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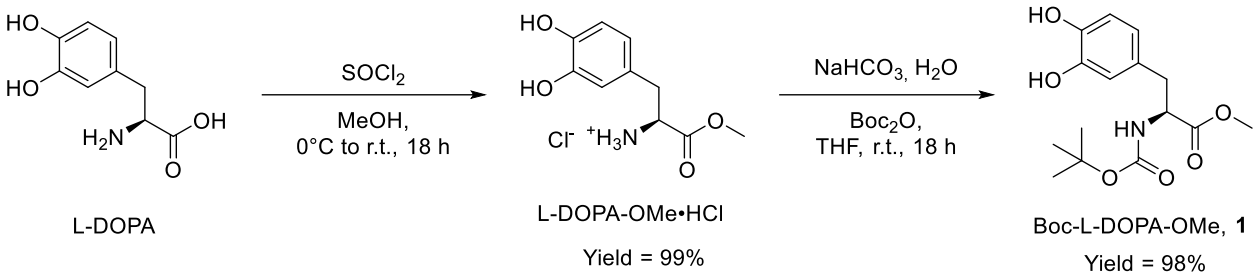
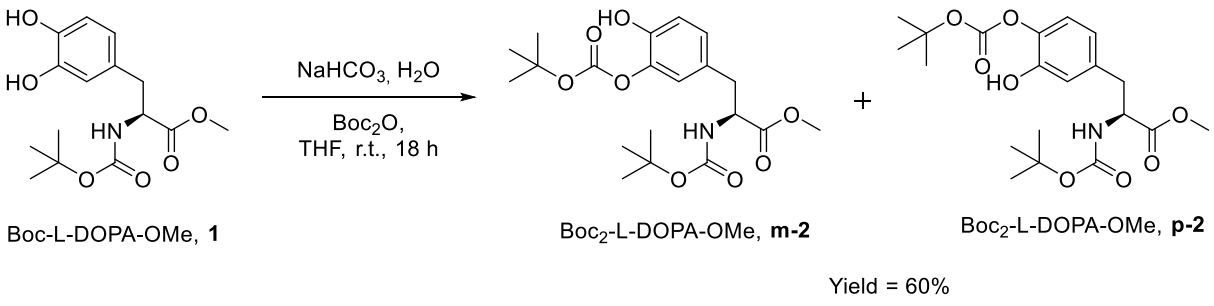
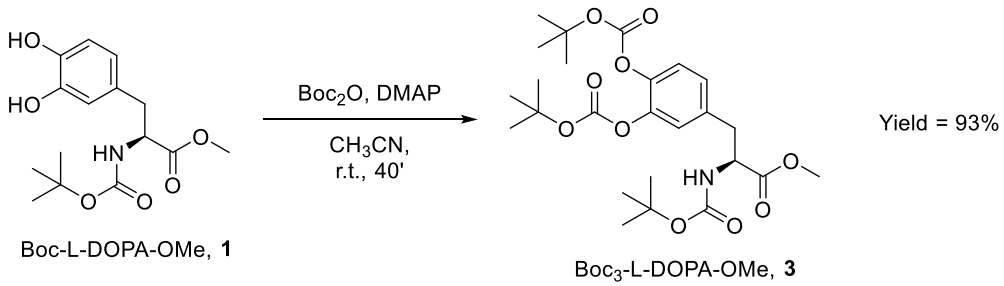


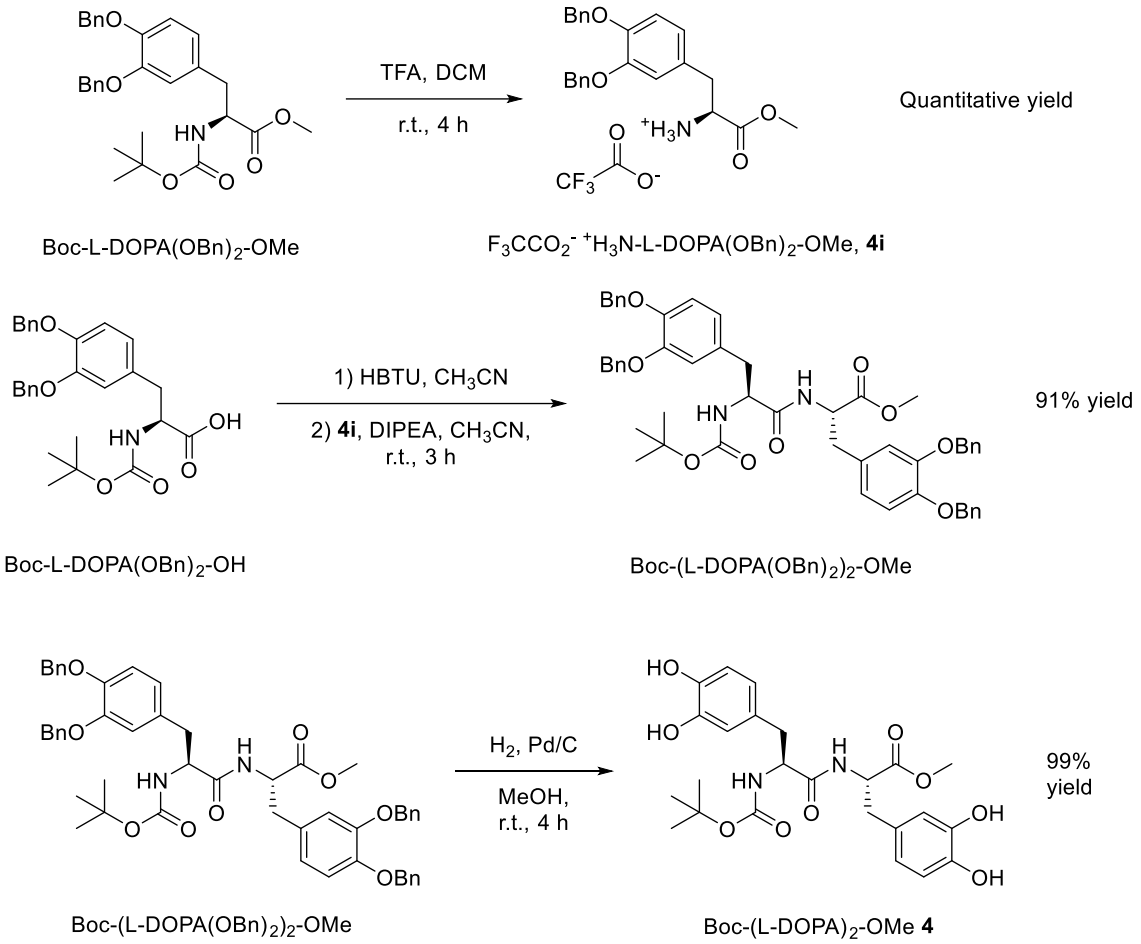
Scheme S1. Synthesis of Boc-L-DOPA-OMe, **1**, with yields.



Scheme S2. Synthesis of Boc_2-L-DOPA-OMe, **m-2** + **p-2**, with yield after flash chromatography. In this reaction some interferents are present: the starting material and the di-substituted product Boc_3-L-DOPA-OMe, **3**, are found at the end of the process. The two species ***m*-2** + ***p*-2** are purified as an inseparable mixture with a 1:1 ratio



Scheme S3. Synthesis of Boc_3-L-DOPA-OMe, **3**, with yield after flash chromatography.



Scheme S4. Synthesis of Boc-(L-DOPA)$_2$-OMe, **4**, with yield.

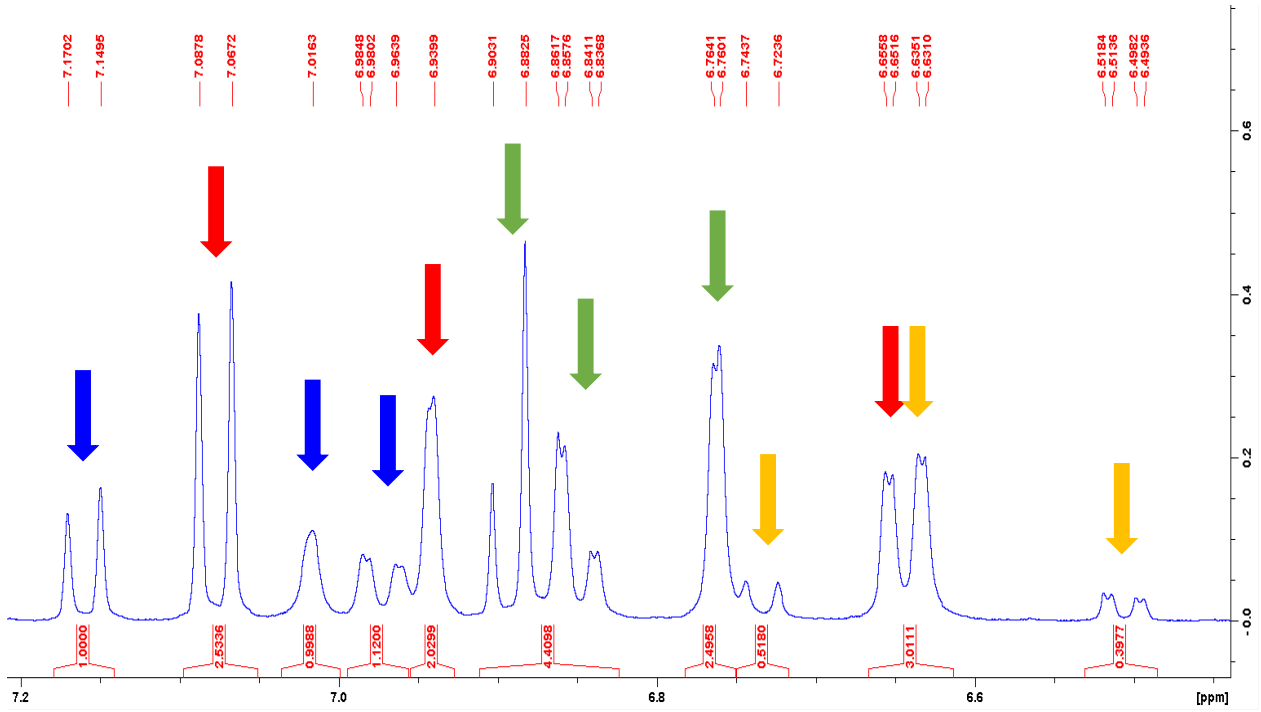


Figure S1. Zoom on the range 6.45 - 7.2 ppm of the ^{1}H-NMR spectrum of the crude of the reaction for Boc_2-L-DOPA-OMe **2** synthesis. Each arrow indicates the shifts of the three H of the aromatic ring for each molecule, divided per color: blue for **3**, red for **p-2**, green for **m-2**, gold for **1**. It is possible to assign the relative ratio of each molecule in the crude: **3** : **p-2** : **m-2** : **1** = 1 : 2.5 : 2.5 : 0.5.

