Highly Diastereoselective α-hydroxylation of Fox chiral auxiliary-based Amide Enolates with Molecular Oxygen

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General informations

Commercial reagents were purchased from Aldrich, Acros, or Alfa Aesar and used as received. Trifluoroacetaldehyde-ethylhemiacetal was generously offered by Central Glass Company. Molecular oxygen used was purchased from MESSER (Oxygen 3.5, purity > 99.95%). All oxidation reactions were performed under argon and molecular oxygen atmosphere with oven-dried glassware fitted with rubber septa. Ether and THF were distilled under nitrogen from sodium/benzophenone prior to use. CH_2Cl_2 was distilled under nitrogen from CaH_2 prior to use. Flash chromatography was performed on SDS 60A, (40-63 μm.) silica gel. Thin layer chromatography was performed on precoated aluminium sheets (Macherey-Nagel Alugram SIL/G 0.2mm). They were visualized under a 254 nm UV light. ^1H NMR spectra, ^{19}F NMR spectra and ^{13}C NMR spectra were recorded on a Brücker Advance 250 DPX (250 MHz ^1H, 235.6 MHz ^{19}F, 69.2 MHz ^{13}C) or a Jeol ECX-400 (400 MHz ^1H, 376.2 MHz ^{19}F, 100.5 MHz ^{13}C). Chemical shift values (δ) are reported in ppm downfield from Me_4Si (δ 0.0 ppm), C_6F_6 (δ -164.9 ppm) or $CDCl_3$ as internal standard (δ 77.0 ppm). Data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), integration, coupling constant (Hz). Infrared (IR-FT) spectra were performed on a Brücker Tensor. GC analyses were performed on a Agilent 6890N (capillary column HP-5MS, 30 m × 250 μm, N_2 as vector gas). HRMS analyses were performed on a Jeol JMS-GC Mate II. Specific rotations were measured on a JASCO P1010 polarimeter.

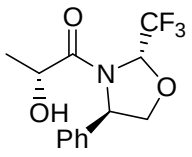
Starting material synthesis.

The starting *N*-acylated oxazolidines **1a-e** were prepared according to our previously reported procedures.[1,2]

Typical procedure for α-hydroxylation reactions in the presence of molecular oxygen and $P(OEt)_3$.

To a solution of amide **1a** (2.27 g, 8.31 mmol) in THF (85 mL) under argon and at –78 °C was added a solution of NaHMDS (8.31 mL, 1.5 M in THF, 16.6 mmol, 2 eq). The reaction mixture was stirred for 45 min at –78 °C and triethylphosphite (1.53 mL, 9.14 mmol, 1.1 eq) was added. Then molecular oxygen was bubbled through the reaction mixture for 2 h. The reaction mixture was quenched with an aqueous 1 N HCl solution (85 mL). The aqueous layer was extracted with diethyl ether (3 x 75 mL). The organic layers were combined and dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 80/20 to 60/40) afforded the alcohol **3a** (2.15 g, 90%, 94% *de*) as a white solid.

(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2-hydroxypropanoyl]-4-phenyl-1,3-oxazolidine ((*R*)-3a).



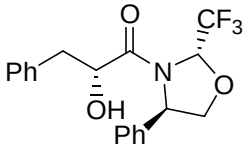
Recrystallisation in cyclohexane (50 mL) gave pure alcohol (*R*)-**3a** (1.56 g, 65%) as a white solid.

(1) Tessier, A.; Pytkowicz, J.; Brigaud, T. *Angew. Chem.* **2006**, *118*, 3759–3763; *Angew. Chem. Int. Ed.* **2006**, *45*, 3677–3681.

(2) Tessier, A.; Lahmar, N.; Pytkowicz, J.; Brigaud, T.; *J. Org. Chem.* **2008**, *73*, 3970-3973.

m.p. = 75 °C; $[\alpha]_D$ –59.0 (*c* 1.0, $CHCl_3$); IR (neat) 3215, 1672, 1410, 1278, 1209, 1177, 1148, 1042, 865, 846, 684 cm^{-1}; ^1H NMR (400 MHz) δ 0.70 (m, 3H), 2.41 (d, 1H, ^3J = 8.7 Hz), 3.93 (m, 1H), 4.12 (d, 1H, ^2J = 8.2 Hz), 4.70 (dd, 1H, ^2J = 8.2 Hz, ^3J = 6.4 Hz), 5.21 (d, 1H, ^3J = 6.4 Hz), 6.13 (m, 1H), 7.22-7.27 (m, 2H), 7.27-7.40 (m, 3H); ^{13}C NMR (100.5 MHz) δ 19.6, 60.1, 67.6, 76.6, 85.5 (q, $^3J_{C\text{-}F}$ = 38.1 Hz), 123.3 (q, $^2J_{C\text{-}F}$ = 288.5 Hz), 126.1, 129.0, 129.6, 141.4, 164.6; ^{19}F NMR (376.2 MHz) δ –79.9 (bs); MS (EI) 289 [M^+] (2), 245 (100), 220 (18), 186 (22), 176 (21), 148 (31), 120 (32), 104 (54), 91 (22), 77 (12); HRMS Calculated 289.0926, Found 289.0883; Anal. Calculated for $C_{13}H_{14}F_3NO_3$: C, 53.98; H, 4.88; N, 4.84. Found C, 54.04; H, 4.75; N, 5.11.

(2*S*,4*R*)-2-trifluoromethyl-3-[(2*R*)-2-hydroxy-3-phenylpropanoyl]-4-phenyl-1,3-oxazolidine (3b).

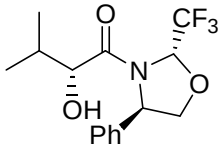


The compound **3b** was obtained as a white solid (3.135 g, 81%, >98% *de*) from the sodium enolate of **1b** (3.597 g, 10.3 mmol) using the typical hydroxylation procedure.

m.p. = 105 °C; $[\alpha]_D$ –67.6 (*c* 1.0, $CHCl_3$); IR (neat) 3404, 2982, 1656, 1178, 1143 1106, 1082, 843, 751, 701, 683 cm^{-1}; ^1H NMR (400 MHz) δ 2.24 (d, 1H, ^3J = 8.9 Hz), 2.31 (d, 1H, ^2J = 12.8 Hz), 2.59 (dd, 1H, ^2J = 12.8 Hz, ^3J = 9.6 Hz), 3.94 (dd, 1H, ^3J = 9.6 Hz, ^3J = 8.9 Hz), 4.09 (d, 1H, ^3J = 8.7 Hz), 4.69 (dd, 1H, ^2J = 8.7 Hz, ^3J = 6.4 Hz), 5.27 (d, 1H, ^3J = 6.4 Hz), 6.13 (q, 1H, $^3J_{H\text{-}F}$ = 3.7 Hz), 6.79 (d, 2H, ^3J = 4.1 Hz), 7.17-7.40 (m, 8H); ^{13}C NMR (100.5 MHz) δ 39.4, 60.2, 72.0, 76.6, 85.6 (q, $^3J_{C\text{-}F}$ = 35.5 Hz), 123.3 (q, $^2J_{C\text{-}F}$ = 289.5 Hz), 126.0, 126.8, 128.5, 129.1, 129.6, 129.7, 136.5, 141.6, 173.2; ^{19}F NMR (376.2 MHz) δ –79.9

(d, $^{3}J_{H\text{-}F}$ = 3.7 Hz); Anal. Calculated for $C_{18}H_{19}F_3NO_3$: C, 62.46; H, 4.97; N, 3.83. Found C, 62.35; H, 4.87; N, 3.99.

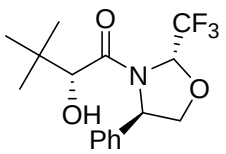
(2*S*,4*R*)-2-trifluoromethyl-3-[(2*R*)-2-hydroxy-3-methylbutanoyl]-4-phenyl-1,3-oxazolidine (3c).



Obtained as a white solid (367 mg, 70%, >98% *de*) from sodium enolate of **1c** (500 mg, 1.66 mmol) using typical hydroxylation procedure.

m.p. = 122 °C; $[\alpha]_D$ –60.2 (*c* 1.50, $CHCl_3$); IR (neat) 3641; 2968, 165, 1417, 1266, 1175, 1145, 1104, 1034, 980, 932, 846, 776, 708, 681 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.45 (m, 3H), 0.75 (m, 3H), 1.47 (m, 1H), 2.17 (d, 1H, ^{3}J = 8.2 Hz), 3.56 (m, 1H), 4.10 (d, 1H, ^{2}J = 6.4 Hz), 4.67 (dd, 1H ^{2}J = 6.4 Hz, ^{3}J = 4.8 Hz), 5.25 (d, 1H, ^{3}J = 4.8 Hz), 6.15 (m, 1H), 7.25-7.32 (m, 2H), 7.32-7.42 (m, 3H); ^{13}C NMR (100.5 MHz) δ 15.7, 19.0, 30.4, 60.2, 75.9, 76.8, 85,8 (q, $^{3}J_{C\text{-}F}$ = 34.5 Hz), 132.3 (q, $^{2}J_{C\text{-}F}$ = 289.5 Hz), 126.1, 128.9, 129.5, 142.0, 173.5; ^{19}F NMR (376.2 MHz) δ –76.4 (bs); HRMS Calculated 317.1239, Found 317.1227; Anal. Calculated for $C_{15}H_{18}F_3NO_3$: C, 56.78; H, 5.72; N, 4.41. Found: C, 56.32; H, 5.78; N, 4.36.

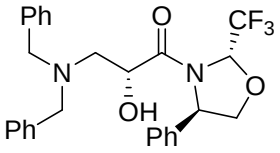
(2*S*,4*R*)-2-trifluoromethyl-3-[(2*R*)-2-hydroxy-3,3-dimethylbutanoyl]-4-phenyl-1,3-oxazolidine (3d).



Obtained as a white solid (222 mg; 42%, >98% *de*) from sodium enolate of **1d** (500 mg, 1.59 mmol) using typical hydroxylation procedure.

m.p. = 115 °C; $[\alpha]_D$ –64.4 (*c* 1.65, $CHCl_3$); IR (neat) 3586, 3417, 2962, 1654, 1386, 1363, 1324, 1273, 1179, 1146, 1110, 980, 938, 846; 704, 681 cm^{-1}; ^1H NMR (400 MHz) δ 0.74 (s, 9H), 2.13 (d, 1H, ^3J = 8.0 Hz), 3.54 (d, 1H, ^3J = 8.0 Hz), 4.08 (d, 1H, ^2J = 8.2 Hz), 4.65 (m, 1H), 5.29 (m, 1H), 6.14 (m, 1H), 7.15-7.28 (m, 2H), 7.28-7.42 (m, 3H); ^{13}C NMR (100.5 MHz) δ 25.5, 34.8, 60.5, 76.6, 78.0, 85.7 (q, $^3J_{C\text{-}F}$ = 34.5 Hz), 123.4 (q, $^2J_{C\text{-}F}$ = 289.5 Hz), 124.8, 128.7, 129.4, 152.7, 172.3; ^{19}F NMR (376.2 MHz) δ –79.2 (bs); HRMS Calculated 331.1395, Found 331.1411; Anal. Calculated for $C_{16}H_{20}F_3NO_3$: C, 58.00; H, 6.08; N, 4.23. Found: C, 57.71; H, 6.19; N, 4.16.

(2*S*,4*R*)-3-[(2*R*)-3-dibenzylamino-2-hydroxypropanoyl]-2-trifluoromethyl-4-phenyl-1,3-oxazolidine (3e).



Obtained as a white solid (386 mg, 75%, >98% *de*) from sodium enolate of **1e** (500 mg, 1.07 mmol) using typical hydroxylation procedure.

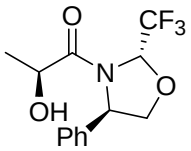
m.p. = 83 °C; $[\alpha]_D$ –15,8 (*c* 0.72, $CHCl_3$); IR (neat) 3327, 3033, 1643, 1494, 1450, 1380, 1272, 1178, 1141, 1112, 1029, 985, 933, 892, 834, 794, 694, 637 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, 298 K, two conformers showing coalescence on heating at 323 K) δ 2.30 (dd, 1H, ^2J = 13.7 Hz, ^3J = 4.1 Hz), 2.45 (dd, 1H, ^2J = 13.7 Hz, ^3J = 7.3 Hz), 3.11 (d, 2H, ^2J = 14.2 Hz), 3,26 (d, 2H, ^2J = 14.2 Hz), 3.90 (td, 1H, ^3J = 7.3 Hz, ^3J = 4.1 Hz), 4.02 (d, 1H, $^2J_{C\text{-}F}$ = 8.7 Hz), 4.53 (dd, 1H, ^2J = 8.7 Hz, ^3J = 6.4 Hz), 5.53 (d, 1H, ^3J = 6.4 Hz), 5.68 (d, 1H, ^3J = 7.3 Hz), 6.34 (q, 1H, $^3J_{H\text{-}F}$ = 5.1 Hz), 7.05-7.12 (m, 3H), 7.12-7.42 (m, 12H); ^{13}C NMR (100.5 MHz, DMSO-d_6, 298 K) δ 54.4, 56.9, 59.0, 67.5, 76.1, 84.4 (q, $^3J_{C\text{-}F}$ = 33.4 Hz), 123.4 (q, $^2J_{C\text{-}F}$ = 289.5 Hz), 125.8, 126.7, 128.0, 128.4, 129.1, 138.8, 142.4, 172.1; ^{19}F NMR (376.2 MHz,

DMSO-d_6, 298 K) δ major conformer : –78.7 (d, $^3J_{H\text{-}F}$ = 5.1Hz), minor conformer : –79.7 (bs); HRMS Calculated 484.1974, Found 484.1980; Anal. Calculated for $C_{27}H_{27}F_3N_2O_3$: C, 66.93; H, 5.62; N, 5.78. Found: C, 66.87; H, 5.68; N, 5.79.

Oxidation procedure using Vedejs' reagent.

To a solution of the amide **1a** (0.325 g, 1.19 mmol) in THF (10 mL) under argon at –78 °C was added a solution of NaHMDS (0.89 mL, 2M in THF, 1.79 mmol, 1.5 eq). The reaction mixture was stirred at –78 °C for 2 h and freshly prepared MoOPH[3] (770 mg, 1.79 mmol, 1.5 eq) was added. The mixture was warmed up to –40 °C and stirred for 19 h. The crude reaction mixture was treated with brine (15 mL) and an aqueous 3N HCl solution (10 mL) was added. The mixture was extracted with diethyl ether (3 x 25 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 90/10 to 60/40) afforded the alcohol **3a** (167 mg, 49%, 62% *de*) as a mixture of two diastereomers ((*R*)-**3a**/(*S*)-**3a** : 81/19). The spectral data of each diastereomer were determined in the crude mixture.

(2*S*,4*R*)-2-trifluoromethyl-3-[(*S*)-2-hydroxypropanoyl]-4-phenyl-1,3-oxazolidine ((*S*)-3a).

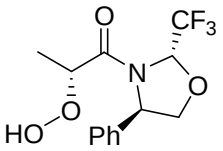


^{1}H NMR (250 MHz) δ 1.35 (d, 3H, ^3J = 6.8 Hz), 3.40 (d, 1H, ^3J = 7.5 Hz), 3.89 (m, 1H), 4.11 (m, 1H), 4.70 (m, 1H), 4.97 (d, 1H, ^3J = 6.4 Hz), 6.23 (q, 1H, $^3J_{H\text{-}F}$ = 4.9 Hz), 7.19-7.34 (m, 5H); ^{13}C NMR (62.9 MHz) δ 21.0, 60.1, 66.5, 76.5, 85.4 (q, $^3J_{C\text{-}F}$ = 35.6 Hz), 123.3 (q, $^2J_{C\text{-}F}$ =

(3) *Organic Syntheses, Coll. Vol. 7* **1990**, 277 ; **1986**,*Vol. 64*, p.127.

289.1 Hz), 125.3, 129.0, 129.7, 140.2, 176.2; ^{19}F NMR (376.2 MHz) δ –81.2 (d, 3F, $^{3}J_{H\text{-}F}$ = 4.9 Hz).

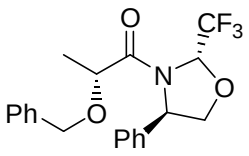
(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2-hydroperoxypropanoyl]-4-phenyl-1,3-oxazolidine (4).



To a solution of the amide **1a** (0.150 g, 0.55 mmol) in THF (6 mL) under argon and at –78 °C was added a solution of NaHMDS (0.55 mL, 2 M in THF, 1.1 mmol). The reaction mixture was stirred at –78 °C for 45 min. Then molecular oxygen was bubbled through the reaction mixture for 2 h. The mixture was quenched with water (5 mL). The aqueous layer was extracted with dichloromethane (3 x 15 ml). The organic layers were combined and dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude hydroperoxide **4** as a white solid (143 mg, 85%).

IR (neat) 3306, 2922, 2855, 1658, 1177, 1145, 705, 683 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.72 (d, 3H, ^{3}J = 6.4 Hz), 4.13 (d, 1H, ^{2}J = 8.6 Hz), 4.31 (q, 1H, ^{3}J = 6.4 Hz), 4.73 (dd, 1H, ^{2}J = 8.6 Hz, ^{3}J = 6.9 Hz,), 5.26 (d, 1H, ^{3}J = 6.9 Hz), 6.19 (q, 1H, $^{3}J_{H\text{-}F}$ = 4.8 Hz), 7.24-7.40 (m, 5H), 8.77 (m, 1H); ^{13}C NMR (100.5 MHz) δ 13.6, 60.1, 76.8, 79.5, 85.6 (q, $^{3}J_{C\text{-}F}$ = 35.6 Hz), 123.3 (q, $^{2}J_{C\text{-}F}$ = 289.5 Hz), 126.2, 129.1, 129.7, 141.4, 171.5; ^{19}F NMR (376.2 MHz) δ –80.1 (d, $^{3}J_{H\text{-}F}$ = 4.8 Hz); MS (EI) 287 [M^{+}–H_2O] (6), 244 (95), 216 (56), 201 (59), 173 (100), 153 (26), 124 (79), 104 (52), 91 (47).

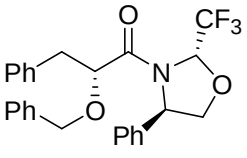
(2*S*,4*R*)-3-[(*R*)-2-benzyloxypropanoyl]-2-trifluoromethyl-4-phenyl-1,3-oxazolidine (5a).



To a solution of alcohol (*R*)-**3a** (1.50 g, 5.19 mmol) in THF (18 mL) cooled to 0 °C and under argon atmosphere was added NaH (259 mg, 6.48 mmol, 1.25 eq). The mixture was stirred at 0 °C for 45 min. Benzyl bromide (1.55 mL, 13.0 mmol, 2.5 eq) was added and the mixture was allowed to warm up to room temperature and stirred overnight. The mixture was quenched with water (30 mL). The aqueous layer was extracted with dichloromethane (3 x 25 mL). The organic layers were combined and dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/ethyl acetate 95/5 to 85/15) afforded the protected alcohols **5a** (1.93 g, 98%, >98% *de*) as a white solid.

m.p. = 89 °C; $[\alpha]_D$ –70.9 (*c* 1.0, $CHCl_3$); IR (neat) 1662, 1409, 1326, 1270, 1103, 1061, 902, 876, 828, 751, 697,687 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.85 (d, 3H, ^3J = 6.4 Hz), 3.75 (q, 1H, ^3J = 6.4 Hz), 4.00 (d, 1H, ^2J = 8.7 Hz), 4.39 (d, 1H, ^2J = 11.9 Hz), 4.50 (d, 1H, ^2J = 11.9 Hz), 4.59 (dd, 1H, ^2J = 8.7 Hz ^3J = 6.9 Hz), 4,75 (d, 1H, ^3J = 6.9 Hz), 6.19 (q, 1H, $^3J_{H\text{-}F}$ = 4.7 Hz), 6.98-7.00 (m, 2H), 7.31-7.44 (m, 8H); ^{13}C NMR (100.5 MHz) δ 15.3, 60.2, 69.6, 72.6, 76.6, 85.3 (q, $^3J_{C\text{-}F}$ = 34.5 Hz), 123.5 (q, $^2J_{C\text{-}F}$ = 288.5 Hz), 125.9, 128.0, 128.2, 128.8, 129.5, 137.8, 141.5, 172.4; ^{19}F NMR (376.2 MHz) δ –80.3 (d, $^3J_{H\text{-}F}$ = 4.7 Hz); HRMS Calculated 379.1395, Found 379.1432; Anal. Calculated for $C_{20}H_{20}F_3NO_3$: C, 63.32; H, 5.31; N, 3.69. Found: C, 63.74; H, 5.40; N, 3.75.

(2*R*,4*S*)-3-[(2*R*)-2-benzyloxy-3-phenylpropanoyl]-2-trifluoromethyl-4-phenyl-1,3-oxazolidine (5b).



Obtained from alcohol **3b** (460 mg, 1.26 mmol) using a similar procedure as for **5a**. Purification by flash chromatography (cyclohexane/ethyl acetate 95/5 to 90/10) afforded the protected alcohols **5b** (550 mg, 96%, >98% *de*) as a white solid.

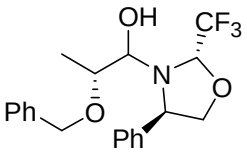
m.p. = 82 °C; $[\alpha]_D$ –118.4 (*c* 1.0, $CHCl_3$); IR (neat) 2986, 1661, 1203, 1180, 1143, 1092, 841, 728, 689 cm^{-1}; ^1H NMR (400 MHz) δ 2.09 (dd, 1H, ^2J = 14.2 Hz, ^3J = 3.7 Hz), 2.85 (dd, 1H, ^2J = 14.2 Hz, ^3J = 9.6 Hz), 3.85 (dd, 1H, ^3J = 9.6 Hz, ^3J = 3.7 Hz), 3.94 (d, 1H, ^2J = 8.7 Hz), 4.37 (s, 2H), 4.42 (d, 1H, ^3J = 6.9 Hz), 4.53 (dd, 1H, ^2J = 8.7 Hz, ^3J = 6.9 Hz), 6.18 (q, 1H, $^3J_{H\text{-}F}$ = 4.8 Hz), 6.65-6.68 (m, 2H), 6.88-7.00 (m, 2H), 7.00-7.09 (m, 2H), 7.09-7.38 (m, 9H); ^{13}C NMR (100.5 MHz) δ 36.6, 60.0, 70.4, 76.5, 76.6, 85.3 (q, $^3J_{C\text{-}F}$ = 35.5 Hz), 123.4 (q, $^2J_{C\text{-}F}$ = 288.5 Hz), 128.1, 128.7, 129.0, 129.7, 137.1, 137.7, 141.7, 171.5; ^{19}F NMR (376.2 MHz) δ –79.9 (d, $^3J_{H\text{-}F}$ = 4.8 Hz); HRMS Calculated 455.1708; Anal. Calculated for $C_{26}H_{24}F_3NO_3$: C, 68.56; H, 5.31; N, 3.08. Found: C, 70.13; H, 5.74; N, 2.98.

Typical procedure for the chiral auxiliary removal

To a solution of the amide **5a** (250 mg, 0.66 mmol) in diethyl ether (6 mL) cooled at –10 °C and under argon atmosphere, was slowly added $LiAlH_4$ (100 mg, 2.64 mmol, 4 eq). The reaction mixture was stirred at –10 °C for 2 h. Water (95 μL, 5.27 mmol, 8 eq), aqueous NaOH 15% (28 μL, 0.11 mmol, 0.16 eq) and water (285 μL, 15.8 mmol, 24 eq) were sequentially added. The resulting mixture was filtered and the white powder was abundantly washed with diethyl ether. The filtrate was concentrated under reduced pressure to afford 250 mg of a mixture of hemiaminal **6a** (30%),[4] aldehyde **7a** (35%),[5] and oxazolidine **8** (35%).[5] The conversion of the hemiaminal **6a** into **7a** and **8** was completed by stirring the reaction mixture for 2 h in a slightly acidic chloroform solution (0.09 mmol acetic acid in 25 mL chloroform). The reaction mixture was then concentrated under reduced pressure to afford 240 mg (96%) of a mixture of aldehyde **7a** and Fox chiral auxiliary **8**. The spectral data of **6a** and **7a** were determined in the mixture. The spectral data of **8** are given in our previous report.[1]

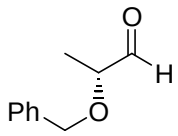
(4) The ratio of **6a**, **7a** and **8** were determined by ^1H NMR.

(2*S*,4*R*)-3-[(*R*)-2-benzyloxy-1-hydroxypropyl]-2-trifluoromethyl-4-phenyl-1,3-oxazolidine (6a).



^{1}H NMR (400 MHz) : δ 1.12 (d, 3H, ^{3}J = 6.0 Hz); 2.62 (m, 1H); 3.13 (d, 1H, ^{3}J = 1.4 Hz); 3.33 (dq, 1H, ^{3}J = 6.0 ^{3}J = 1.4 Hz); 4.09-4.13 (m, 1H); 4.21-4.24 (m, 1H); 4.36 (d, 1H, ^{2}J = 11.0 Hz); 4.48-4.54 (m, 1H); 4.59 (d, 1H, ^{2}J = 11.0 Hz); 5.95 (q, 1H, $^{3}J_{H\text{-}F}$ = 5.8 Hz); 7.25-7.43 (m, 10H); ^{19}F NMR (376.5 MHz) : δ –83.2 (d, $^{3}J_{H\text{-}F}$ = 5.8 Hz).

(*R*)-2-benzyloxypropanal (7a).



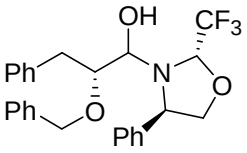
^{1}H NMR spectral data are in accordance with the literature.[5]

^{1}H NMR (400 MHz) δ 1.32 (d, 3H, ^{3}J = 6.9 Hz), 3.89 (dq, 1H, ^{3}J = 1.37, ^{3}J = 6.9 Hz), 4.59 (d, 1H, ^{2}J = 11.9 Hz), 4.65 (d, 1H, ^{2}J = 11.9 Hz), 7.31-7.40 (m, 5H), 9.66 (s, 1H); ^{13}C NMR (100.5 MHz) δ 15.4, 72.1, 79.6, 128.5, 128.2, 128.1, 137.5, 203.6.

In a similar manner, the $LiAlH_4$ reduction of **5b** (500 mg, 1.10 mmol) gave the hemiaminal **6b**. The hydrolysis of **6b** afforded an equimolar mixture of aldehyde **7b** and Fox chiral auxiliary **8** (504 mg) in a quantitative yield.

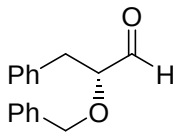
(5) Dubost, C.; Leroy, B.; Markó, I. E.; Tinant, B.; Declercq, J.–P.; Bryans, J. *Tetrahedron* **2004**, *60*, 7693–7704.

(2*S*,4*R*)-3-[(*R*)-2-benzyloxy-1-hydroxy-3-phenylpropyl]-2-trifluoromethyl-4-phenyl-1,3-oxazolidine (6b).



^{1}H NMR (400 MHz) : δ 2.53 (dd, 1H, ^{2}J = 14.0 Hz, ^{3}J = 7.8 Hz); 2.97 (d, 1H, ^{3}J = 2.8 Hz); 3.04 (dd, 1H, ^{2}J = 14.0 Hz, ^{3}J = 3.7 Hz); 3.94-3.98 (m, 1H); 4.13-4.07 (m, 1H); 4.21 (d, 1H, ^{2}J = 10.7 Hz); 4.23-4.27 (m, 1H); 4.27 (d, 1H, ^{2}J = 10.7 Hz); 4.59 (m, 1H); 5.38 (q, 1H, $^{3}J_{H\text{-}F}$ = 6.0 Hz); 7.09-7.38 (m, 15H); ^{19}F NMR (376.5 MHz) : δ –82.8 (d, $^{3}J_{H\text{-}F}$ = 6.0 Hz)

(*R*)-2-benzyloxy-3-phenylpropanal (7b).



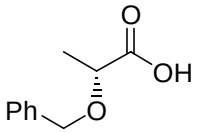
^{1}H NMR (400 MHz) δ 2.93 (dd, 1H, ^{2}J = 14.2 Hz, ^{3}J = 8.6 Hz), 3.03 (dd, 1H, ^{2}J = 14.2 Hz, ^{3}J = 5.0 Hz), 3.97 (ddd, 1H, ^{3}J = 8.6 Hz, ^{3}J = 5.0 Hz, ^{3}J = 2.3 Hz), 4.47 (d, 1H, ^{2}J = 11.9 Hz), 4.59 (d, 1H, ^{2}J = 11.9 Hz), 7.16-7.4 (m, 10H), 9.68 (d, 1H, ^{3}J = 2.3 Hz); ^{13}C RMN (100.5 MHz) δ 36.8, 72.9, 84.3, 126.9, 128.0, 128.1, 128.5, 128.6, 129.6, 136.6, 137.2, 203.2.

Typical procedure for the preparation of enantiopure α-benzyloxycarboxylic acids (9a,b).

The $LiAlH_4$ reduction of **5a** (797 mg, 2.10 mmol), followed by a slightly acidic medium hydrolysis gave an equimolar mixture of aldehyde **7a** and oxazolidine **8** (800 mg). To a solution of this crude mixture in *tert*-butanol (35 mL) at room temperature were added a solution of 2-methylbut-2-ene (11.5 mL, 2M in THF, 23.1 mmol, 11 eq) and a solution of $NaClO_2$ (1.897 g, 21.0 mmol, 10 eq) and NaH_2PO_4 (2.618 g, 16.8 mmol, 8 eq) in water (25

mL). The resulting yellow solution was stirred at room temperature for 1 h 30 min. THF and *t*-butanol were removed under reduced pressure. Water (25 mL) was added and the aqueous layer was extracted with a mixture of cyclohexane and ethyl acetate (90/10) (3 x 50 mL). The organic layers were combined, dried over $MgSO_4$, filtered and concentrated under reduced pressure to give the oxazolidine **8** (261 mg, 57%) as a colourless oil. The aqueous layer was acidified to pH 2 with an aqueous 3N HCl solution and was then extracted with ethyl acetate (3 x 75 mL). The organic layers were combined and dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude mixture was purified by flash chromatography (dichloromethane/ methanol 95/5) to afford acid **9a** (310 mg, 82%) as a pale yellow solid. Spectral data and optical rotation of **7a** were consistent with literature values.[6,7]

(*R*)-2-benzyloxypropanoic acid (9a).



