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for the paper

IMDAV Reaction between 3-(Isoxazol-3-yl)allylamines and Maleic Anhydrides. Unusual Approach to Pyrrolo[3,4-*c*]pyridine Derivatives, Possessing Anti-Inflammatory Activity

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1. General information

All reagents and solvents were purchased from commercial suppliers (Acros Organics, Aldrich, Alfa Aesar, AstaTech and Reachim) and used without further purification. No reactions require absolute solvents ($CHCl_3$, MeOH, PhH, PhMe, *o*-xylene, THF) and in an inert atmosphere. Thin layer chromatography, when necessary, was carried out on aluminum backed silica plates Sorbfil. The plates were visualized under UV light (254 nm) or in I_2 vapor. Organic layers were dried over anhydrous $MgSO_4$ or Na_2SO_4 and concentrated *in vacuo*. Melting points for all crystalline compounds were measured on a capillary point apparatus Stuart SMP 10 equipped with a digital thermometer and were uncorrected. IR spectra were obtained in KBr pellets using an Infralum FT-801 IR-Fourier spectrometer. LC-MS mass spectra were taken on Agilent 1100 series LC/MSD spectrometer with an API-ES/APCI ionization mode. The samples for the ESI-TOF-HRMS experiments were prepared in 1.8 mL glass vials with screwtop caps fitted with Teflon-lined septa (Agilent Technologies). High-resolution mass spectra (HRMS) were recorded on a Bruker maXis q-TOF (tandem quadrupole/time-of-flight mass analyzer) mass spectrometer equipped with an electrospray ionization (ESI) source. The *m/z* scanning range was 50–3000. The measurements were carried out in positive ion mode (+) (grounded spray needle, –4500 V high-voltage capillary; 500 V HV End Plate) and in negative ion mode (–) (grounded spray needle, +4000 V high-voltage capillary; –500 V HV End Plate Offset). External calibration of the mass scale was carried out using a low-concentration calibration solution "Tuning mix" (Agilent Technologies). Samples were injected using a 500 μL Hamilton RN 1750 syringe (Switzerland). The flow rate during injection was controlled with a syringe pump (3 μL/min). Nitrogen was used as a nebulizer gas (1.0 bar) and dry gas (4.0 L/min, 200 °C). The data were processed using Bruker Data Analysis 4.0 software. NMR spectra were run in deuterated (>99%) solvents on Jeol JNM-ECA 600 (600.2 MHz for ^{1}H, 150.9 MHz for ^{13}C and 564.7 for ^{19}F) or Bruker Avance NEO 700 (700.2 MHz for ^{1}H, 176.1 MHz for ^{13}C and 658.8 MHz for ^{19}F) spectrometer for 2−8% solutions in $CDCl_3$ or DMSO-d_6 at 23−25 °C. Residual signals of deuterated solvents were used as internal standards ($CDCl_3$: 7.25 ppm for ^{1}H nuclei, 77.2 ppm for ^{13}C nuclei; DMSO-d_6: 2.50 ppm for ^{1}H nuclei, 39.5 ppm for ^{13}C nuclei). MW-assisted reactions were carried out in a Monowave 400 reactor from Anton Paar GmbH; the reaction temperature was monitored by an IR sensor. Standard 10 mL G10 reaction vials, sealed with silicone septa, were used for the MW irradiation experiments.

2. The X-ray part

X-ray diffraction experiments were performed with a Bruker KAPPA APEX II automatic four-circle area-detector diffractometer. Unit cell parameters were refined over the whole dataset together with data reduction [1]. Absorption corrections using the SADABS program [2]. The structures were solved by the intrinsic phasing method (SHELXT [3]) and refined by the full-matrix least-squares method (SHELXL-2018 [4]) on F^2 over the whole dataset in the anisotropic approximation for all non-hydrogen atoms. The H atoms connected with C ones were placed in geometrically calculated positions with U_{iso} = 1.2U_{eq}(C) for CH and CH_2 groups and U_{iso} = 1.5U_{eq}(C) for CH_3 ones. The H atoms of NH groups in **10c**, **11b** and **11o** were located from difference Fourier-syntheses and refined with U_{iso} = 1.2U_{eq}(N). In **11g** and **11a**, the H atoms of NH groups were placed in geometrically calculated positions with U_{iso} = 1.2U_{eq}(N). The absolute structure of **11a**, containing two crystallographically independent formula units, was not determined. The structure **11b** is partially disordered (Figures S1−S5).

Crystallographic data and experimental details are given in Tables 1S−5S.

The crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (depositions CCDC 2350931−2350935).

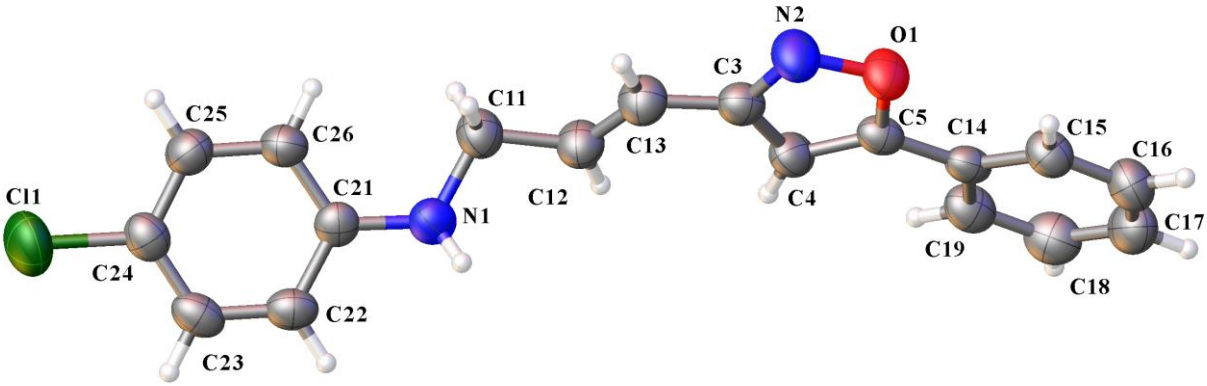

Figure S1. Molecular structure of **10c**.

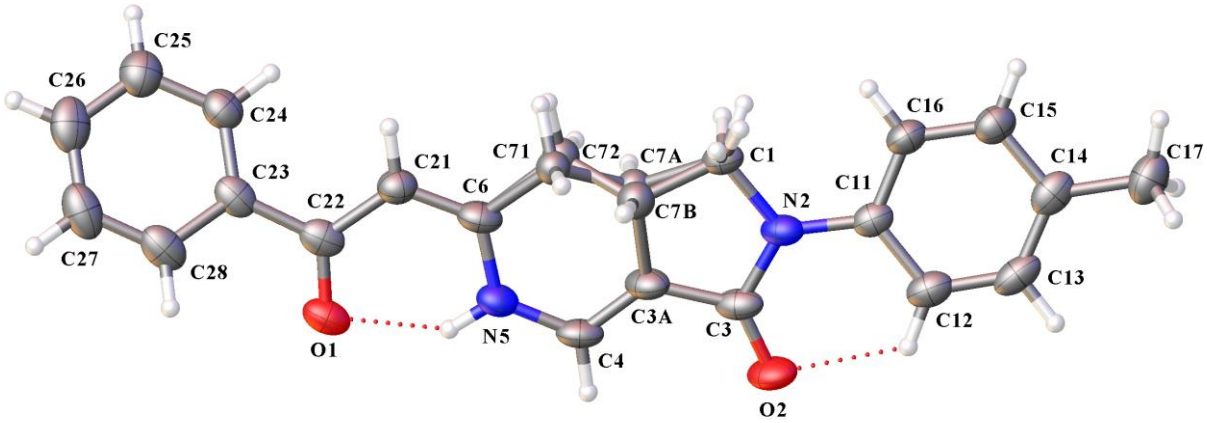

Figure S2. Molecular structure of **11b**. Dotted lines show H-bonding interactions.

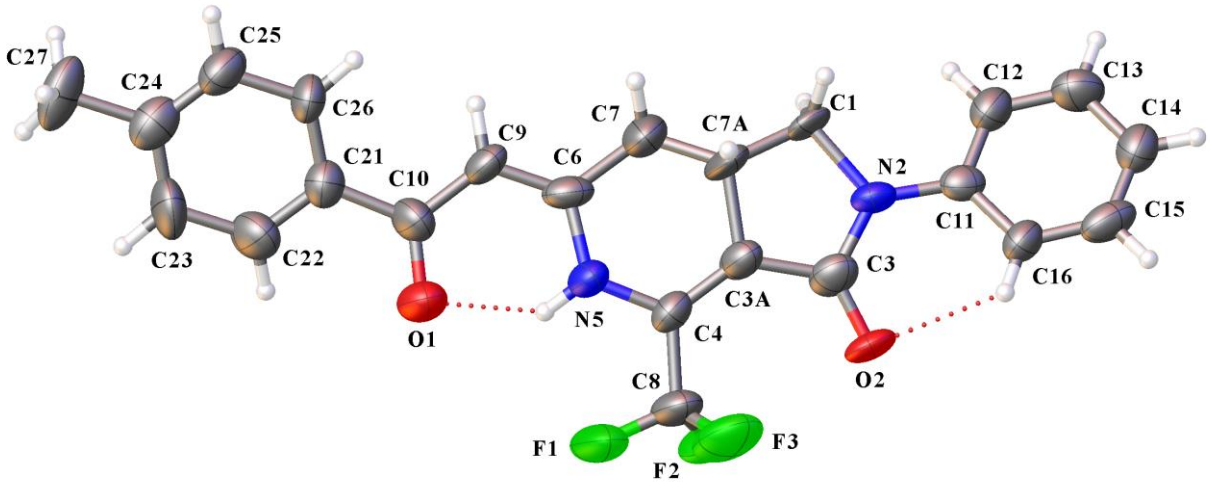

Figure S3. Molecular structure of **11g**. Dotted lines show H-bonding interactions.

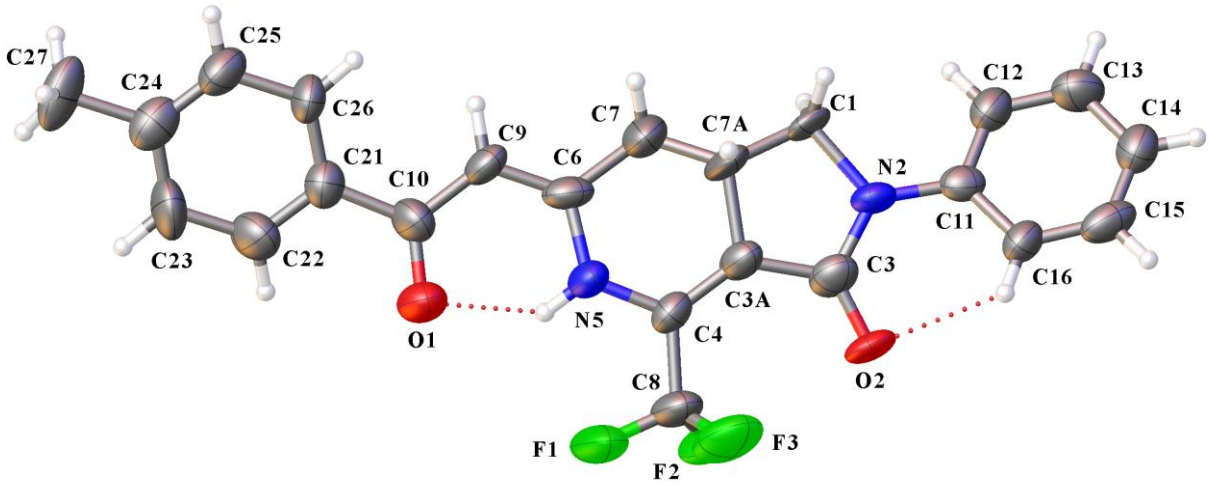

Figure S4. Molecular structure of **11o**. Dotted lines show H-bonding interactions.

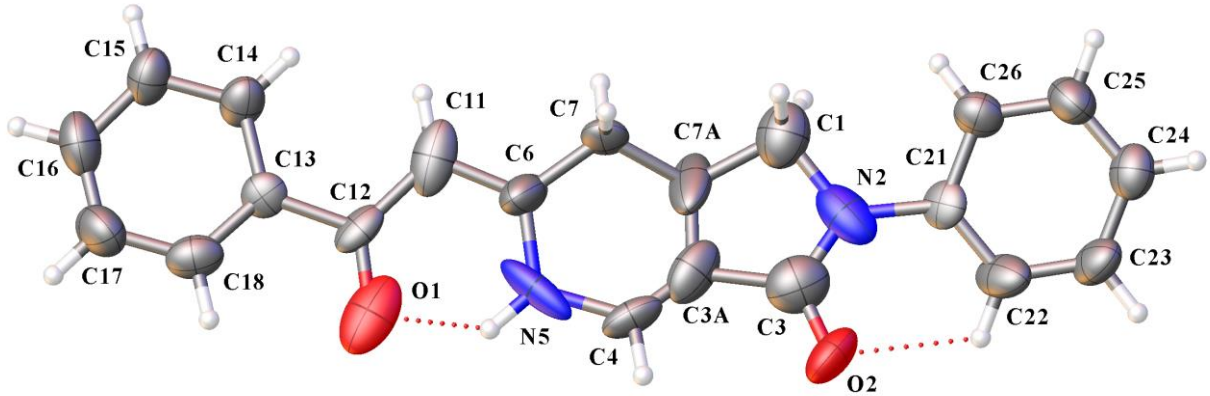

Figure S5. Molecular structure of **11a**. Dotted lines show H-bonding interactions. Only one of the two crystallographically independent molecules is shown.

Table 1S. Crystal data and structure refinement for 10c.

CCDC deposition number	2350931
Empirical formula	$C_{18}H_{15}N_2OCl$
Formula weight	310.77

Temperature/K	296(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	18.3294(19)
b/Å	14.7101(15)
c/Å	5.7414(5)
α/°	90
β/°	93.577(6)
γ/°	90
Volume/$Å^3$	1545.0(3)
Z	4
$\rho_{calc}g/cm^3$	1.336
μ/mm^{-1}	0.250
F(000)	648.0
Crystal size/mm^3	0.4 × 0.2 × 0.03
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	8.606 to 54.994
Index ranges	$-23 \leq h \leq 23$, $-19 \leq k \leq 19$, $-7 \leq l \leq 7$
Reflections collected	14964
Independent reflections	3539 [R_{int} = 0.1061, R_{sigma} = 0.1098]
Data/restraints/parameters	3539/0/202
Goodness-of-fit on F^2	0.923
Final R indexes [I>=2σ (I)]	R_1 = 0.0581, wR_2 = 0.1228
Final R indexes [all data]	R_1 = 0.1804, wR_2 = 0.1679
Largest diff. peak/hole / e $Å^{-3}$	0.17/-0.34

Table 2S. Crystal data and structure refinement for 11b.

CCDC deposition number	2350932
Empirical formula	$C_{22}H_{20}N_2O_2$
Formula weight	344.40
Temperature/K	100(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	13.6337(12)
b/Å	12.0340(9)
c/Å	11.0008(9)
α/°	90
β/°	107.466(5)
γ/°	90
Volume/$Å^3$	1721.7(2)
Z	4
$\rho_{calc}g/cm^3$	1.329
μ/mm^{-1}	0.086
F(000)	728.0
Crystal size/mm^3	0.4 × 0.08 × 0.06
Radiation	MoKα (λ = 0.71073)

2Θ range for data collection/°	8.186 to 54.982
Index ranges	$-17 \leq h \leq 16$, $-15 \leq k \leq 15$, $-14 \leq l \leq 14$
Reflections collected	15890
Independent reflections	3937 [R_{int} = 0.0717, R_{sigma} = 0.0847]
Data/restraints/parameters	3937/1/238
Goodness-of-fit on F^2	1.003
Final R indexes [I>=2σ (I)]	R_1 = 0.0579, wR_2 = 0.1147
Final R indexes [all data]	R_1 = 0.1381, wR_2 = 0.1414
Largest diff. peak/hole / e $Å^{-3}$	0.27/-0.21

Table 3S. Crystal data and structure refinement for 11g.

CCDC deposition number	2350933
Empirical formula	$C_{22}H_{19}N_2O_2Cl$
Formula weight	378.84
Temperature/K	296(2)
Crystal system	monoclinic
Space group	C2/c
a/Å	40.8182(17)
b/Å	6.3454(3)
c/Å	14.8844(6)
α/°	90
β/°	108.250(2)
γ/°	90
Volume/$Å^3$	3661.3(3)
Z	8
$\rho_{calc}g/cm^3$	1.375
μ/mm^{-1}	0.229
F(000)	1584.0
Crystal size/mm^3	0.18 × 0.16 × 0.06
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	8.076 to 54.998
Index ranges	$-52 \leq h \leq 52$, $-8 \leq k \leq 8$, $-19 \leq l \leq 19$
Reflections collected	14340
Independent reflections	4194 [R_{int} = 0.0644, R_{sigma} = 0.0612]
Data/restraints/parameters	4194/0/245
Goodness-of-fit on F^2	1.002
Final R indexes [I>=2σ (I)]	R_1 = 0.0628, wR_2 = 0.1476
Final R indexes [all data]	R_1 = 0.1620, wR_2 = 0.1902
Largest diff. peak/hole / e $Å^{-3}$	0.39/-0.21

Table 4S. Crystal data and structure refinement for 11o.

CCDC deposition number	2350934
Empirical formula	$C_{23}H_{19}N_2O_2F_3$
Formula weight	412.40
Temperature/K	296(2)
Crystal system	monoclinic

Space group	$P2_1/c$
a/Å	5.4100(14)
b/Å	27.059(7)
c/Å	13.460(3)
α/°	90
β/°	96.408(18)
γ/°	90
Volume/Å^3	1958.1(8)
Z	4
ρ_{calc}g/cm^3	1.399
μ/mm^{-1}	0.109
F(000)	856.0
Crystal size/mm^3	0.4 × 0.1 × 0.02
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	8.158 to 49.998
Index ranges	$-6 \leq h \leq 6$, $-30 \leq k \leq 32$, $-15 \leq l \leq 15$
Reflections collected	14588
Independent reflections	3447 [R_{int} = 0.3564, R_{sigma} = 0.3764]
Data/restraints/parameters	3447/1/275
Goodness-of-fit on F^2	0.937
Final R indexes [I>=2σ (I)]	R_1 = 0.1167, wR_2 = 0.2072
Final R indexes [all data]	R_1 = 0.3628, wR_2 = 0.3037
Largest diff. peak/hole / e Å^{-3}	0.26/-0.27

Table 5S. Crystal data and structure refinement for 11a.

CCDC deposition number	2350935
Empirical formula	$C_{21}H_{18}N_2O_2$
Formula weight	330.37
Temperature/K	100(2)
Crystal system	orthorhombic
Space group	$Pca2_1$
a/Å	23.2034(17)
b/Å	6.2396(5)
c/Å	22.4373(18)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	3248.5(4)
Z	8
ρ_{calc}g/cm^3	1.351
μ/mm^{-1}	0.088
F(000)	1392.0
Crystal size/mm^3	0.3 × 0.16 × 0.03
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	8.258 to 50.976
Index ranges	$-27 \leq h \leq 26$, $-7 \leq k \leq 7$, $-26 \leq l \leq 27$
Reflections collected	22620

Independent reflections	5945 [R_{int} = 0.0623, R_{sigma} = 0.0609]
Data/restraints/parameters	5945/17/451
Goodness-of-fit on F^2	1.025
Final R indexes [I>=2σ (I)]	R_1 = 0.1018, wR_2 = 0.2458
Final R indexes [all data]	R_1 = 0.1448, wR_2 = 0.2764
Largest diff. peak/hole / e $Å^{-3}$	0.67/-0.56
Flack parameter	0.1(9)

Table 6S. Parameters of intramolecular H-bonds.

D-H···A	**d(D-H)/Å**	**d(H···A)/Å**	**d(D···A)/Å**	**D-H···A/°**
11b				
N5-H5···O1	0.889(15)	1.913(18)	2.668(2)	141.7(19)
C12-H12A···O2	0.95	2.24	2.860(3)	122
11g				
N9-H9A···O1	0.86	1.96	2.624(3)	133
C12-H12A···O2	0.93	2.26	2.861(4)	122
11o				
N5-H5···O1	0.86(2)	1.93(7)	2.594(11)	133(9)
C16-H16A···O2	0.93	2.33	2.866(13)	116
11a				
N5-H5A···O1	0.88	1.76	2.437(15)	132
C22-H22A···O2	0.95	2.20	2.758(15)	116
N5B-H5BA···O1B	0.88	1.96	2.632(13)	132
C22B-H22B···O2B	0.95	2.26	2.859(15)	120

3. Synthetic procedures

General Procedure for the Synthesis of Products 9a-g and Characterization Data.

A mixture of the corresponding isoxazole-3-carbaldehyde (5.78 mmol) and (triphenylphosphoranylidine)acetaldehyde (1.76 g, 5.78 mmol) in dry $CHCl_3$ (20 mL) was refluxed until the process was complete (TLC and GC/MS monitoring, ~6 h). The reaction mixture was cooled to 25°C, concentrated, and then purified by column chromatography (SiO_2; 15 × 3 cm, eluent: heptane/ethyl acetate 50:1).

(**2*E*)-3-(5-Phenylisoxazol-3-yl)acrylaldehyde (9a).** A mixture of *cis*- and *trans*-isomers of 1.07 g (93%) 3-(5-phenylisoxazole-3-yl) acrylaldehyde **9a** was obtained as colorless crystals. The isomeric isoxazole acrylic aldehydes **9a** were kept in the presence of I_2 (10 mol%, 0.105 g) in boiling acetic acid (20 mL), then poured into H_2O (100 ml), the resulting precipitate was filtered off, washed with *aq*. $Na_2S_2O_3$ (5 ml), and air dried. *Trans*-**9a** was isolated in yields of 80% (0.84 g). M.p. 160-161 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 9.80 (d, J = 7.6 Hz, 1H), 7.83-7.81 (dd, J = 7.6, 2.0 Hz, 2H), 7.58 (d, J = 16.1 Hz, 1H), 7.53-7.49 (m, 3H), 6.77 (dd, J = 7.6, 16.1 Hz, 1H), 6.76 (s, 1H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 192.8, 171.4, 160.2, 138.7, 134.4, 130.9 (2C), 129.3, 126.8, 126.0 (2C), 97.1. IR (KBr, cm^{-1}): ν_{max} = 1679 (C=O), 1572, 1611 (C=C). MS (ESI): *m/z* = 200 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{12}H_{10}NO_2$ $[M+H]^+$, 200.0706; found, 200.0702, (Δ = -2.00 ppm).

(2*E*)-3-[5-(4-Methylphenyl)isoxazol-3-yl]acrylaldehyde (9b). A mixture of *cis*- and *trans*-isomers of 1.14 g (93%) 3-(5-tolylisoxazole-3-yl) acrylaldehyde **9b** was obtained as colorless crystals. The isomeric isoxazole acrylic aldehydes **9b** were kept in the presence of I_2 (10 mol%, 0.136 g) in boiling acetic acid (20 mL), then poured into H_2O (100 ml), the resulting precipitate was filtered off, washed with *aq*. $Na_2S_2O_3$ (5 ml), and air dried. *Trans*-**9b** was isolated in yields of 92% (1.05 g). M.p. 125-126 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 9.79 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 8.1 Hz, 2H), 7.56 (d, J = 16.1 Hz, 1H), 7.30 (d, J = 8.1 Hz, 2H), 6.76 (dd, J = 7.6, 16.1 Hz, 1H), 6.70 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 192.9, 171.6, 160.2, 141.3, 138.8, 134.3, 129.9 (2C), 125.9 (2C), 124.1, 96.4, 21.6. IR (KBr, cm^{-1}): ν_{max} = 1679 (C=O), 1619, 1508 (C=C). MS (ESI): *m/z* = 214 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{13}H_{12}NO_2$ $[M+H]^+$, 214.0863; found, 214.0862, (Δ = -0.47 ppm).

(2*E*)-3-[5-(2,5-Dimethylphenyl)isoxazol-3-yl]acrylaldehyde (9c). Yield: 0.30 g (99%); colourless powder. M.p. 113-115 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 9.81 (d, J = 7.6 Hz, 1H), 7.60 (d, J = 16.2 Hz, 1H), 7.55 (s, 1H), 7.23-7.20 (m, 2H), 6.78 (dd, J = 7.6, 16.2 Hz, 1H), 6.64 (s, 1H), 2.49 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 192.8, 171.6, 159.8, 138.8, 136.0, 134.2, 133.2, 131.5, 131.4, 129.0, 126.0, 100.0, 21.0, 20.9. IR (KBr,

cm^{-1}): ν_{max} = 1683 (C=O), 1573 (C=C). MS (ESI): *m/z* = 228 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{14}H_{14}NO_2$ $[M+H]^+$, 228.1019; found, 228.1016, (Δ = -1.31 ppm).

(2*E*)-3-[5-(3,4-Dimethylphenyl)isoxazol-3-yl]acrylaldehyde (9d). Yield: 1.09 g (83%); colourless powder. M.p. 123-125 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 9.79 (d, *J* = 7.6 Hz, 1H), 7.58 (s, 1H), 7.56 (d, *J* = 16.2 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 1H), 6.74 (dd, *J* = 16.2, 7.6 Hz, 1H), 6.69 (s, 1H), 2.34 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 192.8, 171.7, 160.1, 140.0, 138.9, 137.6, 134.2, 130.4, 127.0, 124.3, 123.4, 96.3, 19.9, 19.8. IR (KBr, cm^{-1}): ν_{max} = 1679 (C=O), 1619, 1572 (C=C). MS (ESI): *m/z* = 228 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{14}H_{14}NO_2$ $[M+H]^+$, 228.1019; found, 228.1021, (Δ = 0.88 ppm).

(2*E*)-3-[5-(4-Ethylphenyl)isoxazol-3-yl]acrylaldehyde (9e). Yield: 1.14 g (87%); colourless powder. M.p. 134-136 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 9.79 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.57 (d, *J* = 16.2 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 2H), 6.76 (dd, *J* = 16.2, 7.6 Hz, 1H), 6.71 (s, 1H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 7.6, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 192.9, 171.6, 160.2, 147.6, 138.8, 134.3, 128.8 (2C), 126.1 (2C), 124.3, 96.5, 28.9, 15.4. IR (KBr, cm^{-1}): ν_{max} = 1679 (C=O), 1617, 1596 (C=C). MS (ESI): *m/z* = 228 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{14}H_{14}NO_2$ $[M+H]^+$, 228.1019; found, 228.1015, (Δ = -1.75 ppm).

(2*E*)-3-[5-(4-*tert*-Butylphenyl)isoxazol-3-yl]acrylaldehyde (9f). Yield: 1.19 g (81%); colourless powder. M.p. 181-182 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 9.79 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 16.2 Hz, 1H), 7.52 (d, *J* = 8.6 Hz, 2H), 6.77 (dd, *J* = 16.2, 7.6 Hz, 1H), 6.72 (s, 1H), 1.36 (s, 9H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 192.9, 171.5, 160.2, 154.4, 138.8, 134.4, 126.2 (2C), 125.8 (2C), 124.0, 96.5, 35.1, 31.2 (3C). IR (KBr, cm^{-1}): ν_{max} = 1693 (C=O), 1615 (C=C). MS (ESI): *m/z* = 256 $[M+H]^+$. MS (ESI): *m/z* = 256 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{16}H_{18}NO_2$ $[M+H]^+$, 256.1332; found, 256.1321, (Δ = -4.29 ppm).

(2*E*)-3-[5-(1-Naphthyl)isoxazol-3-yl]acrylaldehyde (9g). A mixture of *cis*- and *trans*-isomers of 1.31 g (91%) 3-(5-naphthylisoxazole-3-yl)acrylaldehyde **9g** was obtained as colorless crystals. The isomeric isoxazole acrylic aldehydes **9g** were kept in the presence of I_2 (10 mol%, 0.134 g) in boiling acetic acid (20 mL), then poured into H_2O (100 ml), the resulting precipitate was filtered off, washed with *aq*. $Na_2S_2O_3$ (5 ml), and air dried. *Trans*-**9g** was isolated in yields of 67% (0.88 g). M.p. 121-123 °C. ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 9.84 (d, *J* = 7.6 Hz, 1H), 8.27 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 6.9 Hz, 1H), 7.65 (d, *J* = 16.2 Hz, 1H), 7.63-7.57 (m, 3H), 6.85 (s, 1H), 6.82 (dd, *J* = 16.2, 7.6 Hz, 1H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 192.8, 171.4, 159.9, 138.6, 134.4, 133.8, 131.5, 130.2, 128.9, 128.0, 127.7, 126.7, 125.2, 124.7, 124.3, 101.2. IR (KBr, cm^{-1}): ν_{max} = 1682 (C=O),

1565 (C=C). MS (ESI): *m/z* = 250 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{16}H_{12}NO_2$ $[M+H]^+$, 250.0863; found, 250.0859, (Δ = -1.60 ppm).

(2*E*)-3-[5-(4-Nitrophenyl)isoxazol-3-yl]acrylaldehyde (9h). Yield: 0.89 g (63%); colourless powder. M.p. 181-183 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 9.83 (d, *J* = 7.6 Hz, 1H), 8.39 (d, *J* = 8.8 Hz, 2H), 8.01 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 16.2 Hz, 1H), 6.94 (s, 1H), 6.80 (dd, *J* = 16.2, 7.6 Hz, 1H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 192.4, 168.7, 160.5, 148.9, 137.6, 134.9, 132.0, 126.8 (2C), 124.6 (2C), 99.6). IR (KBr, cm^{-1}): ν_{max} = 1688 (C=O, C=C), 1518, 1339 (NO_2). MS (ESI): *m/z* = 245 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{12}H_8N_2O_4$ $[M+H]^+$, 245.0557; found, 245.0548, (Δ = -3.67 ppm).

General Procedure for the Synthesis of Products 10a-n and Characterization Data. To a solution of the corresponding aniline (2.59 mmol) in MeOH (30 mL), corresponding isoxazole acrylic aldehydes **9** (2.59 mmol) was added at room temperature. The mixture was stirred for 24 h, diluted with THF (5 mL), and then $NaCNBH_3$ (0.41 g, 6.48 mmol) and AcOH (1-2 drops) were added. The mixture was refluxed vigorously for 12 h (TLC control), then poured into H_2O (30 ml) and extracted with CH_2Cl_2 (3×10 ml), the combined organic layers were dried over anhydrous $MgSO_4$, concentrated, and purified by column chromatography (SiO_2, 23 × 1.6 cm, eluent: heptane/ethyl acetate 10:1).

***N*-[(2*E*)-3-(5-Phenylisoxazol-3-yl)prop-2-en-1-yl]aniline (10a).** Yield: 0.69 g (97%); colorless powder. M.p. 112-113 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 7.78 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.49-7.43 (m, 3H), 7.22 (t, *J* = 8.1 Hz, 2H), 6.78-6.73 (m, 2H), 6.68 (d, *J* = 8.1 Hz, 2H), 6.62 (s, 1 H), 6.54 (dt, *J* = 16.1, 5.6 Hz, 1 H), 4.02 (dd, *J* = 5.6, 2.0 Hz, 2H), 4.00 (br.s, 1H, NH). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 169.8, 161.7, 147.7, 135.6, 130.3, 129.5 (2C), 129.1 (2C), 127.5, 125.9 (2C), 119.3, 118.0, 113.1 (2C), 96.7, 45.7. IR (KBr, cm^{-1}): ν_{max} = 3371 (NH), 1601, 1505 (C=C). MS (ESI): *m/z* = 277 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{18}H_{17}N_2O$ $[M+H]^+$, 277.1335; found, 277.1340, (Δ = 1.80 ppm).

(4-Methylphenyl)[(2*E*)-3-(5-phenylisoxazol-3-yl)prop-2-en-1-yl]amine (10b). Yield: 0.40 g (53%); colorless powder. M.p. 123-124 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 7.79 (m, 2H), 7.49-7.45 (m, 3H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.74 (dt, *J* = 16.2, 1.7 Hz, 1H), 6.62 (d, *J* = 8.6 Hz, 2H), 6.61 (s, 1H), 6.54 (dt, *J* = 16.2, 5.3 Hz, 1H), 4.00 (dd, *J* = 5.3, 1.7 Hz, 2H), 3.83 (br.s, 1H, NH), 2.27 (s, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 169.7, 161.7, 145.3, 135.8, 130.2, 129.9 (2C), 129.0 (2C), 127.4, 127.2, 125.8 (2C), 119.2, 113.2 (2C), 96.6, 46.0, 20.4. IR (KBr, cm^{-1}): ν_{max} = 3361 (NH), 1612, 1520 (C=C). MS (ESI): *m/z* = 291 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{19}H_{19}N_2O$ $[M+H]^+$, 291.1492; found, 291.1494, (Δ = 0.69 ppm).

(4-Chlorophenyl)[(2*E*)-3-(5-phenylisoxazol-3-yl)prop-2-en-1-yl]amine (10c). Yield: 0.43 g (53%); colorless powder. M.p. 152-154 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 7.79-7.77

(m, 2H), 7.49-7.44 (m, 3H), 7.14 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 16.0 Hz, 1H), 6.61 (s, 1H), 6.58 (d, *J* = 8.8 Hz, 2H), 6.50 (dt, *J* = 5.0 Hz, 16.0 Hz, 1H), 4.00 (br.d, *J* = 5.0 Hz, 3H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 169.8, 161.5, 146.1, 134.9, 130.3, 129.2 (2C), 129.0 (2C), 127.3, 125.8 (2C), 122.5, 119.5, 114.1 (2C), 96.6, 45.7. IR (KBr, cm^{-1}): ν_{max} = 3354 (NH), 1599, 1494 (C=C). MS (ESI): *m/z* = 311 $[M+H]^+$ (for ^{35}Cl), 313 $[M+H]^+$ (for ^{37}Cl). HRMS (ESI-TOF): calcd. for $C_{18}H_{16}ClN_2O$ $[M+H]^+$, 311.0946 (for ^{35}Cl), 313.0917 (for ^{37}Cl); found, 311.0943 (for ^{35}Cl), 313.0916 (for ^{37}Cl), (Δ = -0.96, -0.32 ppm).

***N*-{(2*E*)-3-[5-(4-Methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10d).** Yield: 0.46 g (61%); colorless powder. M.p. 134-135 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) *there are no signal* NH 7.68 (d, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 7.1 Hz, 2H), 7.21 (t, *J* = 7.1 Hz, 2H), 6.77-6.72 (m, 2H), 6.68 (d, *J* = 8.1 Hz, 2H), 6.56 (s, 1H), 6.52 (dt, *J* =16.2, 5.6 Hz, 1H), 4.02 (br.d, *J* = 5.6 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 170.0, 161.7, 147.7, 140.6, 135.4, 129.8 (2C), 129.5, 125.8 (2C), 124.8, 119.4, 118.0 (2C), 113.1 (2C), 96.1, 45.7, 21.6. IR (KBr, cm^{-1}): ν_{max} = 3378 (NH), 1601, 1506 (C=C). MS (ESI): *m/z* = 291 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{19}H_{19}N_2O$ $[M+H]^+$, 291.1492; found, 291.1499, (Δ = 2.40 ppm).

(4-Methylphenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10e). Yield: 0.70 g (89%); colorless powder. M.p. 129-130 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 7.67 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 7.1 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.72 (dt, *J* = 16.2, 1.5 Hz, 1H), 6.61 (d, *J* = 8.6 Hz, 2H), 6.56 (s, 1H), 6.52 (dt, *J* = 16.2, 5.6 Hz, 1H), 3.96 (dd, *J* = 5.6, 1.5 Hz, 2H), 3.83 (br.s, 1H), 2.41 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 170.0, 161.7, 145.4, 140.6, 135.7, 129.9 (2C), 129.8, 127.3, 125.8 (2C), 124.8, 119.4 (2C), 113.3 (2C), 96.1, 46.1, 21.6, 20.5. IR (KBr, cm^{-1}): ν_{max} = 3374 (NH), 1617, 1520 (C=C). MS (ESI): *m/z* = 305 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{20}H_{21}N_2O$ $[M+H]^+$, 305.1648; found, 305.1648, (Δ = 0.00 ppm).

(4-Fluorophenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10f). Yield: 0.48 g (60%); colorless powder. M.p. 129-130 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 7.68 (d, *J* = 7.9 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 6.92 (t, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 16.2 Hz, 1H), 6.61-6.60 (m, 2H), 6.56 (s, 1H), 6.50 (dt, *J* = 16.2, 5.3 Hz, 1H), 3.98 (br.d, *J* = 5.2 Hz, 2H), 3.88 (br.s, 1H), 2.41 (s, 3H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 170.0, 161.5, 156.1 (d, *J* = 235.0 Hz, 1C), 143.9, 140.6, 135.1, 129.7 (2C), 125.7 (2C), 124.7, 119.5, 115.8 (d, *J* = 23.0 Hz, 2C), 113.9 (d, *J* = 6.8 Hz, 2C), 96.0, 46.2, 21.5. ^{19}F NMR (658.8 MHz, $CDCl_3$): δ (ppm) -127.5. IR (KBr, cm^{-1}): ν_{max} = 3357 (NH), 1596, 1509 (C=C). MS (ESI): *m/z* = 309 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{19}H_{18}FN_2O$ $[M+H]^+$, 309.1398; found, 309.1386, (Δ = -3.88 ppm).

(4-Chlorophenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10g). Yield: 0.56 g (66%); colorless powder. ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 7.67 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 7.1 Hz, 2H), 7.14 (d, J = 9.1 Hz, 2H), 6.70 (d, J = 16.2 Hz, 1H), 6.59 (d, J = 9.1 Hz, 2H), 6.56 (s, 1H), 6.48 (dt, J = 16.2, 5.1 Hz, 1H), 4.00 (dd, J = 5.1, 1.5 Hz, 2H), 3.99 (br.s, 1H), 2.41 (s, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 170.1, 161.5, 146.2, 140.6, 134.7, 129.8 (2C), 129.3 (2C), 125.8, 124.7, 122.6, 119.7 (2C), 114.2 (2C), 96.0, 45.8, 21.6. IR (KBr, cm^{-1}): ν_{max} = 3358 (NH), 1598, 1496 (C=C). MS (ESI): *m/z* = 325 $[M+H]^+$ (for ^{35}Cl), 327 $[M+H]^+$ (for ^{37}Cl). HRMS (ESI-TOF): calcd. for $C_{19}H_{18}ClN_2O$ $[M+H]^+$, 325.1102 (for ^{35}Cl), 327.1074 (for ^{37}Cl); found, 325.1097 (for ^{35}Cl), 327.1071 (for ^{37}Cl), (Δ = -1.54, -0.92 ppm).

(4-Bromophenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10h). Yield: 0.54 g (57%); colorless powder. M.p. 154-155 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) *there are no signal* NH 7.67 (d, J = 8.1 Hz, 2H), 7.28-7.27 (m, 4H), 6.71 (d, J = 16.2 Hz, 1H), 6.55 (s, 1H), 6.54 (d, J = 8.6 Hz, 2H), 6.48 (dt, J = 16.2, 5.1 Hz, 1H), 3.98 (dd, J = 5.1, 1.5 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 170.1, 161.5, 146.6, 140.6, 134.7, 132.1 (2C), 129.8 (2C), 125.8 (2C), 124.7, 119.7, 114.7 (2C), 109.6, 96.0, 45.6, 21.6. IR (KBr, cm^{-1}): ν_{max} = 3358 (NH), 1595, 1494 (C=C). MS (ESI): *m/z* = 369 $[M+H]^+$ (for ^{79}Br), 371 $[M+H]^+$ (for ^{81}Br). HRMS (ESI-TOF): calcd. for $C_{19}H_{18}BrN_2O$ $[M+H]^+$, 369.0597 (for ^{79}Br), 371.0577 (for ^{81}Br); found, 369.0590 (for ^{79}Br), 371.0586 (for ^{81}Br), (Δ = -1.90, 2.42 ppm);

***N*-{(2*E*)-3-[5-(2,5-Dimethylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10i).** Yield: 0.39 g (49%); colorless powder. ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 7.54 (s, 1H), 7.23-7.16 (m, 4H), 6.77-6.75 (m, 2H), 6.69 (dd, J = 8.6, 0.9 Hz, 2H), 6.55 (dt, J = 16.2, 5.3 Hz, 1H), 6.49 (s, 1H), 4.03 (dd, J = 5.3, 1.7 Hz, 2H), 3.98 (s, 1H), 2.47 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 170.0, 161.3, 147.6, 135.8, 135.3, 133.1, 131.3, 130.8, 129.4 (2C), 129.0, 126.7, 119.4, 117.9, 113.0 (2C), 99.7, 45.7, 21.0, 20.9. IR (KBr, cm^{-1}): ν_{max} = 3397 (NH), 1602, 1504 (C=C). MS (ESI): *m/z* = 305 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{20}H_{21}N_2O$ $[M+H]^+$, 305.1648; found, 305.1650, (Δ = 0.66 ppm).

***N*-{(2*E*)-3-[5-(3,4-Dimethylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10j).** Yield: 0.39 g (50%); colorless powder. M.p. 113-114 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 7.56 (s, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.23-7.20 (m, 3H), 6.77-6.72 (m, 2H), 6.68 (d, J = 7.6 Hz, 2H), 6.55 (s, 1H), 6.52 (dt, J = 16.2, 5.3 Hz, 1H), 4.02 (dd, J = 5.3, 1.7 Hz, 2H), 3.97 (s, 1H), 2.33 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 170.1, 161.6, 147.6, 139.2, 137.3, 135.2, 130.2, 129.4 (2C), 126.9, 125.0, 123.3, 119.4, 117.9, 113.0 (2C), 95.9, 45.7, 19.8 (2C). IR (KBr, cm^{-1}): ν_{max} = 3381 (NH), 1601, 1504 (C=C). MS (ESI): *m/z* = 305 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{20}H_{21}N_2O$ $[M+H]^+$, 305.1648; found, 305.1655, (Δ = 2.29 ppm).

***N*-{(2*E*)-3-[5-(4-Ethylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10k).** Yield: 0.61 g (77%); colorless powder. M.p. 120-122 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 7.70 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.21 (t, J = 7.6 Hz, 2H), 6.77-6.72 (m, 2H), 6.68 (d, J = 7.6 Hz, 2H), 6.57 (s, 1H), 6.52 (dt, J = 16.2, 5.1 Hz, 1H), 4.02 (br.d, J = 5.1 Hz, 2H), 3.98 (s, 1H), 2.71 (q, J = 7.6 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 170.0, 161.7, 147.7, 146.9, 135.4 (2C), 129.5 (2C), 128.6, 125.9 (2C), 125.0, 119.5 (2C), 118.0, 113.1, 96.1, 45.7, 28.9, 15.4. IR (KBr, cm^{-1}): ν_{max} = 3382 (NH), 1601, 1508 (C=C). MS (ESI): *m/z* = 305 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{20}H_{21}N_2O$ $[M+H]^+$, 305.1648; found, 305.1640, (Δ = 2.62 ppm).

***N*-{(2*E*)-3-[5-(4-*tert*-Butylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10l).** Yield: 0.58 g (68%); colorless powder. M.p. 124-125 °C; ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 7.71 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 8.6 Hz, 2H), 7.22 (t, J = 7.6 Hz, 2H), 6.77-6.73 (m, 2H), 6.68 (d, J = 7.6 Hz, 2H), 6.57 (s, 1H), 6.53 (dt, J = 16.2, 5.0 Hz, 1H), 4.02 (br.s, 2H), 3.96 (br.s, 1H), 1.36 (s, 9H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 170.0, 161.7, 153.7, 147.7, 135.4, 129.5 (2C), 126.0 (2C), 125.7 (2C), 124.7, 119.5, 118.0, 113.1 (2C), 96.2, 45.7, 35.0, 31.3 (3C). IR (KBr, cm^{-1}): ν_{max} = 3348 (NH), 1603, 1509 (C=C). MS (ESI): *m/z* = 333 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{22}H_{25}N_2O$ $[M+H]^+$, 333.1961; found, 333.1959, (Δ = -0.60 ppm).

***N*-{(2*E*)-3-[5-(1-Naphthyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10m).** Yield: 0.44 g (52%); colorless powder. M.p. 113 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 8.28 (d, J = 8.3 Hz, 1H), 7.96 (d, J = 8.1 Hz, 1H), 7.92 (d, J = 7.9 Hz, 1H), 7.79 (d, J = 7.2 Hz, 1H), 7.58-7.53 (m, 3H), 7.20 (t, J = 7.6 Hz, 2H), 6.79 (d, J = 16.2 Hz, 1H), 6.74 (t, J = 7.2 Hz, 2H), 6.69-6.67 (m, 2H), 6.57 (dt, J = 16.2, 4.5 Hz, 1H), 4.04 (br.s, 1H), 4.03 (d, J = 4.5 Hz, 2H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 169.7, 161.4, 147.6, 135.7, 133.8, 130.9, 130.3, 129.4 (2C), 128.7, 127.6, 127.4, 126.4, 125.1 (2C), 125.0, 119.2, 117.9, 113.0 (2C), 100.8, 45.6. IR (KBr, cm^{-1}): ν_{max} = 33577 (NH), 1598, 1495 (C=C). MS (ESI): *m/z* = 327 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{22}H_{19}N_2O$ $[M+H]^+$, 327.1492; found, 327.1497, (Δ = 1.53 ppm).

***N*-{(2*E*)-3-[5-(4-Nitrophenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10n).** Yield: 0.37 g (44%); yellow powder. M.p. 152-153 °C; ^{1}H NMR (700.2 MHz, $CDCl_3$): δ (ppm) 8.34 (d, J = 8.8 Hz, 2H), 7.94 (d, J = 8.8 Hz, 2H), 7.21 (t, J = 7.6 Hz, 2H), 6.79-6.74 (m, 3H), 6.68 (d, J = 7.6 Hz, 2H), 6.53 (dt, J = 16.2, 5.0 Hz, 1H), 4.05 (dd, J = 5.2, 1.7 Hz, 2H), 4.04 (br.s, 1H). ^{13}C NMR (176.1 MHz, $CDCl_3$): δ (ppm) 167.1, 161.9, 148.5, 147.5, 136.5, 132.7, 129.4 (2C), 126.5 (2C), 124.4 (2C), 118.6, 118.0, 113.0 (2C), 99.4, 45.6. IR (KBr, cm^{-1}): ν_{max} = 3422 (NH), 1605 (C=C), 1515, 1352 (NO_2). MS (ESI): *m/z* = 322 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{18}H_{16}N_3O_3$ $[M+H]^+$, 322.1186; found, 322.1185, (Δ = -0.31 ppm).

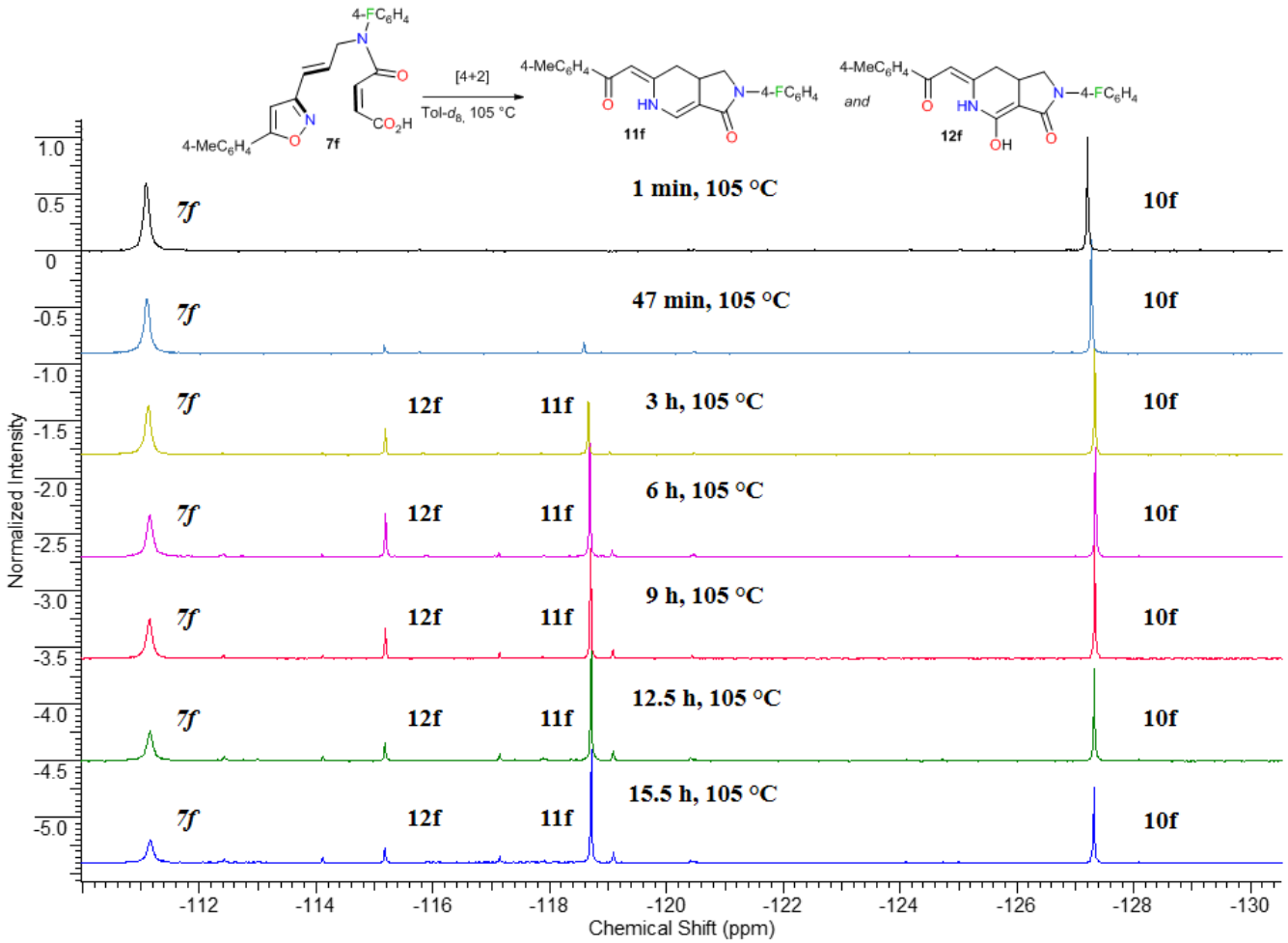

Fig. S6. Real-time ^{19}F NMR-experiment to monitor the formation of amide **7f**, the product of the IMDAV reaction **11f** and the product of the oxidation **12f.**

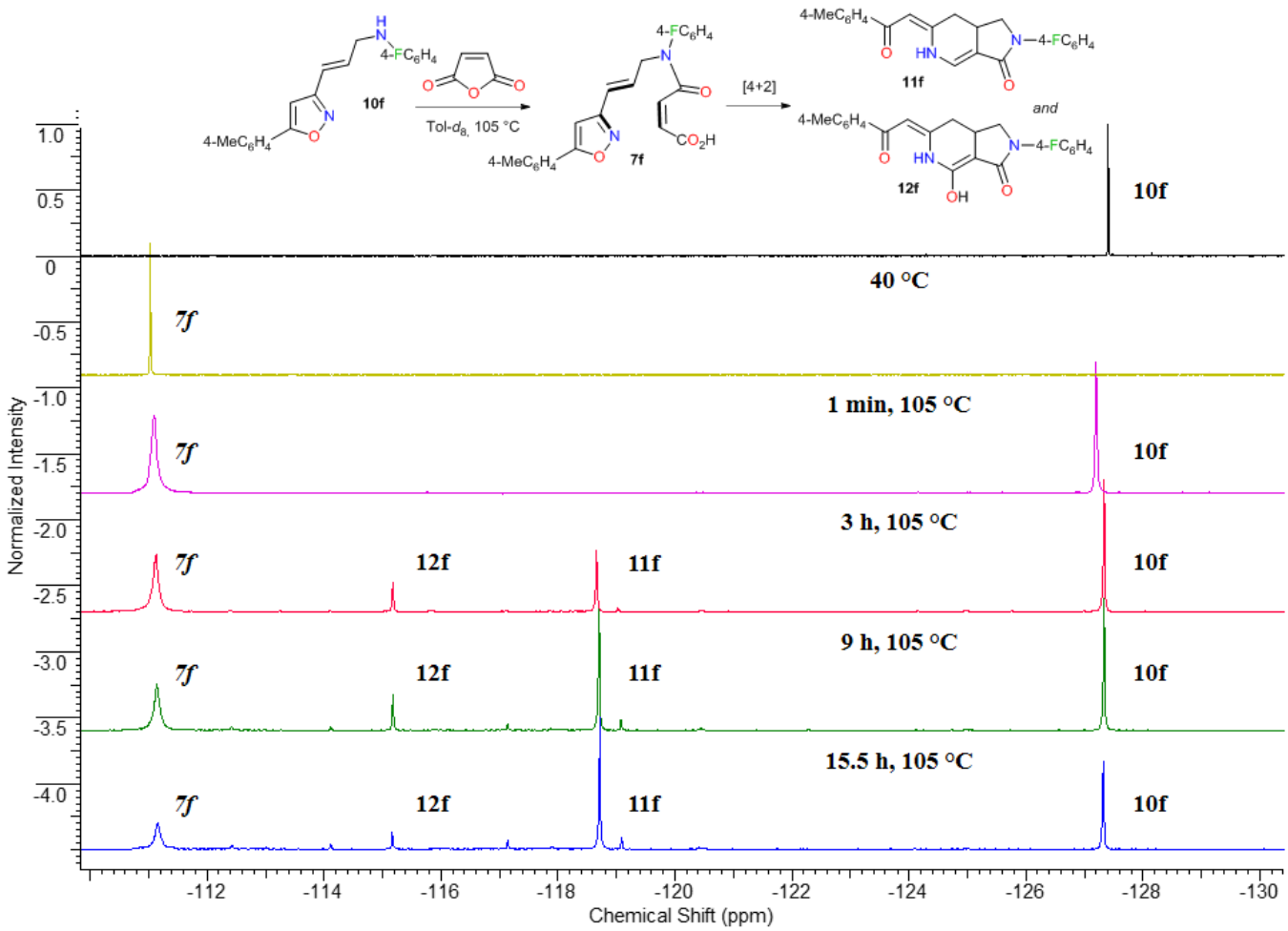

Fig. S7. Real-time ^{19}F NMR-experiment to monitor the formation of amide **7f**, the product of the IMDAV reaction **11f** and the product of the oxidation **12f.**

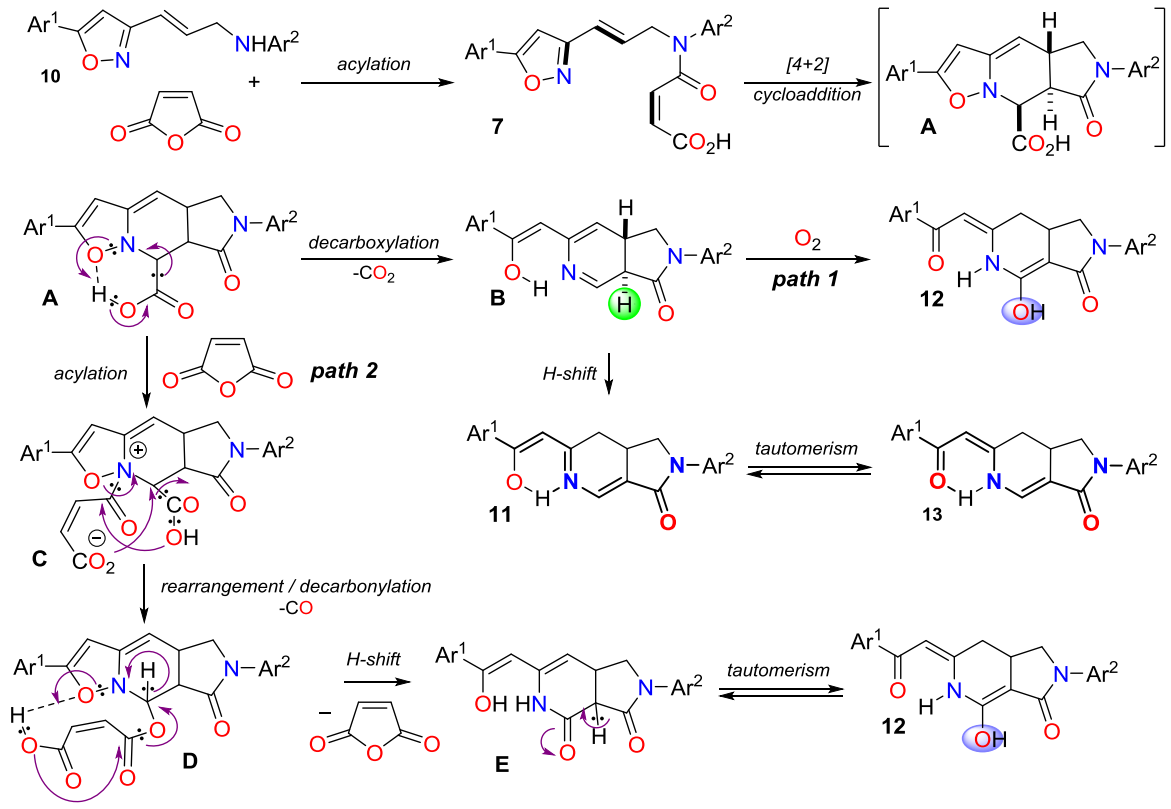

Fig. S8. Plausible pathways of the conducted transformation.

General Procedure for the Synthesis of Products 11a-q and Characterization Data. Method A. Maleic anhydride (0.05 g, 0.5 mmol) was added to the corresponding allylamine **10** (0.5 mmol) diluted in PhMe (5 mL). The resulting mixture was heated at reflux for 12 hours and then cooled to room temperature. The resulting precipitate was filtered off, washed with PhH (5 ml), Et_2O (2×5 ml), and air dried to give the title pyrrolo[3,4-*c*]pyridines **11a-h** as yellow solid powders.

Method B. A solution of appropriate allylamine **10** (0.5 mmol) and maleic (0.05 g, 0.5 mmol, for **11a-n**) or trifluoromethylmaleic anhydride (0.083 g, 0.5 mmol, for **11o-q**) in PhMe (5.0 mL) was irradiated in a microwave reactor at 180 °C (200 °C for **11l**) for 60 min with stirring until complete, monitoring the reaction progress by TLC. The resulting mixture was cooled to room temperature. The resulting precipitate was filtered off, washed with PhH (5 ml), Et_2O (2×5 ml), and air dried to give the title pyrrolo[3,4-*c*]pyridines **11a-q** as yellow solid powders.

(6*Z*)-6-(2-Oxo-2-phenylethylidene)-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11a). According to general procedure **A**, 59.4 mg of **11a** were obtained as a yellow solid (36% yield), contains an impurity of *hydroxy*-**12a** (~9%). According to general procedure **B**, 69.3 mg of **11a** were obtained as a yellow solid (42% yield). M.p. 262-263 °C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.88 (d, J = 4.3 Hz, 1H), 7.98 (d, J = 7.1 Hz, 2H), 7.70 (d, J = 7.9 Hz, 2H), 7.58 (t, J = 7.1 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.6 Hz, 2H), 7.28 (dd, J = 3.0 Hz, 4.5 Hz, 1H), 7.13 (t, J = 7.4 Hz, 1H), 6.26 (s, 1H), 4.12 (t, J = 9.1 Hz, 1H), 3.65 (dd, J = 9.1, 7.9 Hz, 1H), 3.15-3.09 (m, 1 H), 2.97 (dd, J = 15.5, 5.7 Hz, 1H), 2.69 (t, J = 15.5 Hz, 1H).^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 189.1, 166.1, 155.4, 140.3, 139.3, 132.3, 129.2 (2C), 129.1 (2C), 128.0, 127.7 (2C), 124.1, 119.5 (2C), 115.5, 96.5, 52.5, 33.2, 27.1. IR (KBr, cm^{-1}): ν_{max} = 3065 (NH), 1673 (C=O), 1605, 1582, 1548 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{21}H_{18}N_2O_2$ $[M+H]^+$, 331.1441; found, 331.1433, (Δ = 2.41 ppm); calcd. for $C_{21}H_{18}N_2O_2$ $[M+Na]^+$, 353.1260; found, 353.1247, (Δ = 3.68 ppm). HRMS (ESI-TOF) of *hydroxy*-**12a**: calcd. for $C_{21}H_{18}N_2O_3$ $[M+H]^+$, 347.1390; found, 347.1395, (Δ = 1.44 ppm).

(6*Z*)-2-(4-Methylphenyl)-6-(2-oxo-2-phenylethylidene)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11b). According to general procedure **A**, 49.9 mg of **11b** were obtained as a yellow solid (29% yield), contains an impurity of *hydroxy*-**12b** (~17%). According to general procedure **B**, 61.9 mg of **11b** were obtained as a yellow solid (36% yield). M.p. > 250 °C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.84 (br.s, 1H), 7.95 (d, J = 7.6 Hz, 2H), 7.58-7.49 (m, 5H), 7.25 (br.s, 1H), 7.19 (d, J = 7.9 Hz, 2H), 6.19 (s, 1H), 4.11 (t, J = 8.9 Hz, 1H), 3.60 (t, J = 8.2 Hz, 1H), 3.10-3.15 (m, 1H), 2.96-2.99 (dd, J = 15.1, 5.5 Hz, 1H), 2.67 (t, J = 15.1 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 189.4, 165.8,

155.5, 139.6, 138.0, 133.3, 132.1, 129.5 (2C), 128.9 (2C), 127.6 (2C), 121.5, 119.7 (2C), 115.7, 96.5, 52.7, 33.4, 27.4, 20.8. IR (KBr, cm^{-1}): ν_{max} = 3029 (NH), 1668 (C=O), 1604, 1578, 1548 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{22}H_{20}N_2O_2$ $[M+H]^+$, 345.1598; found, 345.1586, (Δ = 3.48 ppm); calcd. for $C_{22}H_{20}N_2O_2$ $[M+Na]^+$, 367.1417; found, 367.1410, (Δ = 1.91 ppm). HRMS (ESI-TOF) of *hydroxy*-**12b**: calcd. for $C_{22}H_{20}N_2O_3$ $[M+H]^+$, 361.1547; found, 361.1538, (Δ = 2.49 ppm).

(6*Z*)-2-(4-Chlorophenyl)-6-(2-oxo-2-phenylethylidene)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11c). According to general procedure **A**, 54.7 mg of **11c** were obtained as a yellow solid (30% yield), contains an impurity of *hydroxy*-**12c** (~5%). According to general procedure **B**, 62.0 mg of **11c** were obtained as a yellow solid (34% yield). M.p. 230 °C; ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.87 (d, *J* = 4.3 Hz, 1H), 7.97 (d, *J* = 7.4 Hz, 2H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 9.1 Hz, 2H), 7.28 (dd, *J* = 4.3, 2.9 Hz, 1H), 6.26 (s, 1H), 4.11 (t, *J* = 9.1 Hz, 1H), 3.62 (dd, *J* = 8.8, 8.1 Hz, 1H), 3.14-3.08 (m, 1H), 2.96 (dd, *J* = 15.5, 6.0 Hz, 1H), 2.67 (t, *J* = 15.5 Hz, 1H).^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 189.2, 166.2, 155.3, 139.2 (2C), 132.4, 129.1 (2C), 129.0 (2C), 128.4, 127.8, 127.7 (2C), 120.9 (2C), 115.0, 96.7, 52.5, 33.1, 27.0. IR (KBr, cm^{-1}): ν_{max} = 3067 (NH), 1669 (C=O), 1608, 1578, 1548 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{21}H_{17}ClN_2O_2$ $[M+H]^+$, 365.1051 (for ^{35}Cl), 367.1022 (for ^{37}Cl); found, 365.1034 (for ^{35}Cl), 367.1015 (for ^{37}Cl) , (Δ = 4.66, 1.91 ppm); calcd. for $C_{21}H_{17}ClN_2O_2$ $[M+Na]^+$, 387.0871 (for ^{35}Cl), 389.0841 (for ^{37}Cl); found, 387.0854 (for ^{35}Cl), 389.0833 (for ^{37}Cl) , (Δ = 4.39, 2.06 ppm).

(6*Z*)-6-[2-(4-Methylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11d). According to general procedure **A**, 49.9 mg of **11d** were obtained as a yellow solid (28% yield). According to general procedure **B**, 61.9 mg of **11d** were obtained as a yellow solid (40% yield). M.p. > 250 °C (decomp); ^{1}H NMR (600.2 MHz, DMSO-d_6): δ (ppm) 11.81 (s, 1H), 7.85 (d, *J* = 7.6 Hz, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.26 (t, *J* = 3.6 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.15 (s, 1H), 4.15 (t, *J* = 9.1 Hz, 1H), 3.61 (t, *J* = 8.6 Hz, 1H), 3.17-3.11 (m, 1H), 2.97 (dd, *J* = 15.1, 6.1 Hz, 1H), 2.67 (t, *J* = 15.1 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (150.9 MHz, DMSO): δ (ppm) 189.0, 166.2, 155.1, 142.6, 140.4, 136.7, 129.7 (2C), 129.2 (2C), 128.1, 127.9 (2C), 124.2, 119.6 (2C), 115.2, 96.6, 52.6, 33.3, 27.2, 21.6. HRMS (ESI-TOF): calcd. for $C_{22}H_{20}N_2O_2$ $[M+H]^+$, 345.1598; found, 345.1587, (Δ = 3.19 ppm).

(6*Z*)-2-(4-Methylphenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11e). According to general procedure **A**, 60.9 mg of **11e** were obtained as a yellow solid (34% yield), contains an impurity of *hydroxy*-**12e** (~13%). According to general procedure **B**, 77.0 mg of **11e** were obtained as a yellow solid (43% yield). M.p. > 250

°C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.83 (s, 1H), 7.86 (d, J = 7.6 Hz, 2H), 7.58 (d, J = 7.6 Hz, 2H), 7.32-7.18 (m, 5H), 6.17 (s, 1H), 4.11 (t, J = 9.1 Hz, 1H), 3.60 (t, J = 8.2 Hz, 1H), 3.14-3.11 (m, 1H), 2.96 (d, J = 14.9 Hz, 1H), 2.66 (t, J = 14.9 Hz, 1H), 2.39 (s, 3H), 2.30 (s, 3H).^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 189.2, 165.9, 155.1, 142.4, 138.1, 137.0, 133.3, 129.5 (4C), 127.8 (2C), 127.6, 119.7 (2C), 115.5, 96.5, 52.8, 33.4, 27.4, 21.4, 20.8. IR (KBr, cm^{-1}): ν_{max} = 3034 (NH), 1678 (C=O), 1604, 1581 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{23}H_{22}N_2O_2$ $[M+H]^+$, 359.1754; found, 359.1768, (Δ = 3.90 ppm). HRMS (ESI-TOF) of *hydroxy*-**12e**: calcd. for $C_{23}H_{22}N_2O_3$ $[M+H]^+$, 375.1703; found, 375.1723, (Δ = 5.33 ppm).

(6*Z*)-2-(4-Fluorophenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11f). According to general procedure **B**, 68.8 mg of **11f** were obtained as a yellow solid (38% yield). M.p. > 250 °C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.85 (s, J = 4.5 Hz, 1H), 7.87 (d, J = 8.1 Hz, 2H), 7.72 (dd, J = 9.1, 5.0 Hz, 2H), 7.31 (d, J = 7.9 Hz, 2H), 7.27 (dd, J = 4.5, 3.1 Hz, 1H), 7.23 (t, J = 9.1 Hz, 2H), 6.25 (s, 1H), 4.11 (t, J = 9.1 Hz, 1H), 3.64 (dd, J = 9.1, 7.9 Hz, 1H), 3.14-3.08 (m, 1H), 2.96 (dd, J = 15.5, 6.0 Hz, 1H), 2.67 (t, J = 15.0 Hz, 1H), 2.38 (s, 3H).^{13}C NMR (176.1 MHz, DMSO): δ (ppm) 188.9, 166.0, 158.8 (d, J = 243.1 Hz, 1C), 155.0, 142.5, 136.8, 136.6, 129.6 (2C), 128.1, 127.8 (2C), 121.4 (d, J = 8.1 Hz, 2C), 115.8 (d, J = 21.6 Hz, 2C), 114.9, 96.5, 52.7, 33.2, 27.1, 21.6. ^{19}F NMR (658.8 MHz, DMSO-d_6): δ (ppm) -118.8. IR (KBr, cm^{-1}): ν_{max} = 3444 (NH), 1678 (C=O), 1603, 1509 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{22}H_{19}FN_2O_2$ $[M+H]^+$, 363.1503; found, 363.1490, (Δ = 3.58 ppm); calcd. for $C_{22}H_{19}FN_2O_2$ $[M+Na]^+$, 385.1323; found, 385.1306, (Δ = 4.41 ppm).

(6*Z*)-2-(4-Chlorophenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11g). According to general procedure **A**, 70.1 mg of **11g** were obtained as a yellow solid (37% yield). According to general procedure **B**, 72.0 mg of **11g** were obtained as a yellow solid (38% yield). M.p. > 250 °C (decomp); ^{1}H NMR (600.2 MHz, DMSO-d_6): δ (ppm) 11.85 (d, J = 4.5 Hz, 1H), 7.88 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 9.1 Hz, 2H), 7.44 (d, J = 8.6 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.28 (dd, J = 4.5, 2.5 Hz, 1H), 6.25 (s, 1H), 4.11 (t, J = 9.1 Hz, 1H), 3.62 (t, J = 9.1, 7.5 Hz, 1H), 3.14-3.07 (m, 1H), 2.94 (dd, J = 15.6, 6.1 Hz, 1H), 2.66 (t, J = 15.6 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (150.9 MHz, DMSO-d_6): δ (ppm) 189.0, 166.3, 154.9, 139.3, 136.7, 129.7 (2C), 129.1 (2C), 128.5, 128.1, 127.9 (3C), 121.0 (2C), 114.7, 96.7, 52.5, 33.2, 27.1, 21.6. IR (KBr, cm^{-1}): ν_{max} = 3102 (NH), 1675 (C=O), br. 1598 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{22}H_{19}ClN_2O_2$ $[M+H]^+$, 379.1208 (for ^{35}Cl), 381.1178 (for ^{37}Cl); found, 379.1197 (for ^{35}Cl), 381.1167 (for ^{37}Cl), (Δ = 2.90, 2.89 ppm); calcd. for $C_{22}H_{19}ClN_2O_2$ $[M+Na]^+$, 401.1027 (for ^{35}Cl), 403.0998 (for ^{37}Cl); found, 401.1018 (for ^{35}Cl), 403.0993 (for ^{37}Cl), (Δ = 2.24, 1.24 ppm)

(6*Z*)-2-(4-Bromophenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11h). According to general procedure **A**, 46.5 mg of **11h** were obtained as a yellow solid (22% yield). According to general procedure **B**, 71.9 mg of **11h** were obtained as a yellow solid (34% yield). M.p. 240-242 °C (decomp); ^{1}H NMR (600.2 MHz, $CDCl_3$): δ (ppm) 12.14 (br.s, 1H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.57 (d, *J* = 9.1 Hz, 2H), 7.49 (d, *J* = 9.1 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H), 7.21 (dd, *J* = 4.5, 3.0 Hz, 1H), 6.03 (s, 1H), 4.10 (t, *J* = 9.1 Hz, 1H), 3.55 (t, *J* = 9.1, 7.6 Hz, 1H), 3.22-3.15 (m, 1H), 2.90 (dd, *J* = 15.1, 5.6 Hz, 1H), 2.64 (t, *J* = 15.1 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (150.9 MHz, $CDCl_3$): δ (ppm) 190.6, 170.8, 153.8, 142.9, 138.8, 136.4, 131.9 (2C), 129.3 (2C), 127.6 (2C), 125.8, 120.9 (2C), 117.1, 114.2, 97.2, 52.7, 33.8, 27.6, 21.7. IR (KBr, cm^{-1}): ν_{max} = 3107 (NH), 1678 (C=O), 1599, 1581 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{22}H_{19}BrN_2O_2$ $[M+H]^+$, 423.0703 (for ^{79}Br), 425.0682 (for ^{81}Br); found, 423.0696 (for ^{79}Br), 425.0679 (for ^{81}Br), (Δ = 1.65, 0.71 ppm); calcd. for $C_{22}H_{19}BrN_2O_2$ $[M+Na]^+$, 445.0522 (for ^{79}Br), 447.0502 (for ^{81}Br); found, 445.0510 (for ^{79}Br), 447.0491 (for ^{81}Br), (Δ = 2.69, 2.46 ppm).

(6*Z*)-6-[2-(2,5-Dimethylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11i). According to general procedure **B**, 32.2 mg of **11i** were obtained as a yellow solid (18% yield). M.p. 222-224 °C; ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.72 (d, *J* = 4.5 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.38 (dd, *J* = 8.6, 7.6 Hz, 2H), 7.32 (s, 1H), 7.27 (dd, *J* = 4.5, 2.9 Hz, 1H), 7.16-7.11 (m, 3H), 5.77 (s, 1H), 4.09 (t, *J* = 9.1 Hz, 1H), 3.61 (dd, *J* = 9.1, 7.6 Hz, 1H), 3.12-3.06 (m, 1H), 2.88 (dd, *J* = 15.5, 6.0 Hz, 1H), 2.63 (t, *J* = 15.5 Hz, 1H), 2.36 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 194.3, 166.1, 154.6, 140.9, 140.3, 135.2, 133.1, 131.5, 130.9, 129.2 (2C), 128.4, 128.0, 124.1, 119.5 (2C), 115.3, 100.3, 52.5, 33.1, 27.1, 21.0, 20.2. IR (KBr, cm^{-1}): ν_{max} = 3197 (NH), 1672 (C=O), 1602, 1564 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{23}H_{22}N_2O_2$ $[M+H]^+$, 359.1754; found, 359.1736, (Δ = 5.01 ppm); calcd. for $C_{23}H_{22}N_2O_2$ $[M+Na]^+$, 381.1573; found, 381.1558, (Δ = 3.94 ppm).

(6*Z*)-6-[2-(3,4-Dimethylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11j). According to general procedure **B**, 32.2 mg of **11j** were obtained as a yellow solid (18% yield). ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.84 (s, 1 H), 7.75-7.69 (m, 4H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.27-7.26 (m, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 6.24 (s, 1H), 4.12 (t, *J* = 8.8 Hz, 1H), 3.64 (t, *J* = 8.1 Hz, 1H), 3.13-3.08 (m, 1H), 2.95 (dd, *J* = 15.3, 5.3 Hz, 1H), 2.66 (t, *J* = 15.3 Hz, 1H), 2.30 (s, 3H), 2.29 (s, 3H).^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 189.2, 166.1, 154.8, 141.3, 140.4, 137.0, 136.9, 130.1, 129.2 (2C), 128.8, 128.1, 125.4, 124.1, 119.5 (2C), 115.1, 96.6, 52.5, 33.2, 27.2, 20.0, 19.9. HRMS (ESI-TOF): calcd. for $C_{23}H_{22}N_2O_2$ $[M+H]^+$, 359.1754; found, 359.1740, (Δ = 3.90 ppm).

(6*Z*)-6-[2-(4-Ethylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11k). According to general procedure **B**, 60.9 mg of **11k** were obtained as a yellow solid (34% yield). M.p. 237-239 °C; ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) *the NH signal is less intense due to proton exchange* 11.83 (br.s, 0.2H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.69 (d, *J* = 8.1 Hz, 2H), 7.39 (t, *J* = 7.9 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.27 (br.d, *J* = 2.6 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.17 (s, 1H), 4.14 (t, *J* = 9.1 Hz, 1H), 3.63 (dd, *J* = 9.1, 7.9, 1H), 3.13-3.10 (m, 1H), 2.97 (dd, *J* = 15.5, 6.0 Hz, 1H), 2.71-2.65 (m, 3H), 1.23 (t, *J* = 7.6 Hz, 3H).^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 189.3, 166.1, 154.7, 148.6, 140.5, 137.2, 129.1 (2C), 128.3 (2C), 127.9 (2C), 127.7, 124.1, 119.7 (2C), 115.2, 96.6, 52.7, 33.4, 28.5, 27.4, 15.4. IR (KBr, cm^{-1}): ν_{max} = 3049 (NH), 1681 (C=O), 1601, 1579 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{23}H_{22}N_2O_2$ $[M+H]^+$, 359.1754; found, 359.1746, (Δ = 2.23 ppm).

