Supporting Information

Novel Linker Variants of Antileishmanial / Antitubercular 7-Substituted 2-Nitroimidazooxazines Offer Enhanced Solubility

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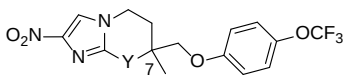
Table S1. Complete *in vitro* antiparasitic and antitubercular data for the compounds of Table 1 (all data for **8**, **10**, **59** and **60** from ref S1; all data for **11** and **12** from ref S2).

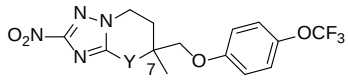
Compd	IC_{50} (μM)[a,b]				Select.	MIC_{90} (μM)[b,d]	
	L. infantum	*T. cruzi*	*T. brucei*	MRC-5	Index[c]	MABA	LORA
10	0.047 ± 0.021[e]	0.061 ± 0.028[f]	>64	>64	>1362	5.2 ± 2.6[g]	4.7 ± 2.6[h]
8	0.13 ± 0.05[e]	0.14 ± 0	>64	>64	>492	0.94 ± 0.04	6.8 ± 3.1[f]
11	0.13 ± 0.07[f]	0.18 ± 0.05	>64	>64	>492	0.86 ± 0.10	7.0 ± 5.1
12	0.45 ± 0.05[f]	0.45 ± 0.15	>64	>64	>142	1.3 ± 0.4	5.0 ± 3.2
15	0.15 ± 0.02[f]	0.45 ± 0.03	>64	>64	>427	1.7 ± 0.3	10 ± 6
18	0.18 ± 0.07[i]	0.50 ± 0.29	>64	>64	>356	0.17 ± 0.07	8.1 ± 5.0
20	0.29 ± 0.07[f]	0.45 ± 0.24	>64	>64	>221	0.65 ± 0.21	10 ± 6
22	0.93 ± 0.54	1.2 ± 0.3	>64	>64	>69	7.2 ± 3.2	36 ± 5
24	0.22 ± 0.02[f]	1.1 ± 0.5[f]	>64	>64	>291	0.11 ± 0.01	6.5 ± 3.9[f]
26	0.27 ± 0.02[f]	0.65 ± 0.32[f]	23 ± 0	52 ± 18[f]	193	0.091 ± 0.034	6.9 ± 3.8
28	0.31 ± 0.02[f]	0.51 ± 0.08	>64	>64	>206	0.23 ± 0.02	3.9 ± 2.6[f]
30	0.48 ± 0.19	0.59 ± 0.34	>64	>64	>133	1.3 ± 0.4	8.2 ± 6.2
35	2.2 ± 0.5	4.2 ± 0.4	>64	>64	>29	12 ± 0	31 ± 10
40	0.13 ± 0	0.55 ± 0.02	>64	>64	>492	0.24 ± 0.01	7.1 ± 0.8
43	1.5 ± 0.8[f]	3.8 ± 1.2	56 ± 5[f]	>64	>43	(2.2)	(31)
44	1.4 ± 0.1	6.1 ± 0.6	59 ± 5	>64	>46	(2.5)	(32)
45	1.3 ± 0.2	4.4 ± 0.9	>64	>64	>49	0.82 ± 0.16	22 ± 9
46	9.9 ± 3.6	2.7 ± 0.8	>64	>64	>6.5	(31)	(54)
47	2.0 ± 0.1	6.5 ± 2.5	>64	>64	>32	1.8 ± 0.1	12 ± 1
48	1.7 ± 0.5	20 ± 11	>64	>64	>38	3.9 ± 0.3	14 ± 2
49	3.3 ± 1.2	3.6 ± 0.9	1.4 ± 0.7[f]	>64	>19	0.61 ± 0.20[f]	3.8 ± 0
51	1.4 ± 0	2.8 ± 0.1	9.2 ± 1.6	40 ± 12	29	0.82 ± 0.13	8.6 ± 1.9
53	1.8 ± 0.3	4.0 ± 0.3	36 ± 6	>64	>36	0.90 ± 0	19 ± 5
55	0.16 ± 0.02	1.8 ± 0.4	>64	>64	>400	0.90 ± 0.07	5.3 ± 0.1
57	2.2 ± 1.0	3.8 ± 1.4	>64	>64	>29	0.88 ± 0.06	14 ± 2
58	2.0 ± 0.1	2.0 ± 0.4	>64	>64	>32	5.5 ± 1.1	24 ± 2
59	0.12 ± 0.05[g]	1.2 ± 0.7[f]	>64	>64	>533	1.0 ± 0.5[f]	7.5 ± 3.4[f]
60	0.30 ± 0.07[f]	0.75 ± 0.41[f]	>64	>64	>213	0.55 ± 0.23[f]	3.3 ± 1.7[f]
64	0.49 ± 0.04	2.2 ± 0.5	46 ± 18	>64	>131	0.55 ± 0.30	3.7 ± 0.1
65	0.36 ± 0.22	0.88 ± 0.53	5.5 ± 1.6[f]	>64	>178	0.58 ± 0.21	12 ± 3
66	0.36 ± 0.04	1.6 ± 0.3	33 ± 1[f]	>64	>178	0.34 ± 0.02	7.3 ± 0.4
68	0.14 ± 0.01	2.3 ± 0.8	19 ± 11	>64	>457	0.085 ± 0.036	1.0 ± 0.1
69	0.20 ± 0	4.3 ± 2.1	48 ± 16	>64	>320	0.39 ± 0.21	2.9 ± 0.6
70	0.64 ± 0.10	1.7 ± 0.1	>64	>64	>100	(3.6)	(37)
71	0.18 ± 0.03	2.8 ± 0.3	32 ± 8	>64	>356	0.94 ± 0.01	7.3 ± 0.1
72	0.32 ± 0	1.7 ± 0.1	>64	44 ± 20	138	1.8 ± 0	6.3 ± 0.3
73	0.79 ± 0	1.6 ± 0.1	8.0 ± 0.3	43 ± 21	54	2.8 ± 0.8	3.4 ± 0.1
74	1.3 ± 0.8	2.1 ± 0.1	8.2 ± 0.1	>64	>49	1.7 ± 0.2	46 ± 18

