

Heteroaromatic Swapping in Aromatic Ketones

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Table of Contents

1.	General	S2–S3
2.	Starting materials	S4
3.	Optimization	S5–S6
4.	Mechanistic study	S7–S12
5.	Preparation of starting materials	S13–S18
6.	Heteroaromatic swapping	S19–S37
7.	Synthetic applications	S38–S42
8.	Computational Studies	S43–S93
9.	X-ray crystal structure analysis	S94–S95
10.	References	S96–S99
11.	¹ H NMR, ¹³ C NMR, and ¹⁹ F NMR	S100–S257

1. General

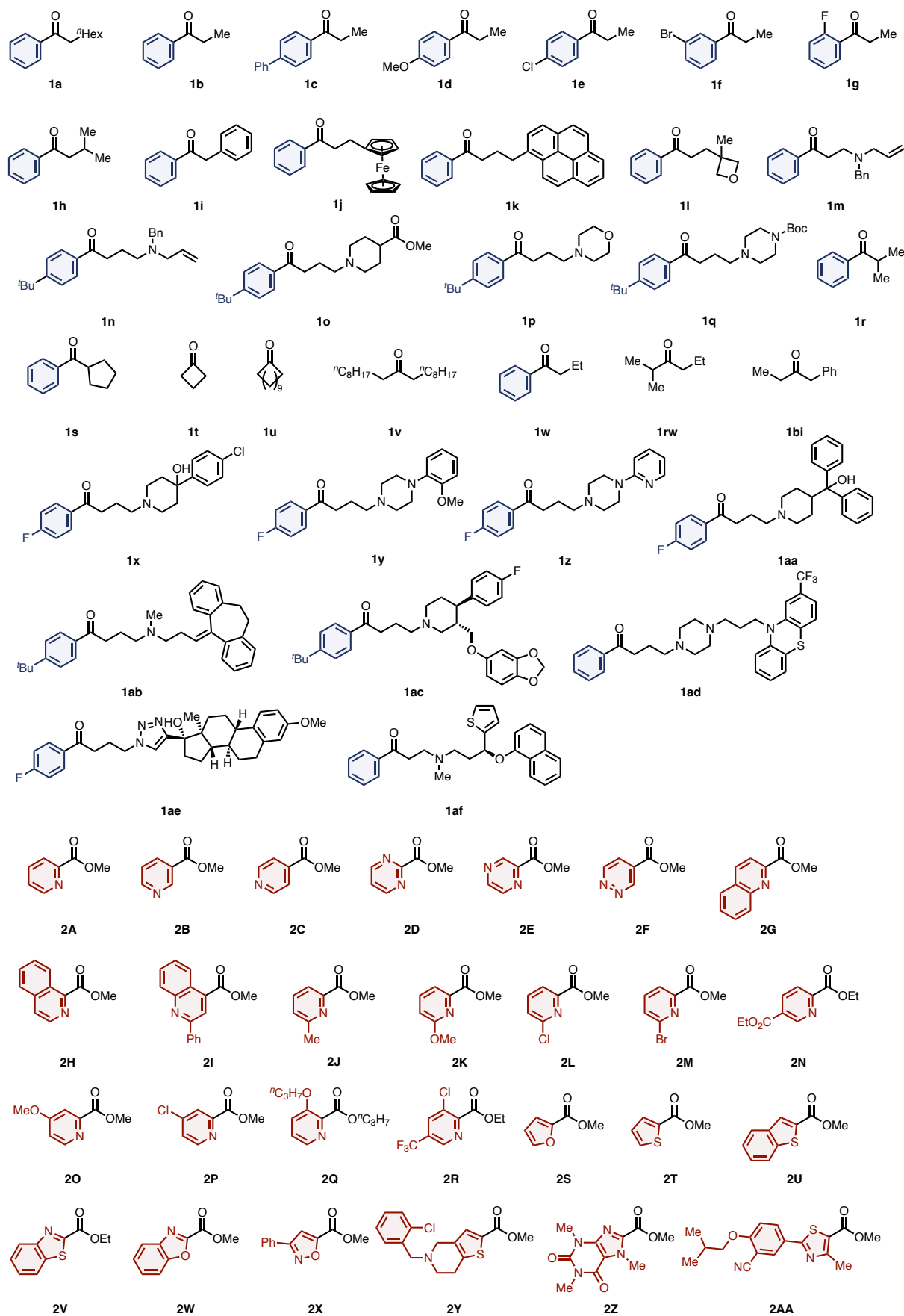
Unless otherwise noted, all reactants or reagents including dry solvents were obtained from commercial suppliers and used as received. NaHMDS, NaOH, *t*BuOK, (2-aminophenyl)methanol, AcOH, BnBr, and NEt₃ were obtained from KANTO Chemical. NaH, benzophenone, Pd/C, Raney Ni, TsNHNH₂, benzoyl cyanide, 1-phenyloctan-1-one (**1a**), propiophenone (**1b**), 1-([1,1'-biphenyl]-4-yl)propan-1-one (**1c**), 1-(4-methoxyphenyl)propan-1-one (**1d**), 1-(4-chlorophenyl)propan-1-one (**1e**), 1-(4-chlorophenyl)propan-1-one (**1f**), 1-(2-fluorophenyl)propan-1-one (**1g**), 3-methyl-1-phenylbutan-1-one (**1h**), 1,2-diphenylethan-1-one (**1i**), 2-methyl-1-phenylpropan-1-one (**1r**), cyclopentyl(phenyl)methanone (**1s**), cyclobutanone (**1t**), cyclododecanone (**1u**), nonadecan-10-one (**1v**), 2-methylhexan-3-one (**1w**), 1-phenylbutan-2-one (**1bi**), haloperidol (**1x**), methyl picolinate (**2A**), methyl nicotinate (**2B**), methyl isonicotinate (**2C**), methyl pyrimidine-2-carboxylate (**2E**), methyl 6-methylpicolinate (**2J**), methyl 6-bromopicolinate (**2M**), diethyl pyridine-2,5-dicarboxylate (**2N**), methyl 4-methoxypicolinate (**2O**), methyl 4-chloropicolinate (**2P**), propyl 3-propoxypicolinate (**2Q**), ethyl 3-chloro-5-(trifluoromethyl)picolinate (**2R**), methyl thiophene-2-carboxylate (**2S**), and ethyl benzo[*d*]thiazole-2-carboxylate (**2V**) were obtained from Tokyo Chemical Industry (TCI). THF was purified by a Glass Contour Ultimate Solvent System. 3-Ferrocenyl-1-(pyridin-2-yl)propan-1-one (**1j**),^[1] 3-(3-methyloxetan-3-yl)-1-phenylpropan-1-one (**1l**),^[2] fluanisone (**1y**),^[3] azaperone (**1z**),^[3] terfenadone (**1aa**),^[4] methyl pyrazine-2-carboxylate (**2D**),^[5] methyl pyridazine-4-carboxylate (**2F**),^[6] methyl quinoline-2-carboxylate (**2G**),^[7] methyl isoquinoline-1-carboxylate (**2H**),^[8] methyl 2-phenylquinoline-4-carboxylate (**2I**),^[9] methyl 6-methoxypicolinate (**2K**),^[10] methyl 6-chloropicolinate (**2L**),^[11] methyl thiophene-2-carboxylate (**2T**),^[7] methyl benzo[*b*]thiophene-2-carboxylate (**2U**),^[7] methyl benzo[*d*]oxazole-2-carboxylate (**2W**),^[12] methyl 3-phenylisoxazole-5-carboxylate (**2X**),^[13] methyl 5-(2-chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridine-2-carboxylate (**2Y**),^[14] methyl 1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purine-8-carboxylate (**2Z**),^[12] methyl 2-(3-cyano-4-isobutoxyphenyl)-4-methylthiazole-5-carboxylate (**2AA**),^[12] methyl isonicotinate-¹⁵N (**¹⁵N-2C**),^[15] 1-(pyridin-2-yl)propan-1-one (**3bA**),^[16] 1-(pyridin-2-yl)butan-1-one (**3wA**)^[16], 4-methoxybenzoyl cyanide^[17], (1*H*-benzo[*d*][1,2,3]triazol-1-yl)(furan-3-yl)methanone,^[18] and (1*H*-benzo[*d*][1,2,3]triazol-1-yl)(thiophen-3-yl)methanone^[18] were synthesized according to procedures and the spectra matched with those of compounds reported in the literature. Unless otherwise noted, all reactions were performed with dry solvents in dried glassware using standard vacuum-line techniques. All reactions were performed in 8-mL glass tubes and heated (IKA Plate RCT Digital) in a 16-well aluminum reaction block (IKA DB4.3 Block) unless otherwise noted. All work-up and purification procedures were carried out with reagent-grade solvents under air unless otherwise noted.

Analytical thin-layer chromatography (TLC) was performed using Silica-gel 70 TLC Plate-Wako (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm). Flash column chromatography was performed with Biotage Isolera[®] equipped with Biotage Sfär Cartridge Silica D

columns and hexane/EtOAc or $\text{CHCl}_3/\text{MeOH}$ as an eluent. Preparative thin-layer chromatography (PTLC) was performed using Wakogel B5-F silica coated plates (0.75 mm) prepared in our laboratory. High-resolution mass spectra (HRMS) were conducted on Bruker Compact QTOF (APCI). Optical rotation values were recorded on a JASCO P-2200. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-ECS-400 (^1H 400 MHz, ^{13}C 101 MHz, ^{19}F 376 MHz), JEOL JNM-ECZ-400 (^1H 400 MHz, ^{13}C 101 MHz, ^{19}F 376 MHz). Chemical shifts for ^1H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm). Chemical shifts for ^{13}C NMR are expressed in ppm relative to CDCl_3 (δ 77.0 ppm). Chemical shifts for ^{19}F NMR are expressed in ppm relative to fluorobenzene (δ -113.15 ppm) or trifluorotoluene (δ -63.72 ppm) as an internal standard.

Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, td = triplet of doublets, q = quartet, m = multiplet, brs = broad singlet), coupling constant (Hz), and integration.

2. Starting materials

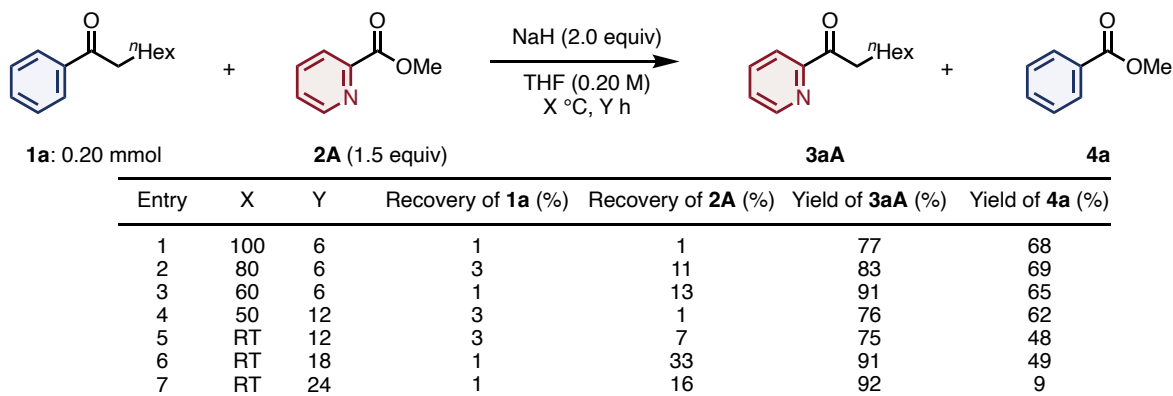


3. Optimization

*In optimization, the yield reliability of methyl benzoate (**4a**) cannot be guaranteed due to its volatility.

3-1. Optimization of heteroaromatic swapping

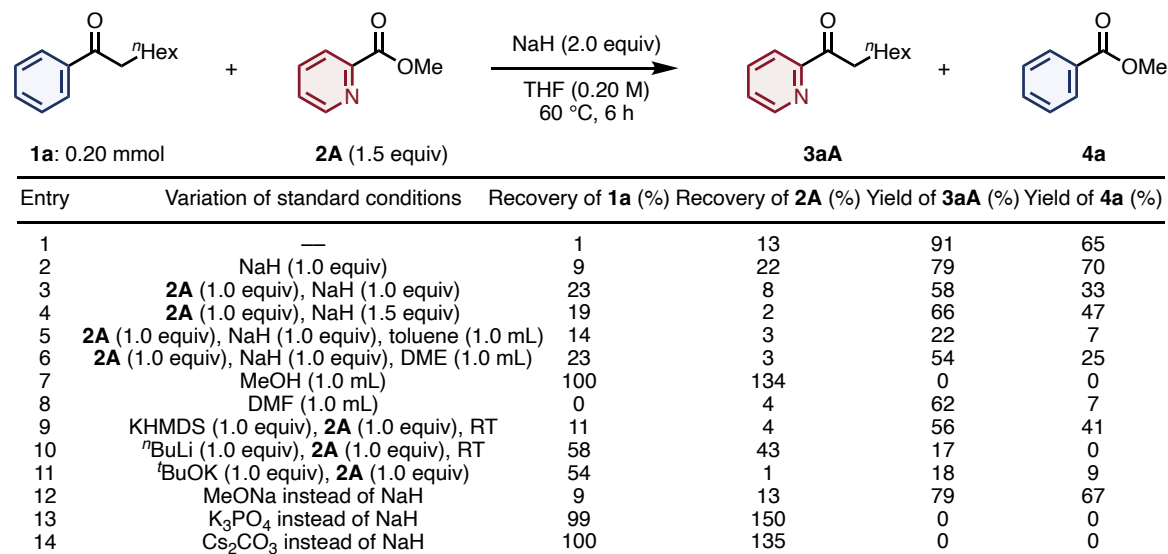
3-1-1. Effect of temperature



Yields were determined by ^1H NMR analysis using CH_2Br_2 as an internal standard.

Table S1

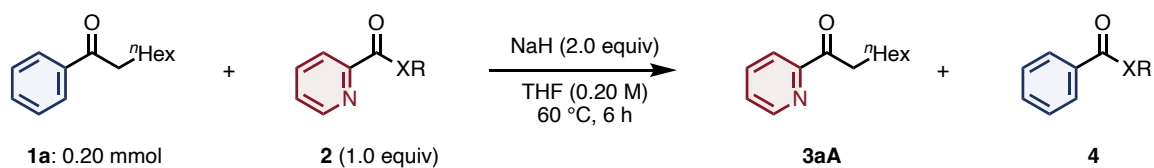
3-1-2. Effect of parameter



Yields were determined by ^1H NMR analysis using CH_2Br_2 as an internal standard.

Table S2

3-1-3. Effect of ester moiety

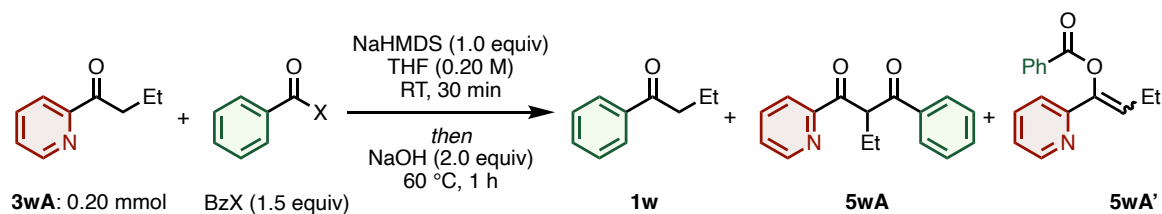


Entry	XR	Yield of 3aA (%)	Yield of 4a (%)
1	OMe	71	37
2	OBn	61	65
3	OCy	0	0
4	OPh	6	4
5	S ⁿ Hex	11	11

Yields were determined by ¹H NMR analysis using CH₂Br₂ as an internal standard.

Table S3

3-2. Optimization of swapping to other aromatics



Entry	X	Recovery of 3wA (%)	Recovery of BzX (%)	Yields of 1w (%)	Yields of 5wA (%)	Yields of 5wA' (%)
1	OMe	99	72	0	0	0
2	Cl	18	10	37	2	48
3 ^a	Cl	8	10	0	3	85
4	CN	17	0	56	24	0
5	Bt	27	0	54	15	0
6	OC ₆ F ₅	73	0	5	0	0

Yields were determined by ¹H NMR analysis using CH₂Br₂ as an internal standard.
[a] without 2nd step

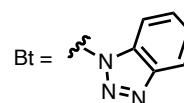
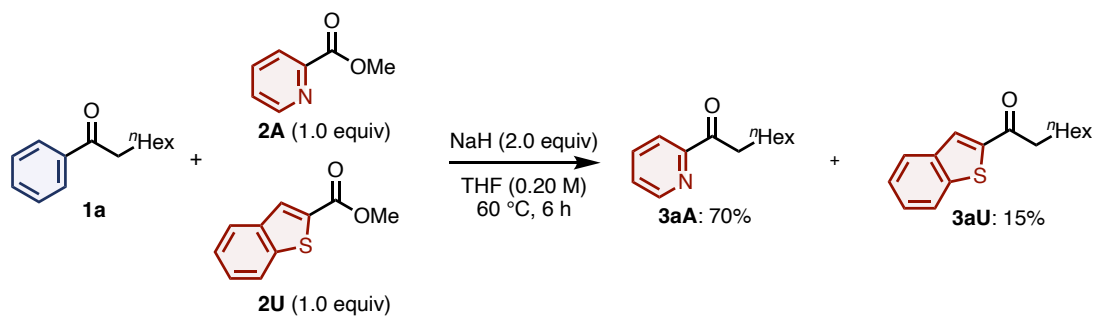


Table S4

4. Mechanistic studies

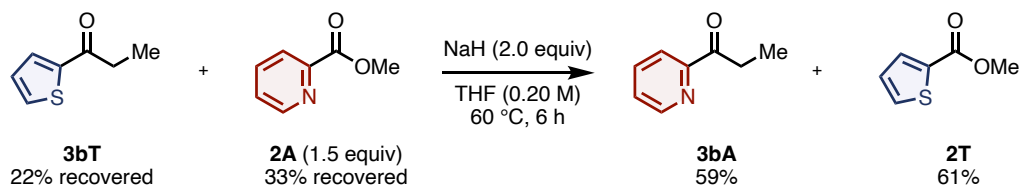
4-1. Comparative study of different heteroaromatic ring (2A vs 2U)



Yields were determined by ^1H NMR analysis using CH_2Br_2 as an internal standard.

Figure S1

4-2. Comparative study of different heteroaromatic ring (2A vs 2T)



Yields were determined by ^1H NMR analysis using CH_2Br_2 as an internal standard.

Figure S2

4-3. Hammett plot

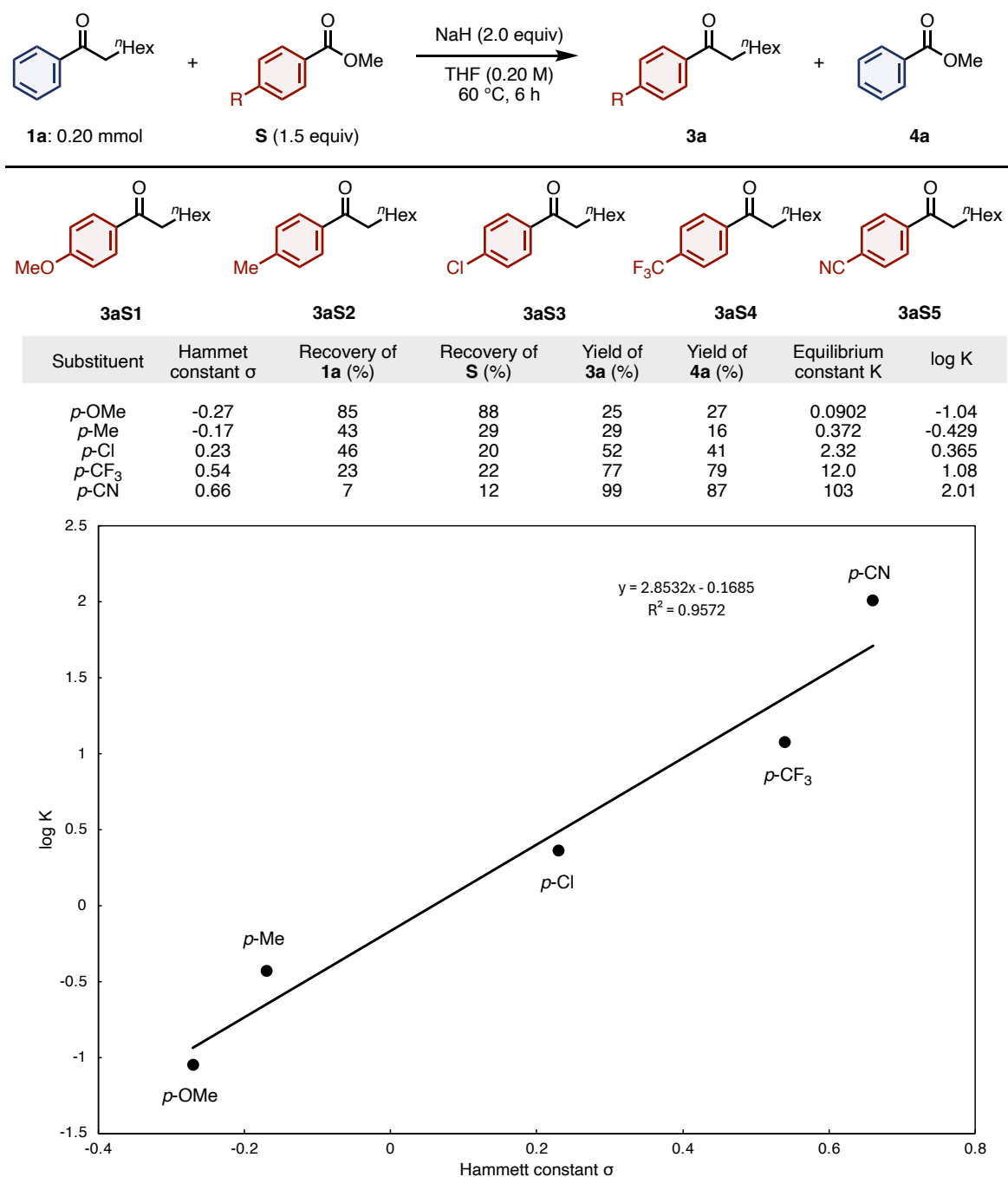


Figure S3

An 8-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N₂ gas after cooling to room temperature. To this tube were added 1-phenyloctan-1-one (1a: 43.7 μ L, 0.20 mmol, 1.0 equiv), substituted methyl benzoates S (0.30 mmol, 1.5 equiv), and THF (1.0 mL), followed by the addition of NaH (16 mg, 0.40 mmol, 2.0 equiv). The vessel was sealed with a screw cap and then heated at 60 °C for 6 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH₄Cl aq. and extracted three times with EtOAc. The combined

organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. Yields were determined by ¹H NMR analysis of crude mixture by using CH₂Br₂ as an internal standard. Hammett reaction constant was obtained from the literature^[19]. Hammett plot of the reaction is shown in Figure S7. X-axis represents Hammett constant σ of various substituents and Y-axis represents common logarithm of equilibrium constant K which is calculated from yields of **1a**, **2**, **3a**, and **4a**.

4-4. Attempt of heteroaromatic swapping of methyl ketone

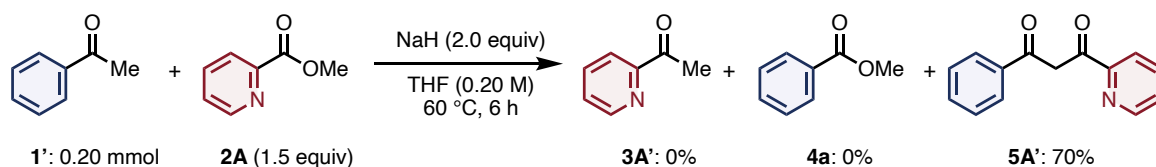
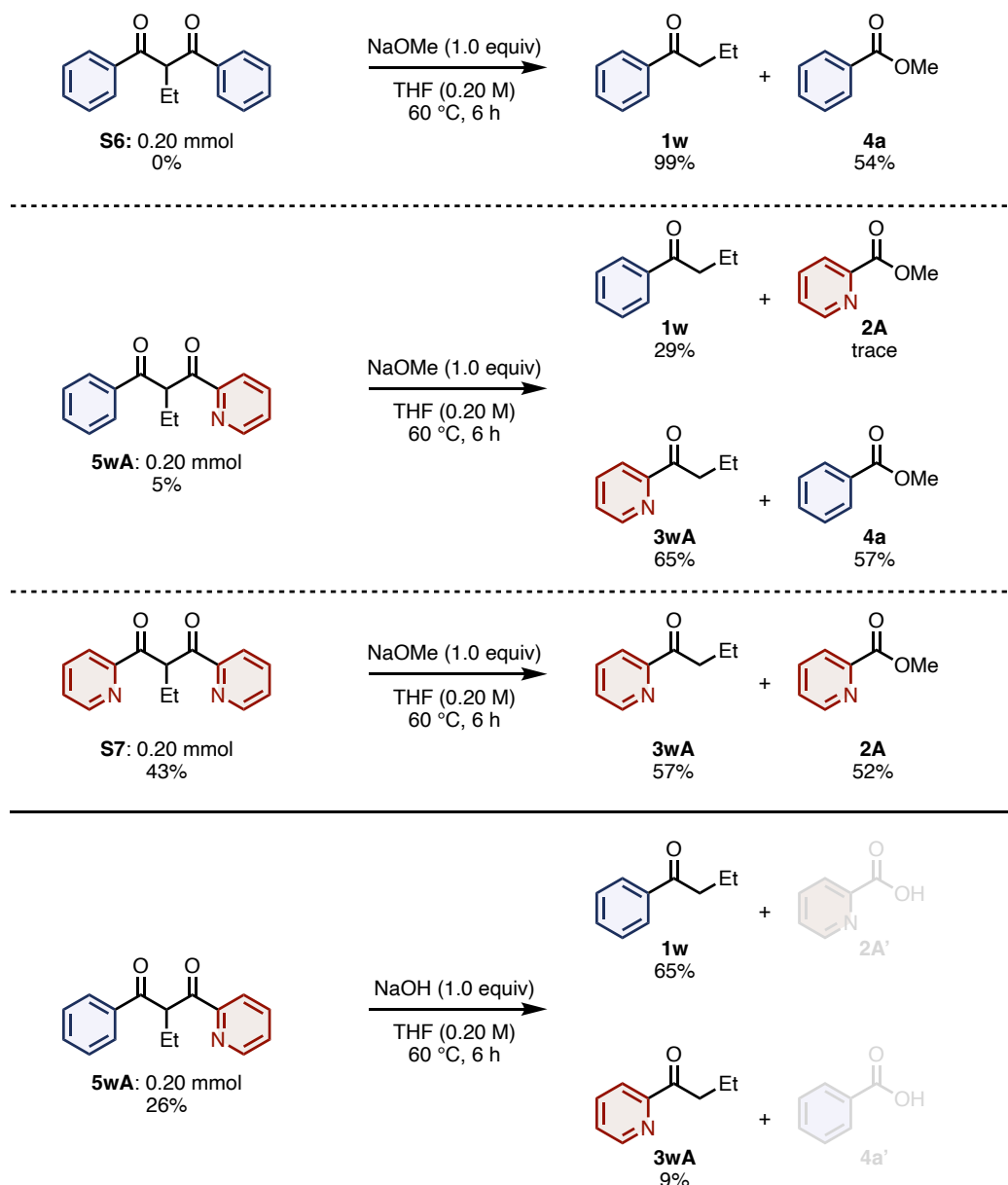


Figure S4

4-5. Control experiments for the retro-Claisen condensation



Yields were determined by ^1H NMR analysis using CH_2Br_2 as an internal standard.

Figure S5

An 8-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N_2 gas after cooling to room temperature. To this tube were added diketone (0.20 mmol, 1.0 equiv), NaOMe (10.8 mg, 0.10 mmol, 1.0 equiv) {or NaOH (8.0 mg, 0.10 mmol, 1.0 equiv)}, and THF (1.0 mL). The vessel was sealed with a screw cap and then heated at 60 °C for 6 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH_4Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Yields were determined by ^1H NMR analysis of crude mixture by using CH_2Br_2 as an internal standard.

4-6. Investigation of reversibility

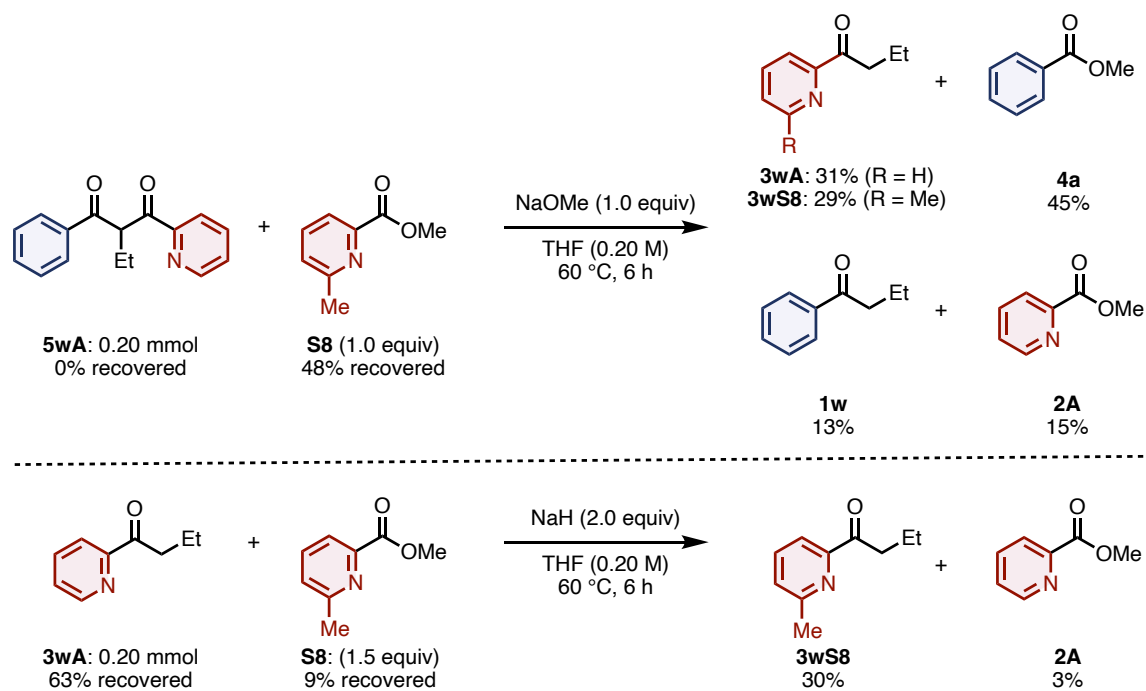
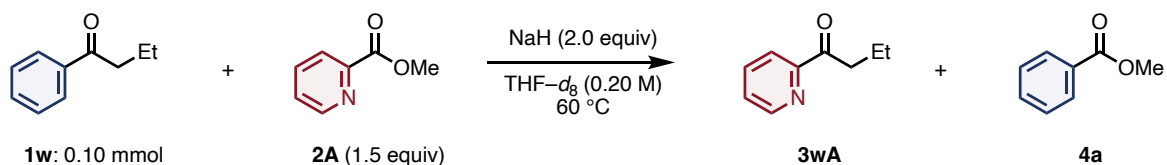


Figure S6

4-7. Time course plot of heteroaromatic swapping



A Wilmad[®] screw-cap NMR tube was dried with a heat gun *in vacuo* and filled with N₂ gas after cooling to room temperature. To this tube were added **1w** (15.0 μ L, 0.10 mmol, 1.0 equiv), **2A** (17.6 μ L, 0.15 mmol, 1.5 equiv), NaH (8.0 mg, 0.20 mmol 2.0 equiv), mesitylene (internal standard: 13.9 μ L) and THF-*d*₈ (0.50 mL). The tube was sealed with a screw cap and heated at 60 $^\circ$ C. The reaction progress was monitored by ¹H NMR spectroscopy every 10 min for 140 min.

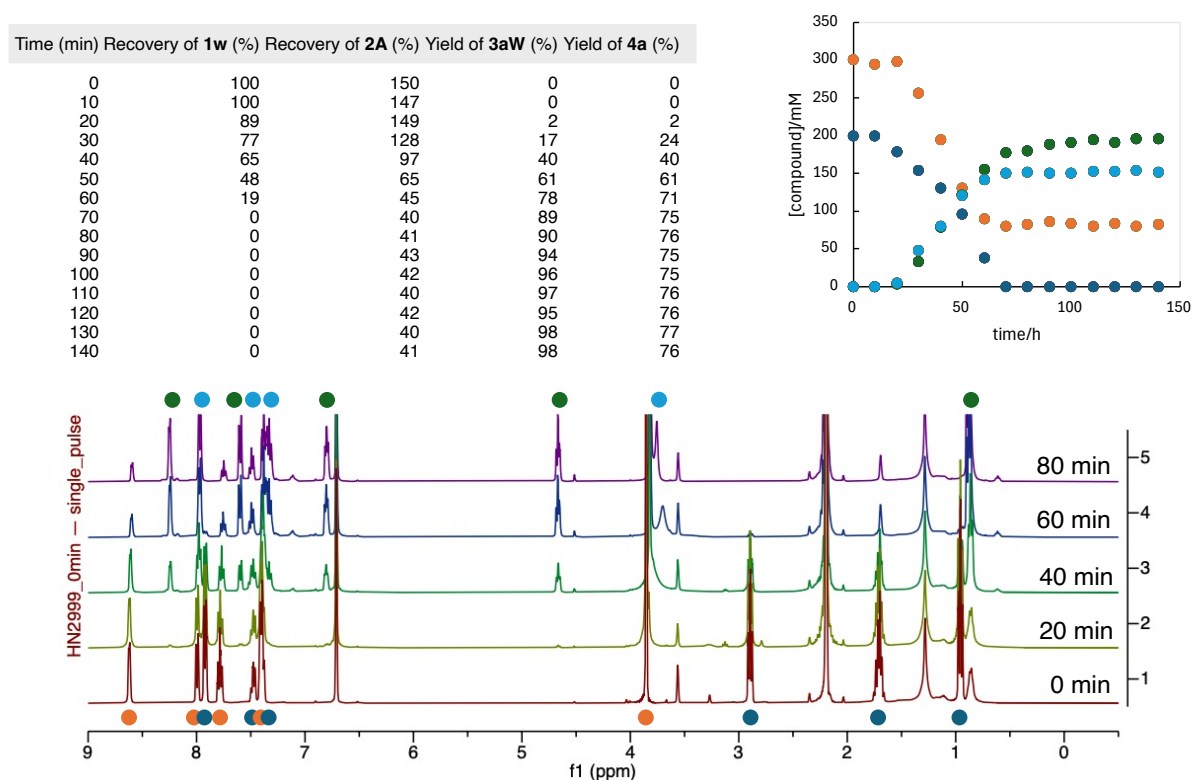
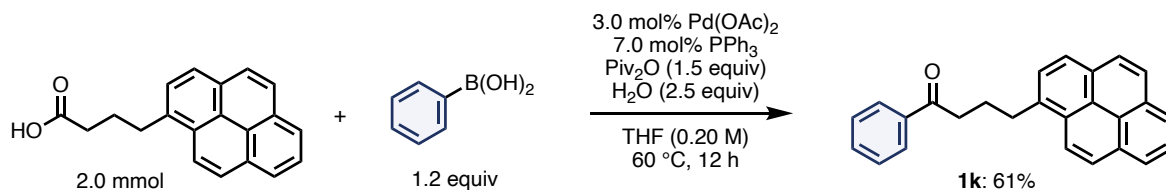


Figure S7

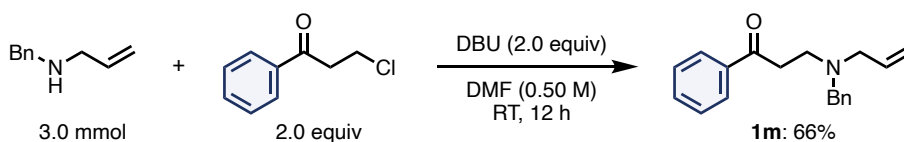
5. Preparation of starting materials

5-1. Preparation of **1k**^[20]



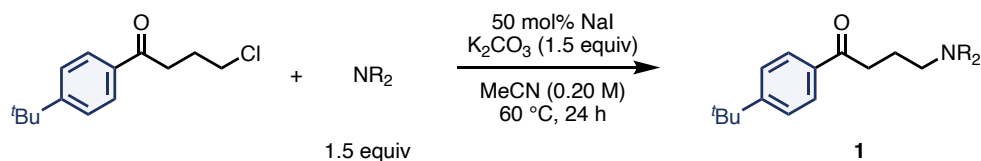
To a 50-mL glass flask containing a magnetic stirring bar were added 4-(pyren-1-yl)butanoic acid (576.7 mg, 2.0 mmol, 1.0 equiv), PhB(OH)₂ (292.6 mg, 2.4 mmol, 1.2 equiv), Pd(OAc)₂ (13.4 mg, 60 μmol, 3.0 mol%), and PPh₃ (36.7 mg, 0.14 mmol, 7.0 mol%). The vessel was placed under vacuum and refilled with N₂ gas three times. To this were added Piv₂O (607.3 μL, 3.0 mmol, 1.5 equiv), degassed H₂O (90 μL, 5.0 mmol, 2.5 equiv), and THF (10 mL). The vessel was heated at 60 °C for 12 h. After cooling the reaction mixture to room temperature, the reaction mixture was concentrated *in vacuo*. Purification by Isolera[®] (hexane/EtOAc = 9:1 to 4:1) afforded 1-phenyl-4-(pyren-1-yl)butan-1-one (**1k**) as a white solid (425.9 mg, 61% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.34 (d, *J* = 8.8 Hz, 1H), 8.19–8.05 (m, 4H), 8.04–7.82 (m, 6H), 7.57–7.47 (m, 1H), 7.45–7.36 (m, 2H), 3.43 (t, *J* = 8.4 Hz, 2H), 3.12–3.03 (m, 2H), 2.36–2.26 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 200.0, 137.0, 136.1, 132.9, 131.4, 130.9, 129.9, 128.8, 128.5, 128.0, 127.5, 127.3, 126.6, 125.8, 125.1, 125.0, 124.84, 124.77, 124.73, 123.4, 37.9, 32.8, 25.9 (One peak is missing due to overlapping); HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₆H₂₁O 349.1587; Found 349.1588.

5-2. Preparation of **1m**



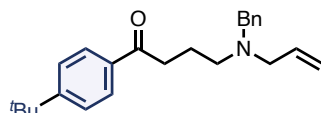
To a 15-mL vial containing a magnetic stirring bar were added 3-chloro-1-phenylpropan-1-one (911.5 μL, 6.0 mmol, 2.0 equiv), DBU (895.5 μL, 6.0 mmol, 2.0 equiv), and DMF (6.0 mL) then added *N*-benzylprop-2-en-1-amine (469.9 μL, 3.0 mmol, 1.0 equiv). The vessel was stirred at room temperature for 12 h. The reaction mixture was concentrated *in vacuo*. Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) afforded 3-(allyl(benzyl)amino)-1-phenylpropan-1-one (**1m**) as a brown liquid (551.3 mg, 66% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.93–7.85 (m, 2H), 7.59–7.50 (m, 1H), 7.48–7.38 (m, 2H), 7.34–7.18 (m, 5H), 5.94–5.79 (m, 1H), 5.24–5.07 (m, 2H), 3.63 (s, 2H), 3.17–3.09 (m, 4H), 2.98–2.90 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 199.4, 139.1, 136.8, 135.5, 132.8, 128.6, 128.4, 128.0, 127.9, 126.7, 117.3, 58.1, 56.8, 48.8, 36.6; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₉H₂₂NO 280.1696; Found 280.1699.

5-3. Preparation of **1**^[3]



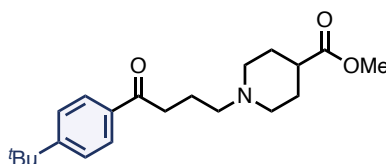
General procedure

To a 100-mL glass flask containing a magnetic stirring bar were added 1-(4-(*tert*-butyl)phenyl)-4-chlorobutan-1-one (1.0 equiv), K_2CO_3 (1.5 equiv), NaI (50 mol%), dialkylamine (1.5 equiv), and MeCN (0.20 M). The vessel was heated at 60 °C for 24 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH_4Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Purification afforded the corresponding product **1**.



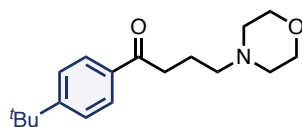
4-(Allyl(benzyl)amino)-1-(4-(*tert*-butyl)phenyl)butan-1-one (**1n**)

Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to 19:1) afforded **1n** as a brown liquid (5.0 mmol scale: 71.8 mg, 4% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.94–7.84 (m, 2H), 7.50–7.43 (m, 2H), 7.36–7.17 (m, 5H), 5.95–5.65 (m, 1H), 5.23–5.08 (m, 2H), 3.58 (s, 2H), 3.09 (d, $J = 6.4$ Hz, 2H), 2.95 (t, $J = 7.2$ Hz, 2H), 2.51 (t, $J = 6.8$ Hz, 2H), 1.97–1.85 (m, 2H), 1.35 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.7, 156.4, 139.1, 135.4, 134.4, 128.9, 128.1, 127.9, 126.8, 125.3, 117.5, 57.8, 56.4, 52.4, 36.0, 34.9, 31.0, 21.4; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{24}\text{H}_{32}\text{NO}$ 350.2478; Found 350.2470.



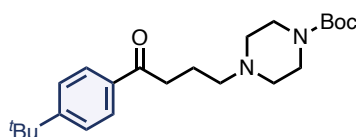
Methyl 1-(4-(4-(*tert*-butyl)phenyl)-4-oxobutyl)piperidine-4-carboxylate (**1o**)

Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to 19:1) afforded **1o** as a brown solid (2.0 mmol scale: 358.7 mg, 52% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, $J = 8.4$ Hz, 2H), 7.47 (d, $J = 8.4$ Hz, 2H), 3.67 (s, 3H), 2.98 (t, $J = 7.2$ Hz, 2H), 2.90–2.83 (m, 2H), 2.39 (t, $J = 7.2$ Hz, 2H), 2.32–2.23 (m, 1H), 2.04–1.82 (m, 6H), 1.78–1.64 (m, 2H), 1.34 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.8, 175.6, 156.6, 134.5, 128.0, 125.5, 57.9, 52.9, 51.6, 41.1, 36.2, 35.1, 31.1, 28.2, 21.7; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{32}\text{NO}_3$ 346.2377; Found 346.2373.



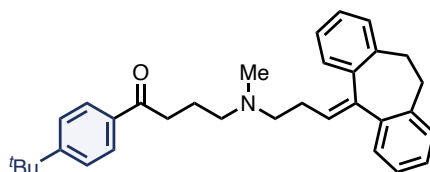
1-(4-(*tert*-Butyl)phenyl)-4-morpholinobutan-1-one (1p)

Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) afforded **1p** as a brown liquid (2.0 mmol scale: 268.4 mg, 46% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.91 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 3.65 (t, *J* = 5.2 Hz, 4H), 2.99 (t, *J* = 7.2 Hz, 2H), 2.47–2.37 (m, 6H), 2.00–1.88 (m, 2H), 1.34 (s, 9H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 199.6, 156.6, 134.5, 128.0, 125.4, 66.8, 58.1, 53.5, 36.0, 35.0, 31.0, 21.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₉H₂₈NO₂ 290.2115; Found 290.2118.



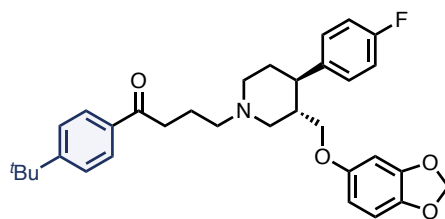
***tert*-Butyl 4-(4-(4-(*tert*-butyl)phenyl)-4-oxobutyl)piperazine-1-carboxylate (1q)**

Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) afforded **1o** as a brown liquid (2.0 mmol scale: 292.7 mg, 42% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 3.38 (t, *J* = 5.2 Hz, 4H), 2.99 (t, *J* = 7.2 Hz, 2H), 2.45–2.34 (m, 6H), 1.98–1.88 (m, 2H), 1.45 (s, 9H), 1.34 (s, 9H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 199.6, 156.6, 154.7, 134.5, 128.0, 125.4, 79.5, 57.7, 52.8, 36.0, 35.0, 31.0, 28.4, 21.4 (One peak is missing due to overlapping); HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₃H₃₇N₂O₃ 389.2799; Found 389.2806.



1-(4-(*tert*-Butyl)phenyl)-4-((3-(10,11-dihydro-5*H*-dibenzo[*a,d*][7]annulen-5-ylidene)propyl)(methyl)amino)butan-1-one (1ab)

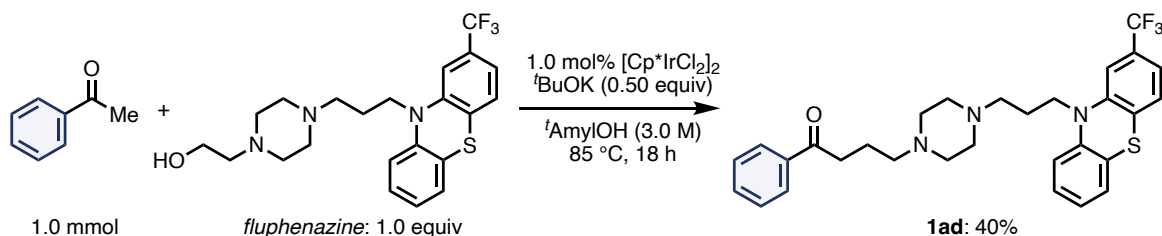
Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) afforded **3aA** as a brown liquid (2.0 mmol scale: 450.9 mg, 48% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.86 (d, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 8.8 Hz, 2H), 7.30–7.23 (m, 1H), 7.19–7.07 (m, 6H), 7.04–6.99 (m, 1H), 5.86 (t, *J* = 7.2 Hz, 1H), 3.46–3.15 (m, 2H), 3.02–2.69 (m, 4H), 2.46 (t, *J* = 7.2 Hz, 2H), 2.38 (t, *J* = 7.2 Hz, 2H), 2.29 (t, *J* = 7.2 Hz, 2H), 2.15 (s, 3H), 1.91–1.81 (m, 2H), 1.34 (s, 9H); HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₃₃H₄₀NO 466.3104; Found 466.3111.



4-((3*S*,4*R*)-3-((Benzo[*d*][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)piperidin-1-yl)-1-(4-(*tert*-butyl)phenyl)butan-1-one (1ac**)**

Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) afforded **1ac** as a brown liquid (1.0 mmol scale: 233.3 mg, 44% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.16–7.06 (m, 2H), 6.95 (t, *J* = 8.4 Hz, 2H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.33 (d, *J* = 2.4 Hz, 1H), 6.12 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.87 (s, 2H), 3.53 (d, *J* = 9.2 Hz, 1H), 3.41 (dd, *J* = 9.2, 5.6 Hz, 1H), 3.23 (d, *J* = 7.2 Hz, 1H), 3.12–2.97 (m, 3H), 2.55–2.36 (m, 3H), 2.16–1.94 (m, 5H), 1.83–1.69 (m, 2H), 1.34 (s, 9H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 199.7, 161.44 (d, *J*_{C-F} = 244.1 Hz), 156.5, 154.4, 148.1, 141.5, 139.8, 134.6, 128.8 (d, *J*_{C-F} = 7.8 Hz), 128.1, 125.5, 115.3 (d, *J*_{C-F} = 21.2 Hz), 107.8, 105.5, 101.0, 97.9, 69.6, 58.1, 57.5, 53.9, 44.1, 41.9, 36.2, 35.1, 34.1, 31.1, 22.0 (Two peaks are missing due to overlapping.); ¹⁹F NMR (376 MHz, CDCl₃) δ -117.5; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₃₃H₃₉FNO₄ 532.2858; Found 532.2871; [α]_D²³ = -19.28 (*c* 0.0071, CHCl₃).

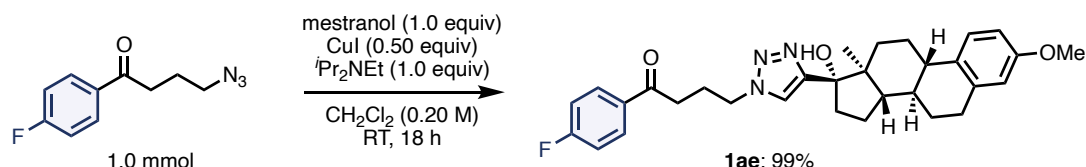
5-4. Preparation of **1ad^[2]**



To an 8-mL glass tube containing a magnetic stirring bar were added fluphenazine (510.4 mg, 1.0 mmol, 1.0 equiv), ^tBuOK (56.1 mg, 0.50 mmol, 0.50 equiv), and [Cp*IrCl₂]₂ (8.0 mg, 10 μmol, 1.0 mol%). The vessel was placed under vacuum and refilled with N₂ gas three times. To this were added acetophenone (117.8 μL, 1.0 mmol, 1.0 equiv) and ^tAmylOH (0.33 mL). The vessel was heated at 85 °C for 18 h. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica-gel pad with CHCl₃/MeOH = 9:1 as an eluent, and then concentrated *in vacuo*. The residue was purified by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) to afford 1-phenyl-4-(4-(3-(2-(trifluoromethyl)-10*H*-phenothiazin-10-yl)propyl)piperazin-1-yl)butan-1-one (**1ad**) as a white solid (214.1 mg, 40% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.96 (d, *J* = 7.2 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.20–7.09 (m, 4H), 7.03 (s, 1H), 6.96–6.88 (m, 2H), 3.94 (t, *J* = 6.8 Hz, 2H), 2.98 (t, *J* = 7.2 Hz, 2H), 2.49–2.34 (m, 12H), 1.98–1.84 (m, 4H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 200.0, 145.7, 144.3, 137.1, 132.8, 129.9, 129.6 (q, *J*_{C-F} = 32.2 Hz) 129.1, 128.5, 128.1, 127.6, 127.5, 127.4, 124.0, 123.8 (q, *J*_{C-F} =

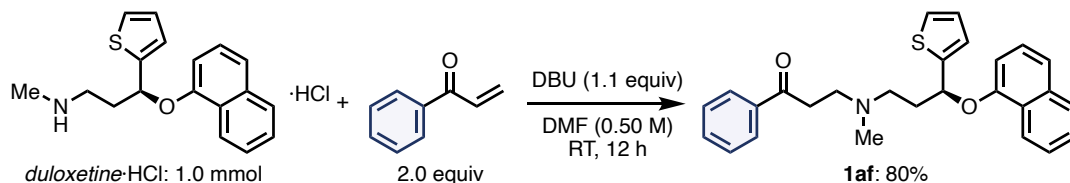
271.3 Hz), 123.0, 119.0 (q, J_{C-F} = 4.0 Hz), 115.9, 111.8 (q, J_{C-F} = 3.8 Hz), 57.7, 55.4, 53.1, 53.0, 45.3, 36.3, 24.1, 21.6 (One peak is missing due to overlapping); ^{19}F NMR (376 MHz, CDCl_3) δ -62.6; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{30}\text{H}_{33}\text{F}_3\text{N}_3\text{OS}$ 540.2291; Found 540.2290.

5-5. Preparation of **1ae**



To a 20-mL glass tube containing a magnetic stirring bar were added 4-azido-1-(4-fluorophenyl)butan-1-one (207.2 mg, 1.0 mmol, 1.0 equiv), mestranol (310.4 mg, 1.0 mmol, 1.0 equiv), CuI (95.2 mg, 0.50 mmol, 0.50 equiv), and $i\text{Pr}_2\text{NEt}$ (174.0 μL , 1.0 mmol, 1.0 equiv), and CH_2Cl_2 (5.0 mL). The vessel was stirred at room temperature for 18 h. The reaction mixture was passed through a short Celite[®] pad with CH_2Cl_2 as an eluent, and then concentrated *in vacuo*. Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH}$ = 1:0 to 19:1) afforded 1-(4-fluorophenyl)-4-(4-((8*S*,9*S*,13*S*,14*S*,17*S*)-17-hydroxy-3-methoxy-9,13-dimethyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl)-1*H*-1,2,3-triazol-1-yl)butan-1-one (**1ae**) as a brown oil (512.0 mg, 99% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.99–7.90 (m, 2H), 7.44 (s, 1H), 7.14–7.04 (m, 3H), 6.67 (dd, J = 8.4, 2.8 Hz, 1H), 6.61 (d, J = 2.8 Hz, 1H), 4.51 (t, J = 6.8 Hz, 2H), 3.76 (s, 3H), 3.00 (t, J = 6.8 Hz, 2H), 2.89–2.74 (m, 3H), 2.46–2.28 (m, 3H), 2.20–2.05 (m, 2H), 1.98–1.84 (m, 3H), 1.64–1.20 (m, 7H), 1.04 (s, 3H), 0.63 (td, J = 12.8, 4.2 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 196.9, 165.8 (d, J_{C-F} = 255.6 Hz), 157.4, 137.9, 132.8 (d, J_{C-F} = 3.1 Hz), 132.4, 130.6 (d, J_{C-F} = 9.3 Hz), 126.3, 126.2, 115.8 (d, J_{C-F} = 21.8 Hz), 113.7, 111.4, 55.1, 49.3, 48.5, 47.3, 43.5, 43.3, 39.4, 38.9, 34.5, 32.9, 32.7, 29.8, 27.3, 26.2, 24.3, 23.3, 14.2; ^{19}F NMR (376 MHz, CDCl_3) δ -105.5; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{31}\text{H}_{37}\text{FN}_3\text{O}_3$ 518.2813; Found 518.2834; $[\alpha]_{\text{D}}^{23}$ = +17.81 (c 0.036, CHCl_3).

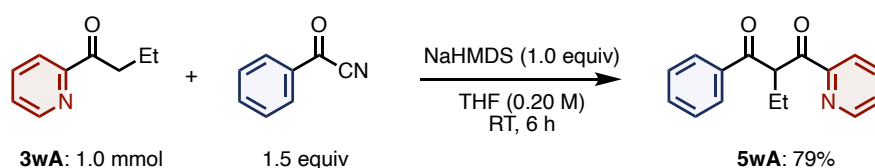
5-6. Preparation of **1af**



To a 15-mL vial containing a magnetic stirring bar were added 1-phenylprop-2-en-1-one (265.4 μL , 2.0 mmol, 2.0 equiv), duloxetine·HCl (264.3 mg, 1.0 mmol, 1.0 equiv), and DMF (2.0 mL) then added DBU (164.2 μL , 1.1 mmol, 1.1 equiv). The vessel was stirred at room temperature for 12 h. The reaction was concentrated and directly purified by Isolera[®] ($\text{CHCl}_3/\text{MeOH}$ = 1:0 to 19:1) to afford (*S*)-3-(methyl(3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propyl)amino)-1-phenylpropan-1-one (**1af**) as a

brown oil (343.5 mg, 80% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.41–8.30 (m, 1H), 7.81–7.71 (m, 3H), 7.55–7.44 (m, 3H), 7.42–7.34 (m, 3H), 7.24 (t, J = 7.6 Hz, 1H), 7.19 (dd, J = 4.8, 3.6 Hz, 1H), 7.04 (d, J = 3.6 Hz, 1H), 6.92 (dd, J = 4.8, 3.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 5.80 (dd, J = 8.0, 4.8 Hz, 1H), 3.05 (t, J = 7.6 Hz, 2H), 2.96–2.67 (m, 3H), 2.62–2.50 (m, 1H), 2.50–2.37 (m, 1H), 2.33 (s, 3H), 2.30–2.13 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 199.3, 153.4, 145.3, 136.8, 134.5, 132.9, 128.5, 127.9, 127.4, 126.5, 126.2, 126.0, 125.7, 125.2, 124.6, 122.0, 120.4, 106.8, 74.0, 53.1, 52.6, 42.5, 36.7, 36.6 (One peak is missing due to overlapping); HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{28}\text{NO}_2\text{S}$ 430.1835; Found 430.1852; $[\alpha]_{\text{D}}^{23} = +35.29$ (c 0.028, CHCl_3).

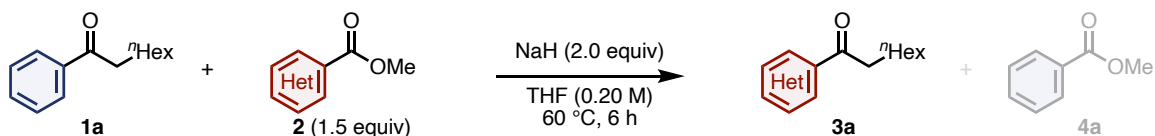
5-7. Preparation of 5wA^[21]



An 20-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N_2 gas after cooling to room temperature. To this tube were added **3wA** (149.2 mg, 1.0 mmol, 1.0 equiv) and THF (5.0 mL), followed by the addition of NaHMDS (1.0 M THF solution: 0.20 mL, 0.20 mmol, 1.0 equiv). To this solution was added benzoyl cyanide (196.7 mg, 1.5 mmol, 1.5 equiv). After stirred at room temperature for 6 h, the reaction was quenched with saturated NH_4Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Purification by Isolera[®] (hexane/EtOAc = 1:0 to 2:1) afforded 2-ethyl-1-phenyl-3-(pyridin-2-yl)propane-1,3-dione (**5wA**) as a white solid (201.3 mg, 79% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.54 (d, J = 4.8 Hz, 1H), 8.07 (d, J = 8.0 Hz, 3H), 7.82 (t, J = 8.0 Hz, 1H), 7.56 (t, J = 7.0 Hz, 1H), 7.50–7.36 (m, 3H), 5.73 (t, J = 6.4 Hz, 1H), 2.22–1.94 (m, 2H), 1.02 (t, J = 7.2 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 197.7, 152.1, 148.7, 137.0, 136.8, 132.9, 128.7, 128.6, 127.2, 122.4, 56.2, 22.1, 12.6; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{16}\text{NO}_2$ 254.1176; Found 245.1177.

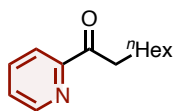
6. Heteroaromatic swapping

6-1. Applicable ester



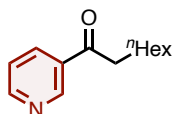
General procedure

An 8-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N₂ gas after cooling to room temperature. To this tube were added 1-phenyloctan-1-one (**1a**: 43.7 μ L, 0.20 mmol, 1.0 equiv), heteroaromatic methylester **2** (0.30 mmol, 1.5 equiv), and THF (1.0 mL), followed by the addition of NaH (16 mg, 0.40 mmol, 2.0 equiv). The vessel was sealed with a screw cap and then heated at 60 °C for 6 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH₄Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification afforded the corresponding heteroaromatic ketone **3a**.



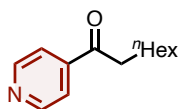
1-(Pyridin-2-yl)octan-1-one (**3aA**)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aA** as a colorless liquid (37.2 mg, 91% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.72–8.65 (m, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 1H), 7.51–7.42 (m, 1H), 3.22 (t, *J* = 6.8 Hz, 2H), 1.90–1.62 (m, 2H), 1.49–1.21 (m, 8H), 0.88 (t, *J* = 6.0 Hz, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 202.2, 153.6, 148.9, 136.8, 126.9, 121.8, 37.7, 31.7, 29.3, 29.1, 24.0, 22.6, 14.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₃H₂₀NO 206.1539; Found 206.1540.



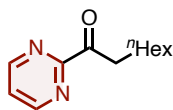
1-(Pyridin-3-yl)octan-1-one (**3aB**)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aB** as a colorless liquid (30.2 mg, 74% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.17 (s, 1H), 8.81–8.74 (m, 1H), 8.27–8.20 (m, 1H), 7.47–7.38 (m, 1H), 2.99 (t, *J* = 7.6 Hz, 2H), 1.81–1.72 (m, 2H), 1.44–1.25 (m, 8H), 0.89 (t, *J* = 7.2 Hz, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 199.3, 153.3, 149.6, 135.3, 132.2, 123.6, 38.9, 31.6, 29.2, 29.1, 24.0, 22.6, 14.0; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₃H₂₀NO 206.1539; Found 206.1541.



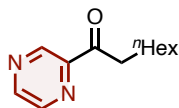
1-(Pyridin-4-yl)octan-1-one (3aC)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aC** as a white solid (27.9 mg, 68% yield). δ 8.81 (d, J = 5.2 Hz, 2H), 7.73 (d, J = 5.2 Hz, 2H), 2.96 (t, J = 7.2 Hz, 2H), 1.80–1.68 (m, 2H), 1.39–1.23 (m, 8H), 0.93–0.85 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.9, 150.9, 142.8, 121.1, 38.9, 31.6, 29.2, 29.1, 23.8, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{20}\text{NO}$ 206.1539; Found 206.1540.



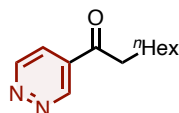
1-(Pyrimidin-2-yl)octan-1-one (3aD)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aD** as a colorless liquid (27.1 mg, 66% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.94 (d, J = 4.8 Hz, 2H), 7.45 (t, J = 4.8 Hz, 1H), 3.23 (t, J = 7.6 Hz, 2H), 1.92–1.56 (m, 2H), 1.46–1.12 (m, 8H), 0.94–0.84 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 200.0, 160.2, 157.6, 122.8, 39.0, 31.7, 29.2, 29.0, 23.9, 22.6, 14.0; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{19}\text{N}_2\text{O}$ 207.1492; Found 207.1494.



1-(Pyrazin-2-yl)octan-1-one (3aE)

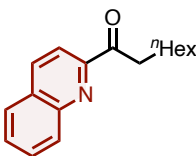
Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aE** as a colorless liquid (30.5 mg, 74% yield). ^1H NMR (400 MHz, CDCl_3) δ 9.23 (d, J = 1.6 Hz, 1H), 8.75 (dd, J = 2.4, 1.6 Hz, 1H), 8.64 (dd, J = 2.4, 1.6 Hz, 1H), 3.18 (t, J = 7.6 Hz, 2H), 1.79–1.67 (m, 2H), 1.43–1.25 (m, 8H), 0.93–0.84 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.6, 147.7, 143.7, 143.5, 37.9, 31.7, 29.2, 29.1, 23.7, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{19}\text{N}_2\text{O}$ 207.1492; Found 207.1493.



1-(Pyridazin-4-yl)octan-1-one (3aF)

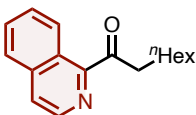
Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aF** as a brown liquid (22.3 mg, 54% yield). ^1H NMR (400 MHz, CDCl_3) δ 9.63–9.54 (m, 1H), 9.46 (d, J = 5.2 Hz, 1H), 7.84 (dd, J = 5.2, 2.4 Hz, 1H), 2.98 (t, J = 7.2 Hz, 2H), 1.80–1.68 (m, 2H), 1.43–1.21 (m, 8H), 0.91–0.77 (m, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.5, 152.5, 148.3, 132.2, 123.4, 39.1, 31.6, 29.02, 29.00, 23.5, 22.6, 14.0; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{19}\text{N}_2\text{O}$ 207.1492; Found 207.1498.



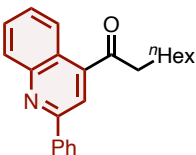
1-(Quinolin-2-yl)octan-1-one (3aG)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aG** as a colorless liquid (28.2 mg, 55% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.25 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.78 (ddd, J = 8.4, 6.8, 1.6 Hz, 1H), 7.64 (ddd, J = 8.4, 6.8, 1.6 Hz, 1H), 3.39 (t, J = 7.6 Hz, 2H), 1.89–1.73 (m, 2H), 1.52–1.22 (m, 8H), 0.99–0.78 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 202.8, 153.2, 147.2, 136.8, 130.5, 129.9, 129.5, 128.4, 127.6, 118.2, 37.4, 31.7, 29.4, 29.2, 24.2, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{22}\text{NO}$ 256.1696; Found 256.1693.



1-(Isoquinolin-1-yl)octan-1-one (3aH)

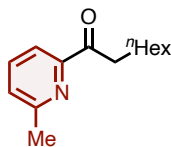
Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aH** as a colorless liquid (31.0 mg, 61% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.85–8.81 (m, 1H), 8.57 (d, J = 5.6 Hz, 1H), 7.87–7.84 (m, 1H), 7.80 (dd, J = 5.6, 0.8 Hz, 1H), 7.74–7.64 (m, 3H), 3.31 (t, J = 7.2 Hz, 2H), 1.82–1.73 (m, 2H), 1.49–1.22 (m, 8H), 0.92–0.84 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 205.0, 153.6, 141.0, 137.0, 130.3, 128.8, 126.9, 126.7, 125.6, 124.2, 40.4, 31.7, 29.3, 29.2, 24.2, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{22}\text{NO}$ 256.1696; Found 256.1694.



1-(2-Phenylquinolin-4-yl)octan-1-one (3aI)

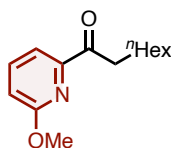
Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aI** as a colorless liquid (47.7 mg, 75% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.27–8.14 (m, 4H), 7.97 (s, 1H), 7.76 (ddd, J = 8.4, 6.8, 1.6 Hz, 1H), 7.64–7.47 (m, 4H), 3.07 (t, J = 7.2 Hz, 2H), 1.87–1.75 (m, 2H), 1.49–1.26 (m, 8H), 0.91–0.80 (m, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 204.8, 156.8, 149.2, 145.0, 139.0, 130.2, 130.0, 129.7,

129.0, 127.6, 127.4, 125.0, 122.8, 116.8, 42.8, 31.6, 29.2, 29.0, 24.0, 22.6, 14.0; HRMS (APCI) m/z $[M+H]^+$ Calcd for $C_{23}H_{26}NO$ 332.2009; Found 332.2018.



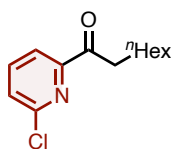
1-(6-Methylpyridin-2-yl)octan-1-one (3aJ)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aJ** as a colorless liquid (35.1 mg, 80% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 3.20 (t, J = 7.2 Hz, 2H), 2.61 (s, 3H), 1.78–1.66 (m, 2H), 1.45–1.29 (m, 8H), 0.94–0.83 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 202.8, 157.8, 153.2, 136.8, 126.5, 118.8, 37.6, 31.7, 29.3, 29.2, 24.4, 24.0, 22.6, 14.1; HRMS (APCI) m/z $[M+H]^+$ Calcd for $C_{14}H_{22}NO$ 220.1696; Found 220.1696.



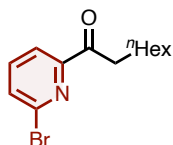
1-(6-Methoxypyridin-2-yl)octan-1-one (3aK)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aK** as a colorless liquid (27.0 mg, 57% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.69 (t, J = 7.2 Hz, 1H), 7.62 (d, J = 7.2 Hz, 1H), 6.92 (d, J = 7.2 Hz, 1H), 3.99 (s, 3H), 3.15 (t, J = 7.2 Hz, 2H), 1.79–1.69 (m, 2H), 1.43–1.23 (m, 8H), 0.98–0.80 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 202.2, 163.2, 151.0, 139.1, 115.0, 114.9, 53.4, 37.8, 31.7, 29.4, 29.2, 24.3, 22.6, 14.1; HRMS (APCI) m/z $[M+H]^+$ Calcd for $C_{14}H_{22}NO_2$ 236.1645; Found 236.1647.



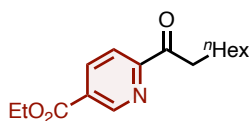
1-(6-Chloropyridin-2-yl)octan-1-one (3aL)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aL** as a colorless liquid (33.2 mg, 69% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.95 (d, J = 7.6 Hz, 1H), 7.80 (t, J = 7.6 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 3.19 (t, J = 7.2 Hz, 2H), 1.76–1.67 (m, 2H), 1.43–1.24 (m, 8H), 0.93–0.83 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 200.8, 153.8, 150.7, 139.5, 127.9, 120.2, 37.6, 31.7, 29.2, 29.1, 23.8, 22.6, 14.1; HRMS (APCI) m/z $[M+H]^+$ Calcd for $C_{13}H_{19}ClNO$ 240.1150; Found 240.1154.



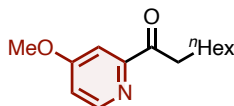
1-(6-Bromopyridin-2-yl)octan-1-one (3aM)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aM** as a colorless liquid (40.2 mg, 71% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.02–7.94 (m, 1H), 7.74–7.62 (m, 2H), 3.17 (t, *J* = 7.2 Hz, 2H), 1.81–1.65 (m, 2H), 1.43–1.26 (m, 8H), 0.94–0.84 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 200.8, 154.3, 141.3, 139.1, 131.6, 120.5, 37.6, 31.7, 29.2, 29.1, 23.8, 22.6, 14.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₃H₁₉BrNO 284.0645; Found 286.0648.



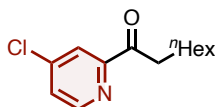
Ethyl 6-octanoylnicotinate (3aN)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aN** as a colorless liquid (33.9 mg, 61% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.26 (dd, *J* = 2.0, 0.8 Hz, 1H), 8.41 (dd, *J* = 8.0, 2.0 Hz, 1H), 8.09 (dd, *J* = 8.0, 0.8 Hz, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 3.23 (t, *J* = 7.2 Hz, 2H), 1.79–1.67 (m, 2H), 1.46–1.22 (m, 11H), 0.91–0.85 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.6, 164.6, 155.8, 150.2, 138.0, 128.7, 121.2, 61.8, 38.0, 31.7, 29.2, 29.1, 23.9, 22.6, 14.2, 14.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₆H₂₄NO₃ 278.1751; Found 278.1752.



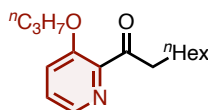
1-(4-Methoxypyridin-2-yl)octan-1-one (3aO)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aO** as a colorless liquid (41.0 mg, 87% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, *J* = 5.6 Hz, 1H), 7.57 (d, *J* = 2.4 Hz, 1H), 6.96 (dd, *J* = 5.6, 2.4 Hz, 1H), 3.90 (s, 3H), 3.19 (t, *J* = 7.6 Hz, 2H), 1.78–1.66 (m, 2H), 1.44–1.22 (m, 8H), 0.94–0.84 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 202.1, 166.4, 155.5, 150.0, 113.7, 106.8, 55.4, 37.8, 31.7, 29.3, 29.1, 24.0, 22.6, 14.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₄H₂₂NO₂ 236.1645; Found 236.1652.



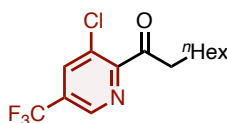
1-(4-Chloropyridin-2-yl)octan-1-one (3aP)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aP** as a colorless liquid (41.2 mg, 86% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.57 (d, *J* = 5.2 Hz, 1H), 8.03 (d, *J* = 2.0 Hz, 1H), 7.46 (dd, *J* = 5.2, 2.0 Hz, 1H), 3.18 (t, *J* = 7.2 Hz, 2H), 1.78–1.66 (m, 3H), 1.42–1.27 (m, 8H), 0.88 (t, *J* = 7.2 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 201.0, 154.7, 149.8, 145.4, 127.0, 122.2, 37.8, 31.7, 29.2, 29.1, 23.9, 22.6, 14.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₃H₁₉ClNO 240.1150; Found 240.1153.



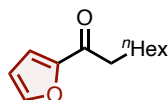
1-(3-Propoxy-2-pyridin-2-yl)octan-1-one (3aQ)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aQ** as a colorless liquid (34.3 mg, 65% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.27–8.08 (m, 1H), 7.44–7.22 (m, 2H), 3.99 (t, *J* = 6.4 Hz, 2H), 3.05 (t, *J* = 7.2 Hz, 2H), 1.93–1.78 (m, 2H), 1.78–1.62 (m, 2H), 1.46–1.18 (m, 8H), 1.06 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 6.0 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 202.5, 154.0, 145.4, 140.4, 126.5, 120.5, 70.3, 41.2, 31.7, 29.2, 29.1, 23.9, 22.6, 22.3, 14.0, 10.5; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₆H₂₆NO₂ 264.1958; Found 264.1959.



1-(3-Chloro-5-(trifluoromethyl)pyridin-2-yl)octan-1-one (3aR)

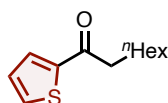
Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aR** as a colorless liquid (30.5 mg, 50% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.78 (s, 1H), 8.03 (s, 1H), 3.07 (t, *J* = 7.2 Hz, 2H), 1.78–1.66 (m, 2H), 1.47–1.22 (m, 8H), 0.89 (t, *J* = 6.4 Hz, 3H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 200.7, 155.4, 143.5 (q, *J*_{C-F} = 4.1 Hz), 136.1 (q, *J*_{C-F} = 3.6 Hz), 129.6, 128.9 (q, *J*_{C-F} = 34.0 Hz), 122.2 (q, *J*_{C-F} = 273.7 Hz), 40.5, 31.6, 29.1, 29.0, 23.5, 22.6, 14.0; ¹⁹F NMR (376 MHz, CDCl₃) δ –62.65; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₄H₁₈ClF₃NO 308.1024; Found 308.1027.



1-(Furan-2-yl)octan-1-one (3aS)

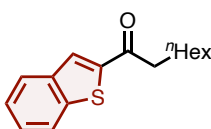
Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:4) afforded **3aS** as a colorless liquid (23.7 mg, 61% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.58 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.17 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.53 (dd, *J* = 3.6, 1.6 Hz, 1H), 2.81 (t, *J* = 7.2 Hz, 2H), 1.81–1.65 (m, 2H), 1.39–1.22 (m, 8H), 0.88

(t, J = 6.8 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 189.9, 152.9, 146.2, 116.8, 112.1, 38.5, 31.7, 29.3, 29.0, 24.3, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{19}\text{O}_2$ 195.1380; Found 195.1382.



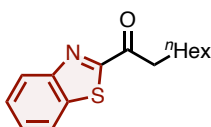
1-(thiophen-2-yl)octan-1-one (3aT)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:4) afforded **3aT** as a colorless liquid (30.1 mg, 72% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.71 (d, J = 3.6 Hz, 1H), 7.62 (d, J = 5.2 Hz, 1H), 7.12 (dd, J = 5.2, 3.6 Hz, 1H), 2.89 (t, J = 7.2 Hz, 2H), 1.81–1.68 (m, 2H), 1.43–1.23 (m, 8H), 0.89 (t, J = 6.4 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 193.6, 144.5, 133.3, 131.6, 128.0, 39.4, 31.7, 29.3, 29.1, 24.8, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{19}\text{OS}$ 211.1151; Found 211.1154.



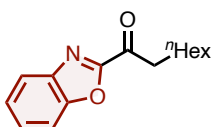
1-(Benzo[b]thiophen-2-yl)octan-1-one (3aU)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aU** as a white solid (48.2 mg, 93% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.95 (s, 1H), 7.88 (t, J = 7.6 Hz, 2H), 7.49–7.38 (m, 2H), 3.00 (t, J = 7.6 Hz, 2H), 1.83–1.74 (m, 2H), 1.45–1.24 (m, 8H), 0.89 (t, J = 7.2 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 195.0, 143.9, 142.4, 139.2, 128.7, 127.2, 125.8, 124.9, 123.0, 39.3, 31.7, 29.3, 29.1, 24.8, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{21}\text{OS}$ 261.1308; Found 261.1308.



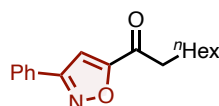
1-(Benzo[d]thiazol-2-yl)octan-1-one (3aV)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aW** as a white solid (41.2 mg, 79% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.19 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.63–7.47 (m, 2H), 3.27 (t, J = 7.2 Hz, 2H), 1.88–1.74 (m, 2H), 1.48–1.22 (m, 8H), 0.89 (t, J = 6.8 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 195.6, 166.6, 153.6, 137.2, 127.5, 126.9, 125.4, 122.4, 38.6, 31.7, 29.1, 29.0, 23.9, 22.6, 14.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{20}\text{NOS}$ 262.1260; Found 262.1261.



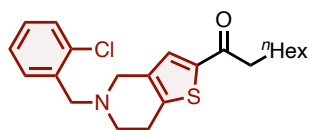
1-(Benzo[d]oxazol-2-yl)octan-1-one (3aW)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aW** as a colorless liquid (29.5 mg, 60% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.53 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.46 (dd, *J* = 8.0, 7.6 Hz, 1H), 3.22 (t, *J* = 7.6 Hz, 2H), 1.87–1.75 (m, 2H), 1.46–1.25 (m, 8H), 0.91–0.85 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 190.4, 157.2, 150.8, 140.4, 128.4, 125.7, 122.2, 111.9, 39.5, 31.6, 29.1, 29.0, 23.8, 22.6, 14.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₅H₂₀NO₂ 246.1489; Found 246.1489.



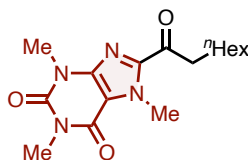
1-(3-Phenylisoxazol-5-yl)octan-1-one (**3aX**)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aX** as a colorless liquid (38.9 mg, 72% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.88–7.80 (m, 2H), 7.52–7.46 (m, 3H), 7.20 (s, 1H), 3.00 (t, *J* = 7.2 Hz, 2H), 1.82–1.71 (m, 2H), 1.44–1.23 (m, 8H), 0.93–0.85 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 189.9, 167.2, 163.1, 130.5, 129.1, 128.0, 126.8, 105.0, 39.8, 31.6, 29.04, 28.98, 23.4, 22.6, 14.0; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₇H₂₂NO₂ 272.1645; Found 272.1647.



1-(5-(2-Chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridin-2-yl)octan-1-one (**3aY**)

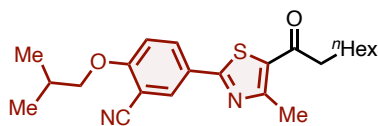
Purification by Isolera[®] (hexane/EtOAc = 1:0 to 0:1) afforded **3aY** as a brown liquid (48.3 mg, 56% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.51 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.38 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.33 (s, 1H), 7.28–7.19 (m, 2H), 3.83 (s, 2H), 3.62 (s, 2H), 2.96–2.92 (m, 2H), 2.90–2.85 (m, 2H), 2.79 (t, *J* = 8.0 Hz, 2H), 1.77–1.66 (m, 2H), 1.36–1.26 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 193.5, 143.3, 141.5, 135.7, 135.3, 134.3, 130.6, 130.1, 129.5, 128.4, 126.8, 58.4, 52.6, 50.2, 39.0, 31.7, 29.3, 29.1, 26.2, 25.1, 22.6, 14.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₂H₂₉ClNOS 390.1653; Found 390.1661.



1,3,7-Trimethyl-8-octanoyl-3,7-dihydro-1H-purine-2,6-dione (**3aZ**)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 0:1) afforded **3aZ** as a white solid (42.0 mg, 66% yield). ¹H NMR (400 MHz, CDCl₃) δ 4.33 (s, 3H), 3.61 (s, 3H), 3.42 (s, 3H), 3.12 (t, *J* = 7.6 Hz, 2H), 1.77–1.66 (m, 2H), 1.43–1.22 (m, 8H), 0.93–0.85 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 194.1,

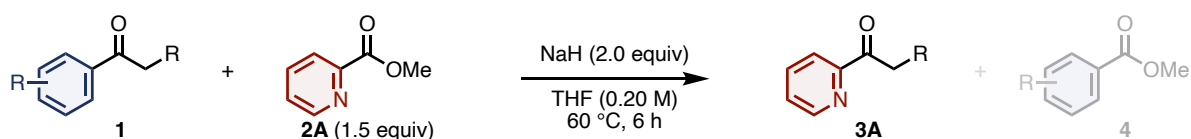
155.8, 151.4, 146.4, 143.6, 110.4, 40.1, 34.7, 31.6, 29.7, 29.1, 29.0, 28.1, 23.9, 22.6, 14.0; HRMS (APCI) m/z $[M+H]^+$ Calcd for $C_{16}H_{25}N_4O_3$ 321.1921; Found 321.1913.



2-Isobutoxy-5-(4-methyl-5-octanoylthiazol-2-yl)benzonitrile (**3aAA**)

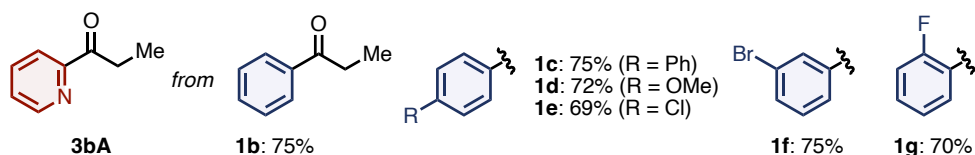
2AA (1.0 equiv) was used. Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3aAA** as a white solid (23.8 mg, 30% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.19 (d, J = 2.4 Hz, 1H), 8.12 (dd, J = 8.8, 2.4 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 3.90 (d, J = 6.4 Hz, 2H), 2.83 (t, J = 7.6 Hz, 2H), 2.77 (s, 3H), 2.28–2.14 (m, 1H), 1.80–1.68 (m, 2H), 1.38–1.23 (m, 8H), 1.09 (d, J = 6.8 Hz, 6H), 0.93–0.85 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 193.2, 166.2, 162.6, 159.6, 132.6, 132.2, 130.7, 125.9, 115.4, 112.6, 103.0, 75.7, 43.3, 31.7, 29.2, 29.1, 28.1, 24.4, 22.6, 19.0, 18.4, 14.1; HRMS (APCI) m/z $[M+H]^+$ Calcd for $C_{23}H_{31}N_2O_2S$ 399.2101; Found 399.2109.

6-2. Substrate scope



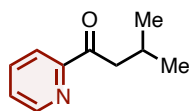
General procedure

An 8-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N₂ gas after cooling to room temperature. To this tube were added ketone **1** (0.20 mmol, 1.0 equiv), methyl picolinate (**2A**: 35.2 μ L, 0.30 mmol, 1.5 equiv), and THF (1.0 mL), followed by the addition of NaH (16 mg, 0.40 mmol, 2.0 equiv). The vessel was sealed with a screw cap and then heated at 60 °C for 6 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH₄Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification afforded the corresponding 2-pyridyl ketone **3A**.



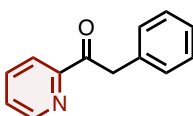
1-(pyridin-2-yl)propan-1-one (**3bA**)

The yields of **3bA** were determined by ¹H NMR analysis of crude mixture by using CH₂Br₂ as an internal standard. The spectra were matched with those of literature.^[16]



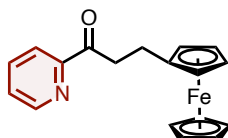
3-Methyl-1-(pyridin-2-yl)butan-1-one (3hA)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3hA** as a colorless liquid (20.3 mg, 62% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J* = 4.8 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.83 (t, *J* = 8.0 Hz, 1H), 7.48–7.44 (m, 1H), 3.11 (d, *J* = 6.8 Hz, 2H), 2.40–2.25 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 6H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.8, 153.8, 148.8, 136.9, 126.9, 121.8, 46.4, 24.6, 22.8; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₀H₁₄NO 164.1070; Found 164.1076.



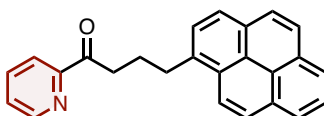
2-Phenyl-1-(pyridin-2-yl)ethan-1-one (3iA)

This reaction was performed at 80 °C using methyl picolinate (**3A**; 3.0 equiv) and NaH (3.0 equiv). Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3iA** as a brown liquid (32.0 mg, 81% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.72 (d, *J* = 4.8 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.81 (td, *J* = 8.0, 1.6 Hz, 1H), 7.48–7.44 (m, 1H), 7.38–7.19 (m, 5H), 4.55 (s, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 199.1, 153.0, 148.9, 136.9, 134.7, 129.9, 128.4, 127.2, 126.7, 122.3, 43.9; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₃H₁₂NO 198.0913; Found 198.0923.



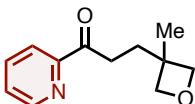
3-Ferrocenyl-1-(pyridin-2-yl)propan-1-one (3jA)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3jA** as a brown liquid (40.8 mg, 64% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.72–8.66 (m, 1H), 8.06 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.84 (td, *J* = 7.6, 1.6 Hz, 1H), 7.51–7.43 (m, 1H), 4.16–4.11 (m, 7H), 4.08–4.03 (m, 2H), 3.49 (t, *J* = 7.6 Hz, 2H), 2.78 (t, *J* = 8.0 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.4, 153.4, 149.0, 136.8, 127.1, 121.8, 88.3, 68.5, 68.1, 67.2, 39.0, 23.8; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₈H₁₈FeNO 320.0732; Found 320.0724.



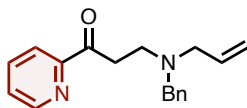
4-(Pyren-1-yl)-1-(pyridin-2-yl)butan-1-one (3kA)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3kA** as a white solid (61.8 mg, 88% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.69–8.63 (m, 1H), 8.38 (d, *J* = 9.2 Hz, 1H), 8.20–8.07 (m, 4H), 8.06–7.95 (m, 4H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.86–7.76 (m, 1H), 7.48–7.40 (m, 1H), 3.51–3.37 (m, 4H), 2.39–2.27 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.8, 153.5, 148.9, 136.8, 136.4, 131.4, 130.9, 129.9, 128.8, 127.5, 127.34, 127.27, 127.0, 126.6, 125.8, 125.1, 125.0, 124.8, 124.7, 123.5, 121.7, 37.4, 33.1, 26.0 (One peak is missing due to overlapping.); HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₅H₂₀NO 350.1539; Found 250.1535.



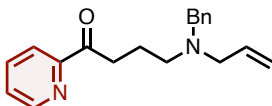
3-(3-Methyloxetan-3-yl)-1-(pyridin-2-yl)propan-1-one (3IA)

Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3IA** as a colorless liquid (40.6 mg, 99% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.72–8.65 (m, 1H), 8.05 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.85 (td, *J* = 8.0, 1.6 Hz, 1H), 7.53–7.45 (m, 1H), 4.50 (d, *J* = 5.6 Hz, 2H), 4.39 (d, *J* = 5.6 Hz, 2H), 3.26–3.17 (m, 2H), 2.14–2.05 (m, 2H), 1.37 (s, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.5, 153.1, 148.9, 136.9, 127.2, 121.8, 82.6, 38.9, 33.0, 32.8, 23.2; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₂H₁₆NO₂ 206.1176; Found 206.1184.



4-(Allyl(benzyl)amino)-1-(pyridin-2-yl)propan-1-one (3mA)

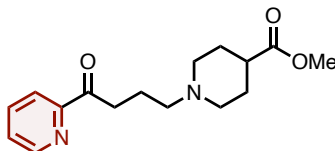
Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 9:1) afforded **3mA** as a brown liquid (27.9 mg, 50% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.63 (d, *J* = 4.4 Hz, 1H), 8.01 (d, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.44 (dd, *J* = 7.6, 4.4 Hz, 1H), 7.29–7.15 (m, 5H), 5.87–5.75 (m, 1H), 5.22–5.05 (m, 2H), 3.63 (s, 2H), 3.41 (t, *J* = 7.2 Hz, 2H), 3.11 (d, *J* = 6.4 Hz, 2H), 2.97 (t, *J* = 7.2 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.5, 153.4, 148.8, 139.4, 136.8, 135.8, 128.8, 128.1, 127.0, 126.7, 121.7, 117.3, 57.8, 56.5, 48.6, 35.4; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₈H₂₁N₂O 281.1648; Found 281.1659.



4-(Allyl(benzyl)amino)-1-(pyridin-2-yl)butan-1-one (3nA)

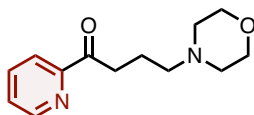
Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 9:1) afforded **3nA** as a colorless liquid (35.8 mg, 61% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.71–8.63 (m, 1H), 8.05–7.97 (m, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 7.50–7.40 (m, 1H), 7.34–7.13 (m, 5H), 5.91–5.79 (m, 1H), 5.21–5.07 (m, 2H), 3.57 (s, 2H), 3.23

(t, $J = 7.2$ Hz, 2H), 3.08 (d, $J = 6.4$ Hz, 2H), 2.57–2.47 (m, 2H), 2.00–1.88 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.8, 153.5, 148.8, 139.5, 136.8, 136.0, 128.9, 128.0, 126.9, 126.7, 121.7, 117.2, 57.9, 56.5, 52.6, 35.4, 21.4; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}$ 295.1810; Found 295.1807.



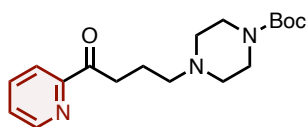
Methyl 1-(4-oxo-4-(pyridin-2-yl)butyl)piperidine-4-carboxylate (**3oA**)

Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3oA** as a brown solid (42.1 mg, 72% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.67 (d, $J = 4.8$ Hz, 1H), 8.05 (dt, $J = 8.0, 1.6$ Hz, 1H), 7.83 (td, $J = 7.6, 1.6$ Hz, 1H), 7.50–7.42 (m, 1H), 3.66 (s, 3H), 3.22 (t, $J = 7.2$ Hz, 2H), 2.89–2.80 (m, 2H), 2.41 (t, $J = 6.4$ Hz, 2H), 2.30–2.18 (m, 1H), 2.04–1.91 (m, 4H), 1.86–1.75 (m, 2H), 1.65–1.50 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.3, 175.6, 153.6, 148.8, 136.8, 126.8, 121.7, 58.0, 52.7, 51.5, 41.0, 35.4, 27.9, 21.8; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_3$ 291.1703; Found 291.1709.



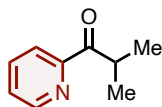
4-Morpholino-1-(pyridin-2-yl)butan-1-one (**3pA**)

Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3pA** as a colorless liquid (31.6 mg, 67% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.71–8.64 (m, 1H), 8.09–8.02 (m, 1H), 7.84 (td, $J = 7.6, 1.6$ Hz, 1H), 7.50–7.42 (m, 1H), 3.57 (t, $J = 4.8$ Hz, 4H), 3.24 (t, $J = 7.2$ Hz, 2H), 2.46–2.38 (m, 6H), 2.03–1.91 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.3, 153.6, 148.8, 136.8, 126.9, 121.7, 66.8, 58.2, 53.4, 35.3, 21.5; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_2$ 235.1441; Found 235.1443.



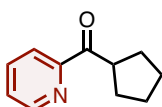
tert-Butyl 4-(4-oxo-4-(pyridin-2-yl)butyl)piperazine-1-carboxylate (**3qA**)

Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3qA** as a colorless liquid (33.2 mg, 50% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.71–8.64 (m, 1H), 8.05 (dt, $J = 8.0, 1.2$ Hz, 1H), 7.83 (td, $J = 7.6, 1.6$ Hz, 1H), 7.50–7.42 (m, 1H), 3.29 (t, $J = 5.2$ Hz, 4H), 3.24 (t, $J = 7.2$ Hz, 2H), 2.43 (t, $J = 7.2$ Hz, 2H), 2.40–2.33 (m, 4H), 2.07–1.92 (m, 2H), 1.44 (s, 9H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.2, 154.6, 153.6, 148.8, 136.8, 126.8, 121.6, 79.4, 57.7, 52.6, 35.2, 28.3, 21.6; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{28}\text{N}_3\text{O}_3$ 334.2125; Found 334.2134.



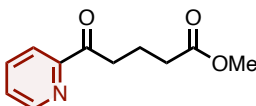
2-Methyl-1-(pyridin-2-yl)propan-1-one (3rA)

This reaction was performed at 80 °C using methyl picolinate (**3A**; 3.0 equiv) and NaH (3.0 equiv). Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3rA** as a colorless liquid (20.6 mg, 69% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.69 (d, *J* = 4.8 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.84 (td, *J* = 7.6, 1.6 Hz, 1H), 7.50–7.42 (m, 1H), 4.17–4.06 (m, 1H), 1.22 (d, *J* = 6.8 Hz, 6H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 205.8, 152.9, 148.9, 136.9, 126.8, 122.5, 34.2, 18.6; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₉H₁₂NO 150.0913; Found 150.0919.



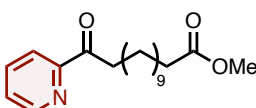
Cyclopentyl(pyridin-2-yl)methanone (3sA)

This reaction was performed at 80 °C using methyl picolinate (**3A**; 3.0 equiv) and NaH (3.0 equiv). Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3sA** as a colorless liquid (17.3 mg, 49% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.72–8.66 (m, 1H), 8.06 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H), 7.49–7.41 (m, 1H), 4.32–4.19 (m, 1H), 2.07–1.62 (m, 8H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 204.3, 153.5, 148.9, 136.8, 126.7, 122.3, 45.2, 29.7, 26.3; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₁H₁₄NO 176.1070; Found 176.1074.



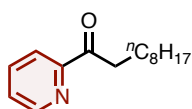
Methyl 5-oxo-5-(pyridin-2-yl)pentanoate (3tA)

This reaction was performed at room temperature using NaHMDS (1.0 equiv) instead of NaH. Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3tA** as a colorless liquid (21.8 mg, 53% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.67 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.04 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.84 (td, *J* = 7.6, 1.6 Hz, 1H), 7.51–7.44 (m, 1H), 3.68 (s, 3H), 3.30 (t, *J* = 7.2 Hz, 2H), 2.46 (t, *J* = 7.2 Hz, 2H), 2.14–2.02 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.1, 173.7, 153.2, 148.9, 136.9, 127.1, 121.7, 51.5, 36.8, 33.3, 19.1; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₁H₁₄NO₃ 208.0968; Found 208.0968.



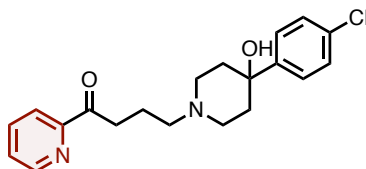
Methyl 14-oxo-14-(pyridin-2-yl)tetradecanoate (3uA)

This reaction was performed at room temperature using NaHMDS (1.0 equiv) instead of NaH. Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3uA** as a colorless liquid (29.1 mg, 46% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.68 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.50–7.42 (m, 1H), 3.67 (s, 3H), 3.21 (t, *J* = 7.6 Hz, 2H), 2.30 (t, *J* = 7.6 Hz, 2H), 1.79–1.63 (m, 2H), 1.67–1.56 (m, 2H), 1.42–1.24 (m, 14H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 207.8, 197.8, 152.5, 148.9, 137.0, 127.2, 122.3, 58.8, 39.5, 26.4, 25.7, 25.3, 24.4, 23.9, 23.8, 23.1, 22.8, 22.0 (One peak is missing due to overlapping.); HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₉H₃₀NO₃ 320.2220; Found 320.2223.



1-(Pyridin-2-yl)decan-1-one (3vA)

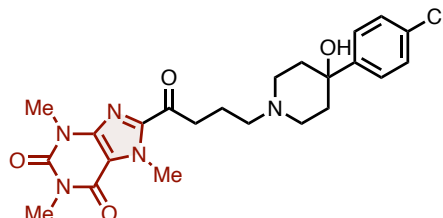
This reaction was performed at room temperature using NaHMDS (1.0 equiv) instead of NaH. Purification by Isolera[®] (hexane/EtOAc = 1:0 to 1:2) afforded **3vA** as a colorless liquid (35.8 mg, 77% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J* = 5.2 Hz, 1H), 8.04 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.50–7.42 (m, 1H), 3.21 (t, *J* = 7.2 Hz, 2H), 1.79–1.67 (m, 2H), 1.44–1.22 (m, 12H), 0.92–0.84 (m, 3H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 202.2, 153.6, 148.9, 136.8, 126.9, 121.8, 37.7, 31.9, 29.5, 29.33, 29.27, 24.0, 22.6, 14.1 (One peak is missing due to overlapping.); HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₅H₂₄NO 234.1852; Found 234.1857.



4-(4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl)-1-(pyridin-2-yl)butan-1-one (3xA)

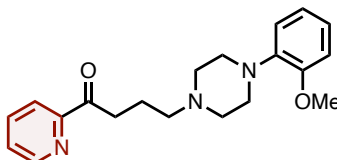
A 100-mL glass flask containing a magnetic stirring bar was dried with a heat gun in vacuo and filled with N₂ gas after cooling to room temperature. To this tube were added haloperidol (**1x**: 3.0 g, 7.98 mmol, 1.0 equiv), methyl picolinate (**2A**: 1.4 mL, 11.97 mmol, 1.5 equiv), and THF (40 mL), followed by the addition of NaHMDS (1M THF solution; 7.98 mL, 7.98 mmol, 1.0 equiv). The vessel was sealed with a screw cap and then stirred at room temperature for 6 h. The reaction was quenched with saturated NH₄Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. To this crude was added 6 M HCl (pH 1–4) and washed with Et₂O. To this solution was added 6 M NaOH (pH 8–10) and extracted three times with EtOAc. The combined organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. Recrystallization (CH₂Cl₂/hexane) afforded **3xA** as a white solid (3 g scale: 2.63 g, 92% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.72–8.65 (m, 1H), 8.07 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.83 (td, *J* = 7.6, 1.6 Hz, 1H), 7.50–7.42 (m,

1H), 7.41–7.33 (m, 2H), 7.33–7.24 (m, 2H), 3.24 (t, $J = 7.2$ Hz, 2H), 2.77 (d, $J = 11.2$ Hz, 2H), 2.49 (t, $J = 7.6$ Hz, 2H), 2.39 (t, $J = 12.0$ Hz, 2H), 2.07–1.95 (m, 2H), 1.89 (td, $J = 12.8, 4.4$ Hz, 2H), 1.68–1.58 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.3, 153.7, 148.9, 147.0, 136.8, 132.6, 128.3, 126.8, 126.1, 121.6, 70.9, 57.9, 49.1, 38.2, 35.4, 22.0; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{24}\text{ClN}_2\text{O}_2$ 359.1521; Found 359.1521.



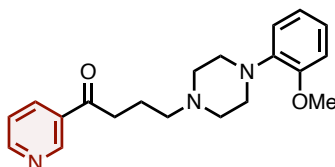
8-(4-(4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl)butanoyl)-1,3,7-trimethyl-3,7-dihydro-1H-purine-2,6-dione (3xAA)

2AA was used as heteroaromatic ester. Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3xAA** as a white solid (93.5 mg, 99% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.39–7.24 (m, 4H), 4.34 (s, 3H), 3.60 (s, 3H), 3.42 (s, 3H), 3.15 (t, $J = 7.2$ Hz, 2H), 2.76 (d, $J = 11.2$ Hz, 2H), 2.49 (t, $J = 7.2$ Hz, 2H), 2.43 (td, $J = 12.0, 2.4$ Hz, 2H), 2.06–1.95 (m, 2H), 1.86 (td, $J = 12.8, 4.4$ Hz, 2H), 1.70–1.61 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 193.3, 155.9, 151.5, 146.8, 146.5, 144.0, 132.8, 128.4, 125.9, 110.3, 70.9, 57.6, 49.0, 38.3, 38.1, 34.8, 29.7, 28.2, 22.3; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{23}\text{H}_{29}\text{ClN}_5\text{O}_4$ 474.1903; Found 474.1905.



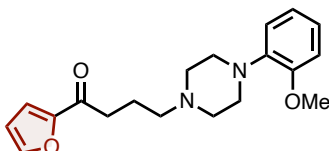
4-(4-(2-Methoxyphenyl)piperazin-1-yl)-1-(pyridin-2-yl)butan-1-one (3yA)

Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3yA** as a brown liquid (1.0 mmol scale: 312.4 mg, 95% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.68 (d, $J = 4.0$ Hz, 1H), 8.05 (d, $J = 8.4$ Hz, 1H), 7.82 (t, $J = 7.6$ Hz, 1H), 7.49–7.41 (m, 1H), 7.03–6.94 (m, 1H), 6.93–6.82 (m, 3H), 3.85 (s, 3H), 3.26 (t, $J = 7.2$ Hz, 2H), 2.97 (brs, 4H), 2.63 (brs, 4H), 2.50 (t, $J = 7.6$ Hz, 2H), 2.05–1.97 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.3, 153.6, 152.2, 148.8, 141.3, 136.7, 126.8, 122.7, 121.7, 120.9, 118.0, 111.0, 57.9, 55.2, 53.1, 50.4, 35.4, 21.8; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{26}\text{N}_3\text{O}_2$ 340.2020; Found 340.2025.



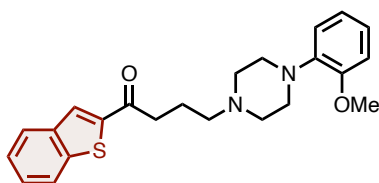
4-(4-(2-Methoxyphenyl)piperazin-1-yl)-1-(pyridin-3-yl)butan-1-one (3yB)

2B was used as heteroaromatic ester. Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 9:1) afforded **3yB** as a brown liquid (0.50 mmol scale: 114.5 mg, 68% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.21–9.19 (m, 1H), 8.77 (d, *J* = 4.8 Hz, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.42 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.01–6.81 (m, 4H), 3.85 (s, 3H), 3.09–2.95 (m, 6H), 2.63 (brs, 4H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.06–1.97 (m, 2H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 198.8, 153.3, 152.2, 149.7, 141.3, 135.4, 132.5, 123.6, 122.9, 120.9, 118.1, 111.1, 57.6, 55.3, 53.3, 50.5, 36.6, 21.5; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₀H₂₆N₃O₂ 340.2020; Found 340.2023.



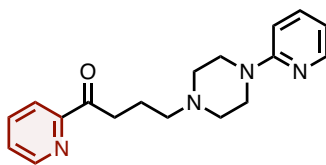
1-(Furan-2-yl)-4-(4-(2-methoxyphenyl)piperazin-1-yl)butan-1-one (3yS)

2S was used as heteroaromatic ester. Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 49:1) afforded **3yS** as a brown liquid (1.5 mmol scale: 452.6 mg, 92% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.60–7.54 (m, 1H), 7.18 (d, *J* = 3.6 Hz, 1H), 7.04–6.80 (m, 4H), 6.56–6.48 (m, 1H), 3.85 (s, 3H), 3.01 (brs, 4H), 2.87 (t, *J* = 7.2 Hz, 2H), 2.63 (brs, 4H), 2.47 (t, *J* = 7.2 Hz, 2H), 2.04–1.91 (m, 2H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 189.2, 152.9, 152.2, 146.0, 141.2, 122.8, 120.9, 118.1, 116.6, 112.1, 111.0, 57.7, 55.2, 53.1, 50.4, 36.2, 21.6; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₉H₂₅N₂O₃ 329.1860; Found 329.1867.



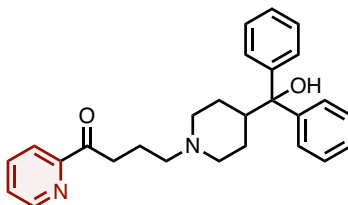
1-(Benzo[*b*]thiophen-2-yl)-4-(4-(2-methoxyphenyl)piperazin-1-yl)butan-1-one (3yU)

2U was used as heteroaromatic ester. Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 9:1) afforded **3yU** as a brown liquid (0.50 mmol scale: 161.4 mg, 82% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.99 (s, 1H), 7.87 (t, *J* = 7.6 Hz, 2H), 7.50–7.35 (m, 2H), 7.04–6.79 (m, 4H), 3.85 (s, 3H), 3.11–2.97 (m, 6H), 2.64 (brs, 4H), 2.50 (t, *J* = 7.0 Hz, 2H), 2.10–1.97 (m, 2H); ¹³C {¹H} NMR (101 MHz, CDCl₃) δ 194.5, 152.2, 144.2, 142.4, 141.3, 139.2, 128.7, 127.2, 125.8, 124.9, 123.0, 122.8, 120.9, 118.2, 111.1, 57.6, 55.3, 53.3, 50.5, 37.1, 22.1 HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₃H₂₇N₂O₂S 395.1788; Found 395.1789.



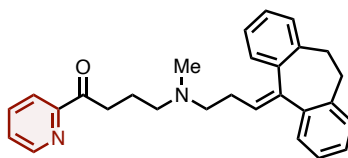
1-(Pyridin-2-yl)-4-(4-(pyridin-2-yl)piperazin-1-yl)butan-1-one (3zA)

Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 9:1) afforded **3zA** as a colorless liquid (57.7 mg, 92% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.68 (d, *J* = 4.8 Hz, 1H), 8.17 (d, *J* = 4.8 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H), 7.50–7.41 (m, 2H), 6.64–6.55 (m, 2H), 3.42 (t, *J* = 4.8 Hz, 4H), 3.27 (t, *J* = 7.2 Hz, 2H), 2.53 (t, *J* = 5.2 Hz, 4H), 2.48 (dd, *J* = 8.0, 6.4 Hz, 2H), 2.07–1.96 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.4, 159.5, 153.6, 148.8, 147.9, 137.3, 136.8, 126.9, 121.7, 113.1, 106.9, 57.9, 52.8, 44.9, 35.4, 21.7; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₁₈H₂₃N₄O 311.1866; Found 311.1861.



4-(4-(Hydroxydiphenylmethyl)piperidin-1-yl)-1-(pyridin-2-yl)butan-1-one (3aaA)

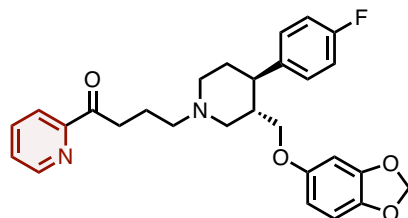
Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 9:1) afforded **3aaA** as a brown liquid (42.3 mg, 51% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.68–8.62 (m, 1H), 8.03 (dt, *J* = 8.0, 1.6 Hz, 1H), 7.82 (td, *J* = 8.0, 1.6 Hz, 1H), 7.49–7.40 (m, 4H), 7.32–7.24 (m, 4H), 7.21–7.12 (m, 2H), 3.20 (t, *J* = 7.2 Hz, 2H), 2.95 (d, *J* = 12.0 Hz, 2H), 2.46–2.33 (m, 3H), 2.05–1.85 (m, 4H), 1.47–1.23 (m, 4H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 201.2, 153.6, 148.8, 145.9, 136.8, 128.1, 126.9, 126.5, 125.8, 121.7, 79.4, 57.9, 53.7, 44.0, 35.5, 25.9, 21.7; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₇H₃₁N₂O₂ 415.2380; Found 415.2377.



4-((3-(10,11-Dihydro-5H-dibenzo[a,d][7]annulen-5-ylidene)propyl)(methyl)amino)-1-(pyridin-2-yl)butan-1-one (3abA)

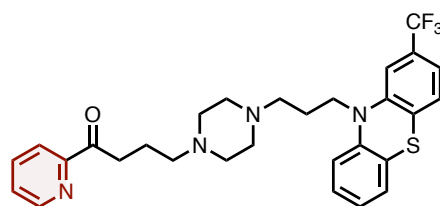
Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 9:1) afforded **3abA** as a colorless liquid (37.7 mg, 46% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.64 (d, *J* = 4.8 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.80 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.47–7.39 (m, 1H), 7.28–7.24 (m, 1H), 7.21–7.07 (m, 6H), 7.05–6.99 (m, 1H),

5.83 (td, $J = 7.2, 1.2$ Hz, 1H), 3.47–3.24 (m, 2H), 3.19 (t, $J = 7.2$ Hz, 2H), 2.95 (brs, 1H), 2.76 (brs, 1H), 2.48–2.35 (m, 4H), 2.29–2.18 (m, 2H), 2.13 (s, 3H), 1.94–1.82 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.6, 153.6, 148.8, 143.3, 141.3, 140.1, 139.3, 137.0, 136.8, 129.9, 129.5, 128.6, 128.2, 128.0, 127.3, 126.91, 126.85, 125.9, 125.7, 121.6, 57.1, 56.7, 41.6, 35.5, 33.7, 32.0, 27.1, 21.7; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{31}\text{N}_2\text{O}$ 411.2431; Found 411.2433.



4-((3*S*,4*R*)-3-((Benzo[*d*][1,3]dioxol-5-yloxy)methyl)-4-(4-fluorophenyl)piperidin-1-yl)-1-(pyridin-2-yl)butan-1-one (3acA)

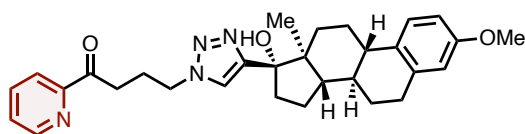
Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3acA** as a brown liquid (40.0 mg, 42% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.72–8.66 (m, 1H), 8.12–8.05 (m, 1H), 7.85 (tt, $J = 7.6, 1.6$ Hz, 1H), 7.50–7.42 (m, 1H), 7.13–7.05 (m, 2H), 6.95 (t, $J = 8.8$ Hz, 2H), 6.62 (d, $J = 8.4$ Hz, 1H), 6.33 (d, $J = 2.4$ Hz, 1H), 6.12 (dd, $J = 8.4, 2.4$ Hz, 1H), 5.87 (s, 2H), 3.56–3.48 (m, 1H), 3.40 (dd, $J = 9.2, 6.4$ Hz, 1H), 3.33–3.16 (m, 3H), 3.01 (d, $J = 11.2$ Hz, 1H), 2.56–2.45 (m, 2H), 2.45–2.35 (m, 1H), 2.10–1.92 (m, 5H), 1.77–1.60 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.3, 161.4 (d, $J_{\text{C-F}} = 244.2$ Hz), 154.4, 153.7, 148.9, 148.1, 141.4, 139.8 (d, $J_{\text{C-F}} = 3.2$ Hz), 136.8, 128.7 (d, $J_{\text{C-F}} = 7.8$ Hz), 126.8, 121.7, 115.3 (d, $J_{\text{C-F}} = 21.1$ Hz), 107.8, 105.5, 101.0, 97.9, 69.6, 58.2, 57.5, 53.8, 44.1, 41.8, 35.5, 34.1, 22.0; ^{19}F NMR (376 MHz, CDCl_3) δ -117.7; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{28}\text{H}_{30}\text{FN}_2\text{O}_4$ 477.2184; Found 477.2194; $[\alpha]_{\text{D}}^{23} = -35.00$ (c 0.0085, CHCl_3).



1-(Pyridin-2-yl)-4-(4-(3-(2-(trifluoromethyl)-10*H*-phenothiazin-10-yl)propyl)piperazin-1-yl)butan-1-one (3adA)

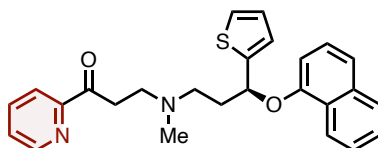
Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3adA** as a brown liquid (43.9 mg, 41% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.65 (d, $J = 4.8$ Hz, 1H), 8.01 (d, $J = 8.0$ Hz, 1H), 7.79 (td, $J = 8.0, 1.6$ Hz, 1H), 7.45–7.40 (m, 1H), 7.20–7.08 (m, 4H), 7.01 (s, 1H), 6.96–6.87 (m, 2H), 3.92 (t, $J = 6.8$ Hz, 2H), 3.20 (t, $J = 6.8$ Hz, 2H), 2.61–2.23 (m, 12H), 2.02–1.84 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.2, 153.6, 148.8, 145.7, 144.2, 136.8, 130.0, 129.5 (q, $J_{\text{C-F}} = 32.5$ Hz), 127.6, 127.5, 127.4, 126.9, 124.1, 123.8 (q, $J_{\text{C-F}} = 271.6$ Hz), 123.1, 122.8, 119.0 (q, $J_{\text{C-F}} = 3.6$ Hz), 115.9,

111.9 (q, $J_{\text{C-F}} = 3.8$ Hz), 57.6, 55.3, 52.6, 45.3, 35.3, 29.7, 23.9, 21.5; ^{19}F NMR (376 MHz, CDCl_3) δ – 62.6; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{29}\text{H}_{32}\text{F}_3\text{N}_4\text{OS}$; Found 541.2257.



4-((8*R*,9*S*,13*S*,14*S*,17*S*)-17-Hydroxy-3-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl)-1*H*-1,2,3-triazol-1-yl)-1-(pyridin-2-yl)butan-1-one (3aeA)

This reaction was performed at room temperature using NaHMDS (1.0 equiv) instead of NaH. Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3aeA** as a brown liquid (38.2 mg, 38% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.58 (d, $J = 4.8$ Hz, 1H), 7.99 (d, $J = 7.6$ Hz, 1H), 7.79 (td, $J = 7.6, 1.6$ Hz, 1H), 7.45 (s, 1H), 7.43–7.37 (m, 1H), 7.08 (d, $J = 8.4$ Hz, 1H), 6.66 (dd, $J = 8.4, 2.8$ Hz, 1H), 6.59 (d, $J = 2.8$ Hz, 1H), 4.49 (t, $J = 7.2$ Hz, 2H), 3.75 (s, 3H), 3.30–3.24 (m, 2H), 2.89–2.76 (m, 3H), 2.44–2.33 (m, 3H), 2.17–2.06 (m, 2H), 1.96–1.84 (m, 3H), 1.68–1.20 (m, 7H), 1.02 (s, 3H), 0.65 (td, $J = 12.8, 4.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 200.4, 157.4, 153.6, 152.8, 149.0, 137.9, 136.9, 132.6, 127.4, 126.3, 121.7, 121.2, 113.7, 111.4, 82.3, 55.2, 49.5, 48.5, 47.3, 43.3, 39.4, 37.8, 34.1, 32.9, 29.8, 27.3, 26.2, 24.4, 23.3, 14.2; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{30}\text{H}_{37}\text{N}_4\text{O}_3$ 501.2860; Found 501.2862; $[\alpha]_{\text{D}}^{23} = +14.00$ (c 0.0013, CHCl_3).

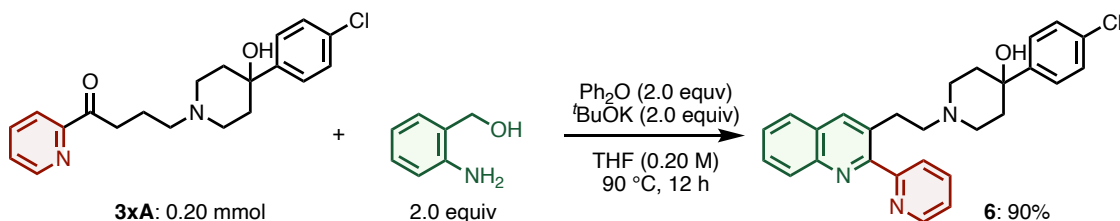


(*S*)-3-(Methyl(3-(naphthalen-1-yloxy)-3-(thiophen-2-yl)propyl)amino)-1-(pyridin-2-yl)propan-1-one (3faA)

This reaction was performed at room temperature using NaHMDS (1.0 equiv) instead of NaH. Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH} = 1:0$ to $9:1$) afforded **3faA** as a brown liquid (43.4 mg, 50% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.63–8.57 (m, 1H), 8.35–8.29 (m, 1H), 7.97 (d, $J = 8.4$ Hz, 1H), 7.78–7.71 (m, 2H), 7.49–7.42 (m, 2H), 7.41–7.32 (m, 2H), 7.25–7.15 (m, 2H), 7.06–6.99 (m, 1H), 6.91 (dd, $J = 5.2, 3.6$ Hz, 1H), 6.81 (d, $J = 7.6$ Hz, 1H), 5.72 (t, $J = 7.2$ Hz, 1H), 3.46–3.26 (m, 2H), 2.96–2.83 (m, 2H), 2.69–2.51 (m, 2H), 2.50–2.34 (m, 1H), 2.30 (s, 3H), 2.22–2.10 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 201.2, 153.4, 153.2, 148.9, 145.4, 136.8, 134.5, 127.4, 127.0, 126.5, 126.2, 126.1, 125.7, 125.1, 124.7, 124.6, 122.2, 121.7, 120.4, 74.4, 53.5, 52.4, 42.2, 36.6, 35.3; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{26}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ 431.1788; Found 431.1770; $[\alpha]_{\text{D}}^{23} = +23.33$ (c 0.0012, CHCl_3).