(6*Z*)-6-[2-(4-*tert*-Butylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11l). According to general procedure **B**, 113.9 mg of **11l** were obtained as a yellow solid (55% yield). M.p. 212-214 °C; ^{1}H NMR (700.2 MHz, DMSO-d_6, 80 °C): δ (ppm) 11.84 (br.s, 1H), 7.89 (d, *J* = 7.9 Hz, 2H), 7.69 (d, *J* = 7.9 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.26 (br.s, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.17 (s, 1H), 4.14 (t, *J* = 9.0 Hz, 1H), 3.62 (t, *J* = 8.6 Hz, 1H), 3.14-3.09 (m, 1H), 2.96 (dd, *J* = 15.3, 5.7 Hz, 1H), 2.67 (t, *J* = 15.3 Hz, 1H), 1.33 (s, 9H). ^{13}C NMR (176.1 MHz, DMSO-d_6, 80 °C): δ (ppm) 189.3, 166.1, 155.3, 155.0, 140.5, 136.9, 129.1 (2C), 127.9, 127.6 (2C), 125.7 (2C), 124.1, 119.7 (2C), 115.3, 96.7, 52.3, 35.1, 33.4, 31.4 (3C), 27.4. IR (KBr, cm^{-1}): ν_{max} = 3067 (NH), 1673 (C=O), 1610, 1579 (NC=O, C=C). HRMS (ESI-TOF) of **11l**: calcd. for $C_{25}H_{26}N_2O_2$ $[M+H]^+$, 387.2067; found, 387.2058, (Δ = 2.32 ppm), calcd. for $C_{25}H_{26}N_2O_2$ $[M+Na]^+$, 409.1886; found, 409.1874, (Δ = 2.93 ppm).

(6*Z*)-6-[2-(1-Naphthyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11m). According to general procedure **B**, 76.0 mg of **11m** were obtained as a yellow solid (40% yield). M.p. > 250 °C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 11.86 (d, *J* = 4.3 Hz, 1H), 8.41 (d, *J* = 8.6 Hz, 1H), 8.06 (d, *J* = 8.1 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 2H), 7.60-7.56 (m, 3H), 7.39 (t, *J* = 8.1 Hz, 2H), 7.32 (dd, *J* = 4.3, 3.3 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 5.94 (s, 1H), 4.11 (t, *J* = 9.1 Hz, 1H), 3.66-3.63 (m, 1H), 3.16-3.12 (m, 1H), 2.93 (d, *J* = 15.5 Hz, 1H), 2.70 (t, *J* = 15.5 Hz, 1H).^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 193.6, 166.1, 155.3, 140.3, 139.0, 133.9, 131.1, 130.0, 129.2 (2C), 128.9, 127.9, 127.4, 126.7, 126.5, 125.9, 125.5, 124.2, 119.5 (2C), 115.8, 100.9, 52.5, 33.1, 27.0. IR (KBr, cm^{-1}): ν_{max} = 3043 (NH), 1676, 1662 (C=O), 1592, 1559 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{25}H_{20}N_2O_2$ $[M+H]^+$, 381.1598; found, 381.1587, (Δ = 2.88 ppm); calcd. for $C_{23}H_{22}N_2O_2$ $[M+Na]^+$, 403.1417; found, 403.1401, (Δ = 3.97 ppm).

(6*Z*)-6-[2-(4-Nitrophenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11n). According to general procedure **B**, 113.9 mg of **11l** were obtained as a yellow solid (23% yield). M.p. > 270 °C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6, 80 °C): δ (ppm) 11.90 (br.s, 1H), 8.32 (d, *J* = 8.8 Hz, 2H), 8.18 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.29 (br.t, *J* = 3.6 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.26 (s, 1H), 4.17 (t, *J* = 9.1 Hz, 1H), 3.66 (dd, *J* = 8.8, 7.9 Hz, 1H), 3.16-3.09 *the signal is superimposed by the peak of water* (m, 1H), 3.02 (dd, *J* = 15.7, 6.0 Hz, 1H), 2.74 (t, *J* = 15.5 Hz, 1H). ^{13}C NMR (176.1 MHz, DMSO-d_6, 80 °C): δ (ppm) 187.0, 165.8, 157.1, 149.8, 144.7, 140.4, 129.1 (2C), 129.0 (2C), 127.4, 124.3, 124.1 (2C), 119.8 (2C), 116.9, 96.7, 52.7, 33.3, 27.1. IR (KBr, cm^{-1}): ν_{max} = 3101 (NH), 1666 (C=O), 1589 (NC=O, C=C), 1569, 1298 (NO_2). MS (ESI): *m/z* = 376 $[M+H]^+$. HRMS (ESI-TOF): calcd. for $C_{21}H_{18}N_3O_4$ $[M+H]^+$, 376.1292; found, 376.1286, (Δ = -1.59 ppm).

(6*Z*)-6-[2-(4-Methylphenyl)-2-oxoethylidene]-2-phenyl-4-(trifluoromethyl)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11o). According to general procedure **B**, 51.5 mg of **11o** were obtained as a yellow solid (25% yield). M.p. > 250 °C (decomp); ^{1}H NMR (600.2 MHz, DMSO-d_6): δ (ppm) 12.91 (s, 1H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.47 (s, 1H), 4.14 (t, *J* = 9.1 Hz, 1H), 3.77 (dd, *J* = 9.1, 7.1 Hz, 1H), 3.35-3.28 (m, 1H), 3.00 (dd, *J* = 16.2, 6.1 Hz, 1H), 2.79 (t, *J* = 16.2 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (150.9 MHz, DMSO-d_6): δ (ppm) 190.5, 162.4, 154.5, 143.4, 139.9, 136.0, 129.8 (2C), 129.3 (2C), 128.2 (2C), 126.9, 125.0, 120.3 (q, *J* = 274.5 Hz, 1C), 120.1 (2C), 117.9, 97.6, 51.7, 31.1, 28.8, 21.6. ^{19}F NMR (564.7 MHz, DMSO-d_6): δ -61.62. IR (KBr, cm^{-1}): ν_{max} = 3029 (NH), 1691, 1664 (C=O), 1622, 1610, 1581 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{23}H_{19}F_3N_2O_2$ $[M+H]^+$, 413.1477; found, 413.1469, (Δ = 1.94 ppm); calcd. for $C_{23}H_{19}F_3N_2O_2$ $[M+Na]^+$, 435.1296; found, 435.1288, (Δ = 1.84 ppm).

(6*Z*)-6-[2-(4-Ethylphenyl)-2-oxoethylidene]-2-phenyl-4-(trifluoromethyl)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11p). According to general procedure **B**, 40.5 mg of **11p** were obtained as a yellow solid (19% yield). M.p. > 250 °C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 12.84 (s, 1H), 7.93 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 7.9 Hz, 2H), 7.41 (t, *J* = 7.9 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.40 (s, 1H), 4.16 (t, *J* = 9.1 Hz, 1H), 3.76 (dd, *J* = 9.1, 7.4 Hz, 1H), 3.38-3.32 (m, 1H), 3.03 (dd, *J* = 15.7, 6.0 Hz, 1H), 2.80 (t, *J* = 15.7 Hz, 1H), 2.71 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 190.5, 162.4, 154.5, 149.4, 139.8, 136.2, 129.2 (2C), 128.6 (2C), 128.2 (2C), 126.8, 125.0, 120.3 (q, *J* = 275.5 Hz, 1C), 120.0 (2C), 117.9, 97.6, 51.6, 31.0, 28.7, 28.6, 15.6. ^{19}F NMR (658.8 MHz, DMSO-d_6): δ -61.72. IR (KBr, cm^{-1}): ν_{max} = 2965 (NH), 1690,

1667 (C=O), 1624, 1584 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{24}H_{21}F_3N_2O_2$ $[M+H]^+$, 426.1555; found, 426.1543, (Δ = 2.81 ppm).

(6*Z*)-6-[2-(1-Naphthyl)-2-oxoethylidene]-2-phenyl-4-(trifluoromethyl)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11q). According to general procedure **B**, 56.0 mg of **11q** were obtained as a yellow solid (25% yield). M.p. > 250 °C (decomp); ^{1}H NMR (700.2 MHz, DMSO-d_6): δ (ppm) 12.77 (s, 1H), 8.46 (d, *J* = 8.1 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.86 (d, *J* = 7.1 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.63-7.58 (m, 3H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.15 (s, 1H), 4.19 (t, *J* = 9.1 Hz, 1H), 3.78 (dd, *J* = 9.1, 7.4 Hz, 1H), 3.43-3.37 (m, 1H), 3.03 (dd, *J* = 16.0, 6.0 Hz, 1H), 2.84 (t, *J* = 16.0 Hz, 1H). ^{13}C NMR (176.1 MHz, DMSO-d_6): δ (ppm) 195.1, 162.3, 154.5, 139.9, 138.1, 134.0, 131.7, 130.0, 129.2 (2C), 128.9, 127.6, 127.0, 126.7 (2C), 125.9, 125.4, 125.0, 120.3 (2C), 120.3 (q, *J* = 274.5 Hz, 1C), 118.6, 101.9, 51.7, 31.2, 29.0. ^{19}F NMR (658.8 MHz, DMSO-d_6): δ -61.62. IR (KBr, cm^{-1}): ν_{max} = 3071 (NH), 1695 (C=O), 1608, 1592, 1559 (NC=O, C=C). HRMS (ESI-TOF): calcd. for $C_{26}H_{19}F_3N_2O_2$ $[M+H]^+$, 449.1471; found, 449.1466, (Δ = 1.11 ppm); calcd. for $C_{23}H_{19}F_3N_2O_2$ $[M+Na]^+$, 471.1291; found, 471.1277, (Δ = 2.97 ppm).

4. Anti-inflammatory assays

Materials and methods

The isolation of murine macrophages

Donor mice of the C57BL/6J strain, pathogen-free and aged 5–6 weeks, were used in this study. Under aseptic conditions, the animals were injected intraperitoneally with 2 mL of a 3% enzymatic peptone solution using a sterile, disposable 5 mL syringe. The mice were maintained under standard vivarium conditions for three days before being euthanized by cervical dislocation. The peritoneal cavity was rinsed with 10 mL of chilled Hanks' solution (+4–6°C, devoid of Ca^{2+} and Mg^{2+}), and the lavage fluid was collected in sterile centrifuge tubes. The fluid was centrifuged twice at 250 g for 15 minutes, after which the supernatant was discarded, and the pellet was resuspended in chilled complete nutrient medium. The medium consisted of DMEM (2 mM L-glutamine, 4.5 g/L glucose) supplemented with 10% heat-inactivated fetal calf serum, 100 U/mL penicillin, and 100 μg/mL streptomycin.

The primary cell suspension was stained with 0.4% trypan blue, and viable cells were counted using a Goryaev chamber. The suspension was then diluted with chilled complete nutrient medium to a concentration of 2×10^6 cells/mL. Cells were seeded into sterile, pyrogen-free 96-well plates at a density of 2×10^5 cells per well. Pre-incubation was carried out in a CO_2 incubator (5% CO_2, 37°C) for two hours. The wells were then washed with DMEM (37°C) to remove dead or unattached macrophages and other non-adherent cell populations. After washing, the medium volume in each well was adjusted to 180 μL using complete nutrient medium, and the cells were incubated for an additional 18 hours.

The following day, solutions of the test compounds were added at a final screening concentration of 100 μM (with a concentration range of 0.1–100 μM used for concentration-activity studies). After a 30-minute incubation, LPS (10 μg/mL, *E. coli* O127:B4, Sigma, USA) was added to all wells except the intact control. The primary incubation period lasted 24 hours, after which the supernatants were collected for LDH testing and nitric oxide measurement using the Griess method. The remaining cells were subsequently subjected to the MTT assay.

Determination of the anti-inflammatory properties of compounds

The anti-inflammatory activity of the studied compounds was assessed by measuring the accumulation of nitrite anion, a stable end product of nitric oxide (NO) degradation, produced by inducible NO synthases. The nitrite concentration was determined using the Griess reagent.[5] This method involves the diazotization of nitrite anion in an acidic medium with sulfanilamide (1% solution in 5% H_3PO_4), followed by the reaction of the resulting diazo compound with N-(1-naphthyl)ethylenediamine (0.1% aqueous solution) to form a red-violet-colored derivative. The

optical density of the reaction product was measured using a microplate reader (Infinite M200 Pro, Tecan, Austria) at a wavelength of 550 nm.

LDH Assay

The LDH assay measures lactate dehydrogenase (LDH) activity based on the conversion of pyruvate to lactate, which is accompanied by the oxidation of NADH. The depletion of NADH serves as an indicator of LDH activity and, consequently, cell viability.[6] For this assay, 20 μL of supernatant was combined with 250 μL of NADH (194 μM) and 25 μL of sodium pyruvate (6.48 mM). The optical density was recorded at 340 nm using a microplate reader at one-minute intervals for 20 minutes. Wells treated with 0.01% Triton-X served as the positive control, while LPS-treated wells served as the negative control.

MTT Assay

The MTT assay evaluates cell viability by measuring the reduction of yellow tetrazolium salt (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) into purple formazan crystals by NADPH-dependent oxidoreductases in viable cells.[7] A 1% MTT solution was added to the culture plate wells at a ratio of 1:10 to the supernatant. After 2.5 hours of incubation, the supernatant was discarded, and 150 μL of 99% DMSO was added to dissolve the formazan crystals. The plates were stirred on a shaker, and the resulting colored solution was analyzed by measuring optical density at 555 nm using a microplate reader.

Evaluation of NLRP3 activity

After an 18-hour incubation, LPS (final concentration: 10 μg/mL) was added to the wells. Following a 20-hour incubation period, the test substances, diluted in DMEM to a final concentration of 100 μM, were introduced into the designated wells. Glibenclamide (Sigma-Aldrich, USA) at an equimolar concentration served as the reference compound. The cells were treated for 1 hour, after which inflammation was induced by adding an ATP solution (5 mM, Sigma-Aldrich, USA). The supernatant was then analyzed for IL-1β content using ELISA commercial kits (Cloud-Clone Corp., USA).

Microscopic examination

Some cells were stained with acridine orange to assess cytotoxic effects, while the remaining cells were stained using the May-Grunwald method with a 0.3% eosin-methylene blue fixative and azure-eosin dye. Microscopy was performed using a ZEISS Primovert microscope (Germany). Macrophage cell area measurements were analyzed using ImageJ software (NIH, USA).

Prediction of toxic properties

Was carried out using Pro-Tox 3.0.

5. References

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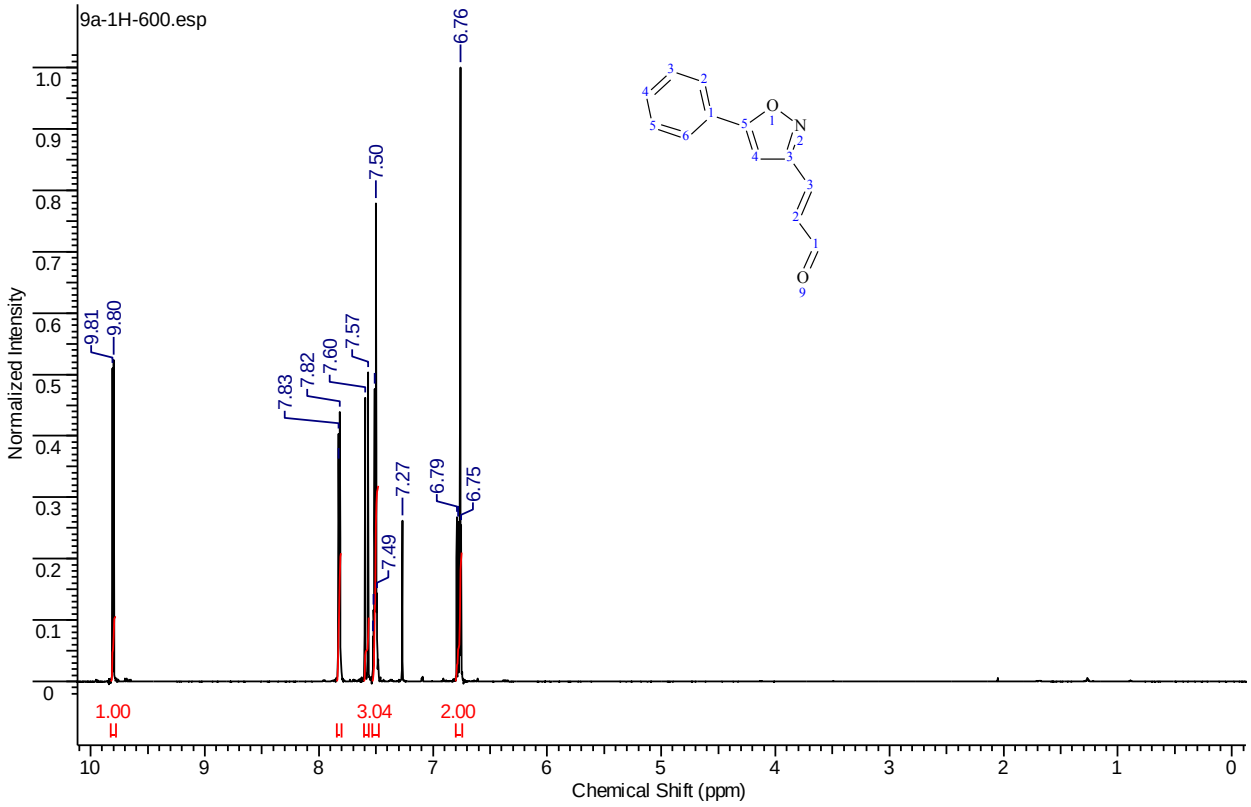
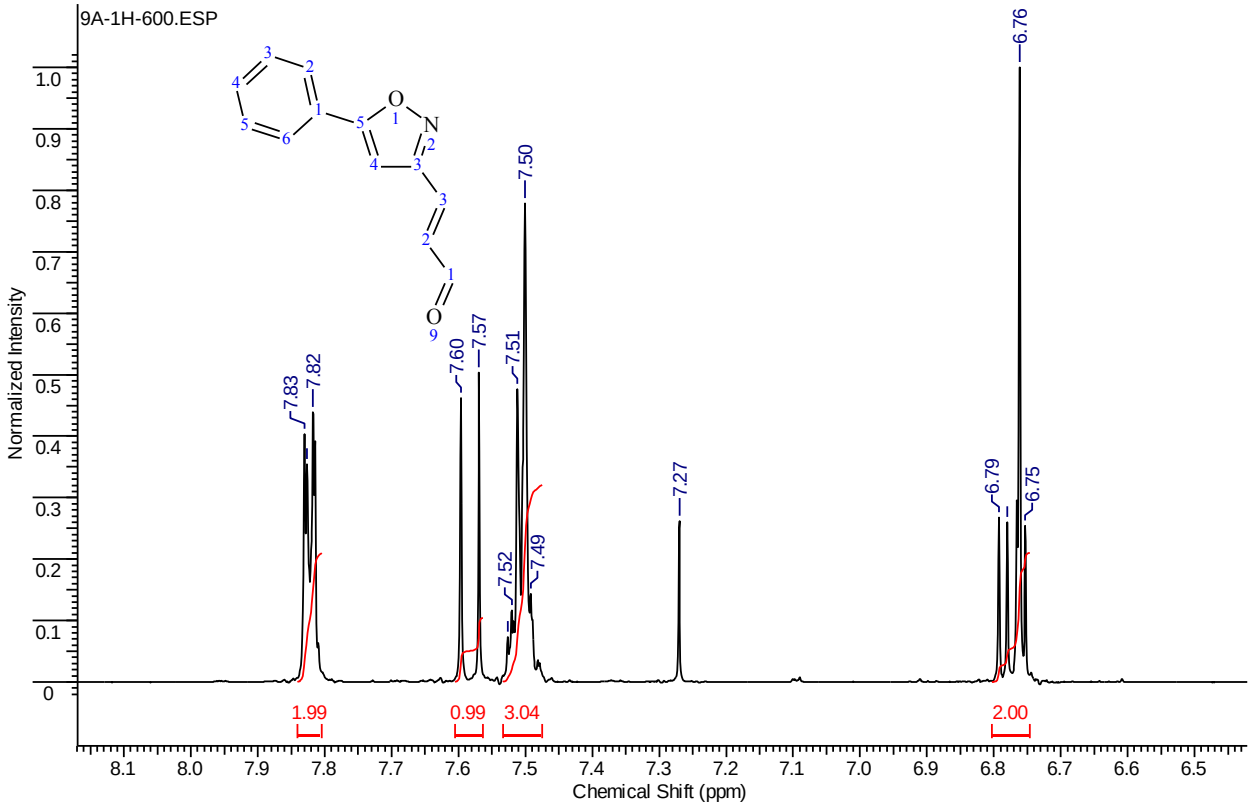
6. Copies of NMR spectra

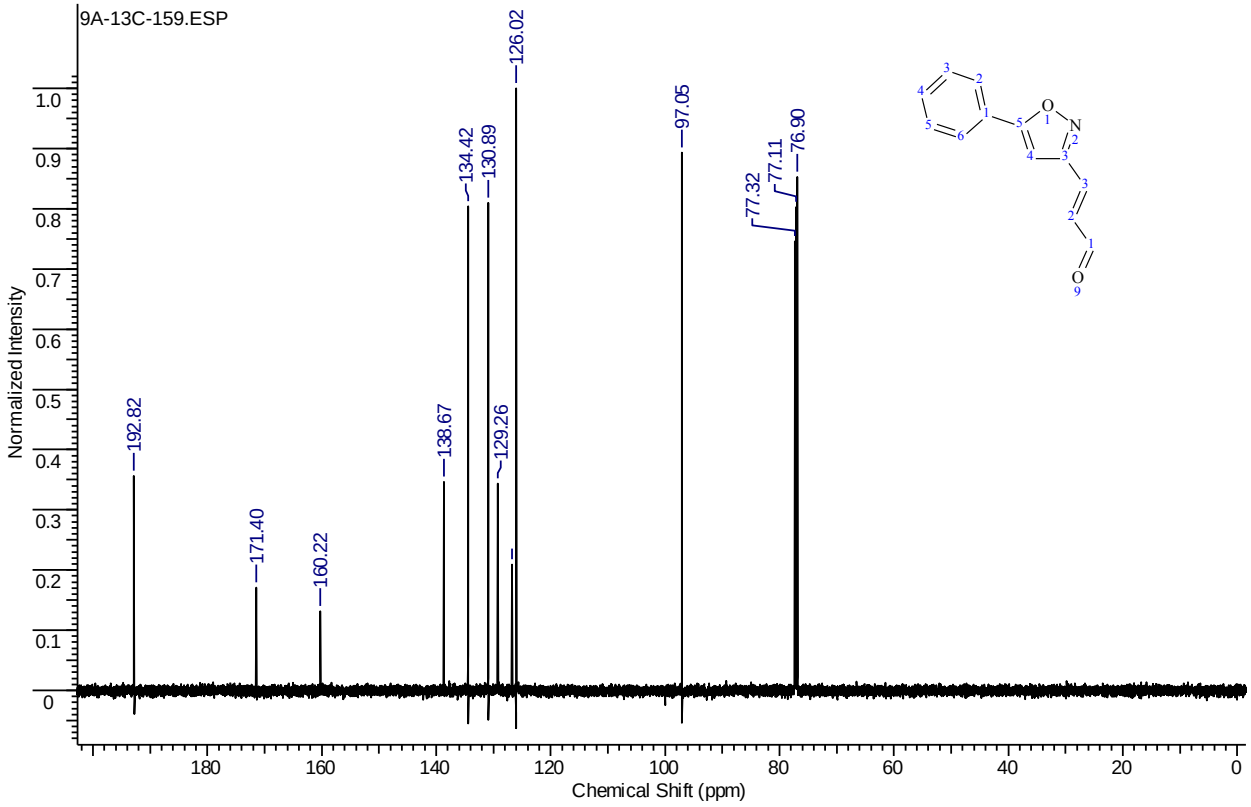
(2E)-3-(5-Phenylisoxazol-3-yl)acrylaldehyde (9a).

^{1}H NMR (600.2 MHz, $CDCl_3$)



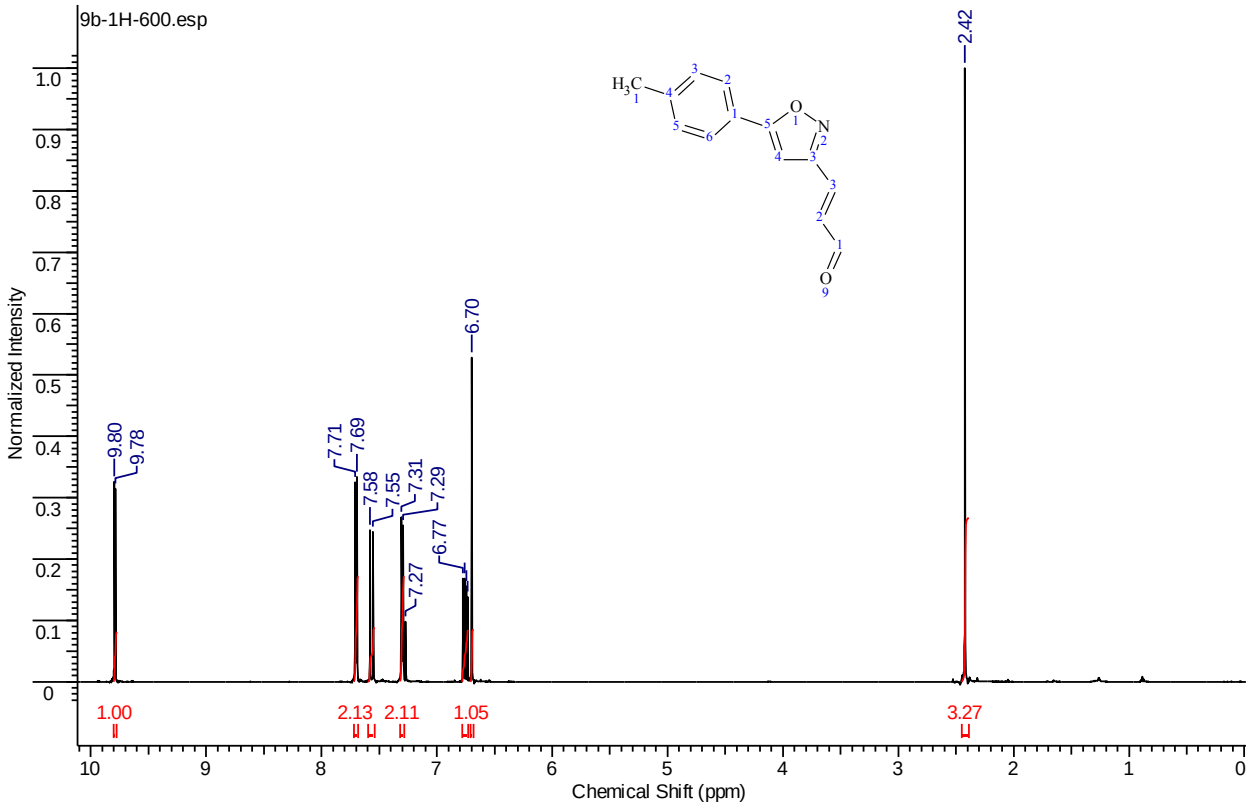


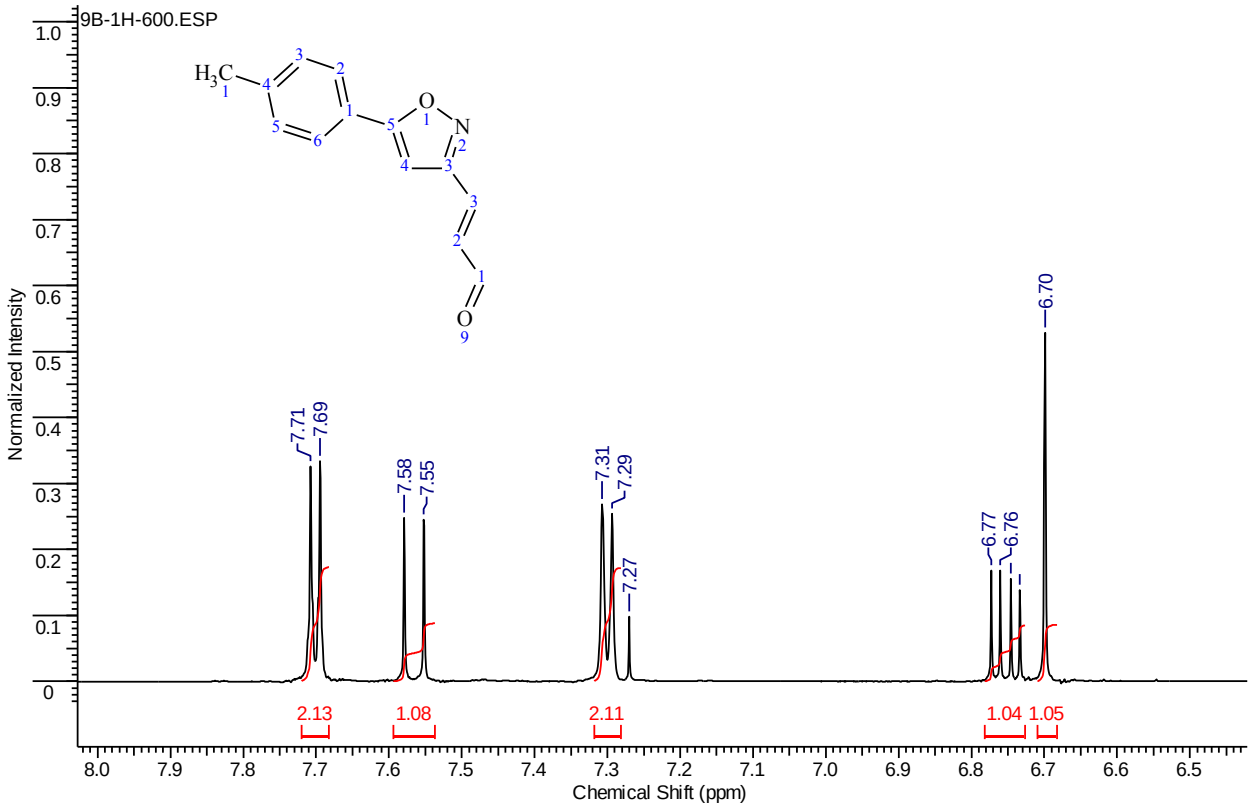
^{13}C NMR (150.9 MHz, $CDCl_3$)



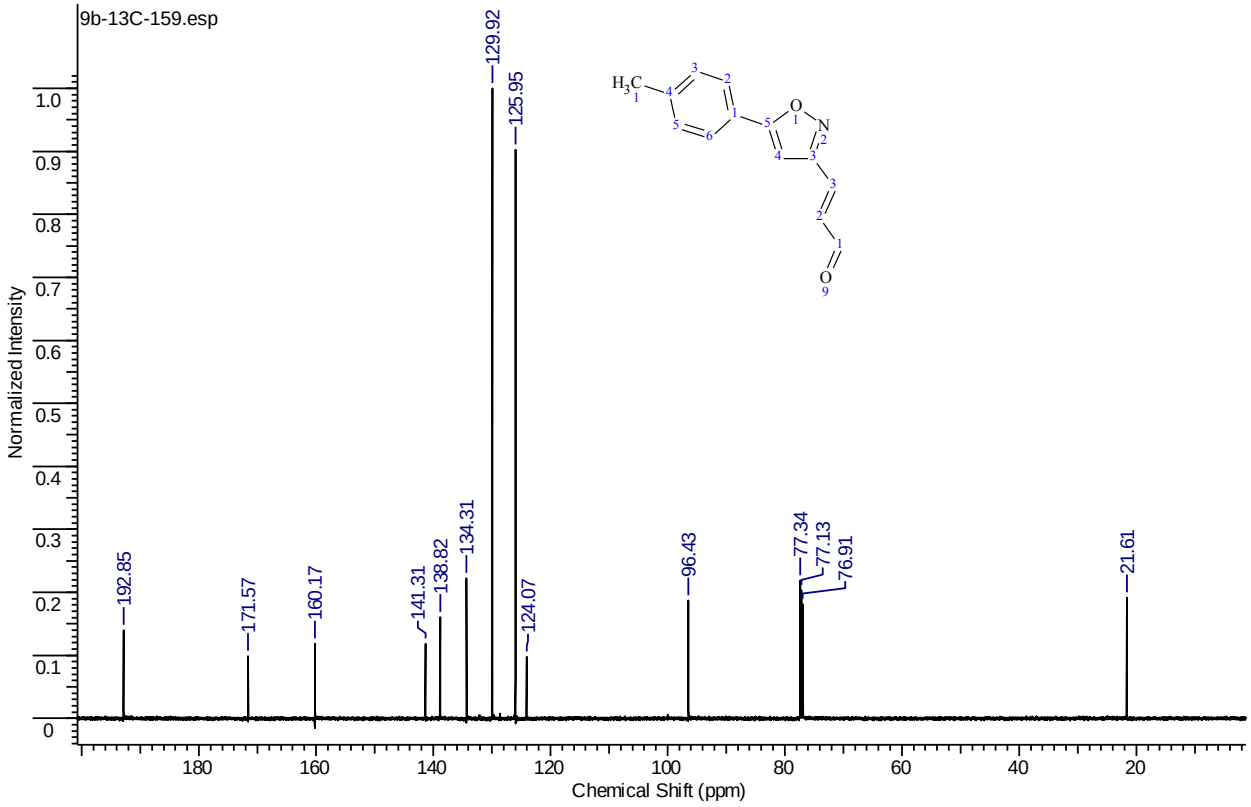
(2*E*)-3-[5-(4-Methylphenyl)isoxazol-3-yl]acrylaldehyde (9b).

^{1}H NMR (600.2 MHz, $CDCl_3$)



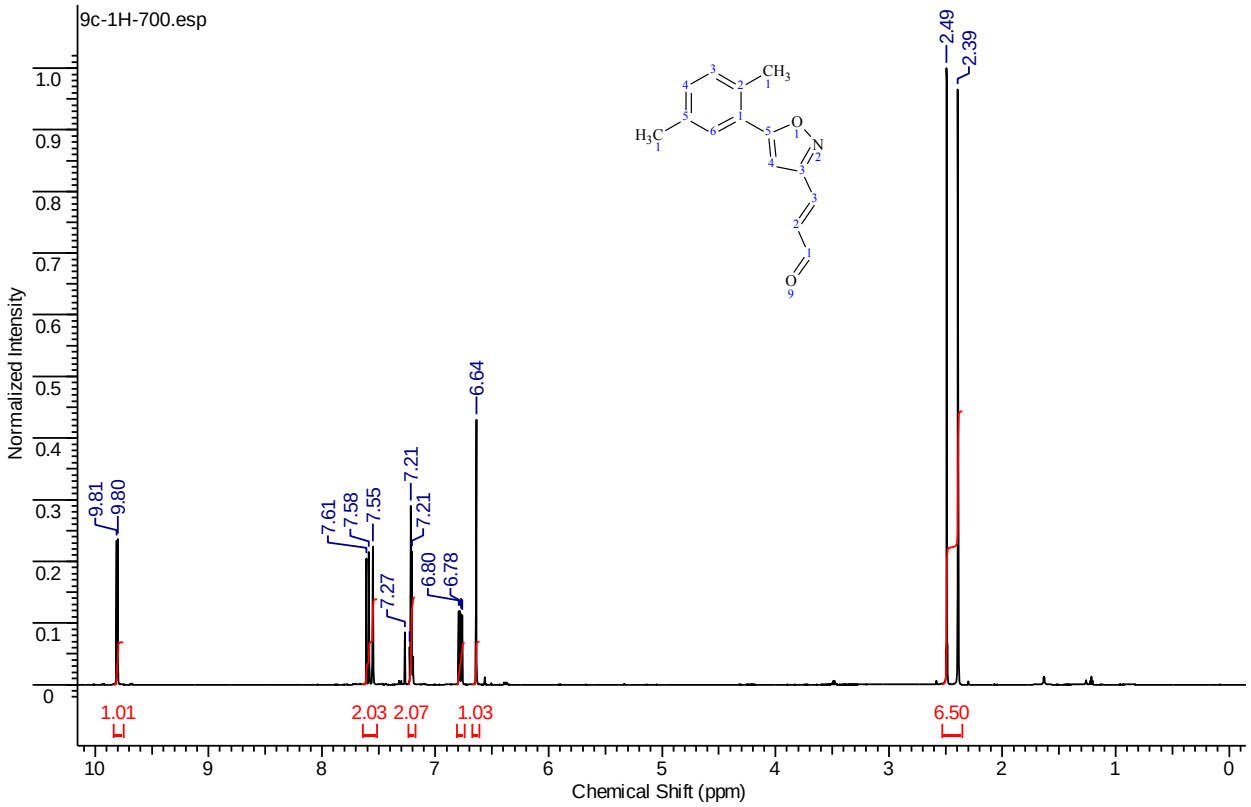


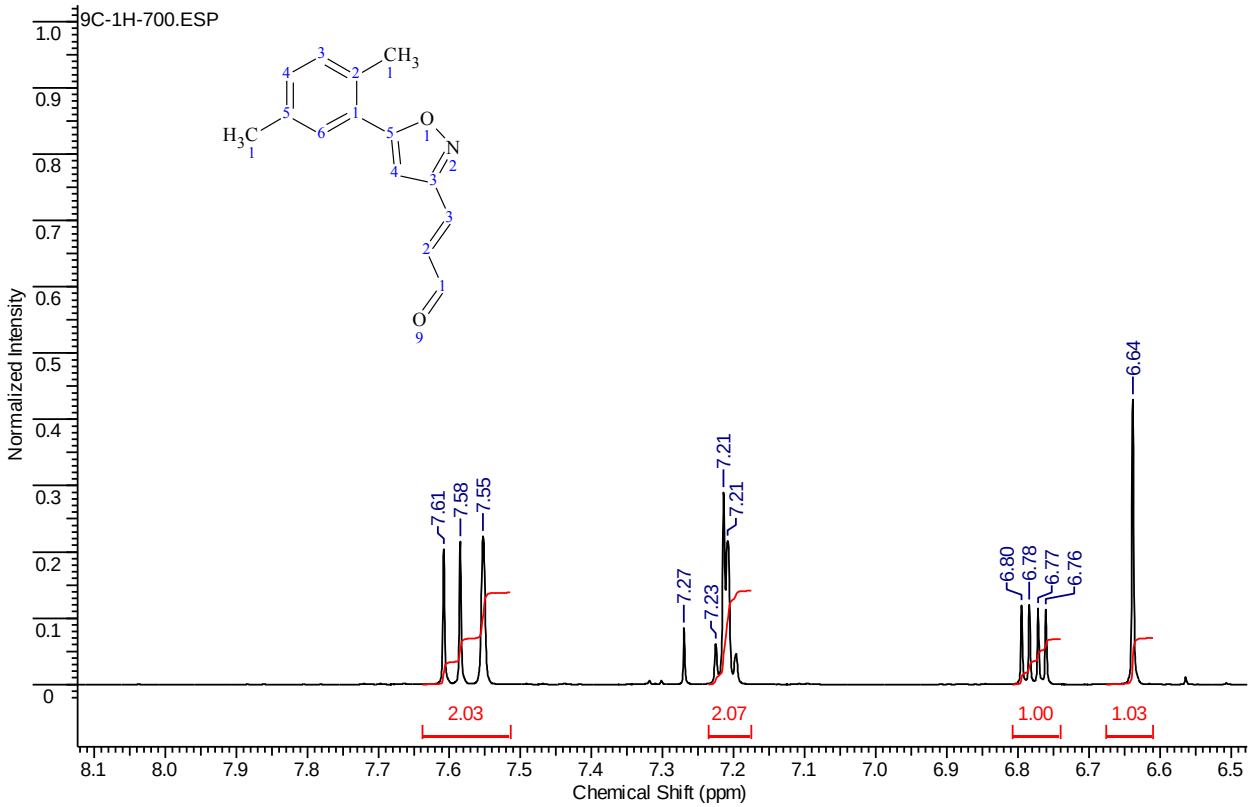
^{13}C NMR (150.9 MHz, $CDCl_3$)



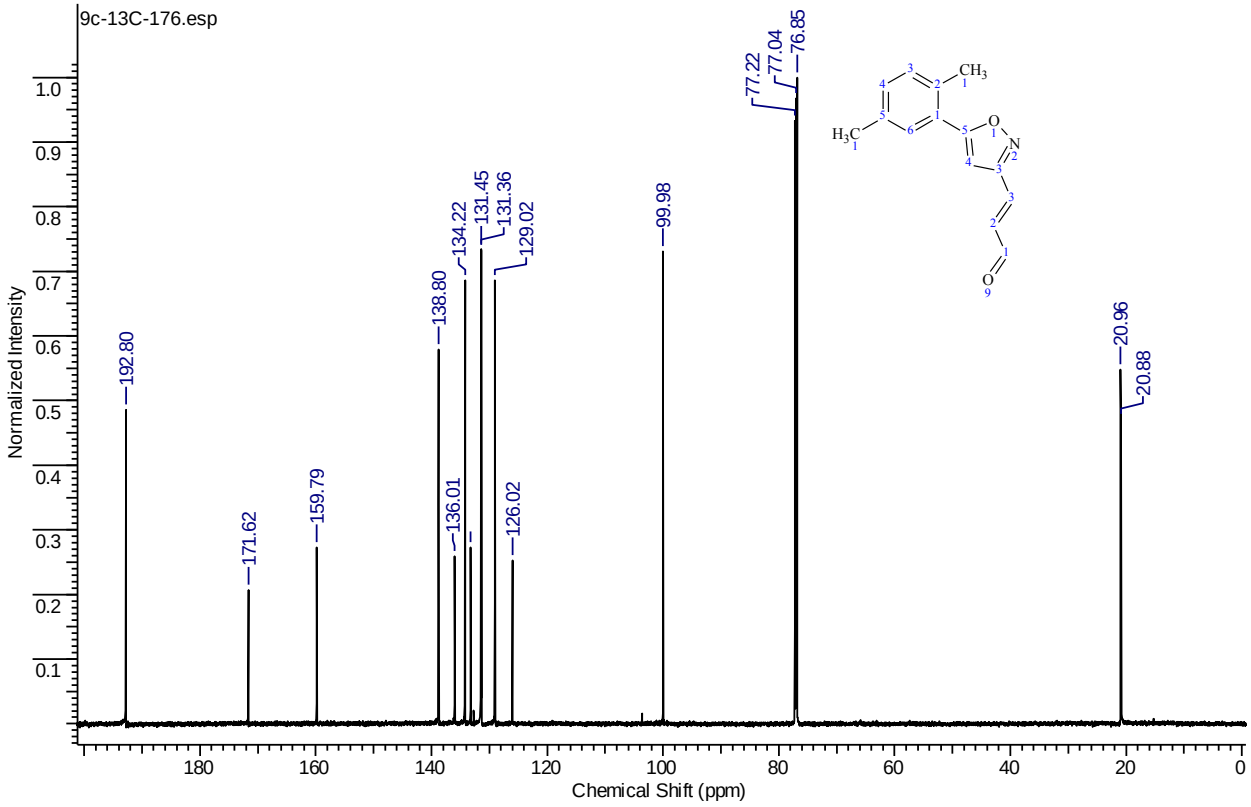
(2*E*)-3-[5-(2,5-Dimethylphenyl)isoxazol-3-yl]acrylaldehyde (9c).

^{1}H NMR (700.2 MHz, $CDCl_3$)



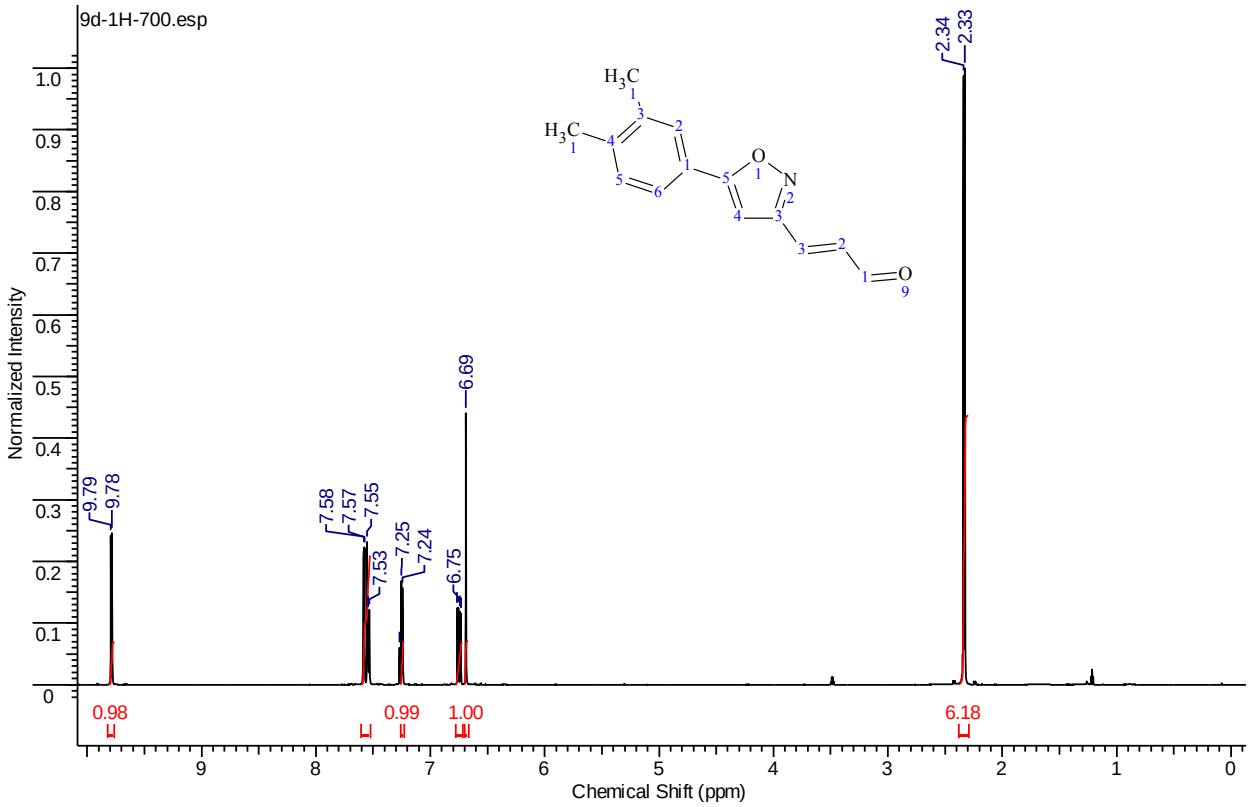


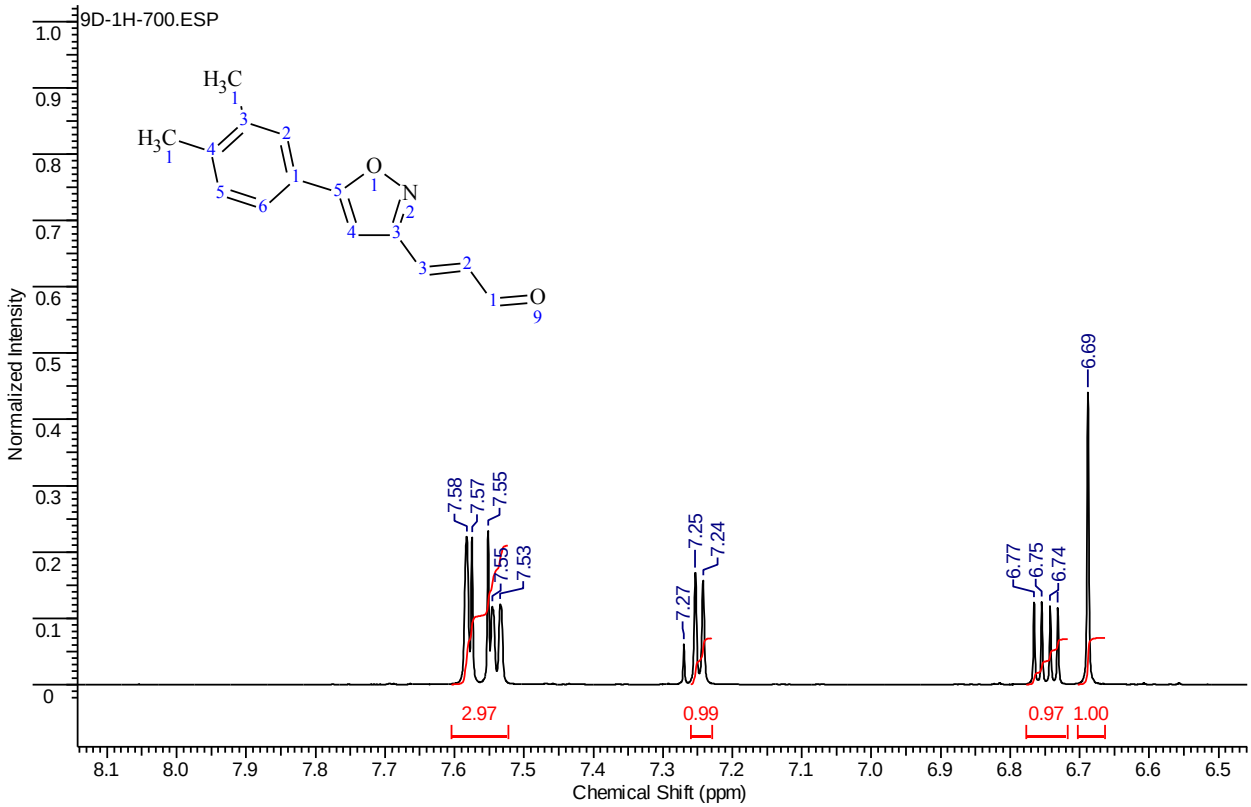
^{13}C NMR (176.1 MHz, $CDCl_3$)



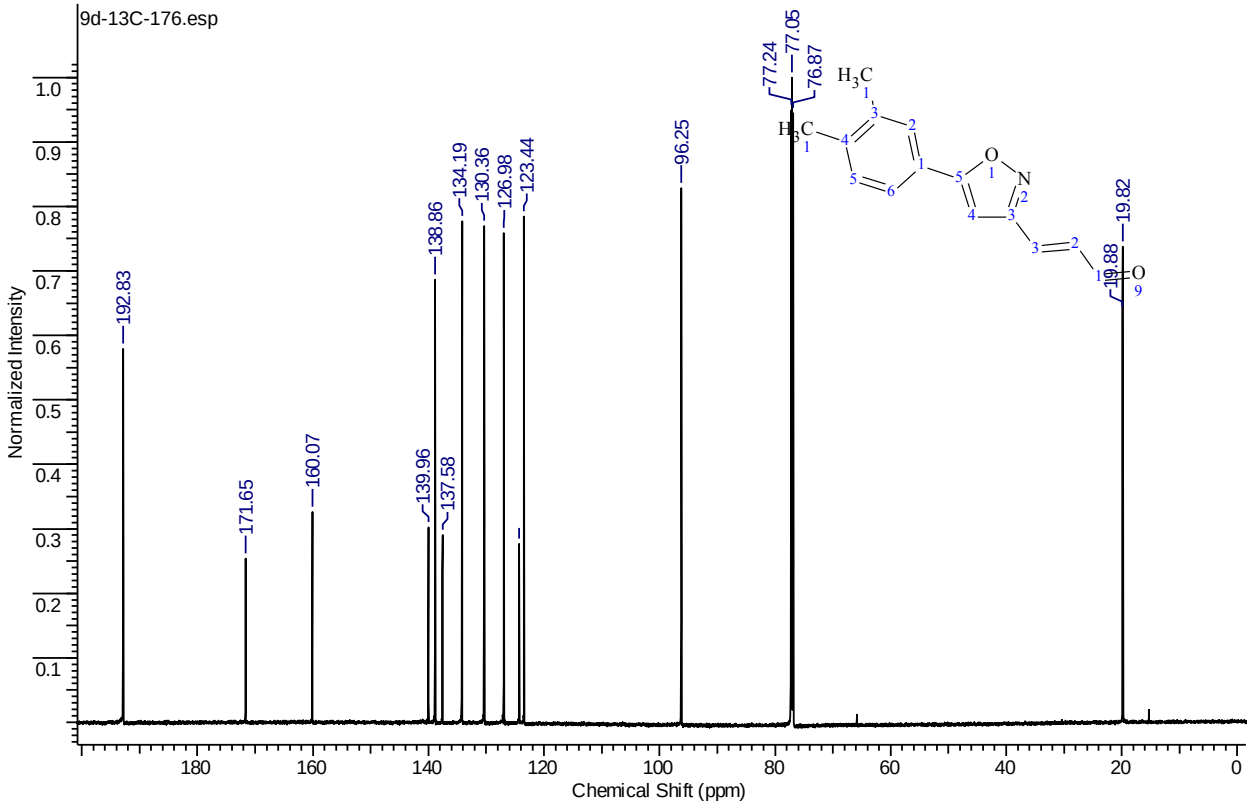
(2*E*)-3-[5-(3,4-Dimethylphenyl)isoxazol-3-yl]acrylaldehyde (9d).

^{1}H NMR (700.2 MHz, $CDCl_3$)



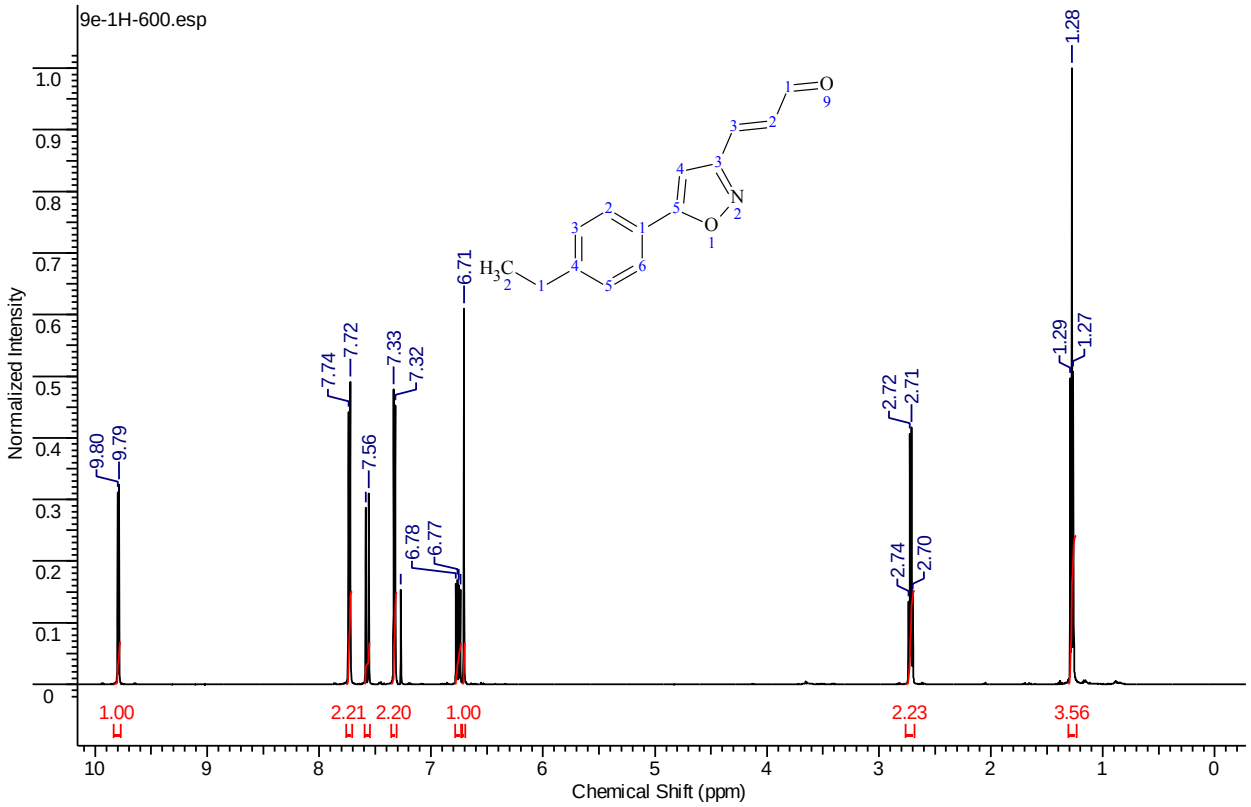


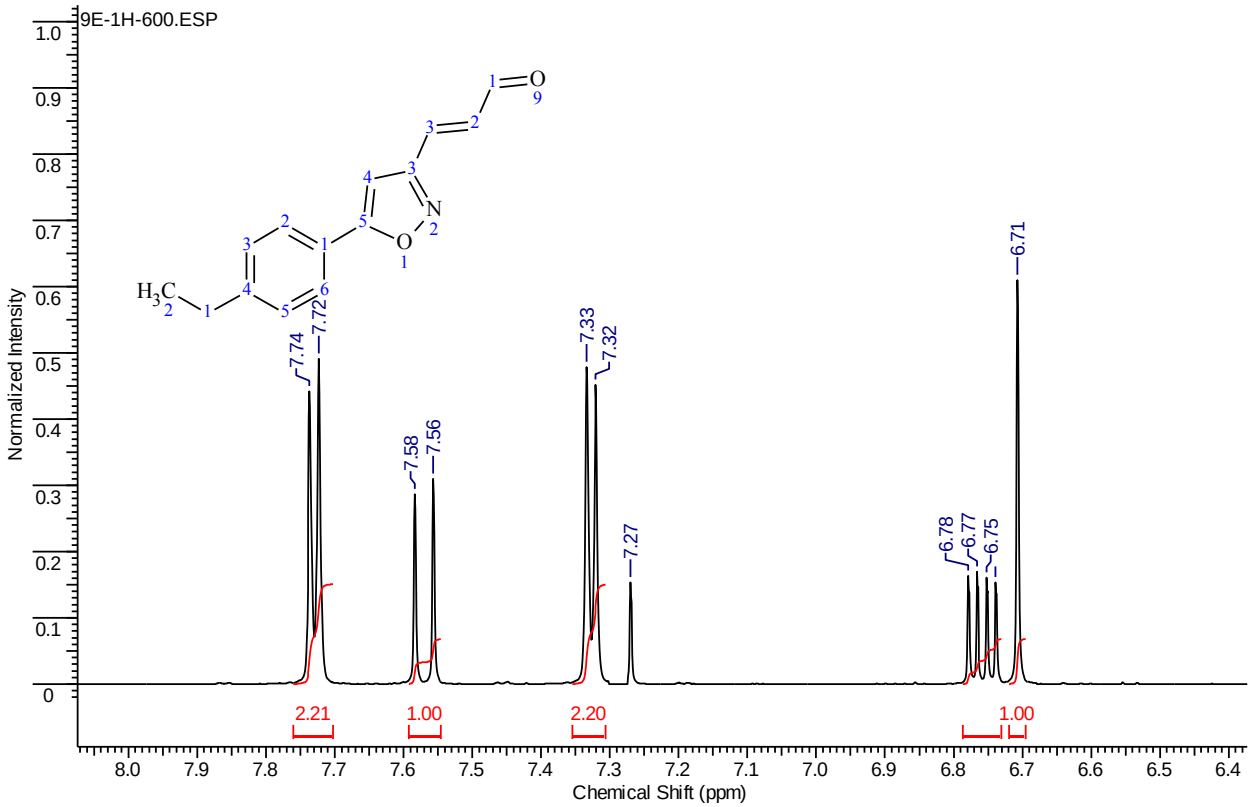
^{13}C NMR (176.1 MHz, $CDCl_3$)



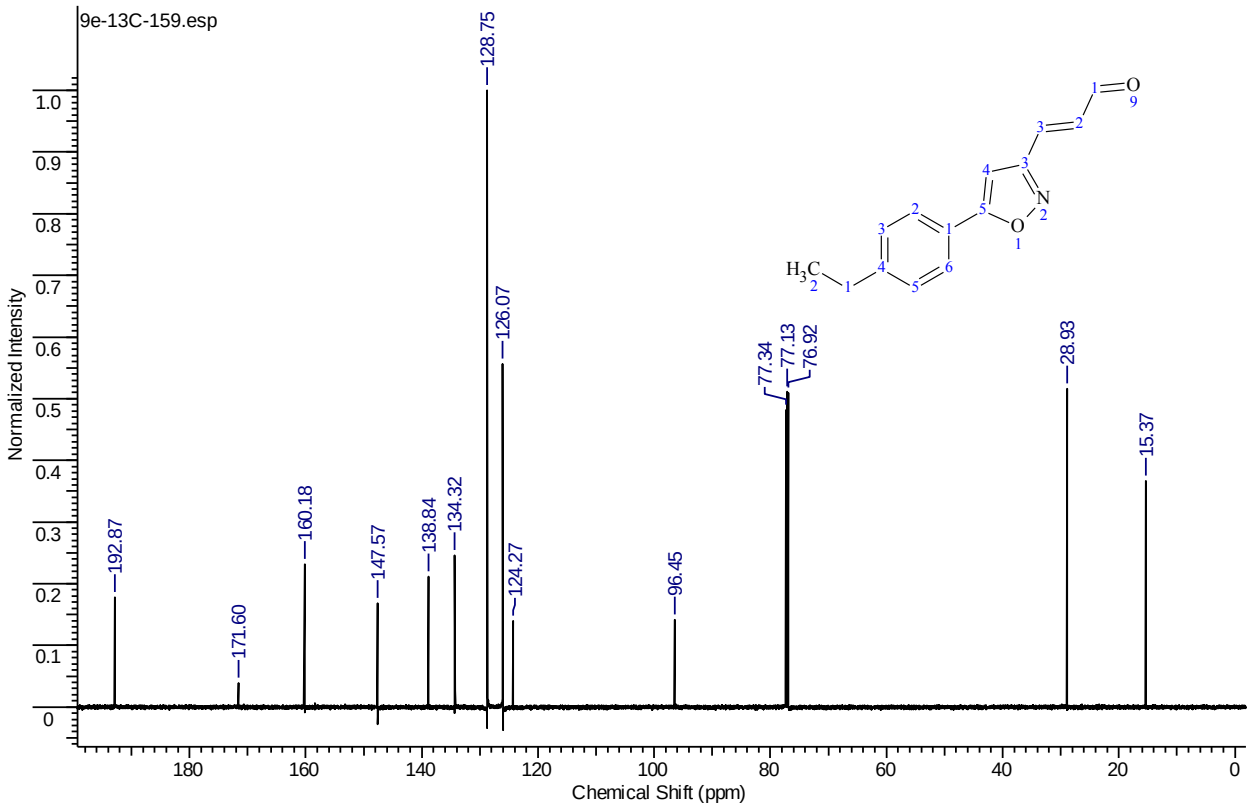
(2*E*)-3-[5-(4-Ethylphenyl)isoxazol-3-yl]acrylaldehyde (9e).

^{1}H NMR (600.2 MHz, $CDCl_3$)



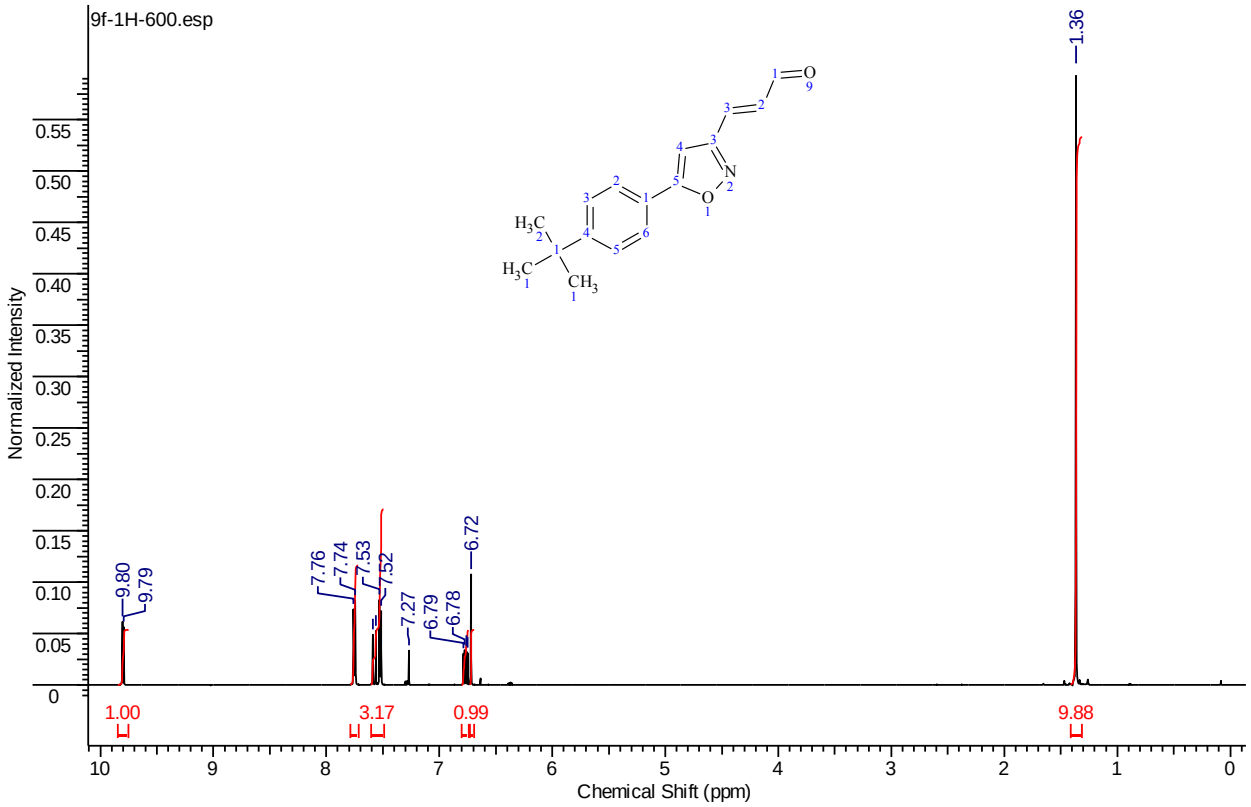


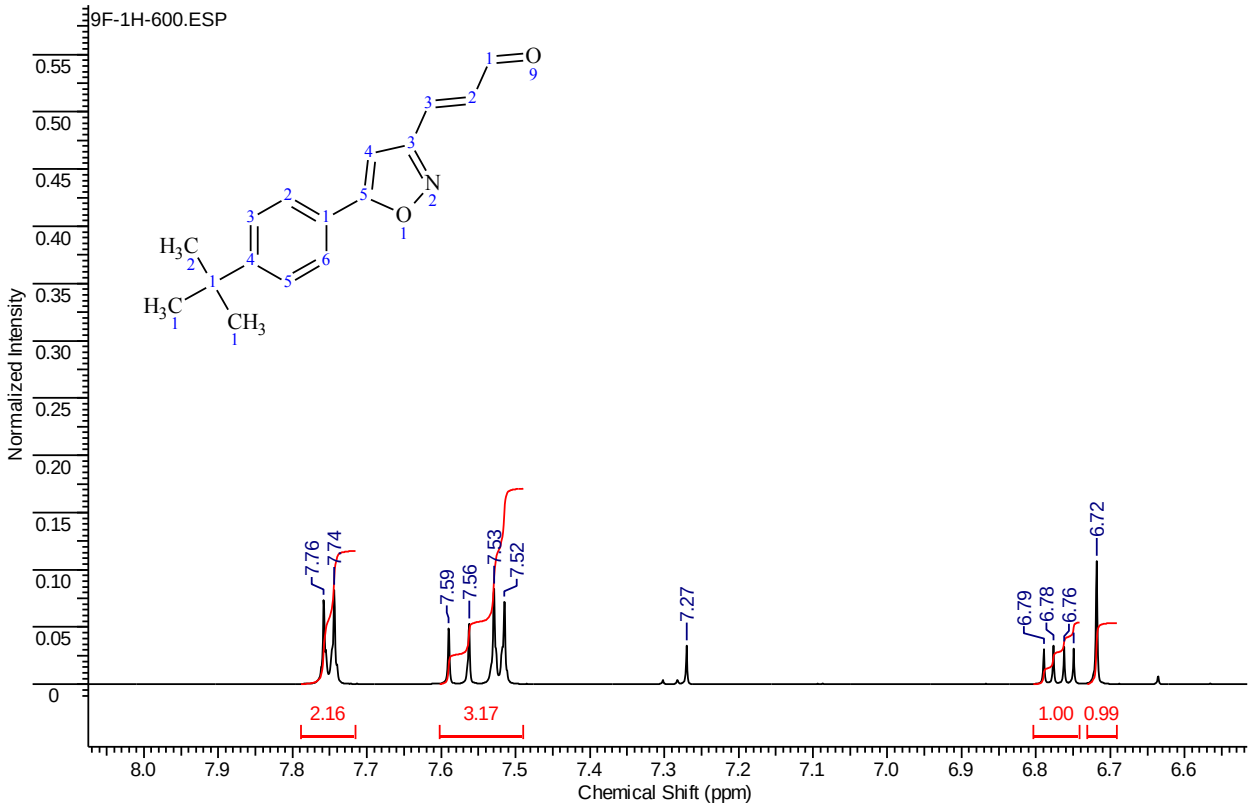
^{13}C NMR (150.9 MHz, $CDCl_3$)



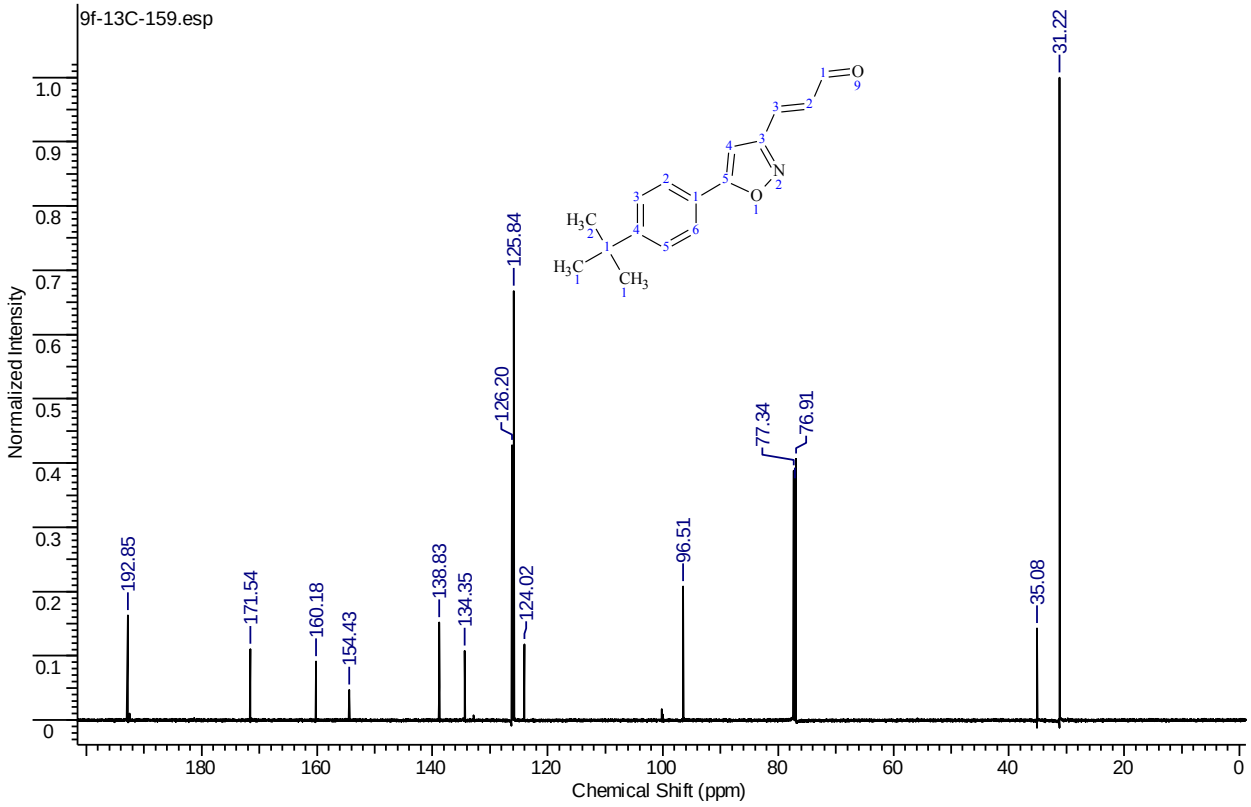
(2*E*)-3-[5-(4-*tert*-Butylphenyl)isoxazol-3-yl]acrylaldehyde (9f).

