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General information

^{1}H NMR and ^{13}C NMR spectra were recorded in deuterated chloroform on a Bruker Avance DPX 500, 400 or 300 spectrometers and were referenced to residual chloroform (7.26 ppm, ^{1}H; 77.00 ppm, ^{13}C). Chemical shifts are expressed in parts per million (ppm). Data for ^{1}H are reported as follows: chemical shift (δ ppm), multiplicity (s = singulet, d = doublet, t = triplet, q = quartet, quint = quintuplet, sept = septuplet, m = multiplet), integration, coupling constant (Hz). Mass spectra and high resolution mass spectra (HRMS) were obtained on a Waters-Micromass Q-Tof micro instrument. IR data were obtained on a PerkinElmer Spectrum 100 FT-IR-spectrometer with only major peaks being reported. Thin layer chromatography (TLC) were performed on silica gel 60 F-254 plates (0.1 mm, Merck). Visualization was accomplished with UV (254 nm) or $KMnO_4$ staining solutions. Dichloromethane was dried and purified on Pure-Solv^{TM} 400 Solvent Purification System. Ethyl acetate (AcOEt) was dried on activated molecular sieves (4Å) and K_2CO_3 was dried by storage for 24 h in an oven at 120°C. Triethylamine (Et_3N) and dicyclohexylamine (Cy_2NH) were employed for Sonogashira coupling without prior purification. $Pd(PPh_3)_4$ was prepared according to known procedure.[1] Pd/C, $PdCl_2(PPh_3)_2$ and CuI were purchased from Alfa Aesar and were used as received. Technical grade N,N-dimethylformamide (DMF) was employed for this work. Catalyst **5** was prepared from (3*S*)-(+)-1-benzyl-3-aminopyrrolidine [114715-38-7] available from TCI**.**[2] Imine **7**[2] and IBX (2-iodoxybenzoic acid)[3] were prepared according to known procedures. 2-Bromopyridine, 2-chloropyrazine, 2-bromopyrimidine, 4-bromopyridine.HCl, 2-chloroquinoline, 2-bromothiazole, 5-nitro-2-chloropyridine, 1,2-dichloropyridine, 2,6-dichloropyrazine, 3-chloropyridine, 3-chloroquinoline and ylide **9** were purchased from chemical suppliers. All hydrogenations were performed in normal vessel under a balloon of H_2.

Chromatographic separations were achieved on silica gel columns (Kieselgel 60, 40–63 μm, Merck). Optical rotations were measured on a Perkin–Elmer 241 LC polarimeter in a 10 cm cell. $[\alpha]_D$ Values are given in units of 10^{-1} deg $cm^2.g^{-1}$. The absolute configuration of the Mannich adducts was deduced from the model presented in our previous study.[2] Melting points were determined on a Electrothermal digital apparatus IA9100 series and are uncorrected. Analytical high performance liquid chromatographies (HPLC) were carried out with a Waters instrument [detector M996 (200–400 nm) and pump 600] and the conditions are indicated for each compounds. Unless otherwise indicated, enantiomeric excess (ee) were determined by chiral HPLC and diastereoisomeric ratio (dr) were measured by ^{1}H NMR on 300 MHz or 400 MHz. The racemic mixture of chiral products were synthesized by employing *rac*-**5** prepared from *rac*-1-benzyl-3-aminopyrrolidine [18471-40-4] available from TCI.

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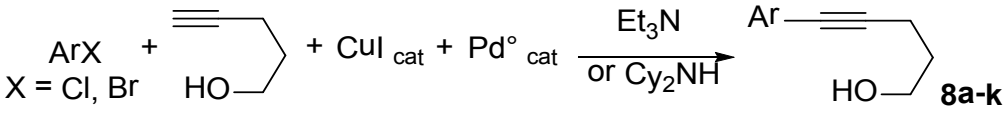
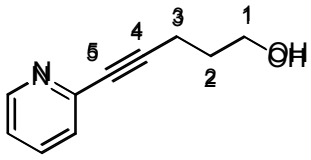
[1] L. Malatesta, M. Angoletta, *J. Chem. Soc.* **1957**, 1186 – 1188.
[2] M. Pouliquen, J. Blanchet, M.-C. Lasne, J. Rouden, *Org. Lett.* **2008**, *10*, 1029 – 1032.
[3] M. Frigerio, M. Santagostino, S. Sputore, *J. Org. Chem.* **1999**, *64*, 4537 – 4538.

Hydroxyls 8a-k



Conditions are detailed for each compound.

5-(Pyridin-2-yl)pent-4-yn-1-ol (8a):[4]



In a one-neck flask under argon atmosphere containing a suspension of 2-bromopyridine (948 mg, 6 mmol, 1 equiv), CuI (58.0 mg, 0.3 mmol, 0.05 equiv), $PdCl_2(PPh_3)_2$ (210 mg, 0.3 mmol, 0.05 equiv) in Et_3N (30 mL) was added dropwise 4-pentyn-1-ol (700 µL, 7.2 mmol, 1.2 equiv) at rt. The suspension was stirred at this temperature for 3 h (TLC monitoring). Then, the suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated under reduced pressure to give 1.3 g of crude alcohol **8a**. The residue was purified by flash chromatography (AcOEt) on silica gel pretreated (washed with 1% Et_3N in AcOEt) to yield 990 mg (>95%) of **8a** as an orange oil.

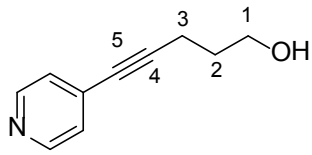
^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.84-1.93 (m, 2H, H_2), 2.57 (t, 3H, *J* = 7.1 Hz, H_3 + O*H*), 3.81 (t, 2H, *J* = 6.2 Hz, H_1), 7.14 (ddd, 1H, *J* = 1.1, 4.9, 6.1 Hz), 7.37 (m, 1 H), 7.60 (dt, 1H, *J* = 1.9, 7.8 Hz), 8.52 (m, 1H) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 149.2 (CH), 143.3 (Cq), 136.1 (CH), 126.6 (CH), 122.2 (CH), 90.7 (Cq), 80.0 (Cq), 60.5 (CH_2), 30.9 (CH_2), 15.6 (CH_2) *ppm*

MS (SCI) *m/z* = 162 (M+H)

$\boldsymbol{R_f}$ = 0.35 (AcOEt)

5-(Pyridin-4-yl)pent-4-yn-1-ol (8b) :



To a solution of 4-bromopyridine (655 mg, 4.1 mmol, 1.0 equiv), CuI (16 mg, $8.20.10^{-2}$ mmol, 0.02 equiv), $PdCl_2(PPh_3)_2$ (29 mg, $4.1.10^{-2}$ mmol, 0.01 equiv) in Et_3N (8 mL) under argon atmosphere was added dropwise 4-pentyn-1-ol (227 µL, 2.45 mmol, 1.3 equiv) at rt. Then, the mixture was heated 90°C for 40 min and cooled to rt. The suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated under reduced pressure to give crude alcohol. The residue was purified by flash chromatography (AcOEt) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 505 mg (77 %) of alcohol **8b** as a yellow solid.

[4] M. Lautens, M. Yoshida, *J. Org. Chem*. **2003**, *68*, 762-769.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.78-1.91 (m, 2H, H_2), 2.55 (t, 2H, J = 7.1 Hz, H_3), 2.81 (broad s, 1H, O*H*), 3.77 (t, 2H, J = 6.2 Hz, H_1), 7.21 (d, 2H, J = 5.2 Hz), 8.48 (d, 2H, J = 5.2 Hz) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.8 (2xCH), 132.4 (Cq), 125.7 (2xCH), 95.6 (Cq), 78.1 (Cq), 60.3 (CH_2), 31.0 (CH_2), 15.7 (CH_2) *ppm*

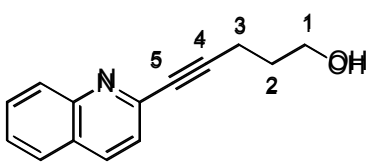
IR (neat): 3200, 2914, 2217, 1599, 1419, 1074, 827, 537 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_{10}N_2O_3$: 162.0919, found: 162.0912

R_f = 0.5 (AcOEt)

mp = 70°C from iPr_2O

5-(Quinolin-2-yl)pent-4-yn-1-ol (8c) :



In an one-neck flask under argon atmosphere containing a solution of 2-chloroquinoline (1.000 g, 6.1 mmol, 1 equiv), CuI (58 mg, 0.3 mmol, 0.05 equiv), $PdCl_2(PPh_3)_2$ (210 mg, 0.3 mmol, 0.05 equiv) in Et_3N (20 mL) was added dropwise 4-pentyn-1-ol (677 µl, 7.2 mmol, 1.2 equiv) at rt. The mixture was allowed to react for 24 h (TLC monitoring). Then, the suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to an oil which was diluted in AcOEt (20 mL) and extracted (3x100 mL) with an aqueous solution of HCl (0.1M). The resulting aqueous layer was separated and washed with Et_2O. The aqueous layer was treated with a saturated solution of $NaHCO_3$ until basic pH (≈ 8) was reached. After extraction of the aqueous layer with AcOEt (3x), the resulting organic layer was dried on $MgSO_4$, filtered and volatiles were removed. The residue was purified by flash chromatography (AcOEt) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 1.15 g (88%) of **8c** as an orange oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.86-1.99 (m, 2H, H_2), 2.54 (broad s, 1H, O*H*), 2.63 (t, 2H, J = 6.9 Hz, H_3), 3.85 (t, 2H, J = 6.2 Hz, H_1), 7.40-7.53 (m, 2H), 7.64-7.76 (m, 2H), 8.05 (d, 2H, J = 8.7 Hz) *ppm*

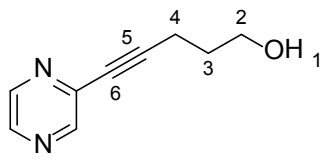
^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.5 (Cq), 143.6 (Cq), 136.0 (CH), 129.8 (CH), 128.5 (CH), 127.2 (CH), 126.7 (Cq), 126.6 (CH), 124.0 (CH), 91.5 (Cq), 81.0 (Cq), 60.7 (CH_2), 30.9 (CH_2), 15.9 (CH_2) *ppm*

IR (neat): 3286, 2927, 223, 1593, 1553, 1500, 1424, 1310, 1052, 827, 754, 731 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{14}H_{14}NO$: 212.1075, found: 212.1070

R_f = 0.7 (AcOEt)

5-(pyrazin-2-yl)pent-4-yn-1-ol (8d):



In an one-neck flask under argon atmosphere containing a solution of 2-chloropyrazine (681 mg, 532 µL, 5.97 mmol, 1.1 equiv), CuI (14.0 mg, $7.34.10^{-2}$ mmol, 0.012 equiv), $PdCl_2(PPh_3)_2$ (51.0 mg, $7.26.10^{-2}$ mmol, 0.012 equiv) in Et_3N (7 mL) was added dropwise 4-pentyn-1-ol (0.5 mL, 6.5 mmol, 1.1 equiv) at rt. The mixture was allowed to react for 22 h (TLC monitoring) at this temperature. Then, the suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to an oil which was purified by flash chromatography (AcOEt) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 760 mg (87%) of **8d** as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.83-1.96 (m, 3H, O*H* + H_2), 2.61 (t, 2H, *J* = 7.1 Hz, H_3), 3.81 (t, 2H, *J* = 6.2 Hz, H_1), 8.42 (m, 1H), 8.48 (m, 1H), 8.59 (s, 1H) *ppm*

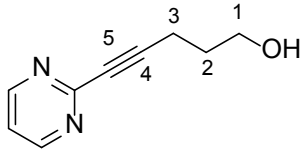
^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.3 (CH), 143.9 (CH), 142.2 (CH), 140.2 (Cq), 95.0 (Cq), 77.6 (Cq), 60.5 (CH_2), 30.6 (CH_2), 15.7 (CH_2) *ppm*

IR (neat): 3368, 2943, 2227, 1462, 1395, 1140, 1057, 1013, 728, 409 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_{10}N_2O_3$: 163.0871, found: 163.0874

$\boldsymbol{R_f}$ = 0.45 (AcOEt)

5-(Pyrimidin-2-yl)pent-4-yn-1-ol (8e):



In an one-neck flask under argon atmosphere containing a solution of 2-bromopyrimidine (300 mg, 1.89 mmol, 1.0 equiv), CuI (8.0 mg, $4.19.10^{-2}$ mmol, 0.02 equiv), $PdCl_2(PPh_3)_2$ (27.0 mg, $3.84.10^{-2}$ mmol, 0.02 equiv) in CH_3CN/Cy_2NH (5.1 mL/ 0.45 mL) was added dropwise 4-pentyn-1-ol (227 µL, 2.45 mmol, 1.3 equiv) at rt. The mixture was allowed to react for 15 h (TLC monitoring). Then, the suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to an oil which was purified by flash chromatography (AcOEt) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 260 mg (86%) of **8e** as an orange oil. In the event, the product can be solubilized in AcOEt and washed with a saturated solution of citric acid to remove traces of Cy_2NH.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.87-1.96 (m, 2H, H_2), 2.26 (broad s, 1H, O*H*), 2.61 (t, 2H, *J* = 6.8 Hz, H_3), 3.82 (t, 2H, *J* = 6.1 Hz, H_1), 7.21 (t, 1H, *J* = 4.8 Hz), 8.68 (d, 2H, *J* = 4.8 Hz) *ppm*

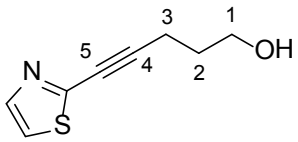
^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.8 (2xCH), 152.2 (Cq), 119.4 (CH), 90.5 (Cq), 79.4 (Cq), 60.3 (CH_2), 30.2 (CH_2), 15.3 (CH_2) *ppm*

IR (neat) : 3338, 2937, 2239, 1720, 1556, 1412, 1042, 801, 724 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_{10}N_2O_3$: 163.0871, found: 163.0868

$\boldsymbol{R_f}$ = 0.3 (AcOEt)

5-(Thiazol-2-yl)pent-4-yn-1-ol (8f):



In an one-neck flask under argon atmosphere containing a solution of 2-bromothiazole (1.77 g, 10.8 mmol, 1.0 equiv), CuI (86 mg, 0.451 mmol, 0.04 equiv), $Pd(PPh_3)_4$ (624 mg, 0.54 mmol, 0.05 equiv) in CH_2Cl_2/Et_3N (20 mL/10 mL) was added dropwise 4-pentyn-1-ol (1.0 mL, 10.8 mmol, 1.0 equiv) at rt. The mixture was stirred for 7 days. Then, the suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to give 1.3 g of crude alcohol which was purified by flash chromatography (Et_2O then AcOEt) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 1.44 g (80%) of **8f** as an orange oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.75 (broad s, 1H, O*H*), 1.82-1.96 (m, 2H, H_2), 2.61 (t, 2H, *J* = 7.1 Hz, H_3), 3.81 (t, 2H, *J* = 6.1 Hz, H_1), 7.28 (d, 1H, *J* = 3.4 Hz), 7.76 (d, 1H, *J* = 3.4 Hz) *ppm*

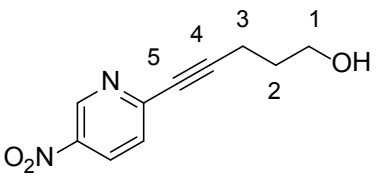
^{13}C NMR (50 MHz, $CDCl_3$) δ = 149.1 (Cq), 142.3 (CH), 119.9 (CH), 96.1 (Cq), 73.6 (Cq), 60.1 (CH_2), 30.4 (CH_2), 15.7 (CH_2) *ppm*

IR (neat): 3353, 2949, 2232, 1482, 1412, 1217, 1135, 1060, 726, 622 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_8H_{10}NOS$: 168.0483, found: 168.0485

R_f = 0.5 (AcOEt)

5-(5-Nitropyridin-2-yl)pent-4-yn-1-ol (8g):



To a solution of 5-nitro-2-chloropyridine (1.72 g, 8.34 mmol, 1 equiv), CuI (103 mg, 0.54 mmol, 0.05 equiv), $PdCl_2(PPh_3)_2$ (380 mg, 0.54 mmol, 0.05 equiv) in Et_3N (35 mL) under argon atmosphere was added dropwise 4-pentyn-1-ol (1 mL, 10.8 mmol, 1.3 equiv) at rt. The mixture was allowed to react for 48 h (TLC monitoring). Then, the suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated under reduced pressure to give the crude alcohol which was purified by flash chromatography (CH_2Cl_2/Et_2O: 5/1 → 3/1) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 1.3 g (58%) of **8g** as a red solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.87-1.96 (m, 2H, H_2), 2.0 (broad s, 1H, O*H*), 2.57 (t, 2H, *J* = 7.1 Hz, H_3), 3.73 (t, 2H, *J* = 6.1 Hz, H_1), 7.47 (d, 1H, *J* = 8.6 Hz), 8.35 (dd, 1H, *J* = 2.7, 8.6 Hz), 9.25 (d, 1H, *J* = 2.7 Hz) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 148.9 (Cq), 145.2 (CH), 142.5 (Cq), 131.4 (CH), 126.9 (CH), 97.2 (Cq), 79.9 (Cq), 61.0 (CH_2), 30.8 (CH_2), 16.1 (CH_2) *ppm*

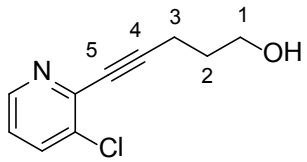
IR (neat): 3261, 3078, 2876, 2217, 1588, 1570, 1522, 1462, 1343, 1272, 1110, 855 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_{10}N_2O_3$: 207.0770, found: 207.0779

R_f = 0.5 (Et_2O/CH_2Cl_2: 1/3)

mp = 55°C from Et_2O

5-(3-Chloropyridin-2-yl)pent-4-yn-1-ol (8h):



To a solution of 1,2-dichloropyridine (1.60. g, 10.6 mmol, 1 equiv), CuI (103 mg, 0.54 mmol, 0.05 equiv), $PdCl_2(PPh_3)_2$ (380 mg, 0.54 mmol, 0.05 equiv) in Et_3N (35 mL) under argon atmosphere was added dropwise 4-pentyn-1-ol (1 mL, 10.8 mmol, 1.0 equiv) at rt. The mixture was allowed to react for 23 h (TLC monitoring). Then, the suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to a residue which was purified by flash chromatography (pentane/Et_2O: 1/3) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to give a mixture of **8h** and unreacted 5-pentyn-1-ol. This mixture was treated with 2.2 mL of HCl (5 M in iPrOH) and the resulting hydrochloride was recrystallized from CH_2Cl_2/Et_2O to yield 300 mg of **8h.HCl** which under treatment with aqueous solution of $NaHCO_3$ (sat), extraction of the aqueous layer with CH_2Cl_2 (3x) and removal of the volatiles afforded 210 mg (10%) of **8h**.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.75 (m, 1H, O*H*), 1.87-1.96 (m, 2H, H_2), 2.65 (t, 2H, *J* = 7.0 Hz, H_3), 3.85 (t, 2H, *J* = 6.1 Hz, H_1), 7.15 (dd, 1H, *J* = 4.7, 8.1 Hz), 7.69 (dd, 1H, *J* = 1.5, 8.1 Hz), 8.42 (dd, 1H, *J* = 1.5, 4.7 Hz) *ppm*

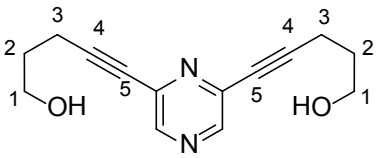
^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.6 (CH), 142.1 (Cq), 136.6 (CH), 133.8 (Cq), 123.1 (CH), 96.1 (Cq), 78.1 (Cq), 61.4 (CH_2), 30.8 (CH_2), 16.1 (CH_2) *ppm*

IR (neat): 3323, 2935, 2230, 1569, 1421, 1136, 1075, 1036, 795, 753, 660 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_{11}NOCl$: 196.0529, found: 196.0538

R_f = 0.13 (CH_2Cl_2/MeOH: 99/1)

5,5'-(Pyrazine-2,6-diyl)bis(pent-4-yn-1-ol) (8i):



In a sealed tube capped with a septum under argon atmosphere, a suspension of 2,6-dichloropyrazine (672 mg, 4.51 mmol, 1 equiv), CuI (24 mg, 0.126 mmol, 0.028 equiv), $PdCl_2(PPh_3)_2$ (88 mg, 0.126 mmol, 0.028 equiv) in Et_3N (7 mL) was treated with 4-pentyn-1-ol (1 mL, 10.8 mmol, 2.4 equiv) introduced dropwise at rt. Then, the septum was removed and the tube was sealed and heated at 50°C for 1 h then cooled to rt. The suspension was filtered through a pad of Celite® washing with AcOEt and the filtrate was concentrated to give the crude alcohol. The residue was purified by flash chromatography (AcOEt) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 1.05 g (95%) of **8i** as yellow solid. In the event, impurities may be removed from **8i** by washing the solid with Et_2O.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.84-1.95 (m, 6H, H_2 + OH), 2.60 (t, 4H, J = 7.1 Hz, H_3), 3.80 (t, 4H, J = 6.2 Hz, H_1), 8.44 (s, 2H) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.5 (CH), 139.2 (Cq), 95.2 (Cq), 77.0 (Cq), 60.2 (CH_2), 30.4 (CH_2), 15.5 (CH_2) *ppm*

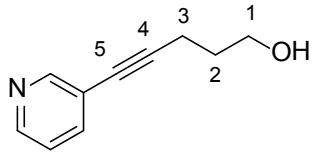
IR (neat): 3320, 2939, 2867, 2230, 1509, 1403, 1256, 1157, 1052, 1009, 729 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{14}H_{17}N_2O_2$: 245.1290, found: 245.1293

$\boldsymbol{R_f}$ = 0.4 (AcOEt)

mp = 44-46°C from Et_2O

5-(Pyridin-3-yl)pent-4-yn-1-ol (8j):



In an one-neck flask connected to a water condenser was added, at rt and under argon atmosphere, 4-pentyn-1-ol (0.55 mL, 5.9 mmol, 1.1 equiv) to a solution of 3-chloropyridine (800 mg, 5.55 mmol, 1 equiv), CuI (20 mg, 0.104 mmol, 0.02 equiv) and $PdCl_2(PPh_3)_2$ (36 mg, $4.98.10^{-2}$ mmol, 0.01 equiv) in Et_3N (1.5 mL). Then, the flask was heated at 90°C for 30 min and cooled to rt. The suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to give an oil which was purified by flash chromatography (AcOEt) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 740 mg (91 %) of **8j** as an orange oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.79-1.88 (m, 2H, H_2), 2.53 (t, 2H, J = 7.2 Hz, H_3), 3.08 (broad s, 1H, O*H*), 3.77 (t, 2H, J = 6.1 Hz, H_1), 7.18 (dd, 1H, J = 4.9, 7.9 Hz), 7.63 (dt, 1H, J = 1.8, 8.1 Hz), 8.42 (d, 1 H, J = 4.9 Hz), 8.57 (s, 1H) *ppm*

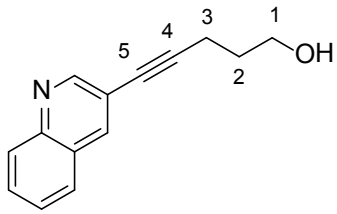
^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.3 (CH), 146.9 (CH), 138.4 (CH), 122.7 (CH), 120.8 (Cq), 93.4 (Cq), 76.8 (Cq), 60.1 (CH_2), 30.9 (CH_2), 15.5 (CH_2) *ppm*

IR (neat): 3331, 2932, 2228, 1565, 1477, 1408, 1265, 1051, 805, 734, 704 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_{12}NO$: 162.0919, found: 162.0911

$\boldsymbol{R_f}$ = 0.6 (AcOEt)

5-(Quinolin-3-yl)pent-4-yn-1-ol (8k):



In a sealed tube capped with a septum containing a solution of 3-bromoquinoline (2.15 g, 1.45 mL, 10.8 mmol, 1 equiv), CuI (15 mg, $7.87.10^{-2}$ mmol, 0.008 equiv), $PdCl_2(PPh_3)_2$ (80 mg, 0.113 mmol, 0.01 equiv) in Et_3N/CH_2Cl_2 (4.8 mL/9.1 mL) was added, under argon atmosphere, 4-pentyn-1-ol (1.0 mL, 10.8 mmol, 1.0 equiv) at rt. Then, the septum was removed and the tube was sealed and heated at 90°C for 5 h then cooled to rt. The suspension was filtered

through a pad of Celite® washing with AcOEt and the filtrate was concentrated to a solid which was purified by flash chromatography (CH_2Cl_2/MeOH: 98/2) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 1.7 g (78 %) of **8k** as a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.85-1.94 (m, 2H, H_2), 2.61 (t, 2H, J = 6.8 Hz, H_3), 2.80 (broad s, 1H, O*H*), 3.84 (t, 2H, J = 5.7 Hz, H_1), 7.48-7.53 (m, 1H), 7.64-7.72 (m, 2H), 8.05 (d, 1H, J = 8.6 Hz), 8.12 (s, 1H), 8.84 (s, 1H) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.7 (CH), 145.6 (Cq), 137.9 (CH), 129.4 (CH), 128.3 (CH), 127.0 (CH), 126.9 (Cq), 126.8 (CH), 117.7 (Cq), 93.3 (Cq), 77.6 (Cq), 60.3 (CH_2), 31.1 (CH_2), 15.7 (CH_2) *ppm*

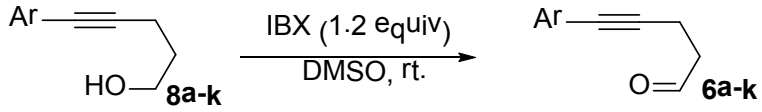
IR (neat): 3256, 2949, 2847, 2232, 1490, 1353, 1275, 1070, 912, 748 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{14}H_{14}NO$: 212.1075, found: 212.1080

R_f = 0.7 (AcOEt)

mp = 61°C

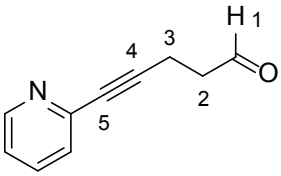
Preparation of aldehydes 6a-k



5-(Pyridin-2-yl)pent-4-ynal (6a):

Representative procedure

To a solution of alcohol **8a** (106 mg, 0.66 mmol, 1 equiv) in DMSO (3.2 mL) was added in one portion IBX (203 mg, 0.72 mmol, 1.2 equiv). After 21 h of reaction (TLC monitoring), water (10 mL) was added and the resultant suspension was filtered. The filtrate was extracted with AcOEt (3x) and the combined organic layers were brined, dried on $MgSO_4$ and filtered. The volatiles were removed under reduced pressure to give 75 mg (72%) of crude aldehyde **6a** as a brown oil, which was used without further purification.



^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.68-2.80 (m, 4H, H_2 + H_3), 7.19 (ddd, 1H, J = 1.2, 4.9, 6.2 Hz), 7.36 (d, 1H, J = 7.7 Hz), 7.61 (dt, 1H, J = 1.9 Hz, 7.7 Hz), 8.53 (d, 1H, J = 4.9 Hz), 9.84 (s, 1H, H_1) *ppm*

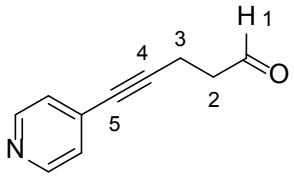
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.9 (CH), 149.7 (CH), 143.2 (Cq), 136.0 (CH), 126.7 (CH), 122.5 (CH), 88.2 (Cq), 80.8 (Cq), 42.1 (CH_2), 12.3 (CH_2) *ppm*

IR (neat): 2918, 2234, 1727, 1582, 1463, 1427, 118, 721 cm^{-1}

HRMS (API +) calcd for $(M+H)^+$ $C_{10}H_{10}NO$: 160.0762, found: 160.0755

R_f = 0.4 (pentane/AcOEt: 1/1)

5-(Pyridin-4-yl)pent-4-yn-1-al (6b):



According to the representative procedure, **8b** (230 mg) was transformed into **6b** (197 mg, 86 %) as a brown oil.

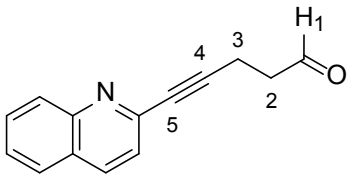
^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.76-2.80 (m, 4H, H_2 + H_3), 7.23 (dd, 2H, J = 1.5, 4.5 Hz), 8.53 (d, 2H, J = 5.5 Hz), 8.61 (s, 1H), 9.85 (s, 1H, H_1) *ppm*

^{13}C NMR (75 MHz, CDCl3) δ = 199.5 (CH), 149.2 (2xCH), 131.4 (Cq), 125.5 (2xCH), 93.1 (Cq), 78.7 (Cq), 41.8 (CH_2), 12.2 (CH_2) *ppm*

IR (neat): 3284, 2916, 2847, 2721, 2226, 1723, 1593, 1407, 1214, 1060, 821, 546 cm^{-1}

$\boldsymbol{R_f}$ = 0.34 (AcOEt/pentane: 1/2)

5-(Quinolin-2-yl)pent-4-yn-1-al (6c):



According to the representative procedure, **8c** (230 mg) was transformed into **6c** (197 mg, 85 %) as a brown oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.79-2.90 (m, 4H, H_2 + H_3), 7.45 (d, 1H, J = 8.3 Hz), 7.53 (t, 1H, J = 7.2 Hz), 7.71 (t, 1H, J = 7.2 Hz), 7.78 (d, 1H, J = 8.3 Hz), 8.08 (t, 2H, J = 8.2 Hz), 9.87 (s, 1H, H_1) *ppm*

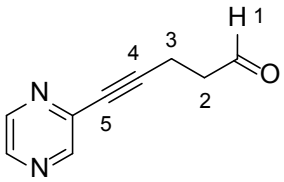
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.6 (CH), 147.5 (Cq), 143.1 (Cq), 135.8 (CH), 129.6 (CH), 128.6 (CH), 127.1 (CH), 126.6 (CH + Cq), 123.7 (CH), 89.0 (Cq), 81.3 (Cq), 41.7 (CH_2), 12.2 (CH_2) *ppm*

IR (neat): 2990, 2901, 2230, 1724, 1594, 1554, 1499, 1425, 831, 758 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{14}H_{12}NO$: 210.0919, found: 210.0907

$\boldsymbol{R_f}$ = 0.55 (Et_2O)

5-(Pyrazin-2-yl)pent-4-yn-1-al (6d):



According to the representative procedure, **8d** (142 mg) was transformed into **6d** (106 mg, 75 %) as a brown oil.

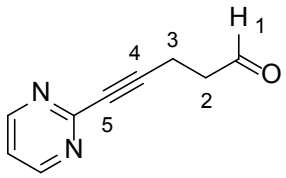
^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.81-2.88 (m, 4H, H_2 + H_3), 8.46 (m, 1H), 8.50 (m, 1H), 8.61 (s, 1H), 9.85 (s, 1H, H_1) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.2 (CH), 147.2 (CH), 143.9 (CH), 142.4 (CH), 139.8 (Cq), 92.6 (Cq), 77.9 (Cq), 41.6 (CH_2), 12.1 (CH_2) *ppm*

IR (neat): 2919, 1735, 2232, 1724, 1665, 1389, 1141, 1011, 849, 411 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_9H_9N_2O$: 161.0715, found: 161.0713

5-(Pyrimidin-2-yl)pent-4-yn-1-al (6e):



According to the representative procedure, **8e** (110 mg) was transformed into **6e** (53 mg, 49 %) as a brown oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.77-2.86 (m, 4H, H_2 + H_3), 7.23 (dt, 1H, J = 0.9, 4.9 Hz), 8.69 (dd, 2H, J = 0.9, 4.9 Hz), 9.84 (s, 1H, H_1) *ppm*

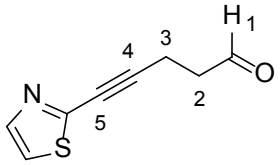
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.3 (CH), 156.9 (2xCH), 152.3 (Cq), 119.5 (CH), 87.6 (Cq), 79.9 (Cq), 41.4 (CH_2), 11.8 (CH_2) *ppm*

IR (neat) = 2922, 2233, 1720, 1549, 1405, 1250, 1021, 802, 540 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_9H_9N_2O$: 161.0715, found: 161.0706

$\boldsymbol{R_f}$ = 0.1 (AcOEt/pentane: 1/2)

5-(Thiazol-2-yl)pent-4-yn-1-al (6f):



According to the representative procedure, **8f** (370 mg) was transformed into **6f** (263 mg, 71 %) as a brown oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.75-2.87 (m, 4H, H_2 + H_3), 7.29 (d, 1H, J = 3.3 Hz), 7.76 (t, 1H, J = 3.3 Hz), 9.84 (s, 1H, H_1) *ppm*

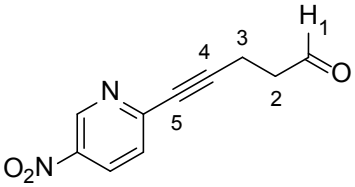
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.1 (CH), 148.0 (Cq), 142.5 (CH), 119.9 (CH), 93.4 (CH), 73.9 (Cq), 41.1 (CH_2), 11.9 (CH_2) *ppm*

IR (neat): 3355, 3119, 1838, 2232, 1721, 1479, 1217, 1131, 621 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ C_8H_8NSO: 166.0327, found: 166.0329

$\boldsymbol{R_f}$ = 0.9 (Et_2O)

5-(5-Nitropyridin-2-yl)pent-4-yn-1-al (6g):



According to the representative procedure, **8g** (322 mg) was transformed into **6g** (280 mg, 87 %) as a brown solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.79-2.88 (m, 4H, H_2 + H_3), 7.53 (d, 1H, J = 8.6 Hz), 8.41 (m, 1H), 9.35 (s, 1H), 9.84 (s, 1H, H_1) *ppm*

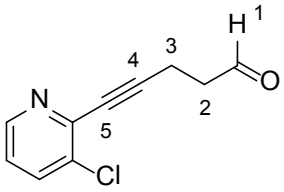
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.2 (CH), 148.2 (Cq), 144.8 (CH), 142.2 (Cq), 131.1 (CH), 126.6 (CH), 94.6 (Cq), 79.7 (Cq), 41.4 (CH_2), 12.1 (CH_2) *ppm*

IR (neat): 3089, 2916, 2221, 1723, 1572, 1342, 1109, 854, 764 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_9N_2O_3$: 205.0613, found: 205.0611

mp = 82 °C

5-(3-Chloropyridin-2-yl)pent-4-yn-1-al (6h):



According to the representative procedure, **8h** (210 mg) was transformed into **6h** (150 mg, 73 %) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.84 (broad s, 4H, H_2 + H_3), 7.17 (d, 1H, J = 4.7, 8.1 Hz), 7.70 (dd, 1H, J = 1.3, 8.1 Hz), 8.44 (broad s, 1H), 9.86 (s, 1H, H_1) *ppm*

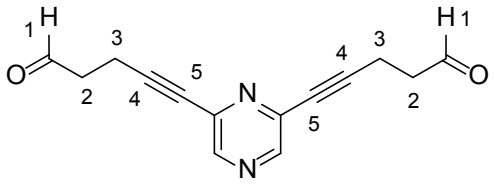
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.6 (CH), 147.3 (CH), 141.5 (Cq), 136.3 (2xCH), 123.1 (Cq), 94.0 (Cq), 78.0 (Cq), 41.8 (CH_2), 12.4 (CH_2) *ppm*

IR (neat): 2834, 2236, 1723, 1569, 1419, 1075, 1034, 795, 753 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_9NOCl$: 194.0373, found: 194.0378

$\boldsymbol{R_f}$ = 0.3 (Et_2O/pentane : 2/1)

5,5'-(Pyrazine-2,6-diyl)bis(pent-4-yn-1-al) (6i):



According to the representative procedure, **8i** (153 mg) was transformed into **6i** (115 mg, 75 %) as a yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.75-2.86 (m, 8H, H_2 + H_3), 8.46 (s, 2H), 9.84 (s, 2H, H_1) *ppm*

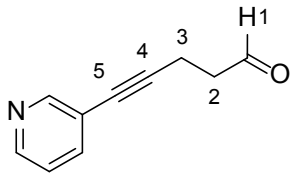
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.3 (CH), 144.9 (CH), 139.1 (Cq), 93.0 (Cq), 77.5 (Cq), 41.6 (CH_2), 12.1 (CH_2) *ppm*

IR (neat): 3387, 2924, 2853, 2233, 1721, 1510, 1403, 1255, 1158, 1008, 477 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{14}H_{13}N_2O_2$: 241.0977, found: 241.0983

$\boldsymbol{R_f}$ = 0.6 (AcOEt)

5-(Pyridin-3-yl)pent-4-yn-1-ol (6j):



According to the representative procedure, **8j** (112 mg) was transformed into **6j** (86 mg, 77 %) as a brown oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 2.69-2.80 (m, 4H, H_2 + H_3), 7.19 (dd, 1H, J = 4.8, 7.7 Hz), 7.63 (d, 1H, J = 7.7 Hz), 8.46 (broad d, 1H, J = 4.3 Hz), 8.58 (s, 1H), 9.82 (s, 1H, H_1) *ppm*

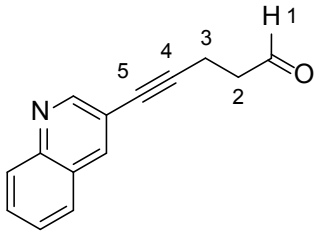
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.8 (CH), 152.0 (CH), 148.0 (CH), 138.4 (CH), 122.8 (CH), 120.3 (Cq), 91.3 (Cq), 77.9 (Cq), 42.2 (CH_2), 12.4 (CH_2) *ppm*

IR (neat): 2918, 2236, 1722, 1652, 1477, 1436, 1407, 1314, 951, 705 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{10}H_{10}NO$: 160.0762, found: 160.0754

$\boldsymbol{R_f}$ = 0.38 (AcOEt/pentane: 1/4)

5-(Quinolin-3-yl)pent-4-yn-1-al (6k):



According to the representative procedure, **8k** (317 mg) was transformed into **6k** (293 mg, 92 %) as a yellow solid.

^{1}H NMR (300 M Hz, $CDCl_3$) δ = 2.80-2.82 (m, 4H, H_2 + H_3), 7.54 (broad t, 1H, *J* = 7.1 Hz), 7.69 (dt, 1H, *J* = 1.5, 7.1 Hz), 7.75 (broad d, 1H, *J* = 8.2 Hz), 8.07 (d, 1H, J = 8.2 Hz), 8.16 (d, 1H, *J* = 1.8 Hz), 8.86 (d, 1H, *J* = 1.8 Hz), 9.88 (s, 1H, H_1) *ppm*

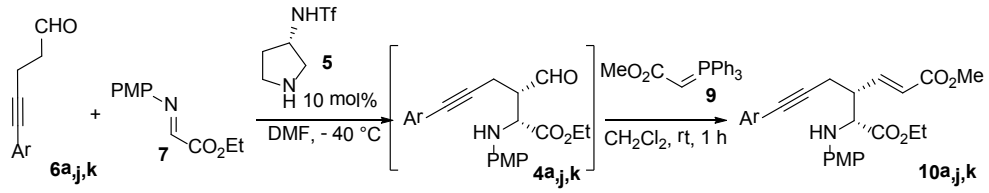
^{13}C NMR (75 MHz, $CDCl_3$) δ = 199.9 (CH), 152.1 (CH), 146.4 (Cq), 138.1 (CH), 129.7 (CH), 129.1 (CH), 127.3 (CH), 127.1 (CH + Cq), 117.4 (Cq), 91.3 (Cq), 78.5 (Cq), 42.3 (CH_2), 12.5 (CH_2) *ppm*

IR (neat): 3059, 2849, 2231, 1716, 1491, 1357, 919, 786, 755 *cm^{-1}*

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{14}H_{23}ON$: 210.0919, found: 210.0912

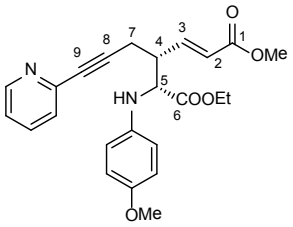
mp = 90 °C

Mannich/Wittig Sequence



Experiment times for Mannich reaction are specified for each compound.

(4*R*,5*R*,*E*)-6-Ethyl-1-methyl-5-((4-methoxyphenyl)amino)-4-(3-(pyridin-2-yl)prop-2-yn-1-yl)hex-2-enedioate (10a):



Representative procedure

To a solution of aldehyde **6a** (1.45 g, 9.12 mmol, 1 equiv) and imine **7** (1.90 g, 9.12 mmol, 1 equiv) in DMF (30 mL) contained in a flask at – 40 °C was added catalyst **5** (198 mg, 0.912 mmol, 0.1 equiv) in one portion. The reaction mixture was allowed to react for 6 h (TLC monitoring). Then, the flask was removed from the cold bath and CH_2Cl_2 (60 mL) followed by ylide **9** (3.04 g, 9.12 mmol, 1.0 equiv) were added. After 1 h of reaction at rt, water was added and the resultant mixture was extracted with AcOEt (3x). Combined organic layers were brined, dried on $MgSO_4$ and filtered. The volatiles were removed under reduced pressure to give 6.04 g of crude compound **10a** which was purified by flash column chromatography (pentane/AcOEt: 1/2 → 1/3) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield **10a** (2.70 g) as an orange oil in 70 % yield, 99% *ee* and dr > 20:1.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.24 (t, 3H, *J* = 7.30 Hz, OCH_2CH_3), 2.67 (dd AB, 1H, *J* = 6.3, 16.8 Hz, H_7), 2.92 (dd AB, 1H, *J* = 8.1, 16.8 Hz, H_7), 3.15 (m, 1H, H_4), 3.73 (s, 3H, O*Me*), 3.75 (s, 3H, O*Me*),

3.88 (d, 1H, *J* = 9.9 Hz, N*H*), 4.12-4.24 (m, 2H, O*CH*$_2$CH$_3$), 4.35 (dd, 1H, *J* = 4.1, 9.9 Hz, H$_5$), 5.97 (d, 1H, *J* = 15.7 Hz, H$_2$), 6.75 (s, 4H), 6.89 (dd, 1H, *J* = 8.7, 15.7 Hz, H$_3$), 7.23 (dd, 1H, *J* = 5.2, 7.7 Hz), 7.38 (d, 1H, *J* = 7.9 Hz), 7.64 (dt, 1H, *J* = 1.7, 7.7 Hz), 8.57 (d, 1H, *J* = 5.2 Hz) *ppm*

^{13}C NMR (75 MHz, CDCl$_3$) δ = 172.5 (Cq), 166.1 (Cq), 153.3 (Cq), 149.9 (CH), 145.4 (CH), 143.3 (Cq), 141.1 (Cq), 136.2 (CH), 127.0 (CH), 124.1 (CH), 122.8 (CH), 116.4 (2xCH), 114.8 (2xCH), 87.1 (Cq), 82.8 (Cq), 61.6 (CH$_2$), 61.0 (CH), 55.7 (CH$_3$), 51.7 (CH$_3$), 44.3 (CH), 21.5 (CH$_2$), 14.3 (CH$_3$) *ppm*

IR (neat): 3373, 2947, 2827, 2235, 1721, 1583, 1511, 1464, 1429, 1235.7, 1180, 1031, 822, 778 *cm^{-1}*

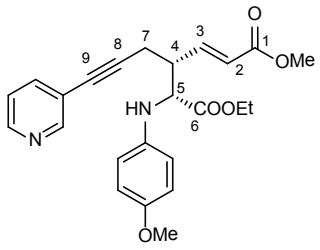
HRMS (TOF MS ES+) calcd for (M+H)$^+$ $C_{24}H_{27}N_2O_5$: 423.1920, found: 423.1901

***R*$_f$** = 0.6 (AcOEt/cyclohexane: 1/1)

Chiral HPLC: Daicel Chiralpak® IC (80% n-heptane, 20% iPrOH), 20°C, 1 mL/min, 327.8 nm, t$_1$ = 21.2 min (*major*), t$_2$ = 24.8 min (*minor*)

[α]$^{20}_D$ = – 14 (c = 0.49, CHCl$_3$)

(4*R*,5*R*,*E*)-6-Ethyl-1-methyl-5-((4-methoxyphenyl)amino)-4-(3-(pyridin-3-yl)prop-2-yn-1-yl)hex-2-enedioate (10j) :



Mannich reaction time: 2 h 45

According to the representative procedure, **6j** (56 mg) was transformed into **10j** (98 mg, 69%, 99% *ee* and dr > 20:1) as an orange oil.

^{1}H NMR (300 MHz, CDCl$_3$) δ = 1.26 (t, 3H, *J* = 7.2 Hz, OCH$_2$*CH$_3$*), 2.67 (dd, 1H, *J* = 6.4, 16.9 Hz, H$_7$), 2.89 (dd, 1H, *J* = 7.9, 16.9 Hz, H$_7$), 3.10 (m, 1H, H$_4$), 3.74 (s, 3H, O*Me*), 3.76 (s, 3H, O*Me*), 3.81 (m, 1H, N*H*), 4.12 (dd, 2H, *J* = 5.3, 7.2 Hz, O*CH$_2$*CH$_3$), 4.33 (broad s, 1H, H$_5$), 5.98 (d, 1H, *J* = 15.7 Hz, H$_2$), 6.70-6.79 (m, 4H), 6.89 (dd, 1H, *J* = 8.7, 15.7 Hz H$_3$), 7.22-7.26 (m, 1H), 7.68 (dt, 1H, *J* = 1.9, 7.8 Hz), 8.52 (m, 1H), 8.65 (s, 1H) *ppm*

^{13}C NMR (75 MHz, CDCl$_3$) δ = 172.2 (Cq), 165.9 (Cq), 153.1 (Cq), 152.1 (CH), 148.2 (CH), 145.2 (CH), 140.9 (Cq), 138.4 (CH), 123.8 (CH), 122.8 (CH), 120.2 (Cq), 116.1 (2xCH), 114.6 (2xCH), 90.1 (Cq), 79.8 (Cq), 61.4 (CH$_2$), 60.7 (CH), 55.4 (CH$_3$), 51.5 (CH$_3$), 44.3 (CH), 21.4 (CH$_2$), 14.1 (CH$_3$) *ppm*

IR (neat): 3348, 2923, 2852, 2250, 1723, 1511, 1237, 1181, 1024, 821, 729, 705 *cm^{-1}*

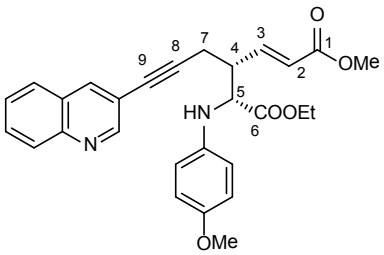
HRMS (TOF MS ES+) calcd for (M+H)$^+$ $C_{25}H_{27}N_2O_5$: 423.1920, found: 423.1906

***R*$_f$** = 0.15 (AcOEt/pentane: 1/3)

Chiral HPLC: Daicel Chiralpak ® IA column (80% n-heptane, 20% iPrOH), 20°C, 1 mL/ min, 239 nm, t$_1$ = 13.5 min (*major*), t$_2$ = 17.0 min (*minor*)

[α]$^{20}_D$ = – 23 (c = 1.35, CHCl$_3$)

(4*R*,5*R*,*E*)-6-Ethyl 1-methyl 5-((4-methoxyphenyl)amino)-4-(3-(quinolin-3-yl)prop-2-yn-1-yl)hex-2-enedioate (10k):



Mannich reaction time: 4 h

According to the representative procedure, **6k** (72 mg) was transformed into **10k** (106 mg, 65%, 87% *ee* and dr > 20:1) as an orange oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.26 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 2.72 (dd AB, 1H, J = 6.2, 16.8 Hz, H_7), 2.95 (dd AB, 1H, J = 8.1, 16.8 Hz, H_7), 3.13 (m, 1H, H_4), 3.73 (s, 3H, O*Me*), 3.77 (s, 3H, O*Me*), 3.87 (broad s, 1H, N*H*), 4.15-4.24 (m, 2H, OCH_2CH_3), 4.37 (broad s, 1H, H_5), 6.01 (d, 1H, J = 15.9 Hz, H_2), 6.73-6.80 (m, 4H), 6.93 (dd, 1H, J = 8.7, 15.9 Hz, H_3), 7.57 (t, 1H, J = 7.7 Hz), 7.69-7.79 (m, 2H), 8.08 (d, 1H, J = 8.4 Hz), 8.19 (s, 1H), 8.89 (s, 1H) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 172.3 (Cq), 166.0 (Cq), 153.2 (Cq), 152.1 (CH), 146.6 (Cq), 145.2 (CH), 140.9 (CH), 138.2 (CH), 129.9 (Cq), 129.2 (CH), 127.4 (CH), 127.2 (CH), 127.1 (Cq), 123.9 (CH), 117.2 (Cq), 116.2 (2xCH), 114.7 (2xCH), 90.1 (Cq), 80.5 (Cq), 61.5 (CH_2), 60.7 (CH), 55.5 (CH_3), 51.6 (CH_3), 44.4 (CH), 21.6 (CH_2), 14.1 (CH_3) *ppm*

IR (neat): 3355, 2948, 2840, 2233, 1722, 1511, 1237, 1033, 908, 821, 728, 547 cm^{-1}

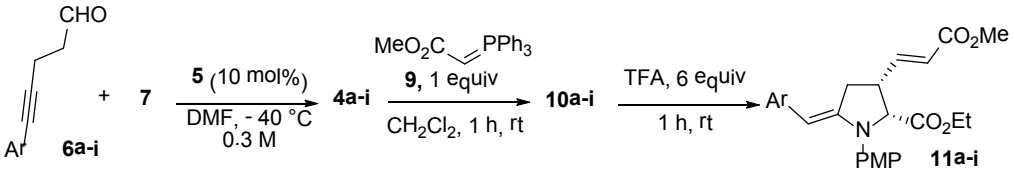
HRMS (TOF MS ES+) calcd for $(M+H)^+$: $C_{28}H_{29}N_2O_5$: 473.2076, found: 473.2070

R_f = 0.55 (AcOEt/pentane: 1/2)

Chiral HPLC: Daicel Chiralpak® IA (80% n-heptane, 20% iPrOH), 20°C, 1 mL/min, 251 nm, t_1 = 19.8 min (*major*), t_2 = 23.6 min (*minor*)

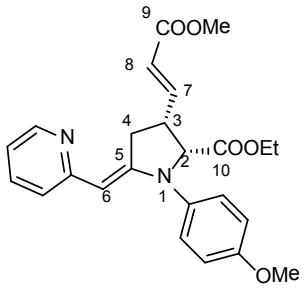
$[\alpha]^{20}_D$ = + 5 (c = 1, $CHCl_3$)

One-pot preparation of pyrrolidines 11a-i



Experiment times of Mannich reactions are specified for each compound.

(2*R*,3*R*,*E*)-Ethyl-3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)-5-(pyridin-2-ylmethylene)pyrrolidine-2-carboxylate (11a):



Representative procedure

In a flask containing a solution of aldehyde **6a** (453 mg, 2.85 mmol, 1 equiv) and imine **7** (590 mg, 2.85 mmol, 1 equiv) in DMF (9.5 mL) at – 40°C was introduced catalyst **5** (62 mg, 0.285 mmol, 0.1 equiv) in one portion. The mixture was allowed to react at – 40°C for 4 h 20 (TLC monitoring). Then, the flask was removed from the cold bath and CH_2Cl_2 (19 mL) followed by ylide **9** (952 mg, 2.85 mmol, 1 equiv) were introduced. After 1 h at rt, TFA (1.3 mL, 6 equiv) was added dropwise triggering the

coloration of the mixture. After 1 h, a saturated aqueous solution of $NaHCO_3$ was carefully added to the mixture which was extracted with AcOEt (3x). Combined organic layers were brined, dried on $MgSO_4$ and filtered. The volatiles were removed to give 2.10 g of crude **8a**. After filtration (AcOEt/cyclohexane: 1/4) on a pad of pretreated silica gel (washed with 1% Et_3N in AcOEt) and concentration of the filtrate, the residue was triturated in iPr_2O to yield 567 mg (48 %, 99% *ee* and dr > 20/1) of **8a** as a yellow solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.19 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 3.21 (dd, 1H, J = 10.6, 16.3 Hz, H_4), 3.50 (m, 1H, H_3), 3.75 (s, 3H, O*Me*), 3.79 (m, 1H, H_4), 3.82 (s, 3H, O*Me*), 4.02-4.24 (m, 2H, OCH_2CH_3), 4.48 (d, 1H, J = 8.2 Hz, H_2), 5.34 (s, 1H, H_6), 6.04 (d, 1H, J = 15.6 Hz, H_8), 6.79-6.96 (m, 5H), 7.23-7.26 (m, 2H), 7.44 (t, 1H, J = 7.4 Hz), 8.38 (d, 1H, J = 4.4 Hz) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.3 (Cq), 166.0 (Cq), 158.5 (Cq), 157.7 (Cq), 151.9 (Cq), 148.5 (CH), 144.7 (CH), 135.3 (CH), 133.7 (Cq), 128.1 (2xCH), 123.3 (CH), 121.2 (CH), 117.1 (CH), 114.6 (2xCH), 94.3 (CH), 69.2 (CH), 60.9 (CH_2), 55.2 (CH_3), 51.4 (CH_3), 42.4 (CH), 35.2 (CH_2), 14.0 (CH_3) *ppm*

IR (neat): 2993, 2949, 1723, 1625, 1583, 1509, 1469, 1175, 1027, 832 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{24}H_{27}N_2O_5$: 423.1920, found: 423.1919

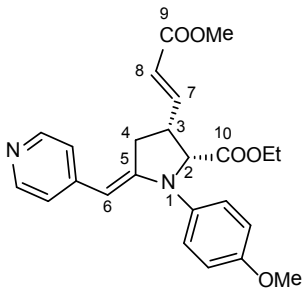
R_f = 0.6 (cyclohexane/AcOEt: 1/1)

mp = 130°C from iPr_2O

Chiral HPLC: Daicel Chiralpak® IC (80% n-heptane, 20% iPrOH), 20°C, 1 mL/min, 328 nm, t_1 = 21.1 min (*major*), t_2 = 24.7 min (*minor*)

$[\alpha]^{20}_D$ = – 161 (c = 0.54, $CHCl_3$)

(2*R*,3*R*,*E*)-Ethyl-3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)-5-(pyridin-4-ylmethylene)pyrrolidine-2-carboxylate (11b):



Mannich reaction time: 3 h

According to the representative procedure, **6b** (70 mg) was transformed into **11b** (75 mg, 40%, 99% *ee* and dr > 20:1) as a yellow oil obtained after purification by flash column chromatography (pentane/AcOEt: 1/2) on silica gel.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.20 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 3.11-3.24 (m, 2H, H_4), 3.53 (m, 1H, H_3), 3.75 (s , 3H, O*Me*), 3.82 (s, 3H, O*Me*), 4.03-4.24 (m, 2H, OCH_2CH_3), 4.47 (d, 1H, J = 8.3 Hz, H_2), 5.16 (s, 1H, H_6), 6.05 (dd, 1H, J = 1.0, 15.6 Hz, H_8), 6.87-6.95 (m, 5H), 7.21 (d, 2H, J = 8.9 Hz), 8.29 (dd, 2 H, J = 1.5, 4.8 Hz) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.1 (Cq), 165.9 (Cq), 158.4 (Cq), 153.1 (Cq), 148.3 (Cq), 147.7 (2xCH), 143.5 (2xCH), 132.9 (CH), 128.4 (2xCH), 124.2 (CH), 120.6 (Cq), 115.0 (2xCH), 93.0 (CH), 69.6 (CH), 61.4 (CH_2), 55.4 (CH_3), 51.8 (CH_3), 42.4 (CH_2), 35.0 (CH), 14.1 (CH_3) *ppm*

IR (neat): 2922, 1725, 1625, 1586, 1509, 1246, 1181, 1029, 835 cm^{-1}

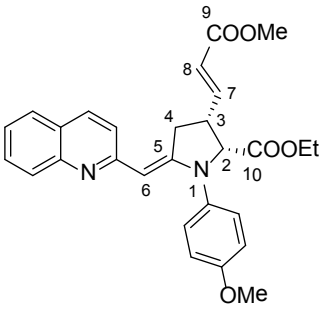
HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{24}H_{27}N_2O_5$: 423.1920 , found: 424.1920

R_f = 0.15 (pentane/AcOEt: 1/2)

Chiral HPLC: Daicel Chiralpak® IC (80% n-heptane, 20% iPrOH), 20°C, 1 mL/min, 328 nm, t_1 = 146.1 min (*major*), t_2 = 284.2 min (*minor*)

$[\alpha]^{20}_D$ = – 240 (c = 0.35, MeOH)

(2*R*,3*R*,*E*)-Ethyl-3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)-5-(quinolin-2-ylmethylene)pyrrolidine-2-carboxylate (11c):



Mannich reaction time: 4 h

According to the representative procedure, **6c** (68 mg) was transformed into **11c** (80 mg, 52%, 99% *ee* and dr > 20:1) as a colorless solid obtained after purification of the crude by filtration (Et_2O/pentane: 2/1) on a pad of pretreated silica gel (washed with 1% Et_3N in AcOEt) followed by removal of the volatiles and trituration (iPr_2O) of the residue.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.13 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 3.30 (ddd, 1H, *J* = 1.6, 10.6, 12.2 Hz, H_4), 3.48 (m, 1H, H_3), 3.69 (s, 3H, O*Me*), 3.75 (s, 3H, O*Me*), 3.97-4.20 (m, 3H, OCH_2CH_3 + H_4), 4.44 (d, 1H, *J* = 8.3 Hz, H_2), 5.39 (s, 1H, H_6), 6.01 (dd, 1H, *J* = 0.8, 15.7 Hz, H_8), 6.87-6.94 (m, 4H), 7.21-7.26 (m, 3H), 7.47-7.56 (m, 2H), 7.73 (d, 1H, *J* = 8.8 Hz), 7.80 (dd, 2H, *J* = 8.4 Hz) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.3 (Cq), 166.1 (Cq), 158.6 (Cq), 158.0 (Cq), 154.2 (Cq), 148.3 (Cq), 144.7 (CH), 134.8 (CH), 128.8 (Cq), 128.2 (2xCH), 128.1 (CH), 127.1 (CH), 125.0 (Cq), 123.8 (CH), 123.5 (CH), 121.9 (CH), 114.7 (2xCH), 94.4 (CH), 69.4 (CH), 61.1 (CH_2), 55.3 (CH_3), 51.6 (CH_3), 42.5 (CH_2), 35.7 (CH), 14.1 (CH_3) *ppm*

IR (neat): 2944, 2846, 1730, 1715, 1583, 1541, 1509, 1369, 1237, 1182, 1024, 840, 755 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{28}H_{29}N_2O_5$: 473.207 , found: 473.2069

R_f = 0.5 (Et_2O/pentane: 1/2)

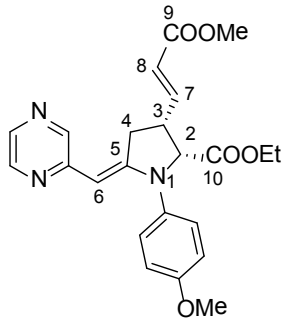
mp =176-178 °C from iPr_2O

Chiral HPLC: Daicel Chiralpak® IC (79.9% n-heptane, 20% iPrOH, 0.1 % Et_3N), 23 °C, 1 mL/min, 328 nm, t_1 = 19.0 min (*major*), t_2 = 23.9 min (*minor*)

$[\alpha]^{20}_D$= – 211 (c = 0.15, MeOH)

(2*R*,3*R*,*E*)-Ethyl-3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)-5-(pyrazin-2-ylmethylene)pyrrolidine-2-carboxylate (11d):

Mannich reaction time: 4 h 45



According to the representative procedure, **6d** (24 mg) was transformed into **11d** (28 mg, 44%, 99% *ee* and dr > 20:1) as a pale yellow solid obtained after purification by flash column chromatography (cyclohexane/AcOEt: 5/1) on silica gel followed by trituration (iPr_2O).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.20 (t, 3H, J = 7.2 Hz, $OCH_2\mathit{CH_3}$), 3.15 (ddd, 1H, J = 1.7, 10.6, 16.9 Hz, H_4), 3.45 (m, 1H, H_3), 3.71 (s, 3H, O*Me*), 3.75 (m, 1H, H_4), 3.79 (s, 3H, O*Me*), 4.04-4.23 (m, 2H, $O\mathit{CH_2}CH_3$), 4.45 (d, 1H, J = 8.4 Hz, H_2), 5.24 (s, 1H, H_6), 6.05 (d, 1H, J = 1.1, 15.6 Hz, H_8), 6.91 (dd, 1H, J = 7.9, 15.6 Hz), 6.95 (d, 2H, J = 9.0 Hz), 7.20 (d, 2H, J = 9.0 Hz), 7.94 (d, 1H, J = 2.6 Hz), 8.03 (s, 1H), 8.26 (m, 1H) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.1 (Cq), 166.0 (Cq), 158.2 (Cq), 154.9 (Cq), 144.2(CH), 143.5 (CH), 142.9 (CH), 136.9 (CH), 133.1 (Cq), 128.2 (2xCH), 123.6 (CH), 114.8 (2xCH), 90.0 (CH), 69.5 (CH), 61.2 (CH_2), 55.3 (CH_3), 55.3 (CH_3), 51.6 (CH_3), 42.4 (CH_3), 35.6 (CH_2), 14.1 (CH_3) *ppm*

IR (neat): 2967, 1724, 1621, 1496, 1469, 1401, 1274, 1244, 1186, 1125, 1006, 837 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{23}H_{26}N_3O_5$: 424.1872, found: 424.1859

$\boldsymbol{R_f}$ = 0.35 (pentane/ Et_2O: 1/2)

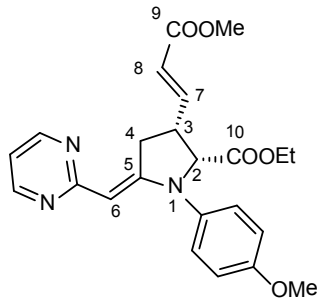
mp = 101 °C from iPr_2O

Chiral HPLC: Daicel Chiralpak® IC (80% n-heptane, 20% iPrOH), 23 °C, 1 mL/min, 328 nm, t_1 = 48.1 min (*minor*), t_2 = 52.5 min (*major*)

$[\alpha]^{17}_D$ = – 260 (c = 0.85, MeOH)

(2*R*,3*R*,*E*)-Ethyl-3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)-5-(pyrimidin-2-ylmethylene)pyrrolidine-2-carboxylate (11e):

Mannich reaction time: 4 h



According to the representative procedure, **6e** (62 mg) was transformed into **11e** (66 mg, 40%, 99% *ee* and dr > 20:1) as a colorless solid obtained after purification by filtration (AcOEt/pentane: 1/1) on a pad of pretreated silica gel (washed with 1% Et_3N in AcOEt) followed by trituration (iPr_2O).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.20 (t, 3H, J = 7.1 Hz, $OCH_2\mathit{CH_3}$), 3.21 (ddd, 1H, J = 1.6, 10.4, 16.9 Hz, H_4), 3.43 (m, 1H, H_3), 3.75 (s, 3H, O*Me*), 3.80 (s, 3H, O*Me*) 3.95 (dd, 1H, J= 7.9, 16.9 Hz, H_4), 4.02-4.27 (m, 2H, $O\mathit{CH_2}CH_3$), 4.49 (d, 1H, J = 8.4 Hz, H_2), 5.44 (s, 1H, H_9), 6.06 (dd, 1H, J = 0.9, 15.6 Hz, H_8), 6.68 (t, 1H, J = 4.8 Hz), 6.85-6.97 (m, 3H), 7.20-7.24 (m, 2H), 8.43 (d, 2H, J = 4.8 Hz) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.2 (Cq), 167.6 (Cq), 166.1 (Cq), 158.4 (Cq), 157.6 (Cq), 156.3 (2xCH), 144.4 (CH), 133.0 (Cq), 128.5 (2xCH), 123.6 (CH), 114.9 (2xCH), 113.9 (CH), 94.2 (CH), 69.8 (CH), 61.3 (CH_2), 55.5 (CH_3), 51.6 (CH_3), 42.4 (CH), 36.0 (CH_2), 14.2 (CH_3) *ppm*

IR (neat): 2965, 2840, 1724, 1620, 1564, 1509, 1434, 1353, 1244, 1184, 1031, 832 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{23}H_{26}N_3O_5$: 424.1872, found: 424.1880

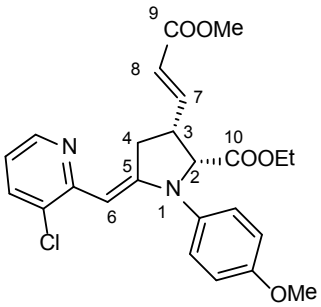
R_f = 0.25 (pentane/Et_2O: 1/2)

mp = 151°C from iPr_2O

Chiral HPLC: Daicel Chiralpak® IC (79.8% n-heptane, 20% iPrOH, 0.2 % Et_3N), 23 °C, 1 mL/min, 328 nm, t_1 = 73.9 min (*major*), t_2 = 102.9 min (*minor*)

$[\alpha]^{20}_D$ = – 35 (c = 0.35, MeOH)

(2*R*,3*R*,*E*)-Ethyl-5-((3-chloropyridin-2-yl)methylene)-3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)pyrrolidine-2-carboxylate (11h):



Mannich reaction time: 6 h

According to the representative procedure, **6h** (66 mg) was transformed into **11h** (81 mg, 54%, 98% *ee* and dr > 20:1) as an orange oil obtained after purification by filtration (Et_2O/pentane: 2/1) on a pad of pretreated silica gel (washed with 1% Et_3N in AcOEt) followed by trituration (iPr_2O).