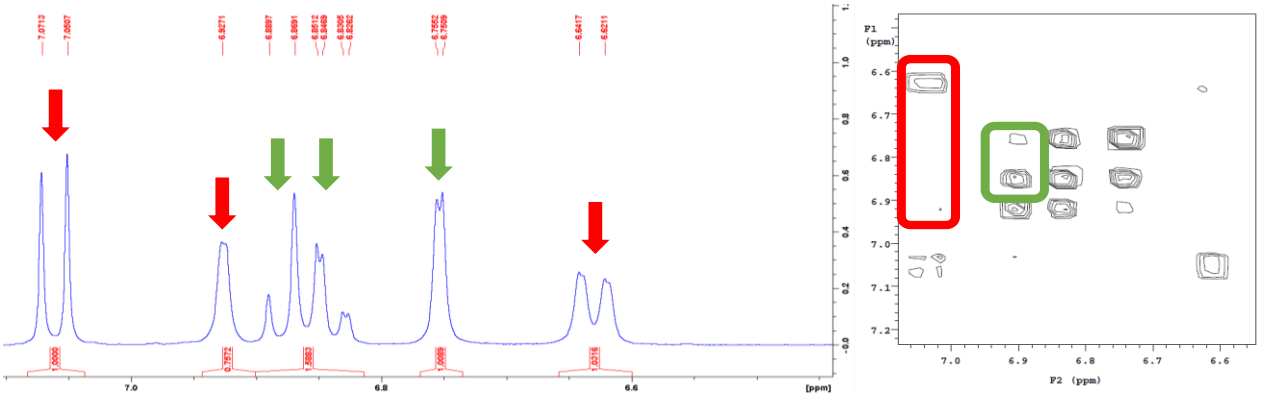
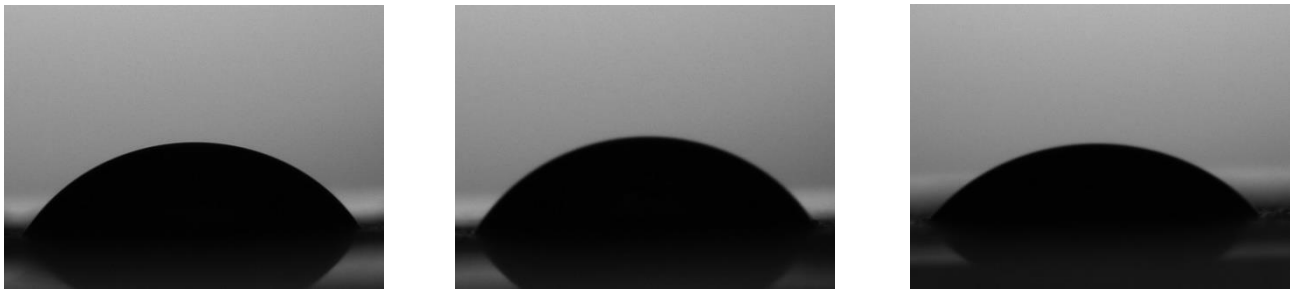


Figure S2. Insets of ^{1}H NMR and *g*-COSY spectra of an inseparable mixture of ***m*-2** and ***p*-2**. The signals of the three aromatic hydrogens, belonging to the two species are highlighted in red and green.

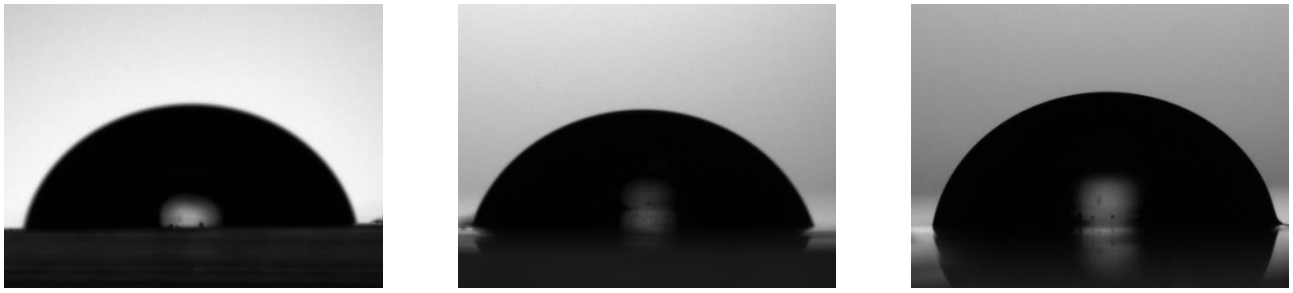


Water
54.7 ± 3.9°

$CaCl_2$
58.0 ± 1.8°

PBS pH 7.4
49.9 ± 1.0°

Figure S3. Pictures of the contact angles of dried surface of **1** with a drop of water, 1M $CalCl_2$ solution or a pH 7.4 PBS solution (from left to right).

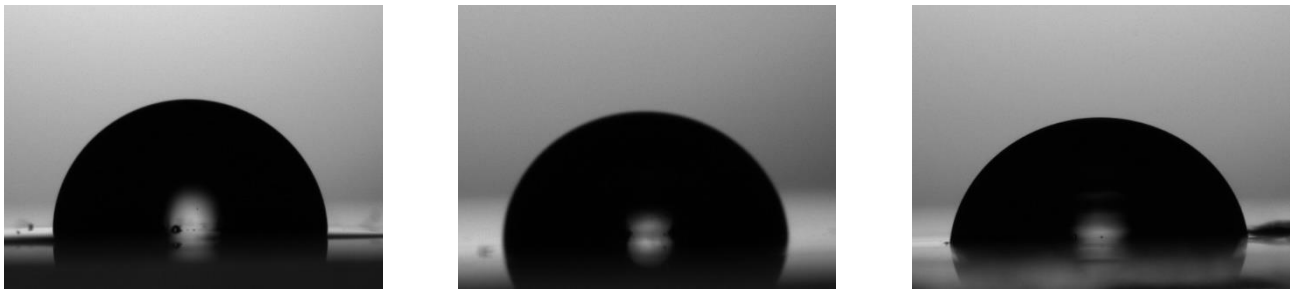


Water
78.2 ± 2.0°

$CaCl_2$
63.7 ± 1.0°

PBS pH 7.4
76.6 ± 5.4°

Figure S4. Pictures of the contact angles of dried surface of **2** (***m*-2** + ***p*-2**) with a drop of water, 1M $CalCl_2$ solution or a pH 7.4 PBS solution (from left to right).



Water
94.0 ± 0.5°

$CaCl_2$
81.1 ± 1.7°

PBS pH 7.4
84.9 ± 1.1°

Figure S5. Pictures of the contact angles of dried surface of **3** with a drop of water, 1M $CaCl_2$ solution or a pH 7.4 PBS solution (from left to right).

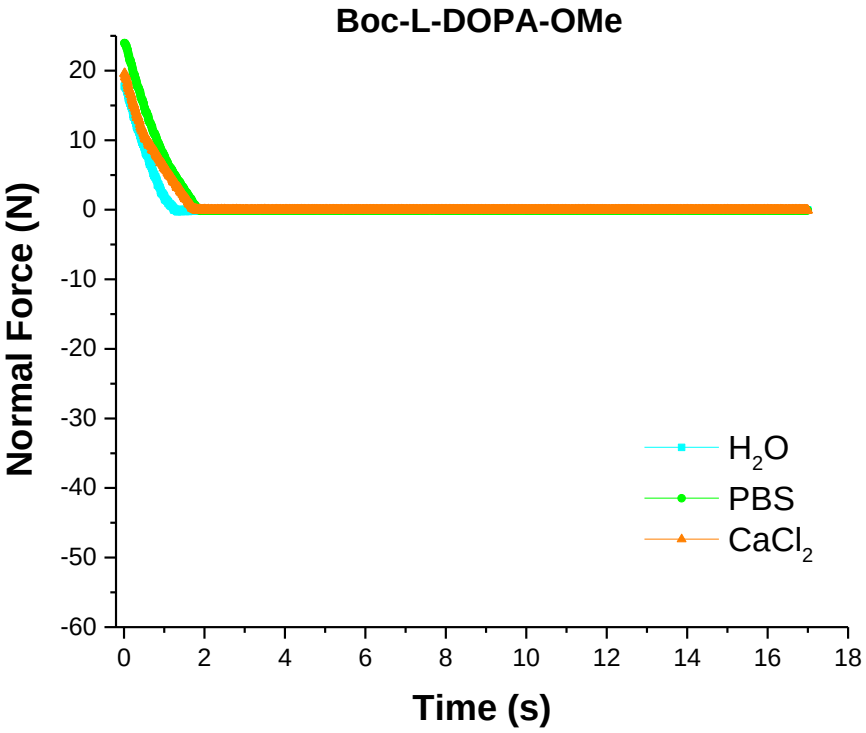
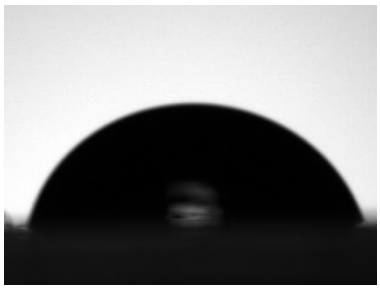
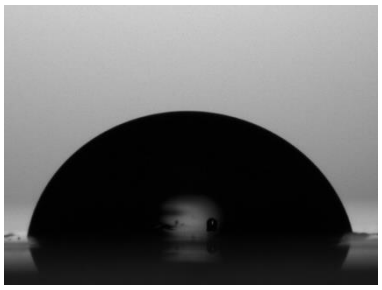


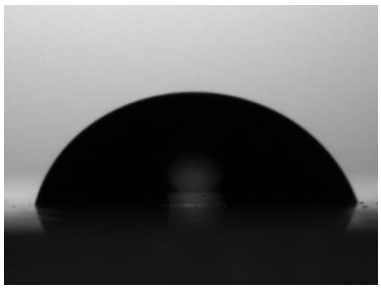
Figure S6. Rheometer tack tests for Boc-L-DOPA-OMe **1** in the three aqueous media.



Water
69.3 ± 2.5°



$CaCl_2$
71.2 ± 2.2°



PBS pH 7.4
67.7 ± 3.9°

Figure S7. Pictures of the contact angles of dried surface of **4** with a drop of water, 1M $CaCl_2$ solution or a pH 7.4 PBS solution (from left to right).

