Construction of three contiguous stereocenters through amine-catalyzed asymmetric aldol reactions

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・Supporting Information

1. General information

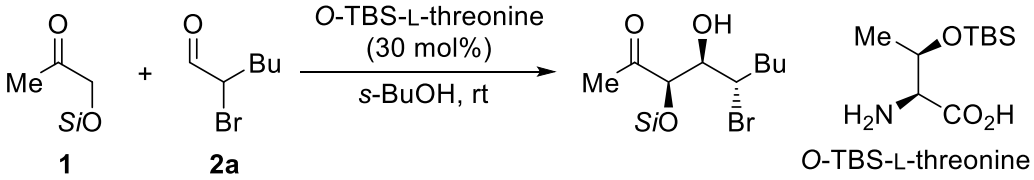
^{1}H NMR spectra were measured on a JEOL JNM-FX300 (300 MHz) spectrometer. Chemical shifts were reported in ppm from tetramethylsilane (for $CDCl_3$) as an internal standard. Data were reported as follow: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = qualtet, m = multiplet, br = broad and app = apparent), coupling constants (Hz), and integration. ^{13}C NMR spectra were measured on a JEOL JNM-FX300 (75 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. ^{19}F NMR spectra were measured on a JEOL JNM-FX300 (283 MHz) spectrometer. Chemical shifts were reported in ppm from benzotrifluoride as an internal standard. Data were reported as follow: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet), coupling constants (Hz). High performance liquid chromategraphy (HPLC) was performed on Shimadzu 20A instruments using Daicel Chiralpak IA-3, IC-3, IF-3, and OD-3 4.6 mm × 25 cm column. High–resolution mass spectra (HRMS) were performed on Thermo SCIENTIFIC Exactive Plus. Optical rotations were measured on a JASCO DIP–1000 digital polarimeter. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel 60N (Kanto Chemical Co. Inc., 40–50 μm).

Acetonitrile (MeCN), 1-methyl-2-pyrrolidone (NMP) and methanol (MeOH) were purchased from Kanto Chemical Co. Inc. Ethanol (EtOH), 2-propanol (*i*-PrOH), dimethyl sulfoxide (DMSO) and tetrahydrofuran (THF) were purchased from Kishida Chemical Co., LTD. Butanol (*n*-BuOH), 2-methyl-2-propanol (*t*-BuOH), *N*,*N*-dimethylformamide (DMF) and toluene were purchased from Sigma-Aldrich Co. LLC. 2-Butanol (*s*-BuOH) and 3-pentanol were purchased from Aldrich or Tokyo Chemical Industry Co., Ltd. (TCI). Dichloromethane (CH_2Cl_2) and chloroform ($CHCl_3$) were purchased from FUJIFILM Wako Pure Chemical Corporation, Ltd. All solvents were stored over molecular sieves.[1] The commercially available aldehydes for one-pot bromination and aldol reaction were distilled and stored under N_2 atmosphere at 4 °C.

TMS-protected hydroxyacetone **1e**[2], TBS-protected dihydroxyacetone **1h**[3], other silyl-protected hydroxyacetones **1a**-**1d**[4], 2-fluorodecanal (**4**)[5], 2-chlorohexanal (**5**)[6], ketone-based brominating agents (KBA)[7], *O*-TBS-L-threonine[8] and **4**[8] were synthesized according to the literature procedures.

2. Screening of *Si*-protecting groups

Table S1. Asymmetric aldol reaction between α-siloxyketones and α-bromohexanal.[a]



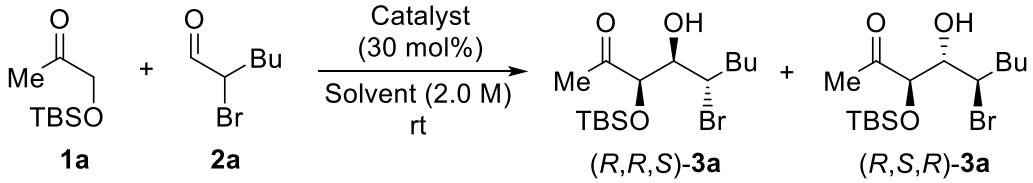
1 **2a**

Entry	*Si*	Time [h]	Yield [%][b]	dr[c]	ee [%][d]
1	TBS (**1a**)	6	88	8.3/1	98
2	TES (**1b**)	6	49	4.7/1	-
3	TBDPS (**1c**)	7	68	2.4/1	-
4	TIPS (**1d**)	7	69	1.3/1	-
5	TMS (**1e**)	6	complex mixture	-	-

[a] Reactions were performed using **1** (0.5 mmol), **2a** (0.1 mmol) and *O*-TBS-L-threonine (0.03 mmol) in *s*-BuOH (0.05 mL). [b] NMR yield. [c] Determined by ^{1}H-NMR. [d] Determined by chiral HPLC methods.

3. Catalyst and solvent screening

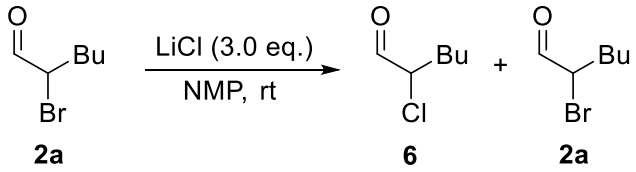
Table S2. Effects of catalysts and solvents on yield and stereoselectivity.[a]



Entry	Catalyst	Solvent	Time [h]	Yield [%][b]	dr[c]	ee [%][d]
1	L-isoleucine	MeCN	20	6	5.0/1	77
2	L-methionine	MeCN	18	8	3.0/1	67
3	L-asparagine	MeCN	18	n.d.	-	-
4	L-phenylalanine	MeCN	19	17	3.3/1	74
5	L-threonine	MeCN	18	n.d.	-	-
6	*O*-TBS-L-threonine	MeCN	6	80	2.1/1	95
7	3,3-diphenyl-L-alanine	MeCN	19	28	4.6/1	80
8	*O*-TBS-L-threonine	H_2O	6	86	3.8/1	99
9	*O*-TBS-L-threonine	EtOH	6	79	3.1/1	96
10	*O*-TBS-L-threonine	*i*-PrOH	6	70	6.3/1	97
11	*O*-TBS-L-threonine	*n*-BuOH	6	68	3.3/1	98
12	*O*-TBS-L-threonine	*s*-BuOH	6	88	8.3/1	98
13	*O*-TBS-L-threonine	*t*-BuOH	6	93	4.2/1	98
14	*O*-TBS-L-threonine	3-pentanol	6	92	2.1/1	97
15	*O*-TBS-L-threonine	DMSO	6	14	>20/1	98
16	*O*-TBS-L-threonine	DMF	6	40	3.1/1	97
17	*O*-TBS-L-threonine	$CHCl_3$	6	77	2.7/1	92
18	*O*-TBS-L-threonine	THF	6	86	3.8/1	96
19	*O*-TBS-L-threonine	toluene	6	66	4.8/1	91

[a] Reactions were performed using **1a** (0.5 mmol), **2a** (0.1 mmol) and *O*-TBS-L-threonine (0.03 mmol) in a solvent (0.05 mL). [b] NMR yield. [c] Determined by ^{1}H-NMR. [d] Determined by chiral HPLC methods.

4. Halogen exchange of α-bromohexanal (2a) with LiCl.[a]

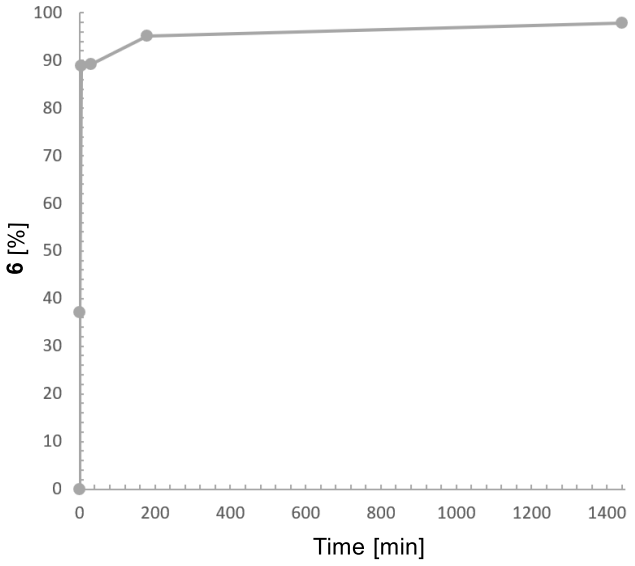


2a **6** **2a**

To a solution of α-bromohexanal (**2a**) (18 mg, 0.1 mmol) in NMP (0.05 mL) was added LiCl (13 mg, 0.3 mmol) at room temperature. After stirring for 1-1440 min, the resulting mixture was filtered through a pad of Celite and silica gel (1:1) with CH_2Cl_2. The filtrate was carefully concentrated under reduced pressure (30 °C, 360 Torr).

Entry	Time [min]	**6**/**2a**[b]
1	1	37/63
2	5	89/11
3	30	89/11
4	180	95/5
5	1440	98/2

[a] Reactions were performed in separate test tubes. [b] Determined by ^{1}H-NMR.



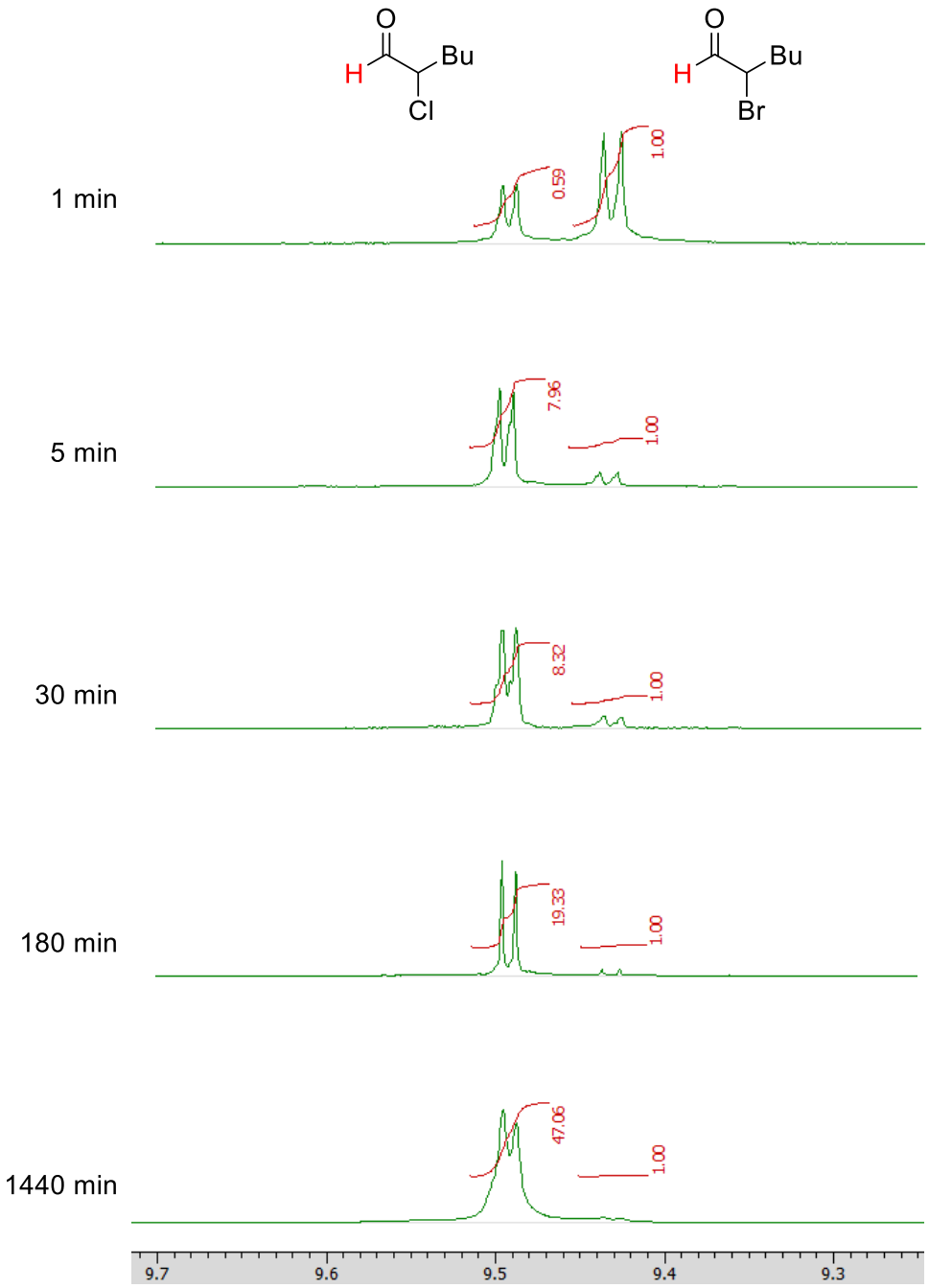
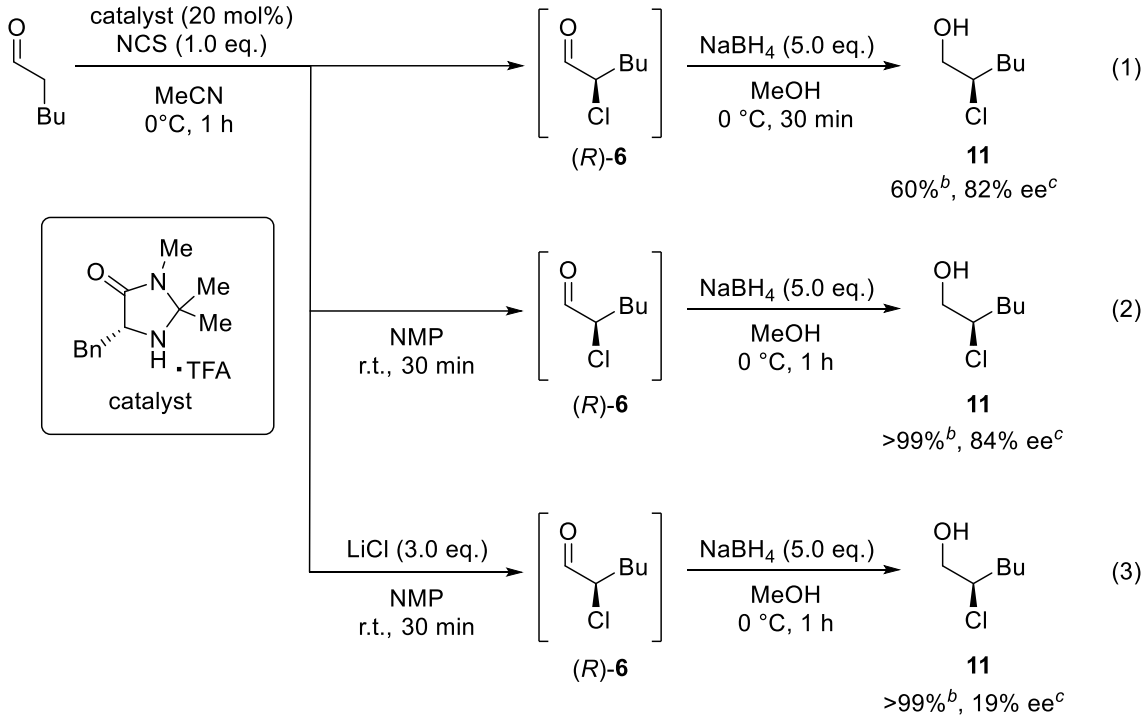


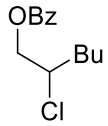
Figure S1. Change over time in the ratio of α-chlorohexanal to α-bromohexanal observed by ^{1}H-NMR.

5. Effects of LiCl and NMP on the racemization of (*R*)-6.[a]



Scheme S1. Asymmetric α-chlorination of hexanal. [a] Reactions were performed using hexanal (0.1 mmol), NCS (0.1 mmol) and catalyst (20 mol%) in MeCN (0.1 mL). If necessary, NMP (0.1 mL) and/or LiCl (0.3 mmol) were added. [b] Determined by ^{1}H-NMR. [c] Enantiomeric excess was determined by converting to the corresponding benzoate (See S50, 51).[9]

2-Chlorohexyl benzoate (12)



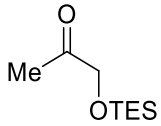
^{1}H-NMR (CDCl$_3$, 300 MHz) δ 8.07 (d, J = 8.1 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 4.56-4.38 (m, 2H), 4.26-4.13 (m, 1H), 1.99-1.68 (m, 2H), 1.53-1.19 (m, 4H), 0.93 (t, J = 7.5 Hz, 3H).

^{13}C-NMR (CDCl$_3$, 75 MHz) δ 166.1, 133.2, 129.72 (Two peaks overlap), 128.4, 68.0, 59.3, 34.5, 28.2, 22.2, 13.9.

HRMS (ESI) m/z calcd. for $C_{13}H_{17}{}^{35}ClO_2SiNa^+$ and $C_{13}H_{17}{}^{37}ClO_2SiNa^+$ ($[M + Na]^+$) : 263.0810 and 265.0780, found 263.0813 and 265.0801.

6. Preparation of α-siloxyketones

1-((Triethylsilyl)oxy)propan-2-one (1b)



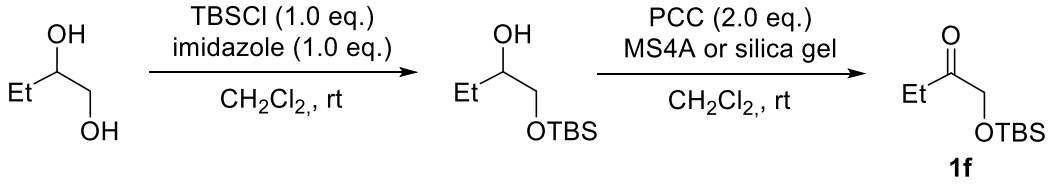
The title compound was synthesized according to the modified literature procedure.[4] To a solution of hydroxyacetone (206 μL, 3.0 mmol) in DMF (0.67 M) were added TESCl (554 μL, 3.3 mmol) and imidazole (266 mg, 3.9 mmol) at room temperature. After stirring for 12 h at the same temperature, the reaction mixture was quenched with H_2O, and extracted with hexane/ethyl acetate (10:1). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flush column chromatography on silica gel (hexane/ethyl acetate = 10:1 as eluent) to give **1b** (182 mg, 0.97 mmol, 32%) as colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.16 (s, 2H), 2.18 (s, 3H), 0.98 (t, J = 7.8 Hz, 9H), 0.64 (q, J = 7.8 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.1, 69.2, 25.9, 6.6, 4.3.

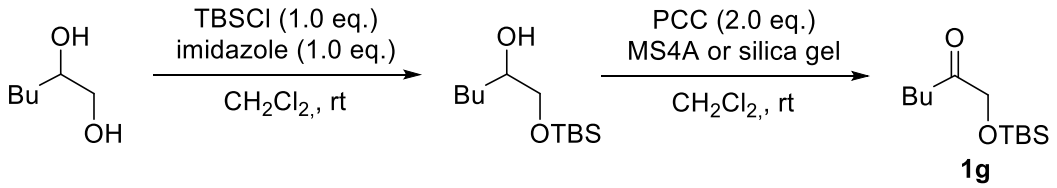
HRMS (ESI$^+$) m/z calcd. for $C_9H_{20}OSiNa^+$ ($[M + Na]^+$) : 211.1125, found 211.1133.

1-((*tert*-Butyldimethylsilyl)oxy)butan-2-one (1f)



The obtained 1-((*tert*-butyldimethylsilyl)oxy)butan-2-ol (906 mg, 4.4 mmol) and MS4A (2.2 g, 240 wt%) in CH_2Cl_2 (22 mL) was added PCC (1.90 g, 8.8 mmol) at room temperature. After stirring for 9 h at the same temperature, the reaction mixture was filtered through a pad of Celite and silica gel (1:1). The filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 10:1 as eluent) to give the title compound **1f** (673 mg, 3.3 mmol 76%) as colorless oil. The spectral data were in agreement with the literature values.[10]

1-((*tert*-Butyldimethylsilyl)oxy)hexan-2-one (1g)

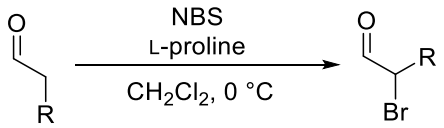


1g

The obtained 1-((*tert*-butyldimethylsilyl)oxy)hexan-2-ol (819 mg, 3.5 mmol) and silica gel (1.8 g, 220 wt%) in CH_2Cl_2 (18 mL) was added PCC (1.51 g, 7.0 mmol) at room temperature. After stirring for 12 h at the same temperature, the reaction mixture was filtered through a pad of Celite and silica gel (1:1). The filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 70:1 as eluent) to give the title compound **1g** (528 mg, 2.3 mmol, 65%) as colorless oil. The spectral data were in agreement with the literature values.[10]

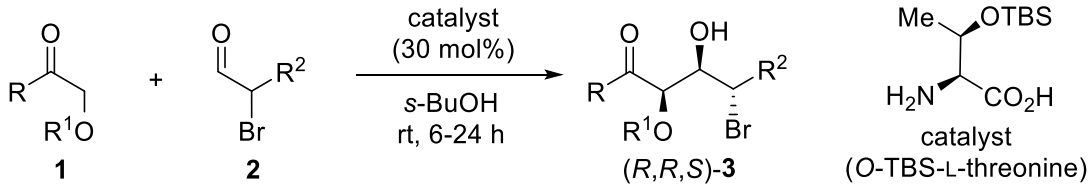
7. Preparation of α-haloaldehydes

General procedure for α-bromoaldehydes



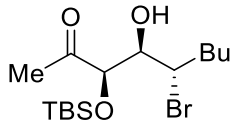
The target product was synthesized according to the modified literature procedure.[11] To a solution of aldehyde (1.0 eq.) in CH_2Cl_2 (0.4 M) were added *N*-bromosuccinimide (1.3 eq.) and L-proline (0.3 eq.) at 0 °C under N_2 atmosphere. After stirring for several hours, the reaction mixture was quenched with saturated $Na_2S_2O_3$ aq. and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by short column chromatography on silica gel (hexane/ethyl acetate as eluent) to give the target product. α-Bromoaldehyde bearing an amide moiety (R = $CH_2CH_2NHCOCF_3$) could not be isolated probably due to the decomposition.

8. General procedure for the aldol reaction of α-bromoaldehydes with α-siloxyketones.



To a solution of α-bromoaldehyde **2** (0.1 mmol) in *s*-BuOH (0.05 mL) were added α-siloxyketone **1** (0.5 mmol) and *O*-TBS-L-threonine (7.0 mg, 0.03 mmol, 30 mol%) at room temperature. After stirring for 6-24 h, the reaction mixture was placed on a silica gel column and eluted with hexane and ethyl acetate to give the aldol adduct **3**.

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3a)



Following the general procedure, the aldol reaction of 2-bromohexanal (**2a**) (18 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 6 h afforded the title compound **3a** (32 mg, 0.088 mmol, 88% yield, 8.3:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.74 (s, 1H), 3.96-3.84 (m, 2H), 2.60-2.46 (m, 1H), 2.25-2.13 (m, 1H), 2.21 (s, 3H), 1.92-1.71 (m, 1H), 1.71-1.52 (m, 1H), 1.51-1.20 (m, 3H), 0.96 (s, 9H), 0.93 (t, J = 7.2 Hz, 3H), 0.15 (s, 3H), 0.12 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.4, 78.4, 75.6, 56.3, 33.7, 29.1, 26.4, 25.8, 22.0, 18.2, 13.9, –4.5, –5.0.

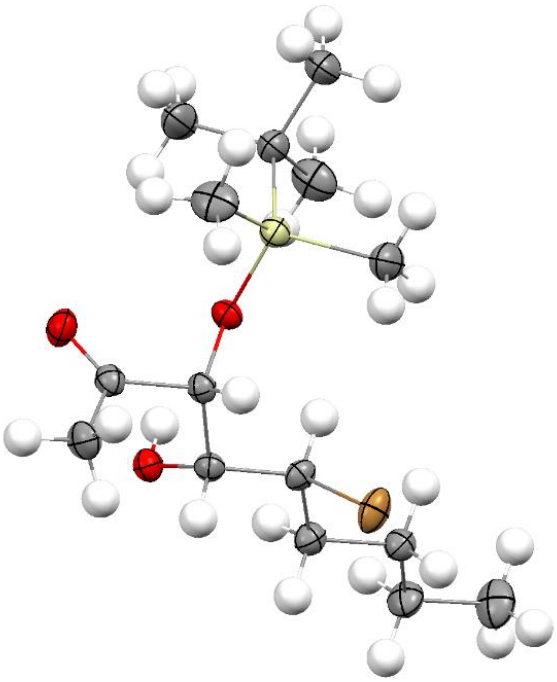
HRMS (ESI$^+$) m/z calcd. for $C_{15}H_{31}{}^{79}BrO_3SiNa^+$ and $C_{15}H_{31}{}^{81}BrO_3SiNa^+$ ($[M + Na]^+$) : 389.1119 and 391.1098, found 389.1124 and 391.1106.

$[\alpha]_D^{31}$ = –12.8 (*c* 0.50, $CHCl_3$, 98% ee)

HPLC analysis Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 300 nm, retention time: 11.4 min (minor) and 12.7 min (major).

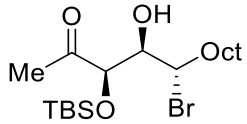
Crystal structure analysis of (3*R*,4*R*,5*S*)-3a

Single crystals of (3*R*,4*R*,5*S*)-**3a** for X-ray diffraction experiments were grown from dichloromethane and hexane at –30 °C. The data were collected at –150 °C on a Rigaku R-AXIS RAPID IP diffractometer with graphite-monochromated Cu Kα radiation (λ = 1.54184 Å). The crystal structure was solved by direct methods using SIR97[12] and refined in SHELXL-97[13] by full matrix least-squares using anisotropic thermal displacement parameters for all non-hydrogen atoms. Crystallographic data for (3*R*,4*R*,5*S*)-**3a**: $C_{15}H_{31}BrO_3Si$, colorless prism, 0.50×0.43×0.40 mm^3, monoclinic, $P2_1$, a = 13.5084(3), b = 8.30240(10), c = 26.1715(5) Å, V = 2864.57(12) $Å^3$, ρ_{calcd} = 1.278 gcm^{-3}, Z = 6, $2\theta_{max}$ = 136.35°, μ = 3.571 mm^{-1}. A total of 33091 reflections were measured. R = 0.0380, and Rw = 0.0895 for 10061 observed reflections with $I > 2.0\sigma(I)$.). Flack parameter = 0.036(5). CCDCCCDC-2189663 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



(3*R*,4*R*,5*S*)-**3a**

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxytridecan-2-one (3b)



Following the general procedure, the aldol reaction of 2-bromodecanal (**2b**) (24 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 6 h afforded the title compound **3b** (31 mg, 0.073 mmol, 73% yield, 6.4:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.74 (s, 1H), 3.89 (br d, J = 4.8 Hz, 2H), 2.53 (br s, 1H), 2.23-2.11 (m, 1H), 2.21 (s, 3H), 1.89-1.70 (m, 1H), 1.69-1.53 (br s, 1H), 1.52-1.38 (br s, 1H), 1.38-1.17 (br s, 10H), 0.96 (s, 9H), 0.88 (t, J = 6.9 Hz, 3H), 0.15 (s, 3H), 0.12 (s, 3H).

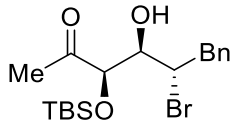
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.4, 78.4, 75.6, 56.3, 34.0, 31.8, 29.4, 29.2, 28.9, 26.9, 26.4, 25.8, 22.6, 18.2, 14.1, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{19}H_{39}{}^{79}BrO_3SiNa^+$ and $C_{19}H_{39}{}^{81}BrO_3SiNa^+$ ($[M + Na])^+$) : 445.1745 and 447.1724, found 445.1742 and 447.1720.

$[\alpha]_D^{31}$ = –15.9 (c 1.00, $CHCl_3$, 97% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 13.8 min (minor) and 15.1 min (major).

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-phenylhexan-2-one (3c)



Following the general procedure, the aldol reaction of 2-bromo-3-phenylpropanal (**2c**) (21 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 6 h afforded the title compound **3c** (39 mg, 0.098mmol, 98% yield, 3.1:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 15:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.37-7.19 (m, 5H), 4.75 (d, J = 1.2 Hz, 1H), 4.08 (ddd, J = 9.9, 9.0, 3.0 Hz, 1H), 3.93 (app t, J = 9.9 Hz, 1H), 3.61 (dd, J = 14.7, 3.0 Hz, 1H), 3.09 (dd, J = 14.7, 9.0 Hz, 1H), 2.72 (d, J = 10.8 Hz, 1H), 2.20 (s, 3H), 0.97 (s, 9H), 0.15

(s, 3H), 0.10 (s, 3H).

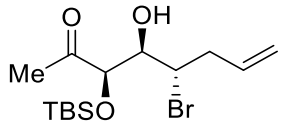
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.2, 137.8, 129.6, 128.3, 126.7, 78.1, 75.2, 56.1, 40.1, 26.4, 25.9, 18.3, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{18}H_{29}{}^{79}BrO_3SiNa^+$ and $C_{18}H_{29}{}^{81}BrO_3SiNa^+$ ($[M + Na])^+$) : 423.0962 and 425.0942, found 423.0959 and 425.0936.

$[\alpha]_D^{30}$ = –15.8 (*c* 1.00, $CHCl_3$, 92% ee).

HPLC analysis Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 14.2 min (minor) and 15.6 min (major).

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxyoct-7-en-2-one (3d)



Following the general procedure for the one-pot bromination and asymmetric aldol reaction (See S20), the bromination of pent-4-enal (8.4 mg, 0.1 mmol) with KBA (41 mg, 0.095 mmol) for 15 h at 0 °C, followed by the aldol reaction with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 6 h afforded the title compound **3d** (25 mg, 0.070 mmol, 70% yield, 6.0:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 30:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.04-5.82 (m, 1H), 5.27-5.19 (m, 1H), 5.19-5.14 (m, 1H), 4.74 (s, 1H), 3.97-3.81 (m, 2H), 3.05-2.87 (m, 1H), 2.80-2.59 (m, 1H), 2.59-2.47 (m, 1H), 2.21 (s, 3H), 0.96 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H).

