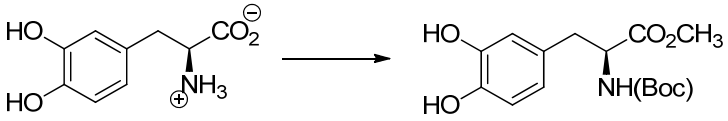
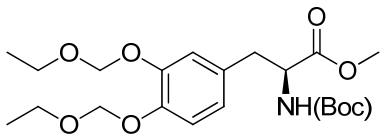
*Synthesis of the diaryliodonium precursor ((S)-methyl-3-(4,5-bis(ethoxymethoxy)2-iodophenyl)-2-(di-(tert-butoxycarbonyl))amino)propanoate)(4-methoxyphenyl)-λ^3-iodane trifluoromethanesulfonate (**ALPDOPA;** Ground Fluor Pharmaceuticals, Inc.)*



(*S*)-methyl-2-((*tert*-butoxycarbonyl)amino)-3-(3,4-dihydroxyphenyl)propanoate: L-DOPA (25.0 g, 127 mmol) was suspended in 250 mL of methanol and the stirred mixture was chilled to 0 °C using an external ice-water bath. Thionyl chloride (11 mL, 152 mmol) was added dropwise to the stirring solution. Upon full addition of thionyl chloride the solid dissolved completely. The ice bath was removed and the reaction was heated at reflux overnight. Methanol was removed by rotary evaporation to give a light yellow solid. The solid was pumped under dynamic vacuum overnight to remove all remaining solvents.

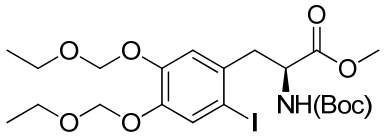
Installation of the Boc group. The remaining off-white solid was suspended in 180 mL of THF in a 1 L round-bottom flask. Saturated aqueous sodium bicarbonate solution (180 mL) was added and the mixture was stirred vigorously to avoid bilayer formation as much as possible. In a separate flask, boc-anhydride (30.5 g, 140 mmol) was dissolved in 140 mL of THF. The boc-anhydride/THF solution was added to the vigorously stirred reaction mixture at a rate of 50 mL/min. The mixture was allowed to stir for 90 minutes. (Reaction progress monitored by TLC with 1:1 ethyl acetate:hexanes mobile phase; R_f = 0.5 for product, reactant was baseline.) At the conclusion of the reaction, as evidenced by a single spot on silica TLC plate, the mixture was transferred to a separatory funnel and the THF layer was separated and collected in an Erlenmeyer flask. The aqueous layer was extracted with 120 mL of ethyl acetate and the aqueous layer was discarded. The ethyl acetate and THF fractions were combined in the separatory funnel and washed with deionized water (2 x 120 mL), 100 mL of

5% aqueous HCl, 100 mL of deionized water, and 100 mL of saturated aqueous sodium chloride. The organic layer was dried over sodium sulfate, and the drying agent was removed by gravity filtration. The mixture was transferred to a 2 L beaker and stirred with a magnetic stir bar. Hexanes (800 mL) were added to the stirring solution at a rate of 50 mL/min and a white precipitate formed. The white solid was collected by vacuum filtration, and traces of solvent were removed under reduced pressure. 1H NMR spectroscopy verified that the solid was (*S*)-methyl-2-((*tert*-butoxycarbonyl)amino)-3-(3,4-dihydroxyphenyl)propanoate (37.5 g, yield 95%). TLC (silica gel plate, mobile phase 1:1 ethyl acetate:hexanes; R_f(product) = 0.5) showed a single spot. ^{1}H NMR (d_6-acetone) 400 MHz δ 1.36 (s, 9H) δ 2.84 (dd, J_1 = 13.9 Hz, J_2 = 8.1 Hz, 1H), δ 2.95 (dd, J_1 = 13.9 Hz, J_2 = 5.8 Hz, 2H), δ 3.66 (s, 3H), δ 4.31 (dd, J_1 = 13.9 Hz, J_2 = 5.8 hz, 1H), δ 5.96 (d, J = 8.8 Hz, 1H), δ 6.55 (dd, J_1 = 8.1 Hz, J_2 = 2.0 Hz, 1H), δ 6.71 (d, J = 2.0 Hz, 1H), δ 6.73 (d, J = 8.1 Hz, 1H), δ 7.79 (s, 2H). ^{13}C NMR (d_6-acetone) 100 MHz δ 28.99, 38.22, 52.60, 56.68, 79.80, 116.51, 117.59, 121.92, 129.99, 145.26, 146.27, 156.63, 173.80. HRMS (HRFAB) calcd. for $C_{15}H_{21}NO_6$ [M^+] 311.1369, found.



(*S*)-methyl-3-(3,4-bis(ethoxymethoxy)phenyl)-2-(*tert*-butoxycarbonyl)amino)propanoate: Under an inert atmosphere (N_2) in a 100 mL round-bottom flask, (*S*)-methyl-2-((*tert*-butoxycarbonyl)amino)-3-(3,4-dihydroxyphenyl)propanoate (2.0 g, 6.4 mmol) was dissolved in 18 mL of dry, distilled THF. *N,N*-Diisopropylethylamine (3.4 mL, 19.3 mmol) was added dropwise to the stirring reaction mixture and the mixture was allowed to stir for 10 minutes before the solution was cooled to 0 °C with an ice-water bath. Chloromethyl ethyl ether (1.8 mL, 19.3 mmol) was added dropwise by syringe, the flask was sealed with a glass stopper and the solution was stirred at 40 °C for 6 hours (reaction progress monitored by silica TLC with 20% ethyl acetate:hexanes; R_f = 0.3 of product). After 6 hours (reaction progress unchanged

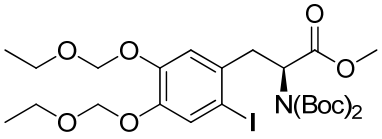
after 21 hours at ~85% completion), the solution was cooled to room temperature and THF was removed by rotary evaporation. The residue was dissolved in 60 mL of MTBE and 40 mL of deionized water was added to the organic solvent. The mixture was transferred to a separatory funnel and the aqueous layer was removed. The organic layer was washed with deionized water (3 x 40 mL) and 5% acetic acid (3 x 40 mL) to remove excess *N,N*-Diisopropylethylamine. Silica gel TLC showed the presence of mono-protected catechol, which was removed from the organic layer with 10% aqueous K_2CO_3 (3 x 30 mL) washes, followed by deionized water (3 x 30 mL) washes. The organic layer was dried over sodium sulfate, filtered by gravity, and the solvents were removed by rotary evaporation to give 2.2 g (82% yield) of (*S*)-methyl-3-(3,4-bis(ethoxymethoxy)phenyl)-2-(*tert*-butoxycarbonyl) amino)propanoate as a colorless oil. ^{1}H NMR ($CDCl_3$) 400 MHz δ 1.21 (t, J = 7.1 Hz, 3H), δ 1.21 (t, J = 7.1 H, 3H), δ 1.41 (s, 9H), δ 3.00 (d, J = 12.0 Hz, 1H), δ 3.01 (d, J = 8.3 Hz, 1H), δ 3.72 (s, 3H), δ 3.74 (quartet, J = 7.1 Hz, 2H), δ 3.74 (quartet, J = 7.1 Hz, 2H), δ 4.53 (dd, J_1 = 13.2 Hz, J_2 = 7.0 Hz, 1H), δ 4.99 Hz (d, J = 8.6 Hz, 1H), δ 5.22 (s, 2H), δ 5.23 (s, 2H), δ 6.68 (dd, J_1 = 8.1 Hz, J_2 = 2.0 Hz, 1H), δ 6.92 (d, J = 2.0 Hz, 1H), δ 7.07 (d, J = 8.1 Hz, 1H). ^{13}C NMR ($CDCl_3$) 100 MHz δ 15.21, 15.25, 28.42, 37.77, 52.33, 54.50, 64.43, 64.49, 79.80, 94.20, 94.26, 116.79, 117.70, 123.26, 130.14, 146.59, 147.49, 155.26, 172.44. HRMS (HRFAB) calcd. for $C_{21}H_{33}NO_8$ [M^+] 427.2206, found.



(*S*)-methyl-3-(4,5-bis(ethoxymethoxy)2-iodophenyl)-2-(*tert*-butoxycarbonyl)amino)propanoate: To a 1 L round-bottom flask fitted with a magnetic stir bar was added solid iodine (7.7 g, 30.0 mmol) and potassium carbonate (9.7 g, 70.0 mmol) under an inert atmosphere (N_2). In a separate flask, (*S*)-methyl-3-(3,4-bis(ethoxymethoxy) phenyl)-2-(*tert*-butoxycarbonyl)amino)propanoate (10 g, 23 mmol) was dissolved in 130 mL

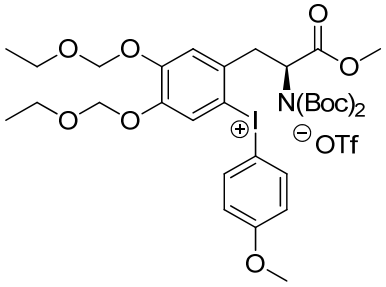
of dry, distilled dichloromethane. The dichloromethane solution was added to the round-bottom flask containing the neat iodine and potassium carbonate, while stirring, and the reaction was allowed to stir for 5 minutes. Bis(trifluoroacetoxy)phenyl-λ^3-iodane (14.1 g, 33.3 mmol) was dissolved in a minimal amount of distilled dichloromethane (yielding an approximately 3 M solution) and this solution was added dropwise to the stirred reaction mixture. Upon completion of the addition, the mixture was stirred under nitrogen for two hours. After 2 hours, the reaction had reached 95% completion, as was determined by ^{1}H NMR spectroscopy of withdrawn aliquots of the reaction. The reaction mixture was transferred to a separatory funnel and the organic layer was washed successively with 10% aqueous potassium carbonate (2 x 200 mL) and 10% sodium chloride (1 x 200 mL). The organic fraction was dried with sodium sulfate, filtered by gravity, and the solvents were removed *in vacuo* to afford a dark yellow oil. The oil was dissolved in 200 mL of acetonitrile, returned to a separatory funnel, and the acetonitrile layer was washed with hexanes (4 x 100 mL) to remove excess iodobenzene and iodine. The acetonitrile was then removed by rotary evaporation to yield the crude product, obtained as an oil. The oil was transferred, neat, onto a 2" length x 2" diameter plug of deactivated silica packed in hexanes. Silica (100 g) was deactivated by stirring the slurry in 350 mL of a 5% triethylamine/hexanes solution, loaded onto the column, and washed with 300 mL of hexanes. The silica column was washed with 100 mL of 10% ethyl acetate to elute any remaining iodobenzene and traces of iodine. The product was eluted using 40% ethyl aceate:hexanes. (*S*)-methyl-3-(4,5-bis(ethoxymethyoxy)-2-iodophenyl)-2-(*tert*-butoxycarbonyl)amino)propanoate (10.4 g, 18.7 mmol 80%) was obtained as a yellow oil. ^{1}H NMR ($CDCl_3$) 400 MHz δ 1.23 (t, J = 7.1 Hz, 3H), δ 1.24 (t, J = 7.1 Hz, 3H), δ 1.38 (s, 9H), δ 3.02 (dd, J_1 = 13.1 Hz, J_2 = 7.1 Hz, 1H), δ 3.20 (dd, J_1 = 13.8 Hz, J_2 = 7.1 Hz, 1H), δ 3.73 (quartet, J = 7.1 Hz, 2H), δ 3.74 (quartet, J = 7.1 Hz, 2H), δ 3.75 (s, 3H), δ 4.59 (dd, J_1 = 13.8 Hz, J_2 = 7.1 Hz, 1H), δ 5.03 (d, J = 9.3 Hz, 1H), δ 5.22 (s, 2H), δ

