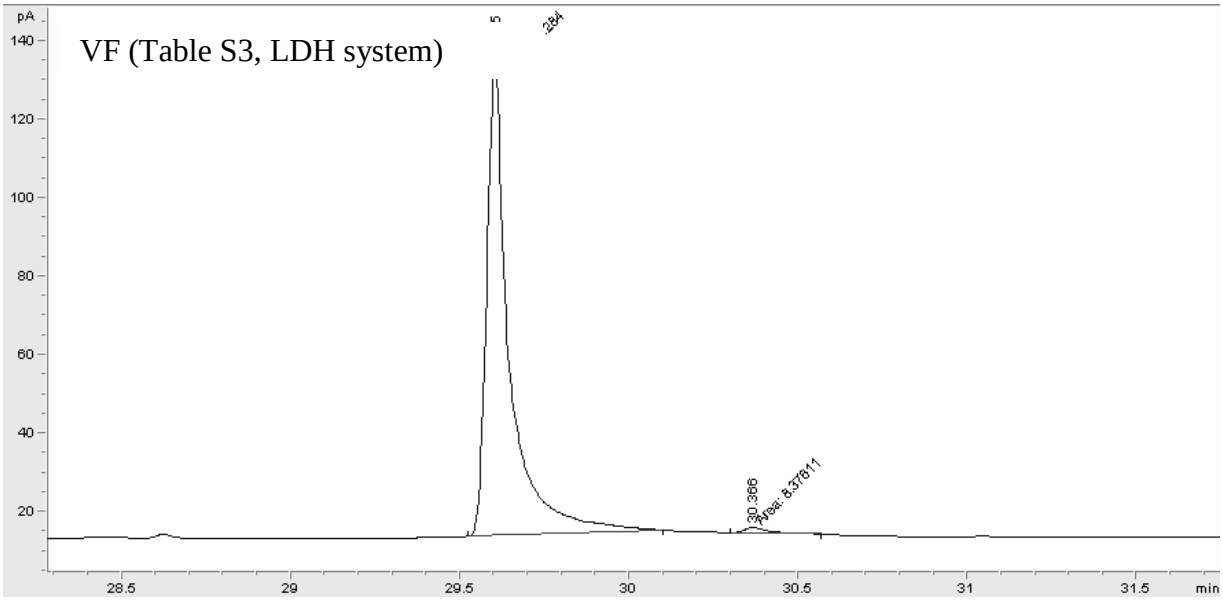
2d

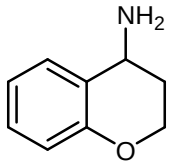
Conversion: method 1, ketone **1d** 20.3 min; amine **2d** 18.3 min.

ee: method A, (*S*)-**2d** 29.6 min; (*R*)-**2d** 30.3 min (derivatised as acetamides). The absolute configuration was assigned by comparison of elution order on GC and coinjection with commercially available racemic and optically pure amines.





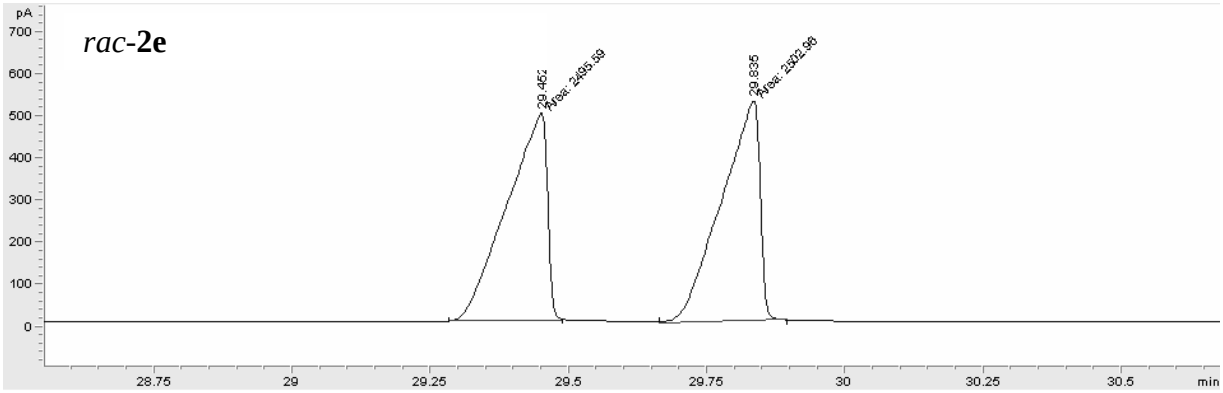

VF (Table S3, LDH system)
pA
140
120
100
80
60
40
20
30.366
Area: 8.37611
28.5
29
29.5
30
30.5
31
31.5
min

