Supporting information.

Synthesis of New Quinolinequinone Derivatives and Preliminary Exploration of their Cytotoxic Properties

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500 MHz ^{1}H-NMR of 5-chloro-8-hydroxy-7-nitroquinoline **(1)** in DMSO

CMK-01-121a-proton
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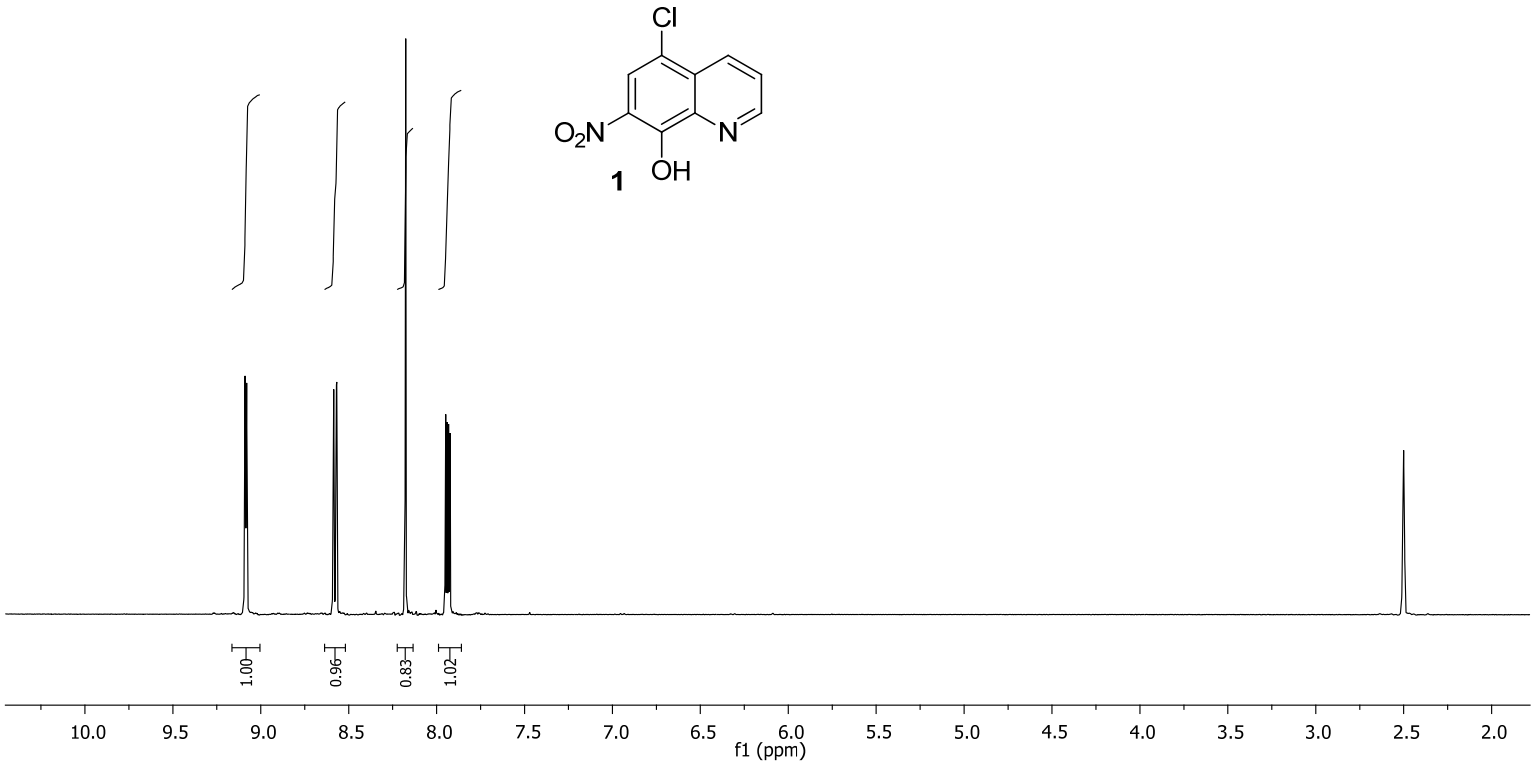
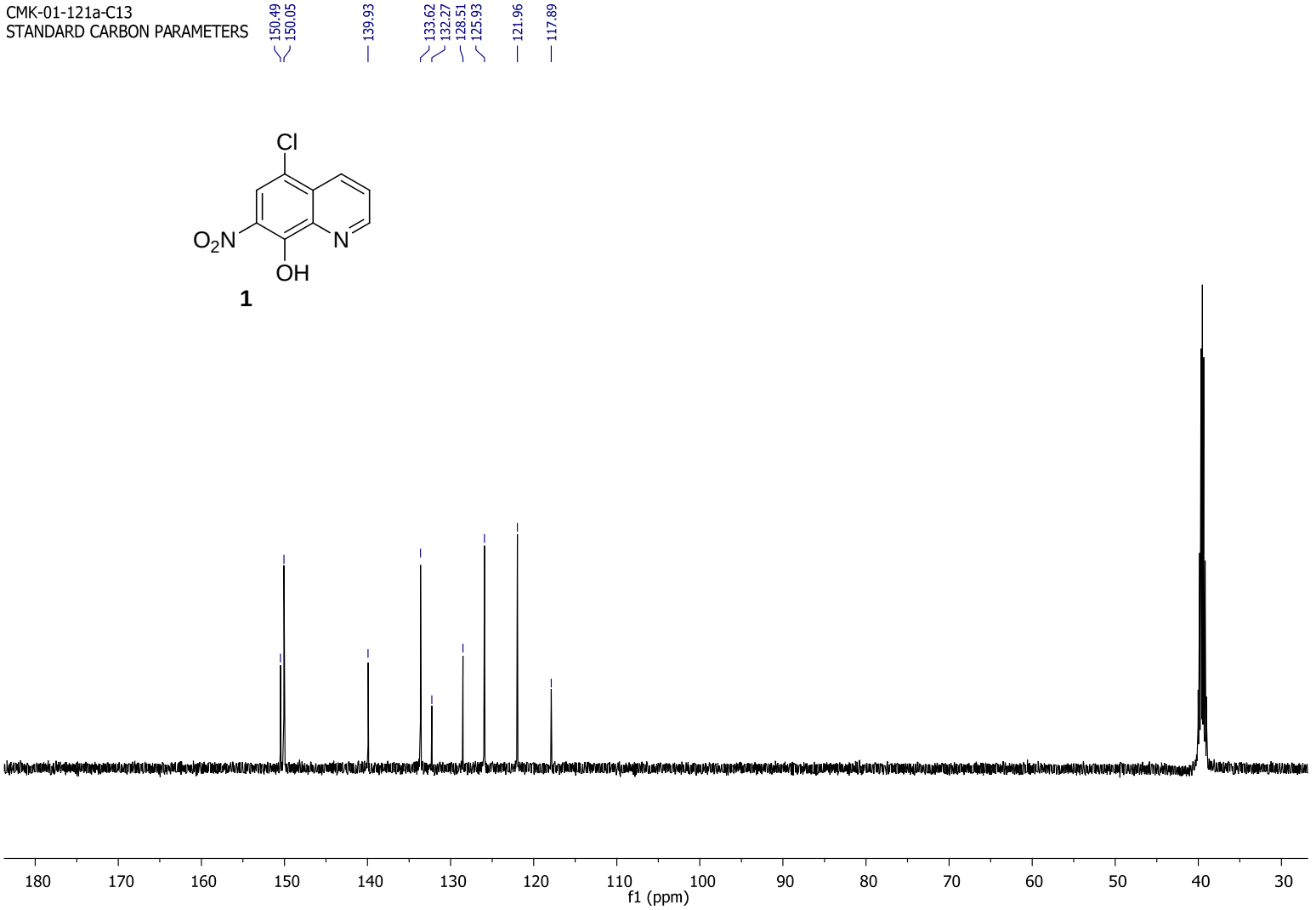
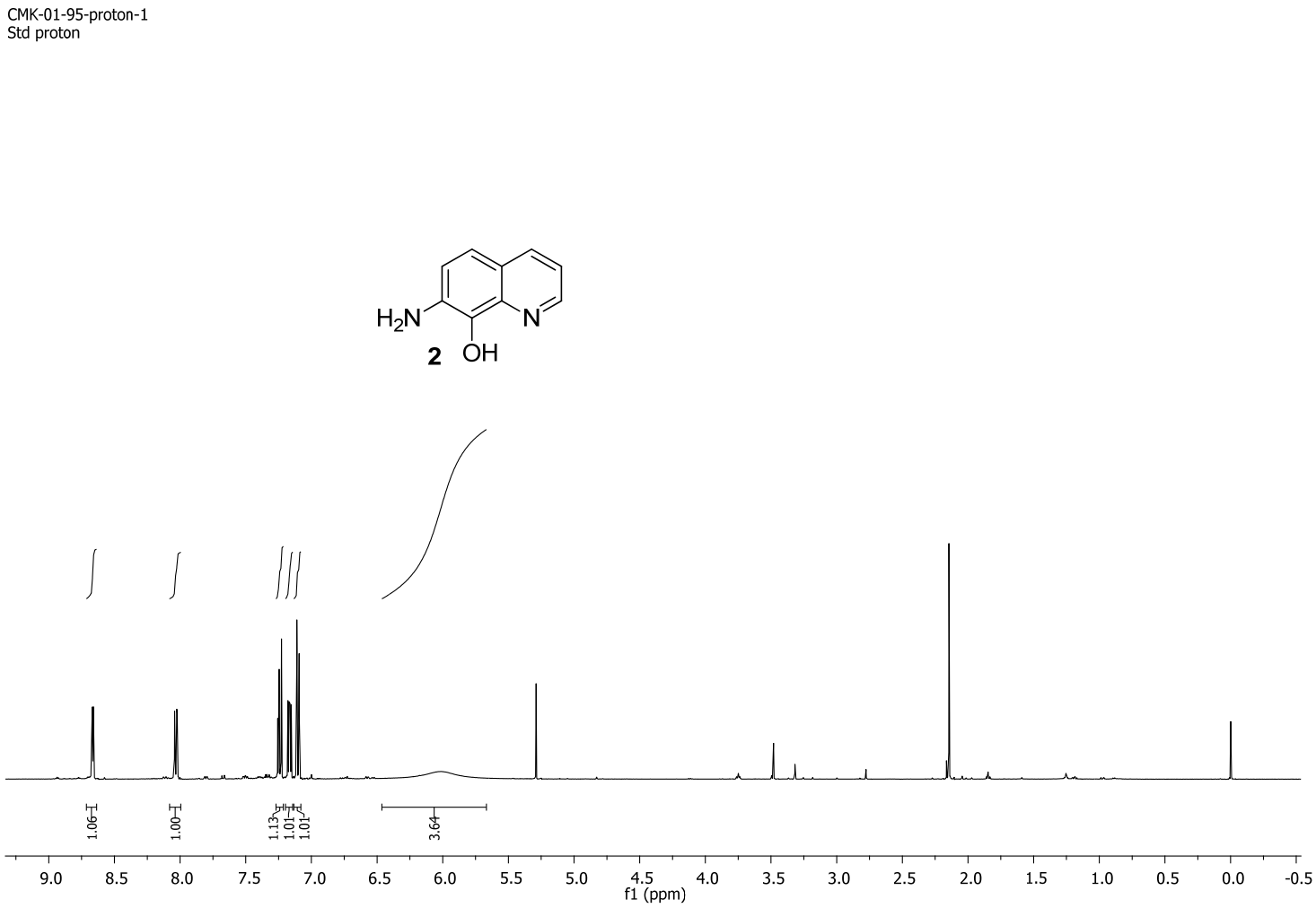


125 MHz ^{13}C-NMR of 5-chloro-8-hydroxy-7-nitroquinoline **(1)** in DMSO



500 MHz ^{1}H-NMR of 7-amino-8-hydroxyquinoline **(2)** in $CDCl_3$



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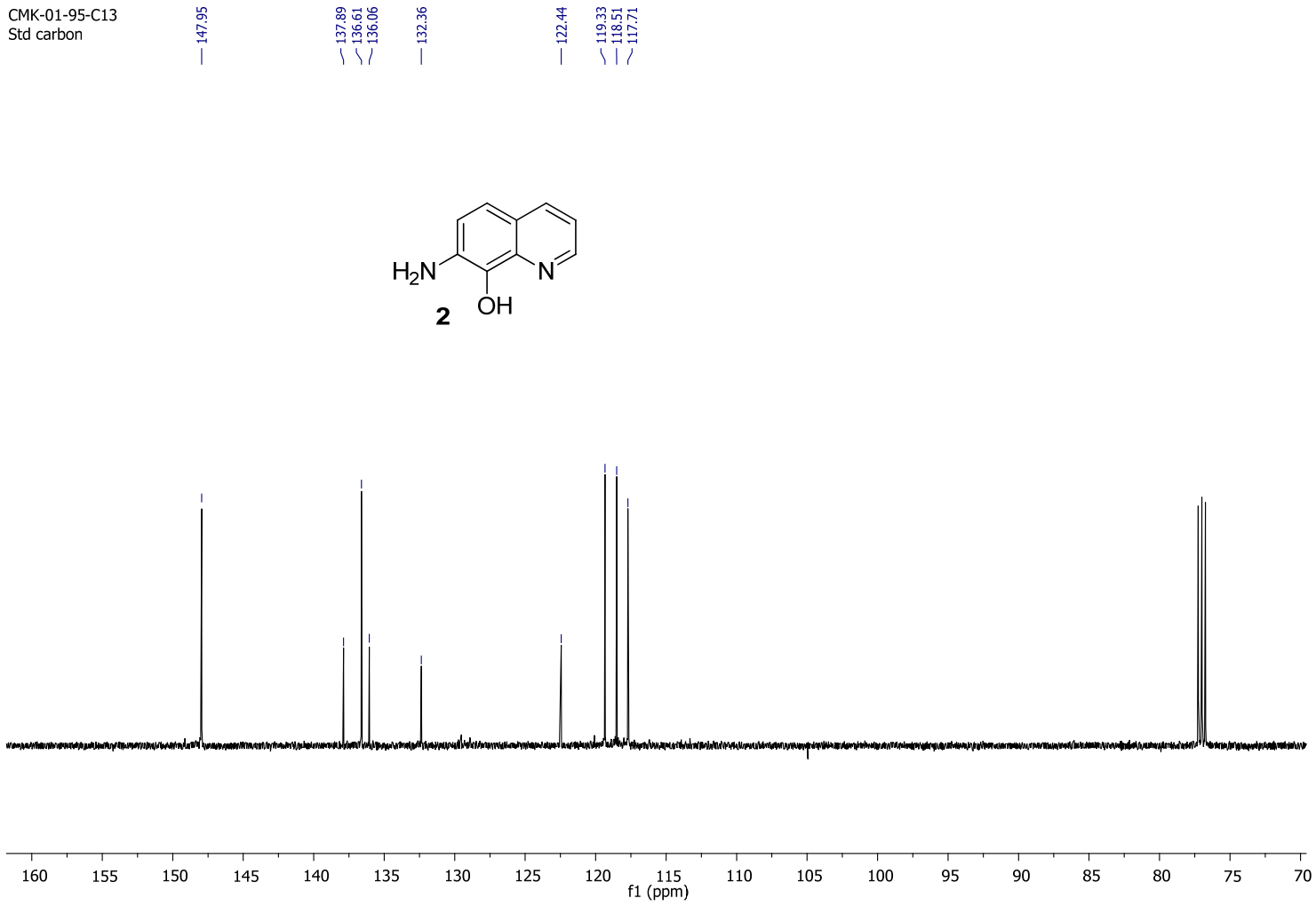

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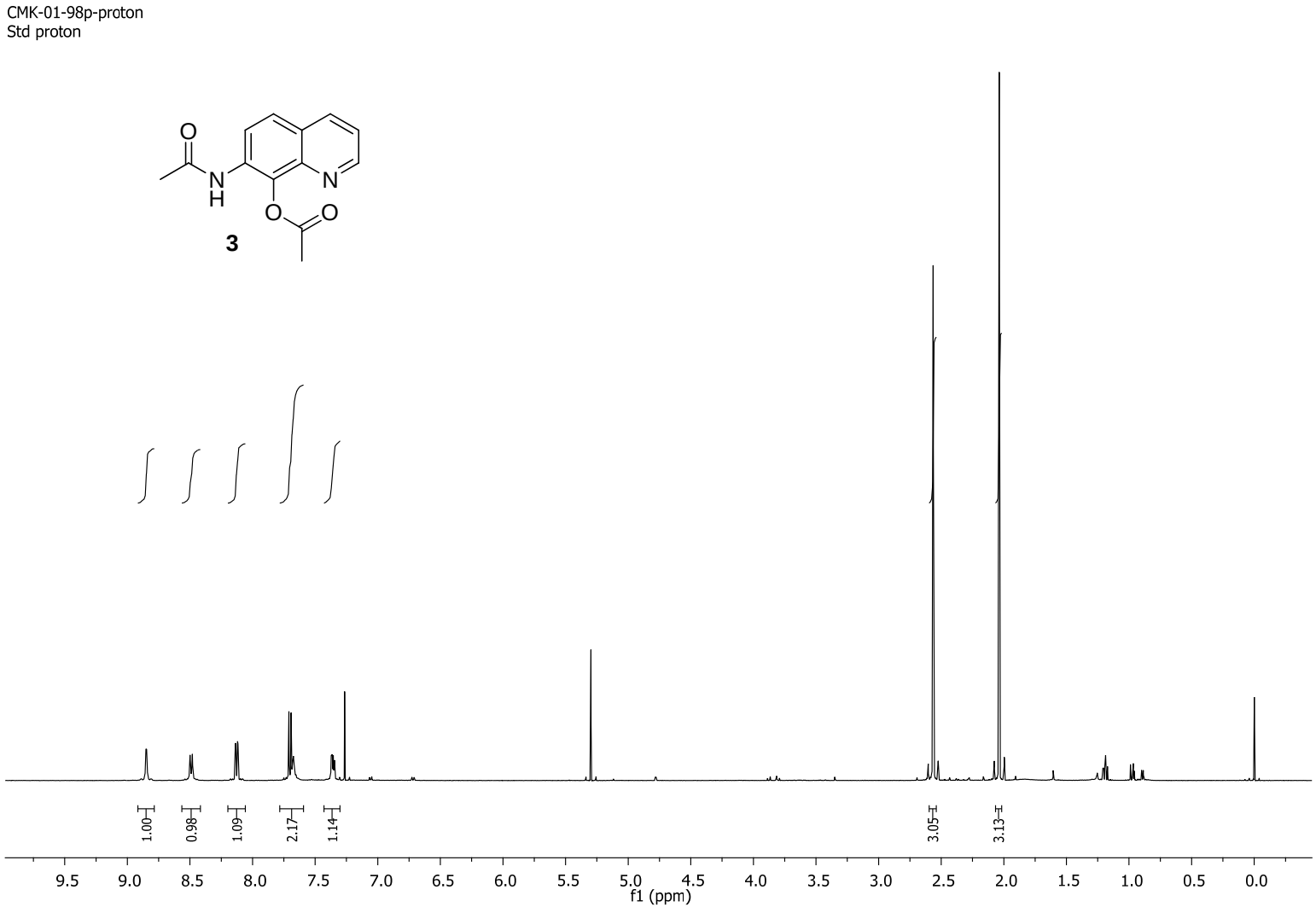

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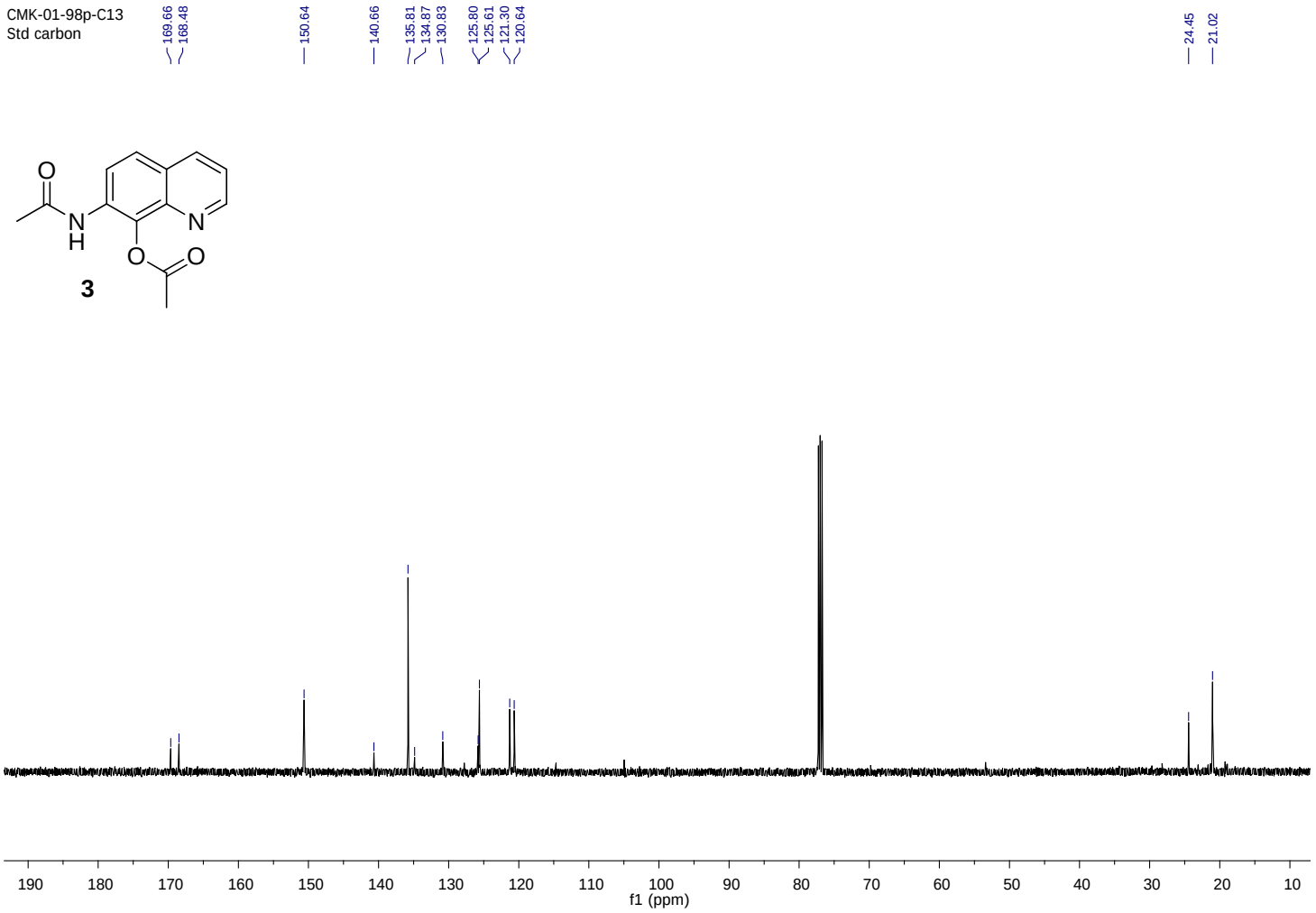

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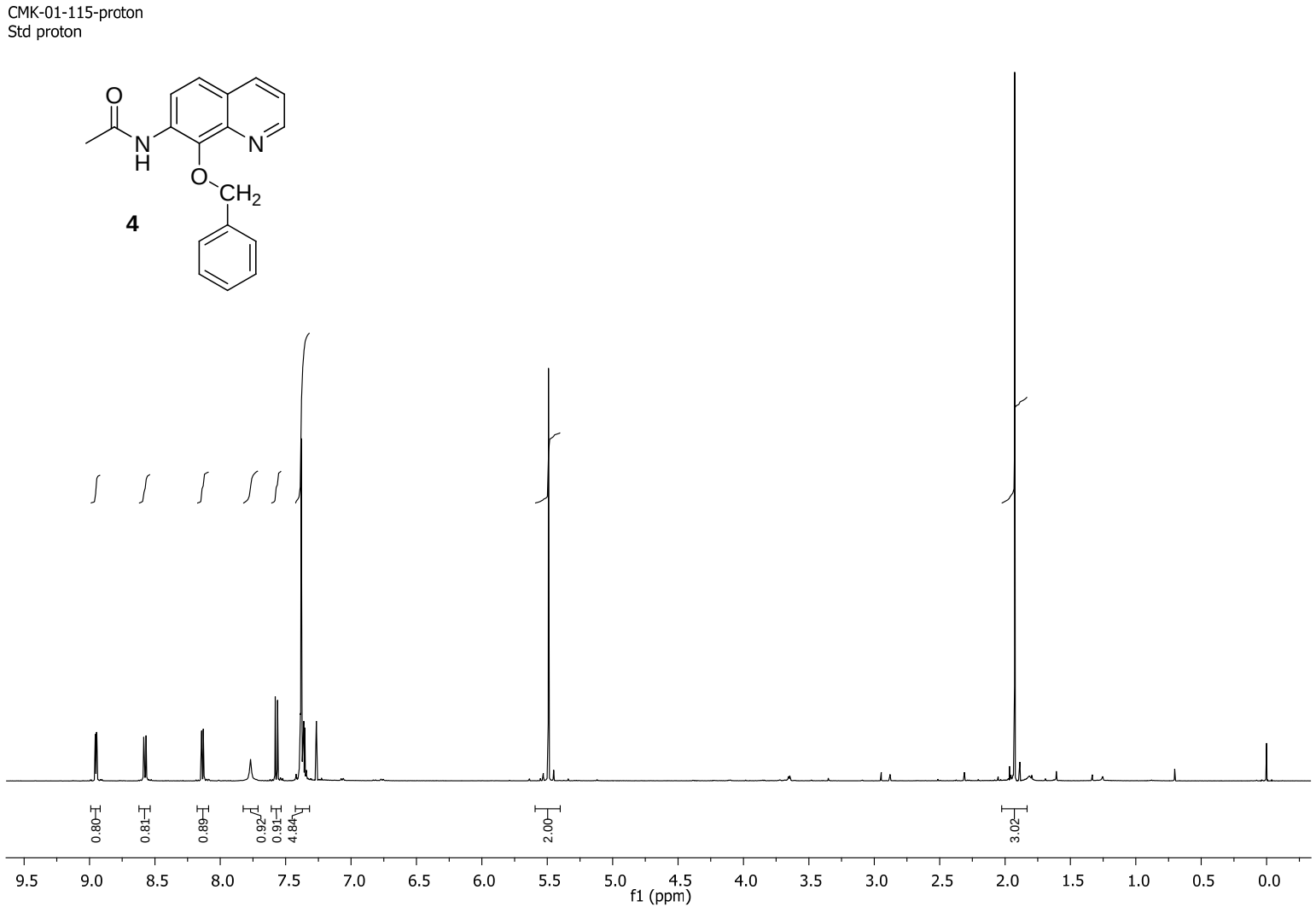