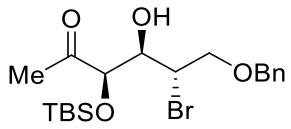
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.3, 134.1, 118.5, 78.1, 75.1, 54.2, 38.2, 26.4, 25.9, 18.2, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{14}H_{27}{}^{79}BrO_3SiNa^+$ and $C_{14}H_{27}{}^{81}BrO_3SiNa^+$ ($[M + Na])^+$) : 373.0806 and 375.0785, found 373.0800 and 375.0775.

$[\alpha]_D^{28}$ = –3.35 (*c* 1.00, $CHCl_3$, 99% ee).

HPLC analysis Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 11.7 min (minor) and 13.3 min (major).

(3*R*,4*R*,5*S*)-6-(benzyloxy)-5-bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxyhexan-2-one (3e)



Following the general procedure, the aldol reaction of 3-(benzyloxy)-2-bromopropanal (**2e**) (18 mg, 0.072 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (68 mg, 0.36 mmol) for 8 h afforded the title compound **3e** (26 mg, 0.060 mmol, 83% yield, 3.5:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 10:1). The obtained diastereomers were inseparable.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.40-7.34 (m, 5H), 4.67 (d, J = 1.5 Hz, 1H), 4.63 (s, 2H), 4.14 (app t, J = 9.3 Hz, 1H), 4.02-3.81 (m, 3H), 2.73 (d, 9.3 Hz, 1H), 2.21 (s, 3H), 0.95 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H).

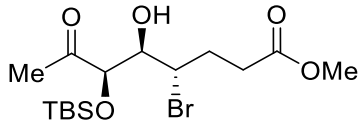
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.4, 137.6, 128.4, 127.8, 127.7, 78.2, 73.8, 73.4, 71.1, 51.5, 25.9, 25.7, 18.3, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{19}H_{31}{}^{79}BrO_4SiNa^+$ and $C_{19}H_{31}{}^{81}BrO_4SiNa^+$ ($[M + Na]^+$) : 453.1068 and 455.1047, found 453.1061 and 455.1039.

$[\alpha]_D^{28}$ = –2.07 (*c* 1.00, $CHCl_3$, 95% ee).

HPLC analysis Daicel Chiralpak IC-3, hexane/*i*-PrOH = 40:1, flow rate 1.0 mL/min, λ= 290 nm, retention time: 7.3 min (minor) and 7.7 min (major).

Methyl (4*S*,5*R*,6*R*)-4-bromo-6-((*tert*-butyldimethylsilyl)oxy)-5-hydroxy-7-oxooctanoate (3f)



Following the general procedure, the aldol reaction of methyl 4-bromo-5-oxopentanoate (**2f**) (21 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 8 h afforded the title compound **3f** (35 mg, 0.087 mmol, 87% yield, 4.0:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 10:1). The obtained diastereomers were inseparable.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.69 (d, J = 1.2 Hz, 1H), 3.99 (td, J = 9.0, 2.4 Hz, 1H),

3.88 (app t, J = 9.9 Hz, 1H), 3.69 (s, 3H), 2.75-2.51 (m, 4H), 2.22 (s, 3H), 2.17-2.01 (m, 1H), 0.96 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H).

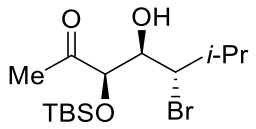
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.6, 173.2, 78.2, 75.6, 54.5, 51.8, 31.5, 29.4, 26.5, 25.8, 18.2, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{15}H_{29}{}^{79}BrO_5SiNa^+$ and $C_{15}H_{29}{}^{81}BrO_5SiNa^+$ ($[M + Na])^+$) : 419.0860 and 421.0840, found 419.0861 and 421.0834.

$[\alpha]_D^{28}$ = –2.59 (c 1.00, $CHCl_3$, 94% ee).

HPLC analysis Daicel Chiralpak IC-3, hexane/i-PrOH = 40:1, flow rate 1.0 mL/min, λ= 290 nm, retention time: 12.4 min (major) and 14.6 min (minor).

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-methylheptan-2-one (3g)



Following the general procedure, the aldol reaction of 2-bromo-3-methylbutanal (**2g**) (17 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 6 h afforded the title compound **3g** (32 mg, 0.091 mmol, 91% yield, 4.3:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1). The obtained diastereomers were inseparable.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.73 (s, 1H), 4.00-3.94 (m, 2H), 2.49-2.43 (m, 1H), 2.34-2.24 (m, 1H), 2.21 (s, 3H), 1.05 (d, J = 6.6 Hz, 1H), 0.96 (d, J = 6.6 Hz, 3H), 0.96 (s, 9H), 0.15 (s, 3H), 0.13 (s, 3H).

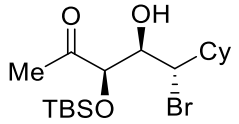
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.5, 78.6, 73.9, 64.8, 28.3, 26.5, 25.9, 22.2, 18.3, 16.0, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{14}H_{29}{}^{79}BrO_3SiNa^+$ and $C_{14}H_{29}{}^{81}BrO_3SiNa^+$ ($[M + Na])^+$) : 375.0962 and 377.0942, found 375.0964 and 377.0946.

$[\alpha]_D^{30}$ = +7.70 (c 1.00, $CHCl_3$, 98% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/i-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 12.4 min (minor) and 15.0 min (major).

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-5-cyclohexyl-4-hydroxypentan-2-one (3h)



Following the general procedure, the aldol reaction of 2-bromo-2-cyclohexylacetaldehyde (**2h**) (21 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 8 h afforded the title compound **3h** (33 mg, 0.083 mmol, 83% yield, 6.9:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1). The obtained diastereomers were inseparable.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.73 (d, J = 0.9 Hz, 1H), 4.03 (app t, J = 11.1 Hz, 1H), 3.94 (dd, J = 10.5, 2.1 Hz, 1H), 2.47 (d, J = 11.1 Hz, 1H), 2.20 (s, 3H), 1.98-1.20 (m, 11H), 0.96 (s, 9H), 0.14 (s, 3H), 0.12 (s, 3H).

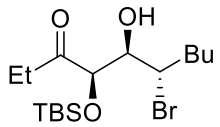
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.5, 78.6, 73.2, 63.4, 38.2, 32.4, 26.6, 26.3, 26.2, 25.9, 25.7, 25.7, 18.3, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{17}H_{33}{}^{79}BrO_3SiNa^+$ and $C_{17}H_{33}{}^{81}BrO_3SiNa^+$ ($[M + Na]^+$) : 415.1275 and 417.1255, found 415.1273 and 417.1256.

$[\alpha]_D^{30}$ = –4.70 (*c* 1.00, $CHCl_3$, >99% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 12.5 min (minor) and 13.2 min (major).

(4*R*,5*R*,6*S*)-6-Bromo-4-((*tert*-butyldimethylsilyl)oxy)-5-hydroxydecan-3-one (3i)



Following the general procedure, the aldol reaction of 2-bromohexanal (**2a**) (18 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)butan-2-one (**1f**) (101 mg, 0.5 mmol) for 12 h afforded the title compound **3i** (23 mg, 0.060 mmol, 60% yield, 12:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 30:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.78 (s, 1H), 3.97-3.83 (m, 2H), 2.62-2.43 (m, 3H), 2.27-2.12 (m, 1H), 1.88-1.72 (m, 1H), 1.72-1.53 (m, 1H), 1.50-1.24 (m, 3H), 1.08 (t, J = 7.5 Hz, 9H), 0.96 (s, 9H), 0.93 (t, J = 6.9 Hz, 3H), 0.14 (s, 3H), 0.11 (s, 3H).

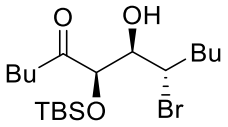
^{13}C-NMR (75 MHz, $CDCl_3$) δ 210.8, 78.0, 75.6, 56.5, 33.8, 31.9, 29.1, 25.9, 22.1, 18.3, 13.9, 7.5, –4.5, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{16}H_{33}{}^{79}BrO_3SiNa^+$ and $C_{16}H_{33}{}^{81}BrO_3SiNa^+$ ($[M + Na]^+$) : 403.1275 and 405.1255, found 403.1276 and 405.1258.

$[\alpha]_D^{30}$ = –11.8 (*c* 1.00, $CHCl_3$, 96% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.8 min (minor) and 12.0 min (major).

(6*R*,7*R*,8*S*)-8-Bromo-6-((*tert*-butyldimethylsilyl)oxy)-7-hydroxydodecan-5-one (3j)



Following the general procedure, the aldol reaction of 2-bromohexanal (**2a**) (18 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)hexan-2-one (**1g**) (0.12 g, 0.5 mmol) for 24 h afforded the title compound **3j** (31 mg, 0.075 mmol, 75% yield, 12:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 70:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.77 (s, 1H), 3.97-3.83 (m, 2H), 2.60-2.42 (m, 3H), 2.21-2.14 (m, 1H), 1.88-1.72 (m, 1H), 1.65-1.50 (m, 4H), 1.48-1.25 (m, 4H), 0.95 (s, 9H), 0.93-0.88 (m, 6H), 0.14 (s, 3H), 0.10 (s, 3H).

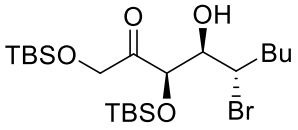
^{13}C-NMR (75 MHz, $CDCl_3$) δ 210.0, 78.2, 75.4, 56.6, 38.3, 33.8, 29.1, 25.9, 25.4, 22.3, 22.1, 18.3, 13.9, 13.8, –4.4, –5.1.

HRMS (ESI$^+$) m/z calcd. for $C_{18}H_{37}{}^{79}BrO_3SiNa^+$ and $C_{18}H_{37}{}^{81}BrO_3SiNa^+$ ($[M + Na]^+$) : 431.1588 and 433.1568, found 431.1588 and 433.1570.

$[\alpha]_D^{30}$ = –15.7 (c 1.00, $CHCl_3$, >99% ee).

HPLC analysis Daicel Chiralpak IA-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.9 min (minor) and 11.9 min (major).

(3*R*,4*R*,5*S*)-5-Bromo-1,3-bis((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3k)



Following the general procedure, the aldol reaction of 2-bromohexanal (**2a**) (18 mg, 0.1 mmol) with 1,3-bis((*tert*-butyldimethylsilyl)oxy)propane-2-one (**1h**) (0.159 g, 0.5 mmol) for 24 h afforded the title compound **3k** (78% yield, 3.7:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 30:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 5.20 (d, J = 1.2 Hz, 1H), 4.38 (d, J = 3.6 Hz, 1H), 4.37 (s, 1H), 4.04 (ddd, J = 10.5, 9.9, 1.2 Hz, 1H), 3.90 (td, J = 9.9, 3.0 Hz, 1H), 2.40 (d, J = 11.1 Hz, 1H), 2.26-2.12 (m, 1H), 1.88-1.72 (m, 1H), 1.69-1.53 (m, 1H), 1.50-1.22 (m, 3H), 0.95 (s, 9H), 0.93 (s, 9H), 0.92 (t, 5.7 Hz, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.6, 76.5, 74.9, 68.3, 55.7, 33.9, 29.1, 25.9, 25.7, 22.1, 18.4, 18.3, 13.9, –4.5, –5.0, –5.4, –5.5.

HRMS (ESI$^+$) m/z calcd. for $C_{21}H_{45}{}^{79}BrO_4SiNa^+$ and $C_{21}H_{45}{}^{81}BrO_4SiNa^+$ ($[M + Na]^+$) : 519.1932 and 521.1912, found 519.1933 and 521.1916.

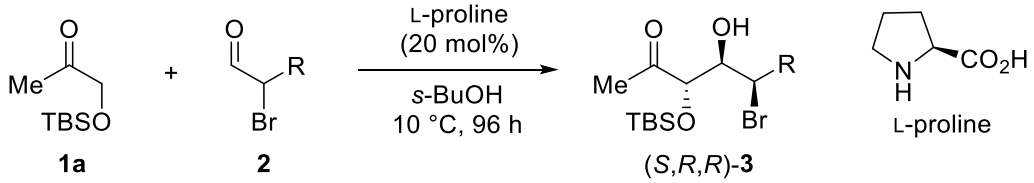
$[\alpha]_D^{31}$ = –25.5 (*c* 1.00, $CHCl_3$, 98% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 11.6 min (minor) and 12.5 min (major).

9. General procedure for the aldol reaction of α-bromoaldehydes with α-siloxy ketones using catalyst 4.

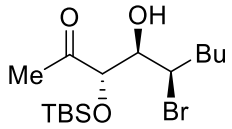
To a mixture of α-bromoaldehyde **2** (0.1 mmol) and **1a** (0.5 mmol) was added **4** (12 mg, 0.03 mmol, 30 mol%) at room temperature. After stirring for several hours at the same temperature or 30 °C, the reaction mixture was placed on a silica gel column and eluted with hexane and ethyl acetate to give the aldol adduct **3**.

10. General procedure for the aldol reaction of α-bromoaldehydes with α-siloxy ketones using L-proline.



To a solution of α-bromoaldehyde **2** (0.1 mmol) in *s*-BuOH (0.05 mL) were added 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a)** (94 mg, 0.5 mmol) and L-proline (3.5 mg, 0.03 mmol, 30 mol%) at 10 °C. After stirring for 96 h at the same temperature, the reaction mixture was placed on a silica gel column and eluted with hexane and ethyl acetate to give the aldol adduct **3**.

(3*S*,4*R*,5*R*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3l)



Following the general procedure, the aldol reaction of 2-bromohexanal (**2a**) (18 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) afforded the title compound **3l** (27 mg, 0.074 mmol, 74% yield, 3.3:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.38 (ddd, J = 9.3, 5.4, 1.8 Hz, 1H), 3.95 (d, J = 5.4 Hz, 2H), 3.48 (ddd, J = 10.5, 5.4, 1.8 Hz, 1H), 2.23 (s, 3H), 2.12-1.97 (m, 1H), 2.05 (d, J = 10.5 Hz, 1H), 1.99-1.80 (m, 1H), 1.51-1.28 (m, 4H), 0.93 (s, J = 7.2 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.05 (s, 3H).

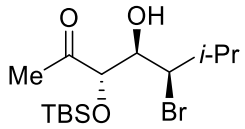
^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.5, 80.1, 74.6, 60.7, 35.6, 30.0, 25.62, 25.57, 21.9, 17.9, 13.9, –4.8, –4.9.

HRMS (ESI$^+$) m/z calcd. for $C_{15}H_{31}{}^{79}BrO_3SiNa^+$ and $C_{15}H_{31}{}^{81}BrO_3SiNa^+$ ($[M + Na])^+$) : 389.1119 and 391.1098, found 389.1119 and 391.1099.

$[\alpha]_D^{30}$ = –15.4 (*c* 1.00, $CHCl_3$, 92% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100/1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 27.2 min (major) and 29.6 min (minor)

(3*S*,4*R*,5*R*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-methylheptan-2-one (3m)



Following the general procedure, the aldol reaction of 2-bromo-3-methylbutanal (**2g**) (17 mg, 0.1 mmol) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) afforded the title compound **3m** (14 mg, 0.041 mmol, 41% yield, 11:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1). The obtained diastereomers were inseparable.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.21 (dd, J = 6.6, 2.1 Hz, 1H), 3.94 (d, J = 8.1 Hz, 1H), 3.65 (ddd, J = 10.5, 8.1, 2.1 Hz, 1H), 2.23 (s, 3H), 2.18-2.07 (m, 1H), 2.12 (d, J = 10.5 Hz, 1H), 1.11 (d, J = 6.6 Hz, 3H), 1.07 (d, J = 6.6 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.05 (s, 3H).

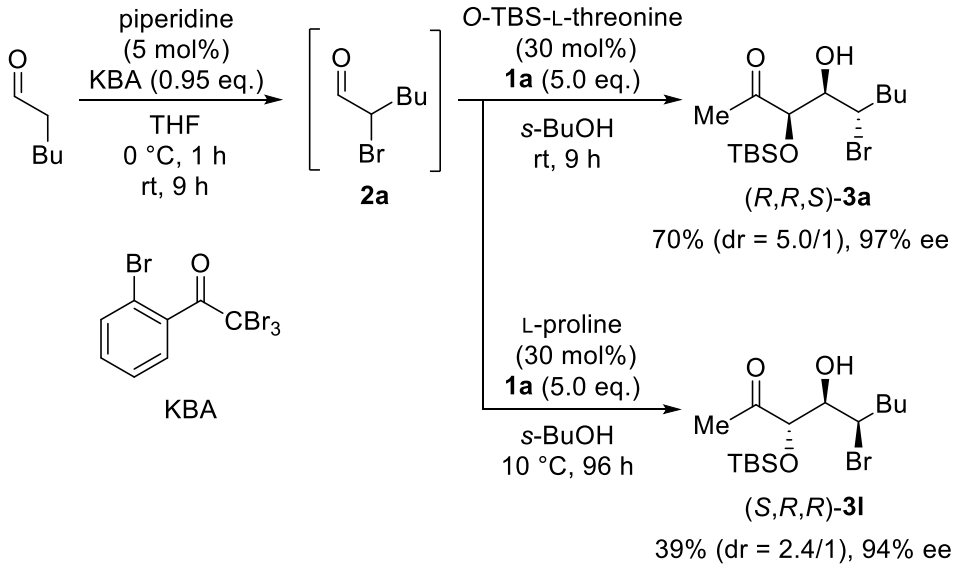
^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.5, 80.0, 73.3, 68.7, 33.2, 25.7, 25.6, 21.2, 20.9, 17.9, –4.8, –5.0.

HRMS (ESI$^+$) m/z calcd. for $C_{14}H_{29}{}^{79}BrO_3SiNa^+$ and $C_{14}H_{29}{}^{81}BrO_3SiNa^+$ ($[M + Na]^+$) : 375.0962 and 377.0942, found 375.0958 and 377.0941.

$[\alpha]_D^{29}$ = –19.2 (*c* 1.00, $CHCl_3$, 95% ee).

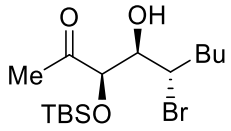
HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100/1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 22.3 min (major) and 22.8 min (minor).

11. General procedure for the one-pot bromination and asymmetric aldol reactions.



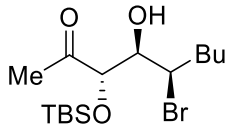
To a solution of hexanal (10 mg, 0.1 mmol) in THF (5 μL) were added KBA (41 mg, 0.095 mmol) and piperidine (0.005 mmol, 5 mol%) at 0 °C. After stirring for 1 h at 0 °C and 9 h at room temperature, *s*-BuOH (0.05 mL), 1-((*tert*-butyldimethylsilyl)oxy) propan-2-one (**1a**) (94 mg, 0.5 mmol), and catalyst (0.03 eq., 30 mol%) were added. After stirring for several hours, the reaction mixture was placed on a silica gel column and eluted with hexane and ethyl acetate to give the aldol adduct **3**.

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3a)



Following the general procedure, the bromination of hexanal (10 mg, 0.1 mmol) with KBA and subsequent aldol reaction with *O*-TBS-L-threonine (7.0 mg, 0.03 mmol) for 9 h afforded the title compound **3a** (27 mg, 0.070 mmol, 70% yield, 5.0:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1).

(3*S*,4*R*,5*R*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3l)



Following the general procedure, the bromination of hexanal (10 mg, 0.1 mmol) with KBA and subsequent aldol reaction with L-proline (3.5 mg, 0.03 mmol) for 96 h afforded the title compound **3l** (14 mg, 0.039 mmol, 39% yield, 2.4:1 dr) as a pale yellow oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1).

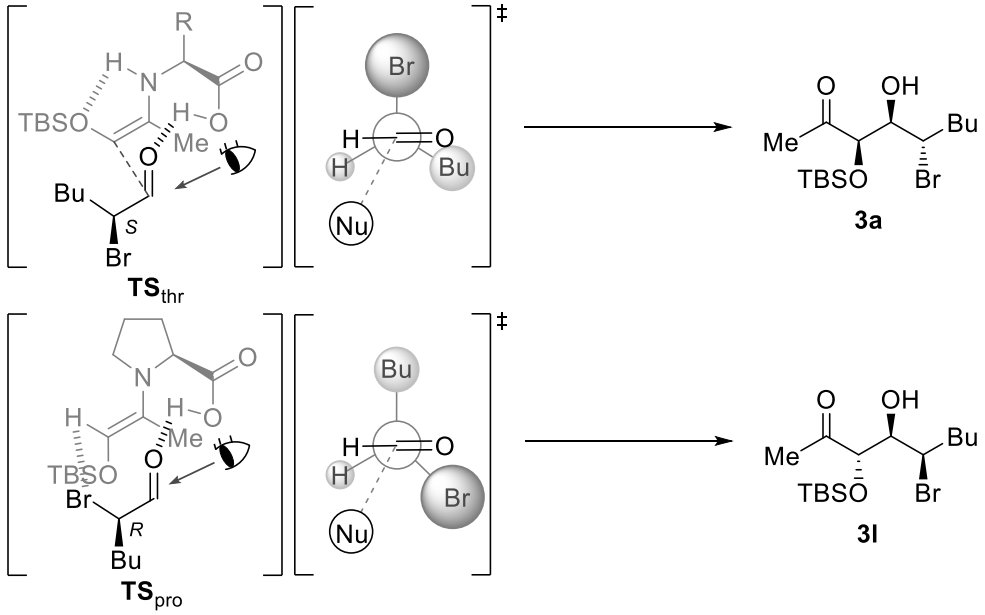
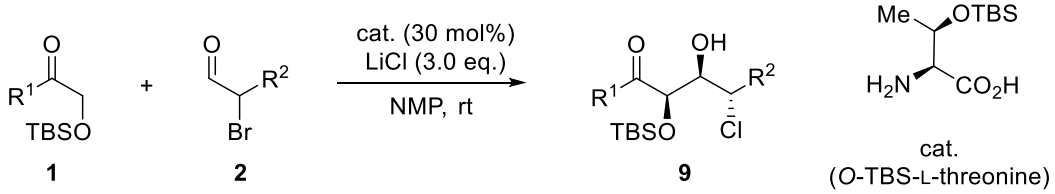


Figure S2. Plausible transition state models using *O*-TBS-L-threonine (TS_{thr}) or L-proline (TS_{pro}).[14]

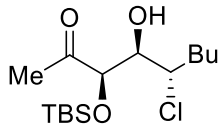
12. General procedure for the aldol reaction of *in-situ* generated α-chloroaldehydes from α-bromoaldehydes with α-siloxyketones using *O*-TBS-L-threonine.



To a solution of α-bromoaldehyde **2** (0.1 mmol) in NMP (0.05 mL) were added LiCl (12.7 mg, 0.3 mmol), α-siloxyketone **1** (0.5 mmol), and *O*-TBS-L-threonine (7.0 mg, 0.03 mmol, 30 mol%) at room temperature. After stirring for 6-24 h, the reaction mixture was

placed on a silica gel column and eluted with hexane and ethyl acetate to give the aldol adduct **9**. The stereochemistry was determined by conversion of **9a** to the corresponding epoxide (See S29).

(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxynonan-2-one (9a)



Following the general procedure, the aldol reaction of 2-chlorohexanal (generated from 2-bromohexanal (**2a**) (18 mg, 0.1 mmol)) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 6 h afforded the title compound **9a** (22 mg, 0.069 mmol, 69% yield, 5.8:1 dr) as a colorless oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.65 (s, 1H), 3.81-3.67 (m, 2H), 2.52-2.40 (m, 1H), 2.21 (s, 3H), 2.20-2.07 (m, 2H) 1.75-1.61 (m, 1H), 1.47-1.29 (m, 3H) 0.96 (s, 9H), 0.93(t, J = 7.5 Hz, 3H), 0.14 (s, 3H), 0.11 (s, 3H).

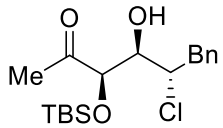
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.7, 77.6, 75.7, 61.7, 33.4, 28.0, 26.5, 25.8, 22.1, 18.2, 13.9, –4.5, –5.2.

HRMS (ESI) m/z calcd. for $C_{15}H_{31}{}^{35}ClO_3SiNa^+$ and $C_{15}H_{31}{}^{37}ClO_3SiNa^+$ ($[M + Na])^+$) : 345.1624 and 347.1594, found 345.1632 and 347.1605.

$[\alpha]_D^{30}$ = –10.9 (*c* 1.00, $CHCl_3$, 95% ee).

HPLC analysis Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 11.0 min (minor) and 12.3 min (major).

(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-phenylhexan-2-one (9b)



Following the general procedure, the aldol reaction of 2-chloro-3-phenylpropanal (generated from 2-bromo-3-phenylpropanal (21 mg, 0.1 mmol) (**2c**)) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) for 6 h afforded the title compound **9b** (27 mg, 0.076 mmol, 76% yield, 3.4:1 dr) as a colorless oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl

acetate = 20:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.42-7.15 (m, 5H), 4.65 (s, 1H), 3.98 (ddd, J = 9.3, 9.0, 3.0 Hz, 1H), 3.79 (app t, J = 10.5 Hz, 1H), 3.50 (dd, J = 14.4, 3.0 Hz, 1H), 2.98 (dd, J = 14.4, 8.7 Hz, 1H), 2.66 (d, J = 10.8 Hz, 1H), 2.20 (s, 3H), 0.96 (s, 9H), 0.14 (s, 3H), 0.09 (s, 3H).

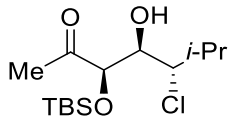
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.4, 137.2, 129.7, 128.3, 126.7, 77.3, 75.2, 61.9, 39.8, 26.5, 25.8, 18.2, –4.5, –5.2.

HRMS (ESI) m/z calcd. for $C_{18}H_{29}{}^{35}ClO_3SiNa^+$ and $C_{18}H_{29}{}^{37}ClO_3SiNa^+$ ([M + Na])$^+$) : 379.1467 and 381.1438, found 379.1473 and 381.1448.

$[\alpha]_D^{31}$ = –14.9 (c 1.00, $CHCl_3$, 96% ee).

HPLC analysis Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 254 nm, retention time: 14.1 min (minor) and 15.6 min (major).

(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-methylheptan-2-one (9c)



The target product was synthesized according to the modified general procedure. To a solution of 2-bromo-3-methylbutanal (**2g**) (16 mg, 0.1 mmol) in NMP (0.05 mL) was added LiCl (13 mg, 3.0 eq.) at room temperature. After stirring for 3 h, 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) and *O*-TBS-L-threonine (7.0 mg, 0.03 mmol, 30 mol%) were added at the same temperature. After stirring for 7 h, the reaction mixture was placed on a silica gel column and eluted with hexane/ethyl acetate (20:1) to give the title compound **9c** (23 mg, 0.070 mmol, 70% yield, 5.2:1 dr) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.62 (s, 1H), 3.89-3.73 (m, 2H), 2.53-2.35 (m, 1H), 2.40 (d, J = 10.5 Hz, 1H), 2.22 (s, 3H), 1.06 (d, J = 6.6 Hz, 3H), 0.96 (d, J = 6.6 Hz, 3H), 0.96 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H).

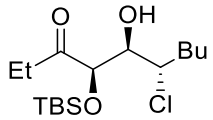
^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.8, 77.9, 73.9, 67.8, 28.3, 26.6, 25.8, 21.0, 18.3, 14.6, –4.5, –5.2.

HRMS (ESI) m/z calcd. for $C_{14}H_{29}{}^{35}ClO_3SiNa^+$ and $C_{14}H_{29}{}^{37}ClO_3SiNa^+$ ([M + Na])$^+$): 331.1467 and 333.1438, found 331.1479 and 333.1454.

$[\alpha]_D^{31}$ = +6.95 (*c* 1.00, $CHCl_3$, 98% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 12.1 min (minor) and 14.5 min (major).

(4*R*,5*R*,6*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-6-chloro-5-hydroxydecan-3-one (9d)



Following the general procedure, the aldol reaction of 2-chlorohexanal (generated from 2-bromohexanal (**2a**) (18 mg, 0.1 mmol)) with 1-((*tert*-butyldimethylsilyl)oxy)butan-2-one (**1f**) (0.10 g, 0.5 mmol) for 7 h afforded the title compound **9d** (16 mg, 0.045 mmol, 45% yield, 11:1 dr) as a colorless oil after purification by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 30:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.68 (s, 1H), 3.86-3.63 (m, 2H), 2.63-2.37 (m, 1H), 2.53 (t, *J* = 7.2 Hz, 2H), 2.25-2.00 (m, 1H), 1.78-1.51 (m, 2H),1.50-1.22 (m, 3H), 1.08 (t, *J* = 7.2 Hz, 3H), 0.95 (s, 9H), 0.93 (t, *J* = 6.9 Hz, 3H), 0.13 (s, 3H), 0.10 (s, 3H).

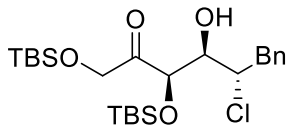
^{13}C-NMR (75 MHz, $CDCl_3$) δ 211.0, 77.2, 75.8, 61.8, 33.4, 32.0, 28.0, 25.8, 22.2, 18.3, 14.0, 7.4, –4.5, –5.2.

HRMS (ESI) m/z calcd. for $C_{16}H_{33}{}^{35}ClO_3SiNa^+$ and $C_{16}H_{33}{}^{37}ClO_3SiNa^+$ ($[M + Na])^+$) : 359.1780 and 361.1751, found 359.1783 and 361.1756.

$[\alpha]_D^{31}$ = –10.2 (*c* 1.00, $CHCl_3$, 98% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.5 min (minor) and 11.5 min (major).