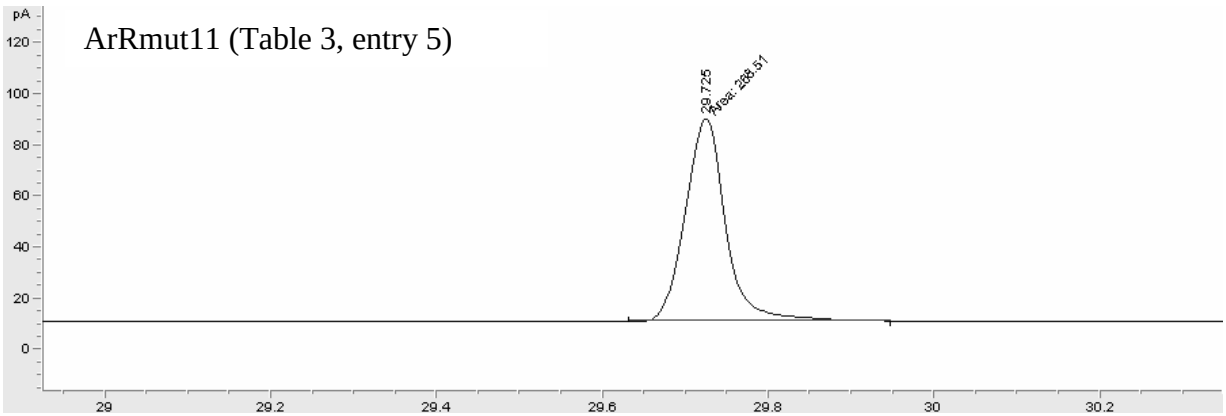


2e

Conversion: method 1, ketone **1e** 19.2 min; amine **2e** 19.5 min.

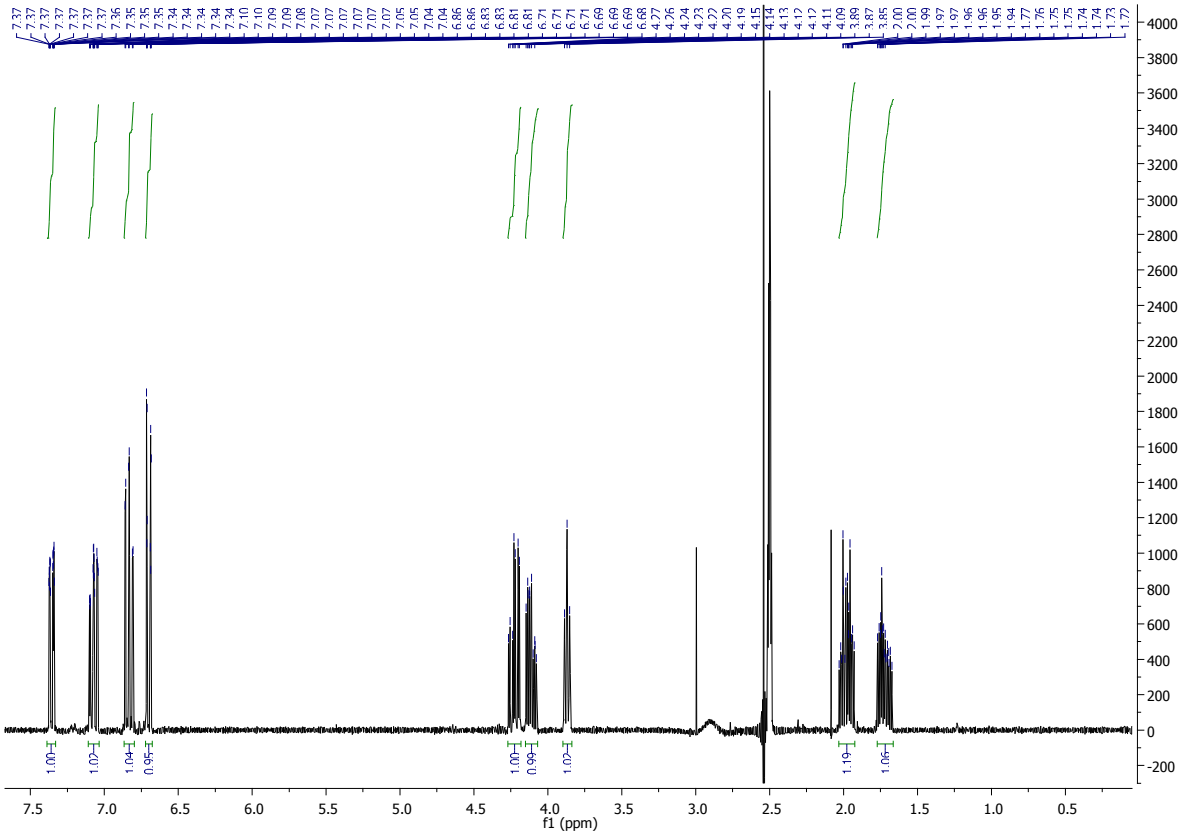
ee: method A, (*S*)-**2e** 29.4 min; (*R*)-**2e** 29.8 min (derivatised as acetamides). Racemic amine was gifted by BASF. The absolute configuration was assigned as follows: the ketone **1e** (70 mg) was aminated employing ArS-ωTA and the amine product was isolated (15.2 mg). The enantiopurity of the amine product was determined by comparison of elution order on GC and coinjection with the available racemic amine. The $[\alpha]_D$ of the amine product was then measured and compared to literature data. Measured: $[\alpha]_D$ = -29.8 (c 0.45, chloroform; ee >99%). Literature: $[\alpha]_D$ = +13.5 (c 1.6, chloroform, *R* enantiomer, *ee* 98%).[5] Thus, the ArS-ωTA produced (*S*)-**2e**.



