Supplementary Information

Enantioselective organocatalytic formal [3+2]-cycloaddition of isatin-derived ketimines with benzylidenemalononitriles and benzylidineindanones

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1 Contents

2 General Experimental

2.1 Naming and Numbering of Compounds

Systematic compound names are those generated by ChemBioDraw™ Ultra version 15.1.0.144 (Perkin Elmer) following IUPAC nomenclature.

2.2 Solvents and reagents

Unless stated otherwise, all other solvents and reagents used were directly obtained from commercial sources. Anhydrous and oxygen-free THF was obtained by distillation from Na/benzophenone. Due to the air and moisture sensitive nature of several of the reactions, glassware was oven-dried prior to use and the reaction performed under an inert (argon) atmosphere, with solvents being dried over 3 Å molecular sieves prior to their use. Anhydrous solvents were degassed with argon for 15 minutes immediately prior to use.

2.3 Purification

Flash column chromatography was carried out using Fluorochem 60 40-63 micron silica gel. Thin-layer chromatography was carried out using Merck Kieselgel 60 F254 (230-400 mesh) fluorescent treated silica, visualized under UV light (254 nm) or by staining with aqueous potassium permanganate solution, ninhydrin or ceric ammonium molybdate solutions.

2.4 Spectroscopy

^{1}H, ^{13}C, and ^{19}F NMR spectra were obtained using Bruker 600, or 400 MHz spectrometers using either $CDCl_3$ or DMSO-d_6 as the solvent. To analyse and process the NMR spectra, TopSpin™ software was used, and spectra were calibrated against residual non-deuteriated solvent peaks as internal standards. The chemical shifts are reported in parts per million (ppm) and coupling constants (*J*) are reported in Hertz (Hz). ^{1}H NMR spectra are reported as follows: δ/ppm (number of protons, multiplicity, coupling constant, assignment of peak (if possible)). The multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. ^{13}C NMR spectra are reported as follows: δ/ppm (assignment). Chemical structures are numbered arbitrarily for the purpose of assignment; this numbering scheme does not necessarily correspond with the systematic name of the compound. Two-dimensional NMR experiments (COSY, HSQC, HMBC, NOESY) were also recorded when necessary to help aid assignment of the proton and carbon peaks.

Infra-red (IR) spectra were recorded on an Agilent Cary 630 spectrometer equipped with an attenuated total reflectance (ATR) accessory. Samples were deposited on the ATR as a thin film or neat solid. Only selected maximum absorbances (ν_{max}) of the most intense peaks are reported (cm^{-1}).

Optical rotations were recorded at the sodium D-line (589 nm) using a Perkin Elmer 341 polarimeter at a temperature of 20 °C and are reported in degrees using concentrations (*c*) in g.100 mL^{-1}. Reported values are the average of eight readings

2.5 Mass Spectrometry

Liquid chromatography-mass spectrometry (LCMS) analyses were conducted using an instrument comprising an Agilent 1260 HPLC (equipped with Infinity II quaternary pump, vial sampler, integrated column compartment and variable wavelength detector) and MSD single quadrupole mass spectrometer. Samples were analysed using an Agilent Infinitylab poroshell 120 column (2.7 µm, 2.1 x 150 mm) under an acetonitrile/water gradient with 0.1% HCOOH additive.

High resolution mass spectra (HRMS) were recorded by Analytical Services and Environmental Projects (ASEP) at Queen's University Belfast on a Waters LCT Premier ToF mass spectrometer using the electrospray ionisation (ESI) technique.

2.6 High-Pressure Liquid Chromatography (HPLC)

HPLC was performed on Agilent 1260 and Agilent 1100 instruments, eluting under reverse phase (acetonitrile-water) and normal phase (hexane/chloroform-isopropanol) conditions respectively. The columns, solvents, flow rates and acquisition wavelengths used for individual compounds can be found in section 3.3.

2.7 Crystallography

Low temperature[1] single crystal Xray diffraction studies were carried out using CuK_α radiation on an Agilent Supernova diffractometer equipped with an area detector and graphite monochromator. Raw frame data were reduced using CrysAlisPRO[2] solved using SHELXT[3] (**3d**) and Superflip (**5a**).[4] Full-matrix least-squares refinement of the structures were carried out using CRYSTALS.[5,6] Full refinement details are given in the supplementary material (CIF). CCDC 2103730, 2103731 and 2114148 contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre and copies can be obtained free of charge *via* www.ccdc.cam.ac.uk/data_request/cif.

2.8 Melting Points

Melting points were determined for compounds where a recrystallization was carried out. These were acquired on a Stuart SMP10 digital melting point apparatus. Values are given in °C and are uncorrected.

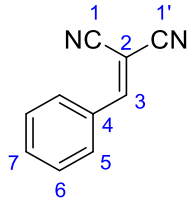
3 Experimental procedures and characterisation data

3.1 Starting materials

General procedure 1 (GP1) for the synthesis of benzylidene derivatives

To a solution of active methylene compound (1 eq.) in EtOH:H_2O (3:7 *v*:*v*) was added the aldehyde (1 eq.) in one portion. The mixture was stirred, placed under argon and warmed to 75 °C, and reaction progress was monitored by TLC. Upon completion, the reaction mixture was cooled to RT and the precipitate filtered under vacuum and washed with pure water (2 mL) or purified by flash column chromatography to afford the products.

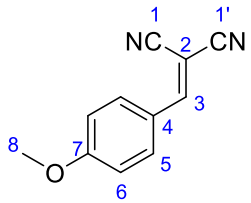
2-Benzylidenemalononitrile (2a)



Synthesised following **GP1** according to a literature procedure, and the data obtained are consistent with those previously reported.[7]

Malononitrile (2.00 g, 30.3 mmol, 1 eq.) and benzaldehyde (3.08 mL, 30.3 mmol, 1 eq.) after 17 h in EtOH:H_2O (3:7, 120 mL) afforded the product (4.58 g, 98%) as a white solid. $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 7.91 (2H, d, *J* 7.6 Hz, **H5**), 7.78 (1H, s, **H3**), 7.64 (1H, t, *J* 7.6 Hz, ***Ar***), 7.54 (2H, t, *J* 7.8 Hz, ***Ar***); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 160.1(**C3**), 134.8 (**C5**), 131.9 (***Ar***), 130.8 (***Ar***), 129.8 (**C4**), 113.7 (**C1'**), 112.7 (**C1**), 83.0 (**C2**).

2-(4-Methoxybenzylidene)malononitrile (2b)

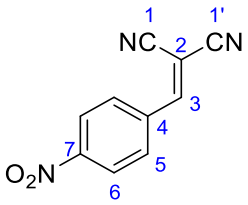


Synthesised following **GP1** according to a literature procedure, and the data obtained are consistent with those previously reported.[7]

Malononitrile (0.5 g, 7.57 mmol, 1 eq.) and 4-methoxybenzaldehyde (0.921 mL, 7.57 mmol, 1 eq.) after 19 h in EtOH:H_2O (3:7, 30 mL) afforded the product (1.39 g, 99%) as a fluffy, yellow solid. $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 7.91 (2H, m, ***Ar***), 7.65 (1H, s, **H3**), 7.01 (2H, m, ***Ar***), 3.91 (3H, s, **H8**); $\boldsymbol{\delta_C}$ (101 MHz,

$CDCl_3$): 165.0 (**C7**), 156.0 (**C3**), 133.6 (***Ar***), 124.2 (**C4**), 115.3 (***Ar***), 114.6 (**C1**), 113.5 (**C1'**), 78.8 (**C2**), 55.8 (**C8**).

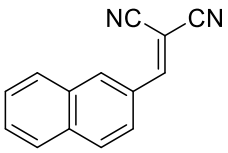
2-(4-Nitrobenzylidene)malononitrile (2c)



Synthesised following **GP1** according to a literature procedure, and the data obtained are consistent with those previously reported.[7]

Malononitrile (0.5 g, 7.57 mmol, 1 eq.) and 4-nitrobenzaldehyde (1.14 g, 7.57 mmol, 1 eq.) after 18 h in EtOH:H_2O (3:7, 30 mL) afforded the product (1.36 g, 90%) as a brown solid. $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 8.39 (2H, d, *J* 8.8 Hz, ***Ar***), 8.07 (2H, d, *J* 8.8 Hz, ***Ar***), 7.88 (1H, s, **H3**); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 156.0 (**C3**), 150.5 (**C7**), 135.9 (**C4**), 131.4 (***Ar***), 124.8 (***Ar***), 112.8 (**C1'**), 111.7 (**C1**), 87.7 (**C2**).

2-(Naphthalen-2-ylmethylene)malononitrile (2d)

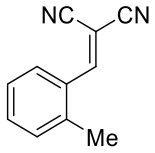


Synthesised following **GP1** according to a literature procedure, and the data obtained are consistent with those previously reported.[7]

Malononitrile (0.25 g, 3.78 mmol, 1 eq.) and 2-naphthaldehyde (0.590 g, 3.78 mmol, 1 eq.) after 1.5 h in EtOH:H_2O (3:7, 15 mL) afforded the product (0.768 g, 99%) as a yellow solid. $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 8.29 (1H, s), 8.07 (1H, dd, *J* 8.7, 1.8 Hz), 7.92 (4H, m), 7.68 (1H, t, *J* 6.9 Hz), 7.61 (1H, t, *J* 7.0 Hz); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 159.9, 136.0, 134.6, 132.8, 130.1, 129.8, 128.7, 128.2, 127.8, 124.4, 114.1, 113.0 82.4.*

* One expected ^{13}C signal is absent due to co-incidence with another peak.

2-(2-methylbenzylidene)malononitrile (2e)

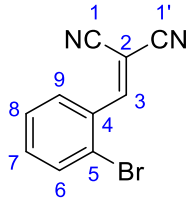


The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[8]

o-Tolualdehyde (0.46 ml, 3.97 mmol, 1 eq.), malononitrile (0.46 ml, 3.92 mmol, 1 eq.), and K_2CO_3 (56 mg, 0.405 mmol, 0.1 eq.) were added into a mortar and ground rapidly at rt for 1 min. The mixture was washed with water and filtered, and the crude product then recrystallized from ethanol, to yield the product as white needles, 280 mg, 43%. M.p. = 107-110 °C (EtOH).

δ_H (400 MHz, $CDCl_3$): 8.10 (1H, s), 8.08 (1H, d, *J* 8.8 Hz), 7.50 (1H, td, *J* 7.5, 1.2 Hz), 7.37 (1H, d, *J* 7.8 Hz), 7.33 (1H, d, *J* 7.8 Hz), 2.45 (3H, s); **δ_C** (101 MHz, $CDCl_3$): 158.3, 139.9, 134.3, 131.5, 130.1, 128.4, 127.2, 113.9, 112.6, 84.2, 19.9; **HRMS** (ESI+): found 201.0979; $C_8H_4N_2OCH_5O$, $[M+MeOH+H]^+$ requires 201.1022; **ν_{max}** (neat): 2967.0, 2221.5, 1572.9, 1371.7, 1230.0, 1058.6.

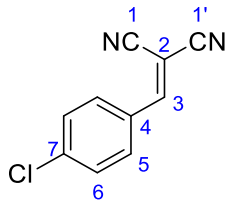
2-(2-Bromobenzylidene)malononitrile (2f)



Synthesised following **GP1** by analogy to a literature procedure,[7] and the data obtained are consistent with those previously reported.[9]

Malononitrile (0.25 g, 3.78 mmol, 1 eq.) and 2-bromobenzaldehyde (0.441 mL, 3.78 mmol, 1 eq.) after 21 h in EtOH:H_2O (3:7, 15 mL) afforded the product (0.499 g, 57%) as a brown solid. **δ_H** (400 MHz, $CDCl_3$): 8.22 (1H, s, **H3**), 8.12 (1H, dd, *J* 7.6, 1.8 Hz, ***Ar***), 7.74 (1H, dd, *J* 7.8, 1.5 Hz, ***Ar***), 7.47 (2H, m, **H7-8**); **δ_C** (101 MHz, $CDCl_3$): 158.9 (**C3**), 135.1 (***Ar***), 134.2 (***Ar***), 131.0 (**C5**), 130.0 (***Ar***), 128.5 (***Ar***), 126.6 (**C4**), 113.3 (**C1'**), 111.9 (**C1**), 86.2 (**C2**).

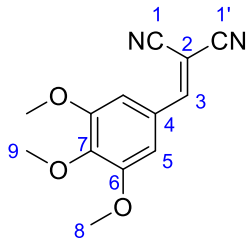
2-(4-Chlorobenzylidene)malononitrile (2g)



Synthesised following **GP1** according to a literature procedure, and the data obtained are consistent with those previously reported.[7]

Malononitrile (0.25 g, 3.78 mmol, 1 eq.) and 4-chlorobenzaldehyde (0.531 g, 3.78 mmol, 1 eq.) after 1 h in EtOH:H_2O (3:7, 15 mL) afforded the product (0.65 g, 91%) as a white powder. $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 7.85 (2H, d, *J* 8.6 Hz, ***Ar***), 7.73 (1H, s, **H3**), 7.52 (2H, d, *J* 8.6 Hz, ***Ar***); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 158.4 (**C3**), 141.3 (**C7**), 132.0 (***Ar***), 130.2 (***Ar***), 129.4 (**C4**), 113.6 (**C1**), 112.5 (**C1'**), 83.5 (**C2**).

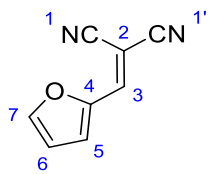
2-(3,4,5-Trimethoxybenzylidene)malononitrile (2h)



Synthesised following **GP1** according to a literature procedure.[7]

Malononitrile (0.25 g, 3.78 mmol, 1 eq.) and 3,4,5-trimethoxybenzaldehyde (0.741 g, 3.78 mmol, 1 eq.) after 1.5 h in EtOH:H_2O (3:7, 15 mL) afforded the product (0.886 g, 96%) as a bright yellow solid. $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 7.65 (1H, s, **H3**), 7.19 (2H, s, **H5**), 3.98 (3H, s, **H9**), 3.91 (6H, s, **H8**); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 159.5 (**C3**), 153.4 (**C6**), 144.2 (**C7**), 126.1 (**C4**), 114.1 (**C1'**), 113.3 (**C1**), 108.5 (**C5**), 80.8 (**C2**), 61.4 (**C9**), 56.5 (**C8**); **HRMS** (ESI+): found 283.0496; $C_{13}H_{12}KN_2O_3$, $[M+K]^+$ requires 283.0485; $\boldsymbol{\nu_{max}}$ (neat): 2939.0, 2219.6, 1567.3, 1498.4, 1343.7, 1321.3, 1258.0, 1127.5, 698.9.

2-(furan-2-ylmethylene)malononitrile (2i)

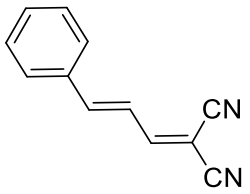


The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported. [8]

Furfural (0.64 ml, 7.73 mmol, 1 eq.), malononitrile (510 mg, 7.72 mmol, 1 eq.), and K_2CO_3 (115 mg, 0.832 mmol. 0.11 eq.) were added into a mortar and ground rapidly at rt for 1 min. The mixture was washed with water and filtered, and the crude product was purified via flash column chromatography (100% DCM), to yield the product as yellow solid, 490 mg, 44 %.

δ_H (400 MHz, $CDCl_3$): 7.80 (1H, d, J 1.4, **H7**), 7.51 (1H, s, **H3**), 7.35 (1H, d, *J* 3.5 Hz, **H5**), 6.71 (1H, dd, *J*, 3.7, 1.7 Hz, **H6**); **δ_C** (101 MHz, $CDCl_3$): 149.7 (**C7**), 148.2 (**C4**), 143.1 (**C3**), 123.6 (**C5**), 114.6 (**C6**), 113.9 (**C1'**), 112.7 (**C1**), 77.7 (**C2**); **HRMS** (ESI+): found 162.0667; $C_8H_4N_2ONH_4$, $[M+NH_4]^+$ requires 162.0662 ; ***ν_{max}*** (neat): 3041.5, 2225.2, 1602.8, 1453.7, 1394.0, 1297.1, 1017.6.

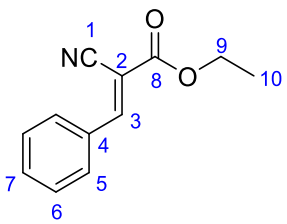
2-(3-phenylpropylidene)malononitrile (2j)



The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[8]

Cinnamaldehyde (0.96 ml, 7.63 mmol, 1 eq.), malononitrile (506 mg, 7.66 mmol, 1 eq.), and K_2CO_3 (118 mg, 0.854 mmol, 0.11 eq.) were added into a mortar and ground rapidly at rt for 10 min. The mixture was washed with water and filtered, and the crude product then recrystallized from ethanol, to yield the product as a yellow solid, 590 mg, 43%. M.p. = 127-130 °C (EtOH). **δ_H** (400 MHz, $CDCl_3$): 7.63-7.53 (3H, m), 7.51-7.42 (3H, m), 7.32-7.21 (2H, m); **δ_C** (101 MHz, $CDCl_3$): 160.2, 150.6, 134.1, 132.2, 129.5, 129.1, 122.4, 113.6, 111.8, 83.1; **HRMS** (ESI+): found 181.0766; $C_{12}H_8N_2H$, $[M+H]^+$ requires 181.0760; ***ν_{max}*** (neat): 2970.7, 2221.5, 1606.5, 1446.2, 1174.1, 1054.8.

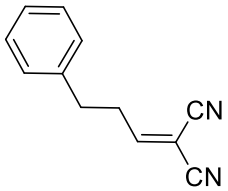
Ethyl-2-cyano-3-phenylacrylate (2l)



Synthesised following **GP1** according to a literature procedure and the data obtained are consistent with those previously reported.[7]

Ethyl cyanoacetate (0.5 mL, 4.70 mmol, 1 eq.) and benzaldehyde (0.477 mL, 4.70 mmol, 1 eq.) were heated at 75 °C for 24 h in EtOH:H_2O (3:7, 15 mL). The mixture was cooled to RT, extracted with EtOAc (3x30 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo.* The residue was purified by flash column chromatography (silica gel, PhMe:Et_2O 99:1) to afford the product (0.245 g, 26%) as a white solid. $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 8.25 (1H, s, **H3**), 7.99 (2H, d, *J* 7.1 Hz, **H5**), 7.53 (3H, m, **H6-7**), 4.39 (2H, q, *J* 7.1 Hz, **H9**), 1.40 (3H, t, 7.1 Hz, **H10**); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 162.6 (**C8**), 155.2 (**C3**), 133.4 (***Ar***), 131.6 (**C4**), 131.2 (**C5**), 129.4 (***Ar***), 115.6 (**C1**), 103.2 (**C2**), 62.9 (**C9**), 14.3 (**C10**).

2-(3-phenylpropylidene)malononitrile (2o)

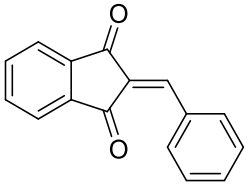


The reaction was carried out according to a literature procedure[10] and the data obtained are consistent with those previously reported.[11]

To a solution of hydrocinnamaldehyde (0.41 mL, 3.48 mmol, 1.0 eq.) and malononitrile (375 mg, 5.68 mmol, 1.6 eq.) under an inert atmosphere of argon in dry CH_2Cl_2 (15 mL) was added K_2CO_3 (262 mg, 1.89 mmol, 0.5 eq.). The reaction mixture was stirred at room temperature for 16 h, after which the solvent was then removed in vacuo and the residue quenched with ice cold water and then extracted with EtOAc (3 x 10 mL). The combined organic layers were then washed with brine, dried over $MgSO_4$, filtered under gravity and then concentrated in vacuo. The crude residue was then purified by short silica plug (30 % DCM:petroleum ether) to afford the product (248 mg, 39%) as a yellow oil.

$\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 7.34 (2H, t, *J* 6.9 Hz), 7.30-7.26 (2H, m) 7.17 (1H, d, *J* 6.8 Hz), 2.96-2.85 (4H, m); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 168.3, 138.3, 129.2, 128.4. 127.3. 112.1, 110.5. 90.8, 34.4, 33.7.

2-benzylidene-1H-indene-1,3(2H)-dione (4a)

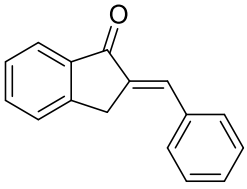


The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[12]

To a round-bottom flask under an inert atmosphere of argon and equipped with a magnetic stir bar, was added 1,3-indandone (438 mg, 3.00 mmol, 1eq.), benzaldehyde (0.35 ml, 3.30 mmol, 1.1 eq.), *L*-proline (104 mg, 0.899 mmol, 0.3 eq.) and dry MeOH (6 ml). The reaction was then left to stir at rt for 20 hours, with a precipitate forming over time. Following this, the precipitate was then filtered under vacuum and washed several times with MeOH to yield the product as a khaki solid, 631 mg, 90 %.

δ_H (400 MHz, $CDCl_3$): 8.46 (2H, d, J 8.3), 8.05-7.99 (2H, m), 7.90 (1H, s), 7.84-7.79 (2H, m), 7.59-7.49 (3H, m).; **δ_C** (101 MHz, $CDCl_3$): 190.4, 189.1, 147.1, 142.7, 140.2, 135.5, 135.3, 134.3, 133.3, 133.2, 129.3, 128.9, 123.5, 123.4; **HRMS** (ESI+): found 235.0764; $C_{16}H_{10}O_2H$, $[M+H]^+$ requires 235.0754; **ν_{max}** (neat): 2113.4, 1681.0, 161.2, 1587.8, 1349.3, 1200.2.

(E)-2-benzylidene-2,3-dihydro-1H-inden-1-one (4b)

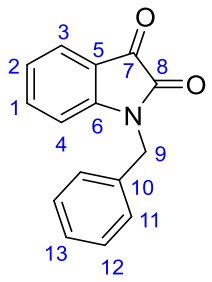


The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[13]

To a round-bottom, equipped with a magnetic stir bar, was added indanone (333 mg, 2.52 mmol, 1 eq.), benzaldehyde (0.27 ml, 2.52 mmol, 1 eq.) and EtOH (1.4 ml). Following this the solution was then cooled down to 0 °C and 10 % NaOH (1.4 ml) solution then added dropwise. The solution was then left to stir at 0 °C for 2 hours. Once the reaction had finished the solid was then filtered under vacuum and washed with H_2O and hexane. The solid was then dried under high vac to yield the product as a faint pink solid, 485 mg, 87%.

δ_H (400 MHz, $CDCl_3$): 7.91 (1H, d, *J* 7.7 Hz), 7.67 (3H, d, *J* 6.7 Hz), 7.61 (1H, td, *J* 7.7, 1.1 Hz), 7.55 (1H, d, *J* 7.6 Hz), 7.49-7.37 (4H, m), 4.05 (2H, s); **δ_C** (101 MHz, $CDCl_3$): 194.4, 149.8, 138.1, 135.5, 134.9, 134.7, 134.0, 130.8, 129.8, 129.1, 127.8, 126.3, 124.6, 32.6; **HRMS** (ESI+): found 221.0935; $C_{16}H_{12}OH$, $[M+H]^+$ requires 221.0961, found 441.1826; $C_{32}H_{12}O_2H$, $[2M+H]^+$ requires 441.1849; **ν_{max}** (neat): 2133.4, 1871.1, 1621.4, 1688.5, 1580.4 1446.2.

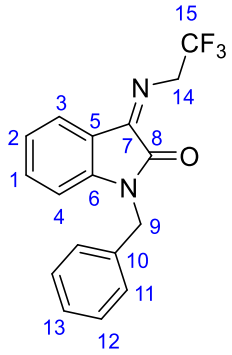
N-Benzyl isatin (S1)



The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[14]

To a stirred solution of isatin (3.00 g, 20.4 mmol) and potassium carbonate (8.45 g, 61.2 mmol, 3 eq.) in acetonitrile (200 mL) was added benzyl bromide (2.67 mL, 22.4 mmol, 1.1 eq.) dropwise *via* syringe. The reaction was heated to 95 °C and refluxed for 4 h until completion. The mixture was cooled to RT and concentrated *in vacuo*. The crude product was recrystallised from PhMe to afford the product (4.42 g, 91%) as a red-orange crystalline solid. M.p. = 136-139 °C (PhMe). ***δ_H*** (400 MHz, $CDCl_3$): 7.61 (1H, d, *J* 7.5 Hz, **H3**), 7.48 (1H, td, *J* 7.8, 1.3 Hz, **H1**) 7.40-7.27 (5H, m, **H11-13**), 7.09 (1H, td, *J* 7.5, 0.8 Hz, **H2**), 6.78 (1H, d, *J* 7.8 Hz, **H4**), 4.93 (2H, s, **H9**); ***δ_C*** (101 MHz, $CDCl_3$): 183.3 (**C7**), 158.4 (**C8**), 150.9 (**C5/6**), 138.4 (**C1**), 134.7 (**C10**), 129.2 (**C12/13**), 128.3 (**C12/13**), 127.6 (**C11**), 125.5 (**C3**), 123.9 (**C2**), 117.9 (**C5/6**), 111.1 (**C4**), 44.2 (**C9**); **HRMS** (ESI+): found 276.0434; $C_{15}H_{11}NO_2K$, $[M+K]^+$ requires 276.0421; ***ν_{max}*** (neat): 1725.8, 1606.5, 1468.6, 1345.6.

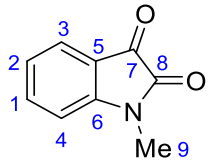
(Z)-1-Benzyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one (1a)



The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[15]

N-benzyl isatin (2.00 g, 8.43 mmol, 1 eq.), 2,2,2-trifluoroethylamine (0.99 mL, 12.6 mmol, 1.5 eq.), *p*-TsOH.H_2O (0.16 g, 0.843 mmol, 0.1 eq.) and $MgSO_4$ (3.00 g, 25.3 mmol, 3 eq.) were dissolved in toluene (75 mL) and refluxed in a sealed tube at 120 °C until completion. The solution was cooled to RT, washed with $NaHCO_3$ (40 mL) and extracted with DCM (2x40 mL). Solvent removed *in vacuo* and the crude residue was recrystallised from MeOH to afford the product (1.96 g, 73%) as an 12:1 mixture of *Z*:*E* isomers as a yellow solid. M.p. = 127-130 °C (MeOH). $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$, major isomer): 7.73 (1H, d, *J* 7.5 Hz, **H3**), 7.38-7.29 (6H, m, **H1**,**11-13**), 7.09 (1H, t, *J* 7.6 Hz, **H2**), 6.74 (1H, d, *J* 7.8 Hz, **H4**), 4.90 (2H, s, **H9**), 4.87 (2H, q, *J* 9.7 Hz, **H14**); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 158.7 (**C8**), 155.7 (**C7**), 145.6 (**C5/6**), 135.1 (**C10**), 133.8 (**C1**), 129.1 (**C12/13**), 128.2 (**C11**), 127.5 (**C12/13**), 125.2 (q, J_{C-F} 277 Hz, **C15**), 123.6 (**C4**), 123.2 (**C3**), 120.9 (**C5/6**), 109.9 (**C2**) 53.8 (q, J_{C-F} 31.5 Hz, **C14**), 43.8 (**C9**); $\boldsymbol{\delta_F}$ (376 MHz, $CDCl_3$): -71.9 (t, *J* 9.7 Hz).

N-Methyl isatin (S2)

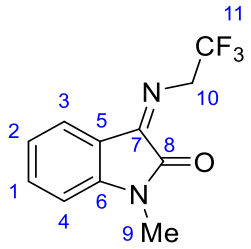


The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[16]

To a stirred solution of isatin (0.5 g, 3.40 mmol) and potassium carbonate (0.94 g, 6.80 mmol, 2 eq.) in DMF (5 mL) in a sealed tube, was added iodomethane (0.423 mL, 6.80 mmol, 2 eq.) dropwise at RT. The reaction was heated to 40 °C until completion. After 22 h, the mixture was cooled to RT, diluted with DCM (20 mL) and H_2O (20 mL), extracted and washed with brine (2x20 mL). The mixture was dried

over $MgSO_4$, filtered and concentrated *in vacuo*, affording the product (0.439 g, 80%) as a red-orange solid. δ_H (400 MHz, $CDCl_3$): 7.62-7.56 (2H, m, **H1,3**), 7.11 (1H, t, *J* 7.8 Hz, **H2**), 6.89 (1H, d, *J* 7.8 Hz, **H4**), 3.24 (3H, s, **H9**); δ_C (101 MHz, $CDCl_3$): 183.5 (**C7**), 158.4 (**C8**), 151.6 (**C5/6**), 138.5 (**C3**), 125.4 (**C1**), 124.0 (**C2**), 117.6 (**C5/6**), 110.1 (**C4**), 26.3 (**C9**).

(Z)-1-Methyl-3-((2,2,2-trifluoroethyl)imino)indolin-2-one (1b)

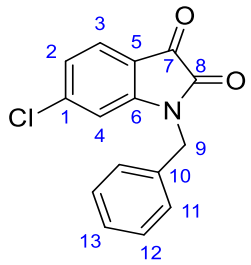


The reaction was carried out by analogy to a literature procedure, and the data obtained are consistent with those previously reported.[15]

N-methyl isatin (252 mg, 1.56 mmol, 1 eq.), 2,2,2-trifluoroethylamine (180 µL, 2.29 mmol, 1.5 eq.) and *p*-TsOH.H_2O (11.8 mg, 0.062 mmol, 0.1 eq.) were dissolved in toluene (9 mL) and refluxed in a sealed tube at 120 °C until completion. After 24 h the solution was cooled to RT, solvent removed *in vacuo* and the crude residue was purified by flash column chromatography (silica gel, petrol:ethyl acetate, 19:1) to afford the product (95.4 mg, 26%) as an 11:1 mixture of Z:E isomers as an orange solid.

δ_H (400 MHz, $CDCl_3$, major isomer): 7.71 (1H, d, *J* 7.7 Hz, **H3**), 7.47 (1H, t, *J* 7.7 Hz, **H1**), 7.12 (1H, t, *J* 7.5 Hz, **H2**), 6.84 (1H, d, *J* 7.9 Hz, **H4**), 4.83 (2H, q, *J* 9.8 Hz, **H10**), 3.22 (3H, s, **H9**); δ_C (101 MHz, $CDCl_3$): 158.8 (**C8**), 155.9 (**C7**), 146.4 (**C5/6**), 133.9 (**C3**), 125.1 (q, $J_{C\text{-}F}$ 276.1 Hz, **C11**), 123.6 (**C2**), 123.1 (**C1**), 120.7 (**C5/6**), 108.9 (**C4**), 53.6 (q, $J_{C\text{-}F}$ 32.3 Hz, **C10**), 26.0 (**C9**); **Major** δ_F (376 MHz, $CDCl_3$): -71.9 (t, *J* 9.9 Hz).

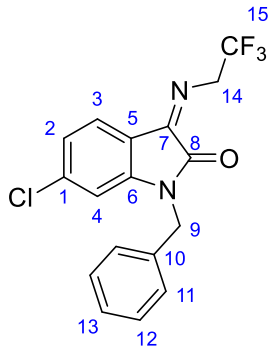
1-Benzyl-6-chloroindoline-2,3-dione (S3)



The reaction was carried out according to a literature procedure.[14]

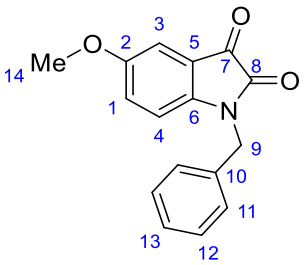
To a stirred solution of 6-chloroisatin (1.00 g, 5.50 mmol, 1 eq.) and potassium carbonate (2.28 g, 16.5 mmol, 3 eq.) in acetonitrile (55 mL) was added benzyl bromide (0.98 mL, 8.26 mmol, 1.1 eq.) dropwise *via* syringe. The reaction was heated to 95 °C and refluxed overnight until completion. The mixture was cooled to RT, filtered under gravity and concentrated *in vacuo*. The crude product was recrystallised from PhMe to afford the product (1.14 g, 76%) as a burnt-orange crystalline solid. M.p. = 175-177 °C (PhMe). δ_H (400 MHz, $CDCl_3$): 7.54 (1H, d, *J* 8.0 Hz, **H3**), 7.40-7.29 (5H, m, **H11-13**), 7.07 (1H, dd, *J* 8.0, 1.6 Hz, **H2**), 6.78 (1H, d, *J* 1.5 Hz, **H4**), 4.91 (2H, s, **H9**); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 181.9 (**C=O**), 158.3 (**C=O**), 151.8 (**C5/6**), 144.8 (**C5/6**), 134.1 (**C10**), 129.3 (**C12/13**), 128.5 (**C12/13**), 127.5 (***C11***), 126.5 (**C3**), 124.2 (**C2**), 116.1 (**C1**), 111.8 (**C4**), 44.3 (**C9**); **HRMS** (ESI+): found 272.0478; $C_{15}H_{10}ClNO_2H$, $[M+H]^+$ requires 272.0472; $\boldsymbol{\nu_{max}}$ (neat): 3078.8, 1731.3, 1608.3, 1425.7, 1347.4, 1254.2, 1071.6.

(Z)-1-benzyl-6-chloro-3-((2,2,2-trifluoroethyl)imino)indolin-2-one (1c)



1-benzyl-6-chloroindoline-2,3-dione **S3** (300 mg, 1.10 mmol, 1 eq.), 2,2,2-trifluoroethylamine (0.13 mL, 1.66 mmol, 1.5 eq.), *p*-TsOH.H_2O (25 mg, 0.13 mmol, 0.12 eq.) and $MgSO_4$ (500 mg, 4.15 mmol, 3.8 eq.) were dissolved in toluene (10 mL) and refluxed in a sealed tube at 120 °C until completion. The solution was cooled to RT, washed with $NaHCO_3$ (20 mL) and extracted with DCM (3x15 mL). Solvent removed *in vacuo* and the crude residue was recrystallised from MeOH to afford the product (122 mg, 31 %) as an 75:1 mixture of *Z*:*E* isomers as a mustard-yellow solid. M.p. = 155-157 °C (MeOH). $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$, major isomer): 7.65 (1H, d, *J* 8.0 Hz, **H3**), 7.37-7.27 (5H, m, **H11-13**), 7.06 (1H, d, *J* 7.9 Hz, **H2**), 6.74 (1H, s, **H4**), 4.88 (2H, s, **H9**), 4.85 (2H, q, *J* 9.8 Hz, **H14**); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 158.6 (**C8**), 154.6 (**C7**), 146.6 (**C5/6**), 139.9 (**C5/6**), 134.6 (**C10**), 129.3 (***Ar***), 128.4 (***Ar***), 127.5 (***Ar***), 125.1 (q, J_{C-F} 276 Hz, **C15**), 124.3 (**C3**), 123.8 (**C2**), 119.3 (**C1**), 110.6 (**C4**), 53.9 (q, J_{C-F} 32.5 Hz, **C14**), 43.9 (**C9**); $\boldsymbol{\delta_F}$ (376 MHz, $CDCl_3$): -71.9 (3F, t, *J* 9.7 Hz); **HRMS** (ESI+): found 353.0669; $C_{17}H_{12}ClF_3N_2OH$, $[M+H]^+$ requires 353.0663; $\boldsymbol{\nu_{max}}$ (neat): 2115.3, 1716.4, 1612.1, 1367.9, 1267.3, 1146.2.

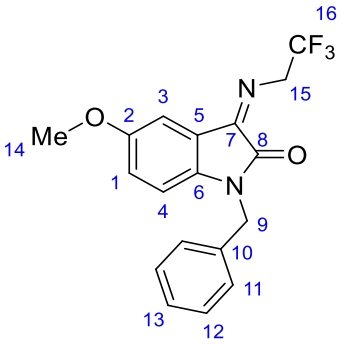
1-benzyl-5-methoxyindoline-2,3-dione (S4)



The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[14]

To a stirred solution of 5-methoxyisatin (1.00 g, 5.64 mmol, 1 eq.) and potassium carbonate (2.34 g, 16.9 mmol, 3 eq.) in acetonitrile (55 mL) was added benzyl bromide (1.00 mL, 8.47 mmol, 1.1 eq.) dropwise *via* syringe. The reaction was heated to 95 °C and refluxed until completion (4 h). The mixture was cooled to RT, filtered under gravity and concentrated *in vacuo*. The crude product was recrystallised from PhMe to afford the product (1.45 g, 96%) as a burgundy crystalline solid. M.p. = 119-121 °C (PhMe). δ_H (400 MHz, $CDCl_3$): 7.37-7.27 (5H, m, **H11-13**), 7.14 (1H, d, *J* 2.8 Hz, **H3**), 7.02 (1H, dd, *J* 8.6, 2.8 Hz, **H1**), 6.68 (1H, d, *J* 8.6 Hz, **H4**), 4.90 (2H, s, **H9**), 3.76 (3H, s, **H14**); δ_C (101 MHz, $CDCl_3$): 183.7 (**C=O**), 158.5 (**C=O**), 156.7 (**C2**), 144.7 (**C5/6**), 134.7 (**C10**), 129.1 (***Ar***), 128.2 (***Ar***), 127.5 (***Ar***), 124.8 (**C1**), 118.2 (**C5/6**), 112.1 (**C3**), 109.7 (**C4**), 56.1 (**C14**), 44.2 (**C9**).

(Z)-1-benzyl-5-methoxy-3-((2,2,2-trifluoroethyl)imino)indolin-2-one (1d)

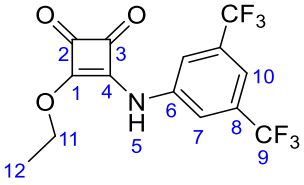


1-benzyl-5-methoxyindoline-2,3-dione **S4** (300 mg, 1.12 mmol, 1 eq.), 2,2,2-trifluoroethylamine (0.15 mL, 1.68 mmol, 1.5 eq.), *p*-TsOH.H_2O (21 mg, 0.11 mmol, 0.10 eq.) and $MgSO_4$ (405 mg, 3.37 mmol, 3.0 eq.) were dissolved in toluene (10 mL) and refluxed in a sealed tube at 120 °C until completion (24 h). The solution was cooled to RT, washed with $NaHCO_3$ (20 mL) and extracted with DCM (3x15 mL). Solvent removed *in vacuo* and the crude residue was recrystallised from MeOH to afford the product (263 mg, 67 %) as an 24:1 mixture of *Z*:*E* isomers as an orange solid. M.p. = 144-147 °C (MeOH). δ_H (400 MHz, $CDCl_3$, major isomer): 7.39-7.26 (6H, m, **H3 + H11-13**), 6.89 (1H, dd, *J*

8.4, 2.2 Hz, **H1**), 6.63 (1H, d, *J* 8.5 Hz, **H4**), 4.89 (2H, q, *J* 9.7 Hz, **H15**) , 4.87 (2H, s, **H9**), 3.79 (3H, s, **H14**); δ_C (101 MHz, $CDCl_3$): 158.8 (**C=O**), 156.6 (**C2**), 156.1 (**C=O**), 139.4 (**C5/6**), 135.2 (**C10**), 129.1 (***Ar***), 128.1 (**Ar**), 127.5 (***Ar***), 125.2 (q, J_{C-F} 276.0 Hz, **C16**), 121.6 (**C5/6**), 120.3 (**C1**), 110.8 (**C4**), 108.0 (**C3**), 56.1 (**C14**), 53.7 (q, J_{C-F} 32.4 Hz, **C15)**, 43.8 (**C9**); δ_F (376 MHz, $CDCl_3$): -71.8 (3F, t, *J* 9.7 Hz); **HRMS** (ESI+): found 349.1164; $C_{18}H_{15}F_3N_2O_2H$, $[M+H]^+$ requires 349.1159; ν_{max} (neat): 3008.0, 2961.4, 2109.7, 1720.2, 1599.0, 1489.1, 1433.3, 1269.2.

3.2 Catalyst synthesis

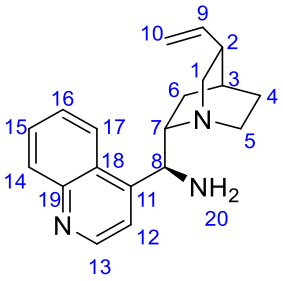
3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-ethoxycyclobut-3-ene-1,2-dione (S5)



The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[17]

To a stirred solution of diethyl squarate (1.36 mL, 9.20 mmol) and $Zn(OTf)_2$ (335 mg, 0.92 mmol, 0.1 eq.) in EtOH (36 mL) at RT, was added 3,5-bistrifluoromethylaniline (1.44 mL, 9.20 mmol, 1 eq.) dropwise *via* syringe. The mixture was left to stir at RT under a flow of argon until consumption of the starting material. After 48 h, the precipitate was filtered, washed with cold EtOH (2 mL), and dried under vacuum. The product (2.36 g, 73%) was obtained as a pale cream solid. δ_H (400 MHz, DMSO-d6): 11.2 (1H, s, **H5**), 8.04 (2H, s, **H7**), 7.79 (1H, s, **H10**), 4.81 (2H, q, *J* 7.1 Hz, **H11**), 1.42 (3H, t, *J* 7.1 Hz, **H12**); δ_C (101 MHz, DMSO-d6): 187.9 (**C2/3**), 184.9 (**C2/3**), 179.7 (**C1/4**), 169.6 (**C1/4**), 140.6 (**C6**), 131.1 (q, J_{C-F} 33.0 Hz, **C8**), 123.0 (q, J_{C-F} 272.9 Hz, **C9**), 119.9 (**C7**), 116.7 (**C10**), 70.5 (**C11**), 15.8 (**C12**); δ_F (376 MHz, DMSO-d6): -61.7 (6F, s).

(S)-Quinolin-4-yl((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methanamine (S6)

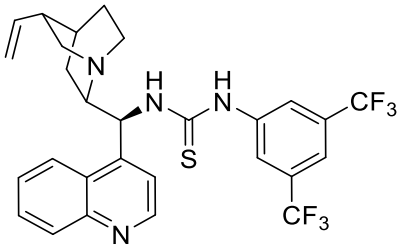


The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[18]

To a solution of PPh_3 (579 mg, 2.21 mmol, 1.3 eq.) and cinchonidine (500 mg, 1.70 mmol, 1 eq.) in dry THF (10 mL) under argon at 0 °C, was added DIAD (434 µL, 2.21 mmol, 1.3 eq.) in one portion. After 15 min, DPPA (475 µL, 2.21 mmol, 1.3 eq.) was added dropwise over 15 min and the reaction mixture was heated to 45 °C. After 40 h, PPh_3 (624 mg, 2.38 mmol, 1.4 eq.) was added in one portion and stirred for a further 3 h. The reaction mixture was cooled to RT, diluted with H_2O (0.5 mL) and stirred for 3 h where-after the crude product was concentrated *in vacuo*. The yellow oil was dissolved in a mixture of DCM:HCl (10% aq. solution) (32 mL) and mixed thoroughly. The aqueous layer was removed and basified to pH 9-10 with *aq*. NH_4OH solution. Solution extracted with EtOAc (3x40 mL), organic layers dried over $MgSO_4$, filtered, and concentrated *in vacuo.* The crude residue was purified by flash column chromatography (silica gel, EtOAc:MeOH:NH_4OH, 90:10:2) to afford the product (0.341 g, 68%) as a yellow oil.

$\boldsymbol{\delta_H}$ (600 MHz, $CDCl_3$): 8.90 (1H, d, *J* 4.6 Hz, **H12/13**), 8.35 (1H, s, **H14/17**), 8.13 (1H, d, *J* 8.3 Hz, **H14/17**), 7.72 (1H, ddd, *J* 8.4, 6.9, 1.4 Hz, **H15/16**), 7.60 (1H, ddd, *J* 8.3, 7.1, 1.2 Hz, **H15/16**), 7.55-7.49 (1H, m, **H12/13**), 5.84-5.76 (1H, m, **H9**), 4.98 (2H, dd, *J* 20.9, 13.8 Hz, **H10**), 4.71 (1H, s, **H8**), 3.28 (1H, dd, *J* 13.8, 10.1 Hz, **H1'**), 3.24-3.17 (1H, m, **H5'**), 3.07 (1H, s, **H7**), 2.84-2.76 (2H, m, **H1/5**), 2.31-2.24 (1H, m, **H2**), 2.03 (2H, s, **H20**), 1.63-1.60 (1H, m, **H3**), 1.58-1.53 (2H, m, **H4**), 1.45-1.38 (1H, m, **H6'**), 0.75 (1H, dd, *J* 13.8, 7.5 Hz, **H6**); $\boldsymbol{\delta_C}$ (151 MHz, $CDCl_3$): 150.5 (**C12/13**), 148.8 (**C8**), 142.0 (**C9**), 132.2 (**C12/13**), 130.6 (**C14/17**), 129.1 (**C15/16**), 128.7 (**C18/19**), 128.6 (**C18/19**), 128.1 (**C11**), 126.6 (**C15/16**), 123.5 (**C14/17**), 119.7 (**C12/13**) 114.4 (**C10**), 62.2 (**C7**), 56.5 (**C1**), 41.1 (**C5**), 40.1 (**C2**) 28.3 (**C4**), 27.8 (**C3**), 26.3 (**C6**); $\boldsymbol{[\alpha]_D^{20}}$ +58.7 (*c* = 0.562, $CHCl_3$).

Cinchonidine derived aryl-thiourea catalyst (C1)



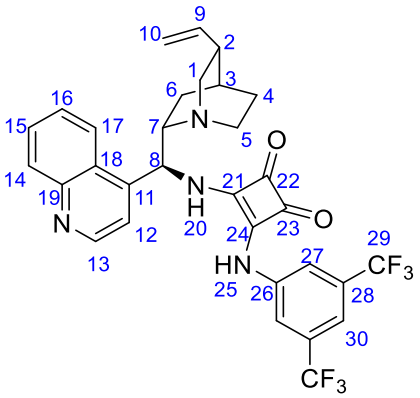
This reaction was carried out according to a literature procedure, and the data obtained are consistent with those previously reported.[19]

A solution of 3,5-bis(trifluoromethyl)phenyl isothiocyanate (0.60 mL, 3.3 mmol, 1.11 eq.) in THF (6 mL) was added slowly to a solution of 9-amino(9-deoxy)epicinchonidine **S6** (870 mg, 2.96 mmol, 1.00 eq.) in THF (20 mL) at room temperature. The reaction mixture was stirred at room temperature for 24 h and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (10 g) using CH_2Cl_2/MeOH/Et_3N 100/2/1 as eluent to afford an off-white solid (1.83 g, 99 %).

$\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$): 8.86 H, d, *J* 3.8 Hz), 8.31 (1H, bs), 8.16 (1H, d, *J* 8.5 Hz), 7.84 (2H, s), 7.76 (1H, t, J 7.5 Hz), 7.69 (1H, s), 7.65 (1H, t, J 7.7 Hz), 7.32 (1H, d, *J* 4.0 Hz), 5.75-5.62 (2H, m), 5.04-4.95 (2H, m), 3.39-3.17 (3H, m), 2.90-2.76 (2H, m), 2.36 (1H, bs), 1.77-1.60 (3H, m), 1.40-1.31 (1H, m), 1.00-0.90 (1H, m); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$):* 181.0, 150.1, 148.7, 140.6, 140.0, 132.7 (q, $J_{C\text{-}F}$ 34.1 Hz,), 130.6, 129.7, 127.2, 123.6, 123.0, 119.0, 118.9, 115.3, 61.6, 55.0, 41.2, 39.2, 27.5, 27.2, 25.6; $\boldsymbol{\delta_F}$ ($CDCl_3$, 376 MHz): -62.3 (6F, s); **HRMS** (ESI) calcd for $C_{28}H_{27}F_6N_4S$ $[M+H]^+$: 565.1860, found: 565.1860; $\boldsymbol{[\alpha]_D^{20}}$ – 87 (*c* = 1.0, $CHCl_3$).

* Signals at ~146 and ~56 ppm were visible as broad humps on the baseline but with insufficient signal:noise to determine precise chemical shift values.

3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((S)-quinolin-4-yl((1S,2S,4S,5R)-5-vinylquinuclidin-2-yl)methyl)amino)cyclobut-3-ene-1,2-dione (C2)



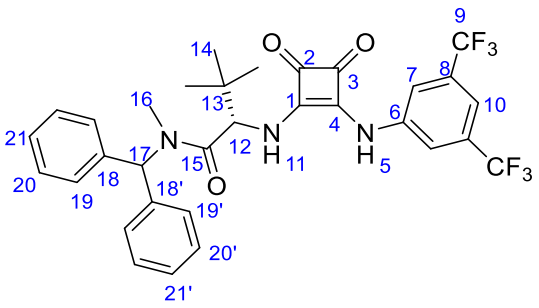
This reaction was carried out according to a literature procedure, and the data obtained are consistent with those previously reported.[20]

To a stirred solution of 3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-ethoxycyclobut-3-ene-1,2-dione (370 mg, 1.05 mmol, 1.2 eq.) in dry MeOH (6 mL) under argon was added (*S*)-quinolin-4-yl((1*S*,2*S*,4*S*,5*R*)-5-vinylquinuclidin-2-yl)methanamine (256 mg, 0.872 mmol, 1 eq.) in dry MeOH (4 mL) in one portion. The reaction mixture was stirred for 24 h under Ar at RT after which the precipitate was filtered under vacuum, washed with cold MeOH (2 mL) and dried to afford the product (0.222 g, 42%) as a white solid.

δ $_H$ (600 MHz, DMSO-d6): 10.25 (1H, s, **H20/25**), 8.98 (1H, d, *J* 4.4 Hz, **H12/13**), 8.47 (1H, d, *J* 8.0 Hz, ***Ar***), 8.39 (1H, s, **H20/25**), 8.09 (1H, d, *J* 8.3 Hz, ***Ar***), 7.98 (2H, s, **H27**), 7.81 (1H, t, *J* 7.7 Hz, ***Ar***), 7.74 (1H, t, *J* 7.7 Hz, ***Ar***), 7.70 (1H, d, *J* 4.6 Hz, **H12/13**), 7.65 (1H, s, **H30**), 6.06 (1H, s, **H8**), 5.99-5.88 (1H, m, **H9**), 4.99 (2H, dd, *J* 16.8, 10.3 Hz, **H10**), 3.34-3.37 (1H, m, **H7**), 3.30-3.18 (2H, m, **H1'+5'**), 2.71 (1H, d, *J* 13.3 Hz, **H1**), 2.69-2.61 (1H, m, **H5**), 2.28 (1H, s, **H2**), 1.62-1.55 (2H, m, **H3+4'**), 1.54-1.47 (1H, m, **H4**) 1.42-1.33 (1H, m, **H6'**), 0.73 (1H, s, **H6**); ***δ*** $_C$ (151 MHz, DMSO-d6): 184.4 (**C22/23**), 180.3 (**C22/23**), 168.8, 162.7, 150.4 (**C12/13**), 148.1, 145.0 (***Ar***), 142.1 (**C9**), 140.9 (***Ar***), 131.2 (q, $J_{C\text{-}F}$ 33.0 Hz, **C28**), 130.0 (***Ar***), 129.4 (***Ar)***, 127.2 (***Ar)***, 126.3 (***Ar***), 125.8 (***Ar***), 124.0 (***Ar***), 123.4 (***Ar***), 123.1 (q, $J_{C\text{-}F}$ 273 Hz, **C29**), 120.4 (**C12/13**), 118.3 (**C27**), 114.9 (**C30**), 114.3 (**C10**), 59.5 (**C7**), 55.5 (**C1**), 40.6 (**C5**), 39.5 (**C2**)*, 27.2 (**C4**), 25.7 (**C6**); ***δ*** $_F$ (376 MHz, DMSO-d6): -61.7 (6F, s); **[α]** $_D^{20}$ -82.9 (*c* = 0.9, DMSO).

* Carbon peak at **C2** is obscured by the DMSO peak, but is visible in the HSQC spectrum

(S)-N-Benzhydryl-2-((2-((3,5-bis(trifluoomethyl)phenyl)amino)-3,4-dioxocyclobut-1-en-1-yl)amino)-N,3,3-trimethylbutanamide (C3)



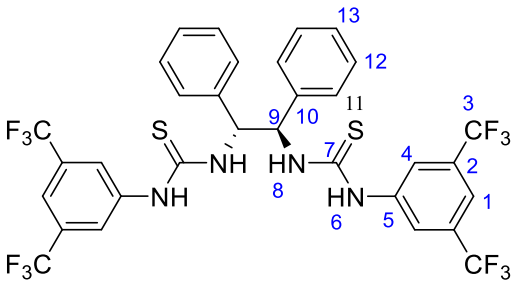
The reaction was carried out according to a literature procedure and the data obtained are consistent with those previously reported.[21]

To a stirred solution of *N*-methylbenzhydrylamine (200 mg, 1.01 mmol, 1.1 eq.), HBTU (383 mg, 1.01 mmol, 1.1 eq.) and *N*-Boc-L-tert-leucine (213 mg, 0.918 mmol, 1 eq.) in dry DCM (15 mL) was added *i*-Pr_2NEt (191 µL, 1.1 mmol, 1.2 eq.) dropwise. The reaction mixture was stirred at RT under Ar until completion. After 5 d, the reaction mixture was washed with 1M HCl (2x25 mL) and extracted with Et_2O (40 mL). The organic layers were washed with aq. $NaHCO_3$ (2x25 mL) and brine (2x25 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. HCl (4M in dioxane, 2.5 mL) was added dropwise to the amide at 0 °C, stirred for 2 h at RT and concentrated to produce the amine hydrochloride. DCM (8 mL) and Et_3N (0.4 mL, 2.75 mmol, 3 eq.) were added and stirred for 15 min before addition of 3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-ethoxycyclobut-3-ene-1,2-dione (325 mg, 0.918 mmol, 1 eq.) in one portion. The reaction mixture was stirred at RT for 48 h where after NaOH (1N, 8 mL) was added and stirred for a further 4 h at RT. Reaction mixture was diluted with DCM (12.5 mL) and H_2O (12.5 mL), washed with brine (15 mL), dried over $MgSO_4$, filtered and concentrated. The crude residue was purified by flash column chromatography (PhMe:EtOAc, 20:1) to afford the product (73.8 mg, 13%) as a white solid.

$\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$, exists as ≈ 5:1 rotamers, resonance of major reported): 10.1 (1H, s, **NH**), 7.92-7.77 (2H, s, ***Ar***), 7.54 (1H, s, **NH**), 7.39-7.32 (4H, m, ***Ar***), 7.24-7.17 (5H, m, ***Ar***), 7.00-6.93 (3H, m, ***Ar***), 5.58-5.46 (1H, m, **H12**), 2.99 (3H, s, **H16**), 1.07 (9H, s, **H14**); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$): 171.4, 169.2, 161.8, 139.8, 138.1, 137.8, 137.2, 133.1 (q, $J_{C\text{-}F}$ 34.0 Hz), 129.4, 129.0, 128.7, 128.5, 128.2, 122.8 (q, $J_{C\text{-}F}$ 273 Hz), 118.9, 61.5 , 60.4 , 36.9, 33.4, 26.1;* $\boldsymbol{\delta_F}$ (376 MHz, $CDCl_3$): -62.9 (6F, s); $\boldsymbol{[\alpha]_D^{20}}$ -48.2 (*c* = 0.28, $CHCl_3$).

* Three ^{13}C signals are not observed, likely due to co-incidence between diastereotopic groups (e.g. 21 and 21').

1,1'-((1R,2R)-1,2-Diphenylethane-1,2-diyl)bis(3-(3,5-bis(trifluoromethyl)phenyl)thiourea) (C4)

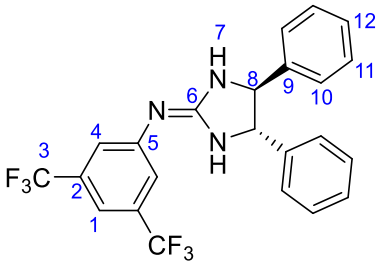


The reaction was carried out by analogy to a literature procedure and the data obtained are consistent with those previously reported.[22,23]

Isothiocyanato-3,5-bistrifluoromethylbenzene (344 µL, 1.88 mmol, 2 eq.) was added dropwise over 2 min to a stirred solution of (1*R*,2*R*)-DPEN (200 mg, 0.942 mmol, 1 eq.) in dry THF (2.5 mL) at 0 °C. The reaction mixture was heated to RT and stirred under a constant flow of argon. After 24 h the THF was removed *in vacuo*. The crude yellow residue was purified by flash column chromatography (silica gel, DCM:MeOH, 95:5) to afford the product (530 mg, 75%) as a white solid.

δ**_H* (400 MHz, DMSO-d6): 10.3 (2H, s, **H6**), 8.73 (2H, s, **H8**), 8.16 (4H, s, **H4**), 7.69 (2H, s, **H1**), 7.30 – 7.18 (10H, m, **H11-13**), 5.96 (2H, s, **H9**); ***δ**_C* (101 MHz, DMSO-d6): 180.4 (**C7**), 141.5 (Ar***), 138.4 (***Ar***), 130.2 (q, $J_{C\text{-}F}$ 32.8 Hz, **C2**), 128.3 (***Ar***), 128.0 (***Ar***), 127.6 (***Ar***), 121.9 (**C4**), 121.7 (q, $J_{C\text{-}F}$ 272.9 Hz, **C3**), 116.4 (**C1**), 62.6 (**C9**); ***δ**_F* (376 MHz, DMSO-d6): -61.8 (s); **[α]**$_D^{20}$ - 39.9 (*c* = 0.8, $CHCl_3$).

N-((4S,5S)-4,5-Diphenylimidazolidin-2-ylidene)-3,5-bis(trifluoromethyl)aniline (C5)



To a stirred solution of (1*R*,2*R*)-DPEN (200 mg, 0.942 mmol, 1 eq.) in dry THF (1.5 mL) was added a solution of isothiocyanato-3,5-bistrifluoromethylbenzene (172 µL, 0.942 mmol, 1 eq.) in dry THF (1 mL) dropwise over 30 min at 0 °C *via* syringe pump. The reaction mixture is stirred at RT for 24 h where after the solvent was removed *in vacuo*. The crude yellow oil was purified by flash column chromatography (silica gel, Petrol:EtOAc:NEt_3, 20:1:0.01 → 10:1:0.01) to afford the product (67.5 mg, 16%) as a white solid.

$\boldsymbol{\delta_H}$ (400 MHz, DMSO-d6): 7.46 (2H, s, **H7**), 7.40-7.26 (13H, m, **H1+4+10-12**), 4.54 (2H, s, **H8**); $\boldsymbol{\delta_C}$ (101 MHz, DMSO-d6): 157.6 (**C6**), 141.9 (**C5**), 131.1 (q, $J_{C\text{-}F}$ 32.0 Hz, **C2**), 129.0 (**C10**), 128.2 (***Ar***), 127.1 (***Ar***), 124.1 (q, $J_{C\text{-}F}$ 273 Hz, **C3**), 112.6 (**C1**), 67.2 (**C8**), possible overlapping with two carbons as speaks is short one peak; $\boldsymbol{\delta_F}$ (376 MHz, DMSO-d6): -61.4 (6F, s); $\boldsymbol{[\alpha]_D^{20}}$ -72.2 (*c* = 0.266, $CHCl_3$); **HRMS** (ESI+): found 450.1334; $C_{23}H_{18}F_6N_3$, $[M+H]^+$ requires 450.1327; $\boldsymbol{\nu_{max}}$ (neat): 3028.5, 2844.0, 1664.3, 1595.3, 1382.8, 1271.0, 1170.4, 1129.4, 698.9, 680.2.

3.3 Spirooxindole products

General procedure for the synthesis of spiro[pyrrolidine-oxindoles]

To a stirred solution of imine (**1a/1b**) (1 eq.) and benzylidene derivatives (1.2 eq.) in DCM (0.1 M) was added catalyst **C1** (0.1 eq.) in one portion. The reaction mixture was stirred under air at RT and monitored by TLC. Upon completion, the solvent was removed *in vacuo* and the crude residue was purified by flash column chromatography to afford the product.

A Note on Purification

In some instances, residual benzylidinemalononitriles present upon completion of the reaction underwent hydrolysis during silica gel chromatography leading to contamination of the product with the corresponding aldehydes. These were removed by dissolving the product in methanol (5 mL), transferring the solution to a separatory funnel, adding saturated aqueous sodium bisulfite (1 mL) and shaking for 30 seconds. The solution was then diluted with water (25 mL) and extracted with $CHCl_3$ (25 mL). The aqueous layer was then extracted three time with chloroform (5 mL). Following this the organic layers were combined, dried over $MgSO_4$, filtered under gravity, and then concentrated *in vacuo.* This procedure was adapted from Furigay *et al.*[24]

A Note on Relative and Absolute Configuration

All spirocyclization reactions produced at least two diastereomeric products identifiable from the crude ^{1}H NMR spectra. In most cases these diastereomers were not separable by chromatography. The relative and absolute stereochemistry of the major diastereomers of all products are assumed to be analogous to the crystal structure obtained for (–)-**3d** (see the main text and section 6 below). With the exception of **3l** and **5b** (which contain an additional stereocentre not common to the other compounds synthesised), we assume the minor diastereomer to be consistent with the following analysis for **3k**.

The relative configuration of the minor diastereomer of **3k** was identified through NOESY analysis (Figure S1). In a mixture containing ~1:1 major:minor diastereomer, a strong nOe enhancement was observed between the *ortho*-CH of the oxindole (H3) and the benzylidene hydrogen (H13), consistent with the C(13)-H(13) and C(7)-C(5) bonds being *syn* relative to the pyrrolidine ring. The presence of strong enhancements between H^{15} and H^{11} for both diastereomers indicates that the CF_3 and Ph groups are *anti* for both the major and minor diastereomers. It should be noted that the absolute stereochemistry of the minor diastereomer is not known.

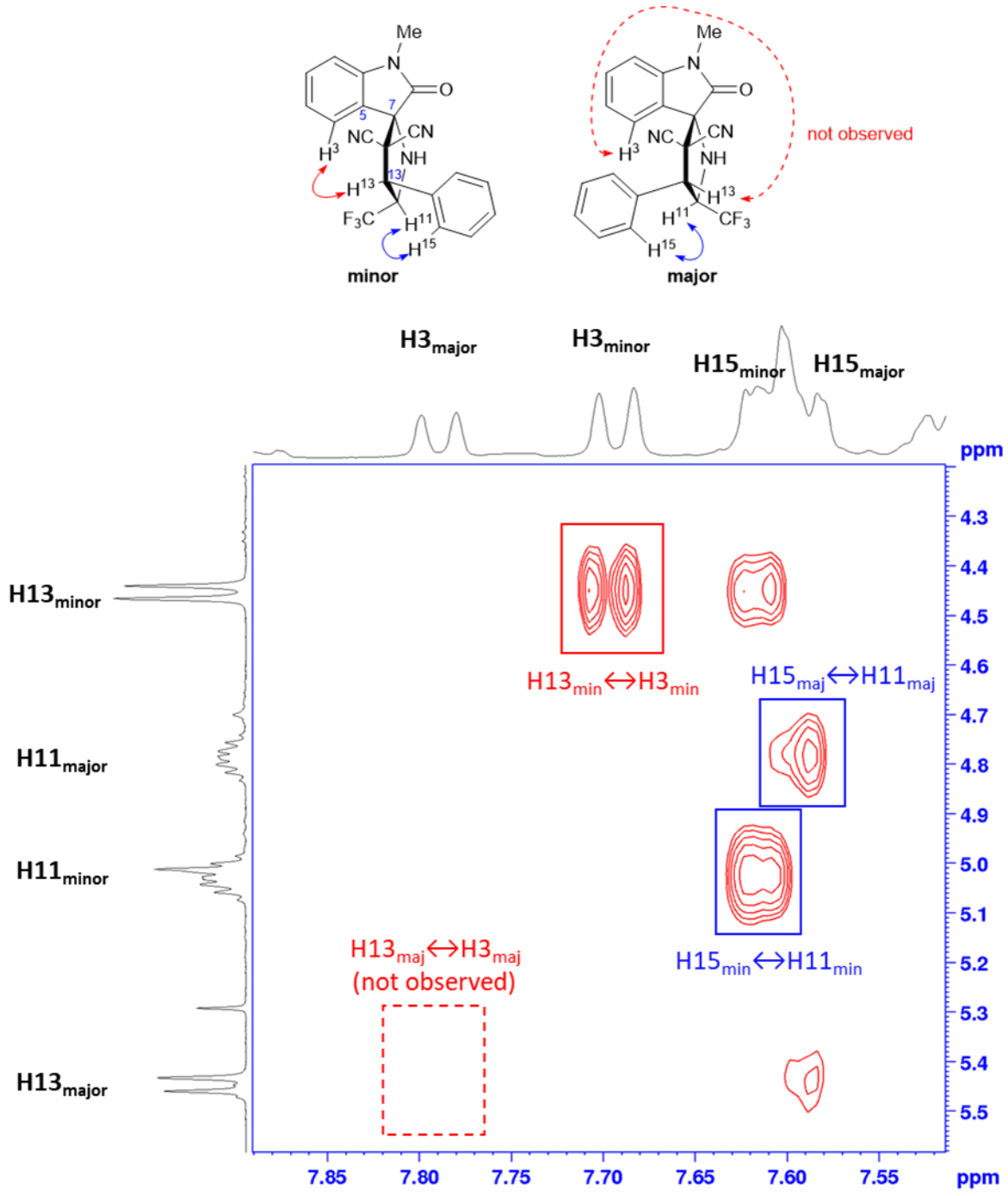
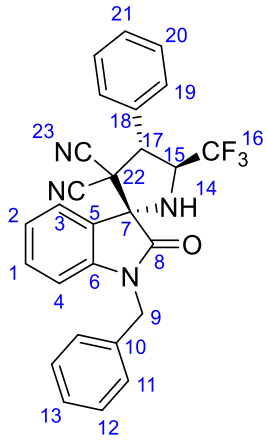


Figure S1. NOESY analysis of spirocycle **3k** ($CDCl_3$, 400 MHz, t_{mix} 0.3 s).

1-Benzyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3a)

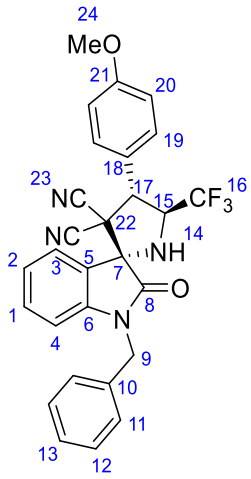


1a (50 mg, 0.157 mmol, 1 eq.), **2a** (29.1 mg, 0.188 mmol, 1.2 eq.) and **C1** (8.9 mg, 0.016 mmol, 0.1 eq.) after 1 day afforded the spirocycle (71.3 mg, 96%, 91% ee, 12:1 d.r.) as a white foam solid. Crude was purified using 1% acetone in toluene. Yield of 250 mg scale, (366 mg, 96%, 90% ee, 6.7:1 d.r.).

Major δ_H (400 MHz, $CDCl_3$): 7.80 (1H, d, *J* 7.8 Hz, **H3**), 7.65-7.60 (2H, m, **H19**), 7.52-7.47 (3H, m, **H20-21**), 7.41-7.26 (6H, m, **H1+11-13**), 7.19 (1H, t, *J* 7.6 Hz, **H2**), 6.80 (1H, d, *J* 7.9 Hz, **H4**), 5.52 (1H, d, *J* 10.8 Hz, **H17**), 5.22 (1H, d, *J* 15.5 Hz, **H9'**), 4.85-4.76 (1H, m, **H15**), 4.69 (1H, d, *J* 15.6 Hz, **H9**), 2.90 (1H, d, *J* 7.5 Hz, **H14**); **Major** δ_C (101 MHz, $CDCl_3$): 173.5 (**C8**), 143.8 (**C10**), 134.6 (***Ar***), 132.5 (**C1**), 130.3 (***Ar***), 129.6 (***Ar***), 129.5 (**C18**), 129.2 (***Ar***), 129.1 (***Ar***), 128.2 (***Ar***), 127.7 (***Ar***), 125.1 (**C3**), 124.0 (**C2**), 122.1 (***Ar***), 111.4 (**C23'**), 111.3 (**C23**), 110.6 (**C4**), 70.7 (**C7**), 60.1 (q, $J_{C\text{-}F}$ 32.2 Hz, **C15**), 51.8 (**C17**), 51.6 (**C22**), 44.8 (**C9**);* **Major** δ_F (376 MHz, $CDCl_3$): -73.5 (3F, d, *J* 6.2 Hz); $[\alpha]_D^{20}$ -34.8 (*c* = 0.94, $CHCl_3$); **HRMS** (ESI+): found 473.1589; $C_{27}H_{19}F_3N_4OH$, $[M+H]^+$ requires 473.1584; ν_{max} (neat): 3371.4, 1709.0, 1612.1, 1287.8, 1140.6, 1094.0, 751.1, 695.1; **HPLC**: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.8 min, t_R (minor) = 10.5 min.

* **C16** not observed due to low signal intensity.

1-Benzyl-4'-(4-methoxyphenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3b)

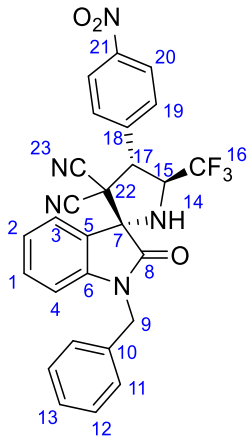


1a (50 mg, 0.157 mmol, 1 eq.), **2b** (46 mg, 0.187 mmol, 1.2 eq.) and **C1** (9 mg, 0.0159 mmol, 0.1 eq.) after 3 days afforded the spirocycle (77 mg, 98%, 93% ee, 2.8:1 d.r.) as a white foam solid. Crude was purified using 0.5% acetone in toluene.

Major δ_H (400 MHz, $CDCl_3$):* 7.79 (1H, d, *J* 7.7 Hz, **H3**), 7.54 (2H, d, *J* 8.7 Hz, ***Ar***), 7.41-7.31 (6H, m, **H1+11-13**), 7.18 (1H, t, *J* 7.7 Hz, **H2**), 7.01 (2H, d, *J* 8.8 Hz, ***Ar***), 6.79 (1H, d, *J* 7.9 Hz, **H4**), 5.47 (1H, d, *J* 10.8 Hz, **H17**), 5.21 (1H, d, *J* 15.7 Hz, **H9'**), 4.78-4.71 (1H, m, **H15**), 4.68 (1H, d, *J* 15.6 Hz, **H9**), 3.84 (3H, s, **H24**), 2.87 (1H, m, **H14**); **Minor** δ_H (400 MHz, $CDCl_3$):†† 7.69 (1H, d, *J* 7.6 Hz, **H3**), 7.56 (2H, m, ***Ar***), 7.41-7.31 (6H, m, **H1+11-13**), 7.22 (1H, d, *J* 7.5 Hz, **H2**), 6.99 (2H, d, *J* 9.0 Hz, ***Ar***), 6.83 (1H, d, 7.8 Hz, **H4**), 5.12 (1H, d, *J* 15.8 Hz, **H9'**), 5.06-4.96 (1H, m, **H15**), 4.82 (1H, d, *J* 15.6 Hz, **H9**), 4.43 (1H, d, *J* 10.0 Hz, **H17**), 3.83 (3H, s, **H24**), 3.13 (1H, m, **H14**); **Major** δ_C (101 MHz, $CDCl_3$): 173.6 (**C8**), 161.0 (**C21**), 143.8 (***Ar***), 134.6 (**C10**), 132.5 (***Ar***), 130.3 (***Ar***), 129.1 (***Ar***), 128.2 (***Ar***), 127.7 (***Ar***), 125.1 (**C3**), 124.0 (**C2**), 122.3 (***Ar***) 121.3 (***Ar***), 114.9 (***Ar***), 111.6 (**C23'**), 111.5 (**C23**), 110.5 (**C4**), 70.4 (**C7**), 60.2 (q, $J_{C\text{-}F}$ 32.2 Hz, **C15**), 55.5 (**C24**), 51.8 (**C22**), 51.4 (**C17**), 44.8 (**C9**);† **Major** δ_F (376 MHz, $CDCl_3$): -73.4 (3F, d, *J* 5.9 Hz), **Minor** δ_F (376 MHz, $CDCl_3$): -73.3 (3F, d, *J* 6.0 Hz); $[\alpha]_D^{20}$ -28.6 (*c* = 1.06, $CHCl_3$); **HRMS** (ESI+): found 503.1695; $C_{28}H_{21}F_3N_4O_2H$, $[M+H]^+$ requires 503.1690; ν_{max} (neat): 3358.3, 1718.3, 1610.2, 1513.3, 1256.1, 1177.8, 1140.6, 752.9, 697.0; **HPLC**: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.3 min, t_R = (minor) 13.7 min.

* Due to significant overlapping in the aromatic region, integration of certain multiplets was inaccurate although where possible, assignment was made *via* 2D analysis.
† **C16** not observed due to low signal intensity.

1-Benzyl-4'-(4-nitrophenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3c)

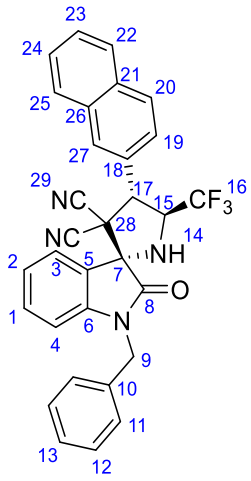


1a (51 mg, 0.160 mmol, 1 eq.), **2c** (38 mg, 0.192 mmol, 1.2 eq.) and **C1** (9 mg, 0.0159 mmol, 0.1 eq.) after 2 days afforded the spirocycle (63 mg, 76%, 97% ee, 48.8:1 d.r.) as a faint-orange foam solid. Crude was purified using 1% acetone in toluene.

Major δ_H (400 MHz, $CDCl_3$): 8.37 (2H, d, *J* 8.8 Hz, ***Ar***), 7.82 (2H, d, *J* 8.8 Hz, ***Ar***), 7.80 (1H, d, *J* 7.6 Hz, **H3**), 7.43-7.27 (6H, m, **H1 + H11-13**), 7.20 (1H, t, *J* 7.7 Hz, **H2**), 6.83 (1H, d, *J* 7.9 Hz, **H4**), 5.66 (1H, d, *J* 10.7 Hz, **H17**), 5.21 (1H, d, *J* 15.6 Hz, **H9'**), 4.90-4.80 (1H, m, **H15**), 4.71 (1H, d, *J* 15.6 Hz, **H9**), 2.97 (1H, d, *J* 7.6 Hz, **H14**); **Major δ_C** (101 MHz, $CDCl_3$)*: 173.3 (**C8**), 149.2 (**C21**), 143.8 (***Ar***), 136.6 (**C18**), 134.3 (***Ar***), 132.8 (***Ar***), 130.3 (***Ar***), 129.2 (***Ar***), 128.3 (***Ar)***, 127.7 (***Ar***), 125.1 (**C3**), 124.6 (***Ar***), 124.2 (**C2**), 121.5 (***Ar***), 111.0 (**C23'**), 110.9 (**C23**), 110.8 (**C4**), 70.8 (**C7**), 60.2 (q, $J_{C\text{-}F}$ 32.8 Hz, **C15**), 51.1 (**C17** & **C22**†), 44.8 (**C9**);‡ **Major δ_F** (376 MHz, $CDCl_3$): -73.5 (3F, d, *J* 6.1 Hz); **$[\alpha]_D^{20}$** -42.5 (*c* = 1.00, $CHCl_3$); **HRMS** (ESI+): found 503.1440; $C_{27}H_{18}F_3N_5O_3H$, $[M+H]^+$ requires 518.1435; **ν_{max}** (neat): 3352.7, 1720.2, 1608.3, 1522.6, 1345.5, 1284.4, 1140.6; **HPLC:** Chiral art Amylose-SB (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 15.0 min, t_R (minor) = 12.8 min.

* No peak visible corresponding to **C22** likely due to co-incidence with another peak.
† As indicated by HMBC and HSQC spectra.
‡ **C16** not observed due to low signal intensity.

1-Benzyl-4'-(naphthalen-2-yl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3d)

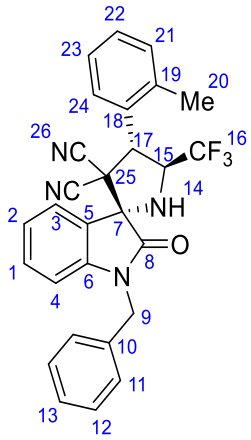


1a (50 mg, 0.158 mmol, 1 eq.), **2d** (38 mg, 0.187 mmol, 1.2 eq.) and **C1** (9 mg, 0.0160 mmol, 0.1 eq.) after 1 day afforded the spirocycle (78 mg, 95%, 87% ee, 10.1:1 d.r.) as a white foam solid. Crude was purified using 1% acetone in toluene.

Major δ_H (400 MHz, $CDCl_3$): 8.13 (1H, s, **H25**), 7.99 (1H, d, *J* 8.7 Hz, ***Ar***), 7.96-7.87 (2H, m, ***Ar***), 7.83 (1H, d, *J* 7.6 Hz, **H3**), 7.72 (1H, d, *J* 8.5, ***Ar***), 7.59-7.54 (2H, m, ***Ar***), 7.44-7.29 (6H, m, **H1+11-13**), 7.20 (1H, t, *J* 7.8 Hz, **H2**), 6.81 (1H, d, *J* 7.9 Hz, **H4**), 5.72 (1H, d, *J* 10.7 Hz, **H17**), 5.25 (1H, d, *J* 15.7 Hz, **H9**), 5.00-4.92 (1H, m, **H15**), 4.71 (1H, d, *J* 15.6 Hz, **H9'**), 2.98 (1H, d, *J* 7.5 Hz, **H14**); **Major δ_C** (101 MHz, $CDCl_3$): 173.6 (**C8**), 143.8 (***Ar***), 134.6 (***Ar***), 134.1 (***Ar***), 133.4 (***Ar***), 132.6 (***Ar***), 129.4 (***Ar***), 129.1 (***Ar***), 128.8 (***Ar***), 128.5 (***Ar***), 128.2 (***Ar***), 127.9 (***Ar***), 127.7 (***Ar***), 127.4 (***Ar***), 127.0 (***Ar$_q$***), 126.9 (***Ar***), 125.4 (***Ar***), 125.1 (**C3**), 124.0 (**C2**), 122.1 (***Ar$_q$***), 111.5 (**C29'**), 111.4 (**C29**), 110.6 (**C4**), 70.8 (**C7**), 60.2 (q, $J_{C\text{-}F}$ 31.7 Hz, **C15**), 52.0 (**C17**), 51.6 (**C28**), 44.8 (**C9**);* **Major δ_F** (376 MHz, $CDCl_3$): -73.4 (3F, d, *J* 5.8 Hz); $[\alpha]_D^{20}$ -19.8 (*c* = 0.95, $CHCl_3$); **HRMS** (ESI+): found 523.1746; $C_{31}H_{21}F_3N_4OH$, $[M+H]^+$ requires 523.1740; ν_{max} (neat): 3360.2, 1710.8, 1612.1, 1468.6, 1366.1, 1285.9, 1138.7; **HPLC**: Chiral art Amylose-SB (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 11.8 min, t_R (minor) = 9.4 min.

* **C16** not observed due to low signal intensity.

1-benzyl-2-oxo-4'-(o-tolyl)-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3e)

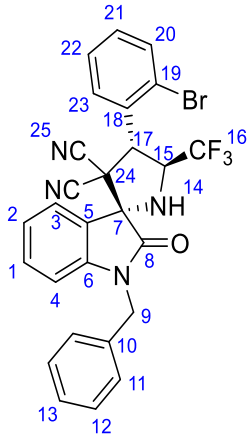


1a (51.3 mg, 0.161 mmol, 1 eq.), **3e** (33.0 mg, 0.196 mmol, 1.2 eq.) and Catalyst **C1** (9 mg,0.0159 mmol, 0.1 eq.) after 2 days afforded the spirocycle **(**72.0 mg, 92 %, 83% ee, 4.0:1 d.r.) as a white solid. Crude was purified using 1% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$): 7.83 (1H, d, *J* 7.6 Hz, **H3**), 7.74-7.71 (1H, m, ***Ar***), 7.39-7.31 (9H, m, ***Ar* + H1**), 7.19 (1H, t, *J* 7.6 Hz, **H2**) 6.78 (1H, d, *J* 7.8 Hz, **H4**), 6.14 (1H, d, *J* 10.8 Hz, **H17**), 5.21 (1H, d, *J* 15.8 Hz, **H9'**), 4.72 (1H, d, *J* 15.8 Hz, **H9**), 4.70-4.64 (1H, m, **H15**), 2.88 (1H, d, *J* 7.4 Hz, **H14**), 2.64 (3H, s, **H20**); **Major δ_C** (151 MHz, $CDCl_3$): 173.7 (**C8**), 143.9 (***Ar***), 139.1 (***Ar***), 134.6 (***Ar***), 132.5 (***Ar***), 131.8 (***Ar***), 129.8 (***Ar***), 129.1 (***Ar***), 128.2 (***Ar***), 127.9 (***Ar***), 127.6 (***Ar***), 127.4 (***Ar***), 126.8 (***Ar***), 125.2 (**C3**), 124.0 (**C2**), 122.2 (***Ar***), 111.7 (**C26** & **C26'**), 110.6 (**C24**), 71.0 (**C22**), 61.3 (q, $J_{C\text{-}F}$ 32.1 Hz, **C15**), 50.2 (**C25**), 46.1 (**C7**), 44.8 (**C9**), 20.0 (**C20**);* **Major δ_F** (564 MHz, $CDCl_3$): -73.7 (3F, d, *J* 6.2 Hz); **$[\alpha]_D^{20}$** -6.4 (*c* = 1.07, $CHCl_3$); **HRMS** (ESI+): found 487.1746; $C_{28}H_{21}F_3N_4OH$, $[M+H]^+$ requires 487.1734; **ν_{max}** (thin film): 3362.1, 1722.0, 1610.2, 1490.9, 1367.9, 1282.2, 1144.3, **HPLC:** Chiral art Amylose-SA (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 11.3 min, t_R (minor) = 6.6 min.

* **C16** not observed due to low signal intensity.

1-Benzyl-4'-(2-bromophenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3f)

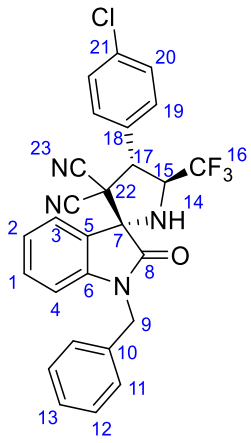


1a (76 mg, 0.239 mmol, 1 eq.), **2f** (67 mg, 0.300 mmol, 1.2 eq.) and **C1** (14 mg, 0.0248 mmol, 0.1 eq.) after 3 days afforded the spirocycle (113 mg, 86%, 80% ee, 9.9:1 d.r.) as a white foam solid. Crude was purified using 1% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$): 7.82 (1H, d, *J* 8.0 Hz, **H3**), 7.78 (1H, dd, *J* 8.0, 1.2 Hz ***Ar***), 7.76 (1H, dd, *J* 8.0, 1.2 Hz, ***Ar***), 7.48 (1H, td, *J* 7.5, 1.2 Hz, ***Ar***), 7.41-7.32 (6H, m, **H1+ *Ar***), 7.28 (1H, m, ***Ar***), 7.19 (1H, td, *J* 7.7, 0.7 Hz, **H2**), 6.78 (1H, d, *J* 7.9 Hz, **H4**), 6.56 (1H, d, *J* 10.8 Hz, **H17**), 5.22 (1H, d, *J* 15.7 Hz, **H9'**), 4.74 (1H, d, *J* 15.7 Hz, **H9**), 4.68-4.62 (1H, m, **H15**), 2.89 (1H, d, *J* 7.5 Hz, **H14**); **Major δ_C** (151 MHz, $CDCl_3$): 173.3 (**C8**), 144.0 (***Ar***), 134.6 (***Ar***), 134.4 (***Ar***), 132.6 (***Ar***), 131.4 (***Ar***), 129.5 (***Ar***), 129.2 (***Ar***), 129.1 (***Ar***), 128.2 (***Ar***), 128.1 (***Ar***), 127.7 (***Ar***), 127.2 (**C10**), 125.1 (**C3**), 123.9 (**C2**), 121.9 (***Ar***), 111.6 (**C25'**), 110.9 (**C25**), 110.7 (**C4**), 71.1 (**C7**), 61.5 (q, $J_{C\text{-}F}$ 32.1 Hz, **C15**), 50.0 (**C24**), 48.7 (**C17**), 44.8 (**C9**);* **Major δ_F** (564 MHz, $CDCl_3$): -73.6 (d, *J* 6.1 Hz); **$[\alpha]_D^{20}$** +15.6 (*c* = 1.01, $CHCl_3$); **HRMS** (ESI+): found 589.0242; $C_{27}H_{18}BrF_3N_4OK$, $[M+K]^+$ requires 589.0246; **ν_{max}** (neat): 3350.9, 1718.3, 1612.1, 1470.4, 1282.2, 1172.2, 1142.4; **HPLC**: Chiral art Amylose-SA (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 13.7 min, t_R (minor) = 9.9 min.

* **C16** not observed due to low signal intensity.

1-Benzyl-4'-(4-chlorophenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3g)

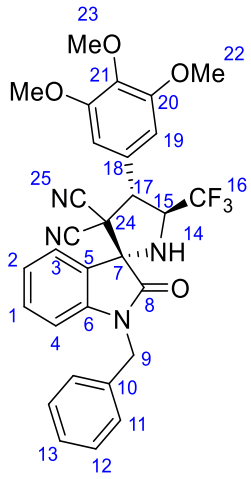


1a (102 mg, 0.321 mmol, 1 eq.), **2g** (73 mg, 0.384 mmol, 1.2 eq.) and **C1** (19 mg, 0.0337 mmol, 0.1 eq.) after 1 day afforded the spirocycle (147 mg, 90%, 93% ee, 8.6:1 d.r.) as a white foam solid. Crude was purified using 1% acetone in toluene.

Major δ_H (400 MHz, $CDCl_3$): 7.79 (1H, d, *J* 7.8 Hz, **H3**), 7.58-7.54 (2H, m, ***Ar***), 7.51-7.47 (2H, m, ***Ar***), 7.41-7.32 (6H, m, **H1, H11-13**), 7.19 (1H, td, *J* 7.9, 1.0 Hz, **H2**), 6.81 (1H, d, *J* 7.9 Hz, **H4**), 5.50 (1H, d, *J* 10.7 Hz, **H17**), 5.21 (1H, d, *J* 15.5 Hz, **H9'**), 4.78-4.72 (1H, m, **H15**), 4.69 (1H, d, *J* 15.7 Hz, **H9**), 2.89 (1H, d, *J* 7.6 Hz, **H14**); **Major δ_C** (101 MHz, $CDCl_3$): 173.4 (**C8**), 143.8 (***Ar***), 136.5 (**C21**), 134.5 (**C10**), 132.6 (***Ar***), 130.4 (***Ar***), 129.8 (***Ar***), 129.2 (***Ar***), 128.3 (***Ar***), 128.1 (**C18**), 127.7 (***Ar***), 125.1 (**C3**), 124.1 (**C2**), 121.9 (***Ar***), 111.3 (**C23'**), 111.2 (**C23**), 110.7 (**C4**), 70.6 (**C7**), 60.1 (q, $J_{C\text{-}F}$ 32.6 Hz, **C15**), 51.4 (**C22**), 51.2 (**C17**), 44.8 (**C9**);* **Major δ_F** (376 MHz, $CDCl_3$): -73.4 (3F, d, J 6.1 Hz); **$[\alpha]_D^{20}$** -37.2 (*c* = 0.98, $CHCl_3$); **HRMS** (ESI+): found 545.0747; $C_{27}H_{18}ClF_3N_4OK$, $[M+K]^+$ requires 545.0758; **ν_{max}** (neat): 3363.9, 1710.8, 1612.1, 1490.9, 1280.3, 1140.6, 1094.0; **HPLC**: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 18.7 min, t_R (minor) = 16.7 min.

* **C16** not observed due to low signal intensity.

1-Benzyl-2-oxo-5'-(trifluoromethyl)-4'-(3,4,5-trimethoxyphenyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3h)

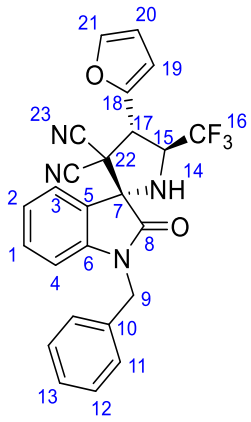


1a (51 mg, 0.160 mmol, 1 eq.), **2h** (47 mg, 0.192 mmol, 1.2 eq.) and **C1** (9 mg, 0.0160 mmol, 0.1 eq.) after 3 days afforded the spirocycle (75 mg, 84%, 92% ee, 7.3:1 d.r.) as a white foam solid. Crude was purified using 1% acetone in toluene.

Major δ_H (400 MHz, $CDCl_3$): 7.79 (1H, d, *J* 7.9 Hz, **H3**), 7.41-7.31 (6H, m, **H1+H11-13**), 7.20 (1H, t, *J* 7.7, **H2**), 6.81 (3H, m, **H4+H19**), 5.43 (1H, d, *J* 10.8 Hz, **H17**), 5.23 (1H, d, *J* 15.7 Hz, **H9'**), 4.79-4.71 (1H, m, **H15**), 4.68 (1H, d, *J* 15.6 Hz, **H9**), 3.92 (6H, s, **H22**), 3.90 (3H, s, **H23**), 2.89 (1H, d, *J* 7.6 Hz, **H14**); **Major δ_C** (101 MHz, $CDCl_3$): 173.6 (**C8**), 153.8 (***Ar***), 143.8 (***Ar***), 139.5 (***Ar***), 134.5 (***Ar***), 132.6 (***Ar***), 129.2 (***Ar***), 128.3 (***Ar***), 127.7 (***Ar***), 125.1 (**C3**), 124.8 (***Ar***), 124.1 (**C2**), 122.1 (***Ar***), 111.7 (**C25'**), 111.6 (**C25**), 110.7 (**C4**), 106.2 (**C19**), 70.7 (**C7**), 61.1 (**C23**), 60.3 (q, $J_{C\text{-}F}$ 31.9 Hz, **C15**), 56.5 (**C22**), 52.3 (**C17**), 51.6 (**C24**), 44.8 (**C9**);* **Major δ_F** (376 MHz, $CDCl_3$): -73.5 (3F, d, *J* 6.1 Hz); **$[\alpha]_D^{20}$** -36.7 (*c* = 0.98, $CHCl_3$); **HRMS** (ESI+): found 601.1465; $C_{30}H_{23}F_3N_4O_4K$, $[M+K]^+$ requires 601.1460; **ν_{max}** (neat): 3326.6, 2931.6, 1710.8, 1593.4, 1464.8, 1284.1, 1250.5, 1125.7; **HPLC**: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 20.7 min, t_R (minor) = 9.9 min.

* **C16** not observed due to low signal intensity.

1-Benzyl-4'-(furan-2-yl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3i)

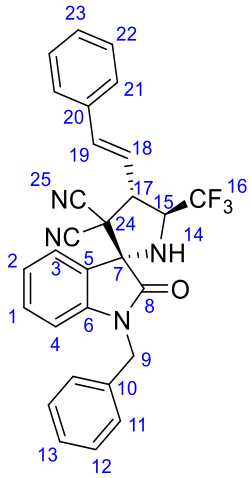


1a (50.6mg, 0.159 mmol, 1 eq.), **2i** (27.6 mg, 0.192 mmol, 1.2 eq.) and **C1** (9 mg, 0.0194 mmol, 0.1 eq.) after 1 day afforded the spirocycle (55 mg, 75 %, 91% ee, 16:1 d.r.) as a yellow solid. Crude was purified using 1% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$): 7.79 (1H, d, *J* 7.8 Hz, **H3**), 7.56 (1H, d, *J* 1.5 Hz, ***Ar***), 7.40-7.27 (6H, m, **H1** + **H11-13**), 7.18 (1H, t, *J* 7.7 Hz, **H2**), 6.79 (1H, d, *J* 7.7 Hz, **H4**), 6.68 (1H, d, *J* 3.4 Hz, **H19**), 6.48 (1H, dd, *J* 3.3, 1.9 Hz, **H20**), 5.62 (1H, d, *J* 10.7 Hz, **H17**), 5.19 (1H, d, *J* 15.7 Hz, **H9'**), 4.87-4.80 (1H, m, **H15**), 4.69 (1H, d, *J* 15.7 Hz, **H9**), 2.94 (1H, d, *J* 7.9 Hz, **H14**); **Major** δ_C (151 MHz, $CDCl_3$): 173.4 (**C8**), 144.7 (***Ar***), 143.9 (***C10***), 143.8 (***C18***), 134.5 (***Ar***), 132.6 (***Ar***), 129.1 (***Ar***), 128.2 (***Ar***), 127.7 (***Ar***), 125.1 (**C3**), 124.0 (**C2**), 121.7 (***Ar***), 111.9 (***Ar***), 111.3 (**C23'**), 111.3 (**C20**), 111.2 (**C23**), 110.6 (**C4**), 70.6 (**C7**), 59.8 (q, $J_{C\text{-}F}$ 32.3 Hz, **C15**), 49.6 (**C22**), 46.6 (**C17**), 44.7 (**C9**);* **Major** δ_F (564 MHz, $CDCl_3$): -74.0 (3F, d, *J* 5.6 Hz); $[\alpha]_D^{20}$ -43.2 (*c* = 1.02, $CHCl_3$); **HRMS** (ESI+): found 463.1382; $C_{25}H_{17}F_3N_4O_2H$, $[M+H]^+$ requires 463.1377; ν_{max} (thin film): 3358.3, 2228.9, 1718.3, 1610.2, 1490.9, 1371.7, 1289.7, 1140.6; **HPLC:** Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.2 min, t_R (minor) 9.2 min.

* **C16** not observed due to low signal intensity.

(E)-1-benzyl-2-oxo-4'-styryl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3j)

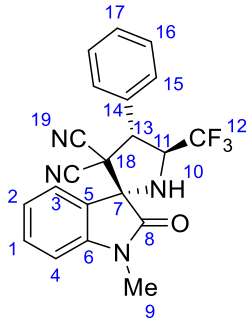


1a (50.0 mg, 0.157 mmol, 1 eq.), **2j** (34.0 mg, 0.189 mmol, 1.2 eq.) and **C1** (9 mg, 0.0159 mmol, 0.1 eq.) after 3 days afforded the spirocycle (52 mg, 67 %, 94% ee, 11.5:1 d.r.) as a yellow solid. Crude was purified using 1% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$): 7.77 (1H, d, *J* 7.6 Hz, **H3**), 7.51-7.47 (2H, m, ***Ar***), 7.41-7.30 (9H, m, ***Ar*+H1**), 7.18 (1H, t, *J* 7.7 Hz, **H2**), 7.02 (1H, d, *J* 15.8 Hz, **H19**), 6.79 (1H, d, *J* 7.7 Hz, **H4**), 6.30 (1H, dd, *J* 15.8, 9.3 Hz, **H18**), 5.20 (1H, d, *J* 15.8 Hz, **H9'**), 5.01 (1H, t, *J* 9.9 Hz, **H17**), 4.67 (1H, d, *J* 15.7 Hz, **H9**), 4.36-4.26 (1H, m, **H15**), 2.18 (1H, d, *J* 7.8 Hz, **H14**); **Major δ_C** (151 MHz, $CDCl_3$): 173.5 (**C8**), 143.8 (***Ar***), 140.2 (**C19**), 135.4 (***Ar***), 134.6 (***Ar***), 132.5 (***Ar***), 129.2 (***Ar***), 129.1 (***Ar)***, 128.9 (***Ar***), 128.2 (***Ar***), 127.7 (***Ar***), 127.3 (***Ar***), 125.0 (**C3**), 124.0 (**C2**), 122.0 (***Ar***), 118.0 (**C18**), 114.4 (**C25**), 113.3 (**C25**), 110.6 (**C4**), 70.5 (**C7**), 62.0 (q, $J_{C\text{-}F}$ 31.6 Hz, **C15**), 51.0 (**C22**), 50.2 (**C17**), 44.8 (**C9**);* **Major δ_F** (564 MHz, $CDCl_3$): -74.0 (3F, d, J 6.5); **$[\alpha]_D^{20}$** -19.8 (*c* = 0.5, $CHCl_3$); **HRMS** (ESI+): found 499.1746; $C_{29}H_{21}F_3N_4OH$, $[M+H]^+$ requires 499.1740; **ν_{max}** (thin film): 3362.1, 2228.9, 1722.0, 1610.2, 1490.9, 1289.7, 1170.4, 1144.3; **HPLC**: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 15.3 min, t_R (minor) = 8.8 min.

* **C16** not observed due to low signal intensity.

