Supporting informations

1.1 General

^{1}H and ^{13}C NMR spectra were recorded in the indicated deuterated solvents in a Bruker Avance™ 400 spectrometer at 400.13 and 100.62 MHz, respectively. Chemical shifts (δ) are given as parts per million relative to the residual solvent peak and coupling constants (J) are in hertz. Column chromatography was performed on silica gel 60 (70-230 mesh) using the specified eluents. Determination of concentrations was obtained by HPLC analyses carried out in a DIONEX® apparatus equipped with a XTerra MS C_{18} (Phenomemex) column (3.5 µm, 3.0x100 mm) using (water + 2.5% formic acid)/acetonitrile mixtures as the mobile phase (and detection by UV-vis detector at 225, 250, 266 and 275 nm). Determination of enantiomeric excesses was obtained by chiral HPLC using a Lux-1 (Phenomemex) column (3.5 µm, 3.0x100 mm) and hexane/isopropanol 85:15 mixture as mobile phase. All HPLC analysis were performed at 25°C. Enantiomeric excesses values of compound **7**, not obtained experimentally, were calculated by using the equations developed by Sih [1] or the derived specific software "SEquential KInetic Resolution" (SEKIRE) [2] developed by the Prof K. Faber (University of Graz, Austria). Optical densities (OD) were measured on a DAD-UV-Visible Agilent® spectrophotometer at 610 nm. ESI-MS spectra were acquired in positive mode in a Waters® Micromass ZQ2000, using a 10 V cone voltage, 3 kV capillary voltage and 150°C source temperature. HR-MS spectra were acquired in positive mode in a Thermofisher Orbitrap Q Exactive, using a 3.2 V cone voltage, and 300°C source temperature. Melting points are uncorrected. The chemicals, solvents and materials for microbiological cultures were obtained from Sigma-Aldrich®, Fluka®, Carlo Erba®, Riedel-de Haen®, Difco® and used without further purification unless expressly specified. *Rhodococcus erythropolis A4* (deposited at the "Culture Collection of Microorganism, Masaryk University, Brno, Czech Republic"), and *Rhodococcus rhodochrous PA34* strains were furnished by the Dr. L. Martinkova (Academy of Sciences of the Czech Republic, Prague) and Prof. T.K. Bhalla (Himachal Pradesh University, Shimla, India) respectively.

1.2. Synthesis of hydroxymethylferrocene (3)

Ferrocenecarboxaldehyde (**2**) (1.12 g, 5.25 mmol) dissolved in a mixture THF/MeOH (60 ml v/v 5:1) was added, in 30 minutes, with $NaBH_4$ (200 mg, 5.28 mmol) under stirring and room temperature. After 30 minutes, the reaction was stopped and evaporated under vacuum at 40°C. The residue was dissolved in AcOEt, extracted with H_2O, washed with brine, and finally dried over Na_2SO_4 anhydrous before to be filtered off and evaporated under vacuum at 40°C to furnish 1.10 g of compound **3** (5.10 mmol, yield: 98%) as a yellow oil. MS (ESI+): m/z 217 $[M+H]^+$, m/z 239

$[M+Na]^+$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.35 (2H, s, $-CH_2O-$), δ 4.26 (2H, t, J=1.6, Cp), δ 4.20 (7H, br, Cp e Cp'). ^{13}C- NMR (100 MHz, $CDCl_3$): δ 88.88 (Cq-Cp), 68.74 ($-CH_2O-$), δ 69.33 (CH-Cp), δ 68.70 (CH-Cp), 68.29 (CH-Cp'), δ 61.17 ($-OCH_3$). Anal. calcd for $C_{11}H_{12}FeO$: C, 61.15; H, 5.60; Found: C, 61.27; H, 5.58.

1.3. Synthesis of methoxymethylferrocene (4)

Hydroxymethylferrocene (**3**) (1.10 g, 5.1 mmol) was dissolved in a MeOH/AcOH mixture (52.5 mL, ratio 4:1 v/v), and refluxed at 80°C for 2 h until complete conversion of the substrate. The reaction was stopped by evaporating the mixture under vacuum at 40°C, and furnished 1.09 g of **4** (4.73 mmol, yield: 98%) as an oil. MS (ESI+): m/z 231 $[M+H]^+$, m/z 253 $[M+Na]^+$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.25 (4H, br s, Cp), δ 4.15 (7H, br s, Cp' e $-CH_2O-$), δ 3.33 (3H, s, $-OCH_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 83.1 (Cq-Cp), δ 70.6 ($-CH_2O-$), δ 69.3 (CH-Cp), δ 68.4 (CH-Cp'), δ 57.6 ($-OCH_3$). Anal. calcd for $C_{12}H_{14}FeO$: C, 62.64; H, 6.13; Found: C, 62.51; H, 6.14.

1.4. Synthesis of (±)-1-formyl-2-methoxymethylferrocene (5)

Methoxymethylferrocene (**4**) (1.09 g, 4.73 mmol) was dissolved in anhydrous Et_2O (20 mL) under an argon atmosphere, and a solution of *t*-BuLi 1.7 M in pentane (3.7 mL, 6.29 mmol) was slowly added at room temperature and under stirring. After 1 hour 446 µl (5.75 mmol) of anhydrous N,N-DMF were added and the reaction mixture was kept at room temperature and under stirring for further 30 minutes. The mixture was then diluted with AcOEt, extracted with H_2O, washed with brine, and finally dried over Na_2SO_4. The mixture was purified by flash chromatography on silica gel using Hex/AcOEt 80:20 v/v as eluents, and yielding 767.7 mg of (±)-**5** (2.97 mmol, yield 70.5 %) as a red oil. MS (ESI+): m/z 259 $[M+H]^+$, m/z 281 $[M+Na]^+$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.10 (1H, s, -CHO), δ 4.80 (1H, m, Cp), δ 4.70 (1H, m, Cp), δ 4.67 (1H, d, J=11.6 Hz, $-CH_{2a}O-$), δ 4.58 (1H, m, Cp), δ 4.44 (1H, d, J=11.6, $-CH_{2b}O-$), δ 4.27 (5H, s, Cp'), δ 3.41 (3H, s, $-OCH_3$). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 193.6 (-CHO), δ 86.3 (Cq-Cp), δ 74.8 (CH-Cp), δ 72.0 (CH-Cp), δ 71.1 (CH-Cp), δ 70.5 (CH-Cp'), δ 68.7 ($-CH_2O-$), δ 58.3 ($-OCH_3$). Anal. calcd for $C_{13}H_{14}FeO_2$: C, 60.50; H, 5.47; Found: C, 60.68; H, 5.46.

1.5. Synthesis of (±)-1-methoxymethyl-2-nitrile-ferrocene (1)

To a homogeneous mixture of (±)-1-formyl-2methoxymethylferrocene (**5**) (230 mg, 0.89 mmol), $NH_2OH{\cdot}HCl$ (221 mg, 3.18 mmol), KI (174.7 mg, 1.05 mmol) and ZnO (92.8 mg, 1.08 mmol) in a round-bottom flask at room temperature under argon was added acetonitrile (14 mL). The resulting mixture was then refluxed for 4 h with efficient stirring and heating (oil bath temperature during the

reflux should not exceed 100°C). Subsequently, aqueous $Na_2S_2O_3$ (5%, 3 mL) was added to the cooled mixture and the stirring was continued for additional 15 min. After the mixture was filtered to remove solid particles, it was diluted with water and extracted with CH_2Cl_2. Collected organic layers were dried on Na_2SO_4 anhydrous, filtered off and concentrated in a rotary evaporator. The mixture was purified by flash chromatography on silica gel using Hex/AcOEt gradient (from 90:10 to 80:20 v/v) as eluents, and yielding 121 mg of (±)-**1** (0.47 mmol, yield 52.6 %) as a red oil. HR-MS (ESI+): m/z 278.02442 $[M+Na]^+$, 533.05959 $[2M+Na]^+$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.65 (1H, m, Cp), δ 4.49 (1H, m, Cp), δ 4.40 (1H, d, J=11.6 Hz, -CH_{2a}O), δ 4.38 (1H, m, Cp), δ 4.34 (1H, d, J=11.6 Hz, -CH_{2b}O), δ 4.30 (5H, s, Cp'), δ 3.37 (3H, s, OCH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 119.25 (-CN), δ 86.85 (Cq-methoxymethyl, Cp), δ 71.85 (-CH_2-), δ 71.62 (CH-Cp), δ 70.95 (5C-Cp'), δ 70.48 (CH-Cp), δ 68.39 (CH-Cp), δ 58.18 (-OCH_3), δ 52.97 (Cq-nitrile, Cp). Anal. calcd for $C_{13}H_{13}FeNO$: C, 61.21; H, 5.14; N, 5.49; Found: C, 61.39; H, 5.13; N, 5.48;

1.6. Synthesis of (±)-1-carboxamide-2-methoxymethyl -ferrocene (6)

To a solution of **(±)-1** (50 mg, 0.19 mmol) in 10 mL of *tert*-butyl alcohol was added 100 mg of finely powdered potassium hydroxide and the mixture was refluxed for 5h under stirring. The reaction mixture was then diluted with satd NH_4Cl solution and extracted with CH_2Cl_2 (3 x 5 mL). The organic phase was washed with brine, dried over Na_2SO_4 and taken to dryness under vacuum to give a residue that was purified on silica gel column (*n*-hexane-AcOEt 4:1) to give pure **(±)-6** (42 mg, 0.15 mmol, 80% yield) [3].