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.19 (t, 3H, J = 7.2 Hz, OCH_2CH_3), 3.23 (ddd, 1H, J = 1.6, 10.6, 12.2 Hz, H_4), 3.50 (m, 1H, H_3), 3.74 (s, 3H, O*Me*), 3.81 (s, 3H, O*Me*), 3.88 (dd, 1H, J = 7.7, 16.9 Hz, H_4), 4.02-4.24 (m, 2H, OCH_2CH_3), 4.50 (d, 1H, J = 8.3 Hz, H_2), 5.78 (s, 1H, H_2), 6.05 (d, 1H, J = 15.7 Hz, H_3), 6.72 (dd, 1H, J = 4.7, 7.9 Hz), 6.88-6.96 (m, 3H), 7.26-7.28 (m, 2H), 7.43 (d, 1H, J = 7.9 Hz), 8.28 (d, 1H, J = 4.7 Hz) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.3 (Cq), 166.2 (Cq), 158.0 (Cq), 155.5 (Cq), 154.6 (Cq), 146.2 (CH), 144.6 (CH), 136.0 (CH), 133.5 (Cq), 127.9 (2xCH), 127.3 (Cq), 123.5 (CH), 117.7 (CH), 114.7 (2xCH), 89.8 (CH), 69.5 (CH), 61.2 (CH_2), 55.4 (CH_3), 51.6 (CH_3), 42.4 (CH_2), 35.6 (CH), 14.1 (CH_3) *ppm*

IR (neat): 3406, 2955, 2839, 1722, 1569, 1507, 1436, 1245, 1178, 1023, 805, 723 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{24}H_{26}N_2O_5Cl$: 457.1530 , found: 457.1525

R_f = 0.7 (AcOEt/ pentane: 1/1)

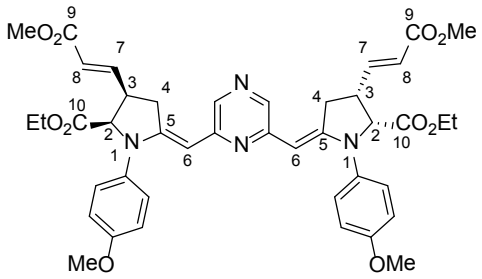
mp = 118-120°C from iPr_2O

Chiral HPLC: Daicel Chiralcel® OD-H (98% n-heptane, 2% iPrOH), 23°C, 1 mL/min, 328 nm, t_1 = 9.4 min (*minor*), t_2 = 11.0 min (*major*)

$[\alpha]^{21}_D$ = – 130 (c = 0.2, $CHCl_3$)

(2*R*,2'*R*,3*R*,3'*R*,5*E*,5'*E*)-Diethyl-5,5'-(pyrazine-2,6-diylbis(methanylylidene))bis(3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)pyrrolidine-2-carboxylate) (11i):

Mannich reaction time: 3 h 45



Following the representative procedure, catalyst **5** (20 mol%), imine **7** (2 equiv), ylide **9** (2 equiv) and TFA (12 equiv) were employed to transform **6i** (129 mg) into crude **11i** (190 mg). Purification of the crude was carried out by flash column chromatography (cyclohexane/AcOEt: 1/1) on silica gel (washed with 1% Et_3N in cyclohexane) to give pyrrolidine **11i** as yellow oil with 36 % yield, 97% *ee* and dr > 20:1

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.17 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 3.20 (ddd, 1H, *J* = 1.7, 10.3, 16.2 Hz, H_4), 3.60 (m, 1H, H_3), 3.73 (s, 3H, O*Me*), 3.79 (m, 1H, H_4), 3.82 (s, 3H, O*Me*), 4.01-4.20 (m, 2H, OCH_2CH_3), 4.48 (d, 1H, *J* = 8.2 Hz, H_2), 5.24 (s, 1H, H_6), 5.96 (dd, 1H, *J* = 1.2, 15.7 Hz, H_8), 6.91 (m, 1H), 6.92 (d, 2H, *J* = 8.9 Hz), 7.23 (d, 2H, *J* = 8.9 Hz), 7.57 (s, 1H) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.4 (Cq), 165.9 (Cq), 158.1 (Cq), 152.6 (Cq), 152.6 (Cq), 144.3 (CH), 137.3 (CH), 133.6 (Cq), 128.2 (2xCH), 123.6 (CH), 114.9 (2xCH), 91.7 (CH), 69.5 (CH), 61.2 (CH_2), 55.5 (CH_3), 51.6 (CH_3), 42.4 (CH_2), 35.7 (CH), 14.2 (CH_3) *ppm*

IR (neat): 2952, 2323, 1728, 1627, 1512, 1487, 1398, 1245, 1190, 1032, 838, 728 cm^{-1}

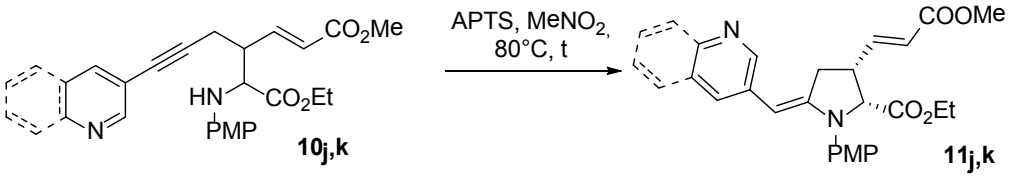
HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{42}H_{47}N_4O_{10}$: 767.3292, found: 767.3282

R_f = 0.36 (Et_2O/pentane: 1/1)

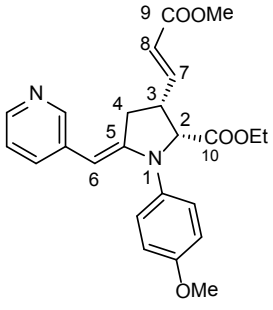
Chiral HPLC: Daicel Chiralpak® IA (80% n-heptane, 20% iPrOH), 20°C, 1 mL/min, 311 nm, t_1 = 26.4 min (*minor*), t_2 = 33.9 min (*major*)

$[\alpha]^{20}_D$ = – 3.5 (c = 1.25, MeOH)

Cyclization of meta-substituted N-heteroaromatic compounds 11j,k



3-((*E*)-((4*R*,5*R*)-5-(Ethoxycarbonyl)-4-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl) pyrrolidin-2-ylidene)methyl)pyridine (11j):



To a solution of **10j** (44 mg, 0.104 mmol, 1 equiv) in $MeNO_2$ (1.04 ml) was introduced *p*-toluene sulfonic acid (90 mg, 0.523 mmol, 5 equiv). After 7 h of reaction at 80 °C (TLC monitoring), the reaction was cooled to rt and quenched with a saturated solution of $NaHCO_3$ and the aqueous layer was extracted with AcOEt (3x). Combined organics layers was washed by brine, dried over $MgSO_4$, filtered and concentrated under vacuum to give crude pyrrolidine **11j** which was purified on preparative TLC (SiO_2, Et_2O/pentane: 1.5/1) as neutral **11j** (23 mg, 54%). Protonation of **11j**

with 20 µL of TFA (in 2 mL of CH_2Cl_2) and evaporation of the volatile were required to stabilize **11j** as a salt for characterization.

Data for 11j.TFA

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.21 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 3.18 (d, 2H, *J* = 9.6 Hz, H_4), 3.60 (m, 1H, H_3), 3.76 (s, 3H, O*Me*), 3.83 (s, 3H, O*Me*), 4.03-4.28 (m, 2H OCH_2CH_3), 4.51 (d, 1H, *J* = 8.3 Hz, H_2), 5.11 (broad s, 1H, H_6), 6.09 (d, 1H, J = 15.7 Hz, H_8), 6.87 (dd, 1H, *J* = 8.1, 15.7 Hz, H_7), 6.95 (d, 2H, *J* = 8.6 Hz), 7.20 (d, 2H, *J* = 8.6 Hz), 7.57 (dd, 1H, *J* = 5.5, 8.1 Hz), 7.84 (d, 1H, *J* = 8.1 Hz), 8.26 (d, 1H, *J* = 5.5 Hz), 8.48 (s, 1H) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 169.8, 165.9, 158.9, 154.6, 142.6, 140.3, 139.2, 137.7, 133.4, 132.1, 128.5, 125.8, 124.6, 115.2, 88.1, 69.8, 61.7, 55.5, 51.8, 42.2, 34.8, 14.1 *ppm*

^{19}F NMR (300 MHz) = – 75.9 Hz

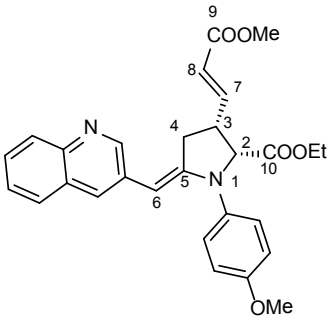
IR (cm^{-1}) : 2927, 1725, 1594, 1510, 1246, 1167, 1028, 798, 721 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{24}H_{27}N_2O_5$: 423.1920, found: 423.1937

R_f (Base) = 0.15 (pentane/Et_2O : 1/1.5)

$[\alpha]^{20}_D$ = – 218 (c = 0.6, $CHCl_3$)

3-((*E*)-((4*R*,5*R*)-5-(Ethoxycarbonyl)-4-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl) pyrrolidine-2-ylidene)methyl)quinolone (11k):



To a solution of **10k** (19 mg, 0.036 mmol, 1 equiv) in $MeNO_2$ (160 µL) was introduced *p*-toluene sulfonic acid (34 mg, 0.197 mmol, 5.4 equiv). After 1 h 30 of reaction at 80 °C, additional $MeNO_2$ (240 µL) was added to the mixture. The heating was pursued 2 h 40 at the same temperature (TLC monitoring). Then the reaction was cooled to rt and quenched with saturated solution of $NaHCO_3$ and aqueous layer was extracted with AcOEt. Combined organics layers were brined, dried over $MgSO_4$, filtered and concentrated under vacuum to give crude pyrrolidine **11k** which was purified on preparative TLC (SiO_2, Et_2O/pentane: 1/1) to give neutral **11k** (13 mg, 68 %). Protonation of **11k** with 6 µL of TFA (in 1 mL of CH_2Cl_2) and evaporation of the volatile were required to stabilize **11k** as a salt for characterization.

Data for 11k.TFA

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.23 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 3.25 (d, 2H, H_4), 3.62 (m, 1H, H_3), 3.77 (s, 3H, O*Me*), 3.85 (s, 3H, O*Me*), 4.07-4.27 (m, 2H, OCH_2CH_3), 4.51 (d, 1H, *J* = 8.2 Hz, H_2), 5.28 (broad s, 1H, H_6), 6.12 (d, 1H, *J* = 15.8 Hz, H_8), 6.91 (dd, 1H, *J* = 8.4, 15.8 Hz, H_7), 6.97 (d, 2H, *J* = 8.7 Hz), 7.22 (d, 2H, *J* = 8.7 Hz), 7.69 (m, 2H), 7.84 (d, 1H, *J* = 8.1 Hz), 8.14 (s, 1H), 8.30 (d, 1H, *J* = 8.1 Hz), 8.96 (broad s, 1H) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.1, 166.0, 158.8, 153.3, 145.1, 143.1, 135.6, 134.7, 129.4, 129.2, 128.6, 127.2, 124.5, 122.3, 115.2, 114.4, 89.0, 69.7, 61.6, 55.5, 51.8, 42.4, 34.8, 14.2 *ppm*

IR (cm^{-1}): 2927, 1726, 1616, 1511, 1247, 1179, 1032, 719 *cm^{-1}*

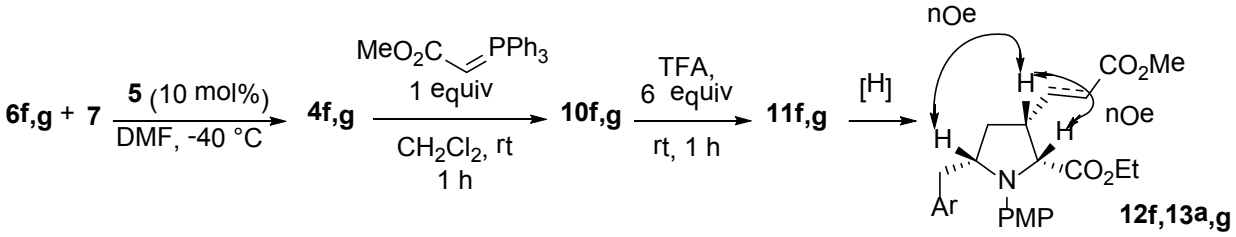
^{19}F NMR (300 MHz) = – 75.6 *ppm*

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{28}H_{29}N_2O_5$: 473.2076, found: 473.2074

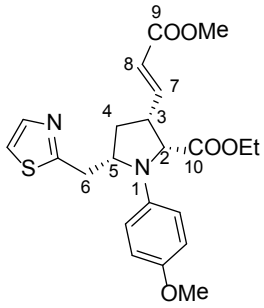
***R*$_f$** (Base) = 0.25 (Et_2O/pentane: 1/1)

$[\alpha]^{20}_D$ = – 331 (c = 0.3, $CHCl_3$)

Preparation of pyrrolidines 12f, 13a and 13g



(2*R*,3*R*,5*S*)-Ethyl-3-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-1-(4-methoxyphenyl)-5-(thiazol-2-ylmethyl)pyrrolidine-2-carboxylate (12f):



To a solution of aldehyde **6f** (78 mg, 0.47 mmol, 1 equiv) and imine **7** (98 mg, 0.47 mmol, 1 equiv) in DMF (1.6 mL) at - 40°C was introduced catalyst **5** (10 mg, 0.047 mmol, 0.1 equiv) in one portion. The mixture was allowed to react at – 40°C for 4 h 30 (TLC monitoring). Then, the flask was removed from the cold bath and CH_2Cl_2 (3.2 mL) followed by ylide **9** (157 mg, 0.47 mmol, 1 equiv) were introduced. After 1 h of reaction at rt, TFA (209 µL, 2.82 mmol, 6 equiv) was added dropwise triggering the coloration of the mixture. After 1 h of reaction, saturated solution of $NaHCO_3$ was carefully added to the solution and the reaction was extracted with AcOEt (3x). Combined organic layers were brined, dried on anhydrous $MgSO_4$ and filtered. The volatiles were removed under reduced pressure to give crude pyrrolidine which was filtrated (Et_2O/pentane: 2/1) on a pad of pretreated silica gel (washed with 1% Et_3N in Et_2O) to obtain the crude **11f** (120 mg). Then, the crude was taken up in $MeNO_2$ (4.7 mL) and $BF_3.Et_2O$ (133 mg, 116 µL, 0.94 mmol, 2 equiv) and $HSiEt_3$ (219 mg, 300 µL, 1.88 mmol, 4 equiv) were added. The reaction was allowed to stir at 30°C for 5 days to reach 90 % of conversion before being quenched with water and extracted with AcOEt (3x). Combined organic layers were brined, dried over $MgSO_4$, filtered and concentrated to a crude (127 mg) containing of **12f** and **11f** in a ratio of 90:10. To complete the conversion, the crude was taken up in CH_3NO_2 (2.7 ml) and $BF_3.Et_2O$ (78 mg, 68 µL, 0.55 mmol), $HSiEt_3$ (175 µL, 1.1 mmol) were added for a second run of 4 days. Work-up led to 110 mg of crude containing cis and trans **12f** (dr = 85:15 according to ^{1}H NMR). The

crude was purified by flash chromatography (cyclohexane/AcOEt: 90/10) on pretreated silica gel (washed with 1% Et_3N in AcOEt) to yield 85 mg of **12f** as a yellow oil in 42 % yield, 95% *ee*. Alternatively, the reaction can be performed at 60°C in 20 h providing **12f** with slightly less selectivity (35%, dr = 75:25).

Data of **12f cis**:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.30 (t, 3H, *J* = 7.2, 14.3 Hz OCH_2CH_3), 2.15-2.23 (m, 1H, H_4), 2.33-2.39 (m, 1H, H_4), 3.10-3.21 (m, 2H, H_3 + H_6), 3.65 (s, 3H, O*Me*), 3.75 (s, 3H, O*Me*), 3.80 (dd, 1H, *J* = 3.1, 14.9 Hz, H_6), 4.17-4.30 (m, 3H, OCH_2CH_3 + H_2), 4.34-4.41 (m, 1H, H_5), 5.90 (dd, 1H, *J* = 1.3, 15.7 Hz, H_8), 6.64 (d, 2H, *J* = 9.1 Hz), 6.82-6.88 (m, 3H), 7.21 (d, 1H, *J* = 3.4 Hz), 7.75 (d, 1H, *J* = 3.4 Hz) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.6 (Cq), 167.3 (Cq), 166.2 (Cq), 152.3 (Cq), 144.6 (CH), 142.8 (CH), 139.8 (Cq), 123.3 (CH), 118.4 (CH), 115.2 (2xCH), 114.1 (2xCH), 68.1 (CH), 61.2 (CH_2), 58.7 (CH), 55.8 (CH_3), 51.6 (CH_3), 43.6 (CH), 37.6 (CH_2), 36.4 (CH_2), 14.3 (CH_3) *ppm*

IR (neat): 2932, 1722, 1656, 1510, 1439, 1363, 1244, 1180, 1181, 1037, 814 cm^{-1}

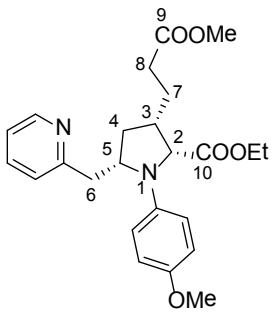
HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{22}H_{27}N_2O_5S$: 431.1641, found: 431.1658

R_f = 0.3 (AcOEt/cyclohexane: 1/3)

Chiral HPLC: Daicel Chiralpak® IC (80% n-heptane, 20% iPrOH), 20°C, 1 mL/min, 210 nm, t_1 = 28.6 min (*minor*), t_2 = 53.7 min (*major*)

[α]$^{20}_D$ = + 40 (c = 0.15, MeOH)

(2*R*,3*S*,5*S*)-Ethyl-3-(3-methoxy-3-oxopropyl)-1-(4-methoxyphenyl)-5-(pyridin-2-ylmethyl)pyrrolidine-2-carboxylate (13a):



To a solution of **11a** (123 mg, 0.291 mmol, 1 equiv) in dry AcOEt (10 ml) was added Pd/C (41 mg, 0.039 mmol, 0.13 equiv) and dry K_2CO_3 (20.1 mg, 0.145 mmol, 0.5 equiv.). The resulting suspension was flushed (3x) with H_2 and was allowed to run under a balloon of H_2 for 11 days to reach 75 % conversion. Additional Pd/C (20 mg, 0.019 mmol, 0.065 equiv) was added and the mixture was allowed to react under a balloon of H_2 for 7 days. The suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to give 140 mg of crude which was purified by flash chromatography (CH_2Cl_2/Et_2O: 2/1) on silica gel to yield 88 mg (71 %) of **13a** as an orange oil (or in 34 % over 4 steps from aldehyde **8a**) from **11a**, 98 % *ee* and dr > 20/1.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.34 (t, 3H, *J* = 7.2 Hz, OCH_2CH_3), 1.56-1.65 (m, 1H, H_7), 1.72-1.84 (m, 2H, H_4 + H_7), 2.09-2.15 (m, 1H, H_4), 2.24-2.33 (m, 1H, H_3), 2.35-2.40 (m, 2H, H_8), 2.76 (AB, 1H, *J* = 9.9, 13.1 Hz, H_6), 3.62 (s, 3H), 3.63 (m, 1H, H_6), 3.74 (s, 3H, OMe), 4.12 (d, 1H, *J* = 8.1 Hz, H_2), 4.23-4.30 (m, 3H, OCH_2CH_3 + H_5), 6.65 (d, 2H, *J* = 8.9 Hz), 6.85 (d, 2H, *J* = 8.9 Hz), 7.11-7.17 (m, 2H), 7.57 (t, 1H, *J* = 1.8, 7.6 Hz), 8.58 (d, 1H, *J* = 4.6 Hz) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 173.7 (Cq), 173.3 (Cq), 159.7 (Cq), 151.5 (Cq), 149.4 (CH), 140.4 (Cq), 136.1 (CH), 123.9 (CH), 121.2 (CH), 114.9 (2xCH), 113.7 (2xCH), 67.8 (CH), 60.9 (CH_2), 58.5 (CH), 55.7 (CH_3), 51.5 (CH_3), 42.3 (CH_2), 40.8 (CH), 37.0 (CH_2), 32.4 (CH_2), 25.3 (CH_2), 14.3 (CH_3) *ppm*

IR (neat): 2940, 1734, 1594, 1511, 1434, 1240, 1161, 1039, 816, 757 cm^{-1}

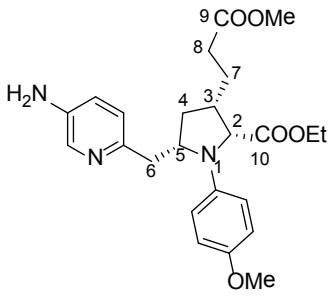
HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{24}H_{31}N_2O_5$: 427.2233 , found: 427.2233

R_f = 0.46 (AcOEt/cyclohexane: 1/1)

Chiral HPLC: Daicel Chiralpak® IC (60% n-heptane, 40% iPrOH), 20°C, 1 mL/min, 252 nm, t_1 = 12.6 min (*minor*), t_2 = 28.2 min (*major*)

$[\alpha]^{20}_D$ = + 33 (c = 1.25, MeOH)

(2*R*,3*S*)-Ethyl-5-((5-aminopyridin-2-yl)methyl)-3-(3-methoxy-3-oxopropyl)-1-(4-methoxyphenyl) pyrrolidine-2-carboxylate (13g):



To a solution of aldehyde **6g** (163 mg, 0.799 mmol, 1equiv) and imine **7** (165 mg, 0.799 mmol, 1 equiv) in DMF (2.4 mL) was introduced at – 40°C catalyst **5** (17.4 mg, 0.0799 mmol, 0.1 equiv) in one portion. The mixture was allowed to react at – 40°C for 4 h 10 (TLC monitoring). Then, the flask was removed from the cold bath and CH_2Cl_2 (4.8 mL) followed by ylide **9** (267 mg, 0.0799 mmol, 1 equiv) were introduced. After 1 h of reaction at rt, TFA (356 µL, 4.79 mmol, 6 equiv) was added dropwise triggering the coloration of the mixture. After 1 h of reaction, a saturated aqueous solution of $NaHCO_3$ was carefully added to the solution and the reaction was extracted with AcOEt (3x). Combined organic layers were brined, dried on $MgSO_4$ and filtered. The volatiles were removed to an oil which was taken up in CH_2Cl_2 before being filtrated (Et_2O/pentane: 2/1) on pretreated silica gel (washed with 1% Et_3N in Et_2O). Evaporation of the volatiles led to 260 mg of the crude **11g**. Owing the instability of **11g**, the crude was taken up in dry AcOEt (79 mL) and transferred into a 250 mL one-neck flask. To the solution was added dry K_2CO_3 (55 mg, 0.398 mmol, 0.5 equiv) and Pd/C (104 mg, 0.098 mmol, 0.12 equiv). The resulting suspension was flushed 3 times with H_2 and was allowed to stir under H_2 for 96 h (TLC monitoring). The reaction mixture was filtered through Celite® washing with AcOEt and the filtrate was concentrated to give 232 mg of the crude pyrrolidine **13g** which was purified by flash chromatography (CH_2Cl_2/AcOEt: 100/0 → 5/1 → 3/1 → 1/1 → 1/2) on pretreated silica gel (washed with 1% Et_3N in CH_2Cl_2) to yield 70 mg of **13g** (20 % yield, 98% *ee* and dr > 20/1) as an orange oil. No other diastereoisomer was isolated from the crude.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.34 (t, 3H, J = 7.2 Hz, OCH_2CH_3), 1.53-1.65 (m, 1H, H_7), 1.70-1.85 (m, 2H, H_4 + H_7), 2.04-2.18 (m, 1H, H_4), 2.22-2.32 (m, 1H, H_3), 2.35-2.41 (m, 2H, H_8), 2.63 (dd, 1H, J = 9.8, 13.4 Hz, H_6), 3.54 (dd, 1H, J = 3.4, 13.4 Hz, H_6), 3.64 (s, 3H, O*Me*), 3.75 (3H, O*Me*), 4.10 (d, 1H,

J = 8.1 Hz, H_2), 4.20-4.29 (m, 3H, O*CH*$_2$CH$_3$ + H_5), 6.66 (d, 2H, *J* = 9.1 Hz), 6.85 (d, 2H, *J* = 9.1 Hz), 6.90-6.98 (m, 2H), 8.10 (dd, 1H, *J* = 0.8, 2.6Hz) *ppm*

^{13}C NMR (75 MHz, $CDCl_3$) δ = 173.7 (Cq), 173.3 (Cq), 151.3 (Cq), 149.2 (Cq), 140.6 (Cq), 140.5 (Cq), 136.8 (CH), 123.7 (CH), 122.1 (CH), 114.8 (2xCH), 113.6 (2xCH), 67.9 (CH), 60.8 (CH_2), 58.8 (CH), 55.7 (CH_3), 51.5 (CH_3), 41.1 (CH), 40.7 (CH_2), 36.9 (CH_2), 32.4 (CH_2), 25.3 (CH_2), 14.3 (CH_3) *ppm*

IR (neat): 3370, 2935, 1733, 1627, 1512, 1492, 1242, 1177, 1039, 818 *cm^{-1}*

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{24}H_{32}N_3O_5$: 442.2342 , found: 442.2322

***R*$_f$** = 0.43 (AcOEt)

Chiral HPLC: Daicel Chiralcel® OD-H (60% n-heptane, 40% iPrOH), 15 °C, 1 mL/min, 328 nm, t_1 = 11.2 min (*minor*), t_2 = 16.7 min (*major*)

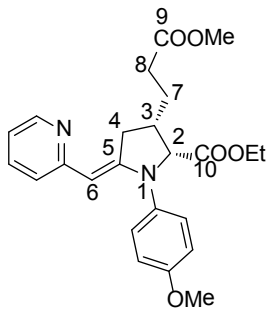
[α]$^{20}_D$ = + 70 (c = 0.25, MeOH)

Synthetic transformations of 11a

(for compound **13a** see above)

(2*R*,3*S*,*E*)-Ethyl-3-(3-methoxy-3-oxopropyl)-1-(4-methoxyphenyl)-5-(pyridin-2-ylmethylene)pyrrolidine-2-carboxylate (16):

To a solution of **11a** (122 mg, 0.289 mmol, 1 equiv) in dry AcOEt (14.5 mL) was added Pd/C (62 mg, 0.058 mmol, 0.2 equiv) and dry K_2CO_3 (20 mg, 0.145 mmol, 0.5 equiv). The resulting mixture was flushed (3x) with H_2 and was allowed to react under H_2 for 1 h 35 (^{1}H NMR monitoring). The suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to give 125 mg (> 95%, 98 % *ee* and dr > 20/1) of **16** as a pale yellow solid.



^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.28 (t, 3H, *J* = 7.1 Hz, OCH$_2$*CH$_3$*), 1.70-1.79 (m, 1H), 1.83-1.92 (m, 1H), 2.51 (t, 2H, *J* = 7.6 Hz), 2.63-2.74 (m, 1H), 2.82 (ddd, 1H, *J* = 1.9, 11.6, 13.7 Hz), 3.69 (s, 3H), 3.74 (dd, 1H, *J* = 7.5, 16.3 Hz), 3.81 (s, 3H), 4.09-4.24 (m, 2H, O*CH$_2$*CH$_3$), 4.37 (d, 1H, *J* = 8.1 Hz), 5.33 (s, 1H, H_6), 6.75 (m, 1H), 6.80 (d, 1H, *J* = 8.1 Hz), 6.89 (d, 2H, *J* = 8.9 Hz), 7.22 (d, 2H, *J* = 8.9 Hz), 7.37 (dt, 1H, *J* = 1.9, 7.8 Hz), 8.38 (dd, 1H, *J* = 1.4, 4.9 Hz) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.4 (Cq), 171.5 (Cq), 159.1 (Cq), 157.7 (Cq), 153.0 (Cq), 148.8 (CH), 135.4 (CH), 134.4 (Cq), 128.1 (2xCH), 121.3 (CH), 117.1 (CH), 114.7 (2xCH), 94.0 (CH), 69.7 (CH), 61.0 (CH_2), 55.5 (CH_3), 51.7 (CH_3), 39.9 (CH), 36.2 (CH_2), 32.5 (CH_2), 25.7 (CH_2), 14.3 (CH_3) *ppm*

IR(neat): 2957, 1735, 1724, 1628, 1583, 1542, 1507, 1467, 1439, 1287, 1239, 1178, 1098, 1029, 801 *cm^{-1}*

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{24}H_{29}N_2O_5$: 425.2076, found: 425.2069

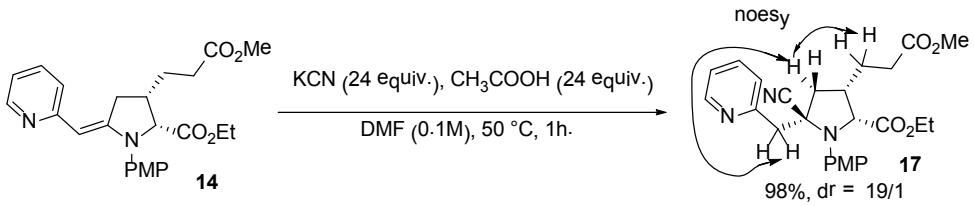
***R*$_f$** = 0.4 (cyclohexane/AcOEt: 1/1)

mp = 102°C from iPr_2O

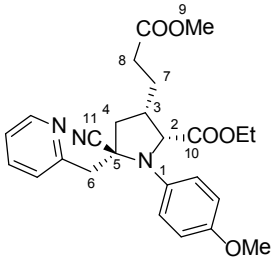
Chiral HPLC: Daicel Chiralpak® IC (60% n-heptane, 40% iPrOH), 20°C, 1 mL/min, 340 nm, t_1 = 12.3 min (*minor*), t_2 = 22.9 min (*major*)

$[\alpha]^{20}_D$ = – 189 (c = 0.54, $CHCl_3$)

Synthesis of 17



(2*R*,3*S*,5*S*)-Ethyl-5-cyano-3-(3-methoxy-3-oxopropyl)-1-(4-methoxyphenyl)-5-(pyridin-2-ylmethyl)pyrrolidine-2-carboxylate (17):



In a flask containing a well stirred solution of pyrrolidine **14** (42 mg, 0.099 mmol, 1 equiv) in DMF (1 mL) was introduced KCN (155 mg, 2.38 mmol, 24 equiv) followed by CH_3CO_2H (136 µL, 2.38 mmol, 24 equiv). The flask was heated at 50 °C for 1 h 15, then the reaction was cooled to rt, quenched with a saturated solution of $NaHCO_3$ and extracted with AcOEt (3x). The combined organic layers were brined, dried on $MgSO_4$ and filtered. The volatiles were removed under reduced pressure to give crude amino nitrile **17** (44 mg) as yellow oil, 98 % yield (crude yield) and dr = 19:1 (determined by HPLC). The relative configuration of **17** was determined by NOE experiments. **Upon attempts of further purification on silica gel, the product was found to be prone to retro-Strecker reaction generating HCN.**

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.28 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 1.60-1.69 (m, 1H, H_7), 1.75-1.84 (m, 1H, H_7), 2.39-2.52 (m, 4H, H_4 + H_8), 2.65-2.75 (m, 1H, H_3), 3.21 (d, 1H, *J* = 13.6 Hz, H_6), 3.66 (s, 3H, O*Me*), 3.78 (s, 3H, O*Me*), 3.85 (d, 1H, *J* = 13.6 Hz, H_6), 4.20-4.25 (m, 3H, OCH_2CH_3 + H_2), 6.88 (d, 2H, *J* = 9.3 Hz), 6.93 (d, 2H, *J* = 9.3 Hz), 7.19 (ddd, 1H, *J* = 1,1, 4.9, 5.9 Hz), 7.23, (m, 1H), 7.62 (dt, 1H, *J* = 1.9, 7.7 Hz), 8.59 (d, 1H, *J* = 4.9 Hz) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.0 (Cq), 172.5 (Cq), 155.4 (Cq), 154.0 (Cq), 149.6 (CH), 136.6 (Cq), 136.5 (CH), 124.7 (CH), 122.3 (CH), 120.9 (CN), 118.2 (2xCH), 114.9 (2xCH), 67.8 (CH), 62.3 (Cq), 61.3 (CH_2), 55.6 (CH_3), 51.7 (CH_3), 44 2 (CH_2), 43.4 (CH_2), 39.6 (CH), 32.2 (CH_2), 24.8 (CH_2), 14.2 (CH_3) *ppm*

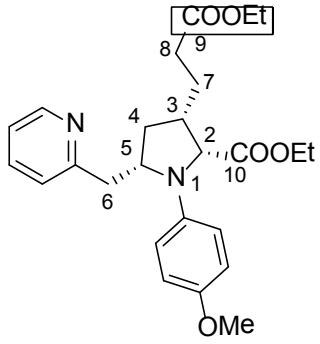
IR (neat): 2937, 1730, 1588, 1512, 1434, 1244, 1173, 1029, 814 cm^{-1}

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{25}H_{30}N_3O_5$: 452.2185, found: 452.2184

***R*$_f$** = 0.2 (AcOEt/cyclohexane: 1/2)

Chiral HPLC: Daicel Chiralpak® IC (60% n-heptane, 40% iPrOH), 20°C, 1 mL/min, 247 nm, t_1 = 19.9 min (*minor diastereoisomer*), t_2 = 27.4 min (*major diastereoisomer*)

(2*R*,3*S*,5*S*)-Ethyl-3-(3-ethoxy-3-oxopropyl)-1-(4-methoxyphenyl)-5-(pyridin-2-ylmethyl)pyrrolidine-2-carboxylate (18):



To a solution of pyrrolidine **11a** (130 mg, 0.308 mmol, 1 equiv) in absolute EtOH (15 mL) was added Pd/C (163 mg, 0.154 mmol, 0.5 equiv) and dry K_2CO_3 (21 mg, 0.154 mmol, 0.5 equiv). The resulting suspension was flushed 3 times with H_2 and was stirred under H_2 for 23 h (TLC monitoring). The suspension was filtered through Celite® washing with AcOEt and the filtrate was concentrated to give a crude (120 mg) which was purified by flash chromatography (EtOAc/cyclohexane: 1/4) on silica gel to yield 95 mg (73 %, 98% *ee*, dr > 20/1) of **18** as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.21 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 1.34 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 1.55-1.65 (m, 1H, H_7), 1.72-1.83 (m, 2H, H_4 + H_7), 2.09-2.17 (m, 1H, H_4), 2.25-2.43 (m, 3H, H_8 + H_3), 2.77 (dd, 1H AB, J = 9.8, 13.3 Hz, H_6), 3.65 (dd AB, 1H, J = 3.3, 13.3 Hz, H_6), 3.74 (s, 3H, O*Me*), 3.74 (s, 3H, O*Me*), 4.08 (q, 2H, J = 7.1 Hz, OCH_2CH_3), 4.12 (d, 1H, J = 8.1 Hz, H_2), 4.24-4.29 (m, 3H, OCH_2CH_3 + H_5), 6.66 (d, 2H, J = 8.9 Hz), 6.86 (d, 2H, J = 8.9 Hz), 7.12-7.18 (m, 2H), 7.57 (dt, 1H, J = 1.8, 7.6 Hz), 8.58 (m, 1H) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.8 (Cq), 173.0 (Cq), 159.9 (Cq), 151.7 (Cq), 149.5 (CH), 140.6 (Cq), 136.2 (CH), 124.0 (CH), 121.3 (CH), 115.1 (2xCH), 113.8 (2xCH), 68.0 (CH) , 60.9 (CH_2), 58.7 (CH), 55.9 (CH_3), 42.5 (CH_2), 41.0 (CH), 37.2 (CH_2), 32.9 (CH_2), 25.5 (CH_2), 14.4 (CH_3), 14.2 (CH_3) *ppm*

IR (neat): 2927, 1732, 1593, 1510, 1365, 1242, 1178, 1039, 817 cm^{-1}

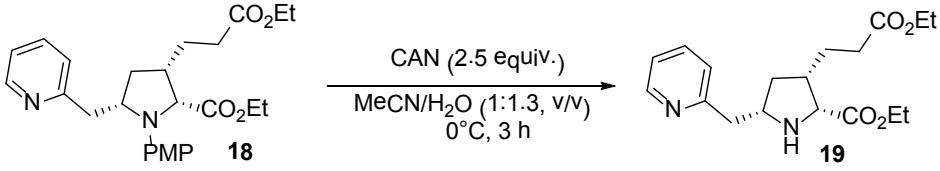
HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{25}H_{33}N_2O_5$: 441.2389 , found: 441.2401

R_f = 0.17 (AcOEt/cyclohexane: 1/4)

Chiral HPLC: Daicel Chiralpak® IC (60% n-heptane, 40% iPrOH), 20°C, 1 mL/min, 252 nm, t_1 = 12.1 min (*minor*), t_2 = 26.8 min (*major*)

$[\alpha]^{20}_D$ = + 13 (c = 0.7, MeOH)

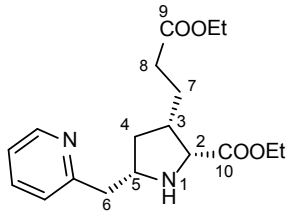
Synthesis of 19



(2*R*,3*S*,5*S*)-Ethyl-3-(3-ethoxy-3-oxopropyl)-5-(pyridin-2-ylmethyl)pyrrolidine-2-carboxylate (19):

In a flask containing a well stirred solution of CAN (115 mg, 0.21 mmol, 2.5 equiv) in H_2O (1.6 mL) at 0°C was introduced dropwise a solution of **18** (37 mg, 0.084 mmol in 1.1 mL of CH_3CN) over 10 min.

Then, the mixture was allowed to react at this temperature for 3 h and was quenched by the addition of aqueous solution of $Na_2S_2O_3$ (1 M). The resulting mixture was extracted with CH_2Cl_2 (3x) and combined organics layers were brined, dried on $MgSO_4$ and filtered. The volatiles were removed under reduced pressure to give 30 mg of crude which was purified by flash column chromatography (AcOEt/MeOH: 95/5) on silica gel to yield **19** (21 mg, 75%) as a pale brown oil.



^{1}H NMR (500 MHz, $CDCl_3$) δ = 1.20-1.24 (m, 4H, OCH_2CH_3 + H_4), 1.29 (t, 3H, J = 7.1 Hz, OCH_2CH_3), 1.43-1.52 (m, 1H, H_7), 1.75-1.83 (m, 1H, H_7), 1.96-2.02 (m, 1H, H_4) 2.33 (t, 2H, H_8), 2.33-2.41 (m, 1H, H_3), 3.01-3.12 (m, 2 H, H_6), 3.62 (m, 1H, H_5), 3.88 (d, 1H, J = 8.6 Hz, H_2), 4.10 (q, 2H, J = 7.10 Hz, OCH_2CH_3), 4.14-4.22 (m, 2H, OCH_2CH_3), 7.12 (ddd, 1H, J = 1.1, 5.0, 6.0 Hz), 7.5 (dt, 1H, J = 1.9, 7.7 Hz), 8.52 (broad d, 1H, J = 4.6 Hz) *ppm*

^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.8 (Cq), 173.1 (Cq), 159.5 (Cq), 149.3 (CH), 136.4 (CH), 123.5 (CH), 121.4 (CH), 63.1 (CH), 60.9 (CH_2), 60.3 (CH_2), 58.7 (CH), 43.7 (CH_2), 42.7 (CH), 37.4 (CH_2), 33.2 (CH_2), 26.2 (CH_2), 14.2 (CH_3), 14.2 (CH_2) *ppm*

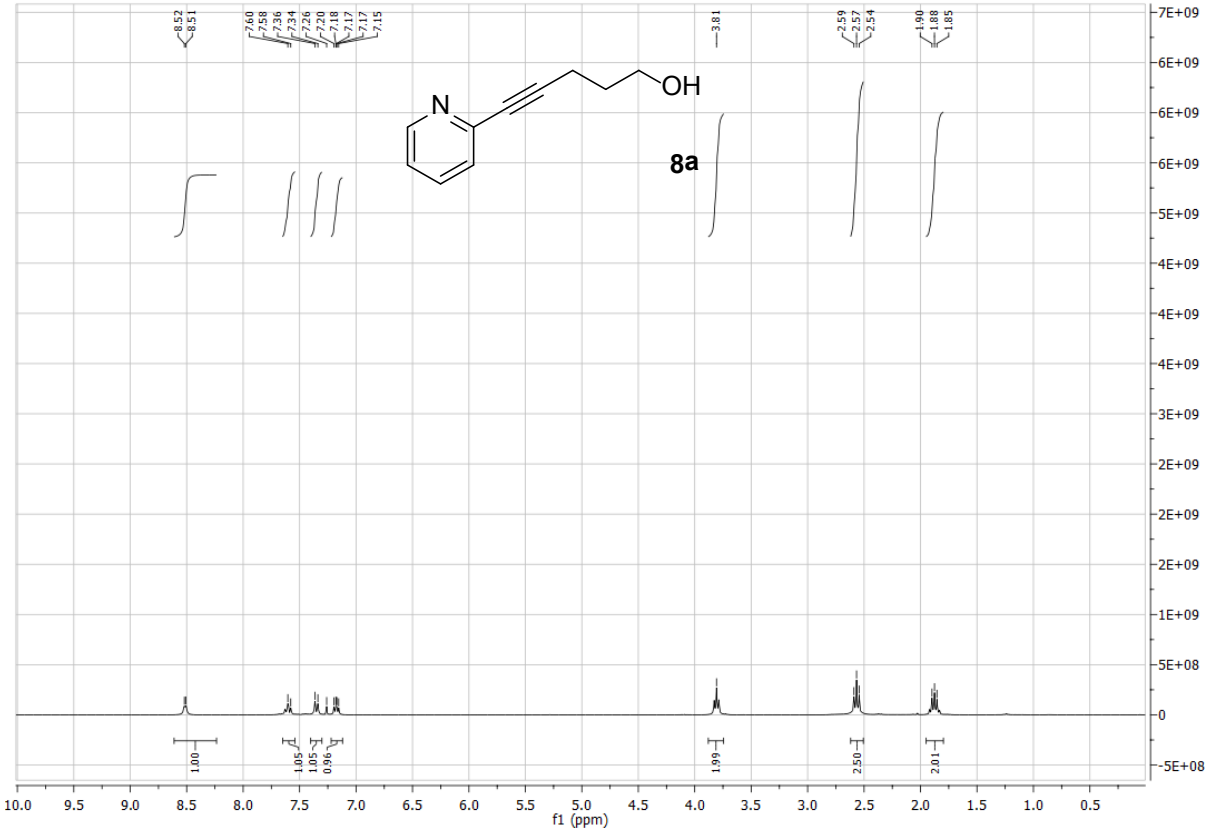
IR (neat): 2927, 1724, 1588, 1568, 1436, 1373, 1178, 1027, 749 cm^{-1}

Chiral HPLC: Daicel Chiralpak® AD (95% n-heptane, 5% iPrOH), 23 °C, 1 mL/min, 254 nm, t_1 = 38.9 min (*major*), t_2 = 55.8 min (*minor*)

HRMS (TOF MS ES+) calcd for $(M+H)^+$ $C_{18}H_{27}N_2O_4$: 335.1971, found: 335.1960

$\boldsymbol{R_f}$ = 0.4 (MeOH/AcOEt: 10/90)