5.23 (s, 2H), δ 6.99 (s, 1H), δ 7.56 (s, 1H). ^{13}C NMR ($CDCl_3$) 100 MHz δ 14.38, 15.22, 15.27, 21.22, 28.47, 42.53, 52.57, 53.93, 60.56, 64.72, 80.03, 91.07, 94.25, 94.39, 118.12, 127.12, 133.38, 147.05, 147.82, 155.16, 172.50. HRMS (HRFAB) calcd. for $C_{21}H_{32}INO_8$ [M^+] 553.1173, found.



(*S*)-methyl-3-(4,5-bis(ethoxymethoxy)2-iodophenyl)-2-(di-(*tert*-butoxycarbonyl))amino)propanoate: In a 500 mL round-bottom flask equipped with a magnetic stirring bar, (*S*)-methyl-3-(4,5-bis(ethoxymethoxy)2-iodophenyl)-2-(*tert*-butoxycarbonyl)amino)propanoate (10.0 g, 18 mmol) was dissolved in 150 mL of acetonitrile. Triethylamine (7.5 mL, 54 mmol) and 4-dimethylaminopyridine (1.1 g, 9 mmol) were added to the stirred reaction mixture. Boc anhydride (5.9 g, 27 mmol) was dissolved in 50 mL of acetonitrile and added to the stirring reaction mixture at a rate of 1 mL/min. The Boc anhydride was added slowly to the reaction mixture as excess boc anhydride was slowly consumed in the presence of DMAP and water. Reaction progress was monitored by silica gel TLC using 20% ethyl acetate:hexanes (R_f = 0.3 of product). After 21 hours, the reaction reached approximately 75% completion. Further addition of Boc anhydride did not drive the reaction to completion. The crude reaction mixture was transferred to a round-bottom flask containing deactivated silica. (Silica was deactivated by stirring silica gel in a 400 mL of 9:1 hexanes:triethylamine solution, filtering, and washing the silica with 300 mL hexanes.) The acetonitrile was removed by rotary evaporation and the silica was dried under dynamic vacuum for 2 hours. A silica gel column (6" x 2") was slurry-packed in 10% triethylamine:hexanes and washed with 200 mL of hexanes to remove unbound triethylamine. The dark orange silica gel was transferred to the top of the column, and the product (R_f = 0.3, 4:1 hexanes:ethyl acetate) was eluted using an ethyl acetate:hexanes gradient (0-5%-10%-

20%). Removal of the solvent by rotary evaporation yielded 8.5 g (72% yield) of (*S*)-methyl-3-(4,5-bis(ethoxymethoxy)-2-iodophenyl)-2-(di-(*tert*-butoxycarbonyl))amino)propanoate as a light yellow oil. ^{1}H NMR ($CDCl_3$) δ 1.19 (t, J = 7.1 Hz, 3H), δ 1.20 (t, J = 7.1 Hz, 3H), δ 1.38 (s, 18H), δ 3.29 (dd, J_1 = 14.2 Hz, J_2 = 11.3 Hz, 1H), δ 3.48 (dd, J_1 = 14.2 Hz, J_2 = 10.1 Hz, 1H), δ 3.71 (quartet, J = 7.1 Hz, 2H), δ 3.72 (quartet, J = 7.1 Hz, 2H), δ 3.76 (s, 3H), δ 5.16 (s, 2H), δ 5.18 (s, 2H), δ 5.22 (dd, J_1 = 10.1 Hz, J_2 = 7.1 Hz, 1H), δ 6.98 (s, 1H), δ 7.54 (s, 1H). ^{13}C NMR ($CDCl_3$) 100 MHz δ 15.18, 15.23, 28.00, 40.36, 52.48, 57.91, 64.58, 64.63, 83.15, 90.84, 94.30, 94.49, 118.81, 126,67, 134.38, 146.77, 148.03, 151.55, 170.63. HRMS (HRFAB) calcd. for $C_{26}H_{40}INO_{10}$ [M^+] 653.1697, found.



((*S*)-methyl-3-(4,5-bis(ethoxymethoxy)2-iodophenyl)-2-(di-(*tert*-butoxycarbonyl))amino)propanoate)(4-methoxyphenyl)-λ^3-iodane trifluoromethanesulfonate: In a N_2 charged glove box, (*S*)-methyl-3-(4,5-bis(ethoxymethoxy)-2-iodophenyl)-2-(di-(*tert*-butoxycarbonyl))amino)propanoate (3.5 g, 5.4 mmol) was dissolved in 30 mL of dry, distilled acetonitrile in a 500 mL round-bottom flask and stirred. In a separate flask, Selectfluor® (2.66 g, 7.51 mmol) was dissolved in 63 mL of dry, distilled acetonitrile and trimethylsilyl acetate (2.1 g, 15.9 mmol) was added neat in a dropwise fashion to the dissolved Selectfluor. The Selectfluor/TMSOAc mixture was added to the stirring iodoarene reaction mixture over the course of two minutes. After the addition was complete, the reaction mixture was sealed with a glass stopper and the solution was stirred for 4 hours. (1H NMR spectroscopy on hourly withdrawn aliquots indicated that the reaction

stalled between 4 and 5 h and could not be pushed to completion.) Potassium (4-methoxyphenyl)trifluoroborate (1.12 g, 5.4 mmol) was added directly to the stirring reaction mixture, followed by an additional 30 mL aliquot of acetonitrile. Trimethylsilyl trifluoroacetate (0.95 g, 5.4 mmol) was diluted with 10 mL of dry acetonitrile and added dropwise to the stirring reaction mixture, and the solution was allowed to stir for 10 minutes before the reaction flask was sealed and removed from the glove box. The solvent was removed under reduced pressure to yield a dark red pasty oil, which was placed under dynamic vacuum for 1 hour. The oil was suspended in 50 mL of dichloromethane and the flask was placed in an ultrasonic bath for 3 minutes. The organic layer was decanted into a 125 mL separatory funnel, and a white residue was left behind in the round-bottom flask. (This material comprises Selectfluor-derived and inorganic salts.) The dichloromethane was washed with acetate buffer (NaOAc: HOAc = 0.5 M: 0.5 M, pH = 5) (3 x 30 mL), dried over sodium sulfate, filtered by gravity, and the solvent was removed by rotary evaporation to yield a brown oil, which was placed under dynamic vacuum for 15 minutes.

The oil was dissolved in 30 mL of acetonitrile and added to an aqueous solution of sodium hexafluorophosphate (2.7 g in 100 mL of deionized water) in a 250 mL separatory funnel. The mixture was vigorously shaken to mix it, which resulted in a heterogenous mixture of brown oil suspended in the aqueous acetonitrile. The aqueous mixture was extracted with dichloromethane (3 x 40 mL). The organic fractions were combined, dried with sodium sulfate, filtered by gravity, and the solvent was removed by rotary evaporation to give a brown oil, which was placed under dynamic vacuum for 15 minutes and became an oily foam. The residue was dissolved in 10 mL of 90:10 acetonitrile/water and loaded onto an Amberlite® IRA-400(Cl) ion-exchange column. (For column preparation instructions, see below.) The 10 mL aliquot was passed through a freshly prepared IRA-400 (Cl) resin,

previously loaded with trifluoromethanesulfonate counterion and eluted with an additional 70 mL of 90:10 acetonitrile:deionized water.

The solvent was removed by rotary evaporation at 40 °C and the remaining residue was exposed to dynamic vacuum for 30 minutes, which left a foamy residue in the flask. The flask was removed from vacuum and 20 mL of MTBE were added to the residue. The solution was brought to a vigorous stir with a magnetic stir bar. After approximately 10 minutes, the residue had completely dissolved. After a total of approximately 20 minutes of stirring, white crystals began to form in the flask. The contents were allowed to stir an additional 3 hours, at which point the solid was collected by vacuum filtration. The off-white solid was washed with 50 mL of ice-cold MTBE. The solid was transferred to a clean 100 mL round-bottom flask and dissolved in 15 mL of acetonitrile. The acetonitrile was removed by rotary evaporation and the oily residue was exposed to dynamic vacuum for 45 minutes, which left behind a white foam. The flask was removed from the vacuum and 15 mL of MTBE was added to the flask. The solution was brought to a vigorous stir with a magnetic stir bar and after approximately 5 minutes, the foamy residue had completely dissolved. After a total of 10 minutes of stirring, large white crystals began to form in the flask. The flask was allowed to stir an additional 3 hours, at which time the solid was collected by vacuum filtration and washed with 50 mL of ice-cold MTBE. NMR confirmed the white solid was pure ((*S*)-methyl-3-(4,5-bis(ethoxymethoxy)2-iodophenyl)-2-(di-(*tert*-butoxycarbonyl))amino)propanoate)(4-methoxyphenyl)-λ^3-iodane trifluoromethanesulfonate (3.1 g, 63% yield) ^{1}H NMR (CD_3CN) 400 MHz δ 1.02 (t, J = 7.6 Hz, 3H), δ 1.19 (t, J = 7.6 Hz, 3H), δ 1.38 (s, 18H), δ 3.36 (dd, J_1 = 11.3 Hz, J_2 = 14.0 Hz, 1H), δ 3.56 (quartet, J = 7.6 Hz, 2H), δ 3.58 (dd, J_1 = 11.3 Hz, J_2 = 14.0 Hz, 1H), δ 3.71 (quartet, J = 7.6 Hz, 2H), δ 3.75 (s, 3H), δ 3.82 (s, 3H), δ 5.14 (dd, J_1 = 4.9 Hz, J_2 = 11.0 Hz, 1H), δ 5.19 (s, 2H), δ 5.27 (s, 2H), δ 7.07 (d, J = 8.6 Hz, 2H), δ 7.21 (s, 1H), 7.60 (s, 1H), 8.02 (d, J = 8.6 Hz, 2H). ^{19}F NMR (CD_3CN) 376 MHz δ -79.29 (3F-OTf).