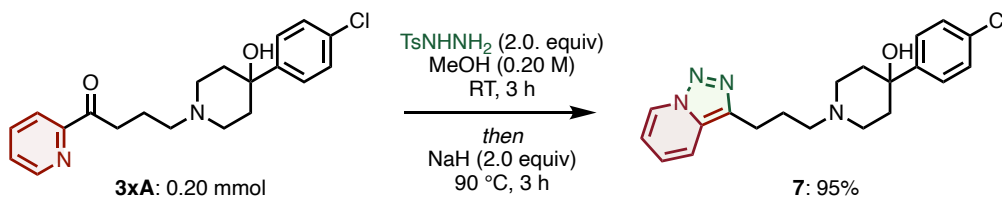
7. Synthetic applications

7-1. Friedlander quinoline synthesis for **6**^[22]



An 8-mL glass tube containing a magnetic stirring bar was added **3xA** (71.8 mg, 0.20 mmol, 1.0 equiv), (2-aminophenyl)methanol (49.3 mg, 0.40 mmol, 2.0 equiv), $t\text{BuOK}$ (44.9 mg, 0.40 mmol, 2.0 equiv), and Ph_2O (72.9 mg, 0.40 mmol, 2.0 equiv), and THF (1.0 mL). The vessel was sealed with a screw cap and then heated at 90 °C for 12 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH_4Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH}$ = 1:0 to 19:1) afforded 4-(4-chlorophenyl)-1-(2-(2-(pyridin-2-yl)quinolin-3-yl)ethyl)piperidin-4-ol (**6**) as a brown solid (80.1 mg, 90% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.71–8.63 (m, 1H), 8.15–8.05 (m, 2H), 7.91 (d, J = 8.0 Hz, 1H), 7.86 (tt, J = 7.6, 1.6 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.72–7.62 (m, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.44–7.35 (m, 2H), 7.34 (d, J = 7.2 Hz, 1H), 7.29–7.25 (m, 2H), 3.34–3.25 (m, 2H), 2.83–2.66 (m, 4H), 2.47 (t, J = 12.0 Hz, 2H), 2.10 (t, J = 12.8 Hz, 2H), 1.75–1.62 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 159.1, 157.7, 148.5, 146.9, 146.6, 137.7, 137.1, 132.9, 132.5, 129.5, 129.2, 128.5, 128.1, 127.1, 127.0, 126.2, 124.6, 123.3, 71.1, 59.8, 49.2, 38.4, 30.3; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{27}\text{ClN}_3\text{O}$ 444.1837; Found 444.1845.

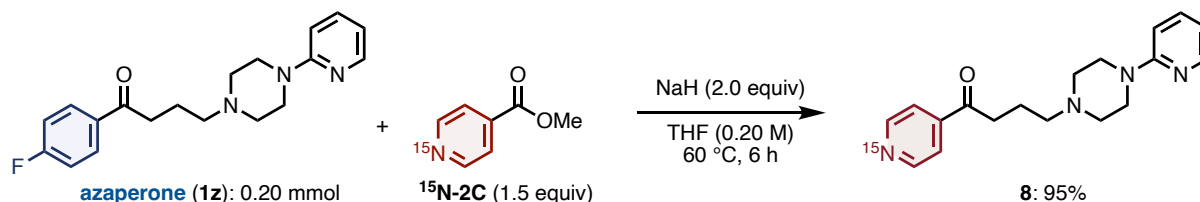
7-2. Synthesis of [1,2,3]triazolo[1,5-*a*]pyridine **7**



An 8-mL glass tube containing a magnetic stirring bar was added **3xA** (71.8 mg, 0.20 mmol, 1.0 equiv), TsNHNH_2 (74.5 mg, 0.40 mmol, 2.0 equiv) and MeOH (1.0 mL). The vessel was stirred at room temperature for 3 h. To this tube was added NaH (16 mg, 0.40 mmol, 2.0 equiv) and sealed with a screw cap and then heated at 90 °C for 3 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH_4Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH}$ = 1:0 to 19:1) afforded 1-(3-([1,2,3]triazolo[1,5-*a*]pyridin-3-yl)propyl)-4-(4-chlorophenyl)piperidin-4-ol (**7**) as a brown solid (70.2 mg, 95% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.65 (d, J = 6.8 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.17 (dd, J = 8.4, 6.8 Hz,

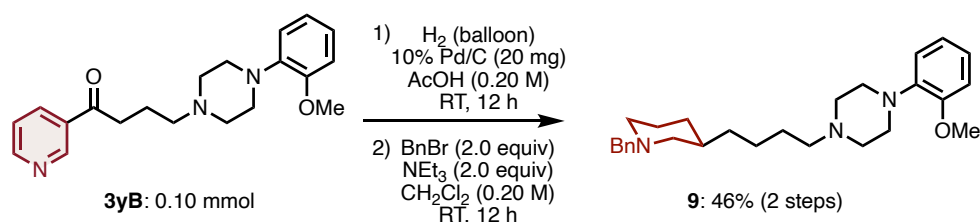
1H), 6.94 (t, J = 6.8 Hz, 1H), 3.05 (t, J = 7.6 Hz, 2H), 2.81 (d, J = 10.4 Hz, 2H), 2.56–2.38 (m, 4H), 2.19–1.98 (m, 4H), 1.72 (d, J = 13.6 Hz, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 146.9, 138.4, 132.7, 131.4, 128.4, 126.1, 125.2, 123.7, 117.6, 115.0, 71.0, 57.8, 49.4, 38.4, 26.7, 23.1; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{20}\text{H}_{24}\text{ClN}_4\text{O}$ 371.1633; Found 371.1629.

7-3. Swapping to ^{15}N -pyridine^[15]

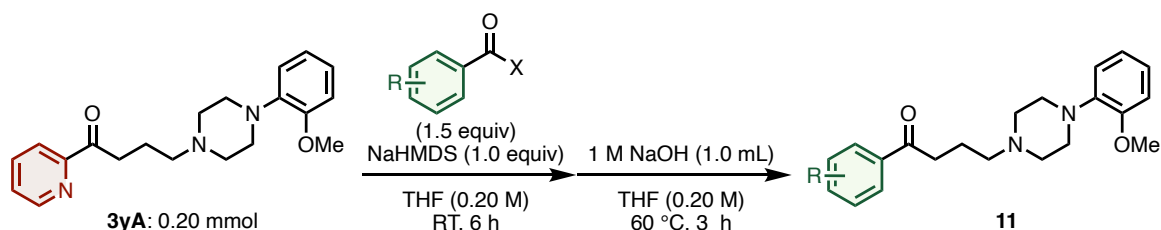


An 8-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N_2 gas after cooling to room temperature. To this tube were added azaperone (**1z**: 65.5 mg, 0.20 mmol, 1.0 equiv), methyl isonicotinate- ^{15}N (^{15}N -2C: 41.4 mg, 0.30 mmol, 1.5 equiv), and THF (1.0 mL), followed by the addition of NaH (16 mg, 0.40 mmol, 2.0 equiv). The vessel was sealed with a screw cap and then heated at 60 °C for 6 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH_4Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Purification by Isolera[®] ($\text{CHCl}_3/\text{MeOH}$ = 1:0 to 19:1) afforded 4-(4-(pyridin-2-yl- ^{15}N)piperazin-1-yl)-1-(pyridin-4-yl)butan-1-one (**8**) as a brown solid (70.2 mg, 95% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.91–8.72 (m, 2H), 8.18 (d, J = 5.2 Hz, 1H), 7.76 (d, J = 5.2 Hz, 2H), 7.47 (t, J = 8.4 Hz, 1H), 6.68–6.54 (m, 2H), 3.44 (t, J = 4.8 Hz, 4H), 3.03 (t, J = 6.8 Hz, 2H), 2.61–2.42 (m, 6H), 2.13–1.92 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 199.2, 159.4, 150.9, 147.9, 143.1, 137.4, 121.1, 113.3, 107.0, 57.5, 52.8, 44.9, 36.4, 21.2; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{23}\text{N}_3\text{O}^{15}\text{N}$ 312.1837; Found 312.1840.

7-4. Saturation of pyridine ring of **3yB**^[23]

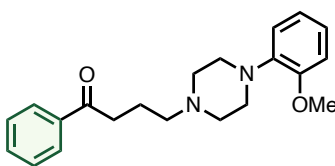


An 8-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N_2 gas after cooling to room temperature. To this tube were added **3yB** (33.9 mg, 0.10 mmol, 1.0 equiv), 10wt% Pd/C (20 mg, 2.0 μmol , 2.0 mol%), and AcOH (0.50 mL). The nitrogen in the reaction vessel was replaced with hydrogen from a balloon, and the reaction was conducted at balloon pressure. After stirring at room temperature for 12 h, the reaction mixture was filtered through pad of Celite[®]. To this was added saturated NaHCO_3 aq. and extracted three times with EtOAc. The combined organic



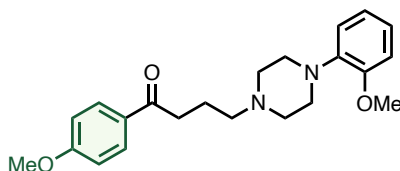
General procedure

An 8-mL glass tube containing a magnetic stirring bar was dried with a heat gun *in vacuo* and filled with N₂ gas after cooling to room temperature. To this tube were added **3yA** (67.9 mg, 0.20 mmol, 1.0 equiv) and THF (1.0 mL), followed by the addition of NaHMDS (1.0 M THF solution: 0.20 mL, 0.20 mmol, 1.0 equiv). After stirred at room temperature for 30 min, to this solution was added Acyl-X (0.30 mmol, 1.5 equiv). After stirred at room temperature for 6 h, to this was added 1M NaOH (1.0 mL, 1.0 mmol, 5.0 equiv). The vessel was heated at 60 °C for 3 h. After cooling the reaction mixture to room temperature, the reaction was quenched with saturated NH₄Cl aq. and extracted three times with EtOAc. The combined organic layer was dried over Na₂SO₄, filtered and concentrated *in vacuo*. Purification afforded the corresponding ketone **11**.



4-(4-(2-Methoxyphenyl)piperazin-1-yl)-1-phenylbutan-1-one (**11a**)

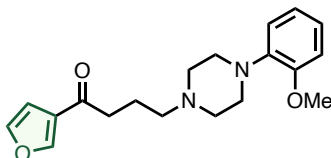
This reaction was performed using benzoyl cyanide (X = CN). Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) afforded 4-(4-(2-methoxyphenyl)piperazin-1-yl)-1-phenylbutan-1-one (**11a**) as a brown liquid (49.1 mg, 73% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.02–6.95 (m, 1H), 6.95–6.88 (m, 2H), 6.85 (d, *J* = 7.6 Hz, 1H), 3.85 (s, 3H), 3.09–2.99 (m, 6H), 2.65 (brs, 4H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.06–1.92 (m, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 200.0, 152.2, 141.3, 137.1, 132.8, 128.5, 128.0, 122.8, 120.9, 118.1, 111.1, 57.8, 55.3, 53.3, 50.5, 36.2, 21.6; HRMS (APCI) *m/z* [M+H]⁺ Calcd for C₂₁H₂₇N₂O₂ 339.2067; Found 339.2057.



1-(4-Methoxyphenyl)-4-(4-(2-methoxyphenyl)piperazin-1-yl)butan-1-one (**11b**)

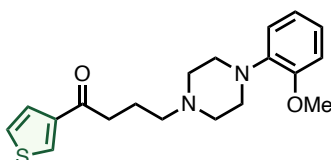
This reaction was performed using 4-methoxybenzoyl cyanide (X = CN). Purification by Isolera[®] (CHCl₃/MeOH = 1:0 to 19:1) afforded 4-(4-(2-methoxyphenyl)piperazin-1-yl)-1-phenylbutan-1-one

(**11b**) as a brown liquid (60.7 mg, 82% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.97 (d, J = 8.0 Hz, 2H), 7.01–6.90 (m, 5H), 6.85 (d, J = 8.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.05 (brs, 4H), 2.98 (t, J = 7.2 Hz, 2H), 2.66 (brs, 4H), 2.49 (t, J = 7.2 Hz, 2H), 2.01–1.94 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 198.7, 163.3, 152.2, 141.3, 130.3, 130.2, 122.8, 120.9, 118.1, 113.6, 111.1, 57.9, 55.4, 55.3, 53.3, 50.6, 36.0, 21.7; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{22}\text{H}_{29}\text{N}_2\text{O}_3$ 369.2173; Found 369.2181.



1-(Furan-3-yl)-4-(4-(2-methoxyphenyl)piperazin-1-yl)butan-1-one (**11c**)

This reaction was performed using (1*H*-benzo[*d*][1,2,3]triazol-1-yl)(furan-3-yl)methanone (X = Bt). Purification by PTLC ($\text{CHCl}_3/\text{MeOH}$ = 49:1) afforded 1-(furan-3-yl)-4-(4-(2-methoxyphenyl)piperazin-1-yl)butan-1-one (**11c**) as a yellow liquid (46.9 mg, 71% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.05–8.04 (m, 1H), 7.43–7.42 (m, 1H), 7.01–6.84 (m, 4H), 6.78–6.76 (m, 1H), 3.85 (s, 3H), 3.05 (brs, 4H), 2.80 (t, J = 7.2 Hz, 2H), 2.64 (brs, 4H), 2.46 (t, J = 6.8 Hz, 2H), 1.98–1.91 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 194.8, 152.2, 147.0, 144.0, 141.3, 127.8, 122.8, 120.9, 118.1, 111.1, 108.6, 57.6, 55.2, 53.2, 50.5, 38.1, 21.5; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{25}\text{N}_2\text{O}_3$ 329.1862; Found 329.1860.



4-(4-(2-Methoxyphenyl)piperazin-1-yl)-1-(thiophen-3-yl)butan-1-one (**11d**)

This reaction was performed using (1*H*-benzo[*d*][1,2,3]triazol-1-yl)(thiophen-3-yl)methanone (X = Bt). Purification by PTLC ($\text{CHCl}_3/\text{MeOH}$ = 49:1) afforded 4-(4-(2-methoxyphenyl)piperazin-1-yl)-1-(thiophen-3-yl)butan-1-one (**11d**) as a brown liquid (48.6 mg, 71% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.07 (d, J = 2.8 Hz, 1H), 7.56 (d, J = 4.8 Hz, 1H), 7.30 (dd, J = 4.8, 2.8 Hz, 1H), 7.01–6.84 (m, 4H), 3.85 (s, 3H), 3.05 (brs, 4H), 2.94 (t, J = 7.2 Hz, 2H), 2.65 (brs, 4H), 2.48 (t, J = 7.2 Hz, 2H), 2.01–1.93 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 194.4, 152.2, 142.5, 141.3, 131.6, 126.9, 126.2, 122.8, 120.9, 118.1, 111.1, 57.7, 55.3, 53.2, 50.5, 37.5, 21.6; HRMS (APCI) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{25}\text{N}_2\text{O}_2\text{S}$ 369.2181; Found 369.2173.

8. Computational Studies

8-1. Computational details

All structures were optimized using density functional theory (DFT) as implemented in Gaussian 16 Revision C.01.^[24] We chose the B3LYP functional^[25,26] with the 6-311+G(d,p)^[27,28,29] basis sets. Dispersion corrections are considered with the D3 version of Grimme's dispersion with Becke–Johnson damping (D3(BJ)).^[30,31] The character of the stationary point was confirmed by performing vibrational frequency analysis; all minimum and transition state structures have zero and one imaginary frequency, respectively. The connectivity of the stationary points was verified with intrinsic reaction coordinate^[32] calculations, followed by geometry optimizations. Thermodynamical corrections (i.e., ΔG) were computed at 333.15 K. The electrophilicity (ω) and nucleophilicity (N) indices (See Section X-2.) as well as stabilization energies of the CH₃ONa clusters were computed at this level of theory (i.e., B3LYP-D3(BJ)/6-311+G(d,p)). For odd-electron systems, unrestricted B3LYP calculations were performed. Solvent effects of tetrahydrofuran was considered using the conductor polarizable continuum model (C-PCM)^[33] without the non-electrostatic contribution.

Interaction energies of enolates (See Section X-3.) were also estimated at this level of theory, B3LYP-D3(BJ)/6-311+G(d,p). For the largest system (**5wA_{enol}**)₄, the vibrational frequency calculation could not be finished, so the thermodynamical correction with a smaller basis set, 6-31G(d), was used instead.

For energy refinement, we performed domain-based local pair natural orbital coupled-cluster singles and doubles with perturbative triples (DLPNO-CCSD(T))^[34,35] single point energy calculations, as implemented in ORCA 5.0.3.^[36] The basis set, as well as the corresponding auxiliary basis set,^[37,38] was def2-TZVPP^[39] for H, C, and Na and def2-TZVPPD^[40] for N and O, which are collectively referred to as def2-TZVPP(D). Solvent effects with C-PCM were also considered based on the perturbation-to-energy (PTE) scheme.^[41]

8-2. Electrophilicity (ω) and nucleophilicity (N) indices

The electrophilicity index (ω) was calculated with the following equation:^[42,43]

$$\omega = \frac{\mu^2}{2\eta}$$

In this study, the chemical potential (μ) was calculated as an average of the ionization potential (IP) and electron affinity (EA), and the chemical hardness (η) as the difference between IP and EA through a finite difference approximation. IP was determined as the difference between the total energy of the cationic (E_{N-1}) and neutral (E_N) states, whereas EA was the difference between the total energy of the anionic (E_{N+1}) and neutral states: IP = $E_{N-1} - E_N$ and EA = $E_{N+1} - E_N$.

The nucleophilicity index N ^[44,45] was calculated as the difference between the energy level of the higher occupied molecular (Kohn–Sham) orbital for the species considered (**X**) and tetracyanoethylene (TCE):

$$N = \varepsilon_{\text{HOMO}}(\text{X}) - \varepsilon_{\text{HOMO}}(\text{TCE})$$

At the theoretical level employed in this study ((U)-B3LYP-D3(BJ)/6-311+G(d,p)), $\varepsilon_{\text{HOMO}}(\text{TCE}) = -0.33550$ hartree.

	ω	N
enolate 1	(1.13)	4.56
ester 2	2.00	(1.58)
enolate 3	(1.14)	4.51
ester 4	1.80	(1.71)

Table S5. The electrophilicity ω and nucleophilicity N indices (unit in eV) computed at the B3LYP-D3(BJ)/6-311+G(d,p) level of theory

8-3. Reaction profiles

Enolization of **5wA** with $(\text{CH}_3\text{ONa})_1$

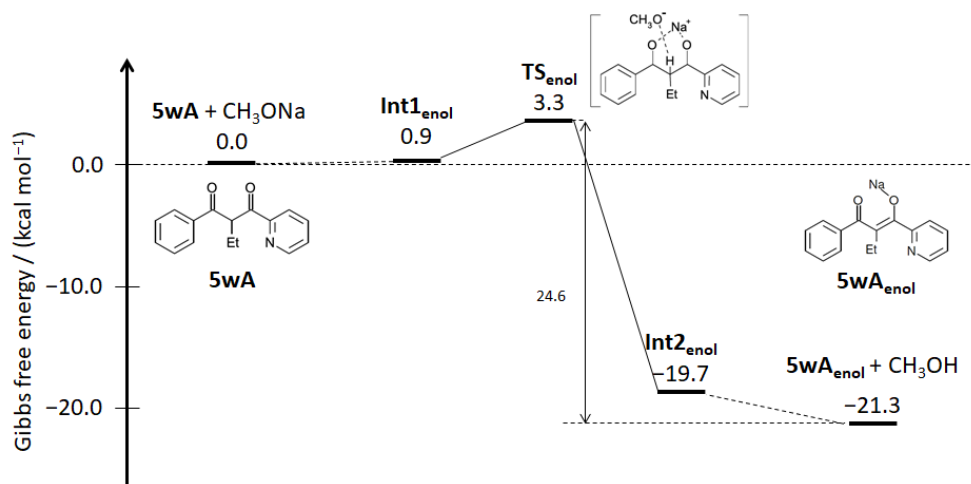


Figure S8. Enolization of **5wA** with $(\text{CH}_3\text{ONa})_1$ at the DLPNO-CCSD(T)/def2-TZVPP(D)//B3LYP-D3(BJ)/6-311+G(d,p) level of theory.

Formation of **1_{enol}** + **2** and **3_{enol}** + **4** from **5wA** with $(\text{CH}_3\text{ONa})_1$

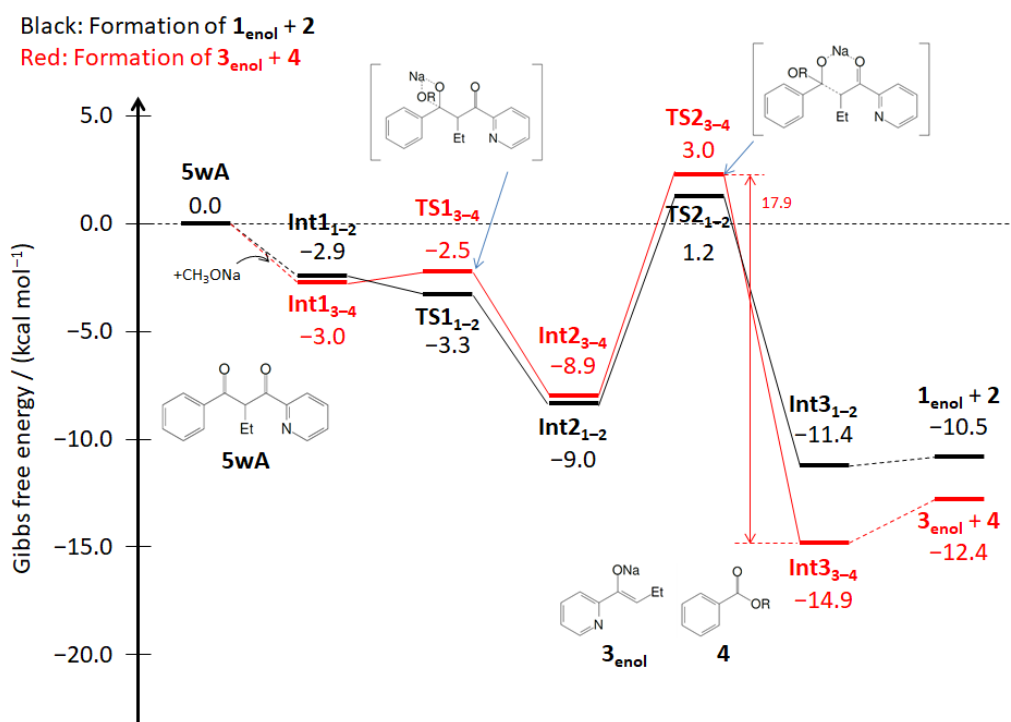


Figure S9. Formation of **1_{enol}** + **2** and **3_{enol}** + **4** from **5wA** with $(\text{CH}_3\text{ONa})_1$ at the DLPNO-CCSD(T)/def2-TZVPP(D)//B3LYP-D3(BJ)/6-311+G(d,p) level of theory.

Enolization of **5wA** with $(\text{CH}_3\text{ONa})_4$

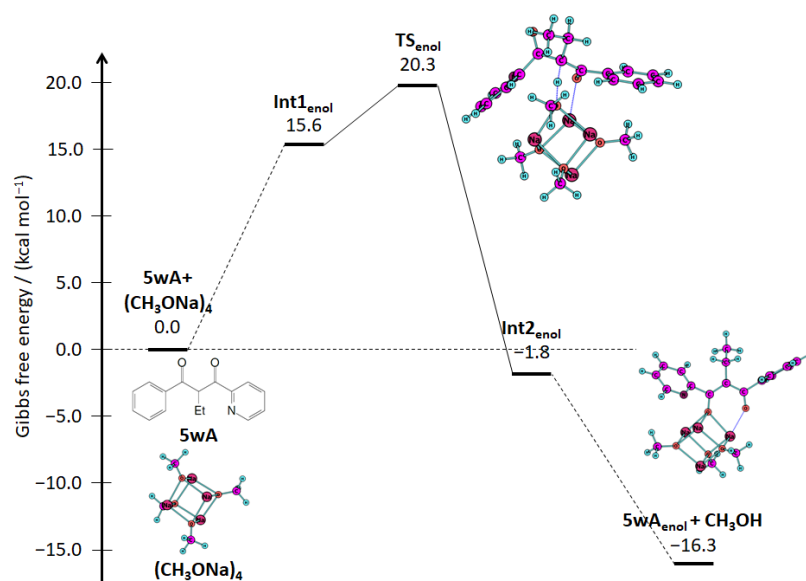


Figure S10. Enolization of **5wA** with $(\text{CH}_3\text{ONa})_4$ at the DLPNO-CCSD(T)/def2-TZVPP(D)//B3LYP-D3(BJ)/6-311+G(d,p) level of theory. The suffix that specifies the CH_3ONa cluster (e.g., “ $-(\text{CH}_3\text{ONa})_4$ ”) is omitted for brevity.

Formation of **1_{enol}** + **2** and **3_{enol}** + **4** from **5wA** with $(\text{CH}_3\text{ONa})_4$

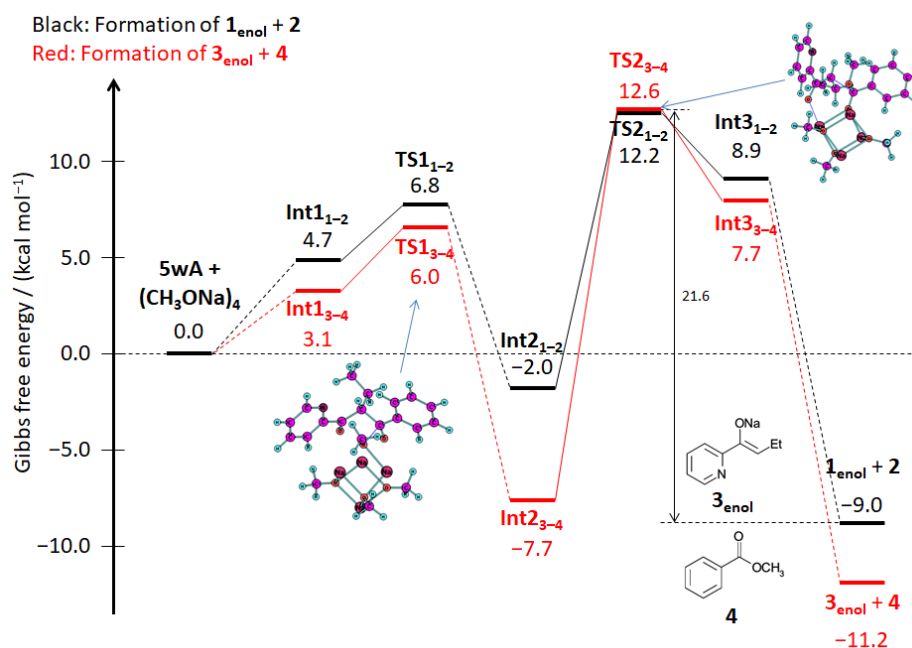


Figure S11. Formation of **1_{enol}** + **2** and **3_{enol}** + **4** from **5wA** with $(\text{CH}_3\text{ONa})_4$ at the DLPNO-CCSD(T)/def2-TZVPP(D)//B3LYP-D3(BJ)/6-311+G(d,p) level of theory. The suffix that specifies the CH_3ONa cluster (e.g., “ $-(\text{CH}_3\text{ONa})_4$ ”) is omitted for brevity.

Formation of **1** + **2**_{ONa} and **3** + **4**_{ONa} from **5wA** and NaOH

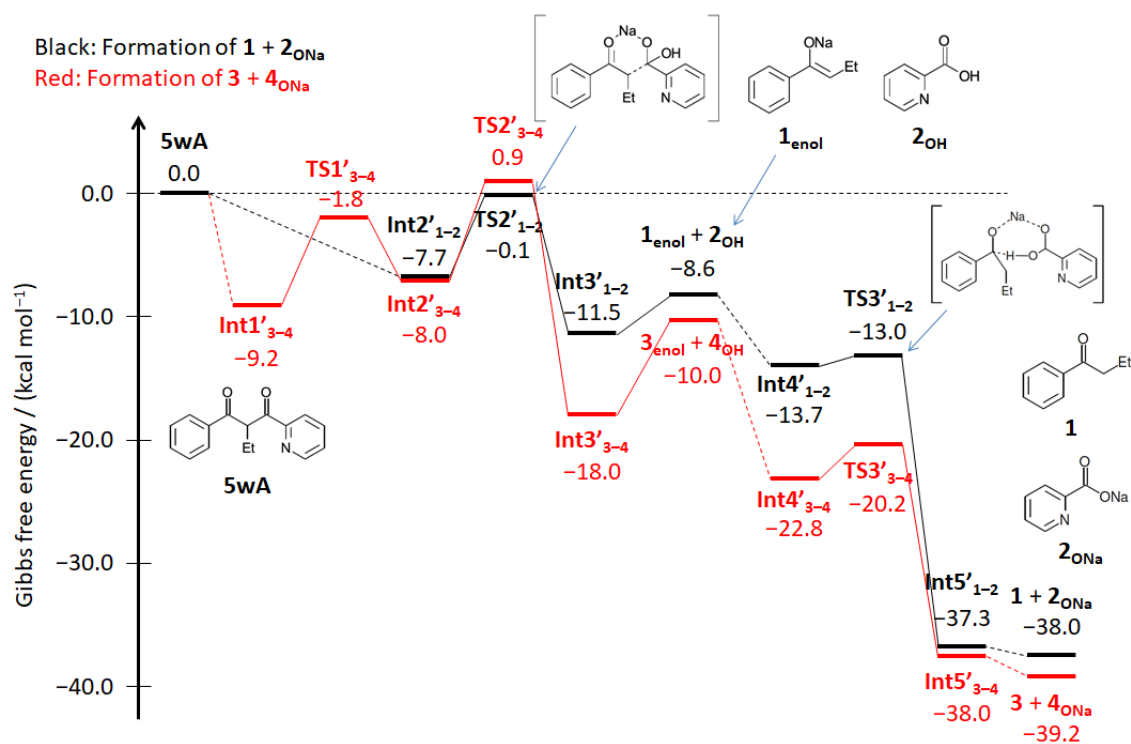


Figure S12. Formation of **1** + **2**_{ONa} and **3** + **4**_{ONa} from **5wA** with NaOH at the DLPNO-CCSD(T)/def2-TZVPP(D)//B3LYP-D3(BJ)/6-311+G(d,p) level of theory.

8-4. Interaction and relative energies of enolates

	$\Delta_{\text{cluster}}E$	$\Delta_{\text{cluster}}G$	$\Delta_{\text{cluster}}G$ per enolate
(1 _{enol})	0.0	0.0	0.0
(1 _{enol}) ₂	−26.2	−8.3	−4.1
(1 _{enol}) ₄	−93.8	−36.6	−9.1
(3 _{enol})	0.0	0.0	0.0
(3 _{enol}) ₂	−24.8	−11.1	−5.5
(3 _{enol}) ₄	−93.9	−44.5	−11.1
(5wA _{enol})	0.0	0.0	0.0
(5wA _{enol}) ₂	−21.3	−6.6	−3.3
(5wA _{enol}) ₄	−83.0	−22.5 ^a	−5.6 ^a

Table S6. Interaction energies of enolates (in kcal mol^{−1}) at the B3LYP-D3(BJ)/6-311+G(d,p) level of theory

^aThermodynamical corrections were computed with a small basis set, 6-31G(d), due to the large computational cost ($N_{\text{basis}} = 2,128$ with the 6-311+G(d,p) basis set).

	ΔG	$\Delta_{\text{cluster}}G$ per enolate	Estimated ΔG
1 _{enol} + 2	−10.7	0.0	−10.7
(1 _{enol}) ₂ + 2	−10.7	−4.1	−14.9
(1 _{enol}) ₄ + 2	−10.7	−9.1	−19.9
(3 _{enol}) + 4	−13.4	0.0	−13.4
(3 _{enol}) ₂ + 4	−13.4	−5.5	−18.9
(3 _{enol}) ₄ + 4	−13.4	−11.1	−24.5
(5wA _{enol})	−18.5	0.0	−18.5
(5wA _{enol}) ₂	−18.5	−3.3	−21.9
(5wA _{enol}) ₄	−18.5	−5.6 ^a	−24.1 ^a

Table S7. Estimated relative energies of products (relative to **5wA**; in kcal mol^{−1}) at the B3LYP-D3(BJ)/6-311+G(d,p) level of theory

^aThermodynamical corrections were computed with a small basis set, 6-31G(d), due to the large computational cost ($N_{\text{basis}} = 2,128$ with the 6-311+G(d,p) basis set).

8-5. Optimized geometries

Optimized geometries in Cartesian coordinates (Å) and energies (hartrees) for stationary points.

8-5-1. Reactants/products

CH₃ONa

6

E(RB3LYP) = -277.525500202

C -0.03620200 -0.06769000 0.23227800

H -1.05846700 -0.26631700 0.62464300

H 0.49182200 -1.04541200 0.29261000

H 0.44994400 0.57187100 1.00223200

O -0.02809800 0.48543500 -1.02852700

Na -0.01567900 1.23561500 -2.96781200

CH₃OH

6

E(RB3LYP) = -115.773256658

C -0.00297700 0.02573500 0.03715600

H -1.05585400 0.05952100 0.33654300

H 0.43342800 -0.90592700 0.39695500

H 0.52825700 0.86447500 0.49940700

O 0.14211900 0.02806400 -1.38603100

H -0.24165200 0.84163200 -1.72860500

1

23

E(RB3LYP) = -463.695522387

C 1.06865800 1.75173300 -2.31490100

C 1.84449500 0.93692100 -1.47828600

C 0.67053500 3.01450200 -1.85602600

C 2.21732200 1.37457700 -0.21359100

C 1.03889100 3.45046300 -0.58567700

C 1.81362700 2.63345400 0.23602600

H 2.14780200 -0.03769200 -1.83877900

H 0.06867500 3.66163900 -2.48005100

H 2.82073400 0.73871600 0.42336400

H 0.72238600 4.42680200 -0.23864900

H 2.10249900 2.97538700 1.22303100

C 0.68805000 1.23232700 -3.66734200

O 0.97300300 0.08927800 -3.99040700

C -0.07754800 2.14795000 -4.60786300

H 0.40063600 3.13281200 -4.61539100

C -0.21715800 1.61397900 -6.03352700

H -0.59348600 0.58835300 -5.99862900

H -0.97508500 2.21174500 -6.54877700

C 1.09288300 1.66144100 -6.82440500

H 1.46760100 2.68747500 -6.89604500

H 1.86419800 1.05285500 -6.34746400

H 0.95078600 1.28665300 -7.84140800

H -1.06621100 2.30399500 -4.15805100

1_{enol}

23

E(RB3LYP) = -625.450969412

C 1.18958600 1.76655900 -2.31351000

C 1.60887300 0.87246900 -1.31756800

C 1.05267100 3.11882100 -1.95866100

C 1.85225200 1.30099800 -0.01337800

C 1.30112600 3.55220000 -0.65914100

C 1.69867700 2.64461500 0.32536200

H 1.73888200 -0.16687100 -1.59104400

H 0.76474700 3.84468100 -2.70910000

H 2.16591400 0.58508200 0.73905700

H 1.19365500 4.60358700 -0.41492600

H 1.89382400 2.98316200 1.33659000
 C 0.92997700 1.23912500 -3.70175000
 O 1.45990000 0.07823800 -3.97827900
 C 0.14425600 1.95728000 -4.56332400
 H -0.27692900 2.90263100 -4.24315100
 C -0.17298600 1.49239200 -5.95694900
 H -0.23909400 0.39725200 -5.97049500
 H -1.16083500 1.86179600 -6.25769800
 C 0.85336600 1.93648500 -7.01781600
 H 0.90064400 3.02795500 -7.07767800
 H 1.85525000 1.57989900 -6.76136400
 H 0.59859100 1.55455300 -8.01327200
 Na 2.08924400 -1.27291600 -5.50797600

2

17

E(RB3LYP) = -476.331339361
 C -1.88544100 0.04840700 -2.24908000
 C -1.22285100 -0.78737900 -1.34931500
 N -2.35166800 1.26023000 -1.92123700
 C -1.03533900 -0.34199200 -0.04507400
 C -2.16553600 1.67546900 -0.66711500
 C -1.51567400 0.91480200 0.30563100
 H -0.87039200 -1.75547200 -1.67675700
 H -0.52534000 -0.96376900 0.68019300
 H -2.55212000 2.66022400 -0.42549400
 H -1.39383000 1.30464700 1.30815900
 C -2.08210600 -0.44275900 -3.65451700
 O -1.69596400 -1.53001800 -4.03425400
 C -2.94019200 0.02069200 -5.80089200
 H -3.54512900 -0.88537500 -5.82689300
 H -1.98792500 -0.15814900 -6.29980600
 O -2.71785200 0.43295700 -4.43509700
 H -3.46794000 0.84799600 -6.26715500

2_{OH}

14

E(RB3LYP) = -437.018032900
 C -1.89069200 0.05492400 -2.25690200
 C -1.22776000 -0.78570400 -1.36215900
 N -2.35568800 1.26639300 -1.92605000
 C -1.03828500 -0.34397700 -0.05689800
 C -2.16771000 1.67777000 -0.67140600
 C -1.51697100 0.91240400 0.29761200
 H -0.87685800 -1.75323900 -1.69335500
 H -0.52805100 -0.96805900 0.66628200
 H -2.55255200 2.66217600 -0.42543200
 H -1.39312900 1.29889400 1.30130400
 C -2.09193500 -0.42459900 -3.66186800
 O -1.71243600 -1.50639000 -4.05859800
 H -2.81297800 0.05441500 -5.32661400
 O -2.73322900 0.45492900 -4.44656100

2_{ONa}

14

E(RB3LYP) = -598.816570033
 C -1.93077400 0.19103800 -2.20240000
 C -1.35290400 -0.74072400 -1.33467400
 N -2.24328100 1.43517100 -1.81246700
 C -1.08868600 -0.37026100 -0.02059100
 C -1.98801600 1.78037600 -0.54716800
 C -1.41312300 0.92018600 0.38675300
 H -1.12352000 -1.73007800 -1.70462200
 H -0.63958900 -1.07331200 0.67125600
 H -2.25483900 2.79436500 -0.26329600
 H -1.22844300 1.25750800 1.39916900
 C -2.22161300 -0.20716500 -3.64801800
 O -1.95412600 -1.39866400 -3.97721100

Na -2.75261100 -0.91433800 -6.14246300

O -2.70675100 0.65583400 -4.42491300

3

22

E(RB3LYP) = -479.736213680

C -0.99498100 2.06629800 -3.94598200

H -1.96910500 2.55695900 -3.86670800

C -0.42222300 2.17879000 -5.35800500

H 0.49791600 1.59172300 -5.42457000

H -0.14305200 3.22252600 -5.53100700

C -1.40534400 1.72902700 -6.44241900

H -1.68477800 0.68093100 -6.31303400

H -2.32055400 2.32858700 -6.41067100

H -0.96876000 1.83864300 -7.43861000

C -1.89299900 0.43036500 -2.15714700

C -2.01321700 -0.86115900 -1.63912600

N -2.42854700 1.50744300 -1.56288500

C -2.72013200 -1.04219000 -0.45605100

C -3.10310700 1.32261200 -0.42651400

C -3.27753600 0.07139500 0.16523900

H -1.55714900 -1.68923400 -2.16436000

H -2.83381200 -2.03039400 -0.02703200

H -3.52515800 2.21048200 0.03360600

H -3.83677900 -0.01991600 1.08785800

C -1.12758900 0.64809900 -3.43795300

O -0.62177900 -0.30372300 -4.00852600

H -0.36068200 2.59095100 -3.22023000

3_{enol}

22

E(RB3LYP) = -641.494866711

C -1.11061200 1.84526700 -4.02956100

H -1.59776100 2.66962100 -3.52522600

C -0.41653700 2.10477200 -5.33531800

H 0.44444400 1.43217300 -5.43397400

H -0.01267800 3.12427400 -5.34792800

C -1.32421900 1.92711400 -6.56868700

H -1.74235200 0.91667600 -6.59838200

H -2.16363400 2.62794500 -6.53555000

H -0.77663500 2.09945700 -7.50232000

C -1.90698200 0.44168900 -2.15024200

C -1.98364500 -0.83341300 -1.56834900

N -2.47185500 1.51301100 -1.55666700

C -2.64914100 -0.99950500 -0.35951400

C -3.10865000 1.34032200 -0.39754100

C -3.22951600 0.11022800 0.24887800

H -1.51688800 -1.66082200 -2.08344800

H -2.71512400 -1.97907200 0.10144800

H -3.54828700 2.23138000 0.04365900

H -3.75892300 0.03351800 1.19051500

C -1.18136100 0.60429300 -3.46124300

O -0.66011600 -0.48645900 -3.95832400

Na 0.10927800 -1.45500500 -5.69913300

4

18

E(RB3LYP) = -460.294534720

C 1.42243600 1.55307800 -1.44205300

C 1.09423700 0.31946100 -0.86869300

C 1.11468700 2.73892600 -0.76460300

C 0.46394500 0.27137100 0.36984400

C 0.48408600 2.68657000 0.47482500

C 0.15819600 1.45490500 1.04293100

H 1.33791200 -0.58990700 -1.40283200

H 1.36923800 3.69141000 -1.20887800

H 0.21111000 -0.68544500 0.81056500

H 0.24685900 3.60537300 0.99754700

H -0.33299700 1.41727000 2.00820900
C 2.09542500 1.55496700 -2.76894500
O 2.38588000 0.55343000 -3.39243100
C 3.00658300 2.89206100 -4.49805000
H 2.38970400 2.43427300 -5.27145300
H 3.97841500 2.39942700 -4.46469000
O 2.35358800 2.79560400 -3.21603600
H 3.12369400 3.95668400 -4.68237800

4_{OH}

15

E(RB3LYP) = -420.981318838
C 1.42499000 1.56475400 -1.44720100
C 1.10020600 0.32721500 -0.87945900
C 1.11501200 2.74820900 -0.76619400
C 0.47051500 0.27357000 0.35853700
C 0.48460300 2.68949800 0.47286800
C 0.16220000 1.45453200 1.03553600
H 1.34600900 -0.57943300 -1.41713700
H 1.36670700 3.70358800 -1.20598600
H 0.21989100 -0.68507900 0.79624700
H 0.24489600 3.60540100 0.99926400
H -0.32882800 1.41199700 2.00064200
C 2.09575800 1.57633000 -2.77047400
O 2.38910900 0.58534500 -3.40721200
H 2.79529100 2.73696000 -4.08435700
O 2.36090800 2.82197500 -3.22186000

4_{ONa}

15

E(RB3LYP) = -582.778618294
C 1.41208500 1.66496100 -1.36461900
C 1.18261200 0.40121000 -0.81094500
C 0.94453900 2.79777300 -0.69063600

C 0.49738900 0.27107600 0.39503700
C 0.25969300 2.67081100 0.51592300
C 0.03435600 1.40632300 1.06141000
H 1.54759500 -0.47078000 -1.33846400
H 1.12624700 3.77228300 -1.12540900
H 0.32416500 -0.71294200 0.81588100
H -0.09833900 3.55508400 1.03097300
H -0.49865000 1.30628600 2.00012200
C 2.15703100 1.80475400 -2.67574400
O 2.56753400 0.75028200 -3.24119900
Na 3.45986600 2.04927600 -4.96894200
O 2.33114400 2.96846400 -3.14017400

5_{wA}

34

E(RB3LYP) = -824.240991168
C 1.71037000 2.96390200 -4.28329800
C 3.09961700 3.14438600 -4.34479400
C 0.97393200 3.64424200 -3.30433800
C 3.74098800 3.98218700 -3.44182100
C 1.61832700 4.49071500 -2.40536600
C 3.00017200 4.65850000 -2.46975200
H 3.66083600 2.61347000 -5.10302100
H -0.10048700 3.53305100 -3.24223100
H 4.81590400 4.10920300 -3.49076100
H 1.04053400 5.01873900 -1.65626600
H 3.50010100 5.31381000 -1.76610400
C 1.06943200 2.04248500 -5.26902900
O 1.68315300 1.64003000 -6.24135500
C -0.37297600 1.60292300 -5.01012000
H -0.99006500 2.48859000 -4.85309000
C -0.94852200 0.78669500 -6.18195400
H -0.34247000 -0.11263500 -6.31282600
H -0.82774200 1.38107500 -7.09047600

C -2.42085000 0.41760900 -5.99086500
 H -2.56799700 -0.24061800 -5.12988700
 H -3.03615800 1.30790700 -5.83605700
 H -2.79884100 -0.10539400 -6.87235600
 C -1.43853000 1.09060200 -2.68734800
 C -1.59963500 0.23621900 -1.59479900
 N -2.16536300 2.20465100 -2.85747100
 C -2.56023700 0.55246700 -0.64106300
 C -3.08156600 2.50142700 -1.93548000
 C -3.31732800 1.70746700 -0.81250600
 H -0.98279400 -0.64829800 -1.51362600
 H -2.71523500 -0.08827400 0.21833600
 H -3.65158200 3.41058100 -2.09640800
 H -4.07554500 1.99429800 -0.09493000
 C -0.41347100 0.76117300 -3.73485200
 O 0.33904900 -0.18487700 -3.58883200

5wA_{enol}

34

E(RB3LYP) = -986.024722953
 C 1.93622000 1.53780400 -0.55489600
 C 2.16904100 1.60628600 -1.93089500
 C 2.28120800 2.62822600 0.24860500
 C 2.72342300 2.75247500 -2.49821700
 C 2.84955400 3.76944400 -0.31480800
 C 3.06668700 3.83692700 -1.69105000
 H 1.91045800 0.76066300 -2.55832100

8-5-2. Enolization of 5wA with (CH₃ONa)₁

Int1_{enol}

40

E(RB3LYP) = -1101.77869971
 C 1.70341900 1.27177900 -0.35152900
 C 2.89443200 1.54825500 -1.03514900

H 2.10430700 2.58187500 1.31757900
 H 2.88911000 2.79815400 -3.56865700
 H 3.11906800 4.60640700 0.31937000
 H 3.50138500 4.72710700 -2.13073500
 C 1.39804400 0.26224300 0.05464500
 O 2.21548400 -0.69814700 0.07075400
 C 0.06049000 0.24767100 0.54151700
 C -0.84130400 1.45237000 0.30172700
 H -1.60928700 1.49744400 1.07548600
 H -0.26999900 2.37589700 0.40451300
 C -1.52039400 1.44604500 -1.07634200
 H -0.77517800 1.44430100 -1.87640800
 H -2.14432400 0.55636000 -1.19919800
 H -2.15709100 2.32688900 -1.20857500
 C -1.92226500 -0.84717200 1.64986100
 C -2.94456300 -1.39345900 0.87023300
 N -2.13824100 -0.32680400 2.86627300
 C -4.24327700 -1.38664000 1.36573900
 C -3.39267800 -0.33506100 3.33639000
 C -4.47644800 -0.84498600 2.62793500
 H -2.71889700 -1.80943600 -0.10381900
 H -5.05842400 -1.79496000 0.77968300
 H -3.53517600 0.09072800 4.32514000
 H -5.47090900 -0.81700300 3.05534300
 C -0.48265900 -0.90071500 1.16936400
 O 0.08388300 -2.00628500 1.39221500
 Na 2.12305900 -2.76117700 0.90106500

C 1.10152900 2.26703300 0.42663000
 C 3.46260600 2.81552200 -0.96430700
 C 1.69093100 3.52568000 0.51778100
 C 2.86265700 3.80575200 -0.18449500
 H 3.35656600 0.76910000 -1.62877000

H 0.20198100 2.03549300 0.98199700
 H 4.37300000 3.03095300 -1.51108000
 H 1.23417400 4.28898500 1.13686000
 H 3.30988000 4.79101700 -0.12232300
 C 1.15035300 -0.11069000 -0.42368500
 O 1.90850900 -1.07106600 -0.32107500
 C -0.32882100 -0.36160900 -0.70556900
 H -0.24673600 -1.06863400 -1.58360100
 C -1.20316700 0.82115000 -1.14588600
 H -1.40475600 1.50717800 -0.32622000
 H -0.64552900 1.38044100 -1.90159800
 C -2.52463300 0.33758900 -1.75095000
 H -2.34668100 -0.34328900 -2.58704400
 H -3.13389700 -0.19315600 -1.01260300
 H -3.11442000 1.18191700 -2.11617400
 C -1.74141000 -0.68746700 1.48252700
 C -2.74271200 -1.47102000 2.05954000
 N -1.45653400 0.55631200 1.89213500
 C -3.49095400 -0.92942800 3.09876000
 C -2.16206000 1.05546100 2.90891300
 C -3.19369500 0.35785000 3.53662100
 H -2.92116400 -2.47229400 1.69127800
 H -4.28637400 -1.50122200 3.56090200
 H -1.89765300 2.05728800 3.23203500
 H -3.74627000 0.81787500 4.34599900
 C -0.89454700 -1.25714600 0.38263500
 O -0.65201600 -2.45784600 0.38901000
 O 0.25547500 -2.17393300 -2.91598300
 C 0.92757200 -1.24393400 -3.68452300
 H 1.01368400 -0.24722800 -3.18965200
 H 1.97342600 -1.53303400 -3.92243200
 H 0.43886100 -1.03975600 -4.65913600
 Na 1.07560200 -3.20769800 -1.14762900

TS_{enol}

40

E(RB3LYP) = -1101.77787517

C 1.74603700 2.65782400 -4.14104900
 C 2.86648700 2.98518900 -4.91264700
 C 1.19597900 3.61012400 -3.27581000
 C 3.41615400 4.26156300 -4.84103000
 C 1.76769500 4.87702100 -3.18458500
 C 2.86931100 5.20832700 -3.97342400
 H 3.29234100 2.23822200 -5.57168700
 H 0.34248100 3.34429700 -2.66352400
 H 4.27202100 4.51708200 -5.45476900
 H 1.35179000 5.60704000 -2.49989000
 H 3.30285100 6.19969900 -3.91067900
 C 1.20586700 1.26428300 -4.18981700
 O 1.99588900 0.31896700 -4.12538100
 C -0.26961100 1.03478700 -4.34635700
 H -0.24760900 0.23904600 -5.27201600
 C -1.14957100 2.21580400 -4.78076700
 H -1.35061700 2.90893900 -3.96534600
 H -0.59741100 2.77537000 -5.54040700
 C -2.47510400 1.74022700 -5.38620400
 H -2.29968000 1.06083000 -6.22364600
 H -3.08575400 1.20942800 -4.64968700
 H -3.06148000 2.58965600 -5.74647000
 C -1.77744200 0.67496200 -2.25190800
 C -2.81639600 -0.14894000 -1.81525500
 N -1.57703000 1.91359100 -1.78076900
 C -3.69934000 0.34514800 -0.86164800
 C -2.41438900 2.36641700 -0.84378600
 C -3.49408800 1.62800200 -0.36175700
 H -2.92054900 -1.14536000 -2.22364100
 H -4.52730400 -0.25949500 -0.51173700
 H -2.21794800 3.36481700 -0.46591600

H -4.15257700 2.05226400 0.38561900
 C -0.77911700 0.15245000 -3.25064900
 O -0.39984600 -1.01192700 -3.12424800
 O -0.03815200 -0.73082100 -6.35012600
 C 0.57931600 0.03515900 -7.33503800
 H 0.85864000 1.04524300 -6.96783200
 H 1.51734700 -0.41727500 -7.70622300
 H -0.06547000 0.20024700 -8.21689400
 Na 1.13600900 -1.82441400 -4.76808700

Int2_{enol}

40

E(RB3LYP) = -1101.81145788

C 1.93985000 1.54909600 -0.54120100
 C 2.33953600 1.65675400 -1.87551100
 C 2.13669900 2.63393200 0.31833800
 C 2.90989200 2.83666700 -2.34991600
 C 2.72551000 3.80711200 -0.14902700
 C 3.10679700 3.91416100 -1.48666600
 H 2.19853000 0.81598100 -2.54454400
 H 1.83023400 2.55600800 1.35554900
 H 3.20364400 2.91339100 -3.39059500
 H 2.88266800 4.63825200 0.52890100
 H 3.55592900 4.83004300 -1.85283700
 C 1.38142400 0.24239700 -0.02588800
 O 2.18776100 -0.72235300 -0.02585900
 C 0.01788800 0.20504800 0.41082700

H -0.19655800 -1.43686400 -1.25063800
 C -0.90756200 1.37164700 0.08708600
 H -1.71405500 1.42096400 0.81902600
 H -0.37369100 2.31831100 0.17488800
 C -1.51573900 1.27968200 -1.32057300
 H -0.73141800 1.26624900 -2.08326100
 H -2.10808400 0.36591200 -1.43100200
 H -2.17123100 2.13142000 -1.52781400
 C -1.89820900 -0.80831100 1.70593200
 C -2.94332800 -1.46948400 1.05643400
 N -2.06455800 -0.14088000 2.85607000
 C -4.21565000 -1.42150900 1.61435500
 C -3.29237200 -0.11557600 3.39123000
 C -4.39756300 -0.72999900 2.80997600
 H -2.75585500 -2.00477400 0.13371400
 H -5.04912400 -1.91474300 1.12793100
 H -3.39496000 0.42696000 4.32621000
 H -5.36946700 -0.66670900 3.28302000
 C -0.48692700 -0.89710400 1.15342000
 O 0.10071400 -1.98004200 1.41822500
 O 0.00777400 -2.26850000 -1.70700200
 C 0.46648600 -1.95445100 -3.02546500
 H 1.42176100 -1.42060300 -2.99588500
 H 0.60591400 -2.89896600 -3.55106200
 H -0.26622500 -1.35111600 -3.56888700
 Na 1.60302400 -2.92503100 -0.00492200

8-5-3. Formation of enolate of 1 and 2 with (CH₃ONa)₁

Int1₁₋₂

40

E(RB3LYP) = -1101.79137608

C 1.59949100 1.31505400 -0.79431300
 C 2.95134600 1.59226800 -1.04382300

C 0.81942100 2.27870400 -0.14127500
 C 3.50870800 2.80654700 -0.66198000
 C 1.38036200 3.49500500 0.24340200
 C 2.72222000 3.76440300 -0.01772700
 H 3.54974600 0.84244200 -1.54546900

H -0.21632100 2.07372200 0.09473500
 H 4.55317200 3.01104500 -0.86743000
 H 0.76860600 4.22939000 0.75445200
 H 3.15497800 4.71253100 0.28003000
 C 1.05534100 -0.00133400 -1.23766300
 O 1.80537700 -0.87424100 -1.68003700
 C -0.45849700 -0.18592200 -1.33633400
 H -0.96038700 0.73755200 -1.07034400
 C -0.85289400 -0.57343000 -2.77468900
 H -0.40978100 -1.54349500 -3.00712300
 H -0.40913900 0.15483500 -3.46115600
 C -2.36855600 -0.61092900 -2.97615500
 H -2.83856400 -1.35749500 -2.33005100
 H -2.82079100 0.35897600 -2.74906100
 H -2.61730300 -0.86308400 -4.01026400
 C -1.82067200 -0.84799700 0.77509100
 C -2.28274900 -1.81677900 1.67082300
 N -2.16557500 0.44338300 0.87046000
 C -3.12554600 -1.42770600 2.70316000
 C -2.97840700 0.80734500 1.86675500
 C -3.48564500 -0.08540700 2.80703800
 H -1.97151200 -2.84443200 1.54368100
 H -3.49648800 -2.15554500 3.41523800
 H -3.23642400 1.86095500 1.91470700
 H -4.14034100 0.26453000 3.59520900
 C -0.90494000 -1.26091900 -0.34199000
 O -0.70606700 -2.45531900 -0.57450500
 Na 1.67191600 -2.65370200 -0.04581100
 C 0.87043900 -0.14225500 2.18653100
 H 1.69994400 -0.41538700 2.86549600
 H -0.06320100 -0.29466300 2.76127800
 O 0.90371700 -0.87046300 1.01288900
 H 0.95624700 0.94722400 2.01517600

TS1₁₋₂

40

E(RB3LYP) = -1101.79074099

C 1.88213900 2.92389700 -4.15963700
 C 3.23155000 3.18235000 -4.44128000
 C 1.13087000 3.90035200 -3.49179500
 C 3.81601200 4.38730700 -4.07110000
 C 1.71918600 5.10573100 -3.11519300
 C 3.05943500 5.35406700 -3.40527800
 H 3.80706100 2.42368200 -4.95611900
 H 0.09519600 3.71739700 -3.23987500
 H 4.85836000 4.57660200 -4.30003800
 H 1.13014000 5.84960700 -2.59159000
 H 3.51350100 6.29433700 -3.11451900
 C 1.31139900 1.60771200 -4.58076800
 O 2.05029500 0.73673300 -5.04371500
 C -0.18994500 1.38888400 -4.53513000
 H -0.68708500 2.30460300 -4.23502300
 C -0.72047400 0.97049600 -5.91814500
 H -0.28763300 0.00261700 -6.17765500
 H -0.36254200 1.69261200 -6.66011700
 C -2.24788600 0.90368000 -5.96952300
 H -2.63681400 0.15784300 -5.27176300
 H -2.69426500 1.86822200 -5.71009800
 H -2.59131700 0.63382200 -6.97180900
 C -1.59432400 0.68226400 -2.47223000
 C -2.17952900 -0.32939600 -1.70598300
 N -1.94107700 1.96987900 -2.34470300
 C -3.14946600 0.00957700 -0.77184900
 C -2.87818700 2.28631800 -1.44460900
 C -3.51064700 1.34872100 -0.63365900
 H -1.86299300 -1.35174400 -1.86008700
 H -3.61811200 -0.75409000 -0.16185000
 H -3.13486100 3.33892900 -1.36932800

H -4.26282700 1.66123200 0.07985100
 C -0.51802600 0.31216300 -3.46985000
 O -0.35559200 -0.89823100 -3.75669300
 Na 1.92761100 -1.07983800 -3.40267600
 C 0.92690500 1.39605600 -1.13614300
 H 1.90144000 1.38567100 -0.62429600
 H 0.18739200 0.97183100 -0.43648800
 O 1.01122200 0.67825500 -2.32862900
 H 0.65421800 2.45059000 -1.29456500

Int2₁₋₂

40

E(RB3LYP) = -1101.79668318
 C 1.82352500 1.54321700 -0.93902800
 C 3.04805700 1.86233900 -1.54232700
 C 1.18752600 2.49973000 -0.13589500
 C 3.62075700 3.11598300 -1.35942600
 C 1.77037600 3.74860800 0.05961300
 C 2.98265500 4.06196400 -0.55545300
 H 3.53452600 1.11723200 -2.15909900
 H 0.25894400 2.25424100 0.36103400
 H 4.56135500 3.35764600 -1.84048400
 H 1.27938200 4.47810200 0.69299600
 H 3.42897100 5.03877200 -0.40871700
 C 1.24231400 0.18854300 -1.17161900
 O 1.96596800 -0.71397800 -1.60214100
 C -0.22730800 -0.05014200 -0.93263700
 H -0.72007000 0.89794500 -0.73401500
 C -0.86532600 -0.69278900 -2.17565400
 H -0.49735500 -1.71690000 -2.26774300
 H -0.51811600 -0.15141100 -3.06264400
 C -2.39516600 -0.69202500 -2.16356500
 H -2.79299800 -1.31294800 -1.35959100
 H -2.78822100 0.31958500 -2.02669600

H -2.78389700 -1.07854900 -3.11003200
 C -1.77530800 -0.66597800 1.01012300
 C -2.55550900 -1.73073300 1.46271300
 N -2.17135000 0.60897300 1.13226100
 C -3.78378900 -1.46828700 2.05875100
 C -3.35717800 0.85351800 1.70074300
 C -4.20160600 -0.14492800 2.17961800
 H -2.17733600 -2.73451700 1.32758400
 H -4.40684300 -2.27876900 2.42047900
 H -3.64737200 1.89792700 1.77681500
 H -5.15224900 0.11137500 2.63089100
 C -0.39484100 -0.95192100 0.36856900
 O -0.15633100 -2.23078500 0.19079500
 Na 1.62360500 -2.91568800 -0.89489000
 C 0.75289100 -0.94798800 2.53122800
 H 1.57127000 -0.45234300 3.05780400
 H 0.99685500 -2.00745700 2.39868900
 O 0.60120200 -0.29235200 1.28826700
 H -0.15435900 -0.87563000 3.14711400

TS2₁₋₂

40

E(RB3LYP) = -1101.78694050
 C 1.71895600 1.44877800 -0.83512300
 C 3.00980700 1.63685700 -1.34905200
 C 1.16419400 2.45208700 -0.02793500
 C 3.72675900 2.79613500 -1.07125400
 C 1.88676900 3.60641600 0.26135100
 C 3.16779600 3.78545400 -0.26104900
 H 3.43679000 0.85761300 -1.96731600
 H 0.18297000 2.31760600 0.40402600
 H 4.72090100 2.92902200 -1.48281500
 H 1.44967700 4.36725300 0.89790000
 H 3.72577400 4.68777800 -0.03854700

C 0.99287700 0.17975700 -1.16981400
 O 1.64825800 -0.76503300 -1.68405400
 C -0.40156800 0.04196600 -0.86529000
 H -0.91127400 0.96765100 -0.62749000
 C -1.20376900 -0.89571300 -1.75985100
 H -1.30462500 -1.87934900 -1.28706100
 H -0.64303400 -1.07191400 -2.68394700
 C -2.59419600 -0.35269700 -2.10187800
 H -3.19309800 -0.19155500 -1.20287100
 H -2.52115700 0.60357300 -2.62889100
 H -3.13957400 -1.04970200 -2.74499500
 C -1.85101200 -0.69827400 1.21082800
 C -2.64347200 -1.84726100 1.17696500
 N -2.35704900 0.51788600 1.45595400
 C -4.01204000 -1.72843600 1.39549900
 C -3.67101900 0.61921300 1.67311300
 C -4.54367800 -0.46767300 1.64846200
 H -2.17378700 -2.80117400 0.98262800
 H -4.65146800 -2.60334000 1.36889200
 H -4.04873800 1.61845100 1.87037000
 H -5.60274400 -0.32304800 1.82182400
 C -0.36197500 -0.83871700 0.92772000
 O 0.10948600 -2.00934200 0.78212000
 Na 1.45283000 -2.85438200 -0.77594000
 C 1.69354300 -0.26707200 2.01309300
 H 2.07786000 0.53034700 2.64867400
 H 2.27678500 -0.29827800 1.09053000
 O 0.32929900 0.05796700 1.76703600
 H 1.78559900 -1.22926600 2.52262200

Int3₁₋₂

40

E(RB3LYP) = -1101.80439991

C 1.54557800 1.33618500 -0.96384200

C 2.88234100 1.57849500 -1.31003300
 C 0.89800100 2.27215800 -0.14293800
 C 3.54302700 2.72716800 -0.87878300
 C 1.55823000 3.41641300 0.29693700
 C 2.88410700 3.65436100 -0.07130300
 H 3.39411100 0.84461900 -1.91991800
 H -0.11394900 2.08123100 0.18997000
 H 4.57480000 2.89684100 -1.16805800
 H 1.04170500 4.11855700 0.94276400
 H 3.39794700 4.54414300 0.27478300
 C 0.88420600 0.07215600 -1.44002100
 O 1.67450400 -0.92724800 -1.72412000
 C -0.48080800 0.02991800 -1.55997100
 H -1.06785300 0.90421300 -1.30660300
 C -1.21754300 -1.16824900 -2.08343200
 H -1.30455800 -1.94895500 -1.30980000
 H -0.63893000 -1.63160700 -2.89311000
 C -2.62687200 -0.83268800 -2.57993300
 H -3.22482600 -0.38968500 -1.77787200
 H -2.59013900 -0.11200000 -3.40277400
 H -3.15272400 -1.72436200 -2.93439700
 C -1.54798100 -0.65930100 1.39597300
 C -2.50267400 -1.62144500 1.06084100
 N -1.85978400 0.60232100 1.72326200
 C -3.84055400 -1.24460300 1.02749900
 C -3.14541400 0.94996000 1.68598000
 C -4.17169400 0.06970300 1.33663900
 H -2.19039400 -2.62987200 0.83057600
 H -4.60718200 -1.96246200 0.76271000
 H -3.37249400 1.97915300 1.94636900
 H -5.19875600 0.41169400 1.31792300
 C -0.10855100 -1.06503800 1.39687900
 O 0.26470600 -2.16496100 1.01002300
 Na 1.39961900 -2.92657400 -0.85805000

C 2.11734700 -0.44898700 1.87829300
H 2.59936600 0.42377700 2.30966000
H 2.44123100 -0.58984000 0.84866800

O 0.70398000 -0.15155600 1.90877400
H 2.32588100 -1.33916200 2.47232200

8-5-4. Formation of enolate of 3 and 4 with (CH₃ONa)₁

Int1₃₋₄

40

E(RB3LYP) = -1101.79138239

C 1.63477600 1.33307700 -0.84632800
C 2.98788100 1.59808500 -1.10233600
C 0.86329800 2.30896800 -0.20128400
C 3.55475300 2.81238100 -0.73485000
C 1.43380800 3.52526900 0.16904600
C 2.77676500 3.78247300 -0.09860300
H 3.57963500 0.83887400 -1.59772300
H -0.17316500 2.11366800 0.03972400
H 4.60002400 3.00742500 -0.94530300
H 0.82864900 4.26925800 0.67402700
H 3.21696700 4.73064300 0.18789400
C 1.07985600 0.01627600 -1.27461800
O 1.82227500 -0.86714300 -1.70893200
C -0.43554100 -0.15764700 -1.36820100
H -0.92969500 0.77277800 -1.11210300
C -0.83593900 -0.55888500 -2.80115700
H -0.40104400 -1.53513000 -3.02298900
H -0.38782700 0.15772000 -3.49699800
C -2.35225900 -0.58666800 -2.99911600
H -2.82679900 -1.32186100 -2.34335400
H -2.79633100 0.38939200 -2.78252400
H -2.60517000 -0.84894300 -4.02969700
C -1.79713100 -0.78434900 0.75460400
C -2.26483700 -1.73943200 1.66214700
N -2.13066500 0.51081600 0.83685700
C -3.10107600 -1.33196900 2.69263400

C -2.93738700 0.89256800 1.83157000
C -3.44932700 0.01449600 2.78297300
H -1.96291100 -2.77104900 1.54511500
H -3.47611900 -2.04878800 3.41368600
H -3.18621600 1.94881200 1.86874200
H -4.09860100 0.37853300 3.56924100
C -0.88846600 -1.21750500 -0.36059000
O -0.70059100 -2.41600500 -0.58038500
Na 1.67846900 -2.62894400 -0.05655900
C 0.90322800 -0.08707800 2.15178700
H 0.99622600 0.99970800 1.96735400
H 1.73302500 -0.35790300 2.83142000
O 0.92739300 -0.82937400 0.98699000
H -0.02951400 -0.22588000 2.73153900

TS1₃₋₄

40

E(RB3LYP) = -1101.78842896

C 1.87461400 2.81102400 -3.96301100
C 3.25243400 2.94527100 -4.16941700
C 1.13752600 3.95311900 -3.63238400
C 3.87928300 4.18157100 -4.04785700
C 1.76117300 5.19498600 -3.51431500
C 3.13374900 5.31524800 -3.72077400
H 3.81739200 2.05965500 -4.43024000
H 0.07341500 3.88885300 -3.45016800
H 4.94802400 4.26382500 -4.21194000
H 1.17175700 6.06805500 -3.25794400
H 3.61760200 6.28091600 -3.62905300

C 1.27572500 1.42446100 -4.09988500
 O 1.99360700 0.52197300 -4.61211700
 C -0.25401900 1.36167700 -4.36895000
 H -0.73248500 2.26379300 -4.00335500
 C -0.52359700 1.22298400 -5.87463400
 H -0.10448100 0.27480500 -6.21706400
 H 0.02340100 2.01685000 -6.39375800
 C -2.01136300 1.31164600 -6.22055900
 H -2.58055400 0.50833600 -5.74305600
 H -2.43783900 2.26264700 -5.88790500
 H -2.16869000 1.23222200 -7.29954100
 C -1.73497200 0.51505300 -2.41214400
 C -2.07186700 -0.50741700 -1.52028800
 N -2.19496400 1.76718100 -2.28343700
 C -2.90523200 -0.21419100 -0.44939500
 C -3.00701200 2.03637100 -1.25693900
 C -3.38680000 1.08625100 -0.31226300
 H -1.67346900 -1.50036100 -1.67781000
 H -3.17641500 -0.98216900 0.26523100
 H -3.36688000 3.05794000 -1.18398000
 H -4.04113900 1.36162000 0.50529700
 C -0.82488900 0.20703000 -3.57322400
 O -0.59902000 -0.96399100 -3.86306500
 Na 1.87994100 -1.11972600 -3.03734900
 C 1.08734300 1.81028600 -1.24873700
 H 1.95692500 2.48348300 -1.19753800
 H 1.02693200 1.27122000 -0.29211100
 O 1.18659500 0.89150200 -2.29803200
 H 0.18909300 2.44069300 -1.32470600

Int2₃₋₄

40

E(RB3LYP) = -1101.79566266

C 1.81265700 1.29767600 -0.50678900

C 2.88191200 1.44235600 -1.38924900
 C 1.32466000 2.43317600 0.14801400
 C 3.45595900 2.69375300 -1.61981800
 C 1.89512900 3.68478100 -0.07402800
 C 2.96346500 3.82036300 -0.96315400
 H 3.25527500 0.55410300 -1.88320600
 H 0.50280000 2.32950600 0.84648500
 H 4.28700100 2.78905200 -2.31052600
 H 1.50956500 4.55477200 0.44649400
 H 3.40709400 4.79401300 -1.13866100
 C 1.18498900 -0.09723200 -0.28471900
 O 1.89030800 -1.08569900 -0.78050300
 C -0.32812100 -0.02737200 -0.81546400
 H -0.77166200 0.89015200 -0.43611500
 C -0.36624100 -0.02867200 -2.34563200
 H 0.02374400 -0.97941600 -2.71551600
 H 0.31738300 0.74681100 -2.70273300
 C -1.76790800 0.22086200 -2.90728400
 H -2.46851500 -0.56021900 -2.59626400
 H -2.16550800 1.17896500 -2.55953000
 H -1.75657500 0.23963100 -4.00064200
 C -2.03192600 -0.93156200 0.91266000
 C -2.45596300 -2.00672200 1.69871800
 N -2.45721900 0.32442800 1.11245300
 C -3.34200000 -1.76572200 2.74133100
 C -3.31914100 0.54298800 2.10766500
 C -3.78582000 -0.46316100 2.95272100
 H -2.08365900 -2.99940700 1.48554300
 H -3.68055700 -2.57562000 3.37640400
 H -3.65183200 1.56788300 2.23983200
 H -4.47785500 -0.22615200 3.75106000
 C -1.07105900 -1.18144800 -0.21765400
 O -0.90411000 -2.33987100 -0.60195600
 Na 1.21967100 -3.11579500 -1.20332100

C 2.12895600 -0.40125500 1.94421800
H 2.78120300 0.48054300 1.88250400
H 2.69522400 -1.27552900 1.60637600
O 0.94394900 -0.22907700 1.19208200
H 1.83154000 -0.54430000 2.98530900

TS2₃₋₄

40

E(RB3LYP) = -1101.78335404

C 1.74124000 1.13961900 -0.43127700
C 2.69073800 1.23924700 -1.45226300
C 1.32613700 2.30309800 0.22678700
C 3.21293900 2.47954800 -1.81534000
C 1.84887300 3.54151000 -0.13315900
C 2.79270900 3.63526900 -1.15852400
H 3.01268200 0.33428000 -1.95117500
H 0.59058300 2.22619700 1.01697200
H 3.94845000 2.54377800 -2.60945800
H 1.52094300 4.43581500 0.38475600
H 3.19736700 4.60071900 -1.43987100
C 1.18333900 -0.21247700 -0.06844500
O 1.72072600 -1.25335800 -0.52429400
C -0.68491700 0.04377800 -1.05159700
H -1.01665000 0.98961000 -0.64204800
C -0.31153900 0.03720500 -2.51229300
H 0.28101500 -0.85512900 -2.73542800
H 0.33280100 0.89480900 -2.72349500
C -1.53157500 0.08245000 -3.44511500
H -2.17827800 -0.78388200 -3.28351500
H -2.12710700 0.98258500 -3.26570100
H -1.22531700 0.08657200 -4.49634500
C -2.07686400 -0.94847000 0.79464200
C -2.30026100 -2.07565000 1.59238900
N -2.53461800 0.26772400 1.13099600

C -2.99892800 -1.93381400 2.78433200
C -3.21289600 0.39173800 2.27475500
C -3.46760500 -0.67109600 3.13930800
H -1.91596200 -3.03236900 1.26648200
H -3.17530300 -2.78931100 3.42620800
H -3.57266300 1.38842100 2.51392600
H -4.01932200 -0.50924100 4.05700700
C -1.30302400 -1.09941800 -0.48988800
O -1.15328100 -2.26850000 -0.94375400
Na 0.88303200 -3.20350500 -1.24589200
C 1.72045200 -0.58206500 2.21571000
H 2.52605400 0.16216600 2.21452500
H 2.14312000 -1.56854500 2.00727100
O 0.70388700 -0.24659600 1.27006800
H 1.24078500 -0.58911900 3.19427500

Int3₃₋₄

40

E(RB3LYP) = -1101.80964290

C 2.01627200 1.11428300 -0.24966300
C 2.75308900 0.79366200 -1.39374100
C 1.60781300 2.43516400 -0.03313200
C 3.08396500 1.78453100 -2.31206900
C 1.93095500 3.42107000 -0.95824200
C 2.67227900 3.09892600 -2.09656500
H 3.06702900 -0.22974300 -1.55315600
H 1.02743700 2.67750200 0.84637400
H 3.65766800 1.53197000 -3.19566800
H 1.60383000 4.44081400 -0.79449000
H 2.92395900 3.87040900 -2.81476800
C 1.69124100 0.03174300 0.71052000
O 1.86804700 -1.15813000 0.48787900
C -1.18946400 0.44101900 -1.13256900
H -1.50278200 1.29743700 -0.54951000

C -0.60250200 0.68042700 -2.49002100
 H 0.01915600 -0.17538100 -2.77293000
 H 0.06054900 1.55201800 -2.45681800
 C -1.65673500 0.91148300 -3.58910700
 H -2.30909100 0.03948800 -3.69054200
 H -2.28877800 1.77181700 -3.34744000
 H -1.18766200 1.10141300 -4.56123200
 C -1.94140400 -0.91407000 0.79297800
 C -2.12107000 -2.19013400 1.35166500
 N -2.25441300 0.19932800 1.48767700
 C -2.61709800 -2.31307800 2.64402500
 C -2.72800900 0.06791300 2.72708500
 C -2.92509200 -1.15950100 3.36016600

H -1.86004600 -3.05143200 0.75333700
 H -2.75783300 -3.29255700 3.08801900
 H -2.96223100 0.99184700 3.25004600
 H -3.30856600 -1.20088500 4.37209800
 C -1.36003300 -0.80194700 -0.59238700
 O -1.02778900 -1.93314000 -1.16245700
 Na 1.05241500 -2.62009300 -1.09473400
 C 0.89516600 -0.50526500 2.87416700
 H 1.79471200 -1.03928400 3.18104000
 H 0.16068900 -1.20423900 2.48058900
 O 1.22862000 0.48377200 1.87578000
 H 0.48020500 0.05707700 3.70543600

8-5-5. Formation of 1 and sodium salt of 2 with NaOH

Int2'₁₋₂

37

E(RB3LYP) = -1062.48492888

C 1.77267600 1.48939300 -0.84610100
 C 3.15797600 1.56775100 -1.05361000
 C 1.10207600 2.61315300 -0.34554300
 C 3.85653800 2.73167500 -0.75858000
 C 1.80001400 3.78340900 -0.05816600
 C 3.17773100 3.84513200 -0.25969700
 H 3.67306000 0.69854800 -1.44148100
 H 0.03362500 2.58862500 -0.18214000
 H 4.92818200 2.77406100 -0.91438100
 H 1.26759700 4.64600800 0.32459000
 H 3.72021200 4.75488900 -0.03014900
 C 1.08028300 0.20744000 -1.17976400
 O 1.68999000 -0.64902800 -1.82978300
 C -0.30690000 -0.06504900 -0.69608400
 H -0.78463600 0.85917000 -0.37852600
 C -1.18464100 -0.76159500 -1.75740300

H -1.22880900 -1.83061600 -1.53160000
 H -0.70662100 -0.67941200 -2.73705700
 C -2.59935000 -0.18215500 -1.83850600
 H -3.12683900 -0.27129500 -0.88638500
 H -2.57154100 0.87859100 -2.10627900
 H -3.19086100 -0.70297200 -2.59694700
 C -1.59306200 -0.99550300 1.26515100
 C -2.37890000 -2.14463600 1.21035600
 N -2.02741300 0.14587400 1.81790300
 C -3.66649300 -2.10299500 1.73478300
 C -3.26290900 0.17690300 2.33008500
 C -4.12381600 -0.91701200 2.30567700
 H -1.96375800 -3.03671900 0.76272500
 H -4.30443300 -2.97894400 1.70106100
 H -3.57721700 1.11564700 2.77632900
 H -5.11848400 -0.83836100 2.72630100
 C -0.17541800 -0.98117400 0.65399900
 O 0.32666600 -2.17023200 0.43706400
 Na 1.57471500 -2.88708200 -1.20082700

H 0.10528300 0.50006000 1.92994700
O 0.66676100 -0.20825400 1.58119000

TS2'₁₋₂

37

E(RB3LYP) = -1062.47964425

C 1.90455200 3.06134900 -4.32587800
C 3.30547000 3.04253600 -4.35698500
C 1.25969700 4.23192200 -3.90628100
C 4.04308500 4.15386400 -3.96365100
C 1.99598000 5.34958200 -3.51997900
C 3.38954600 5.31326300 -3.54276100
H 3.80168400 2.13890300 -4.68711900
H 0.17894500 4.28269300 -3.89069900
H 5.12642500 4.11873600 -3.98306300
H 1.48132400 6.24950500 -3.20356800
H 3.96199300 6.18185800 -3.23825800
C 1.16001500 1.83267100 -4.75511400
O 1.77935200 0.96819600 -5.42438200
C -0.18532300 1.61015500 -4.31056400
H -0.68700900 2.48115200 -3.90445800
C -1.07284400 0.73205700 -5.18059800
H -1.07700900 -0.29737900 -4.80432900
H -0.64427800 0.67248900 -6.18644600
C -2.51206400 1.24828100 -5.26721300
H -2.97324400 1.31005500 -4.27849700
H -2.54114200 2.24816800 -5.71098200
H -3.13142100 0.58921900 -5.88253200
C -1.23852200 0.59340300 -2.11848100
C -2.05259300 -0.53062100 -2.24980500
N -1.65996800 1.72935800 -1.54459300
C -3.36426500 -0.45911500 -1.79285700
C -2.91919700 1.78736700 -1.10179300
C -3.81335900 0.72457200 -1.21214300

H -1.64627200 -1.42759600 -2.69532300
H -4.02577800 -1.31270200 -1.88481500
H -3.22580500 2.72057100 -0.63968400
H -4.82680600 0.82464600 -0.84482800
C 0.18938500 0.58264800 -2.63600900
O 0.71453300 -0.52929100 -2.94517400
Na 1.82366000 -1.21088200 -4.74148200
H 0.41054500 2.14663200 -1.54361300
O 0.99660800 1.44484300 -1.87132200

Int3'₁₋₂

37

E(RB3LYP) = -1062.49616410

C 1.32857800 1.38562900 -0.85102500
C 2.70353400 1.60650300 -1.01594900
C 0.60625000 2.31800200 -0.08770000
C 3.33306900 2.71646000 -0.45531900
C 1.23248000 3.42427600 0.47941600
C 2.60129700 3.63341500 0.29779800
H 3.26548000 0.88151200 -1.59042300
H -0.45160600 2.17506800 0.08410400
H 4.39769000 2.86369100 -0.60311700
H 0.65098200 4.12405900 1.06999900
H 3.08781000 4.49517900 0.74045900
C 0.71797900 0.15328100 -1.46612100
O 1.54659000 -0.71804500 -1.96569000
C -0.64483600 -0.00832800 -1.46654500
H -1.28252900 0.75386100 -1.03711400
C -1.32396200 -1.19487800 -2.08379900
H -1.28977600 -2.06286100 -1.40480800
H -0.76806000 -1.51106300 -2.97481500
C -2.78627800 -0.92408100 -2.45083800
H -3.35980500 -0.62382900 -1.56849400
H -2.86201500 -0.11519400 -3.18419900

H -3.26595500 -1.81123500 -2.87516100
 C -1.11144900 -0.91960300 1.47850200
 C -2.27365300 -1.62579200 1.17858700
 N -1.10580700 0.28069300 2.07603500
 C -3.49191400 -1.02113100 1.46441800
 C -2.27847900 0.85343200 2.34439800
 C -3.49794400 0.24495000 2.04564900
 H -2.21072700 -2.60358700 0.72311000
 H -4.42214400 -1.52647100 1.23592300
 H -2.24520700 1.82977300 2.81560800
 H -4.42623100 0.75079100 2.27777200
 C 0.24150400 -1.47737700 1.18058800
 O 0.43112600 -2.55717400 0.64564900
 Na 1.69549500 -2.80903600 -1.30439200
 H 0.85812400 0.10693300 1.94674500
 O 1.25484800 -0.72156700 1.59881500

Int4'₁₋₂

37

E(RB3LYP) = -1062.49522505
 C 0.14083300 2.37893100 1.37427700
 C 1.52352600 2.16917500 1.46131000
 C -0.57875300 2.55025300 2.56468700
 C 2.16479500 2.10482100 2.69585200
 C 0.06105700 2.49798900 3.80154900
 C 1.43538000 2.26927600 3.87376500
 H 2.08581200 2.05595500 0.54266700
 H -1.64399100 2.74253800 2.52513500
 H 3.23411600 1.92921800 2.74059400
 H -0.51296100 2.64290900 4.71005000
 H 1.93272200 2.22772000 4.83605400
 C -0.50475900 2.41489500 0.00997500
 O 0.24154200 2.79980700 -0.96956700
 C -1.79970600 1.94781900 -0.12400600

H -2.37690500 1.74668000 0.77366900
 C -2.56221100 2.00556900 -1.42339200
 H -1.86241200 1.90837200 -2.25969000
 H -3.03215200 2.99304600 -1.55310800
 C -3.65015700 0.93059500 -1.53558300
 H -3.21902000 -0.07419900 -1.50210600
 H -4.36387600 1.00899000 -0.70915000
 H -4.21107700 1.02590300 -2.46998300
 C 0.20765600 -2.68273700 -0.72520200
 C 1.06594300 -3.25462800 -1.66526900
 N -0.33526600 -3.37081500 0.28756500
 C 1.37552100 -4.60563500 -1.54739200
 C -0.03159800 -4.66550300 0.38956000
 C 0.81655800 -5.32805800 -0.49912800
 H 1.47144300 -2.64493700 -2.46053500
 H 2.03859300 -5.08255100 -2.25872800
 H -0.48400000 -5.20148800 1.21783700
 H 1.02753600 -6.38156200 -0.36561700
 C -0.12255100 -1.22103100 -0.85102300
 O 0.33476000 -0.55046700 -1.77108000
 Na 1.04387000 1.47263500 -2.52784700
 H -1.12044700 0.24342800 -0.04972400
 O -0.91518700 -0.75528100 0.08243000

TS3'₁₋₂

37

E(RB3LYP) = -1062.49392041
 C 1.28024400 0.85647700 -0.41426000
 C 2.67475600 0.88083800 -0.28346900
 C 0.49937400 0.98230300 0.74198700
 C 3.27464500 1.00543900 0.96644100
 C 1.09674500 1.11957800 1.99330900
 C 2.48639500 1.12595800 2.11135200
 H 3.27795300 0.79938000 -1.17897800

H -0.58067300 0.99093200 0.66763400
 H 4.35574100 1.01078500 1.04916400
 H 0.47670000 1.22565200 2.87620700
 H 2.95031500 1.22927200 3.08553300
 C 0.68784900 0.70690000 -1.79410500
 O 1.41295600 1.06555200 -2.77351800
 C -0.55985100 0.07212800 -1.94014000
 H -1.19632000 0.03636200 -1.05861700
 C -1.29296700 0.11309000 -3.26854100
 H -0.64534700 -0.27375300 -4.06286900
 H -1.52007900 1.15026900 -3.55406800
 C -2.59042400 -0.70039800 -3.24480300
 H -2.38993700 -1.75067300 -3.01371300
 H -3.27749900 -0.31989400 -2.48217200
 H -3.10571000 -0.65901800 -4.20859000
 C 1.23698900 -4.42772900 -2.64556800
 C 2.07880400 -4.98680500 -3.60921400
 N 0.65858200 -5.15065300 -1.67744700
 C 2.33041200 -6.35404100 -3.56641600
 C 0.90707000 -6.46165100 -1.64601700
 C 1.73288600 -7.11060700 -2.56398600
 H 2.51613300 -4.35115300 -4.36619700
 H 2.97876000 -6.81812500 -4.29987600
 H 0.42525400 -7.02280000 -0.85127600
 H 1.89771300 -8.17811200 -2.48854600
 C 0.96399800 -2.93920200 -2.69148700
 O 1.48616800 -2.26230600 -3.58669000
 Na 2.23096900 -0.28237000 -4.33586500
 H -0.04418000 -1.34149200 -1.85578300
 O 0.18752600 -2.48281000 -1.76934900

Int5'₁₋₂

37

E(RB3LYP) = -1062.52979934

C 0.12056200 2.31458800 1.47414900
 C 1.04889200 3.35329000 1.63026600
 C -0.37061700 1.66215500 2.61238400
 C 1.47838700 3.73199300 2.89592300
 C 0.06324200 2.03860900 3.88033600
 C 0.98680500 3.07301000 4.02448800
 H 1.42245600 3.85642200 0.74746500
 H -1.08124300 0.85241500 2.51570700
 H 2.19410600 4.53794000 3.00681800
 H -0.31650300 1.52350800 4.75447800
 H 1.32310900 3.36524100 5.01242000
 C -0.30007700 1.92822500 0.09504100
 O 0.25017600 2.43471800 -0.87977600
 C -1.39834200 0.90682000 -0.07127900
 H -2.27246900 1.24115800 0.50005300
 C -1.77898800 0.61292300 -1.51993000
 H -0.88457500 0.32543700 -2.07657700
 H -2.15524800 1.52625400 -1.99075900
 C -2.82769100 -0.49669300 -1.61542900
 H -2.45497200 -1.42720300 -1.17907000
 H -3.74529400 -0.22290800 -1.08513800
 H -3.09134500 -0.69931000 -2.65666000
 C 0.58154300 -2.03506700 -0.90864800
 C 0.26505600 -2.83591800 -2.00945000
 N 0.08402200 -2.27023400 0.31428400
 C -0.58708800 -3.92062700 -1.83562600
 C -0.74148800 -3.30965200 0.46943300
 C -1.10677000 -4.16514800 -0.56790500
 H 0.68534300 -2.59025200 -2.97442800
 H -0.84589300 -4.55850200 -2.67267900
 H -1.13344200 -3.46585200 1.47030500
 H -1.78002000 -4.99277400 -0.38212200
 C 1.49441500 -0.82407300 -1.09298800
 O 1.76477300 -0.49846200 -2.28457300

Na 2.39592200 1.63902800 -1.50232300
H -1.05539900 -0.01179000 0.41924500

O 1.89068900 -0.20538600 -0.0737120

8-5-6. Formation of 3 and sodium salt of 4 with NaOH

Int1'₃₋₄

37

E(RB3LYP) = -1062.48469252

C 1.82449900 1.46464700 -0.85801700

C 3.07083700 1.83211200 -1.38518500

C 1.14738400 2.36243100 -0.02041200

C 3.62353800 3.07379600 -1.09478200

C 1.71224000 3.59775400 0.28623900

C 2.94560800 3.95903400 -0.25461900

H 3.58979900 1.13222100 -2.02774800

H 0.19472000 2.09196900 0.41732000

H 4.58089100 3.35322000 -1.51879200

H 1.18867500 4.27883500 0.94671200

H 3.37773600 4.92549600 -0.02252900

C 1.27988600 0.11297300 -1.19170700

O 2.03712000 -0.75382400 -1.63225700

C -0.18600900 -0.17850100 -0.99054400

H -0.70020400 0.74025200 -0.71577100

C -0.80151400 -0.72038900 -2.28978500

H -0.39728900 -1.71947400 -2.46057200

H -0.47143400 -0.08931800 -3.12288800

C -2.32984900 -0.76154600 -2.27153000

H -2.70175700 -1.45830600 -1.51944600

H -2.75006000 0.22485100 -2.05035700

H -2.71768200 -1.07876500 -3.24365700

C -1.59667400 -0.86289900 1.03463100

C -2.61533000 -1.79719700 1.20304000

N -1.64999700 0.36524700 1.57112000

C -3.73662100 -1.44109900 1.94505400

C -2.72847900 0.69892000 2.28894700

C -3.80009700 -0.16464800 2.49997600

H -2.50309000 -2.77361700 0.75218500

H -4.54770100 -2.14555100 2.09075200

H -2.73495700 1.69866100 2.71300100

H -4.65304700 0.15616100 3.08481700

C -0.33458800 -1.21848600 0.22826200

O -0.21758200 -2.47154100 -0.11041200

Na 2.03497500 -2.58516200 0.02245300

H 0.58816700 -0.05601500 1.64539600

O 0.81842300 -0.87236500 1.18190400

TS1'₃₋₄

37

E(RB3LYP) = -1062.47517763

C 1.88732100 2.80066500 -3.93523700

C 3.15797900 3.11034700 -4.42747500

C 1.16907800 3.78767800 -3.24724900

C 3.70522400 4.37797800 -4.23829900

C 1.71736100 5.05248200 -3.05208800

C 2.98665300 5.35360700 -3.54897400

H 3.70502900 2.34316100 -4.96054300

H 0.18879800 3.56362600 -2.84409900

H 4.69031200 4.60475500 -4.63034900

H 1.15440100 5.80458800 -2.51107500

H 3.40993700 6.34026900 -3.39988600

C 1.34301500 1.41114900 -4.18115200

O 2.07999700 0.55167600 -4.70843700

C -0.18888700 1.31362400 -4.40023900

H -0.65547400 2.24869000 -4.10927100

C -0.49333600 1.04074900 -5.88302800

H -0.07576100 0.06789800 -6.14997100
 H 0.03377600 1.78865300 -6.48392800
 C -1.99013300 1.08977600 -6.19602000
 H -2.54048700 0.32518800 -5.63956900
 H -2.41673800 2.06233900 -5.93359200
 H -2.17236800 0.91923200 -7.26028500
 C -1.70426600 0.61097600 -2.41119400
 C -2.19528000 -0.37942200 -1.55662300
 N -2.06040000 1.89906500 -2.30658500
 C -3.07542300 -0.01494000 -0.54557800
 C -2.90886700 2.23905300 -1.33380300
 C -3.44046700 1.32366600 -0.42682700
 H -1.87829500 -1.40385600 -1.69564700
 H -3.46980500 -0.75819300 0.13704800
 H -3.17747600 3.28926500 -1.27481400
 H -4.12248600 1.65577500 0.34577500
 C -0.74706600 0.22472200 -3.50842600
 O -0.48702300 -0.95915400 -3.69747800
 Na 1.96447900 -1.11438200 -3.09967200
 H 1.43950200 1.59360300 -1.69833600
 O 1.26776500 0.82566400 -2.25017900

Int2'₃₋₄

37

E(RB3LYP) = -1062.48337846
 C 1.76087600 1.33813900 -0.40466700
 C 2.83909800 1.47214900 -1.27904500
 C 1.21449500 2.49168100 0.16820600
 C 3.36724100 2.72950500 -1.57682600
 C 1.73770900 3.74956100 -0.12383000
 C 2.81741700 3.87358600 -1.00079800
 H 3.25740700 0.57241000 -1.71223100
 H 0.38298300 2.39980700 0.85674100
 H 4.20695700 2.81568700 -2.25816700

H 1.30662600 4.63354900 0.33351900
 H 3.22524300 4.85180600 -1.22951500
 C 1.18546600 -0.06432100 -0.10689400
 O 1.96056100 -1.05174200 -0.50368400
 C -0.30412500 -0.09792800 -0.70143500
 H -0.80780600 0.81199100 -0.38279800
 C -0.28037400 -0.16648100 -2.23086400
 H 0.16924100 -1.11164900 -2.54369700
 H 0.37789500 0.62645200 -2.59640700
 C -1.66891900 -0.01115500 -2.85580100
 H -2.34371300 -0.81168500 -2.53728200
 H -2.12490700 0.94030900 -2.56645000
 H -1.61445700 -0.03852000 -3.94760900
 C -2.04922000 -1.01008800 0.98160500
 C -2.49848500 -2.07885000 1.76237000
 N -2.50707900 0.24140300 1.13378800
 C -3.44840700 -1.83615500 2.74688100
 C -3.42726900 0.46183000 2.07447600
 C -3.92542500 -0.53843600 2.90883600
 H -2.09695600 -3.06800300 1.58979100
 H -3.81001400 -2.64115300 3.37537200
 H -3.78331900 1.48291800 2.16977600
 H -4.66664200 -0.30034000 3.66137900
 C -1.02070000 -1.26093300 -0.08702100
 O -0.77809200 -2.42433000 -0.40939300
 Na 1.40088400 -3.12022900 -0.90208400
 H 1.79365400 -0.38320200 1.72305500
 O 0.93565500 -0.12353800 1.36583000

TS2'₃₋₄

37

E(RB3LYP) = -1062.47737444
 C 1.73109600 1.35715800 -0.33812400
 C 2.68690800 1.52278700 -1.34252200

C 1.15709600 2.49450100 0.23972300
 C 3.06367500 2.79759500 -1.76451100
 C 1.52955500 3.76880200 -0.17997200
 C 2.48472400 3.92586400 -1.18622100
 H 3.13084200 0.63808300 -1.78029800
 H 0.41245100 2.38778500 1.01958100
 H 3.80925600 2.90917500 -2.54402500
 H 1.07657300 4.64058100 0.27881900
 H 2.77456500 4.91801000 -1.51284000
 C 1.33934200 -0.05268000 0.08784700
 O 2.03959900 -1.01754100 -0.35038100
 C -0.43547000 -0.12376400 -0.77662500
 H -0.89016500 0.82004900 -0.49137500
 C -0.14303000 -0.24883700 -2.25692500
 H 0.42758400 -1.16326300 -2.43426000
 H 0.49707700 0.58134100 -2.56606300
 C -1.41275200 -0.25617900 -3.11862300
 H -2.05953200 -1.09928000 -2.86045900
 H -1.98859700 0.66313800 -2.97485600
 H -1.16647100 -0.33367500 -4.18227500
 C -1.90803800 -1.02184900 1.06702100
 C -2.90733600 -1.94050400 1.39525500
 N -1.68859200 0.08787800 1.79421300
 C -3.71724700 -1.68626300 2.49640200
 C -2.45634200 0.31320200 2.86383300
 C -3.49084900 -0.53634100 3.24851800
 H -3.03510800 -2.82480600 0.78597300
 H -4.50947900 -2.37432500 2.76656300
 H -2.23277800 1.20770500 3.43597400
 H -4.09375000 -0.30146100 4.11631000
 C -1.03753300 -1.25737300 -0.13782600
 O -0.83423500 -2.44360600 -0.48941100
 Na 1.38082100 -3.13194000 -0.56162400
 H 0.18390800 0.25656700 1.66855300

O 1.06573000 -0.12248500 1.47975700

Int3₃₋₄

37

E(RB3LYP) = -1062.50241663

C 1.88088300 1.10160900 0.26529000
 C 2.10076100 1.48120900 -1.06250600
 C 1.18217200 1.95682400 1.12291700
 C 1.61292100 2.69426100 -1.53261500
 C 0.70677900 3.17841800 0.65493300
 C 0.91524000 3.54505700 -0.67418700
 H 2.63299500 0.80675000 -1.72019200
 H 1.02053100 1.67447200 2.15449400
 H 1.76751300 2.97412900 -2.56783000
 H 0.17277500 3.84155000 1.32506200
 H 0.53452700 4.49137000 -1.04069800
 C 2.39096000 -0.22042600 0.72607100
 O 3.35304600 -0.76945100 0.19764900
 C -1.10775400 -0.13216100 -1.77115300
 H -1.88737100 0.61966400 -1.71771000
 C -0.40346400 -0.31948000 -3.08097500
 H 0.55256600 -0.81768600 -2.89452500
 H -0.16943100 0.65883000 -3.52024400
 C -1.20836100 -1.13791200 -4.10721600
 H -1.41247600 -2.14222700 -3.72473700
 H -2.17090700 -0.66192300 -4.31924300
 H -0.66665600 -1.23737500 -5.05433700
 C -1.49394800 -0.45575700 0.62505500
 C -2.85831900 -0.12857500 0.66452100
 N -0.77606800 -0.47070200 1.76806600
 C -3.45903700 0.19262000 1.87179400
 C -1.35592900 -0.15464000 2.93462200
 C -2.69547300 0.18172100 3.04151200
 H -3.43322800 -0.14835900 -0.25096700

H -4.51408700 0.43813900 1.90780500
H -0.71006000 -0.17199500 3.80648600
H -3.12589600 0.42056900 4.00499300
C -0.77459800 -0.82635300 -0.64155900
O 0.14896900 -1.73437300 -0.54001700
Na 1.80950200 -2.85926600 0.26826700
H 0.70700900 -0.63378900 1.74337600
O 1.76383800 -0.80848000 1.73637700

Int4'₃₋₄

37

E(RB3LYP) = -1062.50510829
C 2.72111100 0.97051000 -0.62745400
C 3.84274000 0.45400300 0.03093000
C 2.82352000 2.17376400 -1.33527200
C 5.05502400 1.13316000 -0.01768600
C 4.03829500 2.85120300 -1.38195200
C 5.15387100 2.33271800 -0.72423300
H 3.75009700 -0.47753200 0.57416100
H 1.95493600 2.57007700 -1.84339600
H 5.92146900 0.73043500 0.49301500
H 4.11548800 3.78214400 -1.93063800
H 6.09880200 2.86199900 -0.76230600
C 1.44022700 0.21495500 -0.55411000
O 1.33486100 -0.84337400 0.05146400
C -2.20827500 -0.34996500 -1.45388500
H -2.62294600 0.64950300 -1.36882500
C -2.05545800 -0.92435600 -2.83680300
H -1.37099500 -1.77702000 -2.79326800
H -1.59673100 -0.18381900 -3.50370100
C -3.38777500 -1.38404100 -3.45615700
H -3.85142500 -2.15850300 -2.83884100
H -4.09210000 -0.54950600 -3.52848500
H -3.24289600 -1.79083400 -4.46284800

C -2.30257400 -0.42176900 1.02068900
C -3.30203200 0.54099800 1.21220600
N -1.50256700 -0.80790100 2.03535100
C -3.46334800 1.12154900 2.46401900
C -1.65801000 -0.23465100 3.23454600
C -2.62012600 0.73281700 3.50320700
H -3.95147300 0.81264200 0.39097900
H -4.23910500 1.86026000 2.62947200
H -0.98204700 -0.56868700 4.01620000
H -2.70862500 1.15784900 4.49495200
C -2.06770500 -1.11144500 -0.31094100
O -1.66327800 -2.33220200 -0.25940700
Na 0.10983000 -2.45252800 1.15614300
H -0.42659600 0.27806200 -1.13415100
O 0.44098000 0.79584300 -1.20155700

TS3'₃₋₄

37

E(RB3LYP) = -1062.50151456
C 3.79880200 0.48778100 -1.44110200
C 4.89101900 -0.05429900 -0.75573800
C 3.93915900 1.71534900 -2.09728300
C 6.10786500 0.62045800 -0.72651400
C 5.15643000 2.39087000 -2.06729000
C 6.24224400 1.84495600 -1.38228800
H 4.77218200 -1.00494700 -0.25202200
H 3.09141200 2.13034500 -2.62599600
H 6.95032200 0.19453600 -0.19416000
H 5.25897900 3.34164700 -2.57716600
H 7.18952900 2.37126500 -1.35974400
C 2.49465100 -0.25904100 -1.45753900
O 2.39093100 -1.33888700 -0.85977200
C -0.89556200 -0.74083200 -2.24207600
H -1.42577400 0.20824600 -2.17727500

C -0.89497400 -1.40253900 -3.60579600
 H -0.20357400 -2.25058100 -3.58763700
 H -0.50589300 -0.69961900 -4.35102200
 C -2.28228900 -1.89075600 -4.05014800
 H -2.67795500 -2.62463600 -3.34260500
 H -2.99070500 -1.05782200 -4.09868200
 H -2.24543700 -2.35854600 -5.03946100
 C -1.12223700 -0.83177400 0.25327100
 C -2.08701400 0.16323600 0.42756500
 N -0.34226400 -1.24936800 1.26880800
 C -2.24816200 0.73996500 1.68344700
 C -0.49118000 -0.67604900 2.46710200
 C -1.43041400 0.31841500 2.72751700
 H -2.71027900 0.46573100 -0.40314100
 H -2.99992600 1.50374500 1.84363700
 H 0.16817900 -1.02925700 3.25390700
 H -1.51623400 0.74222300 3.71994900
 C -0.90045200 -1.53605900 -1.07567900
 O -0.58717800 -2.75559000 -1.02379700
 Na 1.28714900 -2.88802100 0.35608300
 H 0.47040400 -0.23248100 -2.07969400
 O 1.54337400 0.31309900 -2.12436000

Int5'₃₋₄

37

E(RB3LYP) = -1062.53216807
 C 2.18533100 0.40795100 -0.35481200
 C 2.92312500 0.19368900 0.81332100
 C 1.97376300 1.72024400 -0.78669100
 C 3.43795300 1.26699700 1.53665900
 C 2.48501100 2.79728000 -0.06653900
 C 3.21739000 2.57327900 1.09929200

H 3.07728000 -0.82438300 1.14739900
 H 1.39298000 1.87975700 -1.68617700
 H 4.00514800 1.08731900 2.44331300
 H 2.30768900 3.81083200 -0.40888700
 H 3.61248900 3.41057200 1.66366200
 C 1.58202800 -0.76289000 -1.12270500
 O 1.76769000 -1.91917400 -0.63299500
 C -2.42651700 -0.31480900 -2.01609900
 H -3.14807000 0.44279900 -1.69239300
 C -3.08362600 -1.30182800 -2.98035700
 H -2.37798800 -2.10567300 -3.20521000
 H -3.27546000 -0.77857700 -3.92171700
 C -4.39354700 -1.88830900 -2.44729800
 H -4.23126100 -2.43919900 -1.51823200
 H -5.12236500 -1.09631800 -2.24770400
 H -4.83848700 -2.57573900 -3.17146100
 C -1.25111400 -0.05965500 0.28463000
 C -1.35770900 1.32887300 0.23583100
 N -0.62666700 -0.69523900 1.29434000
 C -0.79596500 2.08524500 1.26187500
 C -0.09295400 0.03651400 2.27005400
 C -0.15260700 1.43011200 2.30089100
 H -1.84933000 1.81906000 -0.59195800
 H -0.85145000 3.16621400 1.23753000
 H 0.41677000 -0.50777400 3.05809100
 H 0.31235800 1.97597200 3.11102800
 C -1.79526300 -0.95408200 -0.80317300
 O -1.68719600 -2.16631900 -0.69552100
 Na 0.16888100 -2.94827900 0.57884900
 H -1.61172400 0.22695400 -2.51033100
 O 0.92726200 -0.49990400 -2.15689200

8-5-7. Reactants/products with (CH₃ONa)₄

(CH₃ONa)₄

24

E(RB3LYP) = -1110.23826938

O -0.00344600 -0.03210300 -2.07316800

O 1.67539900 -0.94207800 0.69327900

Na -0.00593000 -1.77528600 -0.60271400

Na 1.52470300 0.88785900 -0.65564300

Na -0.01276300 0.03745200 1.86324900

O -1.69396800 -0.94427900 0.68501300

O -0.01091400 1.96342100 0.64010600

Na -1.53845300 0.88710100 -0.66252800

C -0.00353400 3.26938100 1.10452400

H -0.78291400 3.46688000 1.86990800

H 0.95675000 3.56028100 1.57944500

H -0.17733600 4.02020200 0.30576500

C -2.83174900 -1.60404100 1.12304100

H -3.49685100 -1.92733600 0.29513600

H -2.60962200 -2.52577200 1.70029700

H -3.46855900 -0.98507500 1.78883300

C 2.80724400 -1.60711300 1.13862200

H 2.57782000 -2.54263000 1.69031600

H 3.48998100 -1.90885300 0.31696700

H 3.42805600 -1.00100100 1.83081200

C -0.00017300 -0.06609300 -3.45885500

H 0.88340500 -0.58768100 -3.88242800

H -0.88290300 -0.58566200 -3.88665200

H 0.00208800 0.94243100 -3.92259600

1_{enol}-Na(CH₃ONa)₃

41

E(RB3LYP) = -1458.16655178

O 2.26324900 -1.88796800 -1.85612900

O 3.61153000 -0.93314300 1.07574400

Na 3.37359300 -2.86388700 -0.11691200

Na 2.42763100 -0.00145400 -0.63203300

Na 1.67349500 -1.58800500 2.05813000

O 1.47491500 -3.53971100 0.94075000

Na 0.38515700 -2.35735900 -0.66970700

C 1.07126900 -4.76183700 1.45810000

H 0.01781500 -4.76130400 1.80725600

H 1.14023500 -5.59123200 0.72442600

H 1.67300000 -5.08774300 2.33144000

C 4.68097000 -0.33332300 1.72352800

H 4.43824500 0.67378700 2.12339000

H 5.04962900 -0.91612200 2.59261000

H 5.56403500 -0.18673900 1.06825200

C 2.46009300 -2.08679600 -3.21480500

H 3.50105000 -1.88296200 -3.54032500

H 2.24637500 -3.12620200 -3.53960600

H 1.81913600 -1.44031700 -3.84899300

C 0.03095800 1.85434300 1.26789800

C 1.37150600 2.03239300 1.64885700

C -0.78357000 2.99503000 1.18710800

C 1.87165700 3.29619900 1.95741400

C -0.28436200 4.25918000 1.49095600

C 1.04681000 4.41820000 1.88072400

H 2.02480200 1.16860300 1.70615900

H -1.81278800 2.89201100 0.86484500

H 2.90857200 3.40388900 2.25695300

H -0.93249800 5.12511100 1.41152500

H 1.43613700 5.40294600 2.11219800

C -0.46991900 0.47553100 0.94576800

O 0.43261900 -0.37416600 0.49544800

C -1.77234200 0.14616100 1.16948100

H -2.45296000 0.89197400 1.56462100

C -2.31934600 -1.23355100 0.91865400

H -1.57359600 -1.98263900 1.21636400
H -2.48811900 -1.40174900 -0.15739300
C -3.62933500 -1.50557900 1.66469300
H -3.48831200 -1.41284800 2.74600200
H -4.40347600 -0.78983000 1.37040700
H -4.00775100 -2.51082700 1.45854100

3_{enol}-Na(CH₃ONa)₃

40

E(RB3LYP) = -1474.20866274
O 2.74147700 -0.76224900 -2.07119300
O 3.19162800 -1.93179600 1.05024400
Na 3.01717000 -2.78041000 -1.06047100
Na 2.78527000 0.04960400 0.05143300
Na 0.95026000 -2.19843500 1.12399800
O 0.78133700 -3.21361800 -0.89160500
Na 0.51920000 -1.15625000 -1.80554400
C 0.10860500 -4.38027600 -1.22403200
H -0.99273800 -4.25267600 -1.26924800
H 0.40072500 -4.78615700 -2.21465300
H 0.28149700 -5.20584200 -0.50303400
C 4.12283100 -2.21071500 2.04046600
H 4.11661800 -3.27357200 2.35836400
H 5.16677900 -1.99984300 1.73000700
H 3.96389800 -1.62250300 2.96752000
C 3.34060700 -0.17267100 -3.17415300
H 3.01621800 0.87638200 -3.33469900
H 4.44707300 -0.13472800 -3.10347900
H 3.12167300 -0.70041900 -4.12509800
C -0.01637700 2.16573700 -0.18496300
H -0.57964500 3.03577500 0.13153700
C 0.84874500 2.30193200 -1.40501100
H 1.44921500 1.39953500 -1.55047300
H 1.55848200 3.13119500 -1.27710400

C 0.04101200 2.55615400 -2.69046800
H -0.63657100 1.72082300 -2.89266700
H -0.56861100 3.46017900 -2.59886600
H 0.69914000 2.67776100 -3.55684400
C -1.16207000 0.99573900 1.66015800
C -1.74506800 -0.22053900 2.04953900
N -1.47266000 2.14834700 2.28574000
C -2.65724300 -0.24353800 3.09664900
C -2.34764800 2.11283300 3.29393000
C -2.96730500 0.94925800 3.74557200
H -1.49388700 -1.12144500 1.50788400
H -3.12169000 -1.17516400 3.40006100
H -2.56327000 3.06474700 3.77199200
H -3.66533300 0.98321300 4.57267400
C -0.18270300 1.01284300 0.52098800
O 0.42046500 -0.13435000 0.26520400

5wA-(CH₃ONa)₄

58

E(RB3LYP) = -1934.50358037
O -0.05107900 -0.18125800 -2.05253100
O 0.99961200 0.81522700 0.94674900
Na 0.67047800 -1.15685700 -0.15216400
Na 0.11446300 1.75438500 -0.92485400
Na -1.11602800 0.49757100 1.68750100
O -1.39555300 -1.50026800 0.71493300
O -2.04080200 1.87738000 0.01008500
Na -2.13640300 -0.32518200 -1.11141600
C -1.84940500 3.06444100 0.71121100
H -2.31558300 3.93597500 0.22158200
H -2.26712500 3.03914700 1.73552500
H -0.77826700 3.32590500 0.83707800
C -2.10918600 -2.58480700 1.19957900
H -2.40162100 -3.30528500 0.40814100

H -1.54823400 -3.17839500 1.95033000
 H -3.05820500 -2.29618600 1.69919700
 C 2.08224500 1.32546200 1.64632100
 H 2.38537800 0.69394000 2.50701700
 H 2.99449400 1.43419300 1.02361700
 H 1.89167800 2.33337800 2.07096400
 C 0.13258800 -0.34723700 -3.41611500
 H 0.97578900 0.25104700 -3.82065100
 H 0.34935100 -1.39646900 -3.70358900
 H -0.75485200 -0.05235000 -4.01222700
 C -2.61299600 3.40627400 -2.55297100
 C -1.43526400 3.19582600 -3.28842300
 C -2.95296900 4.71016700 -2.17634600
 C -0.60185200 4.25907000 -3.60756800
 C -2.12601500 5.78077000 -2.51661100
 C -0.94627600 5.55819300 -3.22124400
 H -1.18405300 2.18400100 -3.58145200
 H -3.86342200 4.90662200 -1.62690300
 H 0.31405600 4.08156100 -4.15928100
 H -2.40246400 6.78641900 -2.22283700
 H -0.29850900 6.38978500 -3.47306400
 C -3.44030000 2.20798100 -2.21888400
 O -3.21721600 1.14173200 -2.78035500
 C -4.62803400 2.34293600 -1.27032400
 H -4.63619700 3.31826400 -0.79675800
 C -5.93803700 2.15326600 -2.07559300
 H -5.92965200 1.14704200 -2.50106600
 H -5.92712000 2.85617700 -2.91465200
 C -7.19748600 2.37354500 -1.23768800
 H -7.26777300 1.65024900 -0.42074600
 H -7.20913700 3.37349100 -0.79693900
 H -8.09170200 2.26429600 -1.85645600
 C -4.64295800 1.76009600 1.26414100
 C -4.38571100 0.84401700 2.28966600

N -4.99733300 3.02939100 1.49696000
 C -4.47209400 1.27596500 3.60561000
 C -5.10040000 3.42883700 2.76881800
 C -4.84020400 2.59784300 3.85489900
 H -4.11506300 -0.17276500 2.03709200
 H -4.26204300 0.59694100 4.42351500
 H -5.39693900 4.46123500 2.92559800
 H -4.92511400 2.97799400 4.86512500
 C -4.53099400 1.29954600 -0.16242200
 O -4.48946400 0.10100900 -0.40618800

5wA_{enol}-Na(CH₃ONa)₃

52

E(RB3LYP) = -1818.73596082

O 0.20348200 3.31482700 -4.96654500
 O 2.85303400 4.42088400 -3.24091800
 Na 2.46038000 3.20186400 -5.11330100
 Na 0.58417800 4.49982100 -3.06869600
 Na 2.84064900 2.41437800 -2.19048400
 O 2.64597800 1.18682500 -4.07250400
 Na 0.36511600 1.28170700 -3.90816300
 C 3.35232400 0.05605200 -4.45401600
 H 3.07837300 -0.31012700 -5.46532000
 H 4.45058700 0.21402800 -4.48417200
 H 3.19584100 -0.80736700 -3.77455700
 C 3.62309400 5.51259500 -2.86976900
 H 4.69928300 5.27013400 -2.75029200
 H 3.58657200 6.34376400 -3.60386900
 H 3.31002400 5.95748500 -1.90162100
 C -0.81966600 3.58209400 -5.86416600
 H -0.54652900 3.36670700 -6.91793600
 H -1.73781900 2.98927500 -5.66938500
 H -1.14613400 4.64317700 -5.85479000
 C -3.25340200 0.13013000 -1.44740300