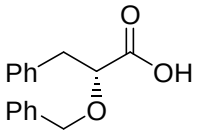
m.p. 43 °C; $[\alpha]_D$ +82.7 (c 2.25, EtOH), lit.[5] $[\alpha]_D$ +97.0 (*c* 0.71, EtOH); IR (neat) 3111, 1729, 1494, 1456, 1408, 1197, 1142, 1120, 804, 732, 694; ^{1}H NMR (400 MHz) δ 1.50 (d, 3H, ^3J = 6.9 Hz), 4.12 (q, 1H, ^3J = 6.9 Hz), 4.53 (d, 1H, ^2J = 11.4 Hz), 4.72 (d, 1H, ^2J = 11.4 Hz), 7.29-7.37 (m, 5H), 10.19 (bs, 1H); ^{13}C NMR (100.5 MHz) δ 18.5, 72.2, 73.6, 128.1, 128.2, 128.7, 137.2, 178.5; HRMS Calculated 180.0787, Found 180.0822; Anal. Calculated for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; Found: C, 65.50; H, 6.76.

(6) Nakata, M.; Arai, M.; Tomooka, K.; Ohsawa, N.; Kinoshita, M. *Bull. Chem. Soc. Jpn* **1989**, *62*, 2618–2635.

(7) Chun, C. C.; Lee, G.-J.; Kim, J. N.; Kim, T. H. *Tetrahedron: Asymmetry* **2005**, 2989–2992.

According to the same procedure from **5b** (300 mg, 0.66 mmol), the acid **9b** (81 mg, 48%) was obtained as a pale yellow solid after purification by flash chromatography (cyclohexane/ ethyl acetate 90/10 to 80/20). The optical rotation of **9b** was consistent with the literature value.[8]

(*R*)-2-(benzyloxy)-3-phenylpropanoic acid (9b)



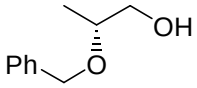
m.p. 49 °C; $[\alpha]_D$ +72.5 (*c* 0.8, EtOH), lit.[8] $[\alpha]_D$ +76.1 (*c* 0.73, EtOH); IR (neat) 3030, 2932, 1722, 1485, 1456, 1391, 1317, 1230, 1158, 1061, 987, 739, 696, 654 cm^{-1}; ^1H NMR (400 MHz) δ 3.05 (dd, 1H, ^2J = 13.7 Hz, ^3J = 8.2 Hz), 3.17 (dd, 1H, ^2J = 14.2 Hz, ^3J = 4.2 Hz), 4.19 (dd, ^3J = 8.2 Hz, ^3J = 4.1 Hz), 4.41 (d, 1H, ^2J = 11.7 Hz), 4.66 (d, 1H, ^2J = 11.7 Hz), 7.14-7.32 (m, 10H), 8.98 (bs, 1H); ^{13}C NMR (100.5 MHz) δ 39.0, 73.0, 78.7, 127.0, 128.1, 128.2, 128.5, 128.5, 129.7, 136.8, 136.9, 176.8; HRMS Calculated 256.1099, Found 256.1097.

Typical procedure for the preparation of enantiopure α-benzyloxyalcohols (10a,b).

The $LiAlH_4$ reduction of **5a** (250 mg, 0.66 mmol), followed by a slightly acidic medium hydrolysis gave an equimolar mixture of aldehyde **7b** and oxazolidine **8** (240 mg). To a solution of this crude mixture in solution in methanol (2 mL) was slowly added $NaBH_4$ (19 mg, 0.50 mmol, 0.8 eq). The reaction mixture was stirred for 1 h 30 min at room temperature. The reaction was quenched with water (10 mL). The aqueous layer was extracted with dichloromethane (3 x 15 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography

(cyclohexane/ethyl acetate 95/5 to 85/15) afforded the expected alcohol **10a** (54 mg, 51%) as a colourless oil, and the oxazolidine **8** (89 mg, 65%) as a colourless oil.

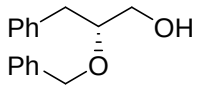
(*R*)-2-benzyloxypropan-1-ol (10a)



$[\alpha]_D$ –46.7 (*c* 0.90, $CHCl_3$); lit.[8] $[\alpha]_D$ −47 (*c* 1.0, $CHCl_3$); IR (neat) 3400, 3063, 3031, 2971, 2928, 2869, 1495, 1453, 1374, 1342, 1208, 1142, 1044, 987, 906, 856, 800, 736, 696 cm^{-1}; ^1H NMR (400 MHz) δ 1.18 (d, 3H, ^3J = 6.0 Hz), 2.09 (s, 1H), 3.47-3.54 (m, 1H), 3.58-3.65 (m, 1H), 3.65-3.72 (m, 1H), 4.49 (d, 1H, ^2J = 11.7 Hz), 4.66 (d, 1H, ^2J = 11.7 Hz), 7-30-7.36 (m, 5H); ^{13}C NMR (100.5 MHz) δ 16.0, 66.5, 70.9, 75.7, 127.9, 128.6, 138.5; HRMS Calculated 166.0994, Found 166.1000.

According to the same procedure from **5b** (500 mg, 1.1 mmol), the alcohol **10b** (222 mg, 83%) was obtained as a colourless oil after purification by flash chromatography (cyclohexane/ diethyl ether 90/10 to 60/40). The oxazolidine **8** (175 mg, 74%) was recovered as a colourless oil.

(*R*)-2-(benzyloxy)-3-phenylpropanol (10b).



$[\alpha]_D$ +15.2 (*c* 1.10, CH_2Cl_2); lit.[9] $[\alpha]_D$ +22.2 (*c* 1.00, CH_2Cl_2); IR (neat) 3402, 3028, 2922, 2868, 1494, 1452, 1349, 1208, 1028, 738, 697 cm^{-1}; ^1H NMR (400 MHz) δ 2.05 (s, 1H), 2.80

(8)Fuganti, C.; Grasselli, P.; Spreafico, R.; Zirotti, C. *J. Org. Chem.* **1984**, *49*, 543–546.

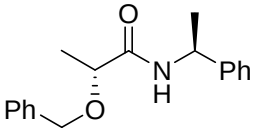
(9) Cardillo, G. *Tetrahedron* **1989**, 45, 1501–1508.

(dd, 1H, ^{2}J = 13.7 Hz, ^{3}J = 6.4 Hz), 2.94 (dd, 1H, ^{2}J = 13.7 Hz, ^{3}J = 6.4 Hz), 3.48-3.52 (m, 1H), 3.63-3.72 (m, 2H), 4.49 (d, 2H, ^{2}J = 11.5 Hz), 4.56 (d, 2H, ^{2}J = 11.5 Hz), 7.18-7.36 (m, 10H); ^{13}C NMR (100.5 MHz) δ 37.6, 63.8, 72.0, 80.97, 126.5, 127.9, 128.6, 129.5, 138.2, 138.3; HRMS Calculated 242.1307, Found 242.1300.

Typical procedure for the determination of the enantiomeric purity of benzyloxycarboxylic acid (9a).

To a solution of acid **9a** (50 mg, 0.28 mmol) in DMF (1 mL), HOBt (56 mg, 0.42 mmol, 1.5 eq) and 1-ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC) (80 mg, 0.42 mmol, 1.5 eq) were added under argon. The reaction mixture was stirred for 10 min, cooled at 0 °C and (*S*)-1-phenylethanamine (44 µL, 3.5 mmol, 1.25 eq) and triethylamine (154 µL, 1.11 mmol, 4 eq) were added. The reaction mixture was stirred at 0 °C for 1 h and overnight at room temperature. Dichloromethane (10 mL) was added and the organic layer was washed twice with water and once with aqueous 1N HCl. The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 89 mg (quantitative yield) of crude amide as a brown oil. Analysis of this crude amide by GC and NMR showed the presence of a single diastereomer.

(2*R*)-2-(benzyloxy)-*N*-((*S*)-1-phenylethyl)propanamide.

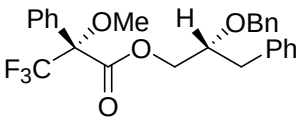


^{1}H NMR (400 MHz) δ 1.39 (d, 3H, ^{3}J = 6.9 Hz), 1,47 (d, 3H, ^{3}J = 6.9 Hz), 3.99 (q, 1H, ^{3}J = 6.9 Hz, 3H), 4.54 (d, 1H, ^{2}J = 11.6 Hz), 4.61 (d, 1H, ^{2}J = 11.6 Hz), 5.11 (dq, 1H, ^{3}J = 6.7 Hz, ^{3}J = 6.9 Hz), 6.79 (d, 1H, ^{3}J = 6.7 Hz) 7.15-7.35 (m, 10H), ^{13}C NMR (100.5 MHz) δ 18.8, 22.2, 41.2, 72.2, 76.5, 126.1, 127.4, 128.0, 128.3, 128.8, 137.4, 143.2, 172.4.

Typical procedure for the determination of the enantiomeric purity of benzyloxyalcohol (10b).

A solution of (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid (70 mg, 0.3 mmol, 3 eq) in toluene (3.5 mL) was concentrated under reduced pressure at 0 °C. Under argon, the acid was dissolved in dichloromethane (1.5 mL) then oxalyl choride (34 µL, 0.4 mmol, 4 eq) and DMF (0.05 mmol) were added. The reaction mixture was stirred at room temperature until gas emission ceased (20 min). The reaction mixture was cooled at 0 °C, and the solvent were removed under reduced pressure for 30 min and then dissolved in dichloromethane (1.5 mL). This solution is slowly added to a solution of alcohol **10b** (24 mg, 1 mmol, 1 eq), DMAP (3 mg, 0.03 mmol, 0.3 eq), and triethylamine (70 µL, 0.5 mmol, 5 eq) in dichloromethane (1 mL). A soft gas emission was observed. The reaction mixture was stirred at room temperature for 24 h. Dichloromethane (15 mL) was added. This organic layer was washed with saturated NH_4Cl (2 x 15 mL), saturated $NaHCO_3$ (2 x 15mL) and water (15 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the crude ester (58 mg, quantitative yield) as a yellow oil. Analysis of this crude ester by NMR showed the presence of a single diastereomer.

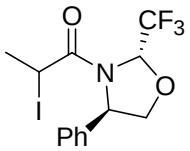
(2*R*)-[(*R*)-2-benzyloxy-3-phenylpropyl]-3,3,3-trifluoro-2methoxy-2-phenylpropanoate



^{1}H NMR (400 MHz) δ 2.80 (dd, 1H, ^2J = 14.0 Hz, ^3J = 6.7 Hz), 2.88 (dd, 1H, ^3J = 14.0 Hz, ^3J = 6.9 Hz), 3.46 (bs, 3H), 3.85 (tdd, 1H, ^3J = 8.7 Hz, ^3J = 6.9 Hz, ^3J = 6.7 Hz), 4.14 (dd, 1H, ^2J = 11.5 Hz, ^3J = 8.7 Hz), 4.32 (d, 1H, ^2J = 11.5 Hz), 4.42 (dd, 1H, ^2J = 11.5 Hz, ^3J = 3.7 Hz), 4.44 (d, 1H, ^2J = 11.5 Hz), 7.10-7.55 (m, 15H); ^{13}C NMR (100.5 MHz) δ 38.1, 55.6, 66.9,

72.2, 77.8, 84.8 (q, $^{3}J_{C\text{-}F}$ = 27.8 Hz), 123.5 (q, $^{2}J_{C\text{-}F}$ = 288.5 Hz), 126.7, 127.6, 127.7, 127.8, 128.4, 128.6, 128.6, 129.6, 129.7, 132.3, 137.4, 138.0, 166.6; ^{19}F NMR (376 MHz) δ –74.64 (s).

Preparation of (2*S*,4*R*)-2-trifluoromethyl-3-(2-iodopropanoyl)-4-phenyl-1,3-oxazolidine (11).



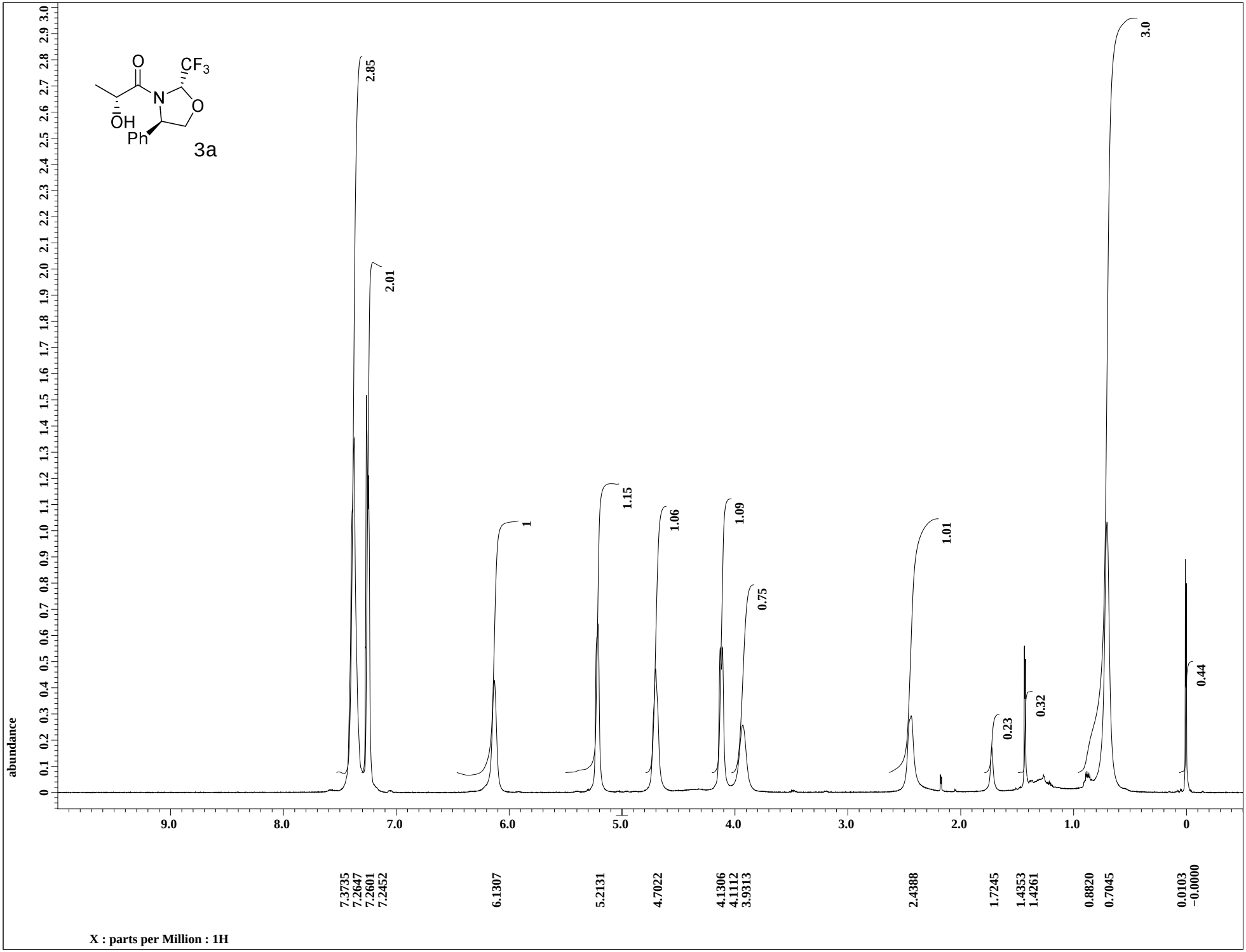
To a solution of the amide **1a** (2.0 g, 7.32 mmol) in THF under argon at –78 °C was added a solution of NaHMDS (7.3 mL, 2M in THF, 14.64 mmol, 2 eq). The reaction mixture was stirred at –78 °C for 45 min then *N*-iodosuccinimide (3.29 g, 14.64 mmol, 2 eq) was added. The mixture was stirred at –78 °C for 3 h. The reaction mixture was quenched with water and extracted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$ and concentrated. Purification by flash chromatography (cyclohexane/ ethyl acetate 95/5 to 85/15) followed by a washing with a saturated sodium bisulfite aqueous solution afforded the iodide **11** (0.568 g, 19%, 82 % *de*) as a white solid.

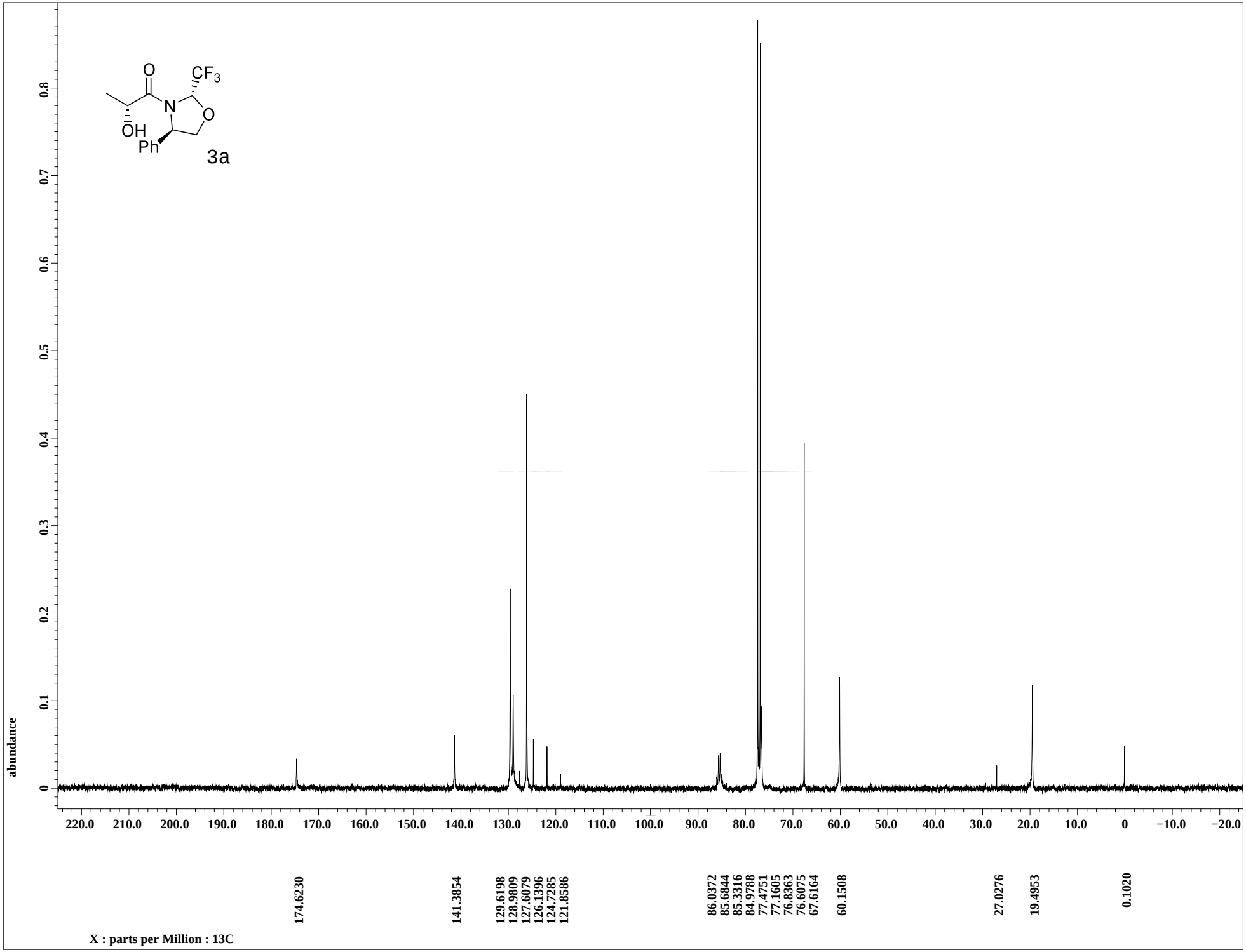
IR (neat) 2915, 1655, 1388, 1279, 1177, 1147, 1104, 993, 932, 880, 847, 700 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.55 (d, 3H, ^{3}J = 6.9 Hz), 4.10 (dd, 1H, ^{2}J = 6.9, ^{3}J = 6.2 Hz), 4.11 (q, 1H, ^{3}J = 6.9 Hz), 4.74 (dd, 1H, ^{2}J = 6.9 Hz, ^{3}J = 6.8 Hz), 5.06 (dd, 1H, ^{3}J = 6.8 Hz, ^{3}J = 6.2 Hz), 6.15 (q, 1H, $^{3}J_{H\text{-}F}$ = 5.1 Hz), 7.19-7.22 (m, 2H), 7.34-7.43 (m, 3H); ^{13}C NMR (100.5 MHz) δ 14.1, 21.9, 60.2, 76.7, 85.6 (q, $^{3}J_{C\text{-}F}$ = 35.5 Hz), 123.4 (q, $^{2}J_{C\text{-}F}$ = 289.5 Hz), 125.2, 129.1, 129.9, 141.2, 171.5; ^{19}F NMR (376.5 MHz) δ –80.3 (d, $^{3}J_{H\text{-}F}$ = 5.1 Hz); HRMS Calculated 398.9943, Found 398.9934.

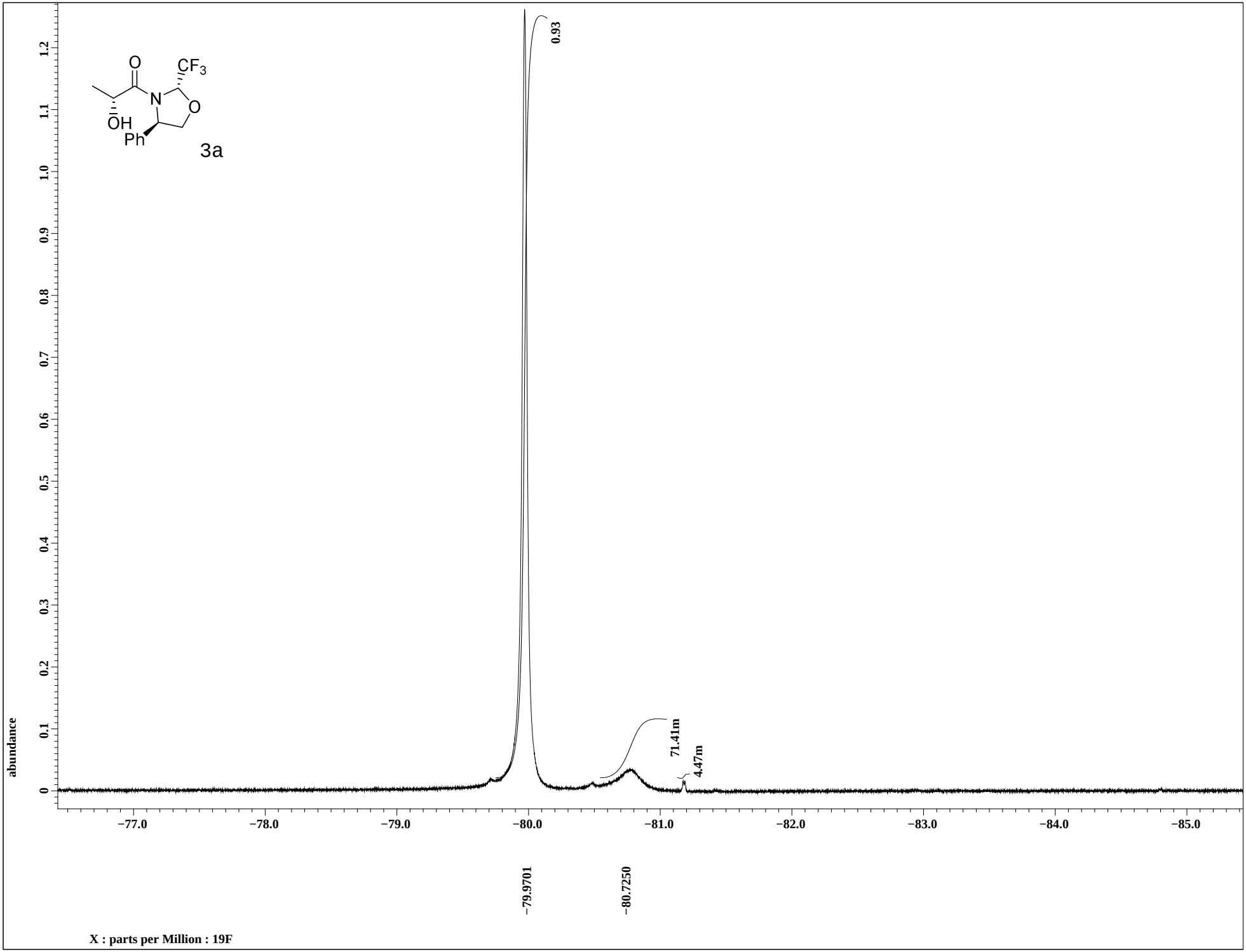
Radical oxygenation of iodide (11)

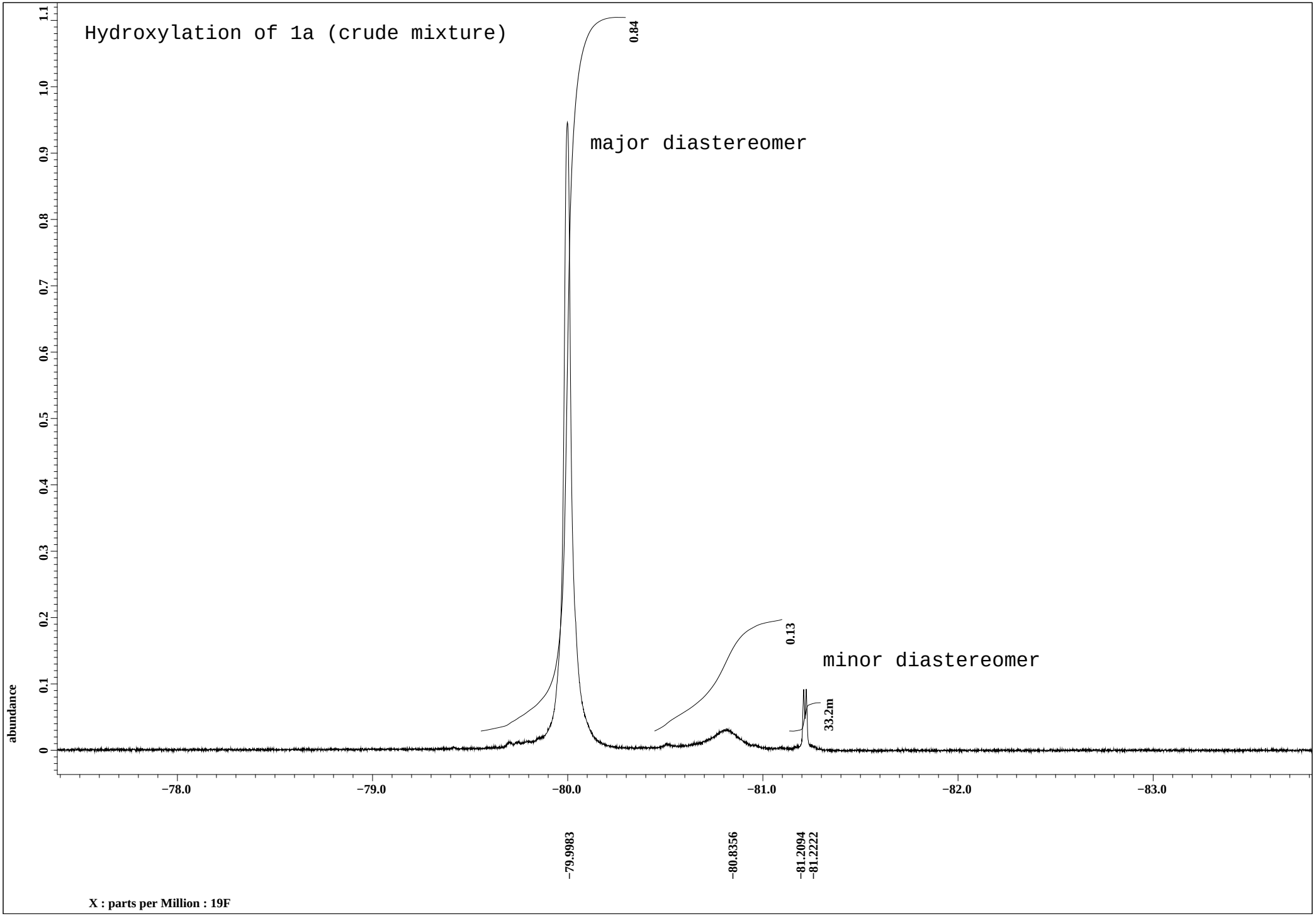
Molecular oxygen was bubbled through a solution of the iodide **11** (215 mg, 0.54 mmol) in dichloromethane (1.5 mL) under argon at −50 °C and triethylborane (1.08 mL, 1 M in hexane, 1.08 mmol) was added. The reaction was followed on TLC plate. The reaction mixture was stirred at −50 °C with oxygen bubbling for 1 h 30 min before triethylborane (1.08 ml, 1 M in hexane, 1.08 mmol) was added once more. No evolution was observed after 1 h 30 min so the reaction mixture was quenched with MeOH and concentrated to furnish a crude mixture of iodide (59%)[10] and alcohols ((*R*)-**3a** (30%) and (*S*)-**3a** (11%)).[4] Purification by flash chromatography (cyclohexane / ethyl acetate 90/10 to 80/20) afforded the alcohol **3a** as a mixture of diastereomers (44 mg, 28%, (*R*)-**3a**/(*S*)-**3a** : 73/27) and the iodide **11** (80 mg, 37%).