(3*R*,4*R*,5*S*)-1,3-Bis((*tert*-butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-phenyl hexane-2-one (9e)



Following the general procedure, the aldol reaction of 2-chloro-3-phenylpropanal (generated from 2-bromo-3-phenylpropanal (21 mg, 0.1 mmol) (**2c**)) with 1,3-bis-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1h**) (0.16 g, 0.5 mmol) for 24 h afforded the title compound **9e** (35 mg, 0.071 mmol, 71% yield, 3.4:1 dr) as a yellow oil after purification

by flash column chromatography on silica gel (eluent with hexane/ethyl acetate = 20:1).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.39-7.18 (m, 5H), 5.14 (d, J = 1.2 Hz, 1H), 4.35 (d, J = 3.9 Hz, 2H), 4.02 (ddd, J = 9.6, 8.1, 3.0, 1H), 3.93 (app t, J = 10.5 Hz, 1H), 3.47 (dd, J = 14.4, 2.7 Hz, 1H), 3.00 (dd, J = 14.4, 8.1, 1H), 2.56 (d, J = 10.5 Hz, 1H), 0.95 (s, 9H), 0.88 (s, 9H), 0.12 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.6, 137.2, 129.8, 128.2, 126.7, 75.3, 74.3, 68.2, 61.4, 39.8, 25.81, 25.77, 18.30, 18.30, –4.5, –5.2, –5.57, –5.63.

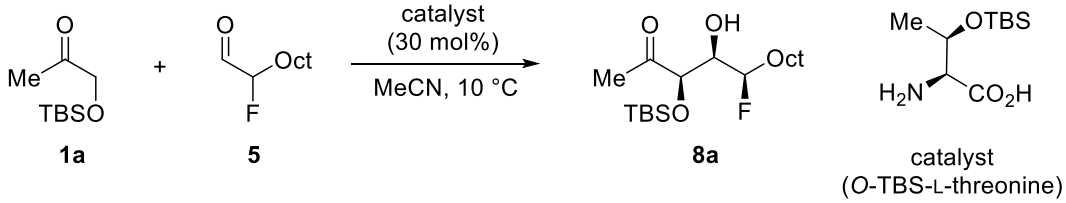
HRMS (ESI) m/z calcd. for $C_{24}H_{43}{}^{35}ClO_3SiNa^+$ and $C_{24}H_{43}{}^{37}ClO_3SiNa^+$ ([M + Na])$^+$) : 509.2281 and 511.2252, found 509.2292 and 511.2270.

$[\alpha]_D^{31}$ = –29.2 (c 1.00, $CHCl_3$, 97% ee).

HPLC analysis Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 254 nm, retention time: 12.9 min (minor) and 13.9 min (major).

13. Asymmetric aldol reaction of α-haloaldehydes with 1a.

(3*R*,4*R*,5*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-fluoro-4-hydroxytridecan-2-one (8a)



To a solution of 2-fluorodecanal (**5**) (17 mg, 0.1 mmol) in MeCN (0.05 mL) were added 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) and *O*-TBS-L-threonine (7.0 mg, 0.03 mmol, 30 mol%) at 10 °C. After stirring for 24 h, saturated $NaHSO_4$ aqueous solution were added and the mixture was extracted with hexane/ethyl acetate (20:1). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flush column chromatography on silica gel (hexane/ethyl acetate = 20:1 as eluent) to give **8a** (21 mg, 0.059 mmol, 59% yield, 3.2:1 dr, 97% ee) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.37 (app t, J = 1.8 Hz, 1H), 4.29 (dtd, J = 48, 8.7, 3.0 Hz, 1H), 3.76-3.64 (m, 1H), 2.36 (d, J = 10.8 Hz, 1H), 2.22 (s, 3H), 1.98-1.70 (m, 1H), 1.61-1.39 (m, 3H), 1.27 (br s, 12H), 0.95 (s, 9H), 0.88 (t, J = 6.9 Hz, 3H), 0.12 (s, 3H), 0.09 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.6, 91.7 (d, J = 173 Hz), 77.0, 73.6 (d, J = 27 Hz),

31.8, 31.6 (d, J = 20 Hz), 29.41, 29.38, 29.2, 26.8, 25.7, 24.8 (d, J = 2.5 Hz), 22.6, 18.2, 14.1, –4.7, –5.5.

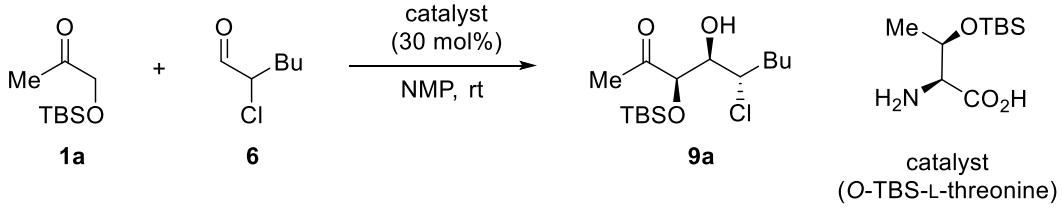
^{19}F-NMR (283 MHz, $CDCl_3$) δ –190.0 (ddd, J = 47, 37, 18 Hz).

HRMS (ESI) m/z calcd. for $C_{19}H_{39}FO_3SiNa^+$ ([M + Na])$^+$): 385.2545, found 385.2549.

$[\alpha]_D^{31}$ = –0.37 (c 1.00, $CHCl_3$, 97% ee).

HPLC analysis Daicel Chiralpak IA-3, hexane/*i*-PrOH = 50:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.1 min (minor) and 11.3 min (major).

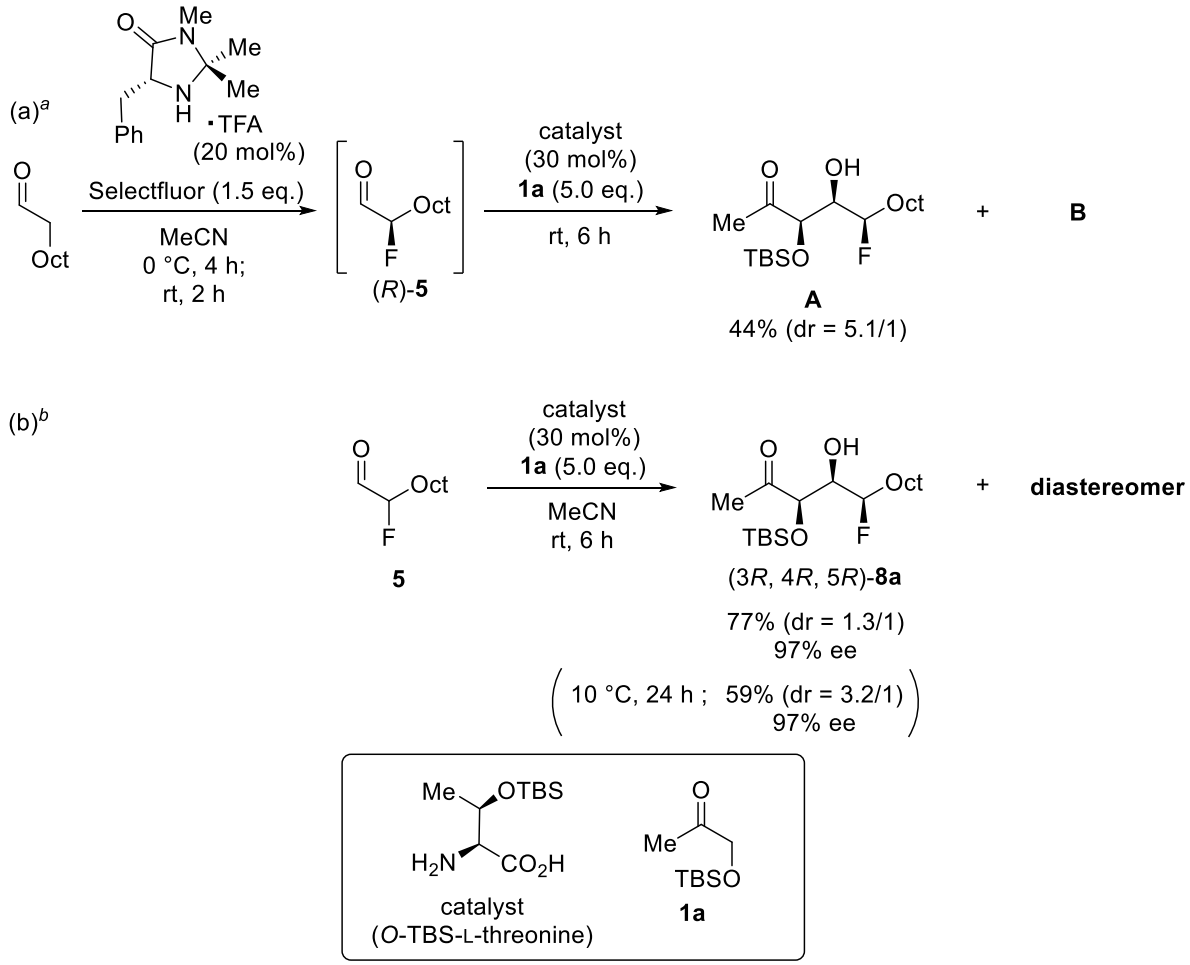
(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxytrihexane-2-one (9a)



To a solution of 2-chlorohexanal (**6**) (13 mg, 0.1 mmol) in NMP (0.05 mL) were added 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) (94 mg, 0.5 mmol) and *O*-TBS-L-threonine (7.0 mg, 0.03 mmol, 30 mol%) at room temperature. After stirring for 6 h at the same temperature, the reaction mixture was placed on a silica gel column and eluted with hexane/ethyl acetate (20:1) to give the title compound **9a** (26 mg, 0.079 mmol, 79% yield, 3.3:1 dr, 97% ee (major)) as a colorless oil.

14. Determination of stereochemistry of 8a and 9a.

The stereochemistry of C5 position of **8a** was determined by using in situ generated (*R*)-2-fluorodecanal ((*R*)-**5**) for the aldol reaction with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**) in the presence of *O*-TBS-L-threonine (scheme S2 (a)).[5,15] The reaction of in situ generated (*R*)-2-fluorodecanal ((*R*)-**5**) proceeded to give the aldol product **A** as a major diastereomer. Since **8a** matches **A**, the absolute configuration of **8a** was determined to be (3*R*,4*R*,5*R*). Interestingly, (*R*)-isomer of **5** was found to react preferentially to give the aldol product, unlike the reaction using 2-bromo- and 2-chloroaldehydes.



Scheme S2. Asymmetric aldol reaction of 2-fluorodecanal (**5**) with 1-((*tert*-butyldimethylsilyl)oxy)propan-2-one (**1a**). [a] Performed using decanal (0.1 mmol), selectfluor (0.15 mmol), (*R*)-5-benzyl-2,2,3-trimethylimidazolidin-4-one trifluoroacetate (20 mol%), **1a** (0.5 mmol), and *O*-TBS-L-threonine (30 mol%) in MeCN (0.1 mL). [b] Performed using **5** (0.1 mmol), **1a** (0.1 mmol), and *O*-TBS-L-threonine (30 mol%) in MeCN (0.1 mL).

Based on the experimental results, possible transition state models for the aldol reaction of α-siloxyketones **1** and α-fluoroaldehydes **5** are shown in Figure S2. Considering the strong electronegativity of fluorine atom, the reaction of (*S*)-2-fluoroaldehyde can give the aldol adduct via the polar-Felkin-Anh-type transition state **TS2**-F. However, since the size of fluorine atom is smaller than R^2 group, the Felkin-Anh product is obtained as a major diastereomer via transition state **TS1**-F.

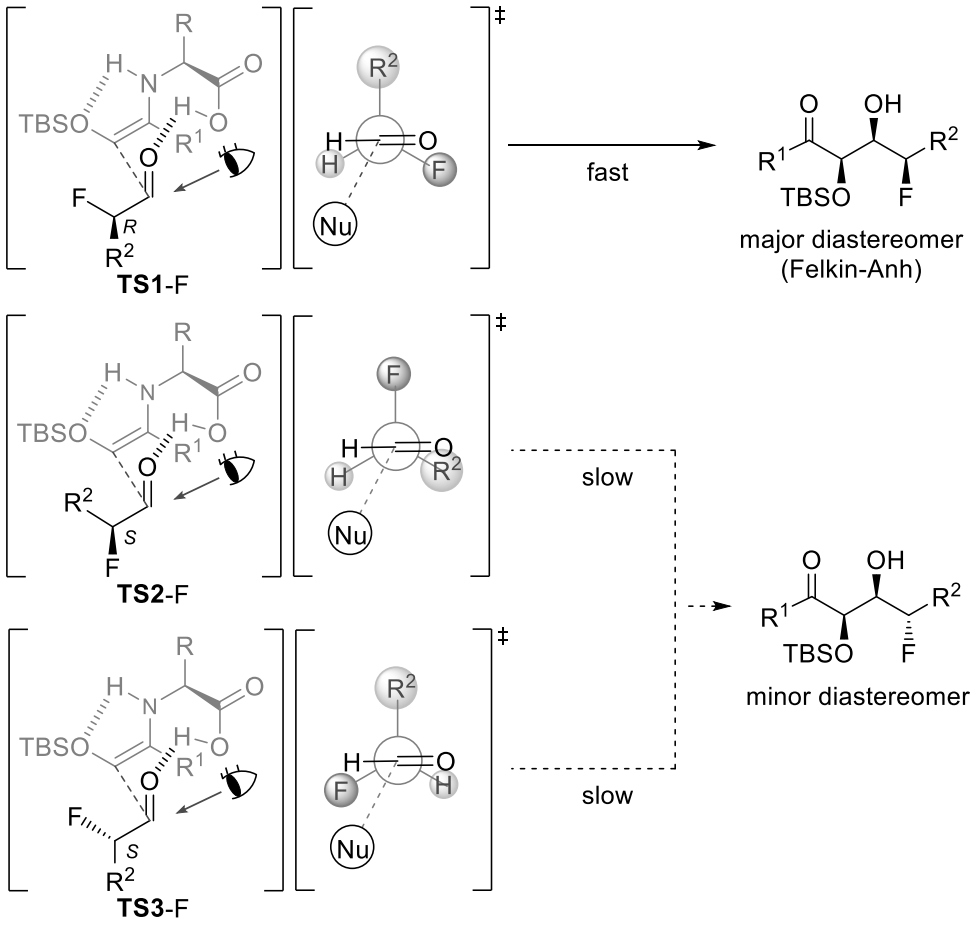
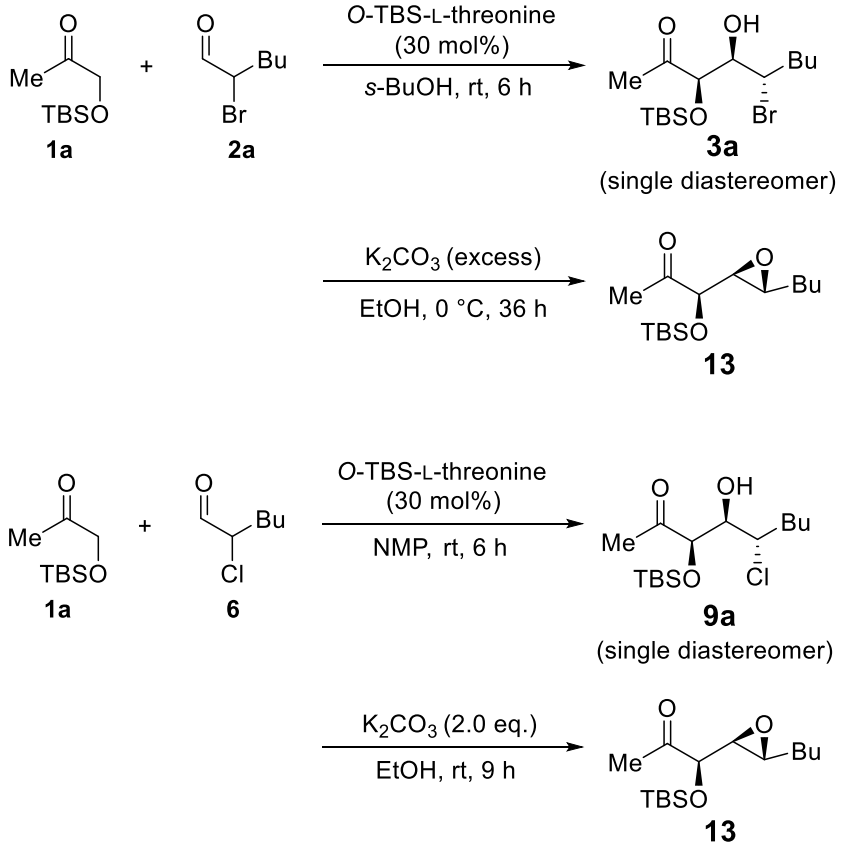
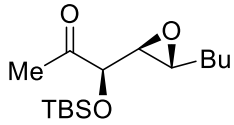


Figure S3. Plausible transition state models.

The stereochemistry of **9a** was determined by conversion of **9a** to the corresponding epoxide **13**.



(*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-1-((2*S*,3*R*)-3-butyloxiran-2-yl)propan-2-one (13)



To a solution of **3a** (11 mg, 0.03 mmol, 97% ee) in EtOH (1.0 mL) was added K_2CO_3 (8 mg, 0.06 mmol) at 0 °C. After stirring 16 h and 21 h, another 1.0 eq. of K_2CO_3 (4+4 mg, 0.03+0.03 mmol) was added. After **3a** was completely converted to **13** (monitored by TLC), the reaction mixture was filtered through a pad of Celite and silica gel (1:1) with CH_2Cl_2 to give the title compound **13** (8.7 mg, 0.03 mmol, >99% yield, 97% ee). Spectroscopic data of **13** synthesized from **3a** and **9a** were in agreement.

^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.83 (d, J = 5.4 Hz, 1H), 2.98 (td, J = 5.7, 2.1 Hz, 1H), 2.84 (dd, J = 5.4, 2.1 Hz, 1H), 2.24 (s, 3H), 1.57-1.49 (m, 2H), 1.49-1.29 (m, 4H), 0.94 (s, 9H), 0.90 (t, J = 7.2 Hz, 9H), 0.13 (s, 3H), 0.09 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.4, 79.8, 59.7, 56.0, 31.2, 27.9, 26.6, 25.7, 22.4, 18.1, 13.9, –4.7, –5.3.

HRMS (ESI) m/z calcd. for $C_{15}H_{30}O_3SiNa^+$ ($[M + Na])^+$) : 309.1857, found 309.1867.

$[\alpha]_D^{29}$ = +30.4 (*c* 0.50, $CHCl_3$, 97% ee).

HPLC analysis Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 300 nm, retention time: 9.5 min (major) and 11.6 min (minor).

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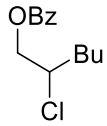
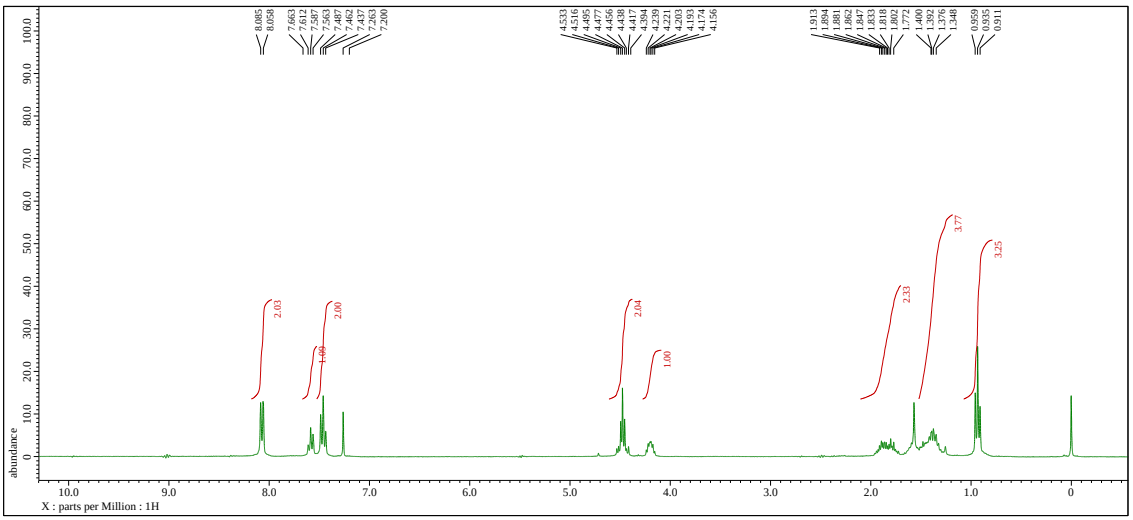
16. ^{1}H, ^{13}C and ^{19}F-NMR spectra

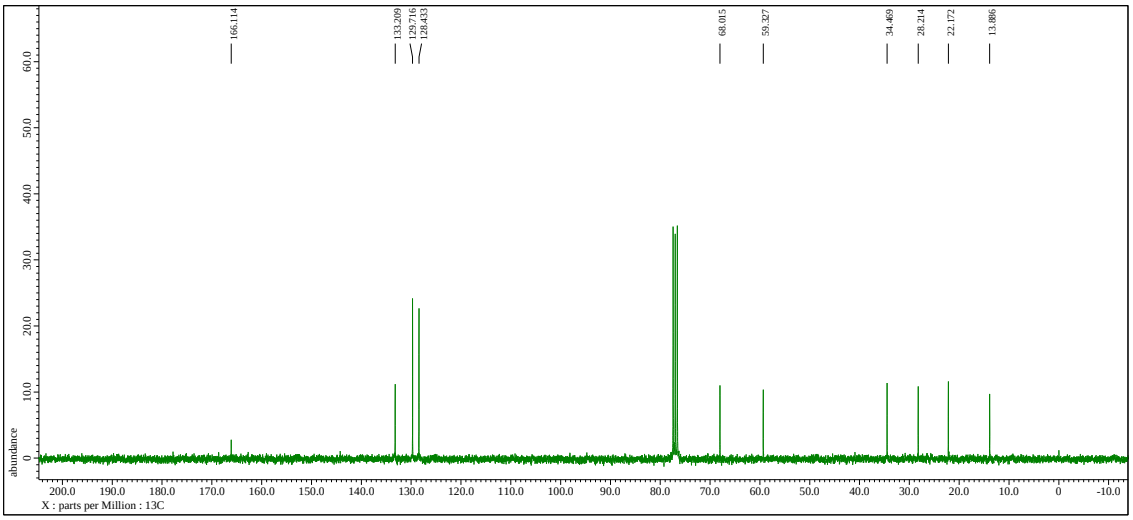
2-Chlorohexyl benzoate (12)



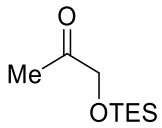
^{1}H-NMR ($CDCl_3$, 300 MHz)



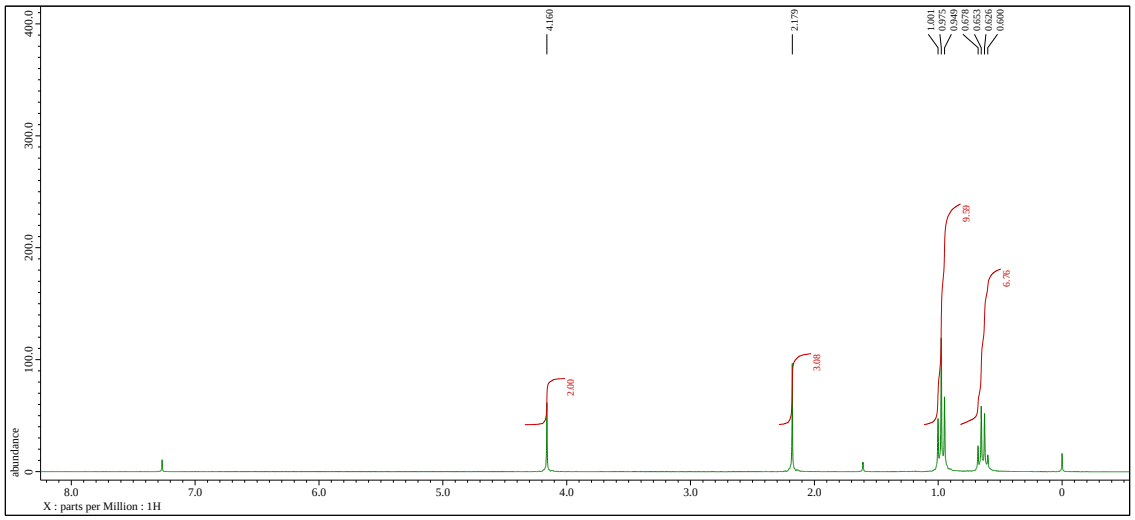
^{13}C-NMR ($CDCl_3$, 75 MHz)



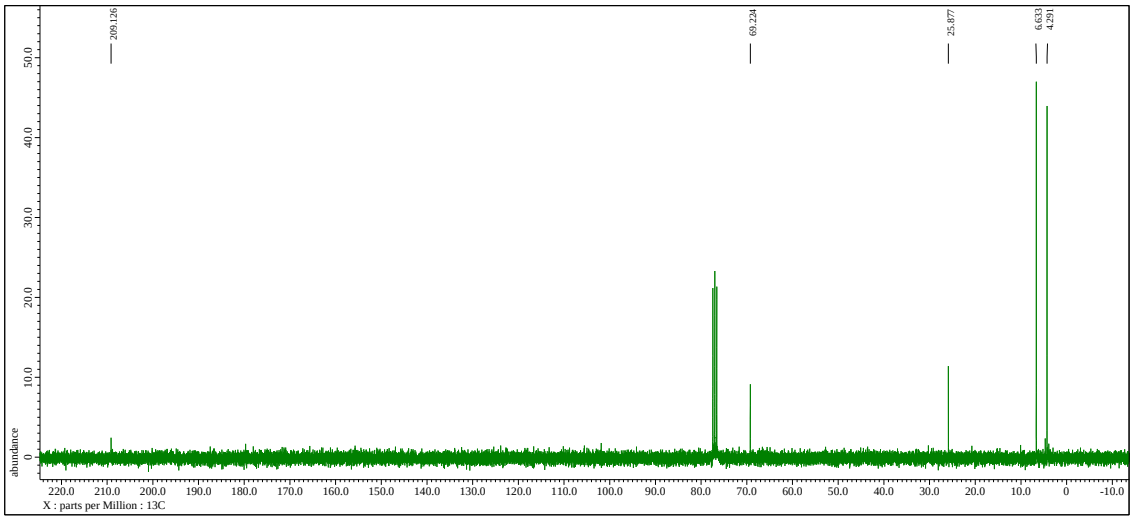
1-((Triethylsilyl)oxy)propan-2-one (1b)



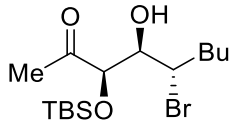
^{1}H-NMR (300 MHz, $CDCl_3$)



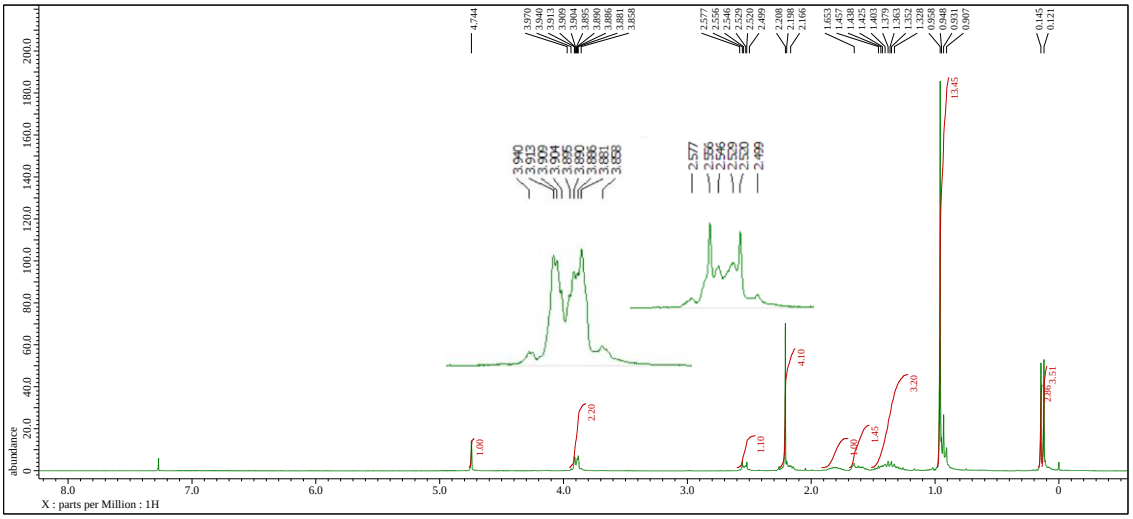
^{13}C-NMR (75 MHz, $CDCl_3$)



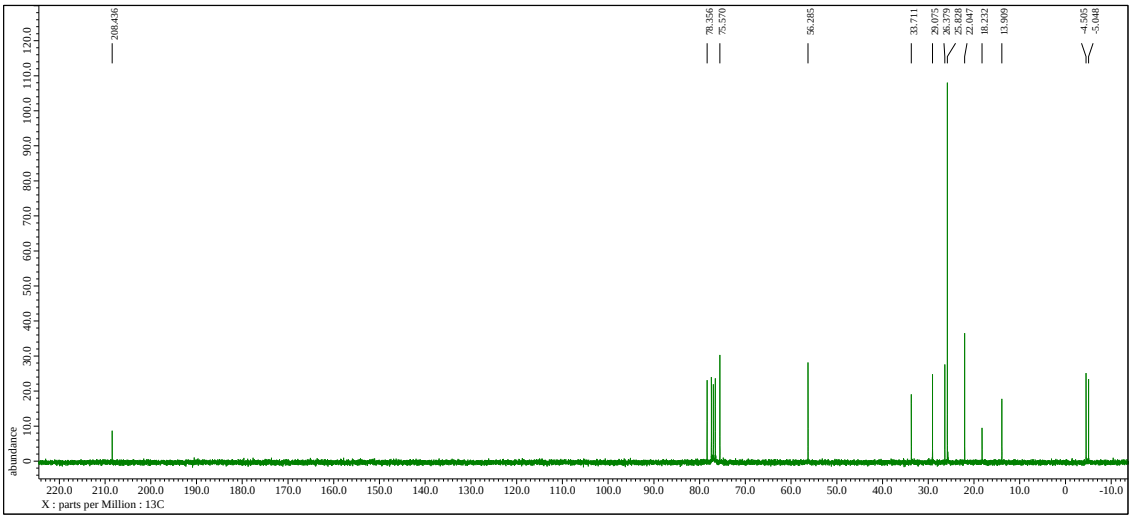
(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3a)