C -4.40299300 0.87831500 -1.71527800
 C -3.38106400 -1.22680800 -1.13816000
 C -5.66127200 0.28023800 -1.67089900
 C -4.63933600 -1.82167400 -1.07407200
 C -5.78330900 -1.06946100 -1.34170200
 H -4.31219100 1.92877300 -1.96847300
 H -2.49107200 -1.81439500 -0.94339000
 H -6.54512900 0.86808200 -1.89093600
 H -4.72697300 -2.87187000 -0.81986300
 H -6.76214600 -1.53274400 -1.29806300
 C -1.87622900 0.74010200 -1.58958500
 O -1.19760800 0.29241600 -2.54258800
 C -1.47140000 1.76055700 -0.66226000
 C -2.35892100 2.07752200 0.53406400
 H -3.39862800 2.17565200 0.21661100
 H -2.08916900 3.05421800 0.93864200

C -2.29564200 1.03387200 1.65971500
 H -2.63397000 0.05735500 1.30533300
 H -1.27470200 0.91231900 2.03191000
 H -2.93109500 1.32531600 2.50181400
 C 0.14523300 3.59160300 0.05993900
 C 0.46990700 3.39971800 1.40270800
 N 0.30621500 4.78014500 -0.55216900
 C 0.97099700 4.47115900 2.13628800
 C 0.76907300 5.80861400 0.16681200
 C 1.11854800 5.70538800 1.51072200
 H 0.34204900 2.42698600 1.85800900
 H 1.24143800 4.34319600 3.17778300
 H 0.87295700 6.75239200 -0.35896000
 H 1.50040100 6.56701300 2.04327300
 C -0.27141000 2.46527600 -0.86888200
 O 0.54139000 2.31804100 -1.83563300

8-5-8. Enolization of 5wA with (CH₃ONa)₄

Int1_{enol}-(CH₃ONa)₄

58

E(RB3LYP) = -1934.49091195

O 2.28395500 -1.05723300 -1.16175900
 O 3.36174600 0.17590000 1.73388100
 Na 3.19791300 -1.81829600 0.75818900
 Na 2.28996700 0.97827200 -0.13728900
 Na 1.14110100 -0.15658400 2.25707000
 O 1.12217300 -2.32851600 1.57337500
 O 0.40857100 1.58567300 0.97932600
 Na 0.42178000 -2.14835600 -0.53552100
 C 0.23569200 2.84774100 1.51581900
 H 0.01315400 3.62526800 0.75183500
 H -0.60724200 2.90931900 2.24039300
 H 1.12258200 3.22185800 2.06841600
 C 0.85859100 -3.33711800 2.49028700

H 1.70564200 -4.04311900 2.61506400
 H 0.63451300 -2.95542100 3.50717500
 H -0.01532000 -3.96074500 2.21574000
 C 4.17370400 0.97634400 2.52048100
 H 4.43809700 0.51251300 3.49363800
 H 5.14233100 1.22656400 2.03975400
 H 3.70948500 1.95310300 2.77512900
 C 2.68670600 -0.97377900 -2.48884900
 H 2.70833700 0.06501600 -2.87372400
 H 3.70396800 -1.38193200 -2.66098700
 H 2.02093900 -1.52252500 -3.18460300
 C -0.34786800 1.03335300 -2.71400400
 C -0.09782000 0.62130400 -4.02778200
 C 0.24134300 2.20951700 -2.23071700
 C 0.71428600 1.38597900 -4.85791800
 C 1.08300900 2.95193400 -3.05372100

C 1.31085100 2.54891700 -4.37036700
 H -0.54832800 -0.29515500 -4.38741000
 H 0.08873500 2.49754300 -1.19773700
 H 0.89270700 1.07069700 -5.87907500
 H 1.55834900 3.84688400 -2.66957700
 H 1.95513400 3.13753100 -5.01303100
 C -1.19580300 0.17196300 -1.84379600
 O -1.17697100 -1.04790200 -1.98512200
 C -2.01725600 0.82499200 -0.74661800
 H -1.24100600 1.17192400 -0.03049900
 C -2.87462500 2.01926400 -1.22147800
 H -3.66766800 1.64198800 -1.87264800
 H -2.25910200 2.68792300 -1.82287700
 C -3.47752700 2.79598500 -0.04977200
 H -4.12556300 2.16335900 0.56357000
 H -2.69256900 3.19972600 0.59540600
 H -4.08091300 3.63206600 -0.41148100
 C -2.55763600 -0.76111800 1.26018200
 C -2.05725700 0.10172000 2.23673700
 N -2.83030500 -2.05524200 1.49780500
 C -1.86909800 -0.39182200 3.52676000
 C -2.59934800 -2.52425700 2.72303200
 C -2.13498000 -1.73182800 3.77525200
 H -1.81279700 1.12523000 1.99720900
 H -1.50731700 0.25880400 4.31441900
 H -2.79596400 -3.58002800 2.87986600
 H -1.98361400 -2.16473400 4.75580700
 C -2.90558800 -0.24560500 -0.10958200
 O -3.89020600 -0.66155100 -0.68722000

TS1_{enol}-(CH₃ONa)₄

58

E(RB3LYP) = -1934.48264834

O 0.00019200 0.48814100 -1.50006000

O 0.68012300 1.98255600 1.38223700
 Na 0.84513800 -0.08672600 0.50510000
 Na -0.28807600 2.53850400 -0.59320500
 Na -1.45875000 1.35927400 1.87545300
 O -1.20072000 -0.78415000 1.24548500
 O -2.34465500 3.00946000 0.46522200
 Na -1.90322000 -0.56524800 -0.86986200
 C -2.28904000 4.25653000 1.10893700
 H -2.38612800 5.10106900 0.40580900
 H -3.08539900 4.38008000 1.86278900
 H -1.33061000 4.38461100 1.63311900
 C -1.40629900 -1.89260200 2.05512800
 H -0.51286500 -2.54665300 2.12926000
 H -1.67265400 -1.62889300 3.09845300
 H -2.22878800 -2.54580200 1.70163100
 C 1.43944700 2.81765100 2.18595700
 H 1.68339000 2.37304800 3.17304200
 H 2.41555200 3.09111200 1.73485700
 H 0.93678800 3.78181800 2.41153400
 C 0.36214700 0.46355400 -2.84172700
 H 0.37477400 1.46765900 -3.30900500
 H 1.37118000 0.03561900 -3.01141400
 H -0.32839700 -0.13548700 -3.46923600
 C -2.84850900 2.50696700 -3.01906900
 C -2.65041300 1.88844100 -4.25874000
 C -2.21864500 3.73230500 -2.76303700
 C -1.85615200 2.48858400 -5.23075600
 C -1.39619500 4.31551800 -3.72333900
 C -1.22121000 3.70068400 -4.96356000
 H -3.12504100 0.93410400 -4.44850600
 H -2.34210200 4.20823600 -1.79947900
 H -1.72081900 2.00469900 -6.19097000
 H -0.89524800 5.25150500 -3.50478100
 H -0.59002800 4.16175500 -5.71426600

C -3.68271500 1.78824800 -1.99846300
 O -3.60459500 0.54493600 -1.96276300
 C -4.48777200 2.54257500 -1.03737800
 H -3.47127000 2.83086000 -0.22858900
 C -5.18989100 3.82113900 -1.52922100
 H -6.04731200 3.54237400 -2.15018700
 H -4.51872300 4.38919400 -2.17078700
 C -5.66979000 4.71720900 -0.38390000
 H -6.36315900 4.18627100 0.27381600
 H -4.83127300 5.06541800 0.22350400
 H -6.19277900 5.59565300 -0.77211700
 C -5.02161400 0.78259100 0.83681900
 C -4.58611200 1.43287300 1.99327900
 N -5.22191500 -0.54063900 0.77548900
 C -4.37248200 0.67601800 3.14296600
 C -4.96736700 -1.25953100 1.87280800
 C -4.55544300 -0.70106900 3.08104400
 H -4.43592400 2.50358000 1.99186100
 H -4.06048400 1.15363400 4.06473600
 H -5.10805300 -2.33231800 1.78574900
 H -4.38160300 -1.33271400 3.94244600
 C -5.45934000 1.61438400 -0.34845300
 O -6.63853700 1.55907600 -0.66087700

Int2_{enol}-(CH₃ONa)₄

58

E(RB3LYP) = -1934.51964266
 O 3.07258100 -0.25084500 -1.14589000
 O 2.85835100 0.54026200 2.00577300
 Na 3.63405700 -1.20747100 0.84602000
 Na 2.38781500 1.54819400 0.04471200
 Na 0.78779600 -0.44928200 1.66059900
 O 1.74142800 -2.42533700 0.96412700
 O 0.24309600 1.98663200 1.08923200

Na 1.32458300 -1.69911300 -1.12209200
 C 0.15322000 3.08377700 2.00425200
 H 0.01270600 4.03034100 1.47417800
 H -0.67079400 2.94281500 2.70965800
 H 1.09070400 3.11485600 2.55682300
 C 1.34708600 -3.62051800 1.54640400
 H 2.07094600 -4.44544700 1.38440800
 H 1.21791900 -3.54875200 2.64637500
 H 0.37502600 -3.99339700 1.16371300
 C 3.03146000 1.11707800 3.25295300
 H 2.09629300 1.15959100 3.85149500
 H 3.76277700 0.57684600 3.88841000
 H 3.39633600 2.16467300 3.20722200
 C 3.75987200 -0.07470500 -2.34204700
 H 4.61102000 0.63201400 -2.25606700
 H 4.19625700 -1.01553100 -2.73603100
 H 3.12058000 0.32330800 -3.15445800
 C -0.64624400 0.62005300 -2.43634100
 C -0.78271900 -0.39843200 -3.38568400
 C 0.06200100 1.77556000 -2.77809700
 C -0.22742300 -0.25991300 -4.65677800
 C 0.62740000 1.90978600 -4.04474100
 C 0.48177200 0.89424500 -4.98877800
 H -1.32818500 -1.29919800 -3.12570600
 H 0.18144400 2.56813700 -2.04927100
 H -0.34721600 -1.05303300 -5.38601100
 H 1.18356800 2.80645600 -4.29307500
 H 0.92044800 0.99956800 -5.97406700
 C -1.16056200 0.38820100 -1.03511000
 O -0.48272500 -0.45085700 -0.36446700
 C -2.27960500 1.11289200 -0.57320200
 H -0.58966800 1.91677700 0.59117000
 C -2.92063700 2.20928300 -1.40386500
 H -4.00724000 2.11786800 -1.31669100

H -2.67531800 2.06733800 -2.45813100
 C -2.52025200 3.62975900 -0.97501800
 H -2.75558400 3.79055100 0.07931900
 H -1.44863100 3.79956500 -1.11329000
 H -3.05360800 4.38505600 -1.56068000
 C -2.56016200 -0.40228300 1.48980500
 C -2.07341800 -0.24414700 2.79128800
 N -2.82064700 -1.60243300 0.95499600
 C -1.77421200 -1.38025200 3.53747300

C -2.55368400 -2.68551300 1.69263200
 C -2.00914300 -2.63199000 2.97344800
 H -1.92453700 0.74886600 3.19675900
 H -1.36924900 -1.29081500 4.53891500
 H -2.78041000 -3.64401100 1.23539300
 H -1.78584300 -3.54431300 3.51127700
 C -2.92562500 0.81986400 0.67516400
 O -3.84722200 1.51811100 1.14435400

8-5-9. Formation of enolate of 1 and 2 with (CH₃ONa)₄

Int1₁₋₂-(CH₃ONa)₄

58

E(RB3LYP) = -1934.50354252

O 2.20406200 -1.78835300 -1.77781200
 O 3.20768400 -0.94240800 1.26661800
 Na 2.98144700 -2.83469900 0.05495900
 Na 2.24793800 0.08379300 -0.52757300
 Na 1.02620500 -1.29638100 1.84935000
 O 0.93369700 -3.32257100 0.81951200
 O 0.28060800 0.53877400 0.62164100
 Na 0.07708300 -2.28188800 -1.03843300
 C 0.60783100 1.70768400 1.30507400
 H 0.30267300 2.62020900 0.76430400
 H 0.13936800 1.76638700 2.30342000
 H 1.69839000 1.79586800 1.47724500
 C 0.19065100 -4.36131500 1.35815900
 H 0.35127000 -5.32926700 0.83981500
 H 0.41958200 -4.55758600 2.42681200
 H -0.90344300 -4.17909600 1.31812300
 C 4.15042700 -0.31963200 2.06788900
 H 4.45673000 -0.93069500 2.94236200
 H 5.09214200 -0.07859800 1.53176400
 H 3.79543200 0.64450400 2.48992500

C 2.41713300 -1.78786000 -3.14686600
 H 3.19832800 -1.06743100 -3.46986500
 H 2.74384300 -2.77283700 -3.53932700
 H 1.50961300 -1.52076300 -3.72592900
 C -0.18754600 1.88188400 -2.09309200
 C 0.93058100 1.71035100 -2.92654800
 C -0.50706200 3.16987400 -1.64703800
 C 1.72261500 2.79451800 -3.28071100
 C 0.27859900 4.26013600 -2.01825400
 C 1.39713500 4.07590300 -2.82715500
 H 1.16704000 0.71236500 -3.27357800
 H -1.36625100 3.33655900 -1.01274300
 H 2.59067800 2.64619800 -3.91254200
 H 0.01888200 5.25202100 -1.66775600
 H 2.01172900 4.92386100 -3.10612800
 C -0.97494900 0.66335800 -1.73462400
 O -0.71994400 -0.40142800 -2.28846600
 C -2.13635300 0.75079300 -0.76262400
 H -2.25525100 1.76016800 -0.38647600
 C -3.44016900 0.31678700 -1.47547600
 H -3.31606900 -0.71477300 -1.81268600
 H -3.55863500 0.93402000 -2.37206700
 C -4.68585800 0.44683400 -0.59820200

H -4.63406800 -0.21045400 0.27377700
H -4.80916700 1.47014700 -0.23442700
H -5.58138200 0.17754500 -1.16404000
C -2.18765500 0.40254500 1.80683300
C -2.13044700 -0.44996600 2.91459700
N -2.53402000 1.69209800 1.91012600
C -2.41542100 0.06388100 4.17247700
C -2.81741400 2.17451600 3.12398400
C -2.76707700 1.40798400 4.28492900
H -1.87349800 -1.49076700 2.76903400
H -2.37265200 -0.57136300 5.04942500
H -3.09614200 3.22292000 3.17045600
H -3.00175900 1.85218900 5.24406100
C -1.87197900 -0.15426700 0.44253900
O -1.69733700 -1.36538600 0.31008300

TS1₁₋₂-(CH₃ONa)₄

58

E(RB3LYP) = -1934.50340260

O -0.12808900 -0.16888200 -2.27227500
O 0.78903000 0.54733000 0.80404200
Na 0.64734400 -1.29613300 -0.48300700
Na -0.09577500 1.66158800 -0.96713100
Na -1.43883700 0.15281800 1.25022900
O -1.38661600 -1.89377600 0.20559200
O -2.04152900 2.19505000 0.20811000
Na -2.25682200 -0.76605300 -1.59692900
C -1.70720000 3.37298900 0.87897200
H -2.02820100 4.27811900 0.33837200
H -2.14887700 3.42927200 1.88740600
H -0.61423900 3.45207400 1.01821600
C -2.16166800 -2.90709000 0.74575500
H -2.22708200 -3.80432900 0.09552100
H -1.78352400 -3.27788300 1.72159400

H -3.21195600 -2.59784900 0.93166300
C 1.60894900 1.11278000 1.76662300
H 1.76588800 0.45816400 2.64939800
H 2.62600900 1.35206500 1.39206600
H 1.21137000 2.06712300 2.17285700
C 0.10629600 -0.16473500 -3.63750200
H 0.86443200 0.58381000 -3.95147400
H 0.47640500 -1.13786500 -4.02125000
H -0.80121100 0.06547800 -4.23271800
C -2.51277200 3.43558400 -2.56790000
C -1.39012800 3.26658600 -3.39541900
C -2.84052600 4.72287500 -2.12550800
C -0.60178000 4.35401300 -3.74861100
C -2.05949500 5.81590600 -2.49686700
C -0.93630700 5.63477500 -3.30055500
H -1.14615000 2.26877900 -3.73687500
H -3.70232800 4.88548900 -1.49359700
H 0.27077400 4.20826900 -4.37480700
H -2.32565500 6.80754200 -2.15056400
H -0.32476600 6.48510800 -3.57902100
C -3.29524400 2.21529500 -2.20616000
O -3.05415100 1.15613500 -2.77694300
C -4.40392900 2.28013700 -1.17693500
H -4.58090500 3.30142400 -0.85861500
C -5.70638800 1.69781500 -1.77519000
H -5.51726600 0.65909500 -2.05445300
H -5.92534700 2.24128300 -2.70026500
C -6.91156400 1.78568100 -0.83792300
H -6.76694800 1.18339300 0.06242600
H -7.09465300 2.81567800 -0.52115900
H -7.81095300 1.42035500 -1.34041200
C -4.42080500 2.06028700 1.39974100
C -4.40854700 1.24040800 2.53252400
N -4.80690400 3.34193200 1.44791500

C -4.78601700 1.77753200 3.75642100
 C -5.17582900 3.84789800 2.62870100
 C -5.17842000 3.11345700 3.81134300
 H -4.12171300 0.20222100 2.43326900
 H -4.78332800 1.16495700 4.65042600
 H -5.48374700 4.88925000 2.62919000
 H -5.48479100 3.57507100 4.74160100
 C -3.99754800 1.47963300 0.07054900
 O -3.75697200 0.26361100 -0.00751500

Int2₁₋₂-(CH₃ONa)₄

58

E(RB3LYP) = -1934.51010790
 O 2.32150300 -1.42965200 -1.55846200
 O 2.72560300 -1.49048400 1.75010600
 Na 2.87145700 -2.96777400 0.02050700
 Na 1.96575600 -0.02699700 0.16855000
 Na 0.61404600 -2.23553500 1.89268000
 O 0.75960300 -3.77819600 0.25043100
 O 0.24125700 1.42542600 0.59929900
 Na 0.15546600 -2.13212900 -1.22163400
 C 0.14940900 2.83342800 0.79240900
 H -0.70073100 3.27320700 0.27238400
 H 0.07306500 3.08854800 1.85207100
 H 1.06979700 3.25525600 0.38028900
 C 0.27245700 -5.07613600 0.26233100
 H -0.80240000 -5.13776700 0.53291900
 H 0.35942100 -5.58534600 -0.71993600
 H 0.79755500 -5.73529300 0.98459800
 C 3.63844700 -1.14937500 2.73645500
 H 3.23882700 -0.41675300 3.46810600
 H 3.97606000 -2.01697500 3.34027700
 H 4.56538400 -0.69025900 2.33399800
 C 2.97355400 -1.37253300 -2.77839200

H 3.65071500 -0.49789800 -2.87477300
 H 3.60926100 -2.26051000 -2.97943200
 H 2.28194100 -1.30602400 -3.64449400
 C -0.25065100 1.91927100 -2.38809400
 C 1.05761600 1.72665700 -2.85102400
 C -0.81568200 3.19752600 -2.42581000
 C 1.79716000 2.80538000 -3.32158500
 C -0.08451400 4.27091800 -2.93021900
 C 1.22499100 4.07893100 -3.36801000
 H 1.48627100 0.73385400 -2.80025600
 H -1.83035000 3.35489400 -2.08093700
 H 2.81775200 2.65620700 -3.65480400
 H -0.53343600 5.25619900 -2.97371400
 H 1.79873300 4.91818700 -3.74383900
 C -0.99867500 0.73190500 -1.88325500
 O -0.84446200 -0.35205900 -2.44017900
 C -1.86089500 0.85515300 -0.65642800
 H -2.18358100 1.88861900 -0.52894000
 C -3.08796200 -0.08106800 -0.72489600
 H -2.83395200 -1.02563700 -0.23711600
 H -3.27502200 -0.32827800 -1.77253600
 C -4.36777700 0.50382400 -0.12232000
 H -4.27953800 0.67624200 0.95067800
 H -4.62028100 1.45916400 -0.59288200
 H -5.20814000 -0.17784100 -0.28209000
 C -1.77431300 0.73454400 1.87541500
 C -2.07874100 -0.33670400 2.71604100
 N -2.24634900 1.96746300 2.10472400
 C -2.86524700 -0.11812300 3.84191500
 C -2.99032200 2.17509400 3.19555200
 C -3.32655900 1.16992500 4.09845500
 H -1.73170400 -1.32449500 2.45551400
 H -3.12160800 -0.93923400 4.50156200
 H -3.34539900 3.19033200 3.34831000

H -3.94174200 1.39088600 4.96177400
C -0.93524500 0.49146000 0.60277300
O -0.41834900 -0.72026100 0.53408600

TS2₁₋₂-(CH₃ONa)₄

58

E(RB3LYP) = -1934.49601771

O 0.05012700 0.20715900 -1.91748700
O 0.39684000 0.11422800 1.39250200
Na 0.54758500 -1.35752400 -0.35331000
Na -0.18235100 1.62567300 -0.20178700
Na -1.68184900 -0.70643600 1.59591500
O -1.57790900 -2.13638600 -0.12834700
O -2.05215700 3.02250900 0.26265100
Na -2.13158800 -0.46955100 -1.60769500
C -2.22041600 4.44965300 0.29497400
H -3.17164000 4.74361500 -0.13550900
H -2.15900000 4.81625800 1.31825200
H -1.40444000 4.84673900 -0.30870300
C -2.07516200 -3.42673400 -0.23900100
H -3.17800700 -3.46114100 -0.35727900
H -1.66638300 -3.97930800 -1.11012100
H -1.85211600 -4.05995300 0.64457700
C 1.32263100 0.39545000 2.38759700
H 0.93672400 1.09361800 3.15865600
H 1.65554800 -0.50553400 2.94261100
H 2.25055000 0.86461000 2.00008800
C 0.62243100 0.25236800 -3.17988500
H 1.29303200 1.12406800 -3.32574200
H 1.23931700 -0.63994900 -3.41213700
H -0.12550500 0.31577900 -3.99700700
C -2.79360300 3.39377300 -2.70957000
C -1.44344300 3.15397800 -2.99225600
C -3.31037700 4.67845600 -2.90717800

C -0.62007500 4.18654700 -3.43085600
C -2.49222800 5.70810400 -3.36914600
C -1.14212800 5.46767500 -3.62271400
H -1.04536400 2.15890700 -2.83372100
H -4.35755300 4.87259400 -2.70614900
H 0.42917500 3.99324500 -3.62549200
H -2.90693400 6.69709400 -3.52817700
H -0.50268400 6.27065200 -3.97146800
C -3.63865700 2.26171700 -2.20326300
O -3.41117400 1.10639400 -2.65883200
C -4.56833800 2.49901800 -1.16558300
H -4.81076600 3.53116500 -0.93888300
C -5.66362900 1.48359200 -0.93023800
H -5.30410200 0.66578500 -0.29394600
H -5.91112300 1.00564200 -1.88523300
C -6.92886400 2.09280900 -0.32105000
H -6.72313700 2.57120900 0.63875900
H -7.35210300 2.85292700 -0.98525100
H -7.69422400 1.32930300 -0.15479400
C -4.06674000 2.32874100 1.55854000
C -4.64914600 1.20919300 2.16619100
N -4.37190200 3.57923700 1.92792100
C -5.57992900 1.40155800 3.17985500
C -5.25997200 3.75194800 2.90878200
C -5.89690500 2.70035700 3.56528300
H -4.37656800 0.21864400 1.83406800
H -6.04977200 0.55115700 3.65979800
H -5.47729000 4.78042100 3.18170100
H -6.61635000 2.89942400 4.34941200
C -3.06602700 2.09024100 0.45791500
O -2.67193900 0.91364100 0.25285600

Int3₁₋₂-(CH₃ONa)₄

58

E(RB3LYP) = -1934.50033146	C 1.28373600 3.76341500 -3.09233900
O 2.48329100 -1.32212400 -1.59654900	H 1.18221400 0.46187900 -2.28359200
O 3.00790600 -1.41682600 1.68510400	H -2.02790200 3.29192600 -2.50660300
Na 3.01606900 -2.90309000 -0.05764200	H 2.78367700 2.22415300 -2.94388800
Na 2.47403700 0.12571600 0.10306400	H -0.44021200 5.05119800 -3.18276100
Na 0.96459500 -2.28176300 2.06511200	H 1.98315100 4.53806500 -3.38608600
O 0.88285700 -3.62174600 0.28110600	C -1.46162200 0.65881800 -1.85702600
O 0.44897300 1.60454000 0.73882000	O -1.14816900 -0.55399100 -2.17568000
Na 0.29921000 -1.95219200 -1.19384500	C -2.55479200 0.99705900 -1.08959100
C 0.09756800 3.00937400 0.65684900	H -2.74070200 2.03820900 -0.85340900
H -0.91826600 3.11966000 0.29393400	C -3.59492000 -0.00436600 -0.68382500
H 0.20393300 3.47220900 1.63408000	H -3.17569800 -0.74998200 0.00709500
H 0.80245500 3.42161700 -0.06151400	H -3.90773800 -0.58973100 -1.55943400
C 0.35779000 -4.90018000 0.15152700	C -4.82098500 0.64161000 -0.03478300
H -0.74336500 -4.90754800 0.01745500	H -4.53758000 1.22385200 0.84614400
H 0.76656900 -5.45350800 -0.71879800	H -5.31942000 1.32118100 -0.73351900
H 0.55406300 -5.54574800 1.03230300	H -5.55110900 -0.10833600 0.28321800
C 3.98652000 -1.17842900 2.64141700	C -1.56714900 0.80286200 1.95863300
H 3.66789400 -0.45613400 3.42082100	C -2.29874200 -0.33770700 2.31629500
H 4.29335500 -2.09217300 3.19034400	N -1.83490700 2.02006700 2.45322200
H 4.92146100 -0.76116400 2.21415500	C -3.36803700 -0.19392600 3.19029000
C 3.05278600 -1.33116600 -2.86186900	C -2.86345500 2.14307900 3.29115100
H 4.12112500 -1.03257100 -2.86210500	C -3.66511700 1.07146700 3.68617200
H 3.02067000 -2.32846100 -3.34664400	H -2.02214200 -1.30151600 1.91590300
H 2.55114900 -0.64162200 -3.57036200	H -3.95885300 -1.05486000 3.47817700
C -0.53417800 1.75213700 -2.31731700	H -3.05610000 3.14165300 3.67077900
C 0.82868700 1.46813900 -2.47663300	H -4.49106000 1.23087300 4.36753300
C -0.97367700 3.05585600 -2.58967500	C -0.37550500 0.60788300 1.08371900
C 1.73000500 2.46415500 -2.84543600	O 0.01268600 -0.52508400 0.80092400
C -0.07698400 4.05092000 -2.97312700	

8-5-10. Formation of enolate of 3 and 4 with (CH₃ONa)₄

Int1₃₋₄-(CH₃ONa)₄

58

E(RB3LYP) = -1934.50353105

O 2.29778500 -1.86672200 -1.67832200

O 3.30188500 -0.81276900 1.32196000
 Na 2.95285700 -2.79354600 0.26265600
 Na 2.42117800 0.09745700 -0.57166300
 Na 1.13072800 -1.01210300 1.94949300
 O 0.85635300 -3.05719300 1.03495200
 O 0.33424900 0.50662700 0.40272800
 Na 0.15344100 -2.11528600 -0.93317000
 C 0.59123900 1.76025300 0.95296200
 H -0.32794600 2.34385600 1.12658200
 H 1.10612600 1.70828000 1.93392300
 H 1.22966800 2.39469800 0.30765900
 C 0.02336400 -3.97998500 1.64879400
 H 0.19963900 -5.02172500 1.31095200
 H 0.13481100 -4.00520800 2.75349800
 H -1.05195500 -3.78209000 1.46245200
 C 4.34818000 -0.26501000 2.04729800
 H 4.14789200 0.77294700 2.38696400
 H 4.58993600 -0.83601100 2.96771900
 H 5.29758400 -0.21118500 1.47497100
 C 2.54947900 -1.93023100 -3.04032700
 H 3.42964200 -1.32932400 -3.35202300
 H 2.75233300 -2.95977500 -3.39978200
 H 1.70360600 -1.55947200 -3.65425600
 C -0.18309300 1.92856200 -2.19928000
 C 0.97039200 1.75833400 -2.98062200
 C -0.55375800 3.22178000 -1.81517100
 C 1.74951300 2.84987000 -3.34174300
 C 0.21679600 4.31942100 -2.19515500
 C 1.37290400 4.13727800 -2.95006500
 H 1.24400200 0.75561600 -3.28523500
 H -1.43998100 3.38749400 -1.21853000
 H 2.64667500 2.70227600 -3.93175200
 H -0.08344200 5.31577500 -1.89290600
 H 1.97713800 4.99097100 -3.23413900

C -0.95340700 0.70160100 -1.82760300
 O -0.68925600 -0.36469600 -2.37353400
 C -2.15235800 0.81098400 -0.89357400
 H -2.19734800 1.79279200 -0.43631800
 C -3.44982900 0.56532600 -1.70236900
 H -3.40531300 -0.44503800 -2.11604100
 H -3.46021300 1.25813700 -2.54994800
 C -4.72033400 0.75090000 -0.87230900
 H -4.77088200 0.03201900 -0.04998300
 H -4.76606000 1.75335700 -0.43911700
 H -5.60829900 0.60838000 -1.49333400
 C -2.21159800 0.25741600 1.64776900
 C -2.07093700 -0.67553800 2.68269800
 N -2.53050800 1.53953300 1.86693000
 C -2.23187700 -0.24833800 3.99253800
 C -2.69625100 1.93688900 3.13348500
 C -2.54990900 1.08964500 4.22767300
 H -1.83317200 -1.70260400 2.43840900
 H -2.11757200 -0.94232900 4.81691700
 H -2.95542800 2.98114200 3.27838400
 H -2.68892200 1.46781100 5.23267900
 C -2.02701300 -0.20855500 0.23080100
 O -1.93632200 -1.40967100 0.00489100

TS1₃₋₄-(CH₃ONa)₄

58

E(RB3LYP) = -1934.50245716

O -0.17775100 -0.91430600 -1.95035900
 O 0.82807000 0.58901500 0.84084200
 Na 0.38490300 -1.49646000 0.12170700
 Na -0.16150700 1.25627700 -1.14396300
 Na -1.32262800 0.64571500 1.52960300
 O -1.75661500 -1.45670900 0.86957900
 O -1.91958400 2.33546000 0.04566400

Na -2.37725100 -0.90101500 -1.28039400
 C -1.70426200 3.53286800 0.73119800
 H -2.64101600 3.98395500 1.09623200
 H -1.05846900 3.38093600 1.61441800
 H -1.20144000 4.29140900 0.10889800
 C -2.52412200 -2.39285600 1.54237500
 H -2.17879500 -3.43581000 1.38789200
 H -2.53408900 -2.24547300 2.64321300
 H -3.59043700 -2.38582900 1.23323300
 C 1.88531200 1.34392900 1.32258000
 H 1.67589200 2.43483000 1.32952900
 H 2.16629800 1.09105500 2.36603300
 H 2.81559400 1.22465600 0.72882600
 C 0.10047300 -1.05611200 -3.29955000
 H 1.15594500 -0.82733900 -3.55793500
 H -0.07927900 -2.08359100 -3.67953300
 H -0.51355600 -0.39040100 -3.94241300
 C -2.42165400 3.62370700 -2.30685100
 C -1.41394600 3.57217800 -3.27886400
 C -2.89986200 4.87674100 -1.90728100
 C -0.88558800 4.73750600 -3.82469300
 C -2.37728300 6.04566900 -2.45772400
 C -1.36631100 5.98181300 -3.41461000
 H -1.06509500 2.60213600 -3.61033000
 H -3.67407200 4.95634600 -1.15676500
 H -0.10669700 4.67655200 -4.57626100
 H -2.75871200 7.00713800 -2.13381800
 H -0.95998600 6.89186600 -3.84051800
 C -2.93671100 2.31645500 -1.75965000
 O -2.48354700 1.25501700 -2.22710400
 C -4.34209000 2.33683200 -1.13430200
 H -4.51259800 3.28612800 -0.63718400
 C -5.38777400 2.14438700 -2.25254500
 H -5.25006100 1.15094700 -2.68603000

H -5.18070400 2.87062600 -3.04447000
 C -6.82326900 2.31976100 -1.75512800
 H -7.07280700 1.58214900 -0.98684700
 H -6.97065400 3.31357500 -1.32285200
 H -7.53669200 2.19964300 -2.57441000
 C -4.58697800 1.63888600 1.35478200
 C -4.38327000 0.66236600 2.33606000
 N -4.91580100 2.90567000 1.64418700
 C -4.49250300 1.02870900 3.67151000
 C -5.04116000 3.23968800 2.93165200
 C -4.82973900 2.34538100 3.97932900
 H -4.12735000 -0.34433600 2.03532900
 H -4.32192100 0.30266700 4.45753300
 H -5.31596700 4.26968000 3.13644200
 H -4.93089700 2.67584000 5.00544000
 C -4.44493900 1.25096900 -0.09007200
 O -4.43204900 0.06463600 -0.38869200

Int2₃₋₄-(CH₃ONa)₄

58

E(RB3LYP) = -1934.51548603
 O 2.85326400 -0.77044900 -2.63341200
 O 3.54422800 -0.63643300 0.66260700
 Na 3.42489100 -2.22656400 -0.97316200
 Na 2.85701100 0.77602100 -0.99398500
 Na 1.37847800 -1.24732100 1.03804500
 O 1.32094500 -2.88689400 -0.53384900
 O -0.54634400 0.00981300 1.38794500
 Na 0.70800900 -1.24987900 -2.02588400
 C -1.27517600 0.45801900 2.52327500
 H -2.20660400 0.95690000 2.24232200
 H -1.52561700 -0.42905900 3.10896500
 H -0.68027200 1.13938300 3.14058400
 C 0.50732400 -3.99868100 -0.38766900

H -0.18827500 -4.14860600 -1.24044500
 H 1.07229400 -4.94895000 -0.29670700
 H -0.14106200 -3.95189100 0.51317900
 C 4.49770700 -0.30984900 1.61379200
 H 4.65987200 -1.10875200 2.36673900
 H 5.49851500 -0.10386400 1.18050400
 H 4.23671200 0.59795700 2.19874600
 C 3.33074900 -0.71058600 -3.93358400
 H 4.42812900 -0.55463800 -3.99120000
 H 3.13259900 -1.63495700 -4.51532400
 H 2.88326900 0.11385400 -4.52673400
 C 0.15546900 2.31662600 0.92380900
 C 1.43965400 2.35657000 1.48452700
 C -0.65233200 3.44868600 1.03733000
 C 1.90450000 3.49747400 2.13048800
 C -0.18552200 4.60100100 1.67513200
 C 1.09332200 4.63100100 2.22389100
 H 2.07158800 1.47750900 1.41798700
 H -1.65504800 3.45131500 0.63023800
 H 2.89923000 3.50405200 2.56242000
 H -0.82680100 5.47265900 1.74293700
 H 1.45481600 5.52364400 2.72130700
 C -0.26943300 0.99727000 0.25034100
 O 0.69209700 0.45876700 -0.47015800
 C -1.63112800 1.11518700 -0.54539100
 H -2.38338400 1.59150400 0.08210500
 C -1.43970900 1.90946500 -1.84324400
 H -0.80014200 1.33062200 -2.51164200
 H -0.89760100 2.83061900 -1.61628500
 C -2.76414100 2.24625600 -2.53101100
 H -3.31552100 1.34024700 -2.79963000
 H -3.40718100 2.84356700 -1.87739900
 H -2.59677100 2.81684300 -3.44848000
 C -3.13061000 -0.90690500 0.08643100

C -3.14927000 -2.29444100 0.25158300
 N -3.99954000 -0.08640300 0.69287500
 C -4.10405000 -2.85038800 1.09305200
 C -4.92978200 -0.63511500 1.47946400
 C -5.01866100 -2.00516500 1.71750100
 H -2.41621600 -2.90243000 -0.26113900
 H -4.13677200 -3.92047000 1.25924800
 H -5.63001100 0.05018200 1.94658800
 H -5.78403000 -2.39369100 2.37751400
 C -2.09716800 -0.29369000 -0.81441000
 O -1.63250300 -0.97483300 -1.72089100

TS2₃₋₄-(CH₃ONa)₄

58

E(RB3LYP) = -1934.49291381

O 0.40354000 0.33158300 -2.06205800
 O 1.16933100 0.59235300 1.19683900
 Na 1.04174700 -1.06877700 -0.39434000
 Na 0.56488100 1.94199900 -0.53528000
 Na -0.88373600 -0.19728300 1.78555800
 O -1.04068800 -1.74014600 0.17419100
 O -2.85120500 1.27223700 2.02627700
 Na -1.71196600 -0.15569600 -1.34845700
 C -3.71803600 1.74093900 3.06936000
 H -4.58648400 2.24103200 2.64365000
 H -4.04060200 0.84936800 3.60296300
 H -3.18502600 2.41169300 3.74524100
 C -1.76238100 -2.92245200 0.24338700
 H -2.43355700 -3.07618400 -0.62747400
 H -1.12080400 -3.82584300 0.28532700
 H -2.42052200 -2.98220000 1.13494300
 C 2.20677200 0.87840500 2.07292300
 H 2.36892000 0.08821400 2.83446500
 H 3.18536800 1.00788000 1.56648400

H 2.04504000 1.81433000 2.64838400
 C 0.69924700 0.33603600 -3.41802000
 H 1.15491100 1.28646500 -3.76372900
 H 1.41363600 -0.46004500 -3.71159700
 H -0.19329800 0.18517900 -4.05972900
 C -2.03291500 3.55109200 1.61638200
 C -0.68759900 3.75821000 1.95691100
 C -2.95126100 4.57911600 1.82813600
 C -0.26990400 4.97899600 2.47994800
 C -2.53004700 5.80303700 2.34430000
 C -1.19020600 6.00934500 2.66834600
 H 0.02132100 2.94582300 1.83510500
 H -3.99131800 4.43411200 1.57748800
 H 0.77206800 5.12268500 2.74158600
 H -3.25262600 6.59732200 2.49051700
 H -0.86686000 6.96336000 3.06793700
 C -2.34042200 2.16422100 1.09921700
 O -1.58649800 1.64066800 0.26263200
 C -4.25645400 2.62746500 -0.28866600
 H -4.96772300 3.09339300 0.38218000
 C -3.57386700 3.48785700 -1.31602100
 H -2.70455400 2.94875900 -1.70307700
 H -3.19448400 4.40231200 -0.84872700
 C -4.49215700 3.87374100 -2.48803500
 H -4.85865700 2.98017900 -2.99998000
 H -5.36151300 4.43722900 -2.13525700
 H -3.96429800 4.49397200 -3.22070800
 C -5.29875600 0.47807300 0.44017600
 C -5.02204600 -0.87974300 0.64300600
 N -6.29846500 1.10391800 1.08324400
 C -5.78914300 -1.60084900 1.54732400
 C -7.04424700 0.39433400 1.93700900
 C -6.83062300 -0.95393800 2.21078300
 H -4.20420600 -1.33534500 0.10319700

H -5.58055300 -2.64832800 1.73359400
 H -7.84946000 0.93137700 2.43042400
 H -7.46190100 -1.47529600 2.91968200
 C -4.43524400 1.26273200 -0.51728000
 O -3.82681500 0.59383600 -1.41164900

Int3₃₋₄-(CH₃ONa)₄

58

E(RB3LYP) = -1934.50029724

O 2.99420400 -1.16557200 -2.17376200
 O 3.08195800 -1.81783700 1.09947400
 Na 3.00732700 -3.01012600 -0.85795800
 Na 3.31454600 -0.04935400 -0.27478000
 Na 0.83802300 -2.15423100 1.15724500
 O 0.77834800 -3.26501000 -0.76336000
 O -0.00371000 0.09251900 1.68605900
 Na 0.71023500 -1.24733100 -1.90226900
 C -0.47998100 0.38712000 3.02335800
 H -1.56482500 0.44904800 3.01614000
 H -0.16006000 -0.45505600 3.63337600
 H -0.03830000 1.30815600 3.39715300
 C -0.05054600 -4.28951300 -1.19328400
 H -0.71676500 -3.99188000 -2.02920500
 H 0.50616300 -5.17591200 -1.55965400
 H -0.72606200 -4.66979900 -0.39944100
 C 3.84400100 -1.98541000 2.24885100
 H 3.83718700 -3.02740200 2.62912300
 H 4.91380200 -1.72917600 2.10613300
 H 3.49901100 -1.35724000 3.09611400
 C 3.49785700 -0.90458700 -3.44075500
 H 3.99018300 0.08640500 -3.52099000
 H 4.25840500 -1.64205700 -3.76905400
 H 2.71785300 -0.91175500 -4.22983800
 C 0.07324700 2.46514800 1.02518700

C 1.05058300 3.40014500 0.66559400
 C -1.16870700 2.90261300 1.49931200
 C 0.80094900 4.76172500 0.80805500
 C -1.42074900 4.26407200 1.61815400
 C -0.43575300 5.19469000 1.28300800
 H 2.00031700 3.05330900 0.27851000
 H -1.95272100 2.18862400 1.71065400
 H 1.56467100 5.48124400 0.53901000
 H -2.39152700 4.60067700 1.96137100
 H -0.63664700 6.25482900 1.38322600
 C 0.38883800 1.03233700 0.80217900
 O 1.05356200 0.64529100 -0.14491300
 C -2.24857500 1.56881200 -1.23297700
 H -2.85278000 2.02617300 -0.46165800
 C -1.61555900 2.46789500 -2.24717400
 H -1.12269800 1.85716000 -3.00893000
 H -0.82021100 3.06387100 -1.76985400

C -2.60443900 3.43836800 -2.91130800
 H -3.37777300 2.89209300 -3.46001500
 H -3.10729300 4.05656900 -2.16037000
 H -2.09954600 4.11046900 -3.61334900
 C -2.65148800 -0.53830100 -0.01732900
 C -2.39125300 -1.91374900 0.09701500
 N -3.37200300 0.11338700 0.92002000
 C -2.87383800 -2.61711800 1.19272600
 C -3.84441400 -0.57862800 1.95967800
 C -3.62351800 -1.94129600 2.15379600
 H -1.79375500 -2.38826700 -0.66605100
 H -2.66843600 -3.67742100 1.29600600
 H -4.42393100 -0.01330900 2.68570200
 H -4.02513400 -2.44489100 3.02444100
 C -2.06039300 0.21516800 -1.18342900
 O -1.36646900 -0.49339500 -2.02788900

8-5-11. Enolate oligomers

(**1**_{enol})₂

46

E(RB3LYP) = -1250.94363659

C 0.94377800 2.16105600 -2.13063300
 C 0.86435100 1.54081300 -0.87408000
 C 1.37774800 3.49564100 -2.17479600
 C 1.18462000 2.22951000 0.29466500
 C 1.70159200 4.18561800 -1.00935800
 C 1.60573700 3.55747700 0.23402800
 H 0.53699700 0.50883300 -0.82730900
 H 1.48135100 3.99129700 -3.13241300
 H 1.10510800 1.72899400 1.25369400
 H 2.04250600 5.21329700 -1.07177900
 H 1.86314600 4.09391100 1.14005500
 C 0.60167100 1.36945800 -3.36229000

O 0.76138100 0.06801000 -3.26481100
 C 0.13872100 2.00423900 -4.47746600
 H 0.01253100 3.08001100 -4.46120900
 C -0.20338300 1.27011600 -5.74584900
 H -0.81022500 0.38371500 -5.51462800
 H -0.83272300 1.90298600 -6.38051100
 C 1.02789700 0.82202500 -6.55589900
 H 1.61098200 1.68778200 -6.88309400
 H 1.68072600 0.19575800 -5.94216300
 H 0.74059900 0.25048300 -7.44535800
 Na 0.29968200 -1.85786800 -4.24329100
 C 2.25600200 -4.67427100 -4.90811300
 C 2.24578000 -3.88692400 -6.07006800
 C 1.96782700 -6.04172500 -5.04157500
 C 1.97853100 -4.44415900 -7.31927900

C 1.69737500 -6.60116600 -6.28790100
 C 1.70255600 -5.80616200 -7.43585500
 H 2.46117600 -2.82887500 -5.97887100
 H 1.93591300 -6.66825200 -4.15840200
 H 1.98629800 -3.81459000 -8.20252800
 H 1.46908300 -7.65875400 -6.36301100
 H 1.48677400 -6.24174600 -8.40468400
 C 2.53748000 -4.02139700 -3.58374100
 O 2.23357500 -2.74510100 -3.50440200
 C 3.09799200 -4.74069800 -2.56941700
 H 3.34217600 -5.78382600 -2.73048500
 C 3.39332700 -4.14303900 -1.22021900
 H 4.11394600 -4.77241600 -0.68709500
 H 3.88101100 -3.16608800 -1.34172800
 C 2.14581000 -3.95578400 -0.33656600
 H 1.40986800 -3.32975600 -0.84748100
 H 1.67397100 -4.91959800 -0.12399300
 H 2.39550400 -3.48228100 0.61945600
 Na 2.62475500 -0.87611900 -2.40266200

(**1_{enol}**)₄

92

E(RB3LYP) = -2501.95327674
 O 2.75427700 -0.95035300 -1.64369000
 O 2.85620300 -1.38486900 1.59307000
 Na 3.00900400 -2.76062000 -0.27460300
 Na 2.39207100 0.38900100 0.20336500
 Na 0.63660700 -1.74953800 1.63540600
 O 0.75647000 -3.16805600 -0.25084700
 Na 0.49505400 -1.32853300 -1.59259900
 C -0.85646300 2.13071000 -0.13058000
 H -1.77899000 2.69388500 -0.19939900
 C 0.42275500 2.84868000 -0.47024100
 H 1.19991700 2.60080200 0.26596300

H 0.26898800 3.92809800 -0.36949100
 C 0.96236200 2.56349200 -1.88480900
 H 1.15262000 1.49748200 -2.02917300
 H 0.23717200 2.87455900 -2.64187100
 H 1.90154900 3.09273500 -2.07230500
 C -2.22313800 0.16468000 0.54222700
 C -2.37357100 -1.22290400 0.38648100
 C -3.32959100 0.88884200 1.01741400
 C -3.58329400 -1.85738400 0.66306300
 C -4.53764800 0.25740400 1.29942000
 C -4.67437300 -1.12086500 1.12029800
 H -1.53707900 -1.81677400 0.04015300
 H -3.66765000 -2.92768100 0.51509900
 H -5.37279400 0.84088500 1.67117100
 H -5.61499100 -1.61178100 1.34197000
 C -0.90837000 0.81541700 0.21674200
 O 0.15361200 0.02506400 0.25723400
 C 0.28144200 -5.22488100 0.85306600
 H -0.32415400 -6.12522900 0.84318600
 C 1.36371500 -5.13500600 1.89176000
 H 1.73739400 -4.10910100 1.95027700
 H 0.95779100 -5.37269300 2.88368200
 C 2.55572500 -6.06956100 1.61866600
 H 3.31716300 -5.98749300 2.40120600
 H 2.23057100 -7.11316500 1.57221700
 H 3.02541700 -5.82792000 0.66031500
 C -1.01595200 -4.50935500 -1.12781900
 C -2.26652000 -5.04235000 -0.78603700
 C -0.80103700 -4.13874200 -2.46372400
 C -3.26642200 -5.19731700 -1.74441300
 C -1.79591900 -4.29518500 -3.42515600
 C -3.03816600 -4.82186700 -3.06838700
 H -2.46068400 -5.31500200 0.24453700
 H -4.23147900 -5.59742400 -1.45359700

H -1.60176400 -4.00799000 -4.45263700
 H -3.81878400 -4.93477500 -3.81172900
 C 0.06717000 -4.29125100 -0.11372000
 C 4.38235800 -2.56503700 2.97502700
 H 3.83060400 -3.47767300 2.75346000
 C 5.51795500 -2.70692400 3.95210300
 H 5.93948200 -1.72754200 4.19105900
 H 6.33964200 -3.29028100 3.51080400
 C 5.08717200 -3.40079000 5.25460600
 H 4.32373300 -2.81241200 5.77255900
 H 4.66082300 -4.38770800 5.04816000
 H 5.93381100 -3.53736100 5.93507700
 C 4.58497600 -0.09812300 2.58534100
 C 3.82243000 1.01297100 2.97683500
 C 5.93940000 0.09887600 2.28984000
 C 4.39820200 2.27687300 3.08244000
 C 6.51838100 1.36387100 2.39125600
 C 5.75110000 2.45748000 2.78879100
 H 2.76919800 0.87701600 3.19839800
 H 3.79297100 3.12116000 3.39341800
 H 7.56699200 1.49622000 2.14879600
 H 6.19909500 3.44165100 2.86235800
 C 3.91593400 -1.43034200 2.39362800
 C 3.38998800 -1.25478000 -3.92009100
 H 3.98336300 -0.86691000 -4.74181500
 C 2.60236800 -2.50972400 -4.16876900
 H 2.24790200 -2.90588000 -3.21175400
 H 3.25292300 -3.28524400 -4.59423300
 C 1.40684400 -2.31523800 -5.11867600
 H 0.69764200 -1.58503900 -4.71746400
 H 1.74234000 -1.94335900 -6.09135000
 H 0.87013500 -3.25482500 -5.28594400
 C 4.24589600 0.65225700 -2.59300000
 C 4.96613300 0.87470400 -1.40844300

C 4.29466600 1.63764600 -3.58847800
 C 5.70524900 2.04061400 -1.22271700
 C 5.03414900 2.80492500 -3.40647200
 C 5.74025400 3.01472600 -2.22147700
 H 4.95552500 0.11931700 -0.63005500
 H 6.24877000 2.18568800 -0.29647600
 H 5.04487200 3.56045200 -4.18444600
 H 6.30590900 3.92786500 -2.07592300
 C 3.41148100 -0.58693800 -2.73558800
 H 0.16775800 -3.74741200 -2.75030900
 H 6.53726900 -0.74341600 1.96225900
 H 3.72478800 1.49697100 -4.49932200
 H -3.23783700 1.95485800 1.18493400

(**3_{enol}**)₂

44

E(RB3LYP) = -1283.02924032

O 3.02749100 -1.27151400 -1.59687100
 Na 2.43261000 0.43033600 -0.23938200
 Na 0.87935100 -1.56164300 -2.05502100
 C -0.89614400 2.04491100 -0.93447100
 H -1.83445800 2.56780100 -0.79723600
 C 0.24791900 2.78106100 -1.57114700
 H 0.87587200 2.06948700 -2.11966000
 H 0.90720300 3.22132500 -0.80470300
 C -0.20520800 3.89760900 -2.51851000
 H -0.80823300 3.49260400 -3.33693600
 H -0.81807900 4.63499000 -1.99058900
 H 0.64862600 4.42351400 -2.95574200
 C -2.00341200 0.07582300 0.08710200
 C -1.88049000 -1.24209700 0.55473200
 N -3.17541700 0.73858900 0.16877200
 C -2.98455800 -1.88156300 1.10650800
 C -4.22610700 0.11461100 0.70253000

C -4.19228000 -1.19397200 1.18508300
 H -0.91911000 -1.73009600 0.47891300
 H -2.90411000 -2.89964800 1.47141400
 H -5.14920300 0.68677800 0.74835700
 H -5.08096200 -1.64788900 1.60556900
 C -0.80578900 0.75237600 -0.51685700
 O 0.28313700 0.01652100 -0.60347100
 C 4.39702000 -1.13309400 -3.52787200
 H 5.40848400 -1.17681000 -3.90909000
 C 3.26898900 -0.84814800 -4.47972200
 H 2.42556700 -1.52197300 -4.27453100
 H 3.58493500 -1.06875100 -5.50476600
 C 2.75735100 0.60344100 -4.41764600
 H 2.42001600 0.84496900 -3.40707700
 H 3.55315100 1.30581600 -4.68153300
 H 1.91939600 0.76527500 -5.10420600
 C 5.37602200 -1.58610600 -1.29497000
 C 5.14703300 -1.94279800 0.04350500
 N 6.62847800 -1.47876600 -1.78368200
 C 6.22656700 -2.19095400 0.88327600
 C 7.65549900 -1.71873300 -0.96725800
 C 7.51696700 -2.07609400 0.37402100
 H 4.12684500 -2.02580300 0.39112700
 H 6.06416400 -2.47101100 1.91828300
 H 8.64607200 -1.61881900 -1.40343500
 H 8.39062900 -2.25560900 0.98807100
 C 4.20094000 -1.31203200 -2.19181200

(**3_{enol}**)₄

88

E(RB3LYP) = -2566.12913163

O 2.60604600 -1.30746400 -1.96650400

O 2.95991300 -0.99753800 1.21744700

Na 2.97689800 -2.79356600 -0.25012800

Na 2.23328300 0.42117300 -0.47114300
 Na 0.77215600 -1.47599000 1.60612300
 O 0.76291800 -3.20184600 0.10767400
 Na 0.38236600 -1.73219300 -1.66563900
 C -1.00690800 2.04067200 0.28078100
 H -1.94603300 2.57708700 0.33326400
 C 0.27021300 2.80895100 0.46982200
 H 0.73940400 3.03681700 -0.50099300
 H 0.99225800 2.18341500 1.00705100
 C 0.08308800 4.11998400 1.23927400
 H -0.61996900 4.78068500 0.72297900
 H -0.31546800 3.93004500 2.24050600
 H 1.02935700 4.65735100 1.34796100
 C -2.35462900 -0.00876100 -0.07777000
 C -2.39268800 -1.41133700 -0.02702100
 N -3.48329500 0.71239400 -0.24082800
 C -3.60680700 -2.07388600 -0.16120200
 C -4.64327900 0.06469200 -0.36125900
 C -4.76670200 -1.32496800 -0.33496200
 H -1.47675200 -1.96791100 0.10629400
 H -3.64088900 -3.15725300 -0.13589600
 H -5.52532300 0.68607000 -0.49287800
 H -5.73667400 -1.79255900 -0.44962700
 C -1.03657800 0.70307600 0.04305500
 O 0.04147800 -0.05845200 -0.06410000
 C 0.49655300 -5.36707300 1.03305500
 H -0.00697400 -6.32457900 0.97002300
 C 1.57497400 -5.23210100 2.06891700
 H 1.84432400 -4.17771500 2.17667400
 H 1.19835000 -5.55986500 3.04672800
 C 2.84241800 -6.04365800 1.74468900
 H 3.60447400 -5.91830500 2.52054800
 H 2.61337300 -7.11062200 1.66607700
 H 3.27472500 -5.73060100 0.78973300

C -0.90010300 -4.61345000 -0.87738100
 C -1.88757200 -5.60431800 -0.74276800
 N -0.90139600 -3.78577600 -1.94310900
 C -2.85457500 -5.75252400 -1.72543000
 C -1.83816900 -3.93919700 -2.88828100
 C -2.83337500 -4.90488400 -2.83391500
 H -1.90601600 -6.23525600 0.13487100
 H -3.62365600 -6.50952500 -1.62401200
 H -1.78943400 -3.24598700 -3.72274600
 H -3.57213800 -4.97993200 -3.62156800
 C 0.17635100 -4.37893500 0.14978400
 C 4.65455700 -1.83603900 2.65773000
 H 4.30524000 -2.84675800 2.44142100
 C 5.77333600 -1.72988700 3.65654200
 H 6.02784000 -0.68254700 3.82841200
 H 6.68431700 -2.19849400 3.25704200
 C 5.43365500 -2.40549200 4.99510700
 H 4.57596700 -1.91797400 5.46855900
 H 5.17533700 -3.45914500 4.84757600
 H 6.27787700 -2.36224400 5.69080000
 C 4.32096800 0.61856900 2.27703900
 C 3.29527000 1.50309700 2.64660100
 N 5.57526500 1.04667200 2.05470200
 C 3.57573300 2.85341400 2.79554200
 C 5.83234900 2.35510300 2.19416400
 C 4.87728800 3.29688800 2.55958100
 H 2.29654800 1.11819100 2.80873400
 H 2.79707900 3.54893200 3.08632900
 H 6.85520900 2.66254200 1.99553700
 H 5.14511800 4.34192400 2.65334400
 C 3.98214000 -0.82837200 2.04908500
 C 3.17676800 -1.90159300 -4.20055700
 H 3.91126400 -1.78539200 -4.98797400
 C 1.95360700 -2.72502400 -4.48410500

H 1.53023900 -3.09933800 -3.54638700
 H 2.23426100 -3.61248600 -5.06446600
 C 0.86245100 -1.96744700 -5.26479700
 H 0.52245400 -1.08662000 -4.71217500
 H 1.24594800 -1.62019400 -6.22856000
 H -0.00593500 -2.60583500 -5.45782900
 C 4.70028000 -0.52453000 -2.81982600
 C 5.15083300 -0.24741200 -1.51774300
 N 5.40706100 -0.12953900 -3.89848300
 C 6.33981900 0.44810300 -1.33130100
 C 6.54766500 0.53673100 -3.70620200
 C 7.06118100 0.85699800 -2.44966300
 H 4.57667000 -0.58157400 -0.66409400
 H 6.68101800 0.66352500 -0.32514300
 H 7.08048300 0.83811600 -4.60438900
 H 7.98971100 1.40710200 -2.36006700
 C 3.41121900 -1.27414000 -3.01760700

(5wA_{enol})₂

68

E(RB3LYP) = -1972.08341609
 C -0.54255800 -0.92676900 -0.53917200
 C -1.08195900 -0.84843200 -1.82052800
 C 0.64728000 -0.25589400 -0.27172400
 C -0.45859400 -0.09576800 -2.80243100
 C 1.26997500 0.50131400 -1.25261100
 C 0.71893000 0.58184900 -2.52141100
 H -1.99563800 -1.38063400 -2.05149400
 H 1.07870800 -0.30291400 0.72078000
 H -0.89096600 -0.04000500 -3.79368700
 H 2.19084500 1.02420400 -1.02675900
 H 1.20693500 1.16637100 -3.29062000
 C -1.14040200 -1.84654400 0.54385700
 O -0.44671000 -2.91752900 0.72820800

C -2.29502800 -1.47681100 1.22149200
 C -3.02287100 -0.18124700 0.87592400
 H -3.30343100 0.34770900 1.78269700
 H -2.34741600 0.47620200 0.33294600
 C -4.29802400 -0.37852300 0.01855200
 H -4.06338600 -0.86281700 -0.92404600
 H -5.02554600 -0.99475000 0.53818100
 H -4.76226600 0.57933300 -0.19943500
 C -4.09498500 -1.89662500 3.03190200
 C -5.21503200 -2.72461800 3.01529500
 N -4.03450500 -0.74734800 3.75135600
 C -6.33956100 -2.36286900 3.73724200
 C -5.14654300 -0.42664500 4.45125200
 C -6.30500700 -1.18977200 4.47208000
 H -5.19614900 -3.63874200 2.43775000
 H -7.22469100 -2.98766900 3.73182000
 H -5.09059600 0.49095300 5.03142500
 H -7.15634300 -0.86912400 5.05680600
 C -2.81766500 -2.33850700 2.26934800
 O -2.34751800 -3.43111700 2.65681800
 Na 1.53997900 -3.13480700 0.45119100
 C 1.71118300 -6.34878100 3.35382400
 C 0.73983000 -7.27765700 2.99172700
 C 2.07851300 -6.25002700 4.69344500
 C 0.16120400 -8.10445200 3.94315900
 C 1.49740400 -7.07168800 5.64513400
 C 0.53937300 -8.00371700 5.27213100
 H 0.43797800 -7.36249200 1.95530600
 H 2.82380100 -5.52283400 4.99100600
 H -0.58724800 -8.82816600 3.64542200
 H 1.79145700 -6.98478000 6.68371900
 H 0.08940400 -8.64769700 6.01657500
 C 2.27106200 -5.37455600 2.29606100
 O 1.41963100 -4.48476000 1.92645100

C 3.58073300 -5.51149400 1.84086000
 C 4.45915300 -6.66423600 2.32088200
 H 5.47812300 -6.32151600 2.48334200
 H 4.09520400 -7.02321500 3.27800100
 C 4.49454700 -7.86532000 1.34156500
 H 3.49821800 -8.27274300 1.19904000
 H 4.87748300 -7.56859000 0.36984000
 H 5.13130300 -8.65716200 1.72635700
 C 5.56516900 -4.73661800 0.37598000
 C 5.84326900 -4.92441400 -0.97531800
 N 6.53340000 -4.57834500 1.31489100
 C 7.16003200 -4.98379000 -1.39926100
 C 7.80792800 -4.62927200 0.86717200
 C 8.16429700 -4.83534300 -0.45861200
 H 5.02855500 -5.01846000 -1.68041400
 H 7.39796300 -5.13763000 -2.44498400
 H 8.57890000 -4.50135500 1.62258100
 H 9.20750300 -4.87370900 -0.74130800
 C 4.08794800 -4.59906200 0.82922100
 O 3.44805700 -3.71212200 0.22085700
 Na -0.54394300 -4.22441600 2.25081600

(5wA_{enol})₄

136

E(RB3LYP) = -3944.23121344

C 0.19201200 -1.07954000 -0.97234000
 C -0.24457700 -1.25643600 -2.28714800
 C 1.45018600 -0.51077400 -0.74180100
 C 0.55973300 -0.87435500 -3.35811000
 C 2.25084900 -0.11571900 -1.81266900
 C 1.80753800 -0.29831700 -3.12381800
 H -1.20387900 -1.71638100 -2.48099200
 H 1.79963000 -0.37669500 0.27648400
 H 0.20224100 -1.04862900 -4.36571800

H 3.22116200 0.32942400 -1.62366700	H -0.15949600 -5.68312300 6.65884200
H 2.43604500 -0.00097900 -3.95552600	H -1.26502200 -7.89029500 6.39354400
C -0.60698300 -1.63233200 0.18318400	C 1.97718500 -6.00095000 2.52351900
O -0.14399400 -2.73200600 0.64224100	O 1.36160800 -5.11166200 1.84146400
C -1.75821500 -0.96803100 0.64259200	C 3.28420800 -6.46157900 2.28399400
C -2.23035300 0.29982500 -0.05326900	C 3.85862700 -7.59104000 3.12586300
H -2.52156800 1.04268200 0.69025000	H 4.88959700 -7.36176000 3.39792900
H -1.39479800 0.73425400 -0.60459400	H 3.30464300 -7.65275600 4.06400400
C -3.40074500 0.07344300 -1.02281600	C 3.81534100 -8.96158400 2.43209400
H -3.12840800 -0.63546700 -1.80908800	H 2.78949600 -9.24392300 2.18170100
H -4.27155300 -0.33123900 -0.49974200	H 4.39115300 -8.94941100 1.50259600
H -3.70236700 1.01063700 -1.50105400	H 4.23400300 -9.74159000 3.07580400
C -3.73908600 -0.76562500 2.22855400	C 5.47637000 -6.39234800 0.99335700
C -4.97908500 -1.40932800 2.19147900	C 5.79796300 -6.98292900 -0.23168000
N -3.56960200 0.45120000 2.76195600	N 6.38600000 -6.16487200 1.94983500
C -6.09061800 -0.75334200 2.70400300	C 7.10978300 -7.37584600 -0.46260600
C -4.64471800 1.06384900 3.27511300	C 7.65263400 -6.52662200 1.70604600
C -5.92266300 0.51301300 3.26111600	C 8.06261100 -7.14233900 0.52723300
H -5.05458700 -2.40330200 1.77204400	H 5.02858100 -7.12045500 -0.97916400
H -7.06792200 -1.22101000 2.67540300	H 7.38626100 -7.84987200 -1.39723200
H -4.47355200 2.04228700 3.71368300	H 8.36983600 -6.31656300 2.49374300
H -6.75788600 1.06162800 3.67818500	H 9.09880500 -7.42596100 0.39159900
C -2.51655800 -1.51076800 1.72706100	C 4.05736100 -5.90503300 1.21752900
O -2.29885500 -2.58889300 2.33129000	O 3.68501300 -5.03570000 0.39288800
Na 1.85862800 -3.72361900 0.05072700	Na -0.70096700 -4.19959900 2.34118300
C 1.15216200 -6.57887800 3.64820800	C -3.42588600 -6.30379900 2.04815000
C 0.53021700 -7.82158000 3.50896400	C -4.48727200 -5.79718200 1.29339800
C 0.89188600 -5.80933300 4.78839300	C -3.42299200 -6.12314900 3.43461800
C -0.33913700 -8.29159000 4.49034400	C -5.53948900 -5.12981200 1.91825100
C 0.03083700 -6.28404800 5.77679700	C -4.46991600 -5.44561400 4.05705800
C -0.58791000 -7.52667000 5.62906500	C -5.53268600 -4.95169400 3.30128300
H 0.70408100 -8.41716100 2.62372600	H -4.49172800 -5.93064100 0.21702500
H 1.36596400 -4.83997500 4.90072000	H -2.60004300 -6.51412500 4.02249000
H -0.82436800 -9.24894700 4.34358800	H -6.36280500 -4.74810800 1.32498200

H -4.45564900 -5.30435700 5.13178800	C 4.85470800 -5.51198600 -3.51980100
H -6.34693600 -4.42554000 3.78554200	H 1.87871100 -7.12511300 -3.20729000
C -2.25875600 -6.96899400 1.35884400	H 2.69762800 -2.91549500 -3.10916100
O -1.42080500 -6.15381400 0.84577700	H 4.28571200 -7.58821300 -3.55504500
C -2.18235400 -8.37539300 1.35776100	H 5.11088500 -3.37622500 -3.43227300
C -3.30073000 -9.18984600 1.99435100	H 5.90934200 -5.71495700 -3.66416600
H -2.88865300 -10.10247900 2.42721700	C 0.67133500 -4.71627300 -2.86753100
H -3.73185400 -8.63858100 2.83040000	O 0.34073800 -4.81321200 -1.63712800
C -4.42246800 -9.55886300 1.01269200	C -0.16387200 -4.36684300 -3.94490300
H -4.88652600 -8.65942500 0.59884500	C 0.40985600 -4.31390700 -5.35446500
H -4.03284100 -10.14767300 0.17748800	H -0.06570300 -3.50745700 -5.91402400
H -5.20277200 -10.14710300 1.50603800	H 1.46884900 -4.05784800 -5.31318300
C -1.02511500 -10.57722200 0.90177600	C 0.24770300 -5.63062200 -6.12797200
C -1.35606600 -11.42281400 -0.15832000	H 0.76004200 -6.44807400 -5.61314200
N -0.54583100 -11.02716300 2.06974400	H -0.80755900 -5.90342500 -6.21884000
C -1.19951900 -12.79447200 0.00721200	H 0.66418900 -5.55099500 -7.13717800
C -0.38451400 -12.34898100 2.21040100	C -2.34932500 -3.56750300 -4.94093700
C -0.70172800 -13.27168200 1.21764300	C -3.31056600 -4.36704800 -5.56198500
H -1.72932600 -11.00852700 -1.08666400	N -2.14039300 -2.28713700 -5.27764400
H -1.45870400 -13.47846900 -0.79245300	C -4.07312300 -3.82056600 -6.58806400
H 0.01270600 -12.68320600 3.16422000	C -2.89567900 -1.76669500 -6.25305800
H -0.56069900 -14.33111400 1.39113900	C -3.86494700 -2.48951300 -6.94269100
C -1.10185800 -9.06940000 0.74348500	H -3.44904400 -5.39307400 -5.24452000
O -0.15393200 -8.58186600 0.08038700	H -4.81751900 -4.41934400 -7.09973400
Na -1.66854800 -4.33493300 -0.56778100	H -2.71112700 -0.72450500 -6.49603300
C 2.13124700 -4.98963000 -3.13900400	H -4.43768900 -2.01995000 -7.73255000
C 2.58674500 -6.30522400 -3.26010100	C -1.55072300 -4.09712300 -3.76370700
C 3.04932100 -3.93711400 -3.20207200	O -2.22471600 -4.22880400 -2.71292300
C 3.94245300 -6.56463500 -3.45511600	Na 0.66453100 -6.53296700 -0.110317
C 4.40556500 -4.19833300 -3.38888200	

9. X-ray crystal structure analysis

Recrystallization from EtOAc/hexane solution gave crystals of **3xA** suitable for X-ray analysis. A suitable crystal was mounted with Immersion Oil Type NVH (Cargille) on a MiTeGen MicroMounts and transferred to Rigaku XtaLAB Synergy-S diffractometer equipped with a HyPix-6000HE Hybrid Photon Counting detector and dual Mo and Cu microfocus sealed tube. Cell parameters were determined and refined, and raw frame data were integrated using CrysAlis^{Pro} (Rigaku Oxford Diffraction, 2021).^[46] The structures were solved by direct methods with (SHELXT)^[47] and refined by full-matrix least-squares techniques against F^2 (SHELXL-2018/3)^[48] by using Olex2 software package.^[49] The intensities were corrected for Lorentz and polarization effects. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed using AFIX instructions.

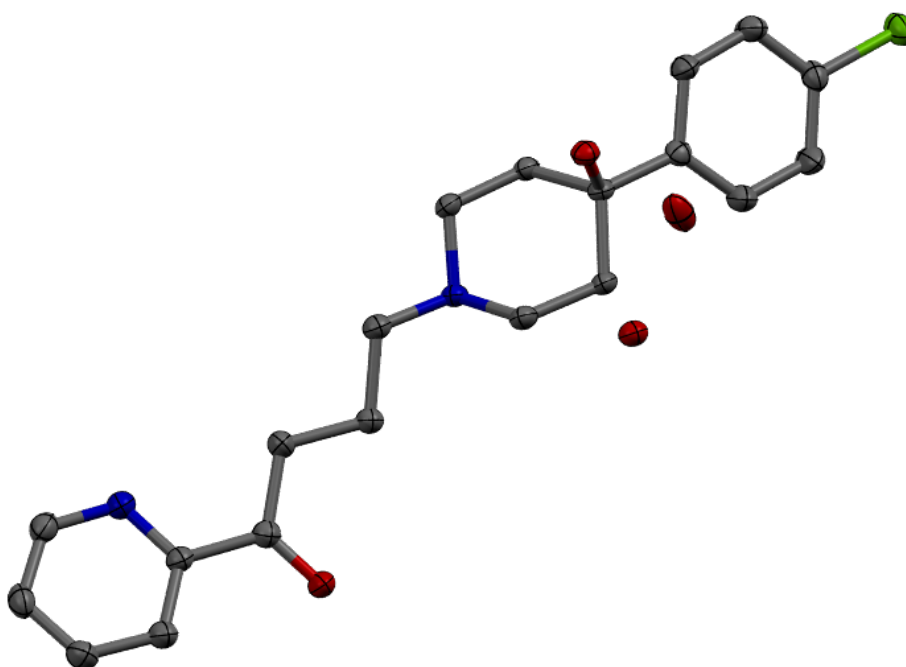


Figure S13. ORTEP drawing of **3xA** with 50% thermal ellipsoid. All hydrogen atoms are omitted for clarity.

Compound	3xA
CCDC Number	2394121
Empirical formula	C ₂₀ H ₂₇ ClN ₂ O ₄
Formula weight	394.88
<i>T</i> / K	100.15
Crystal system	monoclinic
Space group	<i>Pn</i>
<i>a</i> / Å	6.49997(14)
<i>b</i> / Å	11.1943(3)
<i>c</i> / Å	14.0113(3)
α / °	90
β / °	95.358(2)
γ / °	90
<i>V</i> / Å ³	1015.05(4)
<i>Z</i>	2
<i>D</i> _{calc} , / g cm ⁻³	1.292
μ / mm ⁻¹	1.895
<i>F</i> (000)	420.0
Crystal size / mm	0.82 × 0.21 × 0.07
λ / Å	1.54184
2 θ range / °	7.898 to 145.562
Reflections collected	4833
Indep reflns/ <i>R</i> _{int}	2216/0.0386
Params	259
GOF on <i>F</i> ²	1.024
<i>R</i> ₁ , w <i>R</i> ₂ [<i>I</i> > 2 σ (<i>I</i>)]	<i>R</i> ₁ = 0.0468, w <i>R</i> ₂ = 0.1206
<i>R</i> ₁ , w <i>R</i> ₂ [all data]	<i>R</i> ₁ = 0.0477, w <i>R</i> ₂ = 0.1220
Max./Mini. Peak / e Å ⁻³	0.66/−0.39

Table S8. Crystal data and structure refinement for **3xA**.

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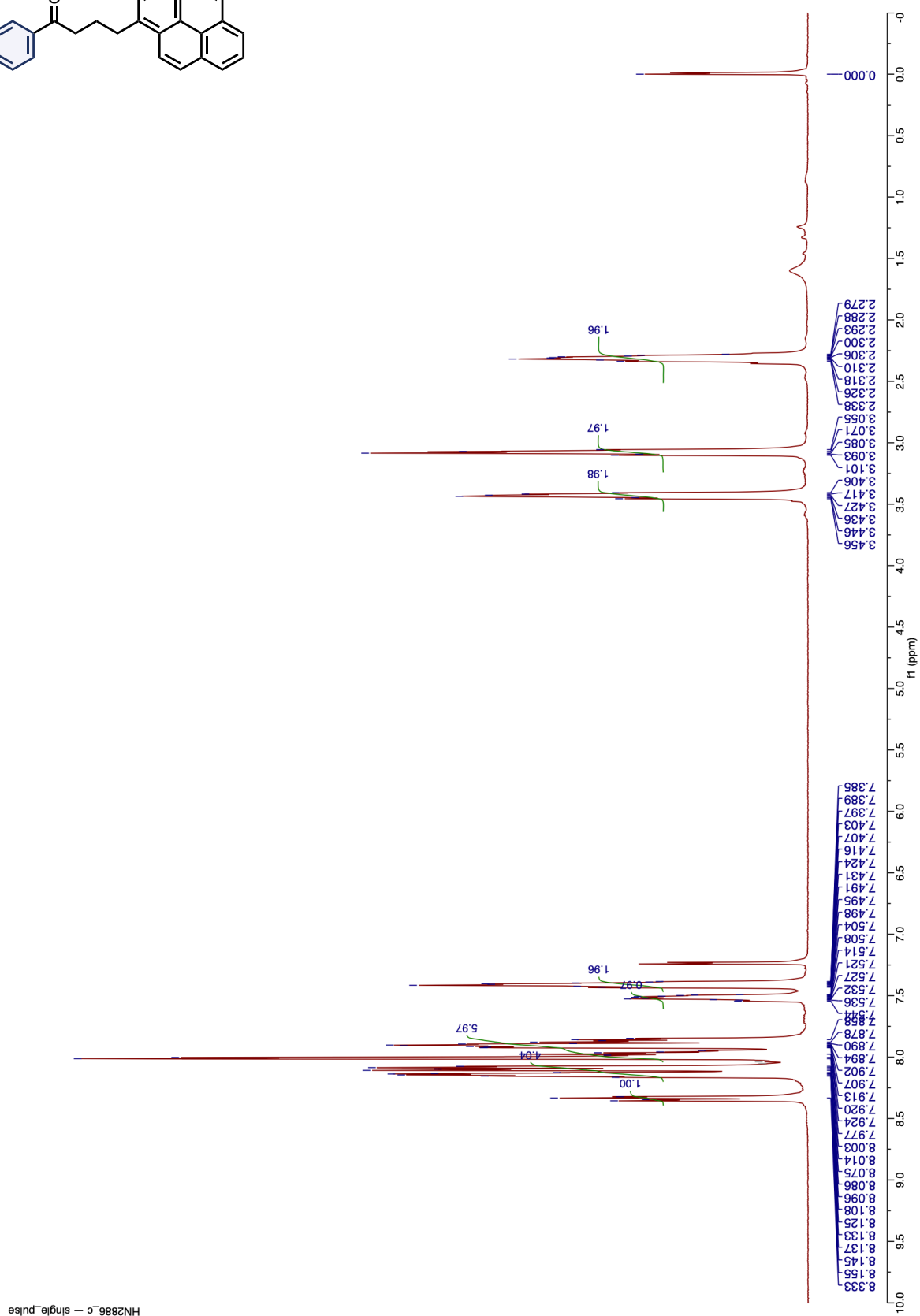
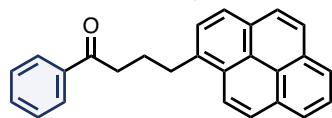
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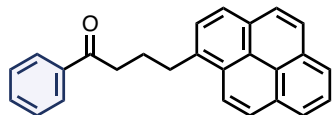
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11. ^1H NMR, ^{13}C NMR, and ^{19}F NMR Spectra

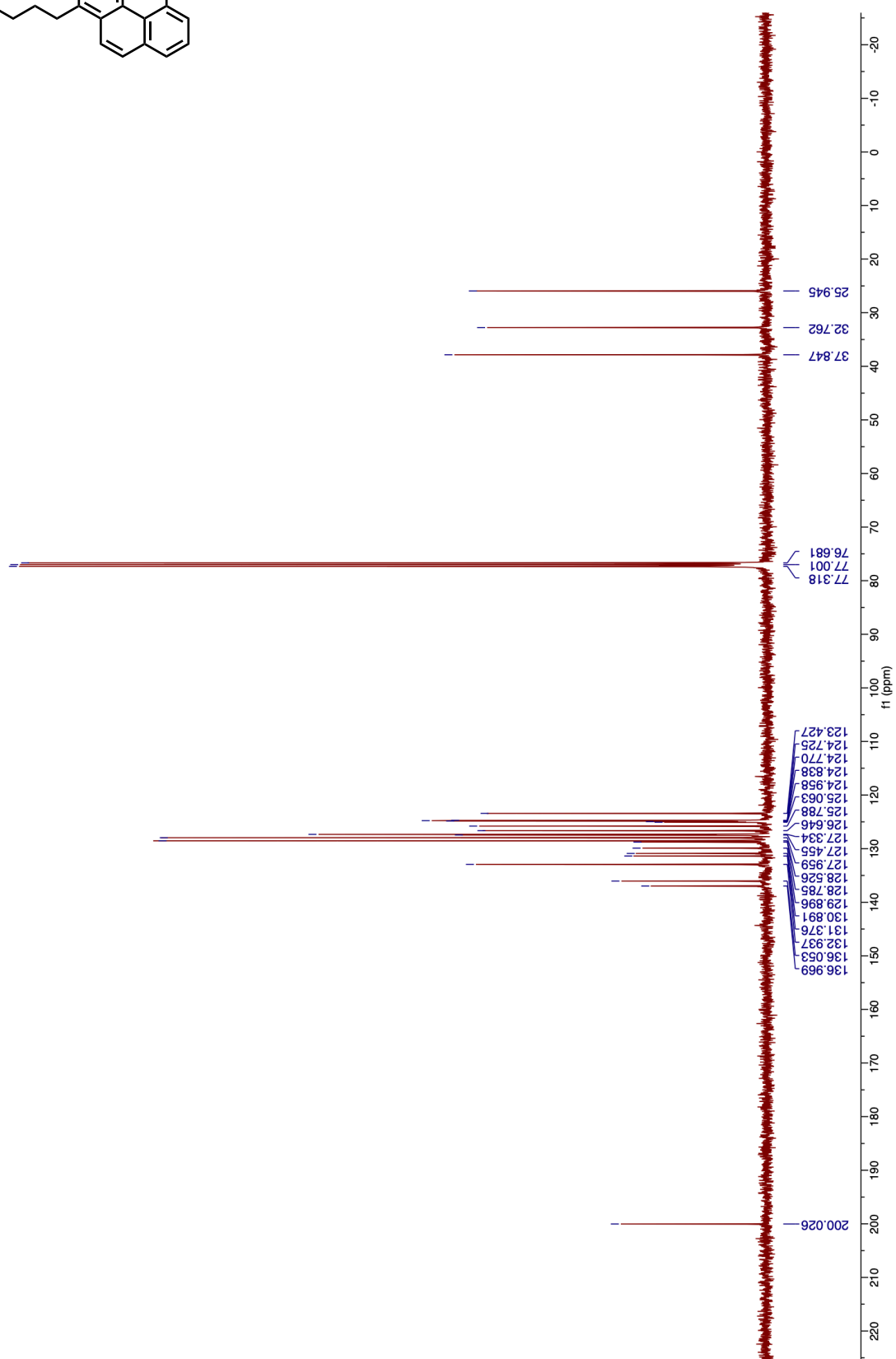
^1H NMR of **1k** (400 MHz, CDCl_3)

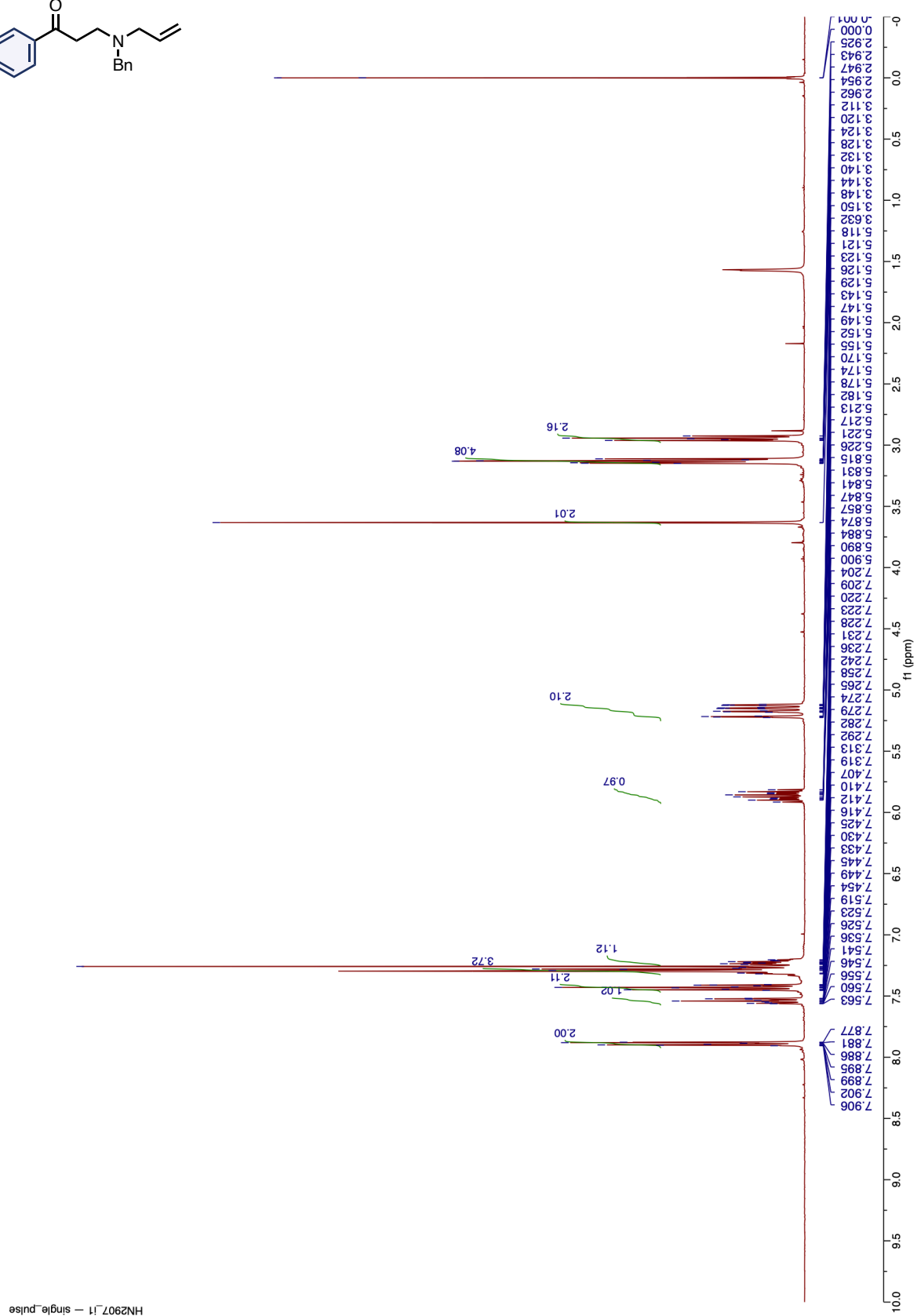


^{13}C NMR of **1k** (101 MHz, CDCl_3)

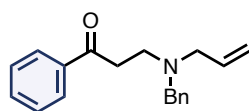


HN2886 — single pulse decoupled gated NOE

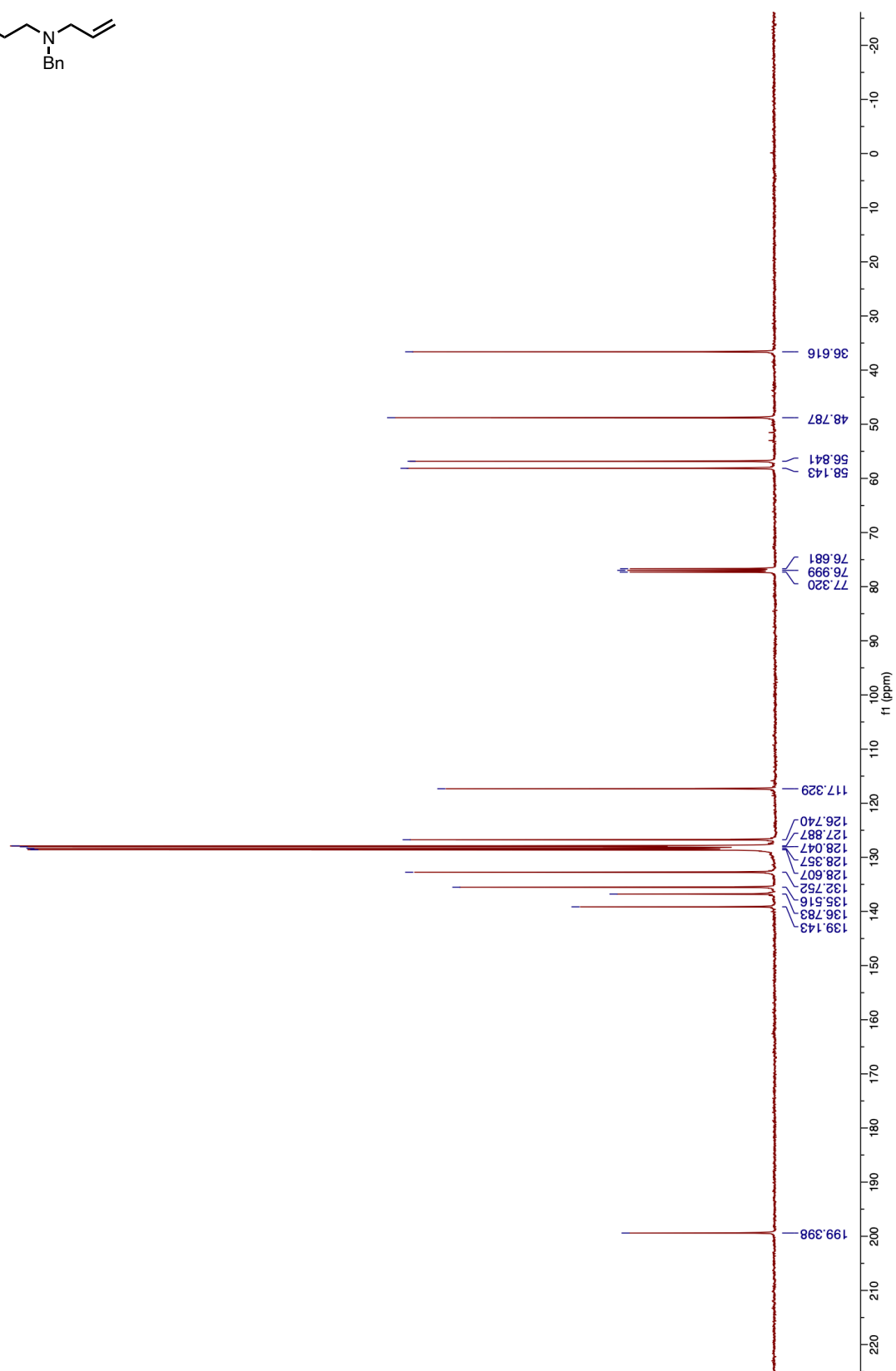


C=CCN(Cc1ccccc1)CCC(=O)c2ccccc2

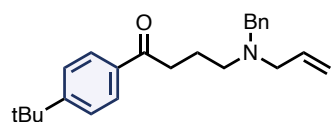
^{13}C NMR of **1m** (101 MHz, CDCl_3)



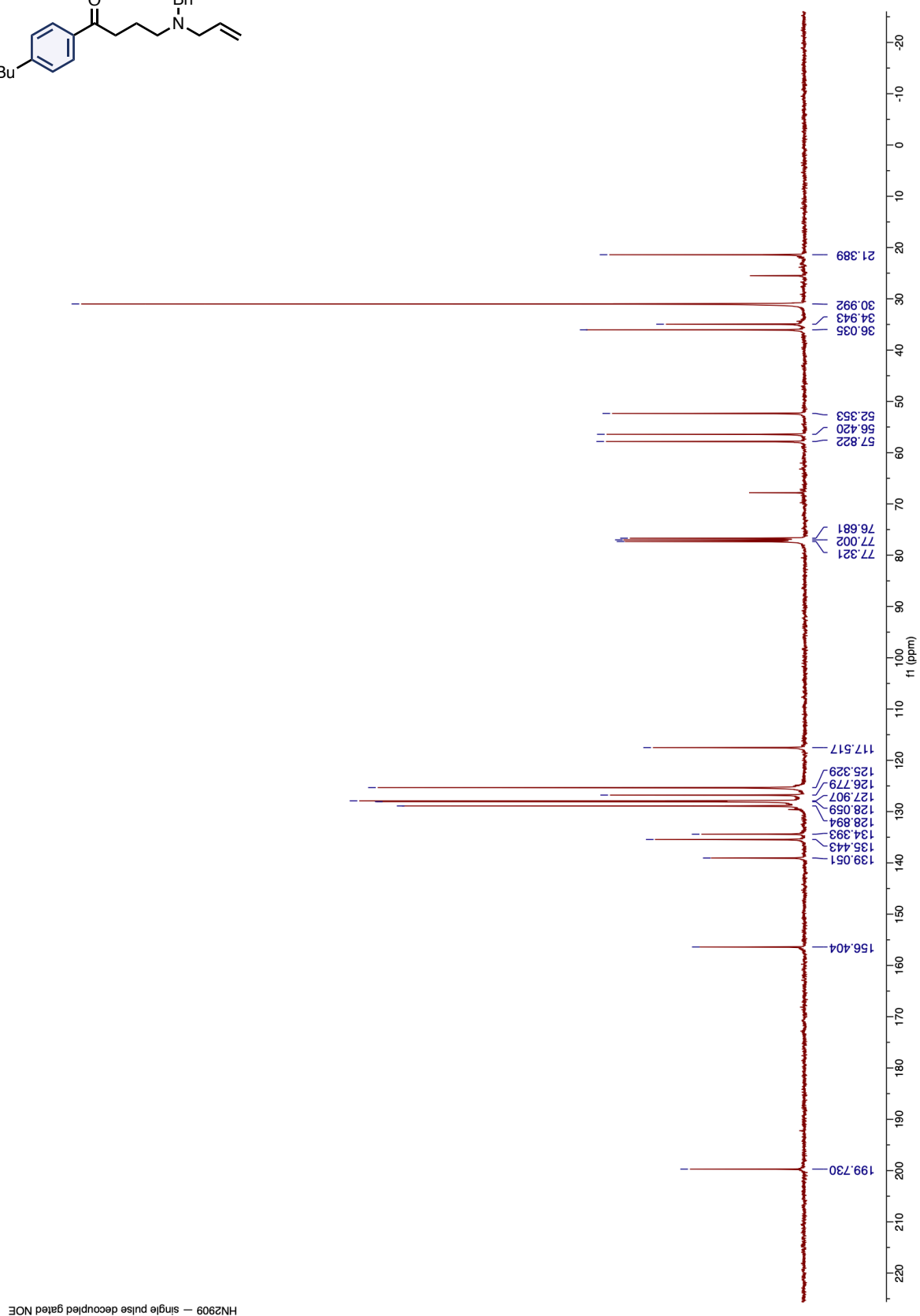
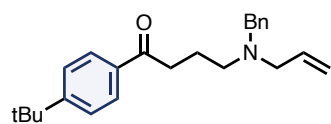
HN2907 — single pulse decoupled gated NOE



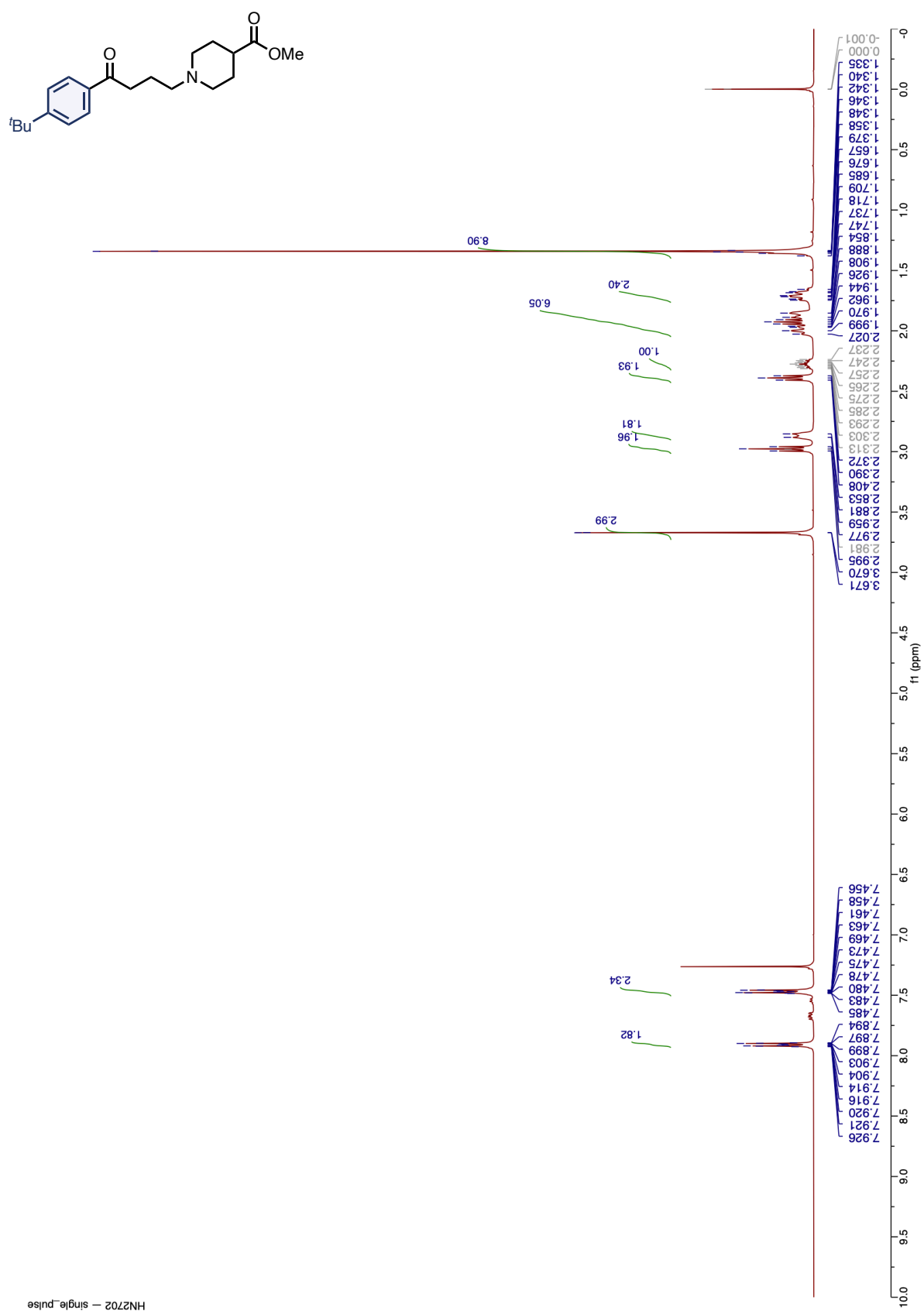
^1H NMR of **1n** (400 MHz, CDCl_3)



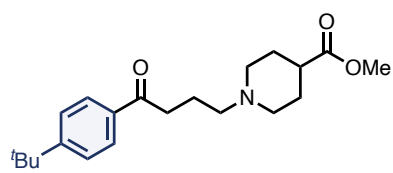
^{13}C NMR of **1n** (101 MHz, CDCl_3)



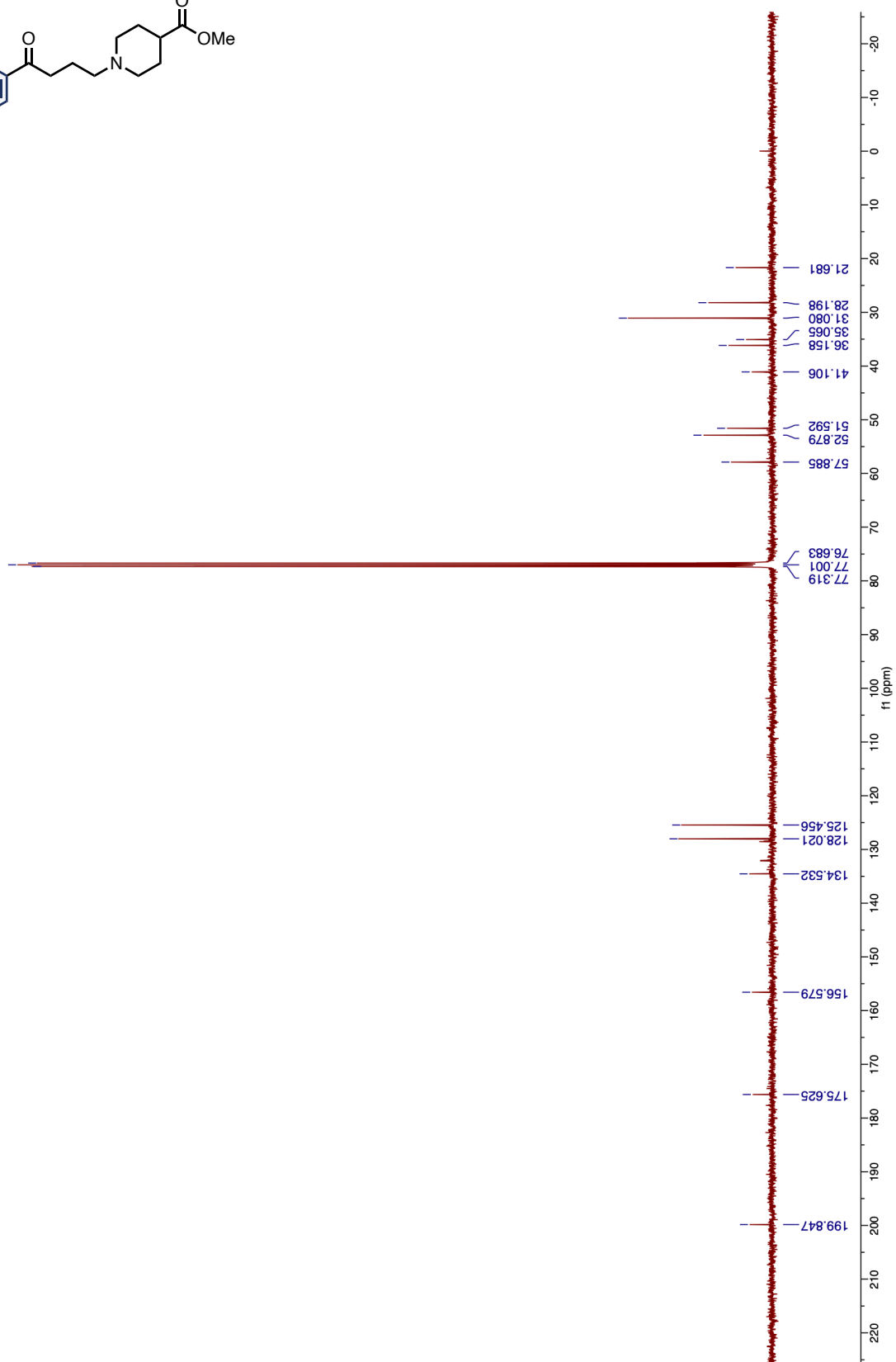
^1H NMR of **1o** (400 MHz, CDCl_3)



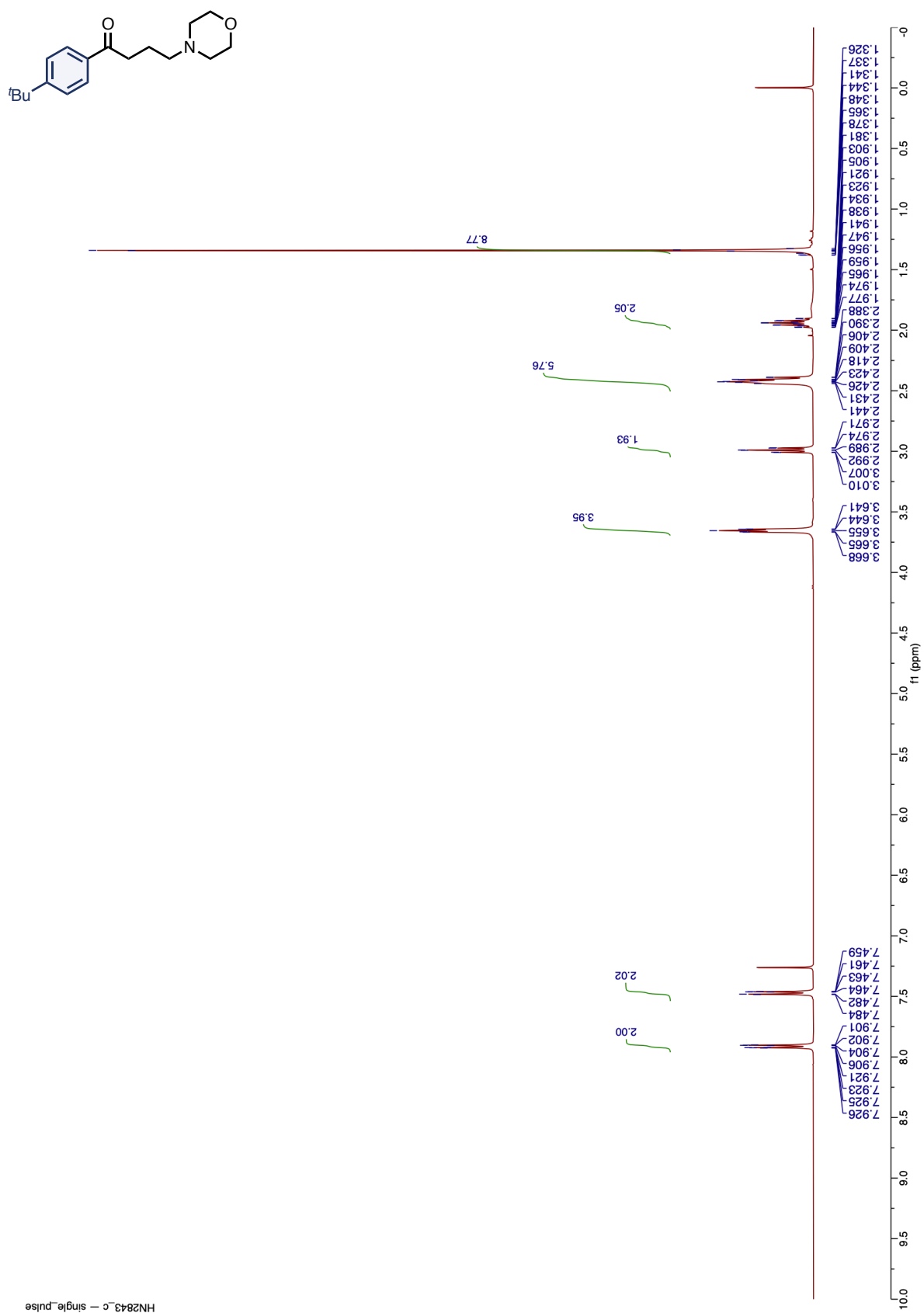
^{13}C NMR of **1o** (101 MHz, CDCl_3)



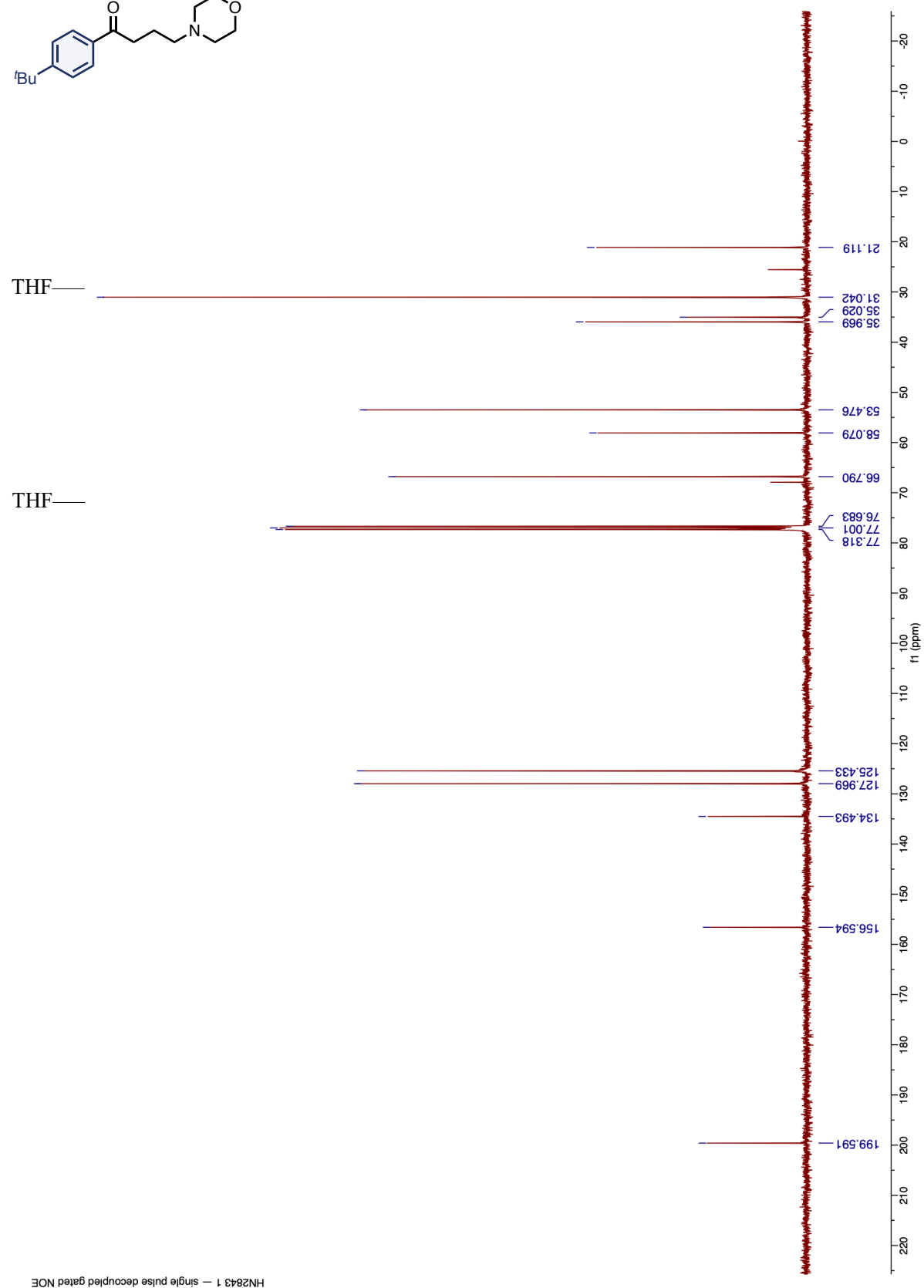
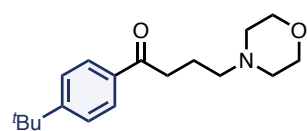
HN2702 — single pulse decoupled gated NOE



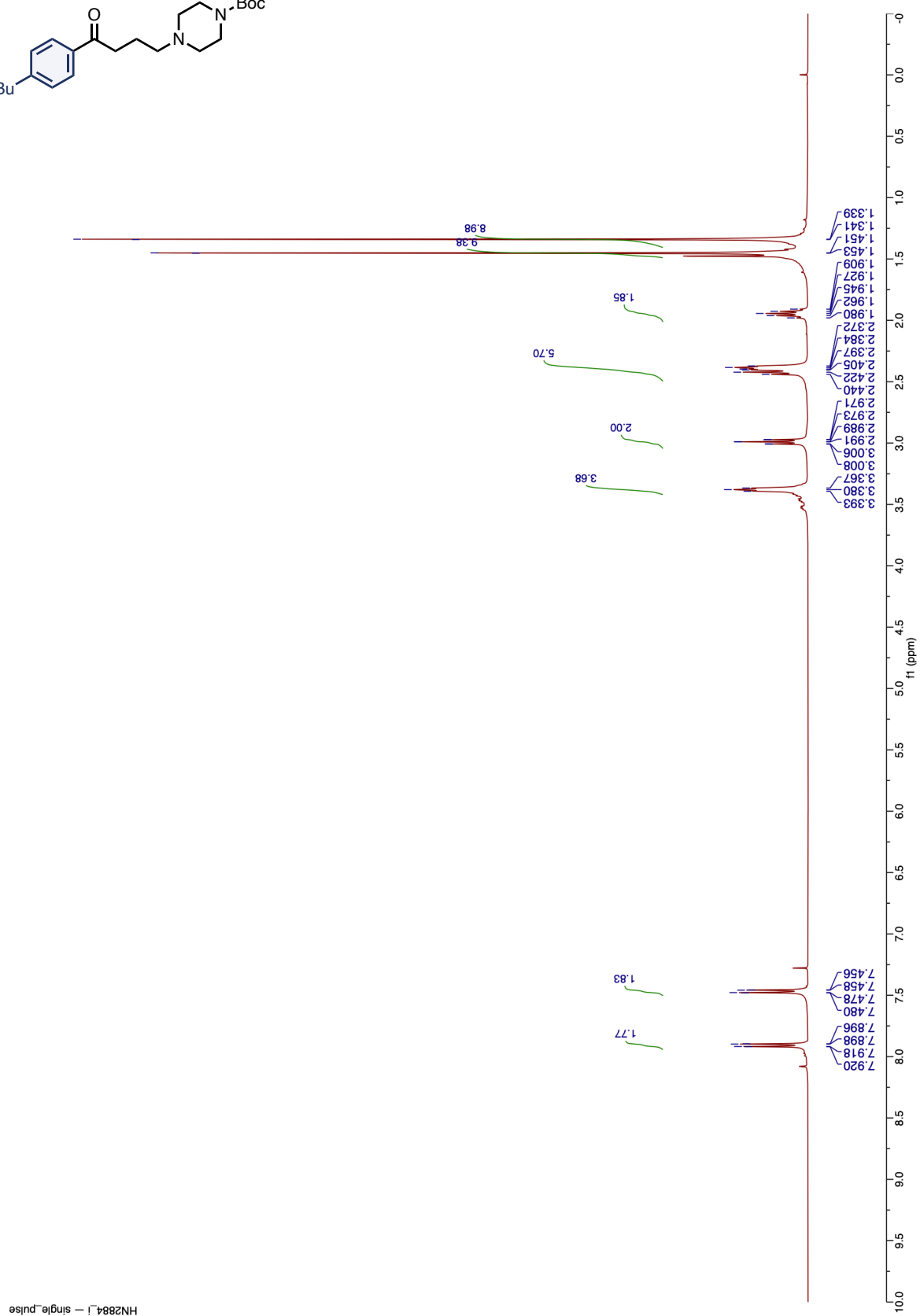
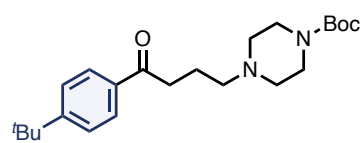
^1H NMR of **1p** (400 MHz, CDCl_3)



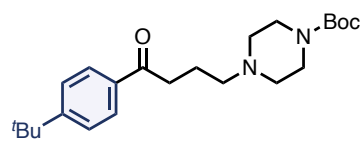
^{13}C NMR of **1p** (101 MHz, CDCl_3)



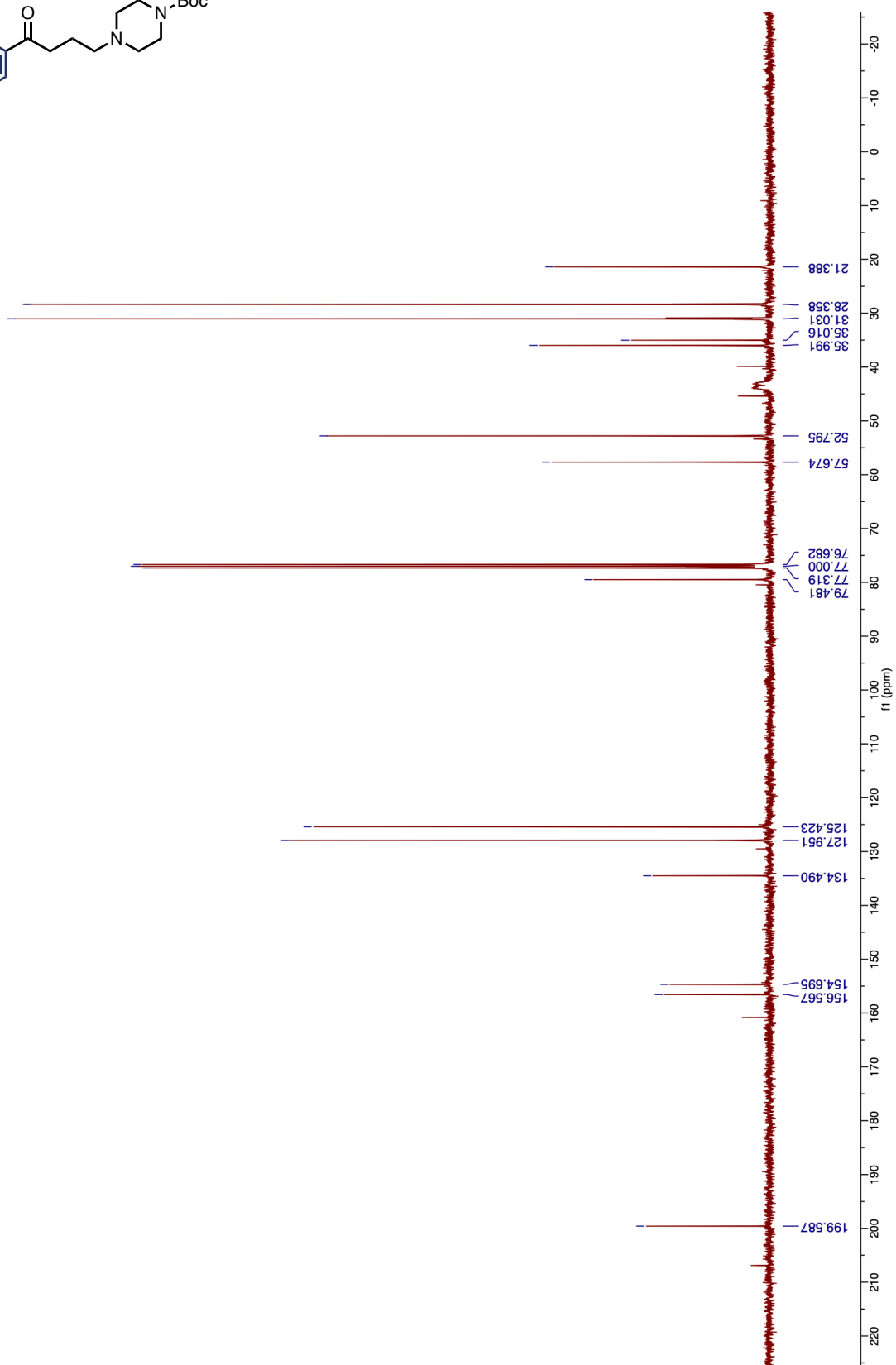
^1H NMR of **1q** (400 MHz, CDCl_3)