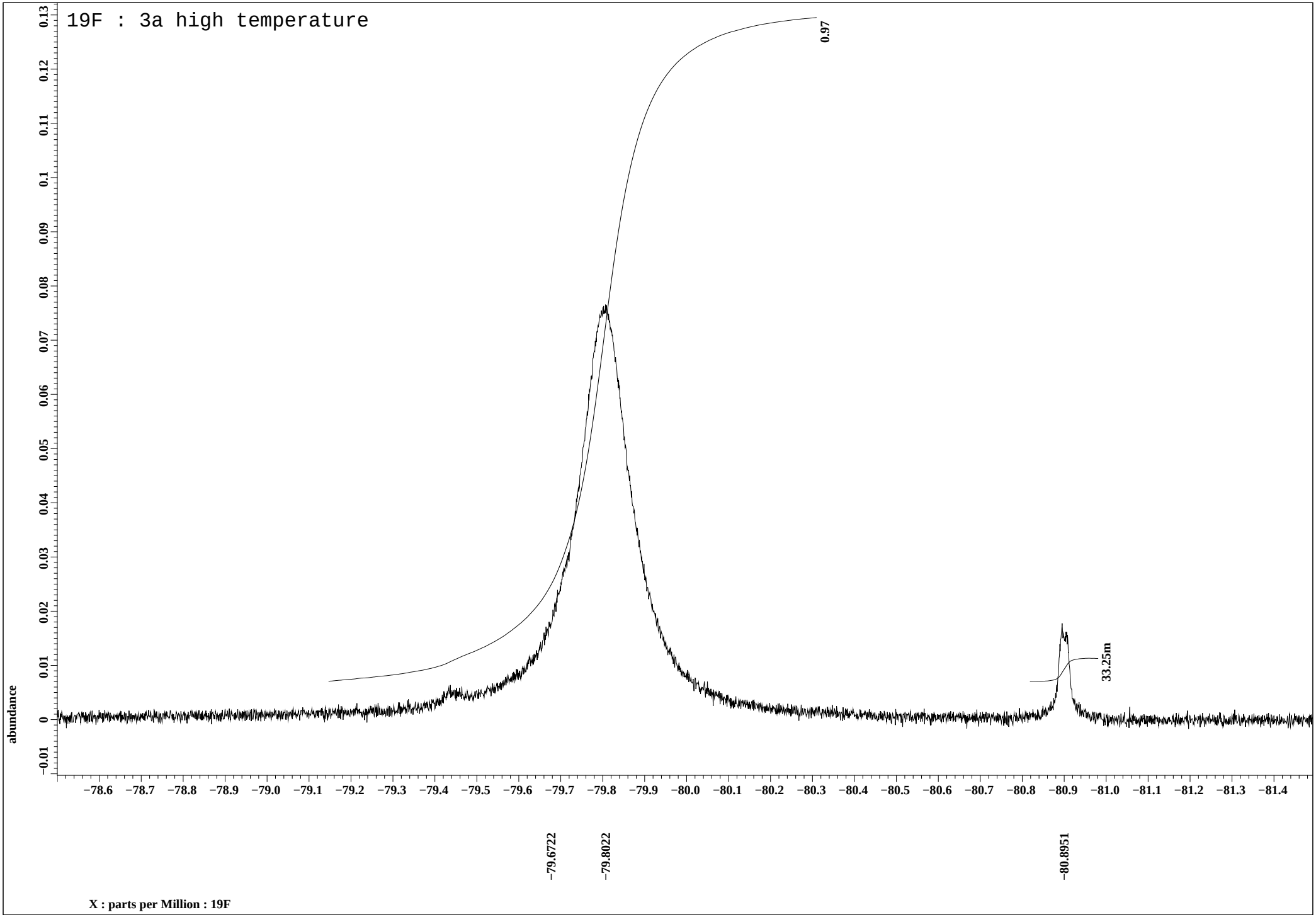
(10) ratio measured by ^{19}F NMR.

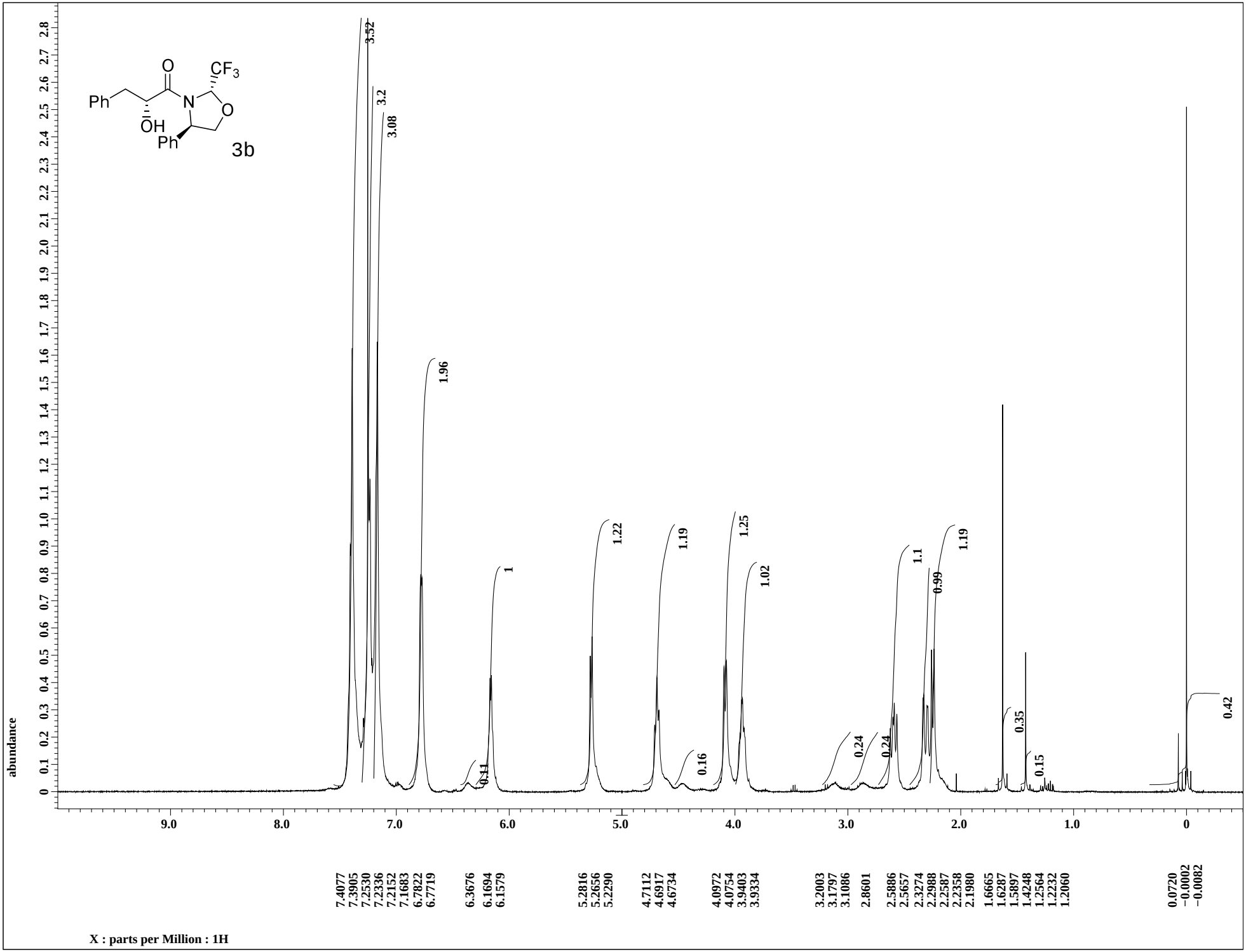

O
CF3
N
O
OH
Ph
3a
abundance
2.85
2.01
1
1.15
1.06
1.09
0.75
1.01
0.23
0.32
3.0
0.44
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.3735
7.2647
7.2601
7.2452
6.1307
5.2131
4.7022
4.1306
4.1112
3.9313
2.4388
1.7245
1.4353
1.4261
0.8820
0.7045
0.0103
−0.0000
X : parts per Million : 1H

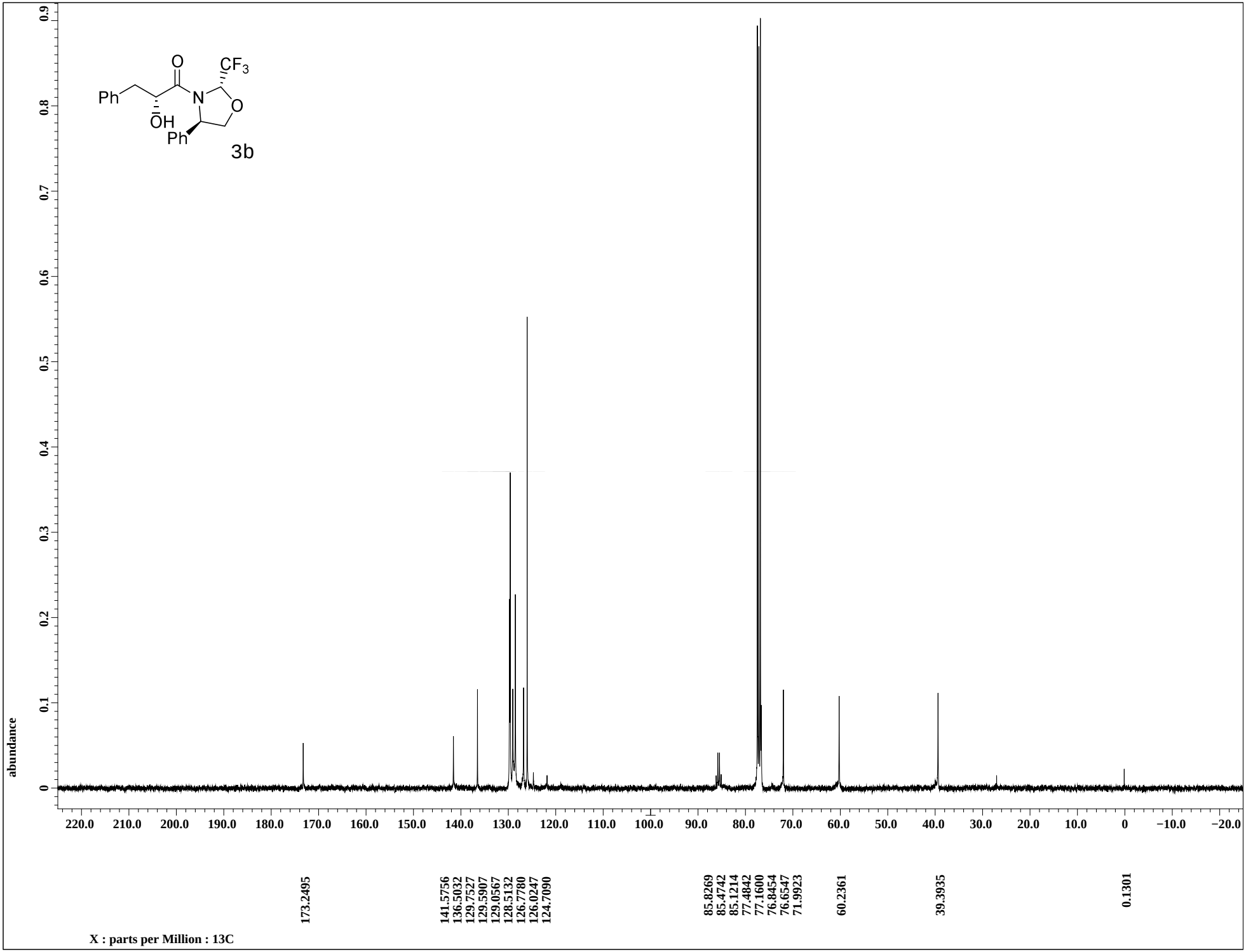

O
CF3
N
O
OH
Ph
3a
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
174.6230
141.3854
129.6198
128.9809
127.6079
126.1396
124.7285
121.8586
86.0372
85.6844
85.3316
84.9788
77.4751
77.1605
76.8363
76.6075
67.6164
60.1508
27.0276
19.4953
0.1020
X : parts per Million : 13C

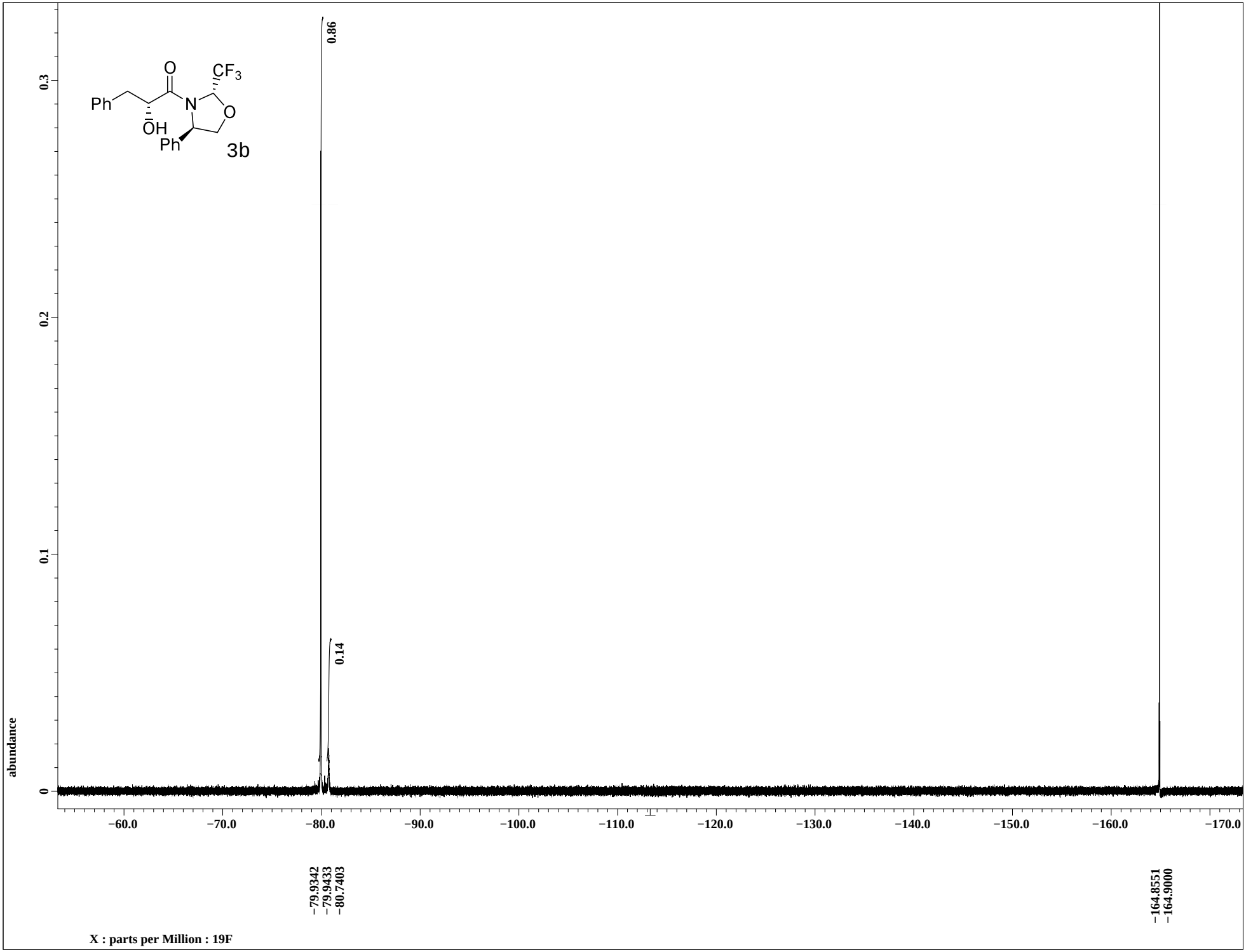

O
CF3
N
O
OH
Ph
3a
0.93
71.41m
4.47m
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
−77.0
−78.0
−79.0
−80.0
−81.0
−82.0
−83.0
−84.0
−85.0
−79.9701
−80.7250
X : parts per Million : 19F

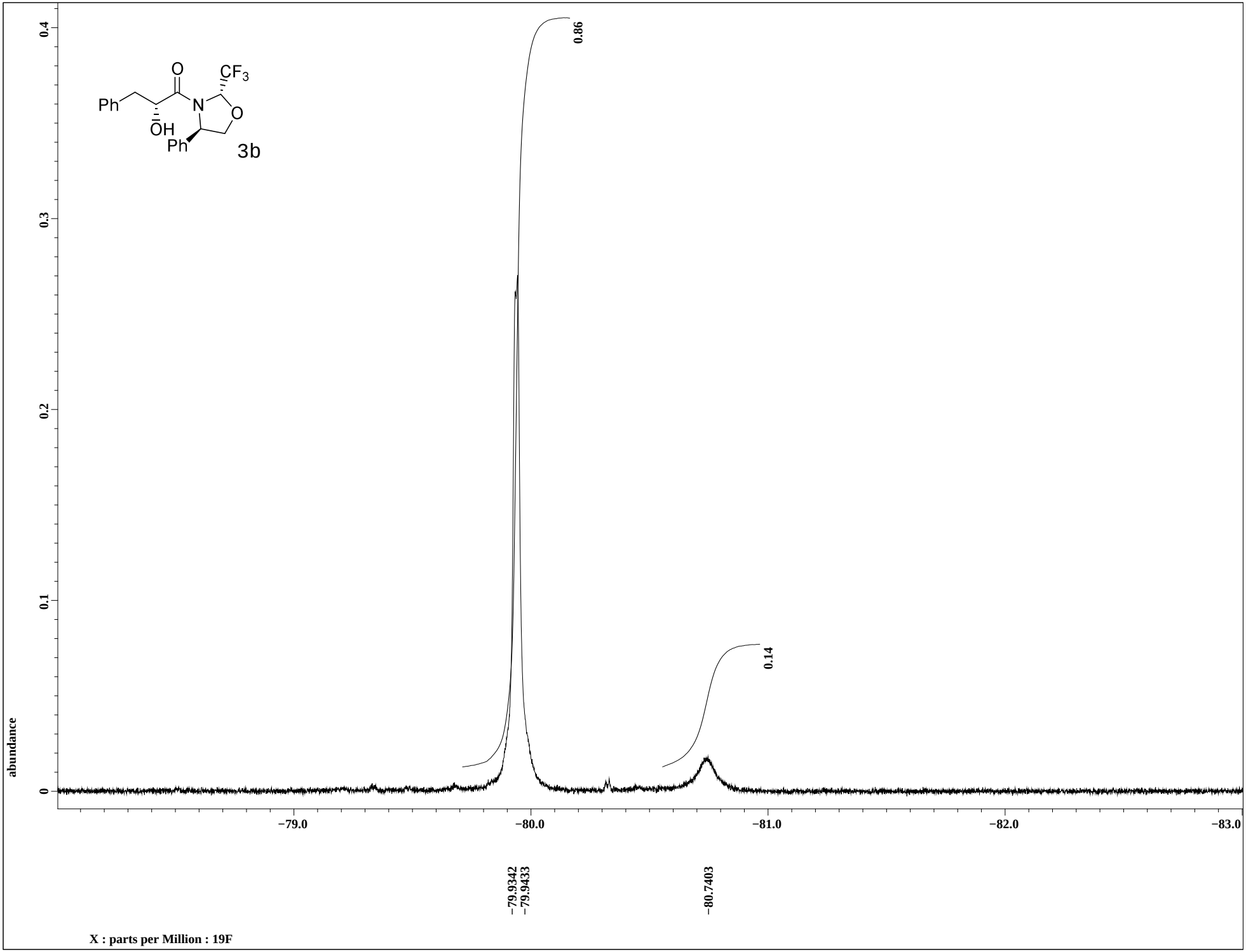

Hydroxylation of 1a (crude mixture)
major diastereomer
minor diastereomer
0.84
0.13
33.2m
abundance
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
−78.0
−79.0
−80.0
−81.0
−82.0
−83.0
−79.9983
−80.8356
−81.2094
−81.2222
X : parts per Million : 19F

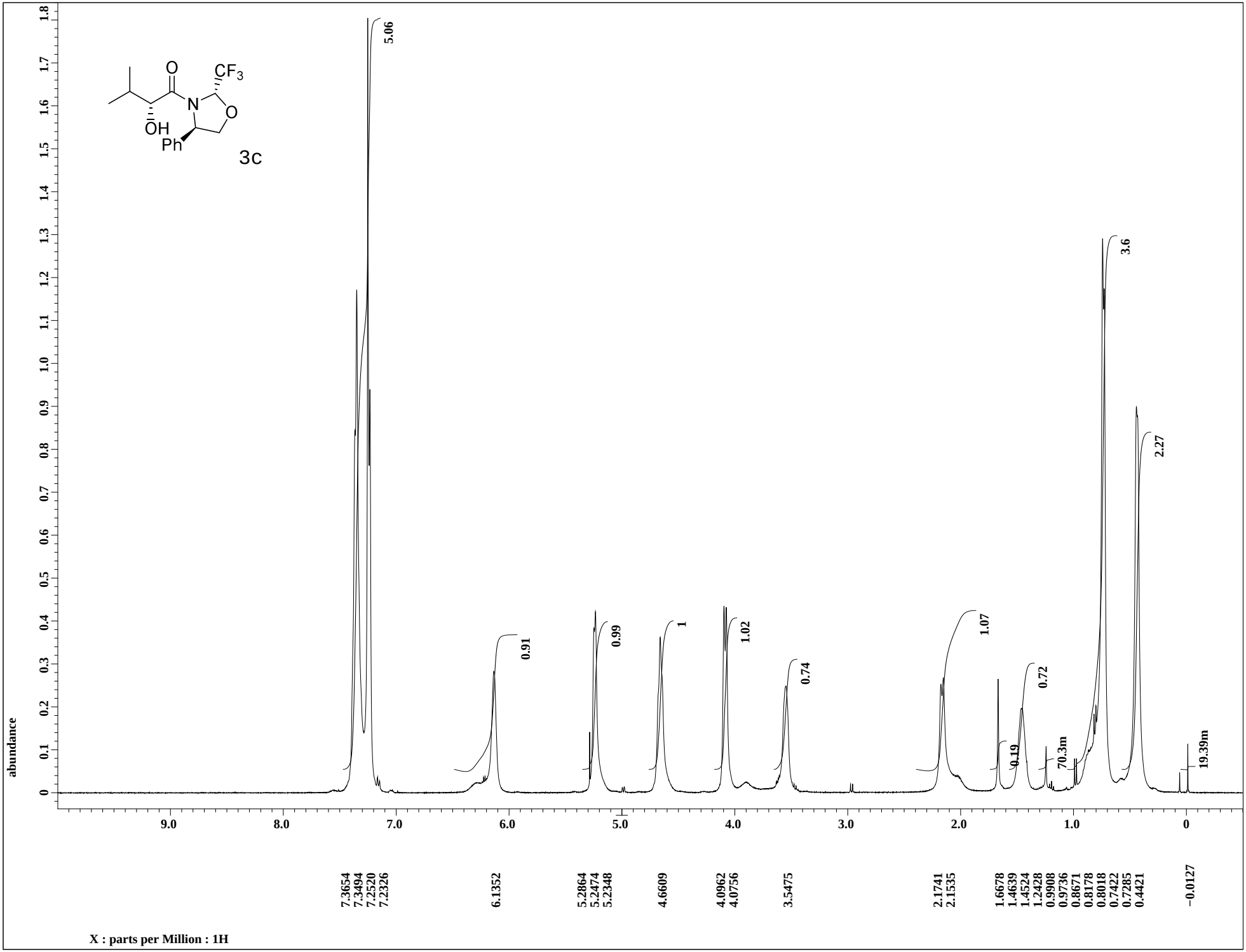

19F : 3a high temperature
0.97
33.25m
abundance
0.13
0.12
0.11
0.1
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
−0.01
−78.6 −78.7 −78.8 −78.9 −79.0 −79.1 −79.2 −79.3 −79.4 −79.5 −79.6 −79.7 −79.8 −79.9 −80.0 −80.1 −80.2 −80.3 −80.4 −80.5 −80.6 −80.7 −80.8 −80.9 −81.0 −81.1 −81.2 −81.3 −81.4
−79.6722
−79.8022
−80.8951
X : parts per Million : 19F

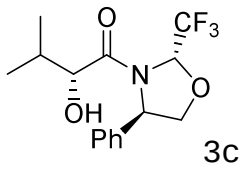

O
CF3
Ph
N
O
OH
Ph
3b
abundance
X : parts per Million : 1H
3.52
3.2
3.08
1.96
1
1.22
1.19
1.25
1.02
1.1
0.99
1.19
0.35
0.42
0.24
0.24
0.16
0.11
0.15
7.4077
7.3905
7.2530
7.2336
7.2152
7.1683
6.7822
6.7719
6.3676
6.1694
6.1579
5.2816
5.2656
5.2290
4.7112
4.6917
4.6734
4.0972
4.0754
3.9403
3.9334
3.2003
3.1797
3.1086
2.8601
2.5886
2.5657
2.3274
2.2988
2.2587
2.2358
2.1980
1.6665
1.6287
1.5897
1.4248
1.2564
1.2232
1.2060
0.0720
−0.0002
−0.0082


O
CF3
Ph
N
O
OH
Ph
3b
abundance
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
173.2495
141.5756
136.5032
129.7527
129.5907
129.0567
128.5132
126.7780
126.0247
124.7090
85.8269
85.4742
85.1214
77.4842
77.1600
76.8454
76.6547
71.9923
60.2361
39.3935
0.1301
X : parts per Million : 13C


0.86
0.14
3b
abundance
X : parts per Million : 19F
−79.9342
−79.9433
−80.7403
−164.8551
−164.9000


O
CF3
Ph
N
O
OH
Ph
3b
0.86
0.14
abundance
0.4
0.3
0.2
0.1
0
−79.0
−80.0
−81.0
−82.0
−83.0
−79.9342
−79.9433
−80.7403
X : parts per Million : 19F


O
CF3
N
O
OH
Ph
3c
abundance
X : parts per Million : 1H
5.06
0.91
0.99
1
1.02
0.74
1.07
0.19
0.72
70.3m
3.6
2.27
19.39m
7.3654
7.3494
7.2520
7.2326
6.1352
5.2864
5.2474
5.2348
4.6609
4.0962
4.0756
3.5475
2.1741
2.1535
1.6678
1.4639
1.4524
1.2428
0.9908
0.9736
0.8671
0.8178
0.8018
0.7422
0.7285
0.4421
−0.0127

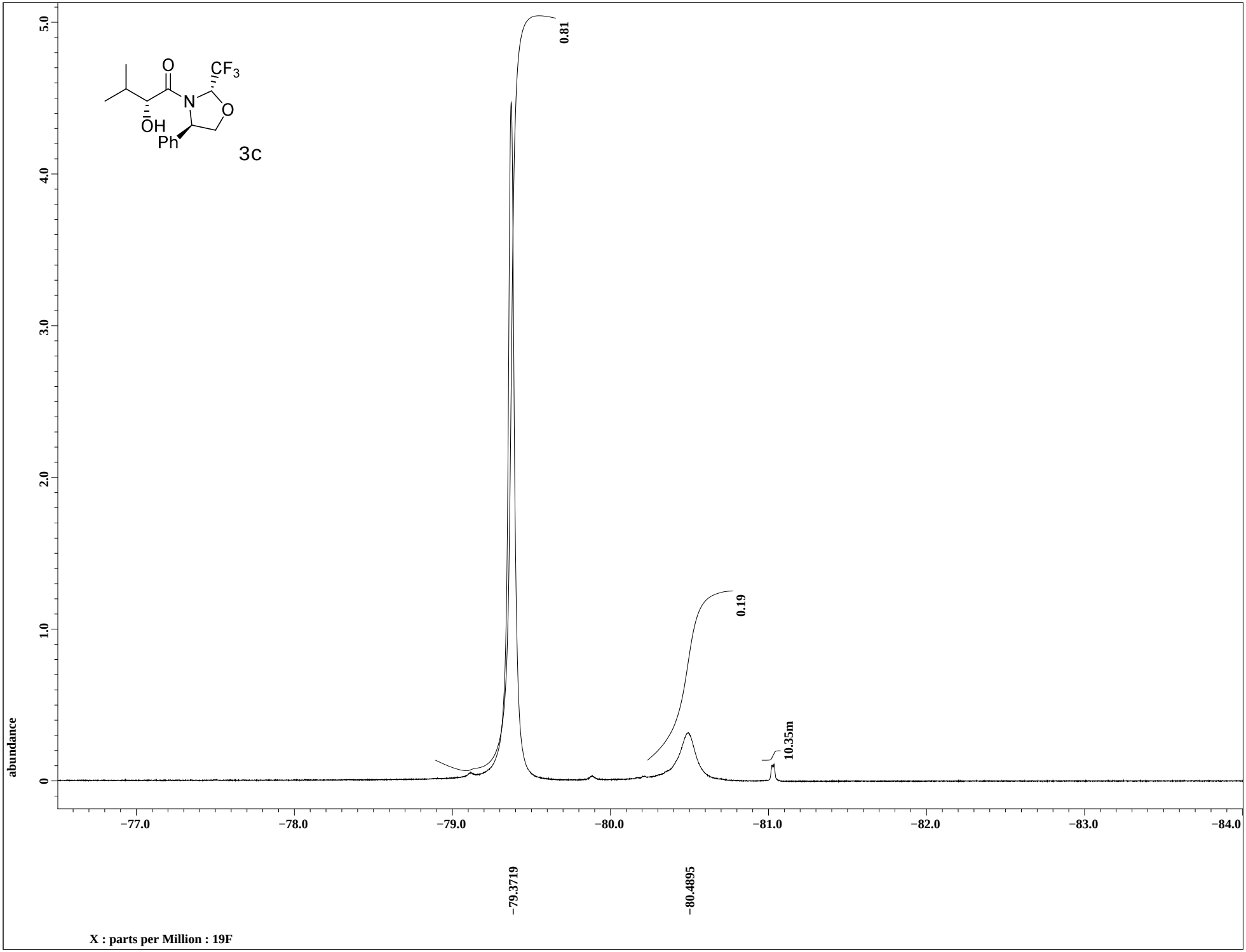


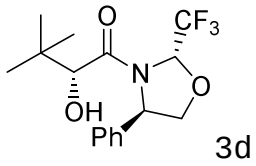
3c

abundance

173.4397
142.0233
129.5044
128.8465
126.0719
124.7752
121.8958
85.9600
85.5976
77.4742
77.1595
76.8449
76.6733
75.9200
65.9469
60.1785
30.3447
18.9891
15.8236
15.3564

