Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Development of a copper-catalyzed enantioselective decarboxylative-aldolization for the preparation of perfluorinated 1,3,5-triols featuring supramolecular recognition properties

Céline Sperandio, Jean Rodriguez, Adrien Quintard,*

Aix Marseille Univ, CNRS, Centrale Marseille, iSm2, Marseille, France

Corresponding author e-mail: adrien.quintard@univ-amu.fr

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General information

NMR spectra were recorded on a Bruker AC 300 (300 MHz), a Bruker AC 400 (400 MHz) and a Bruker 500 (500 MHz) spectrometer. Chemical shifts are given in ppm, using as internal standards the residual $CHCl_3$ signal for ^1H NMR ($\delta = 7.26$) and the deuterated solvent signal for ^{13}C NMR ($\delta = 77.0$). Data for ^{13}C NMR are reported as follows: chemical shift (multiplicity). Data for ^1H NMR are reported as follows: chemical shift (multiplicity [s = singulet, d = doublet, t = triplet, q = quadruplet, m = multiplet, br = broad], coupling constants *J* in Hertz (Hz), integration).

Anhydrous THF was obtained from a Solvent Purification System M Braun SPS-800.

High resolution mass spectra (HRMS) were performed on a QStar Elite (Applied Biosystems SCIEX) spectrometer equipped with atmospheric pression ionization source (API) pneumaticly assisted. Samples were ionized by positive electrospray mode as follows: electrospray tension (ISV): 5500 V; opening tension (OR): 50 V; nebulization gas pression (air): 20 psi.

IR spectra were recorded using a Thermo Nicolet Avatar 330 FT-IR instrument (Thermo Nicolet Corporation, Madison, WI, USA).

Chiral GC analysis were performed on a HP 4890 using 6 bar argon as vector. Column: 25m/0,25 mm. Chromatogram analyzed with ChromNav software.

HPLC analyses for the determination of enantiomeric excesses were performed on a Merck-Hitachi system equipped with Chiralpak ASH.

Optical rotations were measured at 20 °C in $CHCl_3$ with an Anton Paar MCP 200 polarimeter with a 0.2 cm length.

Absolute and relative configuration for the bi-directional reaction were determined on **3c** by X-Ray analysis assuming the same transition states for the other substrates. For the mono-directional products, absolute and relative configuration were determined on **12** by X-ray analysis and by comparison of optical rotation already described in the literature.[1]

Ketoacids compounds were prepared using methods previously described.[2]

Chiral anion TBA((*S*)- BINOL-PO_4) and TBA((*R*)-BINOL-PO_4) were prepared according to a slightly modified literature protocol [3] using commercially available (*S*)- and (*R*)-BINOL-PO_4 and tetrabutylammonium (TBA) hydroxide.

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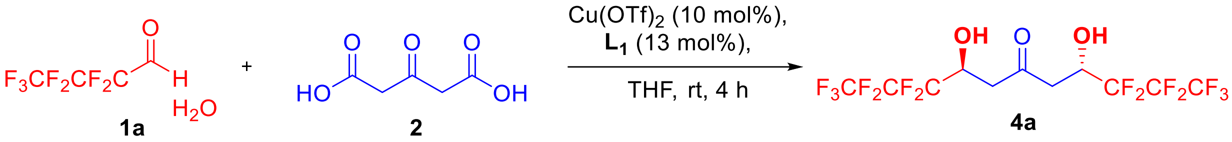
[1] K. Funabiki, Y. Itoh, Y. Kubota, M. Matsui, *J. Org. Chem*. **2011**, *76*, 3545.

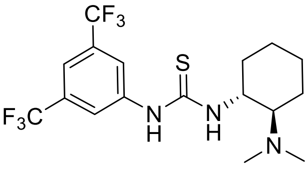
[2] a. V. G. Lisnyak, T. Lynch-Colameta, S. A. Snyder, *Angew. Chem. Int. Ed*. **2018**, *57*, 15162; b. I. Galleano, M. Schiedel, M. Jung, A. S. Madsen, C. A. Olsen, *J. Med. Chem*. **2016**, *59*, 1021

[3] a. J. Y. C. Lim, I. Marques, V. Félix, P. D. Beer, *J. Am. Chem. Soc*. **2017**, *139*, 12228; b. E. Zhou, J. Zhang, Y. Lu, C. Dong, *Arkivoc* **2014**, *5*, 351.

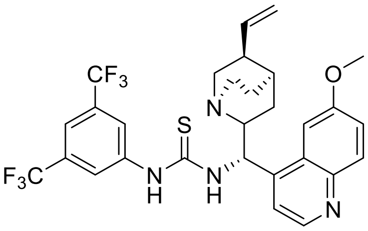
Experimental section

Bi-directional aldolization of 2,2,3,3,4,4,4-Heptafluorobutyraldehyde hydrate with various catalysts

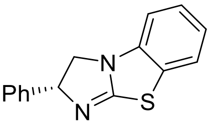




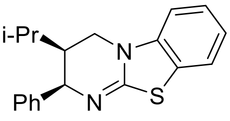
(*S*,*S*)-TUC



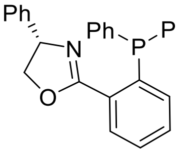
Soòs



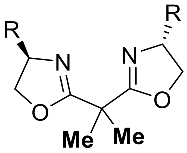
BTM



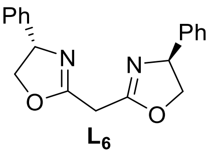
HyperBTM



L$_1$



L$_2$ R = i-Pr
L$_3$ R = t-Bu
L$_4$ R = Bn
L$_5$ R = Ph

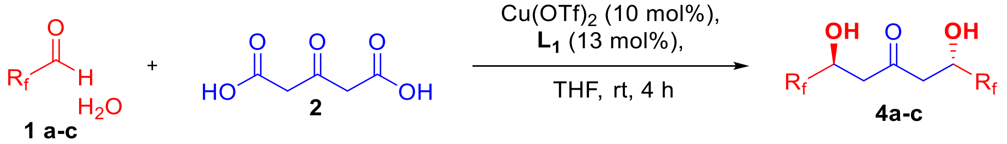


L$_6$

Entry	Catalyst	Isolated Yied	*dr*[a]	*ee*[b]
1	(*S*,*S*)-TUC (10 mol%)	38%	1:1	2%
2	Soòs	45%	1:1	4%
2	Quinine (10 mol%)	Nd	1:1	17%
3	(DHQD)$_2$PHAL (10 mol%)	Nd	1:1	10%
4	BTM	49%	1:1	0%
5	HyperBTM	37%	1:1	0%
6	Cu(OTf)$_2$ (10 mol%) / **L1-4** (13 mol%)	Nd	1:1	0%
7	**Cu(OTf)$_2$ (10 mol%) / L5 (13 mol%)**	**74%[c]**	**4:1 (13:1)**	**88 (97%)[c]**
8	Cu(OTf)$_2$ (10 mol%) / **L6** (13 mol%)	Nd	4:1	-62%
9	Cu(OTf)$_2$ (10 mol%)	73%	1:1	-
10[d]	**L5** (10 mol%)	35	1:1	0%
11[d]	**L5** (10 mol%) in toluene	nd	1:1	0%
12	Cu(OTf)$_2$ (10 mol%) / L5 (13 mol%) at 0°C	46	4:1	88%
13	Cu(OTf)$_2$ (10 mol%) / **L5** (22 mol%)	59%	4:1	88%
14	Cu(OTf)$_2$ (13 mol%) / **L5** (10 mol%)	56%	4:1	82%

[a]: Determined by ^{19}F NMR and GC. [b]: Determined by chiral gas chromatography. [c]: *ee* in parenthesis and yield are given after purification by recrystallization. [d]: reaction run over 12 hours.

General procedure for the bi-directional aldolization:

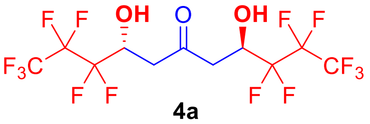


3.61 mg of copper triflate (0.01 mmol, 10 mol%) and 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) are dissolved in 0.1 mL of THF in vial and stirred 30 minutes at room temperature. The corresponding perfluoaldehyde (0.5 mmol, 5 eq) and 16.1 mg of 1,3-acetone-dicarboxylic acid **2** (0.1 mmol, 1 eq) are added and the reaction is stirred at room temperature for 4 hours more before addition of 1 mL of 1M HCl and 1 mL of diethyl ether. The aqueous layer is extracted by 4 times 2 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification by recrystallization from a mixture of diethyl ether and n-hexane provides the corresponding ketodiols.

General procedure for the larger scale

181 mg of copper triflate (0.5 mmol, 5 mol%) and 250 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (13 mmol, 13 mol%) are dissolved in 10 mL of THF on balloon and stirred 30 minutes at room temperature. The corresponding perfluoaldehyde (40 mmol, 4 eq) and 1610 mg of 1,3-acetone-dicarboxylic acid **2** (0.1 mmol, 1 eq) are added and the reaction is stirred at room temperature for 4 hours more before addition of 4 mL of 1M HCl and 4 mL of diethyl ether. The aqueous layer is extracted by 3 times 4 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification by recrystallization from a mixture of diethyl ether and n-hexane provides the corresponding ketodiol.

Carbons -CF_2 was difficult to see and interpret. Similarly, in ^{19}F NMR, many couplings with complex multiplicity were observed with constant values of the order of 290 Hz.



4a

Prepared according to the general procedure using 99.0 mg of 2,2,3,3,4,4,4-Heptafluorobutyraldehyde hydrate (0.5 mmol, 5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 16.1 mg of ketone-dicarboxylic acid **2** (technical grade, 0.1 mmol, 1 eq). Purification by recrystallization from a mixture of diethyl ether chloroforme provides the corresponding ketodiol **4a**. 24.5 mg (0.053 mmol). 54% yield. The product is obtained in 97% *ee* and 13/1 *dr*.

$[\alpha]^{20}_D$ = +11.2° (CH_3CN, c = 0.4), 13/1 *dr*, 97% *ee*).

mp = 99-100 °C.

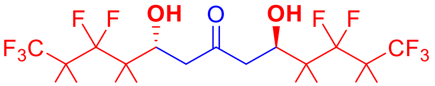
^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 2.81-3.02 (m, 2 C*H*$_2$), 4.65-4.80 (m, 2 C*H*(OH)). ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 44.2 (s, 2 *C*H$_2$), 66.3 (dd, *J* = 28.7, 22.7 Hz, 2 *C*H(OH)), 108.7-123.1 (m, 4 *C*F$_2$ and 2 *C*F$_3$), 203.9 (*C*O).

^{19}F (NMR (376 MHz, CD_3OD): -82.57 (dd, *J* = 11.5, 8.8 Hz, 2 C*F*$_3$), -119.97- -121.14 (m, *AB* syst, *J* = 280, 11.4 Hz, 2 *F*), -125.58- -126.67 (ddd, *AB* syst, *J* = 290.1, 9.1, 4.1 Hz, 2 *F*), -127.40- -128.48 (ddd, *AB* syst, *J* = 290.1, 10.4, 2.6 Hz, 2 *F*), -127.96 -129.11 (m, *AB* syst, *J* = 280 Hz, 2 *F*).

IR: 688.2, 700.4, 1066.7, 1101.1, 1122.9, 1170.2, 1266.9, 3265.8 cm^{-1}

HRMS ESI [M+Na]+ calcd for $C_{11}H_8F_{14}O_3Na$: 477.0142. Observed: 477.0144.

GC enantiomeric excess determination: cyclosil-b; 130°C for 60 min than 1°C/min until 220°C. rt (min) = 29.9 min; rt (maj) = 30.8 min; rt (meso) = 32.0.



4b

Prepared according to the general procedure using 116.0 mg of 2,2,3,3,4,4,5,5,5-Nonafluoropentane-1,1-diol (0.5 mmol, 5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 16.1 mg of ketone-dicarboxylic acid **2** (technical grade, 0.1 mmol, 1 eq). Purification by recrystallization from a mixture of diethyl ether chloroforme provides the corresponding ketodiol **4b**. 33.6 mg (0.06 mmol). 60% yield. The product is obtained in 97% *ee* and 12/1 *dr.*

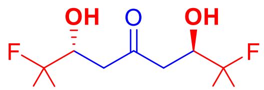
mp = 123-124 °C.

$[\alpha]^{20}_{D}$ = +9.85° (CH_3CN, c = 0.4), 12/1 *dr*, 97% *ee*).
^1H NMR (400 MHz, CD_3OD): δ (ppm) = 2.84-3.06 (m, 2 C*H₂*), 4.73-4.87 (m, 2 C*H*(OH)). ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 44.2 (s, 2 *C*H₂), 66.7 (dd, *J* = 27.4, 22.2 Hz, 2 *C*H(OH)), 108.1-121.1 (m, 6 *C*F₂ and 2 *C*F₃), 203.9 (*CO*).
^{19}F (NMR (376 MHz, CD_3OD): -82.56 (tt, *J* = 9.8, 3.0 Hz, 2 C*F₃*), -119.49- -120.74 (m, *AB* syst, *J* = 288 Hz, 2 *F*), -122.09- -123.24 (m, *AB* syst, *J* = 298 Hz, 2 *F*), -123.59- -124.82 (m, *AB* syst, *J* = 298 Hz, 2 *F*), -125.97- -127.15 (m, *AB* syst, *J* = 292 Hz, 2 *F*), -127.15 – -128.21 (m, *AB* syst, *J* = 292 Hz, 2 *F*), -127.70- -128.86 (m, *AB* syst, *J* = 292 Hz, 2 *F*).

IR: 732.9, 1096.9, 1128.8, 1174.6, 1216.4, 1719.9, 3435.5, 3482.2 cm^{-1}

HRMS ESI [M+Na]+ calcd for $C_{13}H_8F_{18}O_3Na$: 577.0078. Observed: 577.0079.

GC enantiomeric excess determination: cyclosil-b; 120°C for 0 min than 1°C/min until 220°C. rt (min) = 54.6 min; rt (maj) = 56.3 min; 58.9.



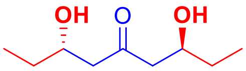
4c

Prepared according to the general procedure using 58.0 mg of trifluoroacetaldehyde monohydrate (0.5 mmol, 5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 16.1 mg of ketone-dicarboxylic acid **2** (technical grade, 0.1 mmol, 1 eq). Purification by recrystallization from a mixture of diethyl ether and chloroforme provides the corresponding ketodiol **4c**. 15.6 mg (0.06 mmol). 71% yield. The product is obtained in 96% *ee* and 12/1 *dr.*
mp = 89-90 °C.
$[\alpha]^{20}_{D}$ = +24.7° ($CHCl_3$, c = 0.8), 12/1 *dr*, 96% *ee*).
^1H NMR (400 MHz, CD_3OD): δ (ppm) = 2.73-2.93 (m, 2 C*H₂*), 4.44-4.56 (m, 2 C*H*(OH)). ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 44.5 (s, 2 *CH₂*), 66.7 (q, *J* = 31.9 Hz, 2 *C*H*(*OH)), 126.7 (q, *J* = 280.9 Hz, 2 *C*F₃), 203.8 (*CO*).
^{19}F (NMR (376 MHz, CD_3OD): -81.35 (s, 2 C*F₃*).

IR: 1088.4, 1128.5, 1166.9, 1264.5, 1300.0, 1728.1, 3326.1, 3389.3 cm^{-1}

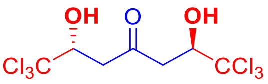
HRMS ESI [M+Na]+ calcd for $C_{13}H_{24}F_2O_3Na$: 277.0270. Observed: 277.0272.

GC enantiomeric excess determination: cyclosil-b; 110°C for 60 min than 1°C/min until 220°C. rt (min) = 81.1 min; rt (maj) = 82.2 min; rt (meso) = 83.2.



6

Prepared according to the general procedure using 32.0 μL of propionaldehyde (0.5 mmol, 5.0 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and mg of 16.1 mg of ketone-dicarboxylic acid **2** (technical grade, 0.1 mmol, 1 eq). The product was isolated as a yellow solid after purification with ethyl acetate / petroleum ether mixture. 5.4 mg (0.031 mmol). 31% yield. R_f = 0.28 (petroleum ether / ethyl acetate (3/7)).
^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.90 (t, *J* = 7.4 Hz, 2 C*H₃*), 1.40-1.53 (m, 2 C*H*₂), 2.52-2.57 (m, 2 C*H*₂), 3.29 (brs, O*H*), 3.92-3.99 (m, 2 C*H*).
Described in the literature.[4]



8

Prepared according to the general procedure using 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) are dissolved in 0.1 mL of THF in vial and stirred 30 minutes at room temperature. 82.5 mg of chloral hydrate (0.5 mmol, 5 eq) and 16.1 mg of 1,3-acetone-dicarboxylic acid **2** (0.1 mmol, 1 eq) are added and the reaction is stirred at room temperature for 4 hours more before addition of 1 mL of 1M HCl and 1 mL of diethyl ether. The aqueous layer is extracted by 4 times 2 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification by recrystallization from a mixture of diethyl ether and *n*-hexane provides the corresponding ketodiol **8.** 23.7 mg (0.04 mmol). 68% yield. The product is obtained in 90% *ee* before purification and 4/1 *dr.*
$[\alpha]^{20}_{D}$ = + 23.3° ($CHCl_3$, c = 0.4), 90% *ee*).
mp= 150-151 °C.

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[4] A. Quintard, J. Rodriguez, *Chem. Eur. J.* **2015**, *21*,14717.

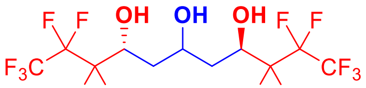
^{1}H NMR (400 MHz, DzMSO-d^6): δ (ppm) = 2.04 - 2.36 (m, C*H*$_2$), 3.66 (ddd, *J* = 8.8, 6.5, 2.3 Hz, CH(O*H*)), 6.09 (d, 2 O*H*). ^{13}C NMR (100 MHz, DMSO-6^9): δ (ppm) = 45.9 (s, *C*H(OH)), 77.6 (s, *C*H$_2$), 104.2 (s, 2 *C*(Cl)$_3$), 203.1 (*C*O).

HRMS ESI [M+NH$_4$]+ calcd for $C_7H_{12}Cl_6NO3$+: 369.8914. Observed: 369.8904

GC enantiomeric excess determination: Cyclosil-b; 140°C for 0 min than 1°C/min until 220°C. rt (m in) = 78.5 min; rt (maj) = 79.7 min.

General procedure for the perfluorinated ketodiols reduction

0.5 mmol (1.0 eq) of the ketodiol are dissolved in 3 mL of dry THF and 0.1 mL of MeOH and cooled to 0°C under argon. 74 mg of NaBH$_4$ (2 mmol, 2.0 eq) are then added and the reaction stirred at 0°C for 35 minutes before addition of 0.12 mL of acetic acid. The reaction mixture is then stirred at room temperature for 30 min before addition of 30 mL of saturated aqueous NaHCO$_3$. The mixture is stirred for further 30 min at room temperature before extraction by 3 times 10 mL of diethyl ether, the combined organic layers washed by 2 times 10 mL saturated aqueous NH$_4$Cl, 10 mL of saturated aqueous NaCl, 15 mL 1M HCl, 10 mL of saturated aqueous NaCl, dried over Na$_2$SO$_4$, filtered and the solvent evaporated. Purification by recrystallization from a mixture of diethyl ether and *n*-hexane yields the pure triol.



3a

Prepared according to the general procedure using 400 mg (0.88 mmol, 1 eq) of the ketodiol and 65.1 mg of NaBH$_4$ (1.76 mmol, 2 eq). Purification by recrystallization from a mixture of diethyl ether and *n*-Hexane yields the pure triol. 372.0 mg (0.81 mmol). 93% yield. The product is obtained in 97% *ee* and 13/1 *dr.*

$[\alpha]^{20}_D$ = +21.4° (CH$_3$CN, c = 0.4), 13/1 *dr*, 97% *ee*).

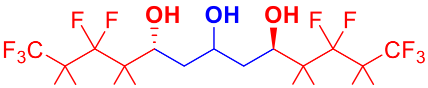
mp = 115-116 °C.

^{1}H NMR (400 MHz, CD$_3$OD): δ (ppm) = 2.75-2.02 (m, 2 C*H$_2$*), 4.09-4.19 (m, C*H*(OH)), 4.29-4.44 (m, 2 C*H*(OH)). ^{13}C NMR (100 MHz, CD3OD): δ (ppm) = 37.1 (s, *C*H$_2$), 37.3 (s, *C*H$_2$), 65.2 (s, *C*H(OH)), 66.6 (ddd, *J* = 100.3, 27.1, 23.2 Hz, 2 *C*H(OH)), 105.5-125.0 (brs, 4 *C*F$_2$ and 2 *C*F$_3$).

^{19}F (NMR (376 MHz, CD$_3$OD): -82.53 (d, *J* = 9.2 Hz, C*F$_3$*), -82.57 (d, *J* = 8.9 Hz, C*F$_3$*), -120.59- -122.01 (m, *AB* syst, *J* = 278.4, 63.8, 26.1 Hz 2*F*), -125.43- -126.67 (m, *AB* syst, *J* = 286.4, 47.1, 4.5 Hz, 2*F*), -127.31- -128.38 (m, *AB* syst, *J* = 290.1, 10.7, 1.7 Hz, 2*F*), -128.21- -129.45 (m, *AB* syst, *J* = 290 Hz, 2*F*).

IR: 733.2, 956.5, 1105.5, 1174.1, 1217.1, 1346.3, 3315.9 cm^{-1}

HRMS ESI [M+Na]+ calcd for $C_{11}H_8F_{14}O_3Na$: 479.0299. Observed: 479.0301.



3b

Prepared according to the general procedure using 400 mg (0.72 mmol, 1 eq) of the ketodiol and 53.4 mg of NaBH$_4$ (1.44 mmol, 1.3 eq). Purification by recrystallization from a mixture of diethyl ether and *n*-Hexane yields the pure triol. 356.3 mg (0.64 mmol). 89% yield.

The product is obtained in 97% *ee* and 12/1 *dr.*

$[\alpha]^{20}_D$ = +17.8° (CH$_3$CN, c = 1), 12/1 *dr*, 97% *ee*).

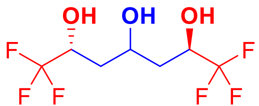
mp = 116-117 °C.

^{1}H NMR (400 MHz, CD$_3$OD): δ (ppm) = 1.66-1.90 (m, 2 C*H$_2$*), 4.09-4.14 (m, 1 C*H*(OH)), 4.09-4.25 (m, 2 C*H*(OH)). ^{13}C NMR (100 MHz, CD3OD): δ (ppm) = 37.1 (s, *C*H$_2$), 37.2 (s, *C*H$_2$), 65.8 (s, *C*H(OH)), 68.6 (ddd, *J* = 100.3, 27.1, 23.2 Hz, 2 *C*H*(*OH)), 100.5-135.0 (brs, 6 *C*F$_2$ and 2 *C*F$_3$).

^{19}F (NMR (376 MHz, CD$_3$OD): -82.56 (ddd, *J* = 12.5, 6.5, 2.9 Hz, 2 C*F$_3$*), -120.58- -121.63 (m, *AB* syst, *J* = 293.0, 87.5, 22.6, 12.1 Hz, 2 *F*), -122.19 – -123.26 (m, *AB* syst, *J* = 294.0, 57.8, 10.1, 9.5, 4.8 Hz, 2 *F*), -123.60- -124.50 (m, *AB* syst, *J* = 294.0, 10.3 Hz, 2 *F*), -126.15- -127.09 (m, *AB* syst, *J* = 293.0, 16.3, 7.9, 3.9 Hz, 2 *F*), -127.64- -128.4 (m, *AB* syst, *J* = 283.0 Hz, 2 *F*), -127.73- -128.66 (m, *AB* syst, *J* = 294.0, 14.6 Hz, 2 *F*).