[a]IC_{50} values for inhibiting the growth of *Leishmania infantum* (in mouse macrophages), *Trypanosoma cruzi* (on MRC-5 cells), and *Trypanosoma brucei*, or for cytotoxicity toward human lung fibroblasts (MRC-5 cells). [b]Each value (except the single test MIC data in parentheses) is the mean of N=2 measurements (± SD), unless noted. [c]Selectivity index: ratio of MRC-5 to *L. inf* IC_{50} values. [d]MIC_{90} against *M. tb* under aerobic (MABA) or hypoxic (LORA) conditions. [e]N=7. [f]N=3. [g]N=4. [h]N=5. [i]N=6.

Table S2. Complete comparative *in vitro* antiparasitic and antitubercular data for some recently reported analogues of **8** (all data for **75** and **76** from ref S2).[S2,S3]



75–79



80

Compd	Y	IC_{50} (μM)[a,b]				MIC_{90} (μM)[b,c]	
		L. infantum	*T. cruzi*	*T. brucei*	MRC-5	MABA	LORA
8	O	0.13 ± 0.05[d]	0.14 ± 0	>64	>64	0.94 ± 0.04	6.8 ± 3.1[e]
75	O[f]	0.098 ± 0.049[g]	0.052 ± 0.001	>64	>64	0.59 ± 0.36	1.4 ± 0.2
76	O[h]	0.17 ± 0.09[i]	0.34 ± 0.03	>64	>64	3.6 ± 0.8	18 ± 12
77	S	62 ± 3[j]	0.46 ± 0.13[j]	>64	>64	0.54 ± 0.35[e]	4.3 ± 0.2
78	SO	41 ± 23[j]	2.4 ± 1.0[j]	18 ± 6	>64	(16)	(61)
79	SO_2	>64	0.69 ± 0.01	>64	>64	(12)	>128
80	O	>64	0.54 ± 0	33 ± 1	>64	(29)	>128

[a]IC_{50} values for inhibiting the growth of *Leishmania infantum* (in mouse macrophages), *Trypanosoma cruzi* (on MRC-5 cells), and *Trypanosoma brucei*, or for cytotoxicity toward human lung fibroblasts (MRC-5 cells). [b]Each value (except the single test MIC data in parentheses) is the mean of N=2 measurements (± SD), unless otherwise noted. [c]MIC_{90} against *M. tb* under aerobic (MABA) or hypoxic (LORA) conditions. [d]N=7. [e]N=3. [f](7*R*)-Enantiomer. [g]N=8. [h](7*S*)-Enantiomer. [i]N=6. [j]N=4.