HR-MS (ESI+): m/z 296.03477 $[M+Na]^+$, 569.08033 $[2M+Na]^+$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.32 (1H, bs, -$CONH_2$), δ 5.64 (1H, bs, -$CONH_2$), δ 4.91 (1H, m, Cp), δ 4.77 (1H, d, J = 11.4, -CH_a-), δ 4.32 (2H, m, Cp), δ 4.22 (5H, s, Cp'), δ 4.20 (1H, d, J = 11.4, -CH_b-), δ 3.38 (3H, s, -OCH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 172.58 (-$CONH_2$), δ 80.6 (Cq-methoxymethyl, Cp), δ 73.86 (-CH_2-), δ 72.86 (CH-Cp), δ 70.27 (5C-Cp', Cq-$CONH_2$ Cp), δ 69.91 (CH-Cp), δ 68.73 (CH-Cp), δ 57.35 (-OCH_3). Anal. calcd for $C_{13}H_{15}FeNO_2$: C, 57.17; H, 5.54; N, 5.13; Found: C, 57.34; H, 5.52; N, 5.13.

1.7. Microorganisms and cultures

The bacterial strains were maintained at 4 °C on meat peptone agar (Bacto beef extract 3 g/L, peptone 10 g/L, NaCl 5 g/L, agar 15 g/L). *Rhodococcus erythropolis* A4 was grown for 2 days at 28°C in shaken 500-mL Erlenmeyer flasks containing 100 mL of basal salts broth according to Di Geronimo and Antoine [4], supplemented with 10 g/L of glycerol and 3 g/L of yeast extract.

Preculture of *R. rhodochrous* PA-34 was prepared by inoculating 50 mL of medium M4 containing 10.0 g/L glycerol, 5.0 g/L peptone, 3.0 g/L malt extract and 3.0 g/L yeast extract (pH 7.0) with a loop full of culture from the slant and was incubated at 30 °C, 160 rpm for 24 h. To the production medium (medium M4 containing 20 mg/L $CoCl_2$), preculture (4%, v/v) and acetonitrile, butyronitrile, valeronitrile, benzonitrile or 3-cyanopyridine (0.2%, v/v) as inducer were added and the solution incubated at 30 °C, 160 rpm for 36 h.

1.8. Preparation of whole-cell catalysts

Whole cells of *Rhodococcus erythropolis* A4 were harvested by centrifugation and washed with Tris-HCl buffer (50 mM, pH 8). Whole cells of *Rhodococcus rhodochrous* PA-34 were harvested by centrifuging the culture at 4000 x g for 15 min, washed twice with 100 mM potassium phosphate buffer (pH 7.0). Biomasses were stored at -4°C, until their usage.

The activities of nitrile-transforming enzymes and amidase were determined with benzonitrile and benzamide, respectively, using the reported assays [5,6]. One unit (U) of NHase activity was defined as the amount of resting cells which converts 1μmol of benzonitrile to benzamide per min under the assay conditions. Analogously one unit of Amidase activity was the amount of cells that catalyses the formation of 1μmol of benzoic acid per min under the assay conditions.

1.9. Preparation of cell-free extract of *Rhodococcus erythropolis* A4

Whole cells of *Rhodococcus erythropolis* A4 suspended in Tris-HCl buffer (50 mM, pH 8) were disrupted using a Retsch MM-200 oscillation mill as described previously [5]. The cell extracts were immediately used for biotransformations. The activities of nitrile hydratase and amidase were approx. 3 and 0.7 U mg^{-1} of protein, respectively.

1.10. Kinetic parameters determination

The kinetic parameters for *Rhodococcus rhodochrous* PA-34 biotransformations were obtained incubating different concentration of substrate, (from 0.1 to 10 mM) with 6.34 mg DCW mL^{-1} of resting cells in a buffered solution prepared with phosphate buffer (50 mM, pH 7.0). (±)-1-Methoxymethyl-2-nitrile-ferrocene (**1**) and (±)-1-carboxamide-2-methoxymethyl-ferrocene (**6**) were used as substrates to evaluate NHase and amidase kinetic parameters, respectively. The assays were carried out in 2 mL volume, at 35°C, for 30 min, under continuous stirring at 200 rpm. The reaction was stopped by adding 1 mL of 0.5 M HCl and centrifuged. Samples of supernatant were analysed for product determination.

1.11. General procedure for biotransformations with whole cells of *Rhodococcus erythropolis* A4

A 10 mM solution of substrate was prepared using a suspension of biomass in Tris-HCl buffer (50 mM, pH 8), having an optical density (OD) value of approx. 15. A percentage of MeOH up to 5% was previously used to solubilise the substrate. The suspension was shaken (200 rpm) at 35°C; aliquots were drawn at regular time intervals and analysed by TLC (80:20 Hex/AcOEt) and HPLC.

1.12. General procedure for biotransformations with whole cells of *Rhodococcus rhodochrous* PA-34

A 10 mM solution (5 mL) of substrate was prepared using a suspension of 50 mg of wet biomass (6.34 mg DCW mL^{-1}) in 100 mM potassium phosphate buffer (pH 7.0). A percentage of MeOH up to 5% was previously used to solubilise the substrate. The suspension was shaken (200 rpm) at 35°C; aliquots were drawn at regular time intervals and analysed by TLC (80:20 Hex/AcOEt) and HPLC.

1.13. Synthesis of (+)-(S_p)-1-carboxamide-2-methoxymethyl-ferrocene (6) and (-)-(R_p) 2-methoxymethyl-ferrocen-1-carboxylic acid (7): biotransformation of (±)-1 catalysed by whole cells from *Rhodococcus rhodochrous* PA-34

Substrate (±)-**1 (**22 mg, 0.086 mmol) was dissolved in 200 μL of MeOH and used to prepare a 5 mL solution with a suspension of whole cells (50 mg wet biomass, 6.34 mg DCW mL^{-1}) from *Rhodococcus rhodochrous* PA-34 (grown up in presence of butyronitrile, OD_{610} = 10) in a 100 mM potassium phosphate buffer (pH 7.0).

The mixture was shaken (200 rpm) at 30°C for 120 hours, and then stopped by centrifugation of the solution. The supernatant was acidified with HCOOH, extracted with CH_2Cl_2, dried over Na_2SO_4 anhydrous, and evaporated under vacuum at 40°C. The mixture was purified by flash chromatography on silica gel using Hex/AcOEt gradient (from 90:10 to 0:100 v/v) as the eluents, and yielded 6.3 mg of compound **6** (0.023 mmol, yield 27%, ee 75.5 %) and 1.5 mg of compound **7** (0.005 mmol, yield 5.5%, ee 98%). The course of the reaction was monitored by TLC and HPLC analysis.

Spectroscopic data of (+)-(S_p)-1-carboxamide-2-methoxymethyl-ferrocene (6) are in accordance with those of the racemic compound synthesized previously (see paragraph 1.6.). [α] = +29.11 ($CHCl_3$, c = 0.13, ee 75.5%). Anal. calcd for $C_{13}H_{15}FeNO_2$: C, 57.17; H, 5.54; N, 5.13; Found: C, 57.34; H, 5.52; N, 5.13.

(-)-(R_p) acid 2-methoxymethyl-ferrocen-1-carboxylic (**7**): HR-MS (ESI+): m/z 297.01746 $[M+Na]^+$, 571.04657 $[2M+Na]^+$, 593.02832 $[(M^-Na^+)+M+Na]^+$. ^{1}H-NMR (400 MHz, CD_3OD): δ 4.98 (1H, d, J = 11.6, -CH_a-), δ 4.76 (1H, s, Cp), δ 4.47 (1H, s, Cp), δ 4.39 (1H, d, J = 11.6, -CH_b-), δ 4.34 (1H, s, Cp), δ 4.17 (5H, s, Cp'), δ 3.36 (3H, s, -OCH_3). ^{13}C-NMR (100 MHz, CD_3OD): δ 174.11 (-COOH), δ 72.71 (Cq-methoxymethyl, -CH_2-), δ 71.38 (CH-Cp), δ 69.74 (5C-Cp', Cq-COOH), δ 69.31 (CH-Cp), δ 68.88 (CH-Cp), δ 56.51 (-OCH_3). [α] = -197,58 (EtOH, c=0.27, ee 98.0%). Anal. calcd for $C_{13}H_{14}FeO_3$: C, 56.97; H, 5.15; Found: C, 57.01; H, 5.14.