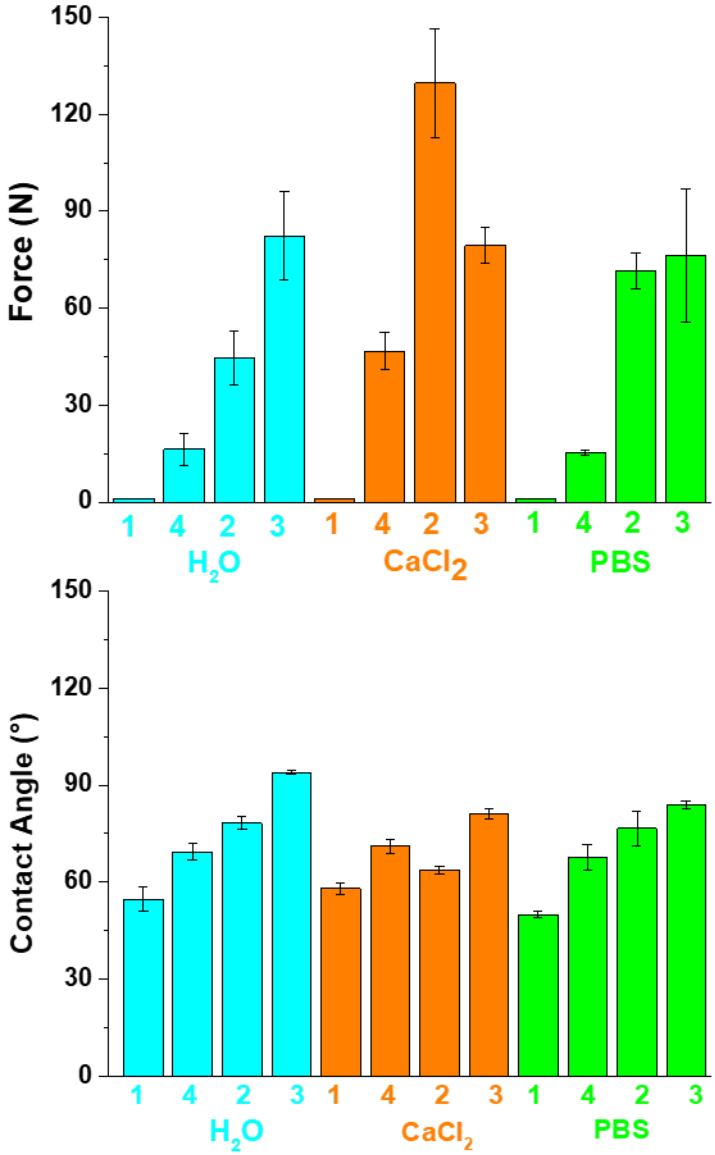


Figure S8. Adhesive forces and contact angles comparison for compounds **1-4** in the three media. Increasing the Boc groups on the catechol (zero for molecules **1** and **4**, one for **2** and two for **3**) adhesive forces increase together with contact angles in all media.

Synthesis and characterization of compounds 1-4

Synthesis: General Remarks. Solvents were dried by distillation before use. All reactions were carried out in dried glassware. The melting points of the compounds were determined in open capillaries and are uncorrected. High quality infrared spectra (64 scans) were obtained at 2 cm^{-1} resolution with an ATR-FT-IR Bruker Alpha System spectrometer. All spectra were obtained in 3 mM solutions in CH_2Cl_2. All compounds were dried *in vacuo* and all the sample preparations were performed in a nitrogen atmosphere. NMR spectra were recorded with a Varian Inova 400 spectrometer at 400 MHz (^{1}H NMR) and at 100 MHz (^{13}C NMR). Chemical shifts are reported in δ values relative to the solvent peak. HPLC-MS was used to check the purity of compounds.

Boc-L-DOPA-OMe 1 - $SOCl_2$ (10 mL, 137 mmol) is added dropwise at 0 °C to a flask containing 60 mL of CH_3OH, then 5 g of L-DOPA (25.4 mmol) is added little by little. The reaction is left under stirring at RT for 24 hours. The solvent is then removed under vacuum, thus obtaining L-DOPA-OMe·HCl with a yield of 99%. The product L-DOPA-OMe·HCl is dissolved in a solution of $NaHCO_3$ (4.27 g, 50.8 mmol) and 58 mL of water, then a solution of Boc_2O (5.82 mL, 25.4 mmol) in THF (30 mL) is added. The solution is stirred for 18 hours. The THF is removed under reduced pressure, the residue is suspended in H_2O (10 mL) and extracted with ethyl acetate (150 mL x 3). The combined organic phase is washed with 1M HCl (2 x 20 mL), with a saturated aqueous $NaHCO_3$ solution (1 x 20 mL) and with H_2O (1 x 20 mL). The organic phase is then dried over Na_2SO_4 and the solvent is evaporated. Boc-L-DOPA-OMe **1** is obtained as a white solid with 98% yield. M.p. = 137-138 °C; $[\alpha]_D^{25}$ +18.0° (c = 0.5 in EtOAc); IR (ATR-IR): ν 3342, 3297, 1739, 1695, 1606, 1514 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz): δ 1.38 (9H, s, *t*-Bu), 2.75 (1H, dd, *J* = 8.4, 13.6 Hz, ArC*H*HCH), 2.89 (1H, dd, *J* = 5.6, 13.6 Hz, ArCH*H*CH), 3.66 (3H, s, OCH_3), 4.25 (1H, dd, *J* = 5.6, 7.6 Hz, CH_2C*H*NH), 6.46 (1H, dd, *J* = 1.6, 8.0 Hz Hz, Ar), 6.61 (1H, d, *J* = 1.6 Hz Ar), 6.66 (1H, d, *J* = 8.0 Hz, Ar); ^{13}C (CD_3OD, 100 MHz): δ 27.3, 36.8, 51.2, 55.3, 79.3, 114.9, 115.9, 120.3, 128.2, 143.8, 144.8, 156.3, 173.0. HPLC-MS (API-ES): 4.22 min, $[M+Na]^+$=334. Anal. Calcd. for $C_{15}H_{21}NO_6$: C, 57.87; H, 6.80; N, 4.50. Found: C, 57.84; H, 6.77; N, 4.53.

***m*-(Boc)$_2$-L-DOPA-OMe *m*-2 + *p*-(Boc)$_2$-L-DOPA-OMe *p*-2** - Boc-L-DOPA-OMe **1** (0.60 g, 1.93 mmol) is dissolved in 4.4 mL of saturated $NaHCO_3$ solution, then Boc_2O (0.44 mL, 1.93 mmol) in THF (4.56 mL) is added. The solution is stirred for 18 hours at room temperature. The THF is removed under vacuum, the residue is suspended in 5 mL HCl 1M and extracted with ethyl acetate (15 mL x 3). The combined organic phase is washed twice with 2.5 mL of 1M HCl, once with 2 mL of a saturated aqueous $NaHCO_3$ solution and with 2 mL of H_2O. The organic phase is then dried over Na_2SO_4 and the solvent is evaporated. Products ***m*-2** and ***p*-2** were obtained as an inseparable mixture in 1:1 ratio after flash chromatography (cyclohexane:ethyl acetate 4:1) with 60% yield as a sticky liquid that becomes a transparent solid in 48 h. IR (ATR-IR): ν 3367, 1756, 1742, 1717, 1685, 1607, 1510 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.40 (9H, s, *t*-Bu), 1.53 (9H, s, *t*-Bu), 2.89-3.08 (2H, m, ArC*H*$_2$CH), 3.69 (3H, s, OCH_3), 4.47-4.57 (1H, m, CH_2C*H*NH), 4.99 (1H, d, *J* = 6.4 Hz, NH), 5.87 (0.5H, bs, OH), 5.87 (0.5H, bs, OH), 6.63 (0.5H, d, *J* = 8.0 Hz, Ar), 6.75 (0.5H, s, Ar), 6.86 (2 x 0.5H, AB, *J* = 8.0 Hz), 6.93 (0.5H, s, Ar), 7.02 (0.5H, d, *J* = 8.0 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 27.6, 28.2, 37.4, 37.7, 52.2, 54.3, 54.4, 60.4, 80.1, 84.3, 117.4, 118.2, 121.4, 122.1, 122.9, 127.5, 128.4, 134.9, 137.9, 146.2, 147.1, 151.2, 151.3, 155.1, 171.2, 172.2. HPLC-MS (API-ES): 8.93 min, $[M+Na]^+$=434. Anal. Calcd. for $C_{20}H_{29}NO_8$: C, 58.38; H, 7.10; N, 3.40. Found: C, 58.40; H, 7.12; N, 3.37.

Boc$_3$-L-DOPA-OMe 3 - Boc-L-DOPA-OMe **1** (1 g, 3.2 mmol) is dissolved in 40 mL of CH_3CN, then 195 mg of DMAP (1.6 mmol) and 1.475 mL of Boc_2O (6.4 mmol) are added. The solution is stirred for 40 minutes at room temperature. The solvent is removed under vacuum, then the residue is suspended in 2 mL of HCl 1M, extracted with ethyl acetate (50 mL x 3) and washed with H_2O (1 x 20 mL). The organic layer is then dried over Na_2SO_4 and concentrated under *vacuum*. The product is eventually purified through flash chromatography (cyclohexane:ethyl acetate 4:1). The pure product is obtained with a 93% yield as a transparent, sticky liquid that becomes a white solid after about 24 hours. M.p: = 95-98 °C; $[\alpha]_D^{25}$ +33.0 ° (c = 0.5 in CH_2Cl_2); IR (ATR-IR): ν 3334, 1737, 1690, 1659, 1587, 1516 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.40 (9H, s, *t*-Bu), 1.52 (18H, s, 2 x *t*-Bu), 3.01-3.10 (2H, m, ArC*H*$_2$CH), 3.68 (3H, s, OCH_3), 4.55 (1H, q, *J* = 6.8 Hz, CH_2C*H*NH), 4.99 (1H, d, *J* = 8.0 Hz, NH), 6.97 (1H, dd, *J* = 1.7, 8.4 Hz, Ar), 7.02 (1H, d, *J* = 1.7 Hz, Ar), 7.16 (1H, d, *J* = 8.4 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.9, 27.6, 28.2, 37.5, 52.3, 54.2, 80.0, 83.7, 113.0, 124.0, 127.1, 134.7, 141.5, 142.3, 150.6, 150.7, 171.9. HPLC-MS (API-ES): 11.30 min, $[M+Na]^+$=534. Anal. Calcd. for $C_{25}H_{37}NO_{10}$: C, 58.70; H, 7.29; N, 2.74. Found: C, 58.75; H, 7.32; N, 2.75.

Boc-(L-DOPA)$_2$-OMe 4 - 1.8 g (3.67 mmol) of Boc-L-DOPA(OBn)$_2$-OMe [1] is deprotected to obtain Boc-L-DOPA(OBn)$_2$-OH.[1]

An equal amount of Boc-L-DOPA(OBn)$_2$-OMe (1.8 g, 3.67 mmol) is dissolved in 25 mL of CH_2Cl_2, then 5.1 mL of TFA (64.8 mmol) are added. The solution is stirred at room temperature for 4 hours. The solvent is removed under reduced pressure and the whole residue, composed of the desired intermediate [F_3CCOO^- ^+H_3N-L-DOPA(OBn)$_2$-OMe] **4i** and the remaining TFA, is used for the next step of the reaction, considering a quantitative yield for this one.