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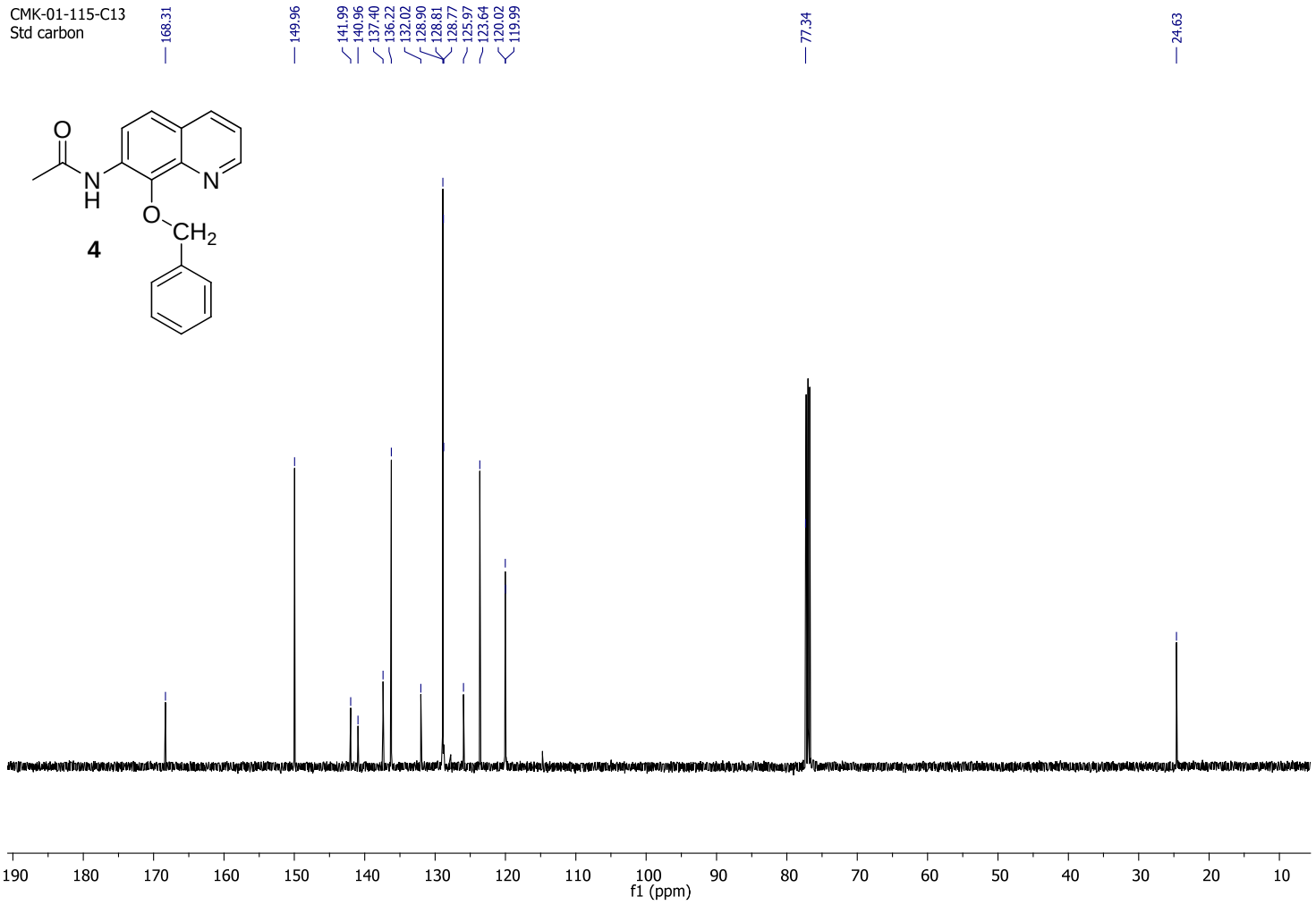

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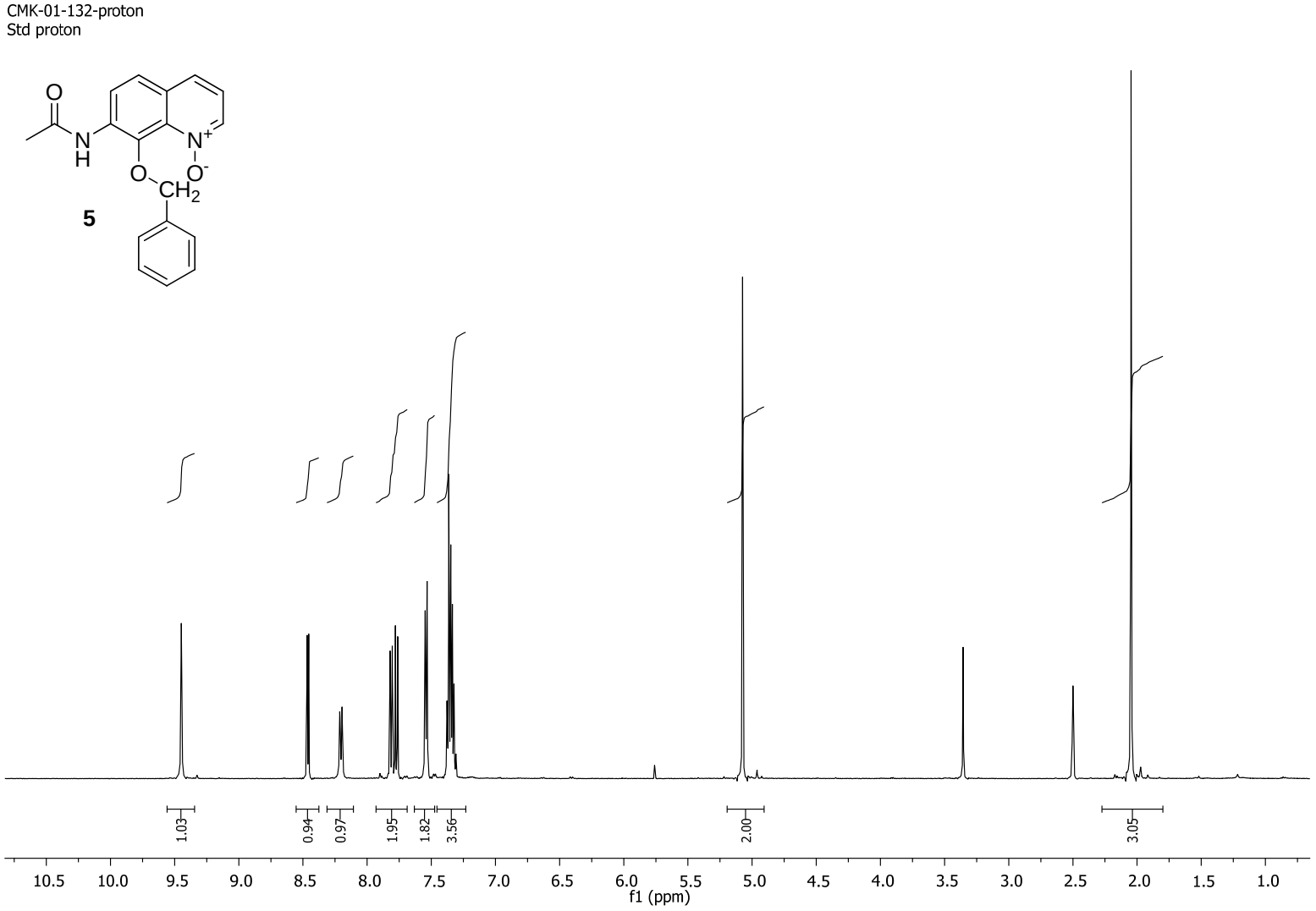
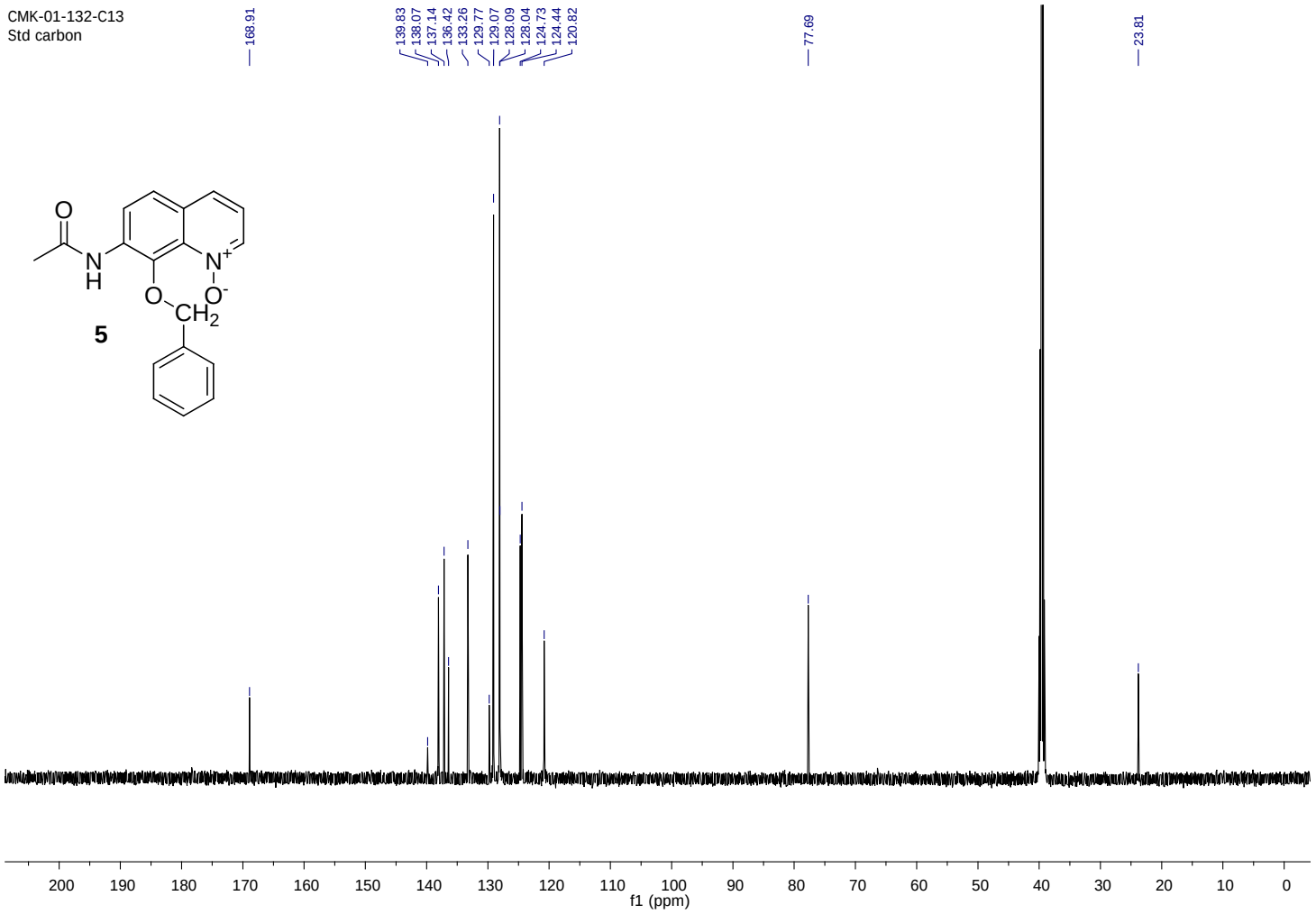


125 MHz ^{13}C-NMR of 7-acetamido-8-benzyloxyquinoline-1-oxide **(5)** in DMSO



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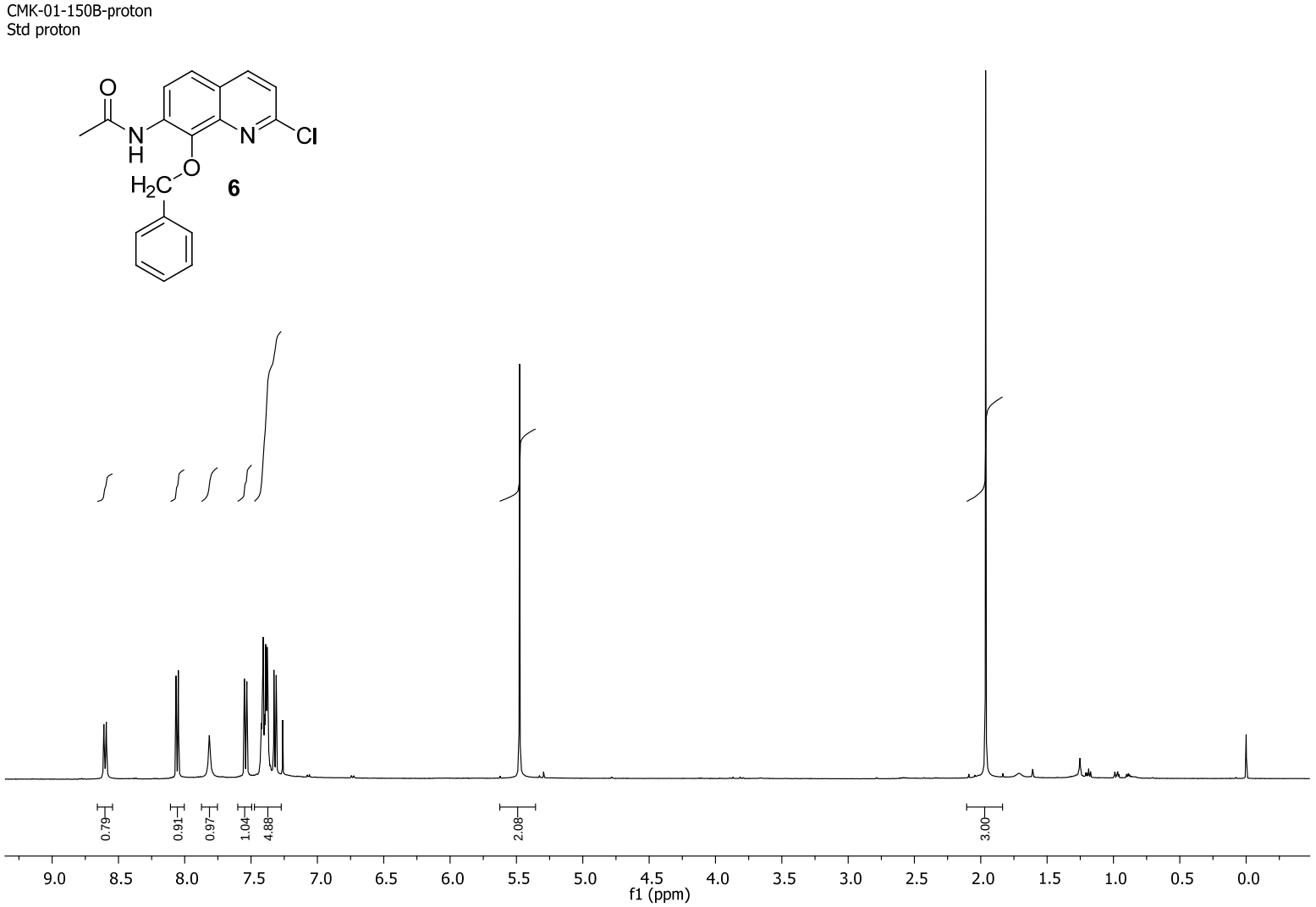

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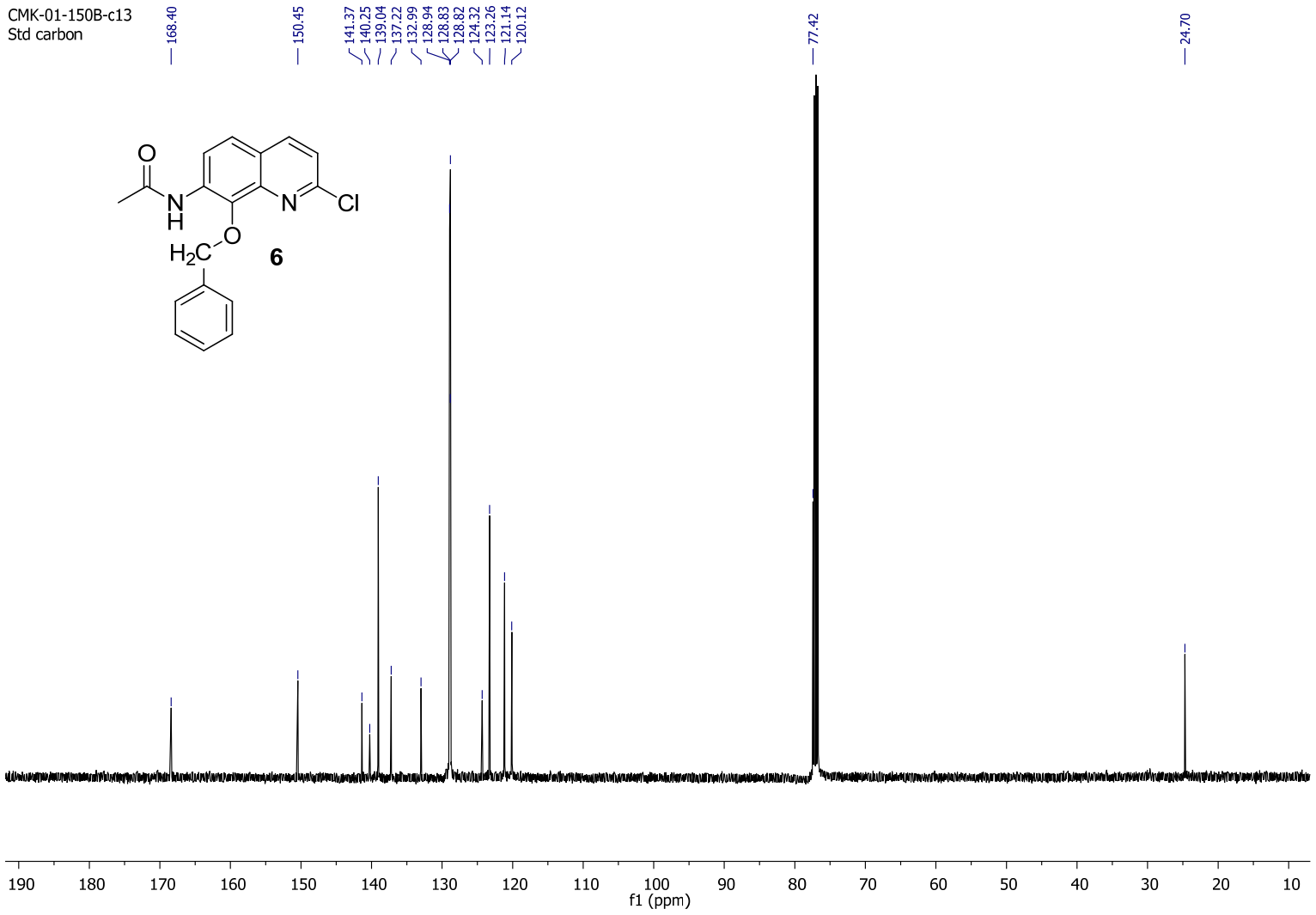

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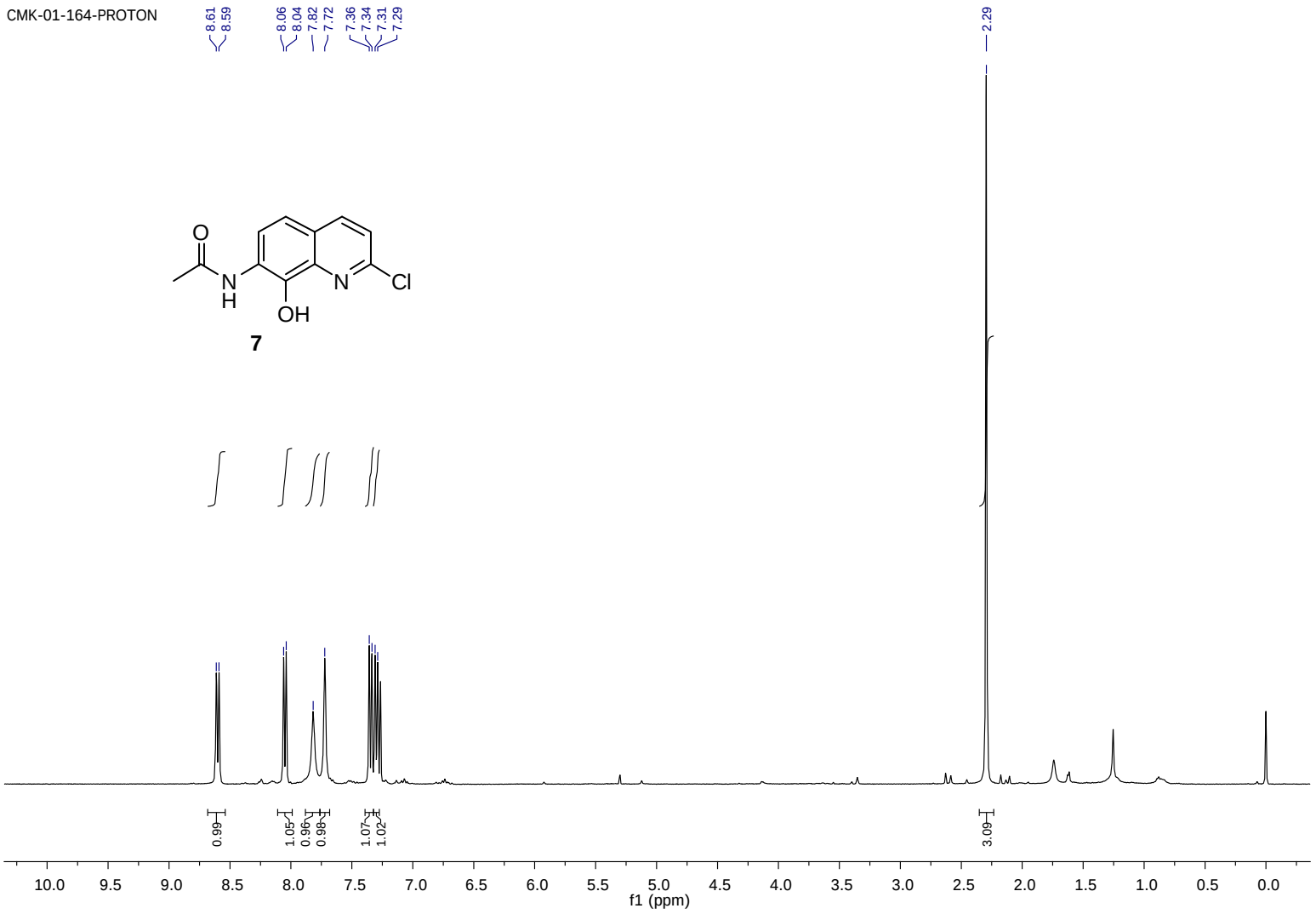

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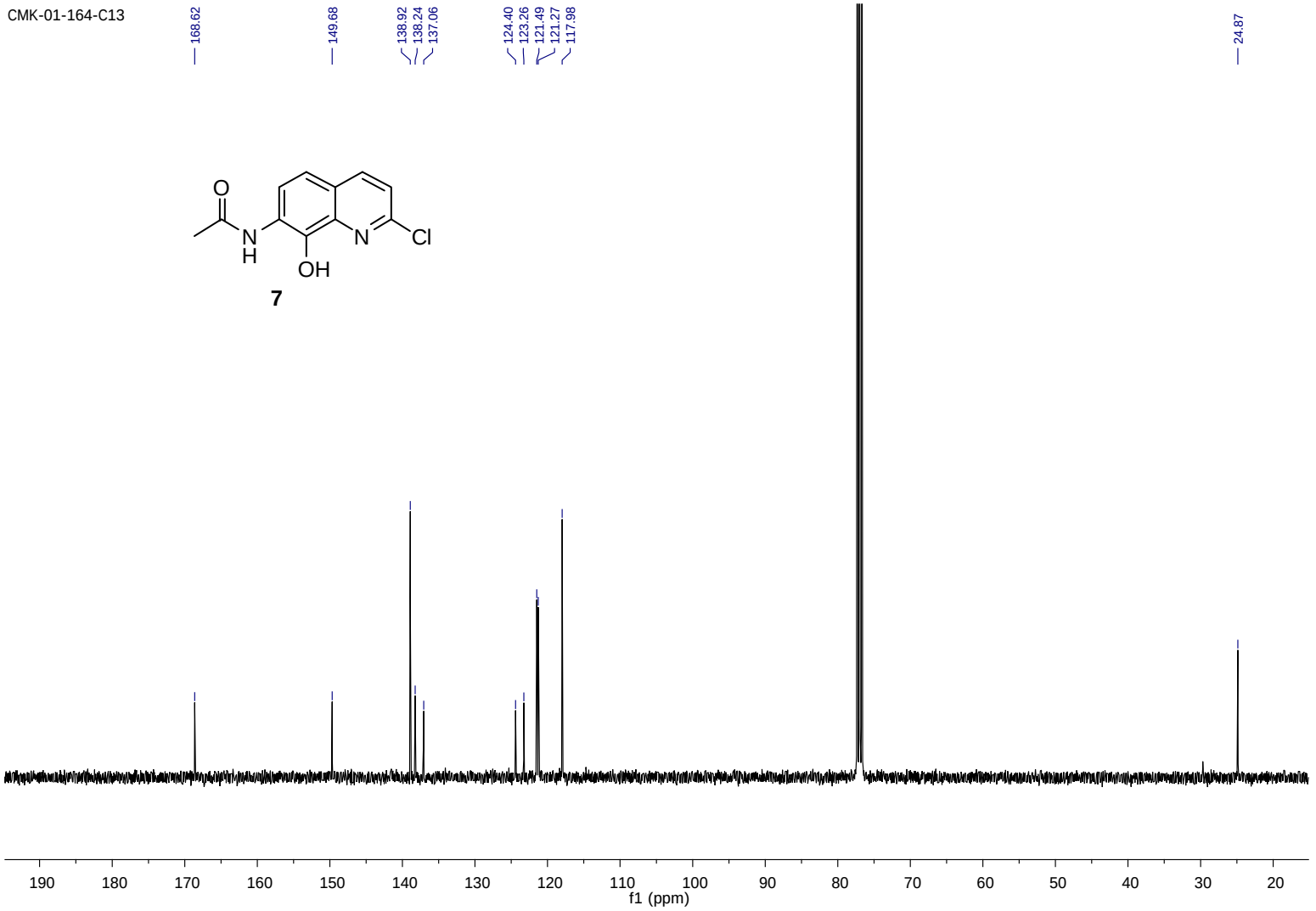