1.14. Synthesis of (±)-1-formyl-2-dimethylaminomethyl-ferrocene (9)

Dimethylaminomethyl-ferrocene (**8**) (1.5 g, 6.17 mmol) was dissolved in anhydrous Et_2O (25.6 mL) under an argon atmosphere, and a solution of t-BuLi 1.7 M in pentane (4.87 mL, 8.28 mmol) was slowly added at room temperature and under stirring. After 1 hour 580 μL (7.49 mmol) of N,N-DMF were added and the reaction mixture was kept at room temperature under stirring for further 30 minutes. The mixture was then diluted with AcOEt, extracted with H_2O, washed with brine, dried over Na_2SO_4, and finally evaporated under vacuum, obtaining quantitatively 1.46 g of product **9** (5,39 mmol). MS (ESI+): m/z 272 $[M+H]^+$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.11 (1H, s, -CHO), δ 4.80 (1H, m, Cp), δ 4.64 (1H, m, Cp), δ 4.58 (1H, m, Cp), δ 4.24 (5H, s, Cp'), δ 3.86 (1H, d, J=16 Hz, -CH_{2a}N), δ 3.39 (1H, d, J=16 Hz, -CH_{2b}N), δ 2.24 (6H, s, (-CH_3)$_2$). Anal. calcd for $C_{14}H_{17}FeNO$: C, 62.02; H, 6.32; N, 5.17; Found: C, 61.78; H, 6.31; N, 5.18.

1.15. Synthesis of (±)-1-dimethylaminomethyl-2-hydroxymethyl-ferrocene (10)

To a solution of (±)-1-formyl-2-dimethylaminomethyl-ferrocene (**9**) (1.5 g, 5.46 mmol) in THF/MeOH (130 mL v/v 5:1) were added 265 mg of $NaBH_4$ (7,00 mmol) at room temperature and under stirring. After 30 minutes, the reaction was stopped, by evaporating the solution under vacuum at 40°C, dissolved in AcOEt, extracted with H_2O, washed with brine, and dried over Na_2SO_4. After evaporation, the mixture was purified by flash chromatography on silica gel using AcOEt/TEA 90:10 v/v as eluents and yielding compound **10** (1.10 g, 4.03 mmol, yield 73.3%) as an oil. MS (ESI+): m/z 272 $[M+H]^+$. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.78 (1H, d, J=12Hz, -CH_{2a}OH), δ 4.19 (1H, m, Cp), δ 4.15 (1H, d, J=12Hz, -CH_{2b}OH), δ 4.10 (1H, m, Cp), δ 4.03 (1H, m, Cp), δ 3.90 (1H, d, J=12.4Hz, -CH_{2a}N), δ 2.78 (1H, d, J=12.4Hz, -CH_{2b}N), δ 2.17 (6H, s, (-CH_3)$_2$). Anal. calcd for $C_{14}H_{19}FeO$: C, 61.56; H, 7.01; N, 5.13; Found: C, 61.37; H, 7.03; N, 5.12.

1.16. Enzymatic resolution of (±)-1-dimethylaminomethyl-2-hydroxymethyl-ferrocene (10)

580 mg (2,12 mmol) of alcohol (±)-**10** dissolved in 20 mL of *t*-BME, were added with 1 mL of vinyl acetate (0.011 mol) in presence of 1 g of *Candida rugosa* lipase. The suspension was shaken (200 rpm) at 45°C; aliquots were drawn at regular time intervals and analysed by TLC (AcOEt/TEA 90:10 v/v) and HPLC. After 18 hours the reaction was stopped by filtering off the enzyme, and evaporated under vacuum. The mixture was purified by flash chromatography on silica gel using AcOEt/TEA 90:10 v/v as eluents and yielding 360 mg (1.32 mmol, yield 62,0 %, ee 41.6%) of alcohol (R_p)-**10** as residual substrate, and 215 mg (0.71 mmol, yield 37.1%, ee 70.5%) of the ester acetate (S_p)-1-dimethylaminomethyl-2-methylacetoxy-ferrocene (**11**).
^{1}H e ^{13}C-NMR spectroscopic data of (S_p)-(**11**) are in accordance with those reported in literature [6].
$[\alpha]$ = +6.6 ($CHCl_3$, c=1, ee 70.5%).

1.17. Synthesis of (S_p)-1-dimethylaminomethyl-2-hydroxymethyl-ferrocene (10)

215 mg (0.71mmol, ee 70.5%) of the ester acetate (S_p)-1-dimethylaminomethyl-2-methylacetoxy-ferrocene (**11**) were dissolved in 12.5 mL of ethanol (EtOH), and reacted with 380 mg of K_2CO_3 (2.75 mmol) at room temperature. After 23 hours the reaction was stopped by evaporating under vacuum at 40°C. The mixture was then dissolved in CH_2Cl_2, extracted with H_2O, washed with brine, dried over Na_2SO_4, and finally evaporated under vacuum, to furnish 161.5 mg (0.59 mmol, yield 75.1%, ee 70.5%) of (R_p)-1-dimethylaminomethyl-2-hydroxymethyl-ferrocene **16**. The reaction was monitored by TLC (AcOEt/TEA 90:10 v/v). $[\alpha]$ = +23.54 ($CHCl_3$, c=1, ee 70.5%).

1.18. Synthesis of (S_p)-1-dimethylaminomethyl-2-formyl-ferrocene (9)

146 mg (0.52mmol, ee 70.5%) of the optically active alcohol (R_p)-**16** were solubilized in 22 mL of CH_2Cl_2 in presence of 1.43 g (16.5 mmol) of MnO_2 at 45°C and under stirring. The reaction was monitored by TLC (AcOEt/TEA 90:10 v/v). After 20 hours the reaction was stopped by filtering off MnO_2, and then extracted with H_2O. The organic fraction was dried over Na_2SO_4, filtered off and finally evaporated under vacuum. The mixture was purified by flash chromatography on silica gel using AcOEt/TEA 95:5 v/v as eluents, and yielding 64 mg (0.23 mmol, yield 43.8%, ee 70.5%,) of (S_p)-1-dimethylaminomethyl-2-formyl-ferrocene (**9**) as an orange oil. $[\alpha]$ = -14.8 ($CHCl_3$, c=1, ee 70.5%).

1.19. Synthesis of (S_p)-1-formyl-2-methoxymethyl-ferrocene (5)

(S_p)-1-dimethylaminomethyl-2-formyl-ferrocene (**9**) (58 mg, 0.21 mmol, ee 70.5%) was dissolved in a mixture composed by 15 mL of MeOH, 3 mL of Ac_2O and 3 mL of AcOH, and the solution refluxed at 80°C. The reaction was monitored by TLC (AcOEt/TEA 95:5 v/v,). After 2 h, the

reaction was stopped by evaporating the solvents-reactants under vacuum, and obtaining as residual product 55 mg (0.21 mmol, yield 95%, ee 70.5%) of (S_p)-1-formyl-2-methoxymethylmethyl-ferrocene **5** optically active. [α] = +3.33 ($CHCl_3$, c=0.98, ee 70.5%).

1.20. Synthesis of *(R_p)*-1-methoxymethyl-2-nitrile-ferrocene (1)

(S_p)-1-formyl-2-methoxymethyl-ferrocene (**5**) (55 mg, 0.21 mmol, ee 70.5%) was dissolved in 8 mL of CH_3CN and added with $NH_2OH{\cdot}HCl$ (107 mg, 1.54 mmol), KI (70.0 mg, 0.42 mmol) and ZnO (40.0 mg, 0.50 mmol) in a round-bottom flask at room temperature under argon. The resulting mixture was then refluxed for 4 h with efficient stirring and heating (oil bath temperature during the reflux should not exceed 100°C). Subsequently, aqueous $Na_2S_2O_3$ (5%, 3 mL) was added to the cooled mixture and the stirring was continued for additional 15 min. After the mixture was filtrated to remove solid particles, it was diluted with water and extracted with CH_2Cl_2. Collected organic layers were dried on Na_2SO_4 anhydrous, filtered off and concentrated in a rotary evaporator. The mixture was purified by flash chromatography on silica gel using Hexane/AcOEt (from 90:10 to 80:20 v/v) as eluents, and yielding 19.8 mg of *(R_p)*-**1** (0.077 mmol, yield 36.0 %, ee 70.5%) as a red oil. [α] = +8.75 ($CHCl_3$, c=0.99, ee 70.5%).