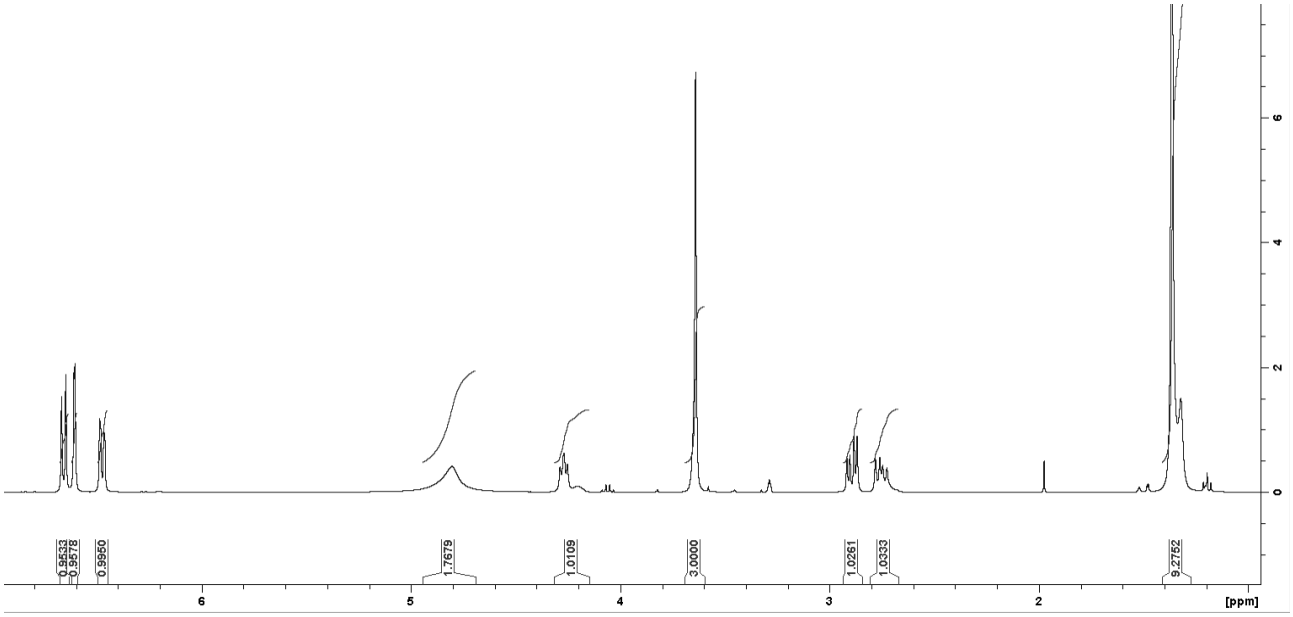
1.75 g of Boc-L-DOPA(OBn)$_2$-OH (3.67 mmol) is dissolved in 40 mL of CH_3CN together with 1.53 g of HBTU (4.0 mmol) and left under stirring at room temperature while a mixture of the previous residue containing **4i**, DIPEA (1.8 mL, 10.3 mmol) (the amount of DIPEA is calculated considering 2.2 equivalents plus 1 equivalent per equivalent of TFA remained in the residue after the solvent removal) and 10 mL of CH_3CN is added dropwise. After two hours the solvent is evaporated under vacuum, the residue is suspended in 10 mL of water, extracted with CH_2Cl_2 (50 mL x 3) and washed with 20 mL of water, HCl, saturated solution of $NaHCO_3$ and water again. The organic layer is dried over Na_2SO_4 and the solvent removed under vacuum. Boc-(L-DOPA(OBn)$_2$)$_2$-OMe is obtained as a white solid with a 94% yield.

0.70 g of Boc-(L-DOPA(OBn)$_2$)$_2$-OMe (0.82 mmol) is dissolved in 50 mL of CH_3OH and 70 mg of Pd/C 10% w/w are added to the solution, then the reaction is left under vigorous stirring for 4 h under H_2 atmosphere. The solution is filtered over Celite, then the solvent is evaporated under vacuum. The product is further purified by washing with n-hexane (2 mL x 3) to obtain a sticky liquid that becomes a white solid in 48 h hours. $[\alpha]_D^{25}$ -3.0 ° (c = 0.5 in CH_3OH); IR (ATR-IR): ν 3310, 1732, 1658, 1608, 1515 cm^{-1}; ^{1}H-NMR (CD_3OD, 400 MHz): δ 1.4 (s, 9H, *t*-Bu), 2.61 (dd, 1H, *J* = 3.2, 12.4 Hz, ArCH*H*NH), 2.81 – 2.97 (m, 3H, ArC*H*HNH + ArC*H*$_2$NH), 3.63 (s, 3H, OCH_3), 4.18 (t, 1H, *J* = 5.6 Hz, CH_2C*H*NH), 4.56 (t, 1H, *J* = 6.0 Hz, CHN*H*Boc), 6.44 (d, 1H, *J* = 7.6 Hz, CHN*H*CO), 6.49 (d, 1H, *J* = 8.4 Hz, CHN*H*CO), 6.58 – 6.65 (m, 4H, Ar); ^{13}C NMR (CD_3OD, 100 MHz): δ 26.5, 27.3, 36.6, 37.2, 51.2, 53.8, 56.1, 79.3, 82.7, 89.7, 114.8, 115.9, 116.3, 117.4, 120.3, 122.0, 123.1, 127.2, 127.6, 128.4, 143.9, 144.8, 152.0, 156.1, 171.8, 172.8. HPLC-MS (API-ES): 8.00 min, $[M+H]^+$=491. Anal. Calcd. for Chemical Formula: $C_{24}H_{30}N_2O_9$: C, 58.77; H, 6.17; N, 5.71. Found: C, 58.76; H, 6.19; N, 5.70.

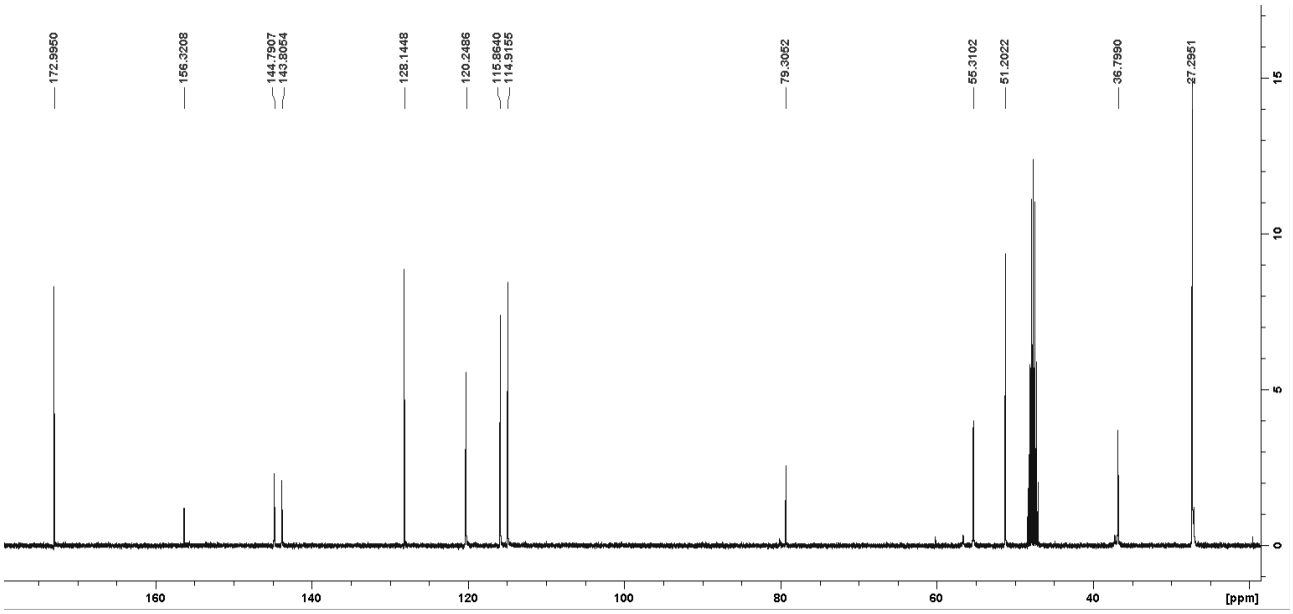
References

(1) A. Gaucher, L. Dutot, O. Barbeau, W. Hamchaoui, M. Wakselman and J. P. Mazaleyrat, *Tetrahedron Asymmetry*, 2005, **16**, 857–864.

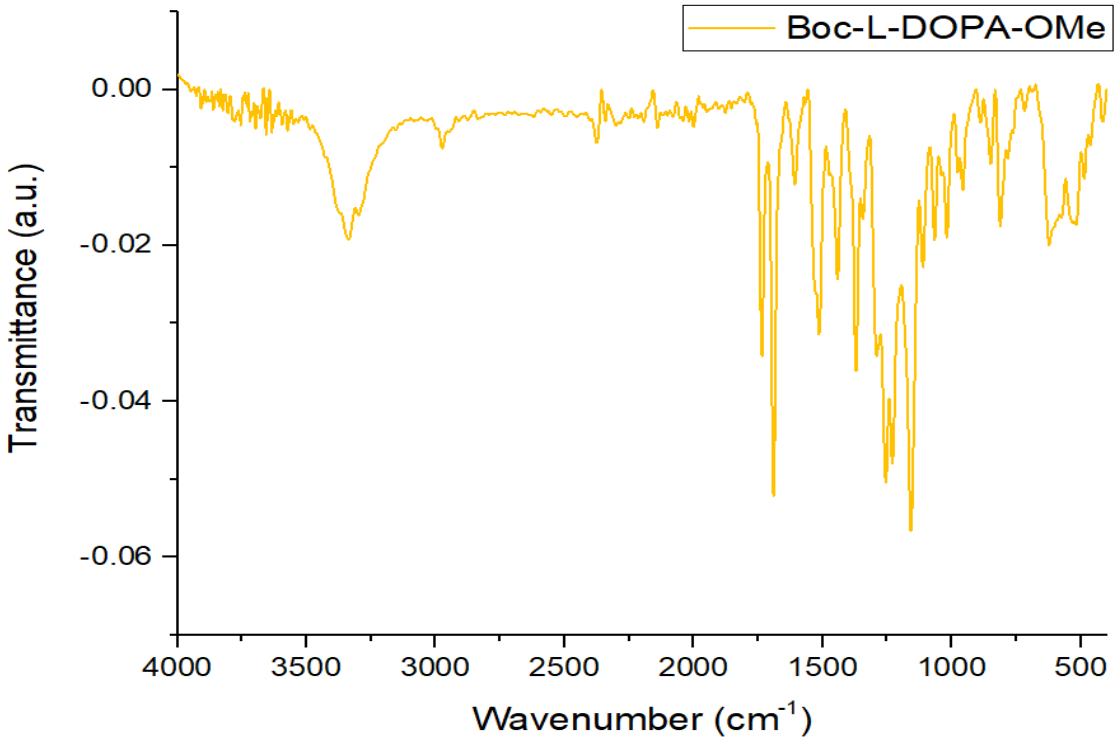
Boc-L-DOPA-OMe, 1



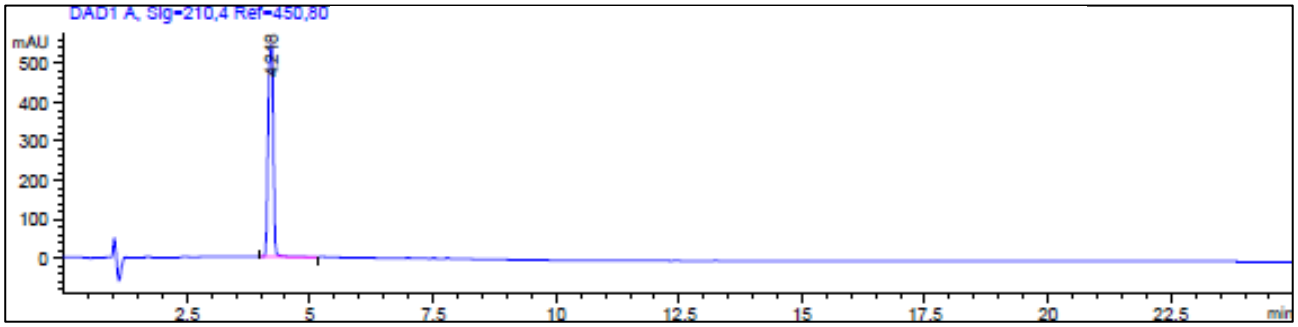
^{1}H-NMR spectrum of Boc-L-DOPA-OMe **1**, registered in CD_3OD. Traces of ethyl acetate (4.12, 2.05, 1.26 ppm) are present.