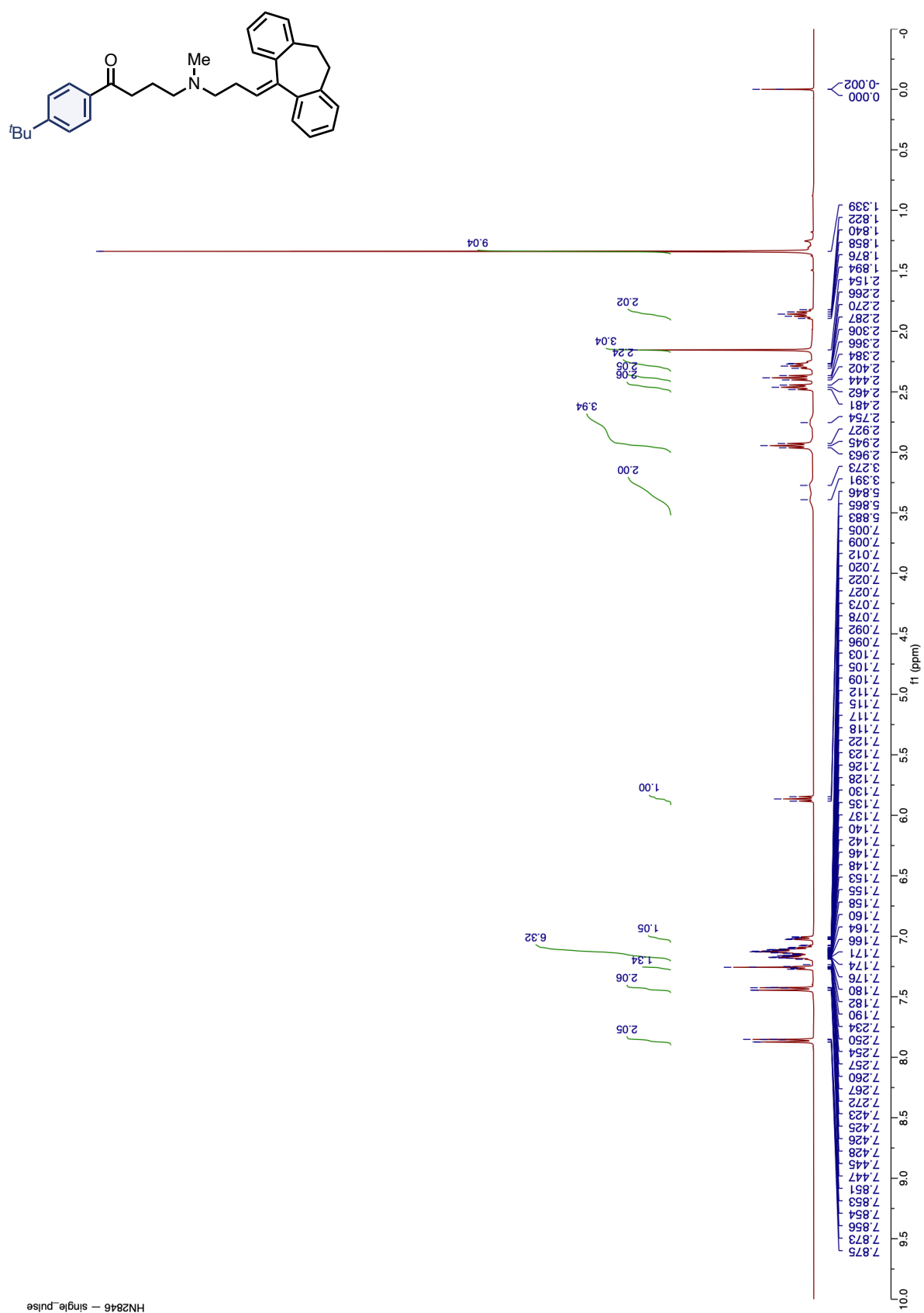
^{13}C NMR of **1q** (101 MHz, CDCl_3)



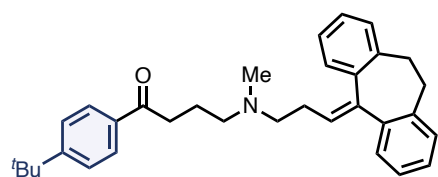
HN2884 — single pulse decoupled gated NOE



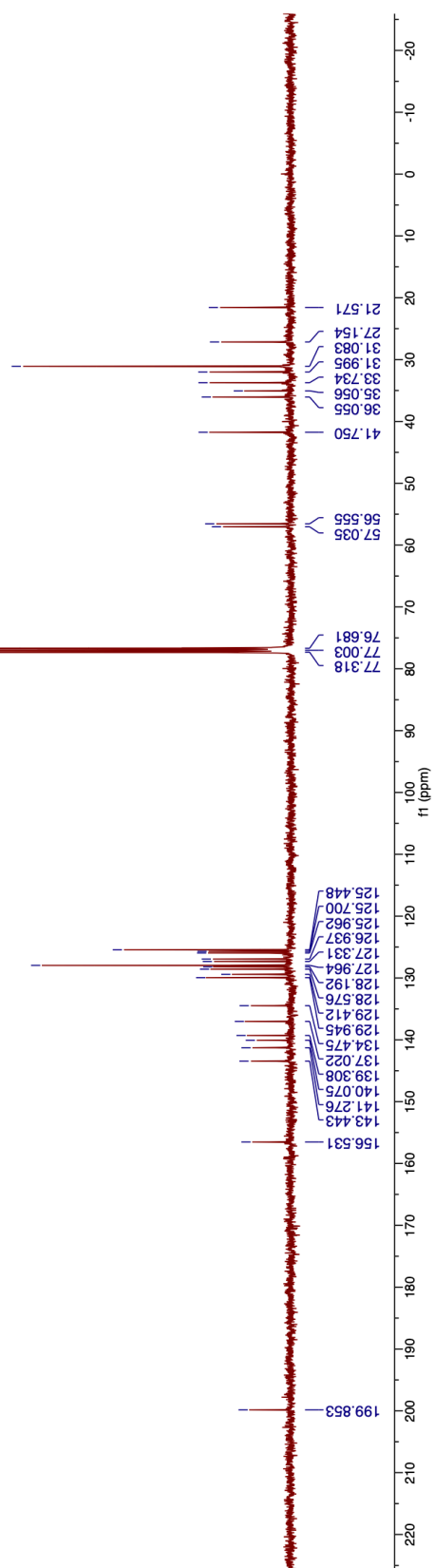
^1H NMR of **1ab** (400 MHz, CDCl_3)



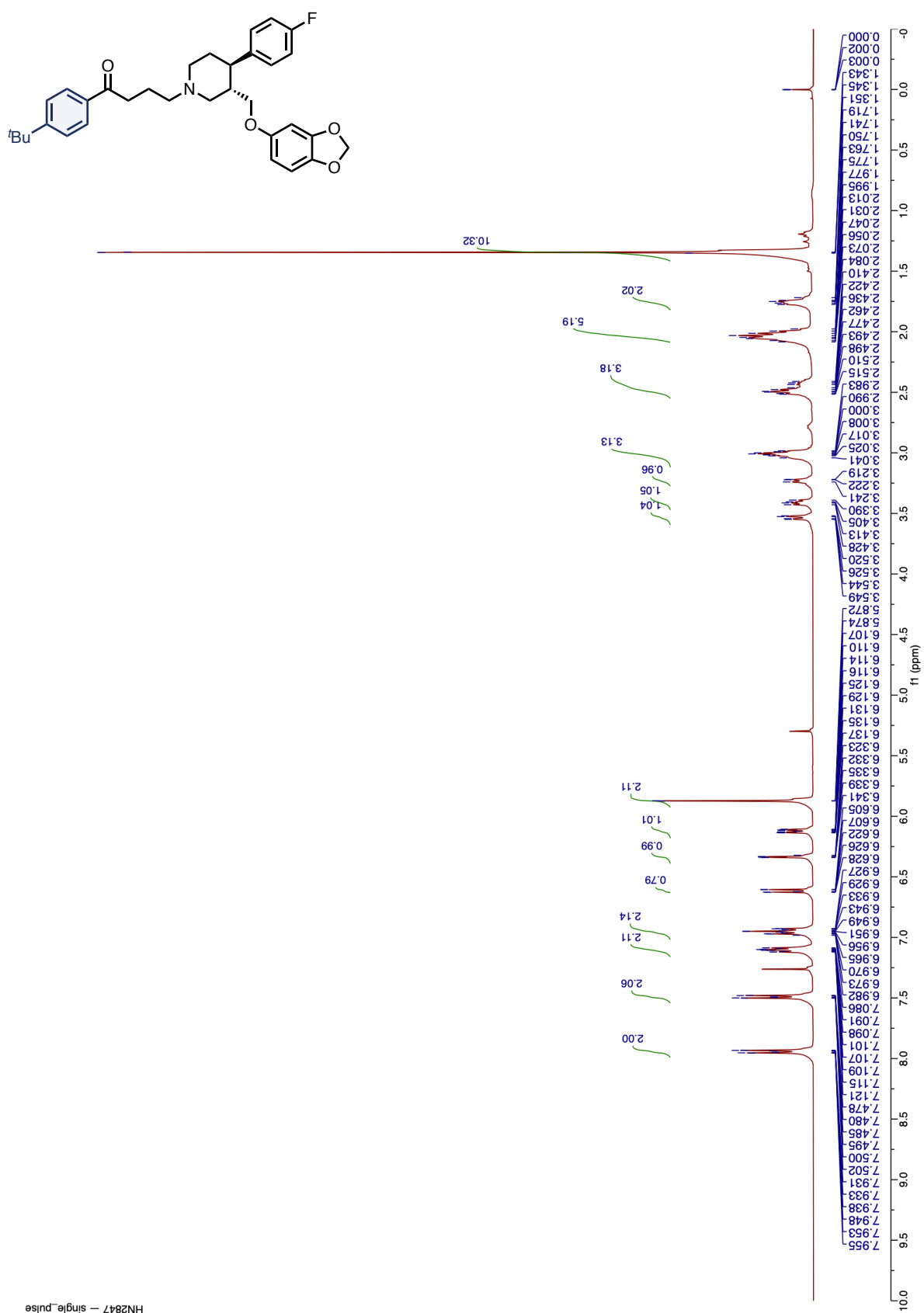
^{13}C NMR of **1ab** (101 MHz, CDCl_3)



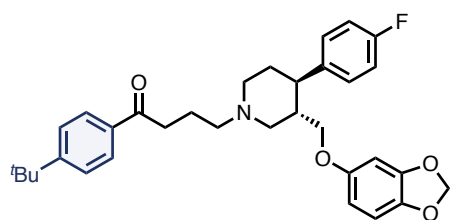
HN2846 — single pulse decoupled gated NOE



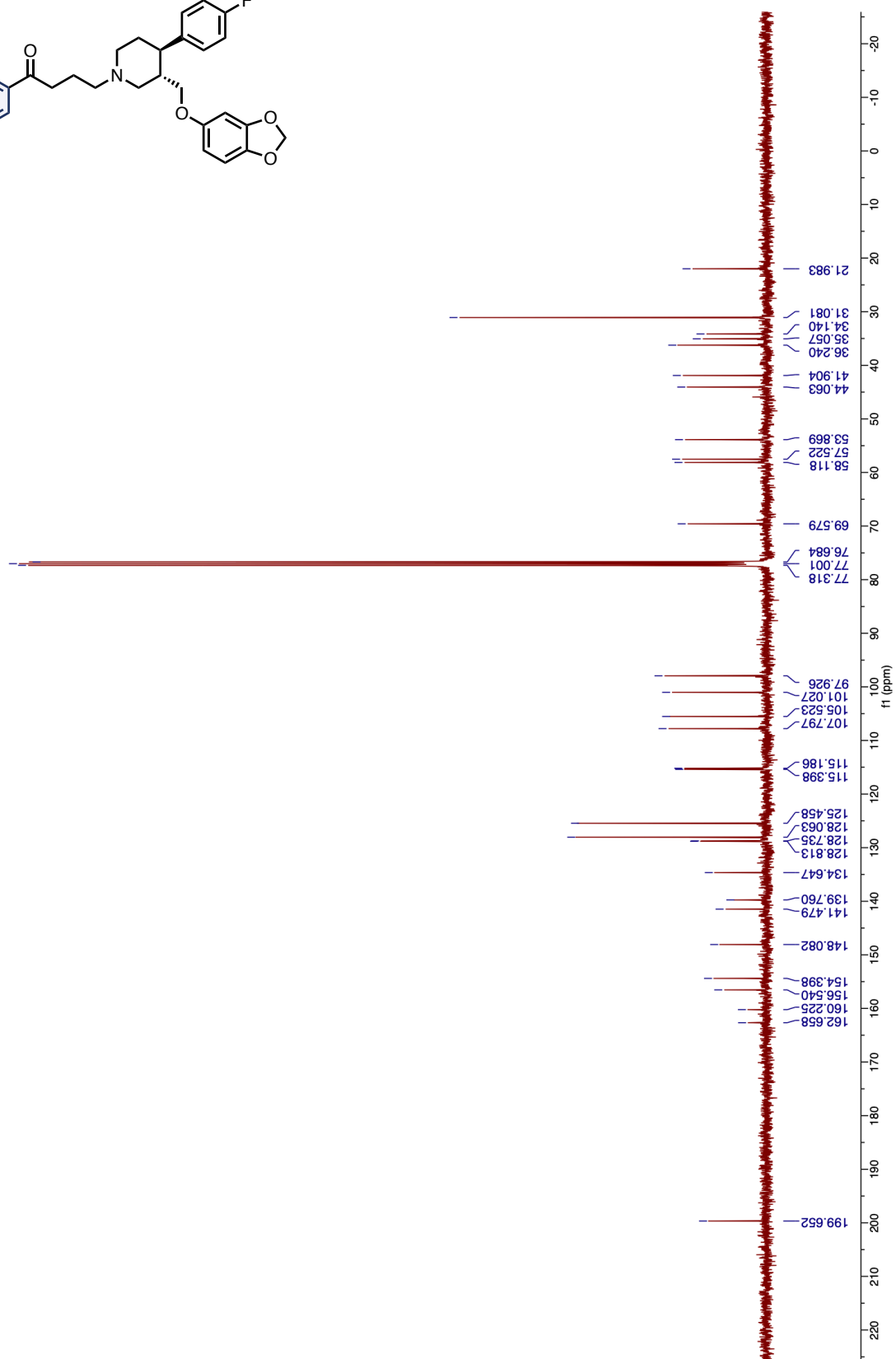
^1H NMR of **1ac** (400 MHz, CDCl_3)



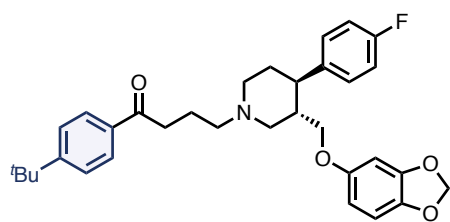
^{13}C NMR of **1ac** (101 MHz, CDCl_3)



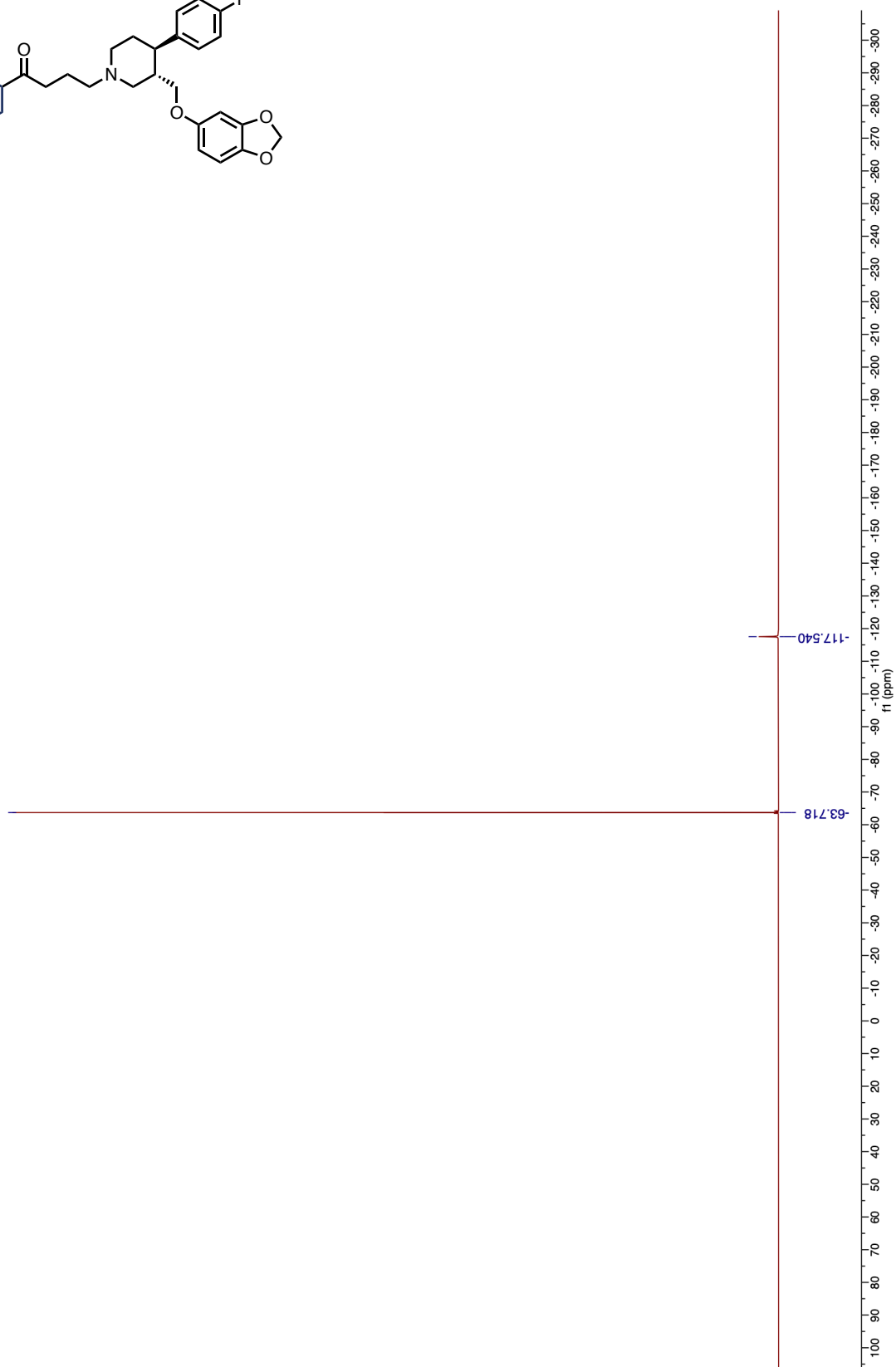
HN2847 — single pulse decoupled gated NOE



^{19}F NMR of **1ac** (376 MHz, CDCl_3)



HN2847 — single pulse decoupled gated NOE

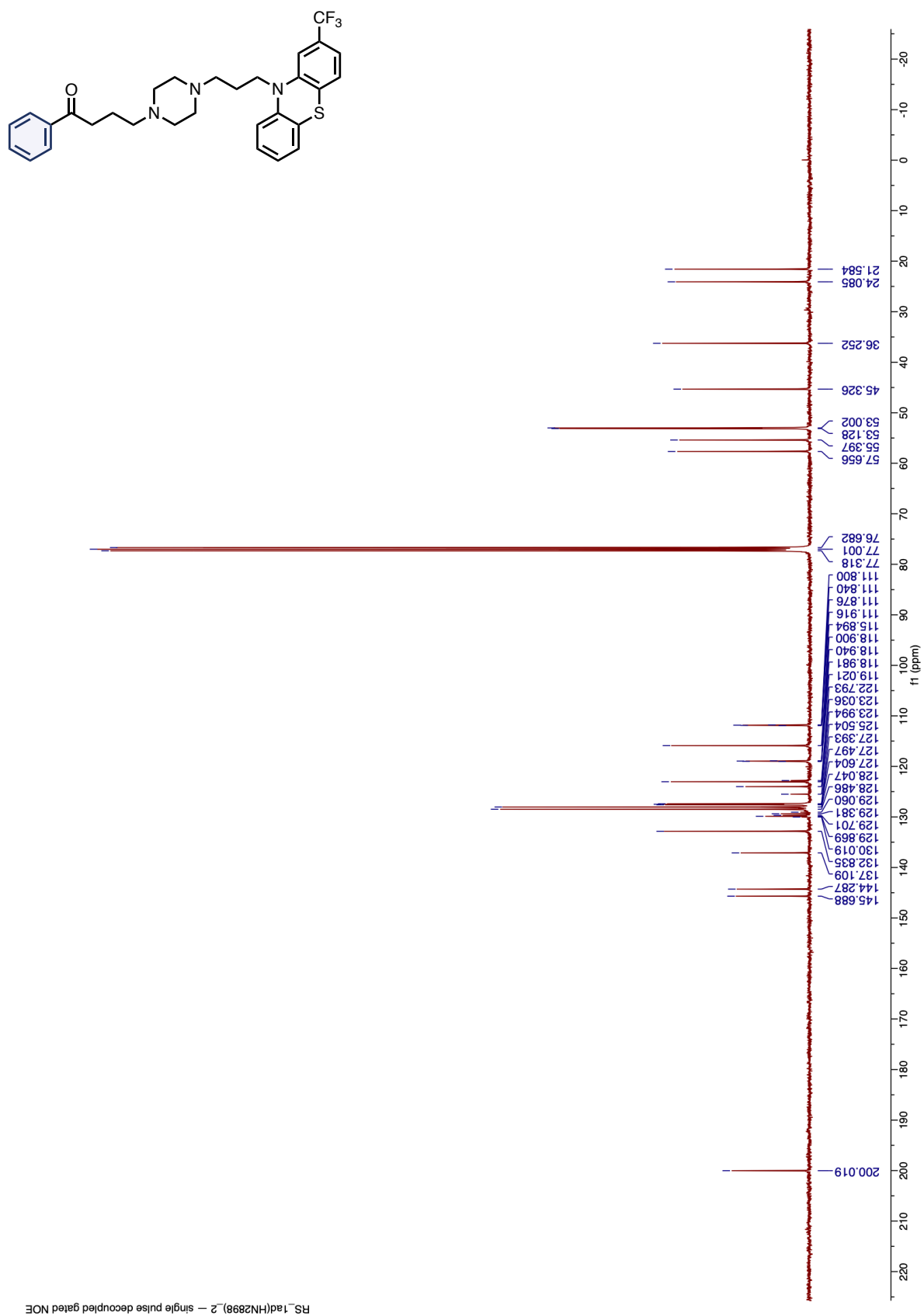


c1ccc(cc1)C(=O)CCCN2CCN(CCN2CCCN3C(=N(C4=CC=CC=C4)S(=O)(=O)C4=CC=C(C=C3)C(F)(F)F)C5=CC=CC=C5)C6=CC=CC=C6

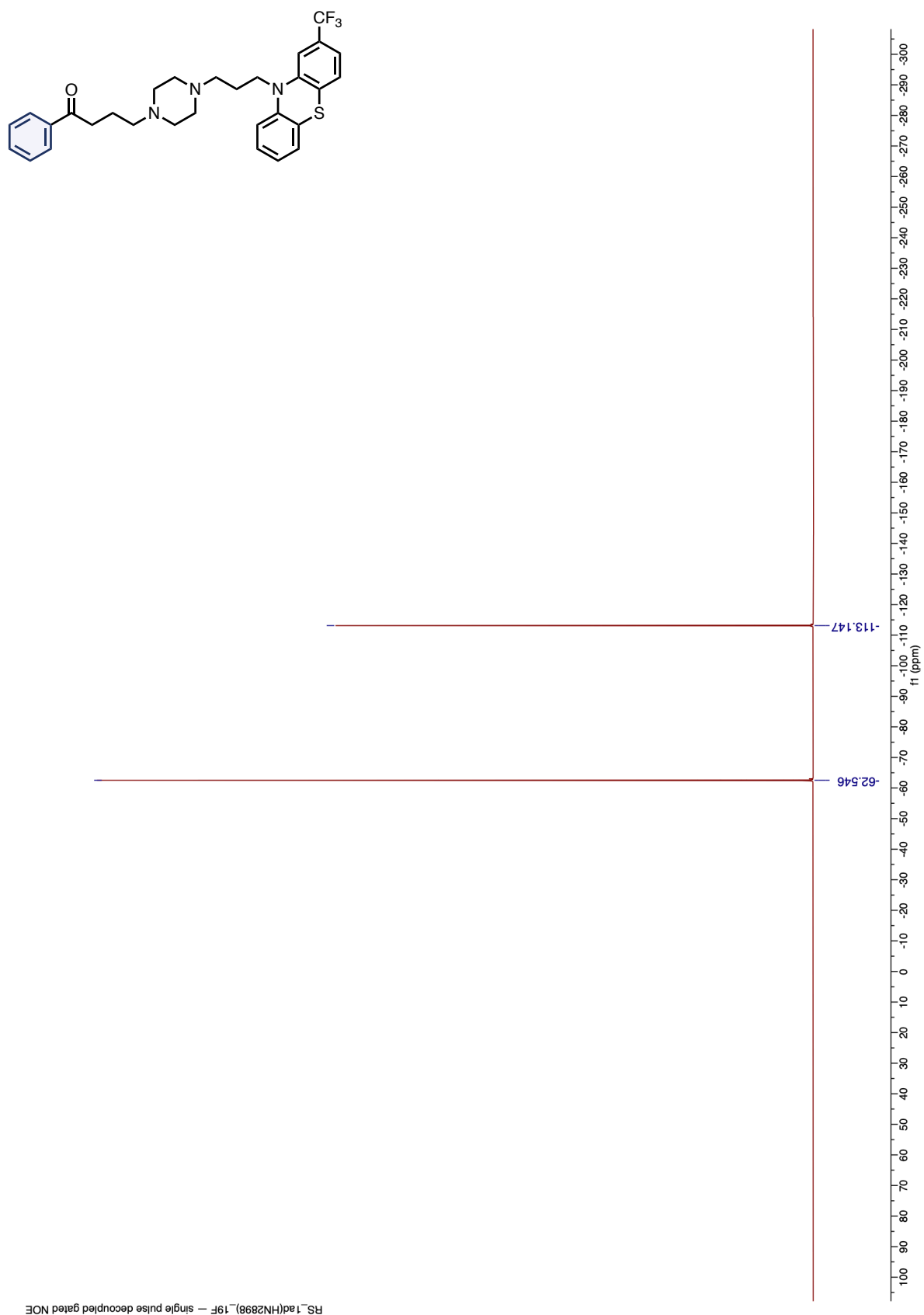
Chemical structure of the compound is shown above the spectrum. The spectrum displays the following peaks (ppm) and integrations:

Chemical Shift (ppm)	Integration
7.971	2.00
7.428 - 7.742	2.12
6.900 - 7.168	4.28
3.924 - 4.001	1.98
2.301 - 3.001	1.96
1.866 - 2.001	4.32
0.000	-

^{13}C NMR of **1ad** (101 MHz, CDCl_3)

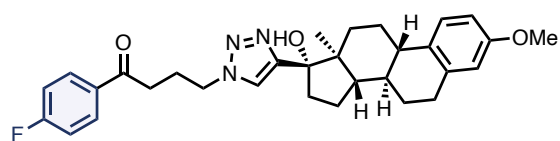


^{19}F NMR of **1ad** (376 MHz, CDCl_3)

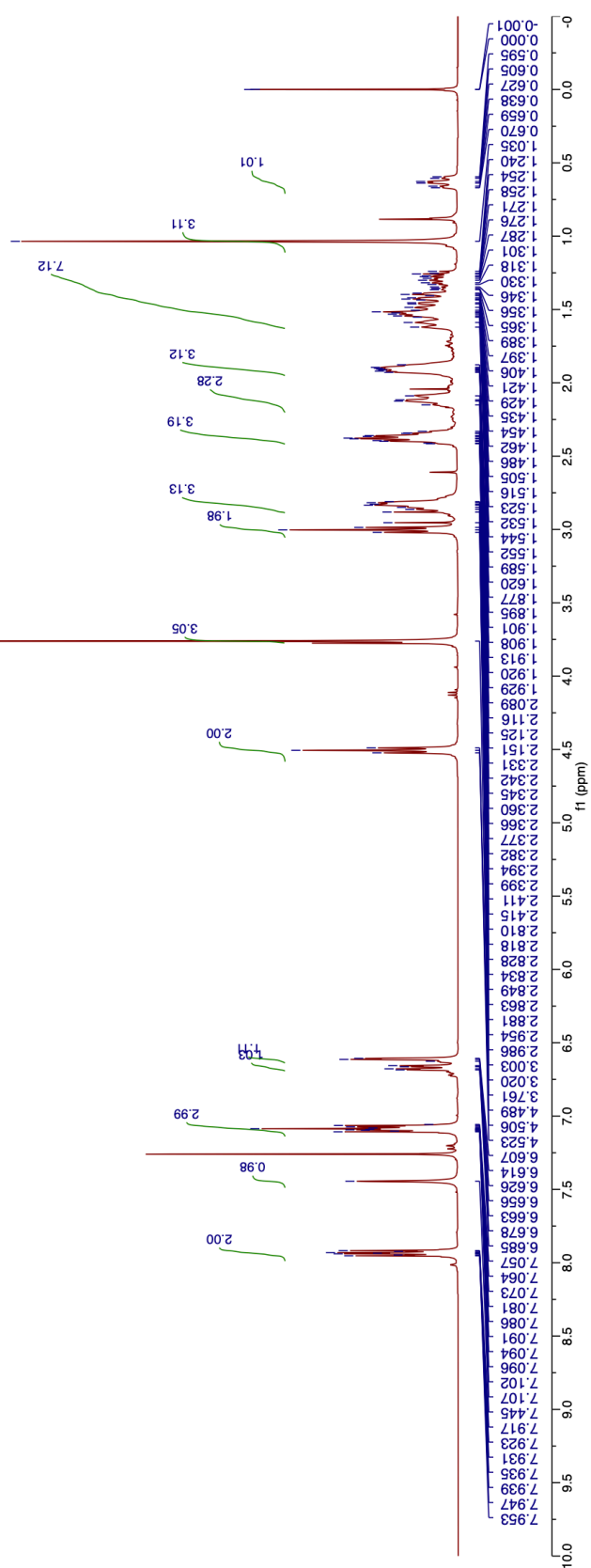


RS_1ad(HN2898)_19F -- single pulse decoupled gated NOE

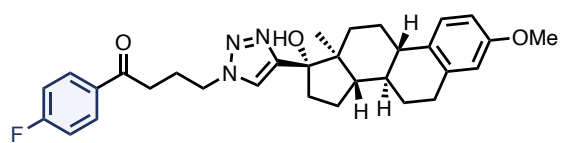
^1H NMR of **1ae** (400 MHz, CDCl_3)



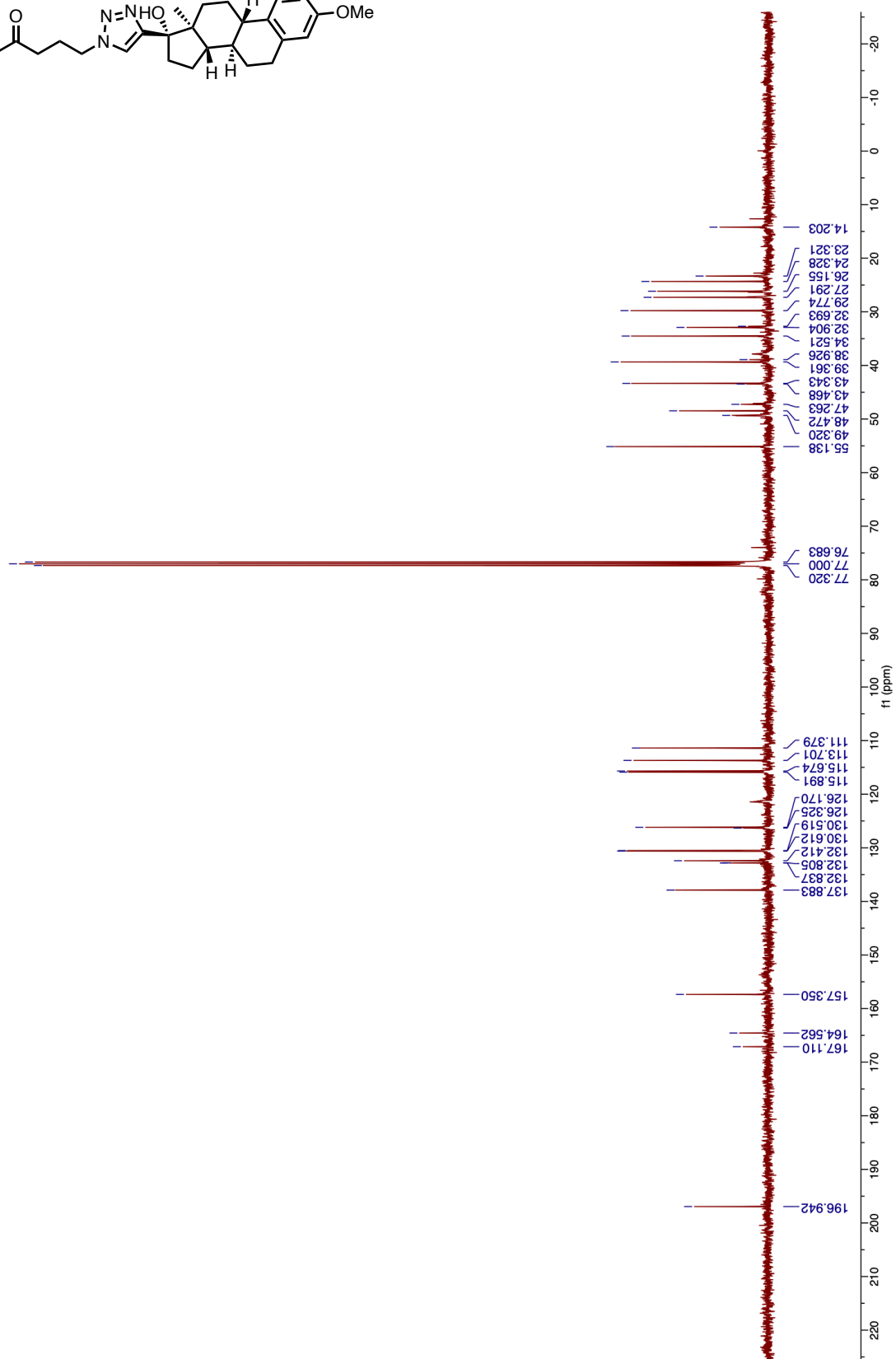
HN2713.f1 - single-pulse



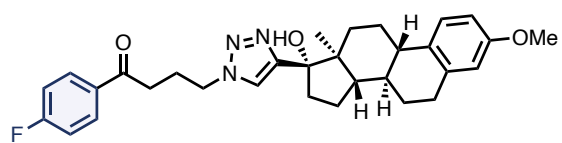
^{13}C NMR of **1ae** (101 MHz, CDCl_3)



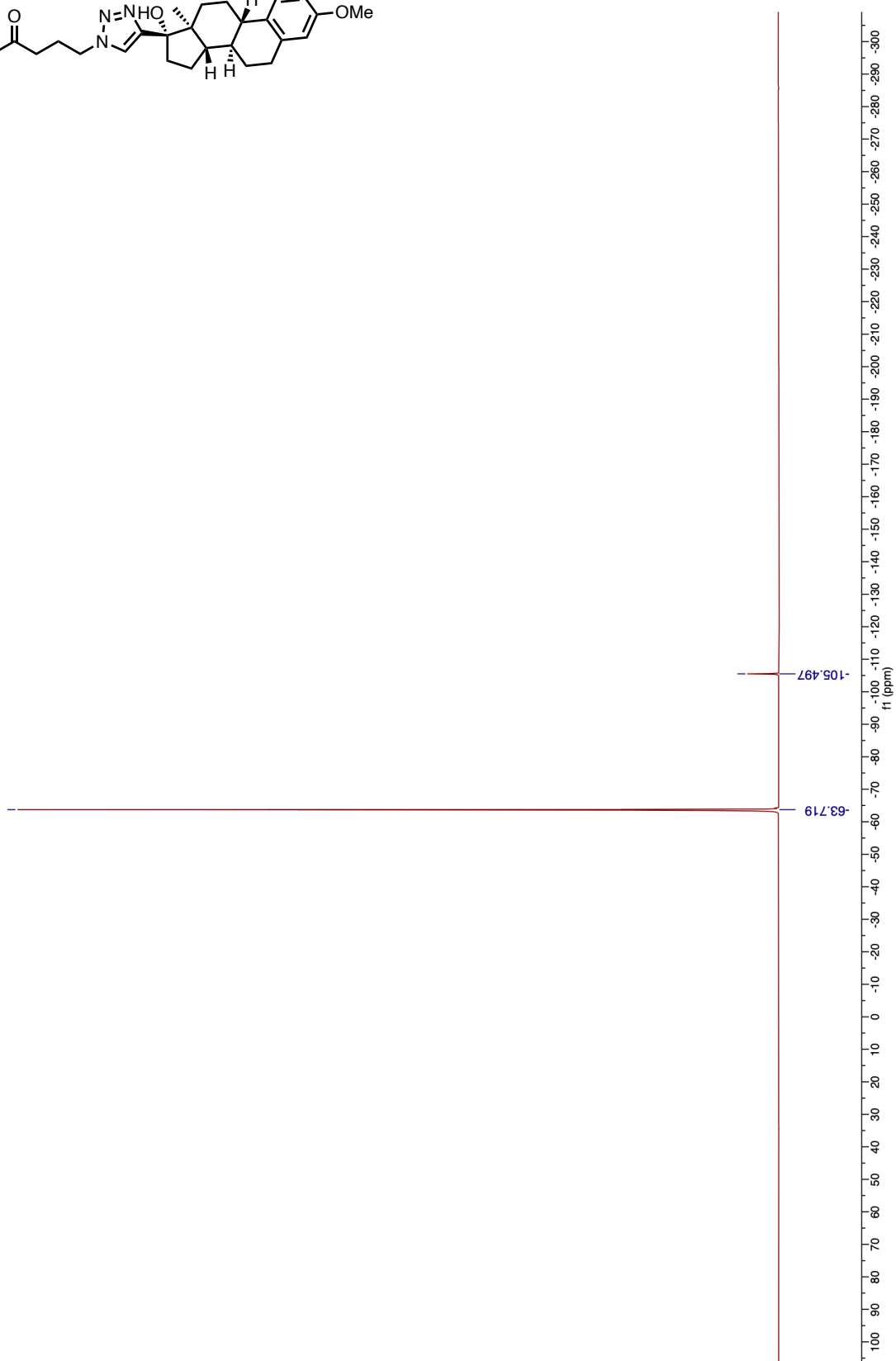
HN2713 — single pulse decoupled gated NOE



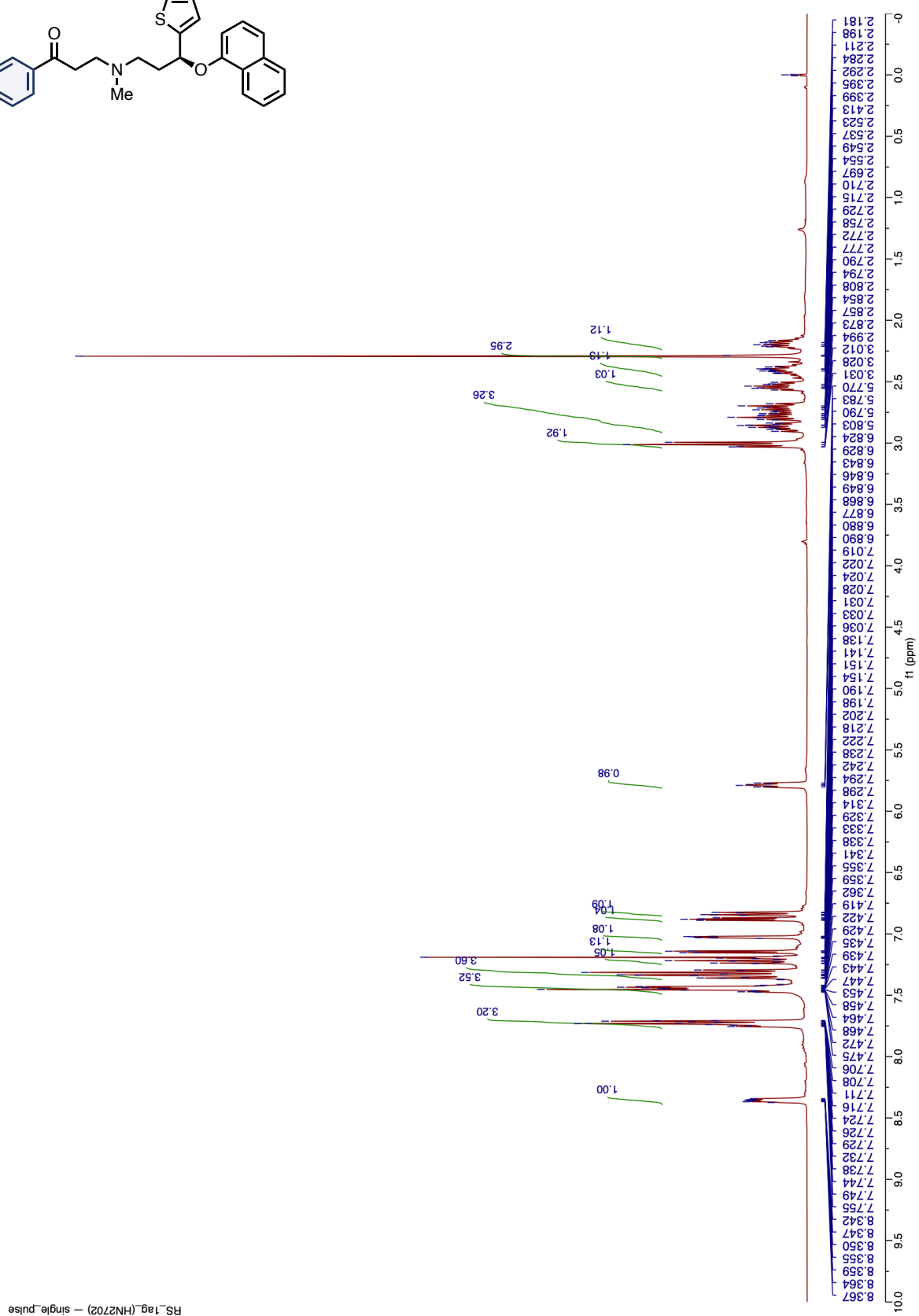
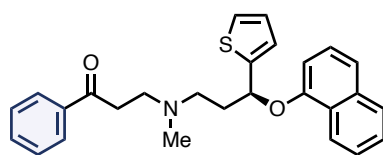
^{19}F NMR of **1ae** (376 MHz, CDCl_3)



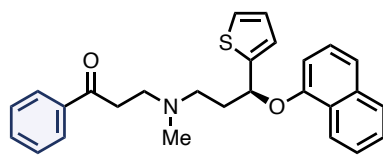
HN2713 — single pulse decoupled gated NOE



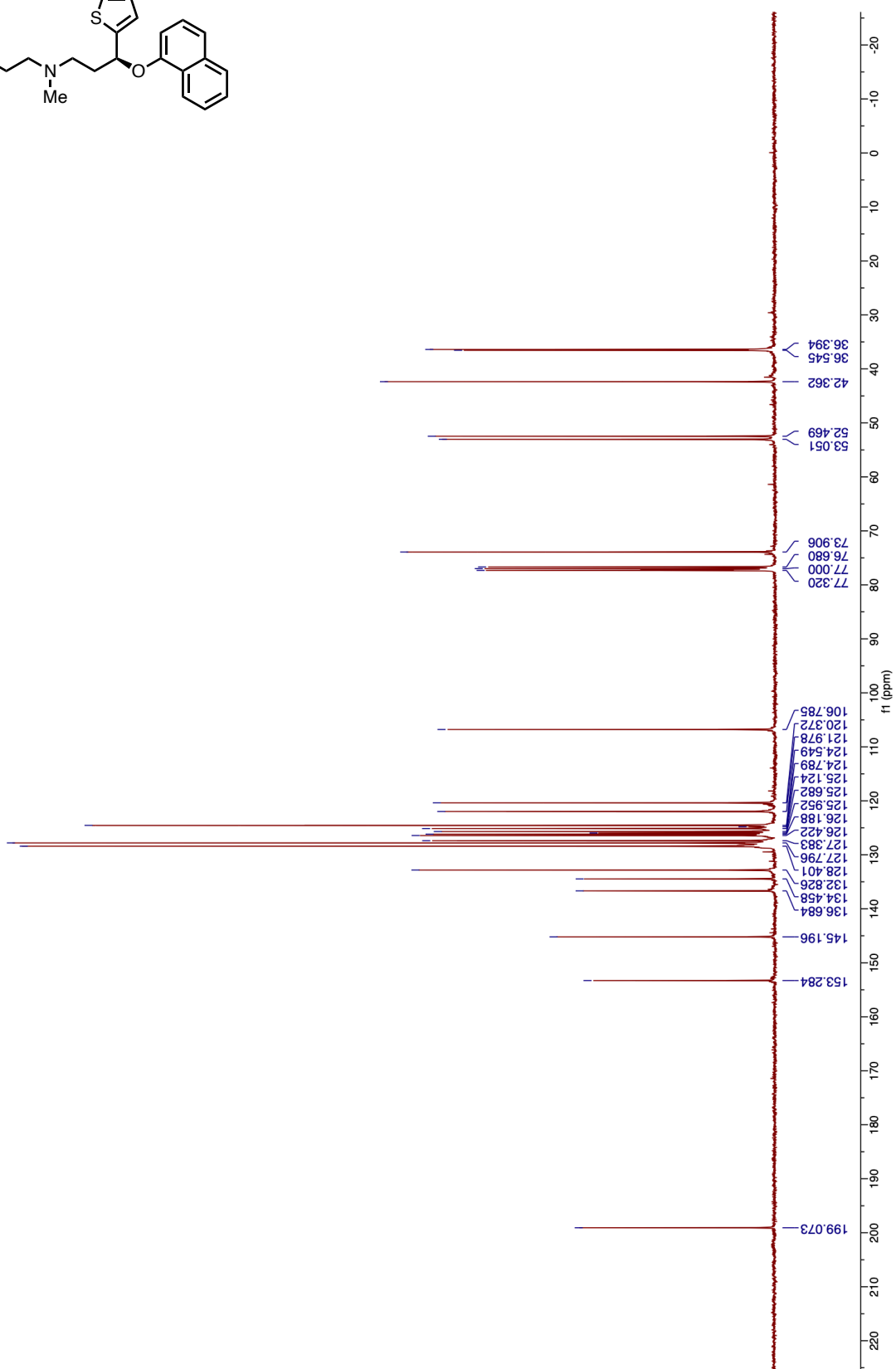
^1H NMR of **1af** (400 MHz, CDCl_3)



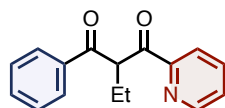
^{13}C NMR of **1af** (101 MHz, CDCl_3)



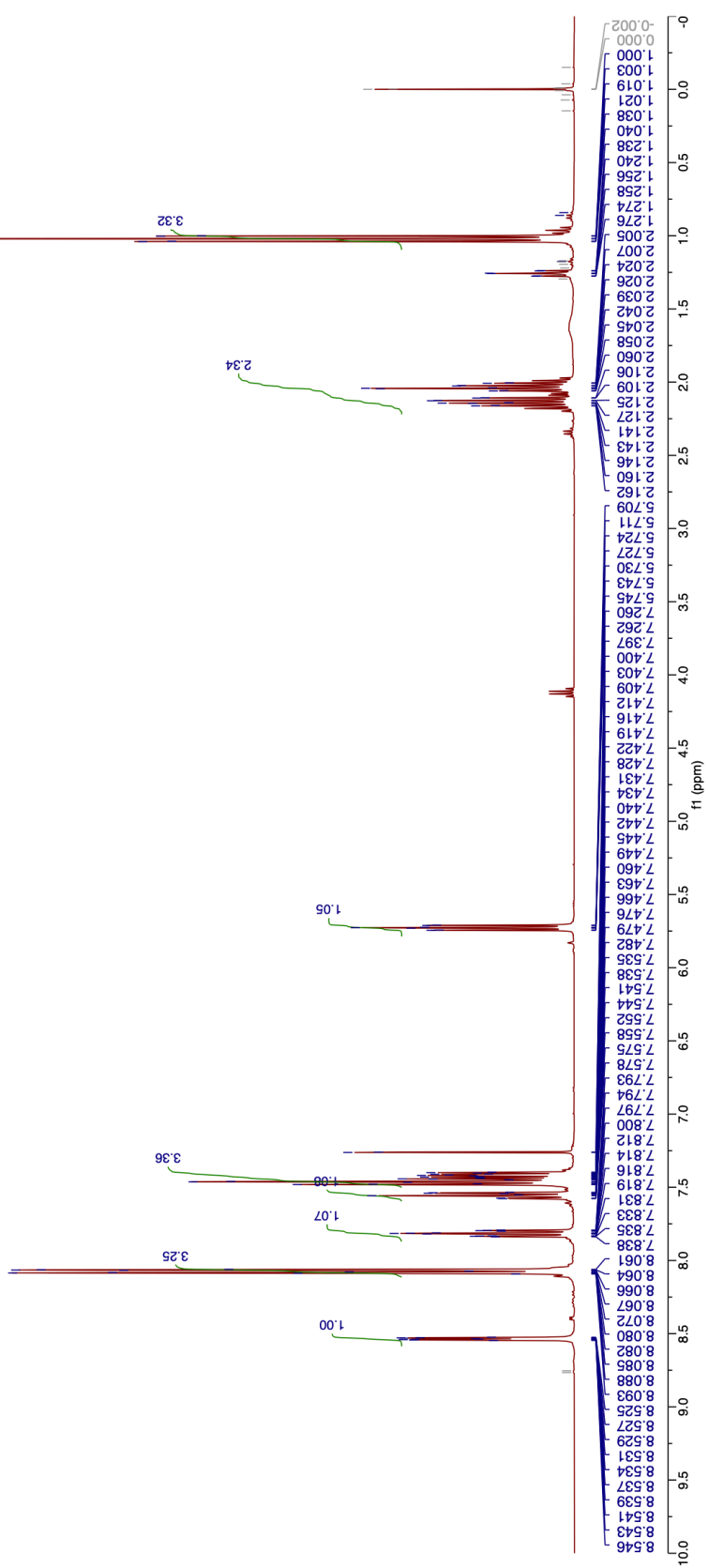
RS_1tag_(HN2702).13C_Kesanaide — single pulse decoupled gated NOE



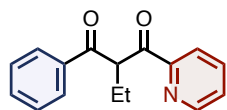
^1H NMR of **5wA** (400 MHz, CDCl_3)



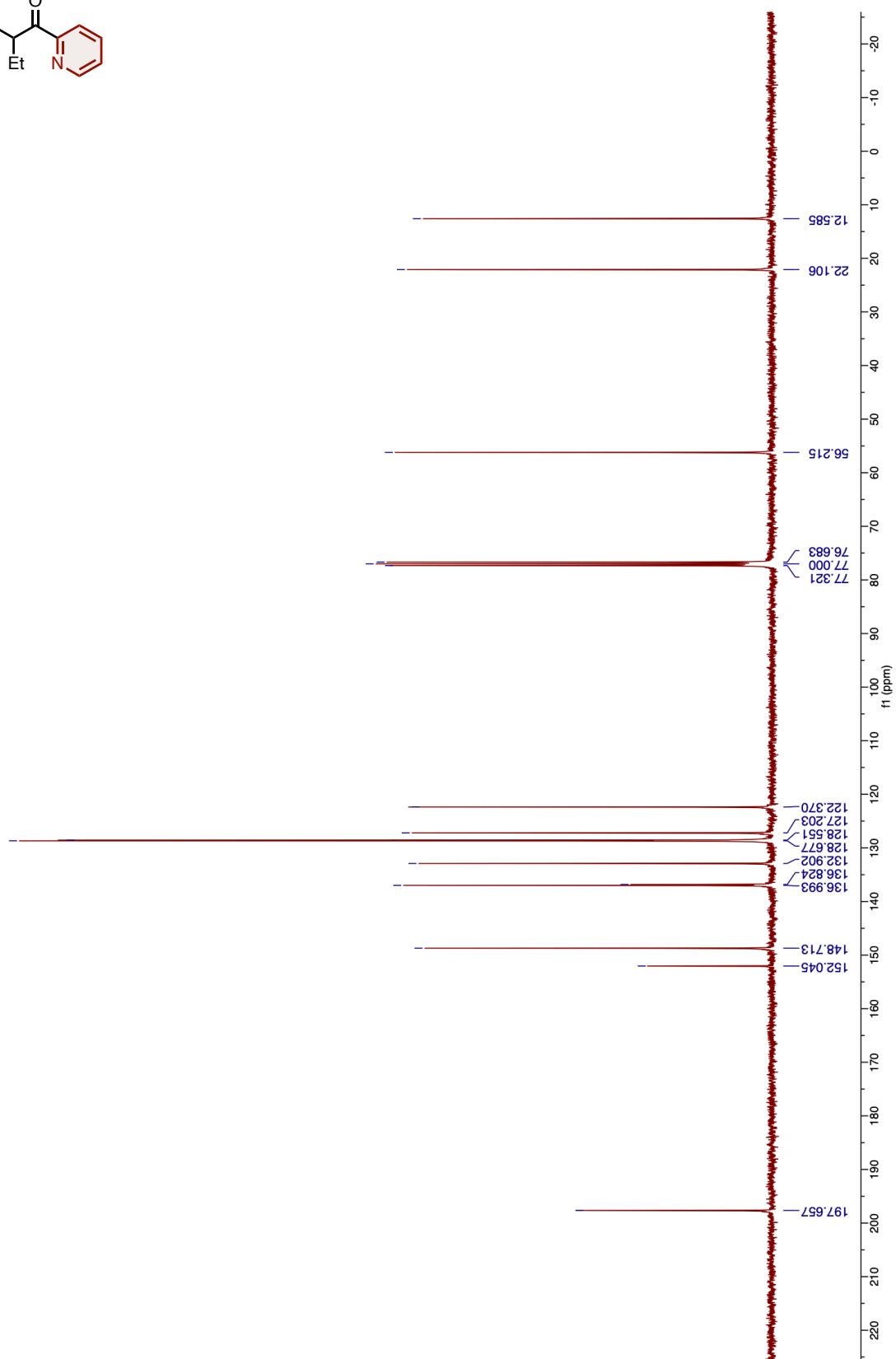
HN2475_76.f1 - single-pulse



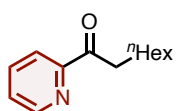
^{13}C NMR of **5wA** (101 MHz, CDCl_3)



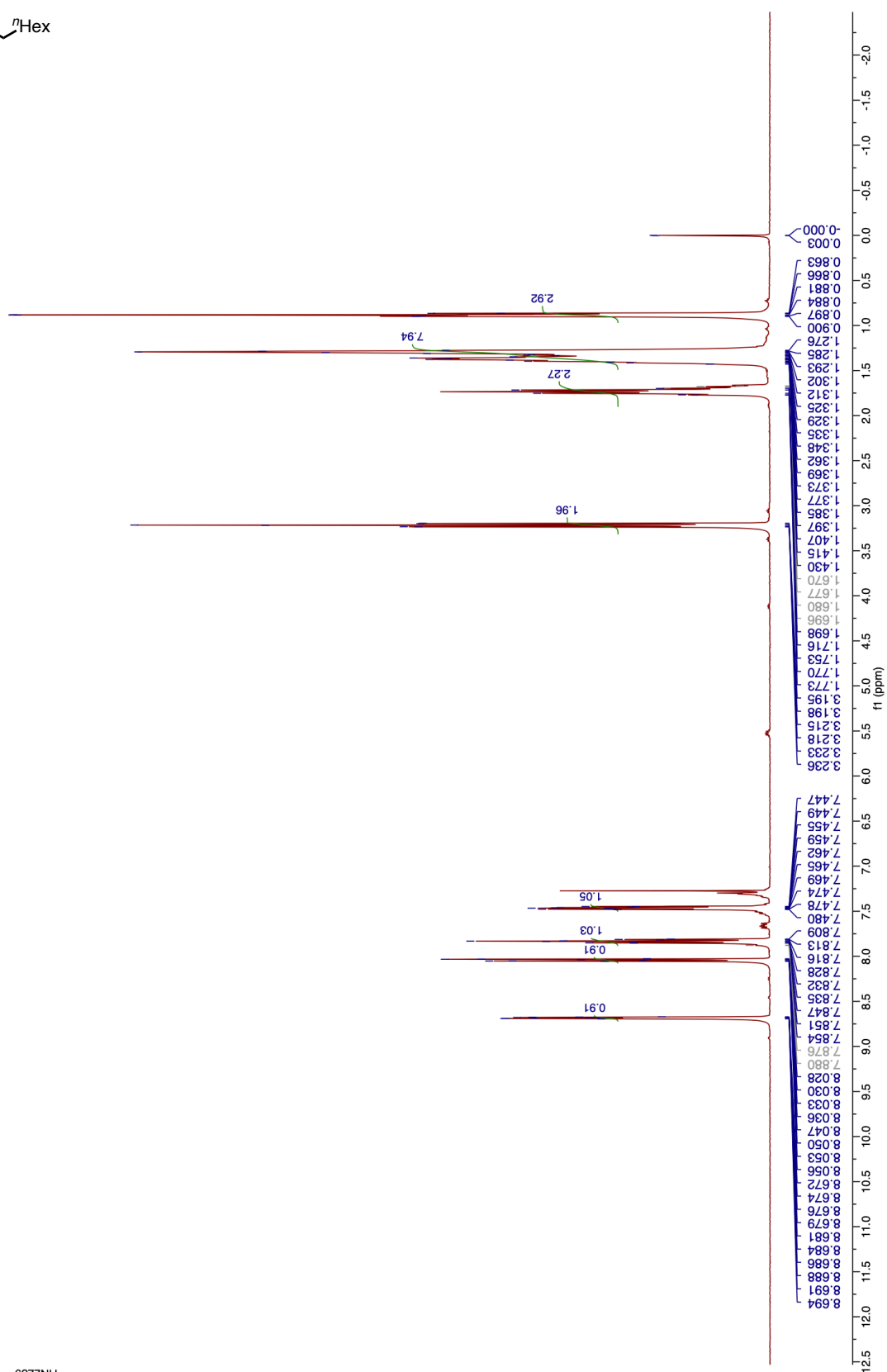
HN2481 — single pulse decoupled gated NOE



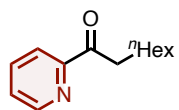
^1H NMR of **3aA** (400 MHz, CDCl_3)



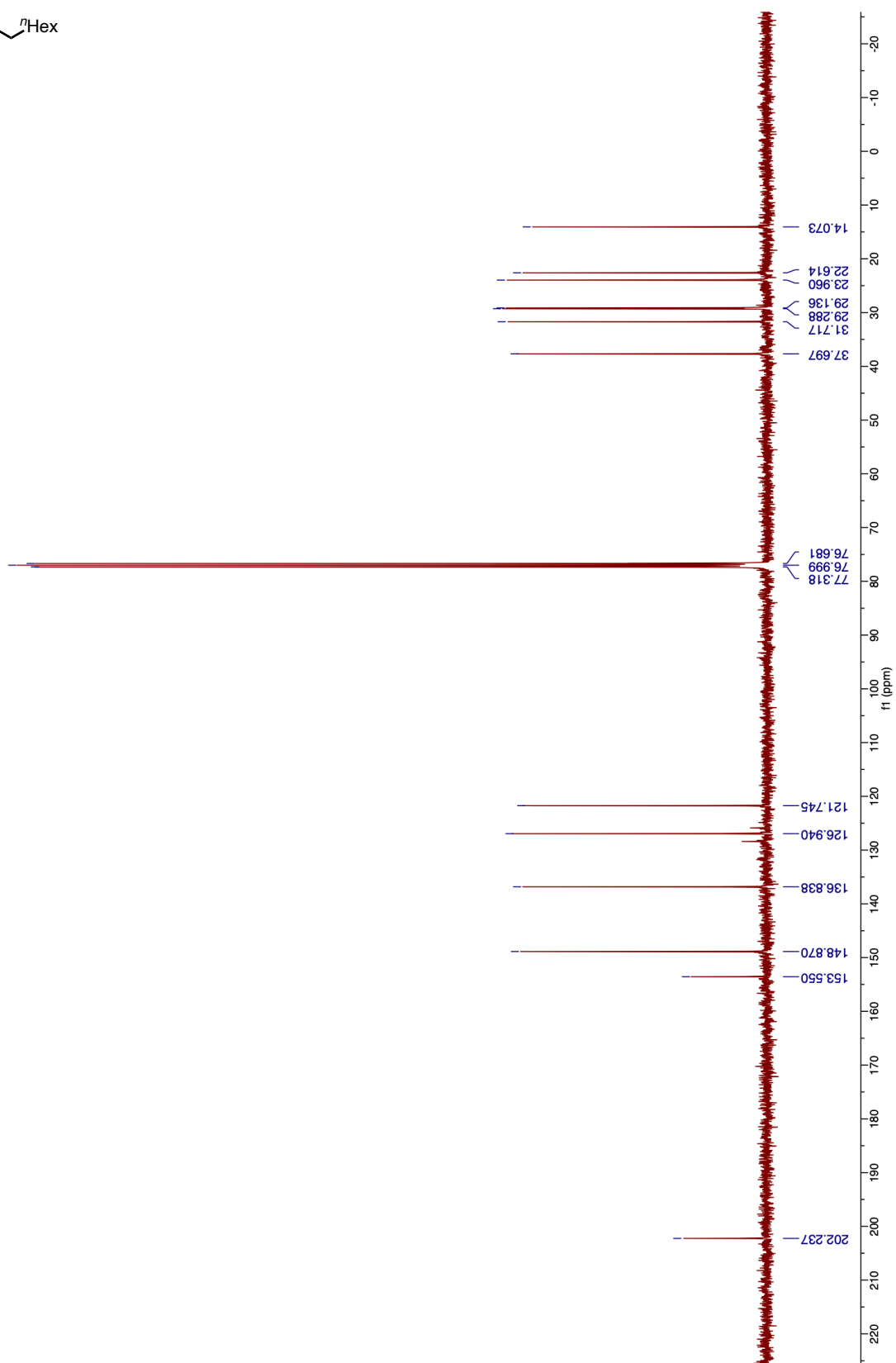
HN2239 — single-pulse



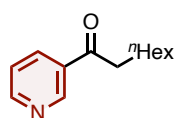
^{13}C NMR of **3aA** (101 MHz, CDCl_3)



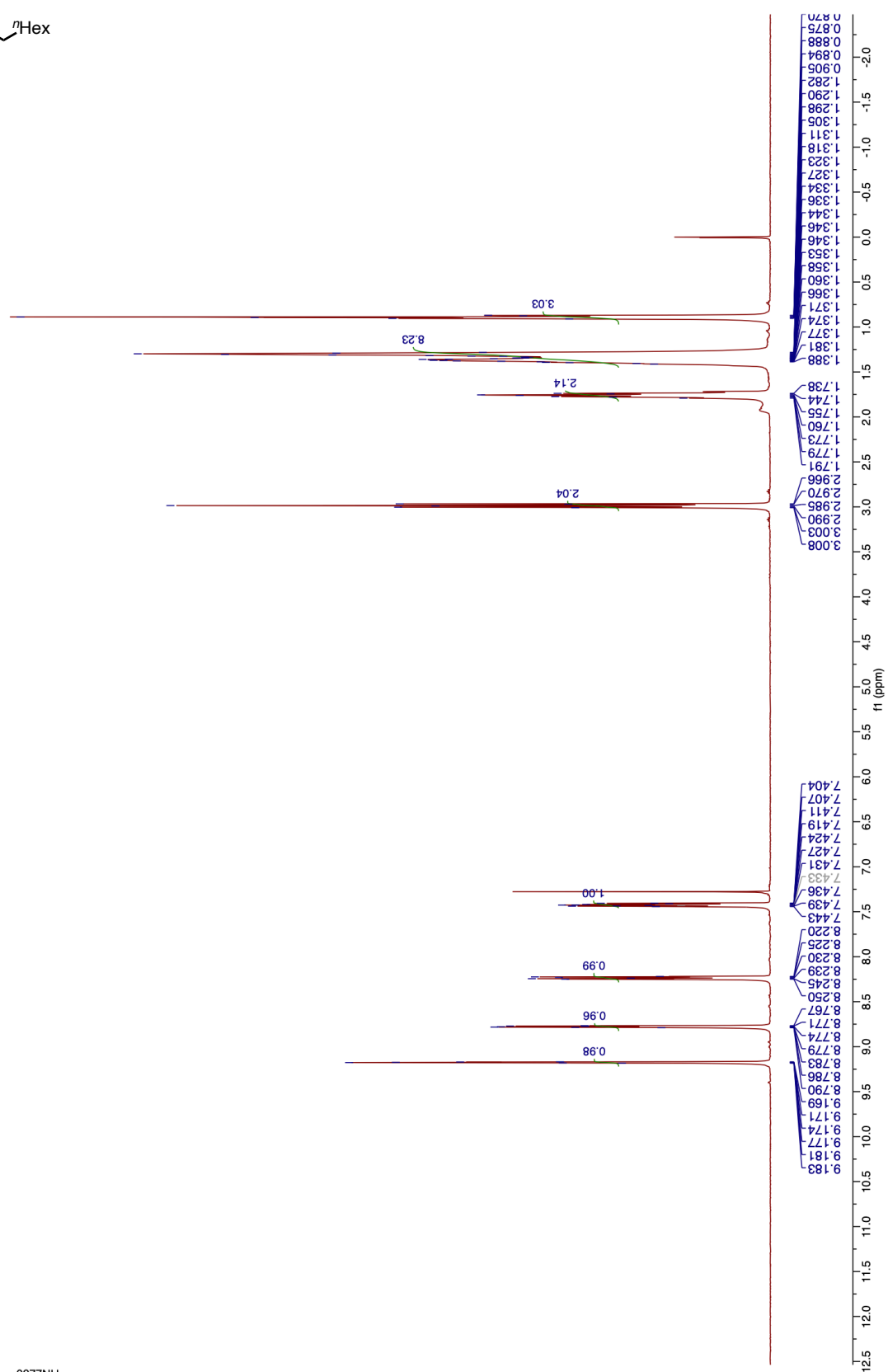
HN2239 — single pulse decoupled gated NOE



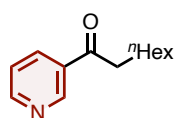
¹H NMR of **3aB** (400 MHz, CDCl₃)



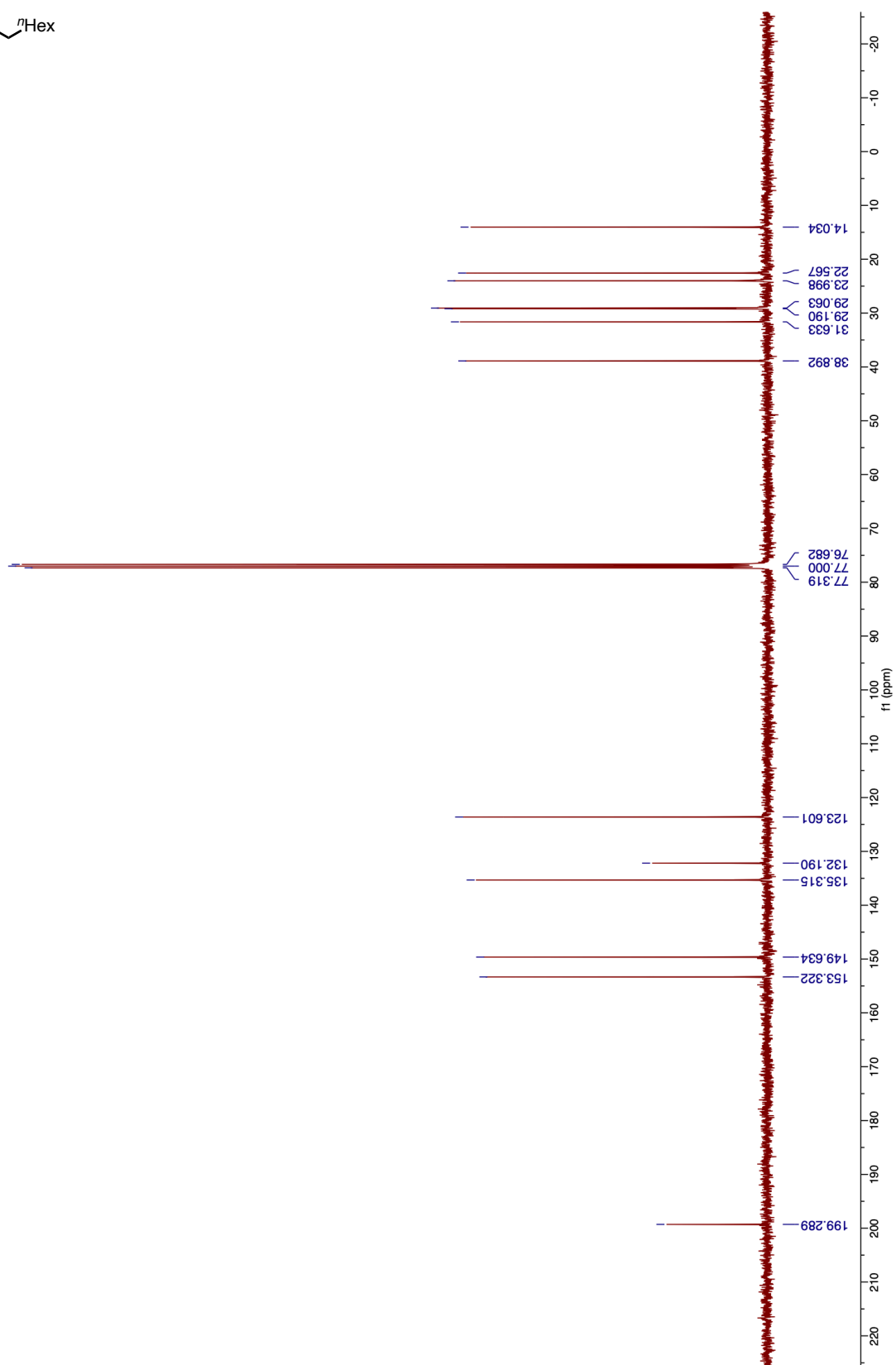
HN2260 — single-pulse

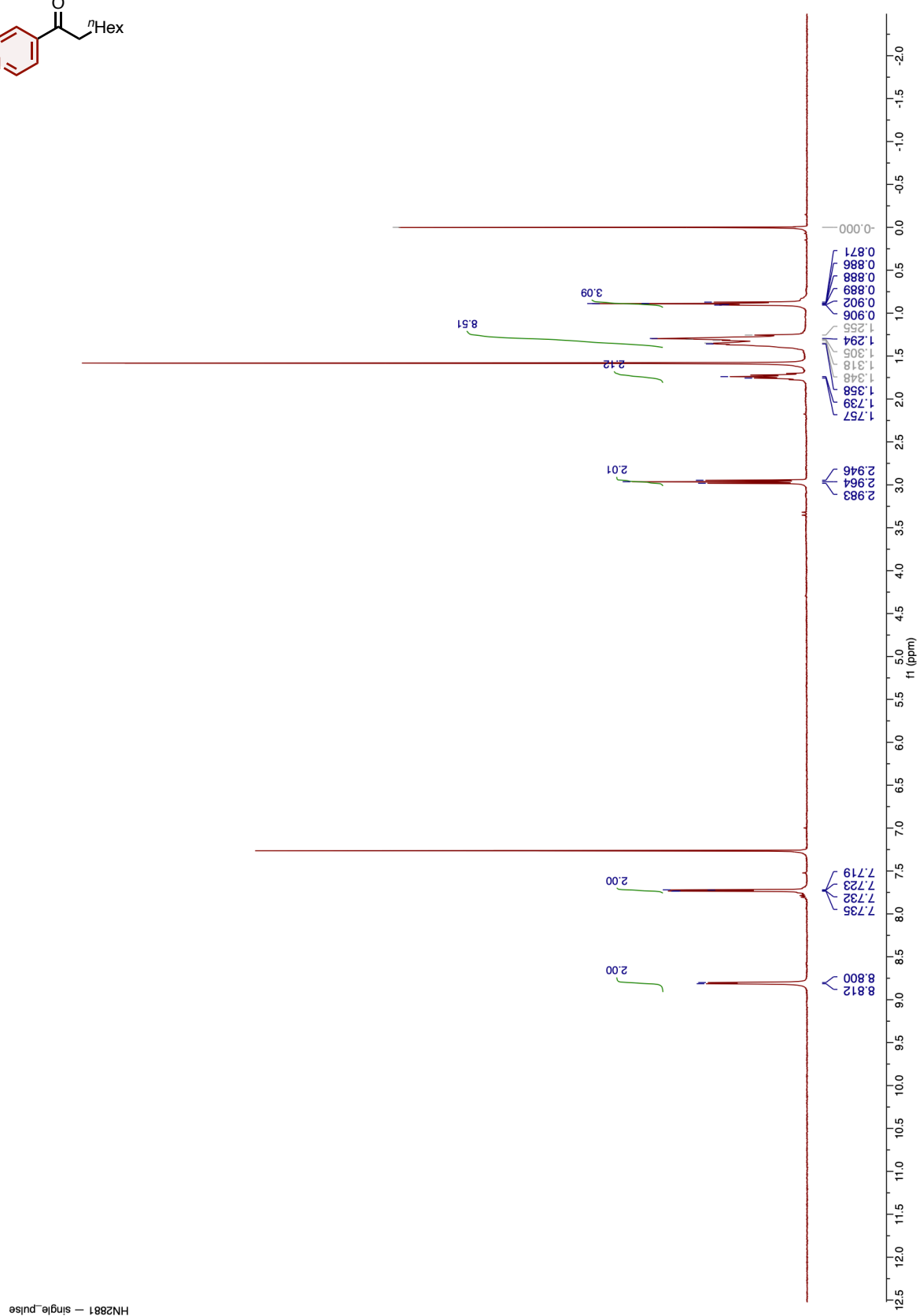


^{13}C NMR of **3aB** (101 MHz, CDCl_3)

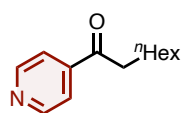


HN2260 — single pulse decoupled gated NOE

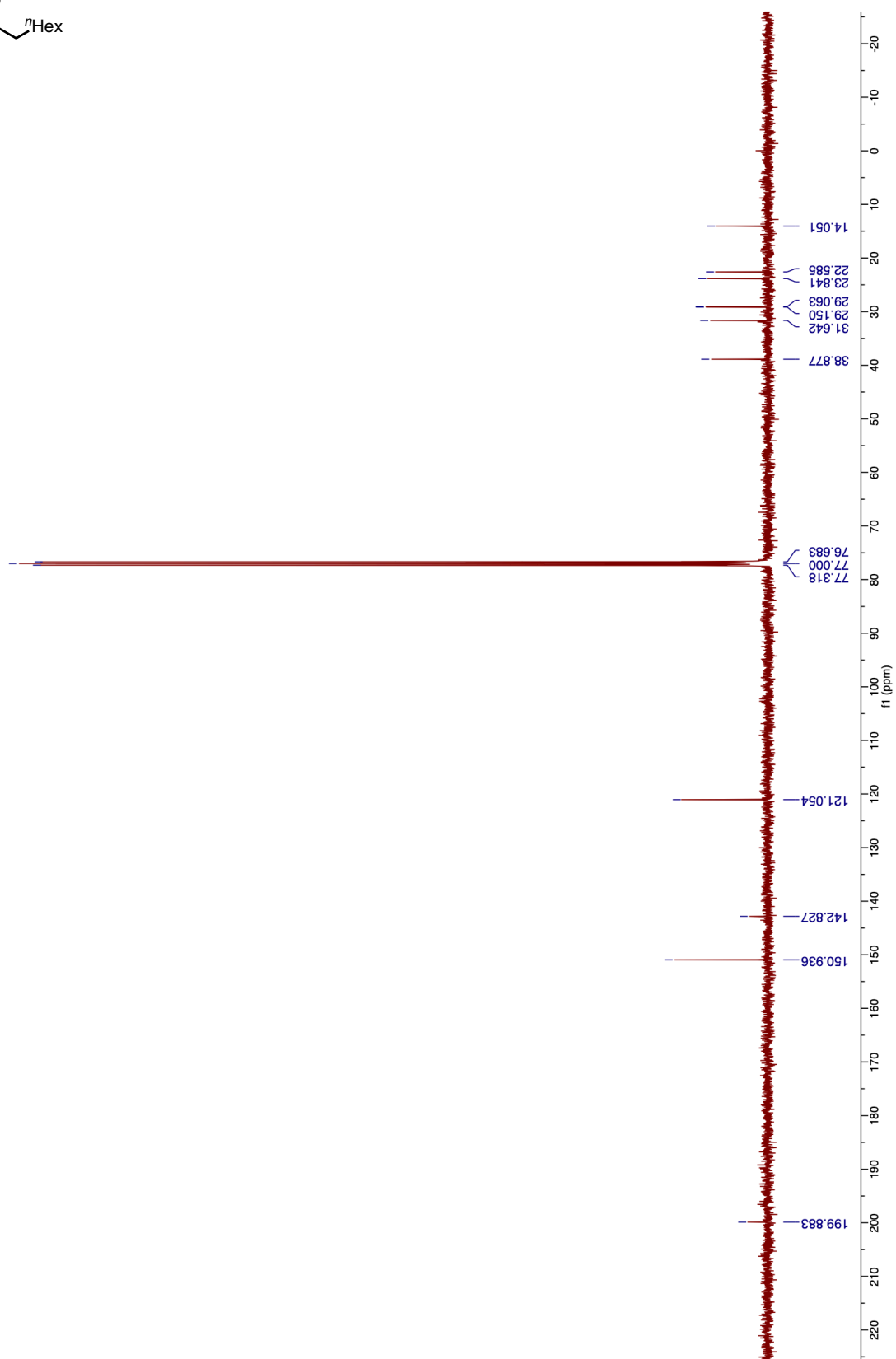




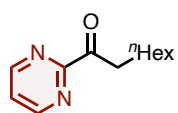
^{13}C NMR of **3aC** (101 MHz, CDCl_3)



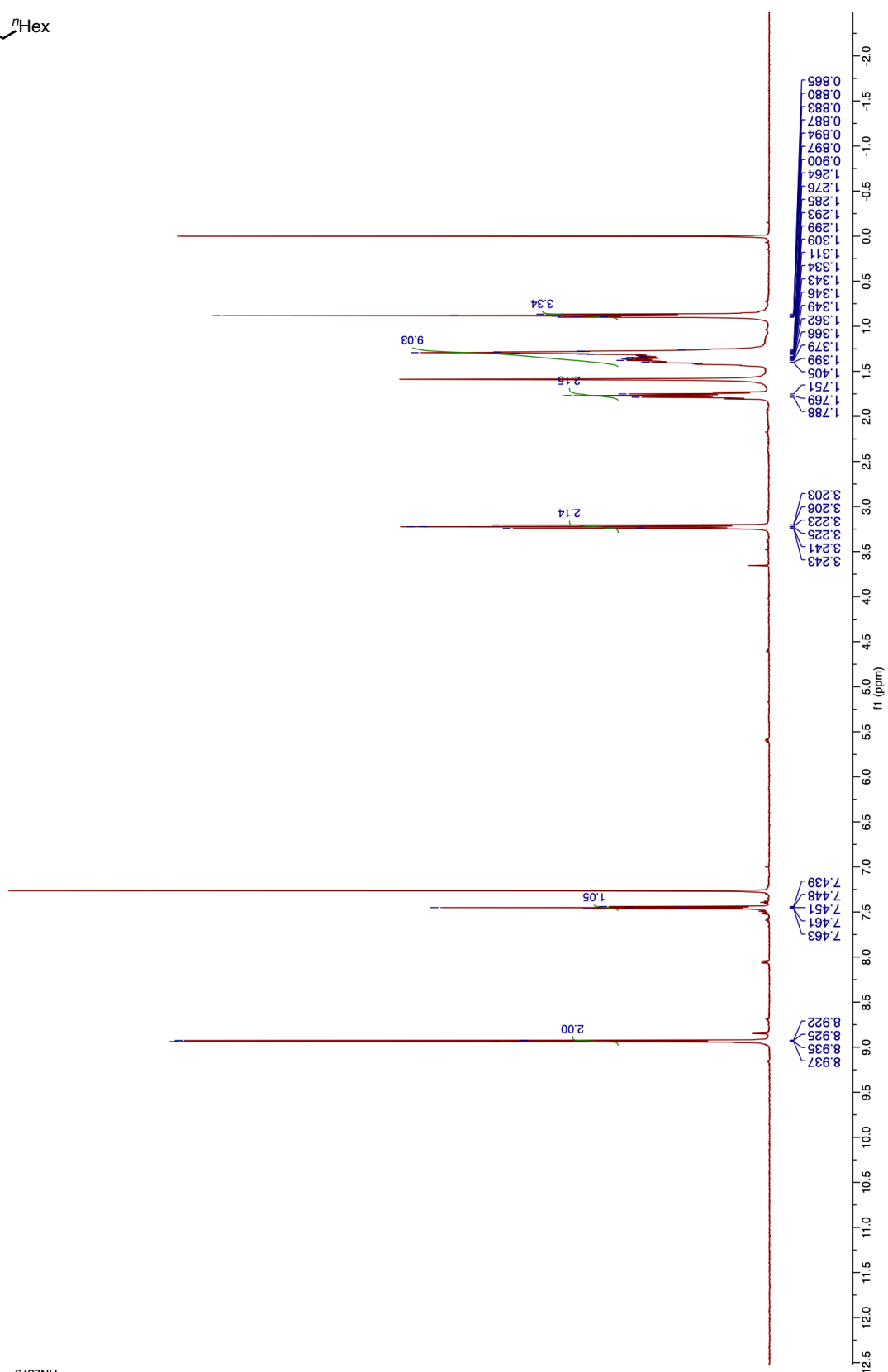
HN2881 — single pulse decoupled gated NOE



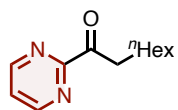
^1H NMR of **3aD** (400 MHz, CDCl_3)



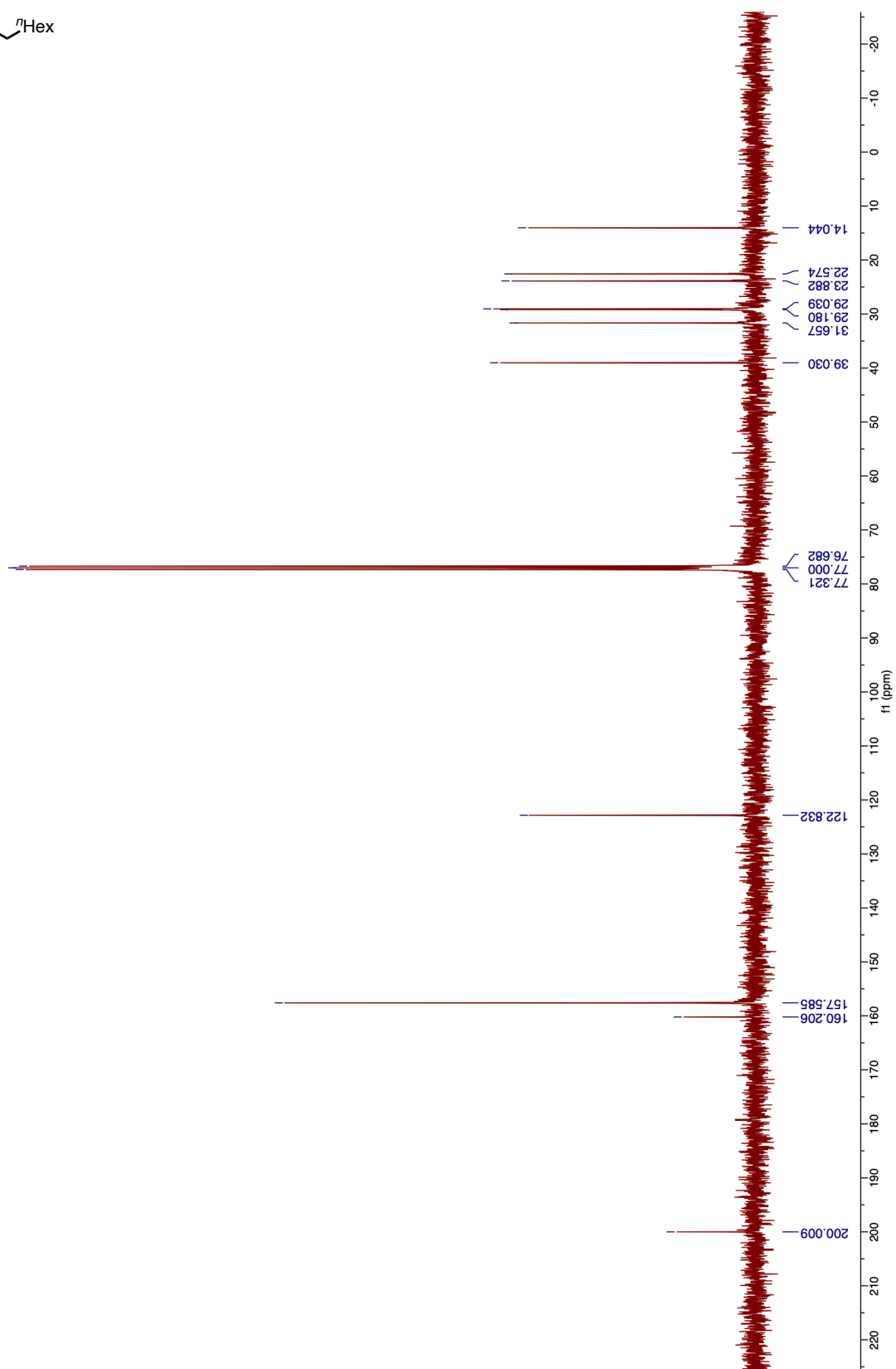
HN2379 — single-pulse



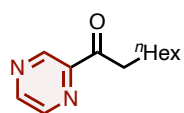
^{13}C NMR of **3aD** (101 MHz, CDCl_3)



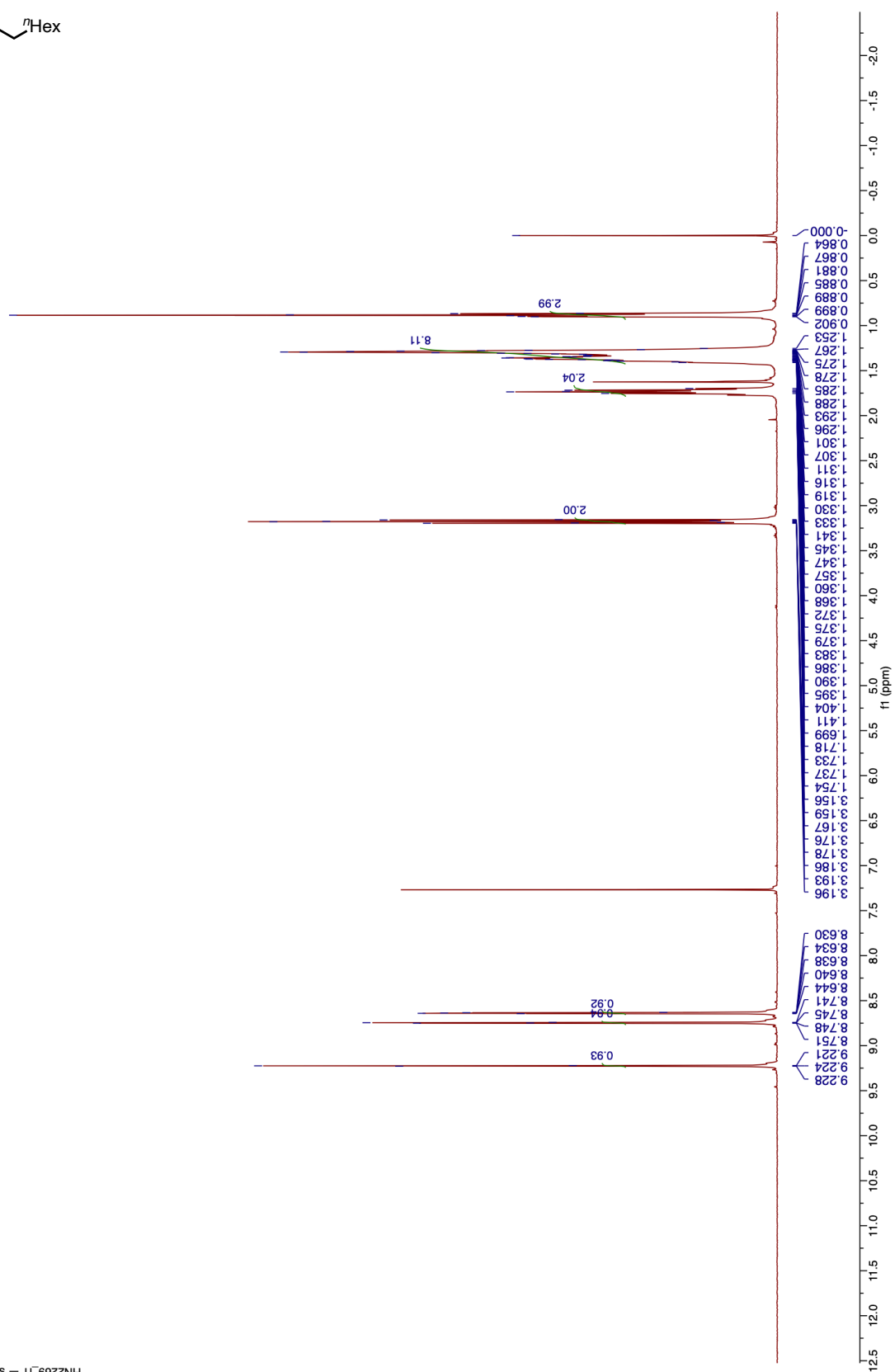
HN2379_11 — single pulse decoupled gated NOE



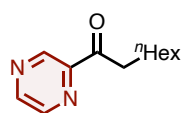
^1H NMR of **3E** (400 MHz, CDCl_3)



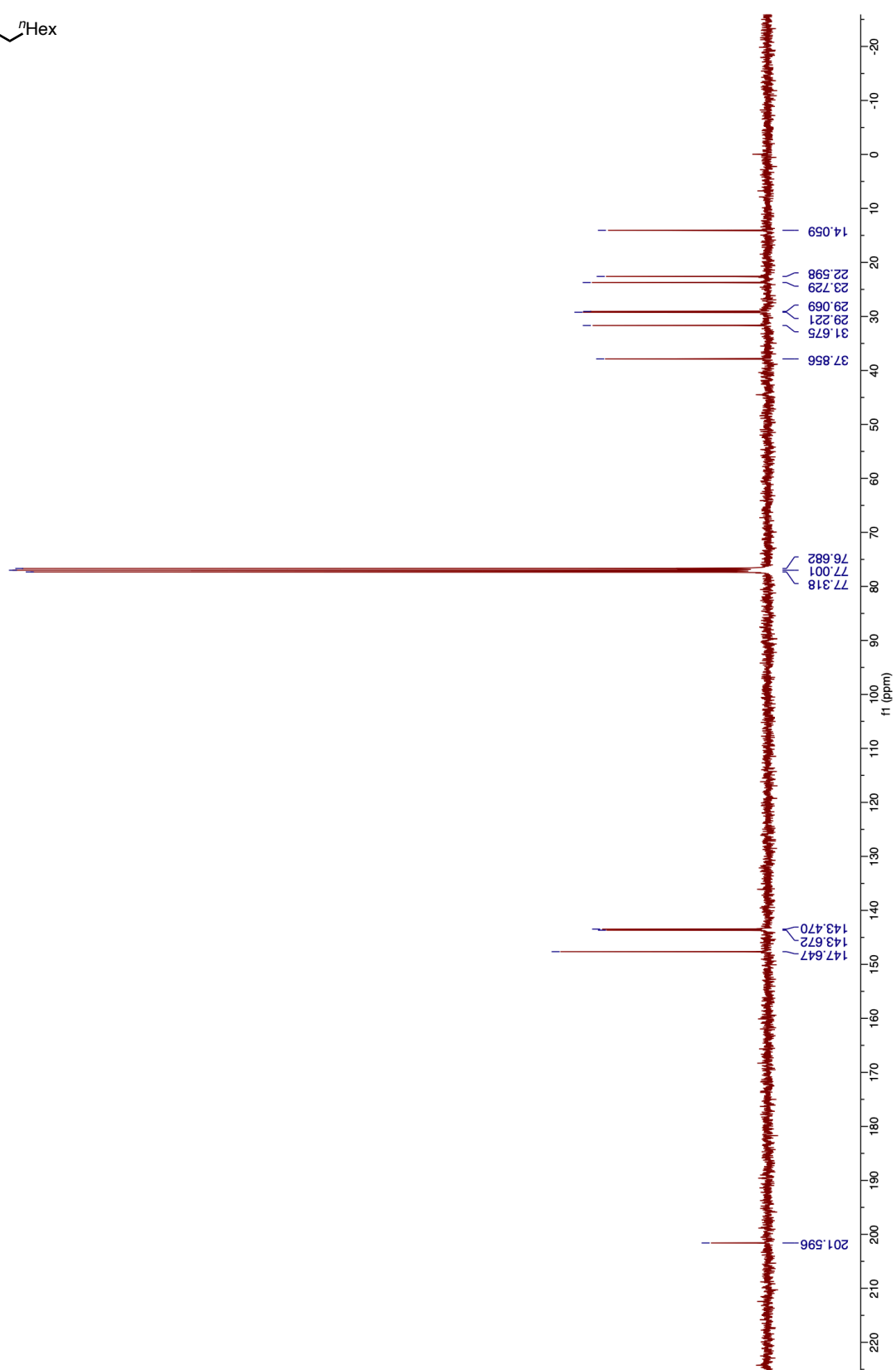
HN2269.f1 — single-pulse



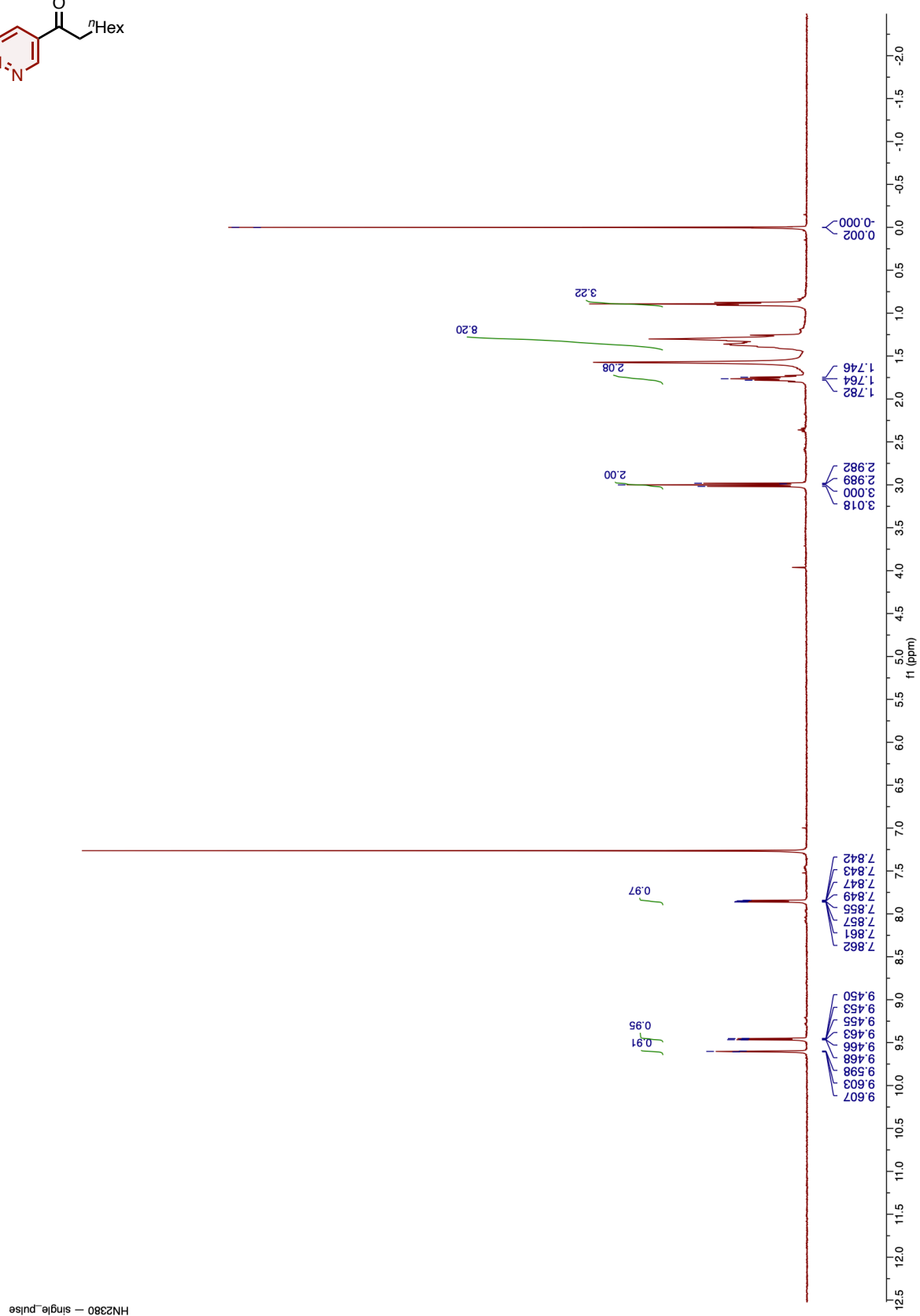
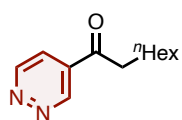
^{13}C NMR of **3aE** (101 MHz, CDCl_3)



HN2268.f1 — single pulse decoupled gated NOE

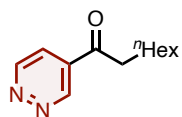


^1H NMR of **3aF** (400 MHz, CDCl_3)

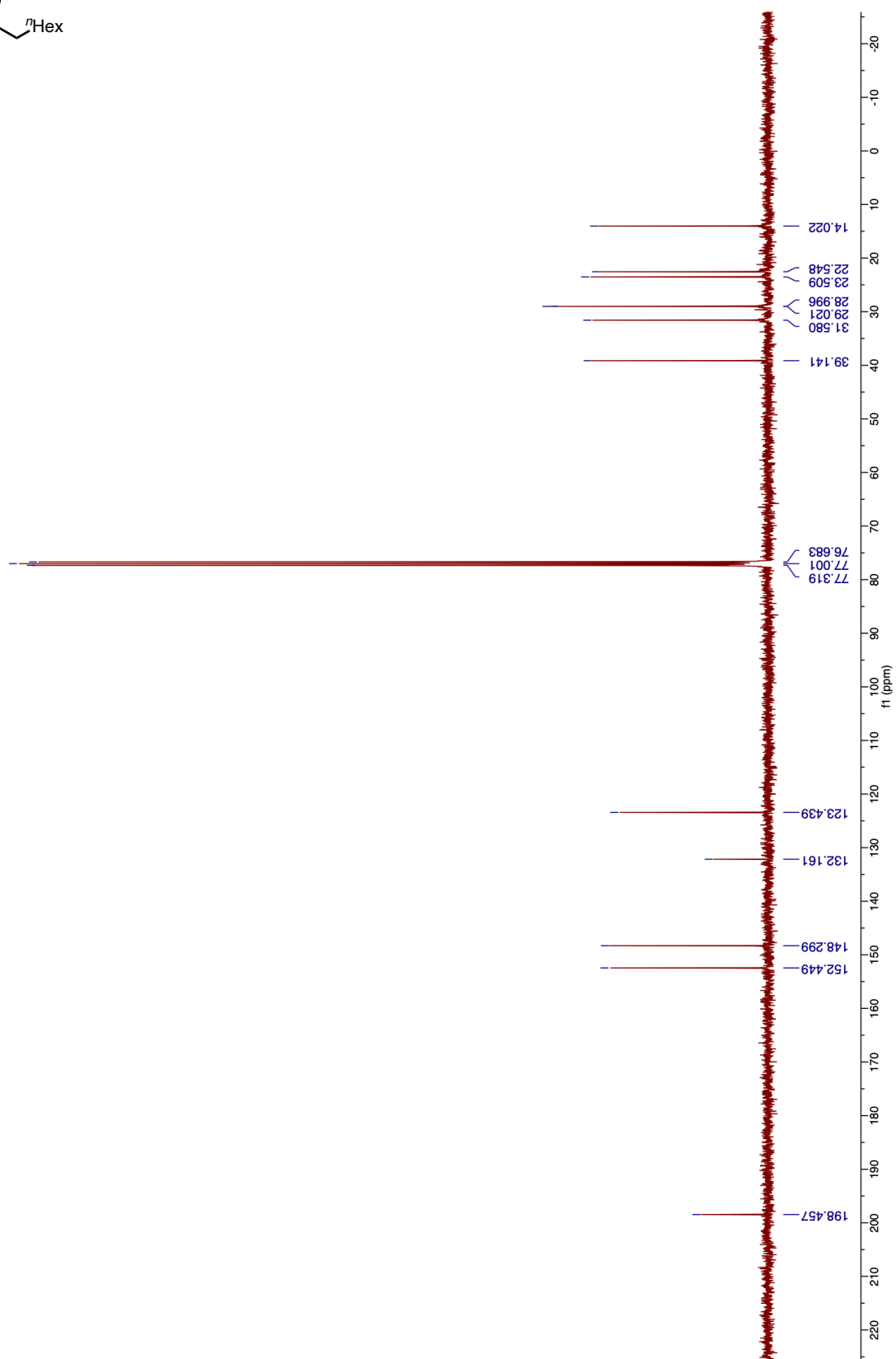


HN2380 — single-pulse

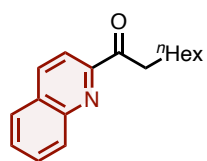
^{13}C NMR of **3aF** (101 MHz, CDCl_3)



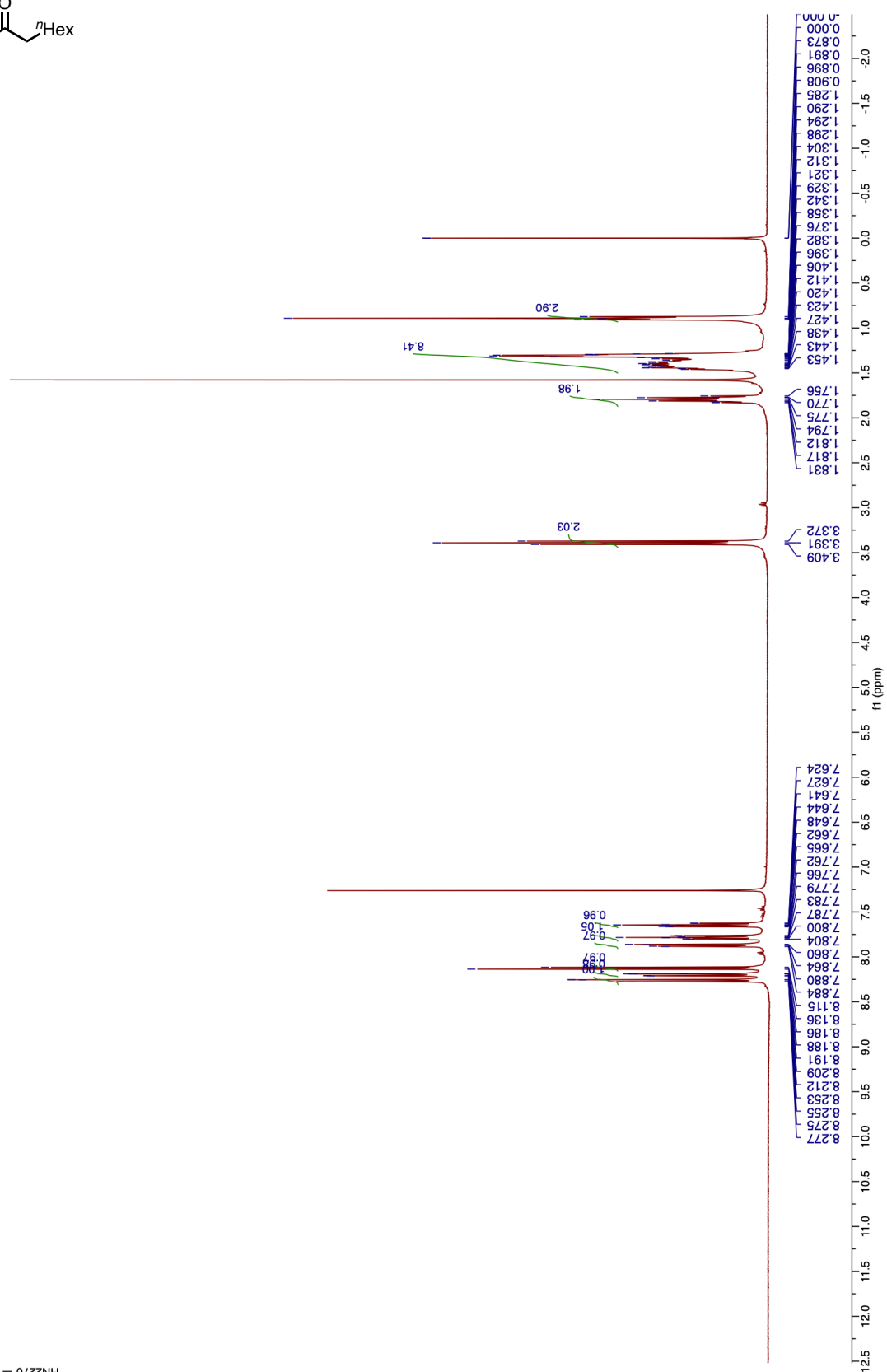
HN2380 — single pulse decoupled gated NOE



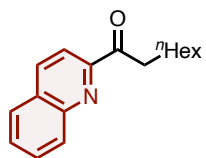
^1H NMR of **3aG** (400 MHz, CDCl_3)



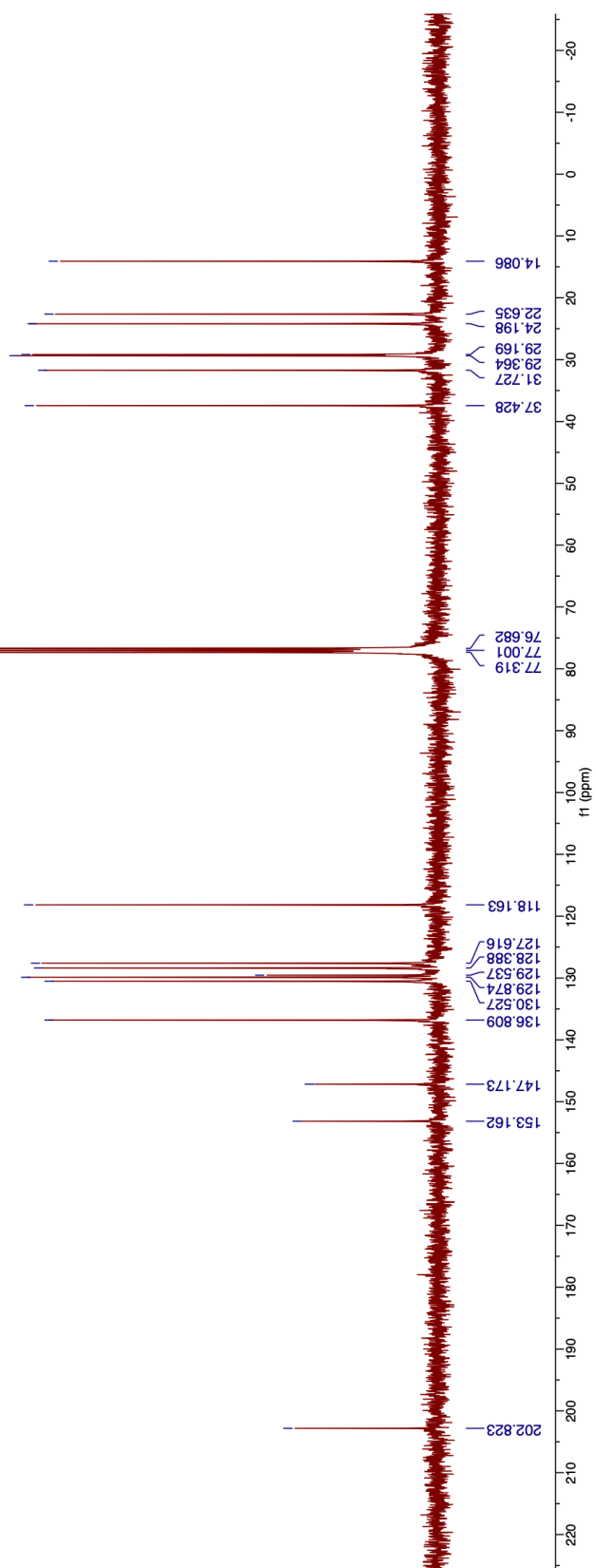
HN2270 — single-pulse



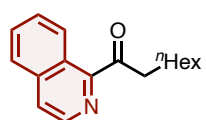
^{13}C NMR of **3aG** (101 MHz, CDCl_3)



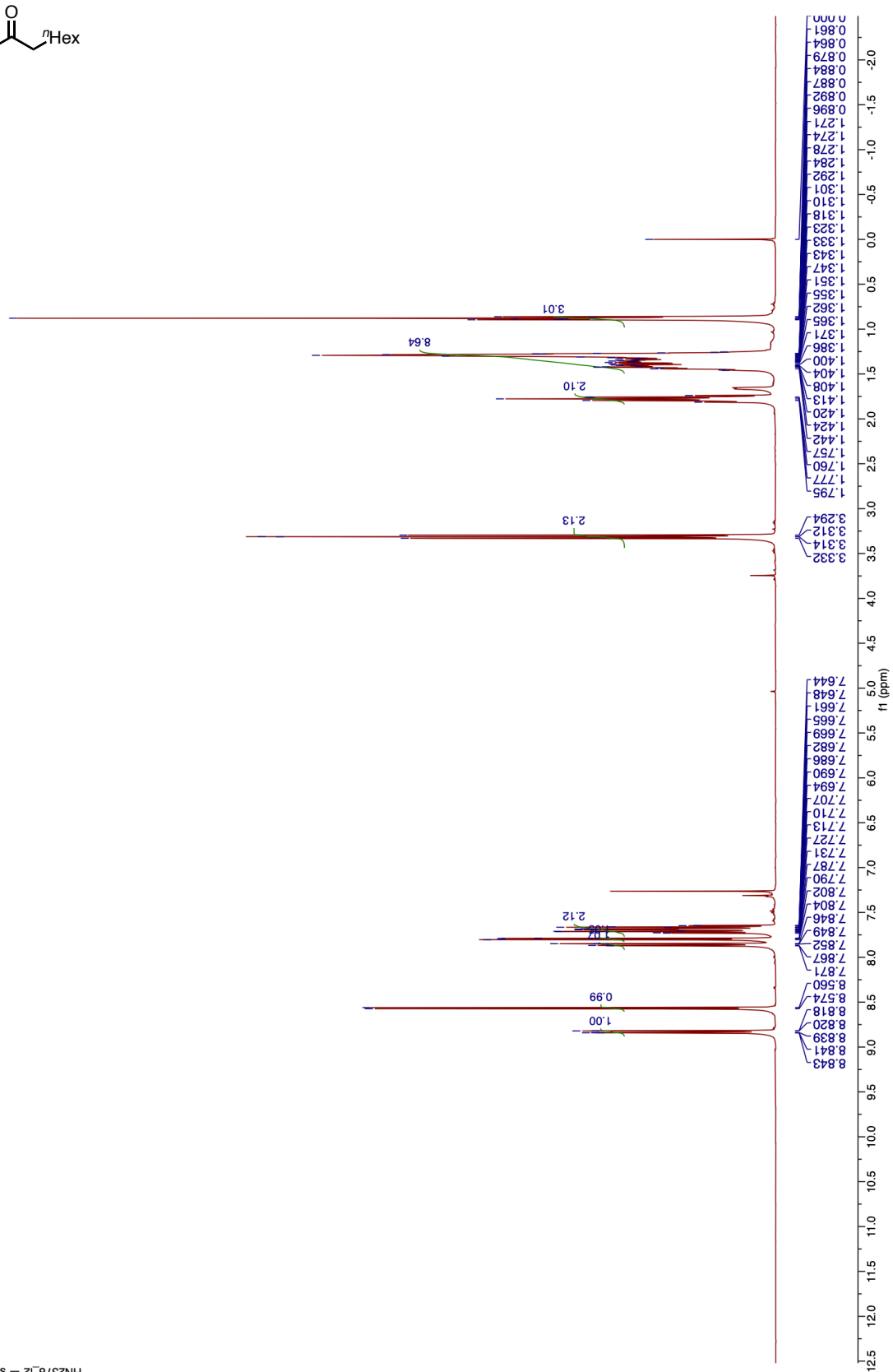
HN2270.f1 — single pulse decoupled gated NOE



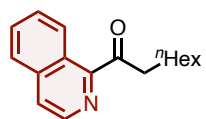
^1H NMR of **3aH** (400 MHz, CDCl_3)