^{1}H NMR (600.2 MHz, $CDCl_3$)



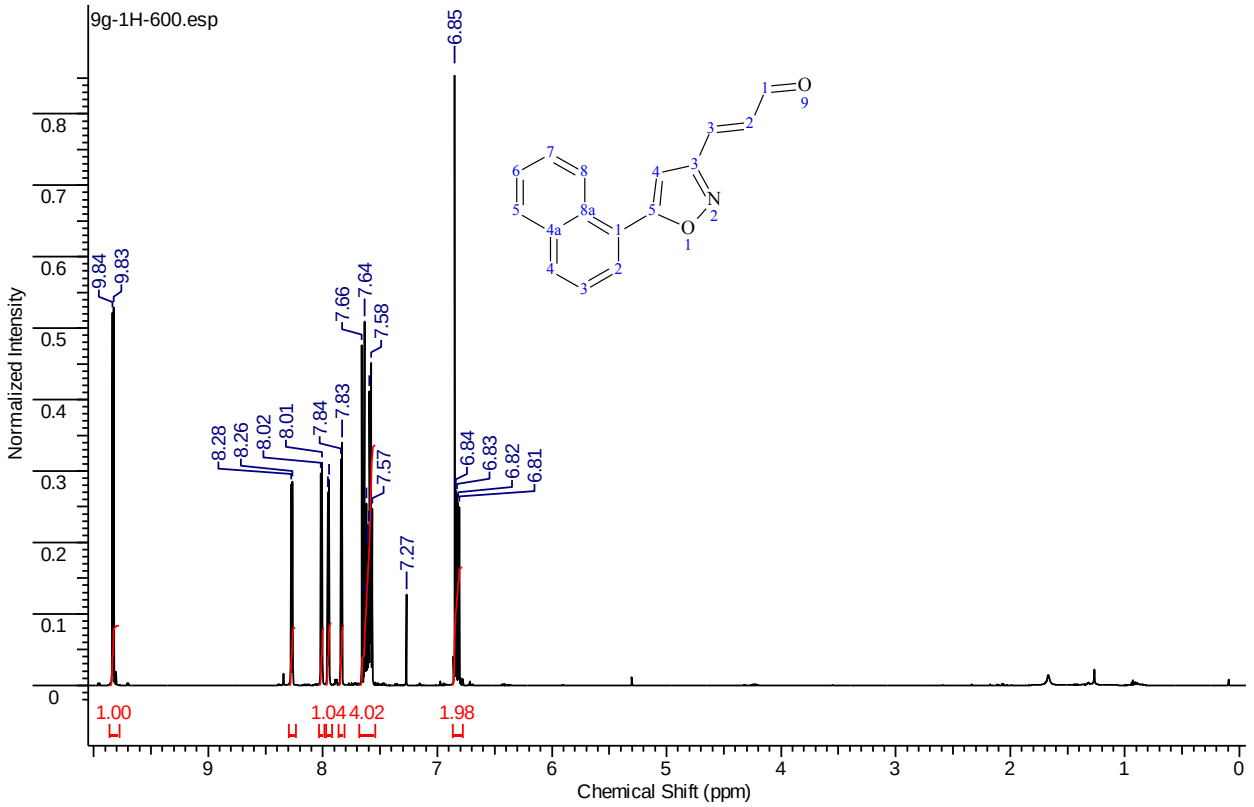


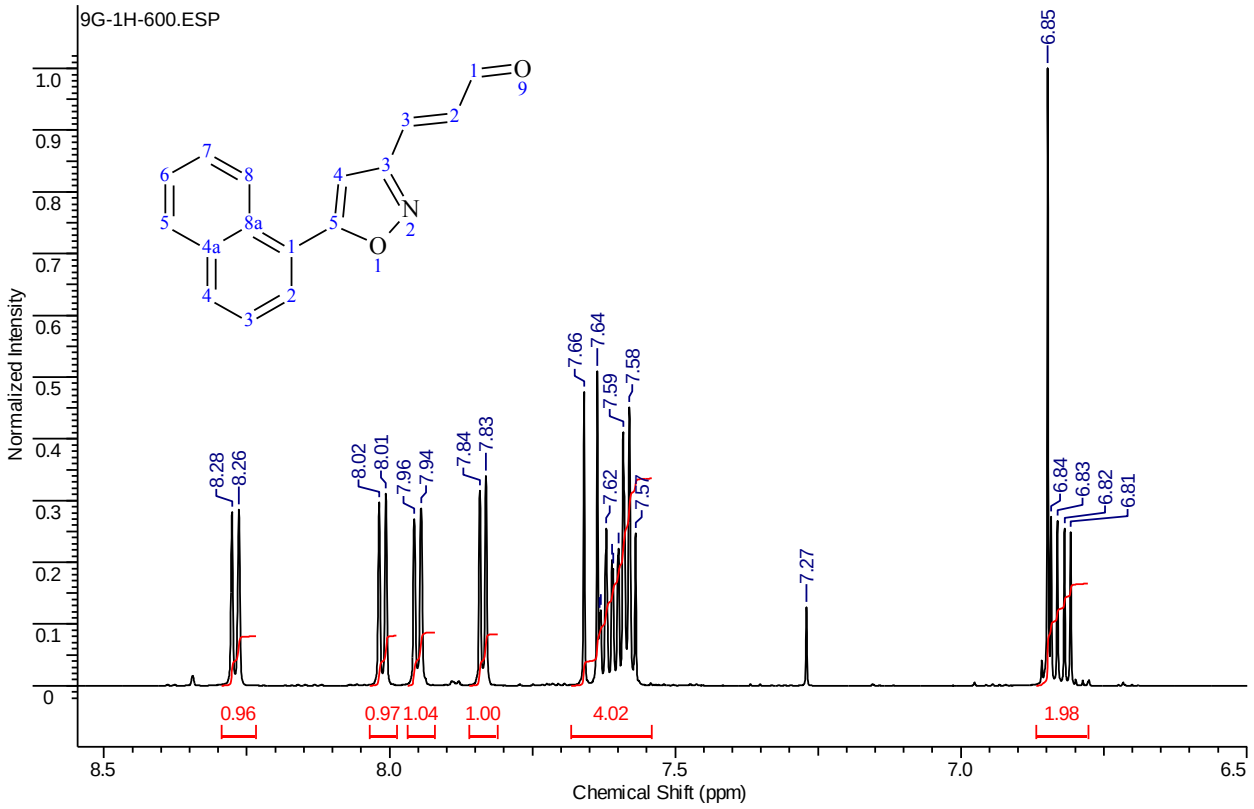
^{13}C NMR (150.9 MHz, $CDCl_3$)



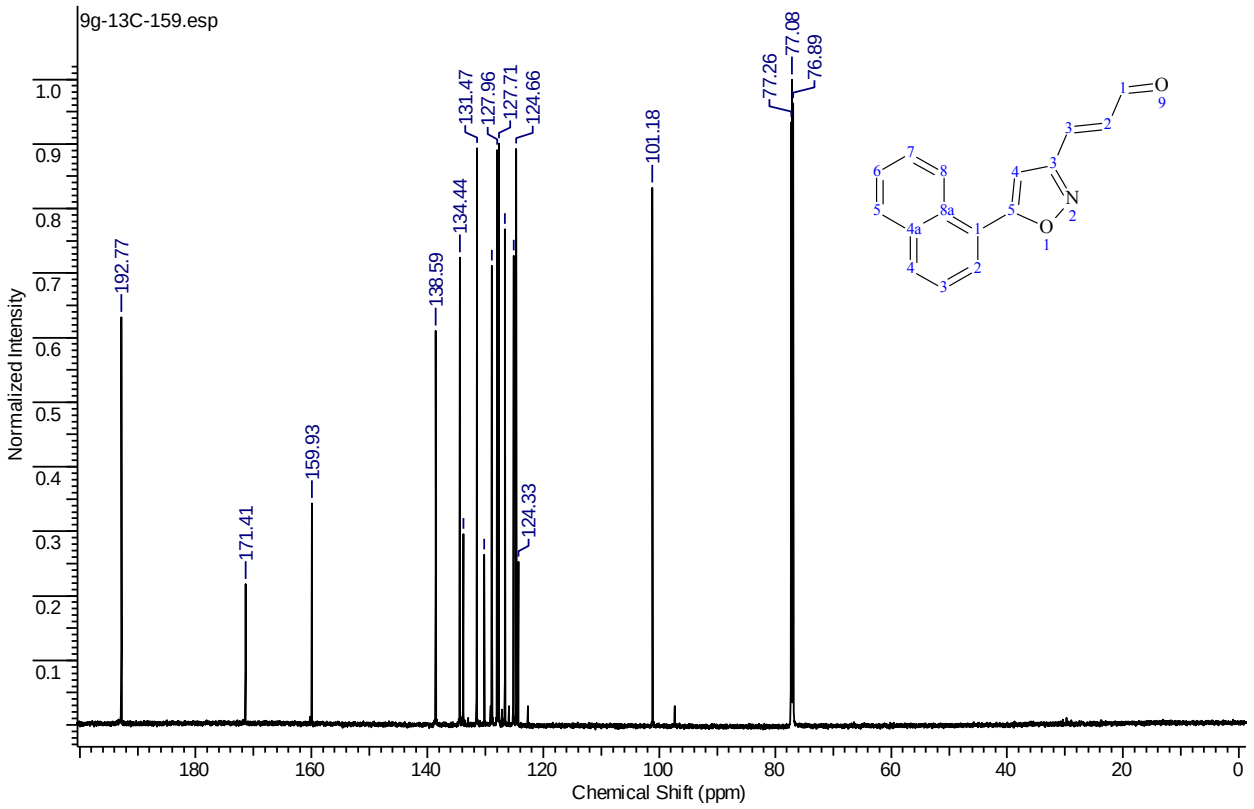
(2*E*)-3-[5-(1-Naphthyl)isoxazol-3-yl]acrylaldehyde (9g).

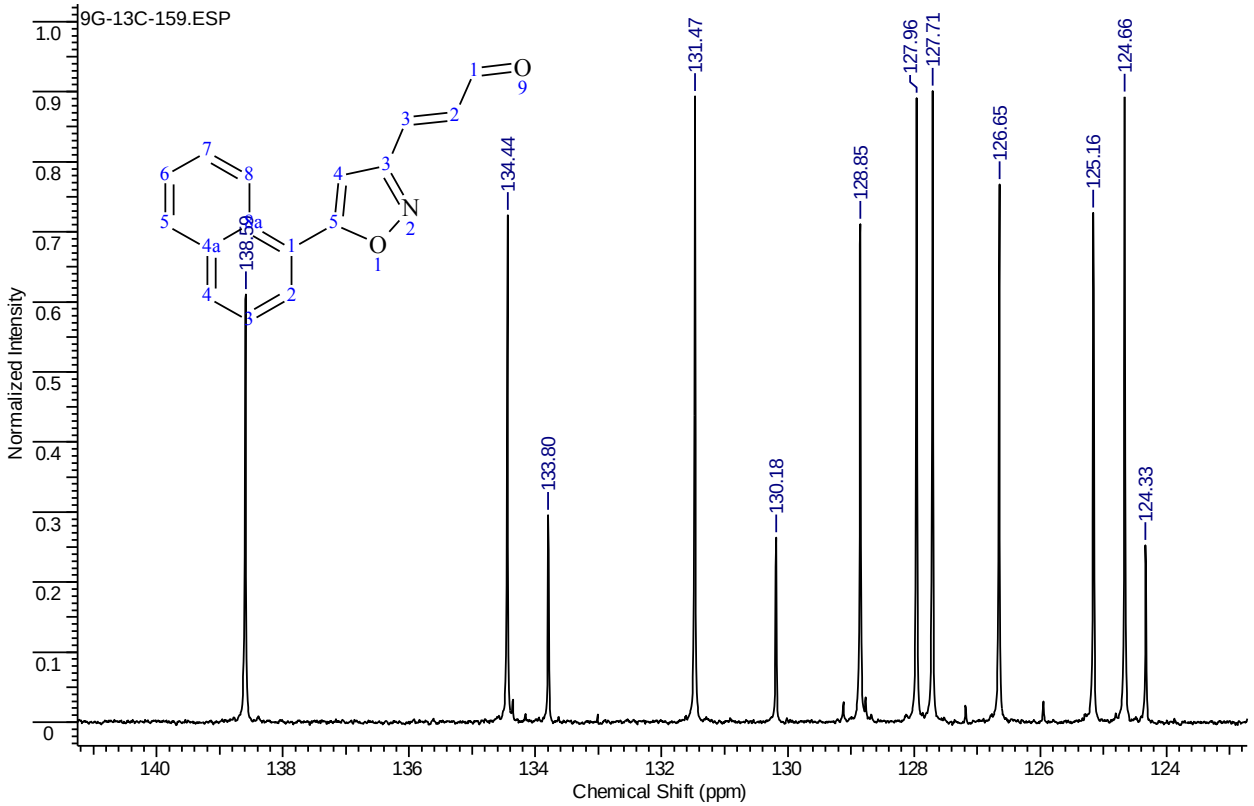
^{1}H NMR (600.2 MHz, $CDCl_3$)





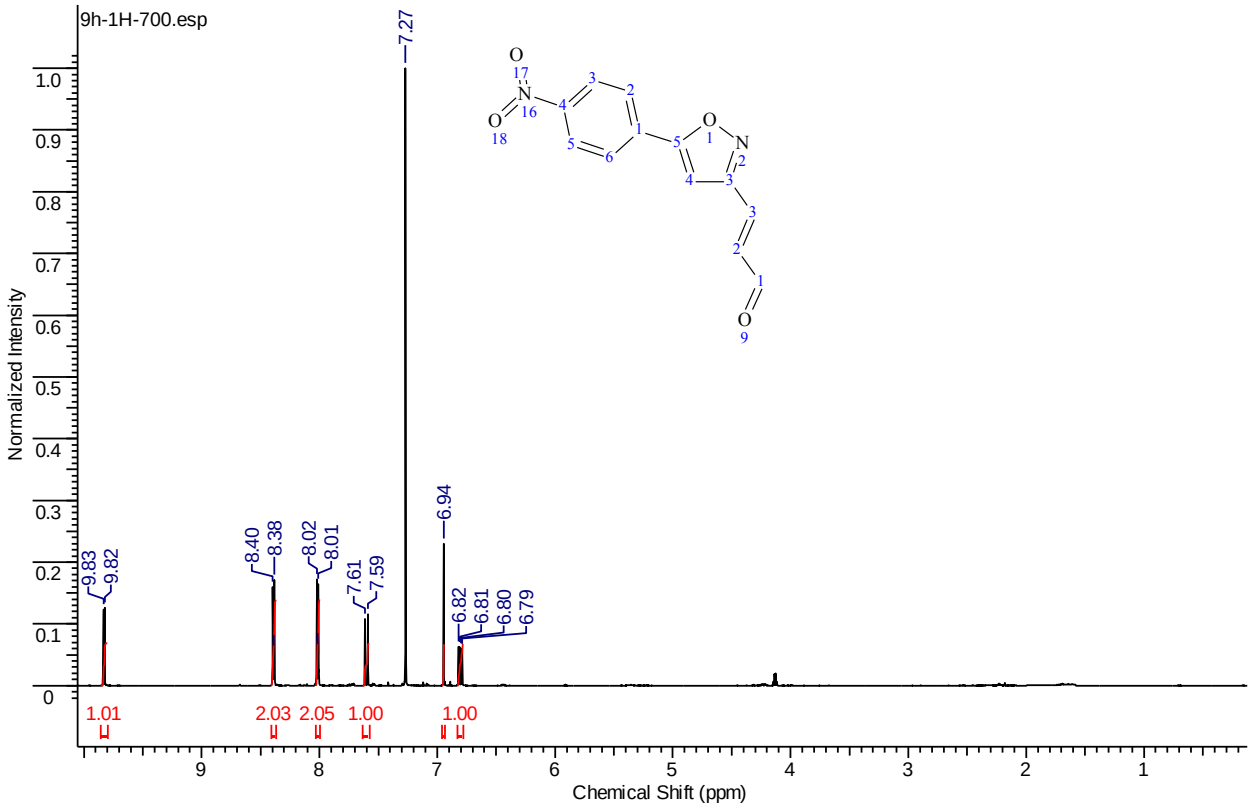
^{13}C NMR (150.9 MHz, $CDCl_3$)



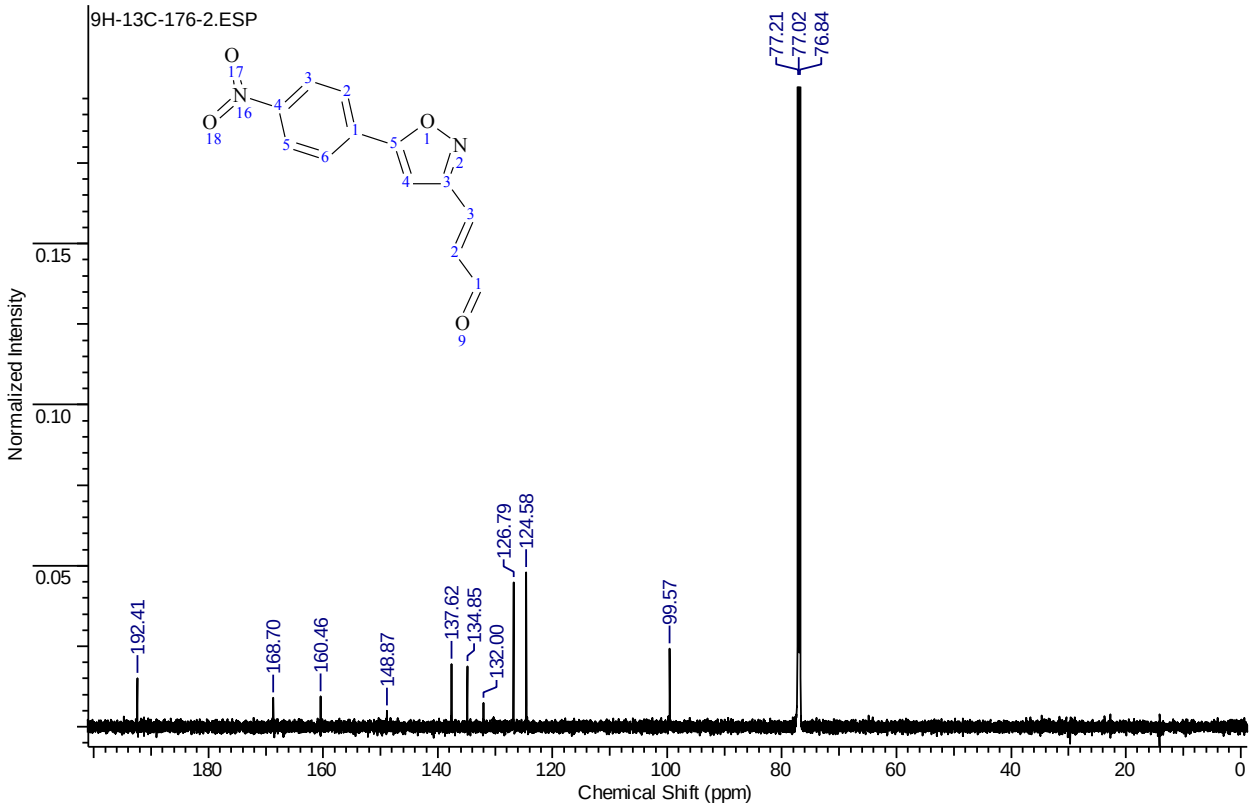


(2*E*)-3-[5-(4-Nitrophenyl)isoxazol-3-yl]acrylaldehyde (9h).

^{1}H NMR (600.2 MHz, $CDCl_3$)

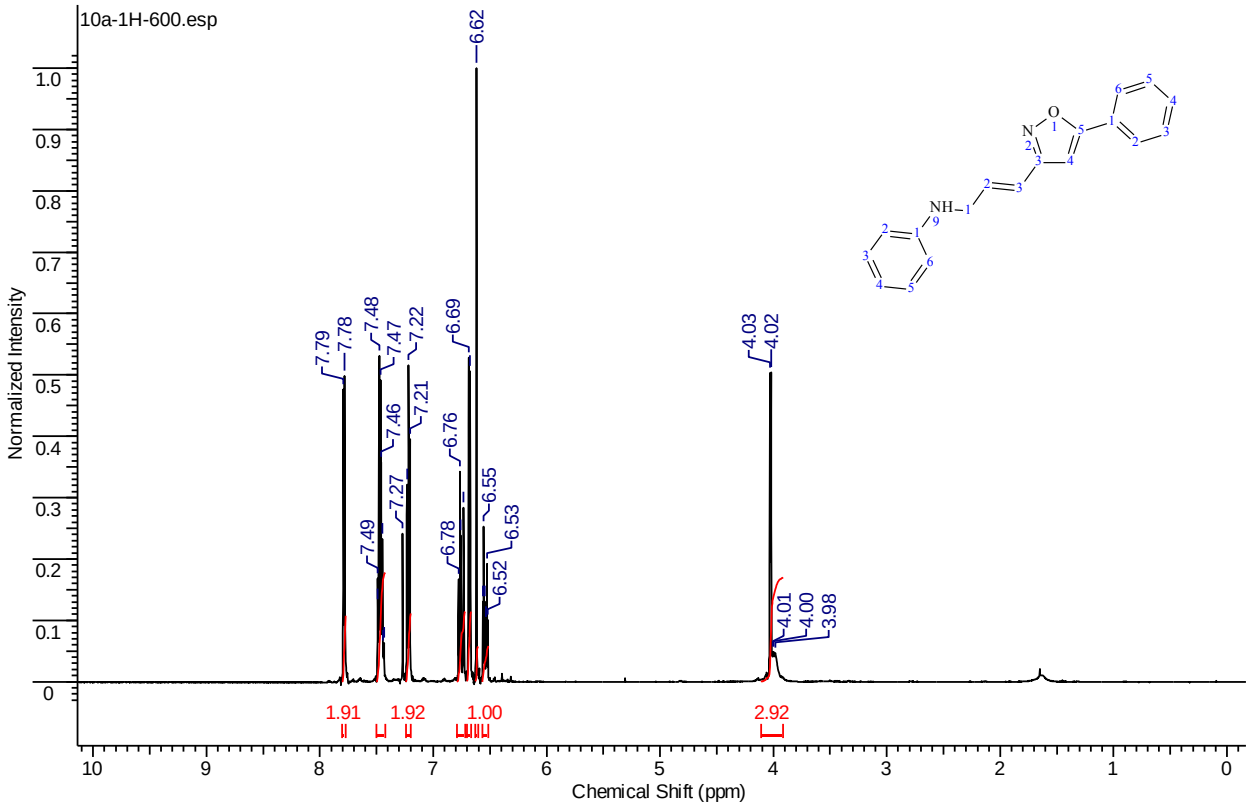


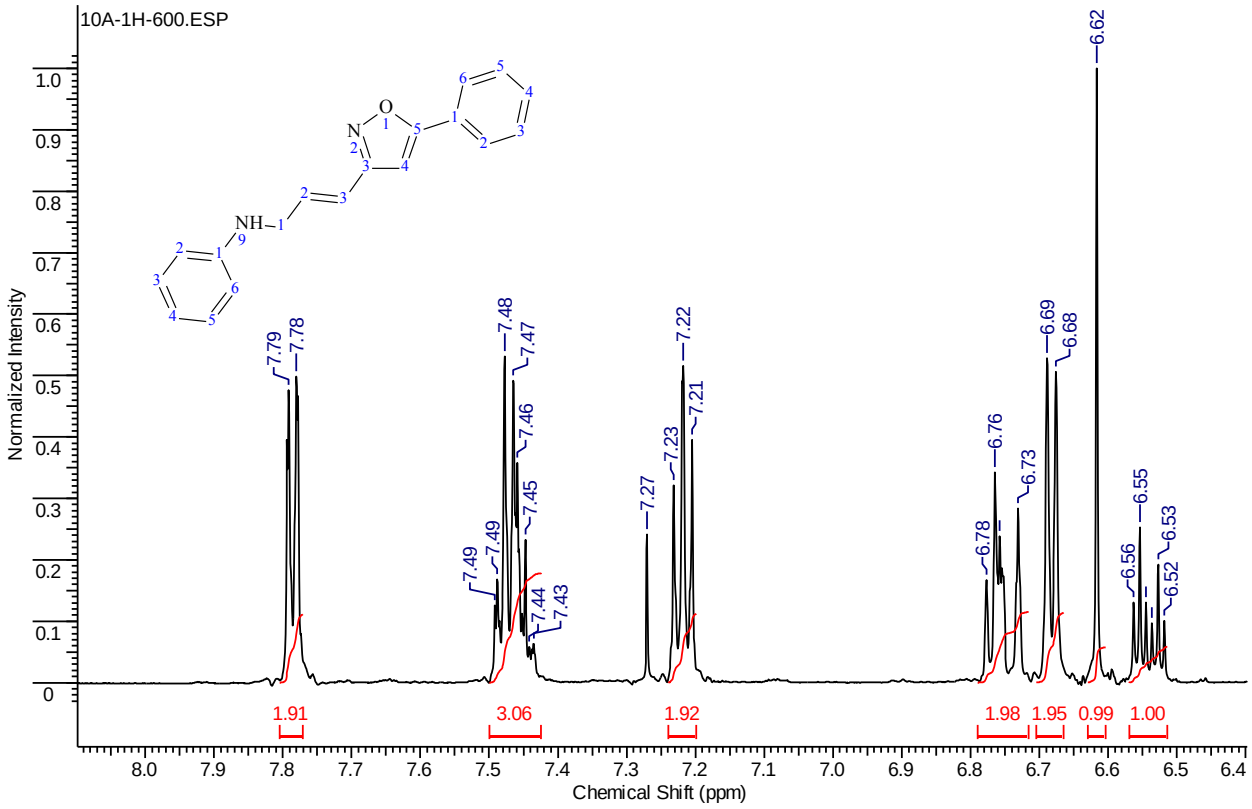
^{13}C NMR (150.9 MHz, $CDCl_3$)



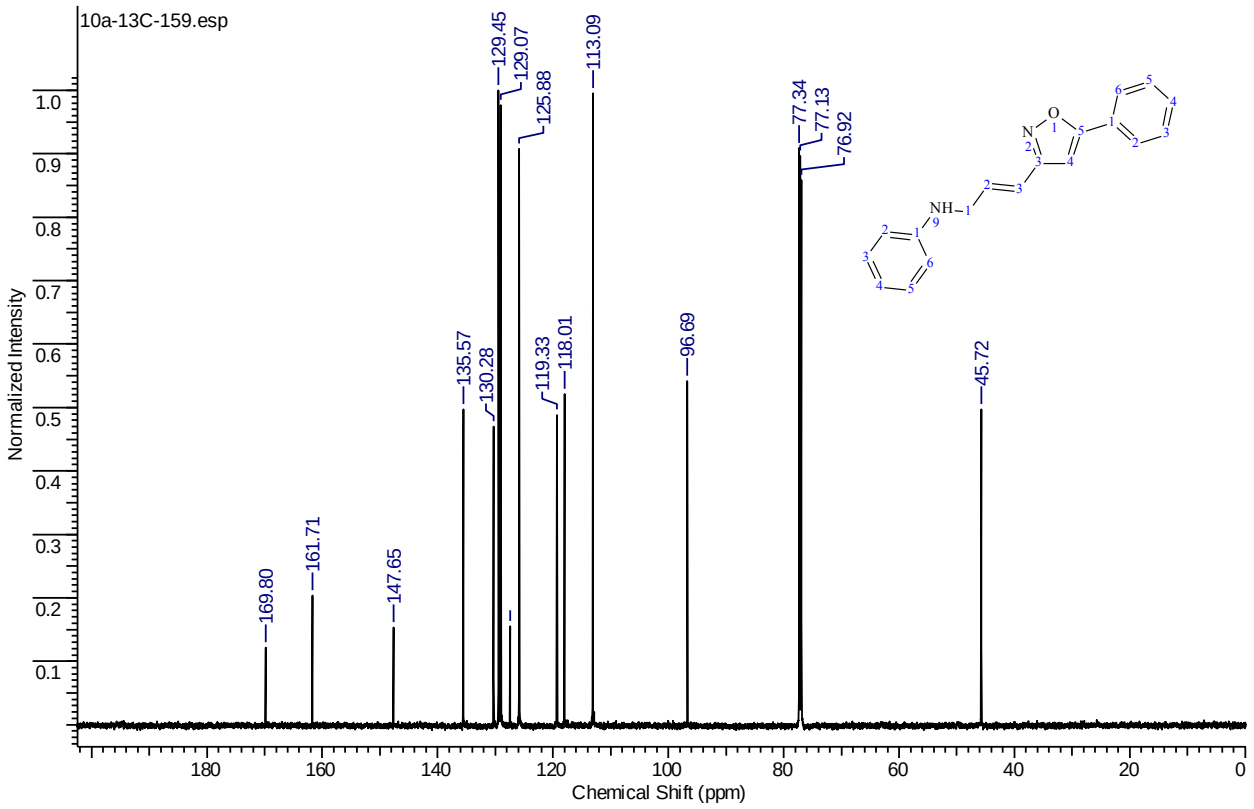
***N*-[(2*E*)-3-(5-Phenylisoxazol-3-yl)prop-2-en-1-yl]aniline (10a).**

^{1}H NMR (600.2 MHz, $CDCl_3$)



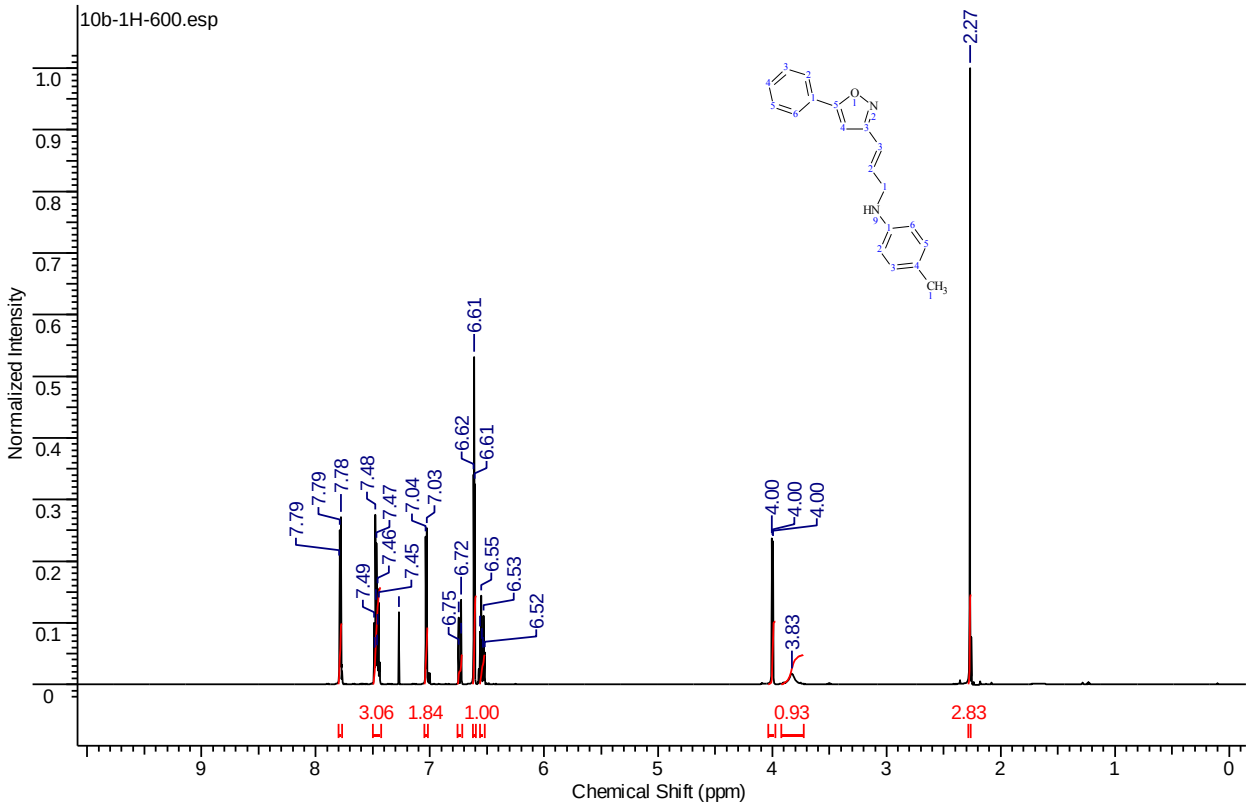


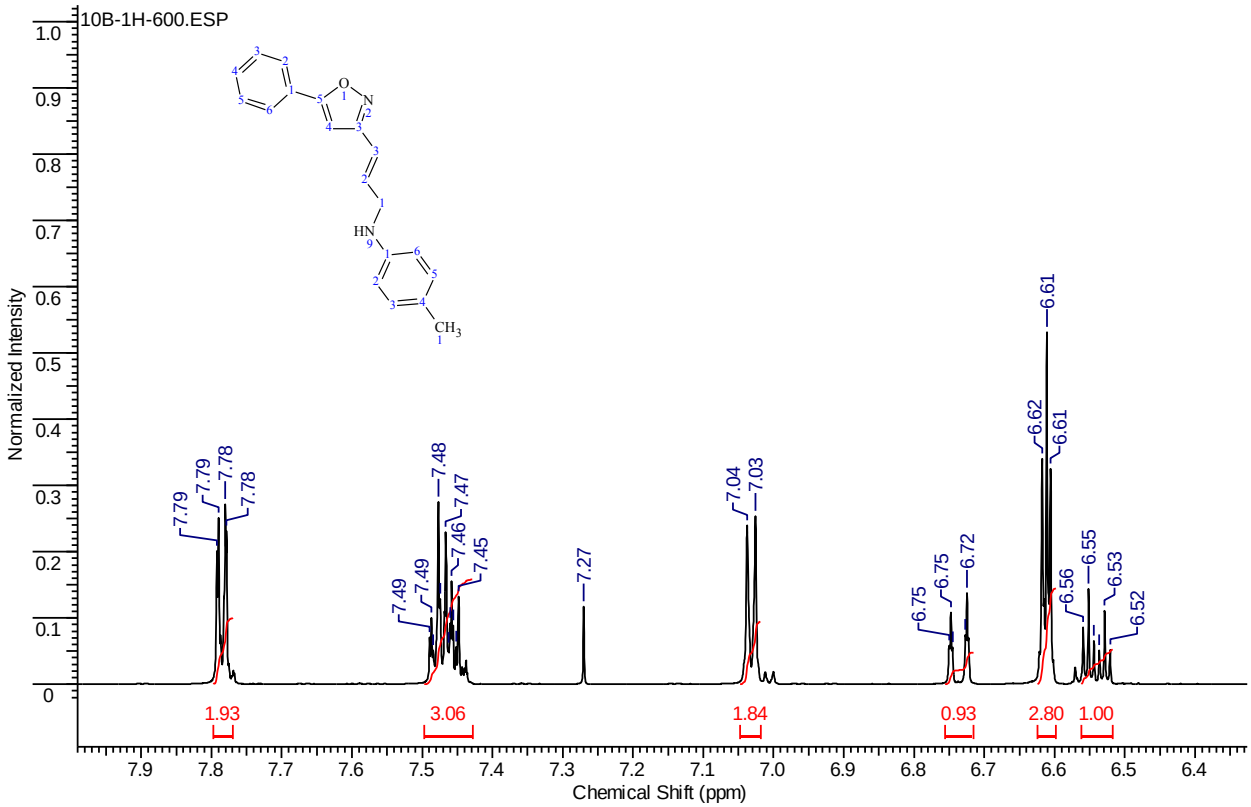
^{13}C NMR (150.9 MHz, $CDCl_3$)



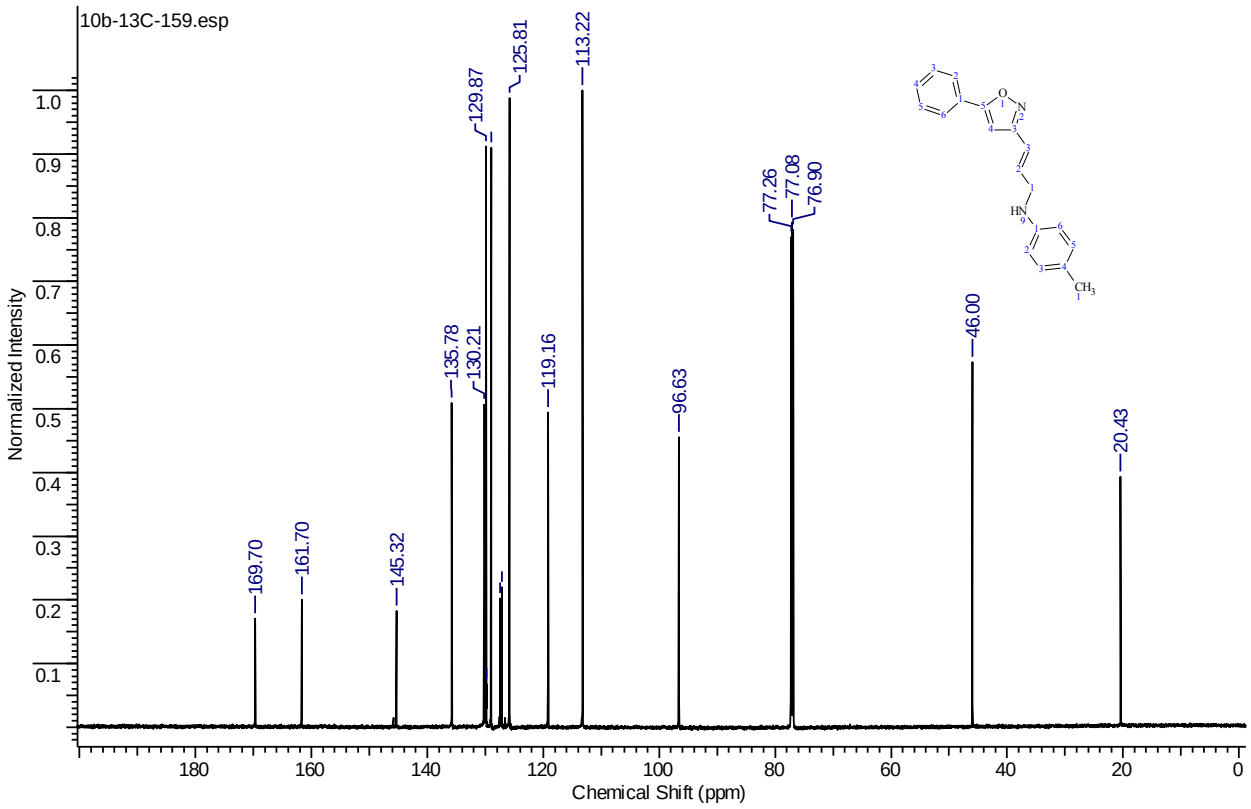
(4-Methylphenyl)[(2*E*)-3-(5-phenylisoxazol-3-yl)prop-2-en-1-yl]amine (10b).

^{1}H NMR (600.2 MHz, $CDCl_3$)



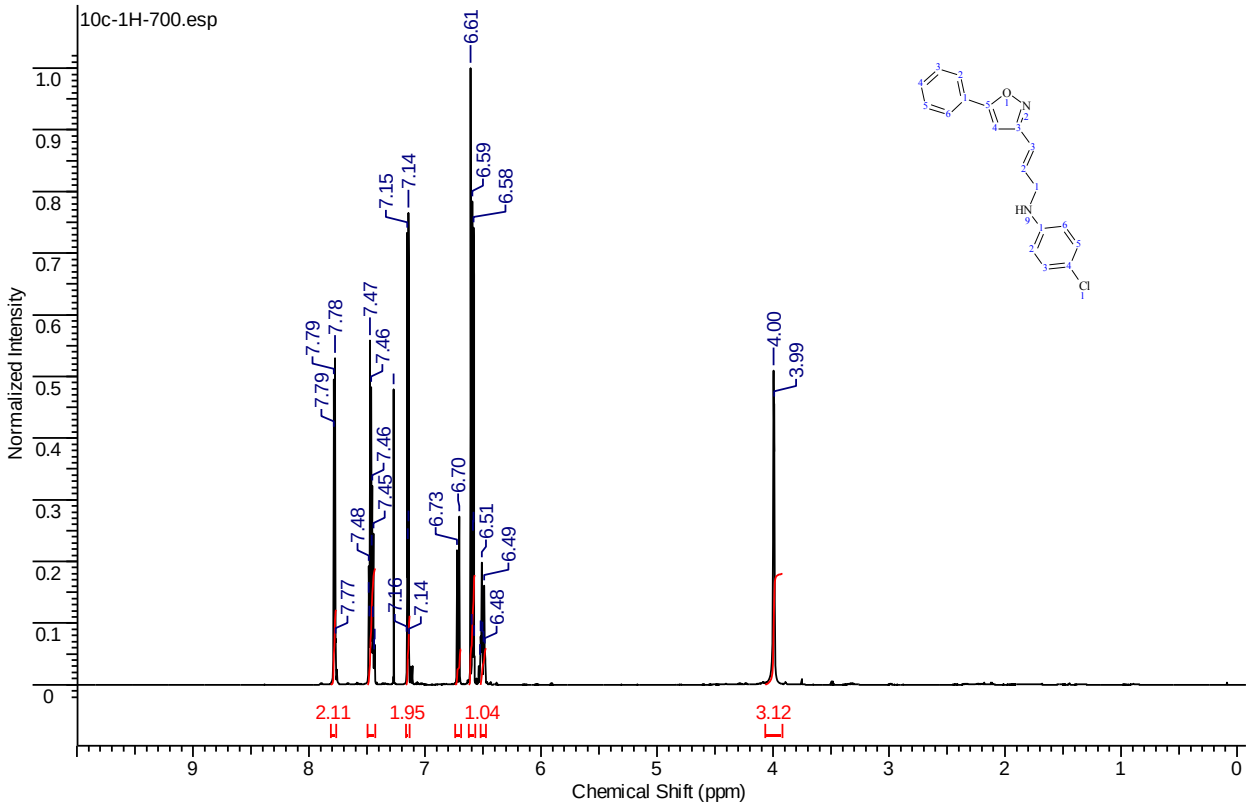


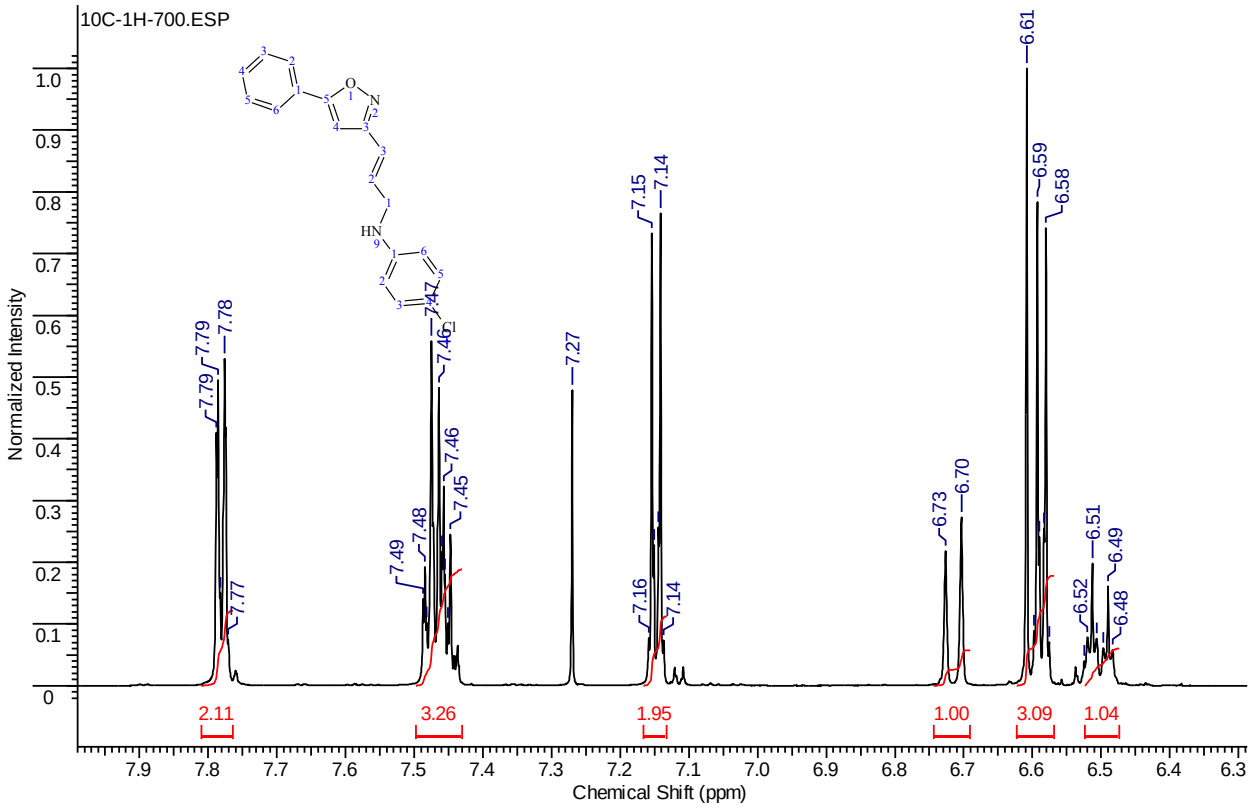
^{13}C NMR (150.9 MHz, $CDCl_3$)



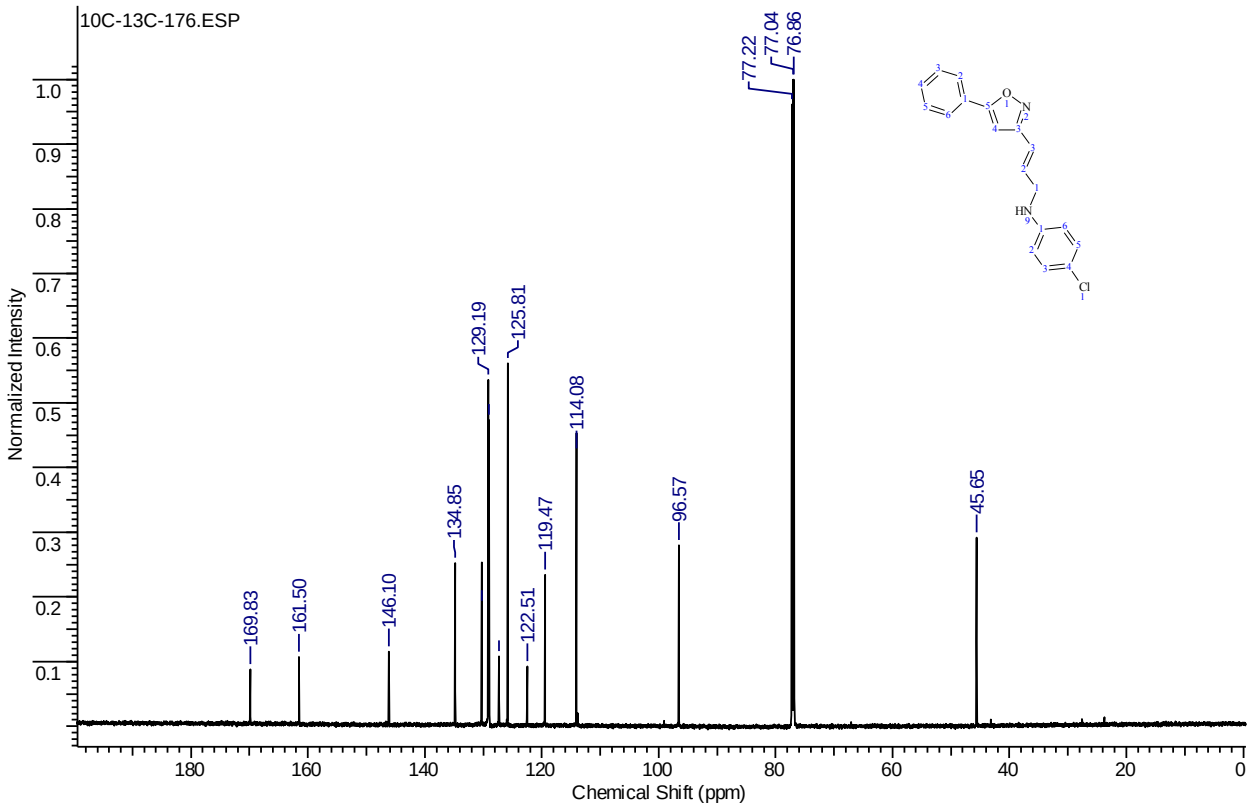
(4-Chlorophenyl)[(2*E*)-3-(5-phenylisoxazol-3-yl)prop-2-en-1-yl]amine (10c).

^{1}H NMR (700.2 MHz, $CDCl_3$)



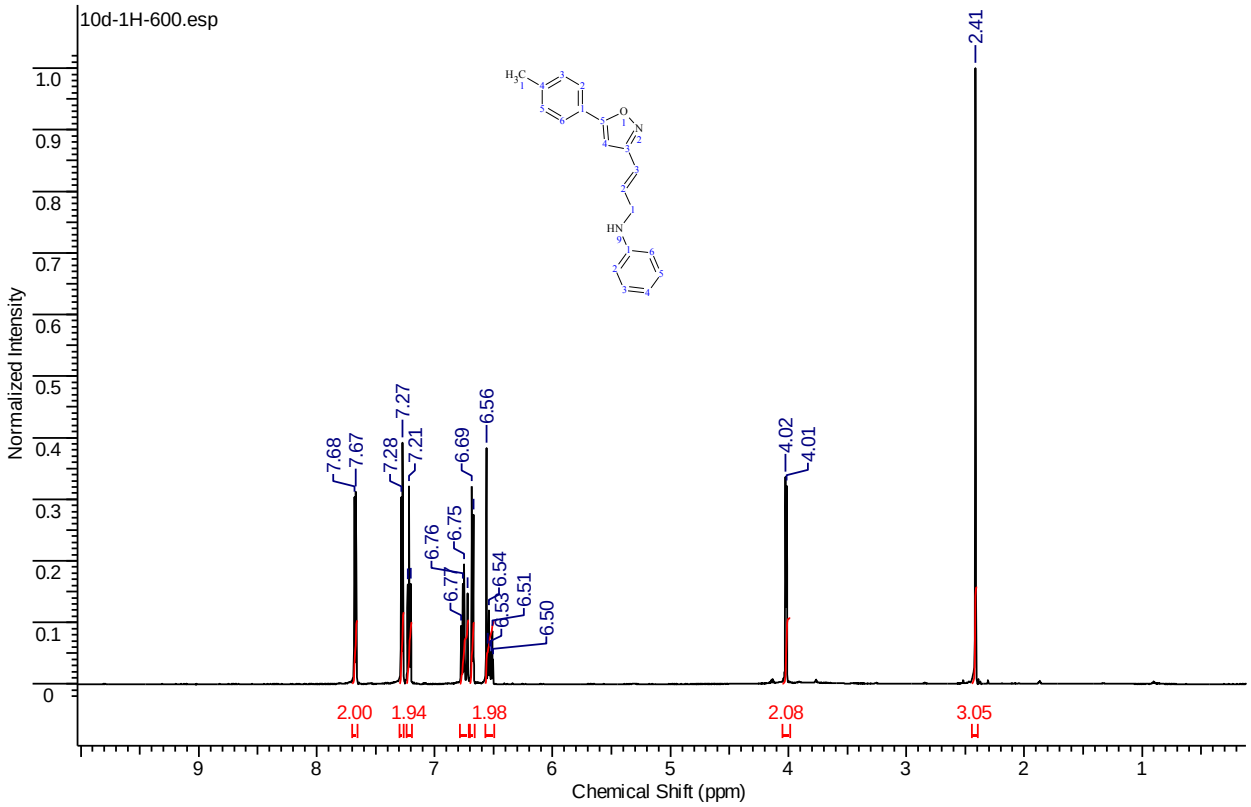


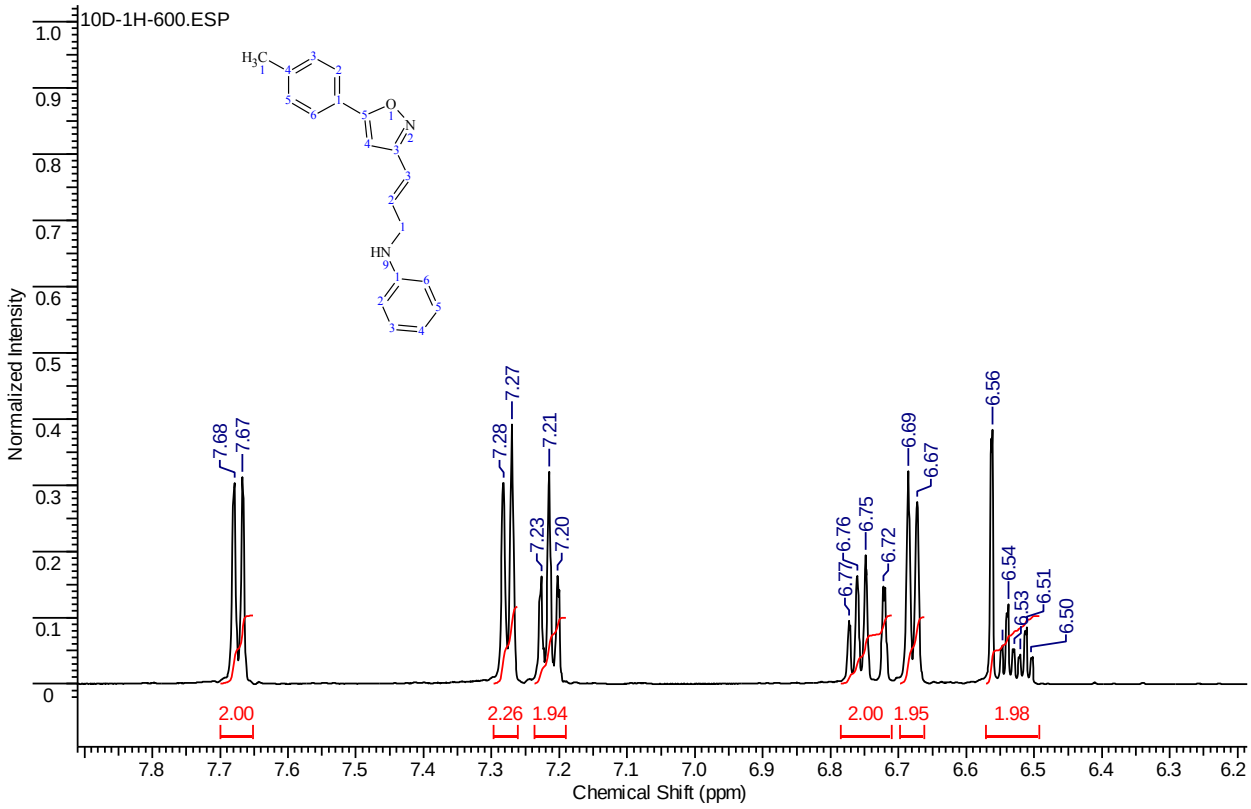
^{13}C NMR (176.1 MHz, $CDCl_3$)



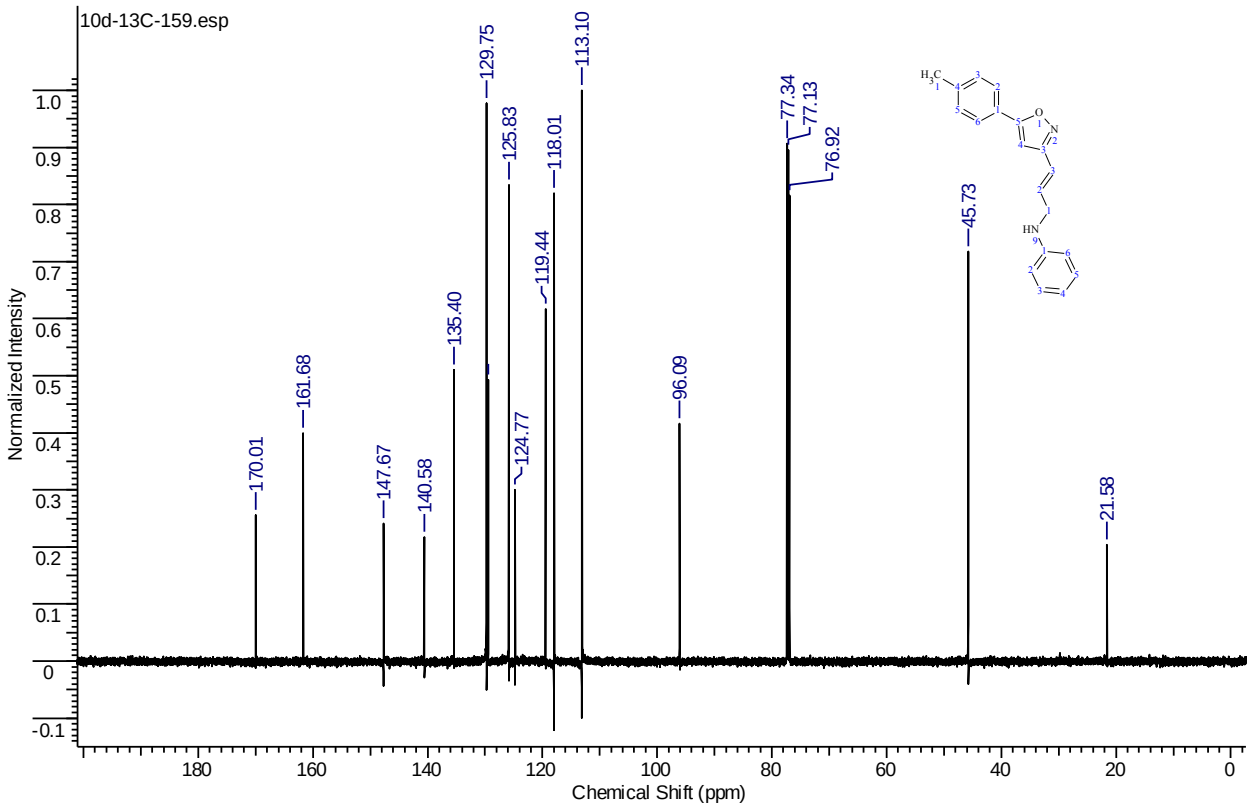
***N*-{(2*E*)-3-[5-(4-Methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10d).**

^{1}H NMR (600.2 MHz, $CDCl_3$)



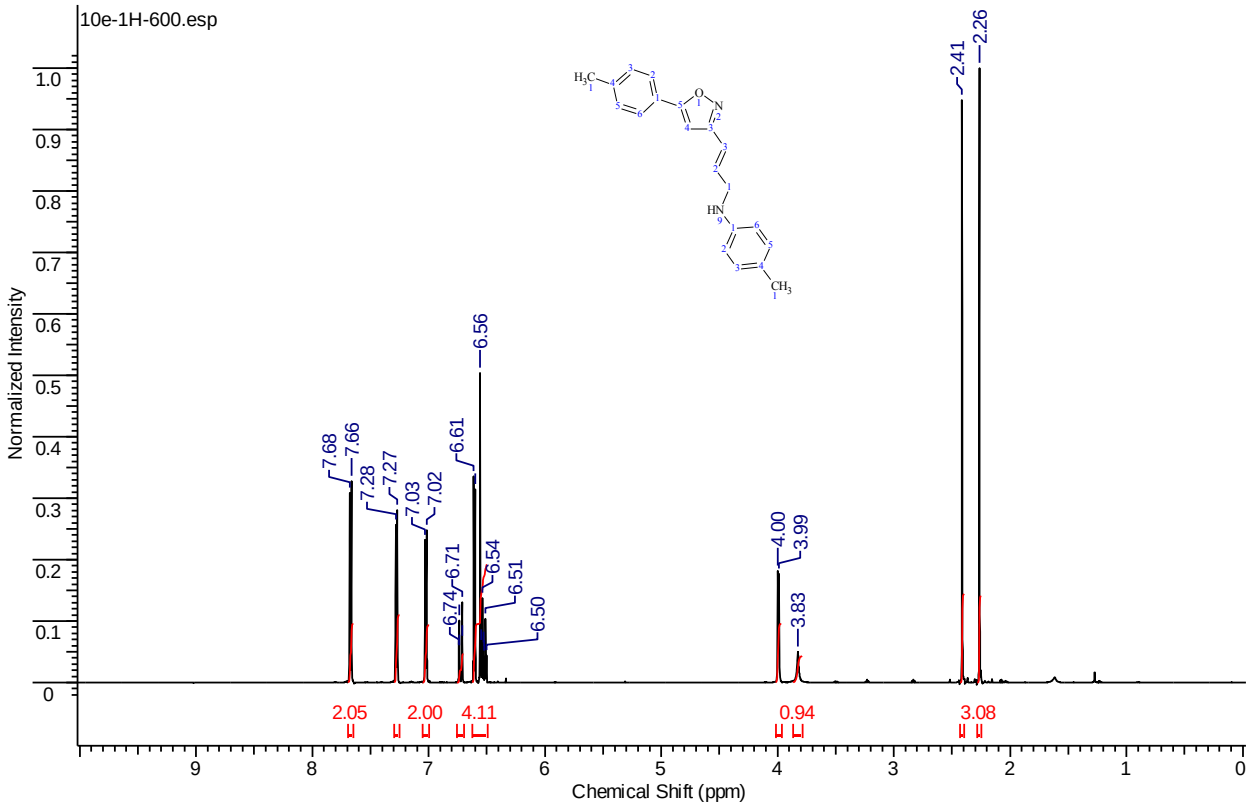


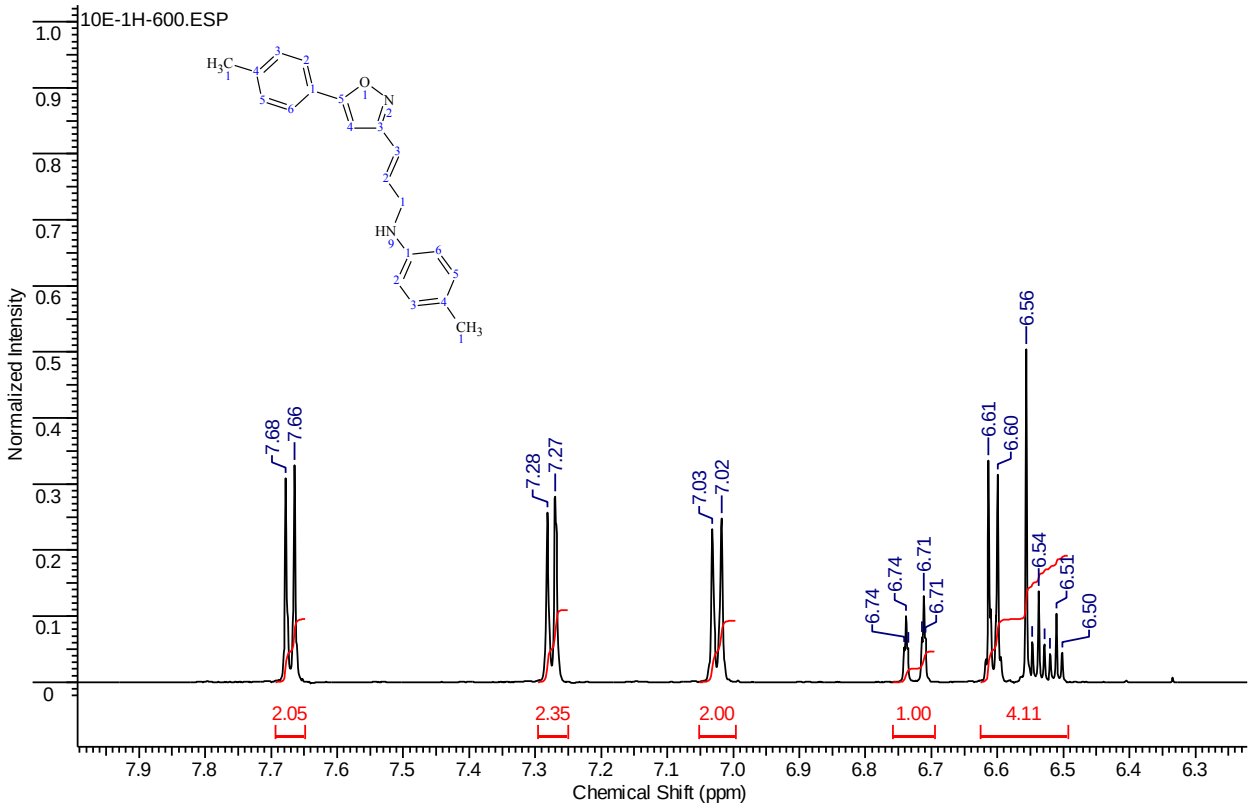
^{13}C NMR (150.9 MHz, $CDCl_3$)



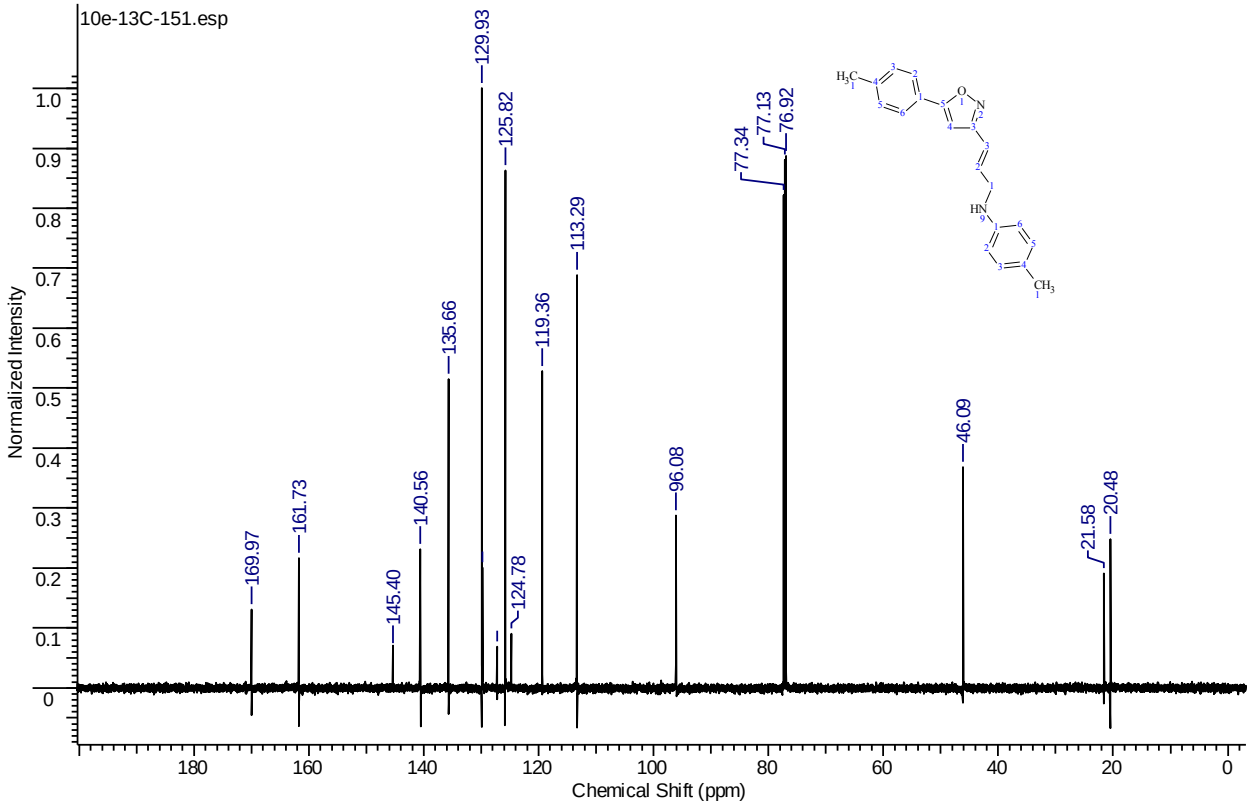
(4-Methylphenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10e).

^{1}H NMR (600.2 MHz, $CDCl_3$)



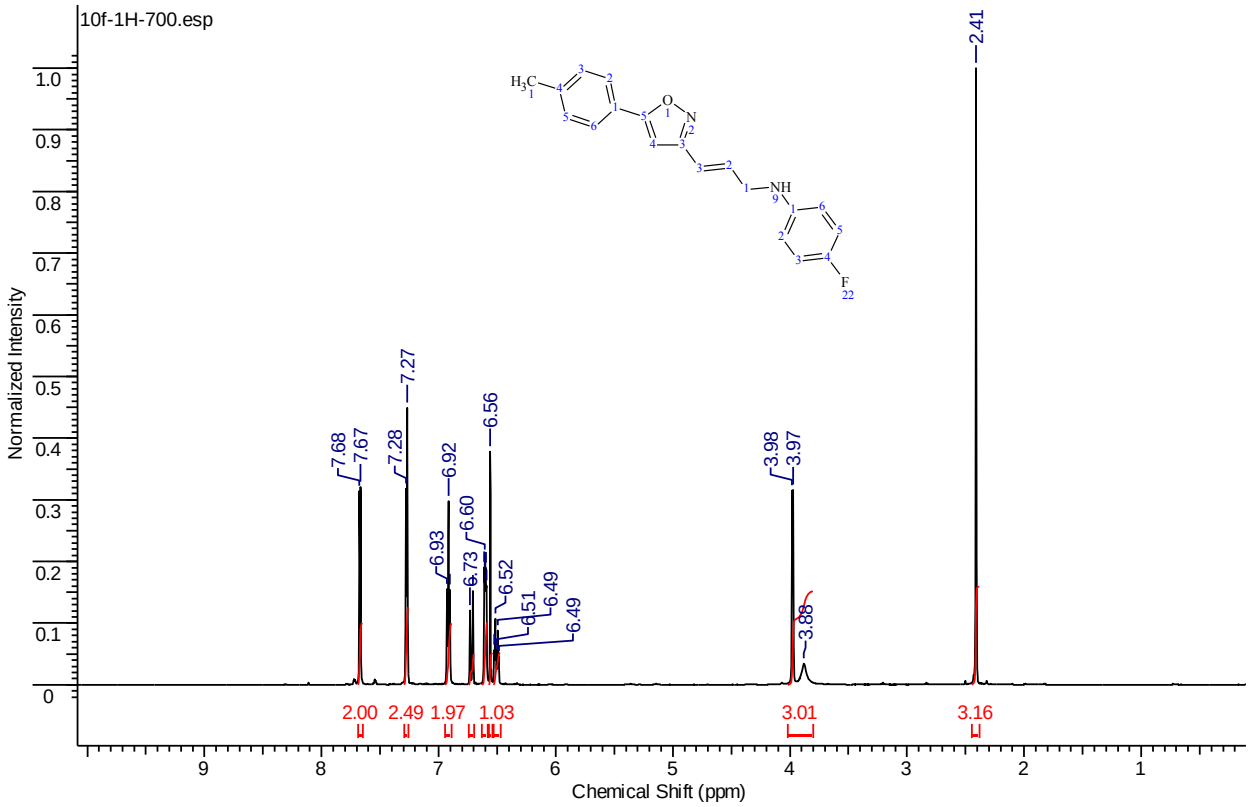


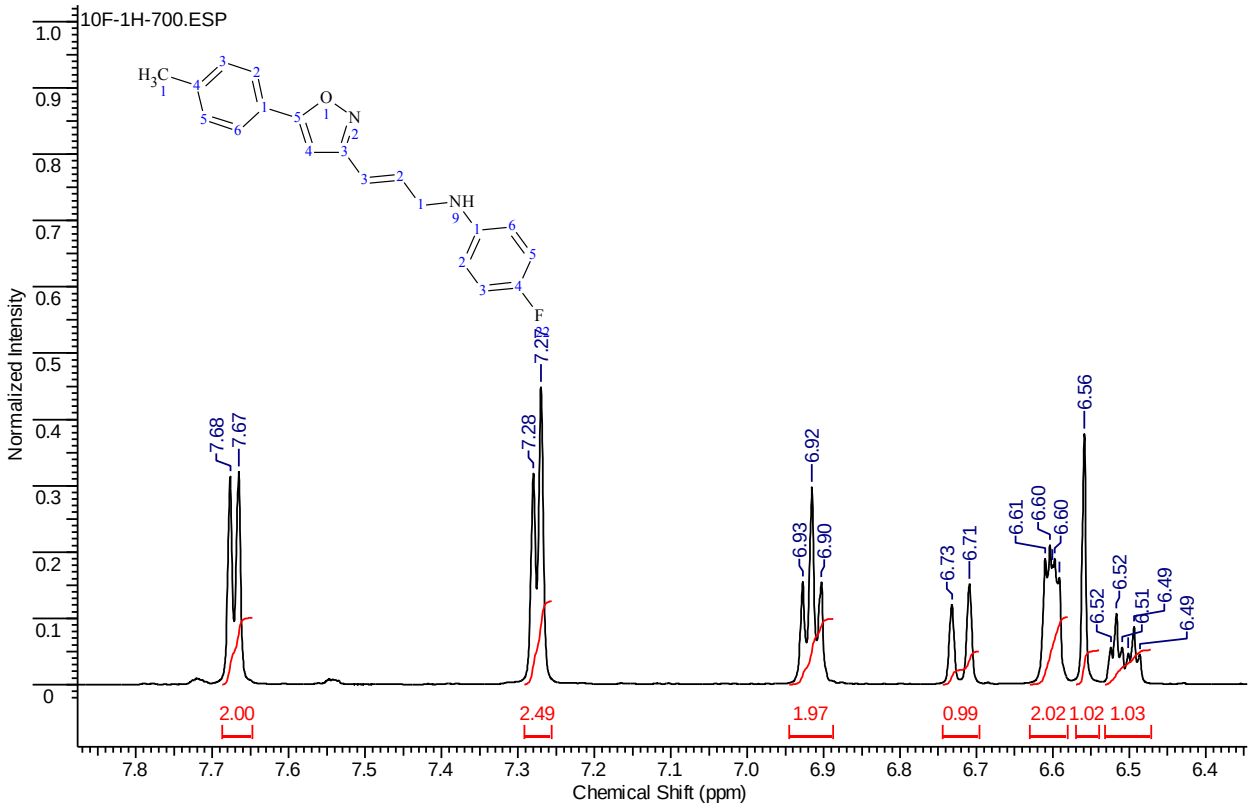
^{13}C NMR (150.9 MHz, $CDCl_3$)



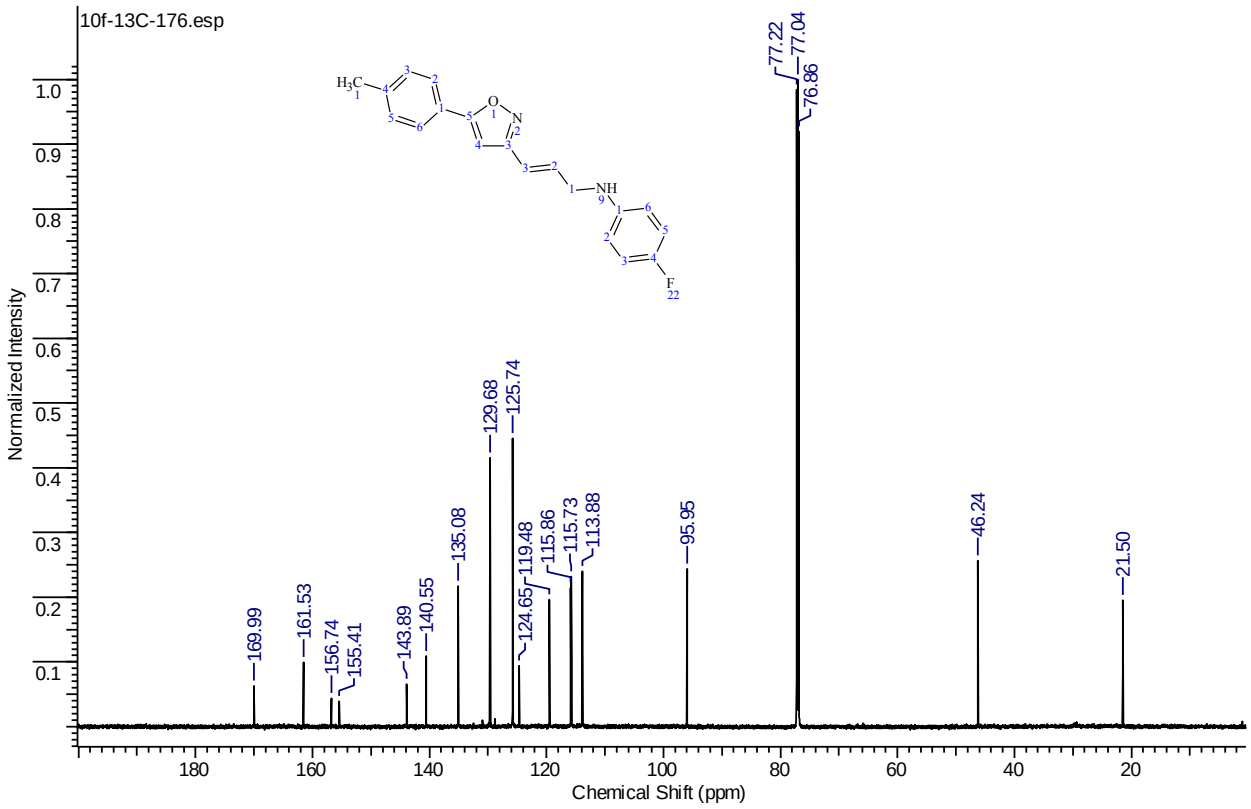
(4-Fluorophenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10f).