Additional discussion

Following on from our observation (in the manuscript) that "across all 7-Me linker derivatives, the association between VL potency and effectiveness against TB was only moderate", we note that further SAR variances were encountered for a few heterocyclic analogues of **8** that we had recently studied[S3] for Chagas disease (**77**-**80**; Table S2). In particular, replacement of the oxygen atom in the oxazine ring of **8** by sulfur (**77**) led to a 477-fold reduction in potency against *L. inf*, compared to a 1.6- to 1.7-fold *increased* effectiveness against *Mycobacterium tuberculosis* (*M. tb*), although this latter activity was greatly reduced (14- to >30-fold) upon S-oxidation (**78** and **79**). However, switching the nitroimidazole ring to a nitrotriazole ring (**80**) was poorly tolerated for both VL and TB, as noted previously for other structurally related scaffolds.[S4,S5]

Table S3. Complete *in vivo* efficacy data for selected analogues in the *L. don* mouse model.

	In Vivo Efficacy Against *L. don* (% Parasite Load Reduction at Dose in mg/kg)[a]					
Compd	50	25	12.5	6.25	3.13	ED_{50} (95% C.I.)[b]
8		100 ± 0	100 ± 0	82.7 ± 8.0	25.1 ± 20.6	4.2 (3.7-4.6)
10		86.9 ± 5.9				
18	99.7 ± 0.2			29.5 ± 37.1		
26	58.3 ± 6.9					
44	70.6 ± 18.9					
51	36.0 ± 15.5					
66	99.95 ± 0.06	97.0 ± 3.4	7.1 ± 15.1			16.3 (14.5-18.4)
68		88.6 ± 7.5	40.4 ± 22.3			
69		51.0 ± 11.1	31.0 ± 8.4			

[a]Dosing was orally, once daily for 5 days consecutively; data are the mean percentage reduction of parasite burden in the liver (± standard deviation). [b]Dose in mg/kg required to achieve a mean 50% reduction in parasite burden (with 95% confidence interval).

Figure S1. Comparative *in vivo* efficacy of selected analogues against *L. don* in the VL mouse model (liver burden only): (a) 50 mg/kg and (b) 25 mg/kg.

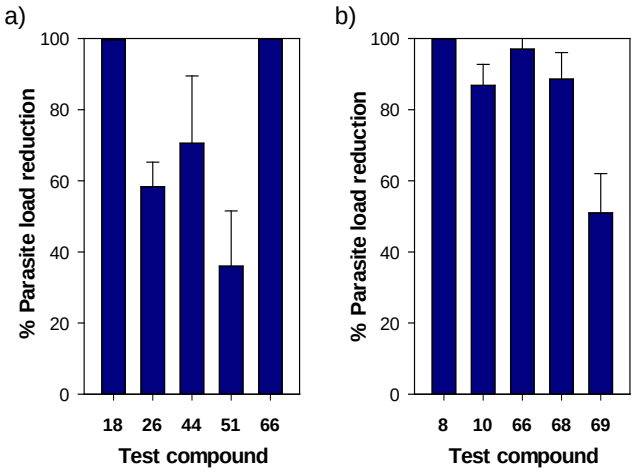
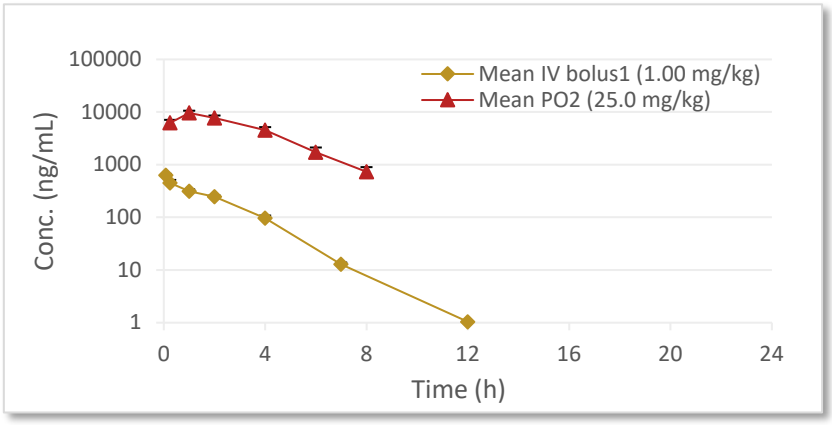