X : parts per Million : 13C


O
CF3
N
O
OH
Ph
3c
5.0
4.0
3.0
2.0
1.0
0
abundance
0.81
0.19
10.35m
−77.0
−78.0
−79.0
−80.0
−81.0
−82.0
−83.0
−84.0
−79.3719
−80.4895
X : parts per Million : 19F



3d

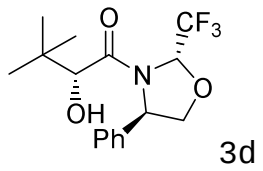
abundance

4.3
0.63
0.75
1.01
0.99
0.71
0.75
81.21m
48.62m
0.21
9
41.04m

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

7.3758
7.3586
7.2544
7.2372
6.1398
5.2853
4.6484
4.0928
4.0722
3.5533
3.5338
2.1375
2.1157
1.7744
1.4261
1.2589
0.9622
0.8958
0.8809
0.8626
0.7377
0.0006

X : parts per Million : 1H



3d

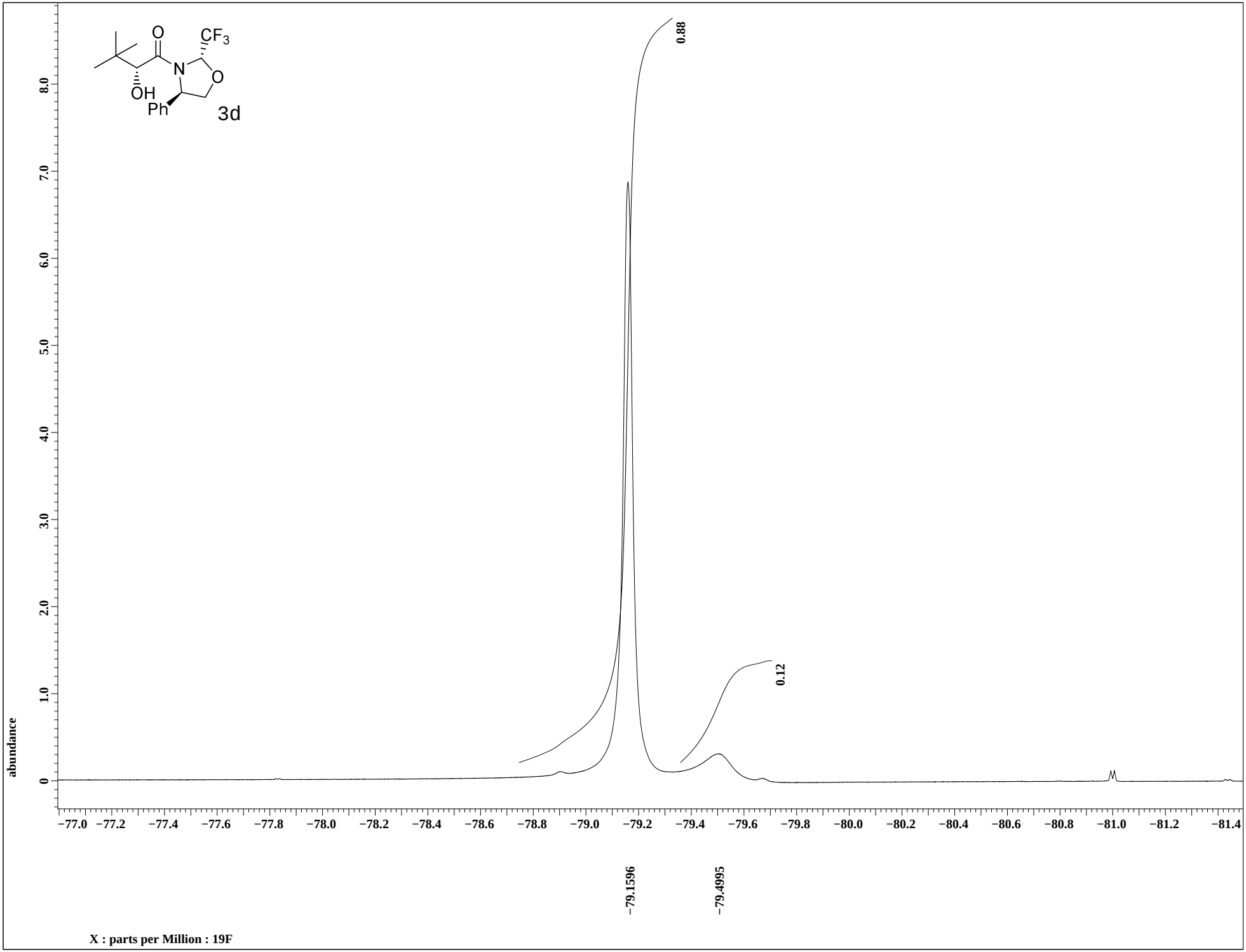
abundance

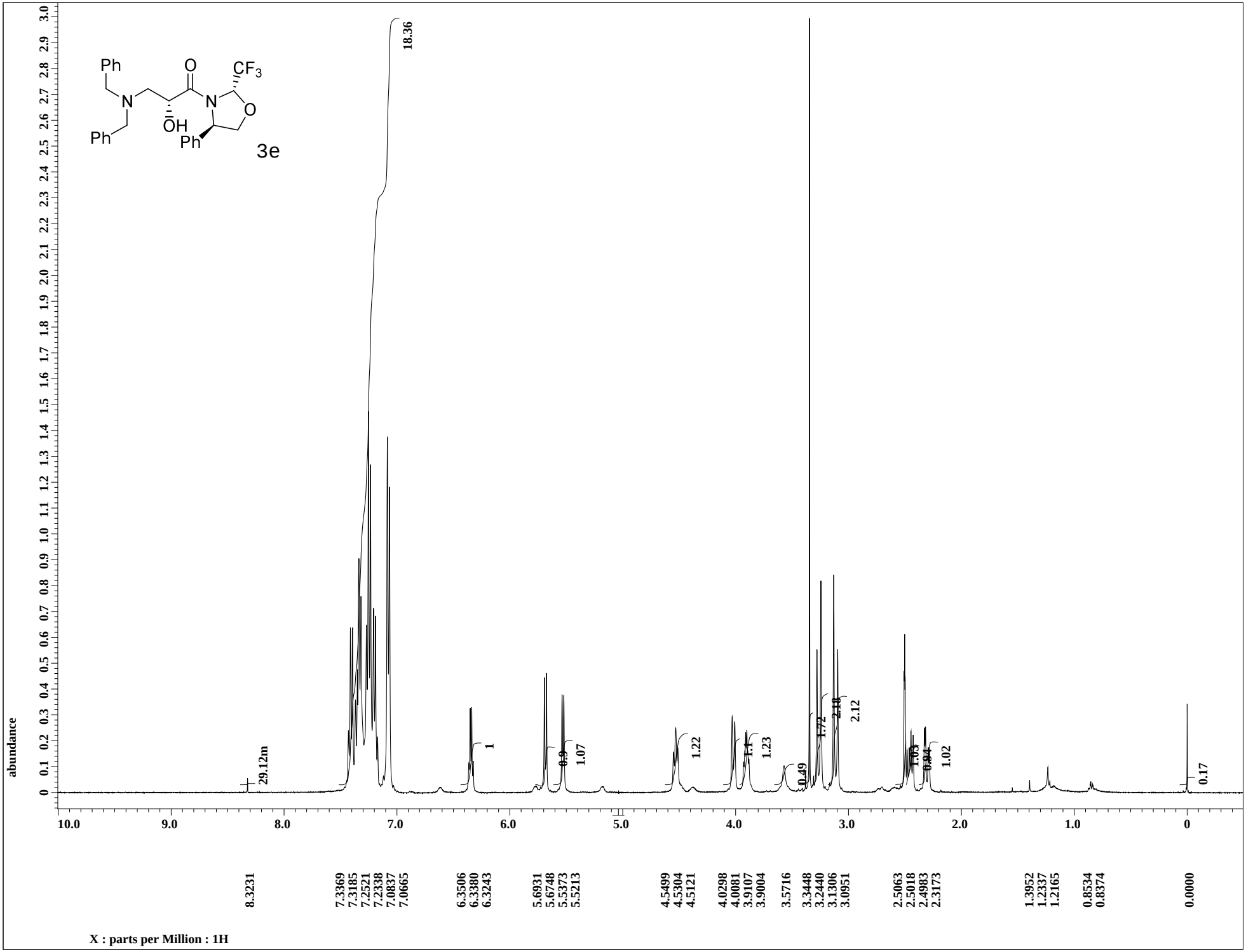
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9

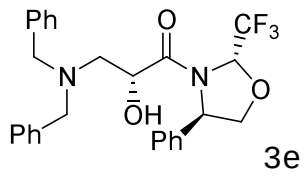
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0

172.3438
142.6722
129.4477
128.6563
127.7220
126.0057
124.8425
121.9631
85.5219
78.0277
77.4747
77.1601
76.8359
76.6547
60.4746
34.7884
29.8018
27.0082
25.4636

X : parts per Million : 13C


O
CF3
N
O
OH
Ph
3d
0.88
0.12
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
−77.0 −77.2 −77.4 −77.6 −77.8 −78.0 −78.2 −78.4 −78.6 −78.8 −79.0 −79.2 −79.4 −79.6 −79.8 −80.0 −80.2 −80.4 −80.6 −80.8 −81.0 −81.2 −81.4
−79.1596
−79.4995
X : parts per Million : 19F


Ph
O
CF3
N
N
O
OH
Ph
Ph
3e
18.36
29.12m
1
0.9
1.07
1.22
1.1
1.23
0.49
1.72
2.18
2.12
1.03
0.94
1.02
0.17
abundance
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.3231
7.3369
7.3185
7.2521
7.2338
7.0837
7.0665
6.3506
6.3380
6.3243
5.6931
5.6748
5.5373
5.5213
4.5499
4.5304
4.5121
4.0298
4.0081
3.9107
3.9004
3.5716
3.3448
3.2440
3.1306
3.0951
2.5063
2.5018
2.4983
2.3173
1.3952
1.2337
1.2165
0.8534
0.8374
0.0000
X : parts per Million : 1H



3e

abundance

0 0.1 0.2 0.3 0.4 0.5 0.6

220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0

172.5677

142.8961
139.3111
129.6144
128.9661
128.5751
127.2212
126.3154
125.4097

85.0879
84.7542

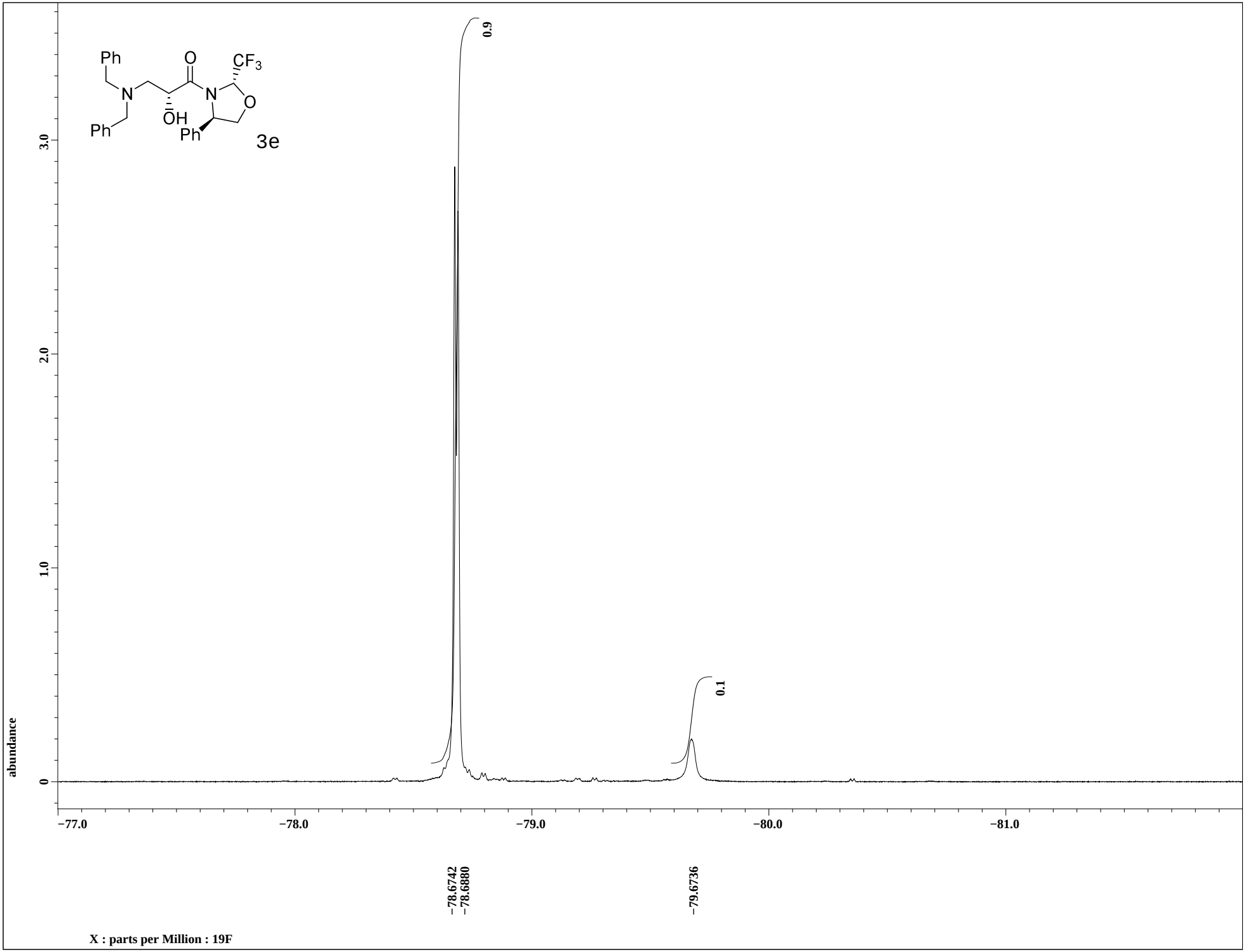
76.6117

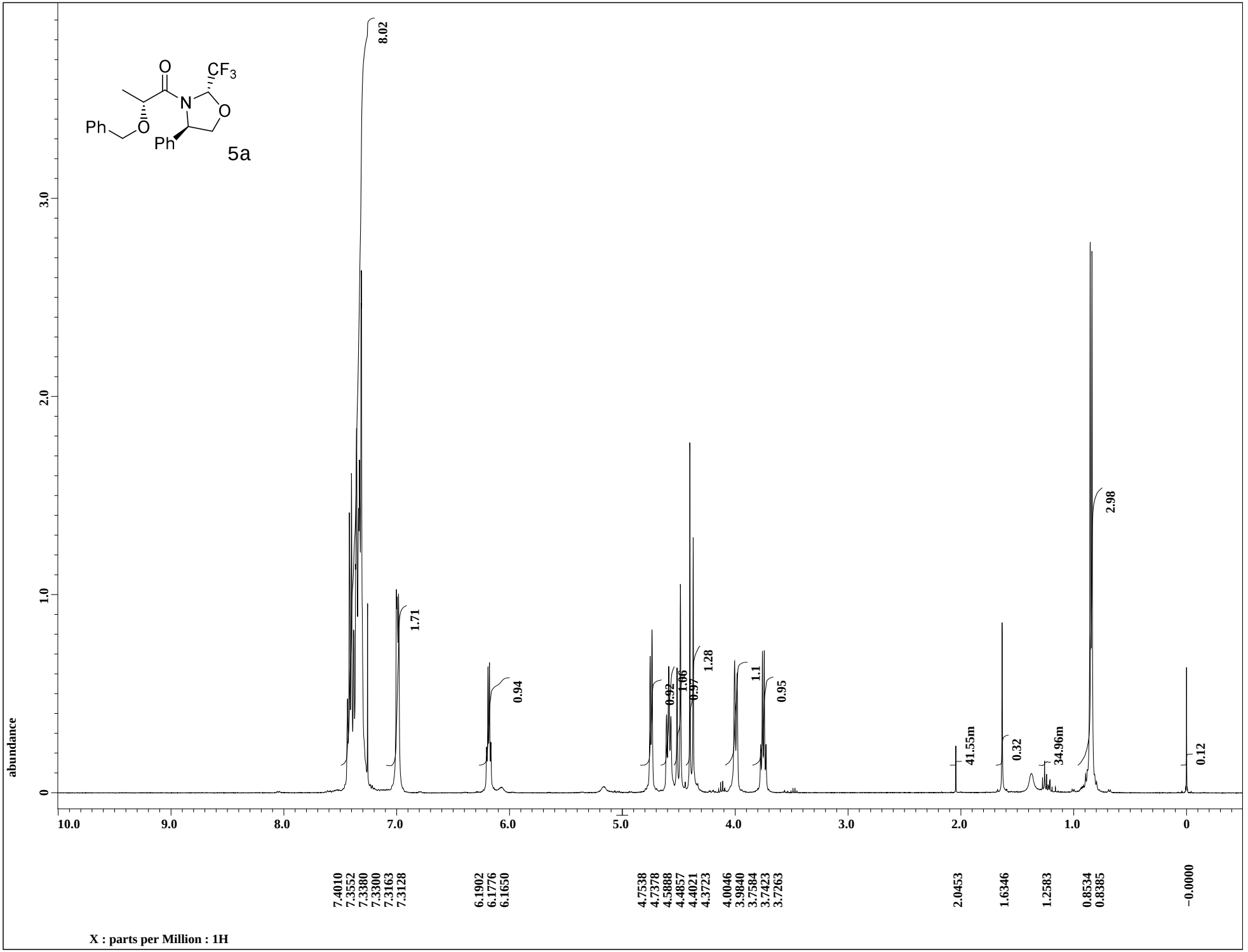
68.0496

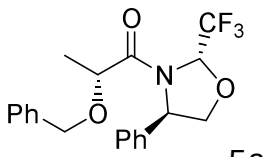
59.5066
57.3900
54.9682

40.2372
40.0275
39.8273

X : parts per Million : 13C


Ph
O
CF3
N
N
O
OH
Ph
Ph
3e
0.9
0.1
3.0
2.0
1.0
0
abundance
−77.0
−78.0
−79.0
−80.0
−81.0
−78.6742
−78.6880
−79.6736
X : parts per Million : 19F


O
CF3
N
O
Ph
O
Ph
5a
abundance
0
1.0
2.0
3.0
8.02
1.71
0.94
0.92
1.06
0.97
1.28
1.1
0.95
41.55m
0.32
34.96m
2.98
0.12
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.4010
7.3552
7.3380
7.3300
7.3163
7.3128
6.1902
6.1776
6.1650
4.7538
4.7378
4.5888
4.4857
4.4021
4.3723
4.0046
3.9840
3.7584
3.7423
3.7263
2.0453
1.6346
1.2583
0.8534
0.8385
−0.0000
X : parts per Million : 1H