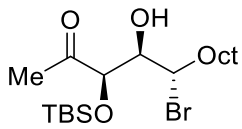
^{1}H-NMR (300 MHz, $CDCl_3$)



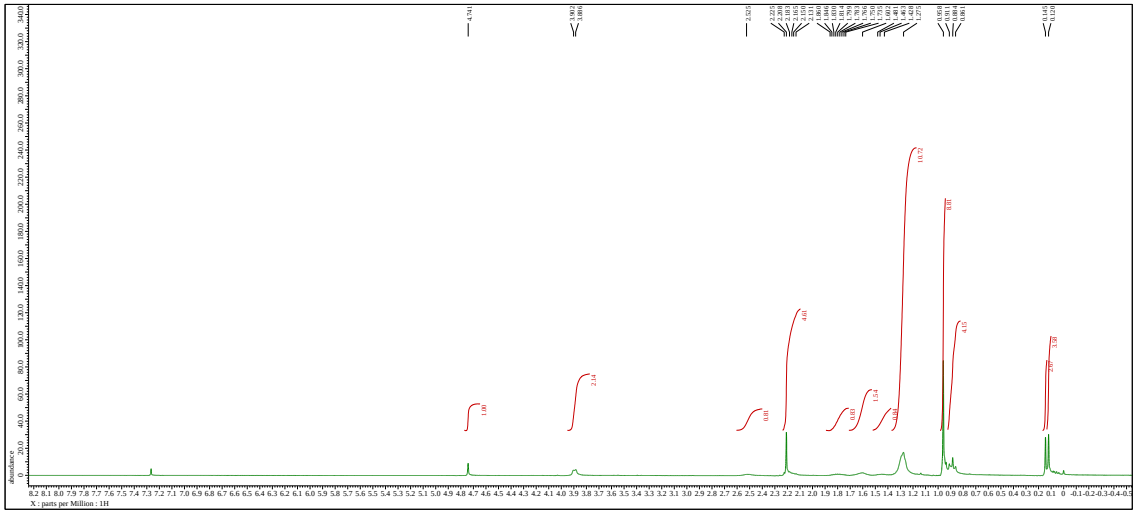
^{13}C-NMR (75 MHz, $CDCl_3$)



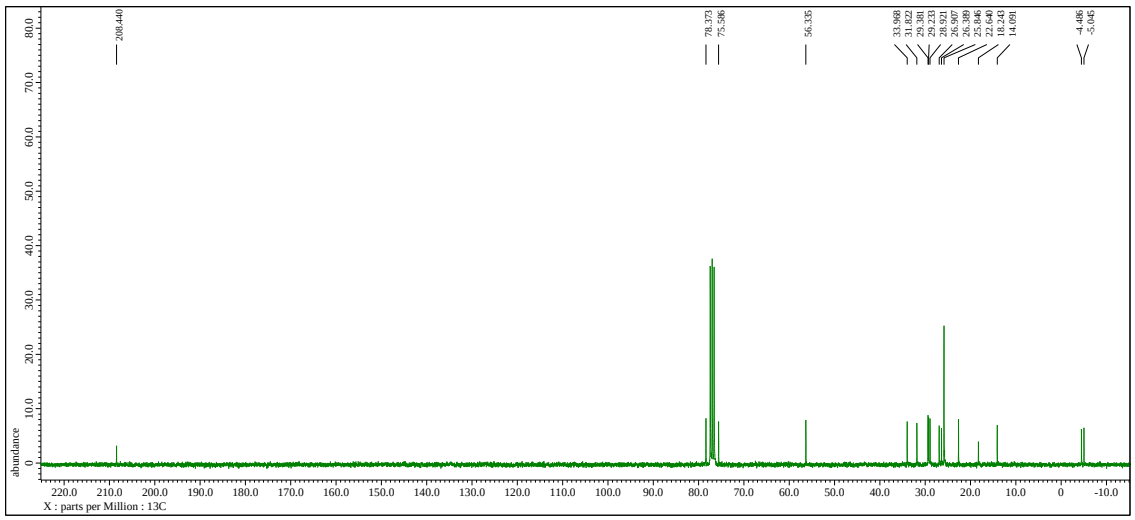
(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxytridecan-2-one (3b)



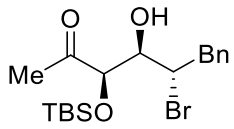
^{1}H-NMR (300 MHz, $CDCl_3$)



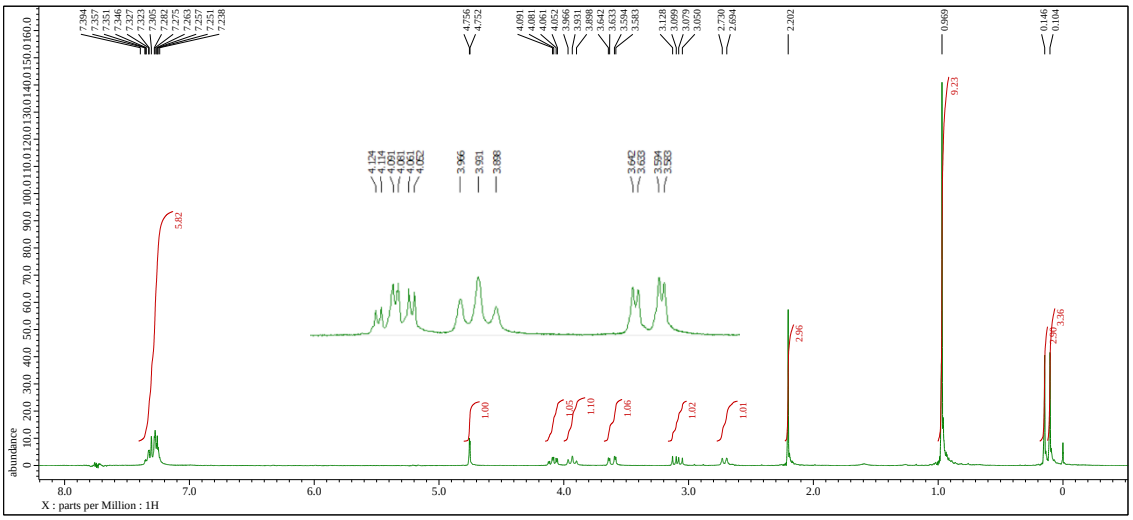
^{13}C-NMR (75 MHz, $CDCl_3$)



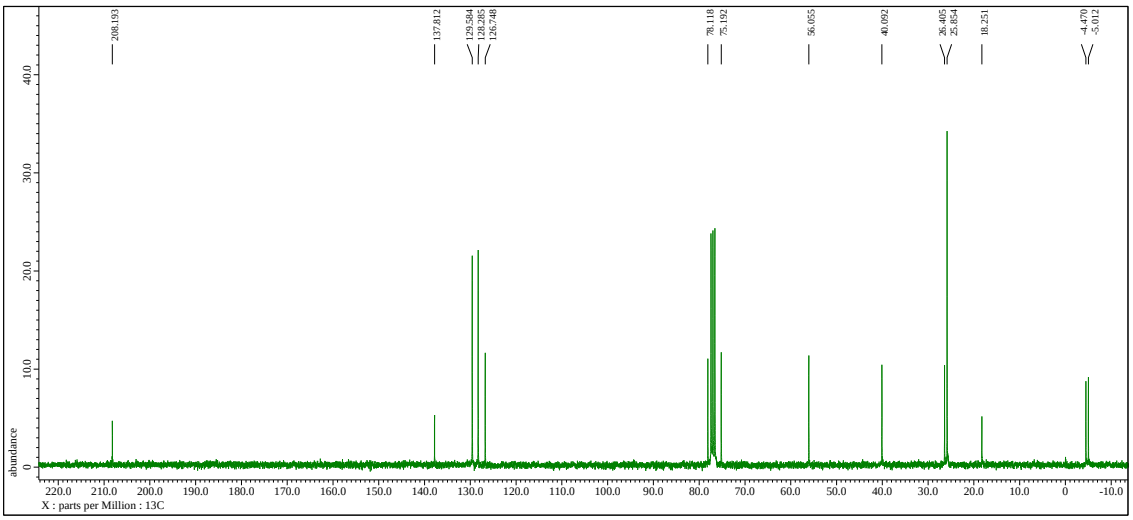
(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-phenylhexan-2-one (3c)



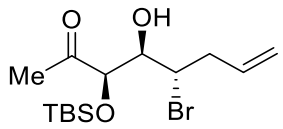
H-NMR (300 MHz, $CDCl_3$)



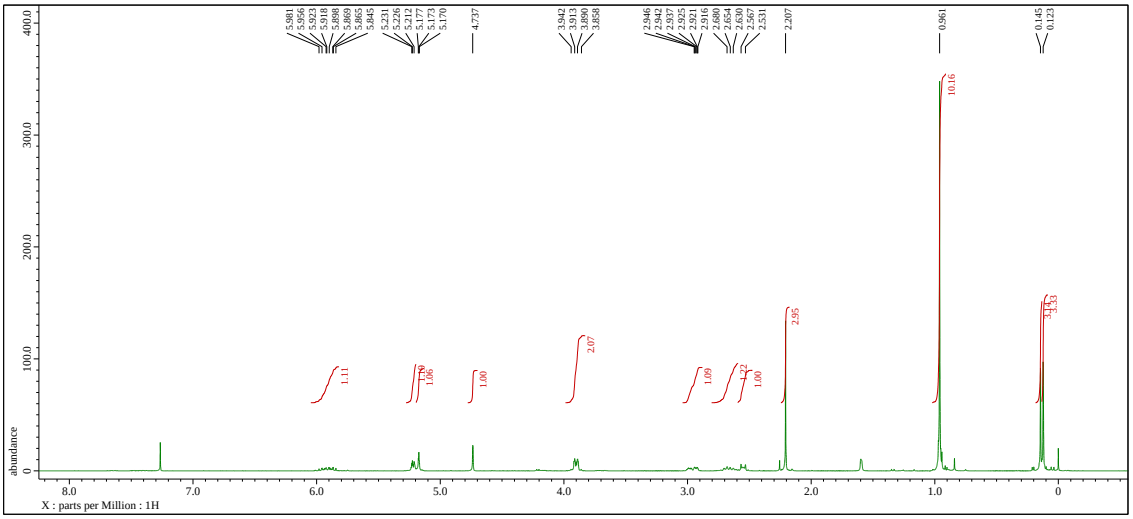
^{13}C-NMR (75 MHz, $CDCl_3$)



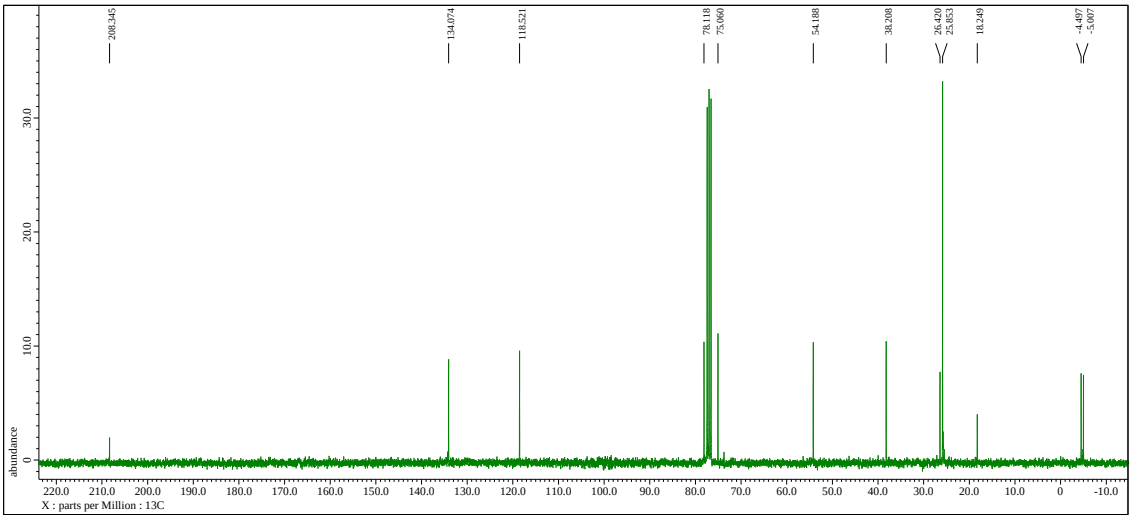
(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxyoct-7-en-2-one (3d)



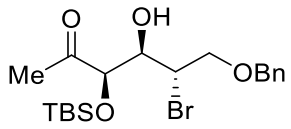
^{1}H-NMR (300 MHz, $CDCl_3$)



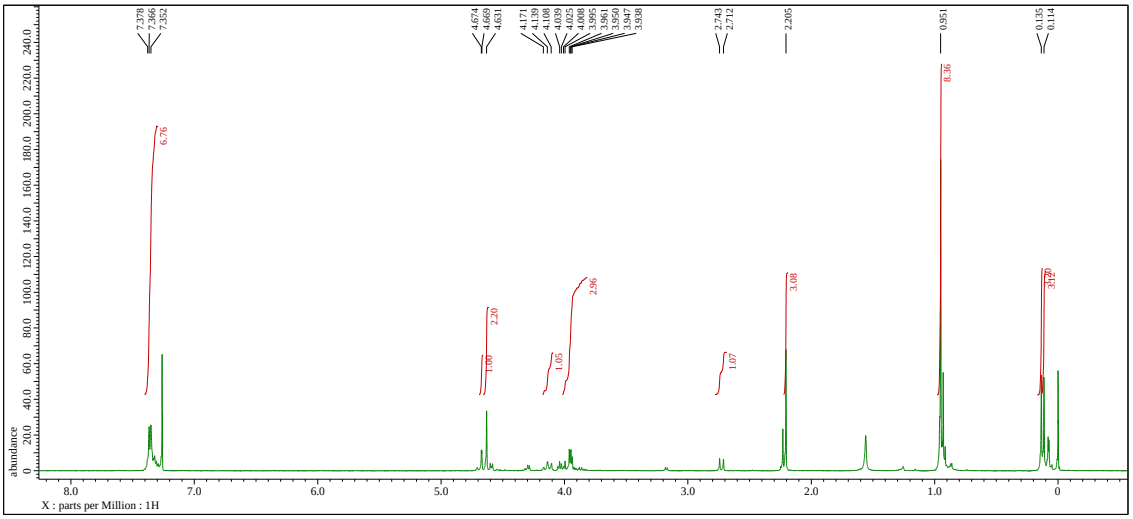
^{13}C-NMR (75 MHz, $CDCl_3$)



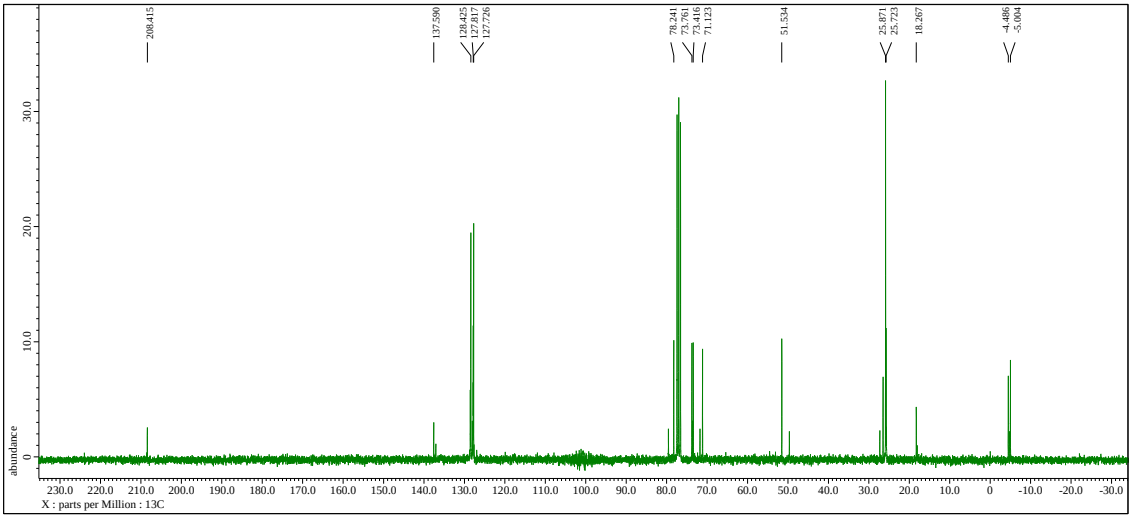
(3*R*,4*R*,5*S*)-6-(Benzyloxy)-5-bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxyhexan-2-one (3e)



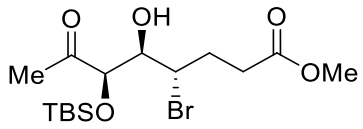
^{1}H-NMR (300 MHz, $CDCl_3$) (diastereomer mixture)



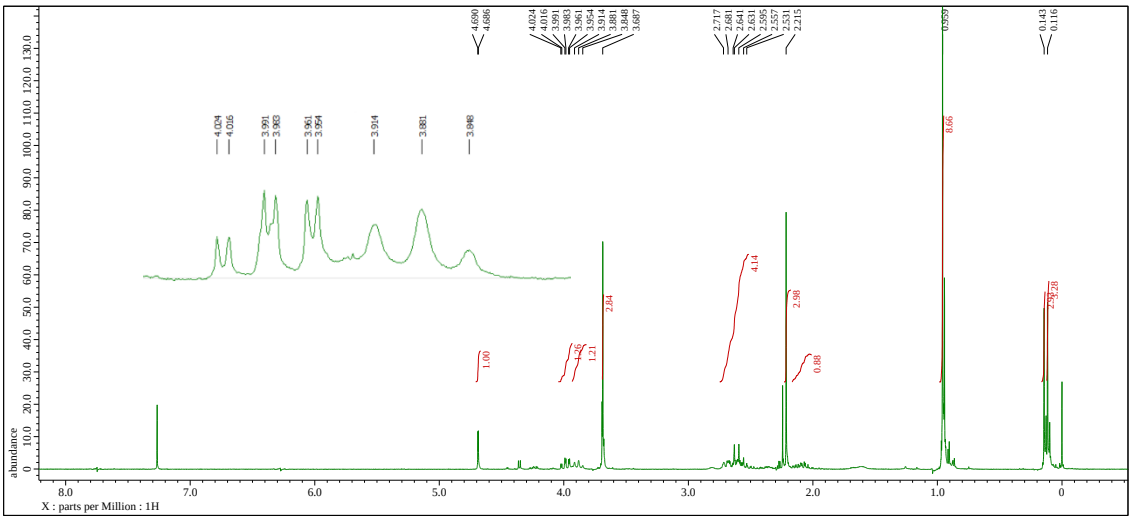
^{13}C-NMR (75 MHz, $CDCl_3$) (diastereomer mixture)



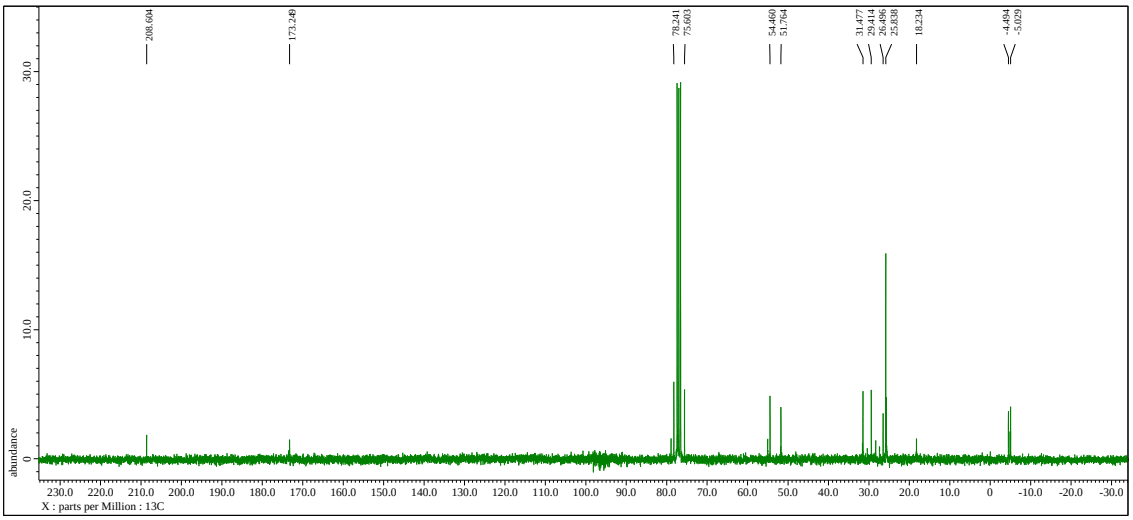
Methyl (4*S*,5*R*,6*R*)-4-bromo-6-((*tert*-butyldimethylsilyl)oxy)-5-hydroxy-7-oxooctanoate (3f)



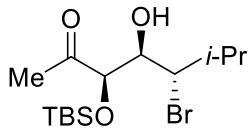
^{1}H-NMR (300 MHz, $CDCl_3$) (diastereomer mixture)



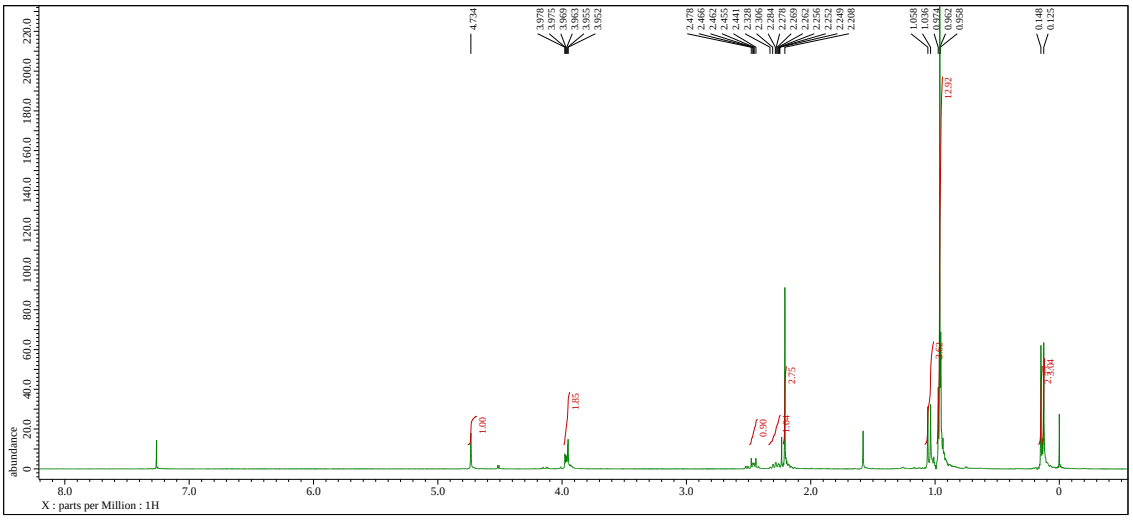
^{13}C-NMR (75 MHz, $CDCl_3$) (diastereomer mixture)



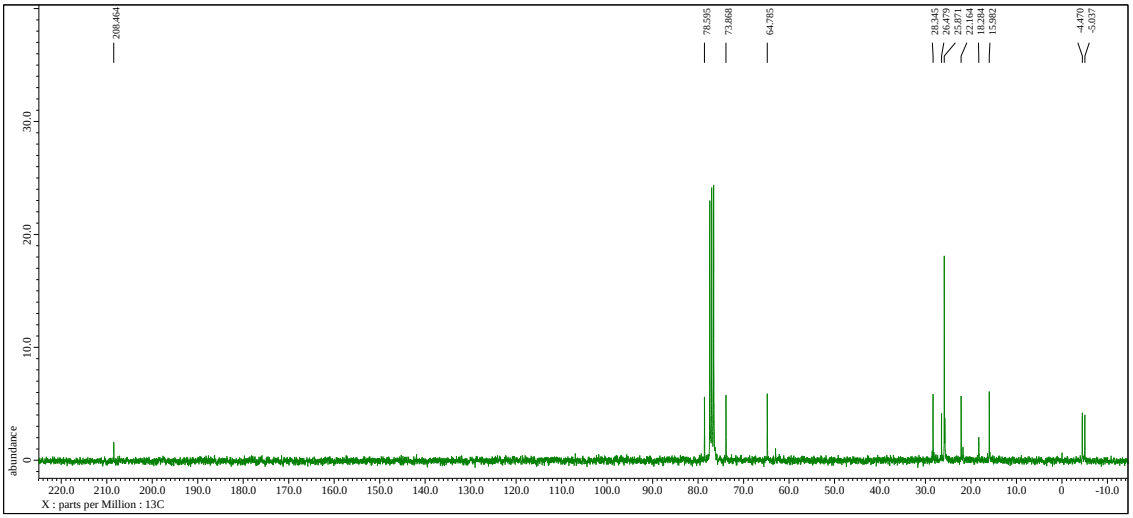
(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-methylheptan-2-one (3g)



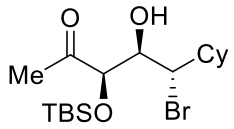
^{1}H-NMR (300 MHz, $CDCl_3$) (diastereomer mixture)



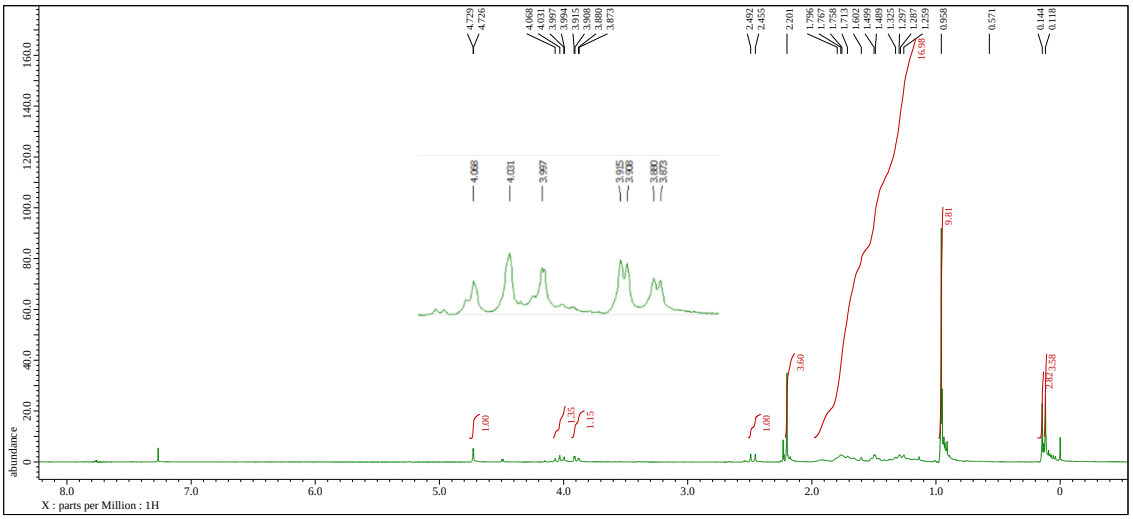
^{13}C-NMR (75 MHz, $CDCl_3$) (diastereomer mixture)



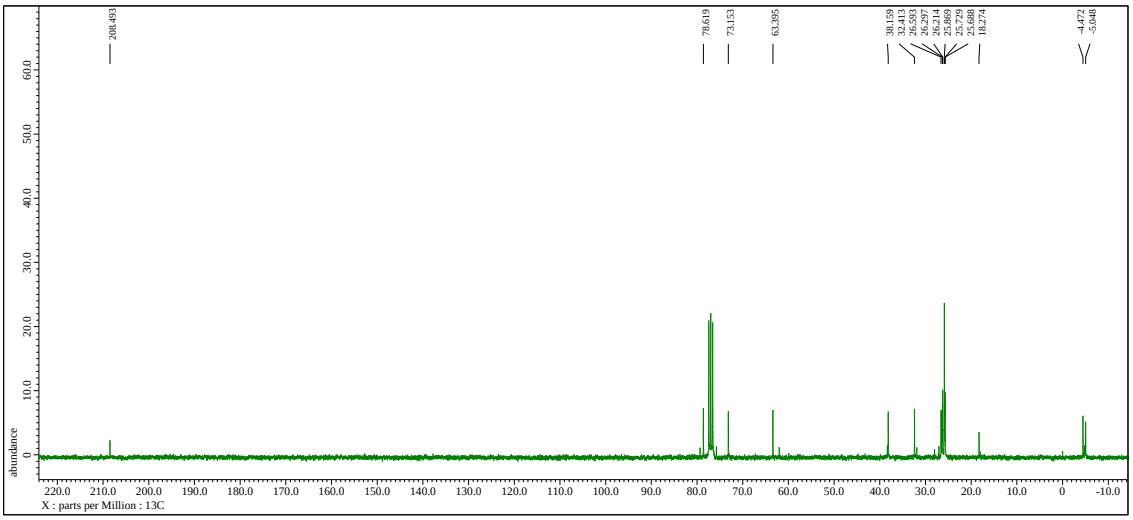
(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-5-cyclohexyl-4-hydroxypentan-2-one (3h)



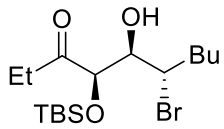
^{1}H-NMR (300 MHz, $CDCl_3$) (diastereomer mixture)



^{13}C-NMR (75 MHz, $CDCl_3$) (diastereomer mixture)



(4*R*,5*R*,6*S*)-6-Bromo-4-((*tert*-butyldimethylsilyl)oxy)-5-hydroxydecan-3-one (3i)