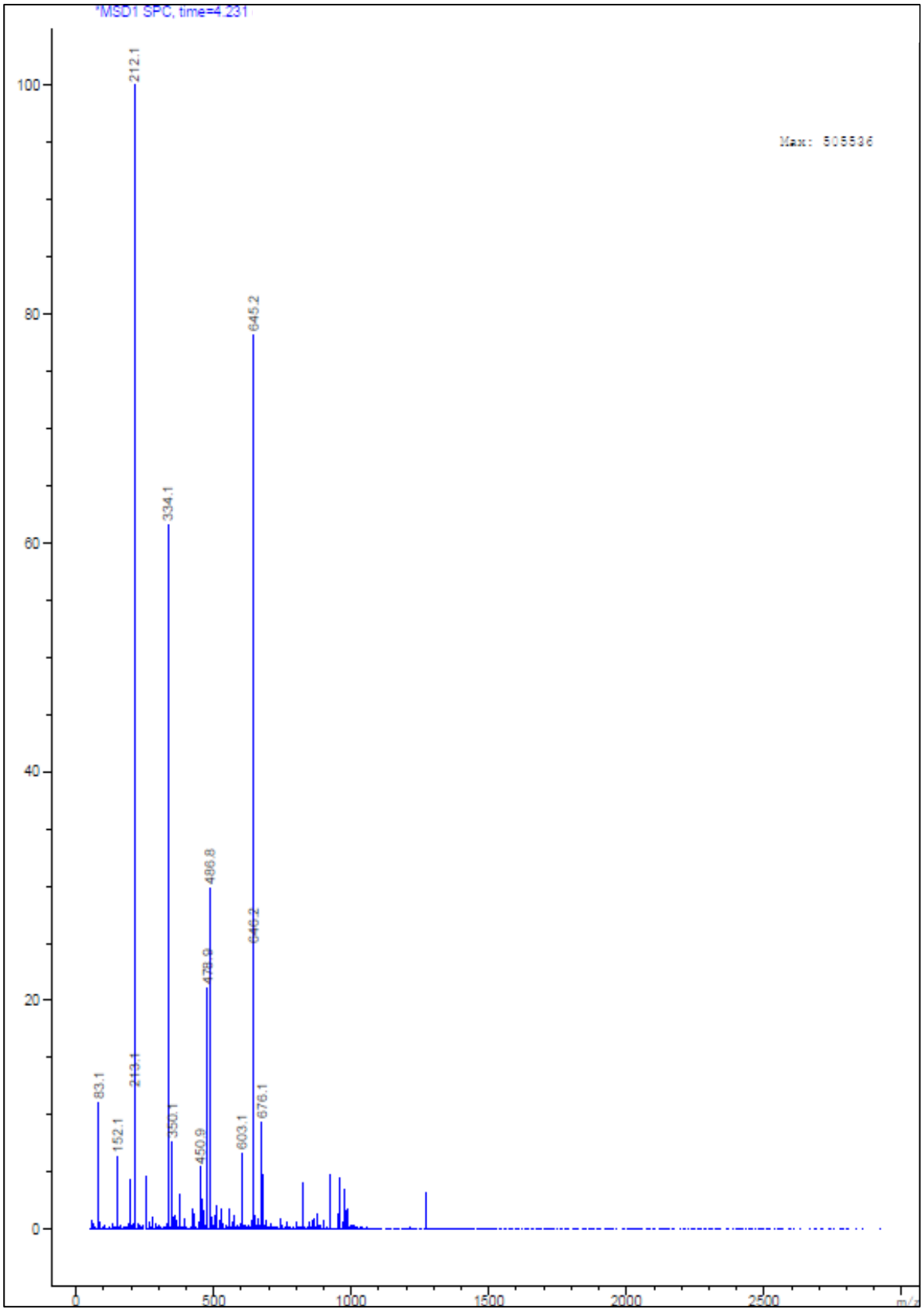
^{13}C-NMR spectrum of Boc-L-DOPA-OMe **1**, registered in CD_3OD.



IR spectrum of Boc-L-DOPA-OMe, **1**, acquired in ATR mode.

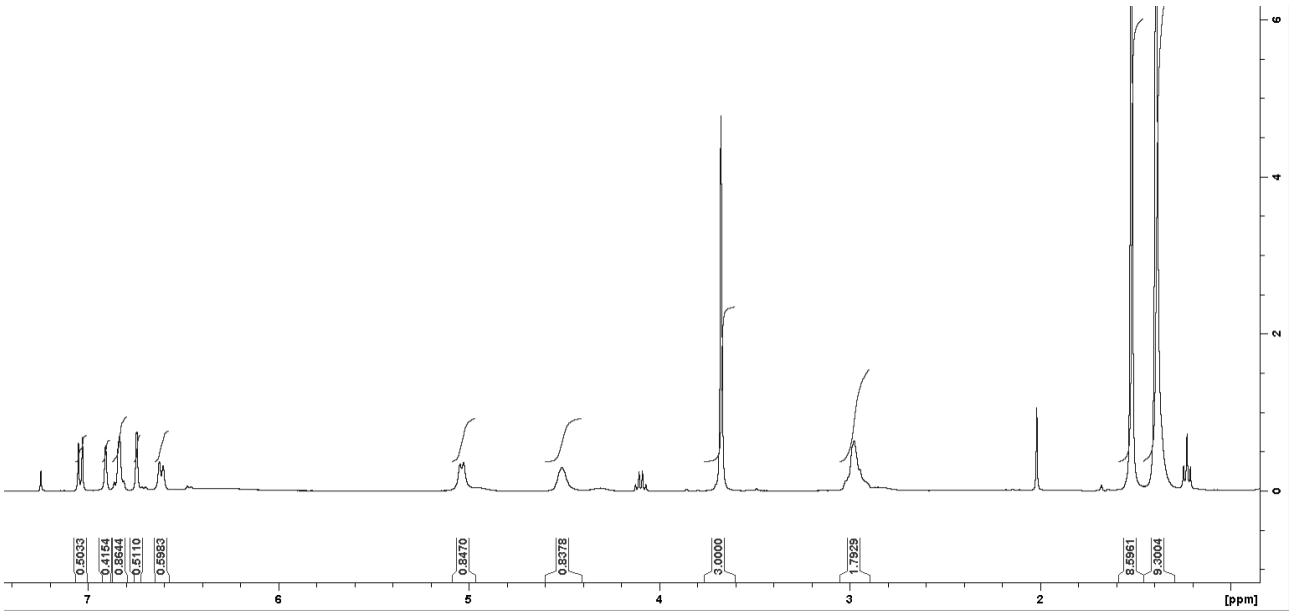


LC-DAD spectrum of Boc-L-DOPA-OMe, **1**, the product elutes at 4.218 min.

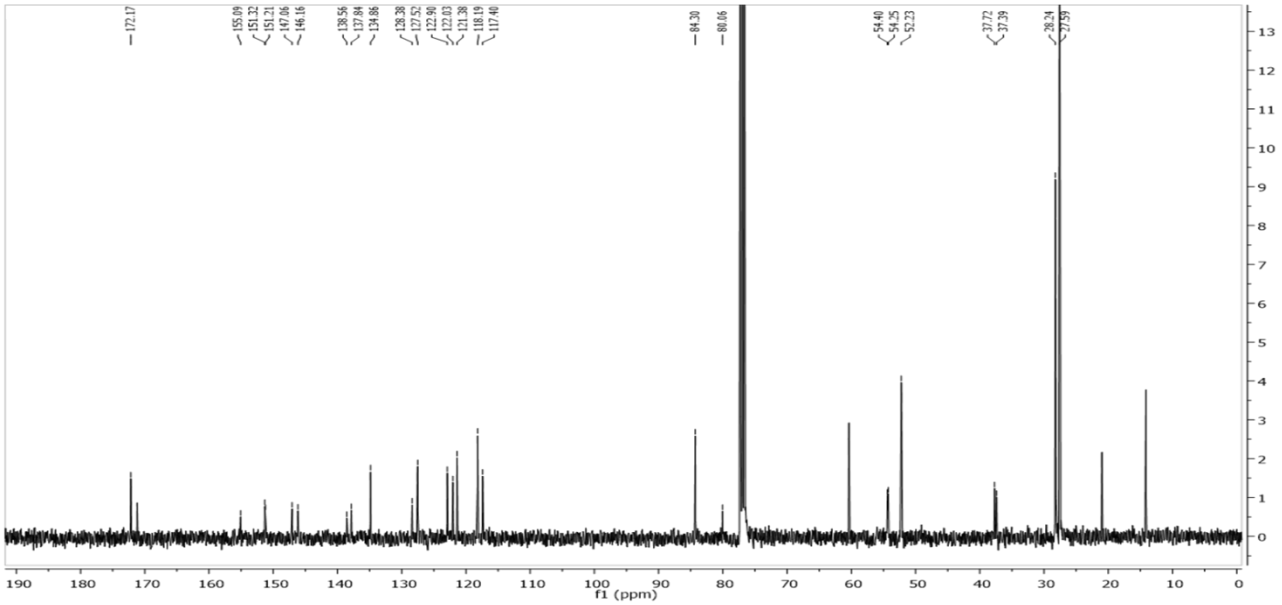


MS spectrum of Boc-L-DOPA-OMe, **1**, at the time 4.231 min.