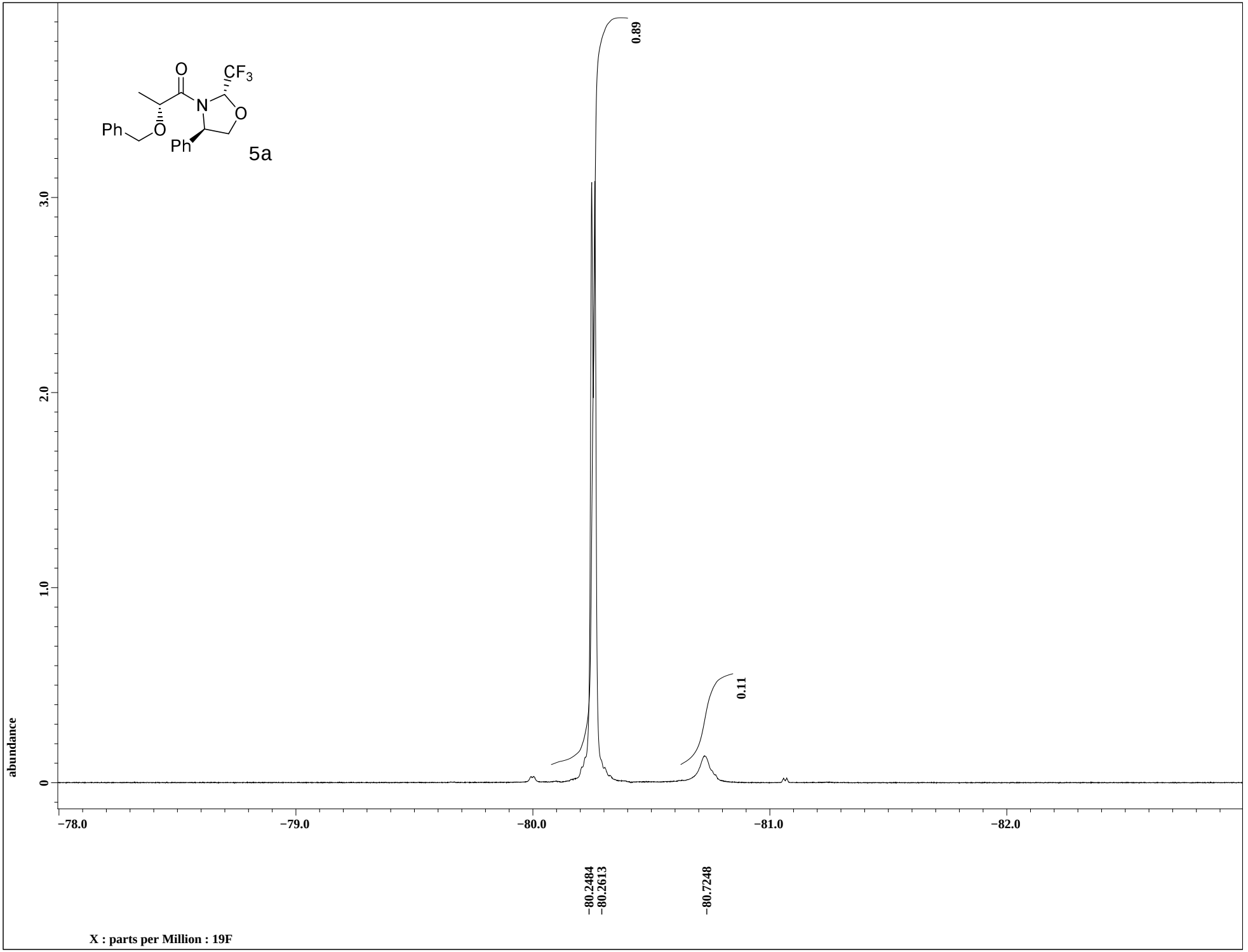


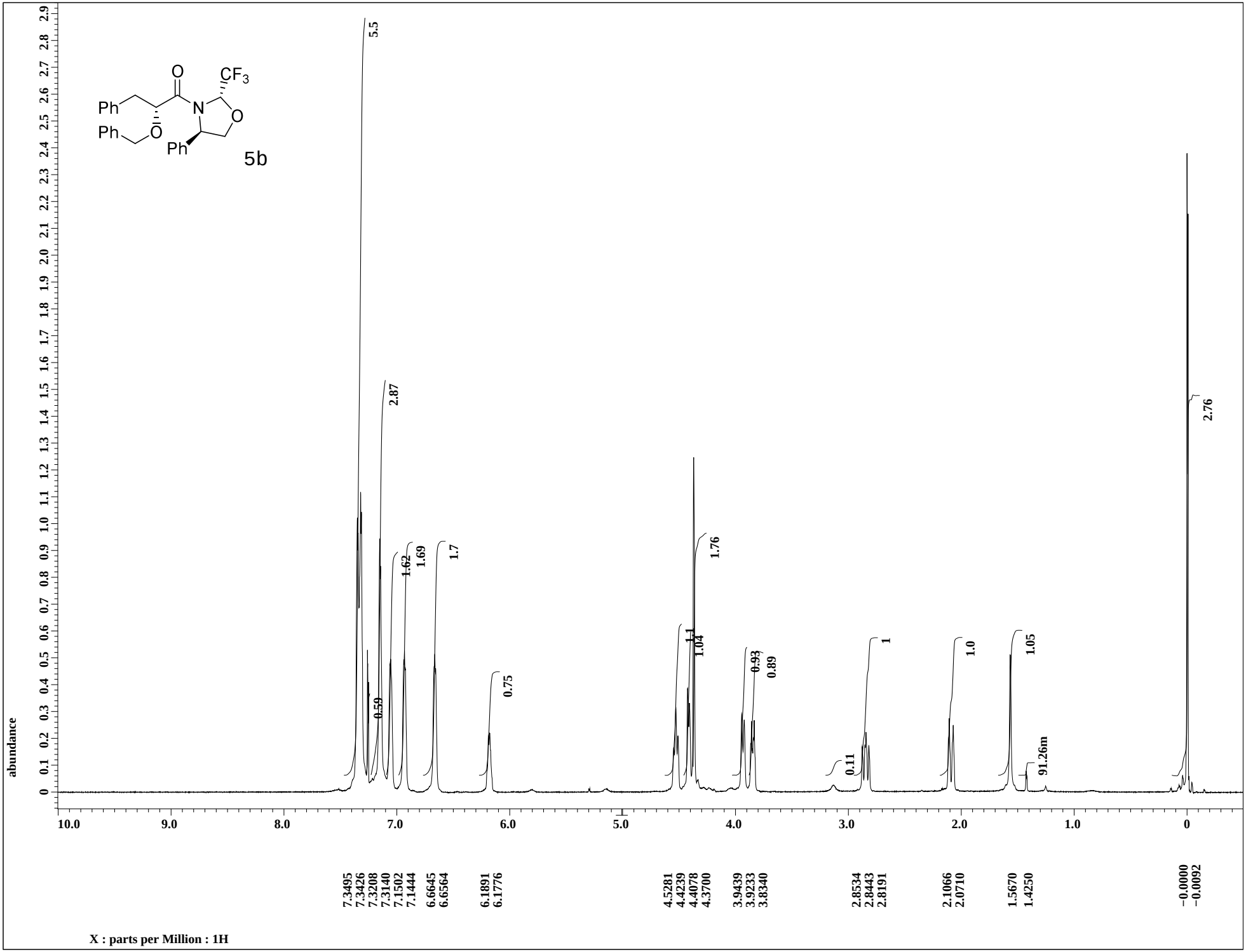
5a

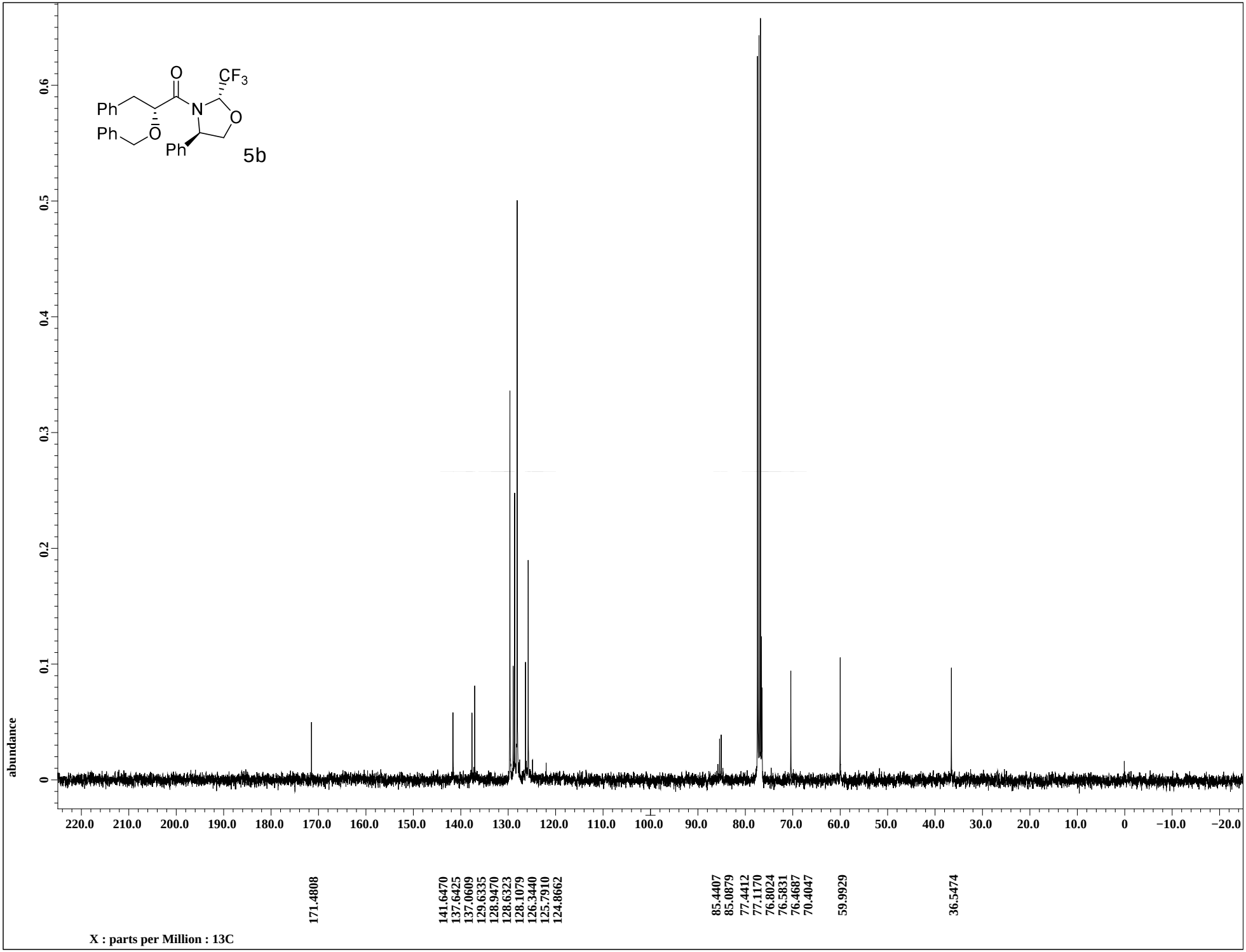
abundance

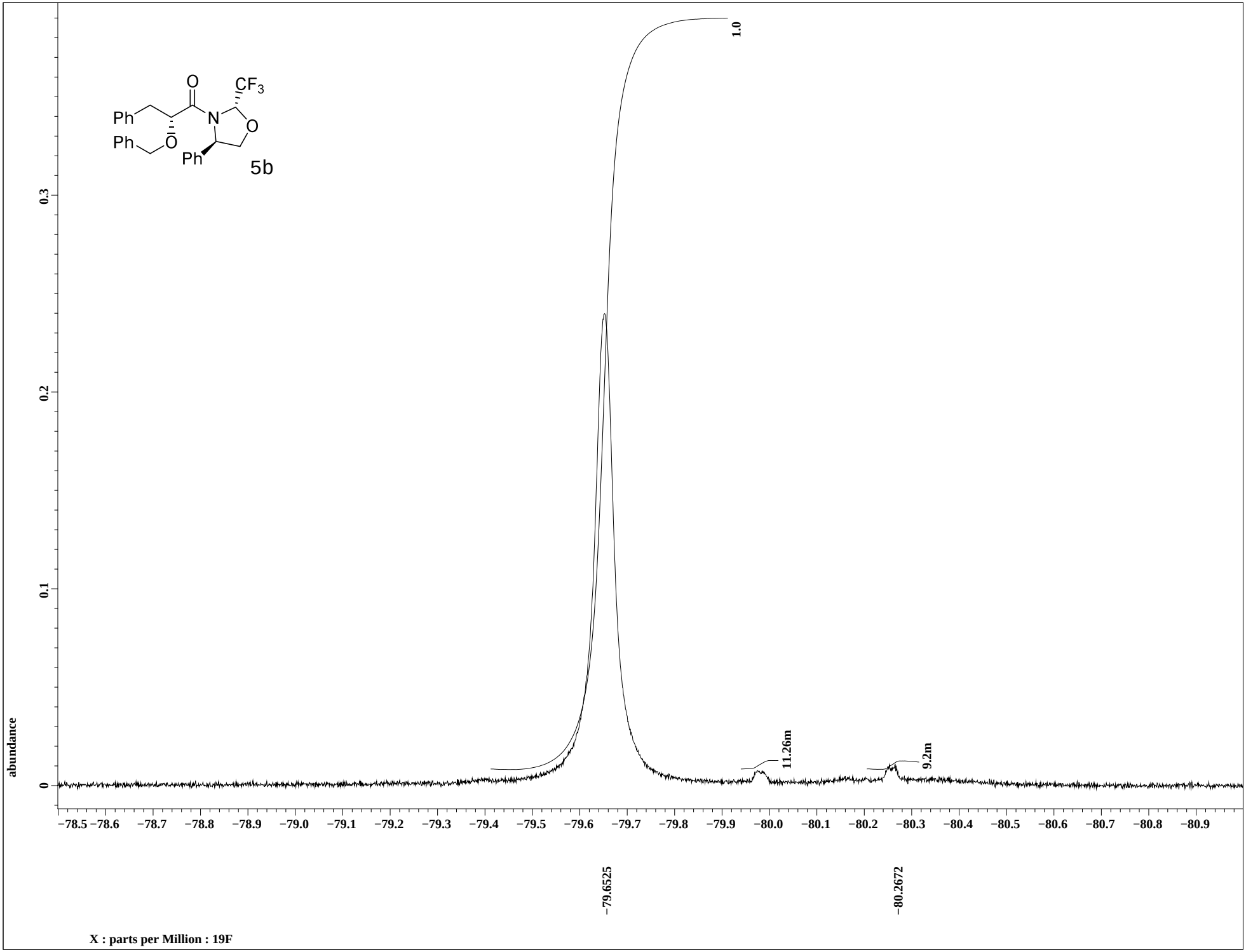
172.3484
141.4277
137.7569
129.4619
128.7277
128.1556
127.9935
125.8959
124.9139
122.0440
85.4693
85.1165
77.4507
77.1265
76.8119
76.5735
72.5976
69.5275
60.1455
15.3139

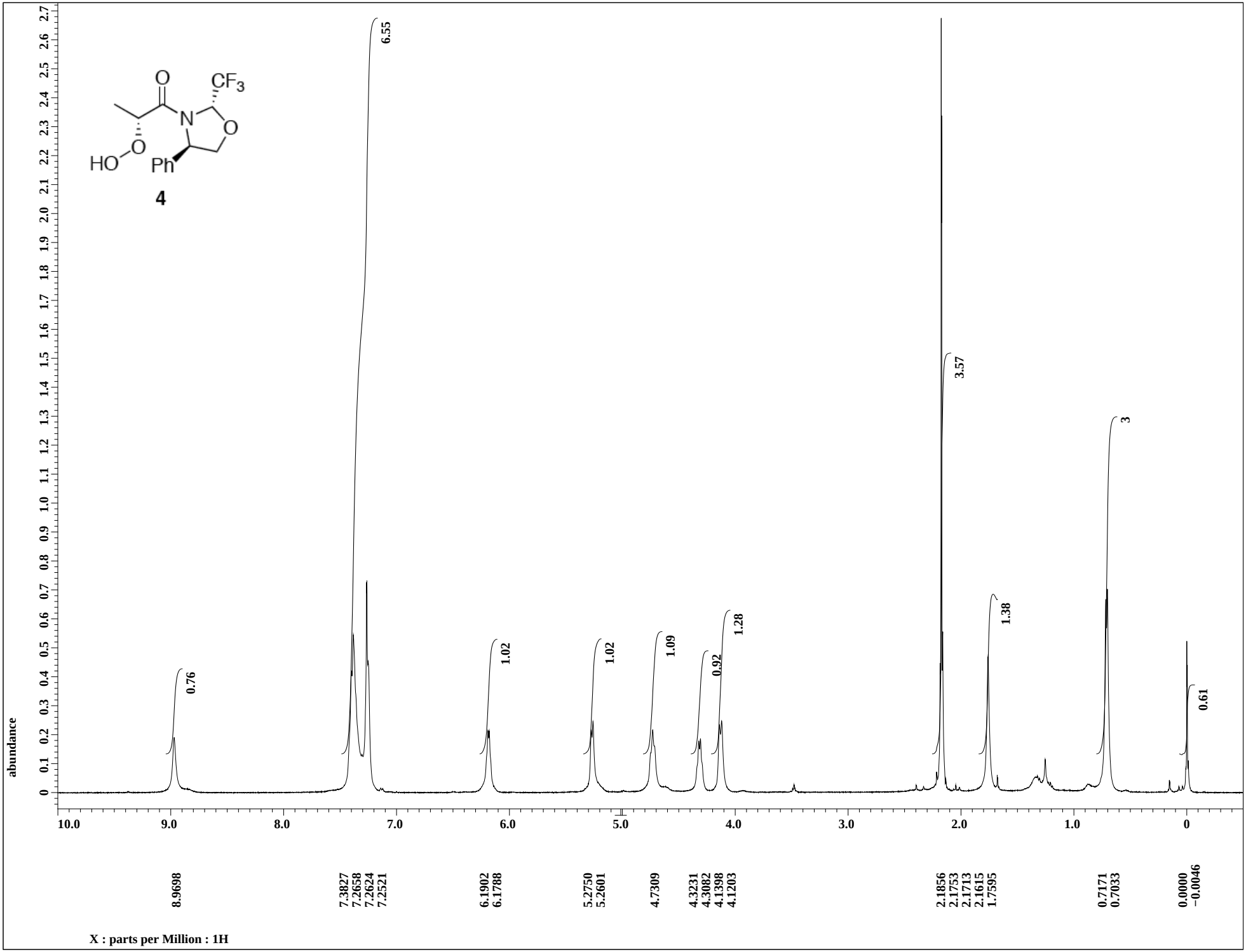
X : parts per Million : 13C

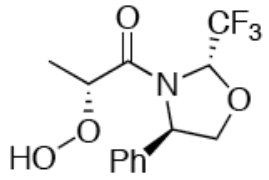

O
CF3
N
O
Ph
O
Ph
5a
0.89
0.11
3.0
2.0
1.0
0
abundance
−78.0
−79.0
−80.0
−81.0
−82.0
−80.2484
−80.2613
−80.7248
X : parts per Million : 19F


O
CF3
Ph
N
O
Ph
O
Ph
5b
abundance
X : parts per Million : 1H
5.5
2.87
0.59
1.62
1.69
1.7
0.75
1.76
1.1
1.04
0.93
0.89
0.11
1
1.0
1.05
91.26m
2.76
7.3495
7.3426
7.3208
7.3140
7.1502
7.1444
6.6645
6.6564
6.1891
6.1776
4.5281
4.4239
4.4078
4.3700
3.9439
3.9233
3.8340
2.8534
2.8443
2.8191
2.1066
2.0710
1.5670
1.4250
−0.0000
−0.0092


O
CF3
Ph
N
O
Ph
O
Ph
5b
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
171.4808
141.6470
137.6425
137.0609
129.6335
128.9470
128.6323
128.1079
126.3440
125.7910
124.8662
85.4407
85.0879
77.4412
77.1170
76.8024
76.5831
76.4687
70.4047
59.9929
36.5474
X : parts per Million : 13C


O
CF3
Ph
N
O
Ph
O
Ph
5b
1.0
0.3
0.2
0.1
0
abundance
11.26m
9.2m
−78.5 −78.6 −78.7 −78.8 −78.9 −79.0 −79.1 −79.2 −79.3 −79.4 −79.5 −79.6 −79.7 −79.8 −79.9 −80.0 −80.1 −80.2 −80.3 −80.4 −80.5 −80.6 −80.7 −80.8 −80.9
−79.6525
−80.2672
X : parts per Million : 19F


O
CF3
N
O
HO
O
Ph
4
abundance
0.76
6.55
1.02
1.02
1.09
0.92
1.28
3.57
1.38
3
0.61
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.9698
7.3827
7.2658
7.2624
7.2521
6.1902
6.1788
5.2750
5.2601
4.7309
4.3231
4.3082
4.1398
4.1203
2.1856
2.1753
2.1713
2.1615
1.7595
0.7171
0.7033
0.0000
−0.0046
X : parts per Million : 1H



4

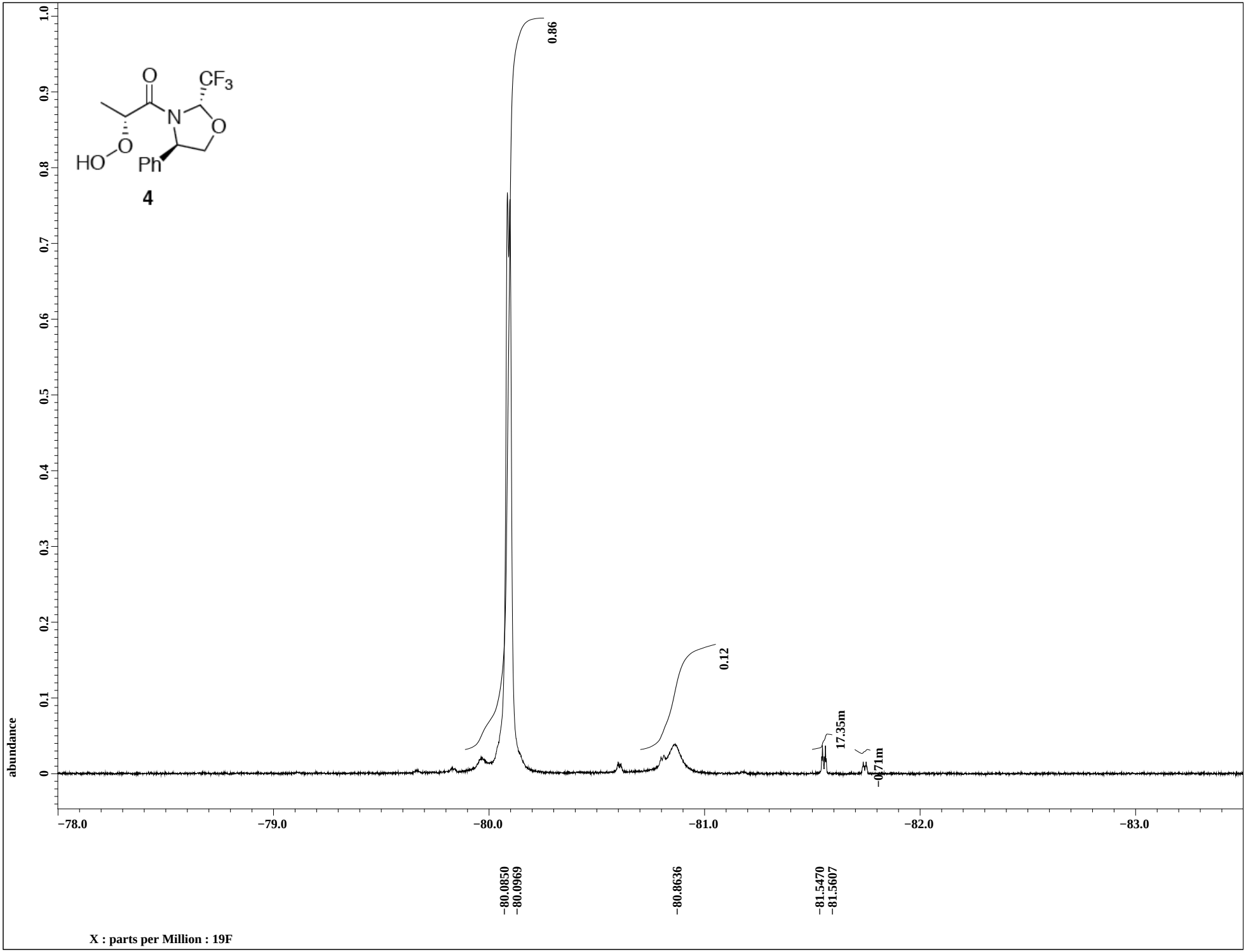
abundance

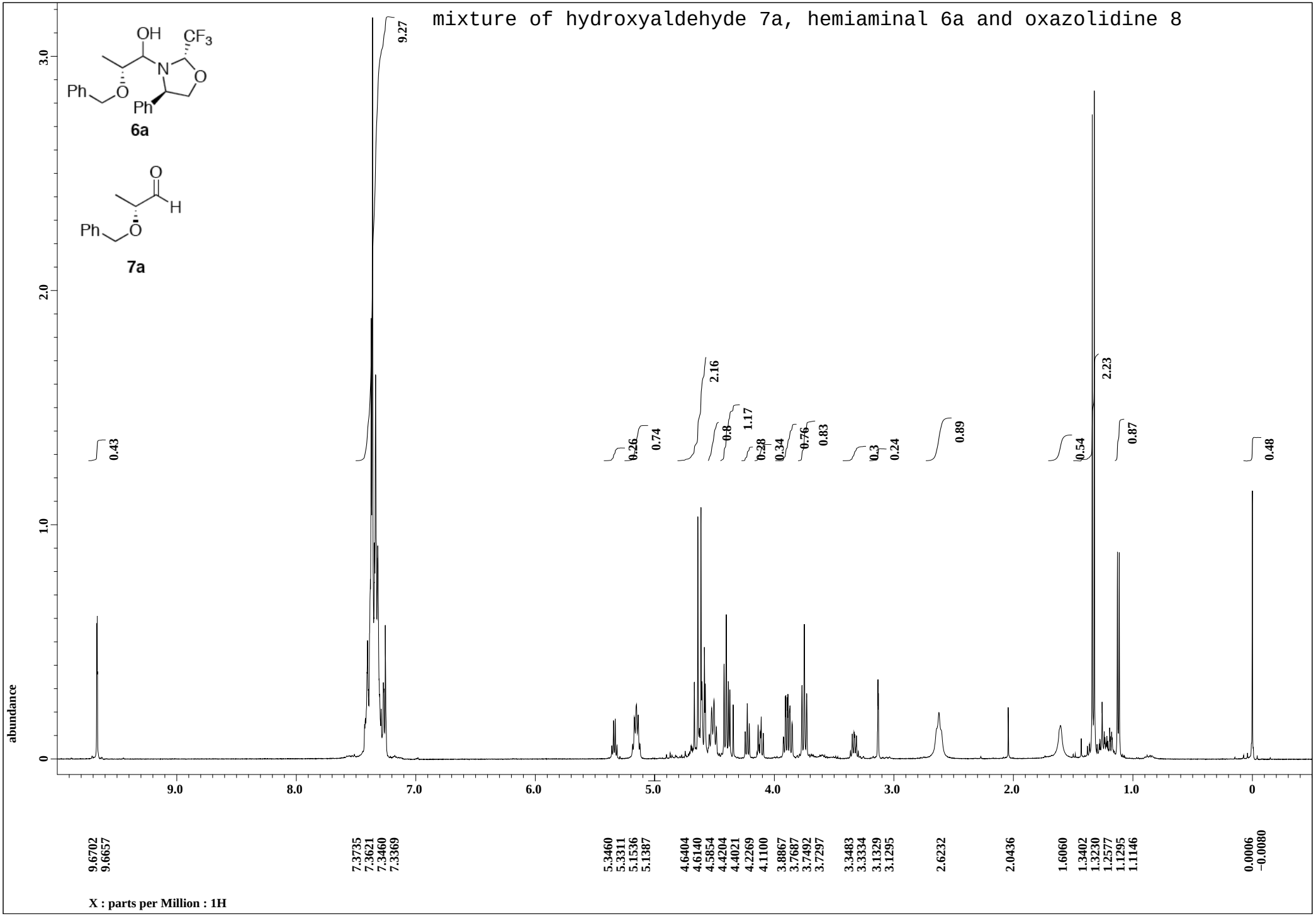
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7

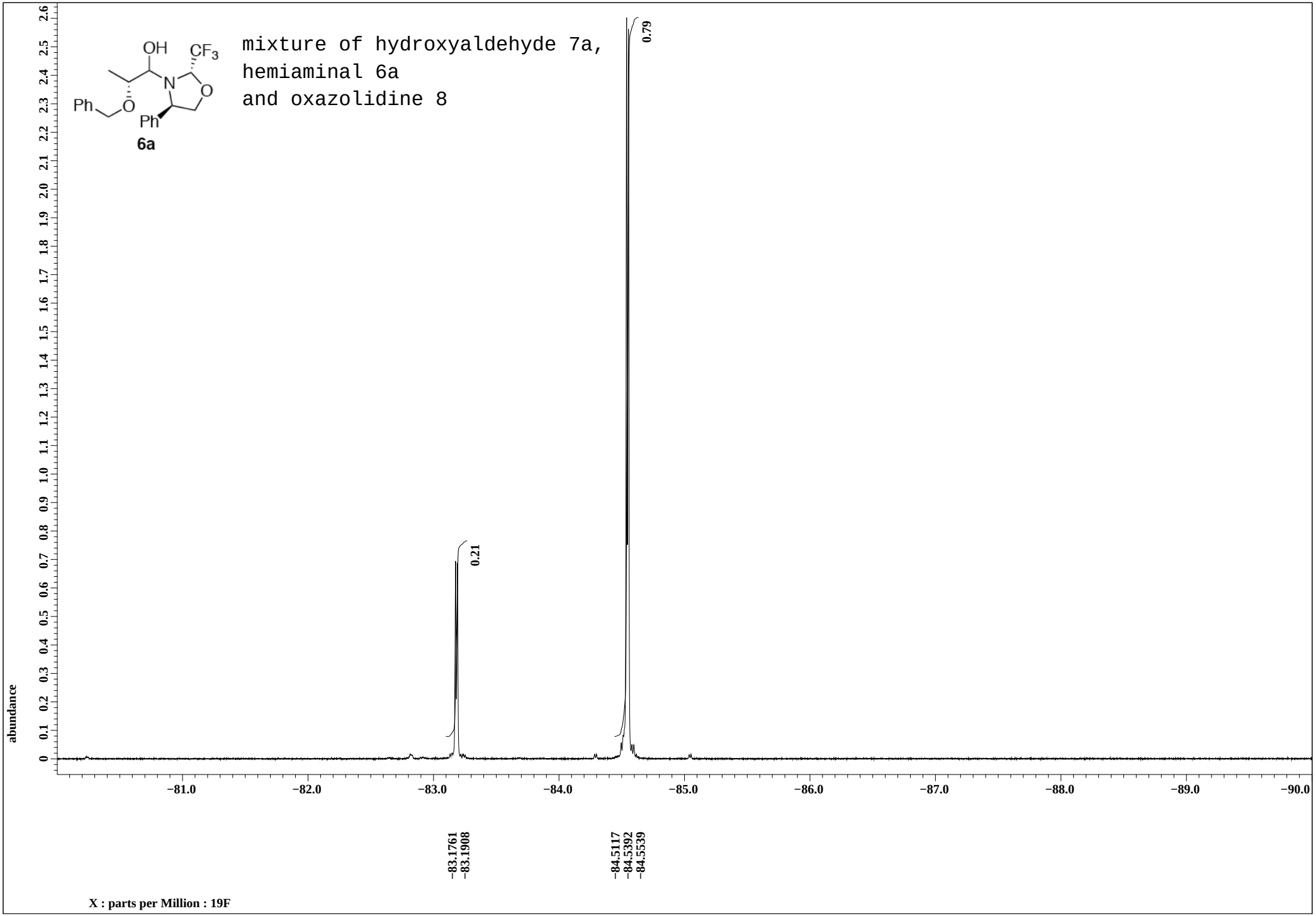
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0

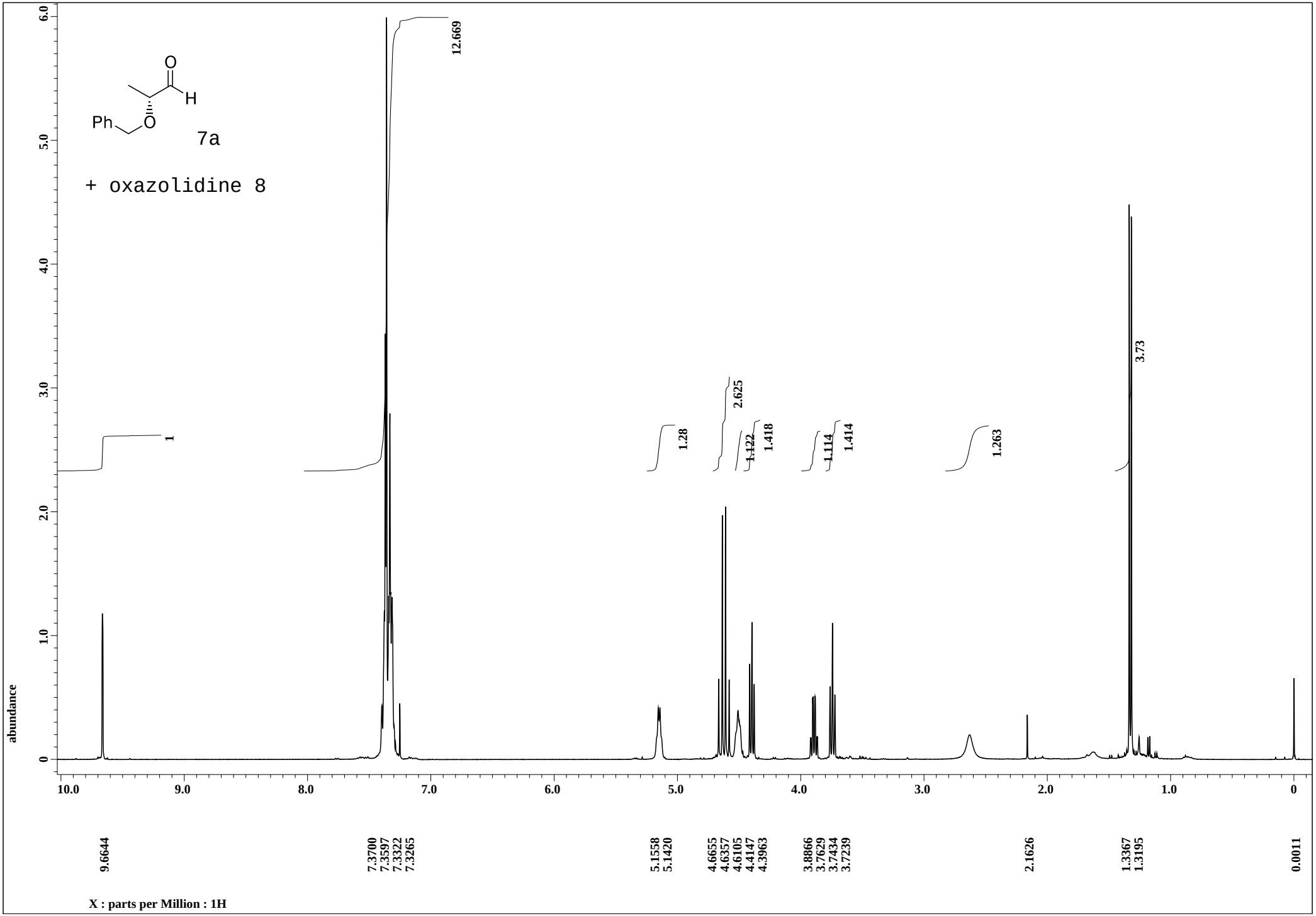
207.3689
171.3949
141.3705
129.6716
129.0328
126.1724
124.7136
121.8342
85.6981
85.3644
79.4148
77.4221
77.1075
76.7928
60.0978
31.0173
13.5595
0.0681