^{1}H NMR (700.2 MHz, $CDCl_3$)

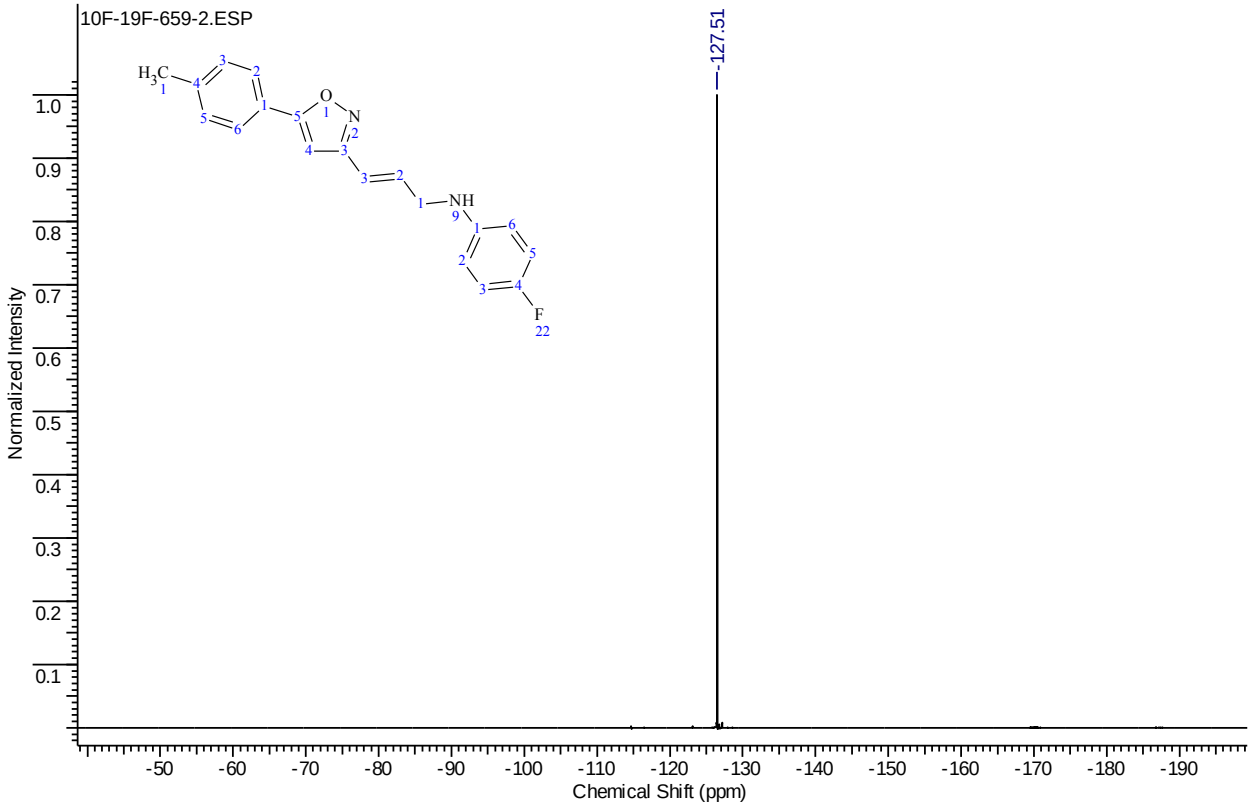




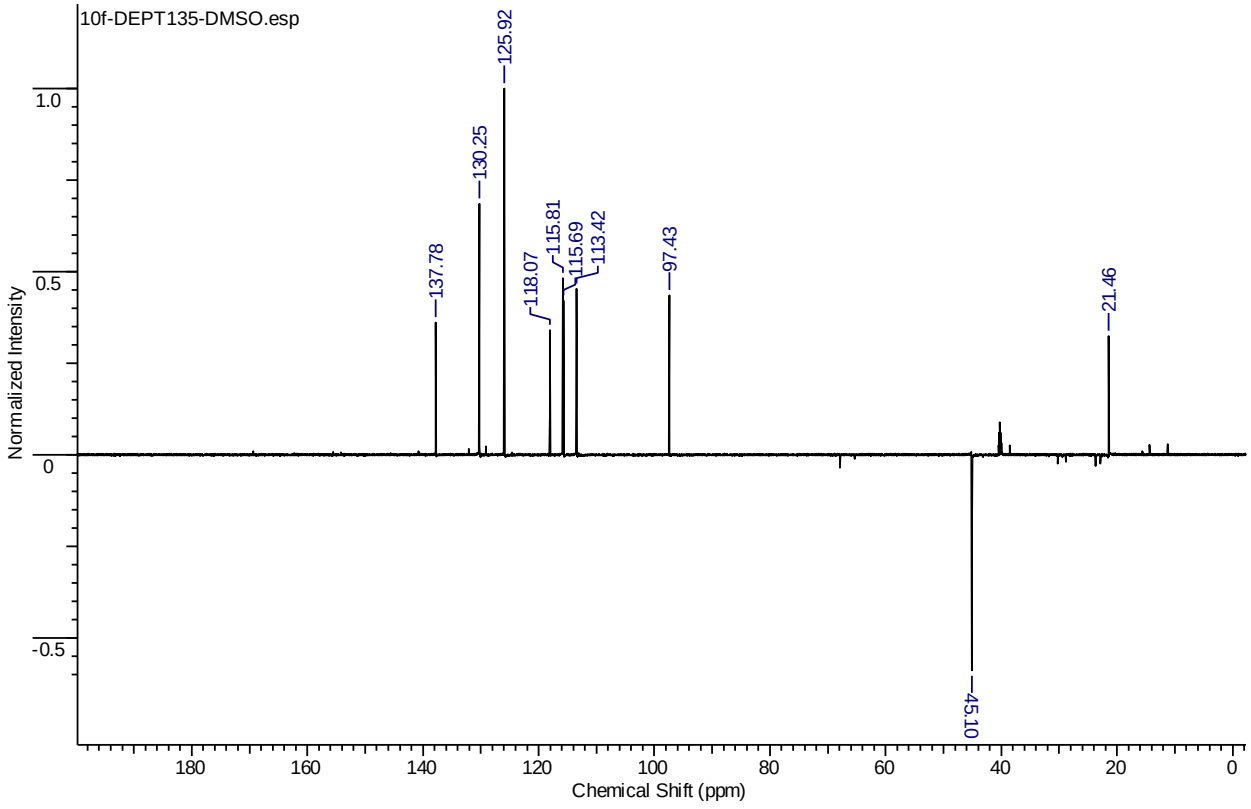
^{13}C NMR (176.1 MHz, $CDCl_3$)



^{19}F NMR (658.8 MHz, DMSO-d_6)



DEPT135



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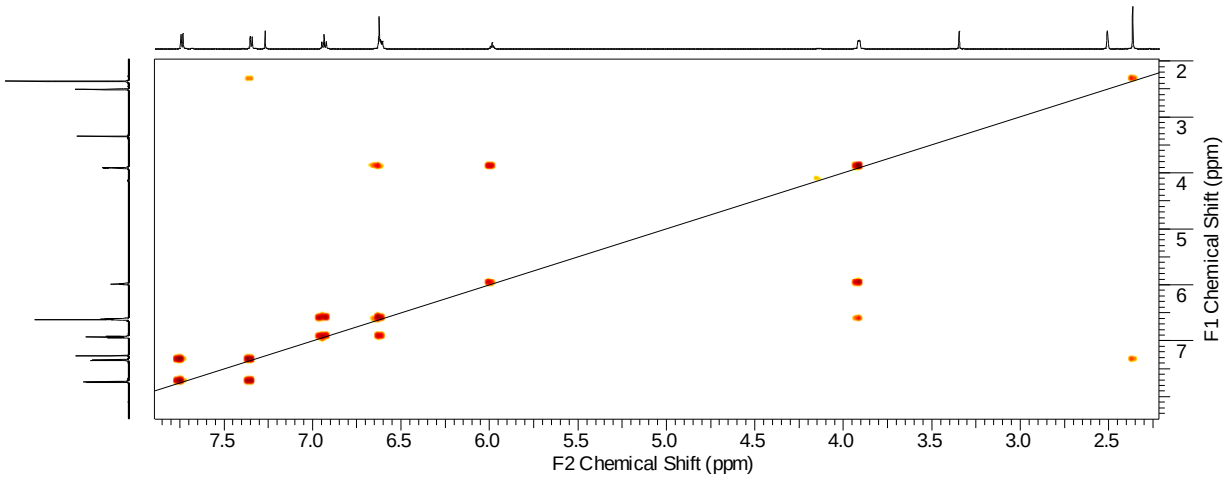
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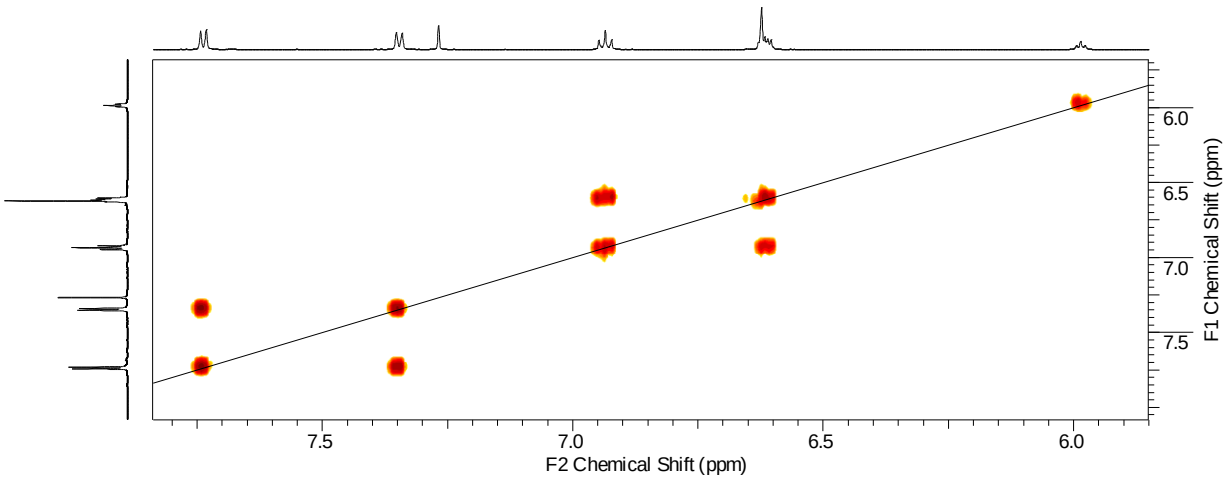
F1 Chemical Shift (ppm)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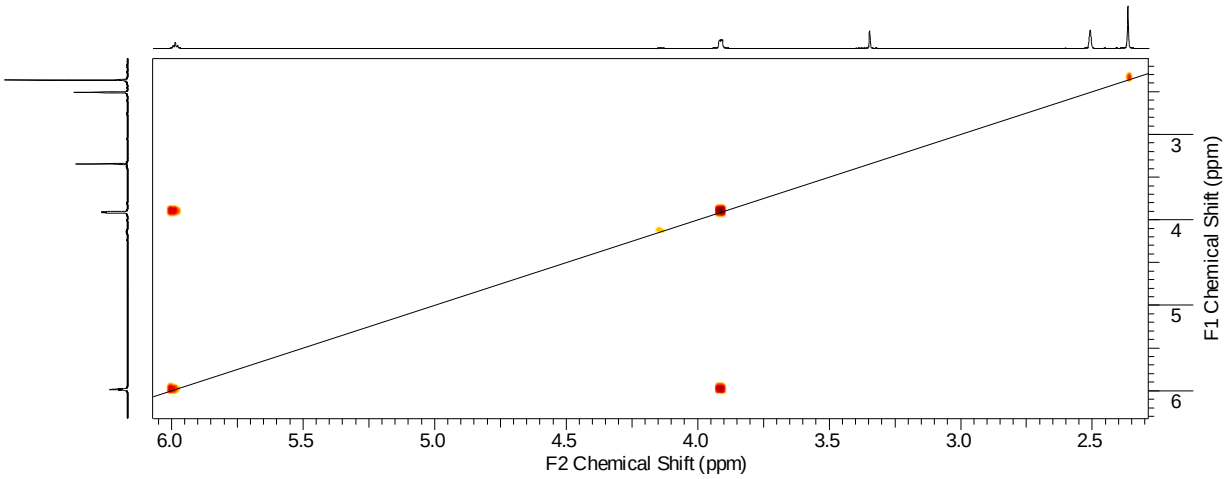
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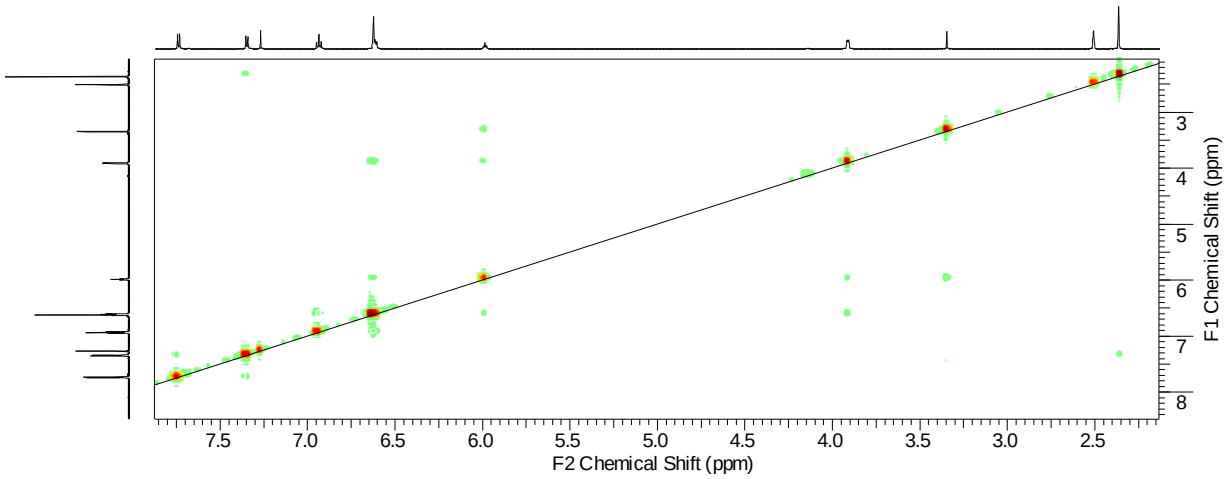
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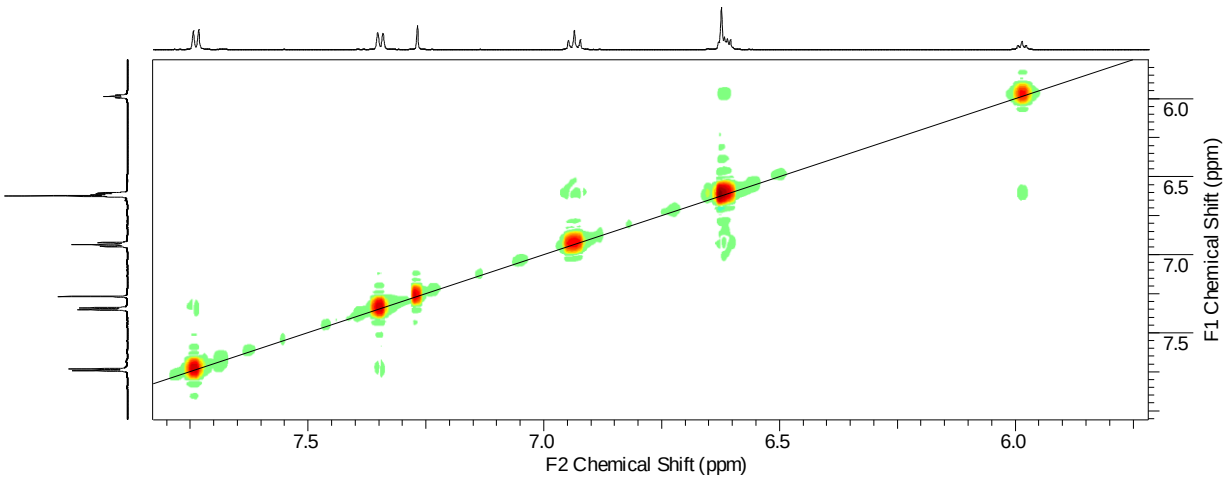
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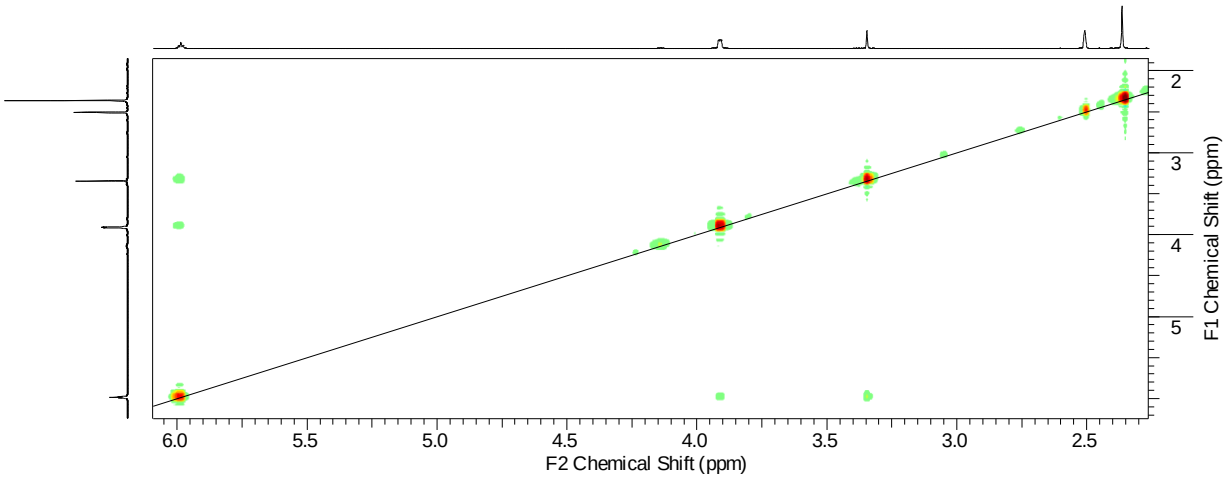
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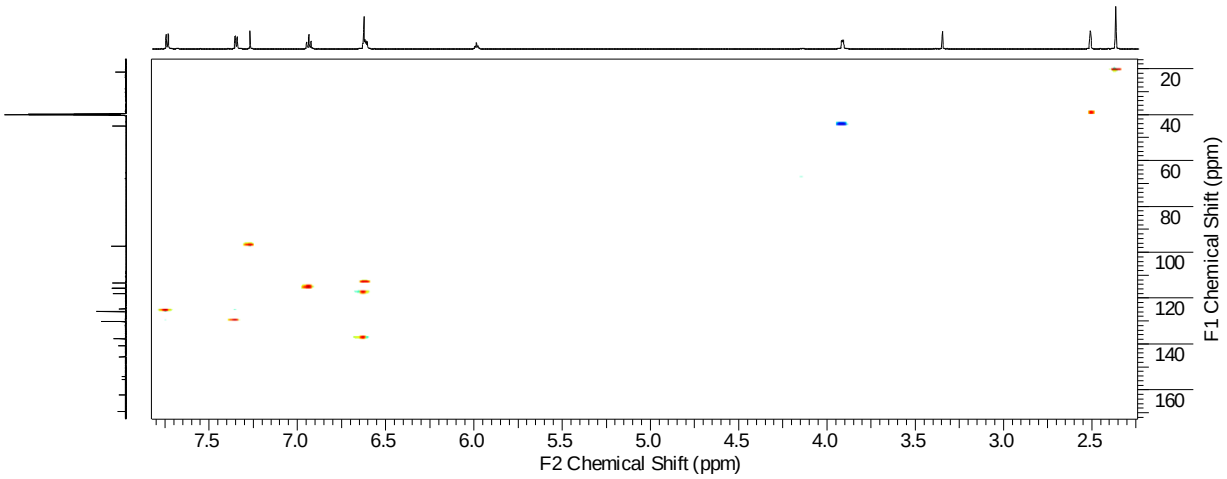
HSQC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3.5
3.0
2.5
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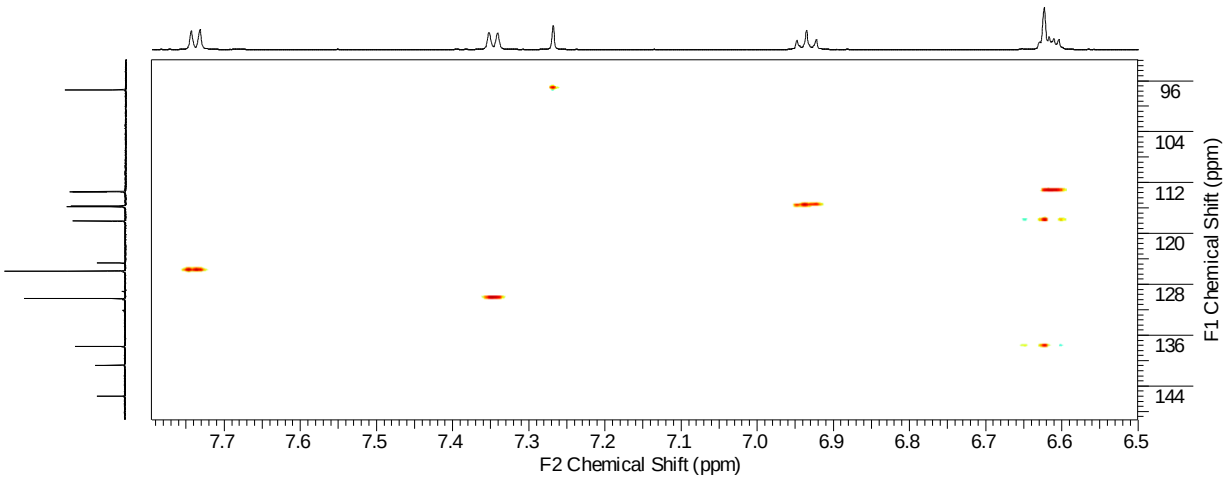
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128
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7.6
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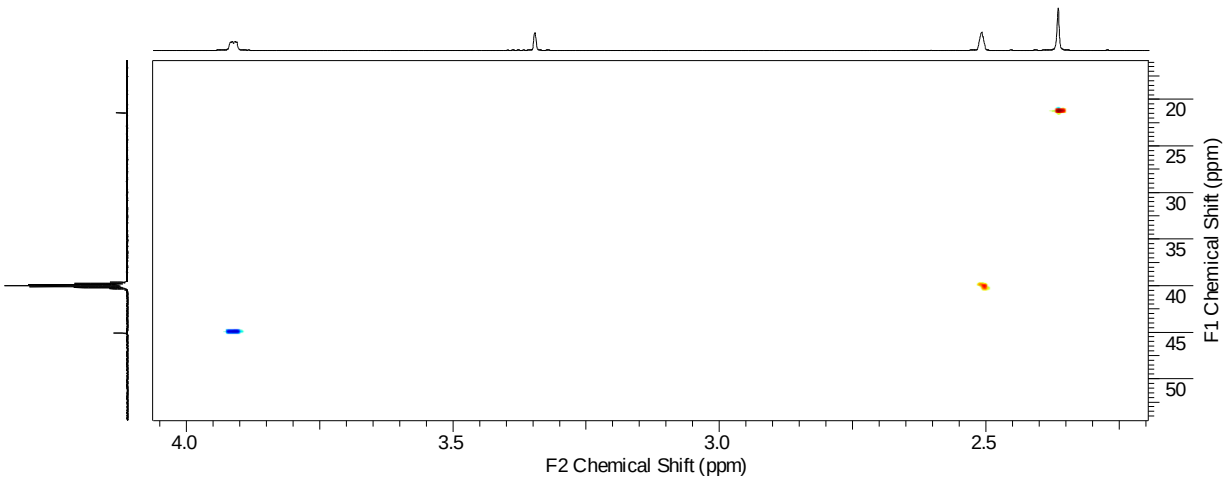
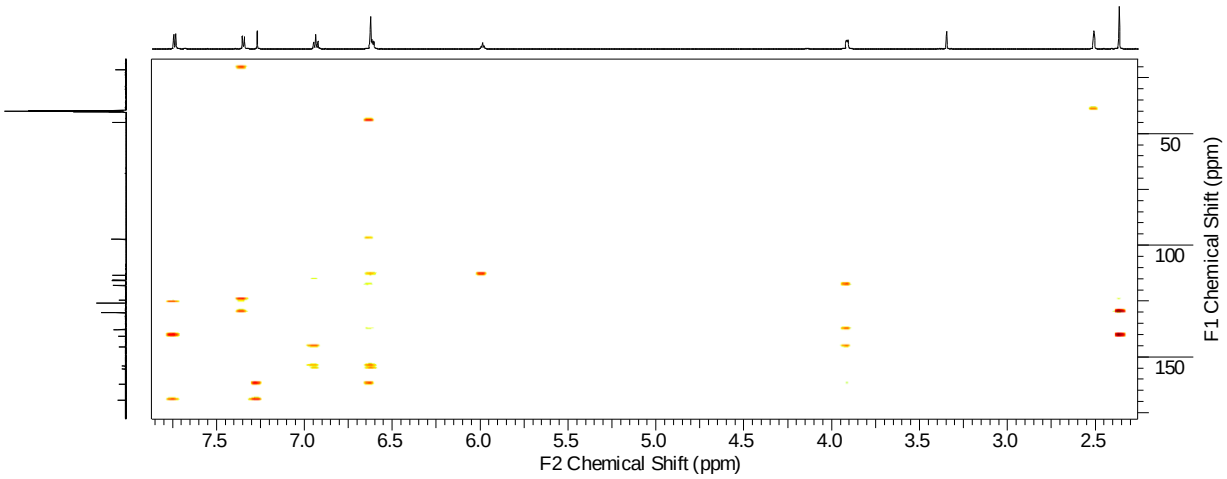
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
6.5
F2 Chemical Shift (ppm)


20
25
30
35
40
45
50
F1 Chemical Shift (ppm)
4.0
3.5
3.0
2.5
F2 Chemical Shift (ppm)

HMBC


50
100
150
F1 Chemical Shift (ppm)
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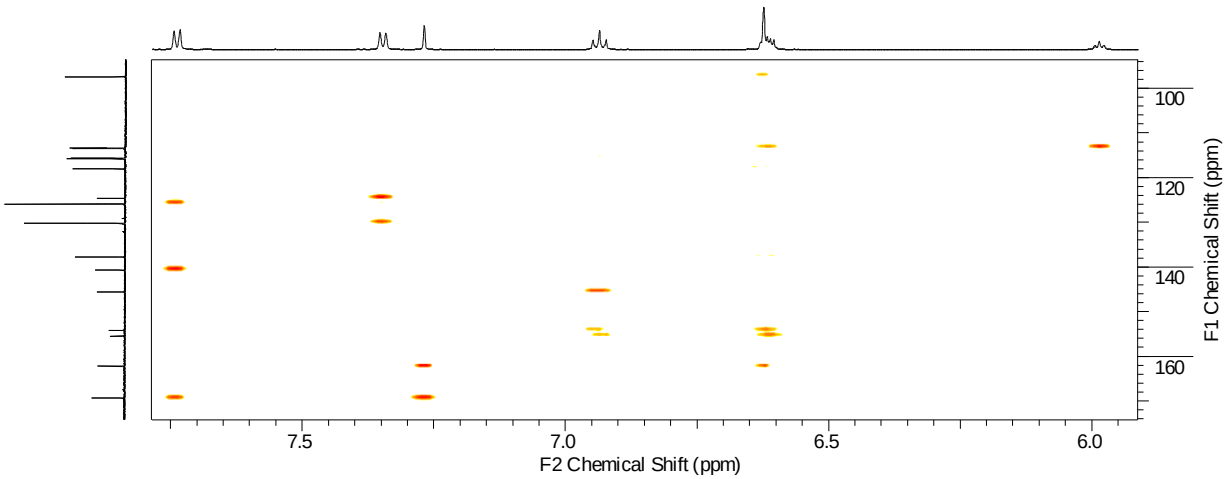
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
F2 Chemical Shift (ppm)


100
120
140
160
F1 Chemical Shift (ppm)
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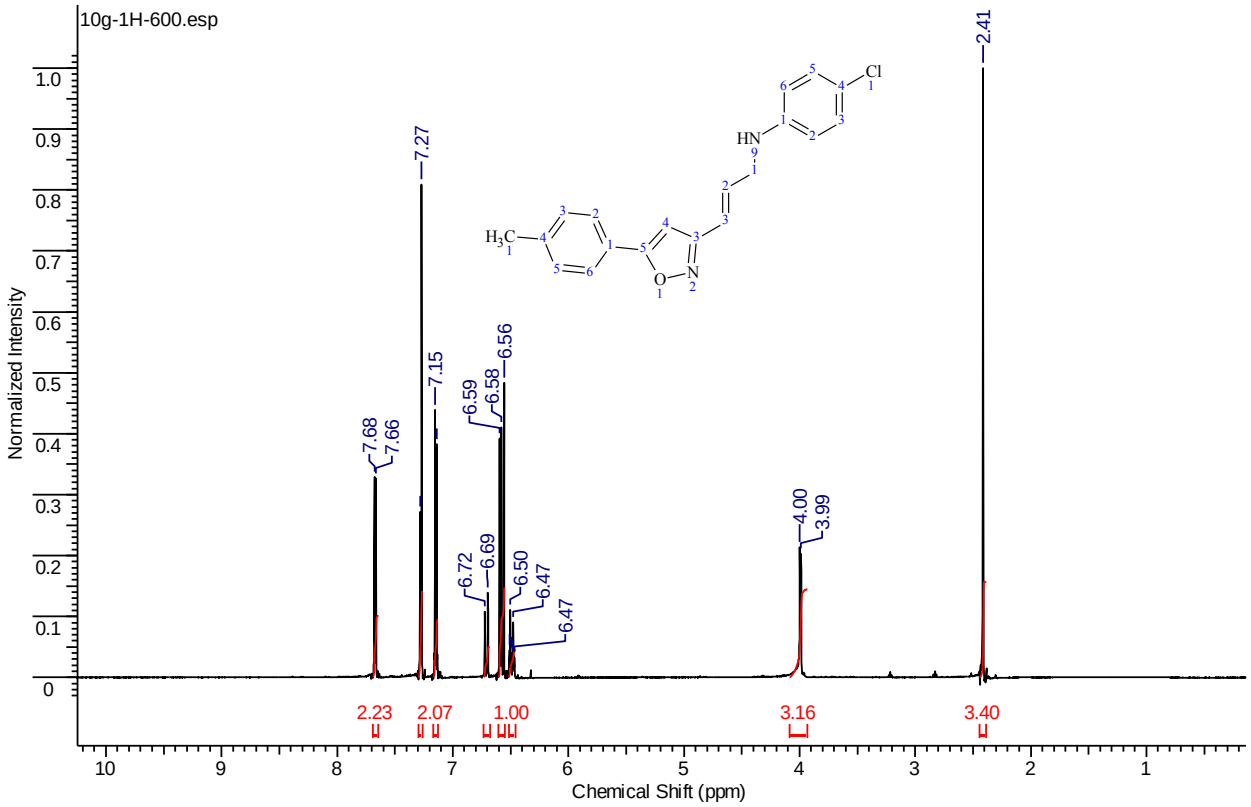
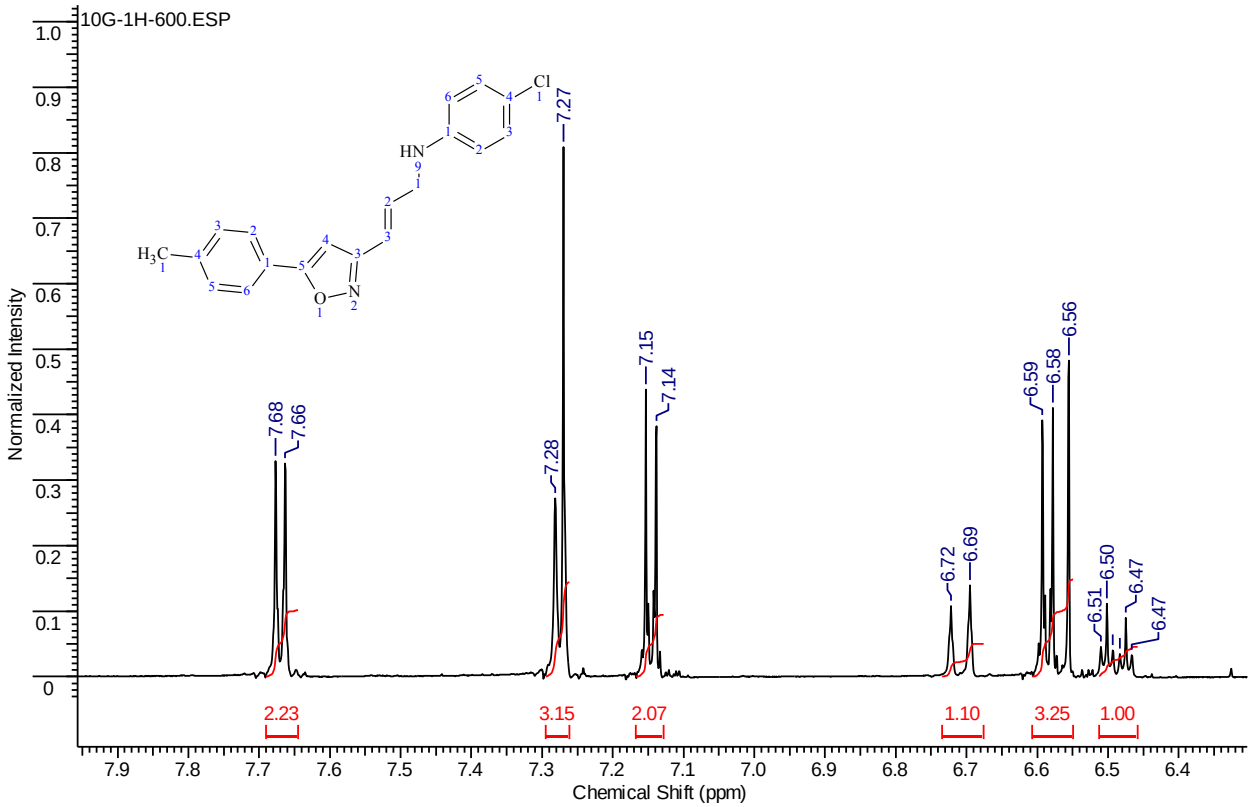
7.0
6.5
6.0
F2 Chemical Shift (ppm)

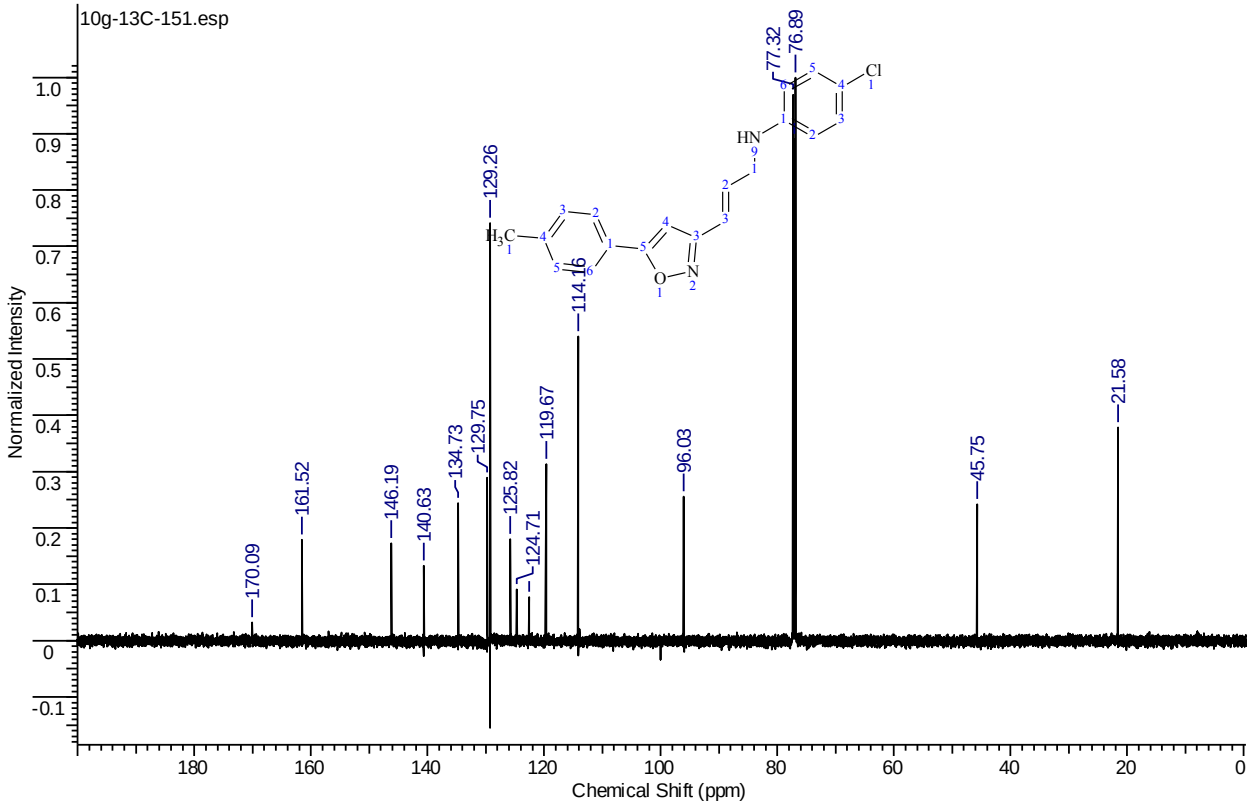
(4-Chlorophenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10g).

^{1}H NMR (600.2 MHz, $CDCl_3$)



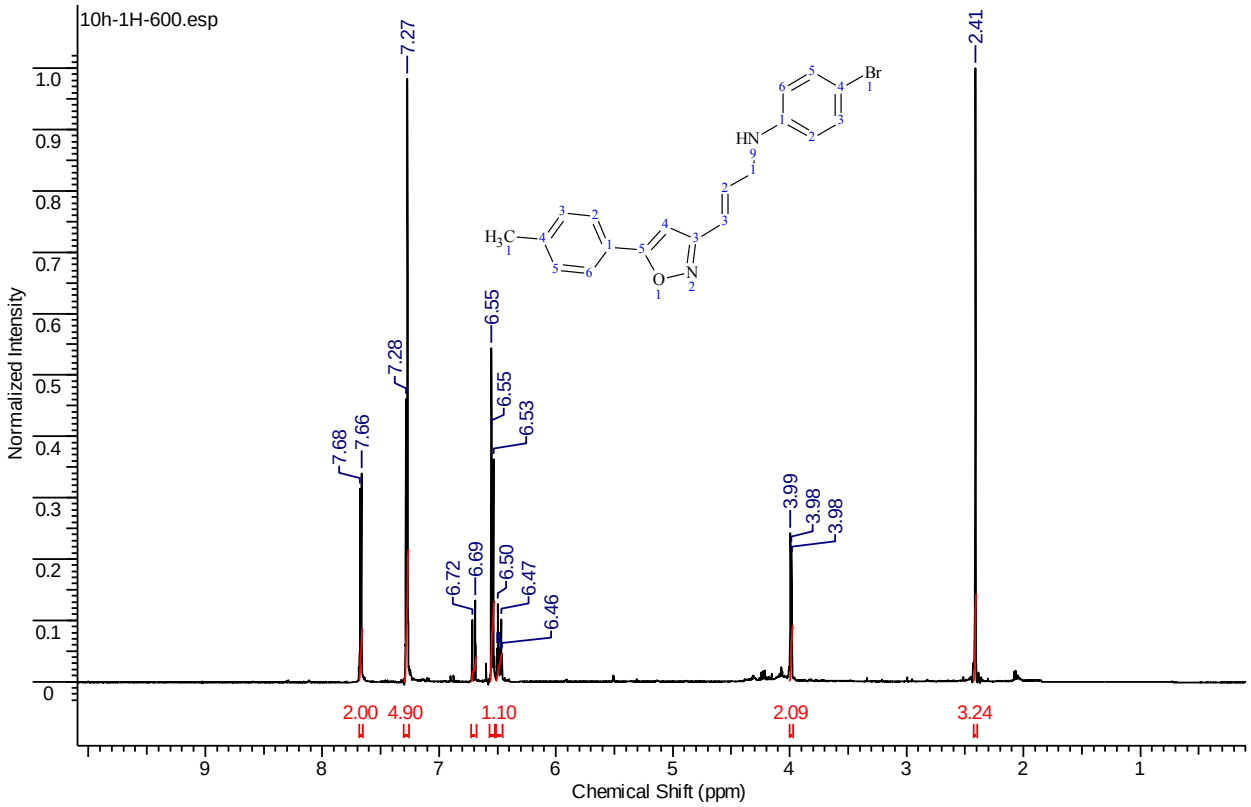


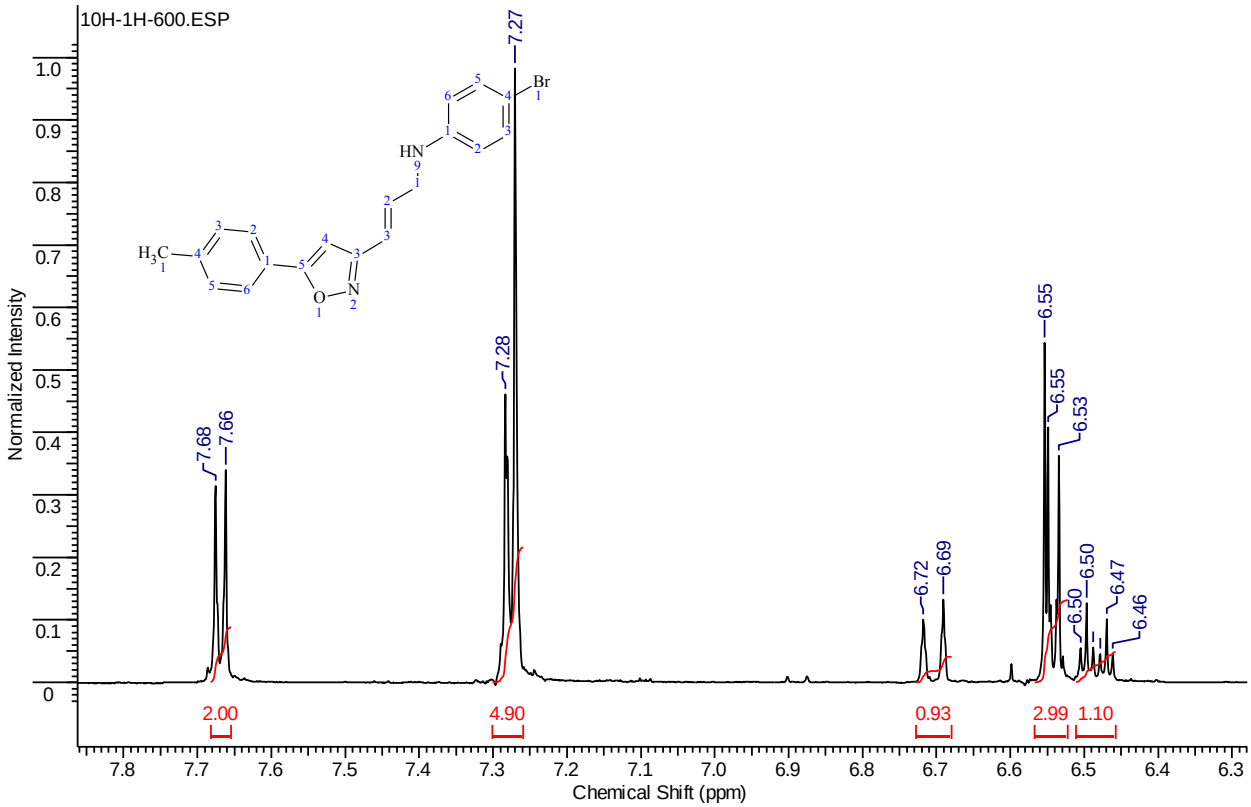
^{13}C NMR (150.9 MHz, $CDCl_3$)



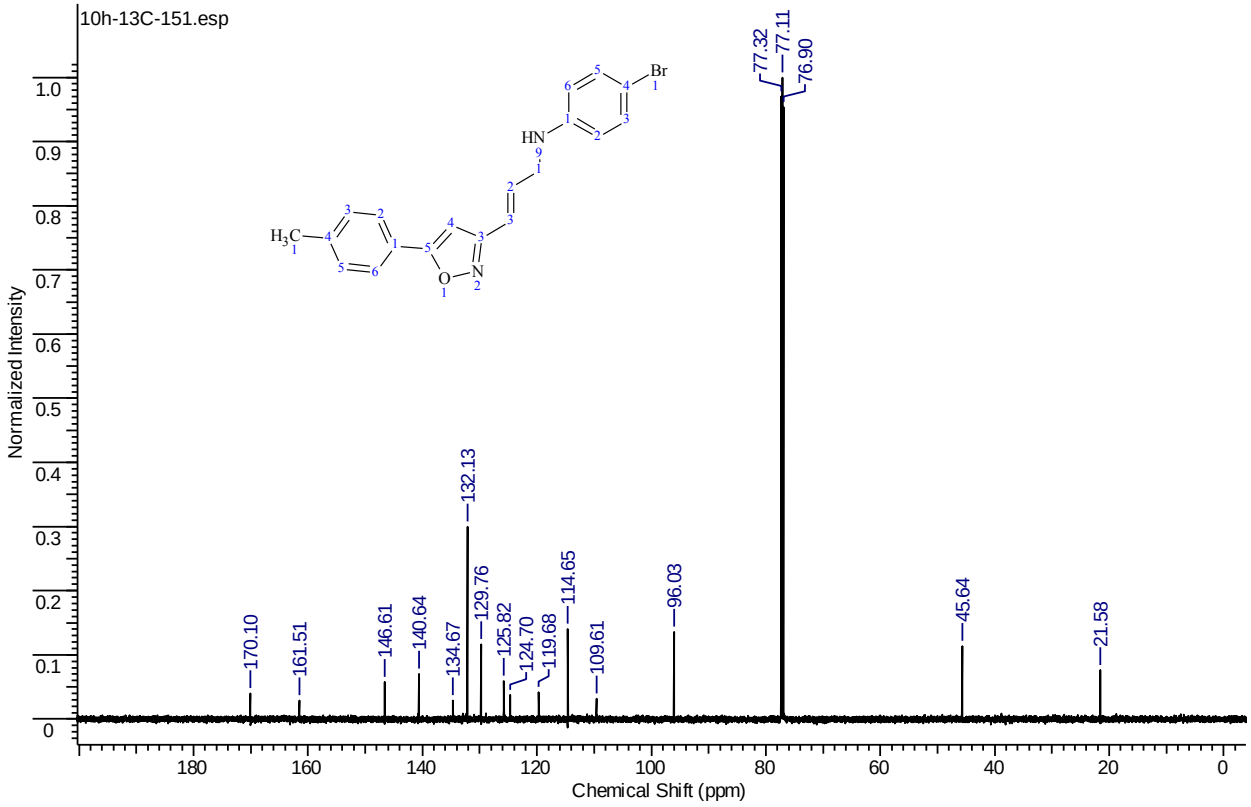
(4-Bromophenyl){(2*E*)-3-[5-(4-methylphenyl)isoxazol-3-yl]prop-2-en-1-yl}amine (10h).

^{1}H NMR (600.2 MHz, $CDCl_3$)



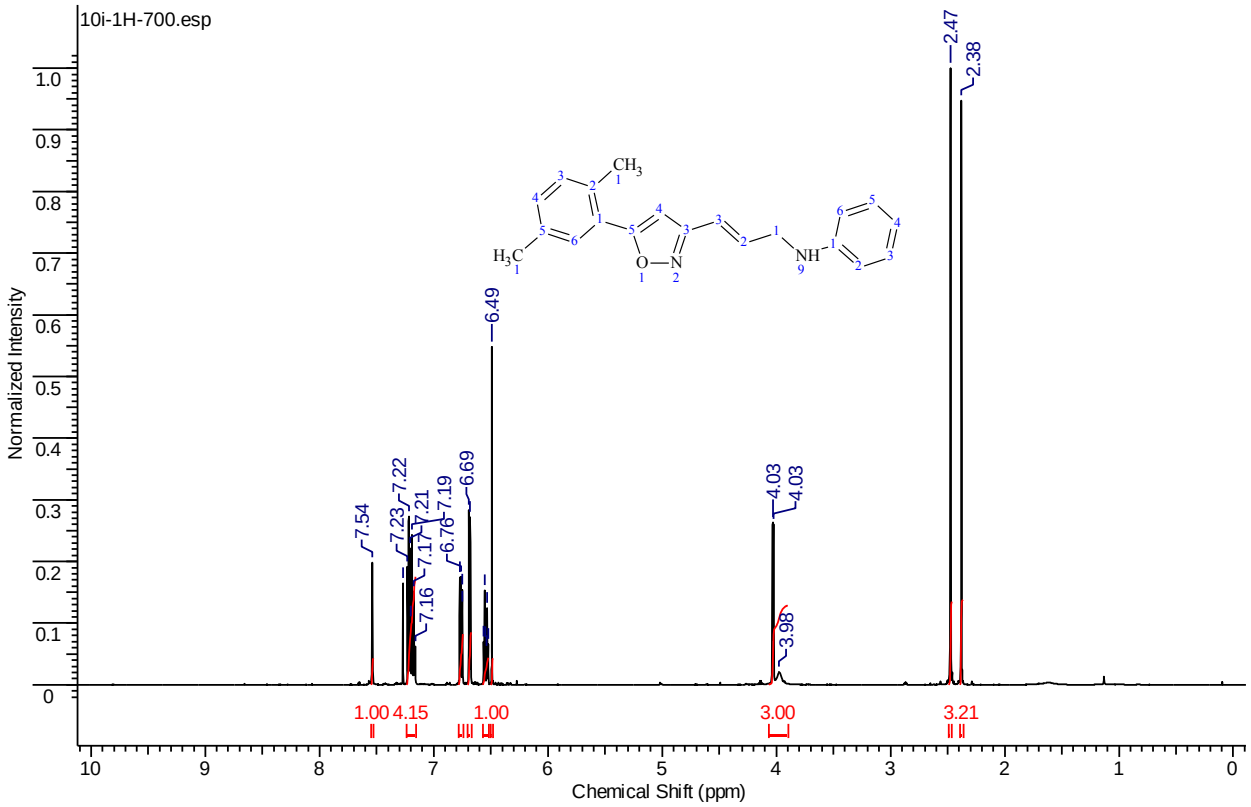


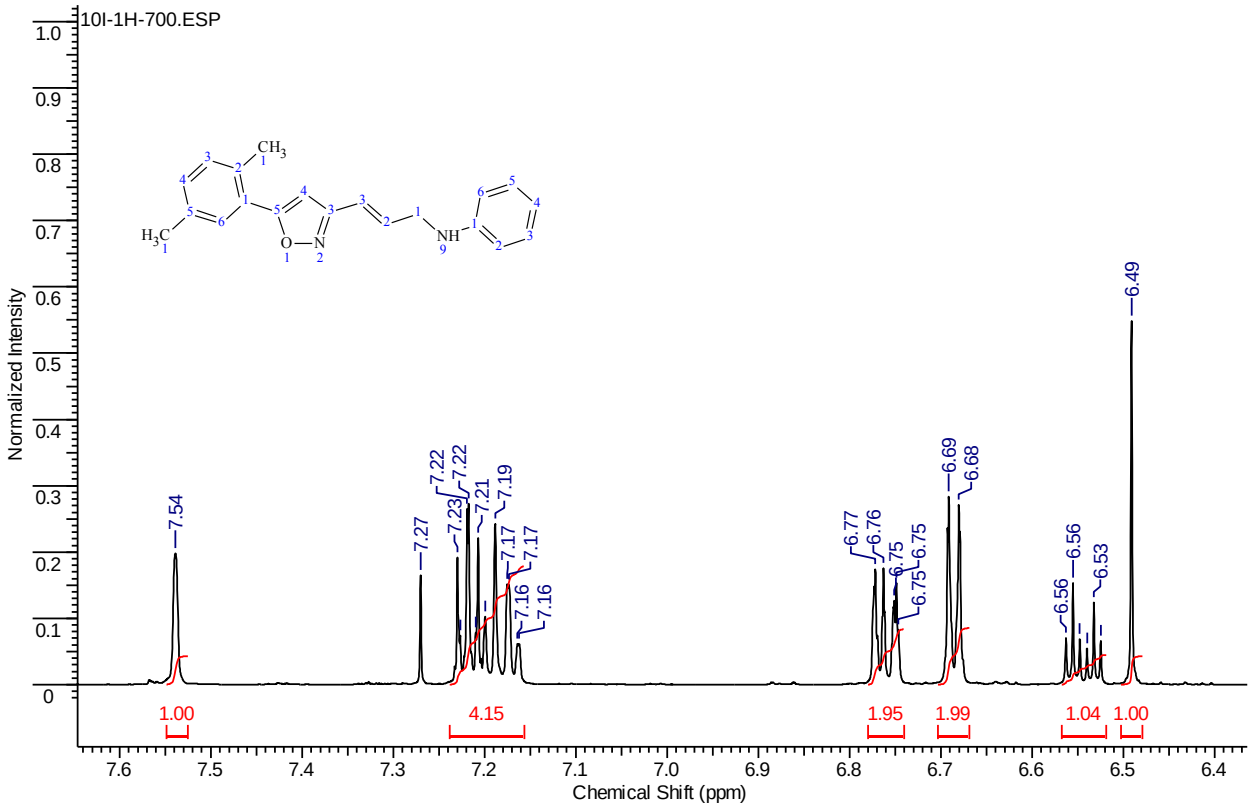
^{13}C NMR (150.9 MHz, $CDCl_3$)



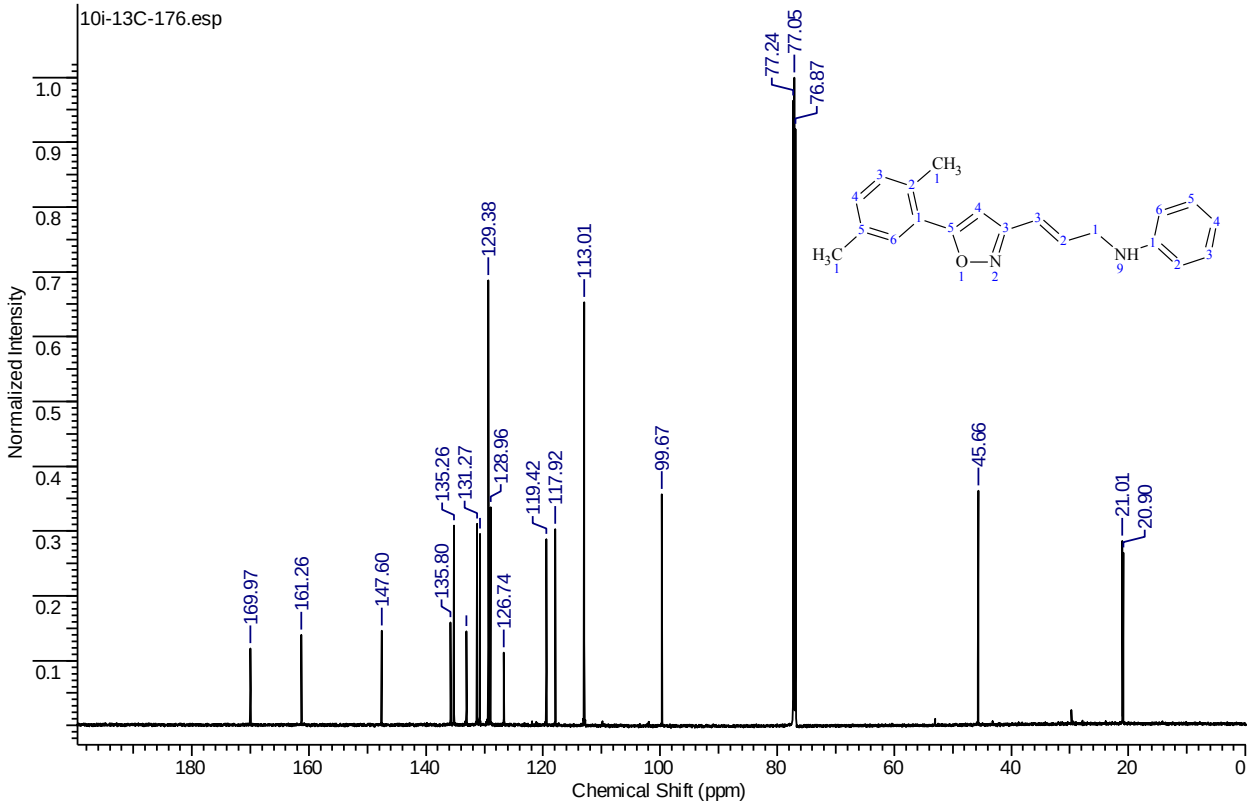
***N*-{(2*E*)-3-[5-(2,5-Dimethylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10i).**

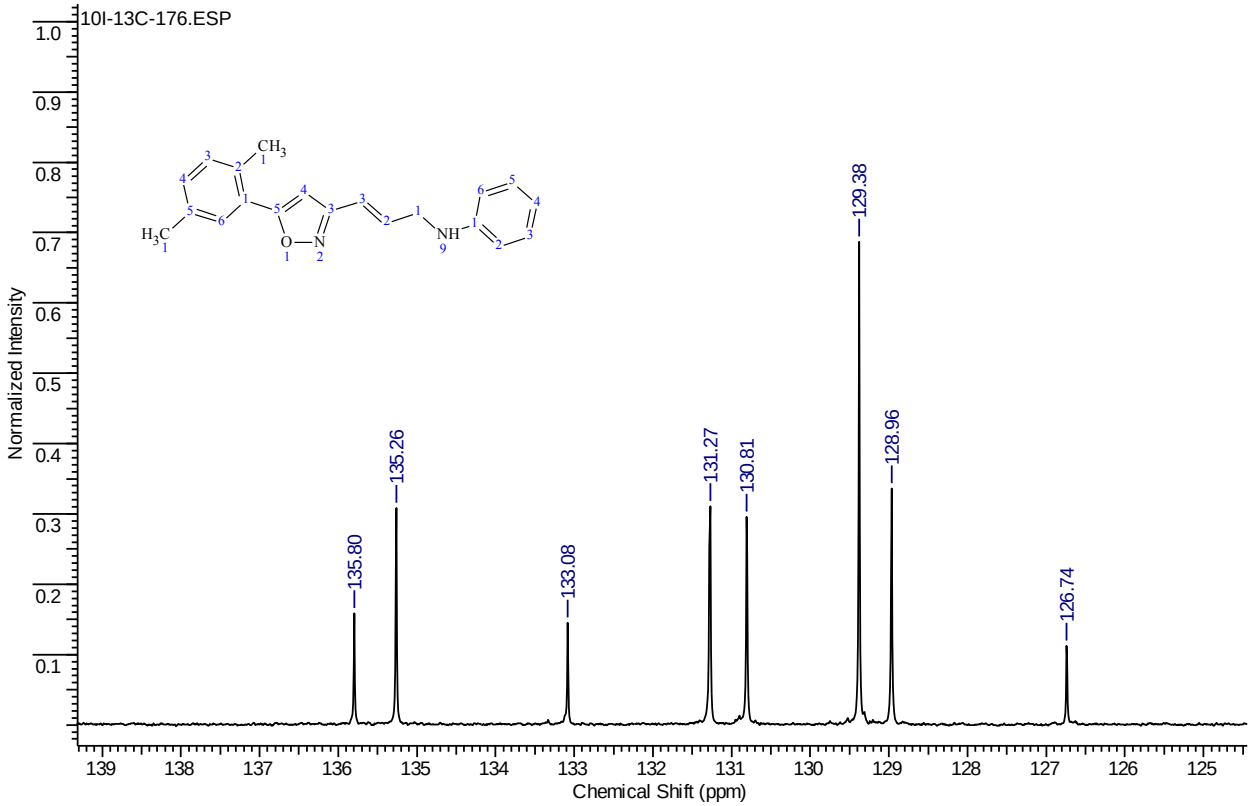
^{1}H NMR (700.2 MHz, $CDCl_3$)





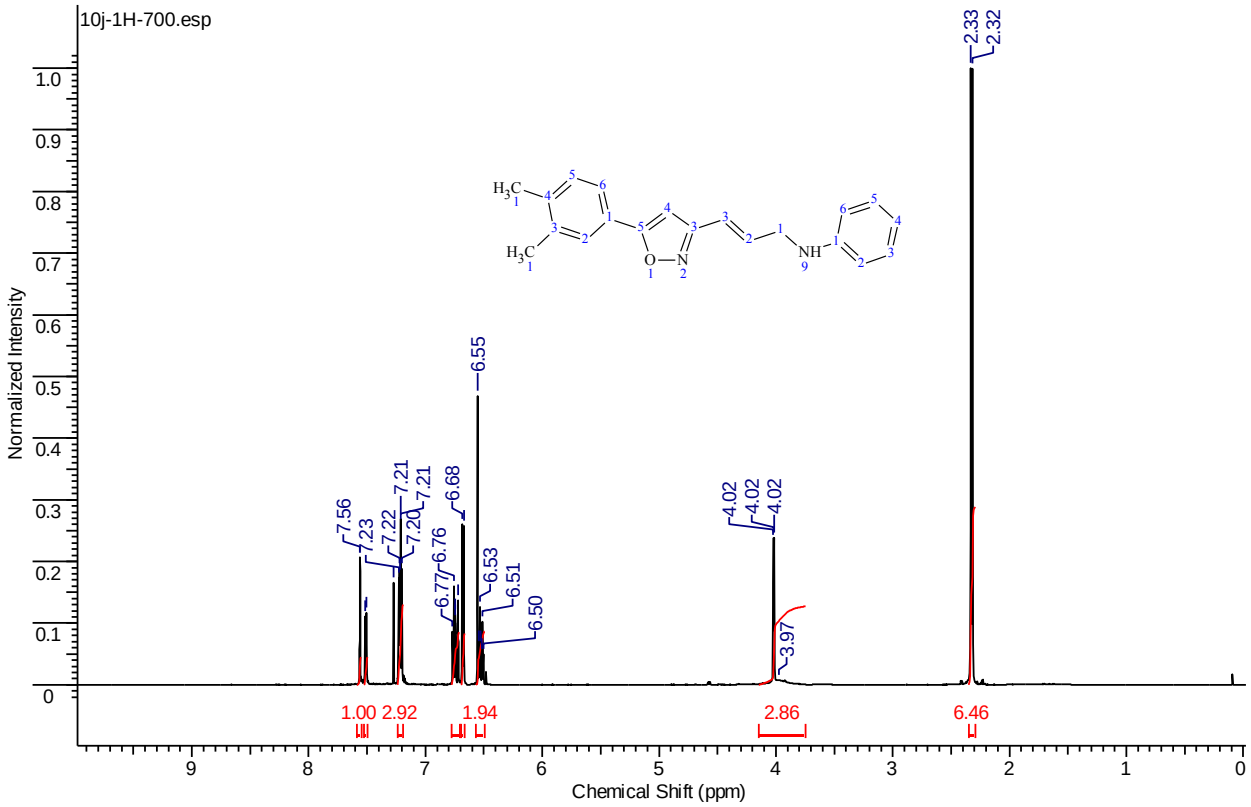
^{13}C NMR (176.1 MHz, $CDCl_3$)

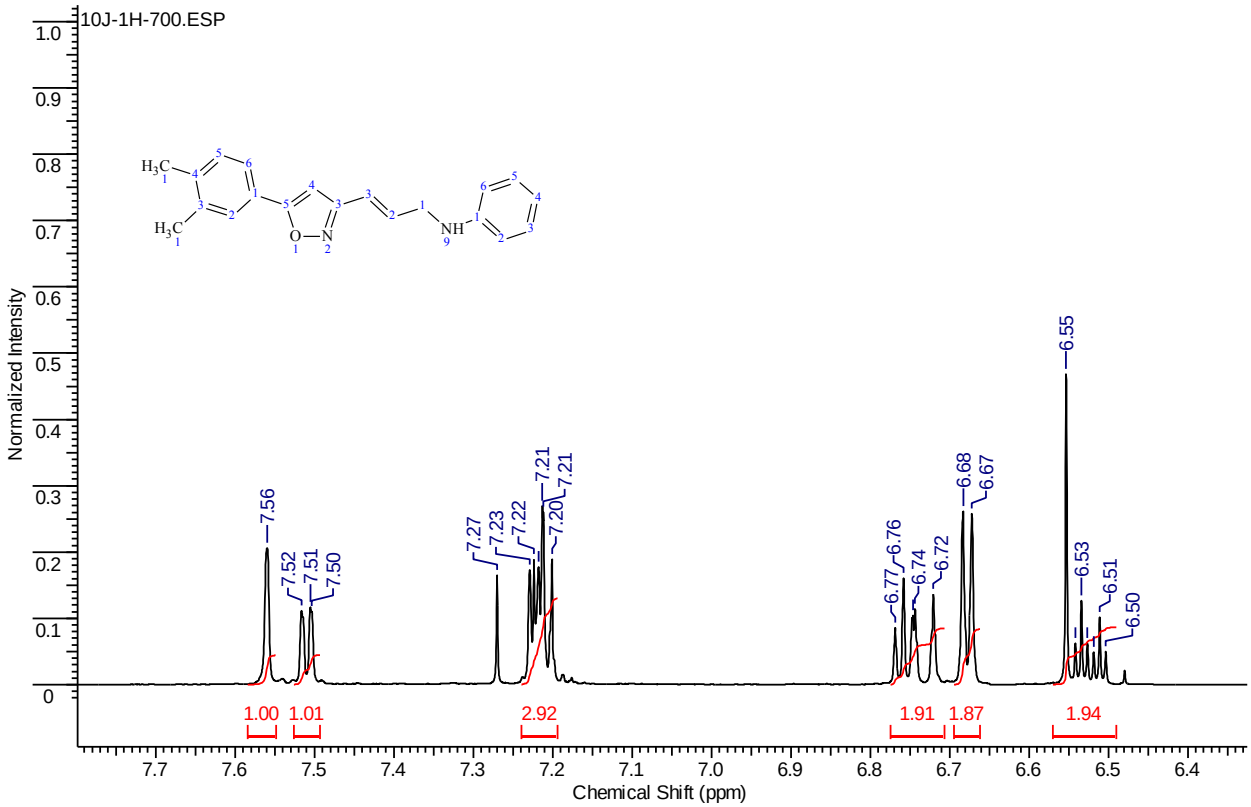




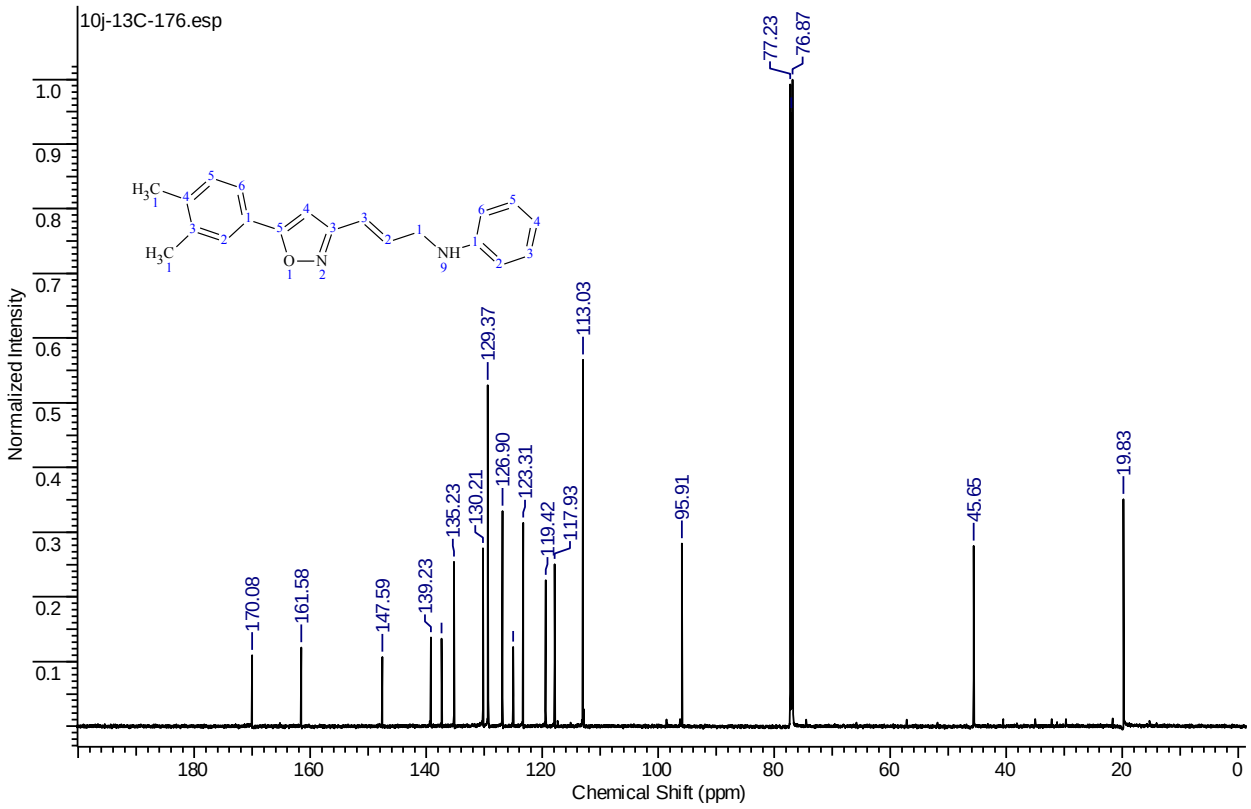
***N*-{(2*E*)-3-[5-(3,4-Dimethylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10j).**

^{1}H NMR (700.2 MHz, $CDCl_3$)



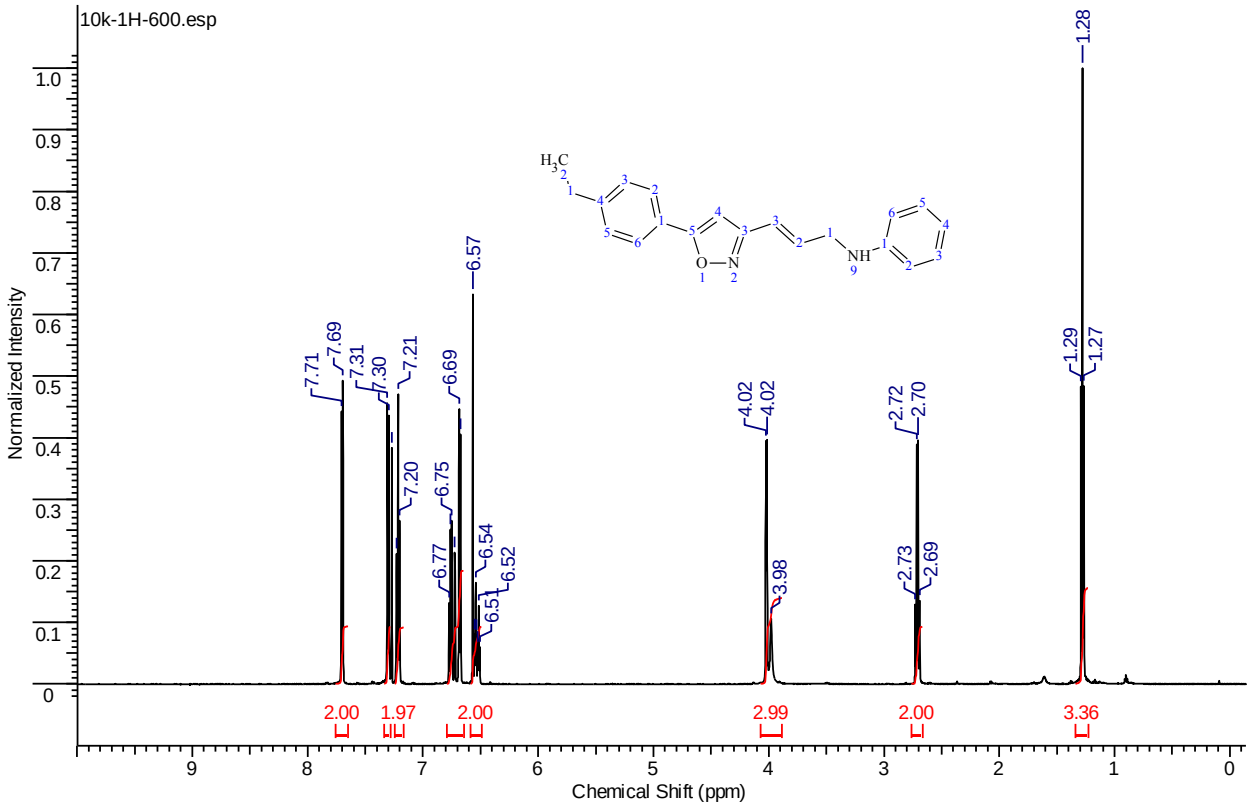


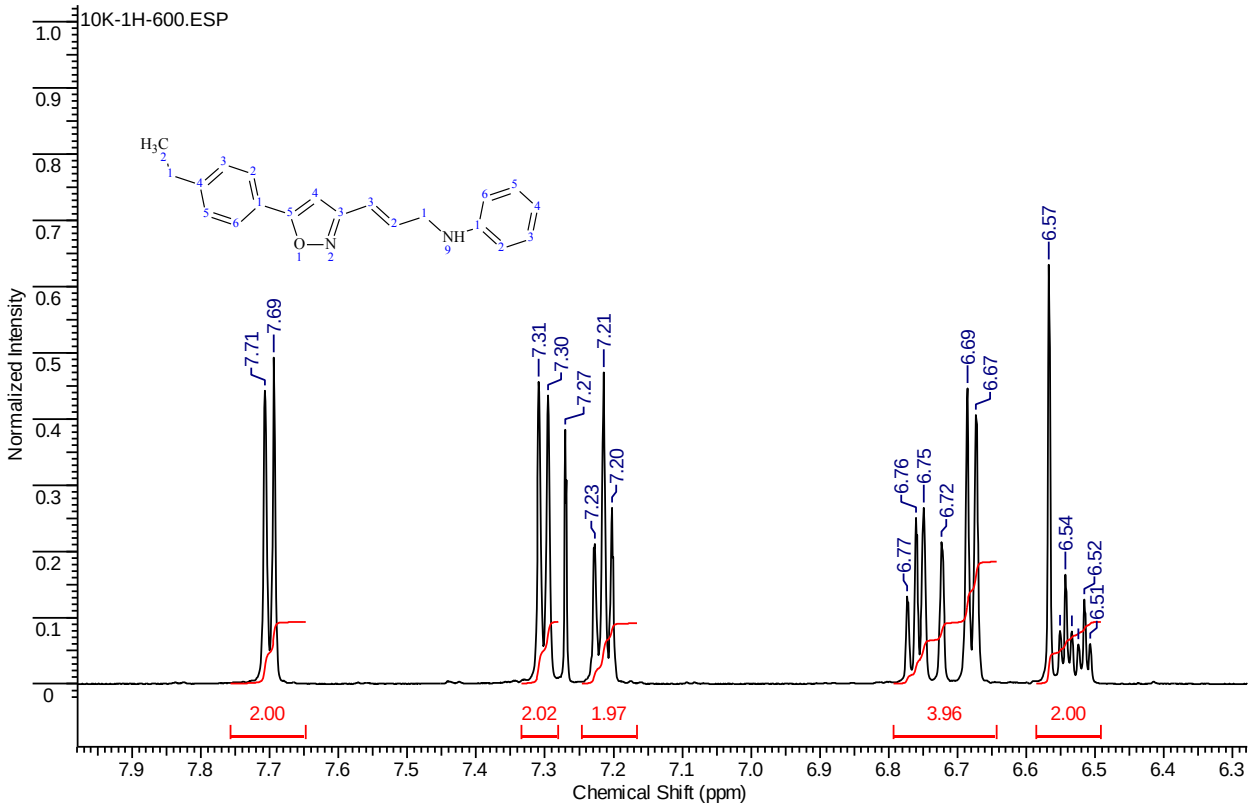
^{13}C NMR (176.1 MHz, $CDCl_3$)



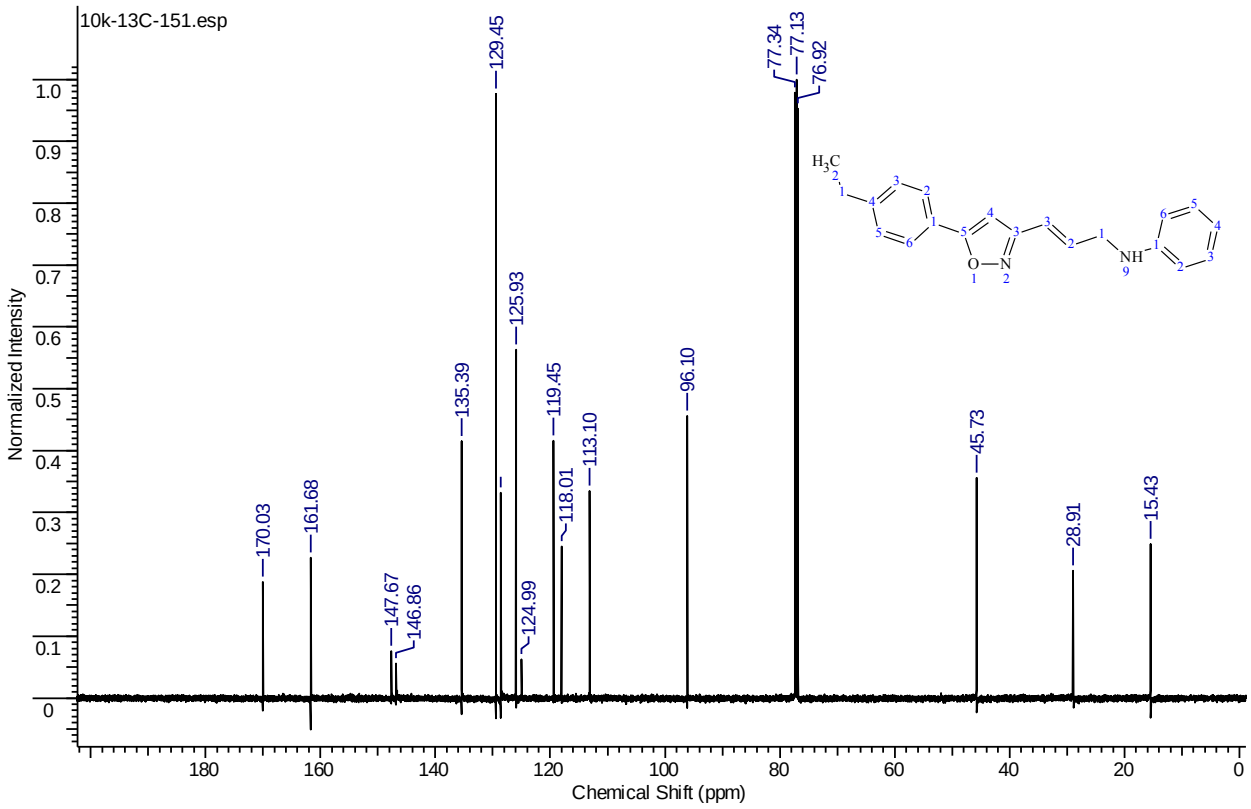
***N*-{(2*E*)-3-[5-(4-Ethylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10k).**