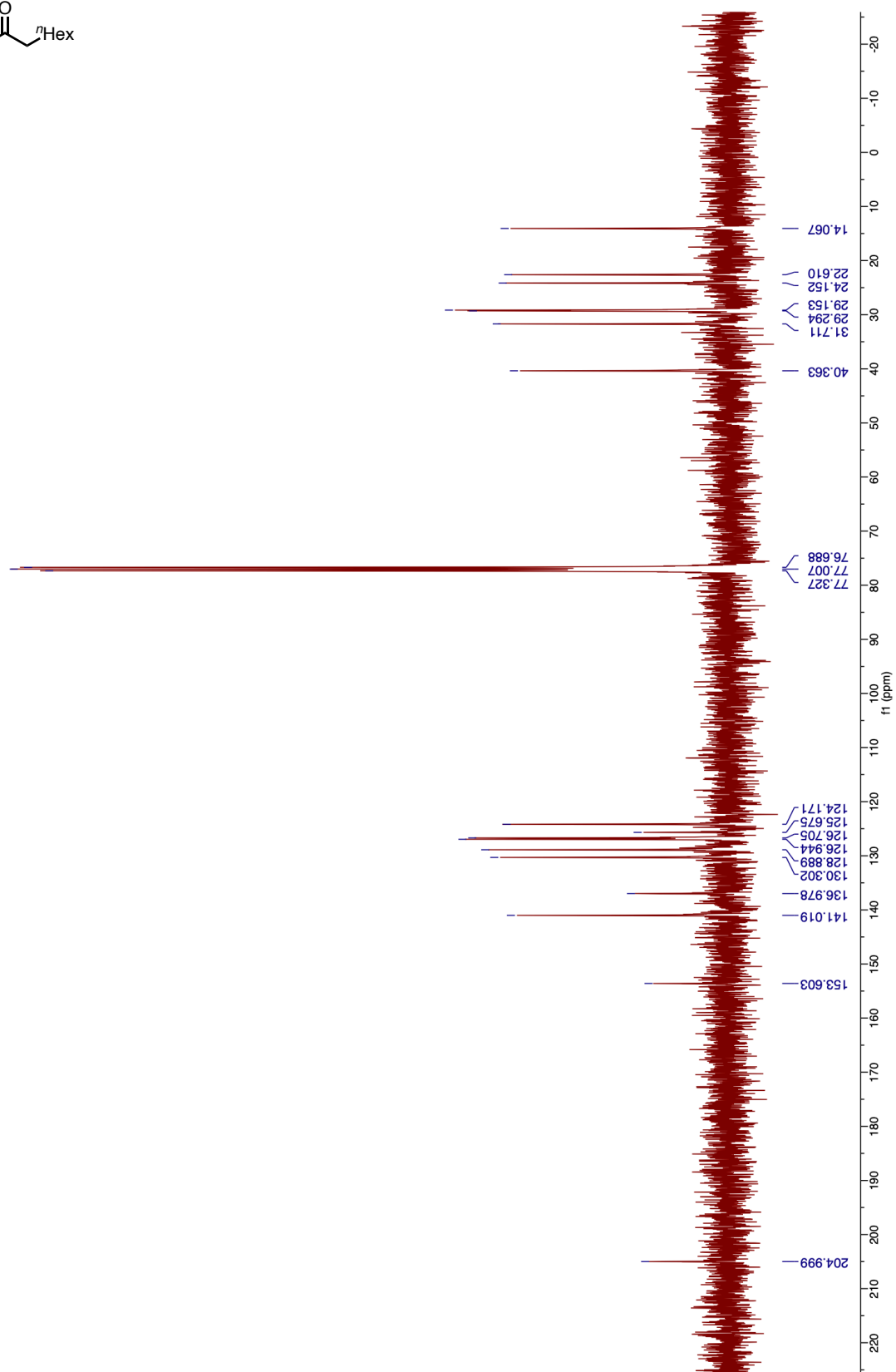
HN2378_12 — single-pulse



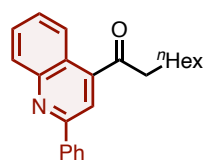
^{13}C NMR of **3aH** (101 MHz, CDCl_3)



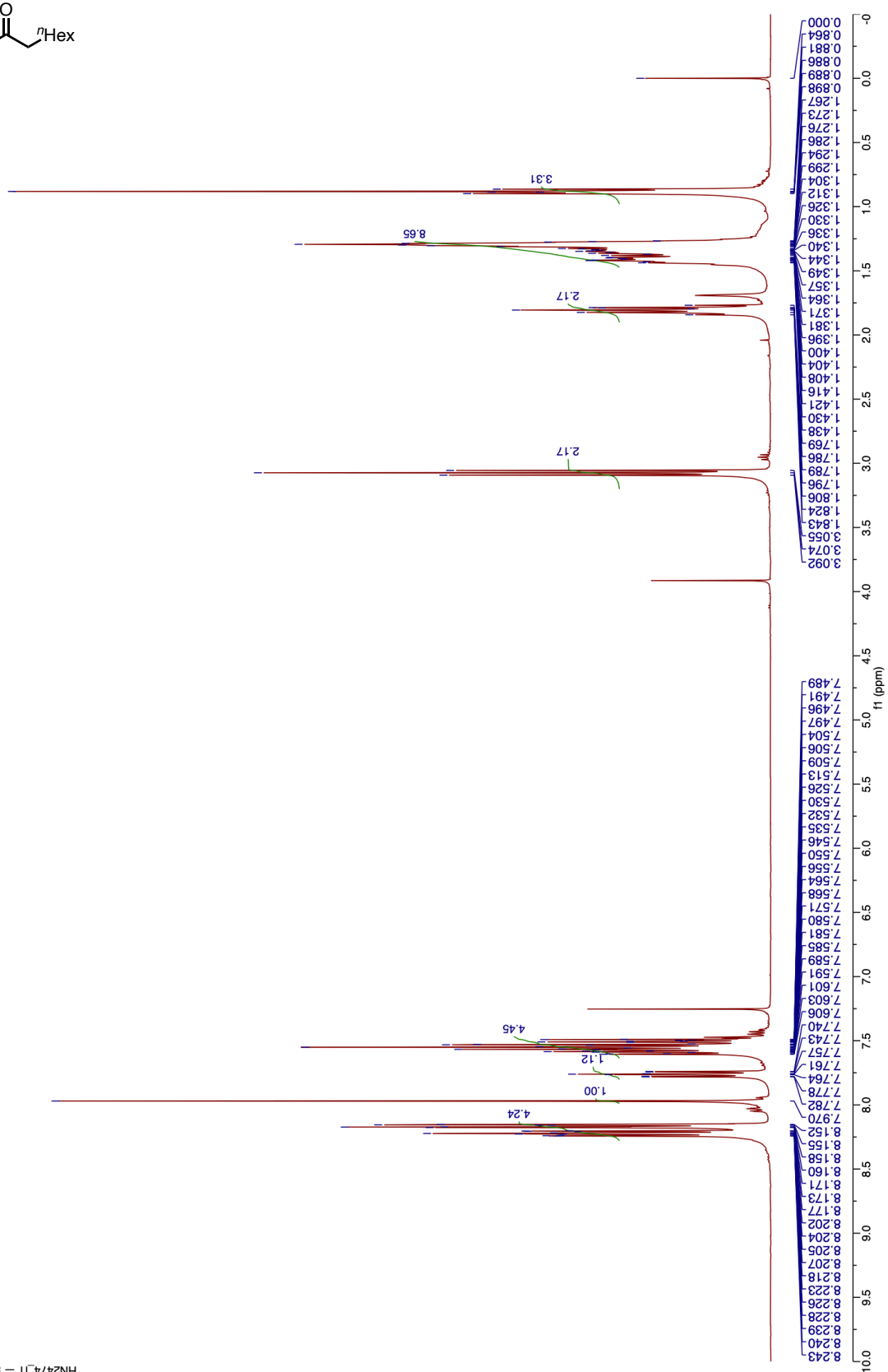
HN2378_12 — single pulse decoupled gated NOE



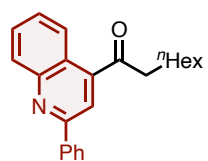
¹H NMR of **3aI** (400 MHz, CDCl₃)



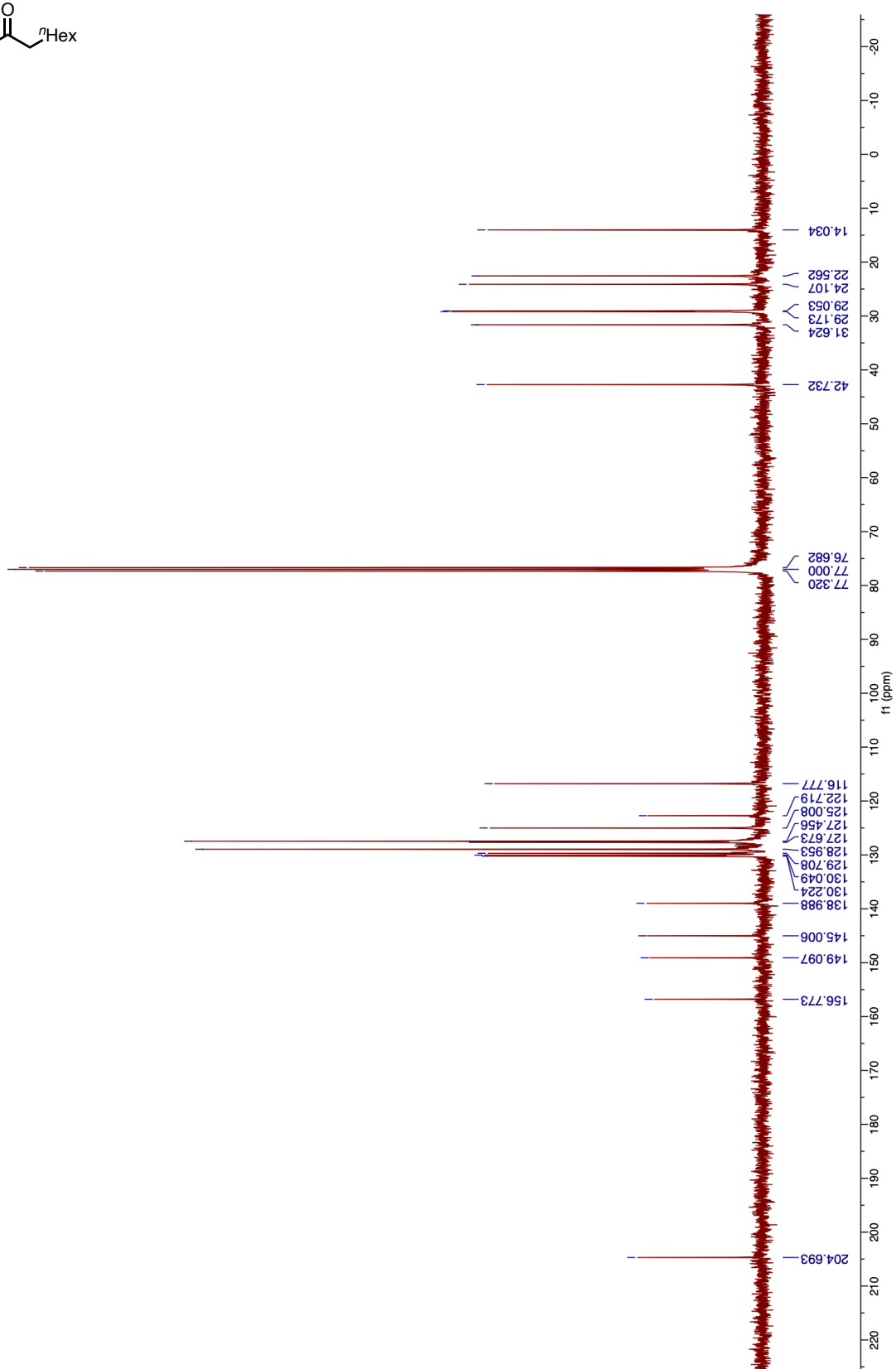
HN2474.f1 - single-pulse



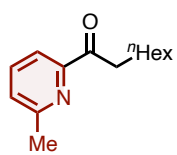
^{13}C NMR of **3aI** (101 MHz, CDCl_3)



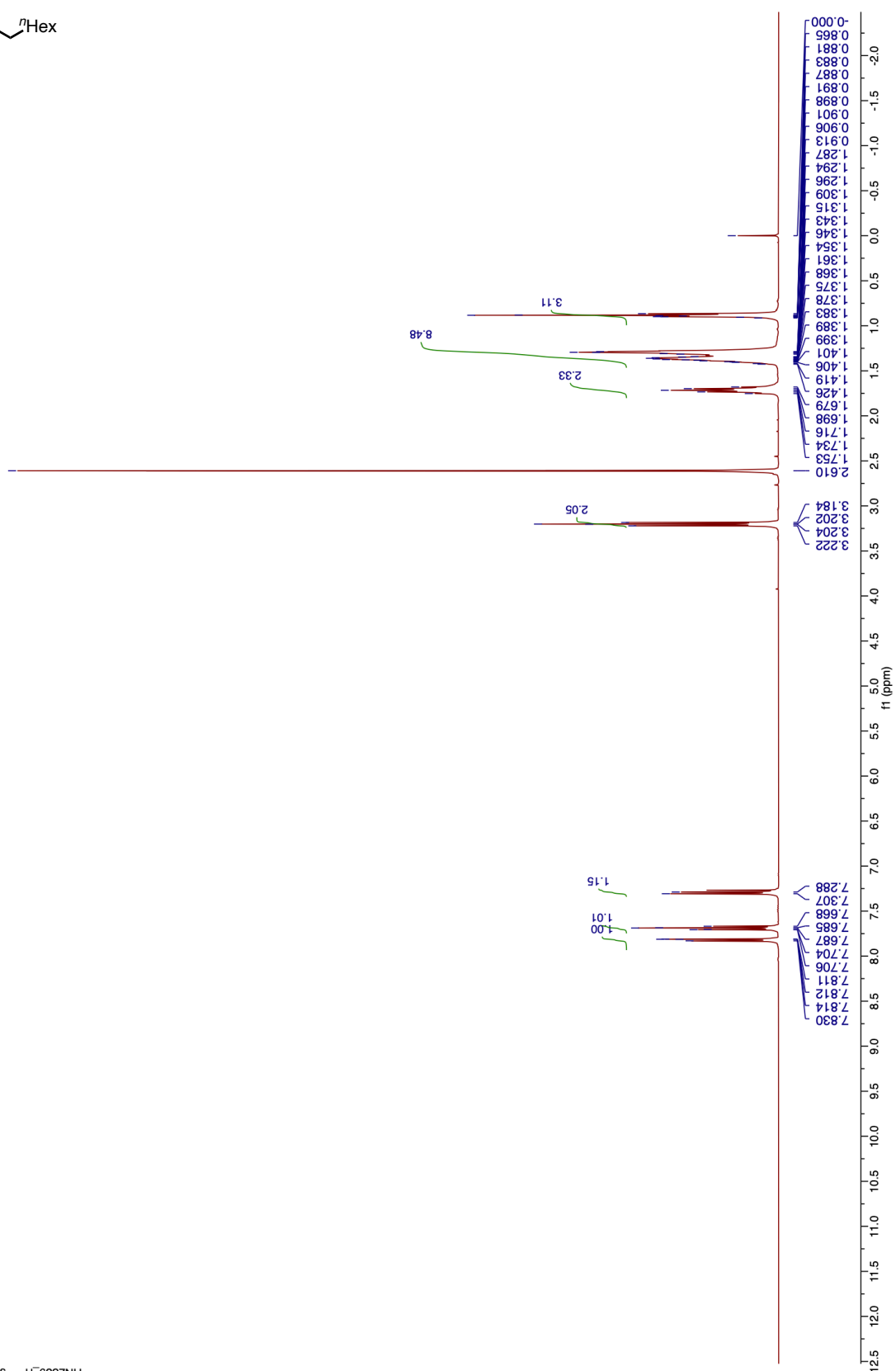
HN2474.f1 — single pulse decoupled gated NOE



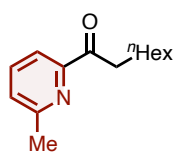
^1H NMR of **3J** (400 MHz, CDCl_3)



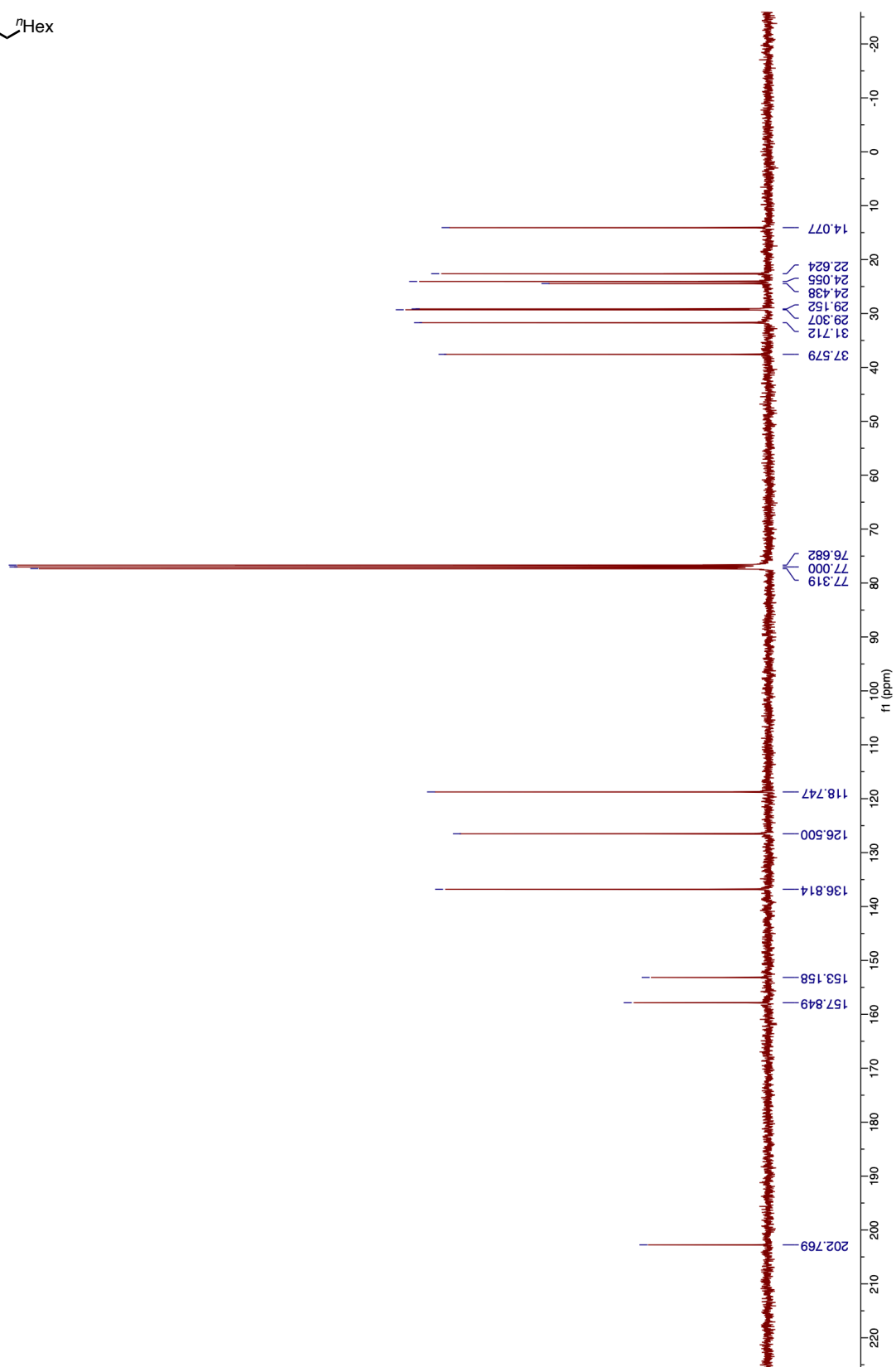
HN2389.f1 — single-pulse



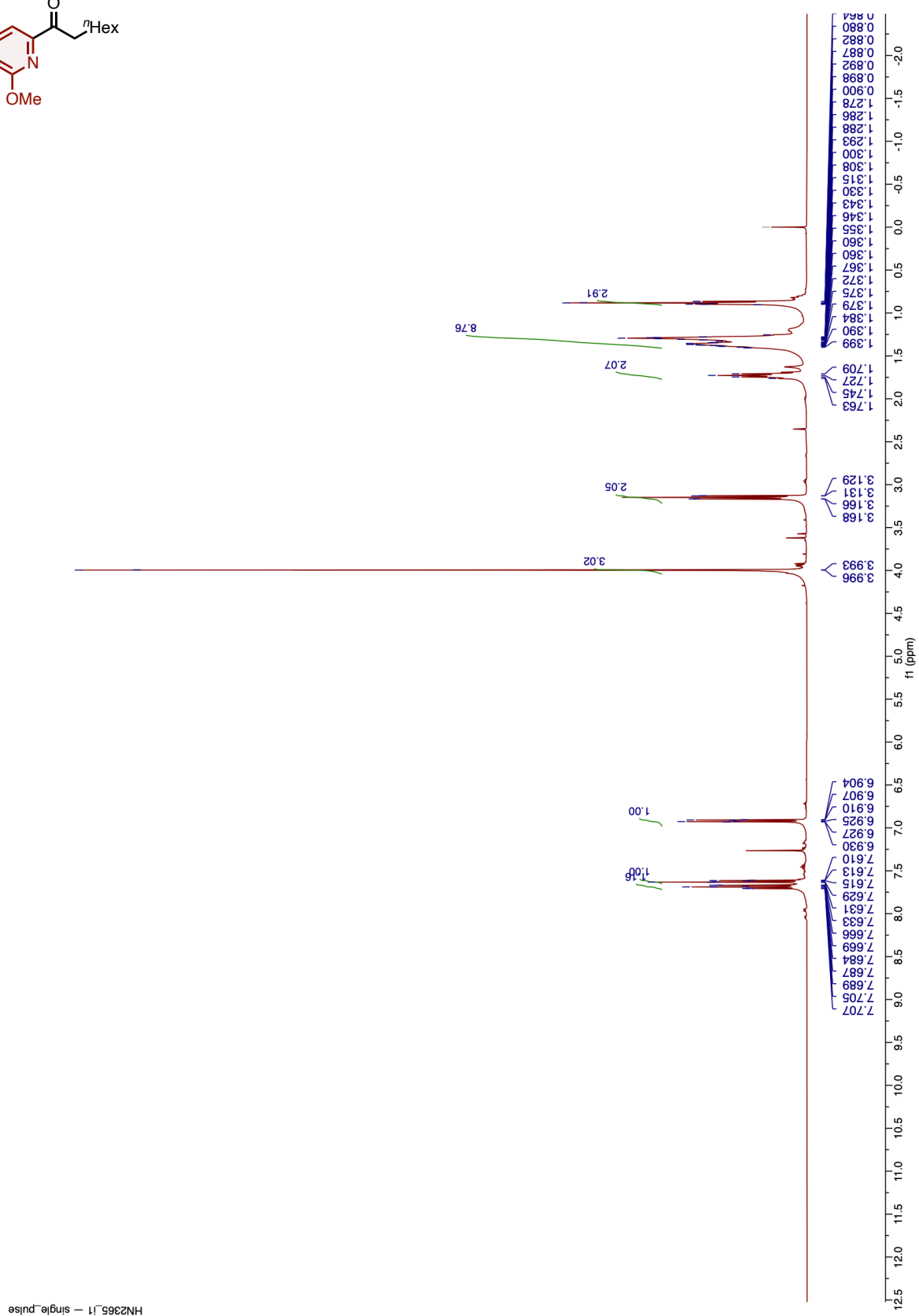
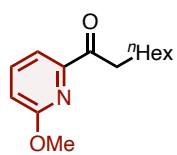
^{13}C NMR of **3aJ** (101 MHz, CDCl_3)



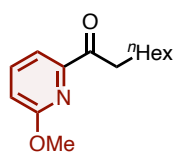
HN2389.f1 — single pulse decoupled gated NOE



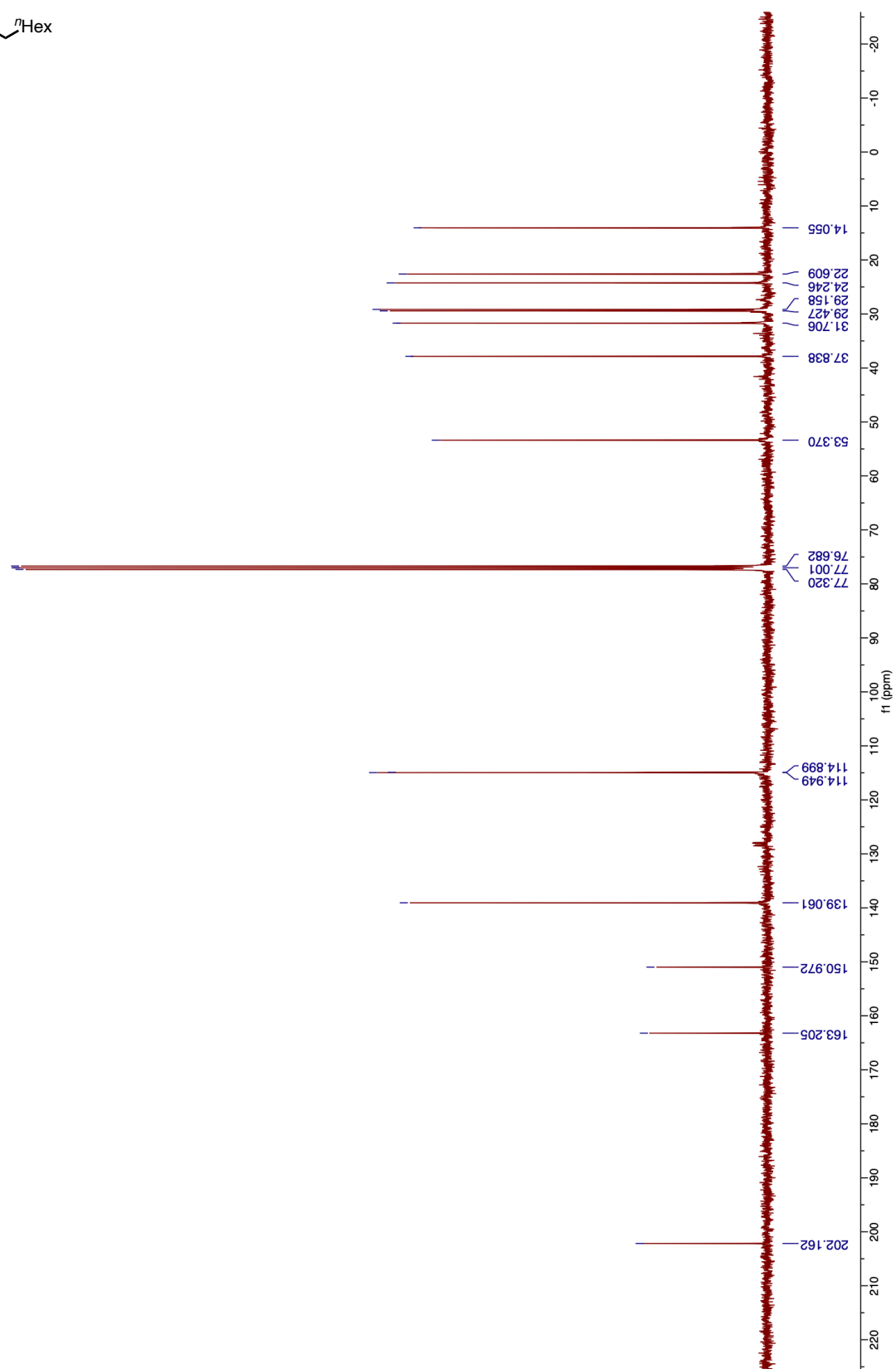
^1H NMR of **3aK** (400 MHz, CDCl_3)

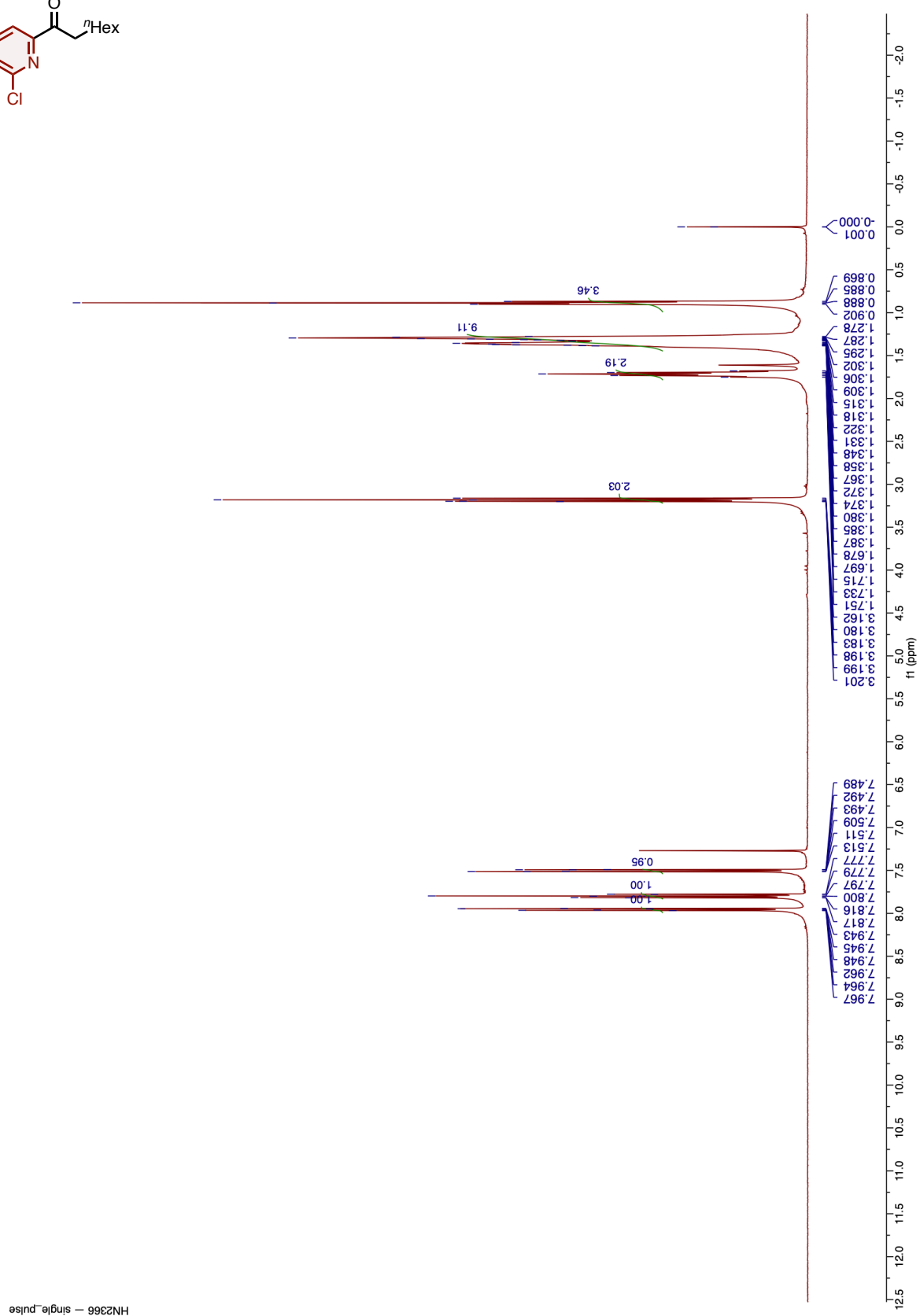


^{13}C NMR of **3aK** (101 MHz, CDCl_3)

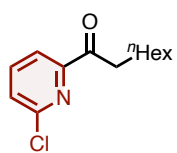


HN2365 — single pulse decoupled gated NOE

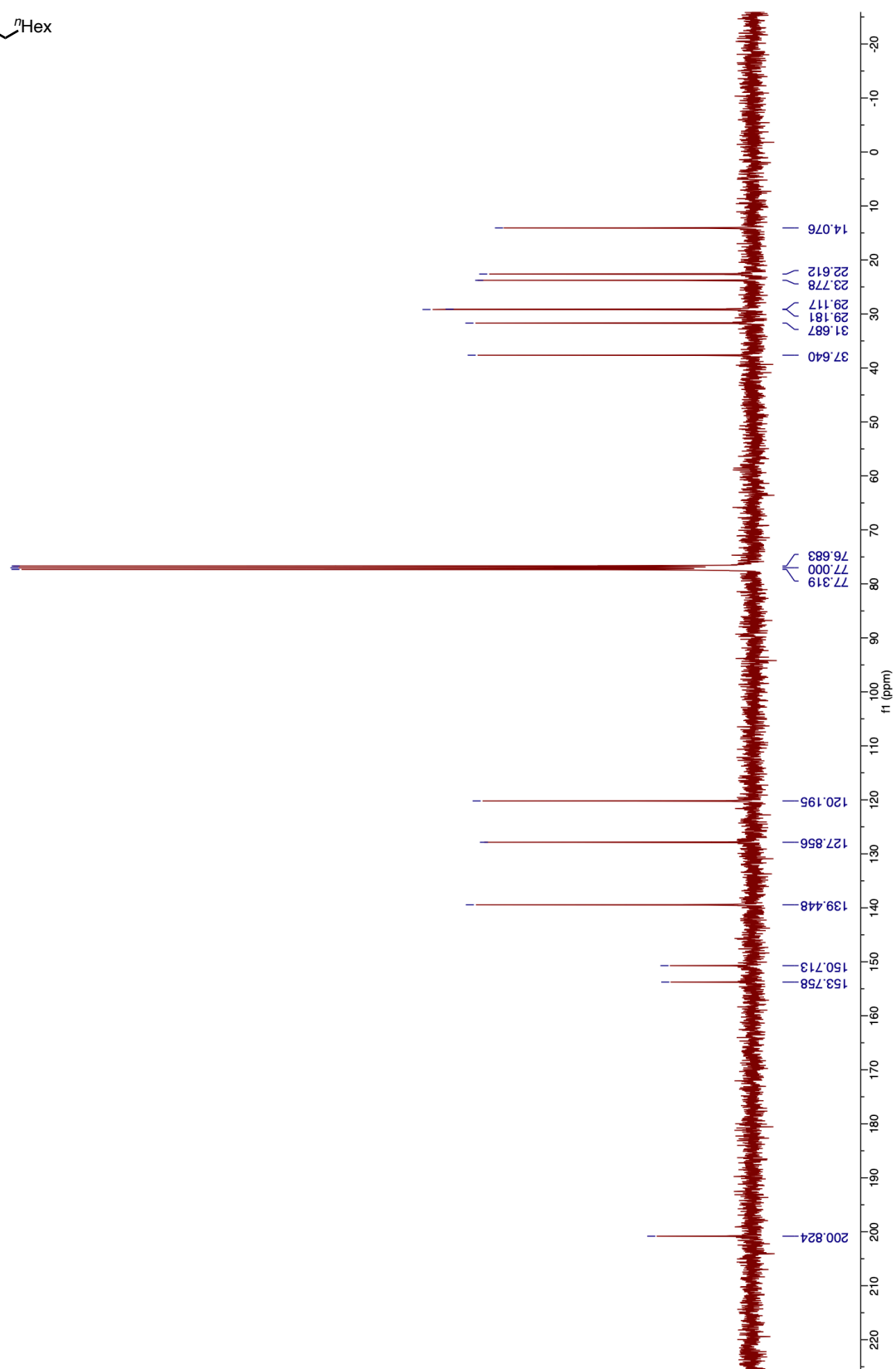


CCCCC(=O)c1cc(Cl)ccn1

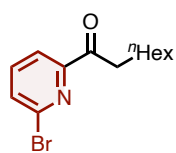
^{13}C NMR of **3aL** (101 MHz, CDCl_3)



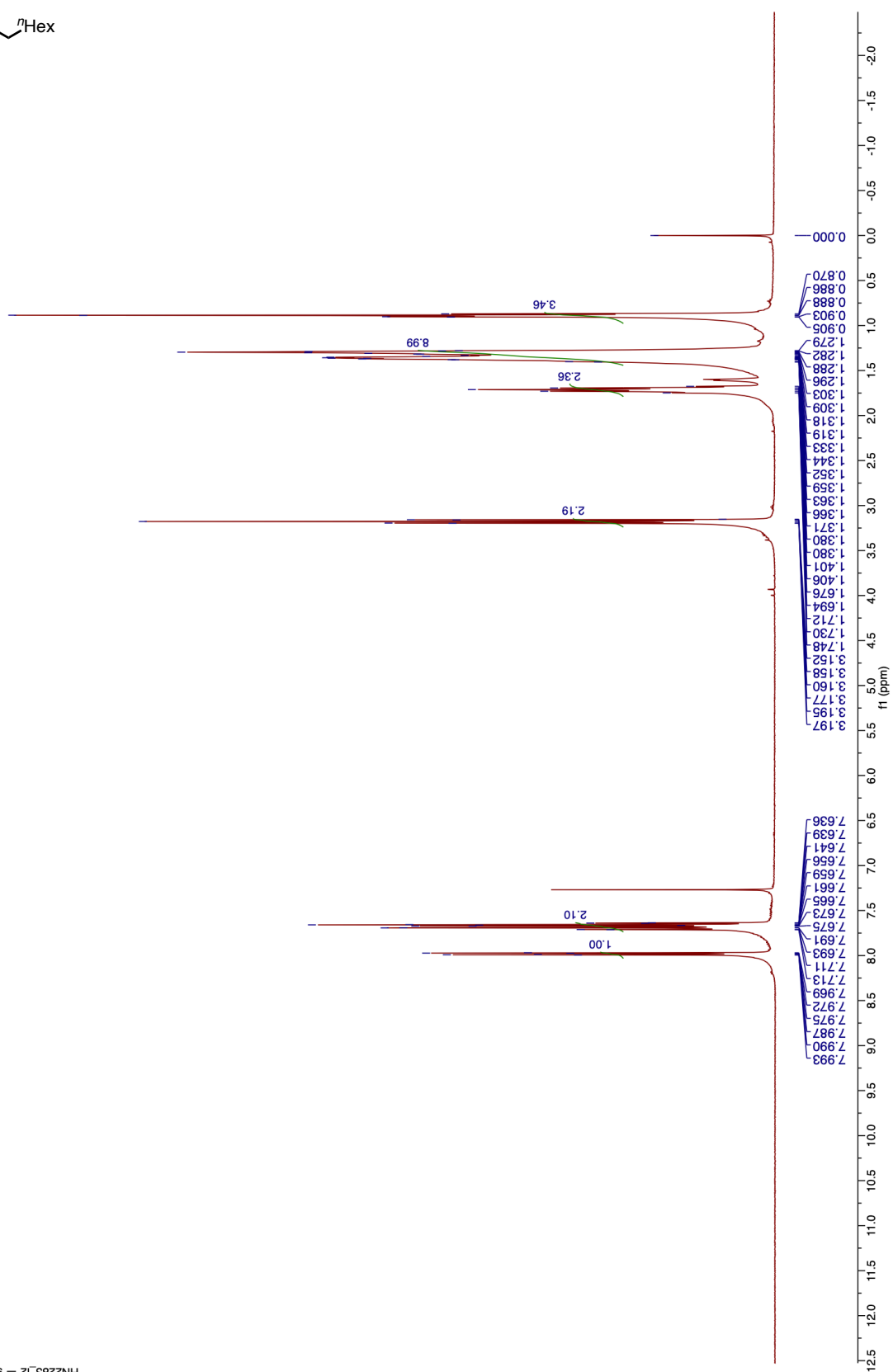
HN2366 — single pulse decoupled gated NOE



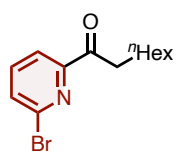
^1H NMR of **3aM** (400 MHz, CDCl_3)



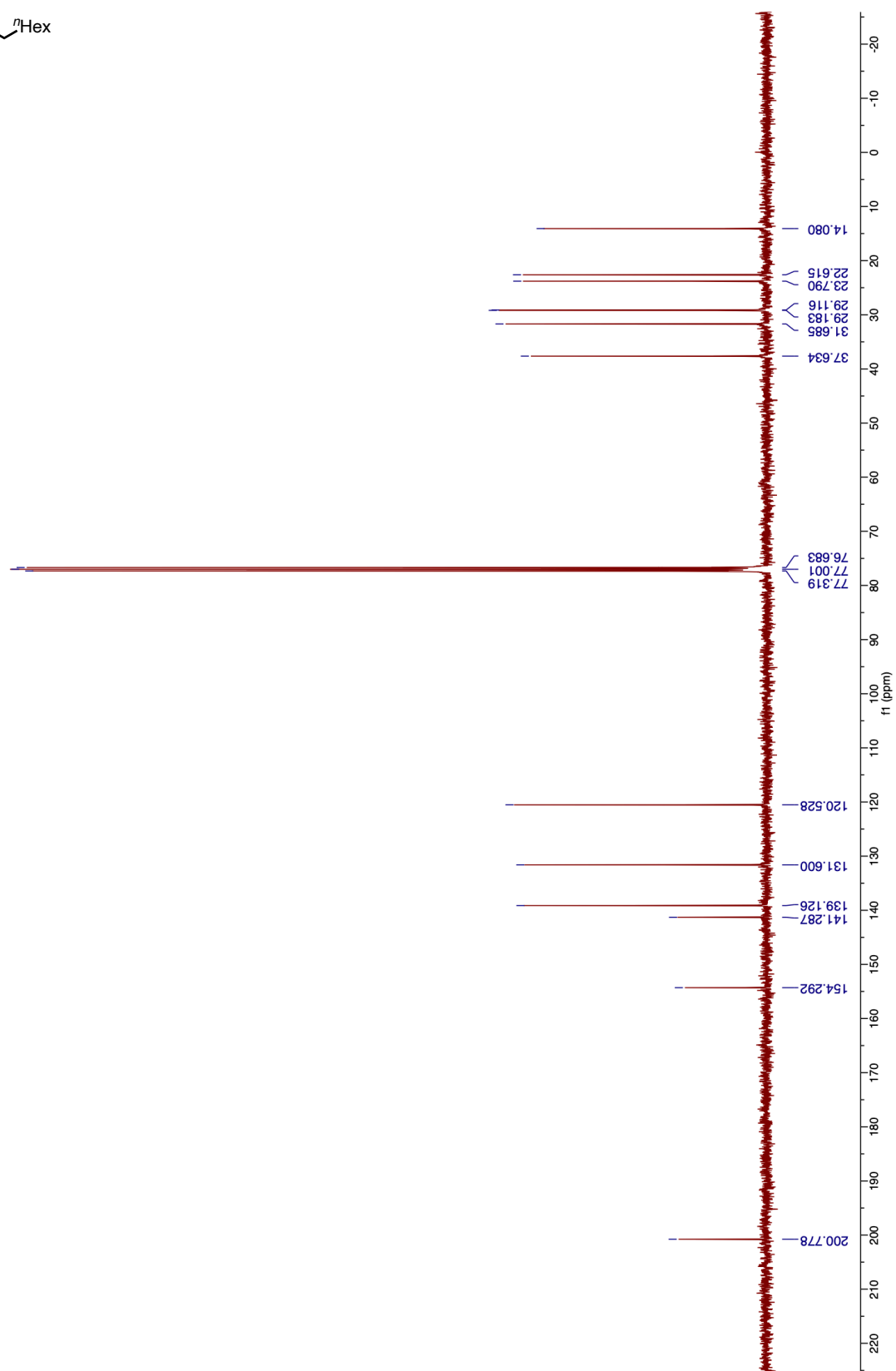
HN2283_12 — single-pulse



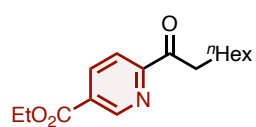
^{13}C NMR of **3aM** (101 MHz, CDCl_3)



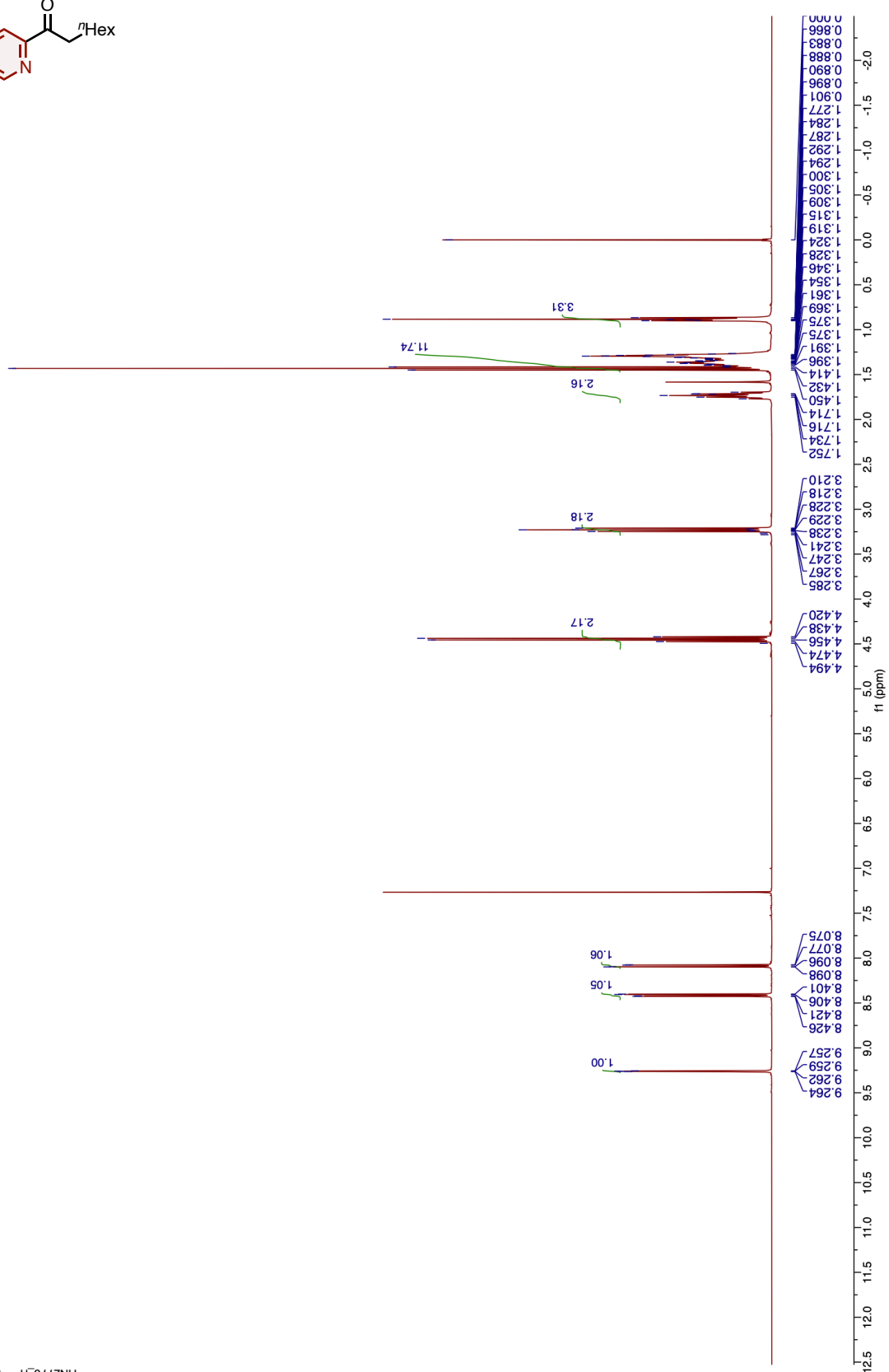
HN2383_12 — single pulse decoupled gated NOE



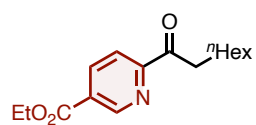
^1H NMR of **3aN** (400 MHz, CDCl_3)



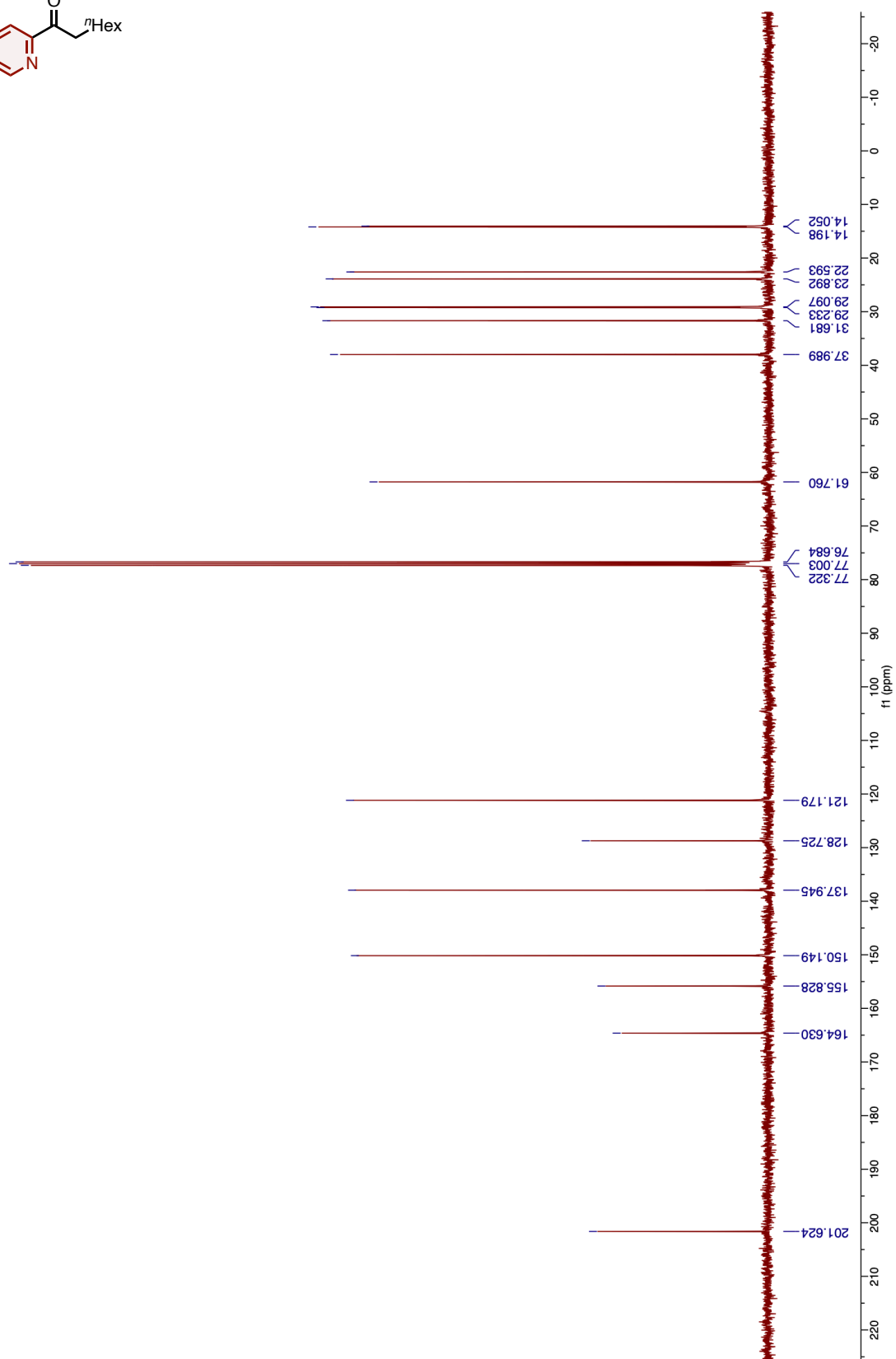
HN2776.f1 — single-pulse



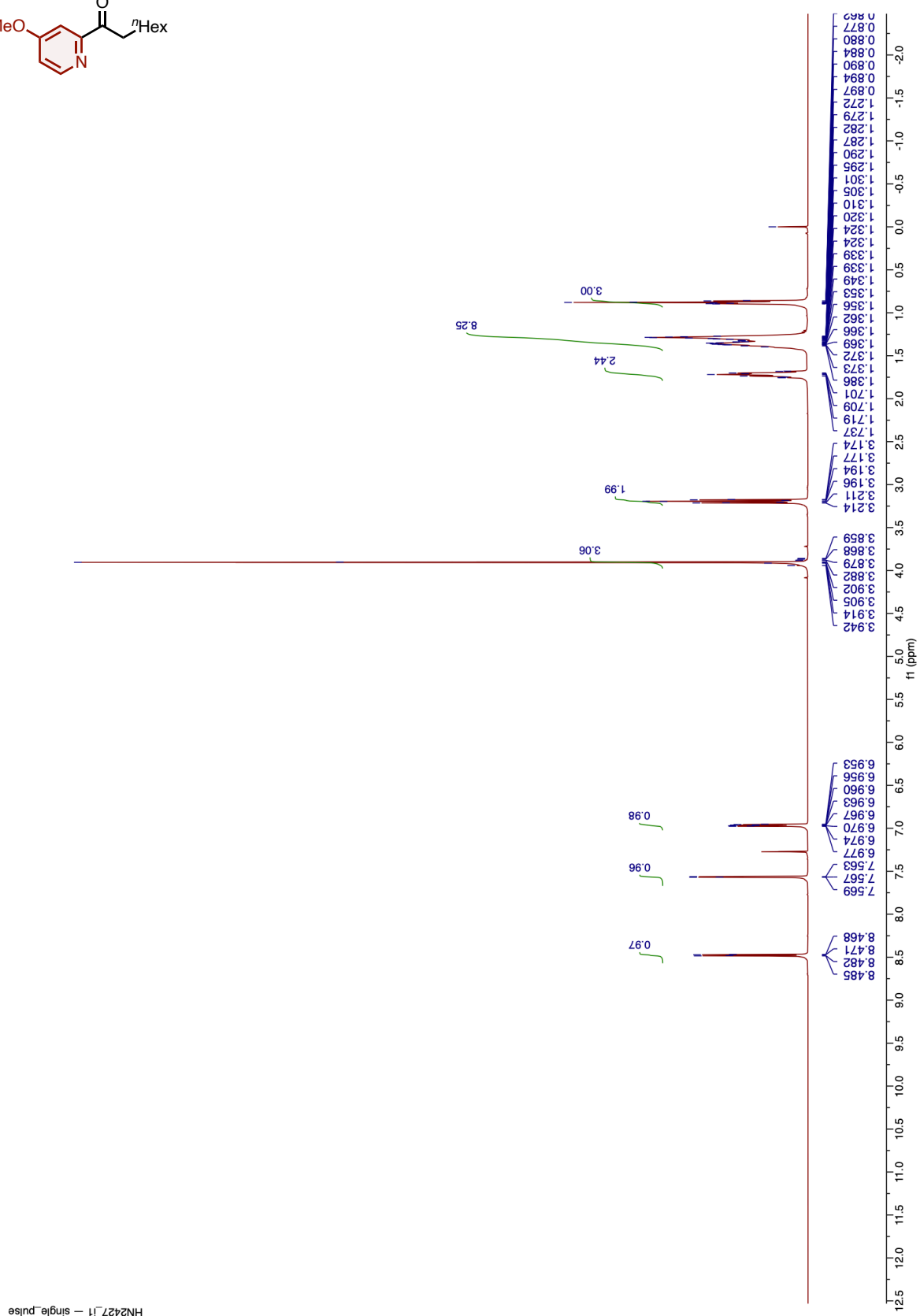
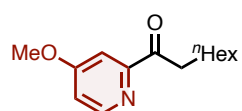
^{13}C NMR of **3aN** (101 MHz, CDCl_3)



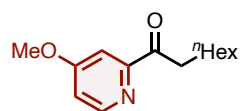
HN2776 — single pulse decoupled gated NOE



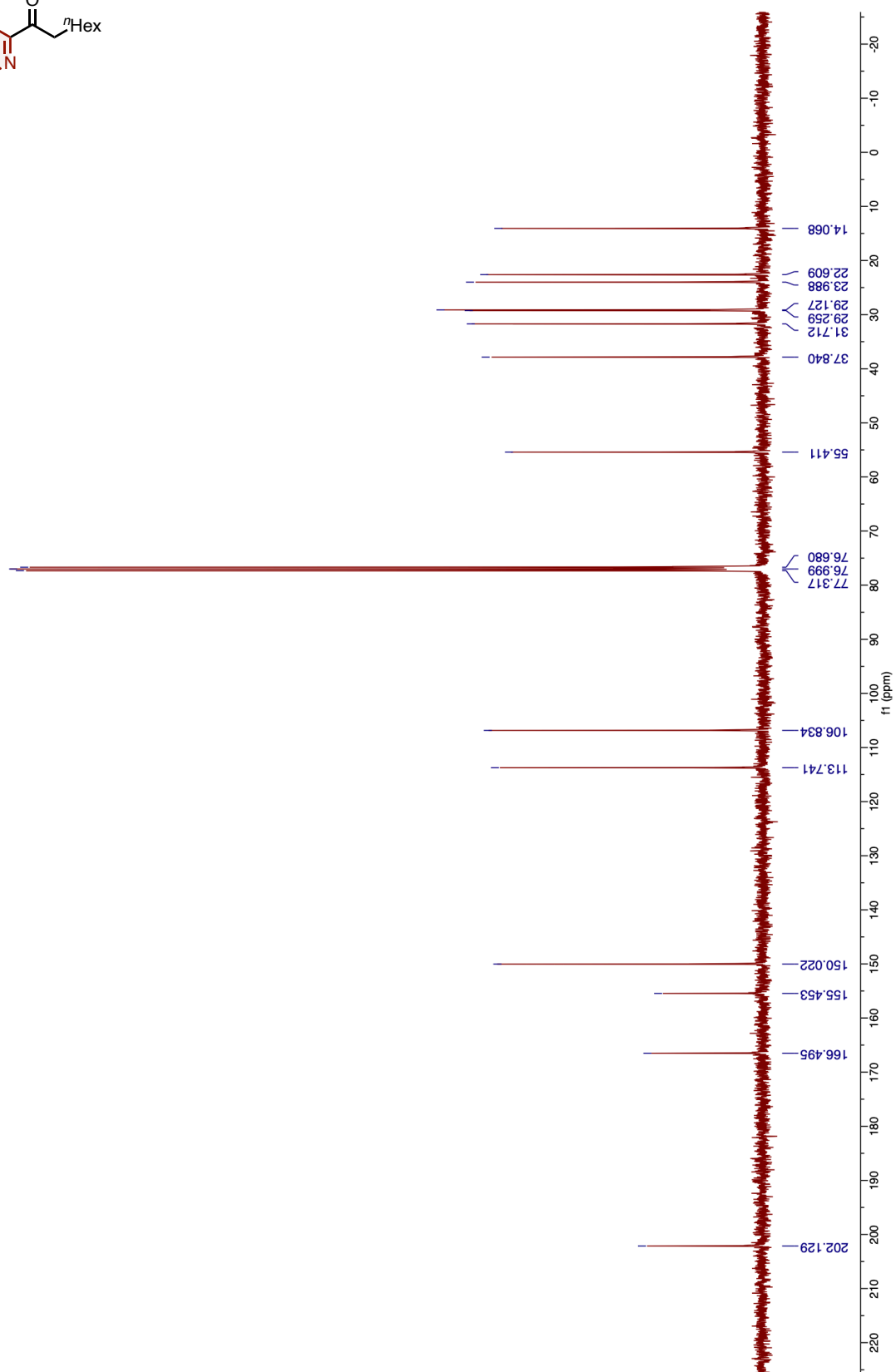
^1H NMR of **3aO** (400 MHz, CDCl_3)



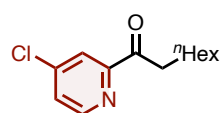
^{13}C NMR of **3aO** (101 MHz, CDCl_3)



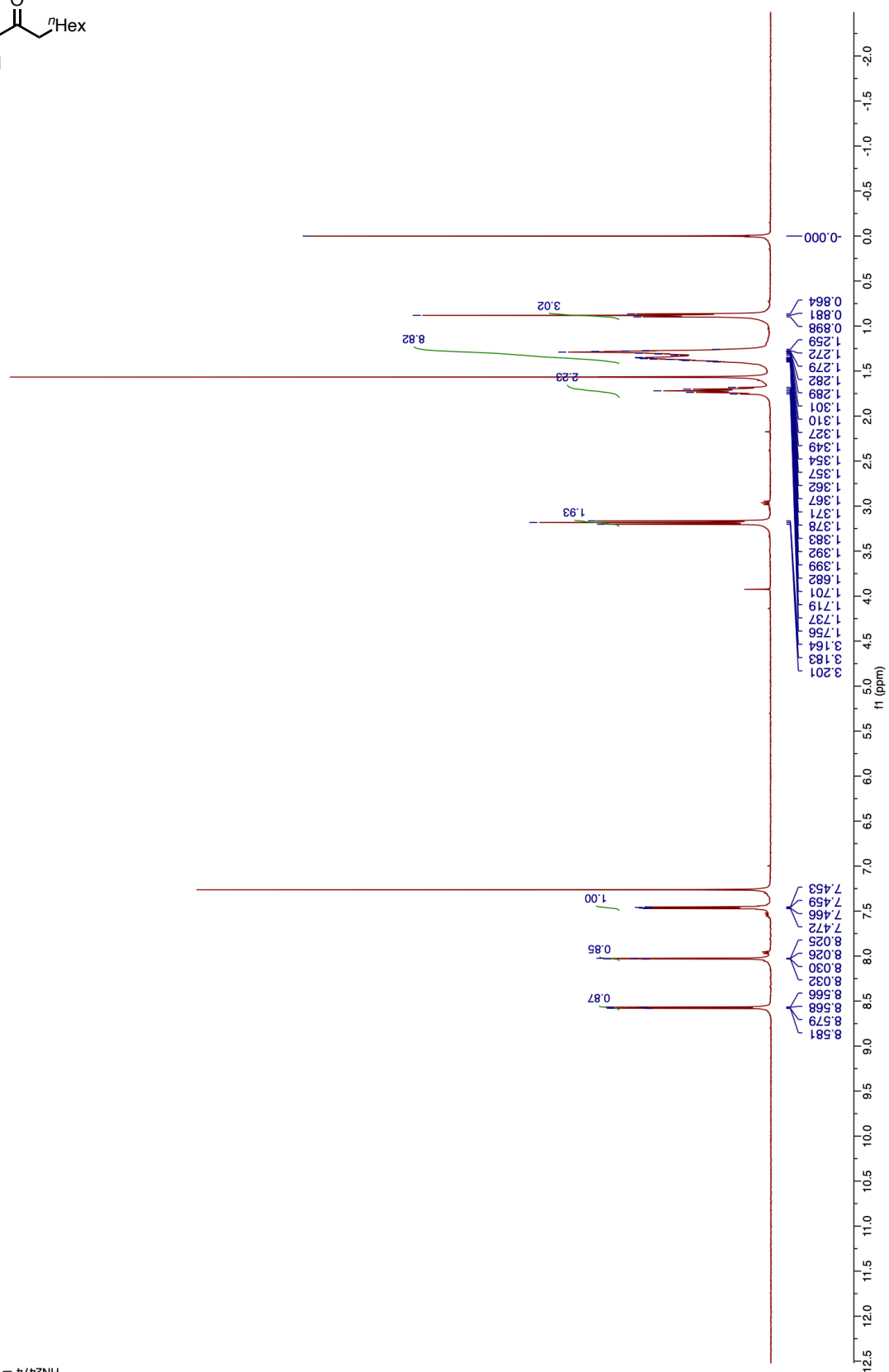
HN2427.f1 — single pulse decoupled gated NOE



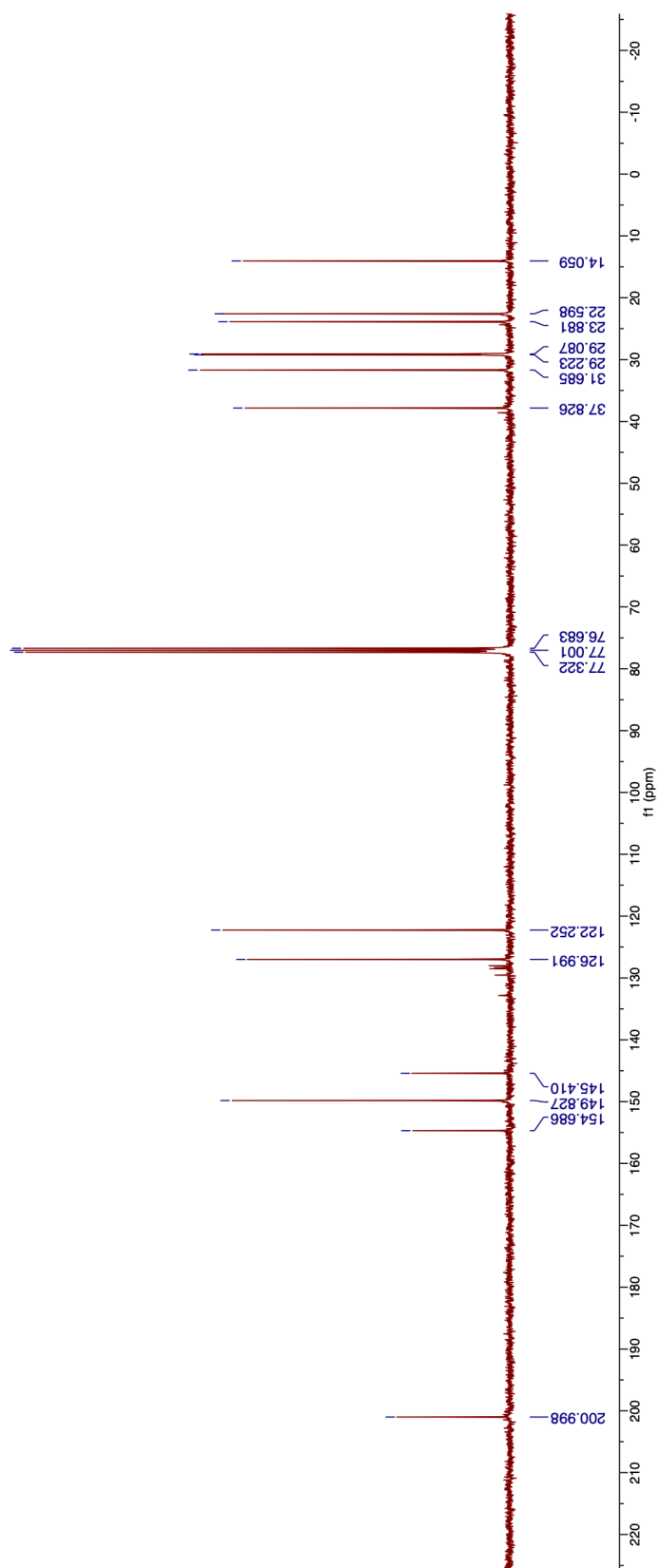
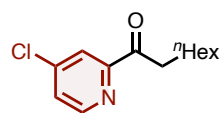
^1H NMR of **3aP** (400 MHz, CDCl_3)



HN2474 — single-pulse

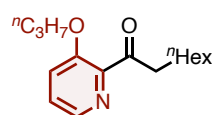


^{13}C NMR of **3aP** (101 MHz, CDCl_3)

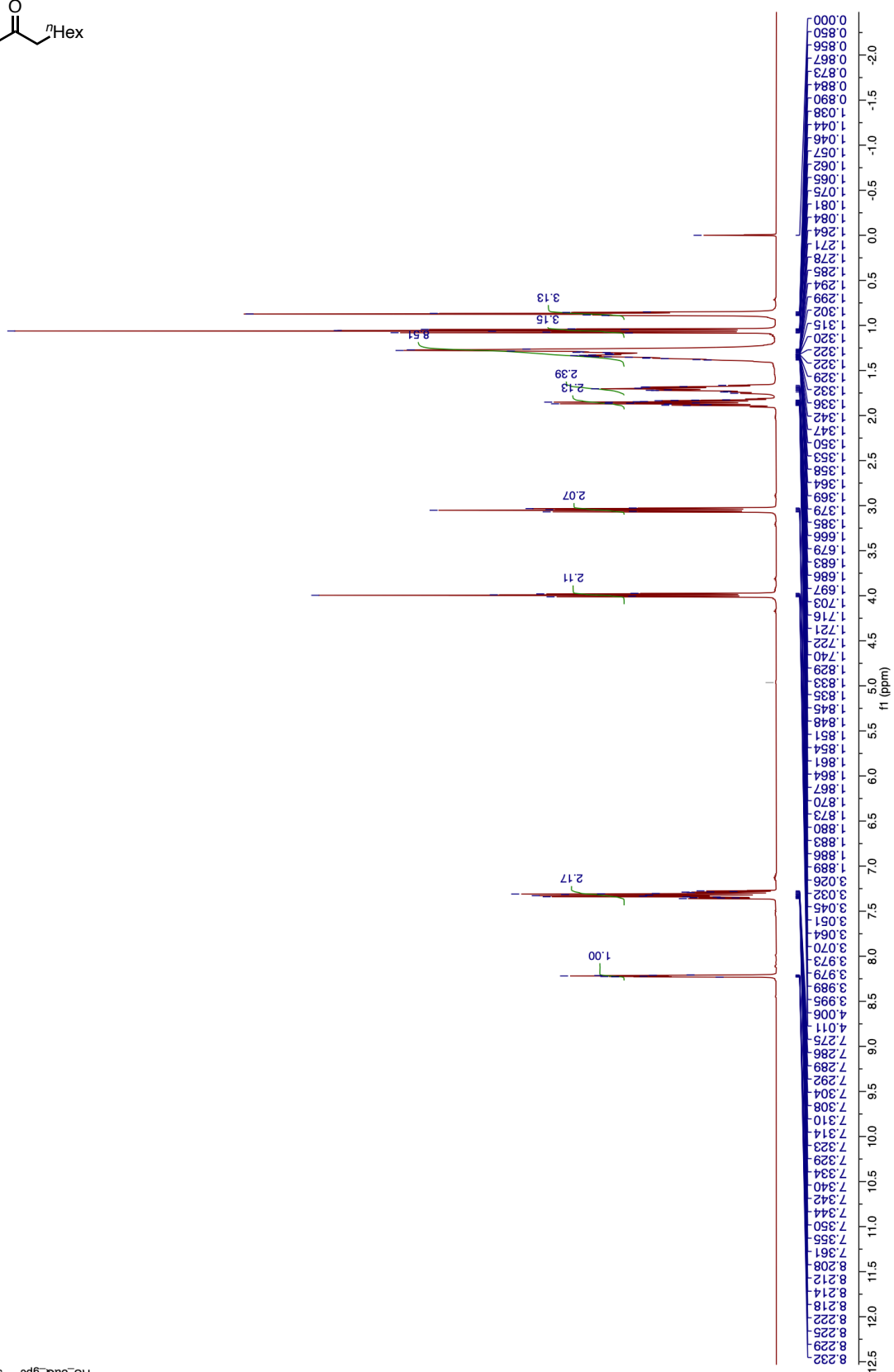


HN2433.f1 — single pulse decoupled gated NOE

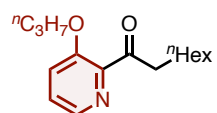
^1H NMR of **3aQ** (400 MHz, CDCl_3)



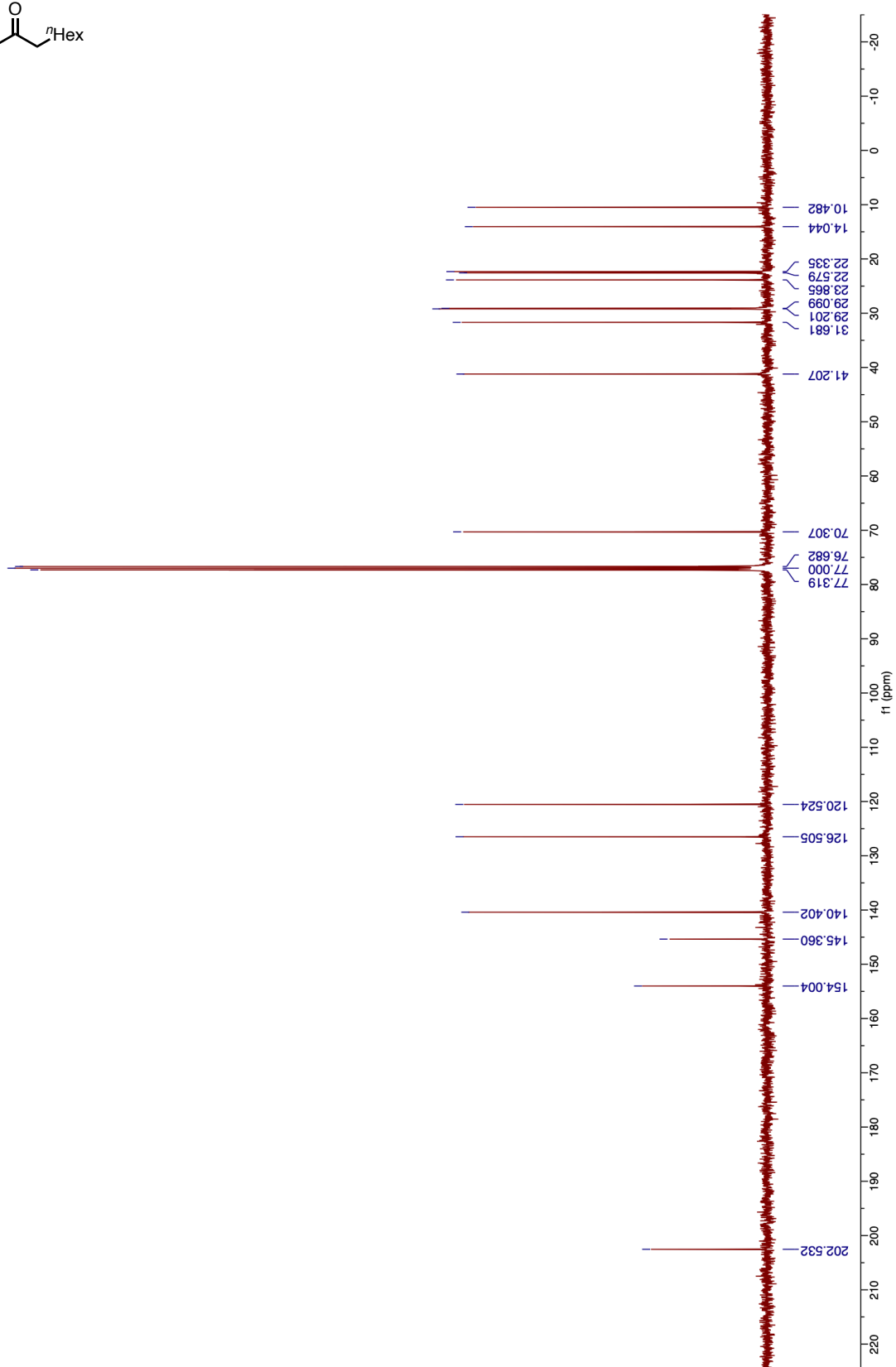
RS_3aQ.gpc — single-pulse



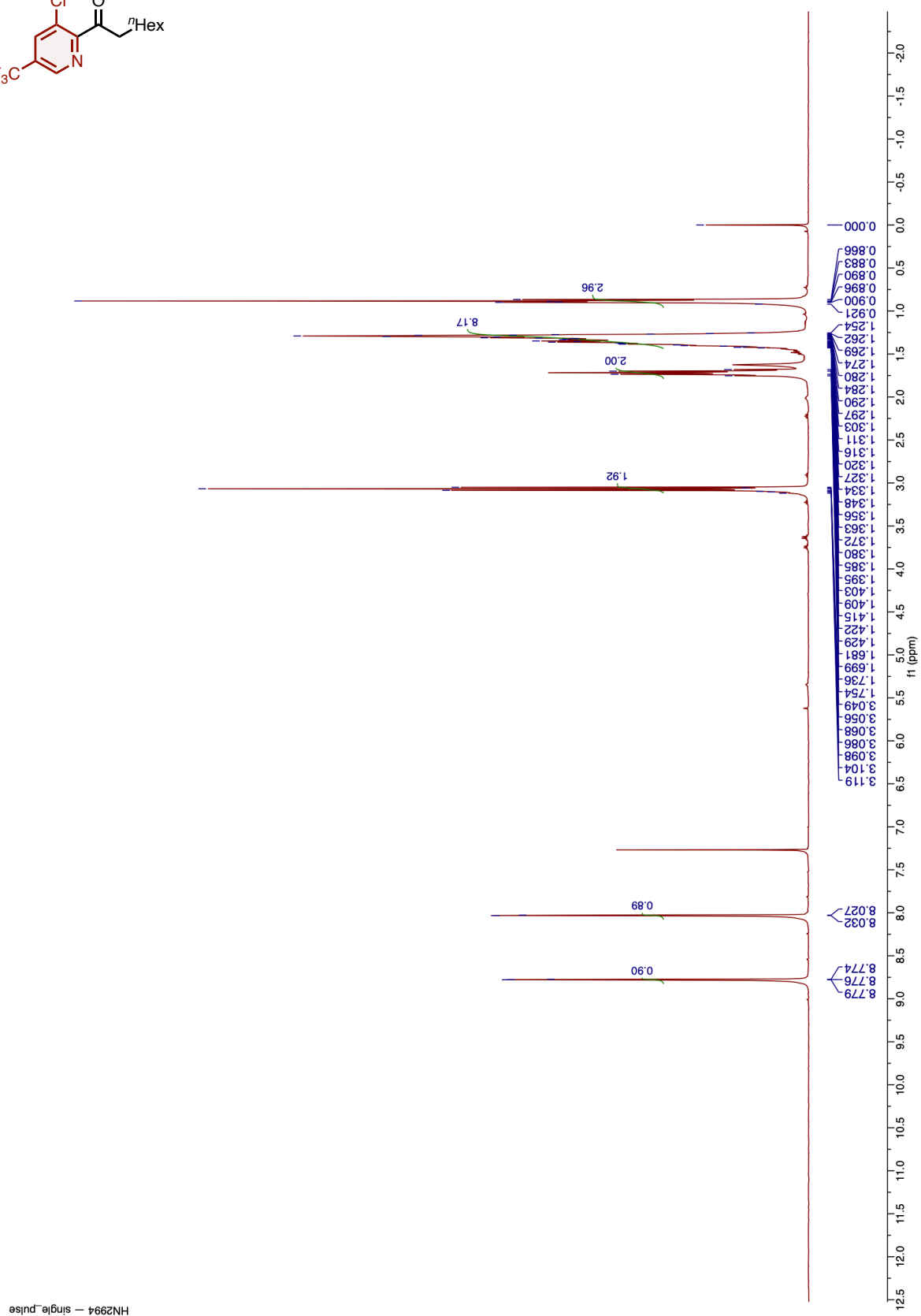
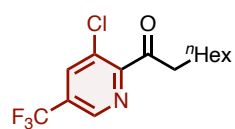
^{13}C NMR of **3aQ** (101 MHz, CDCl_3)



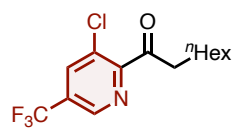
RS_3aQ — single pulse decoupled gated NOE



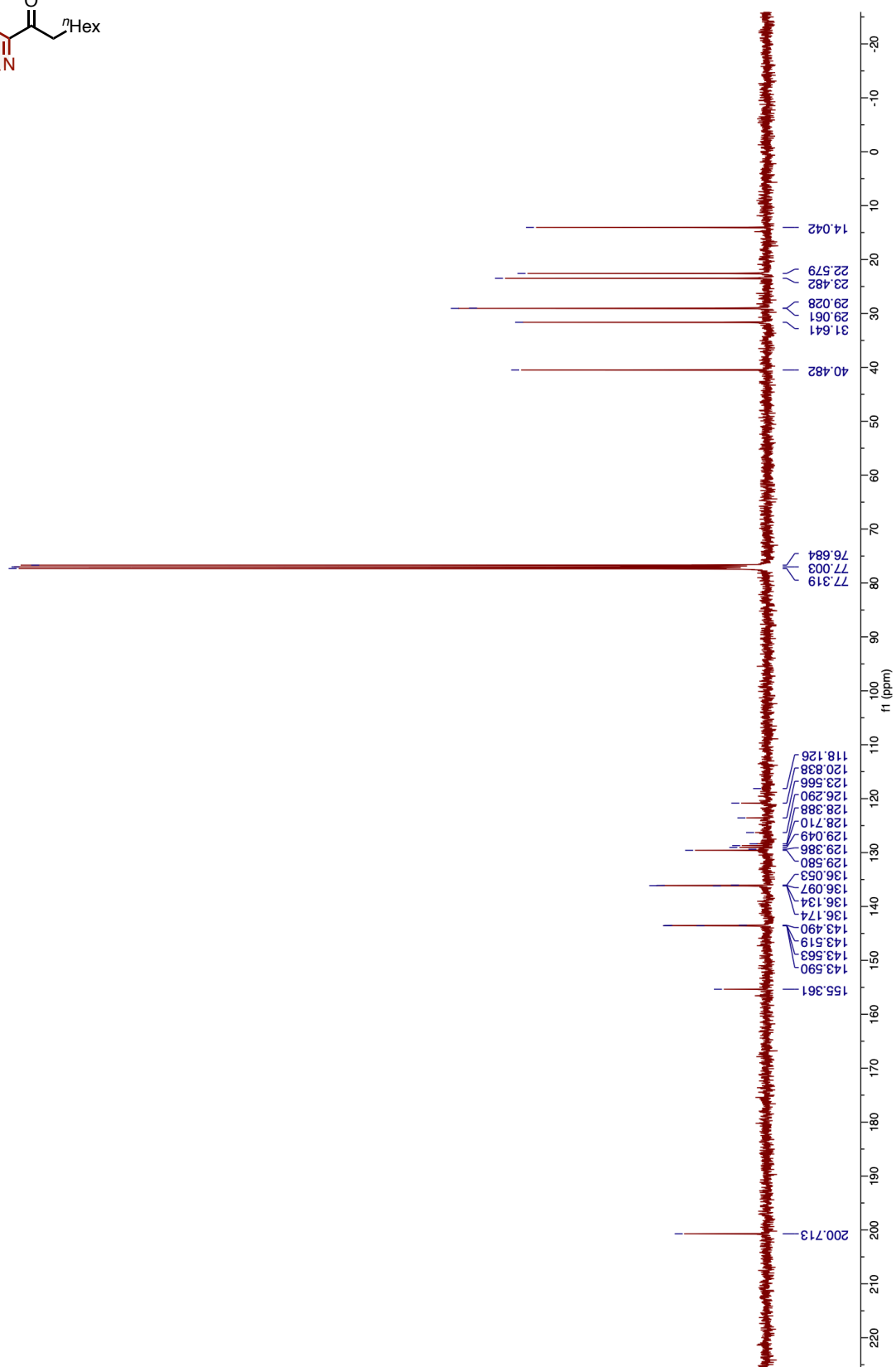
¹H NMR of **3aR** (400 MHz, CDCl₃)



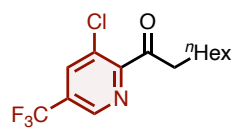
^{13}C NMR of **3aR** (101 MHz, CDCl_3)



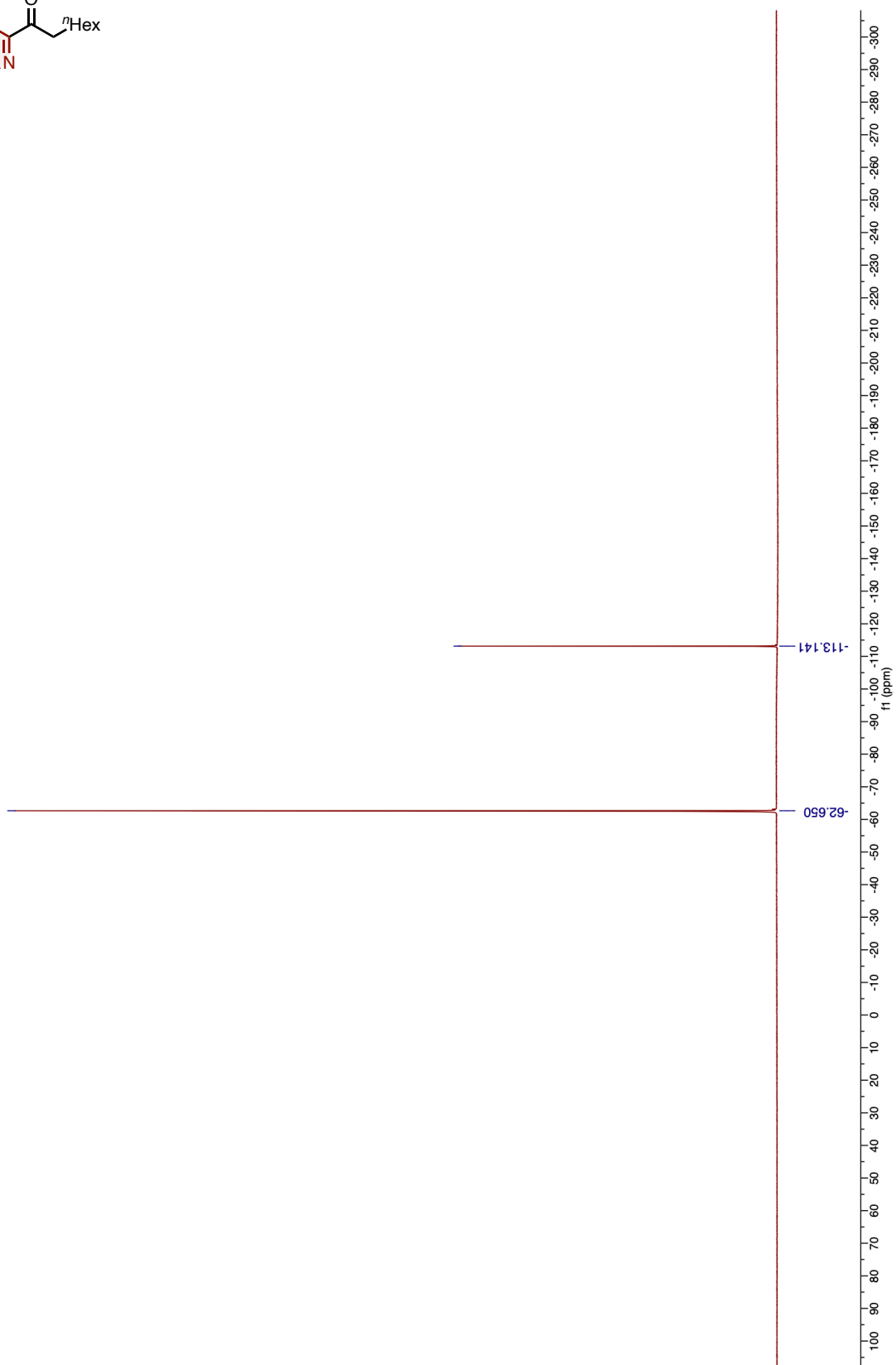
HN2994 — single pulse decoupled gated NOE



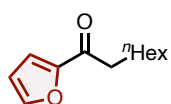
^{19}F NMR of **3aR** (376 MHz, CDCl_3)



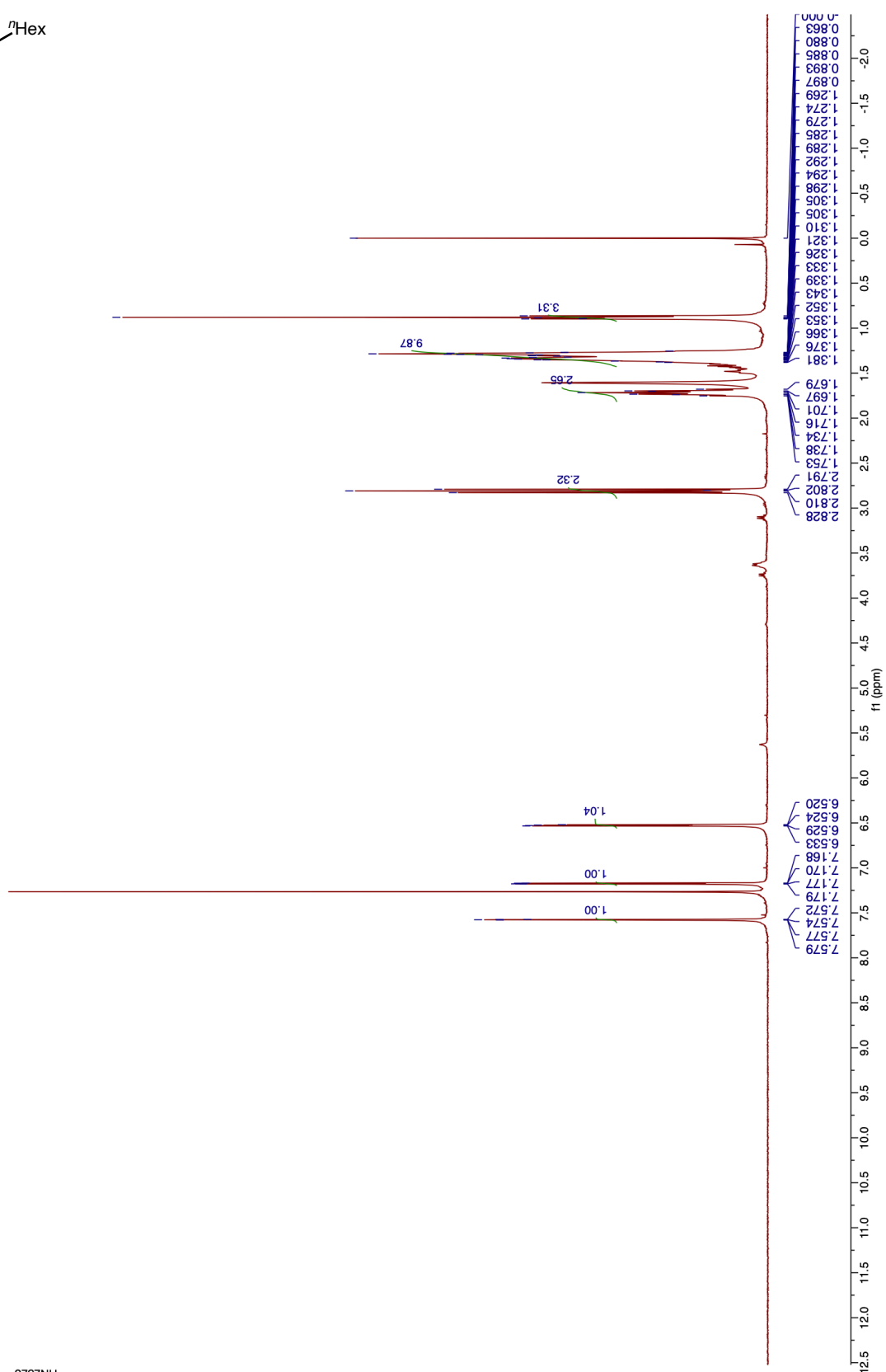
RS_3ar(HN2994)_19F_2 — single pulse decoupled gated NOE



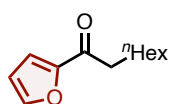
^1H NMR of **3aS** (400 MHz, CDCl_3)



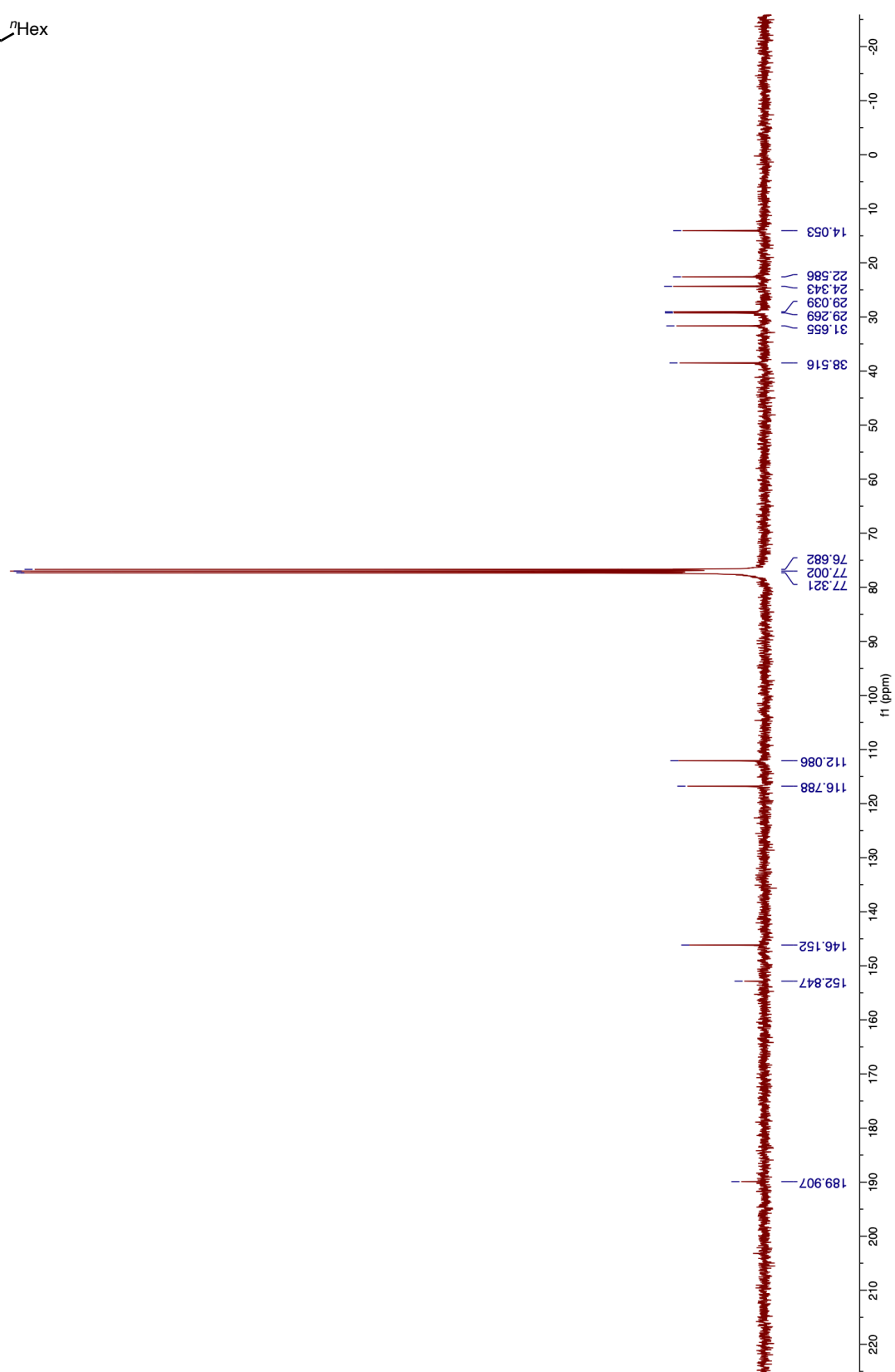
HN2328 — single-pulse



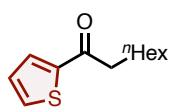
^{13}C NMR of **3aS** (101 MHz, CDCl_3)



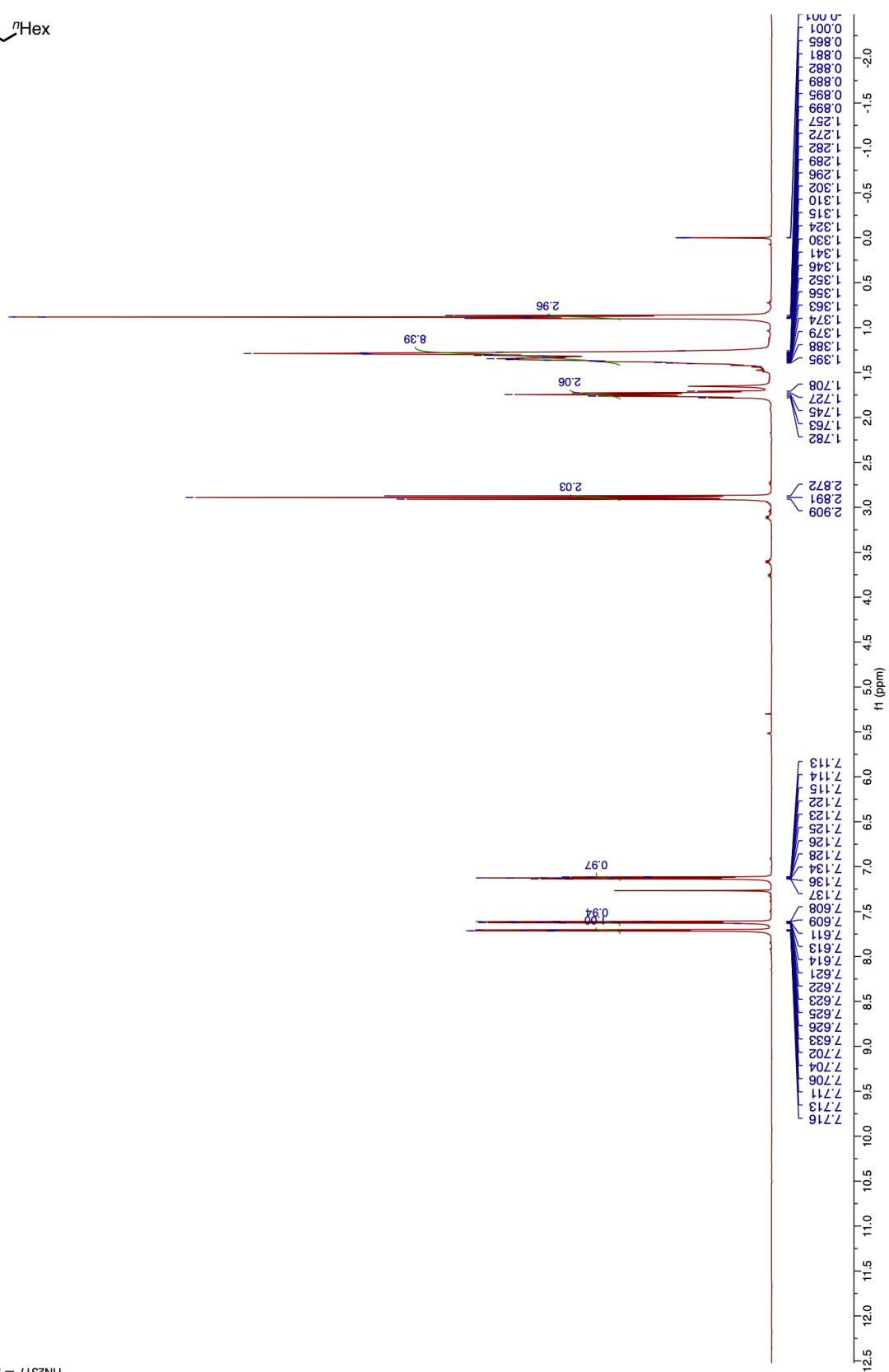
HN2328 — single pulse decoupled gated NOE



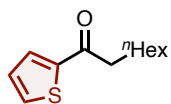
^1H NMR of **3aT** (400 MHz, CDCl_3)



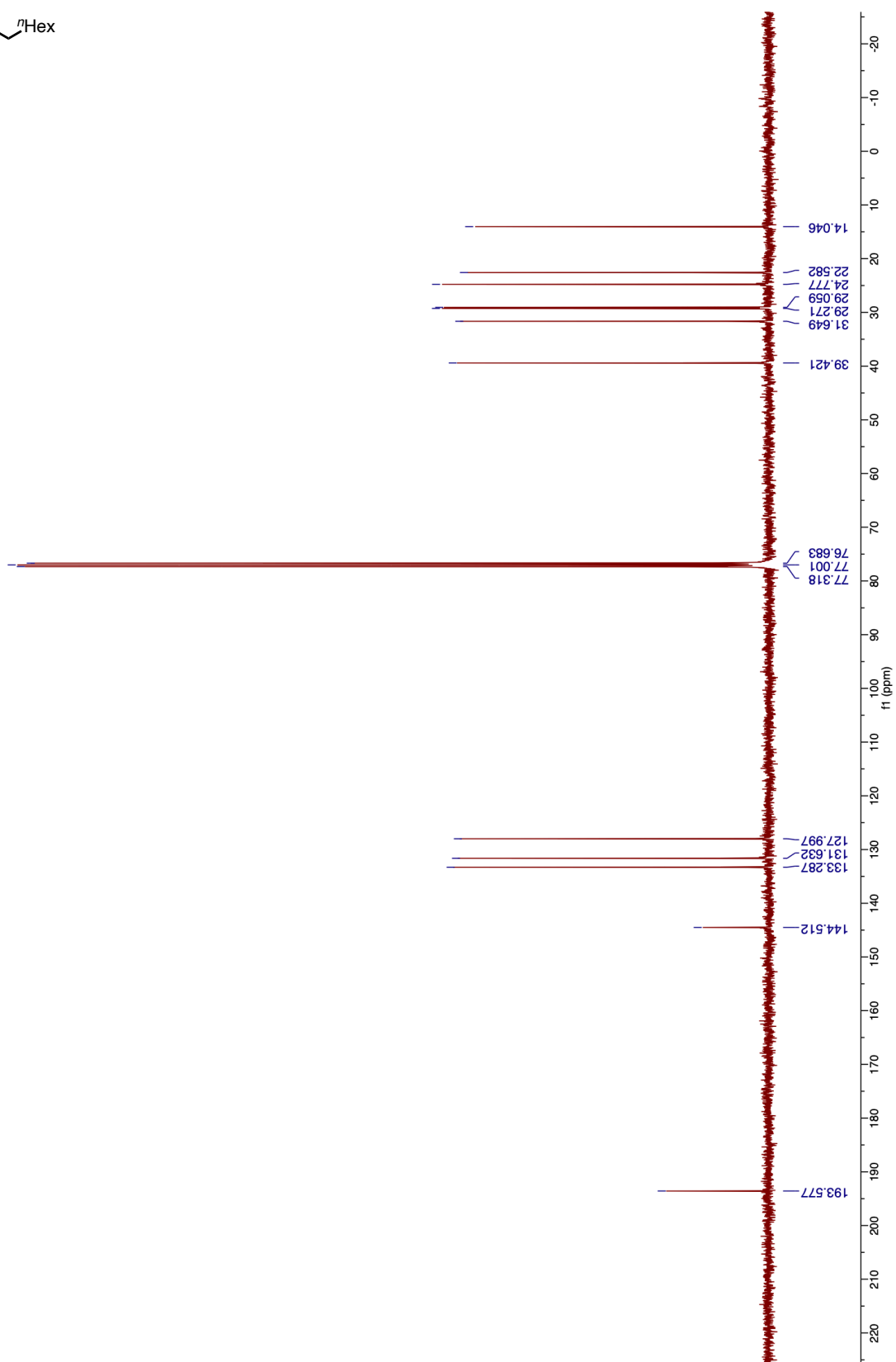
HN2317 — single-pulse



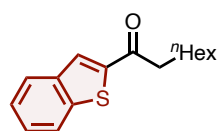
^{13}C NMR of **3aT** (101 MHz, CDCl_3)



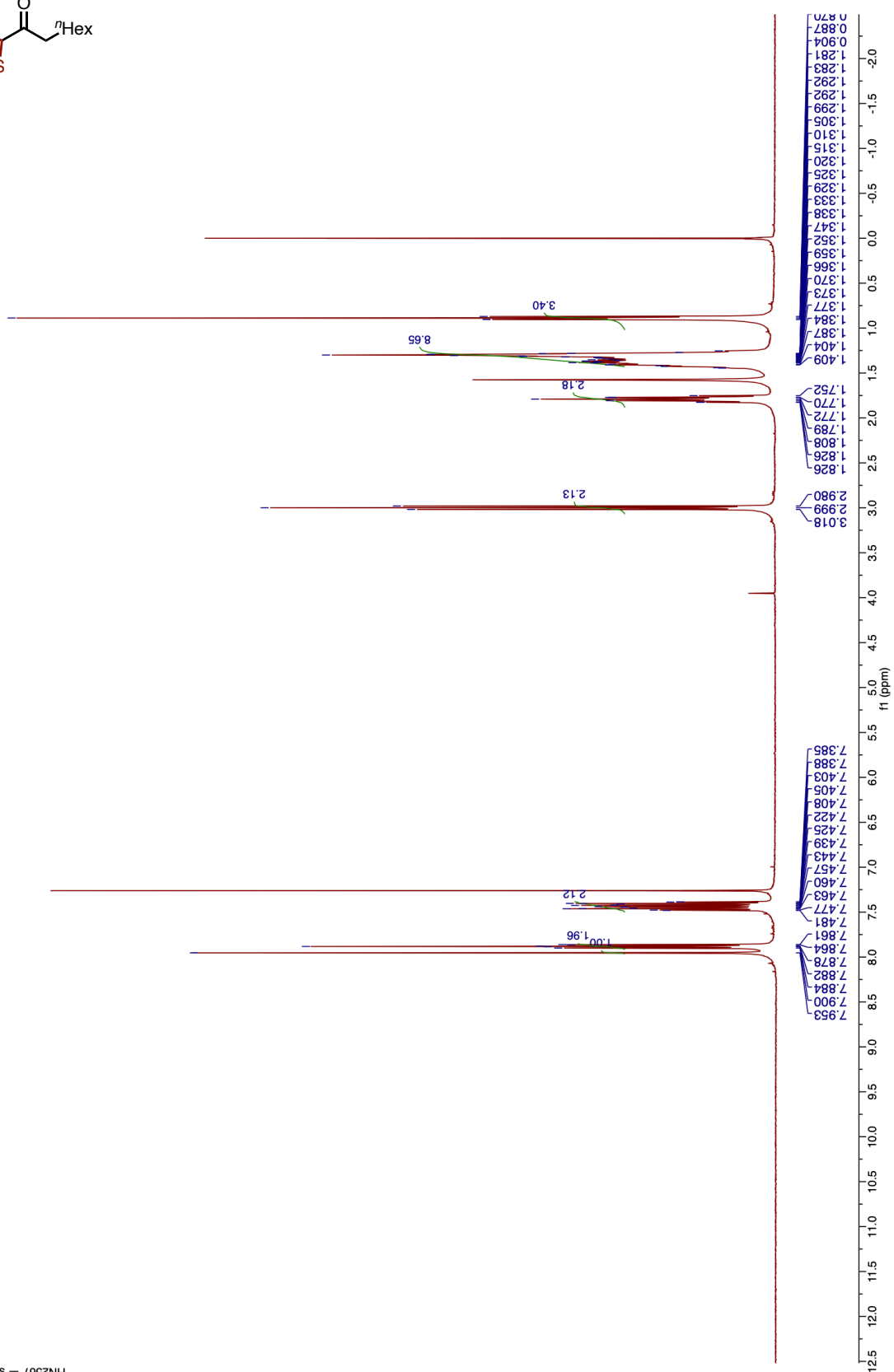
HN2317 — single pulse decoupled gated NOE



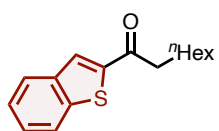
^1H NMR of **3aU** (400 MHz, CDCl_3)



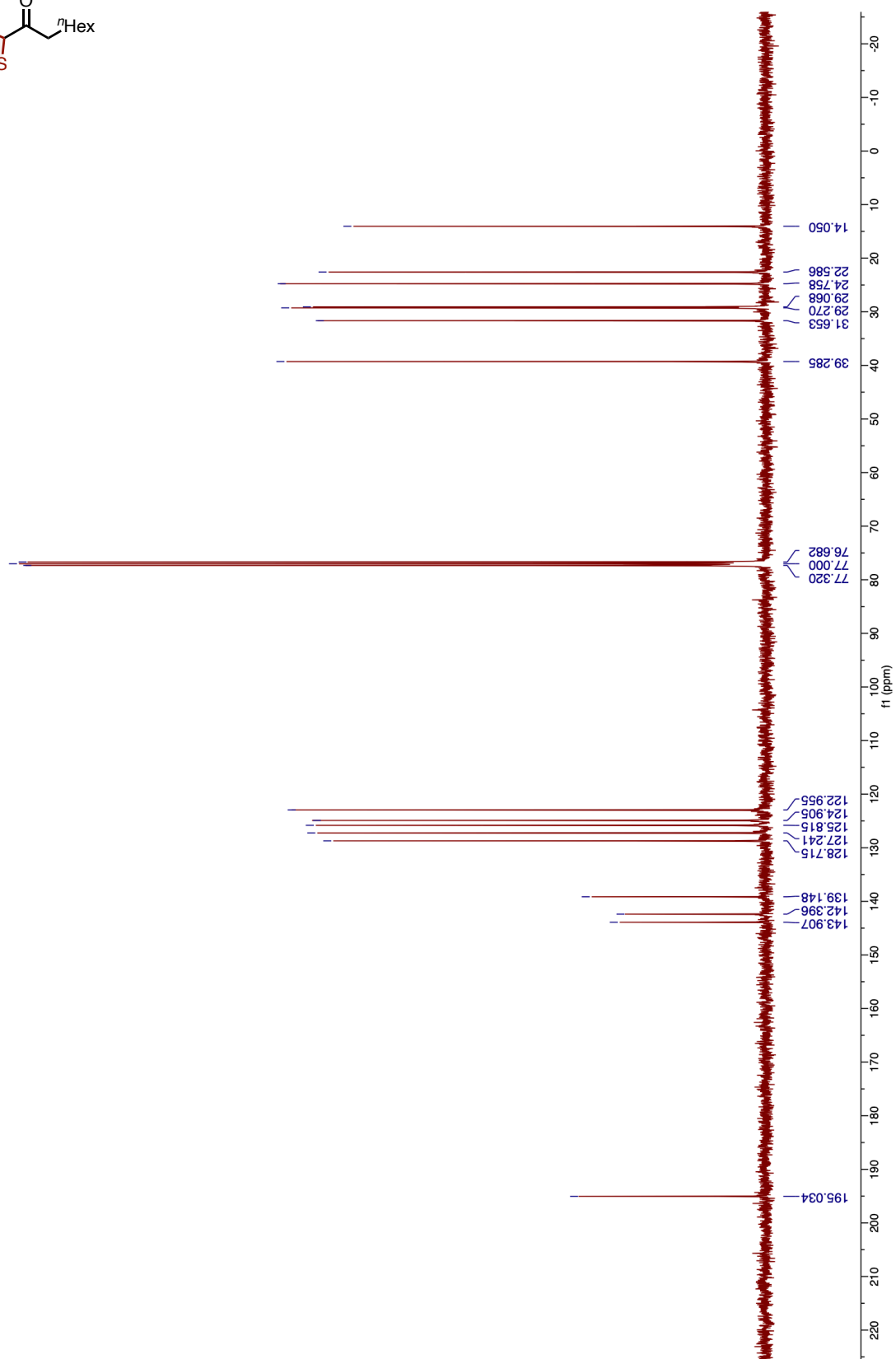
HN2567 — single-pulse



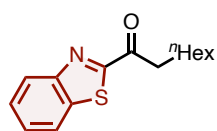
^{13}C NMR of **3aU** (101 MHz, CDCl_3)



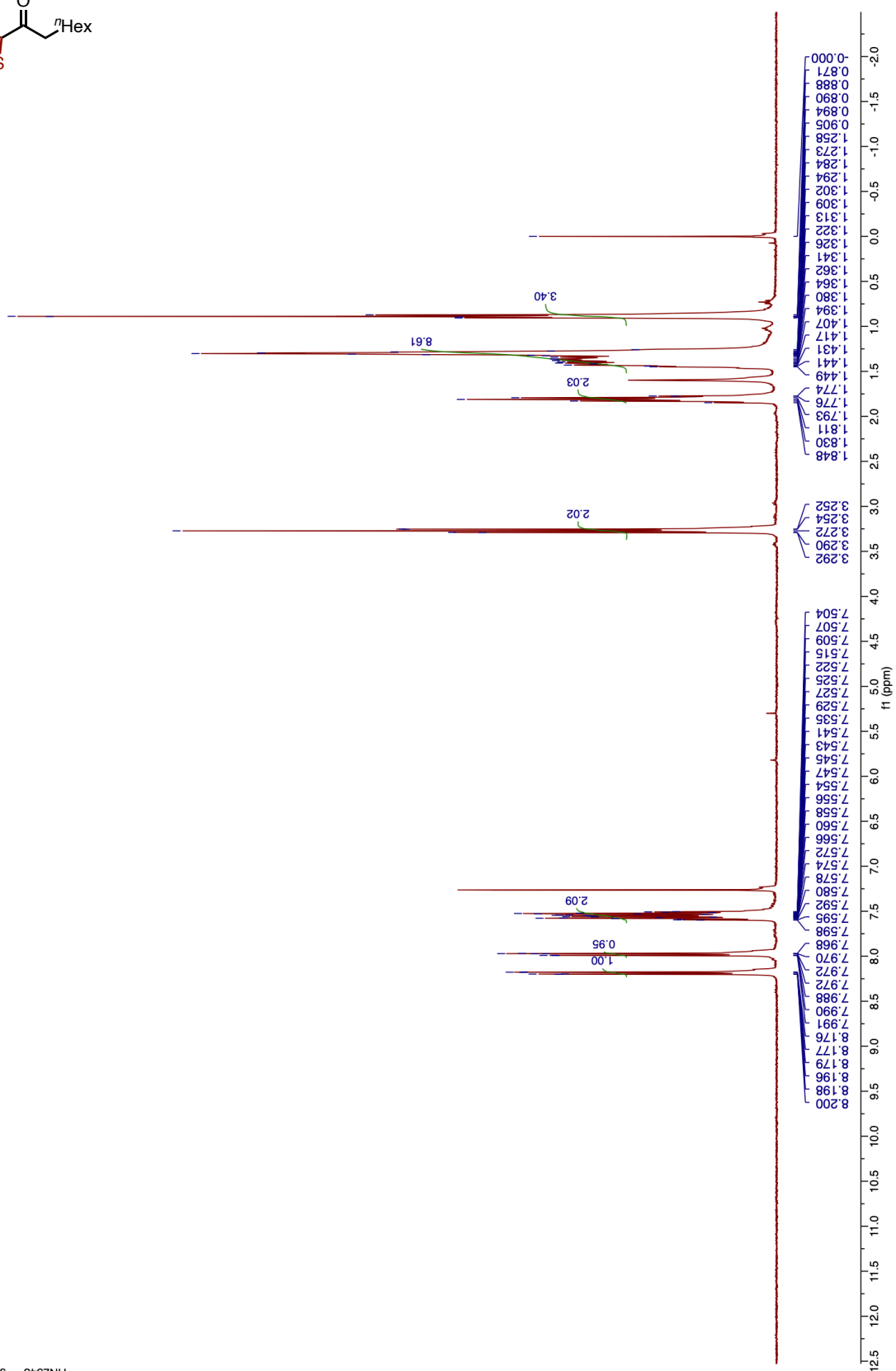
HN2267 — single pulse decoupled gated NOE



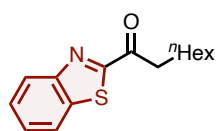
^1H NMR of **3aV** (400 MHz, CDCl_3)