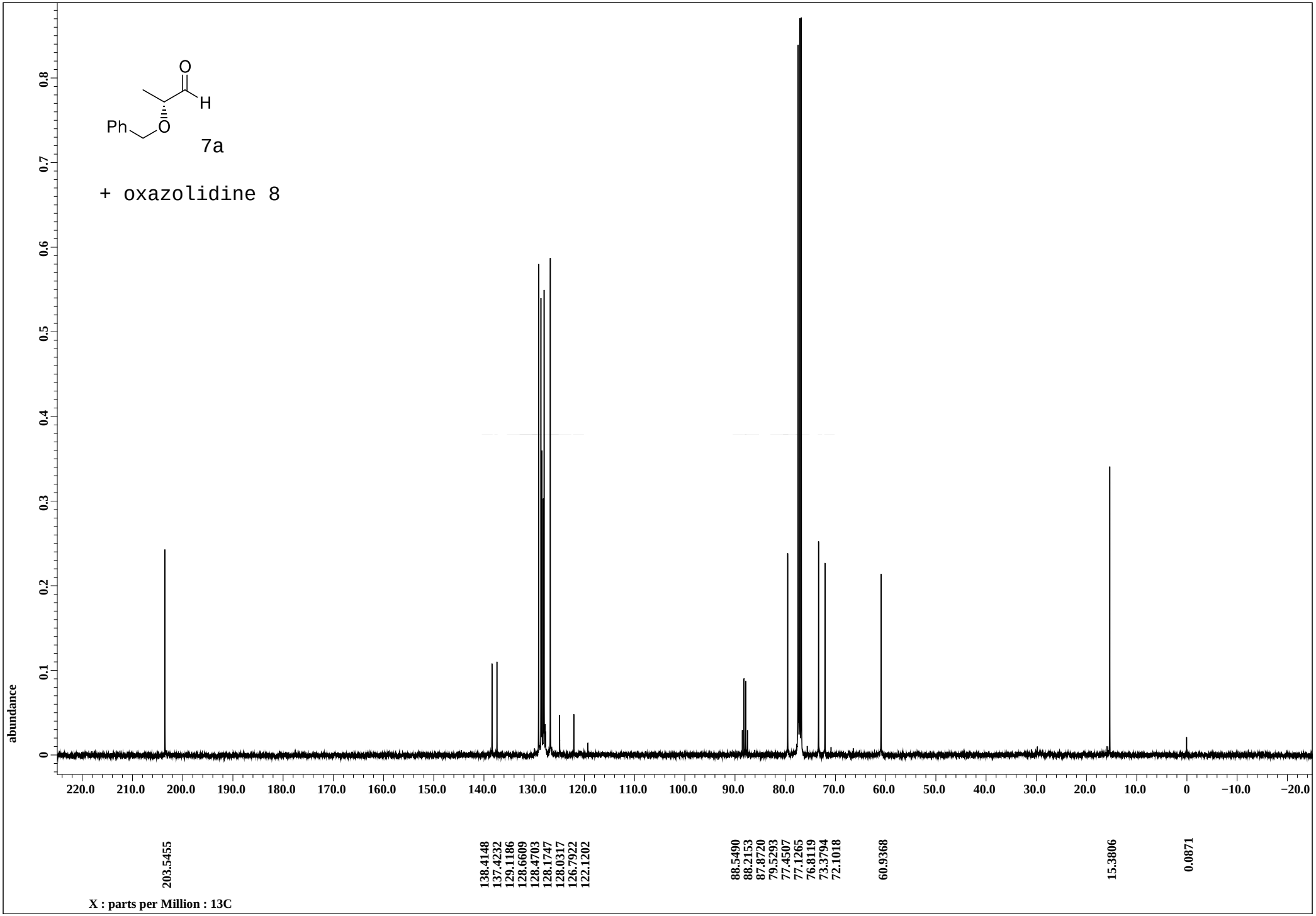
X : parts per Million : 13C

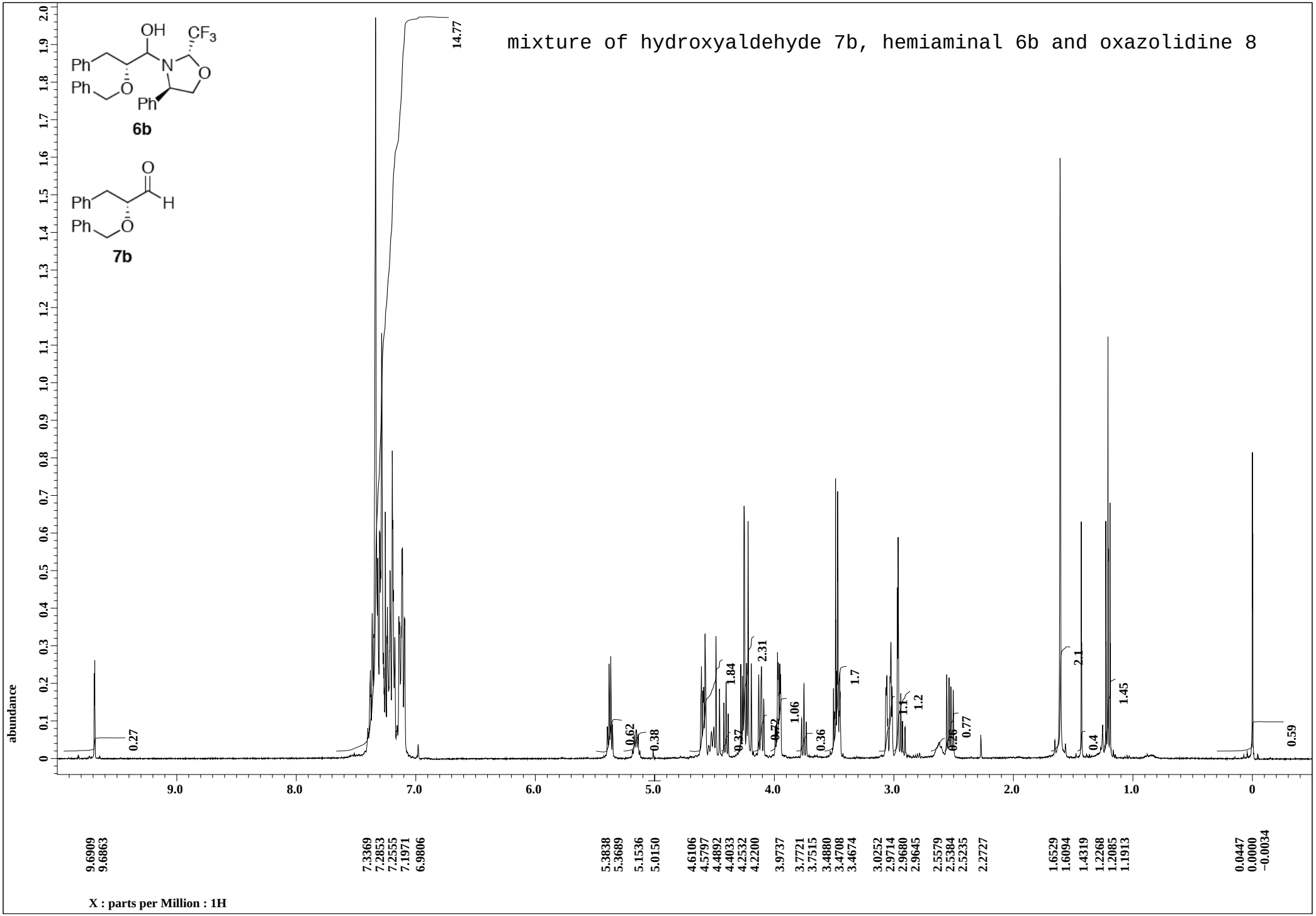

O
CF3
N
O
HO
O
Ph
4
0.86
0.12
17.35m
0.71m
abundance
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
−78.0
−79.0
−80.0
−81.0
−82.0
−83.0
−80.0850
−80.0969
−80.8636
−81.5470
−81.5607
X : parts per Million : 19F


mixture of hydroxyaldehyde 7a, hemiaminal 6a and oxazolidine 8
OH
CF3
N
O
Ph
O
Ph
6a
O
H
Ph
O
7a
abundance
X : parts per Million : 1H

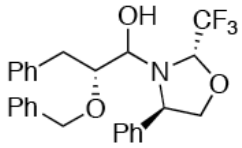

OH
CF3
N
O
Ph
O
Ph
6a
mixture of hydroxyaldehyde 7a,
hemiaminal 6a
and oxazolidine 8
0.79
0.21
abundance
−81.0
−82.0
−83.0
−84.0
−85.0
−86.0
−87.0
−88.0
−89.0
−90.0
−83.1761
−83.1908
−84.5117
−84.5392
−84.5539
X : parts per Million : 19F


O
H
Ph
O
7a
+ oxazolidine 8
12.669
1
1.28
2.625
1.122
1.418
1.114
1.414
1.263
3.73
abundance
6.0
5.0
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.6644
7.3700
7.3597
7.3322
7.3265
5.1558
5.1420
4.6655
4.6357
4.6105
4.4147
4.3963
3.8866
3.7629
3.7434
3.7239
2.1626
1.3367
1.3195
0.0011
X : parts per Million : 1H

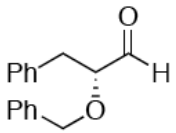

O
H
Ph
O
7a
+ oxazolidine 8
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
203.5455
138.4148
137.4232
129.1186
128.6609
128.4703
128.1747
128.0317
126.7922
122.1202
88.5490
88.2153
87.8720
79.5293
77.4507
77.1265
76.8119
73.3794
72.1018
60.9368
15.3806
0.0871
X : parts per Million : 13C


mixture of hydroxyaldehyde 7b, hemiaminal 6b and oxazolidine 8
OH
CF3
Ph
Ph
O
N
O
Ph
6b
O
H
Ph
Ph
O
7b
abundance
14.77
0.27
0.62
0.38
0.37
1.84
2.31
0.72
1.06
0.36
1.7
1.1
1.2
0.26
0.77
2.1
0.4
1.45
0.59
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.6909
9.6863
7.3369
7.2853
7.2555
7.1971
6.9806
5.3838
5.3689
5.1536
5.0150
4.6106
4.5797
4.4892
4.4033
4.2532
4.2200
3.9737
3.7721
3.7515
3.4880
3.4708
3.4674
3.0252
2.9714
2.9680
2.9645
2.5579
2.5384
2.5235
2.2727
1.6529
1.6094
1.4319
1.2268
1.2085
1.1913
0.0447
0.0000
−0.0034
X : parts per Million : 1H

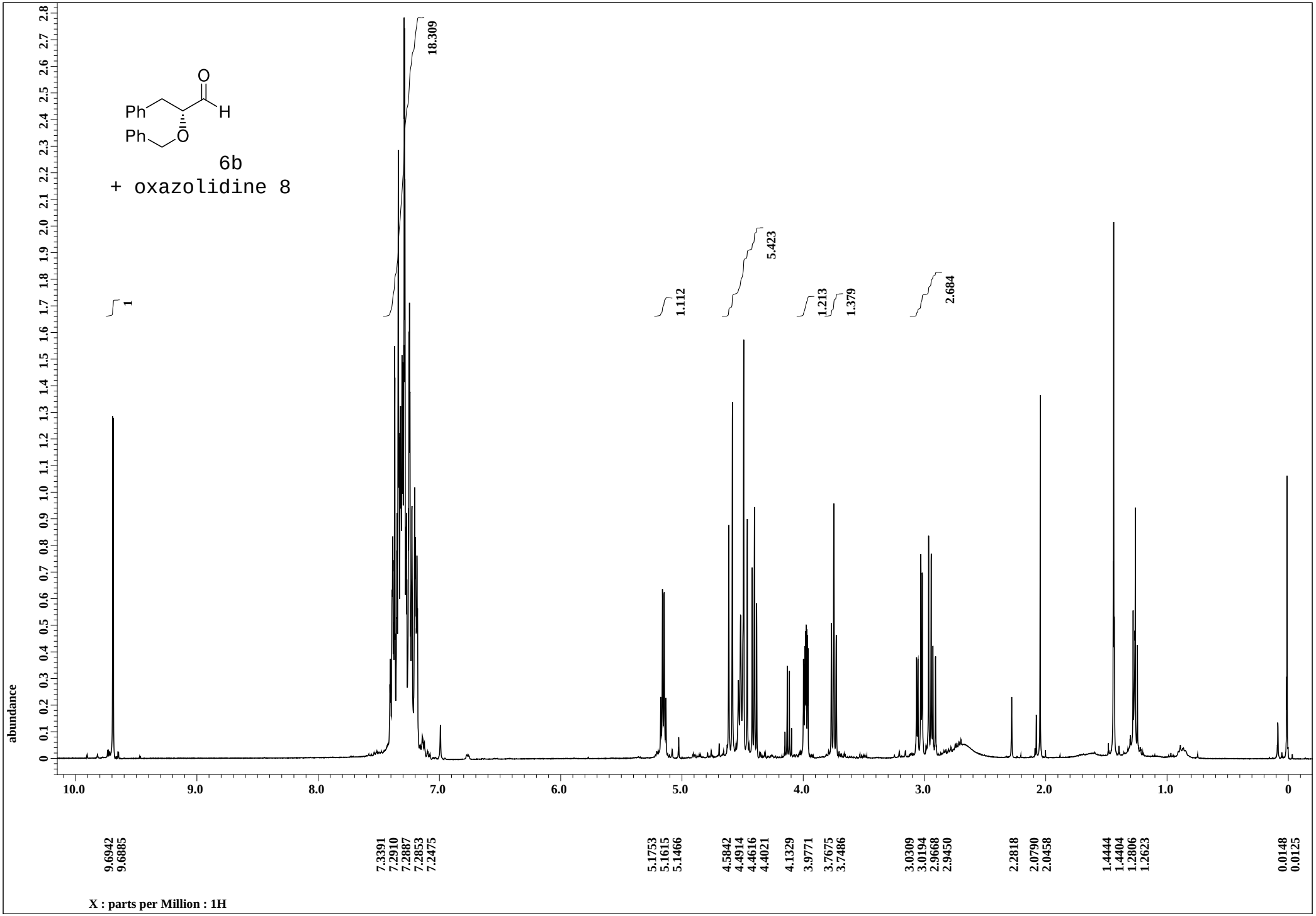
mixture of hydroxyaldehyde 7b, hemiaminal 6b and oxazolidine 8

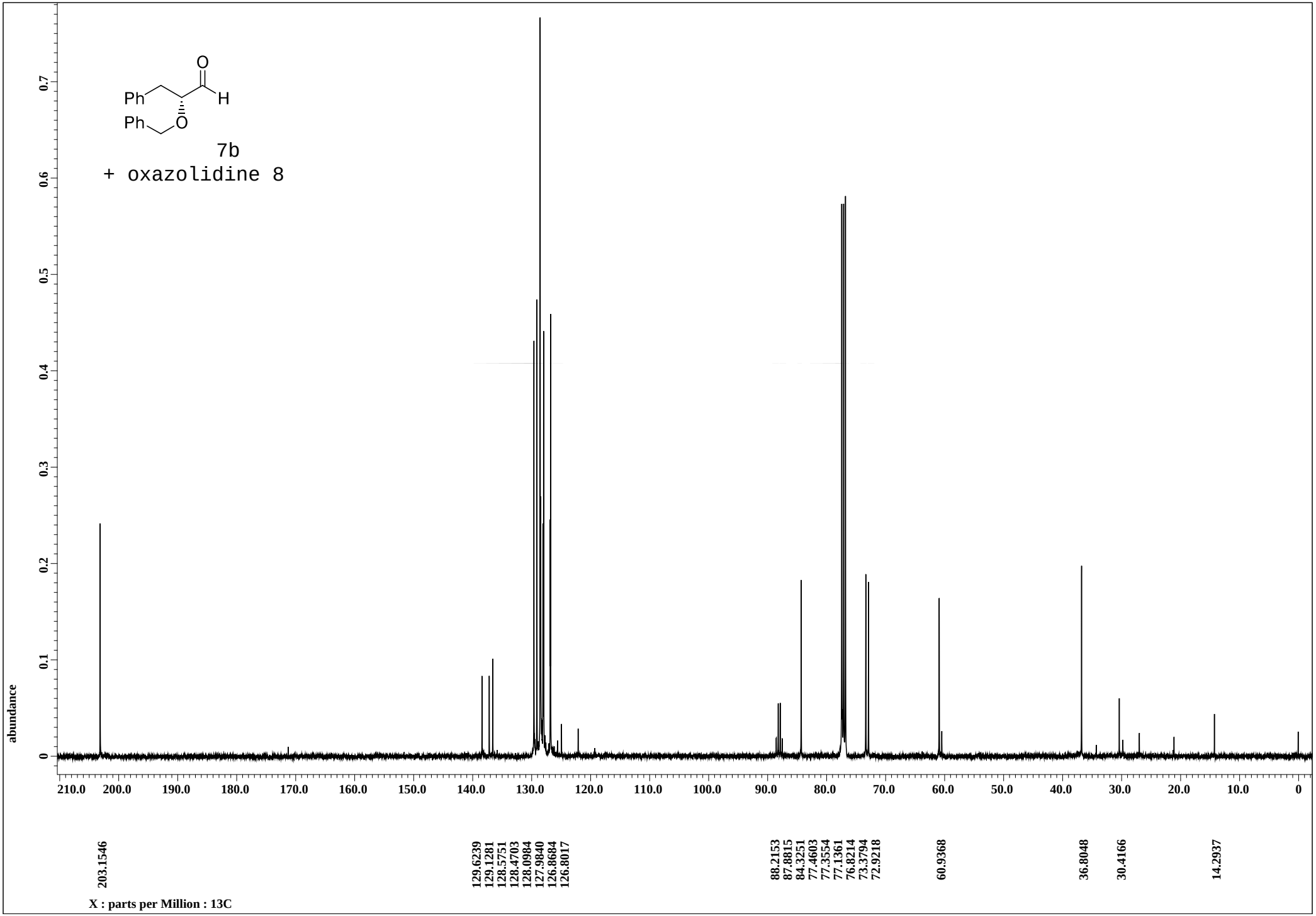


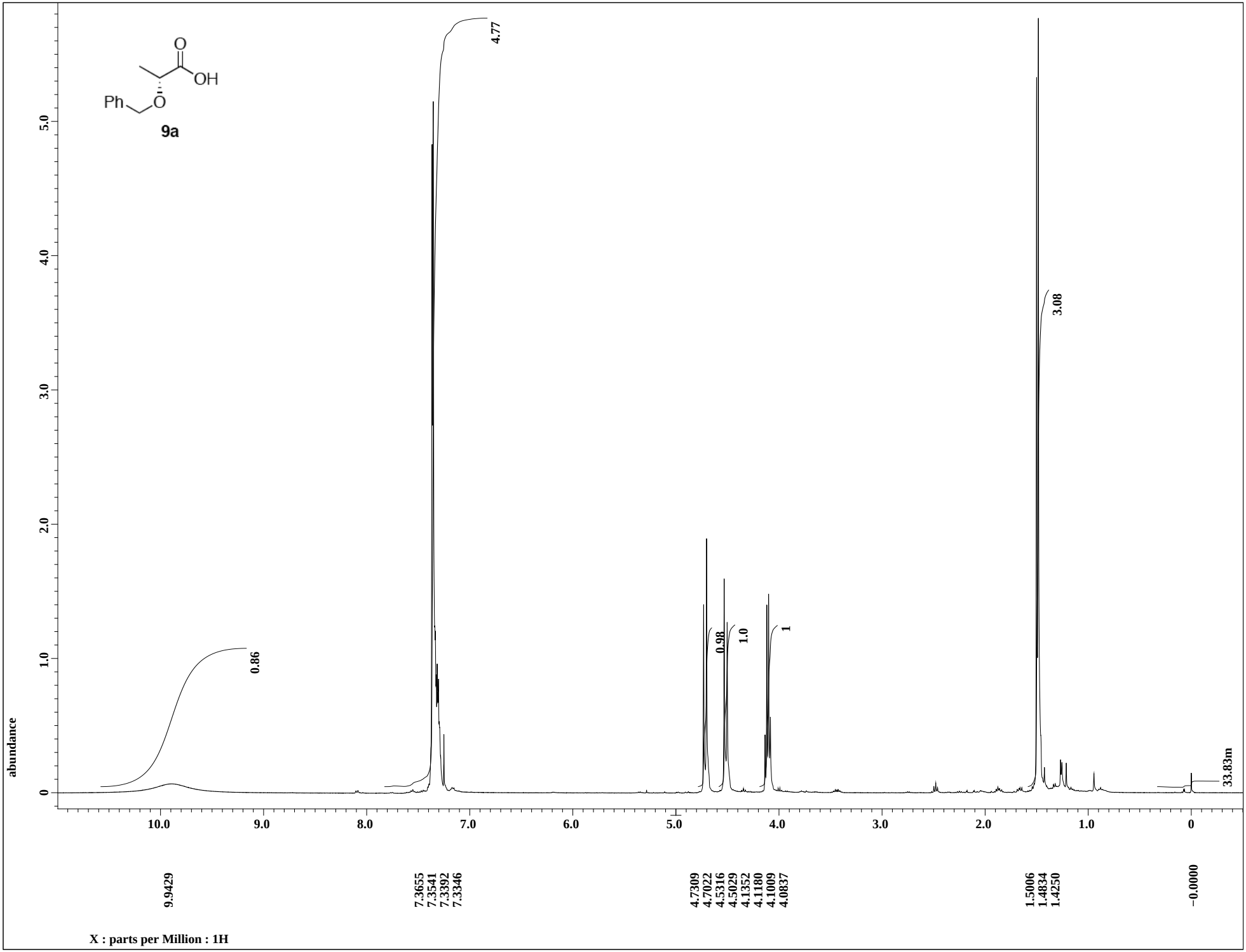
6b

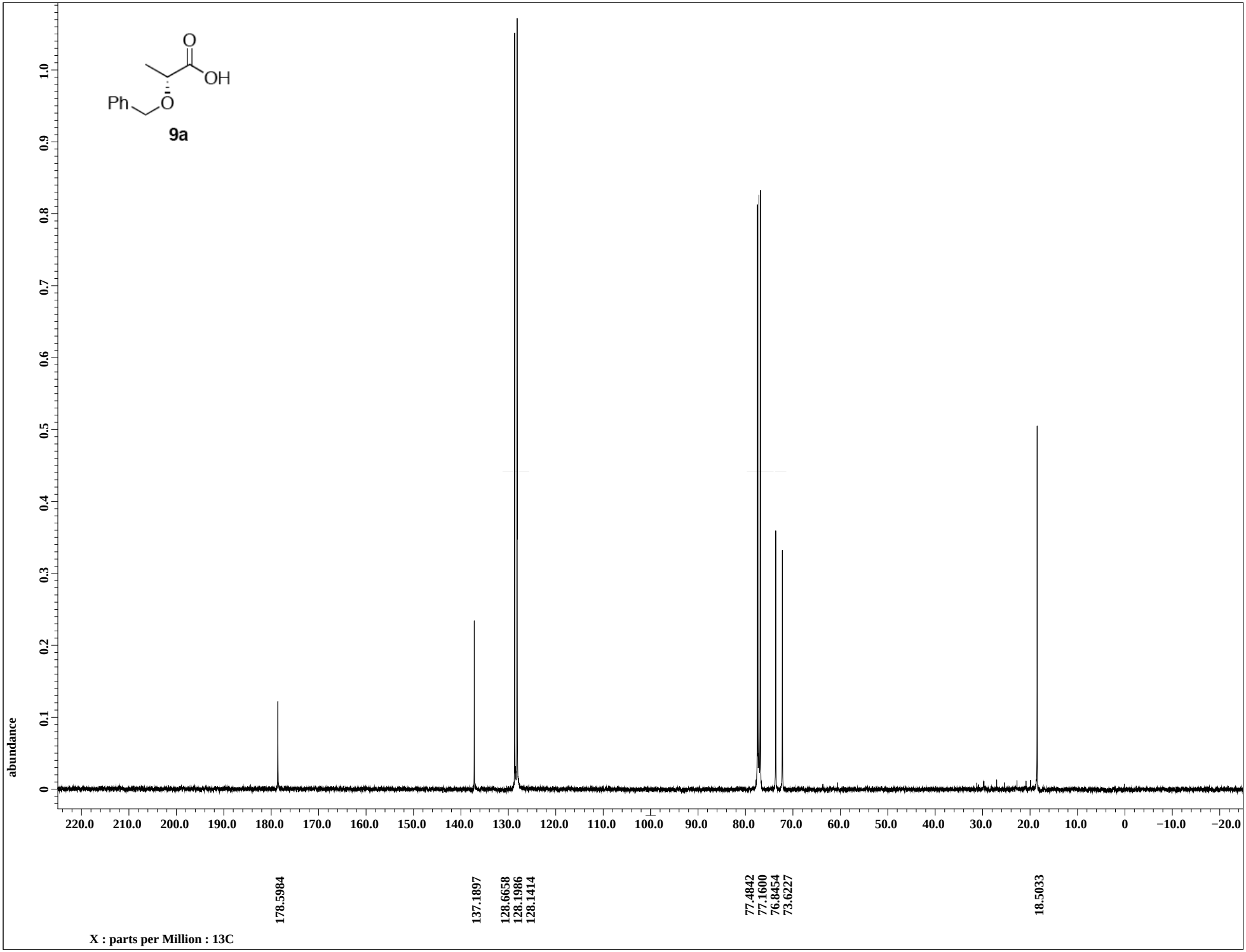


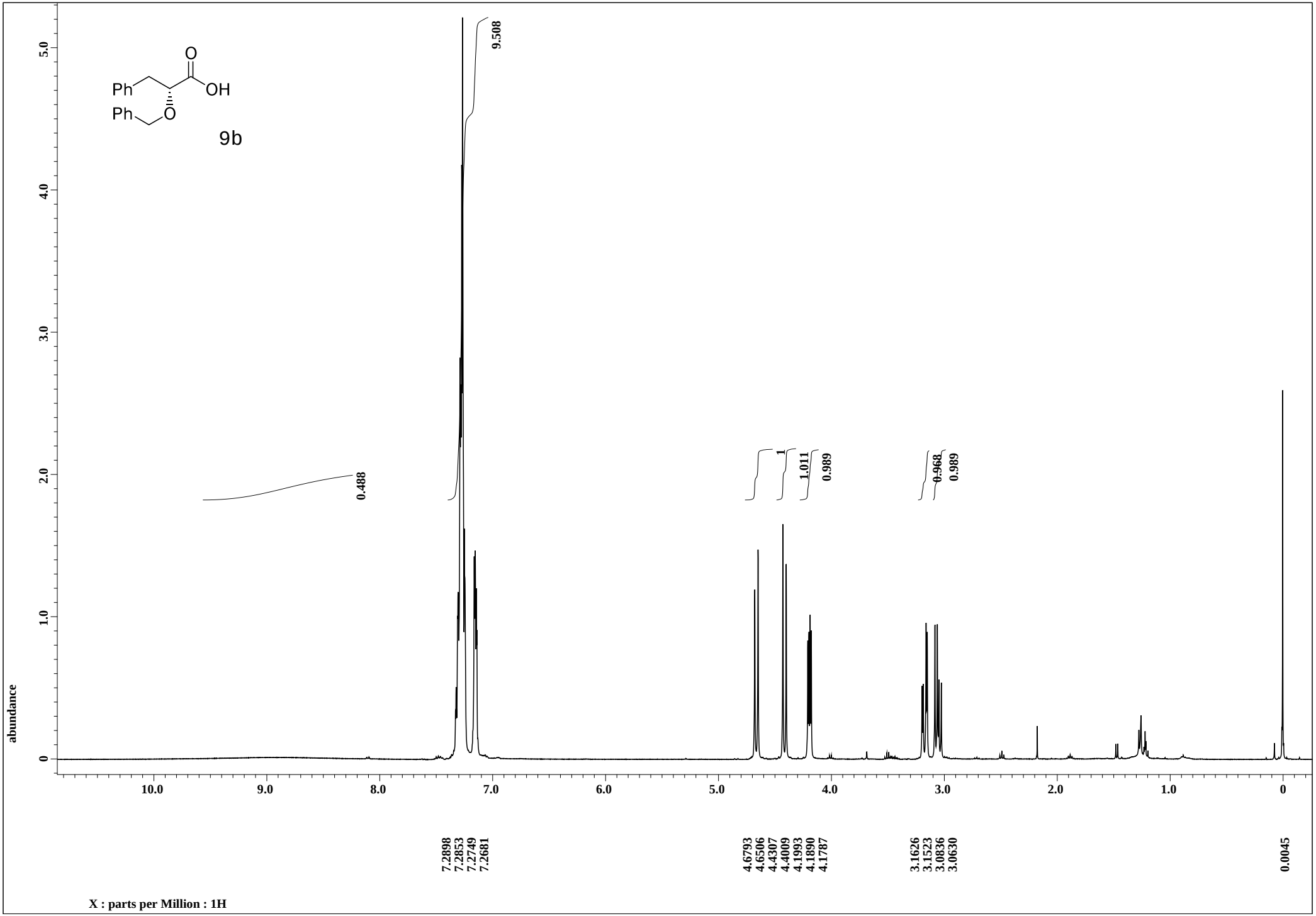
7b

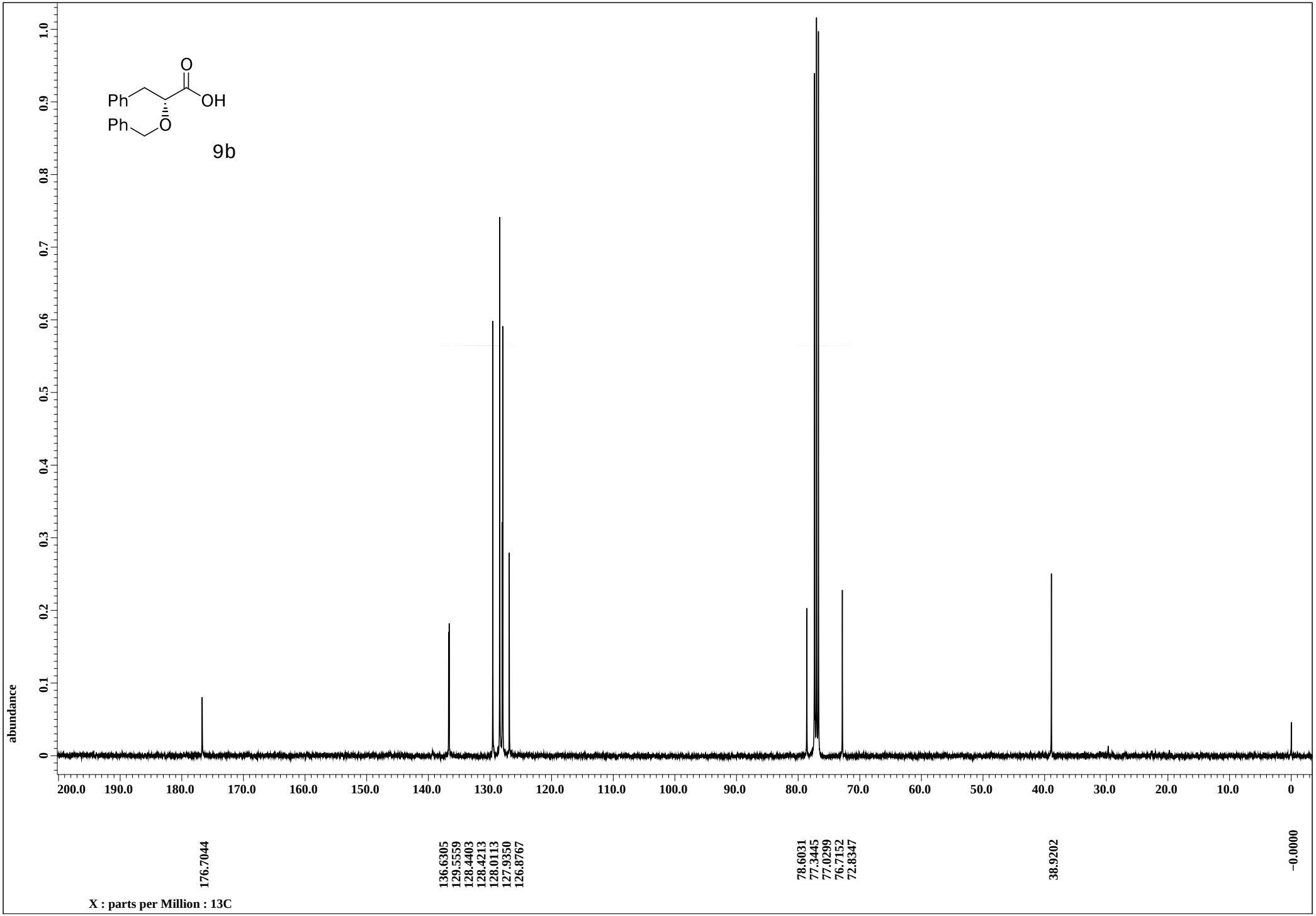

6b
+ oxazolidine 8
Ph
O
H
Ph
O
18.309
1
1.112
5.423
1.213
1.379
2.684
abundance
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9 2.0 2.1 2.2 2.3 2.4 2.5 2.6 2.7 2.8
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
9.6942 9.6885
7.3391 7.2910 7.2887 7.2853 7.2475
5.1753 5.1615 5.1466
4.5842 4.4914 4.4616 4.4021
4.1329
3.9771
3.7675 3.7486
3.0309 3.0194 2.9668 2.9450
2.2818
2.0790 2.0458
1.4444 1.4404 1.2806 1.2623
0.0148 0.0125
X : parts per Million : 1H