^{1}H NMR (600.2 MHz, $CDCl_3$)



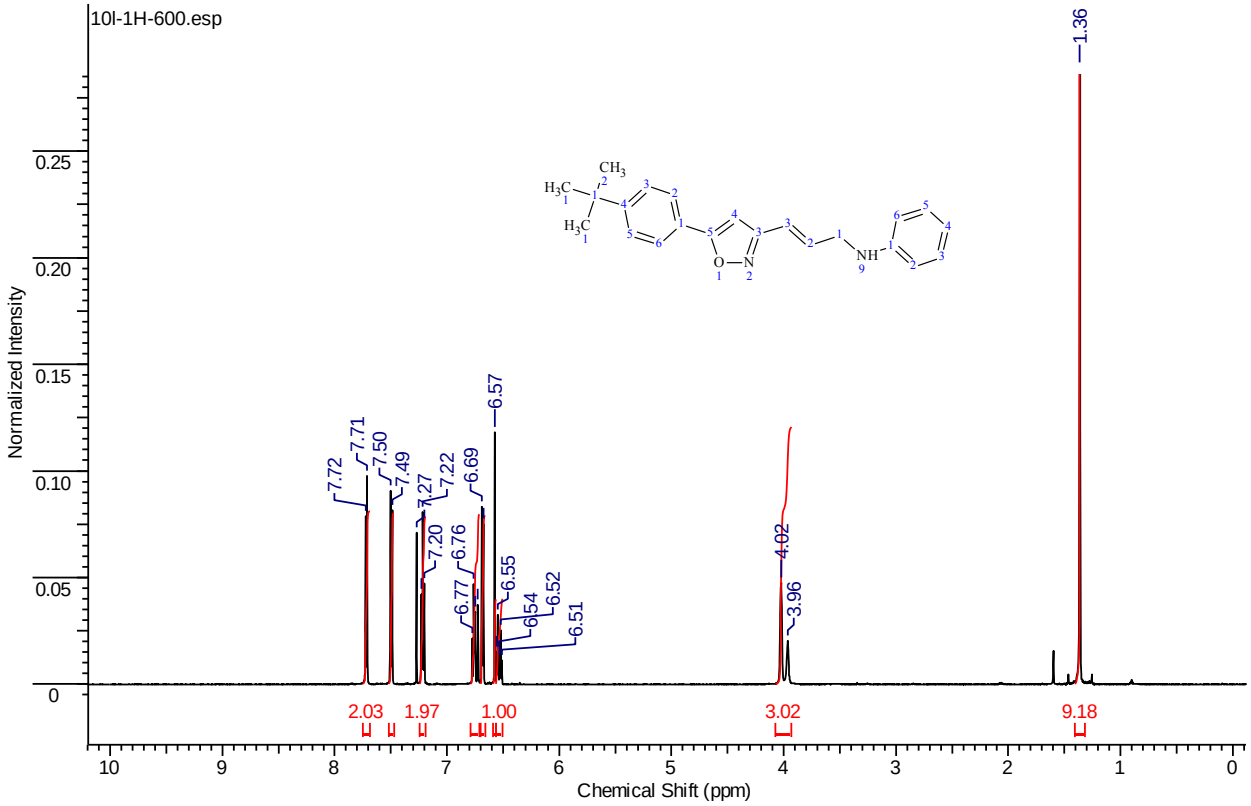


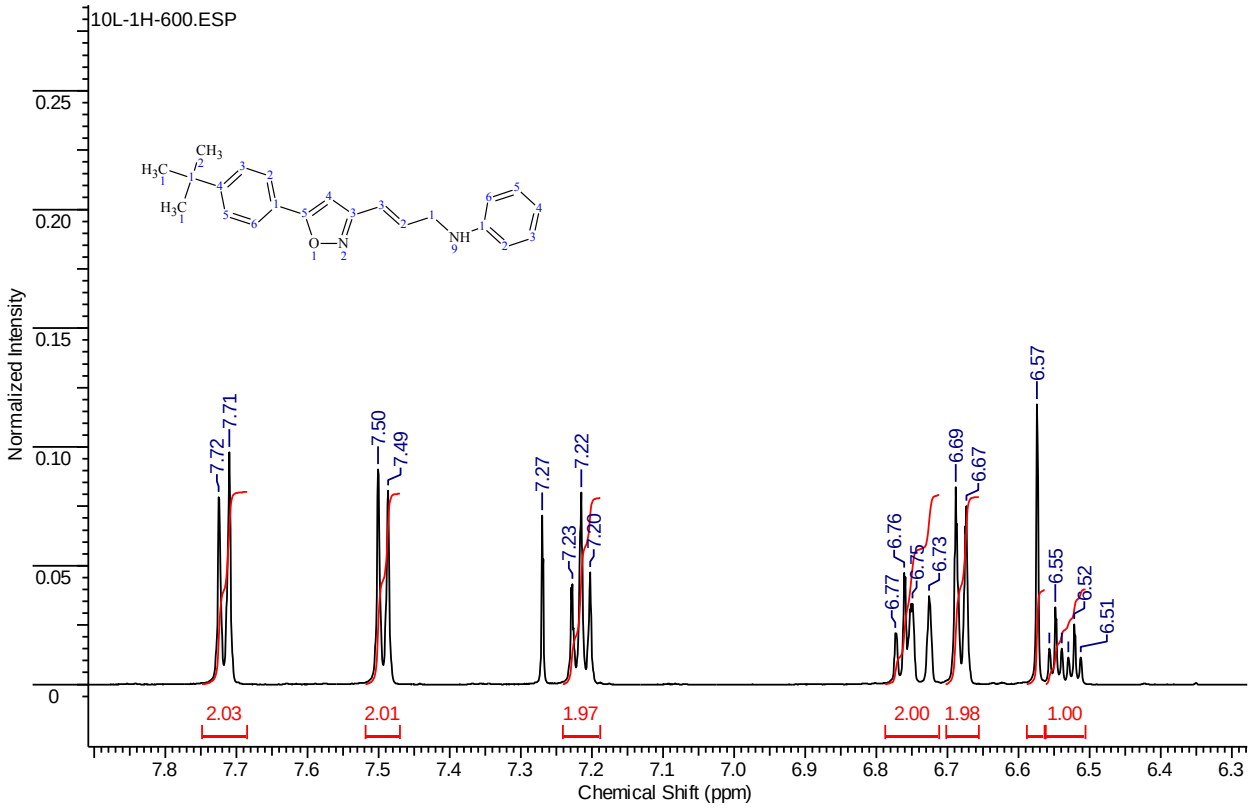
^{13}C NMR (150.9 MHz, $CDCl_3$)



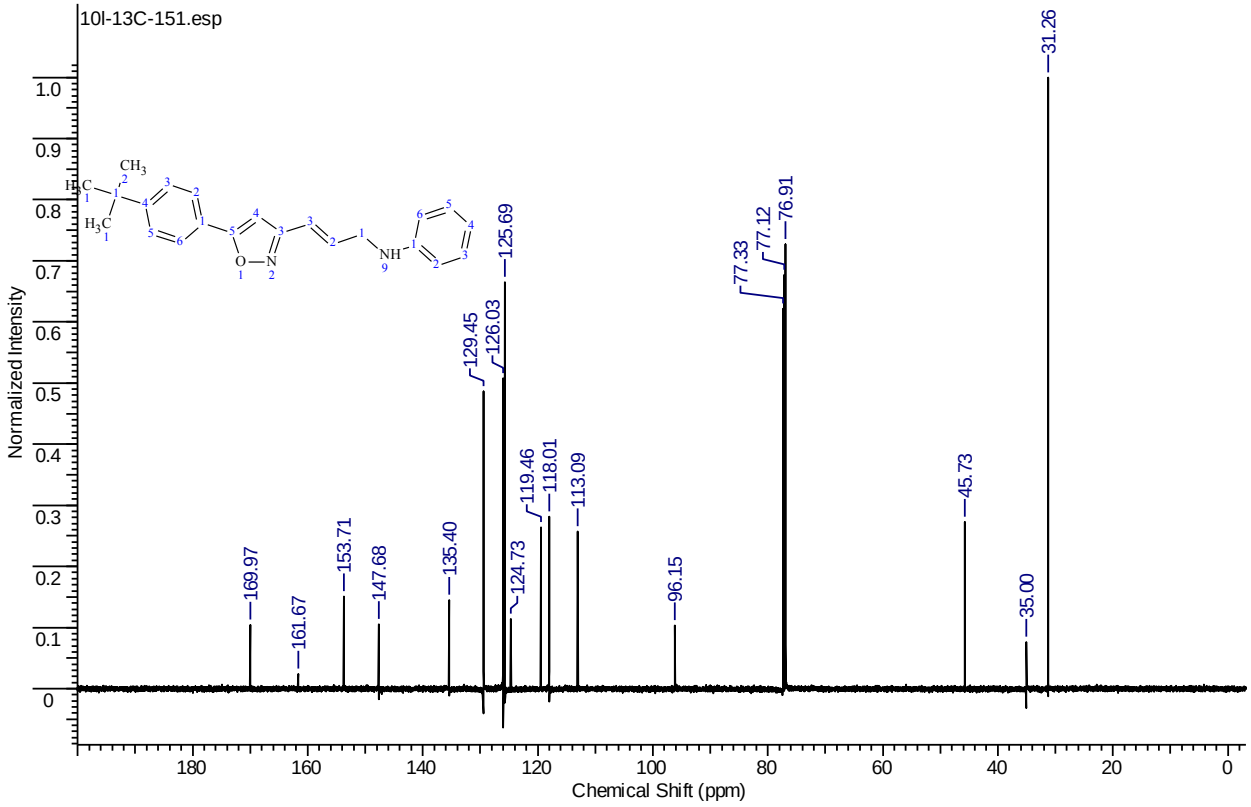
***N*-{(2*E*)-3-[5-(4-*tert*-Butylphenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10l).**

^{1}H NMR (600.2 MHz, $CDCl_3$)



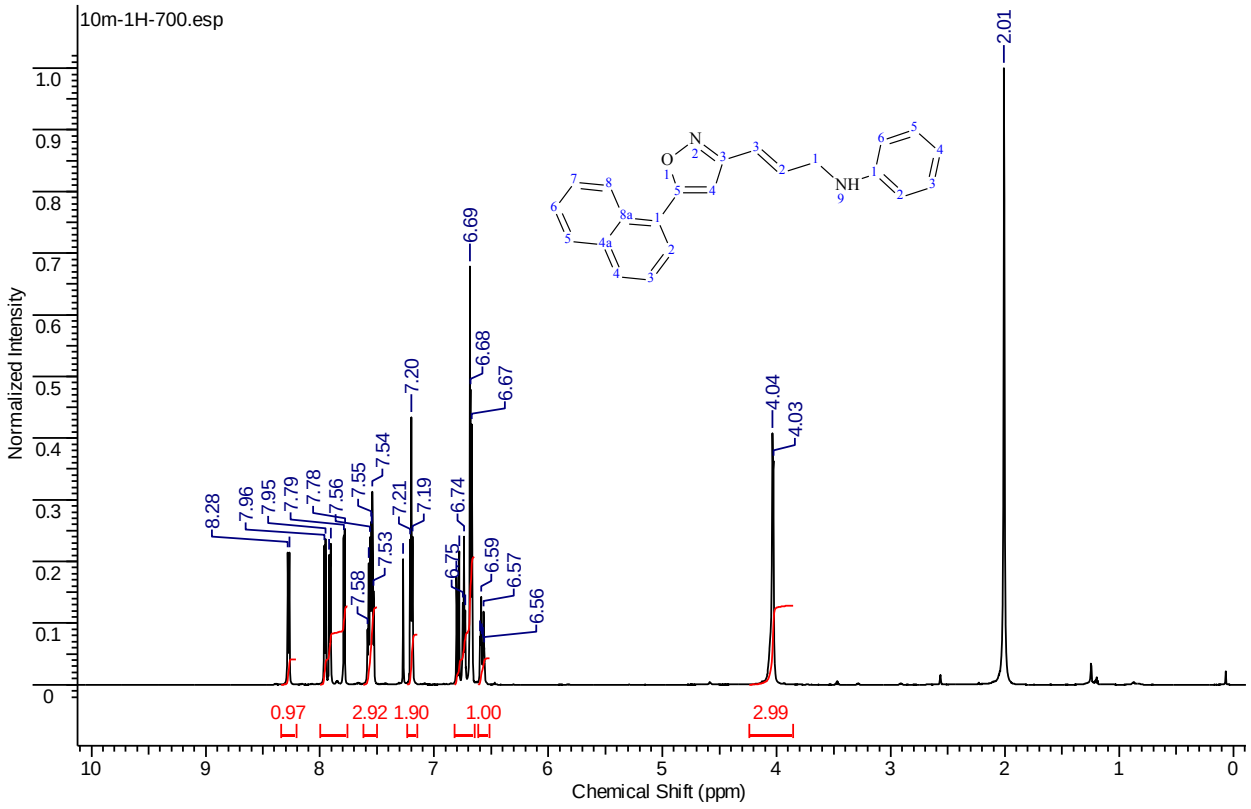


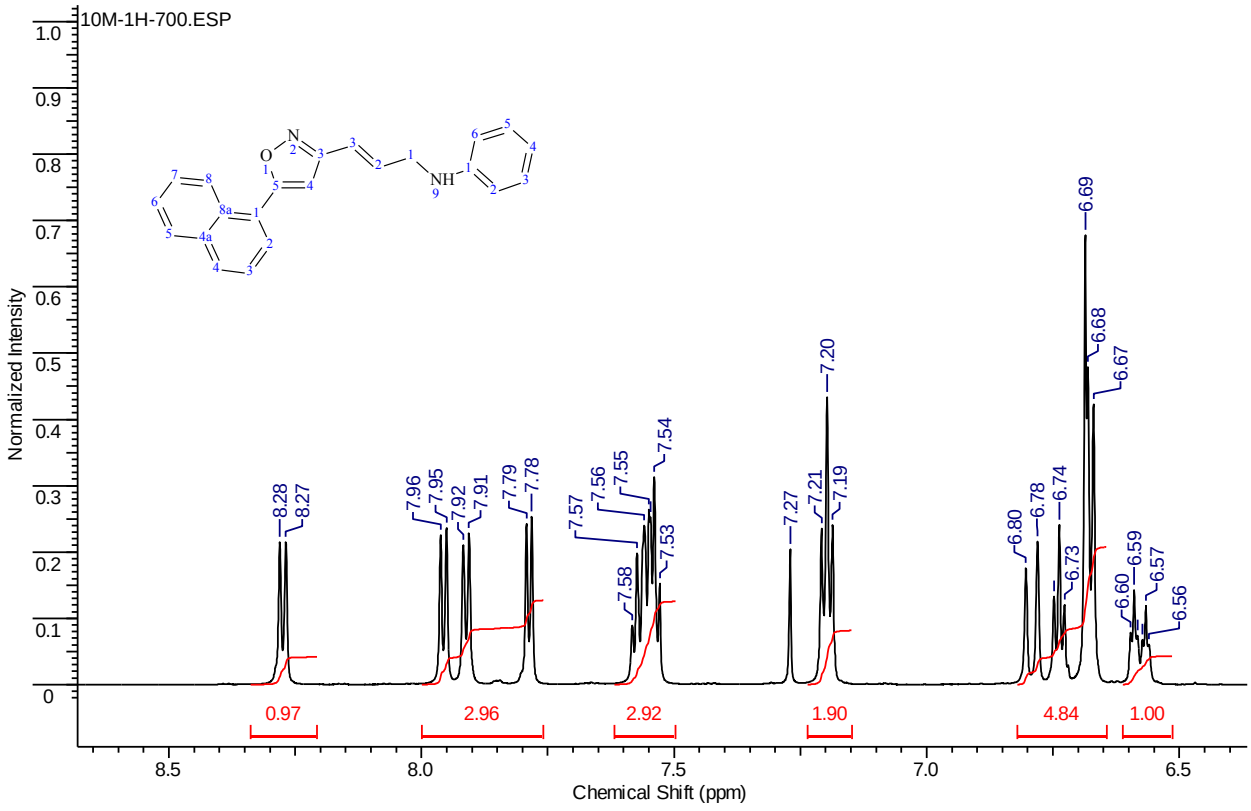
^{13}C NMR (150.9 MHz, $CDCl_3$)



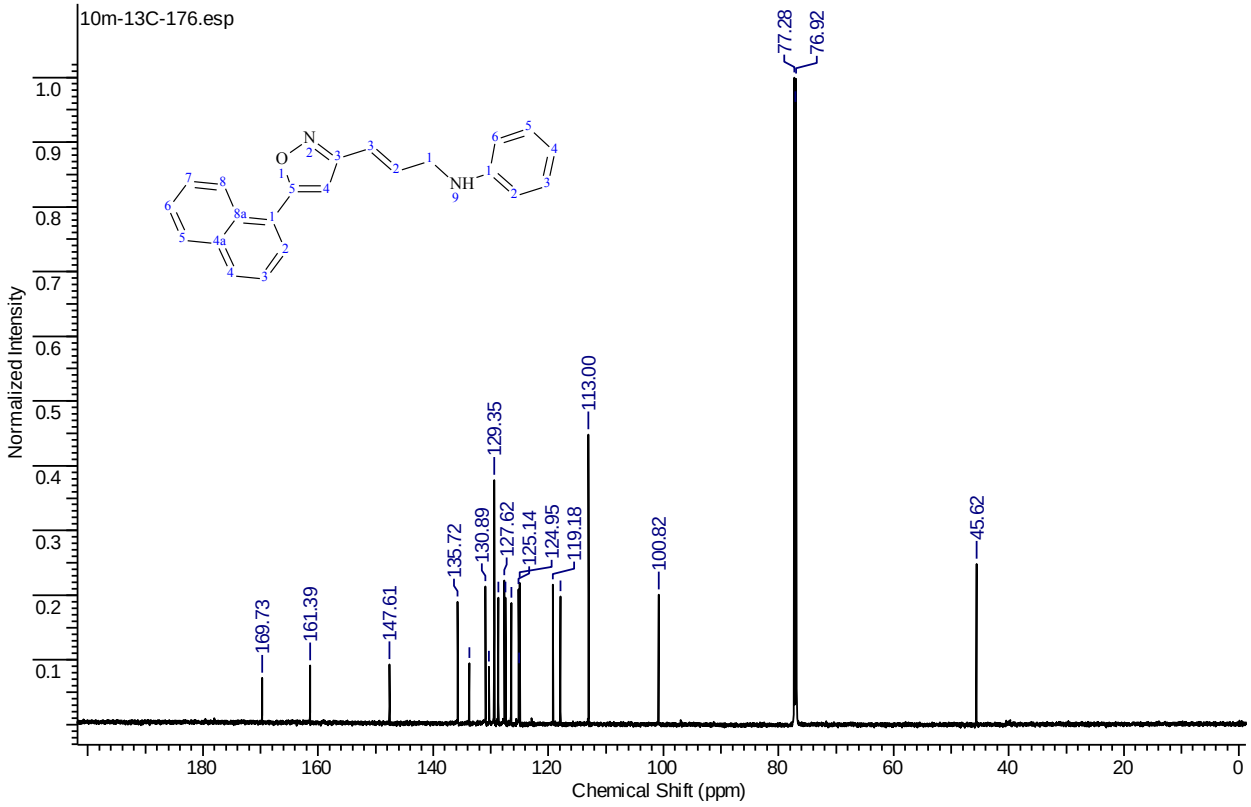
***N*-{(2*E*)-3-[5-(1-Naphthyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10m).**

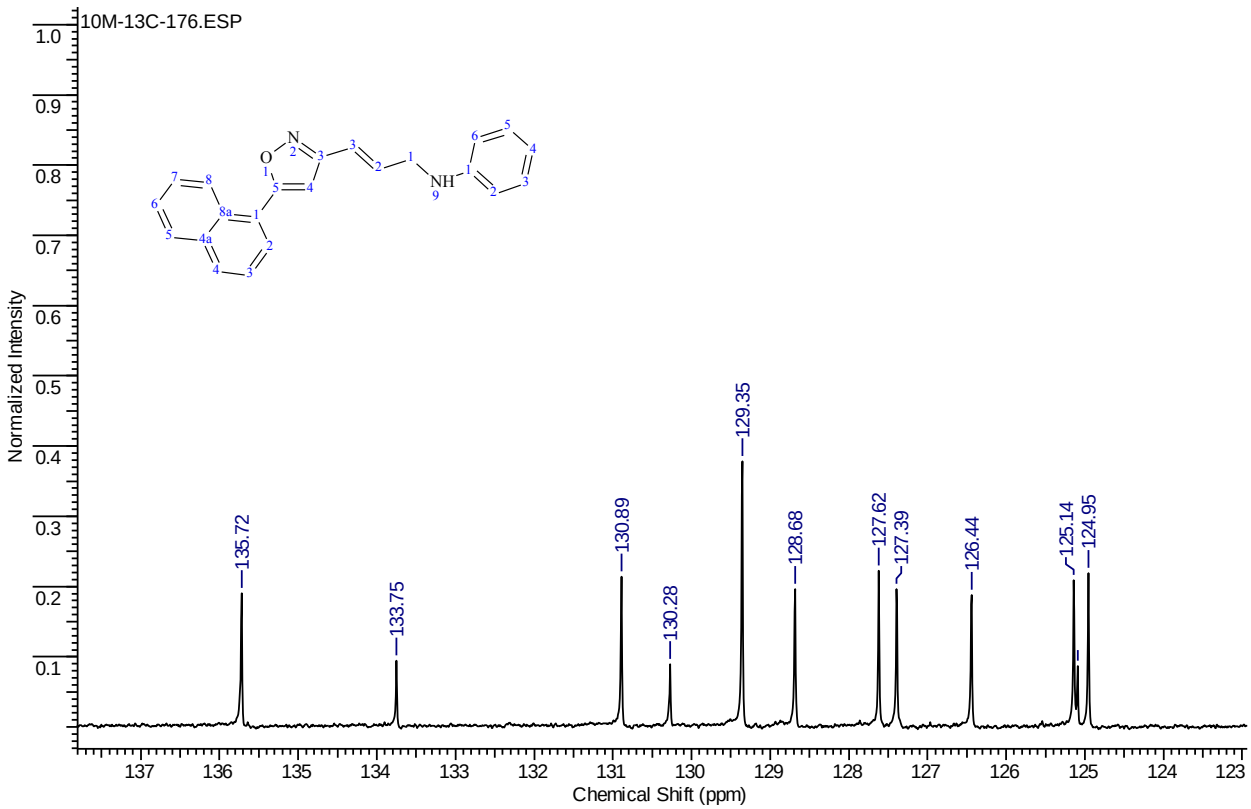
^{1}H NMR (700.2 MHz, $CDCl_3$)





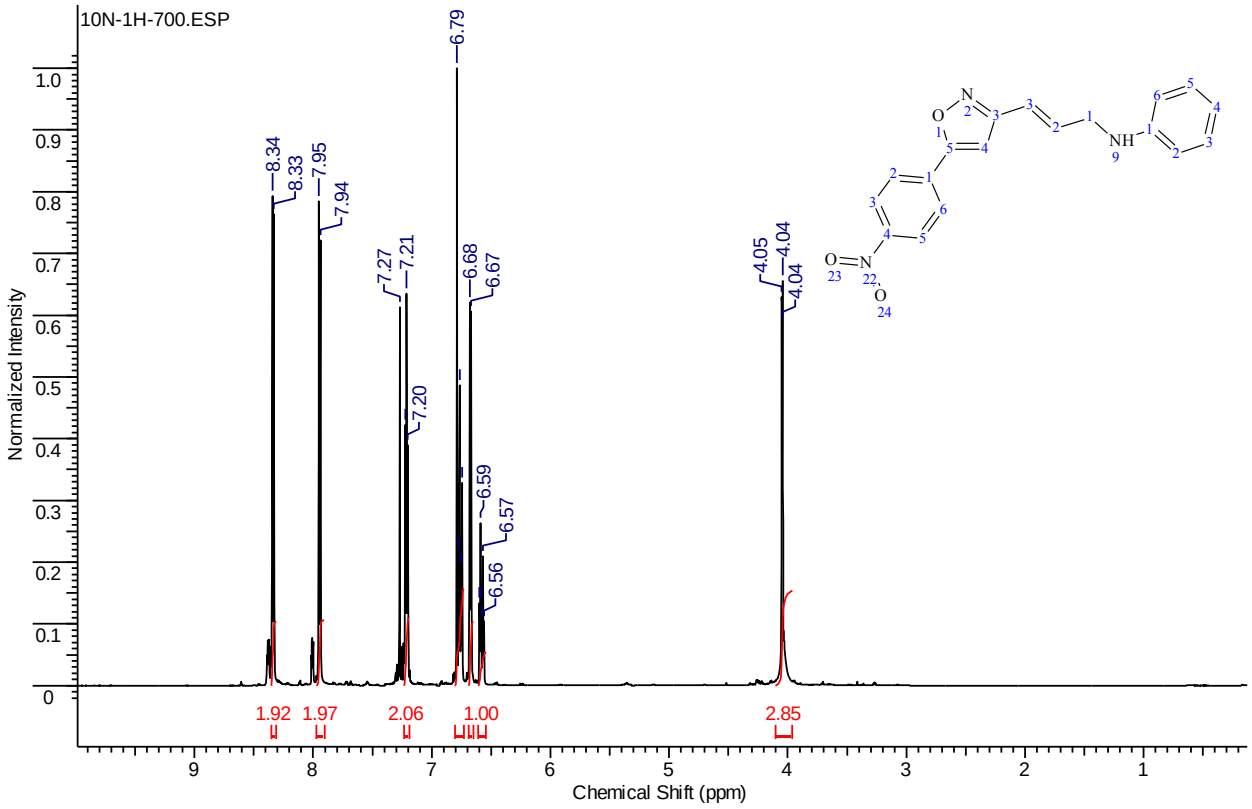
^{13}C NMR (176.1 MHz, $CDCl_3$)

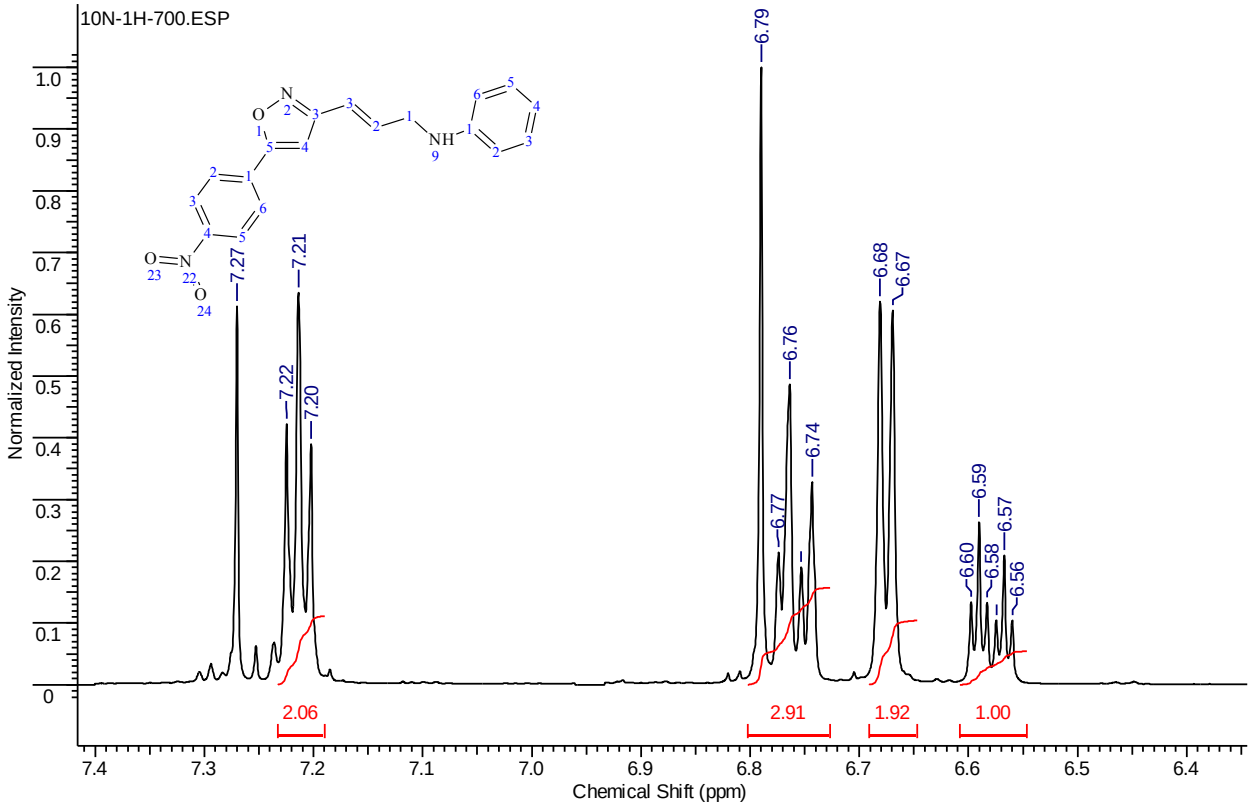




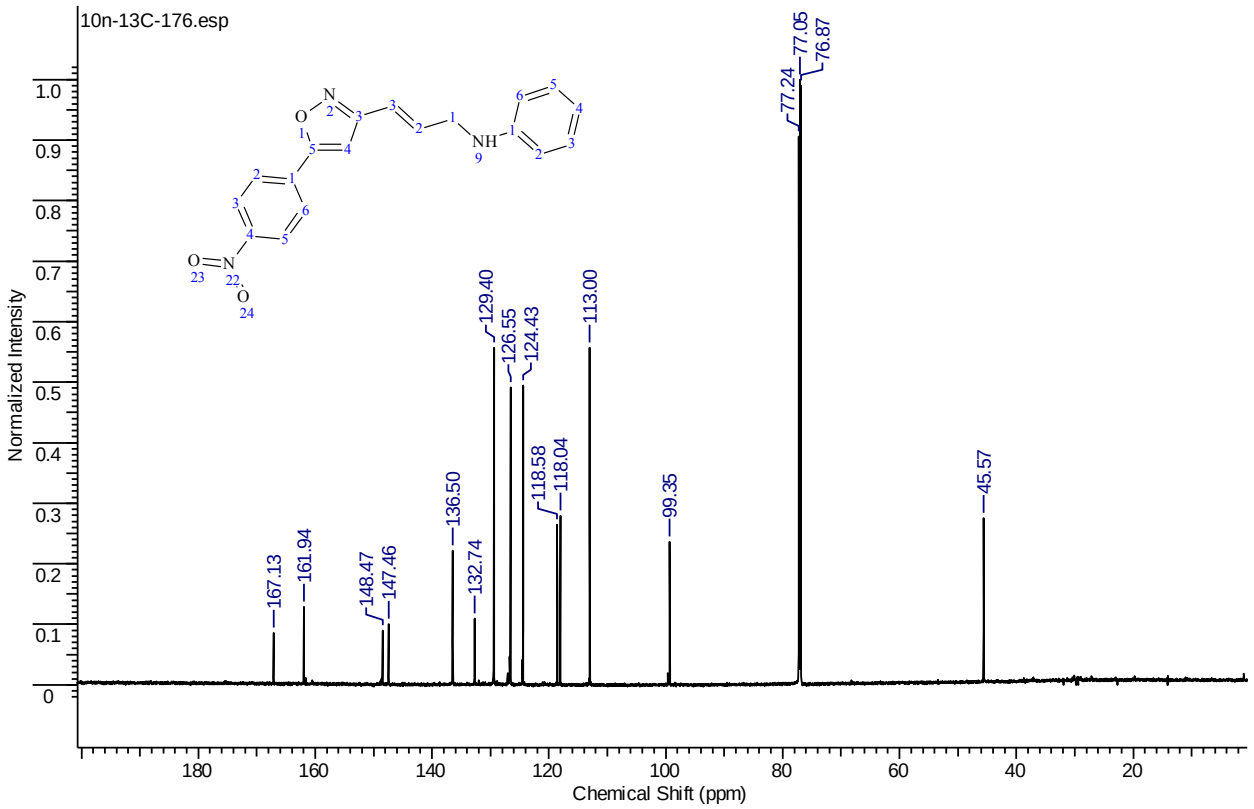
***N*-{(2*E*)-3-[5-(4-Nitrophenyl)isoxazol-3-yl]prop-2-en-1-yl}aniline (10n).**

^{1}H NMR (700.2 MHz, $CDCl_3$)



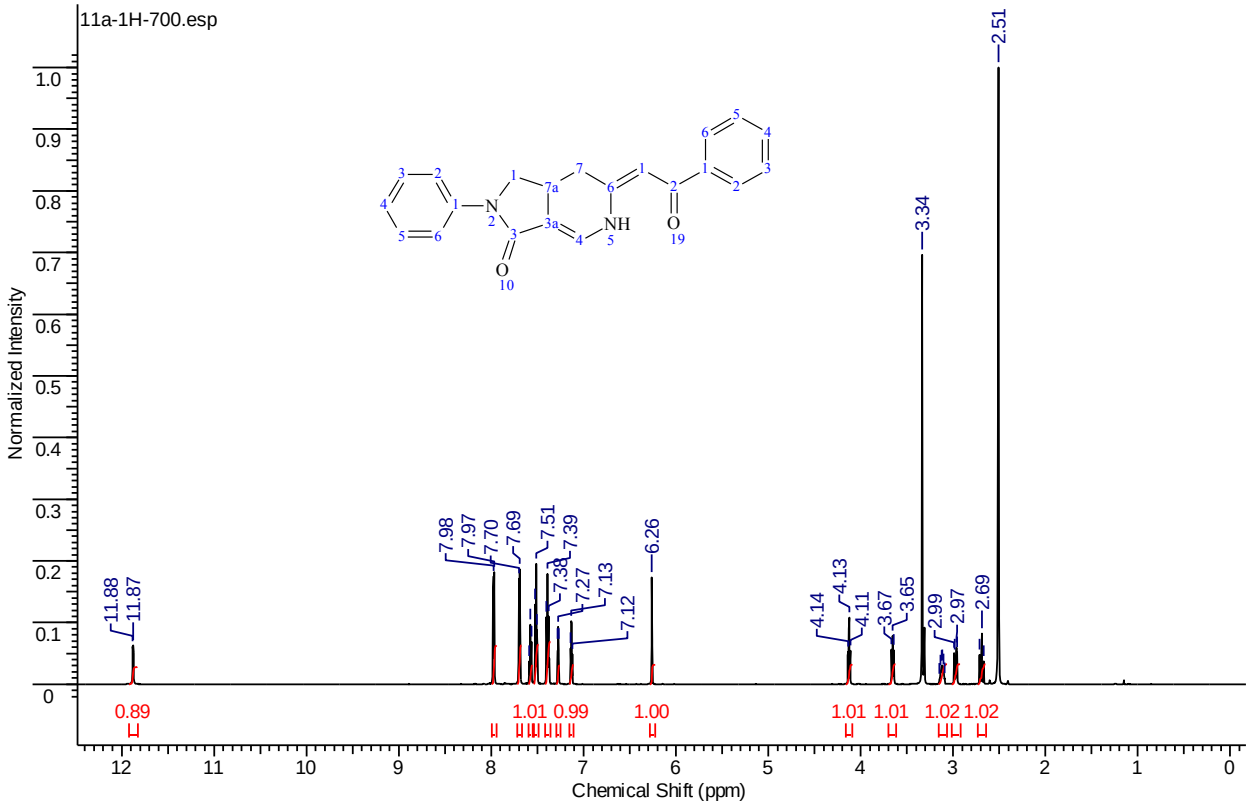


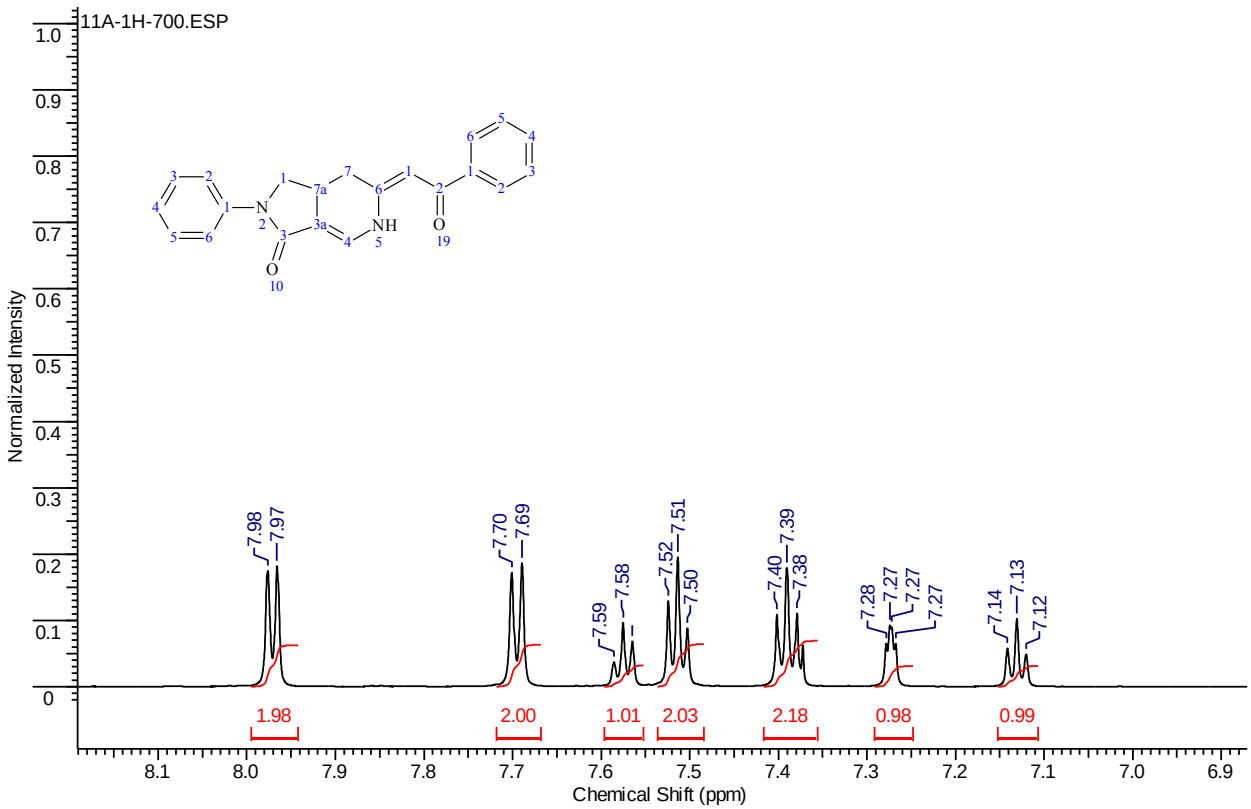
^{13}C NMR (176.1 MHz, $CDCl_3$)



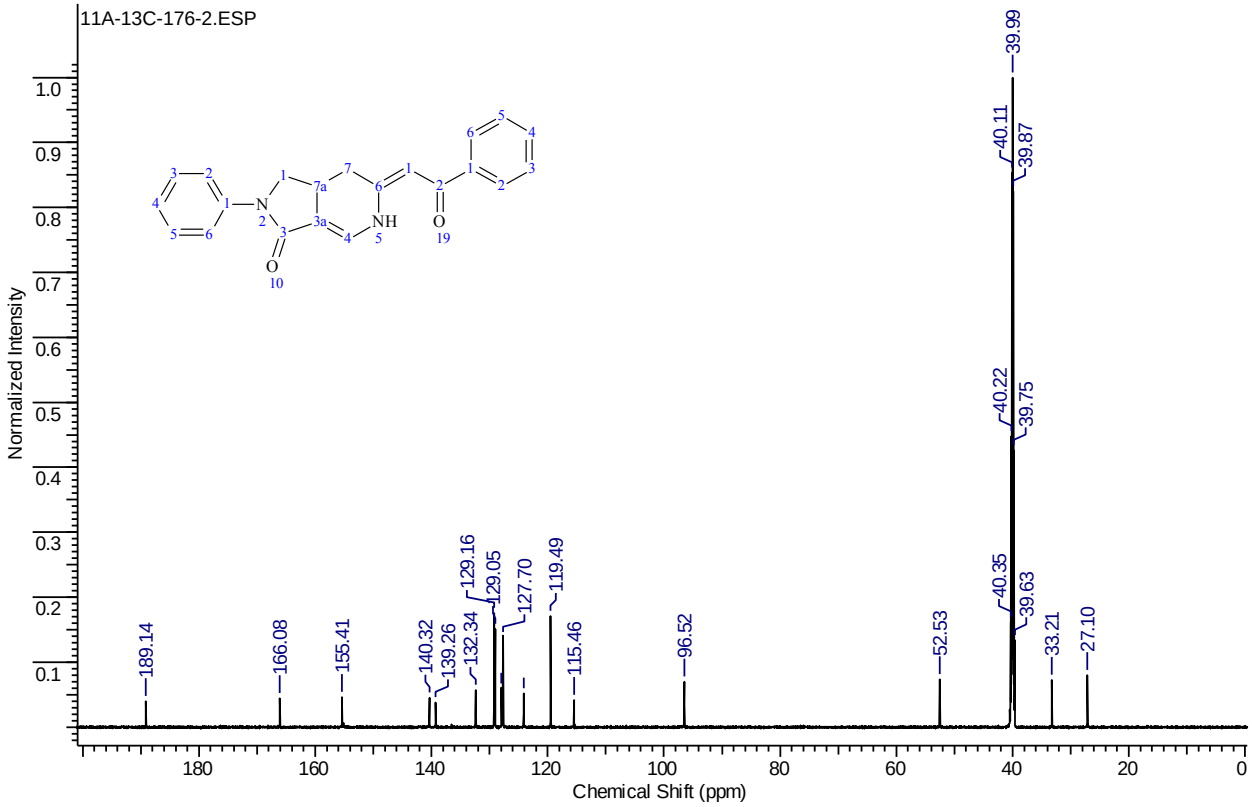
(6*Z*)-6-(2-Oxo-2-phenylethylidene)-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11a).

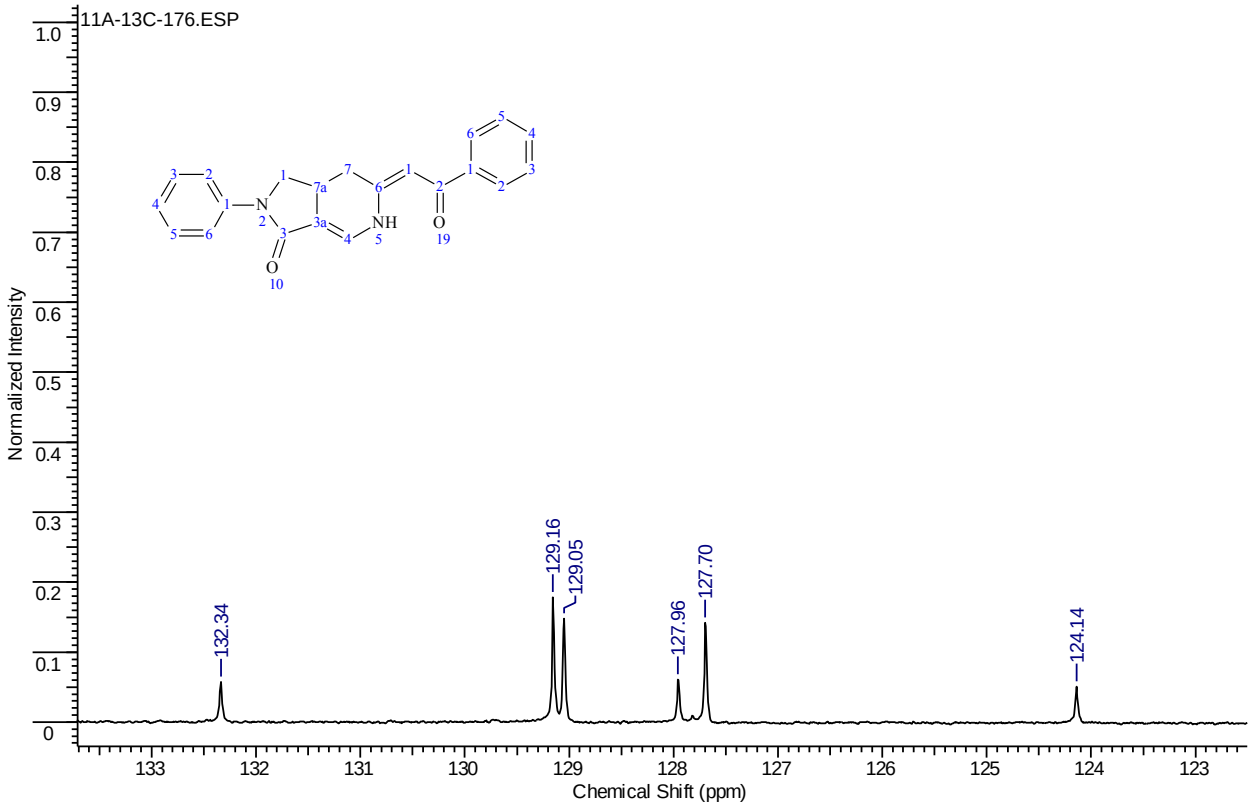
^{1}H NMR (700.2 MHz, DMSO-d_6)





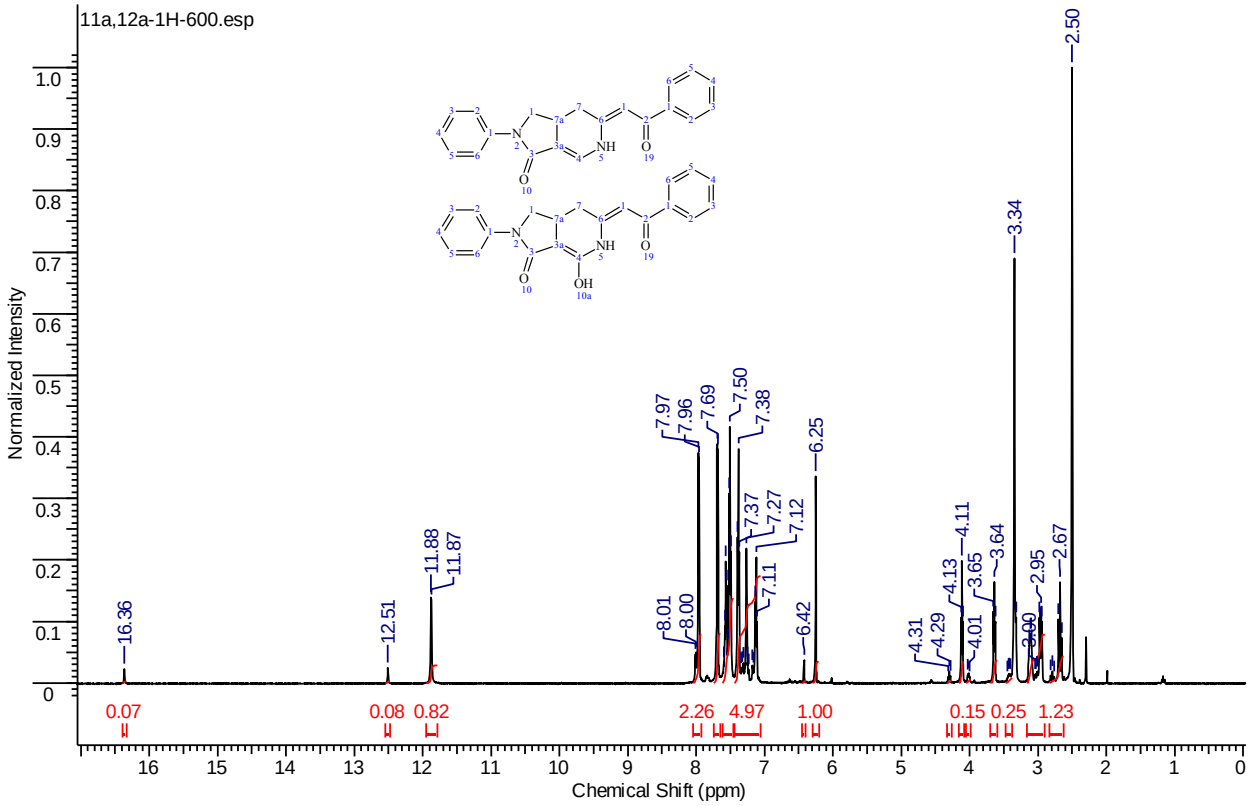
^{13}C NMR (176.1 MHz, DMSO-d_6)

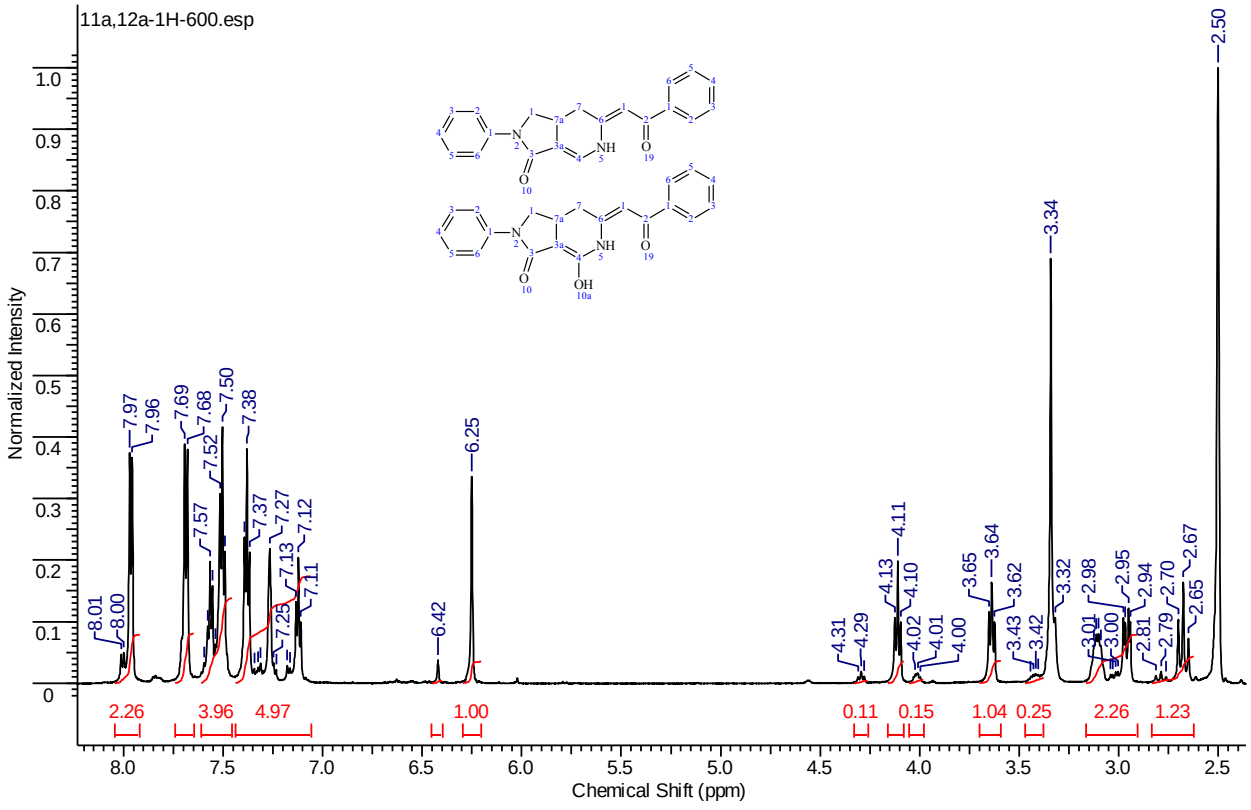




(6*Z*)-6-(2-oxo-2-phenylethylidene)-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11a) and (6*Z*)-4-hydroxy-6-(2-oxo-2-phenylethylidene)-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (12a)

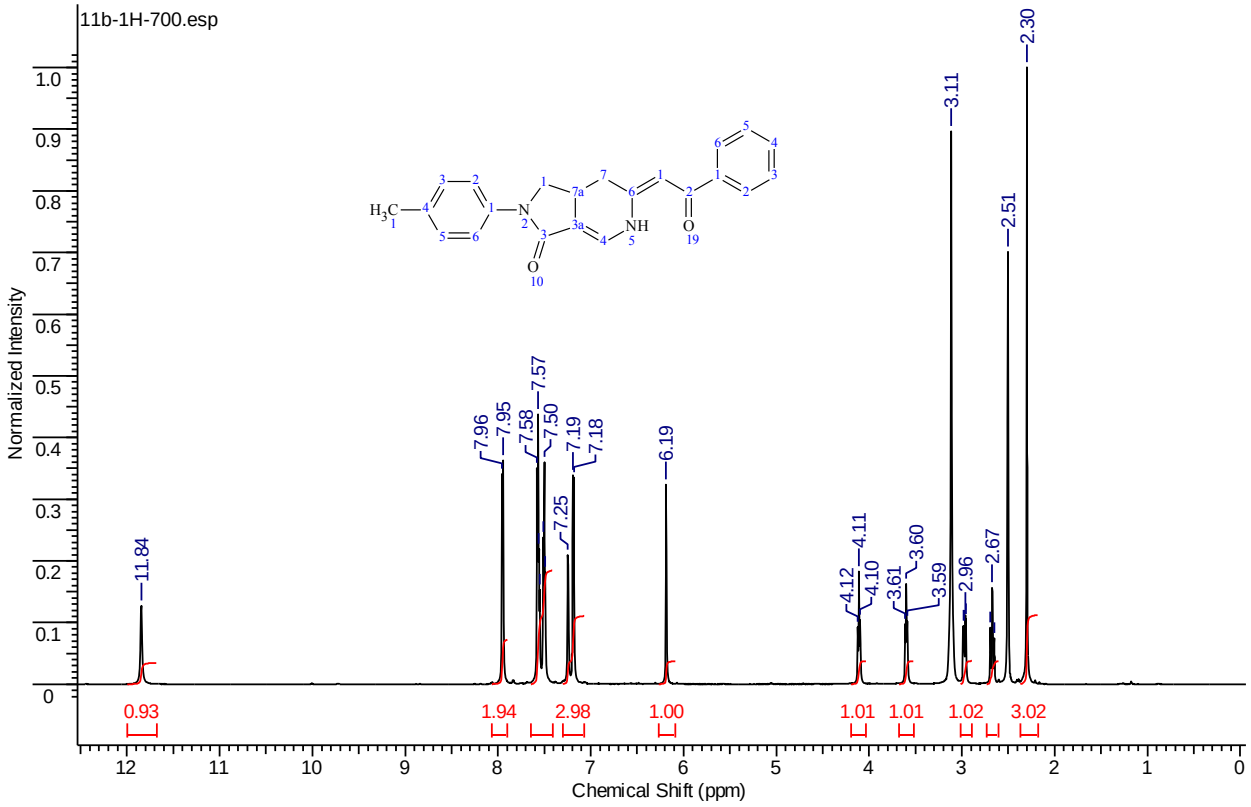
^{1}H NMR (600.2 MHz, DMSO-d_6)



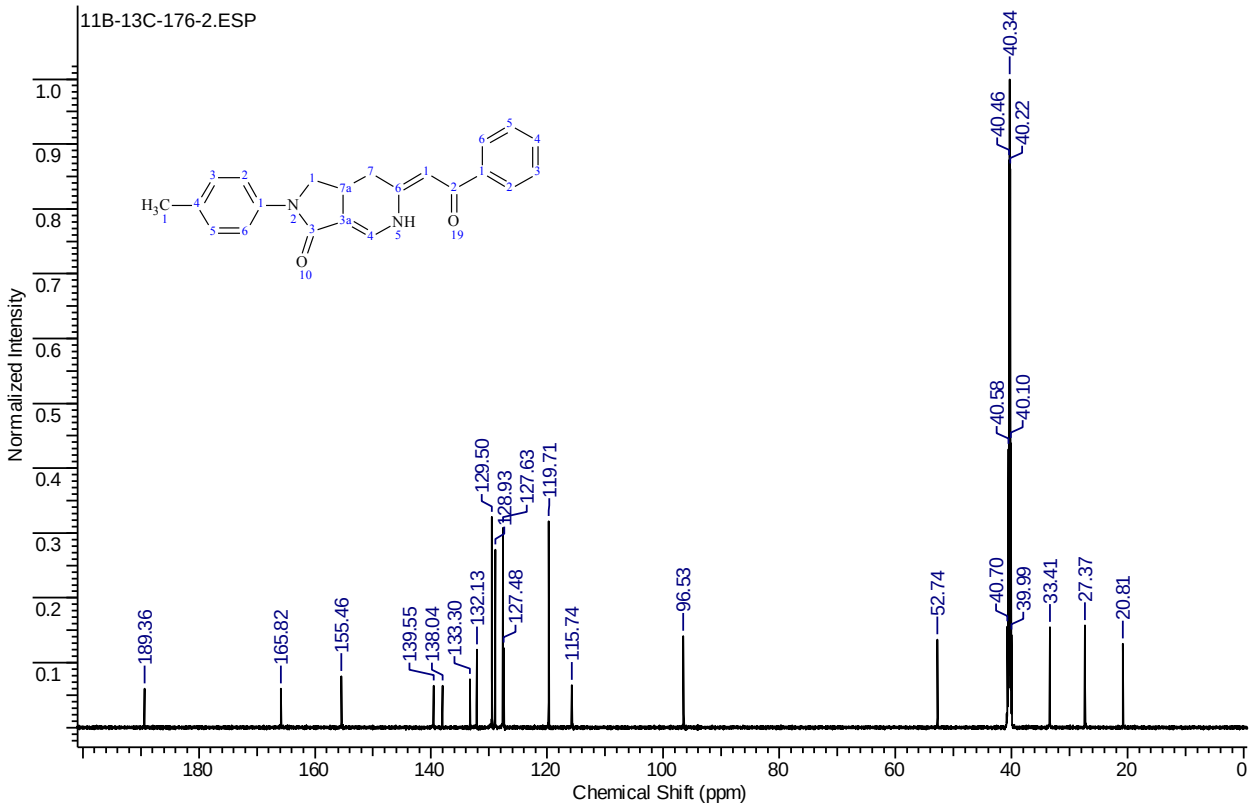


(6*Z*)-2-(4-Methylphenyl)-6-(2-oxo-2-phenylethylidene)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11b).

^{1}H NMR (700.2 MHz, DMSO-d_6)

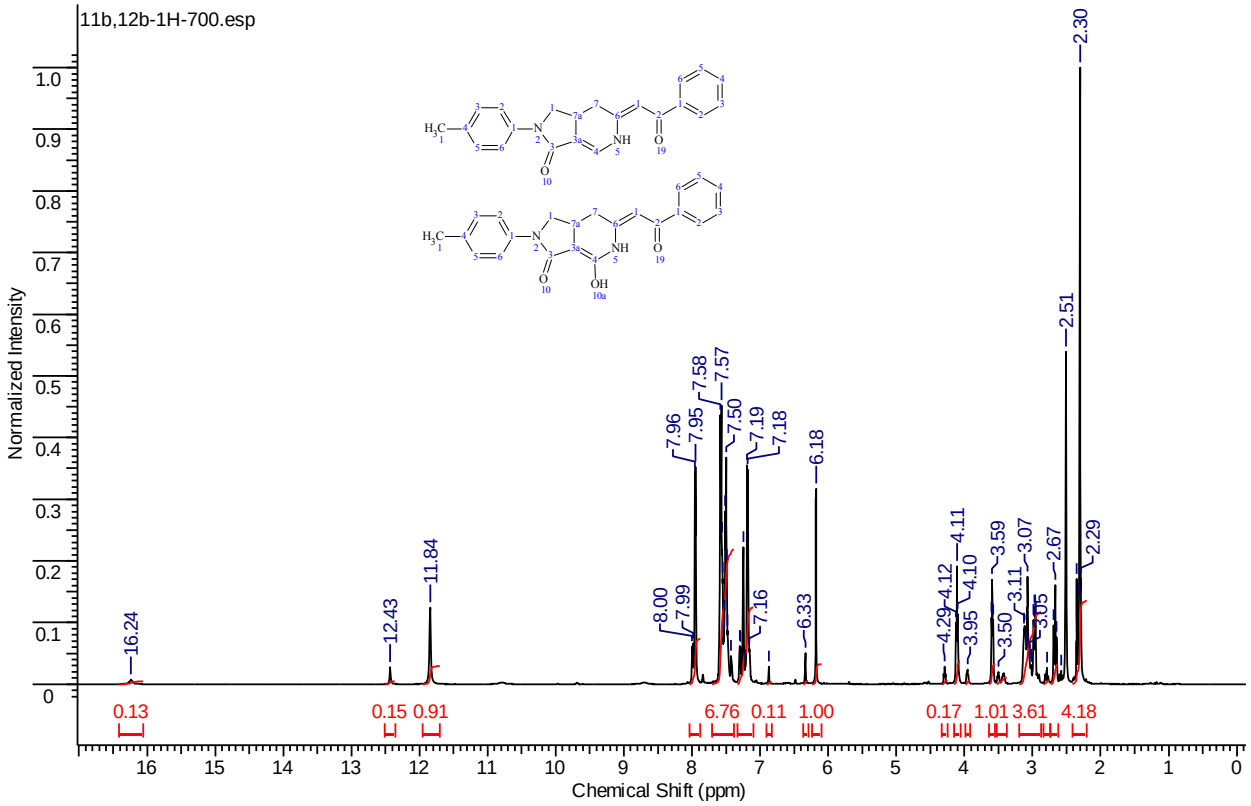


^{13}C NMR (176.1 MHz, DMSO-d_6)

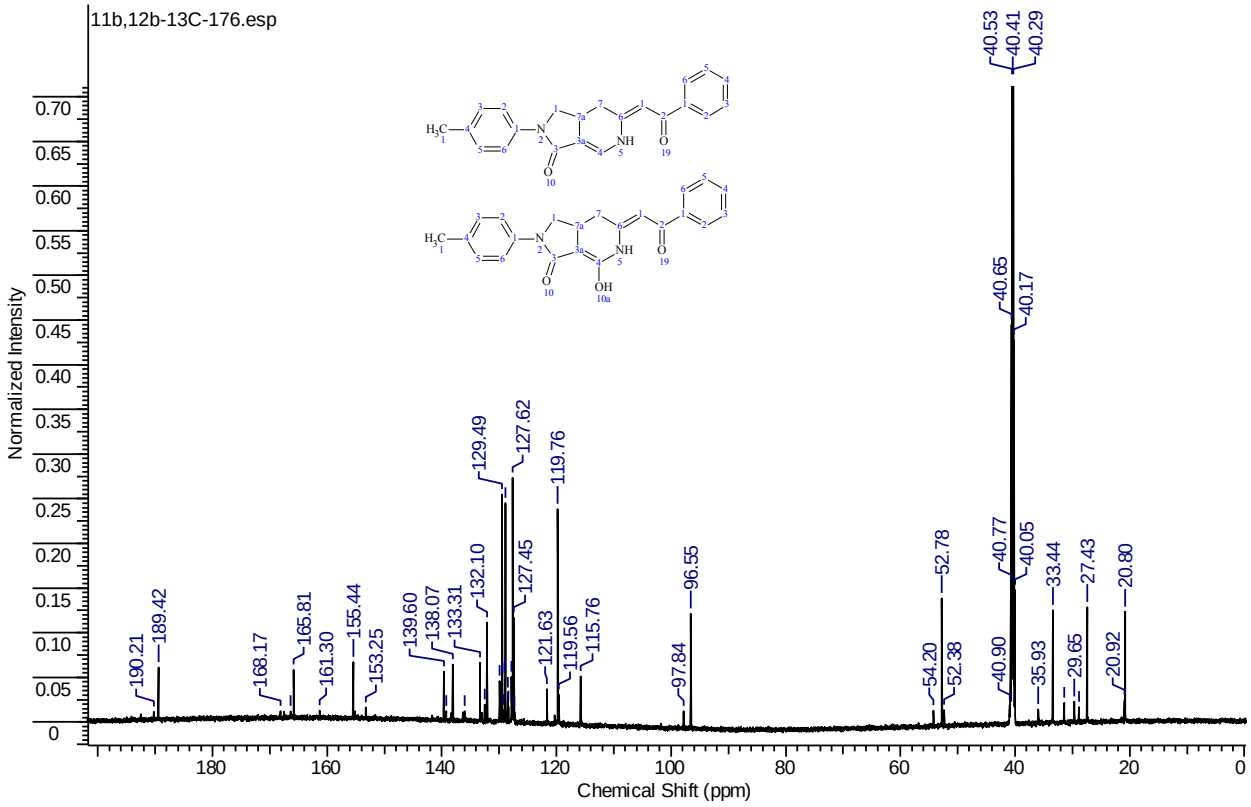


(6*Z*)-2-(4-Methylphenyl)-6-(2-oxo-2-phenylethylidene)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11b) and (6*Z*)-4-hydroxy-2-(4-methylphenyl)-6-(2-oxo-2-phenylethylidene)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (12b)

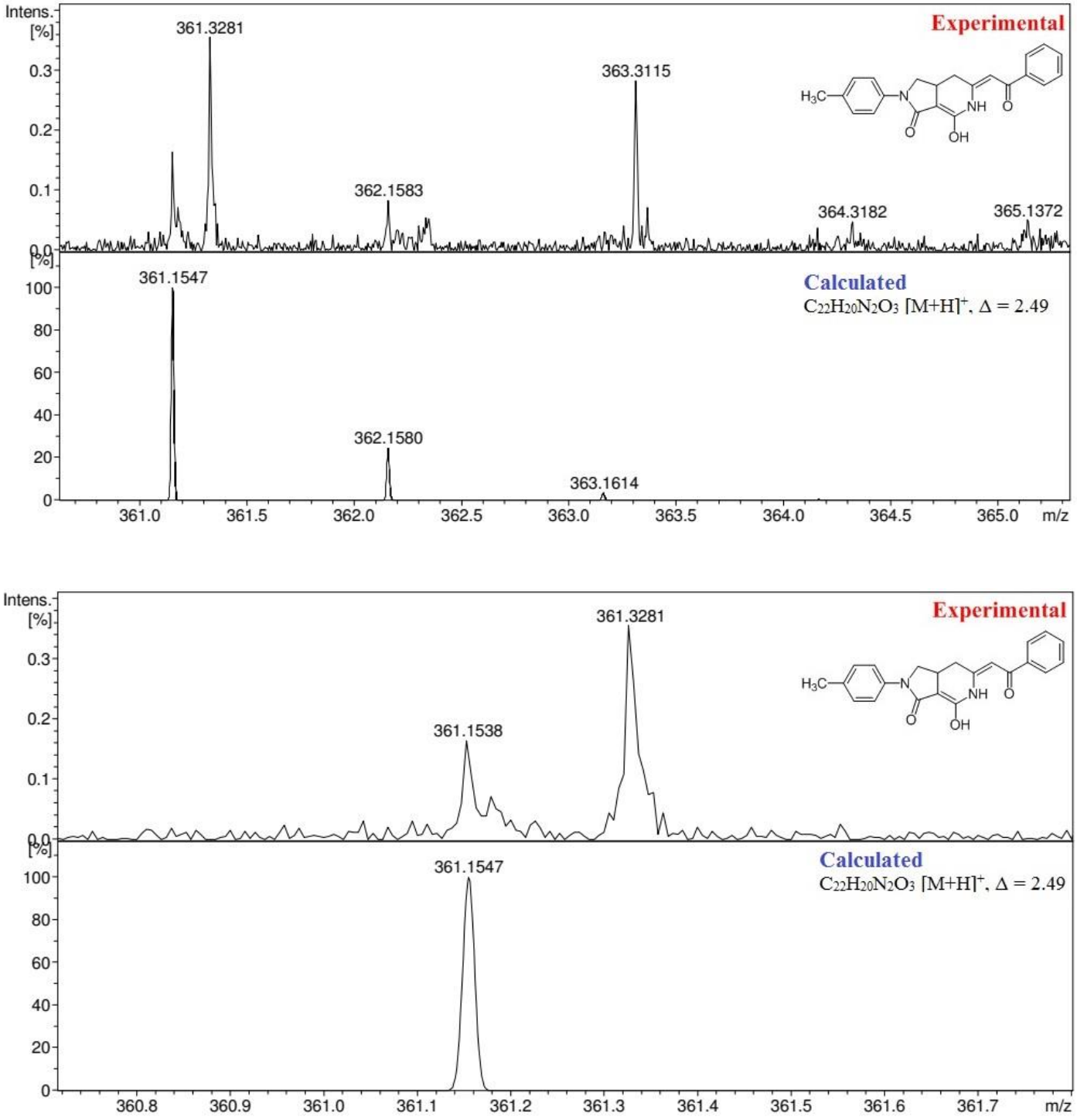
^{1}H NMR (700.2 MHz, DMSO-d_6)



^{13}C NMR (176.1 MHz, DMSO-d_6)

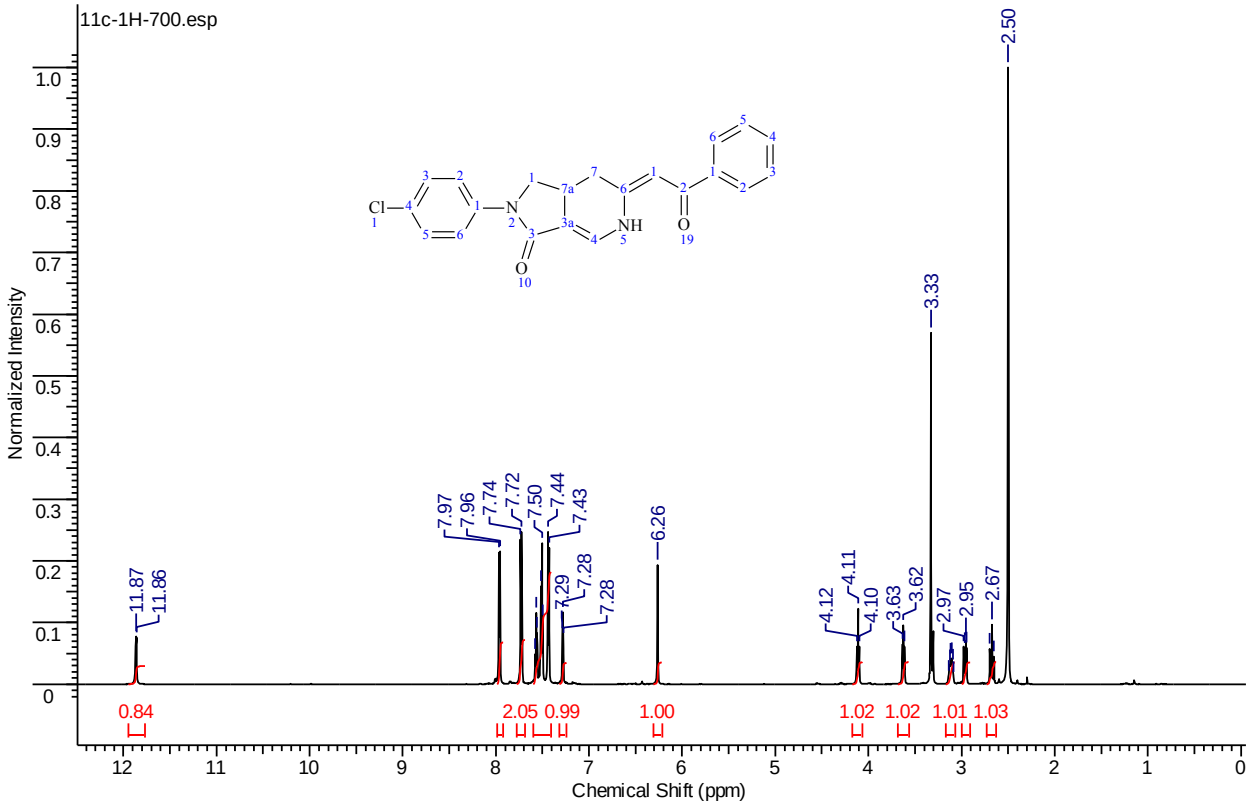


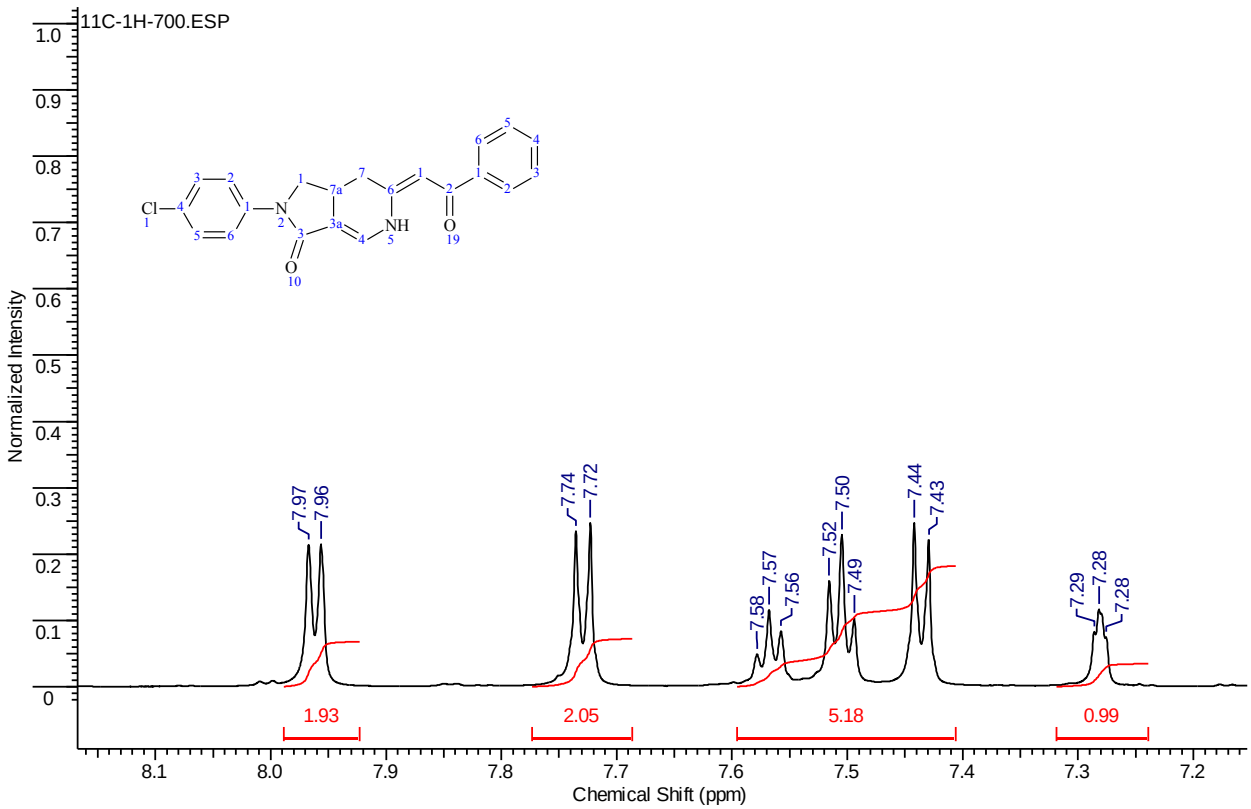
HRMS (ESI) spectrum of (6*Z*)-4-hydroxy-2-(4-methylphenyl)-6-(2-oxo-2-phenylethylidene)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (12b)



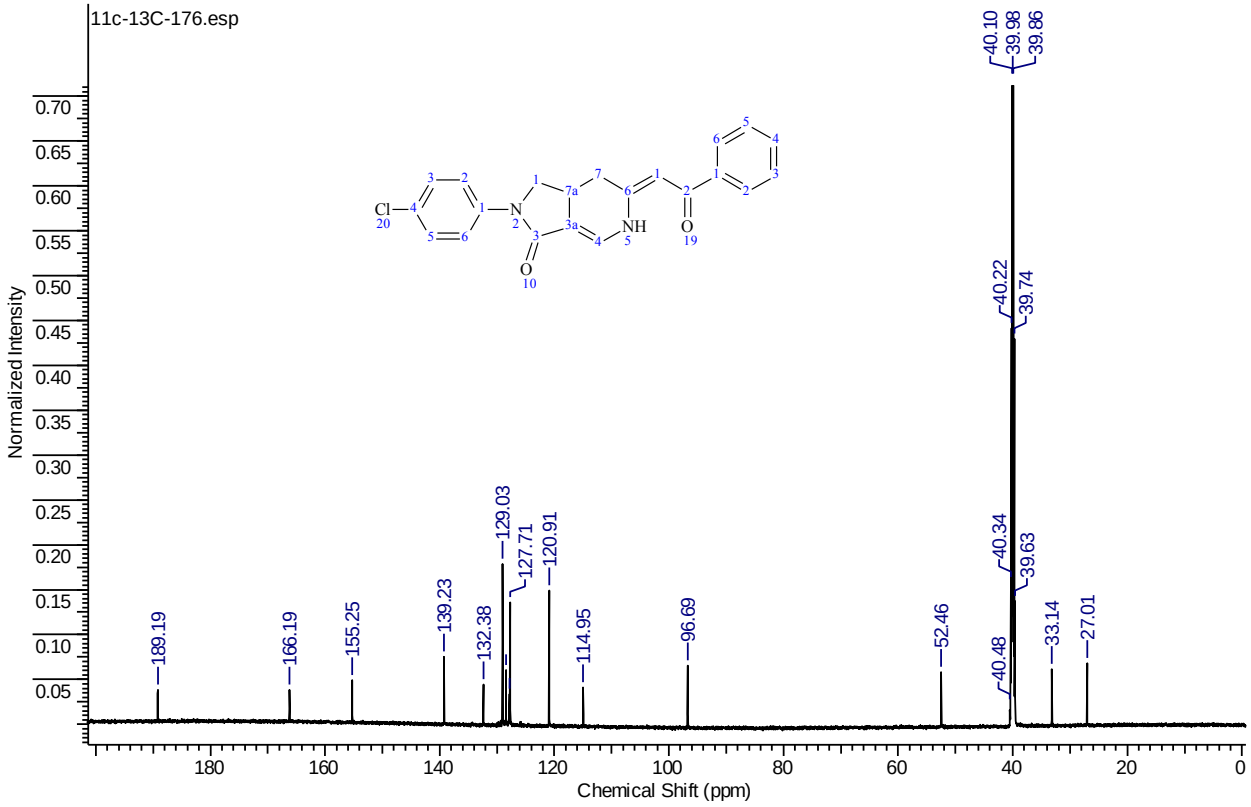
(6*Z*)-2-(4-Chlorophenyl)-6-(2-oxo-2-phenylethylidene)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11c).