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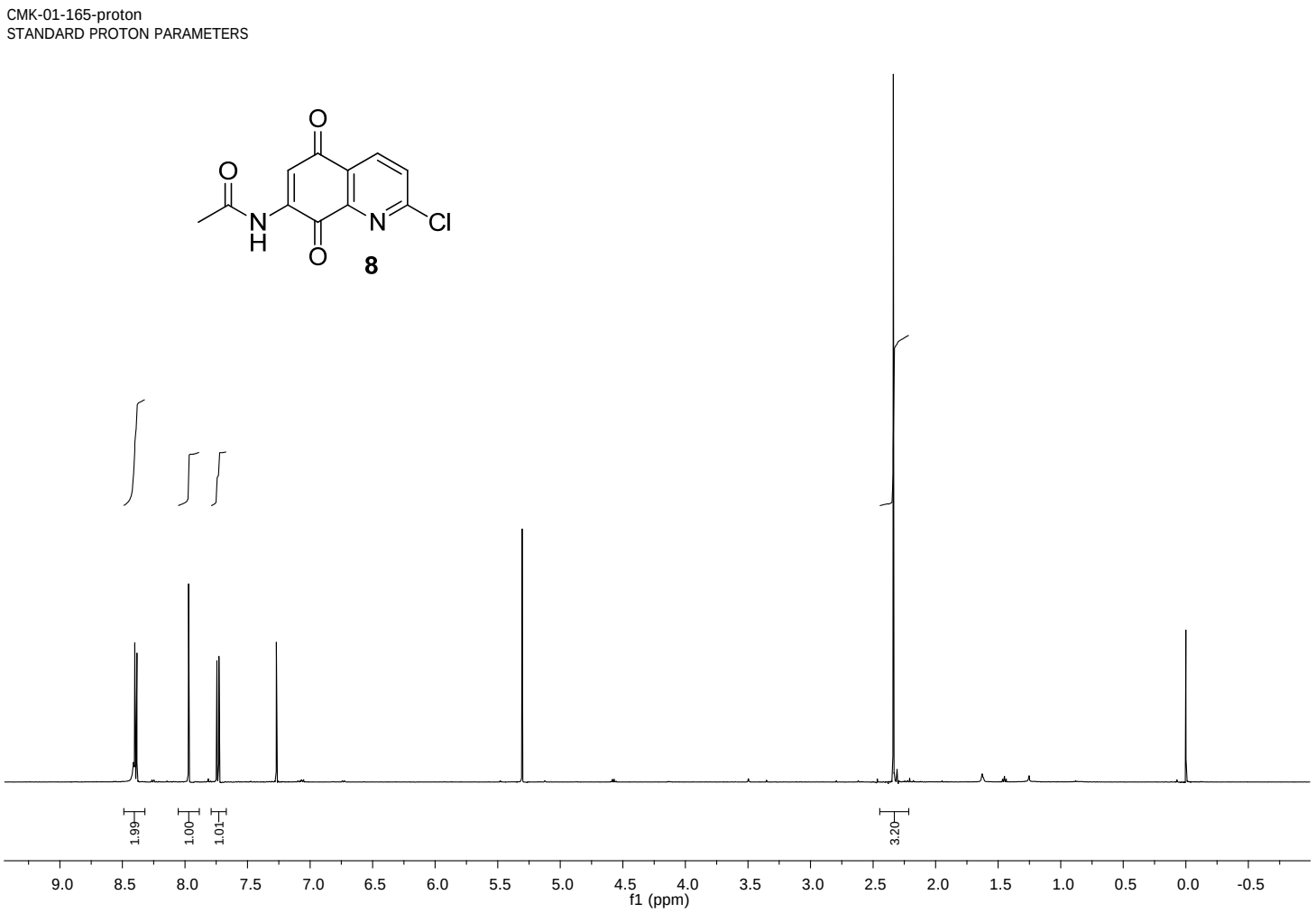

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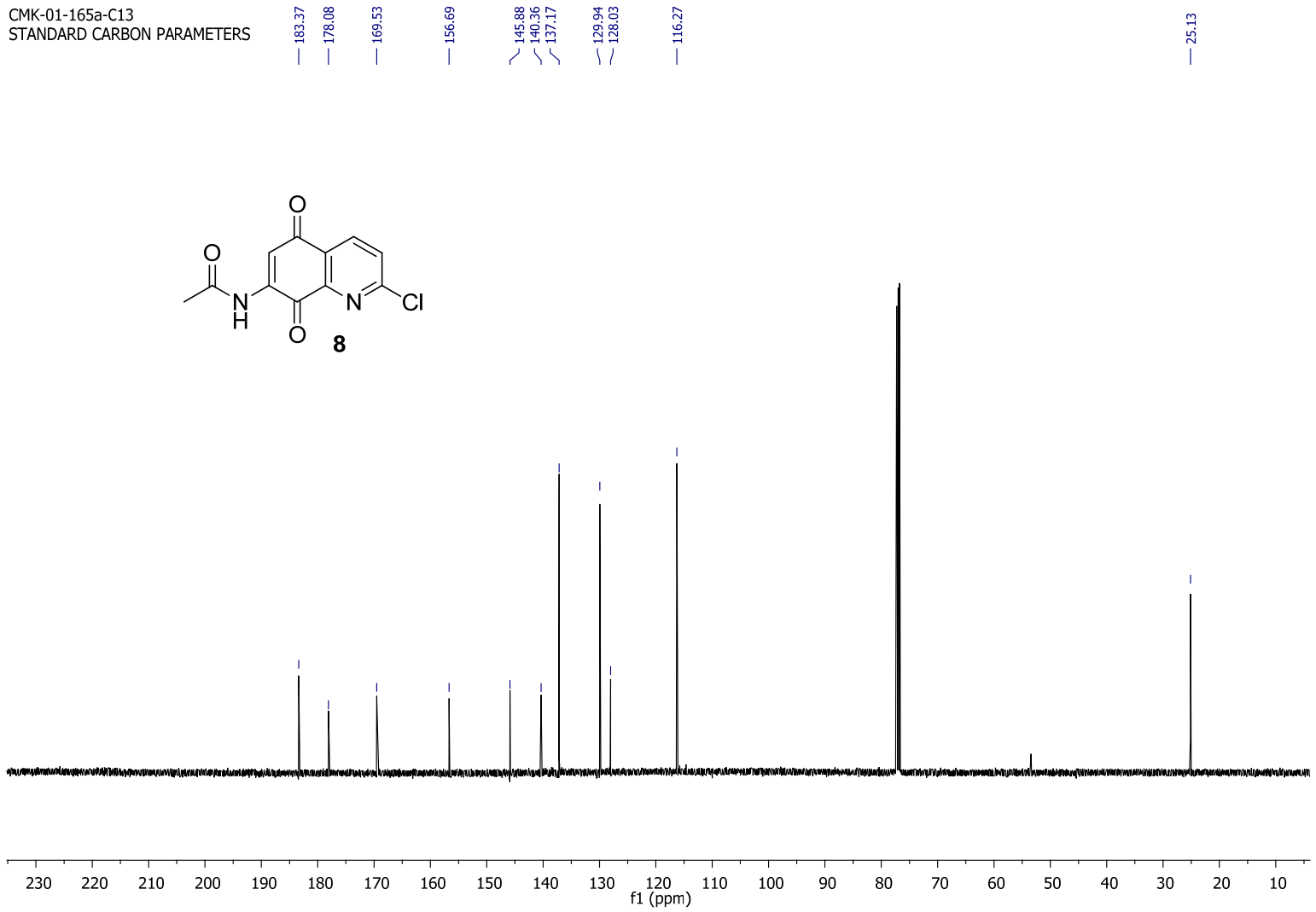

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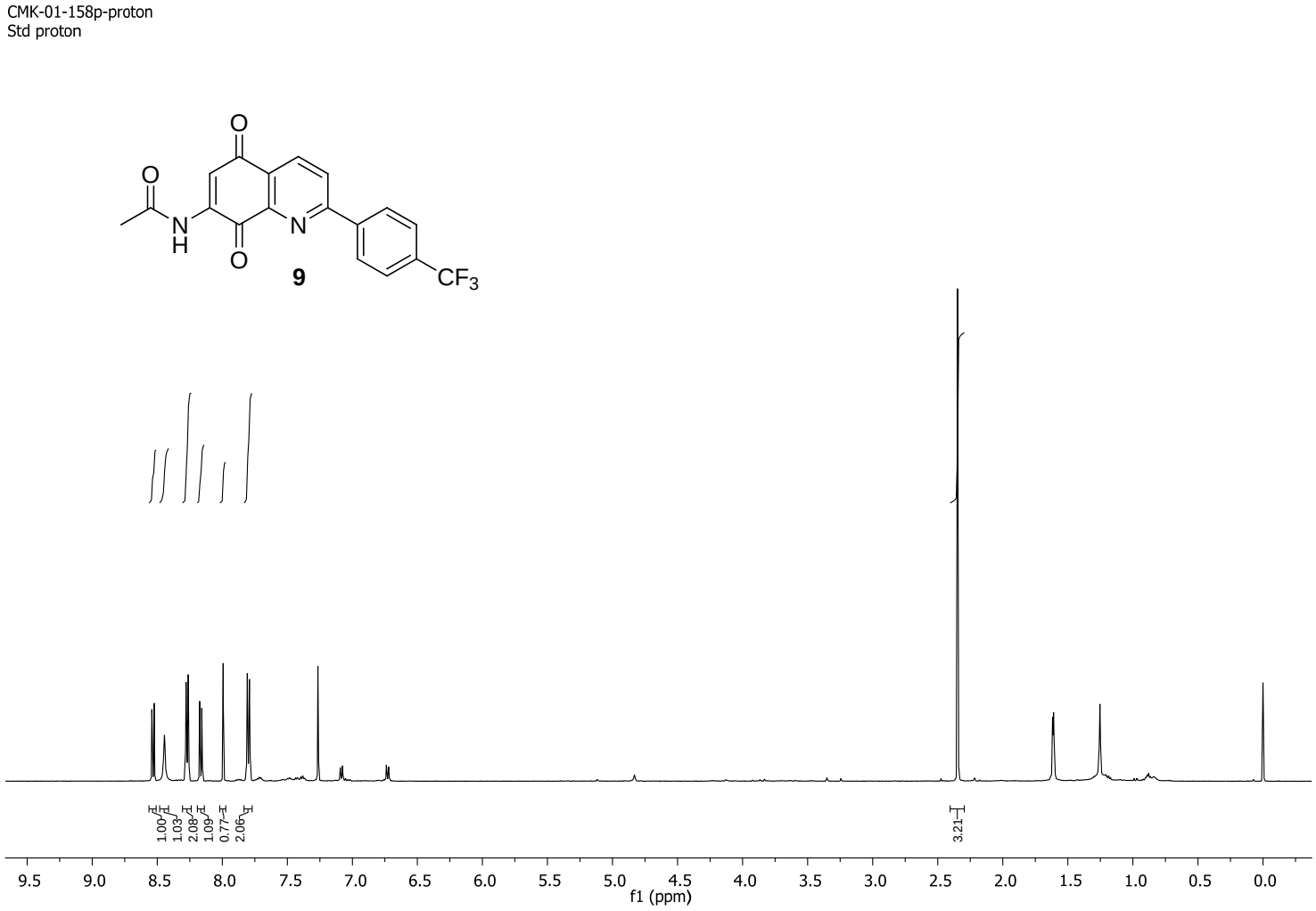

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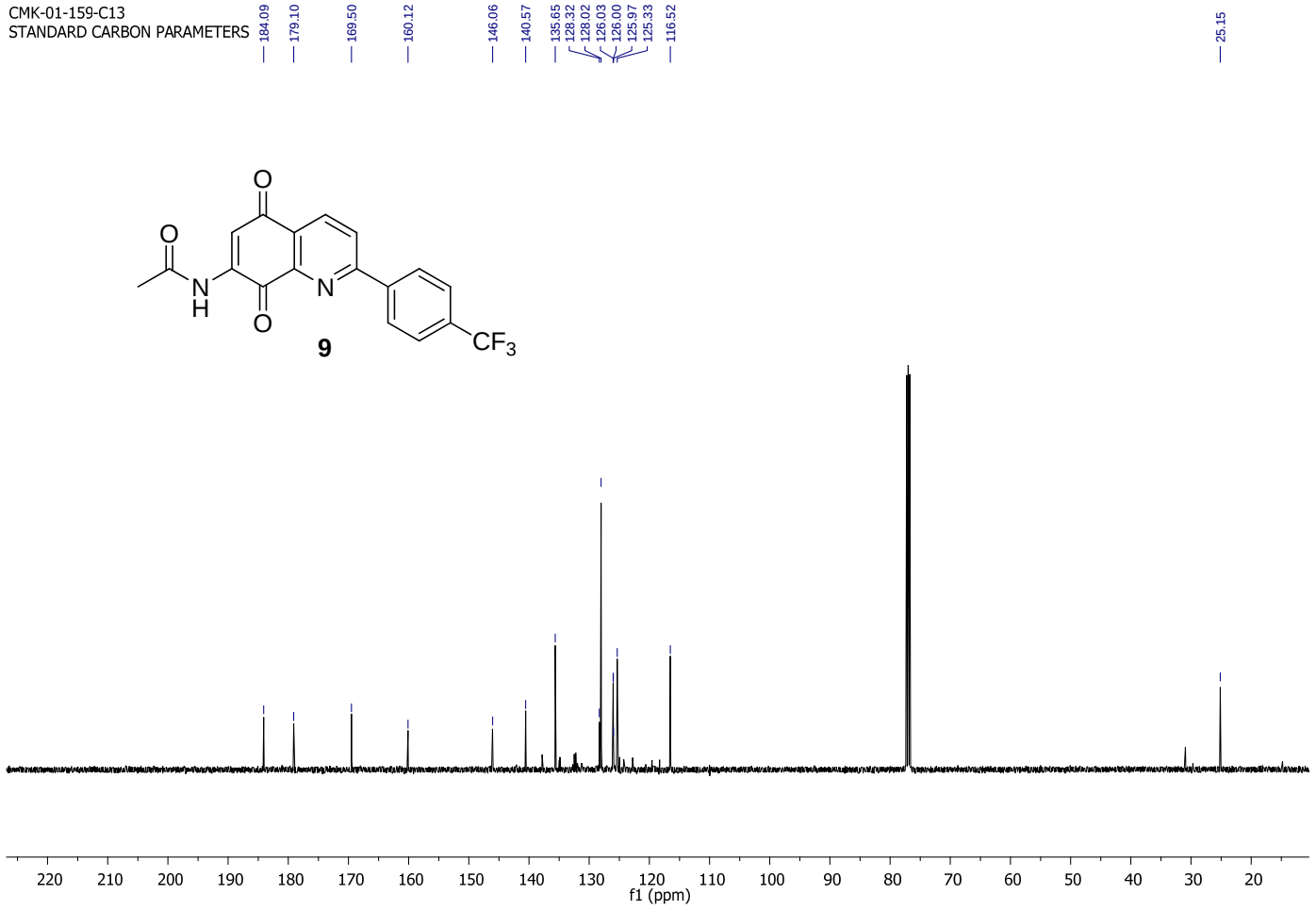

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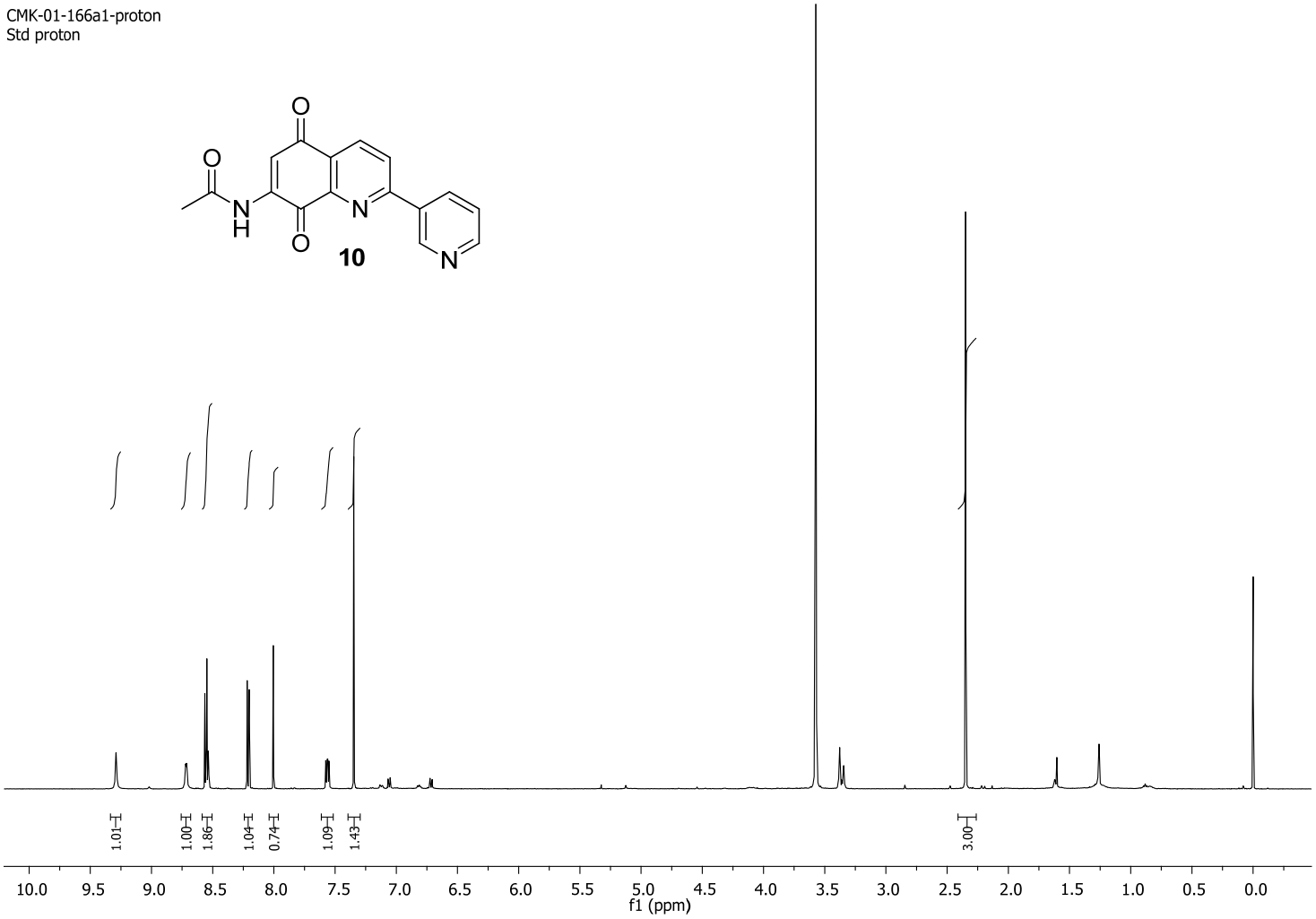
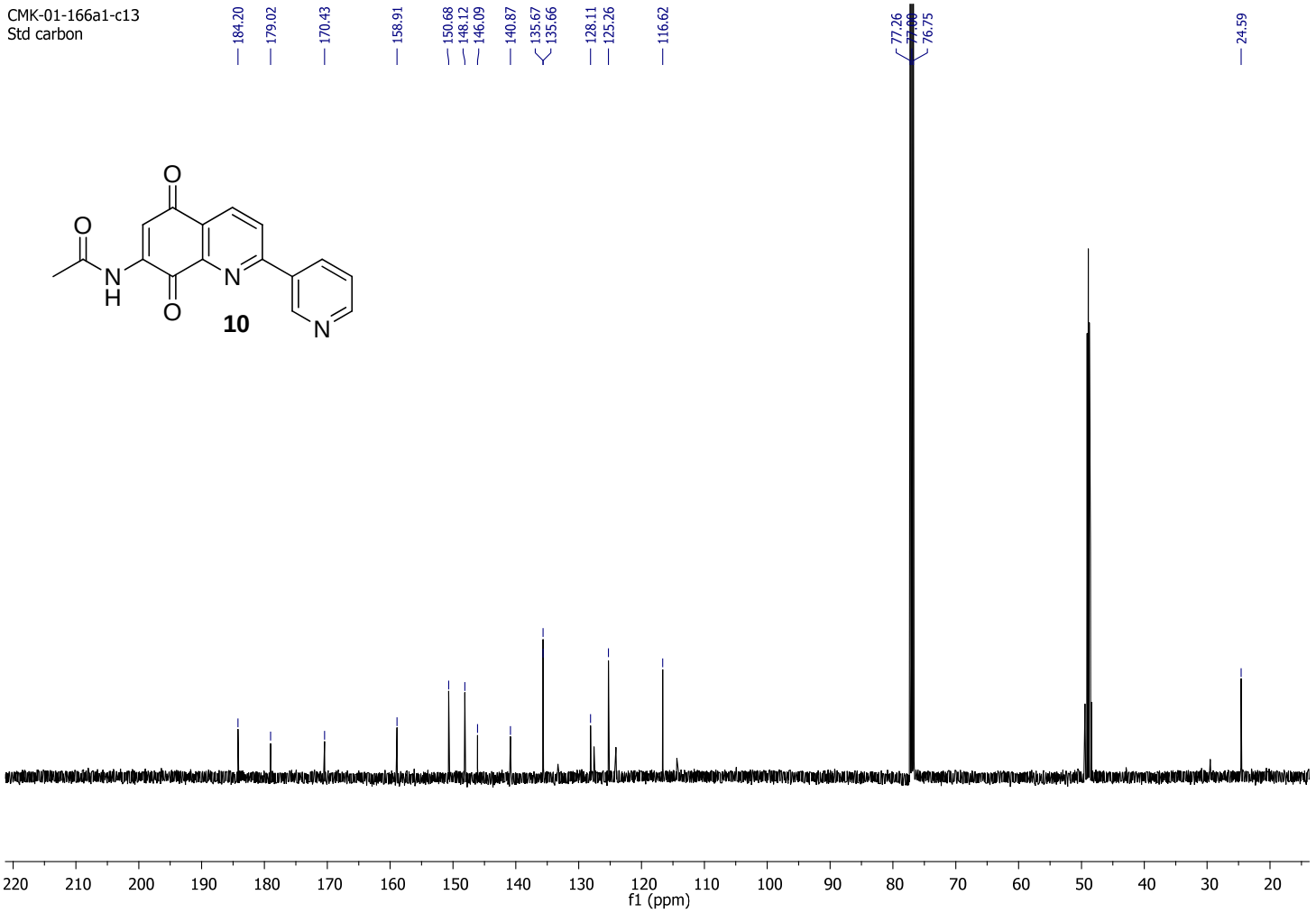


125 MHz ^{13}C-H-NMR of 7-acetamido-2-(3-pyridinyl)quinoline-5,8-dione **(10)** in $CDCl_3/CD_3OD$ mixture



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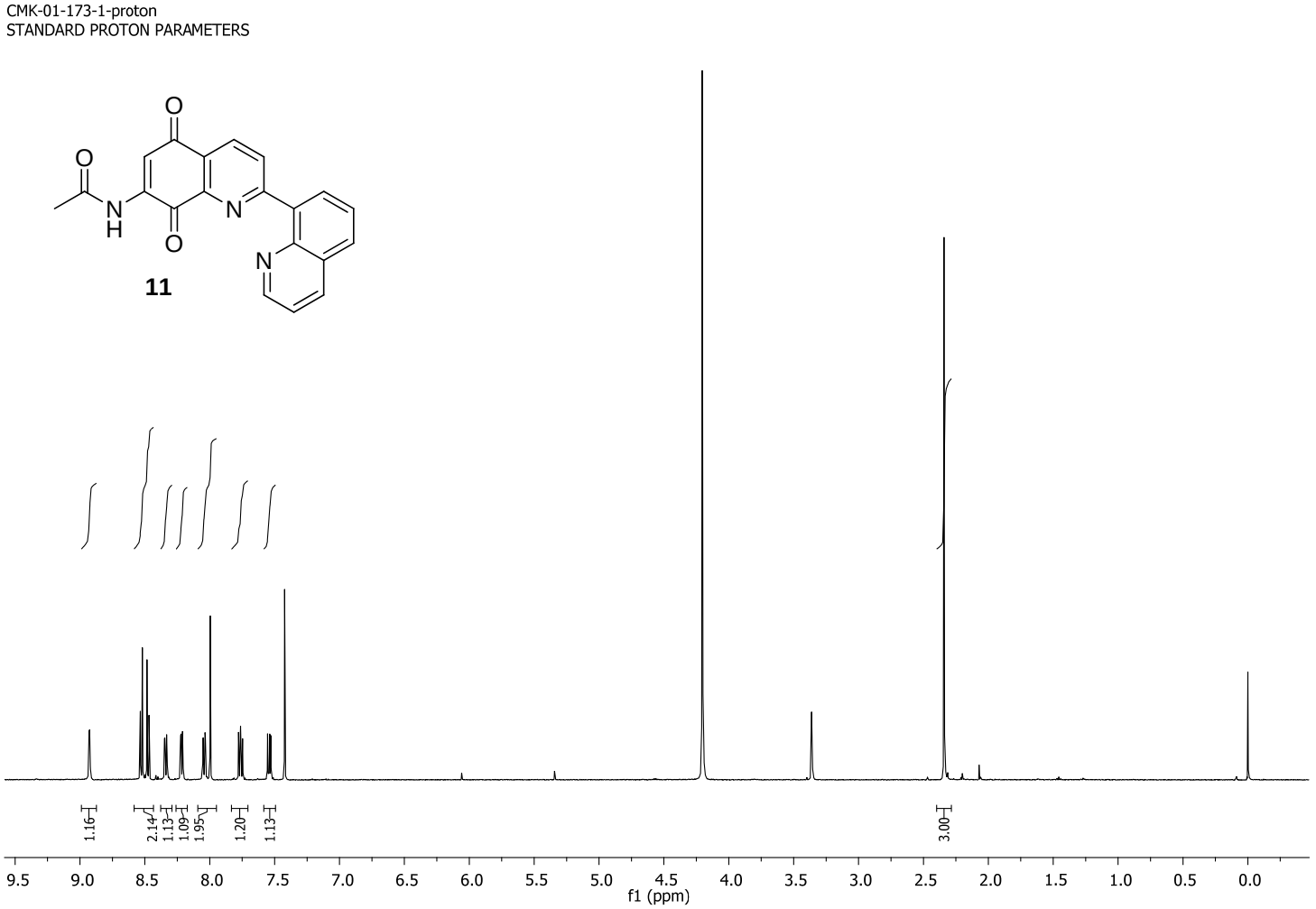
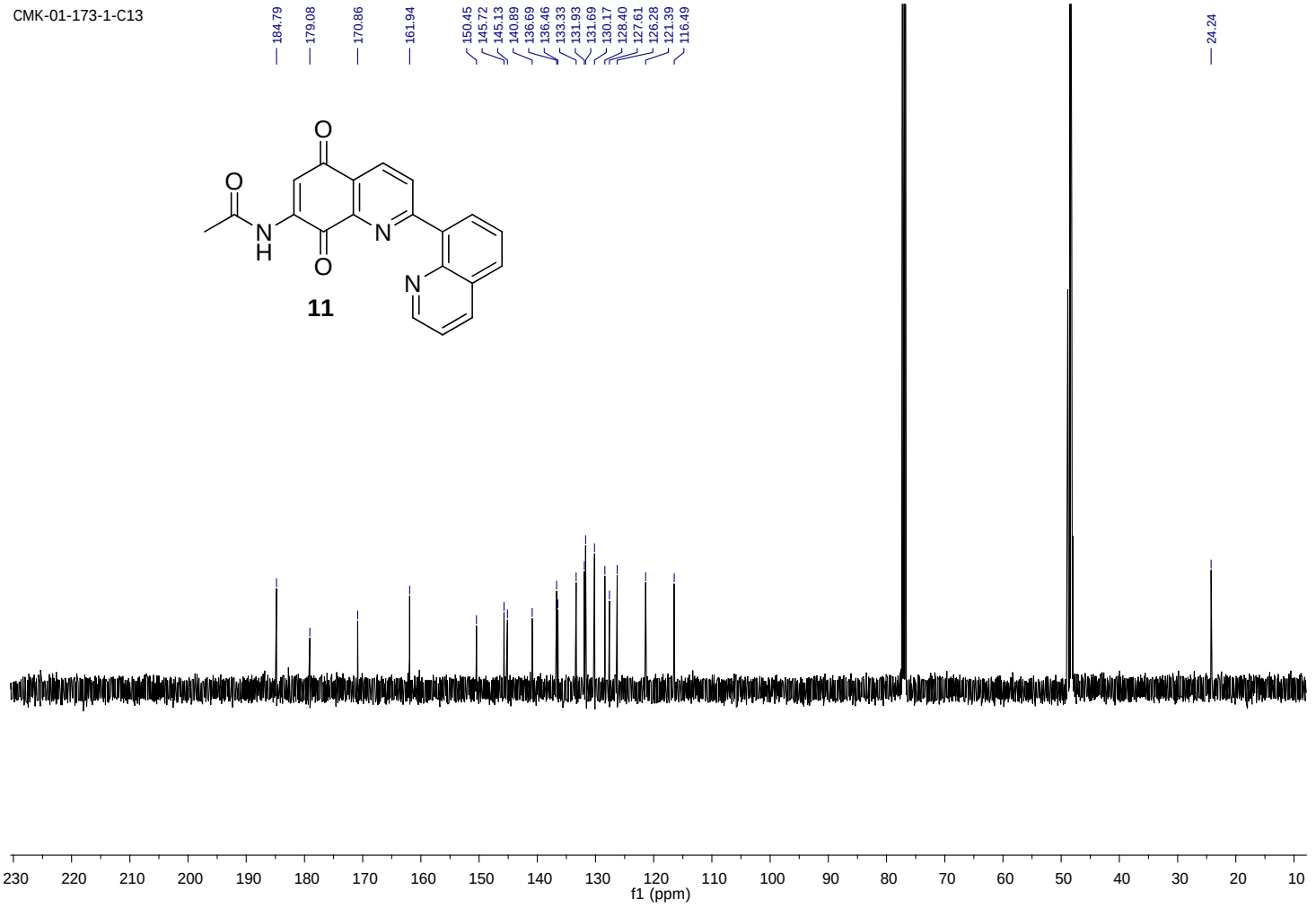
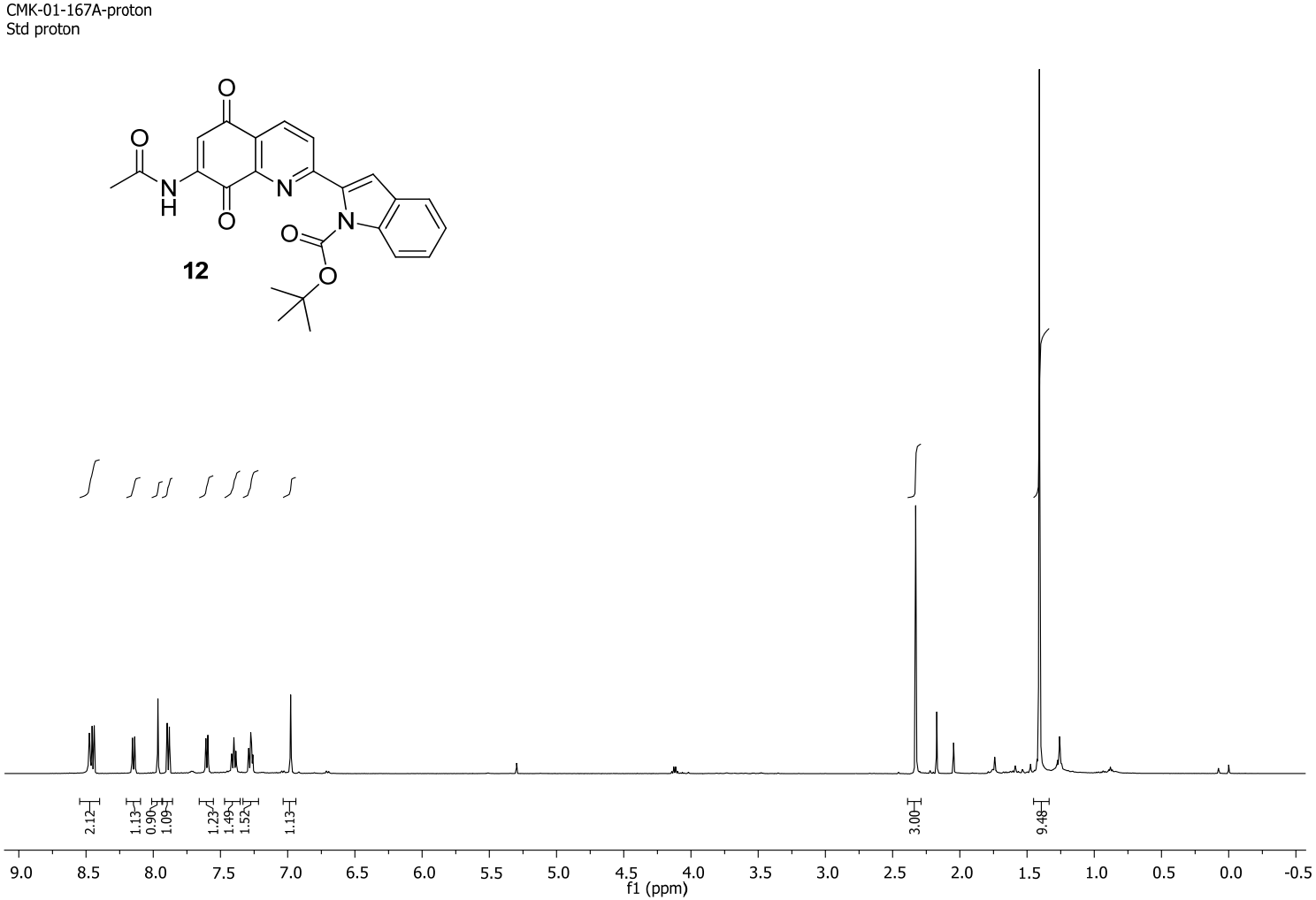