$\boldsymbol{[\alpha]^{20}_D}$ = – 7 (c = 0.35, MeOH)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7.34
7.26
7.20
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7.17
7.17
7.15
3.81
2.59
2.57
2.54
1.90
1.88
1.85
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OH
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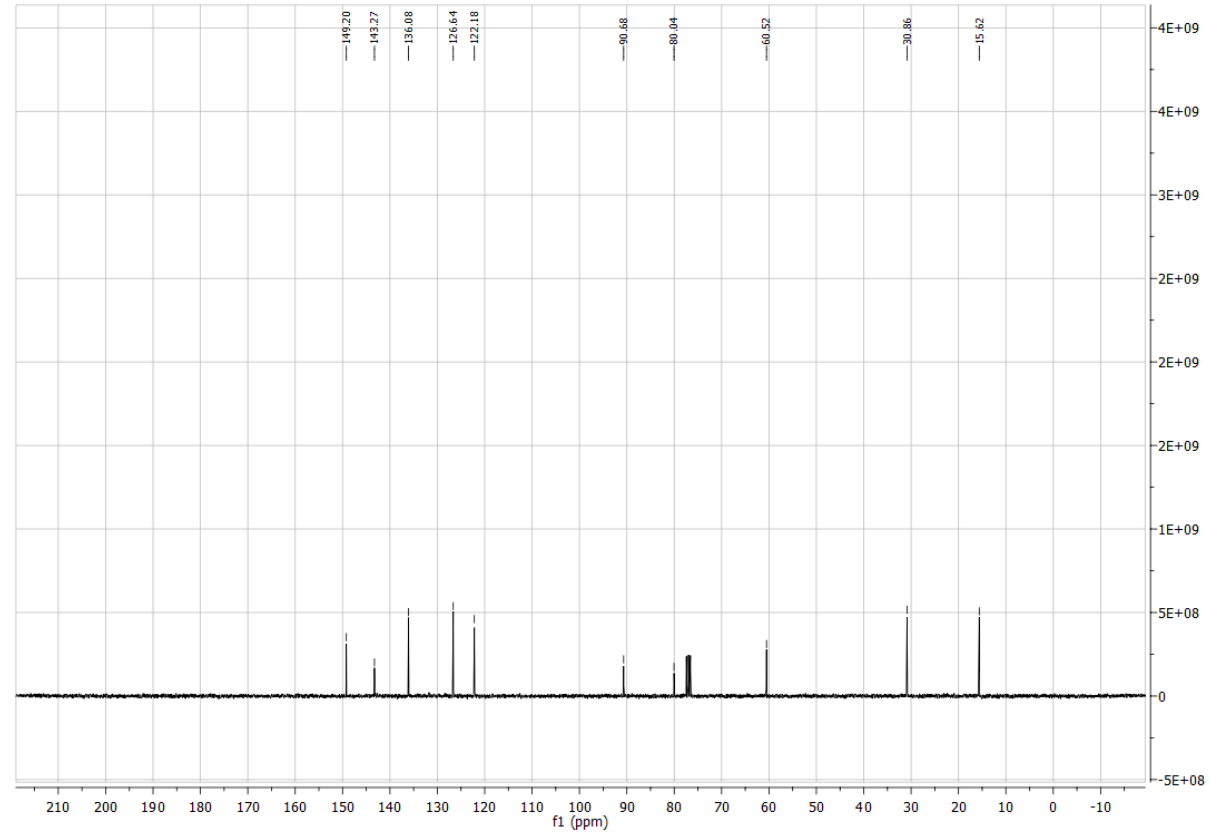
1.05
1.05
0.96
1.99
2.50
2.01
f1 (ppm)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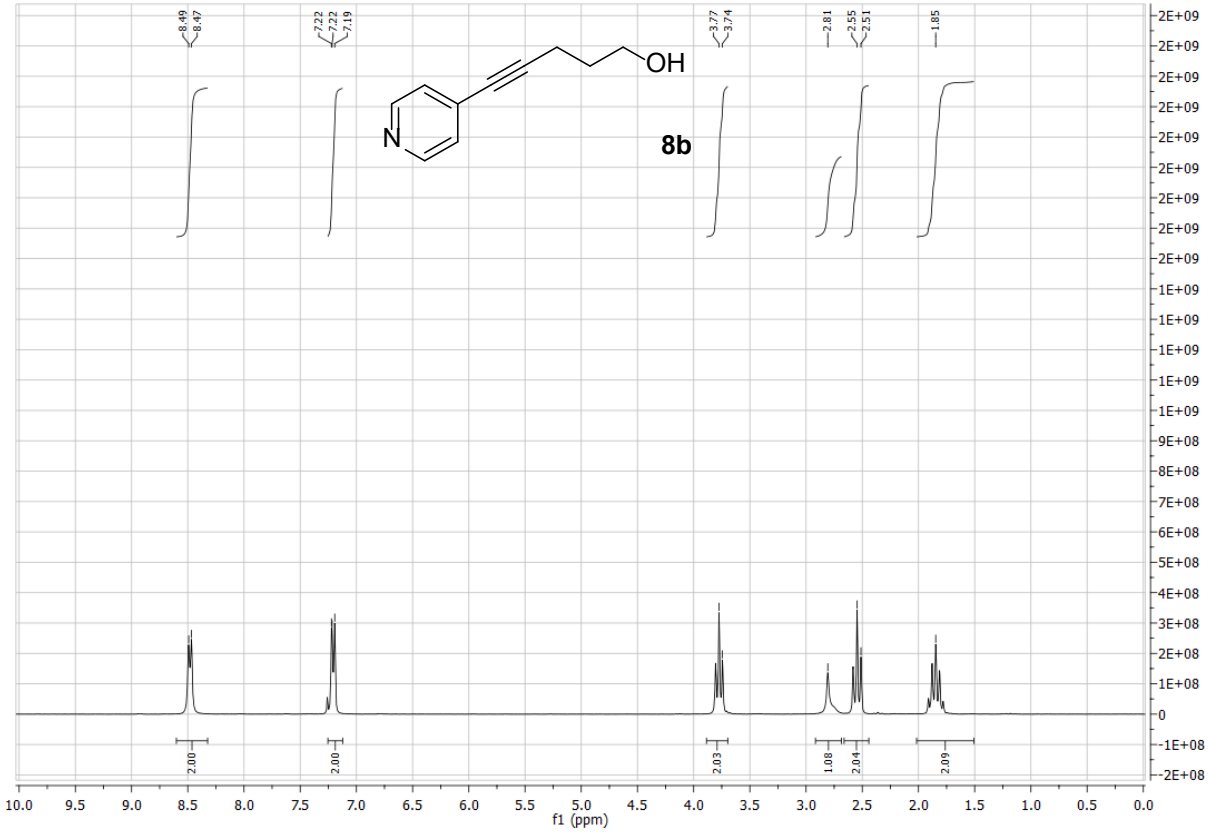
122.18
90.68
80.04
60.52
30.86
15.62
f1 (ppm)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8b
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2.00
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1.08
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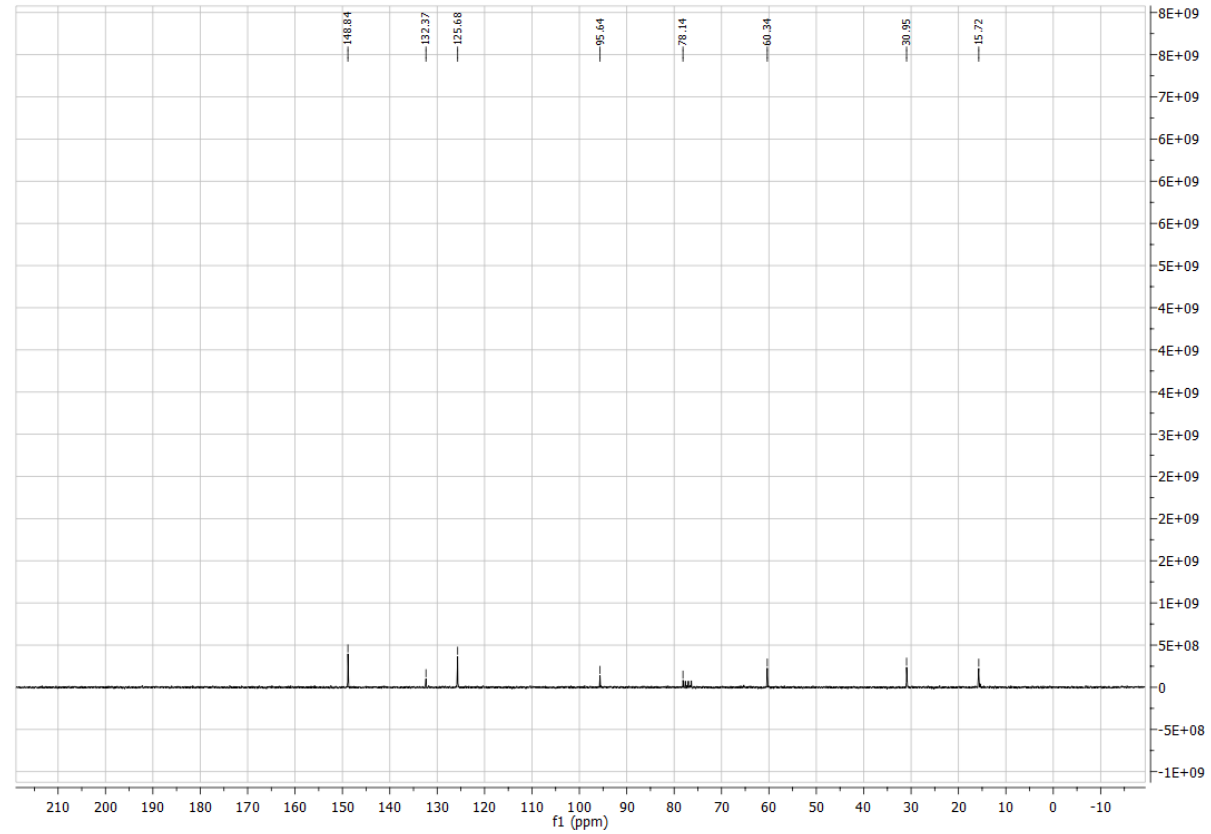
2.09
f1 (ppm)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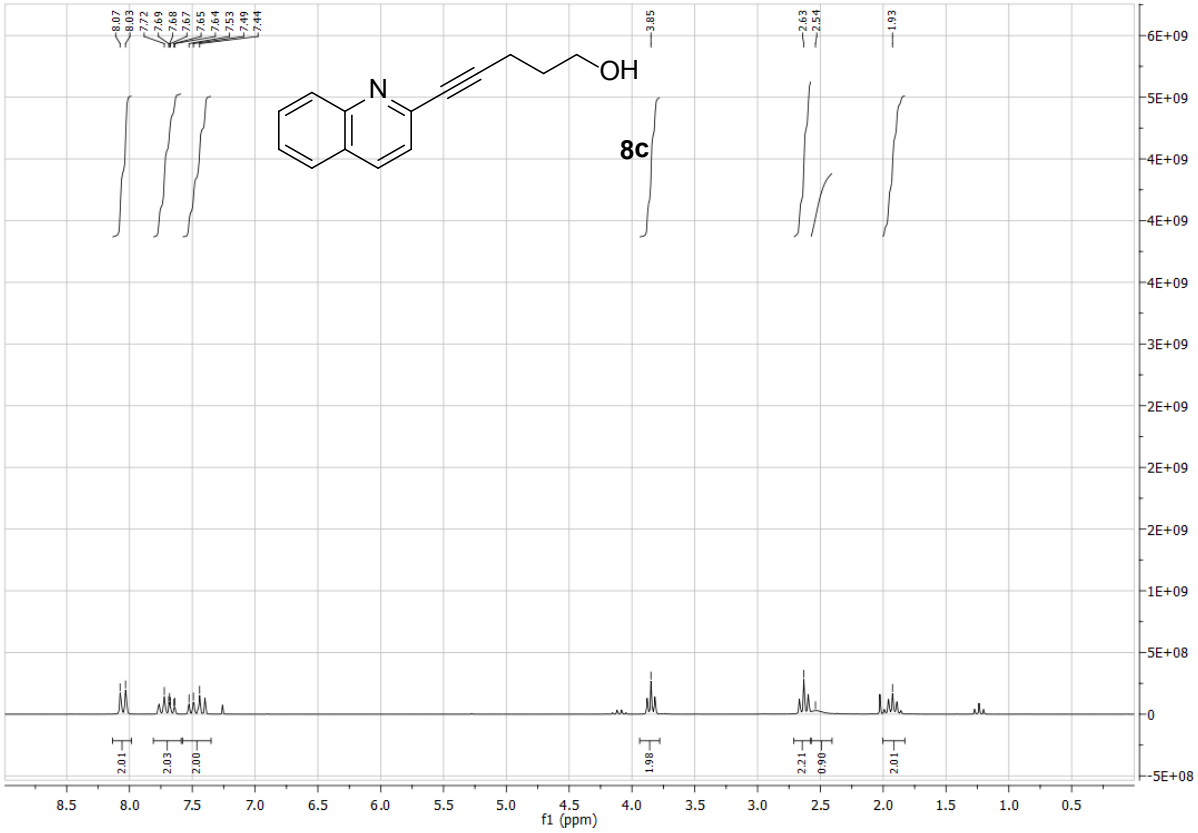
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7.64
7.53
7.49
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2.63
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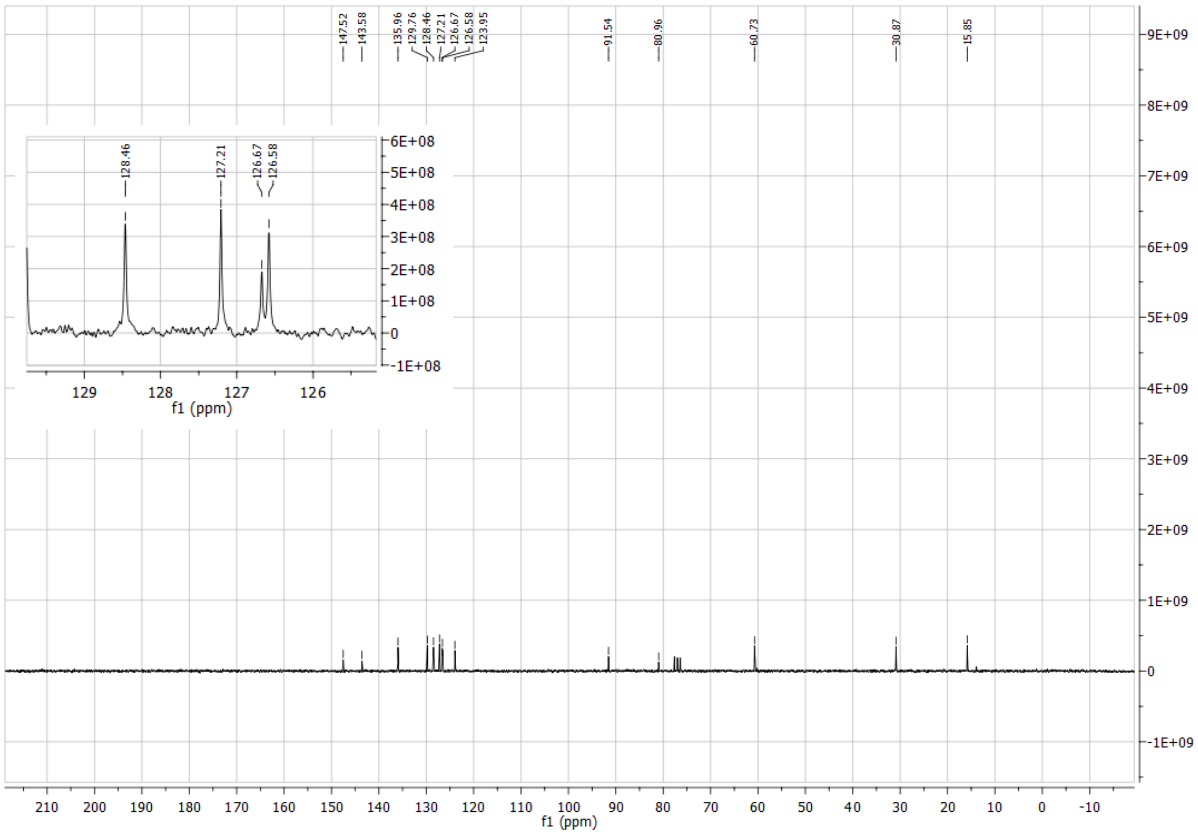
2.01
f1 (ppm)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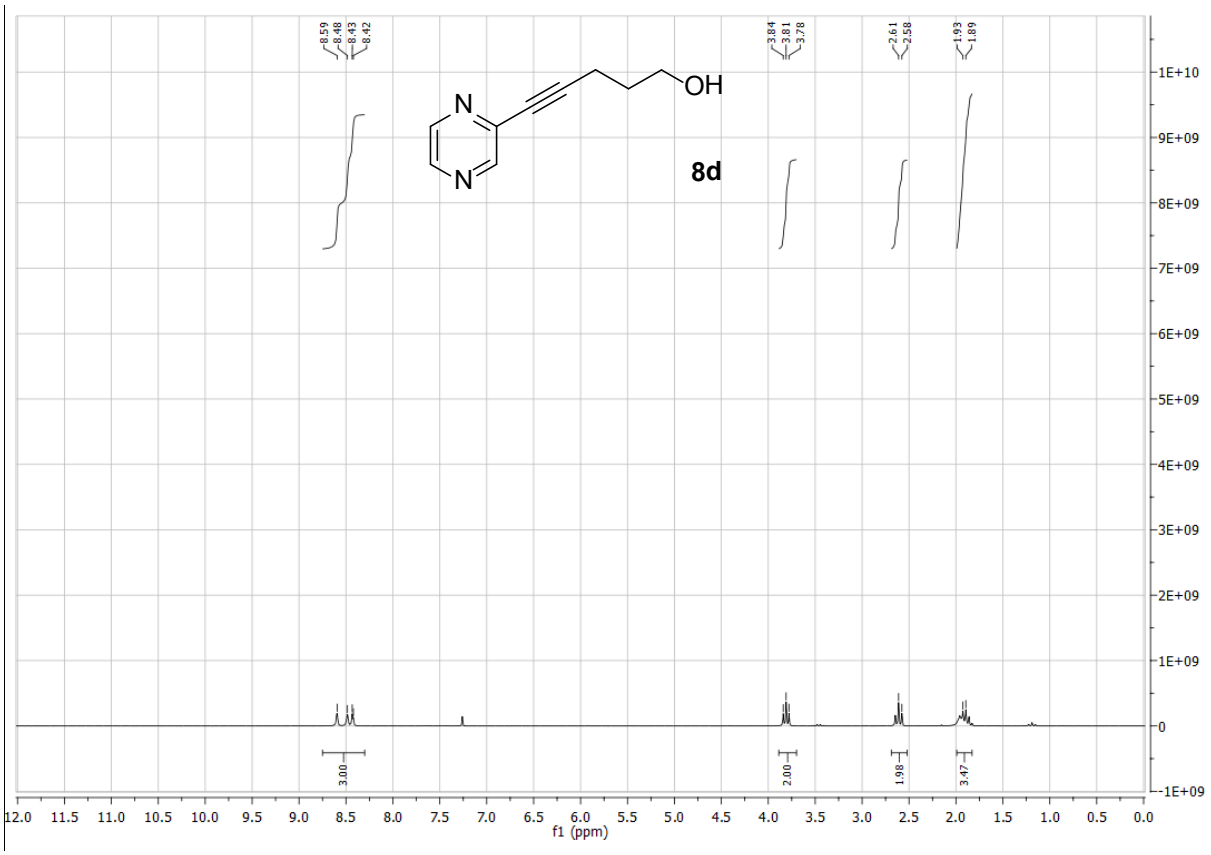
127.21
126.67
126.58
f1 (ppm)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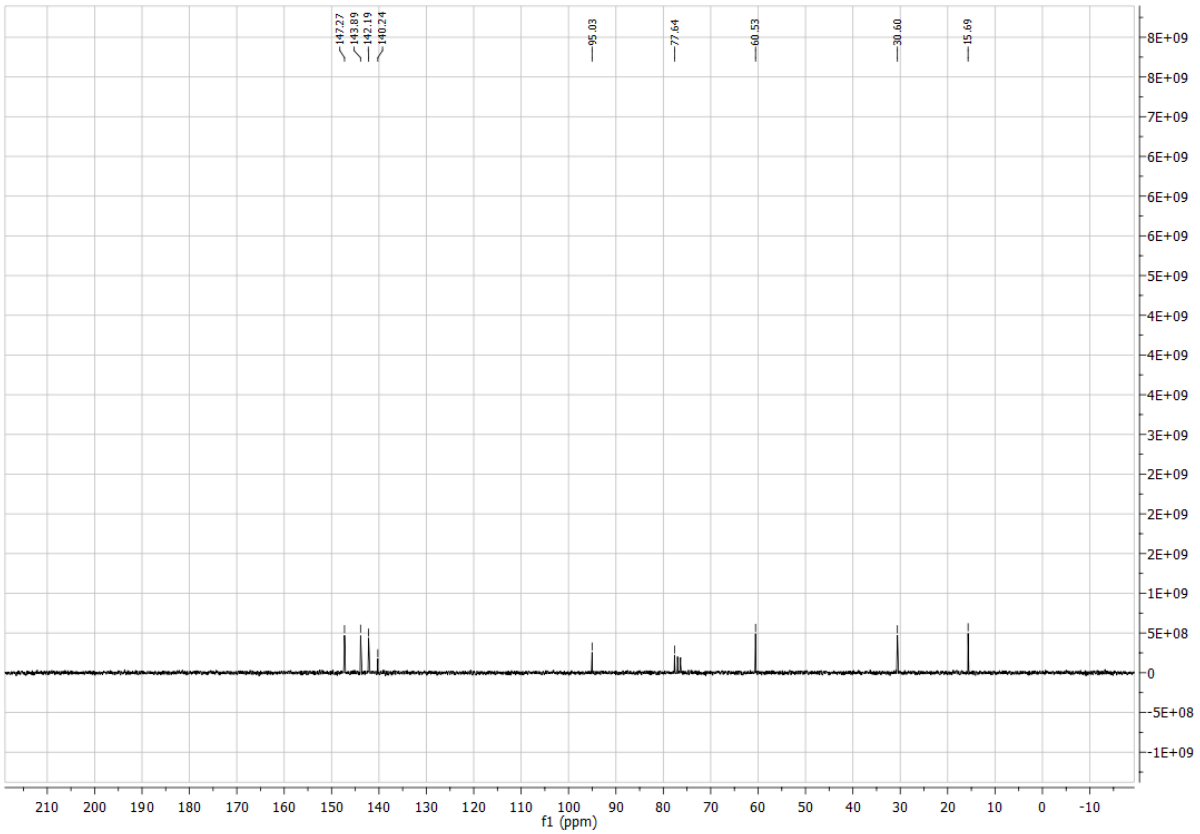
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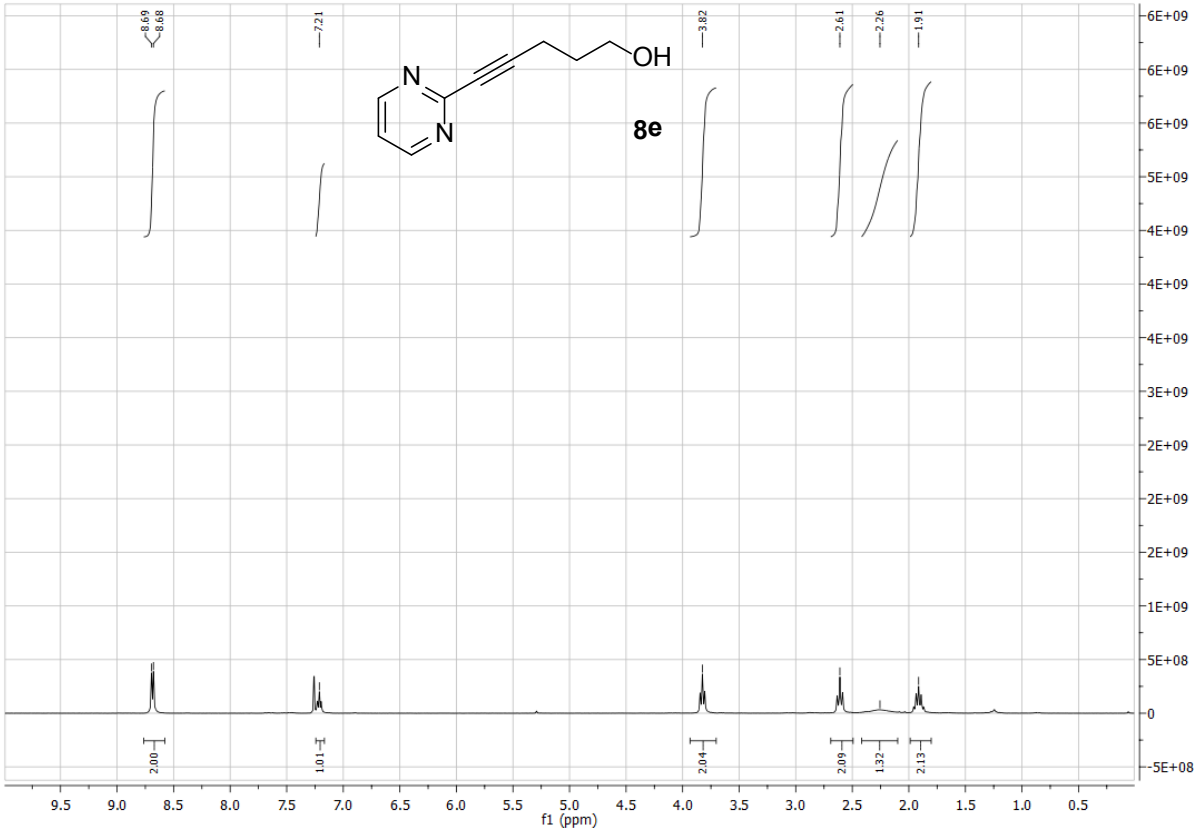
f1 (ppm)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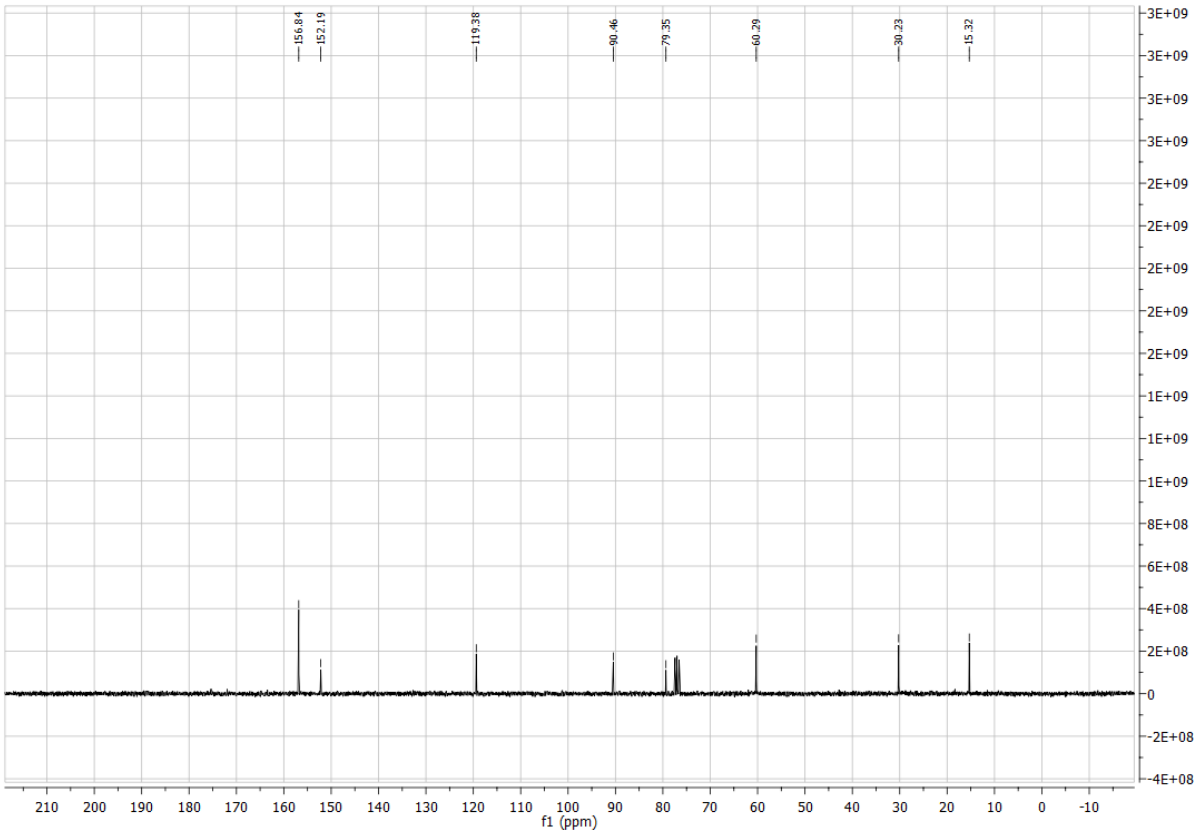
1.01
2.04
2.09
1.32
2.13
f1 (ppm)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152.19
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90.46
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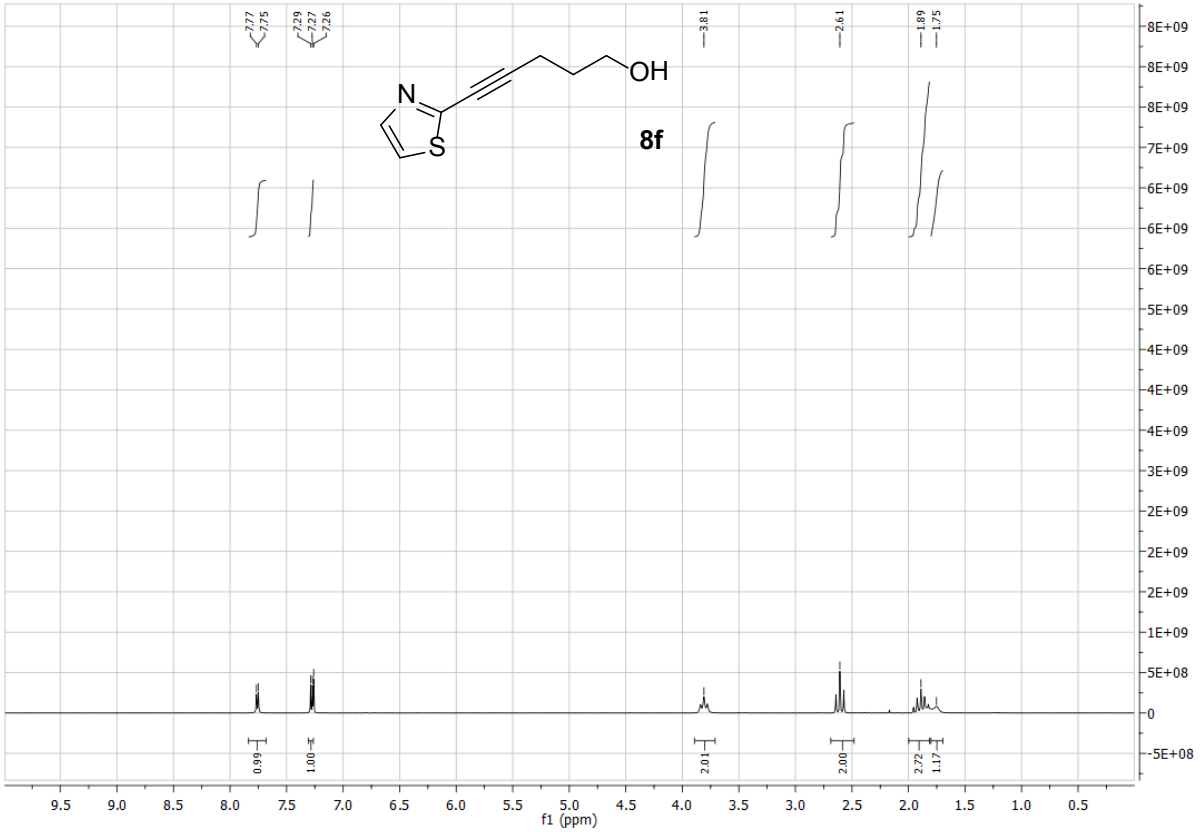
60.29
30.23
15.32
f1 (ppm)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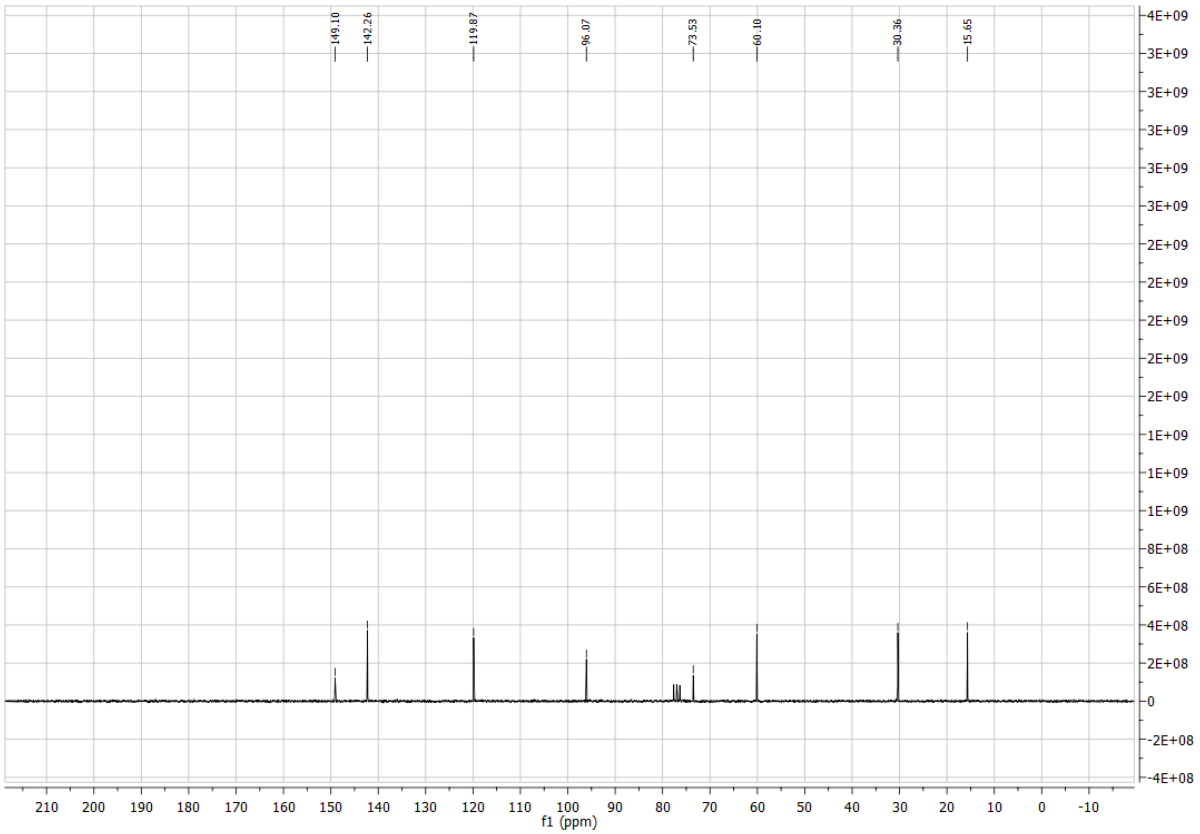
f1 (ppm)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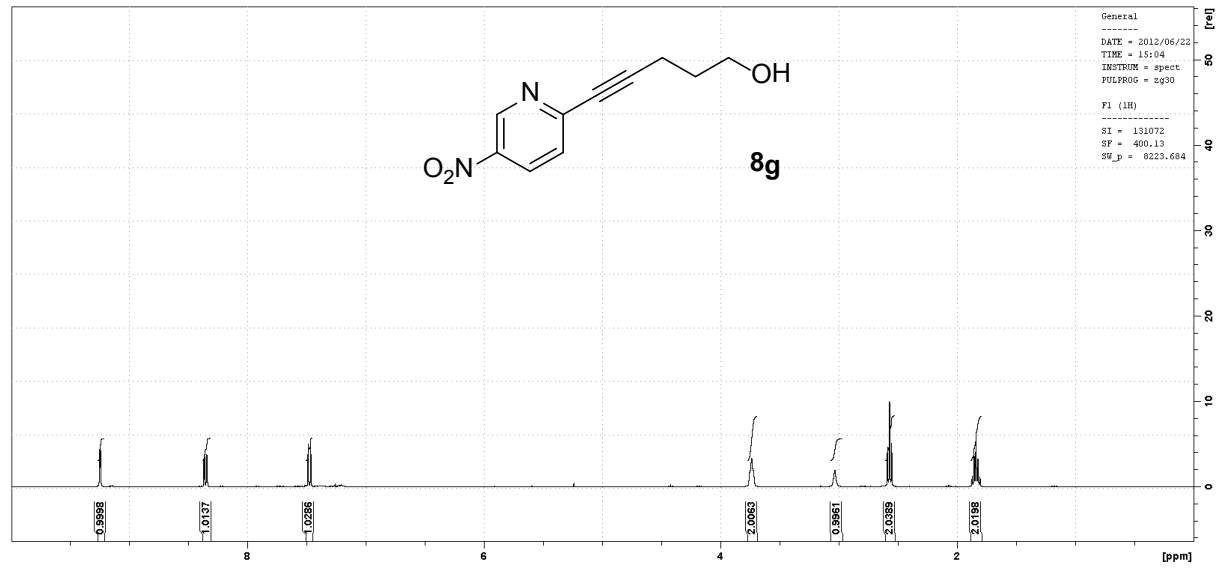
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OH
O_2N
8g
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2.0385
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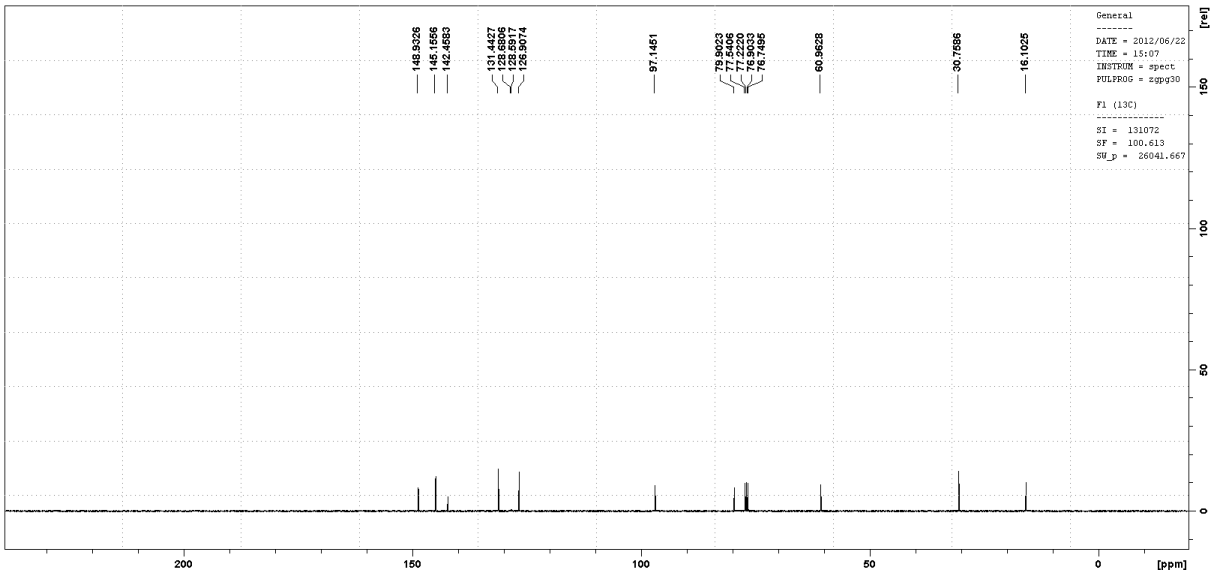
[ppm]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76.9033
76.7495
60.9628
30.7586
16.1025
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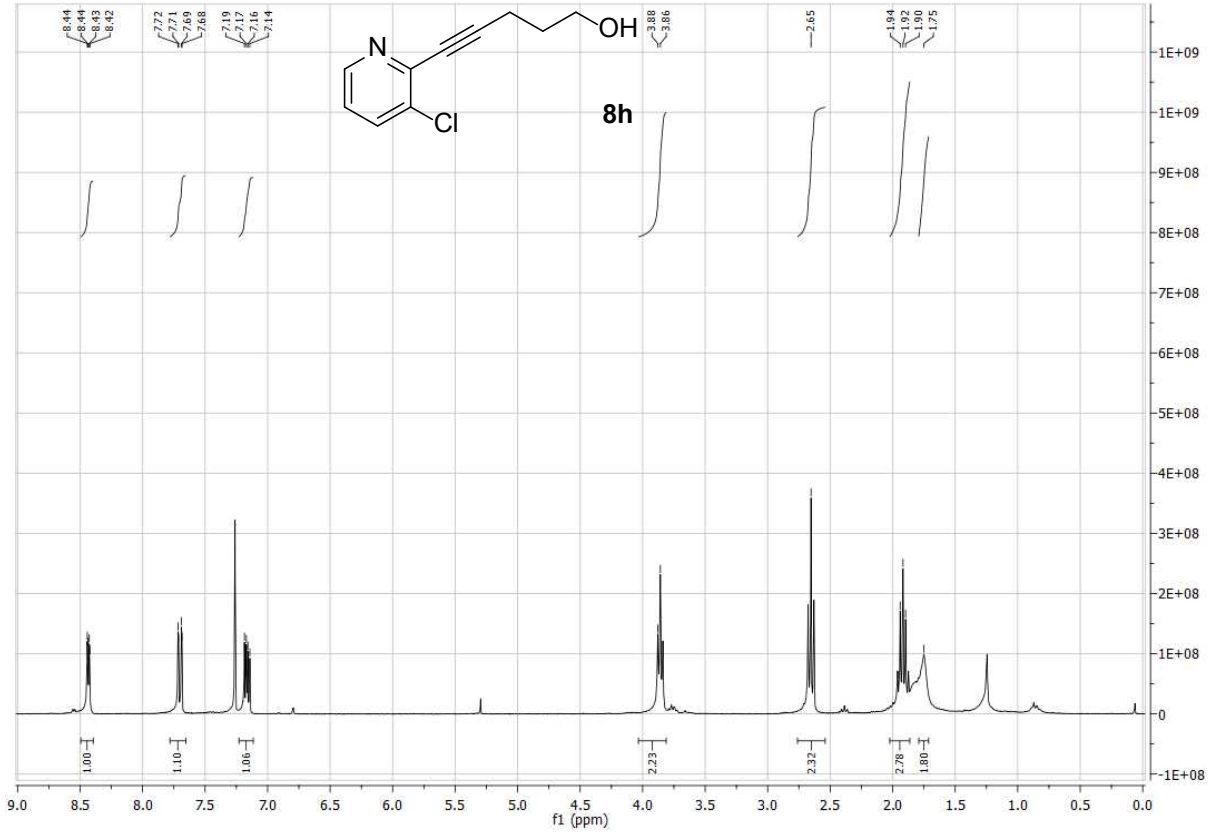
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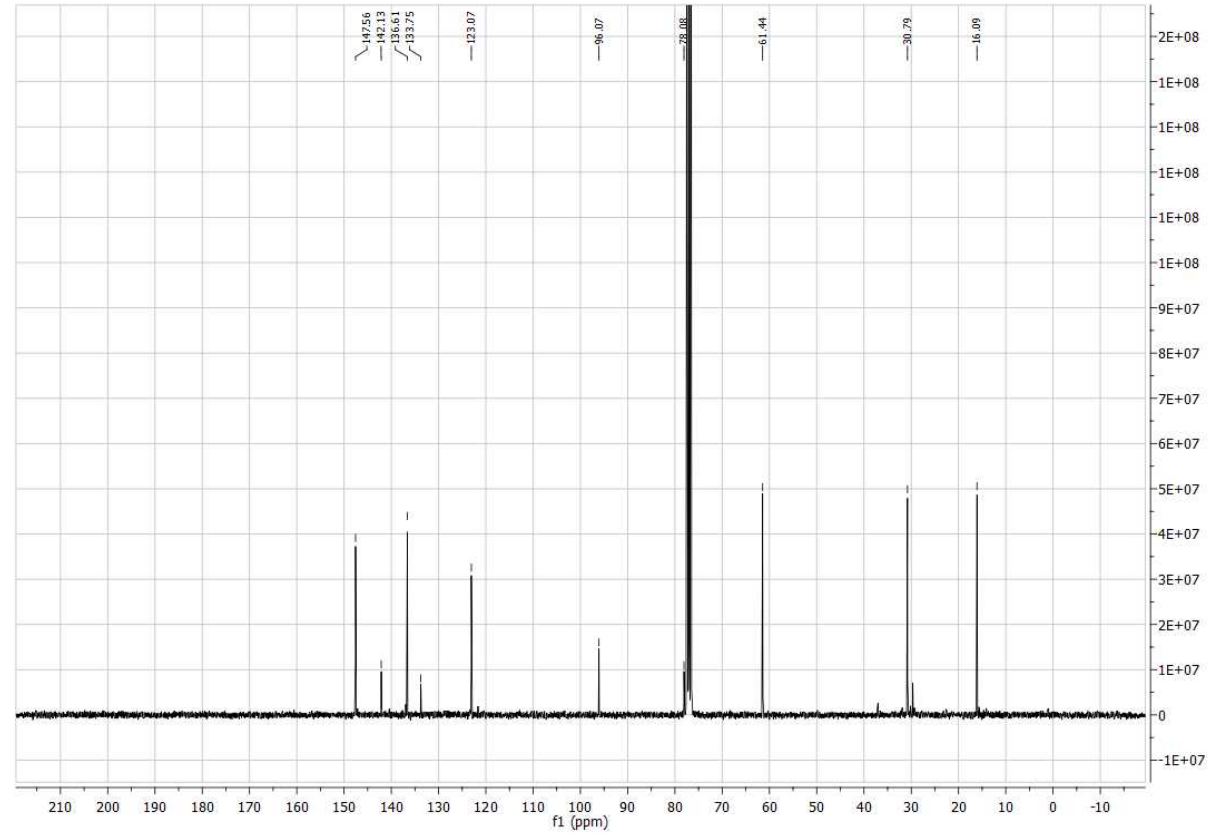
7.19
7.17
7.16
7.14
N
OH
Cl
8h
3.88
3.86
2.65
1.94
1.92
1.90
1.75
1.00
1.10
1.06
2.23
2.32
2.78
1.80
f1 (ppm)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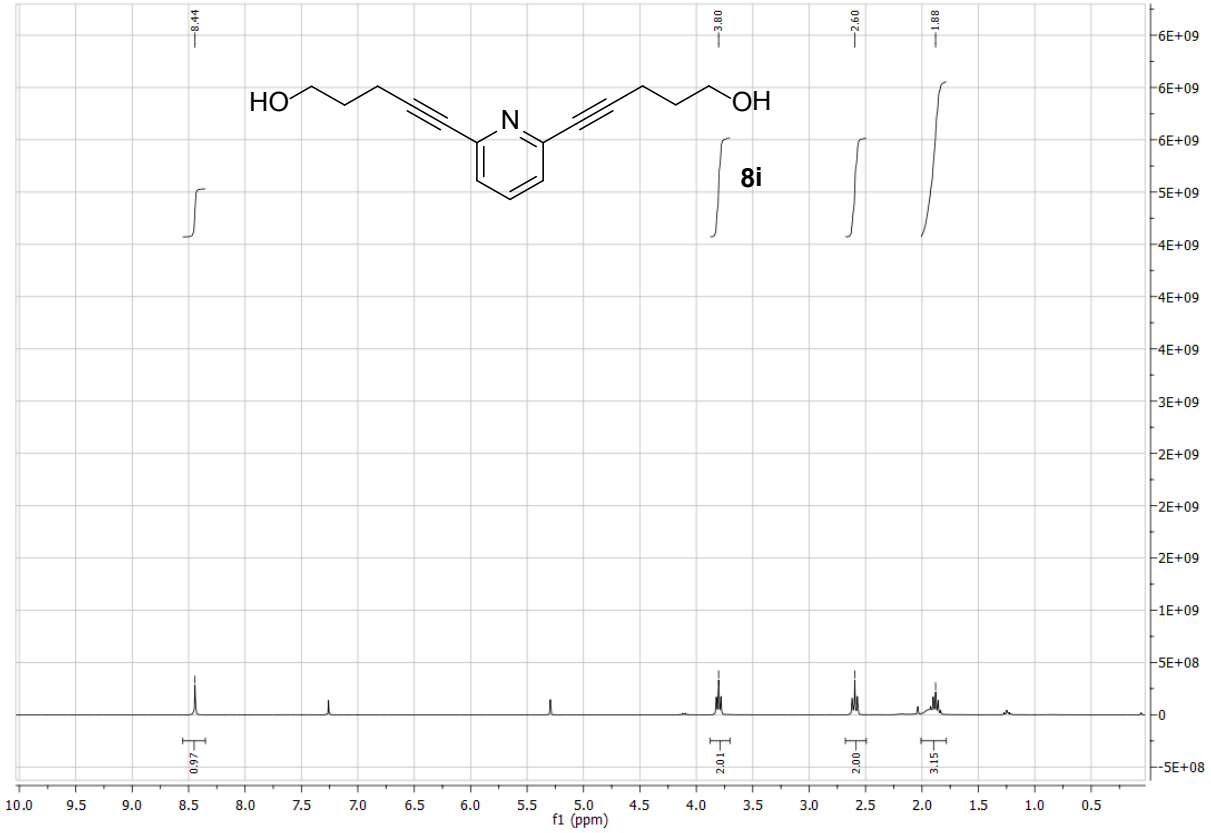
96.07
78.08
61.44
30.79
16.09
f1 (ppm)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HO
N
OH
8i
0.97
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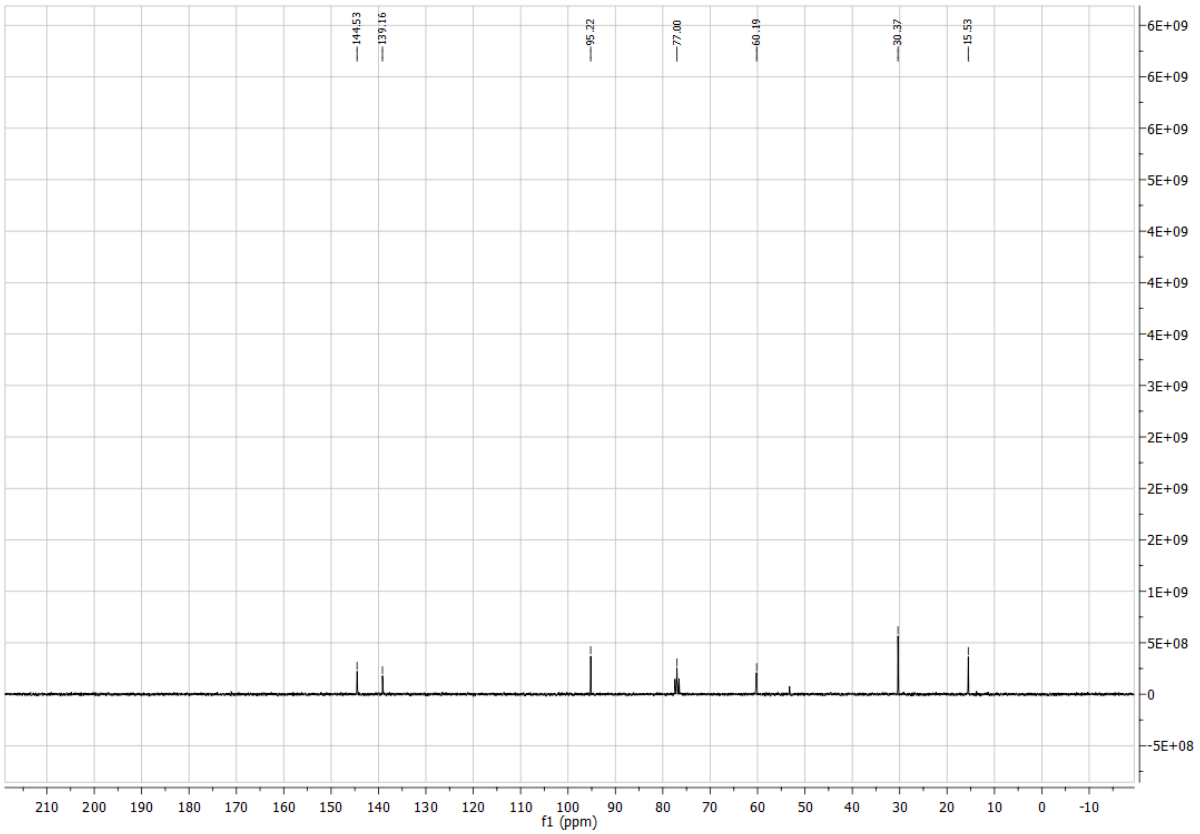
2.00
3.15
f1 (ppm)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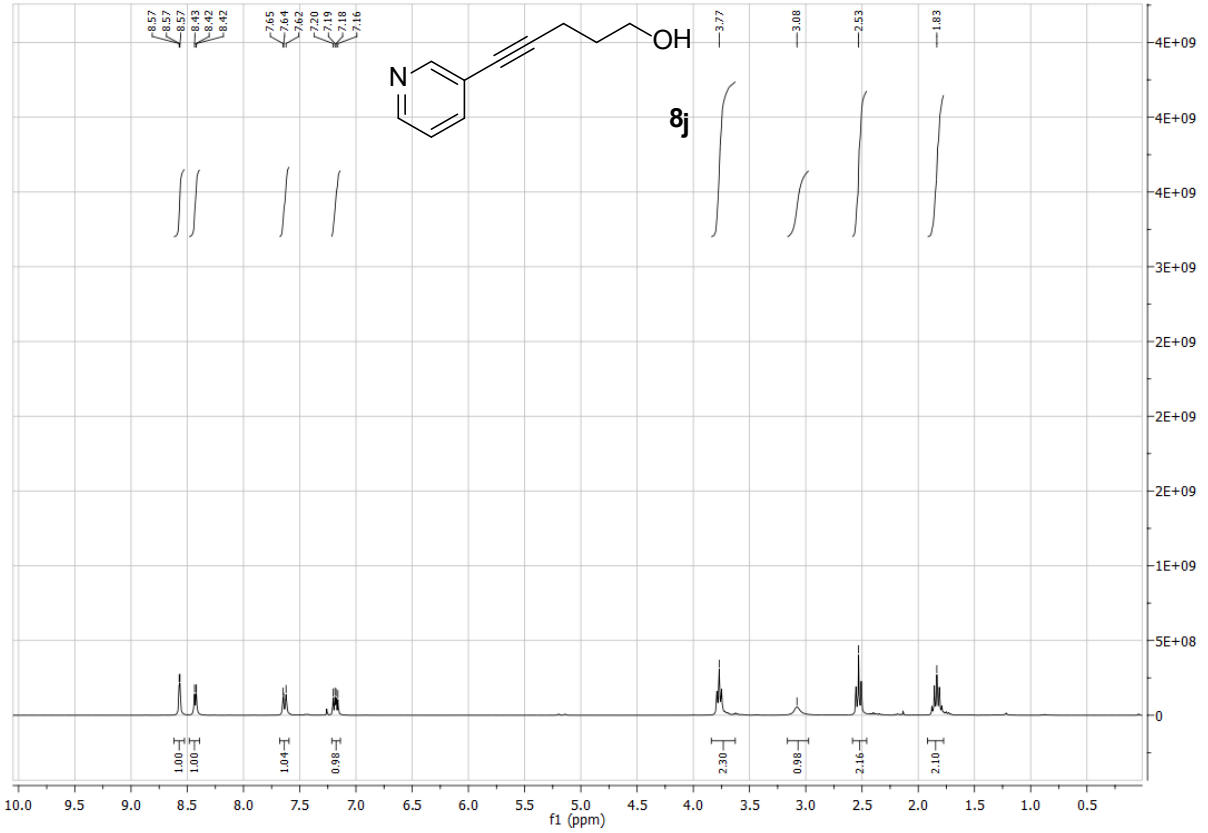
15.53
f1 (ppm)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8.42
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7.64
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7.19
7.18
7.16
3.77
3.08
2.53
1.83
N
OH
8j
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1.00
1.04
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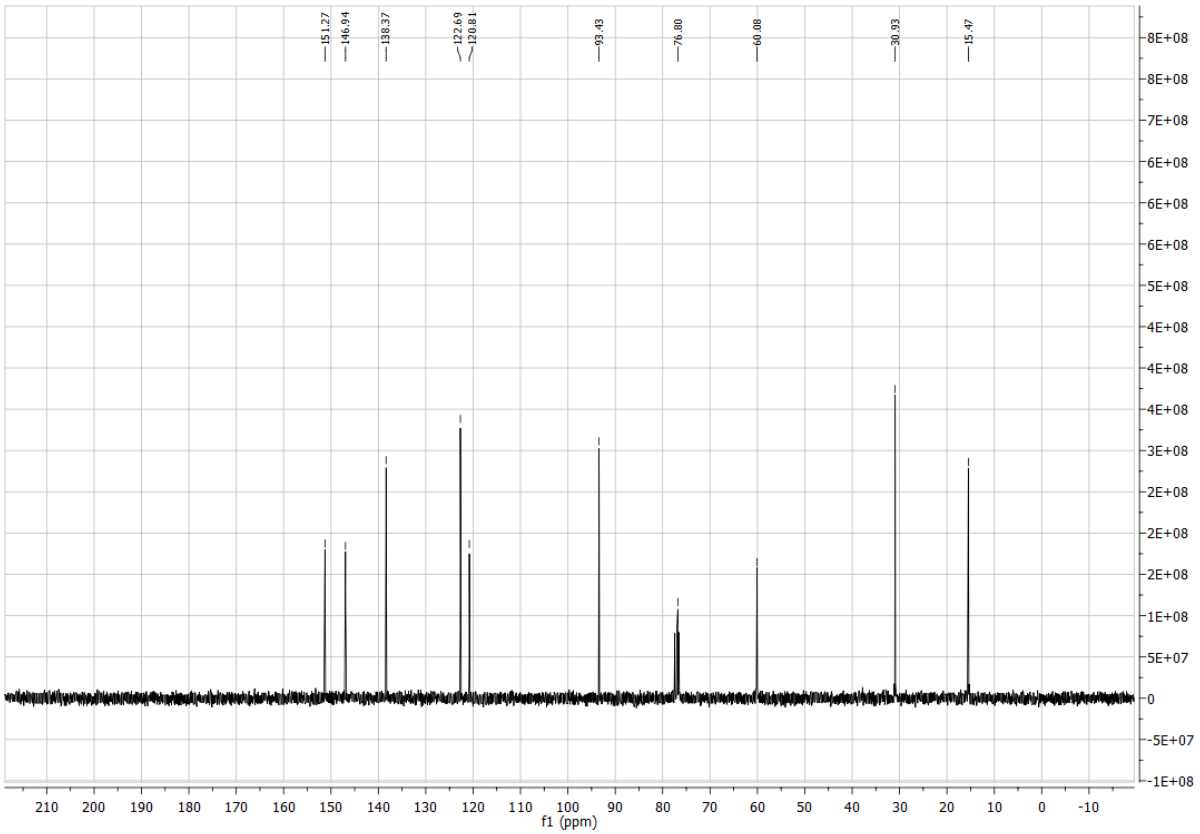
2.30
0.98
2.16
2.10
f1 (ppm)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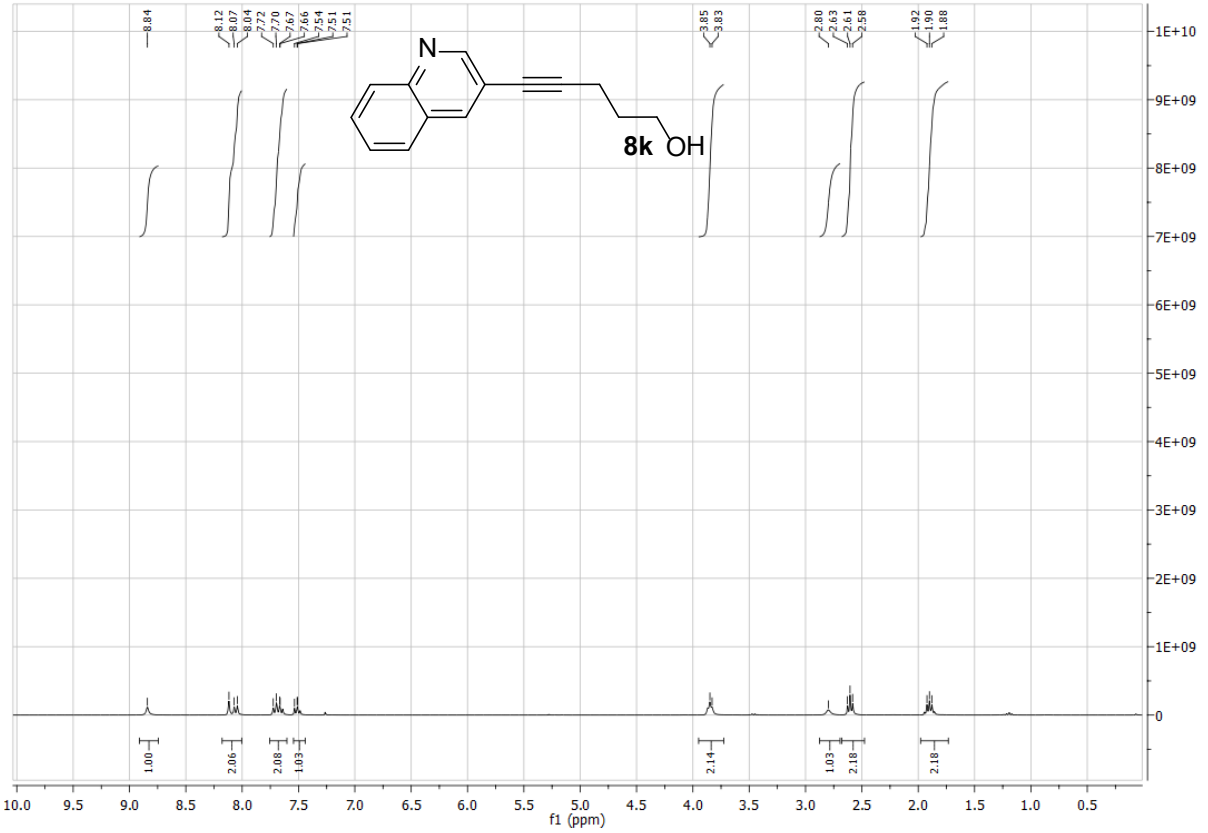
93.43
76.80
60.08
30.93
15.47
f1 (ppm)


8.84
8.12
8.07
8.04
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7.70
7.67
7.66
7.54
7.51
7.51
3.85
3.83
2.80
2.63
2.61
2.58
1.92
1.90
1.88
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8k OH
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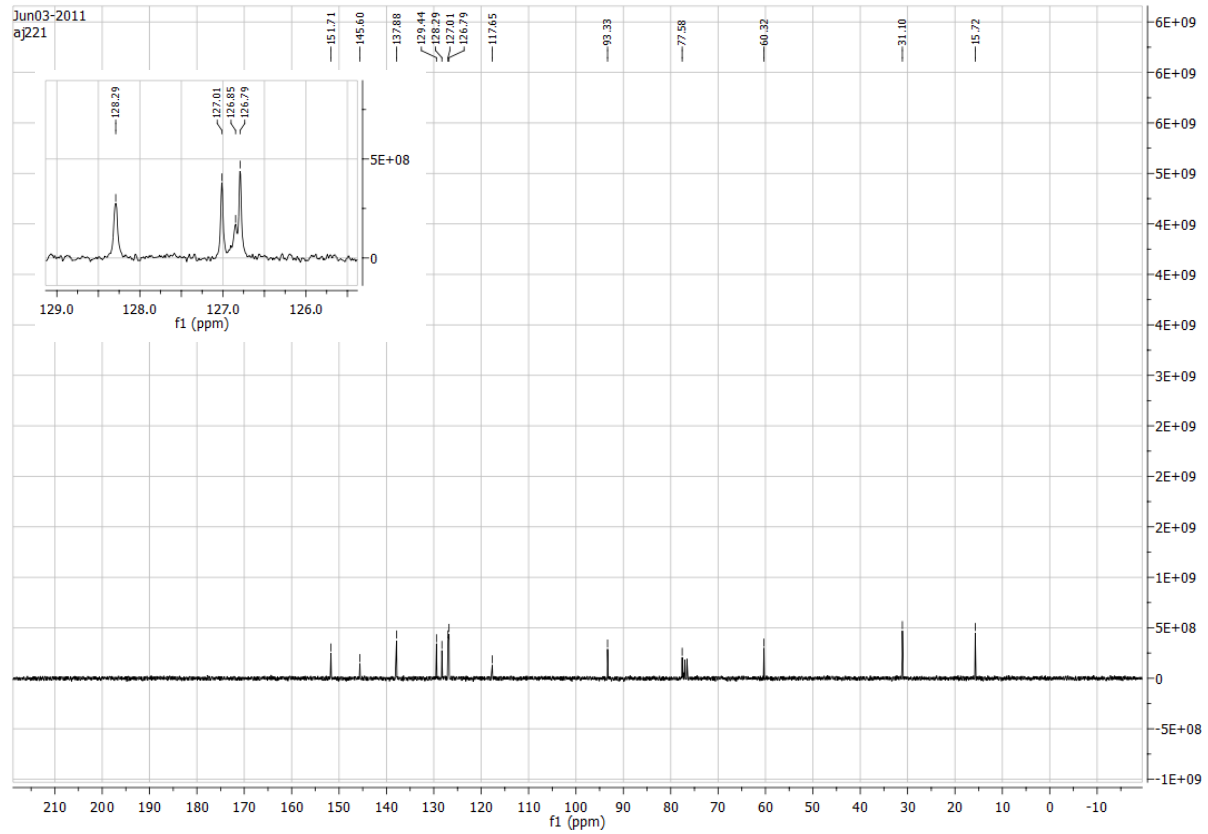
2.06
2.08
1.03
2.14
1.03
2.18
2.18
f1 (ppm)