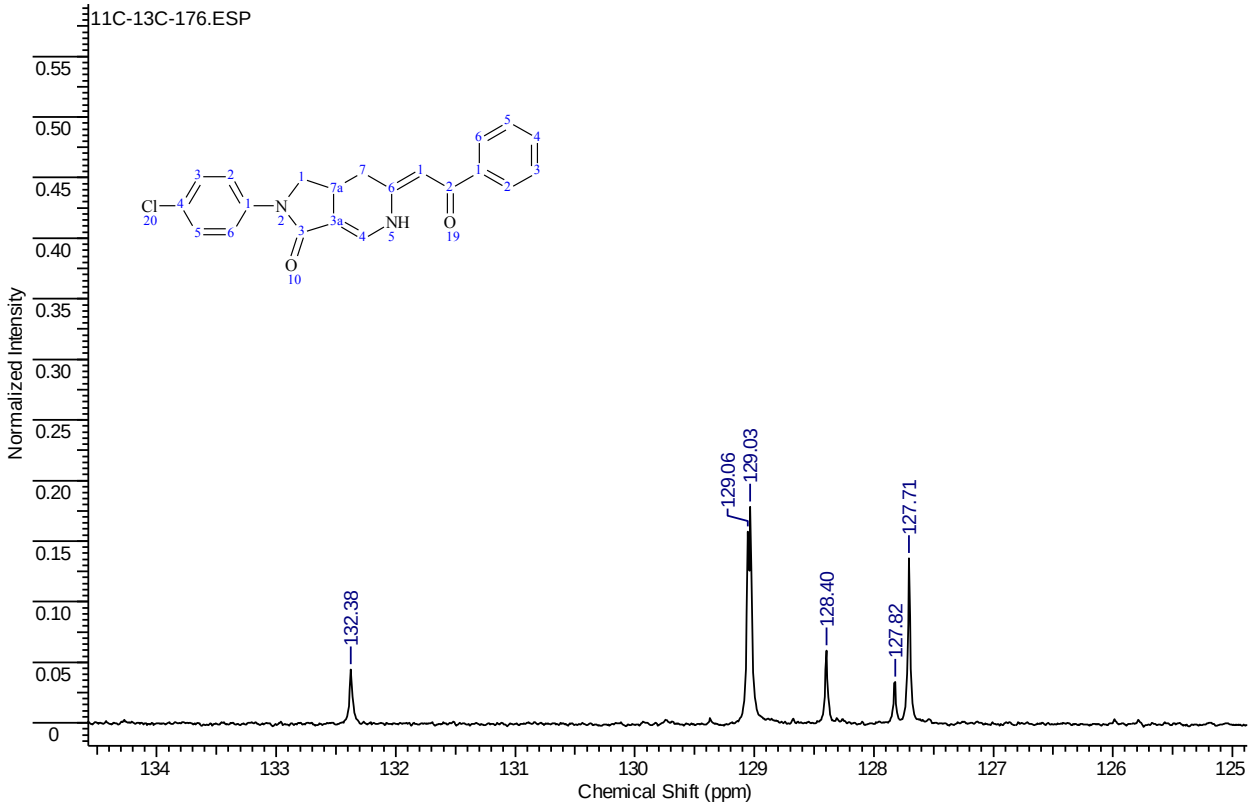
^{1}H NMR (700.2 MHz, DMSO-d_6)





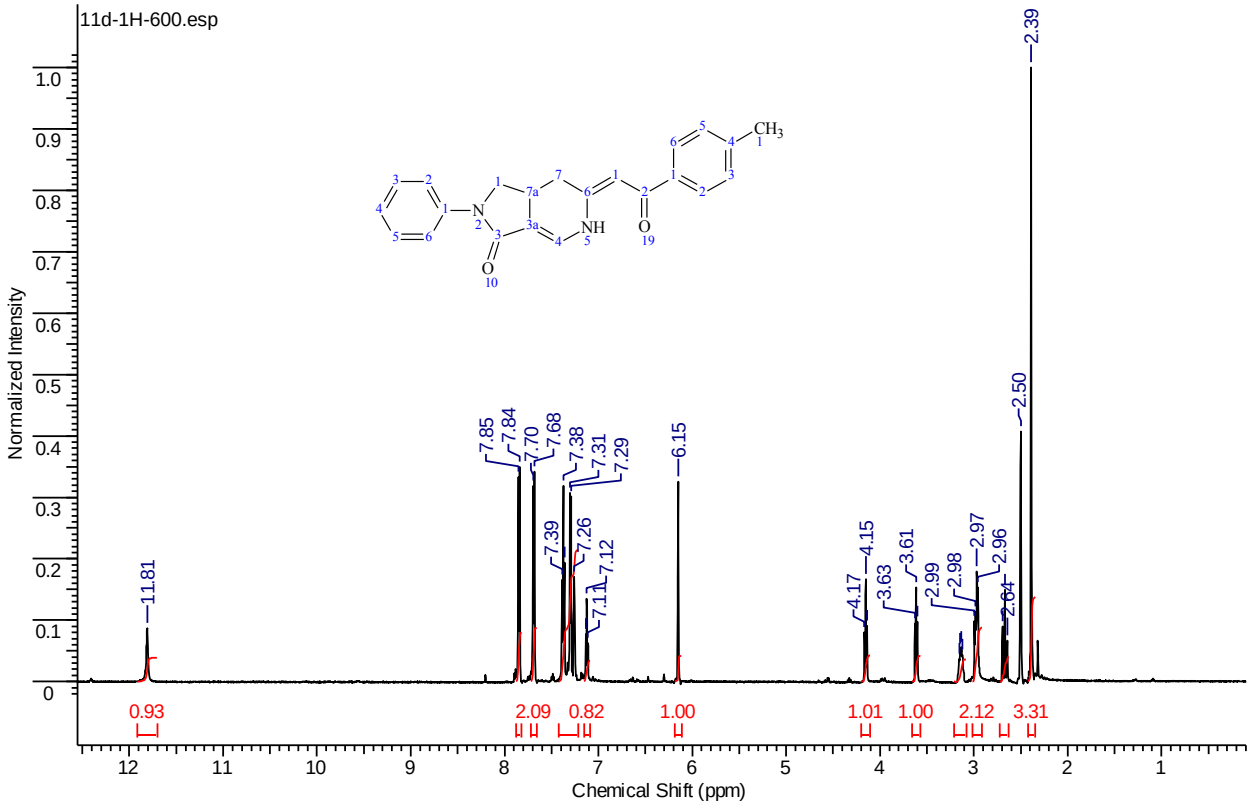
^{13}C NMR (176.1 MHz, DMSO-d_6)

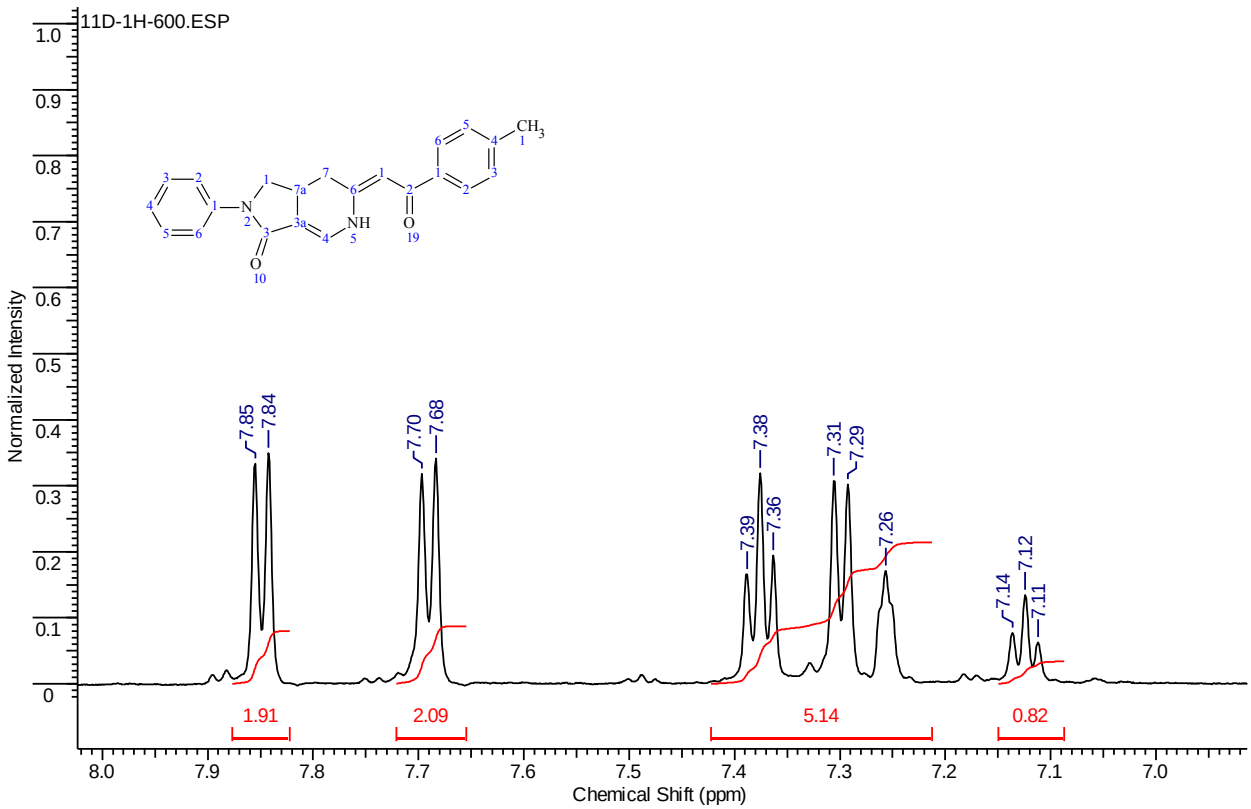


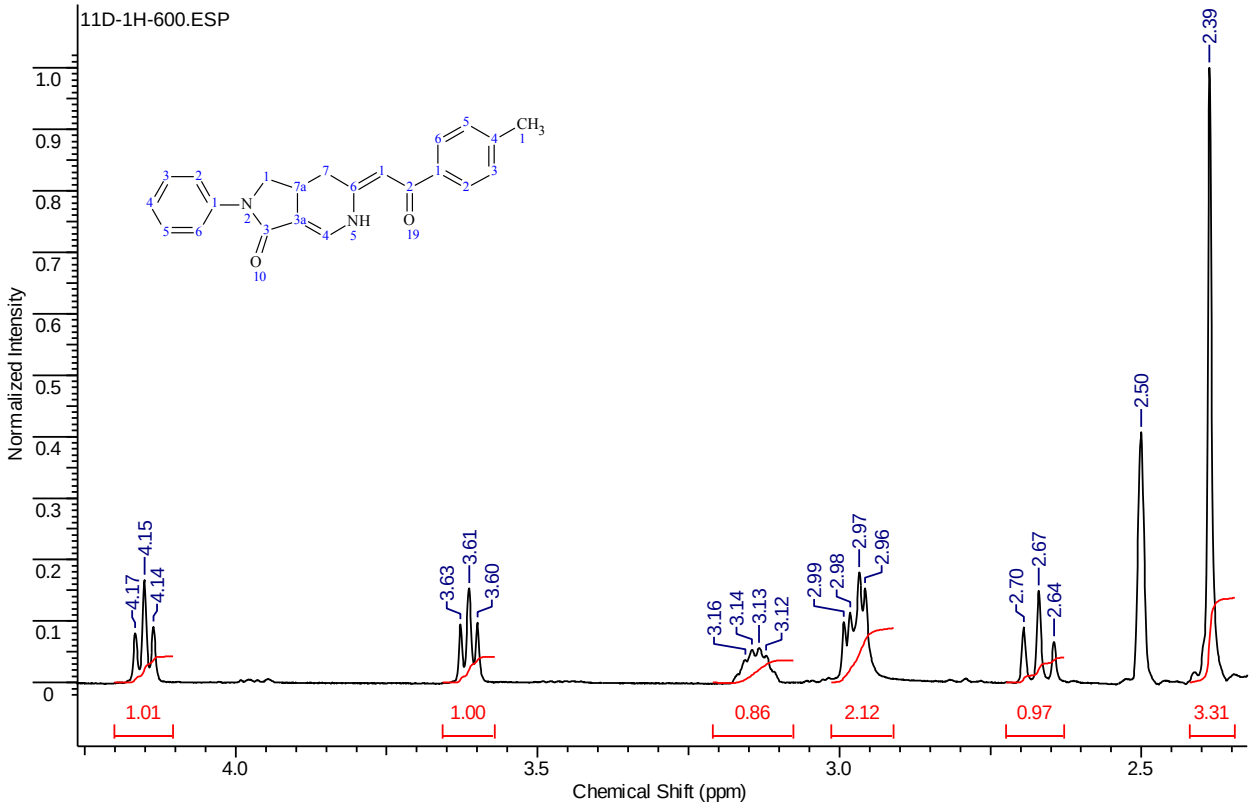


(6*Z*)-6-[2-(4-Methylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11d).

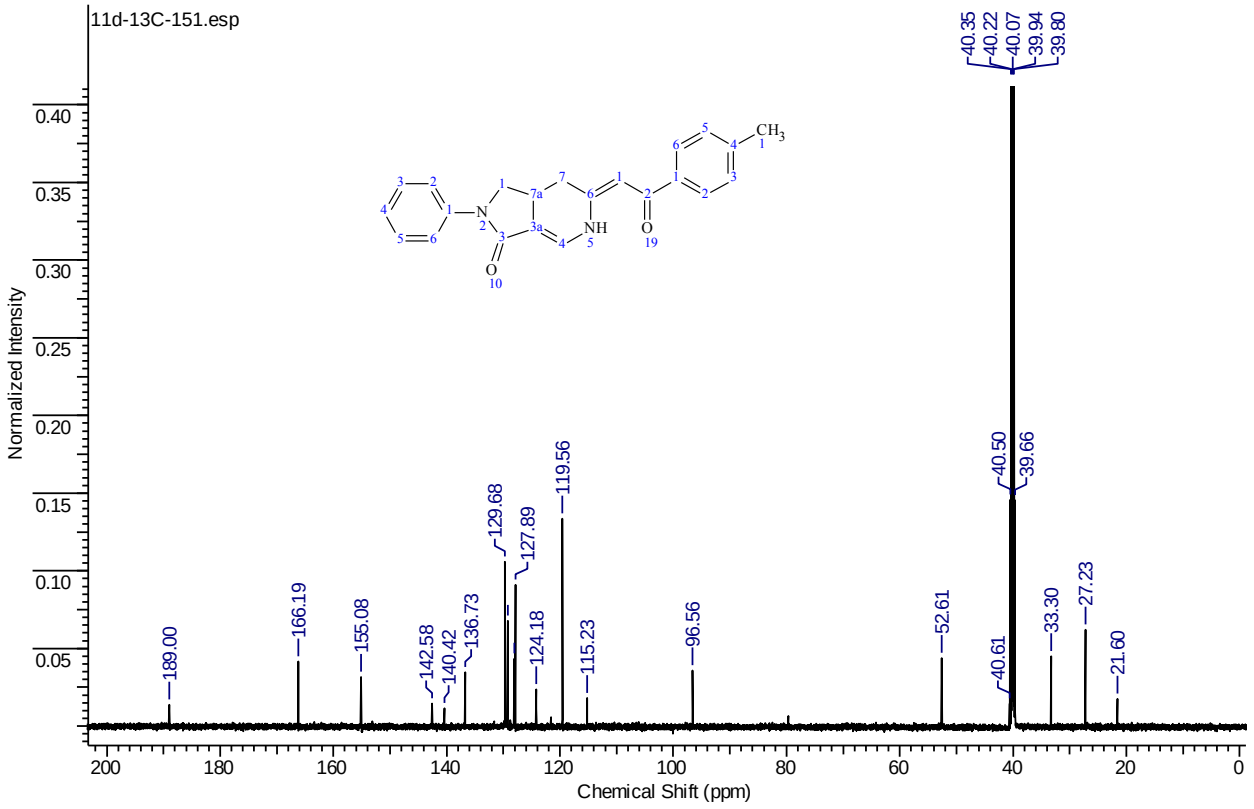
^{1}H NMR (600.2 MHz, DMSO-d_6)





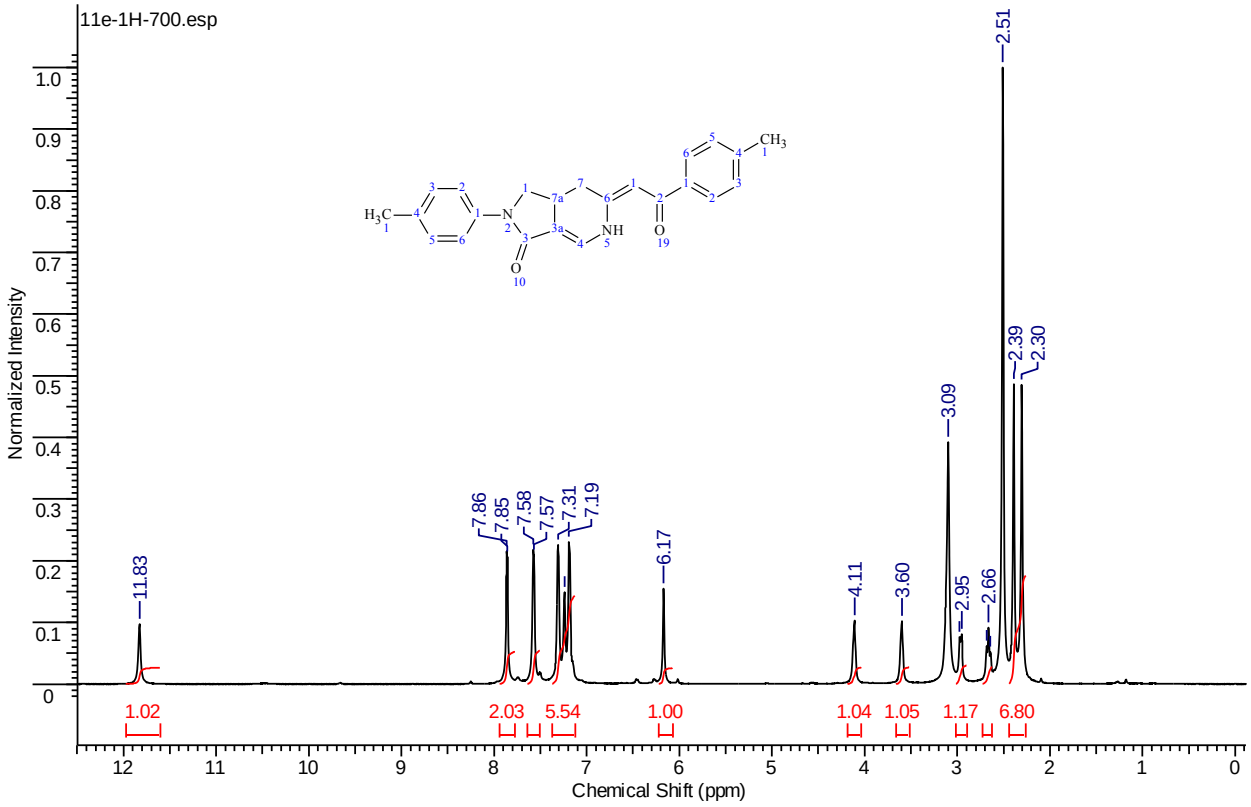


^{13}C NMR (150.9 MHz, DMSO-d_6)

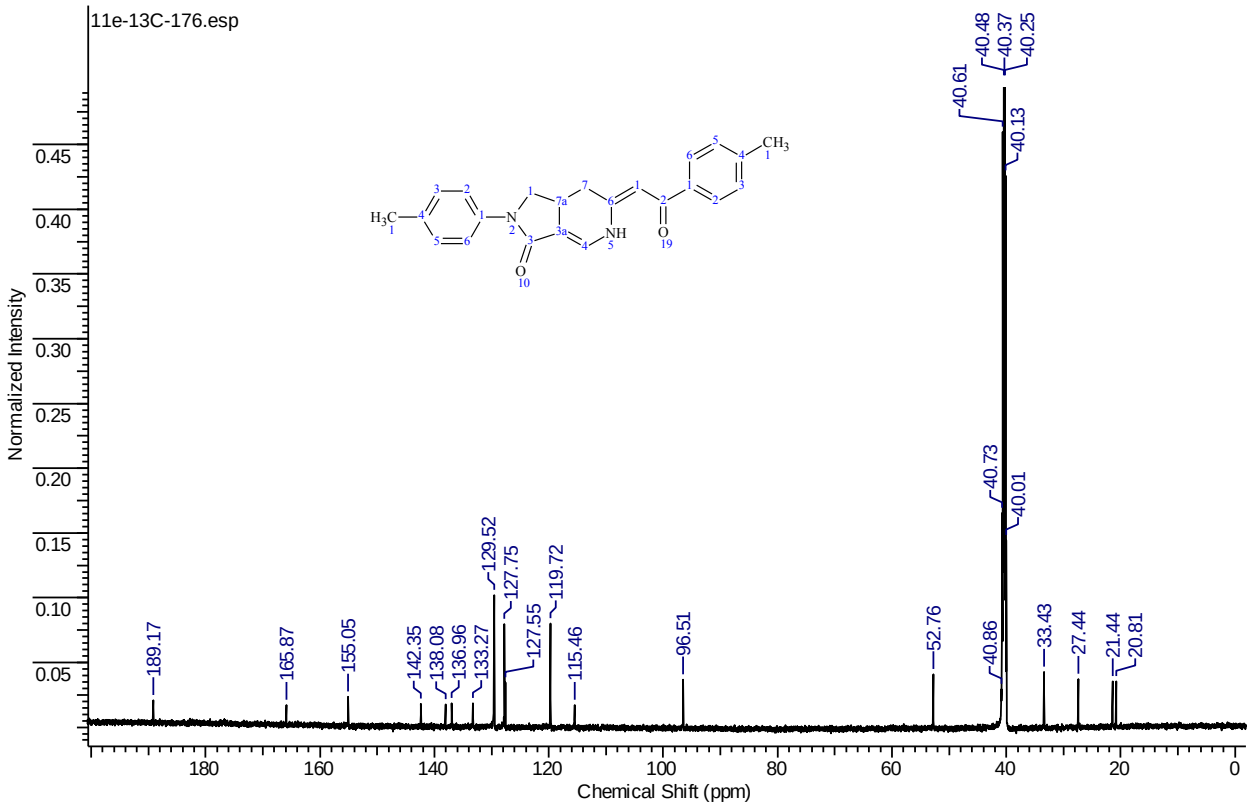


(6*Z*)-2-(4-Methylphenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11e).

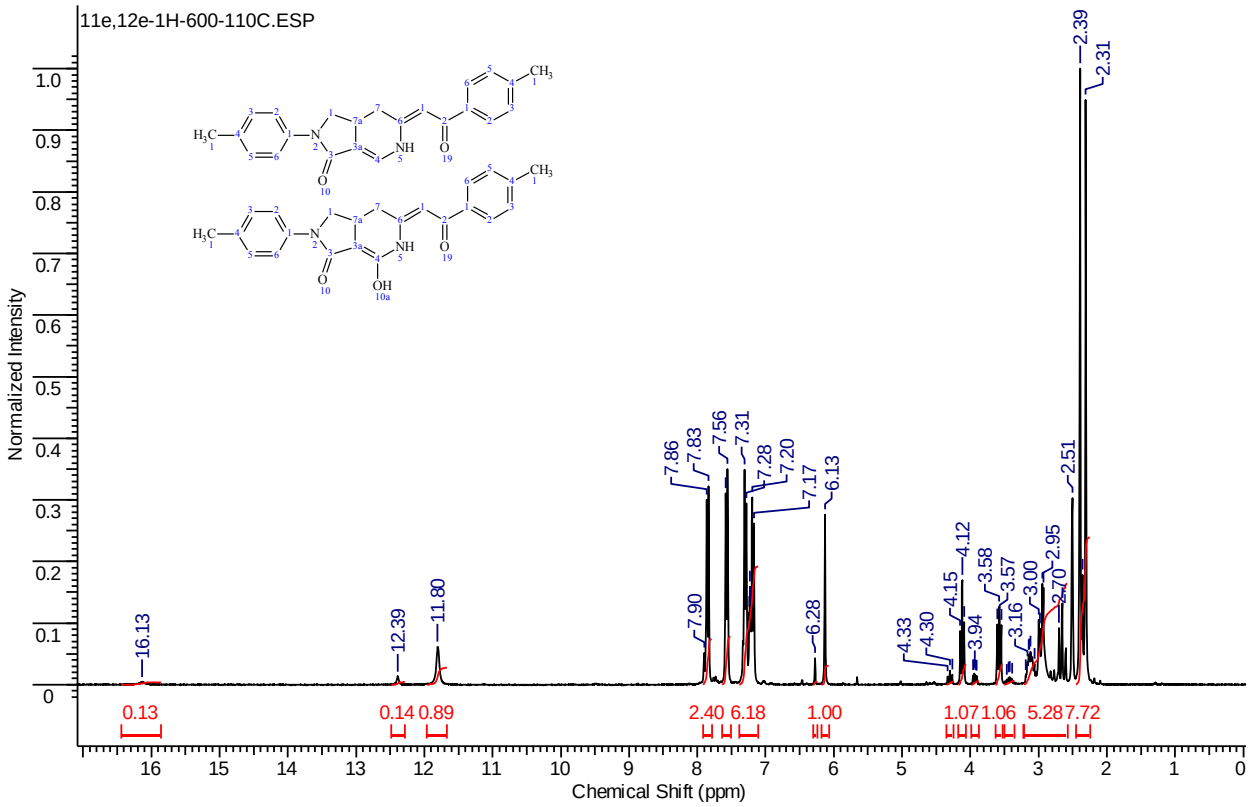
^{1}H NMR (700.2 MHz, DMSO-d_6)



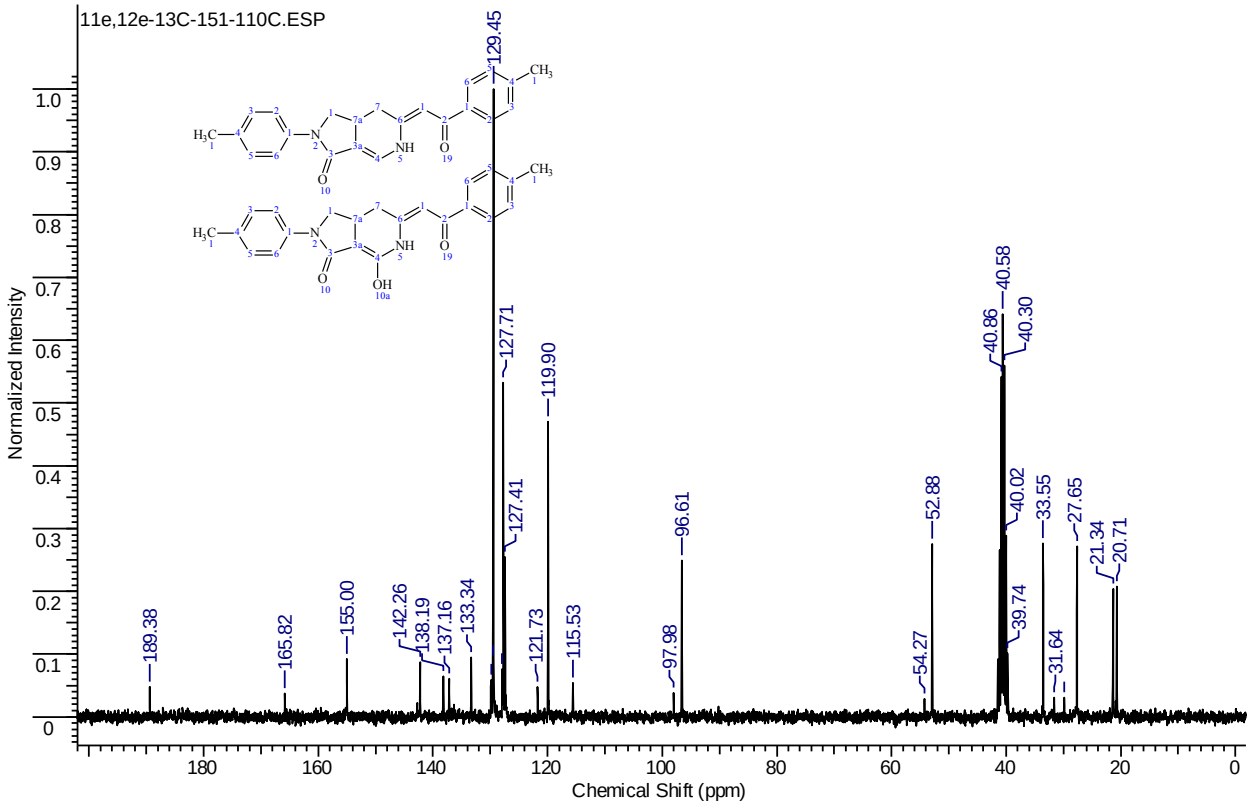
^{13}C NMR (176.1 MHz, DMSO-d_6)



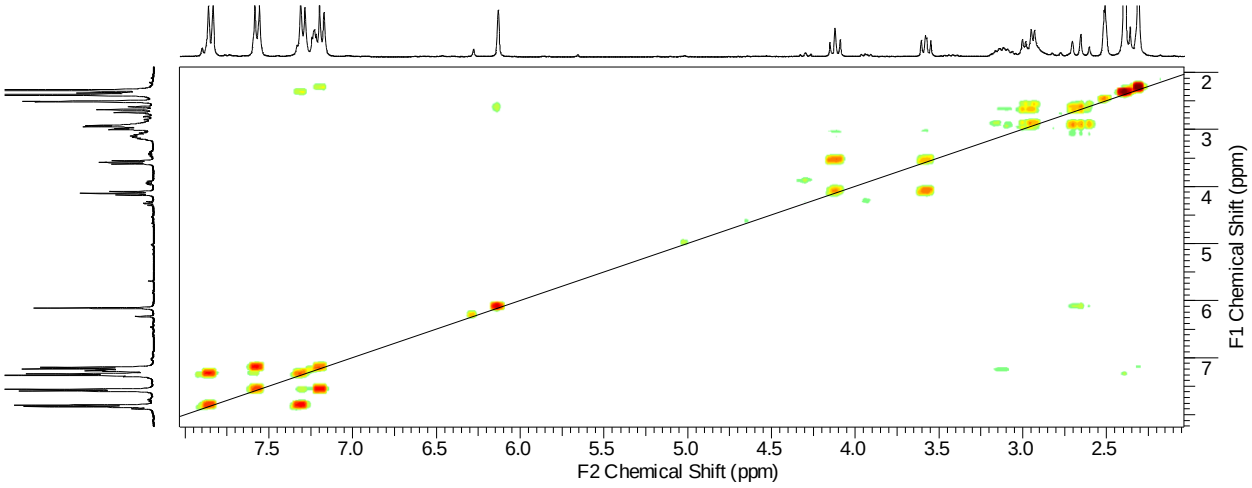
(6*Z*)-2-(4-Methylphenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11e) and (6*Z*)-4-hydroxy-2-(4-methylphenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (12e). ^{1}H NMR (600.2 MHz, DMSO-d_6, 110 °C)

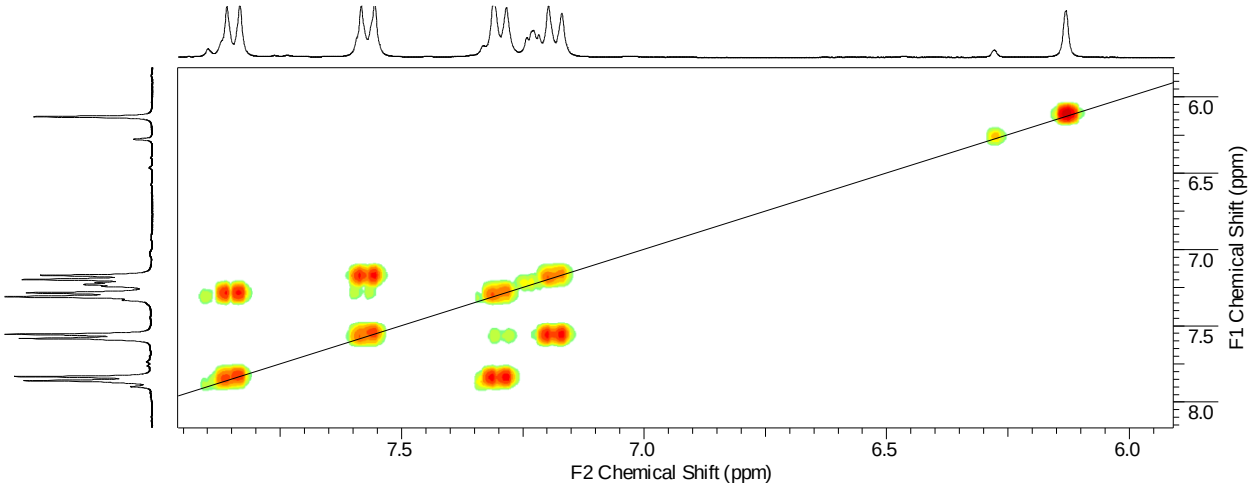


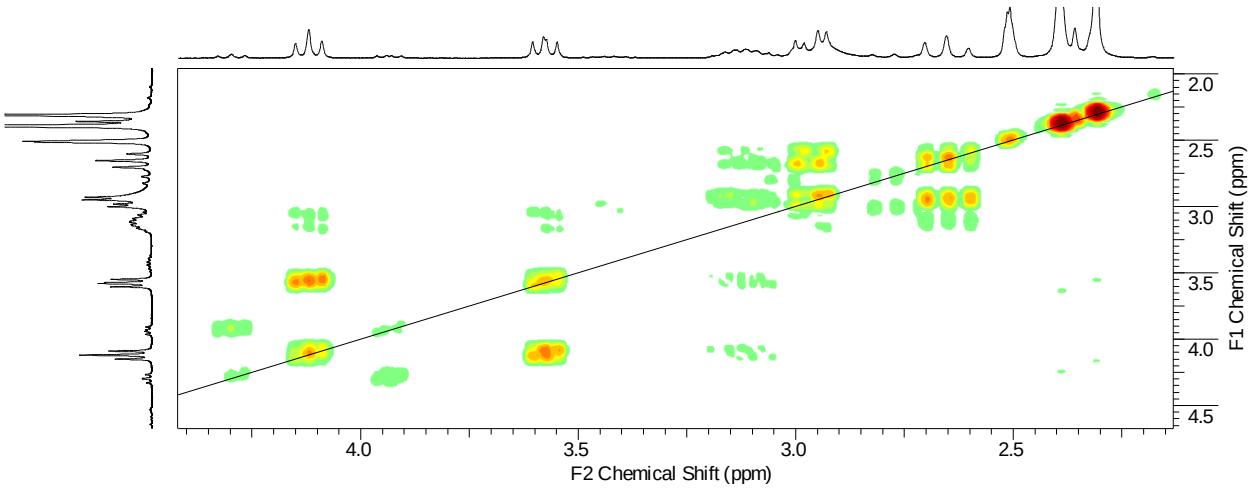
^{13}C NMR (150.9 MHz, DMSO-d_6, 110 °C)



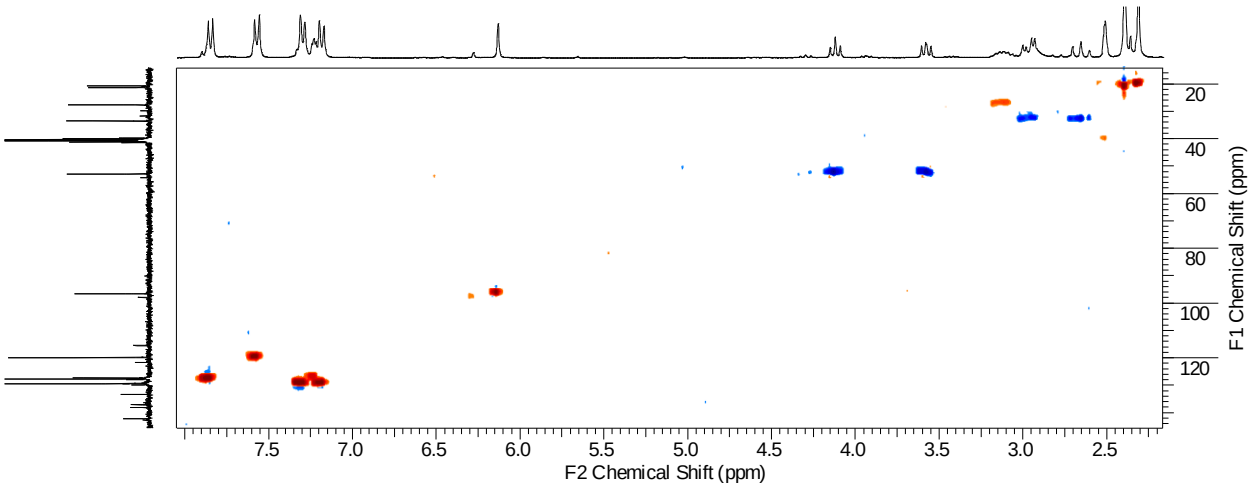
COSY of 11e/12e

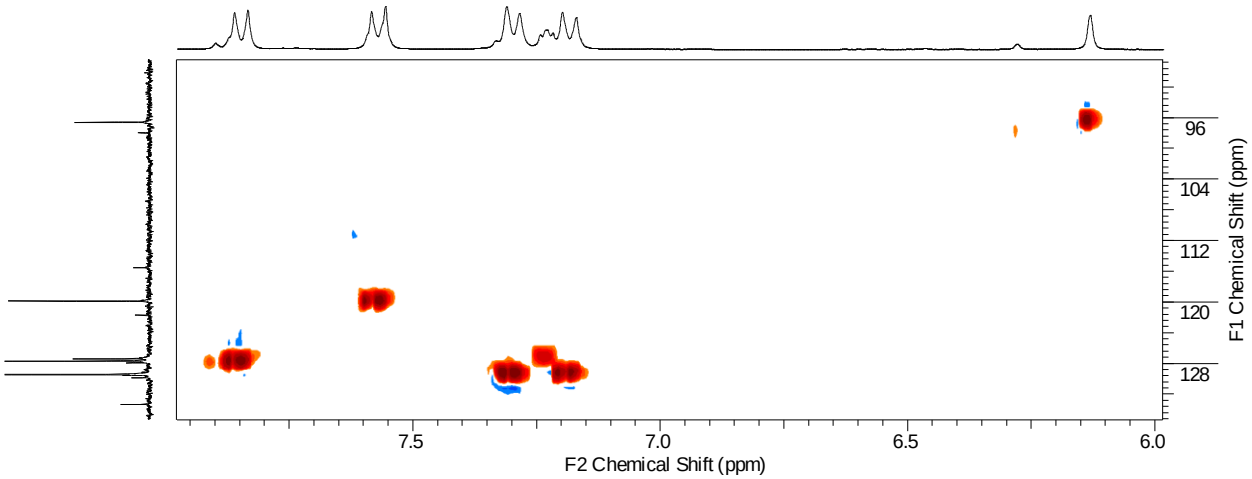


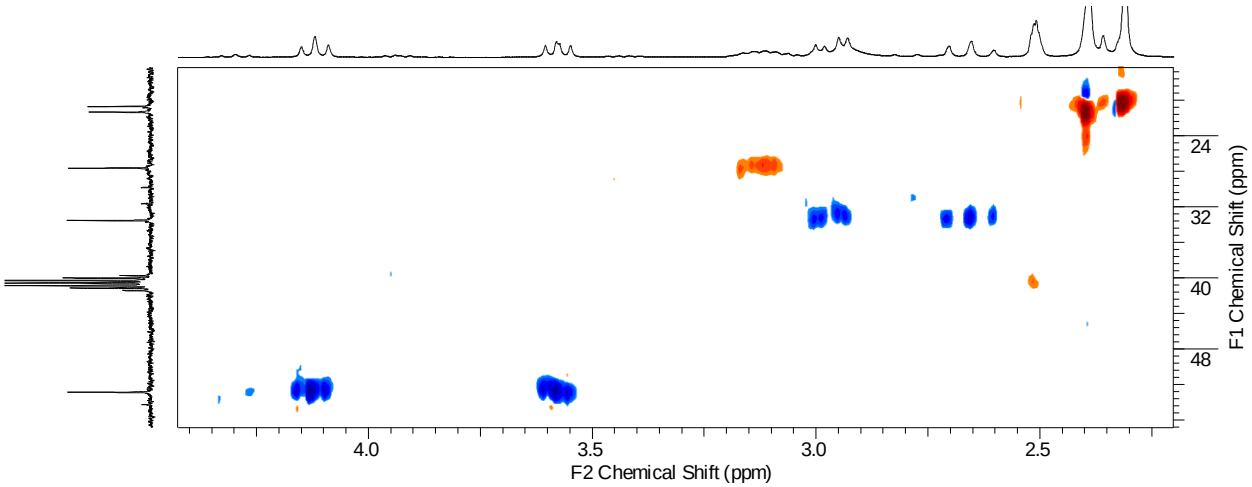




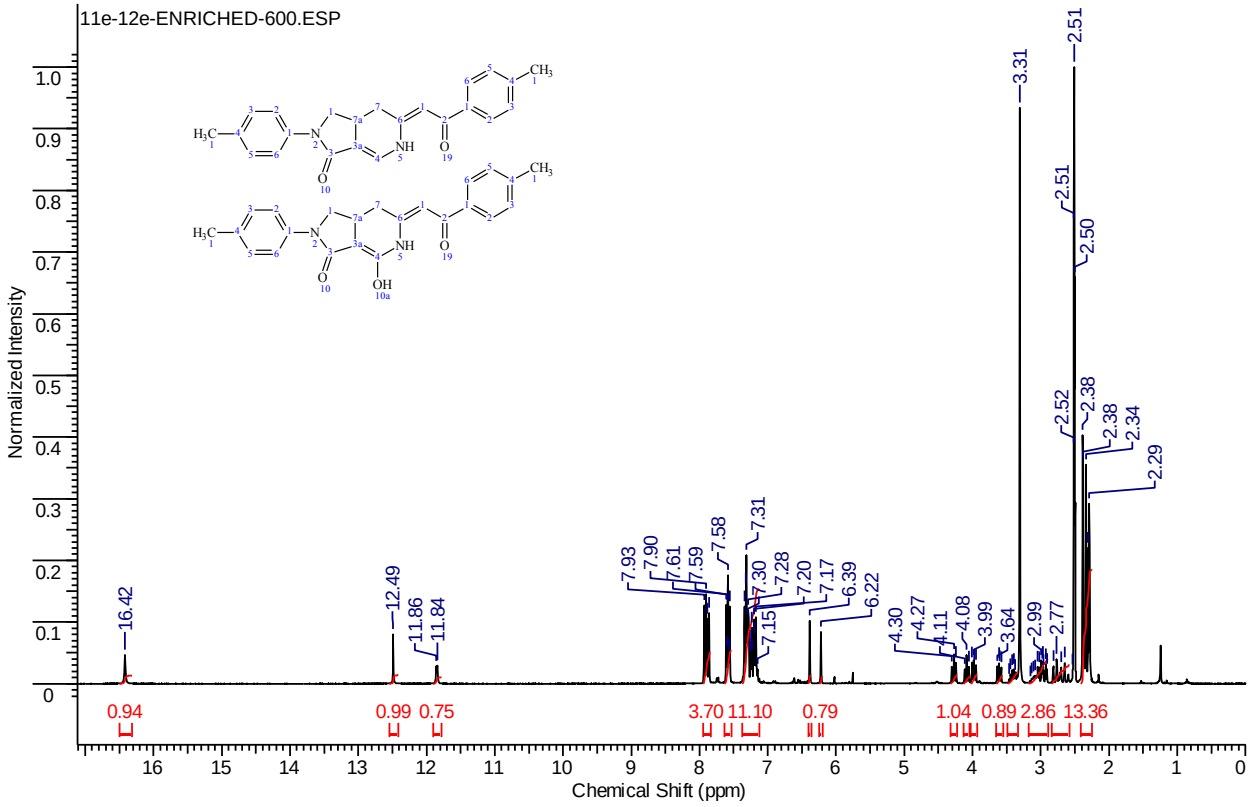
HMQC of 11e/12e



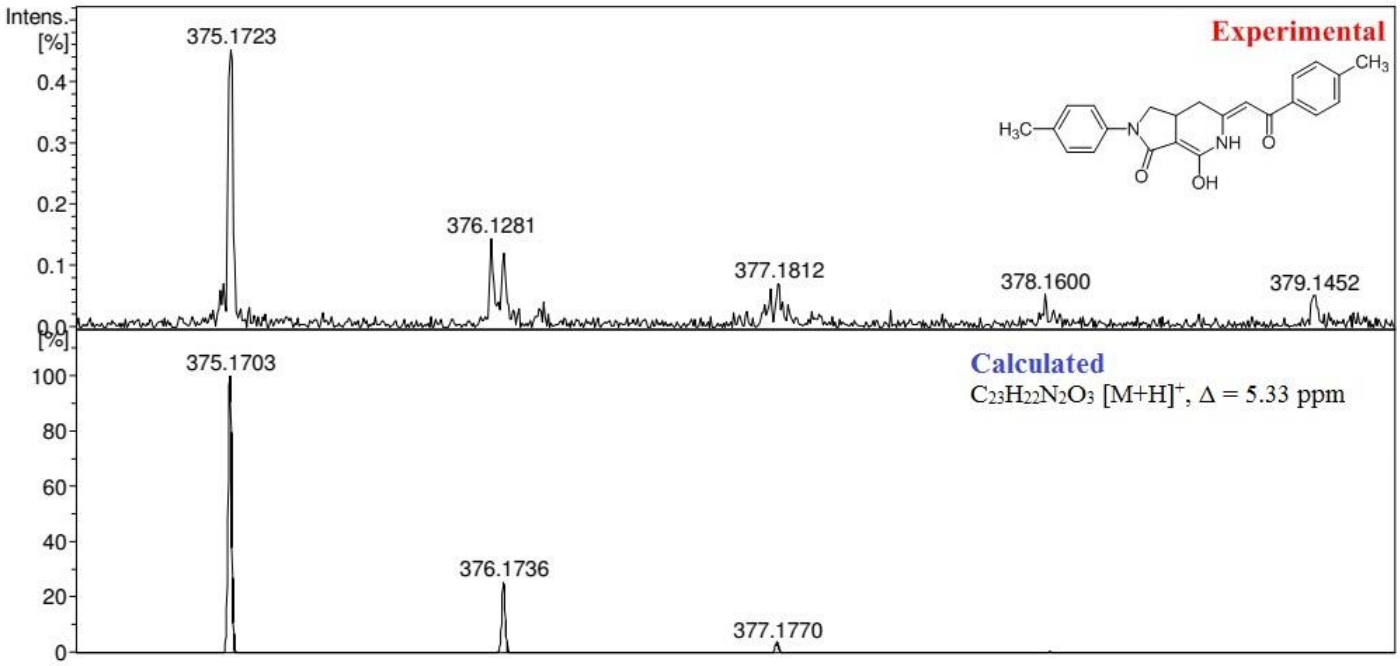




^{1}H NMR (600.2 MHz, DMSO-d_6) *enriched sample for 11e/12e mixture*

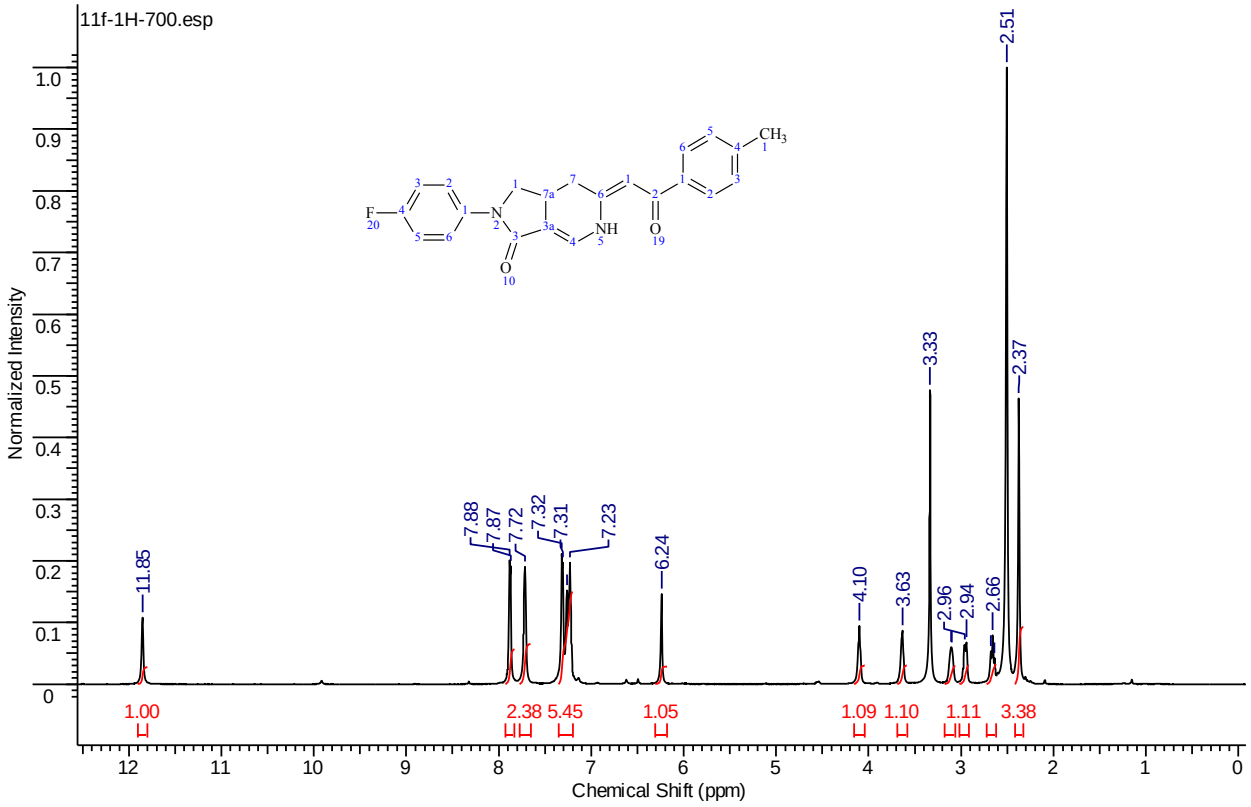


HRMS (ESI) spectrum of (6*Z*)-4-hydroxy-2-(4-methylphenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (12e)

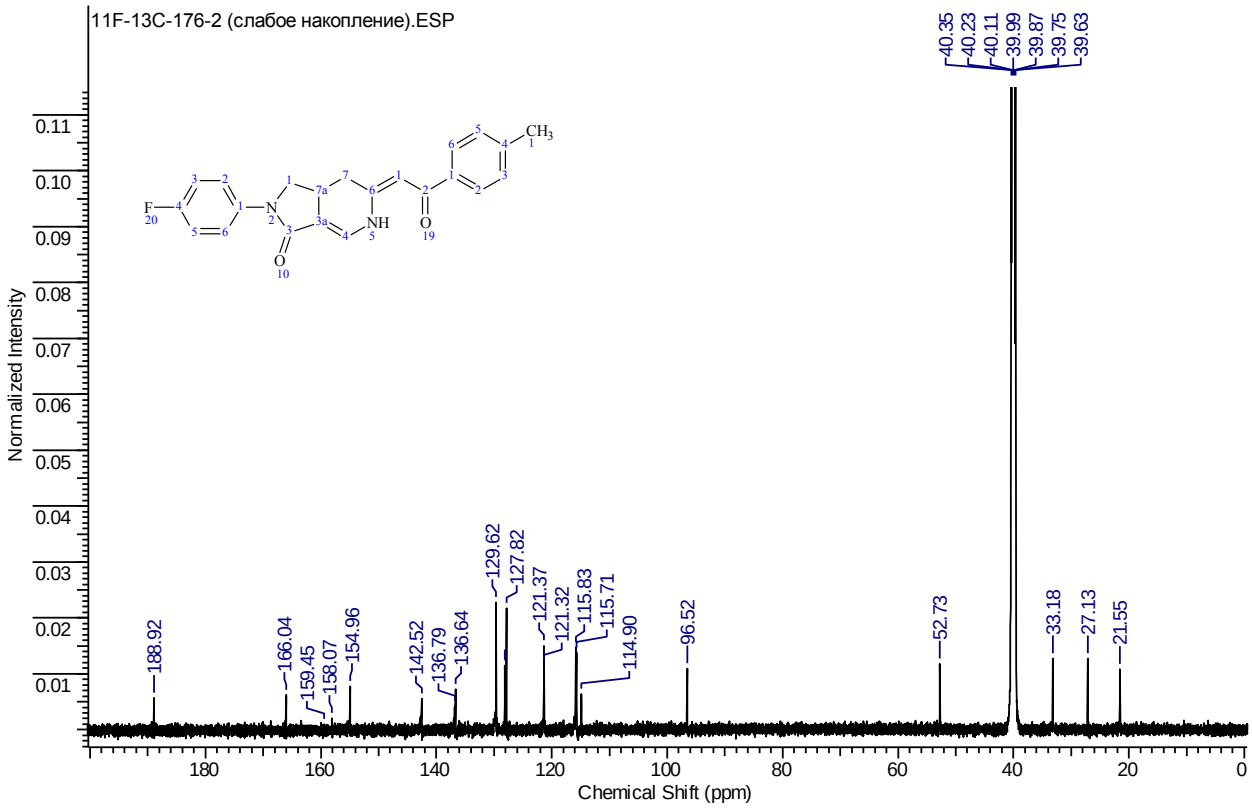


(6*Z*)-2-(4-Fluorophenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11f).

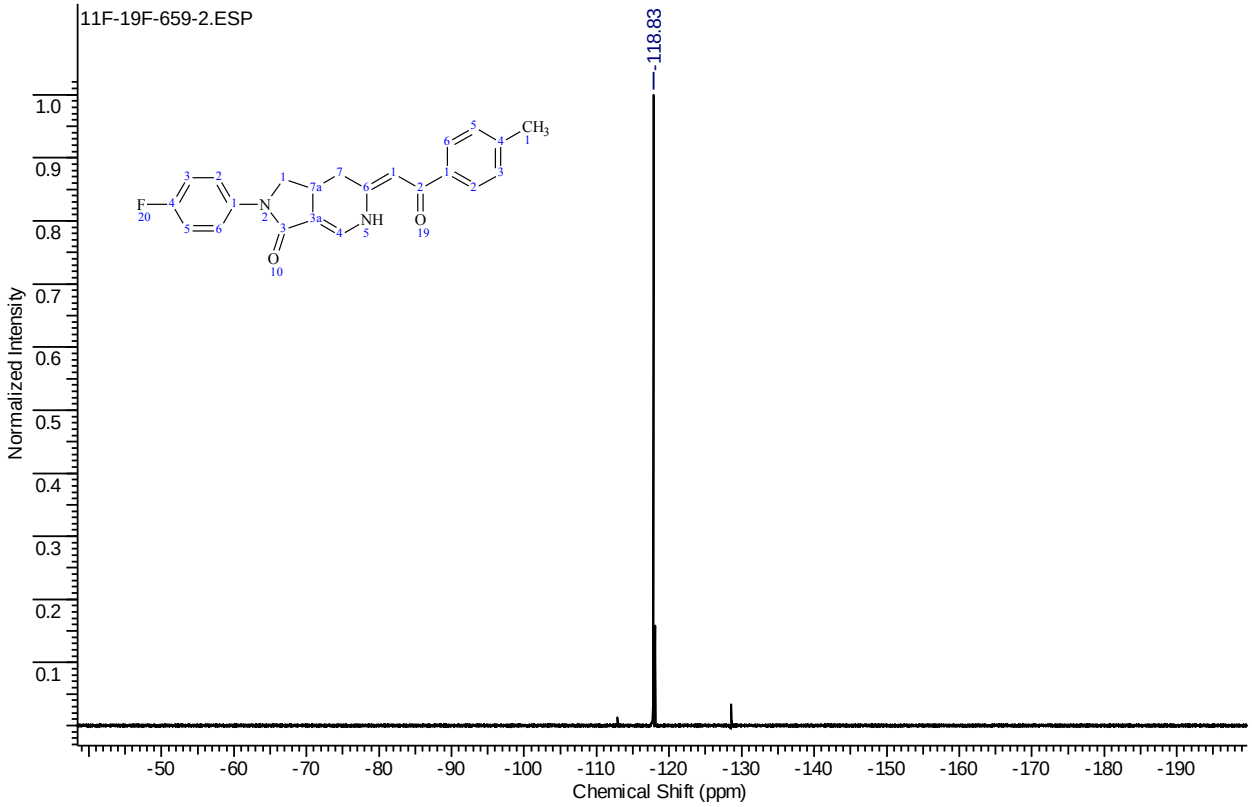
^{1}H NMR (700.2 MHz, DMSO-d_6)



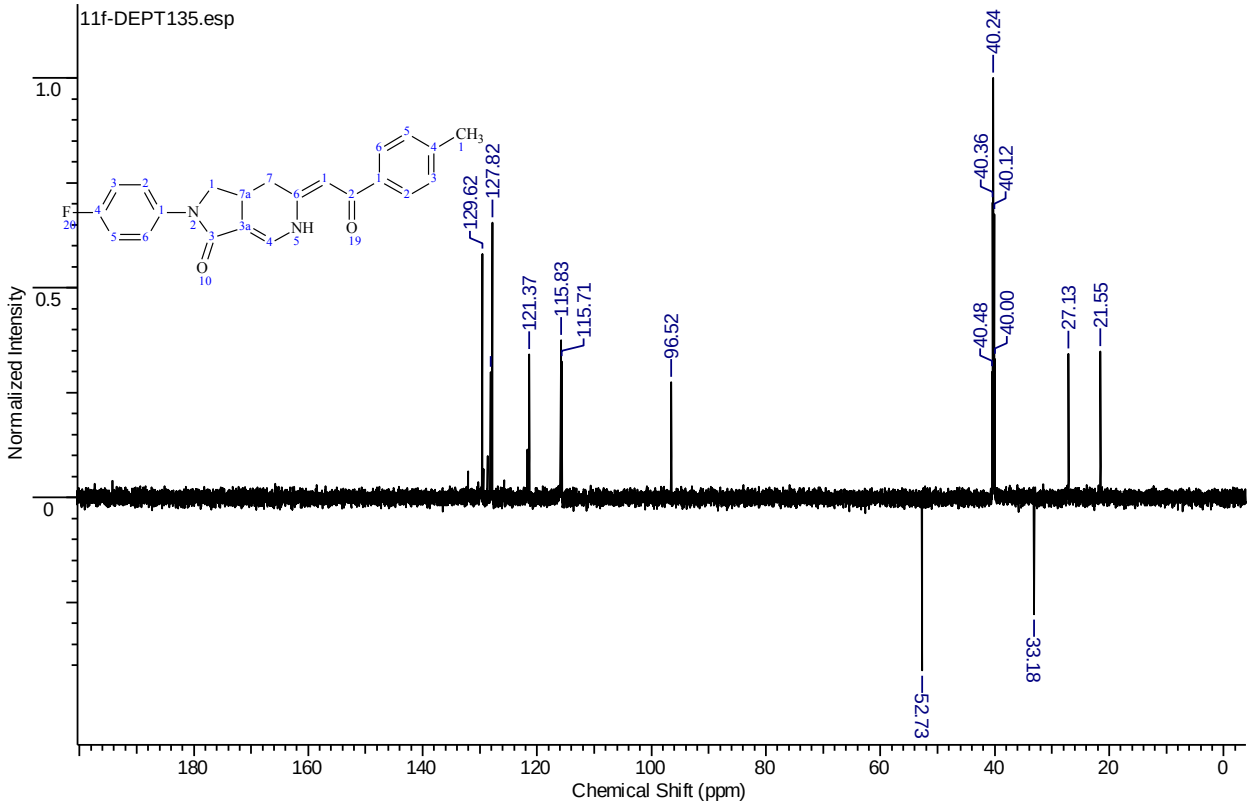
^{13}C NMR (176.1 MHz, DMSO-d_6)



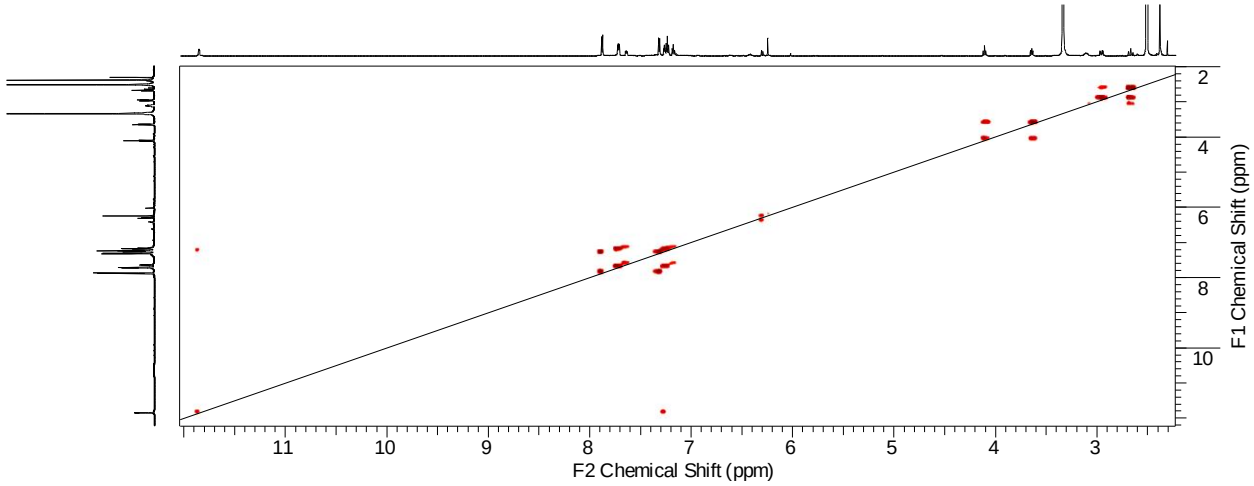
^{19}F NMR (658.8 MHz, DMSO-d_6)

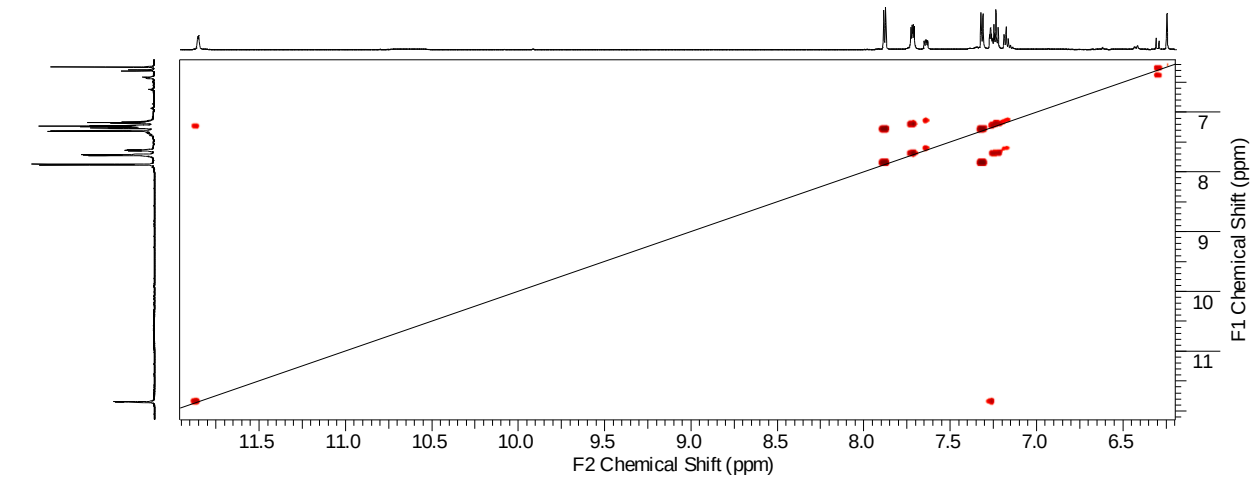


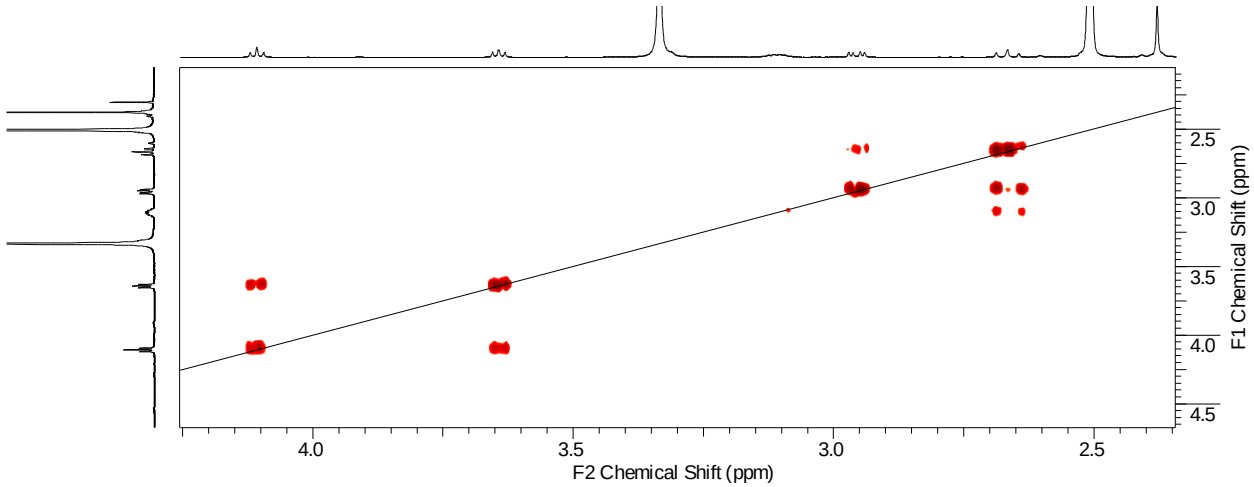
DEPT135



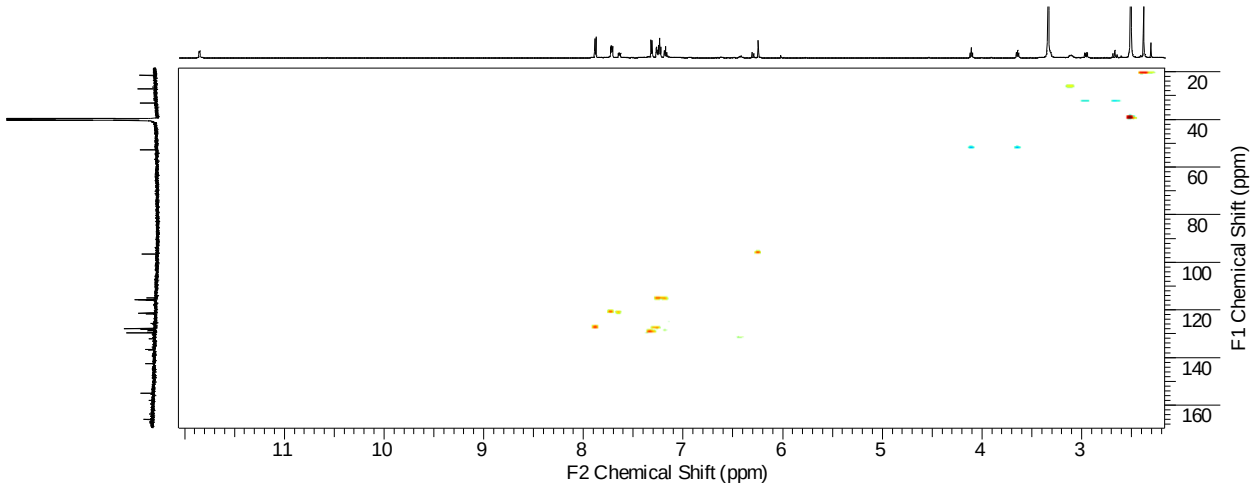
COSY of 11f

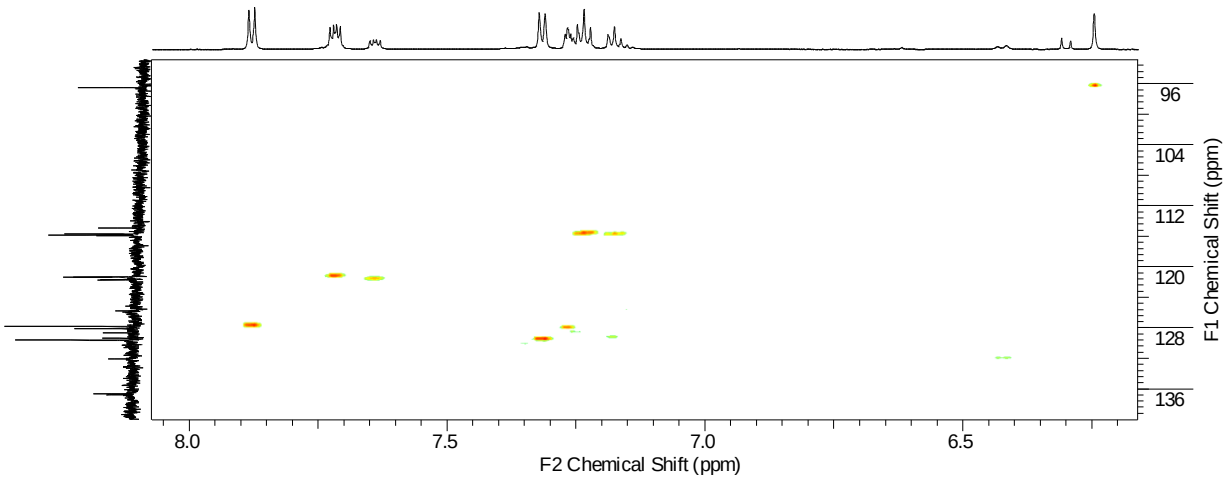

F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

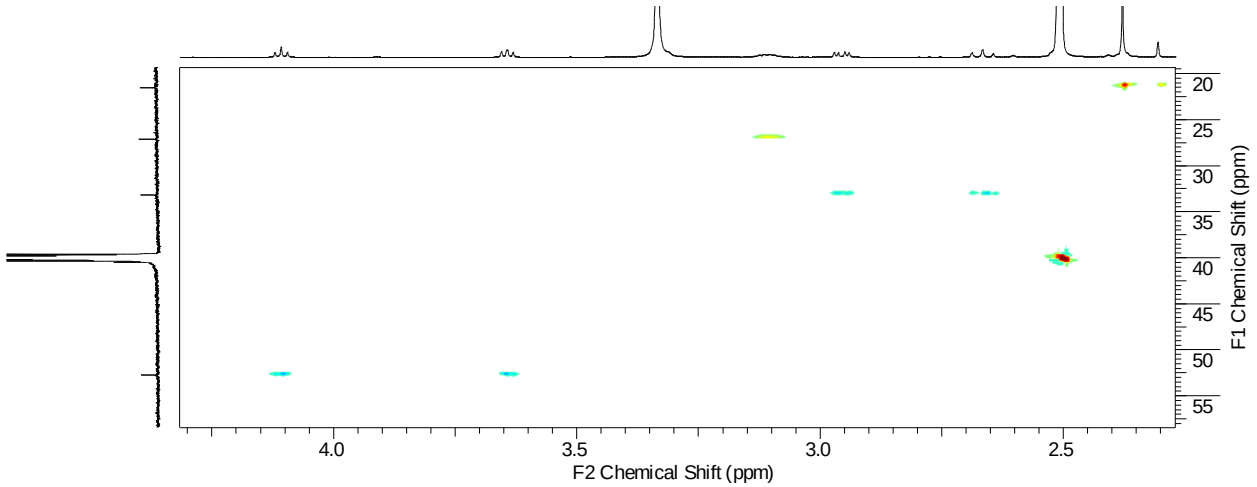

F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)


F2 Chemical Shift (ppm)
F1 Chemical Shift (ppm)