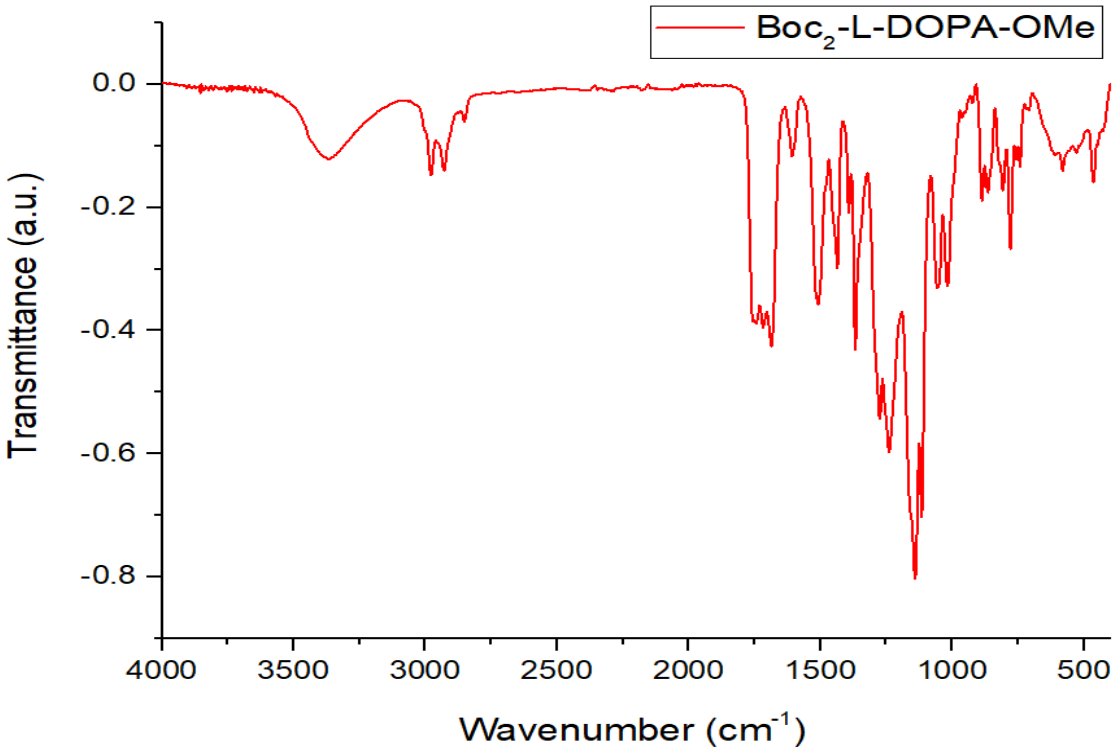
Boc_2-L-DOPA-OMe 2



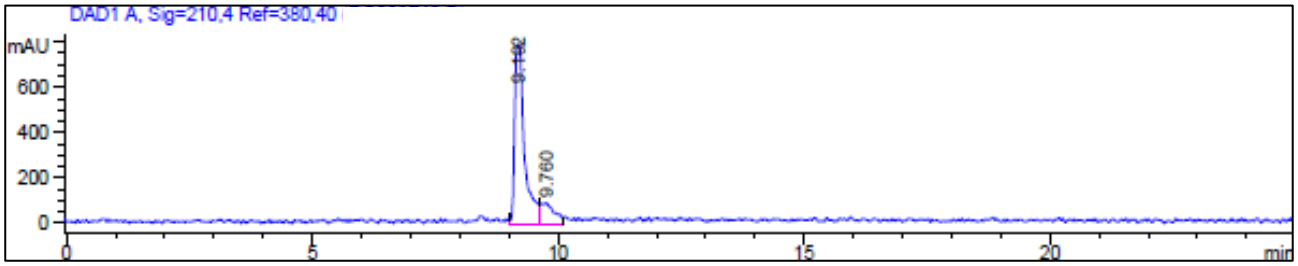
^{1}H-NMR spectrum of Boc_2-L-DOPA-OMe, **2**, registered in $CDCl_3$. Traces of ethyl acetate (4.12, 2.05, 1.26 ppm) are present. The integrals in the aromatic zone suggest the presence of two different species in 1:1 ratio.



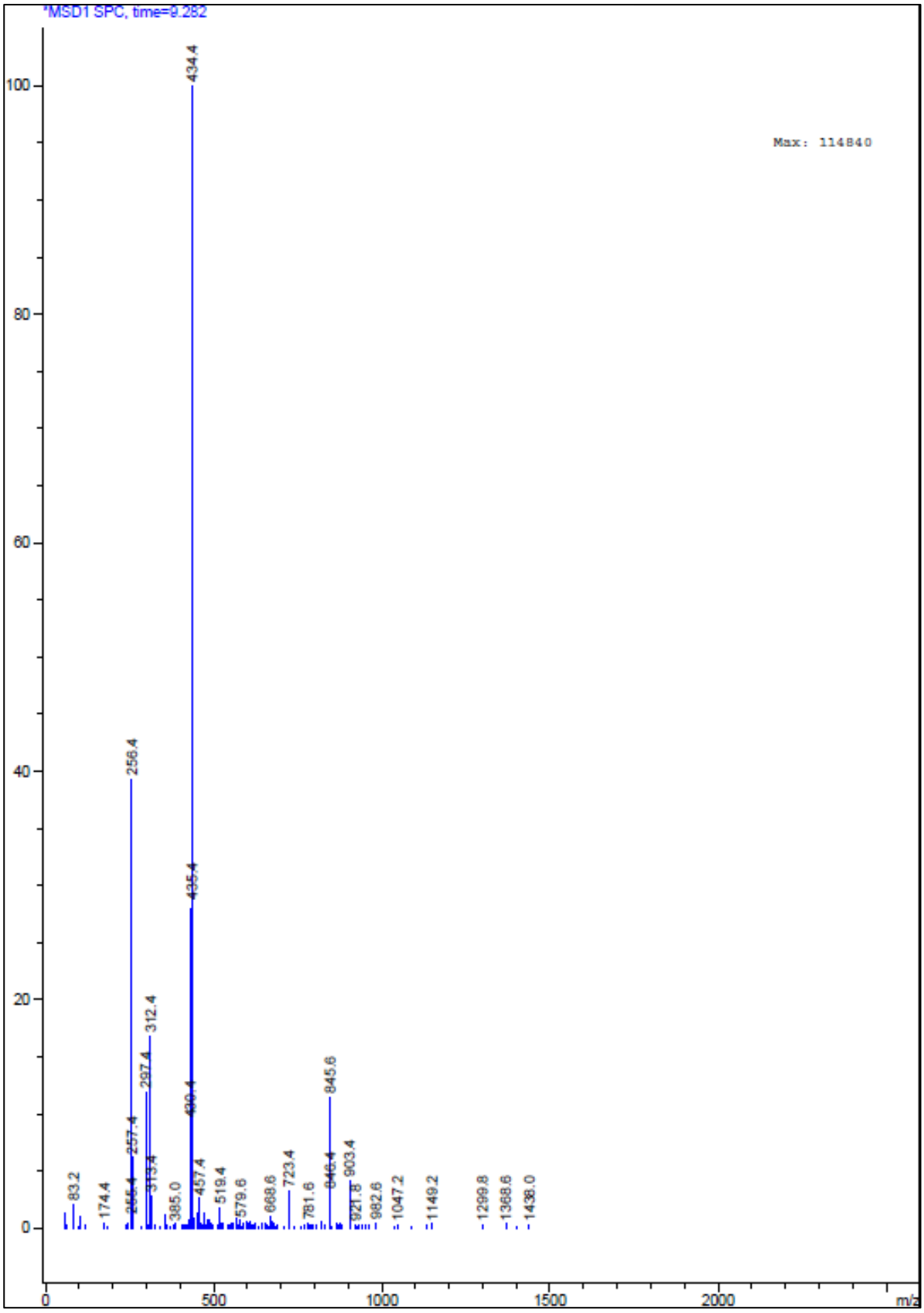
^{13}C-NMR spectrum of Boc_2-L-DOPA-OMe, **2**, registered in $CDCl_3$. Ethyl acetate (4.12, 2.05, 1.26 ppm) is present.



IR spectrum of Boc_2-L-DOPA-OMe **2**, acquired in ATR mode.

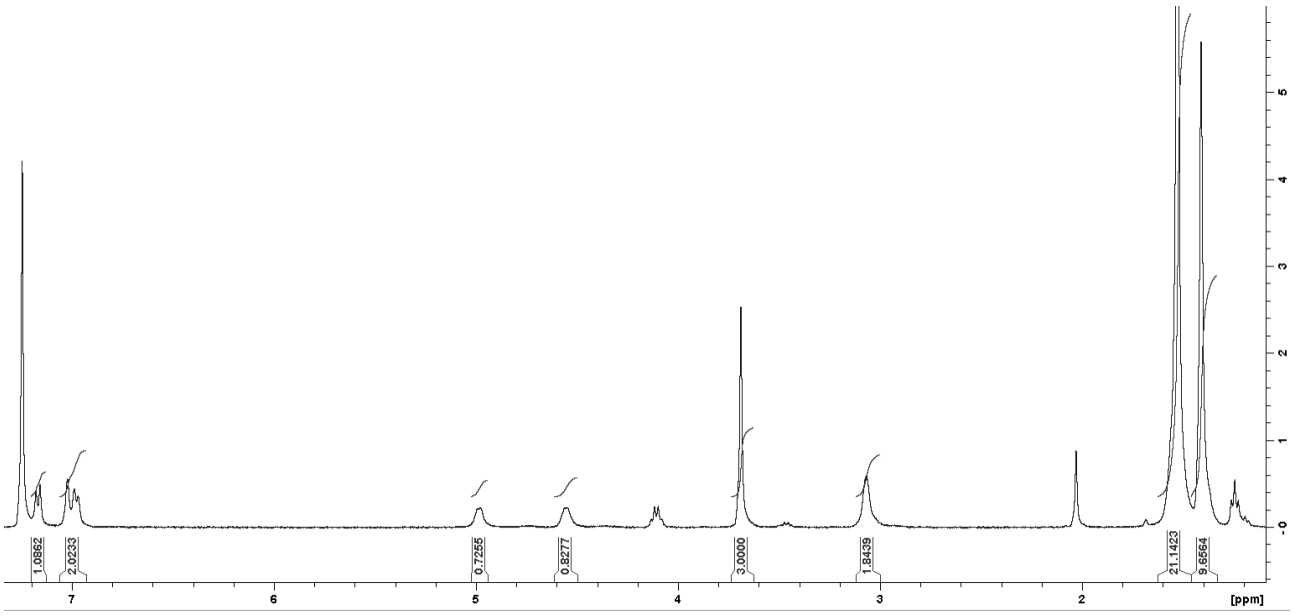


LC-DAD spectrum of Boc_2-L-DOPA-OMe **2**, the products elute between 9.192 and 9.760 min.

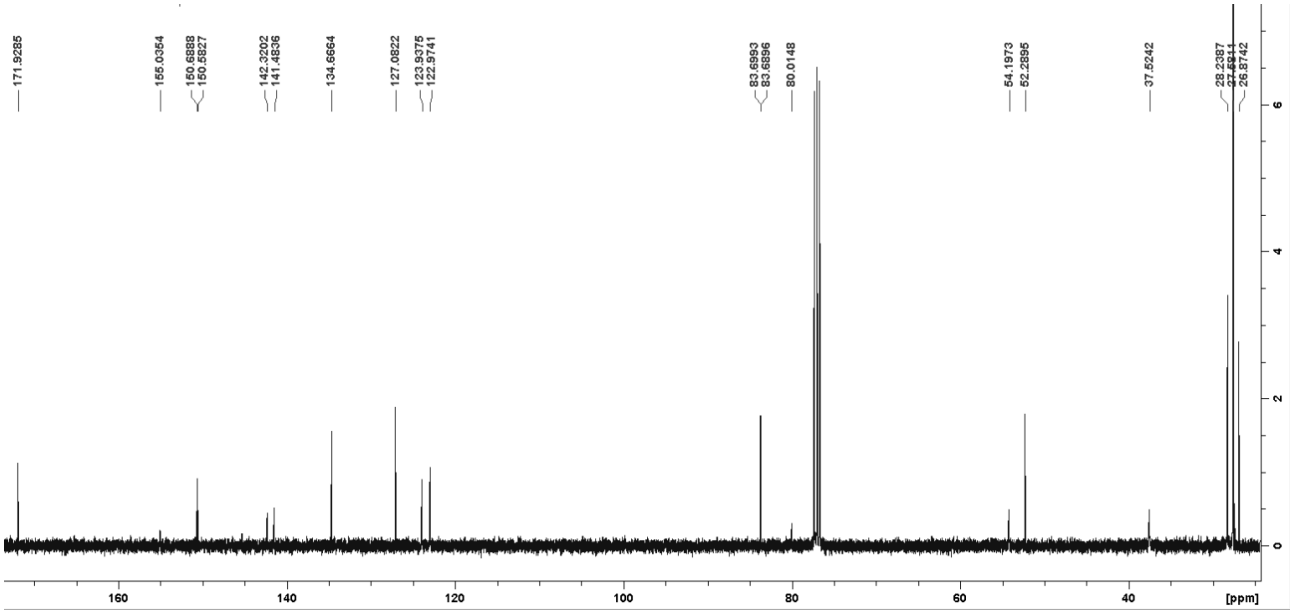


MS spectrum of Boc_2-L-DOPA-OMe **2**, at the time 9.282 min.