125 MHz ^{13}C-NMR of 7-acetamido-2-(8'-(quinolyl))quinoline-5,8-dione **(11)** in $CDCl_3/CD_3OD$ mixture



500 MHz ^{1}H-NMR of 7-acetamido-2-(2-(1-*tert*butoxycarbonylindolyl)quinoline-5,8-dione **(12)** in $CDCl_3$



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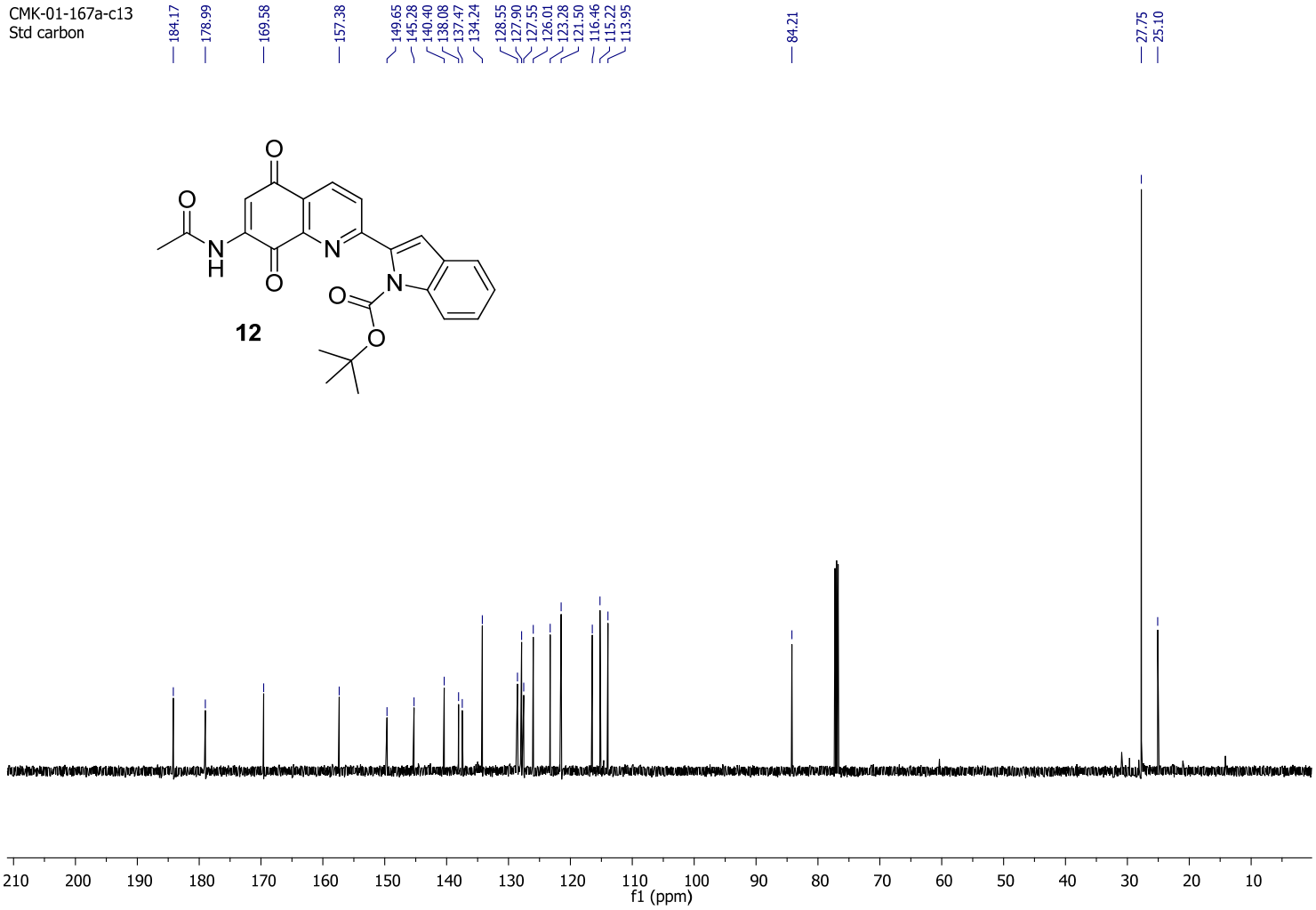
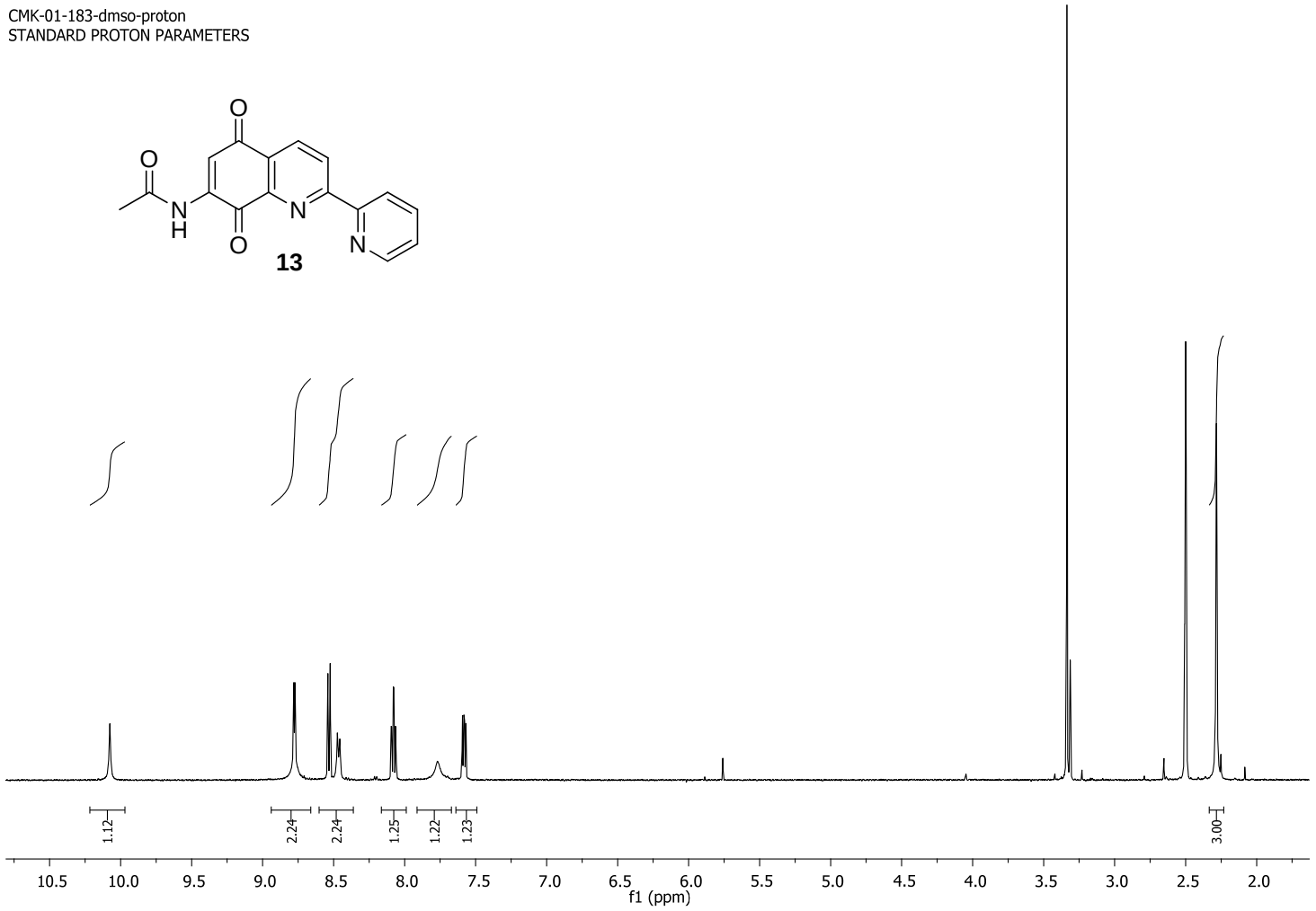


500 MHz ^{1}H-NMR of 7-acetamido-2-(2-(pyridinyl))quinoline-5,8-dione **(13)** in DMSO



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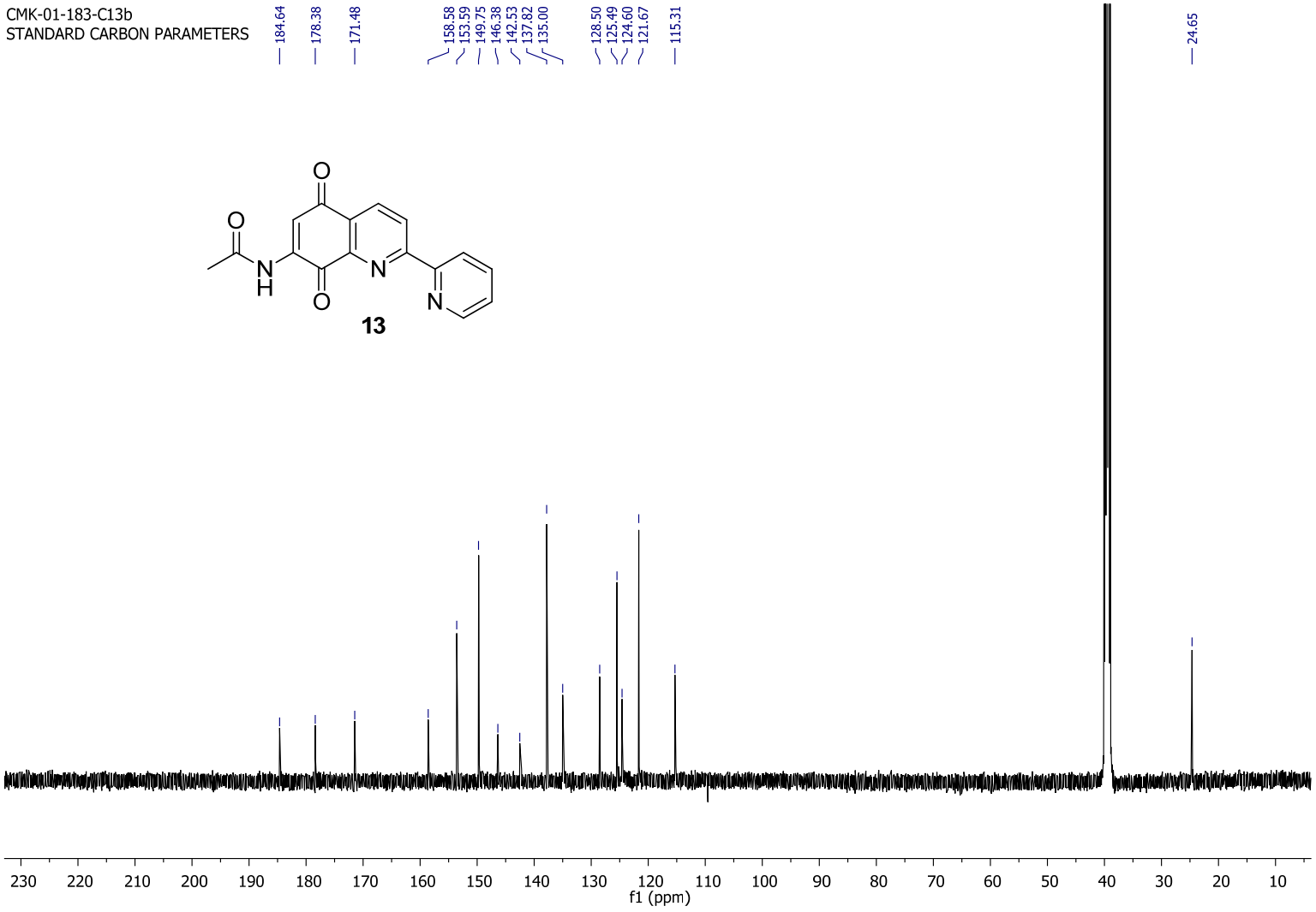
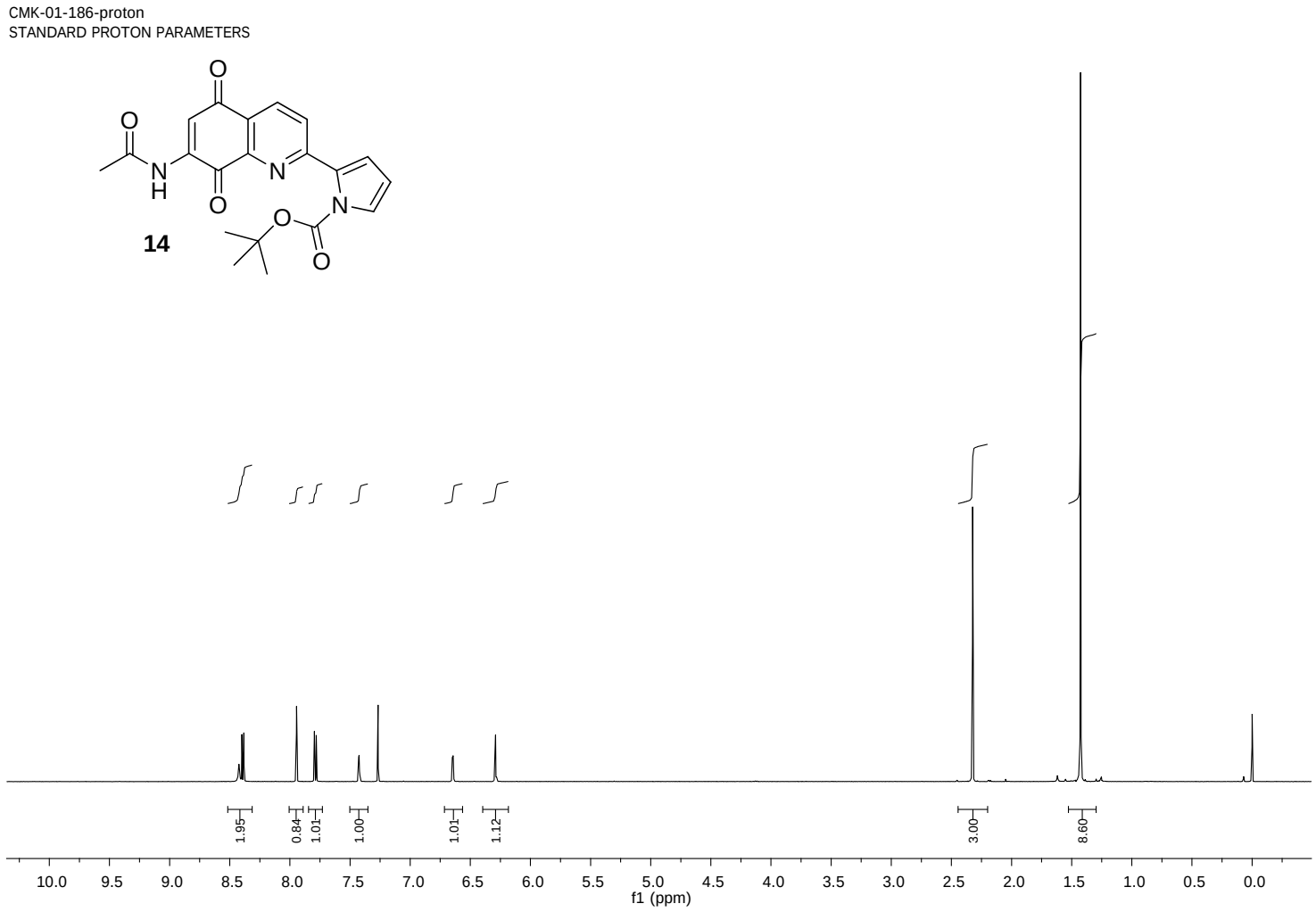
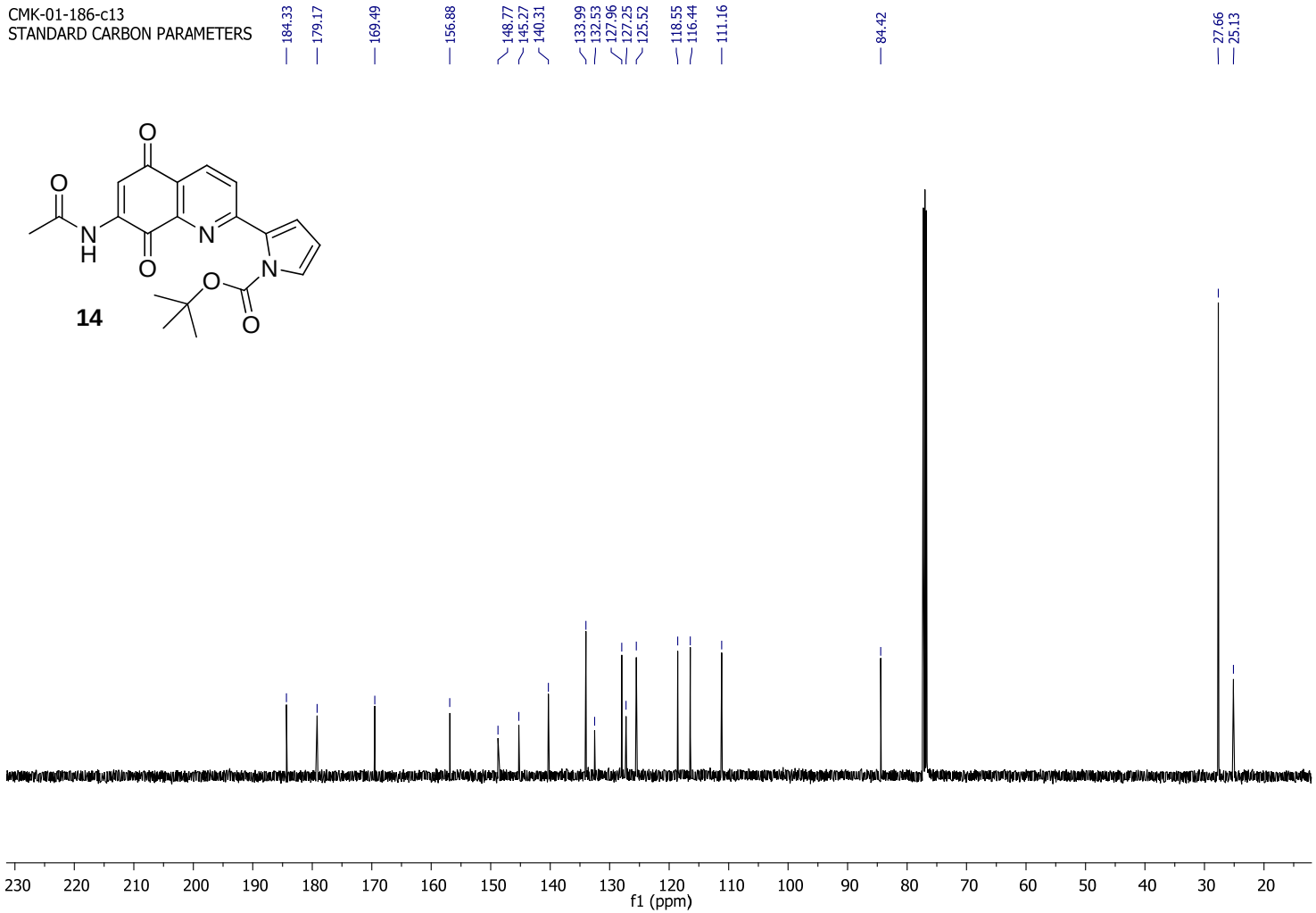


500 MHz ^{1}H-NMR of 7-acetamido-2-(2-(1-*tert*-butoxypyrrolyl))quinoline-5,8-dione **(14)** in $CDCl_3$



125 MHz ^{13}C-NMR of 7-acetamido-2-(2-(1-*tert*-butoxypyrrolyl))quinoline-5,8-dione **(14)** in $CDCl_3$



500 MHz ^{1}H-NMR of 7-acetamido-2-(4-pyrazolyl)quinoline-5,8-dione **(15)** in DMSO

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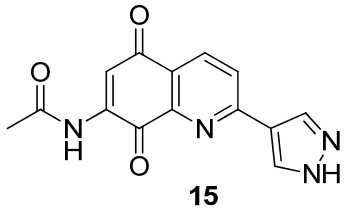
STANDARD PROTON PARAMETERS



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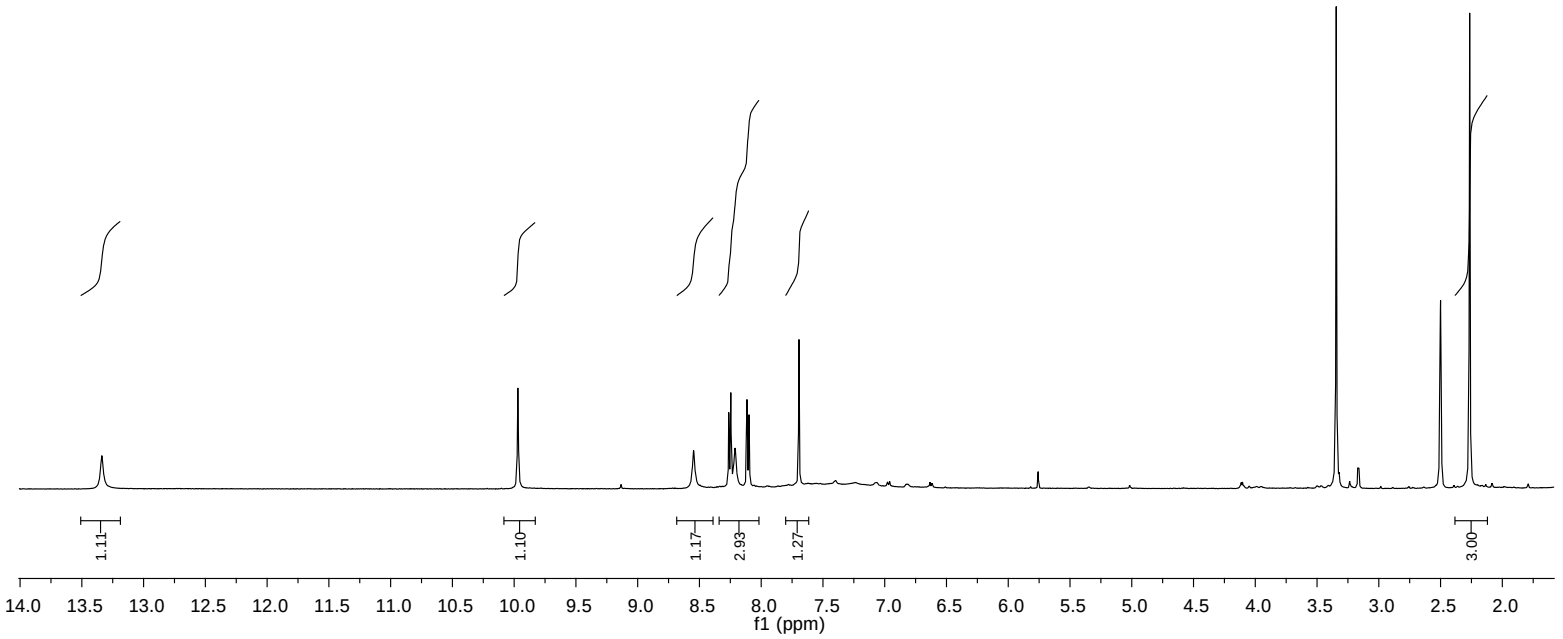