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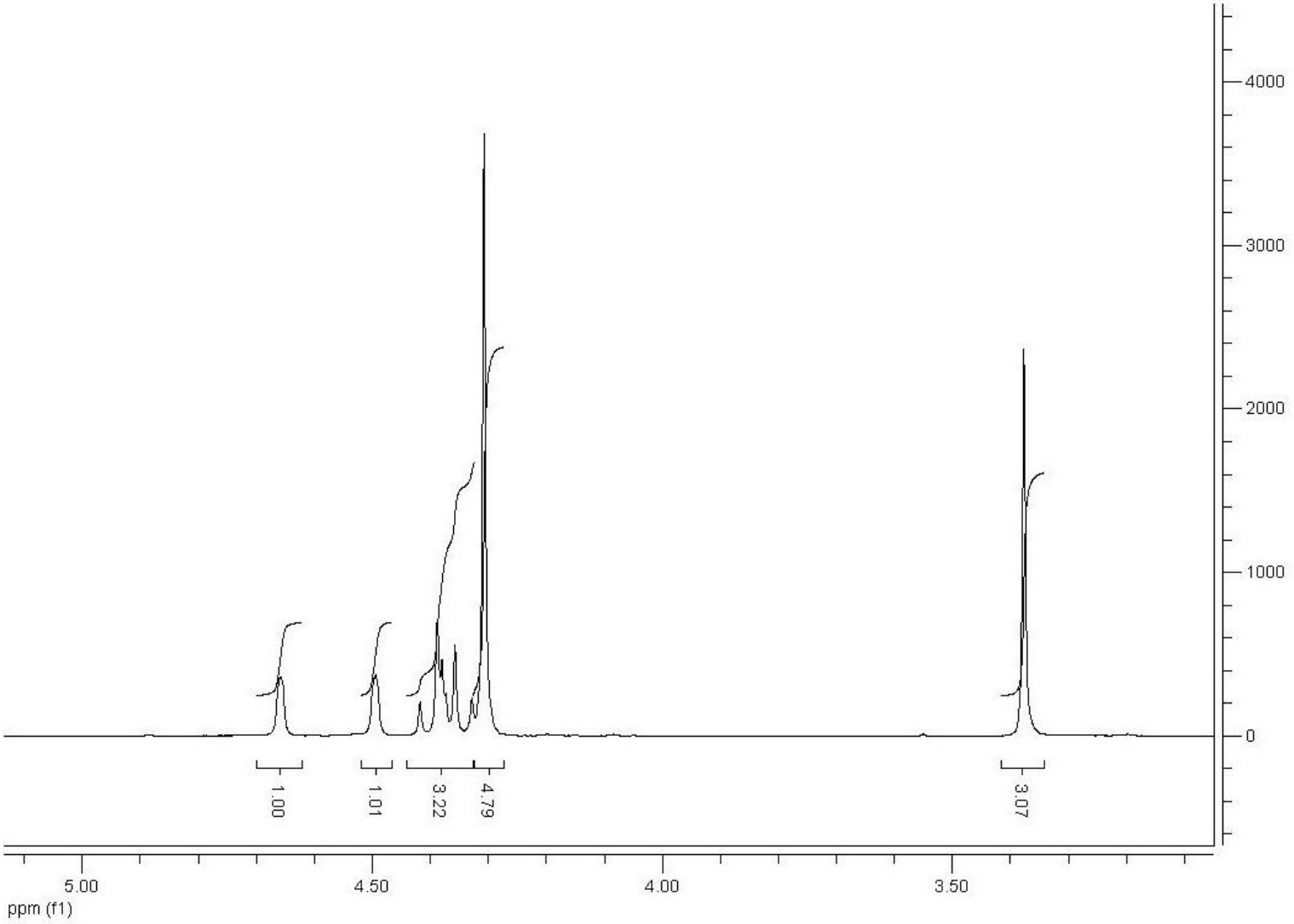
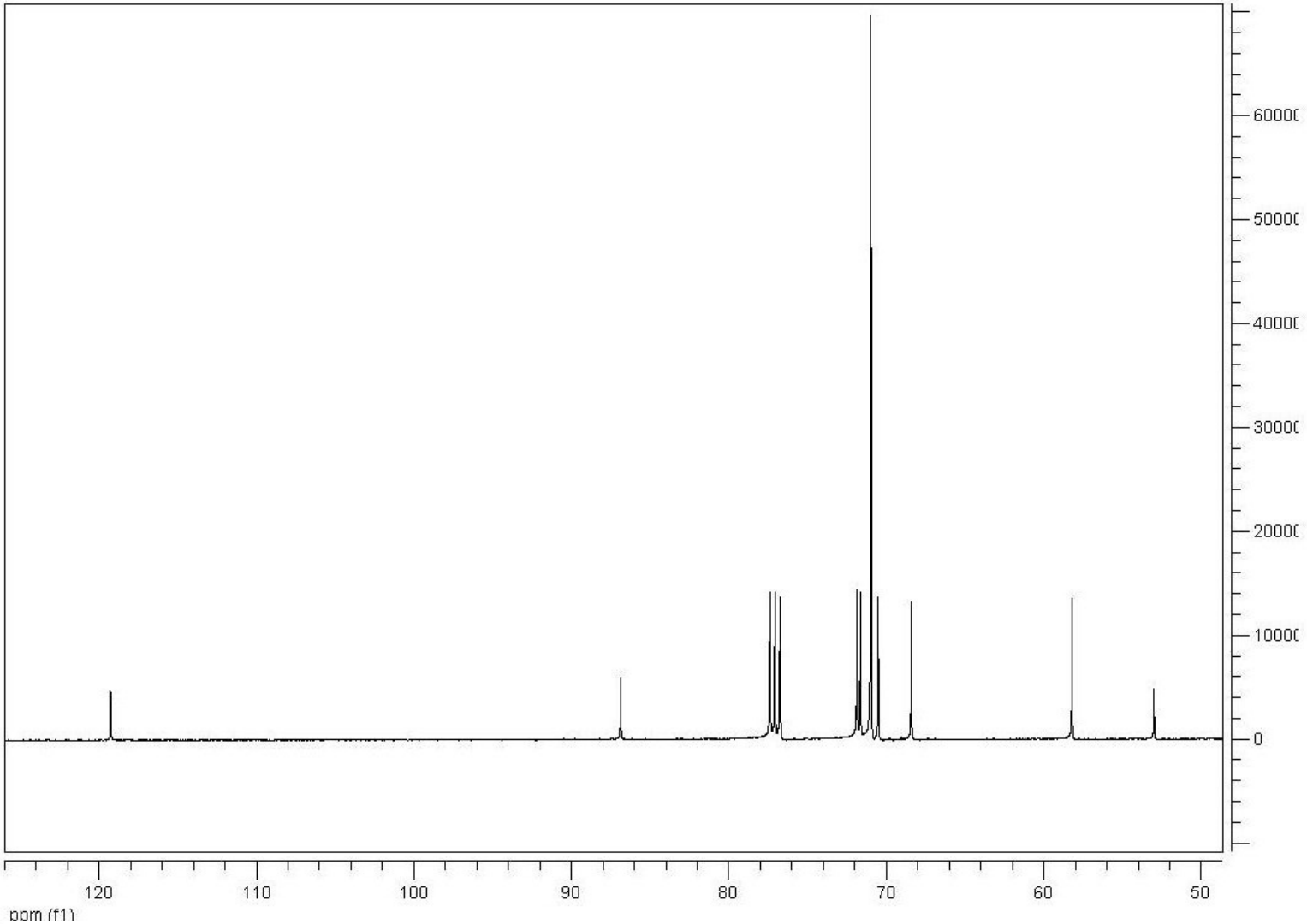


^{1}H-NMR of compound **1** ($CDCl_3$)