Jun03-2011
aj221
151.71
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137.88
129.44
128.29
127.01
126.79
117.65
93.33
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31.10
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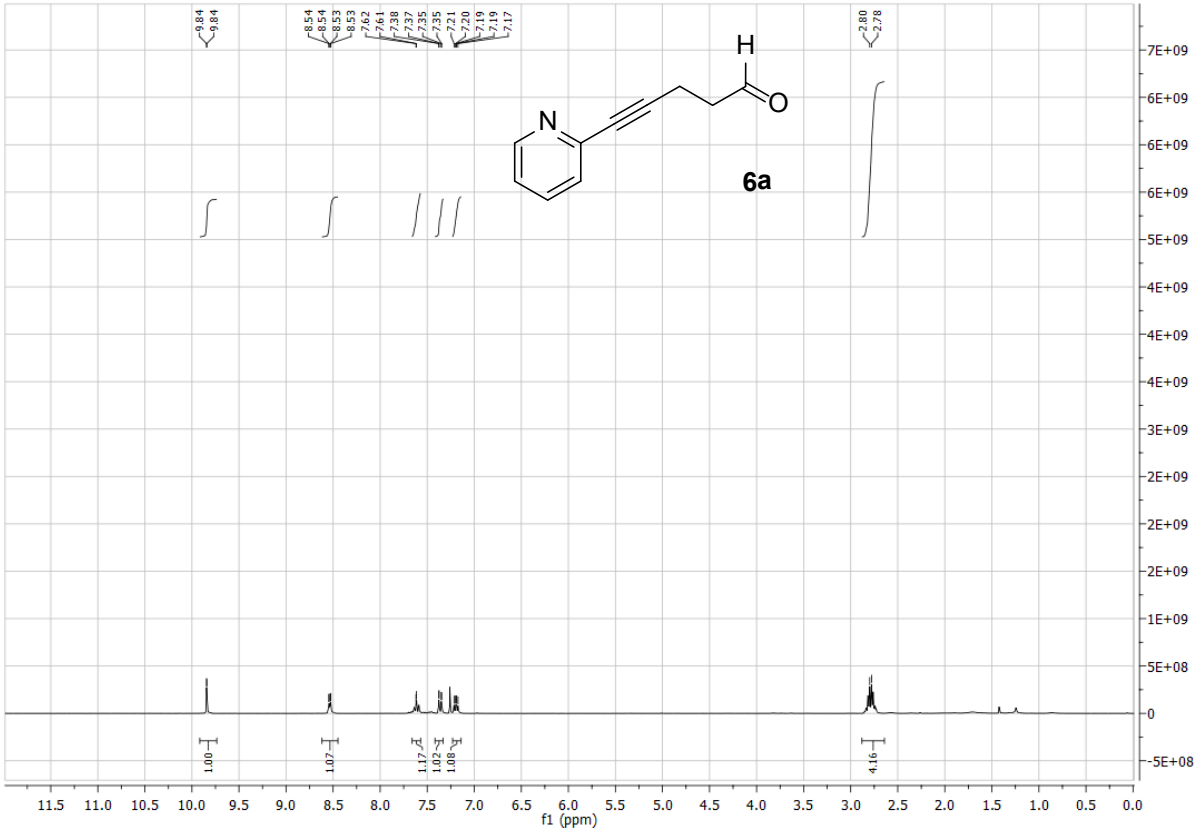
128.29
127.01
126.85
126.79
f1 (ppm)
f1 (ppm)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9.84
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8.53
7.62
7.61
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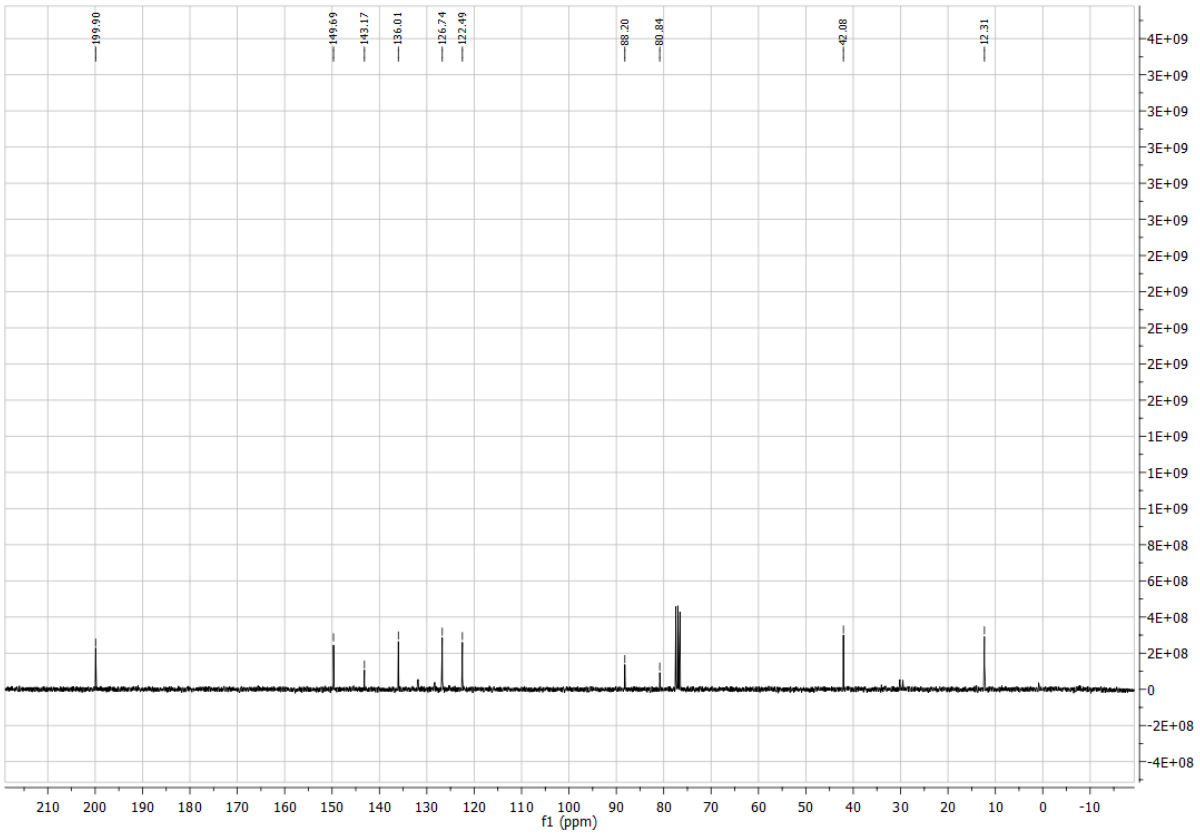
7.37
7.35
7.35
7.21
7.20
7.19
7.19
7.17
2.80
2.78
H
O
N
6a
1.00
1.07
1.17
1.02
1.08
4.16
f1 (ppm)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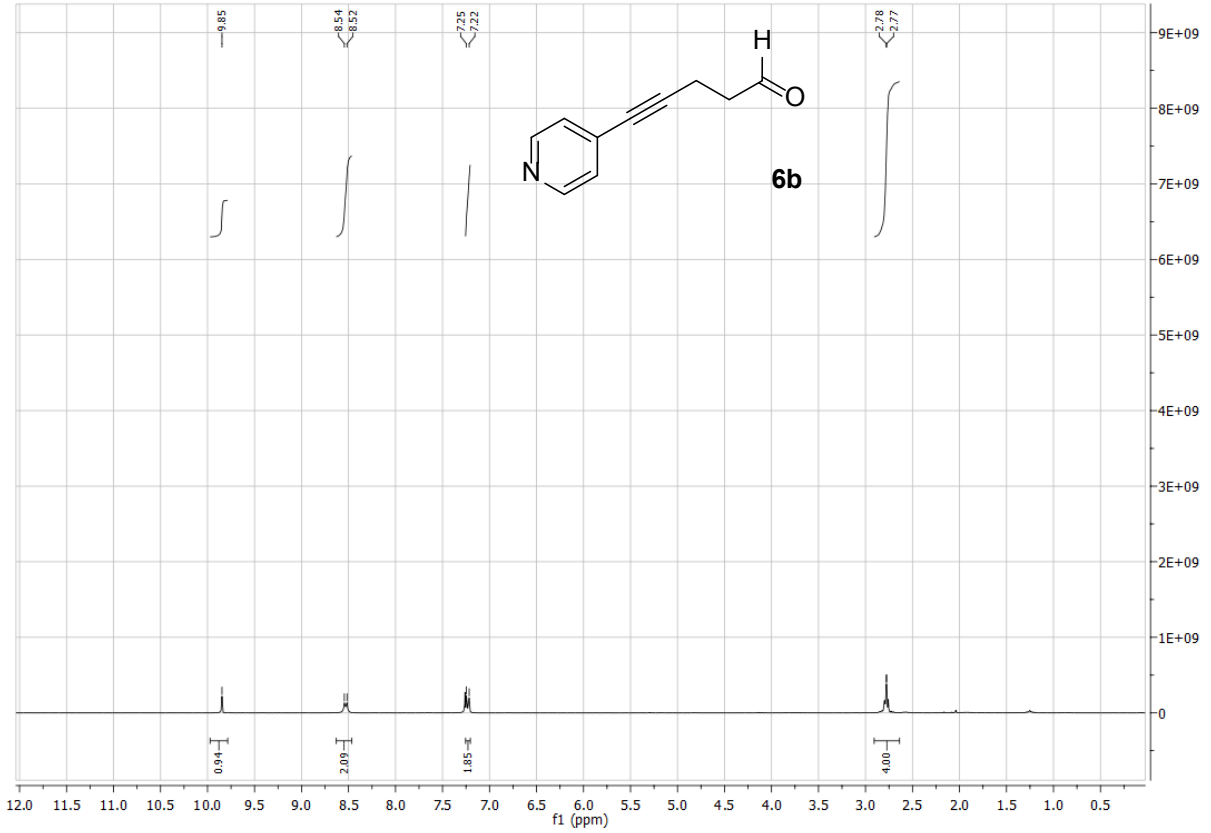
42.08
12.31
f1 (ppm)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8.54
8.52
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2.77
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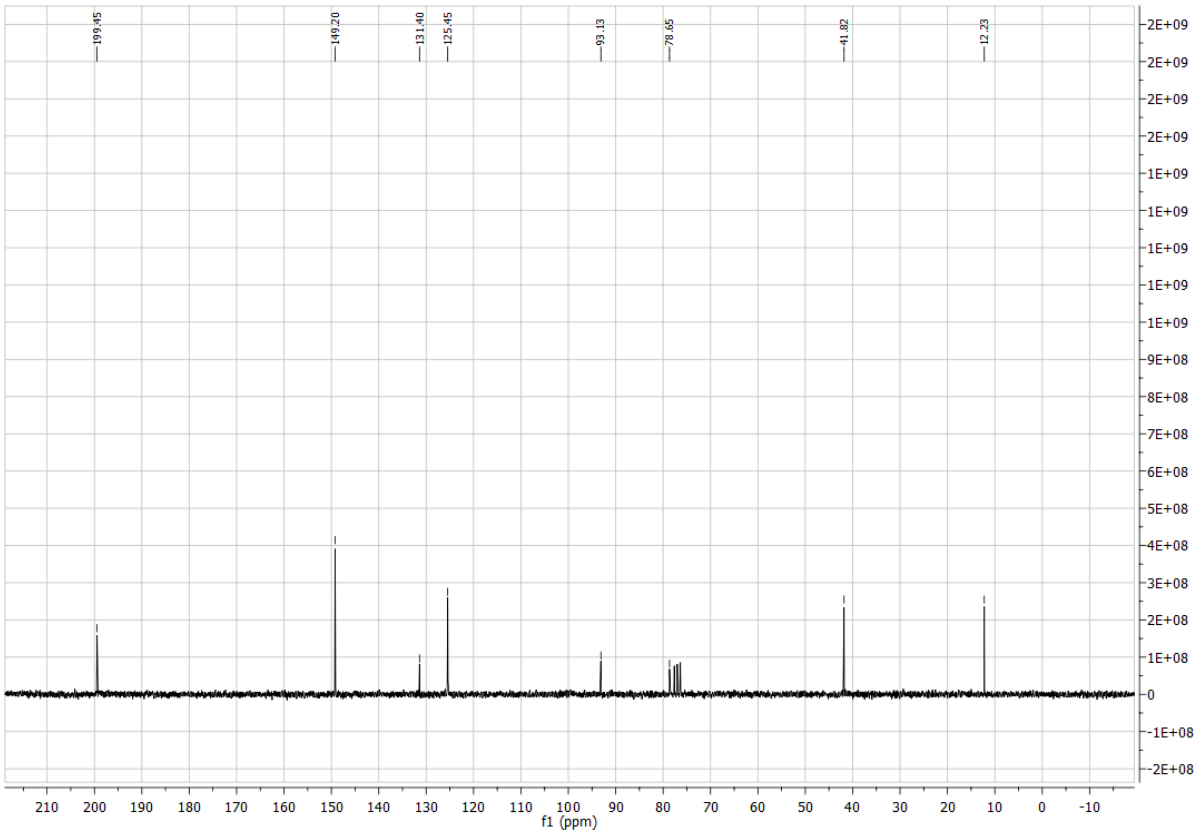
N
6b
0.94
2.09
1.85
4.00
f1 (ppm)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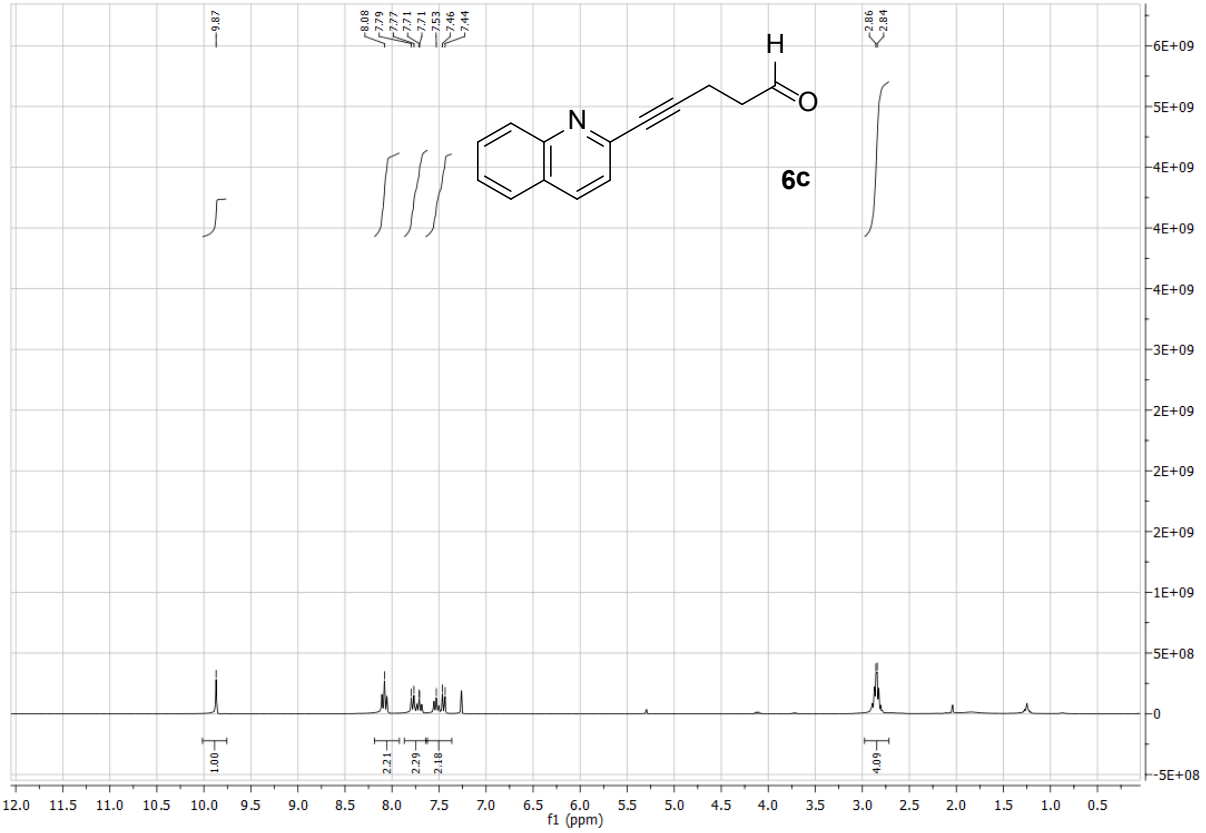
41.82
12.23
f1 (ppm)


9.87
8.08
7.79
7.77
7.71
7.71
7.53
7.46
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N
6c
1.00
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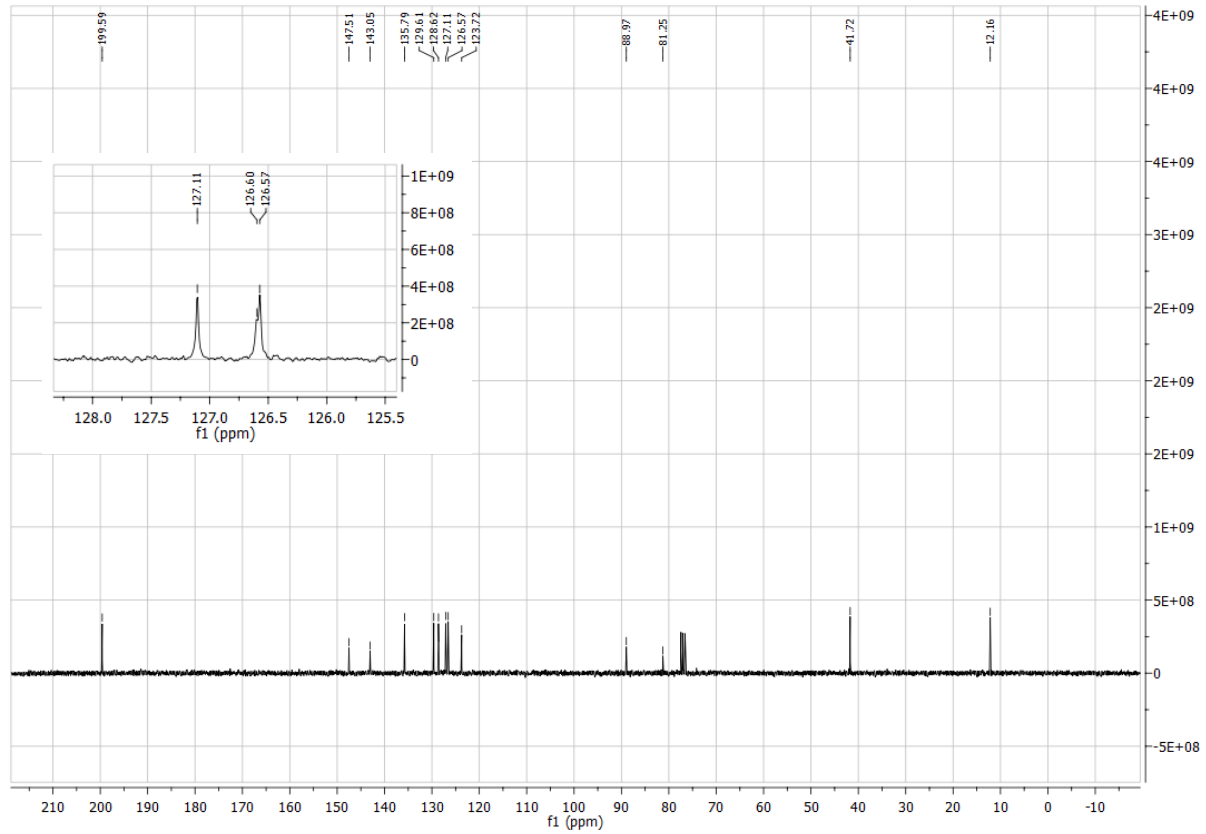
2.29
2.18
4.09
f1 (ppm)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127.11
126.57
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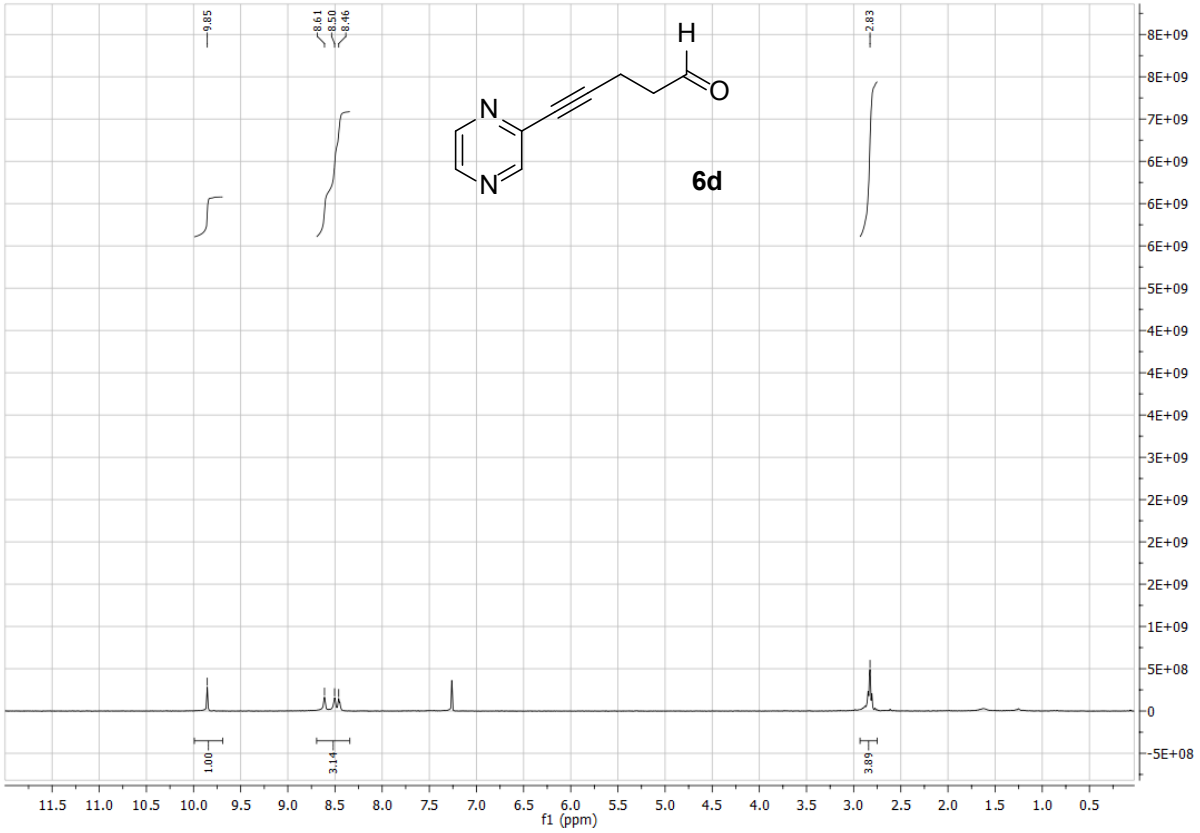
127.11
126.60
126.57
f1 (ppm)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2.83
H
O
N
N
6d
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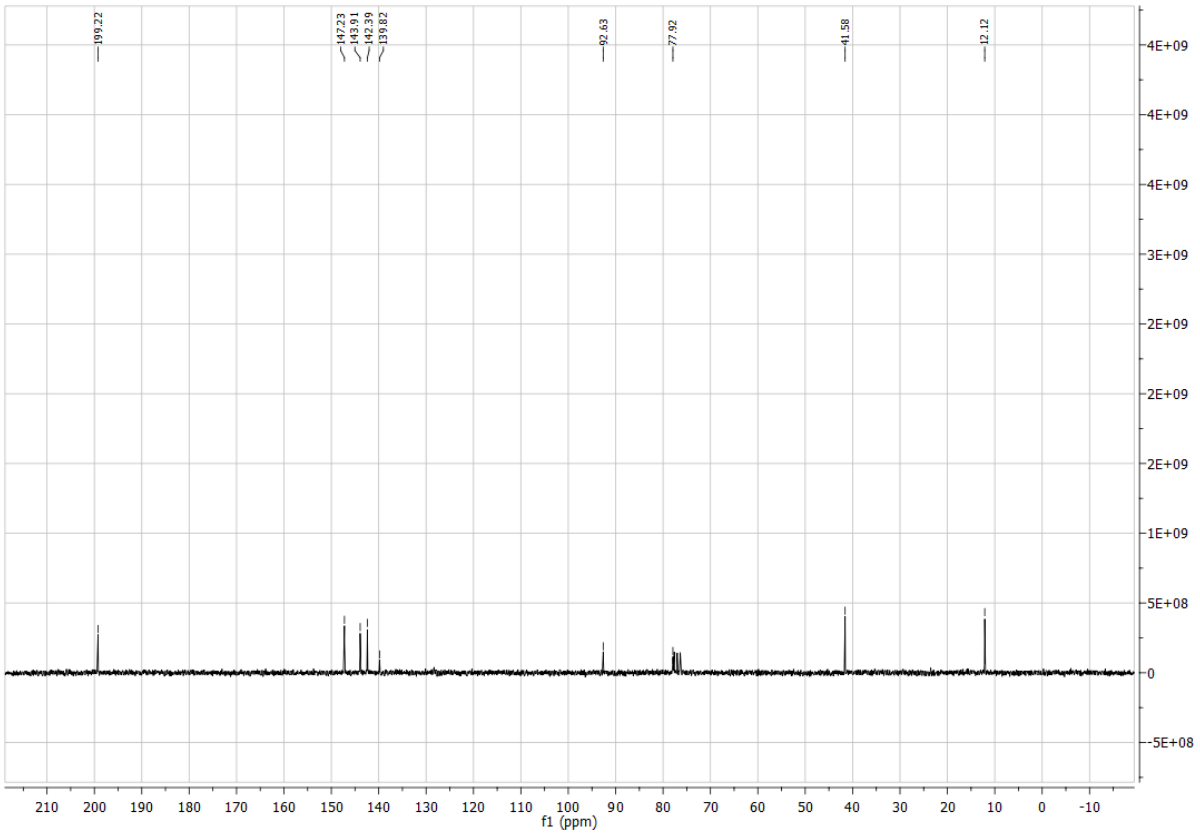
3.14
3.89
f1 (ppm)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147.23
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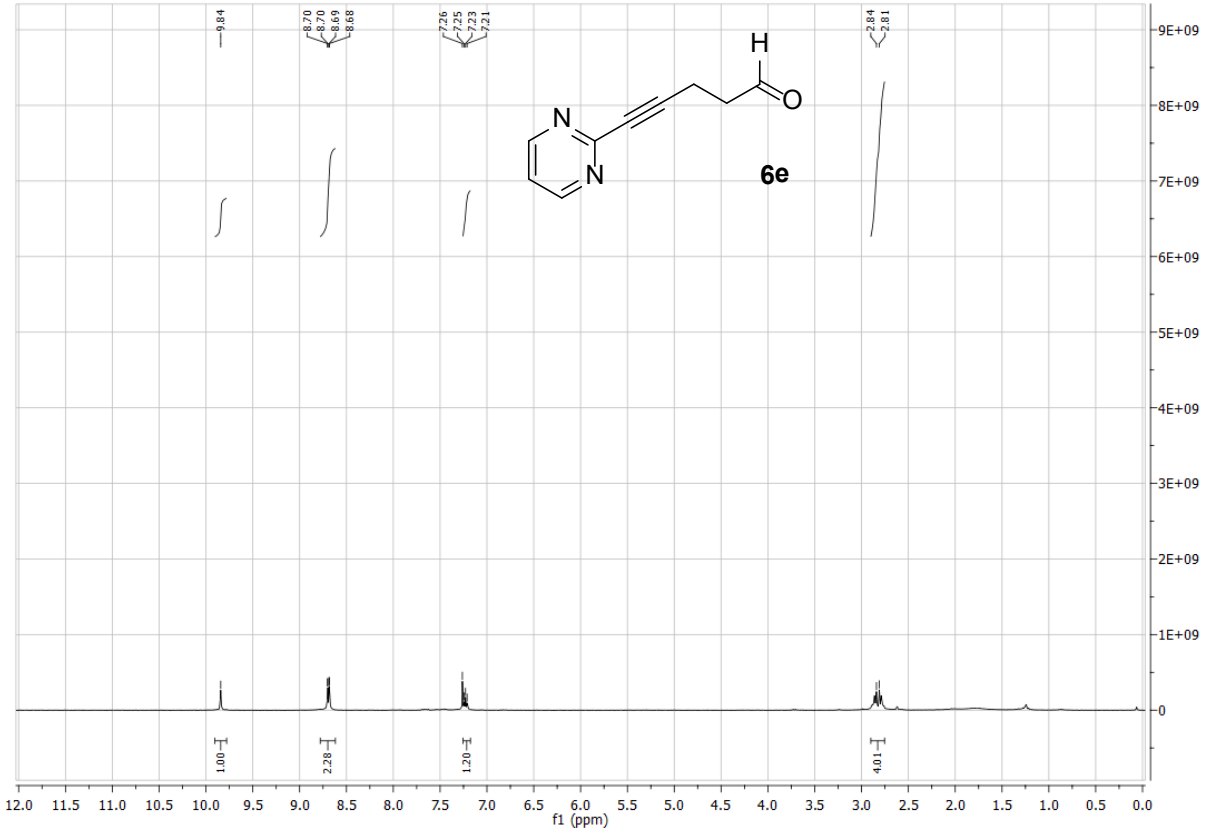
139.82
92.63
77.92
41.58
12.12
f1 (ppm)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8.70
8.69
8.68
7.26
7.25
7.23
7.21
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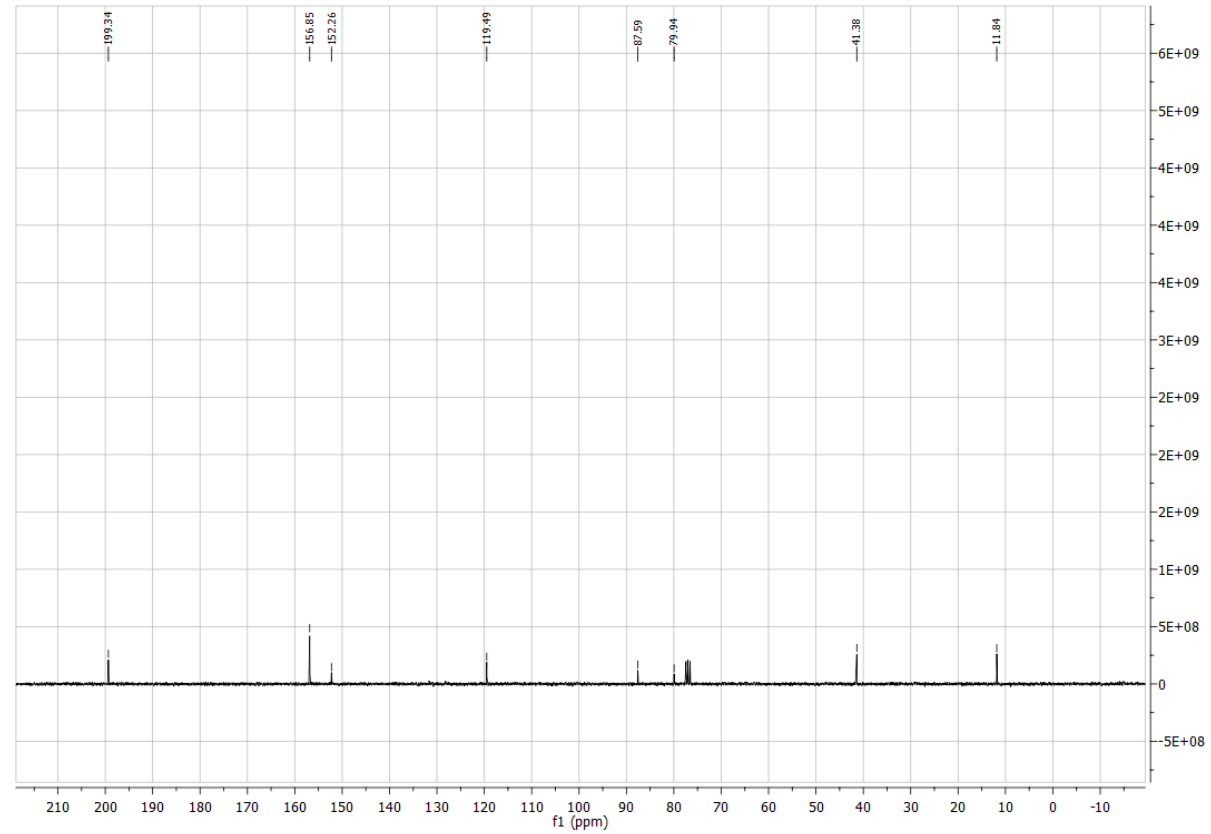
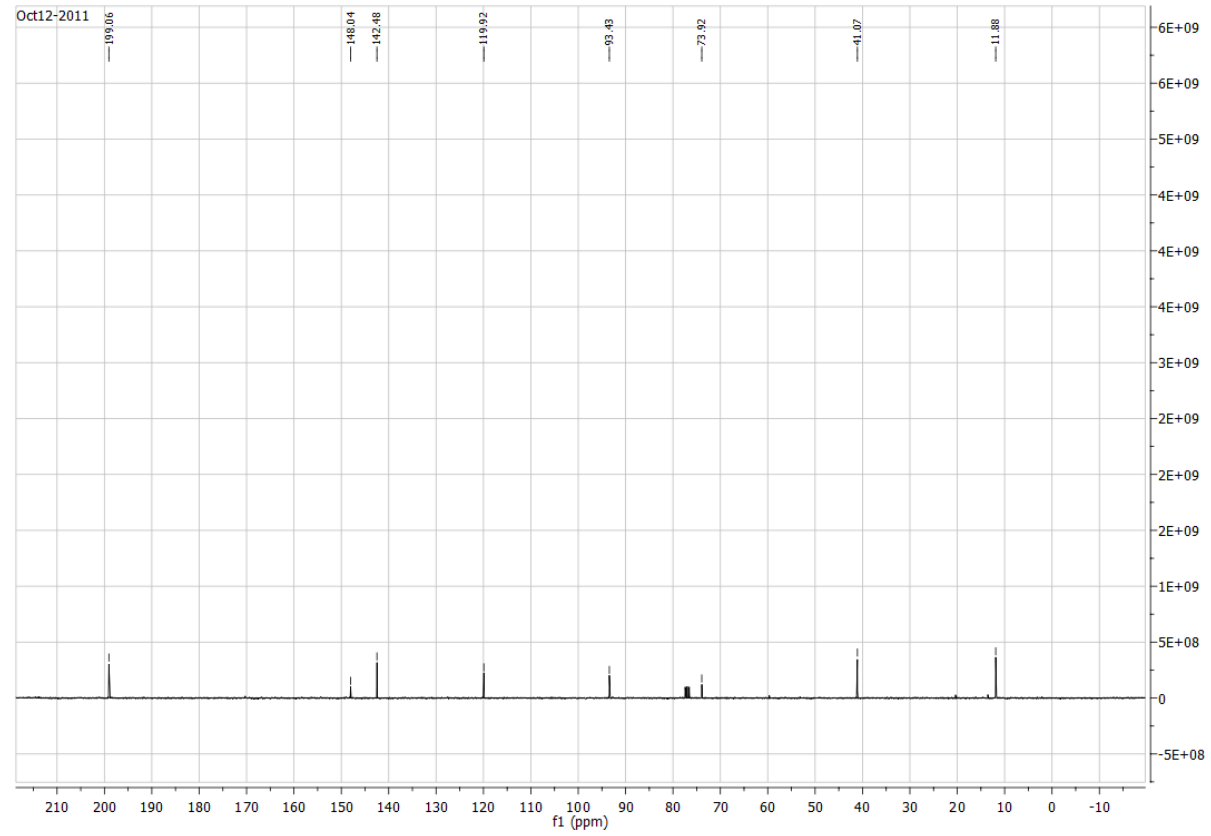
2.81
H
O
N
N
6e
1.00
2.28
1.20
4.01
f1 (ppm)


199.34
156.85
152.26
119.49
87.59
79.94
41.38
11.84
f1 (ppm)


9.84
7.77
7.76
7.30
7.29
7.26
2.84
2.82
2.80
2.79
H
O
N
S
6f
1.00
1.02
1.35
4.26
f1 (ppm)


Oct12-2011
199.06
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119.92
93.43
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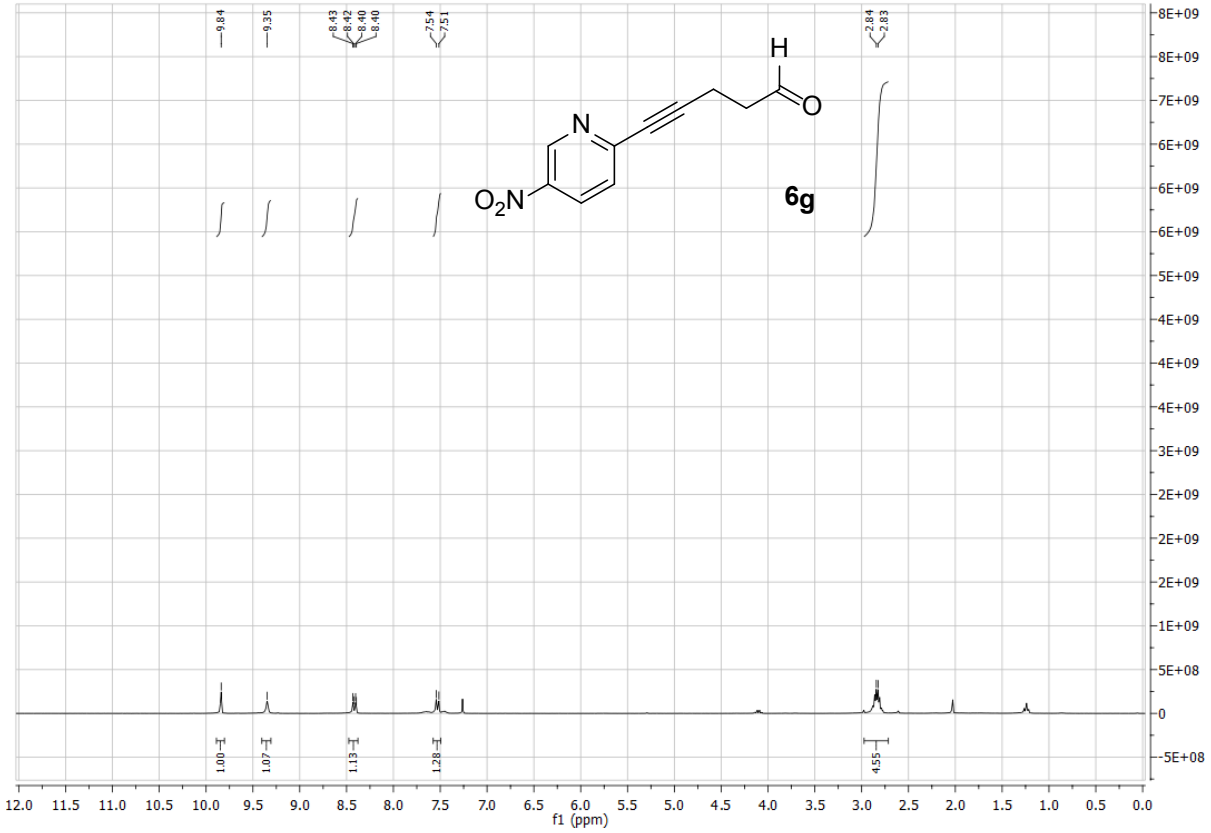
41.07
11.88
f1 (ppm)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8.40
8.40
7.54
7.51
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H
O
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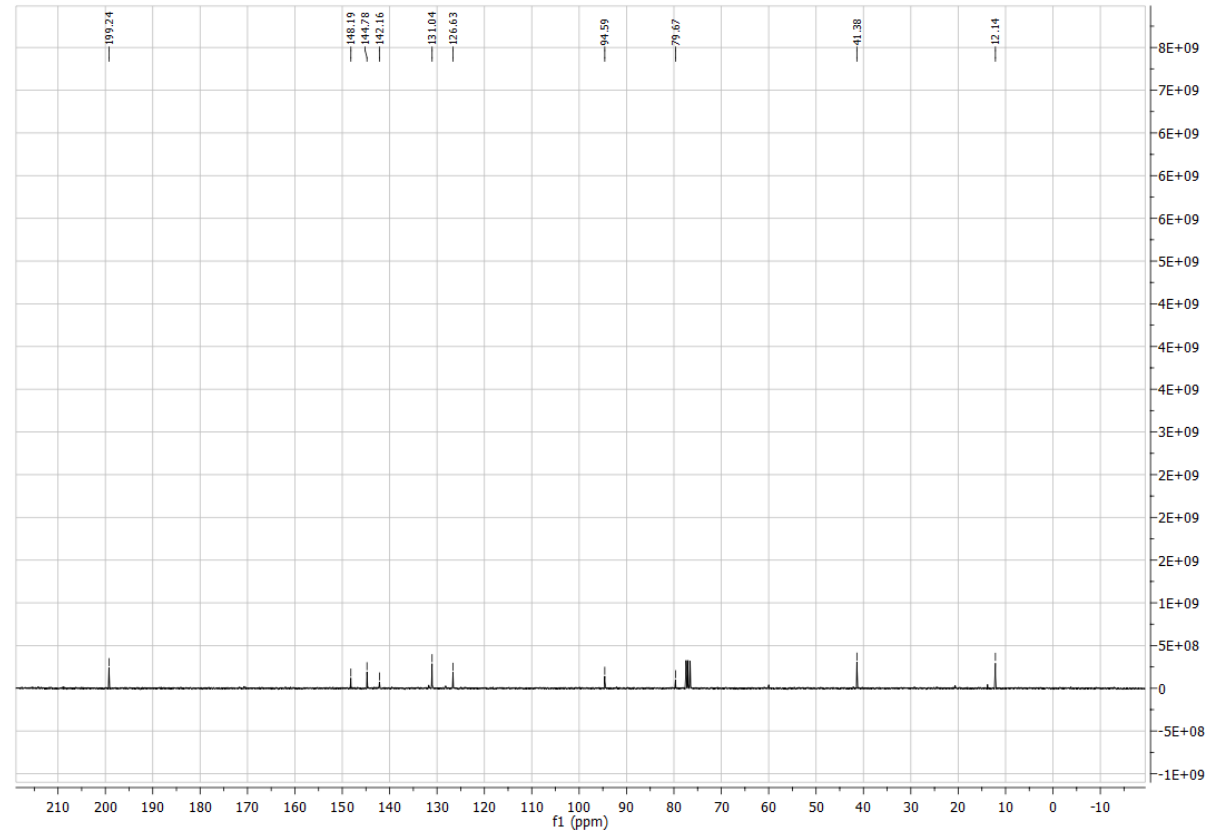
1.13
1.28
4.55
f1 (ppm)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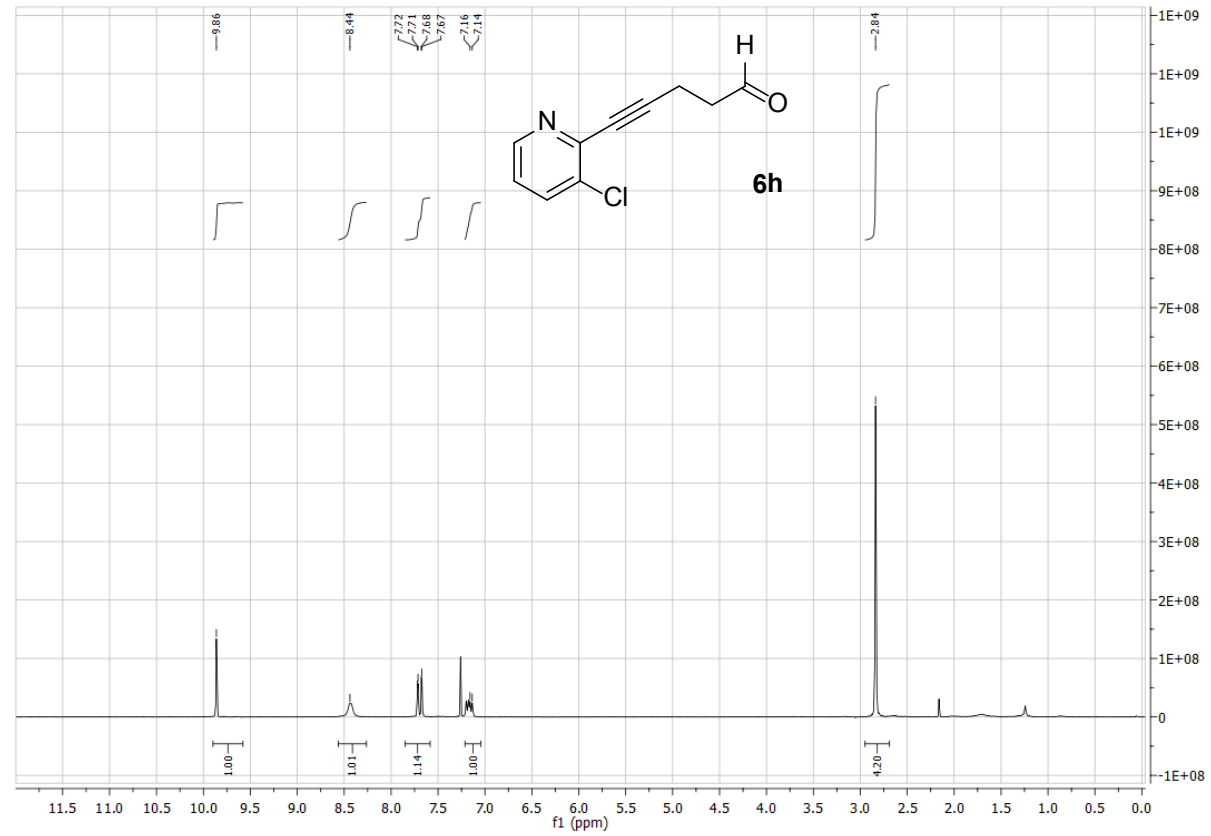
126.63
94.59
79.67
41.38
12.14
f1 (ppm)


9.86
8.44
7.72
7.71
7.68
7.67
7.16
7.14
2.84
H
O
N
Cl
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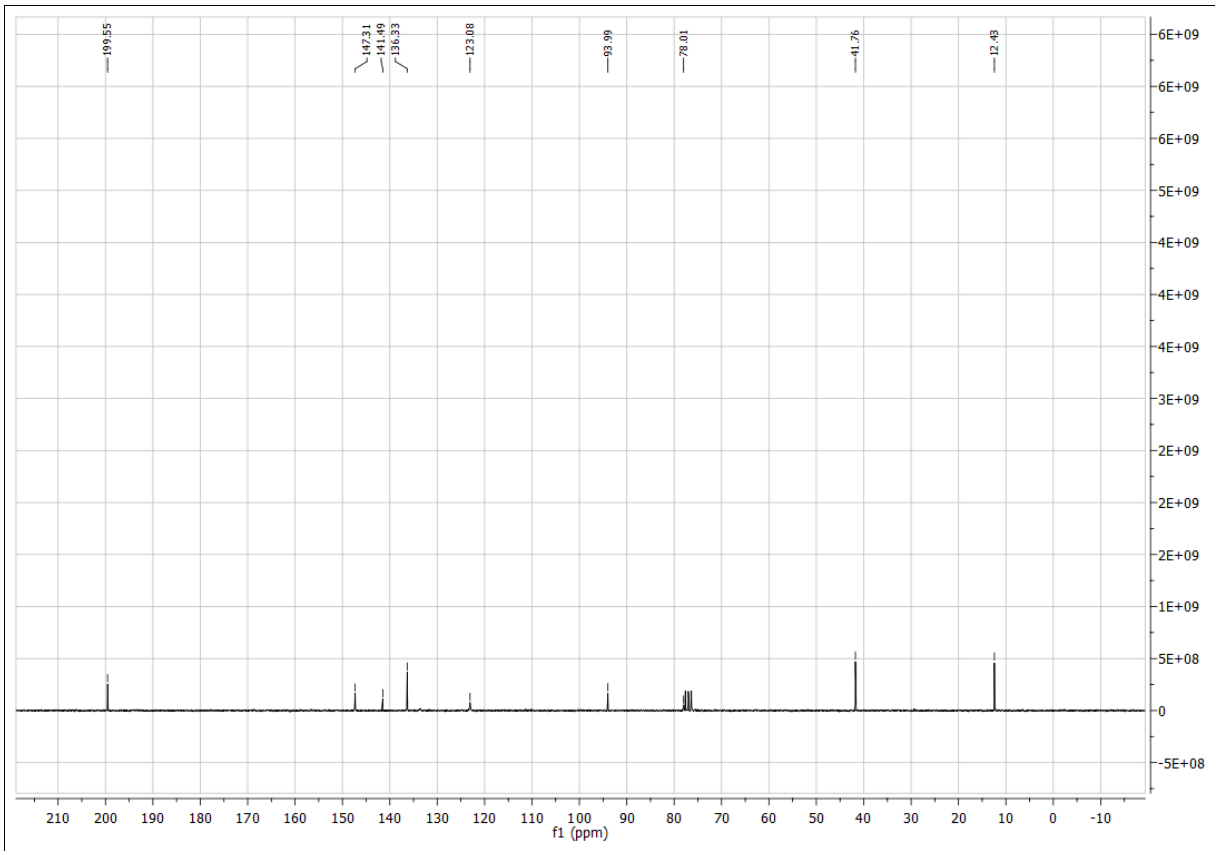
1.01
1.14
1.00
4.20
f1 (ppm)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12.48
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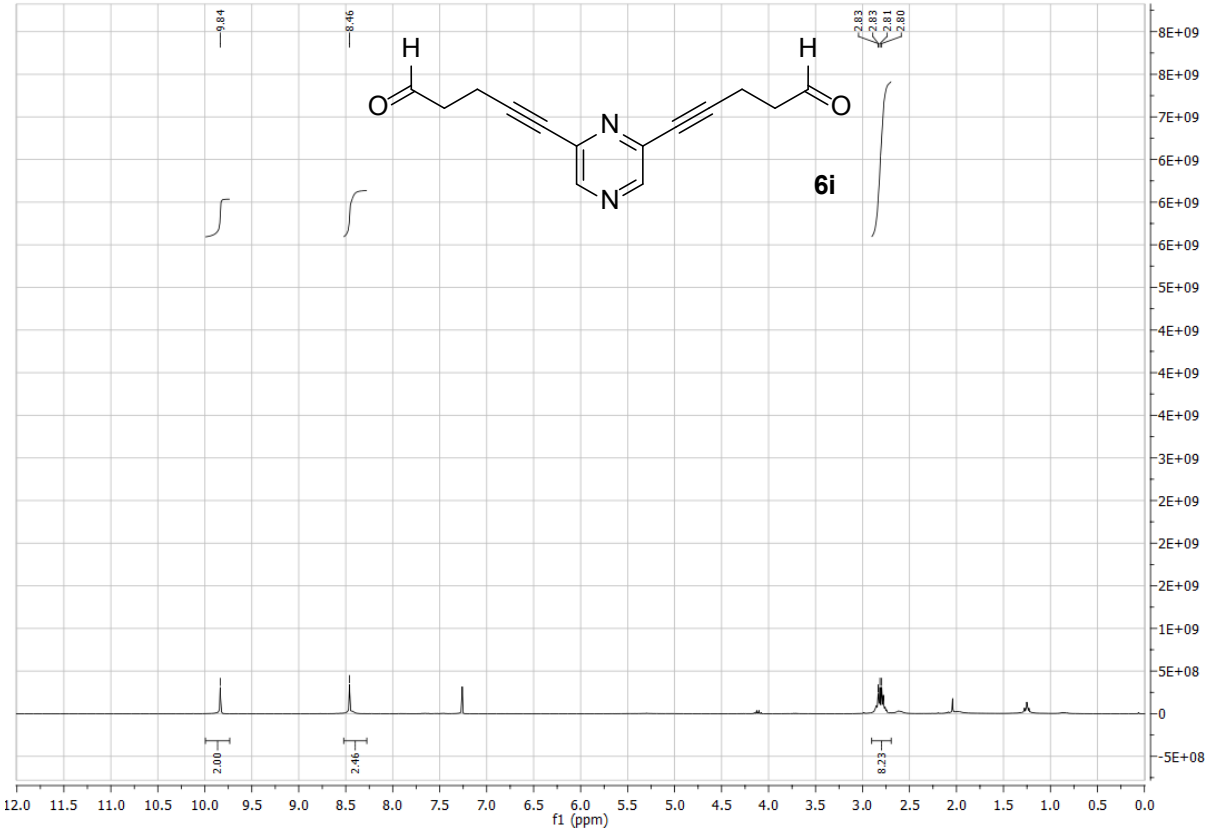
9.84
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2.83
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N
N
H
O
6i
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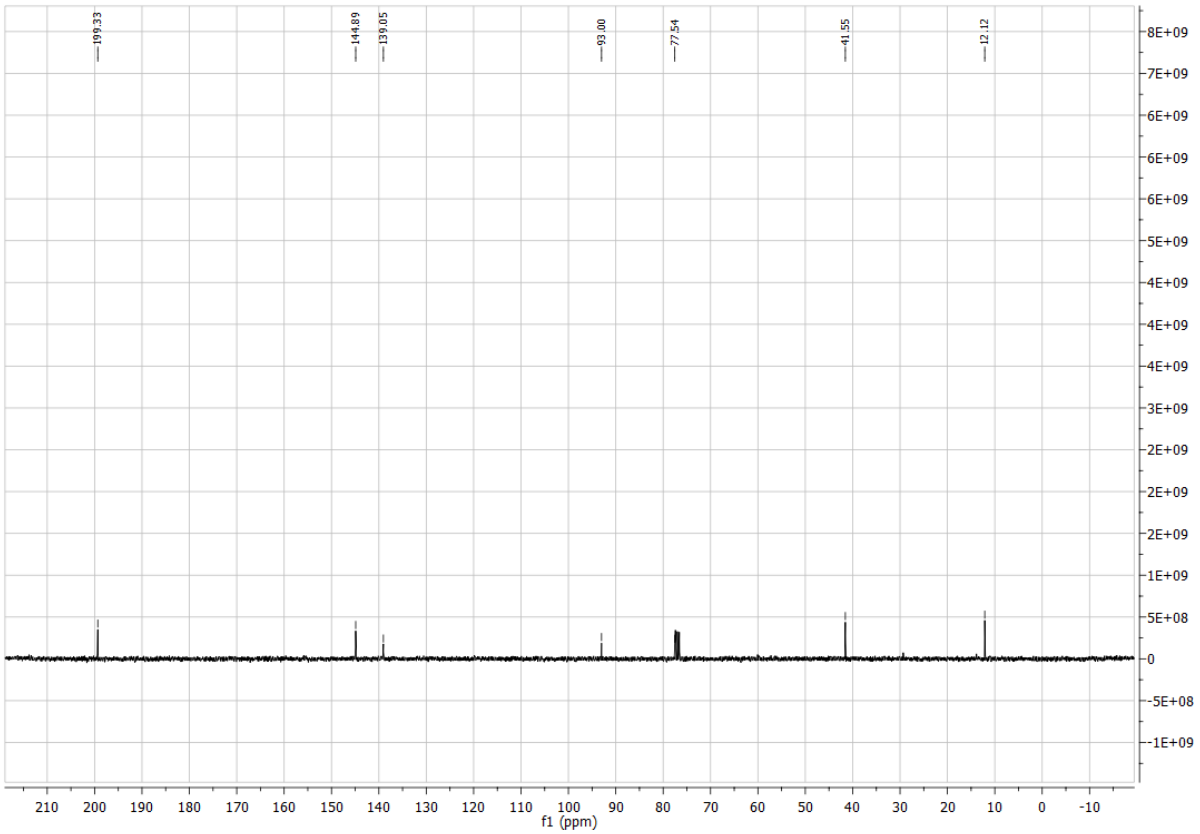
2.46
8.23
f1 (ppm)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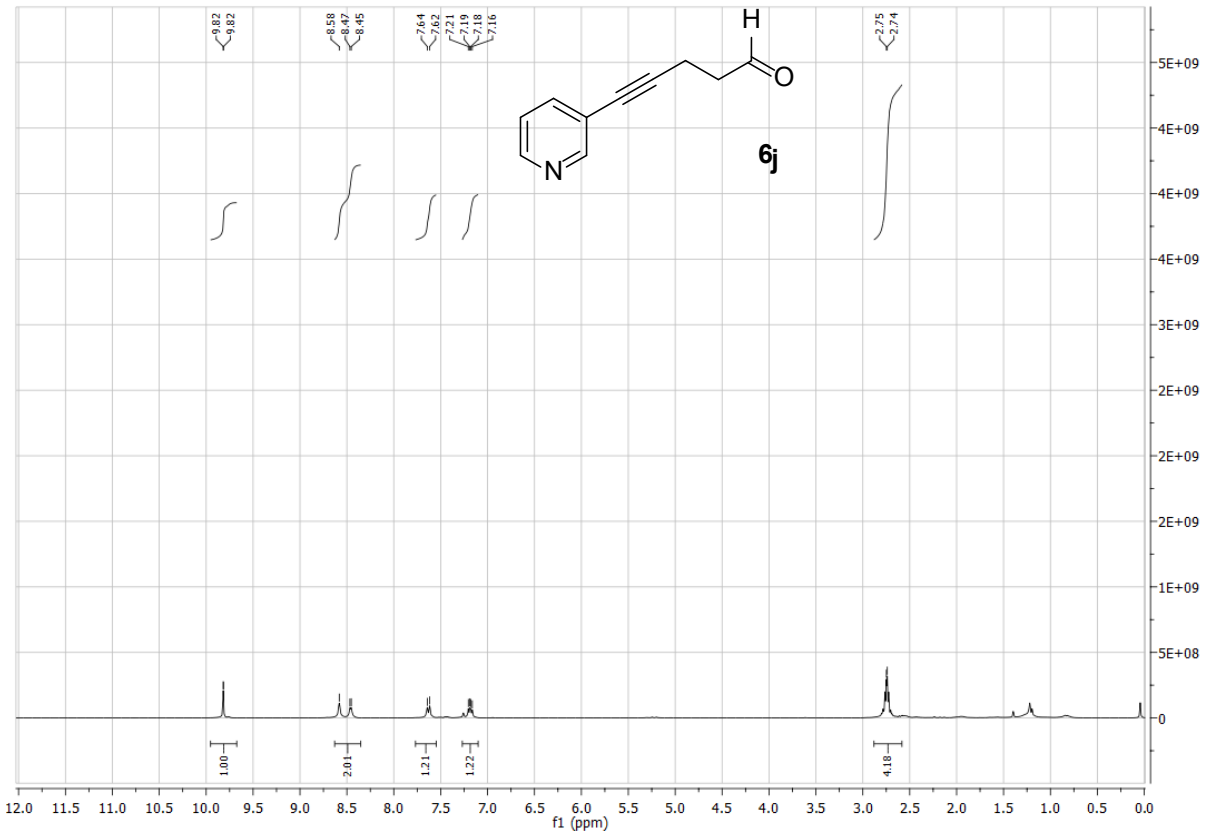
12.12
f1 (ppm)


9.82
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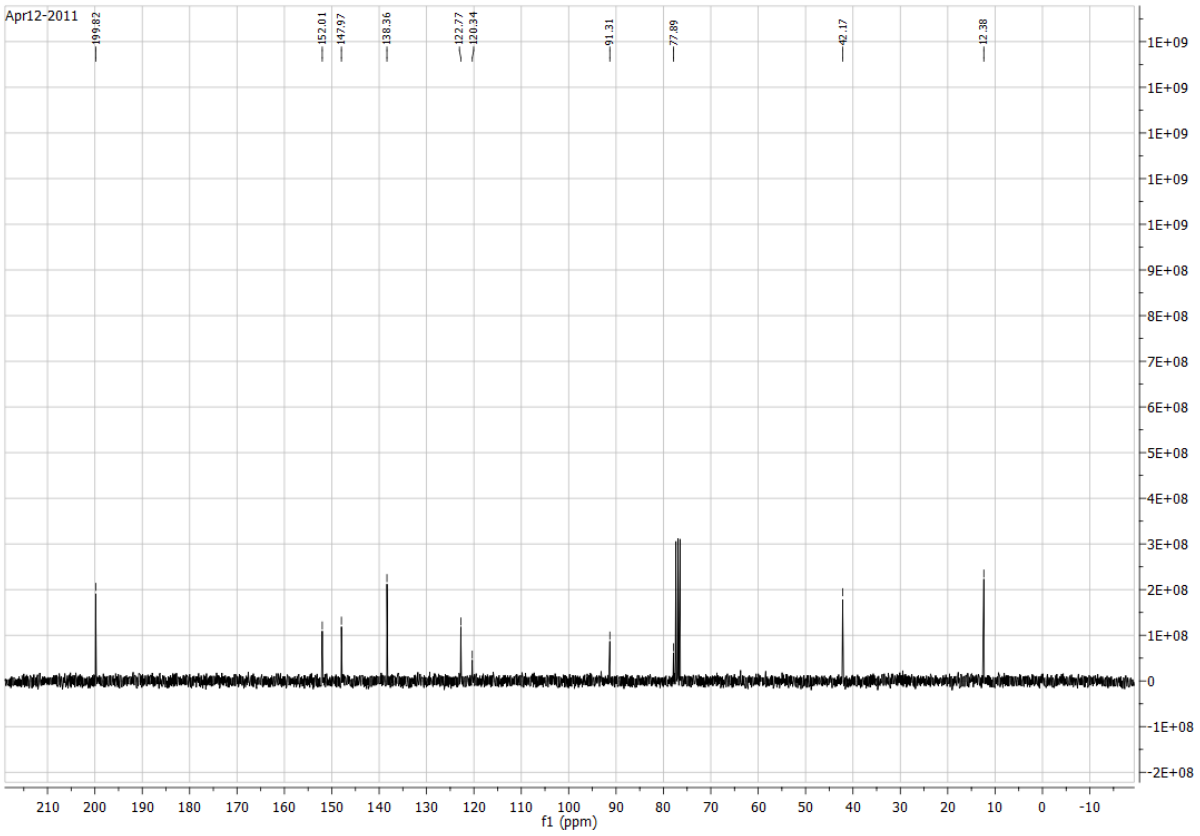
7.62
7.21
7.19
7.18
7.16
2.75
2.74
H
O
N
6j
1.00
2.01
1.21
1.22
4.18
f1 (ppm)