1-Methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3k)



1b (50 mg, 0.206 mmol, 1 eq.), **2a** (38 mg, 0.248 mmol, 1.2 eq.) and **C1** (12 mg, 0.0206 mmol, 0.1 eq.) after 3 days afforded the spirocycle (63 mg, 77%, 85% ee, 2.0:1 d.r.) as a cream coloured glassy solid residue. Crude was purified using 1% acetone in toluene.

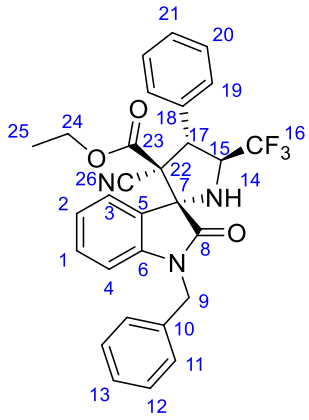
Major δ_H (400 MHz, $CDCl_3$): 7.79 (1H, d, *J* 7.7 Hz, **H3**), 7.61-7.57 (2H, m, **H15**), 7.53-7.46 (4H, m, **H1+16+17**), 7.22 (1H, td, *J* 7.8, 1.1 Hz, **H2**), 6.93 (1H, d, *J* 7.8 Hz, **H4**), 5.44 (1H, d, *J* 10.7 Hz, **H13**), 4.84-4.74 (1H, m, **H11**), 3.27 (3H, s, **H9**), 2.98 (1H, d, *J* 7.5 Hz, **H10**); **Minor δ_H** (400 MHz, $CDCl_3$):* 7.69 (1H, d, J 7.6 Hz, **H3**), 7.61-7.57 (m, ***Ar***), 7.53-7.46 (m, **Ar**), 7.28 (1H, dd, J 7.8 Hz, 1.0 Hz, **H2**), 6.97 (1H, d, *J* 7.8 Hz, **H4**), 5.07-4.98 (1H, m, **H11**), 4.45 (1H, d, *J* 10.3 Hz, **H13**), 3.29 (3H, s, **H9**), 3.32-3.17 (1H, m, **H10**); **Major δ_C** (101 MHz, $CDCl_3$):† 173.4 (**C8**), 144.5 (***Ar***). 132.6 (**C1**), 130.2 (***Ar***), 129.5 (***Ar***), 129.0 (***Ar***), 125.0 (**C3**), 124.0 (**C2**), 122.0 (**Ar**), 111.3 (**C19'**), 111.2 (**C19**), 109.5 (**C4**), 70.9 (**C7**), 60.1 (q, $J_{C\text{-}F}$ 31.3 Hz, **C11)**, 51.7 (**C13**) ,51.6 (**C18**), 26.8 (**C9**);‡ **Minor δ_C** (101 MHz, $CDCl_3$):173.3 (**C8**), 143.3 (***Ar***), 132.6 (***Ar***), 132.1 (***Ar***), 130.3 (***Ar***), 130.1 (***Ar***), 129.5 (***Ar***), 129.3 (***Ar***), 126.1 (***Ar***) 125.6 (***Ar***), 124.2 (***Ar***), 112.5 (**C19'**), 110.4 (**C19**), 109.6 (**C4**), 72.3 (**C7**), 61.2 (q, $J_{C\text{-}F}$ 32.4 Hz, **C11)**, 55.5 (**C13**), 51.5 (**C18**), 27.3 (**C9**); **Major δ_F** (376 MHz, $CDCl_3$): -73.5 (3F, d, *J* 6.1 Hz); **Minor δ_F** (376 MHz, $CDCl_3$): -74.3 (3F, d, *J* 5.9 Hz); **Sole Major diastereomer $[\alpha]_D^{20}$** -71.4 (*c* = 1.01, $CHCl_3$); **Mix of diastereomers $[\alpha]_D^{20}$** -25.5 (*c* = 1.01, $CHCl_3$); **HRMS** (ESI+): found 397.1276; $C_{21}H_{15}F_3N_4OH$, $[M+H]^+$ requires 397.1271; **ν_{max}** (thin film): 3365.8, 2926.0, 1718.3, 1613.9, 1289.7, 1170.4, 1140.6; **HPLC**: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 13.3 min, t_R (minor) = 8.7 min.

* Due to significant overlapping in the aromatic region, integration of certain multiplets was inaccurate and therefore excluded although where possible, assignment was made *via* 2D analysis.

† A small amount of the major diastereomer was able to separated whilst the other fraction contained both diastereomers, therefore assignment was made by subtracting the peaks not present in the major diastereomer spectra

‡ **C14** and **C16** not observed due to low signal intensity.

Ethyl-1-benzyl-3'-cyano-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carboxylate (3l)



Major diastereomer

1a (50 mg, 0.157 mmol, 1 eq.), **2l** (38 mg, 0.189 mmol, 1.2 eq.) and **C1** (9 mg, 0.0160 mmol, 0.1 eq.) after 3 days afforded the spirocycle (78 mg, 95%, 94% ee, 1.8:1:0.05 or 1:0.41:0.02)[*] as a yellow solid. Crude was purified using 0.5→1% acetone in toluene.

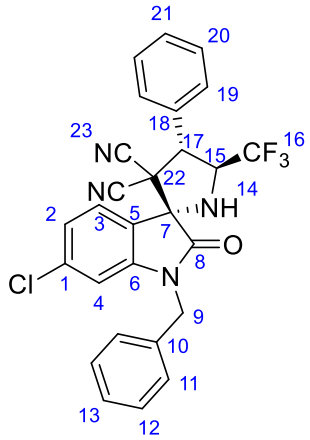
Major δ_H (400 MHz, $CDCl_3$):[†] 7.91 (1H, dd, *J* 7.6 Hz, 0.8 Hz, **H3**), 7.65 (m, ***Ar***), 7.41-7.27 (m, ***Ar***), 7.17 (1H, td, *J* 7.6, 0.9 Hz, **H2**), 6.80 (1H, d, *J* 7.9 Hz, **H4**), 5.43 (1H, d, *J* 10.9 Hz, **H17**), 5.07 (1H, d, *J* 15.6 Hz, **H9'**), 4.76-4.66 (1H, m, **H15**), 4.61 (1H, d, *J* 15.4 Hz, **H9**), 3.79 (1H, dq, *J* 10.7, 7.1 Hz, **H24'**), 3.68 (1H, dq, *J* 10.7, 7.1 Hz, **H24**), 2.79 (1H, d, *J* 8.0 Hz, **H14**), 0.72 (3H, t, *J* 7.2 Hz, **H25**); **Minor δ_H** (400 MHz, $CDCl_3$):[‡] 7.78 (1H, d, *J* 7.5 Hz, **H3**), 7.41-7.27 (m, ***Ar***), 7.09 (1H, td, *J* 7.8, 0.9 Hz, **H2**), 6.78 (1H, m, **H4**), 5.17 (1H, d, *J* 15.6 Hz, **H9'**), 4.89-4.81 (1H, m, **H15**), 4.76-4.66 (2H, m, **H9+H17**), 3.66-3.55 (2H, m, **H24**), 2.79 (1H, d, *J* 8.2 Hz, **H14**), 0.56 (3H, t, *J* 7.2 Hz, **H25**); **δ_C**(101 MHz, $CDCl_3$):[§] 174.5 (**C8, Min**), 174.3 (**C8, Maj**), 163.4 (**C23, Min**), 162.5 (**C23, Maj**), 143.8, 142.6, 135.5, 135.0, 132.2, 132.1, 131.4, 130.8, 130.0, 129.9, 129.2, 129.1, 129.0, 128.8, 128.7, 128.2, 128.1, 128.0, 127.4, 125.8, 125.0, 124.6, 123.5, 123.4, 115.2, 114.1, 109.7, 109.4, 72.3(**C7, Min**) , 70.0 (**C7, Maj**), 63.7 (**C22, Min**), 63.5 (**C22, Maj**), 63.3 (**C24, Min**), 63.2 (**C24, Maj**), 62.7 (q, $J_{C\text{-}F}$ 30.4 Hz, **C15, Min**), 61.8 (q, $J_{C\text{-}F}$ 31.3 Hz, **C15, Maj**), 51.2 (**C17, Min**), 49.0 (**C17, Maj**), 44.9 (**C9, Min**), 44.5 (**C9, Maj**), 13.4 (**C25, Maj**), 13.2 (**C25, Min**);[**] **Major δ_F** (376 MHz, $CDCl_3$): -73.4 (3F, d, *J* 6.4 Hz); **Minor δ_F** (376 MHz, $CDCl_3$): -74.4 (3F, d, *J* 6.0 Hz); **$[\alpha]_D^{20}$** -42.1 (*c* = 1.02, $CHCl_3$); **HRMS** (ESI+): found 558.1405; $C_{29}H_{24}F_3N_3O_3K$, $[M+K]^+$ requires 558.1402; **ν_{max}** (neat): 3330.4,

[*] A further minor diastereomer can observed in the crude NMR.
[†] Due to significant overlapping in the aromatic region, integration of certain multiplets was inaccurate and therefore excluded although where possible, assignment was made *via* 2D analysis.
[‡] H17 peak is absent in minor due to being buried in 4.76-4.66 multiplet, observed *via* 2D analysis
[§] Due to the small d.r. complete assignment of the individual diastereomer carbon peaks are not given, but assignment of certain peaks has been given where possible via 2D NMR.
[**] **C16** not observed due to low signal intensity.

1720.2, 1237.5, 1164.8, 1136.8, 752.9, 697.0; **HPLC:** Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 18.9 min, t_R (minor) = 9.8 min.

The relative and absolute configuration of the major diastereomer (–)-**3l**$_{maj}$ was determined by single crystal x-ray diffraction (see section 6.2 below).

*1-Benzyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (**3m**)*



1c (50 mg, 0.142 mmol, 1 eq.), **2a** (26.2 mg, 0.170 mmol, 1.2 eq.) and **C1** (8.0 mg, 0.014 mmol, 0.1 eq.) after 1 day afforded the spirocycle (66.8 mg, 93%, 89% ee, 2.3:1 d.r.) as a pink foam solid. Crude was purified using 0.5% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$):* 7.72 (1H, d, *J* 8.2 Hz, **H3**), 7.63-7.58 (m, ***Ar***), 7.51-7.47 (m, ***Ar***), 7.40-7.34 (5H, m, **H11-13**), 7.16 (1H, dd, *J* 8.1, 1.8 Hz, **H2**), 6.80 (1H, d, *J* 1.8 Hz, **H4**), 5.46 (1H, d, *J* 10.7 Hz, **H17**), 5.19 (1H, d, *J* 15.7 Hz, **H9'**), 4.82-4.76 (1H, m, **H15**), 4.66 (1H, d, *J* 15.7 Hz, **H9**), 2.87 (1H, d, *J* 7.3 Hz, **H14**); **Minor δ_H** (600 MHz, $CDCl_3$): 7.63-7.58 (m, **H3** + ***Ar***), 7.33-7.29 (5H, m, **H11-13**), 7.20 (1H, dd, *J* 8.1, 1.9 Hz, **H2**), 6.83 (1H, d, *J* 1.7 Hz, **H4**), 5.11 (1H, d, *J* 15.7 Hz, **H9'**), 5.09-5.04 (1H, m, **H15**), 4.77 (1H, d, *J* 15.5 Hz, **H9**), 4.40 (1H, d, *J* 10.1 Hz, **H17**), 3.10 (1H, d, *J* 6.5 Hz, **H14**); **Major δ_C** (151 MHz, $CDCl_3$):†,‡ 173.7 (**C8 Min**), 173.4 (**C8, Maj**), 145.0 (**C5/6, Maj**), 143.8 (**C5/6, Min)**, 138.8 (**C1, Maj**), 138.2 (**C1, Min**), 134.8, 134.0, 133.8, 130.9, 130.4, 130.3, 130.1, 129.8, 129.6, 129.5, 129.42, 129.37, 129.34, 129.29, 129.0, 128.6, 128.5, 127.7, 127.5, 126.9, 126.2 (**C3, Maj**), 124.2 (**C2, Min**), 124.0 (**C2, Maj**), 120.4 (**C5/6, Maj**), 111.28 (**C4, Min**), 111.24 (**C23, Maj**), 111.23 (**C4, Maj**), 110.4 (**C23, Min**), 72.0 (**C7, Min**), 70.4 (**C7, Maj**), 61.3 (q, $J_{C\text{-}F}$ 30.0 Hz, **C15, Min**), 60.0 (q, $J_{C\text{-}F}$ 32.1 Hz, **C15, Maj**), 55.7 (**C22, Min**), 51.7 (**C22, Maj**), 45.0 (**C9, Min**), 44.9 (**C9, Maj**); **Major δ_F** (564 MHz, $CDCl_3$): -73.5 (3F, d, *J* 6.0 Hz); **Minor δ_F** (564 MHz, $CDCl_3$): -74.1 (3F, d, *J* 5.7 Hz); **$[\alpha]_D^{20}$** -33.2 (*c* = 1.00, $CHCl_3$); **HRMS** (ESI+): found 507.1199; $C_{27}H_{18}ClF_3N_4OH$, $[M+H]^+$ requires 507.1193; **ν_{max}** (film): 3339.7, 2922.2, 2253.2, 1720.2, 1608.3, 1490.9, 1284.1, 1142.4; **HPLC:** Chiral ART Amylose-SB (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 13.1 min, t_R (minor) = 7.6 min.

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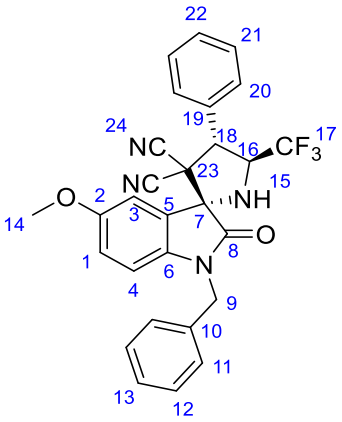
* Due to significant overlapping of major and minor diastereomers in the aromatic region, integration of certain multiplets was inaccurate and therefore omitted. Where possible, assignment was made *via* 2D analysis.

† Due to the low d.r. complete assignment of the individual diastereomer carbon peaks are not given, but assignment of certain peaks has been given where possible via 2D NMR.

‡ **C16** not observed due to low signal intensity.

*1-Benzyl-5-methoxy-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (**3n**)*

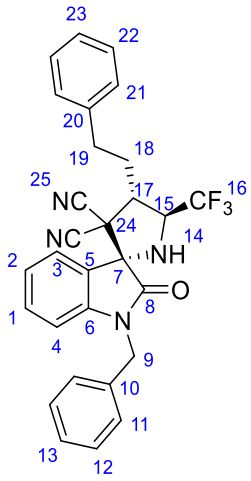


1d (50 mg, 0.144 mmol, 1 eq.), **2a** (26.6 mg, 0.172 mmol, 1.2 eq.) and **C1** (8.1 mg, 0.014 mmol, 0.1 eq.) after 1 day afforded the spirocycle (70.8 mg, 98%, 93% ee, 8.2:1 d.r.) as a white foam solid. Crude was purified using 0.5% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$): 7.63-7.60 (2H, m, **H20/21/22**), 7.51-7.47 (3H, m, **H20/21/22**), 7.40 (1H, d, *J* 2.5 Hz, **H3**), 7.39-7.37 (2H, m, **H11/12**), 7.36-7.32 (2H, m, **H11/12**), 7.31-7.28 (1H, m, **H13**), 6.68 (1H, dd, *J* 8.7, 2.5 Hz, **H1**), 6.69 (1H, d, *J* 8.6 Hz, **H4**), 5.53 (1H, d, *J* 10.7 Hz, **H18**), 5.20 (1H, d, *J* 15.6 Hz, **H9'**), 4.85-4.77 (1H, m, **H16**), 4.66 (1H, d, *J* 15.6 Hz, **H9**), 3.79 (3H, s, **H14**), 2.90 (1H, dd, *J* 7.3, 2.8 Hz, **H15**); **Major δ_C** (151 MHz, $CDCl_3$):* 173.4 (**C8**), 156.8 (**C2**), 136.9 (**C5/6**), 134.7 (**C10**), 130.3 (**C19**), 129.6 (**C20/21/22**), 129.5 (**C20/21/22**), 129.1 (***Ar***), 129.0 (**C20/21/22**), 128.2 (***Ar***), 127.7 (***Ar***), 123.2 (**C5/6**), 117.3 (**C1**), 112.1 (**C3**), 111.5 (**C24'**), 111.4 (**C24**), 111.2 (**C4**), 71.0 (**C7**), 60.1 (q, $J_{C\text{-}F}$ 32.4 Hz, **C16**), 56.1 (**C14**), 51.8 (**C18**), 51.7 (**C23**), 44.9 (**C9**); **Major δ_F** (564 MHz, $CDCl_3$): -7.41 (3F, d, *J* 6.0 Hz); **$[\alpha]_D^{20}$** -8.5 (*c* = 1.05, $CHCl_3$); **HRMS** (ESI+): found 503.1695; $C_{28}H_{21}F_3N_4O_2H$, $[M+H]^+$ requires 503.1690; **ν_{max}** (film): 3363.9, 2924.1, 1994.1, 1716.4, 1455.5, 1284.1, 1144.3; **HPLC**: Chiral ART Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 32.2 min, t_R (minor) = 10.1 min.

* **C16** not observed due to low signal intensity.

*1-benzyl-2-oxo-4'-phenethyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (**3o**)*

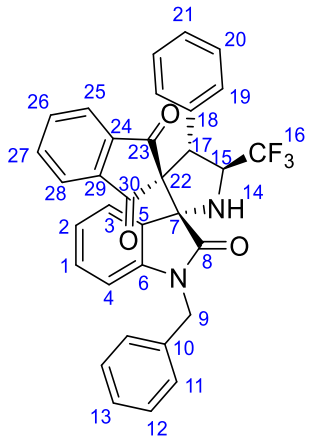


1a (50.0 mg, 0.157 mmol, 1 eq.), **2o** (34.5 mg, 0.190 mmol, 1.2 eq.) and **C1** (9 mg, 0.0157 mmol, 0.1 eq.) after 1 day afforded the spirocycle (71 mg, 90 %, 73% ee, >100:1 d.r.) as a yellow foam solid. Crude was purified using 0.5% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$): 7.74 (1H, d, *J* 7.6 Hz, **H3**), 7.38-7.31 (7H, m, **H1** + ***Ar***), 7.30-7.22 (4H, m, ***Ar***), 7.17 (1H, td, *J* 7.7, 0.8 Hz, **H2**), 6.77 (1H, d, *J* 7.9 Hz, **H4**), 5.15 (1H, d, *J* 15.7 Hz, **H9'**), 4.67 (1H, d, *J* 15.7 Hz, **H9**), 4.35 (1H, td, *J* 10.2, 3.7 Hz, **H17**), 4.03-3.97 (1H, m, **H15**), 3.05 (1H, td, *J* 13.5, 5.3 Hz, **H18'**), 2.95-2.89 (1H, m, **H18**), 2.74 (1H, d, *J* 7.6 Hz, **H14**), 2.44-2.37 (1H, m, **H19'**), 2.32- 2.25 (1H, m, **H19**); **Major δ_C** (151 MHz, $CDCl_3$):* 173.4 (**C8**), 144.0 (**C5/6**), 140.1 (***Ar***), 134.6 (***Ar***), 132.5 (**C1**), 129.1 (***Ar***), 128.9 (***Ar***), 128.4 (***Ar***), 128.2 (***Ar***), 127.7 (***Ar***), 126.7 (***Ar***), 125.0 (**C3**), 123.9 (**C2**), 122.1 (**C5/6**), 112.6 (**C25'**), 111.2 (**C25**), 110.6 (**C4**), 71.2 (**C7**), 63.3 (q, $J_{C\text{-}F}$ 32.1 Hz, **C15**), 48.4 (**C24**), 46.8 (**C17**), 44.7 (**C9**), 33.8 (**C18**), 32.2 (**C19**); **Major δ_F** (564 MHz, $CDCl_3$): -72.9 (3F, d, *J* 6.7 Hz); **$[\alpha]_D^{20}$** -17.1 (*c* = 1.06, $CHCl_3$); **HRMS** (ESI+): found 501.1899; $C_{29}H_{23}F_3N_4OH$, $[M+H]^+$ requires 501.1897; **ν_{max}** (film): 3352.7, 2924.1, 2251.3, 1712.7, 1612.1, 1470.4, 1284.1, 1133.1; **HPLC**: Chiral ART Amylose-SA (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 12.6 min, t_R (minor) = 7.5 min.

* **C16** not observed due to low signal intensity.

1''-Benzyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2''(3H)- dione (5a)

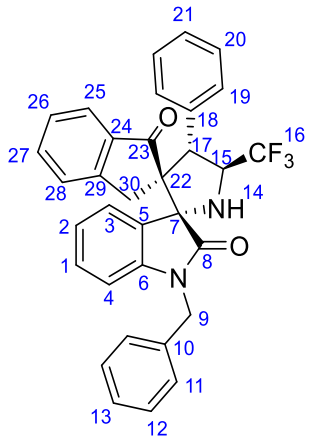


1a (100 mg, 0.315 mmol, 1 eq.), **4a** (90.6 mg, 0.387 mmol, 1.2 eq.) and **C1** (18 mg, 0.0319 mmol, 0.1 eq.) after 1 day afforded the spirocycle (133 mg, 77 %, 85% ee, 23.0:1 d.r.) as a sandy-coloured solid. Crude was purified using 1:1 DCM:hexane; → 100 % DCM.

Major δ_H (600 MHz, $CDCl_3$): 7.69-7.64 (1H, m, **Indanone**), 7.62-7.58 (1H, m **Indanone**), 7.56-7.51 (2H, m, **Indanone**), 7.34 (4H, m, ***Ar***), 7.27 (3H, m, ***Ar***), 7.18 (1H, d, *J* 7.8 Hz, **H3**), 7.18 (2H, d, *J* 7.3, ***Ar***), 7.07-7.04 (1H, m, ***Ar***), 6.97 (1H, t, *J* 7.8 Hz, **H1**), 6.77 (1H, t, *J* 7.6 Hz, **H2**), 6.44 (1H, d, *J* 7.9 Hz, **H4**), 5.50 (1H, d, *J* 10.6 Hz, **H17**), 5.37-5.30 (1H, m, **H15**), 5.28 (1H, d, *J* 13.2 Hz, **H9'**), 4.42 (1H, d, *J* 15.5 Hz, **H9**), 3.19 (1H, d, *J* 8.7 Hz, **H14**); **Major δ_C** (151 MHz, $CDCl_3$): 198.7 (**C8**), 195.4 (C=O), 175.5 (C=O), 143.8 (***Ar***), 142.6 (***Ar***), 141.9 (***Ar***), 136.1 (***Ar***), 136.0 (***Ar***), 135.8 (***Ar***), 132.8 (***Ar***), 130.6 (**C1**), 129.1 (***Ar***), 128.8 (***Ar***), 128.6 (***Ar***), 128.1 (***Ar***), 127.9 (***Ar***), 127.8 (***Ar***), 124.9 (**C3**), 123.7 (***Ar***), 123.1 (***Ar***), 123.0 (***Ar***), 122.4 (**C2**), 109.5 (**C4**), 71.2 (**C7**), 71.0 (**C22**), 61.3 (q, $J_{C\text{-}F}$ 31.0 Hz, **C15**), 49.7 (**C17**), 44.5 (**C9**);* **Major δ_F** (564 MHz, $CDCl_3$): -78.4 (3F, d, *J* 7.0 Hz); **$[\alpha]_D^{20}$** -146.9 (*c* = 1.06, $CHCl_3$); **HRMS** (ESI+): found 553.1722; $C_{33}H_{23}F_3N_2O_3H$, $[M+H]^+$ requires 553.1734; **ν_{max}** (thin film): 3365.8, 2929.7, 2255.0, 1740.7, 1699.7, 1610.2, 1490.9, 1349.3, 1259.8, 1133.1; **HPLC:** Chiral ART Amylose-SA (with column guard), 35% $CHCl_3$-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 10.7 min, t_R (minor) = 5.4 min.

* **C16** not observed due to low signal intensity.

1''-Benzyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (5b)



1a (100 mg, 0.314 mmol, 1 eq.), **4b** (83mg, 0.337 mmol, 1.2 eq.) and **C1** (18 mg, 0.0314 mmol, 0.1 eq.) after 4 days afforded the spirocycle (90 mg, 53 %, 8.0:1 d.r.) as a pale yellow solid. Crude was purified using 1% acetone in toluene.

Major δ_H (600 MHz, $CDCl_3$): 7.45 (1H, d, *J* 7.6 Hz, **H3**),7.40-7.30 (6H, m, ***Ar***), 7.29-7.26 (2H, m, **indanone**), 7.23-7.16 (3H, m, ***Ar***), 7.14 (1H, t, *J* 7.3 Hz, ***Ar***) 6.97 (2H, m, **indanone**), 6.90 (1H, t, *J* 7.7 Hz, **H1**), 6.80 (1H, t, *J* 7.3 Hz, **H2**), 6.31 (1H, d, *J* 7.8 Hz, **H4**), 5.44 (1H, d, *J* 10.9 Hz, **H17**), 5.22 (1H, d, *J* 15.3 Hz, **H9'**), 4.74 (1H, m, **H15**), 4.27 (1H, d, *J* 15.5 Hz, **H9**), 3.48 (1H, d, *J* 16.5 Hz, **H30'**), 3.10 (1H, d, *J* 16.4 Hz, **H30**), 2.75 (1H, s, **H14**); **Major** δ_C (151 MHz, $CDCl_3$): 201.3 (**C23**), 177.5 (**C8**), 151.2 (***Ar***), 143.9 (**C10**), 136.3 (***Ar***), 135.8 (***Ar***), 134.8 (***Ar***), 134.5 (**C10**), 130.0 (***Ar***), 129.5 (**C1**), 128.8 (***Ar***), 128.5 (***Ar***), 127.9 (***Ar***), 127.7 (***Ar***), 127.2 (***Ar***), 126.3 (***Ar***), 125.6 (***Ar***), 125.1 (***Ar***), 124.4 (**C3**), 123.6 (***Ar***), 121.7 (**C2**), 109.1 (**C4**), 73.5 (**C7**), 68.5 (**C22**), 60.6 (q, $J_{C\text{-}F}$ 30.7 Hz, **C15**), 47.7 (**C17**), 44.6 (**C9**), 31.4 (**C30**);* **Major** δ_F (564 MHz, $CDCl_3$): -72.4 (3F, d, J 6.5 Hz); $[\alpha]_D^{20}$ -71.4 (*c* = 1.01, $CHCl_3$). **HRMS** (ESI+): found 539.1933; $C_{33}H_{25}F_3N_2O_2H$, $[M+H]^+$ requires 539.1941; ν_{max} (thin film): 3339.7, 2922.2, 2251.3, 1718.3, 1606.5, 1349.3, 1278.5, 1136.8.

The enantiomeric composition of this material could not be determined since we were unable to produce a racemic standard of the required diastereoisomer. All attempts to do so (DBU, NEt_3/Schreiner's catalyst, and an achiral cinchona-thiourea surrogate catalyst derived from 4-(2-aminoethyl)morpholine and 3,5-bis(trifluoromethyl)phenyl isothiocyanate) gave an insufficient quantity of (±)-**5b** to allow identification of enantiomers by HPLC.

* **C16** not observed due to low signal intensity.

Its relative configuration was determined by NOESY analysis (Figure S2), and assuming the relative configuration of the 3 non-indanone stereocentres are identical to **5a**.

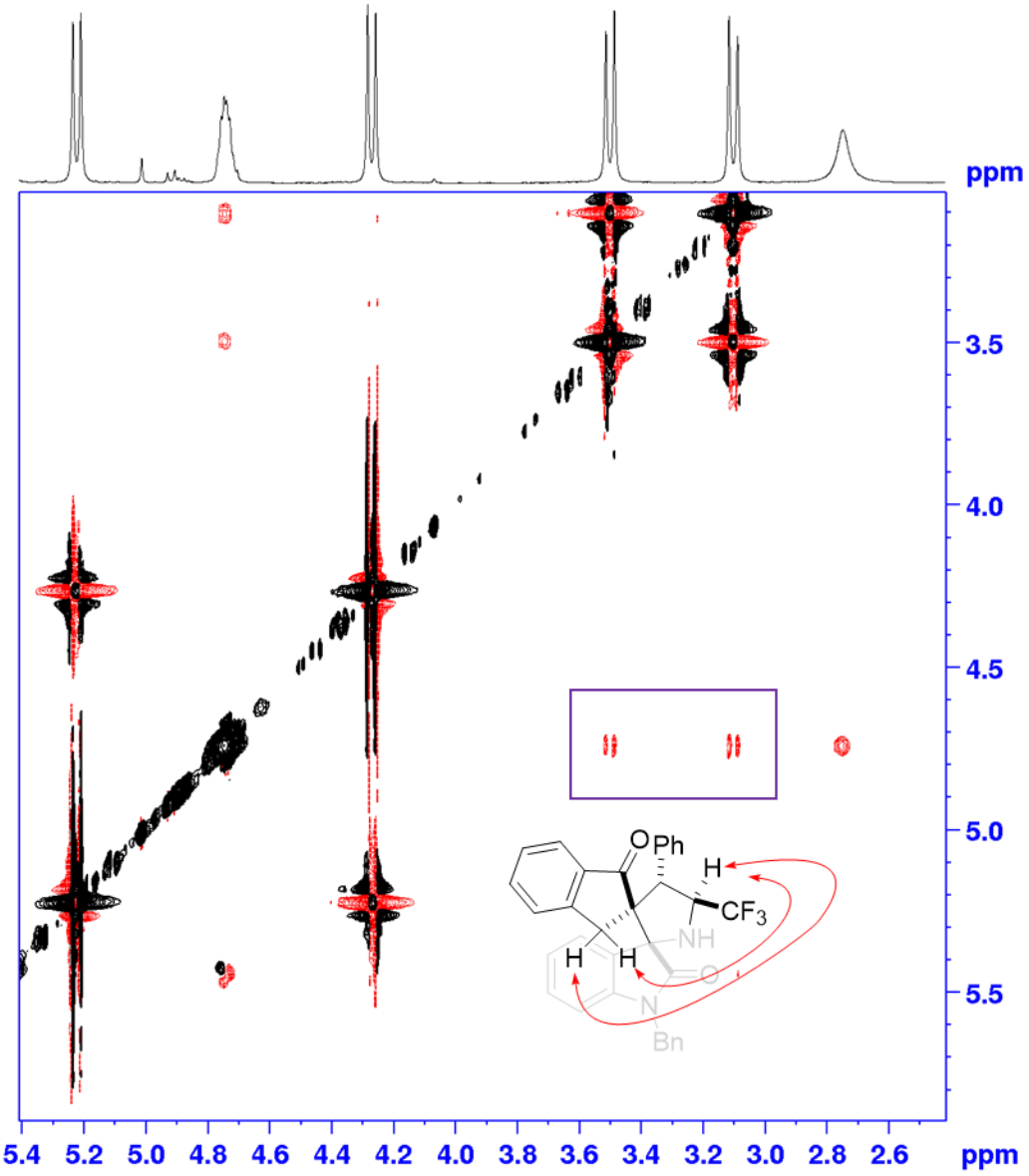
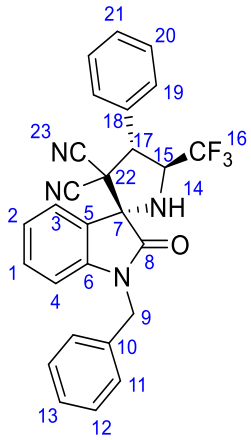


Figure S2. NOESY analysis of indanone **5b** ($CDCl_3$, 600 MHz, t_{mix} 0.3 s). Key stereochemically consequential nOe signals are indicated.

4 HPLC data

1-Benzyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3a)



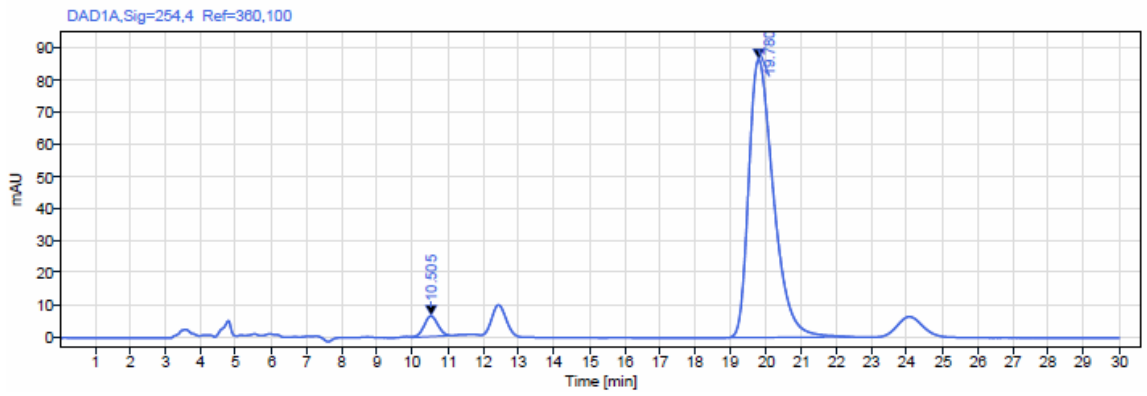
Conditions: Chiral ART Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.8 min, t_R (minor) = 10.5 min.

50 mg scale asymmetric trace: 92% ee

Single Injection Report

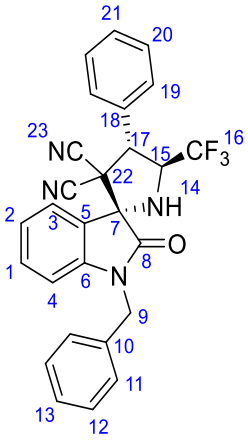
Agilent Technologies

Data file:	WR 2.144.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.144	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-05-03 12:15:33+01:00
Inj. volume:	25.000	**Location:**	3
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.505	VB	1.10	172.76	6.39	3.94	
19.780	BB	3.44	4209.27	86.43	96.06	
		Sum	4382.03			

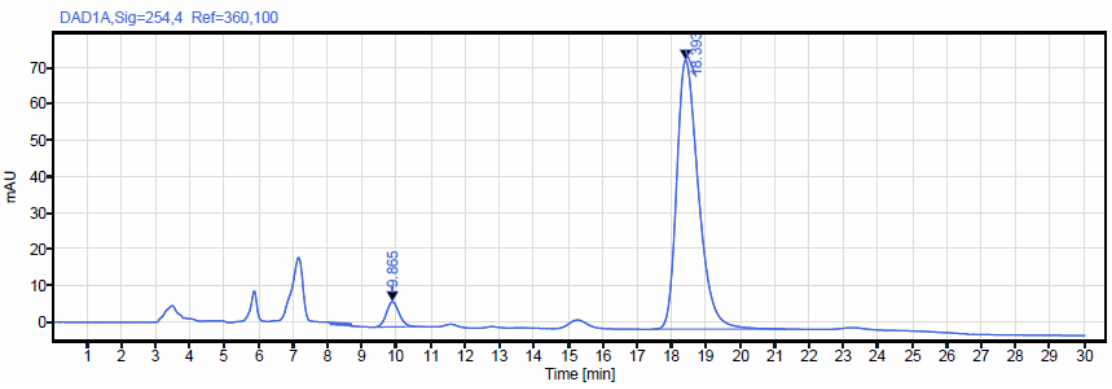


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 18.4 min, t_R (minor) = 9.9 min.

250 mg scale asymmetric trace: 90% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.176 Run 3.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.176 Run 3	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-07-29 08:52:16+01:00
Inj. volume:	25.000	**Location:**	1
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

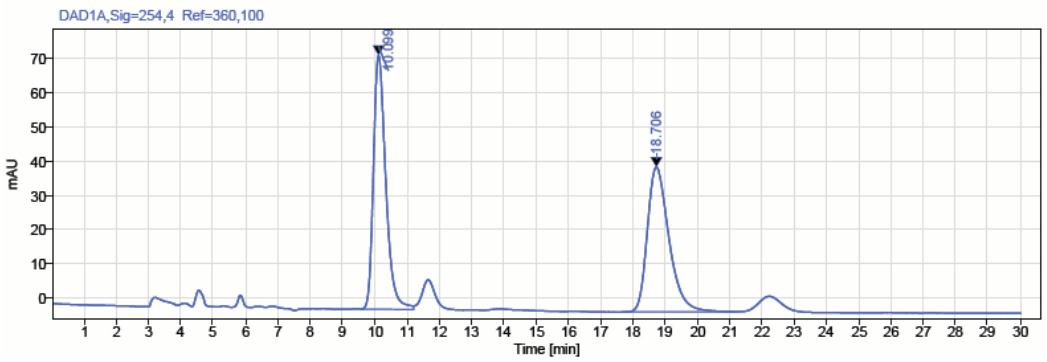
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.865	MM m	0.38	176.80	6.91	5.15	
18.393	BM m	0.66	3253.69	74.06	94.85	
		Sum	3430.49			

Racemic trace

Single Injection Report

Agilent Technologies

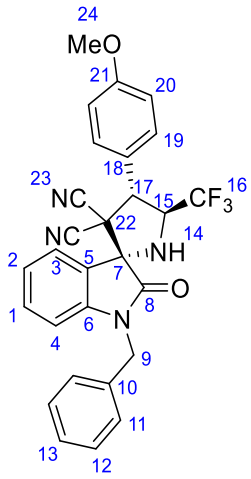
Data file:	WR 2.139 Vial 1.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.139 Vial 1	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-03-25 16:20:05+00:00
Inj. volume:	25.000	**Location:**	1
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.099	BV	1.65	1972.49	74.25	50.00	
18.706	BB	3.46	1972.24	42.35	50.00	
		Sum	3944.73			

1-Benzyl-4'-(4-methoxyphenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3b)

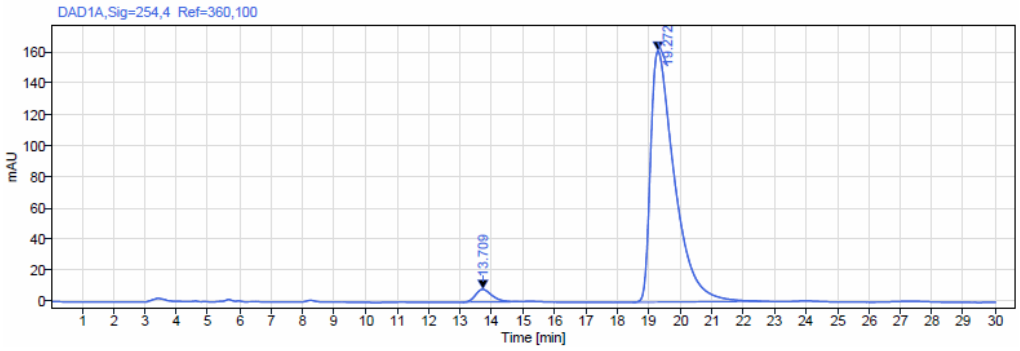


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.3 min, t_R (minor) = 13.7 min.

Asymmetric trace: 93% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.174 Run 2.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.174 Run 2	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-18 15:19:35+01:00
Inj. volume:	25.000	**Location:**	43
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

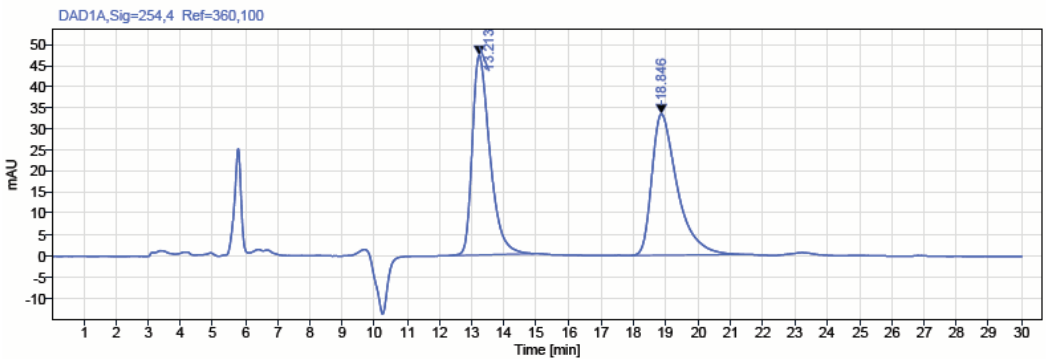
RT [min]	Type	Width [min]	Area	Height	Area%	Name
13.709	BB	1.75	295.57	8.11	3.35	
19.272	BB	4.08	8516.62	161.50	96.65	
		Sum	8812.19			

Racemic trace

Single Injection Report

Agilent Technologies

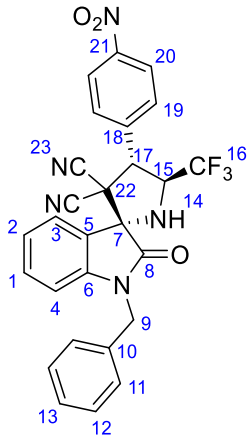
Data file:	WR 2.139 Vial2 (CAD-1-39 rac) re-run.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.139 Vial2 (CAD-1-39 rac) re-run	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-03-30 13:18:00+01:00
Inj. volume:	25.000	**Location:**	5
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
13.213	BB	2.68	1794.29	47.27	49.54	
18.846	BB	3.49	1827.90	33.43	50.46	
		Sum	3622.19			

1-Benzyl-4'-(4-nitrophenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3c)



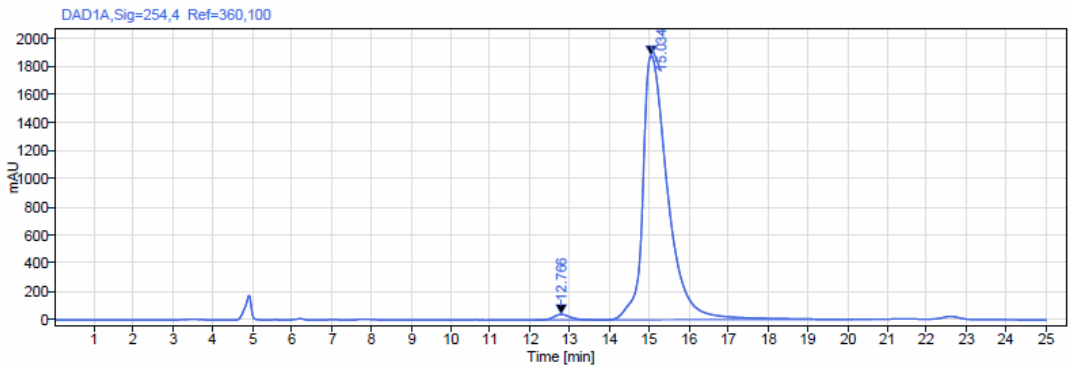
Conditions: Chiral art Amylose-SB (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 15.0 min, t_R (minor) = 12.8 min.

Asymmetric trace: 97% ee

Single Injection Report

Agilent Technologies

Data file:	WR 2.167 (20% IPA-Hex, SB).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.167 (20% IPA-Hex, SB)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-03 14:30:28+01:00
Inj. volume:	25.000	**Location:**	22
Acq. method:	20% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

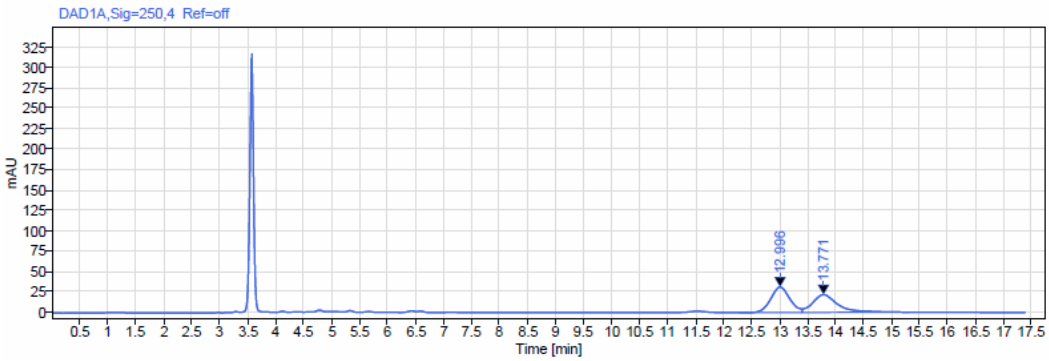
RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.766	VB	1.69	1157.03	39.28	1.38	
15.034	BB	6.77	82564.95	1879.89	98.62	
		Sum	83721.98			

Racemic trace

Single Injection Report

Agilent Technologies

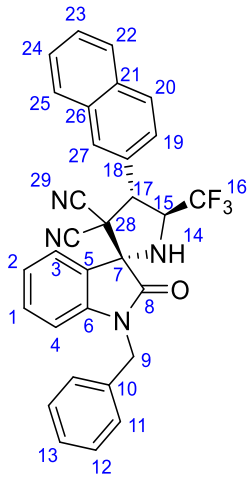
Data file:	PCK 3.74 TLC 20% SB repeat20210312 152812.dx		
Sequence Name:	SingleSample	**Project Name:**	JS
Sample name:	PCK 3.74 TLC 20% SB repeat	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-03-12 15:31:56+00:00
Inj. volume:	25.000	**Location:**	24
Acq. method:	20% IPA-hexane 60 mins 35C.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=250,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
12.996	BV	1.12	737.90	31.27	51.93	
13.771	VB	1.92	683.00	21.73	48.07	
		Sum	1420.90			

1-Benzyl-4'-(naphthalen-2-yl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3d)

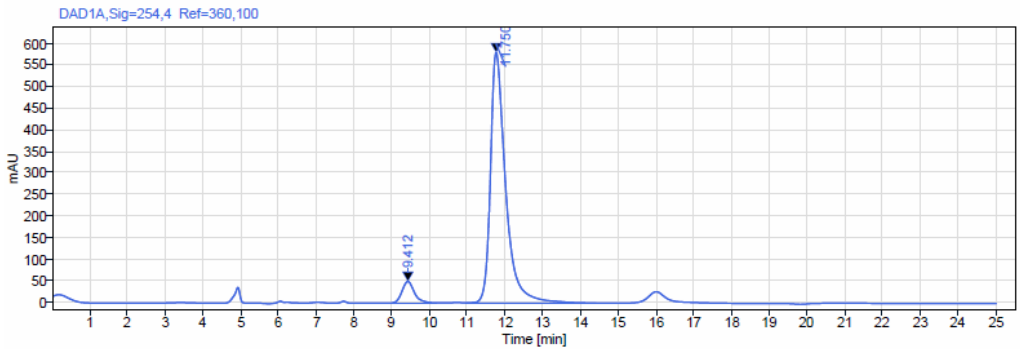


Conditions: Chiral art Amylose-SB (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 11.8 min, t_R (minor) = 9.4 min.

Asymmetric trace: 87% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.164 (20% IPA-Hex, SB).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.164 (20% IPA-Hex, SB)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-03 14:56:46+01:00
Inj. volume:	25.000	**Location:**	13
Acq. method:	20% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

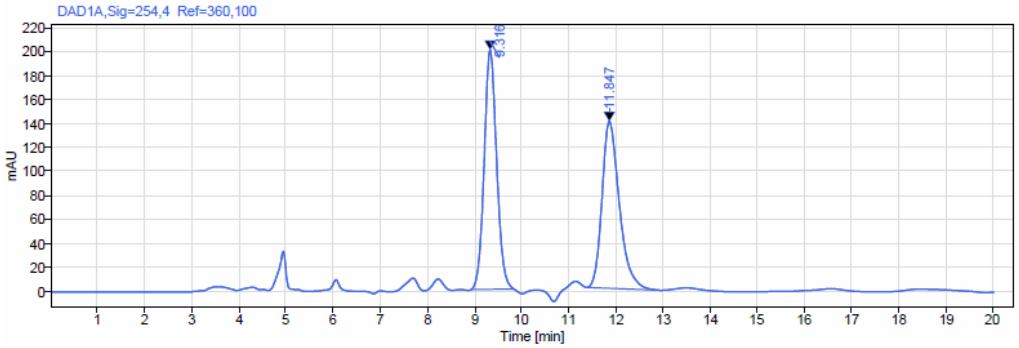
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.412	BV	1.32	1157.58	50.28	6.66	
11.750	VB	3.45	16225.88	579.92	93.34	
		Sum	17383.46			

Racemic trace

Single Injection Report

Agilent Technologies

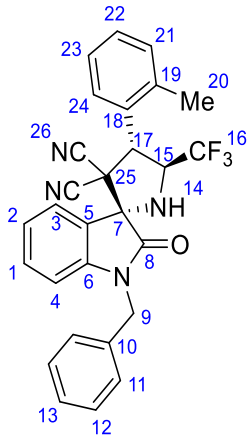
Data file:	WR 2.164 RAC (20% IPA-Hex, SB).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.164 RAC (20% IPA-Hex, SB)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-03 15:23:09+01:00
Inj. volume:	25.000	**Location:**	10
Acq. method:	20% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.316	MM m	0.28	3658.89	199.58	50.75	
11.847	MM m	0.39	3551.20	139.15	49.25	
		Sum	7210.10			

1-benzyl-2-oxo-4'-(o-tolyl)-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3e)

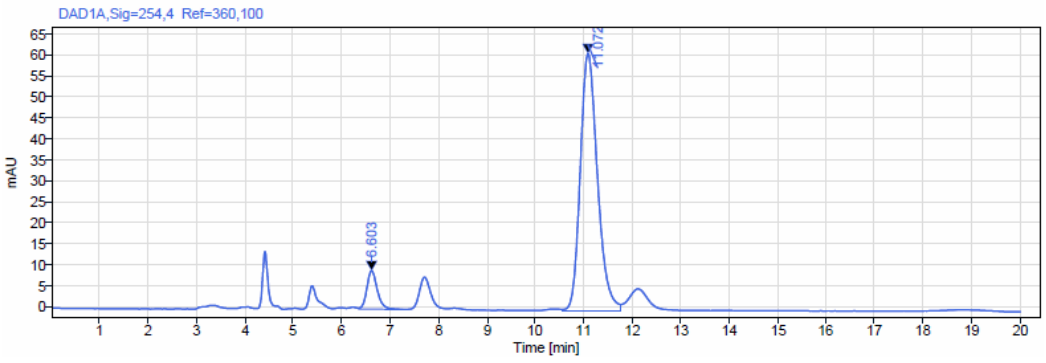


Conditions: Chiral art Amylose-SA (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 11.3 min, t_R (minor) = 6.6 min.

Asymmetric trace: 83% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.160 (20% IPA, 10 uL, SA).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.160 (20% IPA, 10 uL, SA)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-05-06 12:04:52+01:00
Inj. volume:	10.000	**Location:**	1
Acq. method:	20% IPA-HEX 30 mins 10 micro L.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

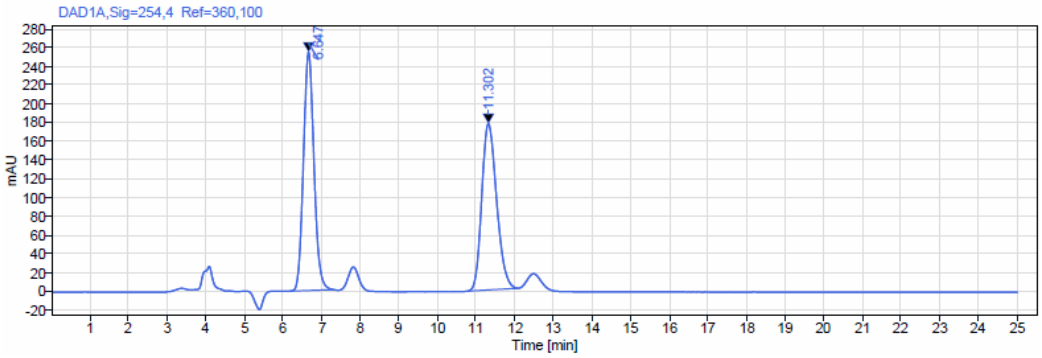
RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.603	VB	0.91	136.69	9.15	8.33	
11.072	VV	1.21	1505.06	61.17	91.67	
		Sum	1641.75			

Racemic traces

Single Injection Report

Agilent Technologies

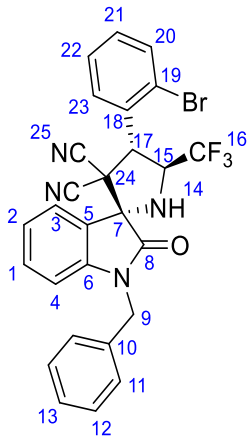
Data file:	WR 2.160 RAC (Run 1).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.160 RAC (Run 1)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-05-07 15:25:04+01:00
Inj. volume:	25.000	**Location:**	1
Acq. method:	20% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.647	MM m	0.29	4813.79	254.30	50.42	
11.302	MM m	0.42	4733.64	177.40	49.58	
		Sum	9547.43			

1-Benzyl-4'-(2-bromophenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3f)

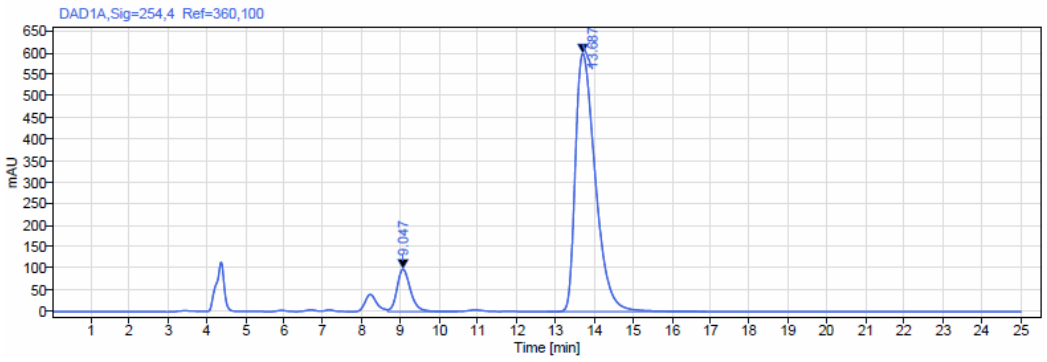


Conditions: Chiral art Amylose-SA (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 13.7 min, t_R (minor) = 9.9 min.

Asymmetric trace: 80% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.158 (20% IPA-Hex, 25 uL).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.158 (20% IPA-Hex, 25 uL)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-02 10:53:00+01:00
Inj. volume:	25.000	**Location:**	11
Acq. method:	20% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

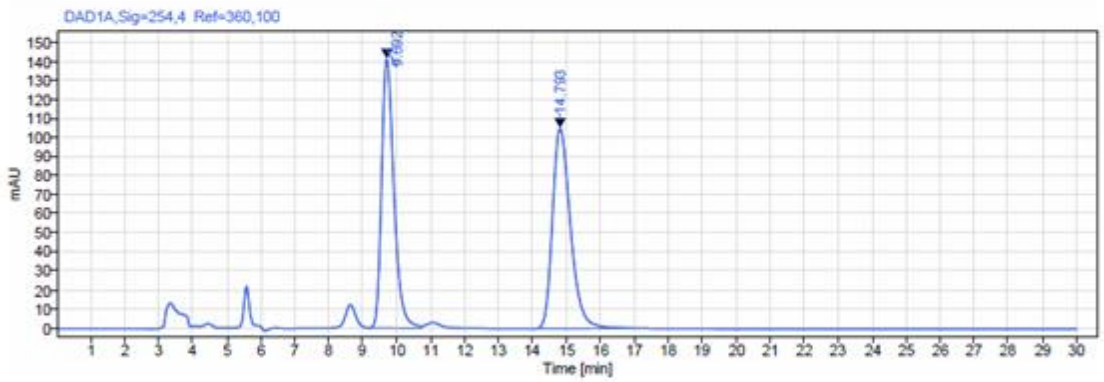
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.047	VV	1.78	2405.32	98.85	10.07	
13.687	BB	4.09	21479.40	600.08	89.93	
		Sum	23884.73			

Racemic trace

Single Injection Report

Agilent Technologies

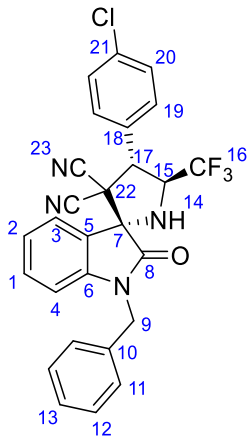
Data file:	WR 2.139 Vial 5 20% IPA.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.139 Vial 5 20% IPA	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-03-25 18:44:47+00:00
Inj. volume:	25.000	**Location:**	5
Acq. method:	20% IPA-HEX 60 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.692	BV	1.57	3561.01	141.36	48.00	
14.793	BB	2.93	3857.83	105.14	52.00	
		Sum	7418.85			

1-Benzyl-4'-(4-chlorophenyl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3g)

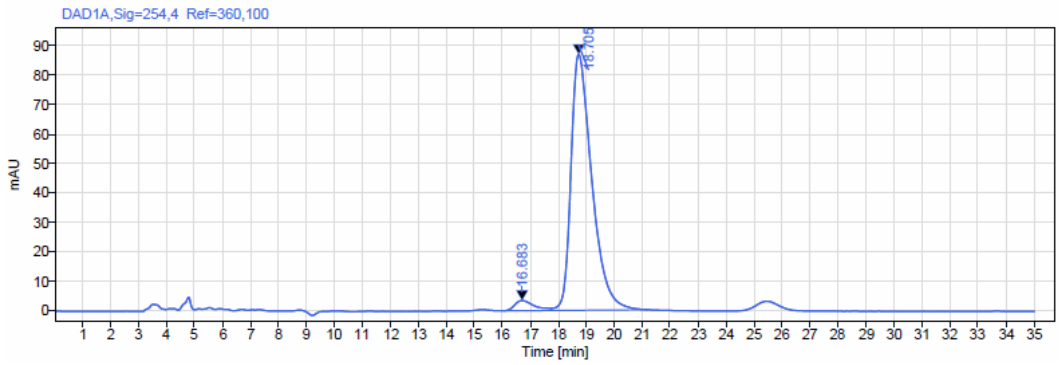


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 18.7 min, t_R (minor) = 16.7 min.

Asymmetric trace: 93% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.145.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.145	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-05-03 12:46:53+01:00
Inj. volume:	25.000	**Location:**	4
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

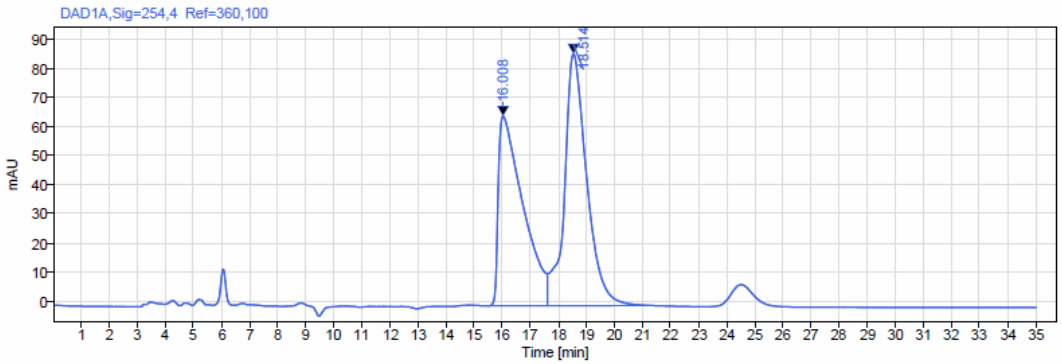
RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.683	BV	1.74	168.04	3.48	3.60	
18.705	VB	3.42	4500.38	86.85	96.40	
		Sum	4668.42			

Racemic trace

Single Injection Report

Agilent Technologies

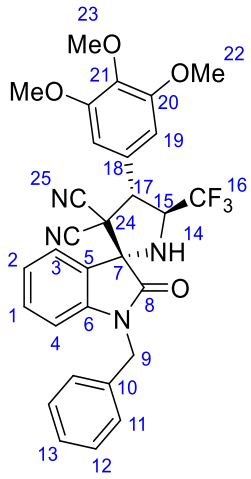
Data file:	WR 2.139 Vial 3.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.139 Vial 3	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-03-25 17:32:50+00:00
Inj. volume:	25.000	**Location:**	3
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
16.008	BV	2.15	3966.36	65.13	45.32	
18.514	VB	3.64	4784.74	86.46	54.68	
		Sum	8751.10			

1-Benzyl-2-oxo-5'-(trifluoromethyl)-4'-(3,4,5-trimethoxyphenyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3h)

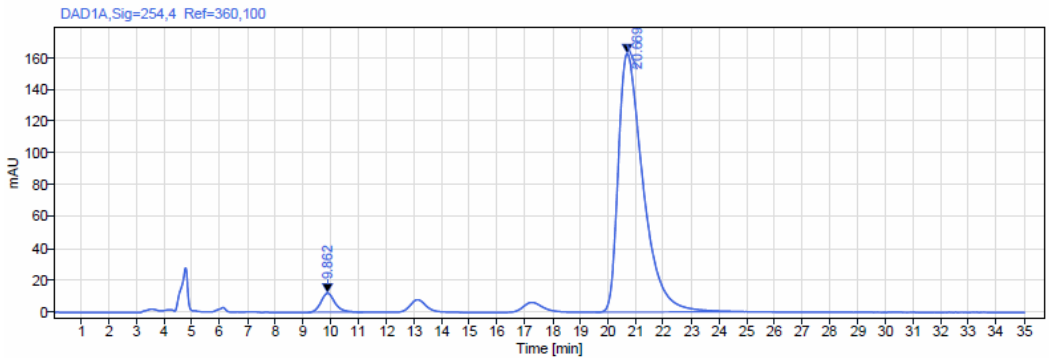


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 20.7 min, t_R (minor) = 9.9 min.

Asymmetric trace: 92% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.143.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.143	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-05-03 11:39:14+01:00
Inj. volume:	25.000	**Location:**	2
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

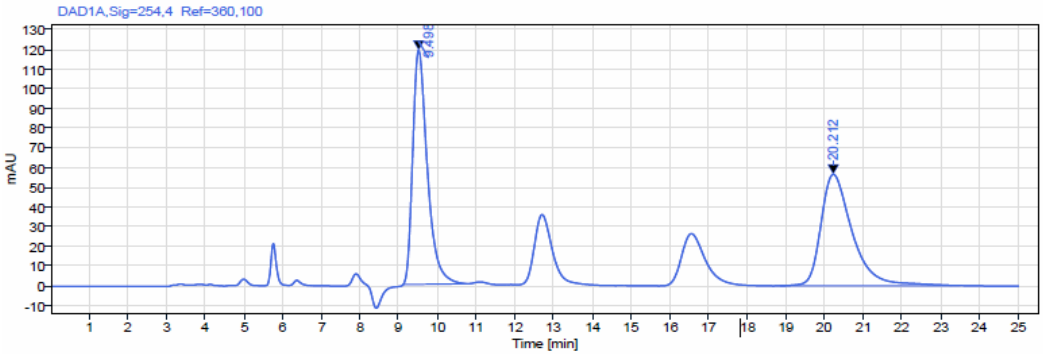
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.862	BV	1.96	423.19	12.02	4.02	
20.669	BB	5.37	10111.75	162.65	95.98	
		Sum	10534.94			

Racemic trace

Single Injection Report

Agilent Technologies

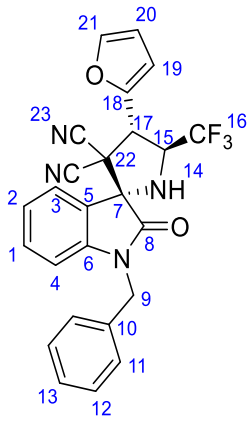
Data file:	CAD-1-46 RAC (15% IPA, 10 uL, SA).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	CAD-1-46 RAC (15% IPA, 10 uL, SA)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-05-06 11:07:52+01:00
Inj. volume:	10.000	**Location:**	3
Acq. method:	15% IPA-HEX 30 mins 10 micro L.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.498	MM m	0.40	3118.86	118.84	49.50	
20.212	BB	4.65	3181.88	56.57	50.50	
		Sum	6300.74			

1-benzyl-4'-(furan-2-yl)-2-oxo-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3i)

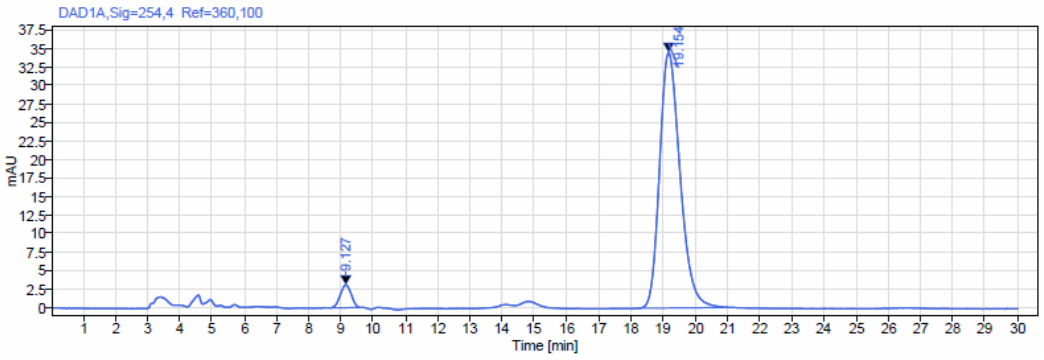


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.2 min, t_R (minor) = 9.2 min.

Asymmetric trace: 91% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.161 (15% IPA-Hex, SA) Run 3 V2.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.161 (15% IPA-Hex, SA) Run 3 V2	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-11 11:15:07+01:00
Inj. volume:	25.000	**Location:**	3
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	None		



Signal: DAD1A,Sig=254,4 Ref=360,100

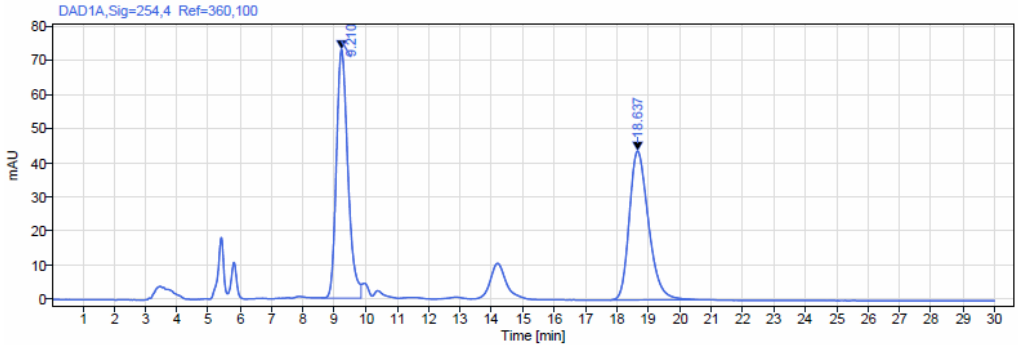
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.127	BB	0.93	72.56	3.07	4.54	
19.154	BB	2.80	1527.09	34.57	95.46	
		Sum	1599.65			

Racemic trace

Single Injection Report

Agilent Technologies

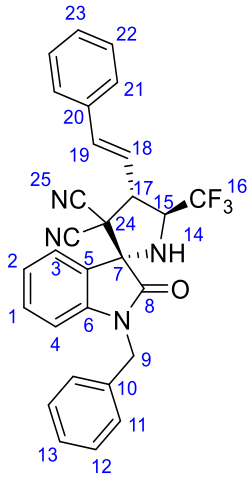
Data file:	WR 2.161 Rac (22-06) Run 3.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.161 Rac (22-06) Run 3	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-22 12:29:08+01:00
Inj. volume:	25.000	**Location:**	41
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.210	BV	1.26	1852.09	72.88	50.03	
18.637	BB	2.80	1849.70	43.65	49.97	
		Sum	3701.79			

(E)-1-benzyl-2-oxo-4'-styryl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3j)

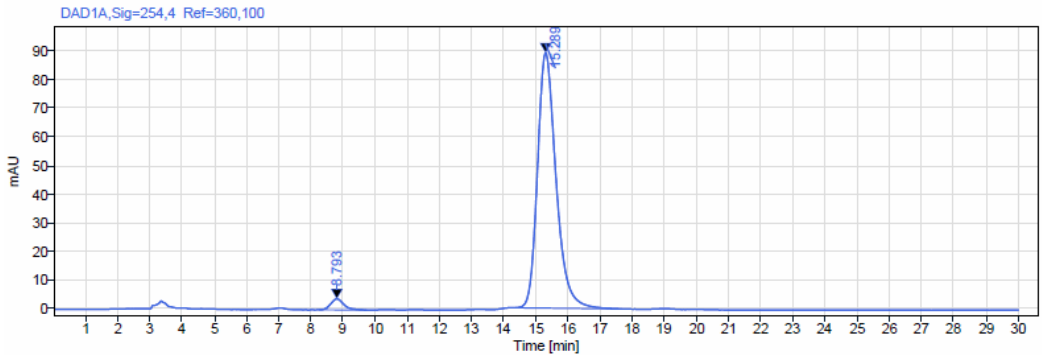


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 15.3 min, t_R (minor) = 8.8 min.

Asymmetric trace: 94% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.162 (15% IPA-Hex, SA) V3.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.162 (15% IPA-Hex, SA) V3	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-14 12:07:06+01:00
Inj. volume:	25.000	**Location:**	10
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

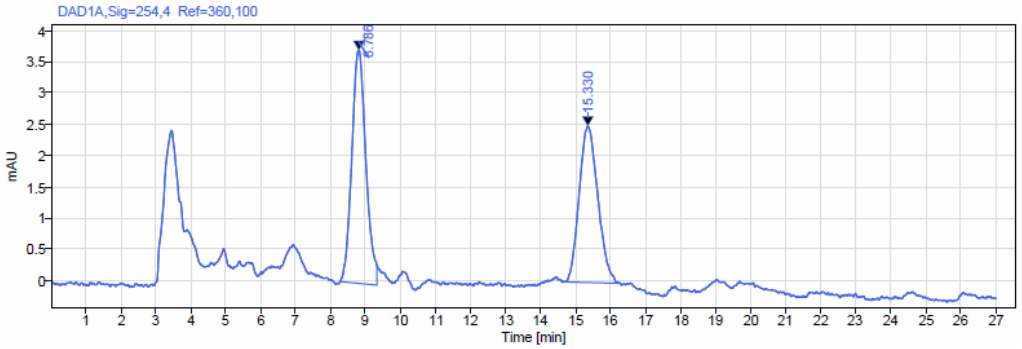
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.793	BB	1.47	107.90	3.84	2.93	
15.289	BB	3.32	3579.20	89.24	97.07	
		Sum	3687.10			

Racemic trace

Single Injection Report

Agilent Technologies

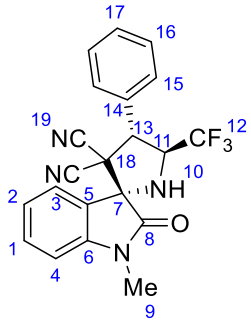
Data file:	WR 2.162 Rac.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.162 Rac	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-18 14:37:00+01:00
Inj. volume:	25.000	**Location:**	42
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.786	MM m	0.42	103.95	3.73	52.88	
15.330	BB	1.49	92.63	2.50	47.12	
		Sum	196.58			

1-Methyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3k)

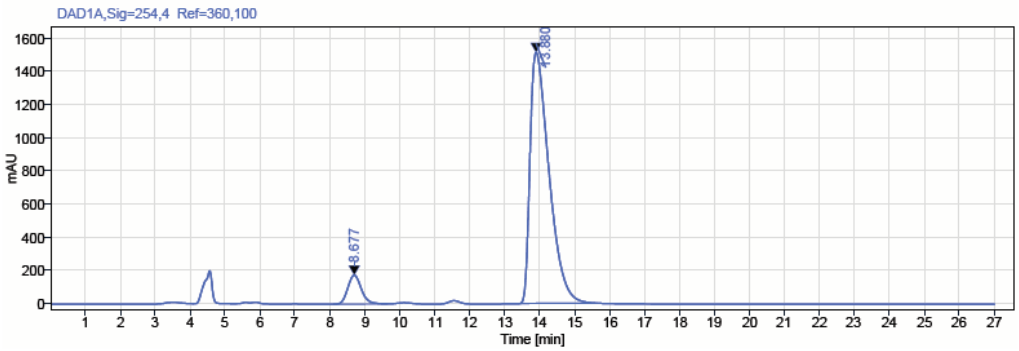


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 13.3 min, t_R (minor) = 8.7 min.

Asymmetric trace: 85% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.168 F1 (15% IPA-Hex, 25 uL) run 2.dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.168 F1 (15% IPA-Hex, 25 uL) run 2	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-03 11:44:12+01:00
Inj. volume:	25.000	**Location:**	12
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

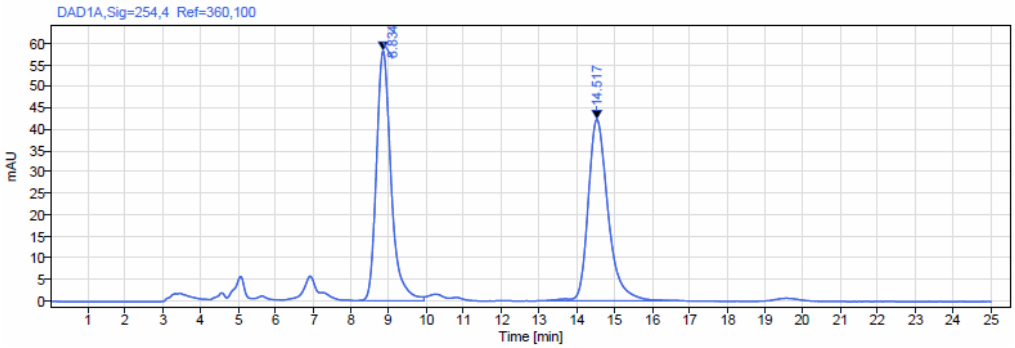
RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.677	VB	1.55	4683.00	174.11	7.58	
13.880	MM m	0.57	57086.10	1514.19	92.42	
		Sum	61769.10			

Racemic trace

Single Injection Report

Agilent Technologies

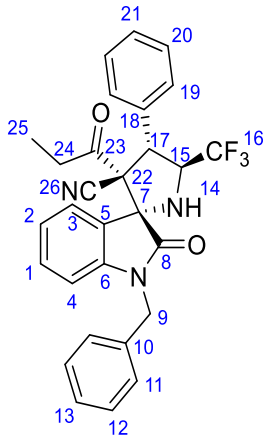
Data file:	WR 2.168 RAC (15% IPA,Hex, SA).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.168 RAC (15% IPA,Hex, SA)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-04 12:08:52+01:00
Inj. volume:	25.000	**Location:**	3
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.834	BV	1.70	1566.70	58.11	50.28	
14.517	BV	3.27	1549.17	42.16	49.72	
		Sum	3115.87			

Ethyl-1-benzyl-3'-cyano-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3'-carboxylate *(3l)*

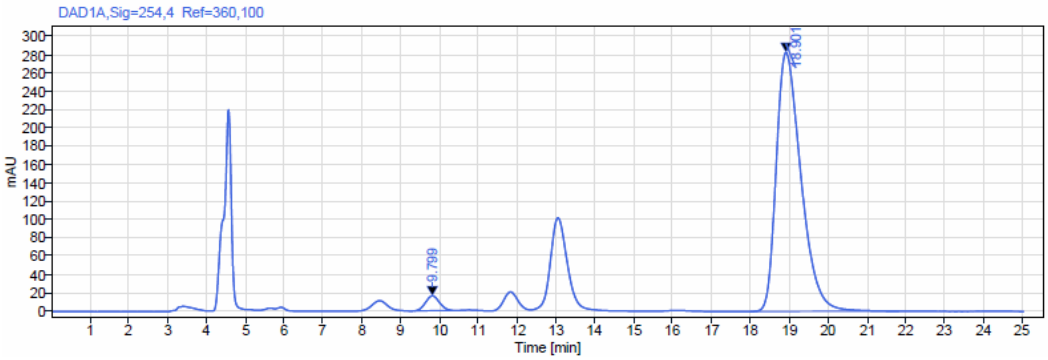


Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 18.9 min, t_R (minor) = 9.8 min.

Asymmetric trace: 94% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.170 (15% IPA,Hex, SA).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.170 (15% IPA,Hex, SA)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-06-04 12:35:11+01:00
Inj. volume:	25.000	**Location:**	4
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

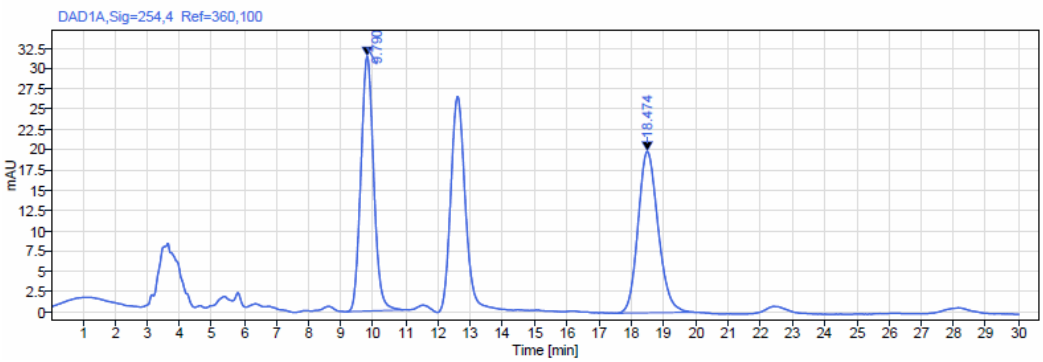
RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.799	MM m	0.38	400.76	16.13	3.10	
18.901	BB	3.83	12516.69	282.80	96.90	
		Sum	12917.46			

Racemic trace

Single Injection Report

Agilent Technologies

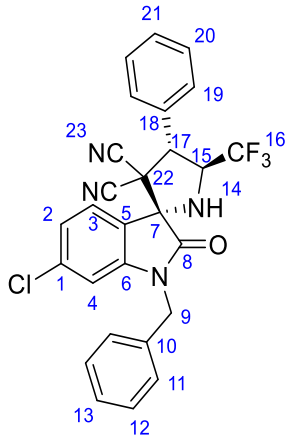
Data file:	WR 2.139 Vial 6 repeat (CAD 1-45 rac).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.139 Vial 6 repeat (CAD 1-45 rac)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-03-30 15:15:07+01:00
Inj. volume:	25.000	**Location:**	7
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
9.790	BB	1.78	864.98	31.38	50.16	
18.474	BB	2.42	859.41	19.90	49.84	
		Sum	1724.40			

*1-Benzyl-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (**3m**)*

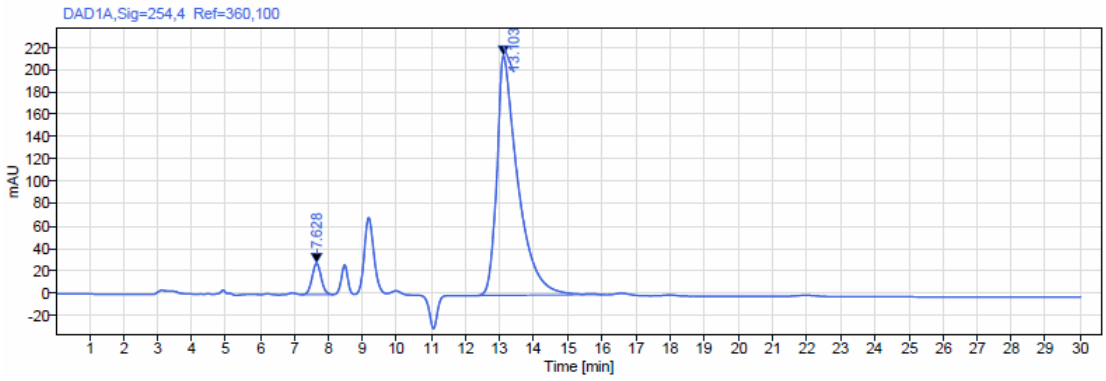


Conditions: Chiral ART Amylose-SB (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 13.1 min, t_R (minor) = 7.6 min.

Asymmetric trace: 89% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.226 Run 2 (20% IPA-Hexane, SB, 25 ul).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.226 Run 2 (20% IPA-Hexane, SB, 25 ul)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-10-11 10:12:13+01:00
Inj. volume:	25.000	**Location:**	1
Acq. method:	20% IPA-HEX 60 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

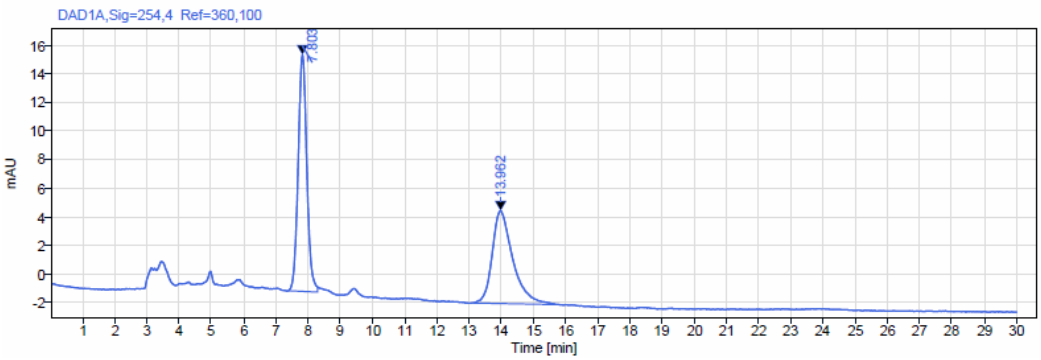
RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.628	VB	0.91	519.38	27.92	5.36	
13.103	MM m	0.60	9162.92	214.79	94.64	
		Sum	9682.31			

Racemic trace

Single Injection Report

Agilent Technologies

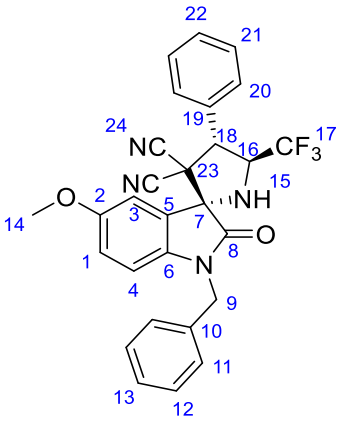
Data file:	WR 2.226 RAC V2 (20% IPA-Hexane, SB, 25 ul).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.226 RAC V2 (20% IPA-Hexane, SB, 25 ul)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-10-11 12:05:56+01:00
Inj. volume:	25.000	**Location:**	11
Acq. method:	20% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.803	MM m	0.29	308.86	16.55	51.74	
13.962	BB	2.59	288.11	6.48	48.26	
		Sum	596.97			

1-benzyl-5-methoxy-2-oxo-4'-phenyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (3n)

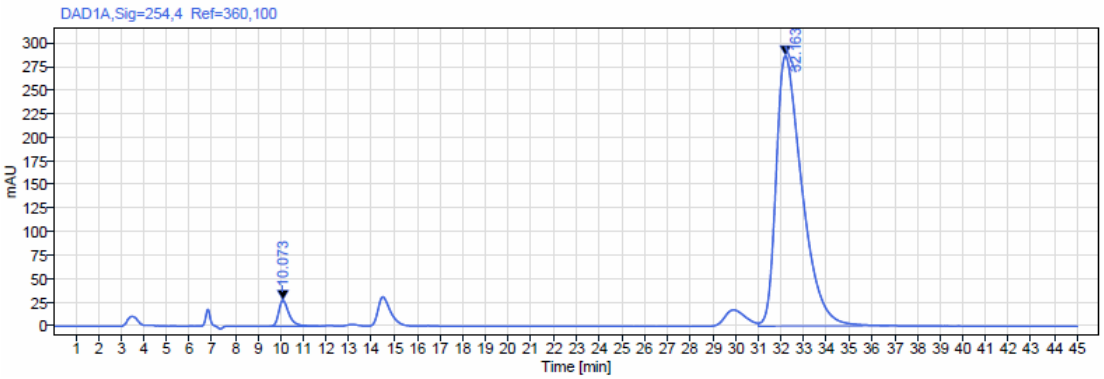


Conditions: Chiral ART Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 32.2 min, t_R (minor) = 10.1 min.

Asymmetric trace: 93% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.231 V2 (15% IPA-Hexane, SA, 25 ul).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.231 V2 (15% IPA-Hexane, SA, 25 ul)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-10-13 16:09:41+01:00
Inj. volume:	25.000	**Location:**	21
Acq. method:	15% IPA-HEX 45 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

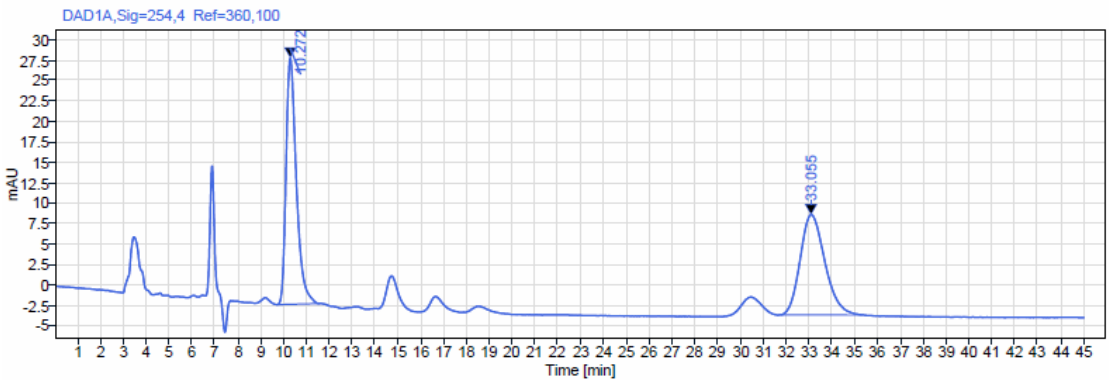
RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.073	BV	2.27	865.03	27.39	3.67	
32.163	VB	5.72	22691.00	287.16	96.33	
		Sum	23556.03			

Racemic trace

Single Injection Report

Agilent Technologies

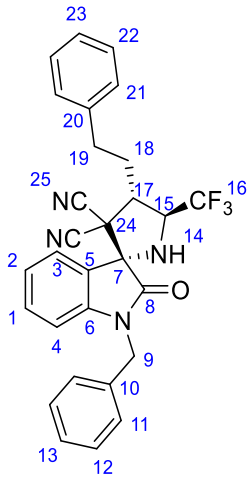
Data file:	WR 2.231 RAC V2 (15% IPA-Hexane, SA, 25 ul).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.231 RAC V2 (15% IPA-Hexane, SA, 25 ul)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-10-13 15:21:21+01:00
Inj. volume:	25.000	**Location:**	22
Acq. method:	15% IPA-HEX 45 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.272	BB	1.84	940.39	30.15	50.52	
33.055	BB	3.54	921.03	12.27	49.48	
		Sum	1861.42			

*1-Benzyl-2-oxo-4'-phenethyl-5'-(trifluoromethyl)spiro[indoline-3,2'-pyrrolidine]-3',3'-dicarbonitrile (**3o**)*

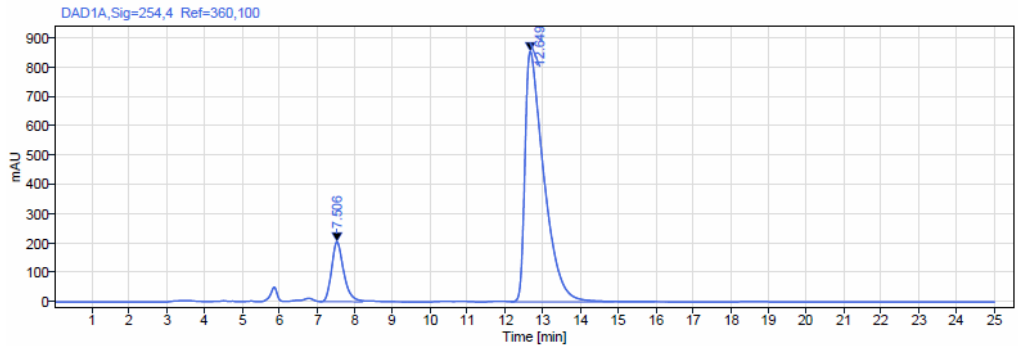


Conditions: Chiral ART Amylose-SA (with column guard), 20% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 12.6 min, t_R (minor) = 7.5 min.

Asymmetric trace: 73% ee

Single Injection Report — Agilent Technologies

Data file:	WR 2.227 (15% IPA-Hexane, SA, 25 ul).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.227 (15% IPA-Hexane, SA, 25 ul)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-10-04 14:44:45+01:00
Inj. volume:	25.000	**Location:**	2
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

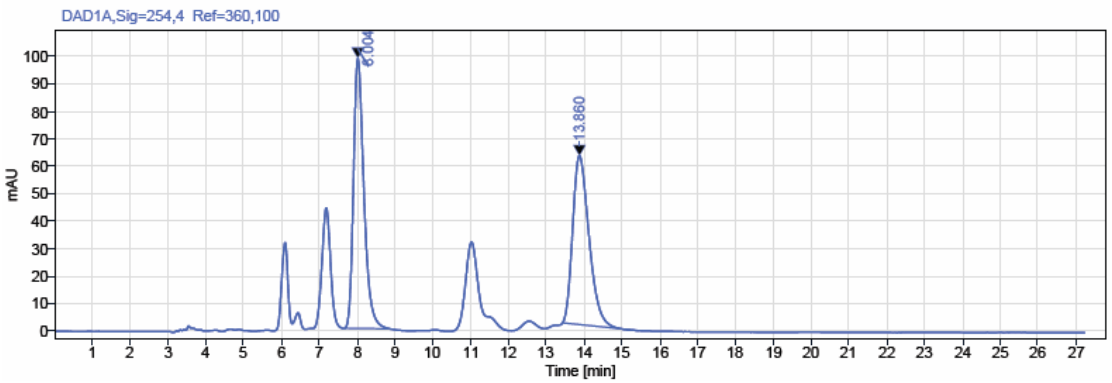
RT [min]	Type	Width [min]	Area	Height	Area%	Name
7.506	MM m	0.34	4565.19	203.95	13.27	
12.649	VV	3.82	29841.96	855.25	86.73	
		Sum	34407.15			

Racemic trace

Single Injection Report

Agilent Technologies

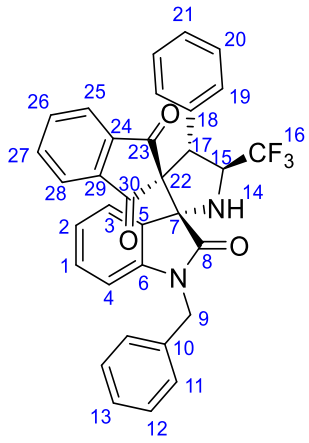
Data file:	WR 2.227 RAC (15% IPA-Hexane, SA, 25 ul).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 2.227 RAC (15% IPA-Hexane, SA, 25 ul)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-10-04 16:14:37+01:00
Inj. volume:	25.000	**Location:**	4
Acq. method:	15% IPA-HEX 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
8.004	MM m	0.29	1877.83	98.58	50.43	
13.860	MM m	0.46	1845.80	61.61	49.57	
		Sum	3723.63			

1''-benzyl-4'-phenyl-5'-(trifluoromethyl)dispiro[indene-2,3'-pyrrolidine-2',3''-indoline]-1,2'',3-trione (5a)

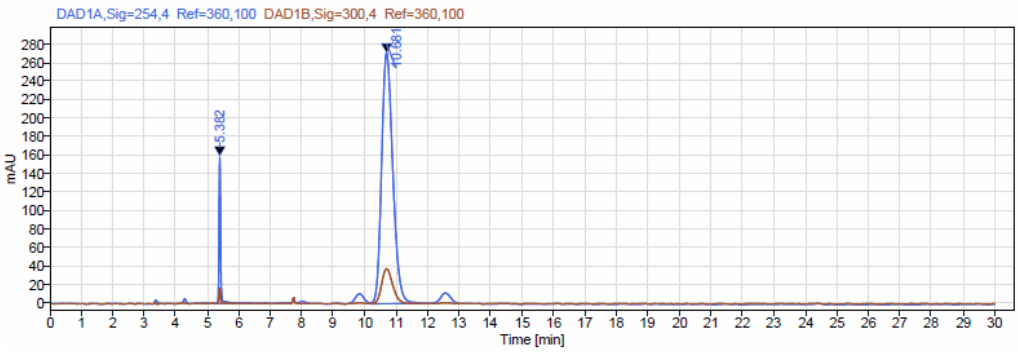


Conditions: Chiral art Amylose-SA (with column guard), 35% $CHCl_3$-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 10.7 min, t_R (minor) = 5.4 min.

Asymmetric trace: 85% ee

Single Injection Report — Agilent Technologies

Data file:	WR 1.136 V3 (35% CHCl3-Hex, SA, 5 uL).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 1.136 V3 (35% CHCl3-Hex, SA, 5 uL)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-07-02 12:51:07+01:00
Inj. volume:	5.000	**Location:**	6
Acq. method:	35% CHCl3 30 mins 5 micro L.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1A,Sig=254,4 Ref=360,100

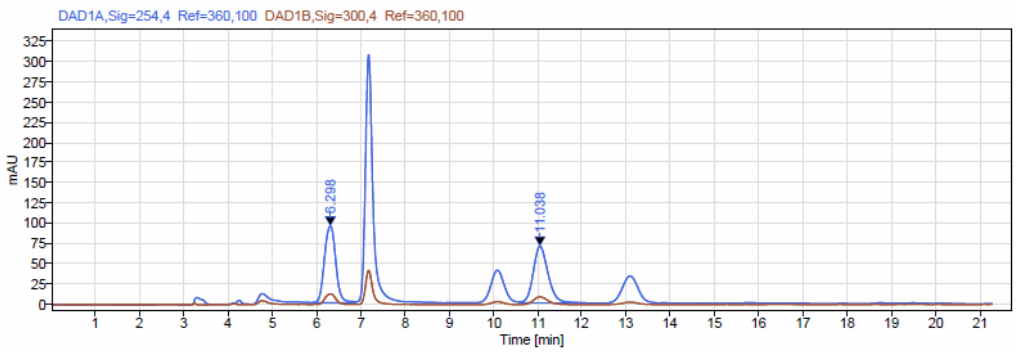
RT [min]	Type	Width [min]	Area	Height	Area%	Name
5.382	VV	0.57	543.23	159.05	7.47	
10.681	VV	1.88	6731.52	270.82	92.53	
		Sum	7274.75			

Racemic trace

Single Injection Report

Agilent Technologies

Data file:	WR 1.136 RAC (35% CHCl3-Hex, SA, 10 uL).dx		
Sequence Name:	SingleSample	**Project Name:**	WR
Sample name:	WR 1.136 RAC (35% CHCl3-Hex, SA, 10 uL)	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2021-07-02 11:44:03+01:00
Inj. volume:	10.000	**Location:**	1
Acq. method:	35% CHCl3 30 mins 10 micro L.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



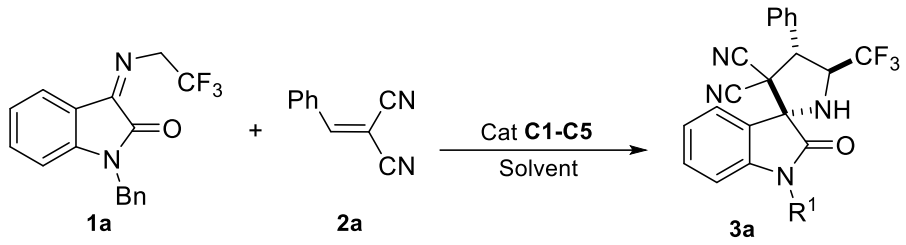
Signal: DAD1A,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%	Name
6.298	BV	0.99	1672.26	94.68	50.82	
11.038	VB	1.56	1618.08	70.05	49.18	
		Sum	3290.35			

5 Kinetic Study

5.1 Kinetic profiling and catalyst screening experiments

Prior to the catalyst screening, a kinetic profiling experiment was carried out with **C1** (**Figure SX**). 10 mol% of catalyst and 50 mol% of EtOAc (NMR standard) were added, and the reaction mixture was subjected to a series of ^{1}H NMR experiments over the course of 24 h. The cyclization proceeds smoothly to complete conversion in around 3.5 h. The reaction mixture was then concentrated *in vacuo*, and the product then purified via prep-TLC to the obtain the *ee* via HPLC: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.8 min, t_R (minor) 10.5 min.