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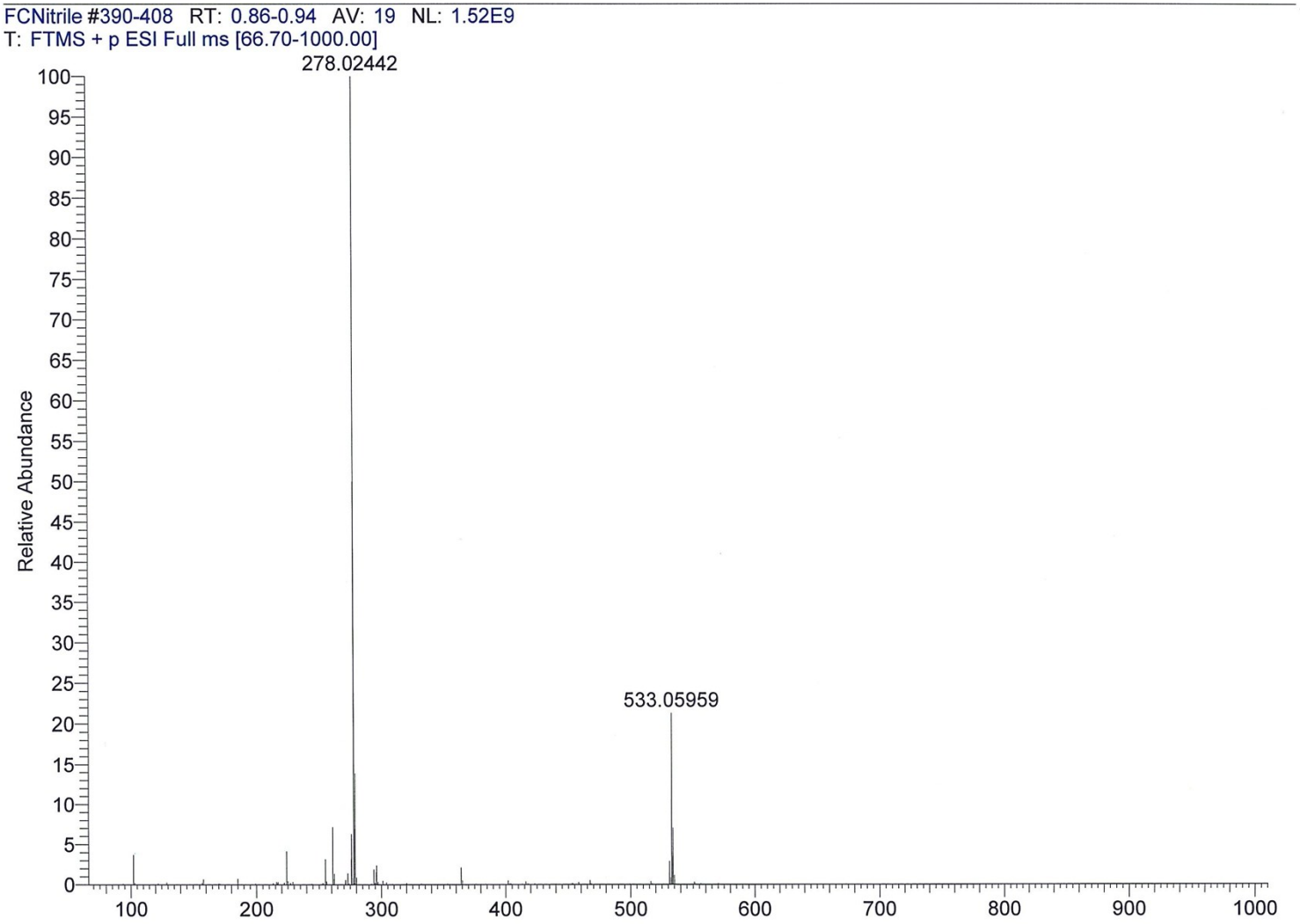