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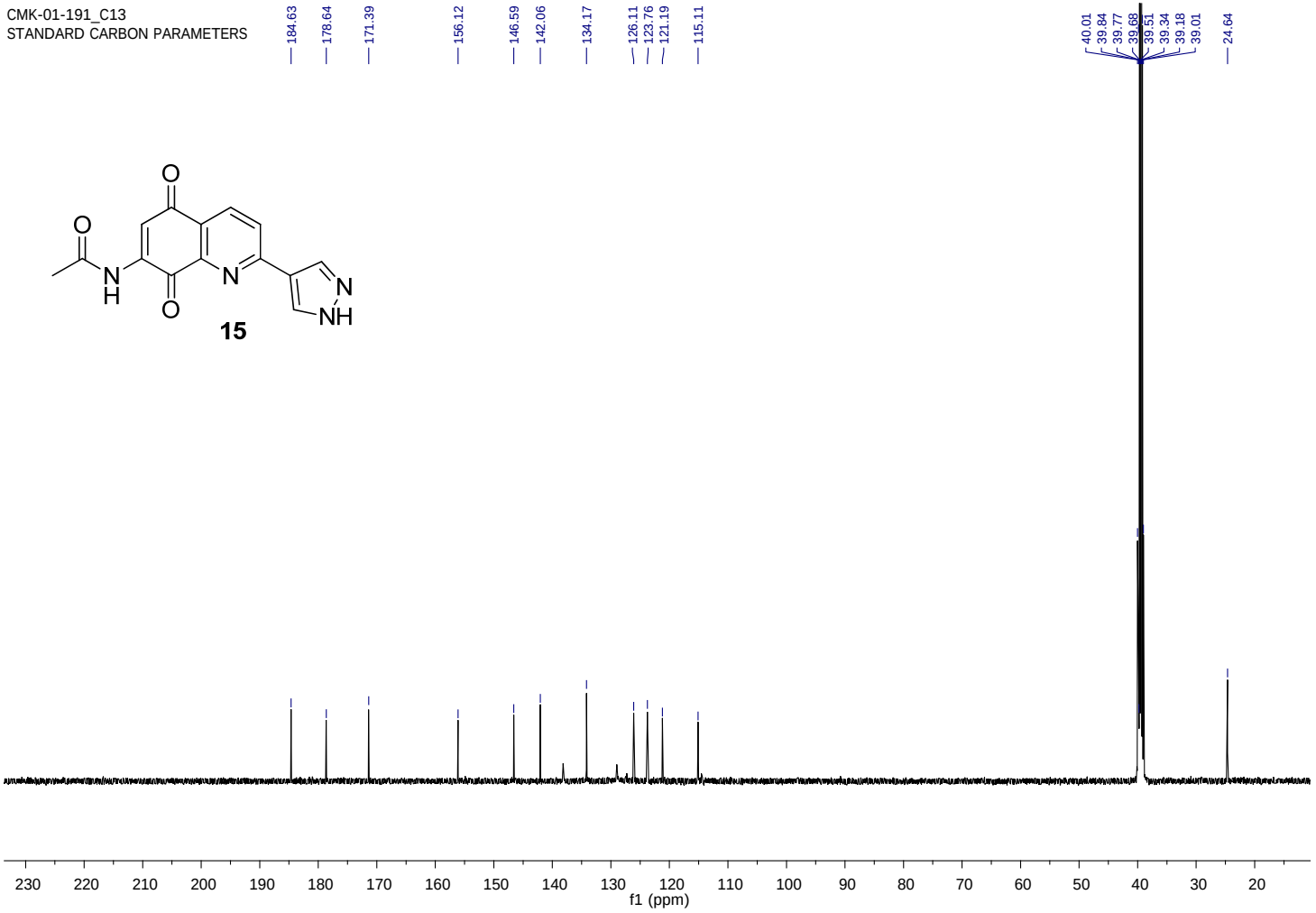
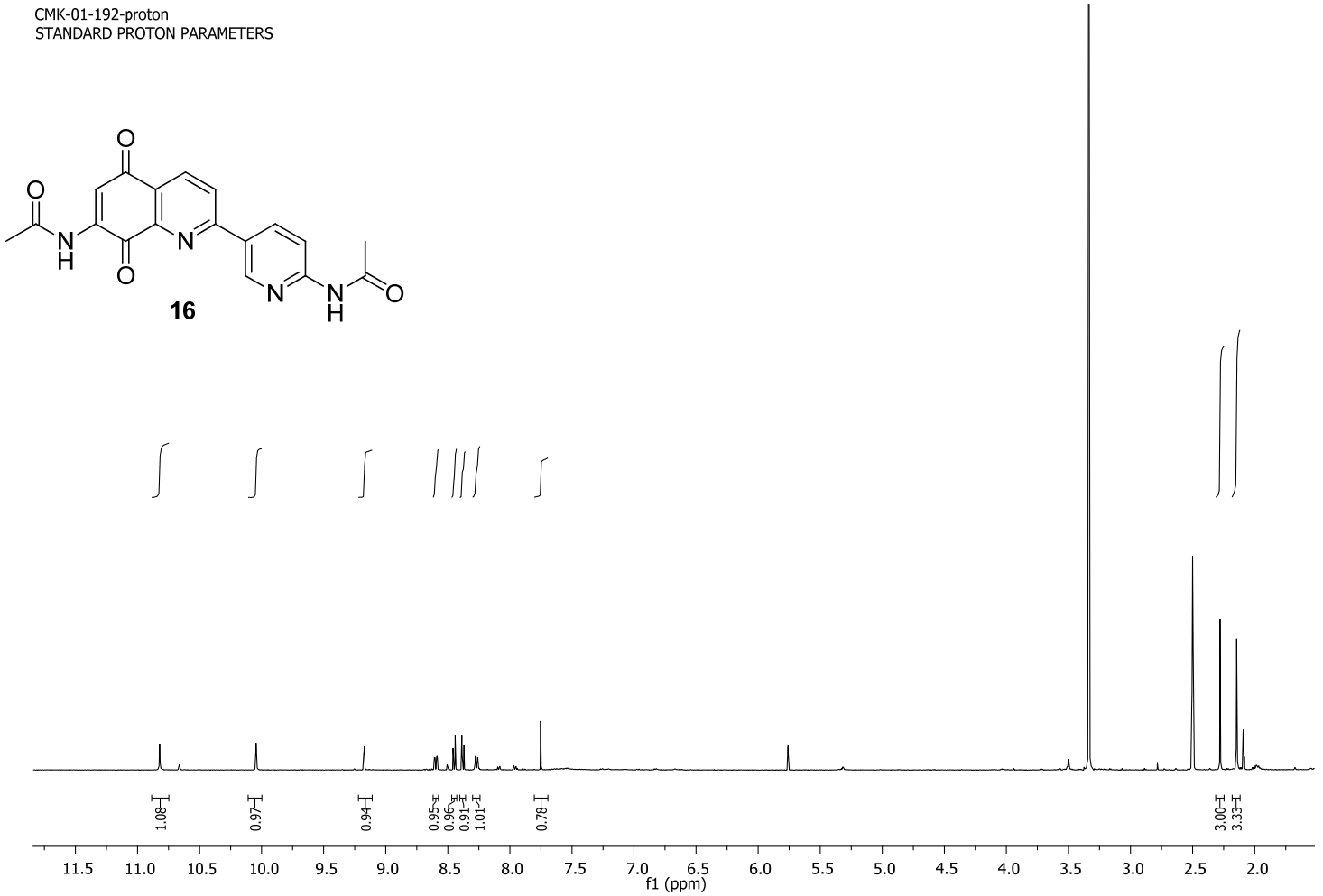
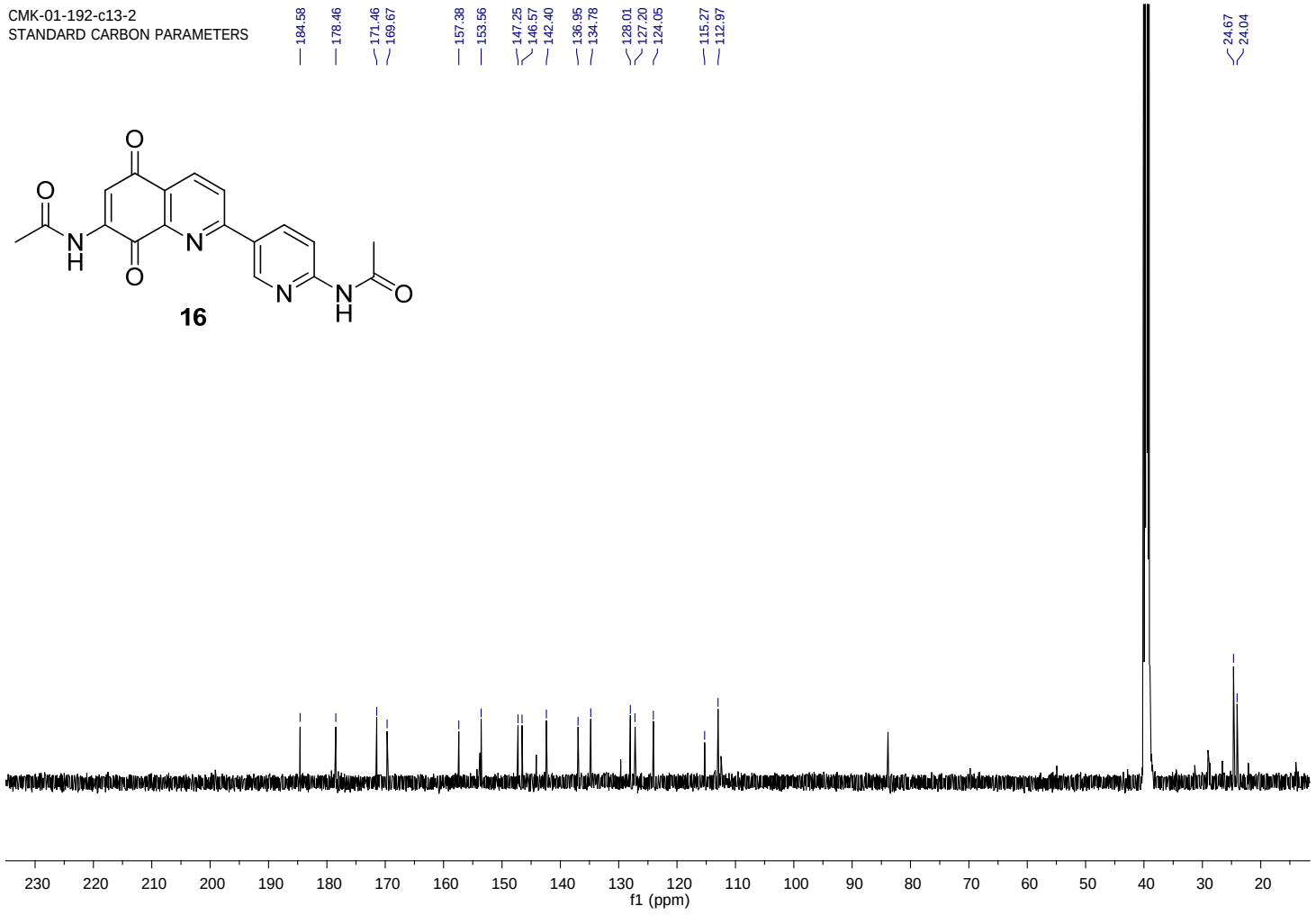


500 MHz ^{1}H-NMR of 7-acetamido-2-(3-(2-acetamidopyridinyl))quinoline-5,8-dione **(16)** in $CDCl_3/CD_3OD$ mixture



125 MHz ^{13}C-NMR of 7-acetamido-2-(3-(2-acetamidopyridinyl))quinoline-5,8-dione **(16)** in $CDCl_3/CD_3OD$ mixture



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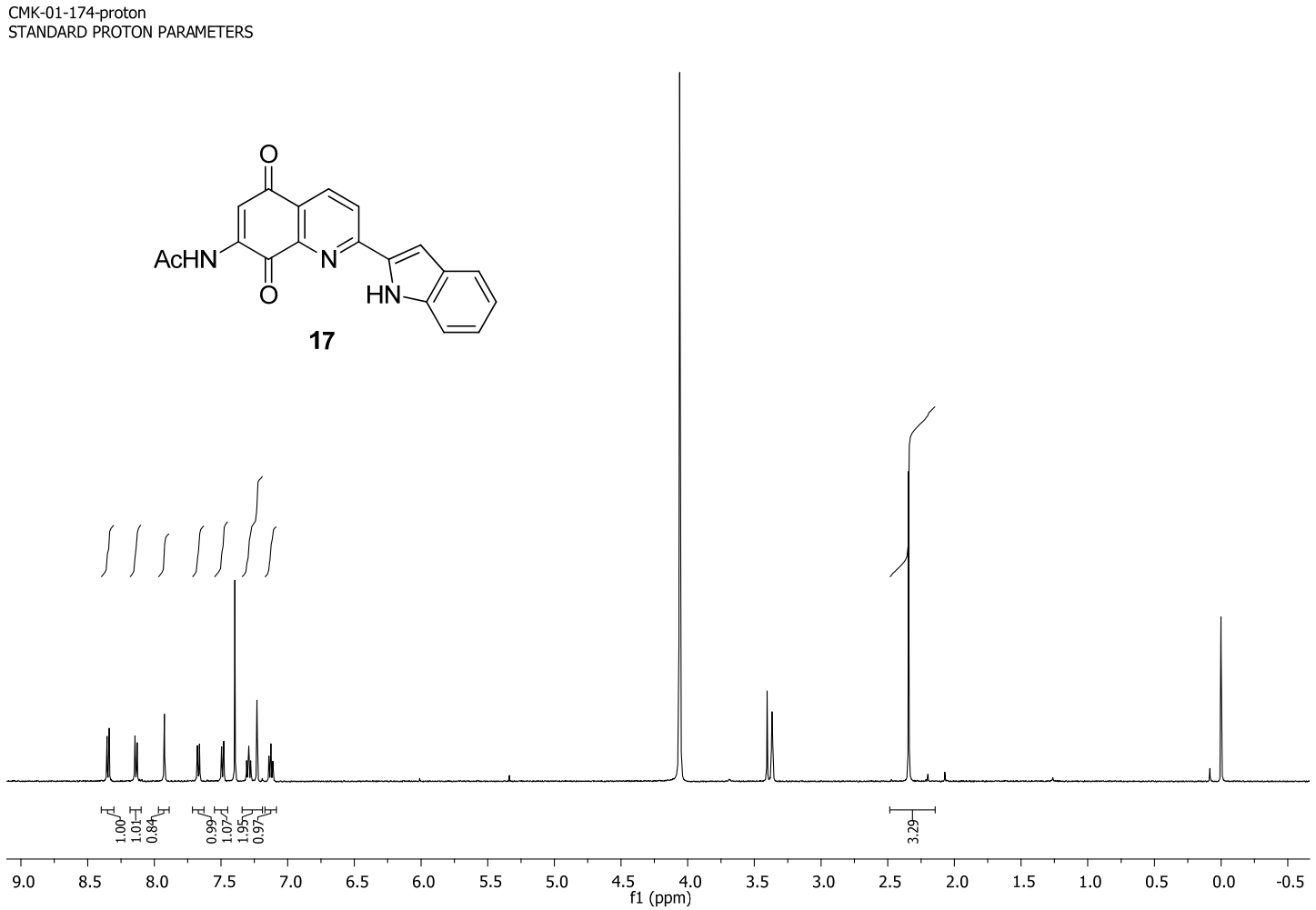
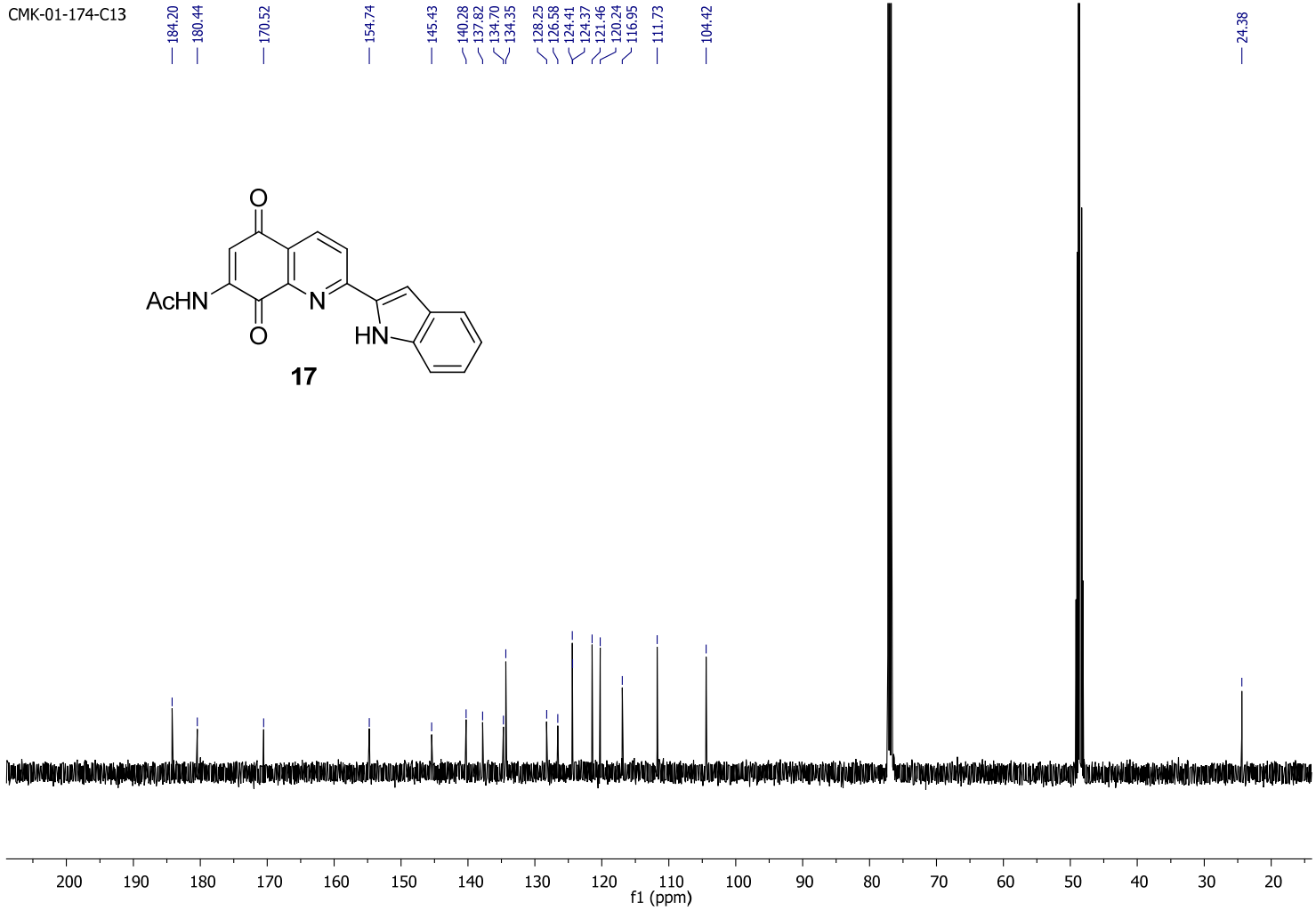
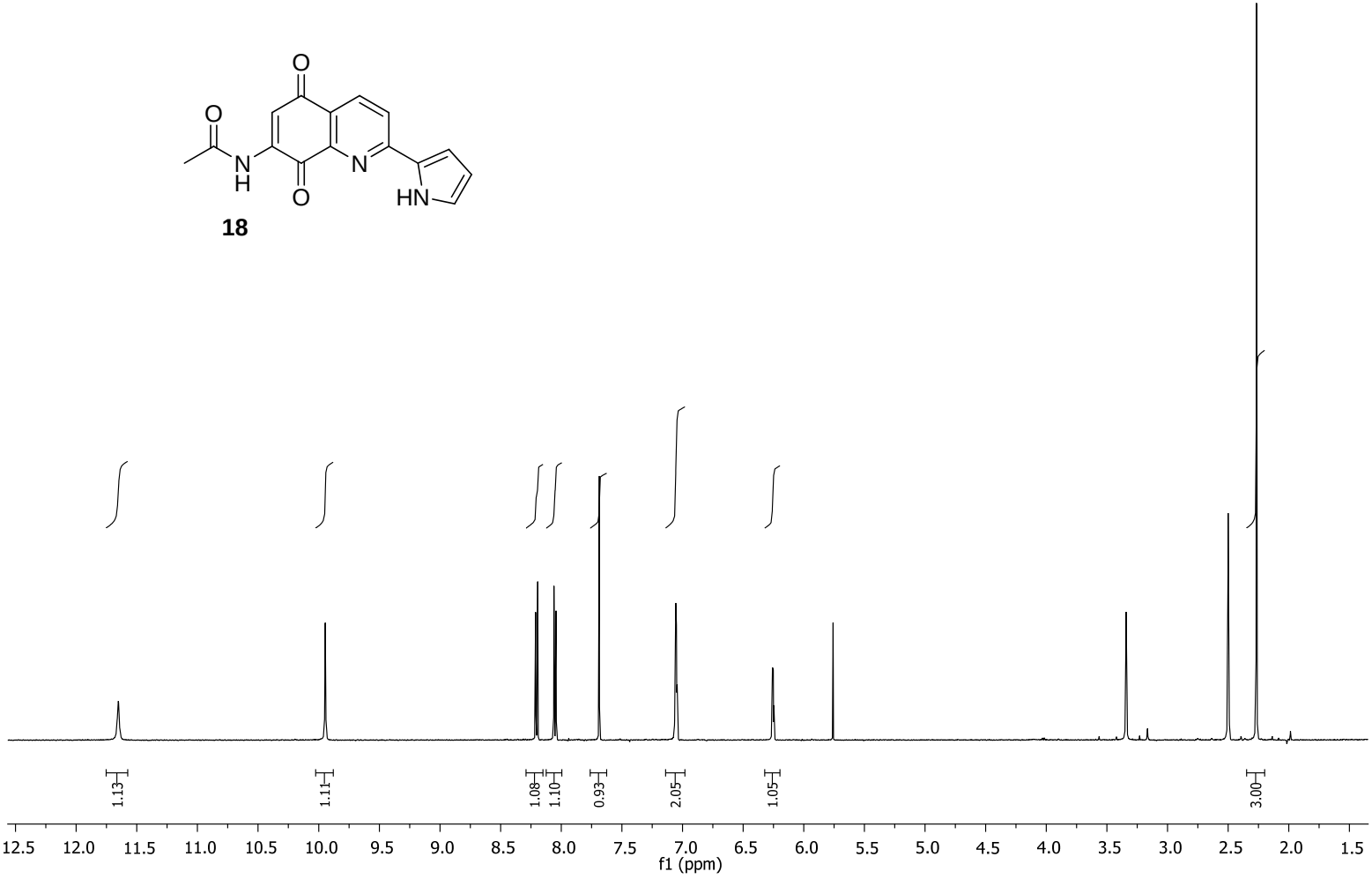