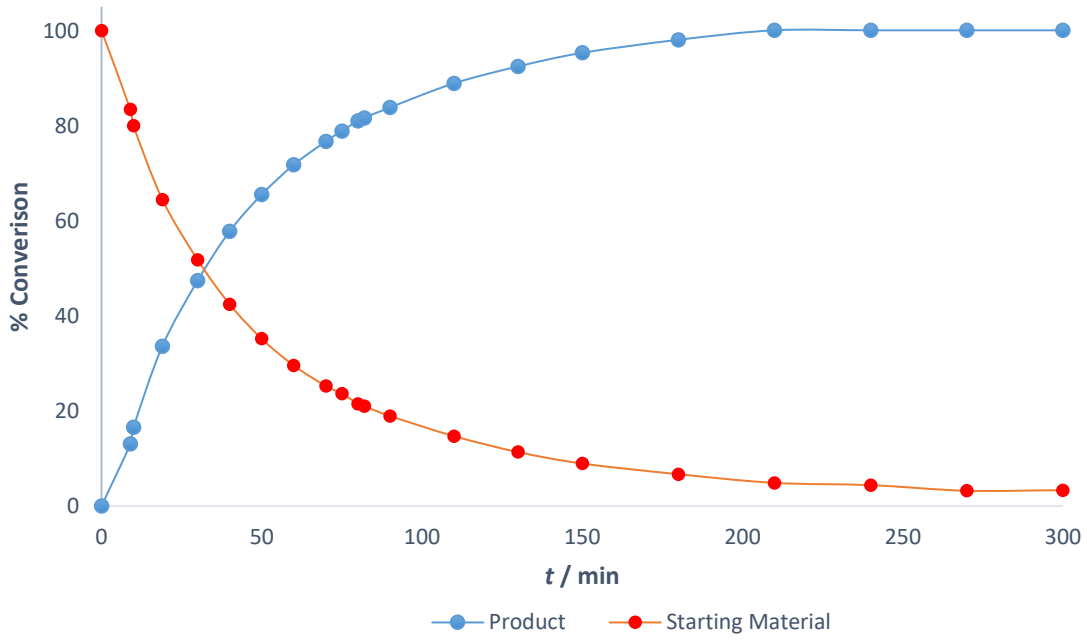
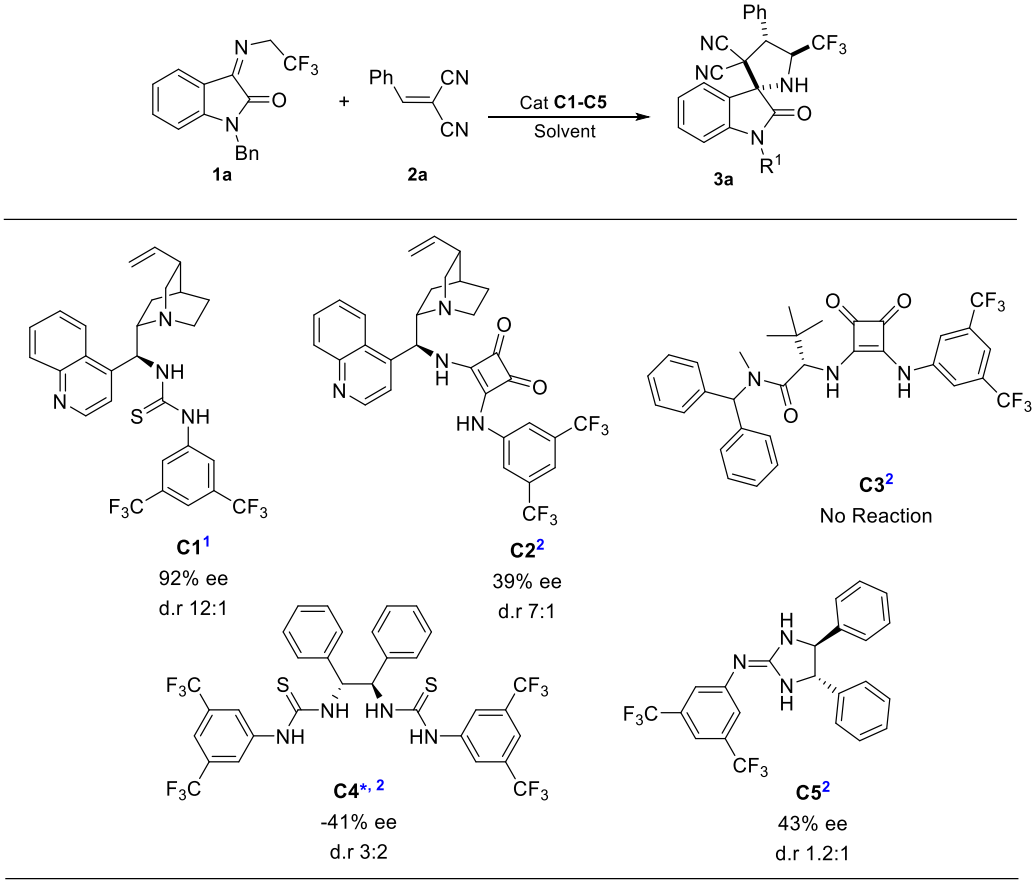


Figure X: Formation of spirocycle **3a** (blue) and consumption of ketimine **1a** (red) as a function of time. Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), **C1** (0.01 mmol), CD_2Cl_2 (1 mL), ethyl acetate (0.05 mmol).

Catalysts **C2**-**C5** the remaining 4 catalysts were screened by the same procedure and subjected to a series of ^{1}H NMR experiments to compare the activity and *ee* from each catalyst (**Scheme S1** and **Figure S3**). All catalysts screened led to a reduction in *ee* and d.r. relative to **C1**.



Scheme S1. [a] Reaction conditions: **108** (0.1 mmol), **111** (0.15 mmol), catalyst (0.01 mmol), CD_2Cl_2 (1 mL), ethyl acetate[1]/triisopropylbenzene[2] (0.05 mmol); *Plus NEt_3 (0.01 mmol).

Internal standards were used to quantitatively measure the conversion and yield. (**Figure S3**). These indicate that the most active catalyst is **C4**,* for which complete consumption of starting material was observed after ~30 min. However, this high reactivity was not mirrored in stereoselectivity: the major diastereomer was formed in 54% yield and -41% *ee*, and the d.r. was a mere 3:2. Squaramide catalysts **C2** and **C3** proved to be poor catalysts in terms of both conversion and stereoselectivity. The poor conversion may be attributed in part to their observed low solubilities in CD_2Cl_2. **C2** formed product slowly, ultimately reaching 72% yield after 25 h, while **C3** yielded no product at all. Lastly guanidine-

* Used alongside NEt_3 as co-catalyst. No product formation was observed after 16 h when NEt_3 was added in the absence of the thiourea.

based catalyst (**C5)** catalysed the spiro-annulation slowly, and gave minimal diastereocontrol (1.2:1 d.r.). The major diastereomer was formed in 28% yield after 26 h, in 46% *ee*.

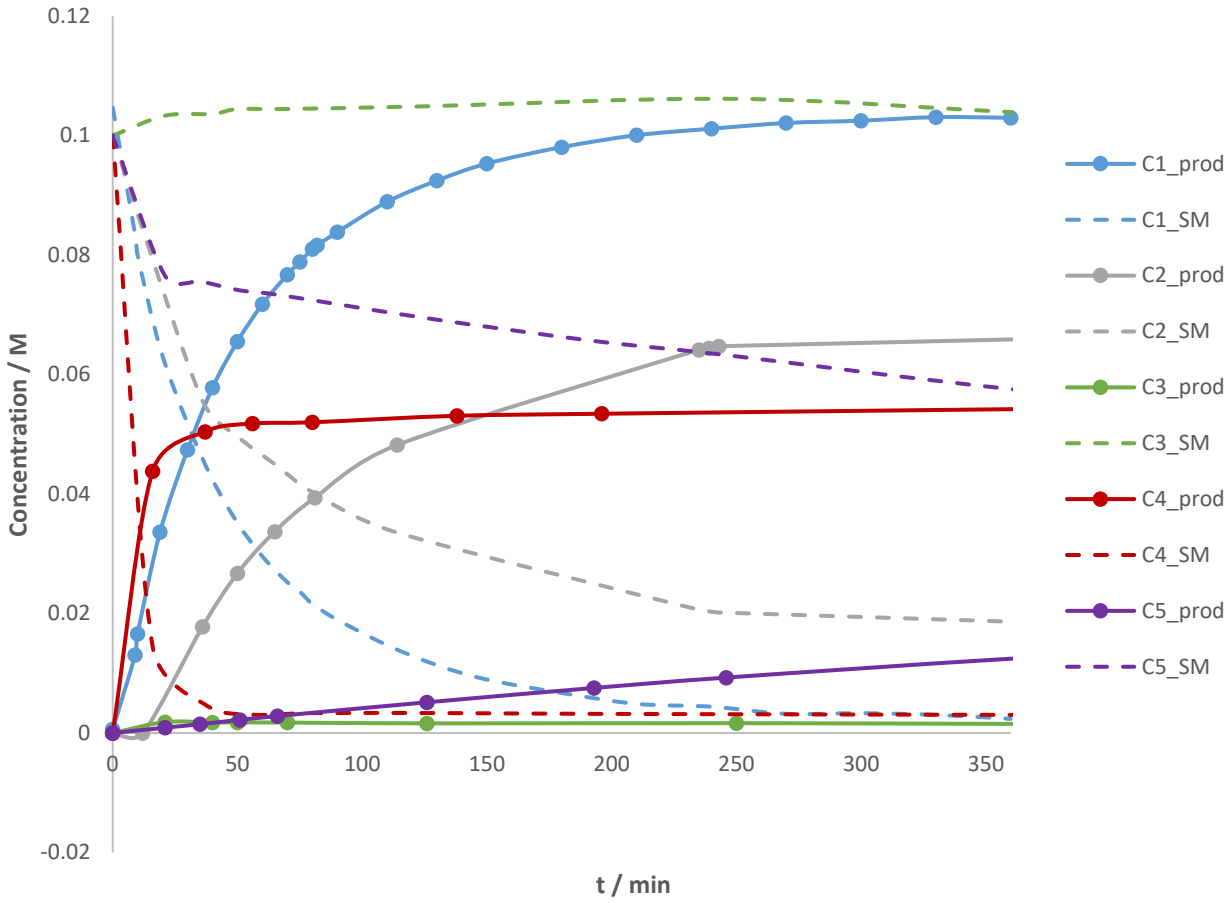


Figure S3: Formation of spirocycle **125** with each catalyst. Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), catalyst (0.01 mmol), CD_2Cl_2 (1 mL), internal standards: ethyl acetate or triisopropylbenzene (0.05 mmol). Solid lines indicate NMR concentration of the major diastereomer (**3a**$_{maj}$), dashed lines indicate NMR concentration of the starting material (**1a**).

5.2 HPLCs Traces for Catalyst Screen

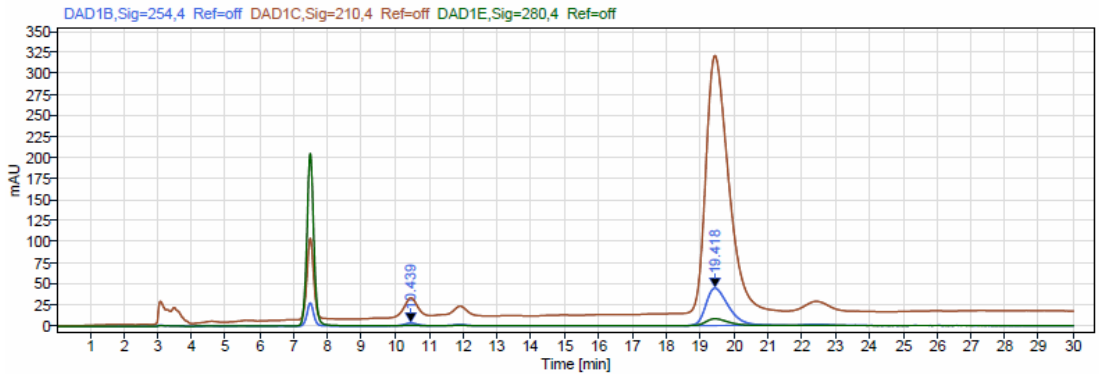
Catalyst C1

Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.4 min, t_R (minor) = 10.4 min.

Asymmetric trace: 92% ee

Single Injection Report — Agilent Technologies

Data file:	CAD-1-17 SA-amylose 15% IPA 30 min.dx		
Sequence Name:	SingleSample	**Project Name:**	CD
Sample name:	CAD-1-17 SA-amylose 15% IPA 30 min	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2020-01-21 16:12:59+00:00
Inj. volume:	25.000	**Location:**	11
Acq. method:	15% IPA 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.439	BB	1.14	83.31	3.16	3.89	
19.418	BB	3.04	2058.89	44.41	96.11	
		Sum	2142.21			

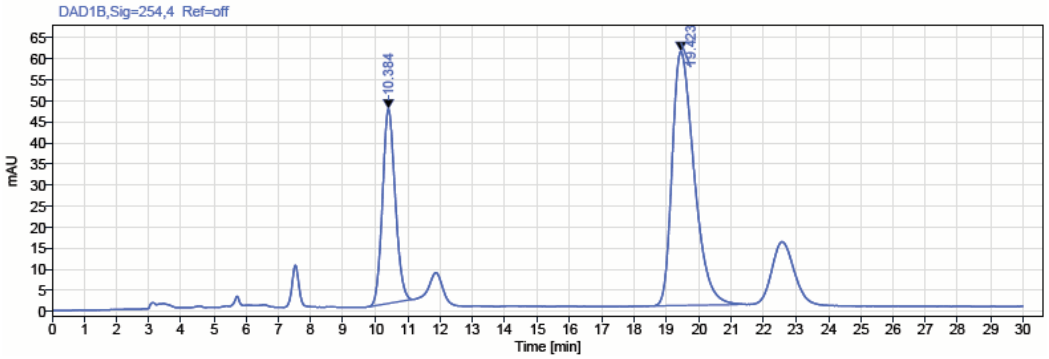
Catalyst C2

Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.4 min, t_R (minor) = 10.4 min.

Asymmetric trace: 38% ee

Single Injection Report — Agilent Technologies

Data file:	CAD-1-30 SA-amylose 15% IPA 30 min.dx		
Sequence Name:	SingleSample	**Project Name:**	CD
Sample name:	CAD-1-30 SA-amylose 15% IPA 30 min	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2020-01-31 11:26:31+00:00
Inj. volume:	25.000	**Location:**	17
Acq. method:	15% IPA 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.384	BB	1.36	1269.46	46.39	30.78	
19.423	BV	2.57	2854.92	60.60	69.22	
		Sum	4124.38			

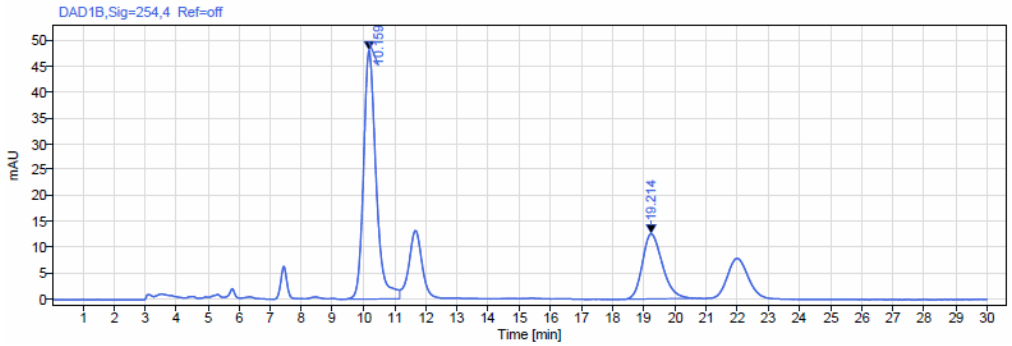
Catalyst C4

Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.3 min, t_R (minor) = 10.3 min.

Asymmetric trace: -41% ee

Single Injection Report — Agilent Technologies

Data file:	CAD-1-25B SA-amylose 15% IPA 30 min.dx		
Sequence Name:	SingleSample	**Project Name:**	CD
Sample name:	CAD-1-25B SA-amylose 15% IPA 30 min	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2020-01-28 15:49:34+00:00
Inj. volume:	25.000	**Location:**	14
Acq. method:	15% IPA 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		



Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.159	BV	1.77	1336.71	47.99	70.52	
19.214	BV	2.23	558.78	12.56	29.48	
		Sum	1895.49			

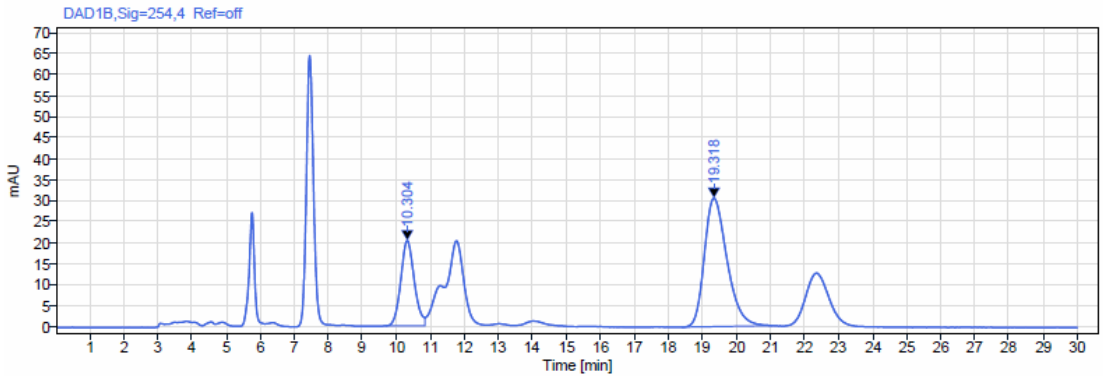
Catalyst C5

Conditions: Chiral art Amylose-SA (with column guard), 15% IPA-hexane 1.0 mL/min, λ = 254 nm, t_R (major) = 19.3 min, t_R (minor) = 10.3 min.

Asymmetric trace: 43% ee

Single Injection Report — Agilent Technologies

Data file:	CAD-1-28B SA-amylose 15% IPA 30 min.dx		
Sequence Name:	SingleSample	**Project Name:**	CD
Sample name:	CAD-1-28B SA-amylose 15% IPA 30 min	**Operator:**	SYSTEM
Instrument:	1100HPLC	**Injection date:**	2020-01-29 16:35:17+00:00
Inj. volume:	25.000	**Location:**	16
Acq. method:	15% IPA 30 mins.amx	**Type:**	Sample
Processing method:	3D UV Quantitative_DefaultMethod.pmx	**Sample amount:**	0.00
Manually modified:	Manual Integration		

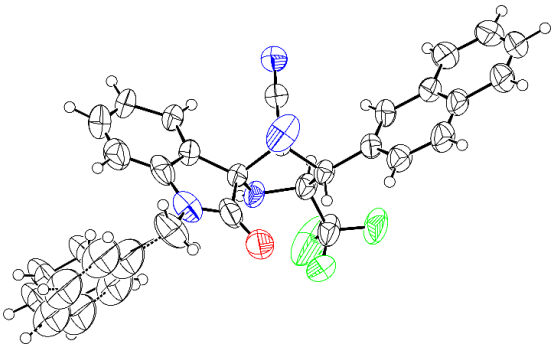


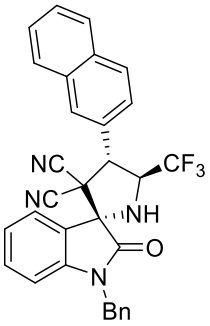
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%	Name
10.304	BV	1.16	557.29	20.28	28.30	
19.318	BB	2.63	1411.73	30.58	71.70	
		Sum	1969.02			

6 X-ray Crystallography

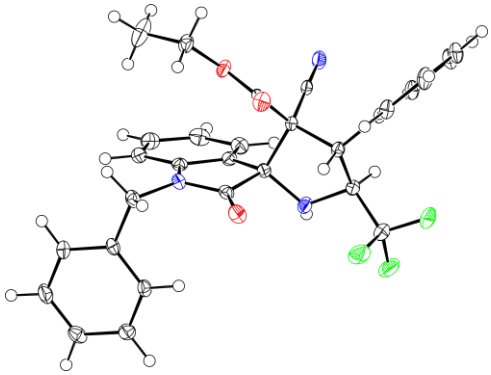
6.1 Single Crystal Data for (–)-3d*maj* (CCDC 2103731)

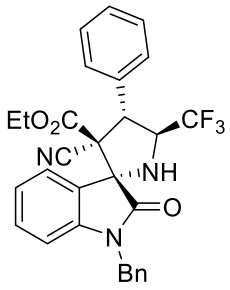




Crystal data	
Chemical formula	$C_{31}H_{21}F_3N_4O$
M_r	522.52
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	150
a, *b*, *c* (Å)	11.6334 (6), 6.6182 (4), 16.7064 (9)
β (°)	91.462 (5)
V (Å^3)	1285.84 (12)
Z	2
Radiation type	Cu *K*α
μ (mm^{-1})	0.82
Crystal size (mm)	0.24 × 0.16 × 0.16
Data collection	
Diffractometer	Oxford Diffraction SuperNova
Absorption correction	Multi-scan *CrysAlis PRO* (Rigaku Oxford Diffraction, 2017)
T_{min}, T_{max}	0.59, 0.88
No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections	39351, 4910, 4258
R_{int}	0.108
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.625
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.108, 0.354, 1.62
No. of reflections	4910
No. of parameters	408
No. of restraints	127
H-atom treatment	H-atom parameters not refined
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.52, −0.66
Absolute structure	Parsons, Flack & Wagner (2013), 1925 Friedel Pairs
Absolute structure parameter	0.11 (7)

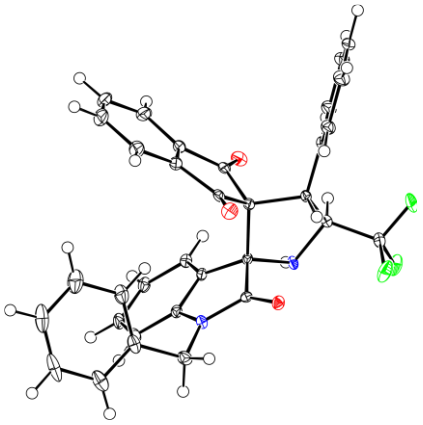
6.2 Single Crystal Data for (–)-3l$_{maj}$ (CCDC 2114148)

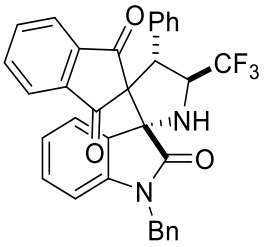




Crystal data	
Chemical formula	C29H24F3N3O3
Mr	519.51
Crystal system, space group	Orthorhombic, P212121
Temperature (K)	100
a, b, c (Å)	11.84750 (1), 13.54710 (1), 15.256700 (14)
V (Å3)	2448.69 (1)
Z	4
Radiation type	Cu Kα
μ (mm−1)	0.91
Crystal size (mm)	0.36 × 0.28 × 0.24
Data collection	
Diffractometer	
Absorption correction	Multi-scan
CrysAlis PRO (Rigaku Oxford Diffraction, 2017)	
Tmin, Tmax	0.55, 0.80
No. of measured, independent and	
observed [I > 2.0σ(I)] reflections	22989, 4737, 4681
Rint	0.000
(sin θ/λ)max (Å−1)	
Refinement	
R[F2 > 2σ(F2)], wR(F2), S	0.026, 0.064, 0.94
No. of reflections	4737
No. of parameters	344
H-atom treatment	H-atom parameters not refined
Δρmax, Δρmin (e Å−3)	0.28, −0.31
Absolute structure	Parsons, Flack & Wagner (2013), 2037 Friedel Pairs
Absolute structure parameter	0.04 (3)

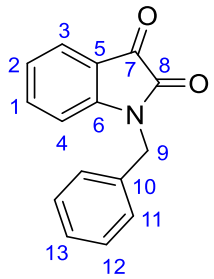
6.3 Single Crystal Data for (±)-5a (CCDC 2103730)





Crystal data	
Chemical formula	$C_{33}H_{23}F_3N_2O_3$
M_r	552.53
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	100
a, b, c (Å)	9.52763 (10), 22.8402 (2), 12.17728 (14)
β (°)	95.6178 (10)
V (Å^3)	2637.20 (5)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	0.87
Crystal size (mm)	0.26 × 0.14 × 0.12
Data collection	
Diffractometer	Oxford Diffraction SuperNova
Absorption correction	Multi-scan *CrysAlis PRO* (Rigaku Oxford Diffraction, 2017)
T_{min}, T_{max}	0.89, 0.90
No. of measured, independent and observed [$I > 2.0\sigma(I)$] reflections	15149, 5075, 4646
R_{int}	0.069
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.615
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.046, 0.123, 1.00
No. of reflections	5074
No. of parameters	374
No. of restraints	4
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.28, −0.33

7 NMR spectra

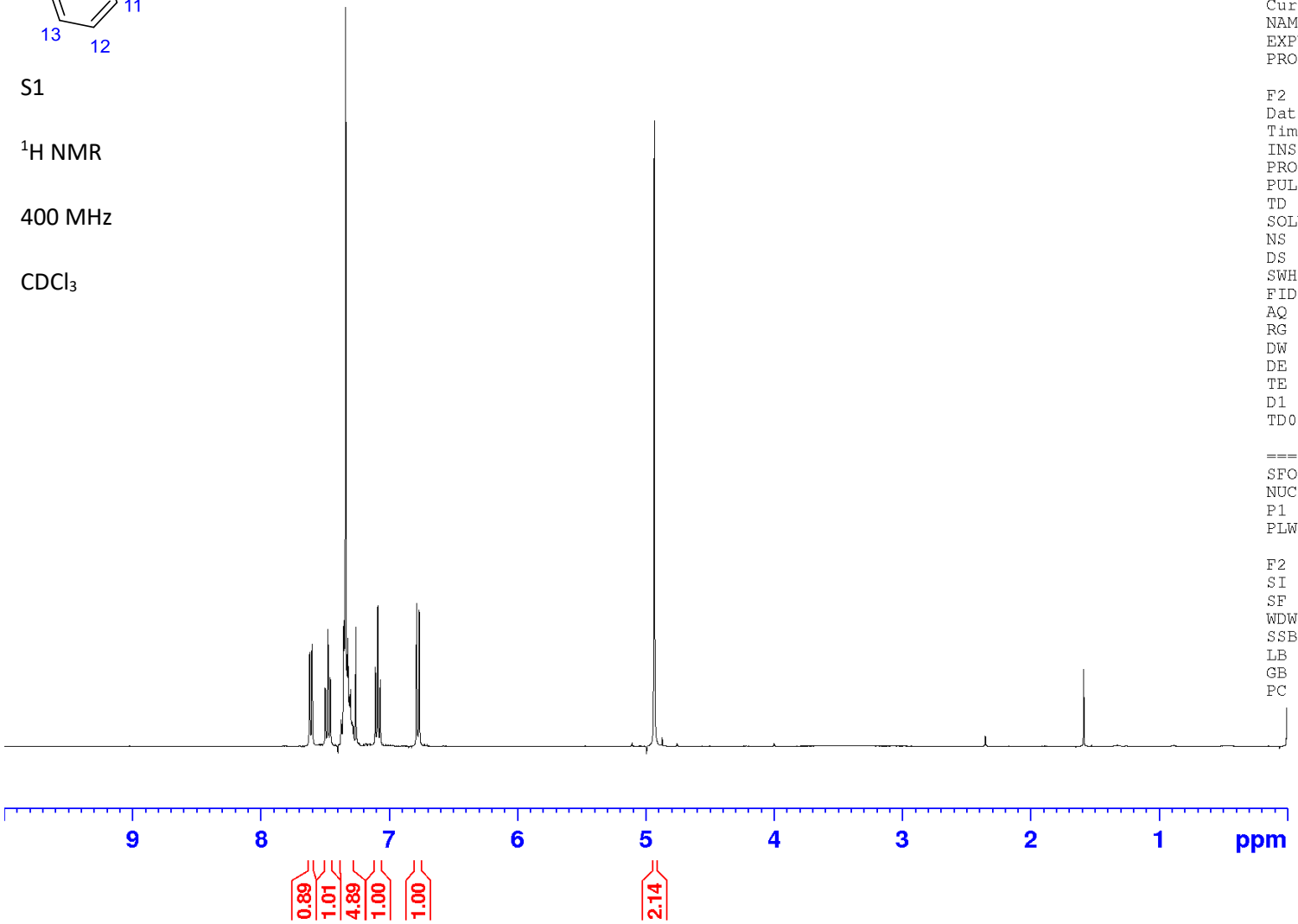


S1

^{1}H NMR

400 MHz

$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-05
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
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Time                14.38
INSTRUM        AVIII_400
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PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                  80.6
DW                60.800 usec
DE                 6.50 usec
TE                297.0 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         399.9124696 MHz
NUC1                   1H
P1                 15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
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WDW                   EM
SSB                    0
LB                  0.30 Hz
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PC                  1.00
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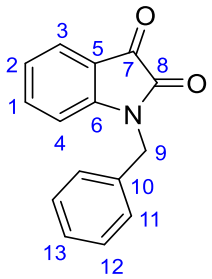
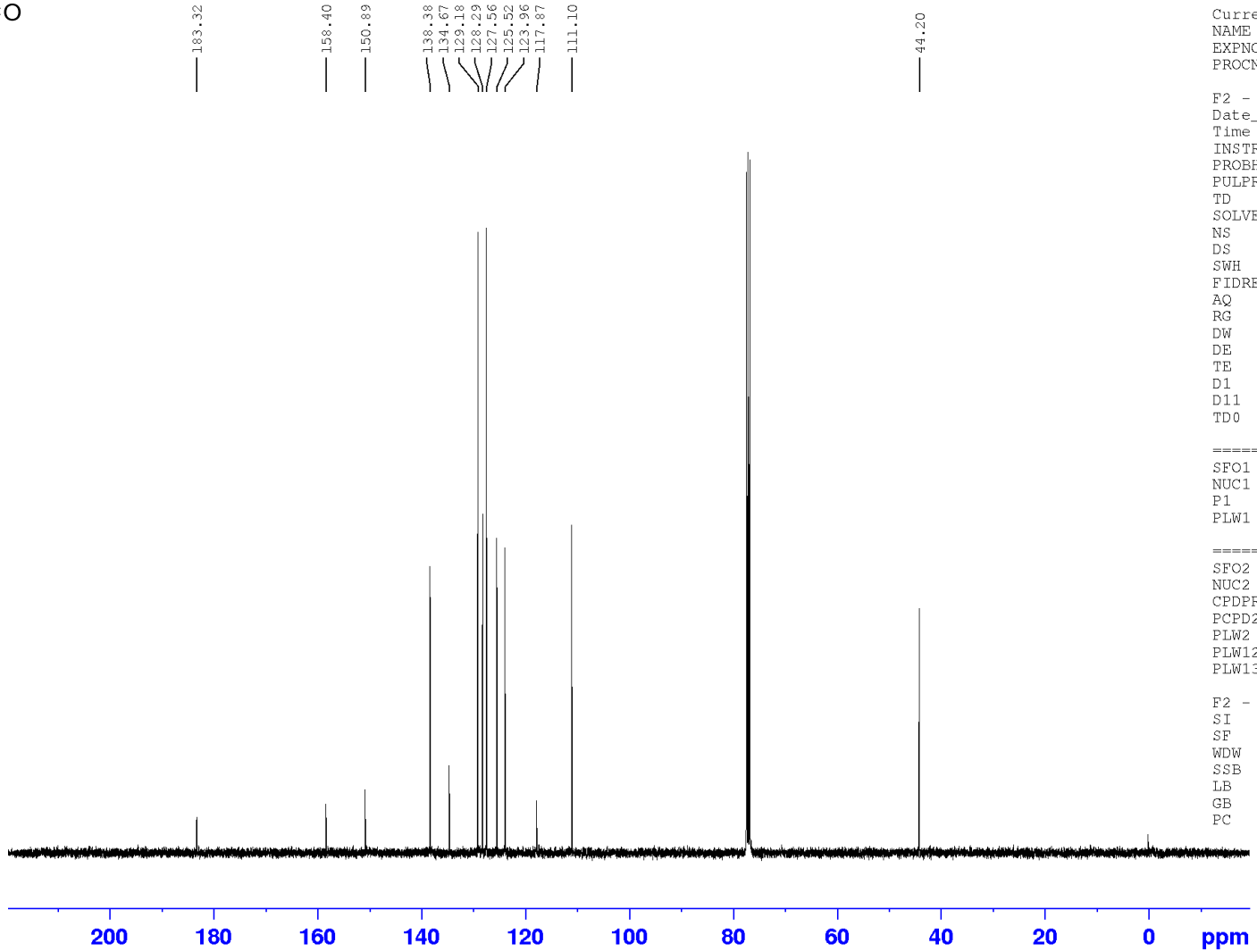


S1

^{13}C NMR

101 MHz

$CDCl_3$

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Current Data Parameters
NAME            CAD-1-05
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191018
Time               20.27
INSTRUM        AVIII_400
PROBHD   5 mm PABBO BB/
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           24038.461 Hz
FIDRES         0.250010 Hz
AQ            1.9999200 sec
RG                   144
DW               20.800 usec
DE                6.50 usec
TE               302.9 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         100.5675047 MHz
NUC1                13C
P1                 9.00 usec
PLW1         96.68000031 W

======== CHANNEL f2 ========
SFO2         399.9115996 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2              90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.38907000 W

F2 - Processing parameters
SI                131072
SF           100.5574367 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
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PC                1.40
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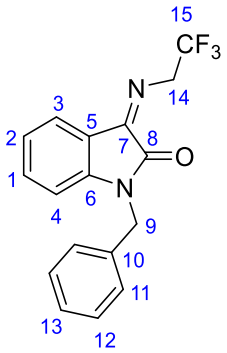
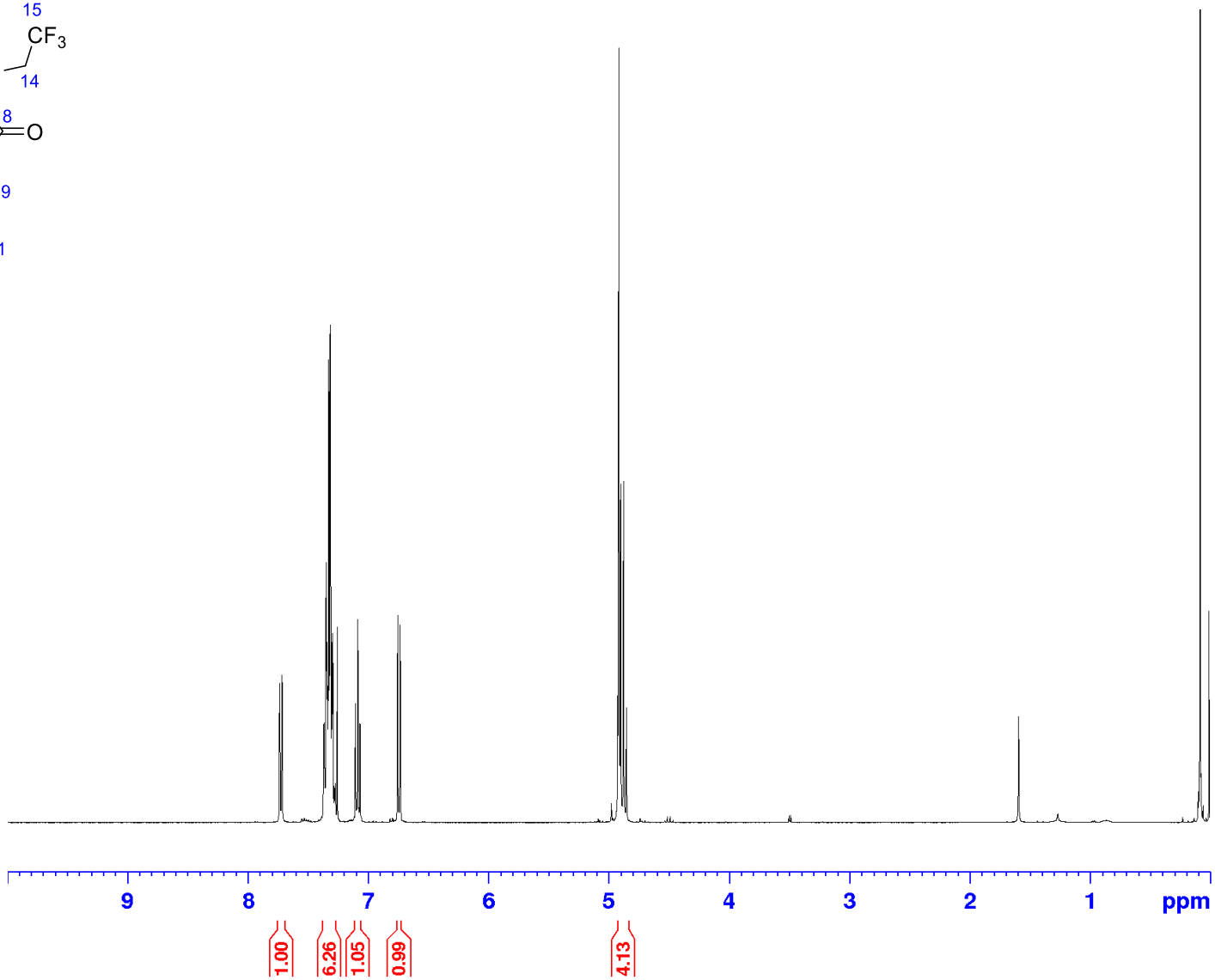


1a

^{1}H NMR

400 MHz

$CDCl_3$

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EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
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Time               16.43 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH              8223.685 Hz
FIDRES           0.250967 Hz
AQ               3.9845889 sec
RG                   144
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100093 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
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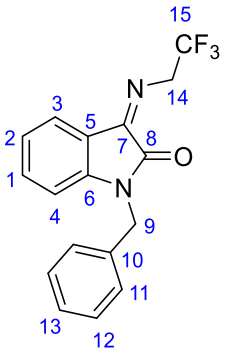
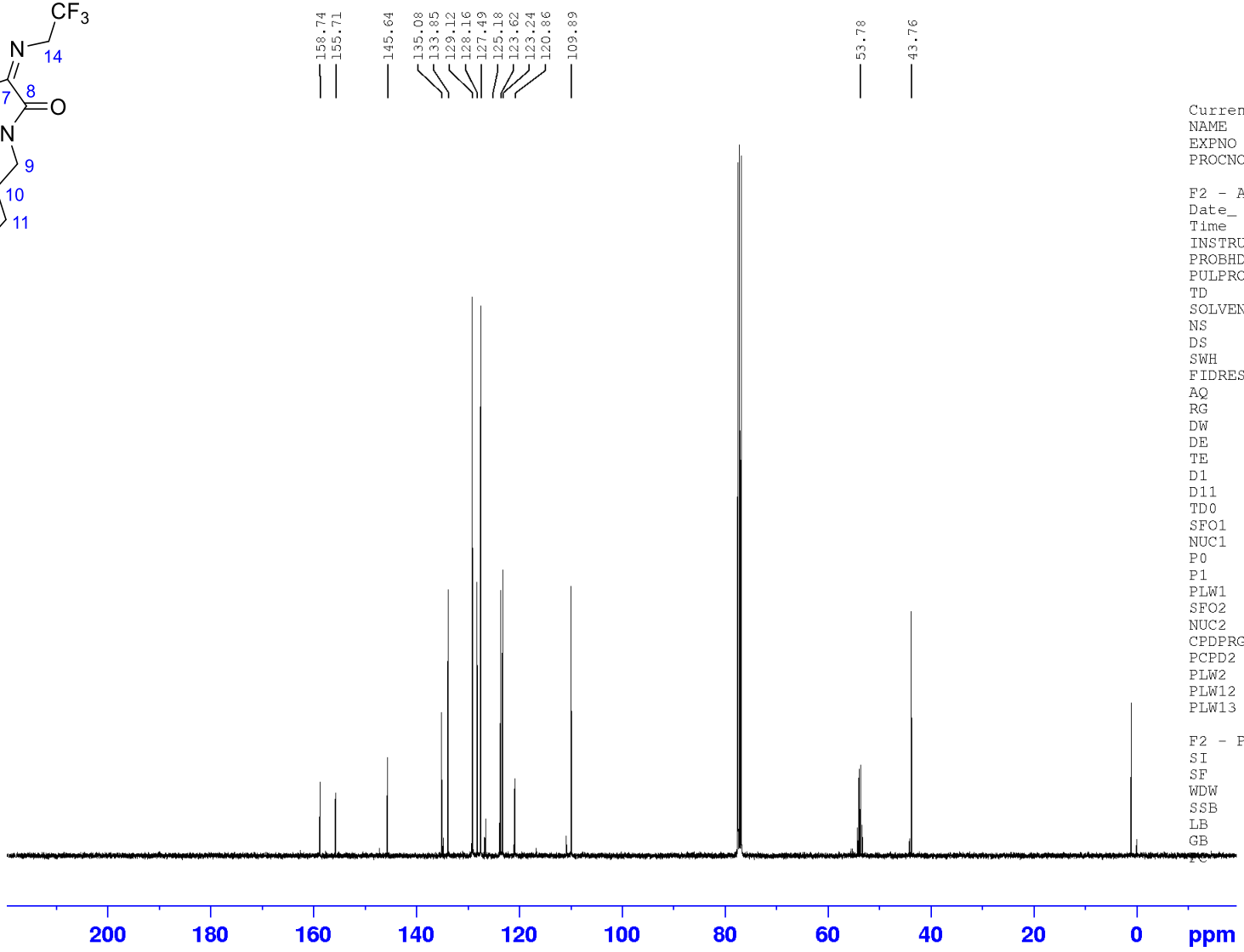


1a

^{13}C NMR

101 MHz

$CDCl_3$

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Current Data Parameters
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EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200214
Time              20.49 h
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PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ              1.9999200 sec
RG                  1030
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1          100.6178003 MHz
NUC1                 13C
P0                 3.00 usec
P1                 9.00 usec
PLW1          96.68000031 W
SFO2          400.1116004 MHz
NUC2                 1H
CPDPRG[2          waltz64
PCPD2             90.00 usec
PLW2          17.29199982 W
PLW12          0.48032999 W
PLW13          0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077268 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
                   1.40
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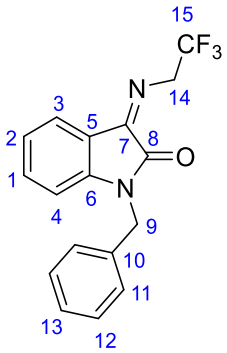
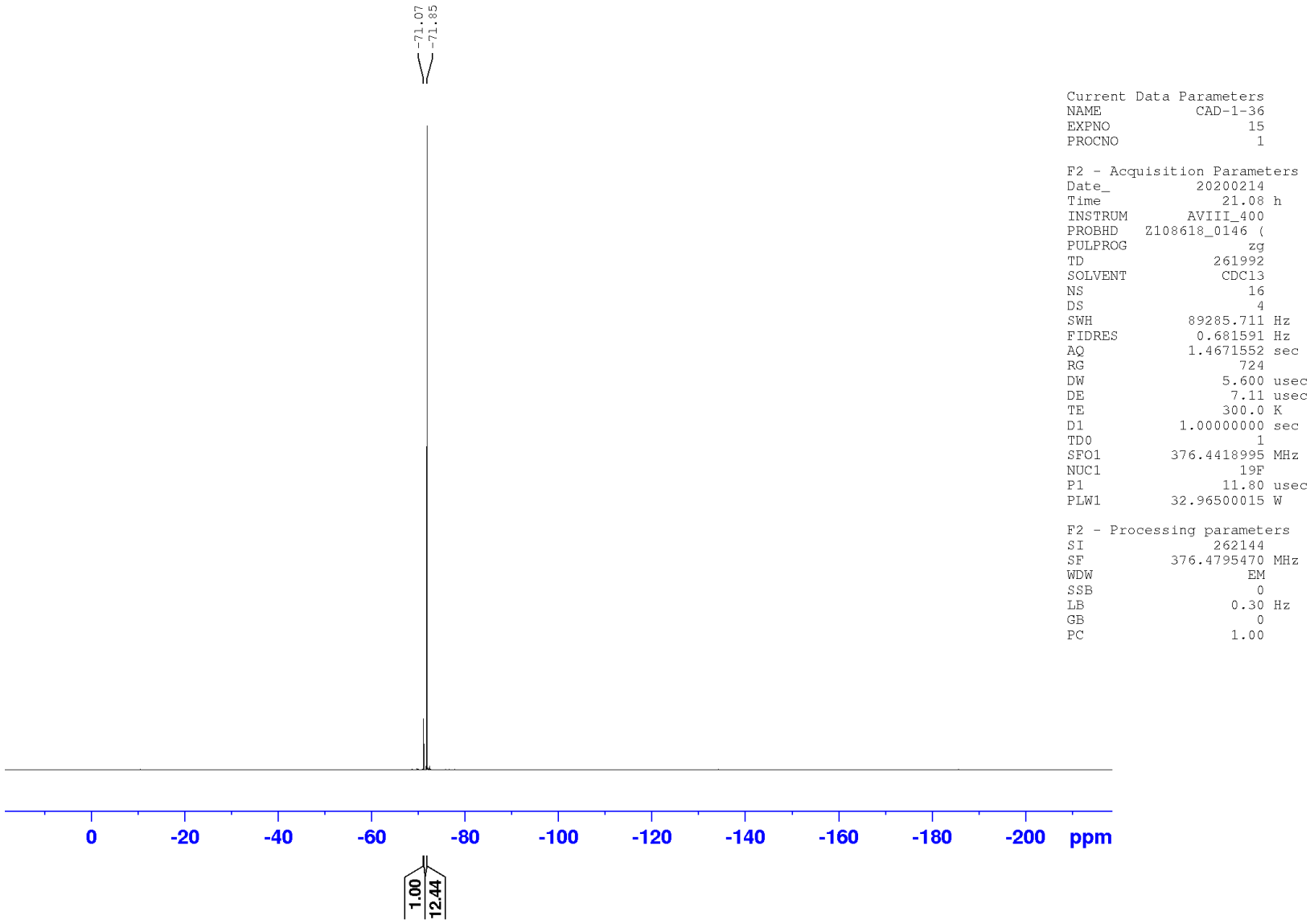


1a

^{19}F NMR

376 MHz

$CDCl_3$

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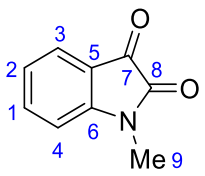
Current Data Parameters
NAME            CAD-1-36
EXPNO                 15
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200214
Time              21.08 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT             CDCl3
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   724
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                 11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

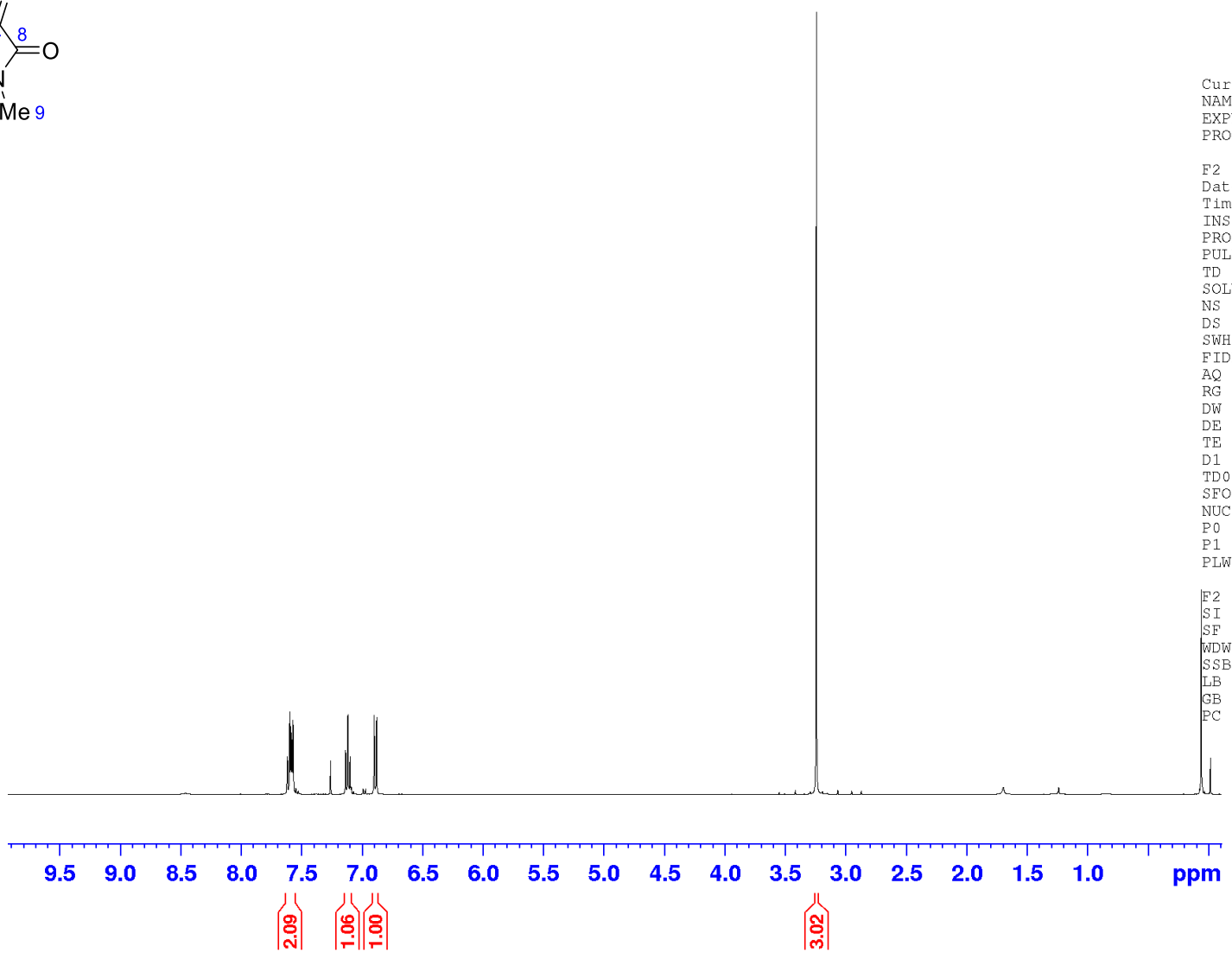


S2

^{1}H NMR

400 MHz

$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-38
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200214
Time              17.02 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   144
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF          400.1100092 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
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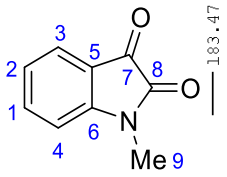


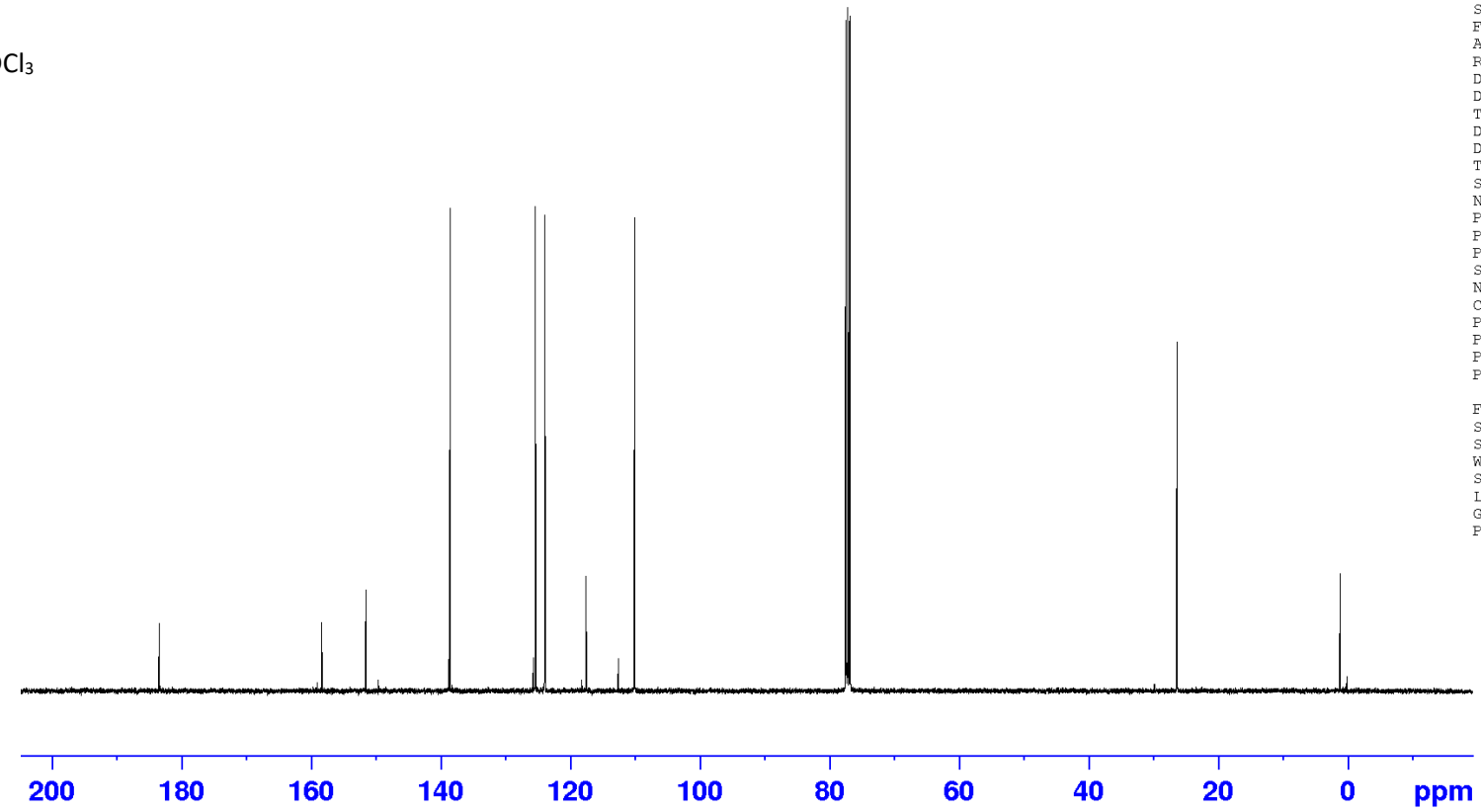
183.47 158.36 151.57 138.54 125.38 123.96 117.55 110.06 26.33

S2

^{13}C NMR

101 MHz

$CDCl_3$

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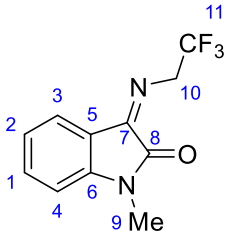
Current Data Parameters
NAME            CAD-1-38
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200214
Time               22.57 h
INSTRUM         AVIII_400
PROBHD    Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ              1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1          100.6178003 MHz
NUC1                 13C
P0                  3.00 usec
P1                  9.00 usec
PLW1          96.68000031 W
SFO2          400.1116004 MHz
NUC2                 1H
CPDPRG[2         waltz64
PCPD2               90.00 usec
PLW2          17.29199982 W
PLW12          0.48032999 W
PLW13          0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077299 MHz
WDW                 EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

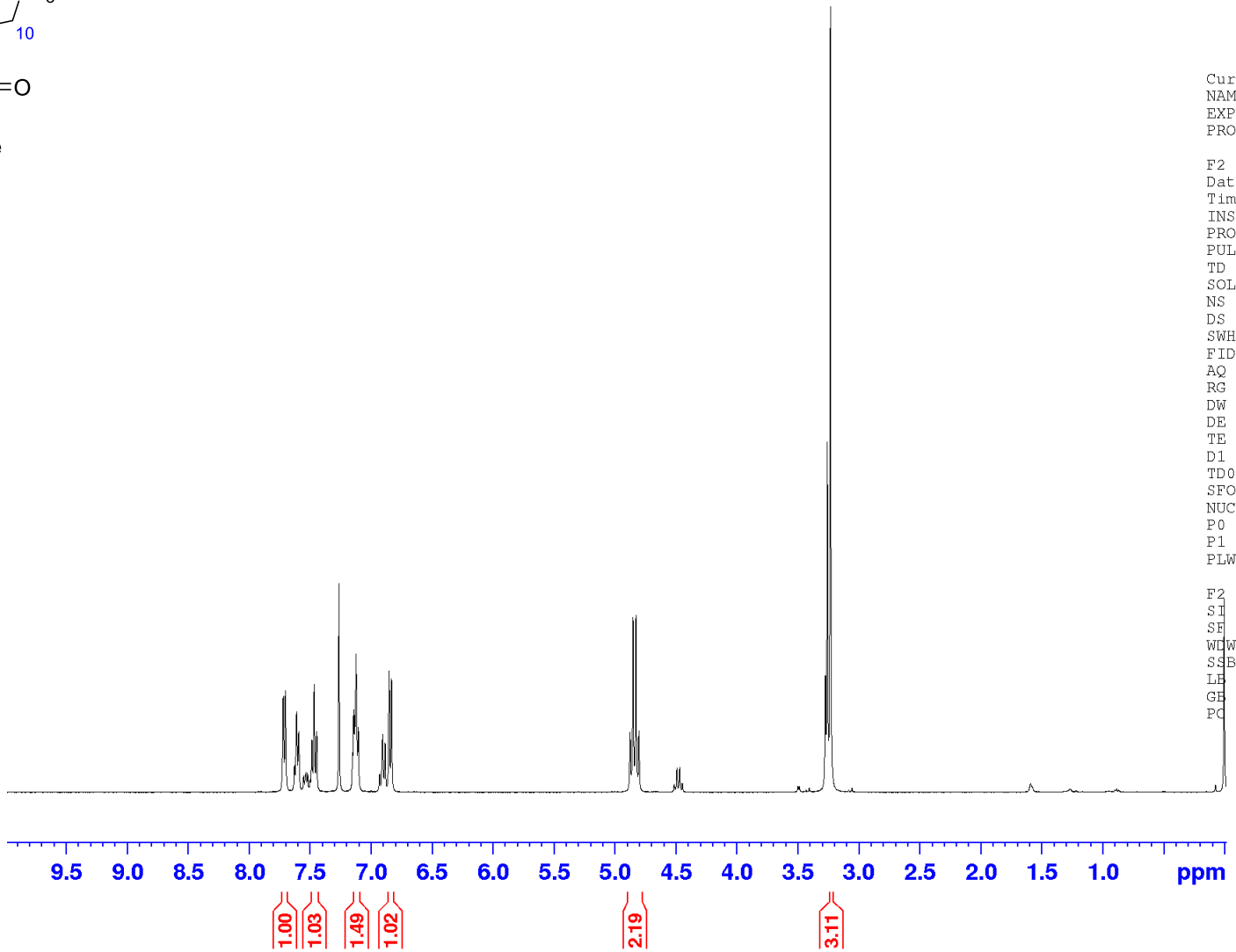


1b

^{1}H NMR

400 MHz

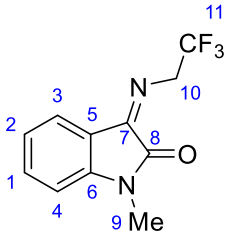
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.163 Crop 1
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20210510
Time              16.39 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100085 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

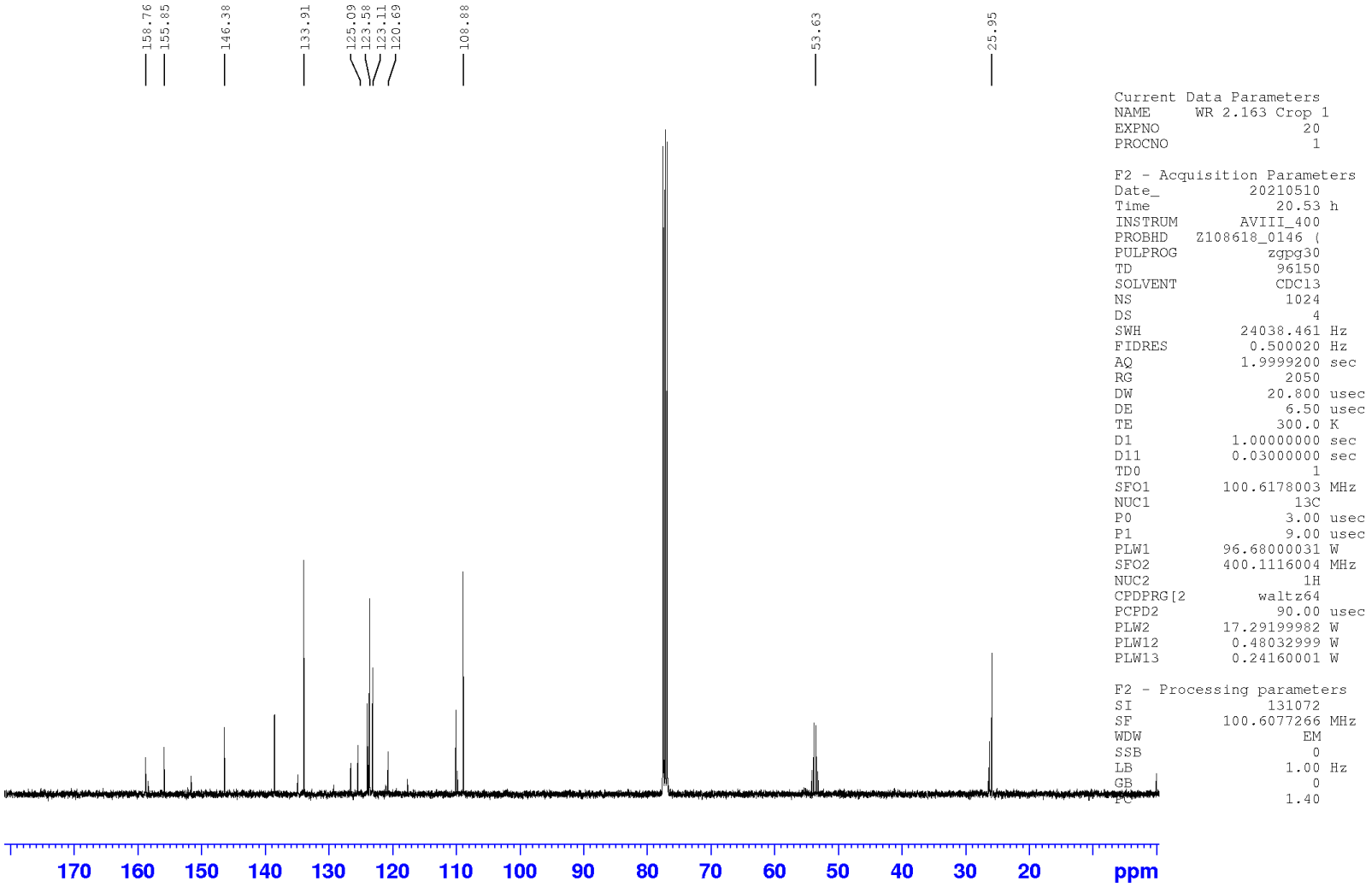


1b

^{13}C NMR

101 MHz

$CDCl_3$

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Current Data Parameters
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PROCNO                 1

F2 - Acquisition Parameters
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Time              20.53 h
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PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1        100.6178003 MHz
NUC1               13C
P0               3.00 usec
P1               9.00 usec
PLW1         96.68000031 W
SFO2        400.1116004 MHz
NUC2               1H
CPDPRG[2        waltz64
PCPD2            90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI               131072
SF          100.6077266 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
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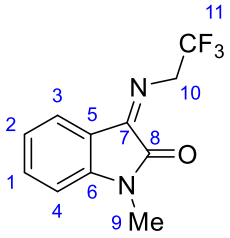
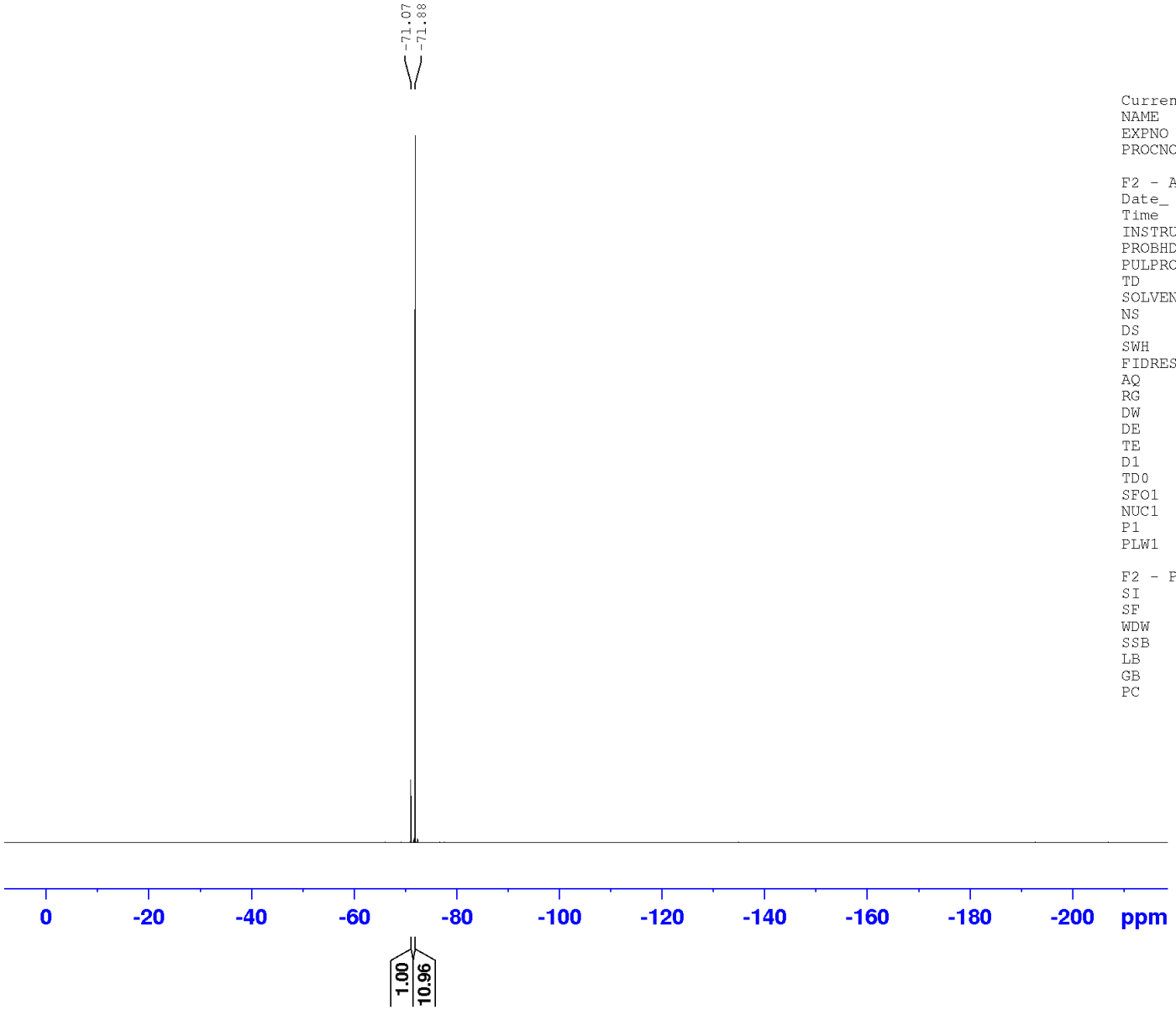


1b

^{19}F NMR

376 MHz

$CDCl_3$

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Current Data Parameters
NAME      WR 2.163 Crop 1
EXPNO                  25
PROCNO                  1

F2 - Acquisition Paramet
Date_            20210510
Time                21.52
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG                 zg
TD                 261992
SOLVENT             CDCl3
NS                     16
DS                      4
SWH             89285.711
FIDRES          0.681591
AQ              1.4671552
RG                    724
DW                  5.600
DE                   7.11
TE                  300.0
D1             1.00000000
TD0                     1
SFO1          376.4418995
NUC1                  19F
P1                  11.80
PLW1          32.96500015

F2 - Processing paramete
SI                 262144
SF            376.4795470
WDW                    EM
SSB                     0
LB                   0.30
GB                      0
PC                   1.00
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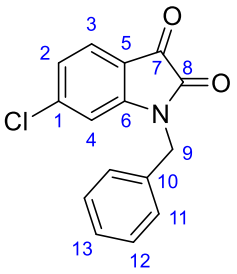
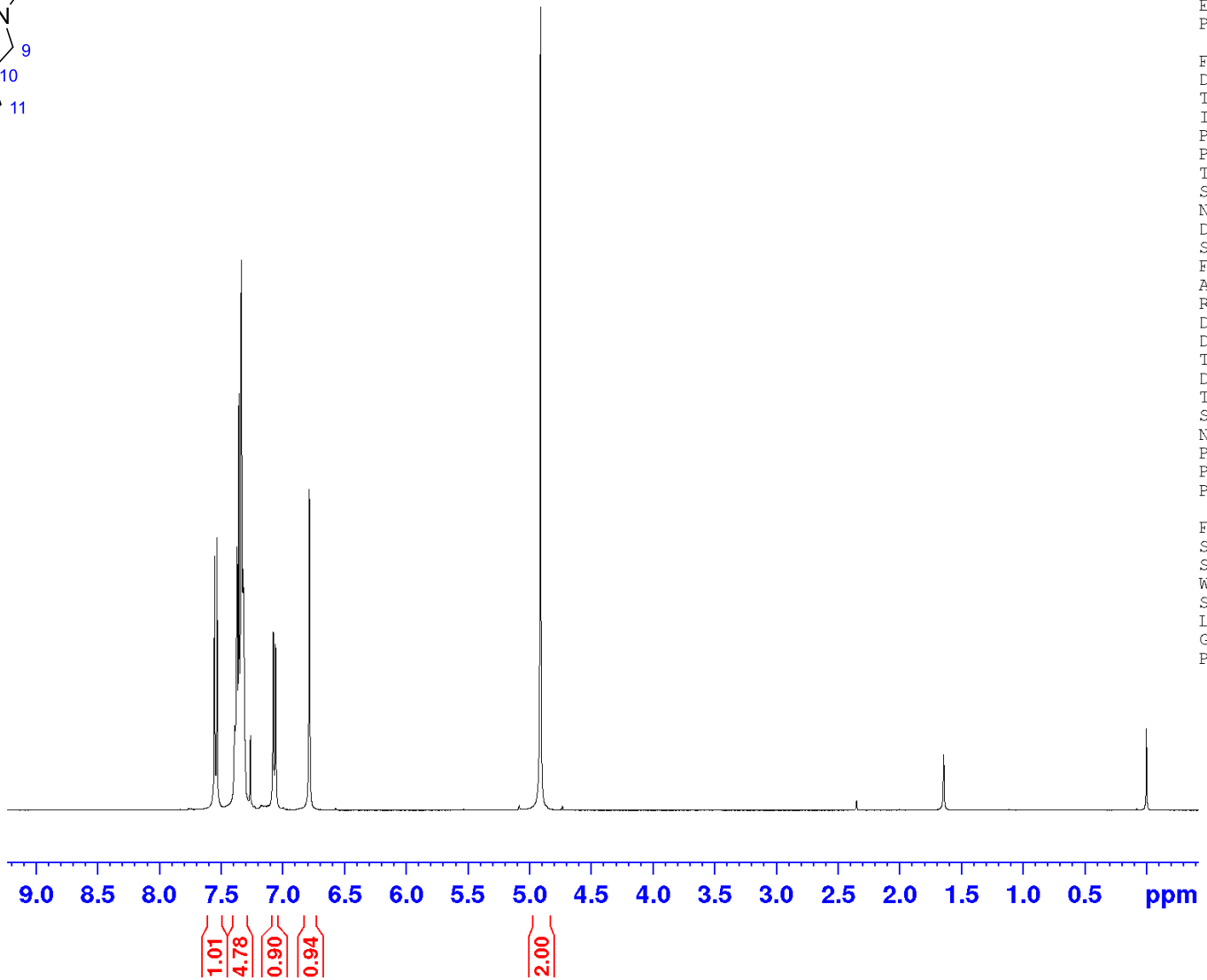


S3

^{1}H NMR

400 MHz

$CDCl_3$




```
Current Data Parameters
NAME         WR 2.220 C1
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210923
Time              17.37 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   128
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100083 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
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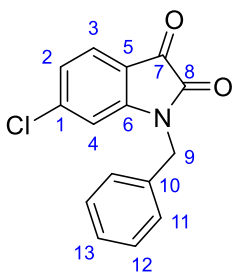
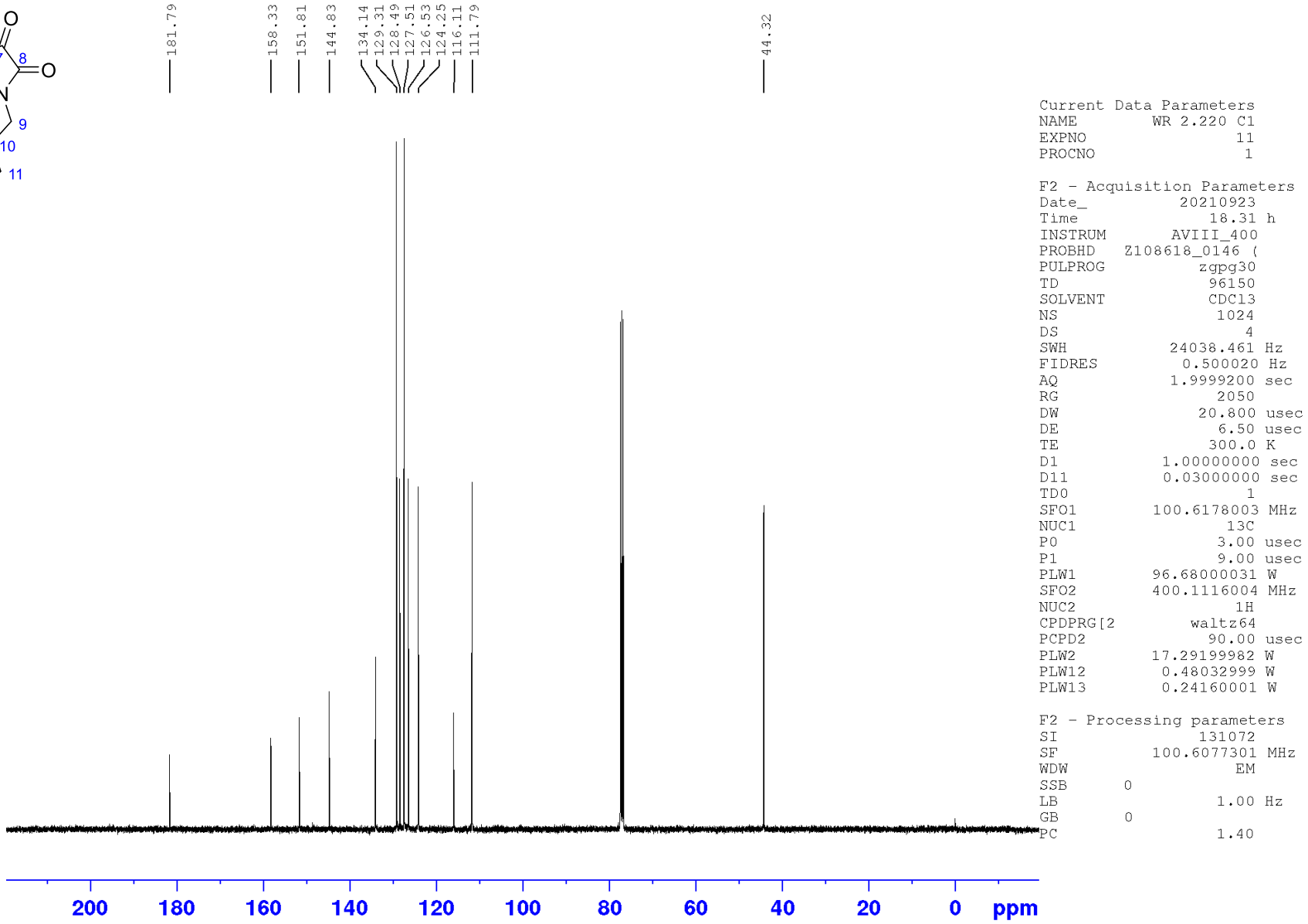


S3

^{13}C NMR

101 MHz

$CDCl_3$




```
Current Data Parameters
NAME         WR 2.220 C1
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20210923
Time              18.31 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6178003 MHz
NUC1               13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2        400.1116004 MHz
NUC2               1H
CPDPRG[2        waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077301 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
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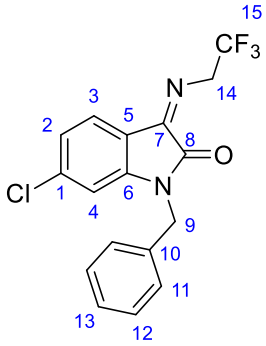
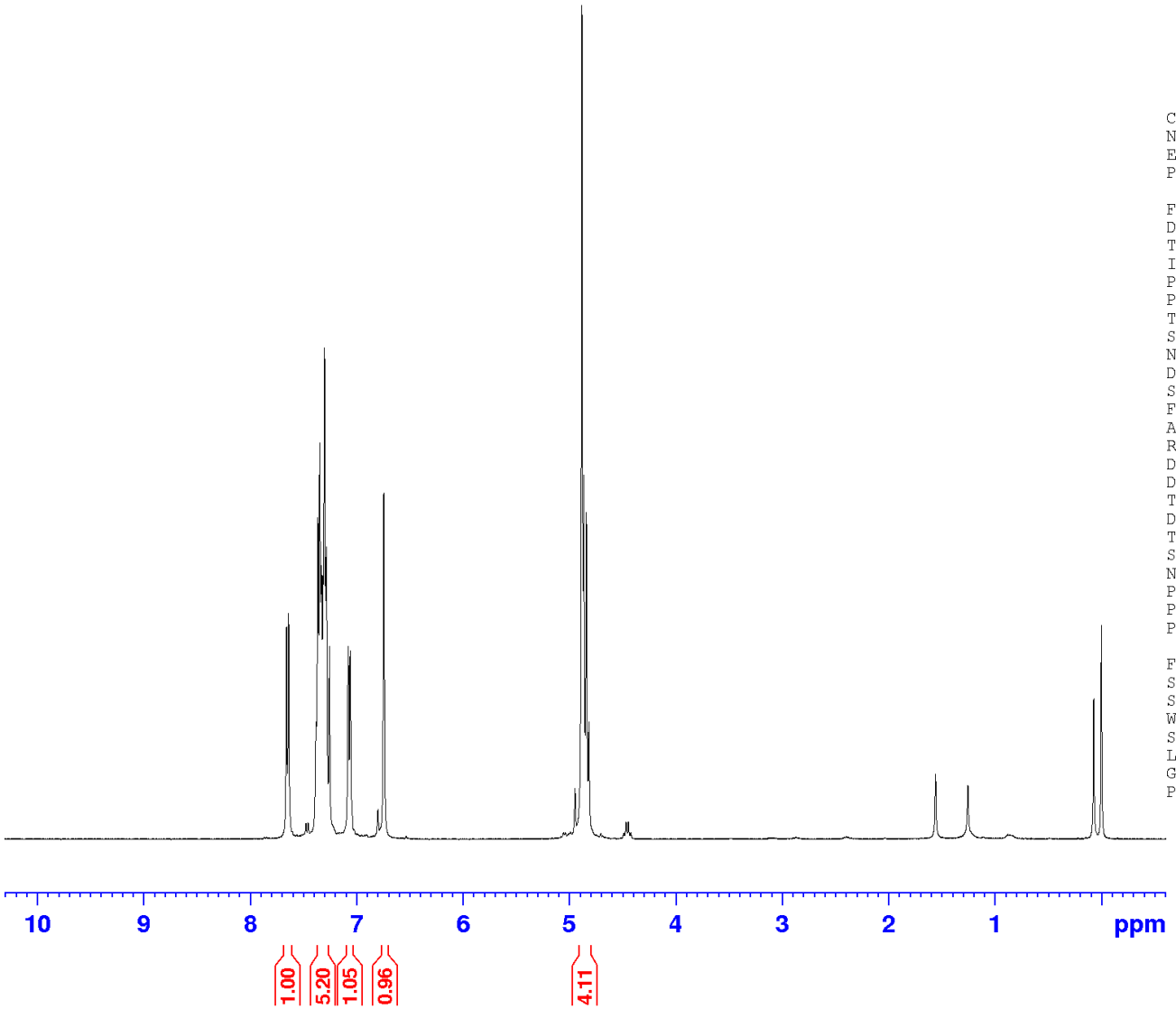


1c

^{1}H NMR

400 MHz

$CDCl_3$

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Current Data Parameters
NAME            WR 2.223
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211014
Time               14.52 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100117 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                  1.00
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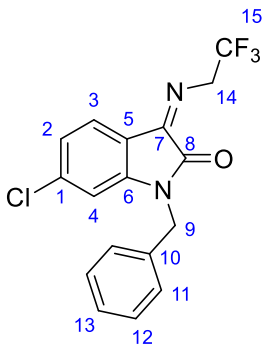
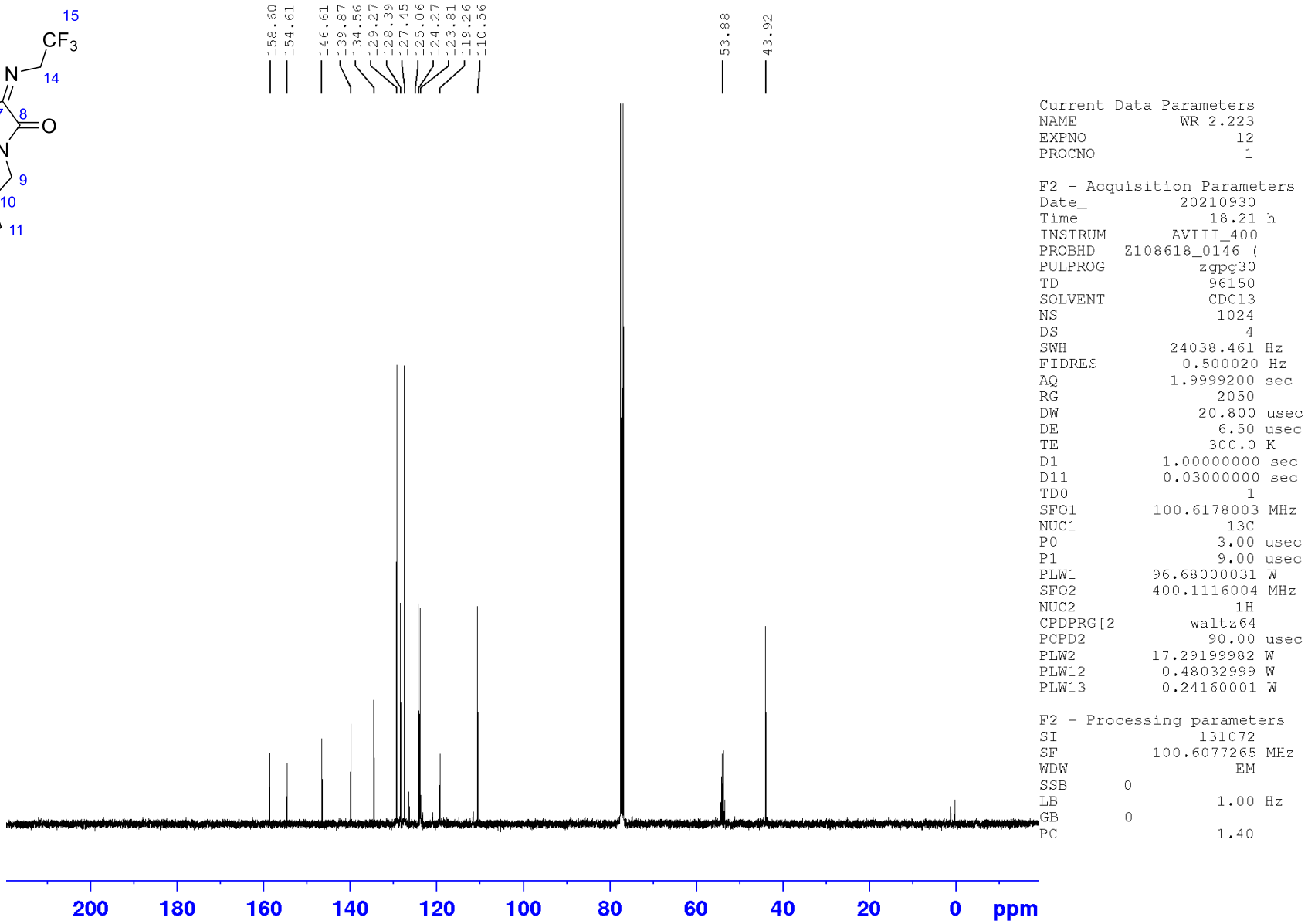


1c

^{13}C NMR

101 MHz

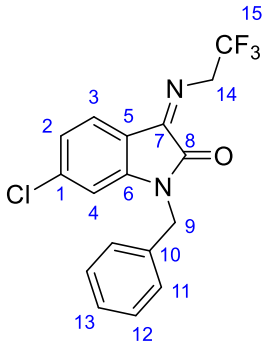
$CDCl_3$




```
Current Data Parameters
NAME                  WR 2.223
EXPNO                       12
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20210930
Time                     18.21 h
INSTRUM               AVIII_400
PROBHD    Z108618_0146 (
PULPROG                 zgpg30
TD                       96150
SOLVENT                  CDCl3
NS                        1024
DS                           4
SWH                  24038.461 Hz
FIDRES                0.500020 Hz
AQ                    1.9999200 sec
RG                        2050
DW                      20.800 usec
DE                       6.50 usec
TE                      300.0 K
D1                    1.00000000 sec
D11                   0.03000000 sec
TD0                          1
SFO1                100.6178003 MHz
NUC1                       13C
P0                       3.00 usec
P1                       9.00 usec
PLW1                96.68000031 W
SFO2                400.1116004 MHz
NUC2                       1H
CPDPRG[2                waltz64
PCPD2                   90.00 usec
PLW2                17.29199982 W
PLW12                0.48032999 W
PLW13                0.24160001 W

F2 - Processing parameters
SI                       131072
SF                  100.6077265 MHz
WDW                         EM
SSB          0
LB                       1.00 Hz
GB           0
PC                       1.40
```

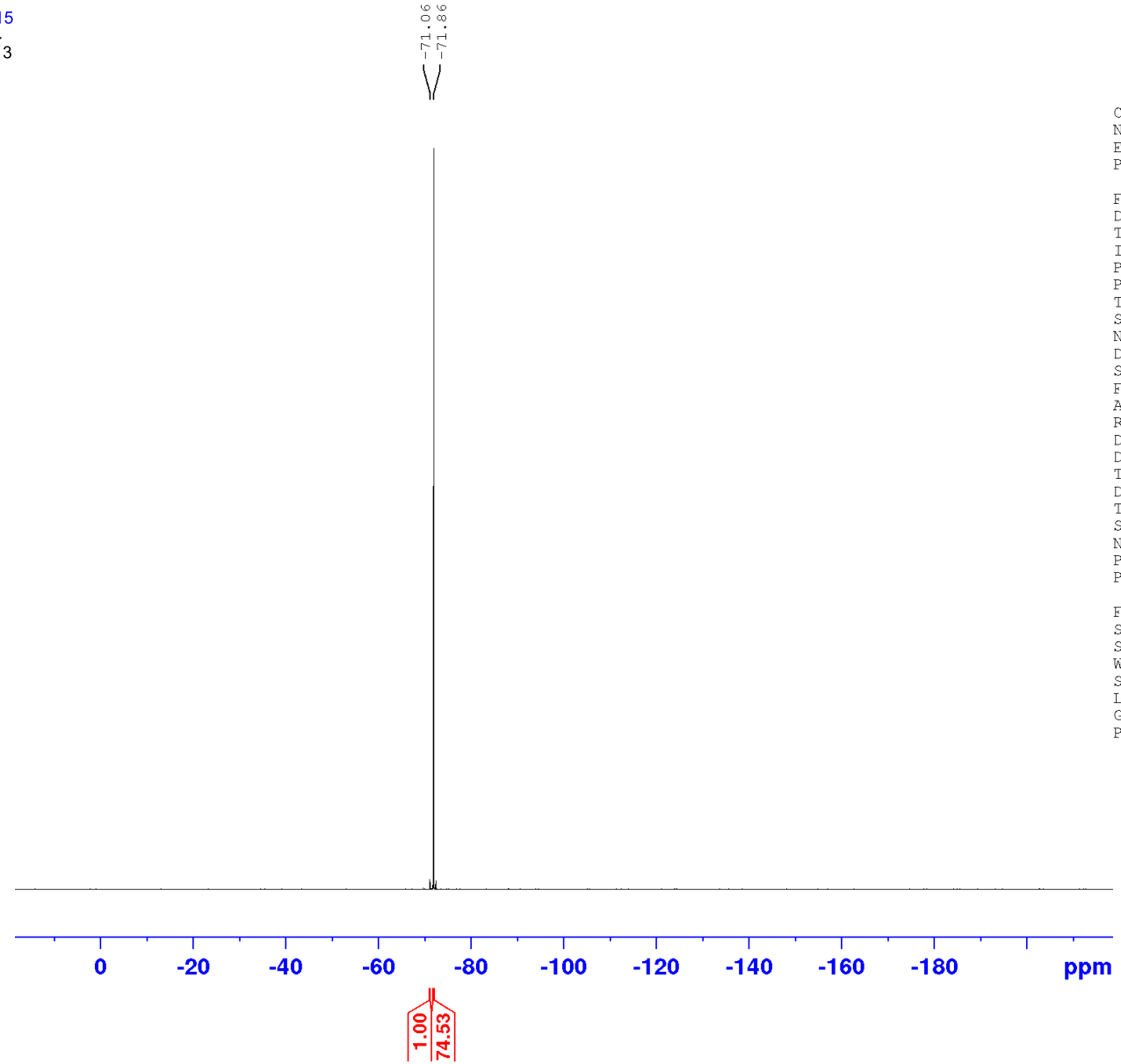


1c

^{19}F NMR

376 MHz

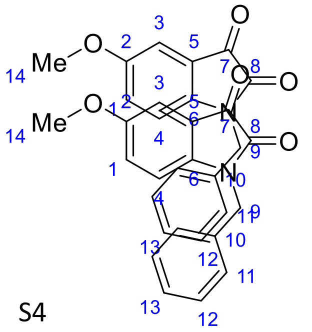
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.223
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210930
Time               15.55 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   645
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



S4

^{1}H NMR

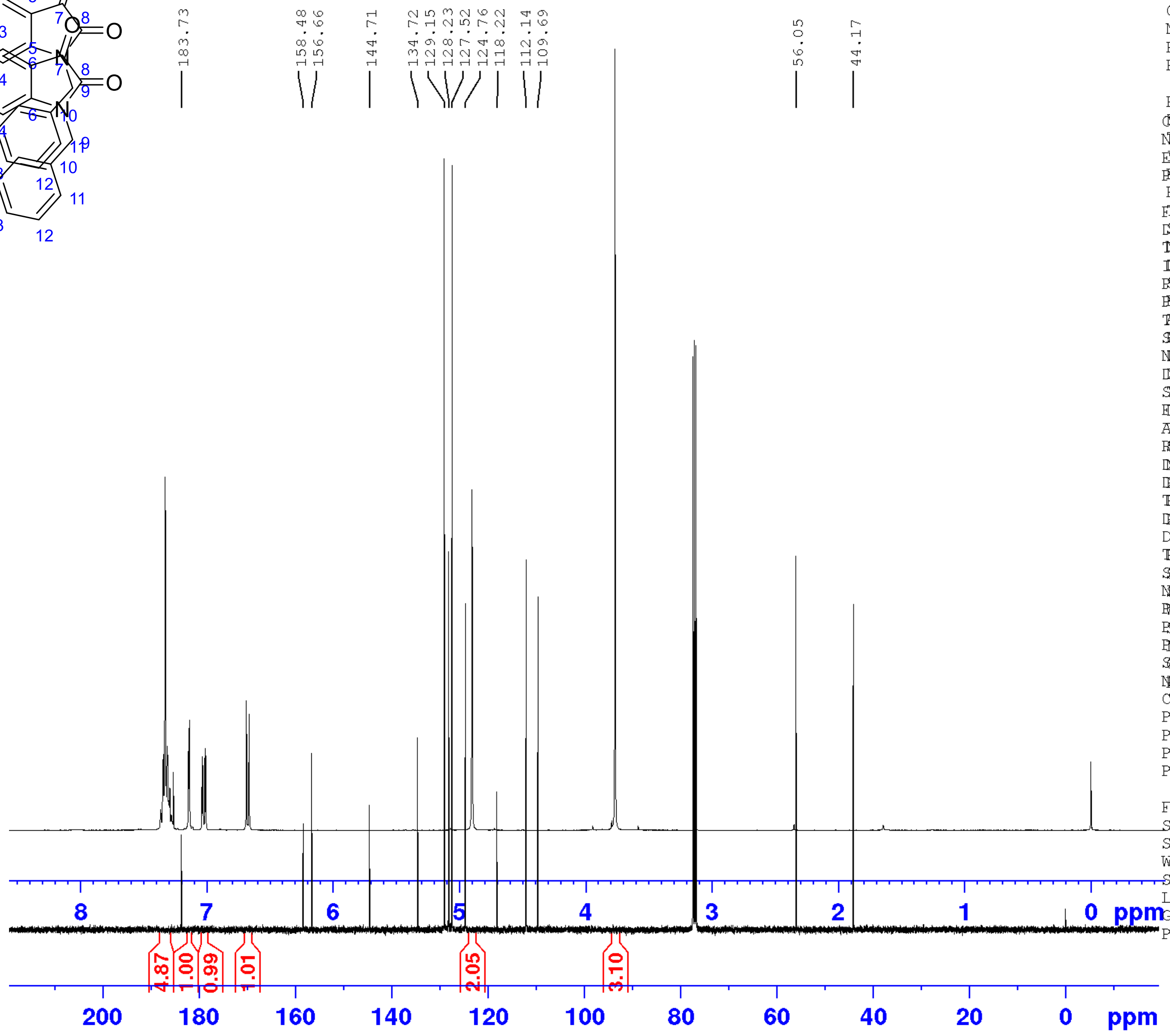
^{13}C NMR

400 MHz

101 MHz

$CDCl_3$

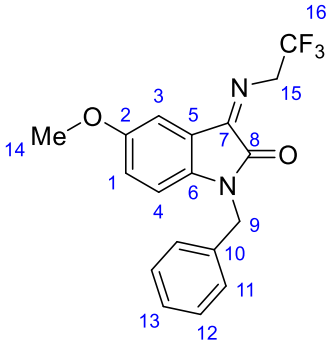
$CDCl_3$



Current Data Parameters
NAME WR 2.229 C1
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
D11 0.03000000 sec
CPDPRG[2 waltz64
PCPD2 90.00 usec
PLW2 17.29199982 W
PLW12 0.48032999 W
PLW13 0.24160001 W

F2 - Processing parameters
SI 131072
SF 100.6077294 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