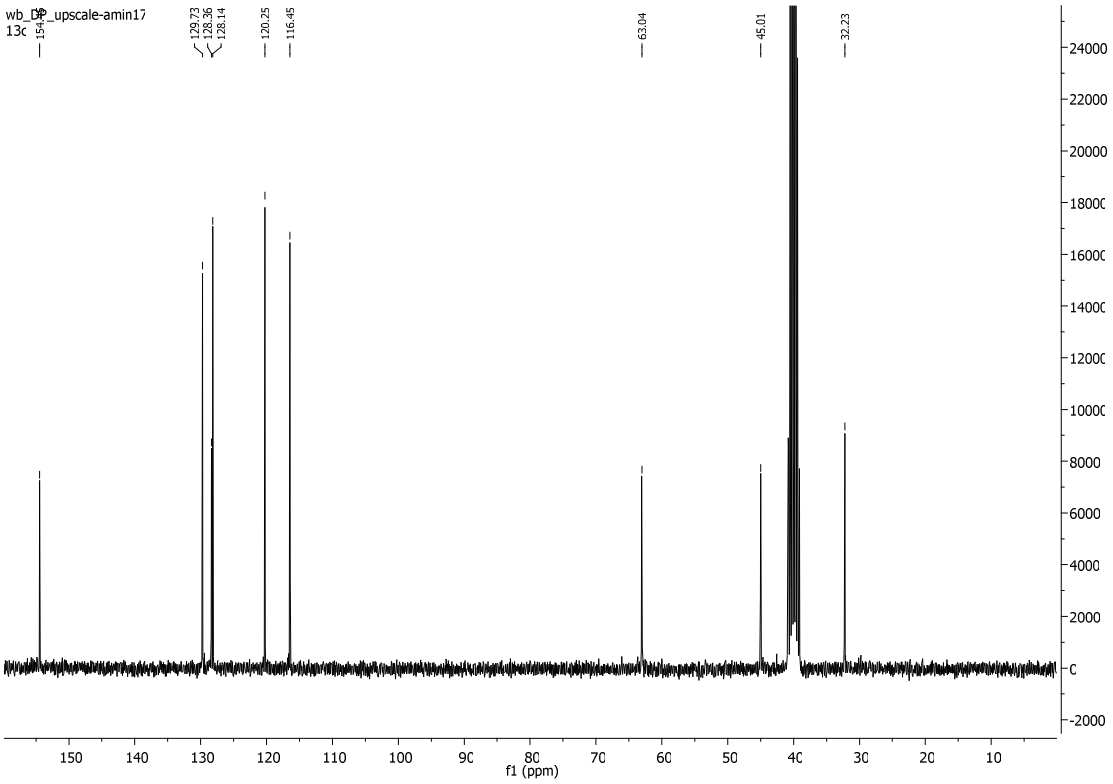


(*S*)-**2e**

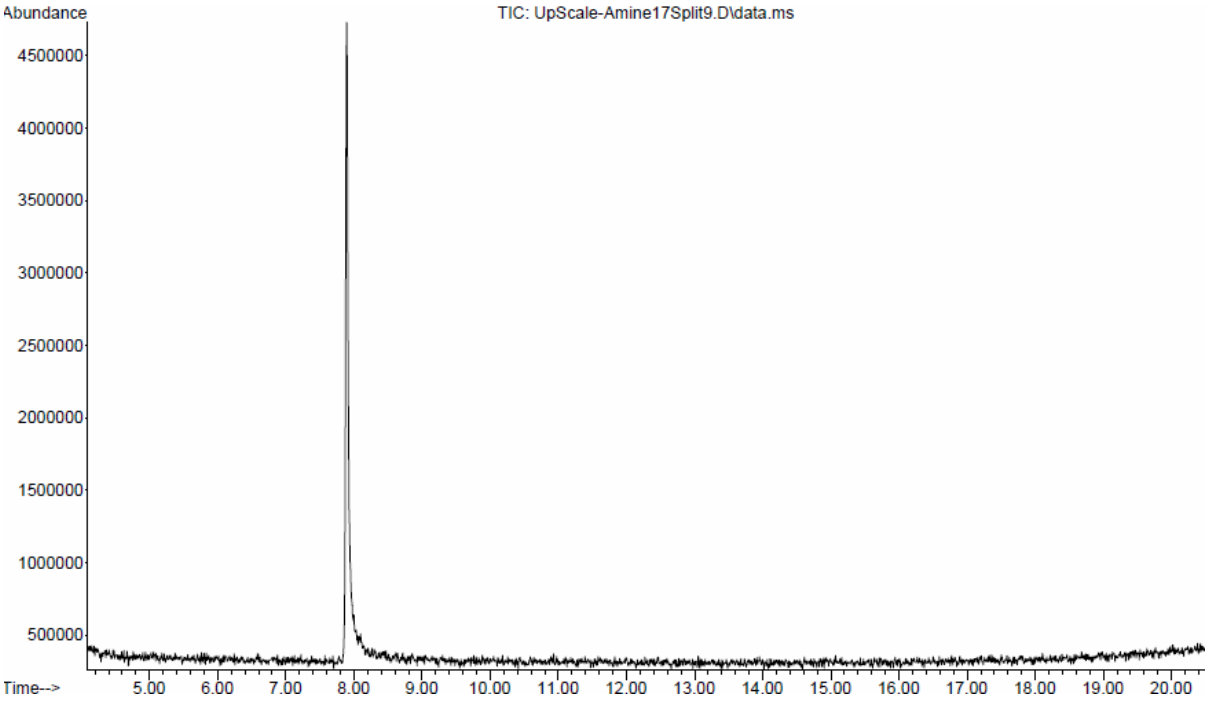
^{1}H-NMR (DMSO-d6, 300 MHz, δ [ppm]): 1.67-1.77 (1H, m), 1.93-2.03 (1H, m), 3.87 (1H, t, ^{3}J = 5.4 Hz), 4.08-4.15 (1H, m), 4.19-4.27 (1H, m), 6.67 (1H, dd, Ar, ^{3}J = 8.2 Hz, ^{4}J = 1.2 Hz), 6.83 (1H, dt, Ar, ^{3}J = 7.4 Hz, ^{4}J = 1.2 Hz), 7.07 (1H, ddd, Ar, ^{3}J = 8.6 Hz, ^{4}J = 1.5Hz, 7.6 Hz), 7.3 (1H, m, Ar).