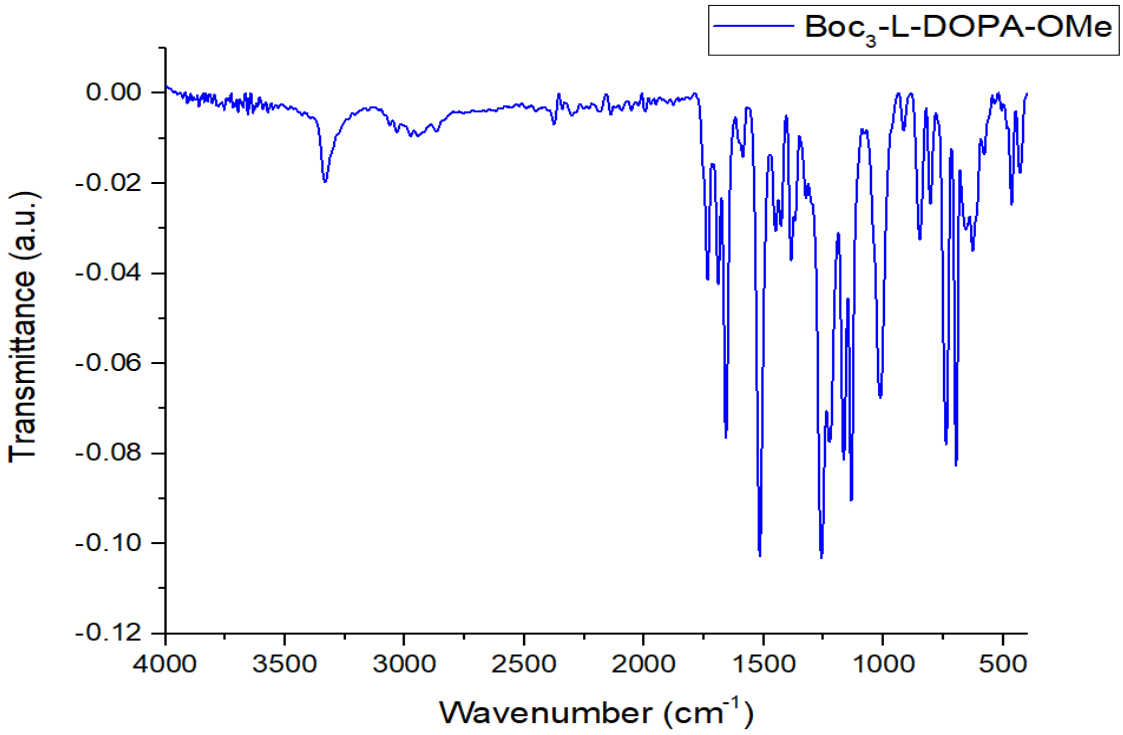
Boc_3-L-DOPA-OMe 3



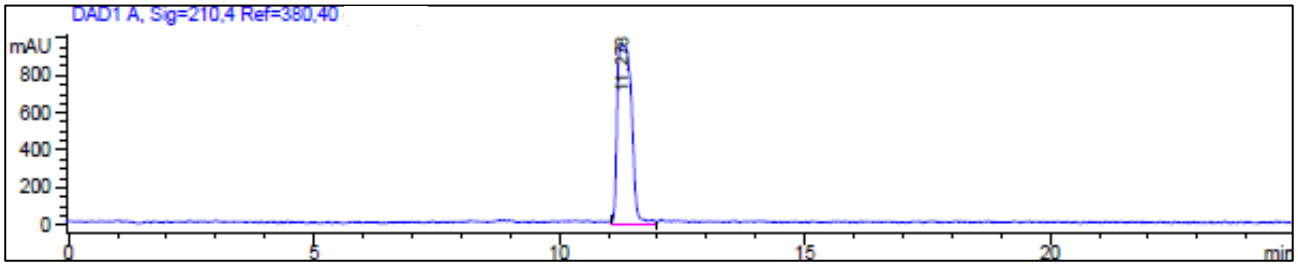
^{1}H-NMR spectrum of Boc_3-L-DOPA-OMe, **3**, registered in $CDCl_3$. Traces of ethyl acetate (4.12, 2.05, 1.26 ppm) are present.



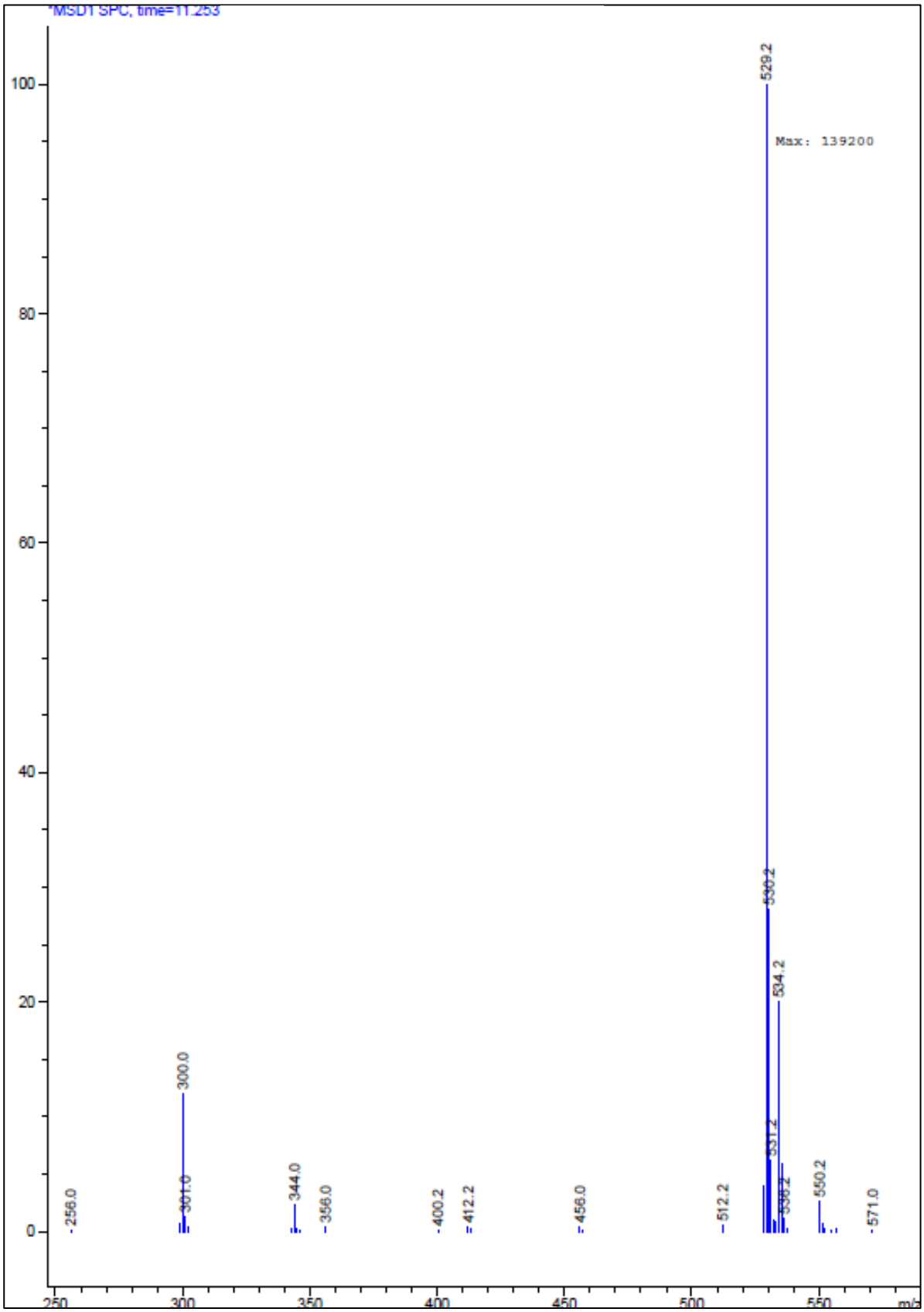
^{13}C-NMR spectrum of Boc_3-L-DOPA-OMe **3**, registered in $CDCl_3$.



IR spectrum of Boc_3-L-DOPA-OMe, **3**, acquired in ATR mode.

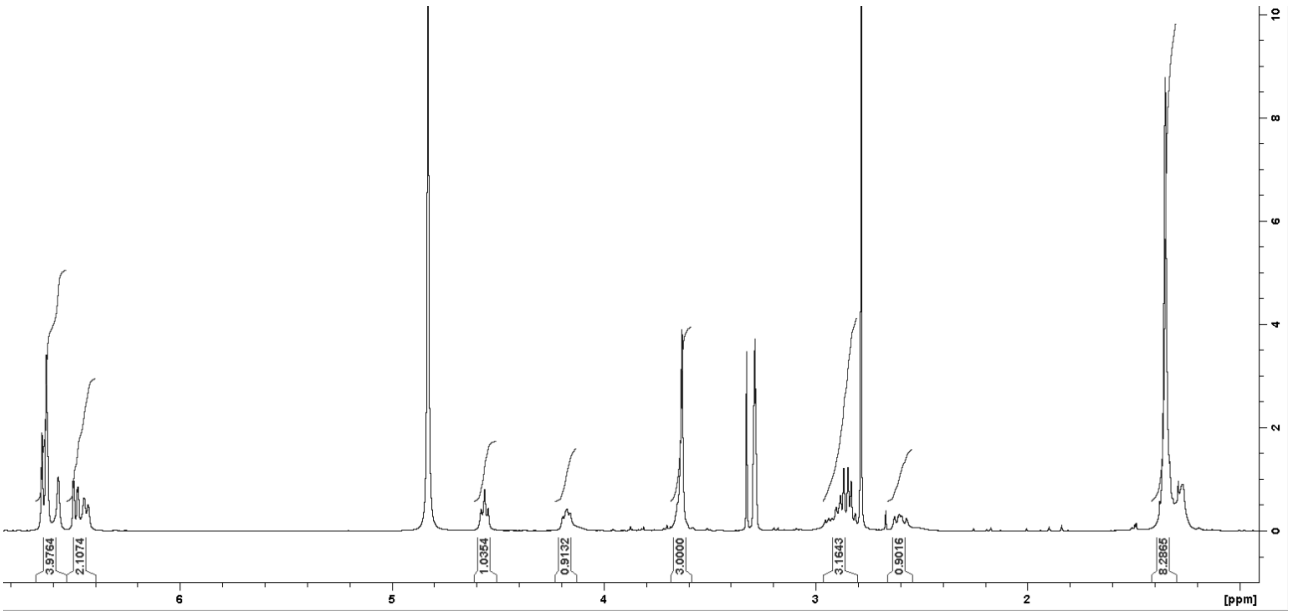


LC-DAD spectrum of Boc_3-L-DOPA-OMe, **3**, the product elutes at 11.278 min.