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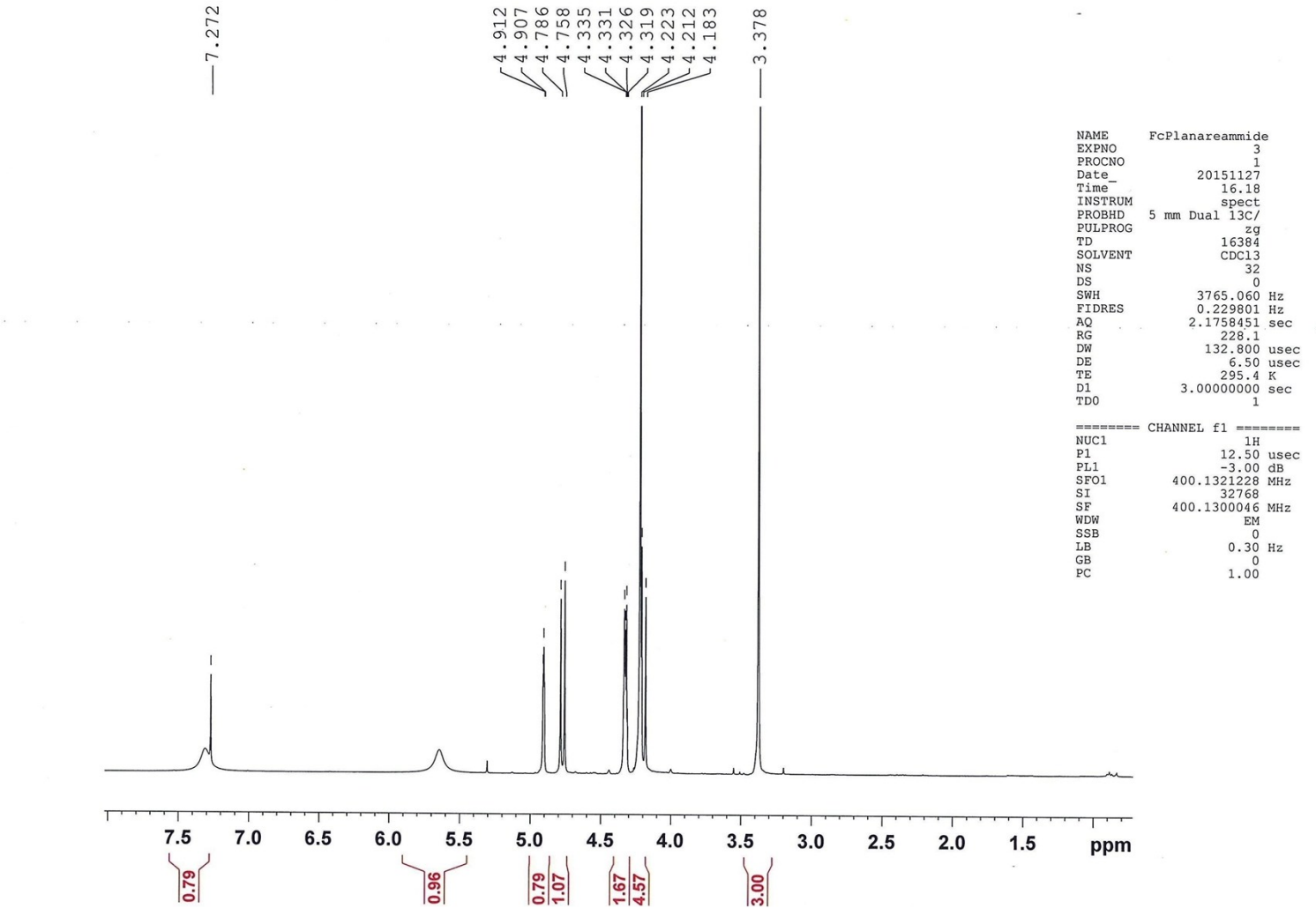
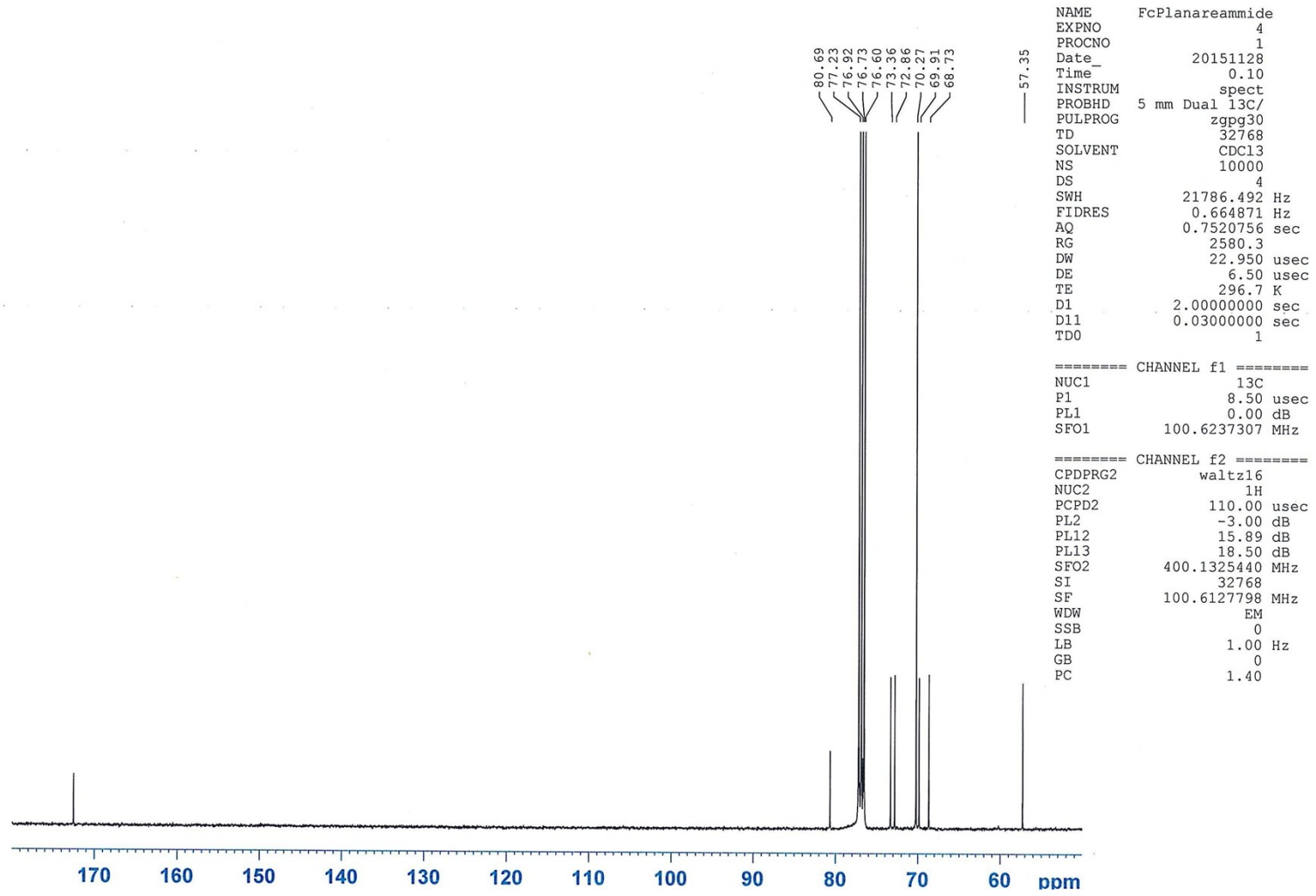
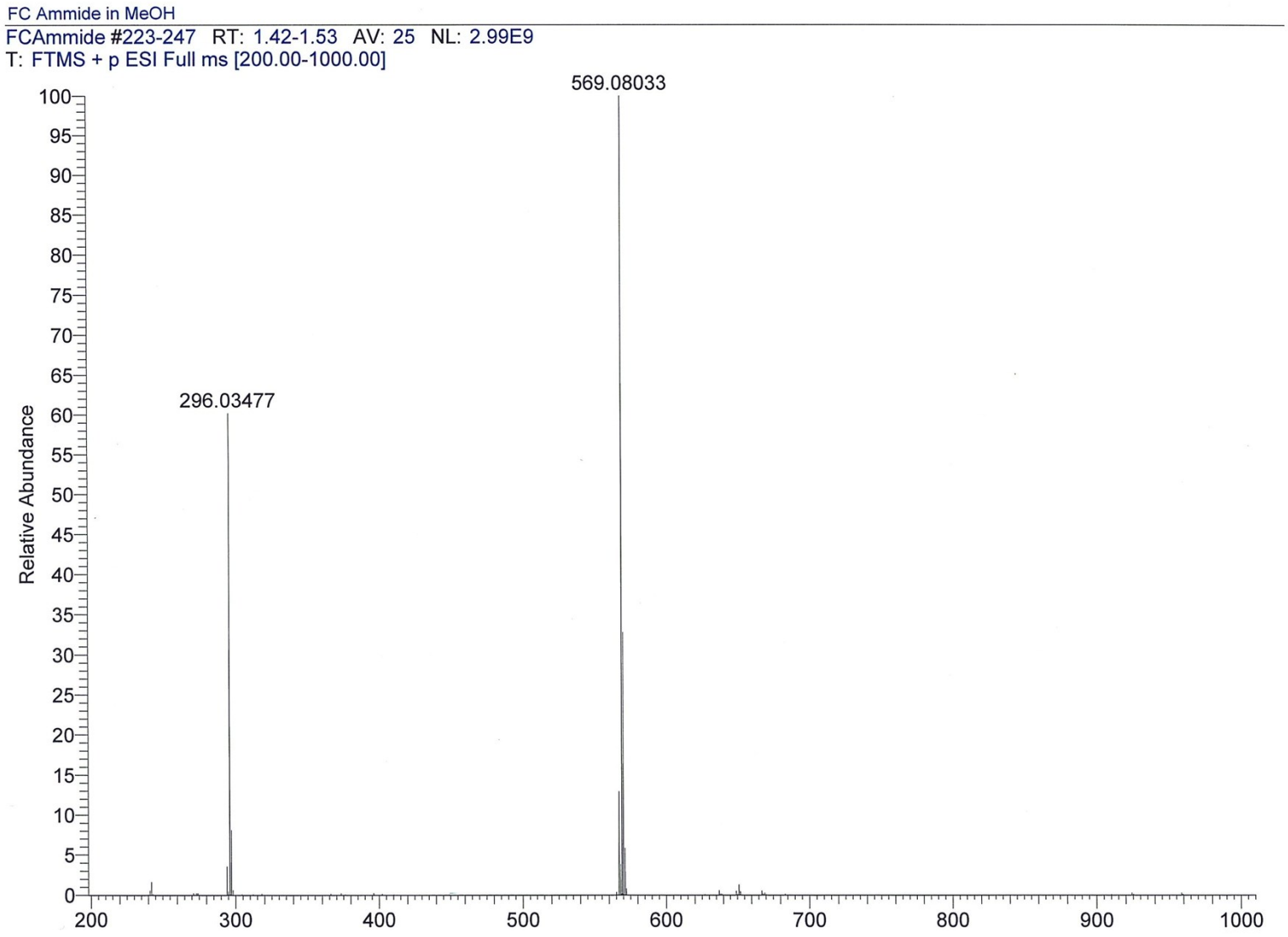


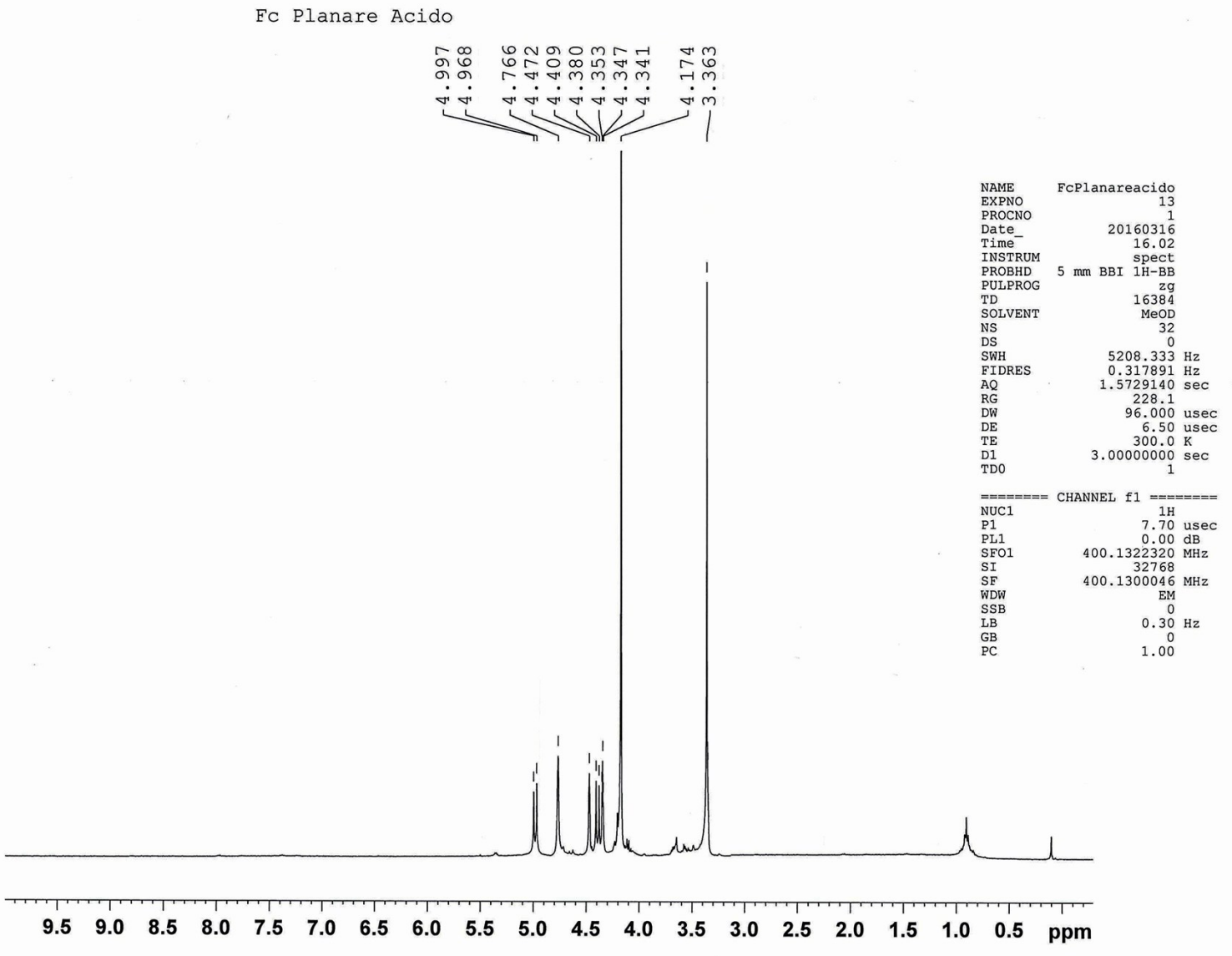
^{1}H-NMR of compound **6** ($CDCl_3$)