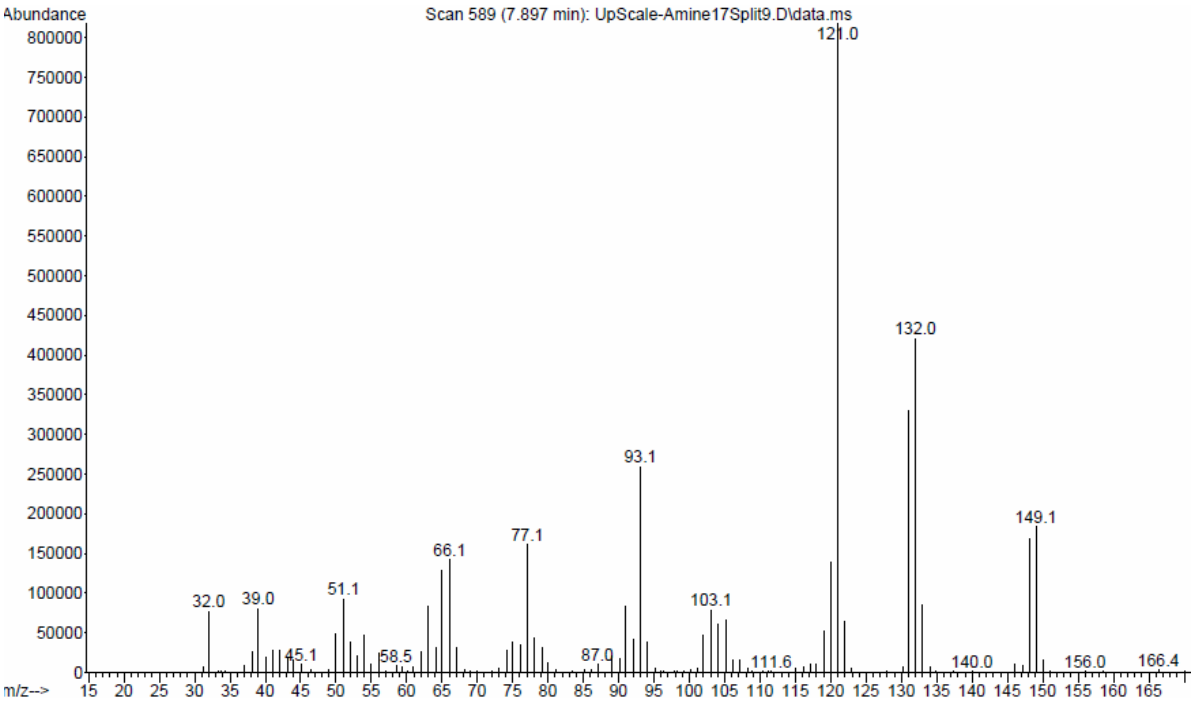


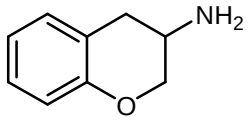
^{13}C-NMR (DMSO-d6, 300 MHz, δ [ppm]): 32.2, 45.0, 63.0, 116.5, 120.3, 128.1, 128.4, 129.7, 154.5.



GC-MS *m/z* (rel. int.): 149 [M^+] (30), 132 (58), 121 (100), 103 (10), 93 (25), 77 (16), 66 (16), 51 (8), 39 (8), 32 (3).