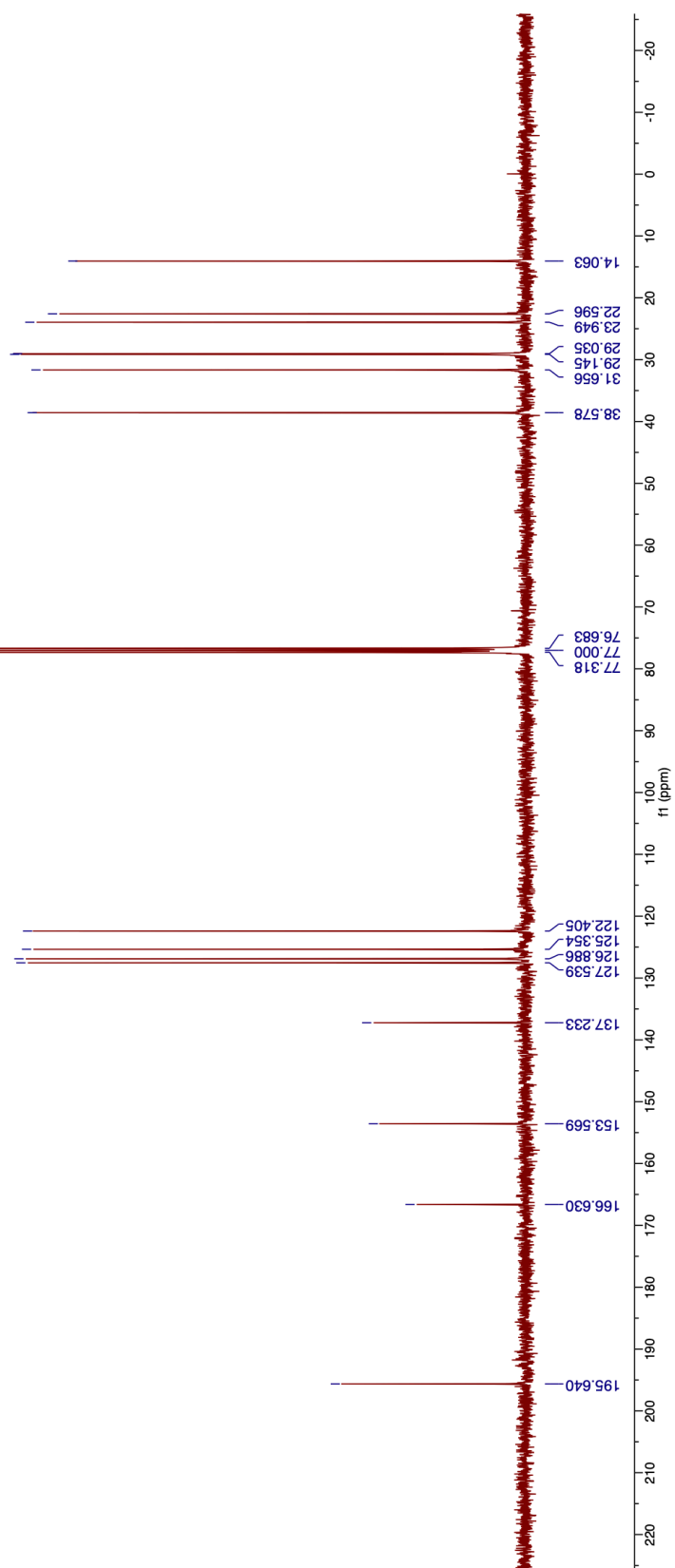
HN2543 — single-pulse



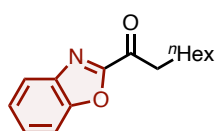
^{13}C NMR of **3aV** (101 MHz, CDCl_3)



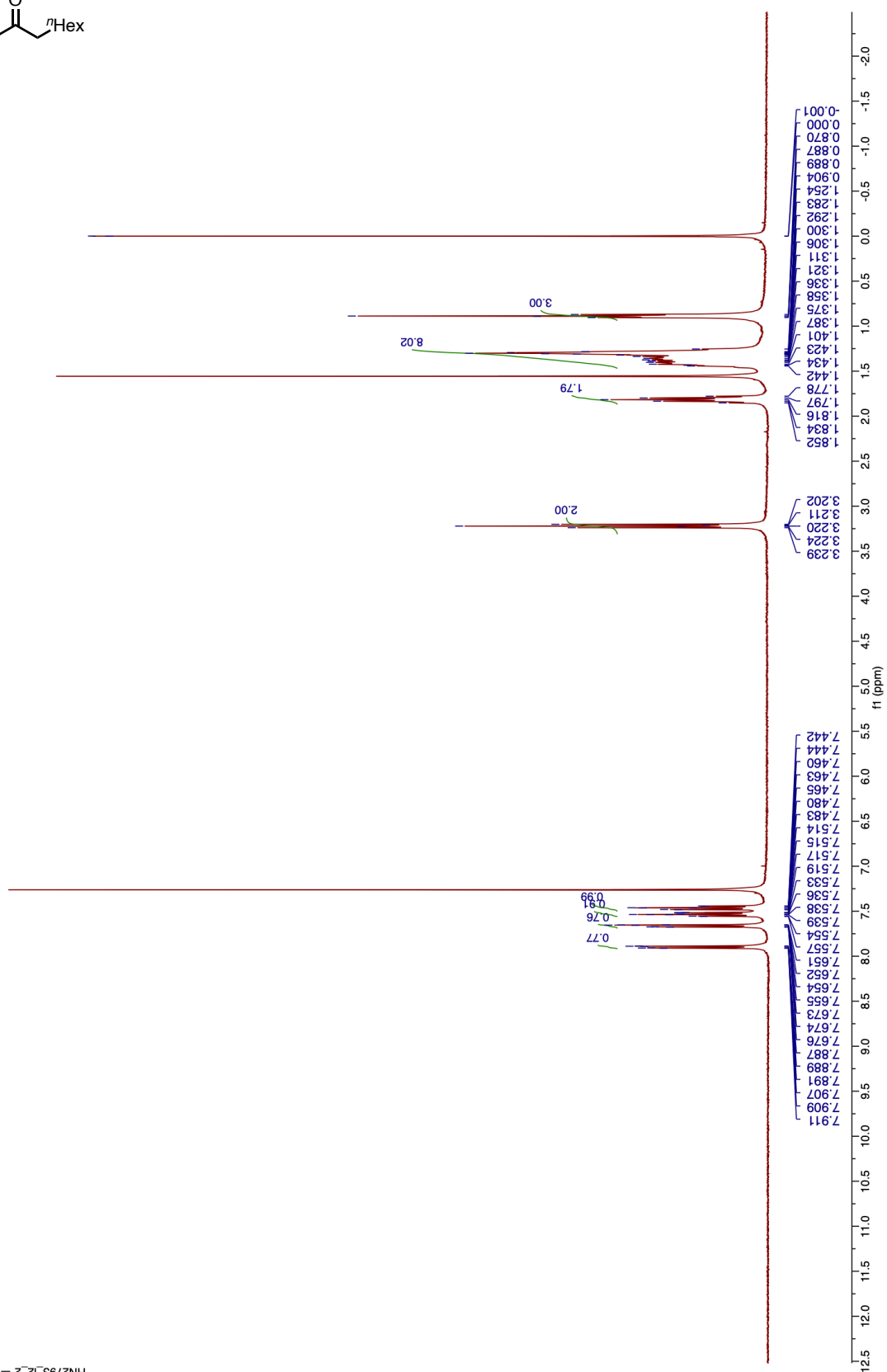
HN2543 — single pulse decoupled gated NOE



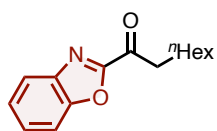
^1H NMR of **3aW** (400 MHz, CDCl_3)



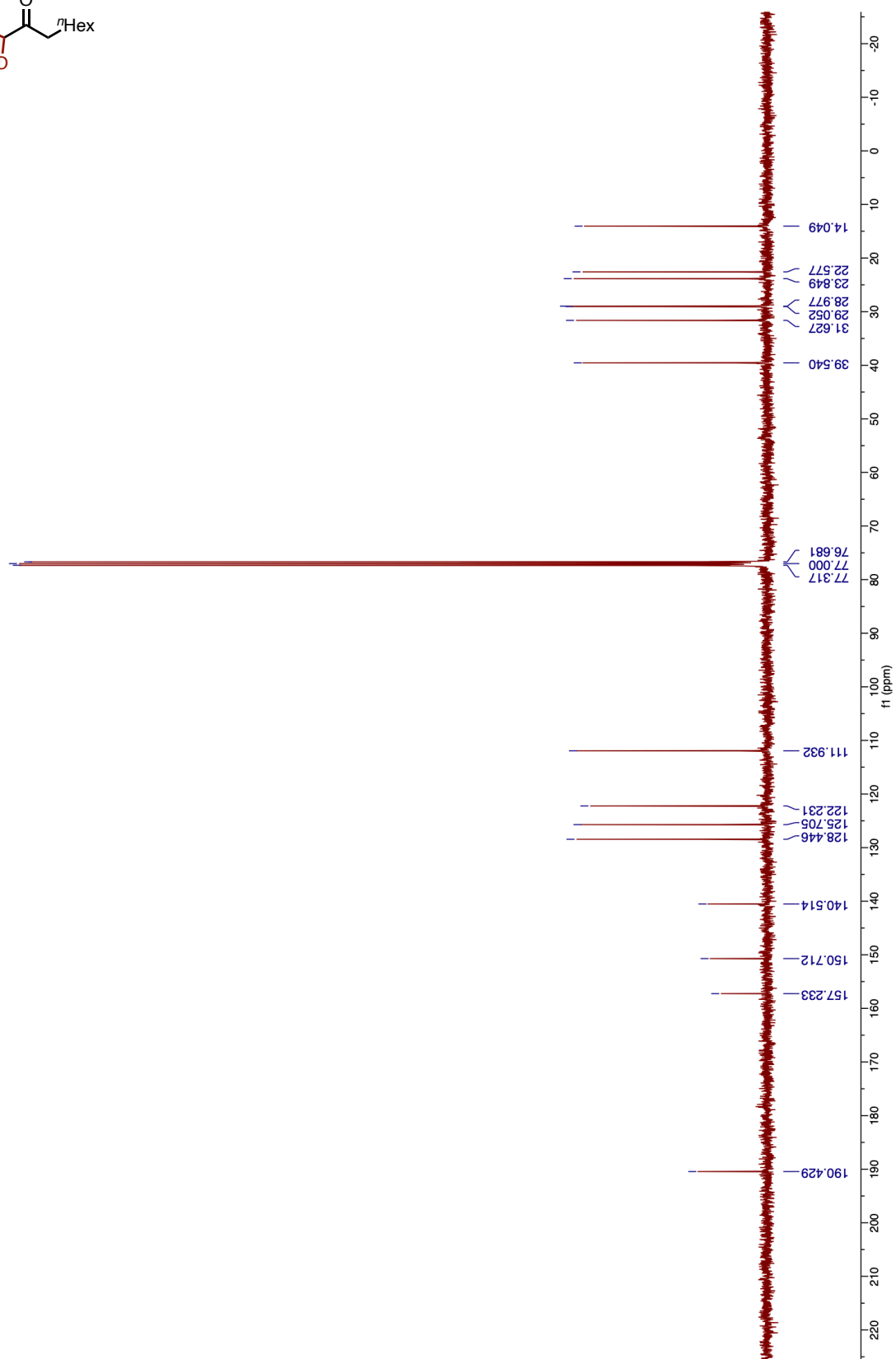
HN2793_i2_2 - single-pulse



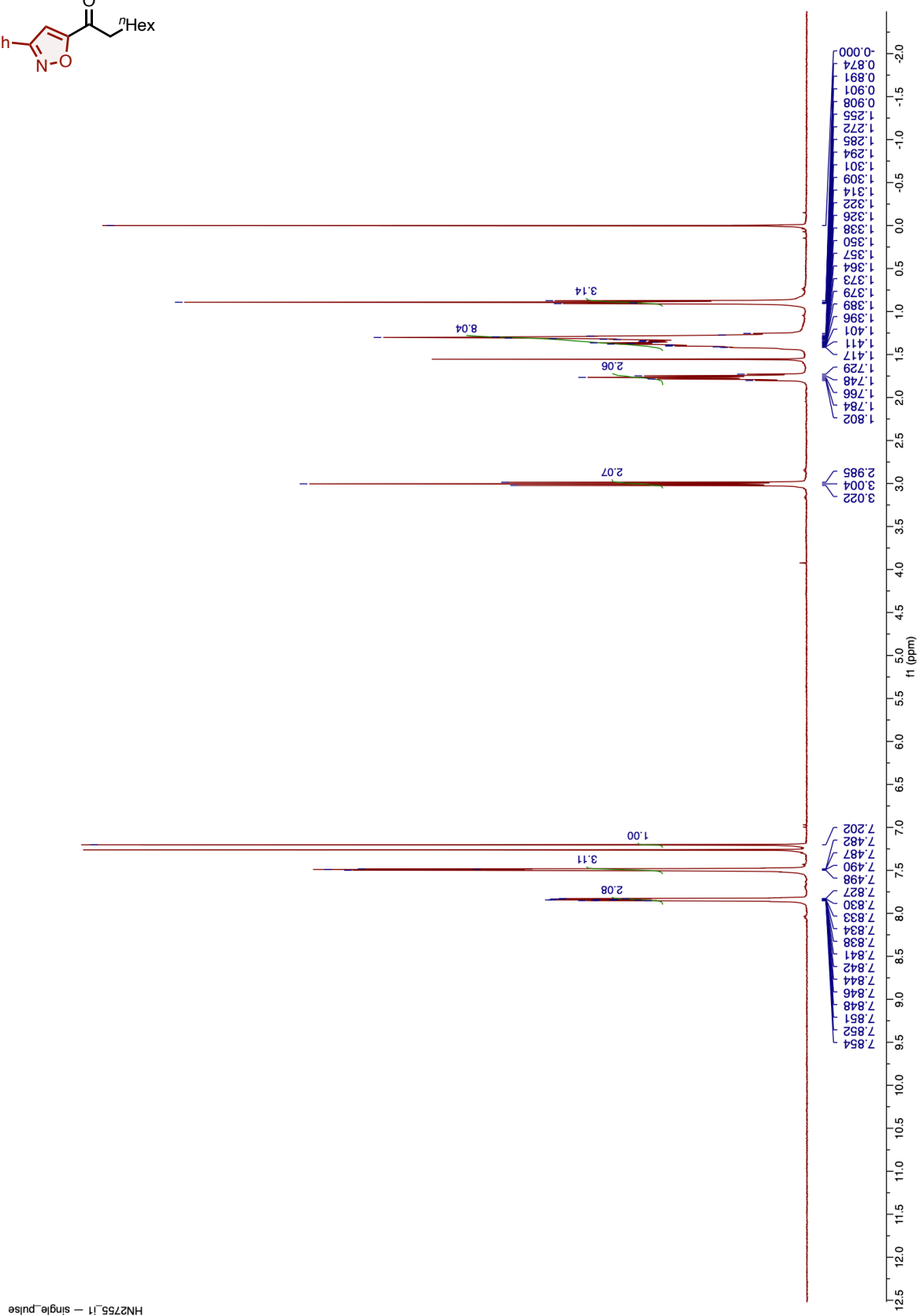
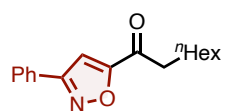
^{13}C NMR of **3aW** (101 MHz, CDCl_3)



HN2793_i2_3 — single pulse decoupled gated NOE

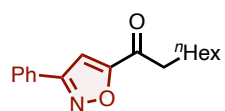


^1H NMR of **3aX** (400 MHz, CDCl_3)

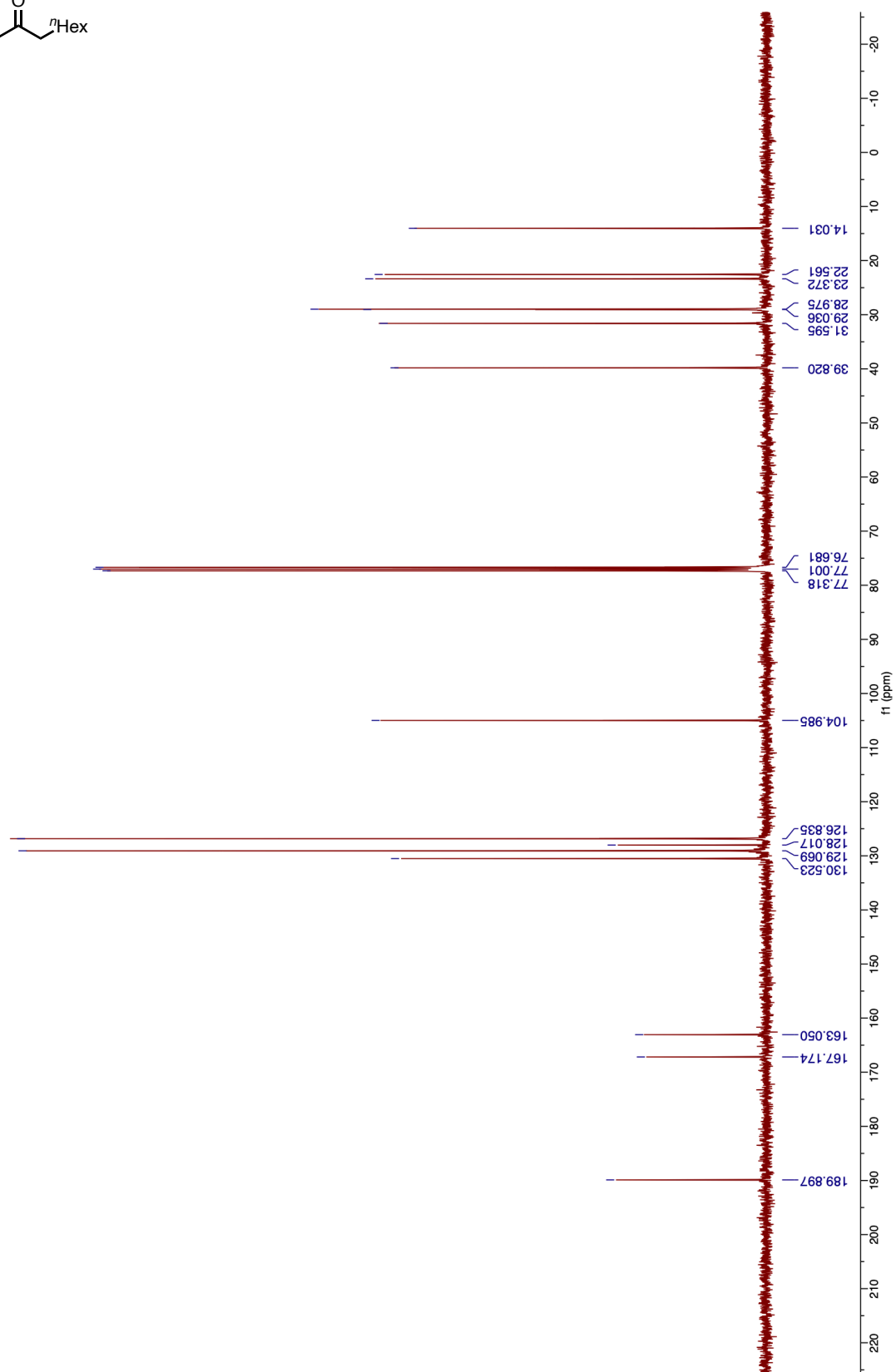


HN2755.f1 - single-pulse

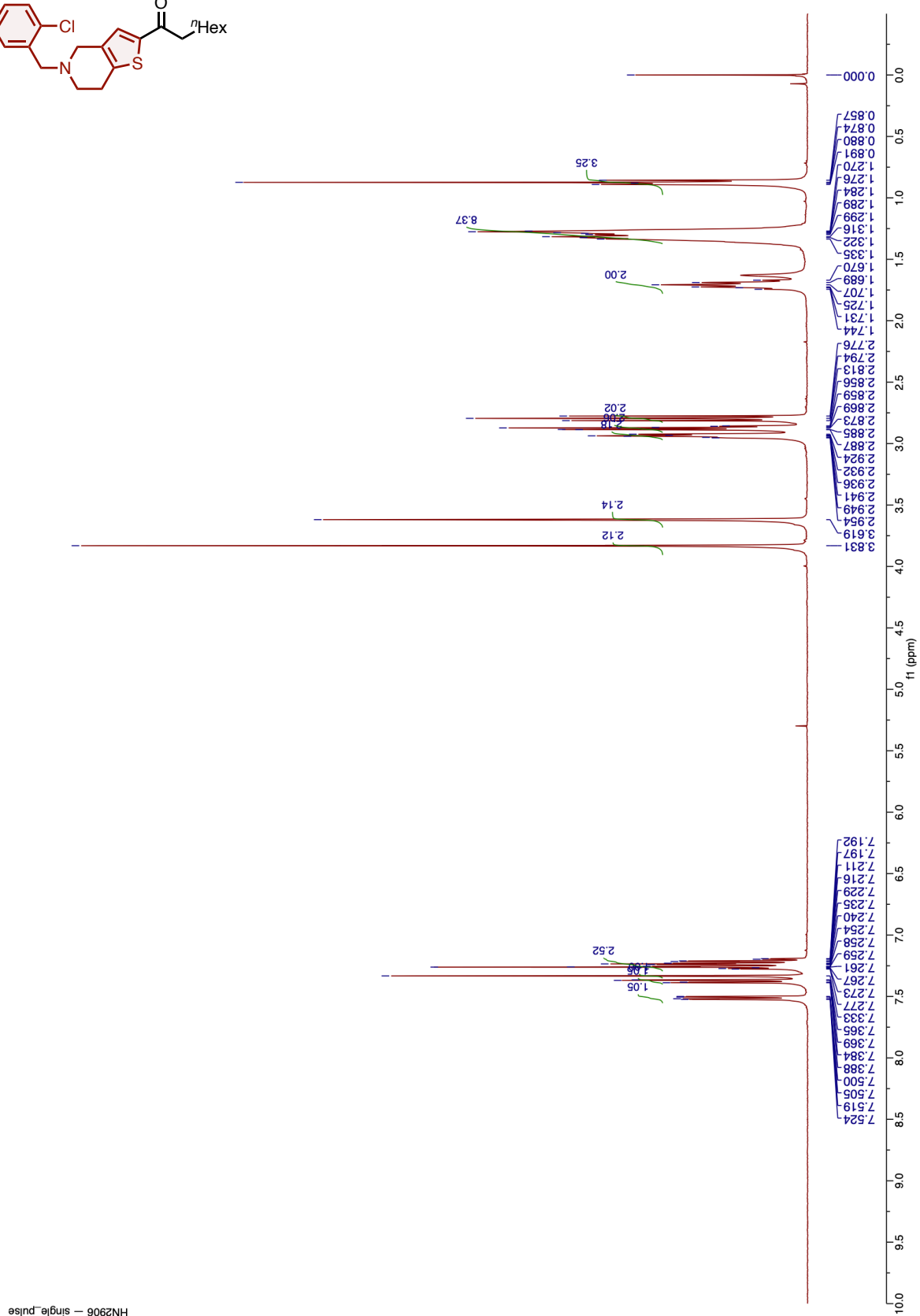
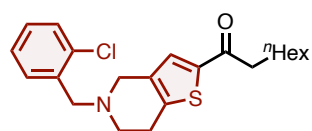
^{13}C NMR of **3aX** (101 MHz, CDCl_3)



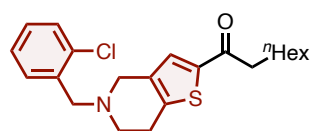
HN2755 — single pulse decoupled gated NOE



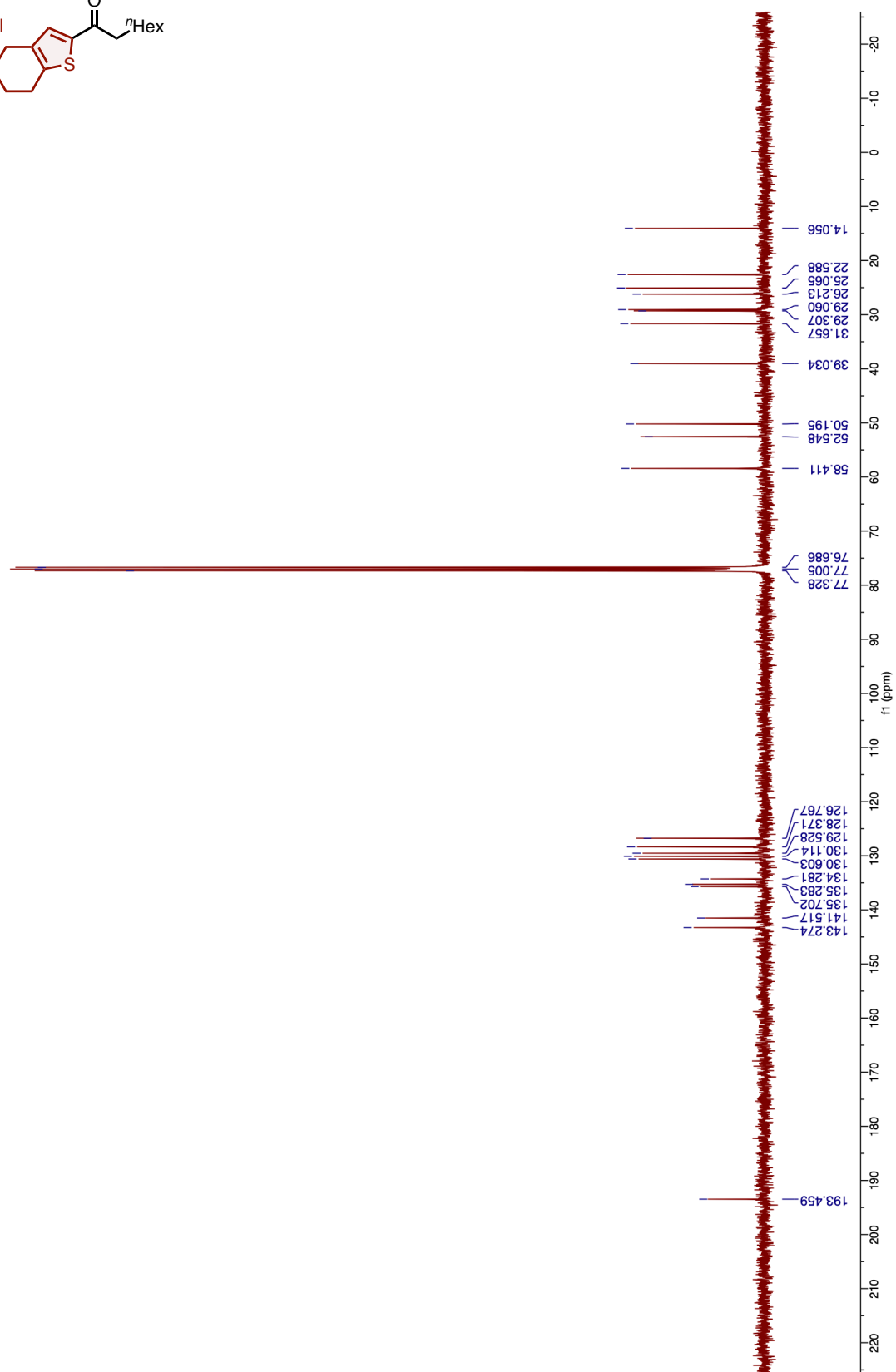
^1H NMR of **3aY** (400 MHz, CDCl_3)



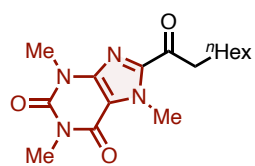
^{13}C NMR of **3aY** (101 MHz, CDCl_3)



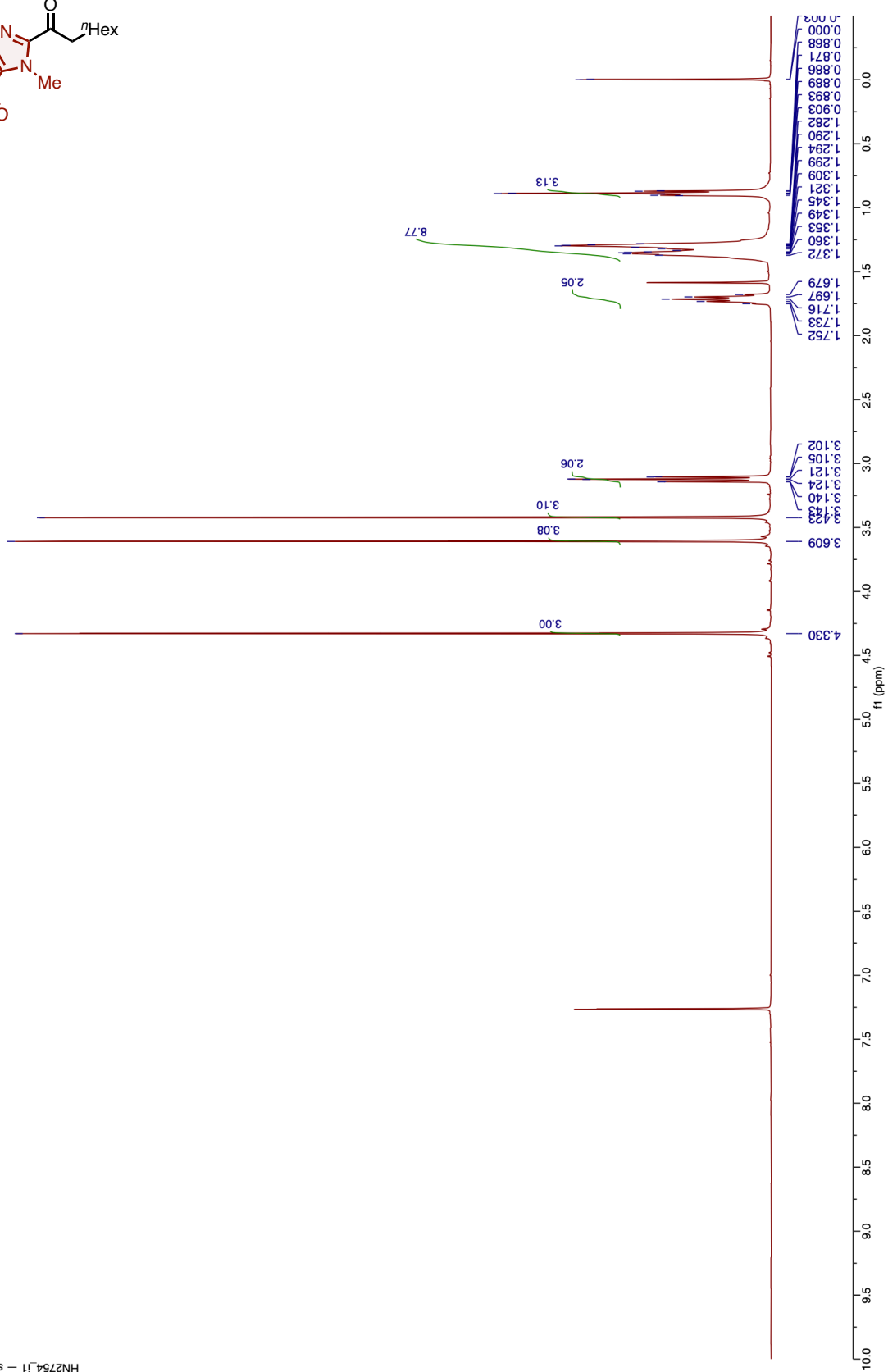
HN2906 — single pulse decoupled gated NOE



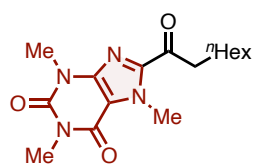
^1H NMR of **3aZ** (400 MHz, CDCl_3)



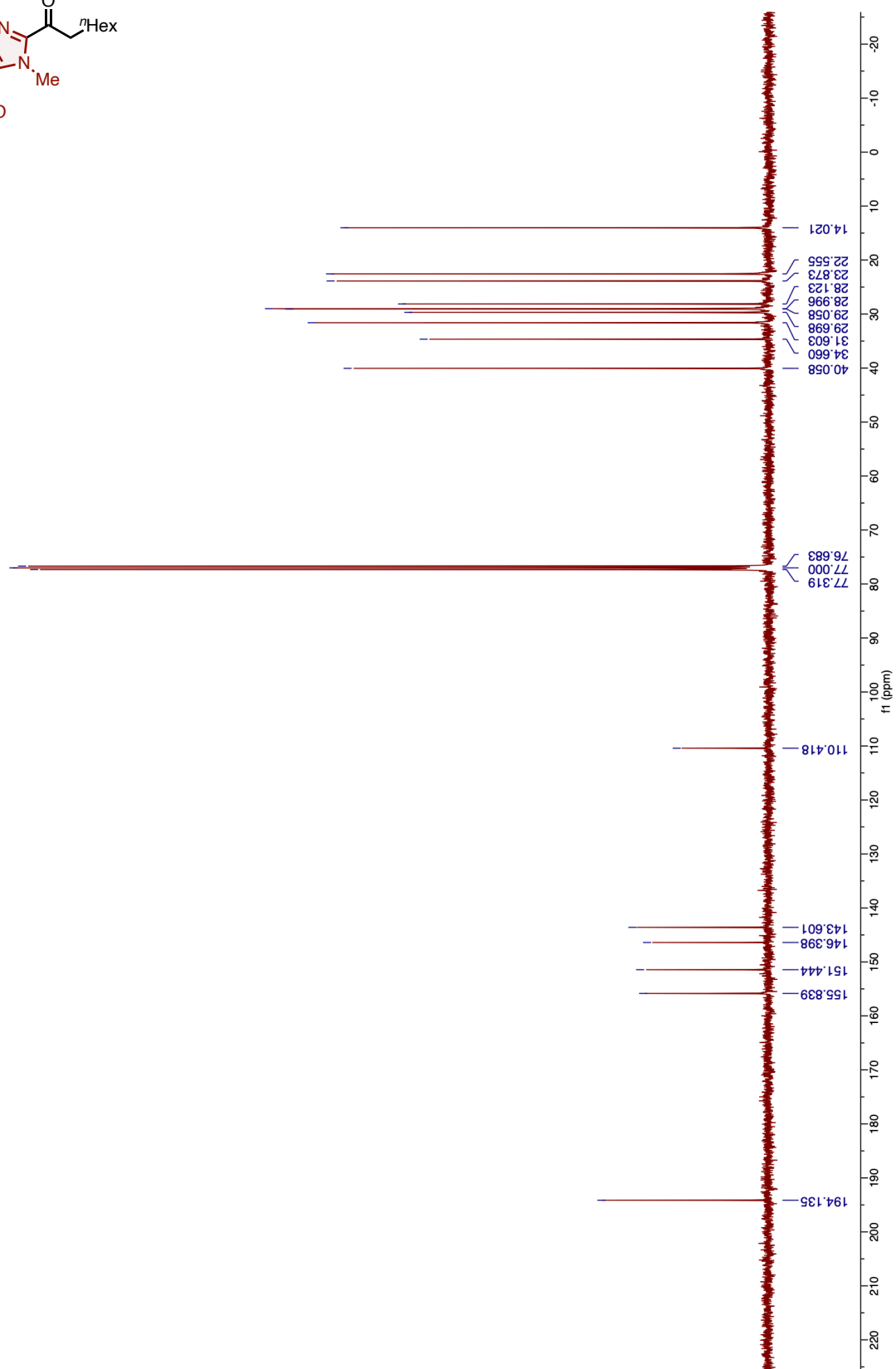
HN2754.f1 — single-pulse



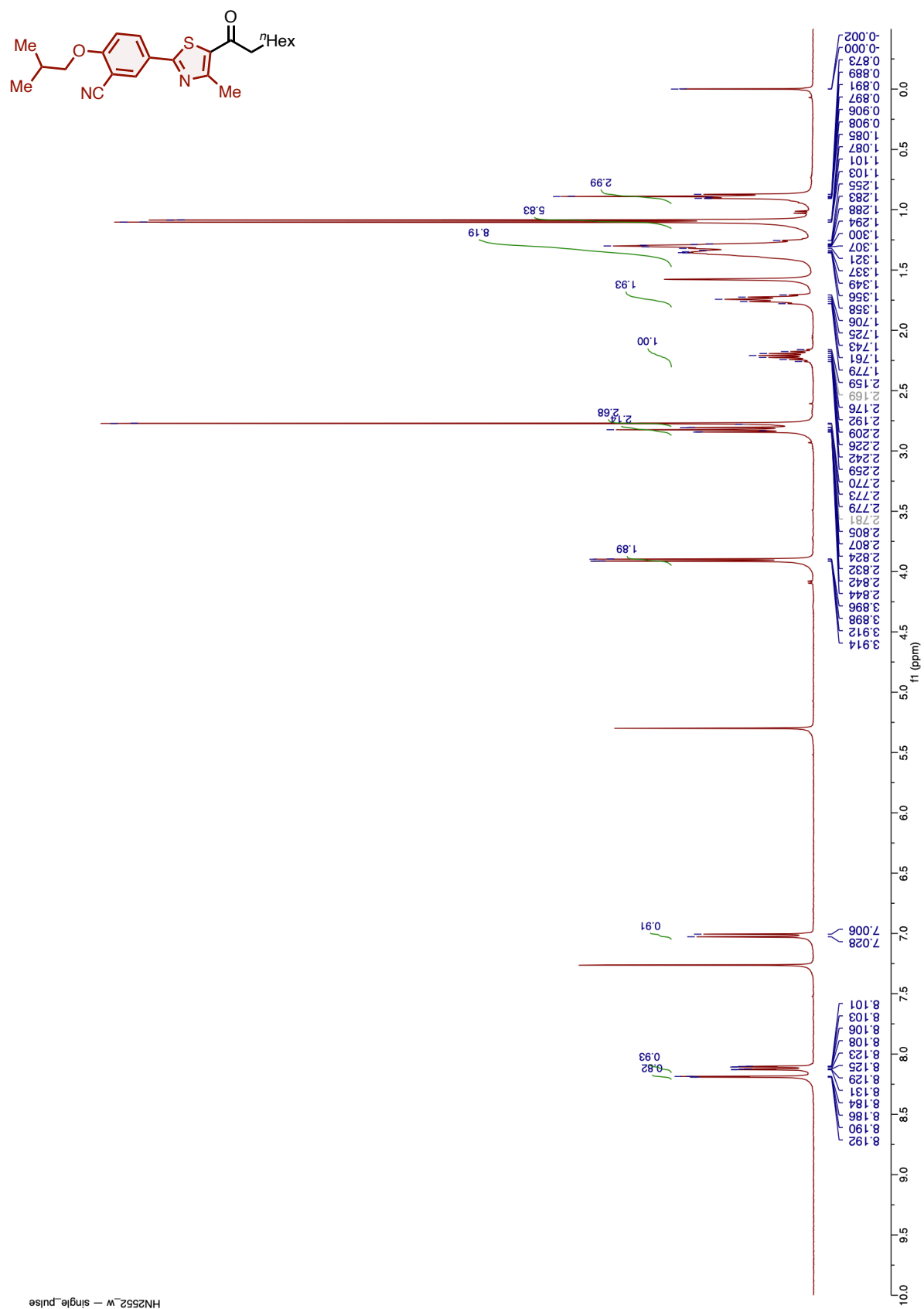
^{13}C NMR of **3aZ** (101 MHz, CDCl_3)



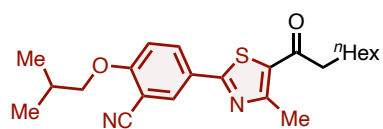
HN2954 — single pulse decoupled gated NOE



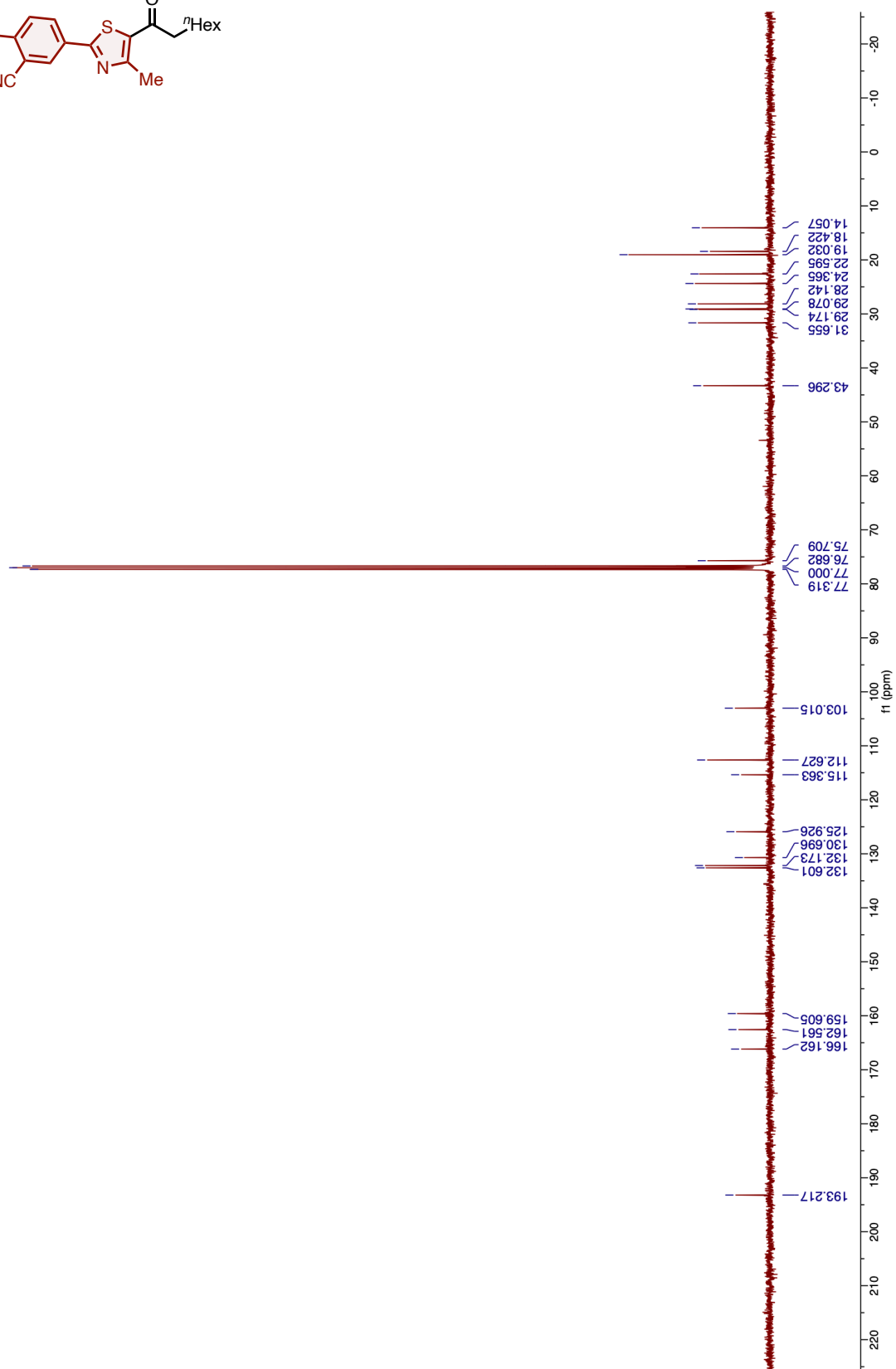
¹H NMR of **3AA** (400 MHz, CDCl₃)



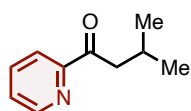
^{13}C NMR of **3aAA** (101 MHz, CDCl_3)



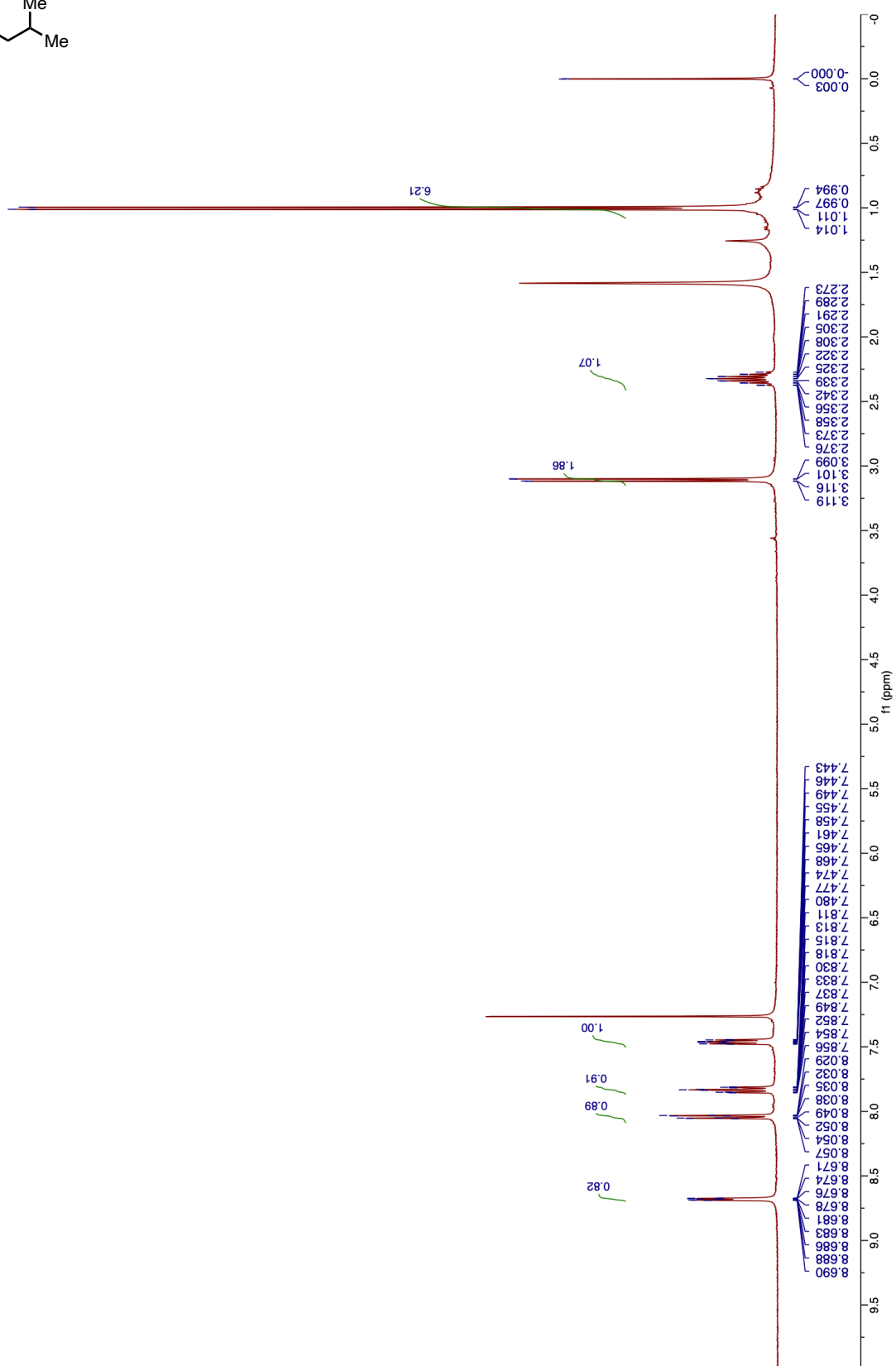
HN2552_w — single pulse decoupled gated NOE



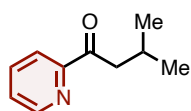
^1H NMR of **3hA** (400 MHz, CDCl_3)



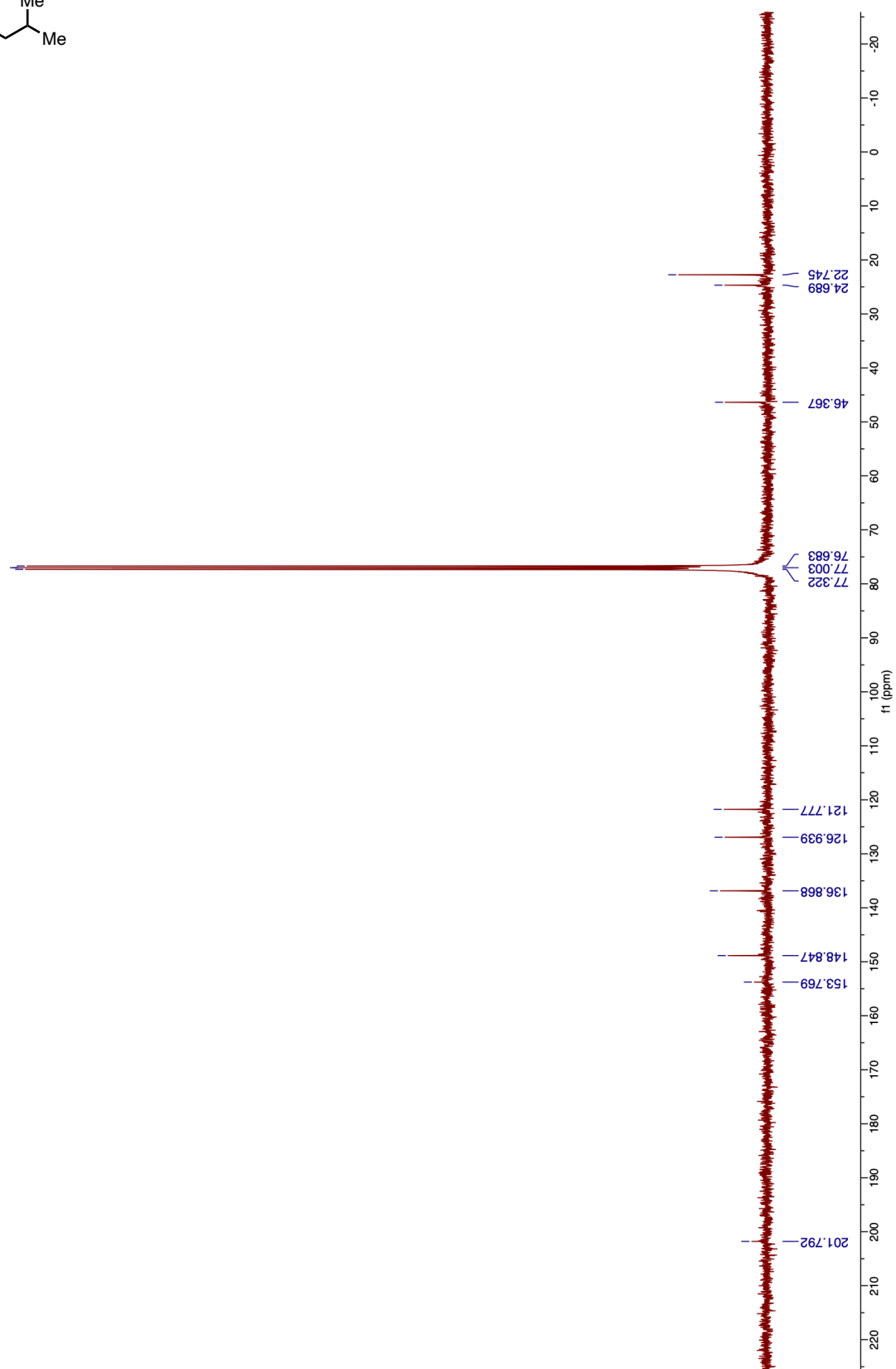
HN2413.f1 - single-pulse



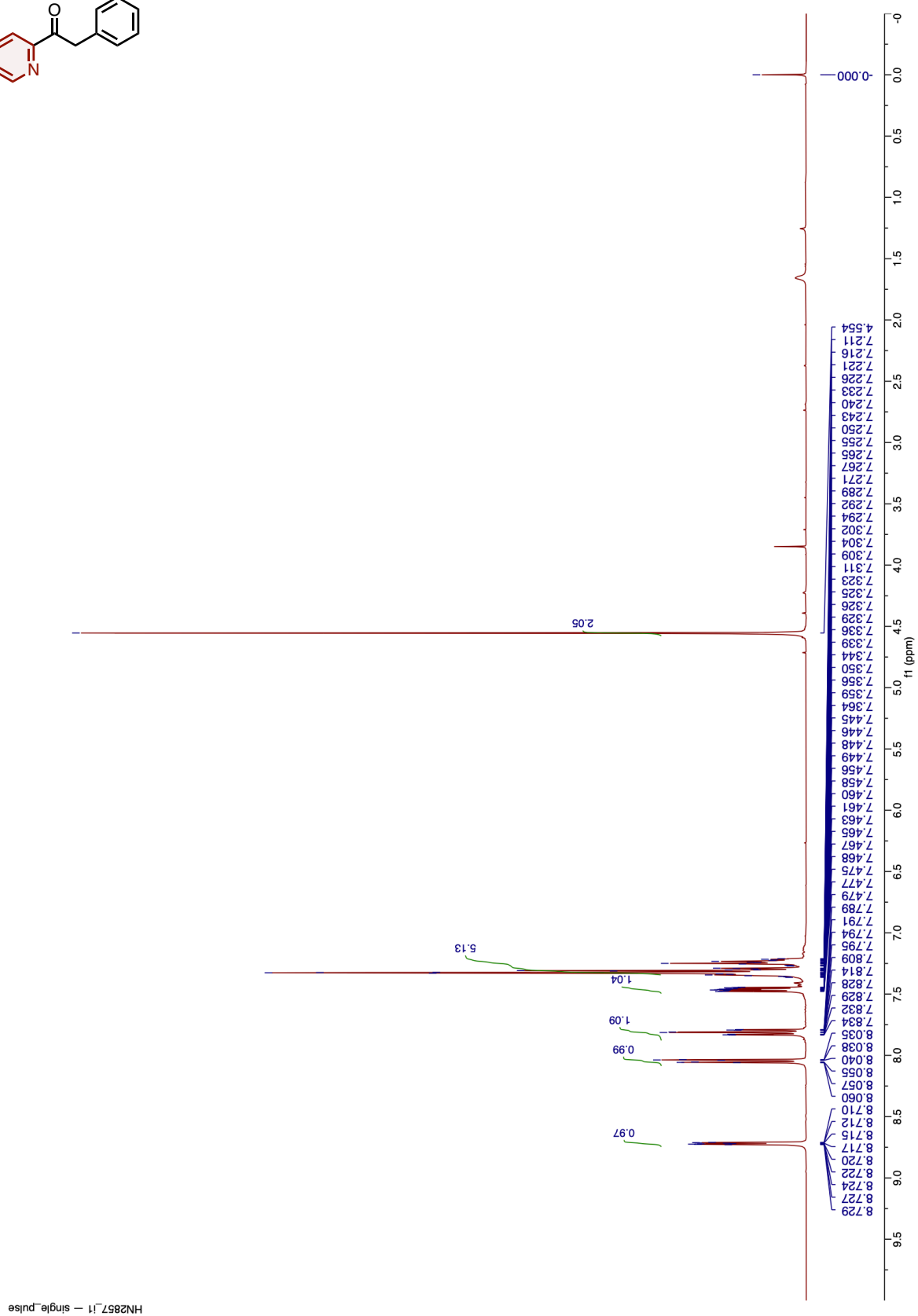
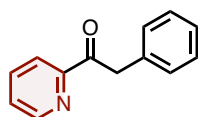
^{13}C NMR of **3hA** (101 MHz, CDCl_3)



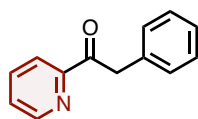
HN2264.f1 — single pulse decoupled gated NOE



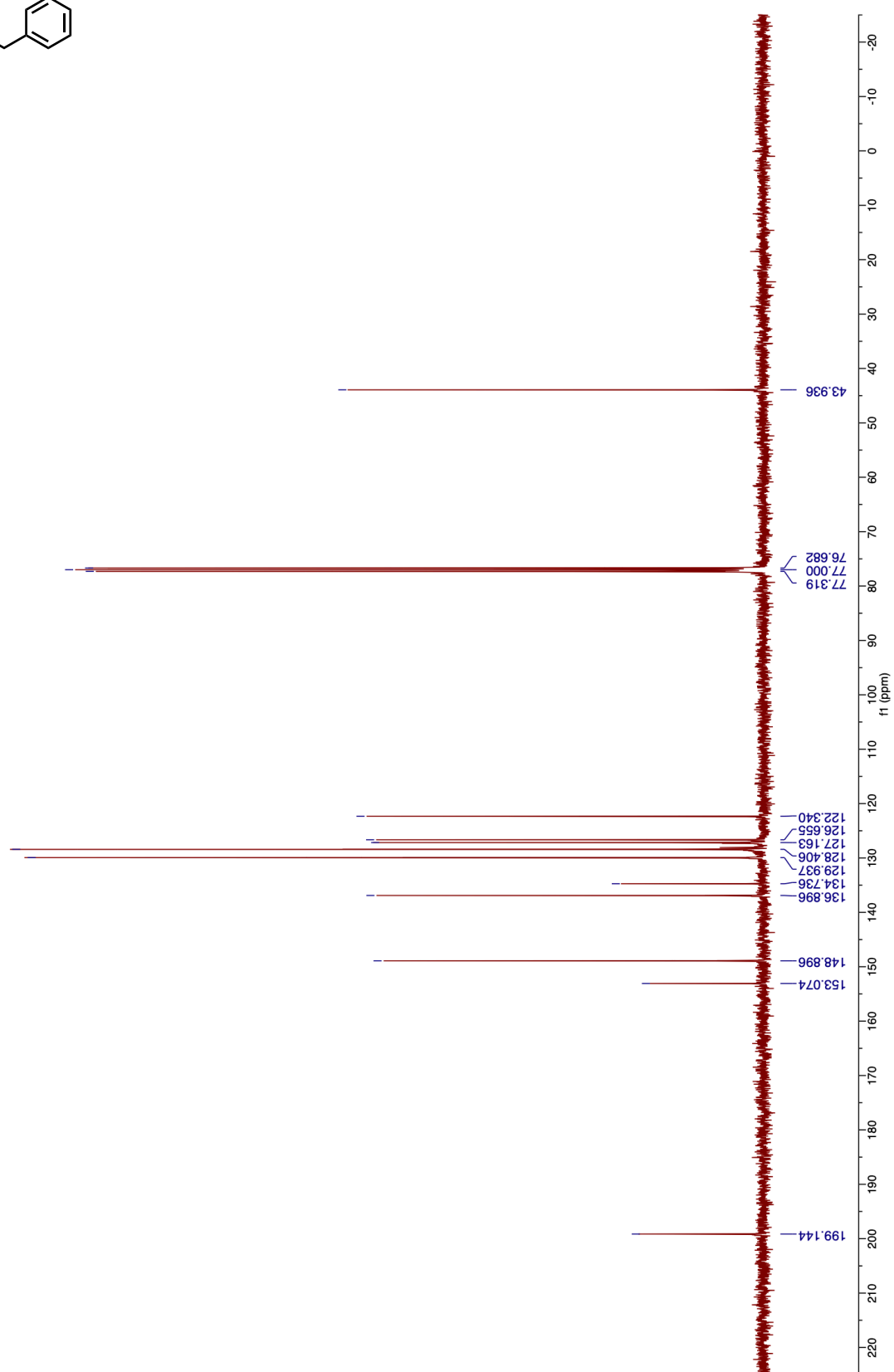
^1H NMR of **3iA** (400 MHz, CDCl_3)



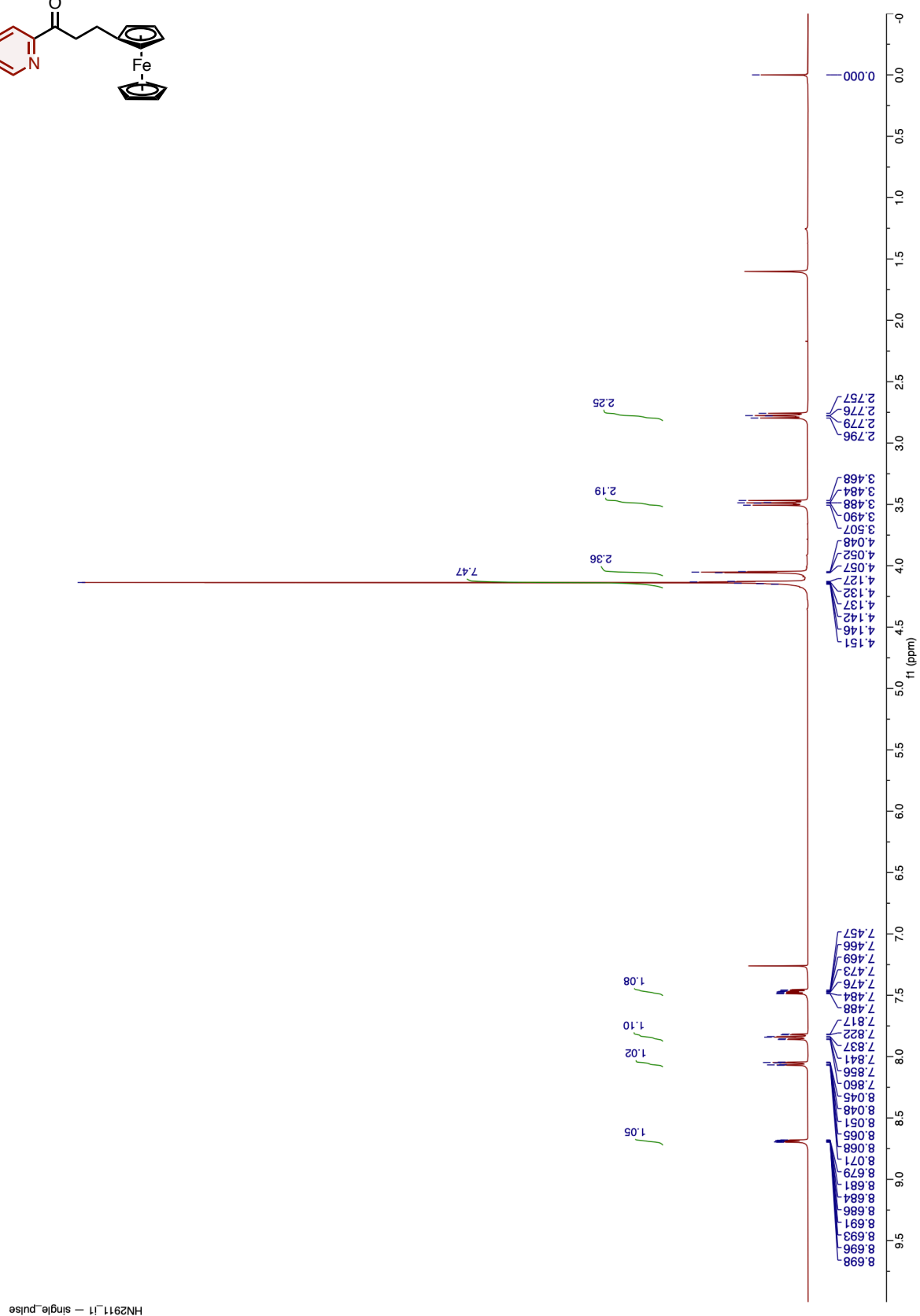
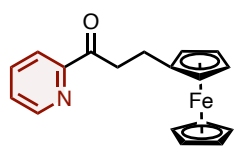
^{13}C NMR of **3iA** (101 MHz, CDCl_3)



HN2857.f1 — single pulse decoupled gated NOE

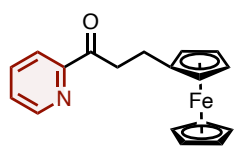


^1H NMR of **3jA** (400 MHz, CDCl_3)

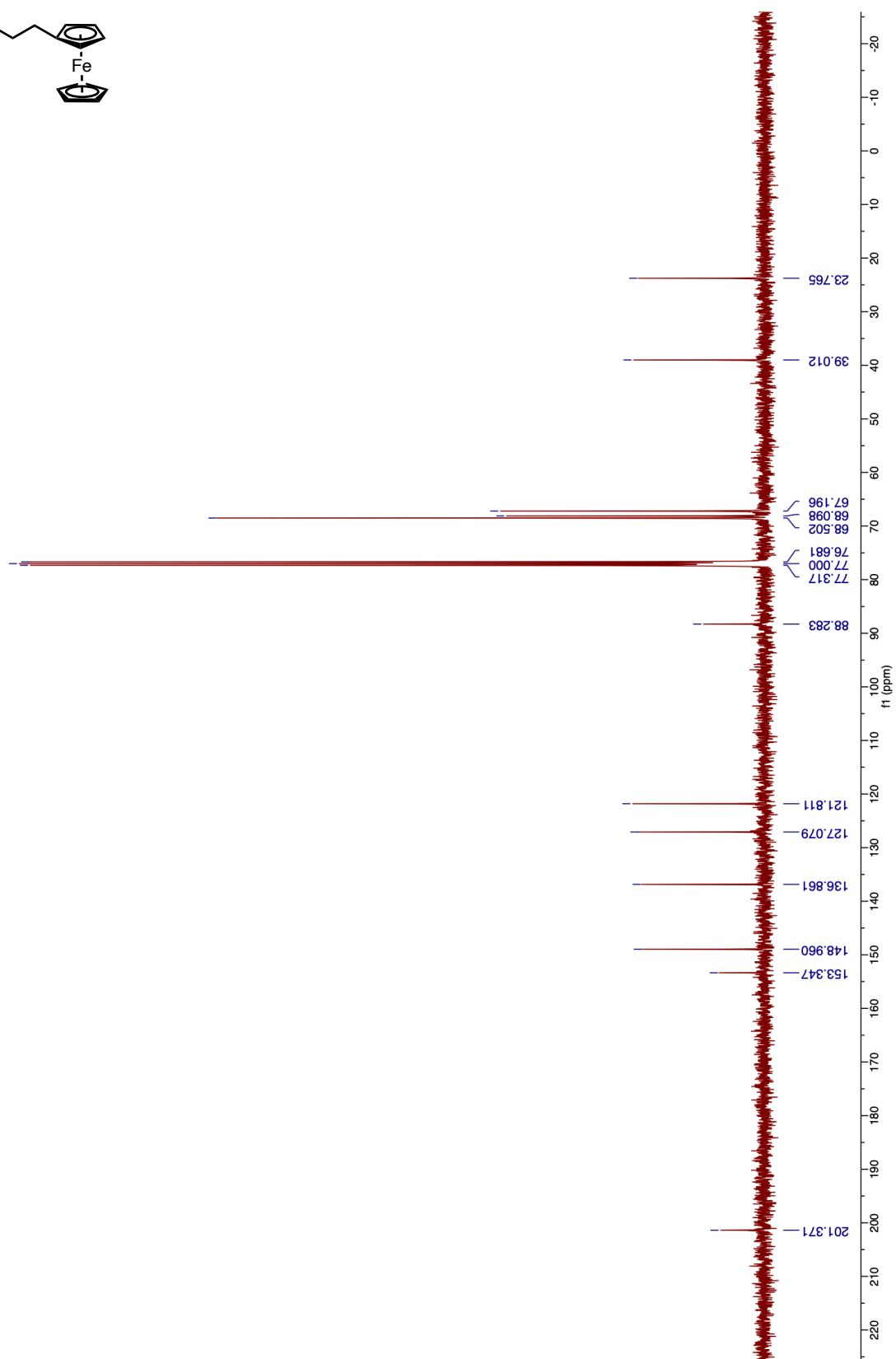


HN2911.f1 — single-pulse

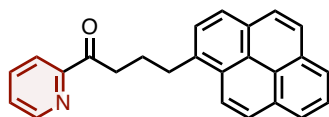
^{13}C NMR of **3jA** (101 MHz, CDCl_3)



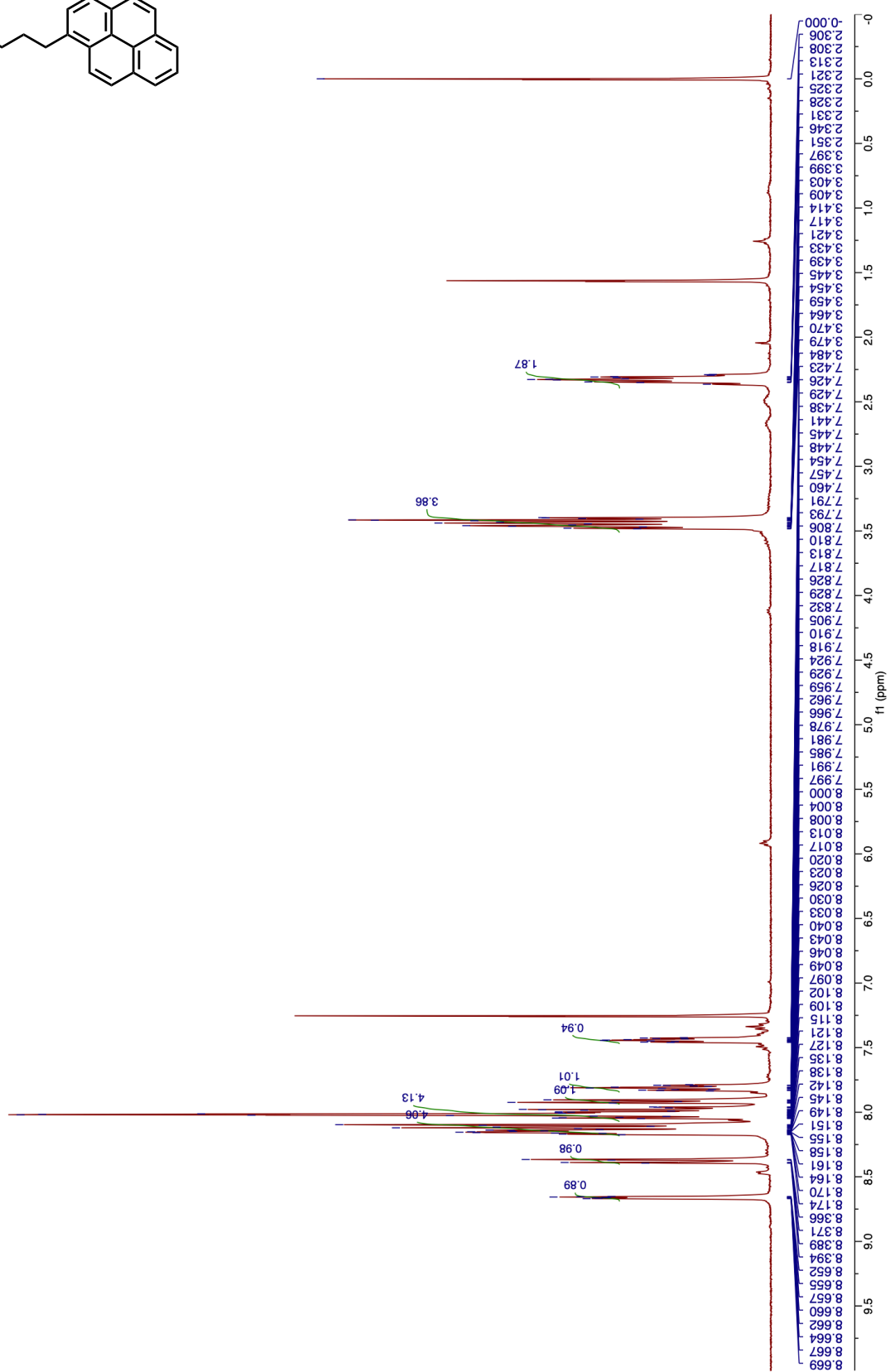
HN2911.f1 — single pulse decoupled gated NOE



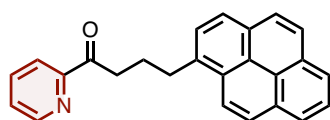
^1H NMR of **3kA** (400 MHz, CDCl_3)



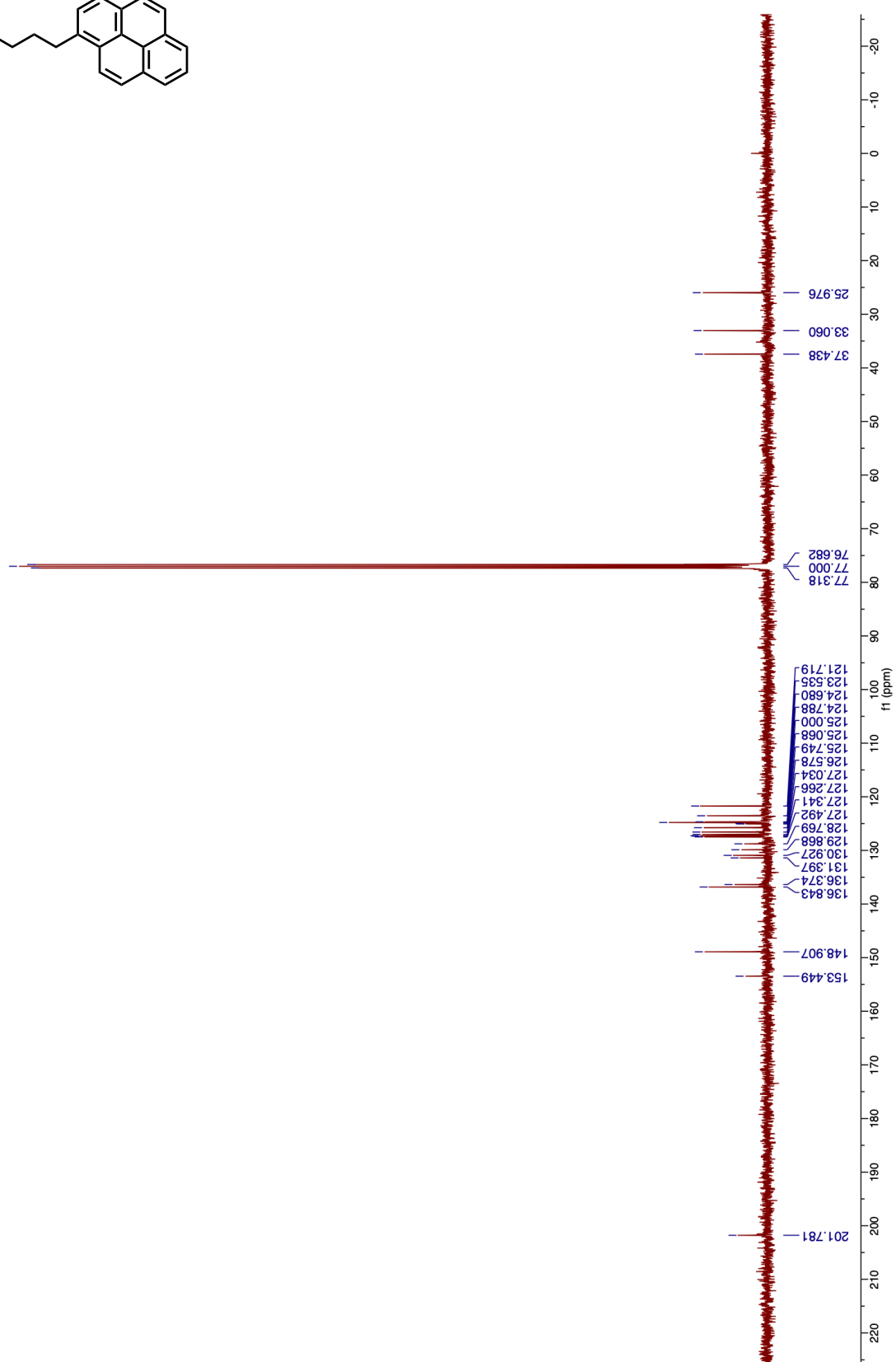
HN2903.f1 - single-pulse



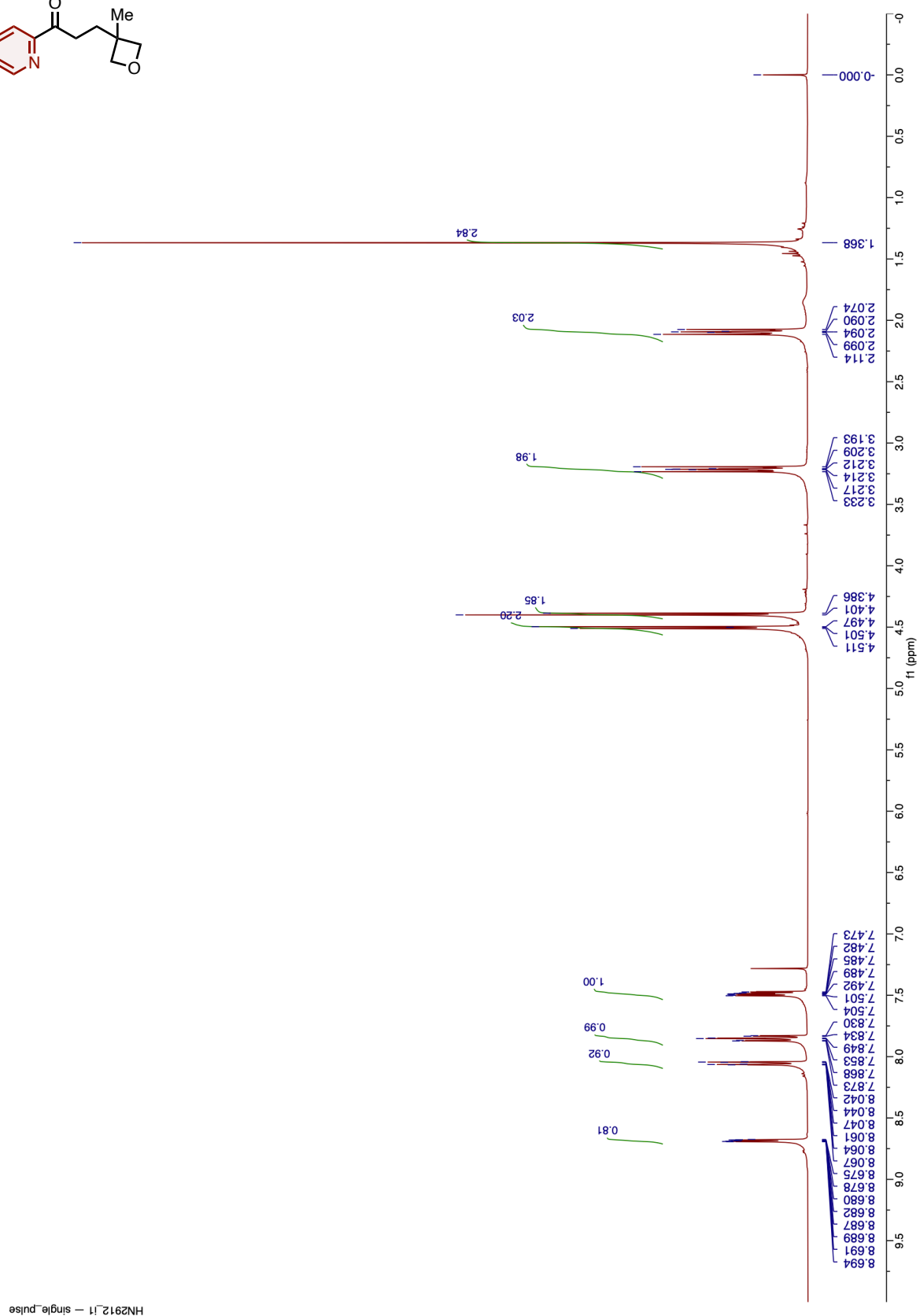
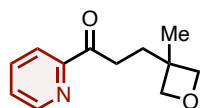
^{13}C NMR of **3kA** (101 MHz, CDCl_3)



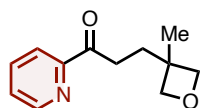
HN2903.f1 — single pulse decoupled gated NOE



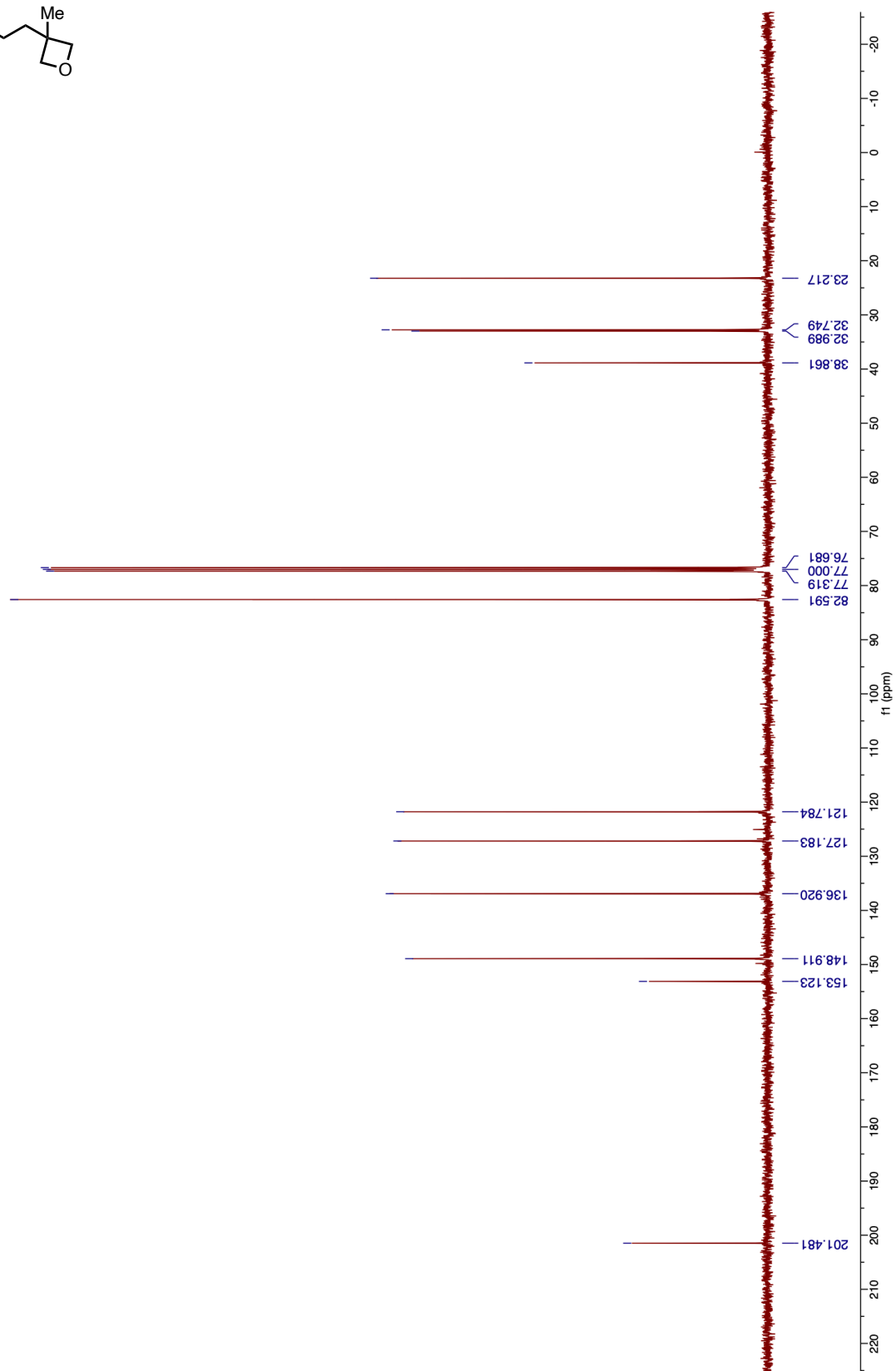
^1H NMR of **31A** (400 MHz, CDCl_3)



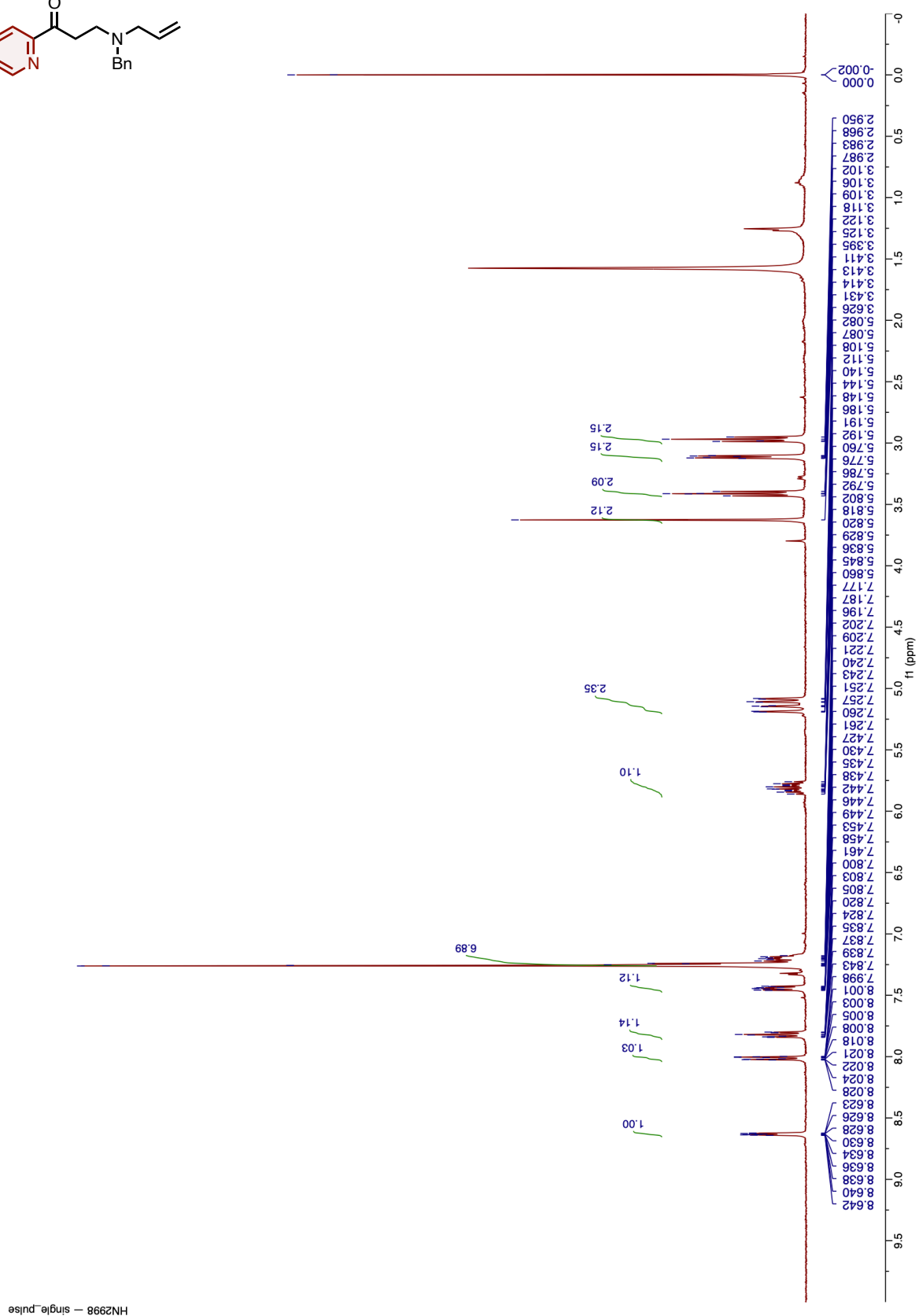
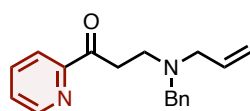
^{13}C NMR of **3IA** (101 MHz, CDCl_3)



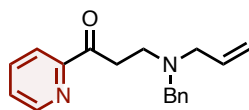
HN2912.f1 — single pulse decoupled gated NOE



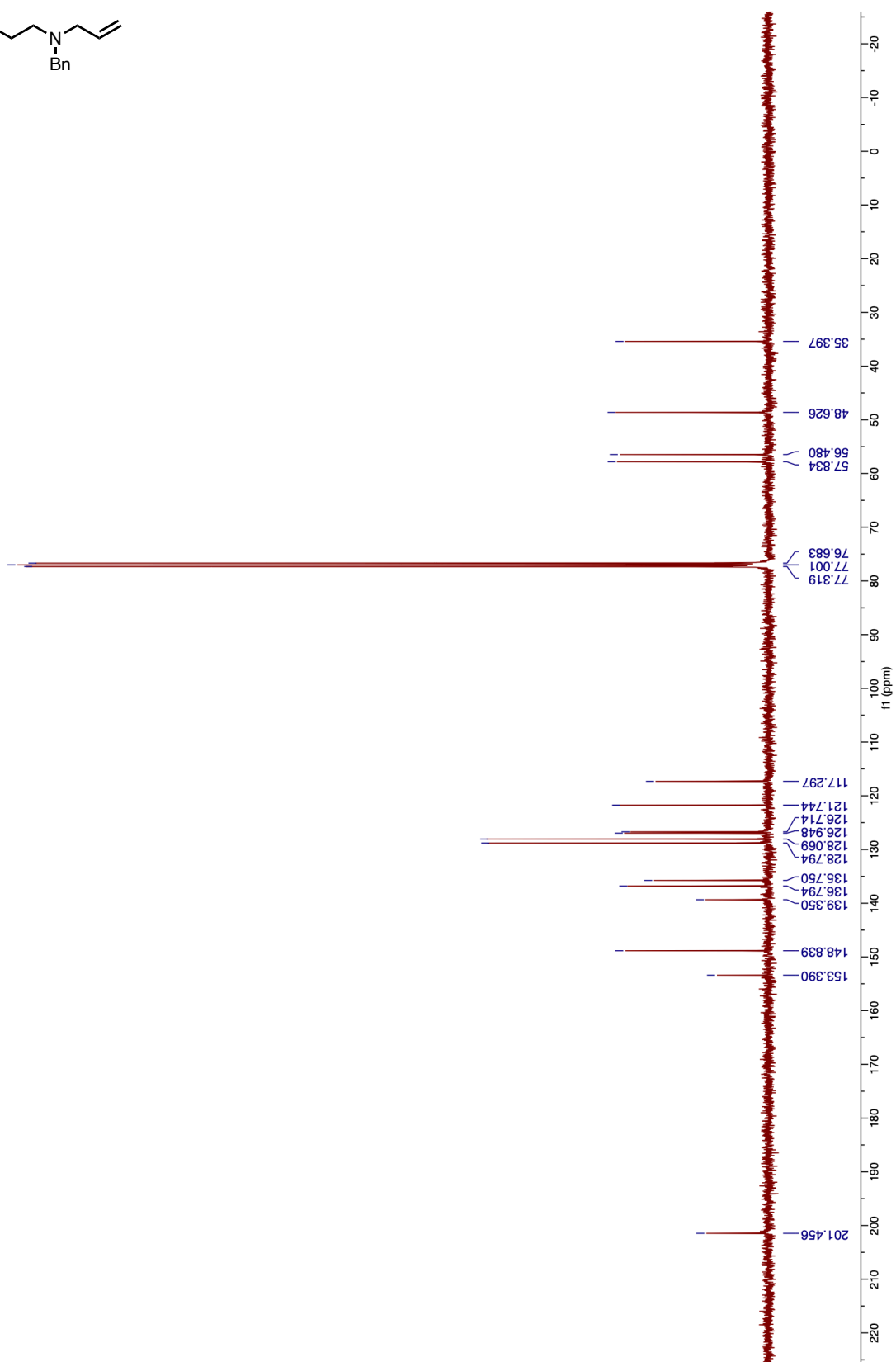
^1H NMR of **3mA** (400 MHz, CDCl_3)

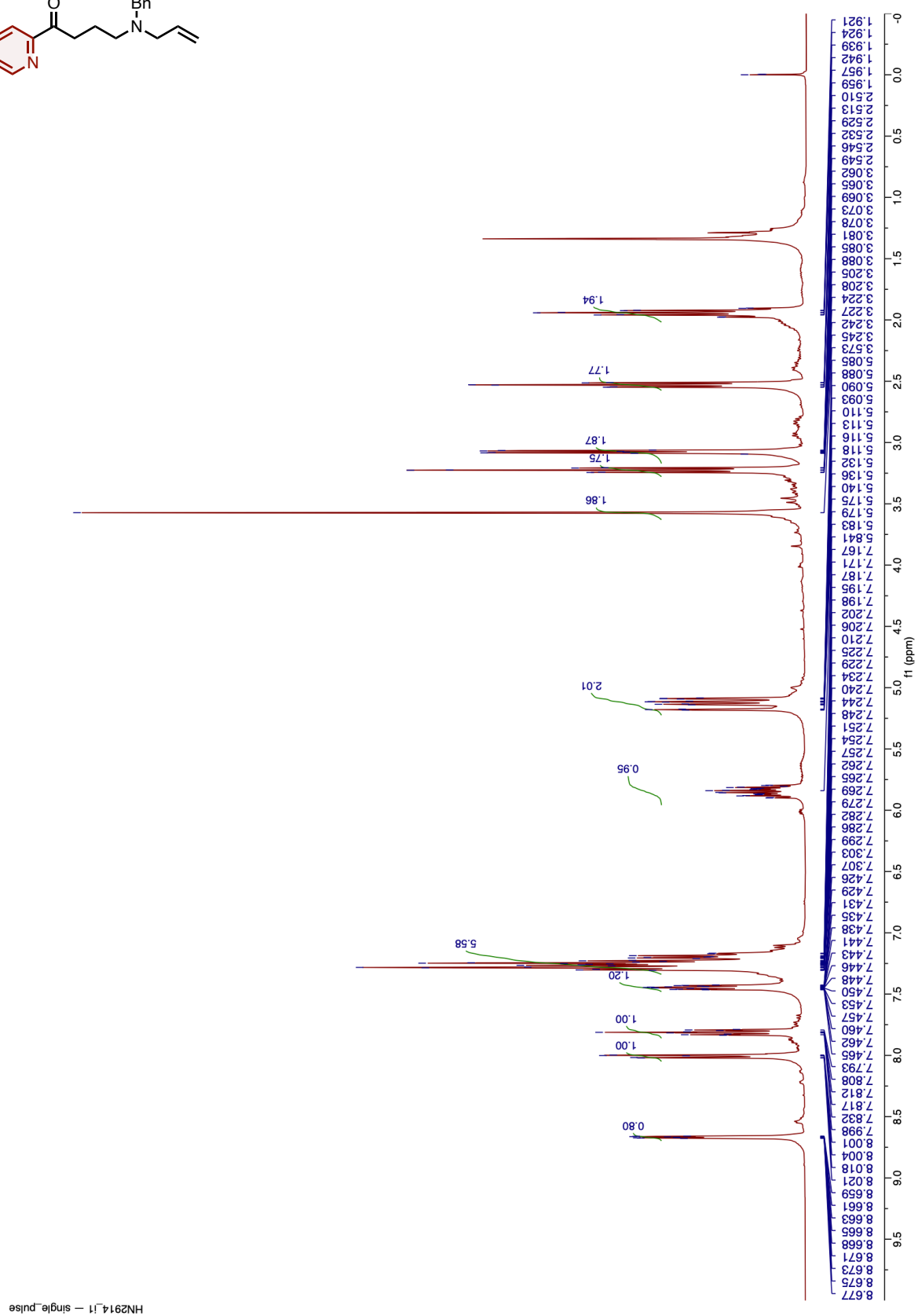
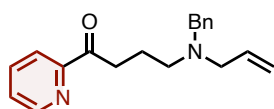


^{13}C NMR of **3mA** (101 MHz, CDCl_3)

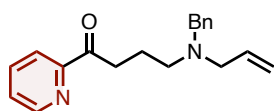


HN2998.f12 — single pulse decoupled gated NOE



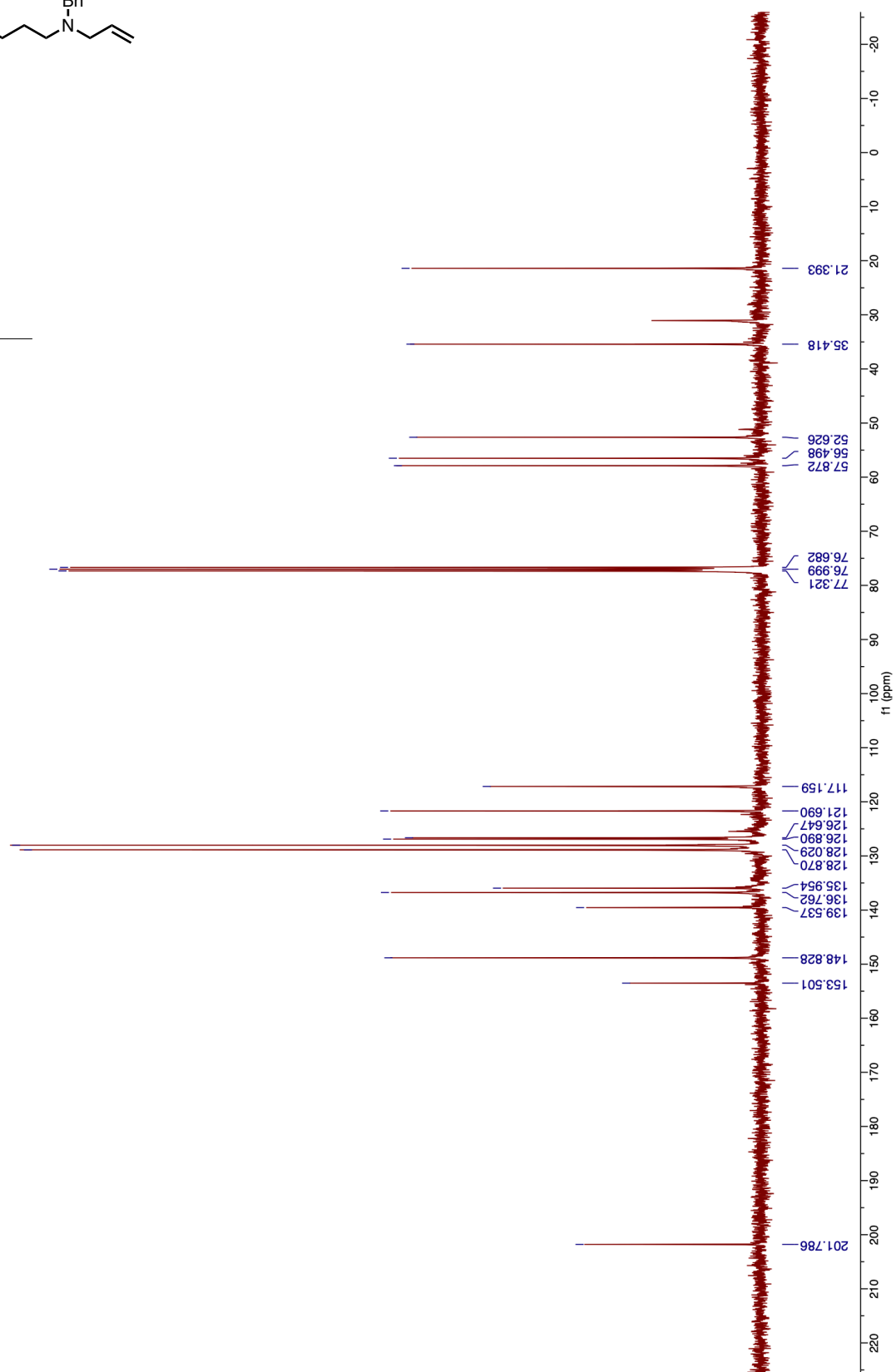
¹H NMR of **3nA** (400 MHz, CDCl₃)

^{13}C NMR of **3nA** (101 MHz, CDCl_3)

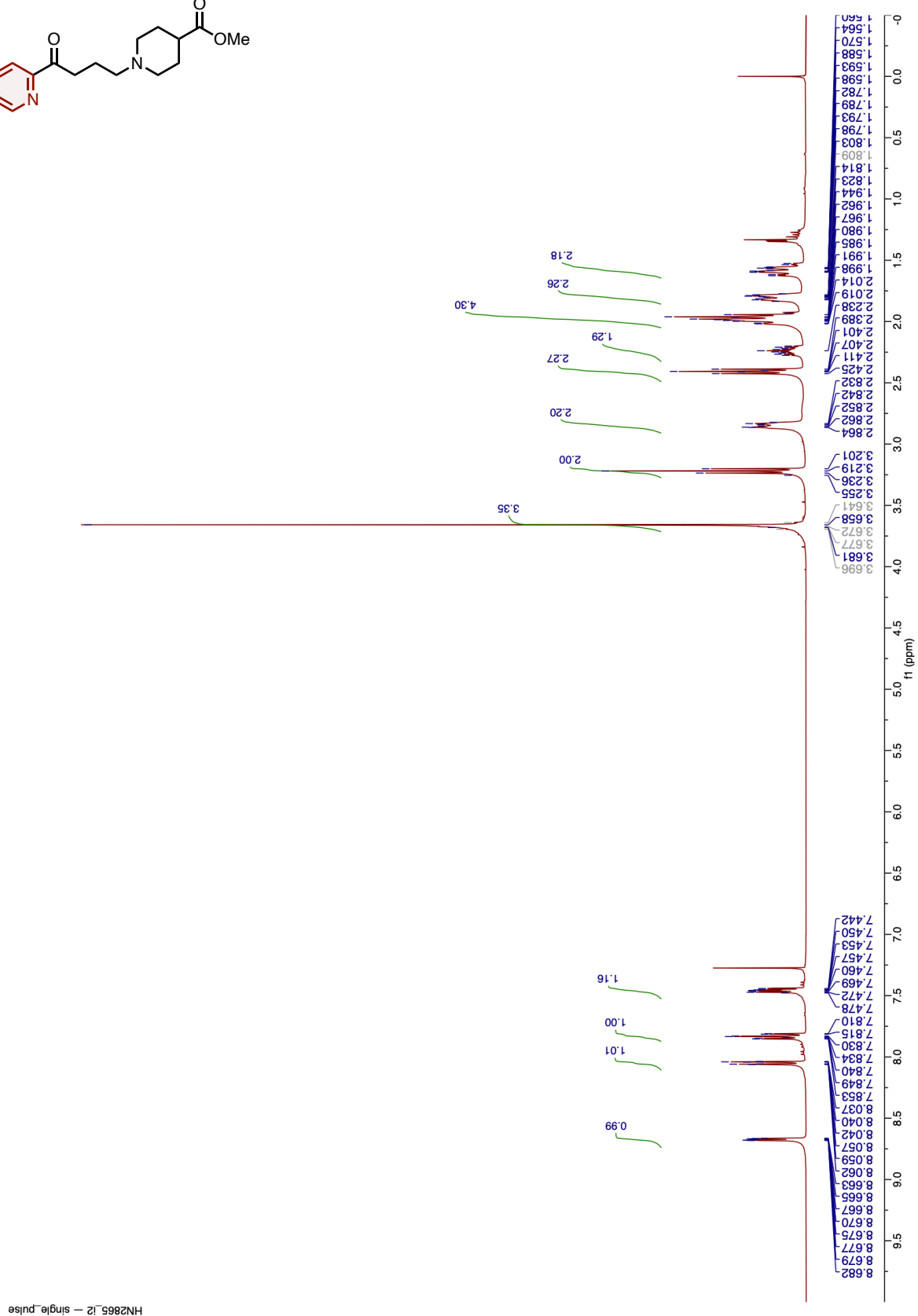
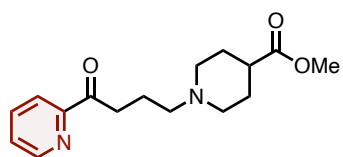


acetone—

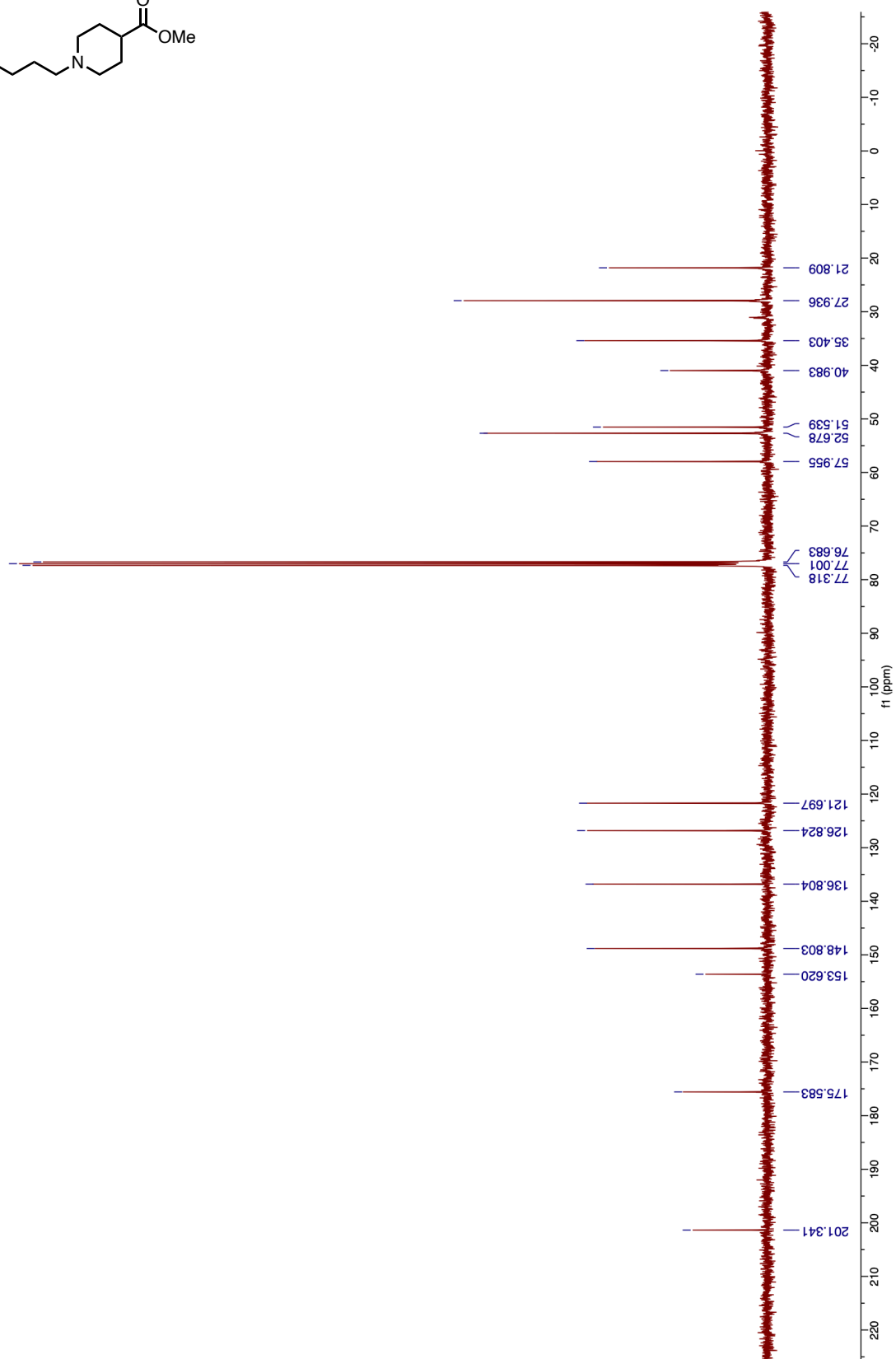
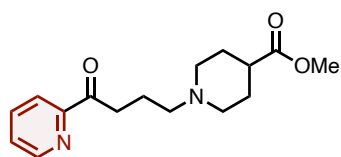
HN2914.f1 — single pulse decoupled gated NOE



^1H NMR of **3oA** (400 MHz, CDCl_3)

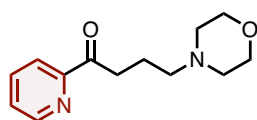


^{13}C NMR of **3oA** (101 MHz, CDCl_3)

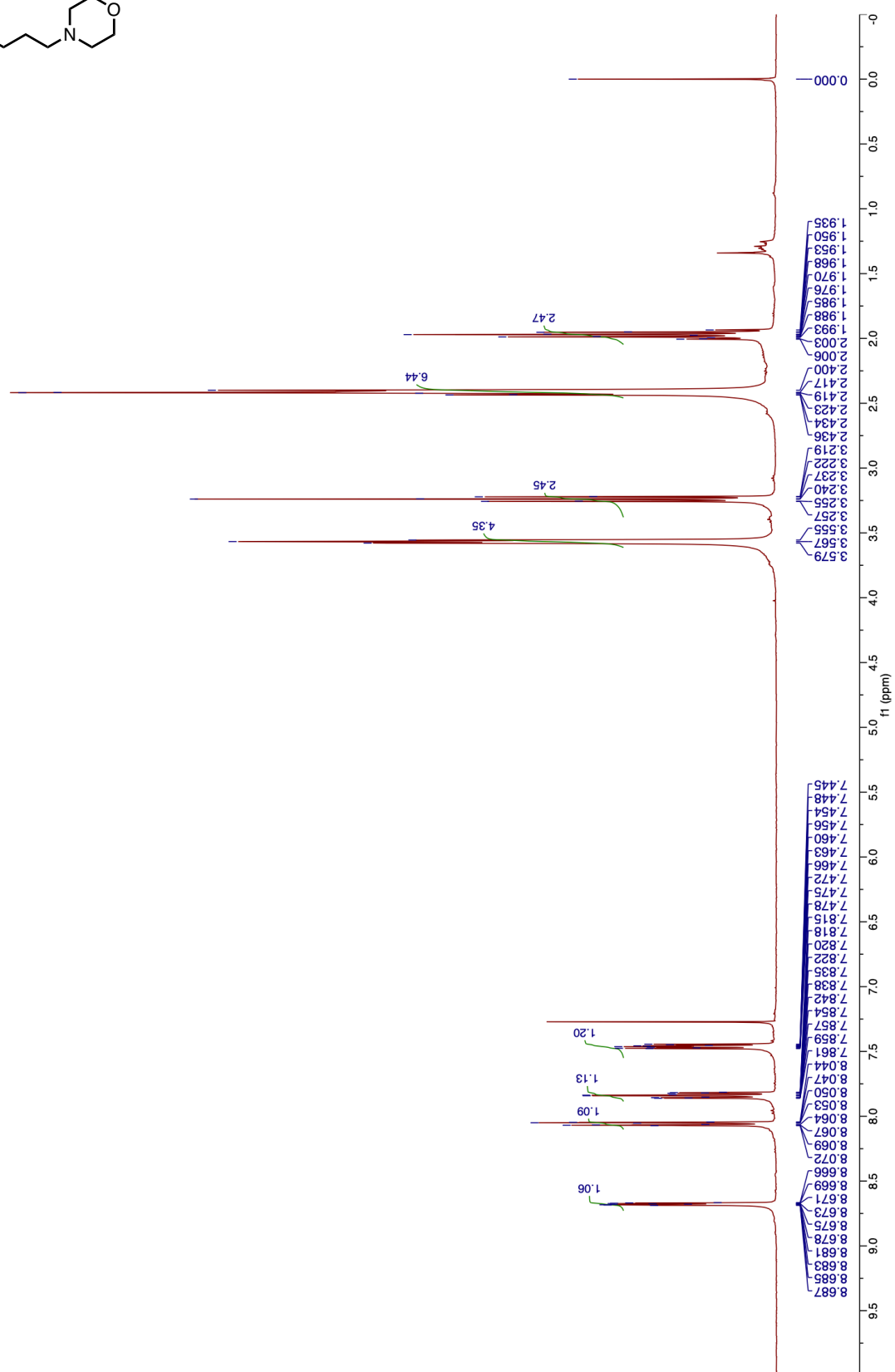


HN2865_12 — single pulse decoupled gated NOE

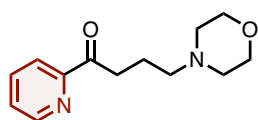
^1H NMR of **3pA** (400 MHz, CDCl_3)