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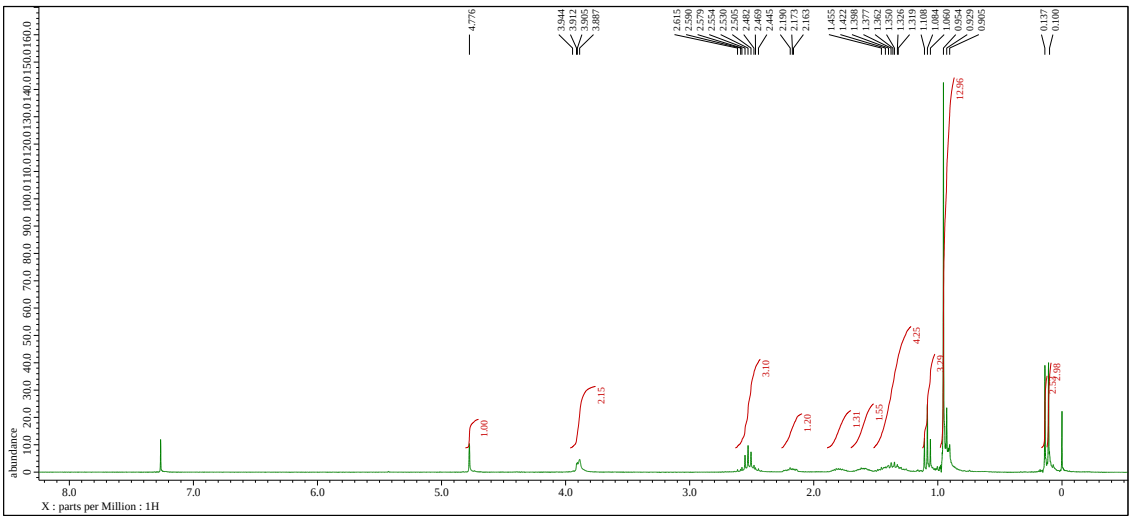

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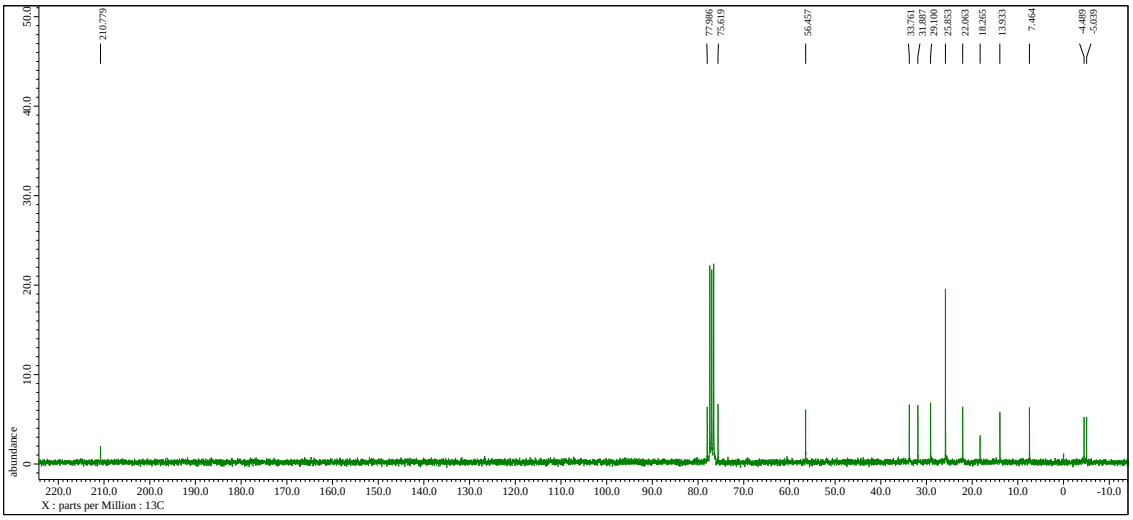
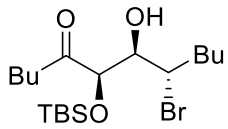


(6*R*,7*R*,8*S*)-8-Bromo-6-((*tert*-butyldimethylsilyl)oxy)-7-hydroxydodecan-5-one (3j)



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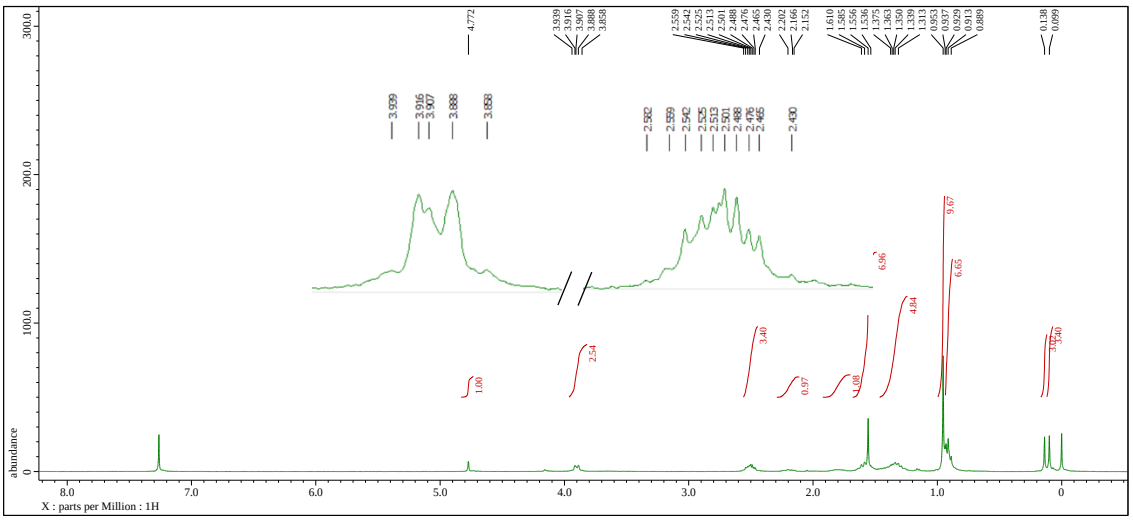

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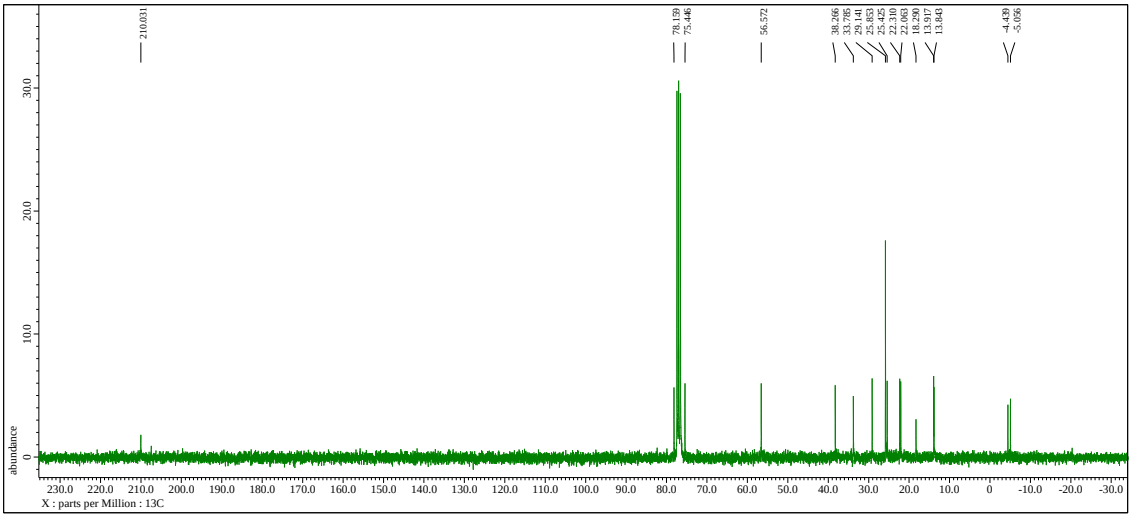
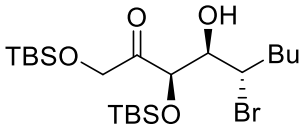
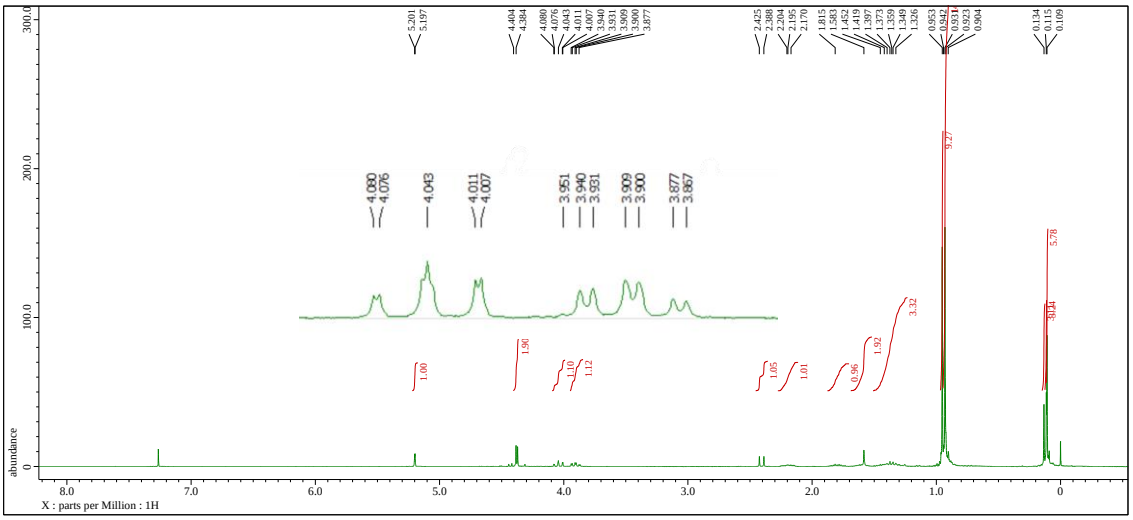


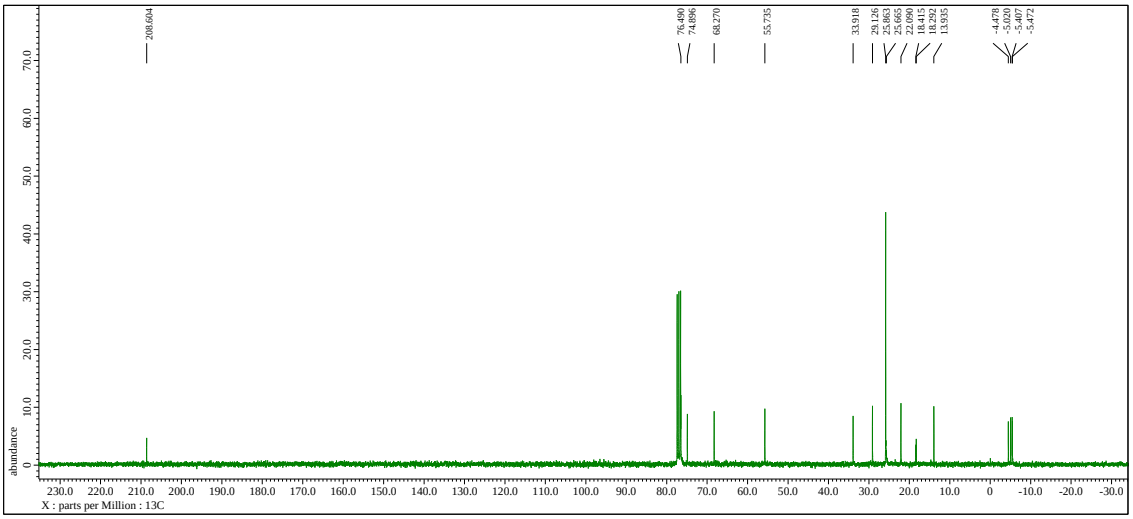
(3*R*,4*R*,5*S*)-1,3-Bis((*tert*-butyldimethylsilyl)oxy)-5-bromo-4-hydroxynonan-2-one (3k)



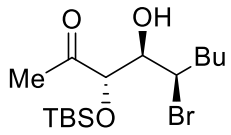
^{1}H-NMR (300 MHz, $CDCl_3$)



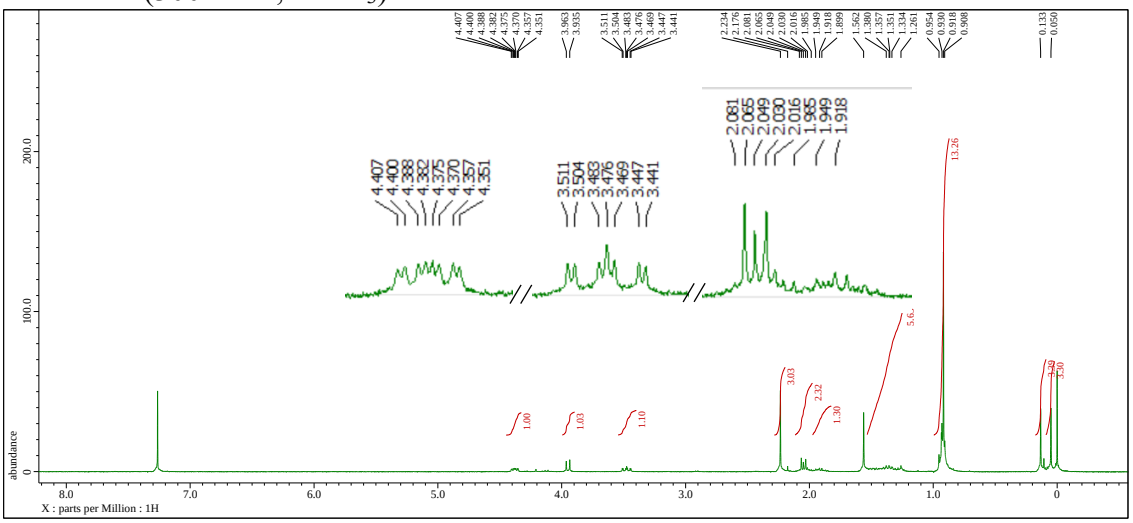
^{13}C-NMR (75 MHz, $CDCl_3$)



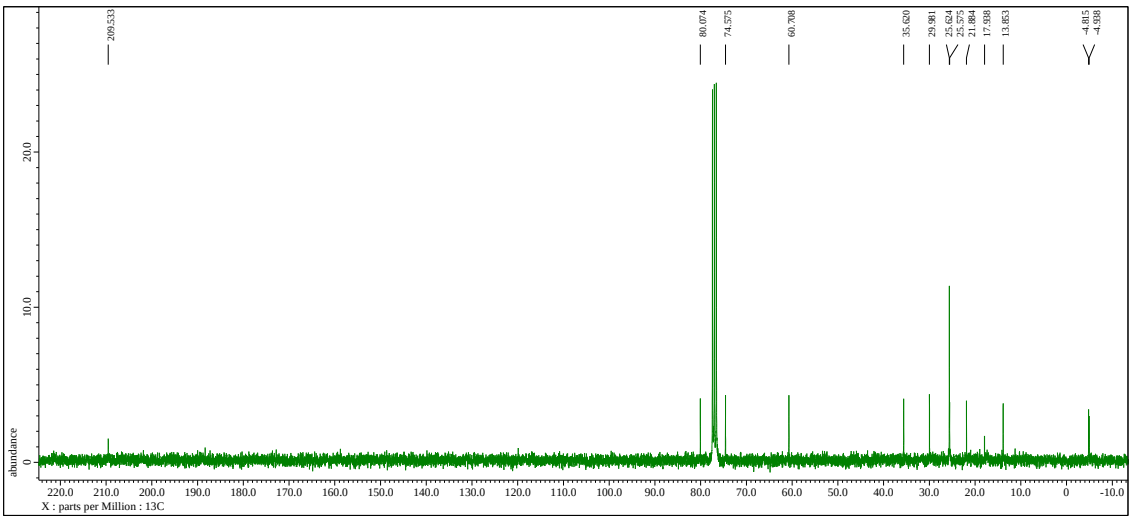
(3*S*,4*R*,5*R*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3l)



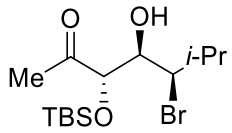
^{1}H-NMR (300 MHz, $CDCl_3$)



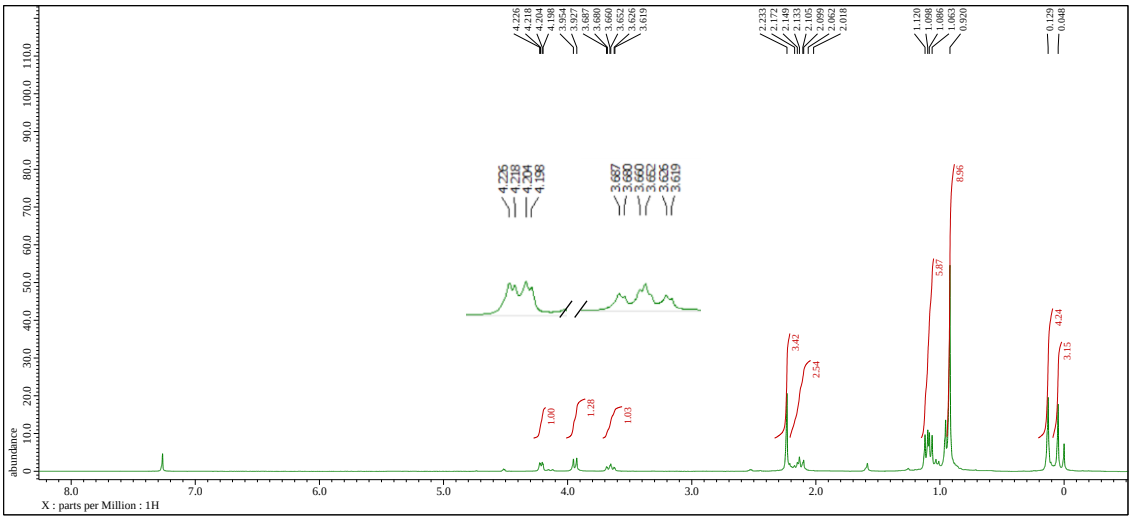
^{13}C-NMR (75 MHz, $CDCl_3$)



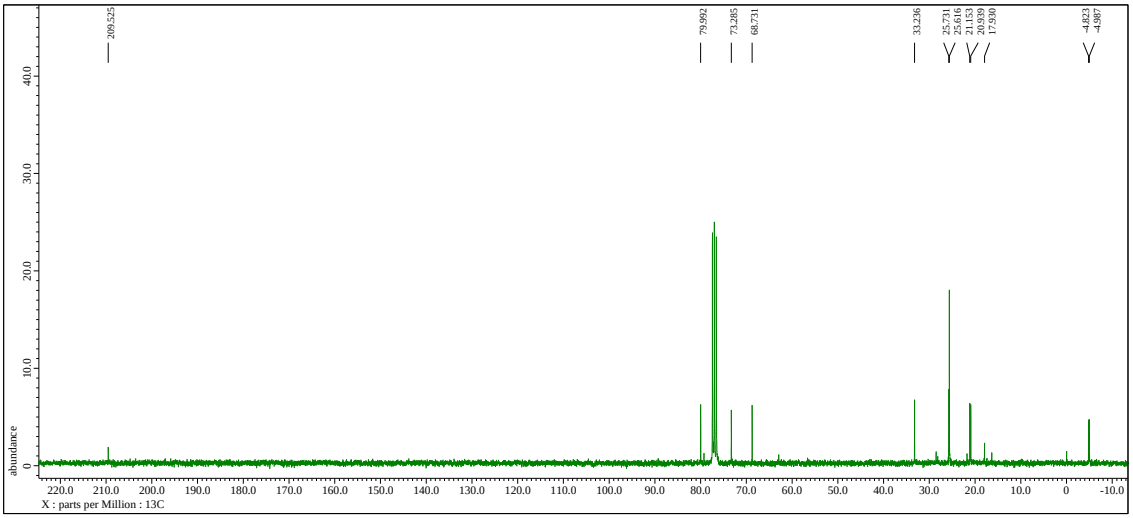
(3*S*,4*R*,5*R*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-methylheptan-2-one (3m)



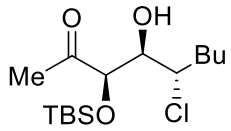
^{1}H-NMR (300 MHz, $CDCl_3$) (diastereomer mixture)



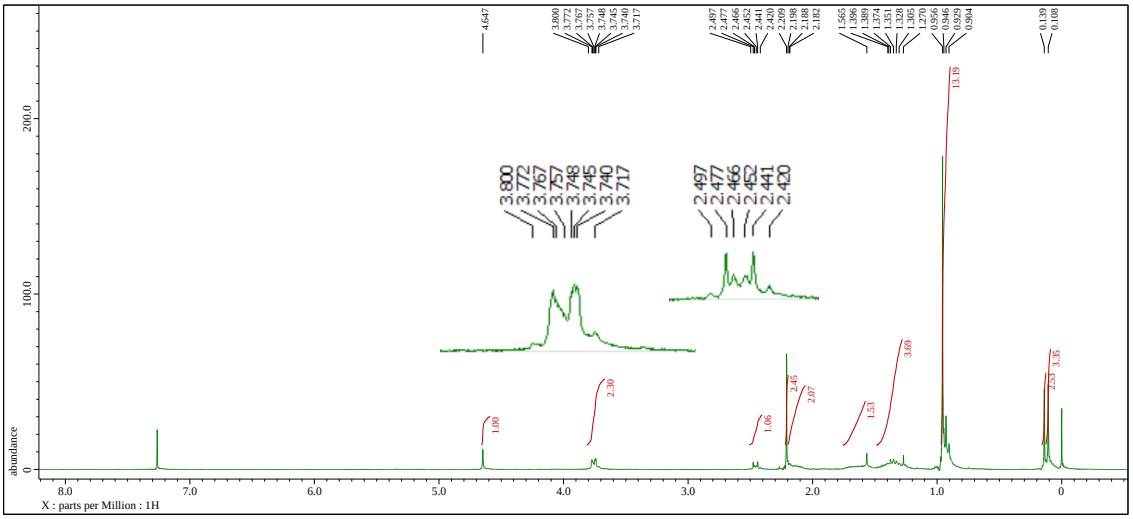
^{13}C-NMR (75 MHz, $CDCl_3$) (diastereomer mixture)



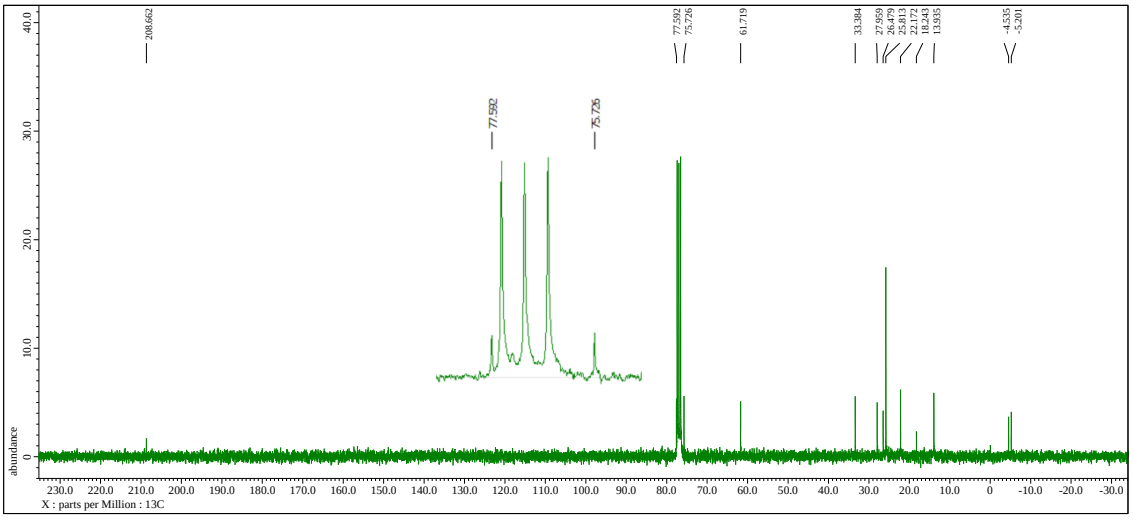
(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxynonan-2-one (9a)



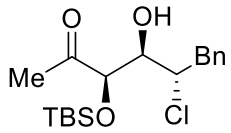
^{1}H-NMR (300 MHz, $CDCl_3$)



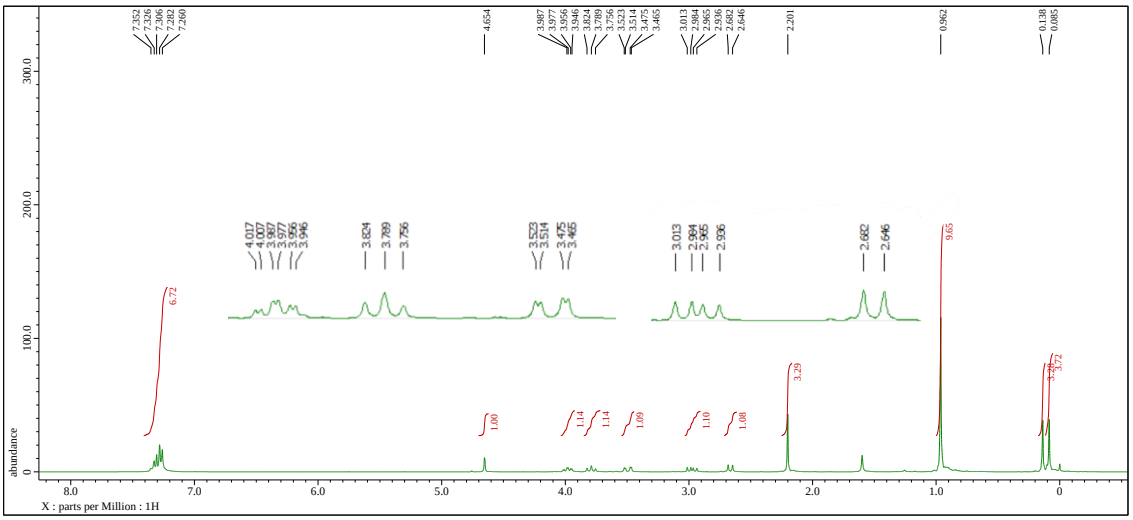
^{13}C-NMR (75 MHz, $CDCl_3$)



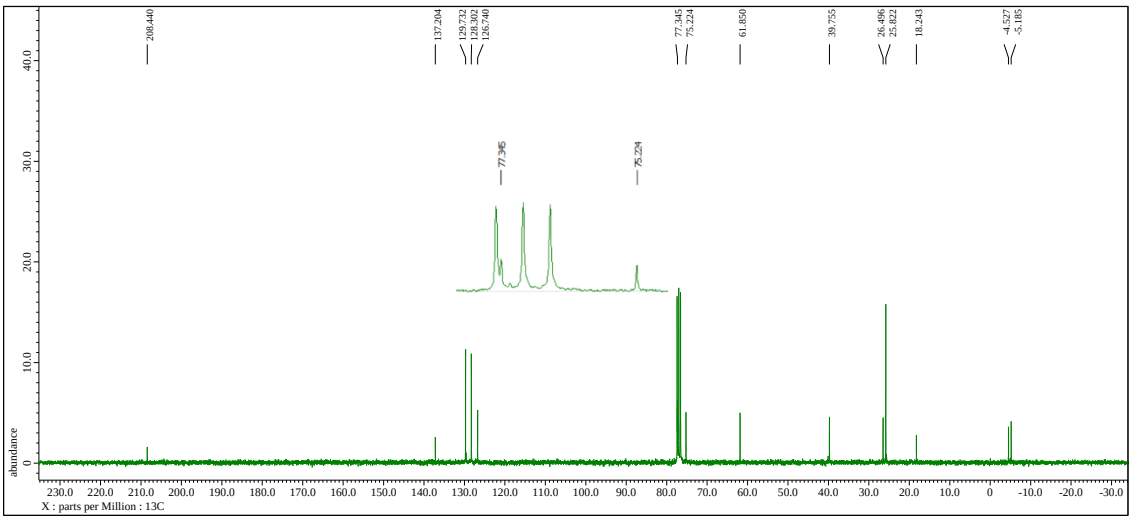
(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-phenylhexan-2-one (9b)



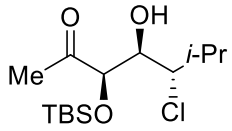
^{1}H-NMR (300 MHz, $CDCl_3$)



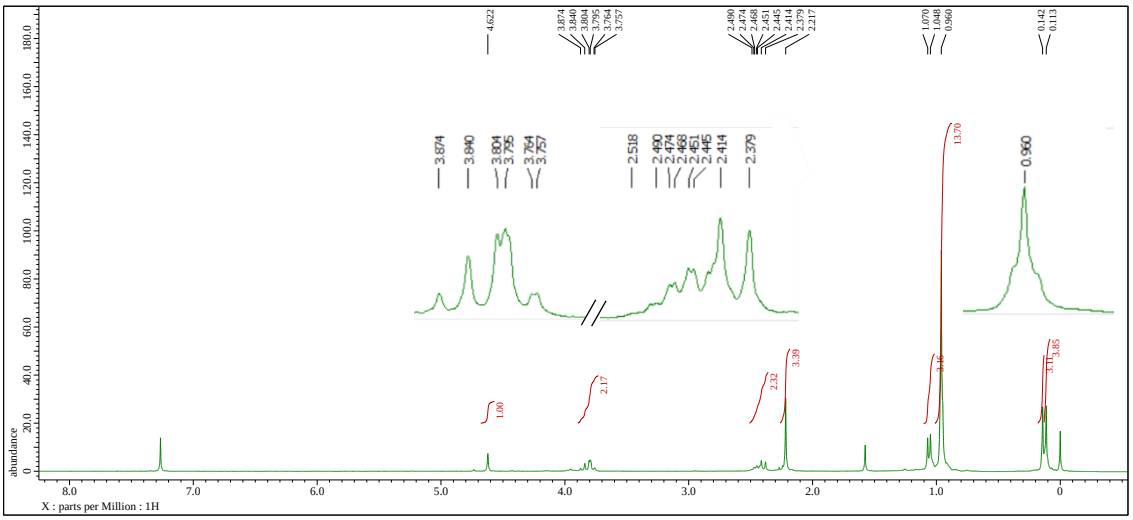
^{13}C-NMR (75 MHz, $CDCl_3$)