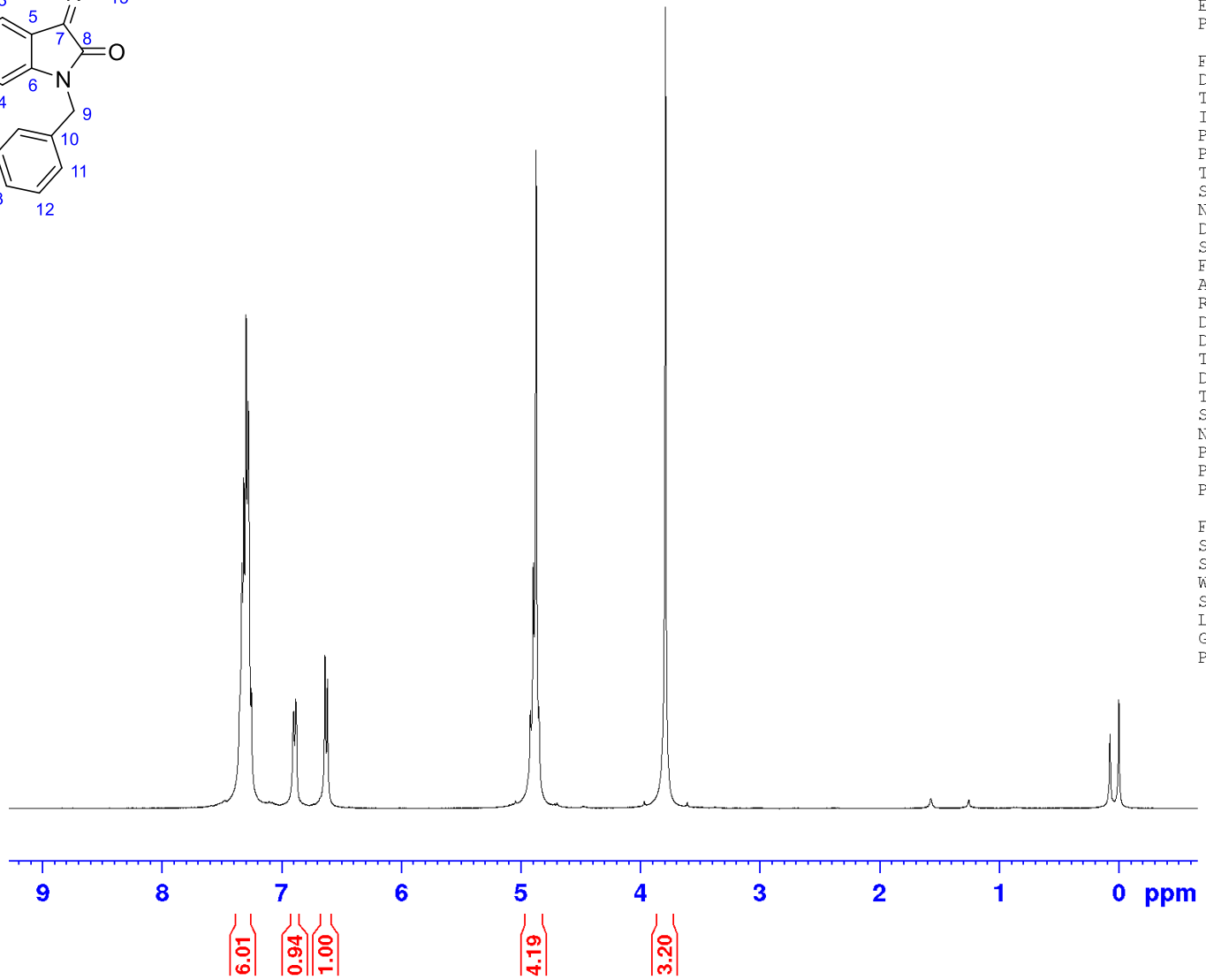


1d

^{1}H NMR

400 MHz

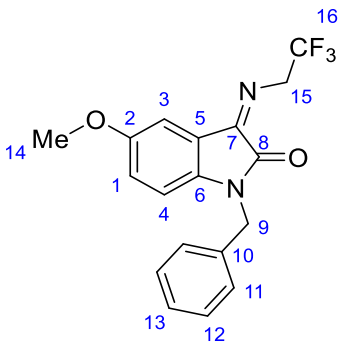
$CDCl_3$




```
Current Data Parameters
NAME         WR 2.230 C1
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211009
Time              16.18 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ             3.9845889 sec
RG                   181
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100121 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

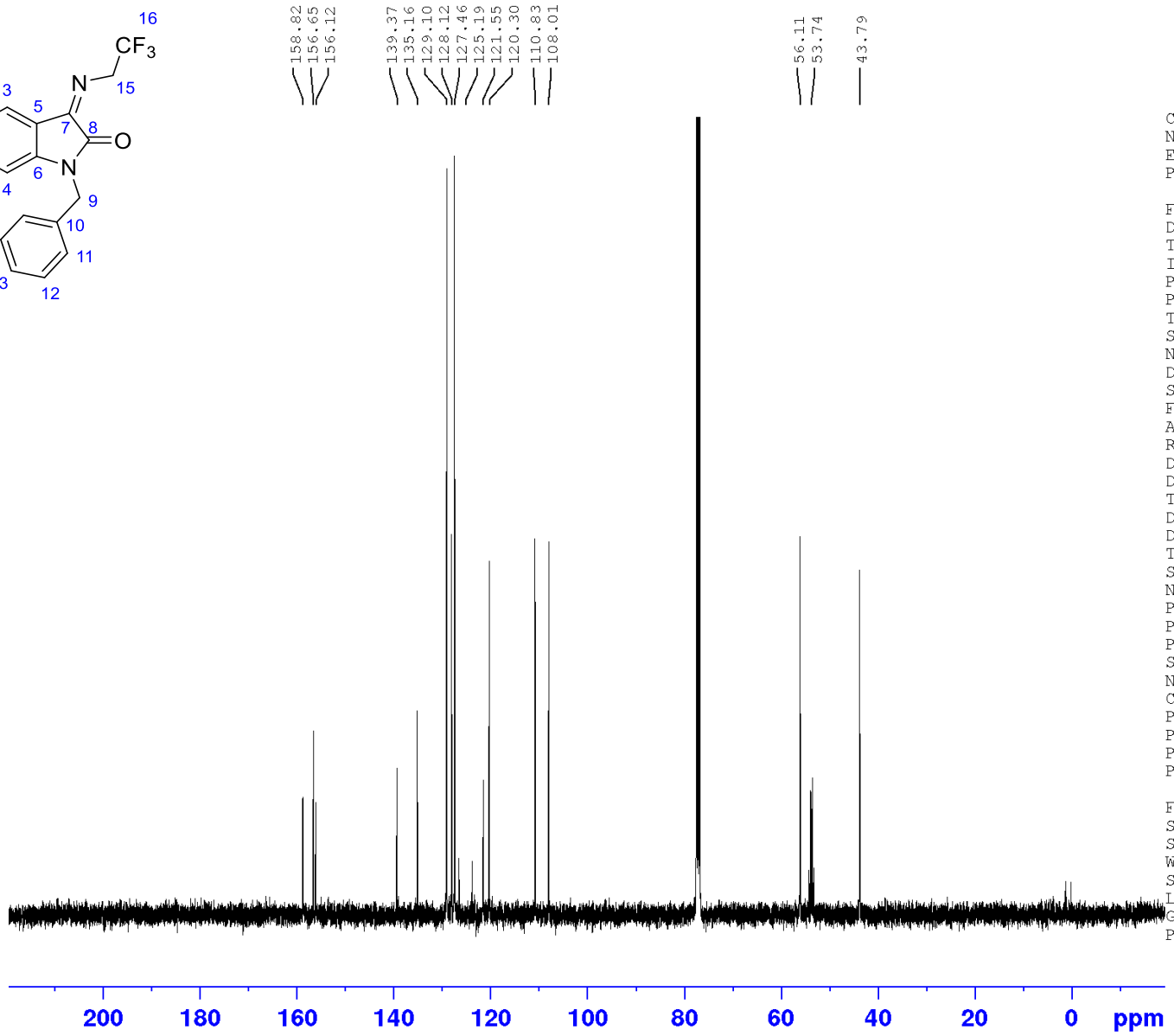


1d

^{13}C NMR

101 MHz

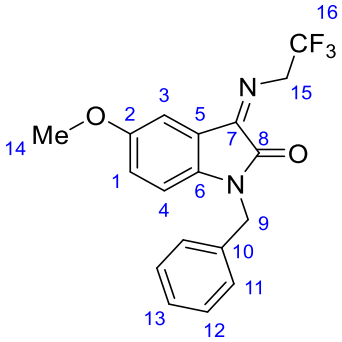
$CDCl_3$




```
Current Data Parameters
NAME         WR 2.230 C1
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20211009
Time              17.12 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6178003 MHz
NUC1                 13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                 1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                 131072
SF           100.6077267 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

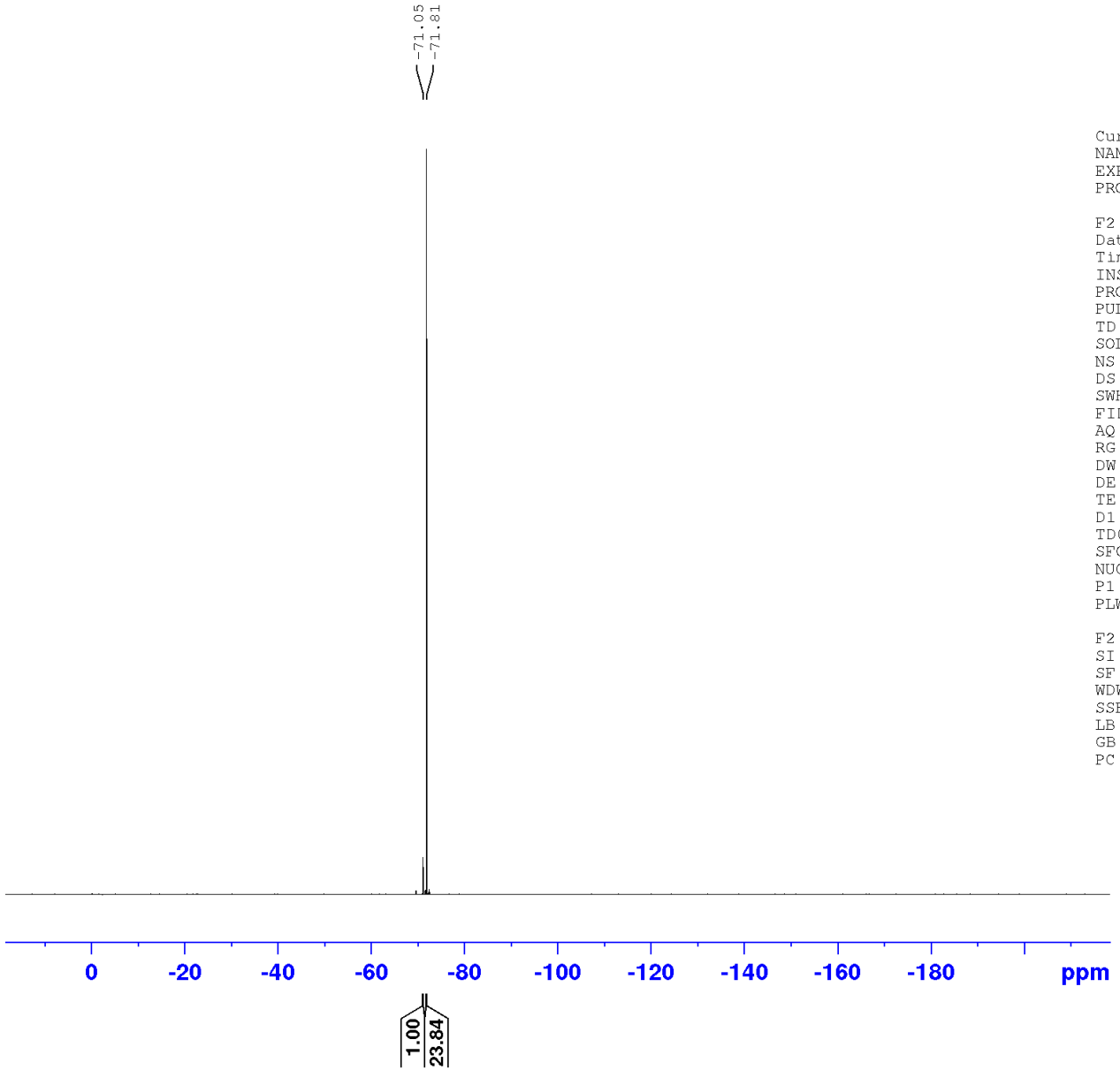


1d

^{19}F NMR

376 MHz

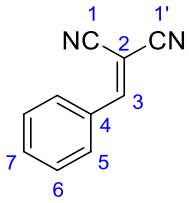
$CDCl_3$




```
Current Data Parameters
NAME         WR 2.230 C1
EXPNO                17
PROCNO                1

F2 - Acquisition Parameters
Date_          20211009
Time              18.29 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG              zg
TD               261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   724
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

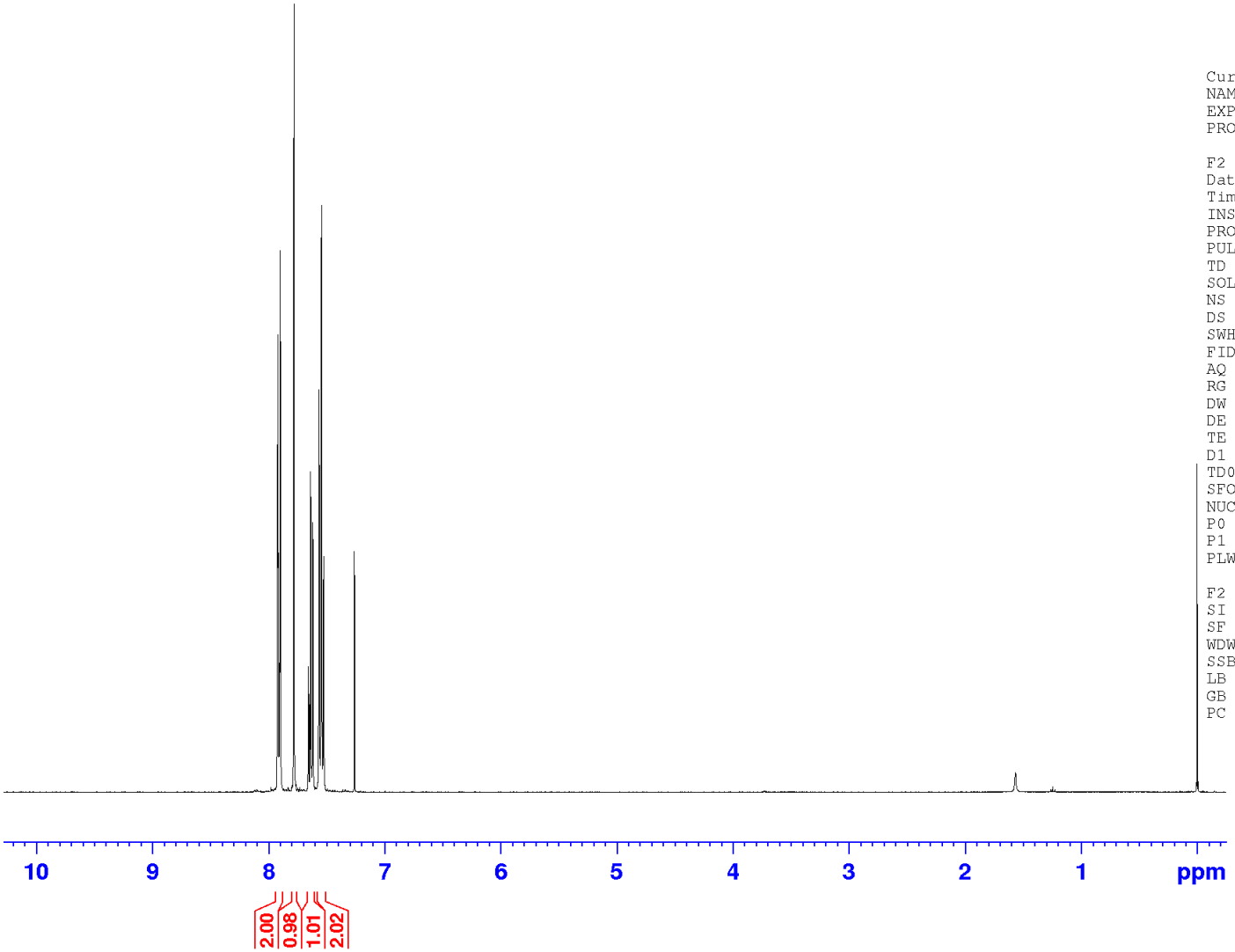


2a

^{1}H NMR

400 MHz

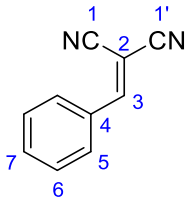
$CDCl_3$




```
Current Data Parameters
NAME      CAD-1-12 Batch 2
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191112
Time               15.04 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   203
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100097 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

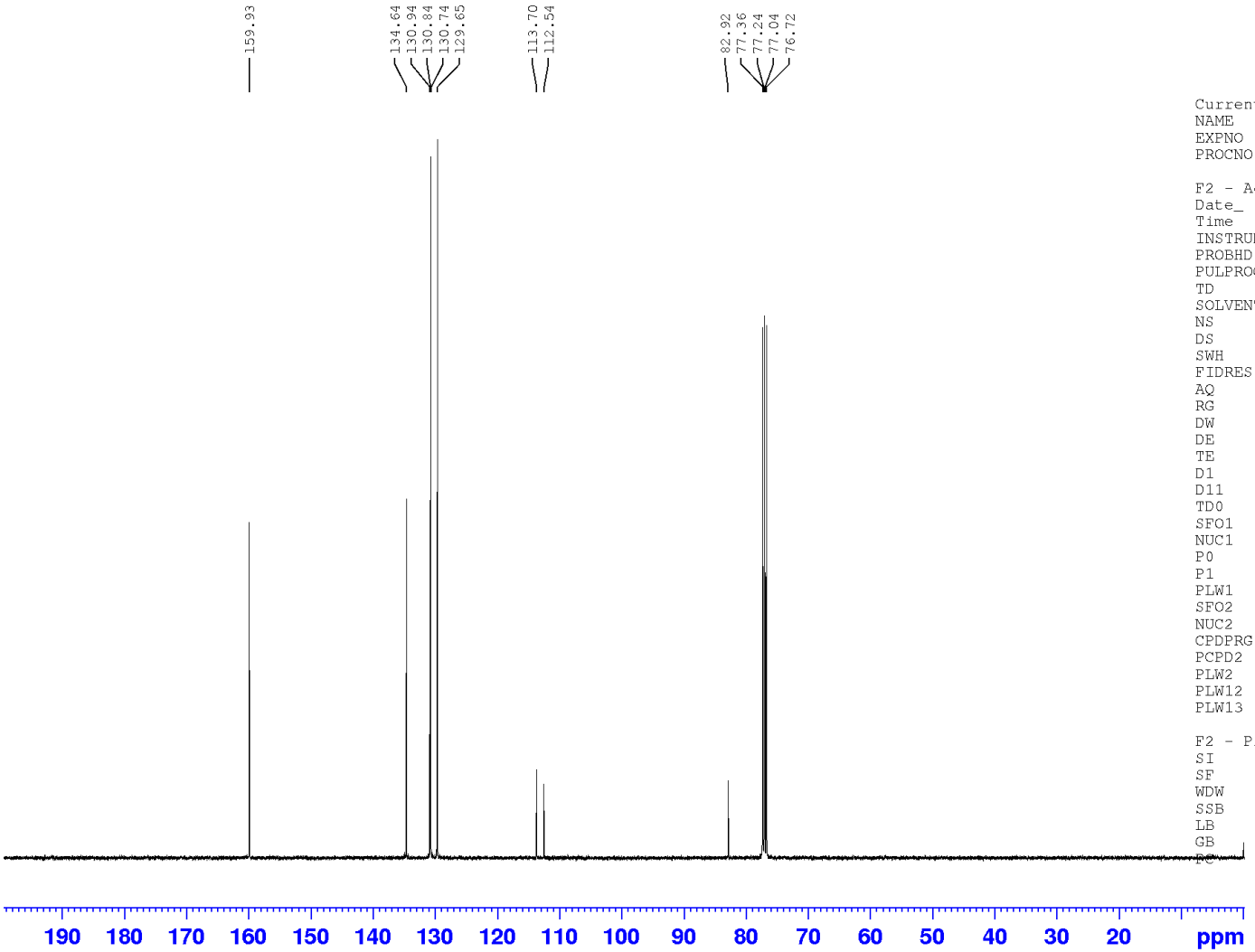


2a

^{13}C NMR

101 MHz

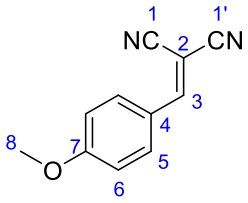
$CDCl_3$




```
Current Data Parameters
NAME      CAD-1-12 Batch 2
EXPNO                  11
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191113
Time                3.03 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 2048
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                 2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1        96.68000031 W
SFO2        400.1116004 MHz
NUC2                1H
CPDPRG[2        waltz64
PCPD2             90.00 usec
PLW2        17.29199982 W
PLW12        0.48032999 W
PLW13        0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077408 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

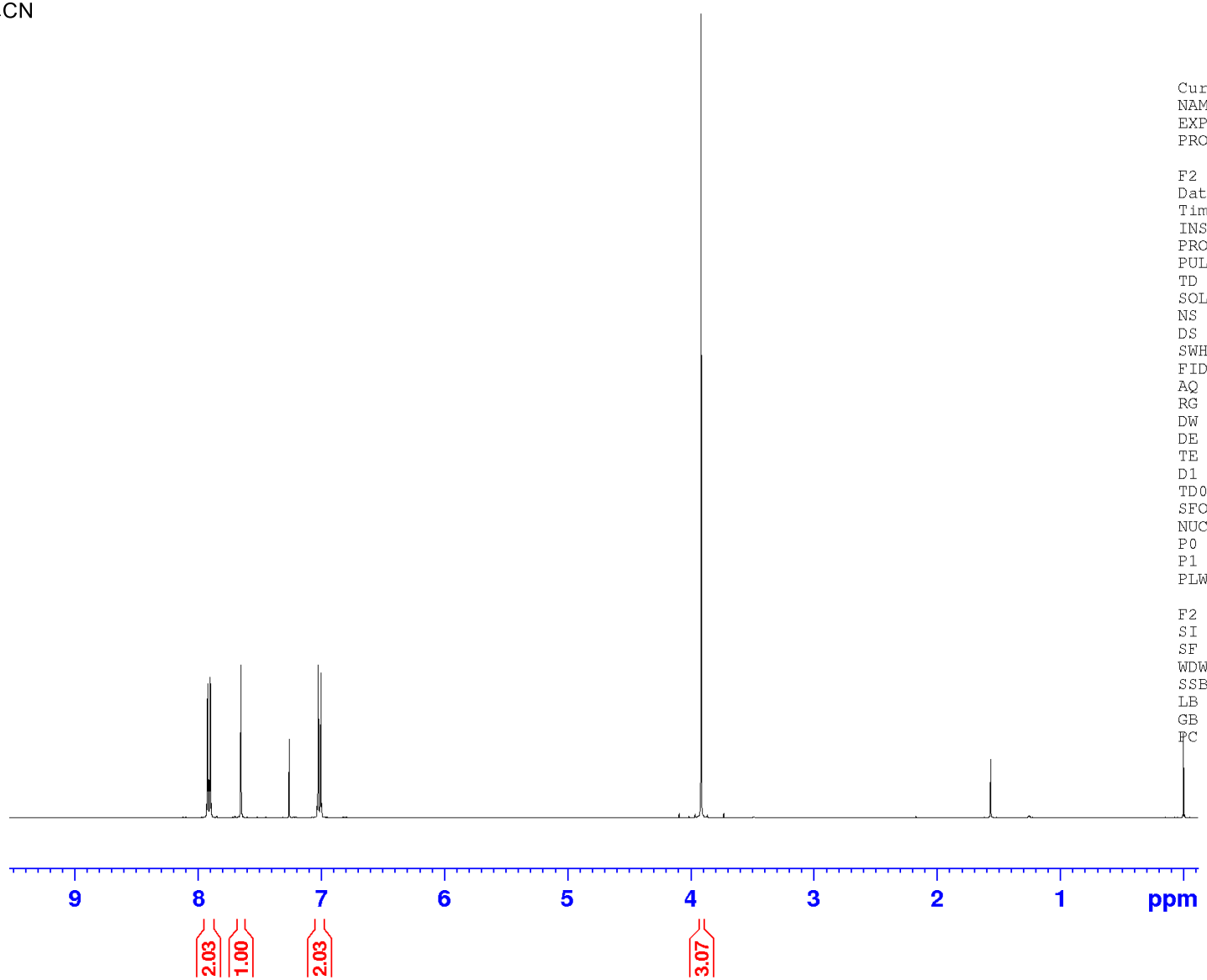


2b

^{1}H NMR

400 MHz

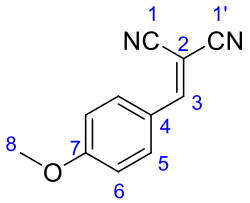
$CDCl_3$




```
Current Data Parameters
NAME                 CAD-1-15
EXPNO                      10
PROCNO                      1

F2 - Acquisition Parame
Date_               20200114
Time                   12.44
INSTRUM             AVIII_400
PROBHD    Z108618_0146 (
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        32
DS                         2
SWH                 8223.685
FIDRES              0.250967
AQ                  3.9845889
RG                       256
DW                    60.800
DE                    17.42
TE                    300.0
D1                 1.00000000
TD0                        1
SFO1             400.1124708
NUC1                      1H
P0                      5.00
P1                     15.00
PLW1             17.29199982

F2 - Processing paramet
SI                     32768
SF               400.1100098
WDW                       EM
SSB                        0
LB                      0.30
GB                         0
PC                      1.00
```

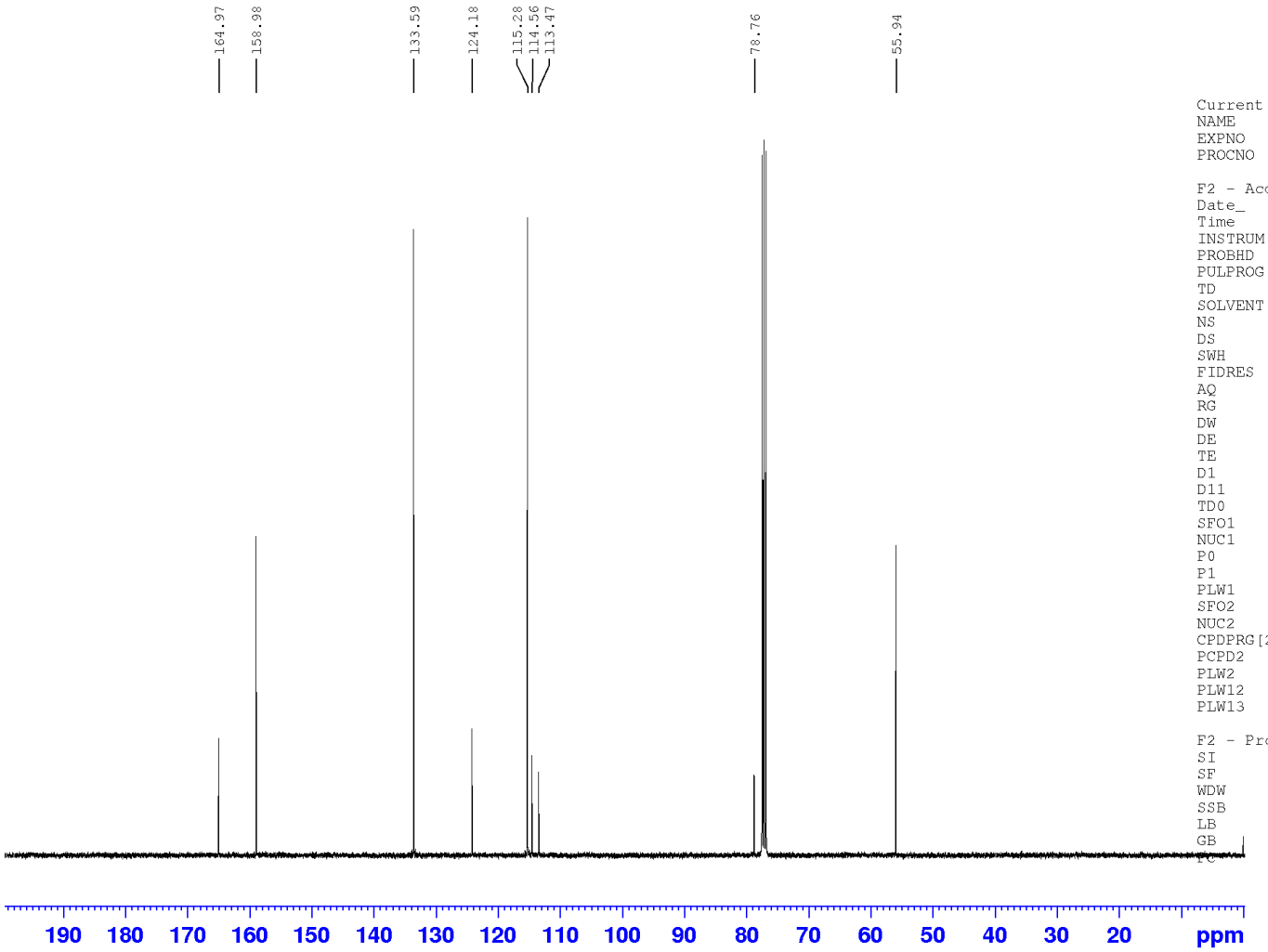


2b

^{13}C NMR

101 MHz

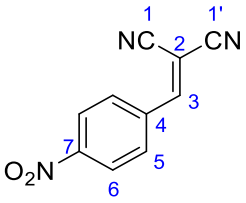
$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-15
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200117
Time                6.33 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ              1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077273 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
                    1.40
```

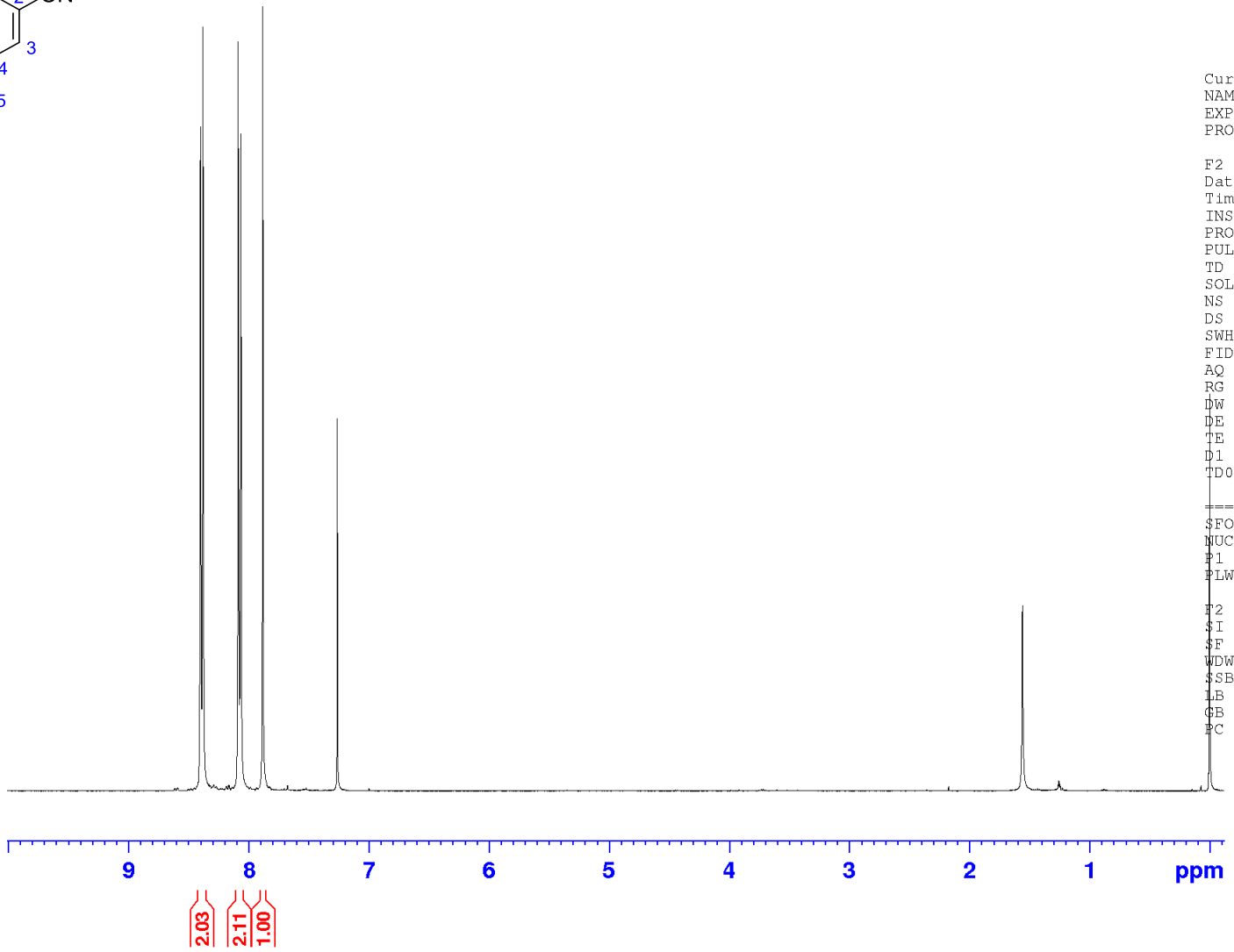


2c

^{1}H NMR

400 MHz

$CDCl_3$

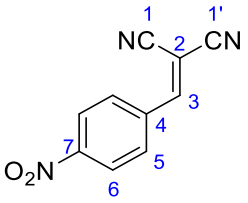



```
Current Data Parameters
NAME      CAD-1-16B high vac
EXPNO                   10
PROCNO                   1

F2 - Acquisition Parameters
Date_           20200117
Time               16.22
INSTRUM         AVIII_400
PROBHD    5 mm PABBO BB/
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     32
DS                      2
SWH              8223.685 Hz
FIDRES           0.125483 Hz
AQ               3.9845889 sec
RG                    128
DW                 60.800 usec
DE                  6.50 usec
TE                 298.2 K
D1            1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
SFO1         399.9124696 MHz
NUC1                   1H
P1                  15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                  32768
SF           399.9100085 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```

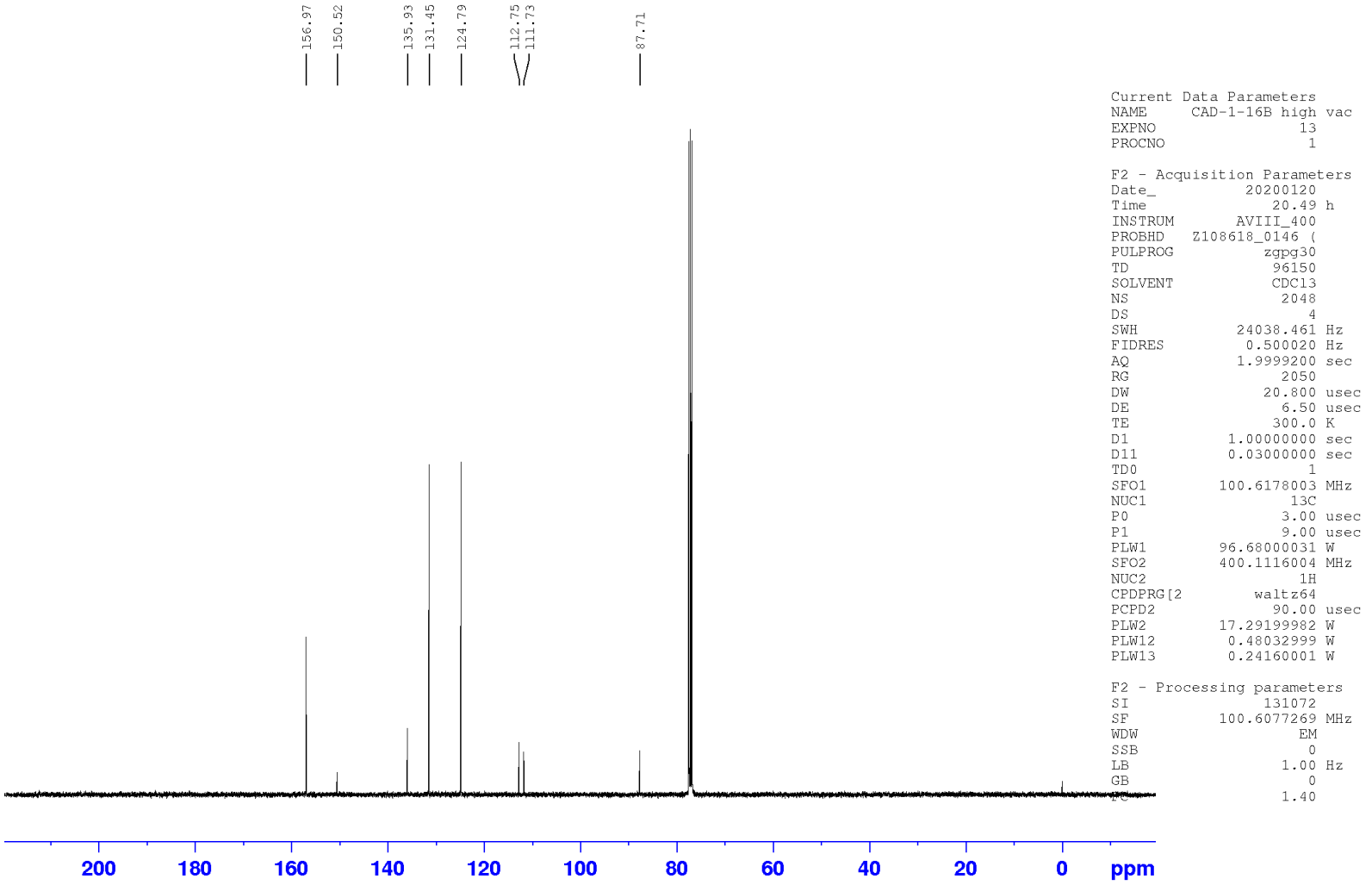


2c

^{13}C NMR

101 MHz

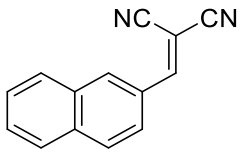
$CDCl_3$




```
Current Data Parameters
NAME      CAD-1-16B high vac
EXPNO                   13
PROCNO                   1

F2 - Acquisition Parameters
Date_             20200120
Time                 20.49 h
INSTRUM         AVIII_400
PROBHD    Z108618_0146 (
PULPROG            zgpg30
TD                  96150
SOLVENT             CDCl3
NS                   2048
DS                      4
SWH             24038.461 Hz
FIDRES           0.500020 Hz
AQ               1.9999200 sec
RG                   2050
DW                 20.800 usec
DE                  6.50 usec
TE                 300.0 K
D1              1.00000000 sec
D11             0.03000000 sec
TD0                     1
SFO1          100.6178003 MHz
NUC1                  13C
P0                  3.00 usec
P1                  9.00 usec
PLW1          96.68000031 W
SFO2          400.1116004 MHz
NUC2                  1H
CPDPRG[2          waltz64
PCPD2               90.00 usec
PLW2          17.29199982 W
PLW12          0.48032999 W
PLW13          0.24160001 W

F2 - Processing parameters
SI                  131072
SF            100.6077269 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
                     1.40
```

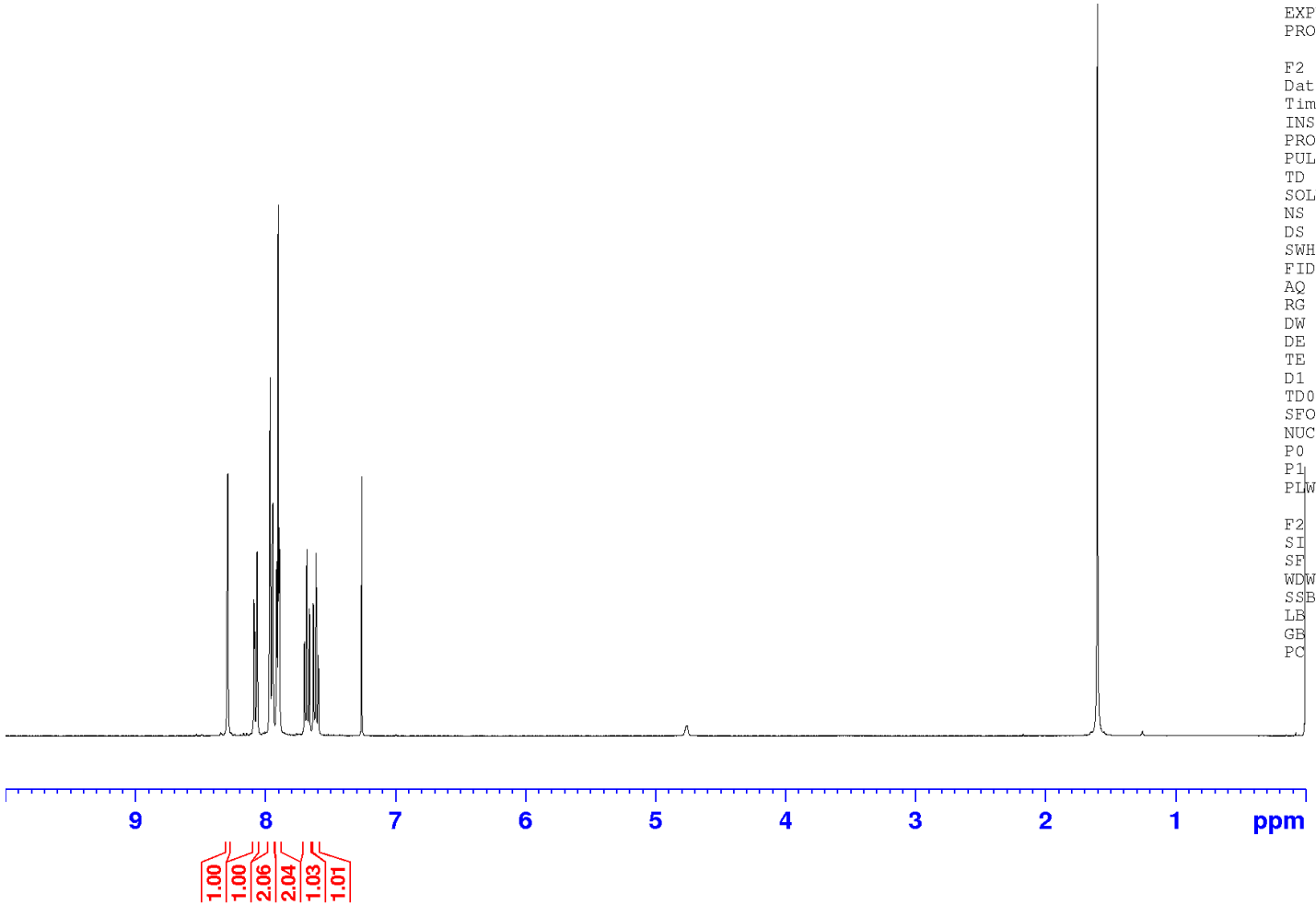


2d

^{1}H NMR

400 MHz

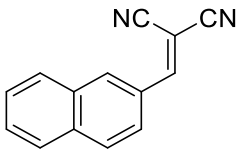
$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-19
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200120
Time              15.38 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ             3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100098 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

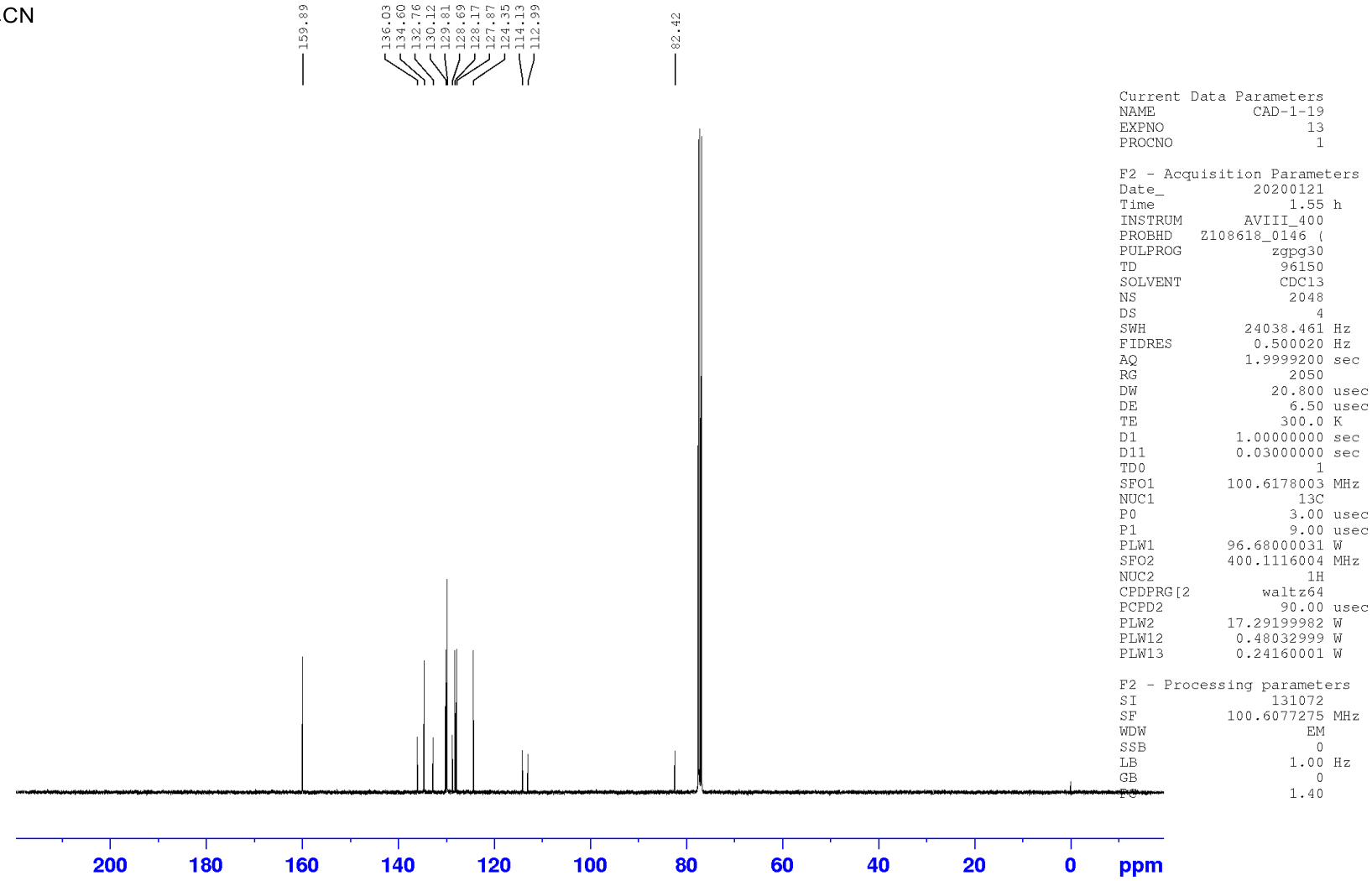


2d

^{13}C NMR

101 MHz

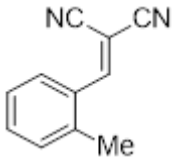
$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-19
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200121
Time                1.55 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 2048
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6178003 MHz
NUC1                13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077275 MHz
WDW                 EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

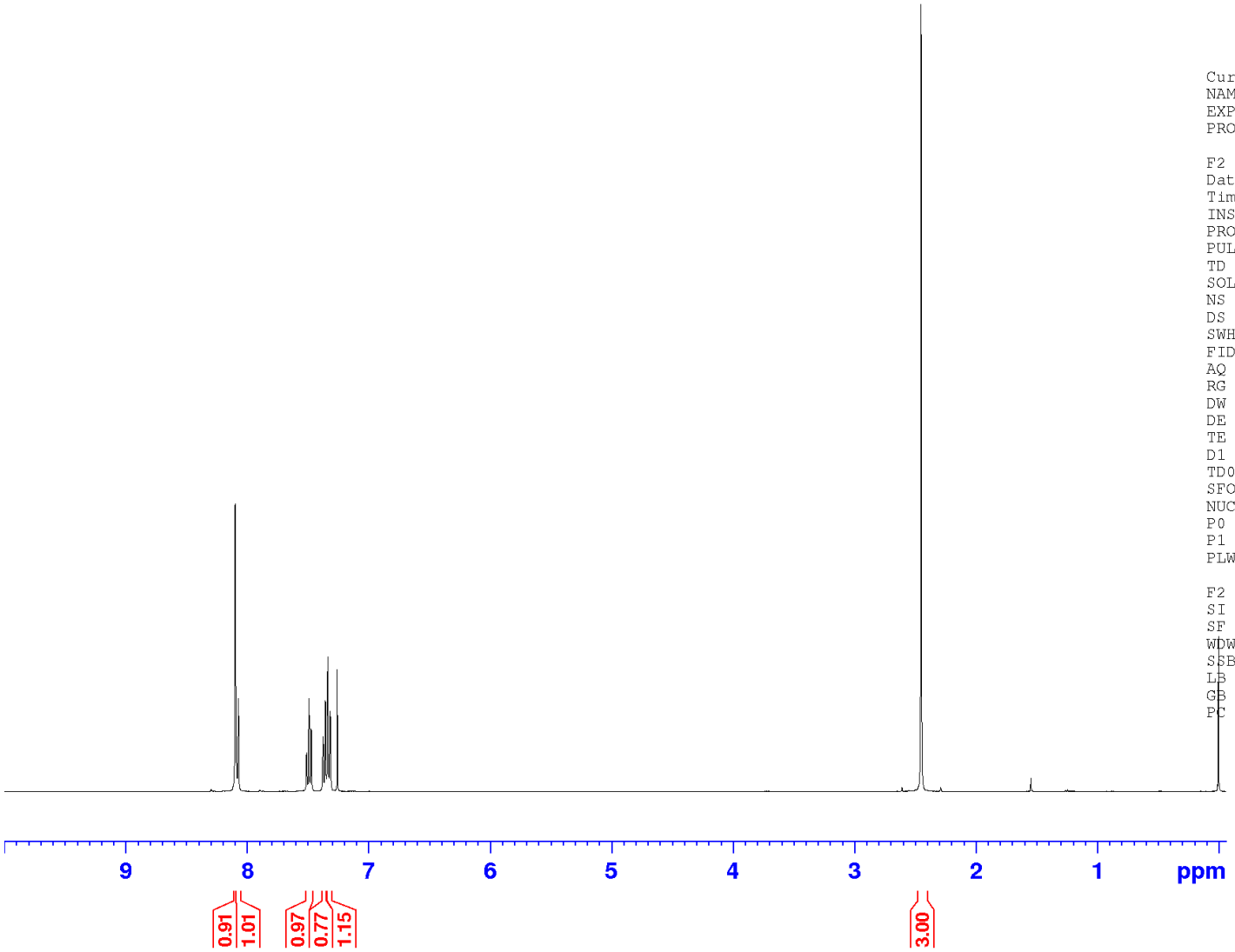


2e

^{1}H NMR

400 MHz

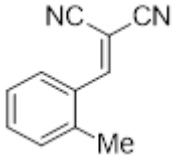
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.159
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210428
Time               13.08 h
INSTRUM         AVIII_400
PROBHD    Z108618_0146 (
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.250967 Hz
AQ               3.9845889 sec
RG                    256
DW                 60.800 usec
DE                 17.42 usec
TE                 300.0 K
D1              1.00000000 sec
TD0                    1
SFO1          400.1124708 MHz
NUC1                  1H
P0                  5.00 usec
P1                 15.00 usec
PLW1          17.29199982 W

F2 - Processing parameters
SI                  32768
SF            400.1100104 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

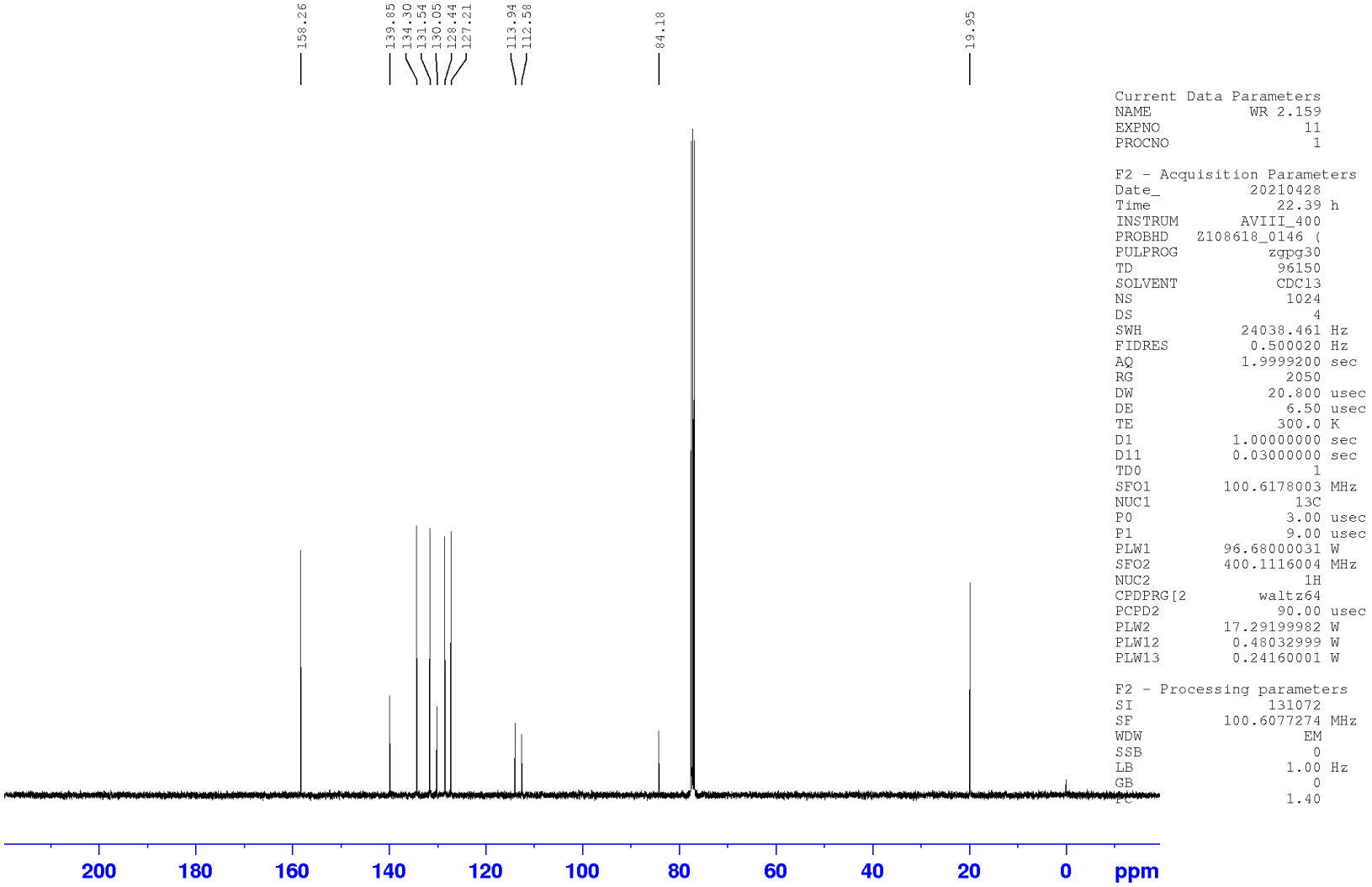


2e

^{13}C NMR

101 MHz

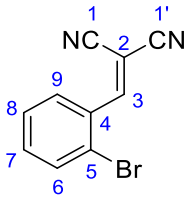
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.159
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210428
Time              22.39 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1        100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1        96.68000031 W
SFO2        400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2        17.29199982 W
PLW12        0.48032999 W
PLW13        0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077274 MHz
WDW                 EM
SSB                    0
LB                1.00 Hz
GB                     0
                  1.40
```

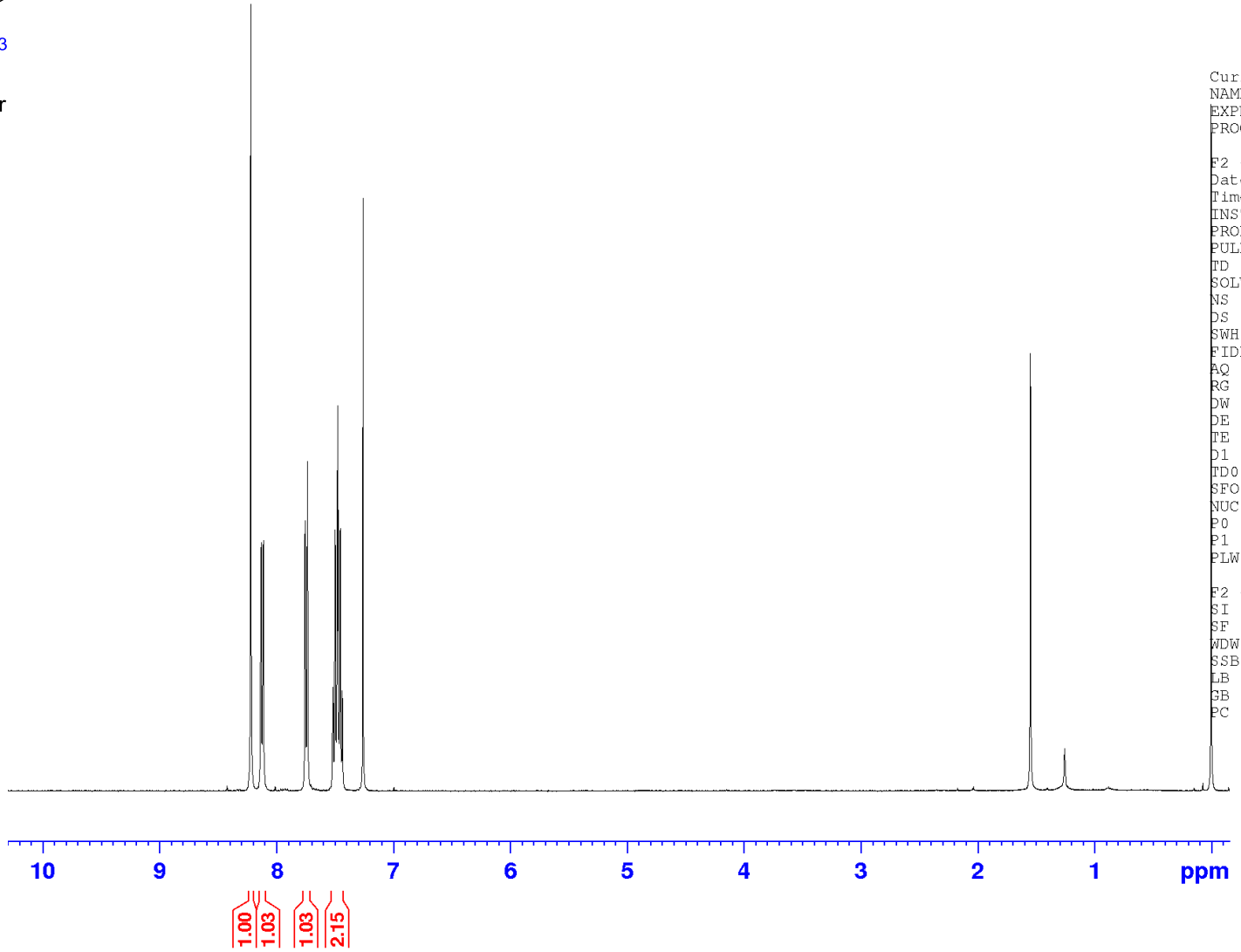


2f

^{1}H NMR

400 MHz

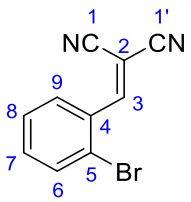
$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-21
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200121
Time              16.53 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100097 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

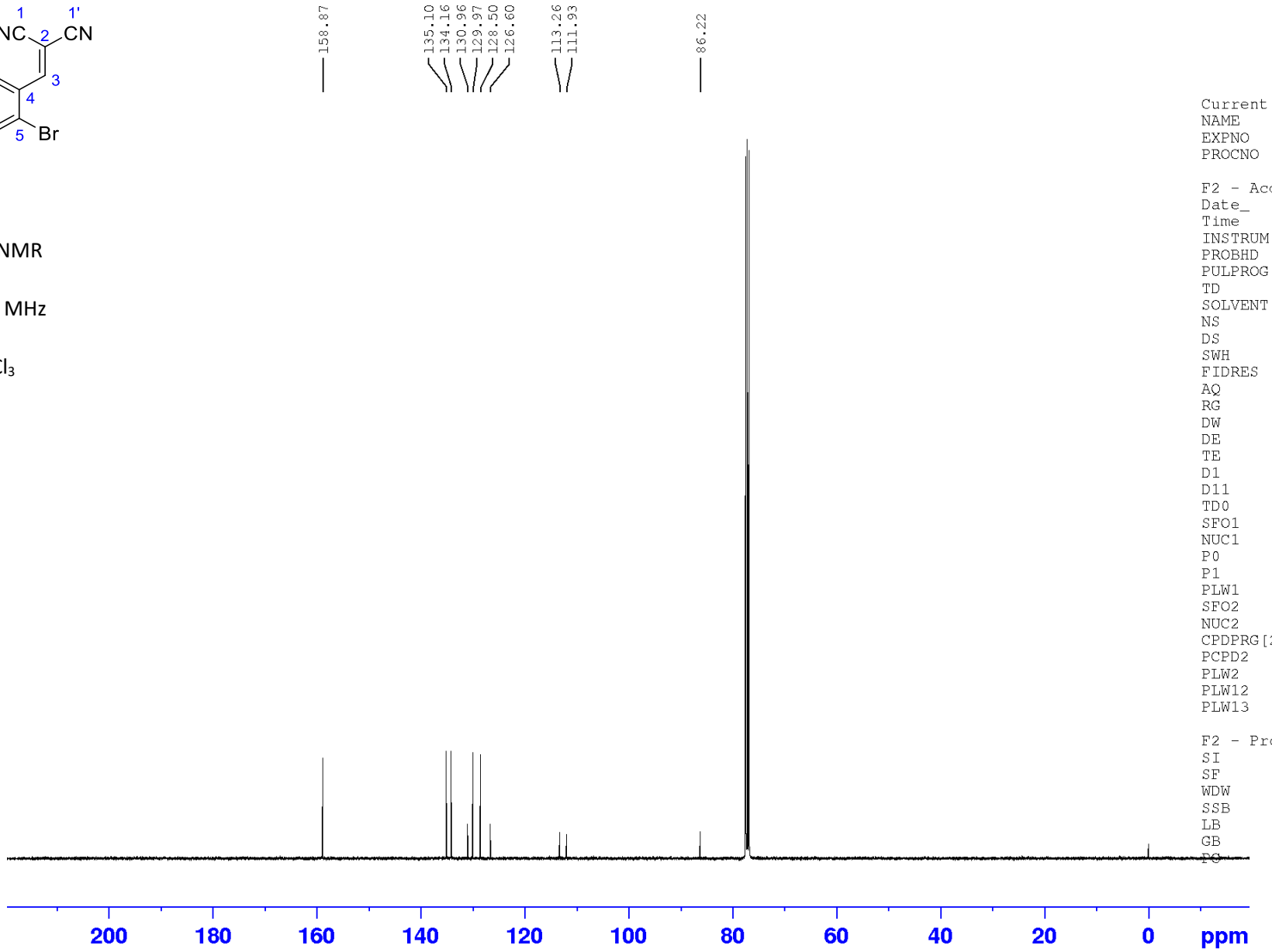


2f

^{13}C NMR

101 MHz

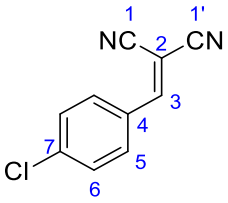
$CDCl_3$




```
Current Data Parameters
NAME                  CAD-1-21
EXPNO                       13
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20200122
Time                      0.24 h
INSTRUM               AVIII_400
PROBHD   Z108618_0146 (
PULPROG                 zgpg30
TD                       96150
SOLVENT                  CDCl3
NS                        4096
DS                           4
SWH                  24038.461 Hz
FIDRES                0.500020 Hz
AQ                    1.9999200 sec
RG                        1620
DW                       20.800 usec
DE                        6.50 usec
TE                       300.0 K
D1                    1.00000000 sec
D11                   0.03000000 sec
TD0                          1
SFO1                100.6178003 MHz
NUC1                       13C
P0                        3.00 usec
P1                        9.00 usec
PLW1                96.68000031 W
SFO2                400.1116004 MHz
NUC2                       1H
CPDPRG[2                waltz64
PCPD2                    90.00 usec
PLW2                17.29199982 W
PLW12                0.48032999 W
PLW13                0.24160001 W

F2 - Processing parameters
SI                       131072
SF                  100.6077258 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```



2g

^{1}H NMR

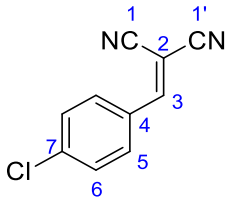
400 MHz

$CDCl_3$


```
Current Data Parameters
NAME           CAD-1-18
EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
Date_          20200120
Time               15.31 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1        17.29199982 W

F2 - Processing parameters
SI                 32768
```

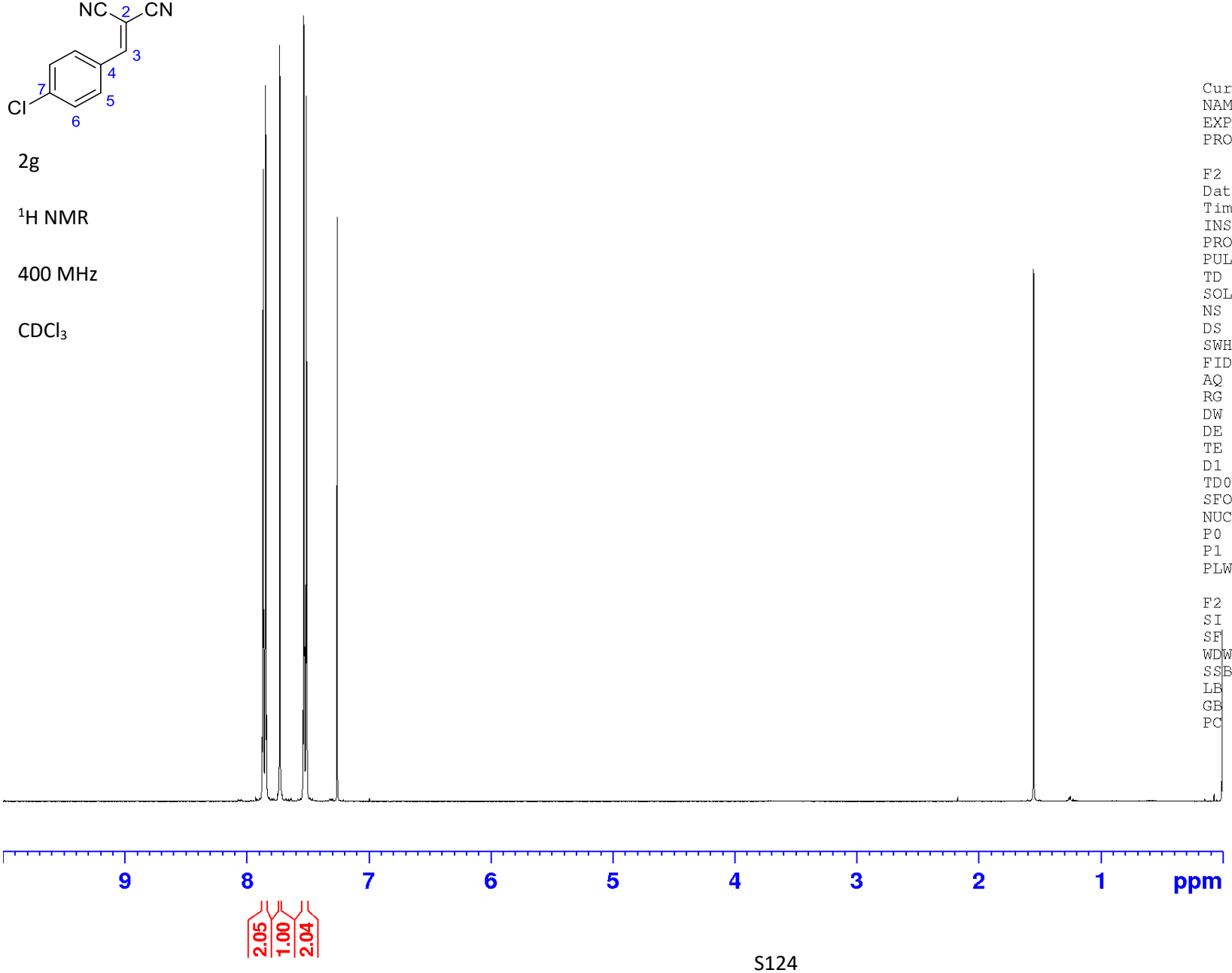


2g

^{1}H NMR

400 MHz

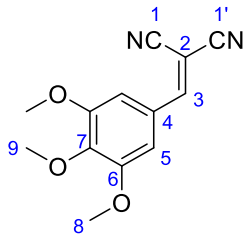
$CDCl_3$




```
Current Data Parameters
NAME                  CAD-1-18
EXPNO                       10
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20200120
Time                     15.31 h
INSTRUM               AVIII_400
PROBHD   Z108618_0146 (
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          32
DS                           2
SWH                   8223.685 Hz
FIDRES                0.250967 Hz
AQ                    3.9845889 sec
RG                         256
DW                      60.800 usec
DE                      17.42 usec
TE                      300.0 K
D1                    1.00000000 sec
TD0                          1
SFO1                400.1124708 MHz
NUC1                        1H
P0                       5.00 usec
P1                      15.00 usec
PLW1                17.29199982 W

F2 - Processing parameters
SI                       32768
SF                  400.1100098 MHz
WDW                         EM
SSB                          0
LB                       0.30 Hz
GB                           0
PC                       1.00
```

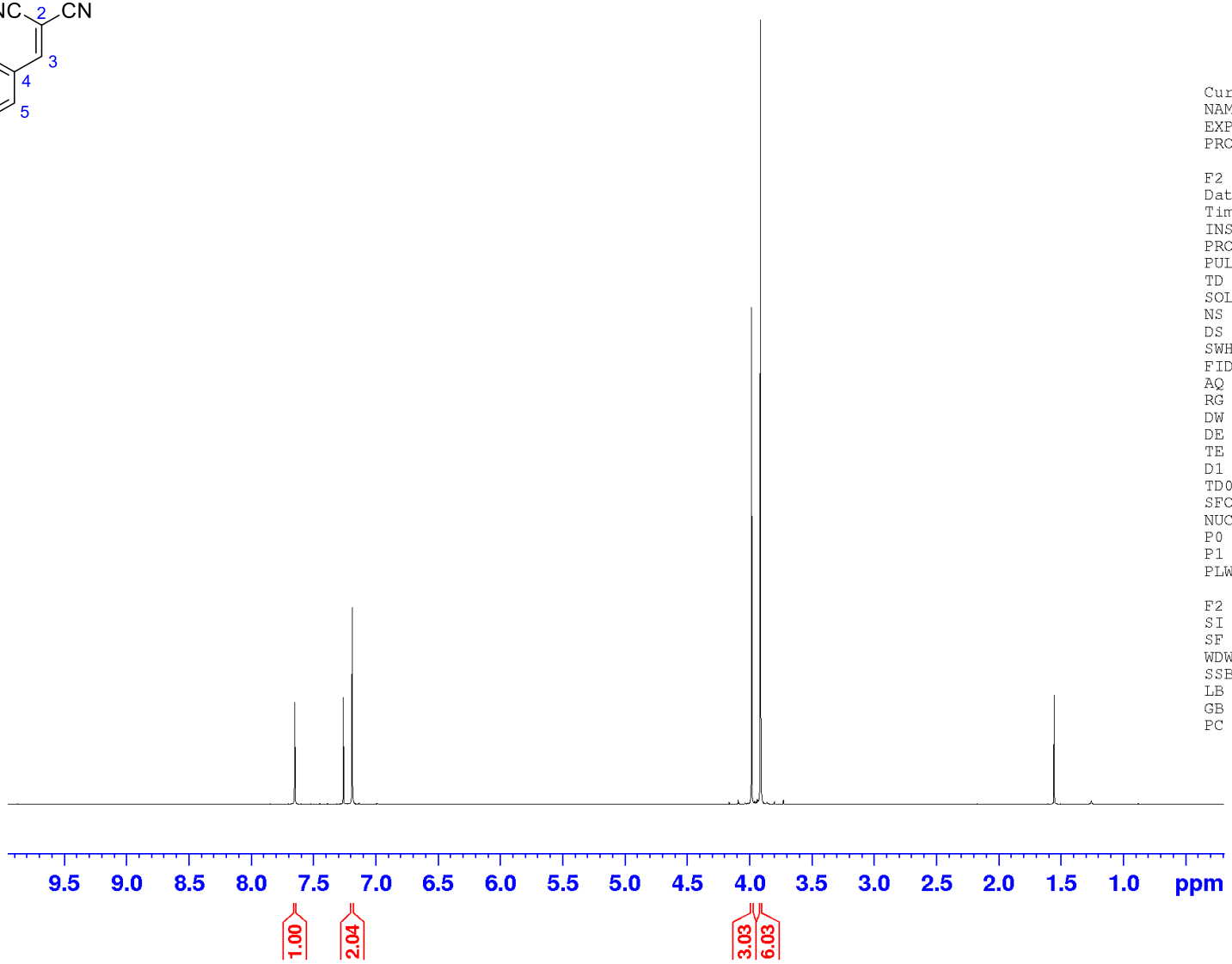


2h

^{1}H NMR

400 MHz

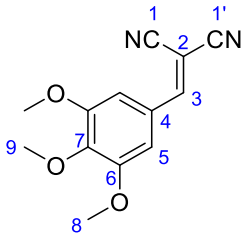
$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-20
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200120
Time              17.23 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ             3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100098 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

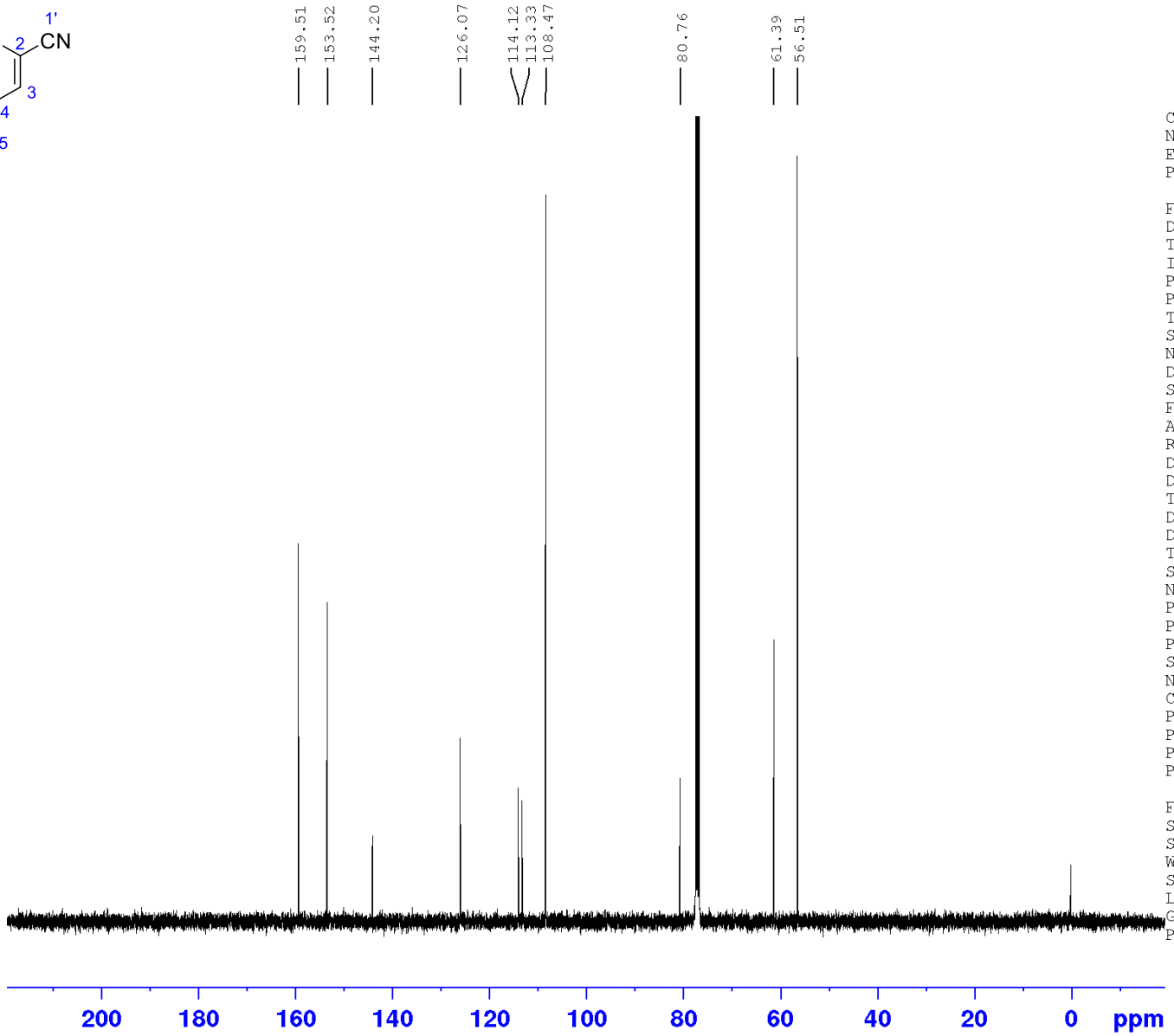


2h

^{13}C NMR

101 MHz

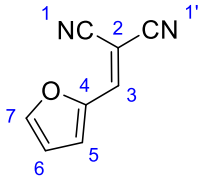
$CDCl_3$




```
Current Data Parameters
NAME            CAD-1-20
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200121
Time               4.28 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 2048
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6178003 MHz
NUC1                 13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                 1H
CPDPRG[2         waltz64
PCPD2            90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077272 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

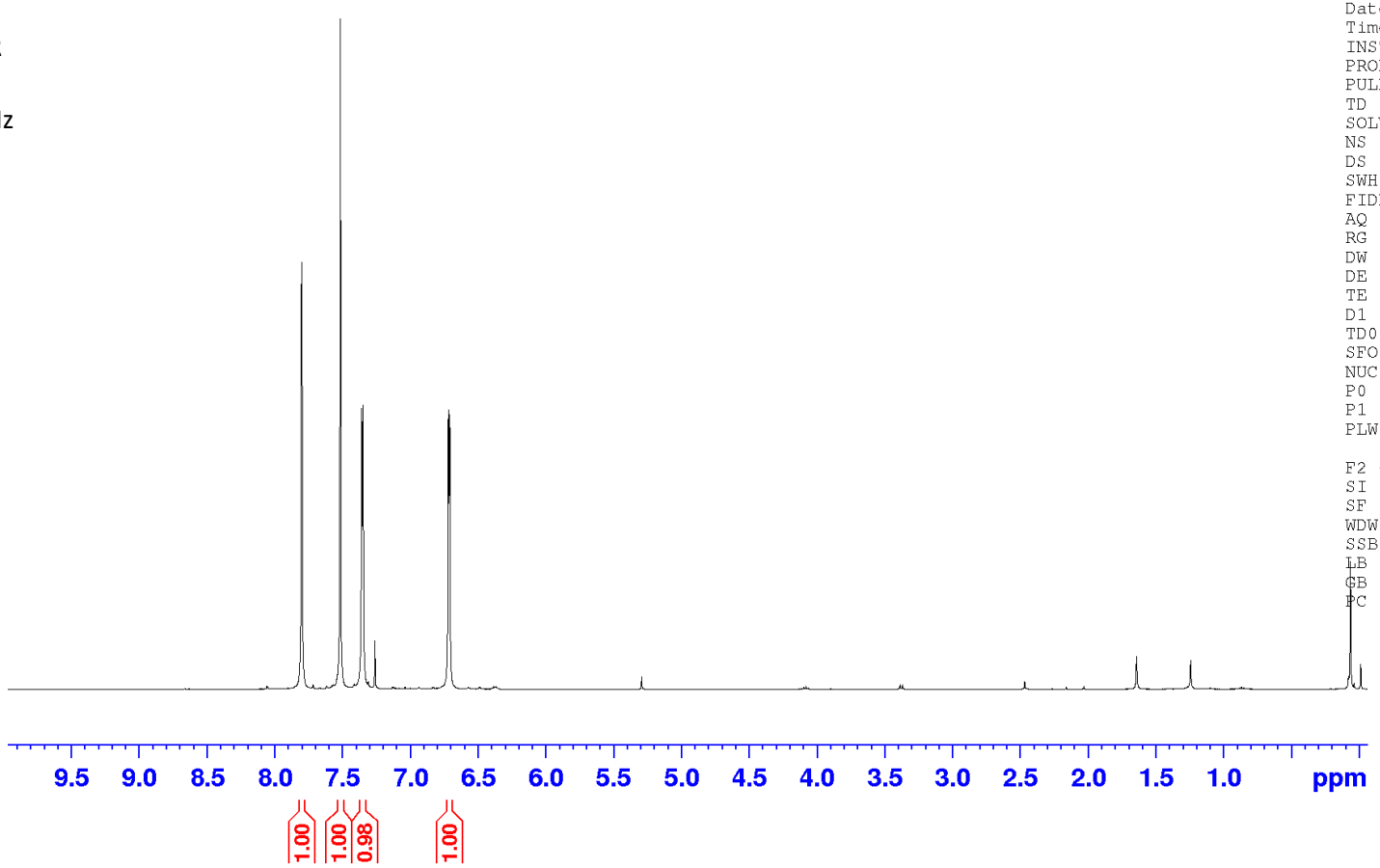


2i

^{1}H NMR

400 MHz

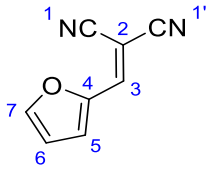
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.153 (Col)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210428
Time              15.00 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDC13
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   128
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100096 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

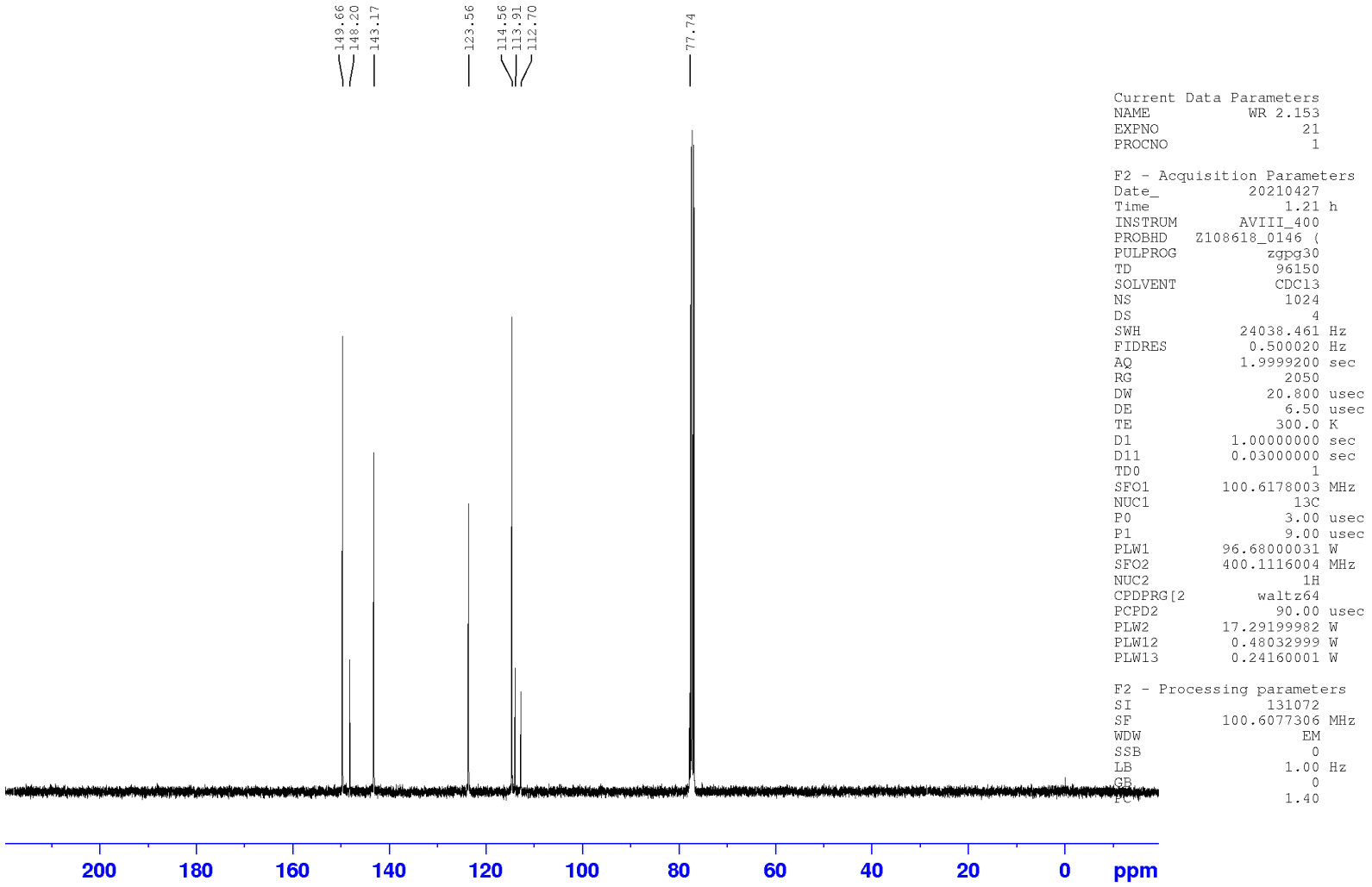


2i

^{13}C NMR

101 MHz

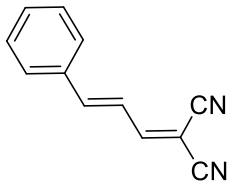
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.153
EXPNO                 21
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210427
Time                1.21 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDC13
NS                  1024
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2              90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077306 MHz
WDW                 EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

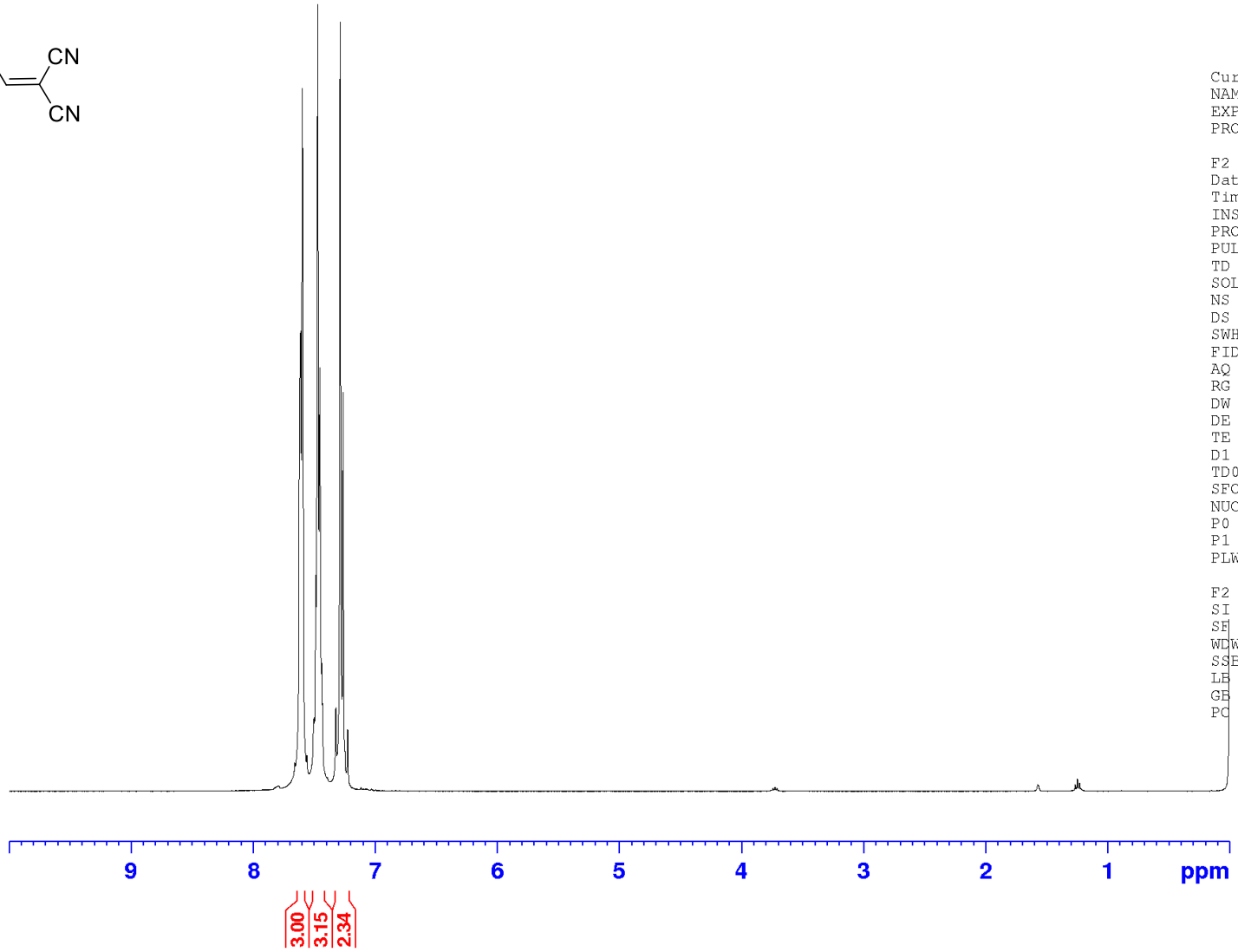


2i

^{1}H NMR

400 MHz

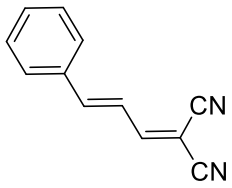
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.154
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210426
Time              12.11 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF          400.1100107 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

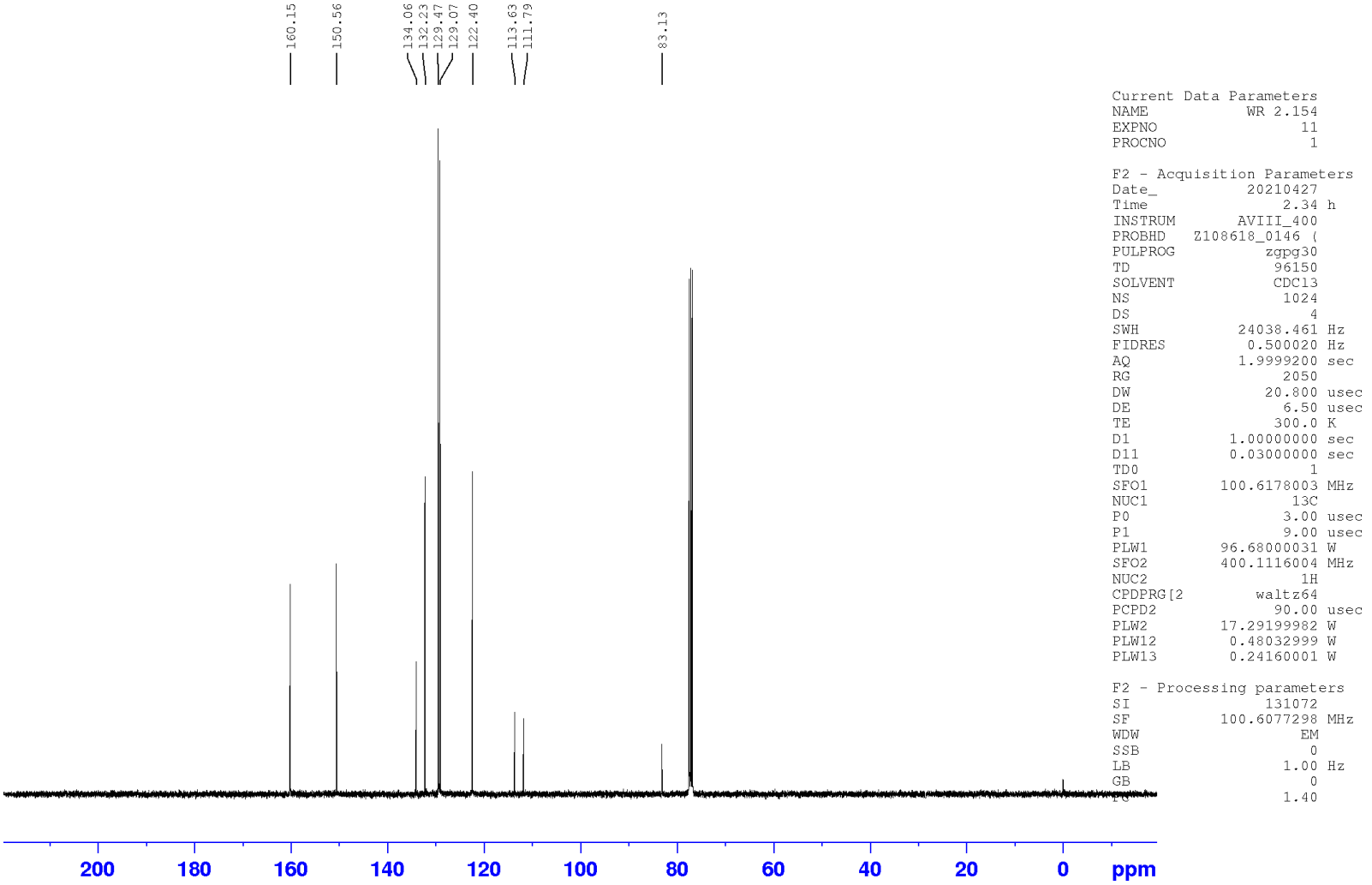


2j

^{13}C NMR

101 MHz

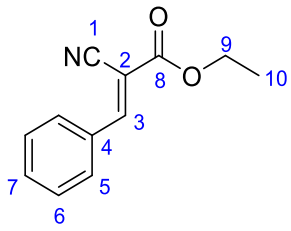
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.154
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210427
Time                2.34 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1        100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2        400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077298 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                  1.40
```

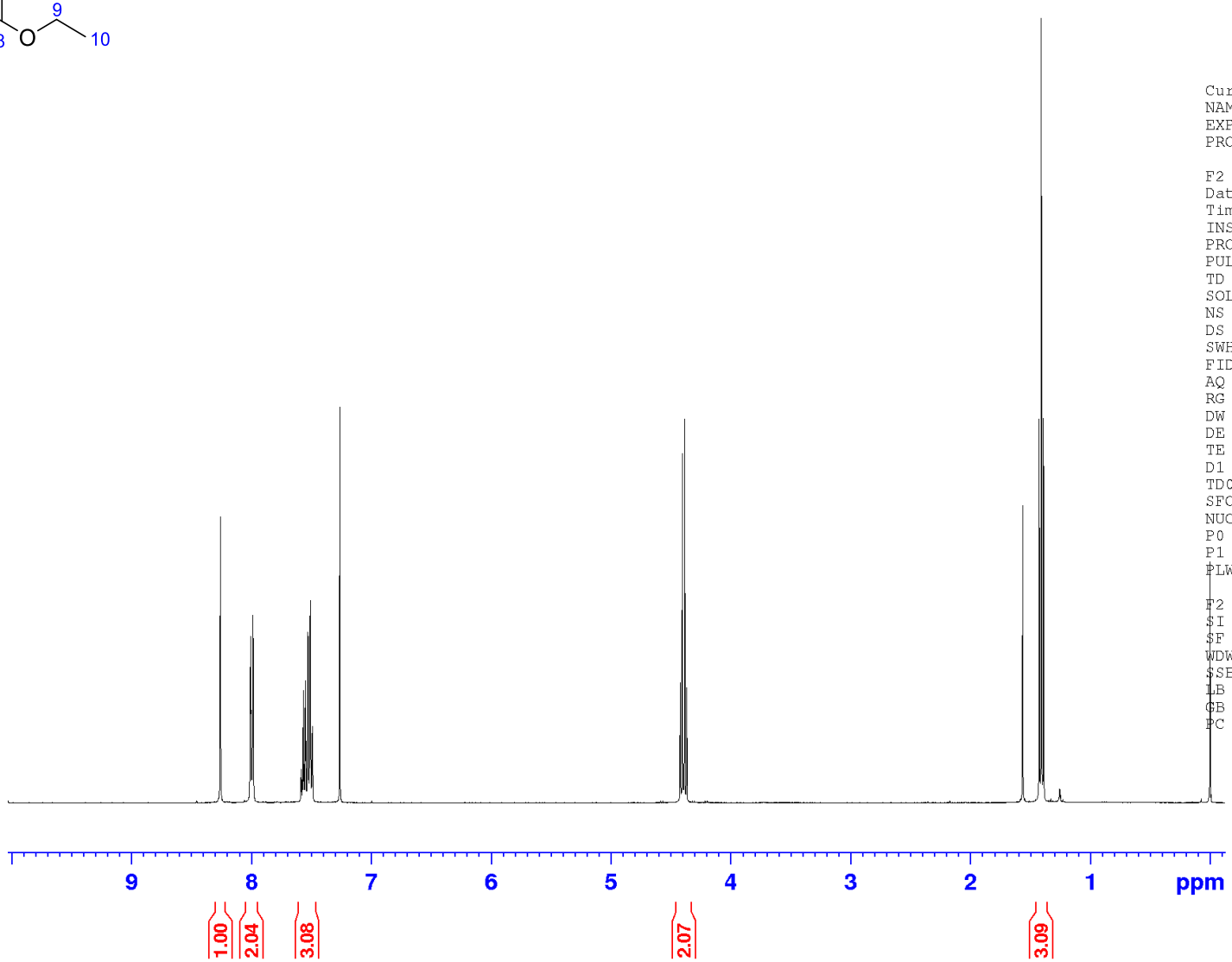


2l

^{1}H NMR

400 MHz

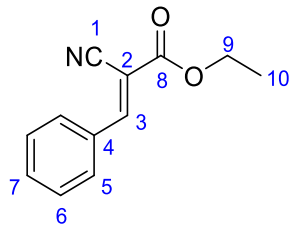
$CDCl_3$




```
Current Data Parameters
NAME      CAD-1-22 spot 1
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200204
Time              17.02 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ             3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF          400.1100090 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