Figure S2. Plasma concentration-time profiles for **65** and **66** in BALB/c mice, following a single intravenous dose of 1 mg/kg or a single oral dose of 25 mg/kg in each case.

65



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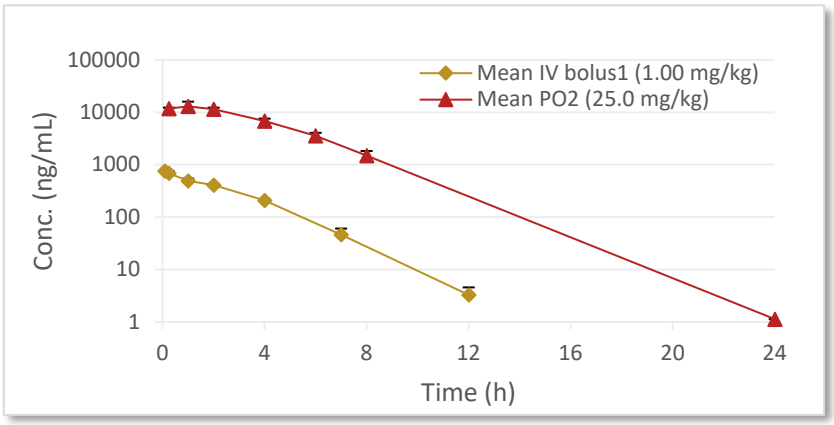
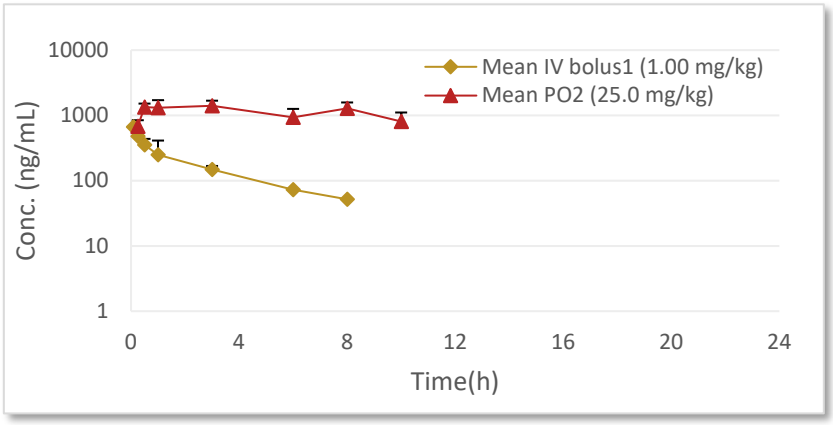


Figure S3. Plasma concentration-time profiles for **8** and **10** in Swiss Albino mice, following a single intravenous dose of 1 mg/kg or a single oral dose of 25 mg/kg in each case.