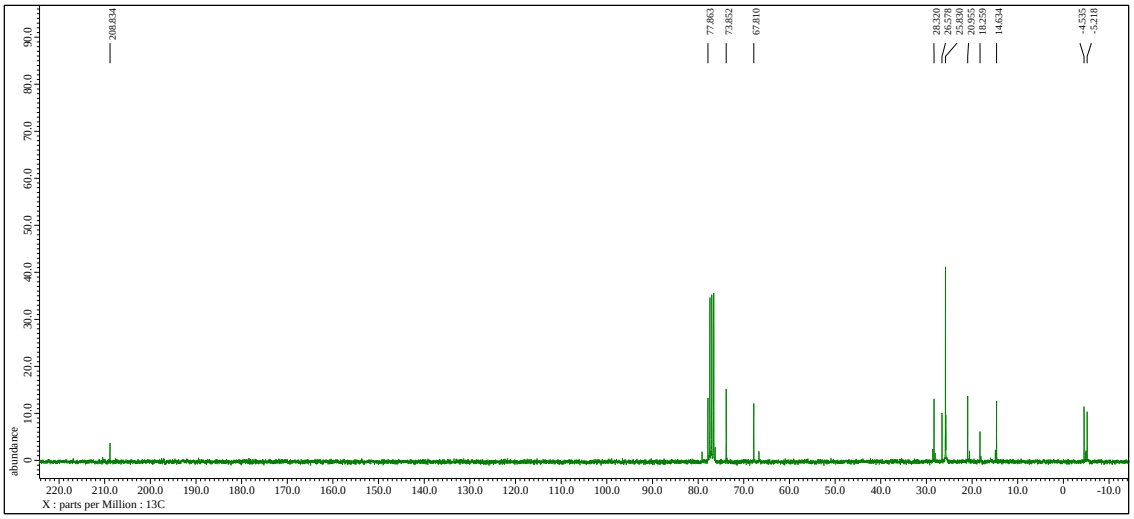
(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-methylheptan-2-one (9c)



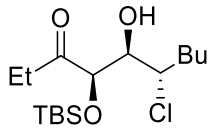
^{1}H-NMR (300 MHz, $CDCl_3$) (diastereomer mixture)



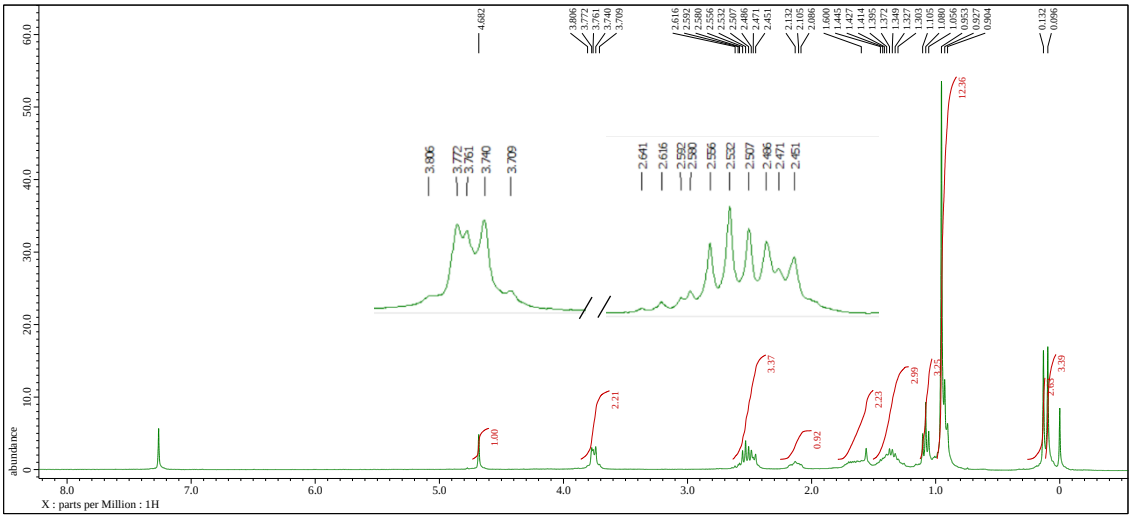
^{13}C-NMR (75 MHz, $CDCl_3$) (diastereomer mixture)



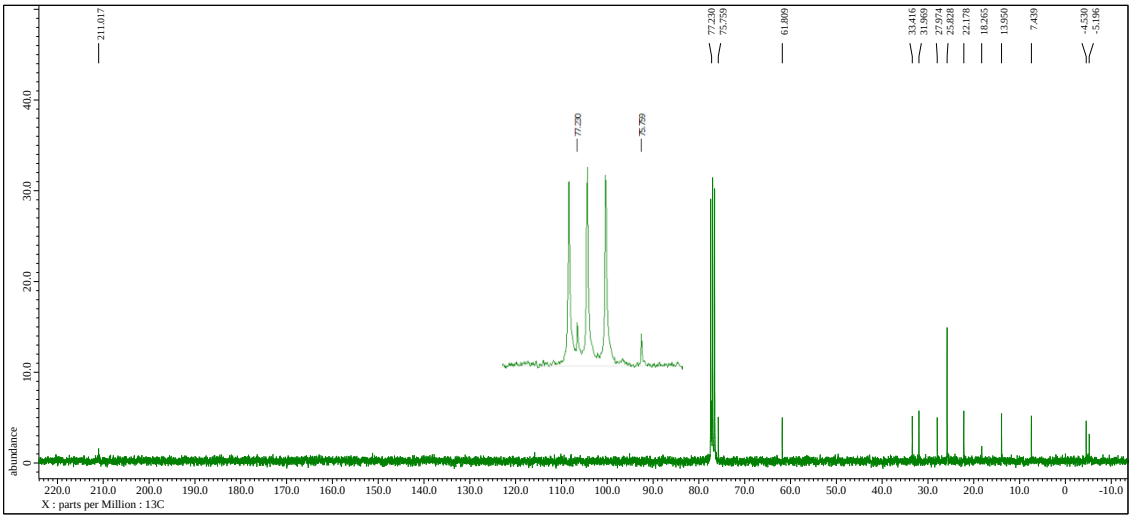
(4*R*,5*R*,6*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-6-chloro-5-hydroxydecan-3-one (9d)



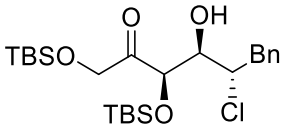
^{1}H-NMR (300 MHz, $CDCl_3$)



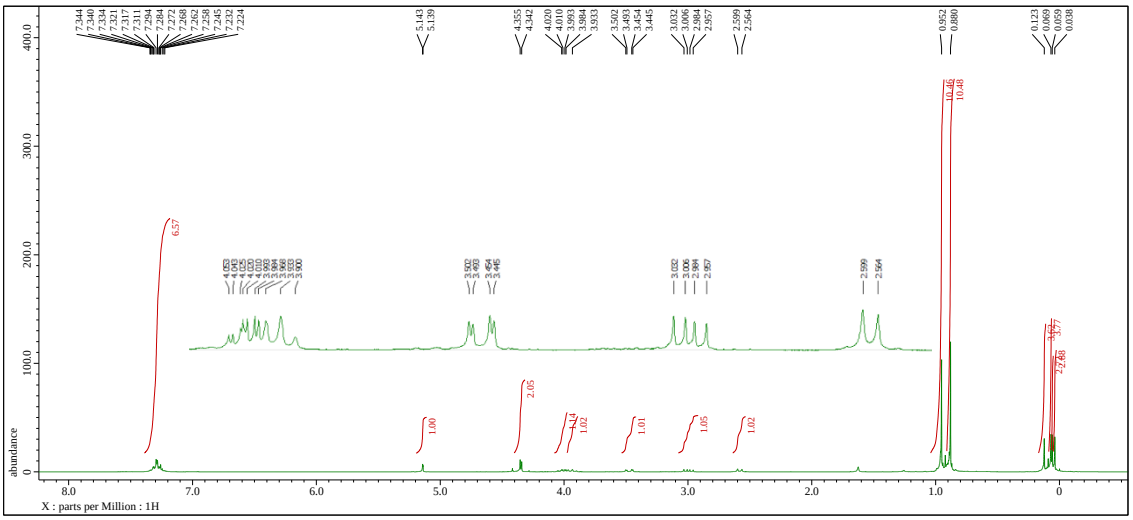
^{13}C-NMR (75 MHz, $CDCl_3$)



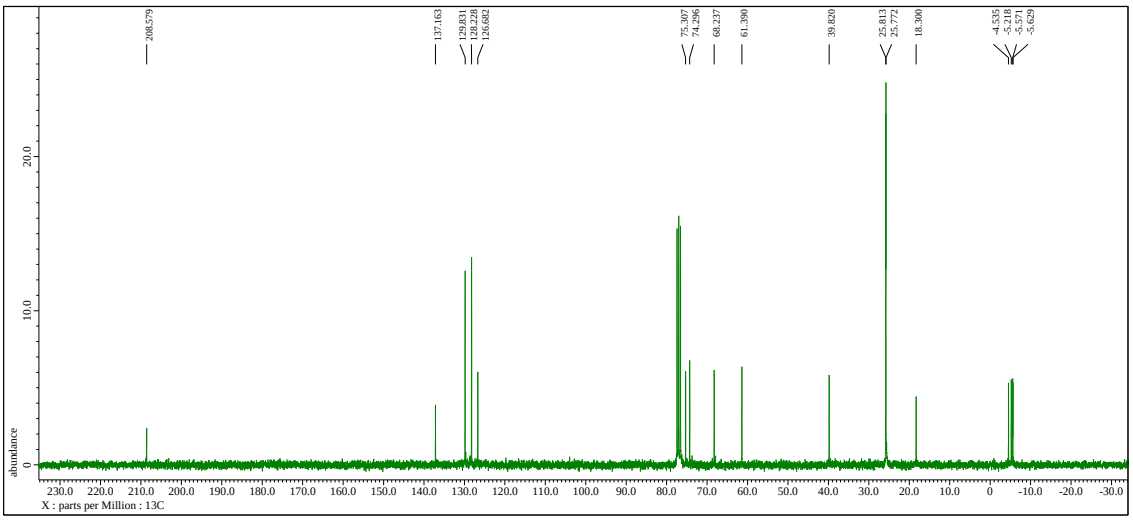
(3*R*,4*R*,5*S*)-1,3-Bis((*tert*-butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-phenyl hexane-2-one (9e)



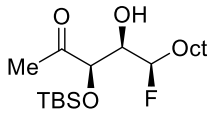
^{1}H-NMR (300 MHz, $CDCl_3$)



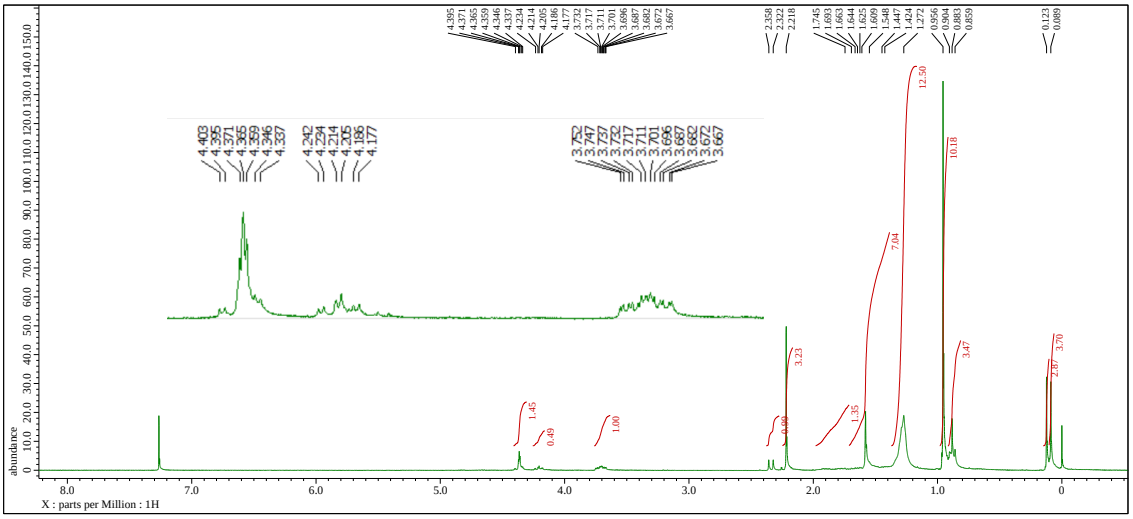
^{13}C-NMR (75 MHz, $CDCl_3$)



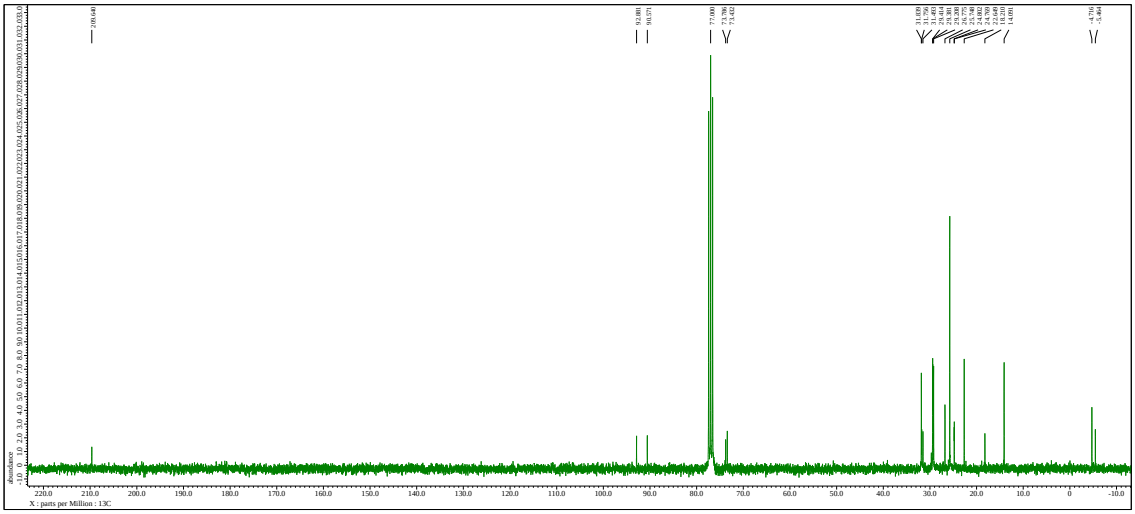
(3*R*,4*R*,5*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-fluoro-4-hydroxytridecan-2-one (8a)



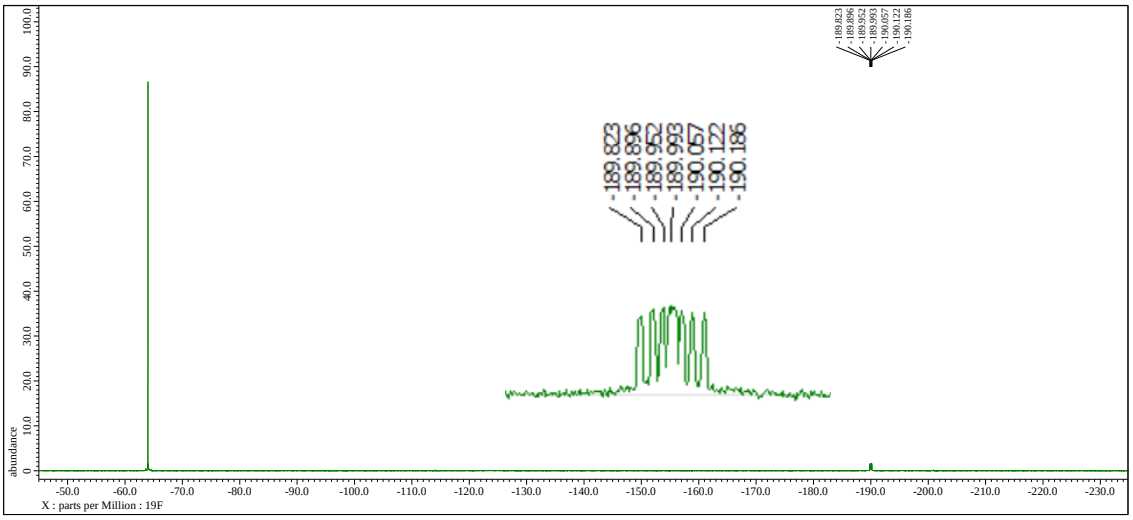
^{1}H-NMR (300 MHz, $CDCl_3$)



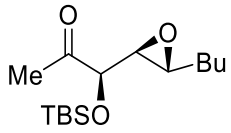
^{13}C-NMR (75 MHz, $CDCl_3$)



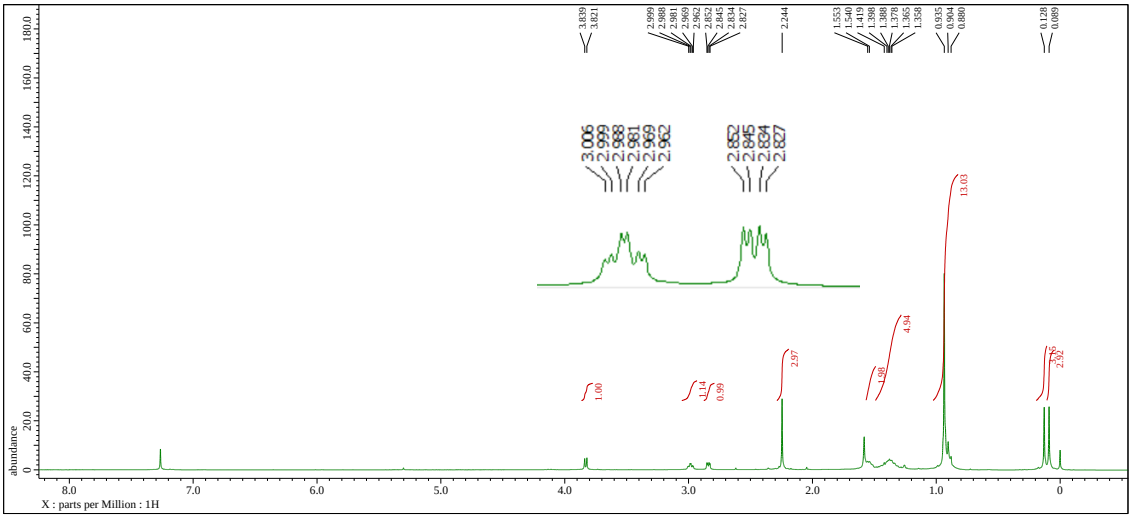
^{19}F-NMR (283 MHz, $CDCl_3$)



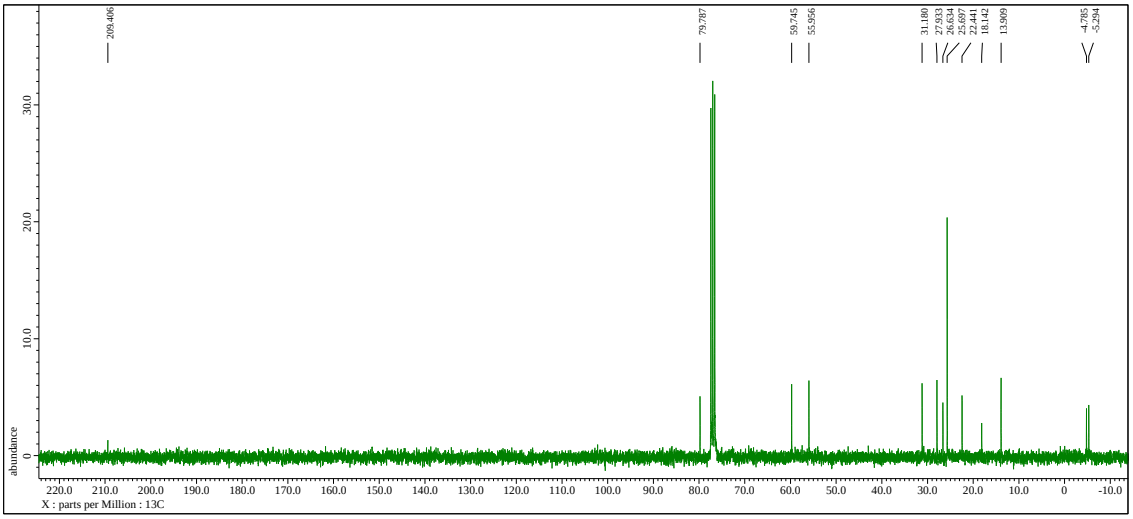
(*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-1-((2*S*,3*R*)-3-butyloxiran-2-yl)propan-2-one (13)



^{1}H-NMR (300 MHz, $CDCl_3$)

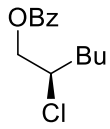


^{13}C-NMR (75 MHz, $CDCl_3$)

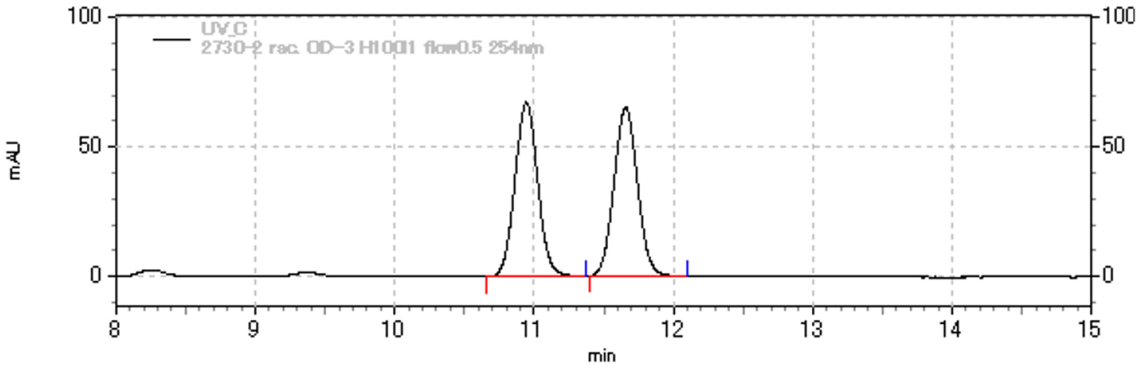


17. HPLC spectra

2-Chlorohexyl benzoate (12)

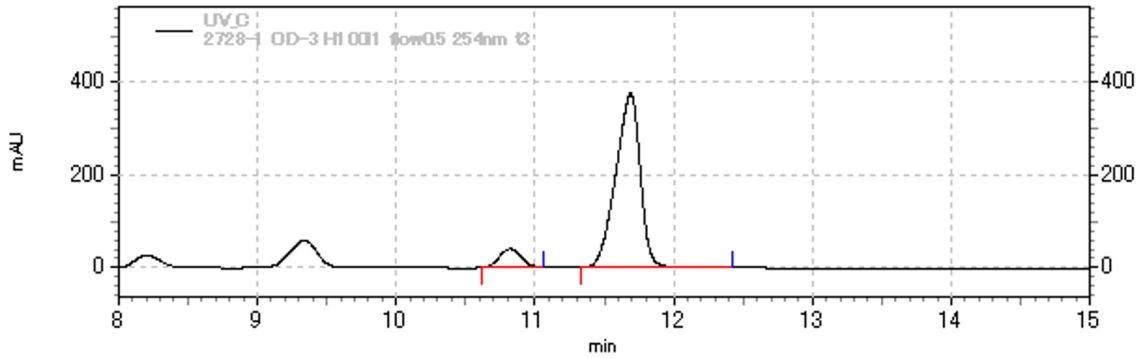


HPLC analysis: Daicel Chiralpak OD–3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ = 254 nm, retention time: 11.0 min (minor) and 11.7 min (major).



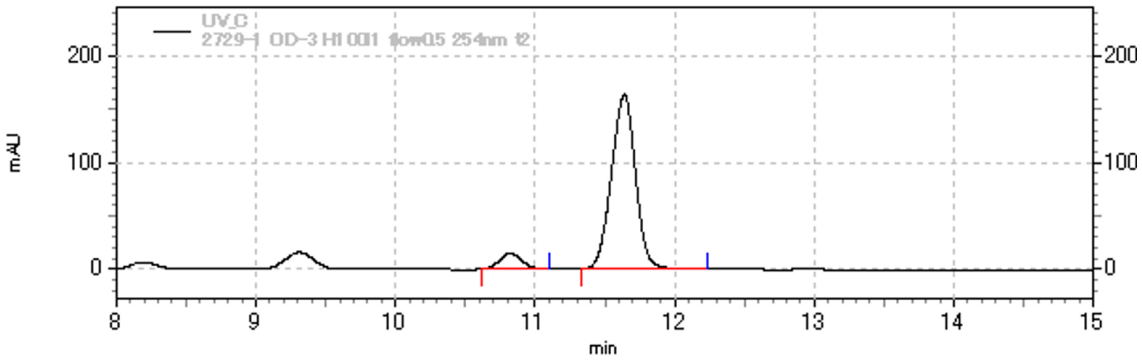
UV_C結果			
No	RT	Area	Area%
1	10.95	766796	50.062
2	11.66	764886	49.938
トータル			
		1531682	100.000

(1)



UV_C結果			
No	RT	Area	Area%
1	10.82	440943	8.690
2	11.69	4632936	91.310
トータル			
		5073879	100.000

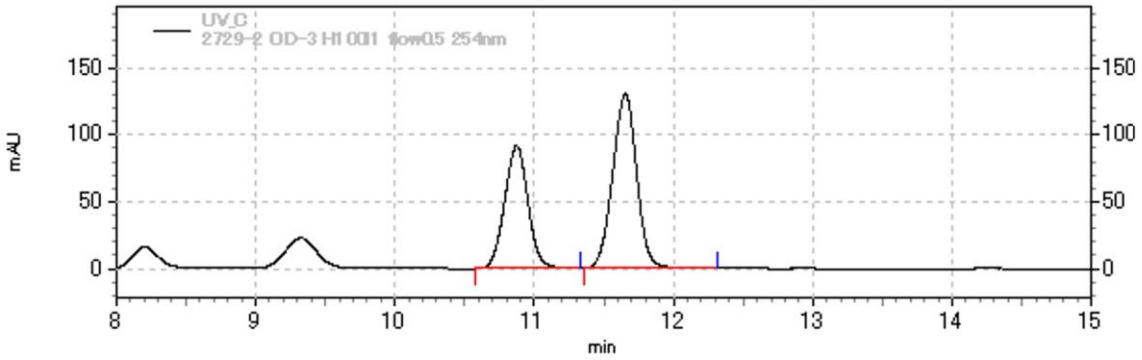
(2)



UV C結果

No	RT	Area	Area%
1	10.82	166004	7.768
2	11.64	1971112	92.232
トータル		2137116	100.000

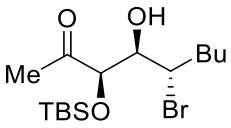
(3)



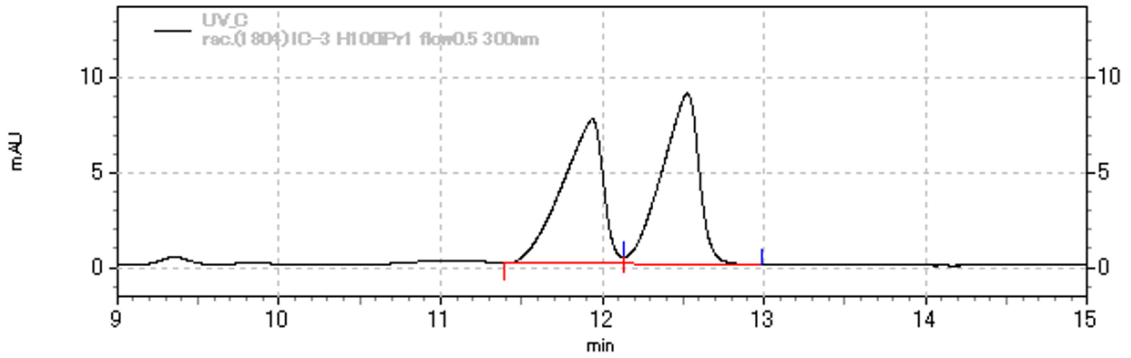
UV C結果

No	RT	Area	Area%
1	10.87	1065049	40.595
2	11.65	1558523	59.405
トータル		2623572	100.000

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3a)

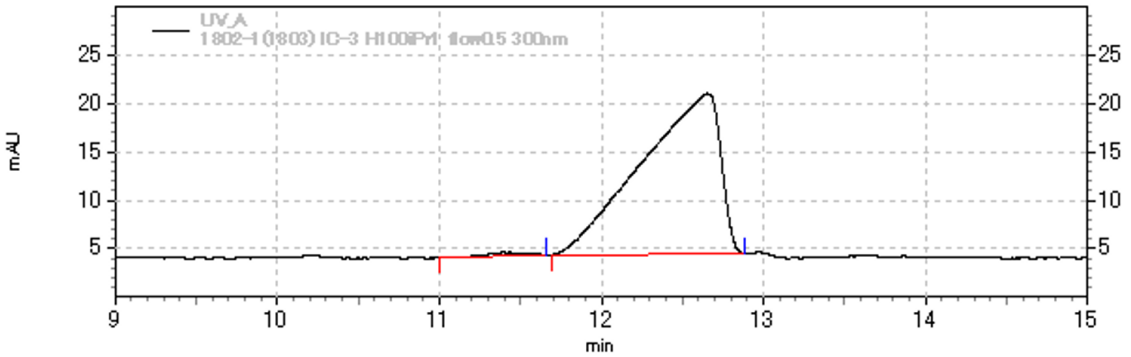


HPLC analysis: Daicel Chiralpak IC–3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ = 300 nm, retention time: 11.4 min (minor) and 12.7 min (major).