Apr12-2011
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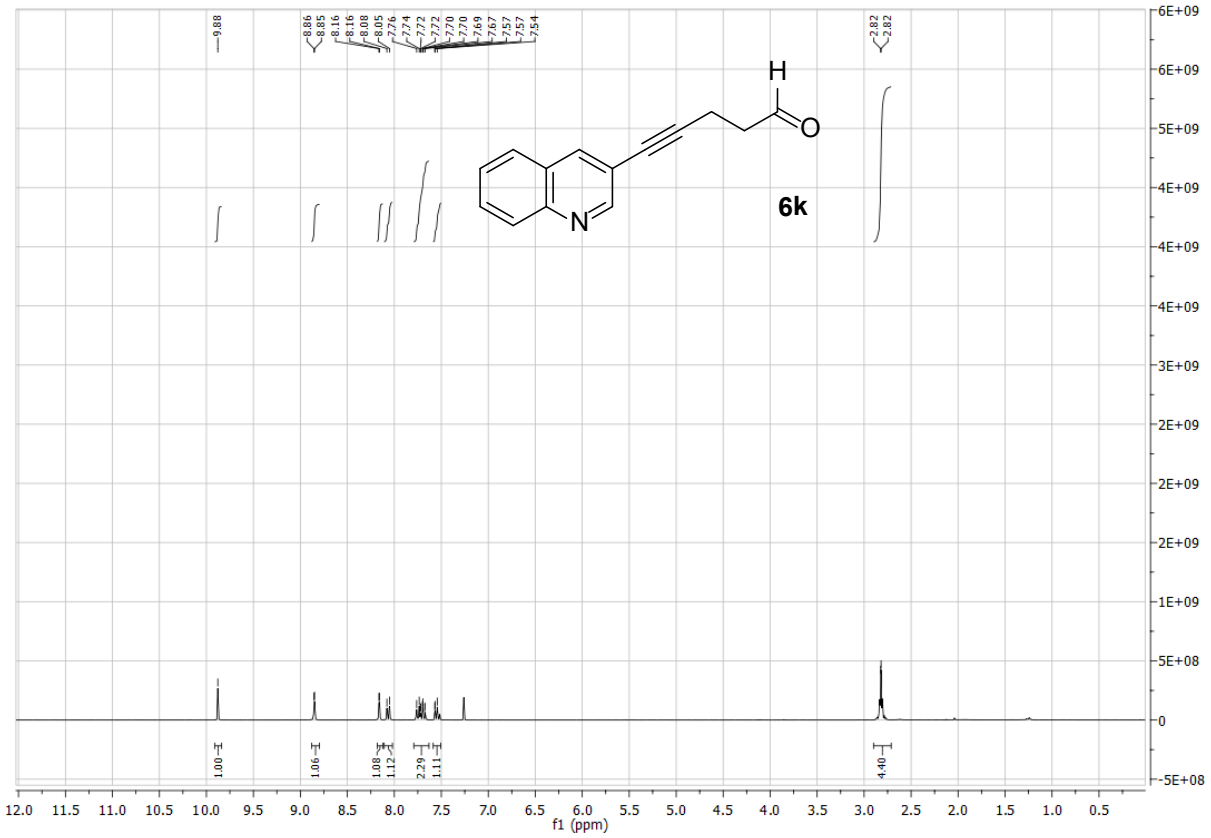
f1 (ppm)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7.72
7.70
7.69
7.67
7.57
7.57
7.54
2.82
2.82
H
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N
6k
1.00
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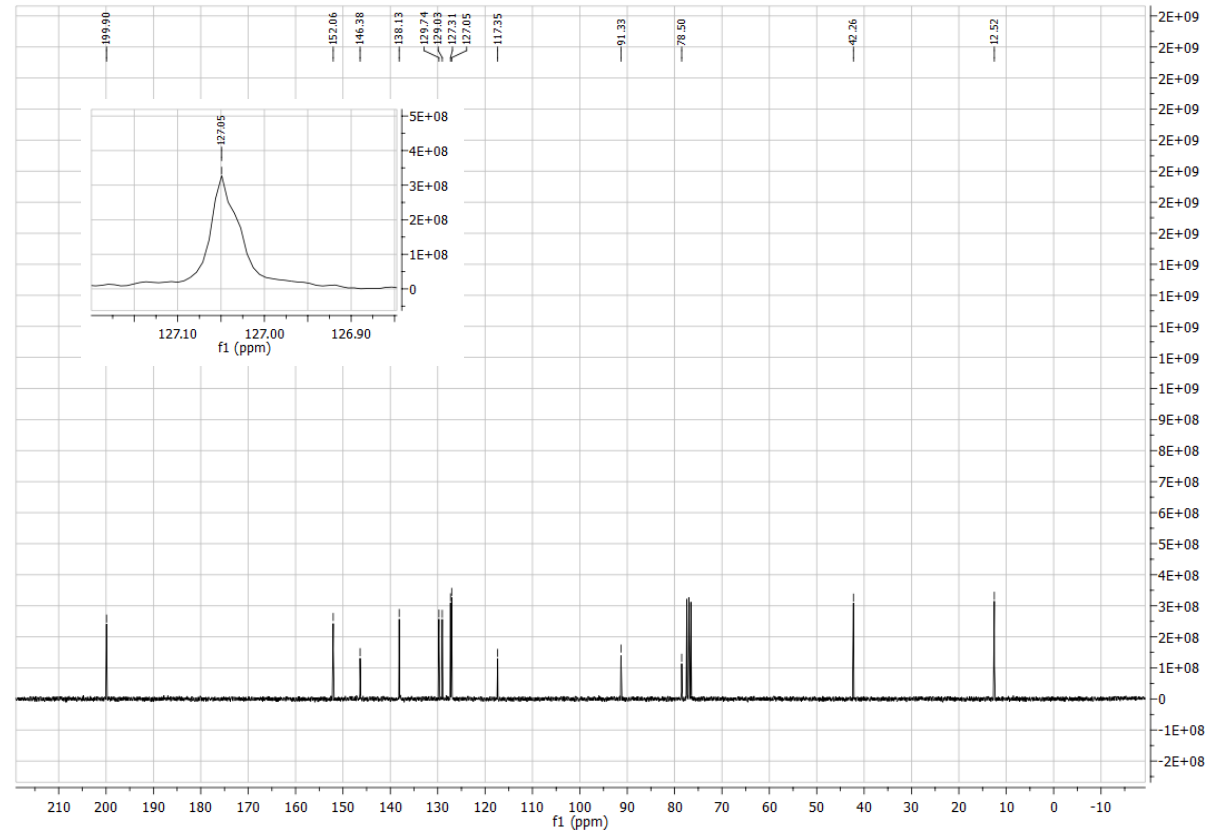
2.29
1.11
4.40
f1 (ppm)


199.90
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127.05
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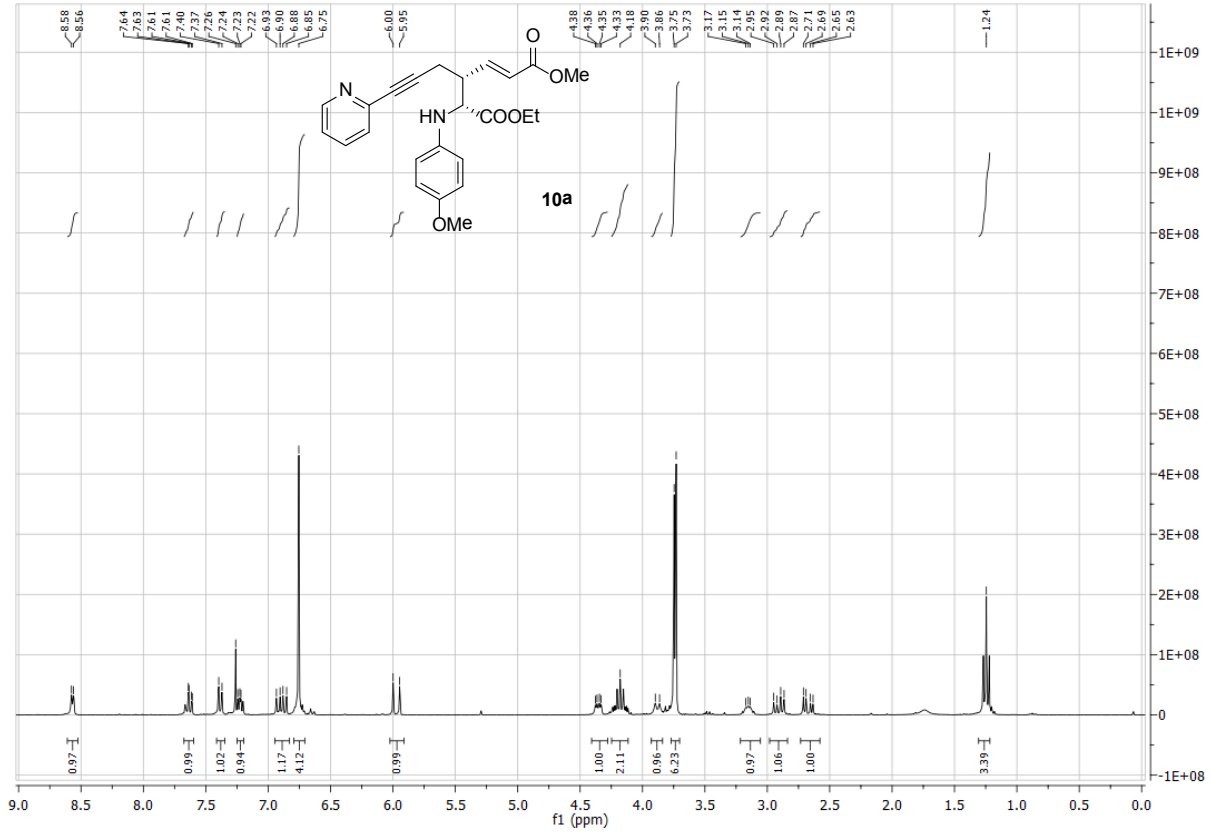
12.52
127.05
f1 (ppm)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7.24
7.23
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6.90
6.88
6.85
6.75
6.00
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4.38
4.36
4.35
4.33
4.18
3.90
3.86
3.75
3.73
3.17
3.15
3.14
2.95
2.92
2.89
2.87
2.71
2.69
2.65
2.63
1.24
O
OMe
N
HN
COOEt
OMe
10a
0.97
0.99
1.02
0.94
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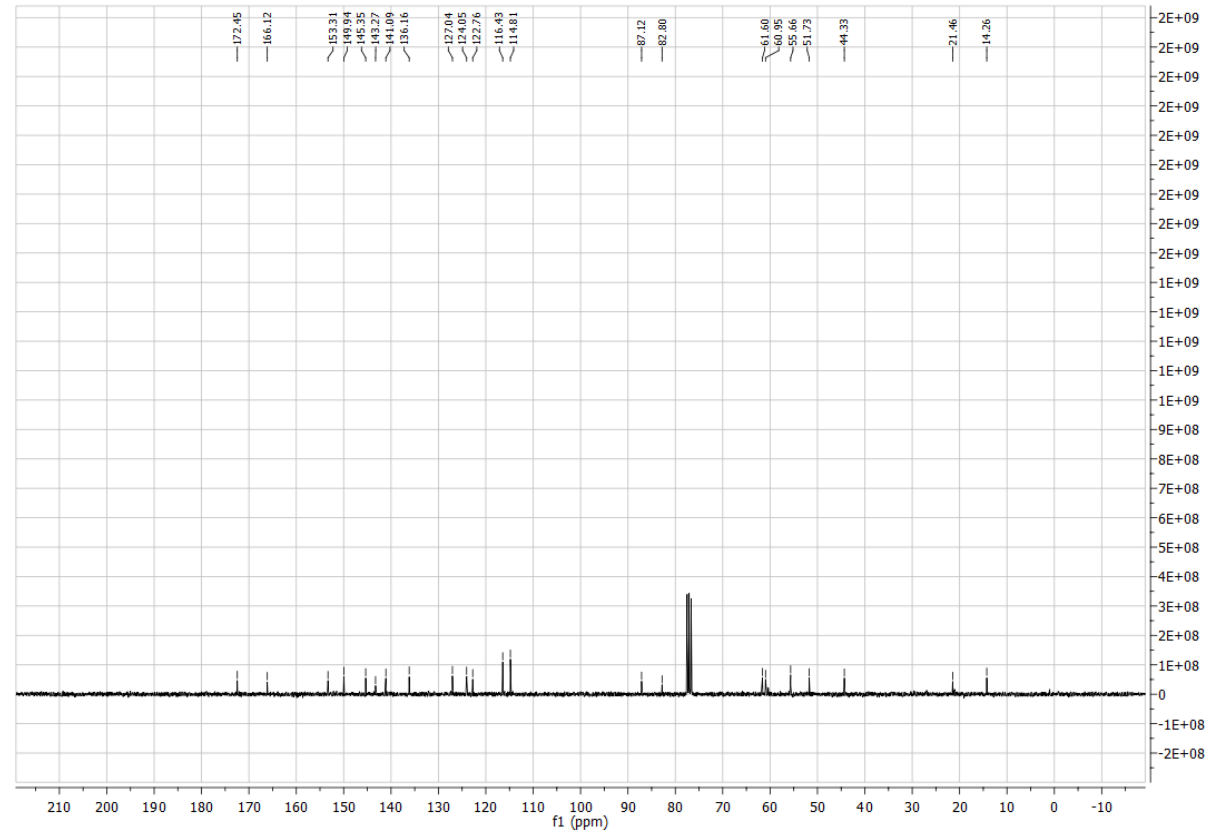
f1 (ppm)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141.09
136.16
127.04
124.05
122.76
116.43
114.81
87.12
82.80
61.60
60.95
55.66
51.73
44.33
21.46
14.26
f1 (ppm)

rac-10a

Instrument Method: IC 1mL80%nhep20%prop_20dC

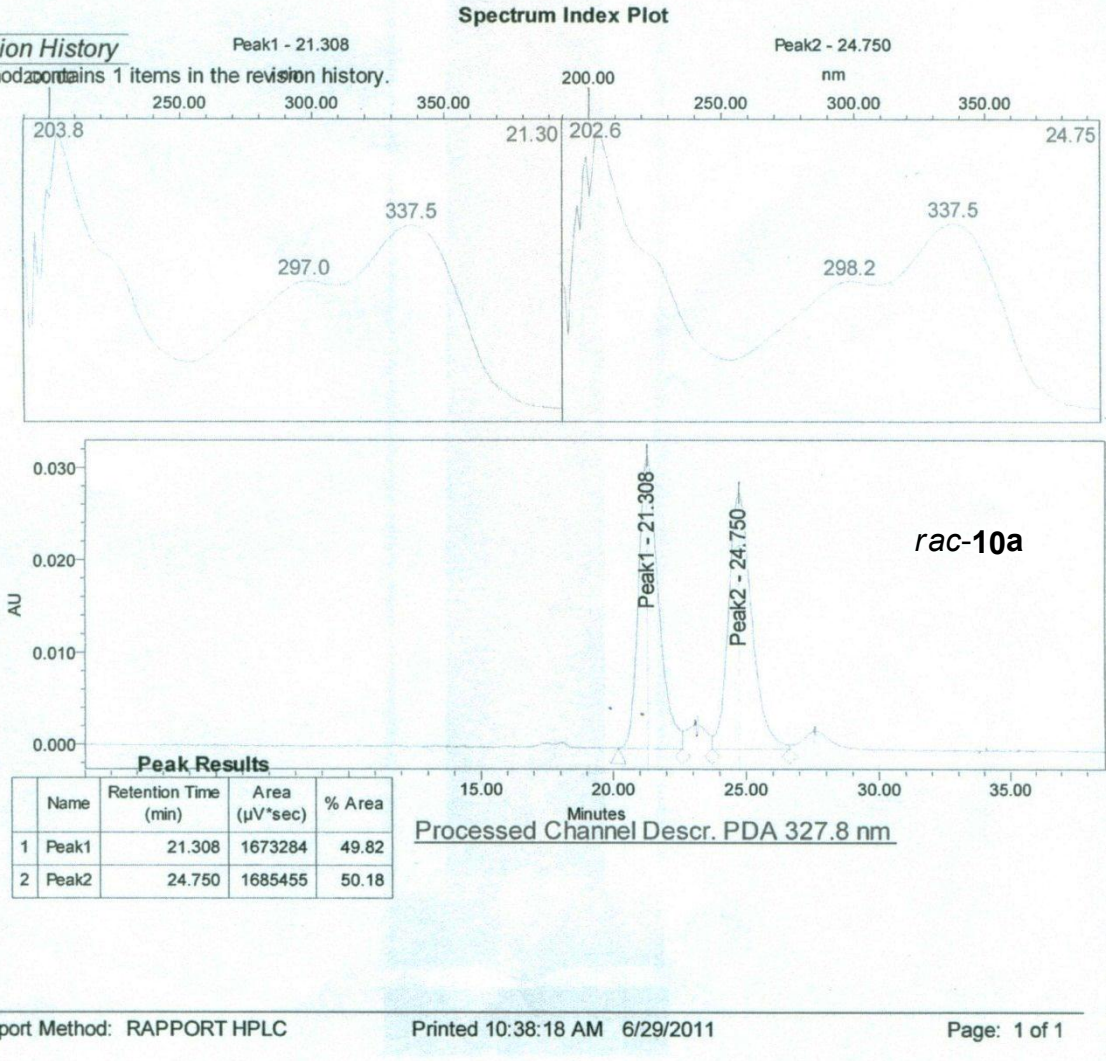
Stored: 1/11/2011 4:19:51 PM

Method Information

Comments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 80%n-heptane20%propanol-2 éch.+col.à 20°C
Modified User	System
Locked	No
Method Id	1095
Method Version	2
Edit User	

Revision History

This method contains 1 items in the revision history.



Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	21.308	1673284	49.82
2	Peak2	24.750	1685455	50.18

Report Method: RAPPORT HPLC Printed 10:38:18 AM 6/29/2011 Page: 1 of 1

Instrument Method: IC 1mL80%nhep20%prop_20dC

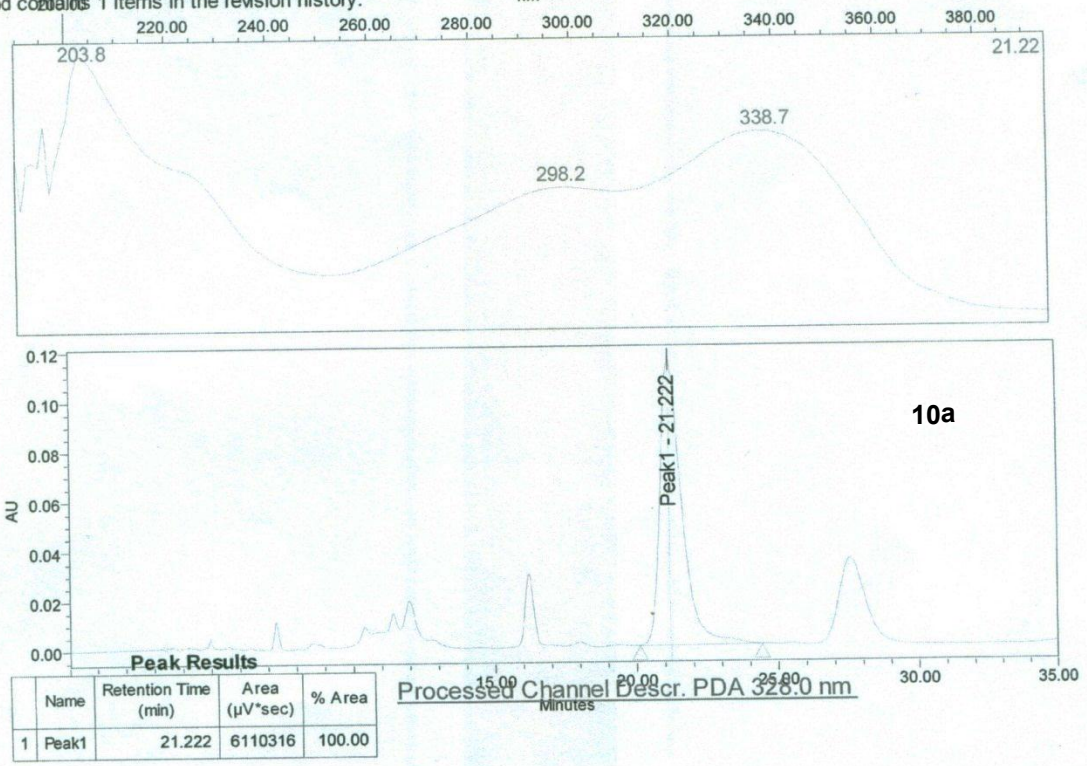
Stored: 1/11/2011 4:19:51 PM

Method Information

Comments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 80%n-heptane20%propanol-2 éch.+col.à 20°C
Modified User	System
Locked	No
Method Id	1095
Method Version	2
Edit User	

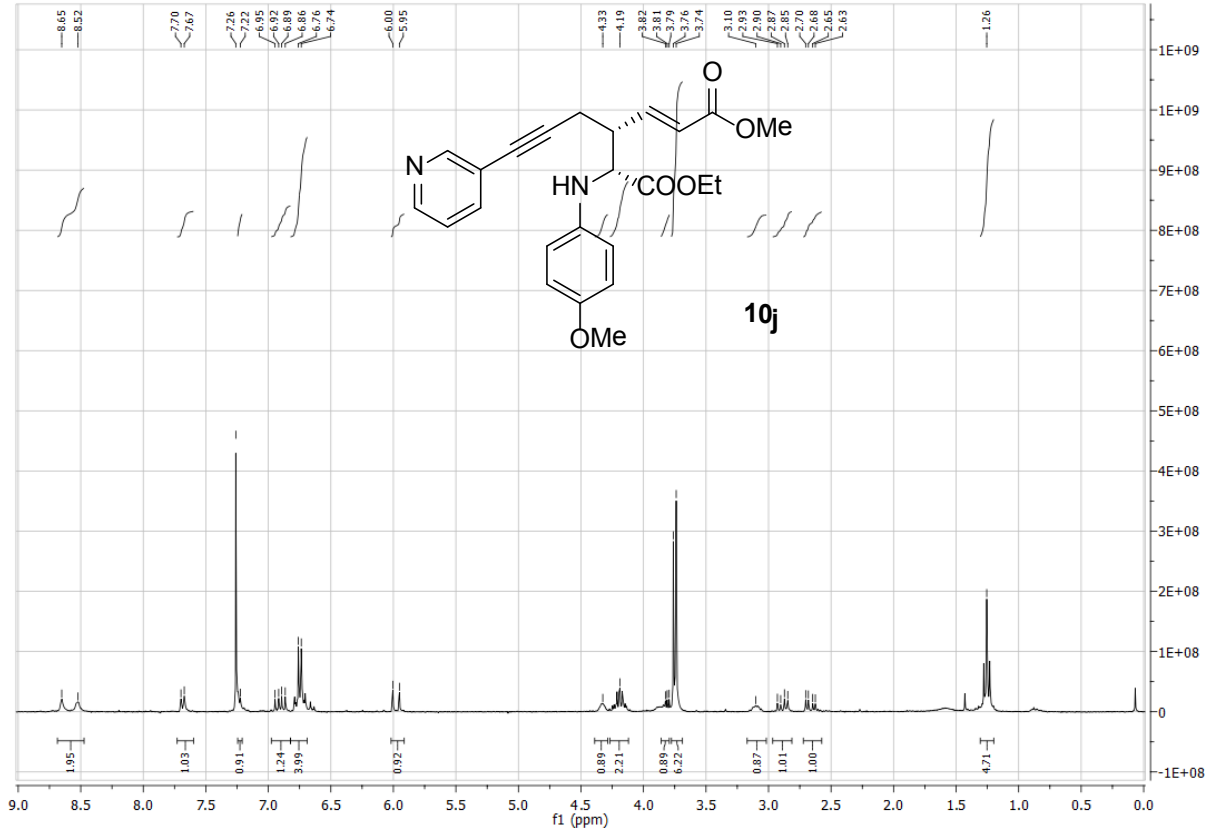
Revision History

This method contains 1 items in the revision history.



Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	21.222	6110316	100.00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7.22
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6.92
6.89
6.86
6.76
6.74
6.00
5.95
4.33
4.19
3.82
3.81
3.79
3.76
3.74
3.10
2.93
2.90
2.87
2.85
2.70
2.68
2.65
2.63
1.26
O
OMe
N
HN
COOEt
OMe
10j
1.95
1.03
0.91
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3.99
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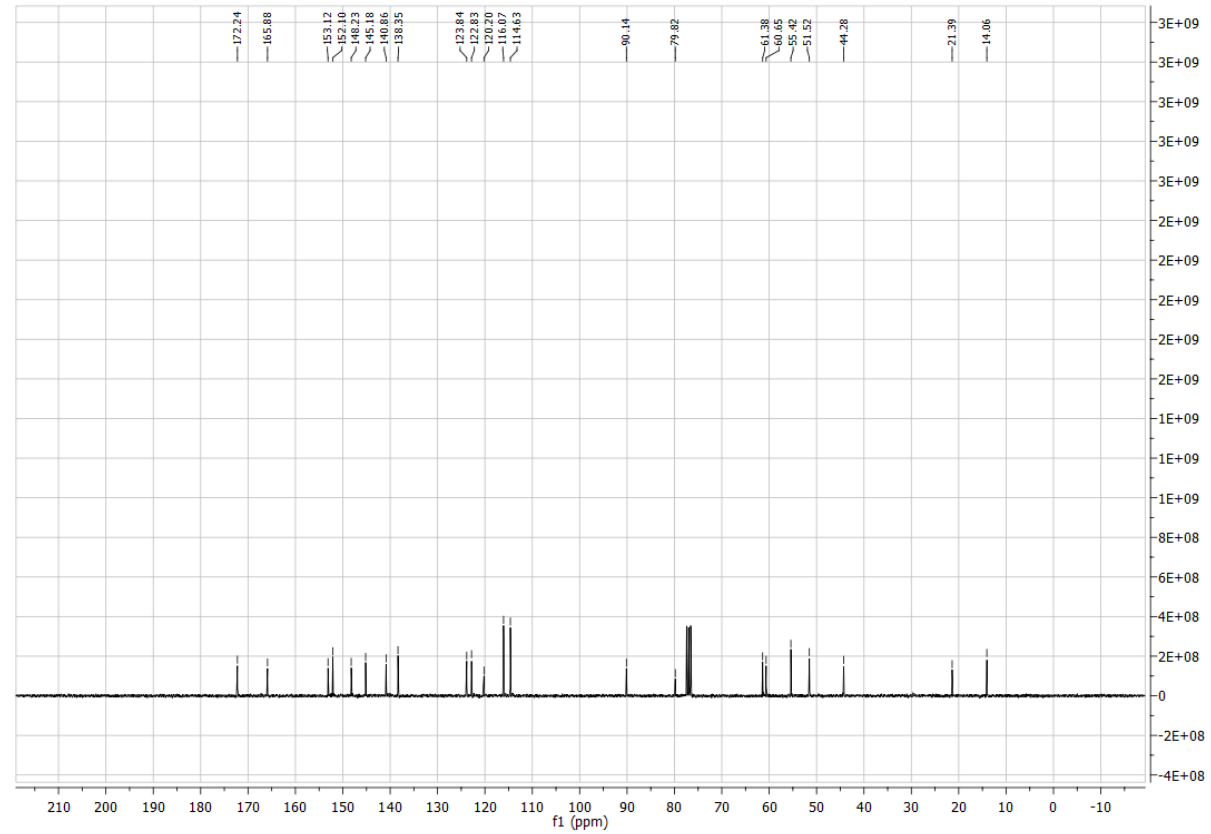
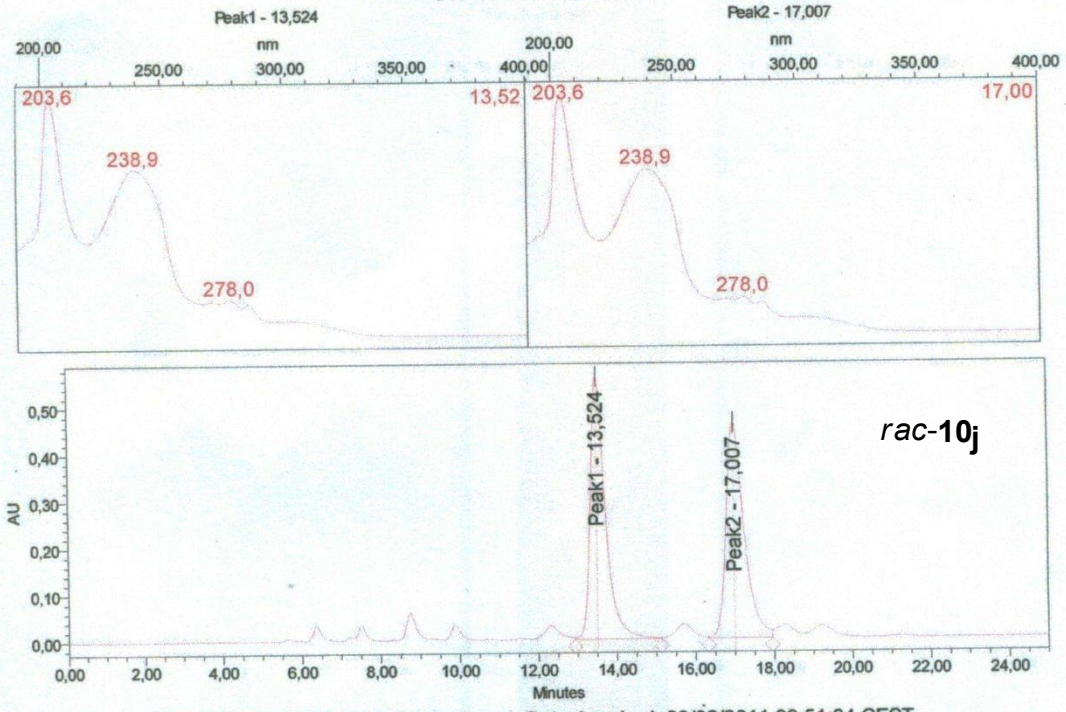
0.89
2.21
0.89
6.22
0.87
1.01
1.00
4.71
f1 (ppm)


172.24
165.88
153.12
152.10
148.23
145.18
140.86
138.35
123.84
122.83
120.20
116.07
114.63
90.14
79.82
61.38
60.65
55.42
51.52
44.28
21.39
14.06
f1 (ppm)

SAMPLE INFORMATION

Sample Name:	AJ185	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	43
Vial:	1	Acq. Method Set:	PM IA 1ml 8020 hept_Prop2 20dc
Injection #:	1	Processing Method:	p
Injection Volume:	10,00 ul	Channel Name:	239,0nm
Run Time:	145,0 Minutes	Proc. Chnl. Descr.:	PDA 239,0 nm
Date Acquired:	09/06/2011 09:51:04 CEST		
Date Processed:	09/06/2011 14:11:51 CEST		

Spectrum Index Plot



rac-**10j**

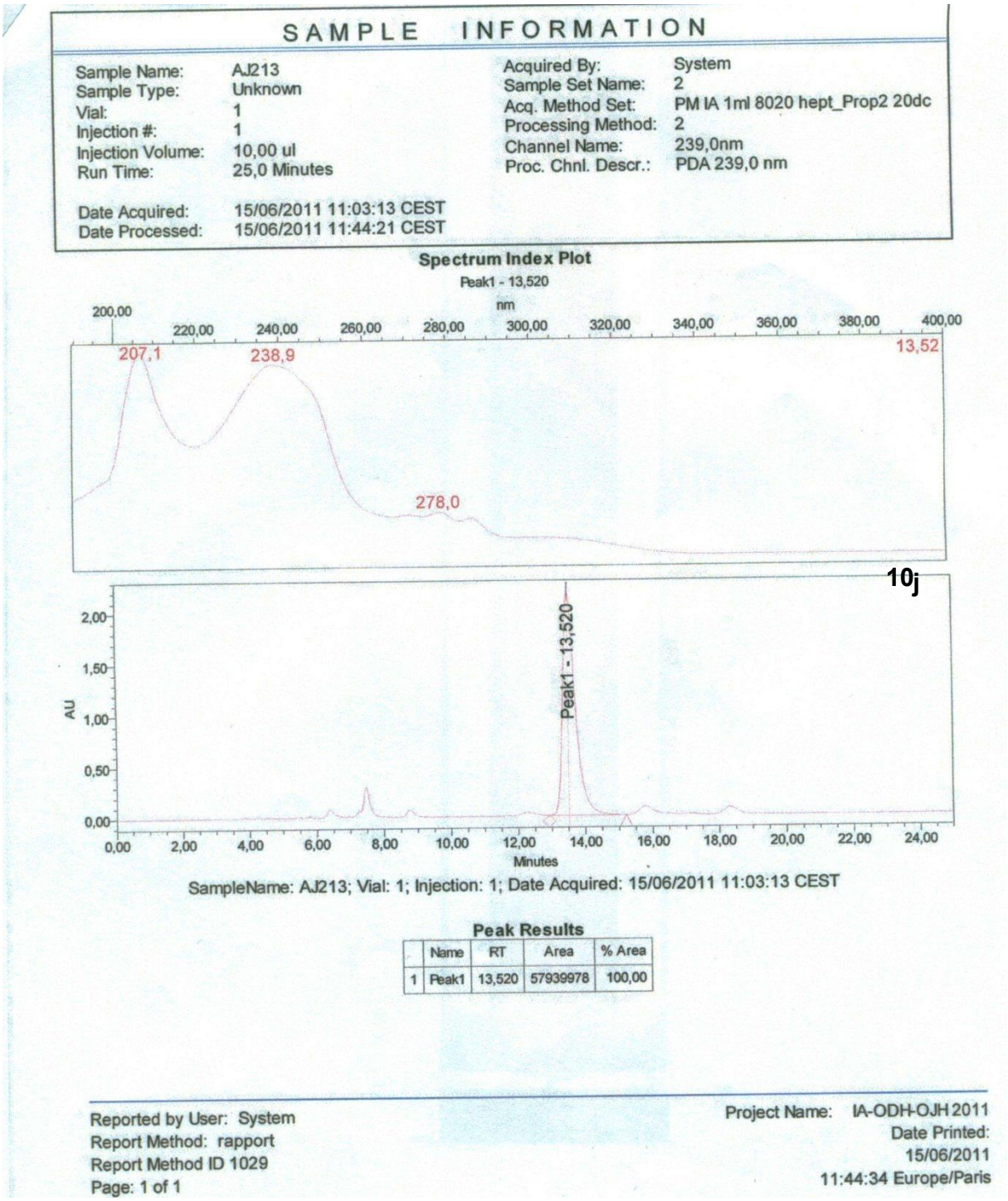
SampleName: AJ185; Vial: 1; Injection: 1; Date Acquired: 09/06/2011 09:51:04 CEST

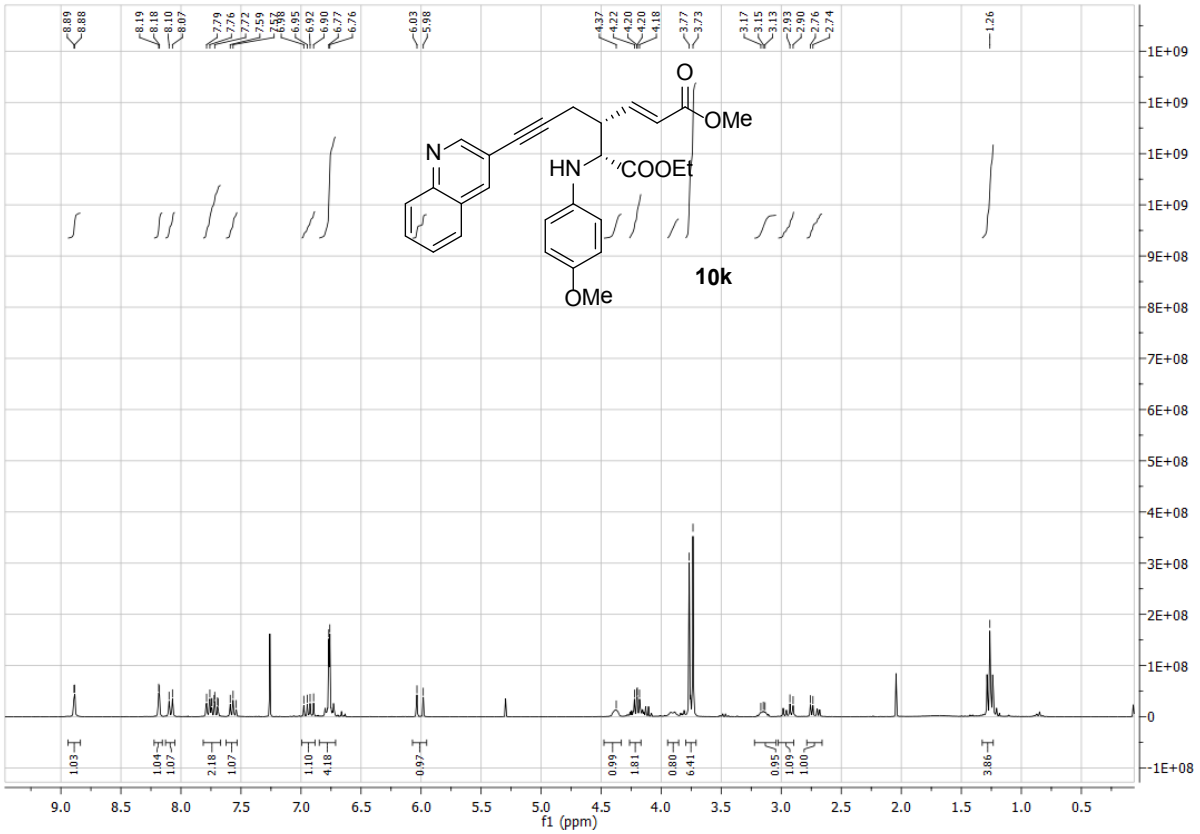
Peak Results

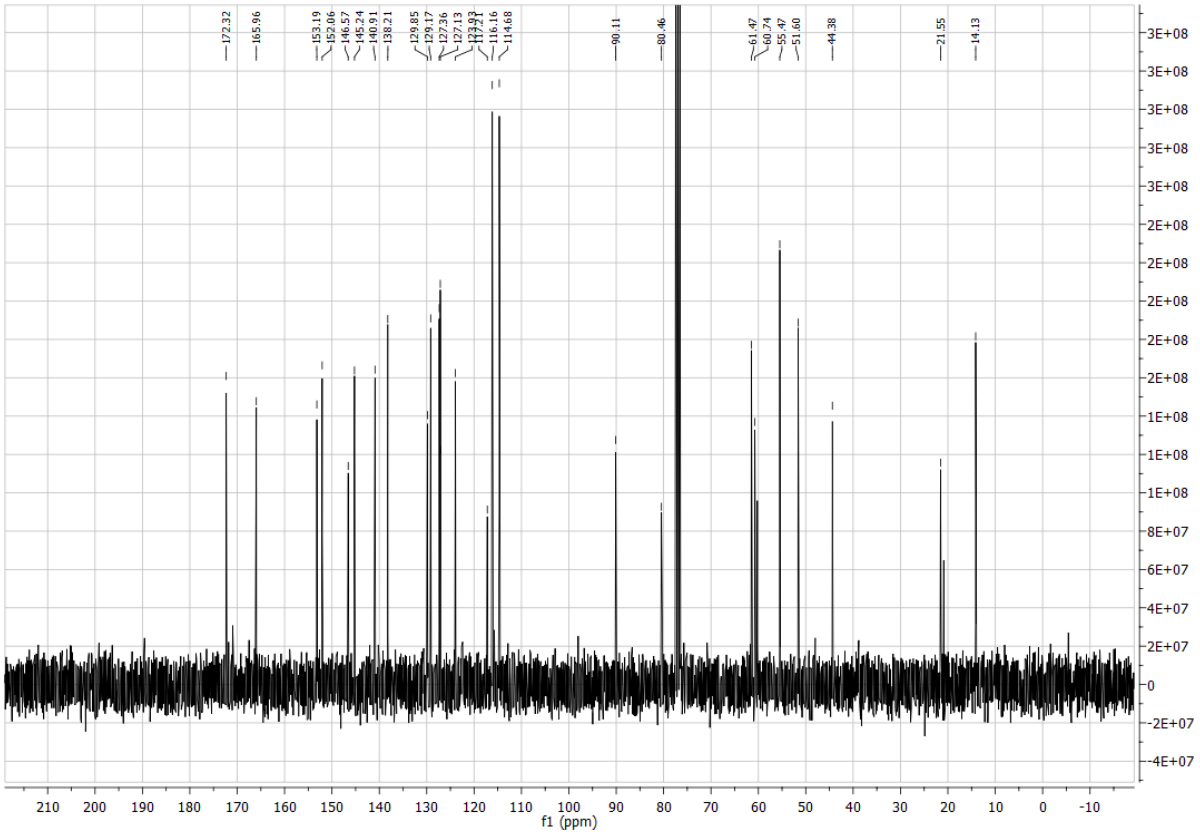
	Name	RT	Area	% Area
1	Peak1	13,524	15065558	50,54
2	Peak2	17,007	14742452	49,46

Reported by User: System
Report Method: rapport
Report Method ID 1029
Page: 1 of 1

Project Name: IA-ODH-OJH 2011
Date Printed:
09/06/2011
14:12:13 Europe/Paris

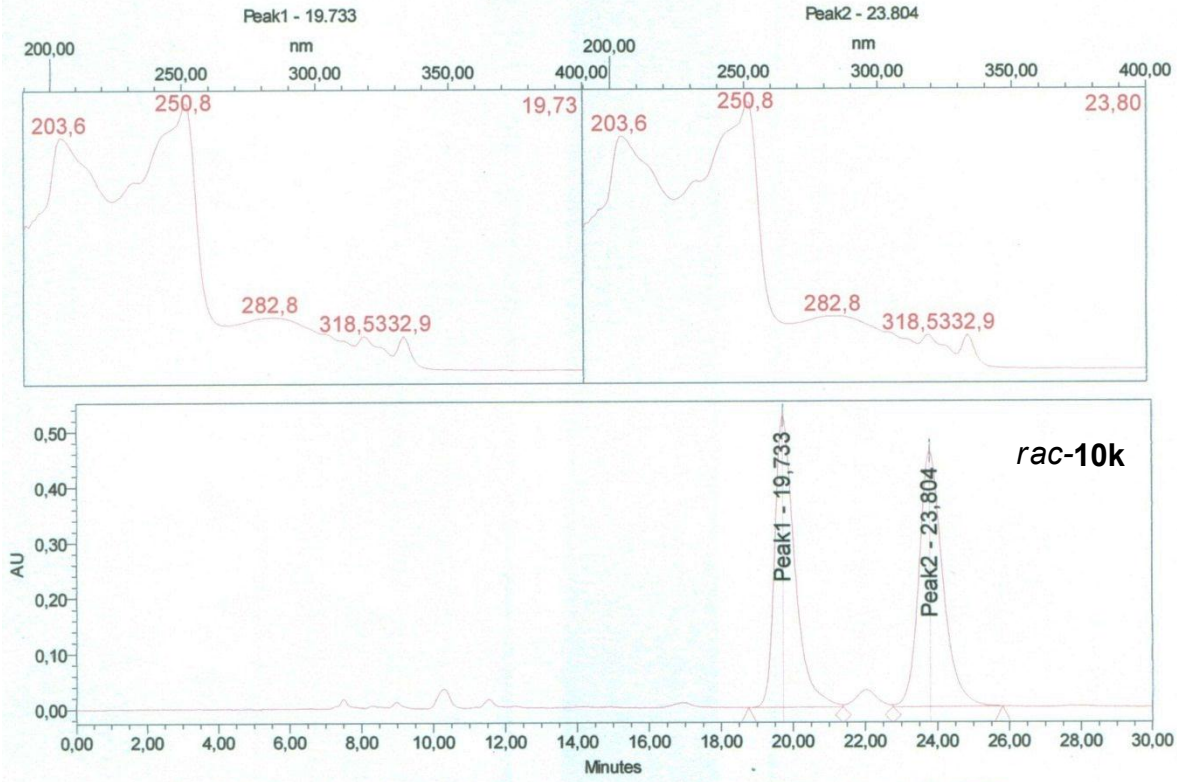

SAMPLE INFORMATION
Sample Name: AJ213
Sample Type: Unknown
Vial: 1
Injection #: 1
Injection Volume: 10,00 ul
Run Time: 25,0 Minutes
Date Acquired: 15/06/2011 11:03:13 CEST
Date Processed: 15/06/2011 11:44:21 CEST
Acquired By: System
Sample Set Name: 2
Acq. Method Set: PM IA 1ml 8020 hept_Prop2 20dc
Processing Method: 2
Channel Name: 239,0nm
Proc. Chnl. Descr.: PDA 239,0 nm
Spectrum Index Plot
Peak1 - 13,520
nm
207,1
238,9
278,0
13,52
10j
Peak1 - 13,520
AU
Minutes
SampleName: AJ213; Vial: 1; Injection: 1; Date Acquired: 15/06/2011 11:03:13 CEST
Peak Results
Name RT Area % Area
1 Peak1 13,520 57939978 100,00
Reported by User: System
Report Method: rapport
Report Method ID 1029
Page: 1 of 1
Project Name: IA-ODH-OJH 2011
Date Printed: 15/06/2011
11:44:34 Europe/Paris


O
OMe
N
HN
COOEt
OMe
10k
f1 (ppm)


f1 (ppm)

Sample Name:	AJ229	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	b
Vial:	2	Acq. Method Set:	PM IA 1ml 8020 hept_Prop2 20dc
Injection #:	1	Processing Method:	3
Injection Volume:	5,00 ul	Channel Name:	251,0nm
Run Time:	30,0 Minutes	Proc. Chnl. Descr.:	PDA 251,0 nm
Date Acquired:	16/06/2011 11:40:02 CEST		
Date Processed:	16/06/2011 13:45:18 CEST		

Spectrum Index Plot



SampleName: AJ229; Vial: 2; Injection: 1; Date Acquired: 16/06/2011 11:40:02 CEST

Peak Results

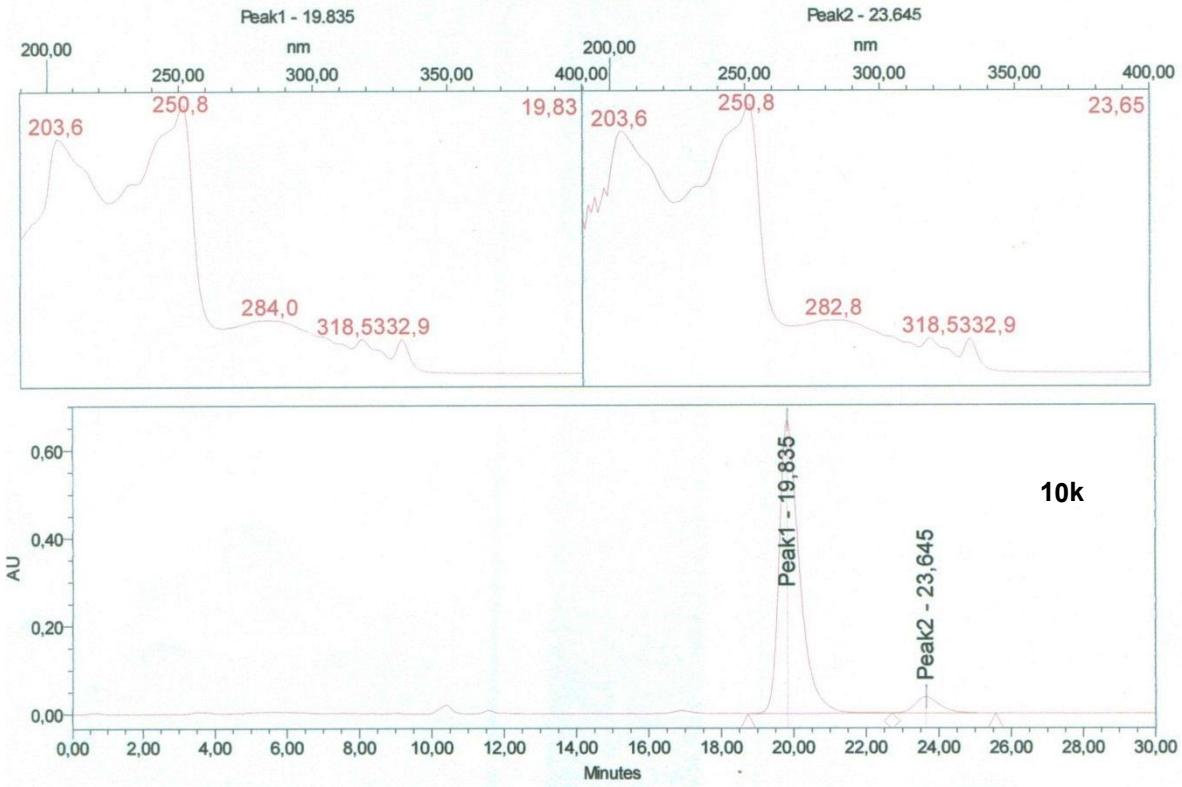
	Name	RT	Area	% Area
1	Peak1	19,733	20337826	49,10
2	Peak2	23,804	21082264	50,90

Reported by User: System
Report Method: rapport
Report Method ID 1029
Page: 1 of 1

Project Name: IA-ODH-OJH 2011
Date Printed: 12/01/2012
09:58:59 Europe/Paris

Sample Name:	AJ228	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	fr
Vial:	2	Acq. Method Set:	PM IA 1ml 8020 hept_Prop2 20dc
Injection #:	1	Processing Method:	3
Injection Volume:	2,00 ul	Channel Name:	251,0nm
Run Time:	30,0 Minutes	Proc. Chnl. Descr.:	PDA 251,0 nm
Date Acquired:	21/06/2011 11:20:04 CEST		
Date Processed:	21/06/2011 11:49:35 CEST		

Spectrum Index Plot



SampleName: AJ228; Vial: 2; Injection: 1; Date Acquired: 21/06/2011 11:20:04 CEST

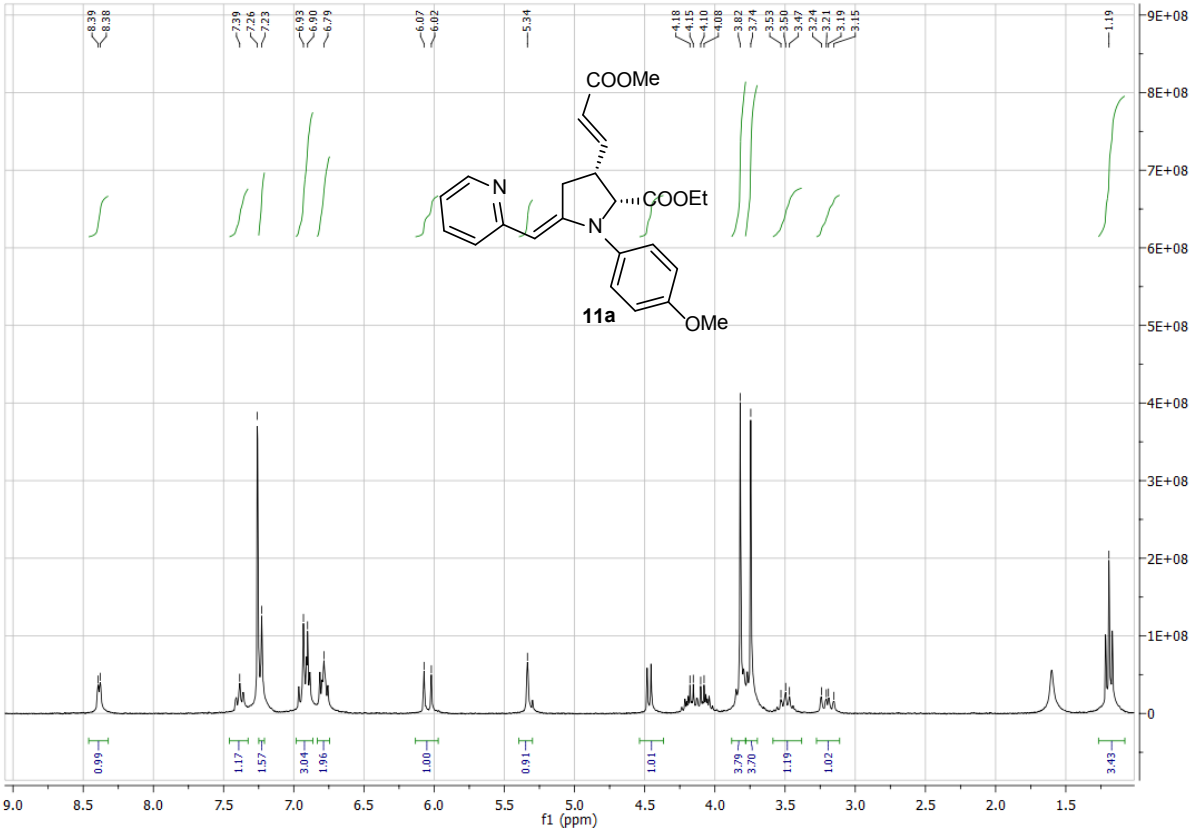
Peak Results

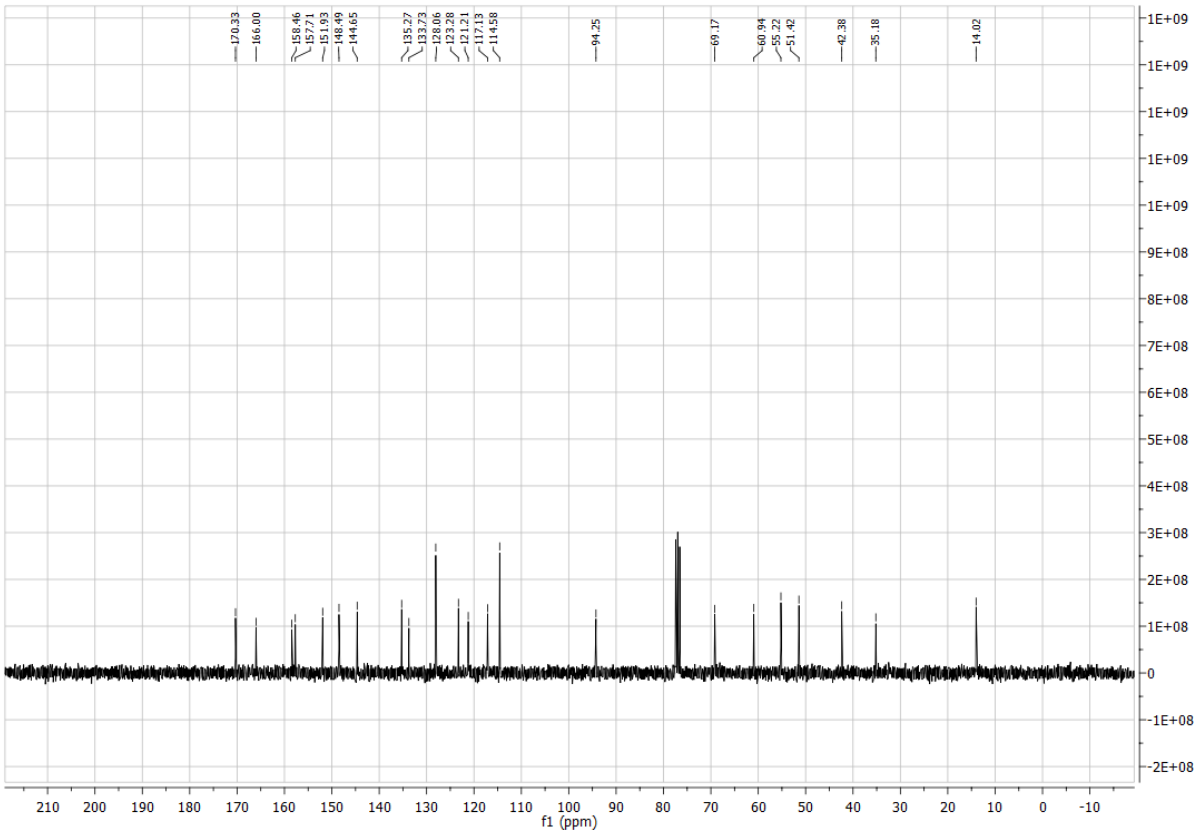
	Name	RT	Area	% Area
1	Peak1	19,835	25904287	93,41
2	Peak2	23,645	1826616	6,59

ee = 87%

Reported by User: System
Report Method: rapport
Report Method ID 1029
Page: 1 of 1

Project Name: IA-ODH-OJH 2011
Date Printed: 12/01/2012
09:58:58 Europe/Paris


COOMe
COOEt
N
N
OMe
11a
f1 (ppm)

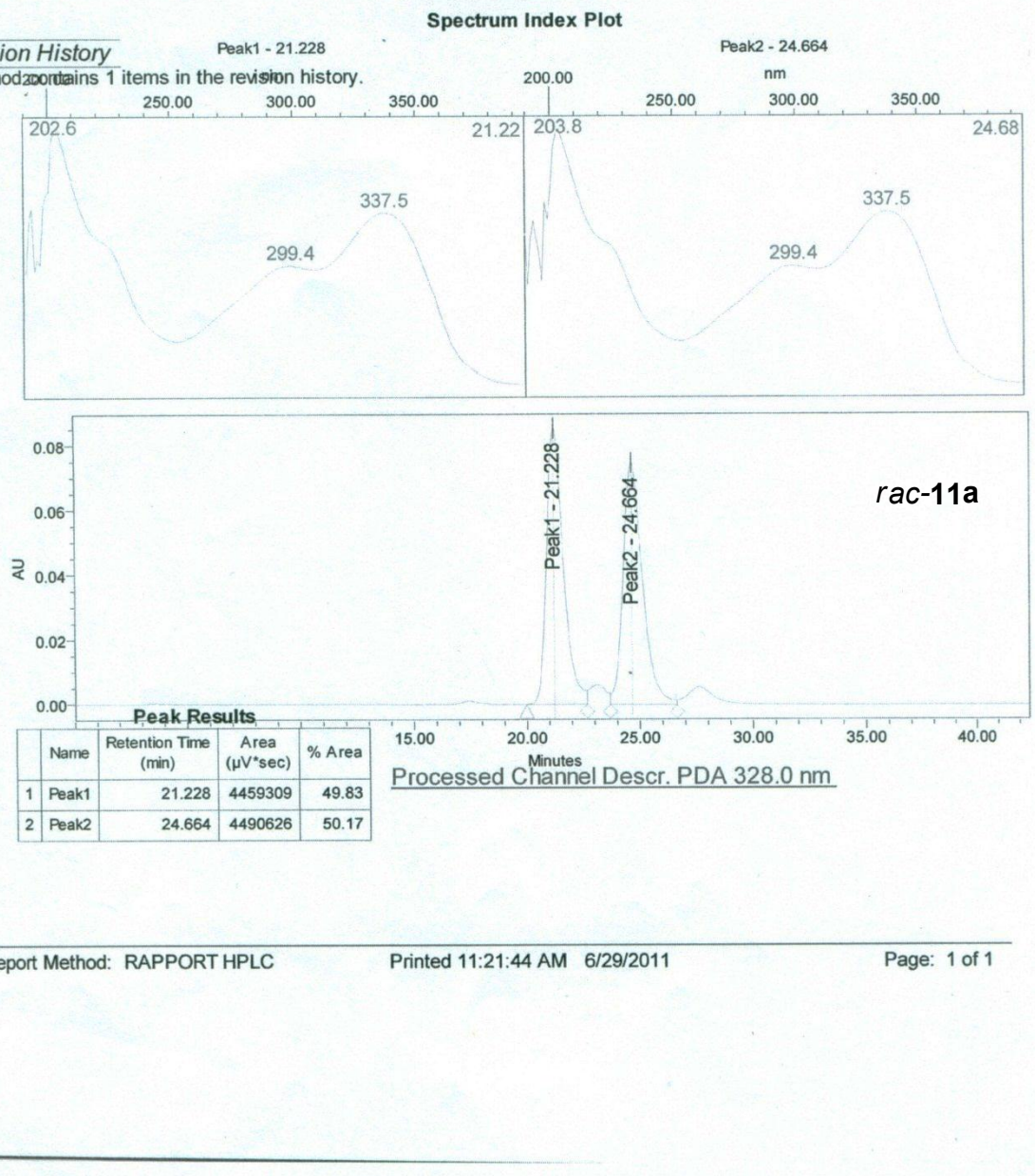

f1 (ppm)

Method Information

Comments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 80%n-heptane20%propanol-2 éch.+col.à 20°C
Modified User	System
Locked	No
Method Id	1095
Method Version	2
Edit User	

Revision History

This method contains 1 items in the revision history.



Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	21.228	4459309	49.83
2	Peak2	24.664	4490626	50.17

Report Method: RAPPORT HPLC Printed 11:21:44 AM 6/29/2011 Page: 1 of 1

Method Information

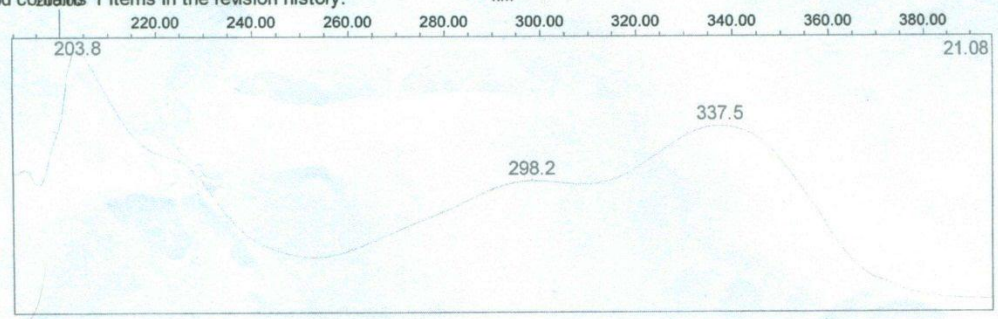
Comments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 80%n-heptane20%propanol-2 éch.+col.à 20°C
Modified User	System
Locked	No
Method Id	1095
Method Version	2
Edit User	

Revision History

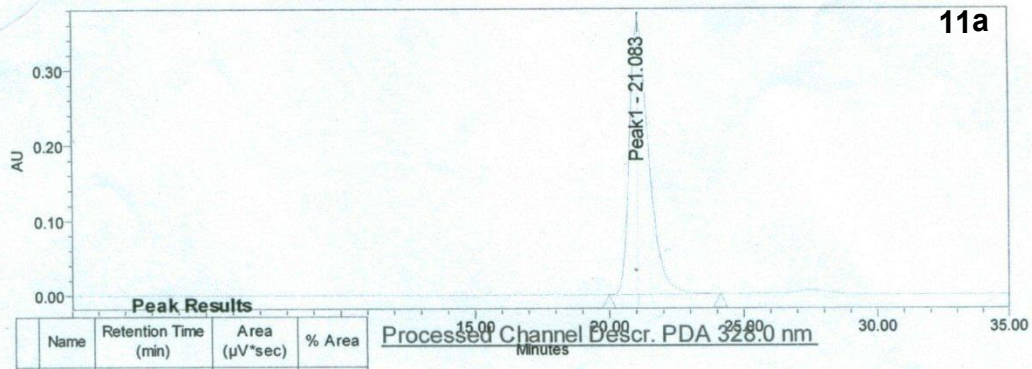
This method contains 1 items in the revision history.

Spectrum Index Plot

Peak1 - 21.083



11a

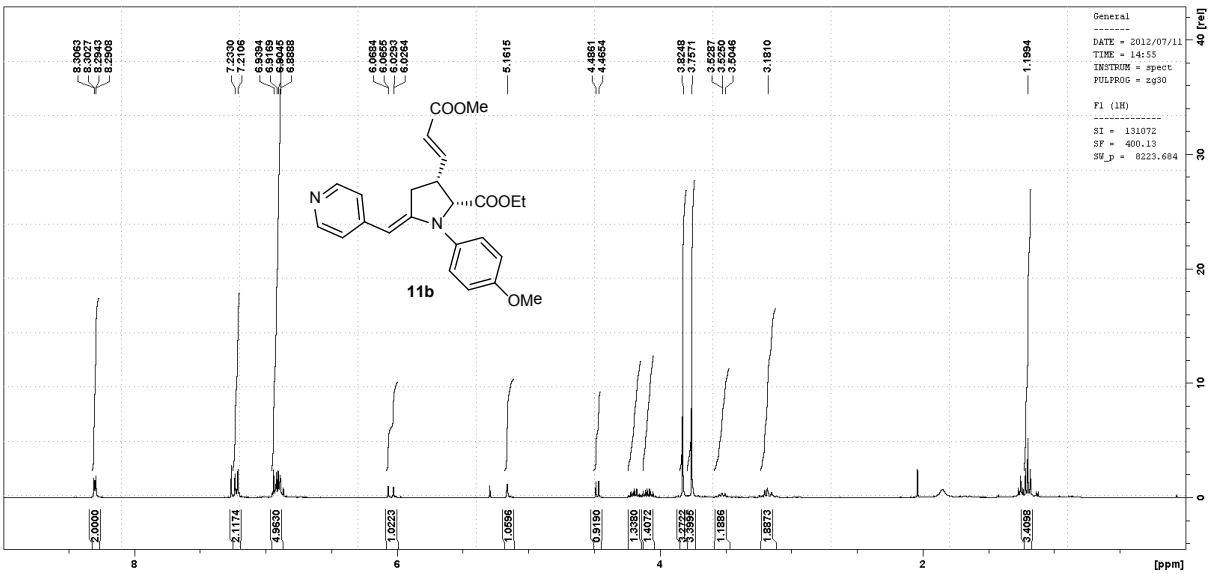


Processed Channel Descr. PDA 326.0 nm

Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	21.083	18203397	100.00

Report Method: RAPPORT HPLC Printed 1:55:05 PM 6/29/2011 Page: 1 of 1


8.3063
8.3027
8.2943
8.2908
7.2330
7.2106
6.9394
6.9169
6.8945
6.8888
6.0684
6.0565
6.0293
6.0264
5.1615
4.4881
4.4654
3.8248
3.7571
3.5287
3.5250
3.5046
3.1810
1.1994
2.0000
2.1174
4.9630
1.0223
1.0596
0.5190
1.3380
1.4072
3.2722
3.3998
1.1886
1.8873
3.4098
COOMe
COOEt
N
N
OMe
11b
General
DATE = 2012/07/11
TIME = 14:55
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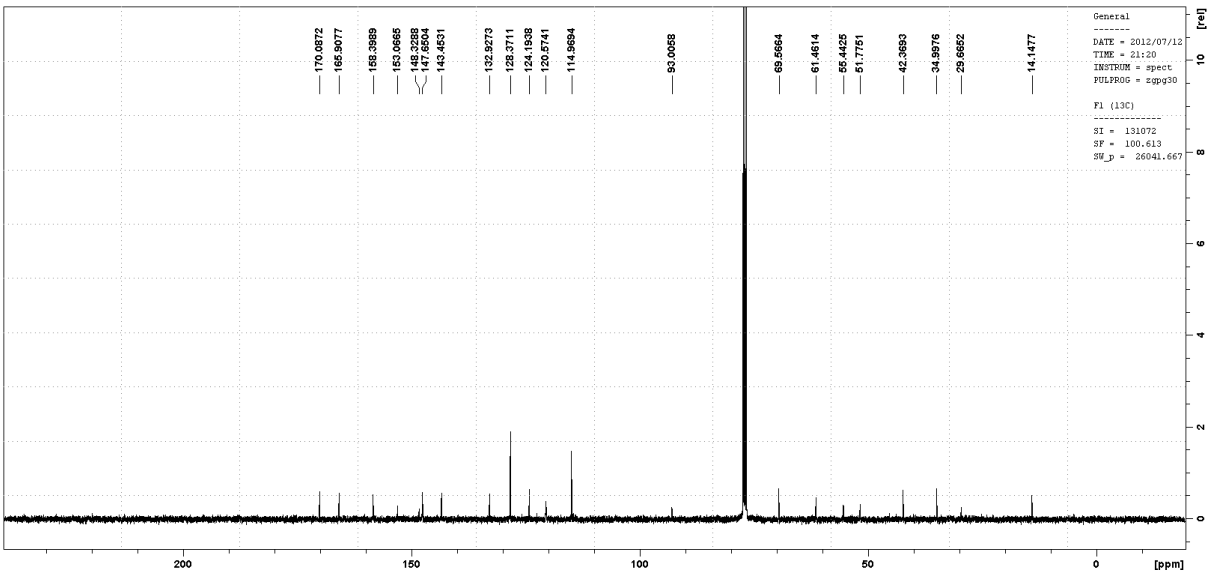
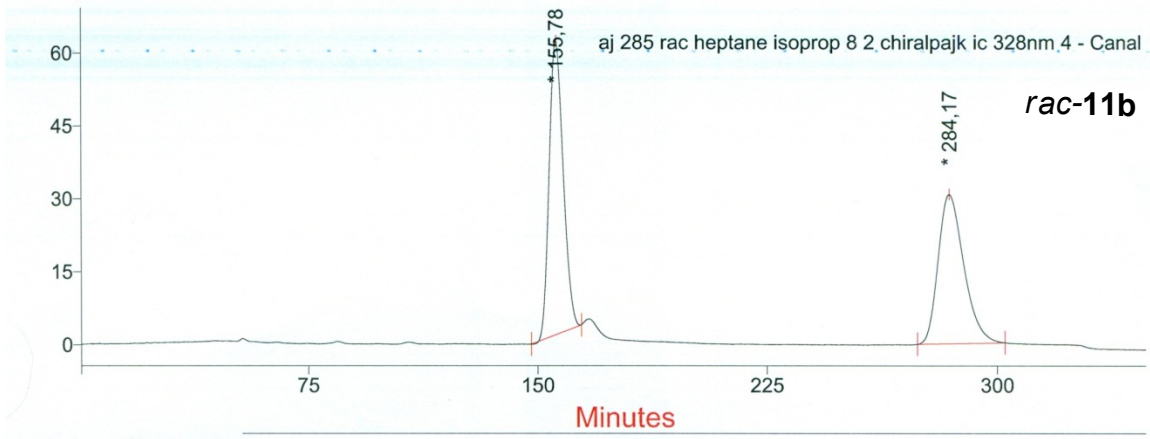
PULPROG = zg30
F1 (1H)
SI = 131072
SF = 400.13
SW_p = 8223.684
[rel]
[ppm]


170.0872
165.9077
158.3989
153.0665
148.3288
147.6804
143.4531
132.9273
128.3711
124.1938
120.5741
114.9694
93.0058
69.5664
61.4614
55.4425
51.7751
42.3693
34.9976
29.6652
14.1477
General
DATE = 2012/07/12
TIME = 21:20
INSTRUM = spect
PULPROG = zgpg30
F1 (13C)
SI = 131072
SF = 100.613
SW_p = 26041.667
[rel]
[ppm]



rac-**11b**

rmations sur l'acquisition

d'acquisition	16/09/2011 12:43:59 (+01:00) (Azur 4.6.0.0)		
ce de l'acquisition :			
	INT7Channel 1		
e	350,02 Minutes	Nb de points	21002
ise d'acquisition	1,00 points/seconde		

Résultats d'intégration

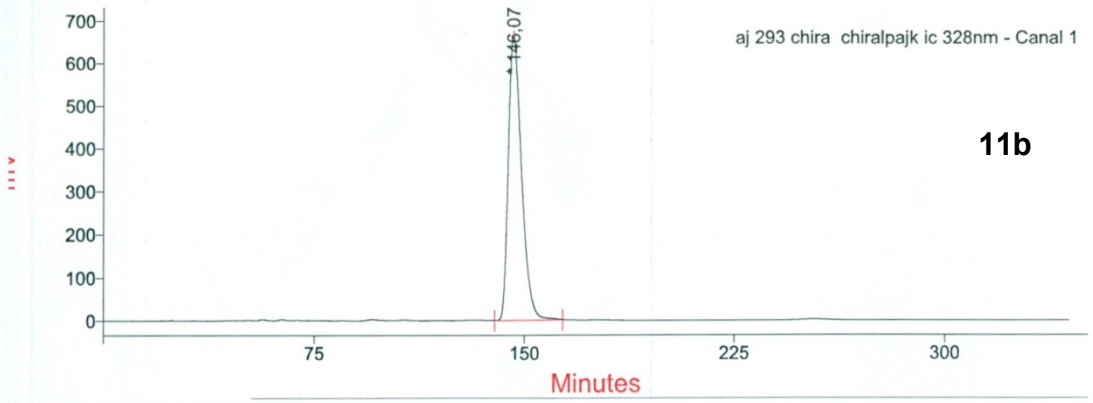
#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		155,78	19275,32	51,86	0,00	0,00
2		284,17	17894,49	48,14	0,00	0,00
MME			**37169,81**	**100,00**	**0,00**	**0,00**

rmations sur l'échantillon

	aj 285 rac heptane isoprop 8 2 chType d'échantillon		Echantillon
lacon	1		
ıtité	0,000000 mg	Volume d'injection	20,00 µl
ion	1	Diviseur	1
valeur initiale modifiée)			
rmations :			

chiralpak ic
Heptane/iPrOH 80/20
@328 nm 1ml/min 20

Analyse : aj 293 chira chiralpajk ic 328nm



11b

ıformations sur l'acquisition

ıte d'acquisition	18/09/2011 13:30:28 (+01:00) (Azur 4.6.0.0)		
ɔurce de l'acquisition :			
	INT7Channel 1		
ırée	344,20 Minutes	Nb de points	20653
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		146,07	216669,38	100,00	0,00	0,00
SOMME			216669,38	100,00	0,00	0,00

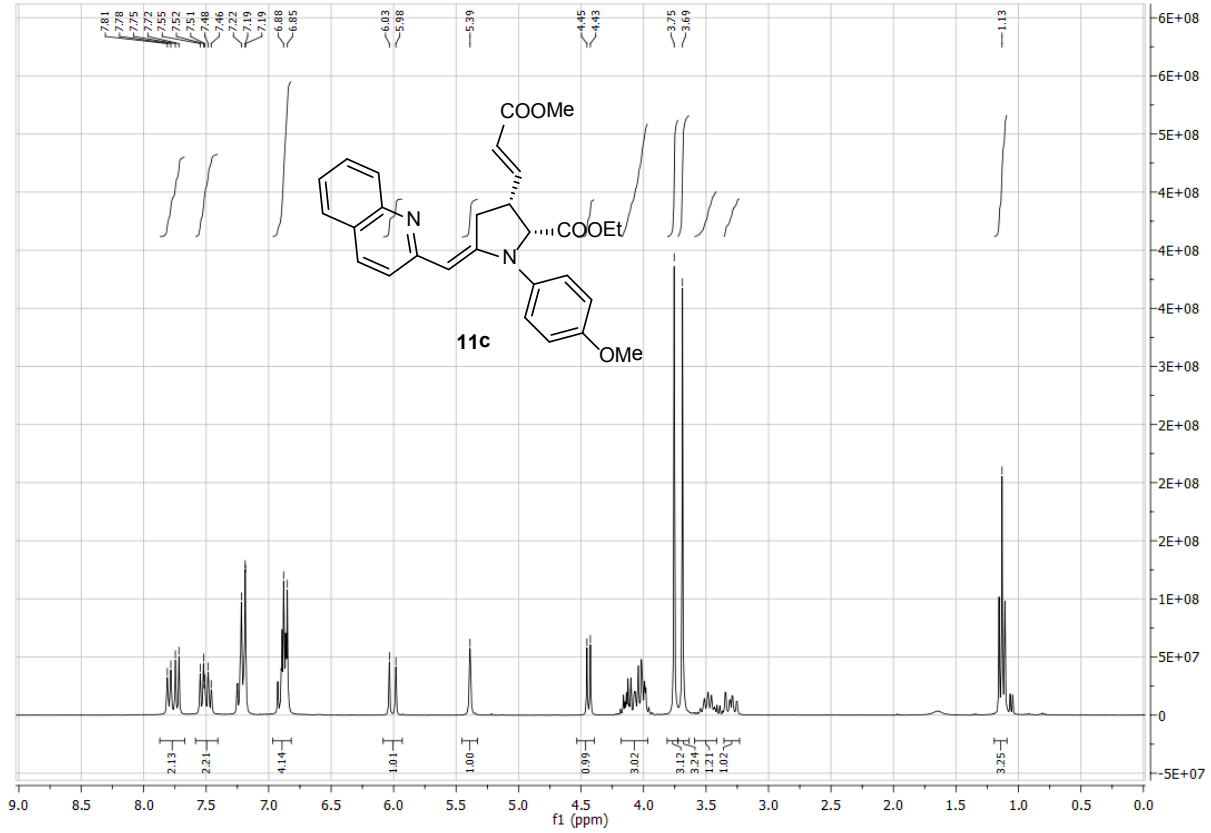
ıformations sur l'échantillon

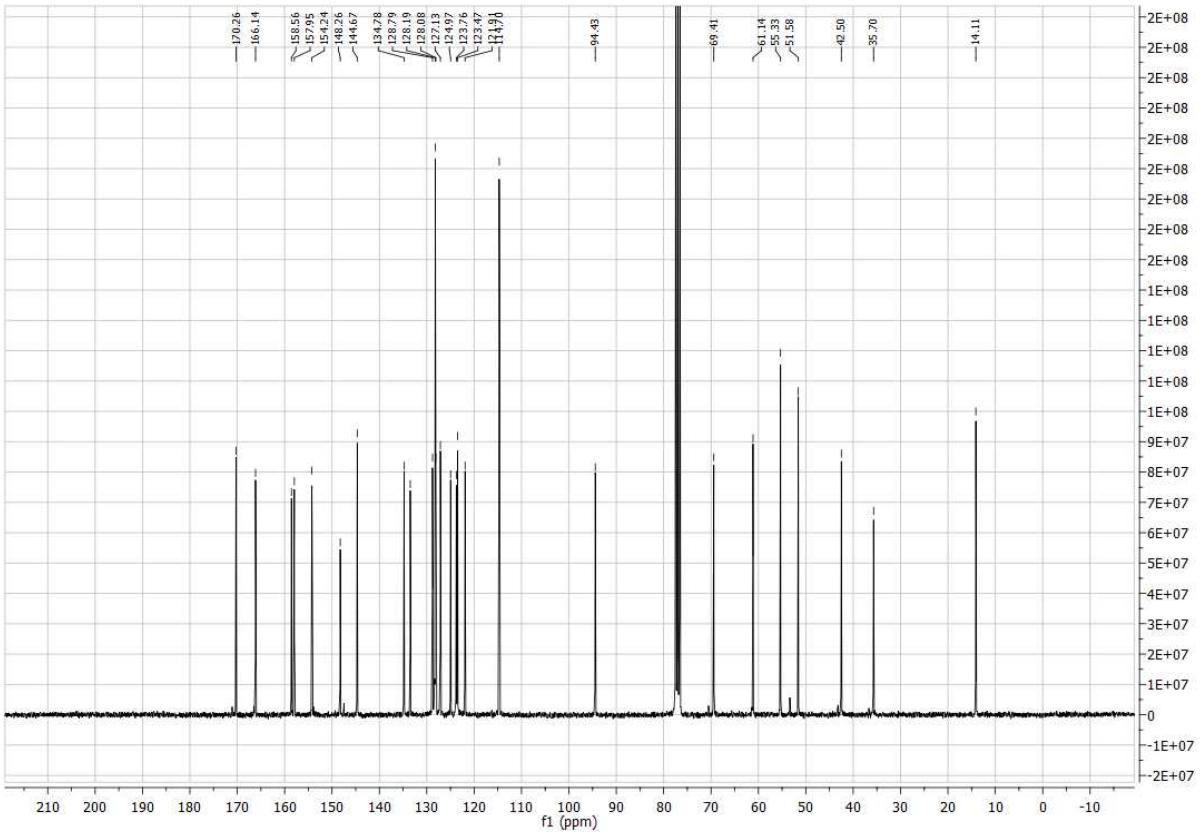
ɔm	aj 293 chira chiralpajk ic 328nm	Type d'échantillon	Echantillon
' Flacon	1		
uantité	0,000000 mg	Volume d'injection	20,00 µl
lution	1	Diviseur	1

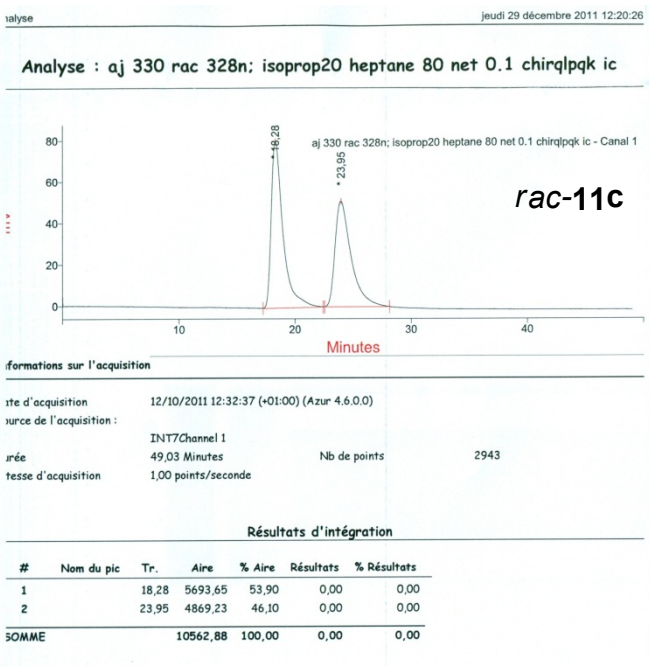
= valeur initiale modifiée)

ıformations :

aj 293chiralpak ic
Heptane/iPrOH/NET3 80/20/0.25
@328 nm 1ml/min


COOMe
COOEt
N
N
OMe
11c
f1 (ppm)


f1 (ppm)



alyse jeudi 29 décembre 2011 12:20:26

Analyse : aj 330 rac 328n; isoprop20 heptane 80 net 0.1 chirqlpqk ic

formations sur l'acquisition

te d'acquisition	12/10/2011 12:32:37 (+01:00) (Azur 4.6.0.0)		
urce de l'acquisition :	INT7Channel 1		
rée	49,03 Minutes	Nb de points	2943
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		18,28	5693,65	53,90	0,00	0,00
2		23,95	4869,23	46,10	0,00	0,00
SOMME			10562,88	100,00	0,00	0,00

Analyse jeudi 29 déc

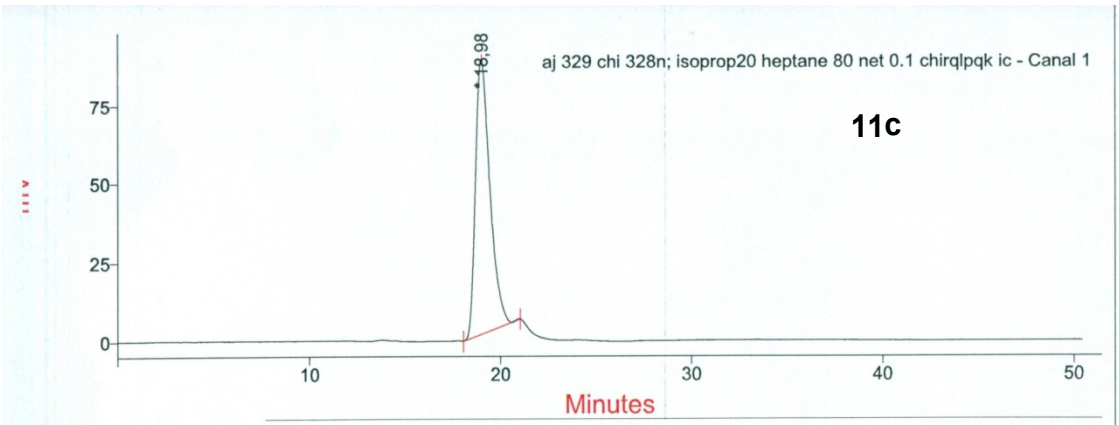
Informations sur l'échantillon

Nom	aj 330 rac 328n; isoprop20 hepta	Type d'échantillon	lpqk ic Echantillon
N° Flacon	1		
Quantité	0,000000 mg	Volume d'injection	20,00 µl
Dilution	1	Diviseur	1

(* = valeur initiale modifiée)

Informations :

Ic
hept/IPA/net3 : 20/80/0.1
1mL/min
UV : 254 nm



ıformations sur l'acquisition

ıte d'acquisition	12/10/2011 13:59:07 (+01:00) (Azur 4.6.0.0)		
ɔurce de l'acquisition :			
	INT7Channel 1		
ırée	50,43 Minutes	Nb de points	3027
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		18,98	4596,17	100,00	0,00	0,00
SOMME			4596,17	100,00	0,00	0,00

ıformations sur l'échantillon

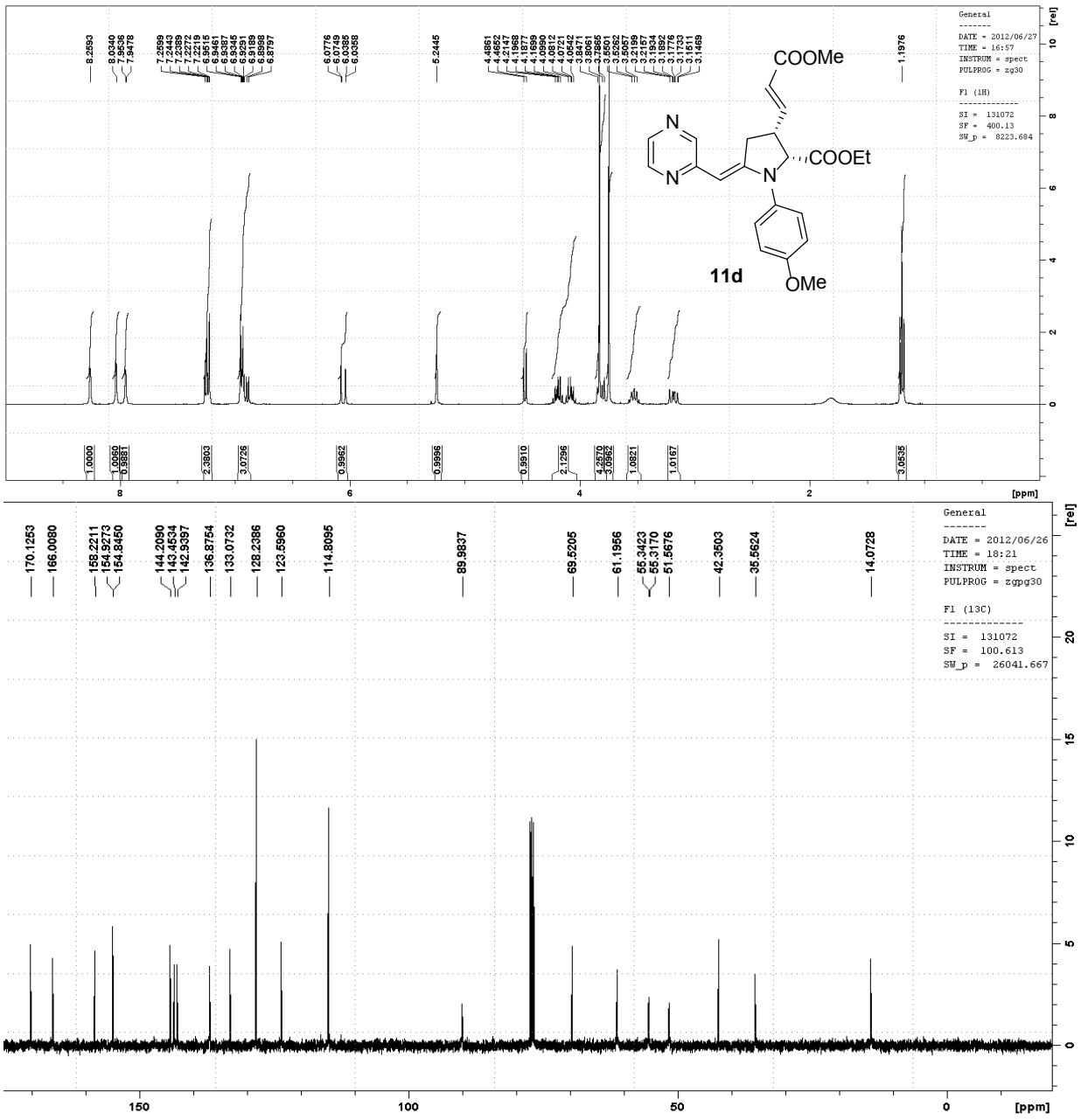
ɔm	aj 329 chi 328n; isoprop20 heptaıType d'échantillonlpqk ic		Echantillon
' Flacon	1		
uantité	0,000000 mg	Volume d'injection	20,00 µl
lution	1	Diviseur	1

= valeur initiale modifiée)

ıformations :

329 Ic
hept/IPA/net3 : 20/80/0.1
1mL/min
UV : 254 nm

329 chi 328n; isoprop20 heptane 80 net 0.1 chirqlpqk ic - Canal 1 Page 1/1


COOMe
COOEt
N
N
N
OMe
11d
General
DATE = 2012/06/27
TIME = 16:57
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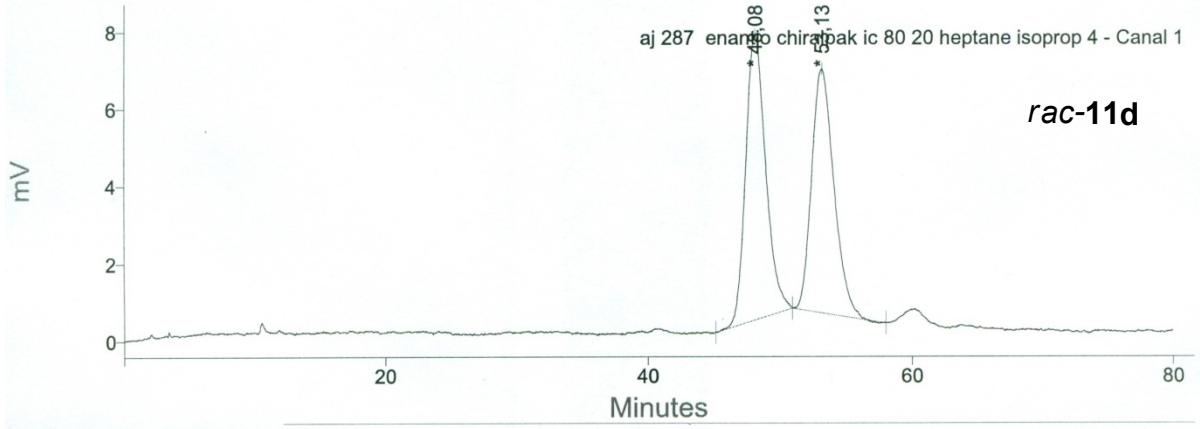
PULPROG = zg30
F1 (1H)
SI = 131072
SF = 400.13
SW_p = 8223.684
[ppm]
[rel]
General
DATE = 2012/06/26
TIME = 18:21
INSTRUM = spect
PULPROG = zgpg30
F1 (13C)
SI = 131072
SF = 100.613
SW_p = 26041.667
[ppm]
[rel]



Informations sur l'acquisition

Date d'acquisition	08/09/2011 16:38:48 (+01:00) (Azur 4.6.0.0)		
Source de l'acquisition :			
	INT7Channel 1		
Durée	80,00 Minutes	Nb de points	4801
Vitesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		48,08	777,83	51,26	0,00	0,00
2		53,13	739,64	48,74	0,00	0,00
SOMME			**1517,48**	**100,00**	**0,00**	**0,00**

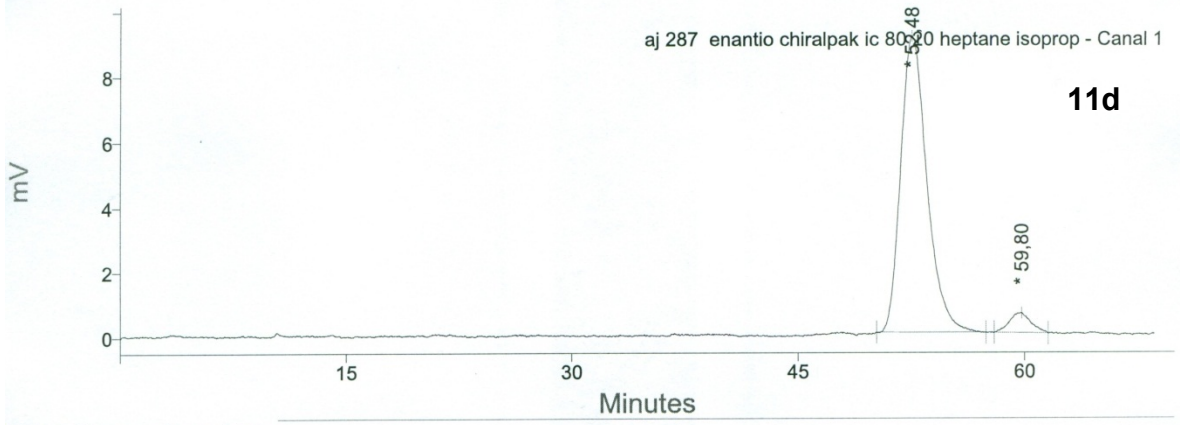
Informations sur l'échantillon

Nom	aj 287 enantio chiralpak ic 80 20	Type d'échantillon	Echantillon
N° Flacon	1		
Quantité	0,000000 mg	Volume d'injection	20,00 µl
Dilution	1	Diviseur	1

(* = valeur initiale modifiée)

Informations :

aj 287
Heptane/iPrOH 80/20
@328 nm 1ml/min



Informations sur l'acquisition

Date d'acquisition	08/09/2011 14:50:53 (+01:00) (Azur 4.6.0.0)		
Source de l'acquisition :			
	INT7Channel 1		
Durée	68,67 Minutes	Nb de points	4121
Vitesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		52,48	1102,80	94,90	0,00	0,00
2		59,80	59,23	5,10	0,00	0,00
SOMME			**1162,03**	**100,00**	**0,00**	**0,00**

Informations sur l'échantillon

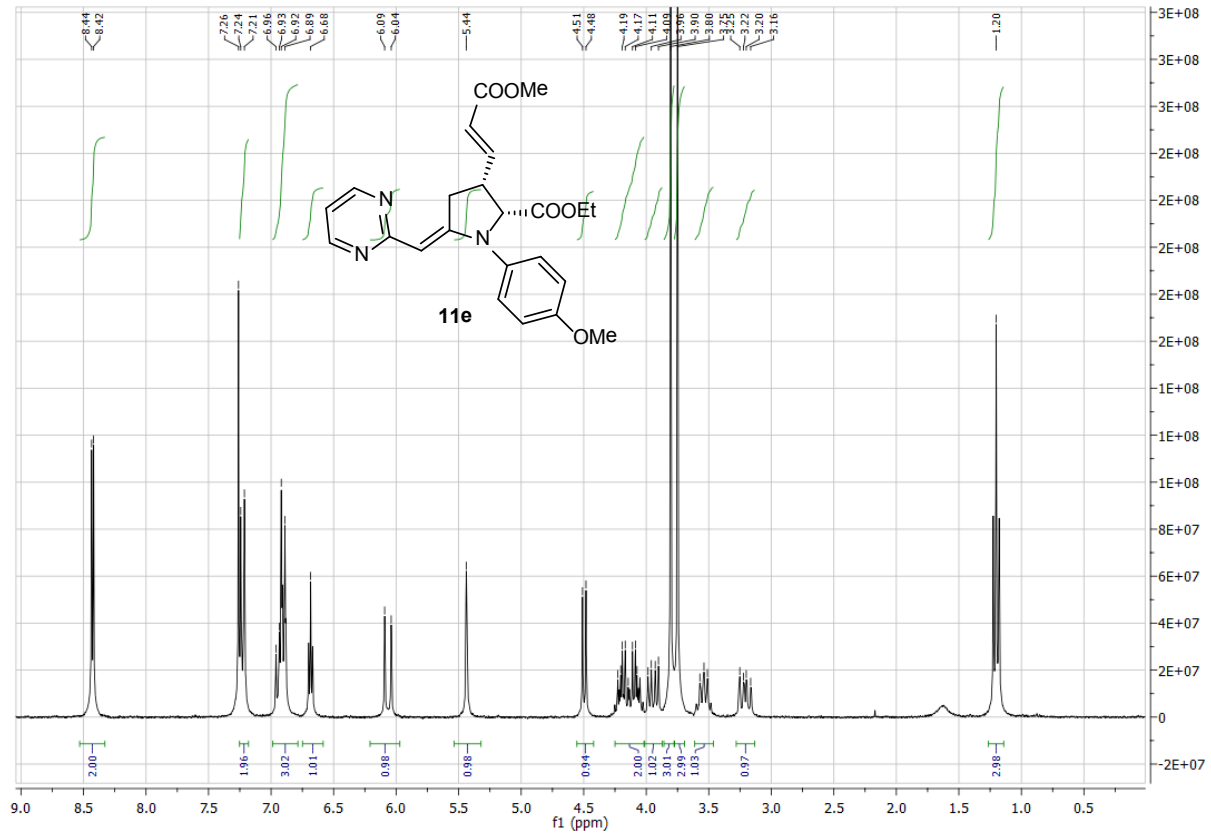
Nom	aj 287 enantio chiralpak ic 80 20	Type d'échantillon	Echantillon
N° Flacon	1		
Quantité	0,000000 mg	Volume d'injection	20,00 µl
Dilution	1	Diviseur	1

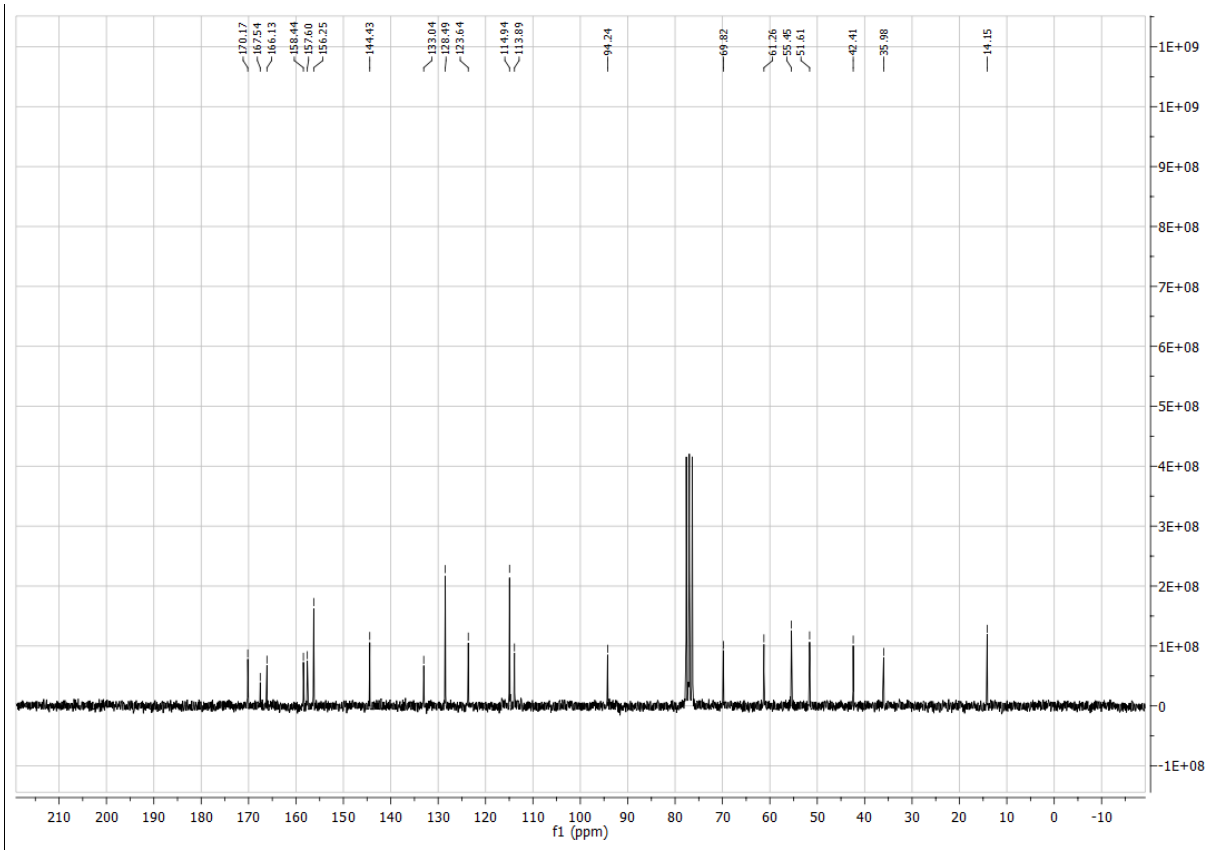
(* = valeur initiale modifiée)

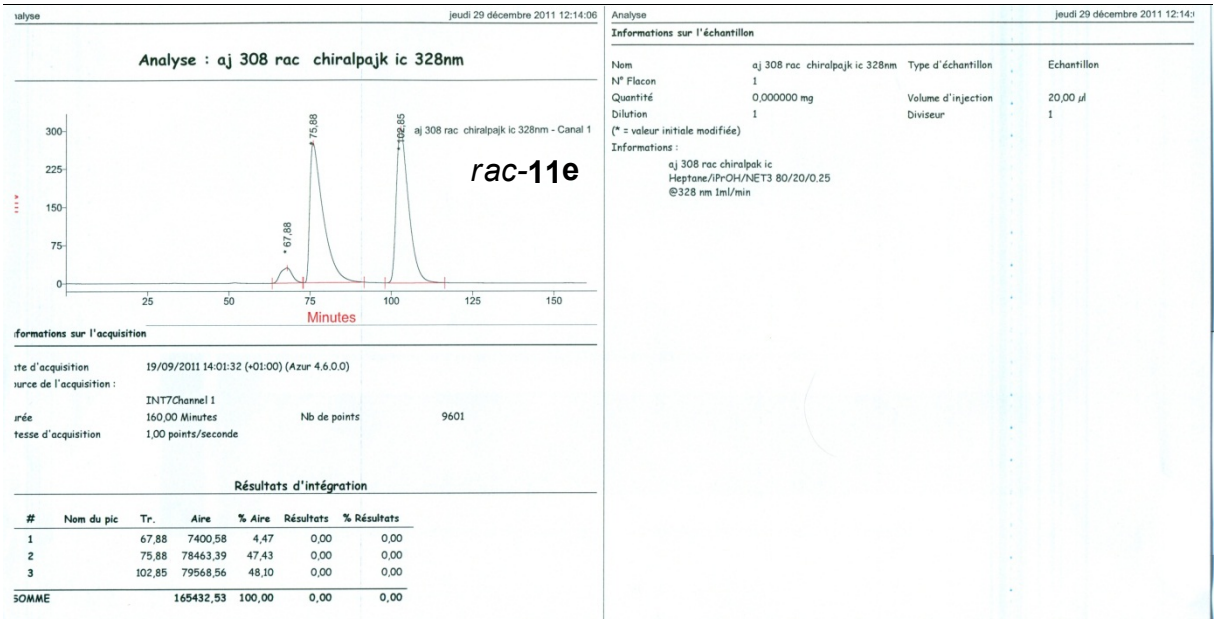
Informations :

aj 287
Heptane/iPrOH 80/20
@328 nm 1ml/min

aj 287 enantio chiralpak ic 80 20 heptane isoprop - Canal 1 Page 1/1


COOMe
COOEt
N
N
N
OMe
11e
f1 (ppm)


f1 (ppm)



alyse jeudi 29 décembre 2011 12:14:06

Analyse : aj 308 rac chiralpajk ic 328nm

formations sur l'acquisition

te d'acquisition	19/09/2011 14:01:32 (+01:00) (Azur 4.6.0.0)		
urce de l'acquisition :			
	INT7Channel 1		
rée	160,00 Minutes	Nb de points	9601
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		67,88	7400,58	4,47	0,00	0,00
2		75,88	78463,39	47,43	0,00	0,00
3		102,85	79568,56	48,10	0,00	0,00
SOMME			165432,53	100,00	0,00	0,00

Analyse jeudi 29 décembre 2011 12:14:

Informations sur l'échantillon

Nom	aj 308 rac chiralpajk ic 328nm	Type d'échantillon	Echantillon
N° Flacon	1		
Quantité	0,000000 mg	Volume d'injection	20,00 µl
Dilution	1	Diviseur	1

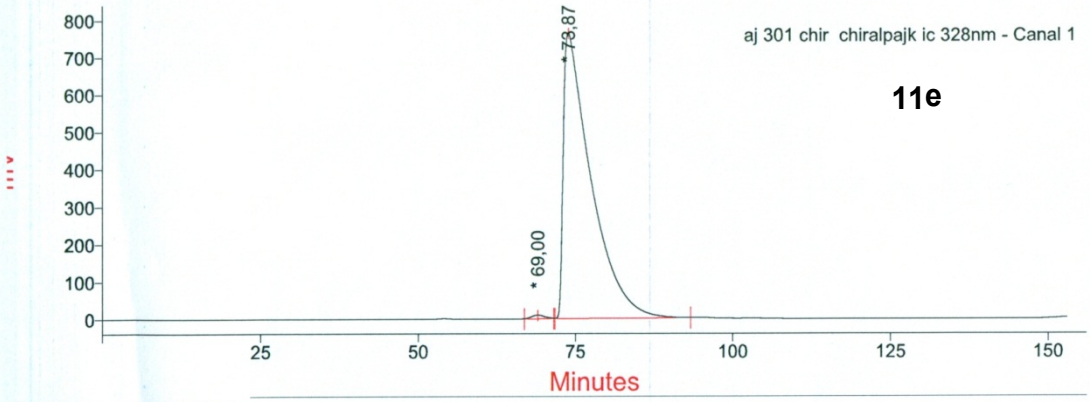
(* = valeur initiale modifiée)

Informations :

aj 308 rac chiralpak ic
Heptane/iPrOH/NET3 80/20/0.25
@328 nm 1ml/min

ıalyse jeudi 29 décembre 2011 12:16:09

Analyse : aj 301 chir chiralpajk ic 328nm



ıformations sur l'acquisition

ıte d'acquisition	19/09/2011 16:49:29 (+01:00) (Azur 4.6.0.0)		
ɔurce de l'acquisition :			
	INT7Channel 1		
ırée	153,00 Minutes	Nb de points	9181
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		69,00	1248,82	0,54	0,00	0,00
2		73,87	230949,39	99,46	0,00	0,00
SOMME			232198,21	100,00	0,00	0,00

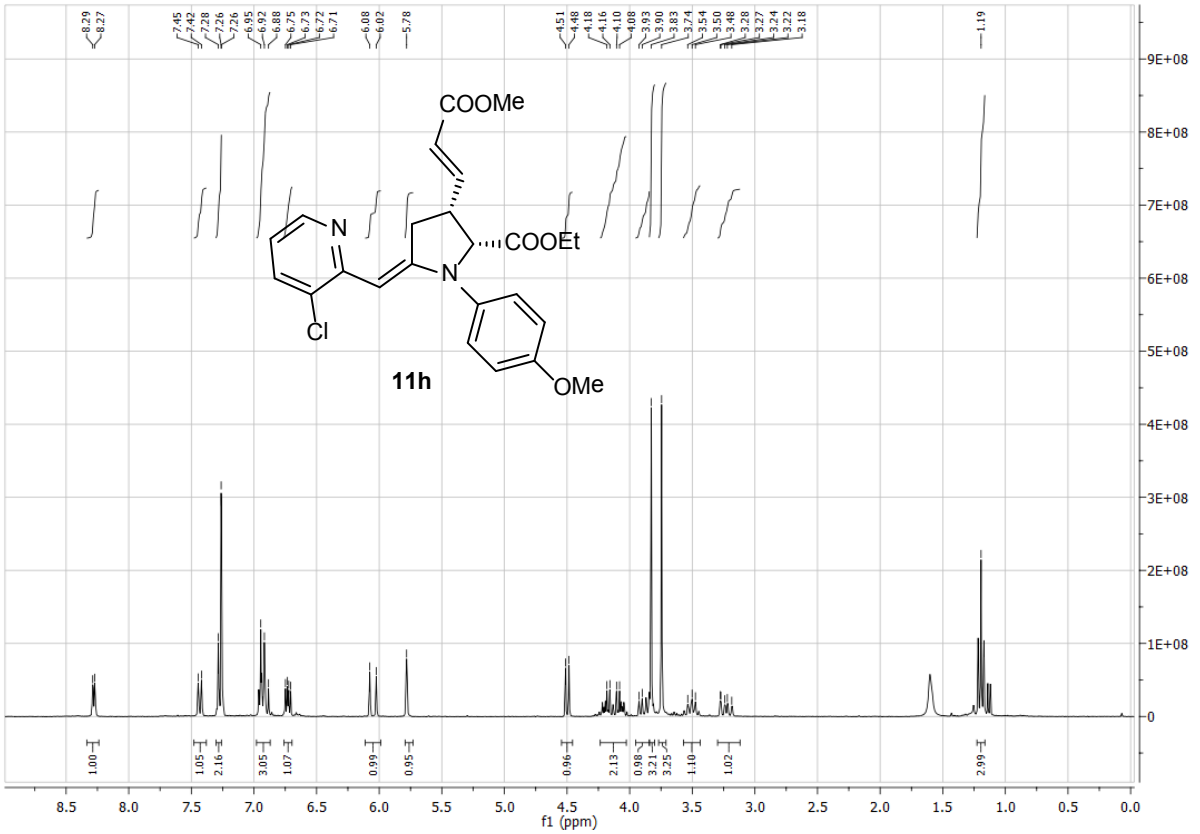
ıformations sur l'échantillon

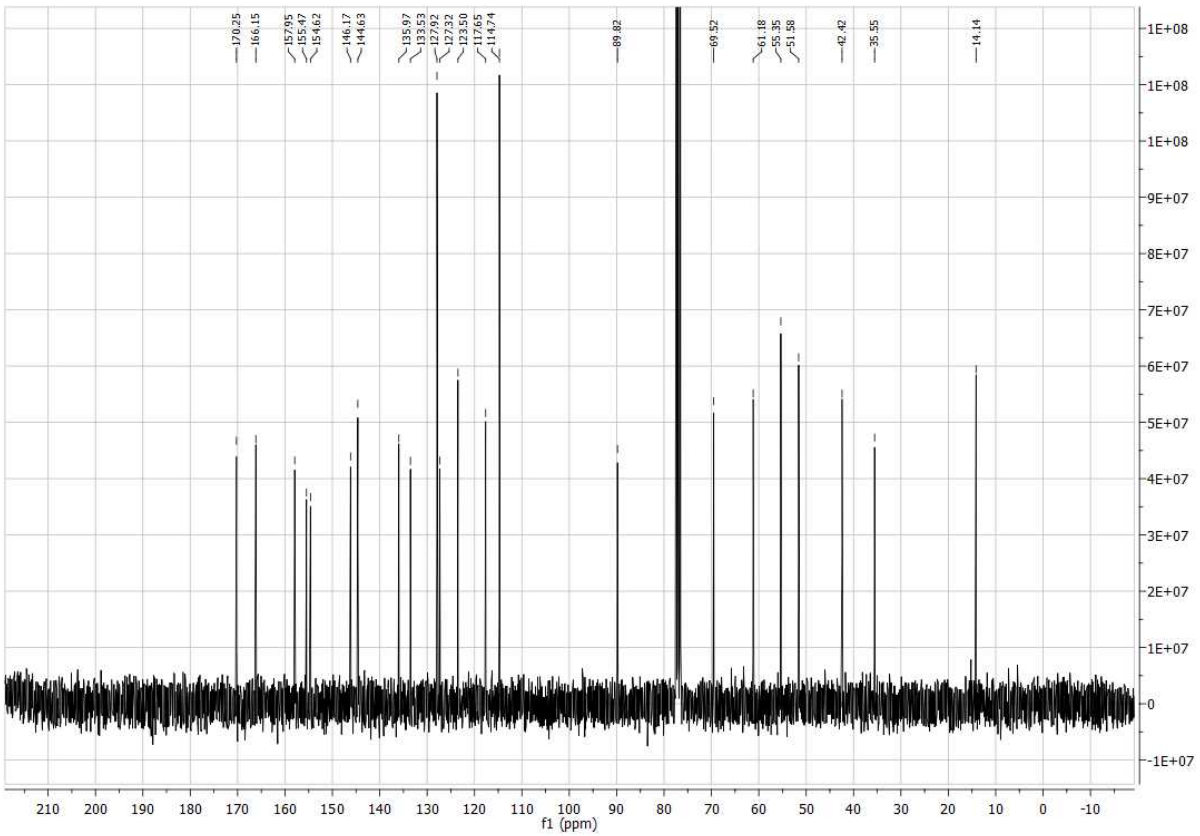
ɔm	aj 301 chir chiralpajk ic 328nm	Type d'échantillon	Echantillon
' Flacon	1		
uantité	0,000000 mg	Volume d'injection	20,00 µl
lution	1	Diviseur	1

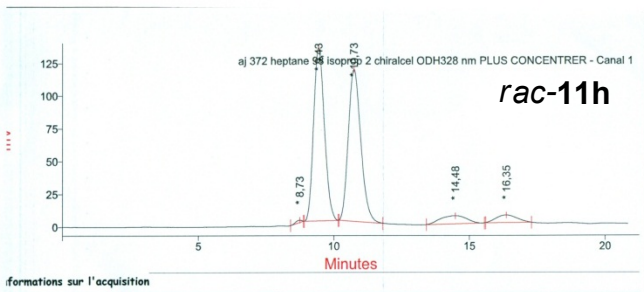
= valeur initiale modifiée)

ıformations :

aj 301 chiral chiralpak ic
Heptane/iPrOH/NET3 80/20/0.25
@328 nm 1ml/min


COOMe
COOEt
N
N
Cl
OMe
11h
f1 (ppm)


f1 (ppm)



Nom	aj 372 heptane 98 isoprop 2 chircType d'échantillonLUS CONCEEchantillon		
N° Flacon	1		
Quantité	0,000000 mg	Volume d'injection	20,00 µl
Dilution	1	Diviseur	1

(* = valeur initiale modifiée)

Informations :

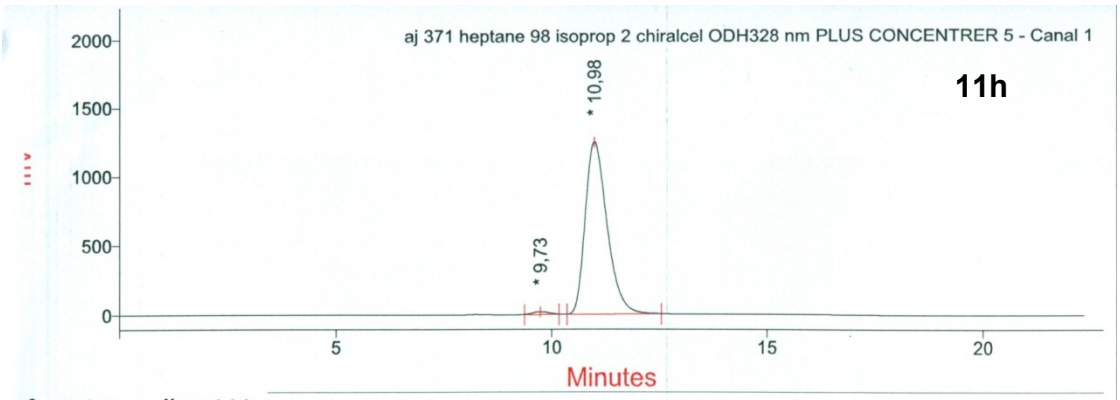
aj 372 heptane 98 isoprop 2 chiralcel ODH328 nm
1mL/min UV : 328 nm

formations sur l'acquisition

te d'acquisition	09/11/2011 17:06:20 (+01:00) (Azur 4.6.0.0)		
urce de l'acquisition :			
	INT7Channel 1		
rée	20,83 Minutes	Nb de points	1251
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		8,73	25,96	0,32	0,00	0,00
2		9,43	3667,17	45,28	0,00	0,00
3		10,73	3704,89	45,74	0,00	0,00
4		14,48	401,43	4,96	0,00	0,00
5		16,35	299,66	3,70	0,00	0,00
SOMME			8099,13	100,00	0,00	0,00



ıformations sur l'acquisition

ıte d'acquisition	10/11/2011 15:47:59 (+01:00) (Azur 4.6.0.0)		
ɔurce de l'acquisition :			
	INT7Channel 1		
ırée	22,33 Minutes	Nb de points	1341
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		9,73	462,00	1,05	0,00	0,00
2		10,98	43583,63	98,95	0,00	0,00
SOMME			44045,64	100,00	0,00	0,00