IR: 720.6, 1086.0, 1130.2, 1198.1, 1216.5, 1354.4, 3344.4 cm^{-1}

HRMS ESI [M+Na]+ calcd for $C_{13}H_{24}F_2O_3Na$: 579.0235. Observed: 579.0234.



3c

Prepared according to the general procedure using 400 mg (1.57 mmol, 1 eq) of the ketodiol and 116.55 mg of $NaBH_4$ (3.15 mmol, 1.3 eq). Purification by recrystallization from a mixture of diethyl ether and *n*-Hexane yields the pure triol 364.2 mg (1.42 mmol). 91% yield. The product is obtained in 96% *ee* and 12/1 *dr.*

mp = 110-111 °C.

$[\alpha]^{20}_{D}$ = +32.4° (CH_3CN, c = 0.4), 12/1 *dr*, 96% *ee*).

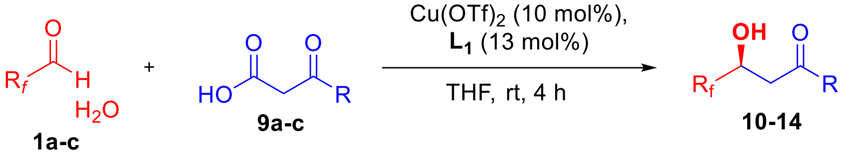
^{1}H NMR (400 MHz, CD_3OD): δ (ppm) = 1.68-1.89 (m, 2 C*H₂*), 4.05-4.23 (m, 3 C*H*(OH)). ^{13}C NMR (100 MHz, CD_3OD): δ (ppm) = 37.8 (s, *C*H₂), 38.7 (s, 2 *C*H₂), 65.1 (s, *C*H*(*OH)), 68.1 (m, 2 *C*H*(*OH)), 124.5-135.0 (m, *J* = 281.6, 32.0 Hz, 2 *C*F₃) 210.2 (*CO*).

^{19}F (NMR (376 MHz, CD_3OD): -81.48 (d, *J* = 2.6 Hz, 2 C*F₃*).

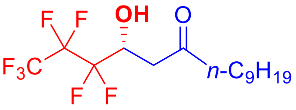
IR: 688.2, 700.4, 1066.7, 1101.1, 1170.2, 1195.5, 1266.9, 3265.8 cm^{-1}

HRMS ESI [M+Na]+ calcd for $C_{13}H_{24}F_2O_3Na$: 279.0426. Observed: 279.0428.

General procedure for the mono-directional aldolization



3.61 mg of copper triflate (0.01 mmol, 10 mol%) and 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) are dissolved in 0.1 mL of THF in vial and stirred 30 minutes at room temperature. 49.5 mg of 2,2,3,3,4,4,4-Heptafluorobutyraldehyde hydrate (0.25 mmol, 2.5 eq) and the corresponding ketone-carboxylic acid are added and the reaction is stirred at room temperature for 4 hours more before addition of 1 mL of 1M HCl and 1 mL of diethyl ether. The aqueous layer is extracted by 4 times 2 ml of diethyl ether, the combined organic layers filtered over a small plug of Na_2SO_4 and silica gel and the solvent evaporated. Purification by recrystallization from a mixture of diethyl ether and *n*-hexane provides the corresponding hydroxyketone.



10

Prepared according to the general procedure using 49.5 mg of 2,2,3,3,4,4,4-Heptafluorobutyraldehyde hydrate (0.25 mmol, 2.5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 21.4 mg of 3-Oxododecanoic acid (0.1 mmol, 1 eq). Purification by recrystallization from a mixture of diethyl ether and *n*-hexane provides the corresponding hydroxyketone **10**. 12.1 mg (0.03 mmol). 33% yield. The product is obtained in 80% *ee.*

$[\alpha]^{20}_{D}$ = +32.4° ($CHCl_3$, c = 1), 80% *ee*).

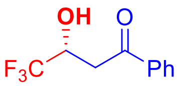
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 0.88 (t, *J* = 6.7 Hz, C*H₃*), 1.27 (t, *J* = 4.8 Hz, 12*H*), 1.59 (m, 2*H*)), 2.49 (t, *J* = 7.4 Hz, 2*H*), 2.72-2.93 (m, 2*H*), 3.55 (brs, O*H*), 4.68 (m, *J* = 18.2, 8.5, 3.6 Hz, C*H*(OH)). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 26.3 (s, *C*H*₃*), 33.56 (s, *C*H₂), 44.83 (s, *C*H₂), 66.77 (dd, *J* = 29.3, 22.6 Hz, *C*H(OH)), 214.9 (*CO*).

^{19}F (NMR (376 MHz, $CDCl_3$): -80.94 (dd, *J* = 11.4, 8.2 Hz, C*F₃*), -119.51- -120.38 (m, *AB* syst, *J* = 283.0, 11.4, 8.2 Hz, 1 *F*), -124.68- -125.50 (ddd, *AB* syst, *J* = 293.0, 9.9, 6.4 Hz, 1 *F*), -126.44- -122.26 (dd, *J* = 294.0, 10.7, 6.3 Hz, 1 *F*), -127.02- -122.89 (m, *AB* syst, *J* = 283.0, 8.3 Hz, 1 *F*).

IR: 1101.3, 1123.2, 1177.1, 1210.9, 1713.0, 2856.8, 2924.4, 2957.3, 3435,5 cm^{-1}

HRMS ESI [M+Na]+ calcd for $C_{15}H_{23}F_7O_2Na$: 391.1478. Observed: 391.1476.

GC enantiomeric excess determination: Hydrodex- β -3P; 140°C for 60 min than 1°C/min until 220°C. rt (m in) = 35.9 min; rt (maj) = 37.3 min.



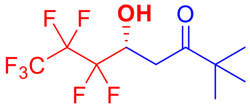
11

Prepared according to the general procedure using 29.0 mg of trifluoroacetaldehyde monohydrate (0.25 mmol, 2.5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 16.4 mg of 3-oxo-3-phenylpropanoic acid (0.1 mmol, 1 eq). Purification by recrystallization from a mixture of diethyl ether and *n*-hexane provides the corresponding hydroxyketone **11**. 14.6 mg (0.07 mmol). 67% yield. The product is obtained in 76% *ee.*

$[\alpha]^{20}_{D}$ = +18.3° ($CHCl_3$, c = 1), 76% *ee*).
mp = 45-46 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 3.25 – 3.46 (m, C*H*$_2$), 4.70 (dqd, *J* = 9.6 Hz, 6.9, 2.7, C*H*(OH)), 7.57 – 7.46 (m, 2*H*)), 7.67 – 7.57 (m, 1*H*), 8.02 – 7.91 (m, 2*H*). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 38.4 (s, *C*H$_2$), 67.2 (q, *J* = 32.2 Hz, *C*H(OH)), 124.94 (d, *J* = 280.0 Hz, *C*F$_3$), 128.4, 129.0, 134.3, 136.2, 197.7 (*CO*).

^{19}F (NMR (376 MHz, $CDCl_3$): -79.27.

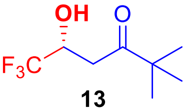
HRMS ESI [M+Na]+ calcd for $C_{15}H_{23}F_7O_2Na$: 241.0447. Observed: 241.0448.
IR (KBr): 645.9, 684.4, 753.9, 881.6, 1104.7, 1119.8, 1151.7, 1276.9, 1583.1, 1598.5, 1683.1, 2508.7, 3380.9 cm^{-1}
HPLC enantiomeric excess determination: Chiralpak ASH; Heptane/isopropanol (95/5), 1 mL/min, rt (m in) = 7.3 min; rt (maj) = 9.35 min.



12

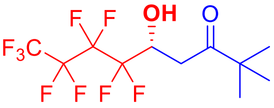
Prepared according to the general procedure using 49.5 mg of 2,2,3,3,4,4,4-Heptafluorobutyraldehyde hydrate (0.25 mmol, 2.5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 14.4 mg of 4,4-dimethyl-3-oxopentanoic acid (0.1 mmol, 1 eq). Purification by recrystallization from a mixture of diethyl ether and *n*-hexane provides the corresponding hydroxyketone **12**. 17.0 mg (0.04 mmol). 57% yield. The product is obtained in 96% *ee* before purification.

$[\alpha]^{20}_{D}$ = + 39.5° (CH_2Cl_2, c = 1), 96% *ee*).
mp = 49-50 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.18 (s, 3 C*H*$_3$), 2.67 – 3.13 (m, C*H*$_2$), 4.74 – 4.58 (m, C*H*(OH)). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 26.3 (s, 3 *C*H$_3$), 35.56 (s, *C*H$_2$), 66.77 (dd, *J* = 29.3, 22.6 Hz, *C*H(OH)), 109.4-125.7 (m, 2 *C*F$_2$ and *C*F$_3$), 214.9 (*CO*).
^{19}F (NMR (376 MHz, $CDCl_3$): -80.96 (dd, *J* = 11.5, 8.3 Hz, C*F$_3$*), -119.51- -120.38 (m, *AB* syst, *J* = 283.0, 11.4, 8.3, 2.2 Hz, 1 *F*), -124.58- -125.63 (ddd, *AB* syst, *J* = 293.0, 9.9, 5.4 Hz, 1 *F*), -126.38- -127.48 (ddd, *AB* syst, *J* = 294.0, 10.7, 2.5 Hz, 1 *F*), -126.90- -128.05 (m, *AB* syst, *J* = 283.0, 10.2, 8.2, 5.4 Hz, 1 *F*).
IR: 1107.9, 1184.4, 1210.6, 1714.7, 2942.9, 2974.8, 2992.9, 3473.7 cm^{-1}
HRMS ESI [M+Na]+ calcd for $C_{10}H_{13}F_7O_2Na$: 321.0696. Observed: 321.0695.
GC enantiomeric excess determination: Hydrodex-β; 120°C for 0 min than 1°C/min until 220°C. rt (m in) = 3.6 min; rt (maj) = 3.8 min.



13

Prepared according to the general procedure using 29.0 mg of trifluoroacetaldehyde monohydrate (0.25 mmol, 2.5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 14.4 mg of 4,4-dimethyl-3-oxopentanoic acid (0.1 mmol, 1 eq). Purification by recrystallization from a mixture of diethyl ether and *n*-hexane provides the corresponding hydroxyketone **13**. 10.7 mg (0.036 mmol). 54% yield. The product is obtained in 82% *ee* before purification.
$[\alpha]^{20}_{D}$ = + 19.5° (CH_2Cl_2, c = 1), 82% *ee*).
mp = 36-37 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.18 (s, 3 C*H*$_3$), 2.71 – 2.96 (m, C*H*$_2$), 3.47 (brs O*H*), 4.53 – 4.44 (m, C*H*(OH)). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 26.2 (s, *C*H$_3$), 36.4 (s, *C*H$_2$), 44.7 (s, C*H*), 67.5 (q, *J* = 32.1 Hz, *C*H(OH)), 123.05 – 126.77 (brs, *C*F$_3$), 214.4 (s, *C*O).
^{19}F (NMR (376 MHz, $CDCl_3$): -79.34.
IR: 787.1, 1024.1, 1128.4; 1402.5, 1636.7, 1705.8, 2942,9, 2974,8, 2992.9, 3473.7 cm^{-1}
HRMS ESI [M+Na]+ calcd for $C_8H_{13}F_3O_2Na$: 221.0760. Observed: 221.0759.
GC enantiomeric excess determination: Cyclosil-b; 110°C for 0 min than 1°C/min until 220°C. rt (m in) = 5.8 min; rt (maj) = 6.1 min.



14

Prepared according to the general procedure using 58.0 mg of 2,2,3,3,4,4,5,5,5-Nonafluoropentane-1,1-diol (0.25 mmol, 2.5 eq), 3.61 mg of copper triflate (0.01 mmol, 10 mol%), 4.34 mg of (+)-2,2′-Isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline] (0.013 mmol, 13 mol%) and 14.4 mg of 4,4-dimethyl-3-oxopentanoic acid (0.1 mmol, 1 eq). Purification by

recrystallization from a mixture of diethyl ether and *n*-hexane provides the corresponding hydroxyketone **14**. 21.1 mg (0.06 mmol). 63% yield. The product is obtained in 62% *ee* before purification.
$[\alpha]^{20}_D$ = + 27.5° (CH_2Cl_2, c = 1), 80% *ee*).
mp = 73-74 °C.
^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.18 (s, 3 C*H*$_3$), 2.79 – 3.02 (m, C*H*$_2$), 3.65 (brs, O*H*), 4.64 – 4.68 (m, C*H*(OH)). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) = 26.2 (s, 3 *C*H$_3$), 35.64 (s, *C*H$_2$), 66.92 (dd, *J* = 29.3, 22.4 Hz, *C*H(OH)), 109.4-125.7 (m, 3 *C*F$_2$ and *C*F$_3$), 215.0 (*CO*).
^{19}F (NMR (376 MHz, $CDCl_3$): -80.98 (tt, *J* = 9.9, 3.3 Hz, C*F*$_3$), -118.93- -120.13 (m, *AB* syst, *J* = 283.0, 24.1, 13.9, 11.4, 5.3, 3.2 Hz, 1 *F*), -121.25- -123.93 (m, *AB* syst, *J* = 293.0,17.4, 9.1, 3.0 Hz, 1 *F*), -124.79- -125.96 (m *AB* syst, *J* = 292.0, 10.4, 3.5 Hz, 1 *F*), -125.90- -127.05 (m, *AB* syst, *J* = 283.0, 15.8, 9.2, 6.4, 3.3 Hz, 1 *F*), -126.65- -127.81 (m, *AB* syst, *J* = 293.0, 15.2, 14.7, 8.1 Hz, 1 *F*).
IR: 1107.9, 1184.4, 1217.4, 1725.7, 2942.9, 2971.4, 2982.8, 3423.9 cm^{-1}
HRMS ESI [M+Na]+ calcd for $C_{11}H_{13}F_9O_2Na$: 371.0664. Observed: 371.0658.
GC enantiomeric excess determination: Cyclosil-b; 80°C for 0 min than 1°C/min until 220°C. rt (m in) = 29.7 min; rt (maj) = 30.1 min.

Additional datas

Single crystal X-ray diffraction:

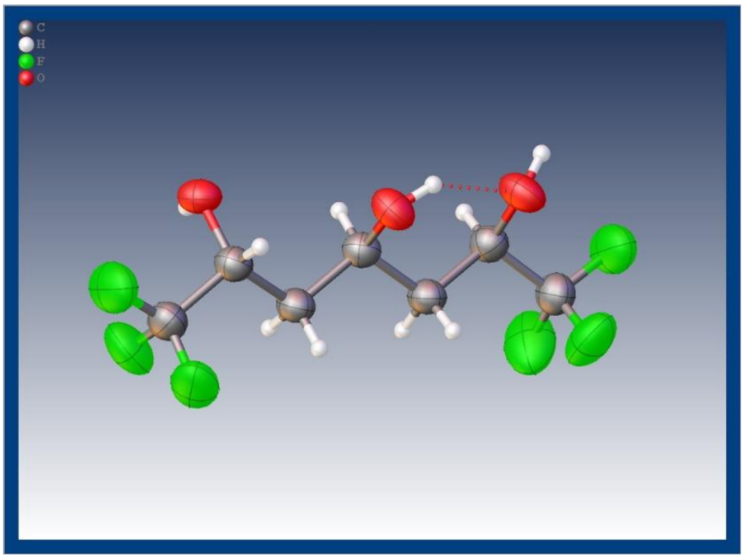


Table 1 Crystal data and structure refinement for 3c.

Identification code	CS641
Empirical formula	$C_7H_{10}F_6O_3$
Formula weight	256.15
Temperature/K	293
Crystal system	monoclinic
Space group	$P2_1$
a/Å	4.90290(10)
b/Å	9.8824(2)
c/Å	10.7838(3)
α/°	90
β/°	100.543(3)
γ/°	90
Volume/Å^3	513.68(2)
Z	2
ρ_{calc}g/cm^3	1.656
μ/mm^{-1}	1.766
F(000)	260.0
Crystal size/mm^3	0.4 × 0.14 × 0.06
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.34 to 136.514
Index ranges	$-5 \le h \le 5$, $-11 \le k \le 11$, $-12 \le l \le 12$
Reflections collected	7133
Independent reflections	1855 [R_{int} = 0.0300, R_{sigma} = 0.0191]
Data/restraints/parameters	1855/1/148
Goodness-of-fit on F^2	1.080
Final R indexes [I>=2σ (I)]	R_1 = 0.0323, wR_2 = 0.0892
Final R indexes [all data]	R_1 = 0.0327, wR_2 = 0.0897
Largest diff. peak/hole / e Å^{-3}	0.22/-0.17

Flack parameter -0.05(7)

Table 2 Fractional Atomic Coordinates ($\times10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2\times10^3$) for cs641. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
F1	1980(6)	9326(2)	730(2)	87.7(8)
F2	5097(6)	9241(3)	2401(3)	103.3(9)
F3	1157(6)	8393(3)	2391(3)	91.7(8)
F4	8345(5)	2034(3)	5020.7(19)	85.6(7)
F5	12137(5)	2551(3)	4462(2)	84.4(7)
F6	10164(6)	683(2)	3865(2)	91.1(8)
O1	1840(5)	6548(2)	506.4(19)	58.5(5)
O2	3672(4)	4147(2)	1455.5(19)	52.0(5)
O3	9572(4)	2495(2)	1905.9(16)	49.3(5)
C1	3103(7)	8553(3)	1698(3)	54.7(7)
C2	4106(6)	7213(3)	1265(2)	45.2(6)
C3	5228(6)	6322(3)	2389(3)	46.2(6)
C4	6065(5)	4912(3)	2020(3)	42.0(5)
C5	7524(6)	4143(3)	3173(2)	45.5(6)
C6	8097(6)	2667(3)	2897(2)	43.3(6)
C7	9680(7)	1972(3)	4063(3)	54.2(7)

Table 3 Anisotropic Displacement Parameters ($Å^2\times10^3$) for cs641. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
F1	131(2)	63.7(12)	68.5(13)	17.5(10)	18.4(13)	39.7(13)
F2	97.9(16)	58.0(12)	141(2)	-32.0(15)	-13.4(16)	2.4(12)
F3	113.0(18)	81.4(16)	95.5(17)	5.3(13)	57.9(15)	29.1(13)
F4	99.0(16)	110.1(18)	53.2(10)	31.3(11)	28.8(10)	31.4(14)
F5	66.9(11)	106.0(18)	70.0(12)	17.0(13)	-14.6(9)	1.6(11)
F6	135(2)	59.2(13)	75.5(14)	12.4(11)	8.4(14)	33.8(14)
O1	75.0(14)	53.8(12)	40.8(10)	7.6(9)	-5.0(9)	-2.5(10)
O2	54.4(10)	48.3(11)	48.2(10)	6.6(9)	-4.3(8)	-7.7(9)
O3	61.1(11)	48.4(10)	38.2(9)	-4.9(8)	8.6(8)	-5.1(9)
C1	61.1(17)	47.3(15)	54.7(17)	1.1(13)	8.0(14)	6.6(13)
C2	52.9(13)	42.1(13)	41.7(13)	2.8(10)	11.4(11)	1.2(11)
C3	55.4(15)	43.8(13)	38.4(13)	-2.1(11)	6.0(11)	2.9(11)
C4	45.6(12)	41.5(13)	39.0(12)	-0.4(10)	7.9(10)	-3.6(10)
C5	52.7(13)	45.2(14)	36.8(12)	-2.7(11)	3.0(10)	1.9(12)
C6	48.4(13)	42.6(13)	38.1(12)	0.7(11)	6.3(10)	-1.1(11)
C7	63.1(17)	55.5(17)	43.8(13)	6.1(13)	9.1(12)	10.1(14)

Table 4 Bond Lengths for cs641.

Atom	Atom	Length/Å
F1	C1	1.329(4)
F2	C1	1.312(4)
F3	C1	1.325(4)
F4	C7	1.321(4)
F5	C7	1.332(4)
F6	C7	1.321(4)
O1	C2	1.415(4)
O2	C4	1.435(3)
O3	C6	1.406(3)
C1	C2	1.516(4)
C2	C3	1.517(4)
C3	C4	1.526(4)
C4	C5	1.520(4)
C5	C6	1.526(4)
C6	C7	1.516(4)

Table 5 Bond Angles for cs641.

Atom	Atom	Atom	Angle/°
F1	C1	C2	111.8(3)
F2	C1	F1	108.3(3)
F2	C1	F3	105.9(3)
F2	C1	C2	112.4(3)
F3	C1	F1	105.9(3)
F3	C1	C2	112.1(3)
O1	C2	C1	108.6(2)
O1	C2	C3	108.9(2)
C1	C2	C3	110.6(2)
C2	C3	C4	113.4(2)
O2	C4	C3	110.7(2)
O2	C4	C5	108.0(2)
C5	C4	C3	110.6(2)
C4	C5	C6	113.2(2)
O3	C6	C5	113.7(2)
O3	C6	C7	108.6(2)
C7	C6	C5	110.8(2)
F4	C7	F5	106.0(3)
F4	C7	C6	112.1(2)
F5	C7	C6	111.7(3)
F6	C7	F4	107.5(3)
F6	C7	F5	106.7(3)
F6	C7	C6	112.5(3)

Table 6 Torsion Angles for cs641.

A	B	C	D	Angle/°
F1	C1	C2	O1	-57.4(3)
F1	C1	C2	C3	-176.8(3)
F2	C1	C2	O1	-179.4(3)
F2	C1	C2	C3	61.1(4)
F3	C1	C2	O1	61.5(3)
F3	C1	C2	C3	-58.0(3)
O1	C2	C3	C4	56.2(3)
O2	C4	C5	C6	51.5(3)
O3	C6	C7	F4	-176.9(3)
O3	C6	C7	F5	64.3(3)
O3	C6	C7	F6	-55.7(3)
C1	C2	C3	C4	175.5(2)
C2	C3	C4	O2	-67.9(3)
C2	C3	C4	C5	172.3(2)
C3	C4	C5	C6	172.8(2)
C4	C5	C6	O3	54.4(3)
C4	C5	C6	C7	177.1(2)
C5	C6	C7	F4	57.5(3)
C5	C6	C7	F5	-61.3(3)
C5	C6	C7	F6	178.7(3)

Table 7 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for cs641.

Atom	*x*	*y*	*z*	U(eq)
H1	1617.87	6849.23	-213.62	88
H2	2723.65	4598.95	900.06	78
H3	10890.96	3018.88	2000.32	74
H2A	5564.52	7374.8	771.14	54
H3A	3823.93	6234.73	2911.67	55
H3B	6829.52	6760.36	2889.69	55
H4	7323.34	4996.59	1414.88	50
H5A	6387.21	4177.72	3819.74	55
H5B	9269.08	4588.97	3502.58	55
H6	6305.71	2207.57	2658.43	52

Experimental

Single crystals of $C_7H_{10}F_6O_3$ **3c** were crystallized from a diethyl ether solution. A suitable crystal was selected and mounted on a SuperNova, Dual, Cu at home/near, AtlasS2 diffractometer. The crystal was kept at 293 K during data collection. Using Olex2,[5] the structure was solved with the ShelXT[6] structure solution program using Intrinsic Phasing and refined with the ShelXL[7] refinement package using Least Squares minimisation.

Crystal structure determination of 3c

Crystal Data for $C_7H_{10}F_6O_3$ (M =256.15 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 4.90290(10) Å, b = 9.8824(2) Å, c = 10.7838(3) Å, β = 100.543(3)°, V = 513.68(2) Å^3, Z = 2, T = 293 K, μ(CuKα) = 1.766 mm^{-1}, $Dcalc$ = 1.656 g/cm^3, 7133 reflections measured (8.34° ≤ 2Θ ≤ 136.514°), 1855 unique (R_{int} = 0.0300, R_{sigma} = 0.0191) which were used in all calculations. The final R_1 was 0.0323 (I > 2σ(I)) and wR_2 was 0.0897 (all data).