8



10

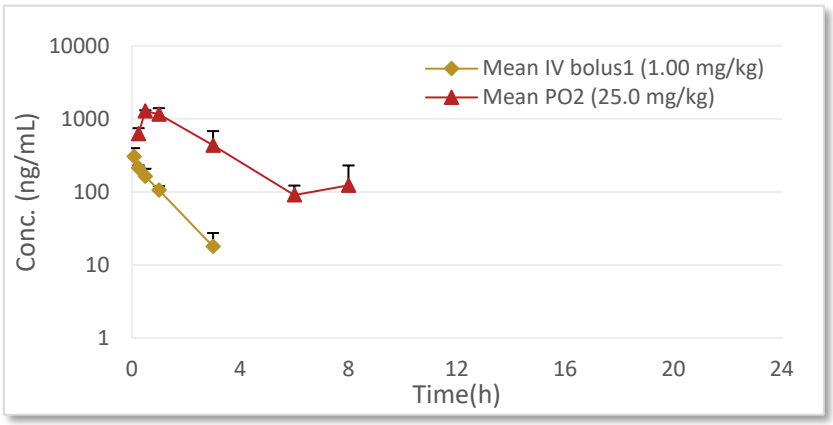
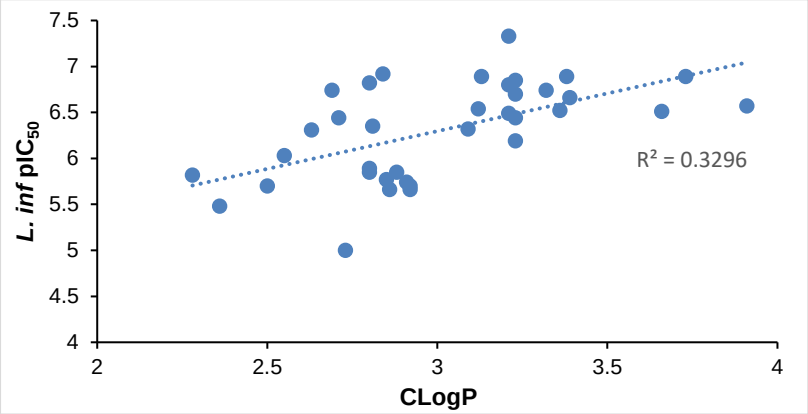
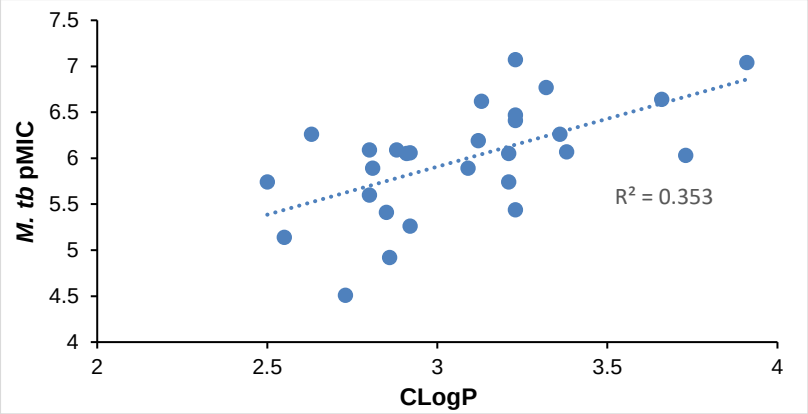


Figure S4. Effect of lipophilicity on potency against *L. inf* or *M. tb* for the compounds of Table 1.