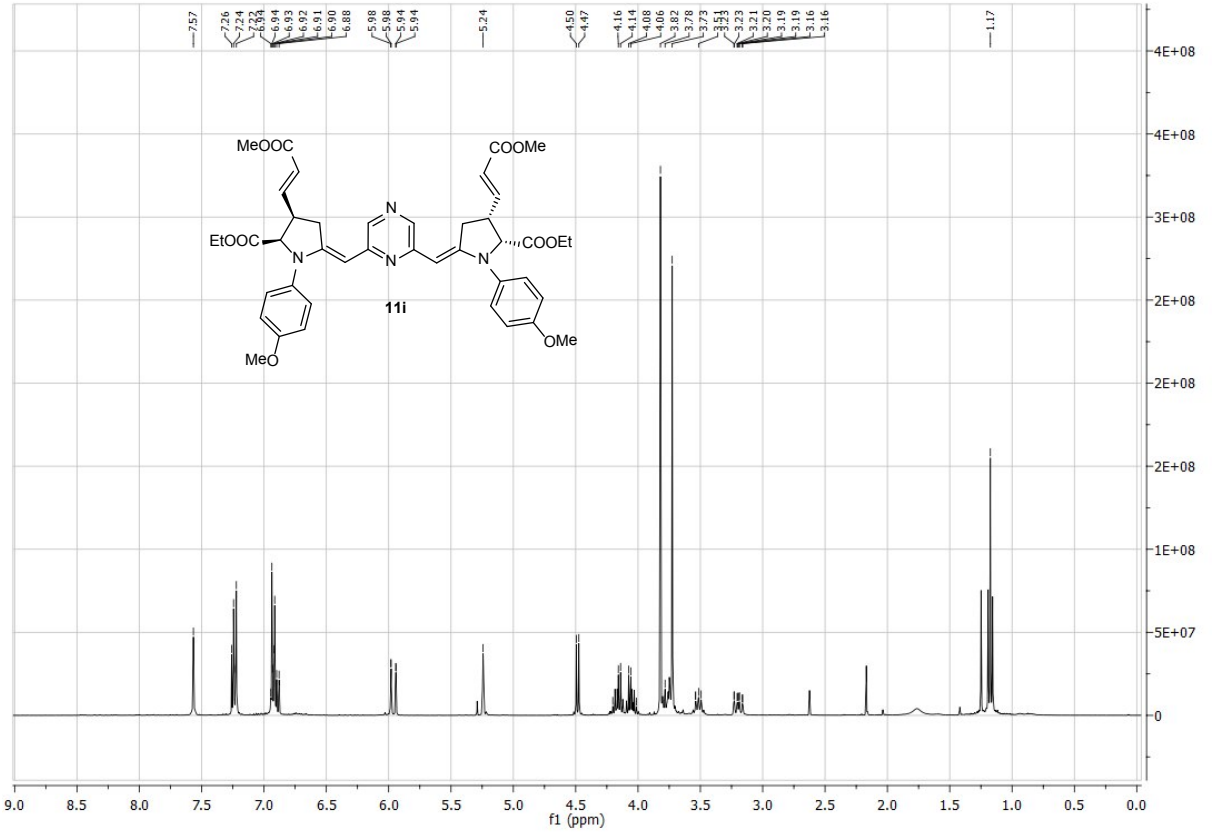
ıformations sur l'échantillon

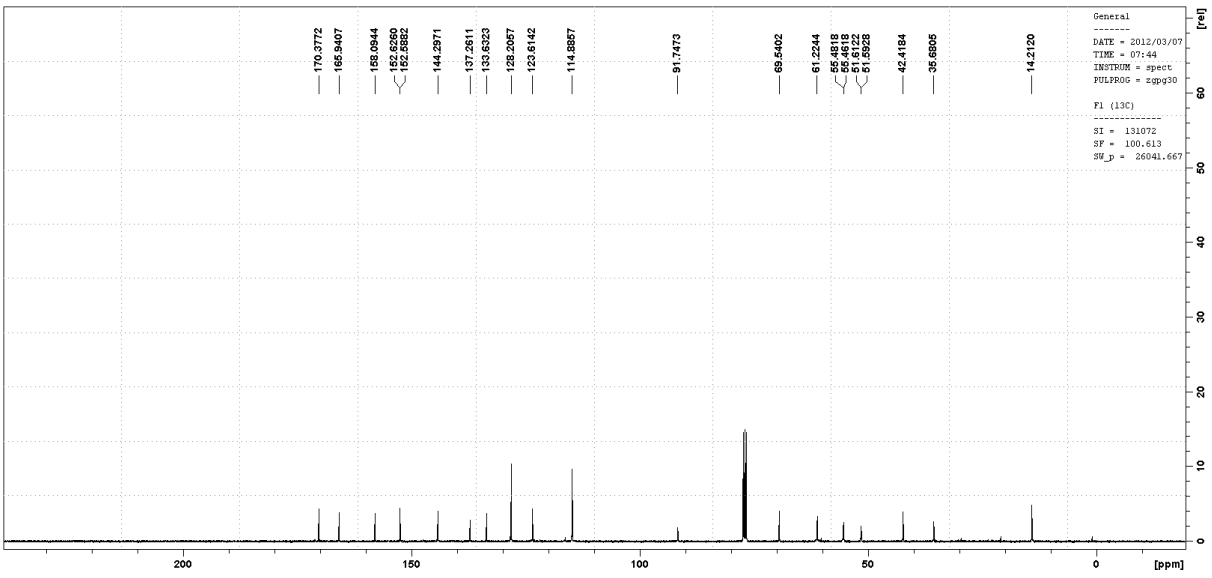
ɔm	aj 371 heptane 98 isoprop 2 chira	Type d'échantillon	LUS CONCEEchantillon
' Flacon	1		
uantité	0,000000 mg	Volume d'injection	20,00 µl
lution	1	Diviseur	1

= valeur initiale modifiée)

ıformations :

aj 371 heptane 98 isoprop 2 chiralcel ODH328 nm
1mL/min UV : 328 nm

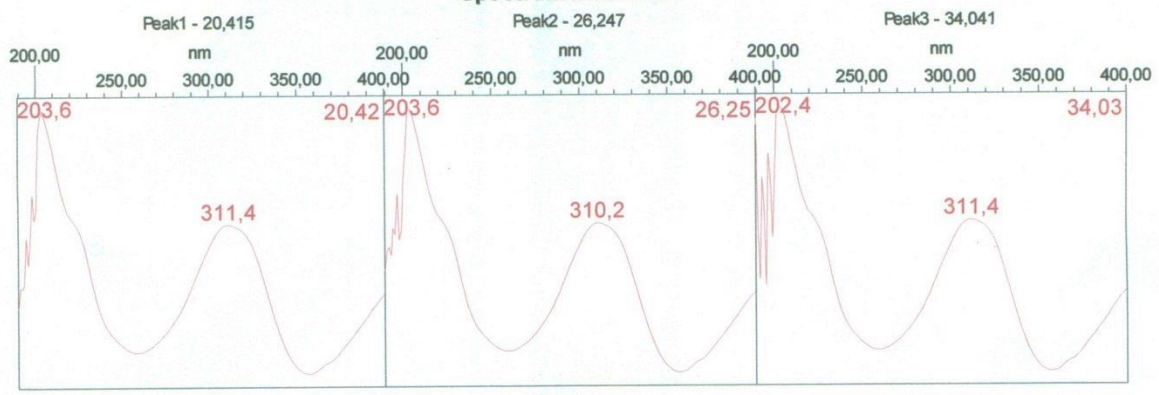

MeOOC
COOMe
EtOOC
COOEt
N
N
N
N
MeO
OMe
11i
f1 (ppm)

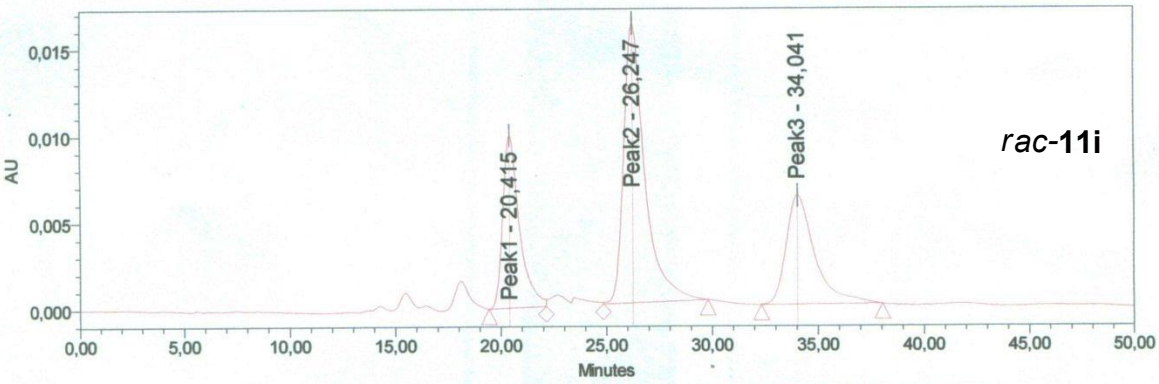

170.3772
165.9407
158.0944
152.6280
152.2882
144.2971
137.2611
133.6323
128.2057
123.6142
114.8857
91.7473
69.5402
61.2244
55.4818
55.4618
51.6122
51.5928
42.4184
35.6805
14.2120
General
DATE = 2012/03/07
TIME = 07:44
INSTRUM = spect
PULPROG = zgpg30
F1 (13C)
SI = 131072
SF = 100.613
SW_p = 26041.667
[rel]
[ppm]

SAMPLE INFORMATION

Sample Name:	AJ494	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	GY1
Vial:	1	Acq. Method Set:	PM IA 1ml 8020 hept_Prop2 20dc
Injection #:	1	Processing Method:	3
Injection Volume:	10,00 ul	Channel Name:	311,0nm
Run Time:	50,0 Minutes	Proc. Chnl. Descr.:	PDA 311,0 nm
Date Acquired:	11/07/2012 16:37:08 CEST		
Date Processed:	12/07/2012 09:52:32 CEST		

Spectrum Index Plot





rac-**11i**

SampleName: AJ494; Vial: 1; Injection: 1; Date Acquired: 11/07/2012 16:37:08 CEST

Peak Results

	Name	RT	Area	% Area
1	Peak1	20,415	546983	24,24
2	Peak2	26,247	1119602	49,62
3	Peak3	34,041	589815	26,14

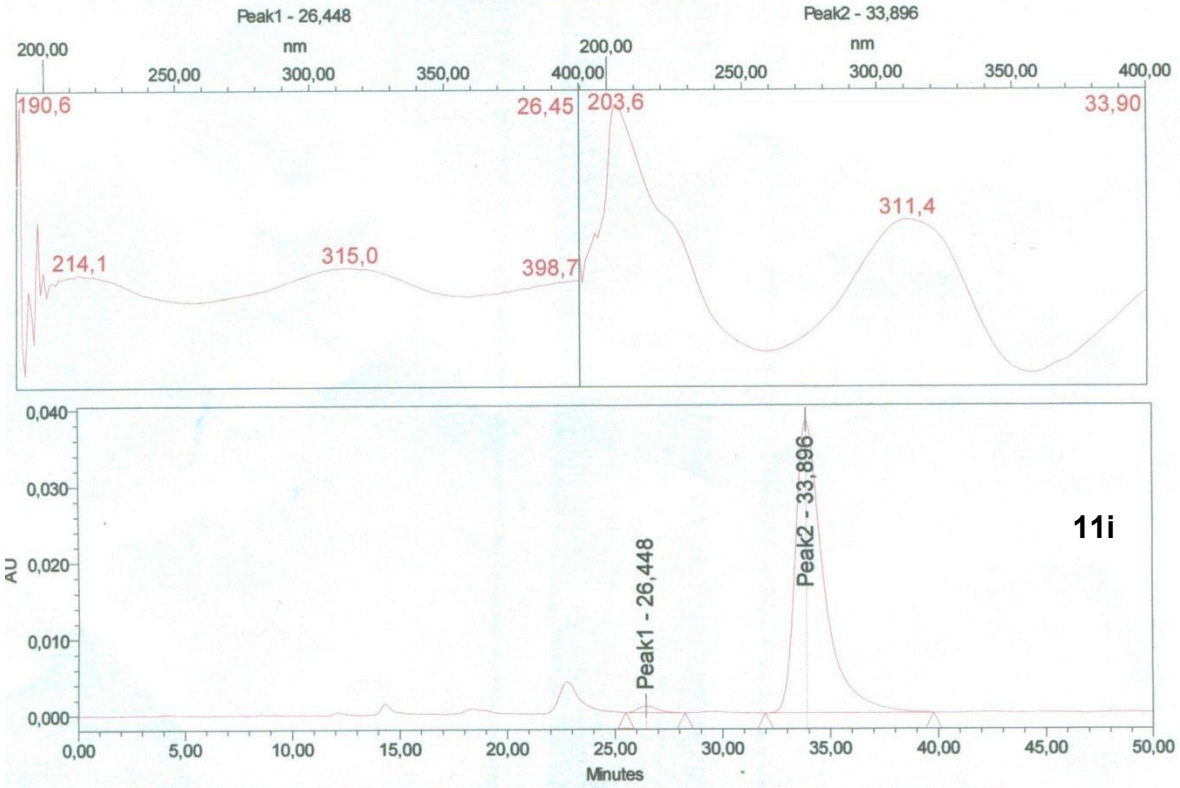
Reported by User: System
Report Method: rapport
Report Method ID 1032
Page: 1 of 1

Project Name: IA-ODH-OJH 2012
Date Printed:
12/07/2012
09:52:55 Europe/Paris

SAMPLE INFORMATION

Sample Name:	AJ495	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	GY1
Vial:	2	Acq. Method Set:	PM IA 1ml 8020 hept_Prop2 20dc
Injection #:	1	Processing Method:	3
Injection Volume:	10,00 ul	Channel Name:	311,0nm
Run Time:	50,0 Minutes	Proc. Chnl. Descr.:	PDA 311,0 nm
Date Acquired:	11/07/2012 17:27:51 CEST		
Date Processed:	12/07/2012 10:26:40 CEST		

Spectrum Index Plot



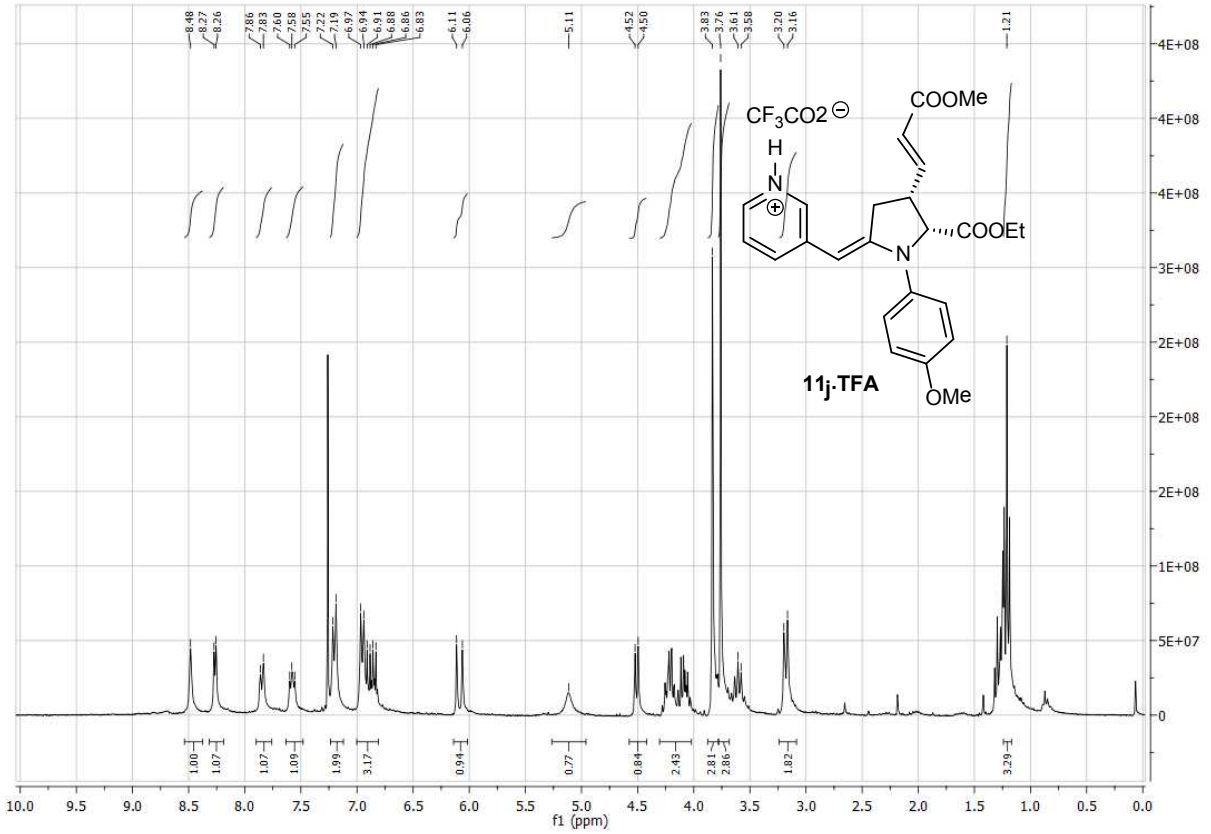
SampleName: AJ495; Vial: 2; Injection: 1; Date Acquired: 11/07/2012 17:27:51 CEST

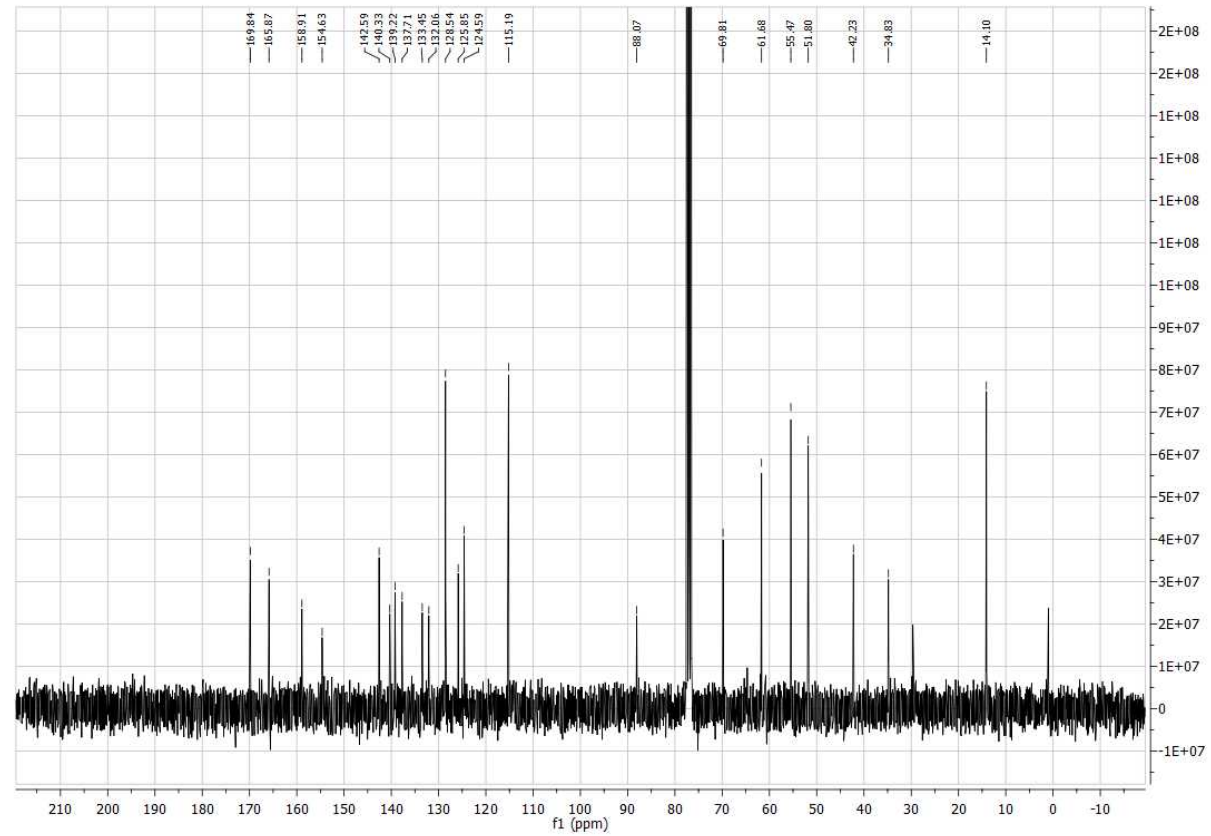
Peak Results

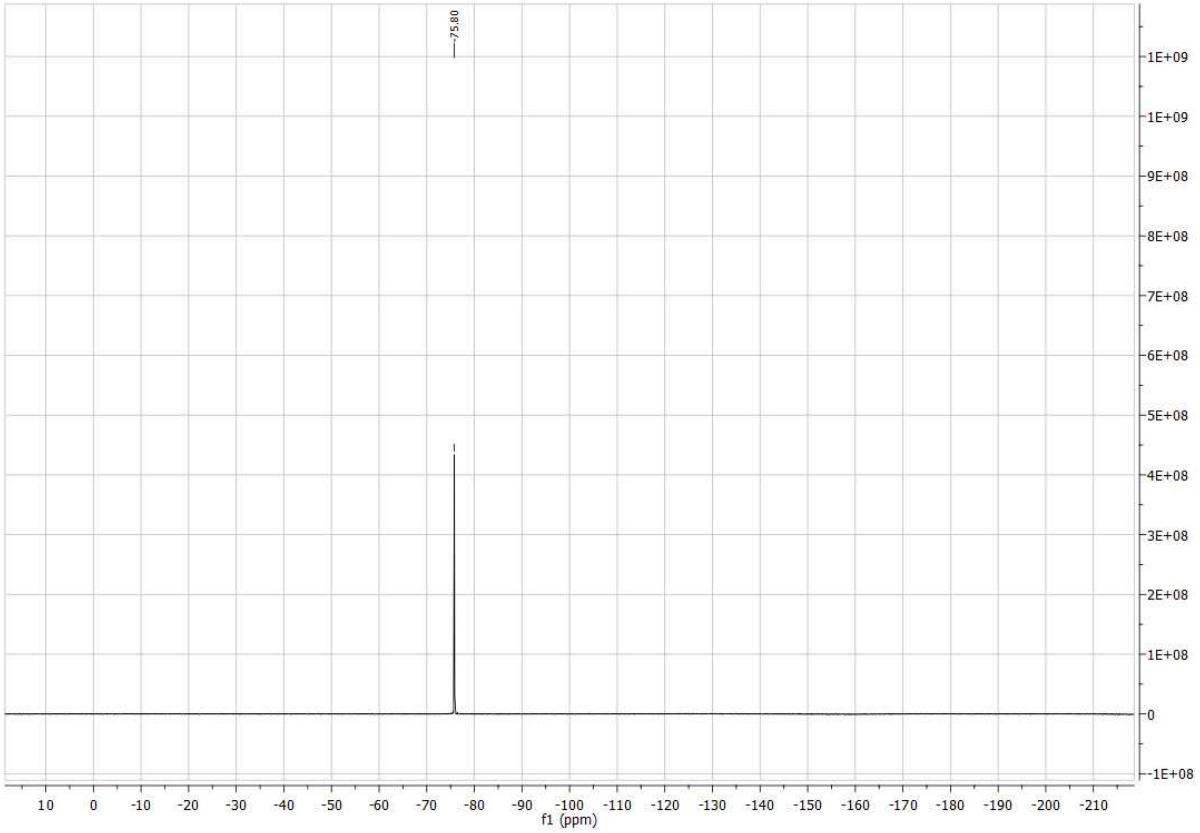
	Name	RT	Area	% Area
1	Peak1	26,448	53919	1,51
2	Peak2	33,896	3513667	98,49

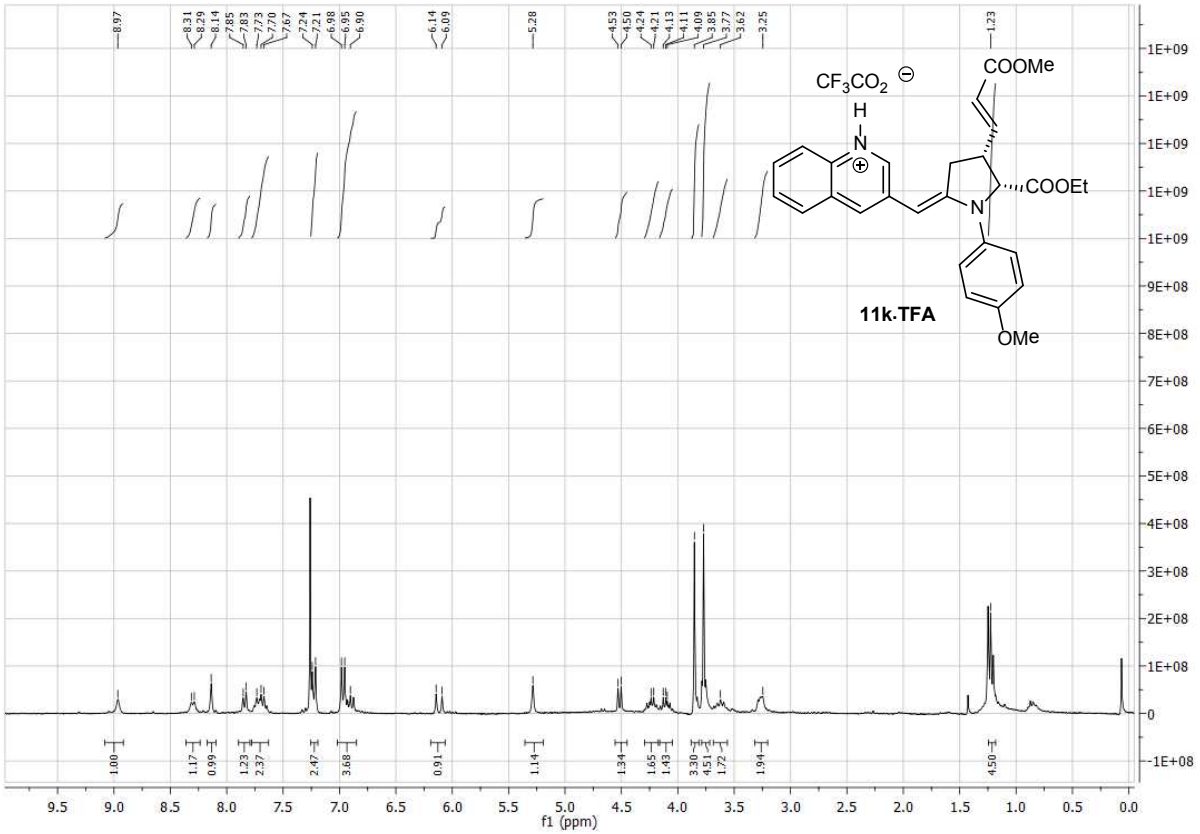
Reported by User: System
Report Method: rapport
Report Method ID 1032
Page: 1 of 1

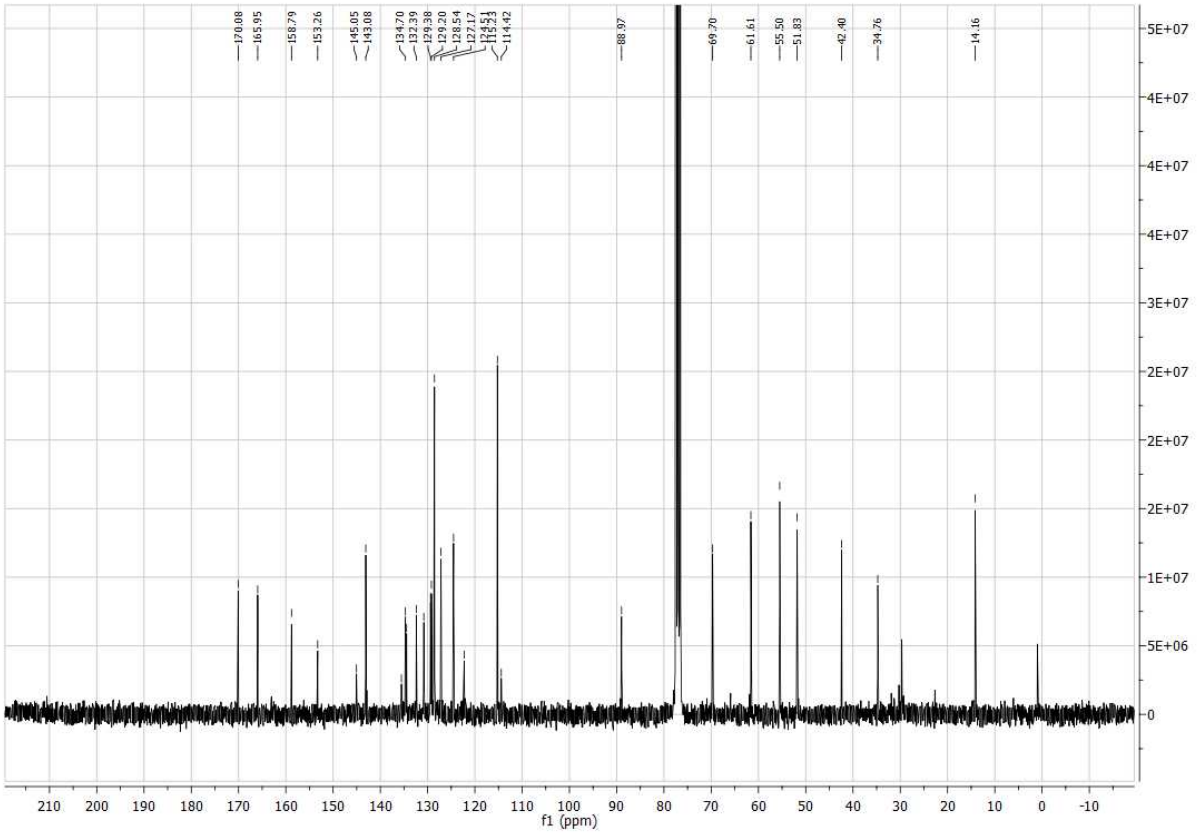
Project Name: IA-ODH-OJH 2012
Date Printed: 12/07/2012
10:26:58 Europe/Paris

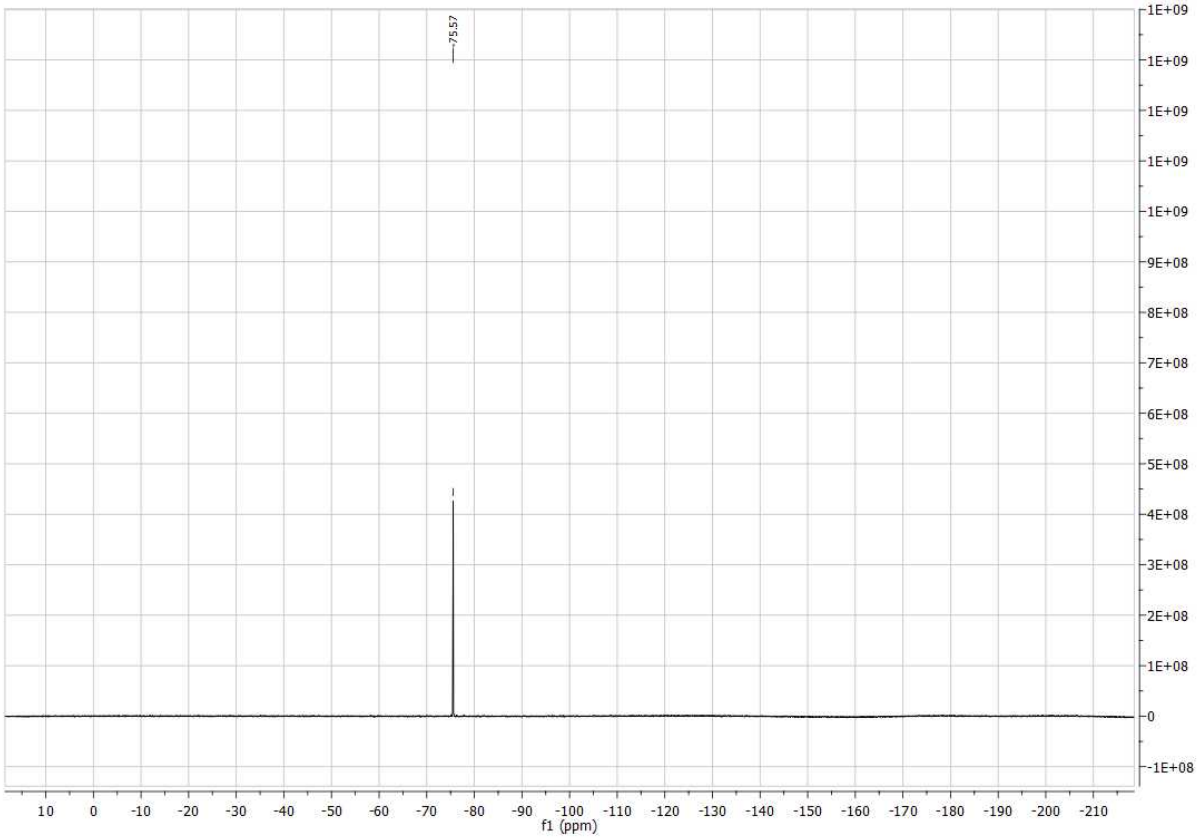

8.48
8.27
8.26
7.86
7.83
7.60
7.58
7.55
7.22
7.19
6.97
6.94
6.91
6.88
6.86
6.83
6.11
6.06
5.11
4.52
4.50
3.83
3.76
3.61
3.58
3.20
3.16
1.21
CF3CO2⊖
H
N
⊕
COOMe
COOEt
N
OMe
11j·TFA
1.00
1.07
1.07
1.09
1.99
3.17
0.94
0.77
0.84
2.43
2.81
2.86
1.82
3.29
f1 (ppm)

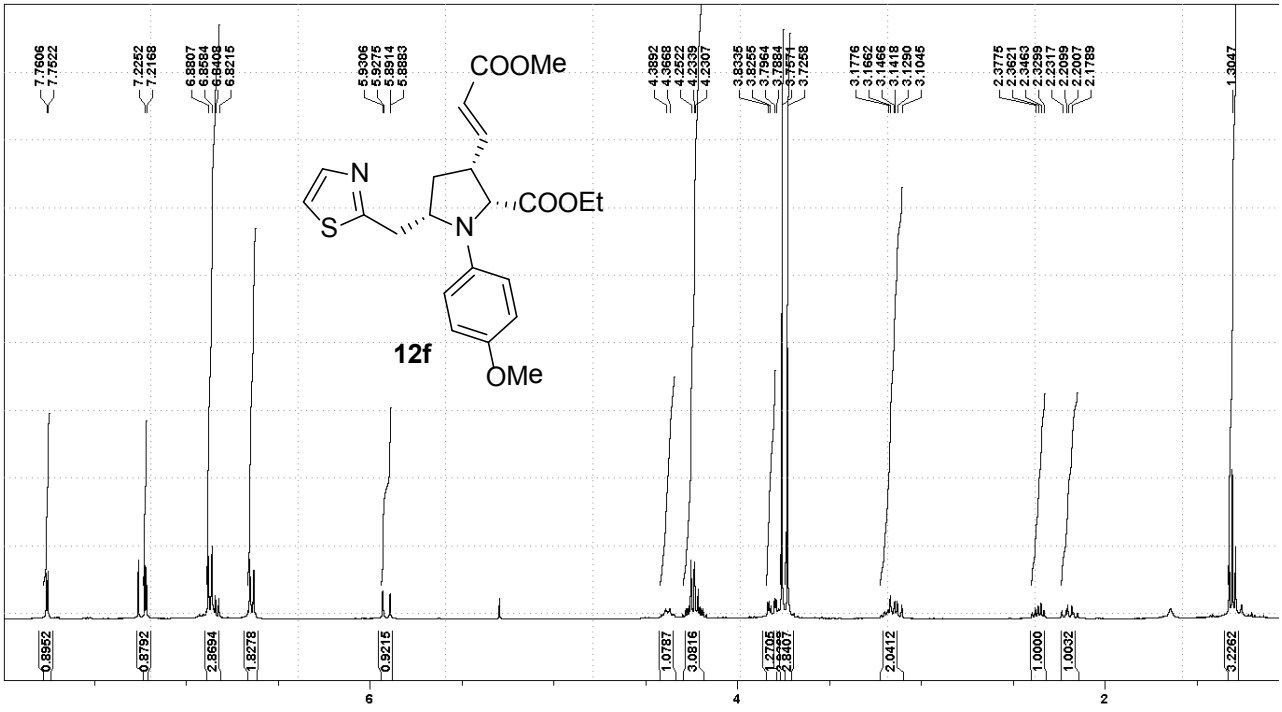

169.84
165.87
158.91
154.63
142.59
140.33
139.22
137.71
133.45
132.06
128.54
125.85
124.53
115.19
88.07
69.81
61.68
55.47
51.80
42.23
34.83
14.10
f1 (ppm)

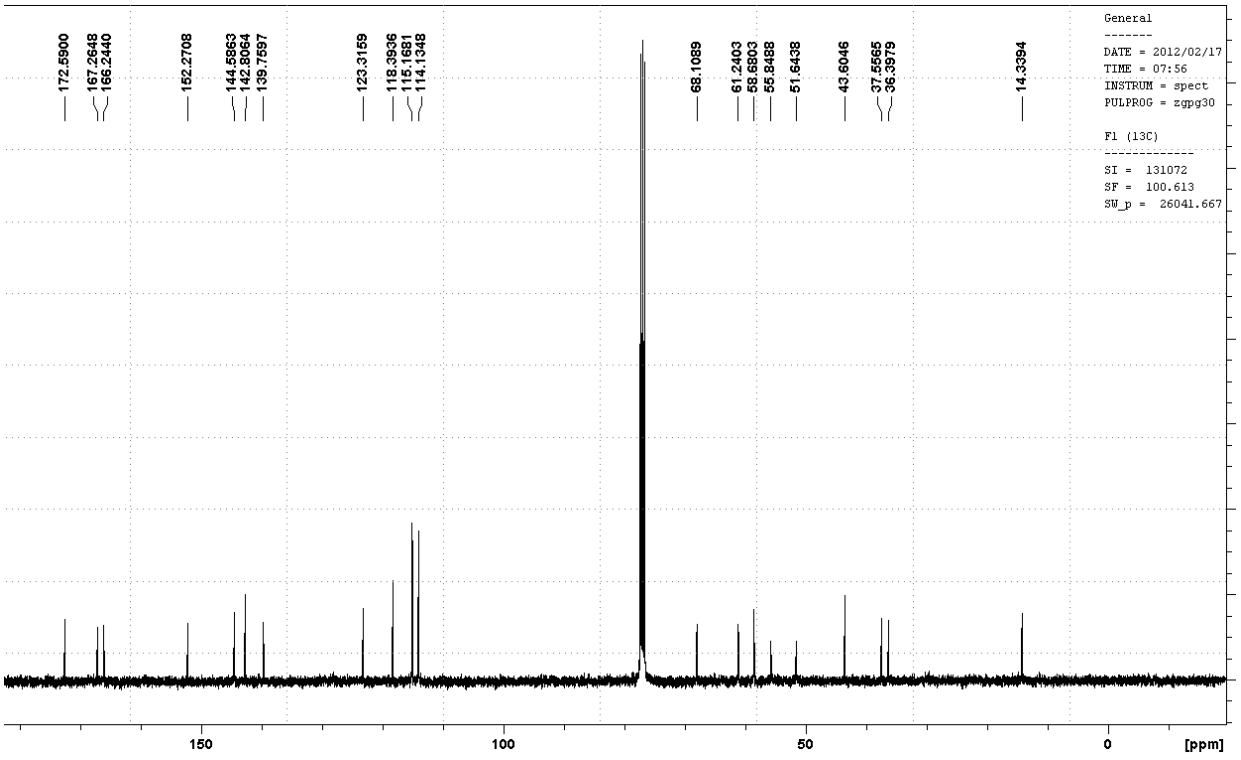

-75.80
f1 (ppm)

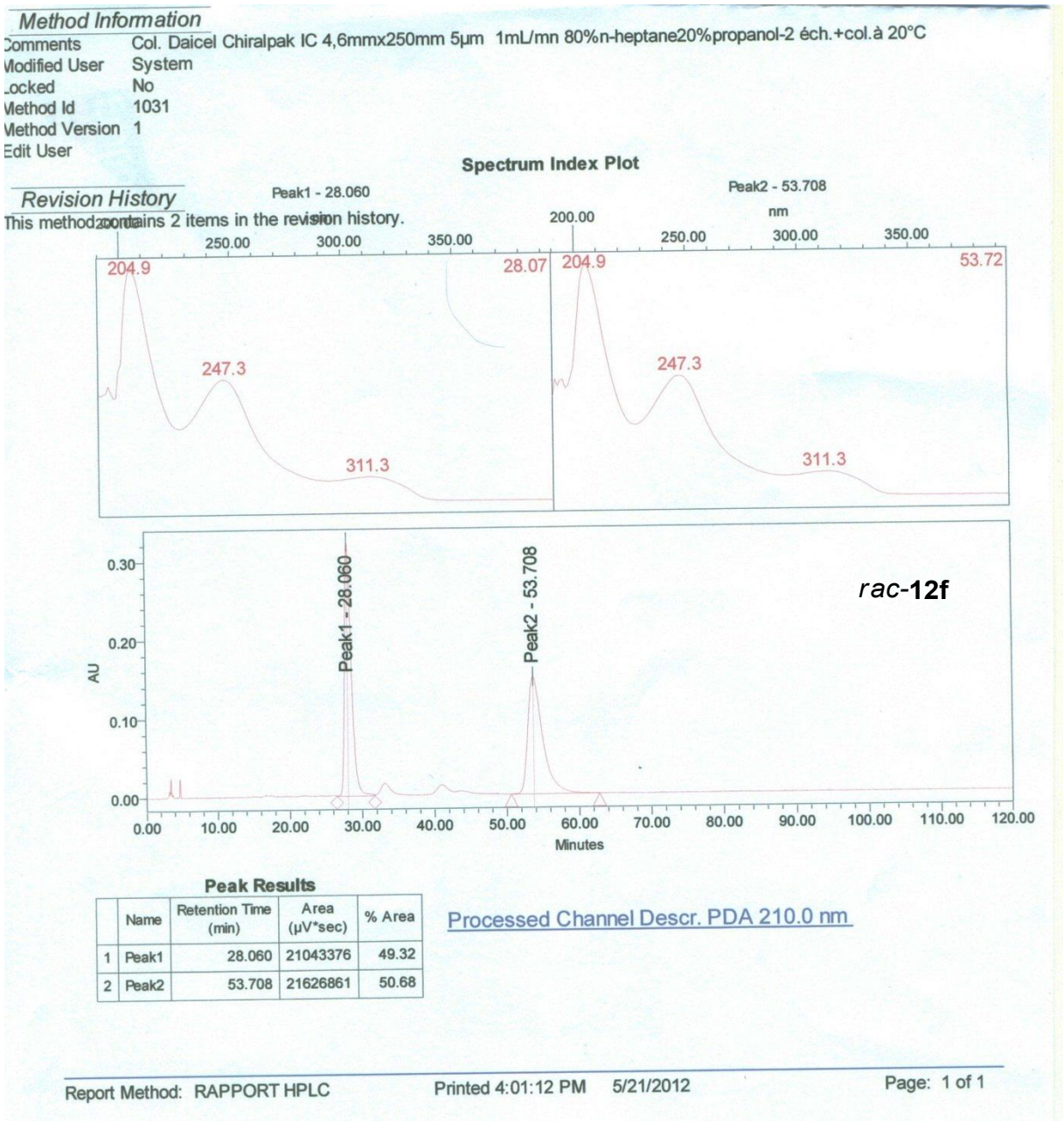

8.97
8.31
8.29
8.14
7.85
7.83
7.73
7.70
7.67
7.24
7.21
6.98
6.95
6.90
6.14
6.09
5.28
4.53
4.50
4.24
4.21
4.13
4.11
4.09
3.85
3.77
3.62
3.25
1.23
CF3CO2
H
N
COOMe
COOEt
N
OMe
11k·TFA
f1 (ppm)


170.08
165.95
158.79
153.26
145.05
143.08
134.70
132.39
129.38
129.20
128.54
127.17
114.42
88.97
69.70
61.61
55.50
51.83
42.40
34.76
14.16
f1 (ppm)


75.57
f1 (ppm)







	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	28.060	21043376	49.32
2	Peak2	53.708	21626861	50.68

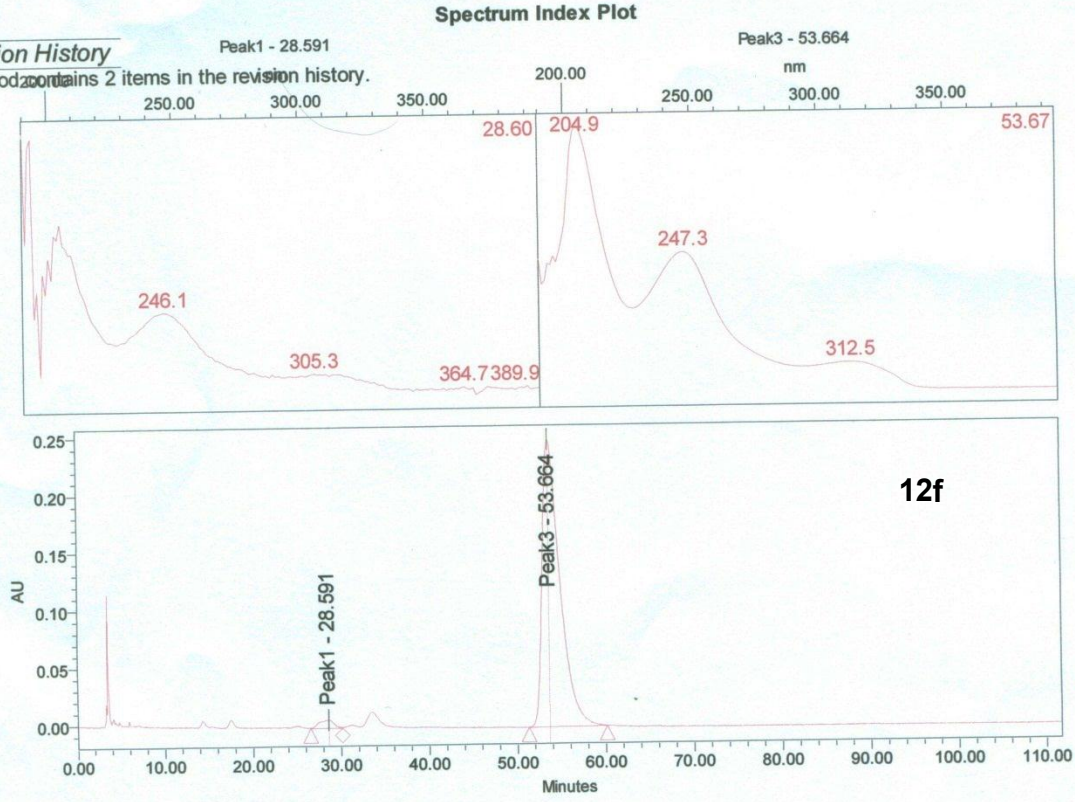
Method Information

Comments Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 80%n-heptane20%propanol-2 éch.+col.à 20°C
Modified User System
Locked No
Method Id 1031
Method Version 1
Edit User

Revision History

This method contains 2 items in the revision history.

Spectrum Index Plot

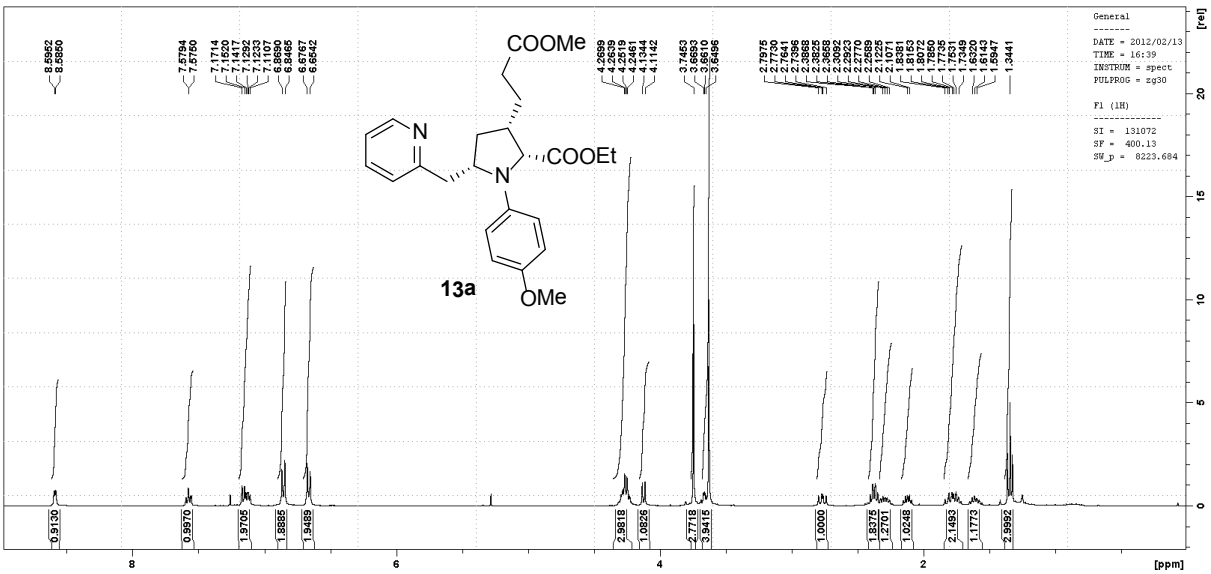


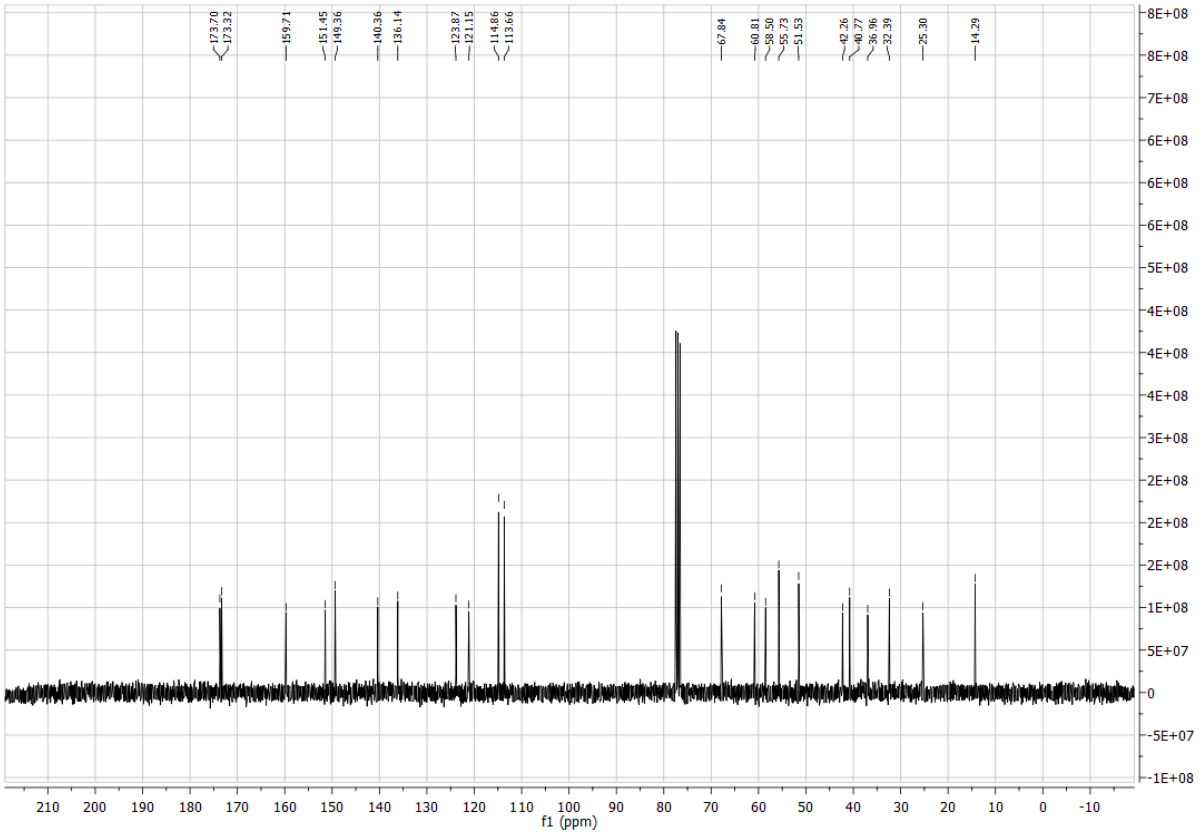
Peak Results

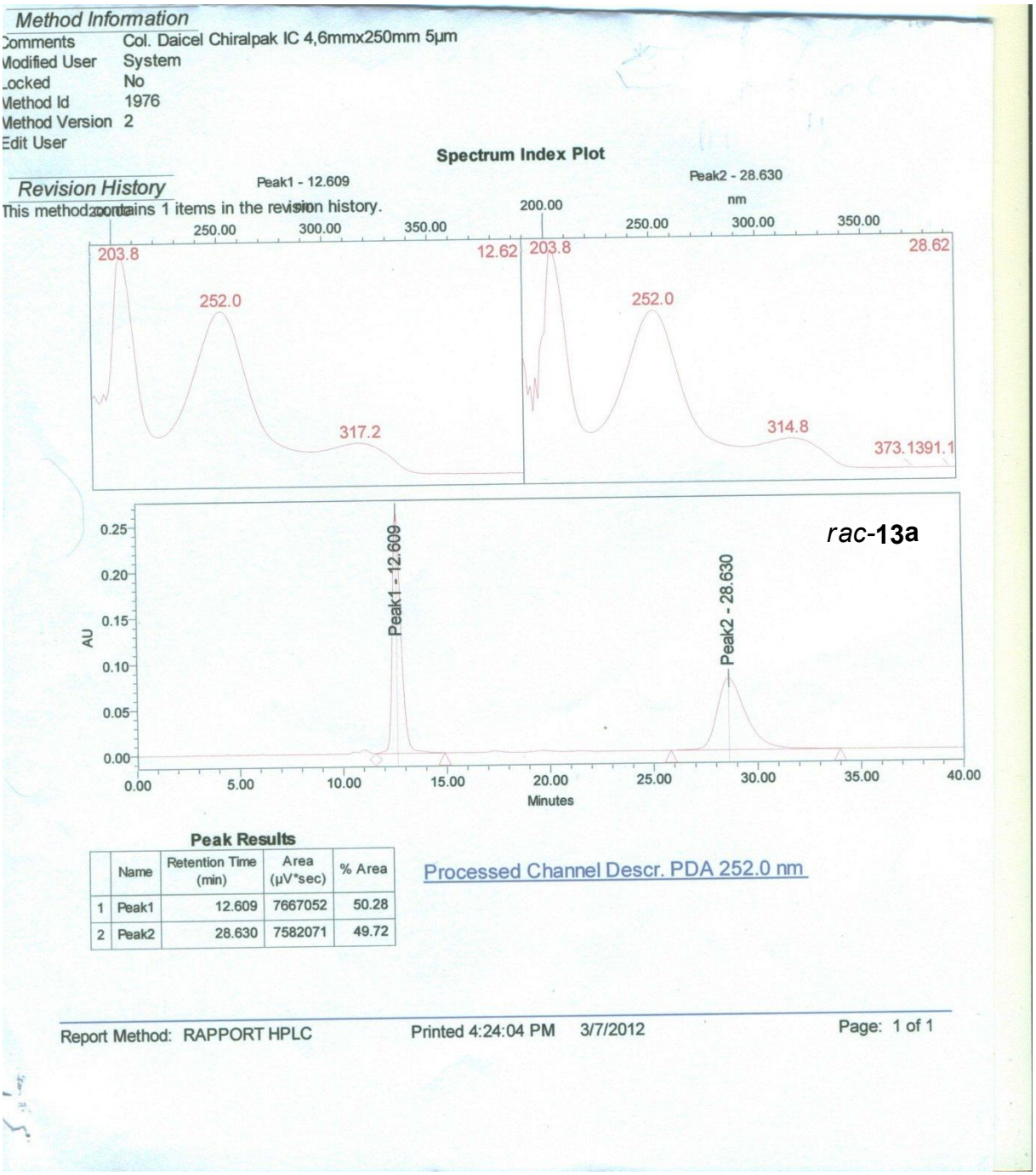
	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	28.591	849184	2.36
2	Peak2	33.506		
3	Peak3	53.664	35072079	97.64

Processed Channel Descr. PDA 210.0 nm

Report Method: RAPPORT HPLC Printed 4:03:26 PM 5/21/2012 Page: 1 of 1


COOMe
COOEt
N
N
13a
OMe
[ppm]
[rel]


f1 (ppm)

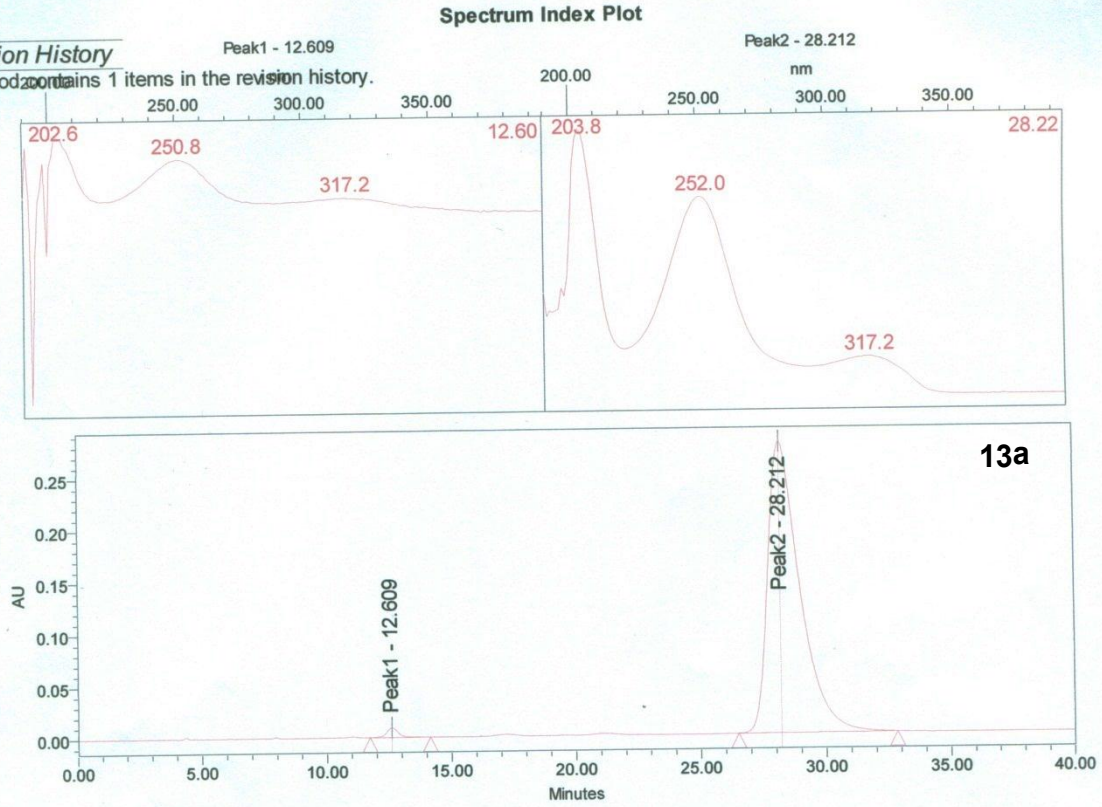

Method Information
Comments Col. Daicel Chiralpak IC 4,6mmx250mm 5µm
Modified User System
Locked No
Method Id 1976
Method Version 2
Edit User
Revision History
This method contains 1 items in the revision history.
Spectrum Index Plot
Peak1 - 12.609
Peak2 - 28.630
nm
200.00
250.00
300.00
350.00
203.8
12.62
252.0
317.2
28.62
314.8
373.1391.1
rac-13a
AU
0.25
0.20
0.15
0.10
0.05
0.00
0.00
5.00
10.00
15.00
20.00
25.00
30.00
35.00
40.00
Minutes
Peak Results
Name
Retention Time (min)
Area (µV*sec)
% Area
1 Peak1 12.609 7667052 50.28
2 Peak2 28.630 7582071 49.72
Processed Channel Descr. PDA 252.0 nm
Report Method: RAPPORT HPLC
Printed 4:24:04 PM 3/7/2012
Page: 1 of 1

Method Information

Comments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm
Modified User	System
Locked	No
Method Id	1976
Method Version	2
Edit User	

Revision History

This method contains 1 items in the revision history.