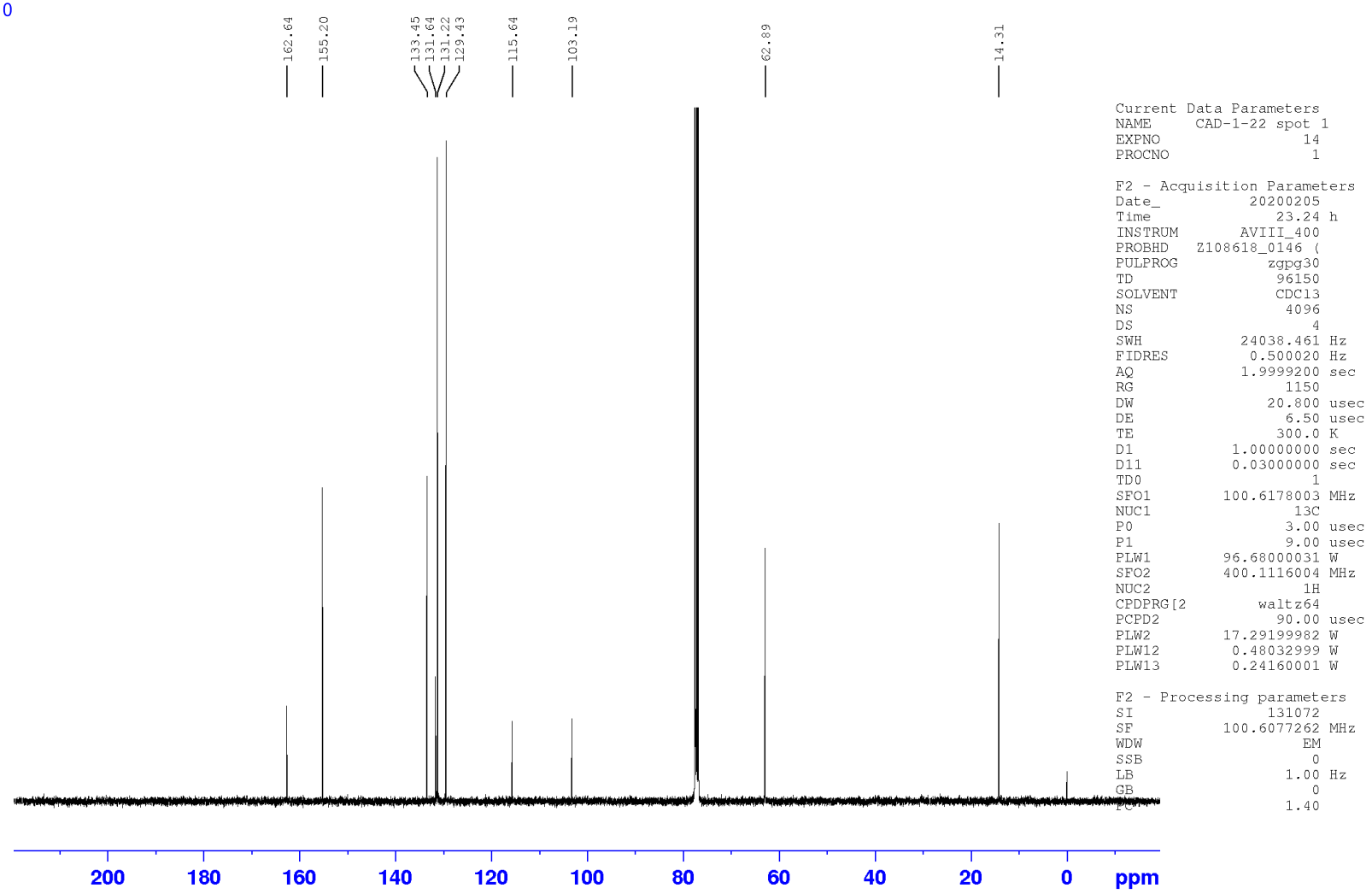


2l

^{13}C NMR

101 MHz

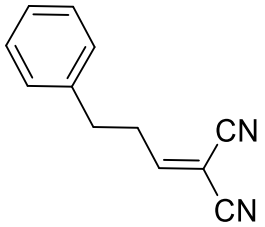
$CDCl_3$




```
Current Data Parameters
NAME      CAD-1-22 spot 1
EXPNO                 14
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200205
Time              23.24 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 4096
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                 1150
DW               20.800 usec
DE                6.50 usec
TE                300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6178003 MHz
NUC1                13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077262 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```

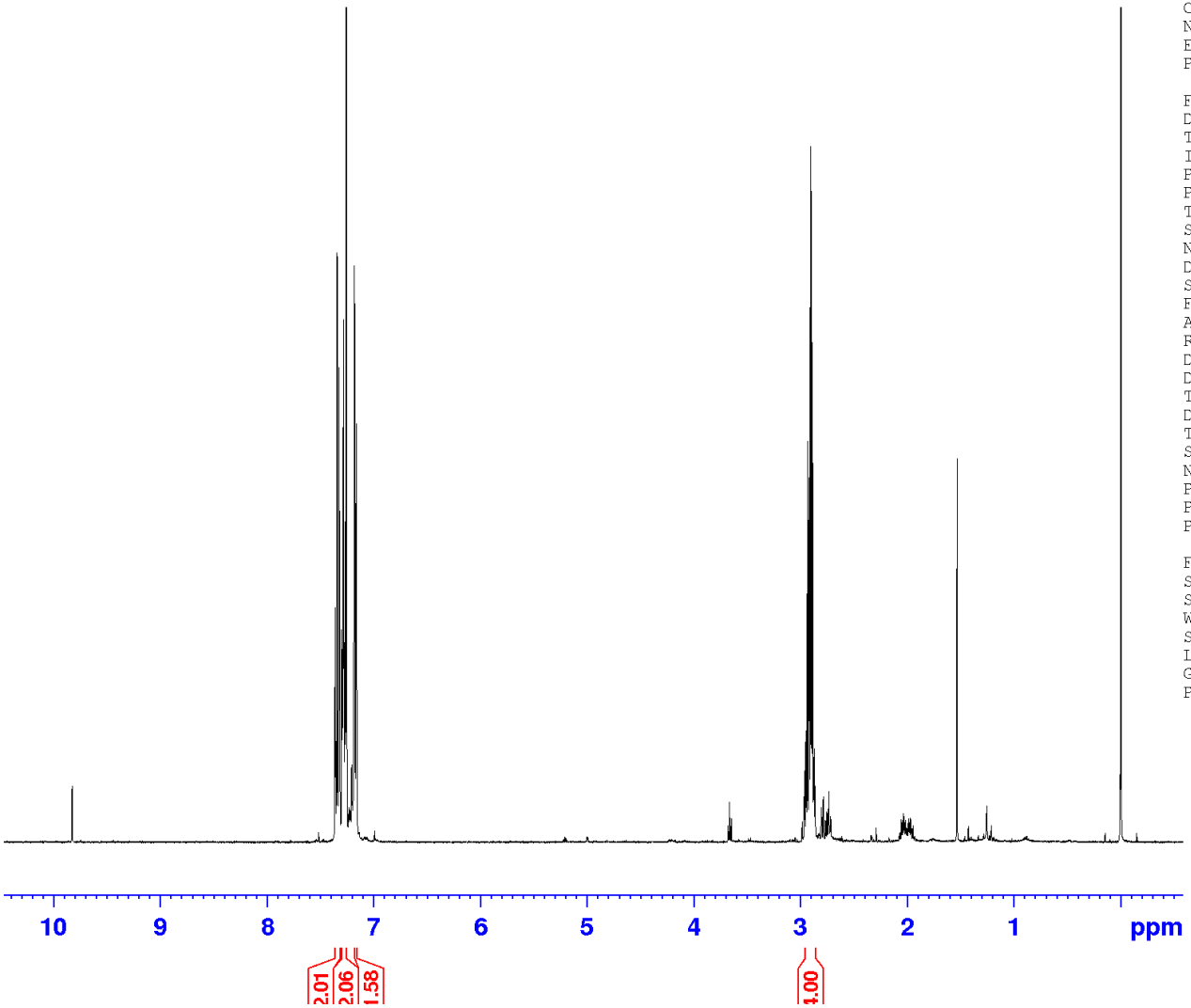


2o

^{1}H NMR

400 MHz

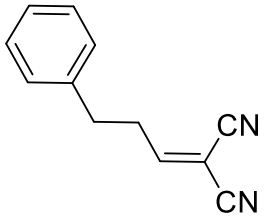
$CDCl_3$




```
Current Data Parameters
NAME         WR 2.225 F1
EXPNO               10
PROCNO               1

F2 - Acquisition Parameters
Date_          20210930
Time             17.24 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           8223.685 Hz
FIDRES        0.250967 Hz
AQ            3.9845889 sec
RG                 256
DW              60.800 usec
DE              17.42 usec
TE              300.0 K
D1           1.00000000 sec
TD0                  1
SFO1        400.1124708 MHz
NUC1                1H
P0               5.00 usec
P1              15.00 usec
PLW1        17.29199982 W

F2 - Processing parameters
SI               32768
SF          400.1100101 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```

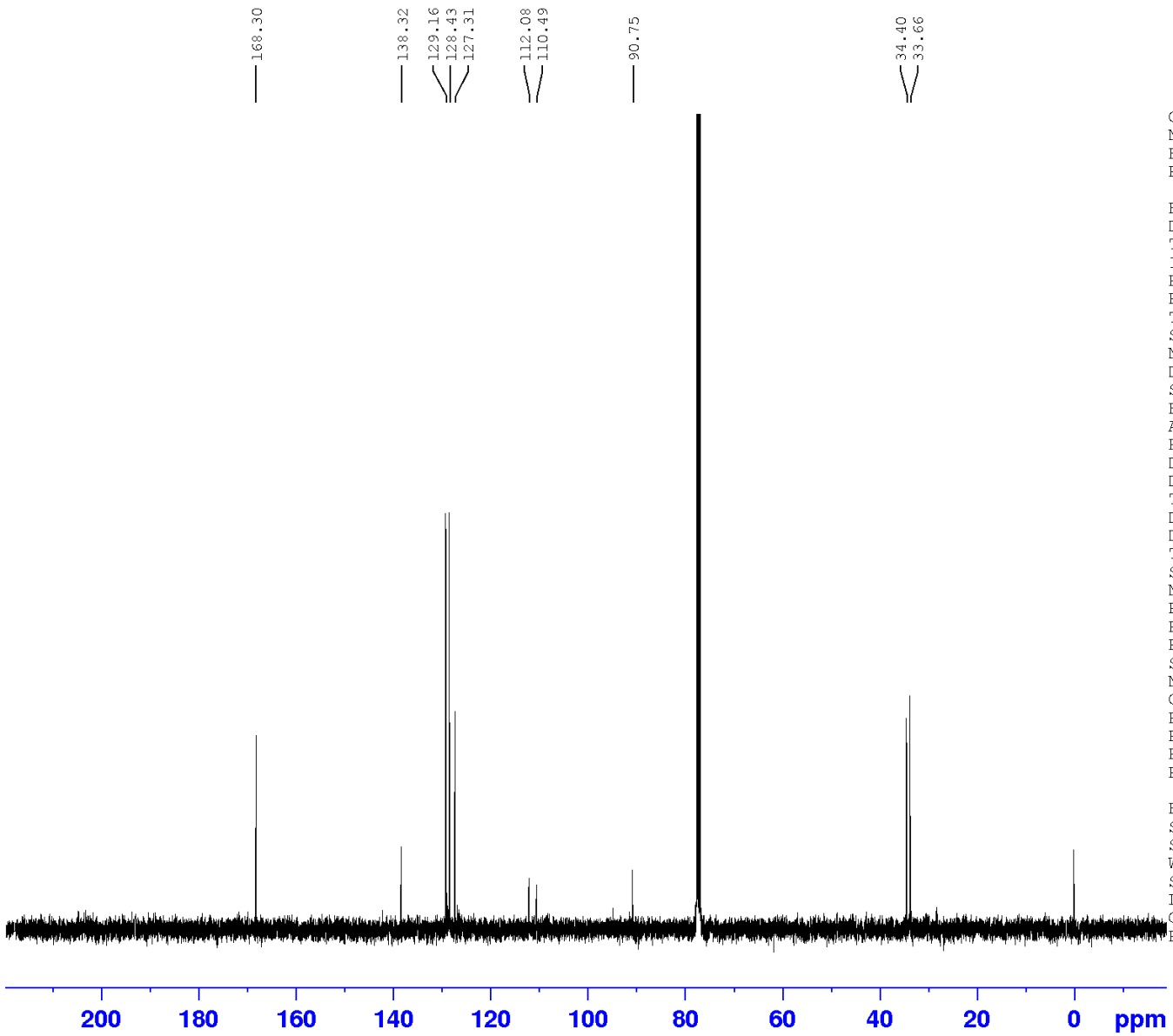


2o

^{13}C NMR

101 MHz

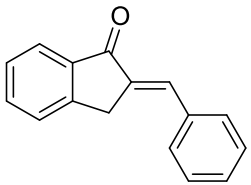
$CDCl_3$




```
Current Data Parameters
NAME         WR 2.225 F1
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20210930
Time              19.50 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                96150
SOLVENT            CDCl3
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE                300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6178003 MHz
NUC1                13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077244 MHz
WDW                 EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

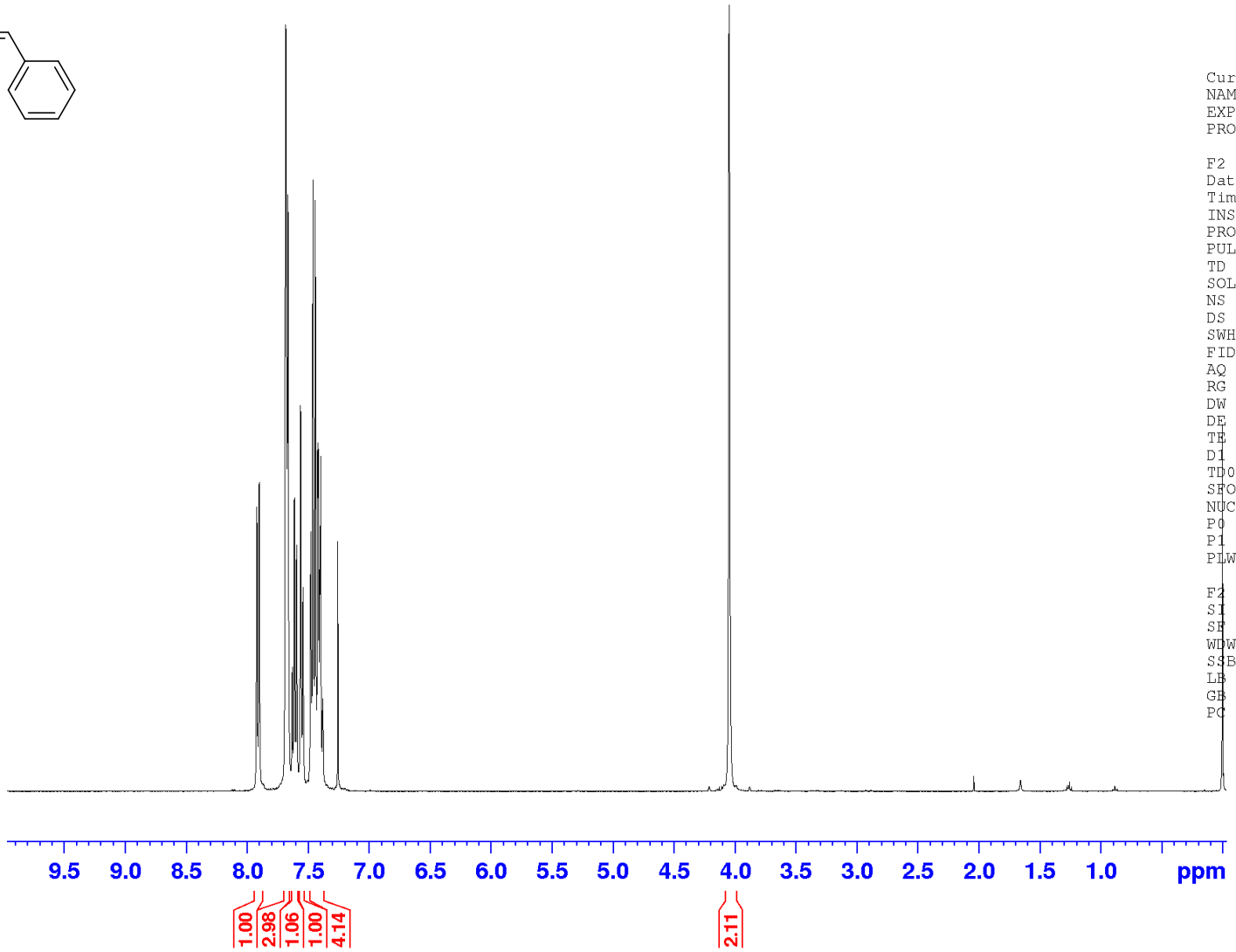


4a

^{1}H NMR

400 MHz

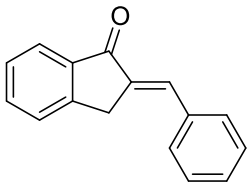
$CDCl_3$




```
Current Data Parameters
NAME       WR 1.128 Rcd
EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
Date_          20210329
Time              16.40 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.250967 Hz
AQ            3.9845889 sec
RG                  144
DW               60.800 usec
DE               17.42 usec
TE               300.0 K
D1            1.00000000 sec
TD0                   1
SFO1        400.1124708 MHz
NUC1                 1H
P0                5.00 usec
P1               15.00 usec
PLW1        17.29199982 W

F2 - Processing parameters
SI                32768
SF          400.1100114 MHz
WDW                  EM
SSB                   0
LB                0.30 Hz
GB                    0
PC                1.00
```

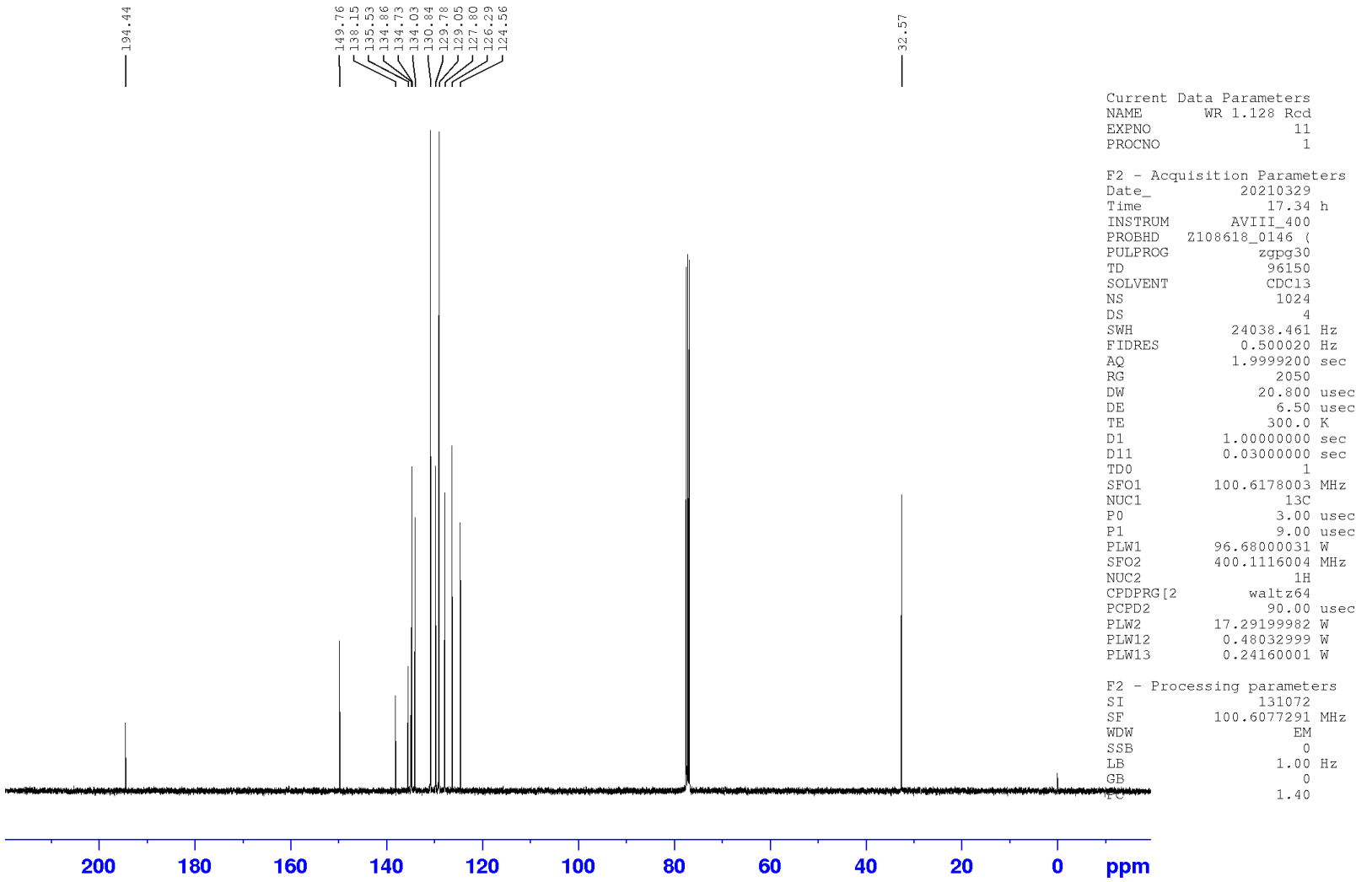


4a

^{13}C NMR

101 MHz

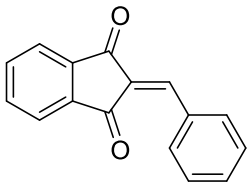
$CDCl_3$




```
Current Data Parameters
NAME        WR 1.128 Rcd
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20210329
Time              17.34 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1        100.6178003 MHz
NUC1                13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2        400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077291 MHz
WDW                 EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

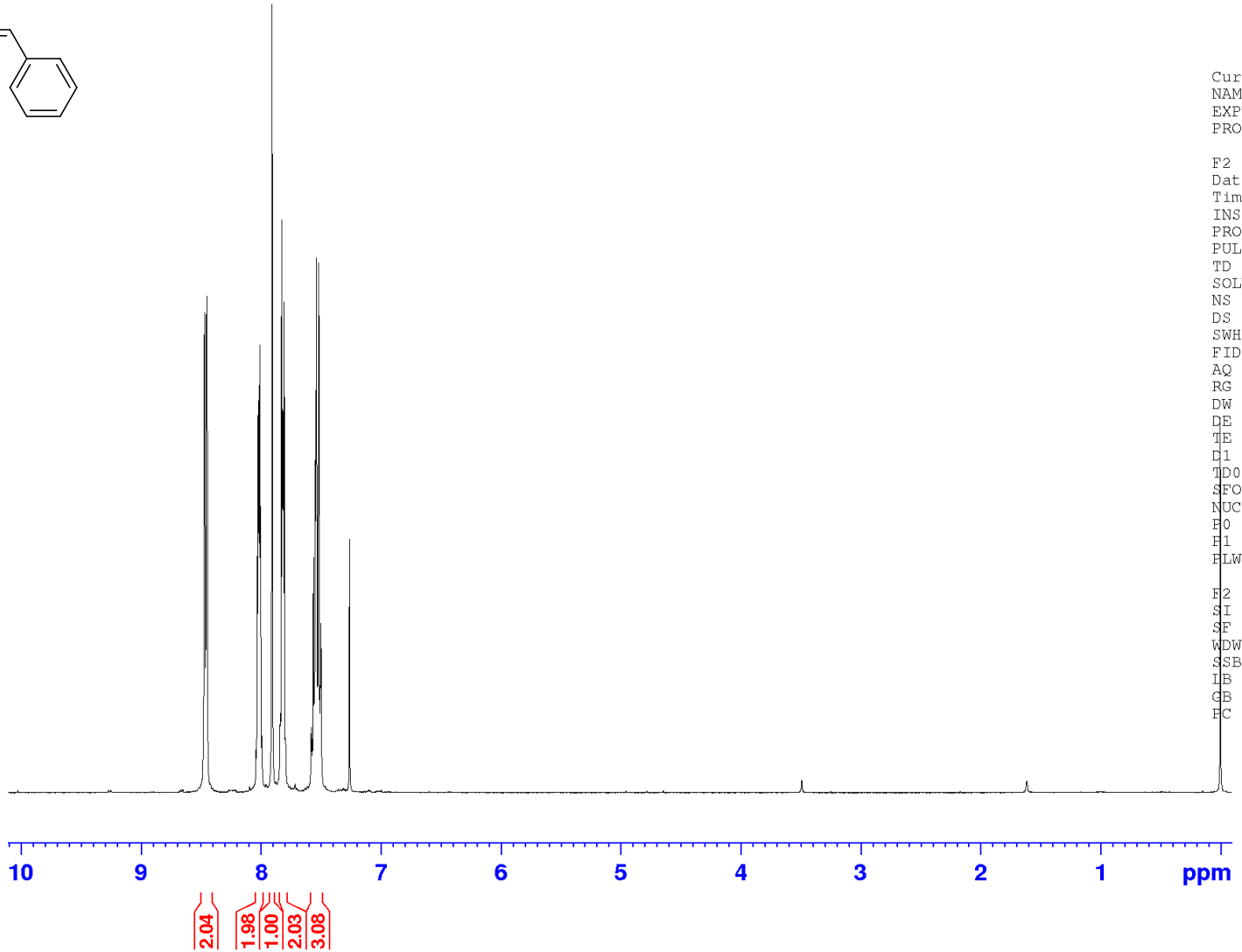


4b

^{1}H NMR

400 MHz

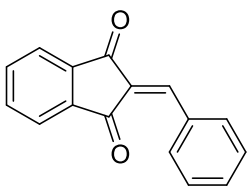
$CDCl_3$




```
Current Data Parameters
NAME      WR 1.132 Re-run
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210318
Time              14.27 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ            3.9845889 sec
RG                   203
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF          400.1100087 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

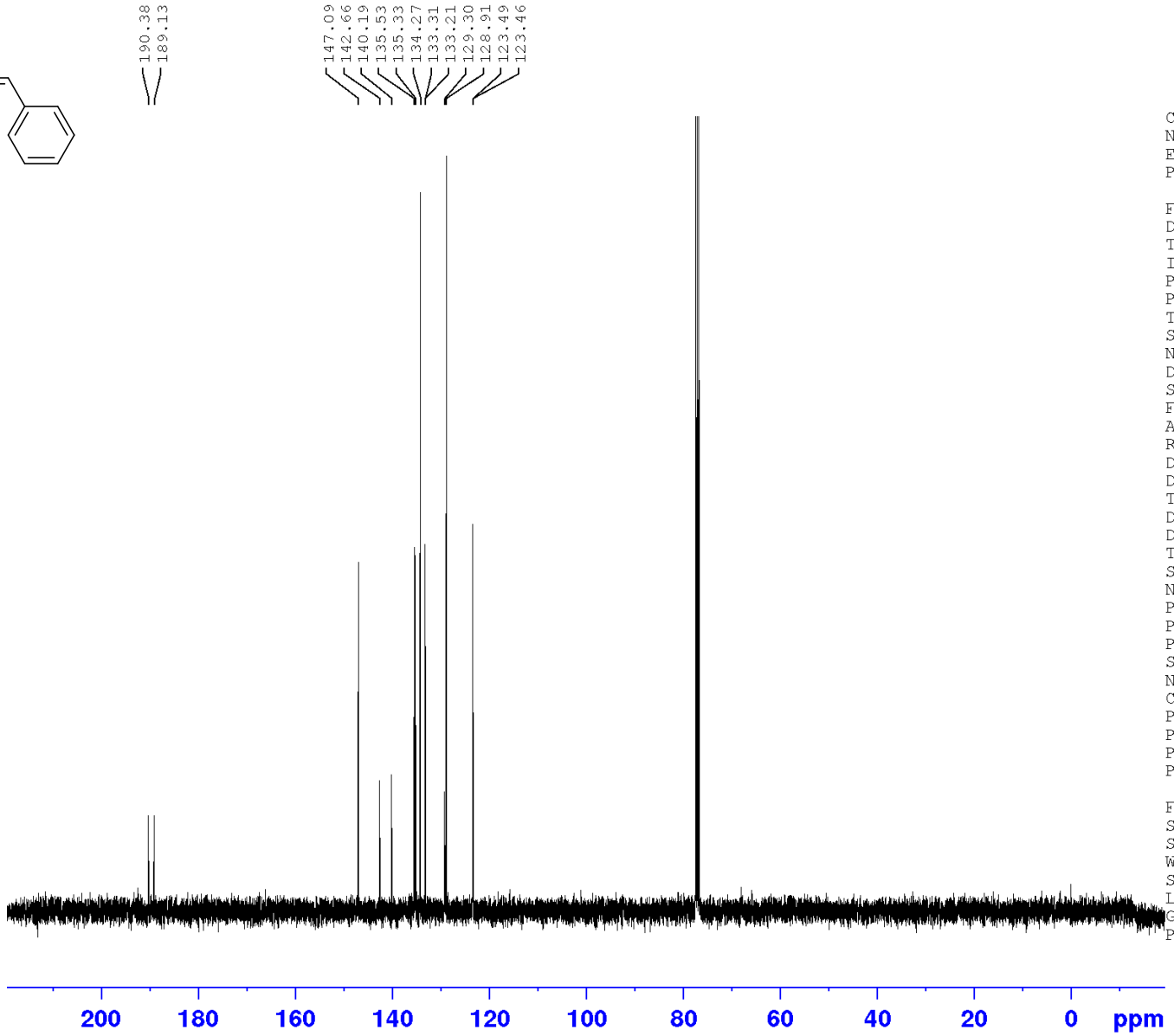


4b

^{13}C NMR

101 MHz

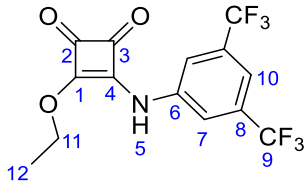
$CDCl_3$




```
Current Data Parameters
NAME      WR 1.132 Re-run
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210318
Time              18.35 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                   128
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ             1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                 13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                 1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                 131072
SF           100.6077293 MHz
WDW                  EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

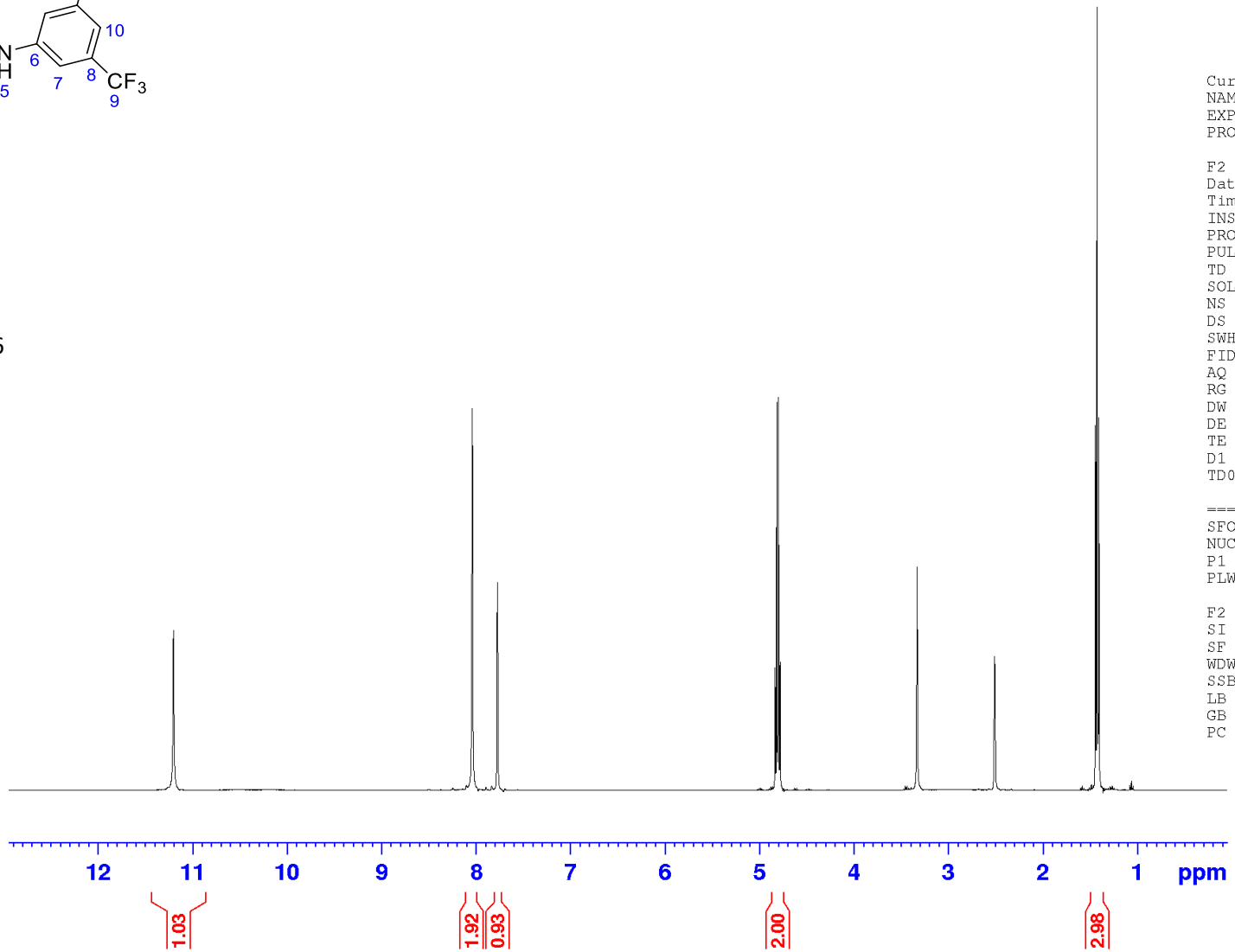


S5

^{1}H NMR

400 MHz

DMSO-D6

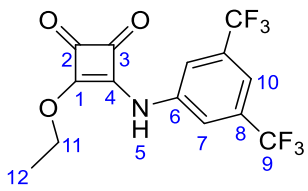



```
Current Data Parameters
NAME            CAD-1-07
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191030
Time               12.12
INSTRUM         AVIII_400
PROBHD    5 mm PABBO BB/
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   80.6
DW                60.800 usec
DE                 6.50 usec
TE                298.5 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          399.9124696 MHz
NUC1                  1H
P1                 15.00 usec
PLW1          17.29199982 W

F2 - Processing parameters
SI                  32768
SF            399.9100000 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

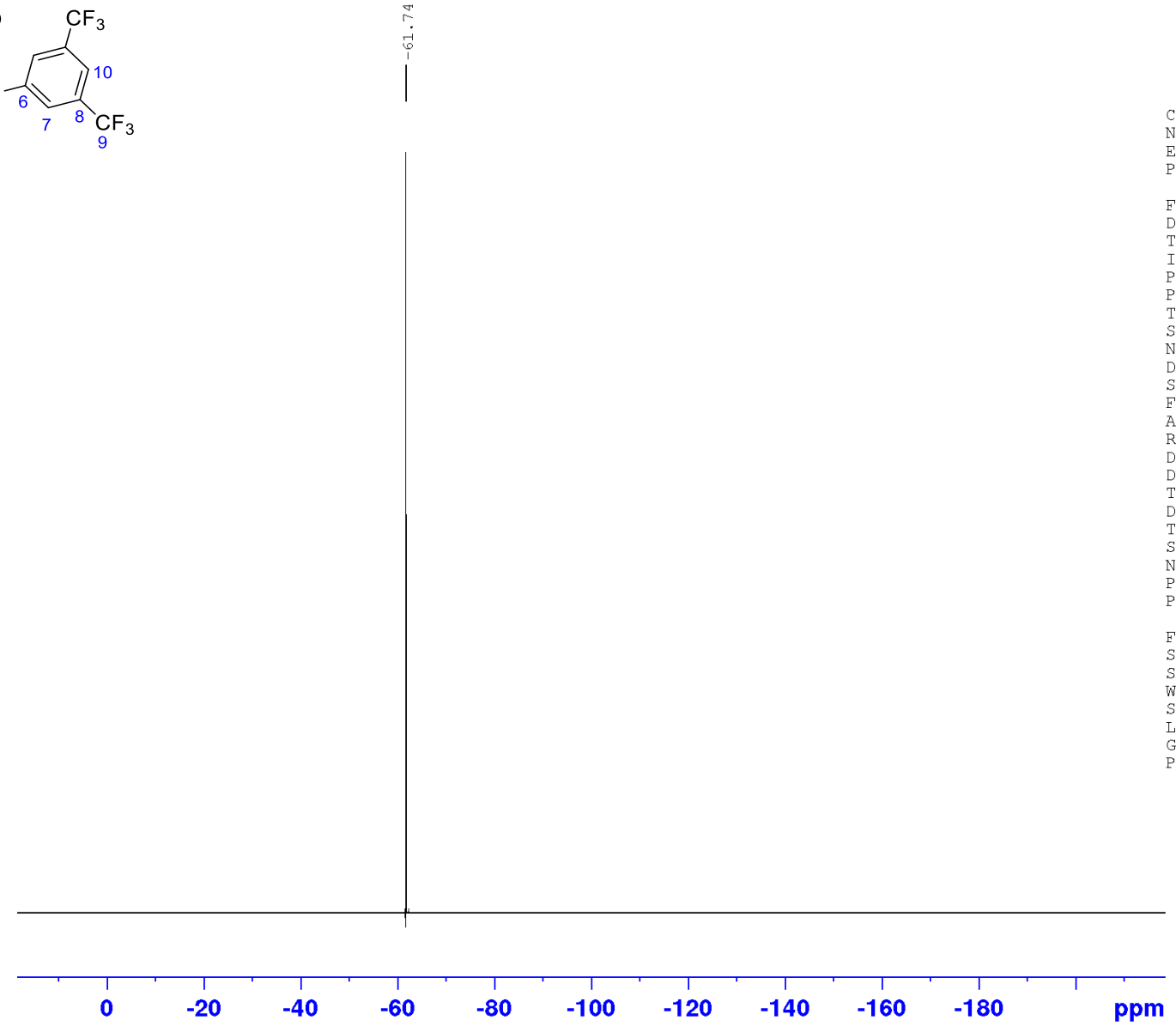


S5

^{19}F NMR

376 MHz

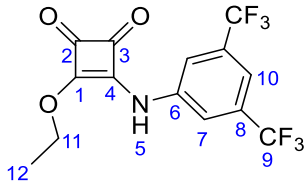
DMSO-D6




```
Current Data Parameters
NAME            CAD-1-07
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191025
Time              12.49 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT             DMSO
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   512
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

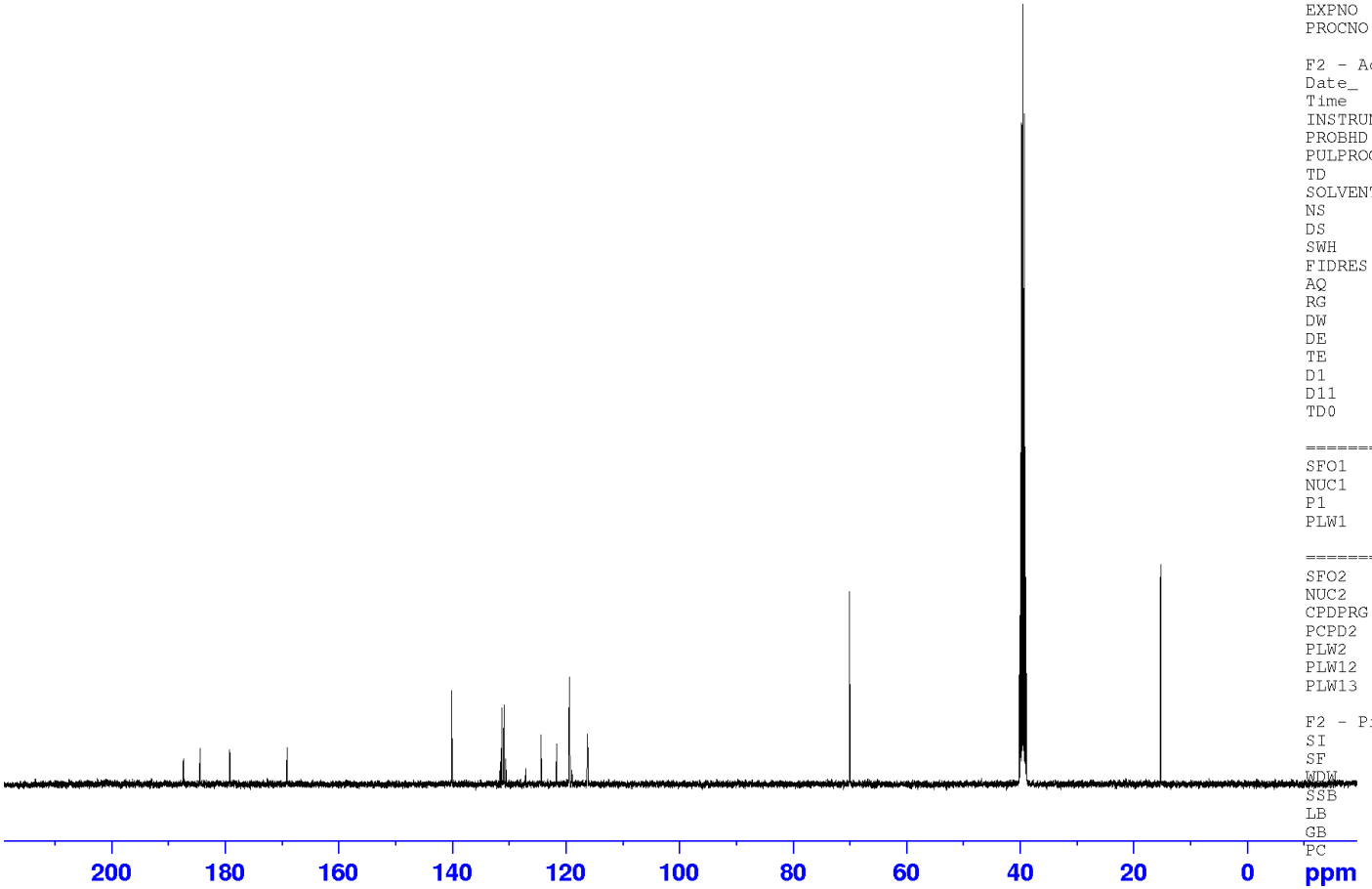


S5

^{13}C NMR

101 MHz

DMSO-D6



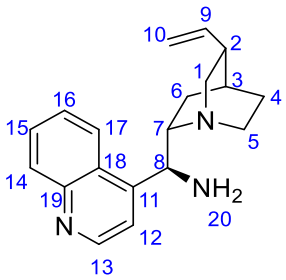

```
Current Data Parameters
NAME            CAD-1-07
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191030
Time               21.54
INSTRUM        AVIII_400
PROBHD   5 mm PABBO BB/
PULPROG           zgpg30
TD                 96150
SOLVENT             DMSO
NS                  1024
DS                     4
SWH           24038.461 Hz
FIDRES         0.250010 Hz
AQ             1.9999200 sec
RG                   181
DW                20.800 usec
DE                 6.50 usec
TE                304.9 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         100.5675047 MHz
NUC1                 13C
P1                  9.00 usec
PLW1         96.68000031 W

======== CHANNEL f2 ========
SFO2         399.9115996 MHz
NUC2                 1H
CPDPRG[2          waltz64
PCPD2              90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.38907000 W

F2 - Processing parameters
SI                 131072
SF           100.5575039 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

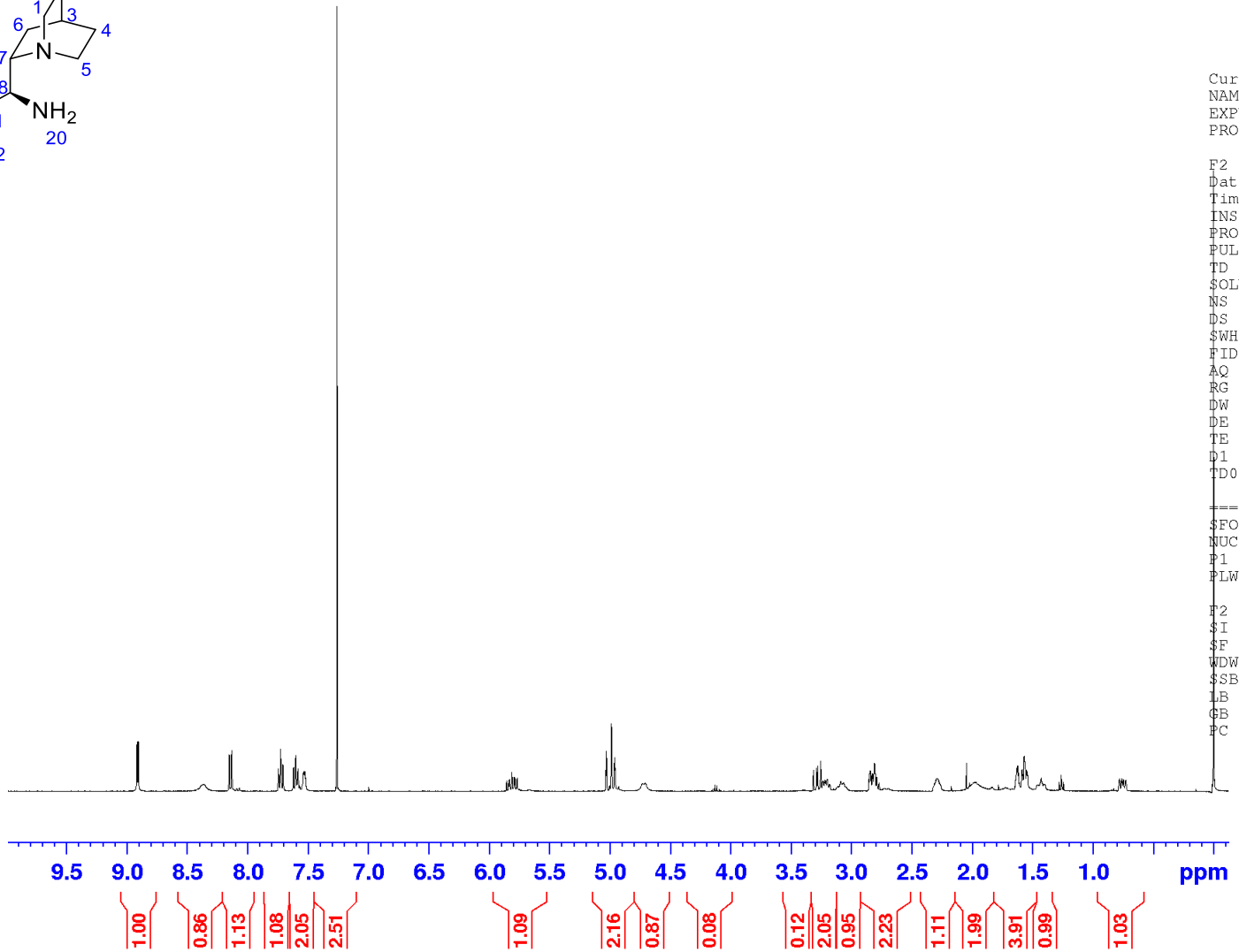


S6

^{1}H NMR

600 MHz

$CDCl_3$

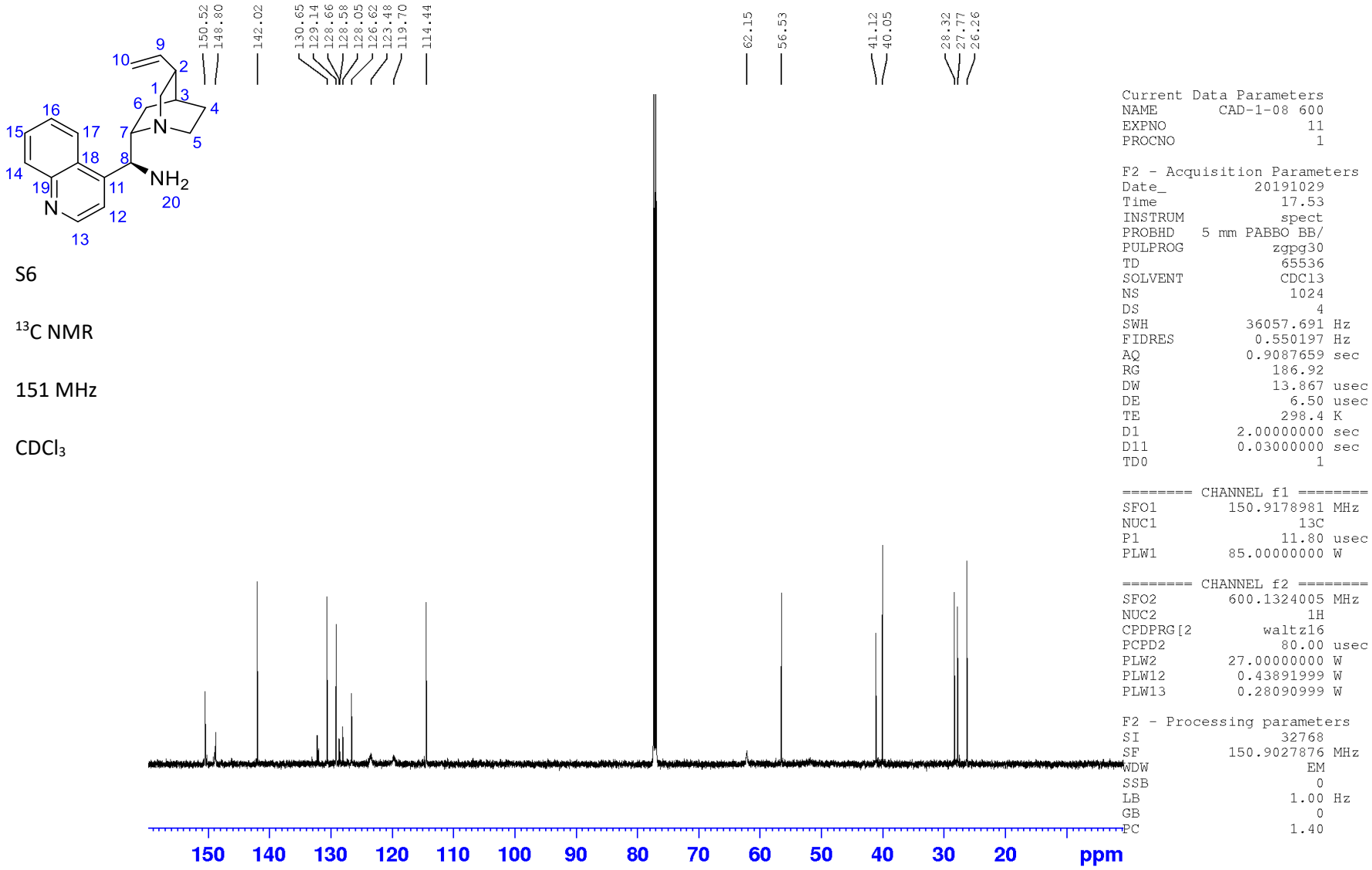



```
Current Data Parameters
NAME          REM1-26-4
EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
Date_          20180213
Time              15.19
INSTRUM       AVIII_400
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES         0.125483 Hz
AQ             3.9845889 sec
RG                  287
DW                60.800 usec
DE                16.82 usec
TE                300.0 K
D1           1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        400.1124708 MHz
NUC1                1H
P1                15.00 usec
PLW1        17.29199982 W

F2 - Processing parameters
SI                32768
SF          400.1100095 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



S6

^{13}C NMR

151 MHz

$CDCl_3$

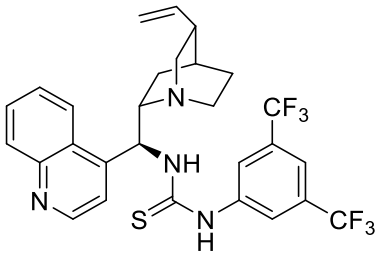
```
Current Data Parameters
NAME       CAD-1-08 600
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20191029
Time              17.53
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36057.691 Hz
FIDRES         0.550197 Hz
AQ            0.9087659 sec
RG               186.92
DW               13.867 usec
DE                6.50 usec
TE               298.4 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        150.9178981 MHz
NUC1                13C
P1                11.80 usec
PLW1        85.00000000 W

======== CHANNEL f2 ========
SFO2        600.1324005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2        27.00000000 W
PLW12        0.43891999 W
PLW13        0.28090999 W

F2 - Processing parameters
SI                32768
SF          150.9027876 MHz
WDW                EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

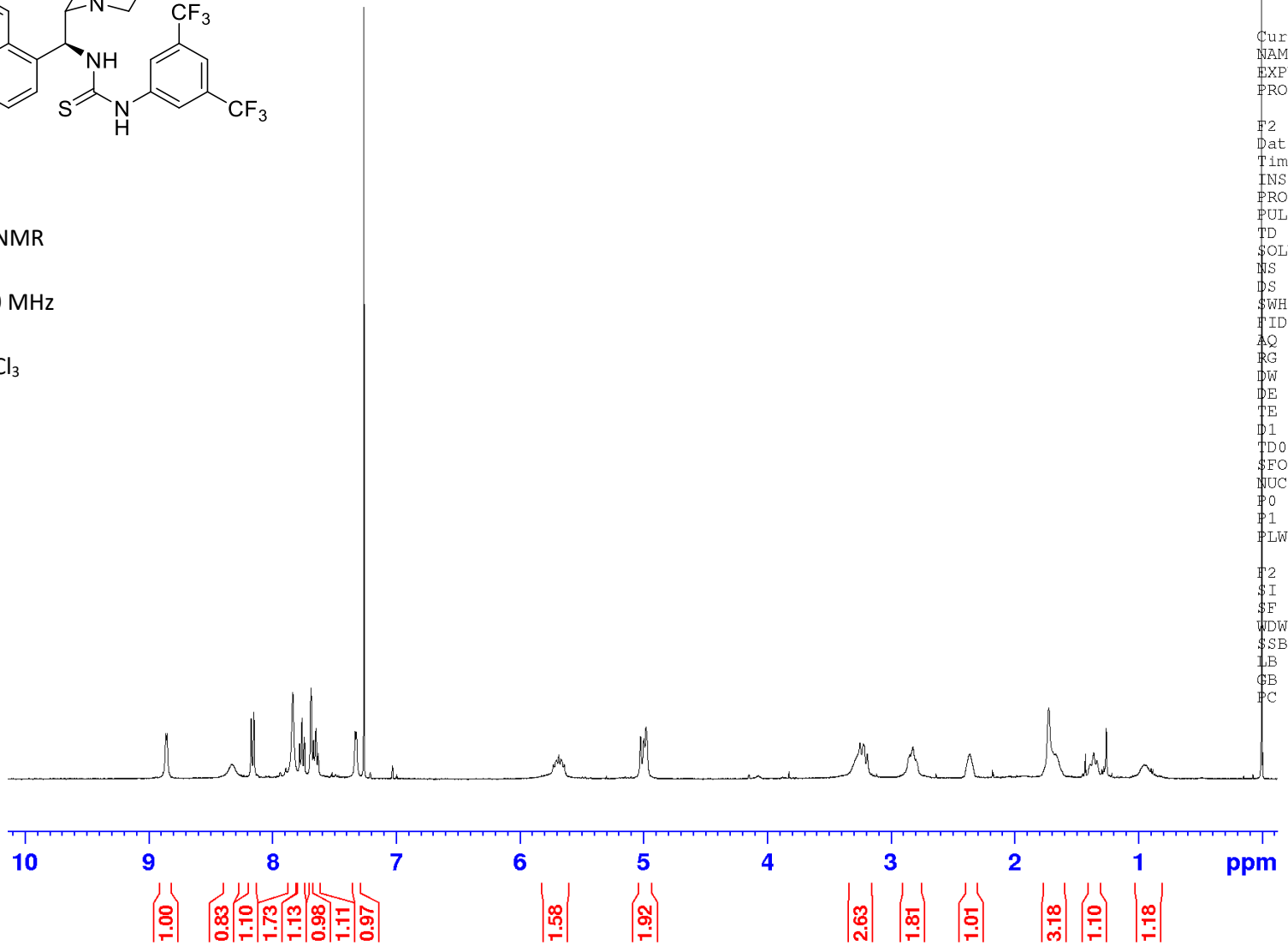


C1

^{1}H NMR

400 MHz

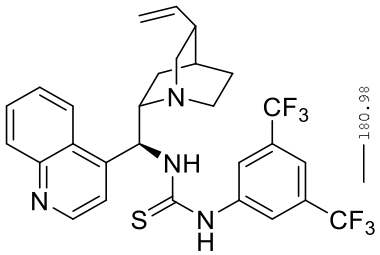
$CDCl_3$




```
Current Data Parameters
NAME            REM2-8-3
EXPNO                 40
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210804
Time              17.18 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1          400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1          17.29199982 W

F2 - Processing parameters
SI                 32768
SF            400.1100091 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

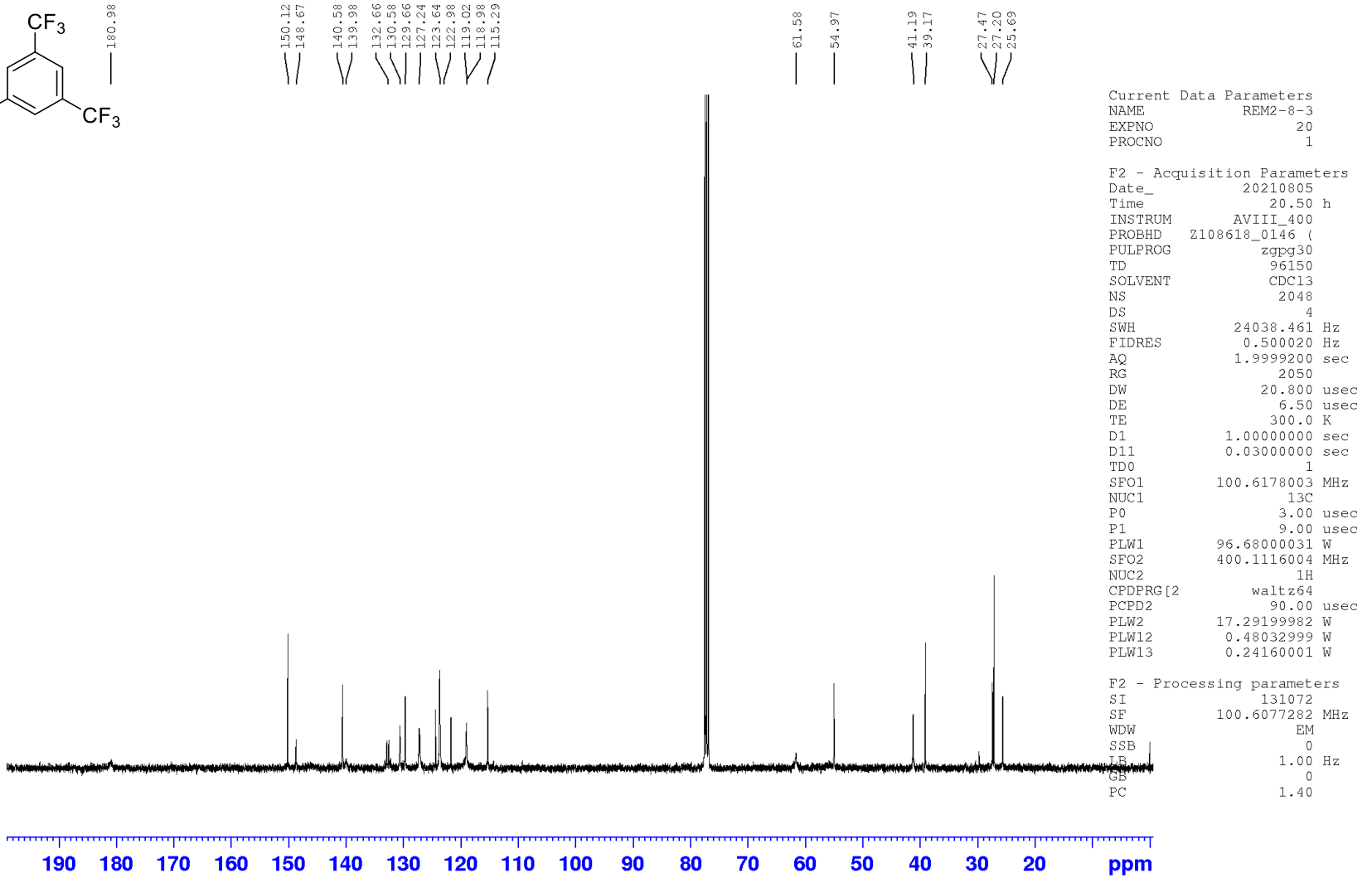


C1

^{13}C NMR

101 MHz

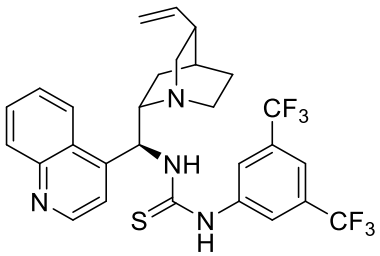
$CDCl_3$




```
Current Data Parameters
NAME            REM2-8-3
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210805
Time              20.50 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077282 MHz
WDW                   EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

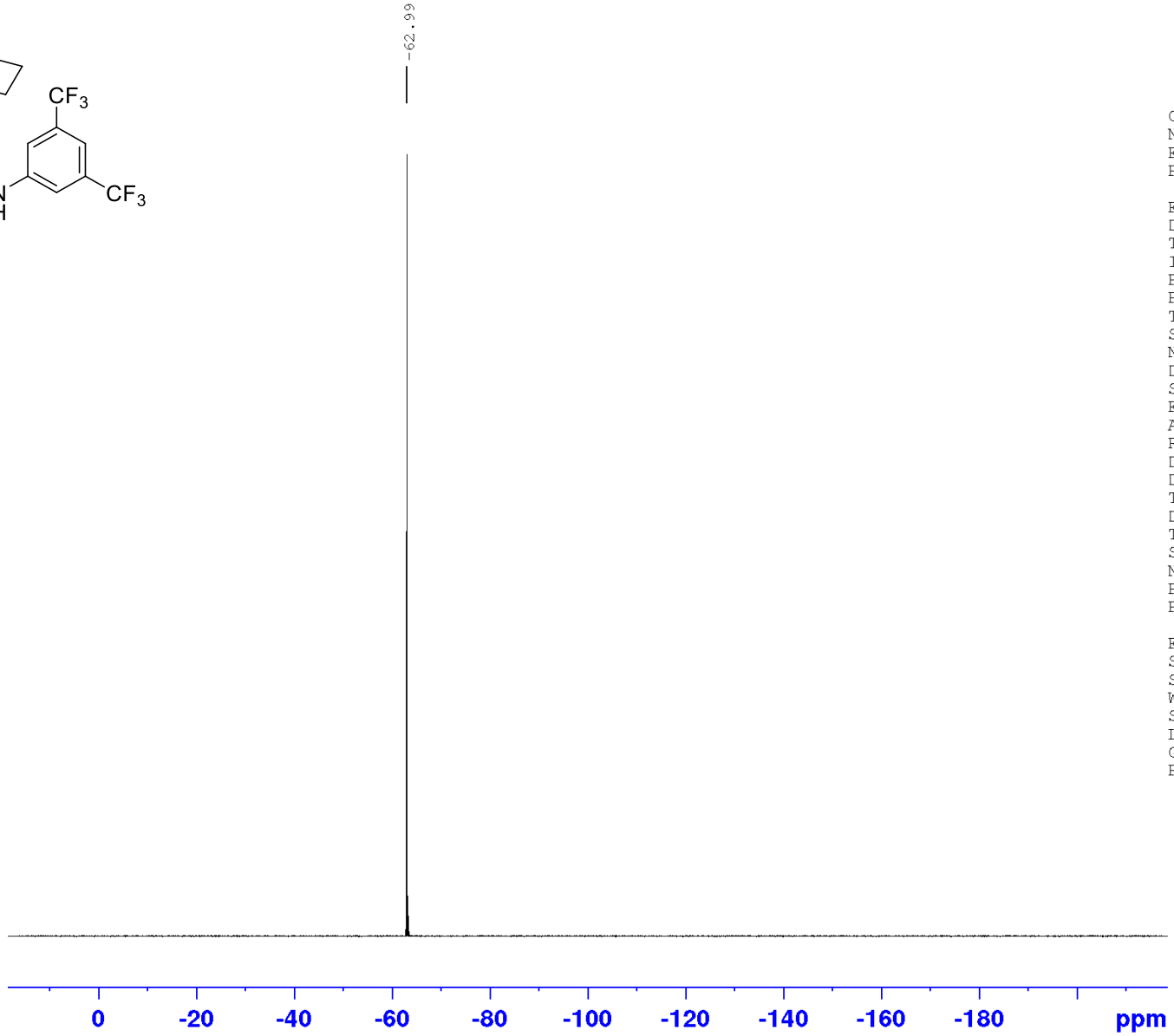


C1

^{19}F NMR

376 MHz

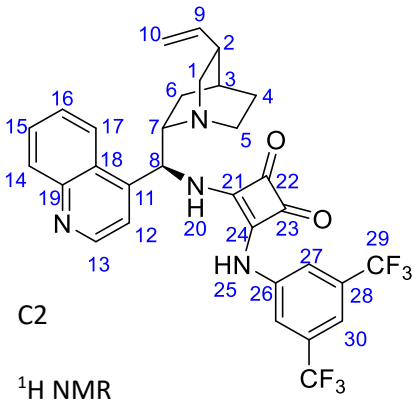
$CDCl_3$




```
Current Data Parameters
NAME            REM2-8-3
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210804
Time              17.13 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   575
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                 11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

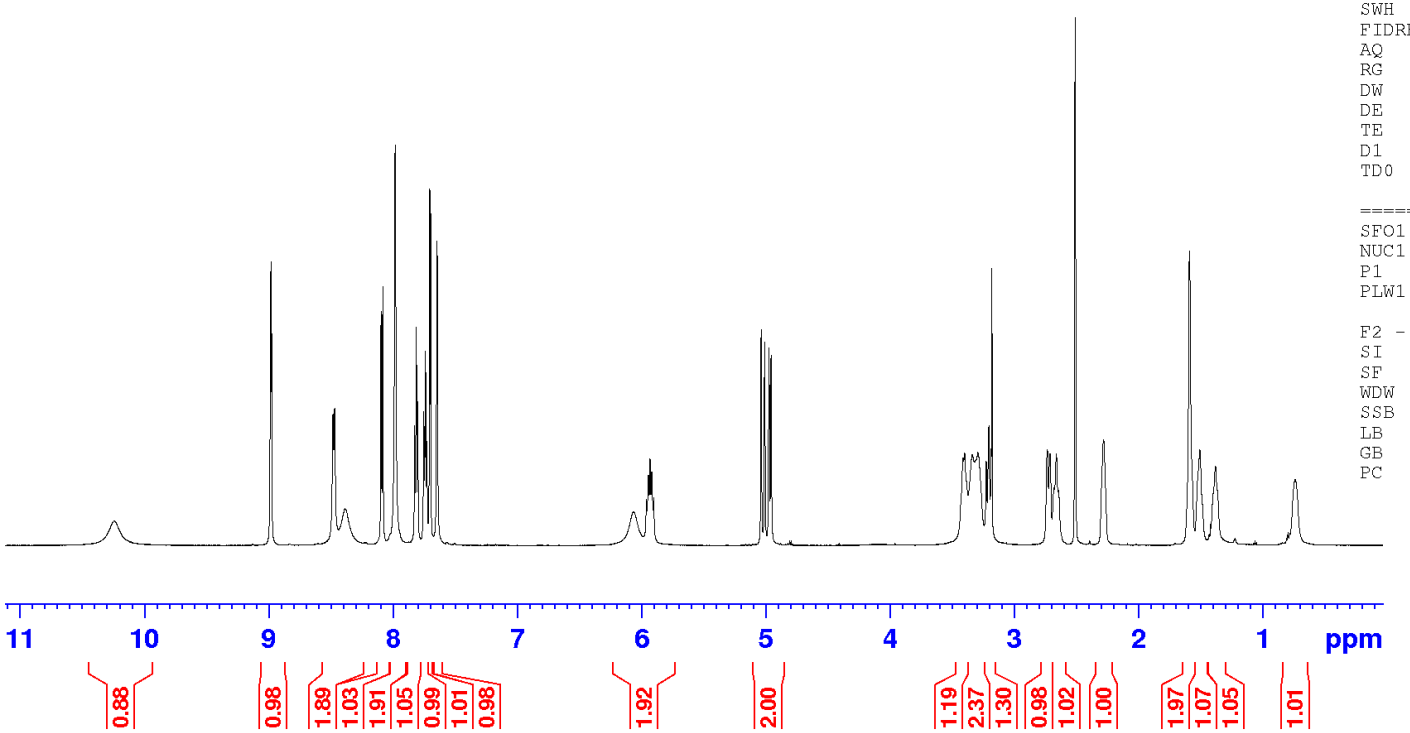


C2

^{1}H NMR

600 MHz

DMSO-d6

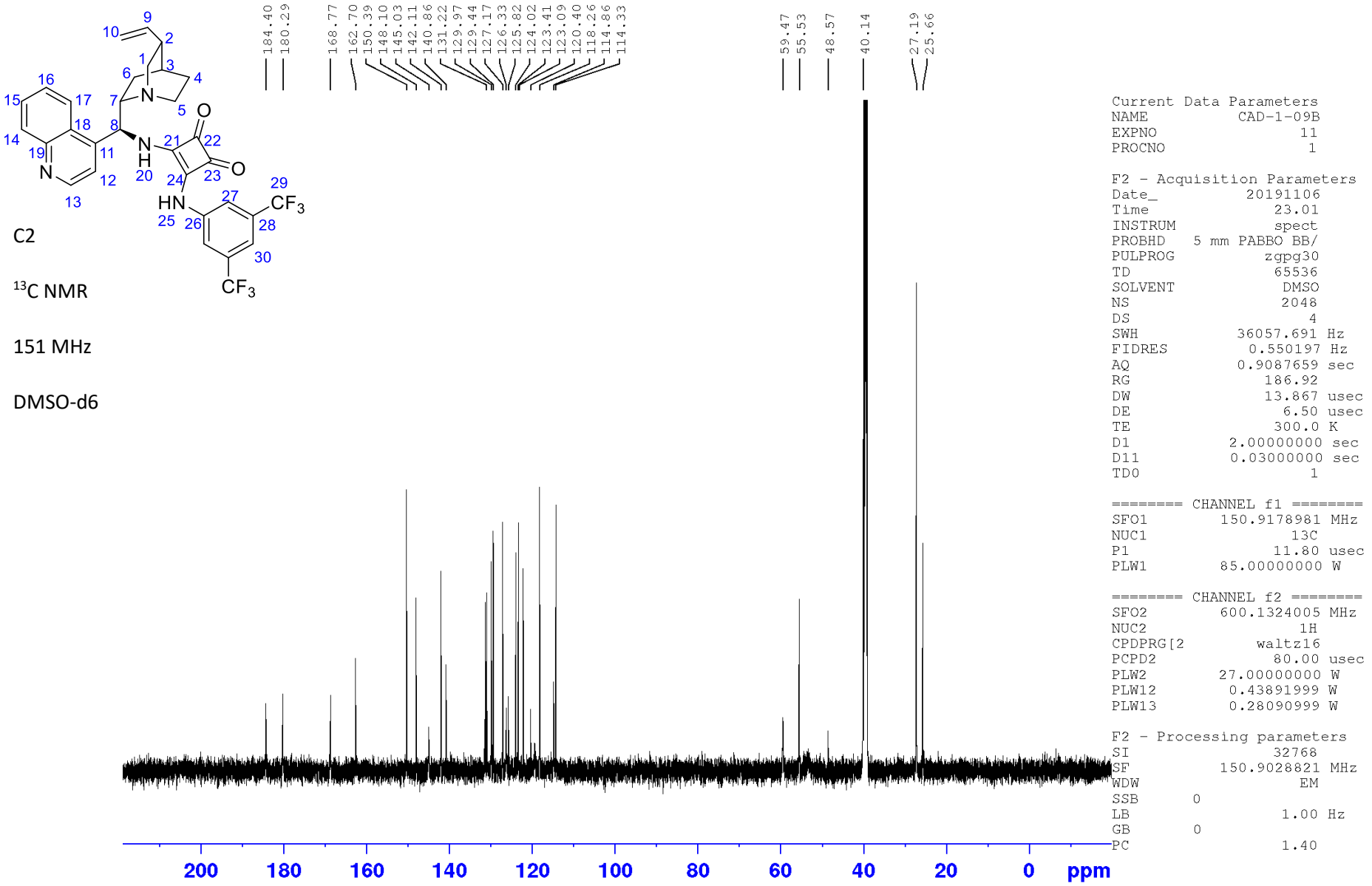


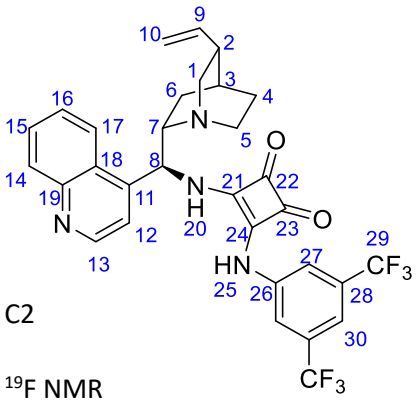

```
Current Data Parameters
NAME           CAD-1-09B
EXPNO                 10
PROCNO                 1

F2 - Acquisition Paramete
Date_           20191106
Time               21.18
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH            12019.230 H
FIDRES          0.183399 H
AQ              2.7262976 s
RG                  97.5
DW                 41.600 u
DE                  6.50 u
TE                 300.0 K
D1              1.00000000 s
TD0                    1

======== CHANNEL f1 =====
SFO1          600.1337060 M
NUC1                1H
P1                 10.00 u
PLW1          26.60000038 W

F2 - Processing paramete
SI                 65536
SF            600.1300000 M
WDW                   EM
SSB                    0
LB                  0.30 H
GB                     0
PC                  1.00
```


184.40
180.29
168.77
162.70
150.39
148.10
145.03
142.11
140.86
131.22
129.97
129.44
127.17
126.33
125.82
124.02
123.41
123.09
120.40
118.26
114.86
114.33
59.47
55.53
48.57
40.14
27.19
25.66
C2
13C NMR
151 MHz
DMSO-d6
Current Data Parameters
NAME CAD-1-09B
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191106
Time 23.01
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 2048
DS 4
SWH 36057.691 Hz
FIDRES 0.550197 Hz
AQ 0.9087659 sec
RG 186.92
DW 13.867 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.9178981 MHz
NUC1 13C
P1 11.80 usec
PLW1 85.00000000 W
======== CHANNEL f2 ========
SFO2 600.1324005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 80.00 usec
PLW2 27.00000000 W
PLW12 0.43891999 W
PLW13 0.28090999 W
F2 - Processing parameters
SI 32768
SF 150.9028821 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm

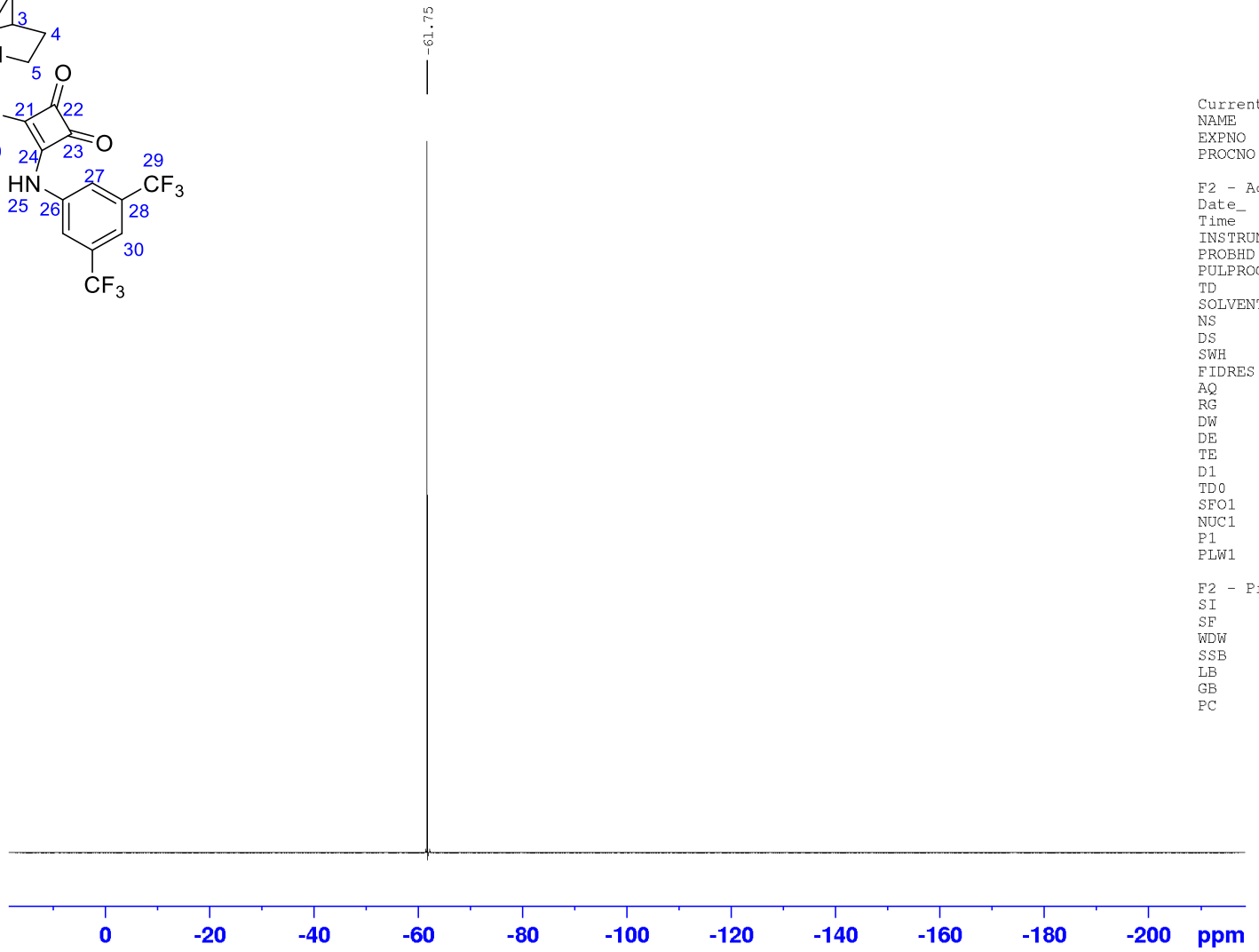


C2

^{19}F NMR

376 MHz

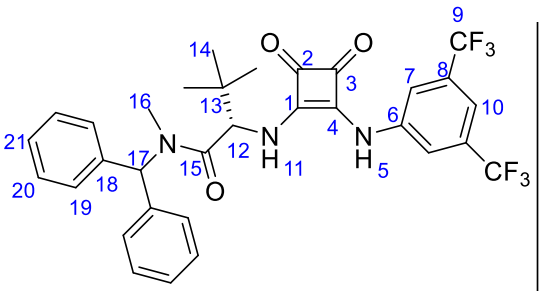
DMSO-d6




```
Current Data Parameters
NAME            CAD-1-09
EXPNO                 23
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191105
Time              14.53 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT             DMSO
NS                    16
DS                     4
SWH           89285.711 Hz
FIDRES         0.681591 Hz
AQ             1.4671552 sec
RG                   575
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1        376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

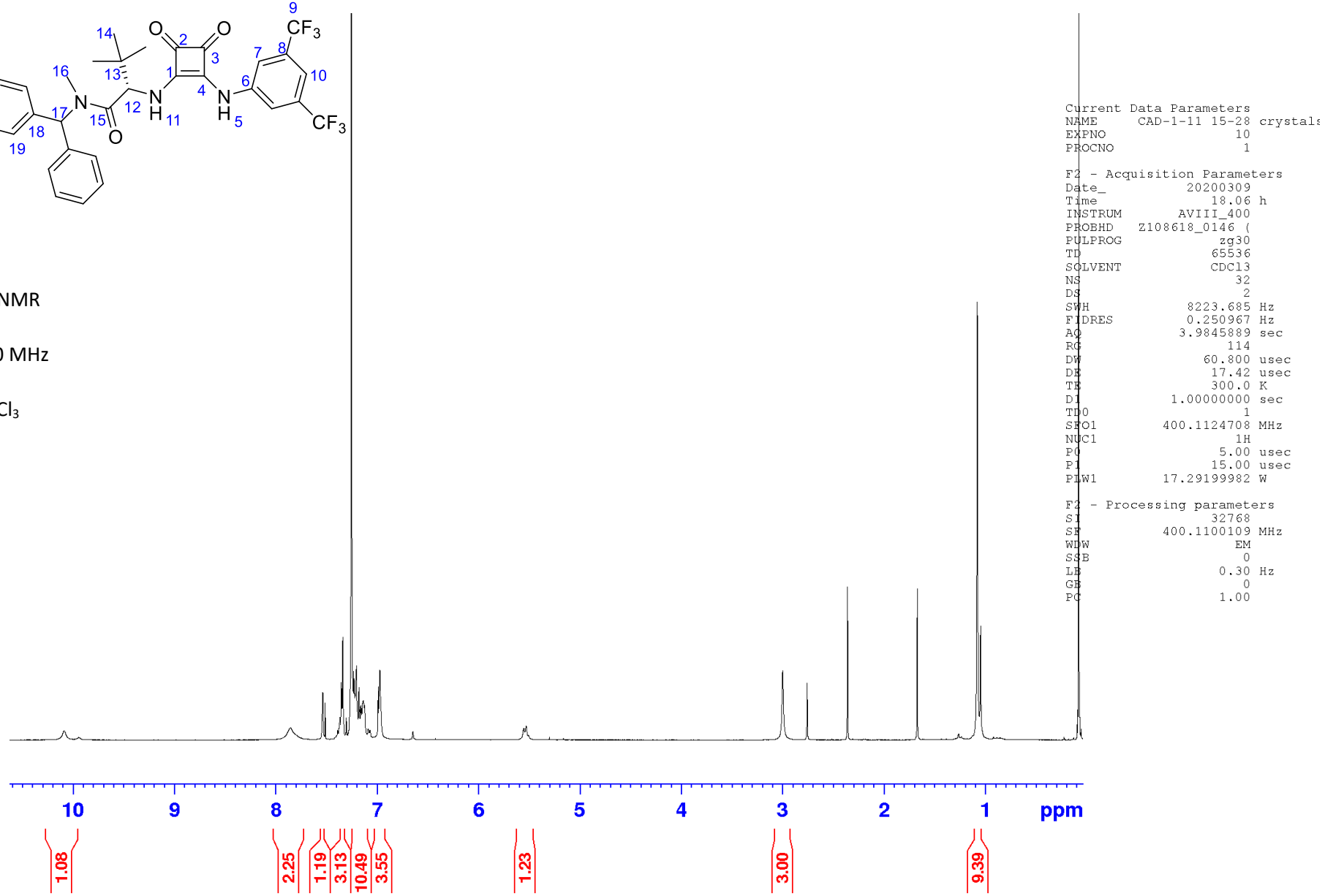


C3

^{1}H NMR

400 MHz

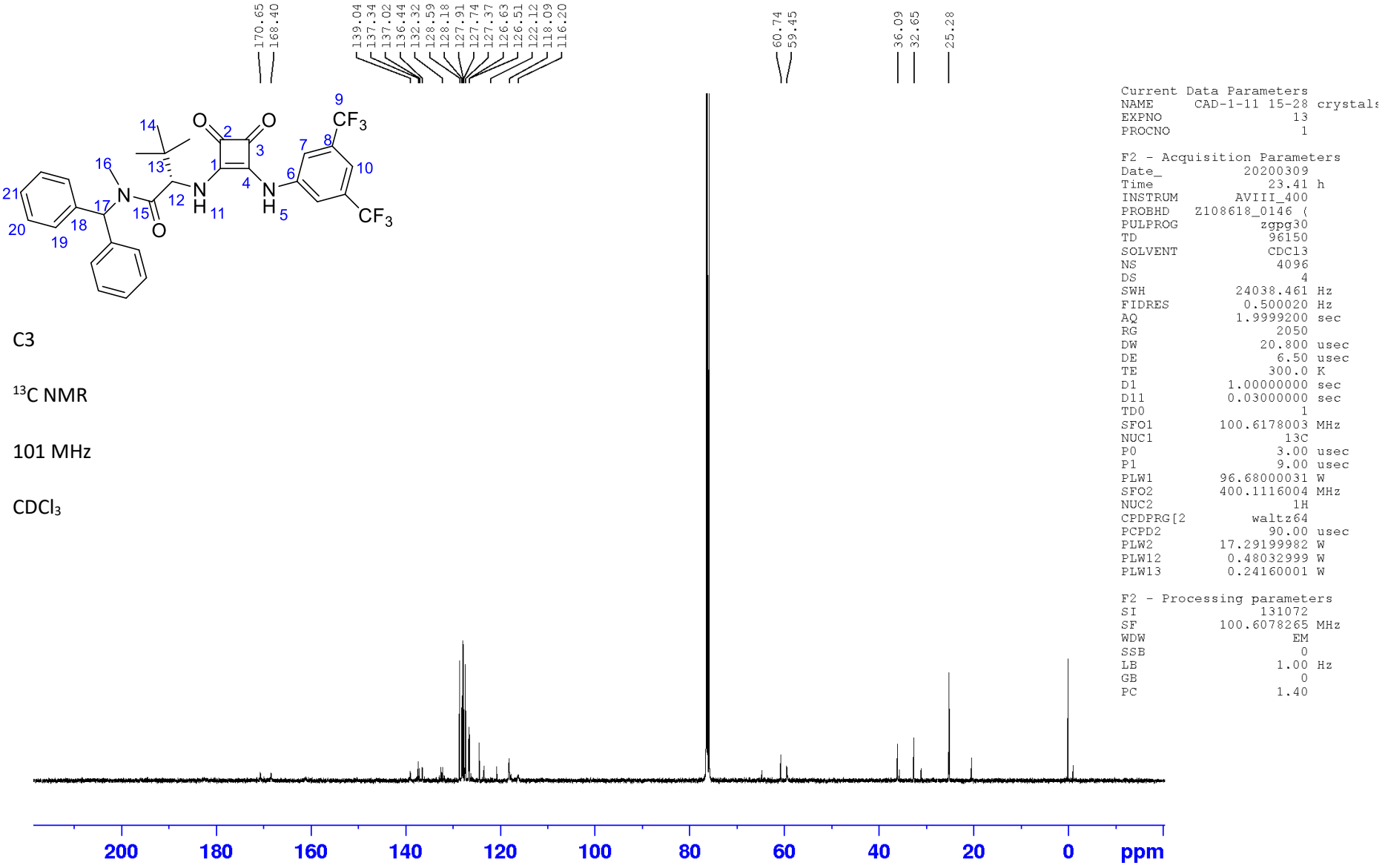
$CDCl_3$

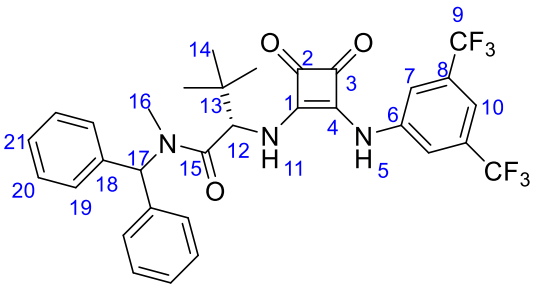



```
Current Data Parameters
NAME      CAD-1-11 15-28 crystals
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200309
Time              18.06 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    32
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   114
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100109 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```


170.65
168.40
139.04
137.34
137.02
136.44
132.32
128.59
128.18
127.91
127.74
127.37
126.63
126.51
122.12
118.09
116.20
60.74
59.45
36.09
32.65
25.28
C3
13C NMR
101 MHz
CDCl3
Current Data Parameters
NAME CAD-1-11 15-28 crystals
EXPNO 13
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200309
Time 23.41 h
INSTRUM AVIII_400
PROBHD Z108618_0146 (
PULPROG zgpg30
TD 96150
SOLVENT CDCl3
NS 4096
DS 4
SWH 24038.461 Hz
FIDRES 0.500020 Hz
AQ 1.9999200 sec
RG 2050
DW 20.800 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 100.6178003 MHz
NUC1 13C
P0 3.00 usec
P1 9.00 usec
PLW1 96.68000031 W
SFO2 400.1116004 MHz
NUC2 1H
CPDPRG[2 waltz64
PCPD2 90.00 usec
PLW2 17.29199982 W
PLW12 0.48032999 W
PLW13 0.24160001 W
F2 - Processing parameters
SI 131072
SF 100.6078265 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm

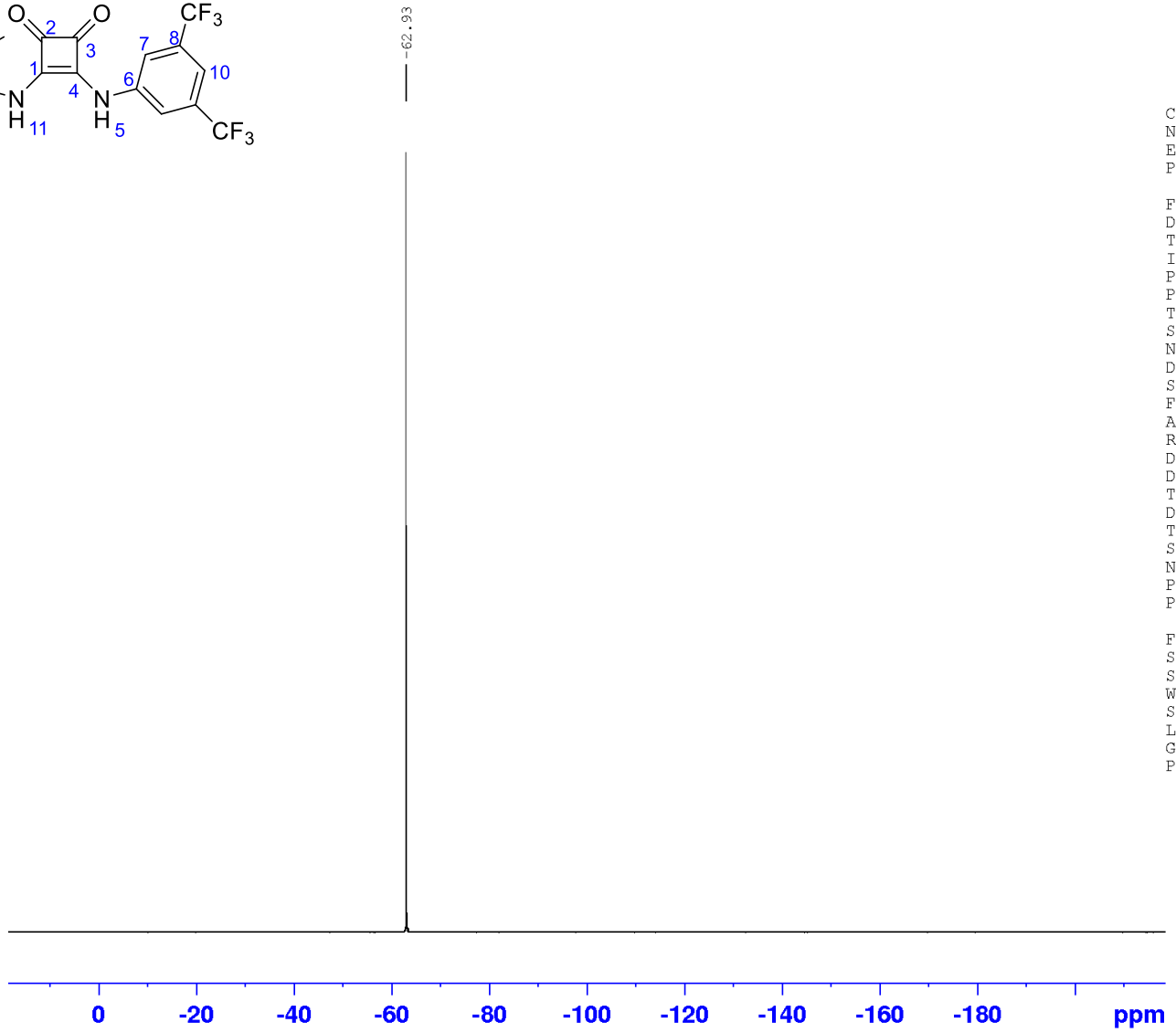


C3

^{19}F NMR

376 MHz

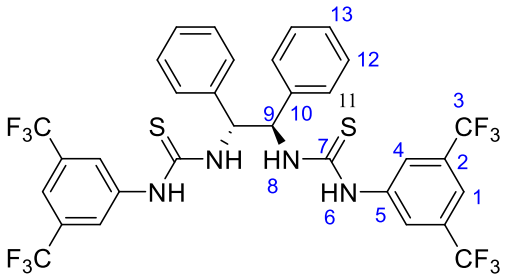
$CDCl_3$




```
Current Data Parameters
NAME      CAD-1-11C 29-77
EXPNO                  15
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191205
Time              17.39 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG                zg
TD                261992
SOLVENT             CDC13
NS                     16
DS                      4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                    645
DW                5.600 usec
DE                7.11 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

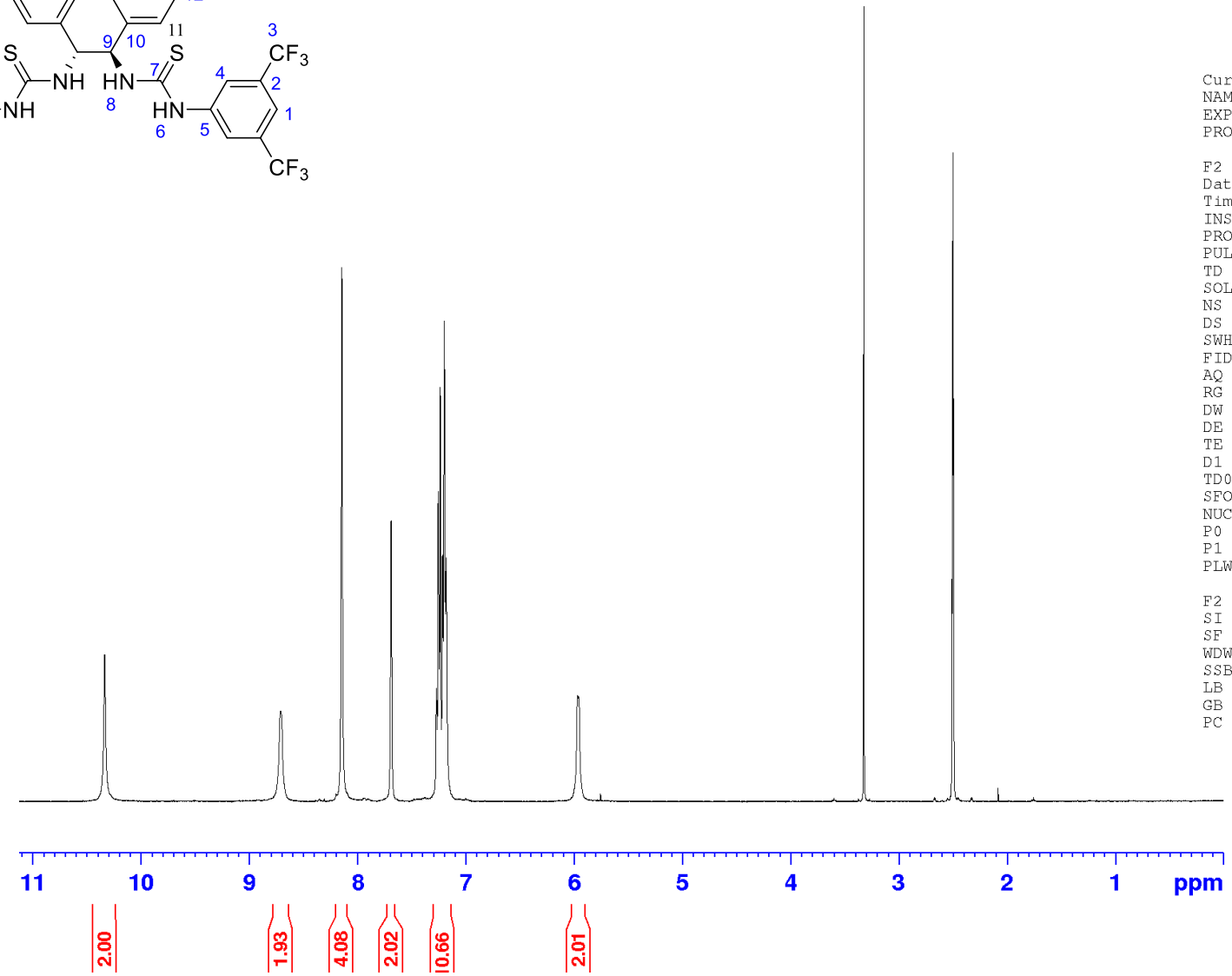


C4

^{1}H NMR

400 MHz

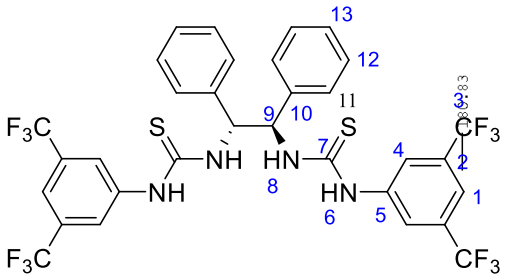
DMSO-d6