Refinement model description

Number of restraints - 1, number of constraints - unknown.

Details:
1. Fixed Uiso
 At 1.2 times of:
  All C(H) groups, All C(H,H) groups
 At 1.5 times of:
  All O(H) groups
2.a Ternary CH refined with riding coordinates:
 C2(H2A), C4(H4), C6(H6)
2.b Secondary CH2 refined with riding coordinates:
 C3(H3A,H3B), C5(H5A,H5B)
2.c Idealised tetrahedral OH refined as rotating group:
 O1(H1), O2(H2), O3(H3)

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[5] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Cryst*. 2009, *42*, 339.

[6] G.M. Sheldrick, *Acta Cryst*. **2015**, A71, 3-8.

[7] G. M. Sheldrick, *Acta Cryst*. 2015, C71, 3-8.

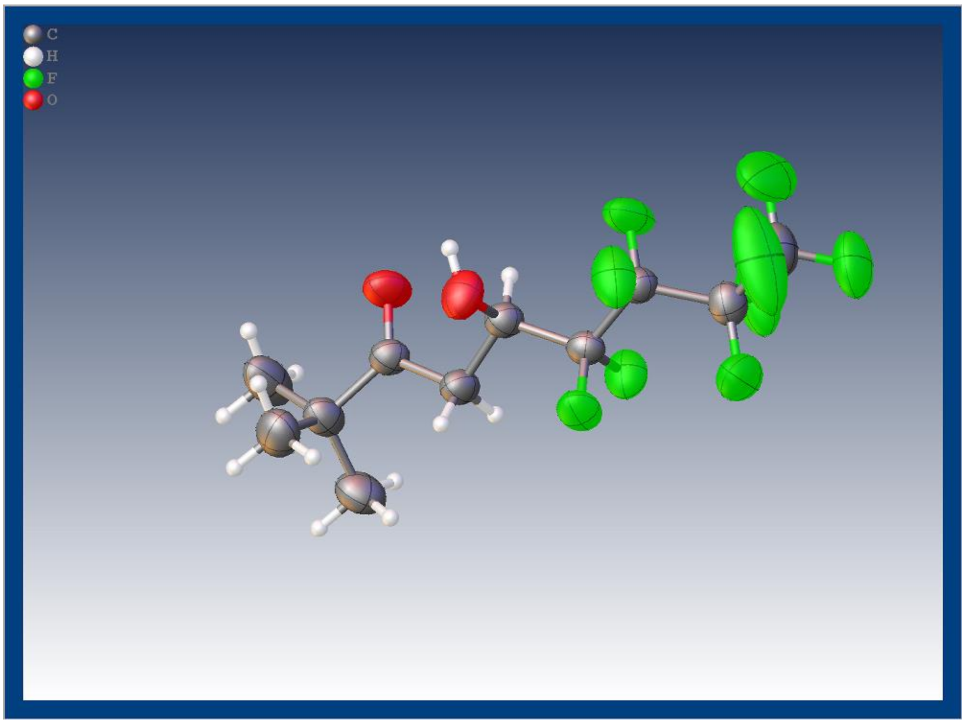

Table 8 Crystal data and structure refinement for 14.

Identification code	cs854
Empirical formula	$C_{11}H_{13}F_9O_2$
Formula weight	348.21
Temperature/K	295
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	5.60440(10)
b/Å	9.5819(2)
c/Å	26.4720(5)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1421.57(5)
Z	4
ρ_{calc}g/cm^3	1.627
μ/mm^{-1}	1.713
F(000)	704.0
Crystal size/mm^3	0.3 × 0.3 × 0.08
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	6.678 to 150.124
Index ranges	$-6 \leq h \leq 6$, $-11 \leq k \leq 11$, $-32 \leq l \leq 32$
Reflections collected	19917
Independent reflections	2746 [R_{int} = 0.0446, R_{sigma} = 0.0176]
Data/restraints/parameters	2746/0/203
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0493, wR_2 = 0.1393
Final R indexes [all data]	R_1 = 0.0508, wR_2 = 0.1416
Largest diff. peak/hole / e Å^{-3}	0.27/-0.21
Flack parameter	-0.01(6)

Table 9 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 12. U_{eq} is defined as 1/3 of of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
F1	8629(3)	5102(3)	5103.0(8)	62.8(6)
F2	6046(5)	6754(2)	4980.5(8)	62.7(6)
F3	3099(4)	5222(4)	5690.1(9)	87.0(9)
F4	6378(7)	4122(2)	5877.1(8)	81.3(8)
F5	8545(6)	6785(4)	5956.5(12)	103.0(11)
F6	5024(8)	7650(3)	5903.6(11)	107.9(13)
F7	3678(10)	5966(7)	6679.7(14)	172(3)
F8	7245(13)	5319(4)	6759.3(12)	175(3)
F9	6357(7)	7412(3)	6845.6(11)	103.8(11)
O1	2047(4)	4020(4)	3922.0(10)	66.9(7)
O2	5210(6)	3082(3)	4897.5(10)	66.2(7)
C1	5148(6)	3851(4)	3296.9(12)	53.9(8)
C2	4134(5)	4160(4)	3822.9(11)	46.0(7)
C3	5848(5)	4704(4)	4219.8(11)	49.0(7)
C4	4912(6)	4484(3)	4751.5(11)	45.5(7)
C5	6272(5)	5400(3)	5120.9(11)	41.5(6)
C6	5476(6)	5287(4)	5678.3(11)	47.3(7)
C7	6247(7)	6519(4)	6023.0(14)	55.3(8)
C8	5868(11)	6288(5)	6589.2(15)	76.4(13)
C9	3106(8)	3607(7)	2927.9(17)	86.3(16)
C10	6716(9)	5048(5)	3125.4(15)	71.7(11)
C11	6627(8)	2513(5)	3340.8(19)	74.6(11)

Table 10 Anisotropic Displacement Parameters (Å^2×10^3) for cs854. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\ldots]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}

F1	33.5(9)	93.0(16)	61.9(11)	-15.6(11)	-2.5(8)	3.4(9)
F2	87.3(16)	47.1(9)	53.8(10)	6.5(8)	-2.8(10)	-2.0(10)
F3	46.6(12)	154(3)	60.2(12)	-24.1(15)	12.1(9)	-24.3(15)
F4	136(3)	54.6(11)	52.8(11)	7.1(9)	-8.7(14)	7.6(14)
F5	74.2(17)	145(3)	90.3(19)	-46.7(19)	7.5(15)	-41.5(19)
F6	175(4)	73.5(16)	75.6(16)	-14.2(13)	-25(2)	49(2)
F7	169(4)	271(6)	75(2)	-57(3)	54(2)	-107(4)
F8	340(8)	127(3)	58.3(17)	-9.3(17)	-54(3)	98(4)
F9	142(3)	104(2)	65.1(14)	-35.0(15)	-8.2(17)	0(2)
O1	36.8(12)	107(2)	57.2(13)	-8.1(14)	-0.1(10)	-7.4(13)
O2	85.6(19)	52.4(13)	60.6(14)	2.4(11)	-7.5(14)	-12.5(13)
C1	40.4(16)	75(2)	46.2(15)	-7.9(15)	-1.6(13)	2.8(15)
C2	36.0(15)	56.4(16)	45.4(14)	1.0(13)	-2.7(12)	-1.0(13)
C3	39.6(15)	63.3(18)	44.0(15)	-2.6(14)	0.0(12)	-7.8(14)
C4	38.9(15)	54.6(16)	43.1(14)	0.4(12)	-0.9(12)	-3.1(13)
C5	34.6(14)	45.1(14)	44.8(14)	1.4(12)	1.3(11)	2.4(11)
C6	42.5(15)	54.5(16)	44.9(15)	1.7(13)	-0.9(12)	-5.1(14)
C7	56(2)	59.2(18)	51.3(17)	-7.3(14)	-3.4(15)	5.2(16)
C8	99(4)	80(3)	50.2(19)	-11.8(18)	-6(2)	2(2)
C9	51(2)	153(5)	55(2)	-30(3)	-8.7(18)	9(3)
C10	70(2)	92(3)	53.4(19)	6.5(19)	12.4(18)	0(2)
C11	60(2)	77(2)	86(3)	-22(2)	3(2)	6(2)

Table 11 Bond Lengths for 12.

Atom	**Atom**	**Length/Å**	**Atom**	**Atom**	**Length/Å**
F1	C5	1.352(4)	C1	C2	1.533(4)
F2	C5	1.355(4)	C1	C9	1.523(5)
F3	C6	1.334(4)	C1	C10	1.515(6)
F4	C6	1.334(4)	C1	C11	1.531(6)
F5	C7	1.325(5)	C2	C3	1.516(4)
F6	C7	1.321(5)	C3	C4	1.517(4)
F7	C8	1.288(7)	C4	C5	1.519(4)
F8	C8	1.289(6)	C5	C6	1.545(4)
F9	C8	1.302(5)	C6	C7	1.553(5)
O1	C2	1.206(4)	C7	C8	1.530(5)
O2	C4	1.408(4)			

Table 12 Bond Angles for 12.

Atom	Atom	Atom	Angle/˚
C9	C1	C2	109.5(3)
C9	C1	C11	109.1(4)
C10	C1	C2	109.9(3)
C10	C1	C9	111.1(4)
C10	C1	C11	110.0(4)
C11	C1	C2	107.1(3)
O1	C2	C1	122.4(3)
O1	C2	C3	120.1(3)
C3	C2	C1	117.5(3)
C2	C3	C4	112.1(3)
O2	C4	C3	110.3(3)
O2	C4	C5	108.4(2)
C3	C4	C5	110.1(2)
F1	C5	F2	106.5(3)
F1	C5	C4	110.2(2)
F1	C5	C6	107.5(2)
F2	C5	C4	109.2(2)
F2	C5	C6	107.5(2)
C4	C5	C6	115.4(2)
F3	C6	C5	108.3(3)
F3	C6	C7	107.4(3)
F4	C6	F3	109.2(3)
F4	C6	C5	109.0(3)
F4	C6	C7	107.4(3)
C5	C6	C7	115.3(3)
F5	C7	C6	109.8(3)
F5	C7	C8	107.0(4)
F6	C7	F5	108.3(4)
F6	C7	C6	109.8(3)
F6	C7	C8	106.3(3)
C8	C7	C6	115.3(3)
F7	C8	F8	109.4(6)
F7	C8	F9	107.6(5)
F7	C8	C7	110.4(4)
F8	C8	F9	106.7(4)
F8	C8	C7	111.3(4)
F9	C8	C7	111.2(4)

Table 13 Torsion Angles for 12.

A	B	C	D	Angle/˚
F1	C5	C6	F3	-164.4(3)
F1	C5	C6	F4	-45.6(3)
F1	C5	C6	C7	75.2(3)
F2	C5	C6	F3	81.3(3)
F2	C5	C6	F4	-159.9(3)
F2	C5	C6	C7	-39.1(4)
F3	C6	C7	F5	-169.1(3)
F3	C6	C7	F6	-50.1(4)
F3	C6	C7	C8	69.9(4)
F4	C6	C7	F5	73.5(4)
F4	C6	C7	F6	-167.6(4)
F4	C6	C7	C8	-47.5(5)
F5	C7	C8	F7	-177.4(5)
F5	C7	C8	F8	-55.6(6)
F5	C7	C8	F9	63.3(5)
F6	C7	C8	F7	67.0(5)
F6	C7	C8	F8	-171.2(5)
F6	C7	C8	F9	-52.4(6)
O1	C2	C3	C4	22.3(5)
O2	C4	C5	F1	62.1(3)
O2	C4	C5	F2	178.8(3)
O2	C4	C5	C6	-59.9(3)
C1	C2	C3	C4	-159.6(3)
C2	C3	C4	O2	77.2(4)
C2	C3	C4	C5	-163.3(3)
C3	C4	C5	F1	-58.5(3)
C3	C4	C5	F2	58.1(3)
C3	C4	C5	C6	179.4(3)
C4	C5	C6	F3	-40.9(4)
C4	C5	C6	F4	77.9(3)
C4	C5	C6	C7	-161.3(3)
C5	C6	C7	F5	-48.3(4)
C5	C6	C7	F6	70.7(4)
C5	C6	C7	C8	-169.3(3)
C6	C7	C8	F7	-54.9(6)
C6	C7	C8	F8	66.9(6)
C6	C7	C8	F9	-174.3(4)
C9	C1	C2	O1	9.5(6)
C9	C1	C2	C3	-168.5(4)
C10	C1	C2	O1	131.8(4)
C10	C1	C2	C3	-46.2(4)
C11	C1	C2	O1	-108.6(4)
C11	C1	C2	C3	73.3(4)

Table 14 Hydrogen Atom Coordinates (Å×10⁴) and Isotropic Displacement Parameters (Å²×10³) for 12.

Atom	x	y	z	U(eq)
H2	3901.32	2731.55	4952.82	99
H3A	6113.86	5692.21	4164.61	59
H3B	7367.98	4229.93	4184.29	59
H4	3213.16	4724.47	4762.88	55
H9A	2074.11	2891.38	3057.33	129
H9B	3738.75	3319.6	2607.36	129
H9C	2217.08	4455.57	2886.38	129
H10A	5832.54	5904.53	3143.6	108
H10B	7217.63	4889.64	2783.37	108
H10C	8091.37	5107.26	3340.4	108
H11A	7947.7	2669.47	3564.66	112
H11B	7214.72	2254.1	3013.28	112
H11C	5646.03	1775.67	3471.99	112

Experimental

Single crystals of $C_{11}H_{13}F_9O_2$ **14** were crystallized from a diethyl ether solution. A suitable crystal was selected and mounted on a SuperNova, Dual, Cu at home/near, AtlasS2 diffractometer. The crystal was kept at 295 K during data collection. Using Olex2,[8] the structure was solved with the ShelXT[9] structure solution program using Intrinsic Phasing and refined with the ShelXL[10] refinement package using Least Squares minimisation.

Crystal structure determination of 14

Crystal Data for $C_{11}H_{13}F_9O_2$ (M =348.21 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 5.60440(10) Å, b = 9.5819(2) Å, c = 26.4720(5) Å, V = 1421.57(5) Å^3, Z = 4, T = 295 K, μ(CuKα) = 1.713 mm^{-1}, *Dcalc* = 1.627 g/cm^3, 19917 reflections measured (6.678° ≤ 2Θ ≤ 150.124°), 2746 unique (R_{int} = 0.0446, R_{sigma} = 0.0176) which were used in all calculations. The final R_1 was 0.0493 (I > 2σ(I)) and wR_2 was 0.1416 (all data).

Refinement model description

Number of restraints - 0, number of constraints - unknown.

Details:
1. Fixed Uiso
 At 1.2 times of:
  All C(H) groups, All C(H,H) groups
 At 1.5 times of:
  All C(H,H,H) groups, All O(H) groups
2.a Ternary CH refined with riding coordinates:
 C4(H4)
2.b Secondary CH2 refined with riding coordinates:
 C3(H3A,H3B)
2.c Idealised Me refined as rotating group:
 C9(H9A,H9B,H9C), C10(H10A,H10B,H10C), C11(H11A,H11B,H11C)
2.d Idealised tetrahedral OH refined as rotating group: O2(H2)

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[8] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, H. Puschmann, *J. Appl. Cryst*. 2009, *42*, 339.

[9] G.M. Sheldrick, *Acta Cryst*. **2015**, A71, 3-8.

[10] G. M. Sheldrick, *Acta Cryst*. 2015, C71, 3-8.

Anion coordination

^{1}H NMR and ^{19}F binding determinations

The anion binding behavior of different polyols was first determined by ^{1}H NMR titration experiments in CD_3CN. The addition of tetrabutylammonium chloride (TBACl) to polyols resulted in large downfield shifts of the hydroxyl hydrogens. In addition, the binding of fluorinated polyols could also be easily monitored by ^{19}F NMR. Association constants was determined using the Thordarson method.[11] For each molecule, the titration experiment was repeated three times.

A solution of **3a** (2.28 mg, 0.005 mmol, 2.5 mM) in CD_3CN (2 ml) was titrated with a solution of TBACl (55,4 mg, 0.2 mmol, 100 mM) in CD_3CN (2 mL) and the ^{1}H NMR signals for the three different hydroxyl hydrogens were monitored.

Cl^- equiv.	**[Cl^-] (mol/L)**	**[triol] (mol/L)**	**δ (OH1) (ppm)**	**δ (OH2) (ppm)**	**δ (OH3) (ppm)**	**Δδ (OH1) (ppm)**	**Δδ (OH2) (ppm)**	**Δδ (OH3) (ppm)**
0	0	0,0025	3,45	4,05	4,34	0	0	0
0,2	0,000508866	0,002497502	3,82	4,41	4,57	0,37	0,36	0,23
0,4	0,001026073	0,00249501	4,2	4,79	4,81	0,38	0,38	0,24
0,6	0,001539133	0,002492522	4,49	4,99	5,1	0,29	0,2	0,29
0,8	0,002091633	0,00249004	4,76	5,16	5,38	0,27	0,17	0,28
1,0	0,002590174	0,002487562	4,97	5,29	5,59	0,21	0,13	0,21
1,4	0,00353598	0,00248139	5,26	5,48	5,89	0,29	0,19	0,3
2,5	0,006148148	0,002469136	5,45	5,6	6,07	0,19	0,12	0,18
3.3	0,008137605	0,00245942	5.46	5.62	6.09	0.01	0.02	0.02

A solution of **3b** (2.78 mg, 0.005 mmol, 2.5 mM) in CD_3CN (2 ml) was titrated with a solution of TBACl (55,4 mg, 0.2 mmol, 100 mM) in CD_3CN (2 mL) and the ^{1}H NMR signals for the three different hydroxyl hydrogens were monitored.

Cl^- equiv.	**[Cl^-] (mol/L)**	**[triol] (mol/L)**	**δ (OH1) (ppm)**	**δ (OH2) (ppm)**	**δ (OH3) (ppm)**	**Δδ (OH1) (ppm)**	**Δδ (OH2) (ppm)**	**Δδ (OH3) (ppm)**
0	0	0,0025	3,45	4,05	4,33	0	0	0
0,24	0,000608766	0,002497502	3,83	4,43	4,56	0,38	0,38	0,23
0,4	0,001009975	0,002493766	4,11	4,71	4,74	0,28	0,28	0,18
0,5	0,001320379	0,002491281	4,43	4,94	5,04	0,32	0,23	0,3
0,7	0,001815017	0,002486325	4,7	5,11	5,31	0,27	0,17	0,27
1,2	0,002882944	0,002485089	5,1	5,38	5,73	0,4	0,27	0,42
1,5	0,003581635	0,002482622	5,19	5,43	5,81	0,09	0,05	0,08
2,1	0,005275455	0,002474023	5,29	5,49	5,9	0,1	0,06	0,09
3.3	0,008137605	0,00245942	5,46	5,62	6,08	0,17	0,13	0,18
4.4	0,010821446	0,002446184	5,5	5,64	6,12	0,04	0,02	0,04

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[11] For the tool used, see http://supramolecular.org and a) P. Thodarson, Determining Association Constants from Titration Experiments in Supramolecular Chemistry. *Chem. Soc. Rev.* **2011**, *40*, 1305; b) D. B. Hibbert, P. Thodarson, The Death of the Job Plot, Transparency, Open Science and Online Tools, Uncertainty Estimation Methods and Other Developments in Supramolecular Chemistry Data Analysis. *Chem. Commun.* **2016**, *52*, 12792.

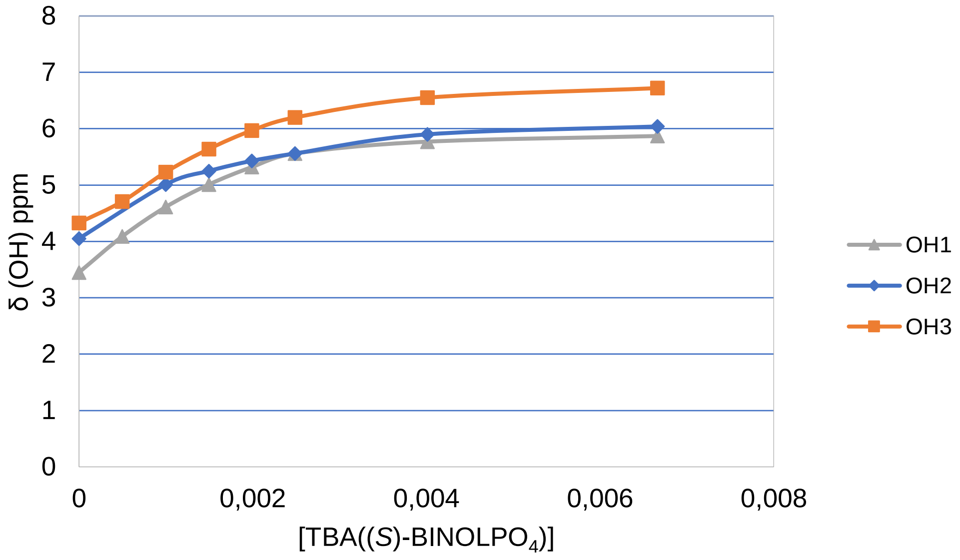
A solution of **3c** (1.28 mg, 0.005 mmol, 2.5 mM) in CD_3CN (2 ml) was titrated with a solution of TBACl (55,4 mg, 0.2 mmol, 100 mM) in CD_3CN (2 mL) and the ^1H NMR signals for the three different hydroxyl hydrogens were monitored.

Cl^- equiv.	**[Cl^-] (mol/L)**	**[triol] (mol/L)**	**δ (OH1) (ppm)**	**δ (OH2) (ppm)**	**δ (OH3) (ppm)**	**Δδ (OH1) (ppm)**	**Δδ (OH2) (ppm)**	**Δδ (OH3) (ppm)**
0	0	0.0025	3.45	4.05	4.34	0	0	0
0.2	0.0005089	0.0024975	3.82	4.41	4.57	0.37	0.36	0.23
0.4	0.0010261	0.002495	4.2	4.79	4.81	0.38	0.38	0.24
0.6	0.0015391	0.0024925	4.49	4.99	5.1	0.29	0.2	0.29
0.8	0.0020916	0.00249	4.76	5.16	5.38	0.27	0.17	0.28
1.0	0.0025902	0.0024876	4.97	5.29	5.59	0.21	0.13	0.21
1.4	0.003536	0.0024814	5.26	5.48	5.89	0.29	0.19	0.3
2.4	0.0061481	0.0024691	5.45	5.6	6.07	0.19	0.12	0.18

Chiral anion recognition:

A solution of **3b** (2.78 mg, 0.005 mmol, 2.5 mM) in CD_3CN (2 ml) was titrated with a solution of (*S*)-BINOL-PO_4) (30.2 mg, 0.05 mmol, 100 mM) in CD_3CN (0.5 mL) and the ^1H NMR signals for the three different hydroxyl hydrogens were monitored.