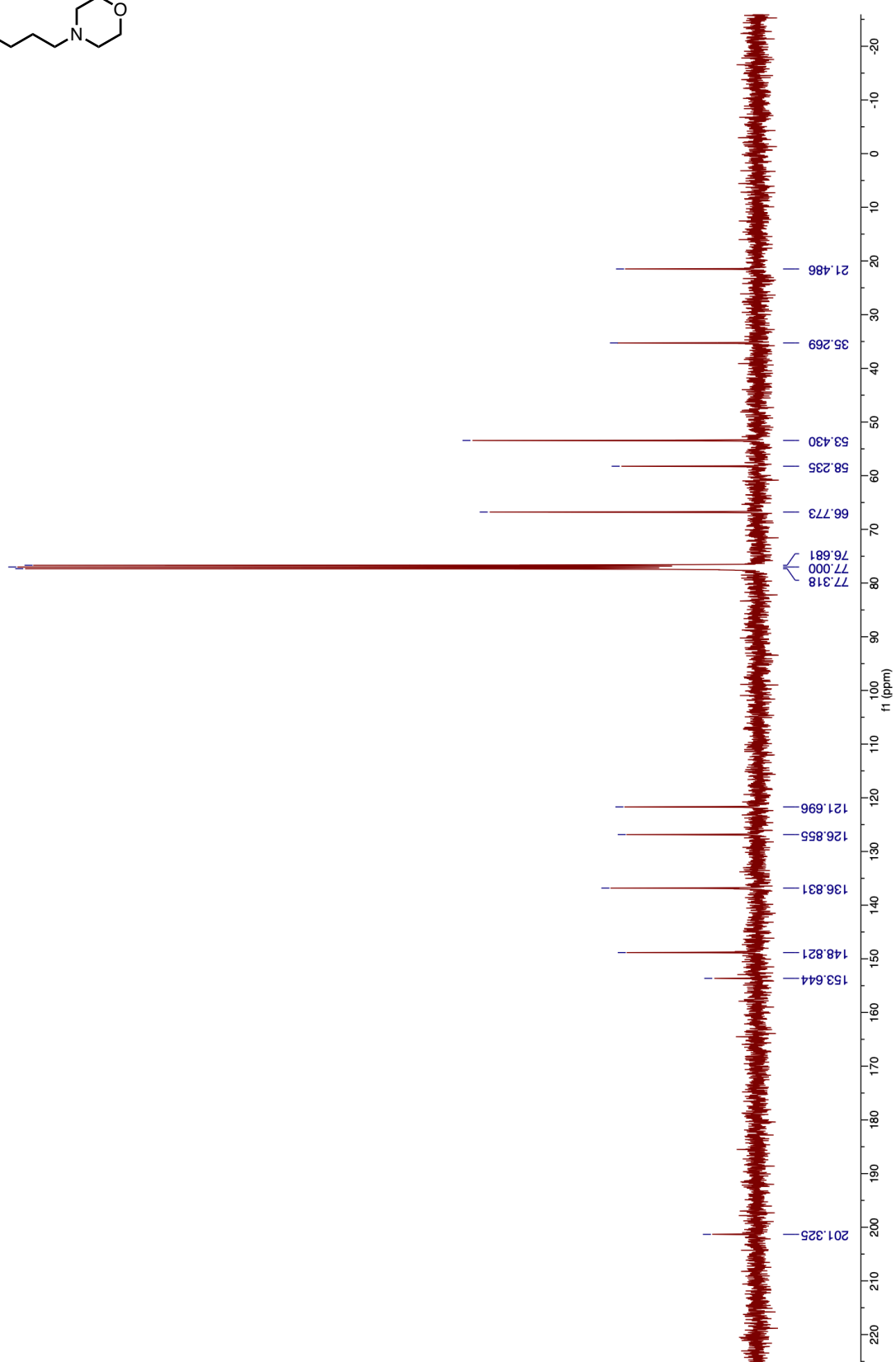
HN2891.f1 — single-pulse



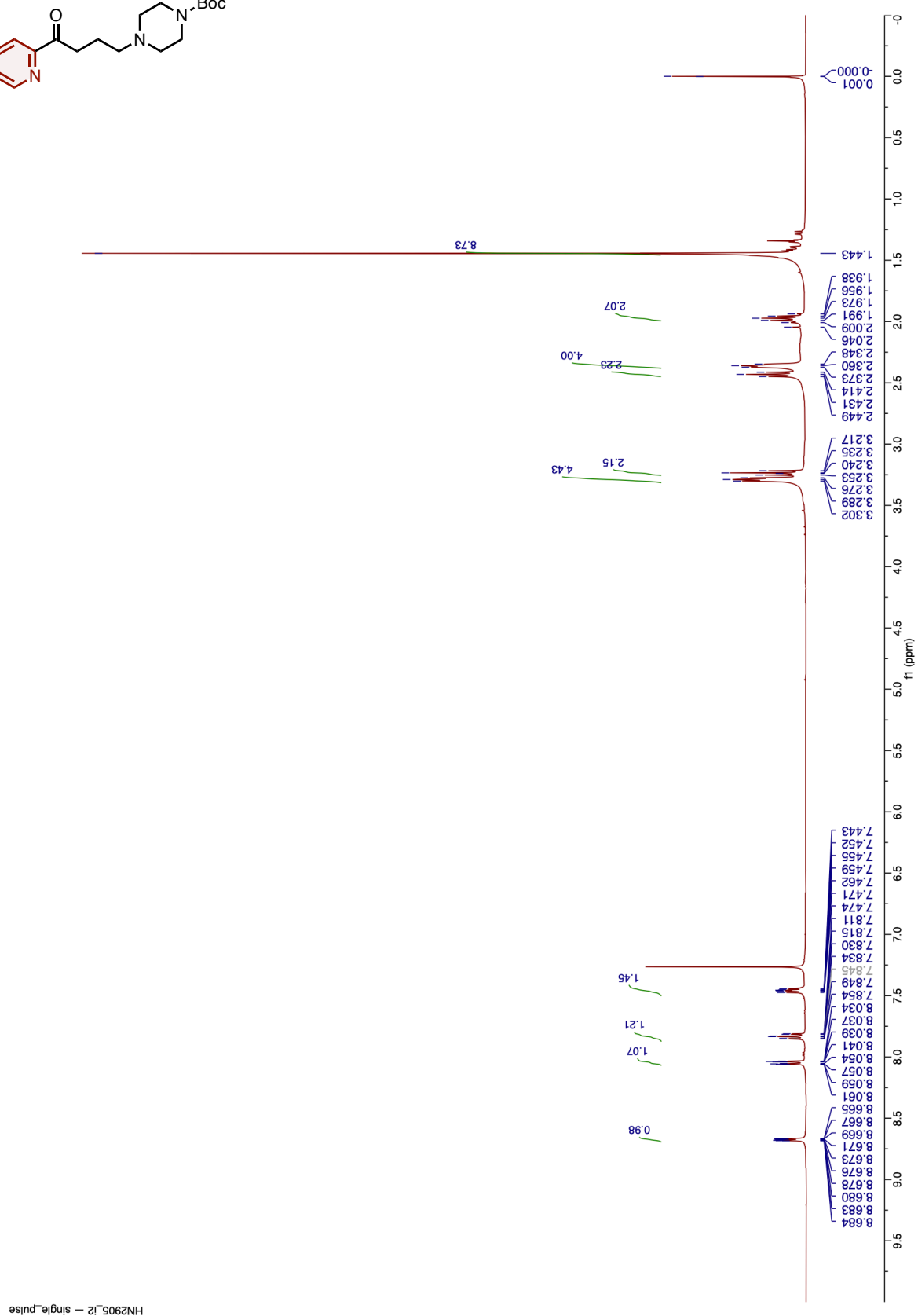
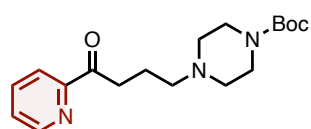
^{13}C NMR of **3pA** (101 MHz, CDCl_3)



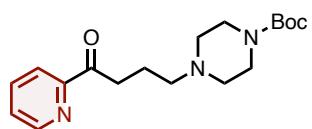
HN2891.f1 — single pulse decoupled gated NOE



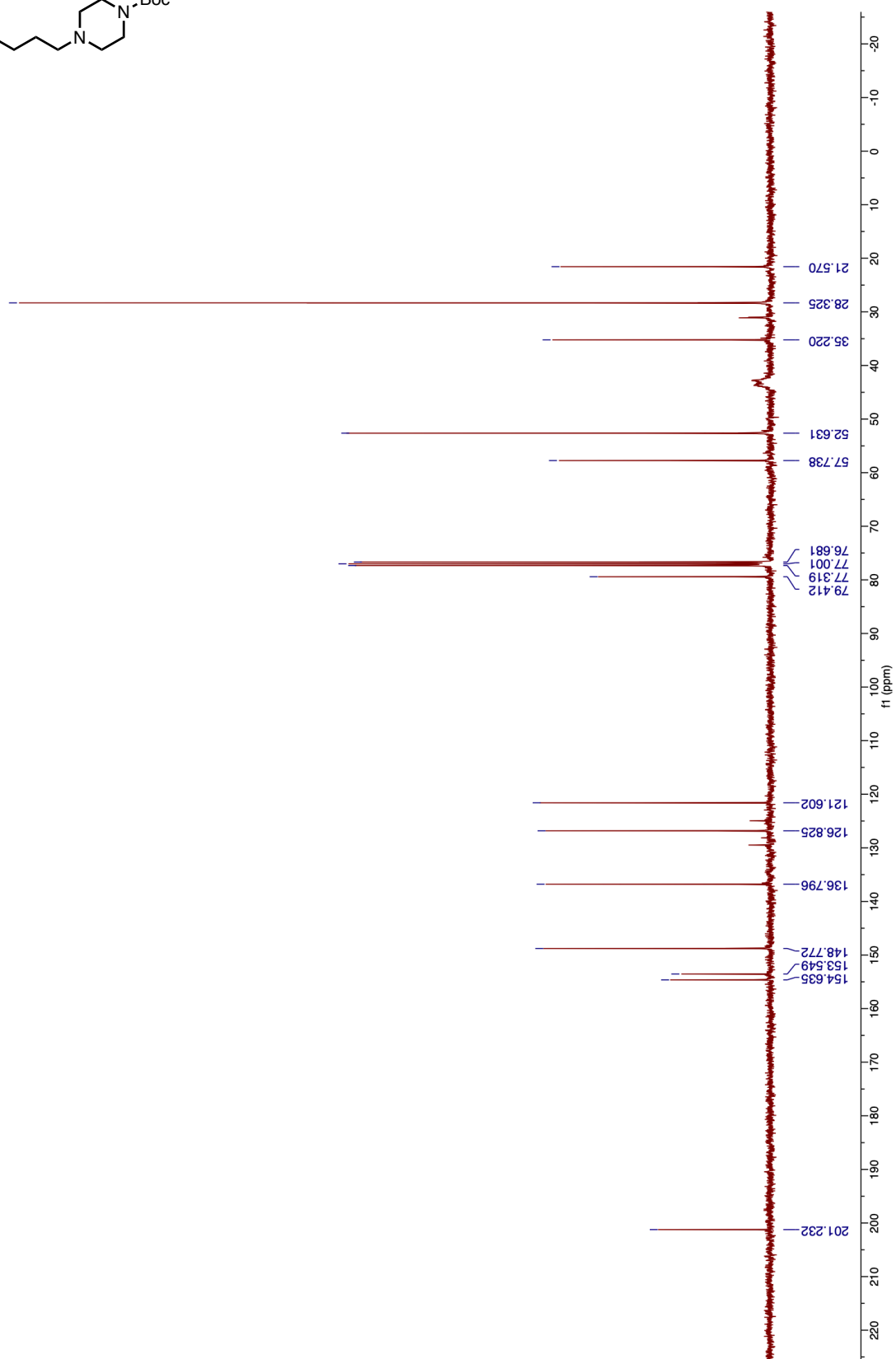
^1H NMR of **3qA** (400 MHz, CDCl_3)



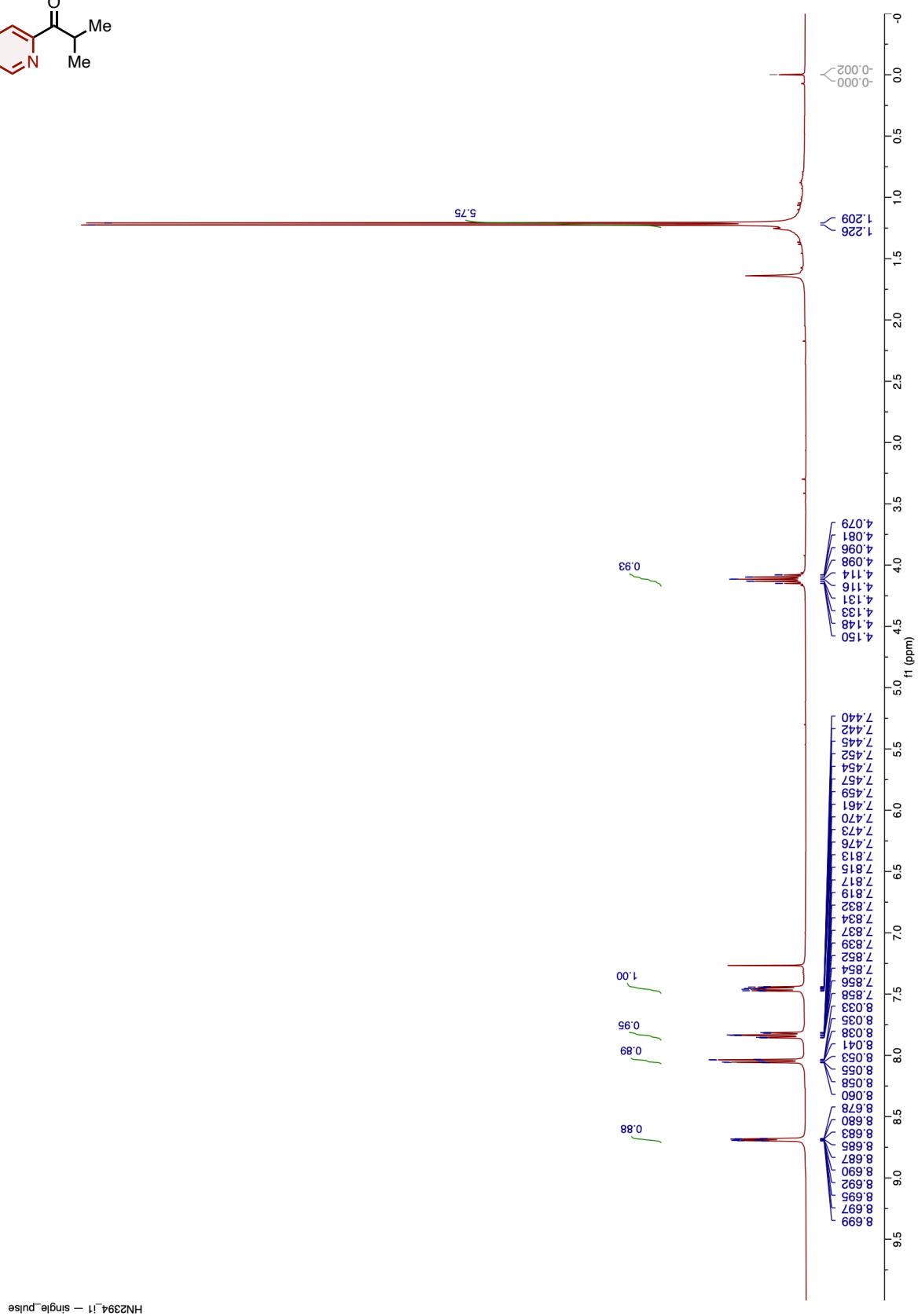
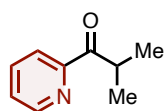
^{13}C NMR of **3qA** (101 MHz, CDCl_3)



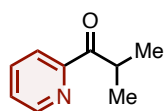
HN2905_12 — single pulse decoupled gated NOE



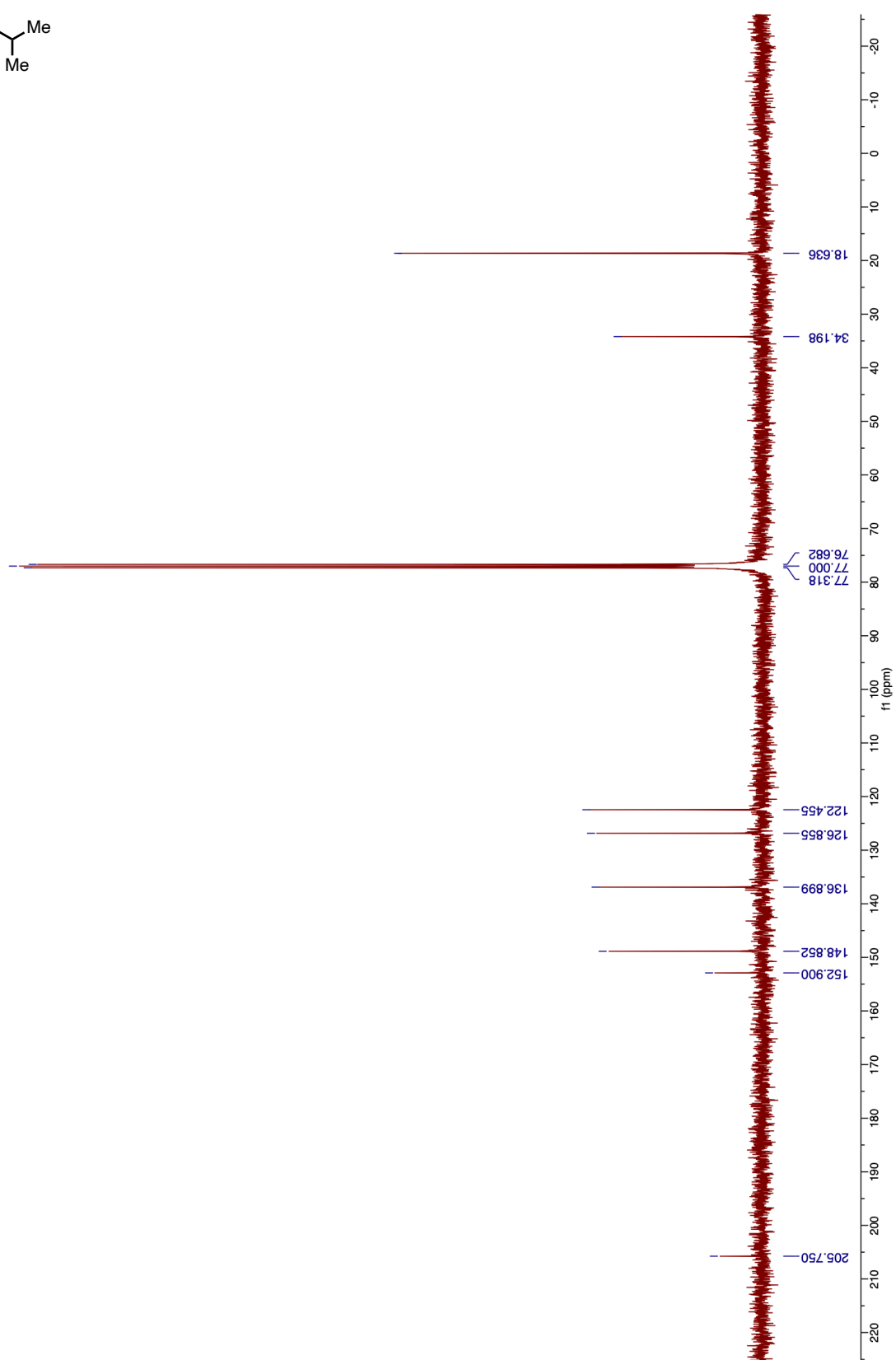
^1H NMR of **3rA** (400 MHz, CDCl_3)



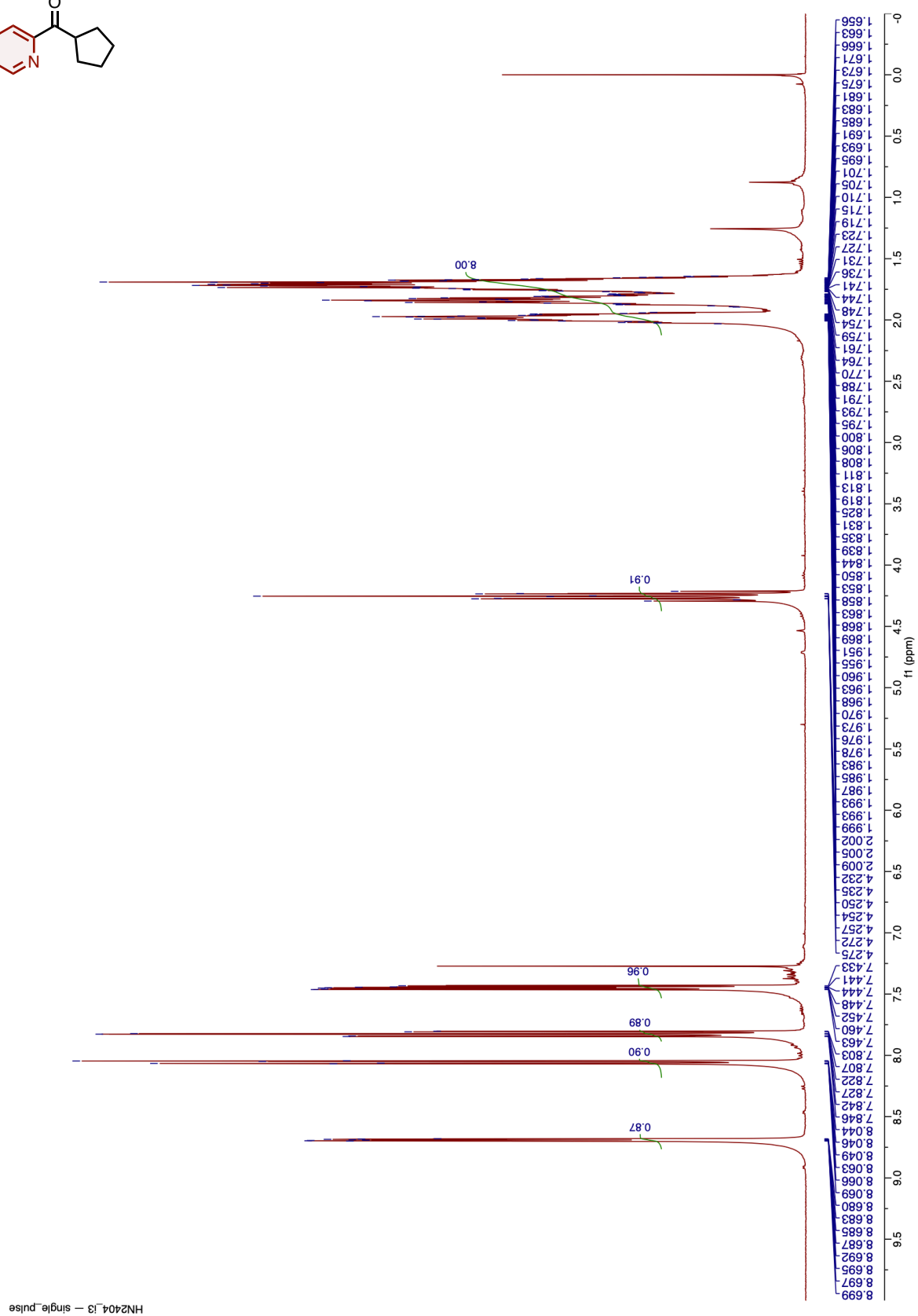
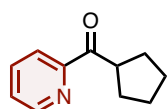
^{13}C NMR of **3rA** (101 MHz, CDCl_3)



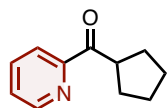
HN2394.f1 — single pulse decoupled gated NOE



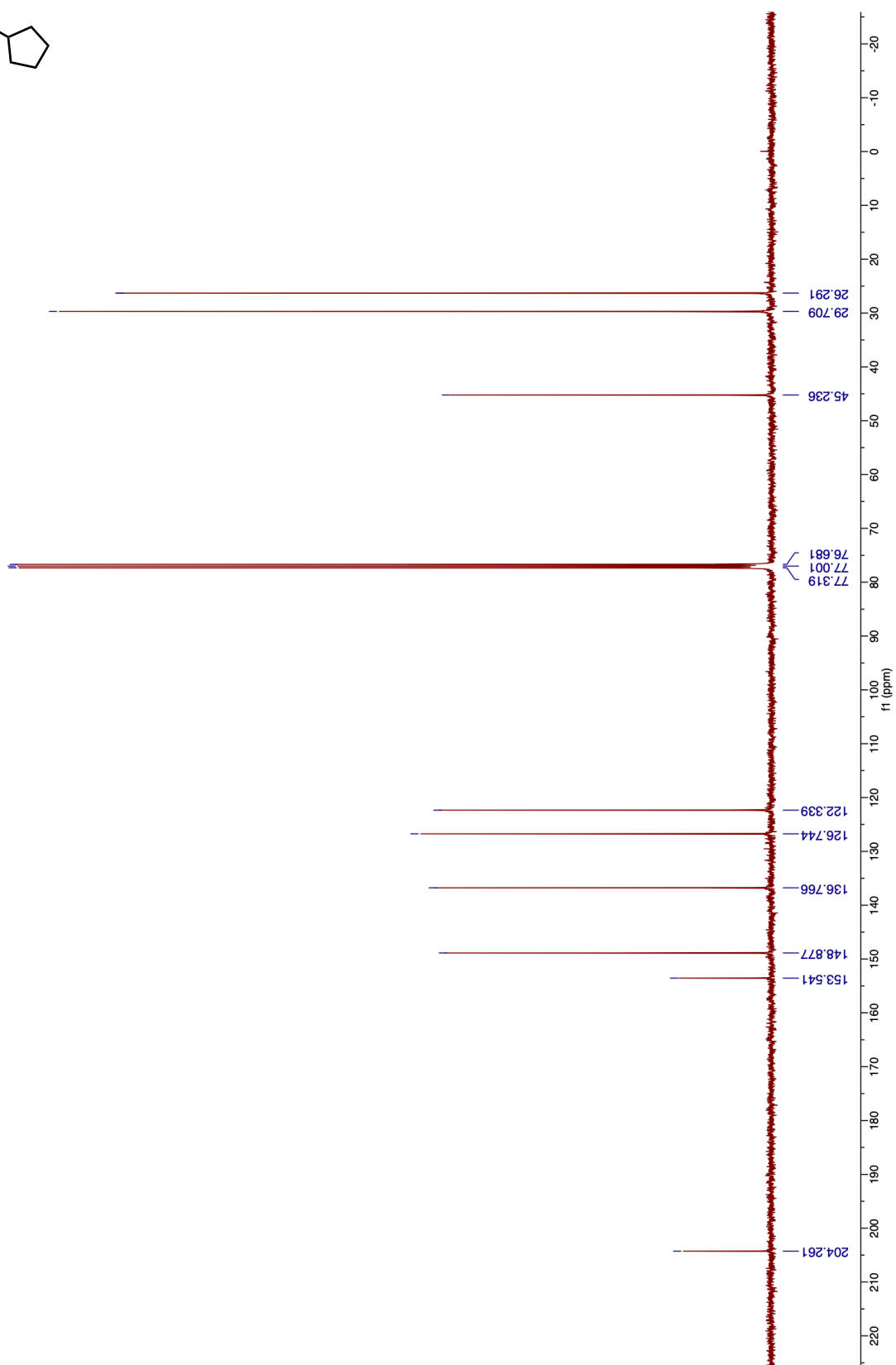
^1H NMR of **3sA** (400 MHz, CDCl_3)



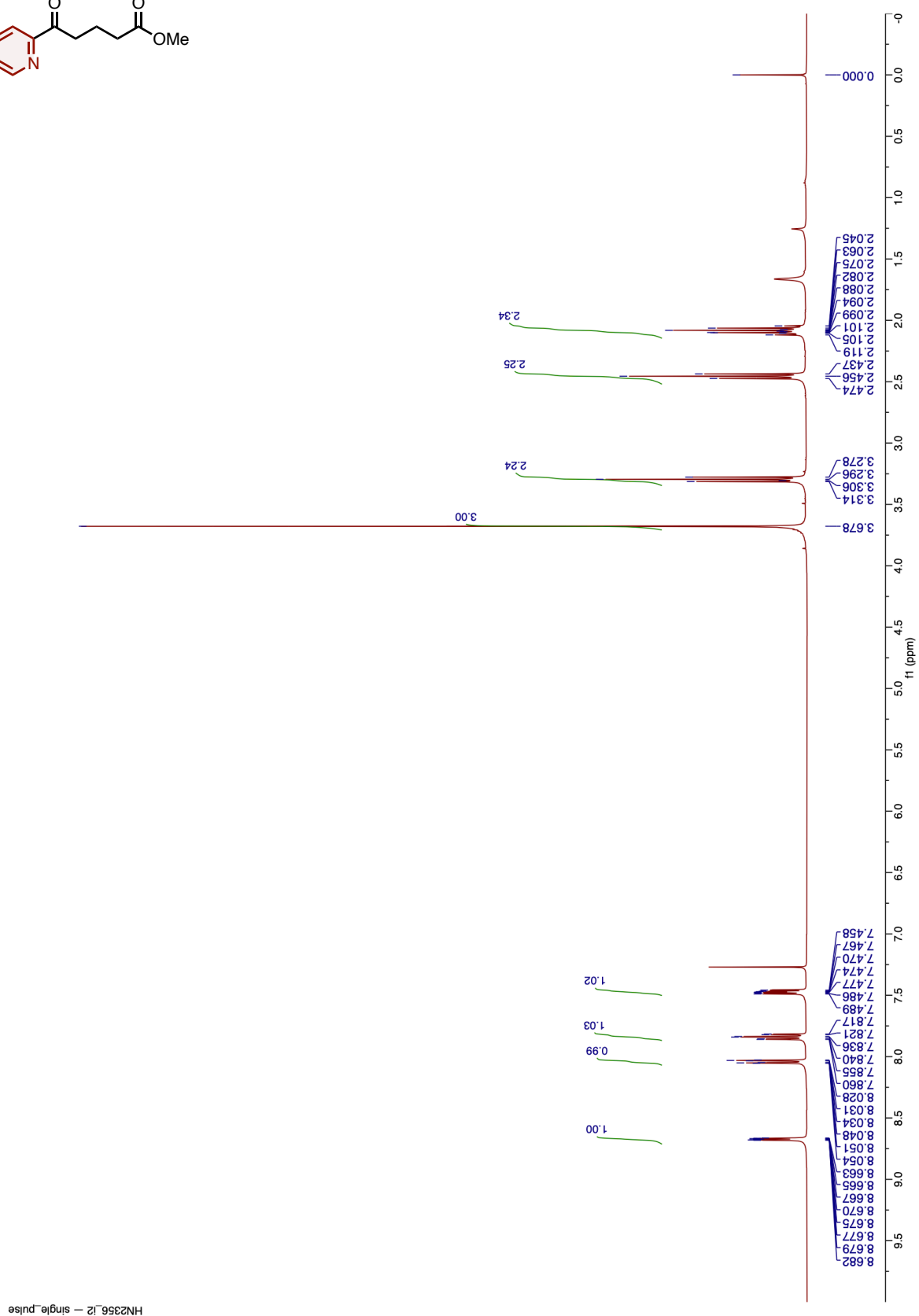
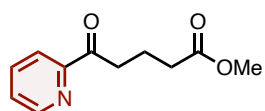
^{13}C NMR of **3sA** (101 MHz, CDCl_3)



RS_3sA(HN2404)_13C — single pulse decoupled gated NOE

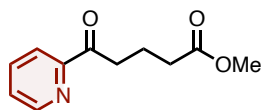


^1H NMR of **3tA** (400 MHz, CDCl_3)

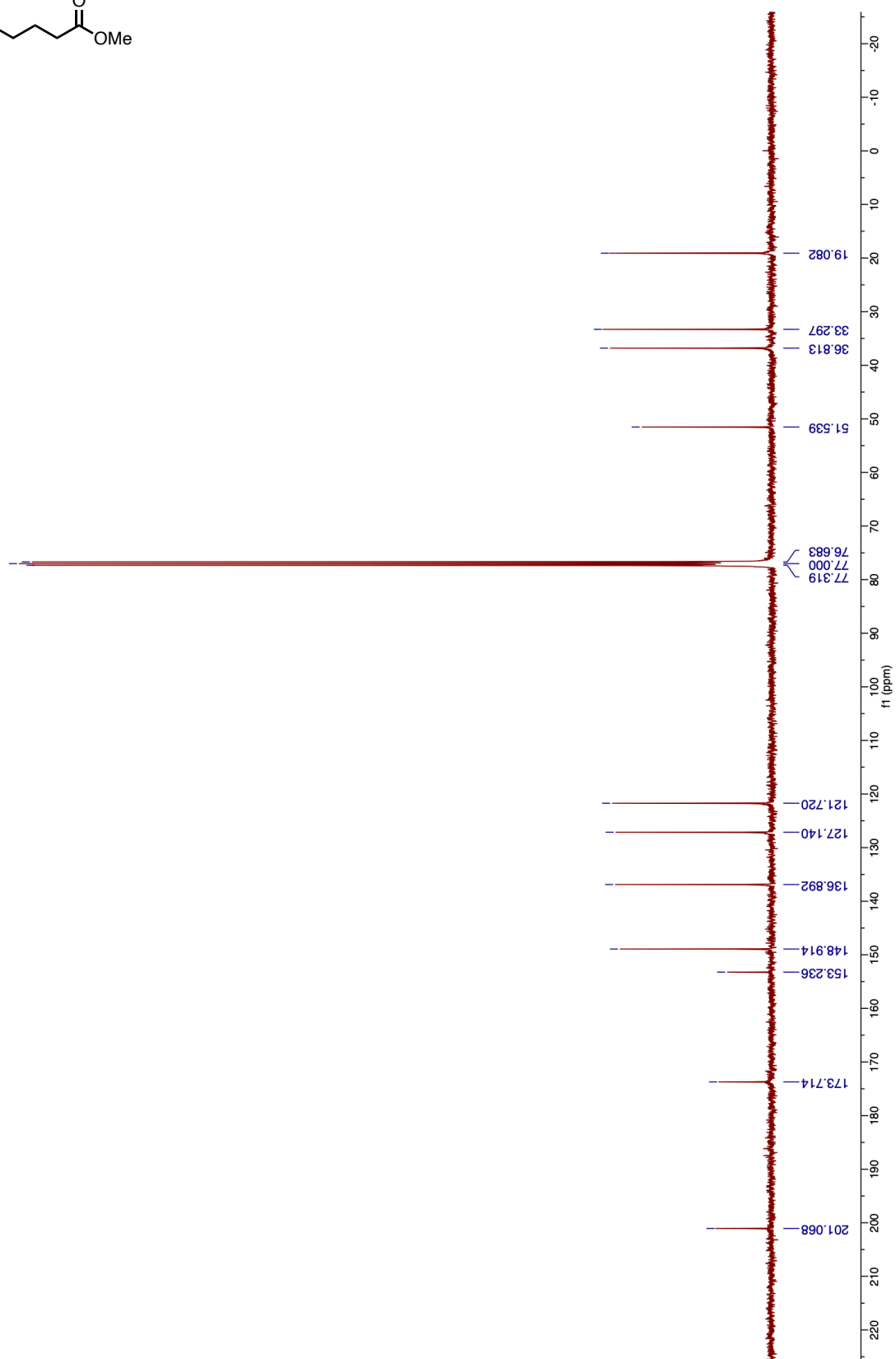


HN2356.f2 — single-pulse

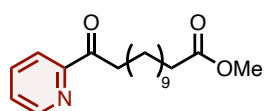
^{13}C NMR of **3tA** (101 MHz, CDCl_3)



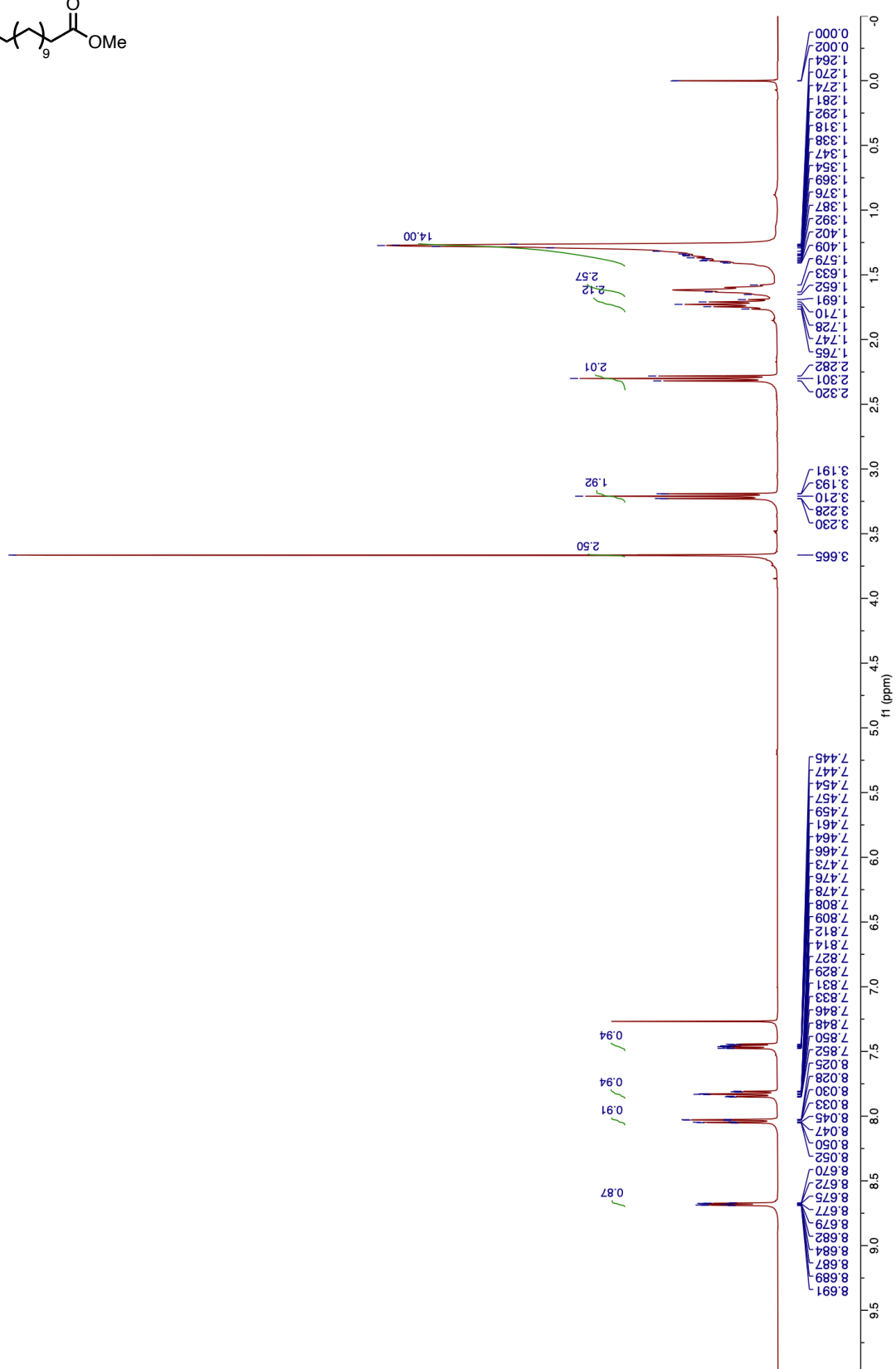
HN2356.f1 — single pulse decoupled gated NOE



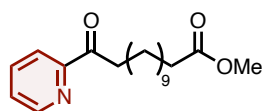
^1H NMR of **3uA** (400 MHz, CDCl_3)



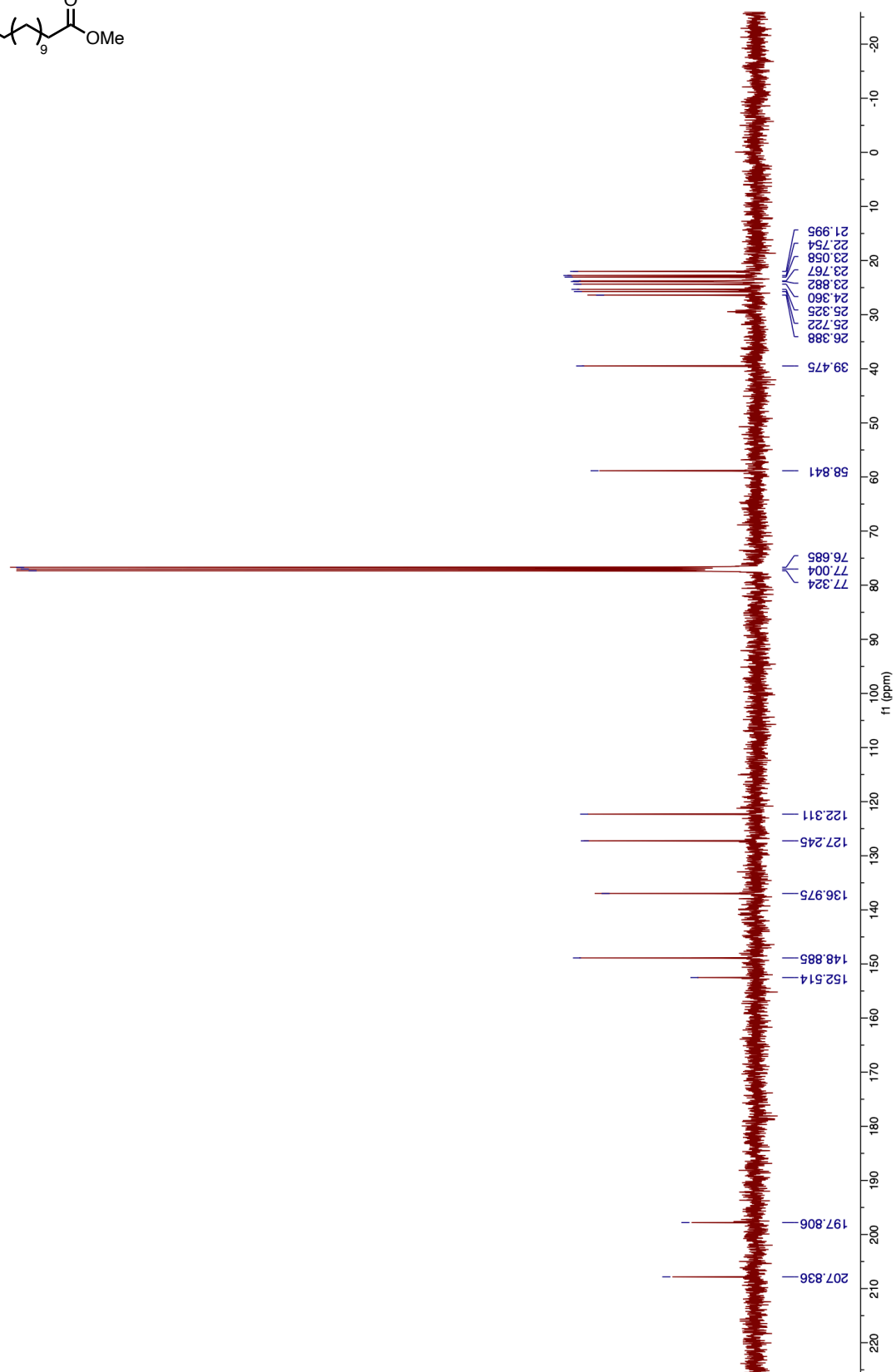
HN2417_12 — single-pulse



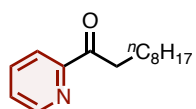
^{13}C NMR of **3uA** (101 MHz, CDCl_3)



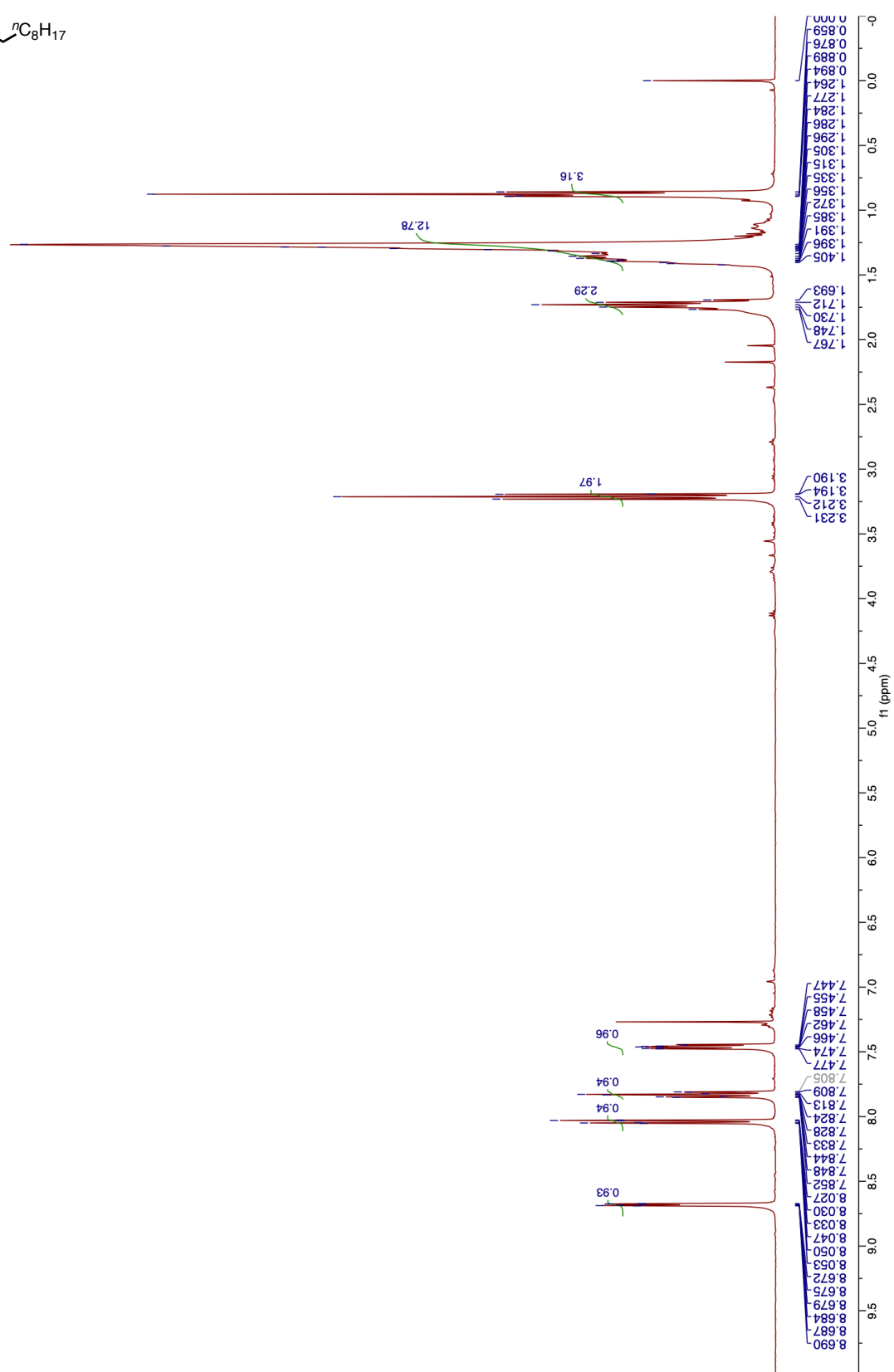
HN2417 — single pulse decoupled gated NOE



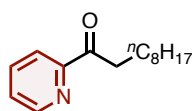
^1H NMR of **3vA** (400 MHz, CDCl_3)



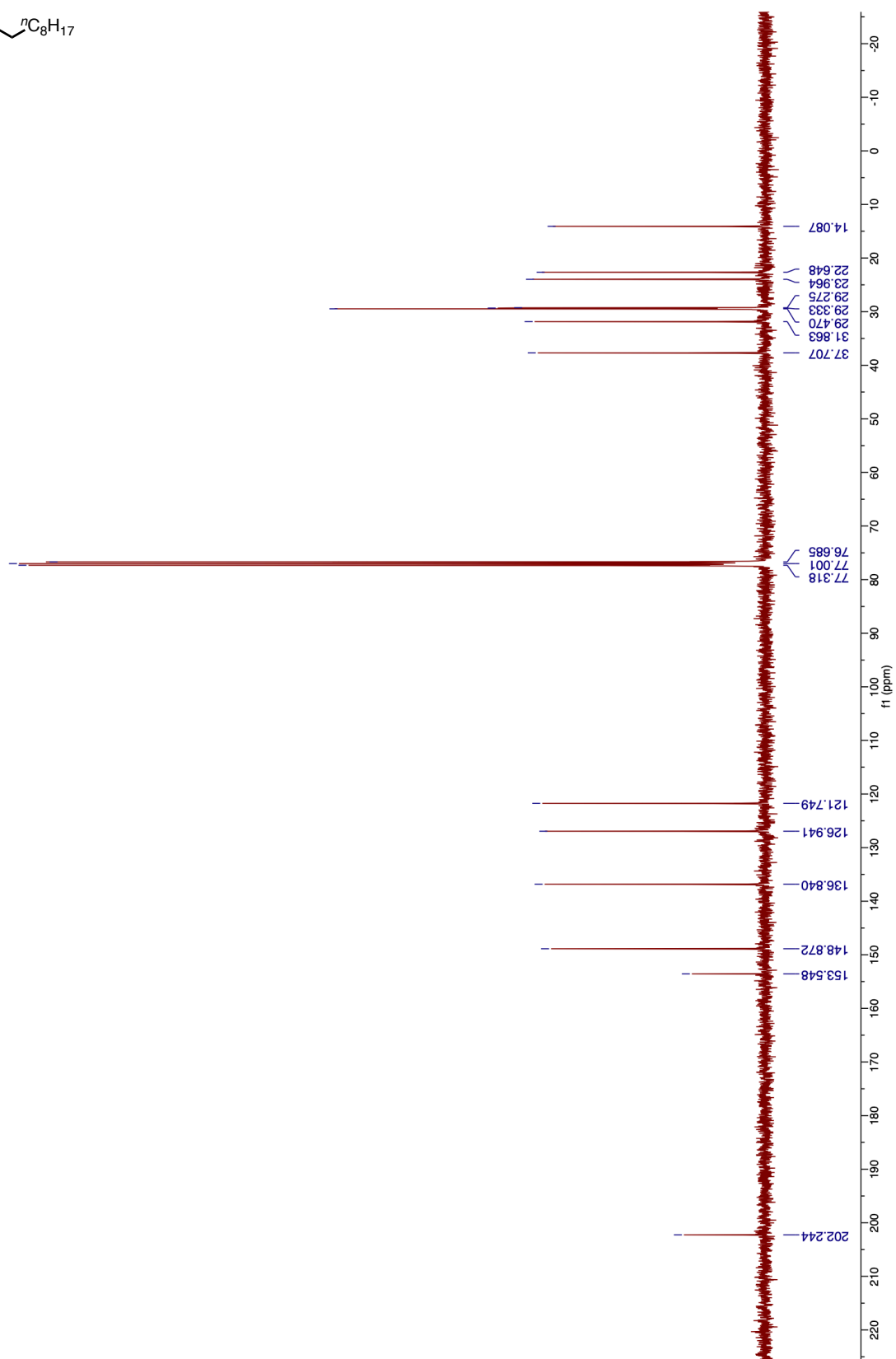
HN2413.f1 - single-pulse



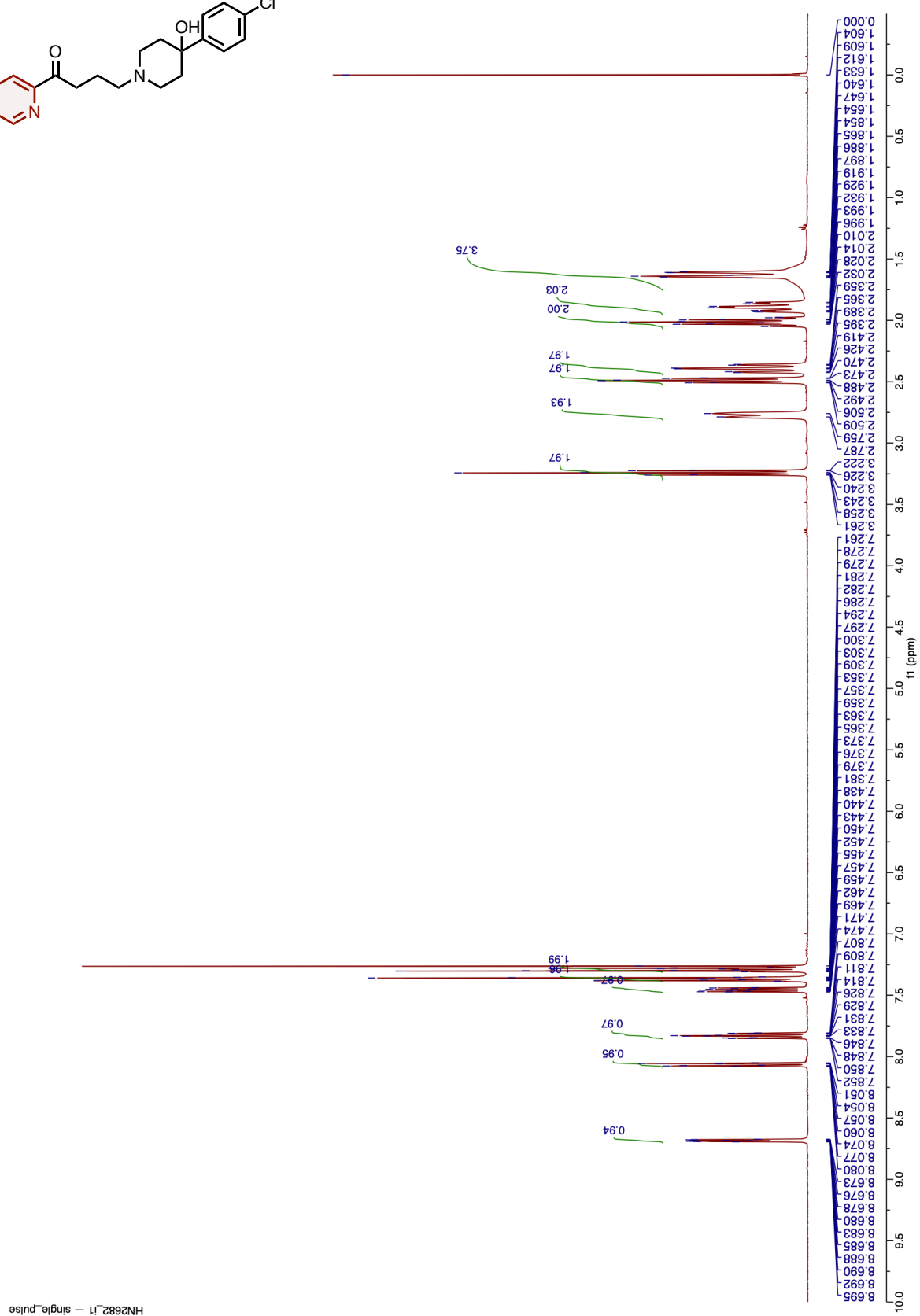
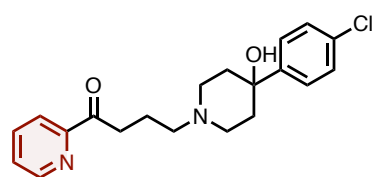
^{13}C NMR of **3vA** (101 MHz, CDCl_3)



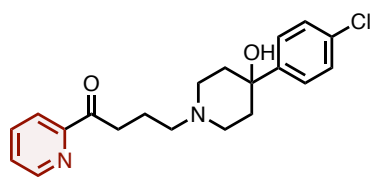
HN2264.f1 — single pulse decoupled gated NOE



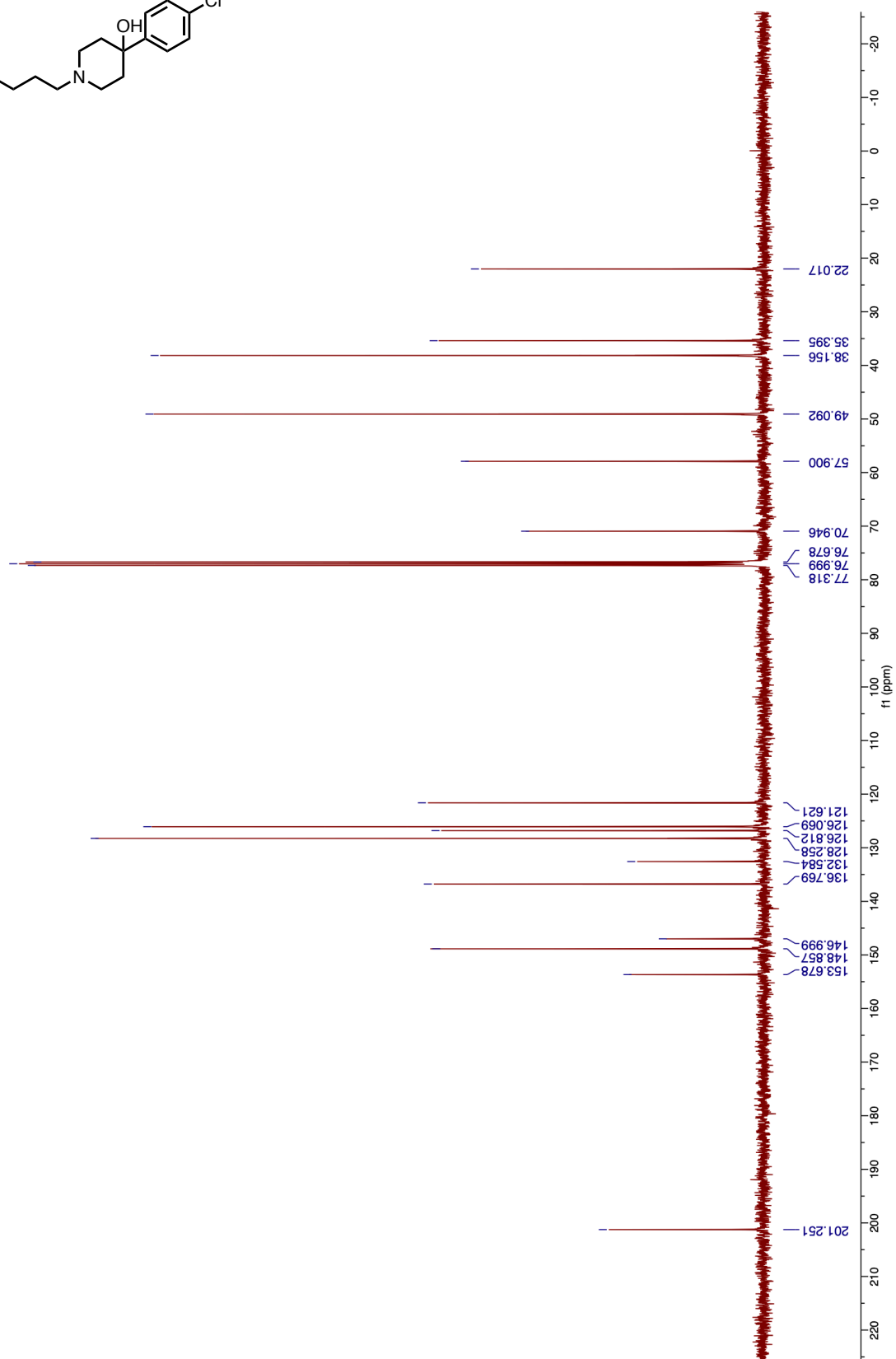
^1H NMR of **3xA** (400 MHz, CDCl_3)



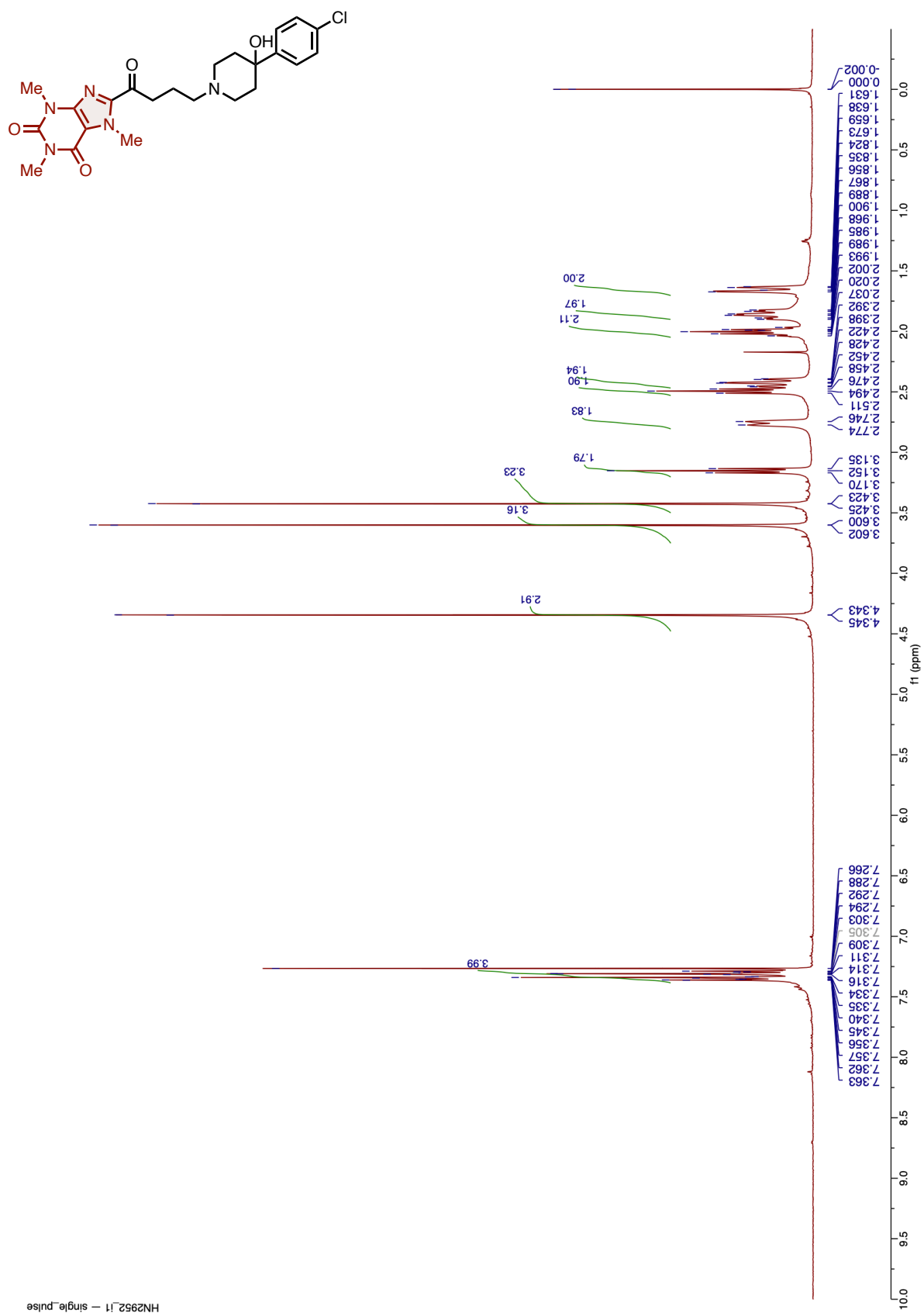
^{13}C NMR of **3xA** (101 MHz, CDCl_3)



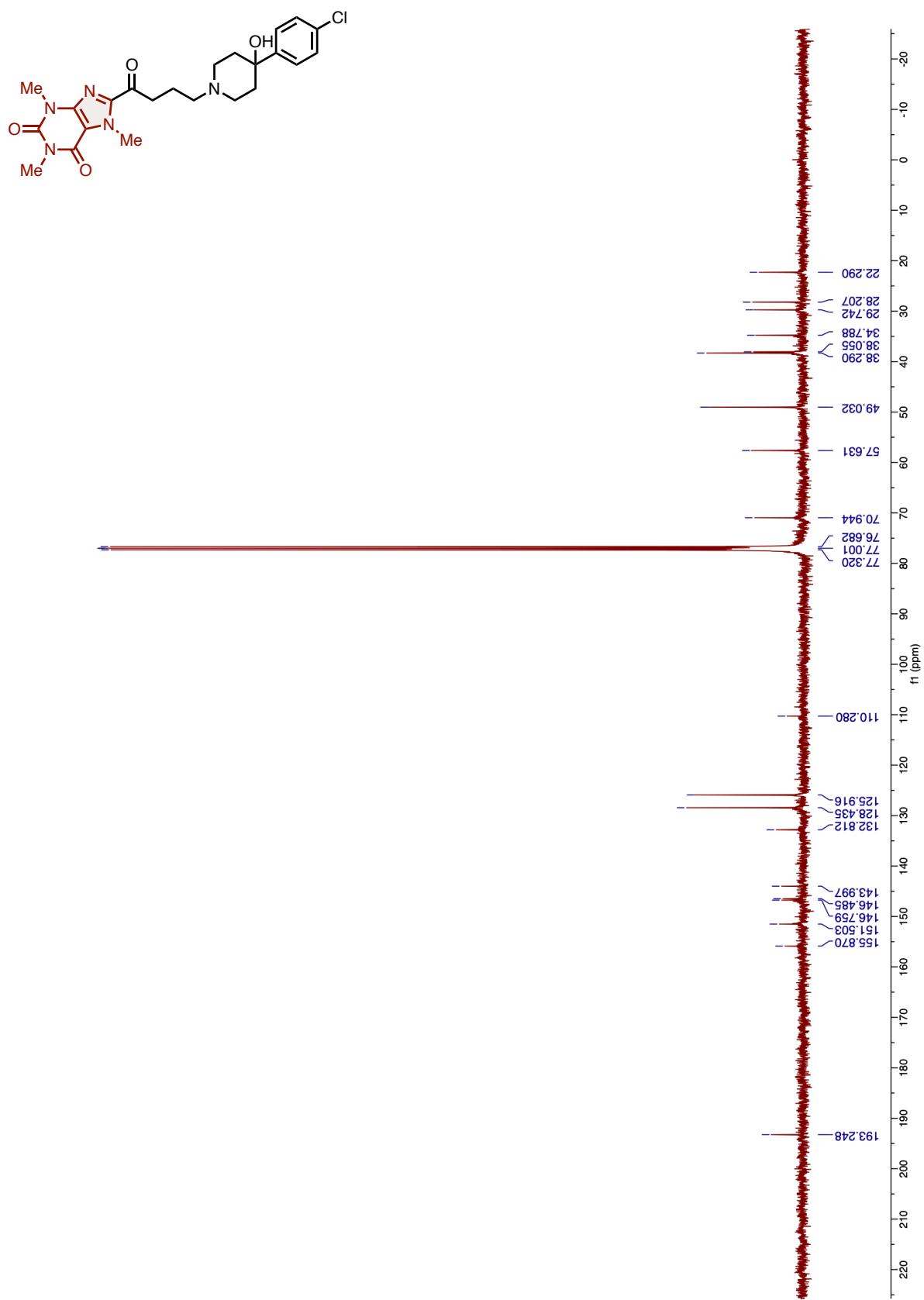
HN2980 — single pulse decoupled gated NOE



^1H NMR of **3xAA** (400 MHz, CDCl_3)

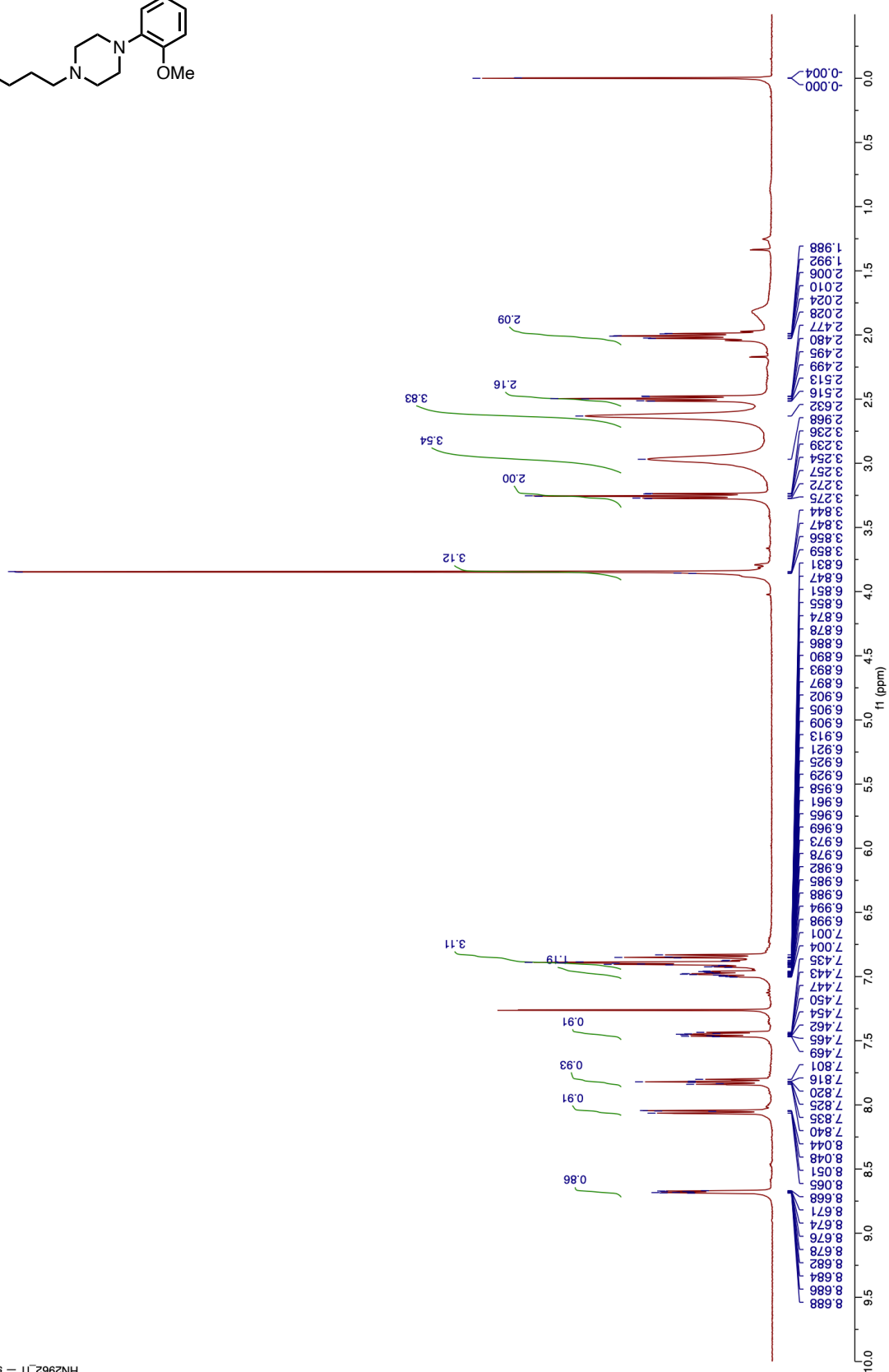
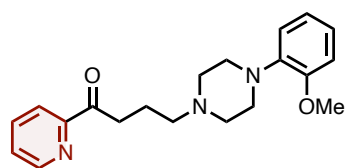


^{13}C NMR of **3xAA** (101 MHz, CDCl_3)



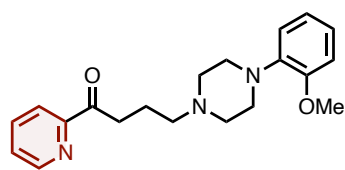
HN2952.f1 — single pulse decoupled gated NOE

^1H NMR of **3yA** (400 MHz, CDCl_3)

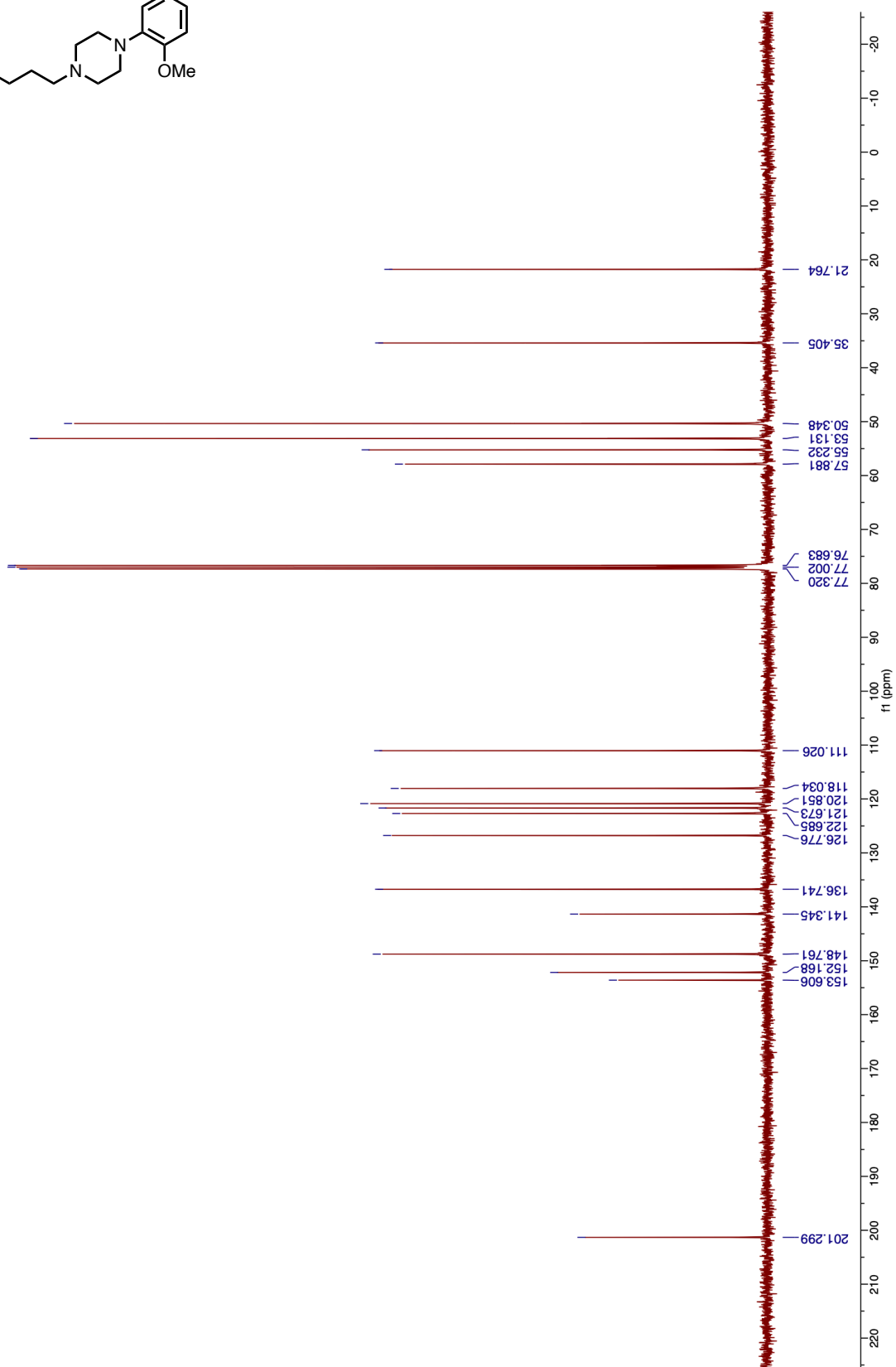


HN2962.f1 - single-pulse

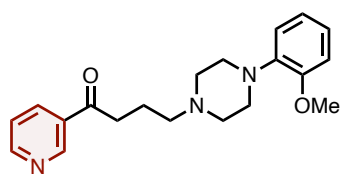
^{13}C NMR of **3yA** (101 MHz, CDCl_3)



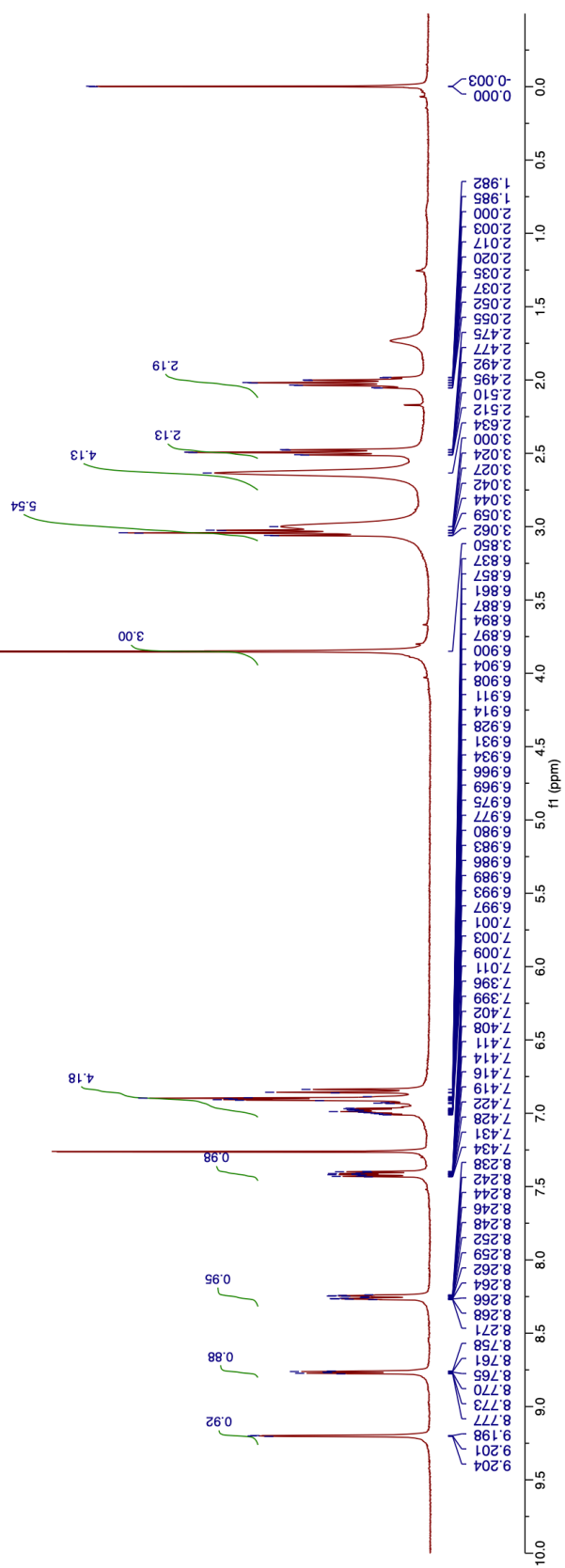
HN2962 — single pulse decoupled gated NOE



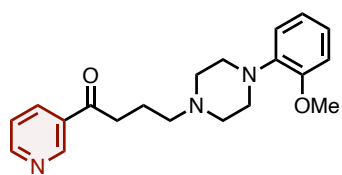
^1H NMR of **3yB** (400 MHz, CDCl_3)



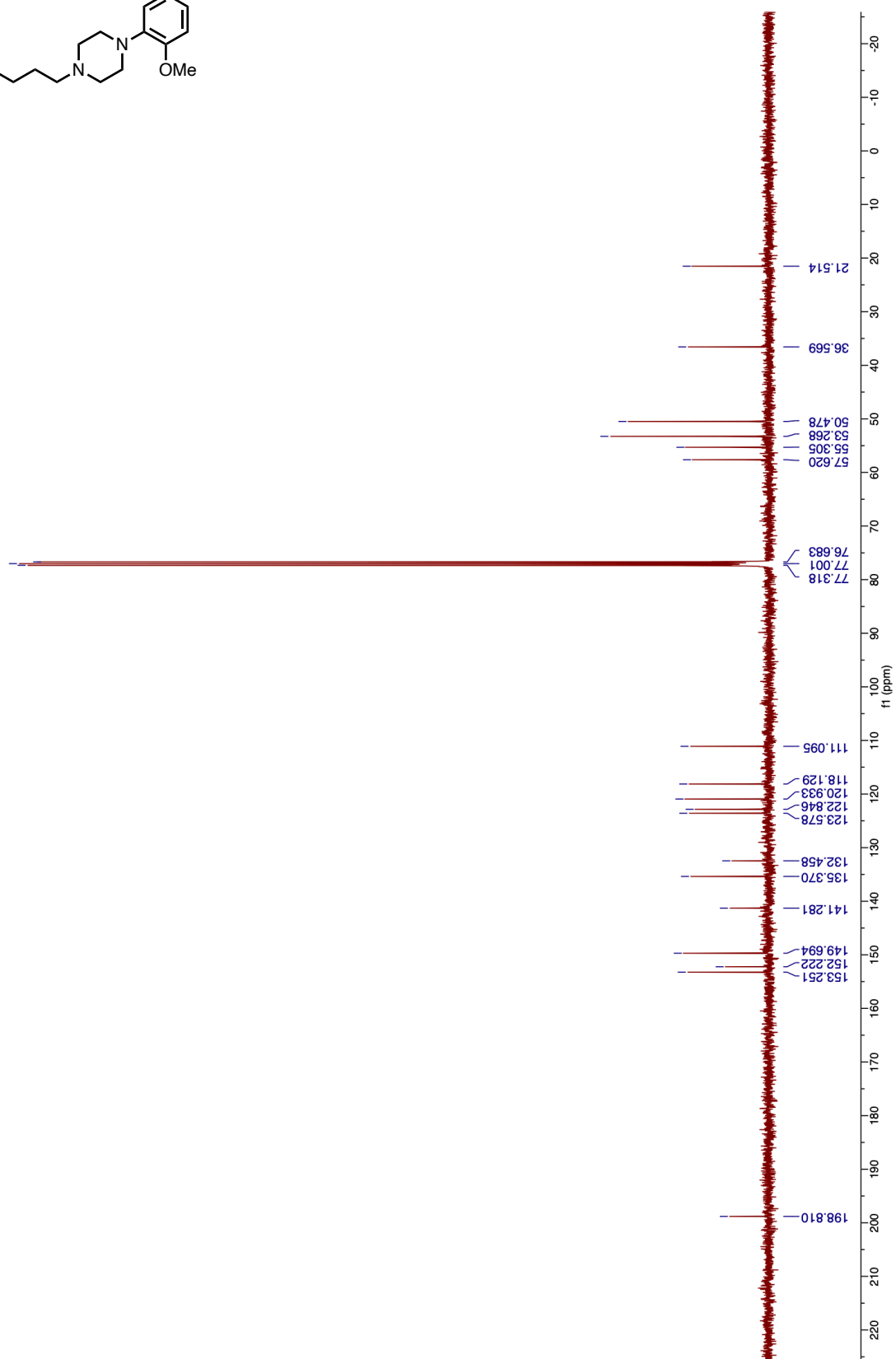
HN2959.f1 — single-pulse



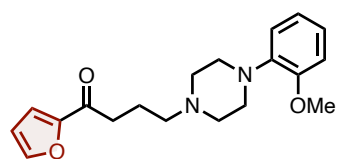
^{13}C NMR of **3yB** (101 MHz, CDCl_3)



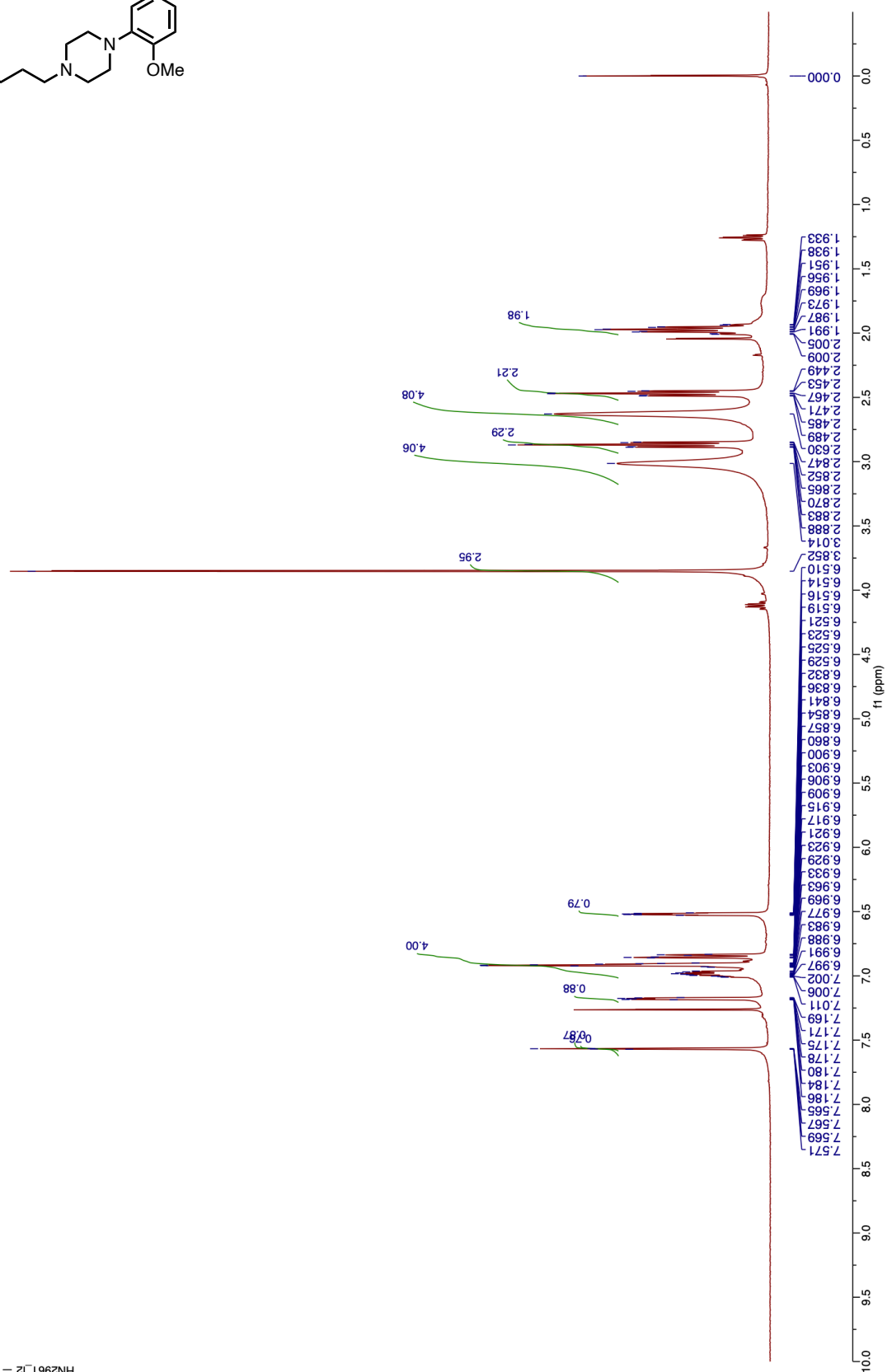
HN2959 — single pulse decoupled gated NOE



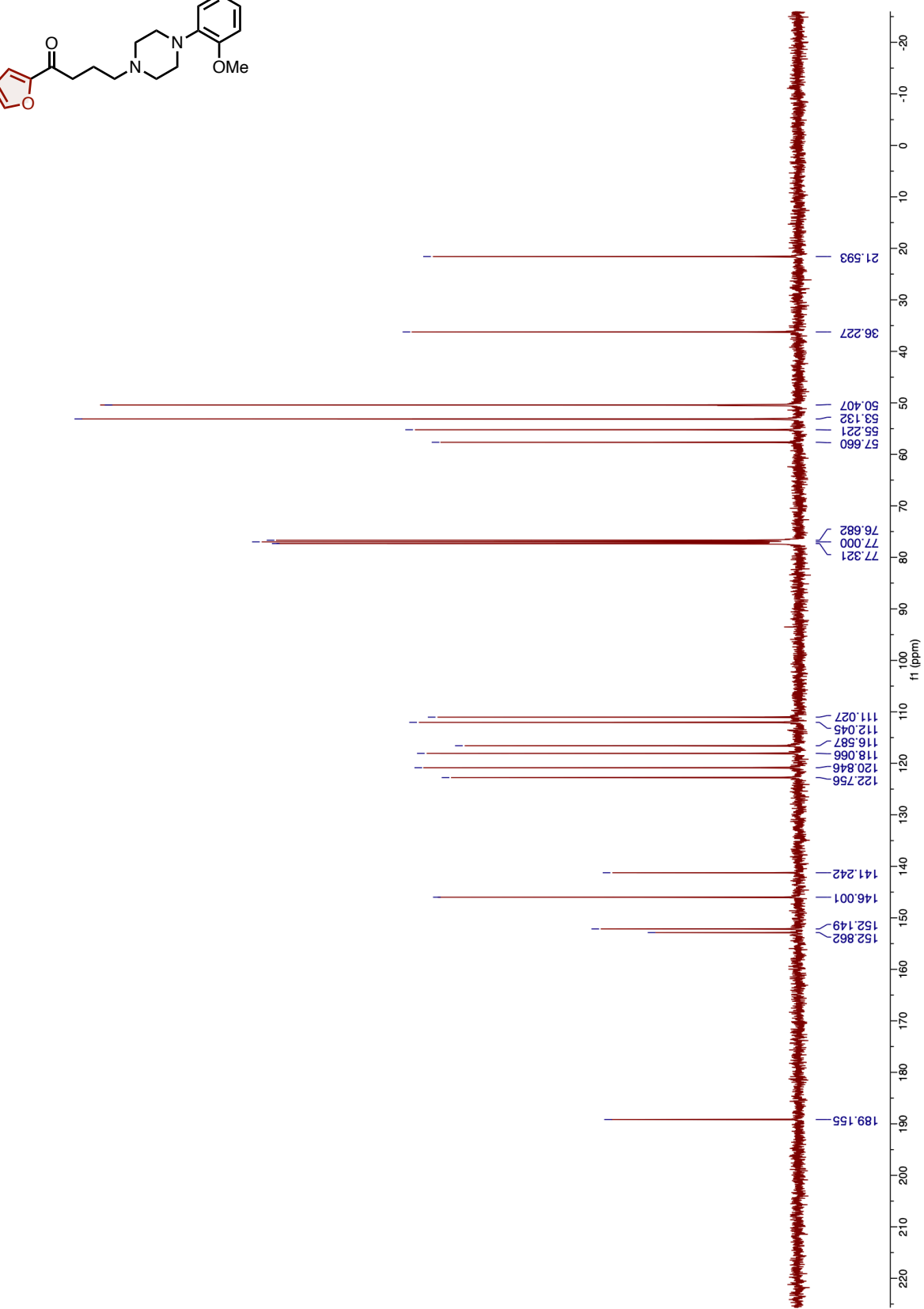
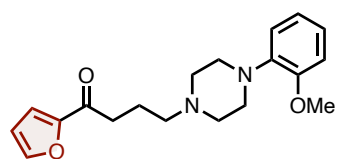
^1H NMR of **3yS** (400 MHz, CDCl_3)



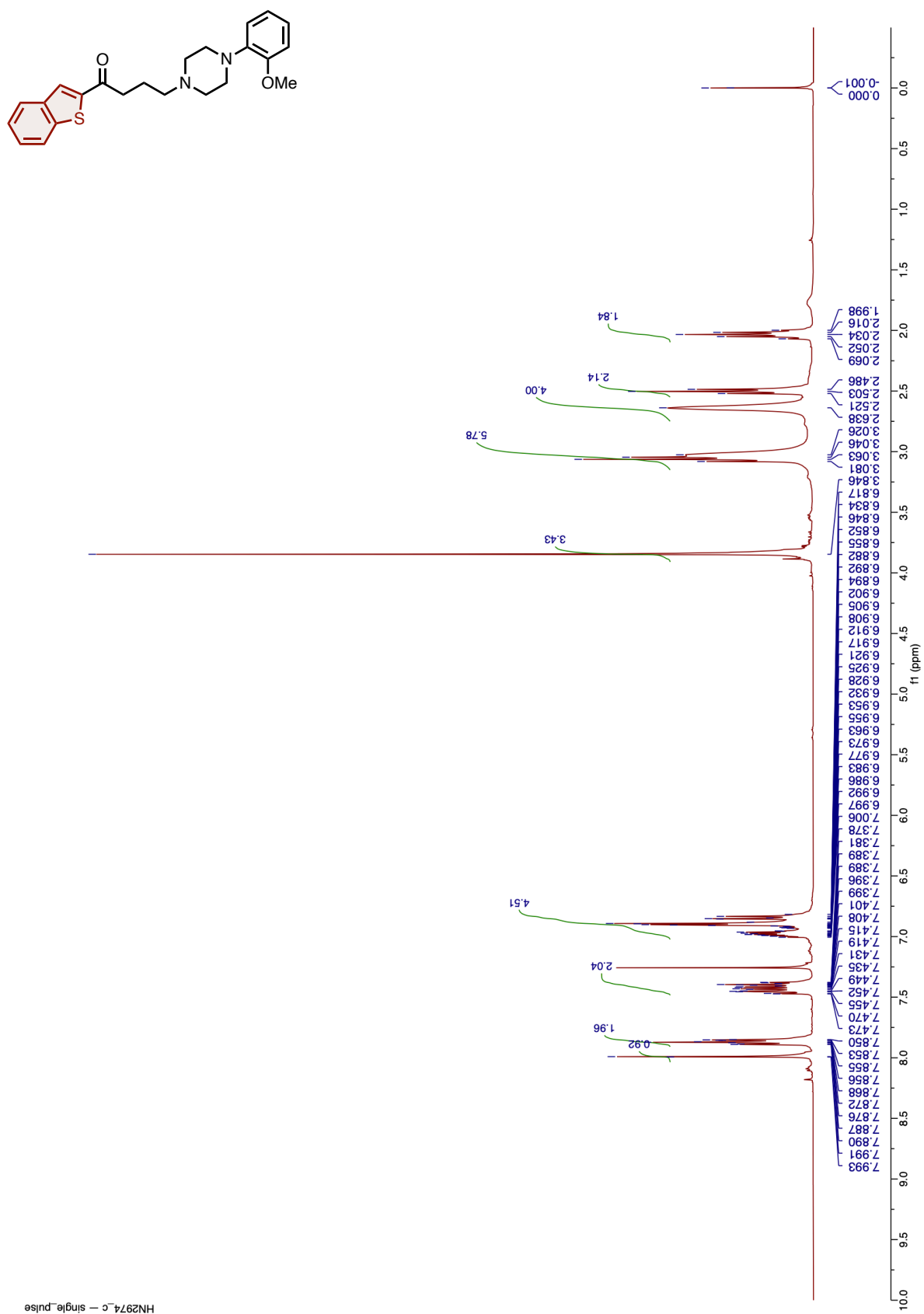
HN2961.f2 — single-pulse



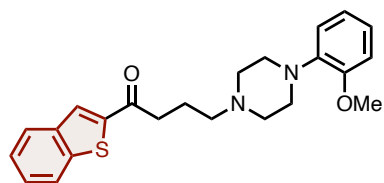
^{13}C NMR of **3yS** (101 MHz, CDCl_3)



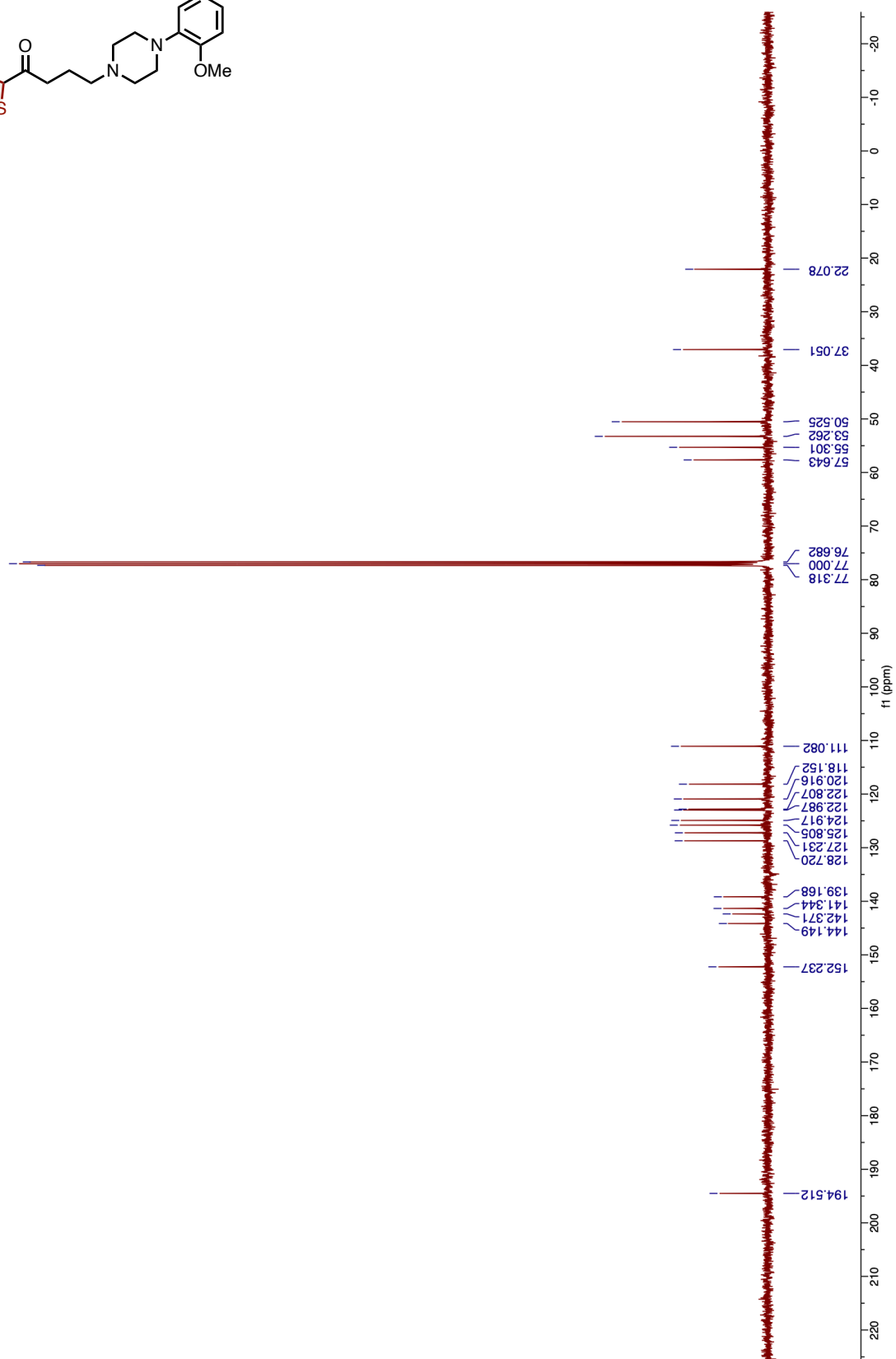
^1H NMR of **3yU** (400 MHz, CDCl_3)



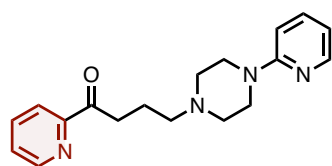
^{13}C NMR of **3yU** (101 MHz, CDCl_3)



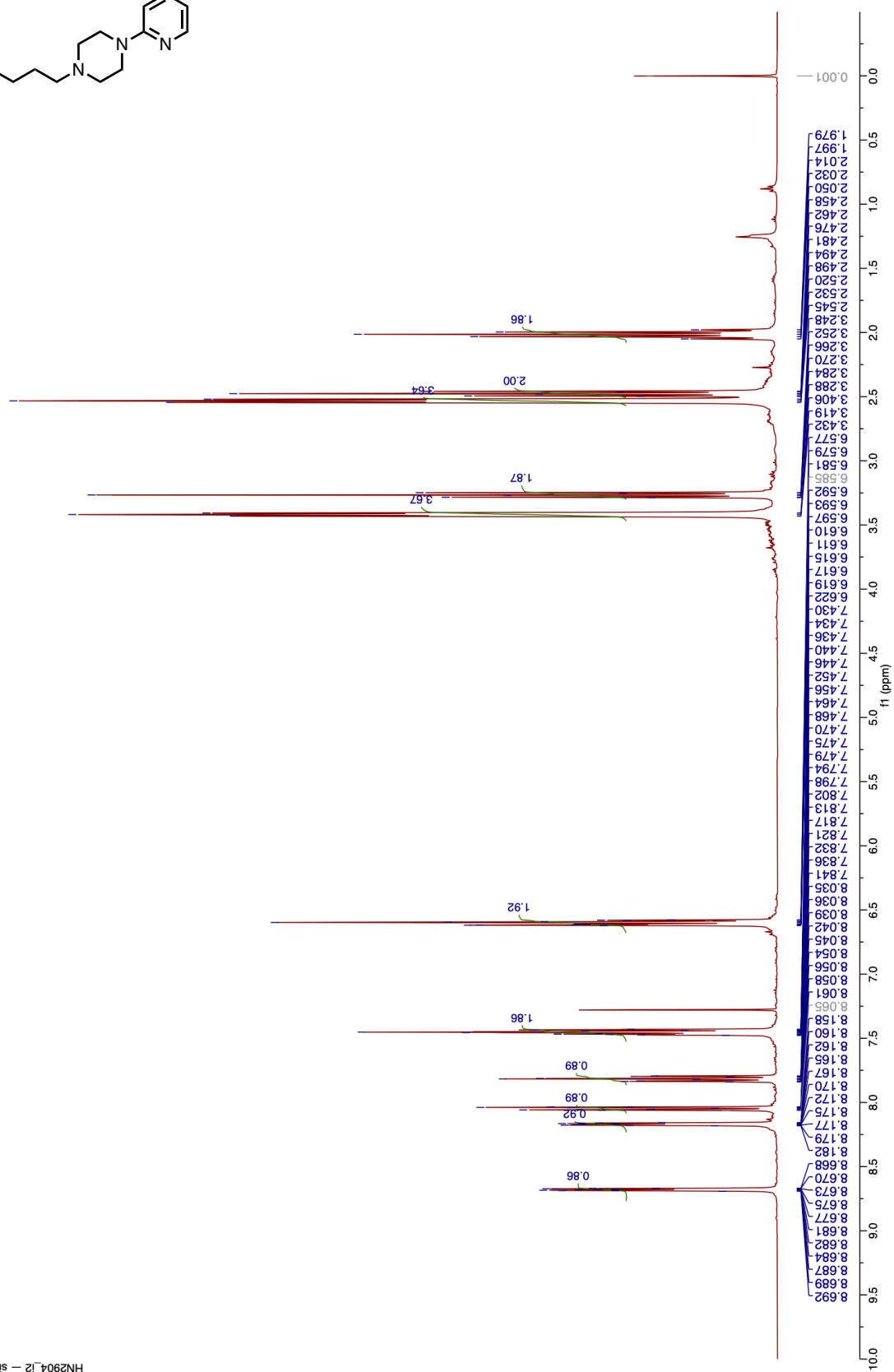
HN2982 — single pulse decoupled gated NOE



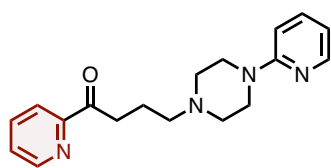
^1H NMR of **3zA** (400 MHz, CDCl_3)



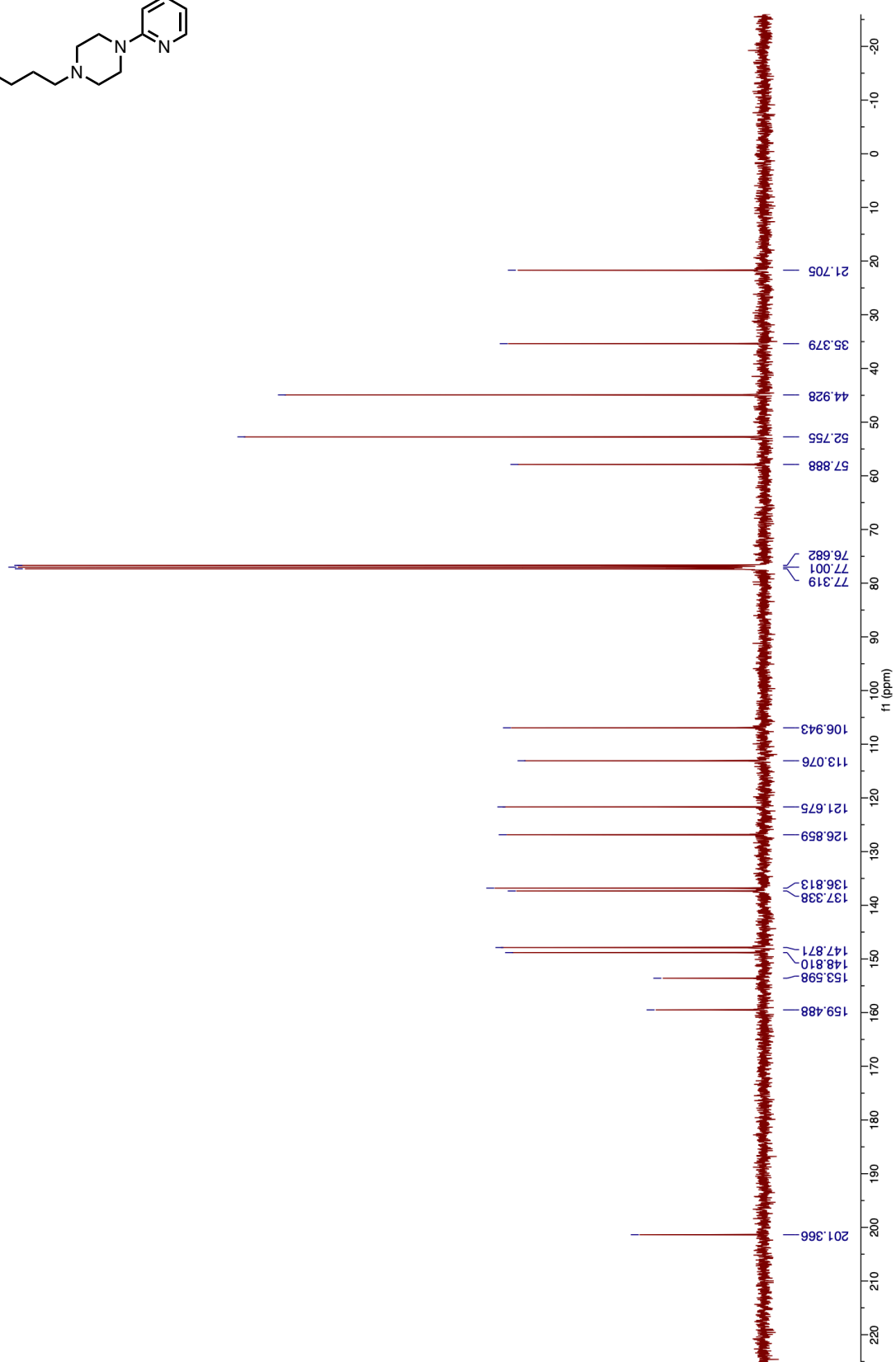
HN2904.f2 — single-pulse



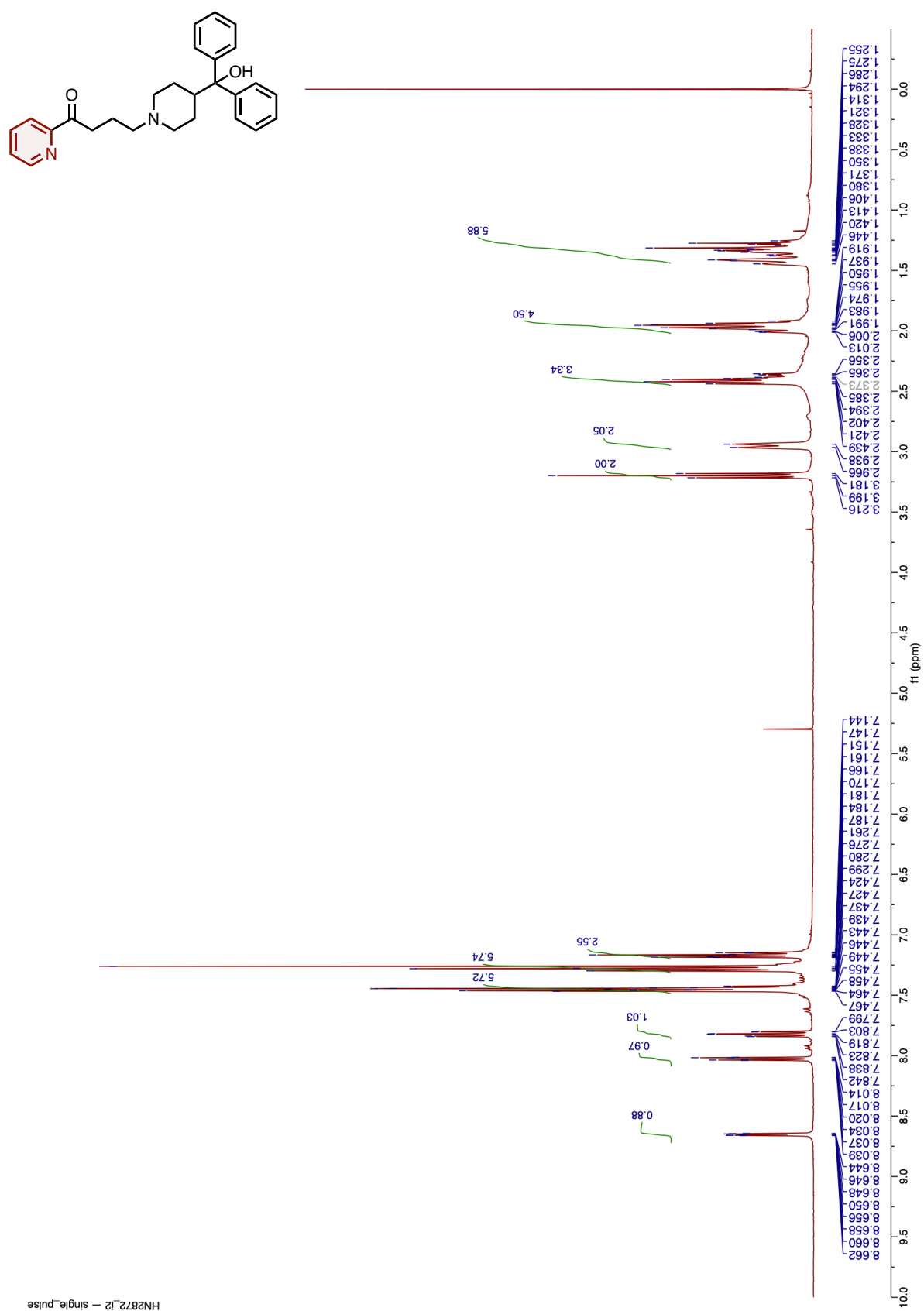
^{13}C NMR of **3zA** (101 MHz, CDCl_3)



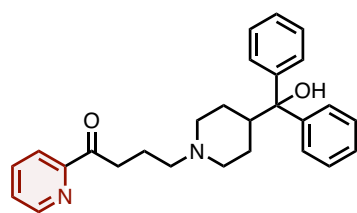
HN2904.f2 — single pulse decoupled gated NOE



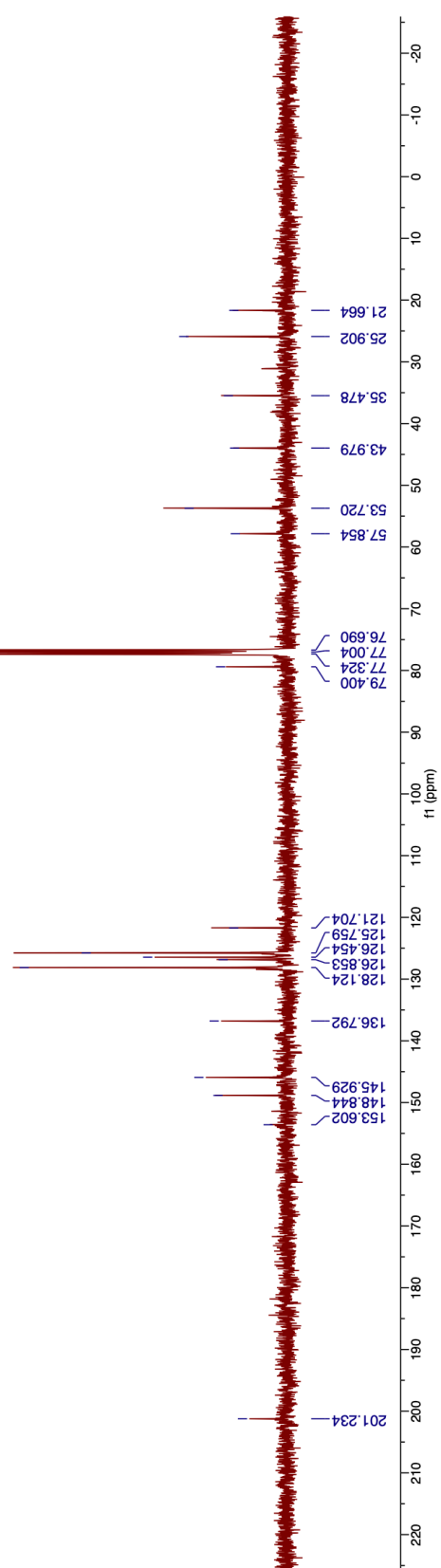
^1H NMR of **3aaA** (400 MHz, CDCl_3)

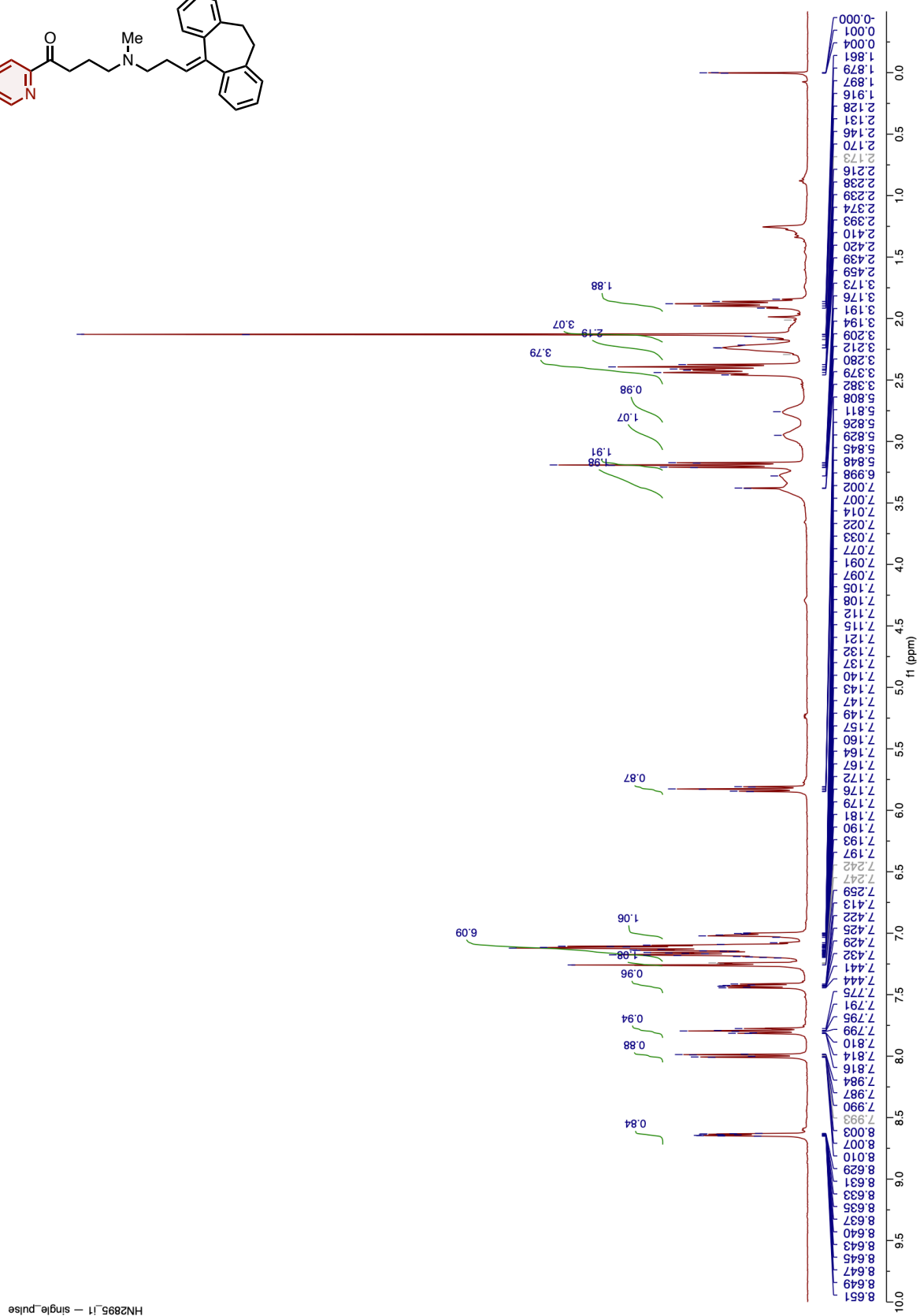
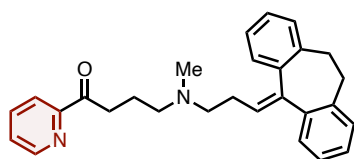


^{13}C NMR of **3aaA** (101 MHz, CDCl_3)