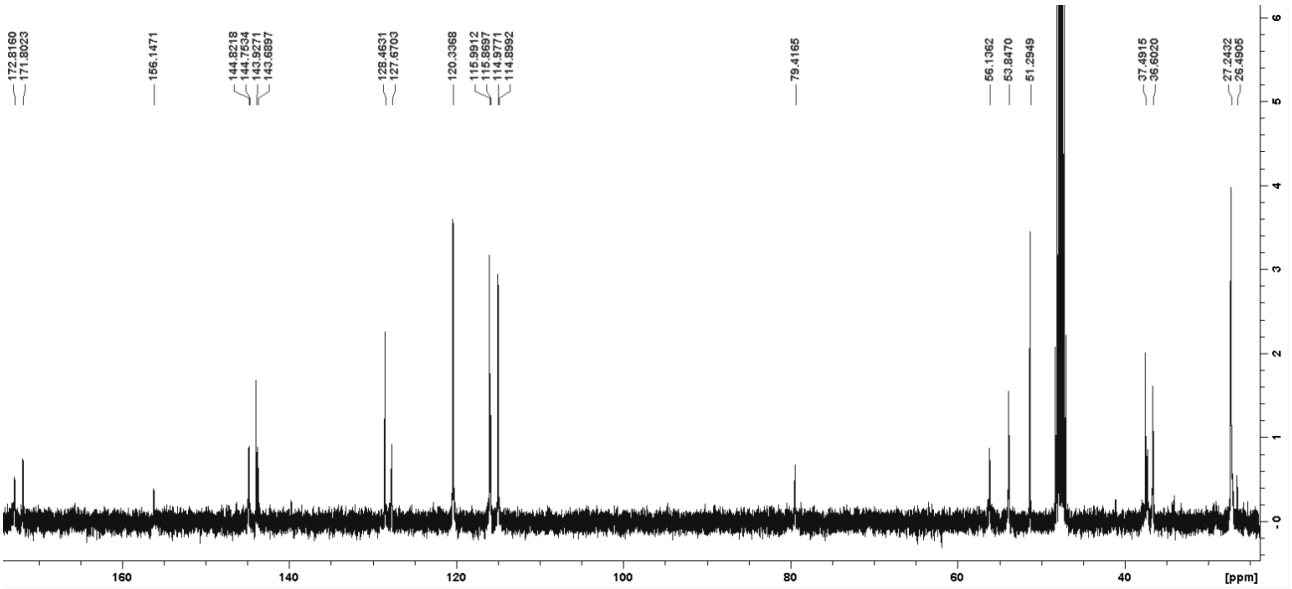


MS spectrum of Boc_3-L-DOPA-OMe, **3**, at the time 11.253 min.

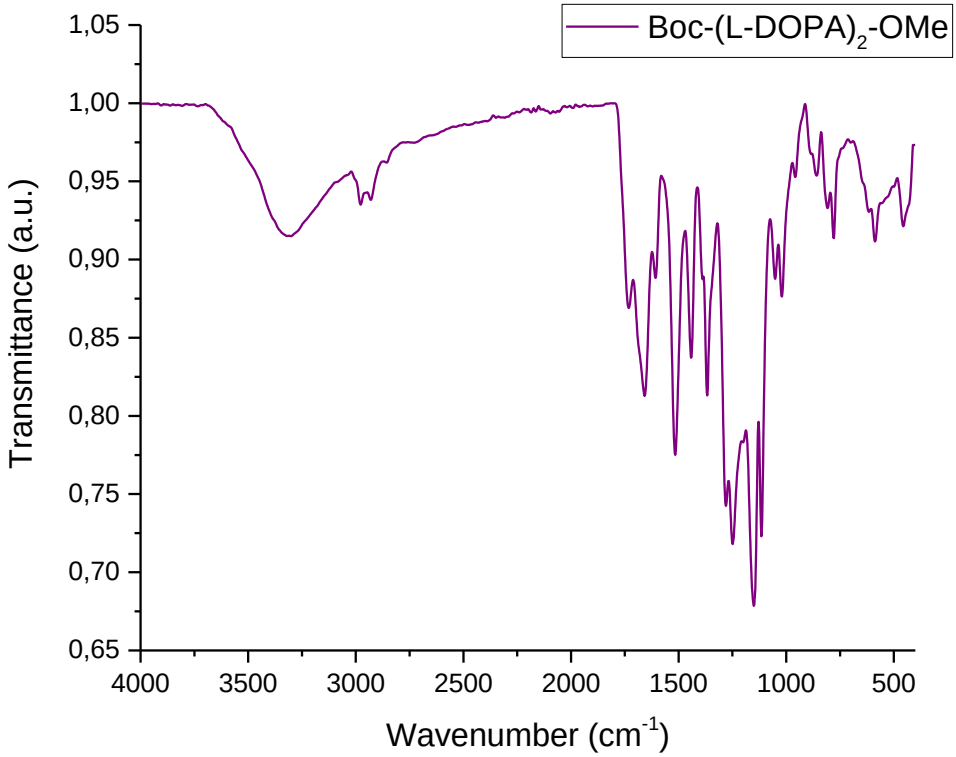
Boc-(L-DOPA)$_2$-OMe 4



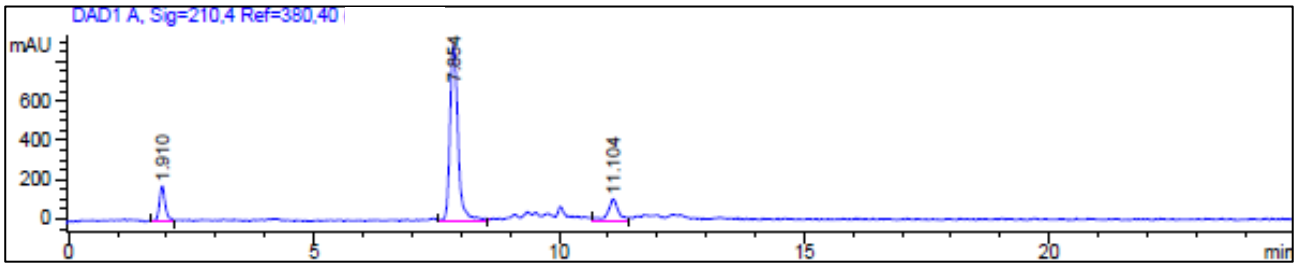
^{1}H-NMR spectrum of Boc-(L-DOPA)$_2$-OMe **4**, registered in CD_3OD. Traces of methanol (3.34 ppm) and tetramethyl urea (2.79 ppm) are present.



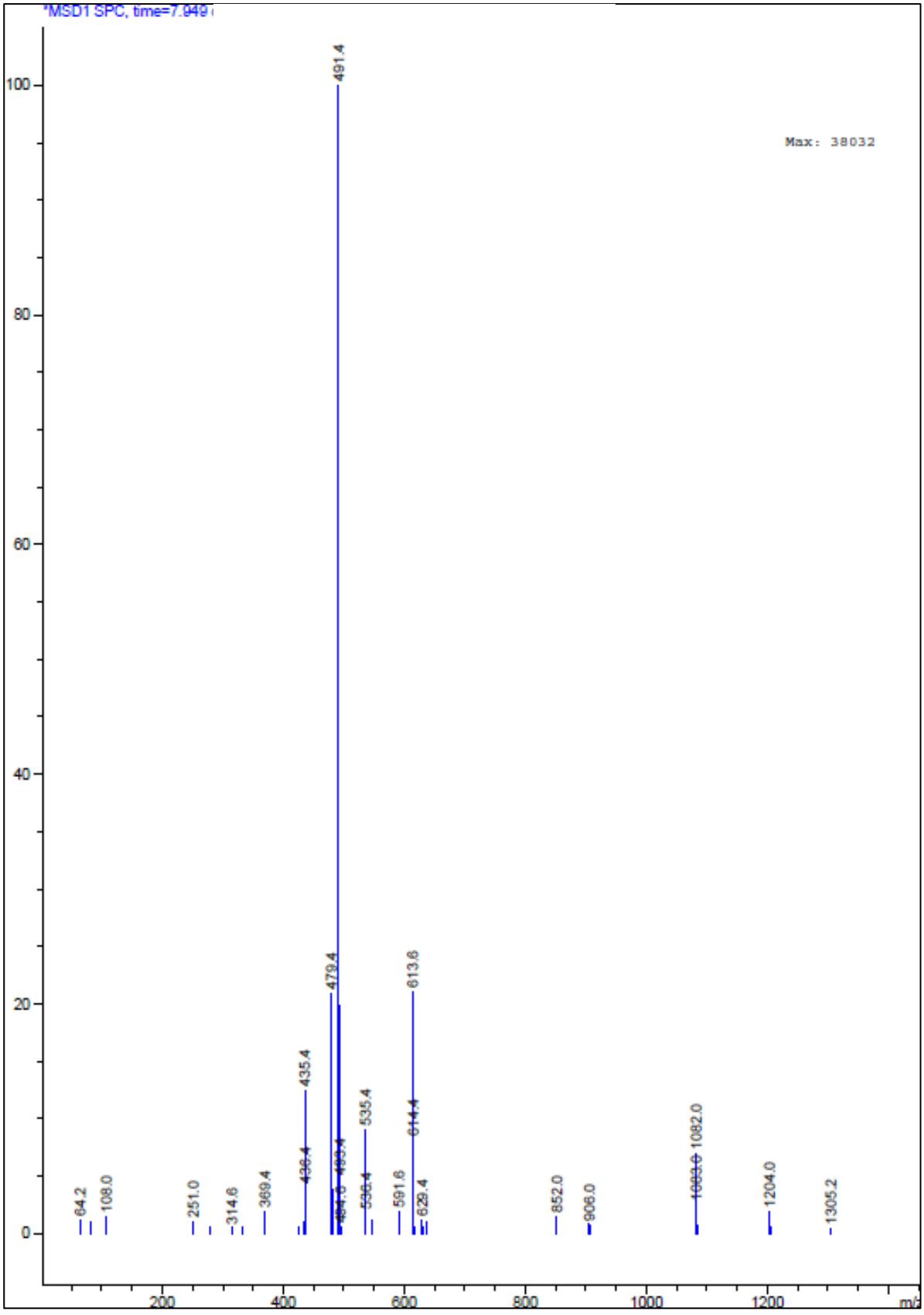
^{13}C-NMR spectrum of Boc-(L-DOPA)$_2$-OMe **4**, registered in CD_3OD.



IR spectrum of Boc-(L-DOPA)$_2$-OMe **4**, acquired in ATR mode.



LC-DAD spectrum of Boc-(L-DOPA)$_2$-OMe **4**, the product elutes at 7.854 min. Some impurities are present.



MS spectrum of Boc-(L-DOPA)$_2$-OMe **4**, at the time 7.949 min.