Cl^- equiv.	**[Cl^-] (mol/L)**	**[triol] (mol/L)**	**δ (OH1) (ppm)**	**δ (OH2) (ppm)**	**δ (OH3) (ppm)**	**Δδ (OH1) (ppm)**	**Δδ (OH2) (ppm)**	**Δδ (OH3) (ppm)**
0	0	0.0025	3.45	4.05	4.33	0	0	0
0.4	0.000998	0.00249501	4.61	5.01	5.23	1.16	0.96	0.9
0.6	0.0014955	0.002492522	5.01	5.25	5.64	0.4	0.24	0.41
0.8	0.001992032	0.00249004	5.32	5.43	5.97	0.19	0.18	0.33
1.0	0.0024876	0.002487562	5.56	5.56	6.2	0.24	0.13	0.23
1.6	0.0037221	0.00248139	5.77	5.9	6.55	0.21	0.34	0.35
2.6	0.0061728	0.002469136	5.87	6.04	6.72	0.1	0.14	0.17



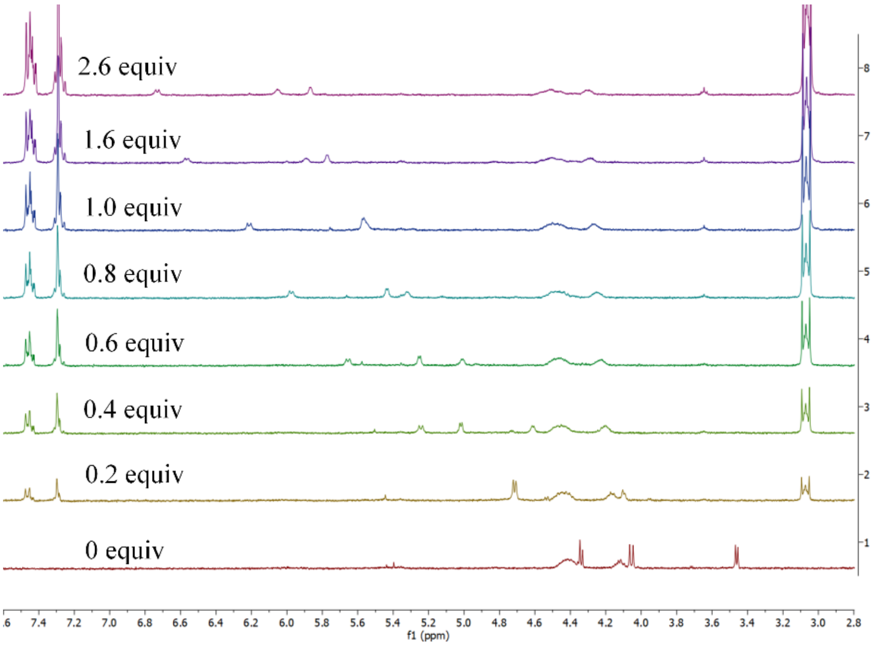
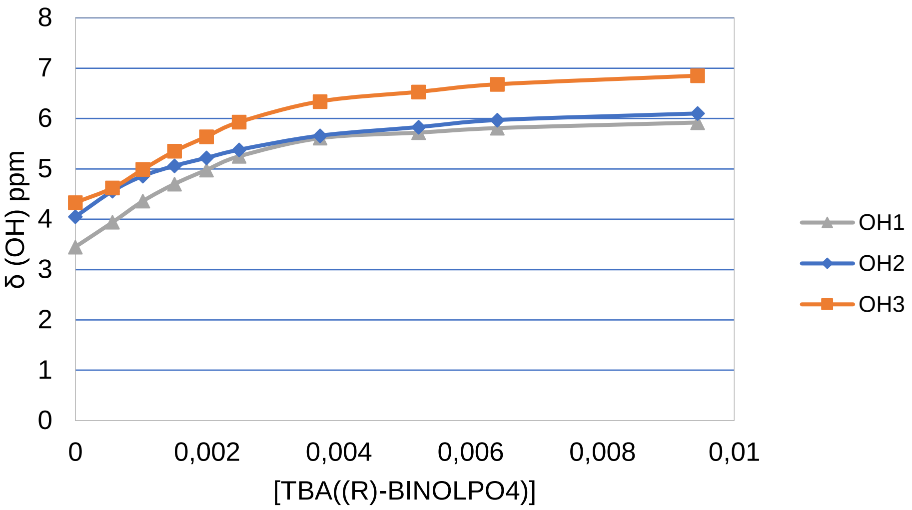


Figure 1 - Titration of 3b in CD_3CN

A solution of **3b** (2.78 mg, 0.005 mmol, 2.5 mM) in CD_3CN (2 ml) was titrated with a solution of (*R*)-BINOL-PO_4) (30.2 mg, 0.05 mmol, 100 mM) in CD_3CN (0.5 mL) and the ^{1}H NMR signals for the three different hydroxyl hydrogens were monitored.

Cl^- equiv.	**[Cl^-] (mol/L)**	**[triol] (mol/L)**	**δ (OH1) (ppm)**	**δ (OH2) (ppm)**	**δ (OH3) (ppm)**	**Δδ (OH1) (ppm)**	**Δδ (OH2) (ppm)**	**Δδ (OH3) (ppm)**
0	0	0,0025	3,45	4,05	4,33	0	0	0
0.2	0,0005651	0,002497502	3,94	4,56	4,62	0,49	0,51	0,29
0.4	0,0010261	0,00249501	4,36	4,86	4,99	0,42	0,3	0,37
0.6	0,0015049	0,002492522	4,7	5,06	5,35	0,34	0,2	0,36
0.8	0,001992	0,00249004	4,98	5,22	5,64	0,28	0,16	0,29
1.0	0,0024876	0,002487562	5,25	5,38	5,93	0,27	0,16	0,29
1.5	0,0037159	0,00248139	5,61	5,66	6,34	0,36	0,28	0,41
2.0	0,0052135	0,002475248	5,72	5,83	6,53	0,11	0,17	0,19
2.5	0,0064074	0,002457002	5,81	5,97	6,68	0,09	0,14	0,15
3.5	0,0094472	0,002469136	5,92	6,1	6,85	0,11	0,13	0,17



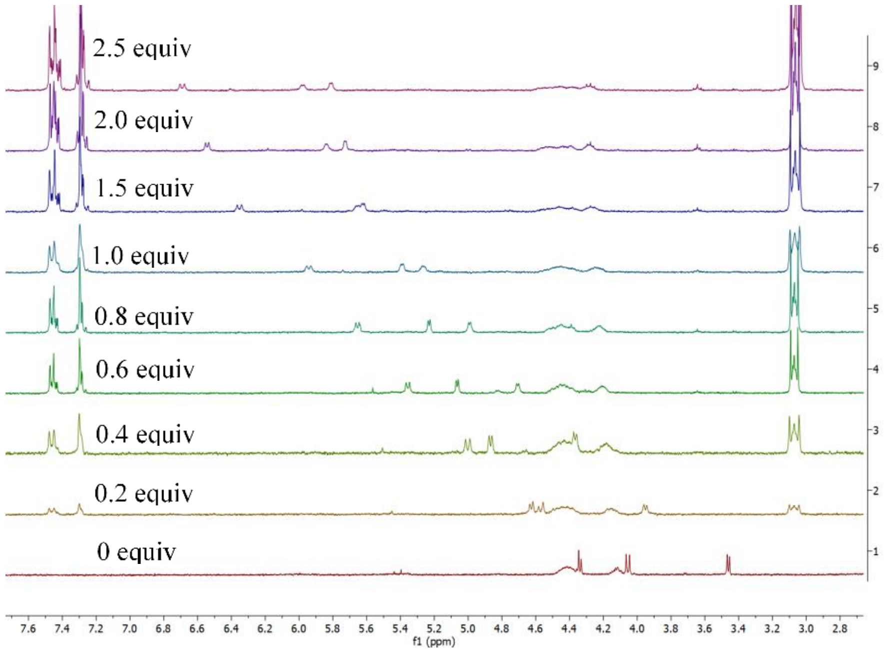
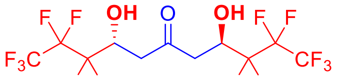
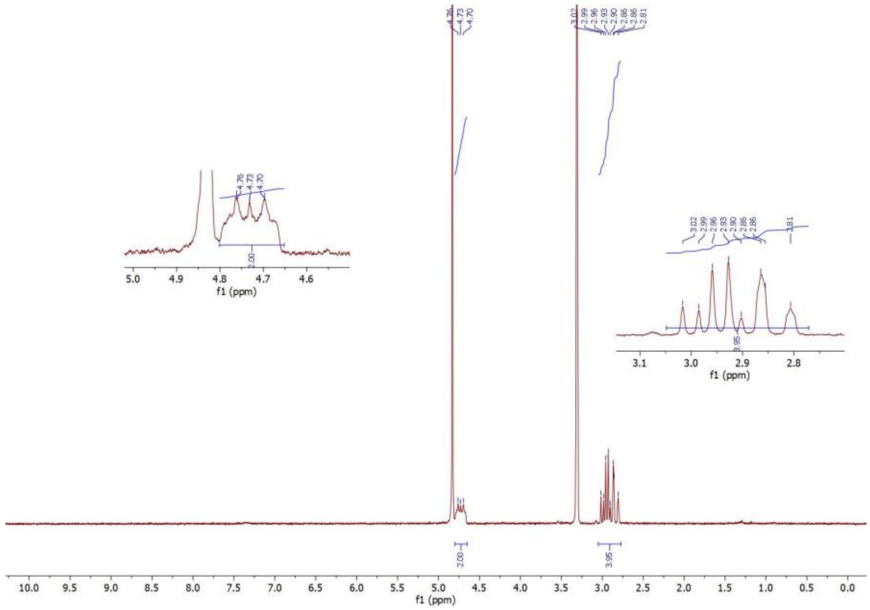


Figure 2 - Titration of 3b in CD_3CN

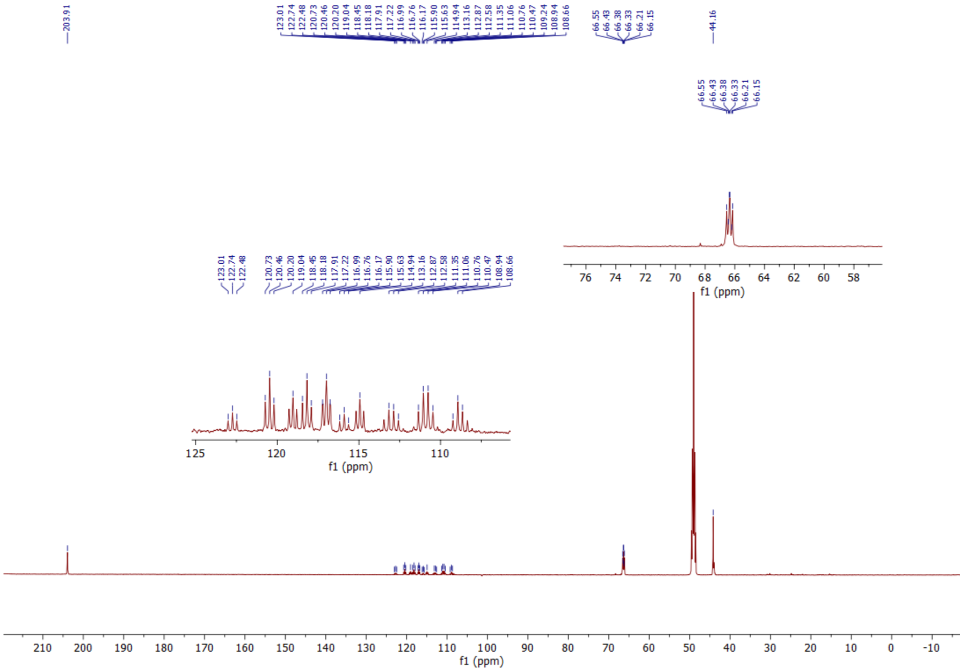
Spectras



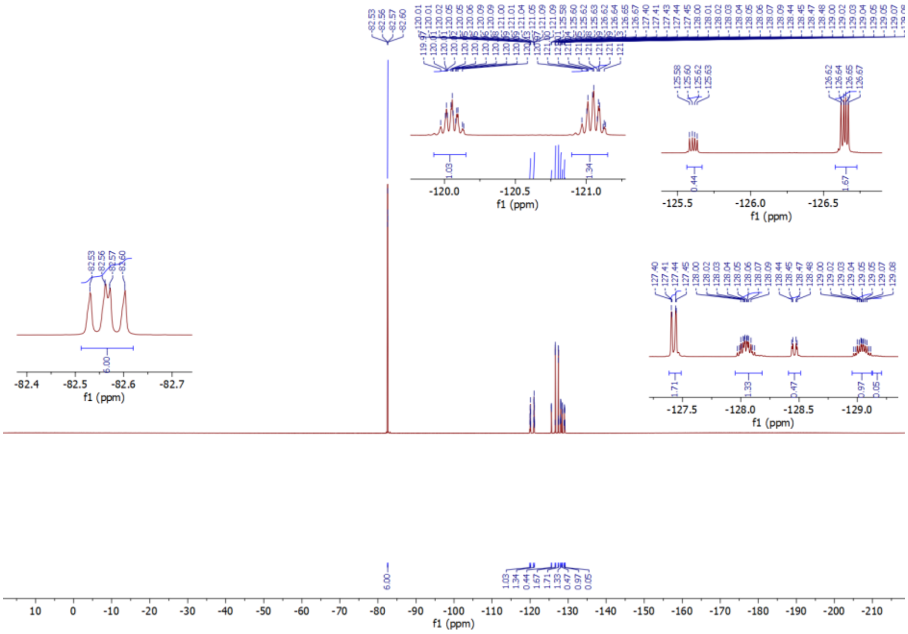
4a



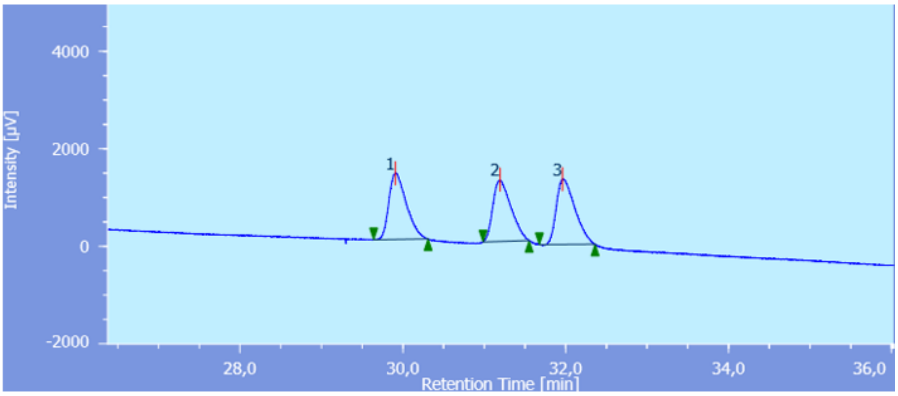
^{13}C NMR (151 MHz, overnight, 20 mg in 0.5 mL of MeOD):

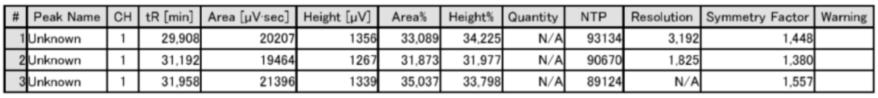


^{19}F NMR:



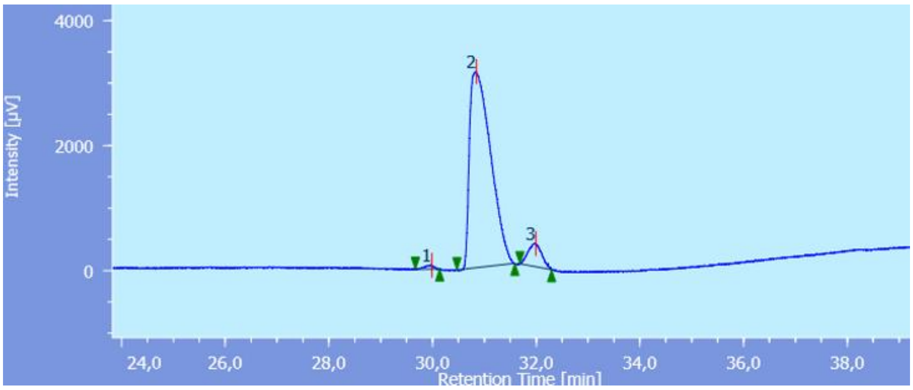
Chiral GC analysis: Racemic version:

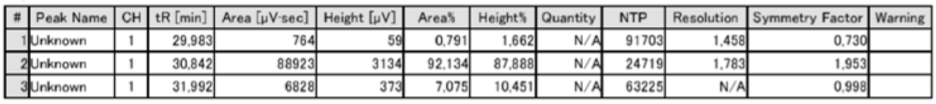




#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	29,908	20207	1356	33,089	34,225	N/A	93134	3,192	1,448	
2	Unknown	1	31,192	19464	1267	31,873	31,977	N/A	90670	1,825	1,380	
3	Unknown	1	31,958	21396	1339	35,037	33,798	N/A	89124	N/A	1,557	

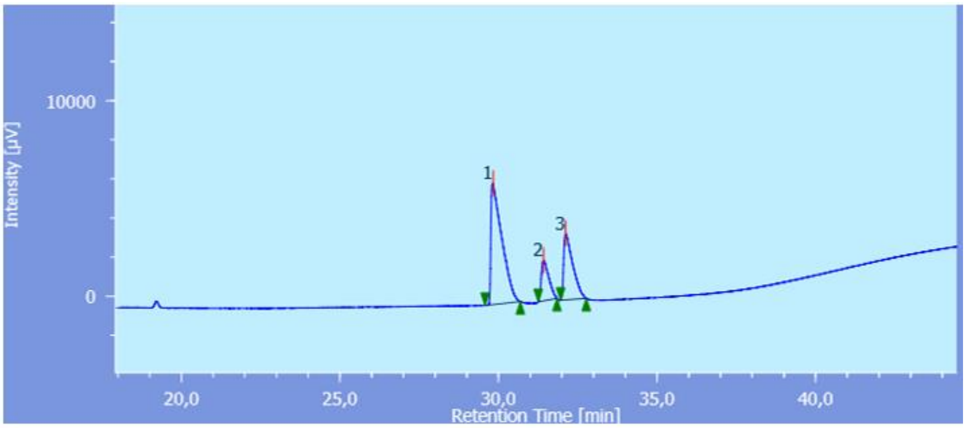
Enantiomeric version:





#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	29,983	764	59	0,791	1,662	N/A	91703	1,458	0,730	
2	Unknown	1	30,842	88923	3134	92,134	87,888	N/A	24719	1,783	1,953	
3	Unknown	1	31,992	6828	373	7,075	10,451	N/A	63225	N/A	0,998	

GC obtained using unoptimal L_6 to confirm peaks attribution:



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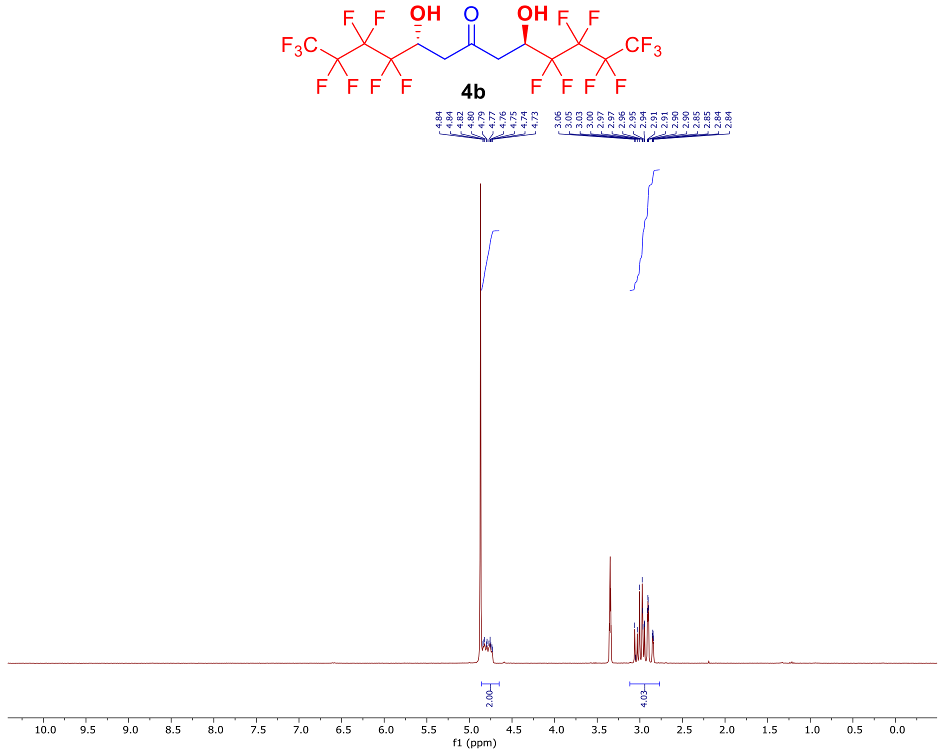
1	Unknown	1	29,825	146897	6203	58,993	53,172	N/A	35646	2,926	3,703	
2	Unknown	1	31,417	34554	2055	13,877	17,617	N/A	75003	1,412	1,805	
3	Unknown	1	32,108	67558	3408	27,131	29,211	N/A	60255	N/A	2,786	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7.5
7.0
6.5
6.0
5.5
5.0
4.5
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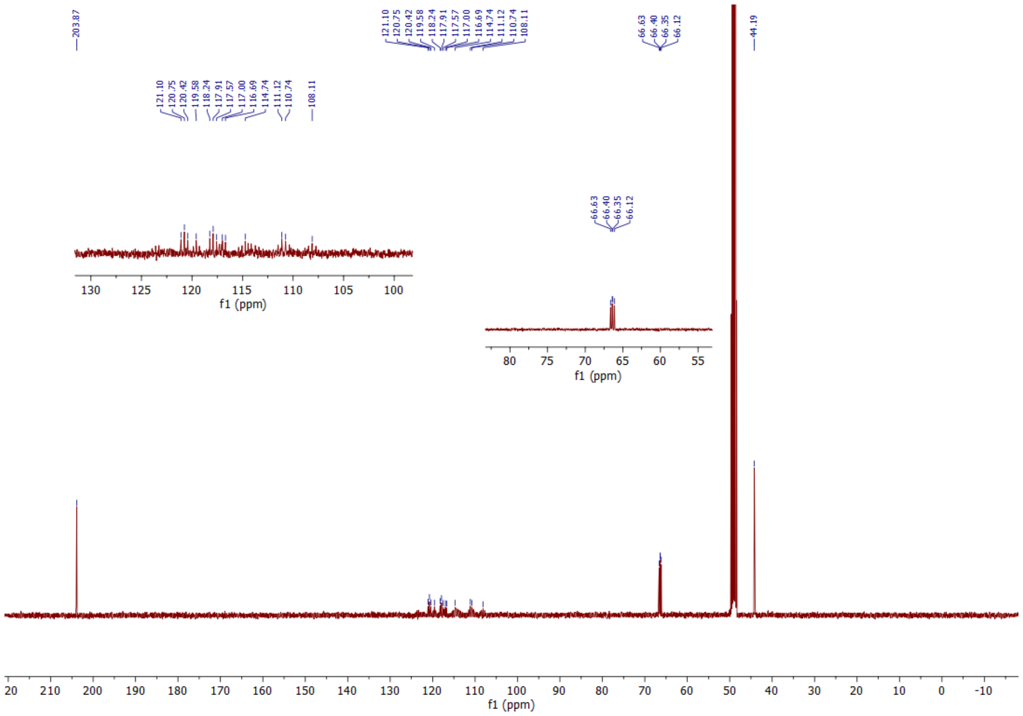
f1 (ppm)