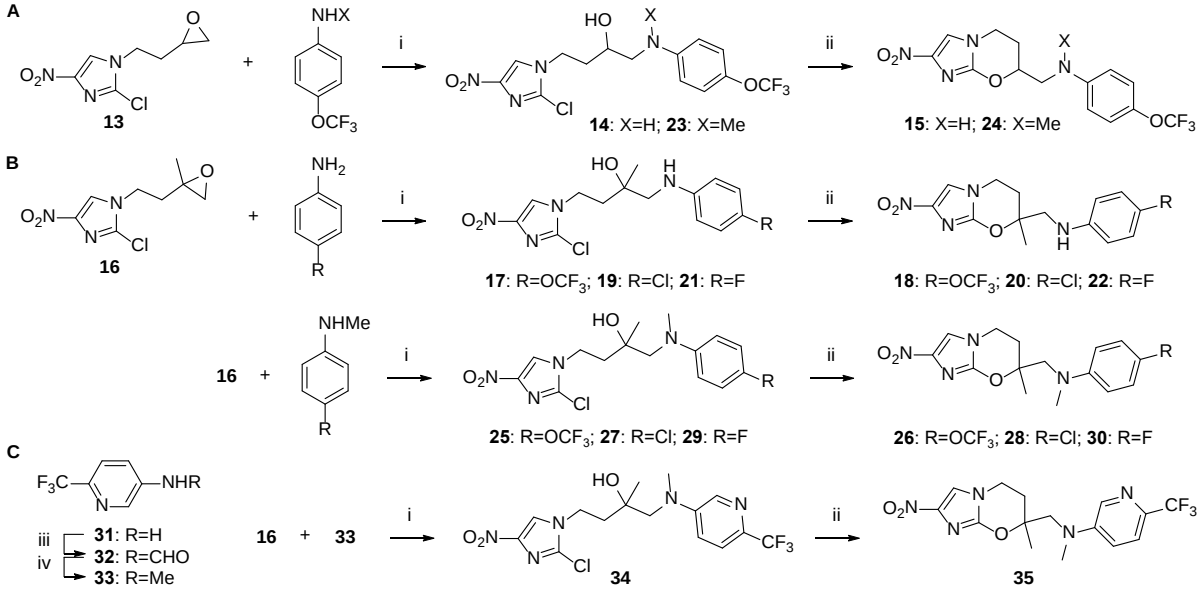
a) CLogP vs potency against *L. inf* (complete dataset)



b) CLogP vs potency against *M. tb* (MABA assay; 7-Me subset only)