^{13}C NMR (CD_3CN) 100 MHz δ 15.70, 15.75, 28.47, 39.77, 53.85, 57.12, 59.51, 65.71, 66.14, 85.33, 95.35, 95.38, 103.26, 109.36, 119.46, 120.51, 124.73, 135.91, 139.04, 149.35, 152.54, 153.28, 164.74, 171.63. HRMS (HRFAB) calcd. for $C_{33}H_{47}INO_{11}[M^+]$ 760.63, found.

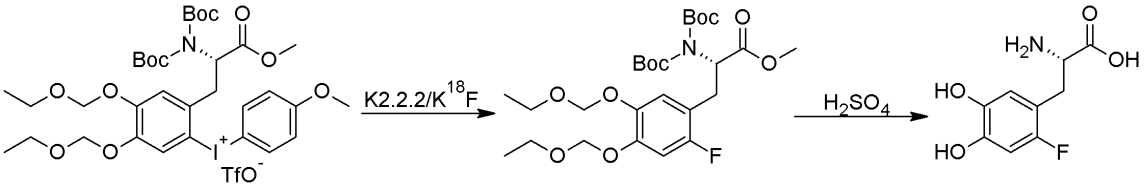
Triflate ion-exchange resin preparation

An aqueous silver nitrate solution (for monitoring the progress of the ion exchange process) was prepared by dissolving 20 mg of silver nitrate in 5 mL of deionized water.

A glass column 3 cm in diameter was filled with 400 mL of deionized water and an IRA-400 (Cl) ion-exchange resin was added to the column until the resin reached 15 cm in length. A 1 M solution of aqueous sodium trifluoromethanesulfonate was eluted through the ion-exchange column at a rate of 5 mL/min. Periodically, 1 mL fractions from the eluant were collected in 15 mm borosilicate glass test tubes and analyzed for the presence of chloride ion with 0.5 mL aliquots of the previously prepared aqueous silver nitrate solution. The chloride was considered fully exchanged when no visible precipitate formed upon addition of the silver nitrate solution to aliquots of column eluent that also contained sodium trifluoromethanesulfonate. The ion-exchange was complete after approximately 800 mL of aqueous 1 M sodium triflate had been eluted through the column.

Upon completion, the column was washed with distilled water and then equilibrated with 90:10 acetonitrile:water.

Radiosynthesis of 6-[18]fluoro-3,4-dihydroxy-L-phenylalanine ([18]FDOPA-H) from diaryliodonium salt precursor.



^{18}fluoride was produced via a $^{18}O(p,n)^{18}F$ reaction using a 10 μAh proton beam. The radioactivity was trapped on a SepPak Accell Plus QMA Plus Light cartridge (Waters). The QMA had been preconditioned by rinsing with 10 mL of 0.5 M K_2CO_3 and 20 mL of demineralised water, respectively, followed by drying under a small stream of argon for at least 15 minutes.

Kryptofix $K_{2.2.2}$ (9.5 mg) and K_2CO_3 (1.7 mg) were dissolved in a mixture of 850 μL of acetonitrile and 150 μL of demineralised water. The solution was passed over the QMA to elute the ^{18}fluoride and collected in a 5 mL conical vial. The conical vial was capped with a septum. The Kryptofix/K[^{18}F]F-complex was dried azeotropically at 100 ºC by three additions of 0.5 mL anhydrous acetonitrile. Complete evaporation of solvent was prevented to avoid degradation of the Kryptofix/K[^{18}F]F-complex at 100 ºC. At room temperature the argon supply was replaced by a vacuum line. Three cycles of vacuum drying (50 seconds) and purging with argon (10 seconds) were performed to remove remaining traces of water and acetonitrile.

The diaryliodonium precursor ALPDOPA, ((*S*)-methyl-3-(4,5-bis(ethoxymethoxy)2-iodophenyl)-2-(di-(*tert*-butoxycarbonyl))amino)propanoate)(4-methoxyphenyl)-λ^3-iodane trifluoromethanesulfonate (Ground Fluor Pharmaceuticals; 12 ± 2 mg), was dissolved in 750 μL anhydrous diglyme. The solution was added to the dried Kryptofix/K[^{18}F]F-complex. The conical vial was capped with a new septum and put inside a heating block set at a temperature of 140 ºC for 5 minutes.

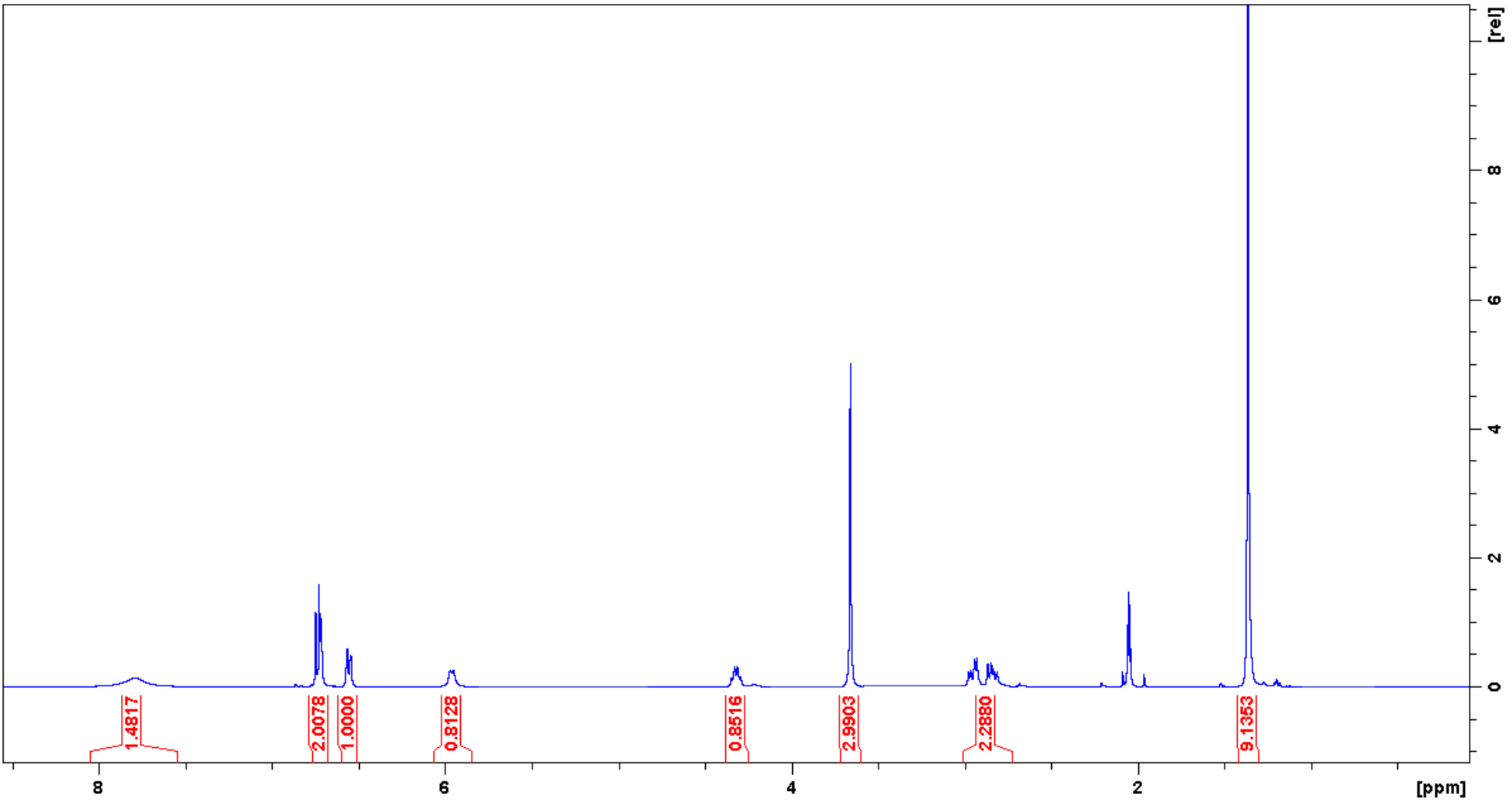
The reaction mixture, diluted with 19 mL of demineralised water, was passed over a SepPak C_{18} Light Plus cartridge (Waters). The SepPak was eluted with 2 mL of ethanol and the eluate was subsequently dried in a 5 mL conical vial at 100 ºC under a small stream of argon. Complete evaporation of solvent was prevented.

To the protected ^{18}FDOPA-H in a small residual volume of ethanol (50-100 µL) 300 µL 3 M H_2SO_4 was added. The acidic mixture was heated in the heating block set at a temperature of 140ºC for 5 minutes. The mixture was neutralised by 800 µL of a solution of 0.48 M Na_2HPO_4, containing 0.04 % (w/v) ascorbic acid, resulting in a solution with a pH of 2.0. The neutralised solution was filtered over a 0.22 µm LG sterile filter (Millex) and a SepPak Alumina N Plus Light cartridge (Waters). Alumina N SepPak pre-purification reduced the amount of free ^{18}fluoride in the HPLC-system and in the product fraction.

The filtered solution was injected onto a 1 mL loop of a semi-preparative RP-HPLC system, equipped with a Hamilton PRP-1 column (part. no.: 79496). The mobile phase (1% ethanol, 50 mM ortho-phosphoric acid, 50 mM monobasic sodium phosphate and 0.04% (w/v) ascorbic acid, pH: 2.0) was run at a speed of 2 mL per minute. The UV detector was set at 254 nm. Free ^{18}fluoride had a retention time of 6 minutes and ^{18}FDOPA eluted at 16 minutes. To obtain a slightly acidic ^{18}FDOPA solution (pH 6.6), suitable for injection, 75 µL of the 1 M NaOH solution, supplemented with 0.04 % (w/v) ascorbic acid, was added to each 925 µL of product fraction.