```
Current Data Parameters
NAME          CAD-1-10B
EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
Date_          20191112
Time              12.35 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG            zg30
TD                65536
SOLVENT            DMSO
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ             3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF          400.1100032 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

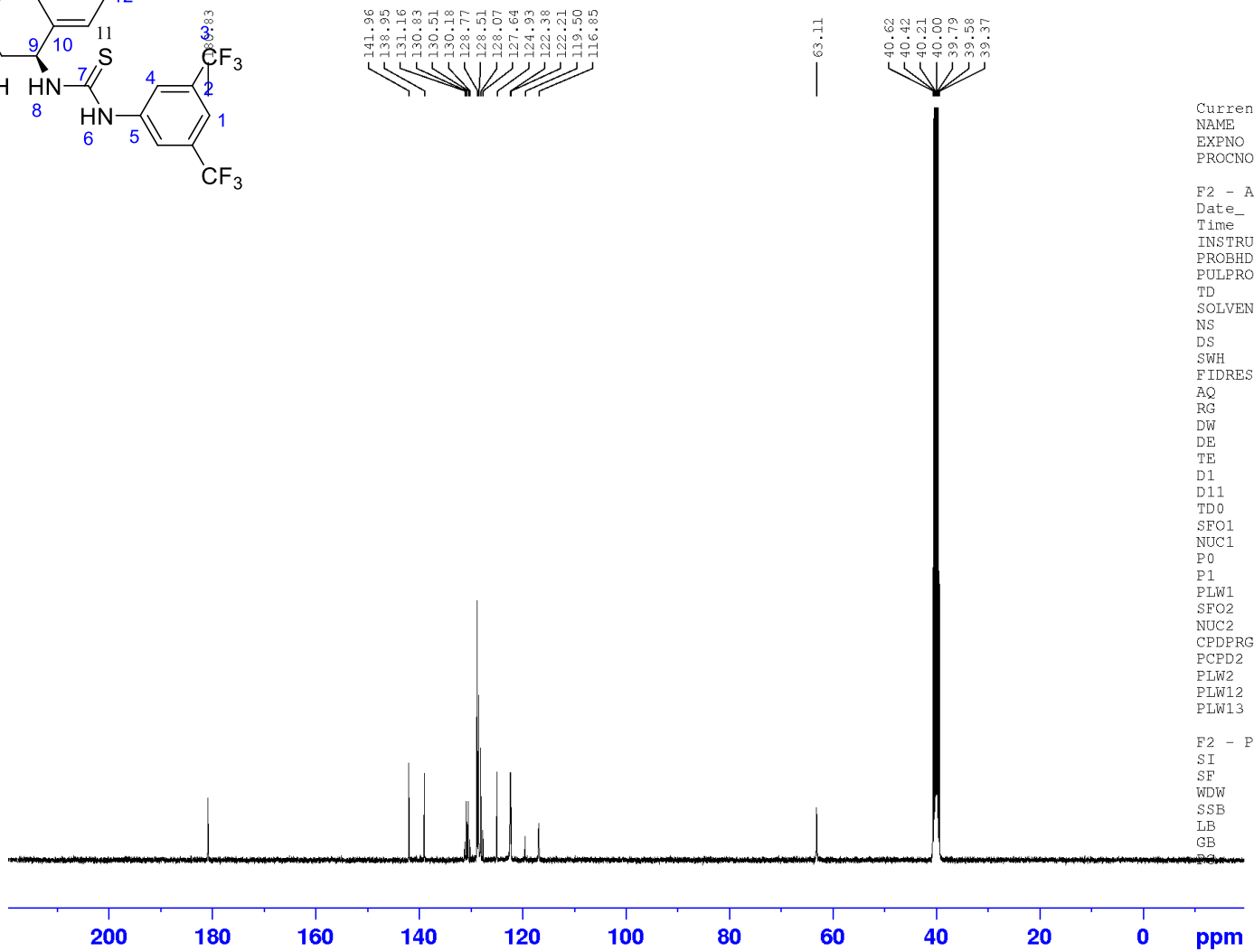


C4

^{13}C NMR

101 MHz

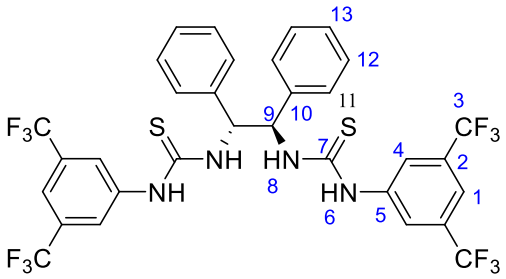
DMSO-d6




```
Current Data Parameters
NAME            CAD-1-10B
EXPNO                  18
PROCNO                  1

F2 - Acquisition Parameters
Date_           20191115
Time                2.50 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT             DMSO
NS                  4096
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ             1.9999200 sec
RG                  1620
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077400 MHz
WDW                 EM
SSB                    0
LB                1.00 Hz
GB                     0
PC                1.40
```

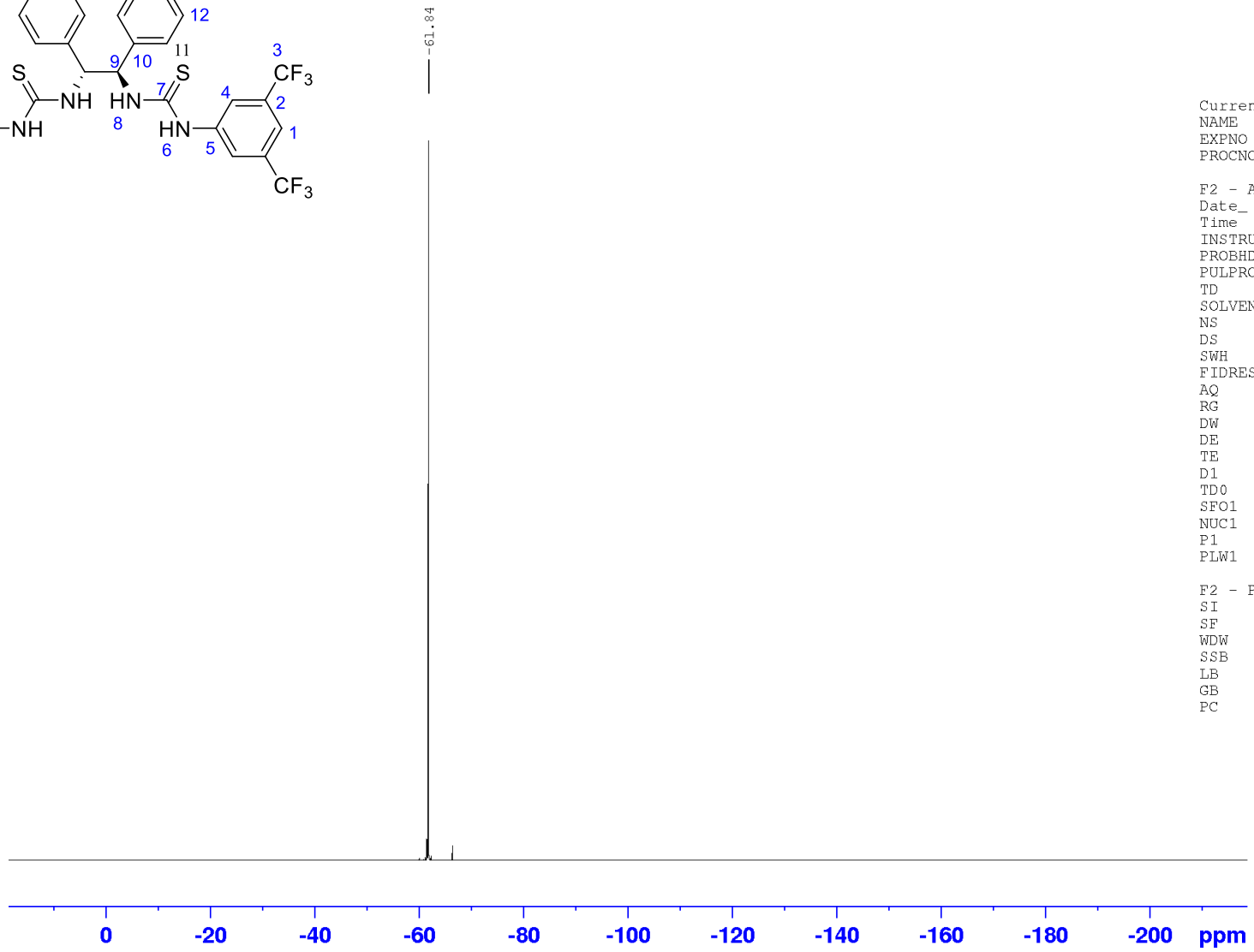


C4

^{19}F NMR

376 MHz

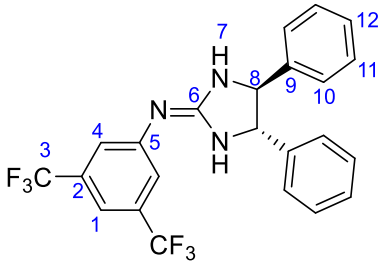
DMSO-d6




```
Current Data Parameters
NAME            CAD-1-10
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20191107
Time               12.50 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG                zg
TD                261992
SOLVENT             DMSO
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                  90.5
DW                 5.600 usec
DE                 7.11 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```

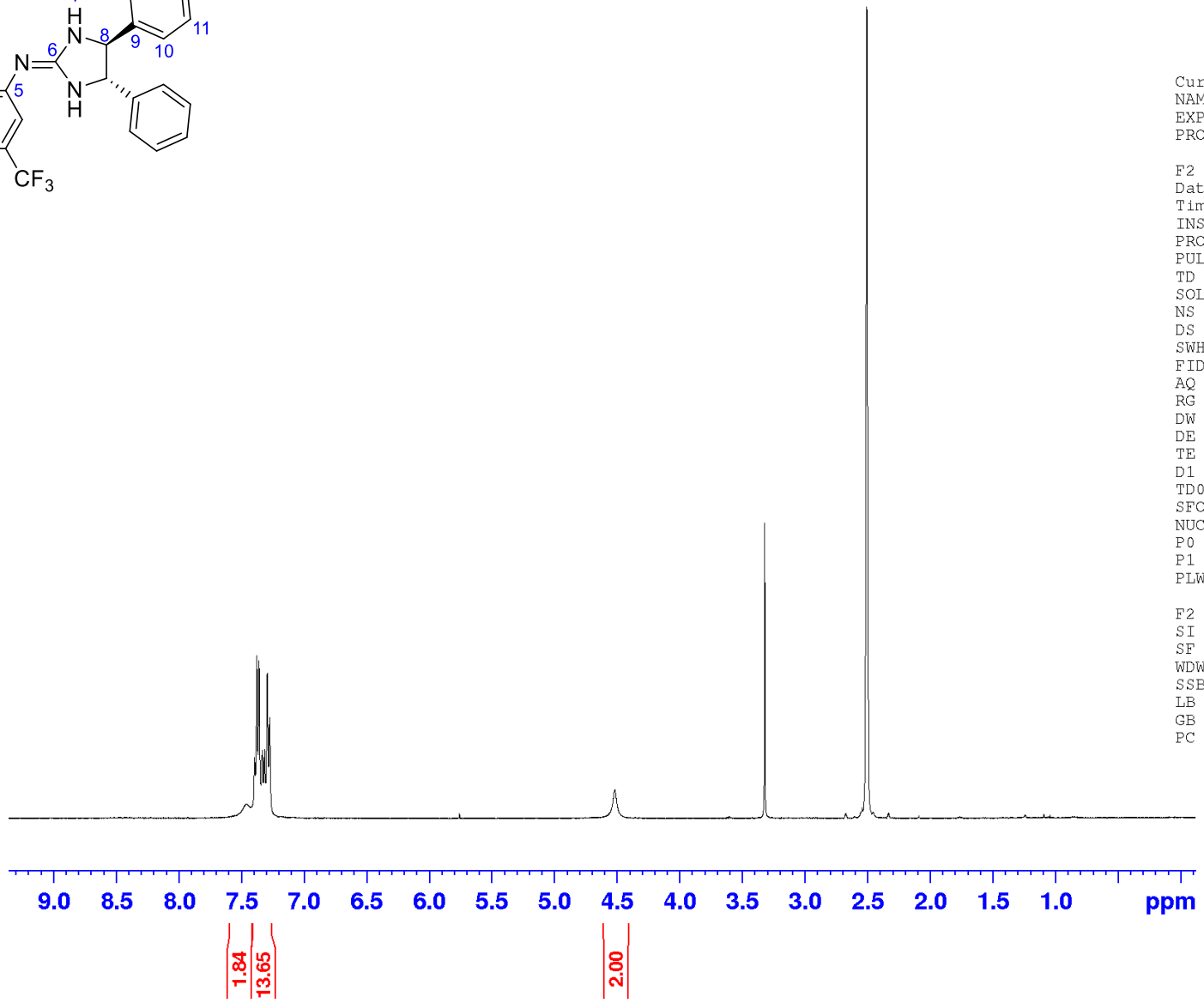


C5

^{1}H NMR

400 MHz

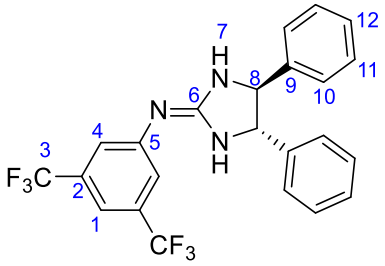
DMSO-d6




```
Current Data Parameters
NAME            CAD-1-14B
EXPNO                  10
PROCNO                  1

F2 - Acquisition Parameters
Date_            20200122
Time                15.46 h
INSTRUM         AVIII_400
PROBHD    Z108618_0146 (
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     32
DS                      2
SWH              8223.685 Hz
FIDRES           0.250967 Hz
AQ               3.9845889 sec
RG                    256
DW                 60.800 usec
DE                 17.42 usec
TE                 300.0 K
D1            1.00000000 sec
TD0                     1
SFO1         400.1124708 MHz
NUC1                   1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                  32768
SF           400.1100034 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

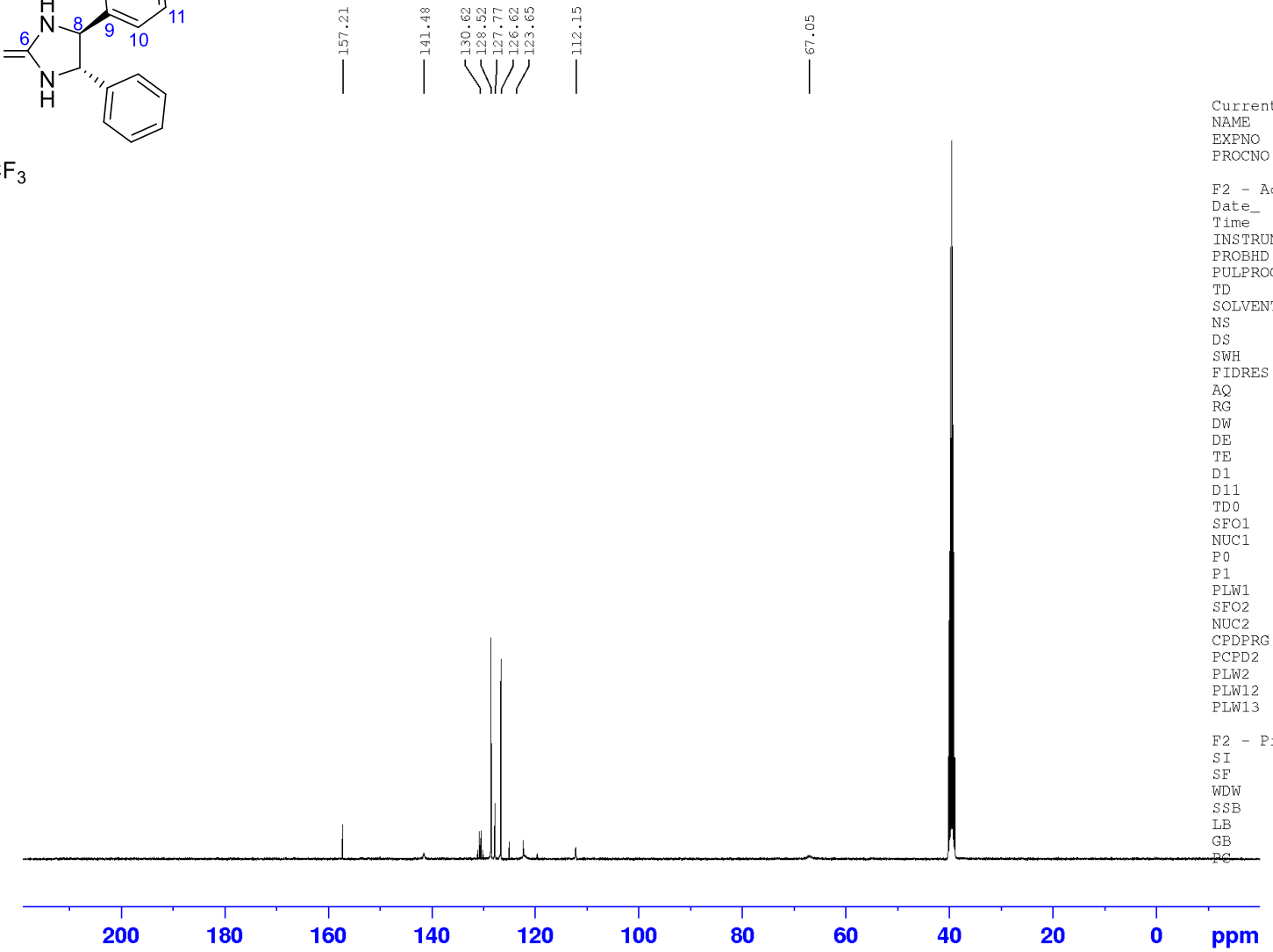


C5

^{13}C NMR

101 MHz

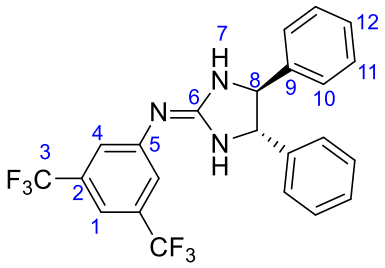
DMSO-d6




```
Current Data Parameters
NAME          CAD-1-14C
EXPNO                14
PROCNO                1

F2 - Acquisition Parameters
Date_          20200130
Time               4.53 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT            DMSO
NS                 4096
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                  912
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1        100.6178003 MHz
NUC1               13C
P0                3.00 usec
P1                9.00 usec
PLW1        96.68000031 W
SFO2        400.1116004 MHz
NUC2               1H
CPDPRG[2        waltz64
PCPD2             90.00 usec
PLW2        17.29199982 W
PLW12        0.48032999 W
PLW13        0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077874 MHz
WDW                 EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

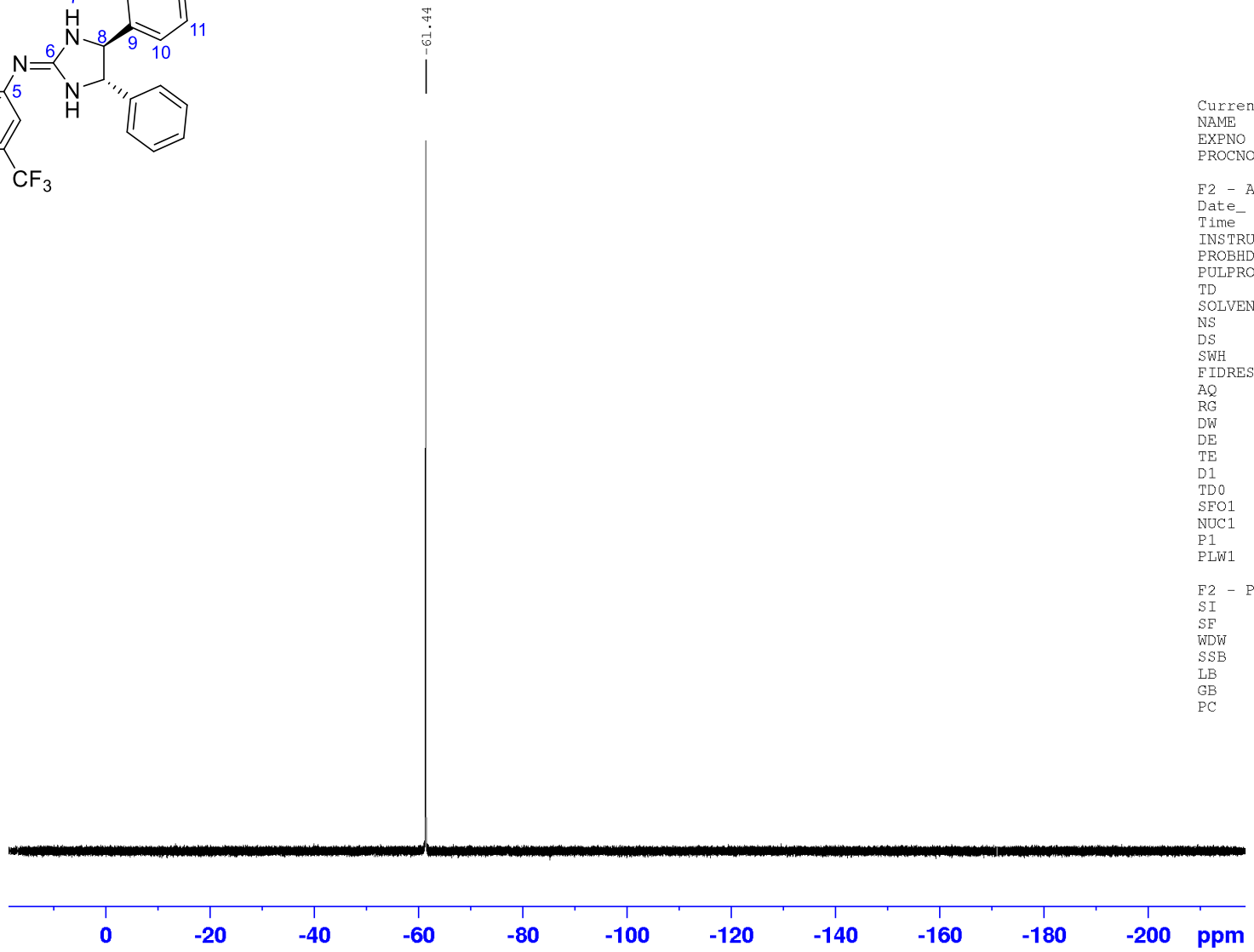


C5

^{19}F NMR

376 MHz

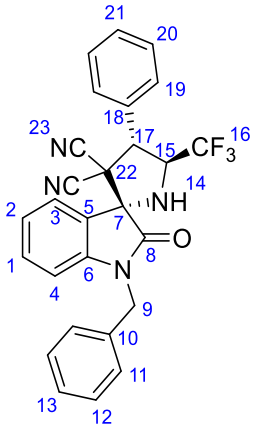
DMSO-d^{6}




```
Current Data Parameters
NAME          CAD-1-14B
EXPNO                11
PROCNO                1

F2 - Acquisition Parameters
Date_          20200122
Time             16.53 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG              zg
TD               261992
SOLVENT            DMSO
NS                   16
DS                    4
SWH           89285.711 Hz
FIDRES         0.681591 Hz
AQ            1.4671552 sec
RG                  512
DW                5.600 usec
DE                7.11 usec
TE                300.0 K
D1           1.00000000 sec
TD0                   1
SFO1        376.4418995 MHz
NUC1                19F
P1                11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```



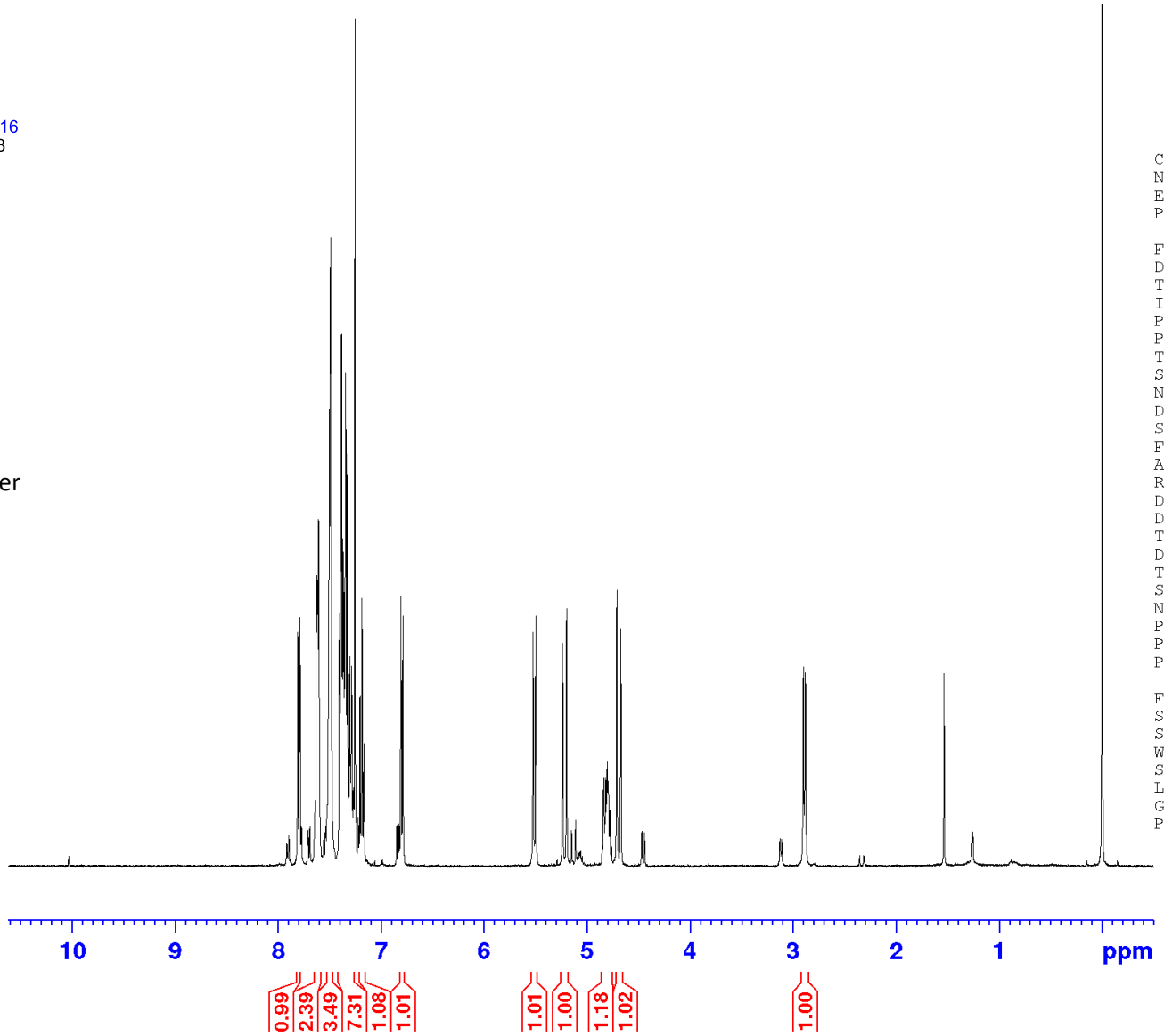
3a

Major diastereomer

^{1}H NMR

400 MHz

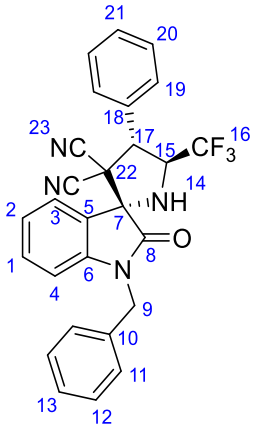
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.176
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210614
Time               15.25 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                    256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1          400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1          17.29199982 W

F2 - Processing parameters
SI                 32768
SF            400.1100113 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



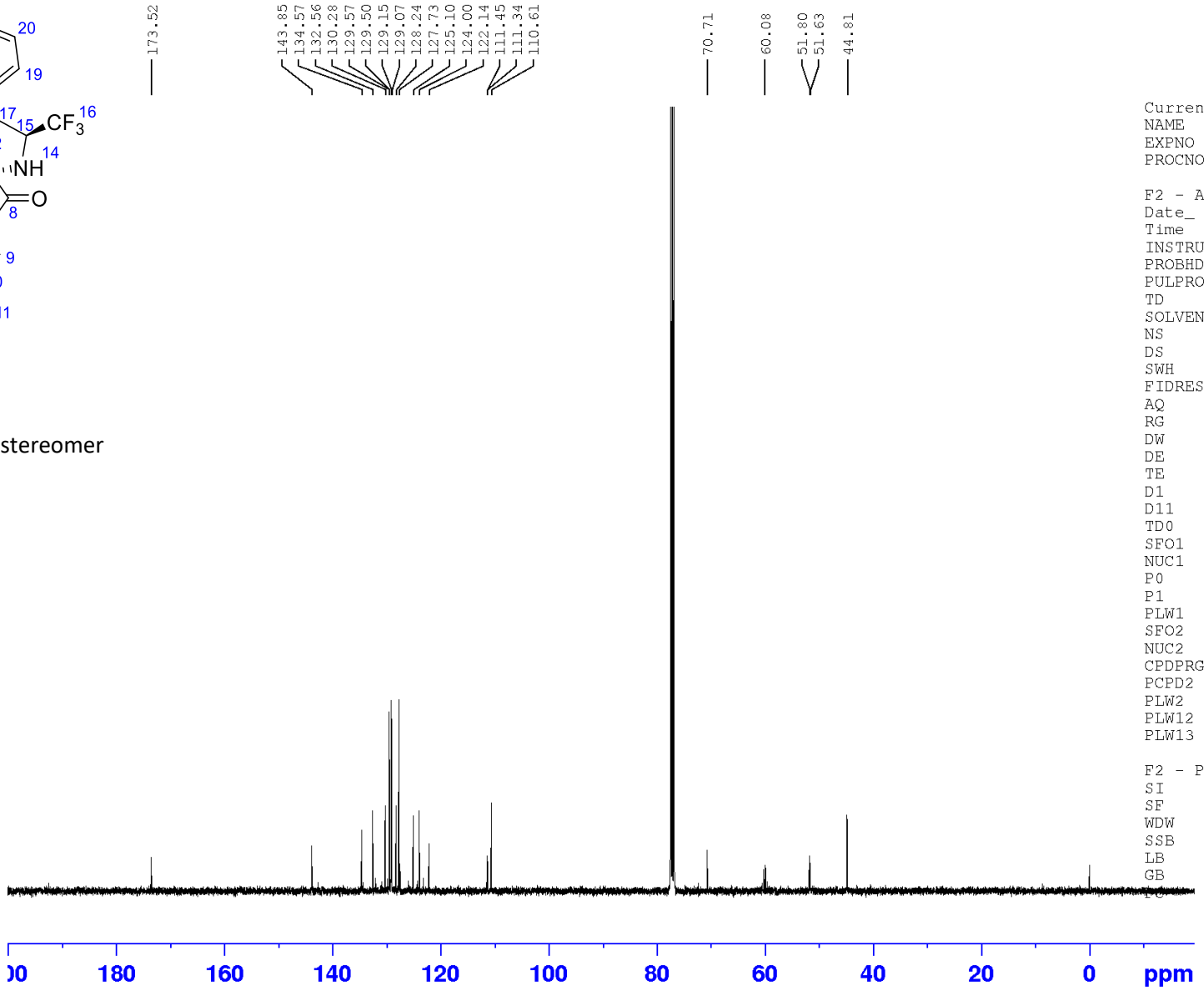
3a

Major diastereomer

^{13}C NMR

101 MHz

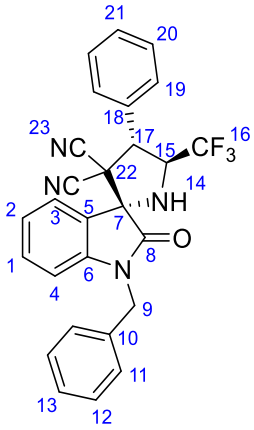
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.176
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210715
Time              19.42 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1        100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2        400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077257 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
                    1.40
```



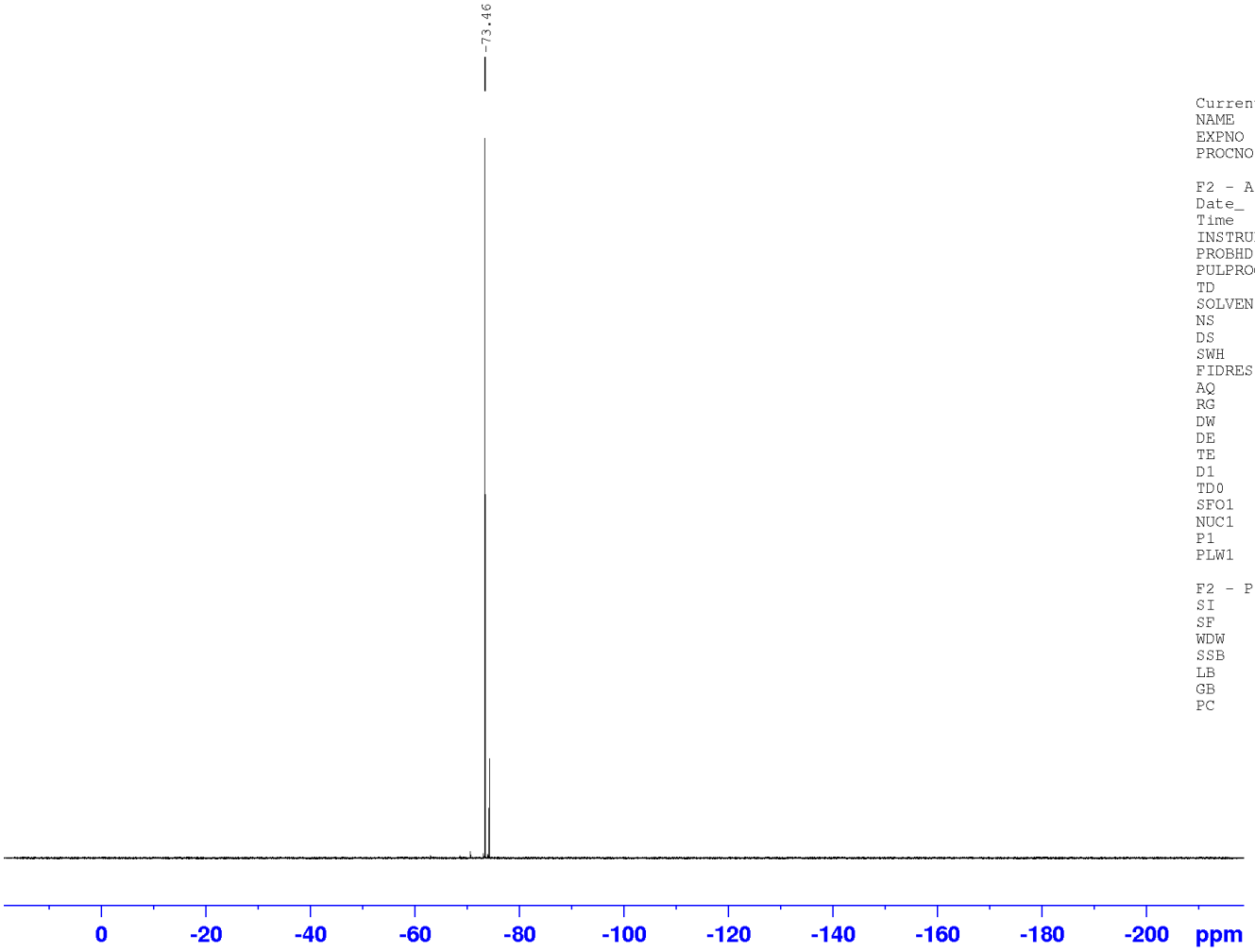
3a

Major diastereomer

^{19}F NMR

376 MHz

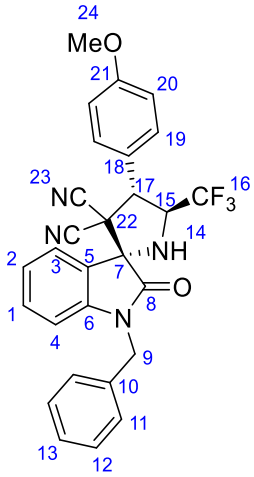
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.176
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210614
Time              15.29 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           89285.711 Hz
FIDRES         0.681591 Hz
AQ            1.4671552 sec
RG                   575
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1        376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



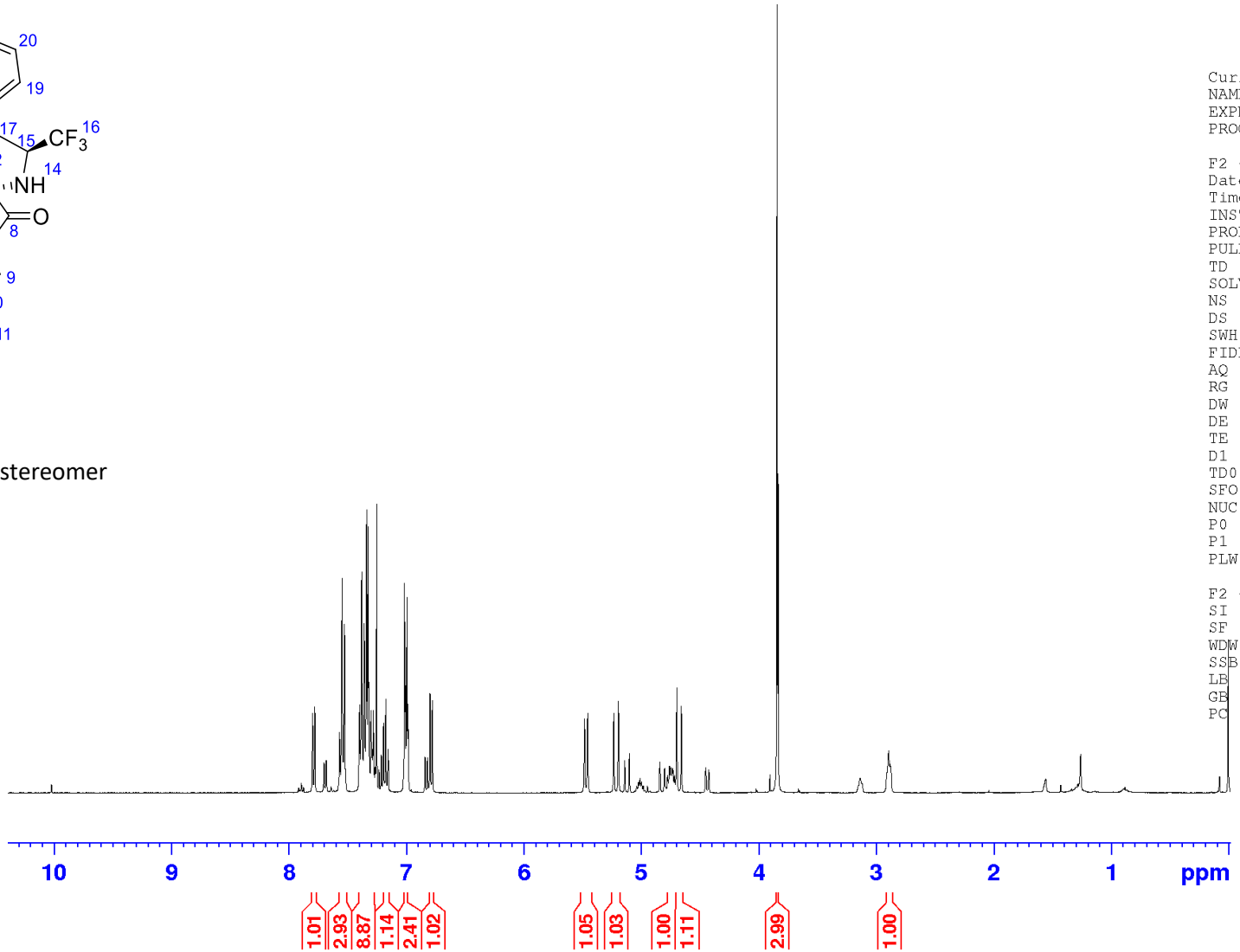
3b

Major diastereomer

^{1}H NMR

400 MHz

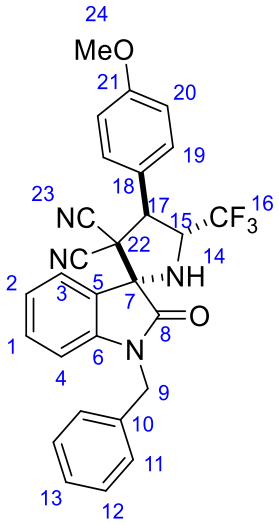
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.174 (V3)
EXPNO                10
PROCNO                1

F2 - Acquisition Parameters
Date_          20210624
Time              14.09 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.250967 Hz
AQ            3.9845889 sec
RG                  144
DW               60.800 usec
DE               17.42 usec
TE               300.0 K
D1            1.00000000 sec
TD0                   1
SFO1        400.1124708 MHz
NUC1                 1H
P0                5.00 usec
P1               15.00 usec
PLW1        17.29199982 W

F2 - Processing parameters
SI                32768
SF          400.1100128 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



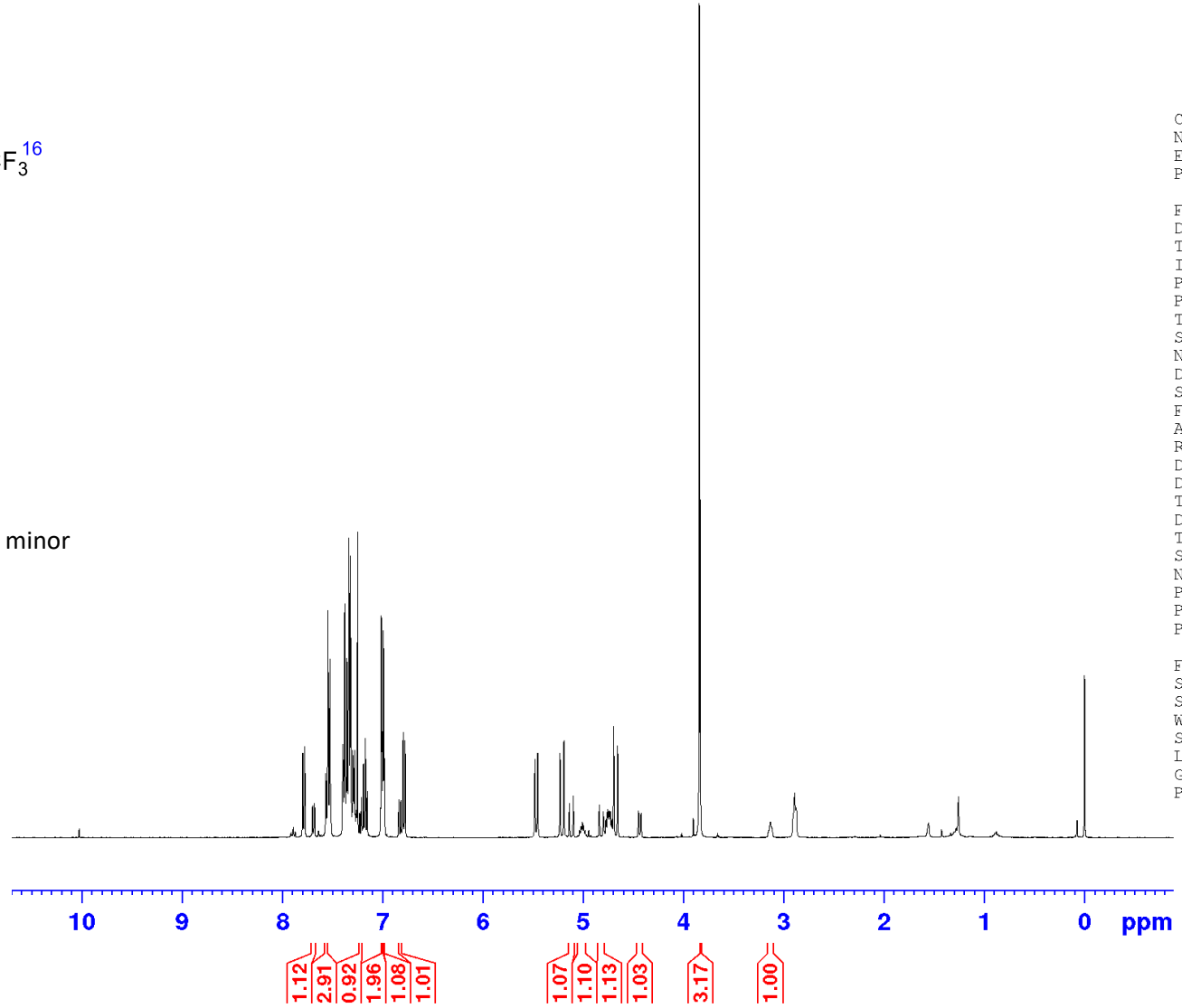
3b

Peaks picked for minor diastereomer

^{1}H NMR

400 MHz

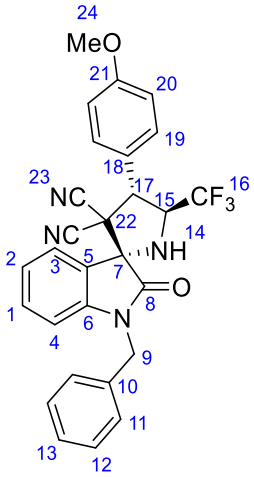
$CDCl_3$




```
Current Data Parameters
NAME       WR 2.174 (V3)
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210624
Time              14.09 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   144
DW                60.800 usec
DE                17.42 usec
TE                 300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF          400.1100128 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



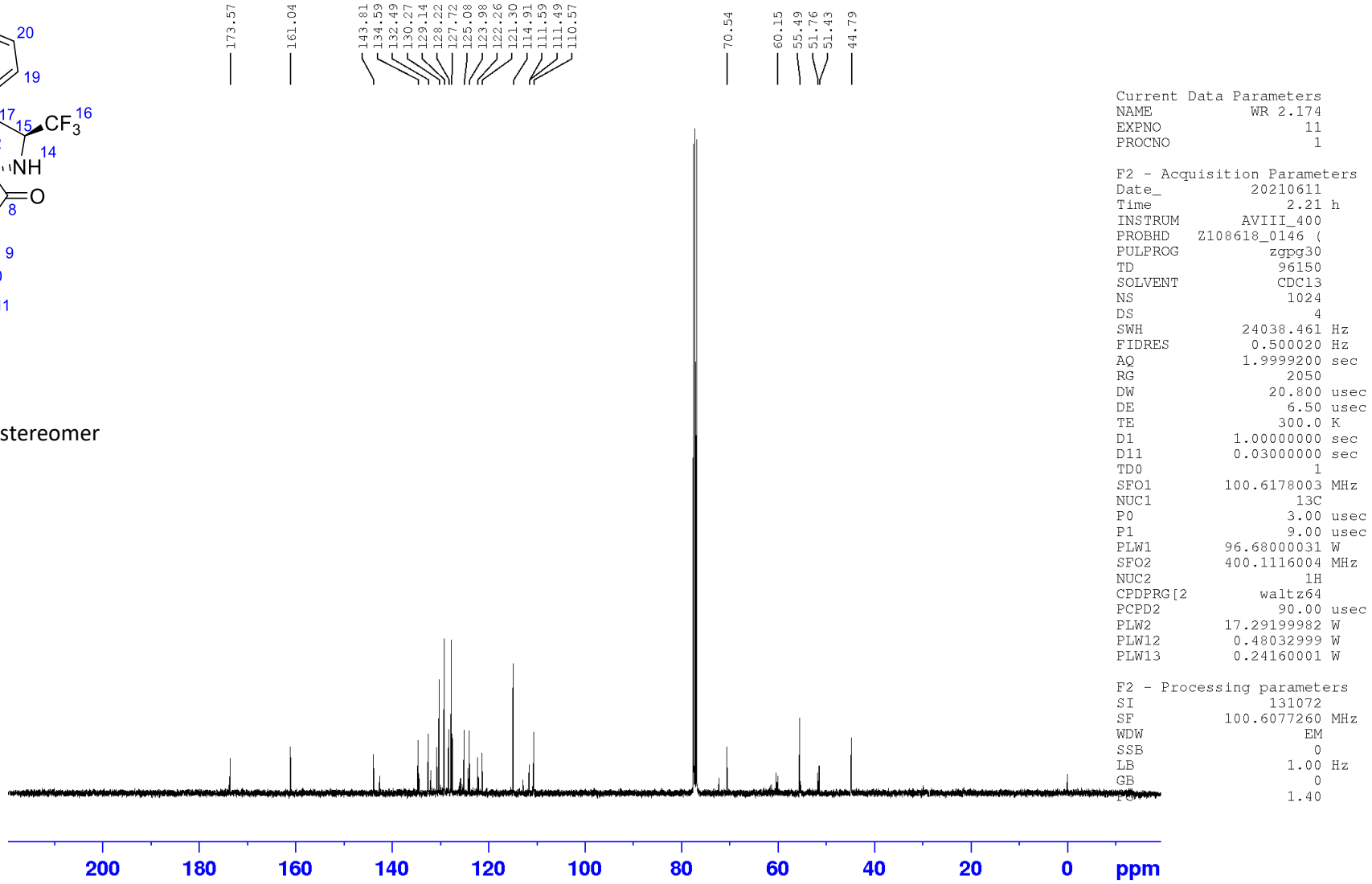
3b

Major diastereomer

^{13}C NMR

101 MHz

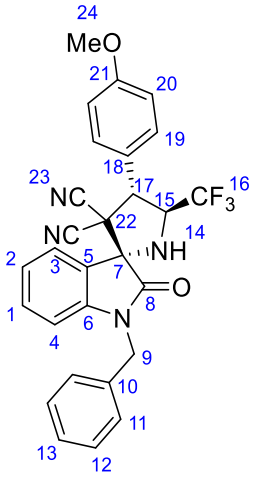
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.174
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210611
Time                2.21 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ              1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077260 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
                    1.40
```



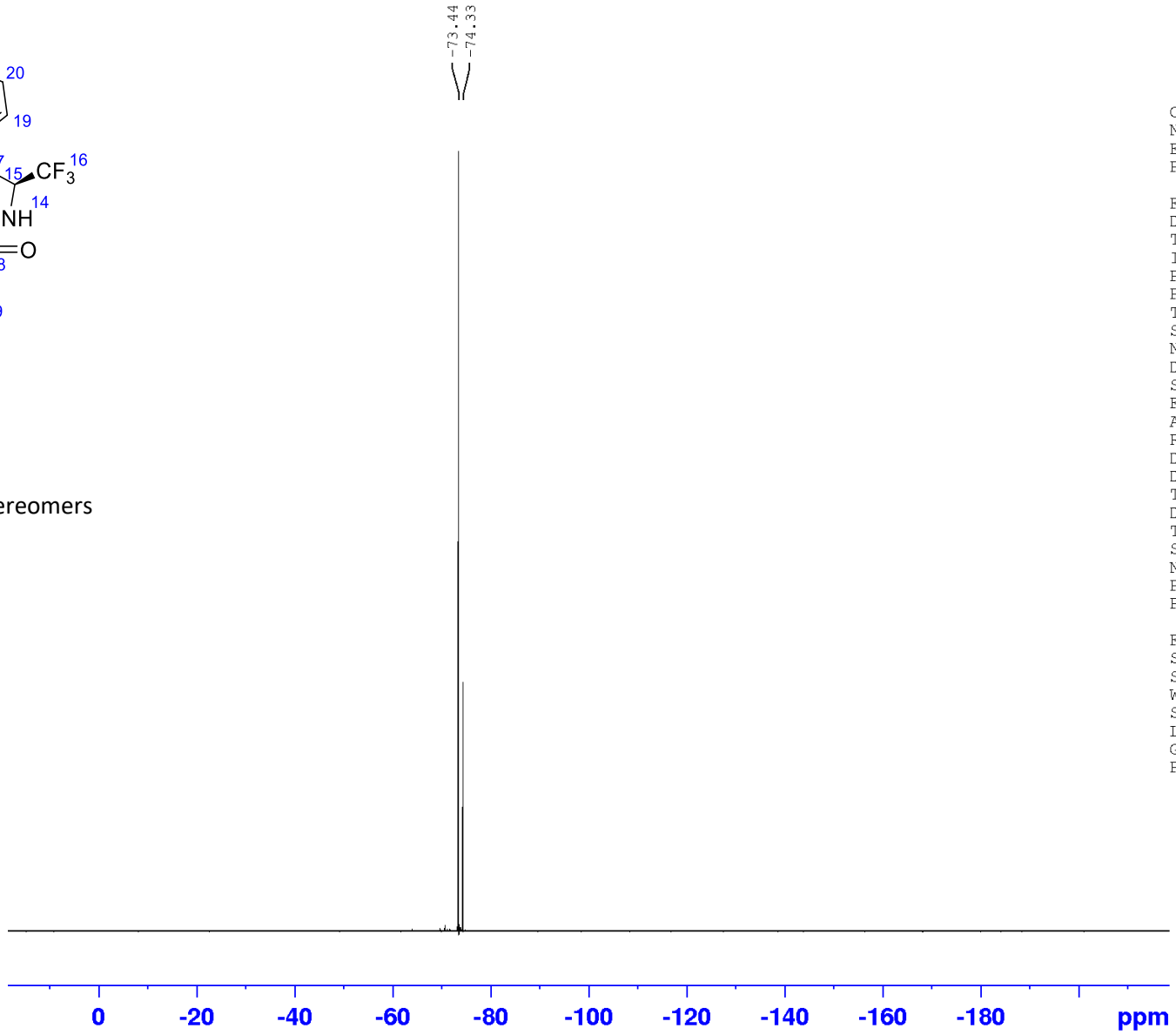
3b

Both diastereomers

^{19}F NMR

376 MHz

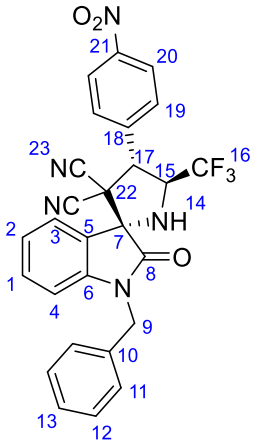
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.174
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210611
Time                3.37 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDC13
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   645
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1        376.4418995 MHz
NUC1                 19F
P1                 11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



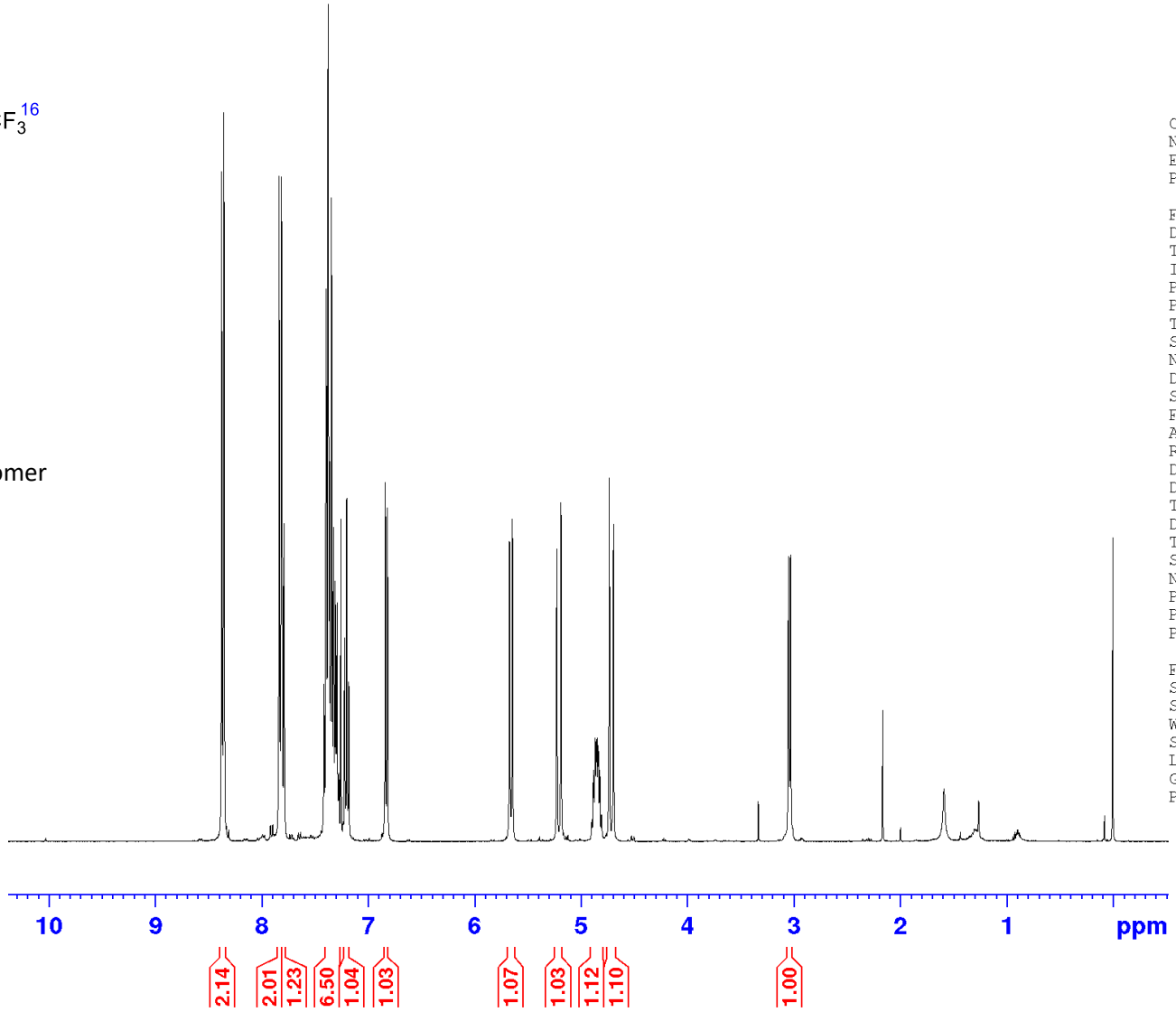
3c

Major diastereomer

^{1}H NMR

400 MHz

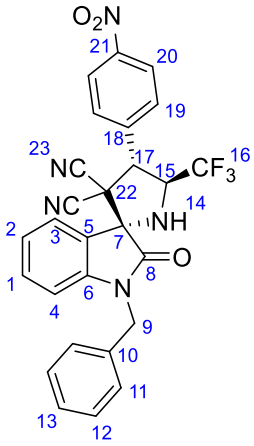
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.167
EXPNO                 50
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210720
Time              17.28 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ             3.9845889 sec
RG                   144
DW                60.800 usec
DE                17.42 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF          400.1100099 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



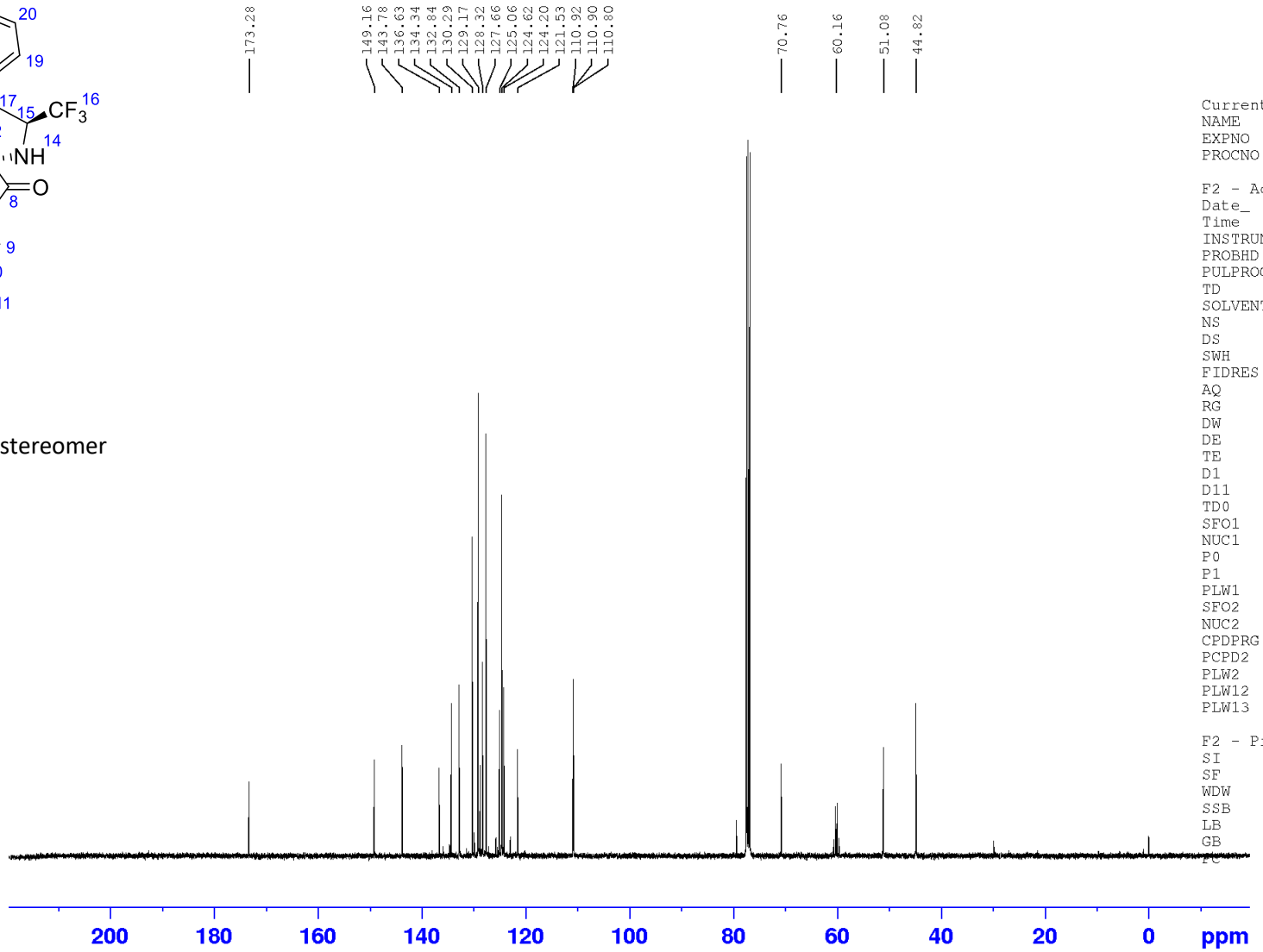
3c

Major diastereomer

^{13}C NMR

101 MHz

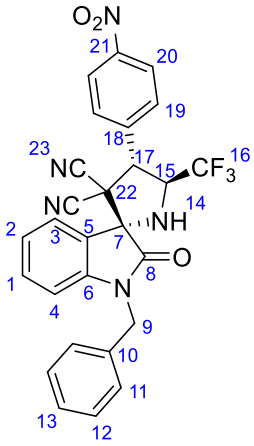
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.167
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210521
Time                0.56 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDC13
NS                  2048
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ              1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077288 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                  1.40
```



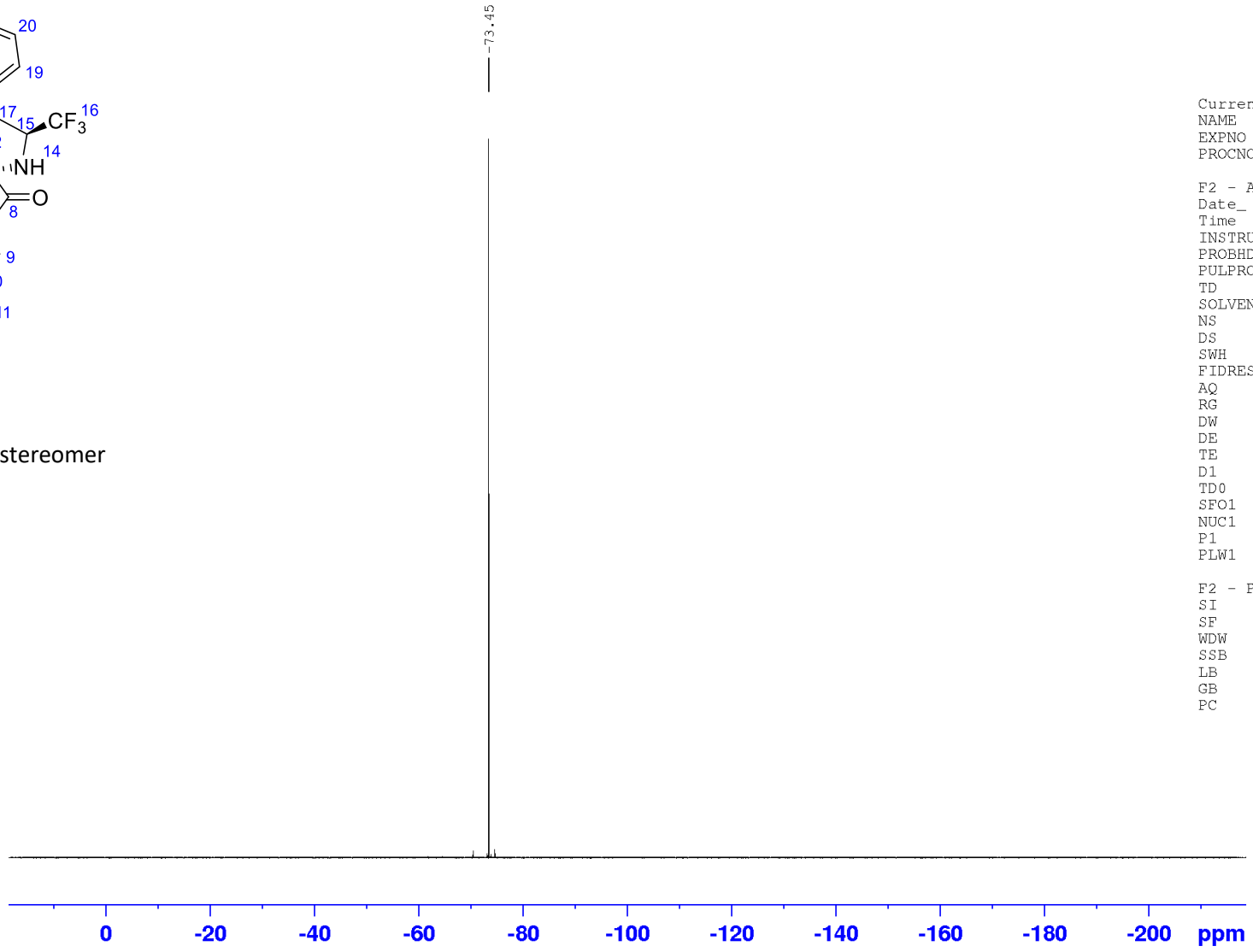
3c

Major diastereomer

^{19}F NMR

376 MHz

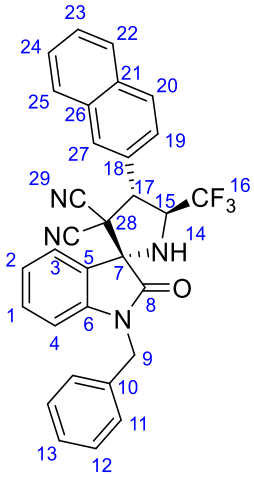
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.167
EXPNO                 21
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210706
Time               15.15 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   645
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                 11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



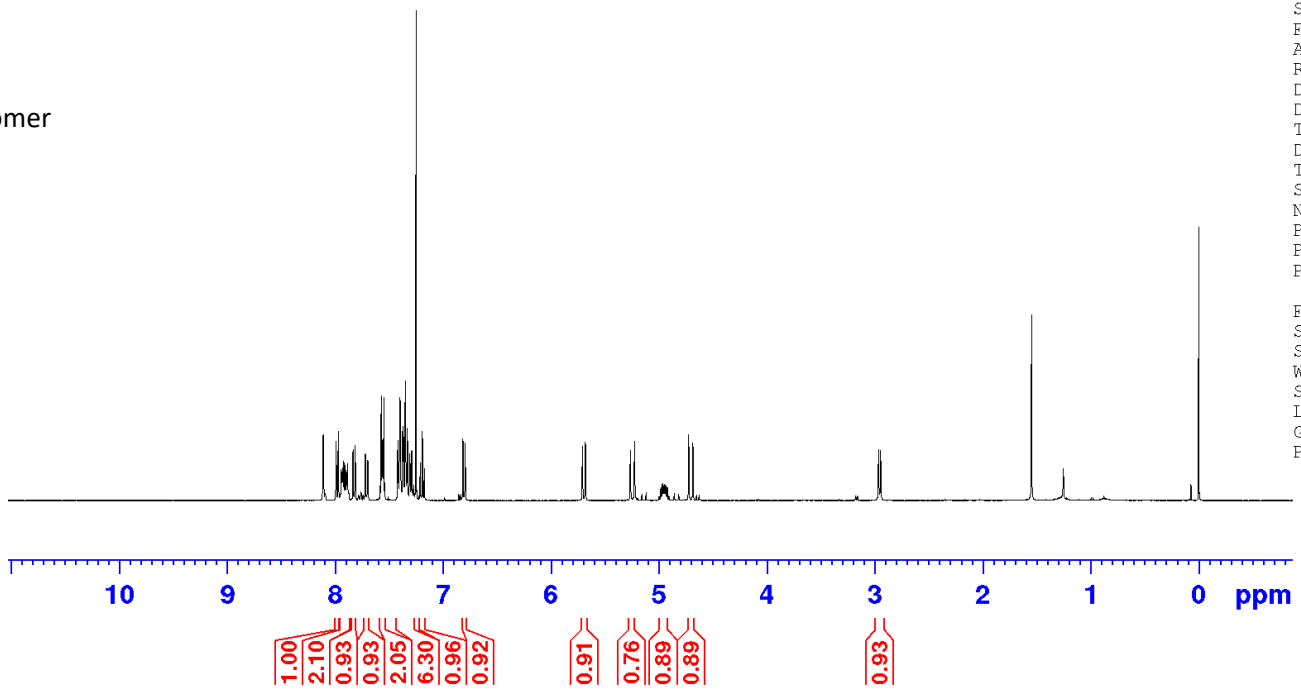
3d

Major diastereomer

^{1}H NMR

400 MHz

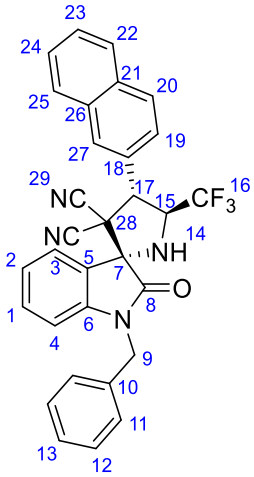
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.164
EXPNO                 50
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210805
Time              16.09 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100116 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



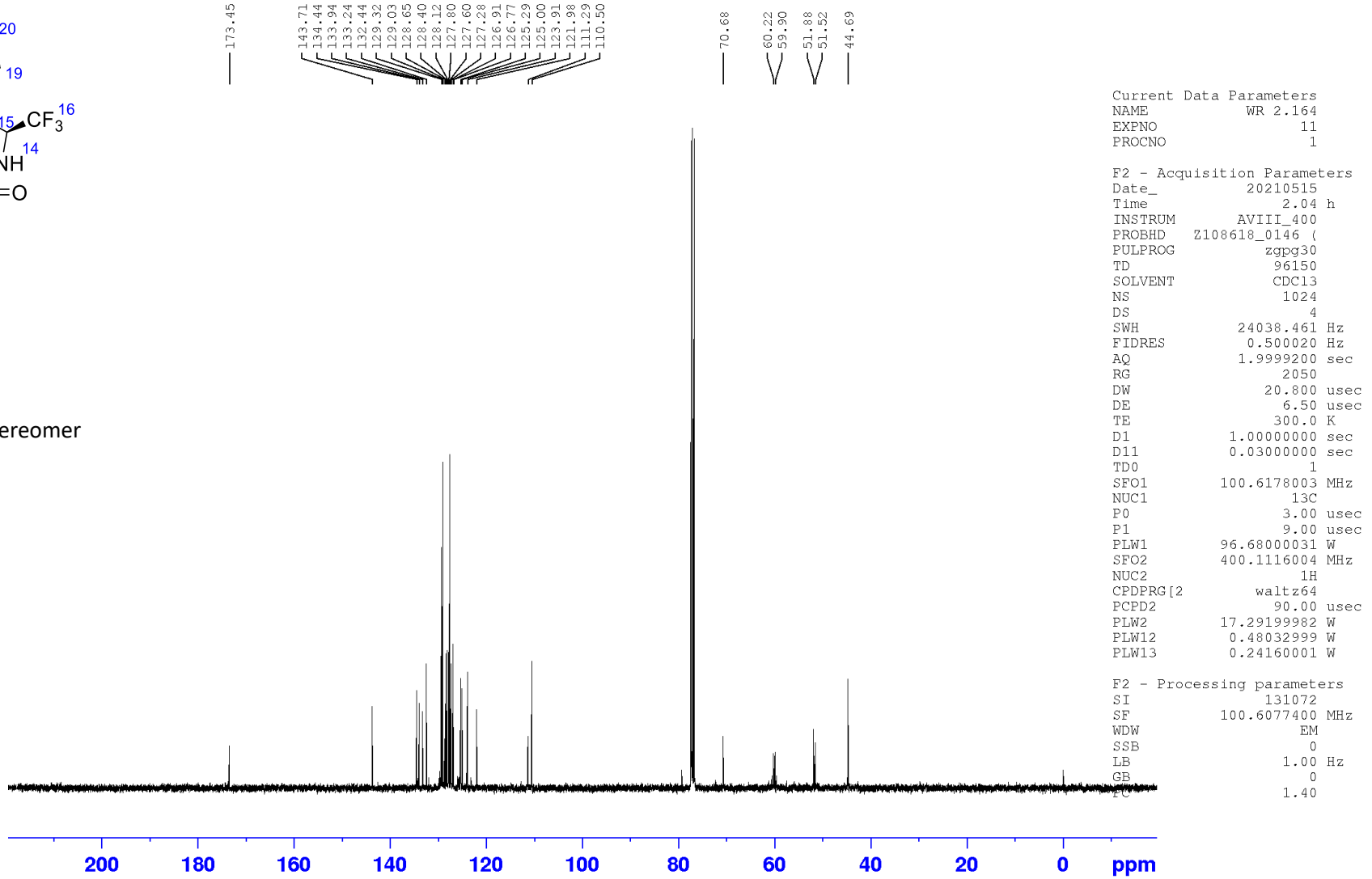
3d

Major diastereomer

^{13}C NMR

101 MHz

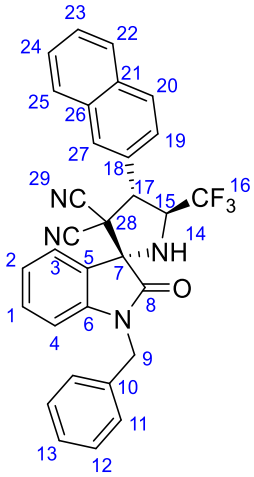
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.164
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210515
Time                2.04 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            24038.461 Hz
FIDRES          0.500020 Hz
AQ              1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077400 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
                    1.40
```



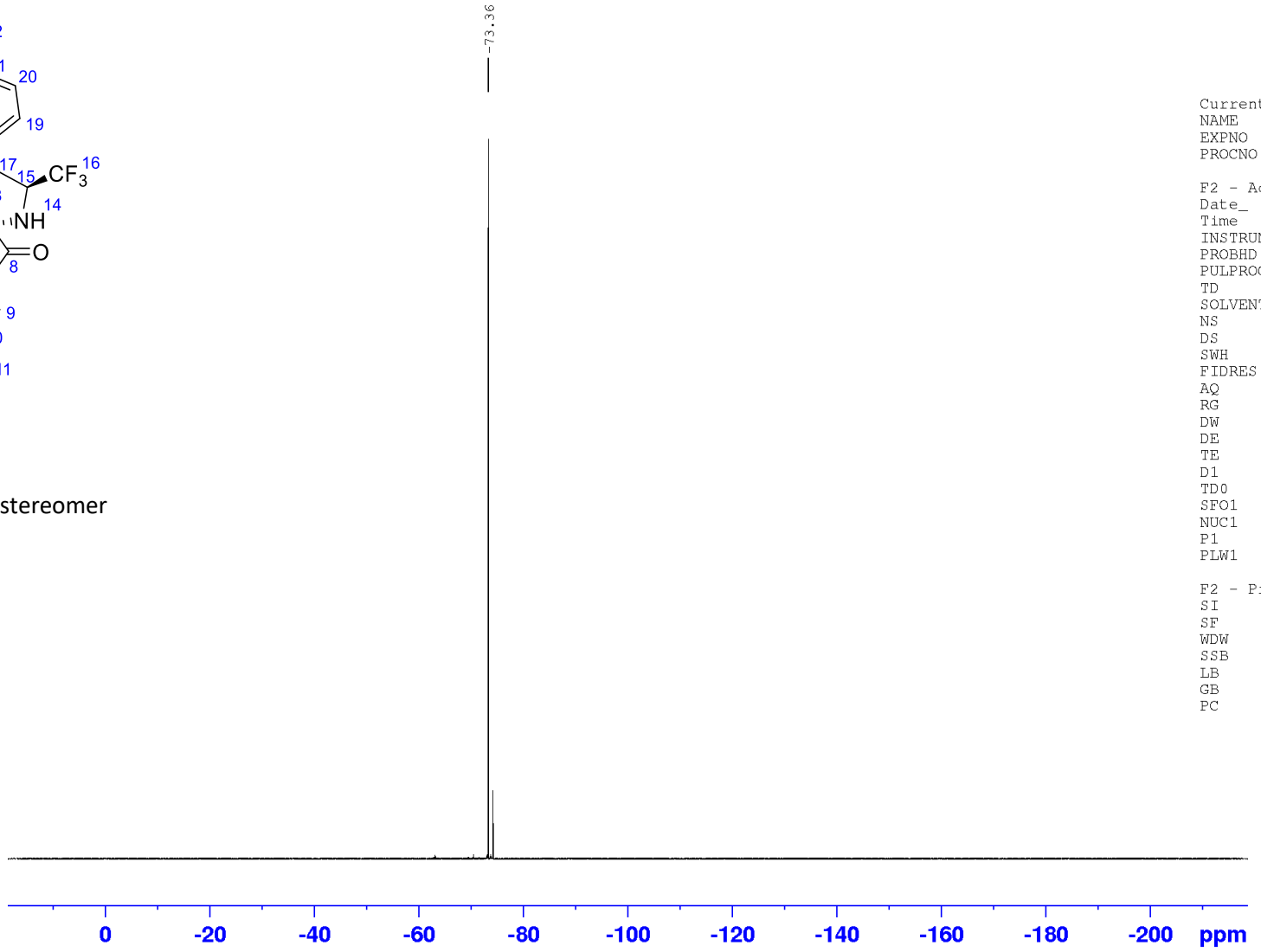
3d

Major diastereomer

^{19}F NMR

376 MHz

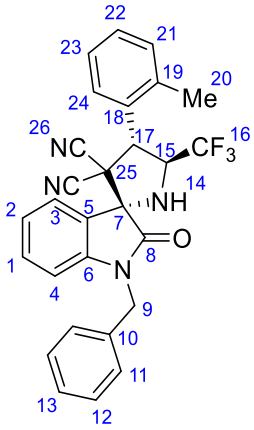
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.164
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210514
Time               18.49 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDC13
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   645
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



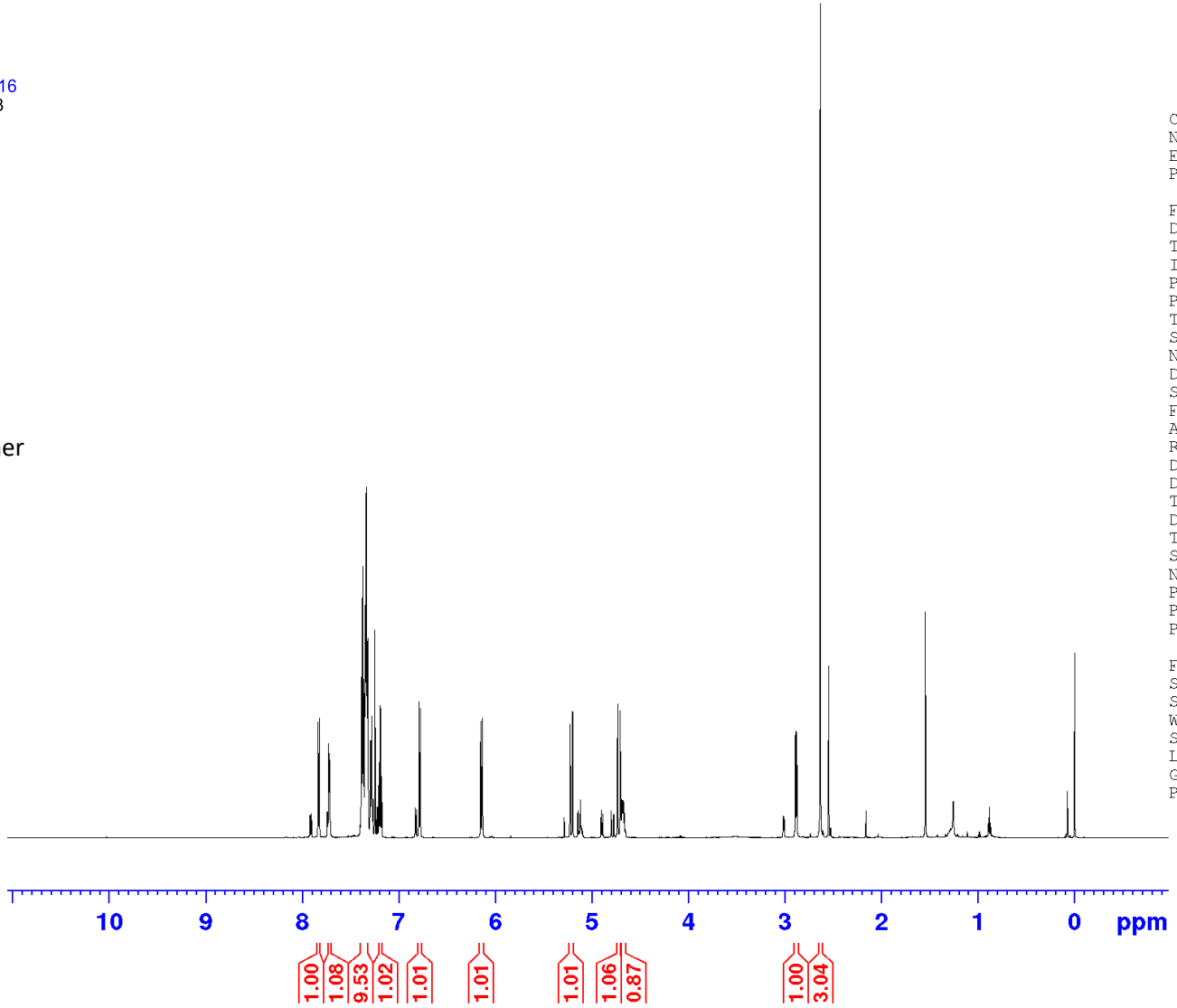
3e

Major diastereomer

^{1}H NMR

600 MHz

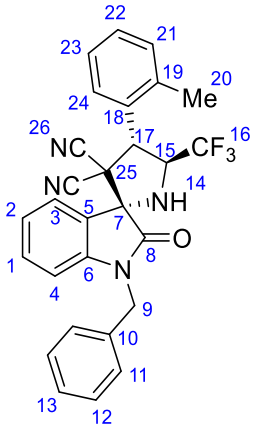
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.160 (600)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210720
Time              17.56 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG                 83.95
DW                41.600 usec
DE                12.10 usec
TE                302.0 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1        26.60000038 W

F2 - Processing parameters
SI                 65536
SF          600.1300193 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



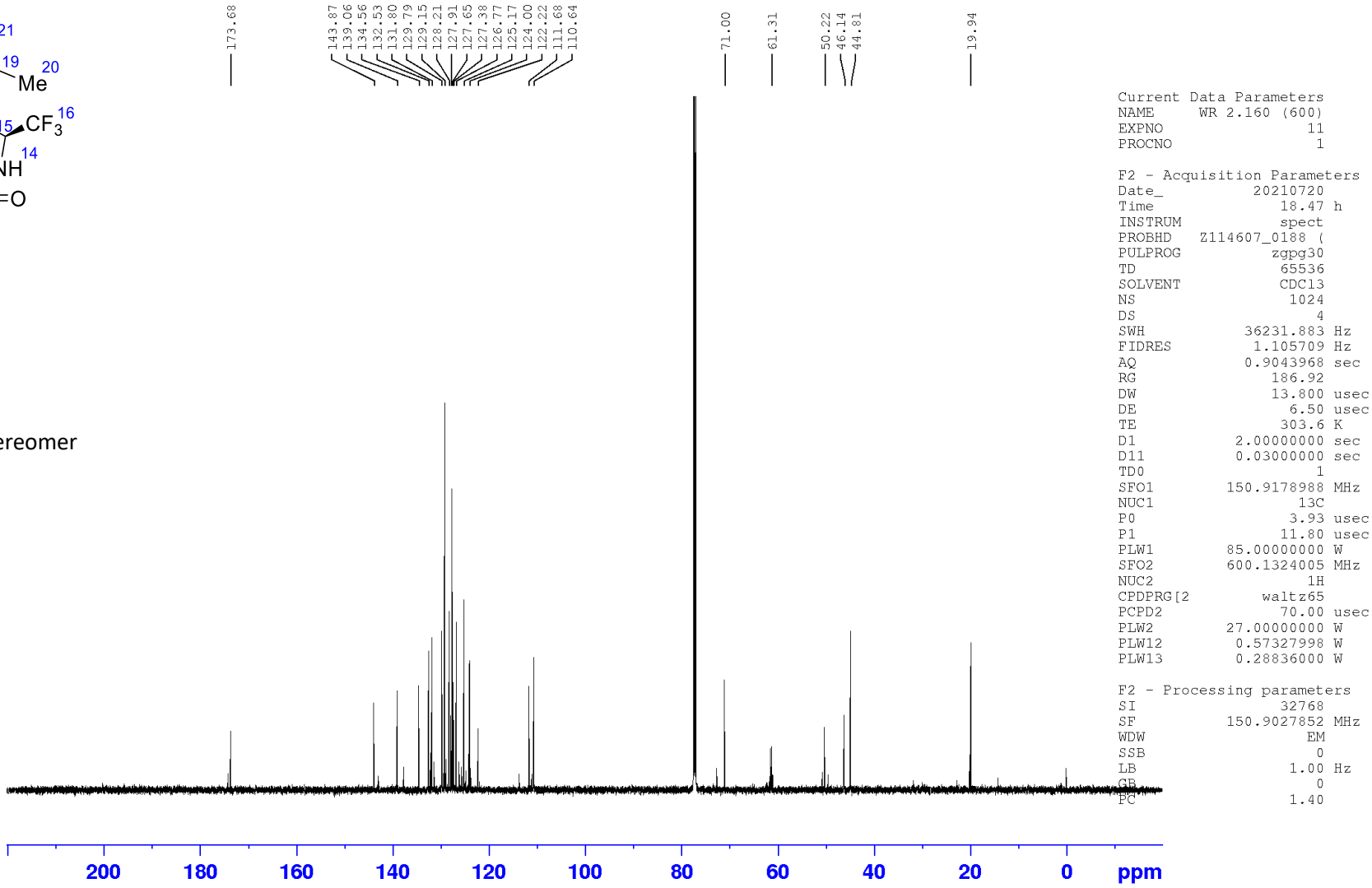
3e

Major diastereomer

^{13}C NMR

151 MHz

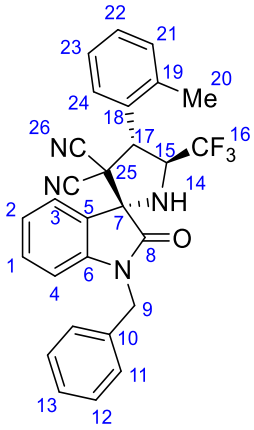
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.160 (600)
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210720
Time              18.47 h
INSTRUM             spect
PROBHD    Z114607_0188 (
PULPROG           zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               186.92
DW               13.800 usec
DE                6.50 usec
TE               303.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.9178988 MHz
NUC1                13C
P0                3.93 usec
P1               11.80 usec
PLW1        85.00000000 W
SFO2        600.1324005 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2            70.00 usec
PLW2        27.00000000 W
PLW12        0.57327998 W
PLW13        0.28836000 W

F2 - Processing parameters
SI                32768
SF          150.9027852 MHz
WDW                EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



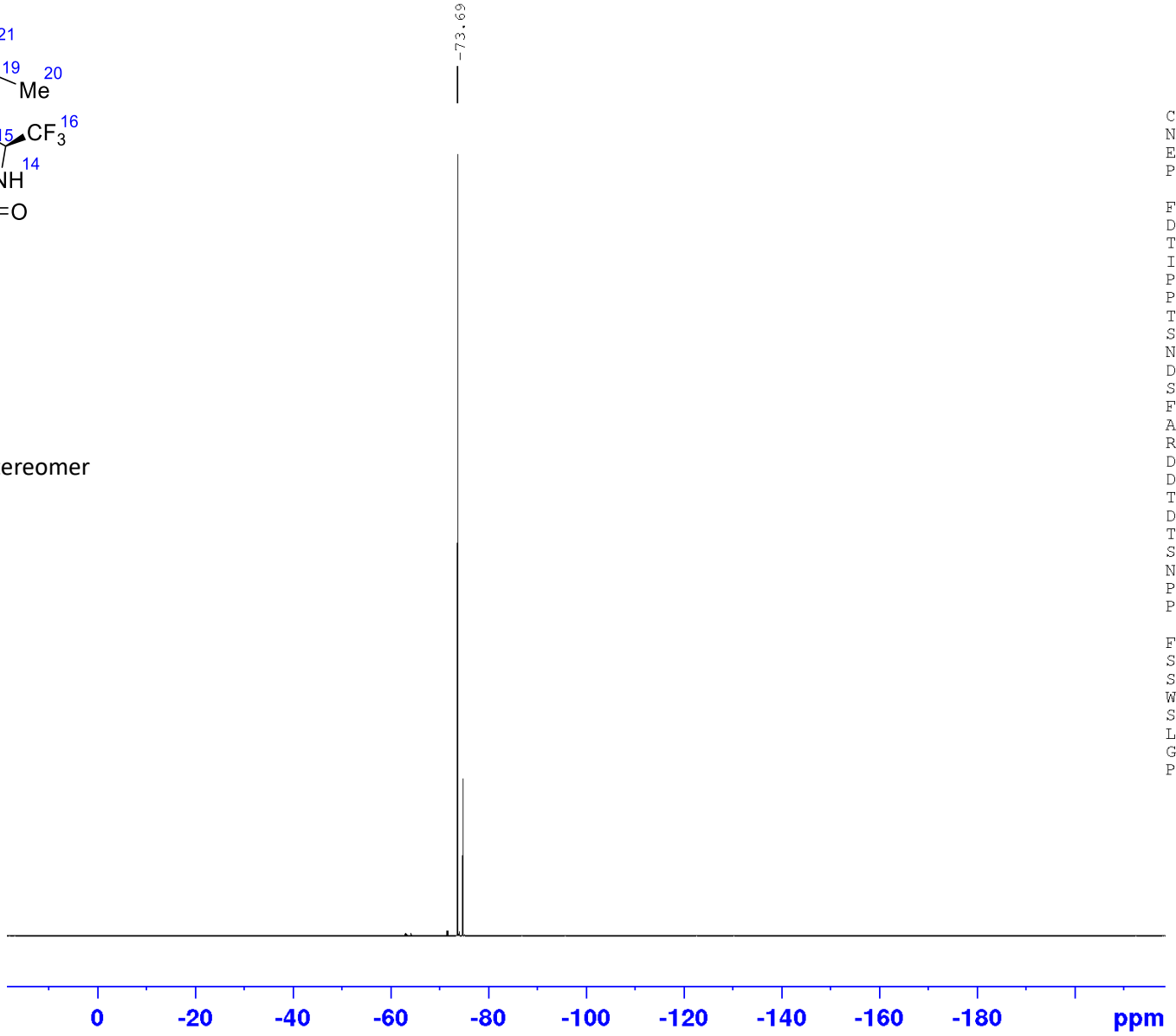
3e

Major diastereomer

^{19}F NMR

564 MHz

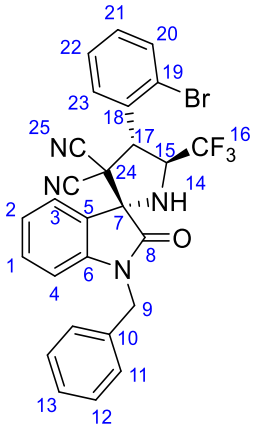
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.160 (600)
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210720
Time              20.57 h
INSTRUM            spect
PROBHD    Z114607_0188 (
PULPROG          zgflqn
TD               261896
SOLVENT           CDCl3
NS                   16
DS                    4
SWH          133928.578 Hz
FIDRES         1.022761 Hz
AQ            0.9777451 sec
RG               186.92
DW                3.733 usec
DE                6.70 usec
TE                301.9 K
D1           4.00000000 sec
TD0                   1
SFO1        564.6299217 MHz
NUC1                19F
P1                12.00 usec
PLW1        49.00000000 W

F2 - Processing parameters
SI               262144
SF          564.6863882 MHz
WDW                  EM
SSB       0
LB                0.50 Hz
GB        0
PC                2.00
```



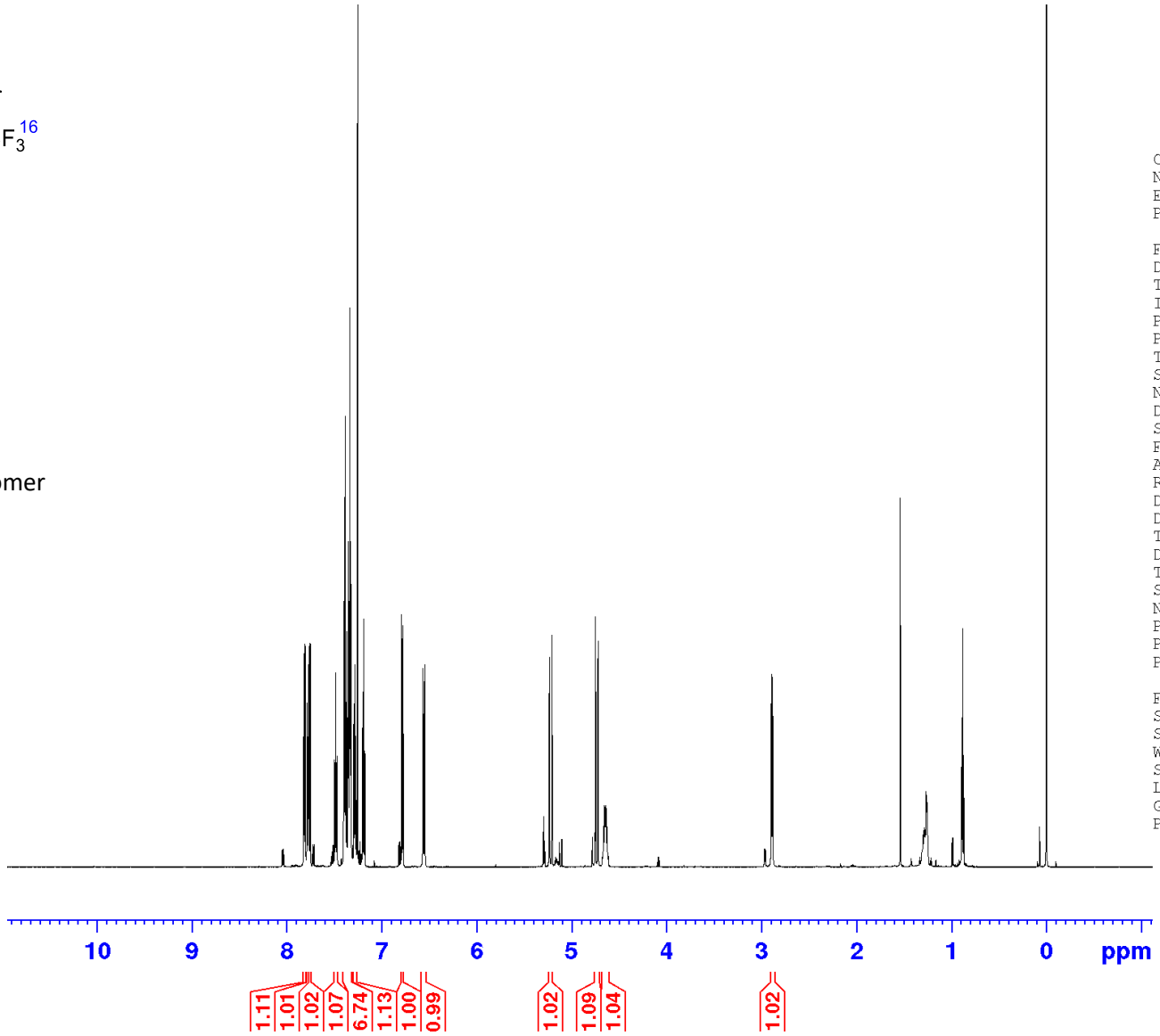
3f

Major diastereomer

^{1}H NMR

600 MHz

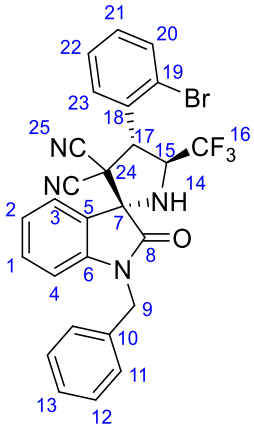
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.158 (600)
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210728
Time              20.44 h
INSTRUM             spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG                 119.2
DW                41.600 usec
DE                12.10 usec
TE                312.0 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300148 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