^{13}C NMR (6 h):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110.74
108.11
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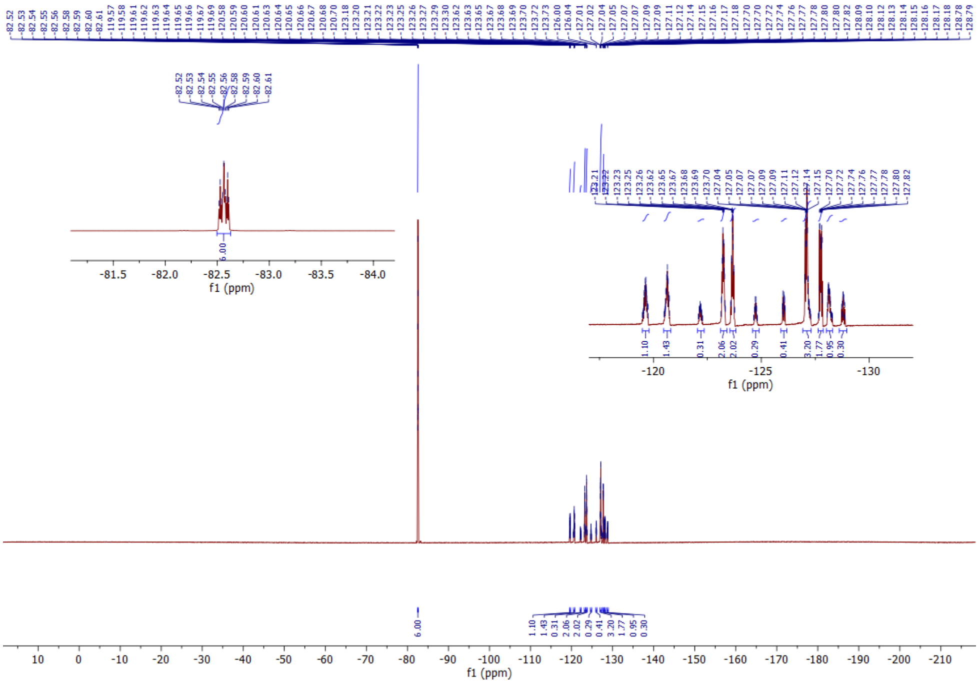
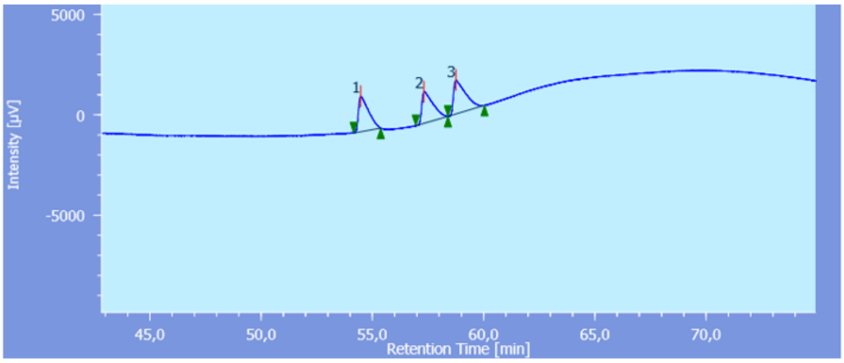
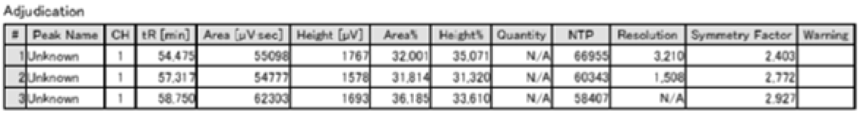
66.40
66.35
66.12
44.19
130
125
120
115
110
105
100
f1 (ppm)
80
75
70
65
60
55
f1 (ppm)
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{19}F NMR:



Chiral GC analysis: Racemic version:

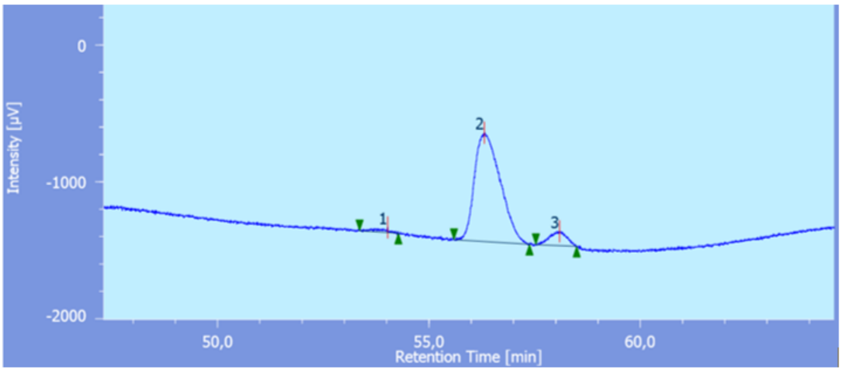


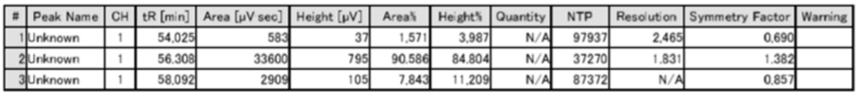


Adjudication

#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	54,475	55098	1767	32,001	35,071	N/A	66955	3,210	2,403	
2	Unknown	1	57,317	54777	1578	31,814	31,320	N/A	60343	1,508	2,772	
3	Unknown	1	58,750	62303	1693	36,185	33,610	N/A	58407	N/A	2,927	

Enantiomeric version:





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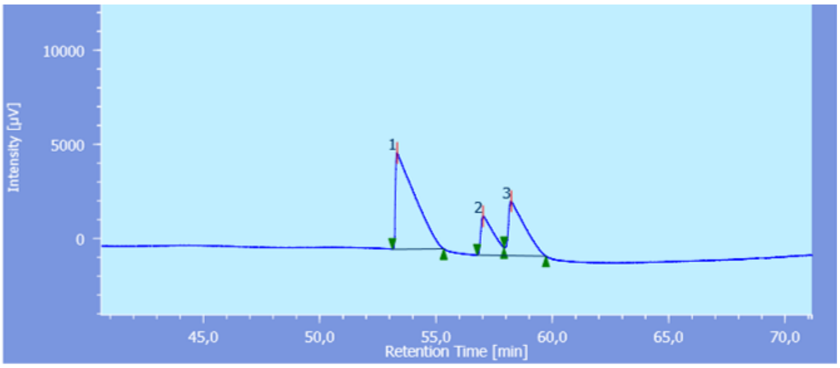
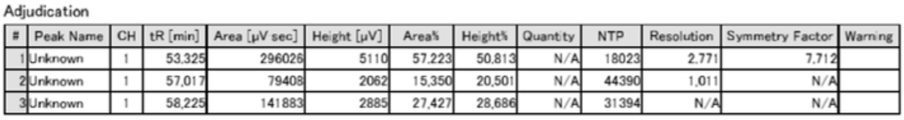
1	Unknown	1	54,025	583	37	1,571	3,987	N/A	97937	2,465	0,690	
2	Unknown	1	56.308	33600	795	90.586	84.804	N/A	37270	1.831	1.382	
3	Unknown	1	58,092	2909	105	7,843	11,209	N/A	87372	N/A	0,857	

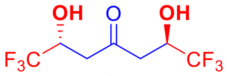
GC obtained using unoptimal L_6 to confirm peaks attribution:





Adjudication

#	Peak Name	CH	tR [min]	Area [µV sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	53,325	296026	5110	57,223	50,813	N/A	18023	2,771	7,712	
2	Unknown	1	57,017	79408	2062	15,350	20,501	N/A	44390	1,011	N/A	
3	Unknown	1	58,225	141883	2885	27,427	28,686	N/A	31394	N/A	N/A	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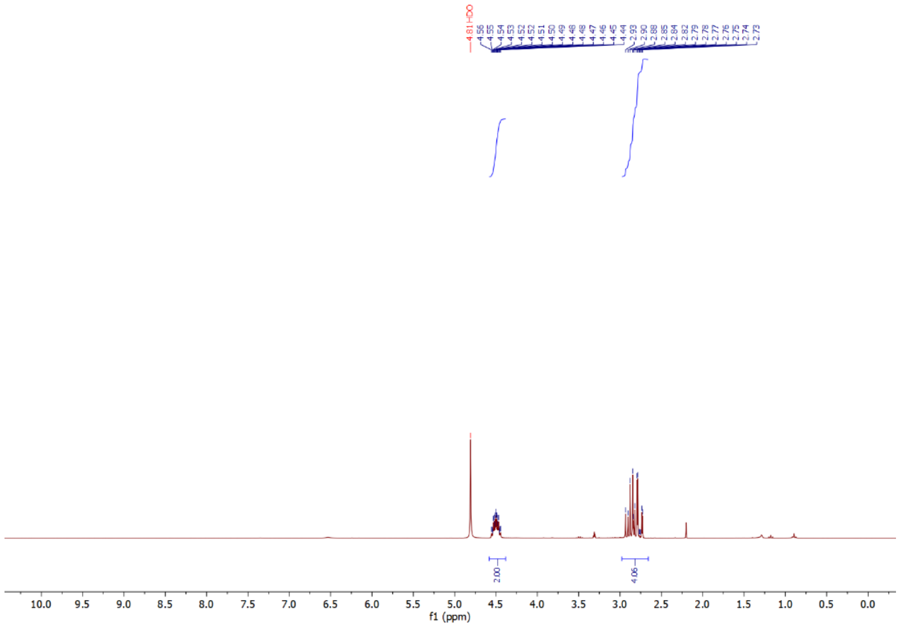
CF3

4c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2.79
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2.77
2.76
2.75
2.74
2.73
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10.0
9.5
9.0
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8.0
7.5
7.0
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5.5
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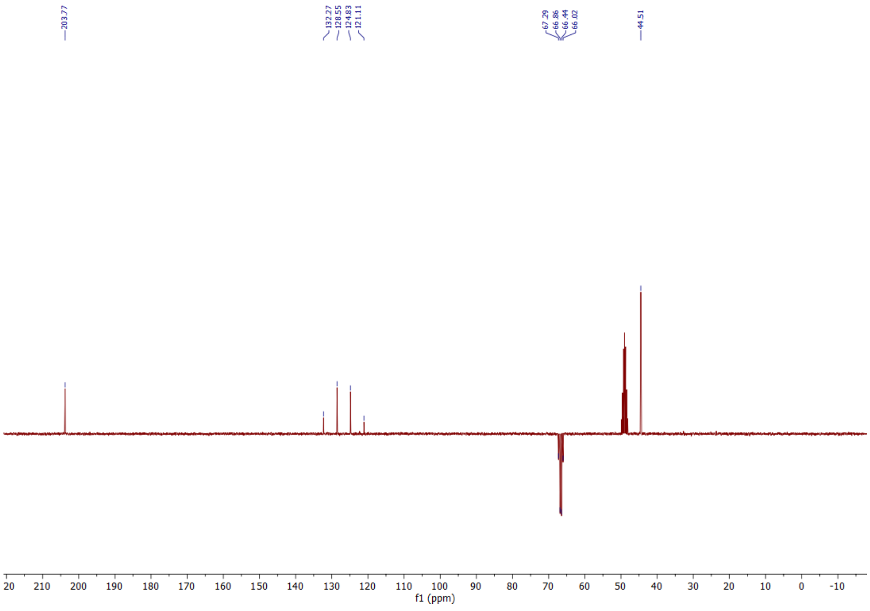
1.0
0.5
0.0
f1 (ppm)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160
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140
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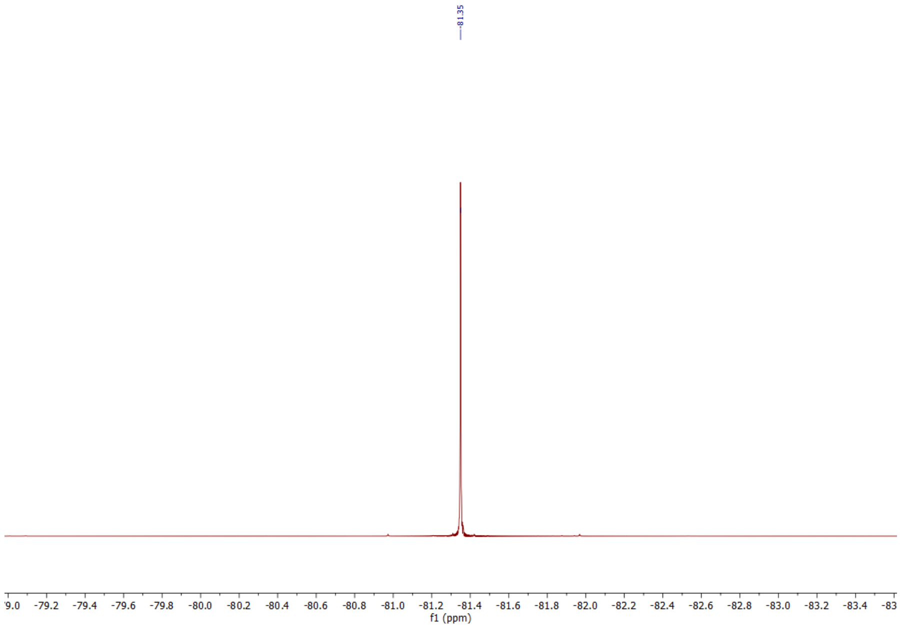
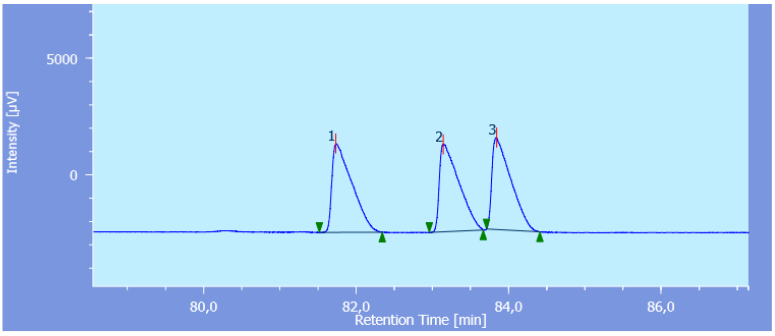
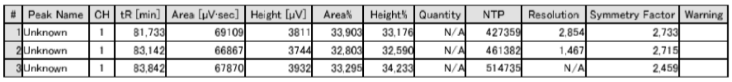
20
10
0
-10
f1 (ppm)

^{19}F NMR:



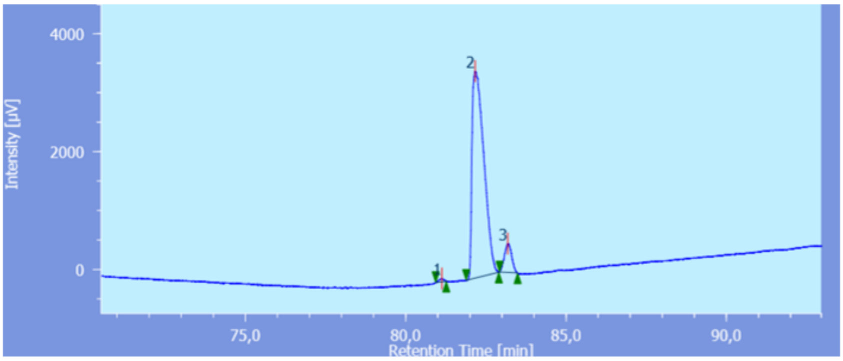
Chiral GC analysis: Racemic version:

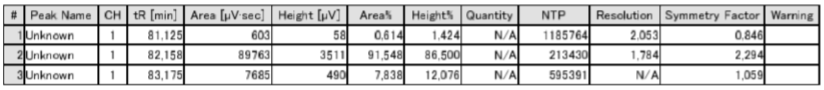




#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	81,733	69109	3811	33,903	33,176	N/A	427359	2,854	2,733	
2	Unknown	1	83,142	66867	3744	32,803	32,590	N/A	461382	1,467	2,715	
3	Unknown	1	83,842	67870	3932	33,295	34,233	N/A	514735	N/A	2,459	

Enantioselective version:





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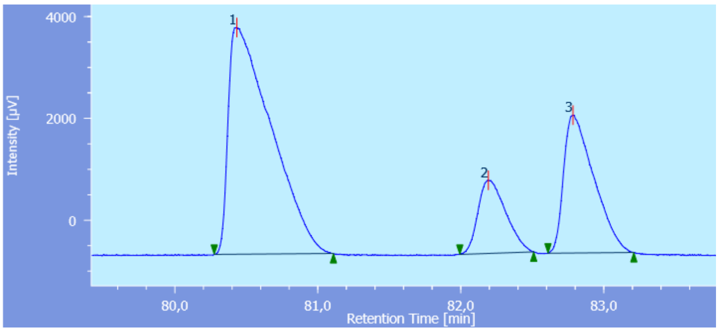
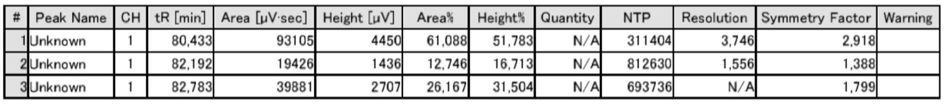
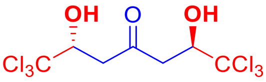
1	Unknown	1	81,125	603	58	0,614	1,424	N/A	1185764	2,053	0,846	
2	Unknown	1	82,158	89763	3511	91,548	86,500	N/A	213430	1,784	2,294	
3	Unknown	1	83,175	7685	490	7,838	12,076	N/A	595391	N/A	1,059	

GC obtained using unoptimal L_6 to confirm peaks attribution:





#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	80,433	93105	4450	61,088	51,783	N/A	311404	3,746	2,918	
2	Unknown	1	82,192	19426	1436	12,746	16,713	N/A	812630	1,556	1,388	
3	Unknown	1	82,783	39881	2707	26,167	31,504	N/A	693736	N/A	1,799	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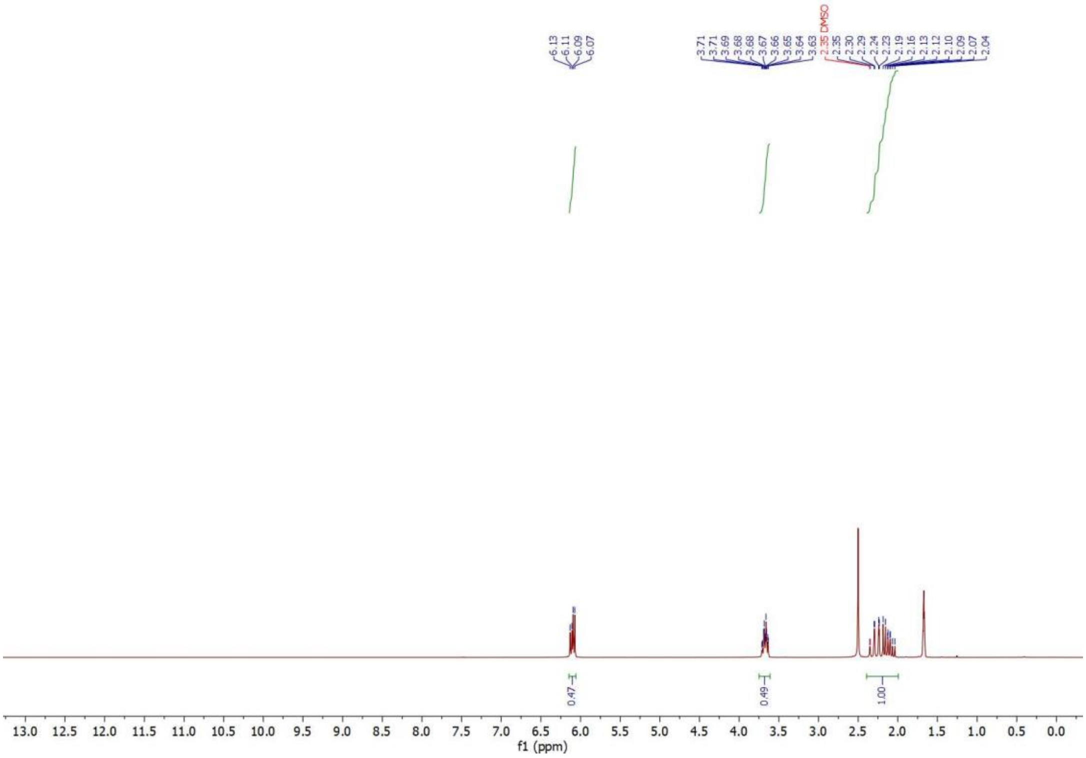
O
OH
Cl3C
CCl3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6.07
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3.71
3.69
3.68
3.68
3.67
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2.35 DMSO
2.35
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2.23
2.19
2.16
2.13
2.12
2.10
2.09
2.07
2.04
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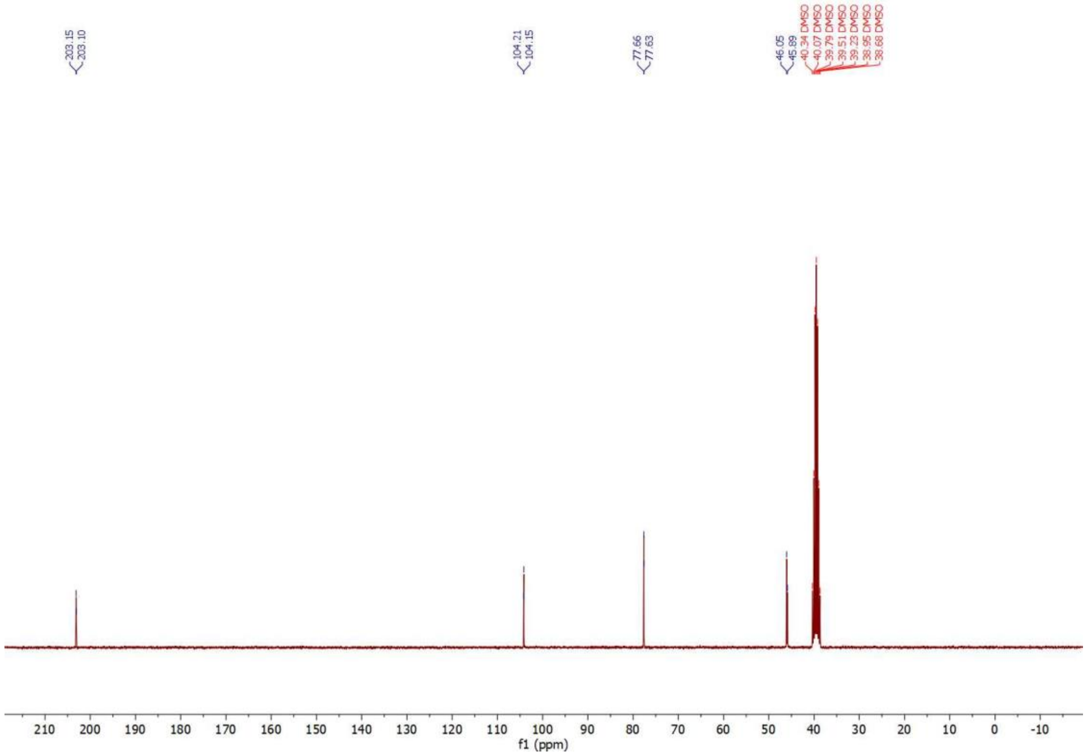
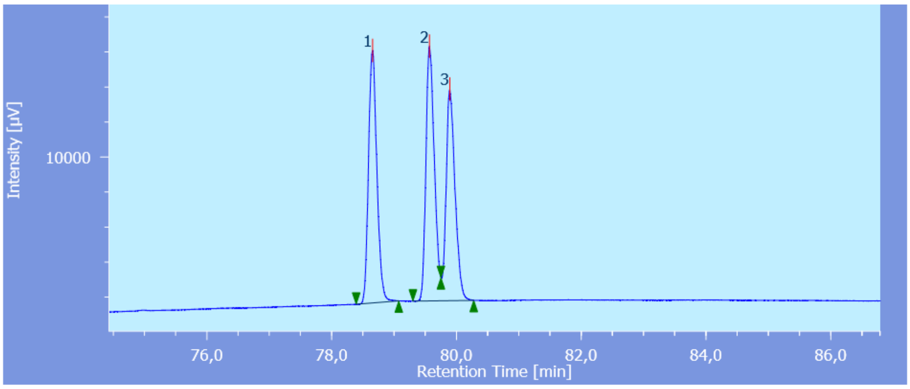
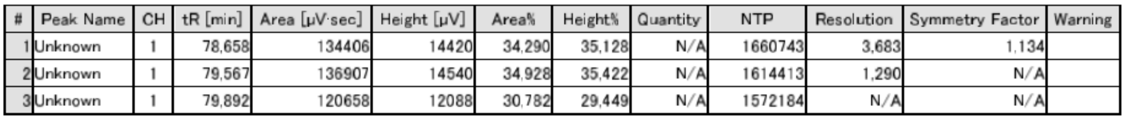
0.49
1.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