The formulated solution was injected onto a 10 µL loop of a quantitative UPLC system, equipped with an Acquity UPLC HSS T3 1.8 µm column (3.0 x 50 mm, part. no.: 186004679). The mobile phase (50 mM monobasic sodium phosphate, pH: 2.5) was run at a speed of 0.8 mL per minute. The UV detector was set at 200 nm. The retention time of ^{18}FDOPA was 1.41 minute. The limit of quantitation was 167 nM. For radio-TLC determination, a spot (1 µL) of the product formulation was applied to a silica plate and te

solvent was evaporated with a heat gun. The plate was developed with n-butanol/acetic acid/water/ethanol (4/1/1.6/0.5) and dried. The plate was mounted on a phosphor storage screen and read by a Cyclone. The R_f of ^{18}FDOPA was 0.43. Enantiomeric excess was determined by a chiral analytical column (Supelco Chirobiotic T2, 4.6 x 25 mm, 5 μm). The mobile phase (50% CH_3CN:H_2O) was run at 0.8 mL per minute. The UV detector was set at 254 nm.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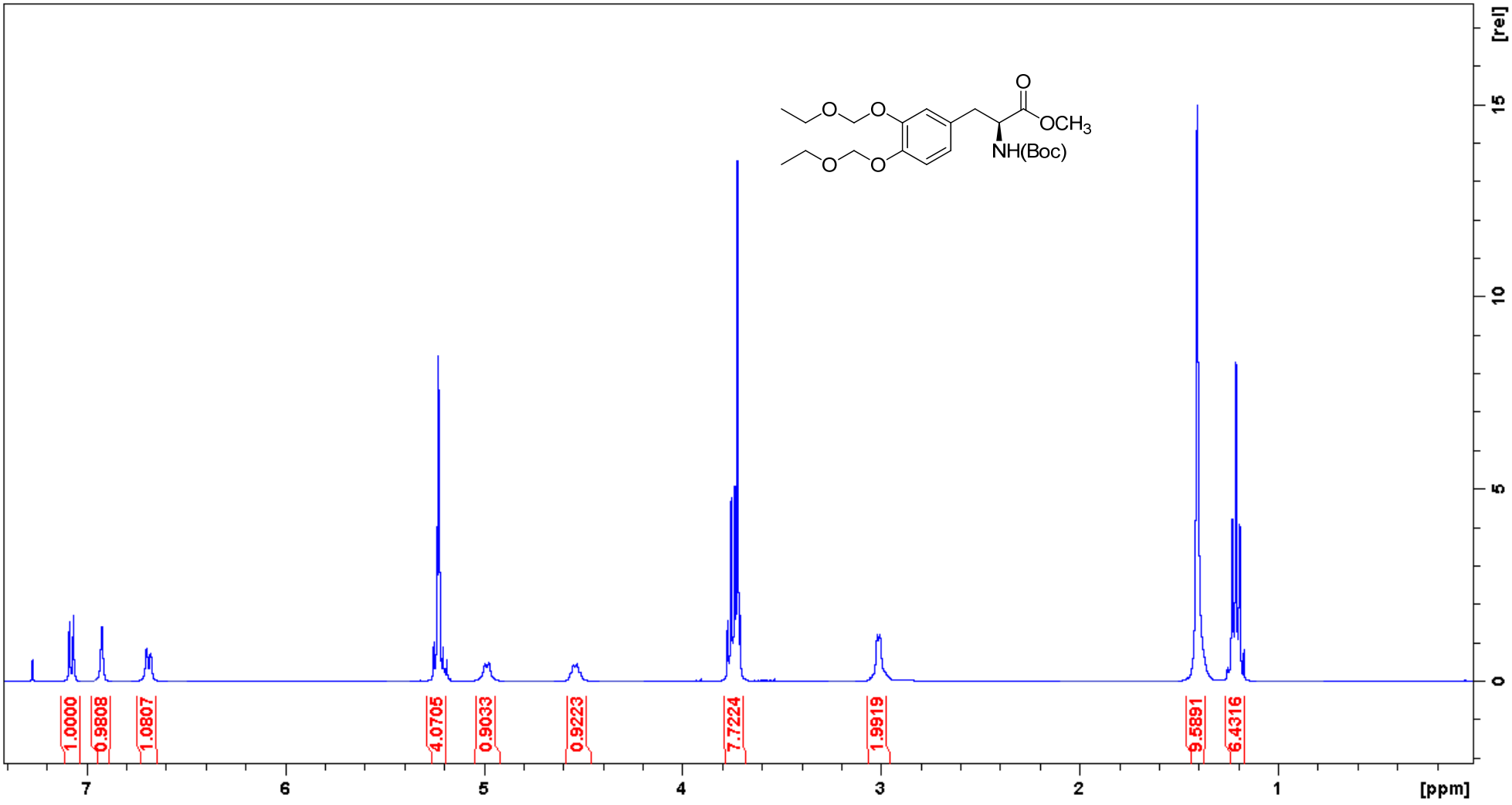
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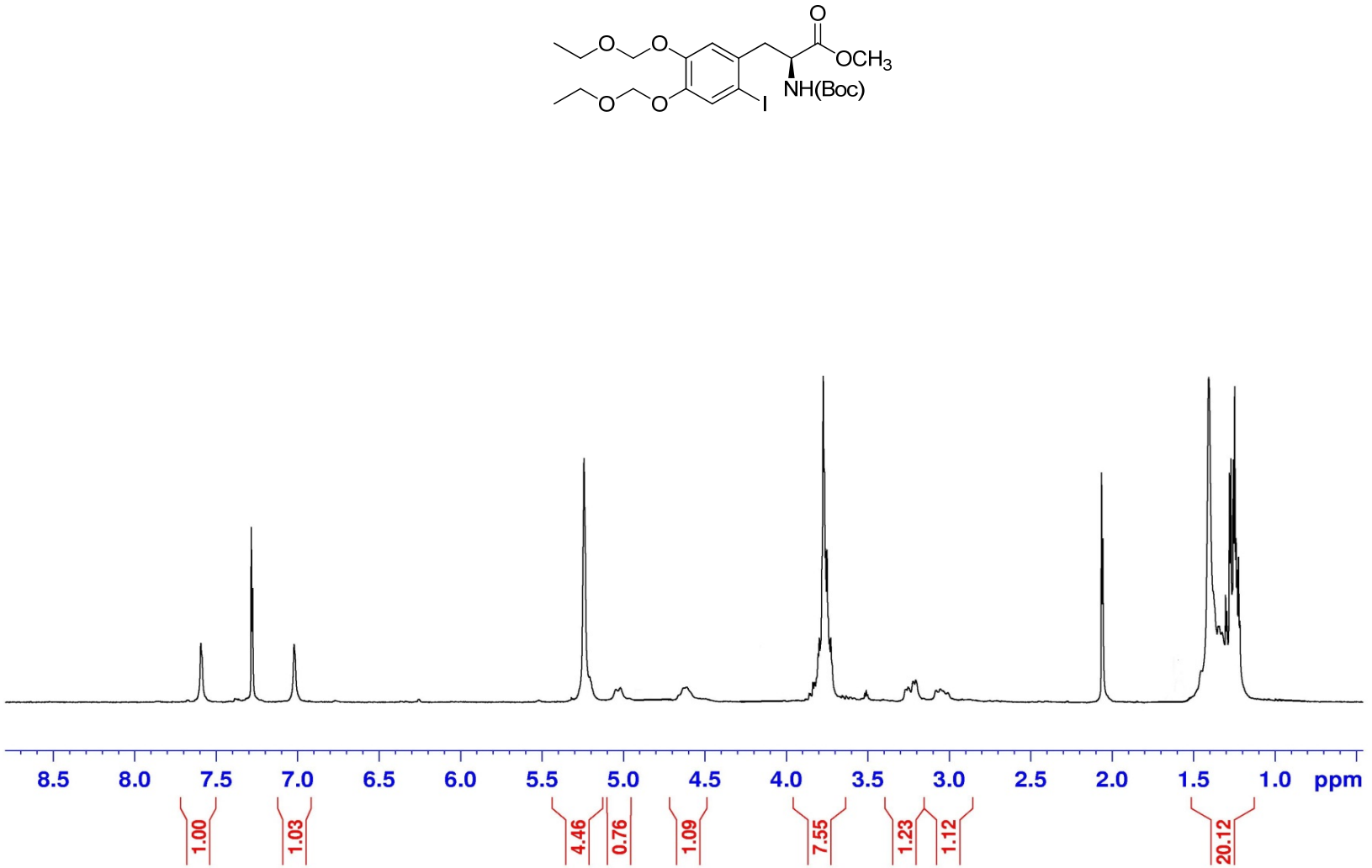
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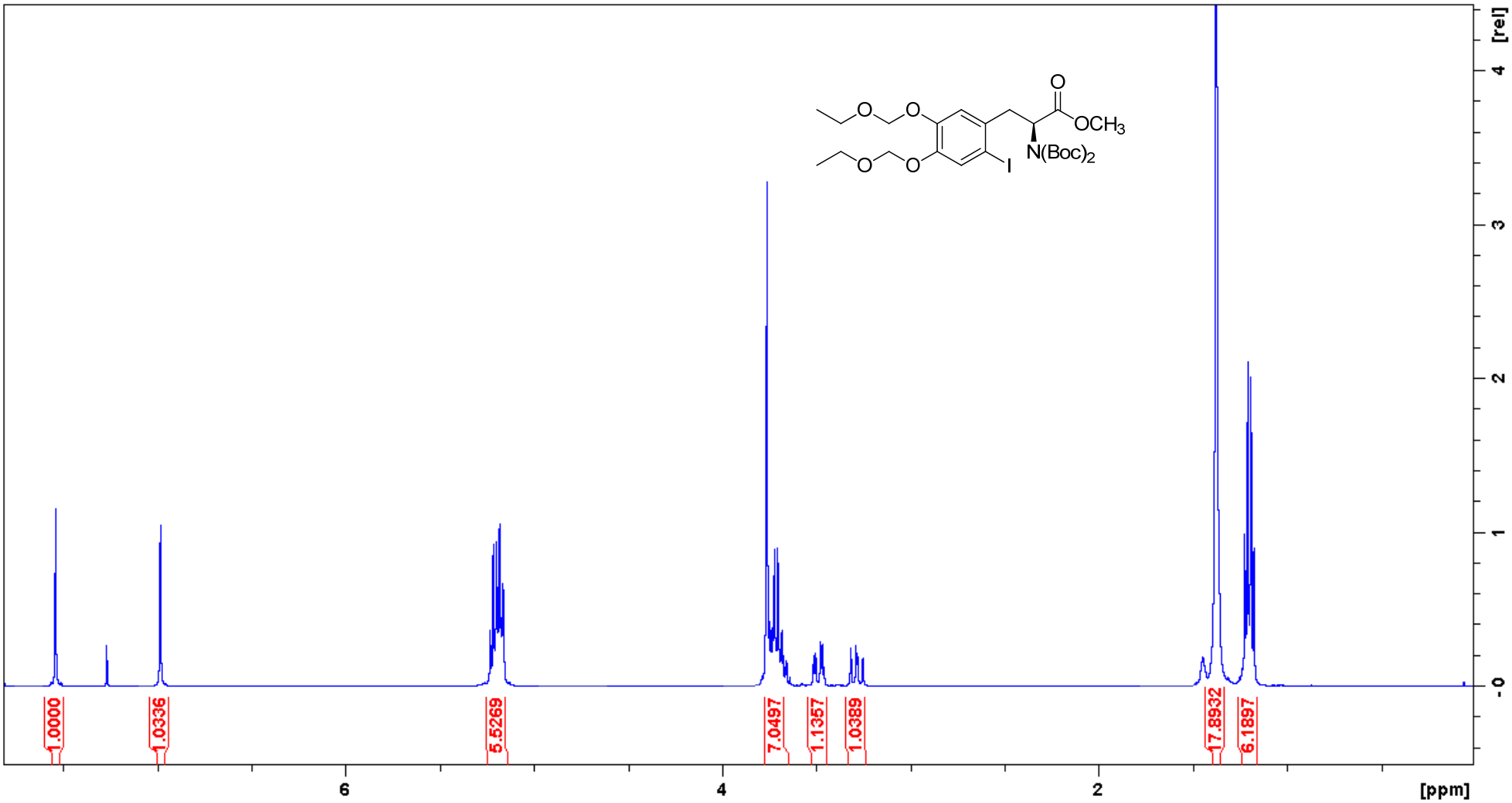
OCH3
NH(Boc)
I
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
1.03
4.46
0.76
1.09
7.55
1.23
1.12
20.12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N(Boc)2
I
[rel]
4
3
2
1
-0
1.0000
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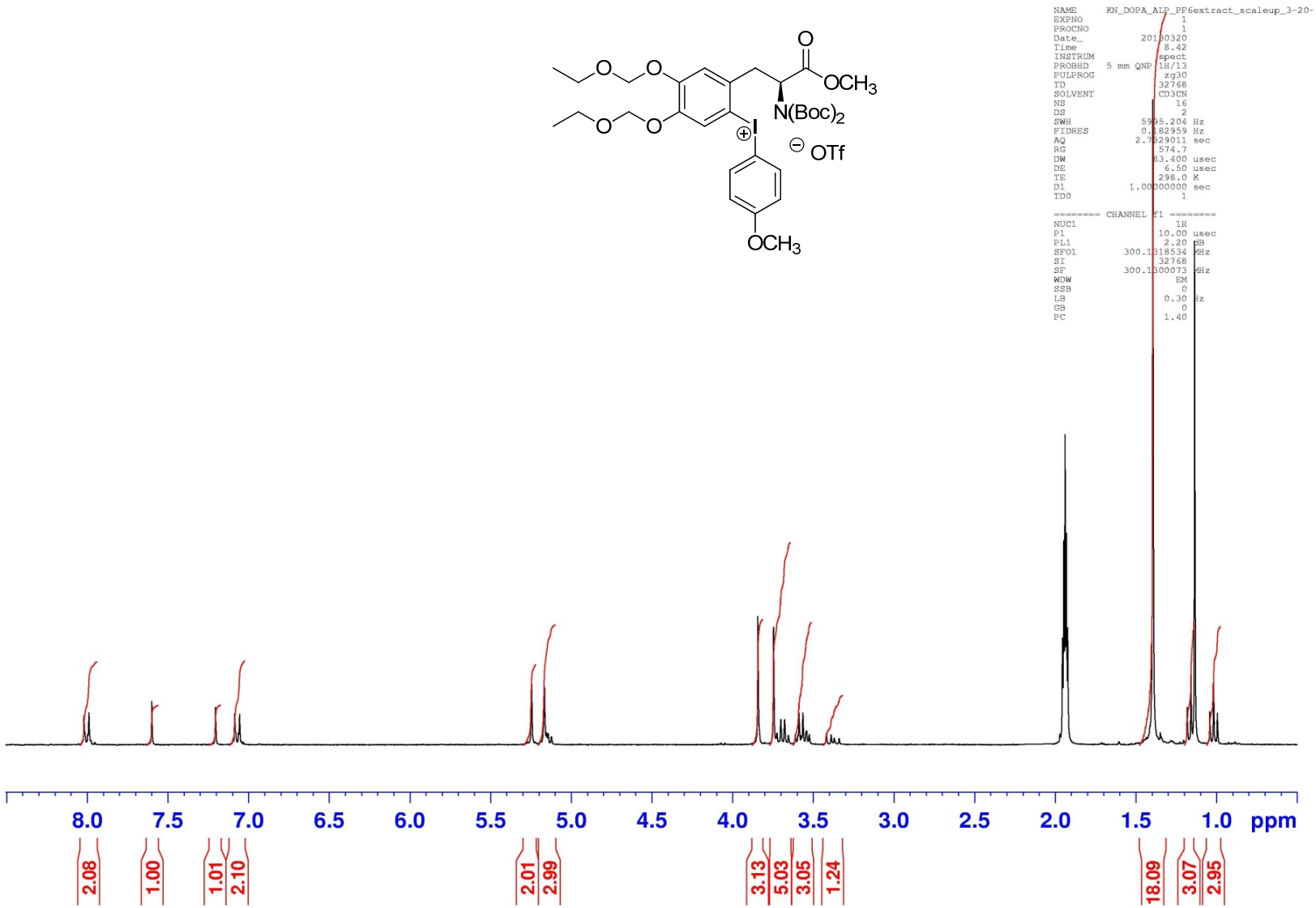
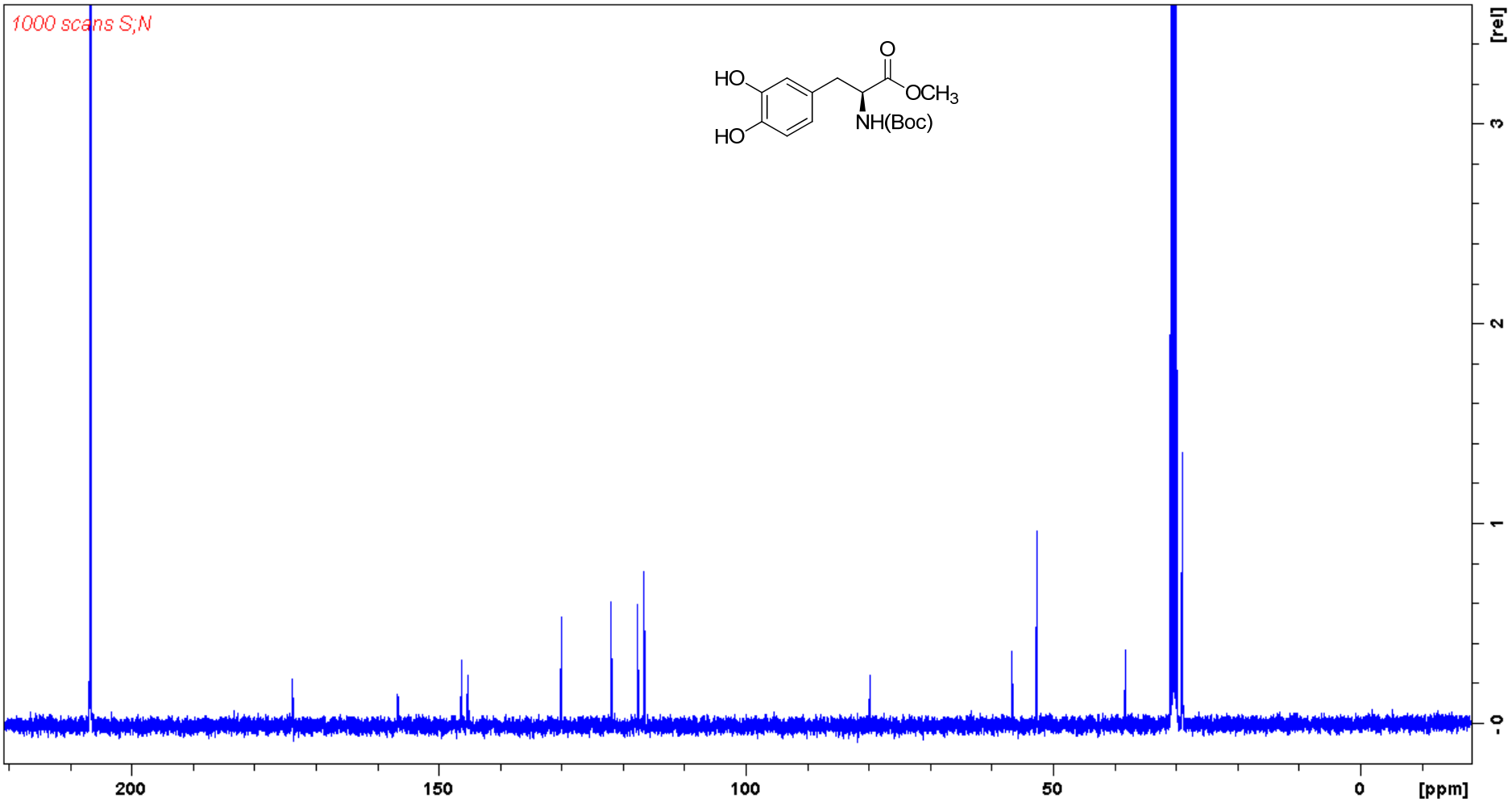
1.0389
17.8932
6.1897
6
4
2
[ppm]