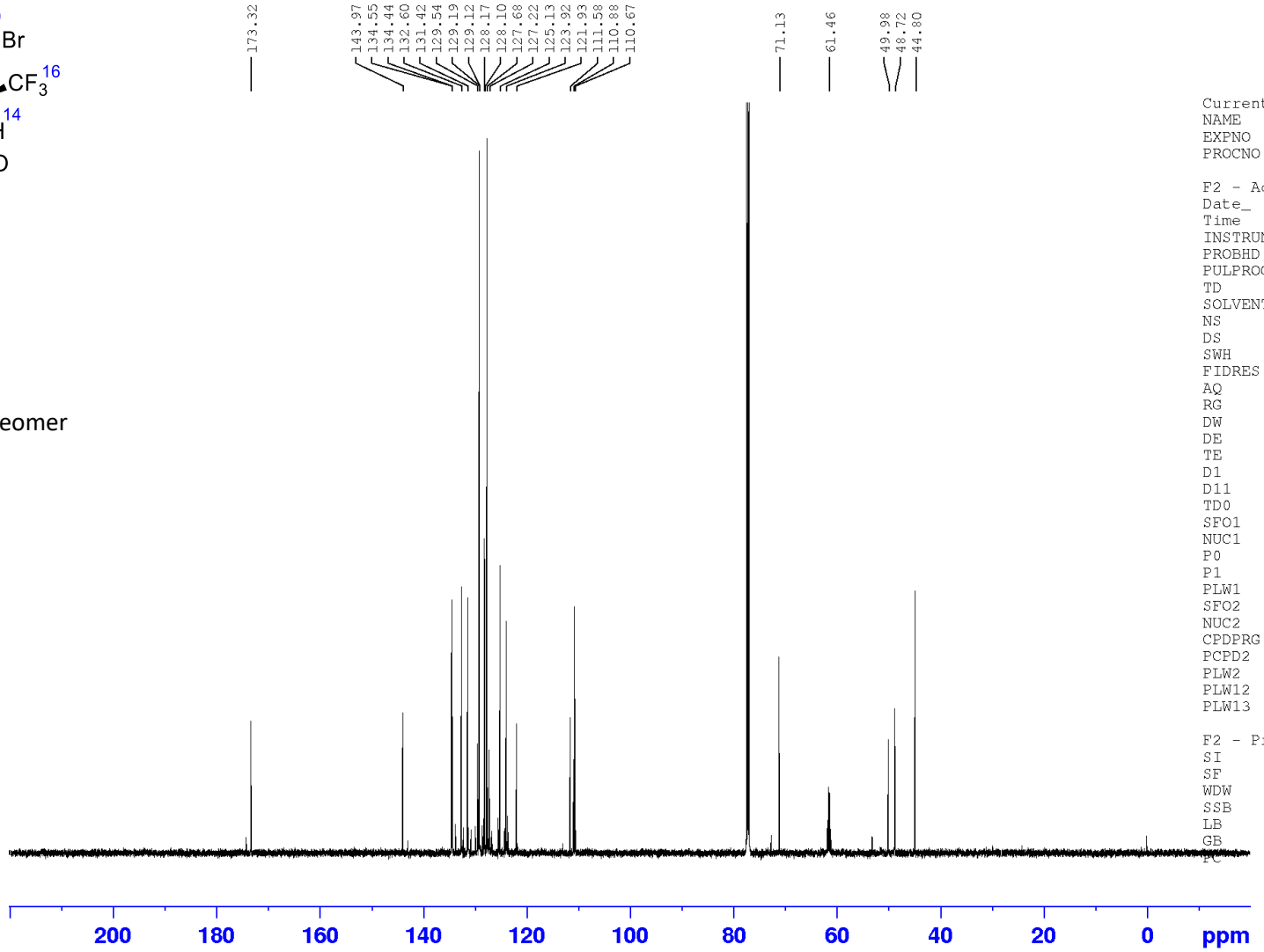
3f

Major diastereomer

^{13}C NMR

151 MHz

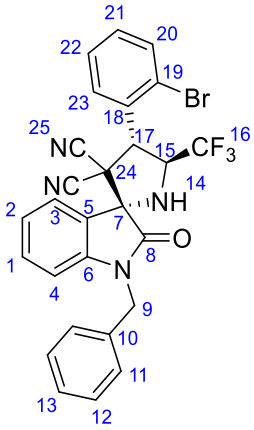
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.158 (600)
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210720
Time              21.55 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ             0.9043968 sec
RG                186.92
DW                13.800 usec
DE                 6.50 usec
TE                303.2 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1        150.9178988 MHz
NUC1                13C
P0                 3.93 usec
P1                11.80 usec
PLW1         85.00000000 W
SFO2         600.1324005 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             70.00 usec
PLW2         27.00000000 W
PLW12         0.57327998 W
PLW13         0.28836000 W

F2 - Processing parameters
SI                32768
SF          150.9027885 MHz
WDW                EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



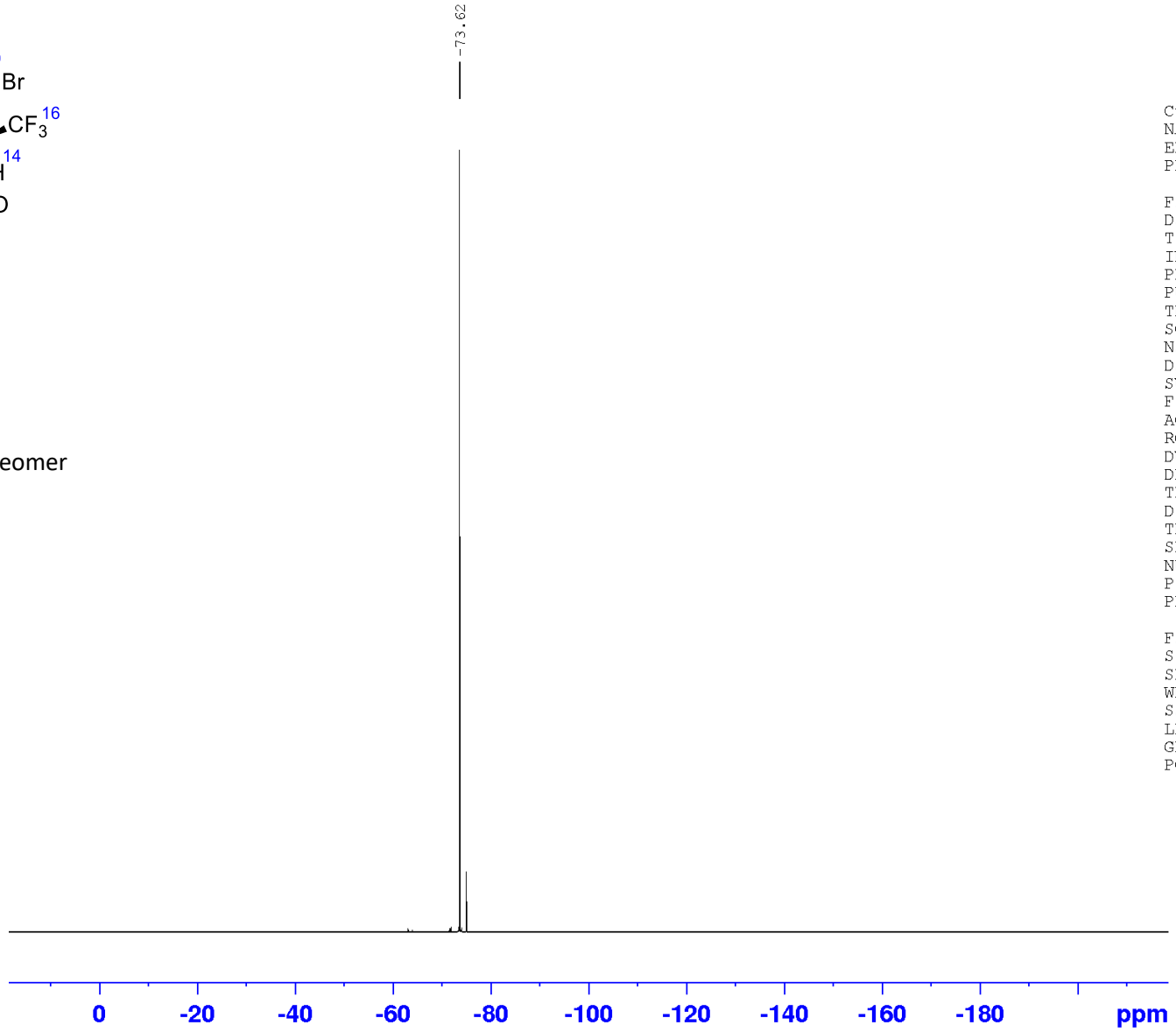
3f

Major diastereomer

^{19}F NMR

564 MHz

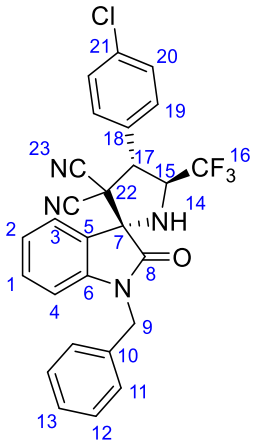
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.158 (600)
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210721
Time                0.04 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG           zgflqn
TD                261896
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           133928.578 Hz
FIDRES          1.022761 Hz
AQ              0.9777451 sec
RG                186.92
DW                 3.733 usec
DE                 6.70 usec
TE                301.2 K
D1           4.00000000 sec
TD0                    1
SFO1         564.6299217 MHz
NUC1                19F
P1                 12.00 usec
PLW1         49.00000000 W

F2 - Processing parameters
SI                262144
SF           564.6863882 MHz
WDW                   EM
SSB                    0
LB                  0.50 Hz
GB                     0
PC                  2.00
```



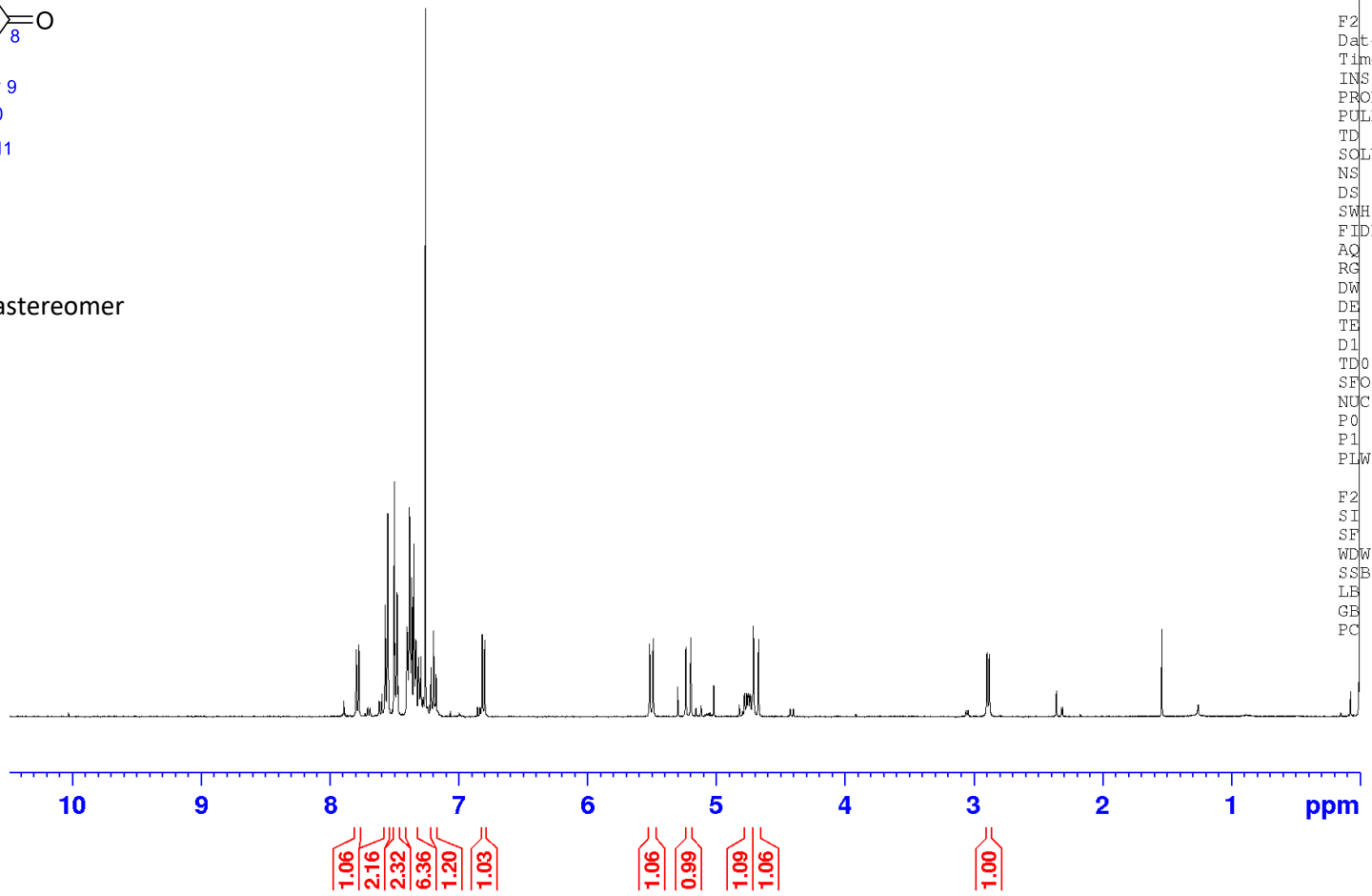
3g

Major diastereomer

^{1}H NMR

400 MHz

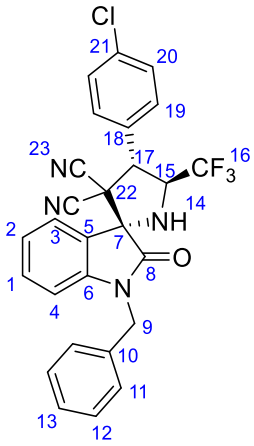
$CDCl_3$




```
Current Data Parameters
NAME                  WR 2.145
EXPNO                       10
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20210415
Time                     18.10 h
INSTRUM              AVIII_400
PROBHD    Z108618_0146 (
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8223.685 Hz
FIDRES                0.250967 Hz
AQ                    3.9845889 sec
RG                         256
DW                      60.800 usec
DE                      17.42 usec
TE                      300.0 K
D1                    1.00000000 sec
TD0                          1
SFO1                400.1124708 MHz
NUC1                        1H
P0                       5.00 usec
P1                      15.00 usec
PLW1                17.29199982 W

F2 - Processing parameters
SI                       32768
SF                  400.1100104 MHz
WDW                         EM
SSB                          0
LB                       0.30 Hz
GB                           0
PC                        1.00
```



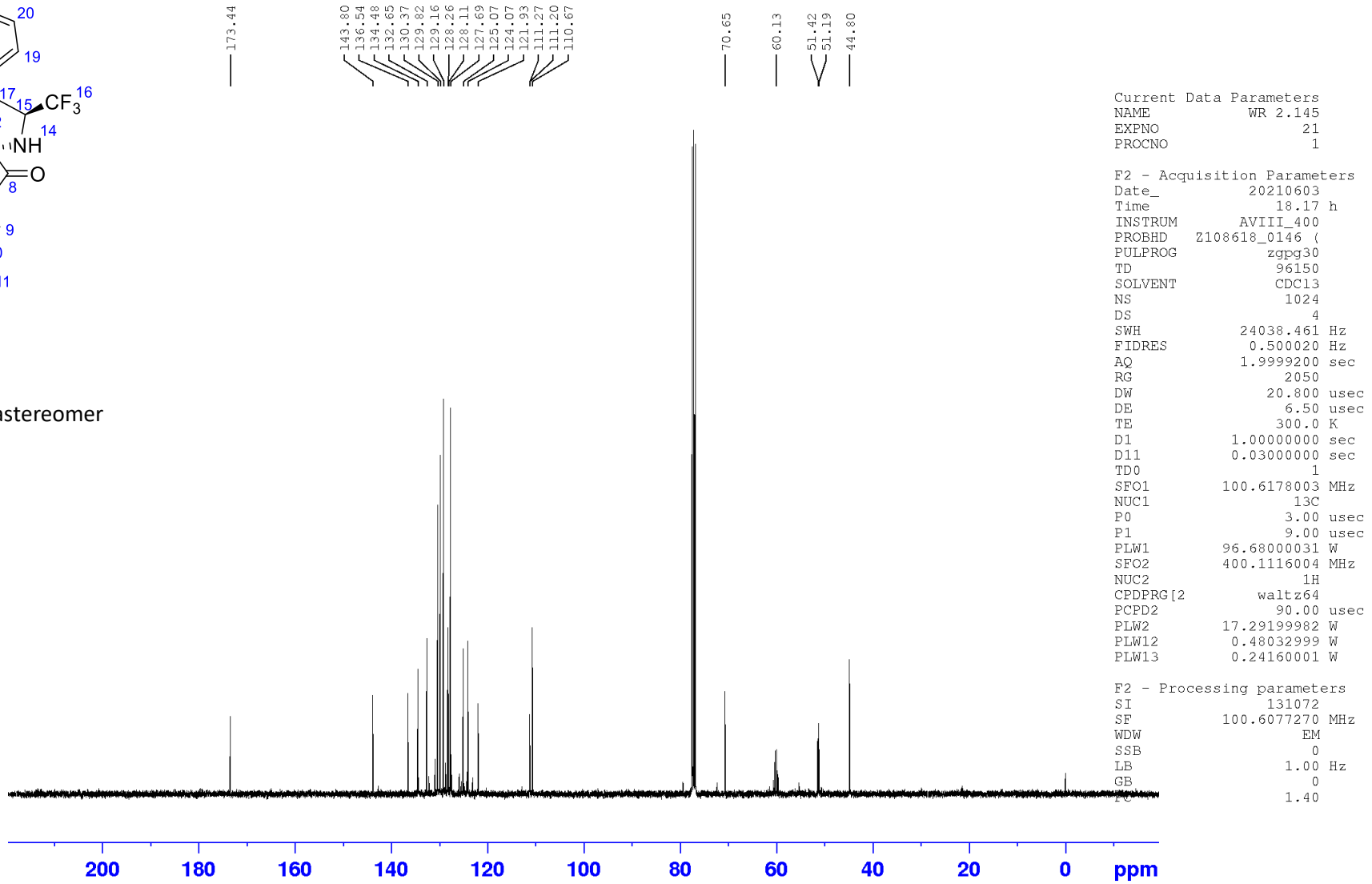
3g

Major diastereomer

^{13}C NMR

101 MHz

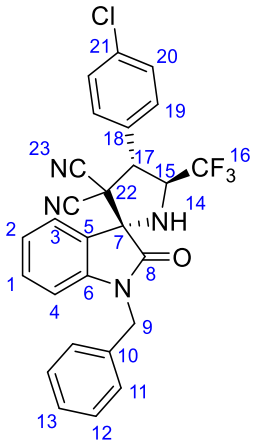
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.145
EXPNO                 21
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210603
Time              18.17 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1        100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2        400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077270 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
                   1.40
```



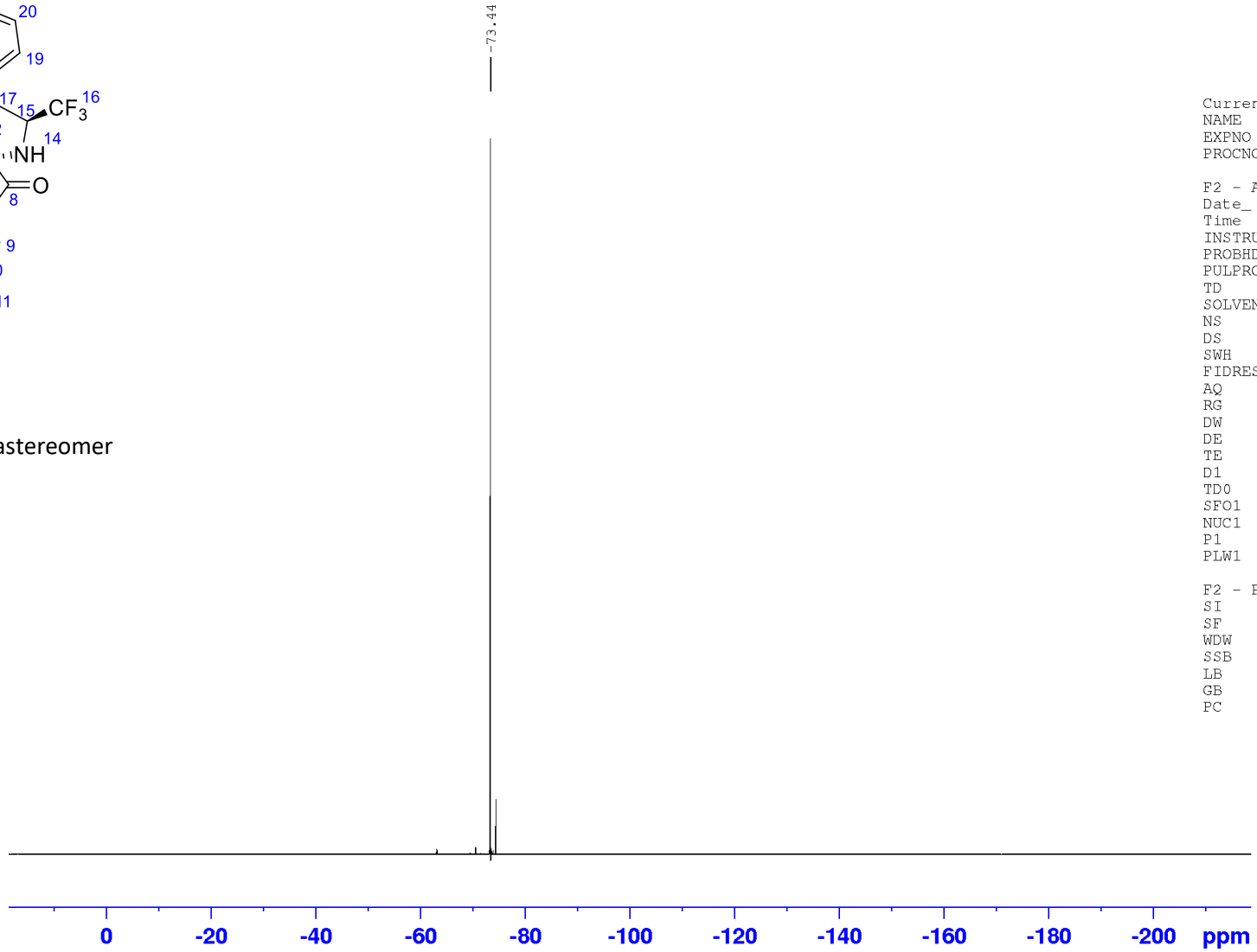
3g

Major diastereomer

^{19}F NMR

376 MHz

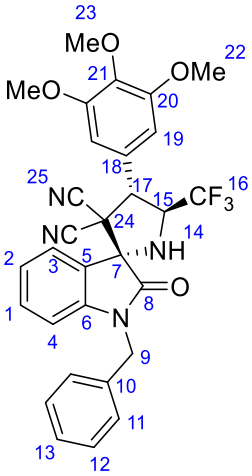
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.145
EXPNO                 27
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210603
Time              17.12 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           89285.711 Hz
FIDRES         0.681591 Hz
AQ            1.4671552 sec
RG                   724
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1        376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



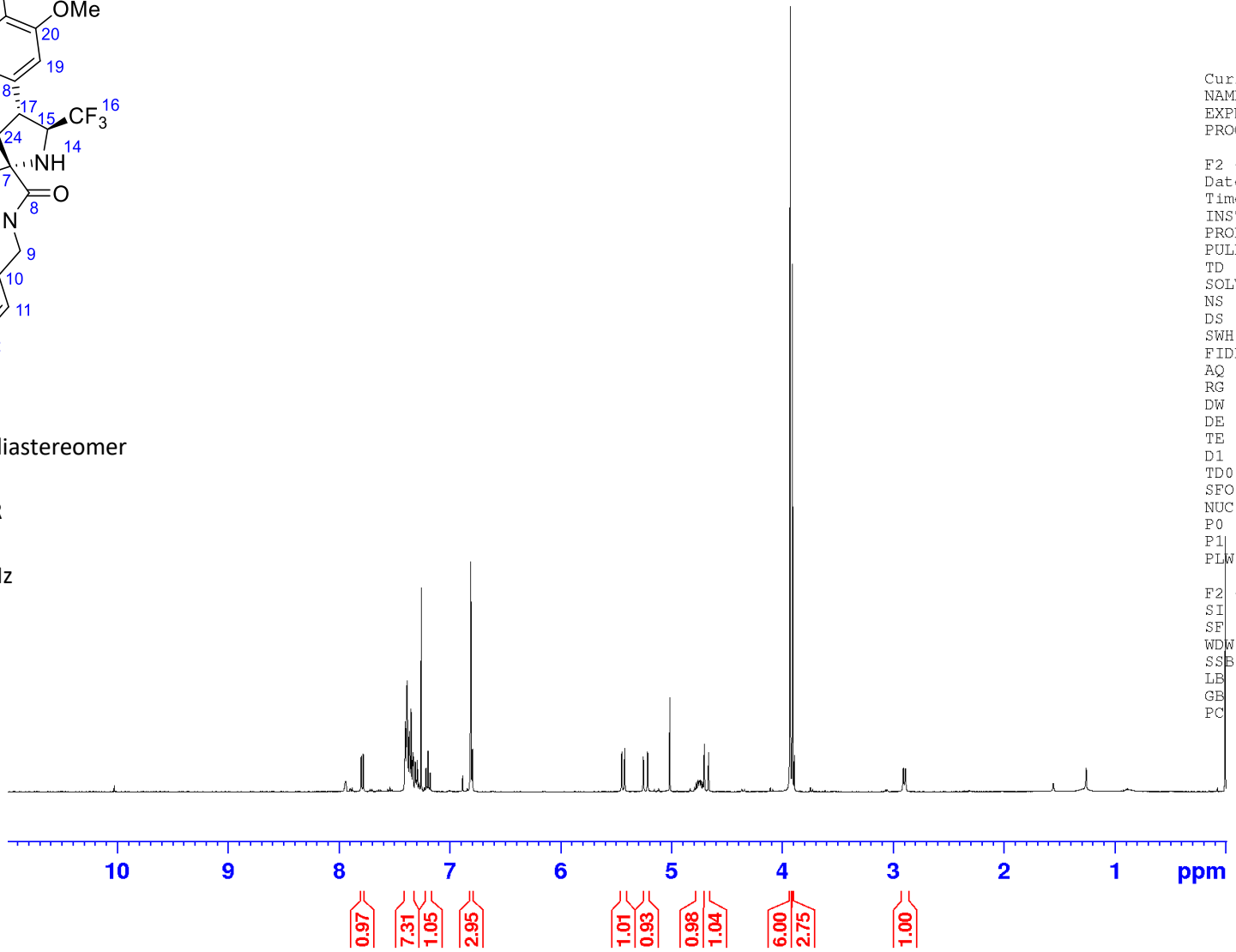
3h

Major diastereomer

^{1}H NMR

400 MHz

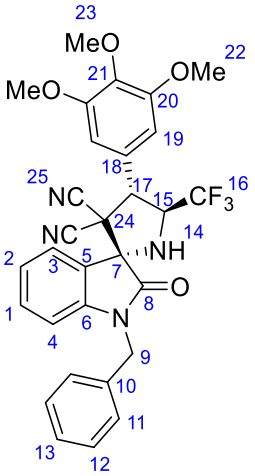
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.143
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210416
Time              17.50 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100102 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



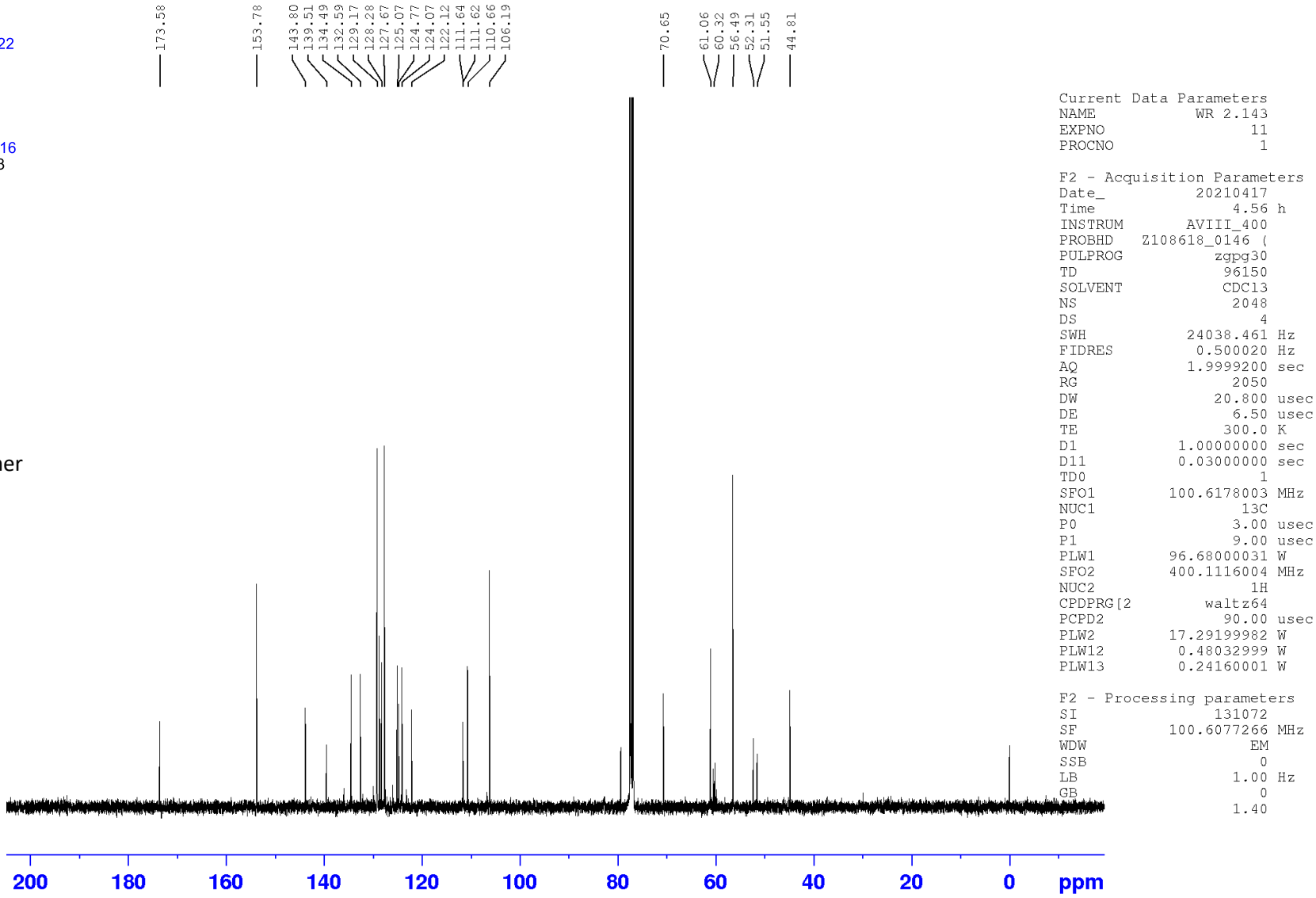
3h

Major diastereomer

^{13}C NMR

101 MHz

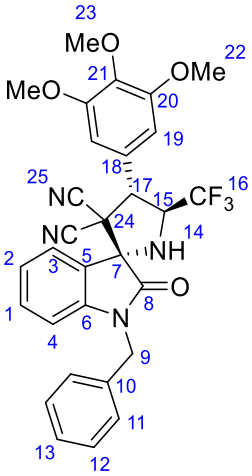
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.143
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210417
Time                4.56 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1           1.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1        100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1        96.68000031 W
SFO2        400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2        17.29199982 W
PLW12        0.48032999 W
PLW13        0.24160001 W

F2 - Processing parameters
SI                131072
SF          100.6077266 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
                   1.40
```



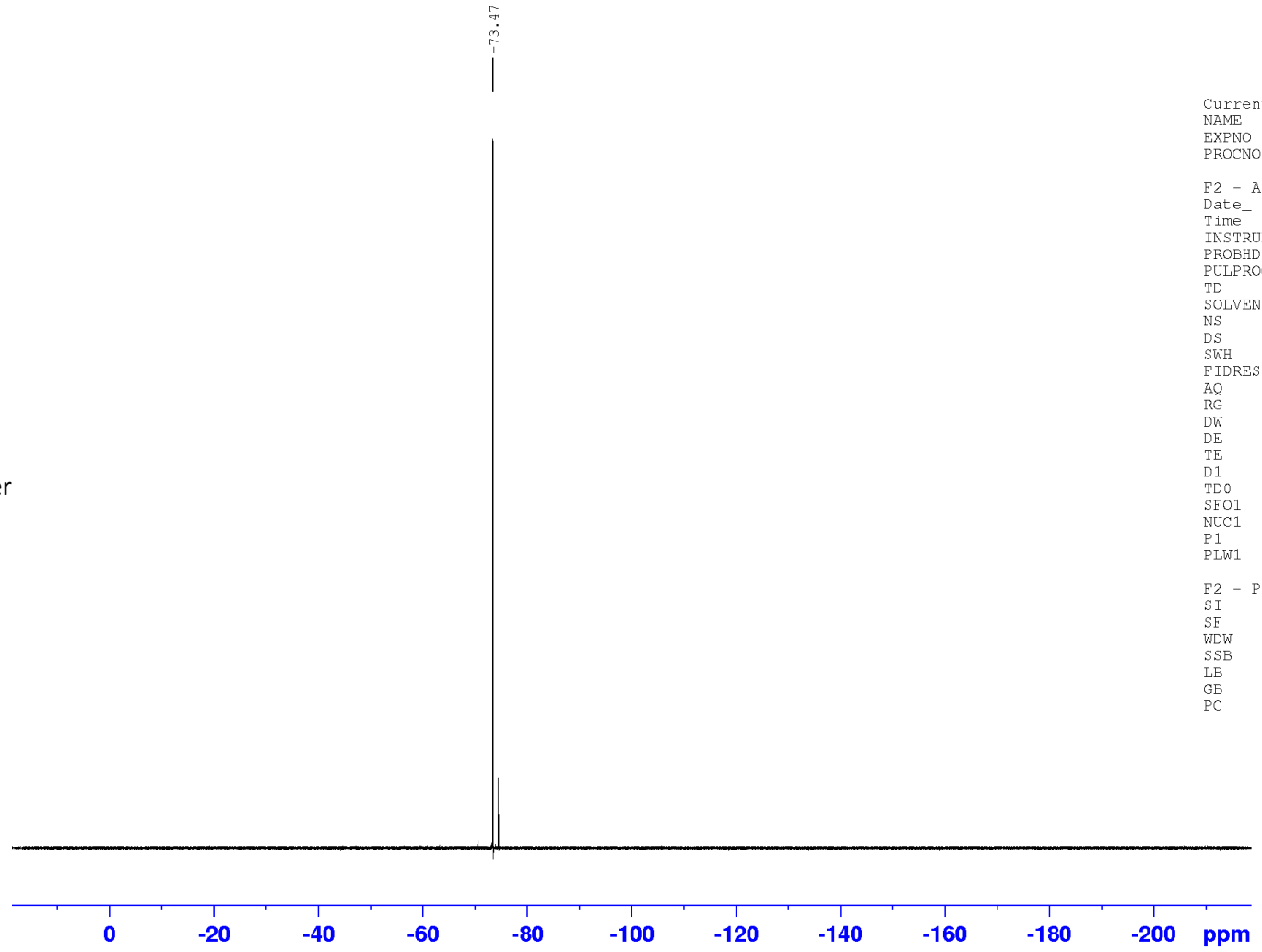
3h

Major diastereomer

^{19}F NMR

376 MHz

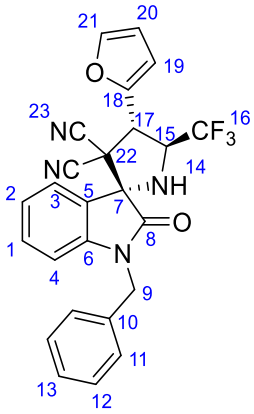
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.143
EXPNO                 33
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210621
Time              18.30 h
INSTRUM       AVIII_400
PROBHD   Z108618_0817 (
PULPROG               zg
TD                261992
SOLVENT            CDC13
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ            1.4671552 sec
RG                   256
DW                 5.600 usec
DE                 7.11 usec
TE                 296.8 K
D1           1.00000000 sec
TD0                    1
SFO1        376.2537307 MHz
NUC1                 19F
P1                11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.2913590 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```



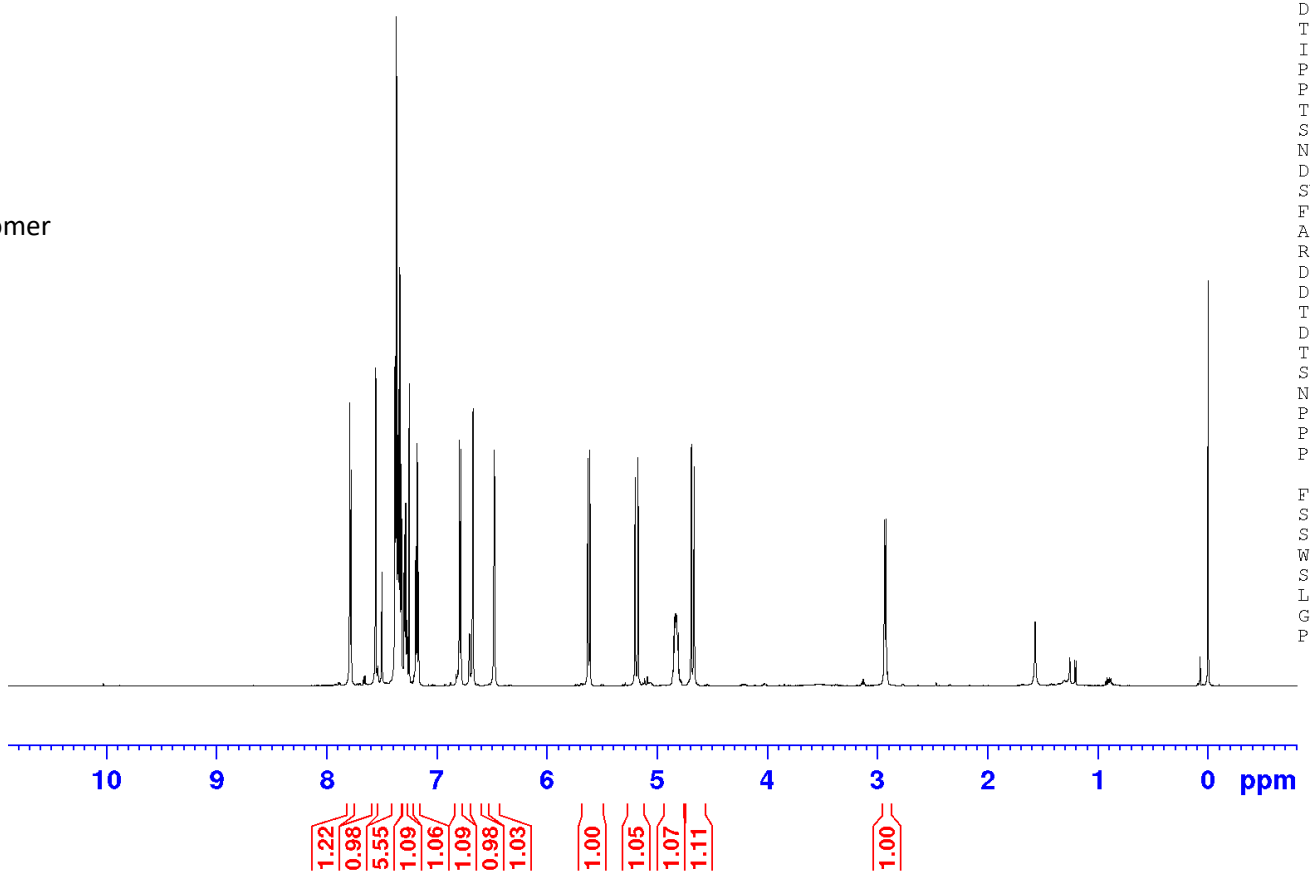
3i

Major diastereomer

^{1}H NMR

600 MHz

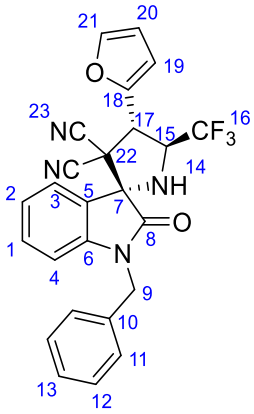
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.161 (600)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210622
Time                3.04 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                 83.95
DW                41.600 usec
DE                12.10 usec
TE                301.7 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300169 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



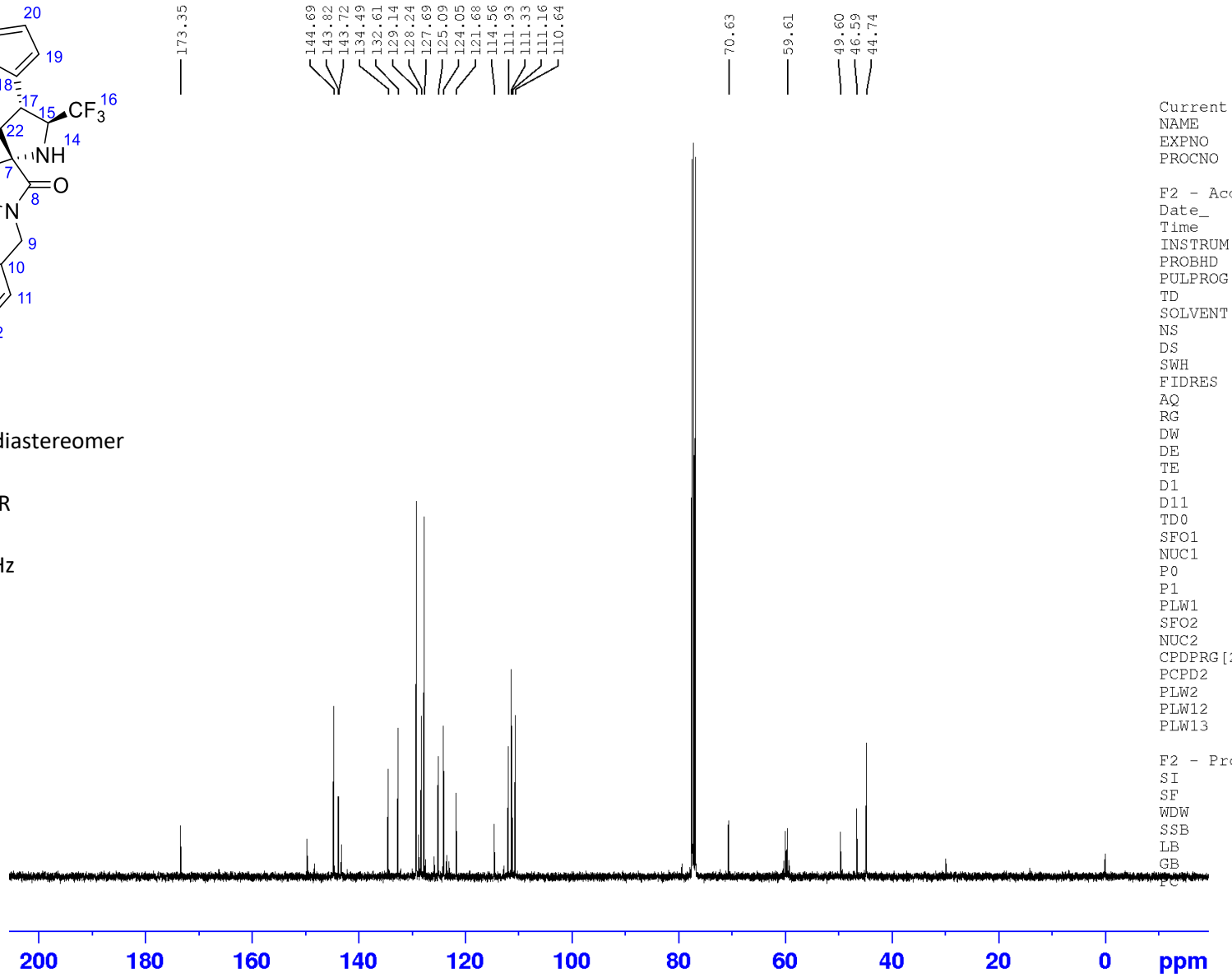
3i

Major diastereomer

^{13}C NMR

151 MHz

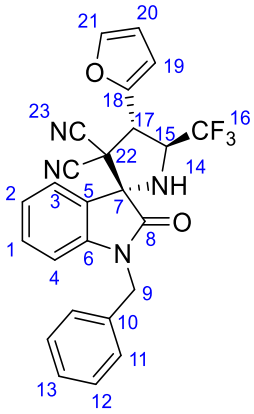
$CDCl_3$




```
Current Data Parameters
NAME                  WR 2.161
EXPNO                       12
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20210430
Time                     18.05 h
INSTRUM              AVIII_400
PROBHD    Z108618_0146 (
PULPROG                 zgpg30
TD                       96150
SOLVENT                  CDCl3
NS                        1024
DS                           4
SWH                  24038.461 Hz
FIDRES                0.500020 Hz
AQ                    1.9999200 sec
RG                        2050
DW                       20.800 usec
DE                        6.50 usec
TE                       300.0 K
D1                 1.00000000 sec
D11                0.03000000 sec
TD0                          1
SFO1               100.6178003 MHz
NUC1                        13C
P0                        3.00 usec
P1                        9.00 usec
PLW1               96.68000031 W
SFO2               400.1116004 MHz
NUC2                        1H
CPDPRG[2                waltz64
PCPD2                    90.00 usec
PLW2               17.29199982 W
PLW12               0.48032999 W
PLW13               0.24160001 W

F2 - Processing parameters
SI                       131072
SF                 100.6077271 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```



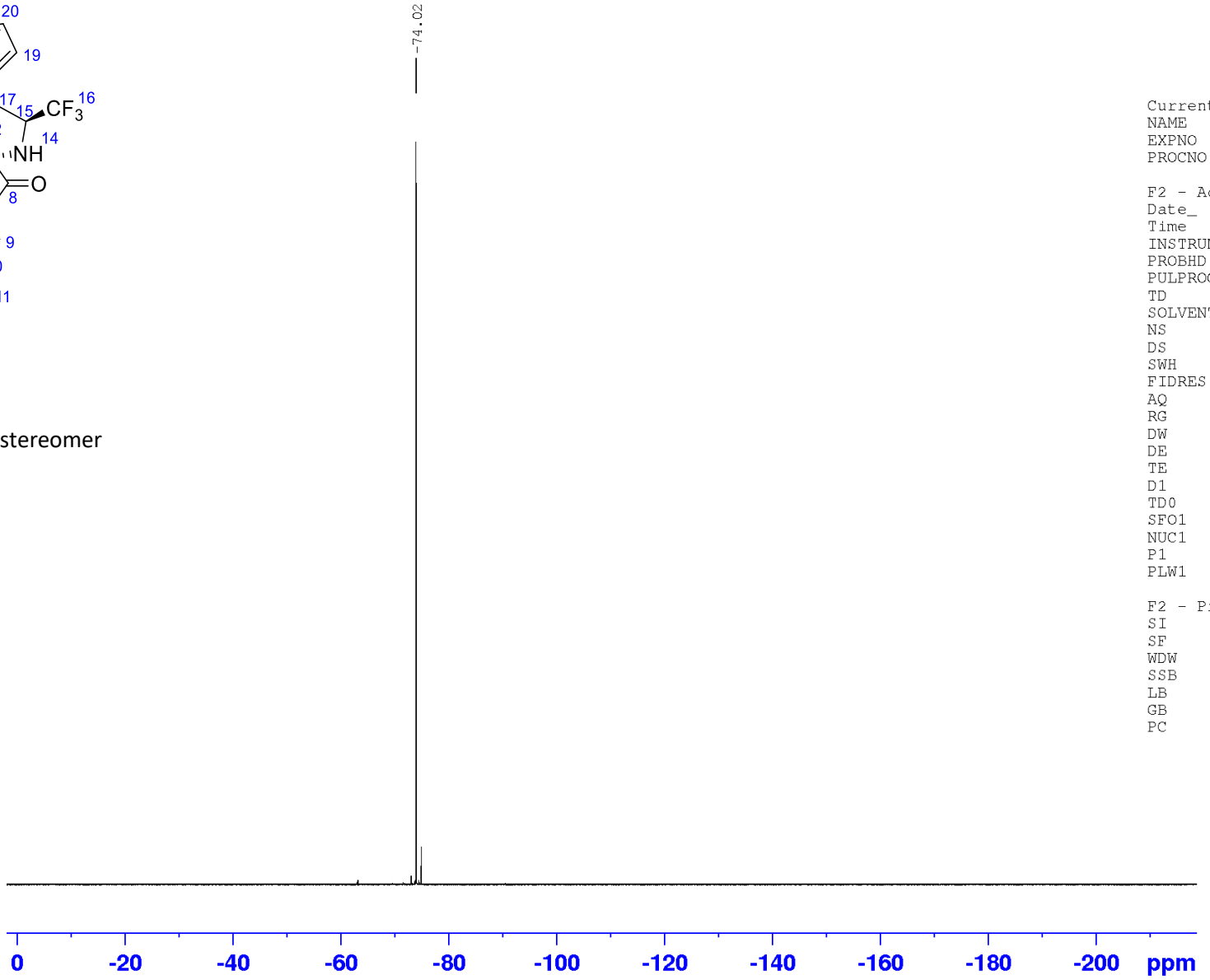
3i

Major diastereomer

^{19}F NMR

564 MHz

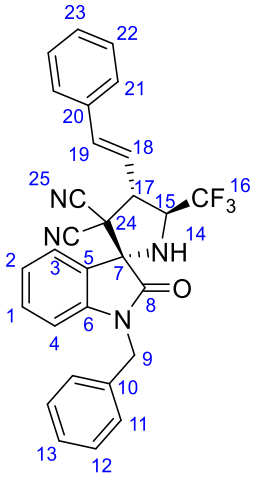
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.161
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210430
Time               16.55 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG                zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ              1.4671552 sec
RG                   645
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



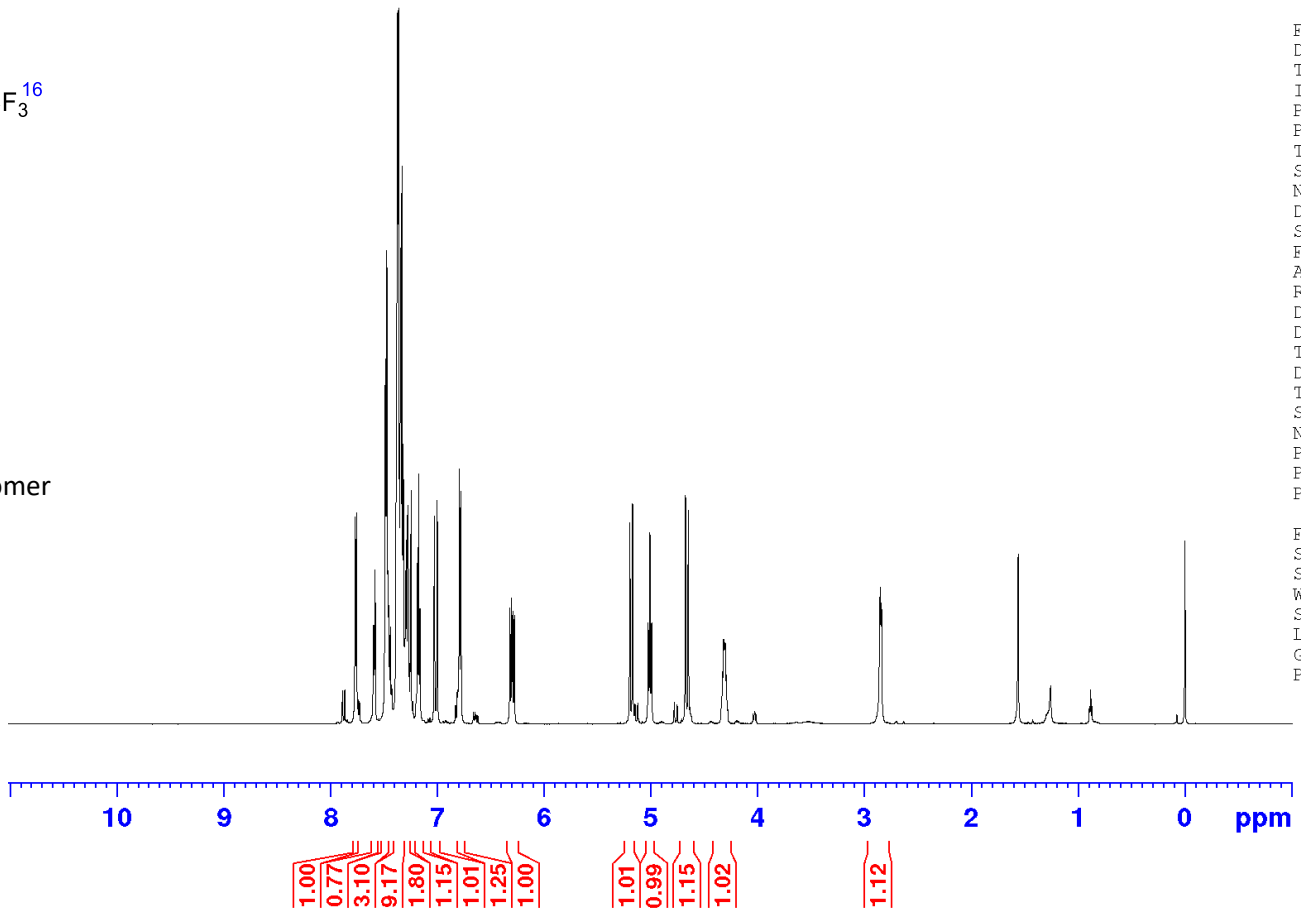
3j

Major diastereomer

^{1}H NMR

600 MHz

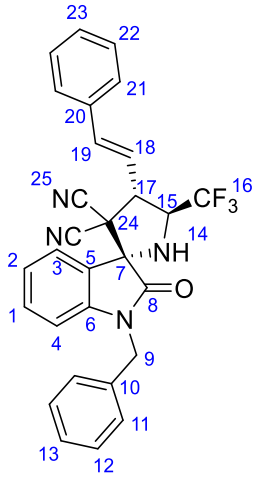
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.162 (600)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210716
Time              17.53 h
INSTRUM             spect
PROBHD    Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           12019.230 Hz
FIDRES         0.366798 Hz
AQ            2.7262976 sec
RG                 74.91
DW                41.600 usec
DE                12.10 usec
TE                303.8 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300211 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



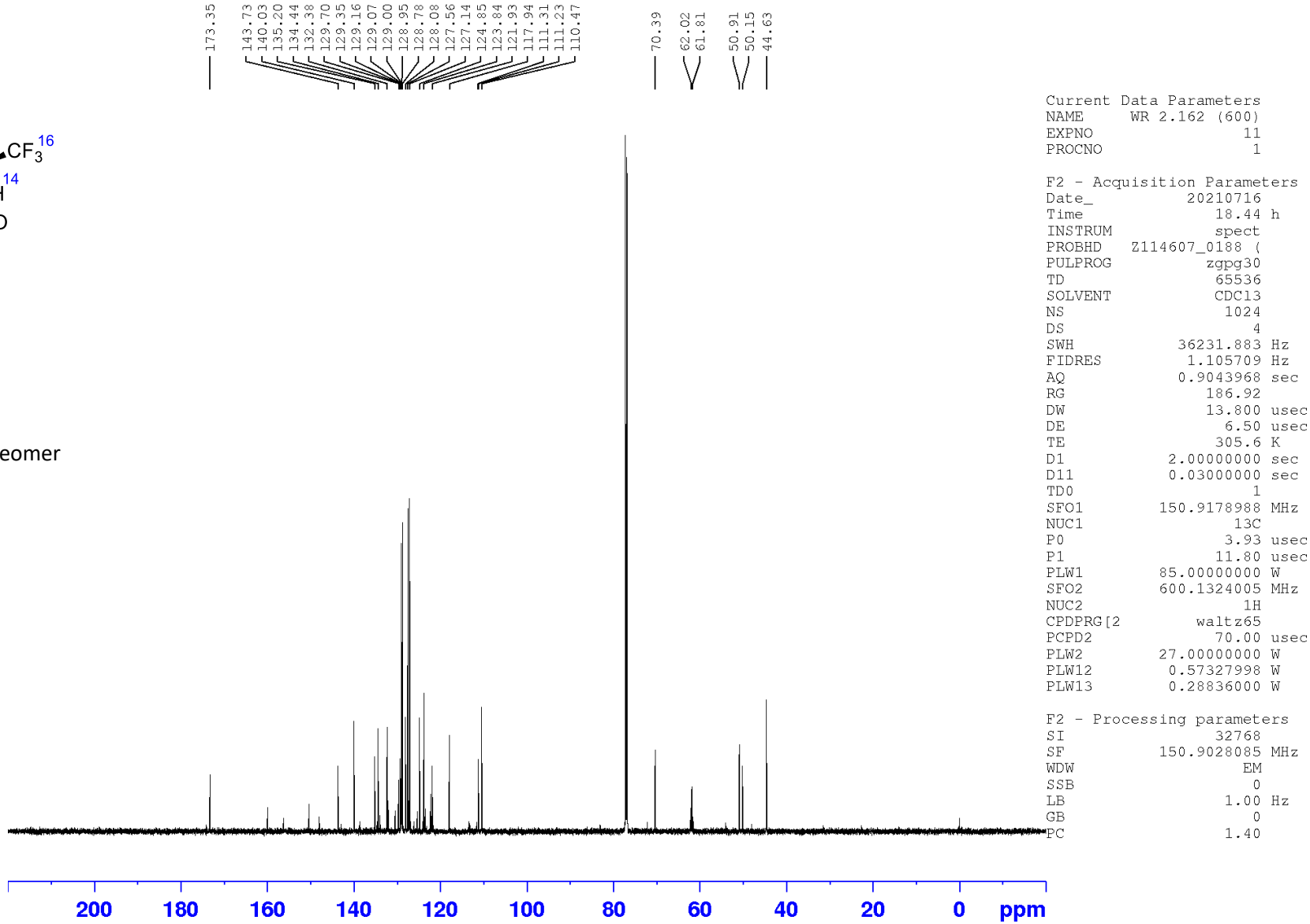
3j

Major diastereomer

^{13}C NMR

151 MHz

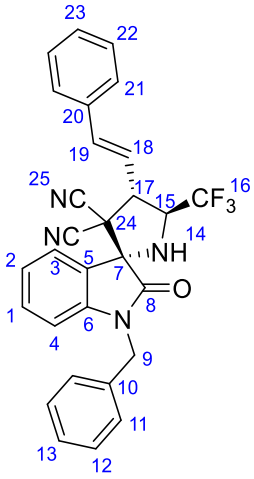
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.162 (600)
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210716
Time              18.44 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               186.92
DW               13.800 usec
DE                6.50 usec
TE               305.6 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.9178988 MHz
NUC1               13C
P0                3.93 usec
P1               11.80 usec
PLW1        85.00000000 W
SFO2        600.1324005 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2            70.00 usec
PLW2        27.00000000 W
PLW12        0.57327998 W
PLW13        0.28836000 W

F2 - Processing parameters
SI                32768
SF          150.9028085 MHz
WDW                EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                1.40
```



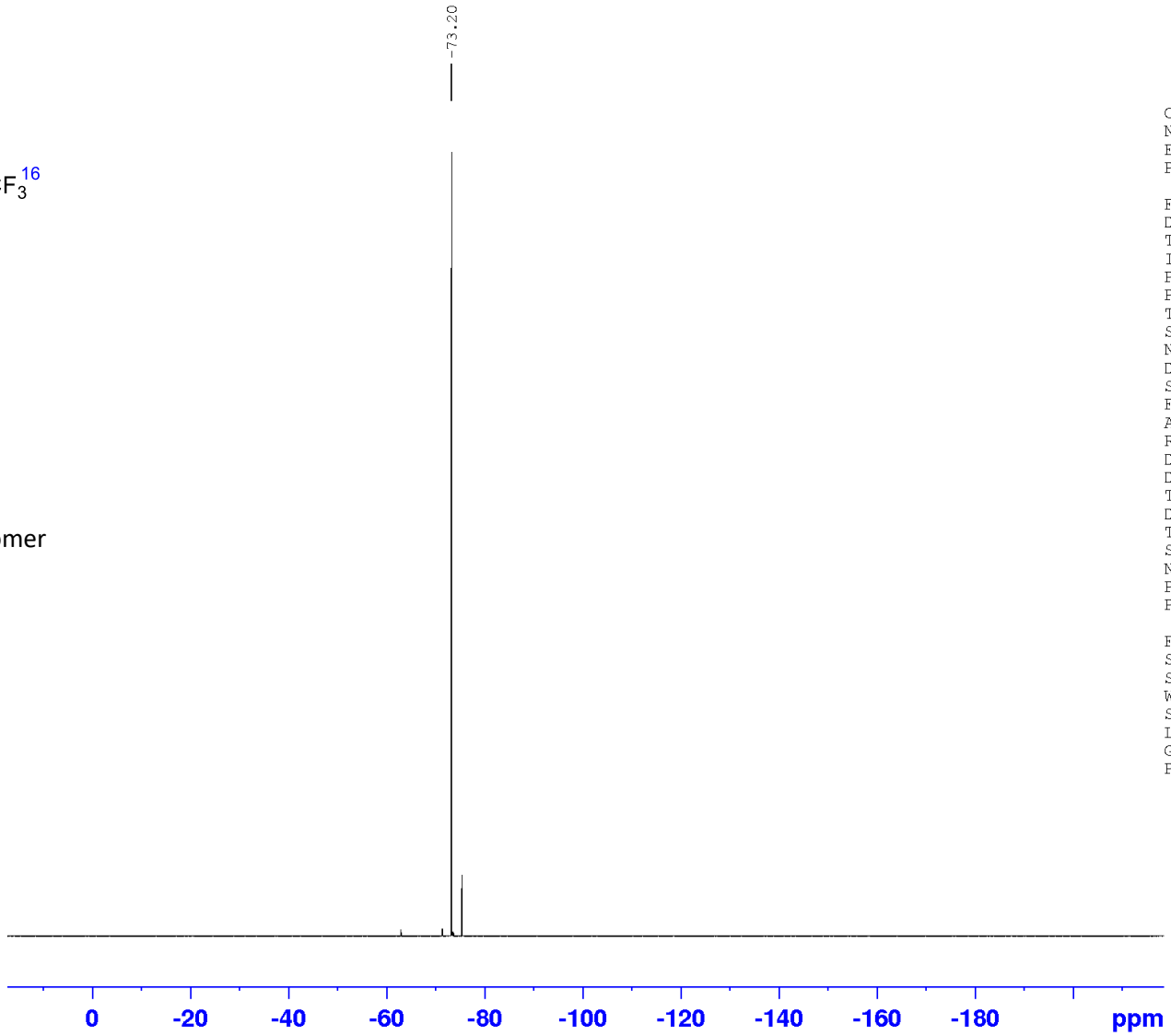
3j

Major diastereomer

^{19}F NMR

564 MHz

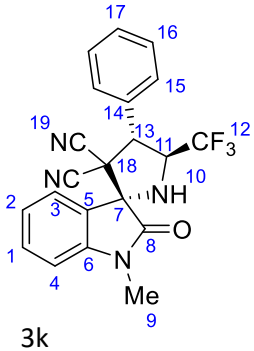
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.162 (600)
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210716
Time              20.53 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG          zgflqn
TD               261896
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           133928.578 Hz
FIDRES          1.022761 Hz
AQ             0.9777451 sec
RG                186.92
DW                 3.733 usec
DE                 6.70 usec
TE                303.9 K
D1           4.00000000 sec
TD0                    1
SFO1         564.6299217 MHz
NUC1                19F
P1                12.00 usec
PLW1         49.00000000 W

F2 - Processing parameters
SI                262144
SF           564.6863882 MHz
WDW                   EM
SSB                    0
LB                  0.50 Hz
GB                     0
PC                  2.00
```



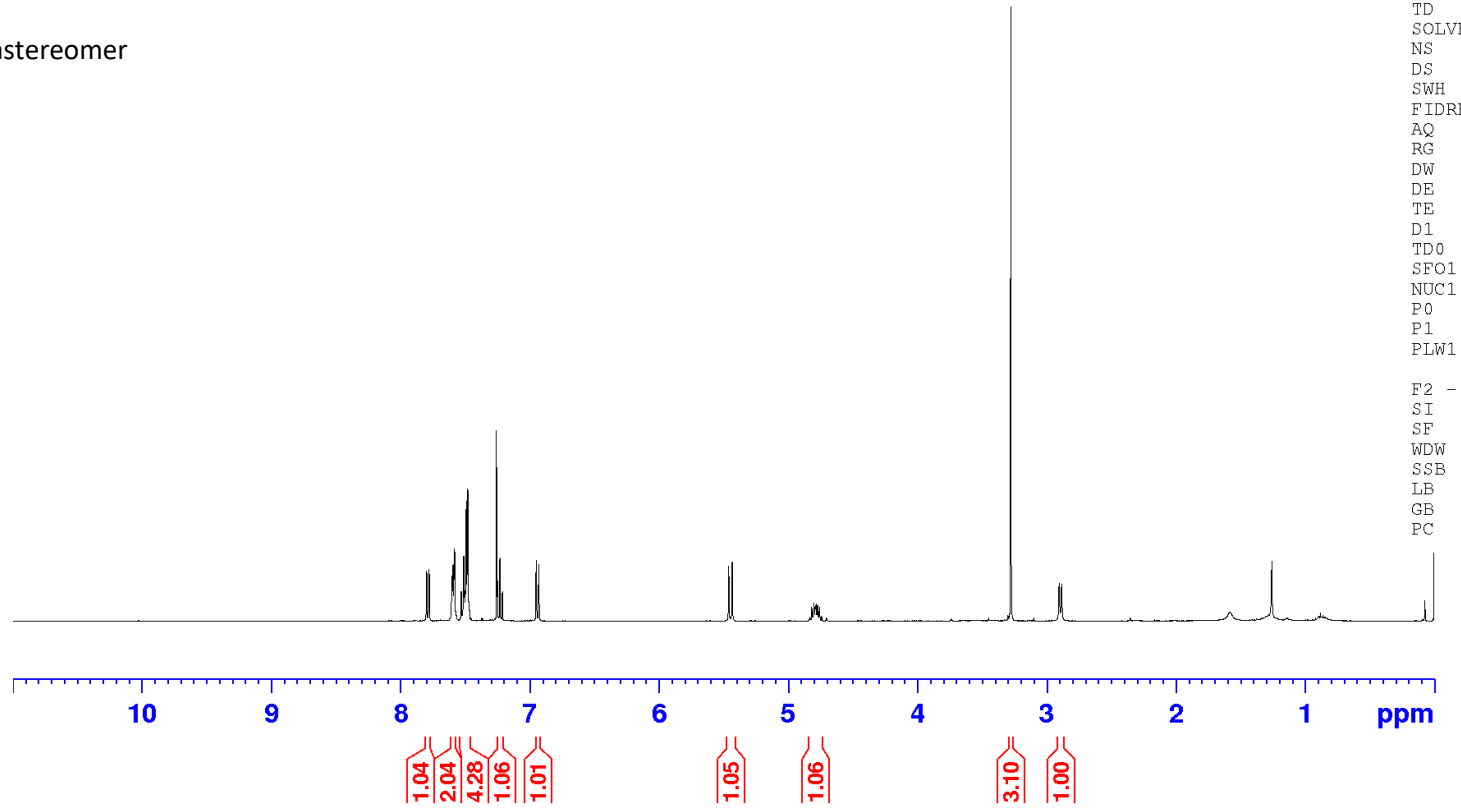
3k

Major diastereomer

^{1}H NMR

400 MHz

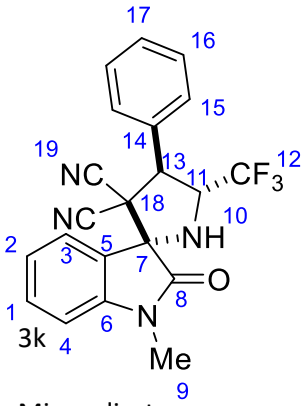
$CDCl_3$




```
Current Data Parameters
NAME         WR 2.168 F1
EXPNO                20
PROCNO                1

F2 - Acquisition Parameters
Date_          20210706
Time              15.20 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES        0.250967 Hz
AQ            3.9845889 sec
RG                  256
DW               60.800 usec
DE               17.42 usec
TE               300.0 K
D1            1.00000000 sec
TD0                   1
SFO1        400.1124708 MHz
NUC1                 1H
P0                5.00 usec
P1               15.00 usec
PLW1        17.29199982 W

F2 - Processing parameters
SI                32768
SF          400.1100105 MHz
WDW                  EM
SSB                   0
LB                0.30 Hz
GB                    0
PC                 1.00
```



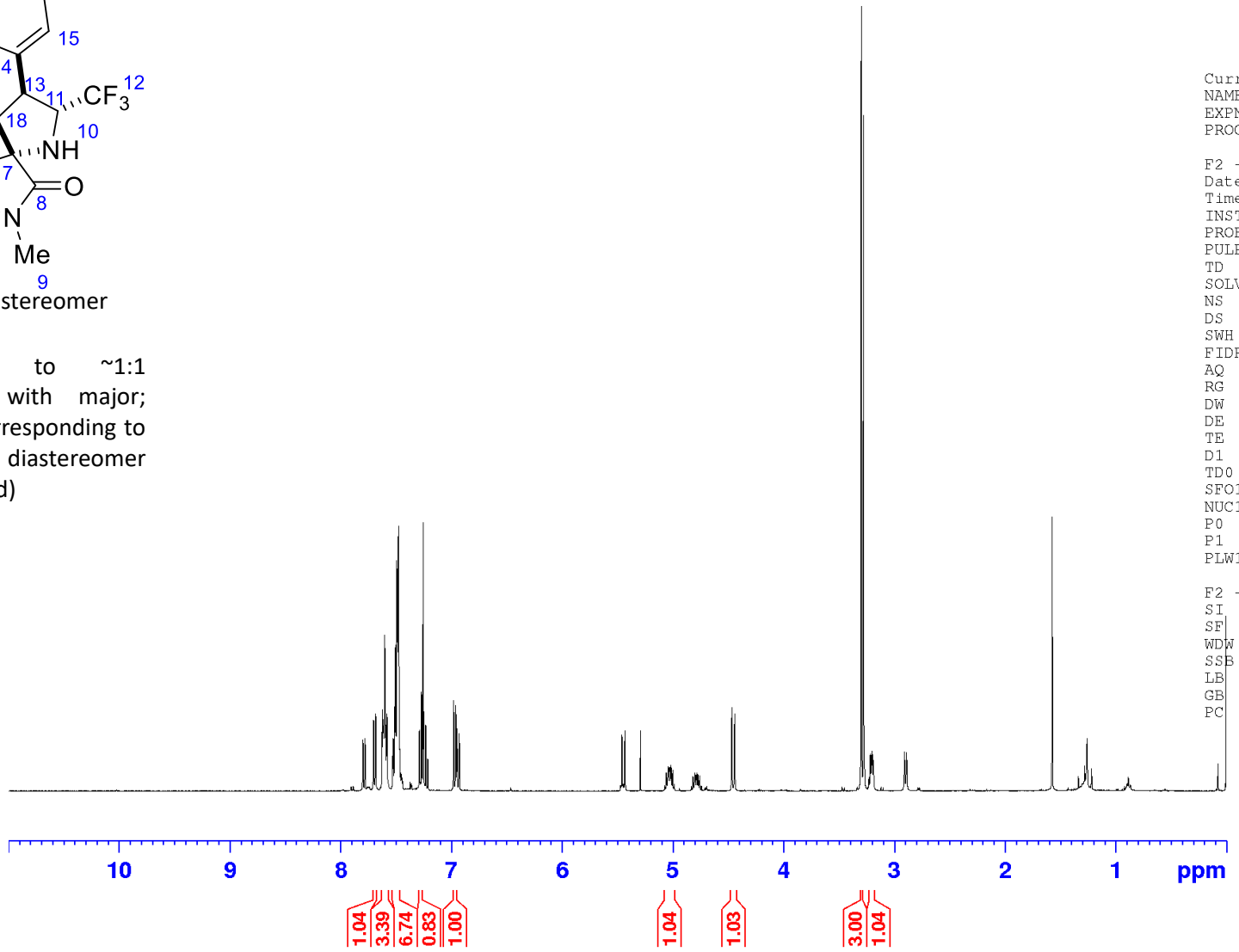
Minor diastereomer

(Purified to ~1:1 mixture with major; peaks corresponding to minor diastereomer integrated)

^{1}H NMR

400 MHz

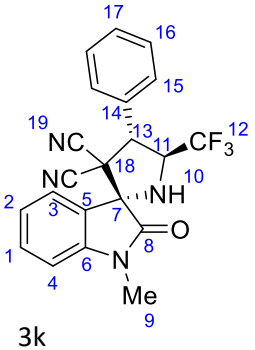
$CDCl_3$




```
Current Data Parameters
NAME         WR 2.168 F2
EXPNO                20
PROCNO                1

F2 - Acquisition Parameters
Date_          20210706
Time              15.28 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH            8223.685 Hz
FIDRES         0.250967 Hz
AQ             3.9845889 sec
RG                  181
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1            1.00000000 sec
TD0                   1
SFO1         400.1124708 MHz
NUC1                 1H
P0                5.00 usec
P1               15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                32768
SF          400.1100109 MHz
WDW                  EM
SSB                   0
LB                 0.30 Hz
GB                    0
PC                 1.00
```



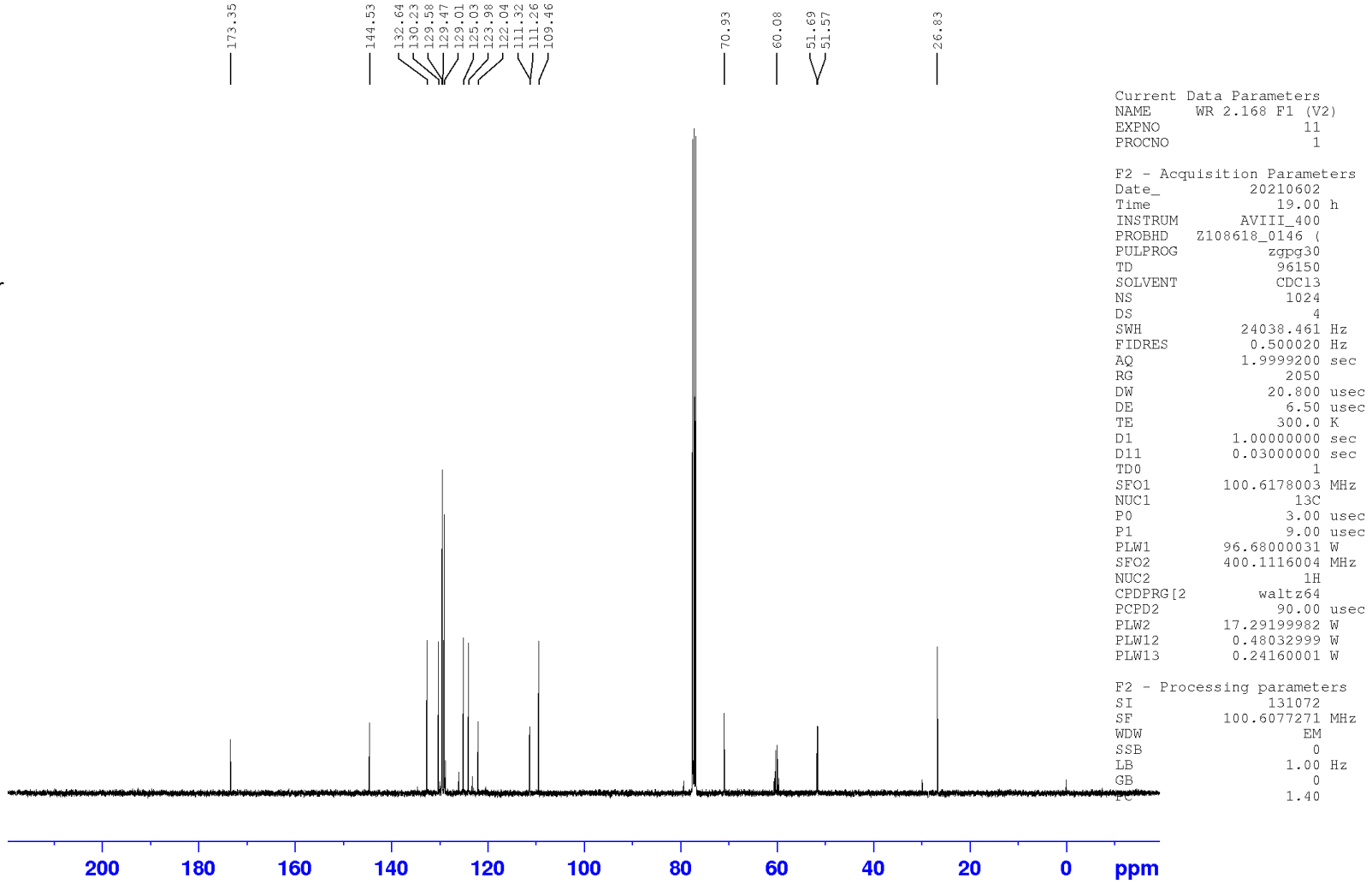
3k

Major diastereomer

^{13}C NMR

101 MHz

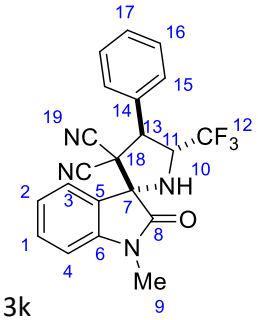
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.168 F1 (V2)
EXPNO                  11
PROCNO                  1

F2 - Acquisition Parameters
Date_           20210602
Time              19.00 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG          zgpg30
TD                96150
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ            1.9999200 sec
RG                 2050
DW               20.800 usec
DE                6.50 usec
TE               300.0 K
D1            1.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6178003 MHz
NUC1                13C
P0                3.00 usec
P1                9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077271 MHz
WDW                 EM
SSB                  0
LB                1.00 Hz
GB                   0
PC                1.40
```



3k

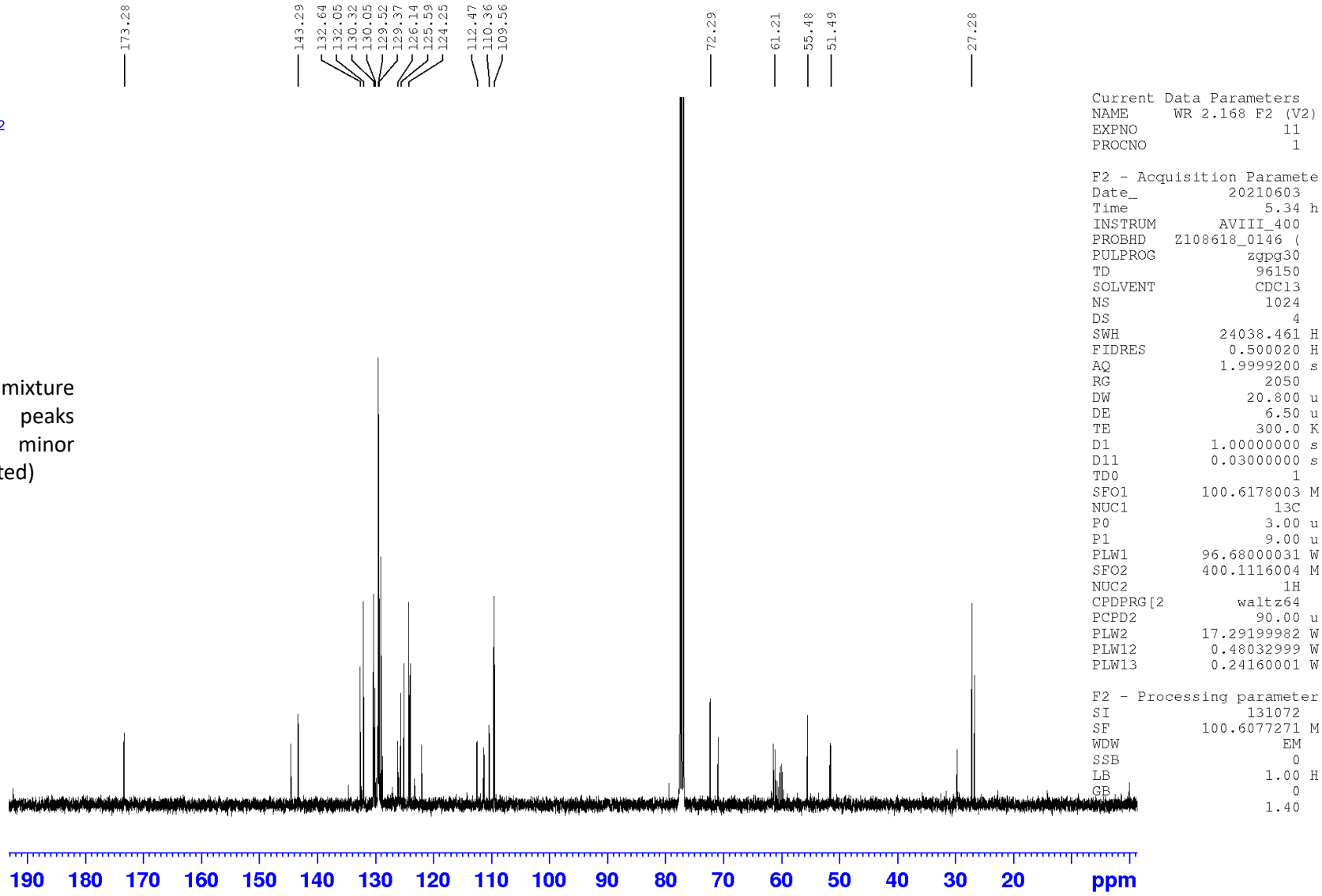
Minor diastereomer

(Purified to ~1:1 mixture with major; peaks corresponding to minor diastereomer indicated)

^{13}C NMR

101 MHz

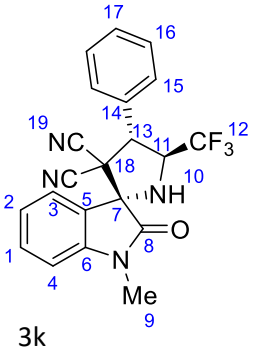
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.168 F2 (V2)
EXPNO                  11
PROCNO                  1

F2 - Acquisition Paramete
Date_            20210603
Time                5.34 h
INSTRUM        AVIII_400
PROBHD    Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDC13
NS                  1024
DS                     4
SWH           24038.461 H
FIDRES         0.500020 H
AQ             1.9999200 s
RG                  2050
DW                20.800 u
DE                 6.50 u
TE                300.0 K
D1           1.00000000 s
D11          0.03000000 s
TD0                    1
SFO1         100.6178003 M
NUC1                 13C
P0                 3.00 u
P1                 9.00 u
PLW1         96.68000031 W
SFO2         400.1116004 M
NUC2                 1H
CPDPRG[2         waltz64
PCPD2             90.00 u
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameter
SI                131072
SF         100.6077271 M
WDW                  EM
SSB                   0
LB                 1.00 H
GB                    0
                   1.40
```



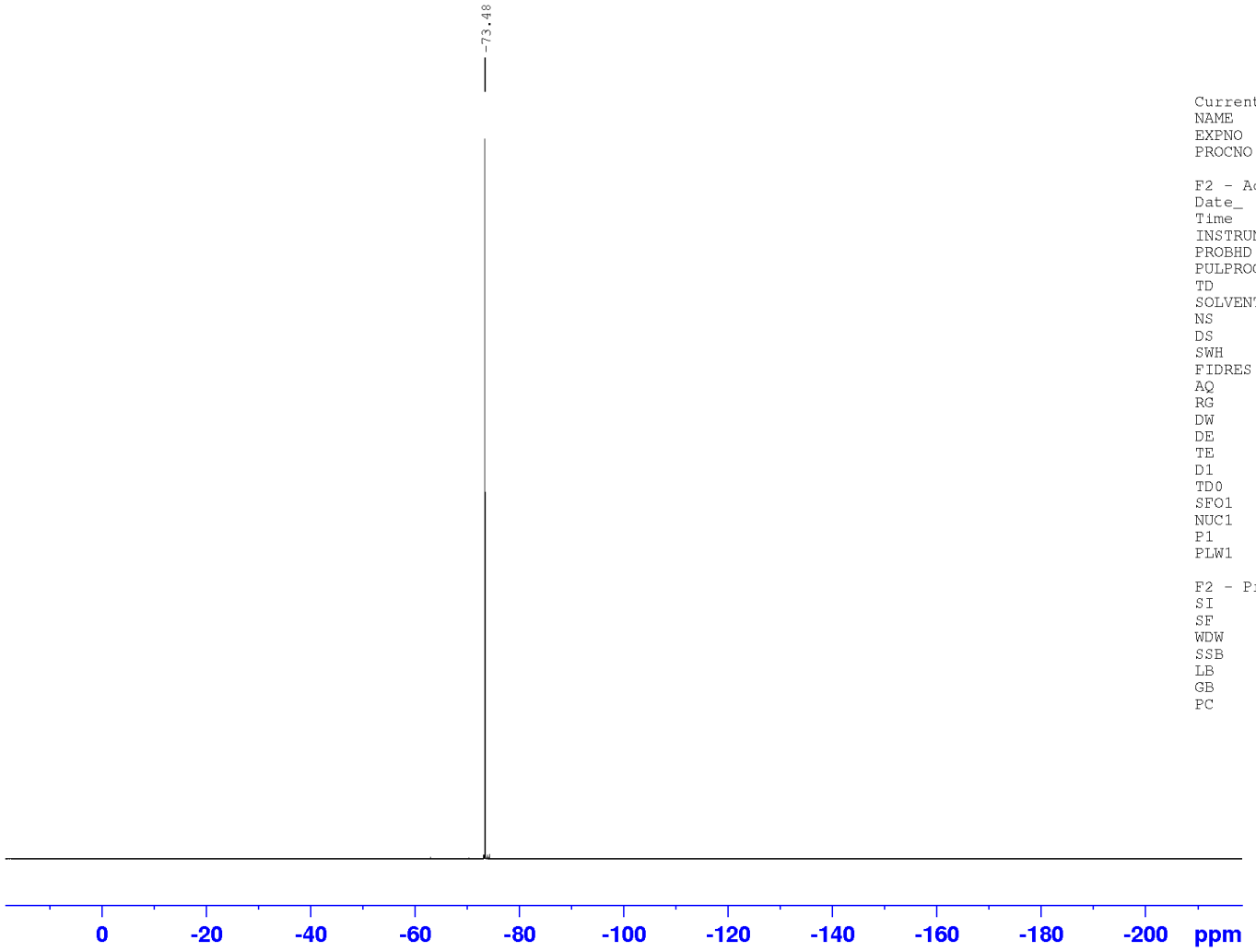
3k

Major diastereomer

^{19}F NMR

376 MHz

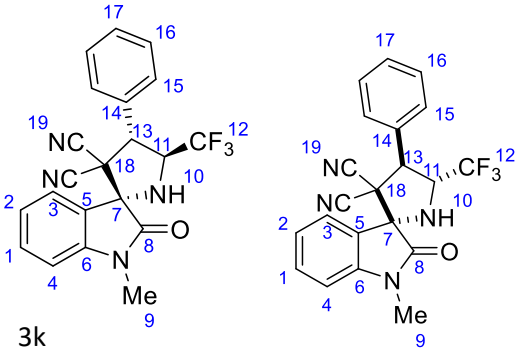
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.168 F1 (V2)
EXPNO                  17
PROCNO                  1

F2 - Acquisition Parameters
Date_           20210602
Time              17.23 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD              261992
SOLVENT           CDCl3
NS                   16
DS                    4
SWH           89285.711 Hz
FIDRES         0.681591 Hz
AQ            1.4671552 sec
RG                  645
DW                5.600 usec
DE                7.11 usec
TE                300.0 K
D1           1.00000000 sec
TD0                   1
SFO1        376.4418995 MHz
NUC1               19F
P1                11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.00
```



3k

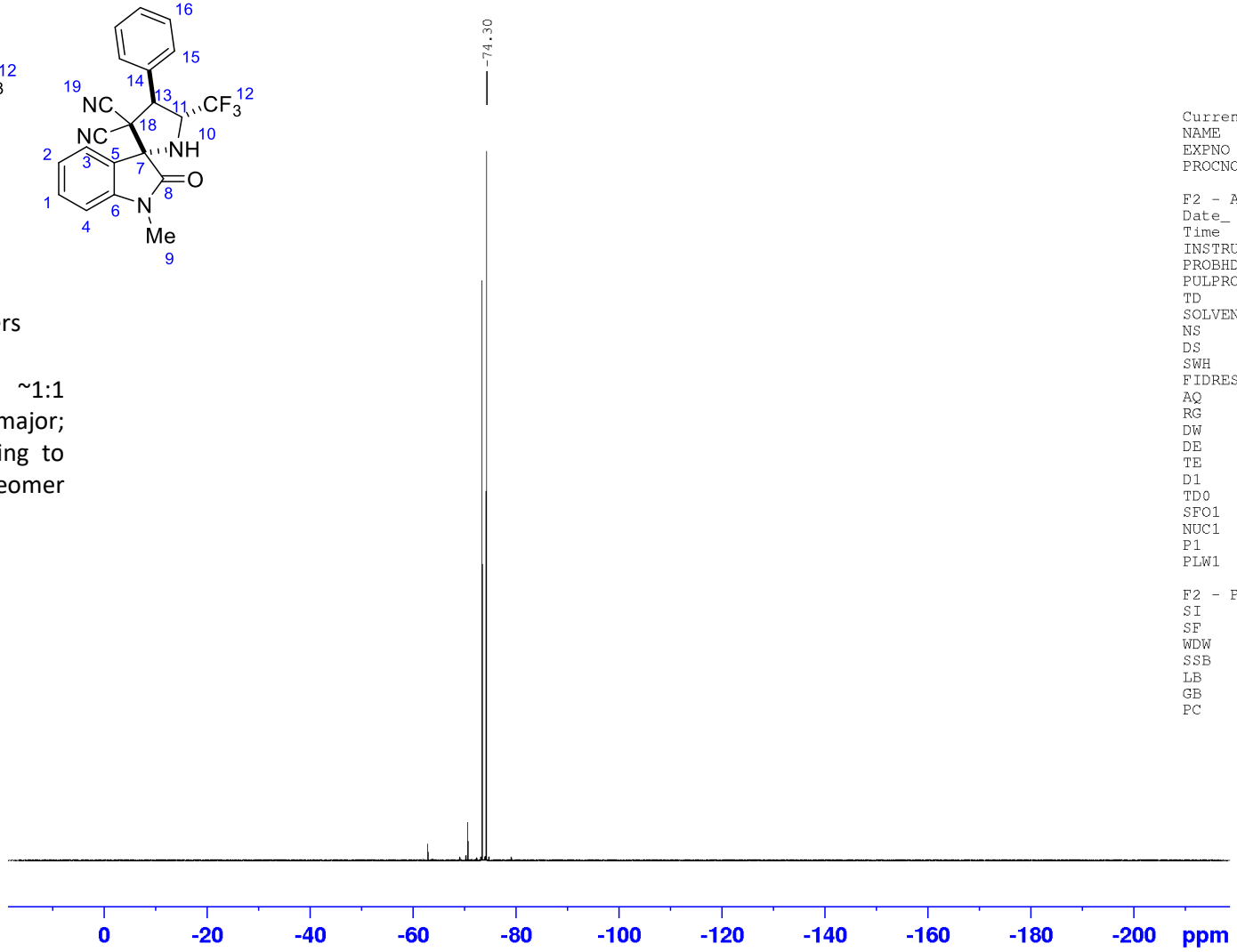
Both diastereomers

(Purified to ~1:1 mixture with major; peak corresponding to minor diastereomer indicated)

^{19}F NMR

376 MHz

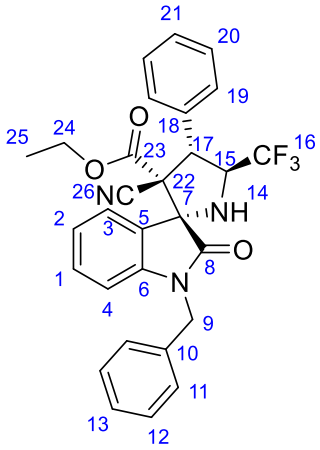
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.168 F2 (V2)
EXPNO                  16
PROCNO                  1

F2 - Acquisition Parameters
Date_           20210602
Time              17.51 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           89285.711 Hz
FIDRES         0.681591 Hz
AQ            1.4671552 sec
RG                   645
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1           1.00000000 sec
TD0                    1
SFO1        376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1        32.96500015 W

F2 - Processing parameters
SI                262144
SF          376.4795470 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



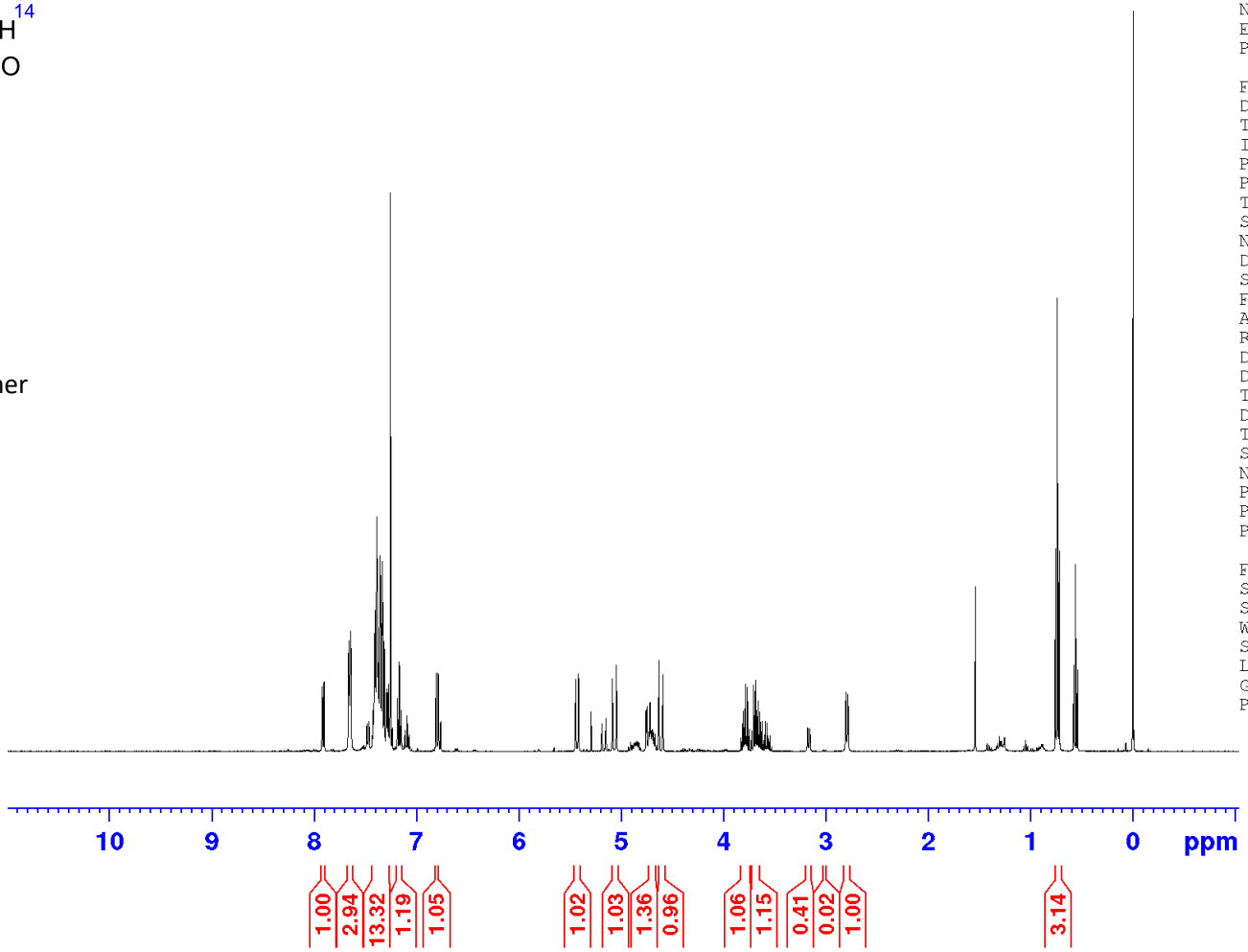
3l

Major diastereomer

^{1}H NMR

400 MHz

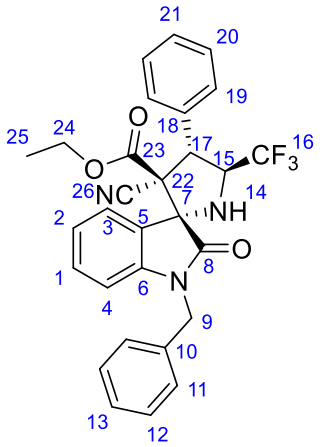
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.170
EXPNO                 30
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210702
Time              16.51 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              3.9845889 sec
RG                   256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1             1.00000000 sec
TD0                    1
SFO1          400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1          17.29199982 W

F2 - Processing parameters
SI                 32768
SF            400.1100108 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



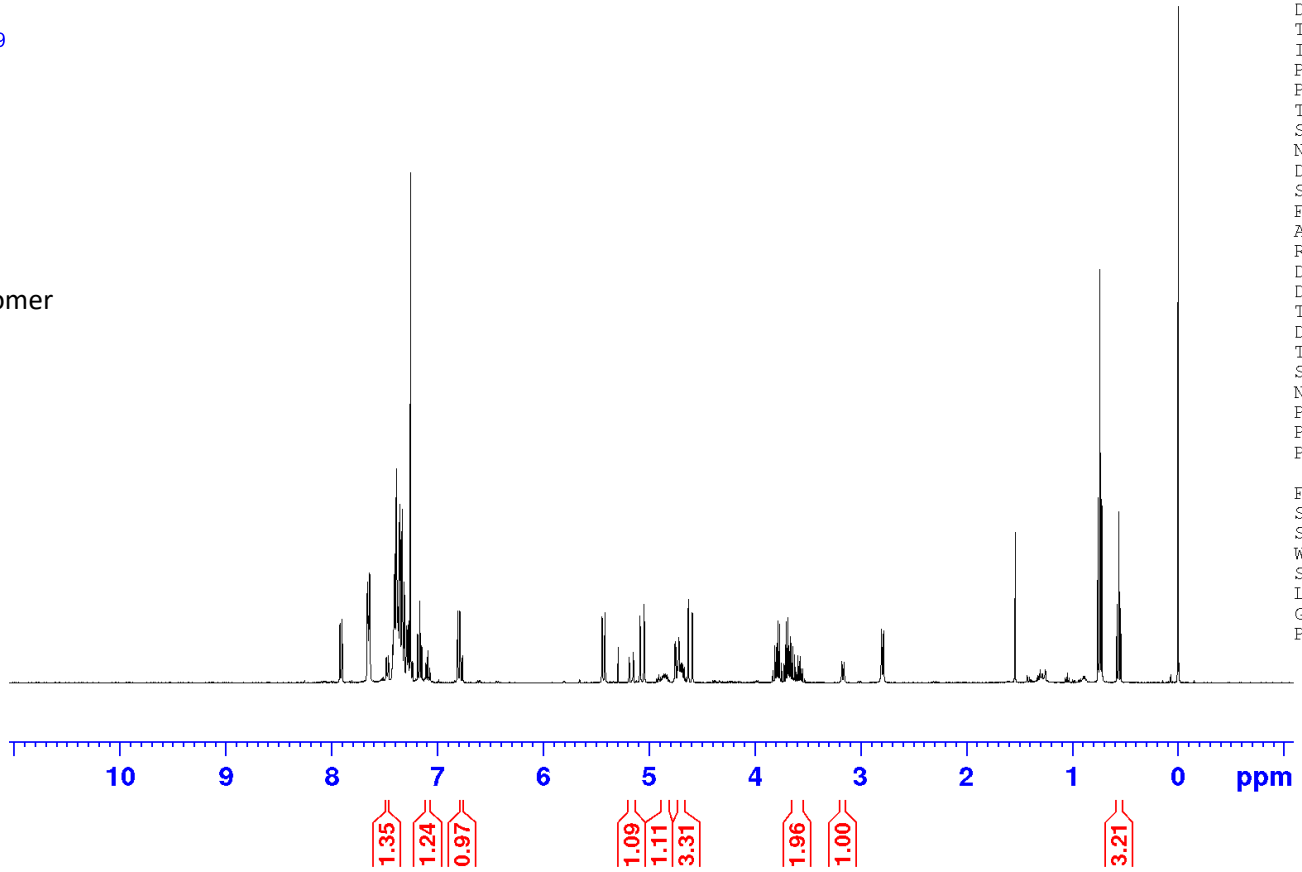
3l

Minor diastereomer

^{1}H NMR

400 MHz

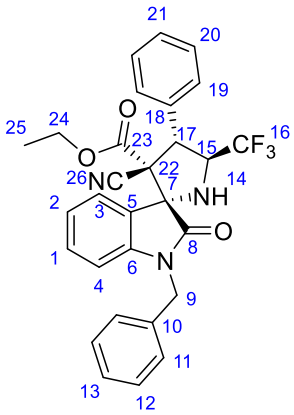
$CDCl_3$

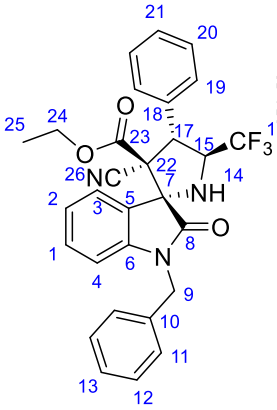