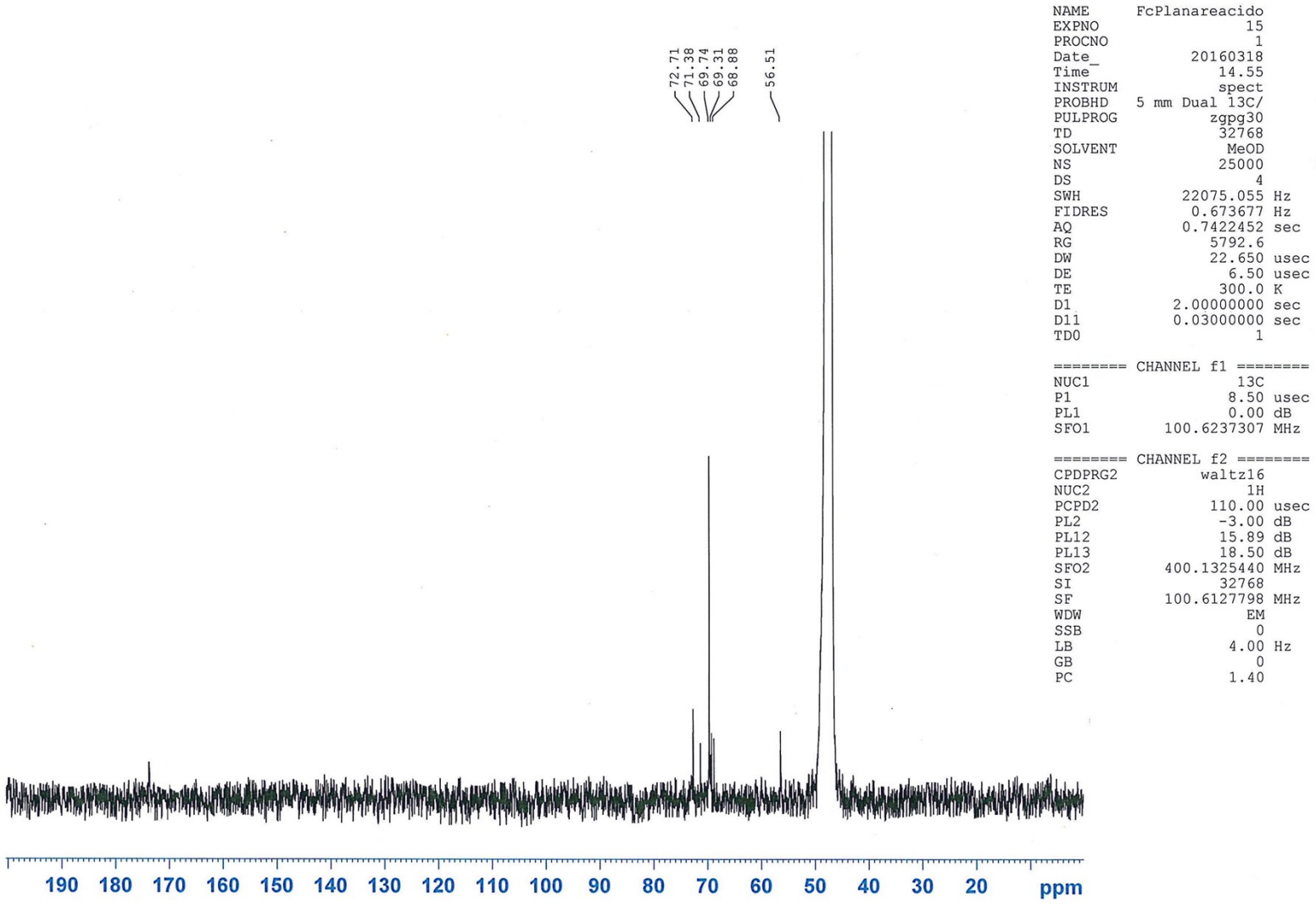
^{13}C-NMR of compound **6** ($CDCl_3$)



HR-MS of compound **6**

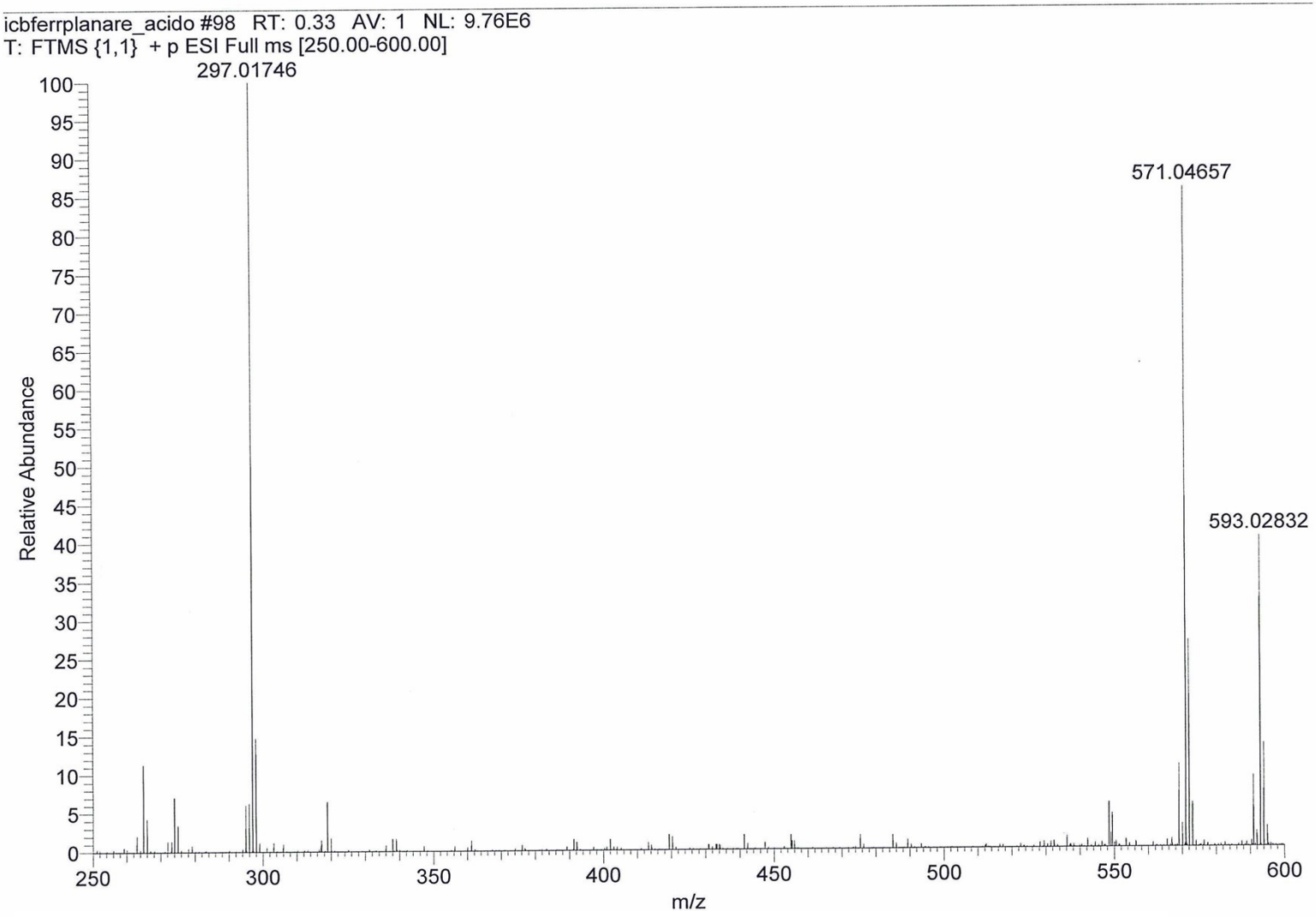


^{1}H-NMR of compound **7** (CD_3OD)