O
OCH3
N(Boc)2
OTf
OCH3
NAME KN_DOPA_ALP_PF6extract_scaleup_3-20-
EXPNO 1
PROCNO 1
Date_ 20130320
Time 8.42
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 32768
SOLVENT CD3CN
NS 16
DS 2
SWH 5995.204 Hz
FIDRES 0.182959 Hz
AQ 2.7329011 sec
RG 574.7
DW 83.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.00 usec
PL1 2.20 dB
SFO1 300.1318534 MHz
SI 32768
SF 300.1300073 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
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
ppm
2.08
1.00
1.01
2.10
2.01
2.99
3.13
5.03
3.05
1.24
18.09
3.07
2.95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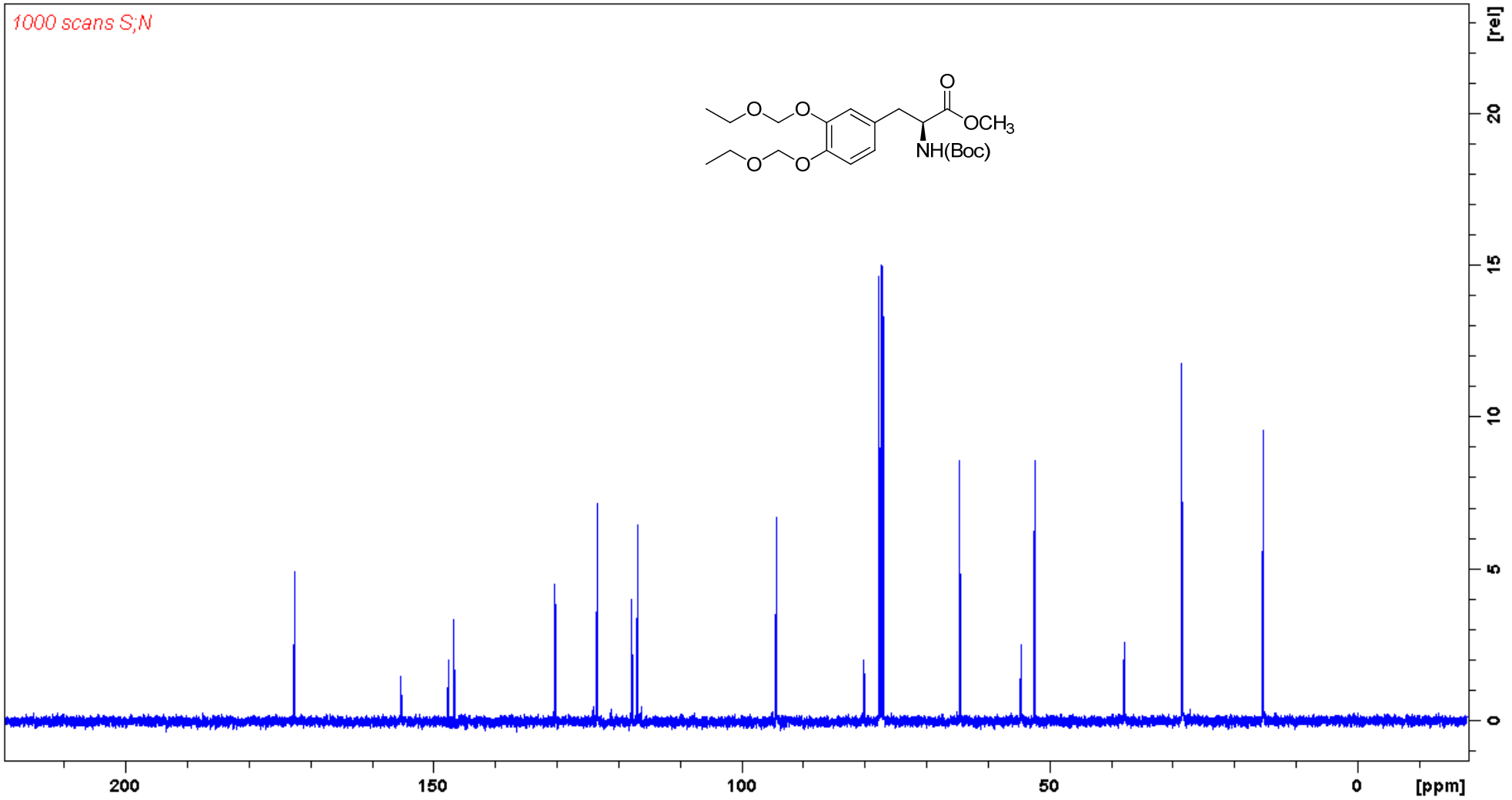
HO
HO
O
OCH3
NH(Boc)
200
150
100
50
0
[ppm]
[rel]
3
2
1
-0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NH(Boc)
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5
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100
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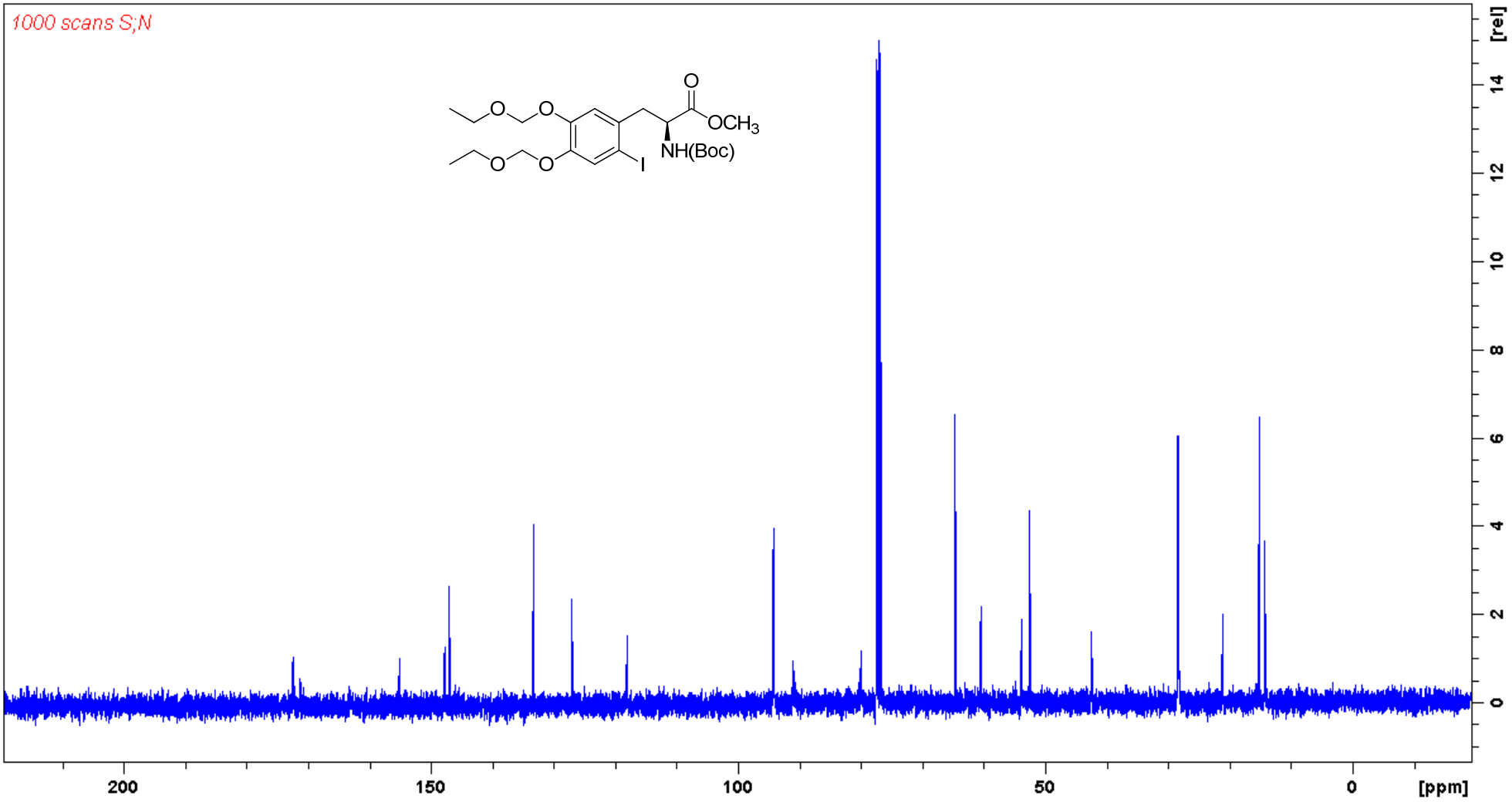
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NH(Boc)
I
[rel]
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12
10
8
6
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2
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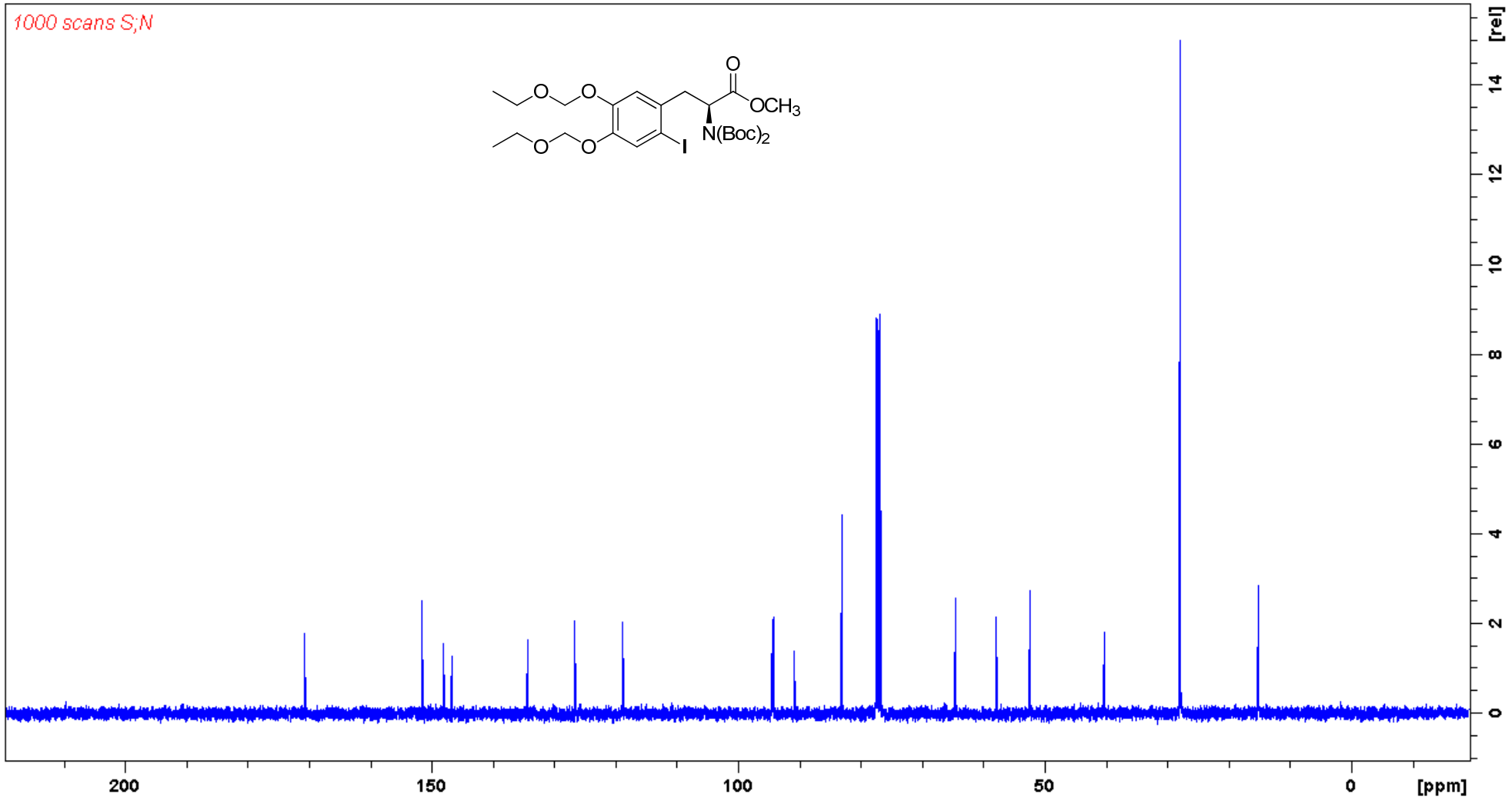
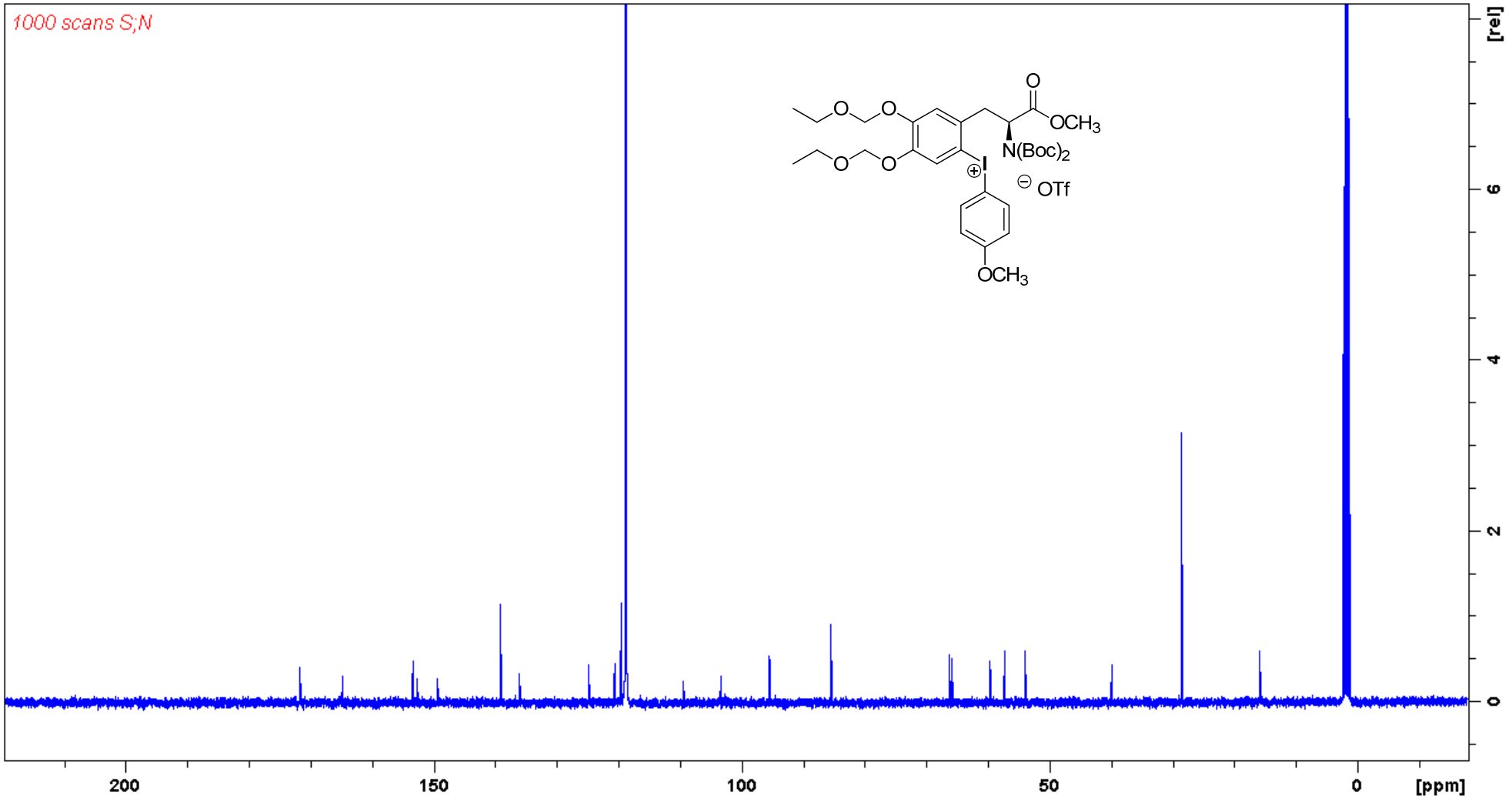
50
0
[ppm]