125 MHz ^{13}C-NMR of 7-acetamido-2-(2-(indolyl))quinoline-5,8-dione **(17)** in $CDCl_3$

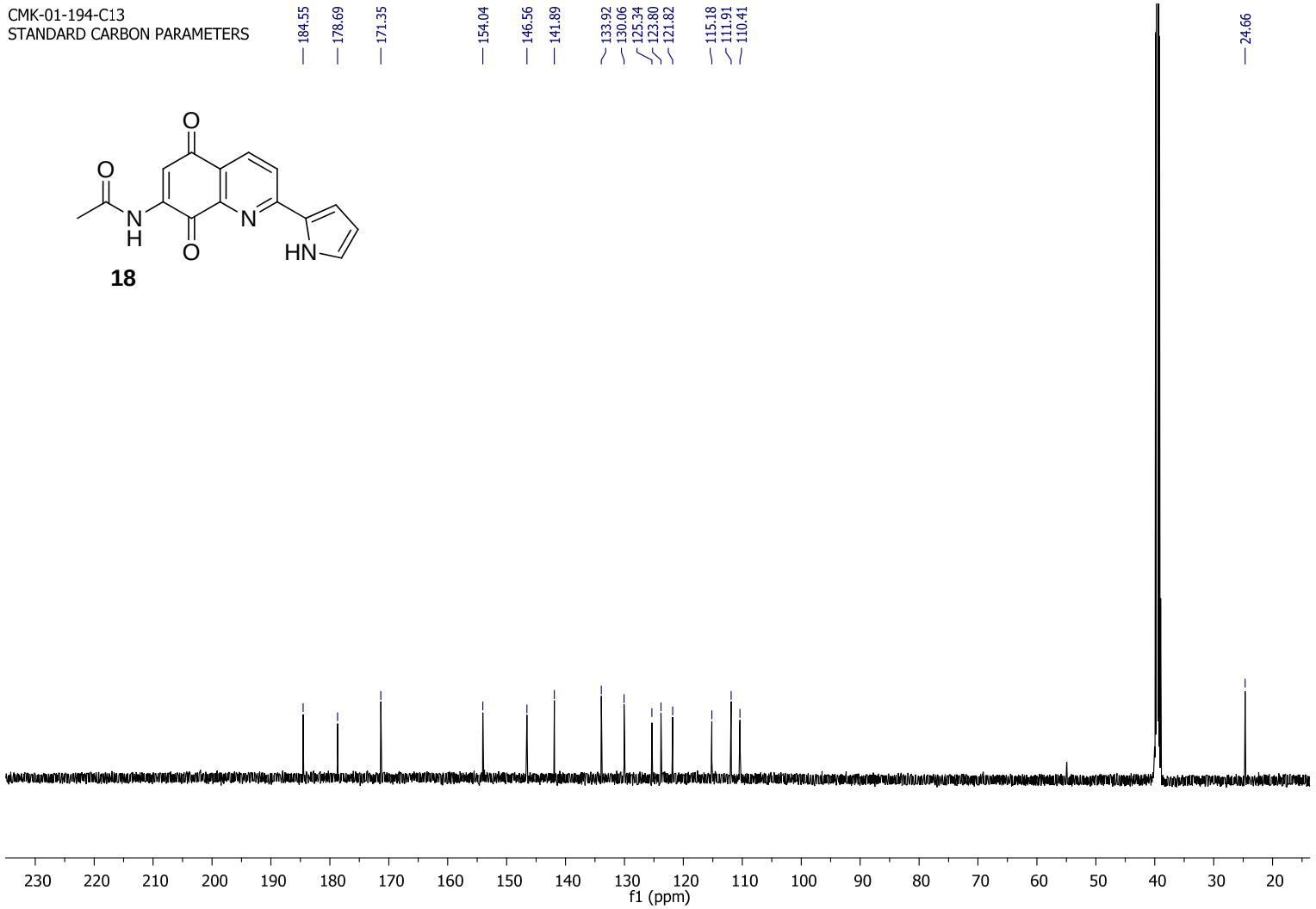


500 MHz ^{1}H-NMR of 7-acetamido-2-(2-(pyrrolyl))quinoline-5,8-dione **(18)** in DMSO

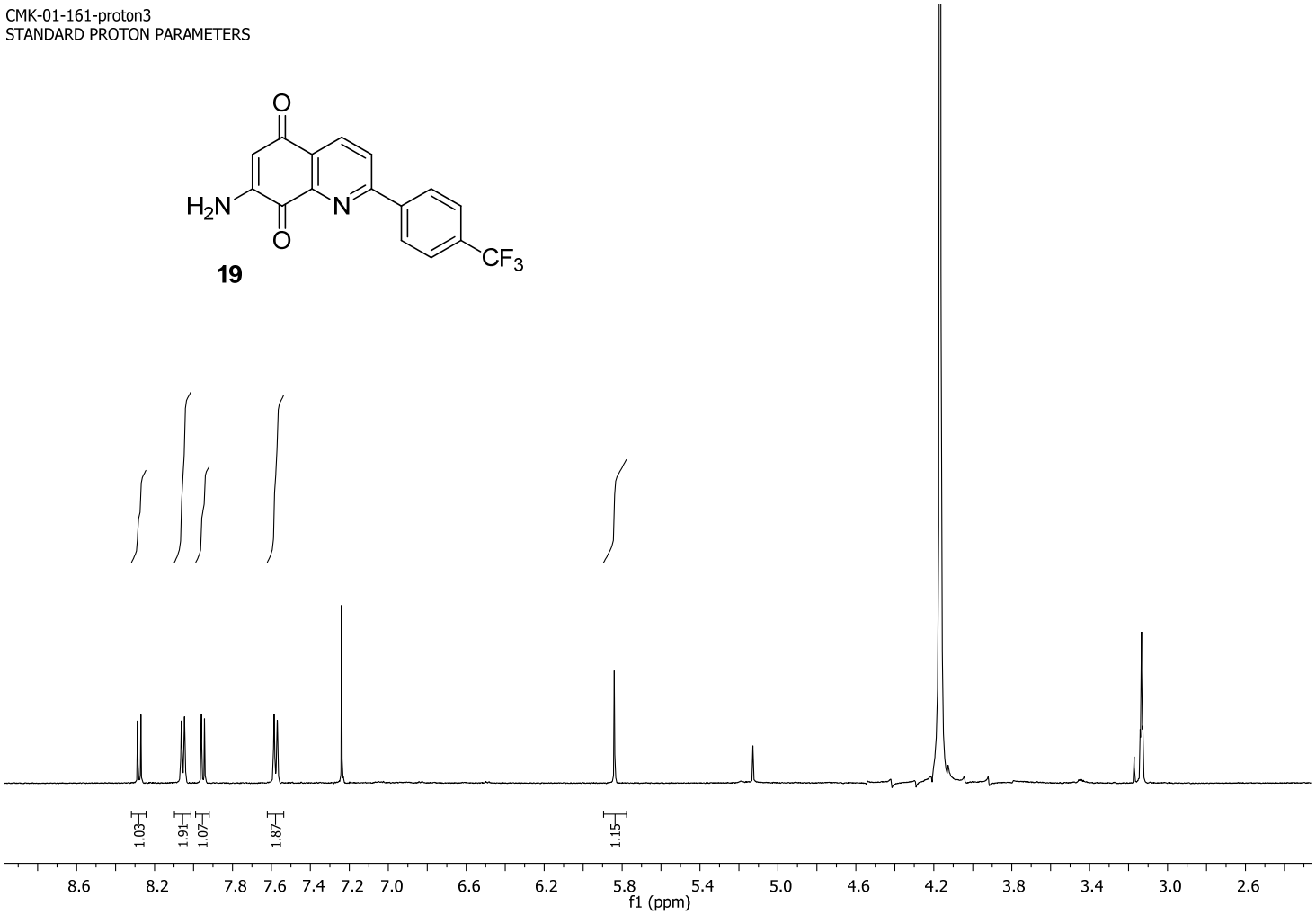
CMK-01-194-dmso-proton
STANDARD PROTON PARAMETERS



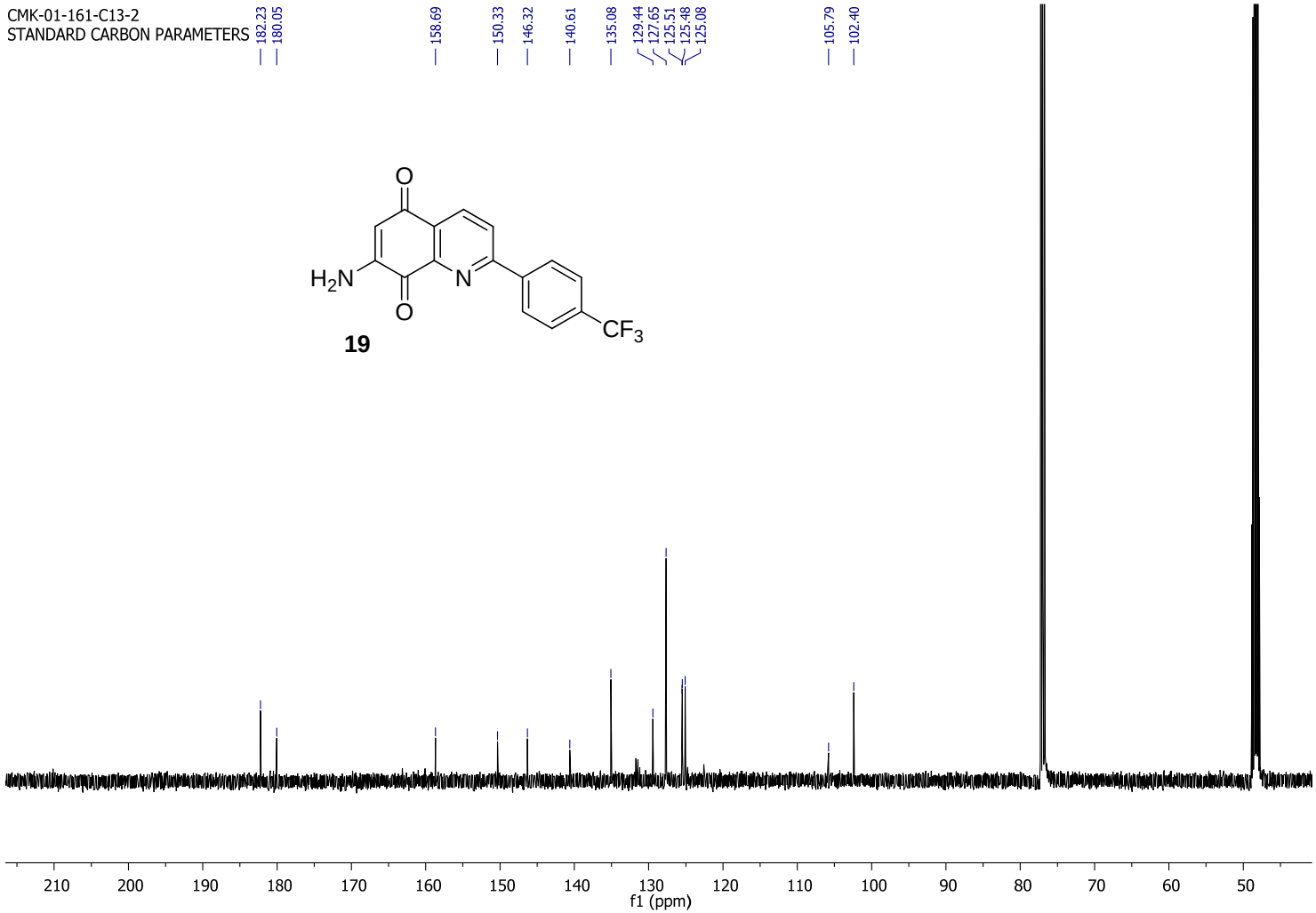
125 MHz ^{13}C-NMR of 7-acetamido-2-(2-(pyrrolyl))quinoline-5,8-dione **(18)** in DMSO



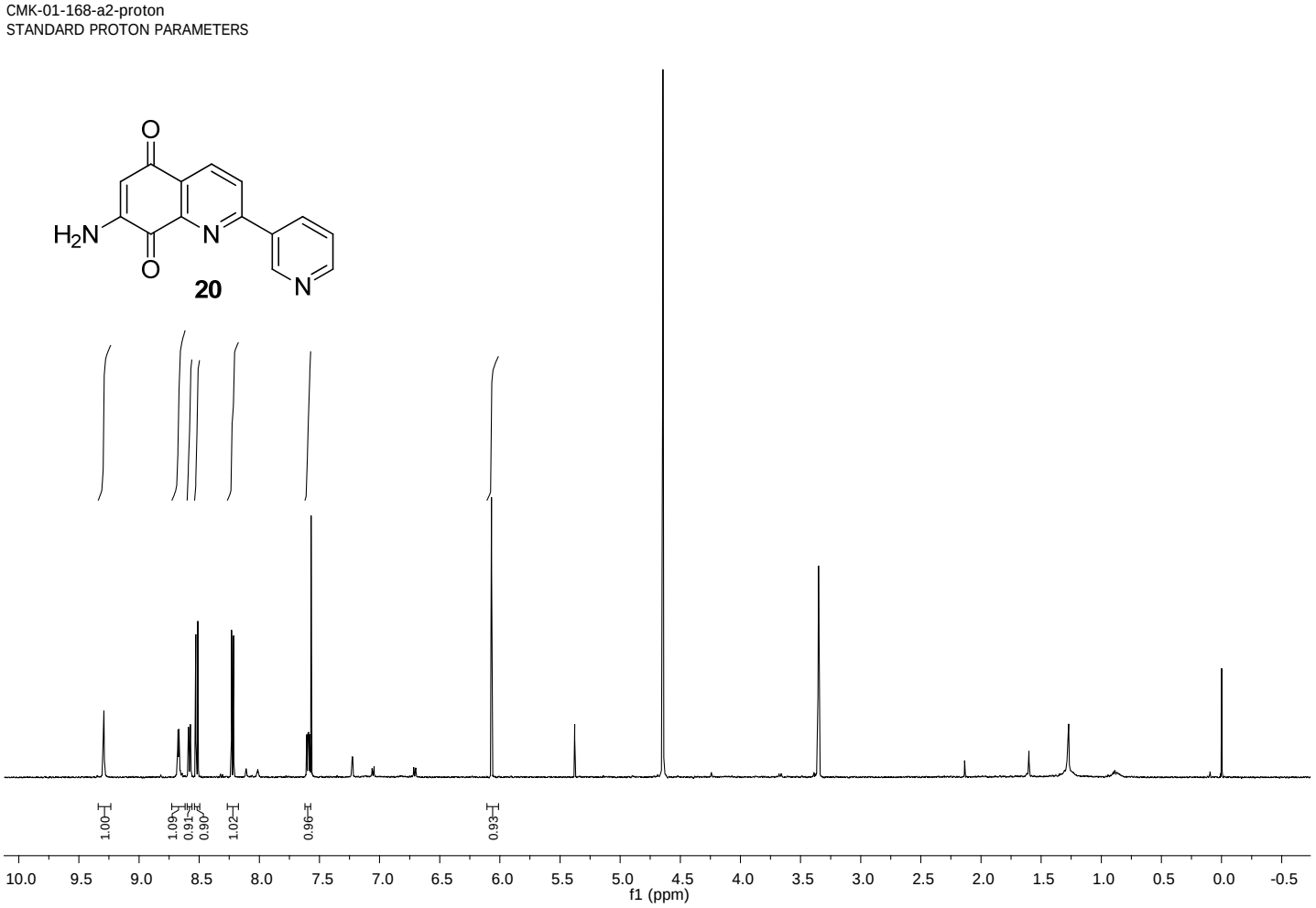
500 MHz ^{1}H-NMR of 7-amino-2-(4-trifluorophenyl)quinoline-5,8-dione **(19)** in $CDCl_3/CD_3OD$ mixture



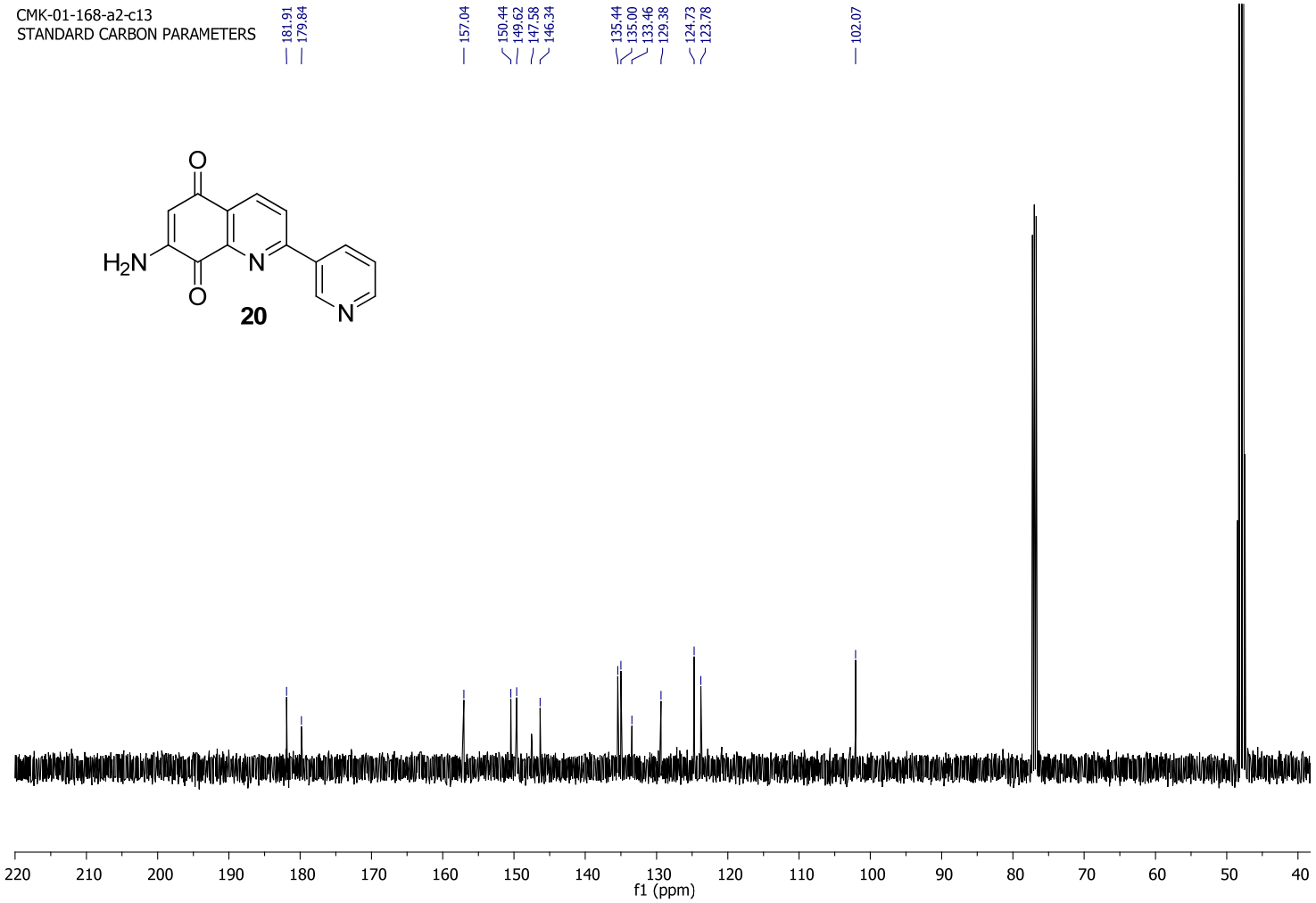
125 MHz ^{13}C-NMR of 7-amino-2-(4-trifluorophenyl)quinoline-5,8-dione **(19)** in $CDCl_3/CD_3OD$ mixture



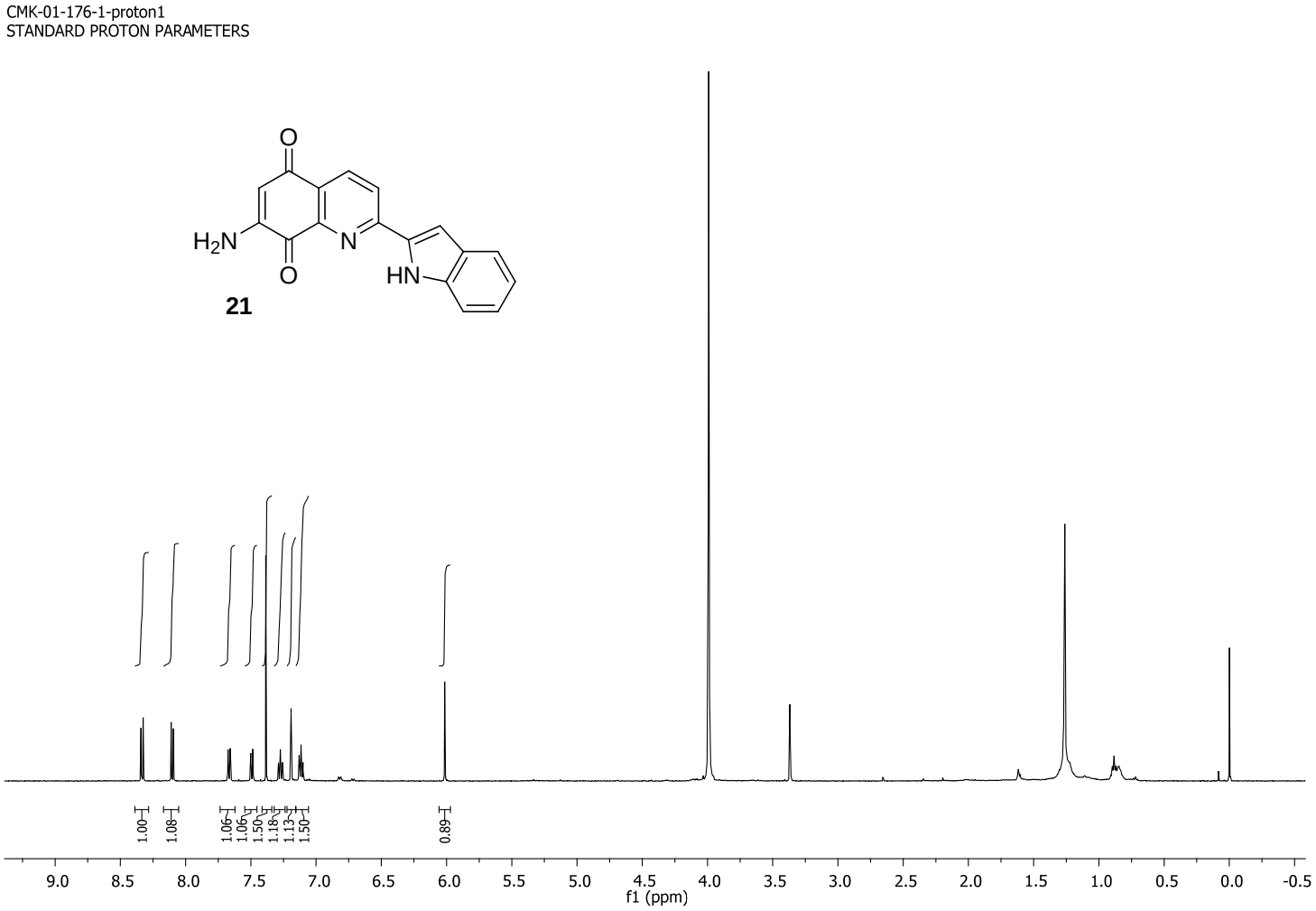
500 MHz ^{1}H-NMR of 7-amino-2-(3-pyridinyl)quinoline-5,8-dione **(20)** in $CDCl_3/CD_3OD$ mixture



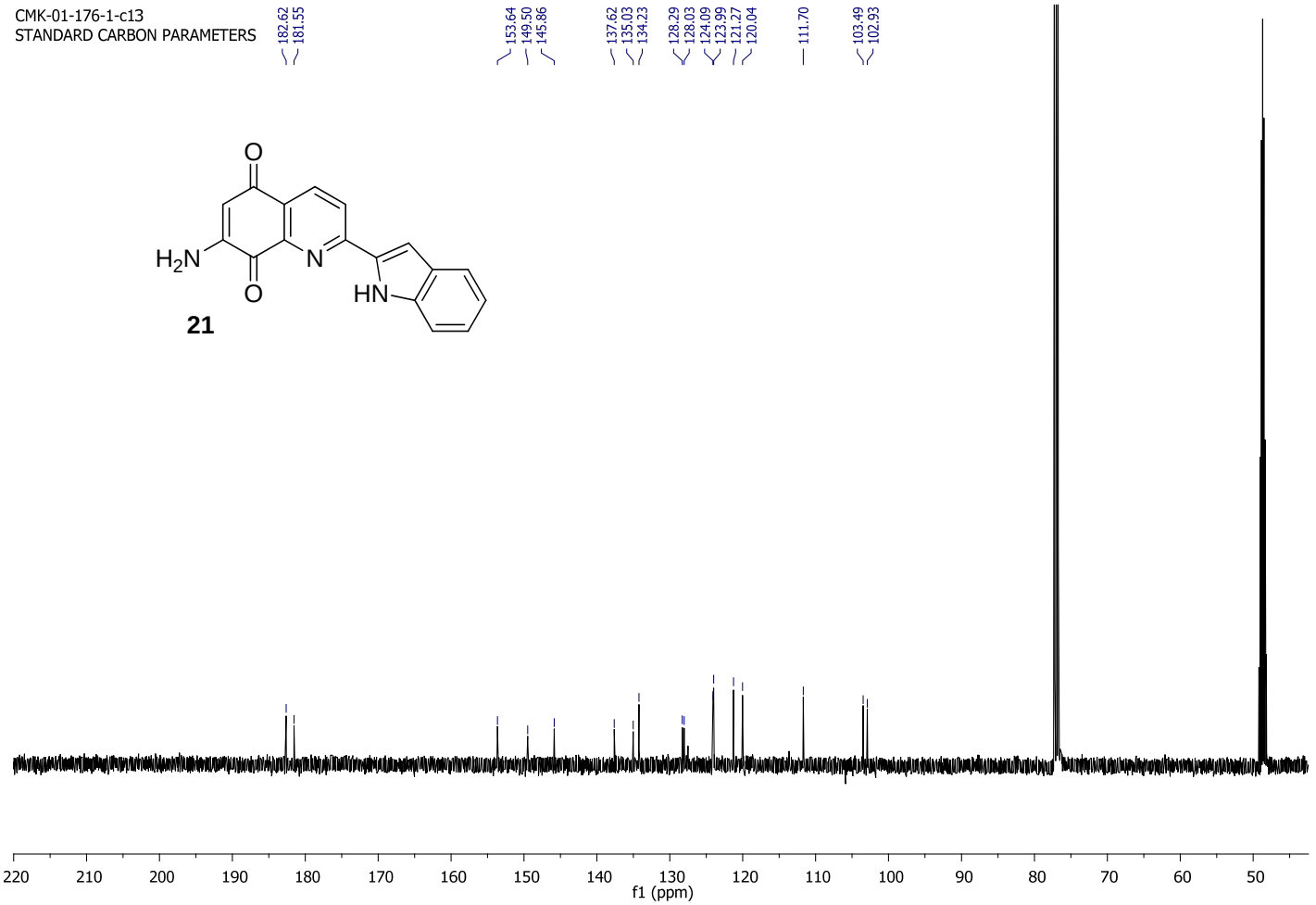
125 MHz ^{13}C-NMR of 7-amino-2-(3-pyridinyl)quinoline-5,8-dione **(20)** in $CDCl_3/CD_3OD$ mixture



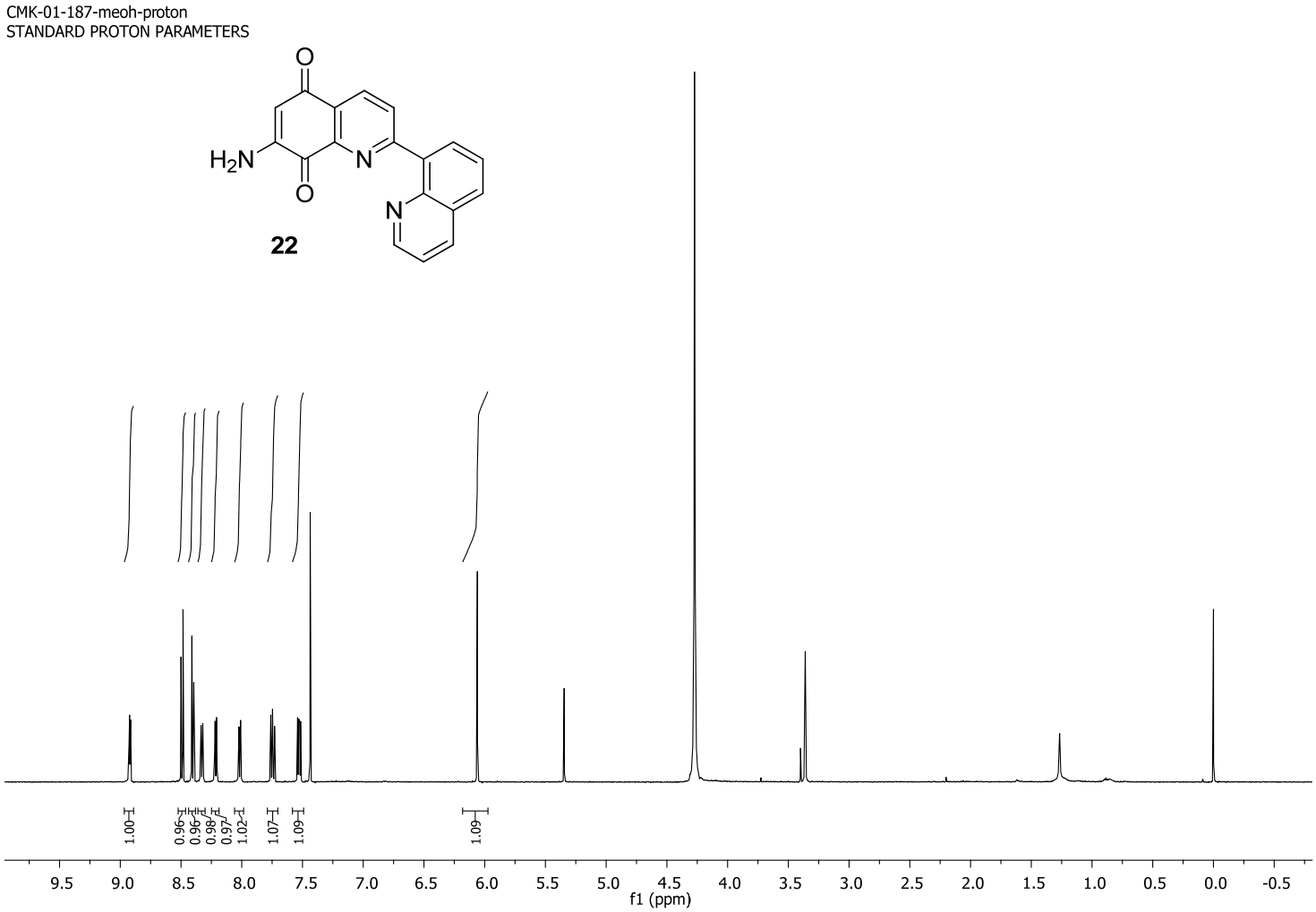
500 MHz ^{1}H-NMR of 7-amino-2-(2-indolyl)quinoline-5,8-dione **(21)** in $CDCl_3/CD_3OD$ mixture