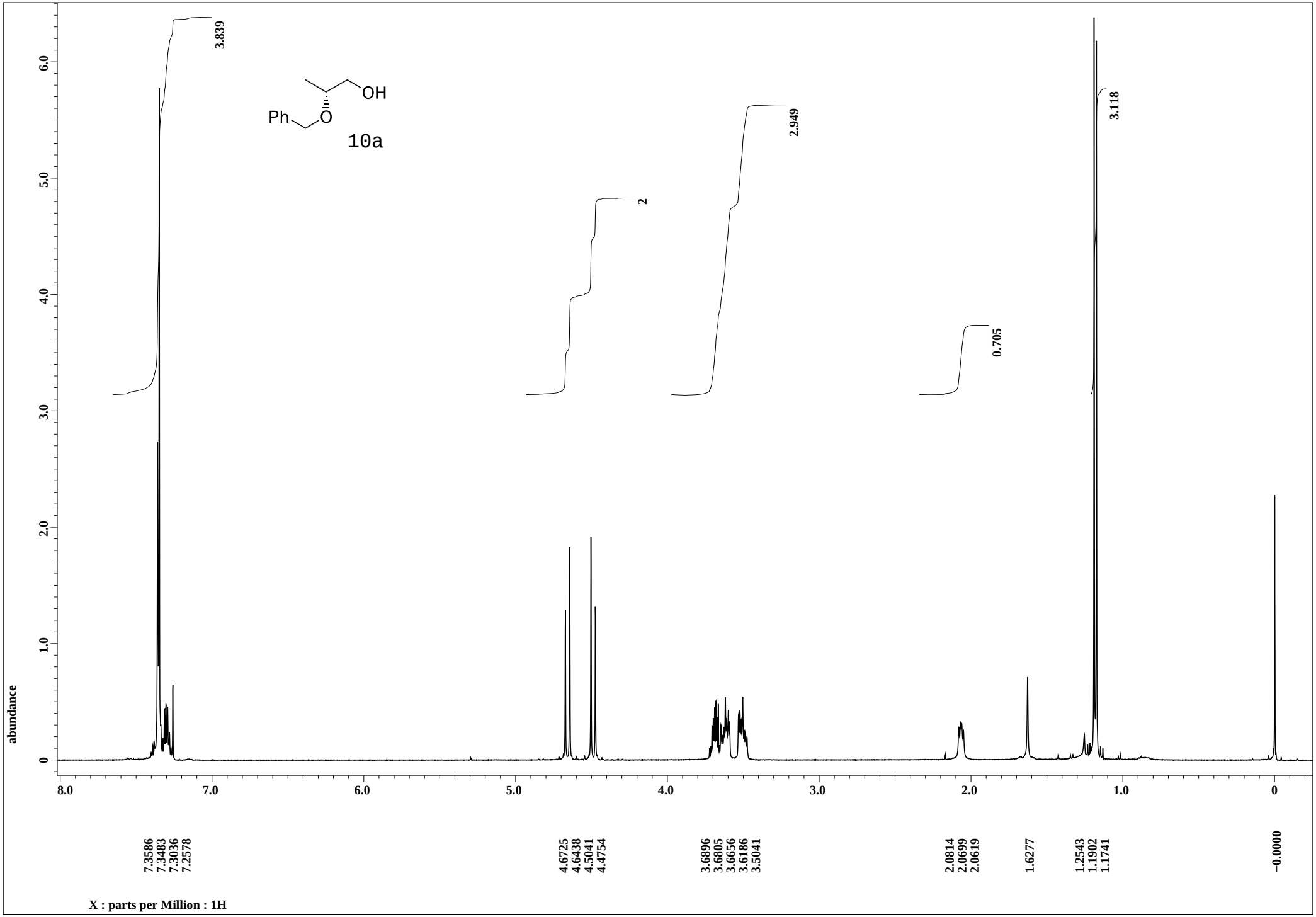

7b
+ oxazolidine 8
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
203.1546
129.6239
129.1281
128.5751
128.4703
128.0984
127.9840
126.8684
126.8017
88.2153
87.8815
84.3251
77.4603
77.3554
77.1361
76.8214
73.3794
72.9218
60.9368
36.8048
30.4166
14.2937
X : parts per Million : 13C

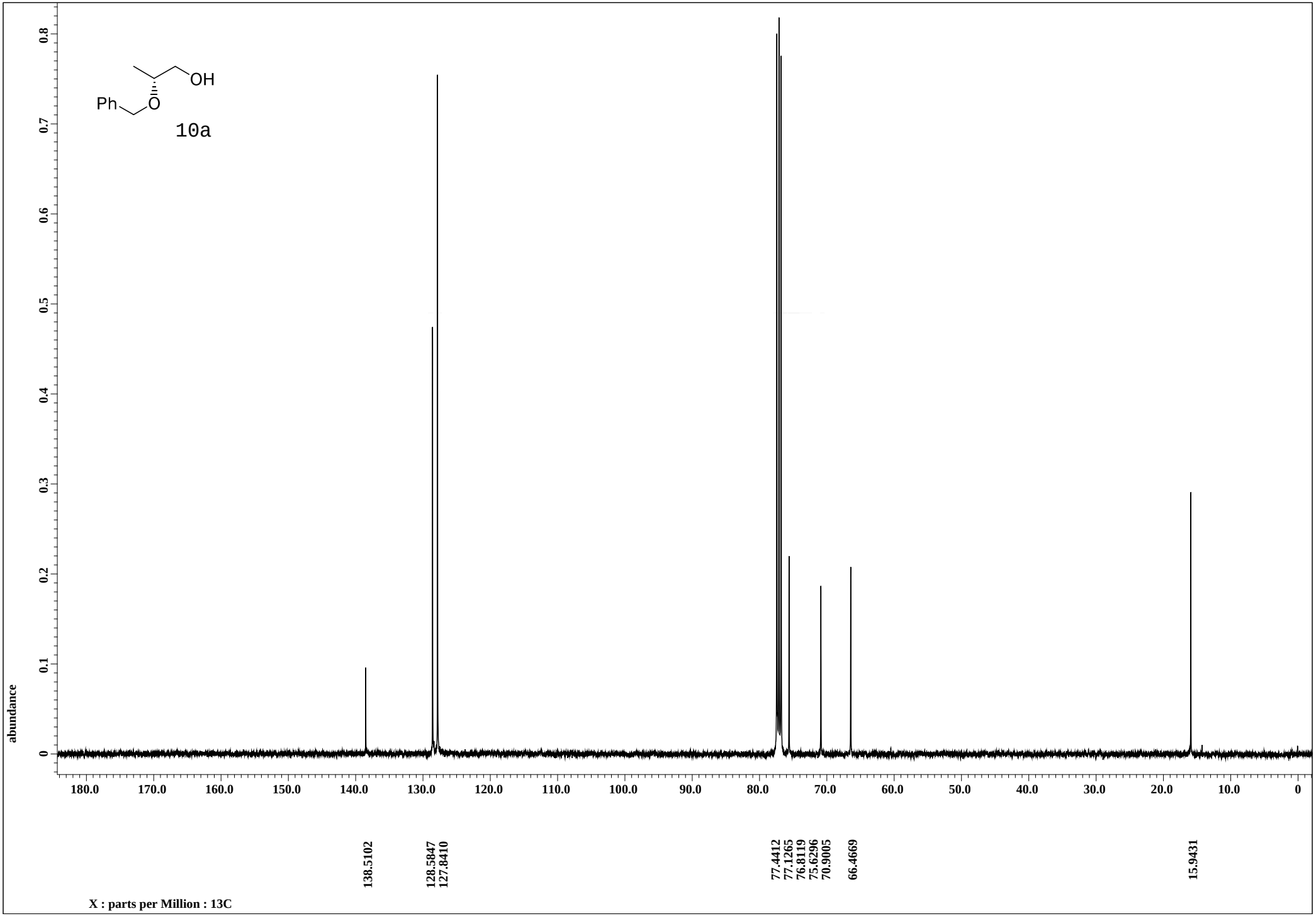

O
OH
Ph
O
9a
4.77
3.08
0.86
0.98
1.0
1
33.83m
abundance
0
1.0
2.0
3.0
4.0
5.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.9429
7.3655
7.3541
7.3392
7.3346
4.7309
4.7022
4.5316
4.5029
4.1352
4.1180
4.1009
4.0837
1.5006
1.4834
1.4250
−0.0000
X : parts per Million : 1H

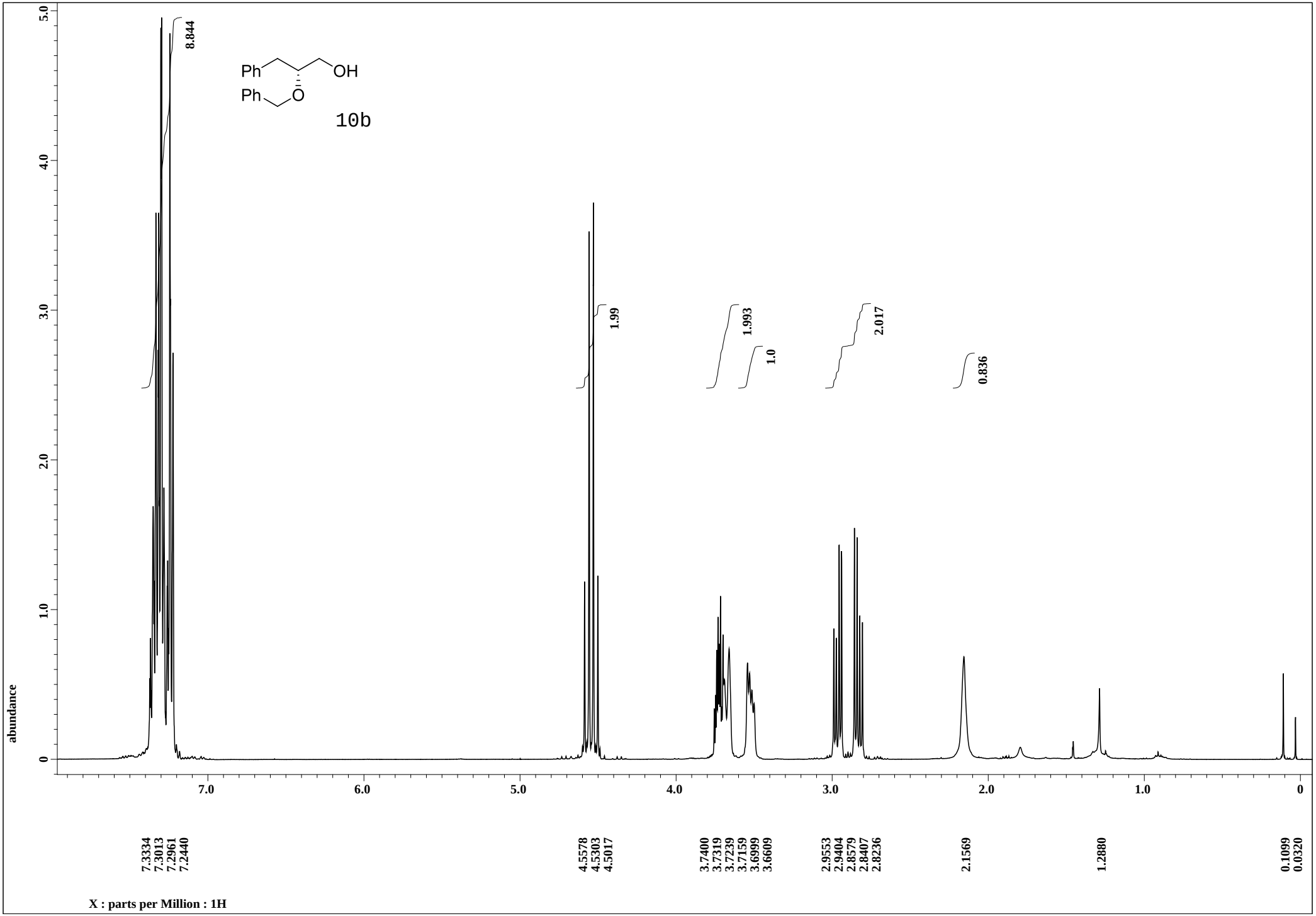

O
OH
Ph
O
9a
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
178.5984
137.1897
128.6658
128.1986
128.1414
77.4842
77.1600
76.8454
73.6227
18.5033
X : parts per Million : 13C

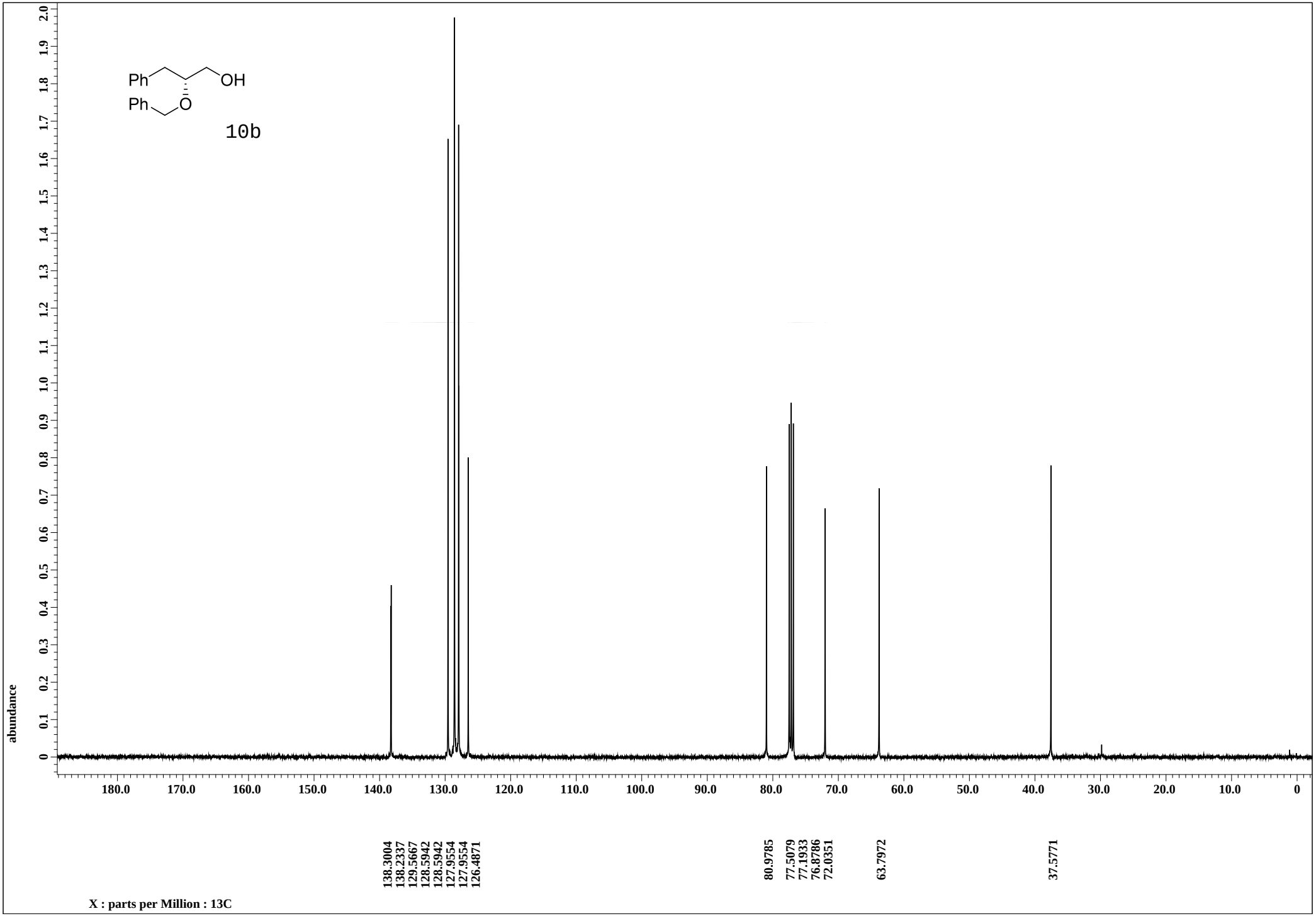

O
Ph
OH
Ph
O
9b
9.508
0.488
1
1.011
0.989
0.968
0.989
abundance
5.0
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.2898
7.2853
7.2749
7.2681
4.6793
4.6506
4.4307
4.4009
4.1993
4.1890
4.1787
3.1626
3.1523
3.0836
3.0630
0.0045
X : parts per Million : 1H

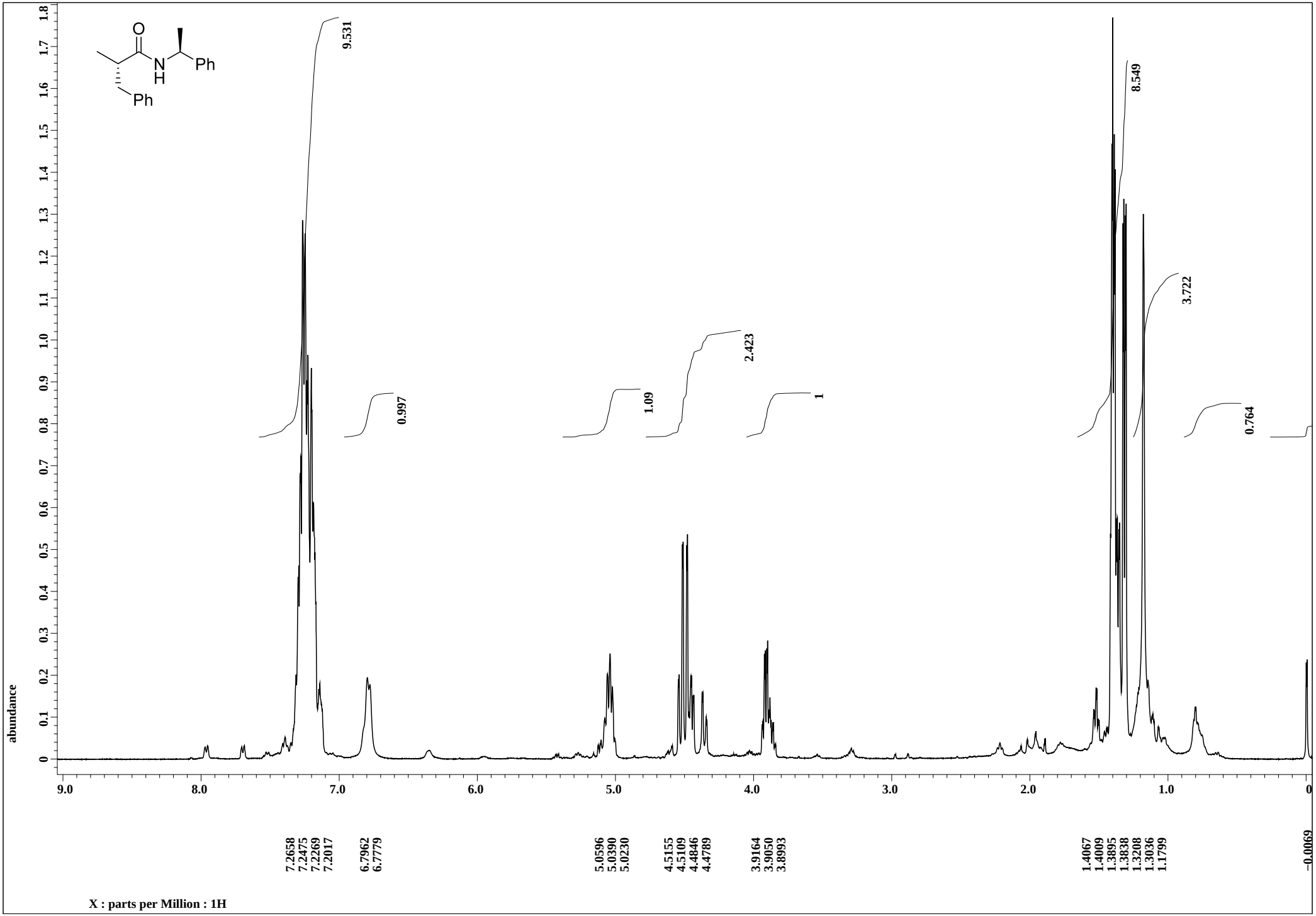

O
Ph
OH
Ph
O
9b
abundance
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
176.7044
136.6305
129.5559
128.4403
128.4213
128.0113
127.9350
126.8767
78.6031
77.3445
77.0299
76.7152
72.8347
38.9202
−0.0000
X : parts per Million : 13C

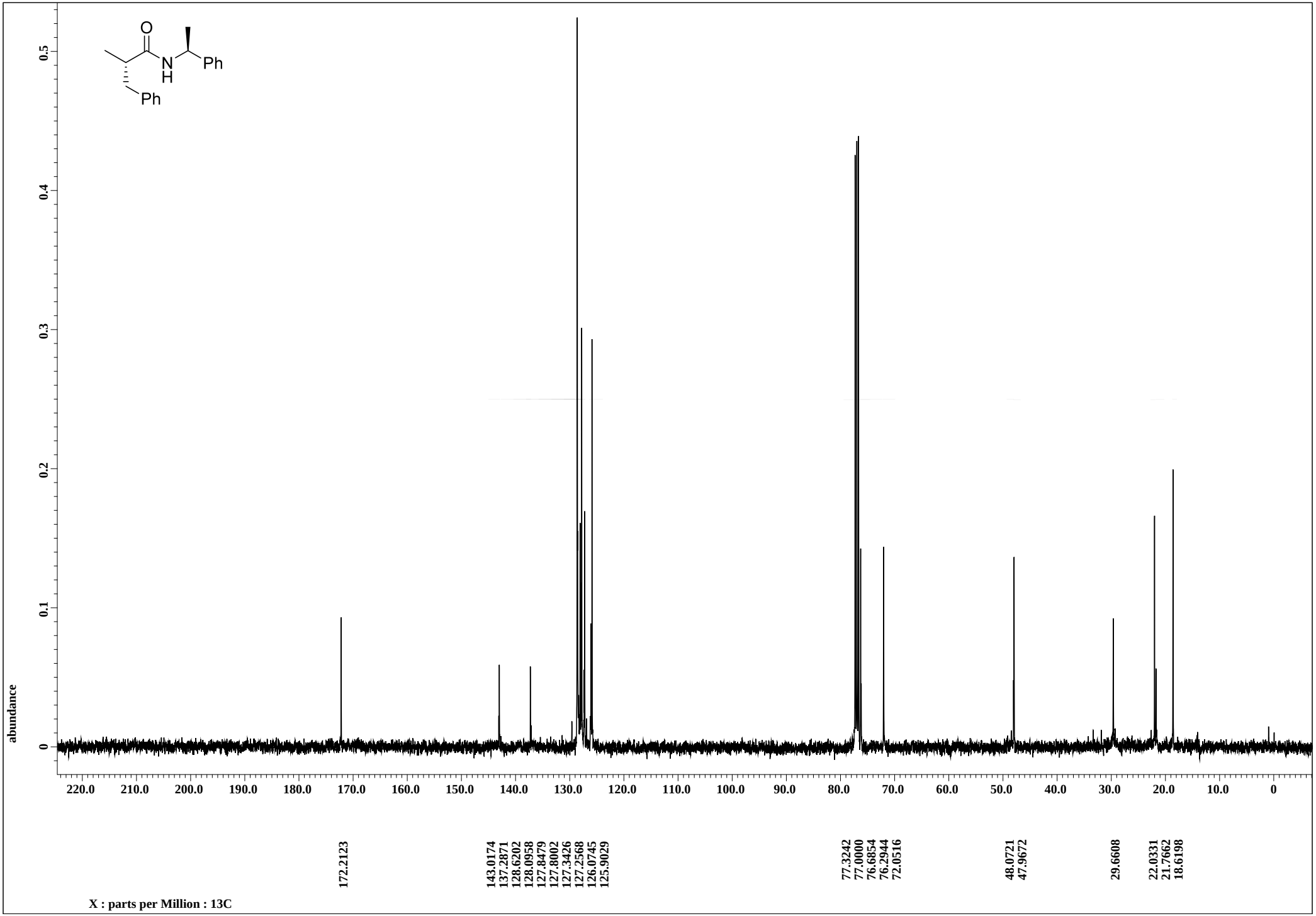

3.839
2
2.949
0.705
3.118
OH
Ph
O
10a
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.3586
7.3483
7.3036
7.2578
4.6725
4.6438
4.5041
4.4754
3.6896
3.6805
3.6656
3.6186
3.5041
2.0814
2.0699
2.0619
1.6277
1.2543
1.1902
1.1741
−0.0000
X : parts per Million : 1H

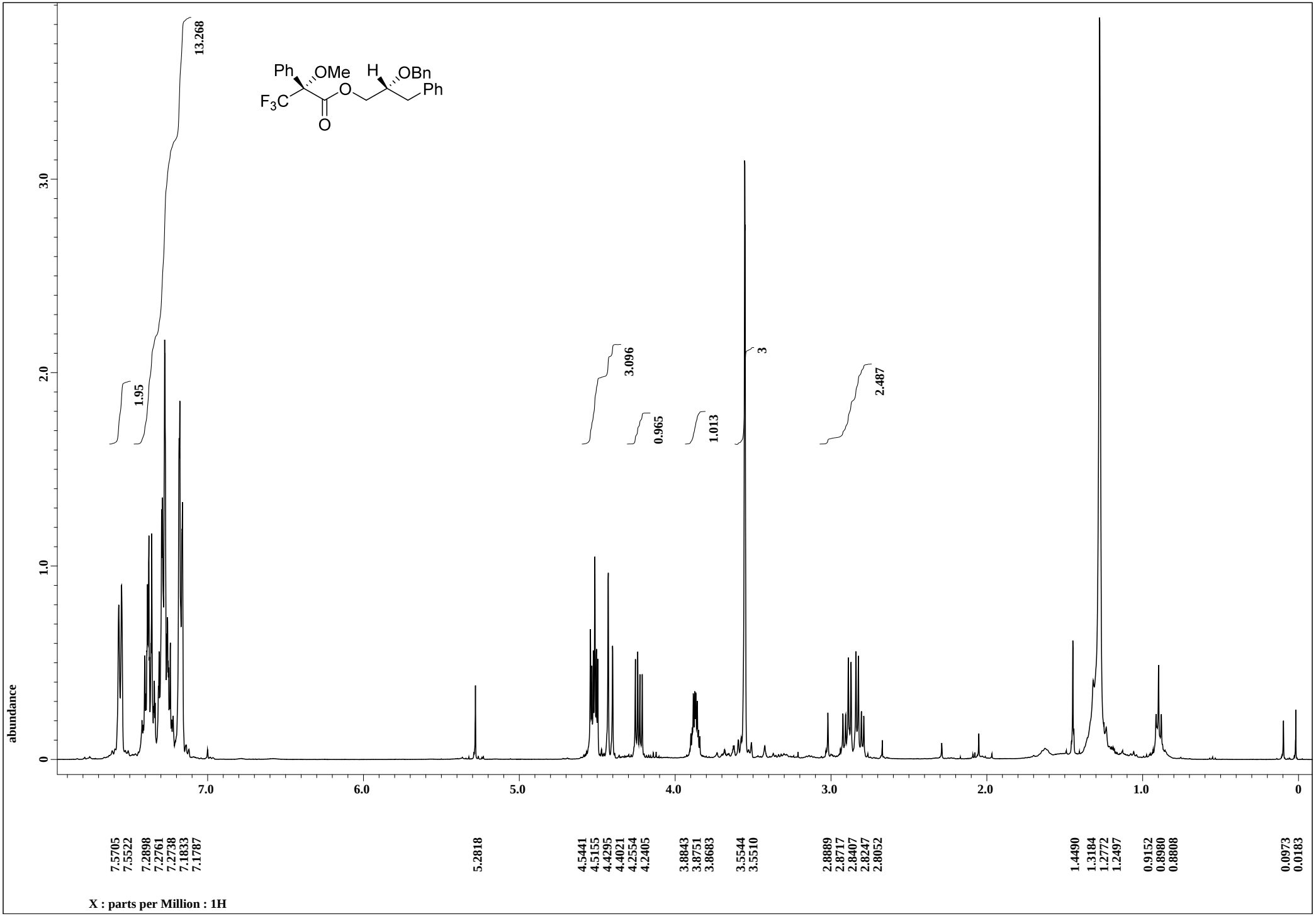

OH
Ph
O
10a
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
138.5102
128.5847
127.8410
77.4412
77.1265
76.8119
75.6296
70.9005
66.4669
15.9431
X : parts per Million : 13C