UV_C結果

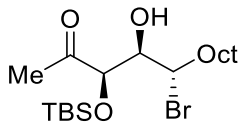
No	RT	Area	Area%
1	11.94	135682	48.434
2	12.53	144455	51.566
トータル		280137	100.000



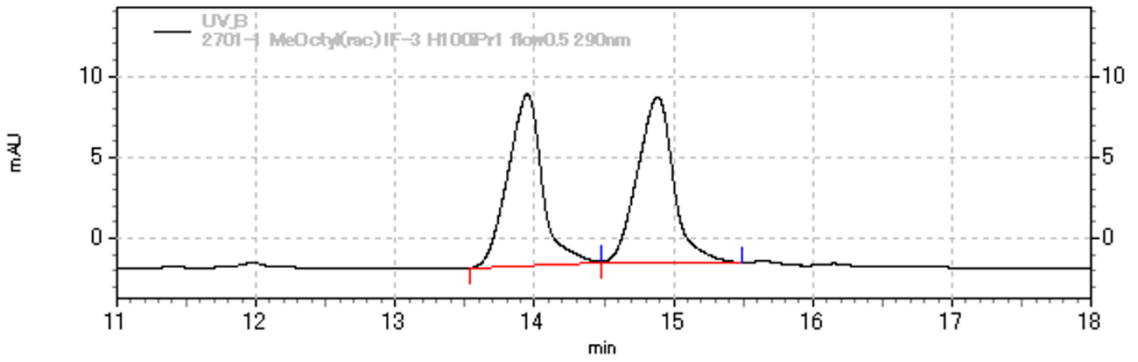
UV_A結果

No	RT	Area	Area%
1	11.40	6330	1.121
2	12.65	558398	98.879
トータル		564728	100.000

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxytridecan-2-one (3b)

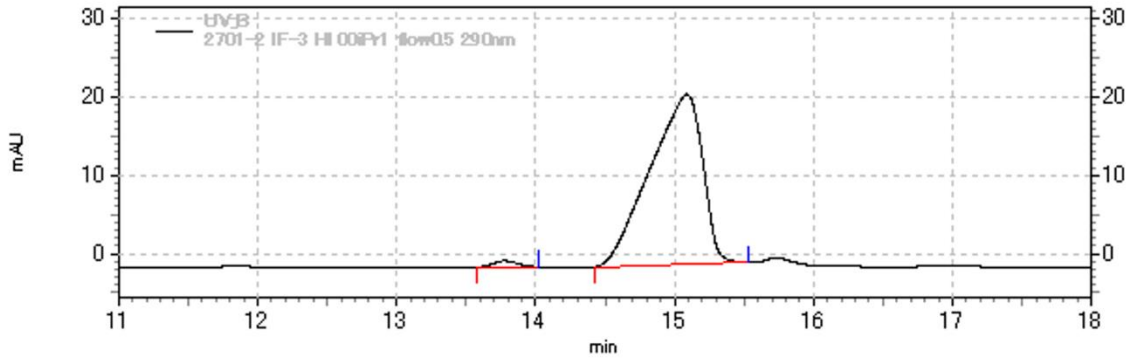


HPLC analysis: Daicel Chiralpak IF–3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ = 290 nm, retention time: 13.8 min (minor) and 15.1 min (major).



UV_B結果

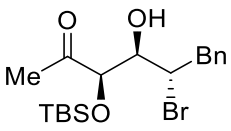
No	RT	Area	Area%
1	13.95	180017	49.612
2	14.88	182832	50.388
トータル		362849	100.000



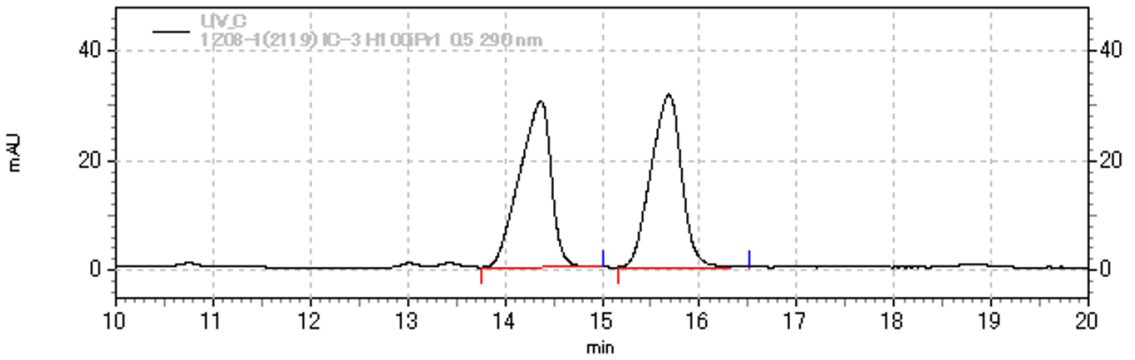
UV_B結果

No	RT	Area	Area%
1	13.78	9548	1.640
2	15.09	572649	98.360
トータル		582197	100.000

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-phenylhexan-2-one (3c)

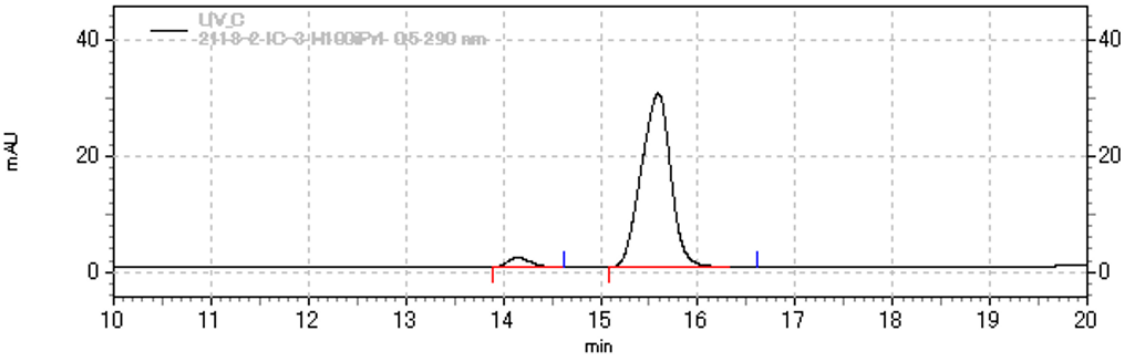


HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min,λ= 290 nm, retention time: 14.2 min (minor) and 15.6 min (major).



UV_C結果

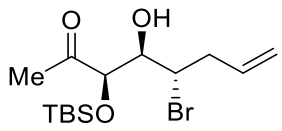
No	RT	Area	Area%
1	14.37	683320	49.811
2	15.69	688504	50.189
トータル		1371824	100.000



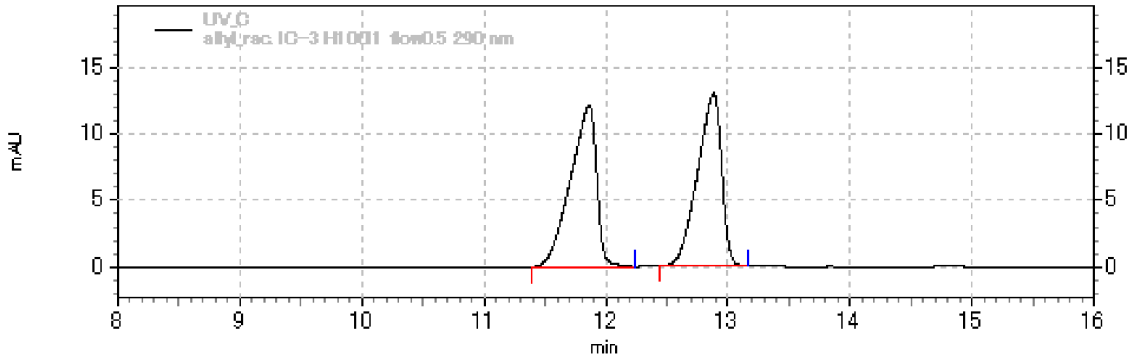
UV_C結果

No	RT	Area	Area%
1	14.15	26746	4.069
2	15.59	630493	95.931
トータル		657239	100.000

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxyoct-7-en-2-one (3d)

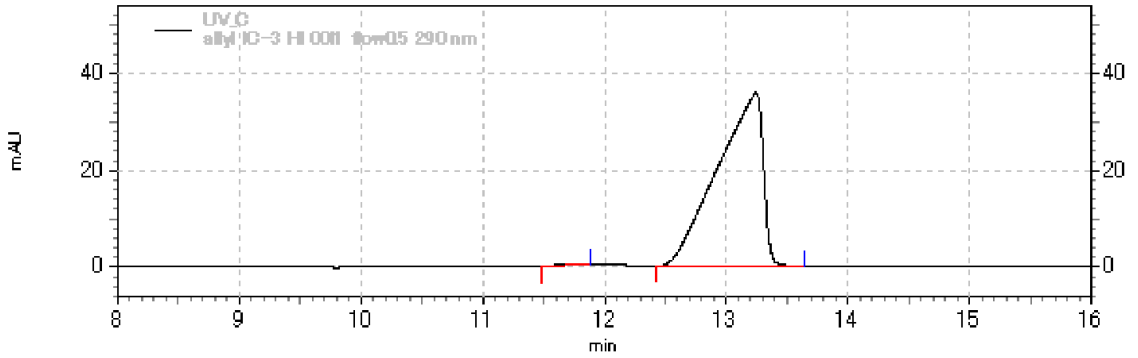


HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 11.7 min (minor) and 13.2 min (major).



UV_C結果

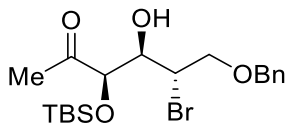
No	RT	Area	Area%
1	11.86	180442	50.357
2	12.88	177885	49.643
トータル		358327	100.000



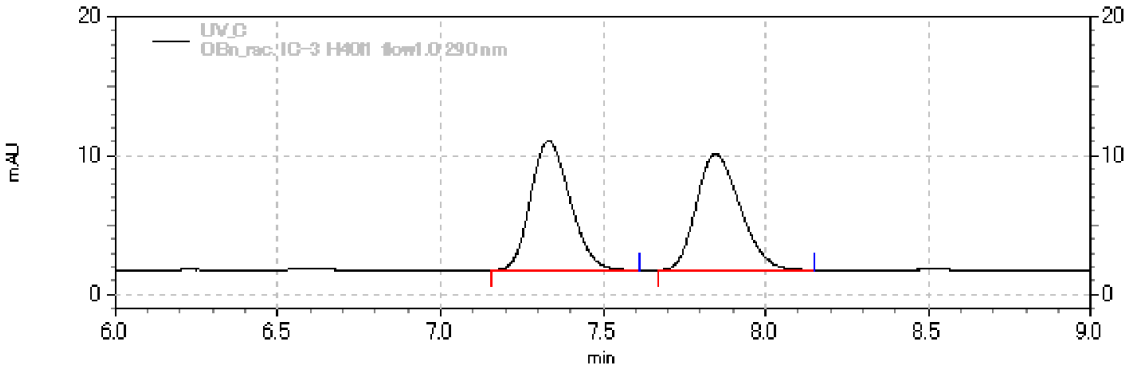
UV_C結果

No	RT	Area	Area%
1	11.70	4952	0.526
2	13.25	936317	99.474
トータル		941269	100.000

(3*R*,4*R*,5*S*)-6-(Benzyloxy)-5-bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxyhexan-2-one (3e)

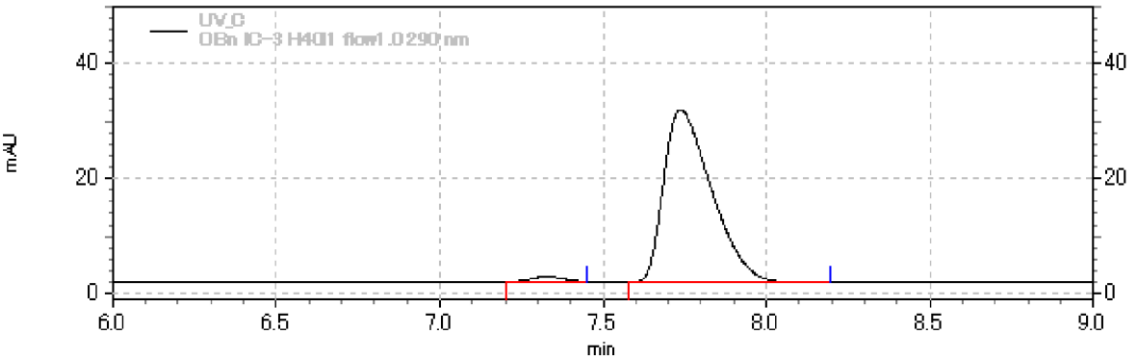


HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 40:1, flow rate 1.0 mL/min, λ= 290 nm, retention time: 7.3 min (minor) and 7.7 min (major).



UV_C結果

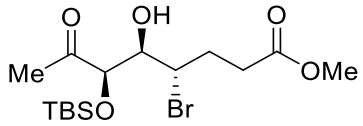
No	RT	Area	Area%
1	7.33	78400	50.166
2	7.85	77882	49.834
トータル		156282	100.000



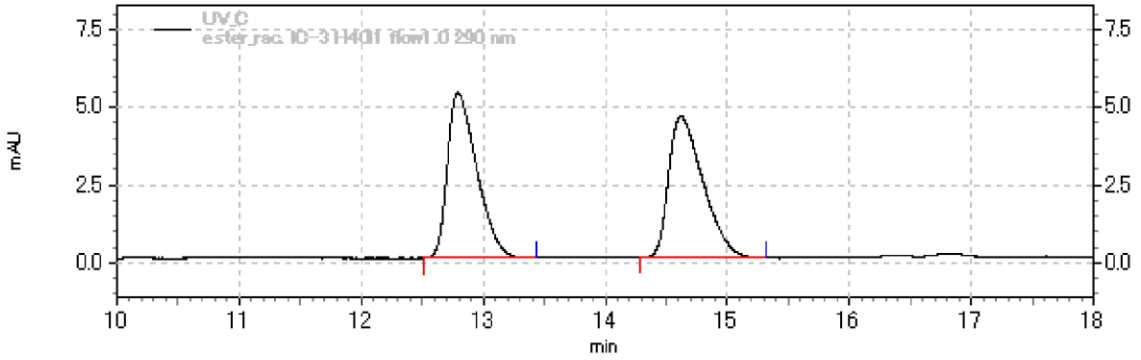
UV_C結果

No	RT	Area	Area%
1	7.33	7272	2.316
2	7.74	306725	97.684
トータル		313997	100.000

Methyl (4*S*,5*R*,6*R*)-4-bromo-6-((*tert*-butyldimethylsilyl)oxy)-5-hydroxy-7-oxooctanoate (3f)

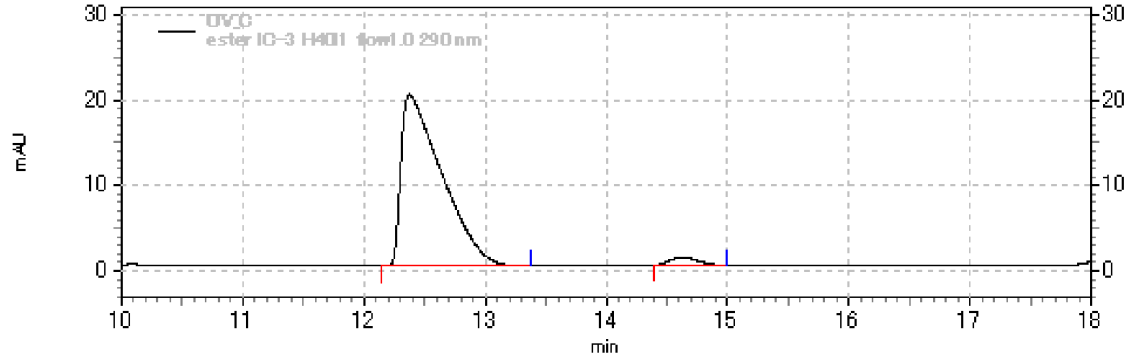


HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 40:1, flow rate 1.0 mL/min, λ= 290 nm, retention time: 12.4 min (major) and 14.6 min (minor).



UV C結果

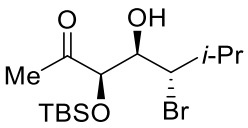
No	RT	Area	Area%
1	12.79	89495	50.066
2	14.62	89260	49.934
トータル		178755	100.000



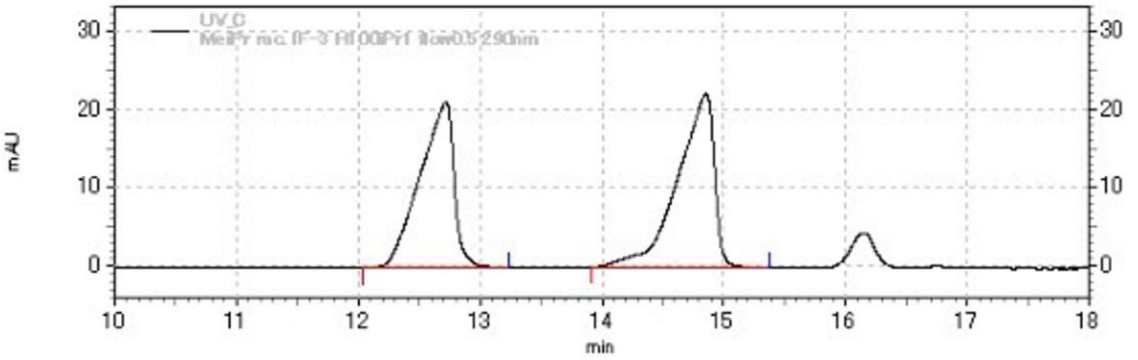
UV C結果

No	RT	Area	Area%
1	12.38	467301	96.827
2	14.62	15311	3.173
トータル		482612	100.000

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-methylheptan-2-one (3g)

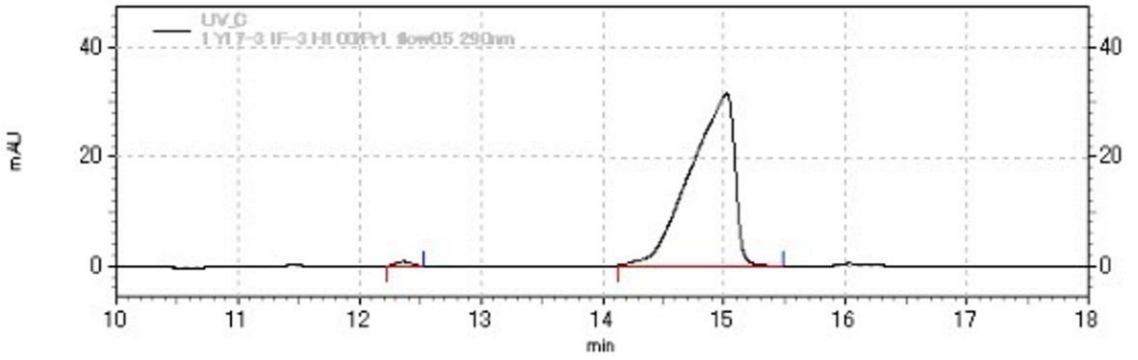


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 12.4 min (minor) and 15.0 min (major).



UV C結果

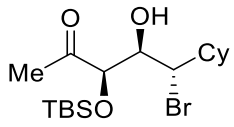
No	RT	Area	Area%
1	12.72	413474	47.011
2	14.85	466059	52.989
トータル		879533	100.000



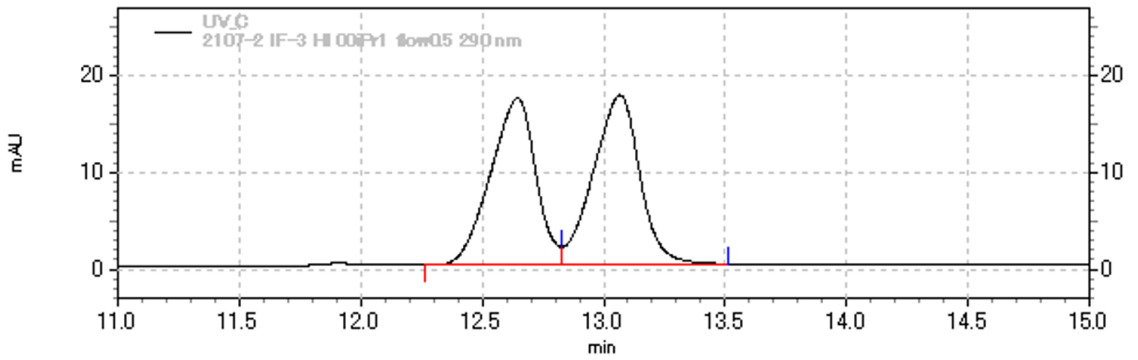
UV C結果

No	RT	Area	Area%
1	12.37	7250	0.906
2	15.02	792737	99.094
トータル		799987	100.000

(3*R*,4*R*,5*S*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-5-cyclohexyl-4-hydroxypentan-2-one (3h)

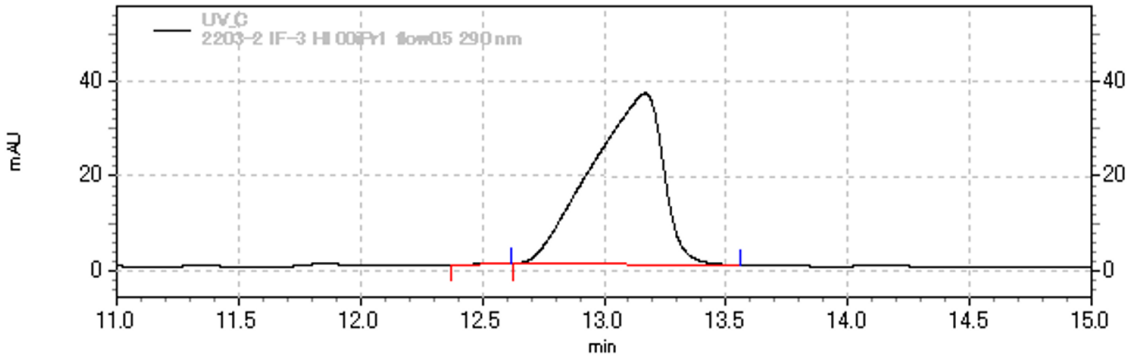


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 12.5 min (minor) and 13.2 min (major).



UV_C結果

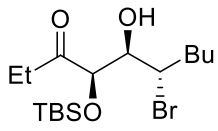
No	RT	Area	Area%
1	12.65	224086	48.573
2	13.07	237254	51.427
トータル		461340	100.000



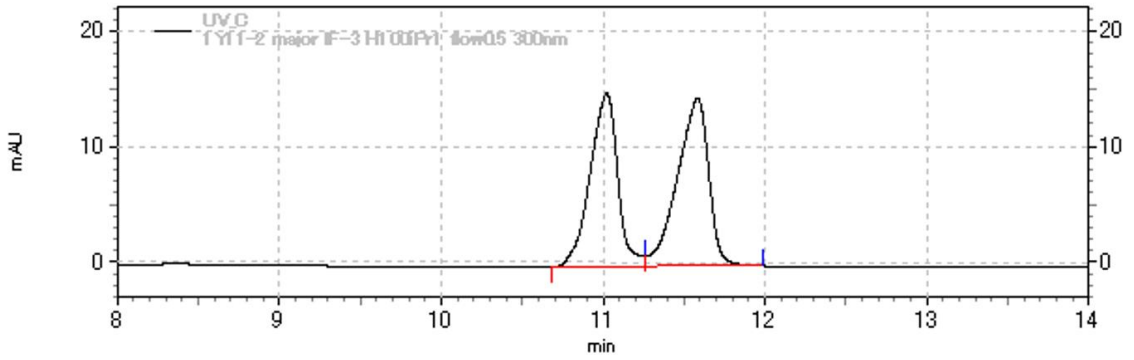
UV_C結果

No	RT	Area	Area%
1	12.53	1218	0.165
2	13.17	735310	99.835
トータル		736528	100.000

(4*R*,5*R*,6*S*)-6-bromo-4-((*tert*-butyldimethylsilyl)oxy)-5-hydroxydecan-3-one (3i)

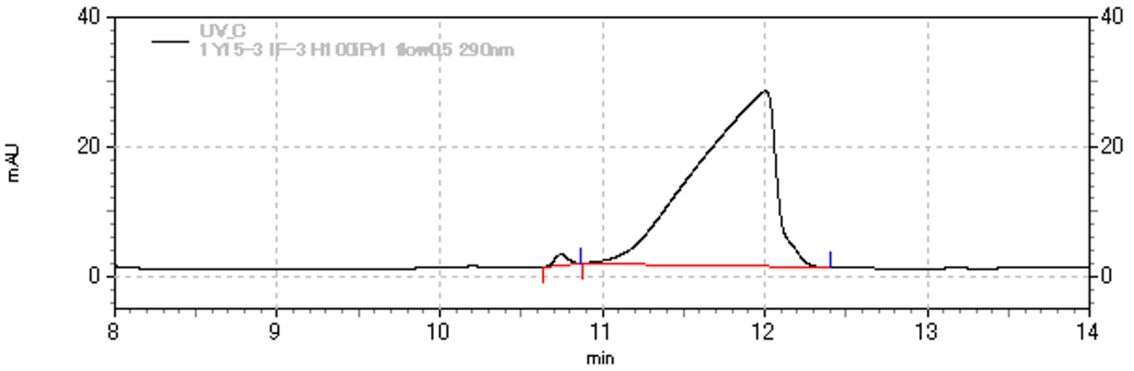


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.8 min (minor) and 12.0 min (major).



UV C結果

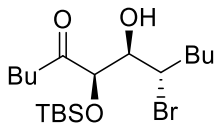
No	RT	Area	Area%
1	11.02	177916	47.630
2	11.58	195619	52.370
トータル		373535	100.000



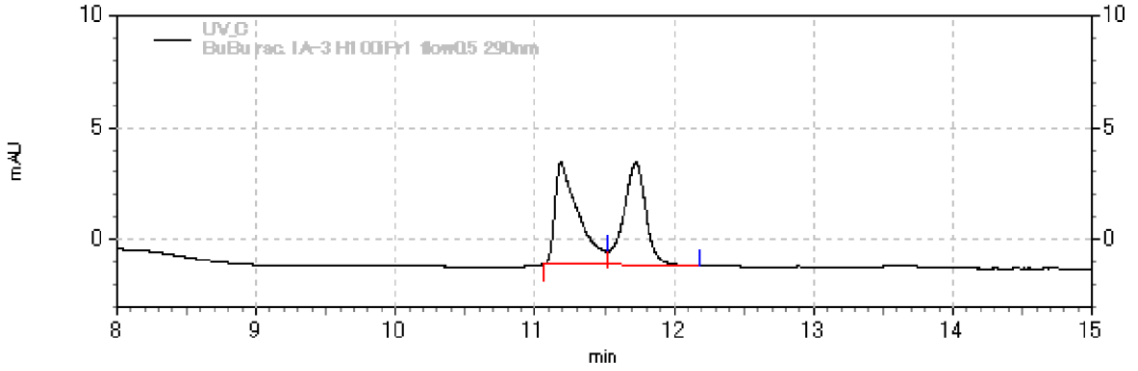
UV C結果

No	RT	Area	Area%
1	10.75	10138	1.103
2	12.00	908645	98.897
トータル		918783	100.000

(6*R*,7*R*,8*S*)-8-Bromo-6-((*tert*-butyldimethylsilyl)oxy)-7-hydroxydodecan-5-one (3j)

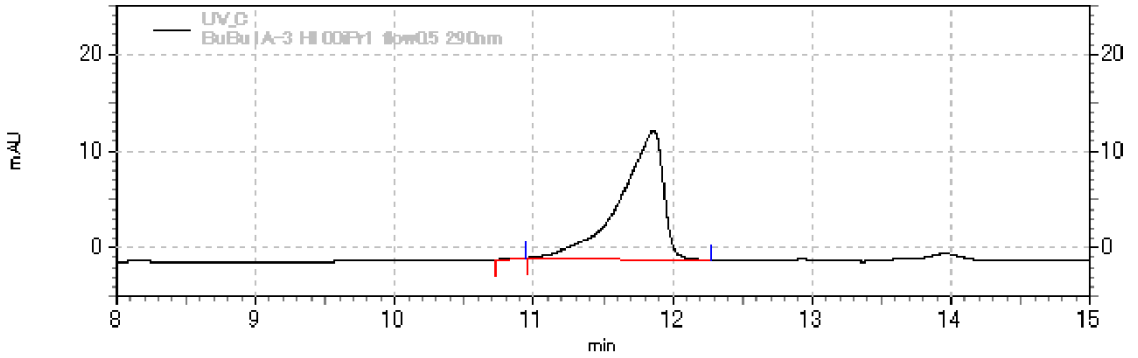


HPLC analysis: Daicel Chiralpak IA-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.9 min (minor) and 11.9 min (major) .



UV_C結果

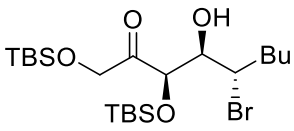
No	RT	Area	Area%
1	11.19	53325	51.232
2	11.73	50761	48.768
トータル		104086	100.000



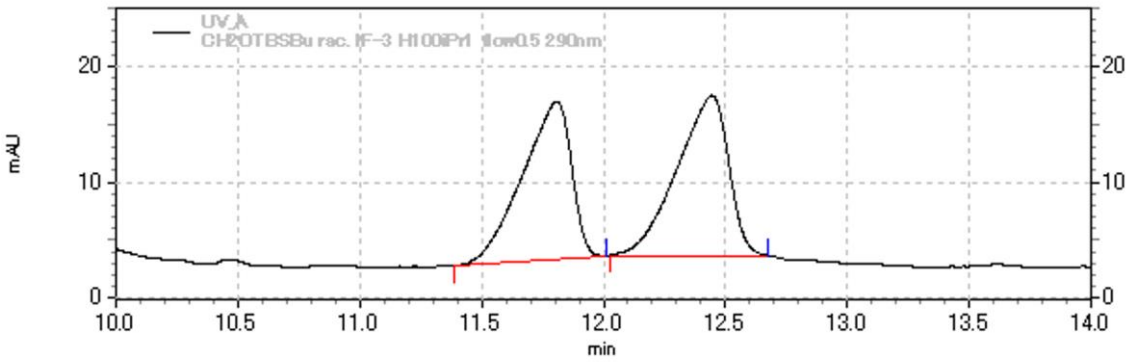
UV_C結果

No	RT	Area	Area%
1	10.94	750	0.262
2	11.86	285009	99.738
トータル		285759	100.000

(3*R*,4*R*,5*S*)-5-Bromo-1,3-bis((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3k)

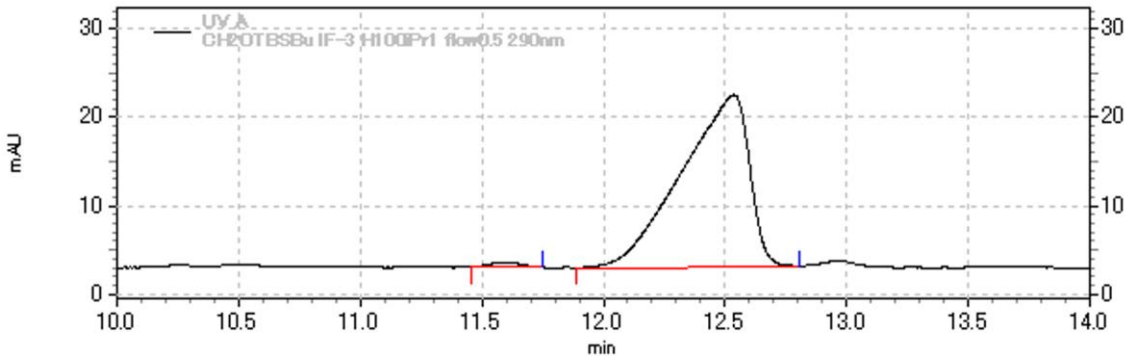


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 11.6 min (minor) and 12.5 min (major).