203.15
203.10
104.21
104.15
77.66
77.63
46.05
45.89
40.34 DMSO
40.07 DMSO
39.79 DMSO
39.51 DMSO
39.23 DMSO
38.95 DMSO
38.68 DMSO
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

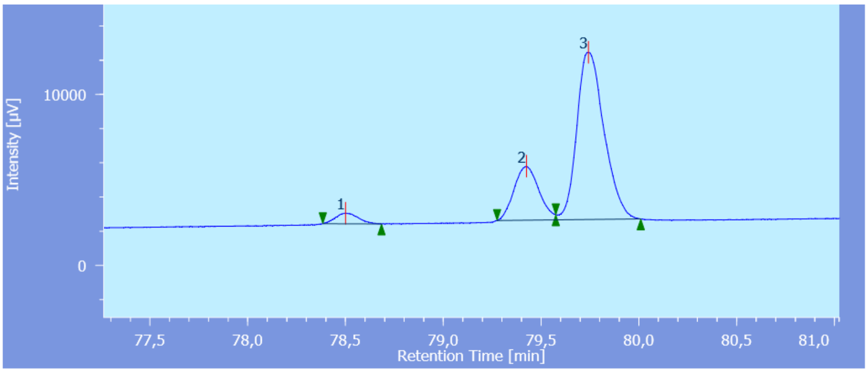
Chiral GC analysis: Racemic version:

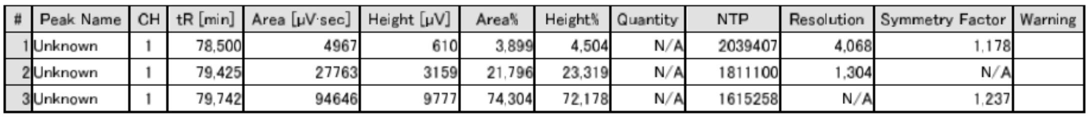




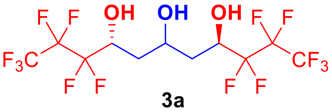
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	78,658	134406	14420	34,290	35,128	N/A	1660743	3,683	1,134	
2	Unknown	1	79,567	136907	14540	34,928	35,422	N/A	1614413	1,290	N/A	
3	Unknown	1	79,892	120658	12088	30,782	29,449	N/A	1572184	N/A	N/A	

Enantiomeric version:

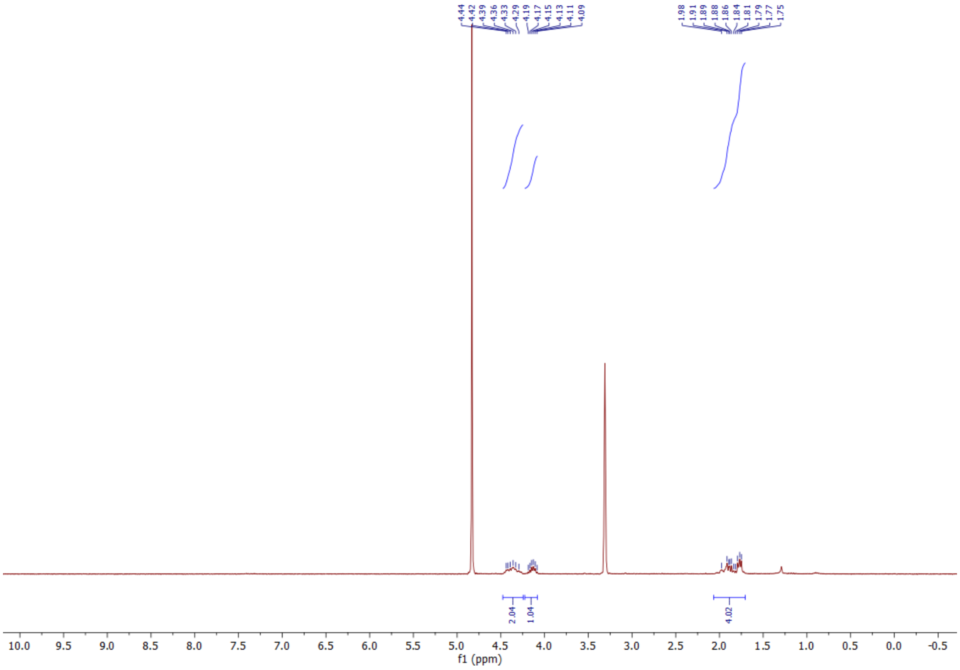




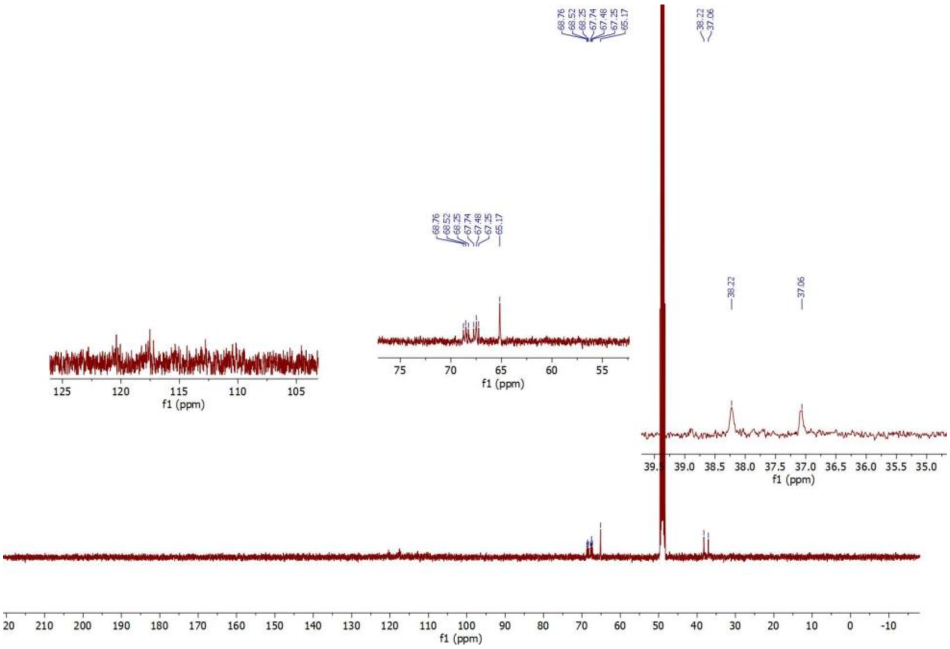
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	78,500	4967	610	3,899	4,504	N/A	2039407	4,068	1,178	
2	Unknown	1	79,425	27763	3159	21,796	23,319	N/A	1811100	1,304	N/A	
3	Unknown	1	79,742	94646	9777	74,304	72,178	N/A	1615258	N/A	1,237	


F
F
OH
OH
OH
F
F
F_3C
CF_3
F
F
F
F

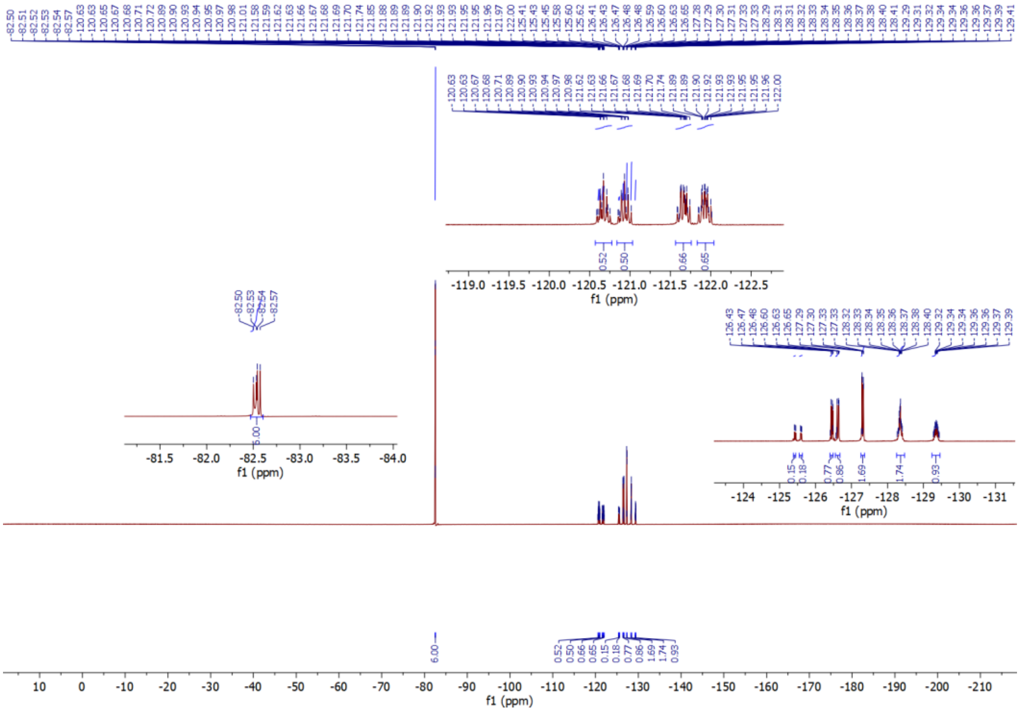
3a

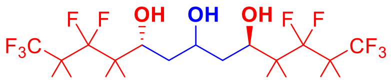

4.44
4.42
4.39
4.36
4.33
4.29
4.19
4.17
4.15
4.13
4.11
4.09
1.98
1.91
1.89
1.88
1.86
1.84
1.81
1.79
1.77
1.75
2.04
1.04
4.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

^{13}C NMR (3h):

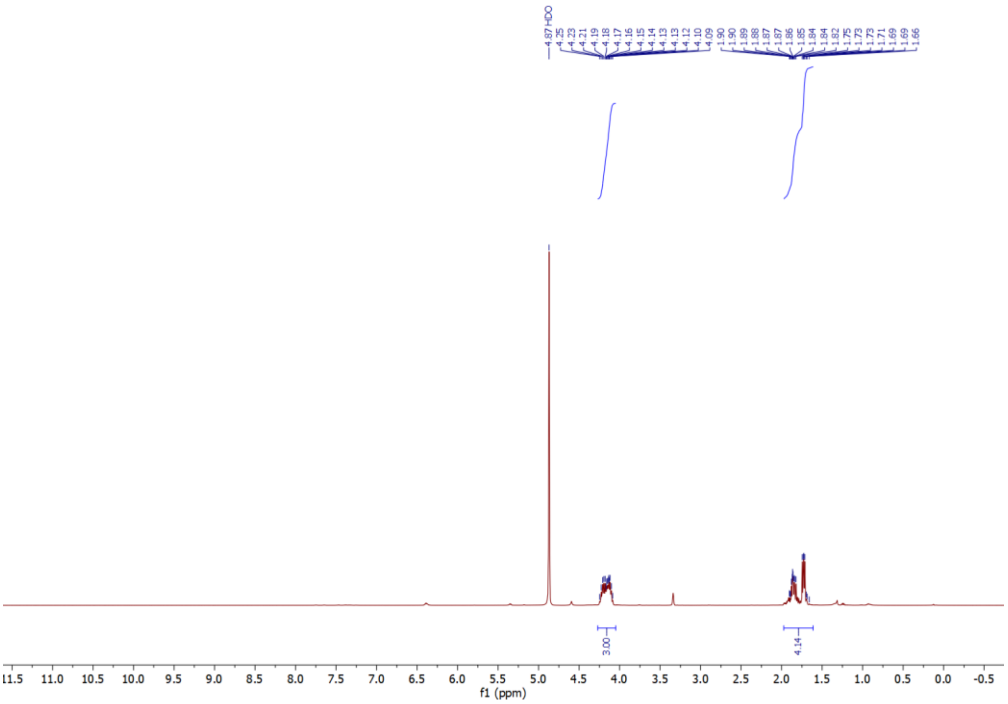

68.76
68.52
68.25
67.74
67.48
67.25
65.17
38.22
37.06
125
120
115
110
105
f1 (ppm)
75
70
65
60
55
f1 (ppm)
39.
39.0
38.5
38.0
37.5
37.0
36.5
36.0
35.5
35.0
f1 (ppm)
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

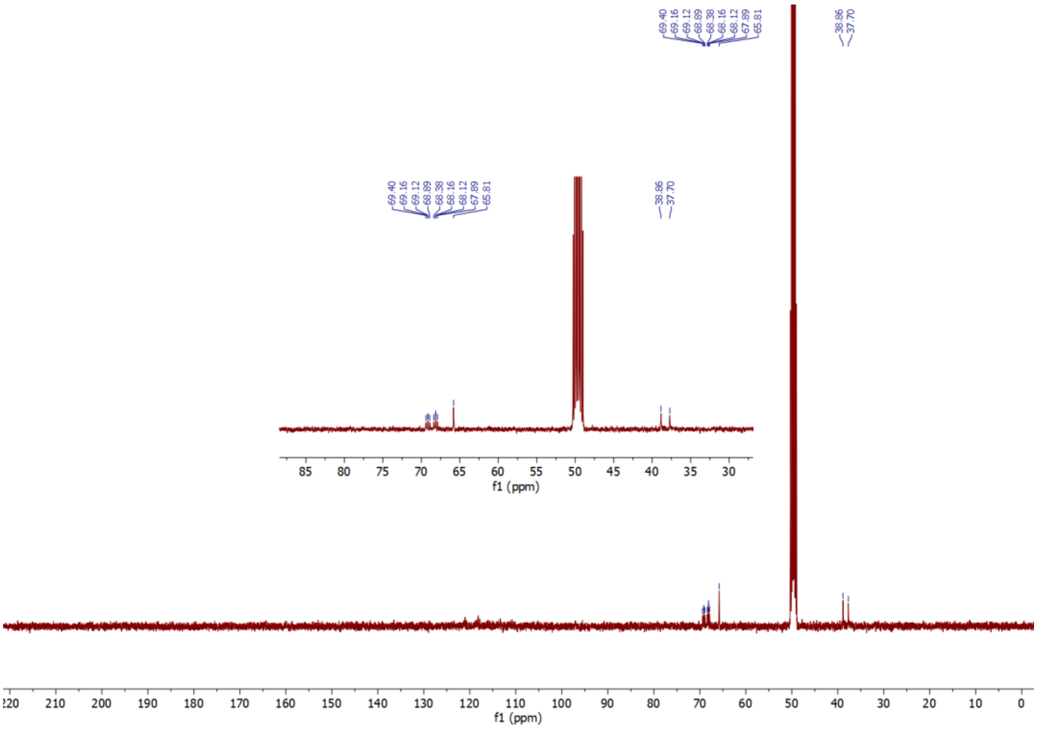
^{19}F NMR:



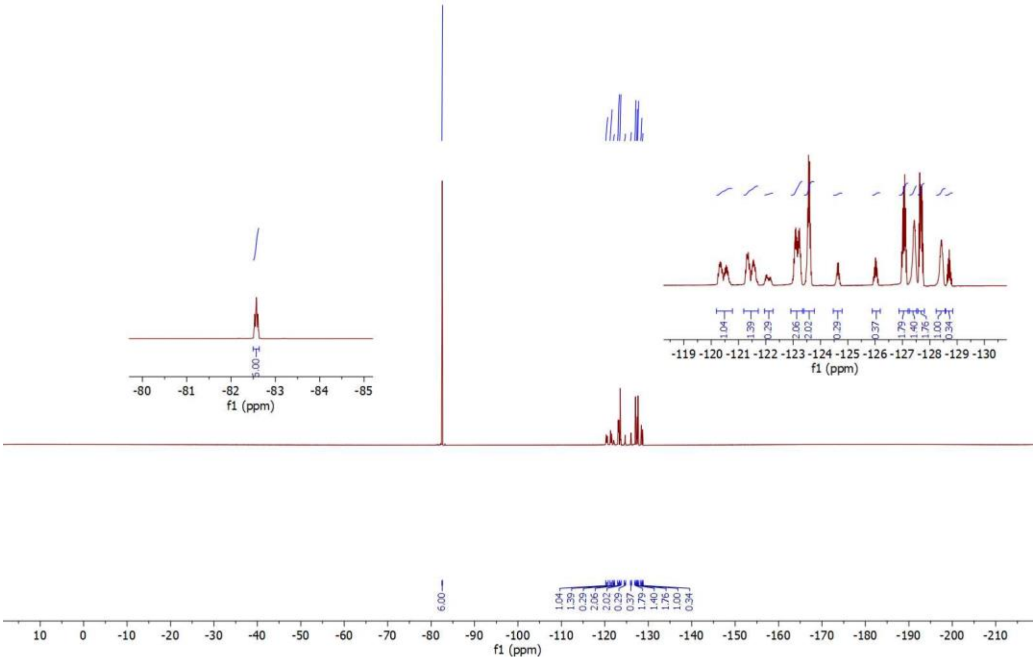

F₃C
F F
OH
OH
OH
F F
CF₃
F F F F
F F F F

3b

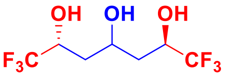

4.87 HDO
4.25
4.23
4.21
4.19
4.18
4.17
4.16
4.15
4.14
4.13
4.13
4.12
4.10
4.09
1.90
1.90
1.89
1.88
1.87
1.87
1.86
1.85
1.84
1.84
1.82
1.75
1.73
1.73
1.71
1.69
1.69
1.66
3.00
4.14
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


69.40
69.16
69.12
68.89
68.38
68.16
68.12
67.89
65.81
38.86
37.70
85 80 75 70 65 60 55 50 45 40 35 30
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

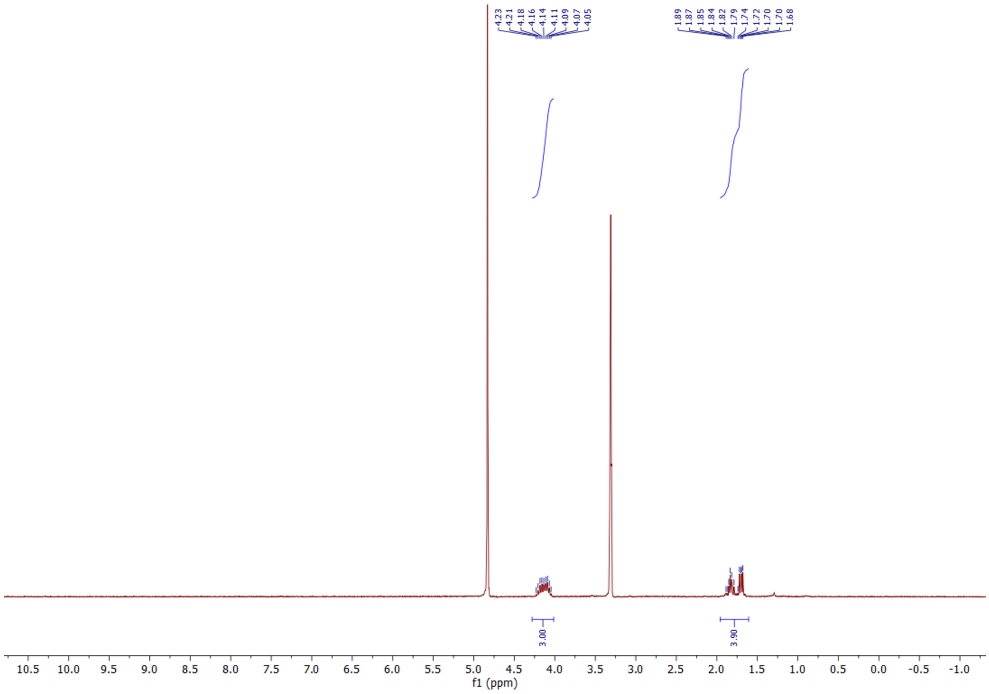
^{19}F NMR:

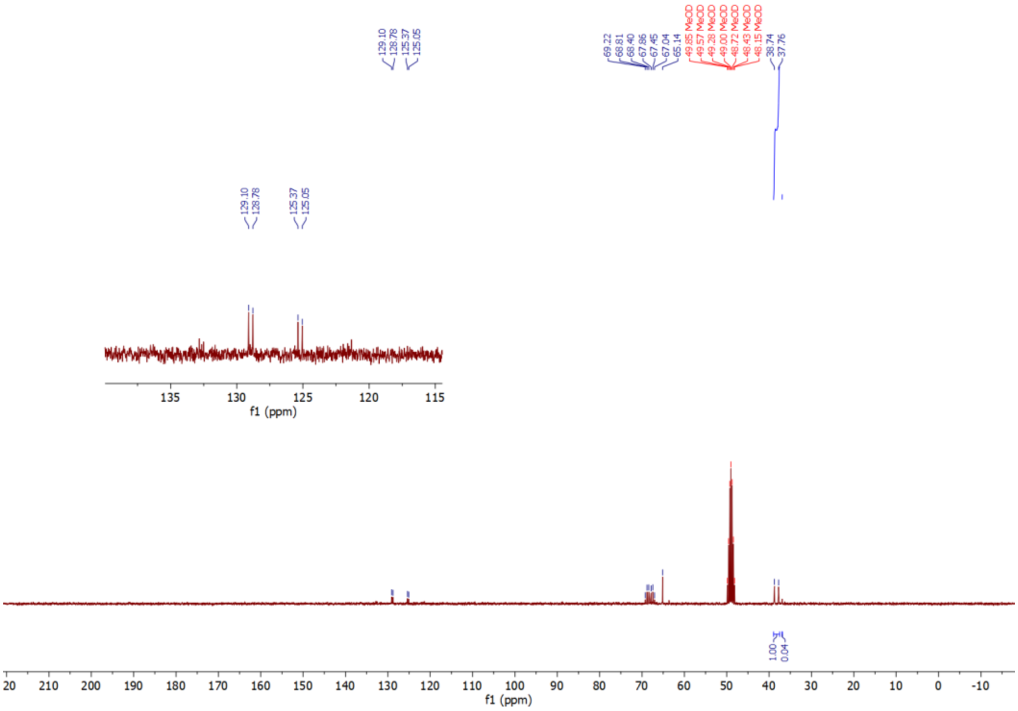


5.00
-80 -81 -82 -83 -84 -85
f1 (ppm)
1.04 1.39 0.29 2.06 2.02 0.29 0.37 1.79 1.40 1.76 1.00 0.34
-119 -120 -121 -122 -123 -124 -125 -126 -127 -128 -129 -130
f1 (ppm)
6.00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

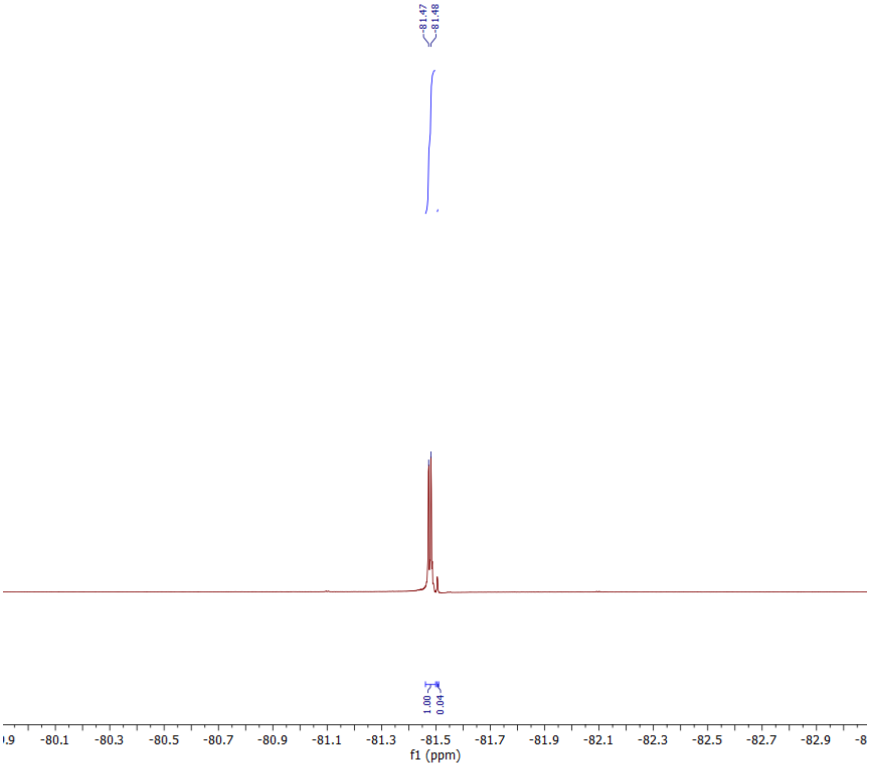

OH
OH
OH
F3C
CF3

3c

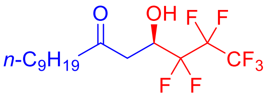

4.23
4.21
4.18
4.16
4.14
4.11
4.09
4.07
4.05
1.89
1.87
1.85
1.84
1.82
1.79
1.74
1.72
1.70
1.70
1.68
3.00
3.90
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