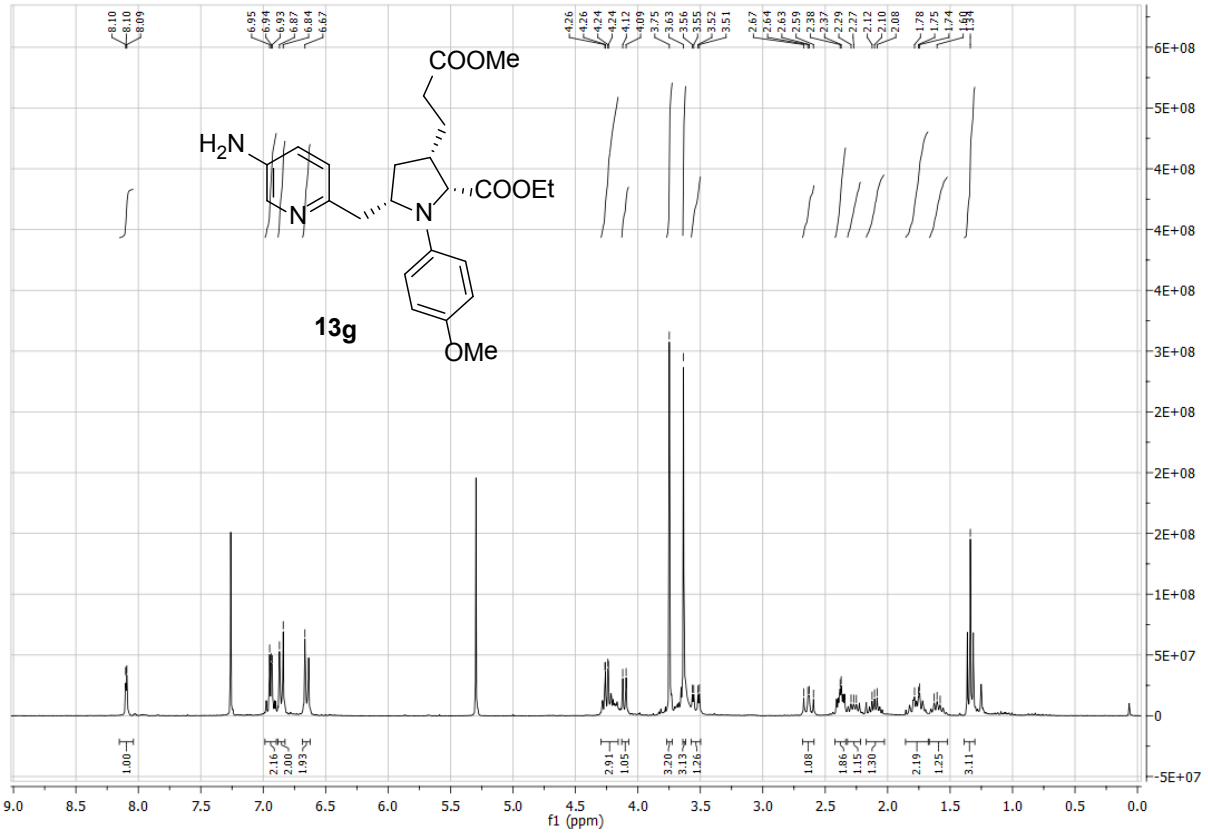


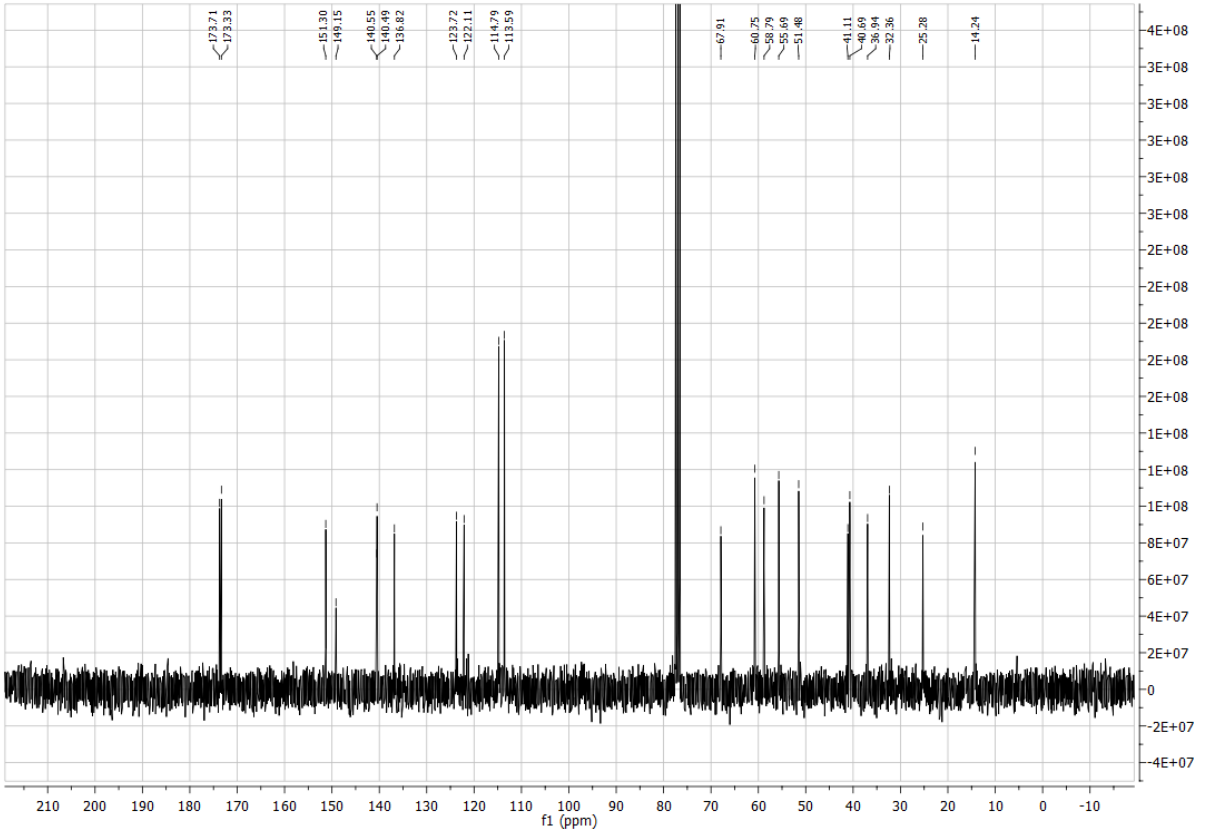
Peak Results

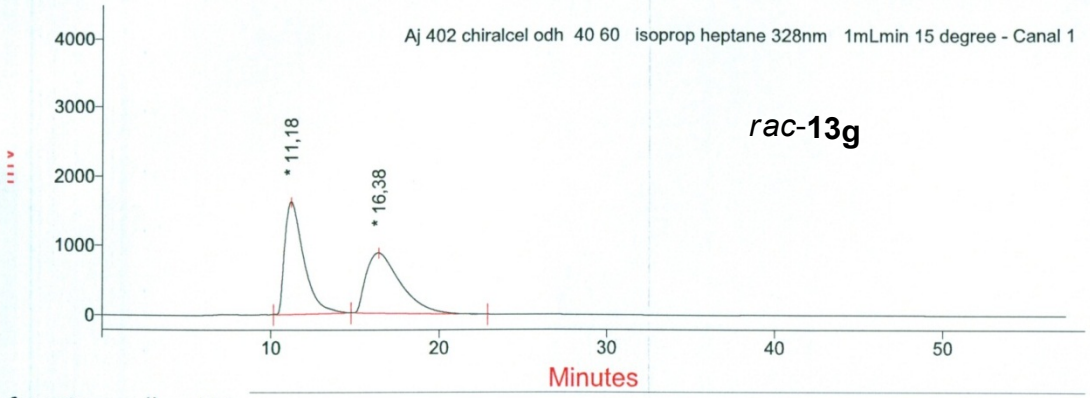
	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	12.609	311511	1.23
2	Peak2	28.212	24947114	98.77

Processed Channel Descr. PDA 252.0 nm

Report Method: RAPPORT HPLC Printed 4:23:52 PM 3/7/2012 Page: 1 of 1


COOMe
H_2N
N
N
COOEt
OMe
13g
f1 (ppm)


f1 (ppm)



ıformations sur l'acquisition

ıte d'acquisition	02/12/2011 14:33:38 (+01:00) (Azur 4.6.0.0)		
ɔurce de l'acquisition :			
	INT7Channel 1		
ırée	57,30 Minutes	Nb de points	3439
tesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		11,18	126894,44	51,01	0,00	0,00
2		16,38	121879,12	48,99	0,00	0,00
SOMME			248773,56	100,00	0,00	0,00

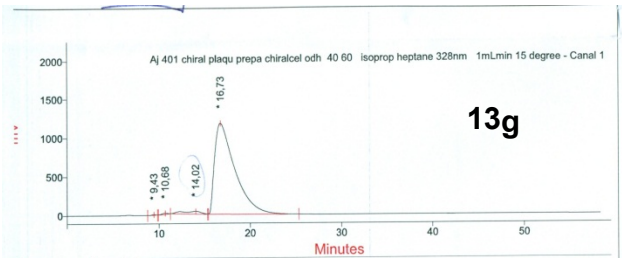
ıformations sur l'échantillon

ɔm	Aj 402 chiralcel odh 40 60 isop	Type d'échantillom	1mLmin 1!Echantillon
' Flacon	1		
uantité	0,000000 mg	Volume d'injection	20,00 µl
lution	1	Diviseur	1

= valeur initiale modifiée)

ıformations :

Aj 402 chiralcel odh 40 60 isoprop heptane 328nm 1mLmin 15 degree



formations sur l'acquisition

te d'acquisition	03/12/2011 17:16:56 (+01:00) (Azur 4.6.0.0)
ource de l'acquisition :	
	INT7Channel 1
rée	58,30 Minutes
Nb de points	3499
tesse d'acquisition	1,00 points/seconde

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
1		9,43	206,17	0,11	0,00	0,00
2		10,68	563,68	0,30	0,00	0,00
3		14,02	4921,40	2,64	0,00	0,00
4		16,73	180847,17	96,95	0,00	0,00
SOMME			186538,42	100,00	0,00	0,00

401 chiral plaqu prepa chiralcel odh 40 60 isoprop heptane 328nm 1mLmin 15 degree - Canal 1 Page 1/2

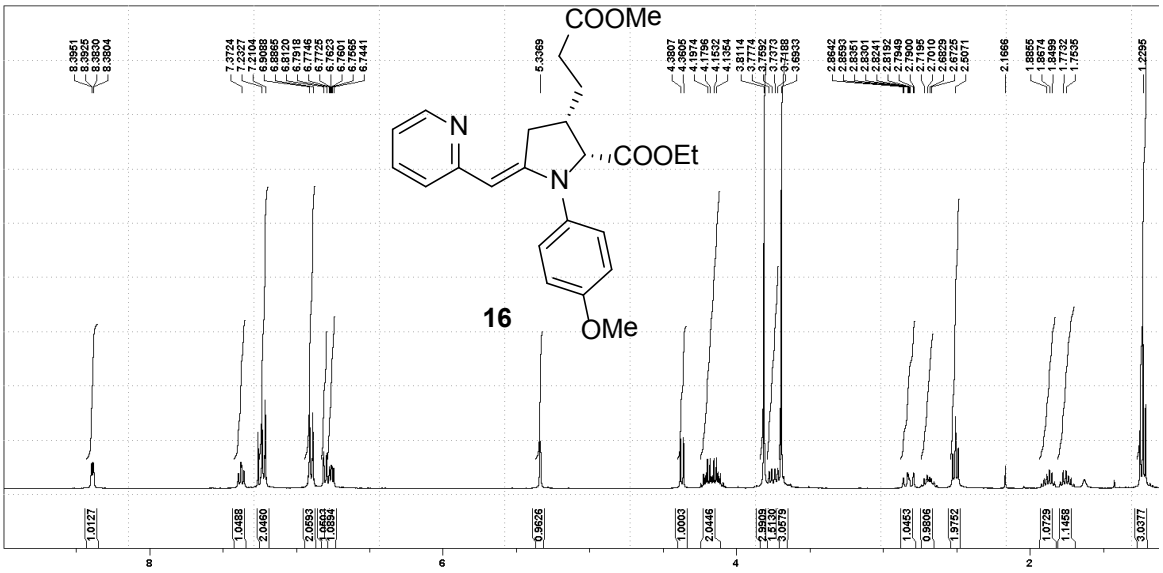
Quantité	0,000000 mg	Volume d'injection	20,00 µl
Dilution	1	Diviseur	1

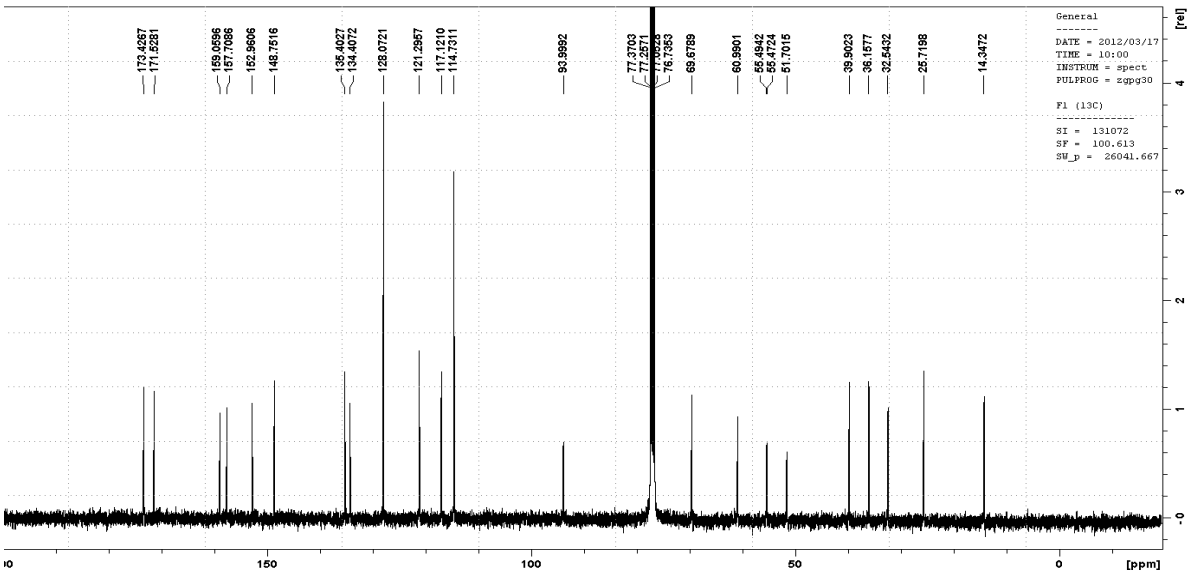
(* = valeur initiale modifiée)

Informations :

Aj 401 chiral plaqu prepa chiralcel odh 40 60 isoprop heptane 328nm 1mLmin 15 degree

Aj 401 chiral plaqu prepa chiralcel odh 40 60 isoprop heptane 328nm 1mLmin 15 degree - Canal 1 Pag





power software

RAPPORT HPLC

Reported by User: System

Project Name: IC_OBH_ASH2012

AJ535

Instrument Method: IC 1mL60%nhep40%prop_20dC

Stored: 1/18/2012 10:25:00 AM

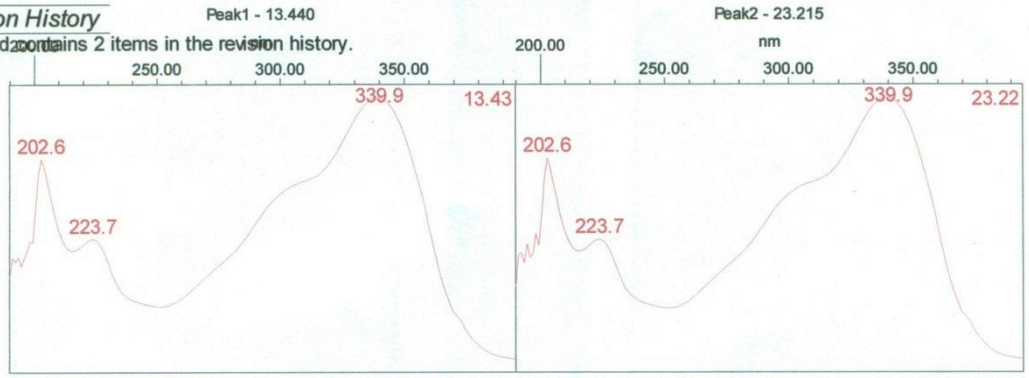
Method Information

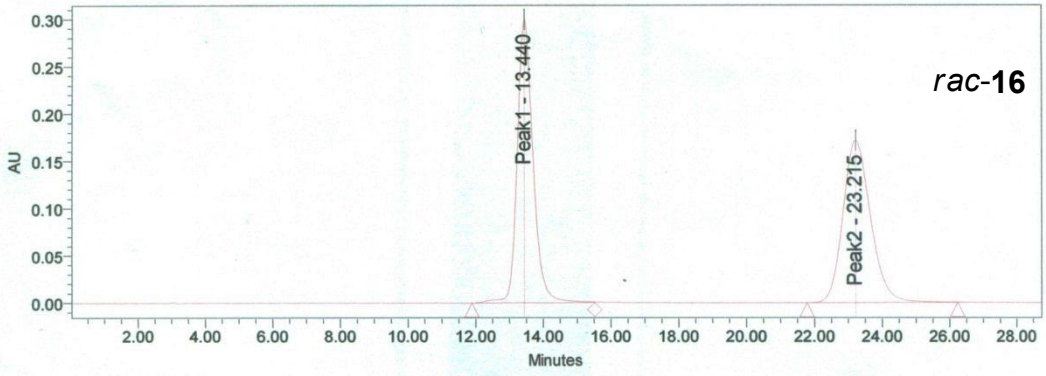
Comments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 60%n-heptane40%propanol-2 éch.+col.à 20°C
Modified User	System
Locked	No
Method Id	1019
Method Version	1
Edit User	

Revision History

This method contains 2 items in the revision history.

Spectrum Index Plot





***rac*-16**

Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	13.440	9855955	50.29
2	Peak2	23.215	9742204	49.71

Processed Channel Descr. PDA 340.0 nm

Report Method: RAPPORT HPLC Printed 10:50:10 AM 4/11/2012 Page: 1 of 1

Empower software

RAPPORT HPLC

Reported by User: System

Project Name: IC_OBH_ASH2012

AJ545

Instrument Method: IC 1mL60%nhep40%prop_20dC

Stored: 1/18/2012 10:25:00 AM

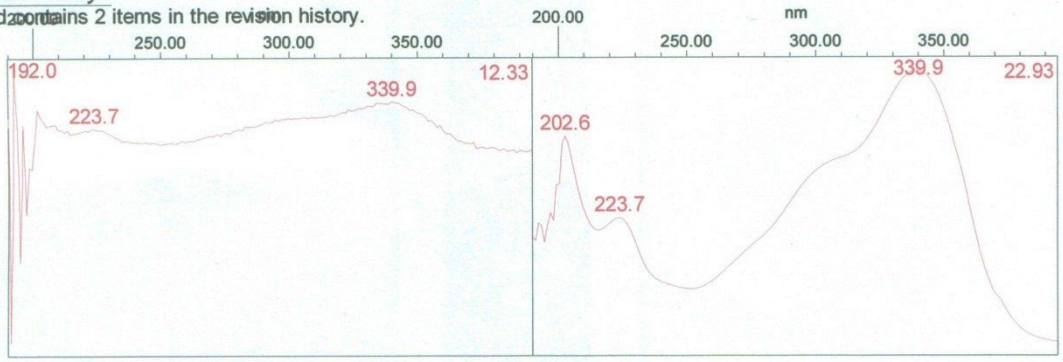
Method Information

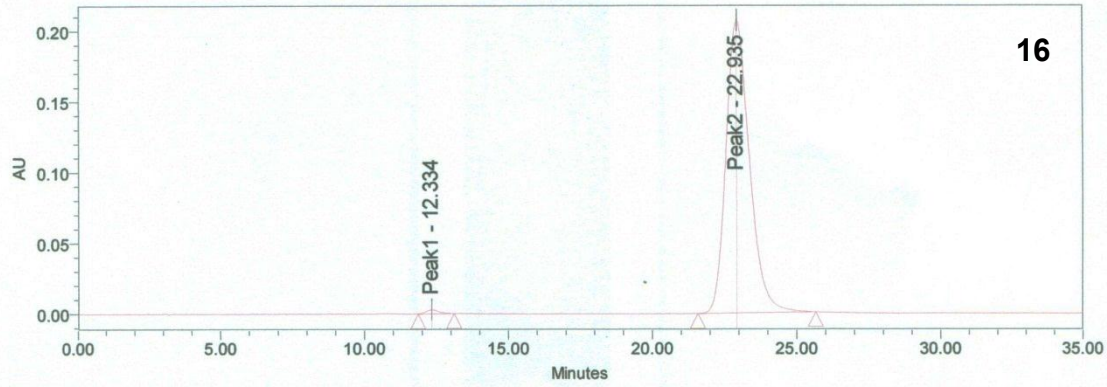
Comments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 60%n-heptane40%propanol-2 éch.+col.à 20°C
Modified User	System
Locked	No
Method Id	1019
Method Version	1
Edit User	

Revision History

This method contains 2 items in the revision history.

Spectrum Index Plot





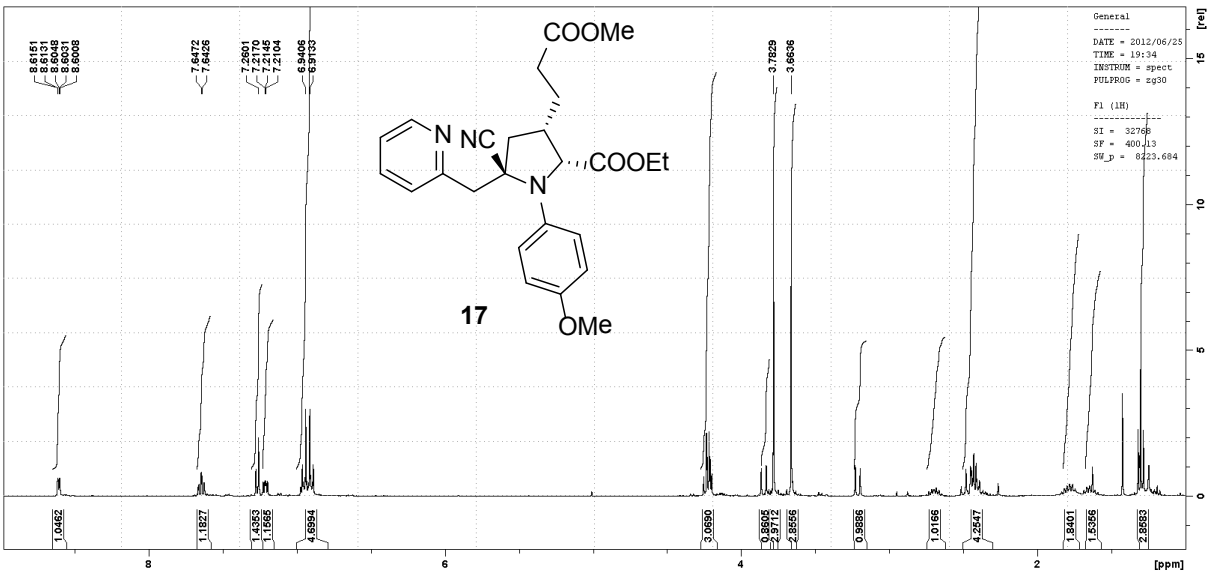
16

Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	12.334	87877	0.74
2	Peak2	22.935	11813784	99.26

Processed Channel Descr. PDA 340.0 nm

Report Method: RAPPORT HPLC Printed 10:47:58 AM 7/20/2012 Page: 1 of 1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8.6043
8.6031
8.6008
7.6472
7.6426
7.2601
7.2170
7.2145
7.2104
6.9406
6.9133
3.7829
3.6636
COOMe
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NC
COOEt
N
OMe
17
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SI = 32768
SF = 400.13
SW_p = 8223.684
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1.1565
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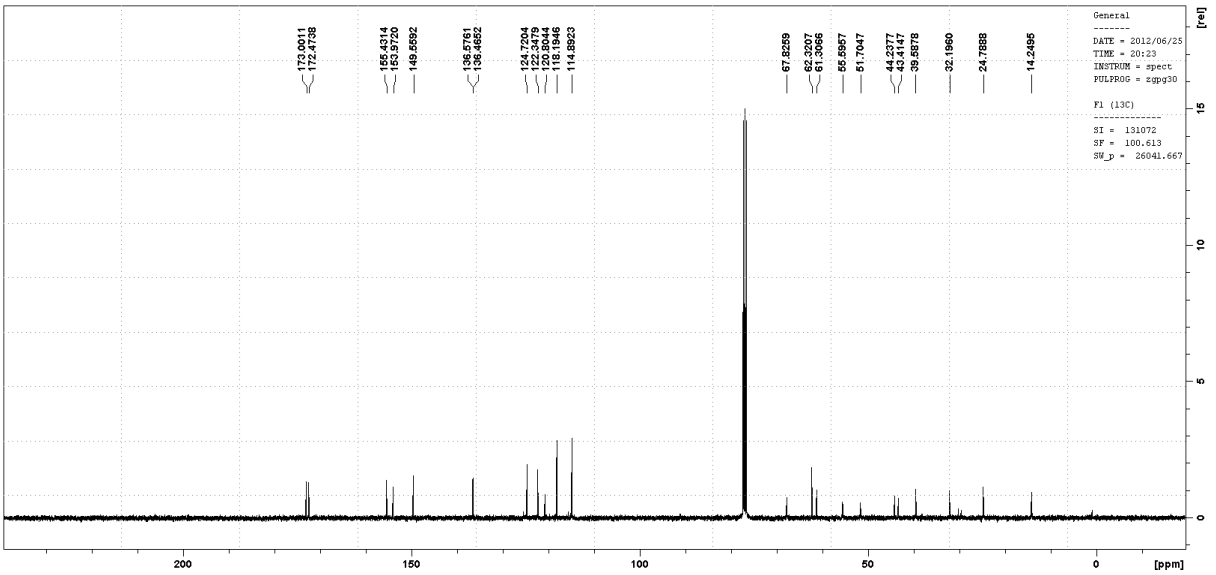
[ppm]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149.5592
136.5761
136.4652
124.7204
122.3479
120.0844
118.1946
114.8923
67.8259
62.3207
61.3066
55.5957
51.7047
44.2377
43.4147
39.5878
32.1960
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TIME = 20:23
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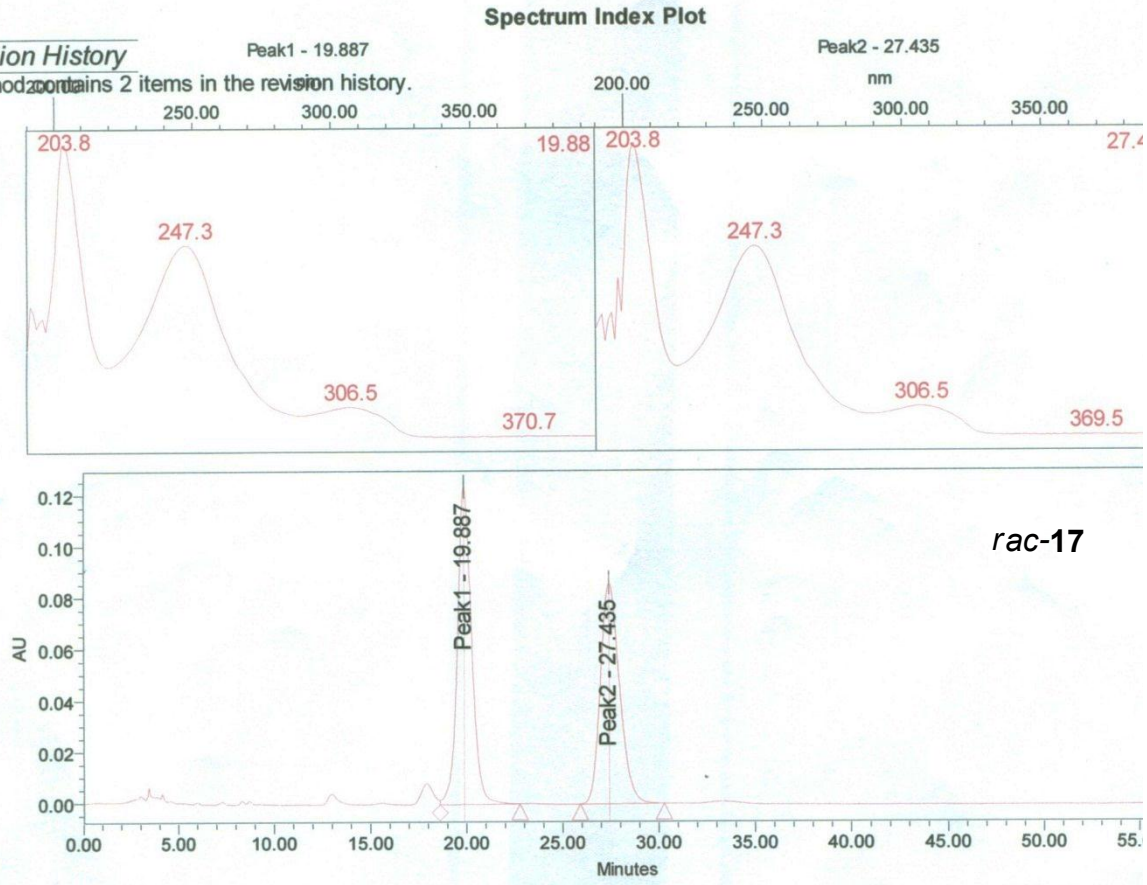
PULPROG = zgpg30
F1 (13C)
SI = 131072
SF = 100.613
SW_p = 26041.667
[rel]
[ppm]

Method Information

ɪmments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 60%n-heptane40%propanol-2 éch.+col.à 20°C
ɔdified User	System
cked	No
ɛthod Id	1019
ɛthod Version	1
lit User	

Revision History

is method contains 2 items in the revision history.



rac-**17**

Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	19.887	6363204	51.48
2	Peak2	27.435	5997001	48.52

Processed Channel Descr. PDA 247.0 nm

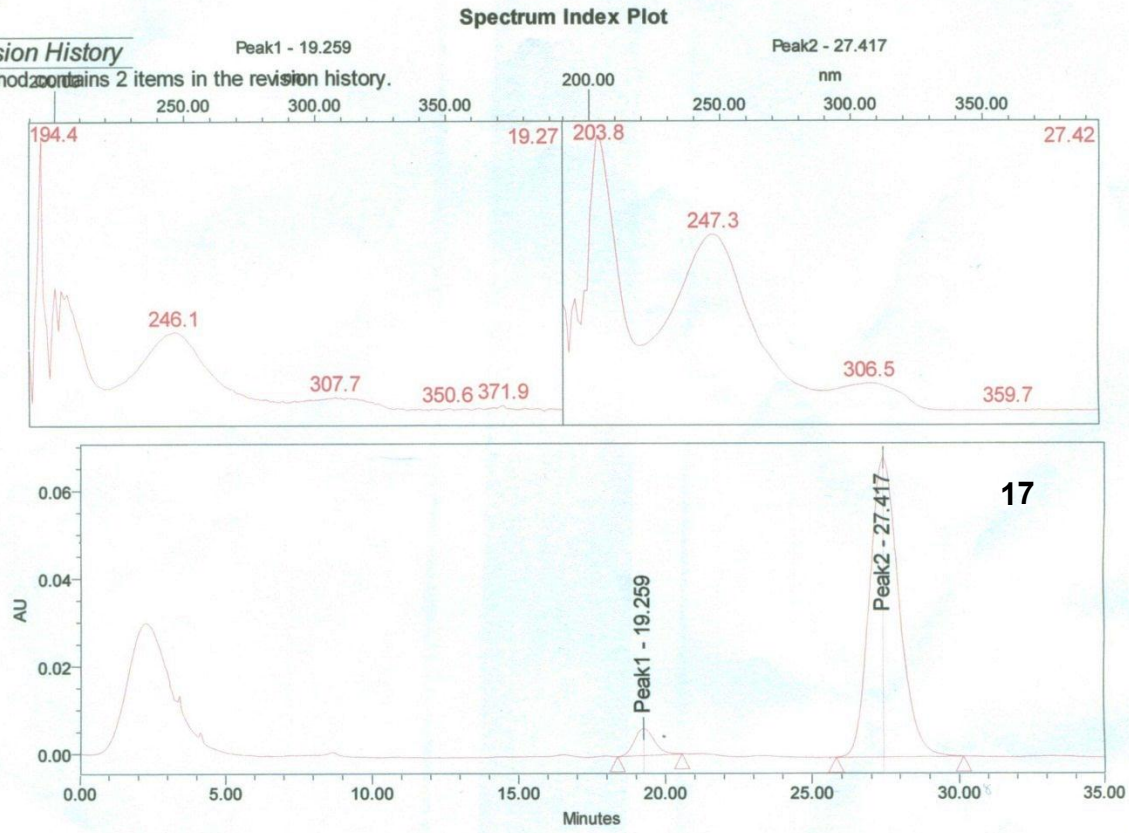
Report Method: RAPPORT HPLC Printed 10:50:10 AM 4/11/2012 Page: 1 of 1

Method Information

›mments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm 1mL/mn 60%n-heptane40%propanol-2 éch.+col.à 20°C
›dified User	System
cked	No
ethod Id	1019
ethod Version	1
lit User	

Revision History

is method contains 2 items in the revision history.

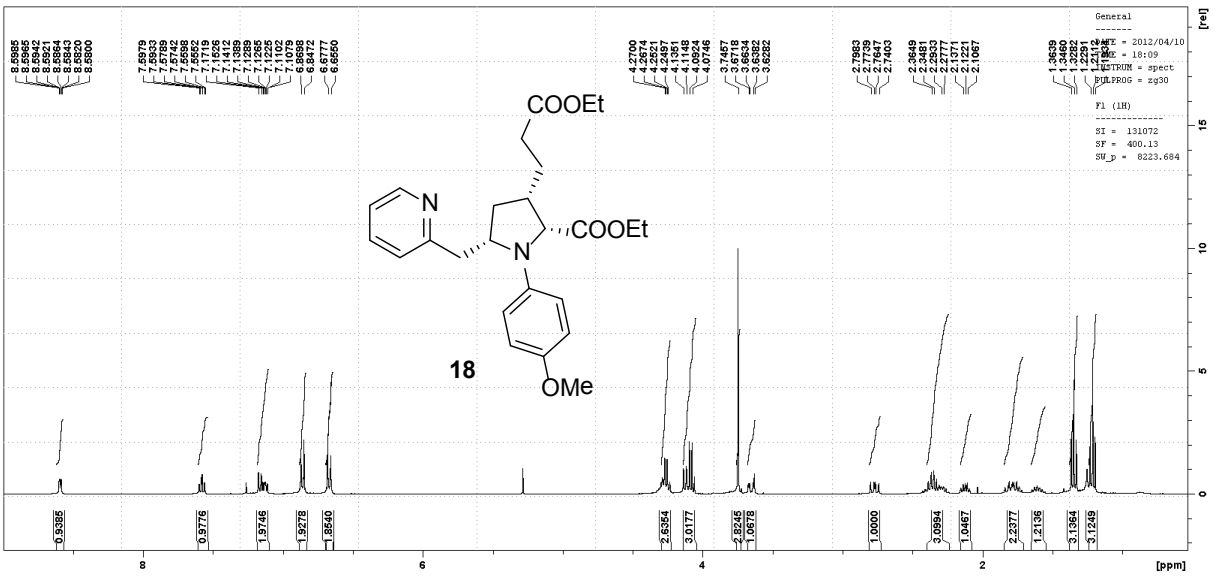


Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	19.259	291856	5.78
2	Peak2	27.417	4760675	94.22

Processed Channel Descr. PDA 247.0 nm

Report Method: RAPPORT HPLC Printed 10:50:02 AM 4/11/2012 Page: 1 of 1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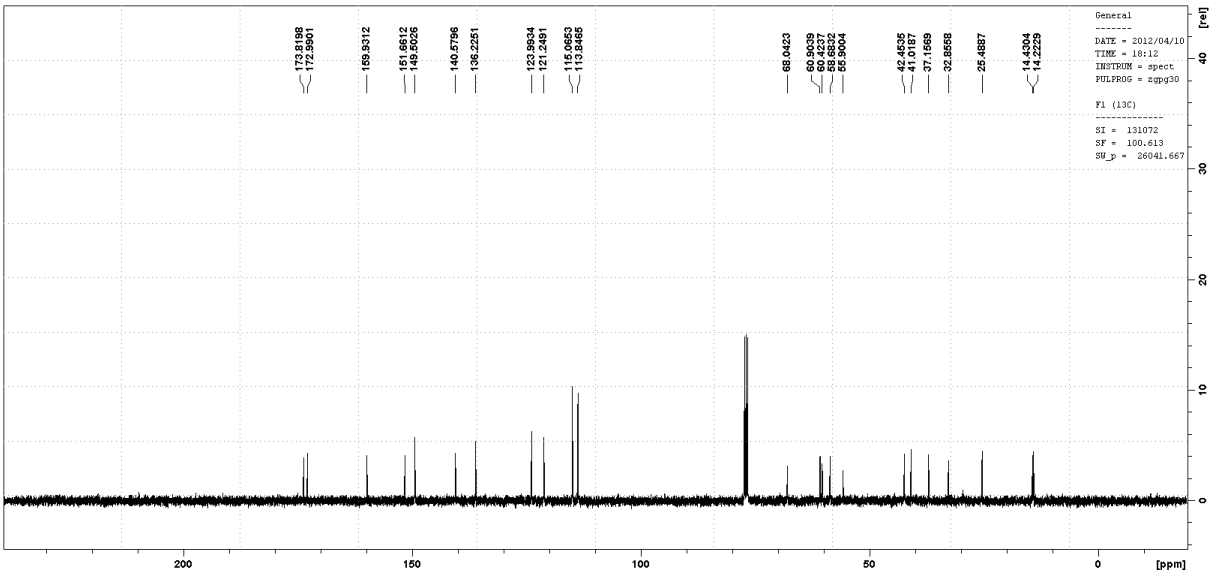
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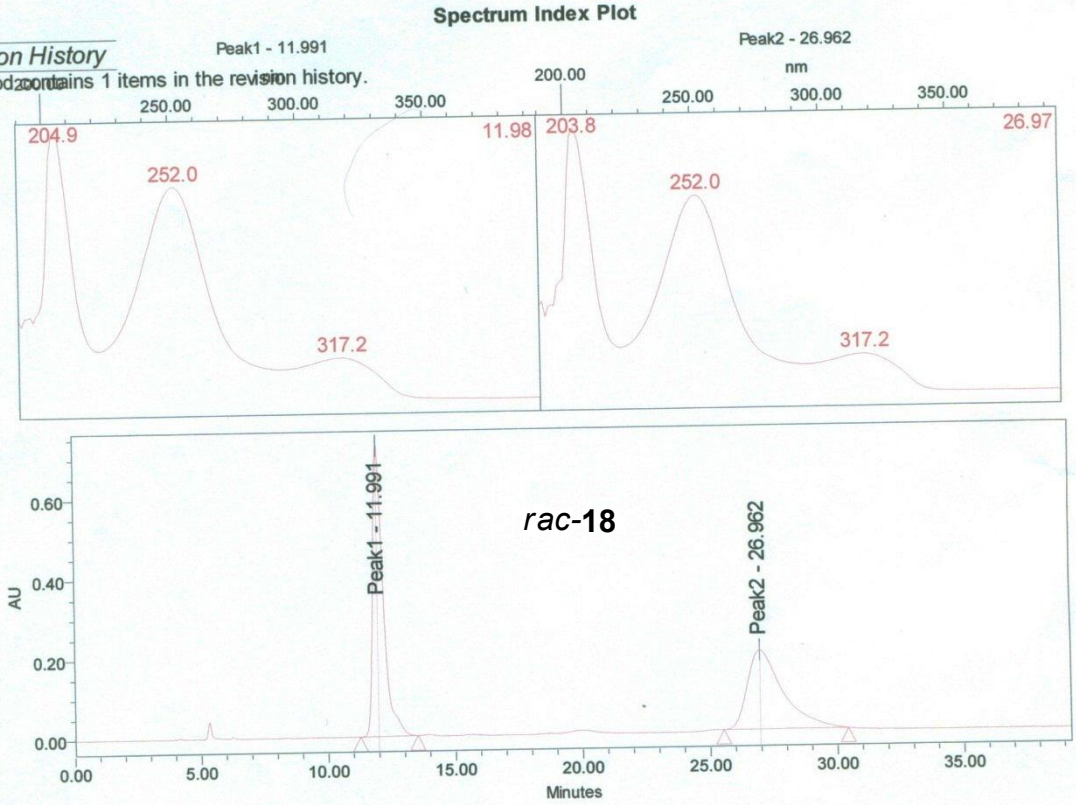
Method Information

omments Col. Daicel Chiralpak IC 4,6mmx250mm 5µm
lodified User System
ocked No
lethod Id 1976
lethod Version 2
dit User

Revision History

his method contains 1 items in the revision history.

Spectrum Index Plot



rac-**18**

Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	11.991	21046716	52.34
2	Peak2	26.962	19165460	47.66

Processed Channel Descr. PDA 252.0 nm

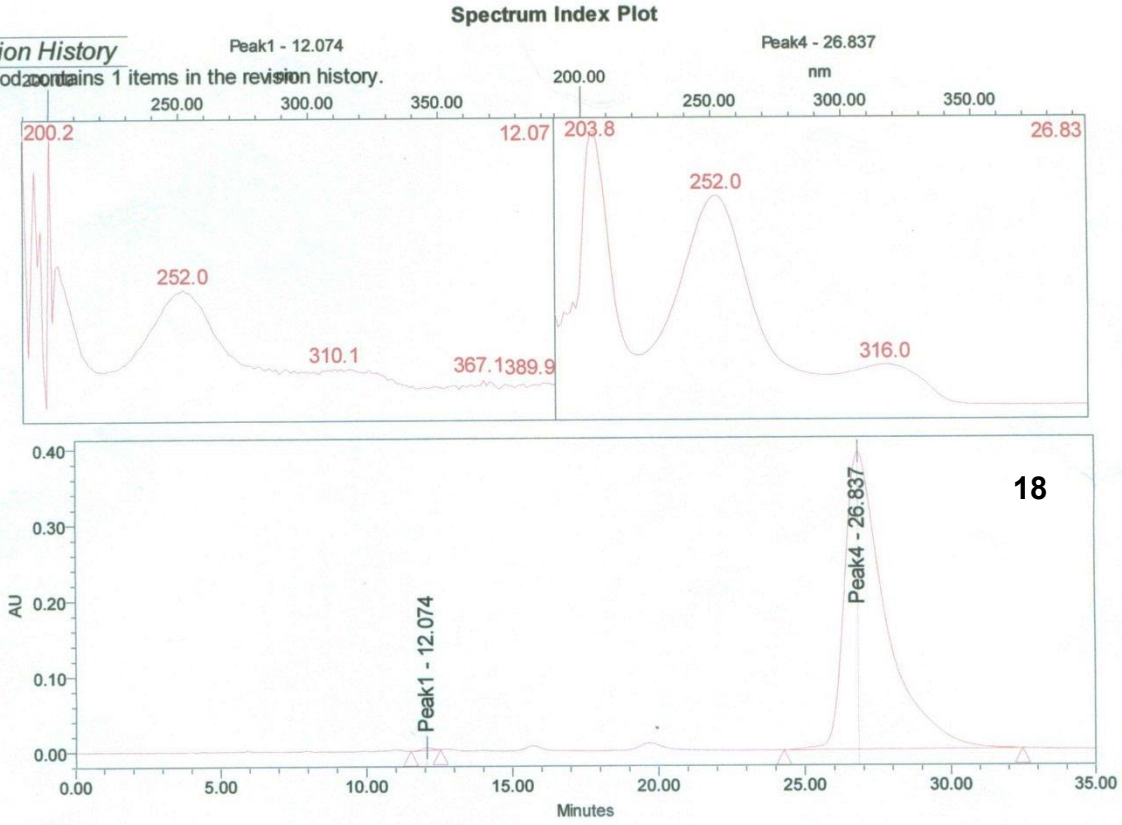
Report Method: RAPPORT HPLC Printed 1:41:18 PM 4/11/2012 Page: 1 of 1

Method Information

›mments	Col. Daicel Chiralpak IC 4,6mmx250mm 5µm
ɔdified User	System
ıcked	No
ethod Id	1976
ethod Version	2
‡it User	

Revision History

his method contains 1 items in the revision history.



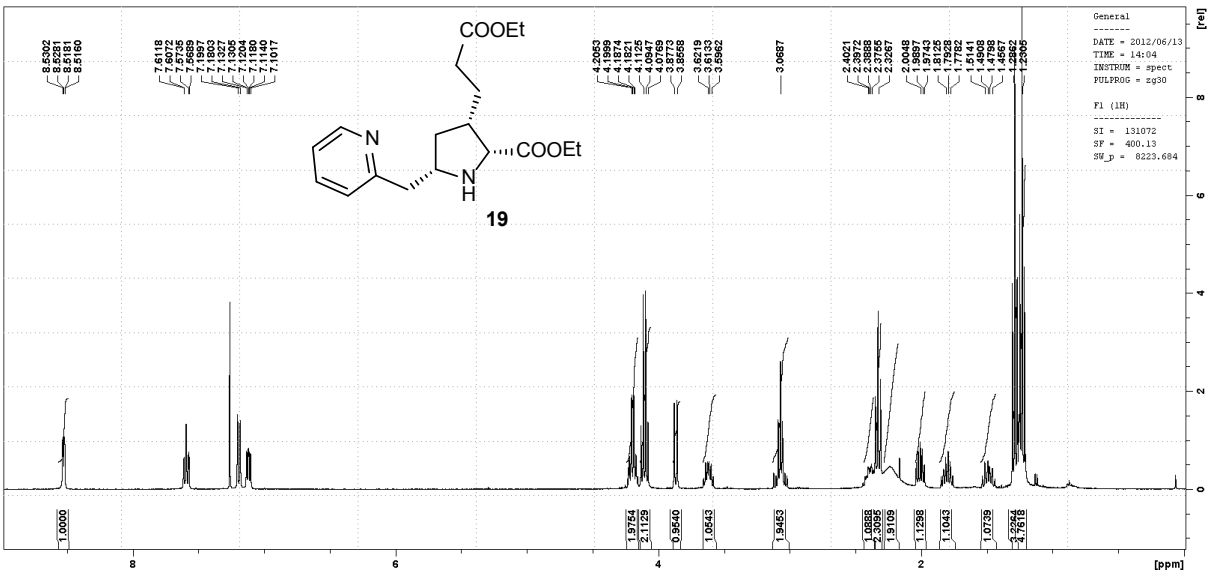
18

Peak Results

	Name	Retention Time (min)	Area (µV*sec)	% Area
1	Peak1	12.074	83901	0.22
2	Peak4	26.837	38467703	99.78

Processed Channel Descr. PDA 252.0 nm

Report Method: RAPPORT HPLC Printed 1:43:34 PM 4/11/2012 Page: 1 of 1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4.1874
4.1821
4.1125
4.0947
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2.3858
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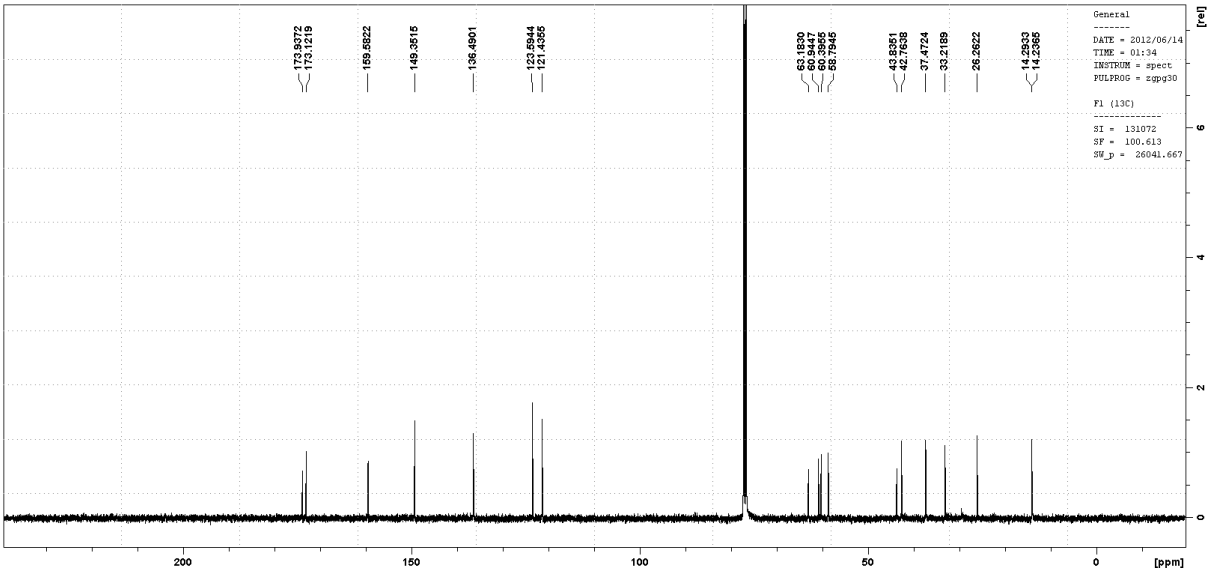
SW_p = 8223.684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26.2622
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PULPROG = zgpg30
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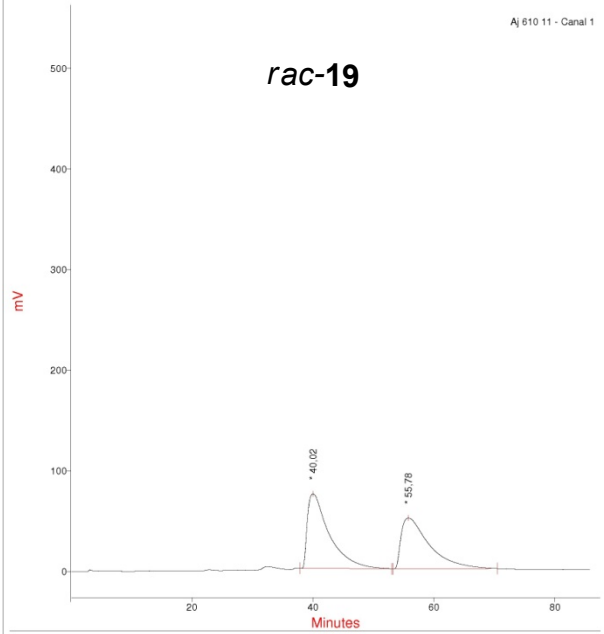
SI = 131072
SF = 100.613
SW_p = 26041.667

Analyse — mardi 7 août 2012 18:29:17

Analyse : Aj 610 11

Aj 610 11 - Canal 1

rac-**19**



Aj 610 11 - Canal 1 — Page 1/2

Analyse — mardi 7 août 2012 18:29:17

Informations sur l'acquisition

Date d'acquisition	01/08/2012 13:24:06 (+01:00) (Azur 4.6.0.0)		
Source de l'acquisition :	INT7Channel 1		
Durée	85,77 Minutes	Nb de points	5147
Vitesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
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2		55,78	16276,02	46,79	0,00	0,00
SOMME			34785,58	100,00	0,00	0,00

Informations sur l'échantillon

Nom	Aj 610	Type d'échantillon	Echantillon
N° Flacon	1		
Quantité	0,000000 mg	Volume d'injection	60,00 µl
Dilution	1	Diviseur	1

(* = valeur initiale modifiée)
Informations :
AD, 254 nm, 23°C
hept/iprOH 95/5
1 mL/min
254

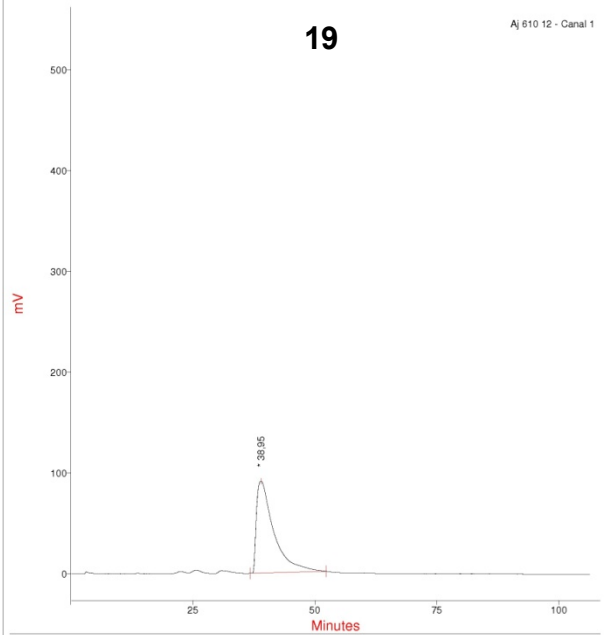
Aj 610 11 - Canal 1 — Page 2/2

Analyse — mardi 7 août 2012 18:32:38

Analyse : Aj 610 12

Aj 610 12 - Canal 1

19



Aj 610 12 - Canal 1 — Page 1/2

Analyse — mardi 7 août 2012 18:32:38

Informations sur l'acquisition

Date d'acquisition	01/08/2012 14:57:12 (+01:00) (Azur 4.6.0.0)		
Source de l'acquisition :	INT7Channel 1		
Durée	106,37 Minutes	Nb de points	6383
Vitesse d'acquisition	1,00 points/seconde		

Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Résultats	% Résultats
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SOMME			22556,85	100,00	0,00	0,00

Informations sur l'échantillon

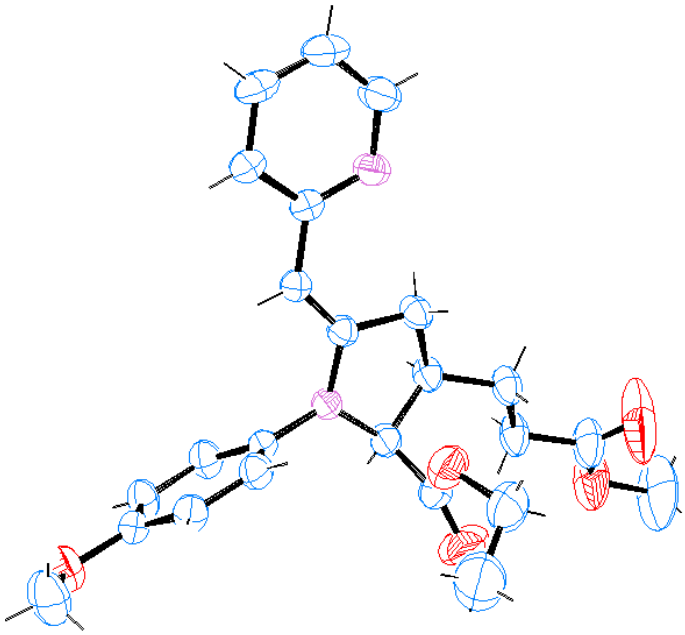
Nom	Aj 610	Type d'échantillon	Echantillon
N° Flacon	1		
Quantité	0,000000 mg	Volume d'injection	60,00 µl
Dilution	1	Diviseur	1

(* = valeur initiale modifiée)
Informations :
AD, 254 nm, 23°C
hept/iprOH 95/5
1 mL/min
254

Aj 610 12 - Canal 1 — Page 2/2

Crystal data of **16**:

Bruker Kappa APEXII CCD diffractometer ($Mo_{K\alpha}$ λ=0.71073 Å; graphite monochromator; *T*=291(2)K). Formula $C_{24}H_{28}N_2O_5$, formula weight 424.48, crystal system monoclinic, space group $P2_1$, crystal dimensions 0.42 x 0.35 x 0.29 mm^3, *a*=6.7414(2), *b*=8.5308(2), *c*=20.2800(4) Å, β=94.853(1)° *V*=1162.11(5) $Å^3$, *Z*=2, ρ_{calcd}=1.213 Mgm^{-3}, μ□=0.085 mm^{-1}, $2\theta_{max}$=61.84°, 17720 measured reflections, 7233 independent reflections (R_{int}= 0.0204), *R*1 [*I*>2σ(*I*)]=0.0462, *wR*2 [*I*>2σ(*I*)]= 0.1247, GOF=1.03, 283 parameters, final difference map within 0.305 and -0.177 $eÅ^{-3}$. The structure was solved using direct methods and refined by full-matrix least-squares analysis on F^2.



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2 -x,1/2+y,-z
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_cell_length_b                  9.2684(11)
_cell_length_c                  22.590(2)
_cell_angle_alpha                90
_cell_angle_beta                 91.848(4)
_cell_angle_gamma                90
_cell_volume                    2288.04
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_atom_site_type_symbol
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N2 N 0.228616 0.615955 0.216317
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C3 C 0.412803 0.817877 0.262657
C2 C 0.529043 0.904823 0.279086
C1 C 0.505878 1.04803 0.248768
C6 C 0.557719 0.896498 0.346894
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C9 C 0.281947 0.833813 0.163741
C10 C 0.207317 0.704435 0.172542
C11 C 0.108856 0.681814 0.132333
C12 C 0.033597 0.570153 0.138271
C13 C 0.053229 0.473008 0.184752
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C20 C 0.312183 1.19777 0.14724
C18 C 0.374671 1.29705 0.053424
C16 C 0.492298 1.10492 0.099444
C17 C 0.473558 1.19955 0.054508
C19 C 0.289055 1.2941 0.100429
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O3 O 0.580587 0.847805 0.483172
O4 O 0.759499 0.693761 0.457994
O2 O 0.501495 1.2327 0.321687
C36 C 0.259119 1.48311 0.005734
C37 C 0.43287 1.32231 0.362115
C44 C 0.762317 0.696206 0.532227
C45 C 0.501252 1.45233 0.370273
N3 N 0.936507 0.004818 0.19585
C21 C 1.00318 0.051035 0.249967
C24 C 0.864238 -0.121614 0.204115
C22 C 1.0302 -0.094208 0.279028
C23 C 0.913245 -0.188778 0.260485
C30 C 0.815428 0.195831 0.148483
C25 C 0.912143 0.103431 0.14832
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C29 C 0.793887 0.289442 0.102597
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C31 C 0.756835 0.47954 0.004051
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O7 O 0.820158 0.147037 0.28993
O8 O 0.996157 0.241233 0.315609
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C39 C 0.536745 -0.449956 0.147888
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C38 C 0.603268 -0.31198 0.129256
C40 C 0.547472 -0.531363 0.188621
C42 C 0.932349 0.351058 0.354011
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