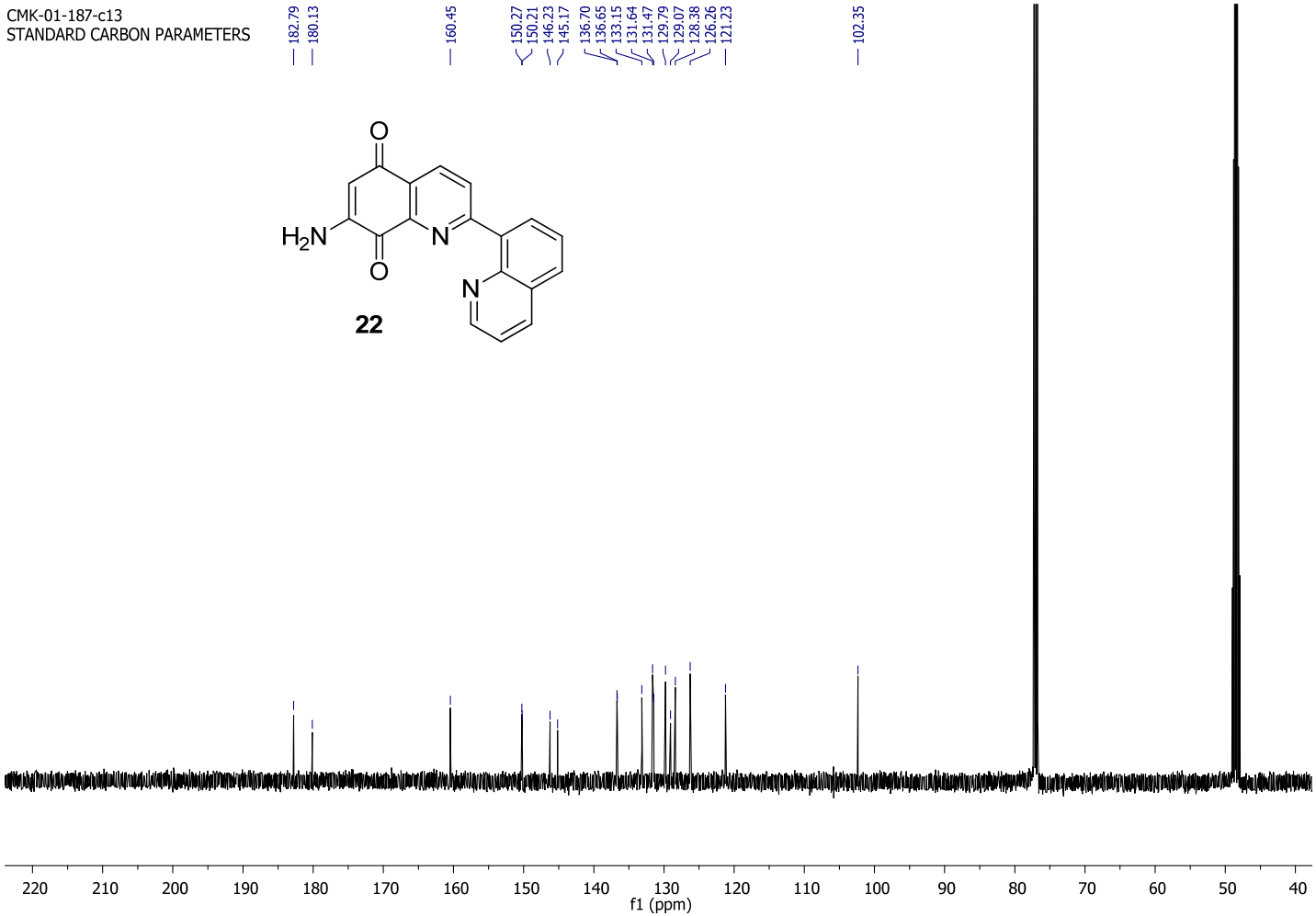
125 MHz ^{13}C-NMR of 7-amino-2-(2-indolyl)quinoline-5,8-dione **(21)** in $CDCl_3/CD_3OD$ mixture



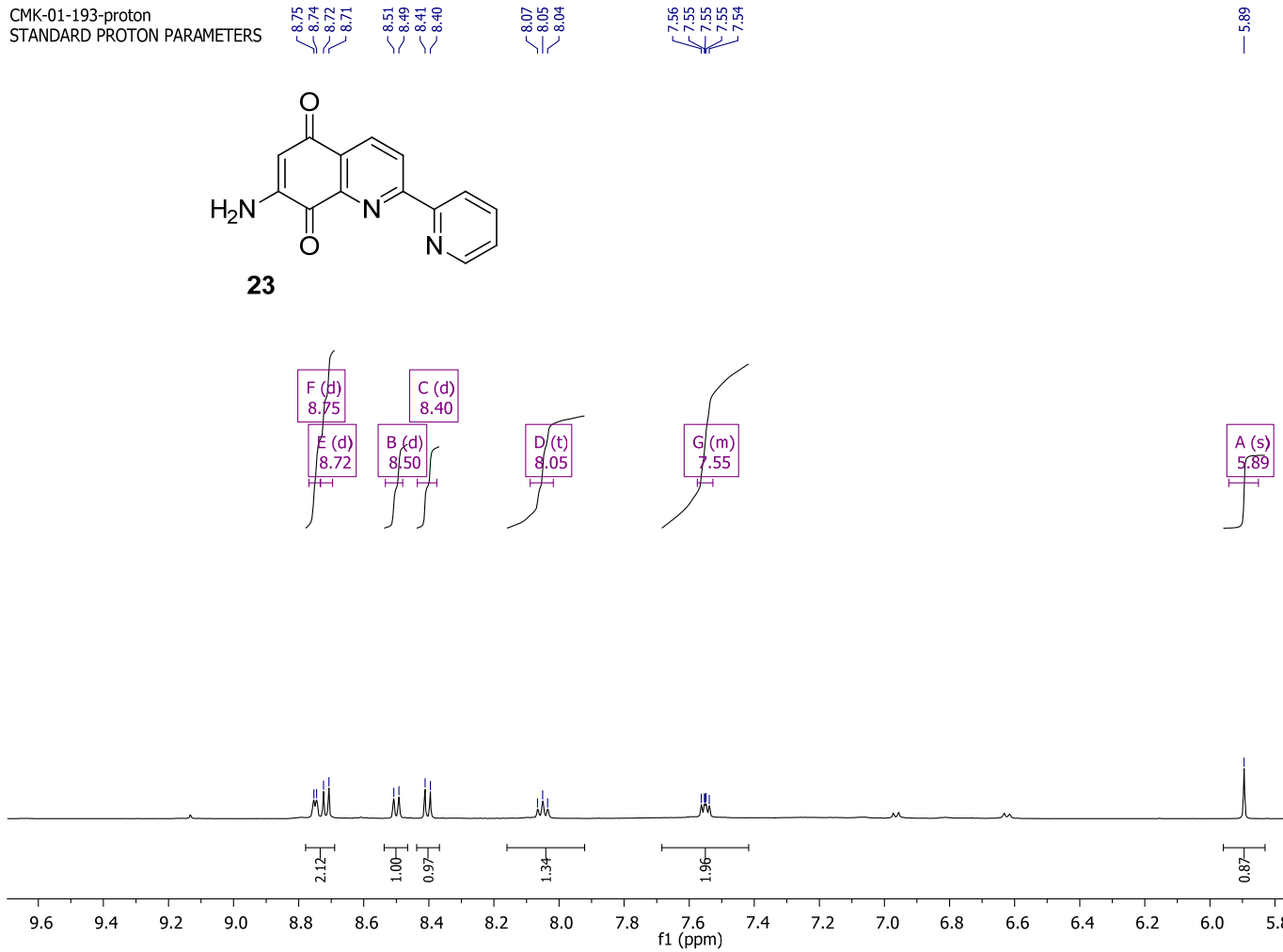
500 MHz ^{1}H-NMR of 7-amino-2-(8'-quinolyl)quinoline-5,8-dione **(22)** in $CDCl_3/CD_3OD$ mixture



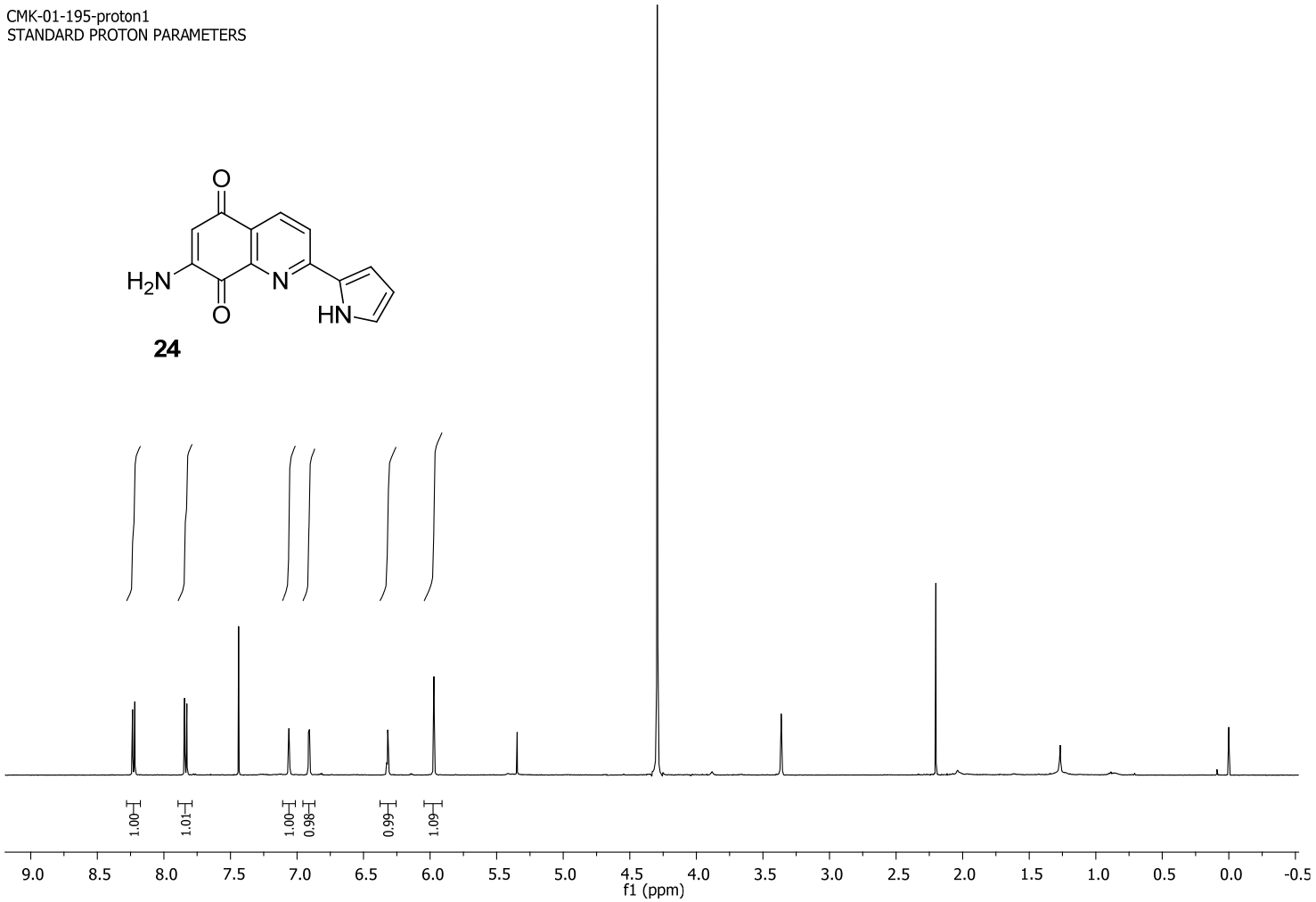
125 MHz ^{13}C-NMR of 7-amino-2-(8'-quinolyl)quinoline-5,8-dione **(22)** in $CDCl_3/CD_3OD$ mixture



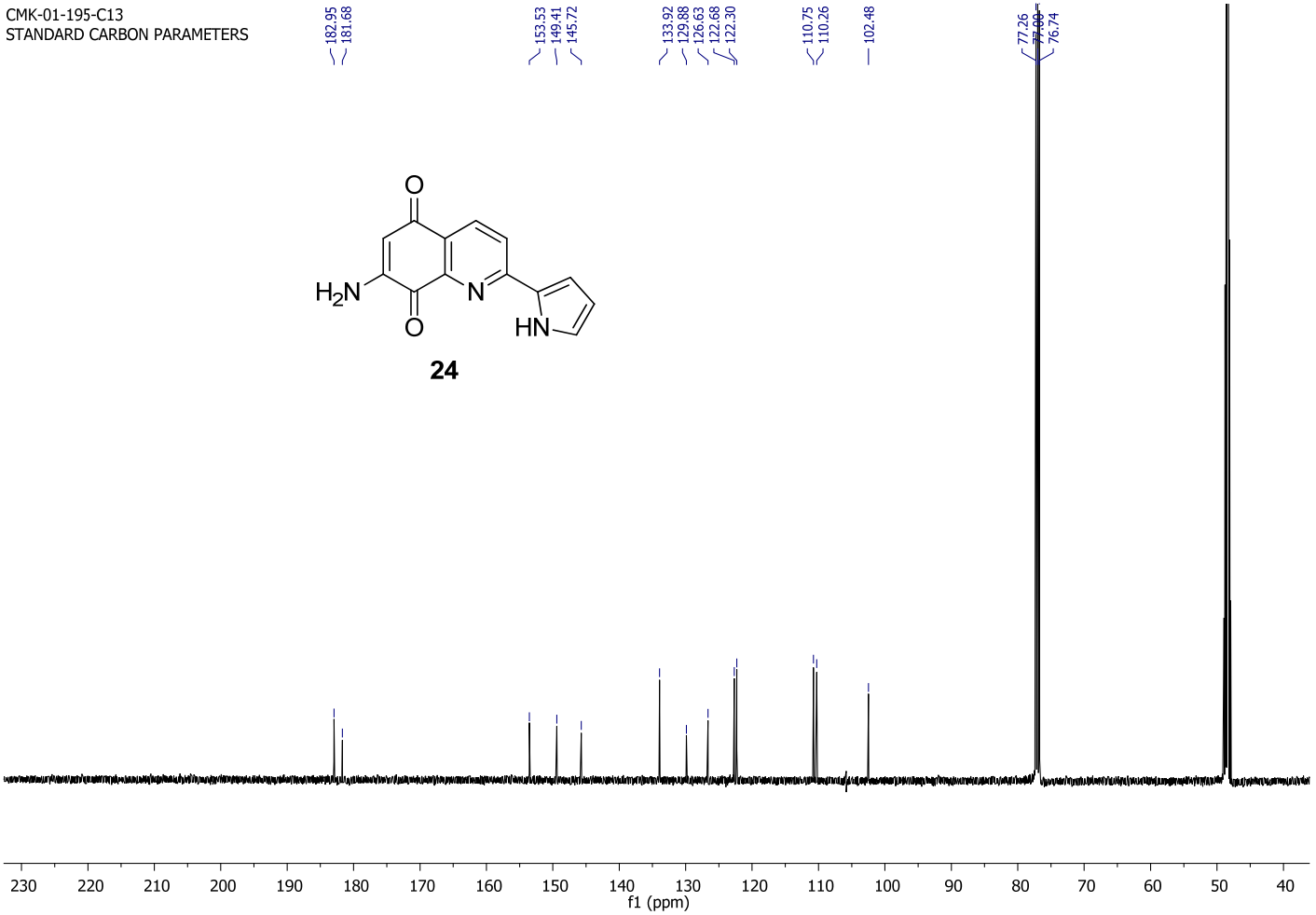
500 MHz ^{1}H-NMR of 7-amino-2-(2-pyridyl)quinoline-5,8-dione **(23)** in DMSO



500 MHz ^{1}H-NMR of 7-amino-2-(2-pyrrolyl)quinoline-5,8-dione **(24)** in $CDCl_3/CD_3OD$ mixture



125 MHz ^{13}C-NMR of 7-amino-2-(2-pyrrolyl)quinoline-5,8-dione **(24)** in $CDCl_3/CD_3OD$ mixture



400 MHz ^{1}H-NMR of the aromatic region of 7-amino-2-(4-trifluorophenyl)quinoline-5,8-dione **(19)** in [$^{2}H_8$]THF

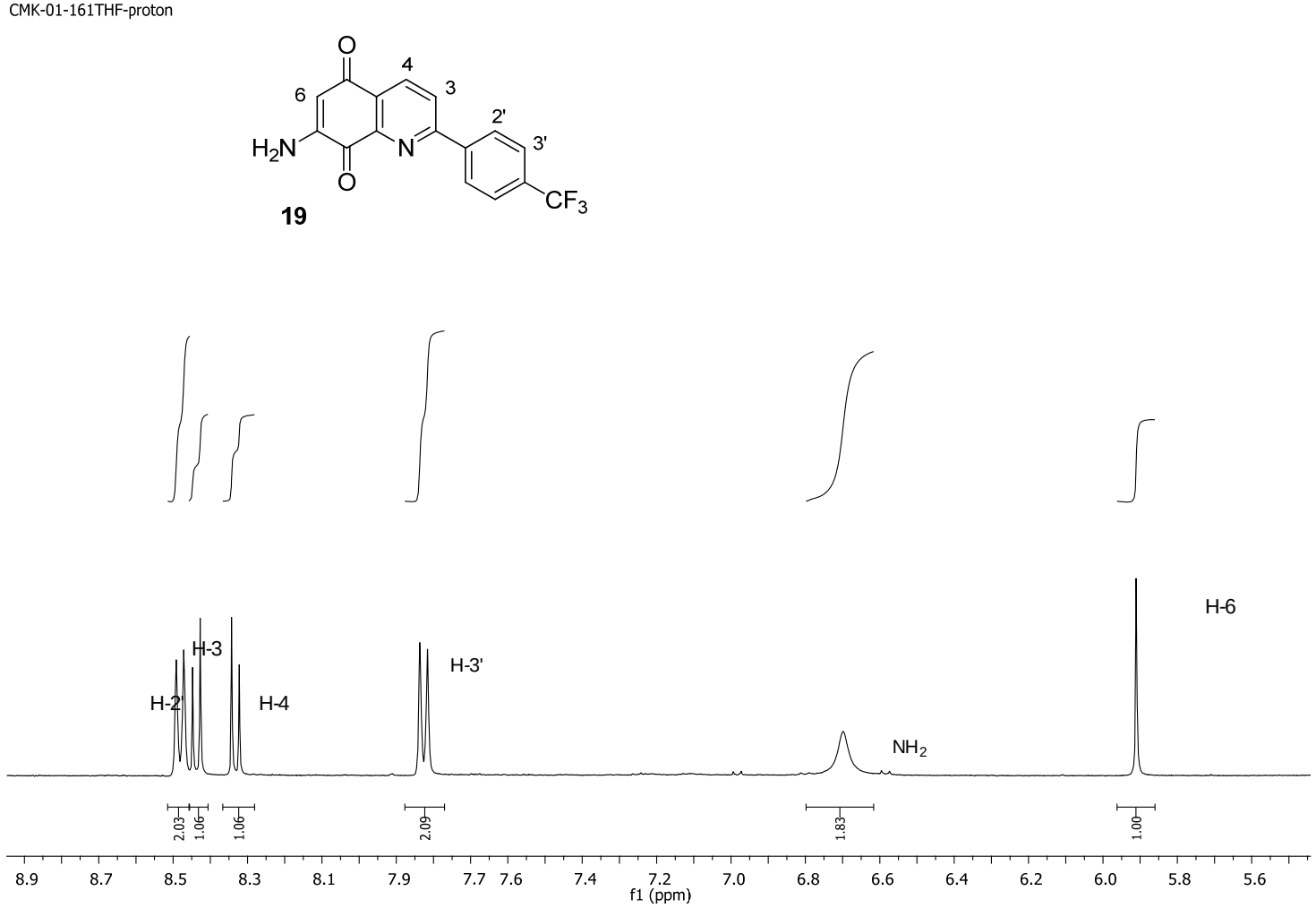


Table S1. Chemical shifts (δ) of protons upon addition of Zinc(II) triflate to **(19)** (^{1}H NMR (400 MHz, THF).

Zn^{2+} equiv.	H-2'	H-3	H-4	H-7'	H-4'	H-5'	H-6'	H-3'	NH_2	H-6
0	8.85 (dd, J = 4.1, 1.8)	8.54 (d, J = 8.2)	8.36 (d, J = 8.2)	8.30 (dd, J = 7.2, 1.3)	8.20 (dd, J = 8.3, 1.7)	7.88 (dd, J = 8.2, 1.2)	7.65 – 7.59 (m)	7.39 (dd, J = 8.3, 4.1)	6.44 (s)	5.90 (s)
1	9.12 (dd, J = 4.6, 1.2)	8.62 (d, J = 8.6)	8.45 (d, J = 8.5)	8.46 (m)	8.64 (dd, J = 8.8, 1.4)	8.19 (d, 8.3)	7.82 (t, J = 7.8)	7.79 (dd, J = 8.1, 4.5)	6.86 (s)	6.05 (s)
2	9.11 (dd, J = 4.8, 1.6)	8.62 (d, J = 8.4)	8.46 (d, J = 8.5)	8.46 (dd, J = 7.8, 0.8)	8.64 (dd, J = 8.4, 1.6)	8.20 (dd, J = 8.1, 0.9)	7.83 (t, J = 7.8)	7.79 (dd, J = 8.2, 4.8)	6.88 (s)	6.07 (s)
3	9.11 (dd, J = 4.8, 1.7)	8.62 (d, J = 8.4)	8.46 (d, J = 8.6)	8.46 (dd, J = 6.8, 1.1)	8.64 (d, J = 8.2, 1.7)	8.20 (d, J = 8.1, 0.9)	7.82 (t, J = 7.8)	7.79 (dd, J = 8.2, 4.8)	6.88 (s)	6.07 (s)
4	9.10 (dd, J = 4.8, 1.6)	8.62 (d, J = 8.3)	8.46 (d, J = 8.5)	8.46 (m)	8.65 (d, J = 9.3, 1.6)	8.19 (m)	7.83 (d, J = 7.8)	7.79 (dd, J = 8.3, 4.8)	6.89 (s)	6.07 (s)
5	9.10 (dd, J = 4.8, 1.6)	8.62 (d, J = 8.4)	8.46 (d, J = 8.2)	8.46 (d, J = 8.2)	8.64 (d, J = 8.2, 1.4)	8.19 (d, J = 8.1)	7.82 (d, J = 7.8)	7.79 (dd, J = 8.3, 4.8)	6.87 (s)	6.08(s)
10	9.09 (dd, J = 4.8, 1.7)	8.62 (d, J = 8.3)	8.46 (d, J = 8.4)	8.46 (d, J = 8.4)	8.64 (dd, J = 8.1, 1.7)	8.19 (dd, J = 8.1, 0.7)	7.81 (d, J = 7.8)	7.78(dd, J = 8.3, 4.8)	6.89 (s)	6.09(s)

400 MHz ^{1}H-NMR of the aromatic region of 7-amino-2-(8'-quinolyl)quinoline-5,8-dione **(22)** in [$^{2}H_8$]THF/$CDCl_3$ mixture

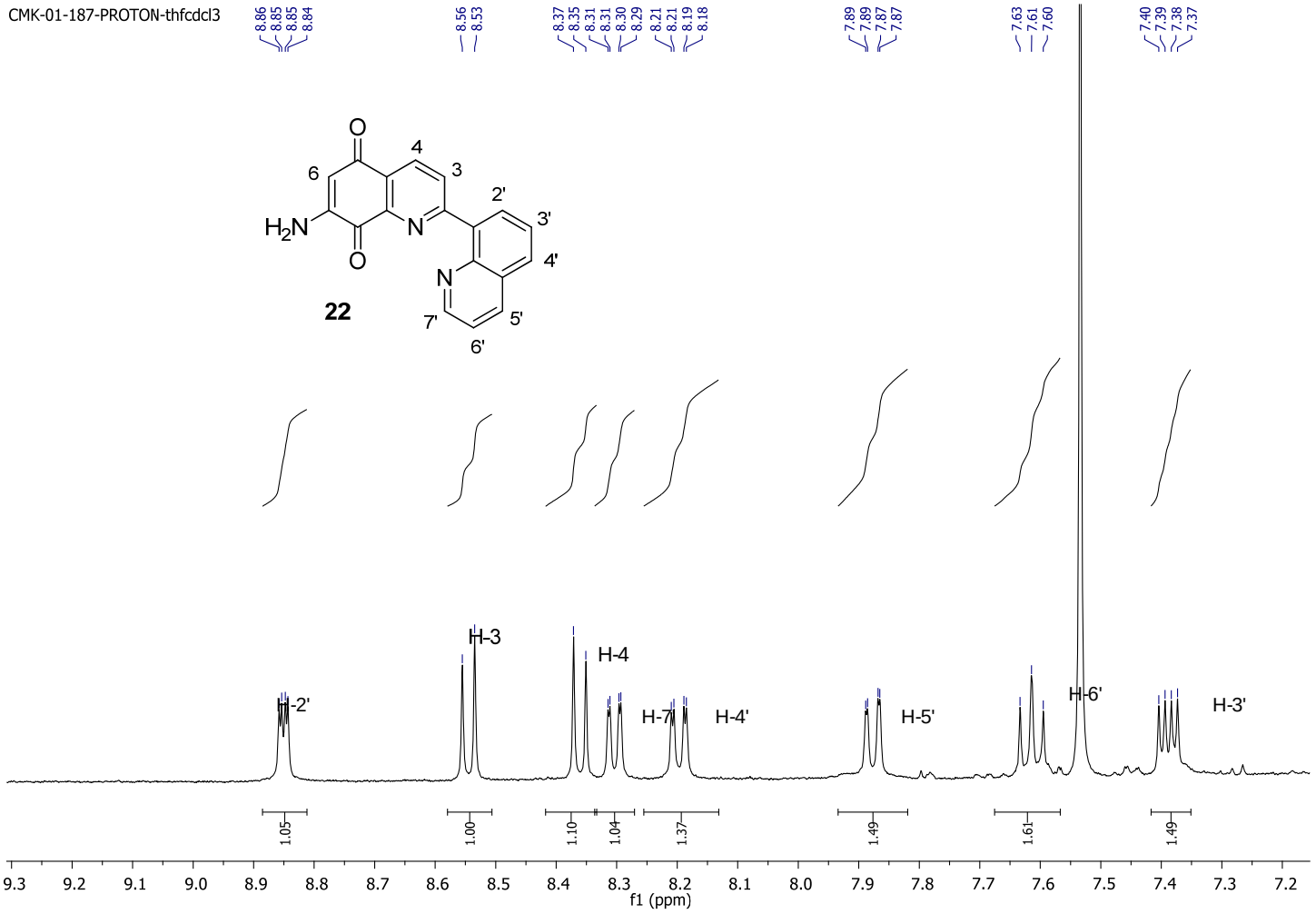


Table S2. Chemical shifts (δ, ppm), multiplicity and coupling constant (*J*, Hz)of **(22)** protons upon addition of Zinc(II) triflate (^{1}H NMR (400 MHz, THF/$CDCl_3$)