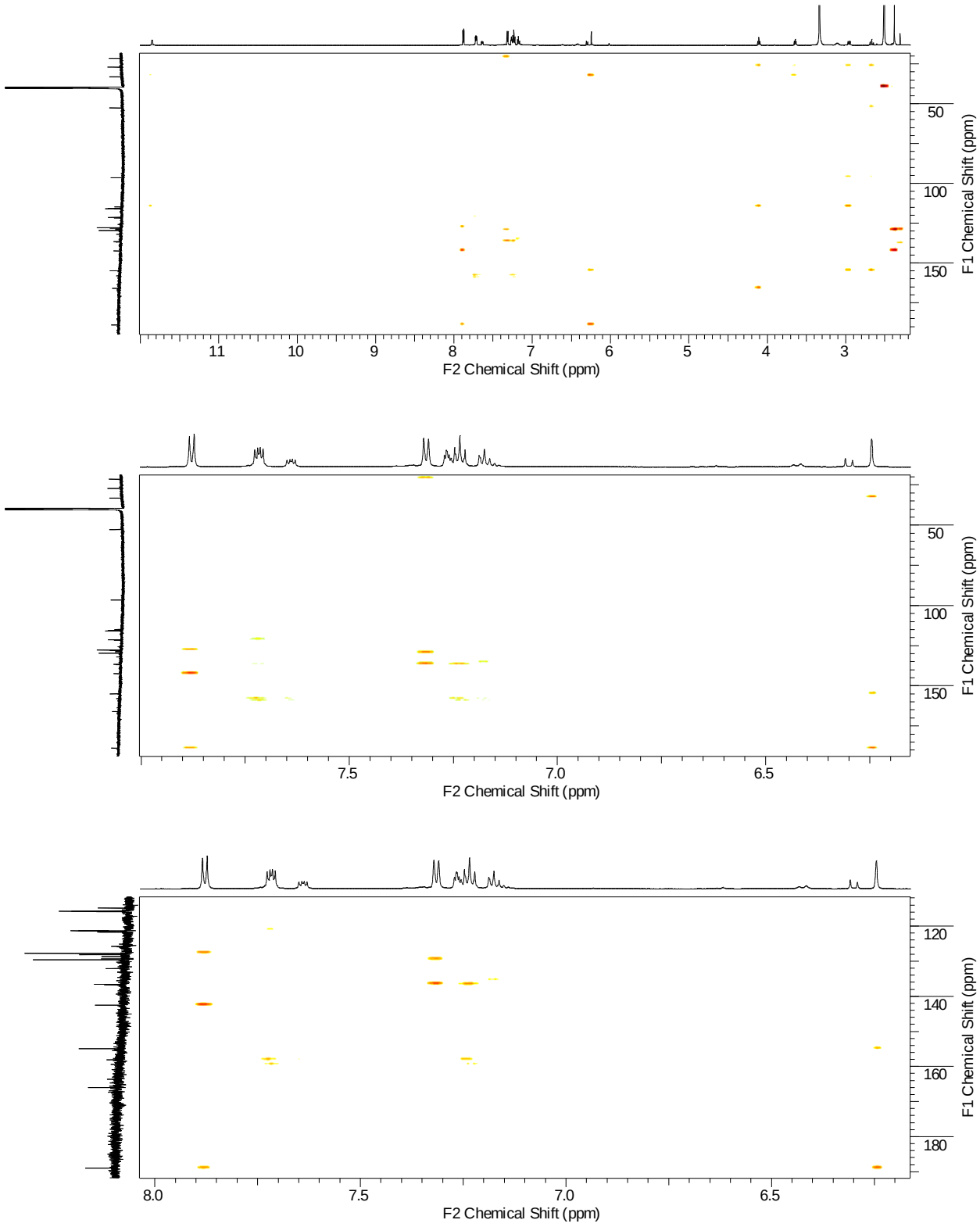
HSQC of 11f

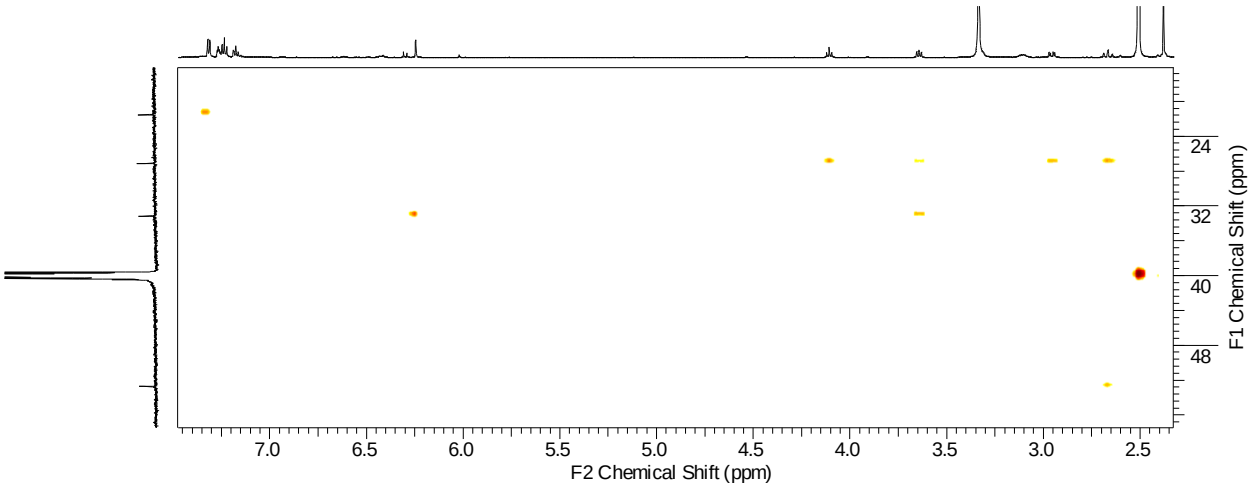

20
40
60
80
100
120
140
160
F1 Chemical Shift (ppm)
11
10
9
8
7
6
5
4
3
F2 Chemical Shift (ppm)


96
104
112
120
128
136
F1 Chemical Shift (ppm)
8.0
7.5
7.0
6.5
F2 Chemical Shift (ppm)


20
25
30
35
40
45
50
55
F1 Chemical Shift (ppm)
4.0
3.5
3.0
2.5
F2 Chemical Shift (ppm)

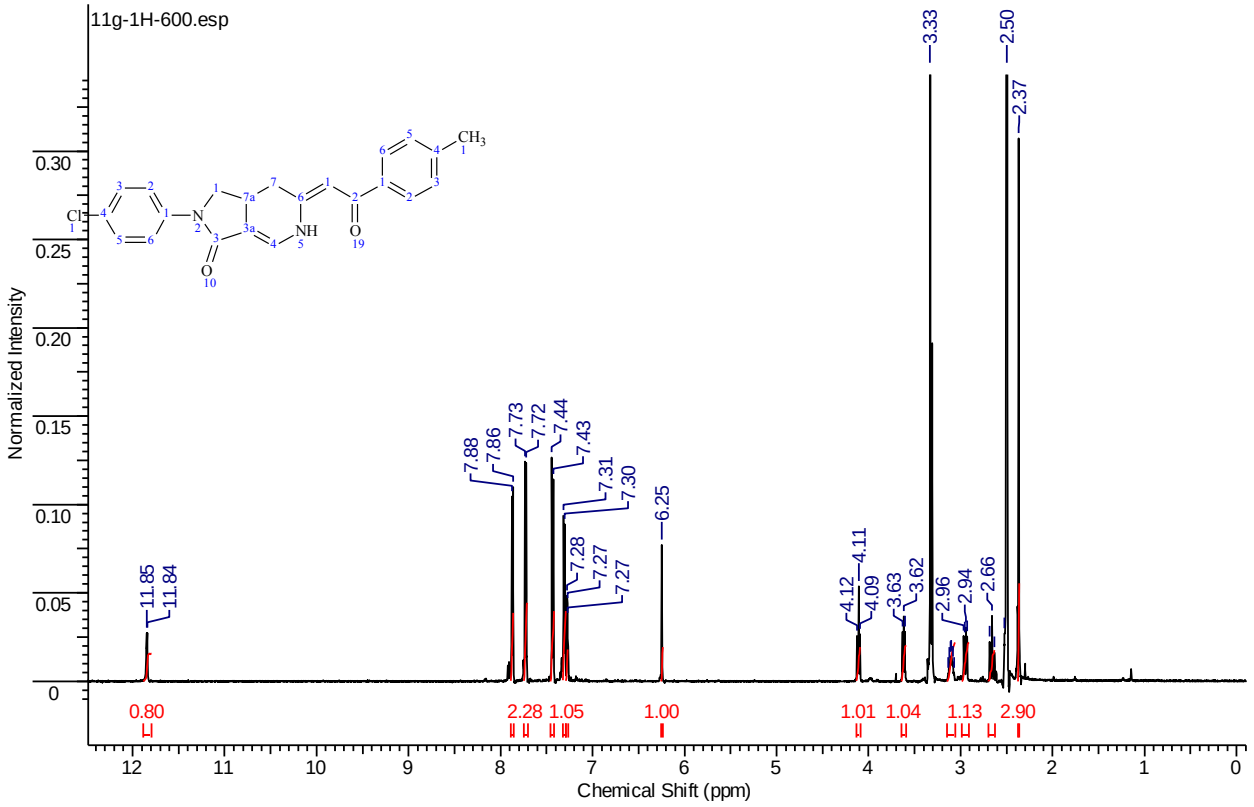
HMBC of 11f

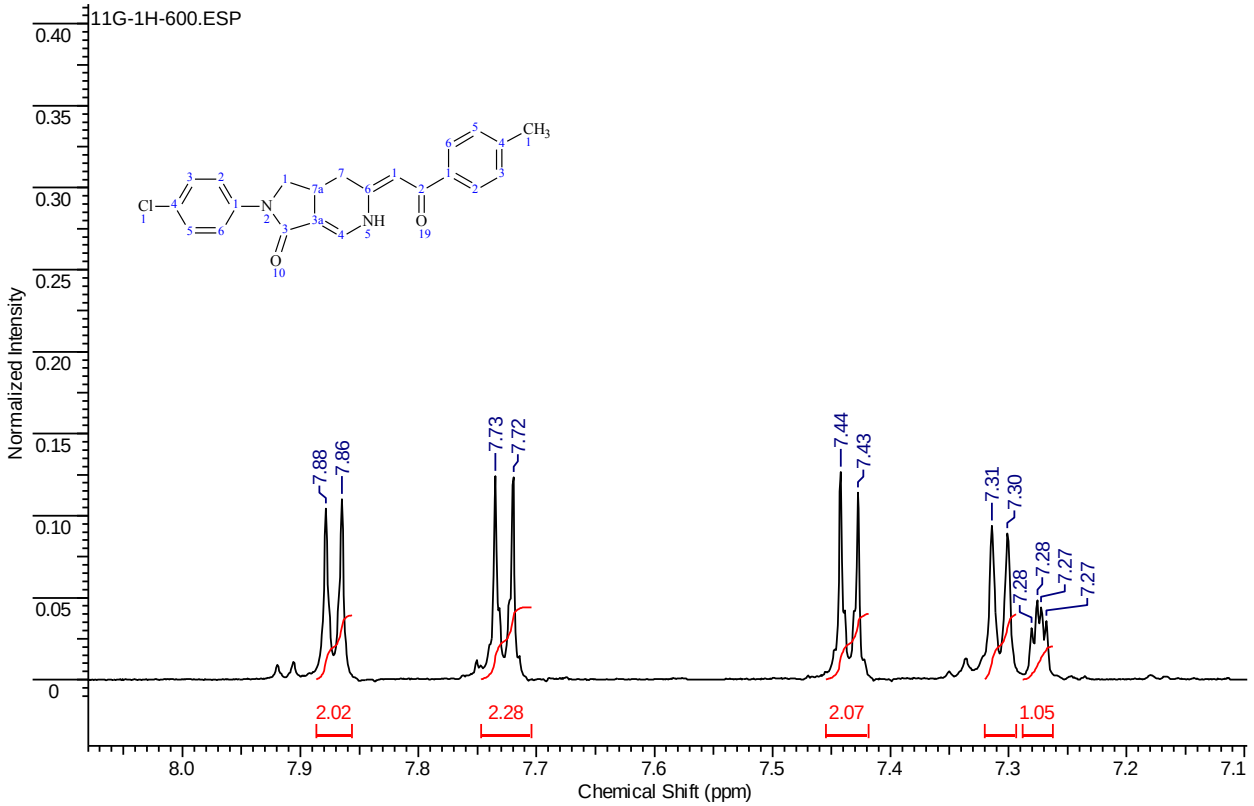

11
10
9
8
7
6
5
4
3
F2 Chemical Shift (ppm)
50
100
150
F1 Chemical Shift (ppm)
7.5
7.0
6.5
F2 Chemical Shift (ppm)
50
100
150
F1 Chemical Shift (ppm)
8.0
7.5
7.0
6.5
F2 Chemical Shift (ppm)
120
140
160
180
F1 Chemical Shift (ppm)

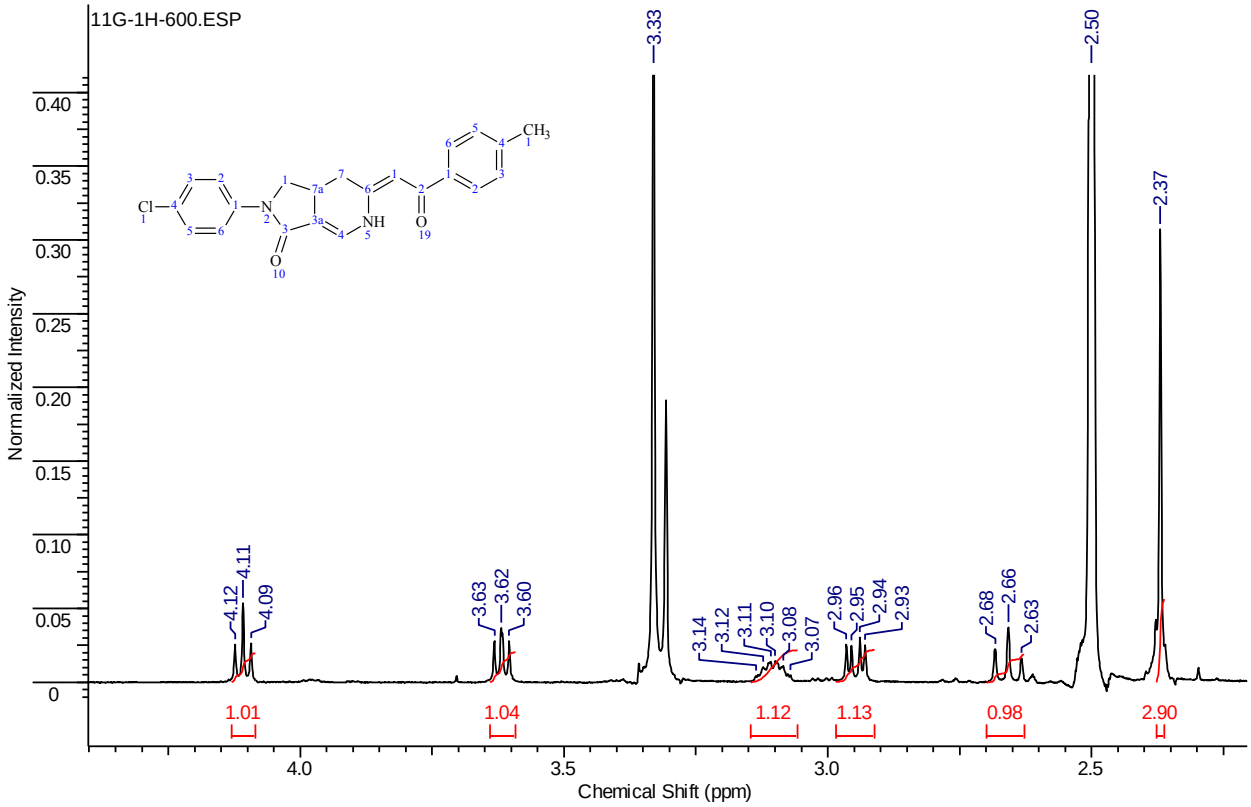

24
32
40
48
F1 Chemical Shift (ppm)
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
F2 Chemical Shift (ppm)

(6*Z*)-2-(4-Chlorophenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11g).

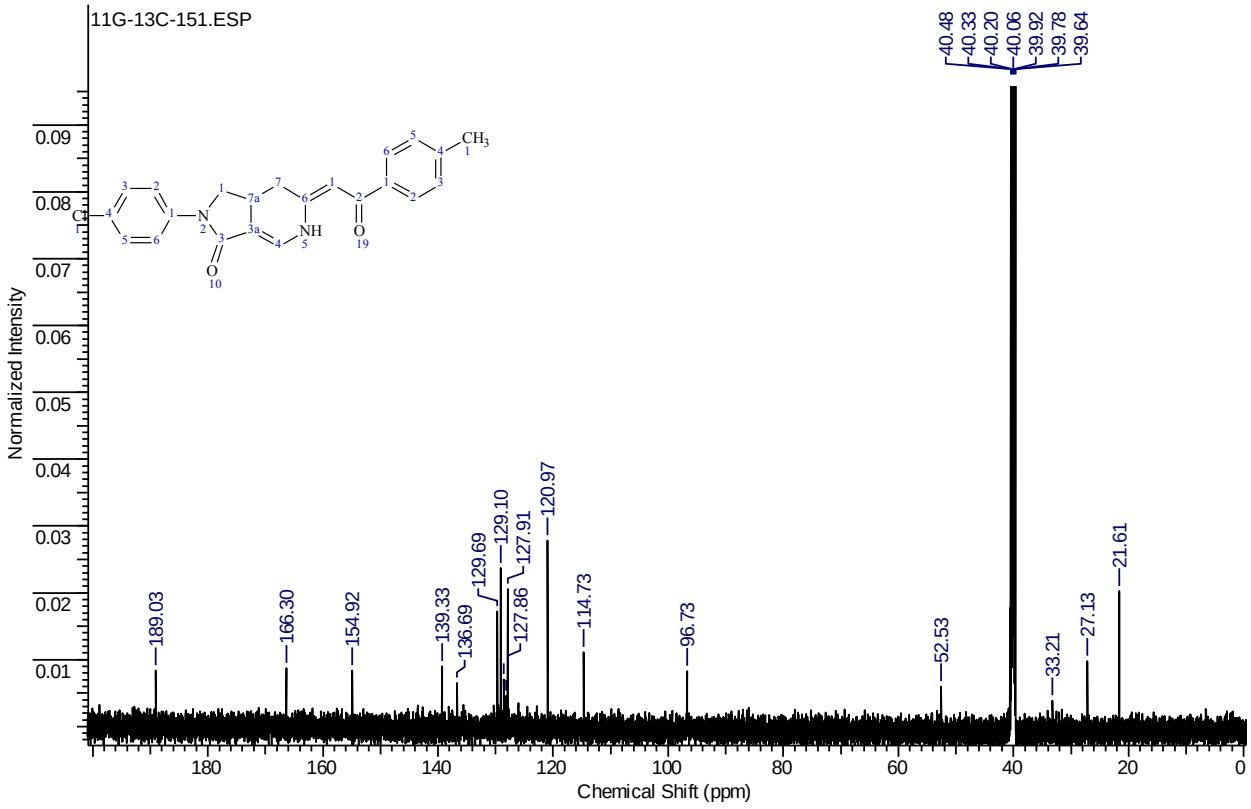
^{1}H NMR (600.2 MHz, DMSO-d_6)





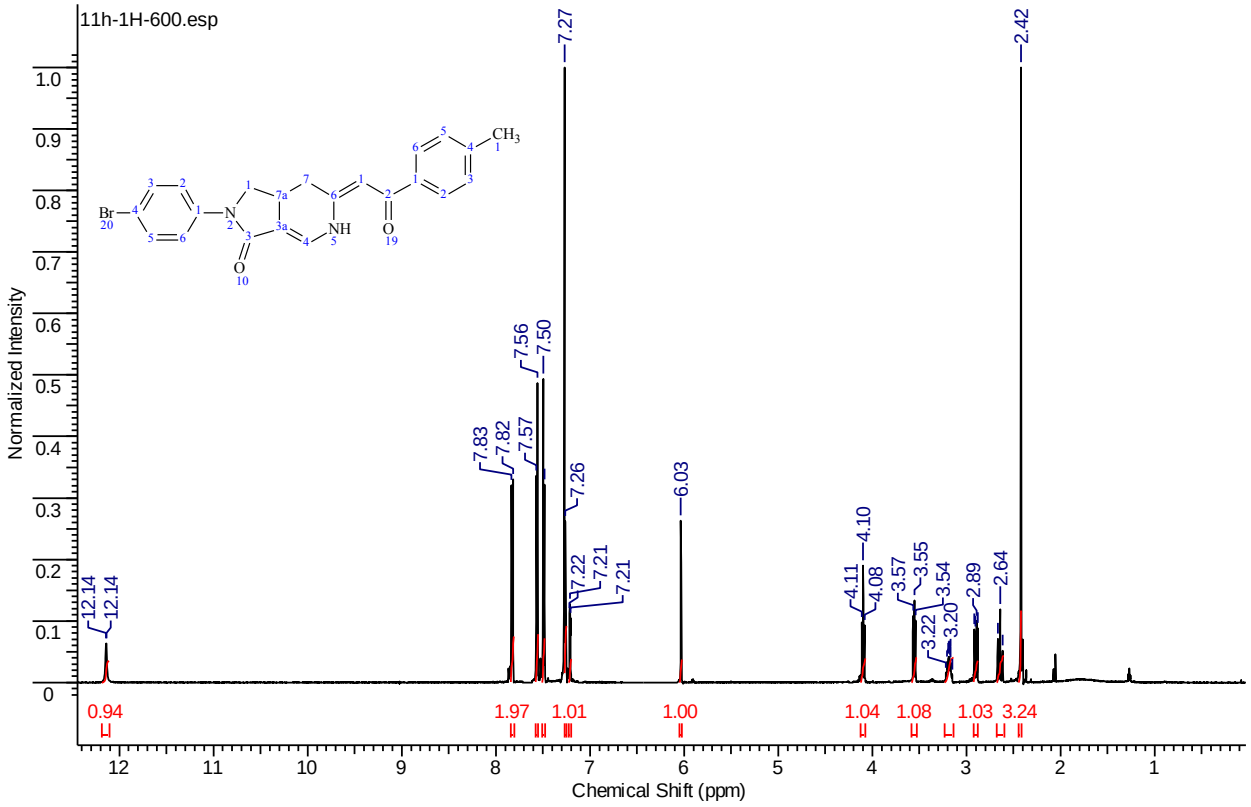


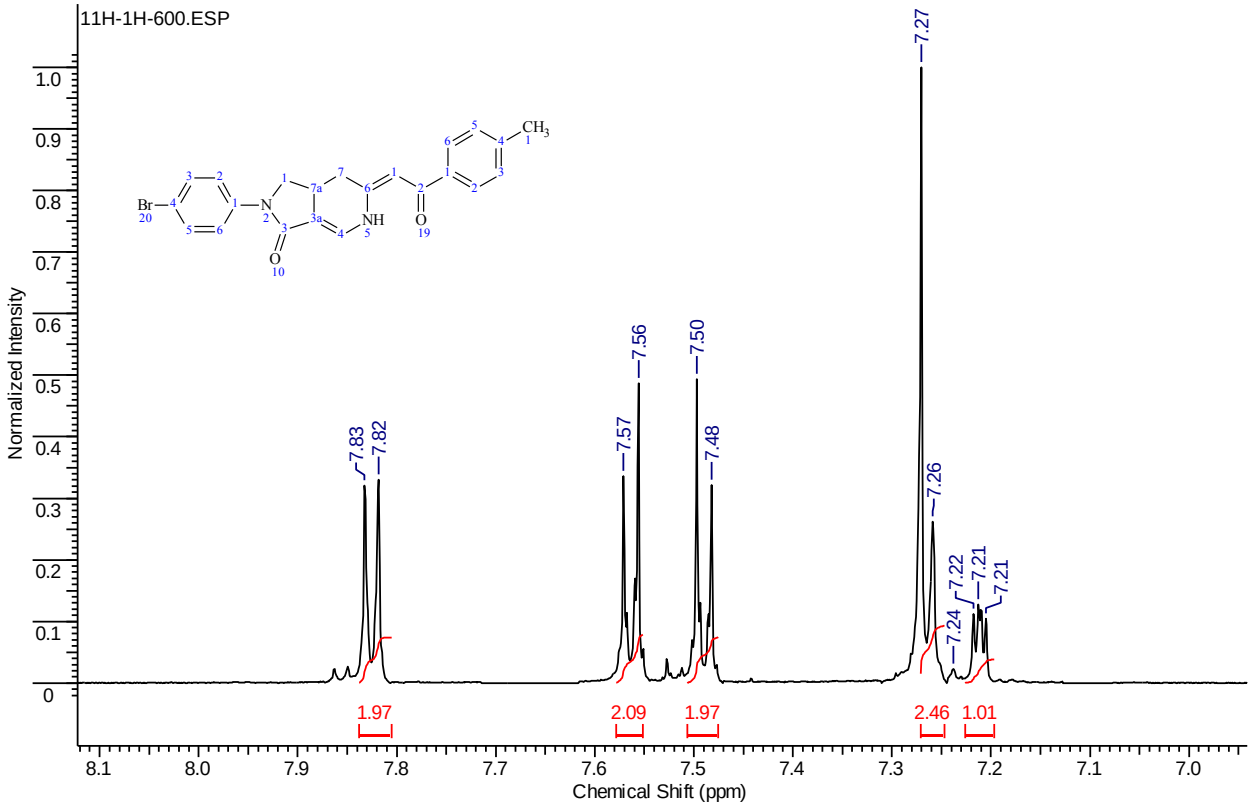
^{13}C NMR (150.9 MHz, DMSO-d_6)



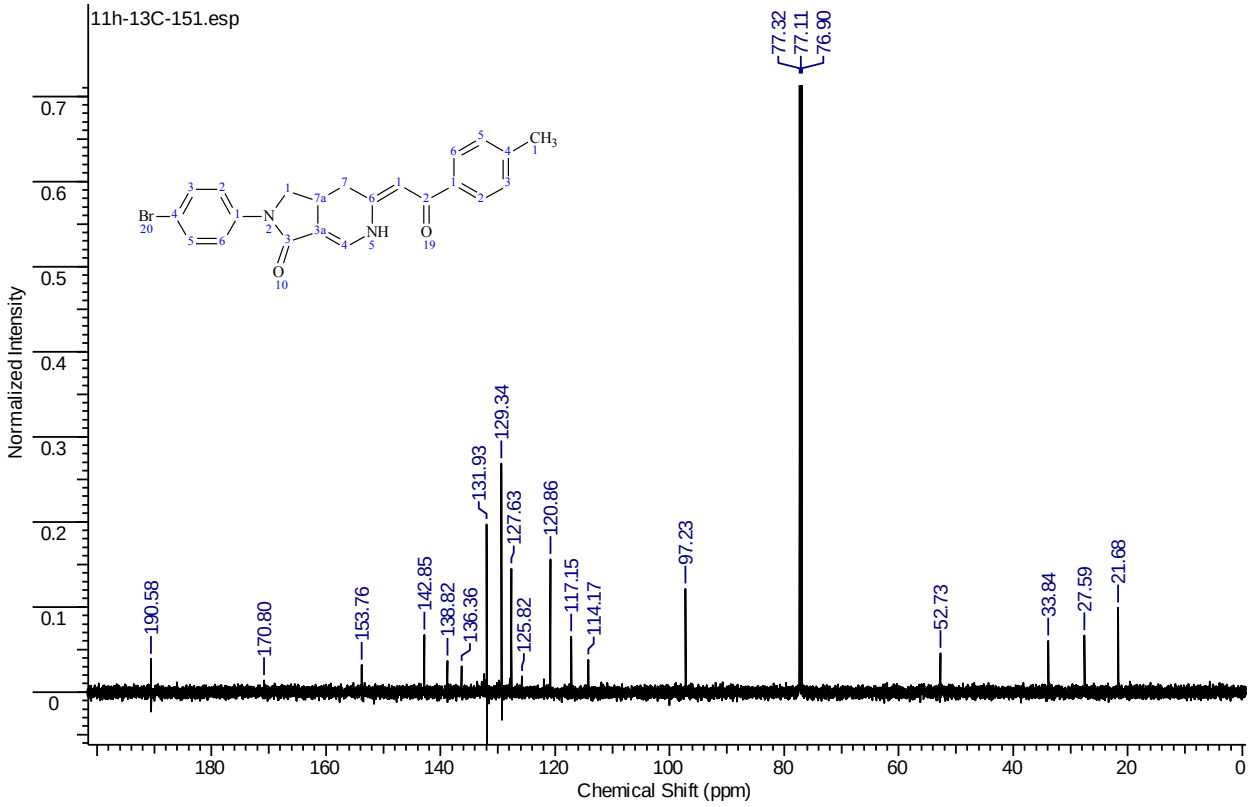
(6*Z*)-2-(4-Bromophenyl)-6-[2-(4-methylphenyl)-2-oxoethylidene]-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11h).

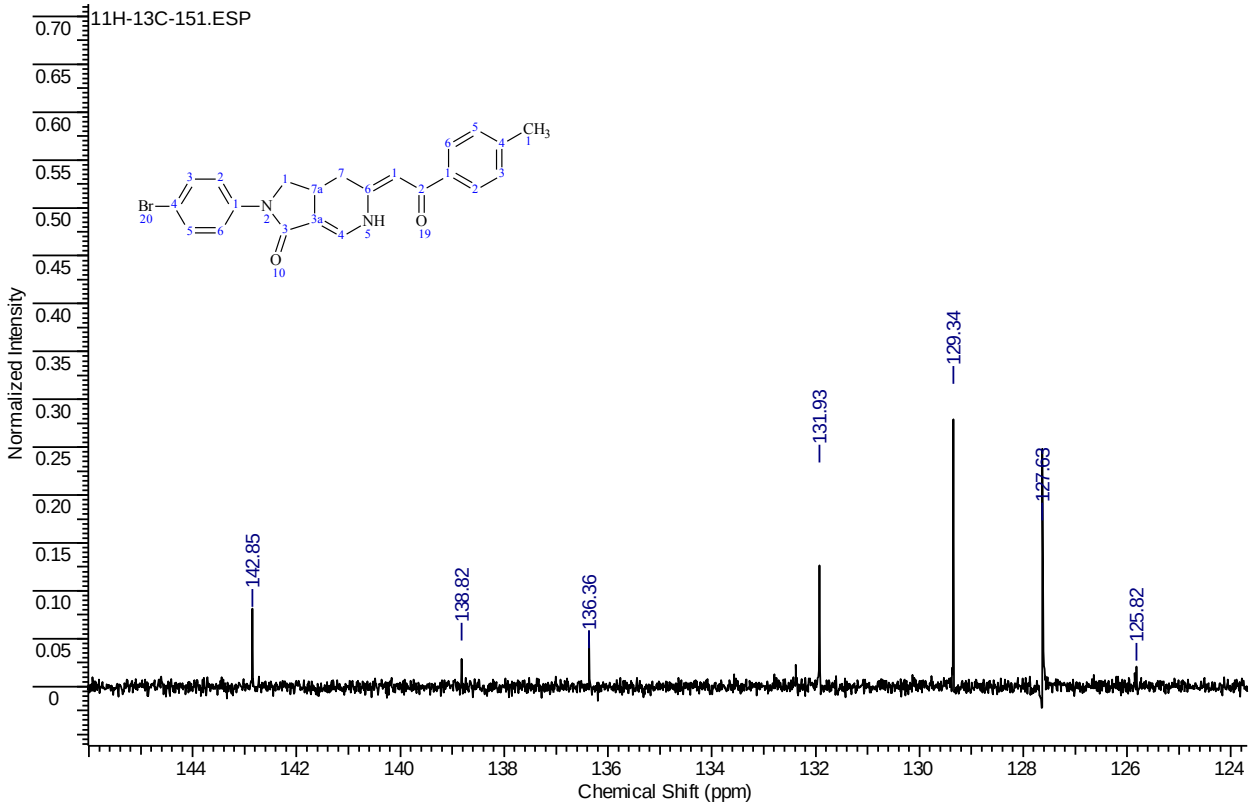
^{1}H NMR (600.2 MHz, $CDCl_3$)





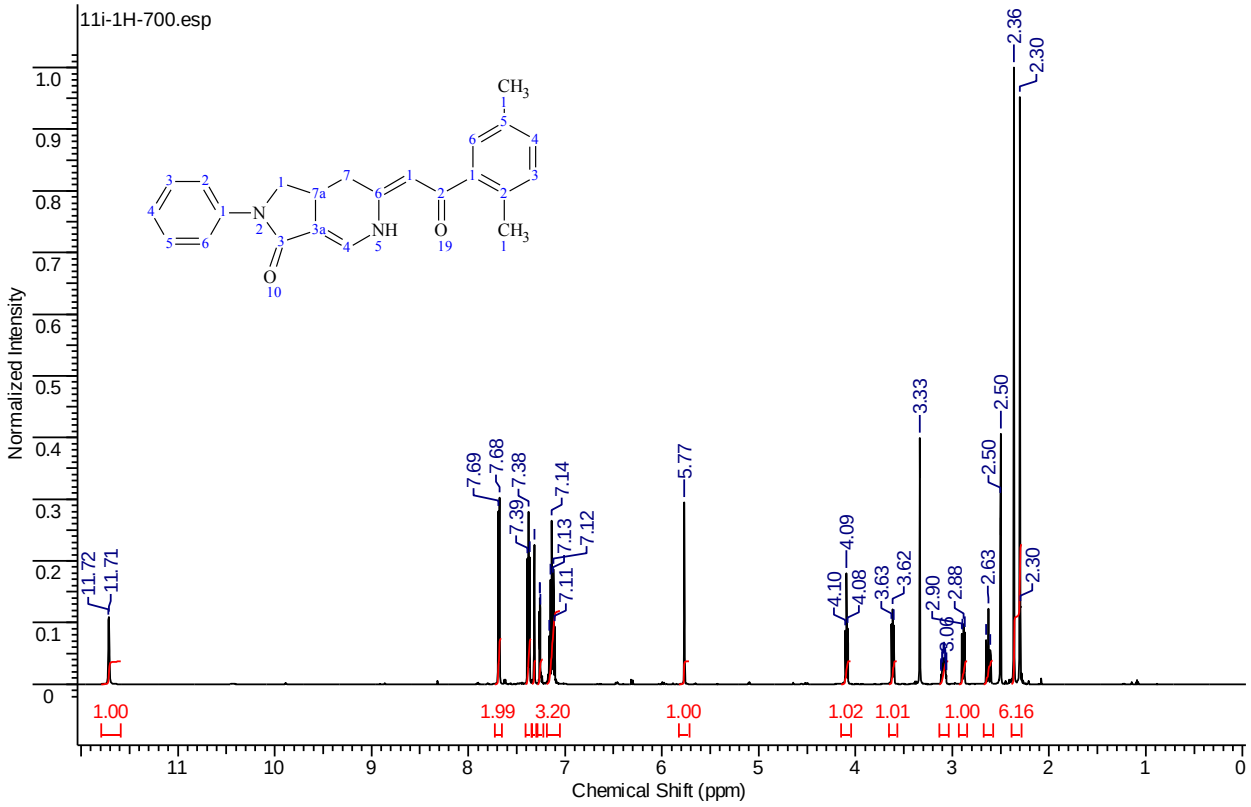
^{13}C NMR (150.9 MHz, $CDCl_3$)

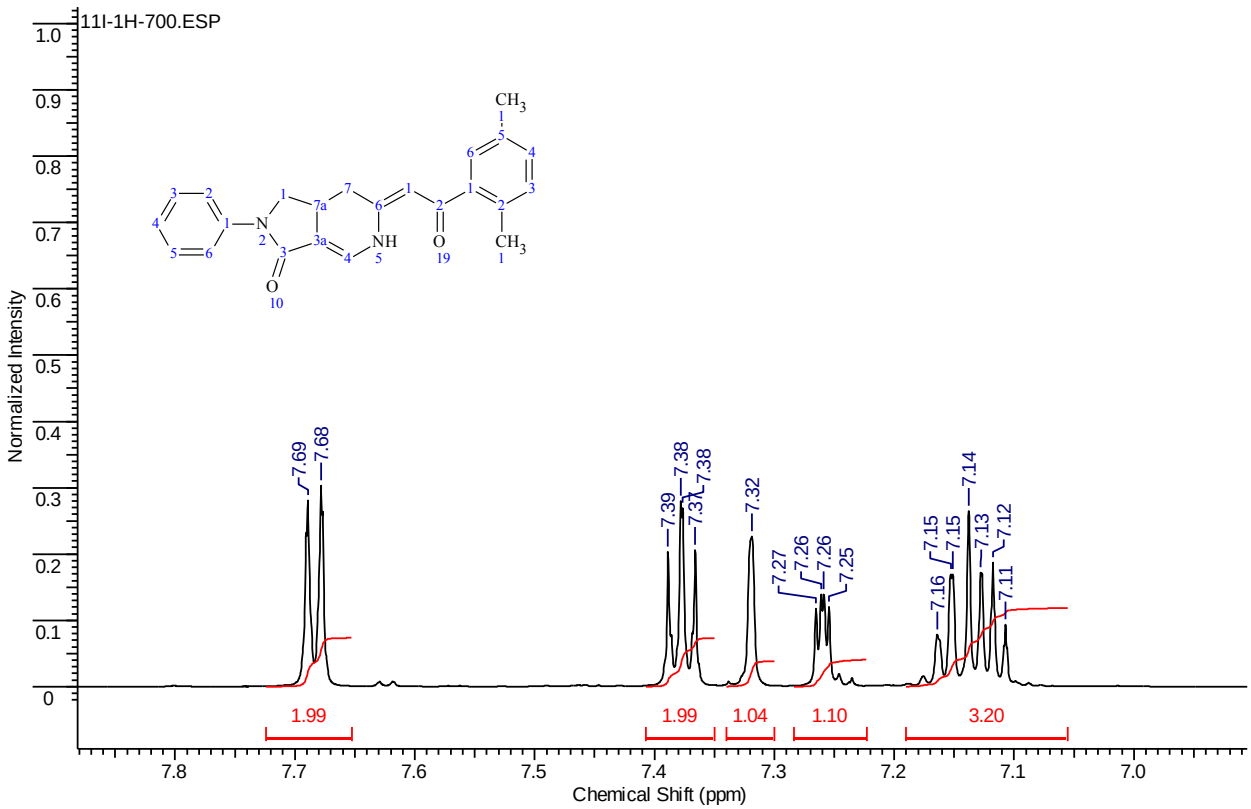




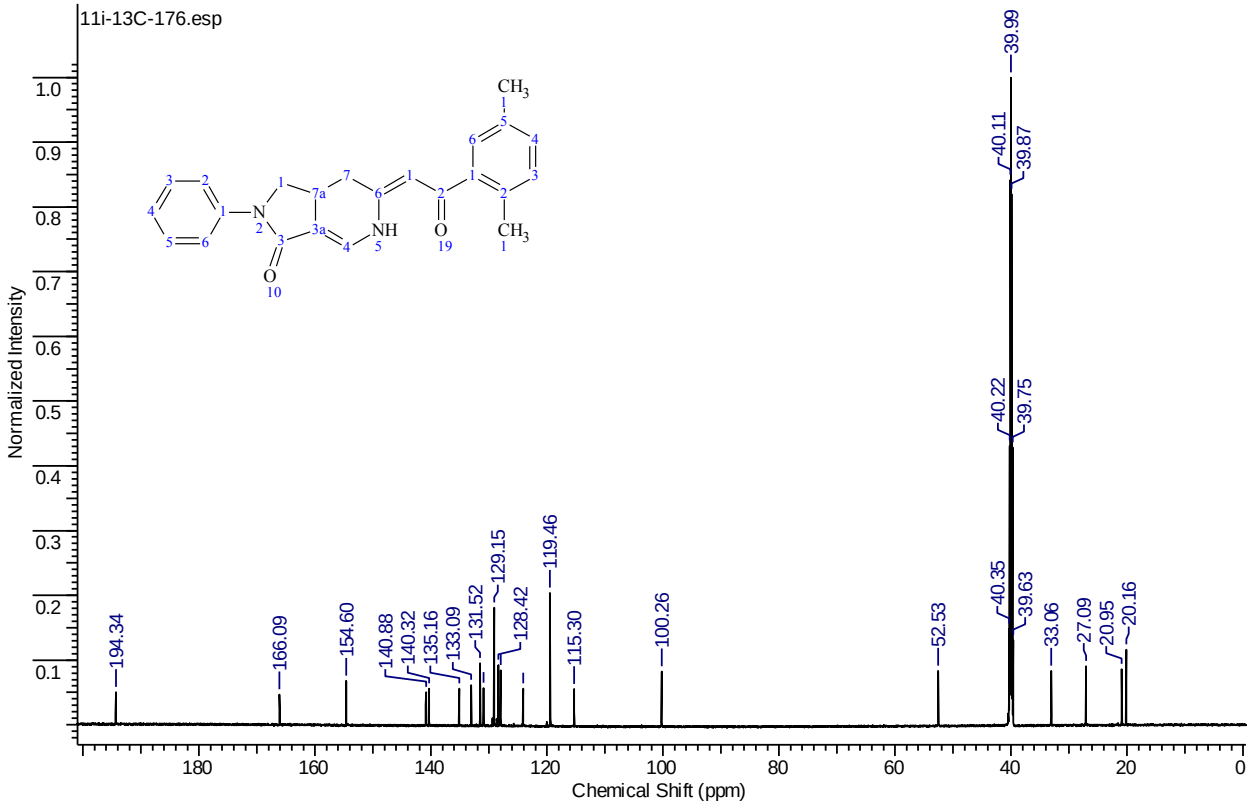
(6*Z*)-6-[2-(2,5-Dimethylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11i).

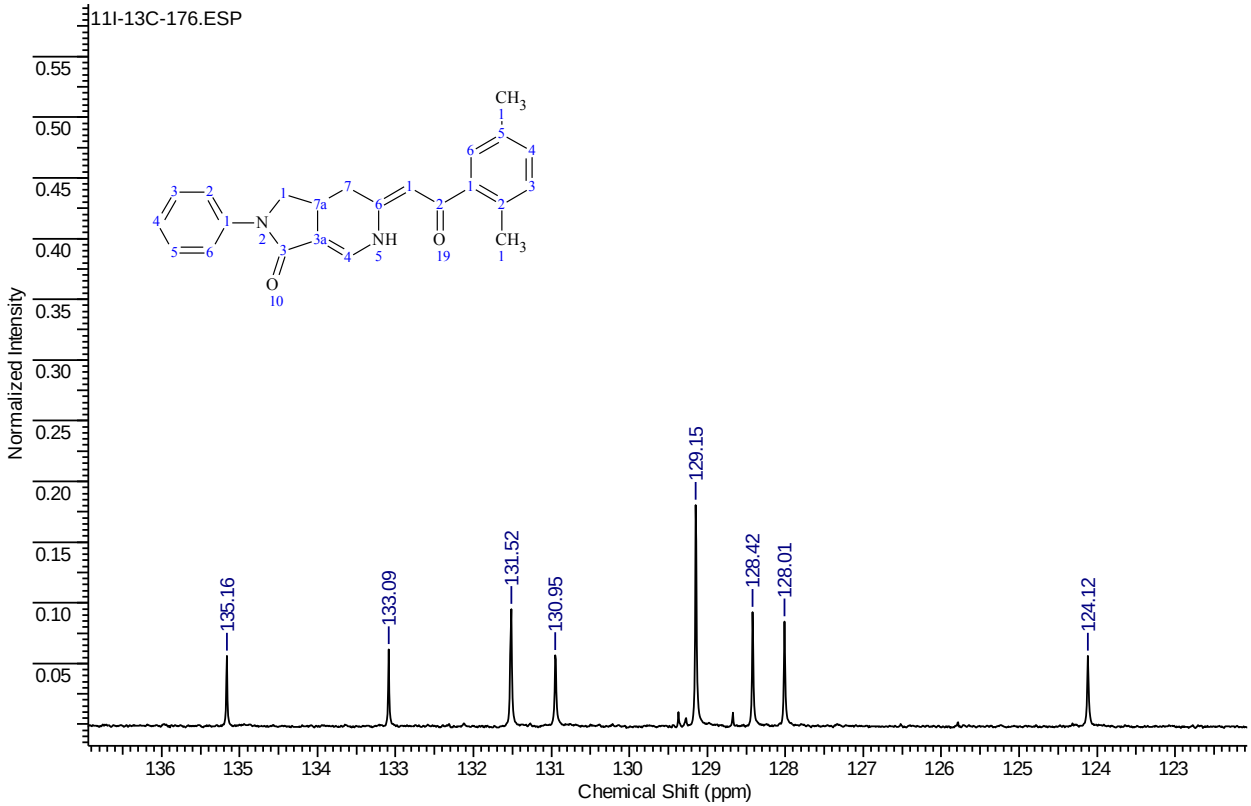
^{1}H NMR (700.2 MHz, DMSO-d_6)





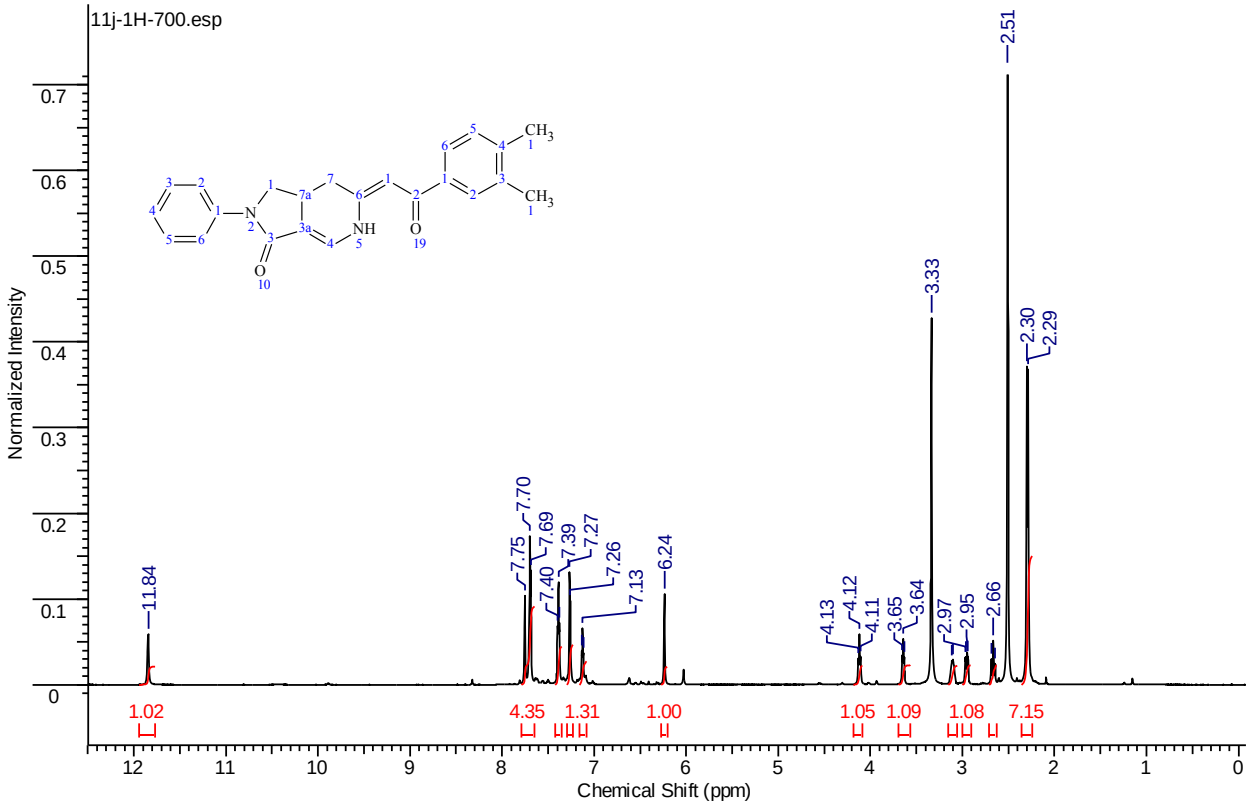
^{13}C NMR (176.1 MHz, DMSO-d_6)

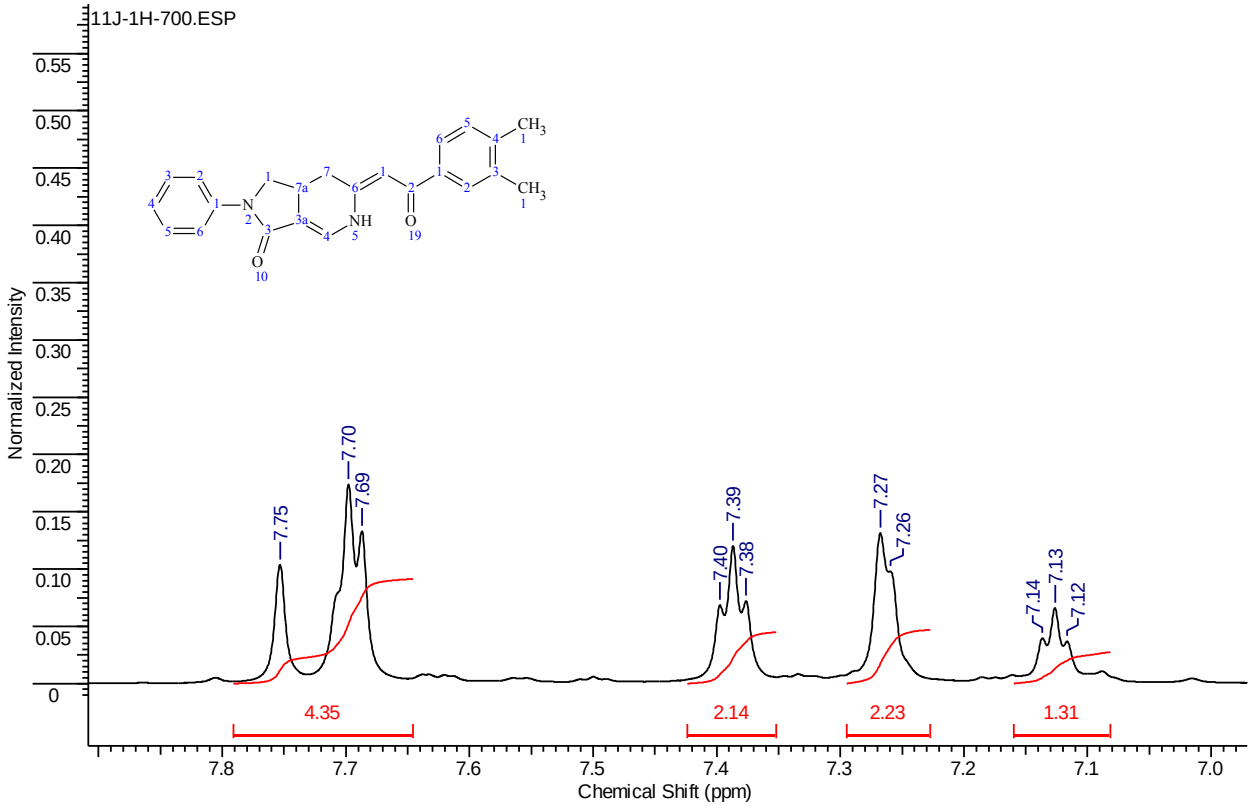




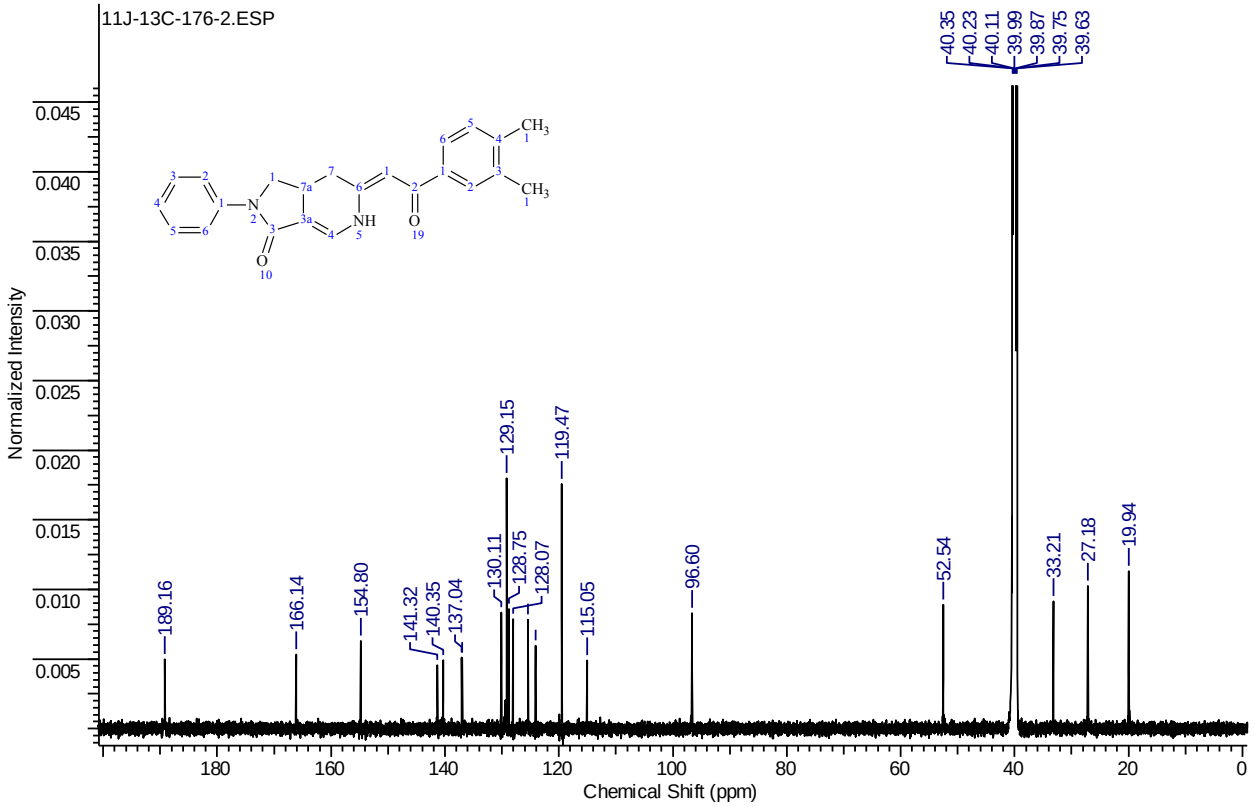
(6*Z*)-6-[2-(3,4-Dimethylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11j).

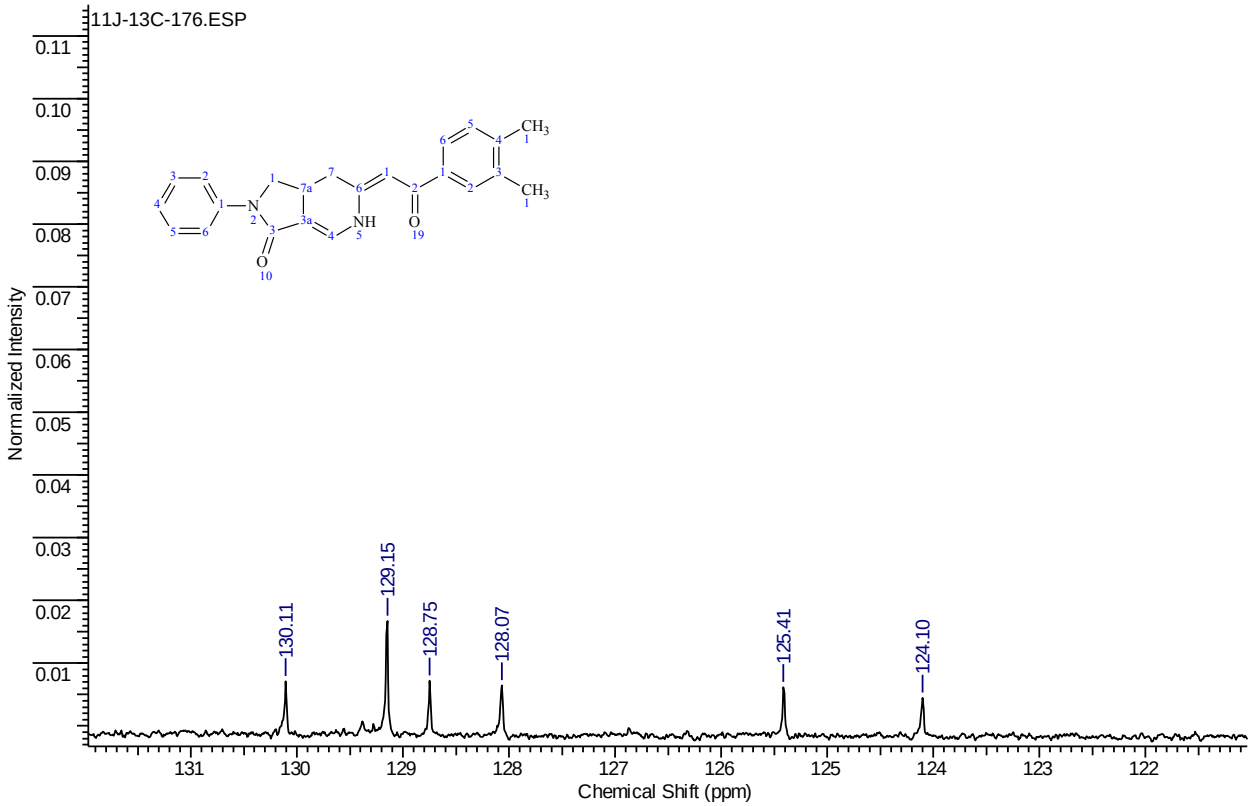
^{1}H NMR (700.2 MHz, DMSO-d_6)





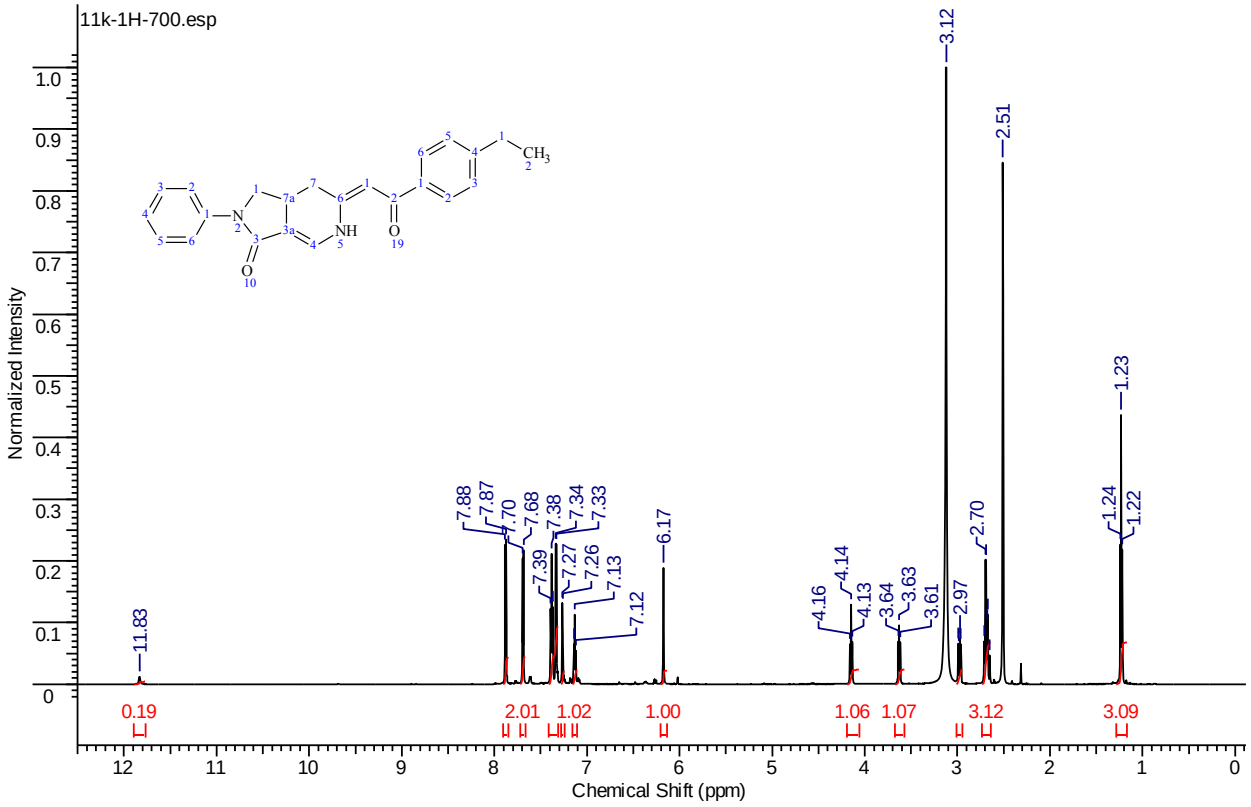
^{13}C NMR (176.1 MHz, DMSO-d_6)

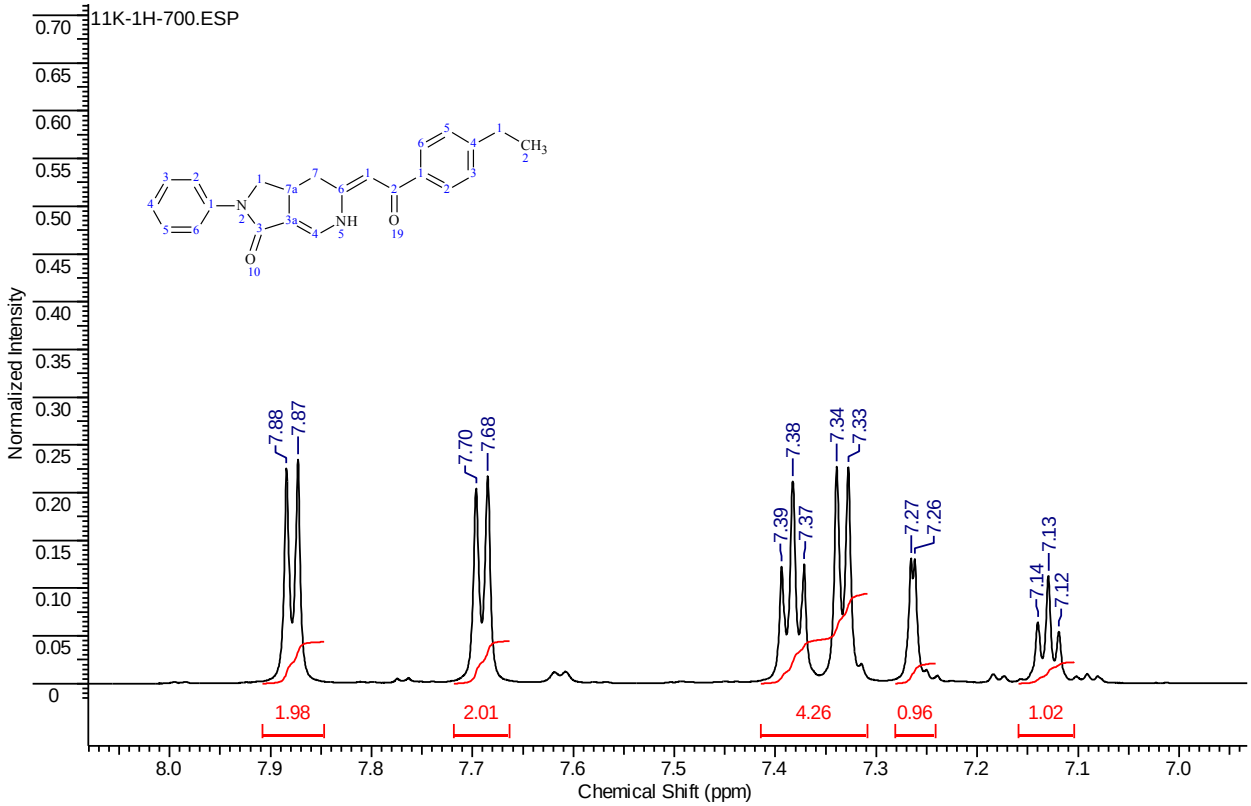




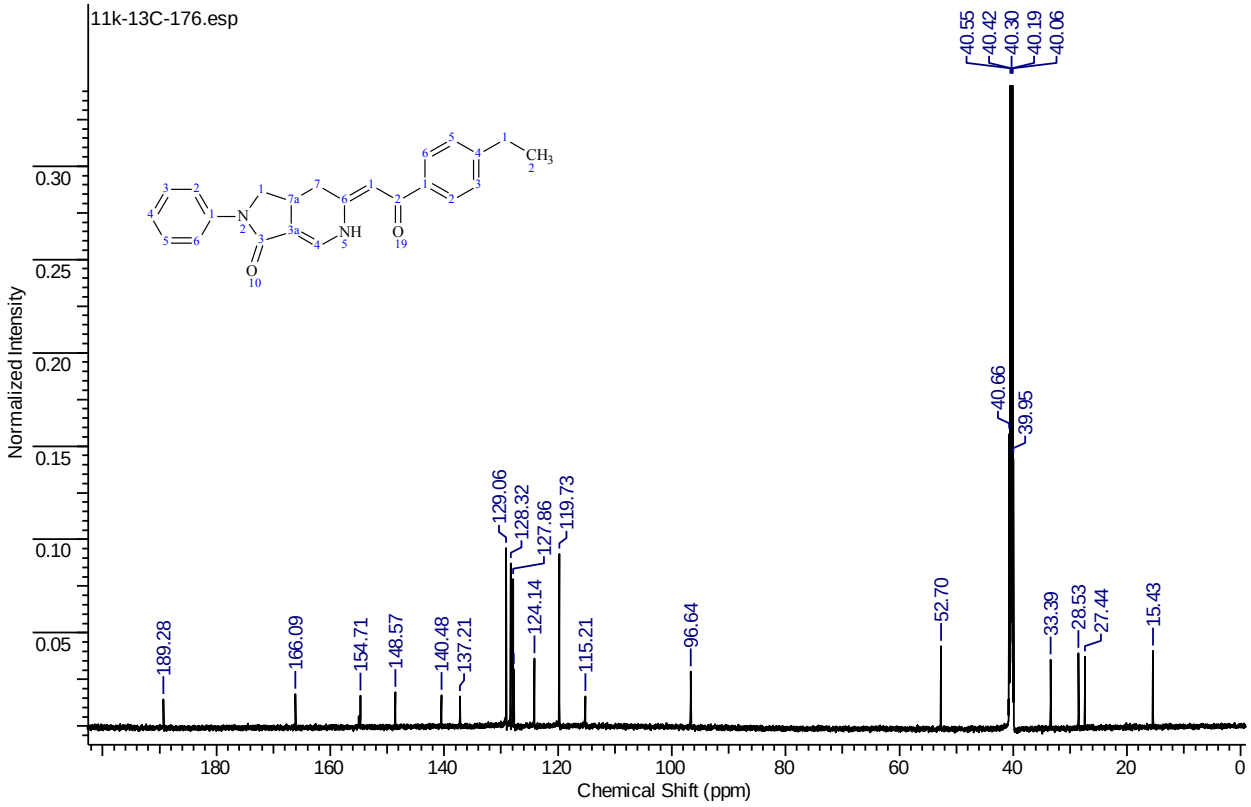
(6*Z*)-6-[2-(4-Ethylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11k).

^{1}H NMR (700.2 MHz, DMSO-d_6)



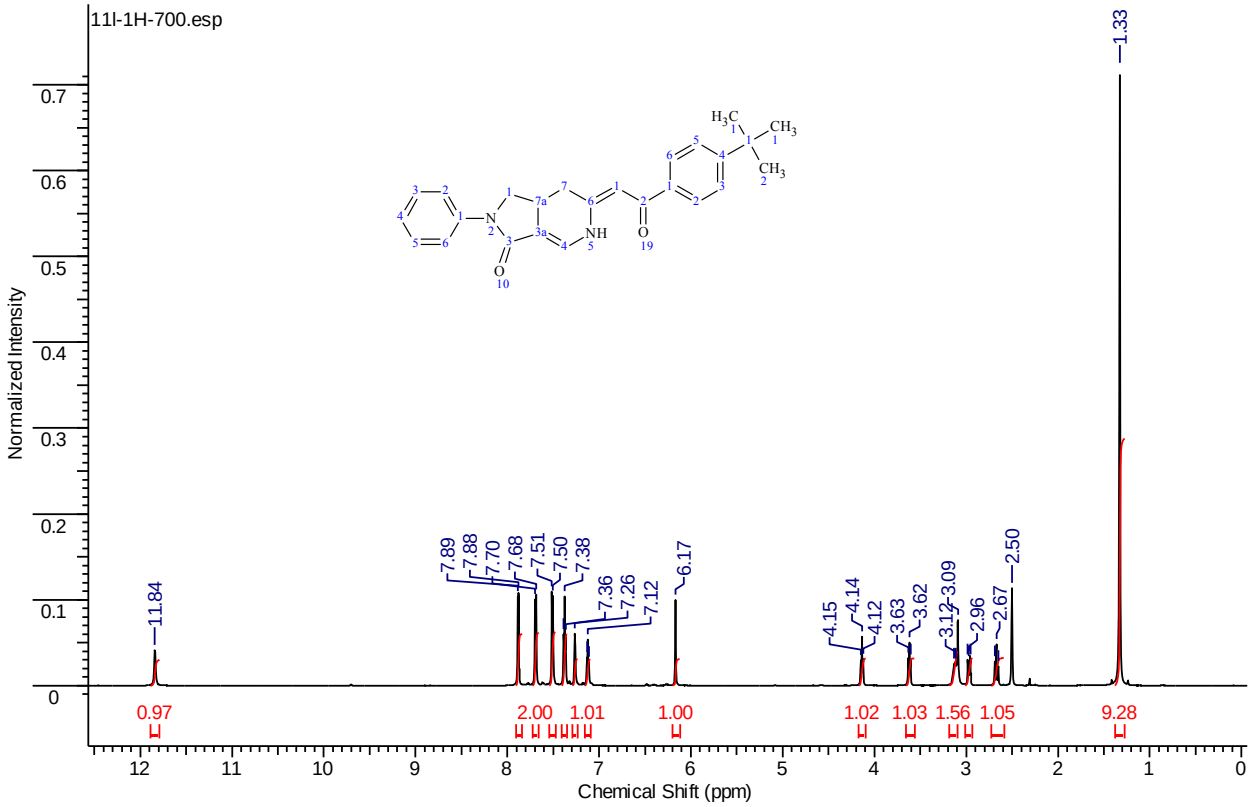


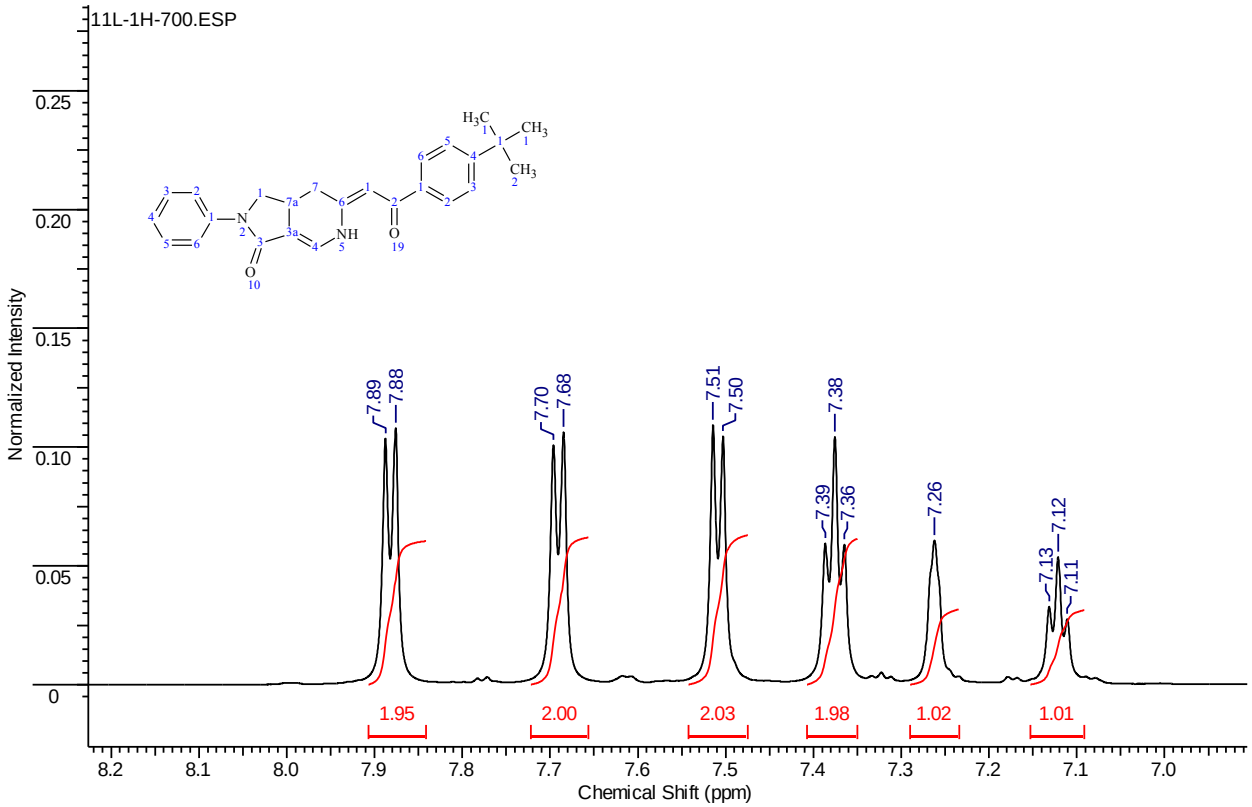
^{13}C NMR (176.1 MHz, DMSO-d_6)



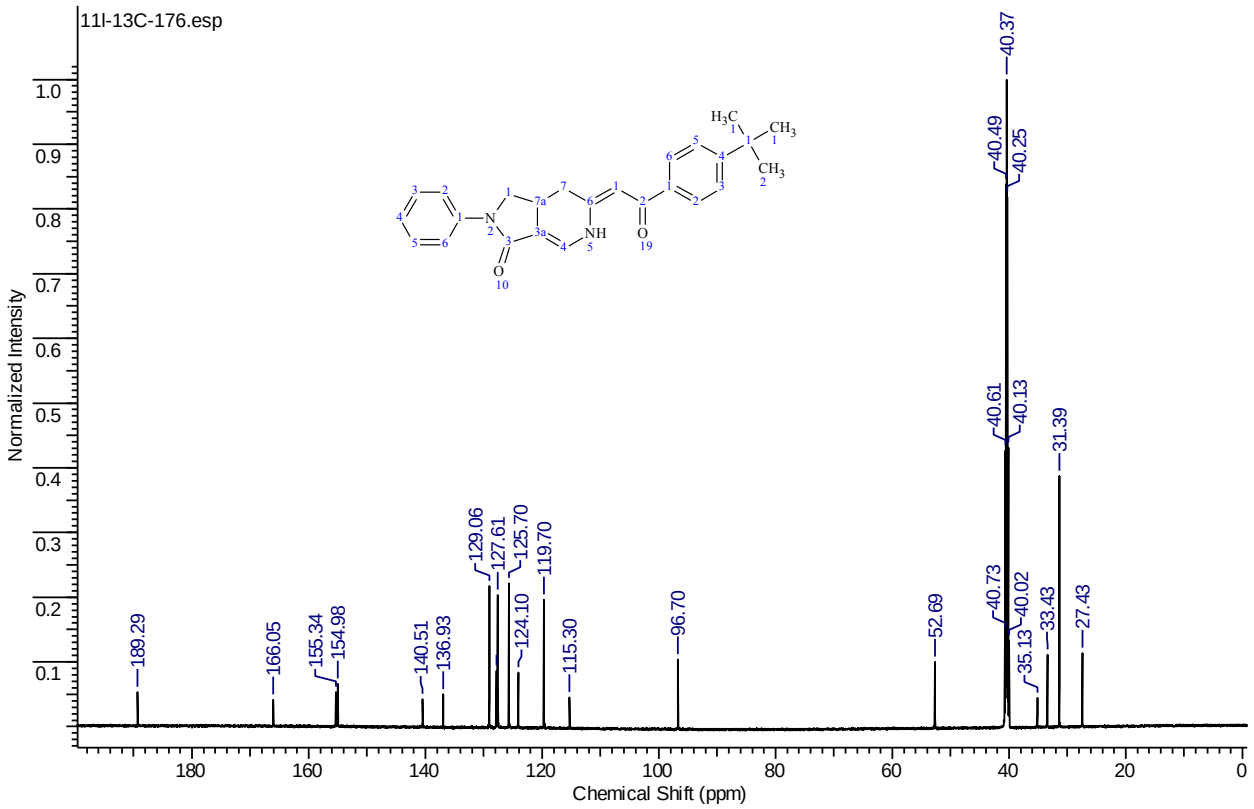
(6*Z*)-6-[2-(4-*tert*-Butylphenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11l).