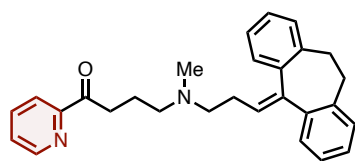


HN2952 — single pulse decoupled gated NOE

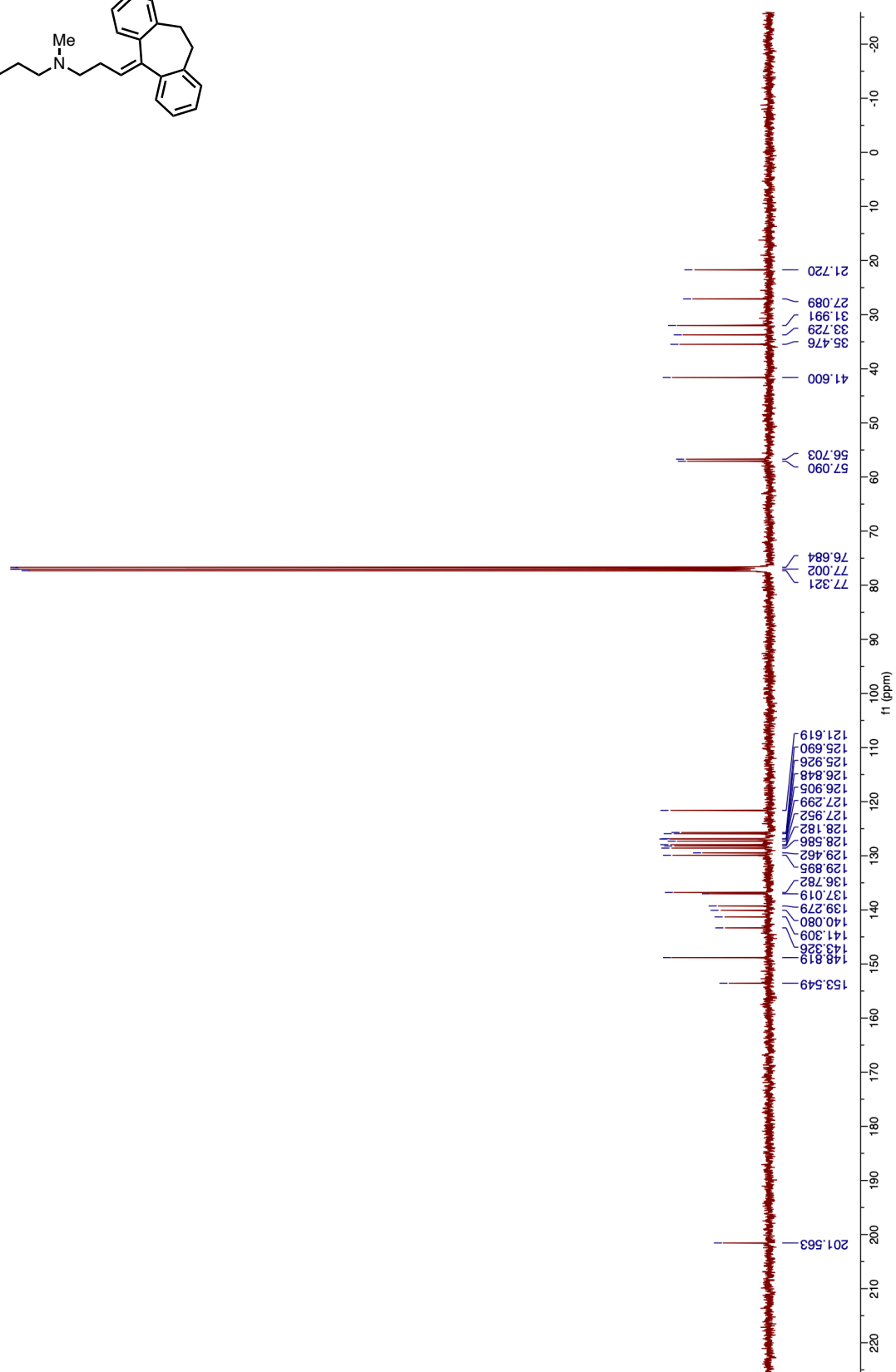




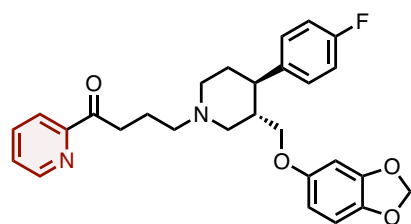
^{13}C NMR of **3abA** (101 MHz, CDCl_3)



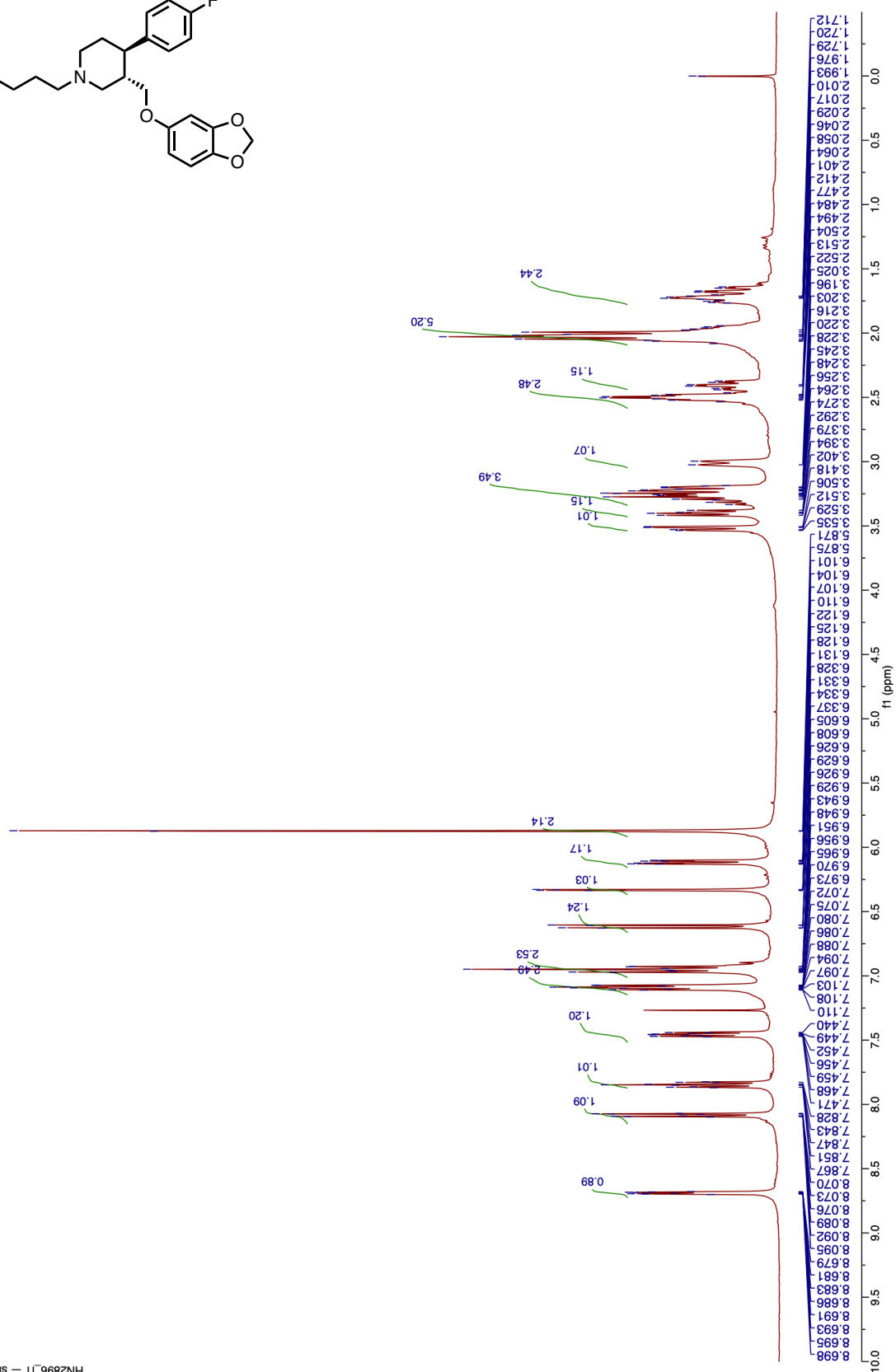
HN2895.f1 — single pulse decoupled gated NOE



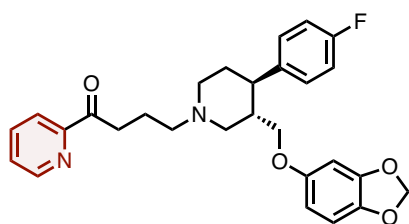
^1H NMR of **3acA** (400 MHz, CDCl_3)



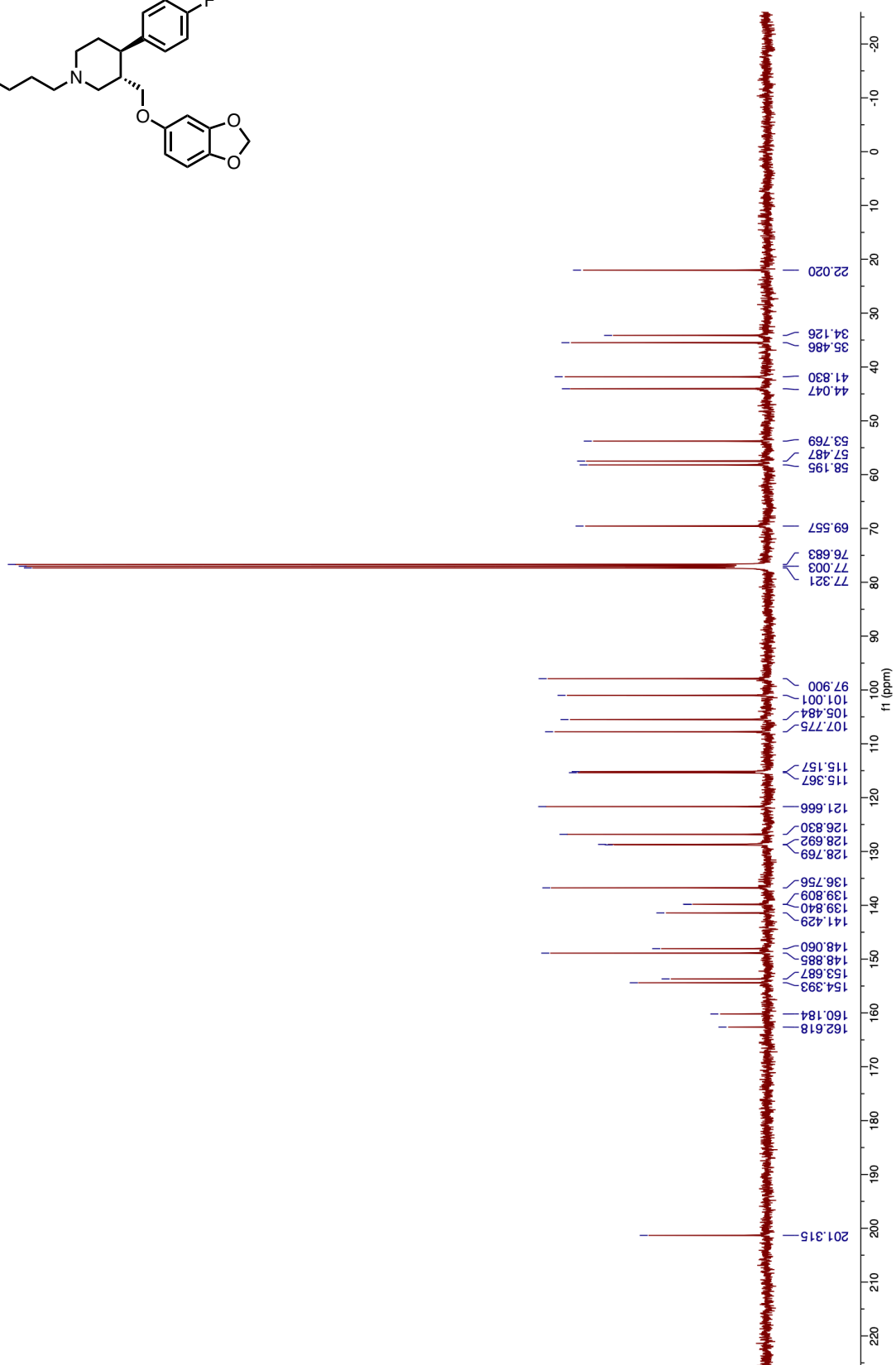
HN2896.f1 - single-pulse



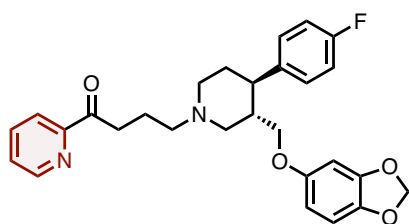
^{13}C NMR of **3acA** (101 MHz, CDCl_3)



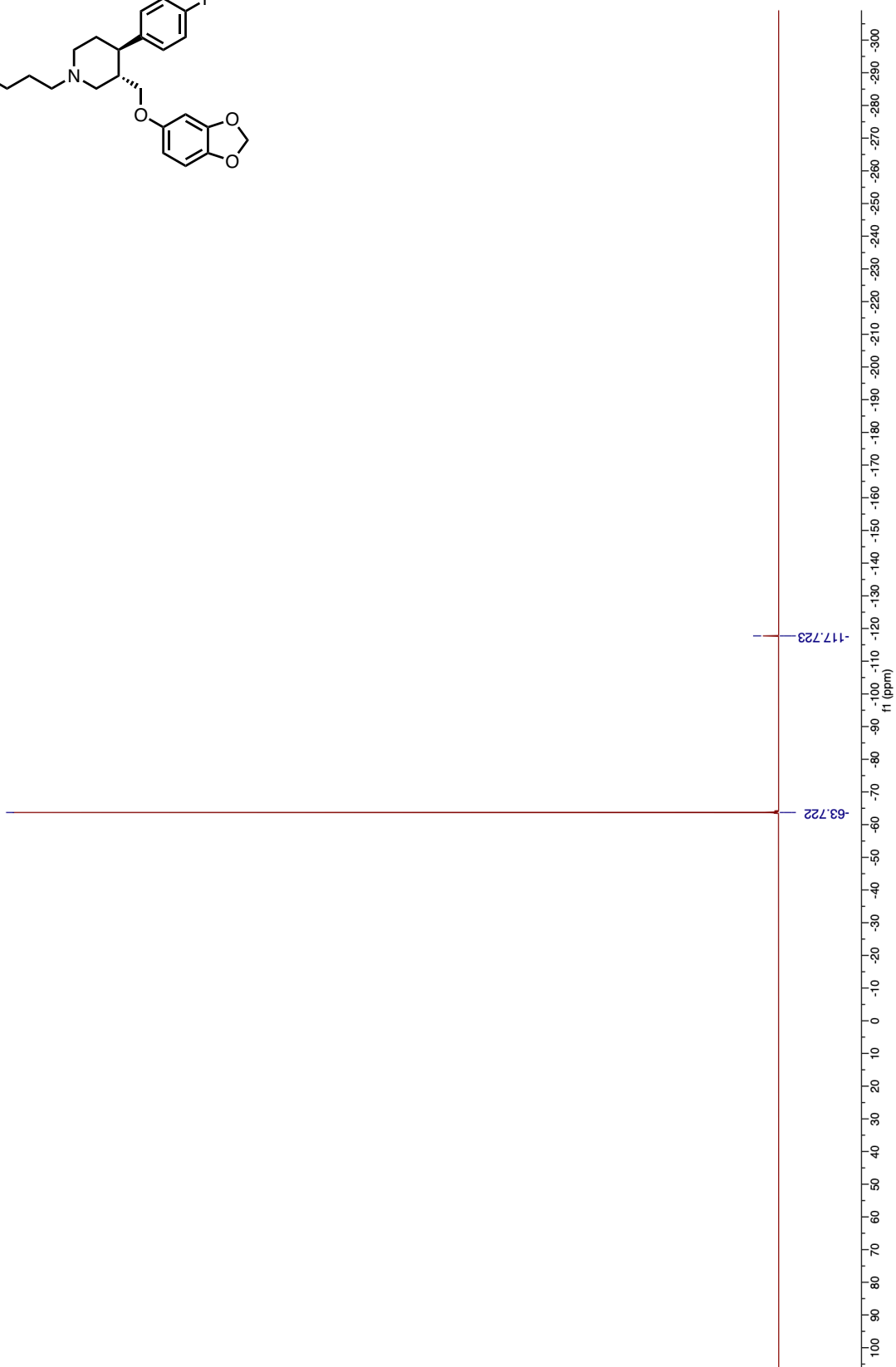
HN2896.f1 — single pulse decoupled gated NOE



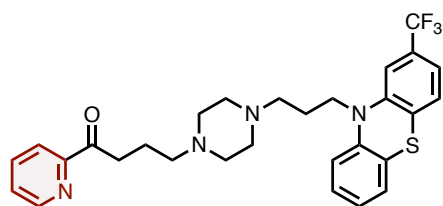
^{19}F NMR of **3acA** (376 MHz, CDCl_3)



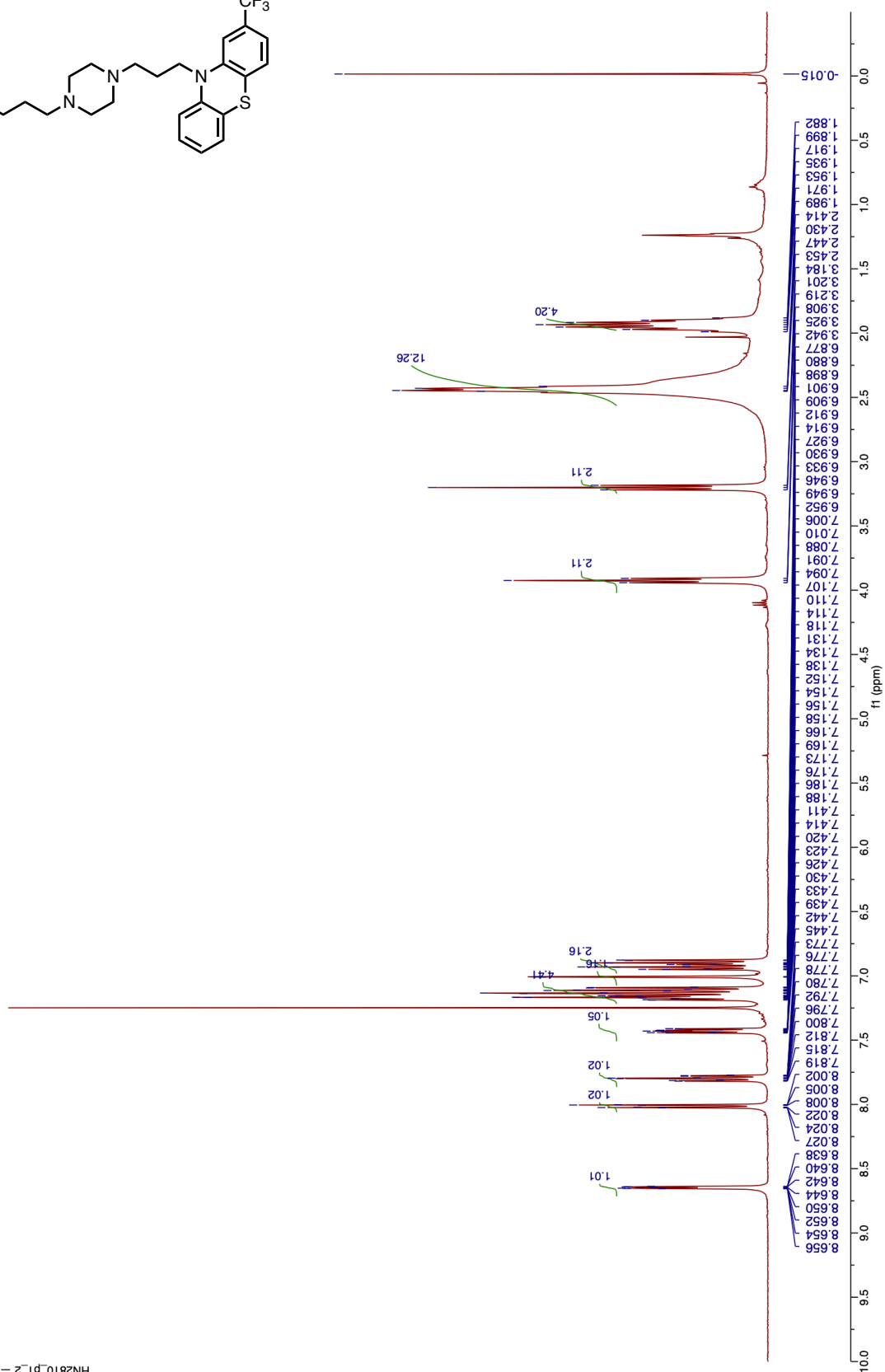
HN2896 — single pulse decoupled gated NOE



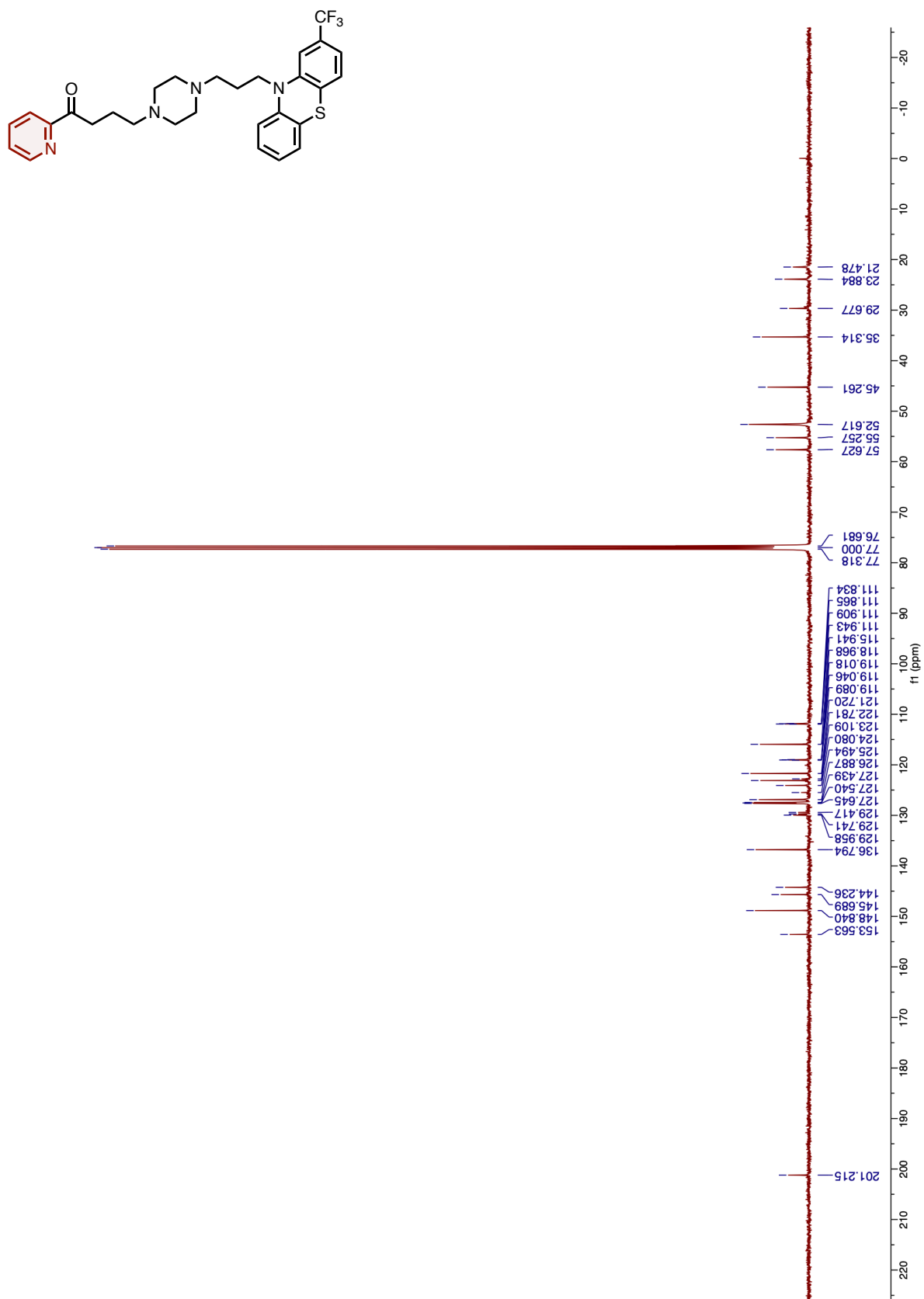
¹H NMR of **3adA** (400 MHz, CDCl₃)



HN2810.p1_2 - single-pulse

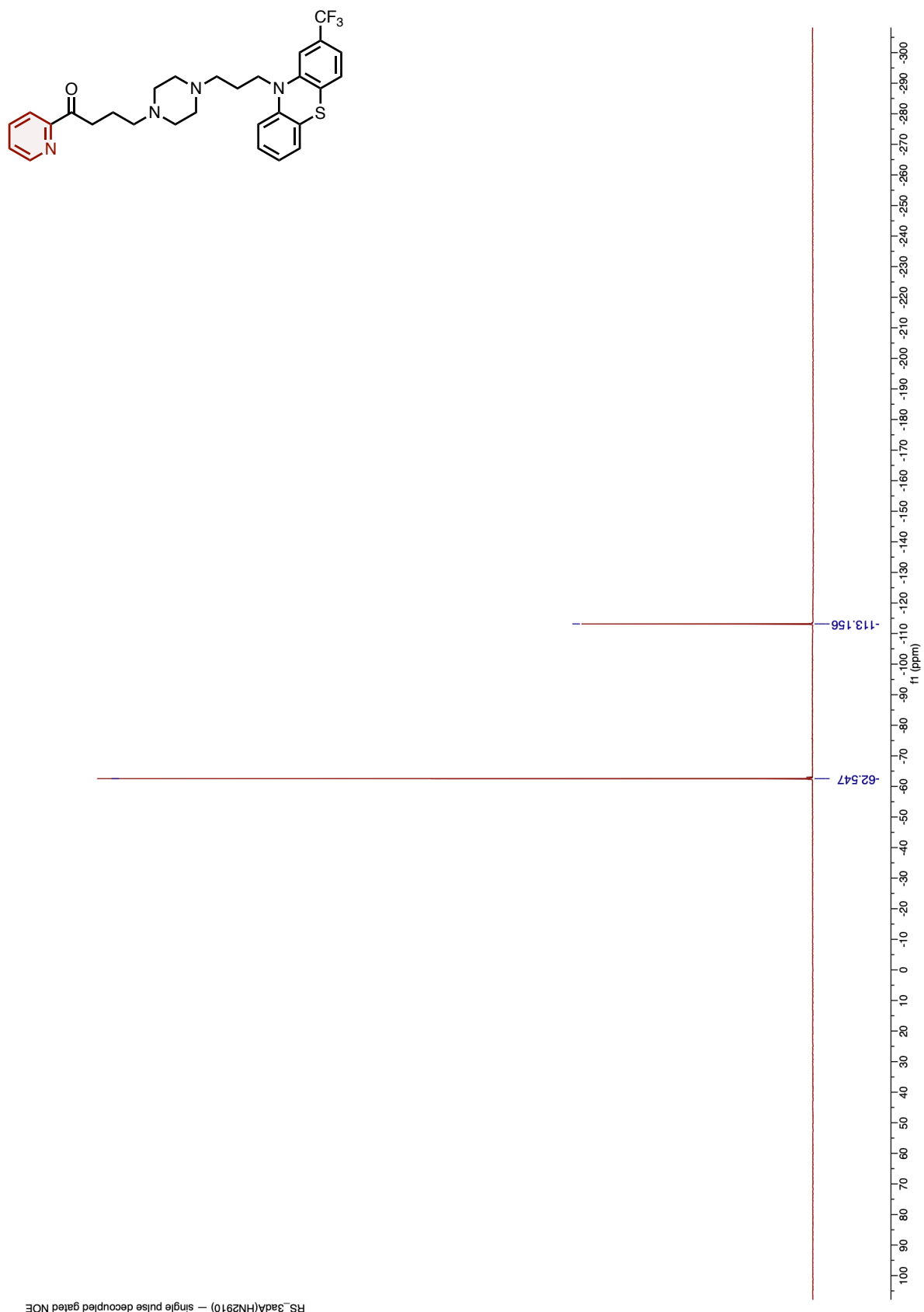


^{13}C NMR of **3adA** (101 MHz, CDCl_3)



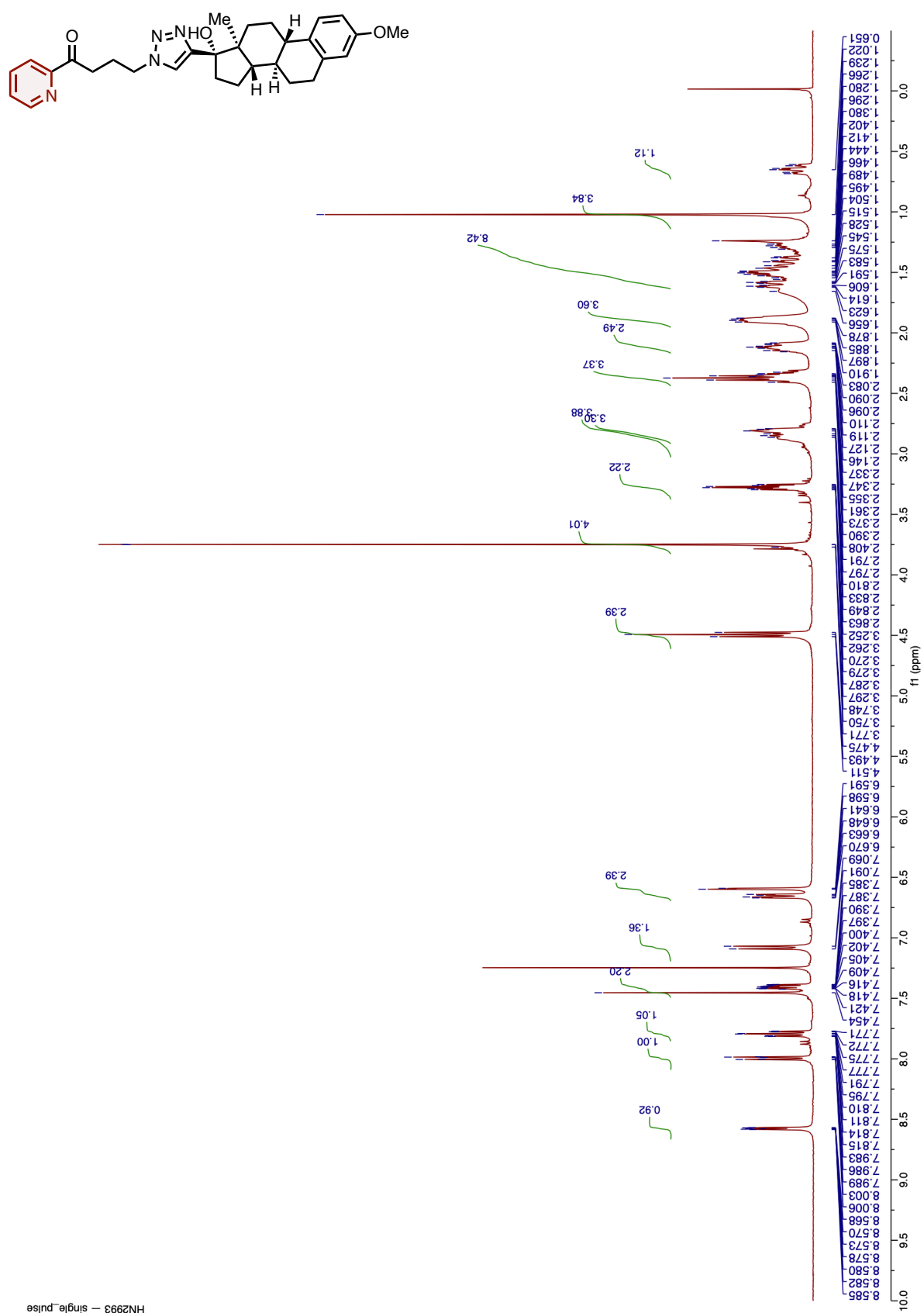
RS_3adA(HN2910)_2 — single pulse decoupled gated NOE

^{19}F NMR of **3adA** (376 MHz, CDCl_3)

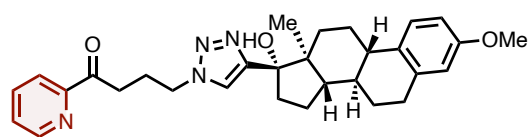


RS_3adA(HN2910) — single pulse decoupled gated NOE

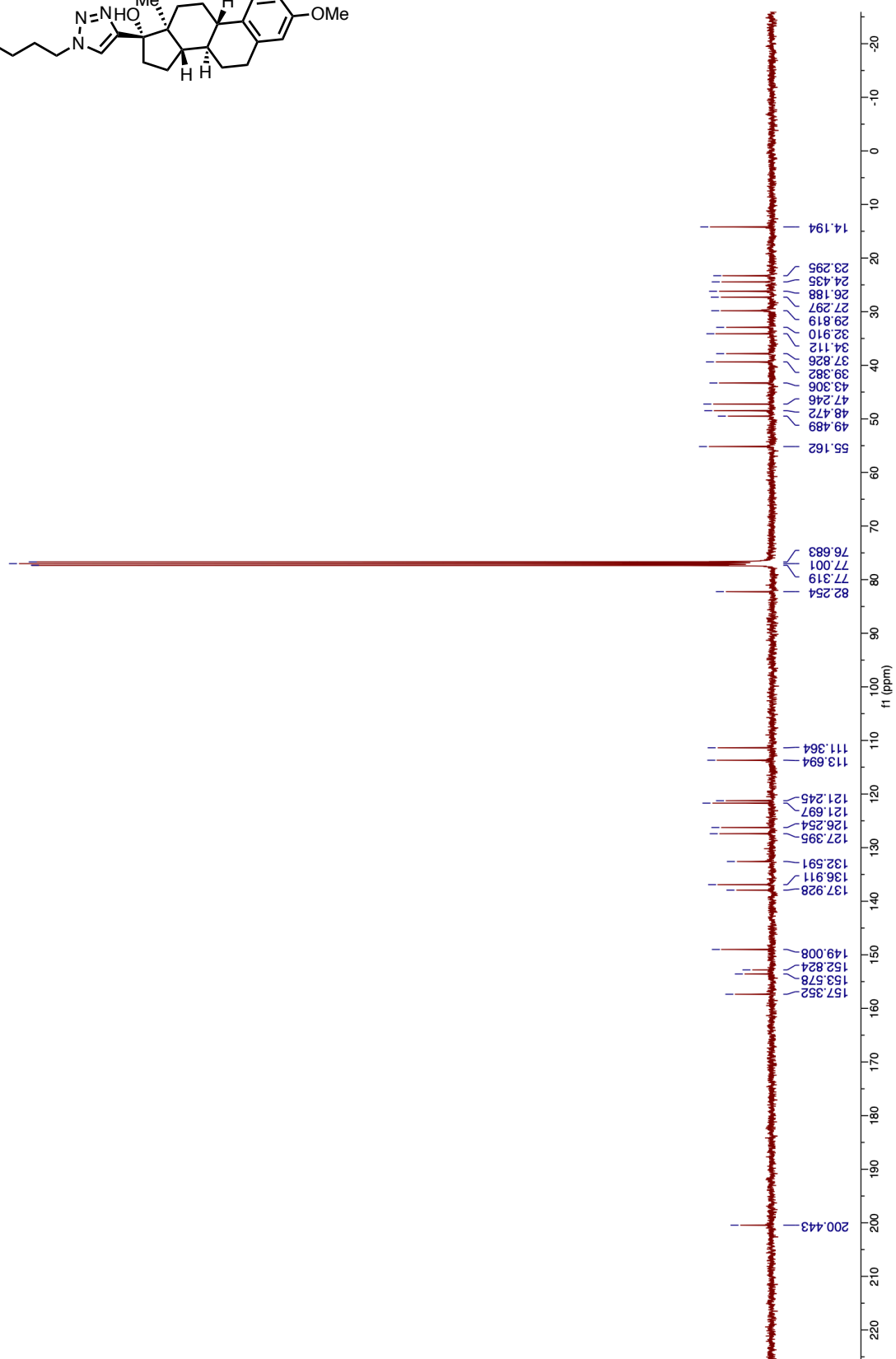
¹H NMR of **3aeA** (400 MHz, CDCl₃)



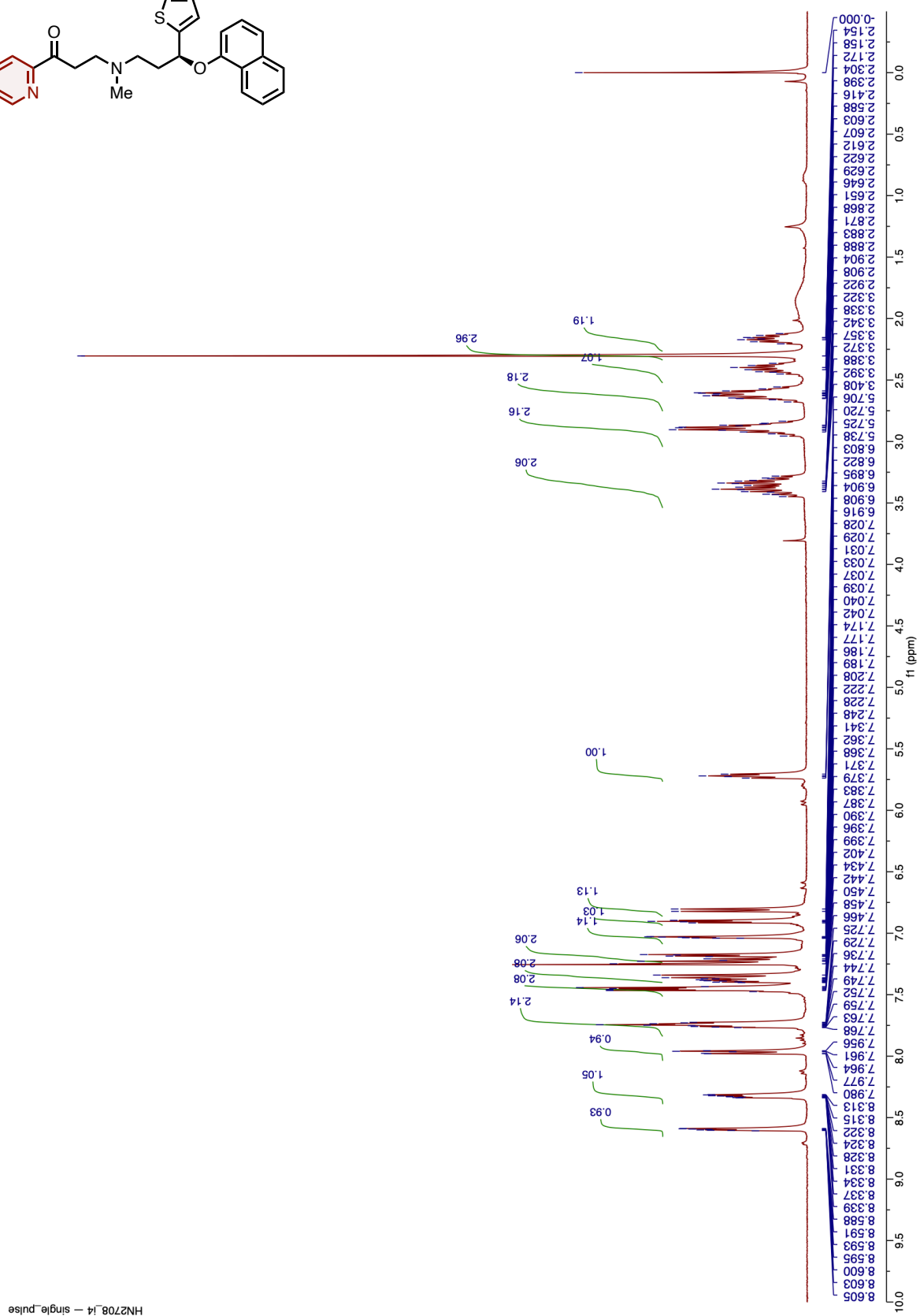
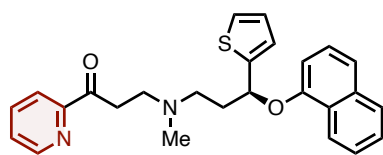
^{13}C NMR of **3aeA** (101 MHz, CDCl_3)



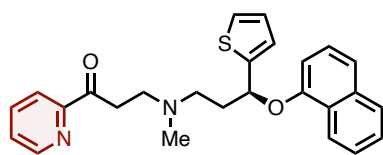
HN2993_2 — single pulse decoupled gated NOE



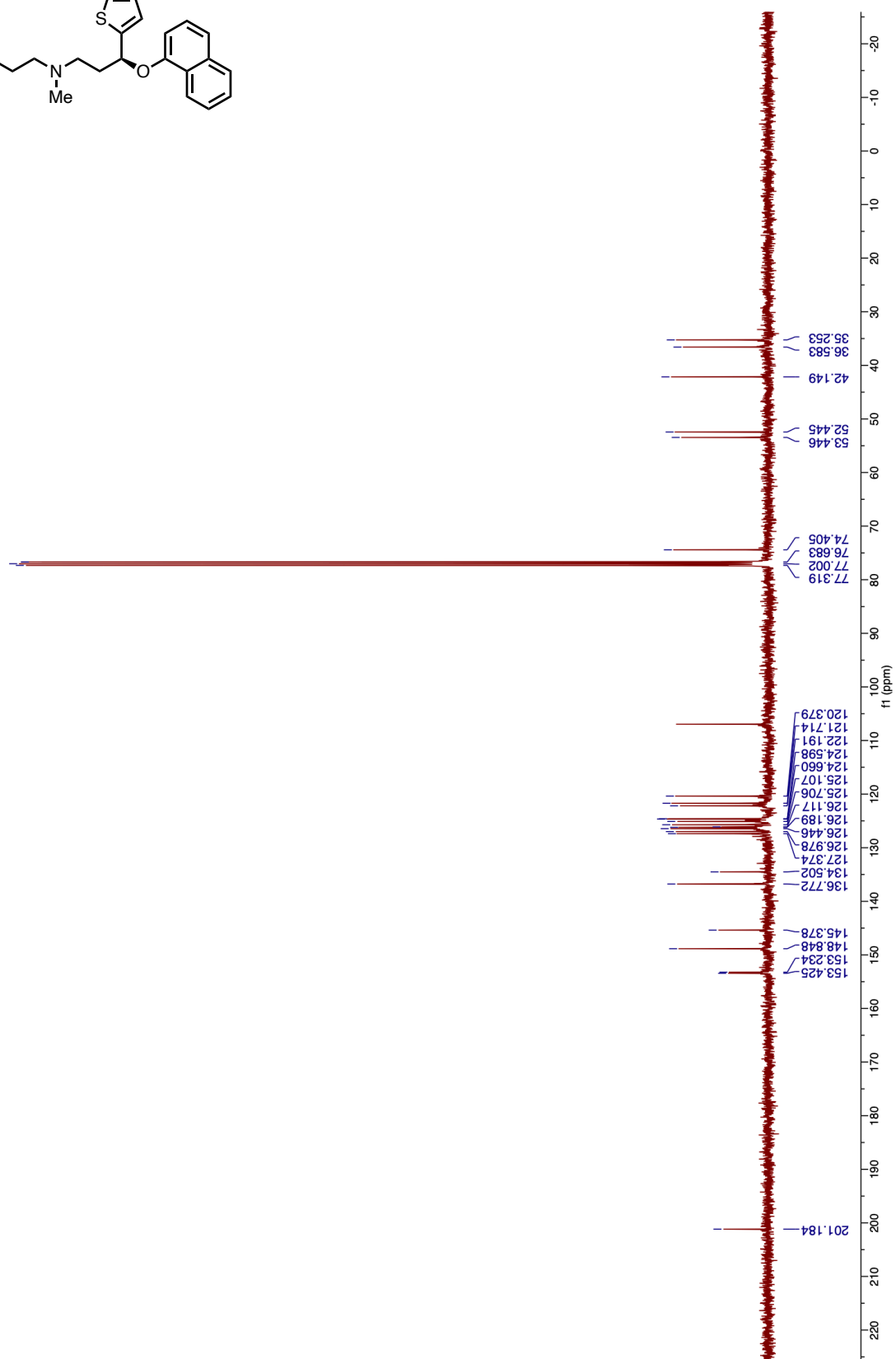
^1H NMR of **3afA** (400 MHz, CDCl_3)



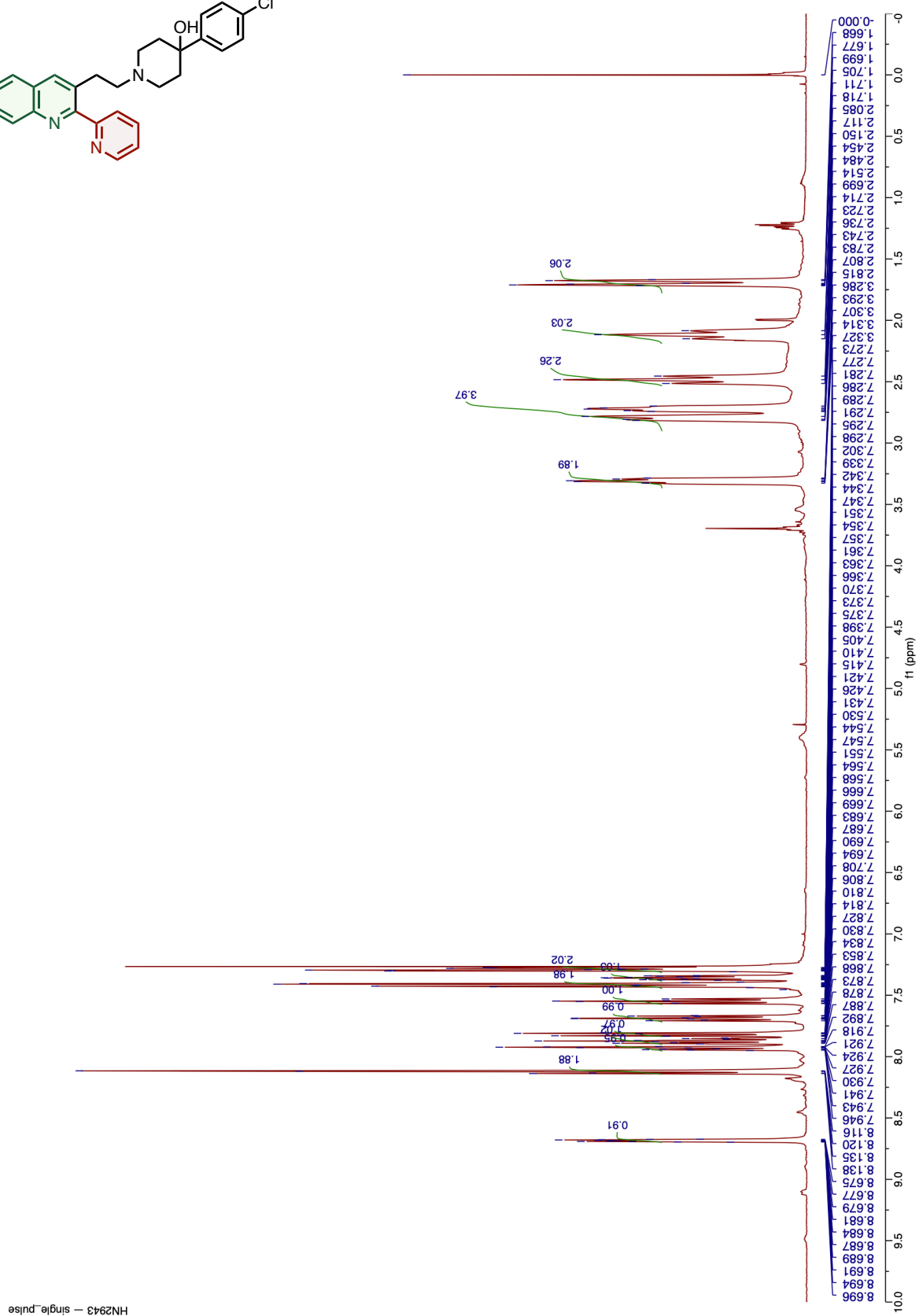
^{13}C NMR of **3afA** (101 MHz, CDCl_3)



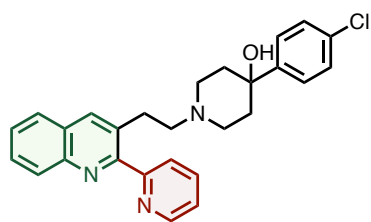
HN2708 — single pulse decoupled gated NOE



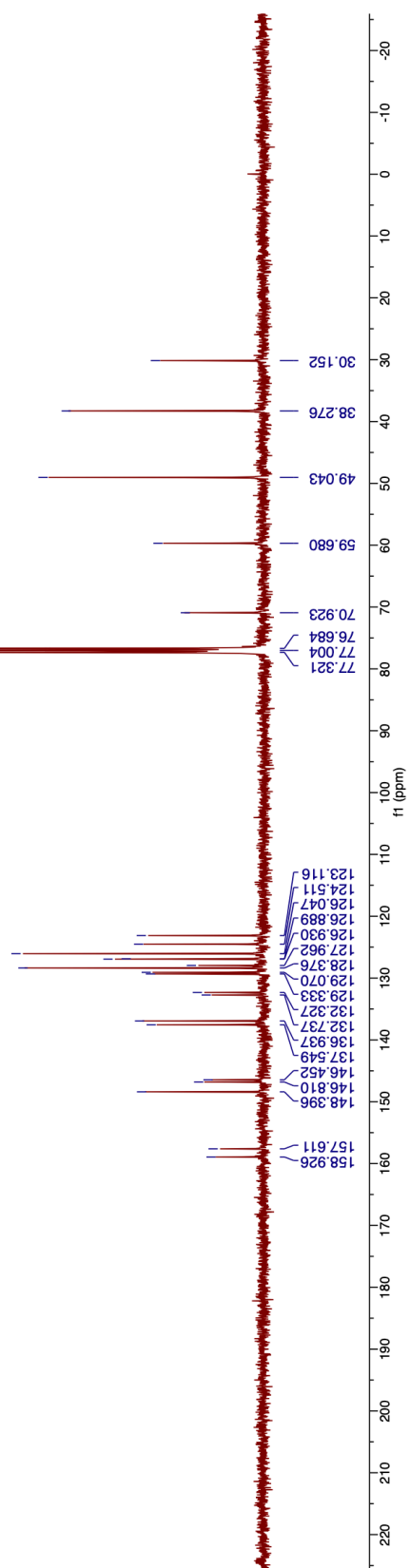
The chemical structure shows a piperazine ring substituted with a 4-chlorophenyl group at the 4-position and a 2-(4-chlorophenyl)-2-hydroxyethyl group at the 1-position. The piperazine ring is also substituted with a 2-(4-chlorophenyl)-2-hydroxyethyl group at the 4-position. The piperazine ring is further substituted with a 2-(4-chlorophenyl)-2-hydroxyethyl group at the 1-position. The piperazine ring is also substituted with a 2-(4-chlorophenyl)-2-hydroxyethyl group at the 4-position.



^{13}C NMR of **6** (101 MHz, CDCl_3)

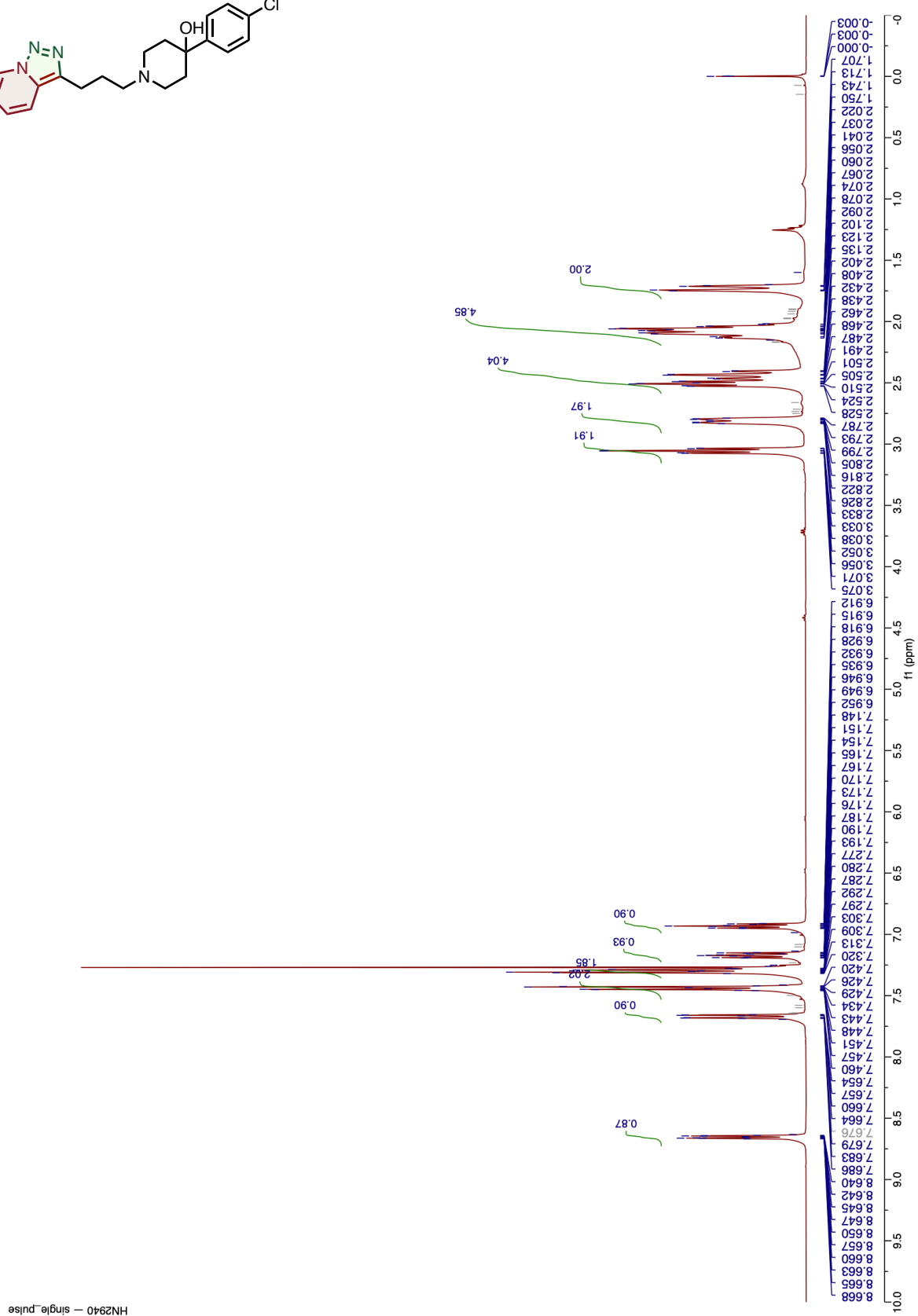


HN2943.f1 — single pulse decoupled gated NOE

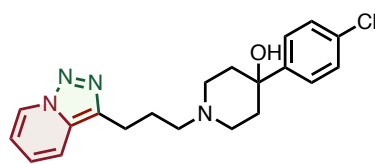




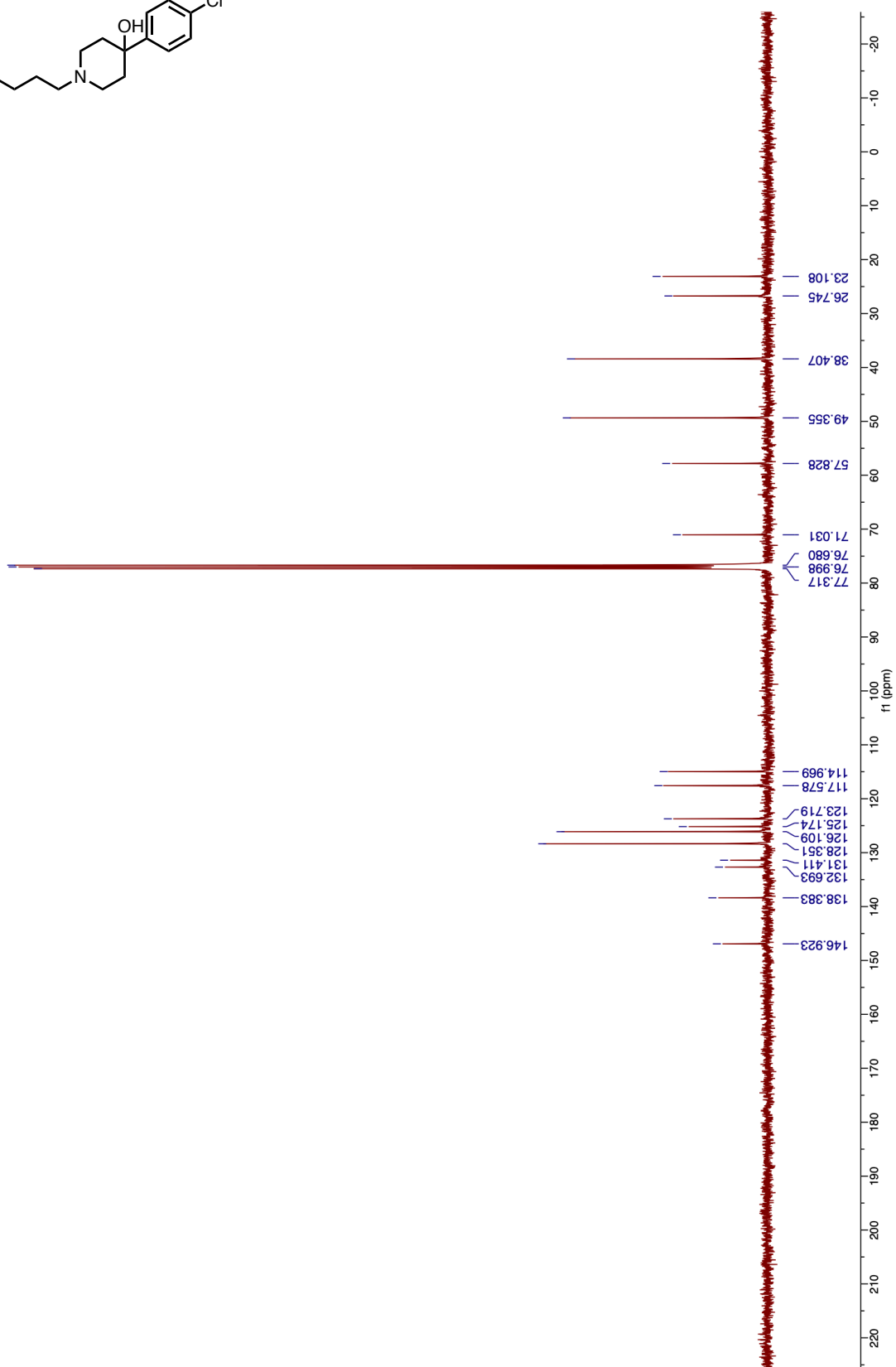
The chemical structure shows a piperidine ring substituted at the 4-position with a hydroxyl group and a 4-(4-(pyrazolo[1,5-a]pyridin-3-yl)butyl) group. The pyrazolo[1,5-a]pyridine moiety is highlighted with a red-to-yellow gradient, and the butyl chain is highlighted in light blue.



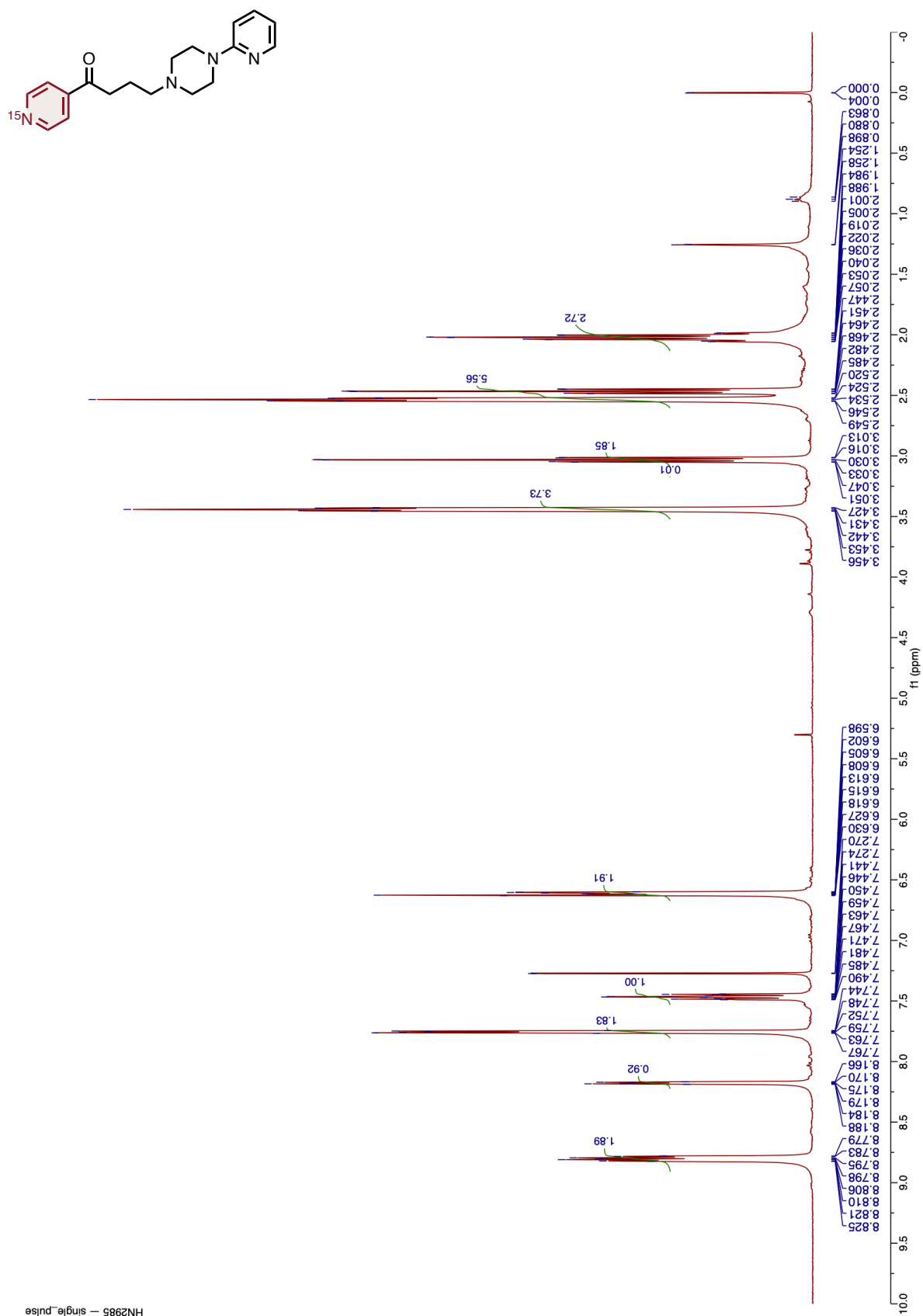
^{13}C NMR of **7** (101 MHz, CDCl_3)



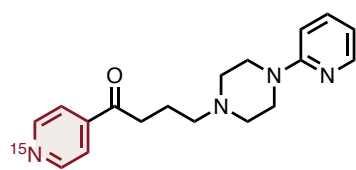
HN2940_2 — single pulse decoupled gated NOE



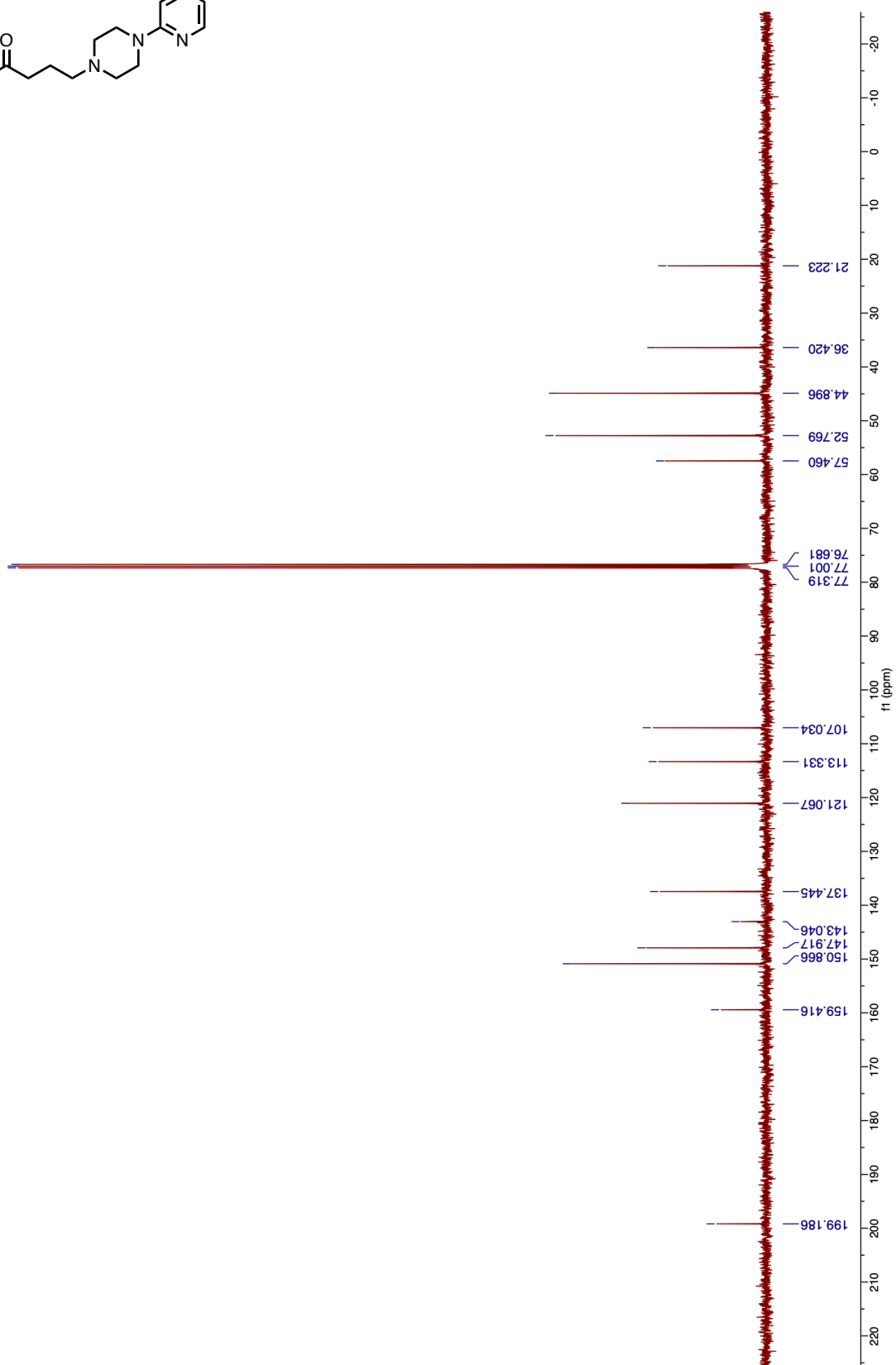
^1H NMR of **8** (400 MHz, CDCl_3)



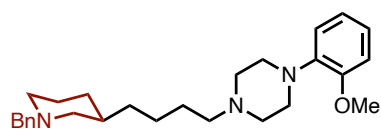
^{13}C NMR of **8** (101 MHz, CDCl_3)



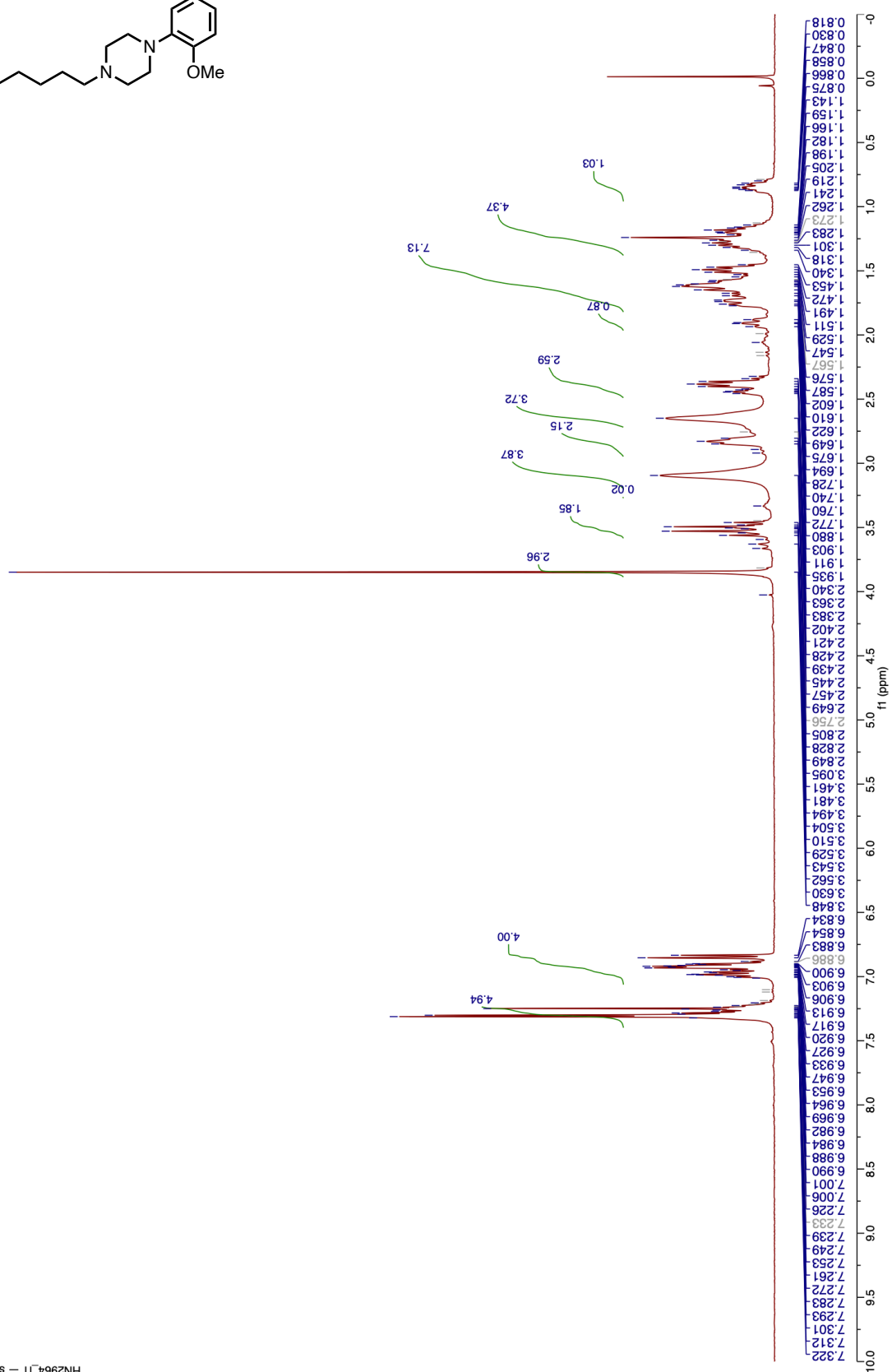
HN2985.f1 — single pulse decoupled gated NOE



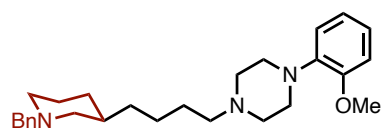
^1H NMR of **9** (400 MHz, CDCl_3)



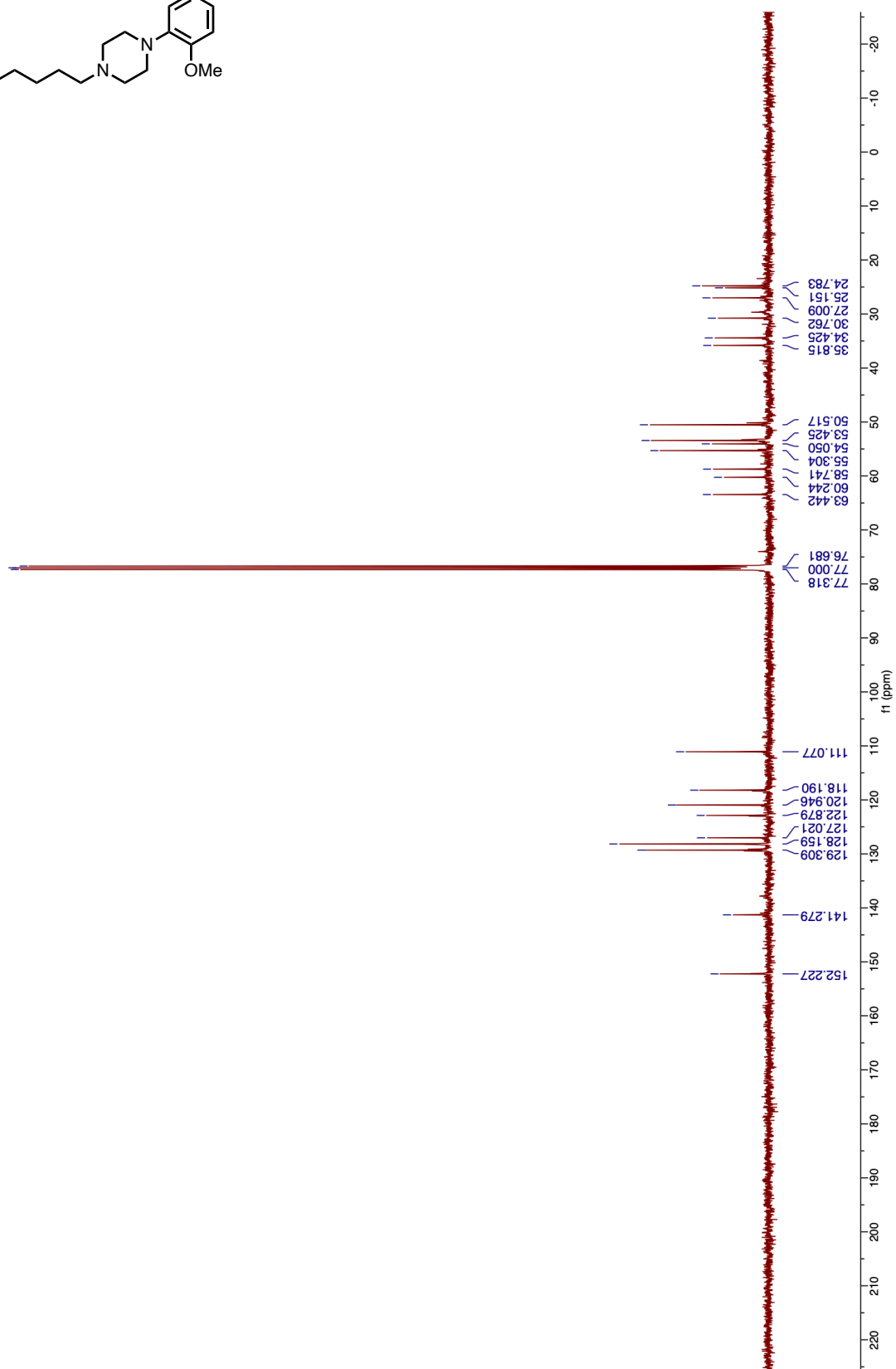
HN2964.f1 - single-pulse



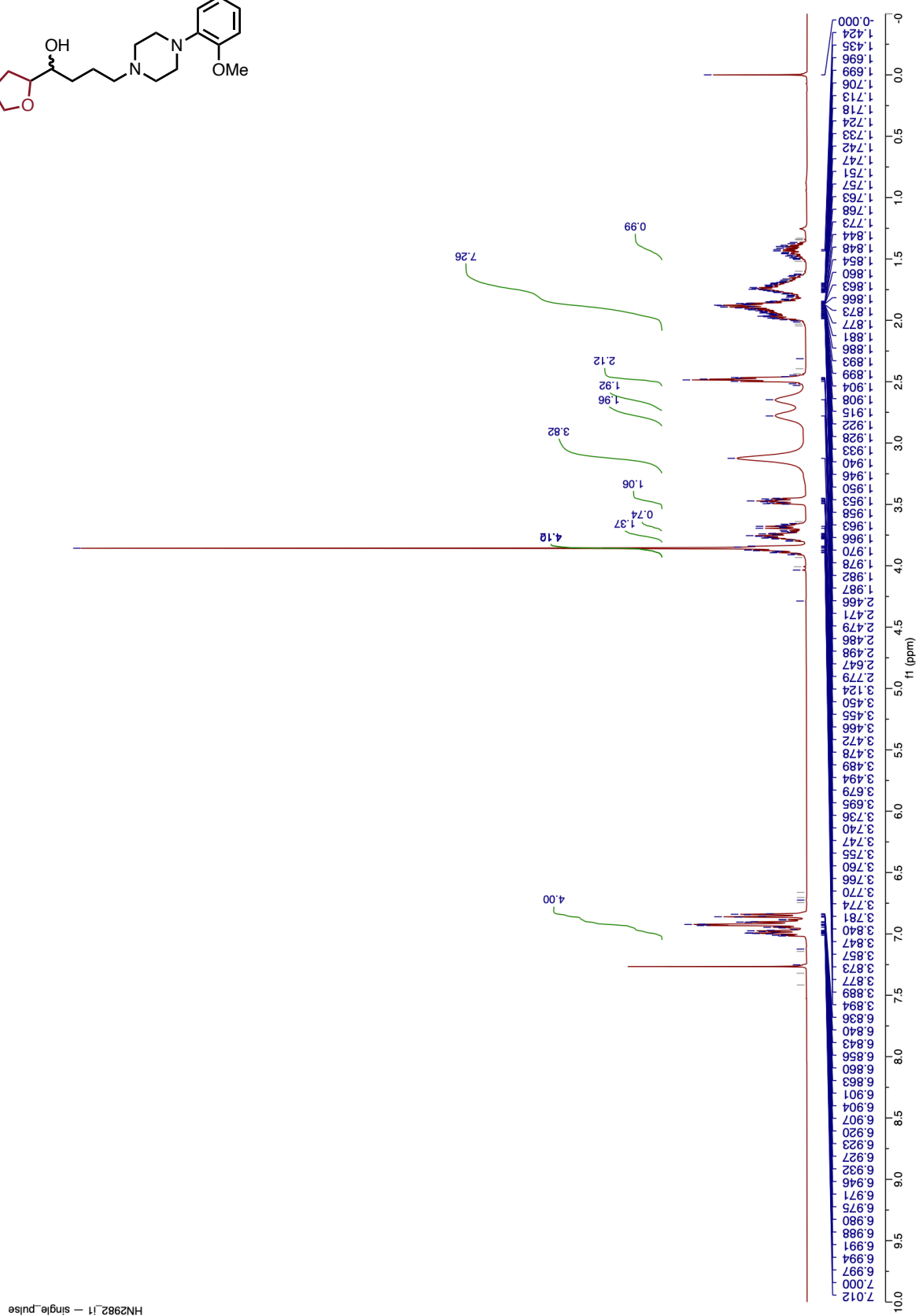
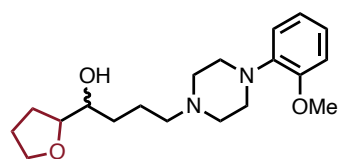
^{13}C NMR of **9** (101 MHz, CDCl_3)



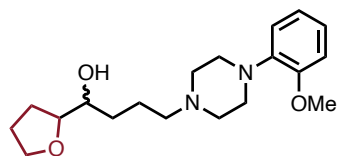
HN2964.f1 — single pulse decoupled gated NOE



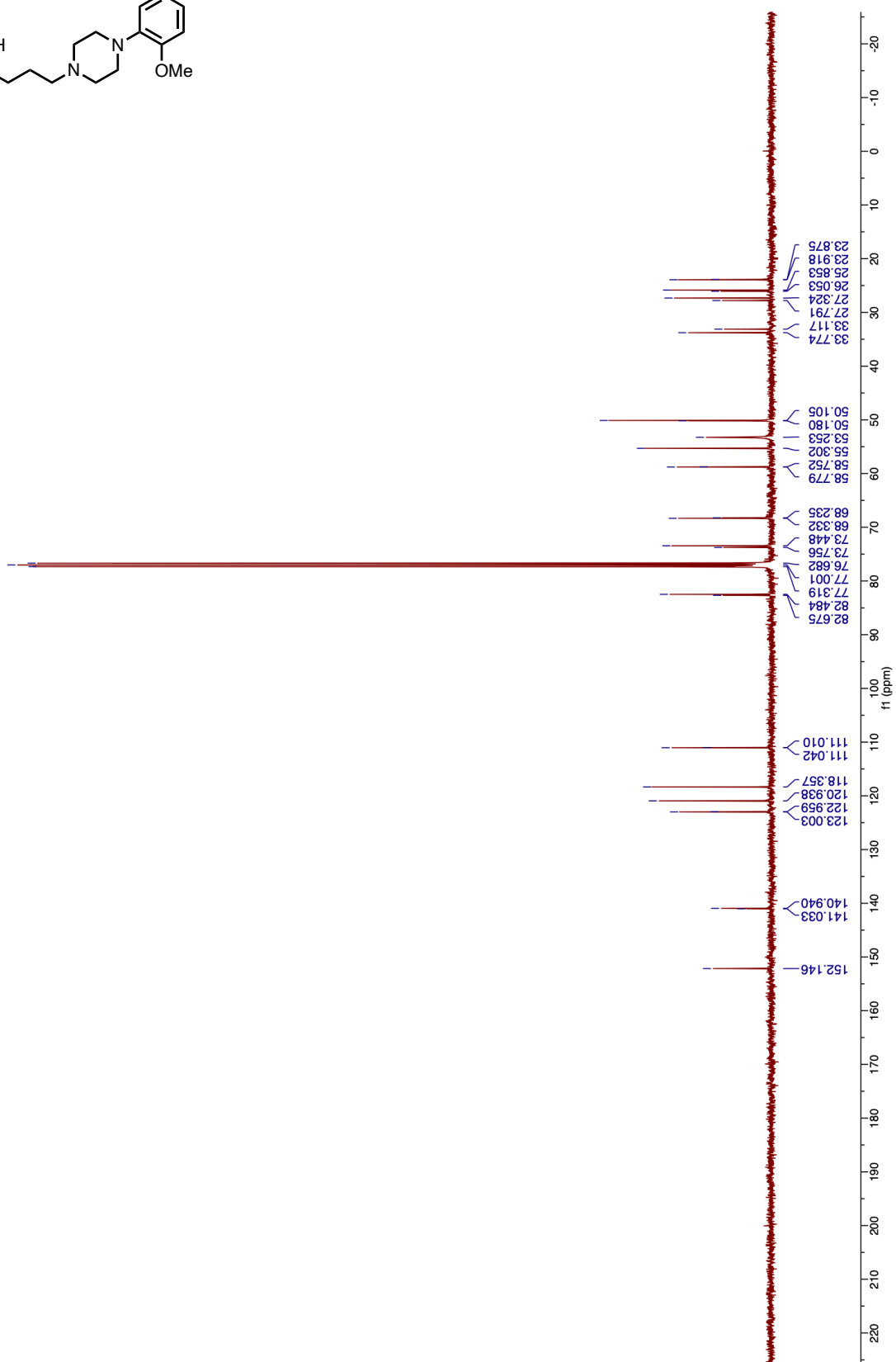
^1H NMR of **10** (400 MHz, CDCl_3)



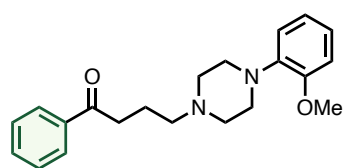
^{13}C NMR of **10** (101 MHz, CDCl_3)



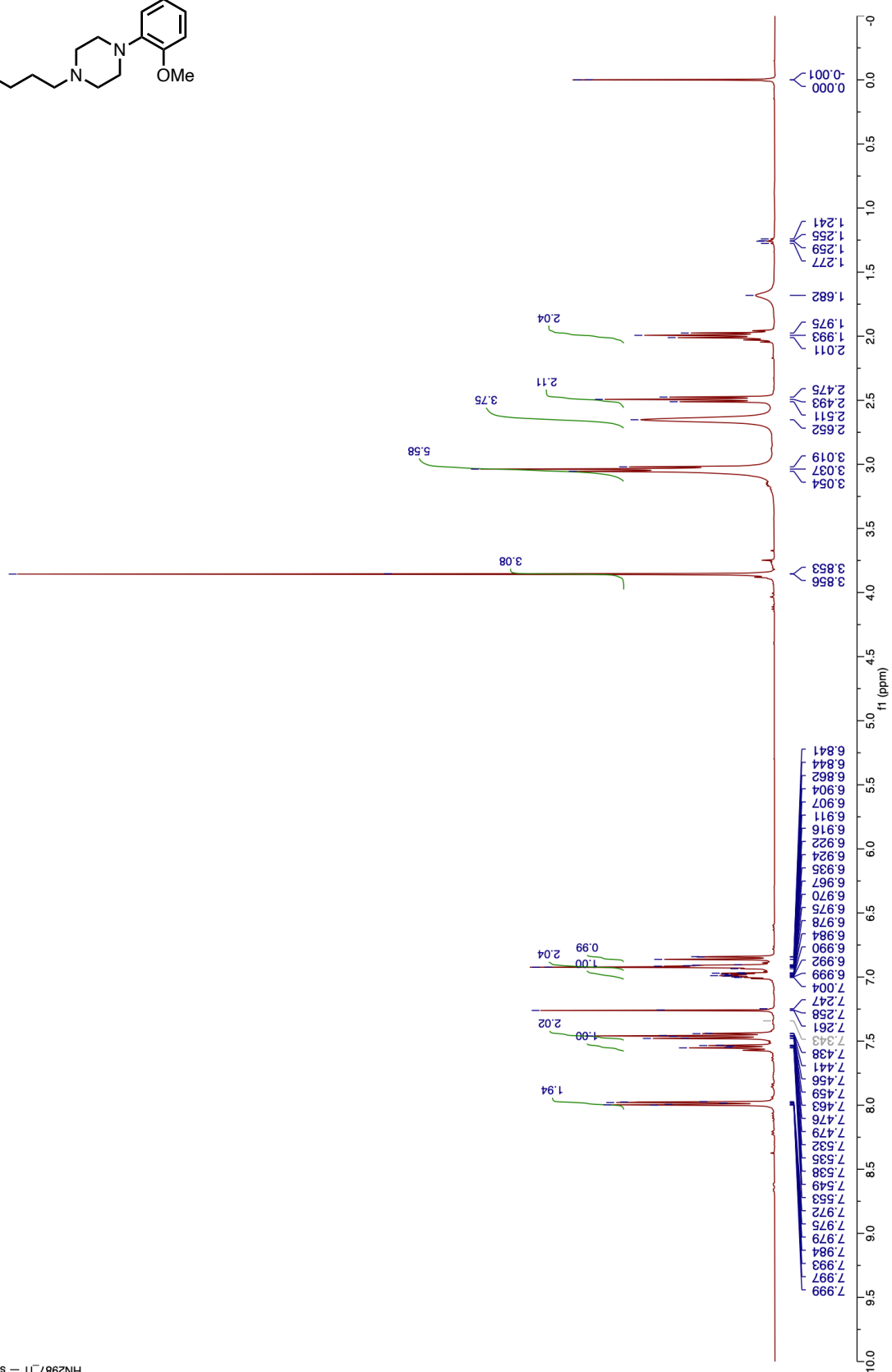
HN2983 — single pulse decoupled gated NOE



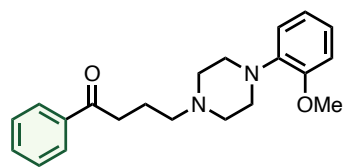
^1H NMR of **11a** (400 MHz, CDCl_3)



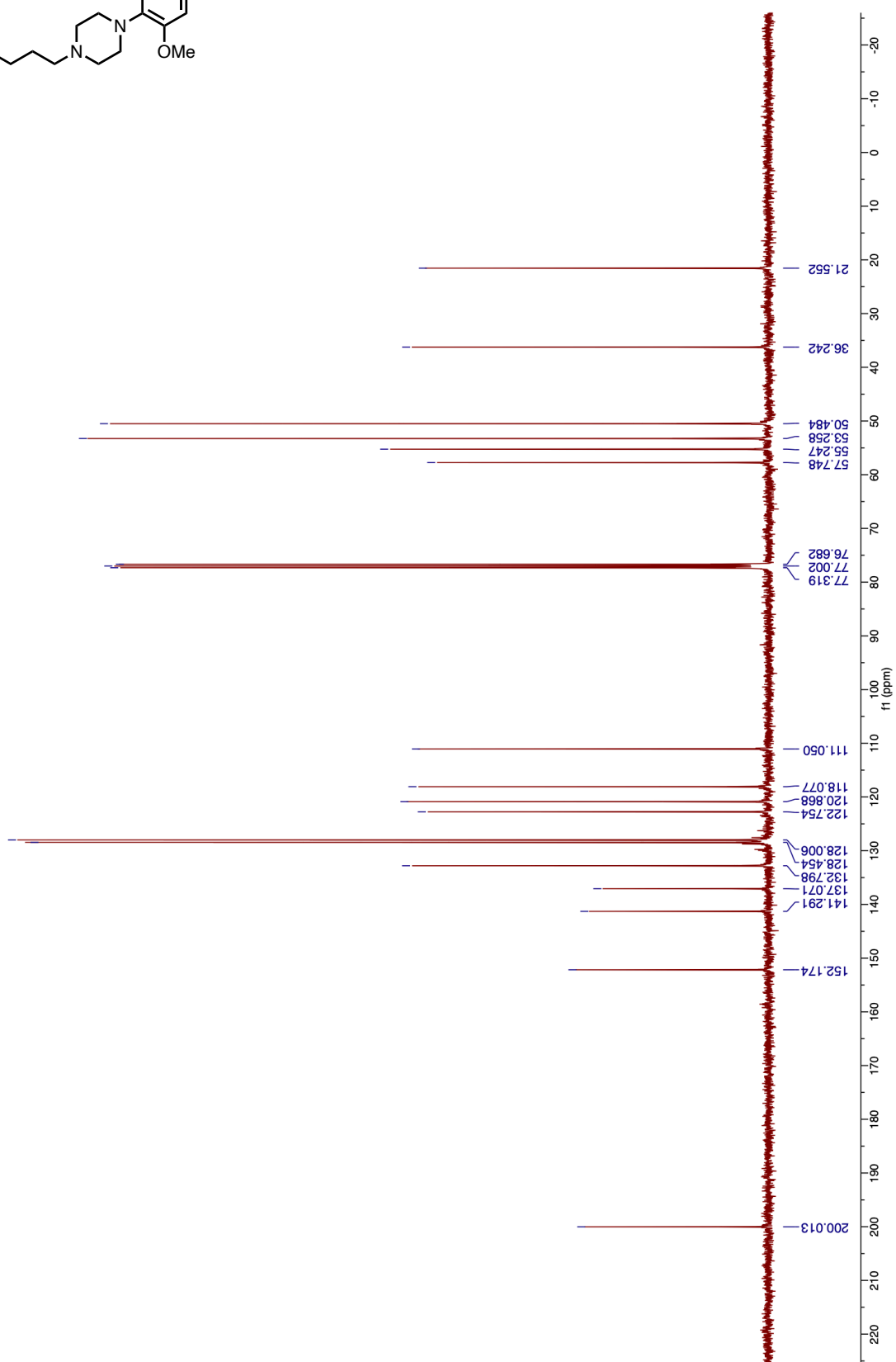
HN2987.f1 - single-pulse



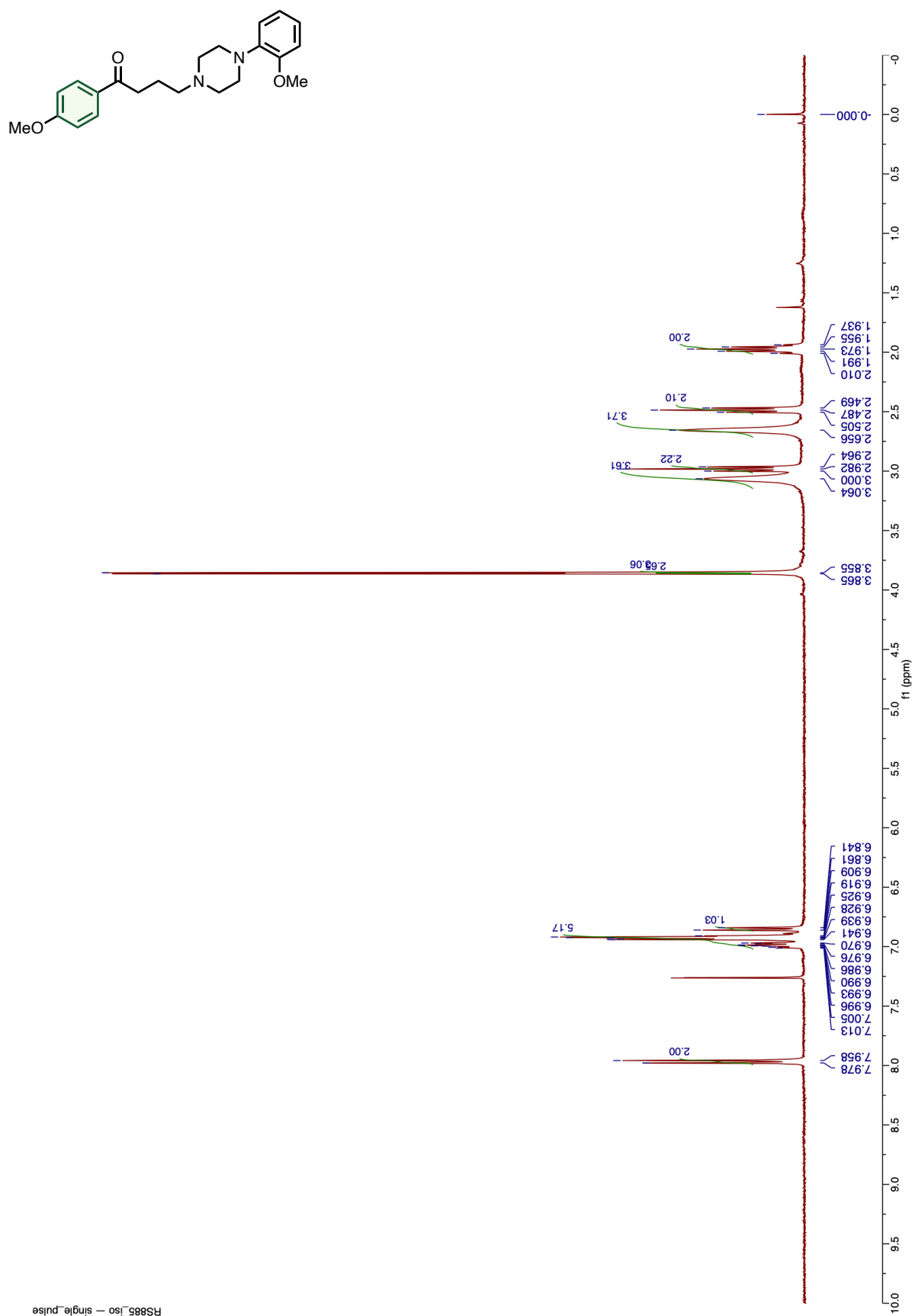
^{13}C NMR of **11a** (101 MHz, CDCl_3)



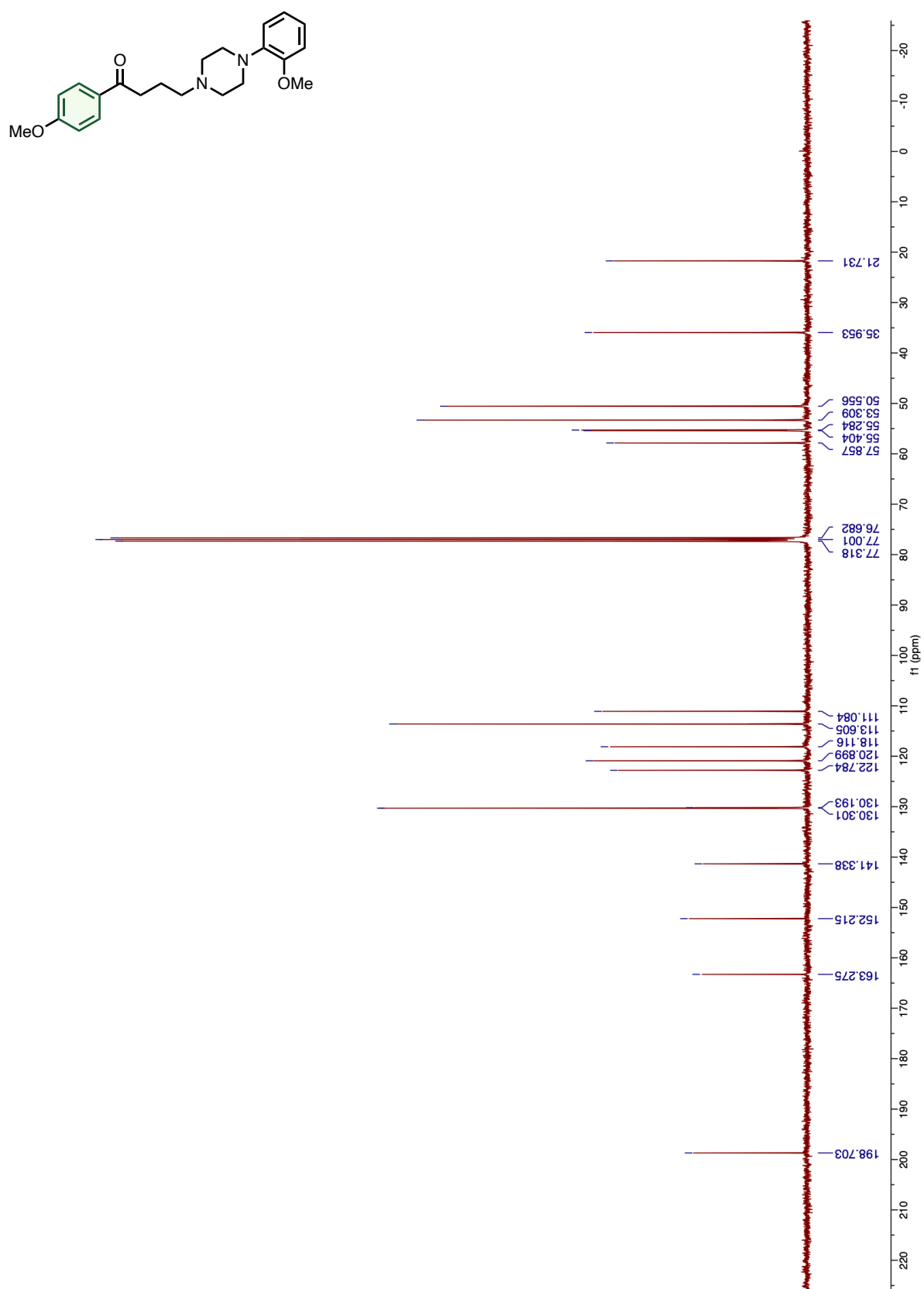
HN2987.f — single pulse decoupled gated NOE



^1H NMR of **11b** (400 MHz, CDCl_3)

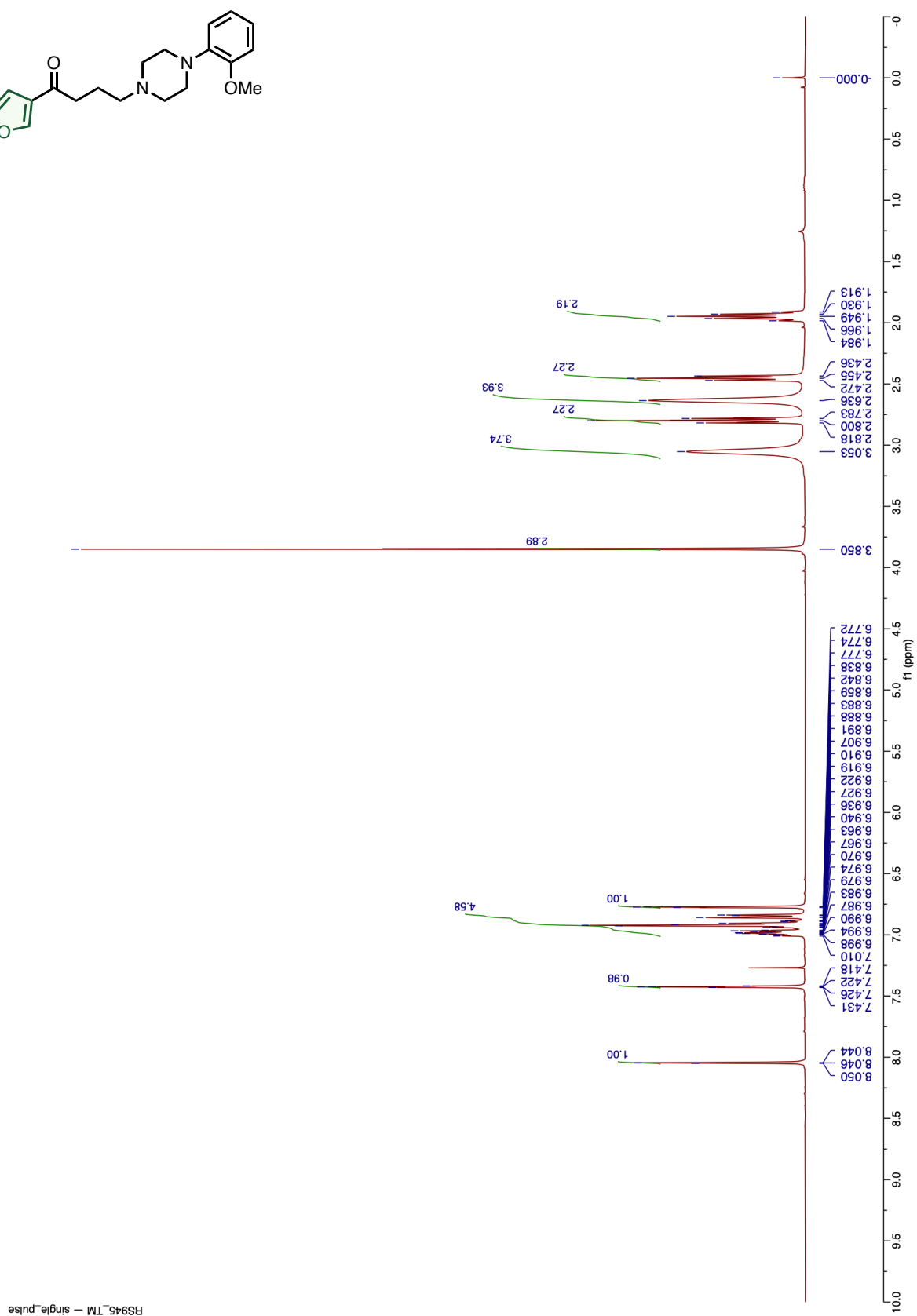
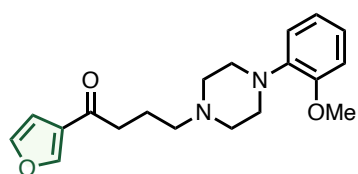


^{13}C NMR of **11b** (101 MHz, CDCl_3)



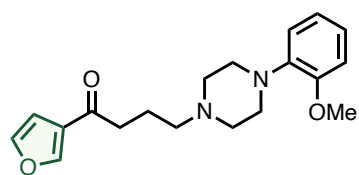
RS885_iso — 消さないでください single pulse decoupled gated NOE

¹H NMR of **11c** (400 MHz, CDCl₃)

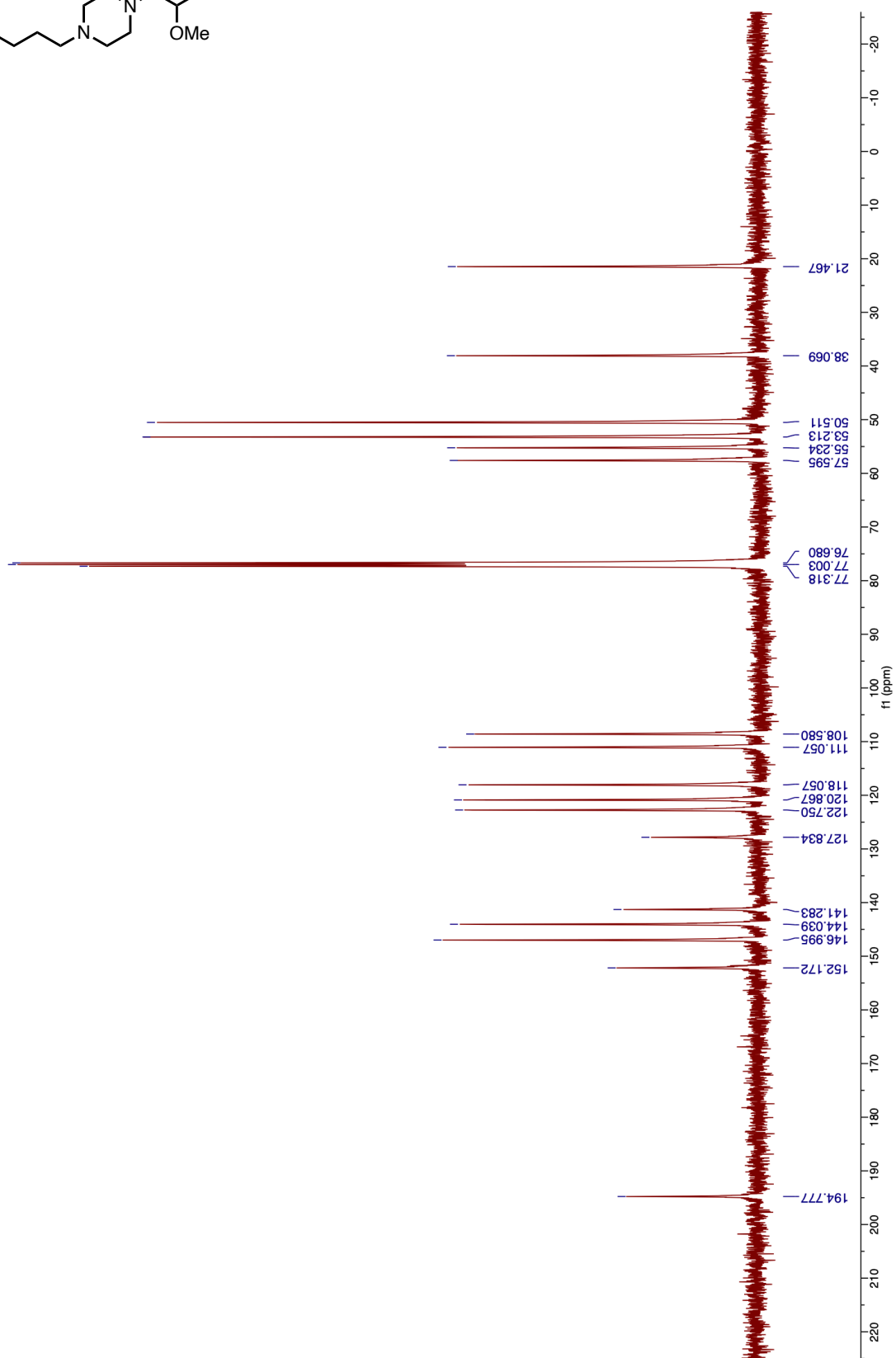


RS945_TM — single-pulse

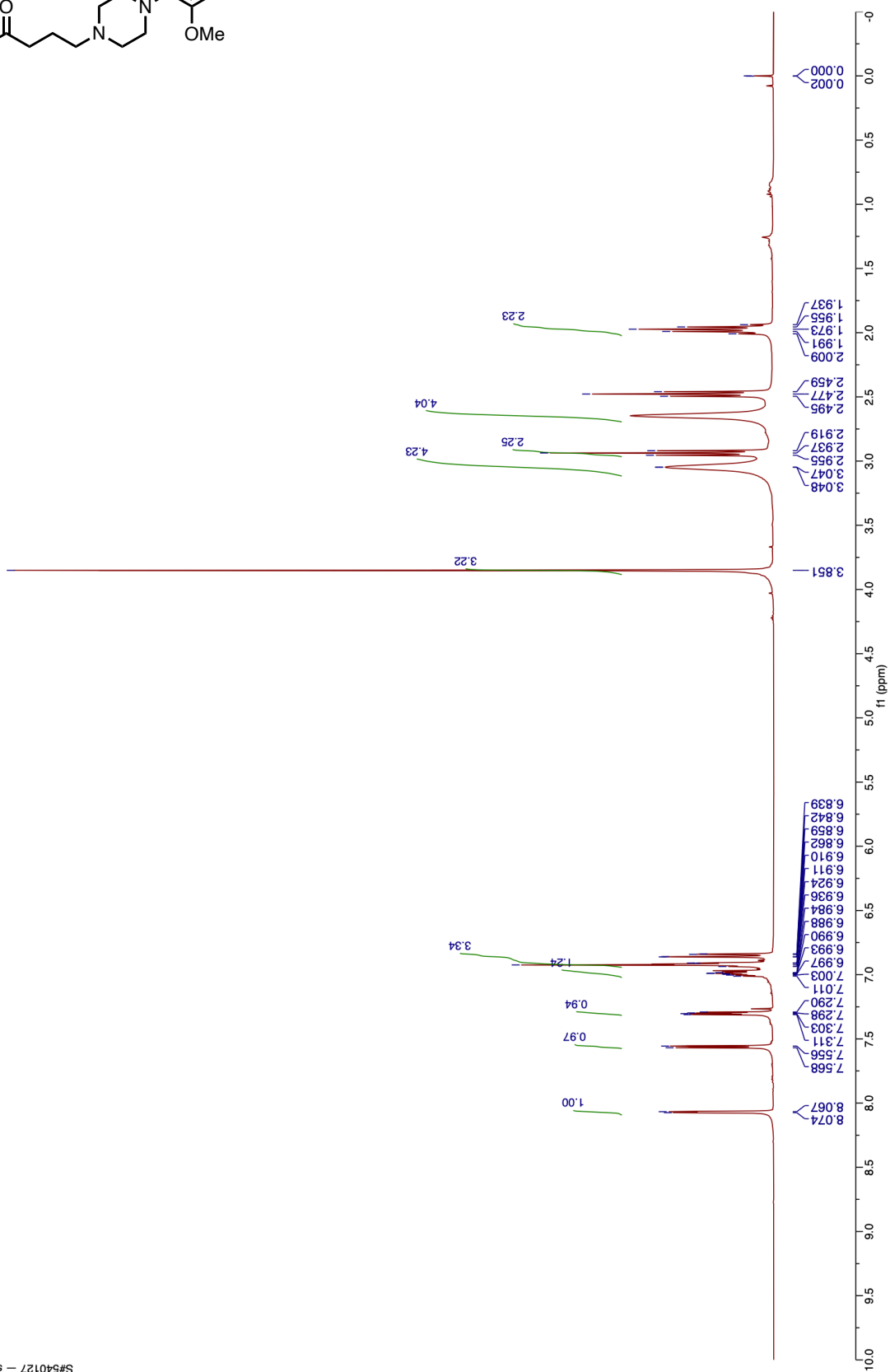
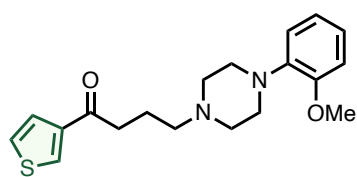
^{13}C NMR of **11c** (101 MHz, CDCl_3)



RS945_TM_13C -- single pulse decoupled gated NOE

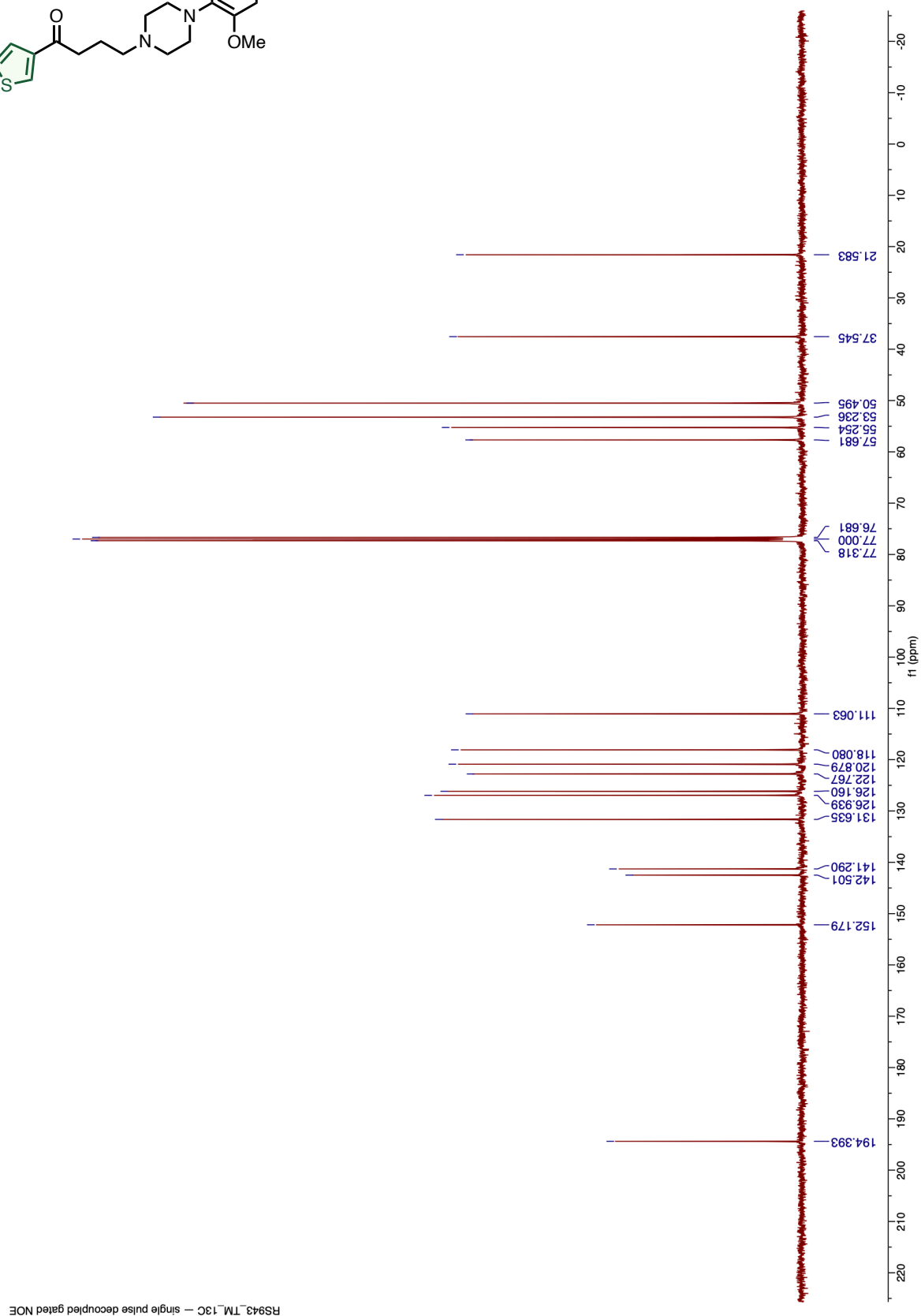
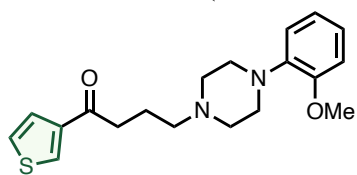


^1H NMR of **11d** (400 MHz, CDCl_3)



S#540127 — single-pulse

^{13}C NMR of **11d** (101 MHz, CDCl_3)



RS943_TM_13C -- single pulse decoupled gated NOE