129.10
128.78
125.37
125.05
69.22
68.81
68.40
67.86
67.45
67.04
65.14
49.85 MeOD
49.57 MeOD
49.28 MeOD
49.00 MeOD
48.72 MeOD
48.43 MeOD
48.15 MeOD
38.74
37.76
129.10
128.78
125.37
125.05
135
130
125
120
115
f1 (ppm)
1.00
0.04
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

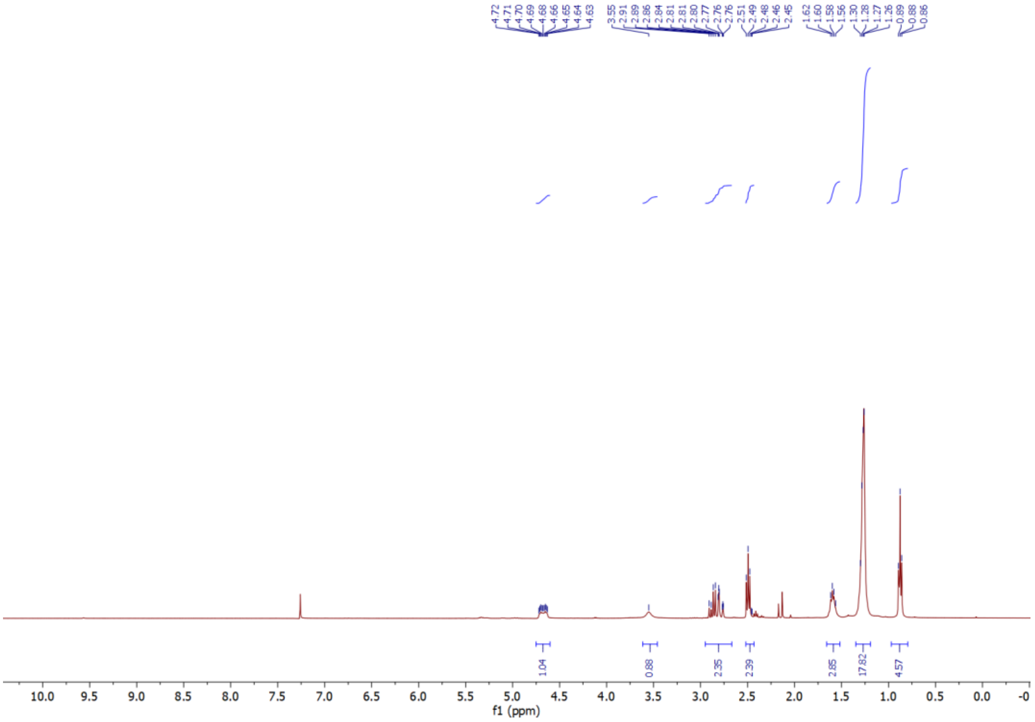
^{19}F NMR:

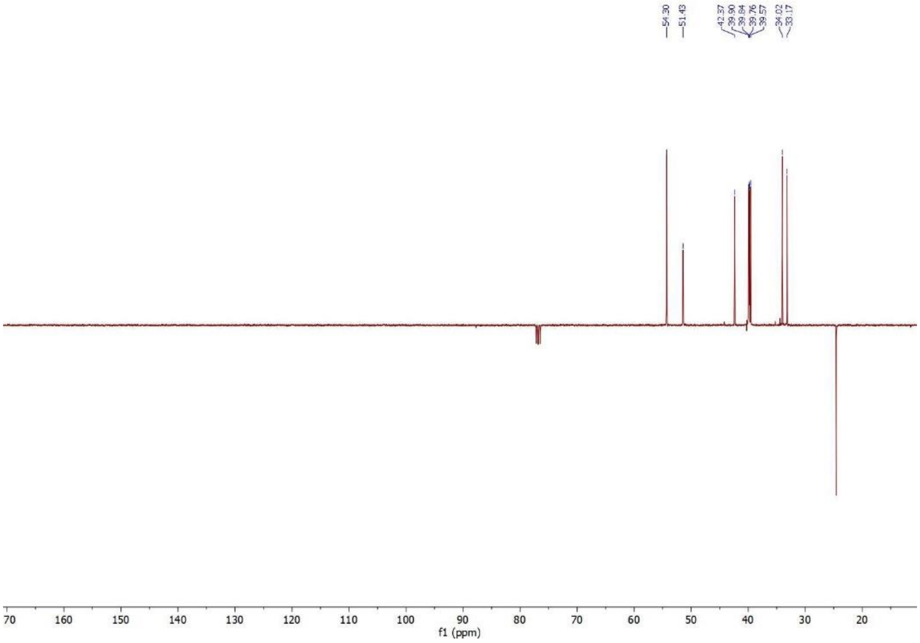


-81.47
-81.48
1.00
0.04
-79.9
-80.1
-80.3
-80.5
-80.7
-80.9
-81.1
-81.3
-81.5
-81.7
-81.9
-82.1
-82.3
-82.5
-82.7
-82.9
-8
f1 (ppm)

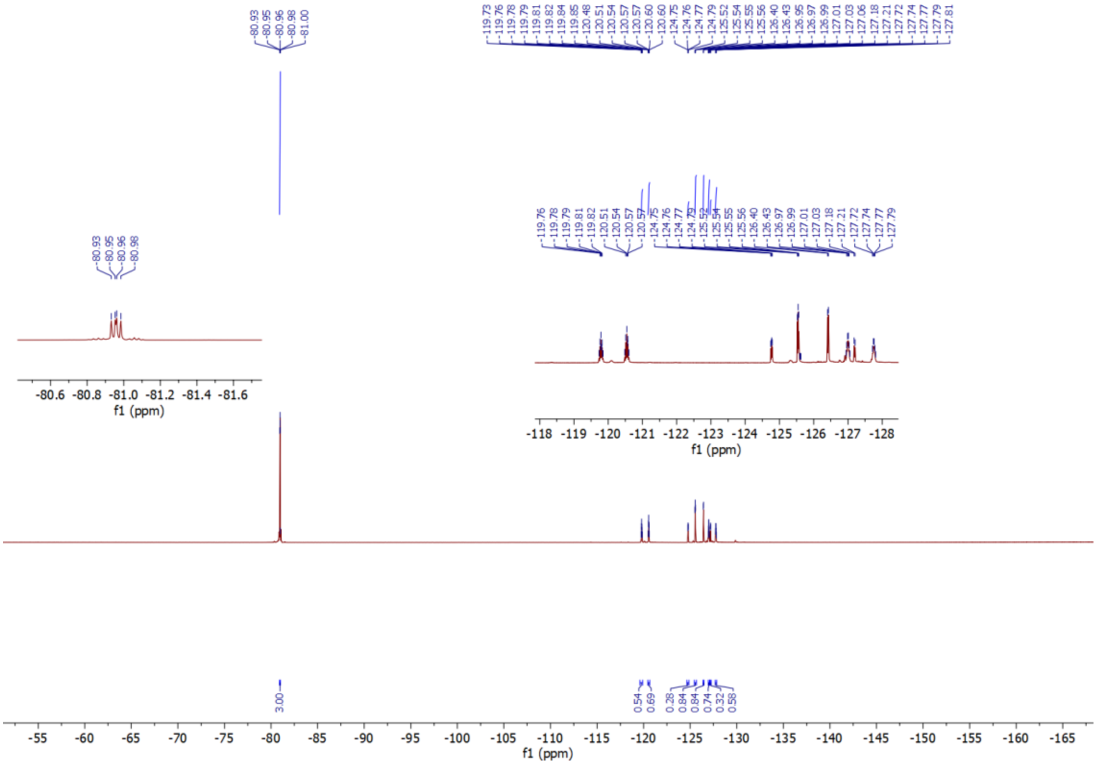

O
OH
F
F
n-C9H19
CF3
F
F

8

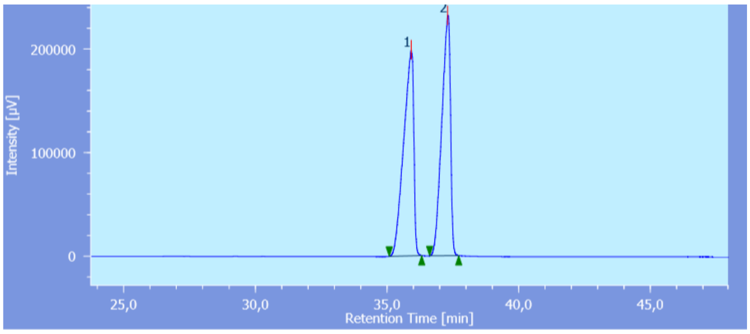

4.72
4.71
4.70
4.69
4.68
4.66
4.65
4.64
4.63
3.55
2.91
2.89
2.86
2.84
2.81
2.81
2.80
2.77
2.76
2.76
2.51
2.49
2.48
2.46
2.45
1.62
1.60
1.58
1.56
1.30
1.28
1.27
1.26
0.89
0.88
0.86
1.04
0.88
2.35
2.39
2.85
17.82
4.57
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

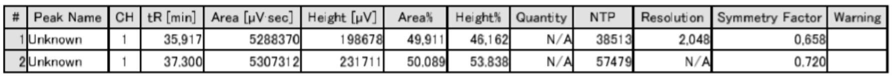

54.30
51.43
42.37
39.90
39.84
39.76
39.57
34.02
33.17
70
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

^{19}F NMR:



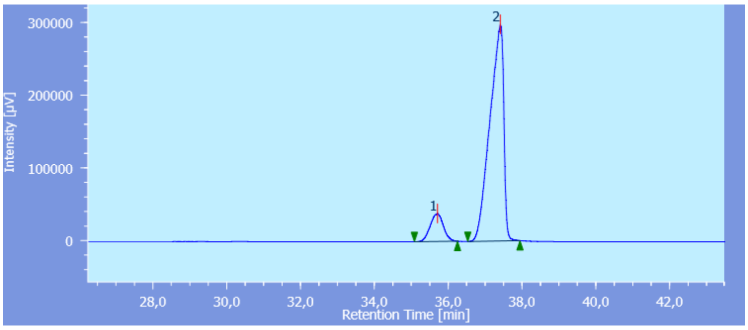
Chiral GC analysis: Racemic mixture:

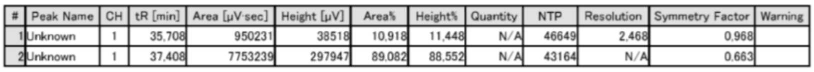




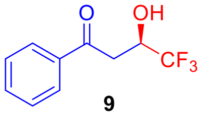
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	35,917	5288370	198678	49,911	46,162	N/A	38513	2,048	0,658	
2	Unknown	1	37.300	5307312	231711	50.089	53.838	N/A	57479	N/A	0.720	

Enantiomeric version:

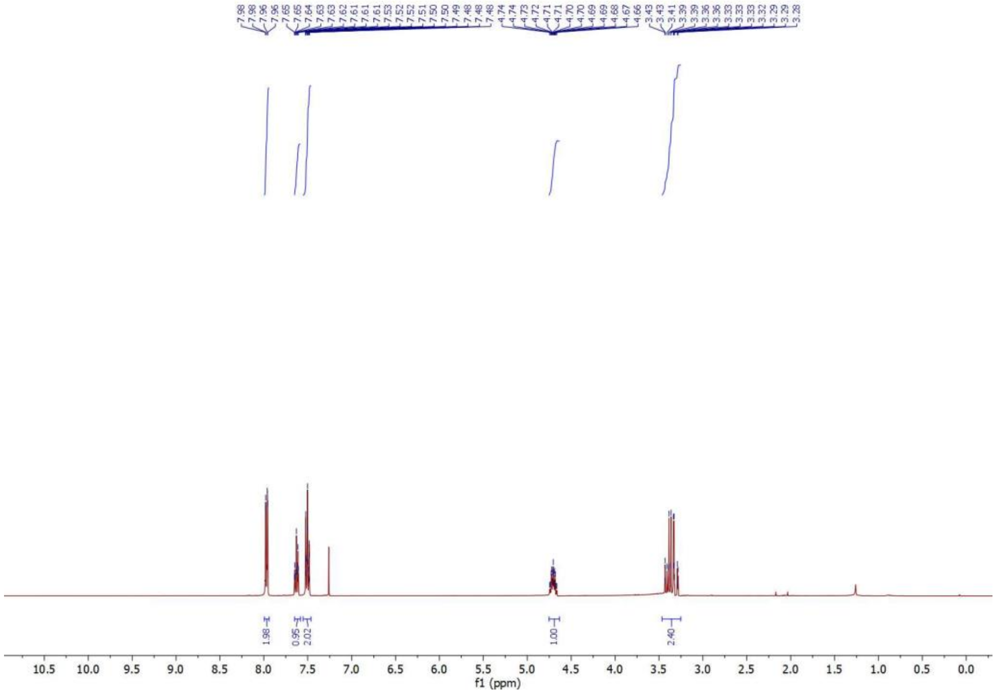


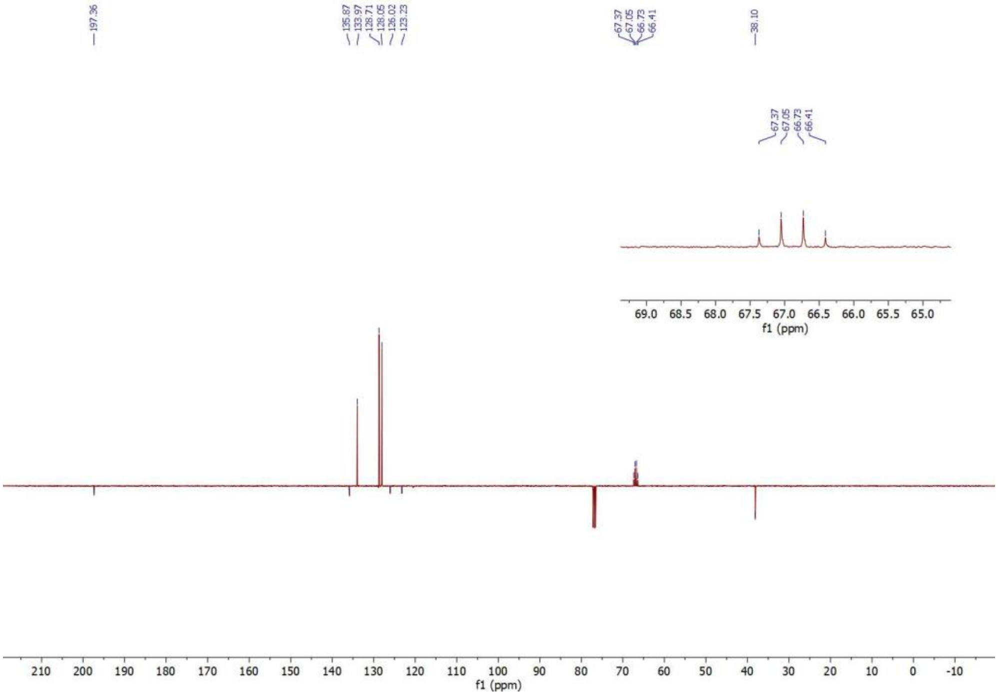


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	35,708	950231	38518	10,918	11,448	N/A	46649	2,468	0,968	
2	Unknown	1	37,408	7753239	297947	89,082	88,552	N/A	43164	N/A	0,663	

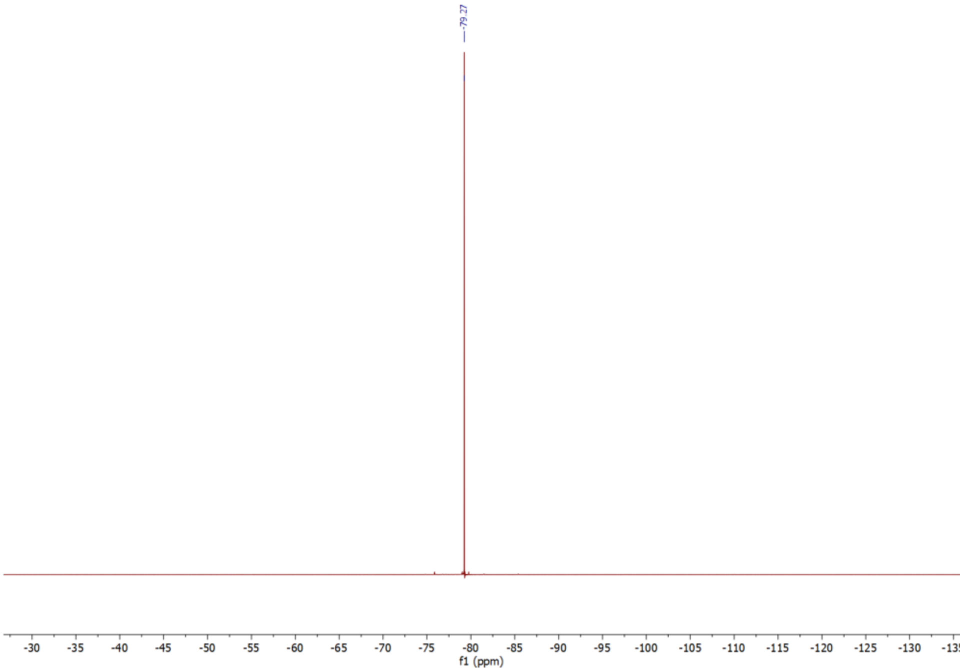


9

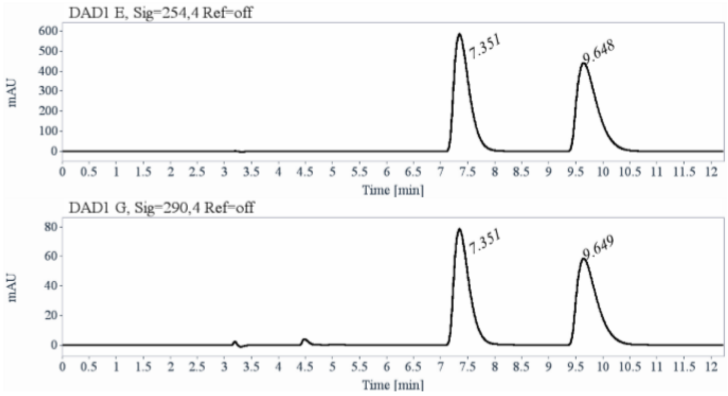

7.98
7.98
7.96
7.96
7.65
7.65
7.64
7.63
7.63
7.62
7.61
7.61
7.61
7.53
7.52
7.52
7.51
7.50
7.50
7.49
7.48
7.48
7.48
4.74
4.74
4.73
4.72
4.71
4.71
4.70
4.70
4.69
4.69
4.68
4.67
4.66
3.43
3.43
3.41
3.39
3.39
3.36
3.36
3.33
3.33
3.33
3.32
3.29
3.29
3.28
1.98
0.95
2.02
1.00
2.40
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

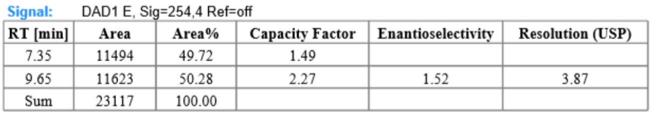

197.36
135.87
133.97
128.71
128.05
126.02
123.23
67.37
67.05
66.73
66.41
38.10
67.37
67.05
66.73
66.41
69.0
68.5
68.0
67.5
67.0
66.5
66.0
65.5
65.0
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{19}F NMR:



HPLC analysis:
Racemic version:

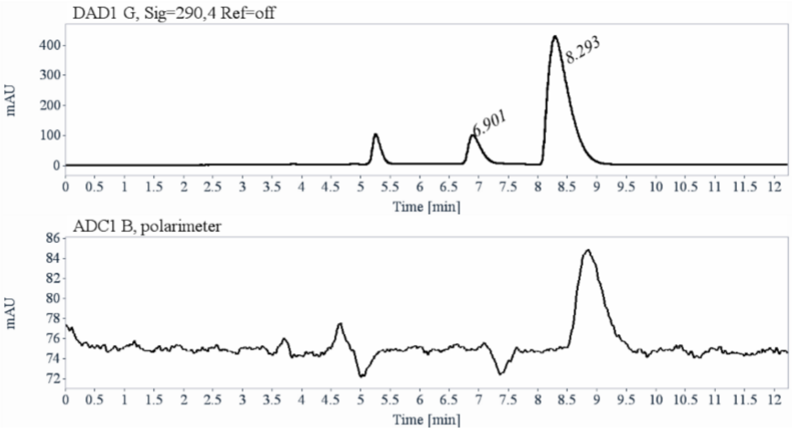




Signal: DAD1 E, Sig=254,4 Ref=off

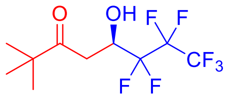
RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
7.35	11494	49.72	1.49		
9.65	11623	50.28	2.27	1.52	3.87
Sum	23117	100.00			

Enantiomeric version:

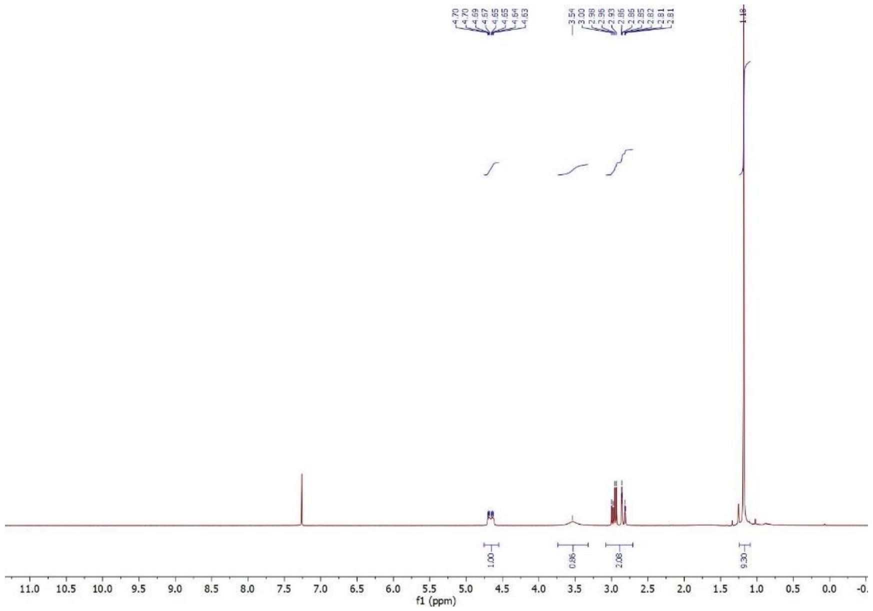


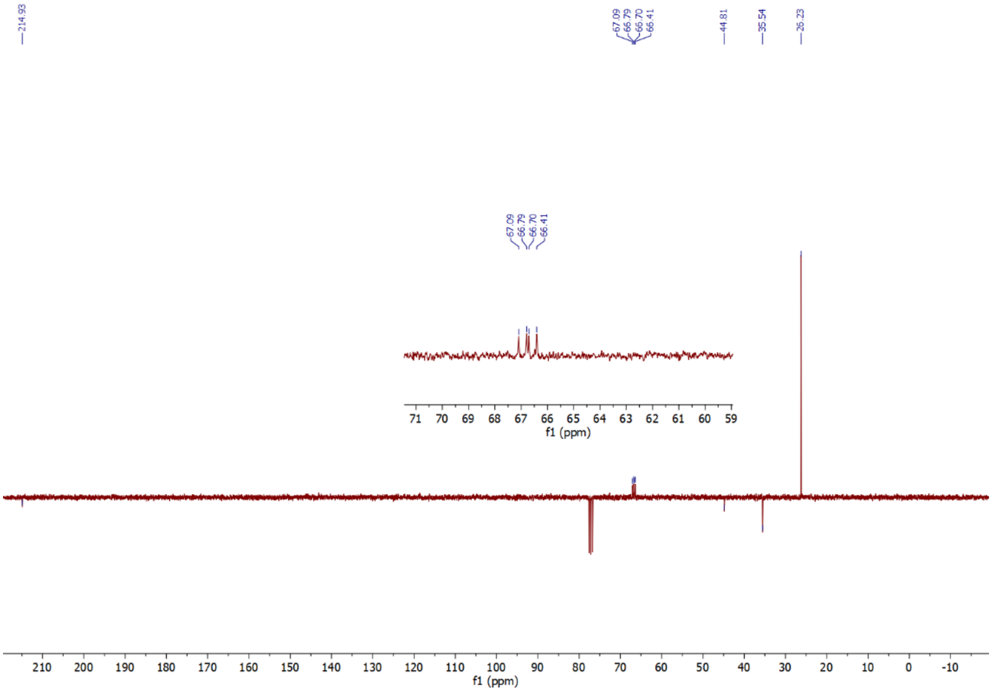
Signal: DAD1 G, Sig=290,4 Ref=off

RT [min]	Area	Area%	Capacity Factor	Enantioselectivity	Resolution (USP)
6.90	1488	12.31	1.34		
8.29	10593	87.69	1.81	1.35	2.64
Sum	12080	100.00			