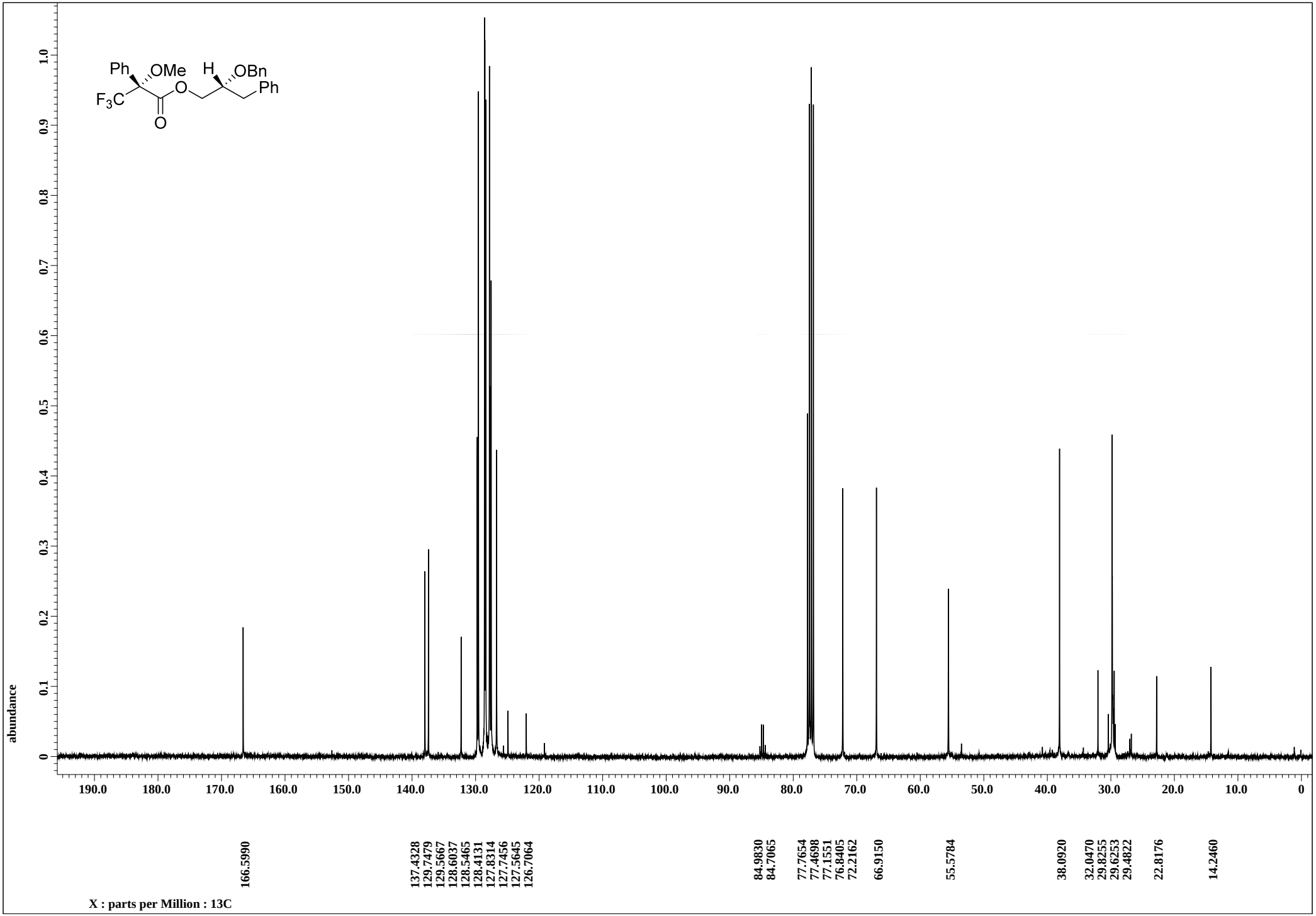

Ph
OH
Ph
O
10b
8.844
1.99
1.993
1.0
2.017
0.836
abundance
X : parts per Million : 1H
7.3334
7.3013
7.2961
7.2440
4.5578
4.5303
4.5017
3.7400
3.7319
3.7239
3.7159
3.6999
3.6609
2.9553
2.9404
2.8579
2.8407
2.8236
2.1569
1.2880
0.1099
0.0320

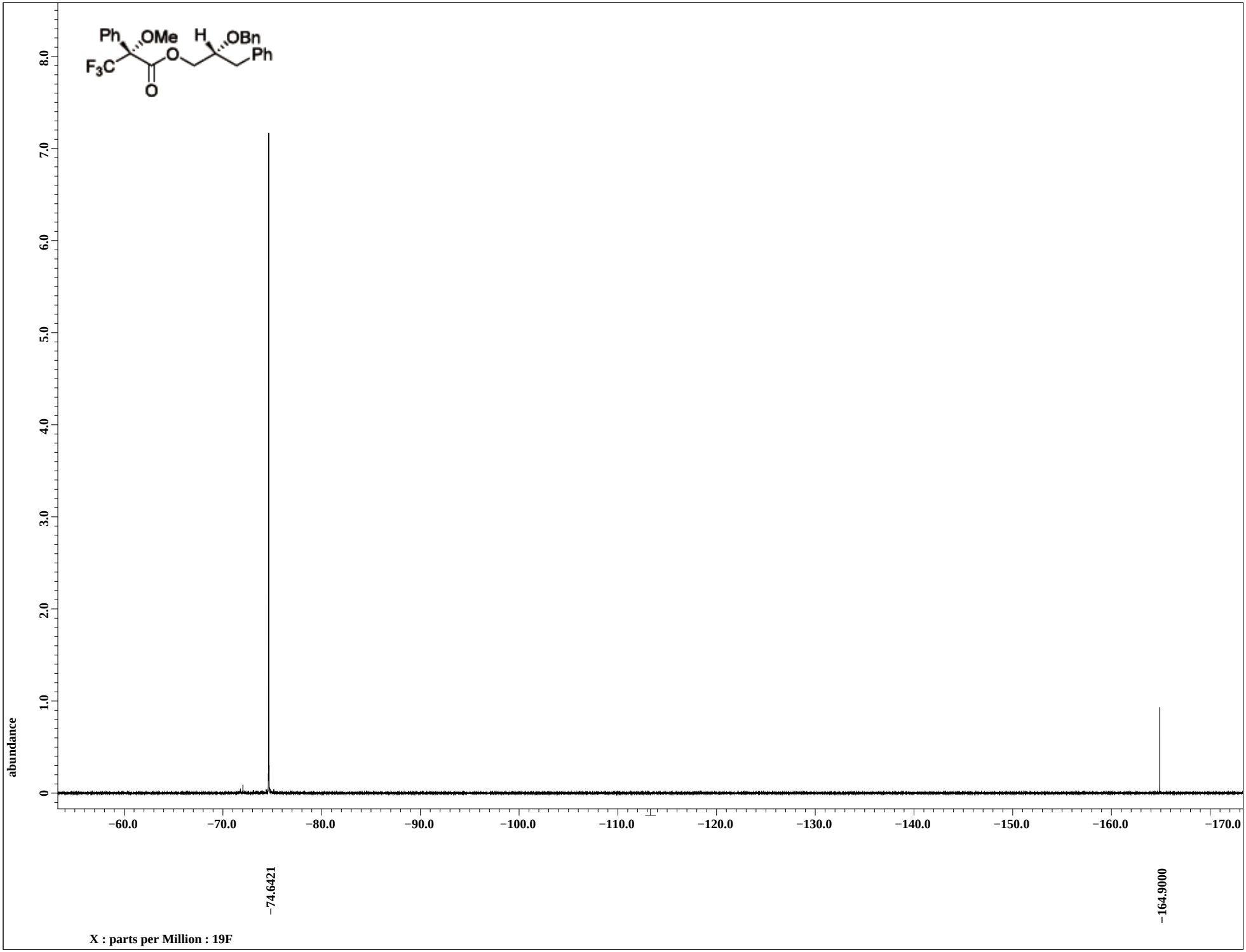

Ph
OH
Ph
O
10b
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
138.3004
138.2337
129.5667
128.5942
128.5942
127.9554
127.9554
126.4871
80.9785
77.5079
77.1933
76.8786
72.0351
63.7972
37.5771
X : parts per Million : 13C

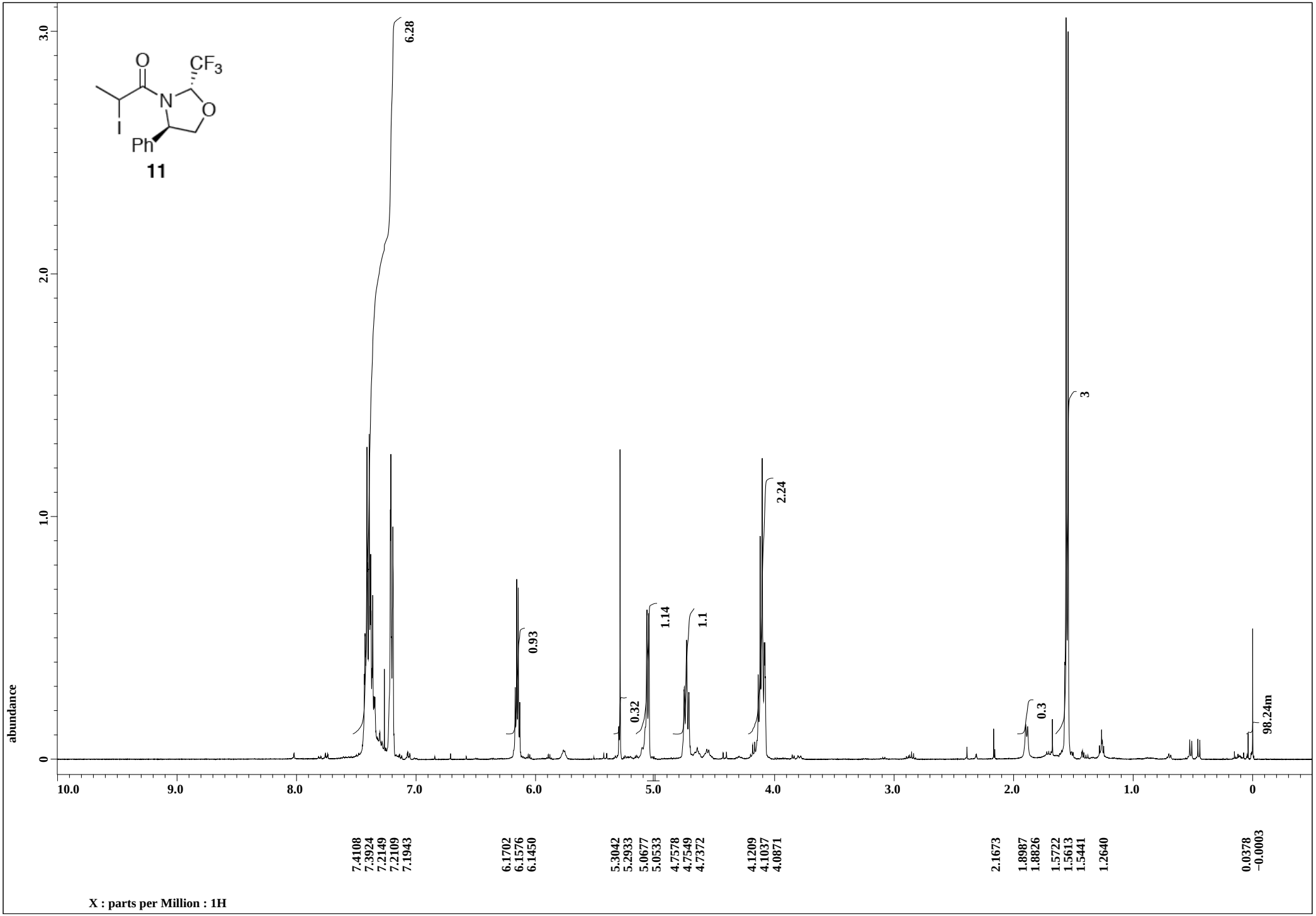

O
N
H
Ph
Ph
9.531
0.997
1.09
2.423
1
8.549
3.722
0.764
abundance
X : parts per Million : 1H
7.2658
7.2475
7.2269
7.2017
6.7962
6.7779
5.0596
5.0390
5.0230
4.5155
4.5109
4.4846
4.4789
3.9164
3.9050
3.8993
1.4067
1.4009
1.3895
1.3838
1.3208
1.3036
1.1799
−0.0069

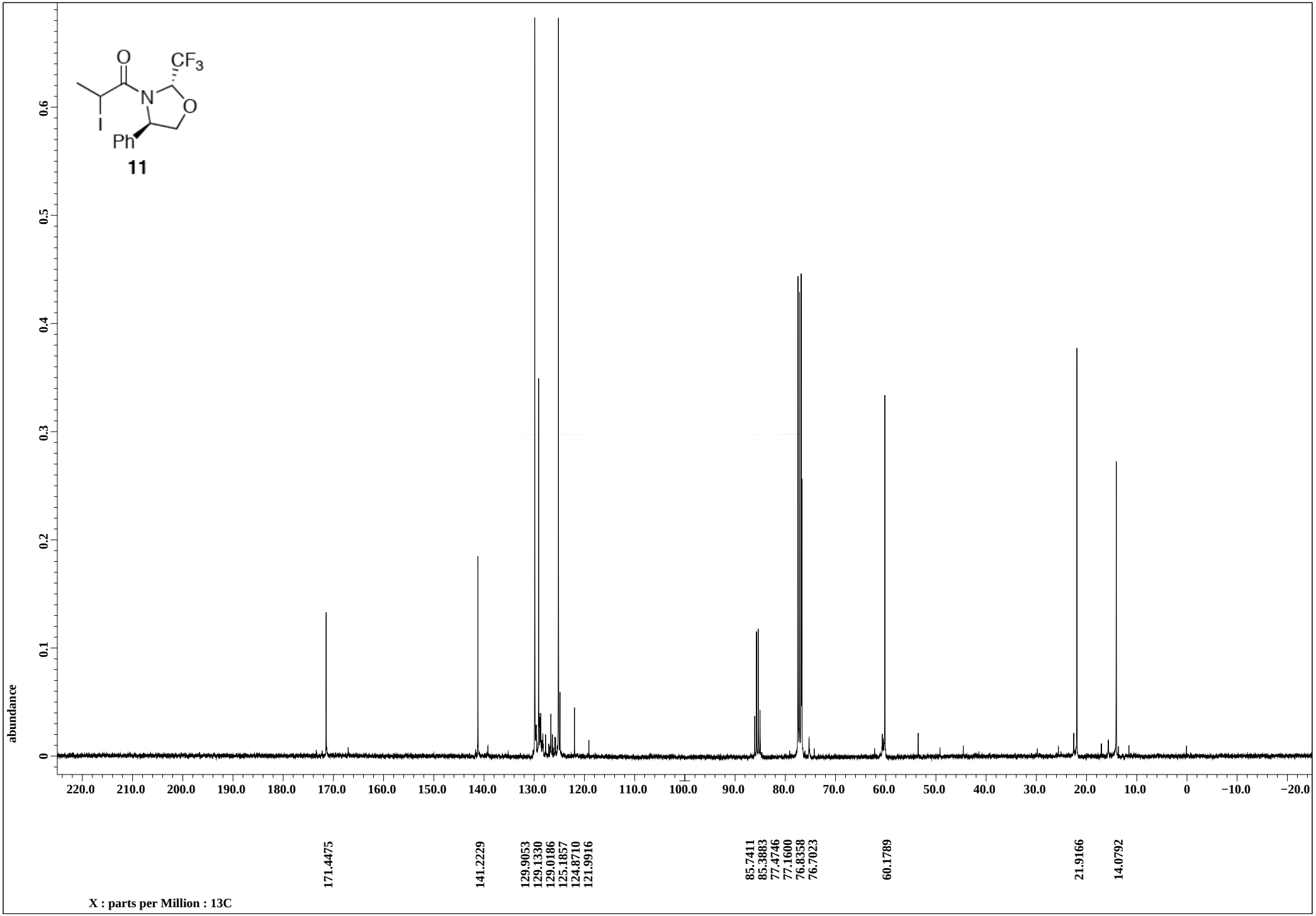

O
N
H
Ph
Ph
abundance
0
0.1
0.2
0.3
0.4
0.5
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
172.2123
143.0174
137.2871
128.6202
128.0958
127.8479
127.8002
127.3426
127.2568
126.0745
125.9029
77.3242
77.0000
76.6854
76.2944
72.0516
48.0721
47.9672
29.6608
22.0331
21.7662
18.6198
X : parts per Million : 13C

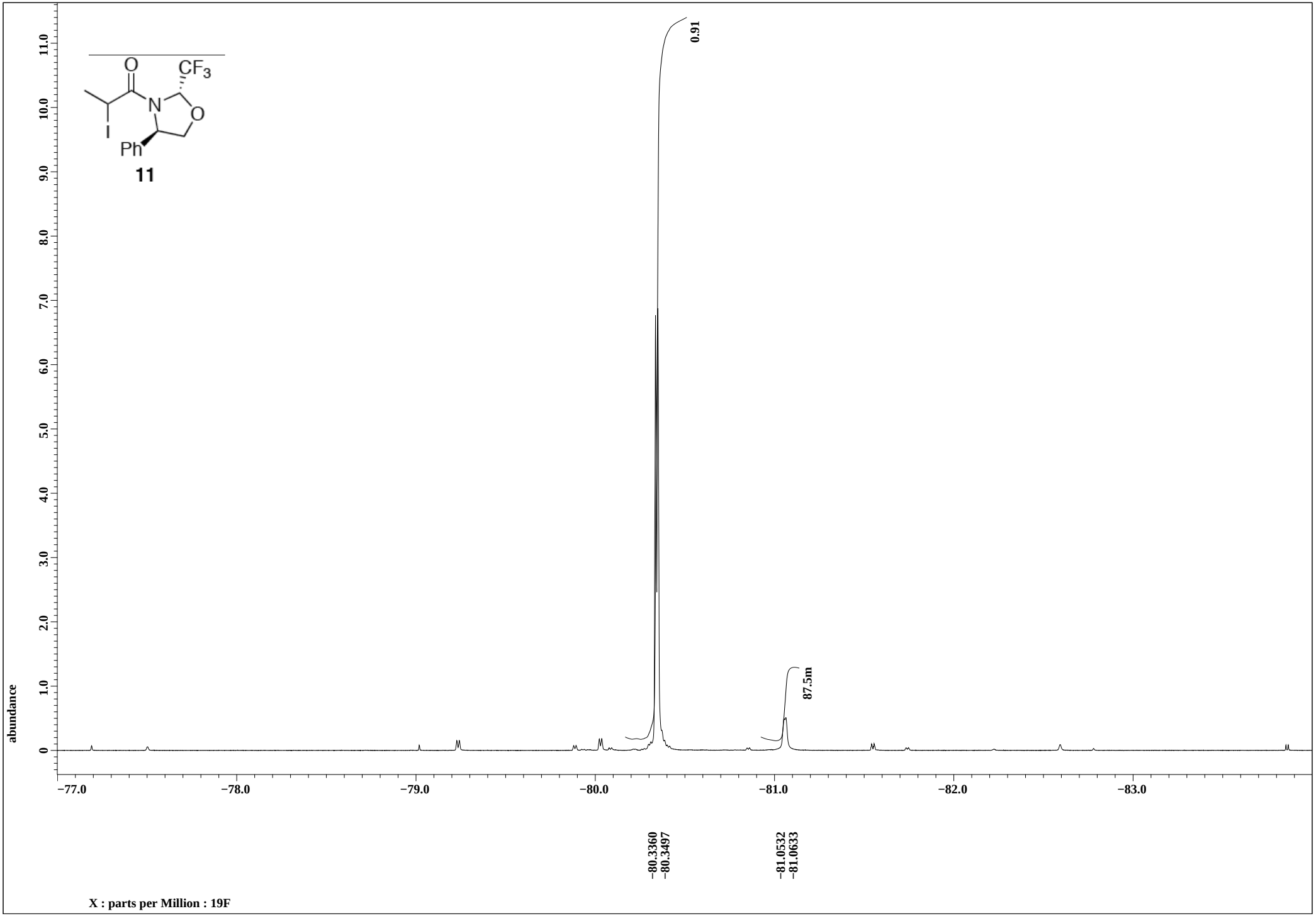

Ph
OMe
H
OBn
F3C
O
O
Ph
13.268
1.95
3.096
0.965
1.013
3
2.487
abundance
3.0
2.0
1.0
0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.5705
7.5522
7.2898
7.2761
7.2738
7.1833
7.1787
5.2818
4.5441
4.5155
4.4295
4.4021
4.2554
4.2405
3.8843
3.8751
3.8683
3.5544
3.5510
2.8889
2.8717
2.8407
2.8247
2.8052
1.4490
1.3184
1.2772
1.2497
0.9152
0.8980
0.8808
0.0973
0.0183
X : parts per Million : 1H

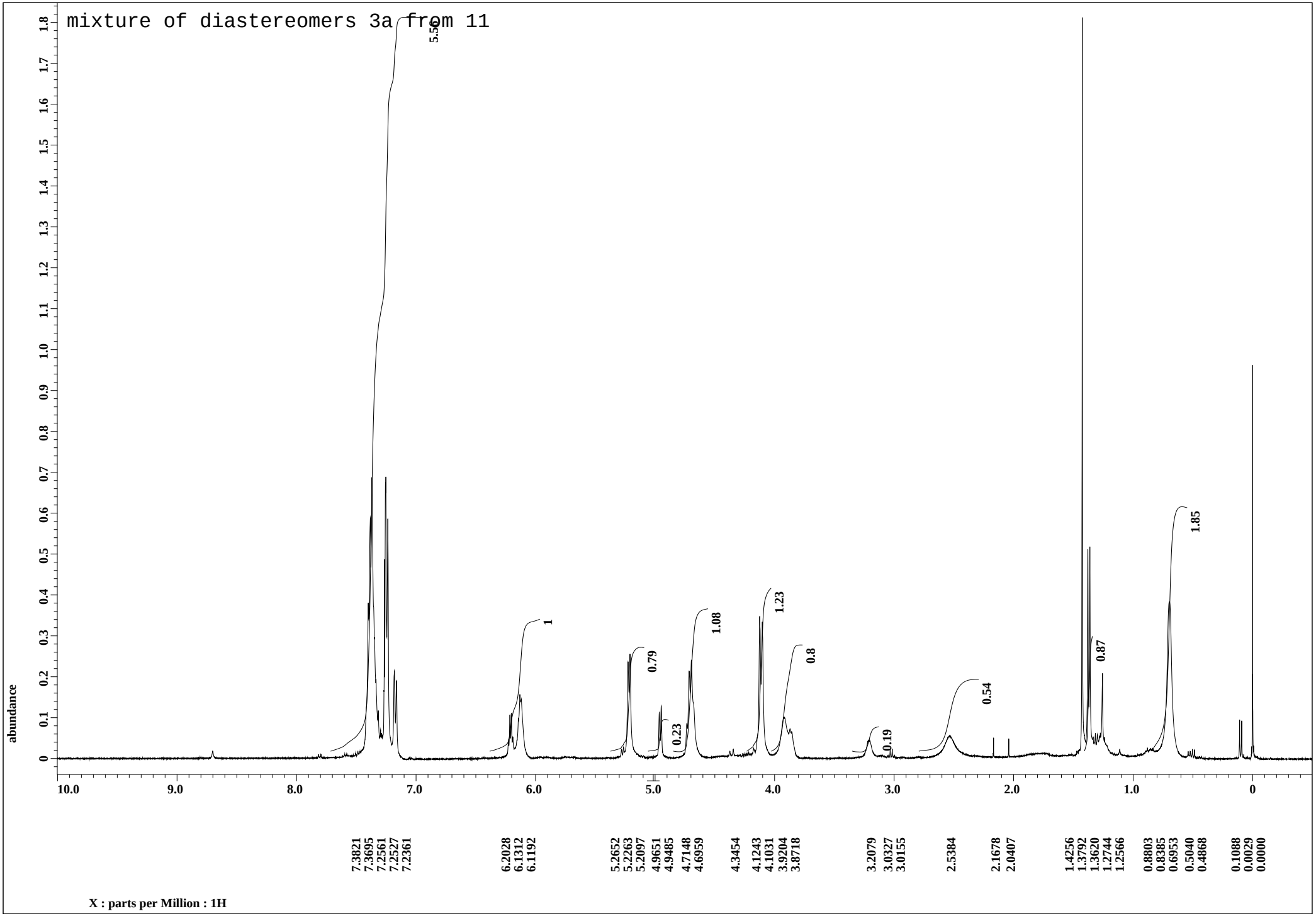

Ph
OMe
H
OBn
F3C
O
O
Ph
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
166.5990
137.4328
129.7479
129.5667
128.6037
128.5465
128.4131
127.8314
127.7456
127.5645
126.7064
84.9830
84.7065
77.7654
77.4698
77.1551
76.8405
72.2162
66.9150
55.5784
38.0920
32.0470
29.8255
29.6253
29.4822
22.8176
14.2460
X : parts per Million : 13C

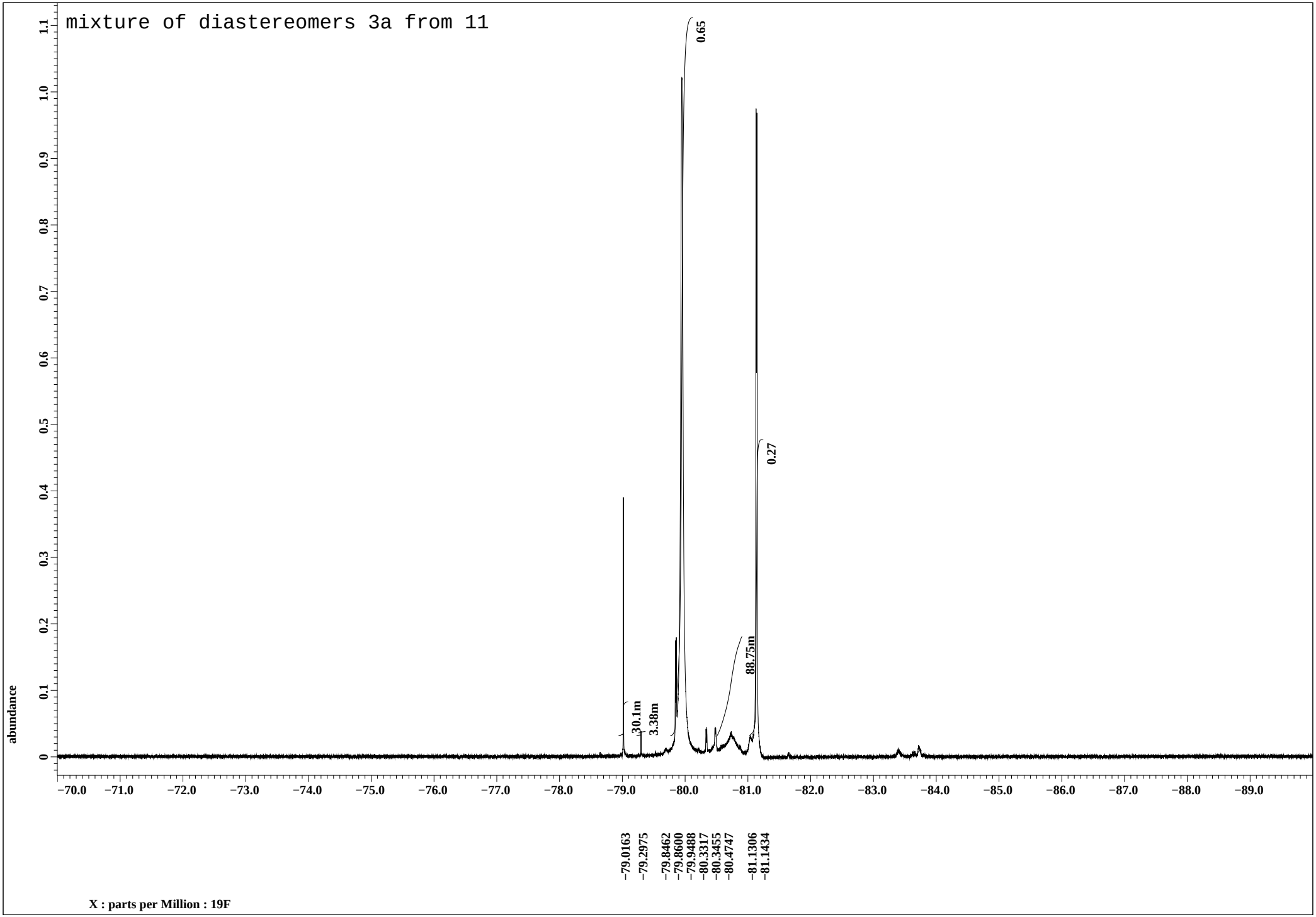

Ph
OMe
H
OBn
F3C
O
O
Ph
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−60.0
−70.0
−80.0
−90.0
−100.0
−110.0
−120.0
−130.0
−140.0
−150.0
−160.0
−170.0
−74.6421
−164.9000
X : parts per Million : 19F


O
CF3
N
O
I
Ph
11
abundance
3.0
2.0
1.0
0
6.28
3
2.24
1.14
1.1
0.93
0.32
0.3
98.24m
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.4108
7.3924
7.2149
7.2109
7.1943
6.1702
6.1576
6.1450
5.3042
5.2933
5.0677
5.0533
4.7578
4.7549
4.7372
4.1209
4.1037
4.0871
2.1673
1.8987
1.8826
1.5722
1.5613
1.5441
1.2640
0.0378
−0.0003
X : parts per Million : 1H


O
CF3
N
O
I
Ph
11
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
−20.0
171.4475
141.2229
129.9053
129.1330
129.0186
125.1857
124.8710
121.9916
85.7411
85.3883
77.4746
77.1600
76.8358
76.7023
60.1789
21.9166
14.0792
X : parts per Million : 13C


O
CF3
N
O
I
Ph
11
0.91
87.5m
abundance
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−77.0
−78.0
−79.0
−80.0
−81.0
−82.0
−83.0
−80.3360
−80.3497
−81.0532
−81.0633
X : parts per Million : 19F


mixture of diastereomers 3a from 11
abundance
X : parts per Million : 1H
1
0.79
0.23
1.08
1.23
0.8
0.19
0.54
0.87
1.85
7.3821
7.3695
7.2561
7.2527
7.2361
6.2028
6.1312
6.1192
5.2652
5.2263
5.2097
4.9651
4.9485
4.7148
4.6959
4.3454
4.1243
4.1031
3.9204
3.8718
3.2079
3.0327
3.0155
2.5384
2.1678
2.0407
1.4256
1.3792
1.3620
1.2744
1.2566
0.8803
0.8385
0.6953
0.5040
0.4868
0.1088
0.0029
0.0000


mixture of diastereomers 3a from 11
0.65
0.27
30.1m
3.38m
88.75m
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
−70.0
−71.0
−72.0
−73.0
−74.0
−75.0
−76.0
−77.0
−78.0
−79.0
−80.0
−81.0
−82.0
−83.0
−84.0
−85.0
−86.0
−87.0
−88.0
−89.0
−79.0163
−79.2975
−79.8462
−79.8600
−79.9488
−80.3317
−80.3455
−80.4747
−81.1306
−81.1434
X : parts per Million : 19F