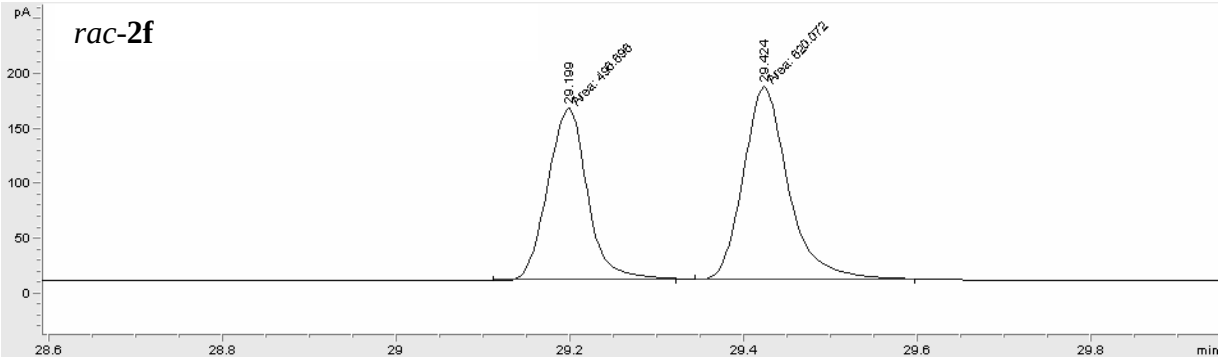


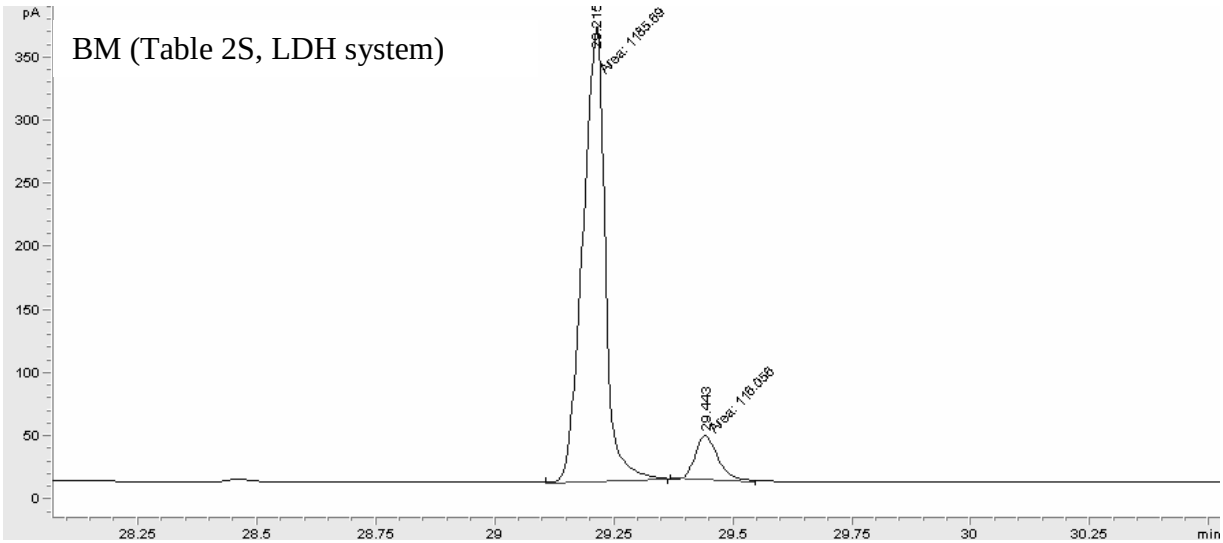


2f

Conversion: method 1, ketone **1f** 17.2 min; amine **2f** 19.8 min.

ee: method A, (*S*)-**2f** 29.1 min; (*R*)-**2f** 29.4 min (derivatised as acetamides). The absolute configuration was assigned as follows: the ketone **1f** was aminated employing ArS-ωTA as reported at paragraph S5, step 4 and the amine product was isolated. The enantiopurity of the amine product was determined by comparison of elution order on GC and coinjection with the racemic amine. The $[\alpha]_D$ of the amine product was measured and compared to literature data. Measured: $[\alpha]_D^{20}$ = +46.4 (c 1.00 as hydrochloride salt in methanol; *ee* >99%). Literature: $[\alpha]_D^{20}$ = +61.3 (c 0.5, as hydrochloride salt in methanol, *R* enantiomer, *ee* 99.5%).[3] NMR spectra and GC-MS chromatogram have been reported in paragraph S5.





S5.

References

(1) a) Koszelewski, D.; Göritzer, M.; Clay, D.; Seisser, B.; Kroutil, W. *ChemCatChem* **2010**, *2*, 73-77; b) Mutti, F. G.; Fuchs, C. S.; Pressnitz, D.; Sattler, J. H.; Kroutil, W. *Adv. Synth. Catal.* **2011**, *353*, 3227–3233; c) Mutti, F. G.; Fuchs, C. S.; Pressnitz, D.; Turrini, N. G.; Sattler, J. H.; Lerchner, A.; Skerra, A.; Kroutil, W. *Eur. J. Org. Chem.* **2012**, *2012*, 1003–1007.

(2) Alami, M.; Peyrat, J.-F.; Belachmi, L.; Brion, J.-D. *Eur. J. Org. Chem.* 2001, 4207-4212.

(3) Brisander, M.; Caldirola, P.; Johansson, A. M.; Hacksell, U. *J. Org. Chem.* 1998, **63**, 5362-5367.

(4) Harris, M. C. J.; Jackson, M.; Lennon, I. C.; Ramsden, J. A.; Samuel, H. *Tetrahedron Lett.* 2000, **41**, 3187-3191.

(5) Guijarro, D.; Pablo, O.; Yus, M. *J. Org. Chem.* 2010, **75**, 5265-5270.