^{1}H NMR (700.2 MHz, DMSO-d_6, 80 °C)



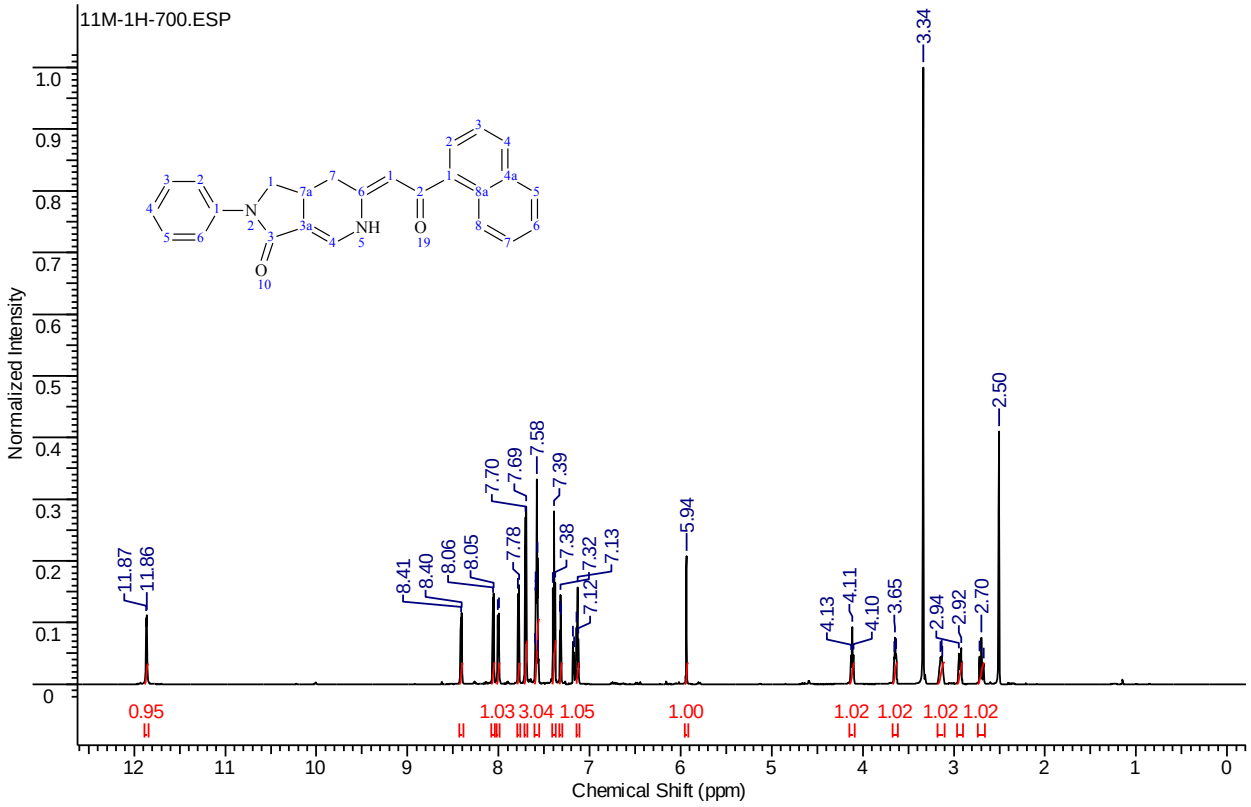


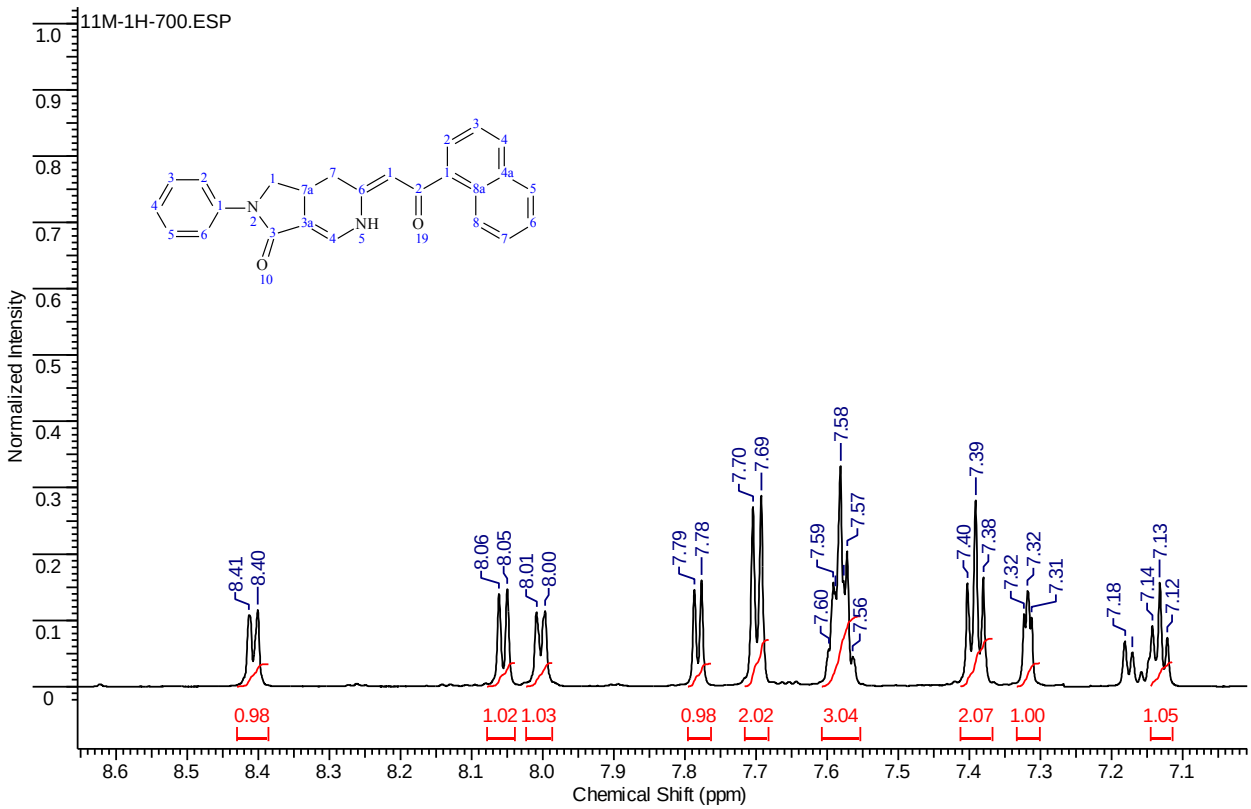
^{13}C NMR (176.1 MHz, DMSO-d_6, 80 °C)



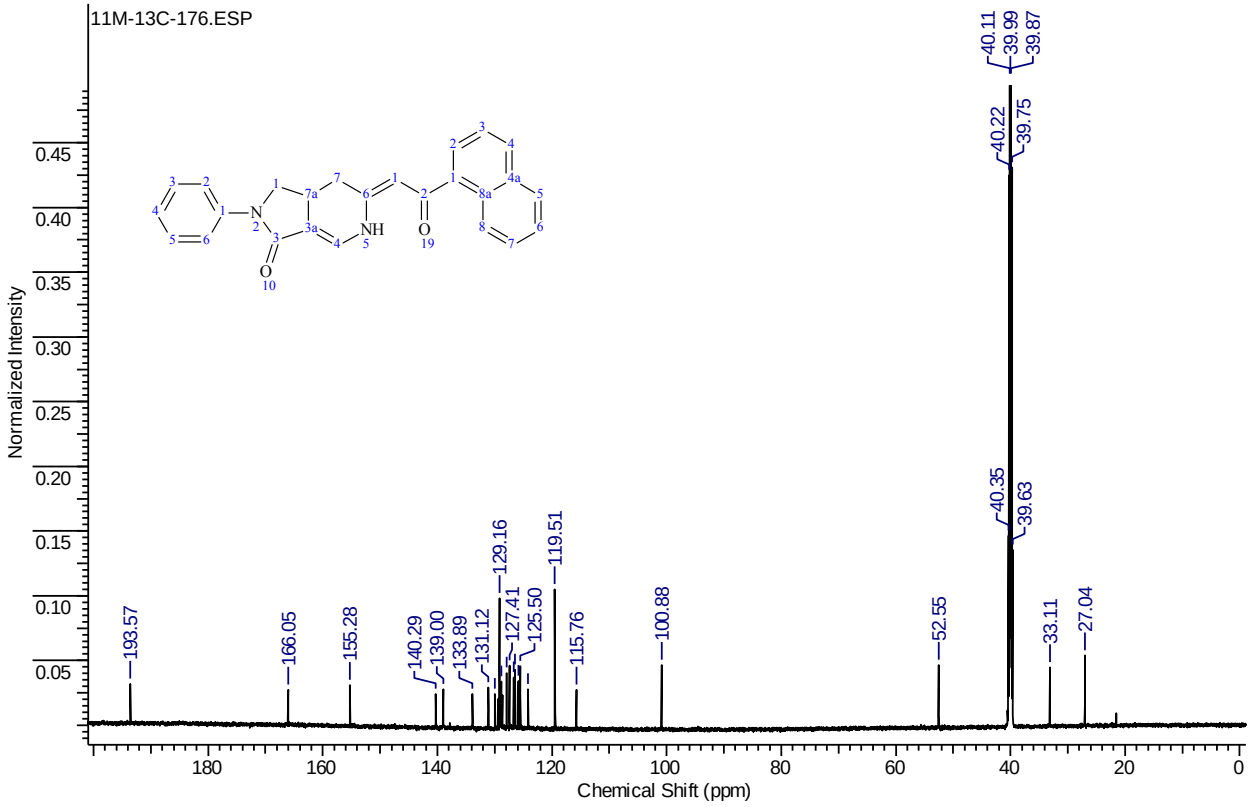
(6*Z*)-6-[2-(1-Naphthyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11m).

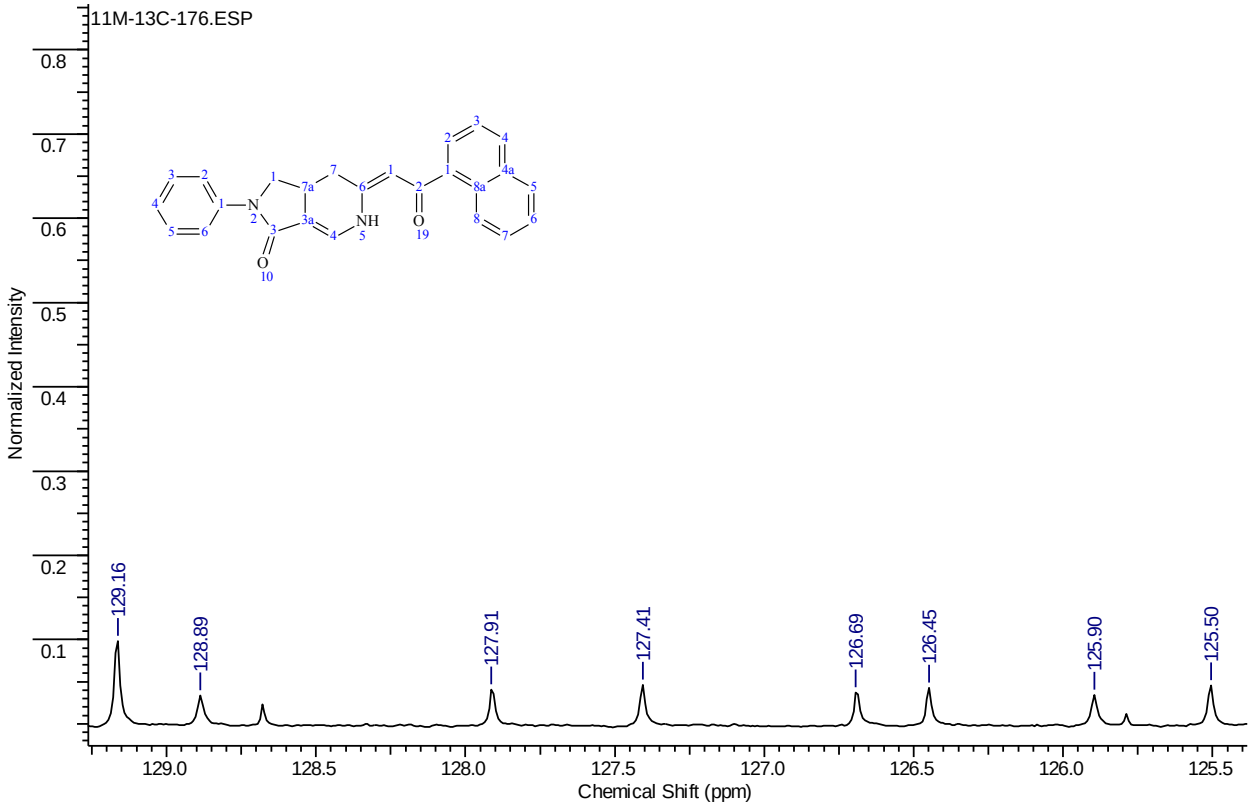
^{1}H NMR (700.2 MHz, DMSO-d_6)





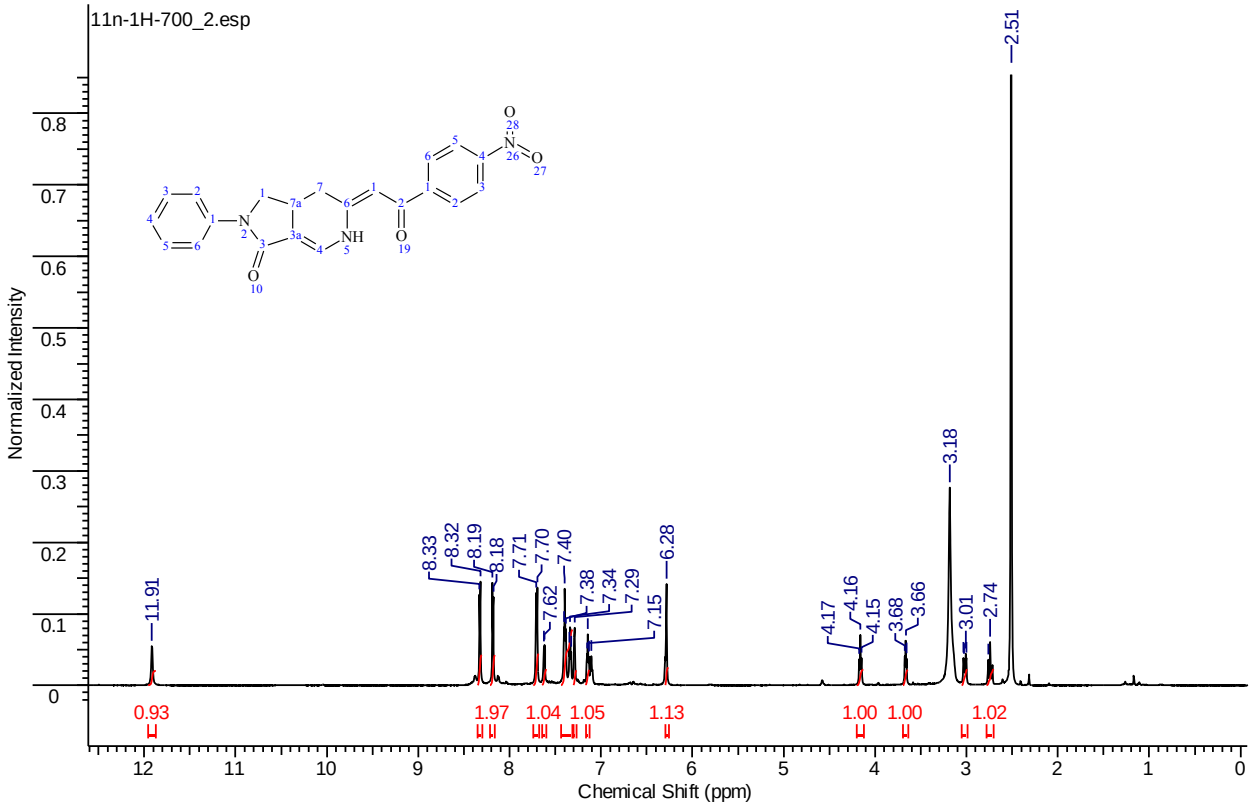
^{13}C NMR (176.1 MHz, DMSO-d_6)

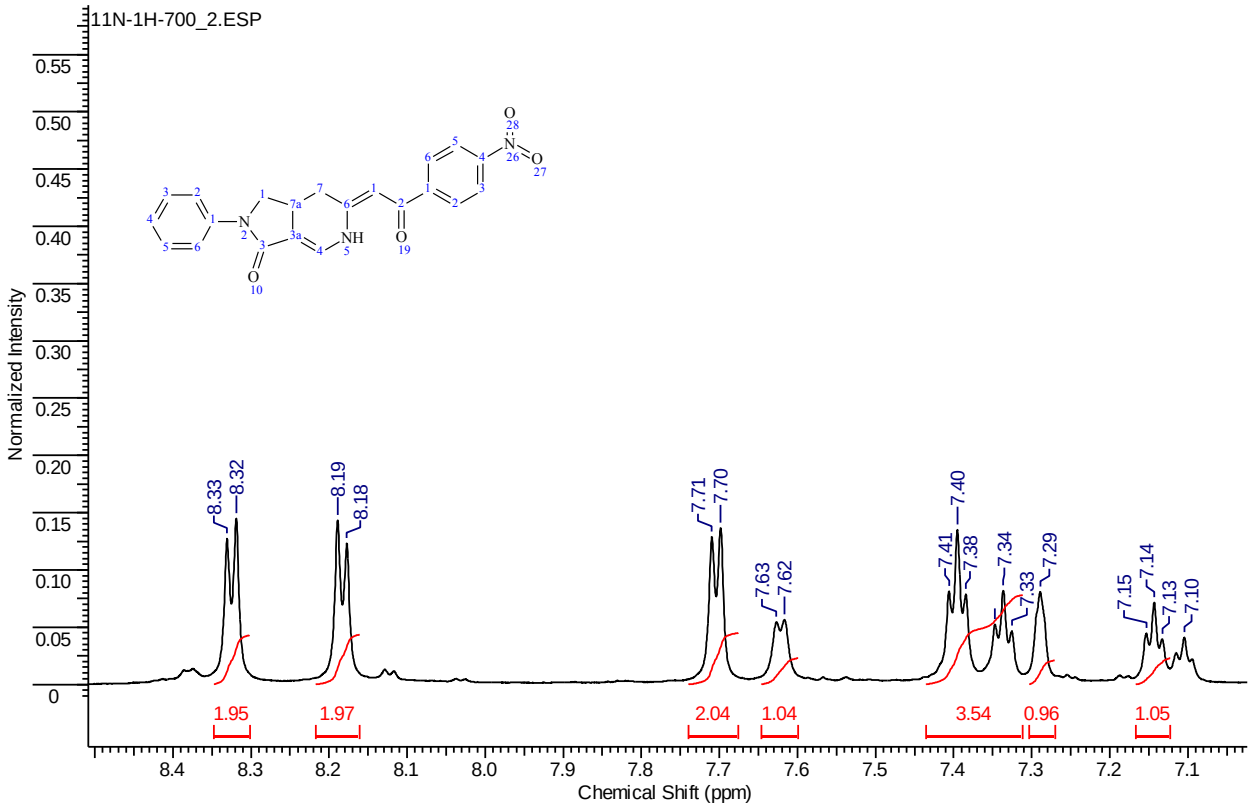




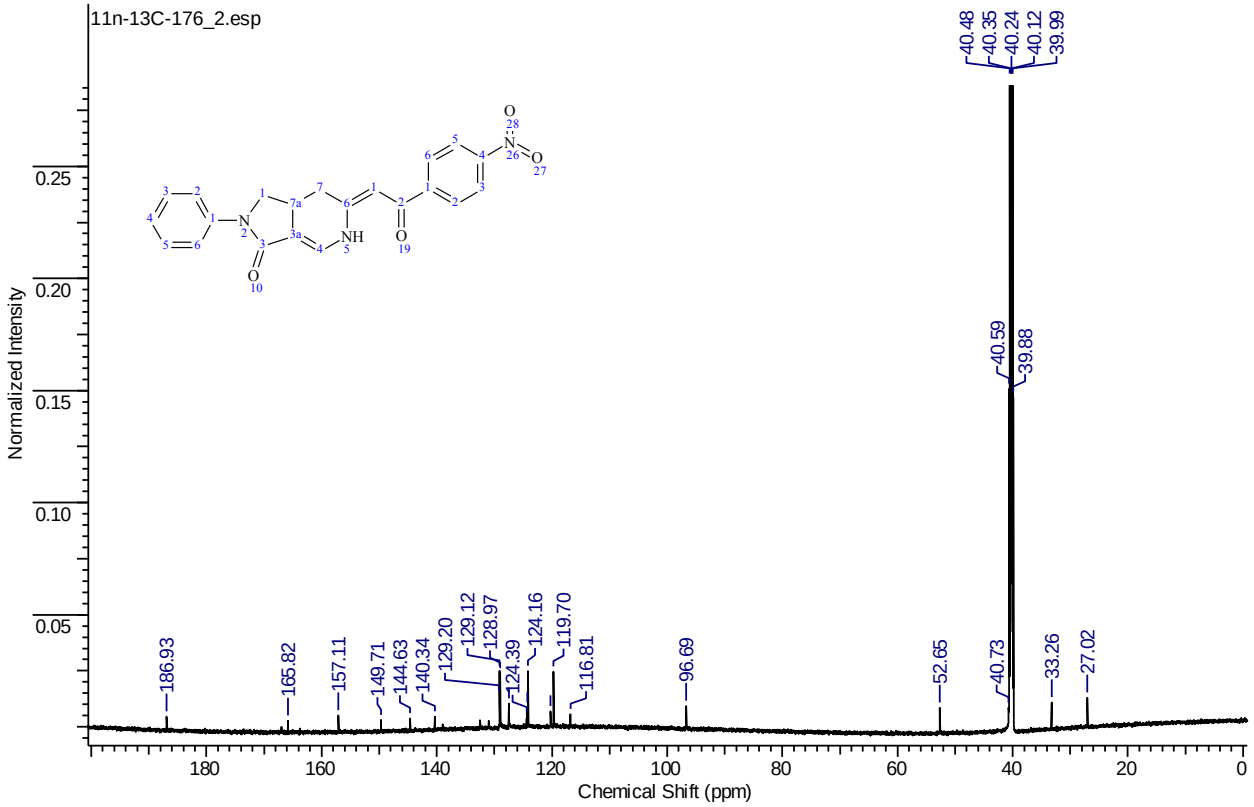
(6*Z*)-6-[2-(4-Nitrophenyl)-2-oxoethylidene]-2-phenyl-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11n).

^{1}H NMR (700.2 MHz, DMSO-d_6, 80 °C)



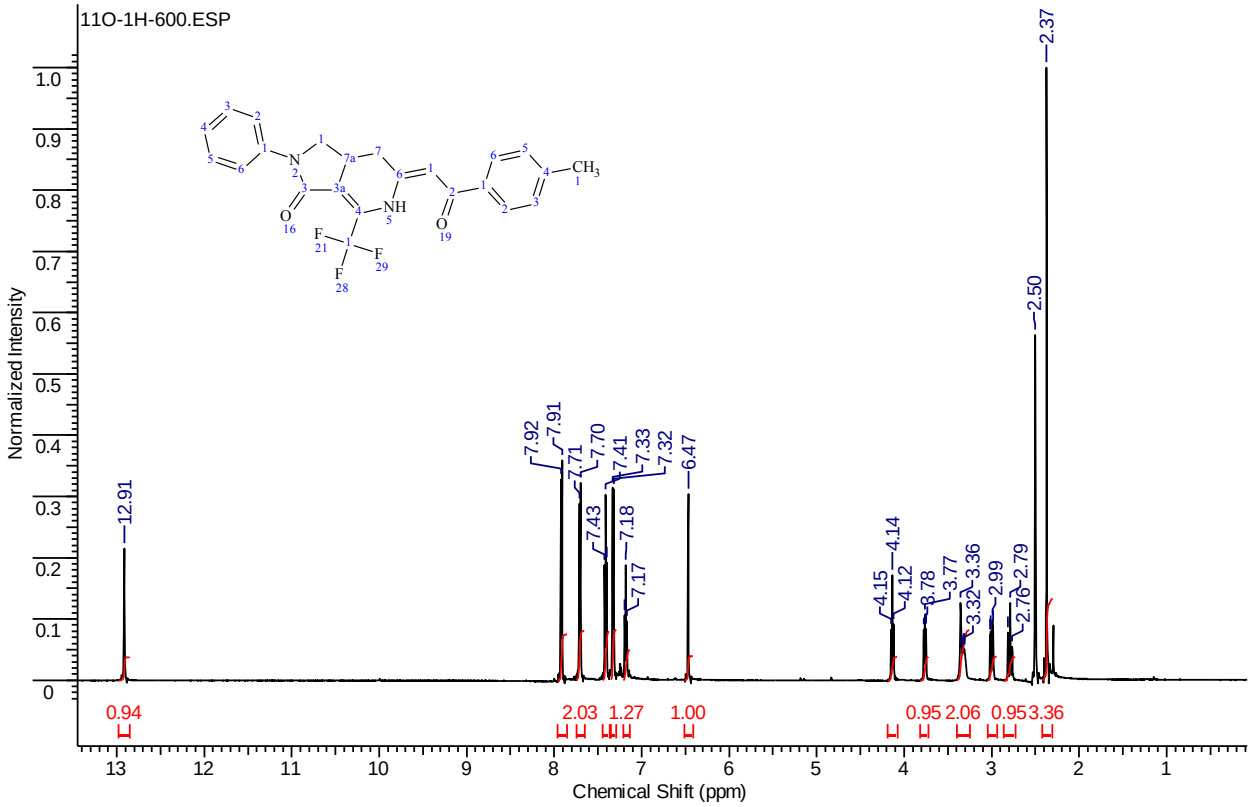


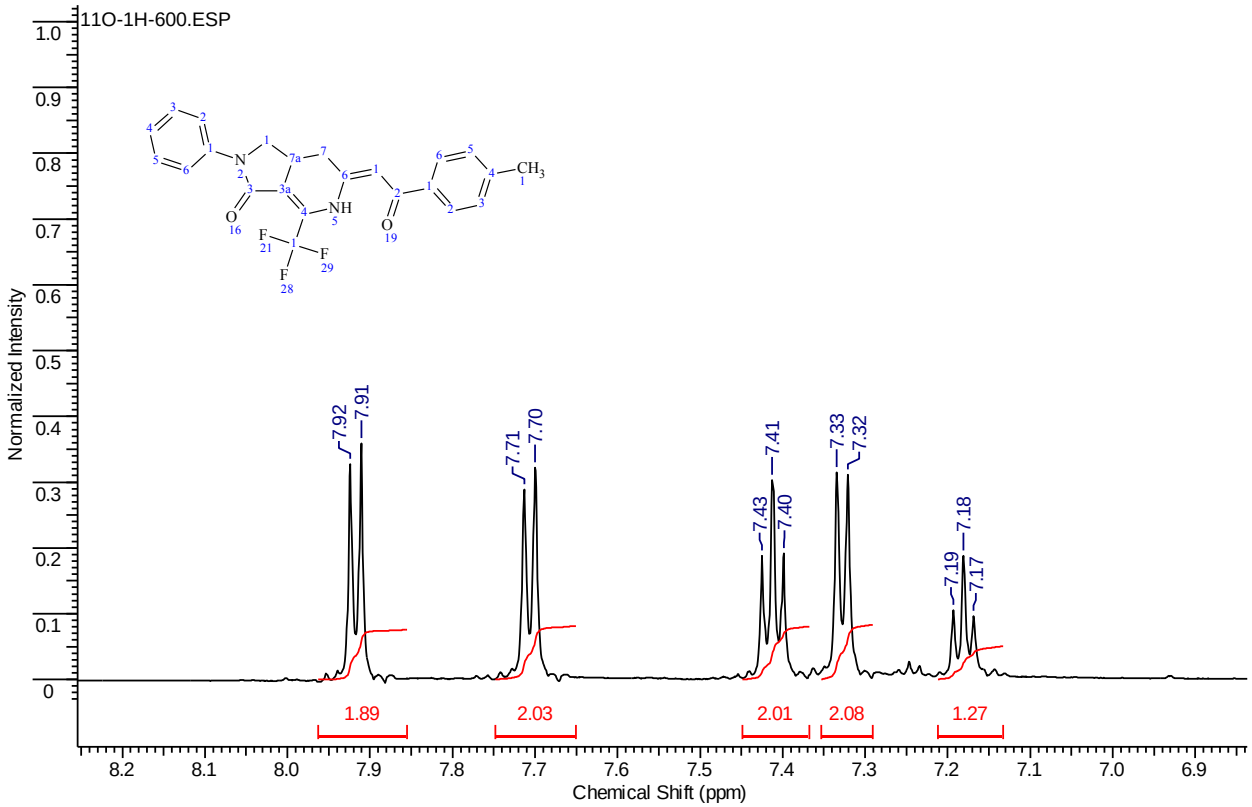
^{13}C NMR (176.1 MHz, DMSO-d_6, 80 °C)

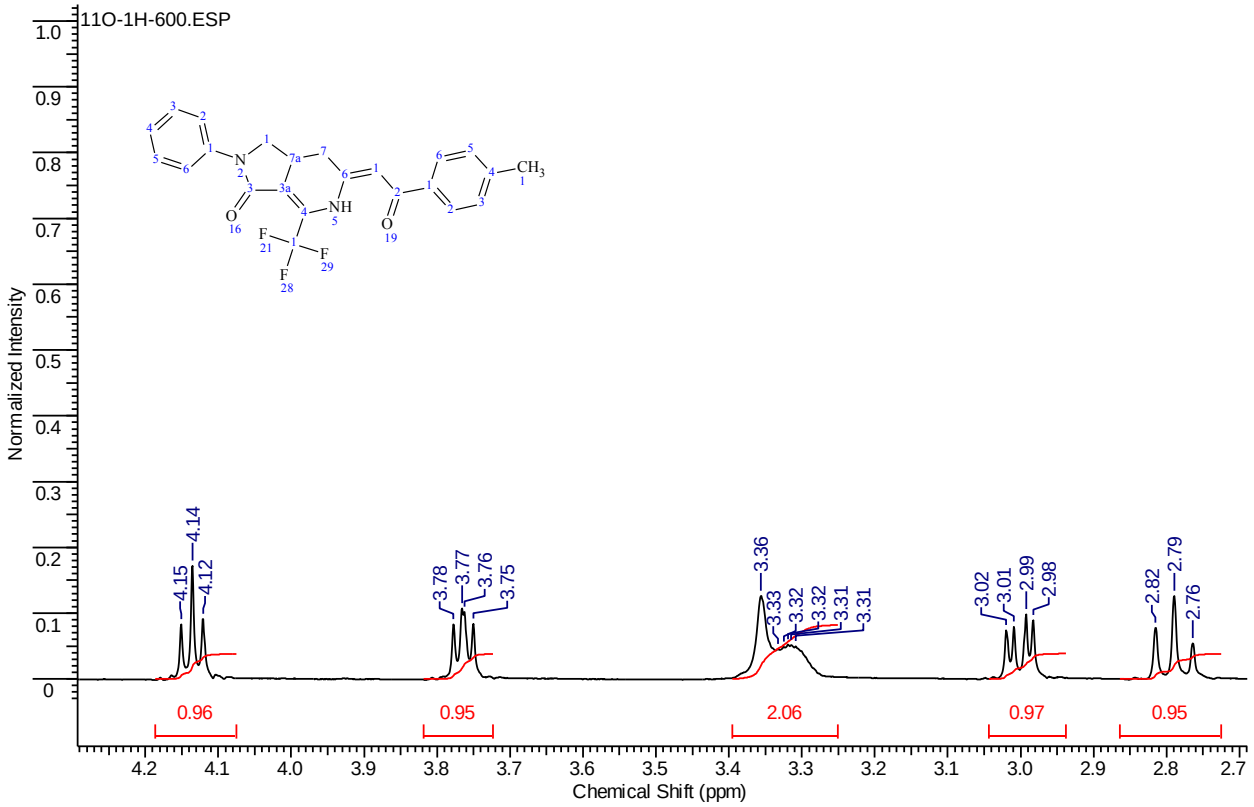


(6*Z*)-6-[2-(4-Methylphenyl)-2-oxoethylidene]-2-phenyl-4-(trifluoromethyl)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11o).

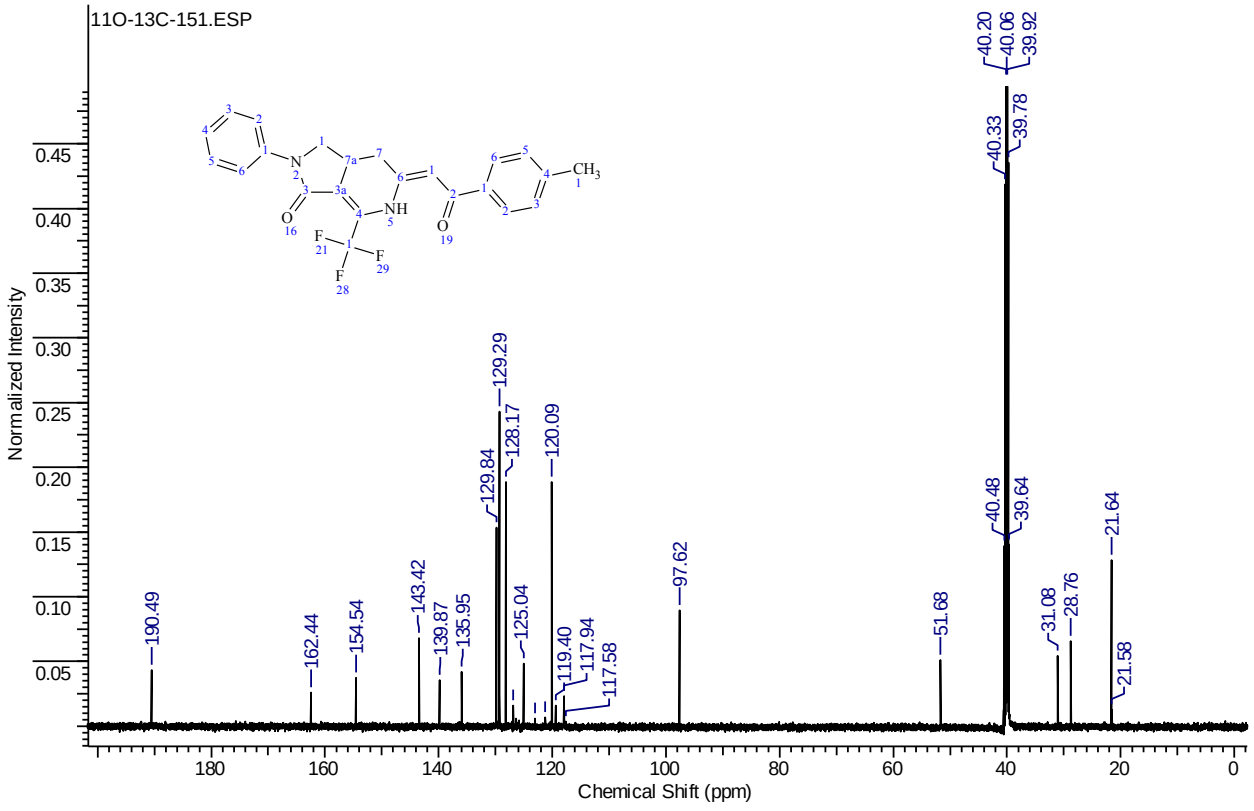
^{1}H NMR (600.2 MHz, DMSO-d_6)

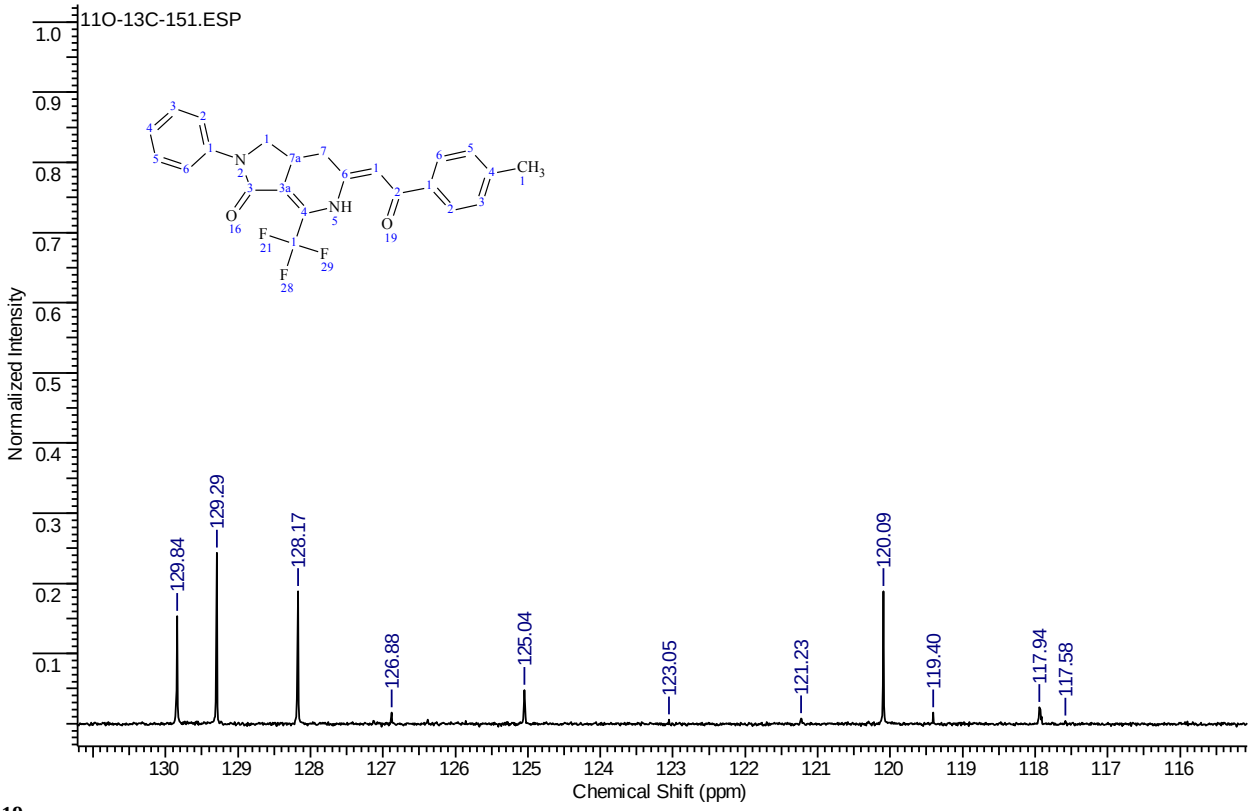




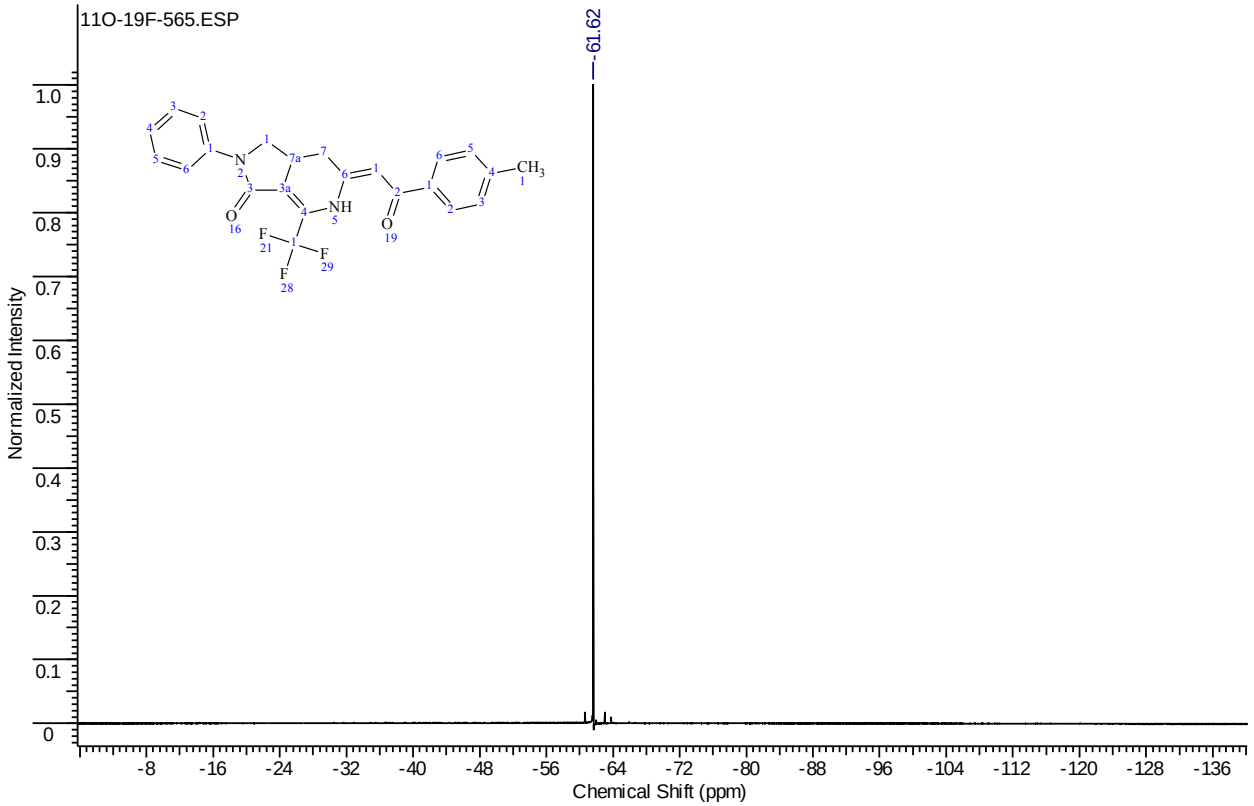


^{13}C NMR (150.9 MHz, DMSO-d_6)



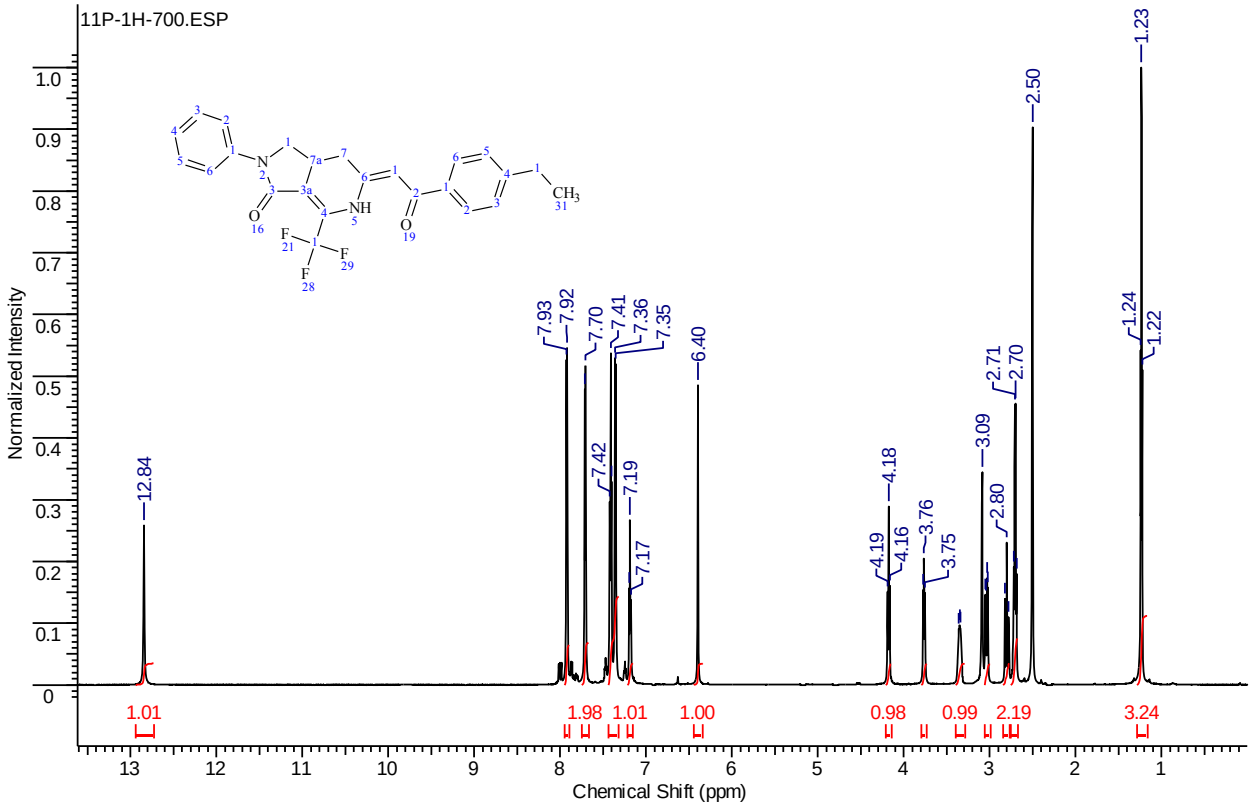


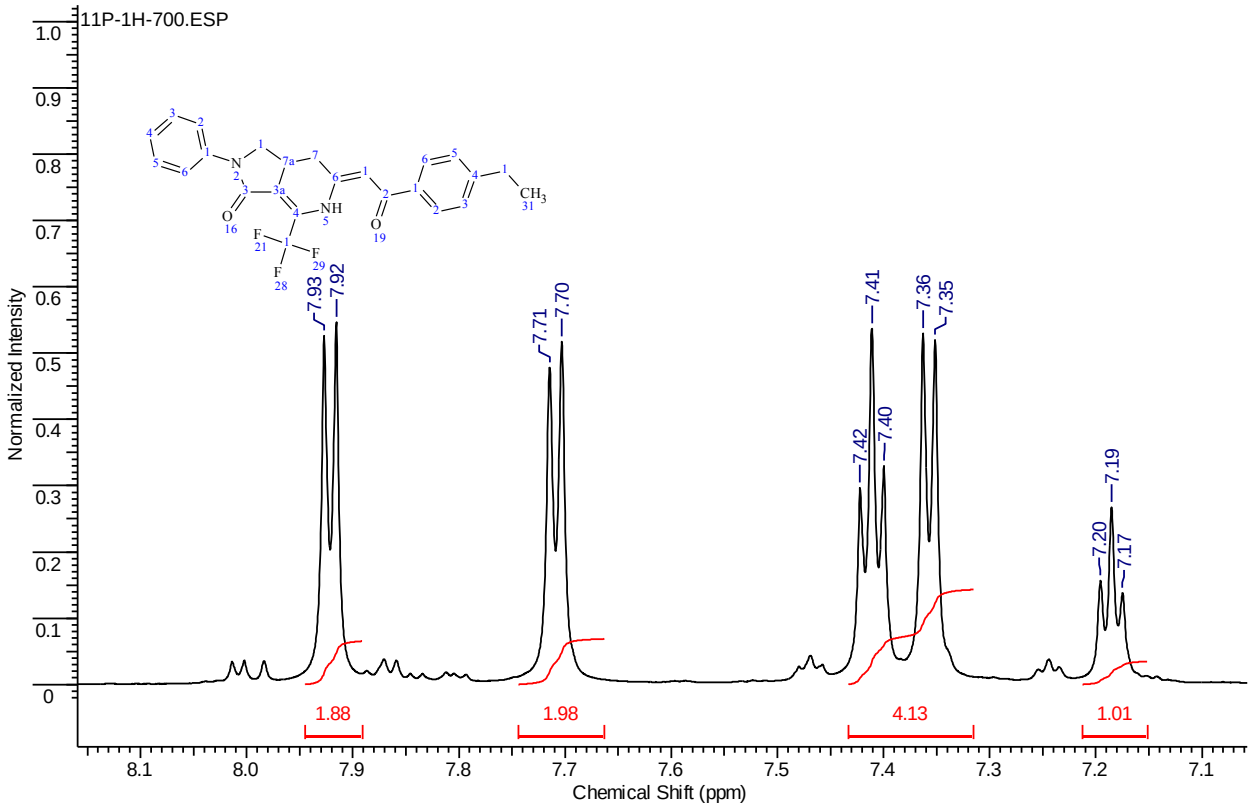
^{19}F NMR (564.7 MHz, DMSO-d_6)

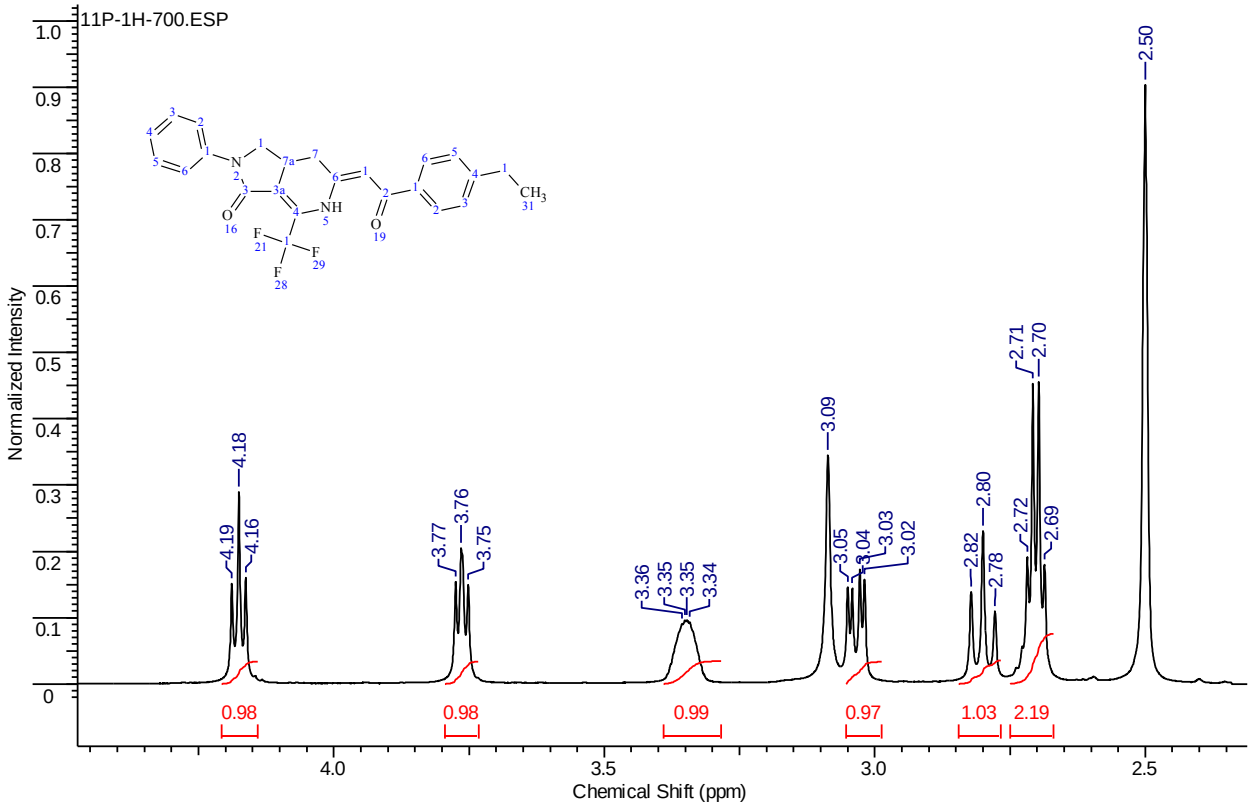


(6*Z*)-6-[2-(4-Ethylphenyl)-2-oxoethylidene]-2-phenyl-4-(trifluoromethyl)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11p).

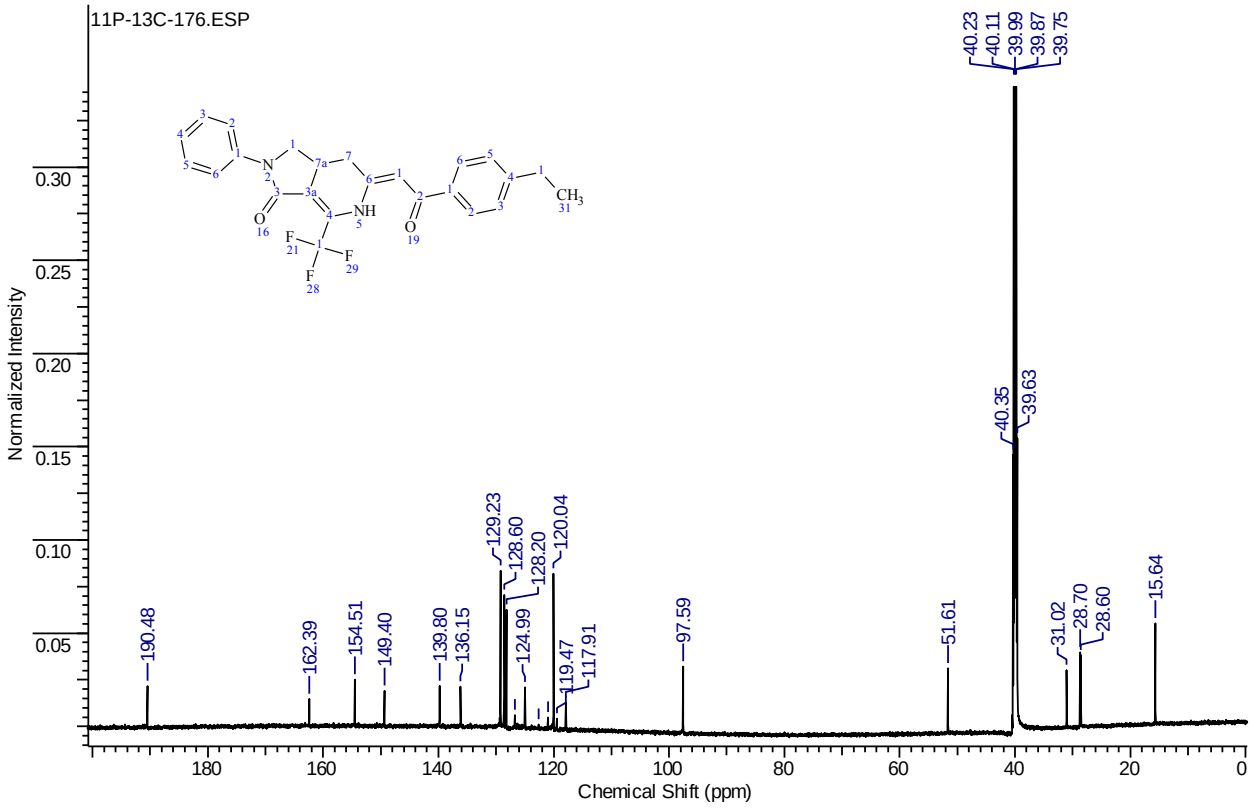
^{1}H NMR (700.2 MHz, DMSO-d_6)

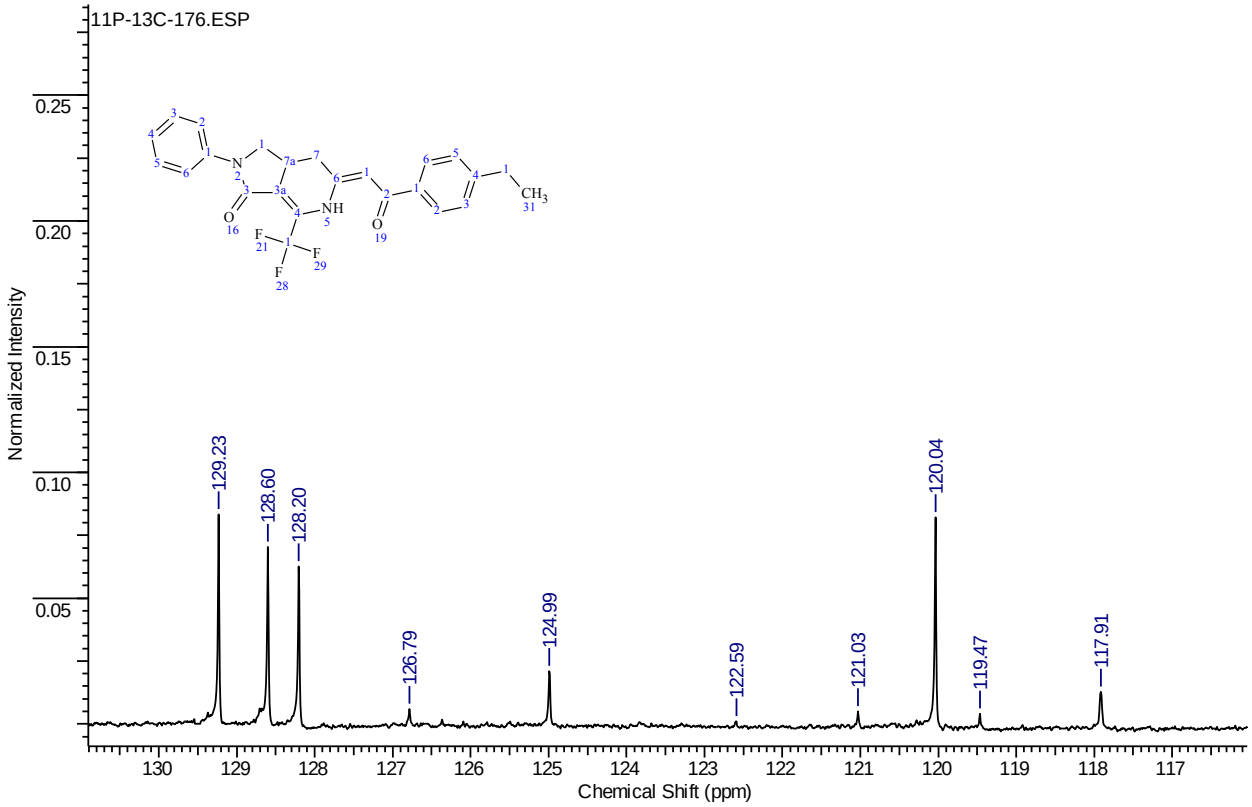




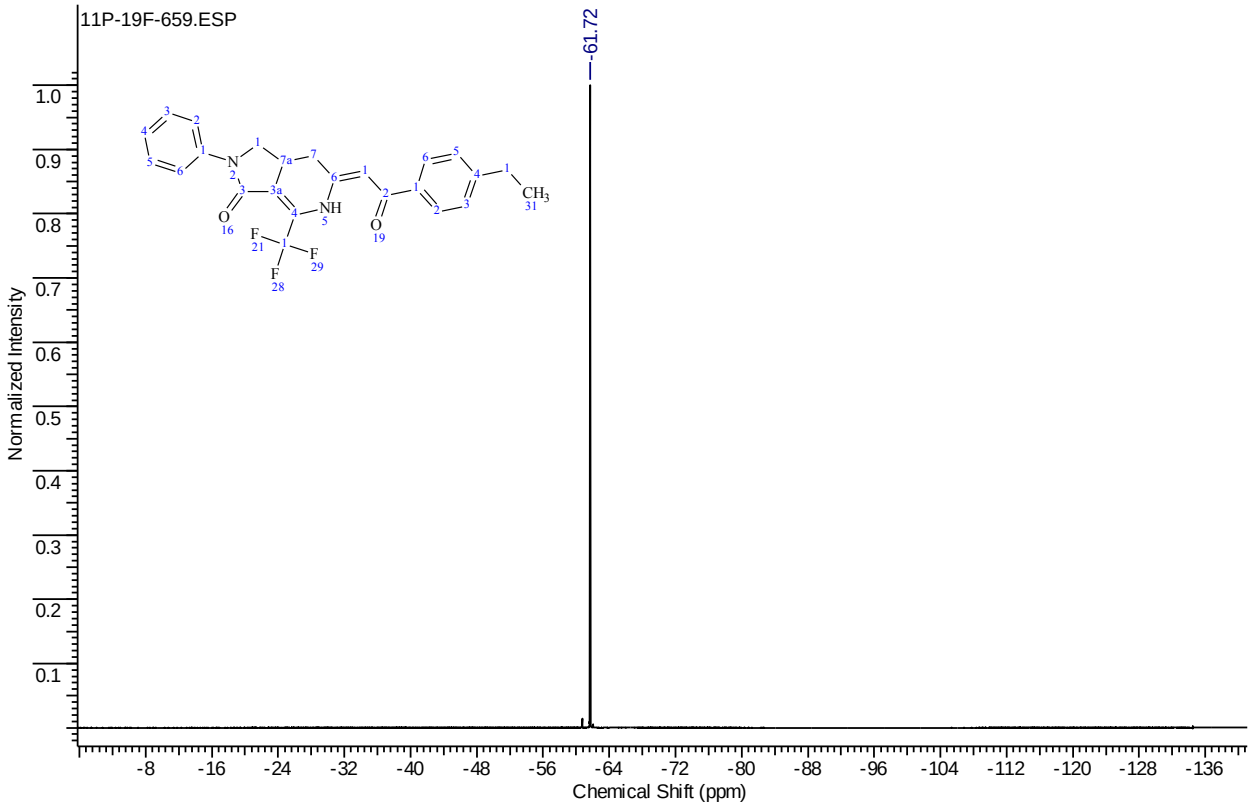


^{13}C NMR (176.1 MHz, DMSO-d_6)



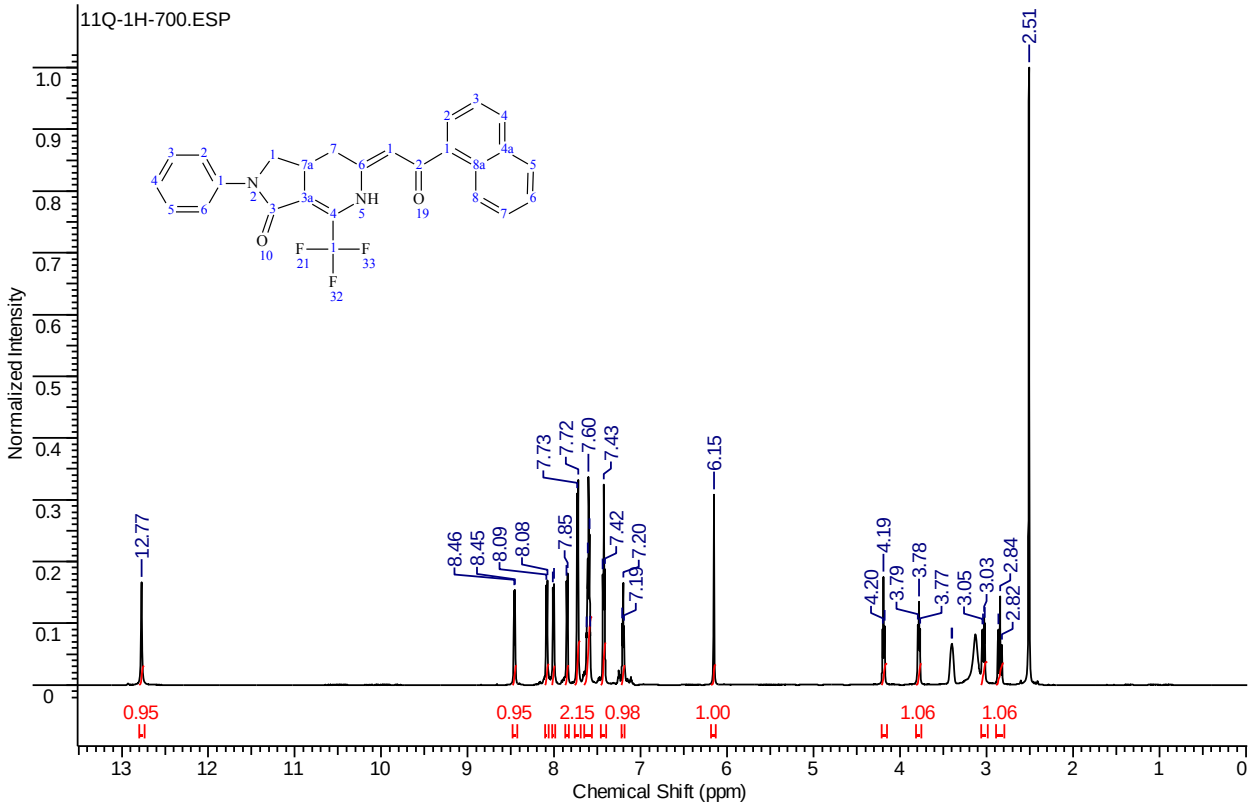


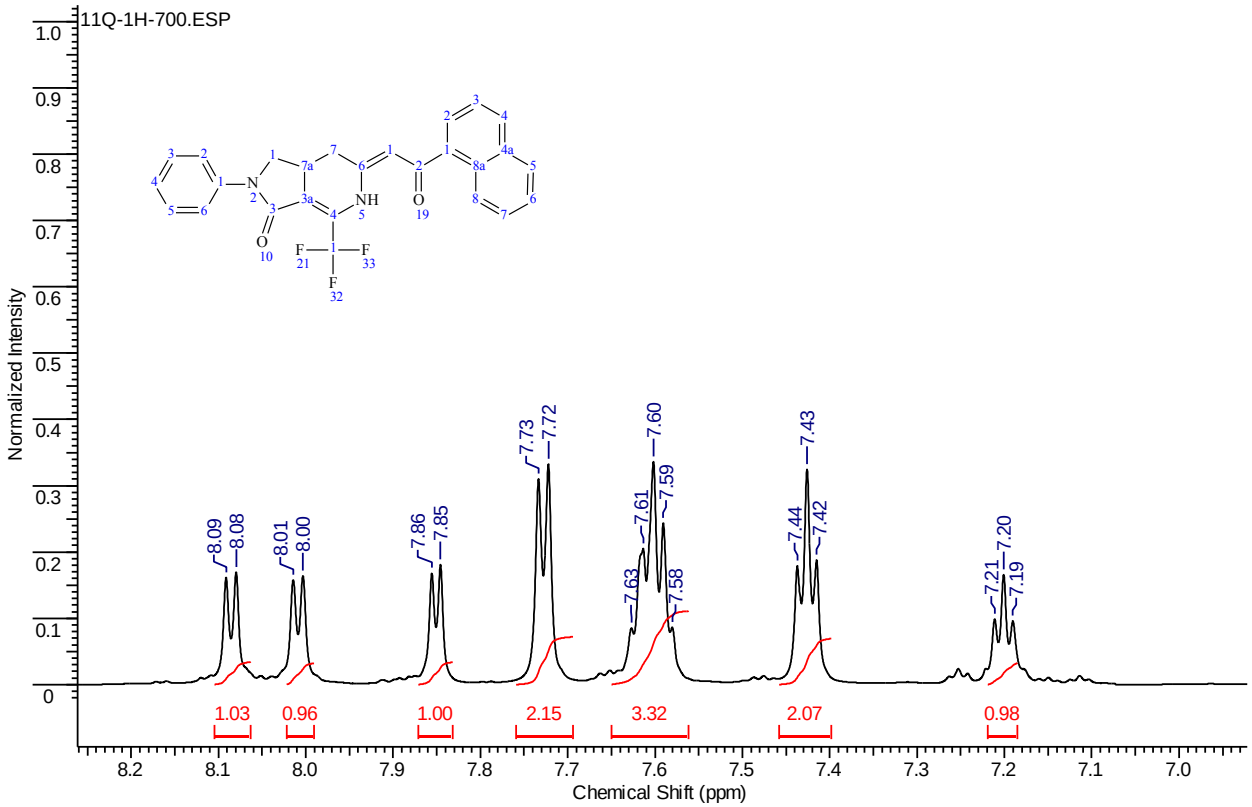
^{19}F NMR (658.8 MHz, DMSO-d_6)

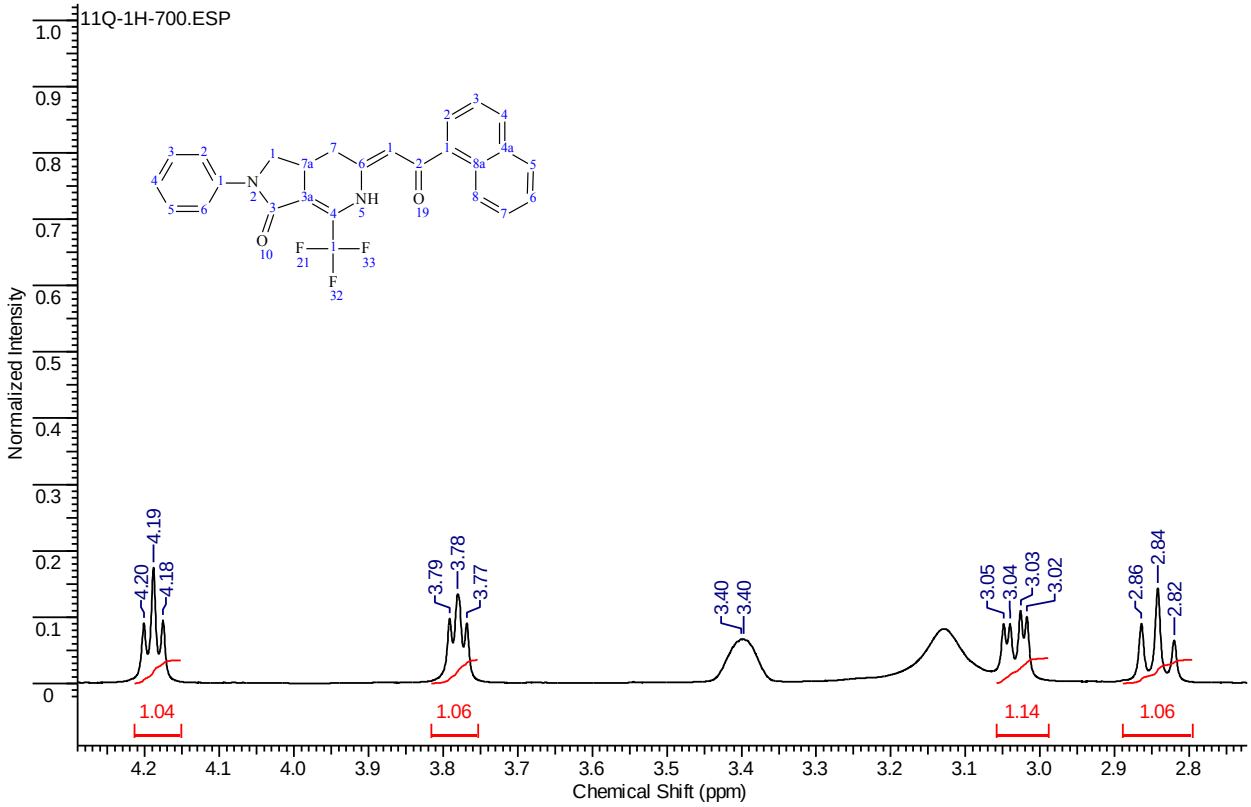


(6*Z*)-6-[2-(1-Naphthyl)-2-oxoethylidene]-2-phenyl-4-(trifluoromethyl)-1,2,5,6,7,7a-hexahydro-3*H*-pyrrolo[3,4-*c*]pyridin-3-one (11q).

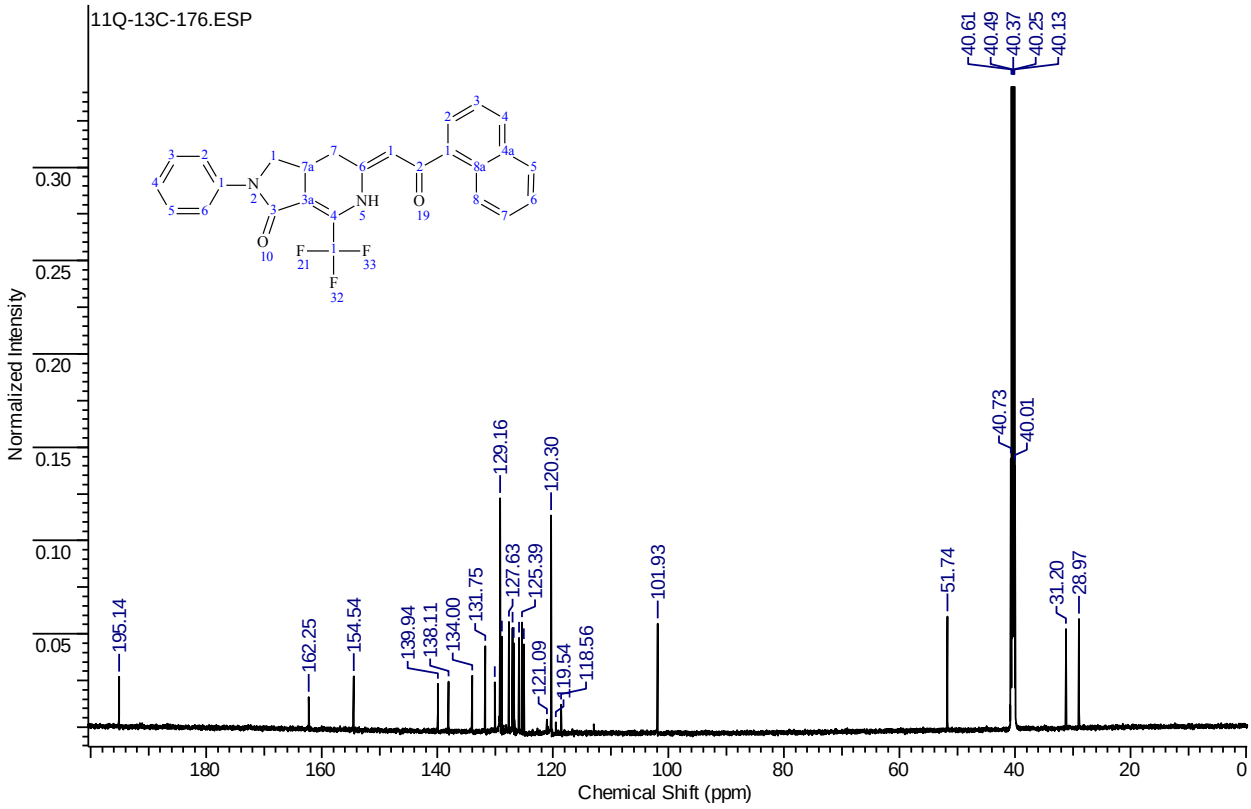
^{1}H NMR (700.2 MHz, DMSO-d_6)

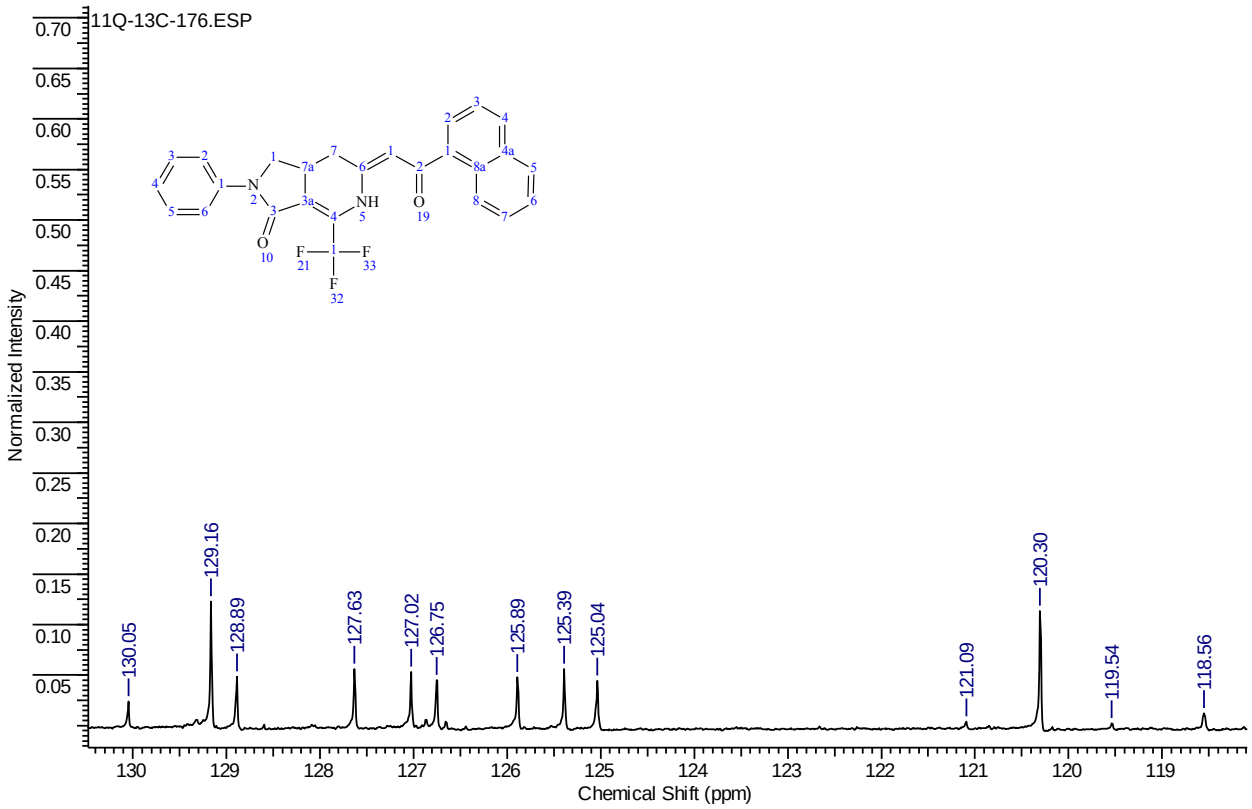






^{13}C NMR (176.1 MHz, DMSO-d_6)





^{19}F NMR (658.8 MHz, DMSO-d_6)