1000 scans S;N
O
OCH3
N(Boc)2
O
O
O
O
I
[rel]
0
2
4
6
8
10
12
14
200
150
100
50
0
[ppm]


1000 scans S;N
O
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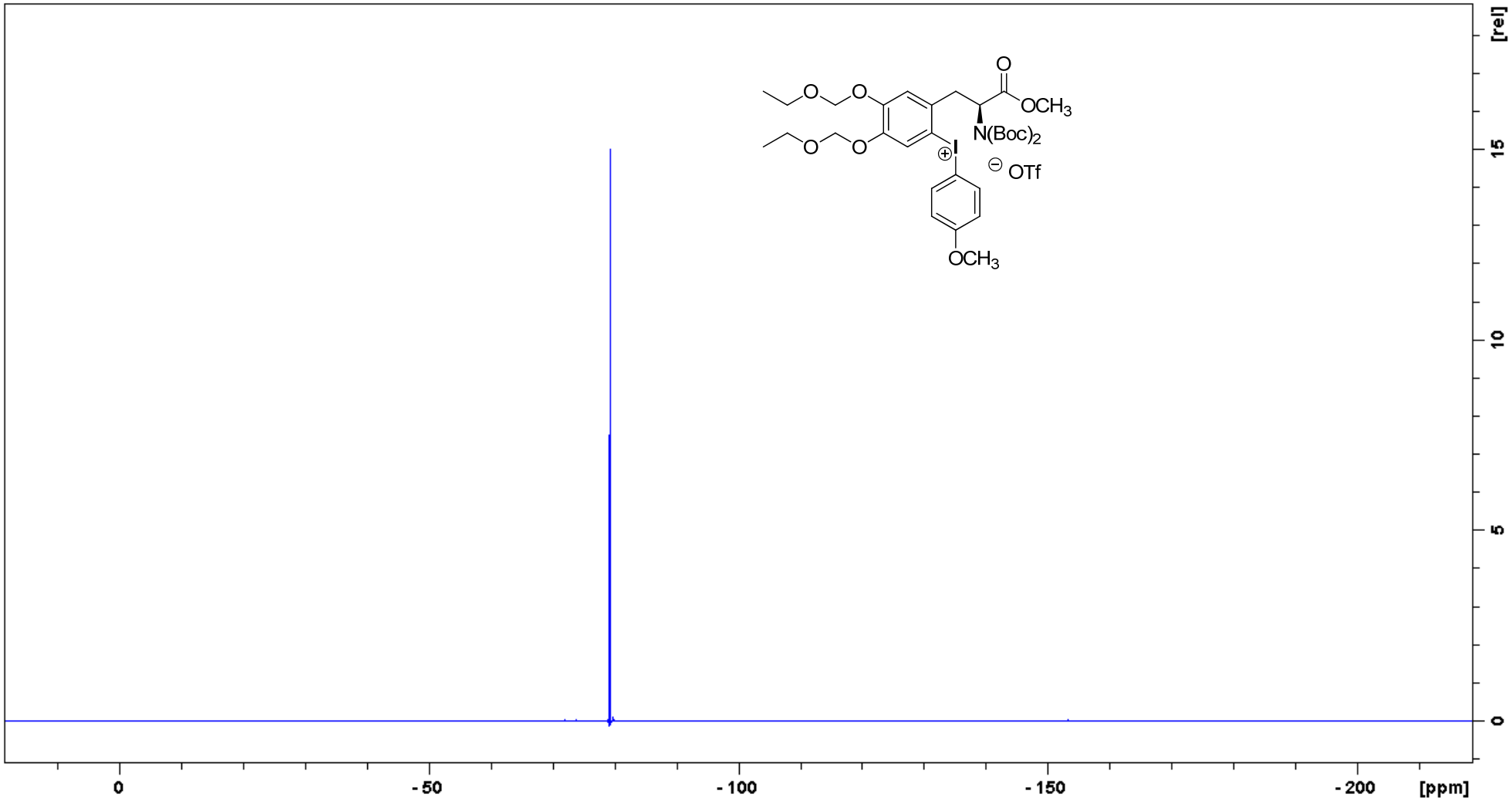
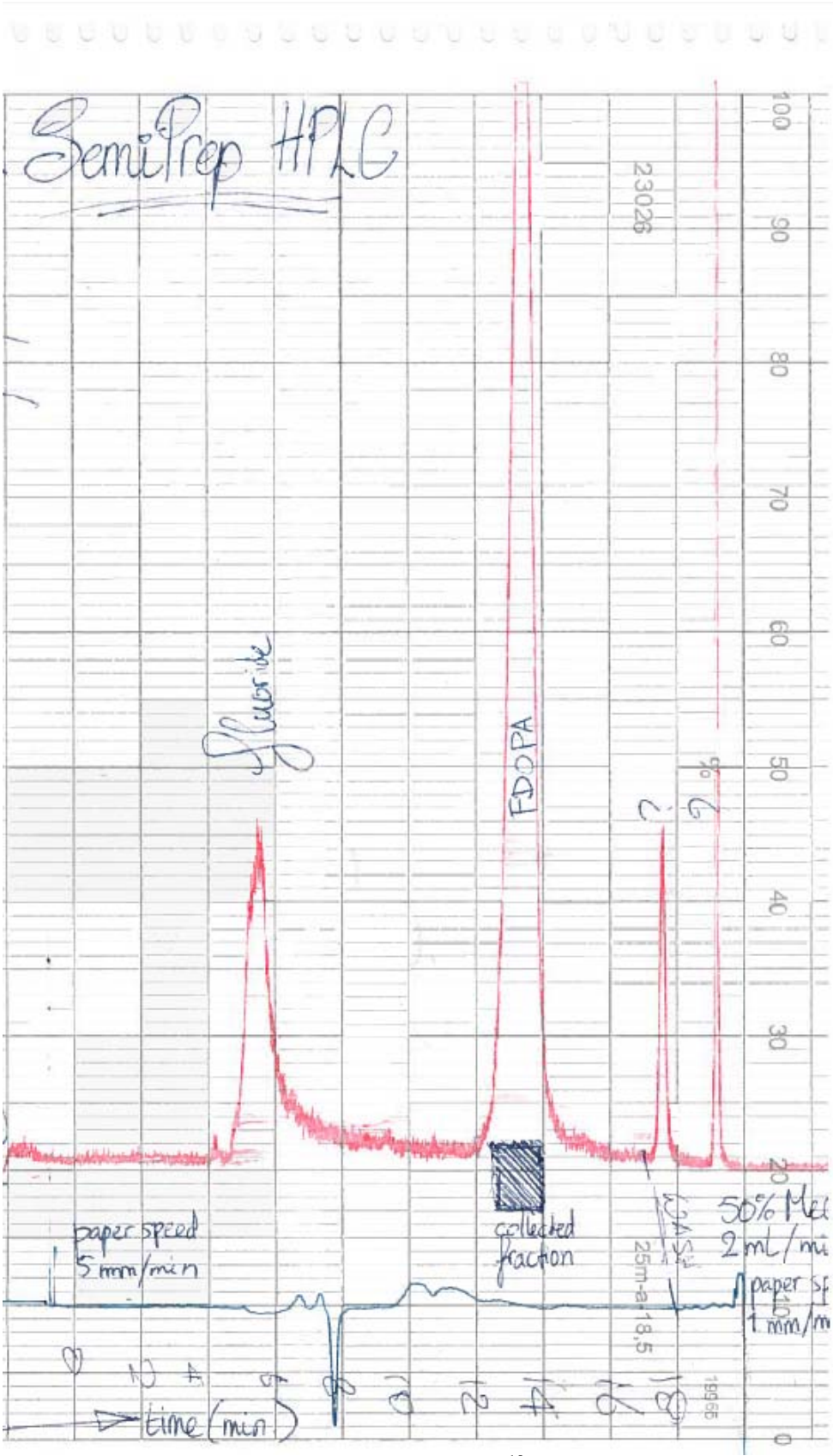
N(Boc)2
I
OTf
OCH3
[rel]
6
4
2
0
200
150
100
50
0
[ppm]