UV_A結果

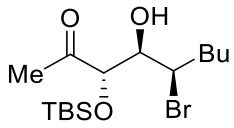
No	RT	Area	Area%
1	11.81	190289	48.424
2	12.44	202678	51.576
トータル		392967	100.000



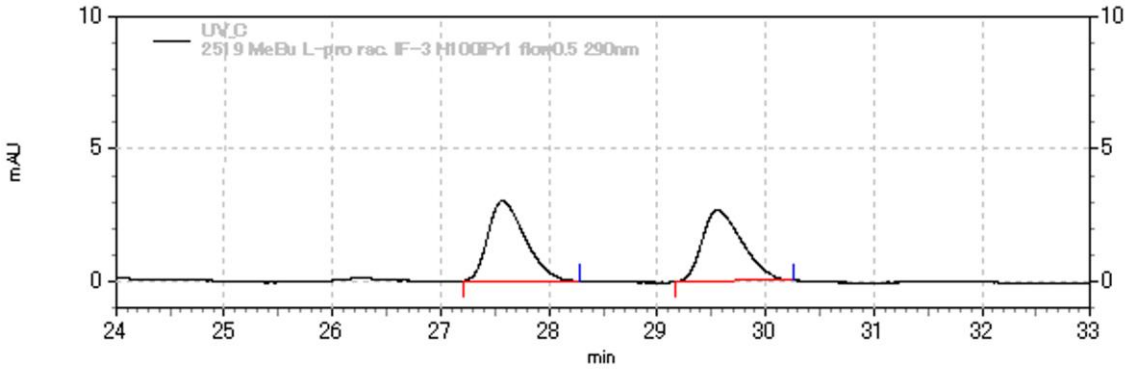
UV_A結果

No	RT	Area	Area%
1	11.58	4738	1.245
2	12.54	375898	98.755
トータル		380636	100.000

(3*R*,4*R*,5*R*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxynonan-2-one (3l)

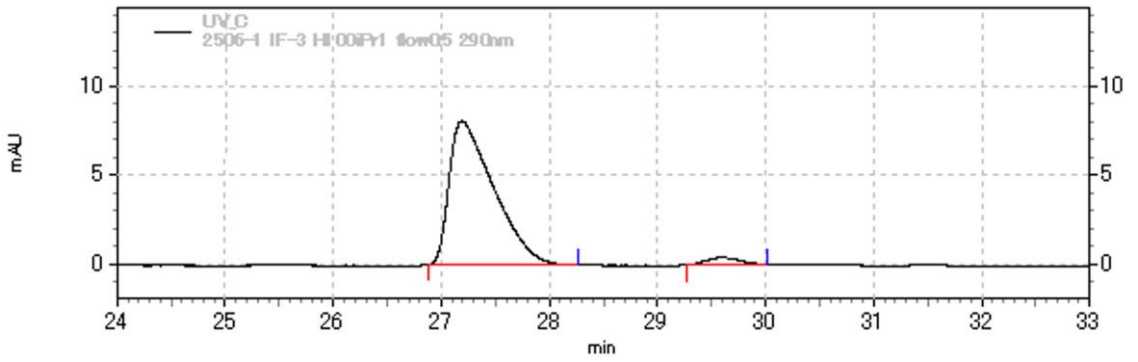


HPLC analysis: Daicel Chiralpak IF–3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ = 290 nm, retention time: 27.2 min (major) and 29.6 min (minor).



UV_C結果

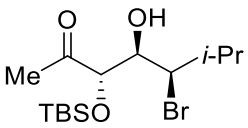
No	RT	Area	Area%
1	27.57	72061	51.078
2	29.56	69019	48.922
トータル		141080	100.000



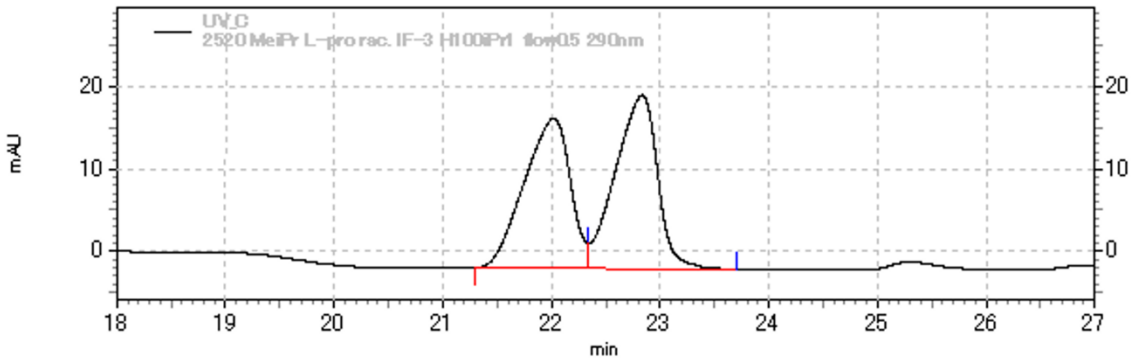
UV_C結果

No	RT	Area	Area%
1	27.19	231923	96.134
2	29.61	9326	3.866
トータル		241249	100.000

(3*R*,4*R*,5*R*)-5-Bromo-3-((*tert*-butyldimethylsilyl)oxy)-4-hydroxy-6-methylheptan-2-one (3m)

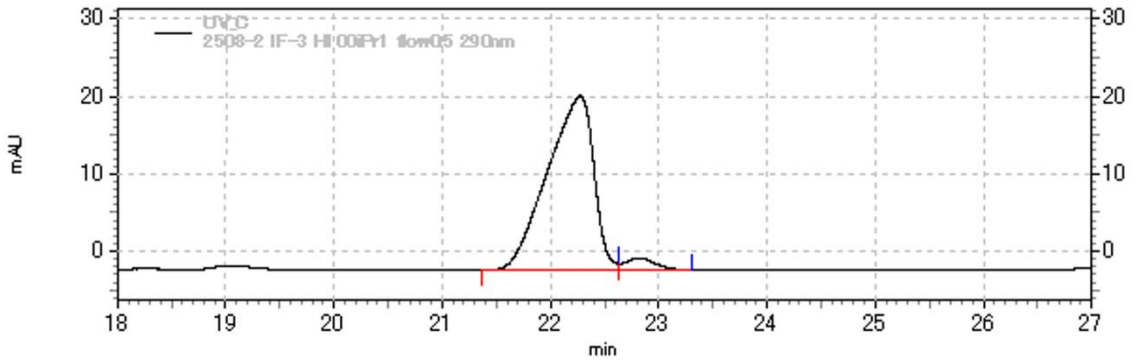


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 22.3 min (major) and 22.8 min (minor).



UV C結果

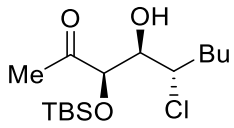
No	RT	Area	Area%
1	22.02	538432	48.610
2	22.83	569222	51.390
トータル		1107654	100.000



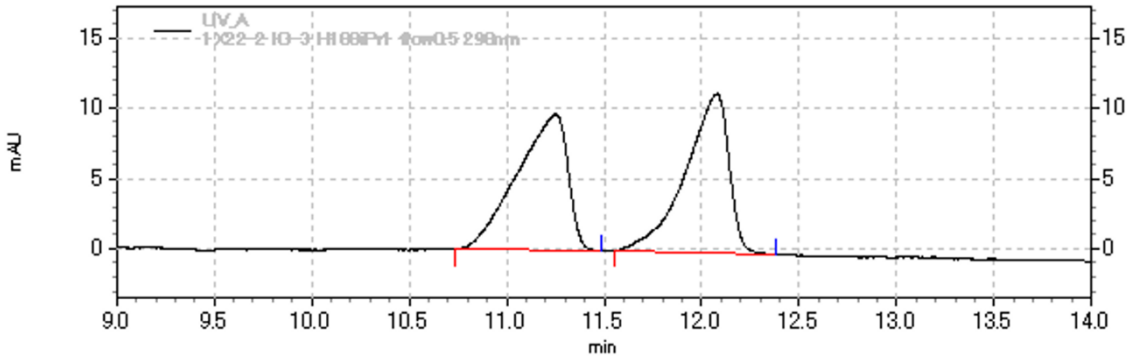
UV C結果

No	RT	Area	Area%
1	22.27	667653	95.841
2	22.81	28974	4.159
トータル		696627	100.000

(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxynonan-2-one (9a)

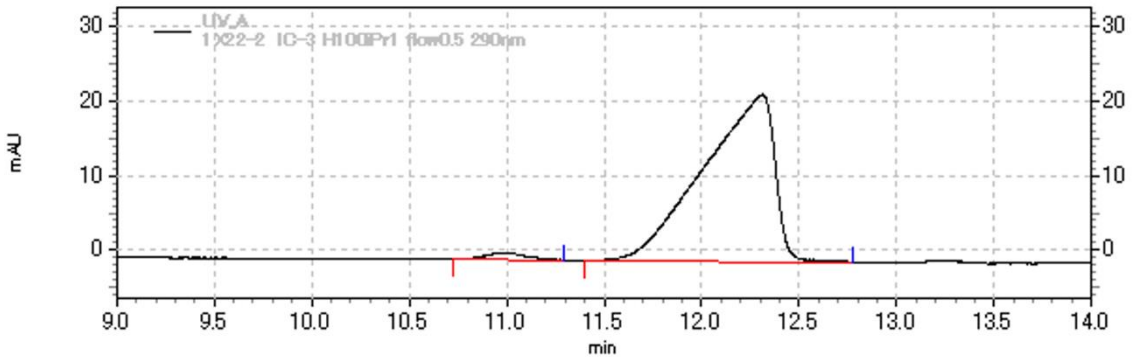


HPLC analysis: Daicel Chiralpak IC–3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ = 290 nm, retention time: 11.0 min (minor) and 12.3 min (major).



UV A結果

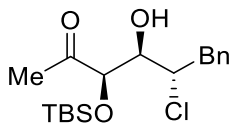
No	RT	Area	Area%
1	11.25	176179	49.937
2	12.08	176621	50.063
トータル		352800	100.000



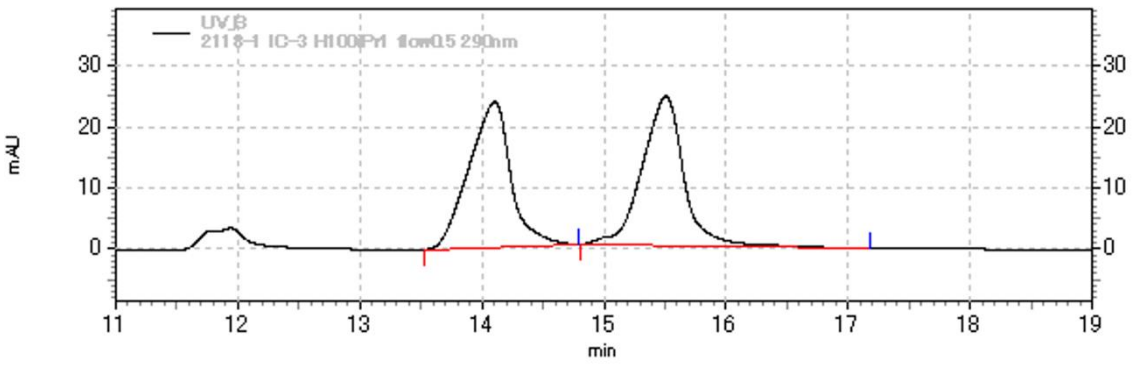
UV A結果

No	RT	Area	Area%
1	10.97	14495	2.456
2	12.31	575626	97.544
トータル		590121	100.000

(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-phenylhexan-2-one (9b)

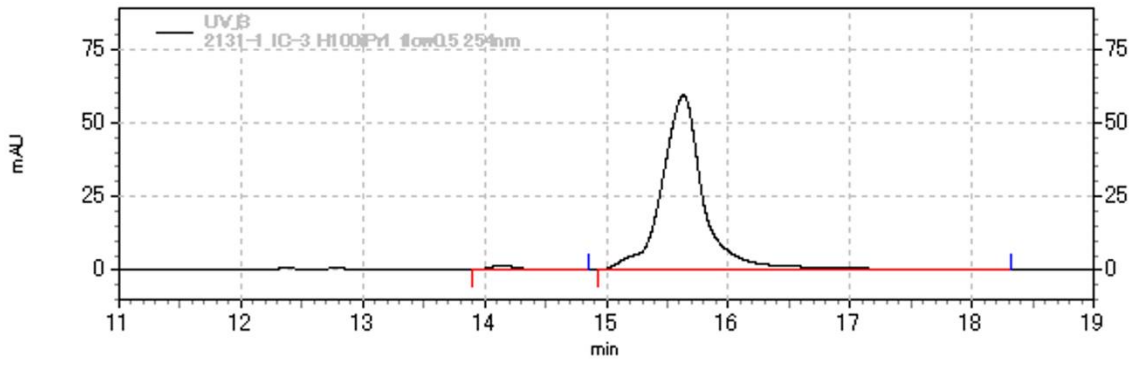


HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min,λ= 254 nm, retention time: 14.1 min (minor) and 15.6 min (major) .



UV_B結果

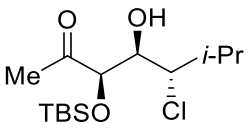
No	RT	Area	Area%
1	14.10	568814	49.376
2	15.51	583198	50.624
トータル		1152012	100.000



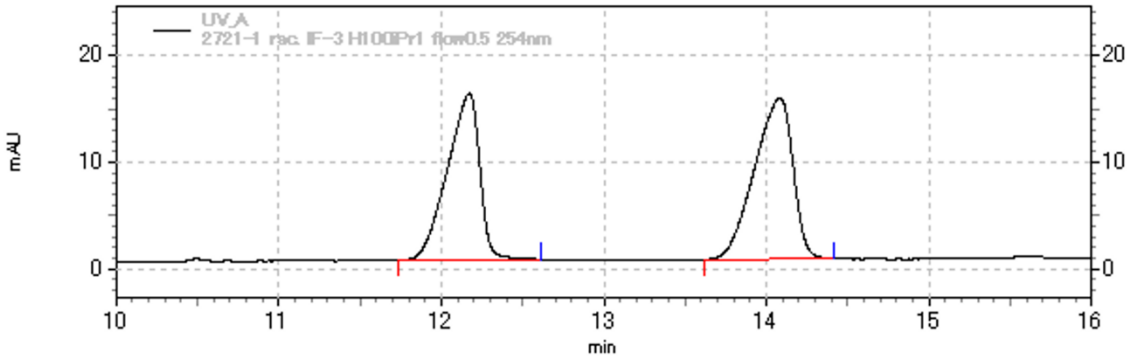
UV_B結果

No	RT	Area	Area%
1	14.14	26607	1.831
2	15.63	1426210	98.169
トータル		1452817	100.000

(3*R*,4*R*,5*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-methylheptan-2-one (9c)

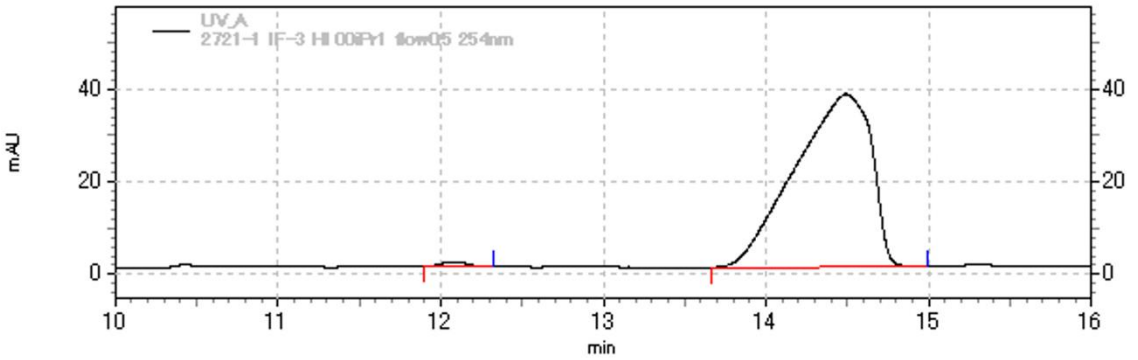


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 12.1 min (minor) and 14.5 min (major).



UV_A結果

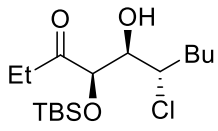
No	RT	Area	Area%
1	12.17	216311	46.522
2	14.08	248654	53.478
トータル		464965	100.000



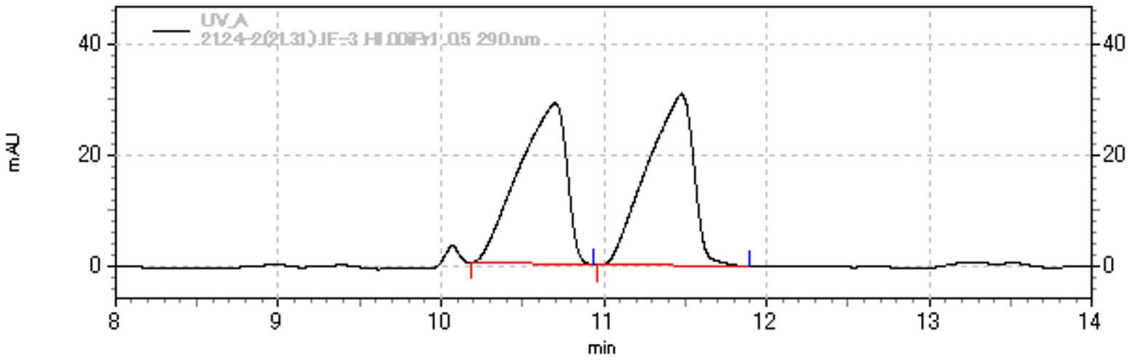
UV_A結果

No	RT	Area	Area%
1	12.08	10986	0.898
2	14.49	1212745	99.102
トータル		1223731	100.000

(4*R*,5*R*,6*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-6-chloro-5-hydroxydecan-3-one (9d)

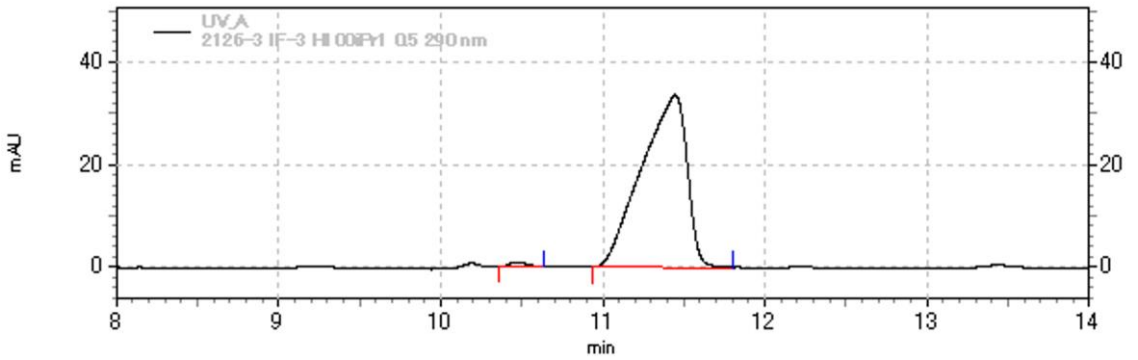


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.5 min (minor) and 11.5 min (major).



UV A結果

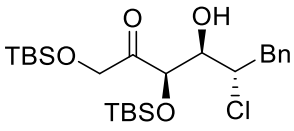
No	RT	Area	Area%
1	10.70	592273	49.104
2	11.48	613893	50.896
トータル		1206166	100.000



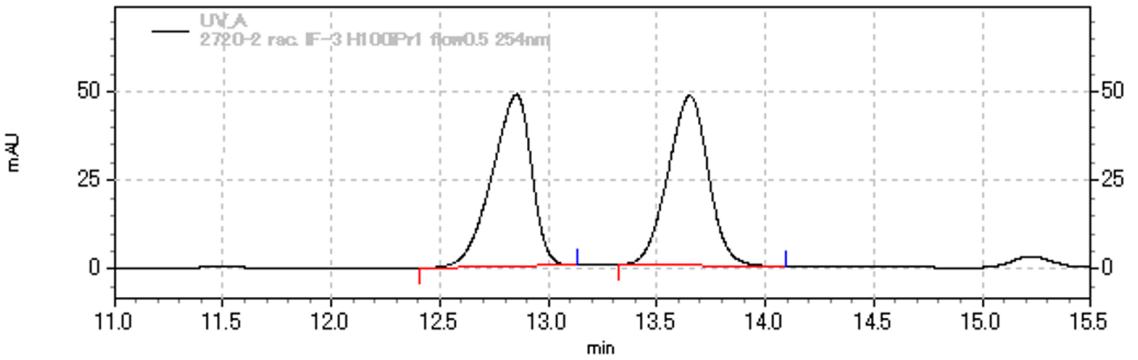
UV A結果

No	RT	Area	Area%
1	10.48	6336	0.961
2	11.45	652908	99.039
トータル		659244	100.000

(3*R*,4*R*,5*S*)-1,3-Bis((*tert*-butyldimethylsilyl)oxy)-5-chloro-4-hydroxy-6-phenylhexane-2-one (9e)

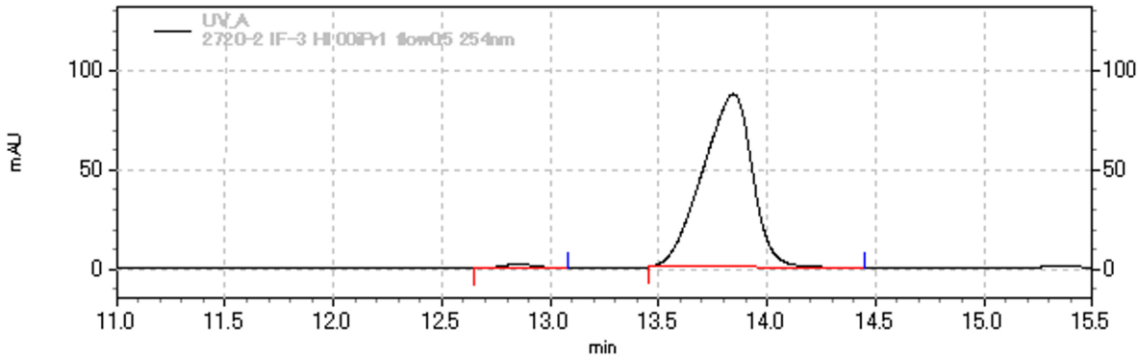


HPLC analysis: Daicel Chiralpak IF-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 254 nm, retention time: 12.9 min (minor) and 13.9 min (major).



UV A結果

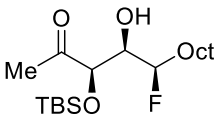
No	RT	Area	Area%
1	12.85	617045	49.864
2	13.65	620421	50.136
トータル		1237466	100.000



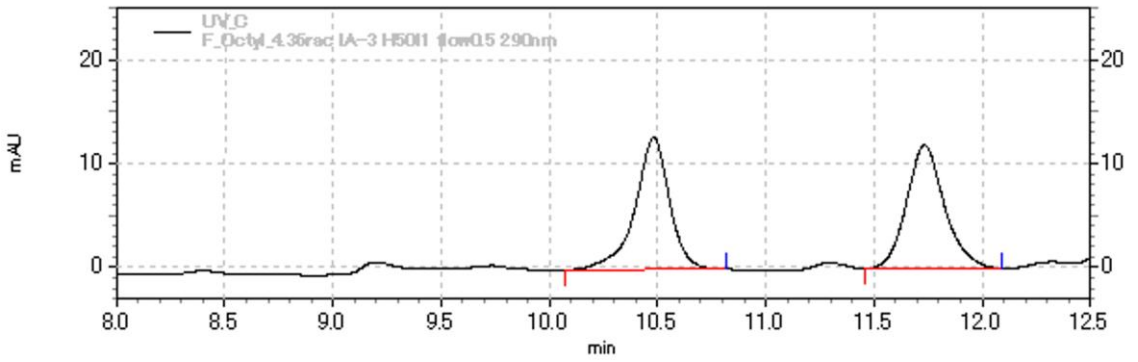
UV A結果

No	RT	Area	Area%
1	12.85	21812	1.548
2	13.85	1387134	98.452
トータル		1408946	100.000

(3*R*,4*R*,5*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-5-fluoro-4-hydroxytridecan-2-one (8a)

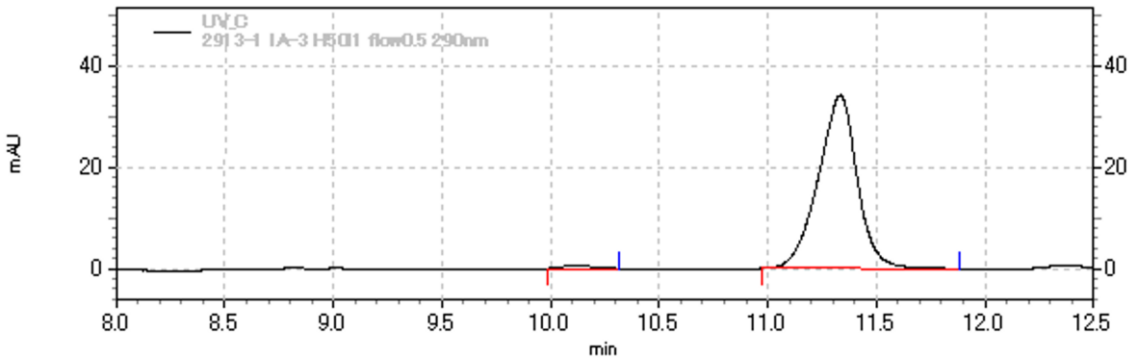


HPLC analysis: Daicel Chiralpak IA-3, hexane/*i*-PrOH = 50:1, flow rate 0.5 mL/min, λ= 290 nm, retention time: 10.1 min (minor) and 11.3 min (major).



UV_C結果

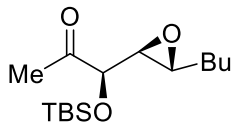
No	RT	Area	Area%
1	10.48	142127	49.551
2	11.74	144703	50.449
トータル		286830	100.000



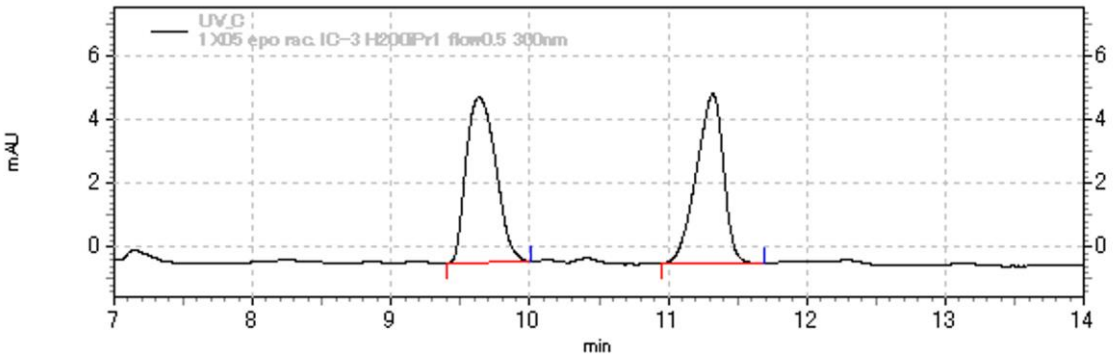
UV_C結果

No	RT	Area	Area%
1	10.11	5645	1.307
2	11.33	426120	98.693
トータル		431765	100.000

(*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-1-((2*S*,3*R*)-3-butyloxiran-2-yl)propan-2-one (13)

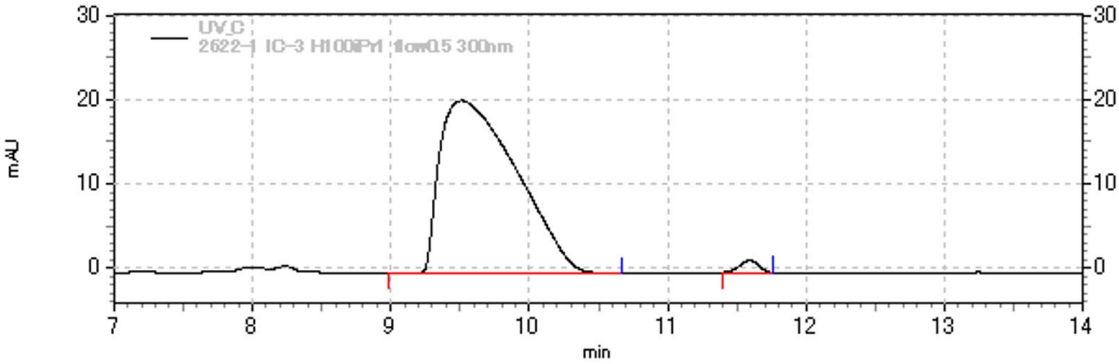


HPLC analysis: Daicel Chiralpak IC-3, hexane/*i*-PrOH = 100:1, flow rate 0.5 mL/min, λ= 300 nm, retention time: 9.5 min (major) and 11.6 min (minor).



UV_C結果

No	RT	Area	Area%
1	9.64	77359	51.664
2	11.32	72375	48.336
トータル		149734	100.000



UV_C結果

No	RT	Area	Area%
1	9.51	790033	98.255
2	11.59	14033	1.745
トータル		804066	100.000