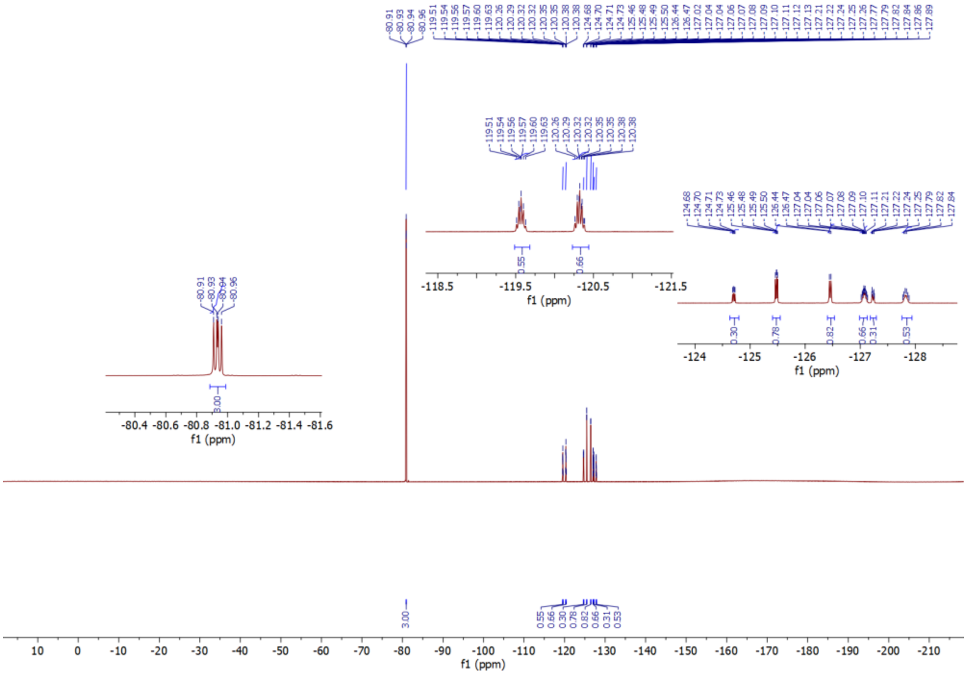

O
OH
F
F
CF3
F
F

10

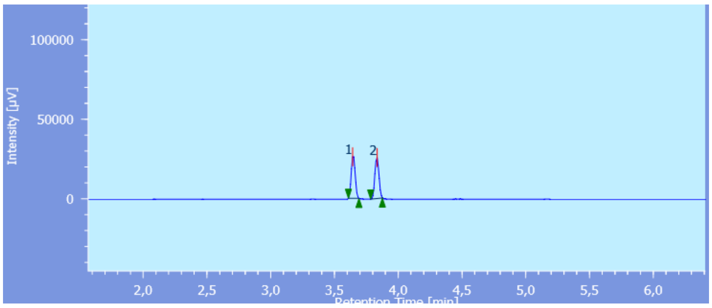

4.70
4.70
4.69
4.67
4.65
4.65
4.64
4.63
3.54
3.00
2.98
2.96
2.93
2.86
2.86
2.85
2.82
2.81
2.81
1.18
1.00
0.86
2.08
9.30
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)


214.93
67.09
66.79
66.70
66.41
44.81
35.54
26.23
67.09
66.79
66.70
66.41
71
70
69
68
67
66
65
64
63
62
61
60
59
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{19}F NMR:

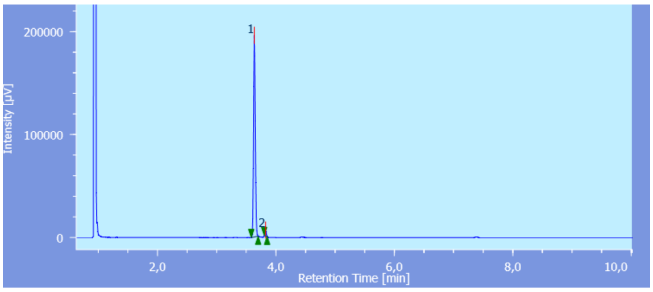


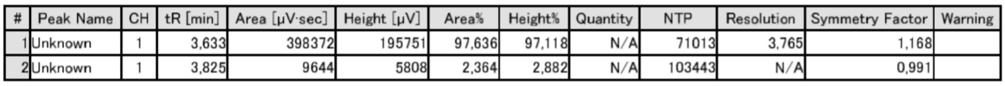
Chiral GC analysis: Racemic version:



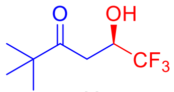
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	3,642	57589	26168	50,236	50,424	N/A	59790	3,202	1,203	
2	Unknown	1	3,833	57049	25727	49,764	49,576	N/A	64426	N/A	0,980	

Enantiomeric version:

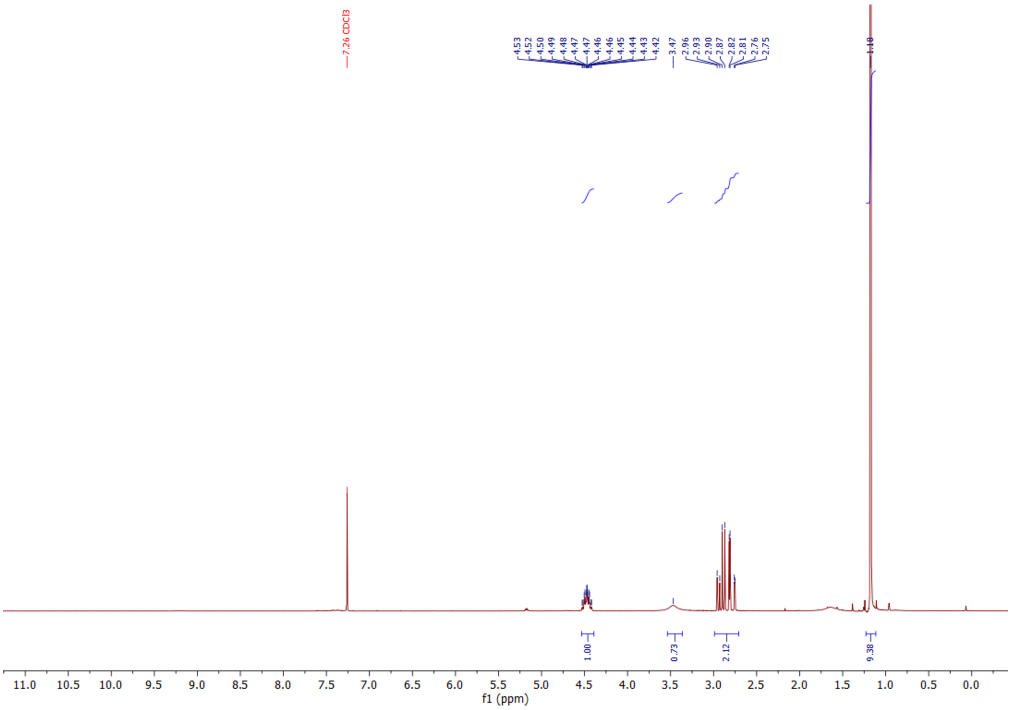


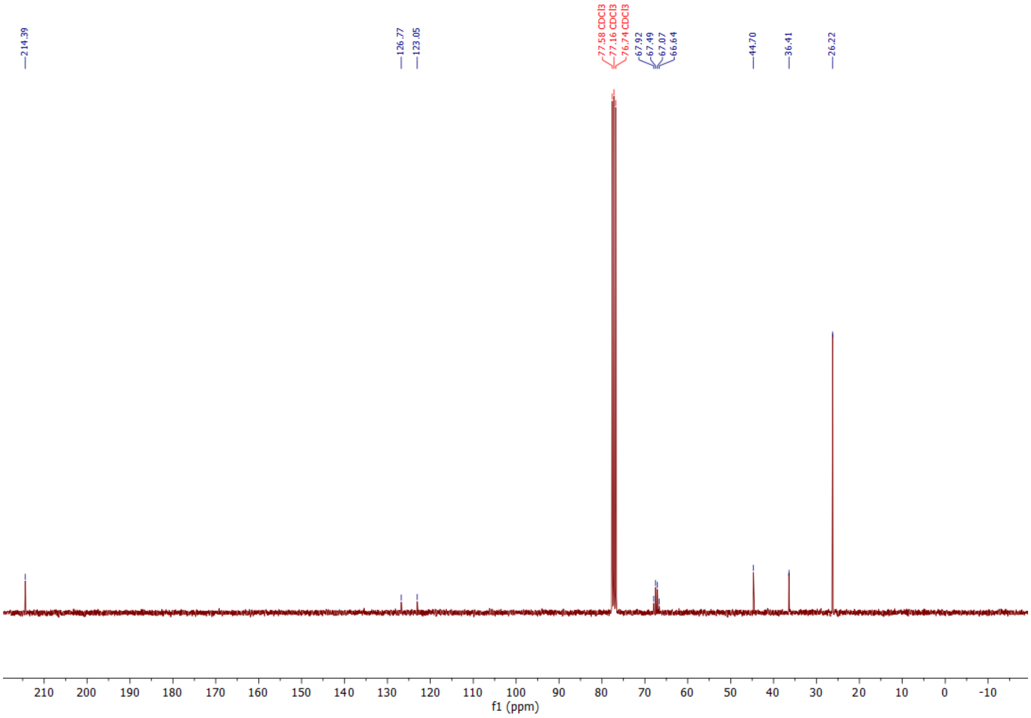


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	3,633	398372	195751	97,636	97,118	N/A	71013	3,765	1,168	
2	Unknown	1	3,825	9644	5808	2,364	2,882	N/A	103443	N/A	0,991	

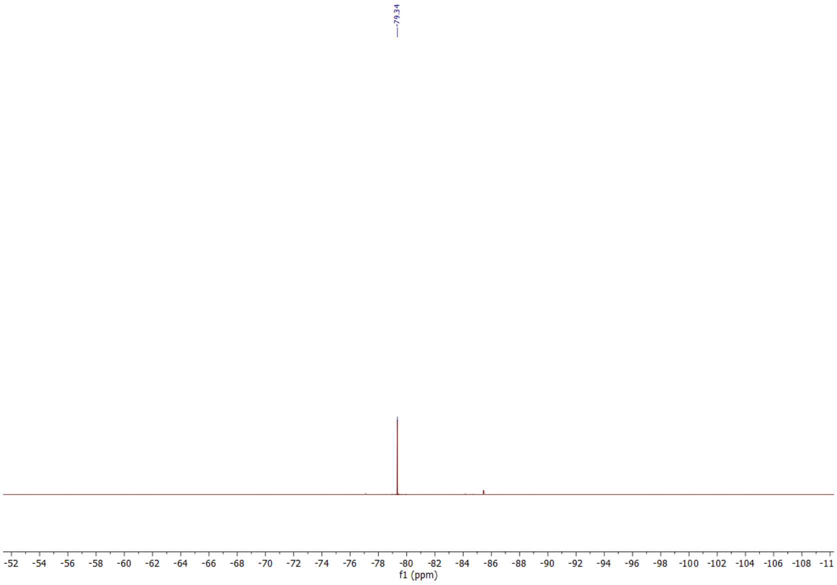

O
OH
CF3

11

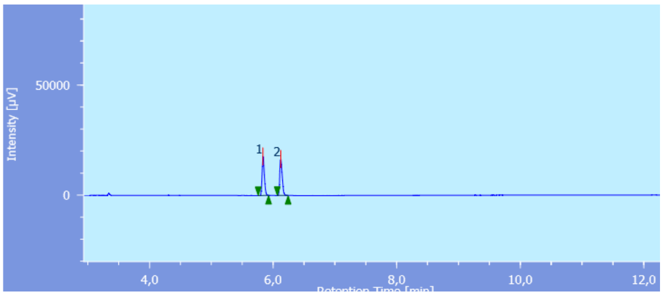

7.26 CDCl3
4.53
4.52
4.50
4.49
4.48
4.47
4.47
4.46
4.46
4.45
4.44
4.43
4.42
3.47
2.96
2.93
2.90
2.87
2.82
2.81
2.76
2.75
1.18
1.00
0.73
2.12
9.38
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


214.39
126.77
123.05
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
67.92
67.49
67.07
66.64
44.70
36.41
26.22
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{19}F NMR:

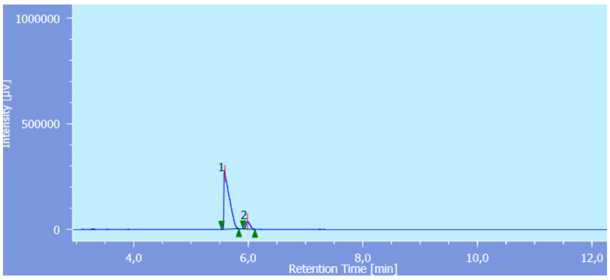


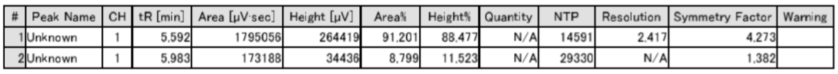
Chiral GC analysis: Racemic version:



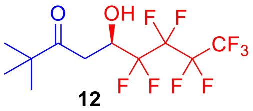
#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	5,833	45066	17737	49,813	51,644	N/A	121626	4,210	1,385	
2	Unknown	1	6,125	45404	16608	50,187	48,356	N/A	115674	N/A	1,214	

Enantiomeric version:

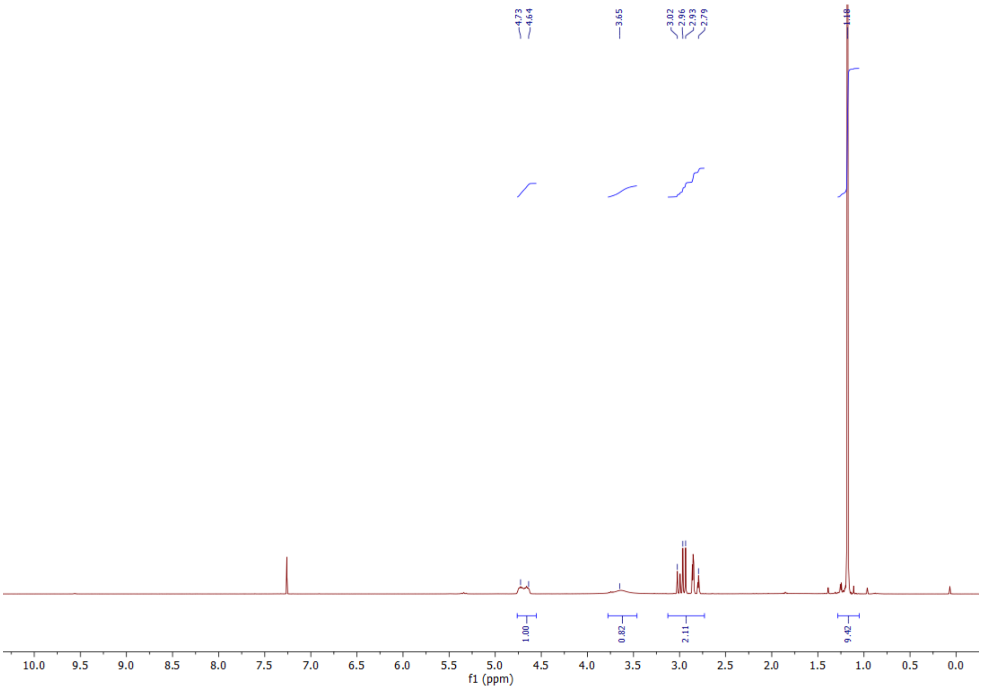


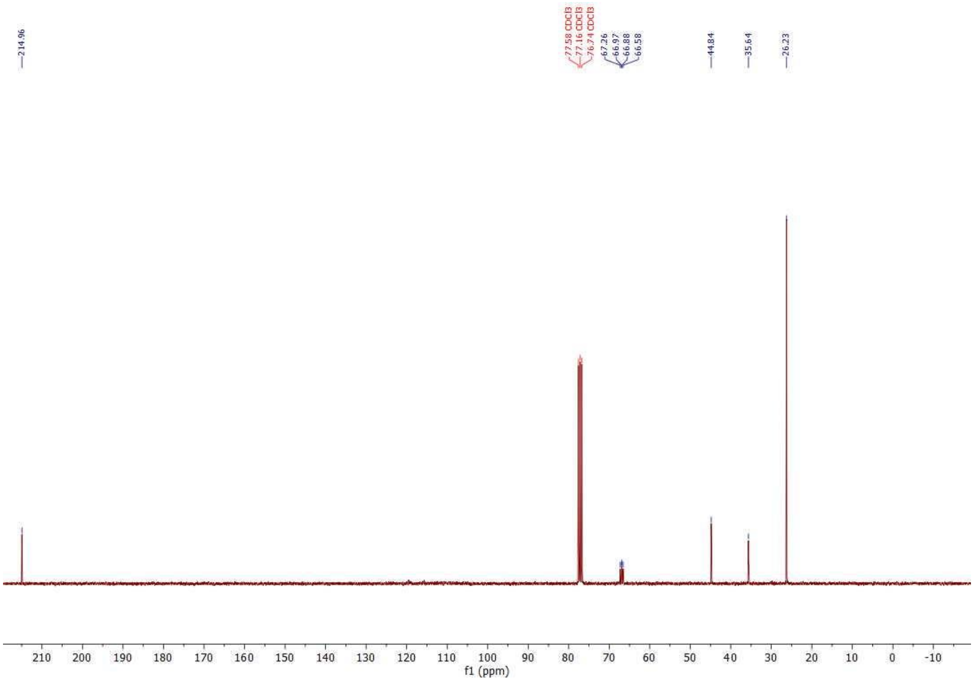


#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	5,592	1795056	264419	91,201	88,477	N/A	14591	2,417	4,273	
2	Unknown	1	5,983	173188	34436	8,799	11,523	N/A	29330	N/A	1,382	

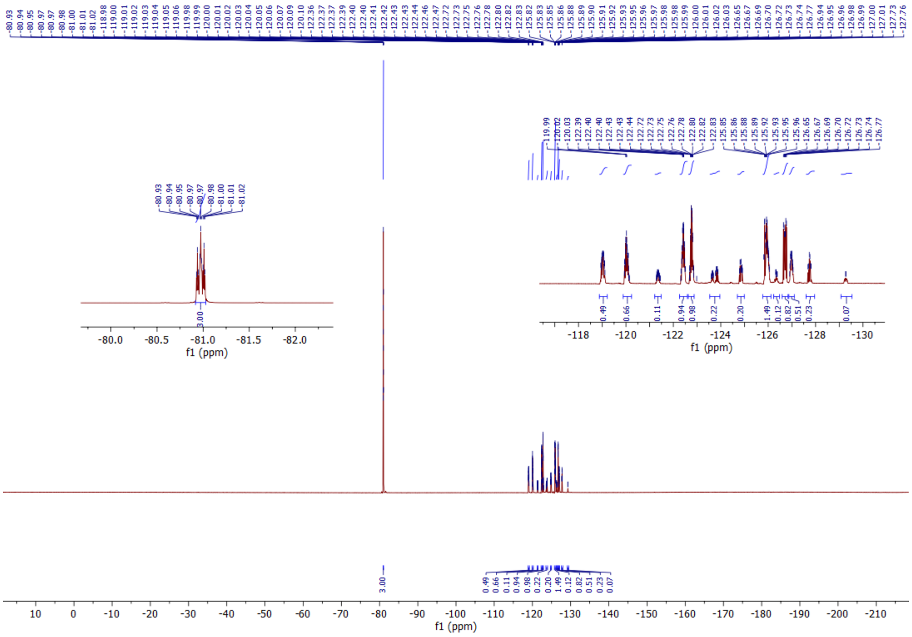

O
OH
F
F
CF3
F
F
F
F

12

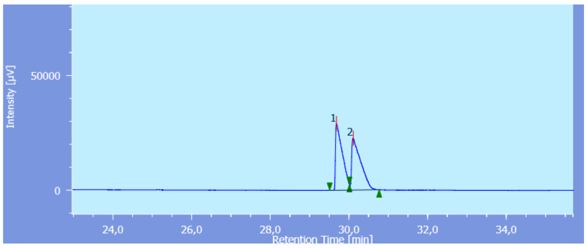

4.73
4.64
3.65
3.02
2.96
2.93
2.79
1.18
1.00
0.82
2.11
9.42
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


214.96
77.58 CDCl3
77.16 CDCl3
76.74 CDCl3
67.26
66.97
66.88
66.58
44.84
35.64
26.23
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

^{19}F NMR:

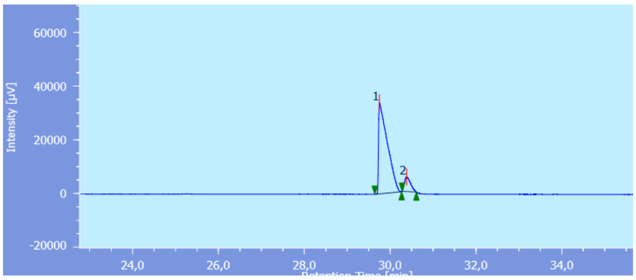


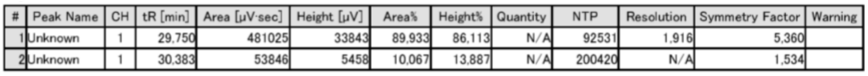
Chiral analysis: Racemic version:



#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	29,683	350675	29038	49,052	56,286	N/A	123752	1,106	N/A	
2	Unknown	1	30,108	364226	22553	50,948	43,714	N/A	77255	N/A	N/A	

Enantiomeric version:





#	Peak Name	CH	tR [min]	Area [µV·sec]	Height [µV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor	Warning
1	Unknown	1	29,750	481025	33843	89,933	86,113	N/A	92531	1,916	5,360	
2	Unknown	1	30,383	53846	5458	10,067	13,887	N/A	200420	N/A	1,534	