O
OCH3
N(Boc)2
OTf
OCH3
[rel]
15
10
5
0
0
-50
-100
-150
-200
[ppm]



Chromatogram semi-preparative HPLC of n.c.a. ^{18}FDOPA-H

Components table

	Peak Name	RT	Area	% Area	Amount (µM)	Units	volume_ml	Max_volume	activity_MBq	time_EOS	SA_GBqmmol	Dilution
1	Ascorbinezuur	0,300					1		2	14:50		1,00000
2	L-dopa	1,000					1		2	14:50		1,00000
3	FDOPA	1,442	958	100,00	0,060		1	251075,60	2	14:50	10375,2	1,00000
4	[18F]DOPA	1,458	132563	92,98			1		2	14:50		1,00000
5	[18F]F-	0,422	10008	7,02			1		2	14:50		1,00000

3 GBq/L / 60 nmol/L = 50 GBq/mmol

Reported by User: Rolf Zijlma (Rolf)
Report Method: FDOPA_m
Report Method ID: 1428
Page: 2 of 3

Date Printed: 22-1-2014
Project Name: WJ FDopa
15:04:34 Europe/Amsterdam

rijksuniversiteit groningen

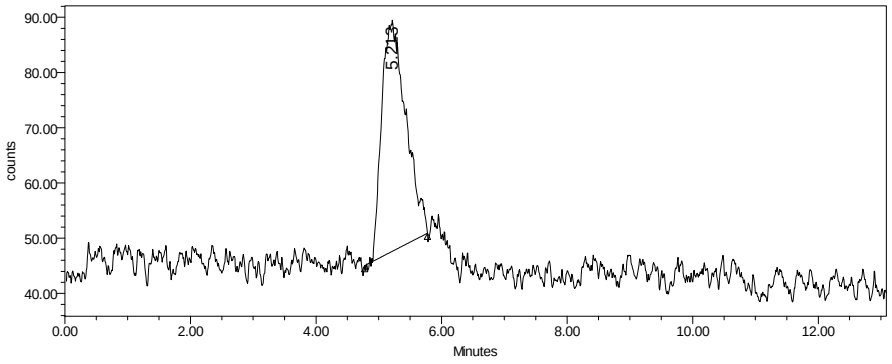
Chromatogram quantitative UPLC of n.c.a. ^{18}FDOPA-H

Identity and Purity Report

UCSF Radiopharmaceutical Facility

SAMPLE INFORMATION

Sample Name:	6FDOPA	Acquired By:	salma
Sample Type:	Unknown	Sample Set Name:	6FDOPA
Vial:	3	Acq. Method Set:	FDOPAChiral
Injection #:	1	Processing Method:	Methionine Radio
Injection Volume:	20.00 ul	Channel Name:	eSATIN-Ch2
Run Time:	15.0 Minutes	Proc. Chnl. Descr.:	Radioactivity
Date Acquired:	8/23/2013 12:07:43 PM PDT		
Date Processed:	8/23/2013 12:22:11 PM PDT		



Channel: eSATIN-Ch2; Processed Channel: Radioactivity; Result Id: 2734; Processing Method: Methionine Radio

Processed Channel Descr.: Radioactivity

	Processed Channel Descr.	RT	Area	% Area
1	Radioactivity	5.213	1124874	100.00

Reported by User: Salma Jivan (salma)
Report Method: Identity and Purity Report
Report Method ID 2598
Page: 1 of 1

Project Name: MET_C11_HPLC
Date Printed:
8/23/2013
12:22:45 PM US/Pacific

Chromatogram chiral analytical column of n.c.a. ^{18}FDOPA-H (determination e.e.)

Components table

	Peak Name	RT	Area	% Area	Amount	Units	volume_ml	Max_volume	activity_MBq	time_EOS	SA_GBqmmol	Dilution
1	Ascorbinezuur	0,300					16		857	14:15		5,00000
2	L-dopa	1,096	152430	1,96	9,434		16	1589,97	857	14:15	1220,7	5,00000
3	FDOPA	1,541	7824180	98,04	609,530		16	16,49	857	14:15	12,7	5,00000
4	[18F]DOPA	1,862	282180	99,28			16		857	14:15		5,00000
5	[18F]F-	0,480	2045	0,72			16		857	14:15		5,00000

Reported by User: Bram Maas (Bram)
Report Method: FDOPA_rm
Report Method ID: 4925
Page: 2 of 3

Date Printed: 1-8-2013
Project Name: FDOPA-
14:24:54 Europe/Amsterdam

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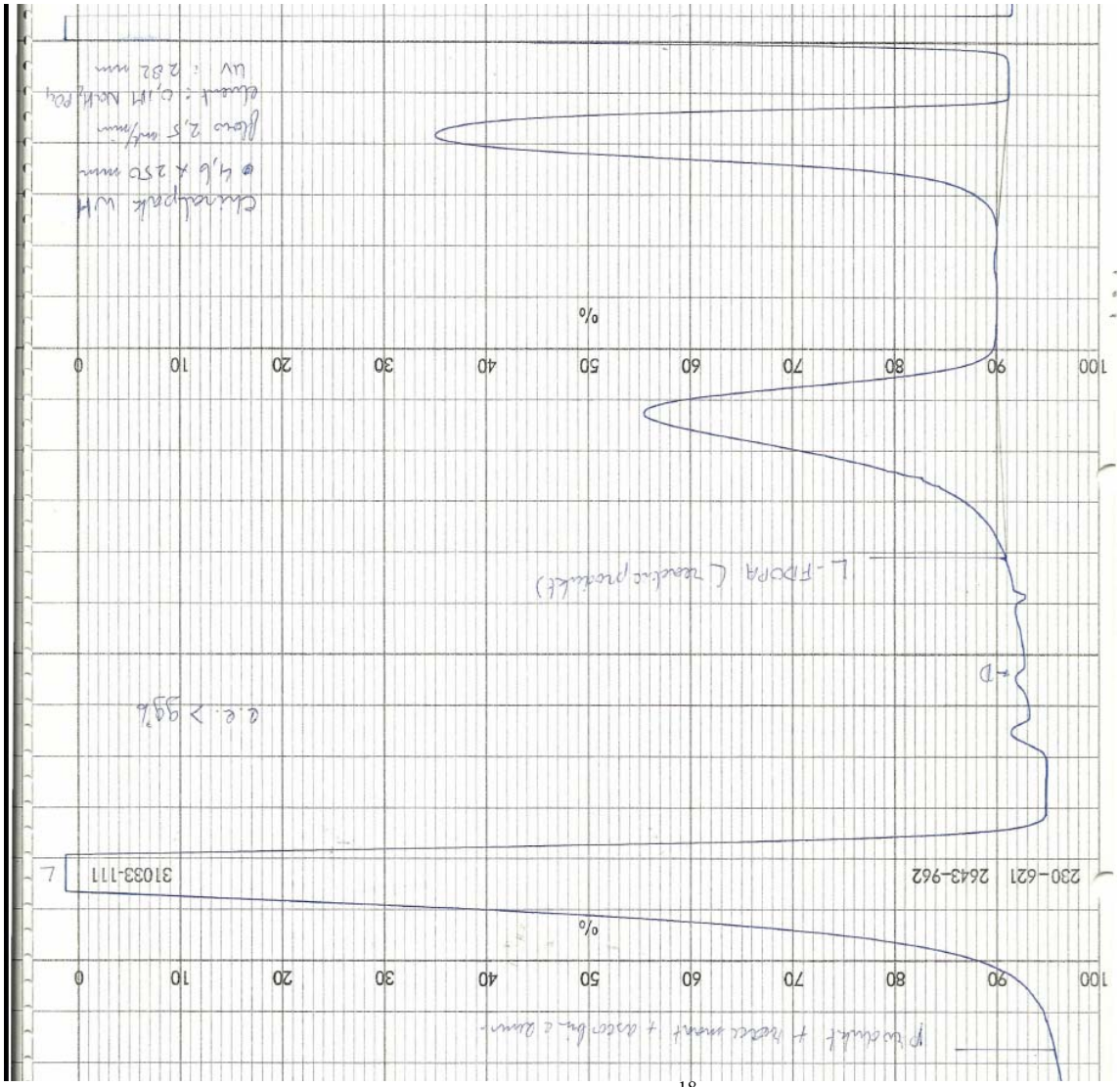
Chromatogram quantitative UPLC of carrier-added ^{18}FDOPA-L



Chromatogram chiral analytical column of carrier-added ^{18}FDOPA-L (determination e.e.)