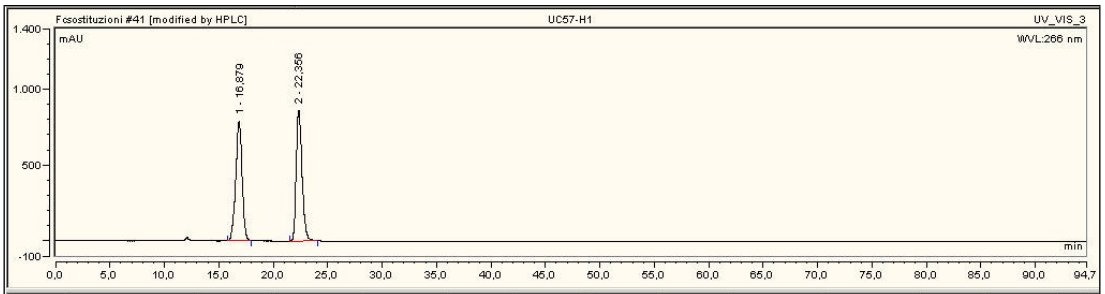


NAME	FcPlanareacido
EXPNO	15
PROCNO	1
Date_	20160318
Time	14.55
INSTRUM	spect
PROBHD	5 mm Dual 13C/
PULPROG	zgpg30
TD	32768
SOLVENT	MeOD
NS	25000
DS	4
SWH	22075.055 Hz
FIDRES	0.673677 Hz
AQ	0.7422452 sec
RG	5792.6
DW	22.650 usec
DE	6.50 usec
TE	300.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	8.50 usec
PL1	0.00 dB
SFO1	100.6237307 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	110.00 usec
PL2	-3.00 dB
PL12	15.89 dB
PL13	18.50 dB
SFO2	400.1325440 MHz
SI	32768
SF	100.6127798 MHz
WDW	EM
SSB	0
LB	4.00 Hz
GB	0
PC	1.40

^{13}C-NMR of compound **7** (CD_3OD)

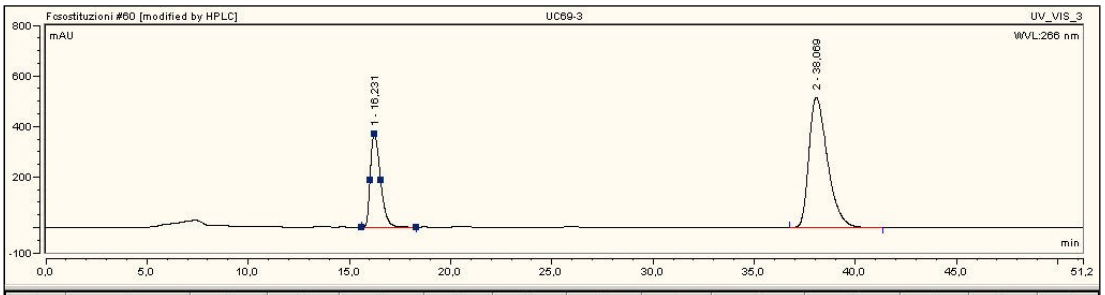


HR-MS of compound **7**



No.	Peakname	Ret.Time min	Area mAU*min	Amount	Type	Height mAU	Rel.Area %	Resolution
1	n.a.	16,879	535,5179	n.a.	BMB	783,583	49,97	5,50
2	n.a.	22,356	536,1676	n.a.	BMB	859,433	50,03	n.a.
Total:			1071,6855	0,0000		1643,016	100,00	

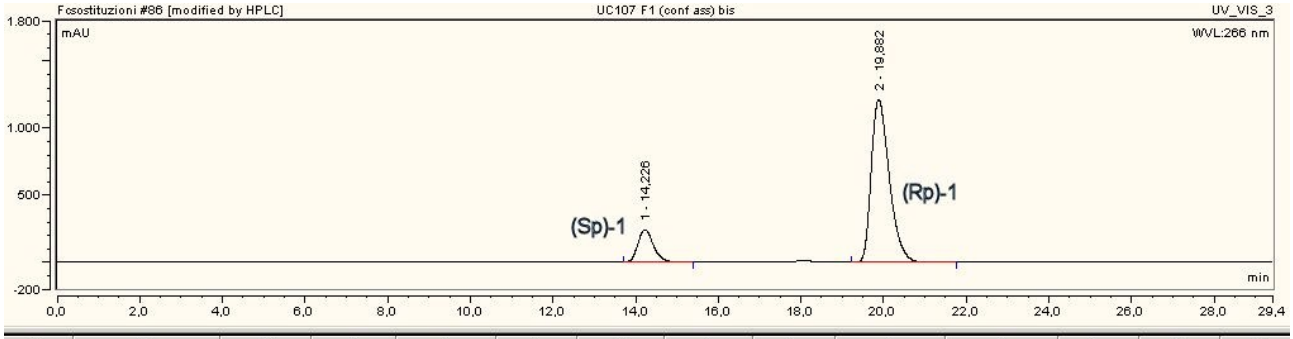
a)



No.	Peakname	Ret.Time min	Area mAU*min	Amount	Type	Height mAU	Rel.Area %	Resolution
1	n.a.	16,231	214,6991	n.a.	BMB	368,663	28,19	17,03
2	n.a.	38,069	547,0460	n.a.	BMB	513,572	71,81	n.a.
Total:			761,7451	0,0000		882,236	100,00	

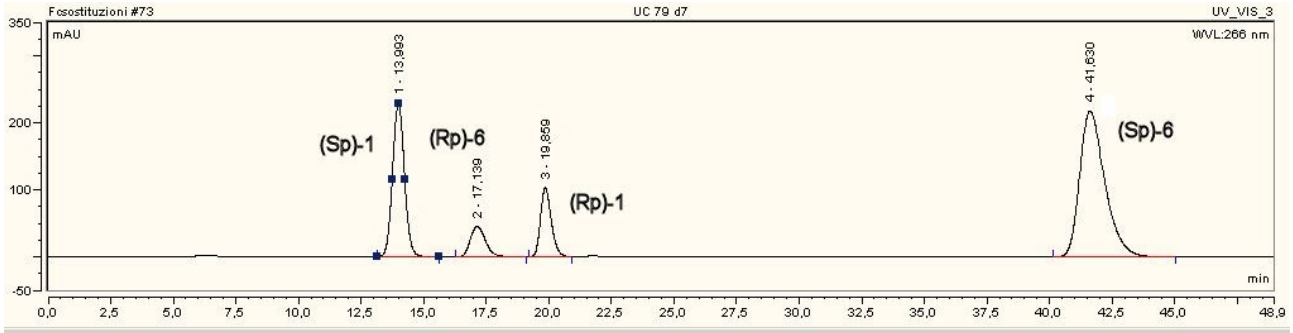
b)

Enantiomeric discrimination by chiral chromatography of: a) (±)-1-methoxymethyl-2-nitrile-ferrocene (**1**); b) 1-carboxamide-2-methoxymethyl-ferrocene (**6**) (sample injected was not racemic).



No.	Peakname	Ret.Time min	Area mAU*min	Amount	Type	Height mAU	Rel.Area %	Resolution
1	n.a.	14,226	106,1039	n.a.	BMB	242,307	14,76	7,72
2	n.a.	19,882	612,9881	n.a.	BMB	1212,819	85,24	n.a.
Total:			719,0920	0,0000		1455,126	100,00	

a)



No.	Peakname	Ret.Time min	Area mAU*min	Amount	Type	Height mAU	Rel.Area %	Resolution
1	n.a.	13,993	125,2340	n.a.	BMB	228,114	27,11	3,20
2	n.a.	17,139	31,5744	n.a.	BMB	45,059	6,83	2,90
3	n.a.	19,859	51,4078	n.a.	BMB	102,943	11,13	16,91
4	n.a.	41,630	253,7873	n.a.	BMB	217,480	54,93	n.a.
Total:			462,0034	0,0000		593,597	100,00	

b)

Determination of absolute configuration by chiral chromatographic comparison: a) (+)-(R_p)-1-methoxymethyl-2-nitrile-ferrocene (**1**) synthesized according Figure 7 in manuscript; b) Biotransformation mixture.