Zn^{2+} equiv.	H-2'	H-3	H-4	H-7'	H-4'	H-5'	H-6'	H-3'	NH_2	H-6
0	8.85 (dd, J = 4.1, 1.8)	8.54 (d, J = 8.2)	8.36 (d, J = 8.2)	8.30 (dd, J = 7.2, 1.3)	8.20 (dd, J = 8.3, 1.7)	7.88 (dd, J = 8.2, 1.2)	7.65 – 7.59 (m)	7.39 (dd, J = 8.3, 4.1)	6.44 (s)	5.90 (s)
1	9.12 (dd, J = 4.6, 1.2)	8.62 (d, J = 8.6)	8.45 (d, J = 8.5)	8.46 (m)	8.64 (dd, J = 8.8, 1.4)	8.19 (d, 8.3)	7.82 (t, J = 7.8)	7.79 (dd, J = 8.1, 4.5)	6.86 (s)	6.05 (s)
2	9.11 (dd, J = 4.8, 1.6)	8.62 (d, J = 8.4)	8.46 (d, J = 8.5)	8.46 (dd, J = 7.8, 0.8)	8.64 (dd, J = 8.4, 1.6)	8.20 (dd, J = 8.1, 0.9)	7.83 (t, J = 7.8)	7.79 (dd, J = 8.2, 4.8)	6.88 (s)	6.07 (s)
3	9.11 (dd, J = 4.8, 1.7)	8.62 (d, J = 8.4)	8.46 (d, J = 8.6)	8.46 (dd, J = 6.8, 1.1)	8.64 (d, J = 8.2, 1.7)	8.20 (d, J = 8.1, 0.9)	7.82 (t, J = 7.8)	7.79 (dd, J = 8.2, 4.8)	6.88 (s)	6.07 (s)
4	9.10 (dd, J = 4.8, 1.6)	8.62 (d, J = 8.3)	8.46 (d, J = 8.5)	8.46 (m)	8.65 (d, J = 9.3, 1.6)	8.19 (m)	7.83 (d, J = 7.8)	7.79 (dd, J = 8.3, 4.8)	6.89 (s)	6.07 (s)
5	9.10 (dd, J = 4.8, 1.6)	8.62 (d, J = 8.4)	8.46 (d, J = 8.2)	8.46 (d, J = 8.2)	8.64 (d, J = 8.2, 1.4)	8.19 (d, J = 8.1)	7.82 (d, J = 7.8)	7.79 (dd, J = 8.3, 4.8)	6.87 (s)	6.08(s)
10	9.09 (dd, J = 4.8, 1.7)	8.62 (d, J = 8.3)	8.46 (d, J = 8.4)	8.46 (d, J = 8.4)	8.64 (dd, J = 8.1, 1.7)	8.19 (dd, J = 8.1, 0.7)	7.81 (d, J = 7.8)	7.78(dd, J = 8.3, 4.8)	6.89 (s)	6.09(s)

400 MHz ^{1}H-NMR of the aromatic region of 7-amino-2-(2-pyridyl)quinoline-5,8-dione **(23)** in [$^{2}H_8$]THF.

CMK-01-193-thf

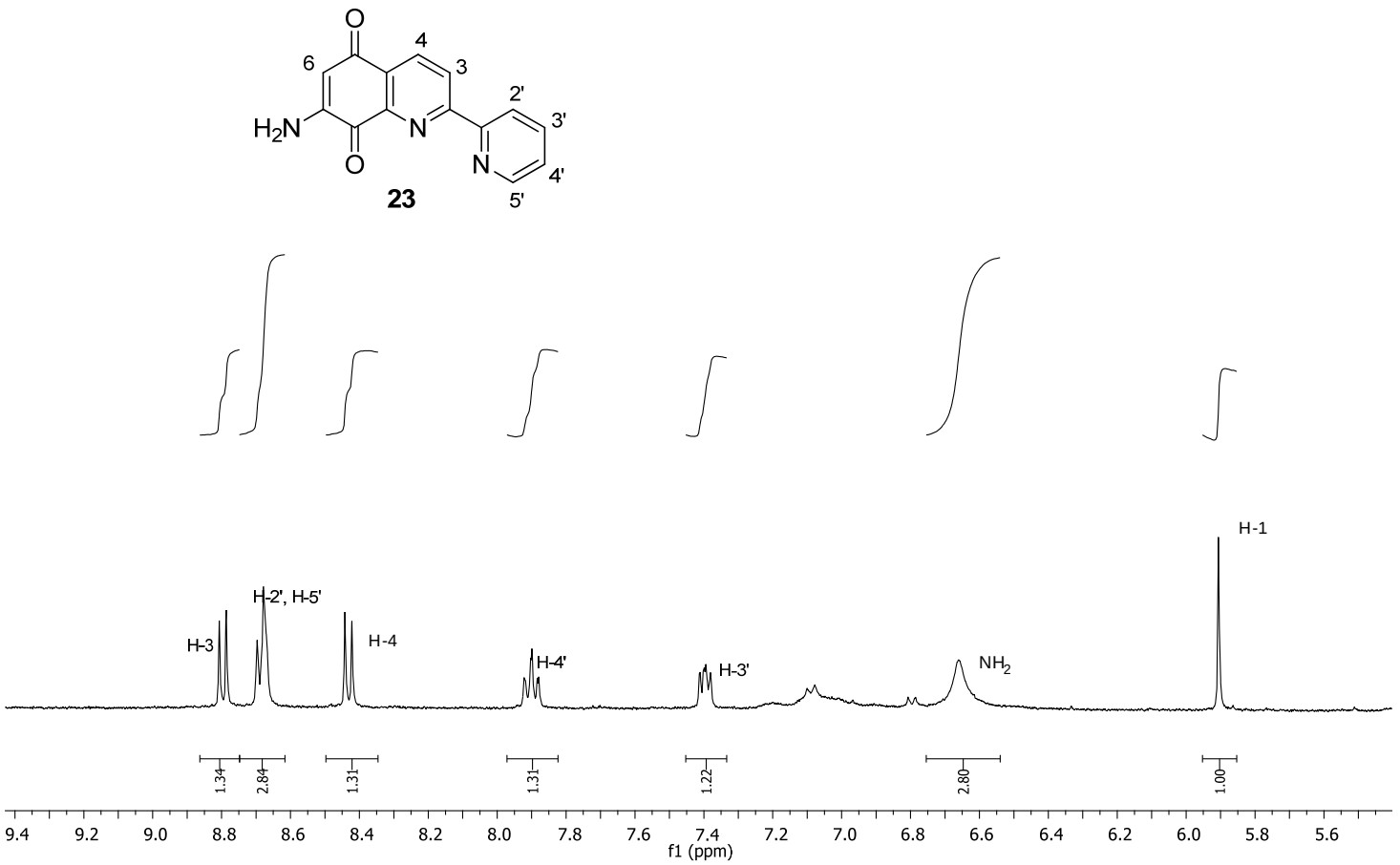
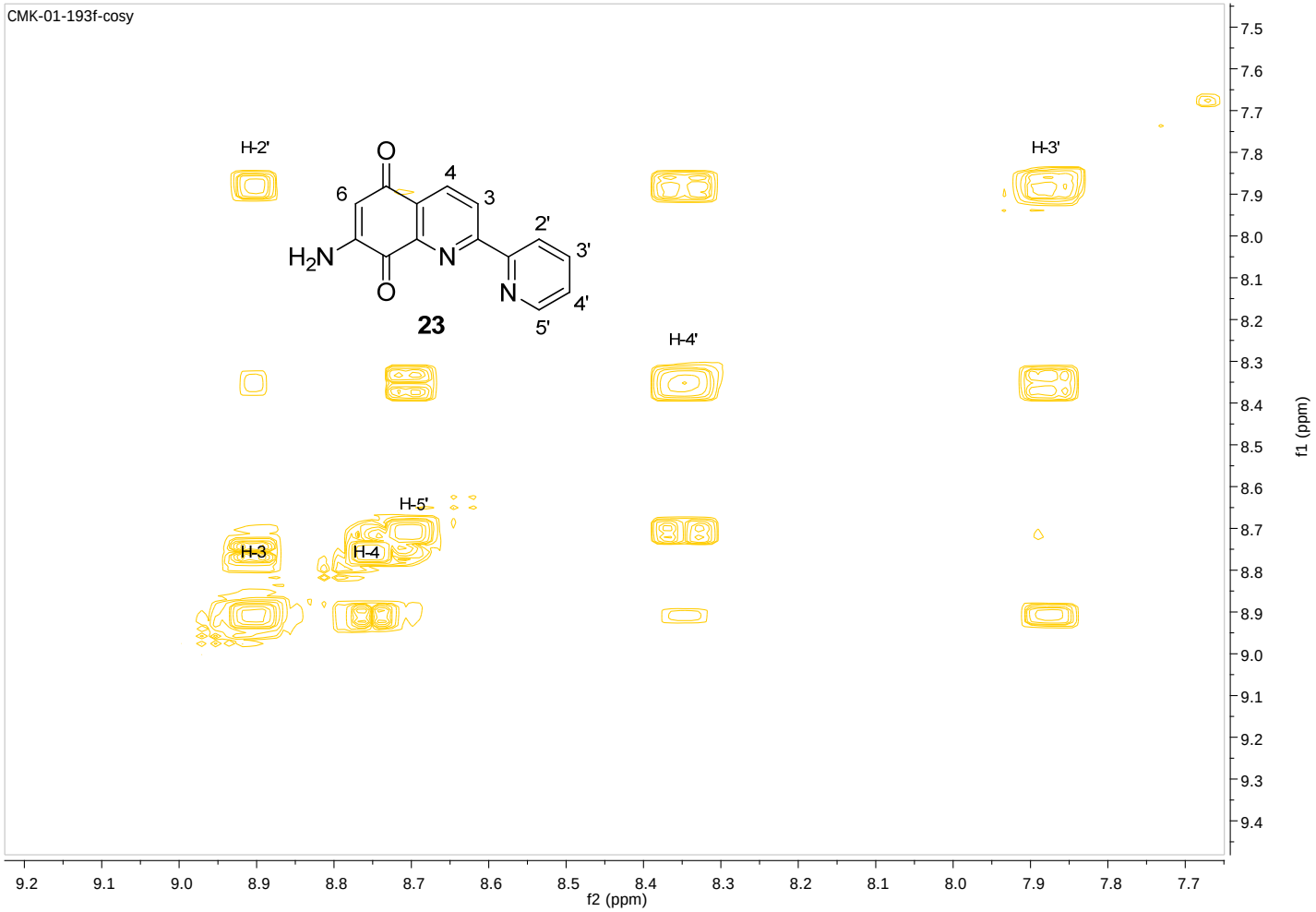


Table S3. Chemical shifts (δ, ppm) and coupling constants (*J*, Hz) of **(23)** protons upon addition of Zinc(II) triflate (^{1}H NMR (400 MHz, [$^2H_8$]THF)

Zn^{2+} equiv.	*H-2'*	*H-3*	*H-4*	*H-3'*	*H-5'*	*H-4'*	*NH_2*	*H-6*
0	*8.69 (d, J = 7.3)*	*8.80 (d, J = 8.2)*	*8.43 (d, J = 8.2)*	*7.40 (dd, 7.2, 5.2)*	*8.68(m)*	*7.90 (td, J = 7.8, 1.5)*	*6.66 (s)*	*5.91 (s)*
1	*8.91 (d, J = 4.7)*	*8.89 (d, J = 8.4)*	*8.75 (d, J = 8.1)*	*7.88 (dd, J = 7.4, 5.4)*	*8.69 (d, J= 8.1)*	*8.35 (td, J = 7.8, 1.3)*	*7.20 (s)*	*6.08 (s)*
2	*8.91 (d, J = 5.5)*	*8.89 (d, J = 8.4)*	*8.75 (d, J = 8.2)*	*7.88 (m)*	*8.69 (d, J = 8.1)*	*8.35 (td, J = 7.9, 1.5)*	*7.20 (s)*	*6.09 (s)*
3	*8.91 (d, J = 6.4)*	*8.89 (d, J = 8.5)*	*8.75 (d, J = 8.2)*	*7.88 (dd, J = 7.4, 5.2)*	*8.70 (d, J = 8.1)*	*8.35 (td, J = 8.0, 1.2)*	*7.20 (s)*	*6.09 (s)*
4	*8.91 (d, J = 5.4)*	*8.89 (d, J = 8.3)*	*8.75 (d, J = 8.2)*	*7.87 (dd, J = 7.4, 5.3)*	*8.70 (d, J = 8.0)*	*8.35 (td, J = 7.8, 1.3)*	*7.20(s)*	*6.09(s)*
5	*8.91 (d, J = 3.9)*	*8.89 (d, J = 8.2)*	*8.75 (d, J = 8.2)*	*7.87 (dd, J = 7.2, 5.5)*	*8.70 (d, J = 8.0)*	*8.35 (td, J = 7.9, 1.4)*	*7.21 (s)*	*6.10(s)*
10	*8.90 (m)*	*8.89 (d, J = 8.2*	*8.75 (d, J = 8.2)*	*7.87 (dd, J = 7.6, 5.2)*	*8.70 (d, J = 8.1)*	*8.35 (td, J = 7.9, 1.4)*	*7.21 (s)*	*6.10(s)*

400 MHz COSY-NMR spectrum of the aromatic region of 7-amino-2-(2-pyridyl)quinoline-5,8-dione **(23)** + 10 equiv. $Zn(SO_3CF_3)_2$ in $[^2H_8]THF$



400 MHz ^{1}H-NMR spectrum of the 7-acetamido-2-(2-pyridyl)quinoline-5,8-dione **(13)** in [$^{2}H_{8}$]THF

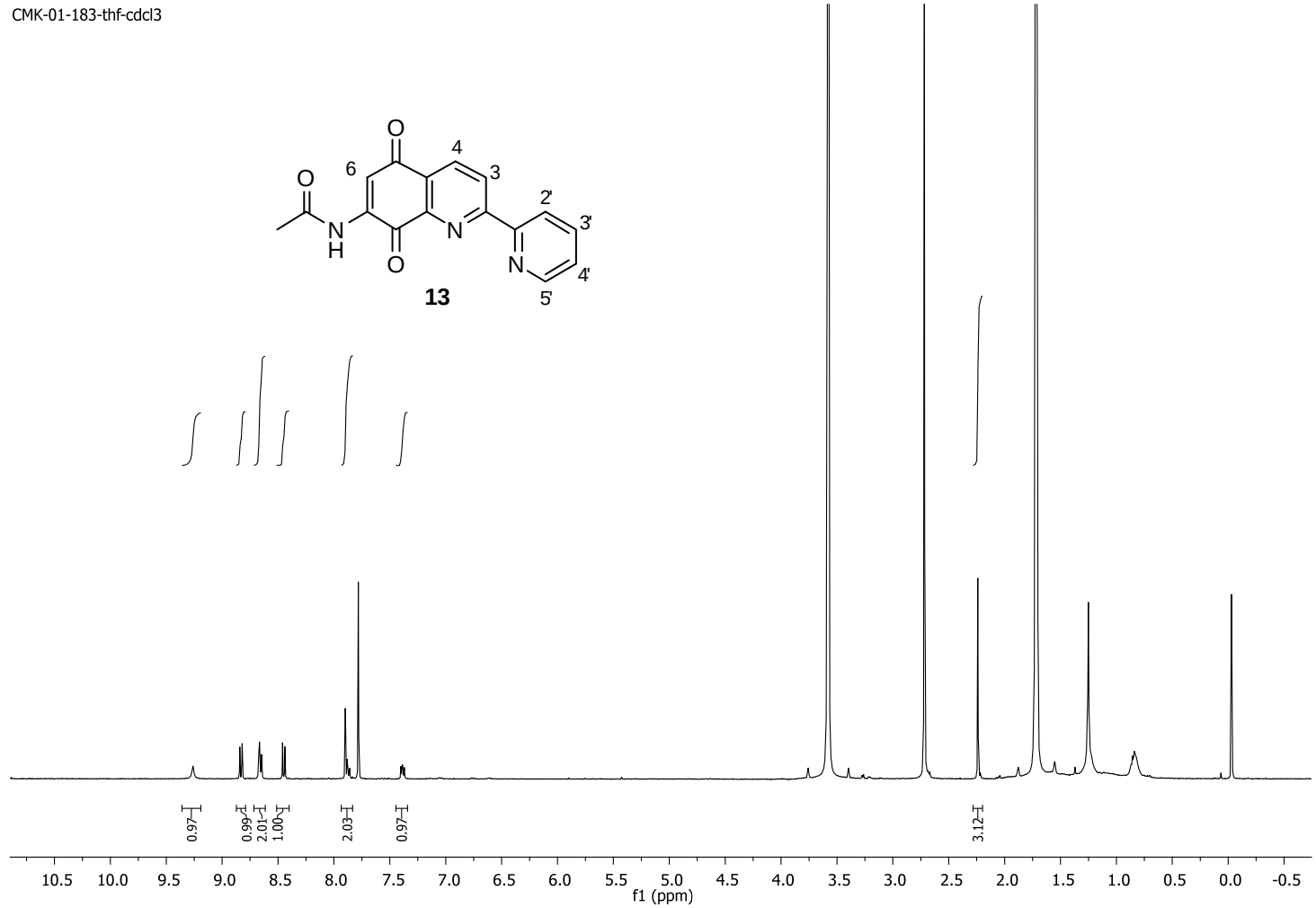
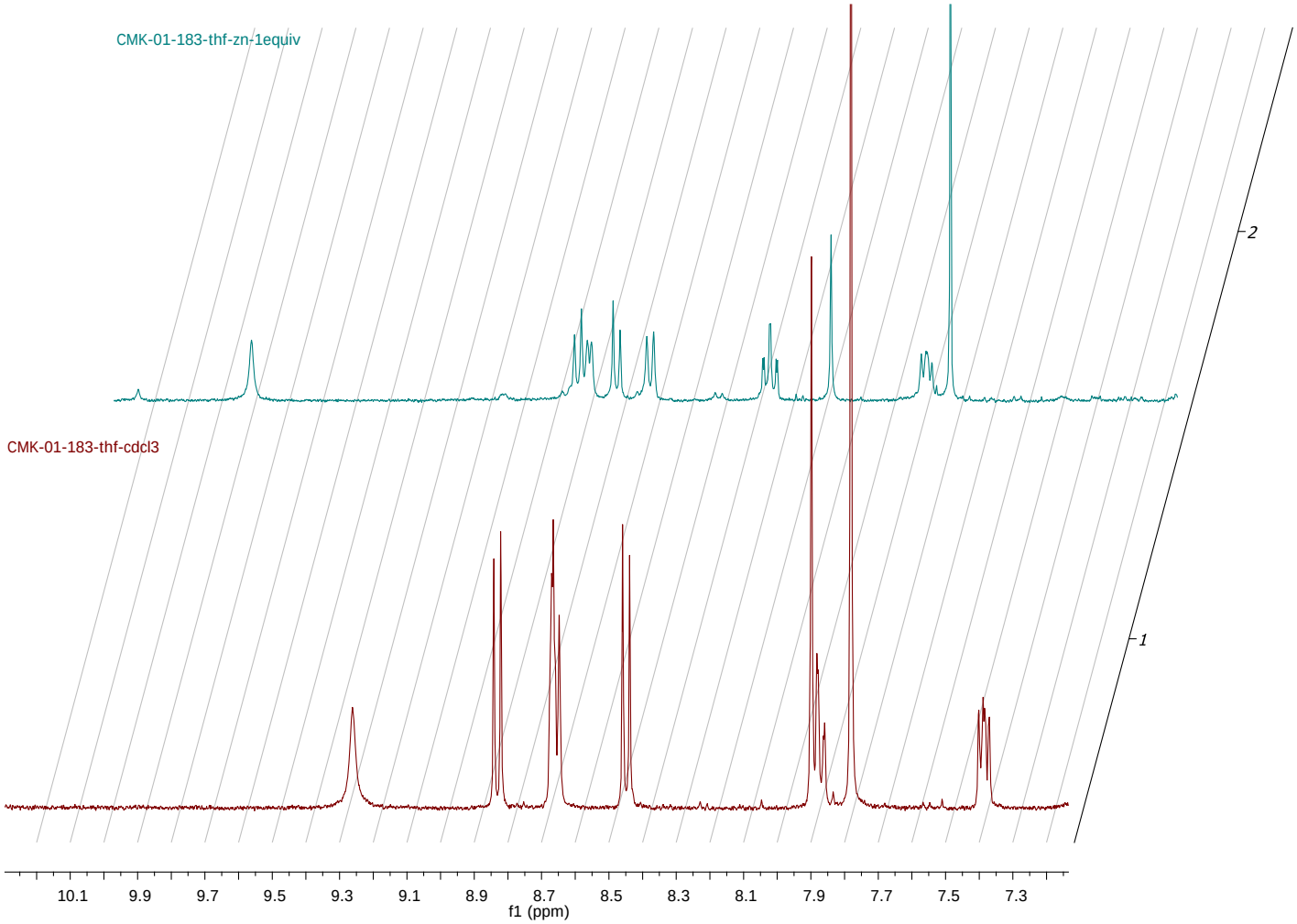


Table S4. Chemical shifts (δ, ppm) and coupling constants (*J*, Hz) of **(13)** protons upon addition of Zinc(II) triflate (^{1}H NMR (400 MHz, [$^2H_8$]THF)

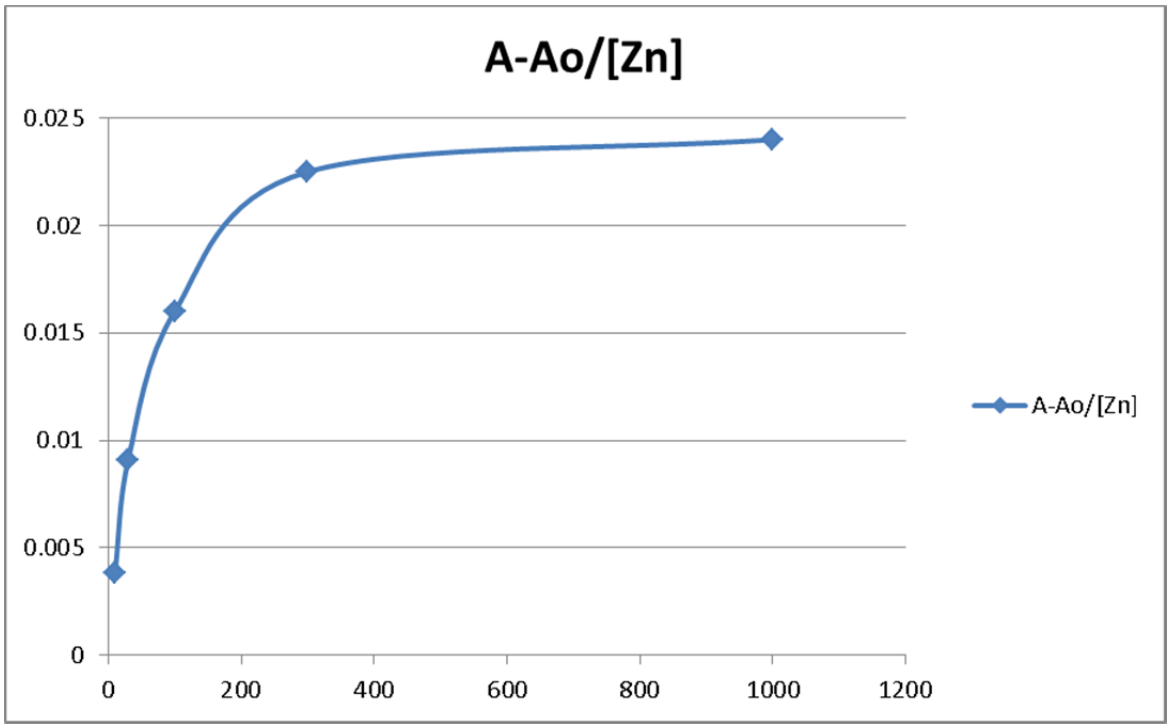
Zn^{2+} equiv.	H-2'	H-3	H-4	H-3'	H-5'	H-4'	NH	H-6	-C<u>H$_3$</u>
0	8.67 (m)	8.83 (d, J = 8.2)	8.45 (d, J = 8.2)	7.39 (m)	8.66(m)	7.87 (dd, J = 7.8, 1.6)	9.26 (s)	7.90 (s)	2.24 (s)
1	8.88 (d, J = 4.8)	8.92 (d, J = 8.3)	8.80 (d, J = 8.2)	7.88 (m)	8.70 (d, J = 8.1)	8.35 (td, J = 7.9, 1.6)	9.89 (s)	8.16 (s)	2.33 (s)
2	8.88 (d, J = 4.7)	8.92 (d, J = 8.4)	8.80 (d, J = 8.3)	7.88 (m)	8.70 (d, J = 8.1)	8.35 (td, J = 7.9, 1.6)	9.89 (s)	8.16 (s)	2.28 (s)
3	8.88 (d, J = 4.7)	8.92 (d, J = 8.4)	8.79 (d, J = 8.3)	7.88 (dd, J = 7.0, 5.5)	8.70 (d, J = 8.0)	8.34 (td, J = 7.8, 1.4)	9.88 (s)	8.16 (s)	2.28 (s)
4	8.88 (d, J = 4.8)	8.92 (d, J = 8.3)	8.79 (d, J = 8.3)	7.88 (dd, J = 7.1, 5.4)	8.70 (d, J = 8.0)	8.34 (td, J = 7.9, 1.6)	9.87 (s)	8.16 (s)	2.27 (s)
5	8.88 (d, J = 4.7)	8.92 (d, J = 8.2)	8.79 (d, J = 8.3)	7.88 (dd, J = 7.2, 5.4)	8.70 (d, J = 8.0)	8.34 (td, J = 7.8, 1.4)	9.87 (s)	8.16 (s)	2.27 (s)
10	8.88 (d, J = 4.6)	8.92 (d, J = 8.3)	8.79 (d, J = 8.3)	7.88 (dd, J = 7.1, 5.5)	8.70 (d, J = 8.0)	8.34 (td, J = 7.8, 1.5)	9.88 (s)	8.15 (s)	2.27 (s)

H-3 H-2', H-5' H-4' H-6

400 MHz ^{1}H-NMR spectrum of the aromatic region of 7-acetamido-2-(2-pyridyl)quinoline-5,8-dione **(13)** in [$^{2}H_8$]THF and addition of 1 equiv. of $Zn(SO_3CF_3)_2$.



Affinity constant for compound **(23)** binding with Zn^{2+}



LC/MS analyses

LC/MS analyses were obtained on a Waters ACQUITY UPLC-series liquid chromatography system equipped with a diode array detector and a Waters Quattro Premier Tandem Quadrupole mass spectrometer (ionization type electrospray). The liquid chromatrography conditions were as follows: a Waters ACQUITY UPLC column (BEH, C18, 1.7 um, 1.0x100 mm) was used, and it was eluted with a gradient made up of two solvent mixtures. Solvent A consisted of water and 0.2% formic acid. Solvent B consisted of methanol. The gradient was processed as follows:

Time (min)	Flow (ml/min)	%A	%B
Initial	0.200	90.0	10.0
1.00	0.200	90.0	10.0
8.00	0.200	5.0	95.0
12.00	0.200	5.0	95.0
12.10	0.200	90.0	10.0
15.00	0.200	90.0	10.0

Compound purity was assigned on the basis of 254-nM detection data assessed by comparing relative peak areas of the signals.

Compound	Retention Time (min)	Purity (%)
9	7.60	95
10	3.99	94.6
11	4.59	100
13	4.70	96
15	4.89	100
17	7.22	100
18	6.35	97.9
19	7.18	97.1
20	3.70	96
21	6.87	97.5
22	4.29	96
23	4.07	89.7
24	5.84	100