```
Current Data Parameters
NAME            WR 2.170
EXPNO                 32
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210702
Time              16.51 h
INSTRUM        AVIII_400
PROBHD   Z108618_0146 (
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8223.685 Hz
FIDRES           0.250967 Hz
AQ               3.9845889 sec
RG                    256
DW                60.800 usec
DE                17.42 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1124708 MHz
NUC1                  1H
P0                 5.00 usec
P1                15.00 usec
PLW1         17.29199982 W

F2 - Processing parameters
SI                 32768
SF           400.1100108 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```





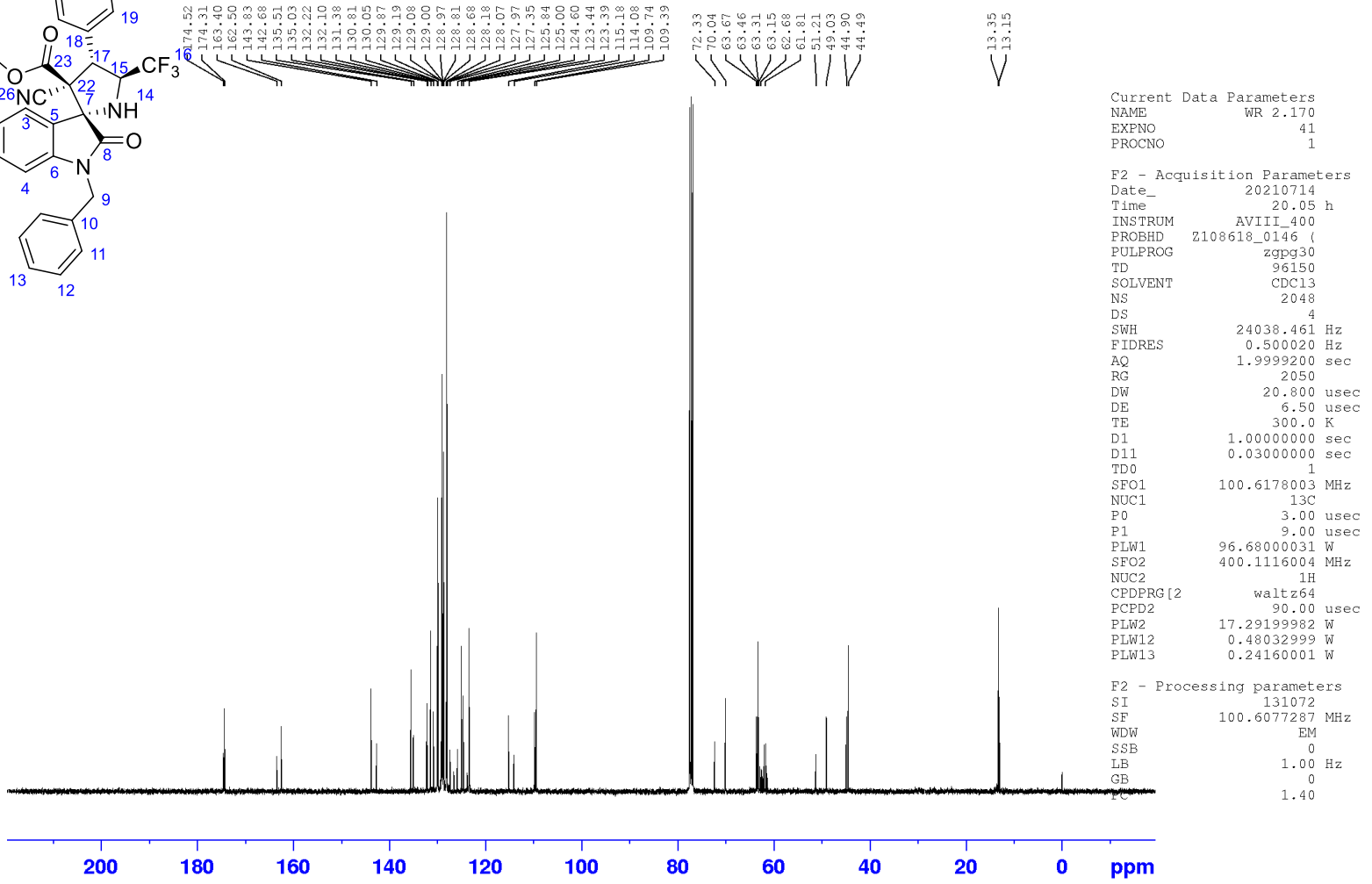
3l

Both diastereomers

^{13}C NMR

101 MHz

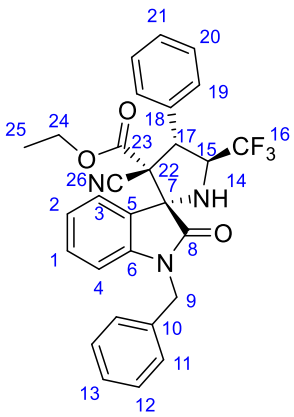
$CDCl_3$

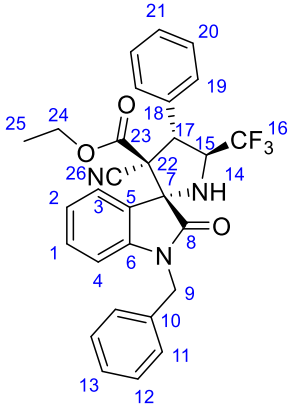



```
Current Data Parameters
NAME            WR 2.170
EXPNO                 41
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210714
Time               20.05 h
INSTRUM       AVIII_400
PROBHD    Z108618_0146 (
PULPROG           zgpg30
TD                 96150
SOLVENT            CDCl3
NS                  2048
DS                     4
SWH           24038.461 Hz
FIDRES         0.500020 Hz
AQ             1.9999200 sec
RG                  2050
DW                20.800 usec
DE                 6.50 usec
TE                300.0 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                    1
SFO1         100.6178003 MHz
NUC1                13C
P0                 3.00 usec
P1                 9.00 usec
PLW1         96.68000031 W
SFO2         400.1116004 MHz
NUC2                1H
CPDPRG[2         waltz64
PCPD2             90.00 usec
PLW2         17.29199982 W
PLW12         0.48032999 W
PLW13         0.24160001 W

F2 - Processing parameters
SI                131072
SF           100.6077287 MHz
WDW                 EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```





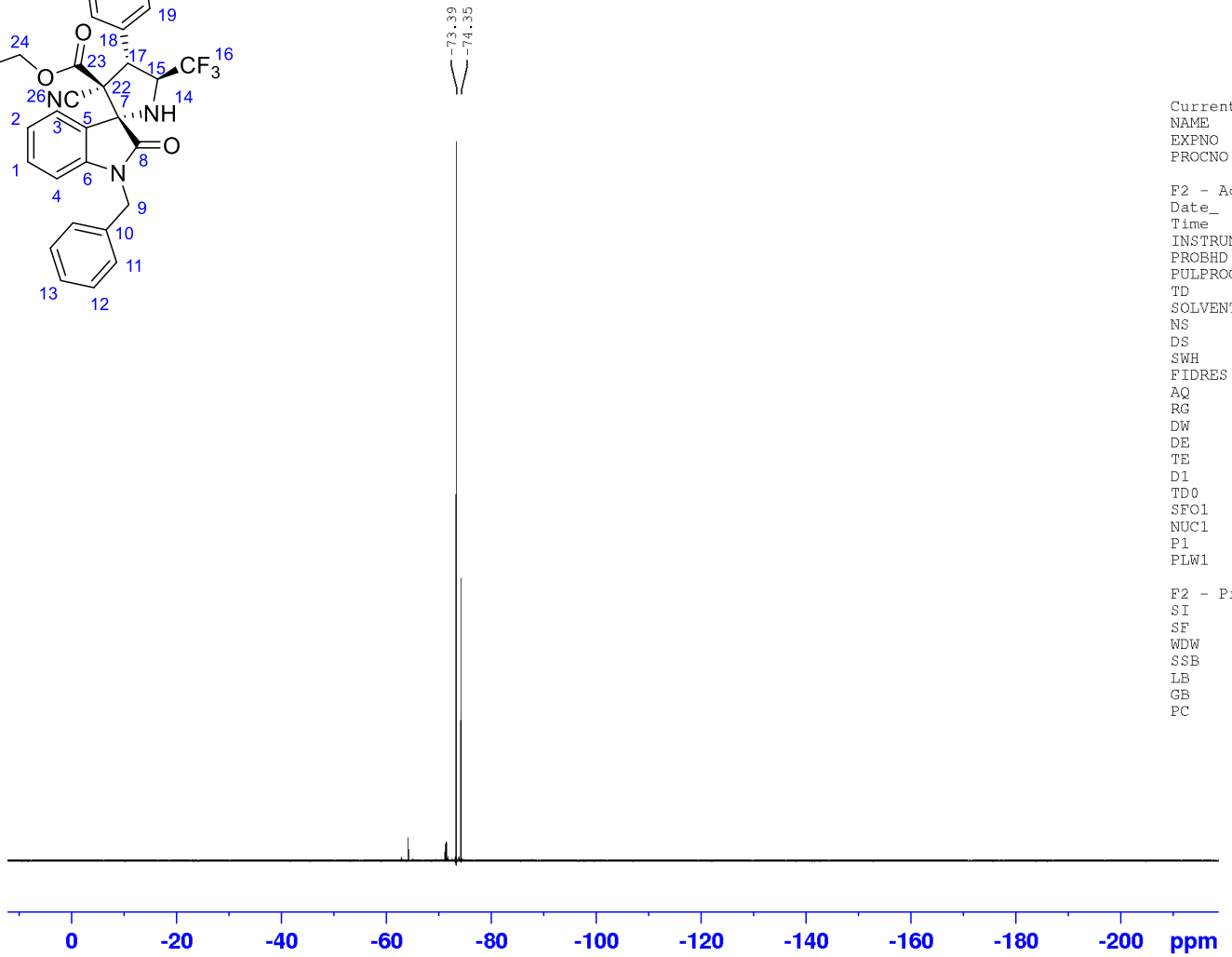
3l

Both diastereomers

^{19}F NMR

376 MHz

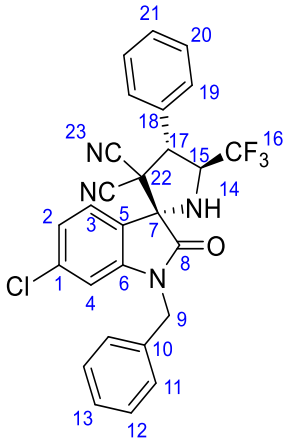
$CDCl_3$




```
Current Data Parameters
NAME            WR 2.170
EXPNO                 31
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210702
Time               16.53 h
INSTRUM       AVIII_400
PROBHD   Z108618_0146 (
PULPROG               zg
TD                261992
SOLVENT            CDCl3
NS                    16
DS                     4
SWH            89285.711 Hz
FIDRES          0.681591 Hz
AQ             1.4671552 sec
RG                   575
DW                 5.600 usec
DE                 7.11 usec
TE                 300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         376.4418995 MHz
NUC1                 19F
P1                11.80 usec
PLW1         32.96500015 W

F2 - Processing parameters
SI                262144
SF           376.4795470 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

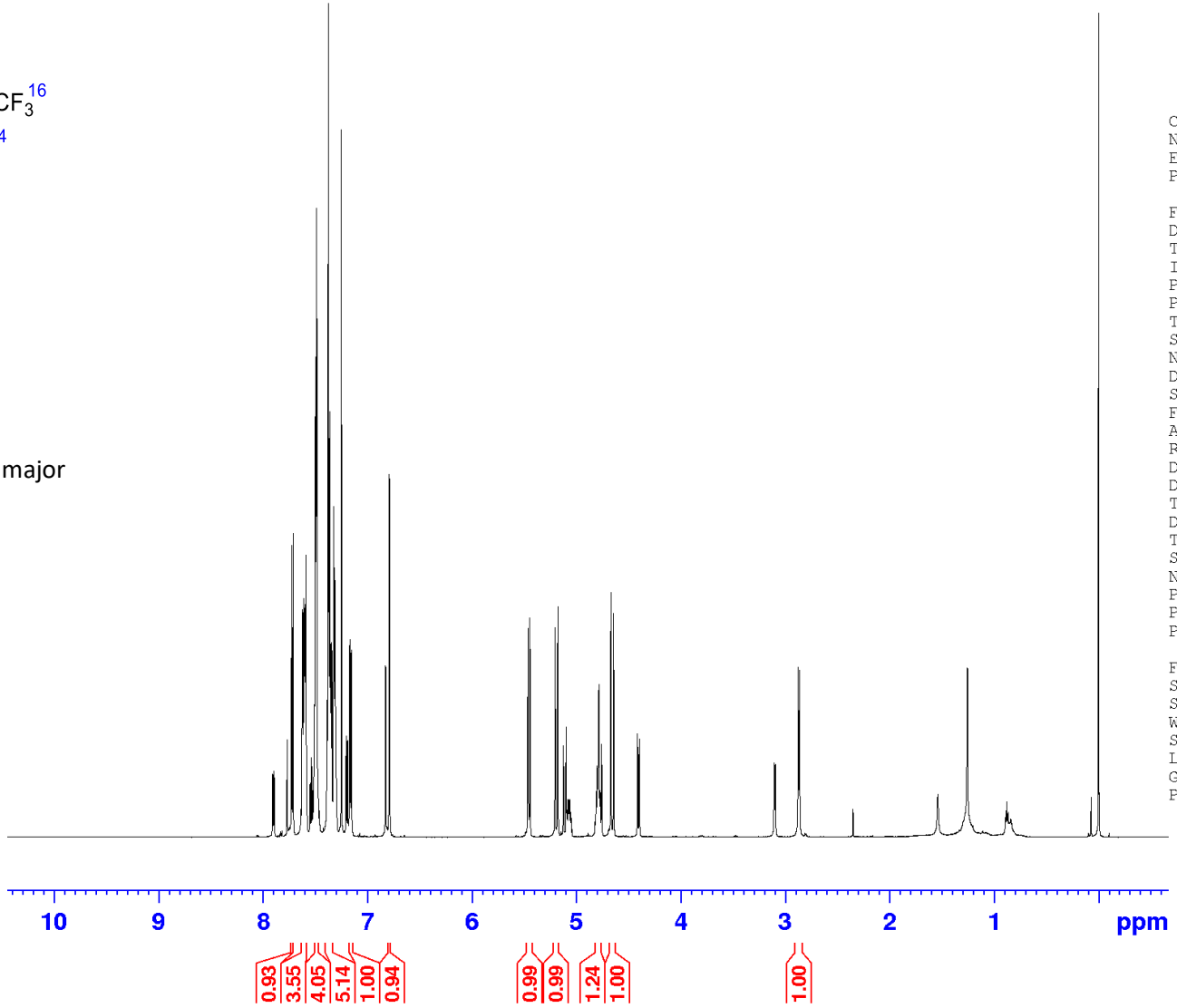


3m

Peaks picked for major diastereomer

^{1}H NMR

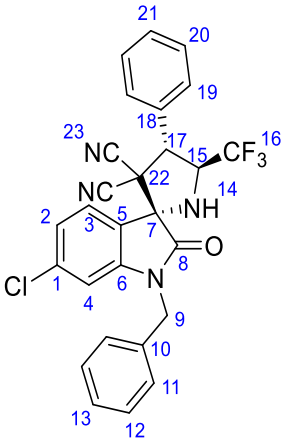
600 MHz




```
Current Data Parameters
NAME      WR 2.226 (600)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211005
Time               15.20 h
INSTRUM             spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                  97.5
DW                41.600 usec
DE                12.10 usec
TE                300.0 K
D1            1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300170 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

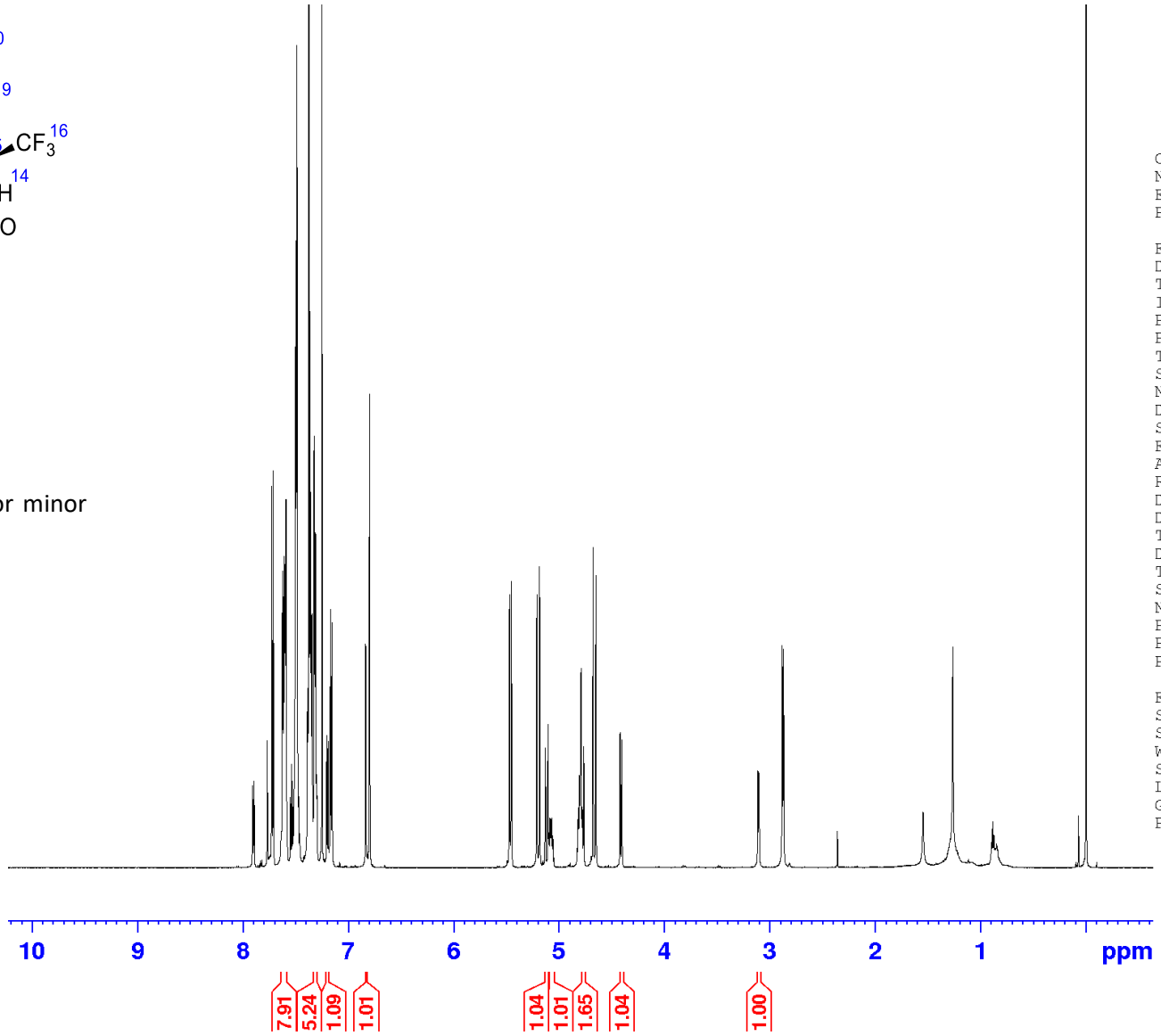


3m

Peaks picked for minor diastereomer

^{1}H NMR

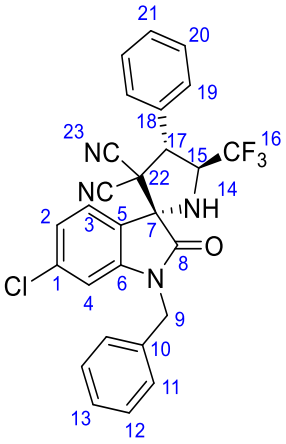
600 MHz




```
Current Data Parameters
NAME      WR 2.226 (600)
EXPNO                 30
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211005
Time               15.20 h
INSTRUM             spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                  97.5
DW                41.600 usec
DE                12.10 usec
TE                300.0 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300170 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



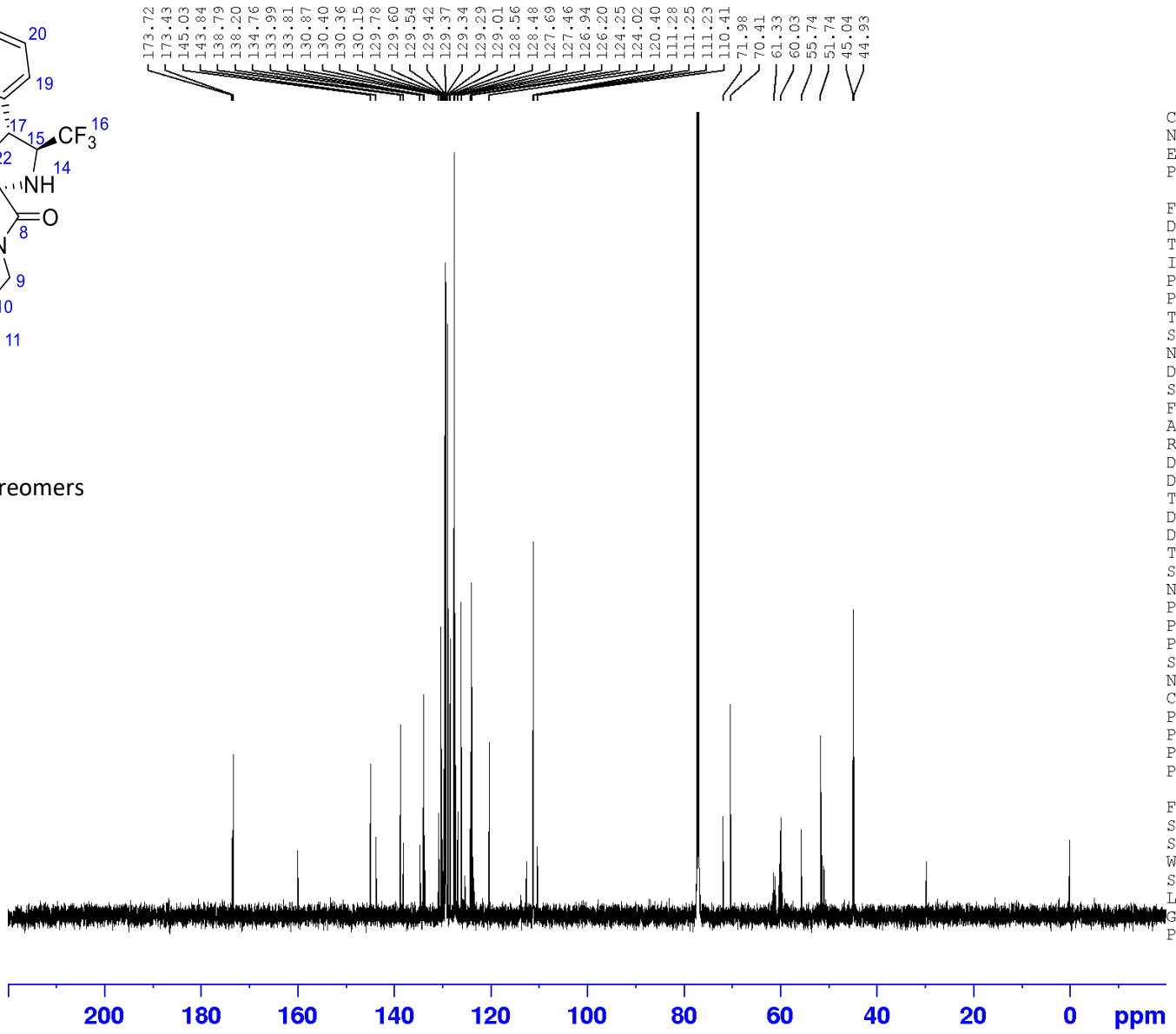
3m

Both diastereomers

^{13}C NMR

151 MHz

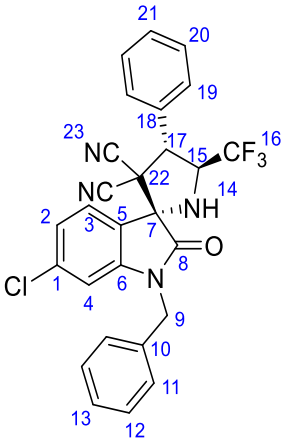
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.226 (600)
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211006
Time              20.43 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               186.92
DW               13.800 usec
DE                6.50 usec
TE               300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.9178988 MHz
NUC1               13C
P0                3.93 usec
P1               11.80 usec
PLW1        85.00000000 W
SFO2        600.1324005 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2            70.00 usec
PLW2        27.00000000 W
PLW12        0.57327998 W
PLW13        0.28836000 W

F2 - Processing parameters
SI                32768
SF          150.9027894 MHz
WDW                EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                1.40
```



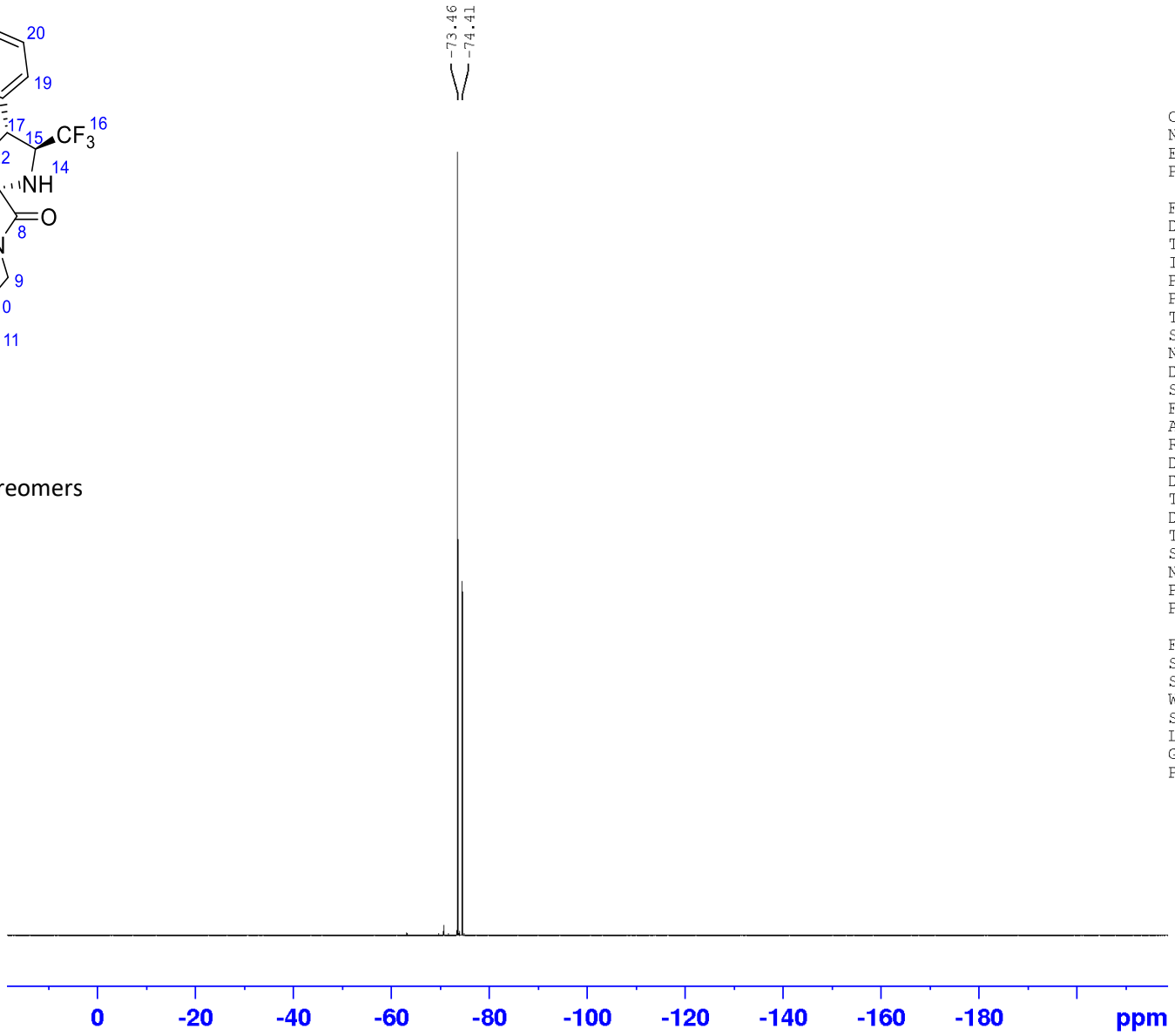
3m

Both diastereomers

^{19}F NMR

564 MHz

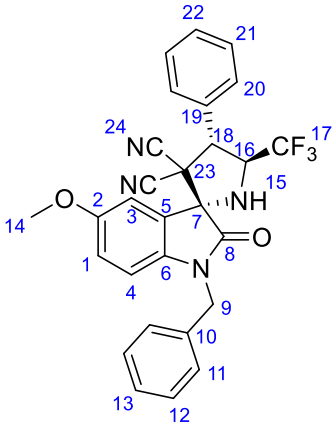
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.226 (600)
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211005
Time              17.29 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG           zgflqn
TD                261896
SOLVENT            CDCl3
NS                    16
DS                     4
SWH          133928.578 Hz
FIDRES         1.022761 Hz
AQ             0.9777451 sec
RG                186.92
DW                 3.733 usec
DE                 6.70 usec
TE                300.0 K
D1           4.00000000 sec
TD0                    1
SFO1        564.6299217 MHz
NUC1                19F
P1                 12.00 usec
PLW1        49.00000000 W

F2 - Processing parameters
SI                262144
SF          564.6863882 MHz
WDW                  EM
SSB                   0
LB                 0.50 Hz
GB                    0
PC                 2.00
```



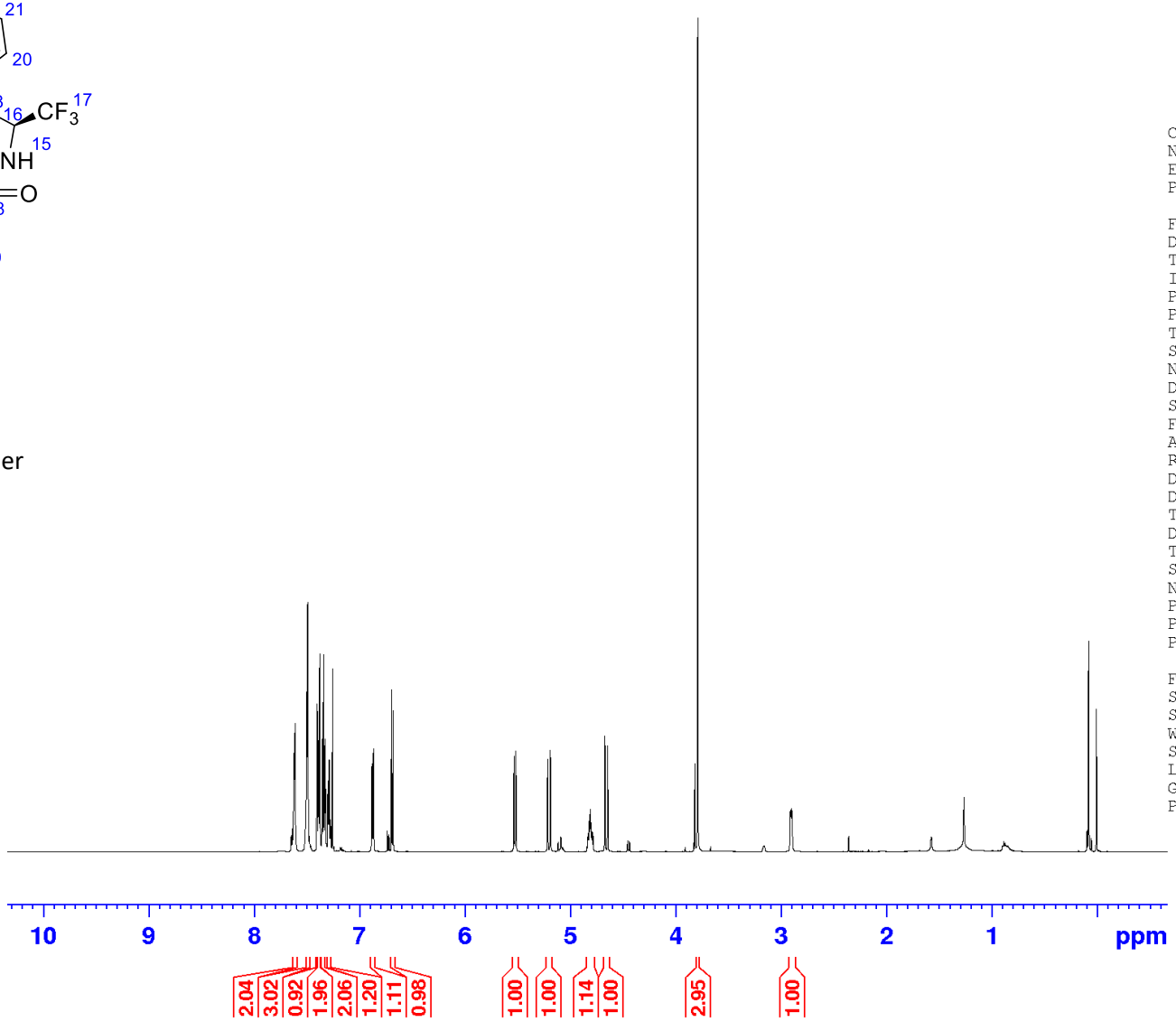
3n

Major diastereomer

^{1}H NMR

600 MHz

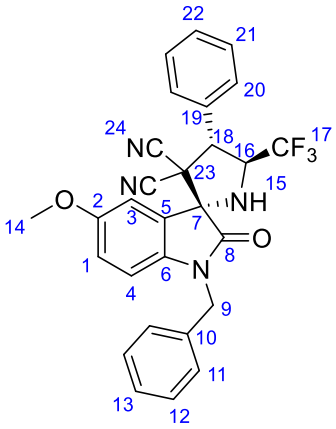
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.231 (600)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211014
Time               12.56 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ              2.7262976 sec
RG                 74.91
DW                41.600 usec
DE                12.10 usec
TE                297.6 K
D1             1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300144 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



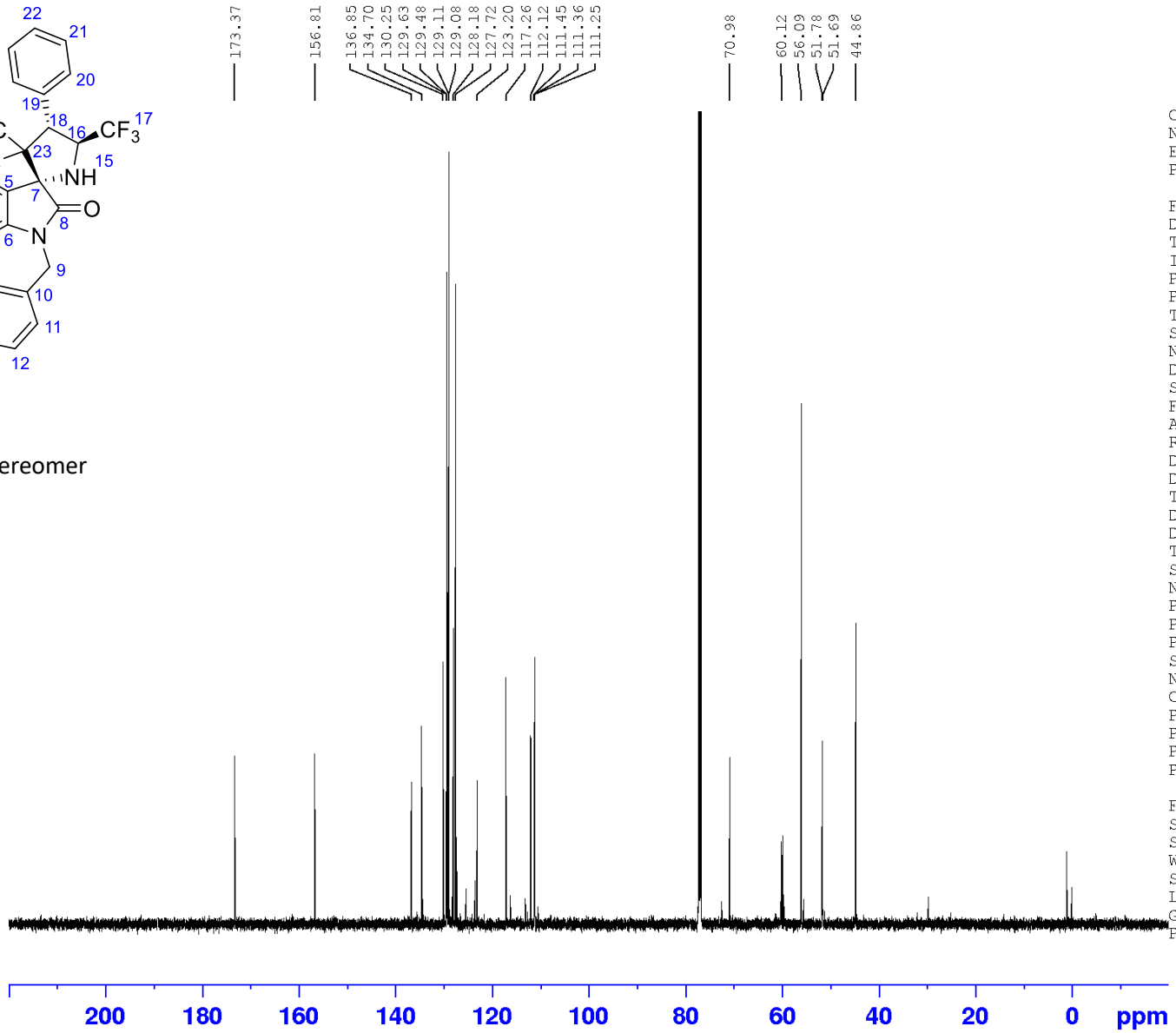
3n

Major diastereomer

^{13}C NMR

151 MHz

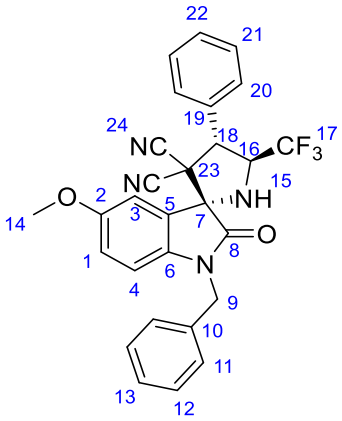
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.231 (600)
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211014
Time               13.48 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ             0.9043968 sec
RG                186.92
DW                13.800 usec
DE                 6.50 usec
TE                299.5 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1        150.9178988 MHz
NUC1               13C
P0                 3.93 usec
P1                11.80 usec
PLW1         85.00000000 W
SFO2        600.1324005 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2             70.00 usec
PLW2         27.00000000 W
PLW12         0.57327998 W
PLW13         0.28836000 W

F2 - Processing parameters
SI                32768
SF          150.9027877 MHz
WDW                EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



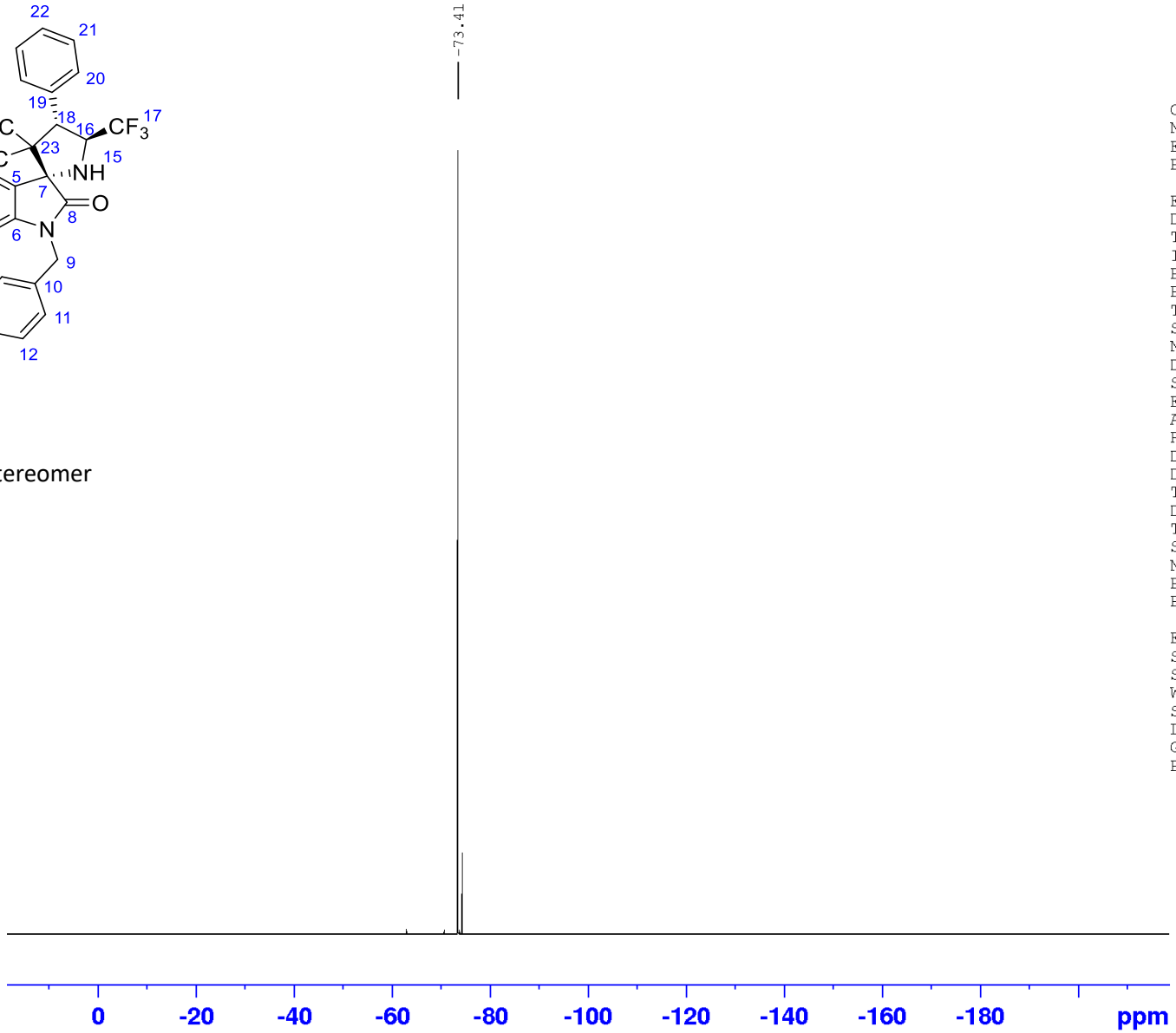
3n

Major diastereomer

^{19}F NMR

564 MHz

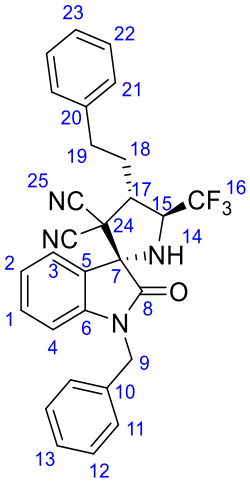
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.231 (600)
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211014
Time               15.33 h
INSTRUM             spect
PROBHD   Z114607_0188 (
PULPROG           zgflqn
TD                261896
SOLVENT             CDCl3
NS                     16
DS                      4
SWH           133928.578 Hz
FIDRES          1.022761 Hz
AQ              0.9777451 sec
RG                186.92
DW                 3.733 usec
DE                 6.70 usec
TE                297.7 K
D1           4.00000000 sec
TD0                    1
SFO1         564.6299217 MHz
NUC1                 19F
P1                12.00 usec
PLW1         49.00000000 W

F2 - Processing parameters
SI                262144
SF           564.6863882 MHz
WDW                  EM
SSB                   0
LB                 0.50 Hz
GB                    0
PC                 2.00
```



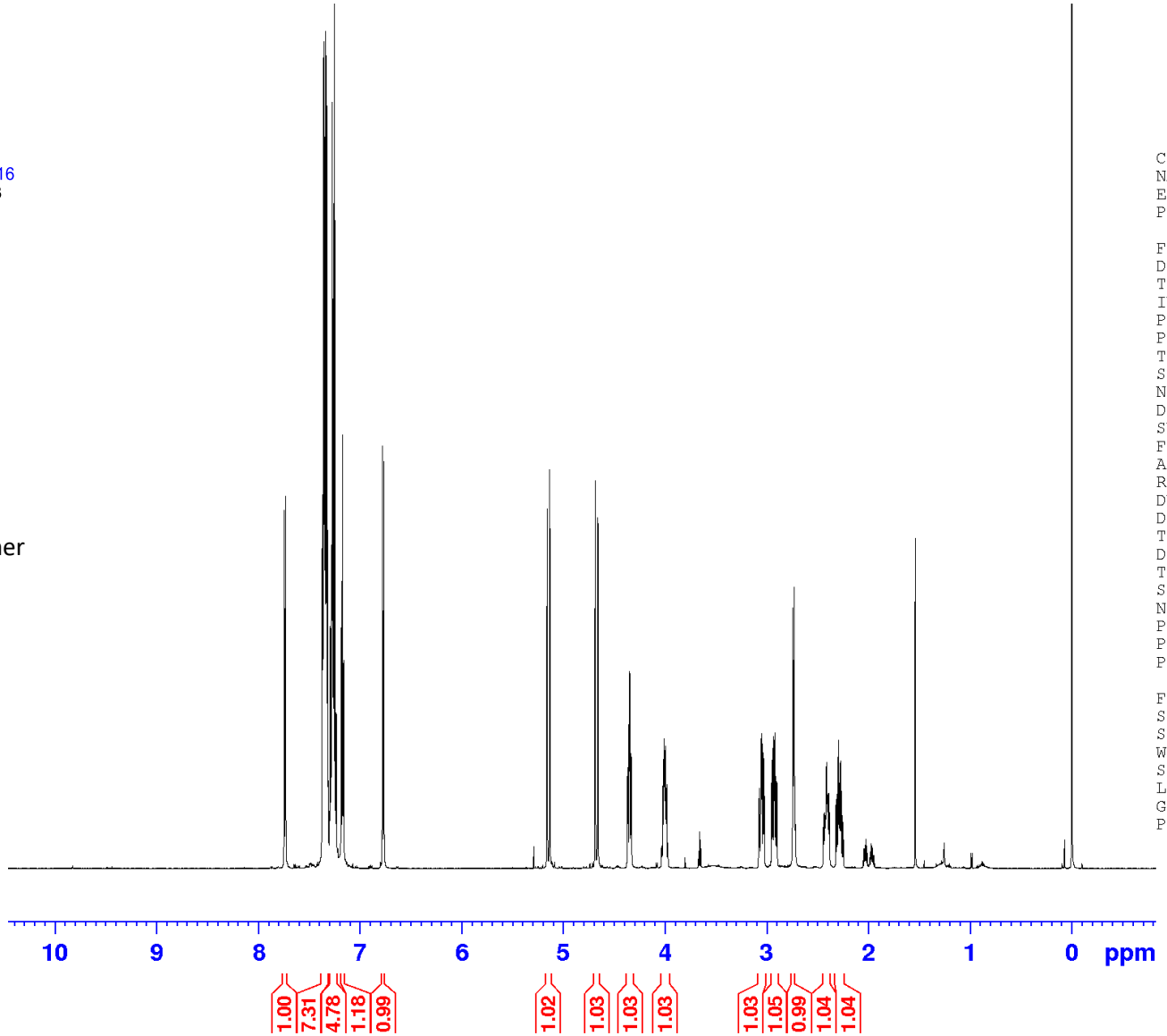
3o

Major diastereomer

^{1}H NMR

600 MHz

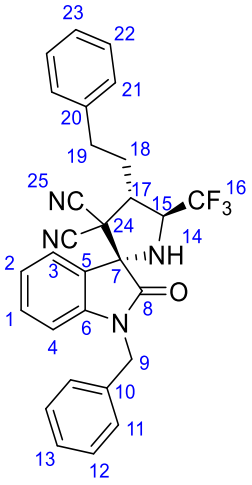
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.227 (600)
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211014
Time               12.51 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                  97.5
DW                41.600 usec
DE                12.10 usec
TE                297.6 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300183 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```



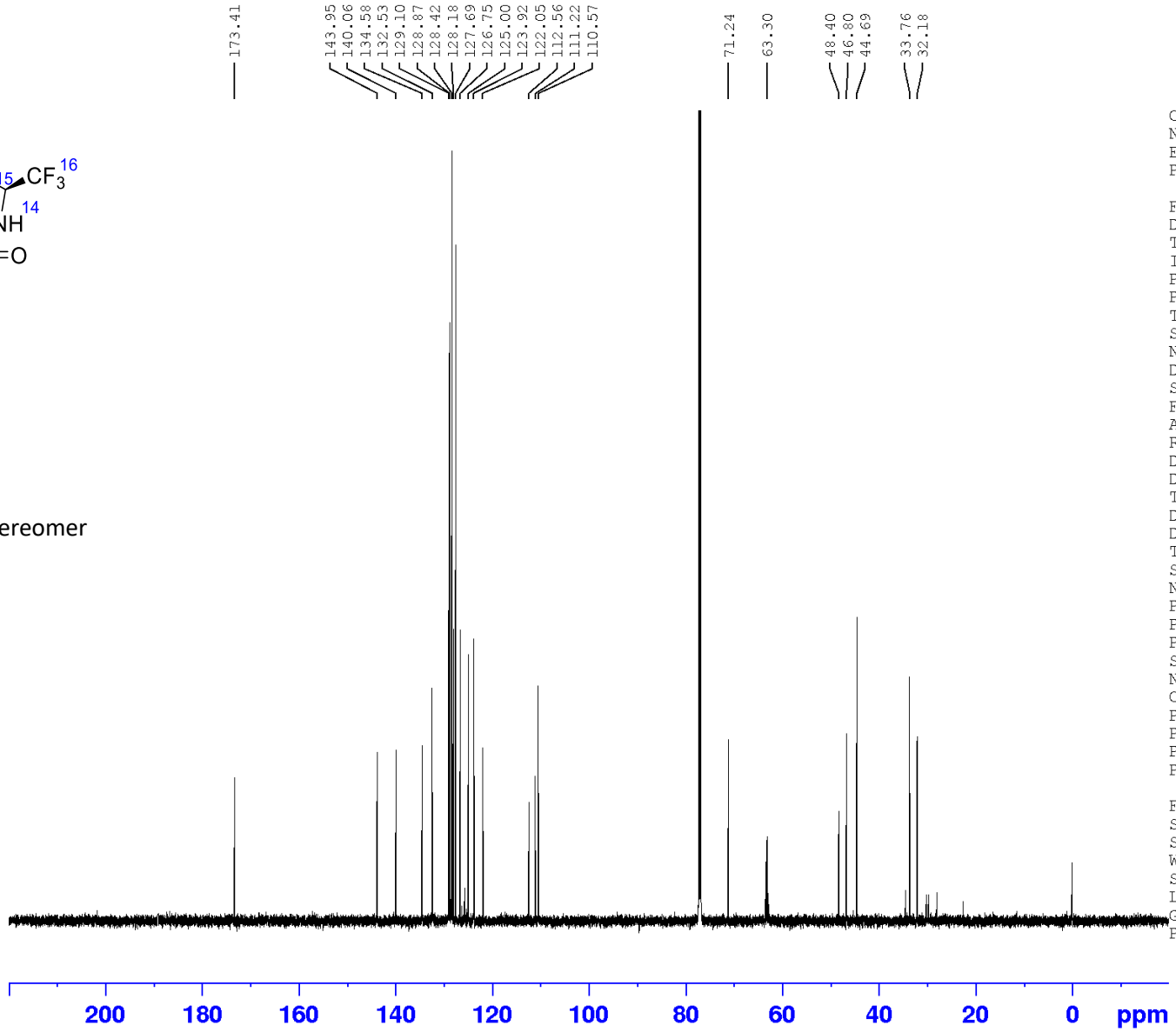
3o

Major diastereomer

^{13}C NMR

151 MHz

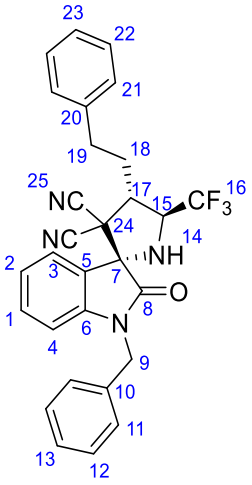
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.227 (600)
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211006
Time              17.38 h
INSTRUM             spect
PROBHD   Z114607_0188 (
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  1024
DS                     4
SWH            36231.883 Hz
FIDRES          1.105709 Hz
AQ              0.9043968 sec
RG                186.92
DW                13.800 usec
DE                 6.50 usec
TE                300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1        150.9178988 MHz
NUC1                13C
P0                 3.93 usec
P1                11.80 usec
PLW1        85.00000000 W
SFO2        600.1324005 MHz
NUC2                1H
CPDPRG[2         waltz65
PCPD2             70.00 usec
PLW2        27.00000000 W
PLW12        0.57327998 W
PLW13        0.28836000 W

F2 - Processing parameters
SI                 32768
SF          150.9027895 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```



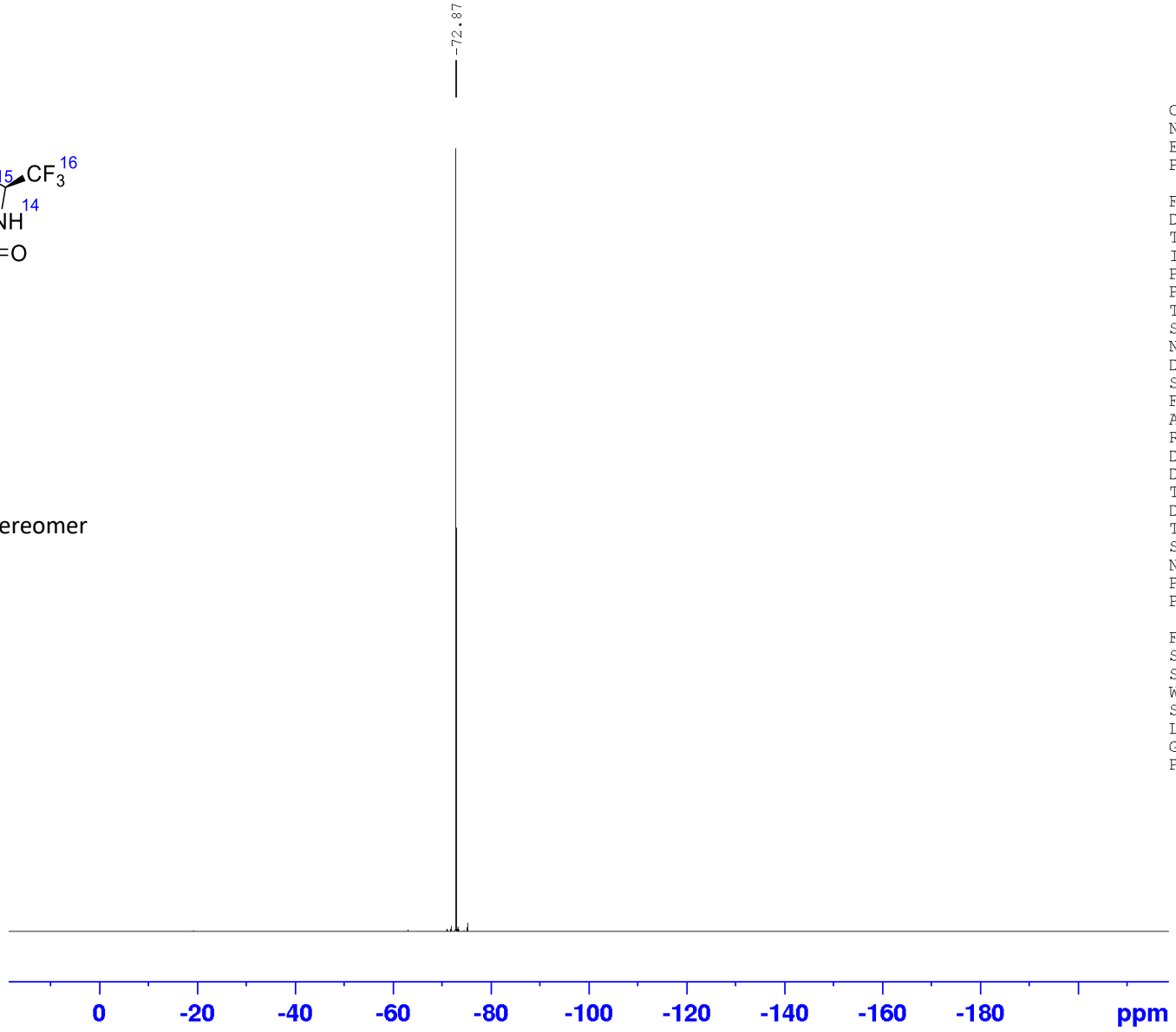
3o

Major diastereomer

^{19}F NMR

564 MHz

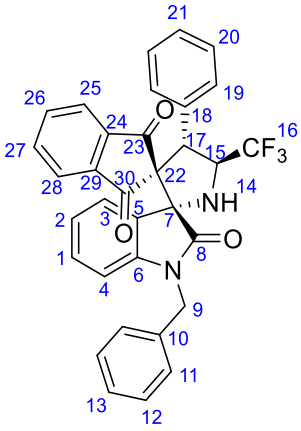
$CDCl_3$




```
Current Data Parameters
NAME      WR 2.227 (600)
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20211006
Time               19.41 h
INSTRUM             spect
PROBHD   Z114607_0188 (
PULPROG           zgflqn
TD                261896
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           133928.578 Hz
FIDRES          1.022761 Hz
AQ              0.9777451 sec
RG                186.92
DW                 3.733 usec
DE                 6.70 usec
TE                300.0 K
D1           4.00000000 sec
TD0                    1
SFO1        564.6299217 MHz
NUC1                19F
P1                 12.00 usec
PLW1        49.00000000 W

F2 - Processing parameters
SI                262144
SF          564.6863882 MHz
WDW                   EM
SSB                    0
LB                  0.50 Hz
GB                     0
PC                  2.00
```



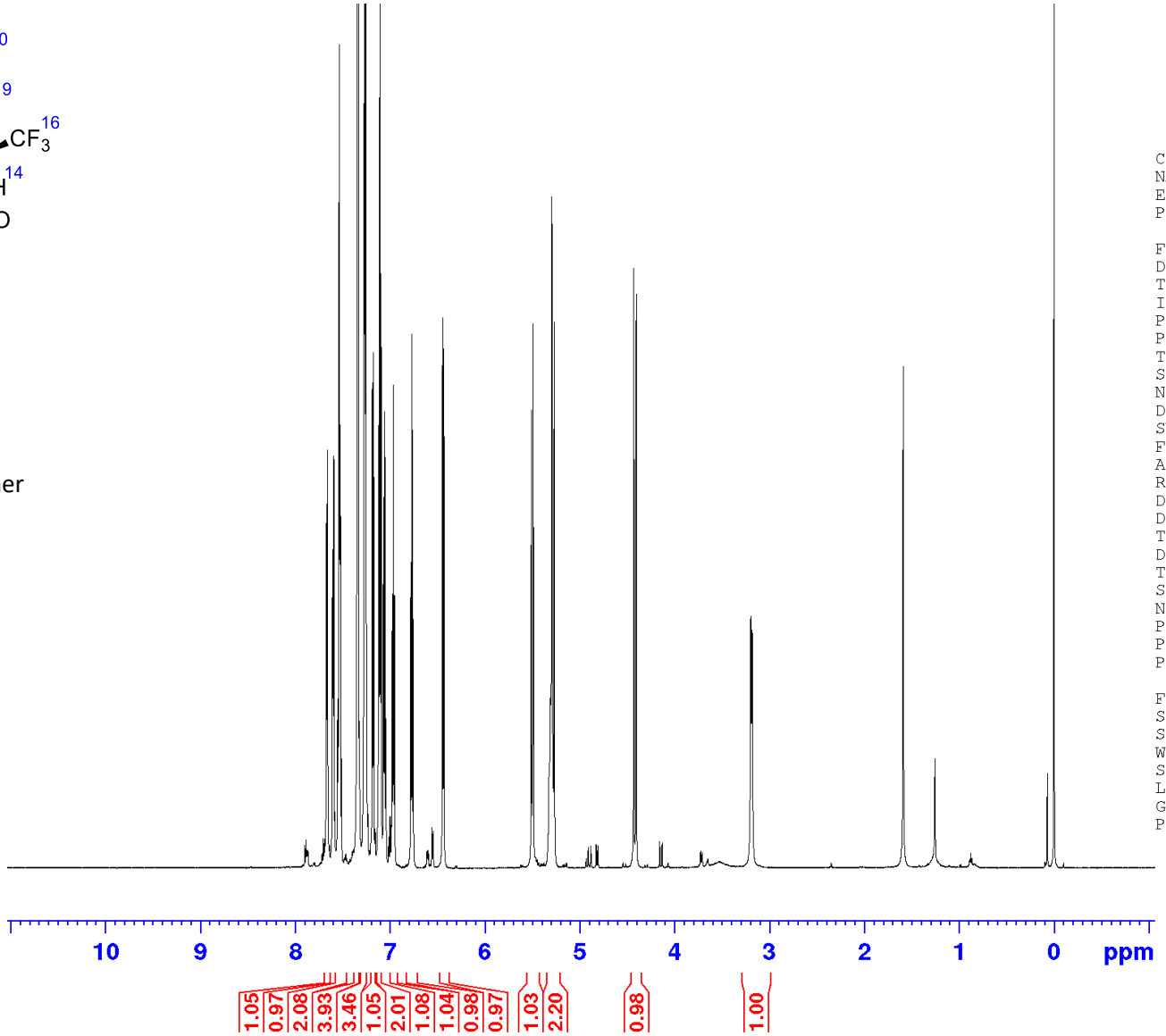
5a

Major diastereomer

^{1}H NMR

600 MHz

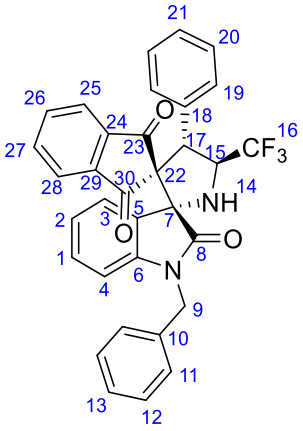
$CDCl_3$




```
Current Data Parameters
NAME      WR 1.136 (600)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210715
Time                2.24 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                 83.95
DW                41.600 usec
DE                12.10 usec
TE                302.4 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1        26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300152 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



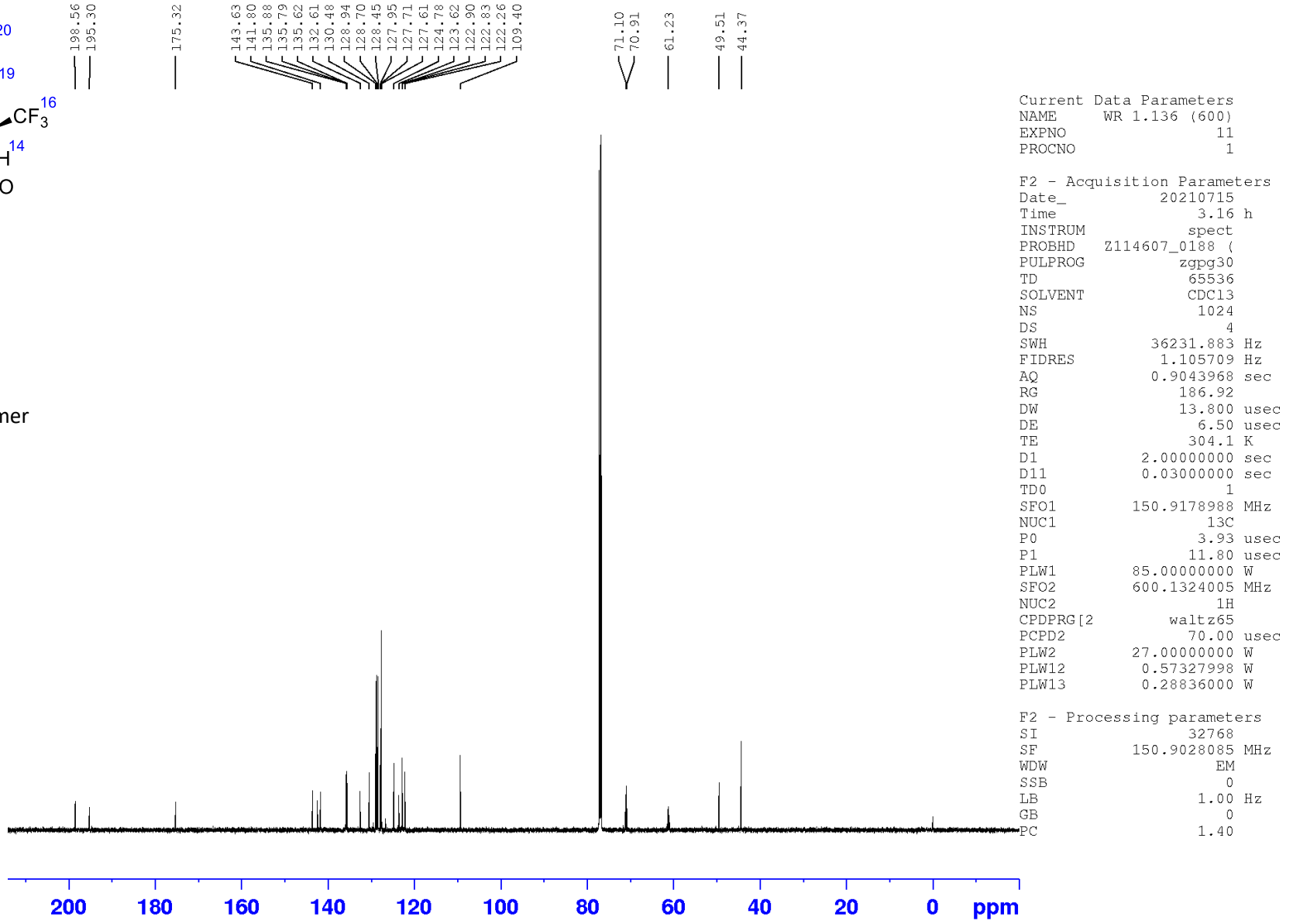
5a

Major diastereomer

^{13}C NMR

151 MHz

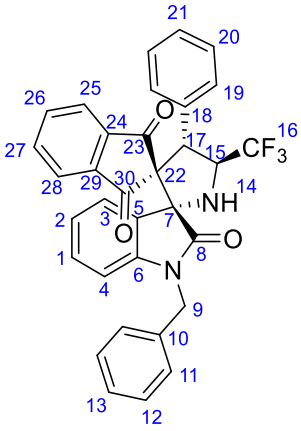
$CDCl_3$




```
Current Data Parameters
NAME      WR 1.136 (600)
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210715
Time                3.16 h
INSTRUM            spect
PROBHD    Z114607_0188 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ            0.9043968 sec
RG               186.92
DW               13.800 usec
DE                6.50 usec
TE               304.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        150.9178988 MHz
NUC1               13C
P0                3.93 usec
P1               11.80 usec
PLW1        85.00000000 W
SFO2        600.1324005 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2            70.00 usec
PLW2        27.00000000 W
PLW12        0.57327998 W
PLW13        0.28836000 W

F2 - Processing parameters
SI                32768
SF          150.9028085 MHz
WDW                EM
SSB                   0
LB                1.00 Hz
GB                    0
PC                1.40
```



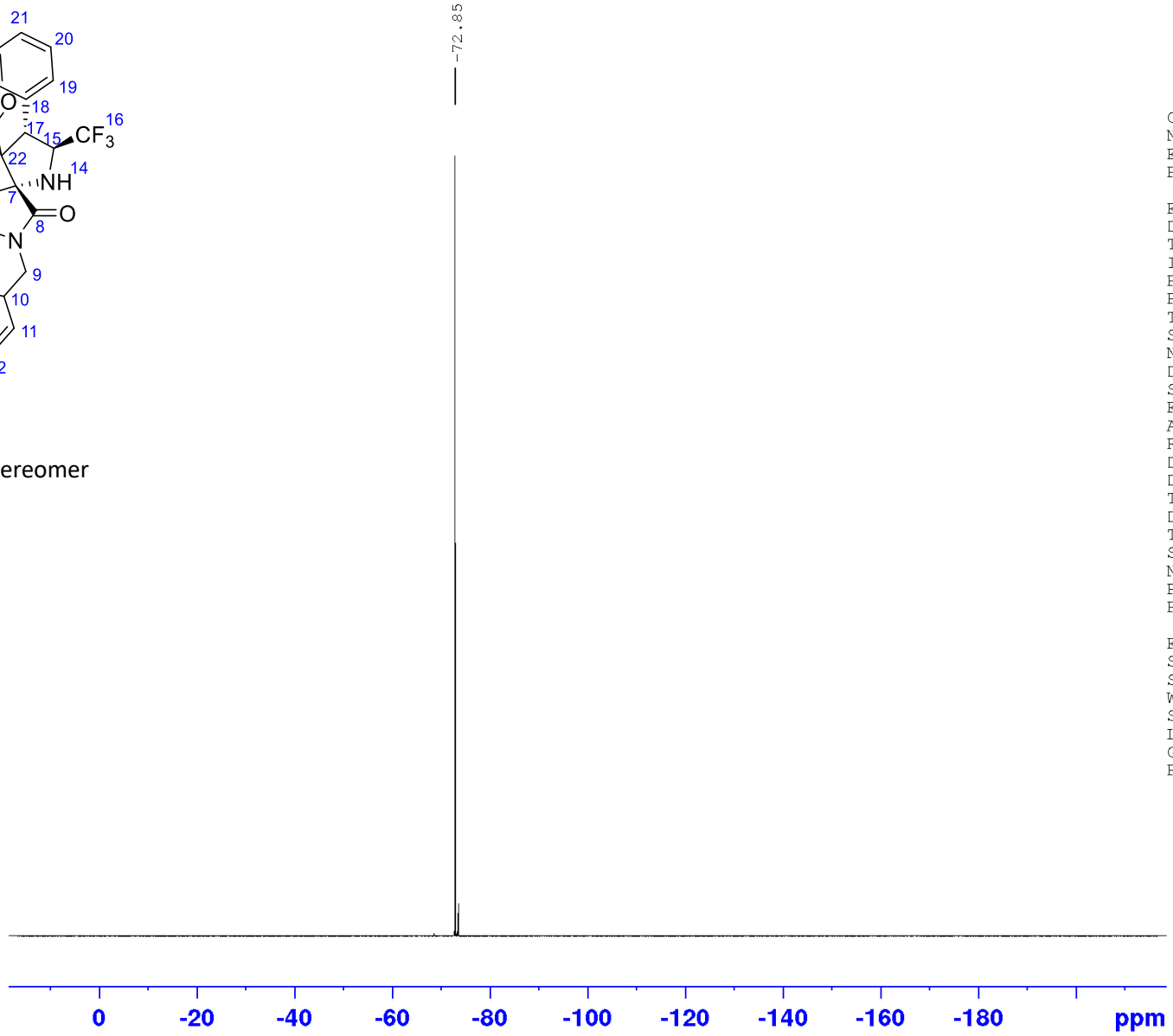
5a

Major diastereomer

^{19}F NMR

564 MHz

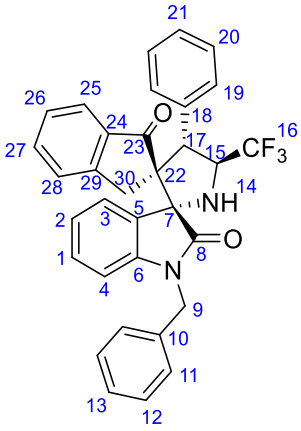
$CDCl_3$




```
Current Data Parameters
NAME      WR 1.136 (600)
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210715
Time               5.25 h
INSTRUM            spect
PROBHD   Z114607_0188 (
PULPROG           zgflqn
TD                261896
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           133928.578 Hz
FIDRES          1.022761 Hz
AQ             0.9777451 sec
RG                186.92
DW                 3.733 usec
DE                 6.70 usec
TE                302.5 K
D1           4.00000000 sec
TD0                    1
SFO1         564.6299217 MHz
NUC1                 19F
P1                12.00 usec
PLW1         49.00000000 W

F2 - Processing parameters
SI                262144
SF           564.6863882 MHz
WDW                  EM
SSB       0
LB                 0.50 Hz
GB        0
PC                 2.00
```



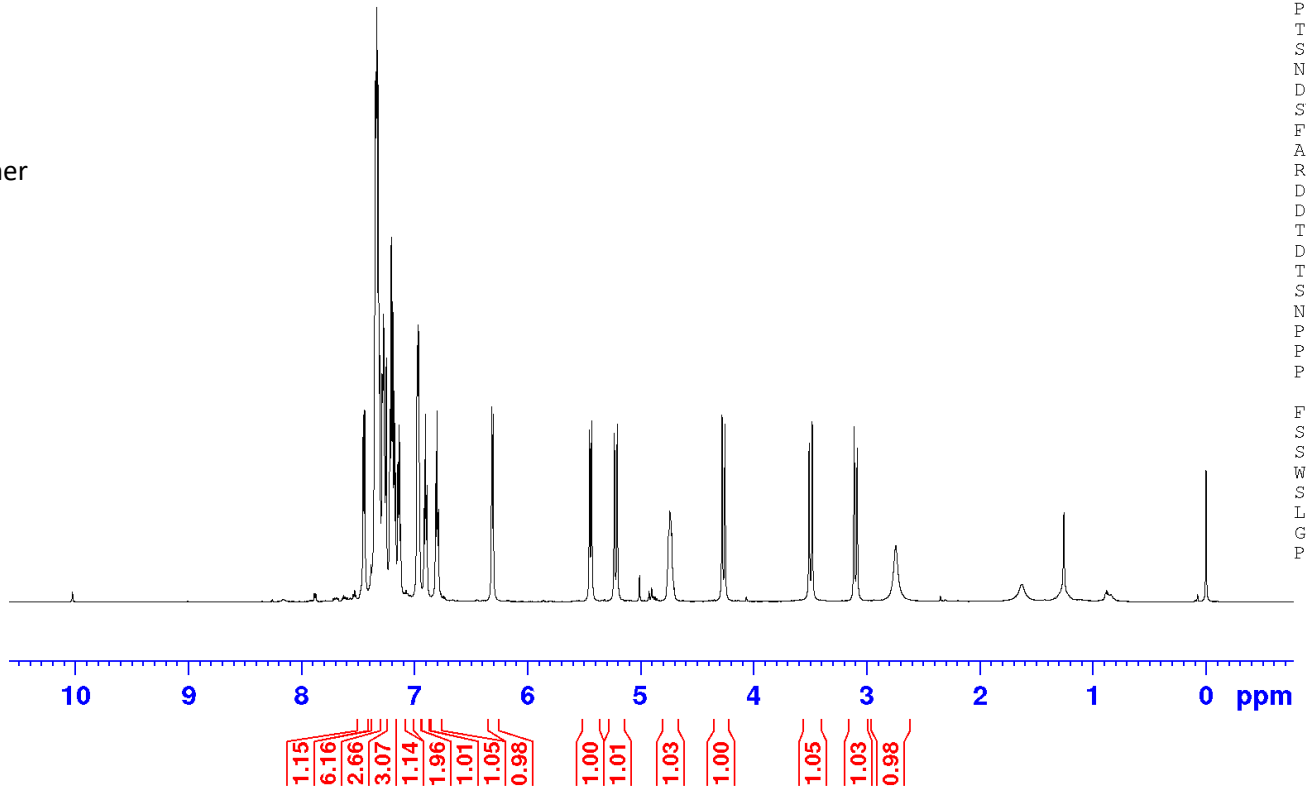
5b

Major diastereomer

^{1}H NMR

600 MHz

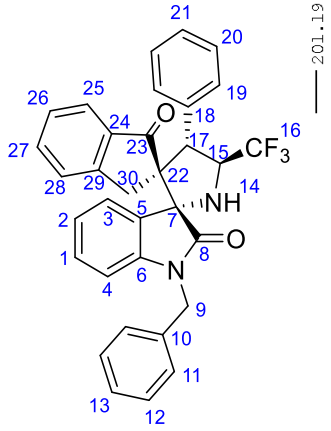
$CDCl_3$




```
Current Data Parameters
NAME      WR 1.131 (600)
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210714
Time               23.18 h
INSTRUM             spect
PROBHD   Z114607_0188 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12019.230 Hz
FIDRES          0.366798 Hz
AQ             2.7262976 sec
RG                    68
DW                41.600 usec
DE                12.10 usec
TE                303.6 K
D1           1.00000000 sec
TD0                    1
SFO1         600.1337058 MHz
NUC1                  1H
P0                 3.33 usec
P1                10.00 usec
PLW1         26.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1300185 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



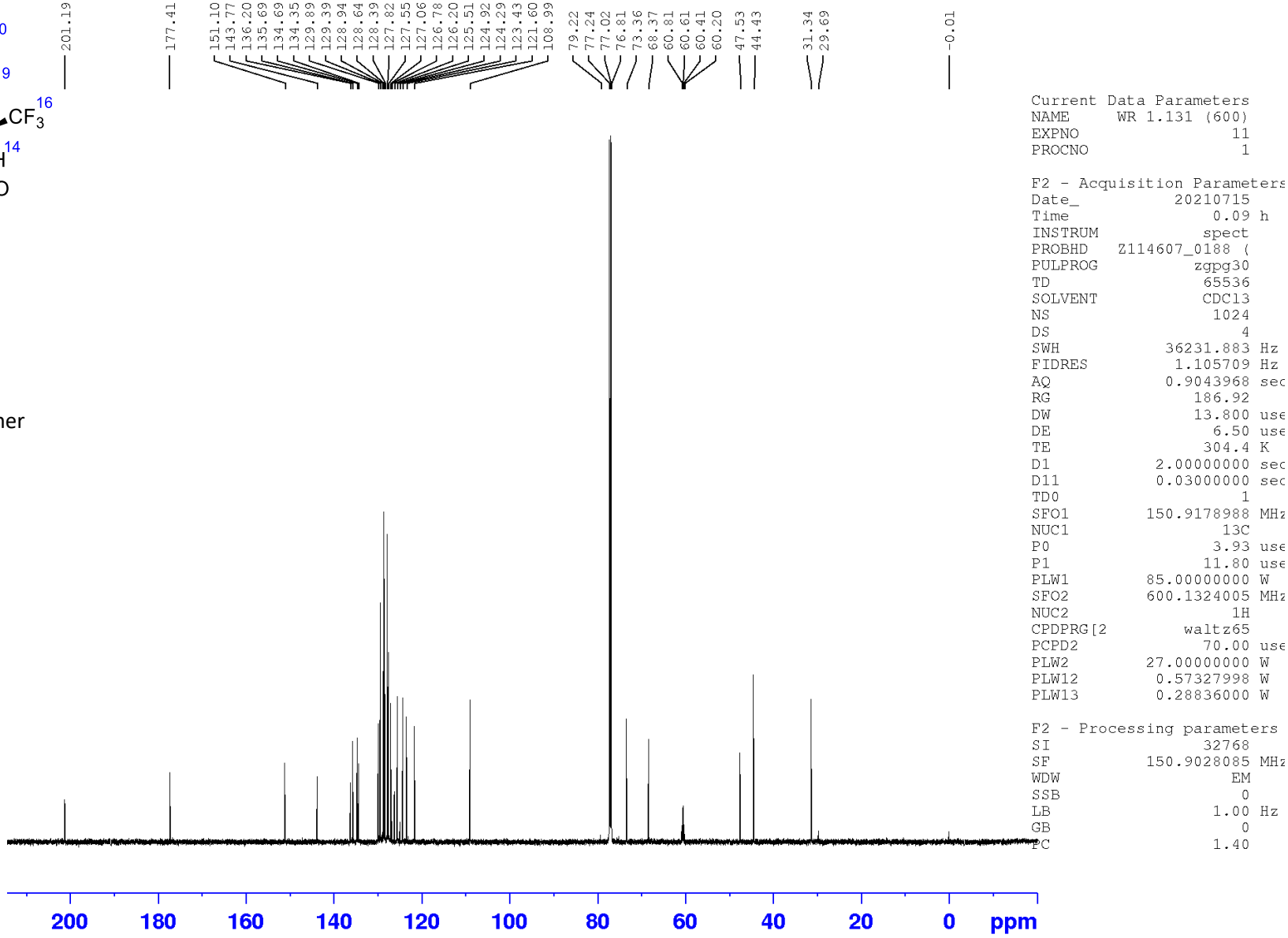
5b

Major diastereomer

^{13}C NMR

151 MHz

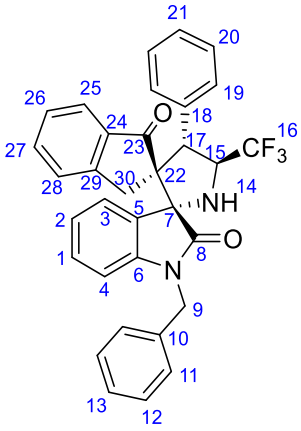
$CDCl_3$




```
Current Data Parameters
NAME      WR 1.131 (600)
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210715
Time                0.09 h
INSTRUM            spect
PROBHD    Z114607_0188 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           36231.883 Hz
FIDRES         1.105709 Hz
AQ             0.9043968 sec
RG               186.92
DW                13.800 use
DE                 6.50 use
TE                304.4 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                   1
SFO1        150.9178988 MHz
NUC1               13C
P0                 3.93 use
P1                11.80 use
PLW1        85.00000000 W
SFO2        600.1324005 MHz
NUC2               1H
CPDPRG[2        waltz65
PCPD2             70.00 use
PLW2        27.00000000 W
PLW12        0.57327998 W
PLW13        0.28836000 W

F2 - Processing parameters
SI                32768
SF          150.9028085 MHz
WDW                EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```



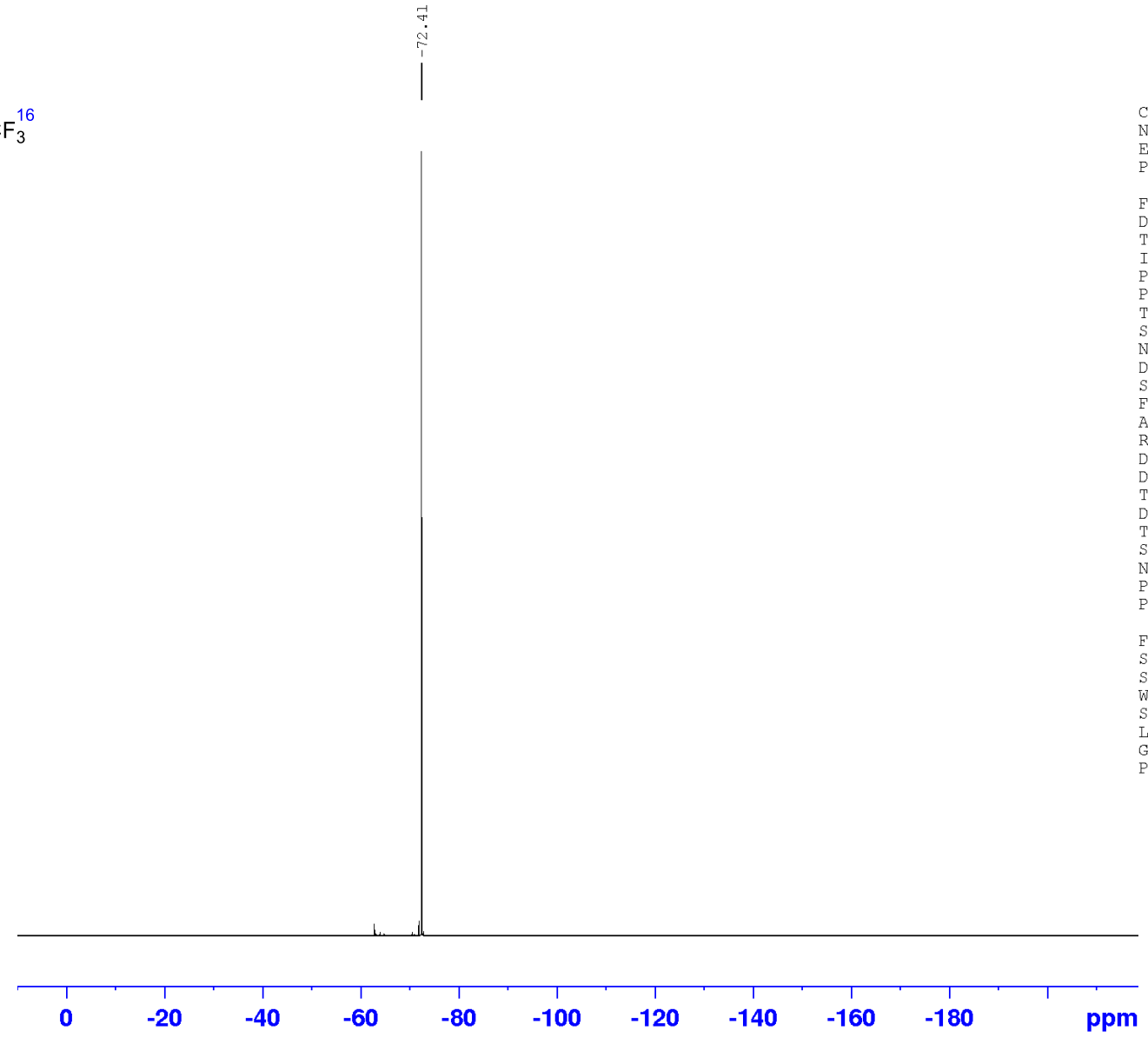
5b

Major diastereomer

^{19}F NMR

564 MHz

$CDCl_3$




```
Current Data Parameters
NAME      WR 1.131 (600)
EXPNO                 18
PROCNO                 1

F2 - Acquisition Parameter
Date_           20210715
Time                2.18 h
INSTRUM            spect
PROBHD    Z114607_0188 (
PULPROG           zgflqn
TD                261896
SOLVENT            CDCl3
NS                    16
DS                     4
SWH           133928.578 H
FIDRES          1.022761 H
AQ              0.9777451 s
RG                186.92
DW                 3.733 u
DE                 6.70 u
TE                302.4 K
D1            4.00000000 s
TD0                    1
SFO1          564.6299217 M
NUC1                19F
P1                12.00 u
PLW1          49.00000000 W

F2 - Processing parameter
SI                262144
SF          564.6863882 M
WDW                 EM
SSB                  0
LB                0.50 H
GB                   0
PC                2.00
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8 References

1 J. Cosier and A. M. Glazer, *J. Appl. Crystallogr.*, 1986, **19**, 105–107.

2 *CrysAlisPRO*, Oxford Diffraction/Agilent Technologies UK Ltd, Yarnton, England.

3 G. M. Sheldrick, *Acta Crystallogr. Sect. A*, 2015, **71**, 3–8.

4 L. Palatinus and G. Chapuis, *J. Appl. Crystallogr.*, 2007, **40**, 786–790.

5 P. W. Betteridge, J. R. Carruthers, R. I. Cooper, K. Prout and D. J. Watkin, *J. Appl. Crystallogr.*, 2003, **36**, 1487.

6 R. I. Cooper, A. L. Thompson and D. J. Watkin, *J. Appl. Crystallogr.*, 2008, **43**, 1100–1107.

7 J. M. G. O. Ferreira, J. B. M. De Resende Filho, P. K. Batista, E. E. S. Teotonio and J. A. Vale, *J. Braz. Chem. Soc.*, 2018, **29**, 1382–1387.

8 M. Zhang, A. Q. Zhang, H. H. Chen, J. Chen and H. Y. Chen, *Synth. Commun.*, 2006, **36**, 3441–3445.

9 Y. Song, H. Jing, B. Li and D. Bai, *Chem. Eur. J*, 2011, **17**, 8731–8738.

10 S. P. Bhoite, A. H. Bansode and G. Suryavanshi, *J. Org. Chem.*, 2020, **85**, 14858–14865.

11 K. Yamashita, T. Tanaka and M. Hayashi, *Tetrahedron*, 2005, **61**, 7981–7985.

12 Z. Li, H. Li, X. Guo, L. Cao, R. Yu, H. Li and S. Pan, *Org. Lett.*, 2008, **10**, 803–805.

13 T. M. Kadayat, S. Banskota, P. Gurung, G. Bist, T. B. Thapa Magar, A. Shrestha, J. A. Kim and E. S. Lee, *Eur. J. Med. Chem.*, 2017, **137**, 575–597.

14 C. S. Buxton, D. C. Blakemore and J. F. Bower, *Angew. Chem. Int. Ed.*, 2017, **56**, 13824–13828.

15 M. Ma, Y. Zhu, Q. Sun, X. Li, J. Su, L. Zhao, Y. Zhao, S. Qiu, W. Yan, K. Wang and R. Wang, *Chem. Commun.*, 2015, **51**, 8789–8792.

16 B. Ma, P. Wu, X. Wang, Z. Wang, H. X. Lin and H. X. Dai, *Angew. Chem. Int. Ed.*, 2019, 58, 13335–13339.

17 C. Jin, M. Zhang, L. Wu, Y. Guan, Y. Pan, J. Jiang, C. Lin and L. Wang, *Chem. Commun.*, 2013, **49**, 2025–2027.

18 C. J. Thomson, D. M. Barber and D. J. Dixon, *Angew. Chem. Int. Ed.*, 2019, **58**, 2469–2473.

19 C. B. Tripathi, S. Kayal and S. Mukherjee, *Org. Lett.*, 2012, **14**, 3296–3299.

20 Y. Zhu, J. P. Malerich and V. H. Rawal, *Angew. Chem. Int. Ed.*, 2010, **49**, 153–156.

21 E. Matador, M. de Gracia Retamosa, D. Monge, J. Iglesias-Sigüenza, R. Fernández and J. M. Lassaletta, *Chem. Eur. J*, 2018, **24**, 6854–6860.

22 F. Yu, Z. Jin, H. Huang, T. Ye, X. Liang and J. Ye, *Org. Biomol. Chem.*, 2010, 8, 4767–4774.

23 N. Akhtar, A. Saha, V. Kumar, N. Pradhan, S. Panda, S. Morla, S. Kumar and D. Manna, *ACS Appl. Mater. Interfaces*, 2018, **10**, 33803–33813.

24 M. H. Furigay, M. M. Boucher, N. A. Mizgier and C. S. Brindle, *J. Vis. Exp.*, 2018, 1–10, doi:10.3791/57639.