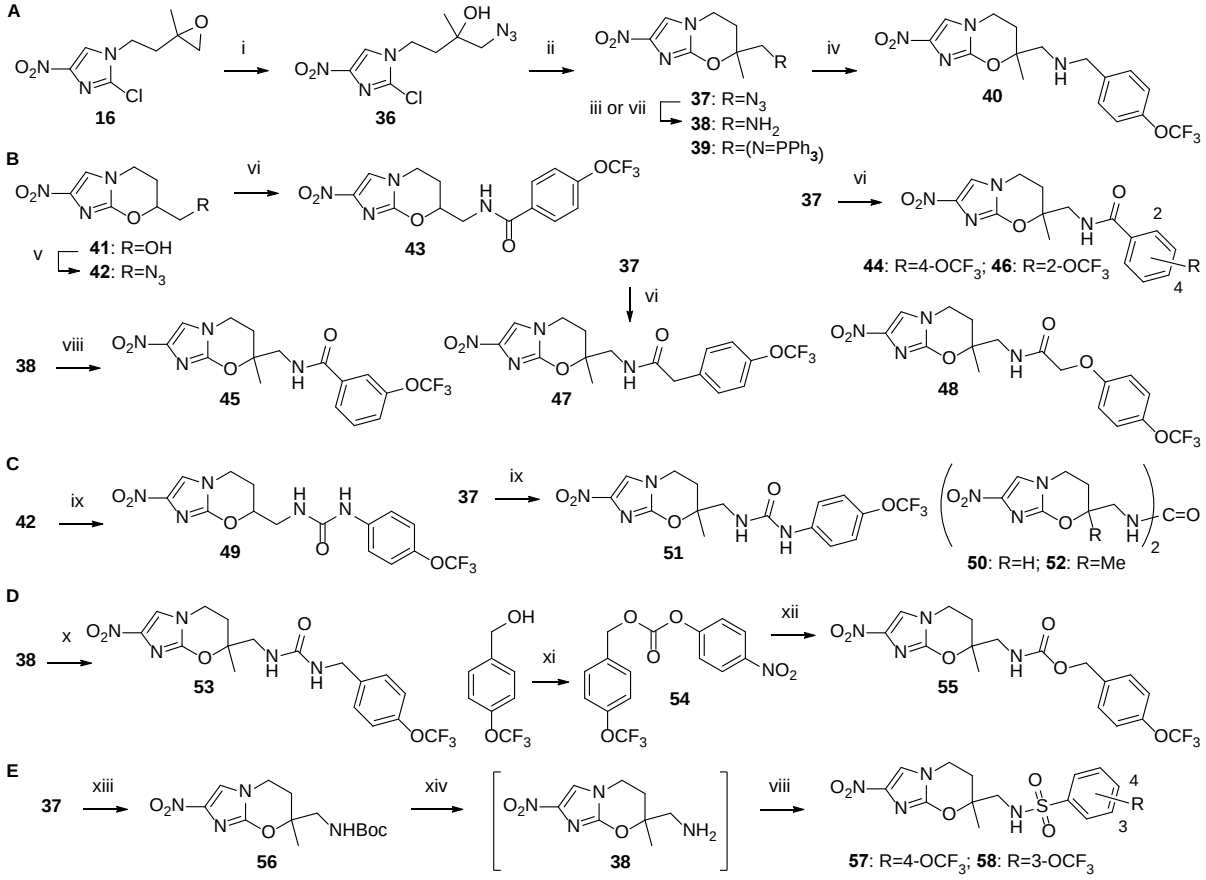


Scheme S1[a]



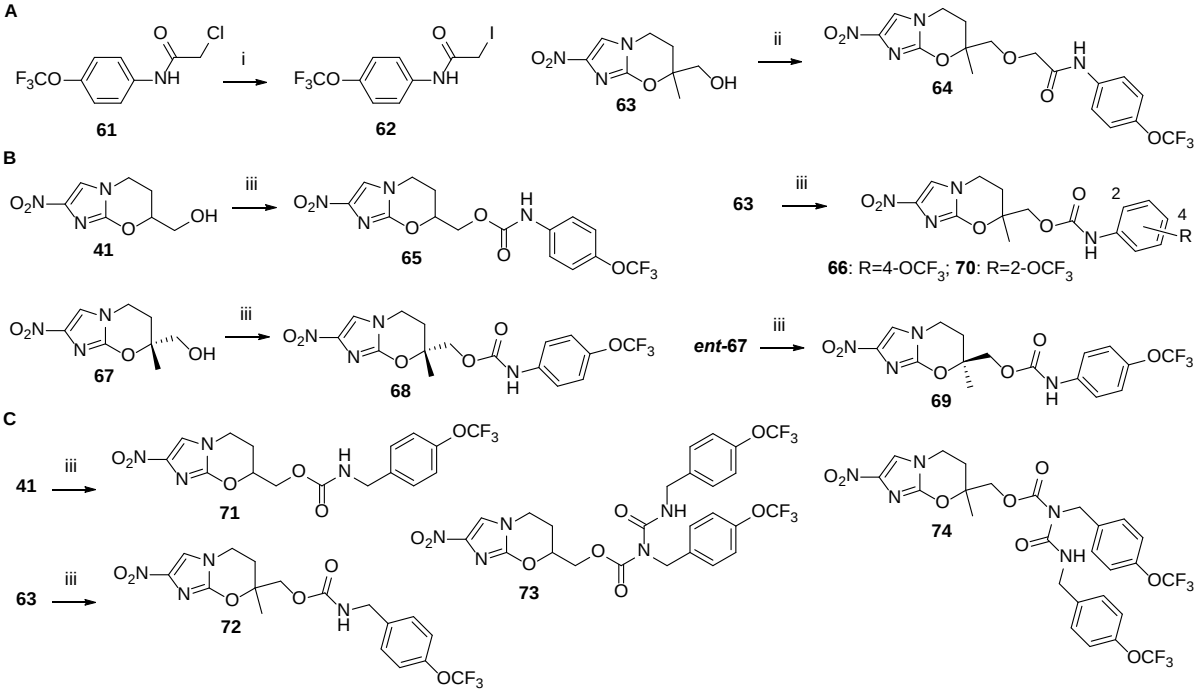
[a]Reagents and conditions: (i) $CoCl_2$, CH_3CN, 65-75 °C, 1-3 d (17-97%); (ii) NaH, DMF, 0-20 °C, 2-4.3 h (or 50-70 °C, 2-3 h) (9-63%); (iii) $HCOOH/Ac_2O$, THF, 20 °C, 23 h (97%); (iv) $Me_2S{\cdot}BH_3$, THF, 0-20 °C, 0.5 h, then 65 °C, 3.5 h (72%).

Scheme S2[a]



[a]Reagents and conditions: (i) NaN_3, CTAB, MeOH, 20 °C, 45 min, then 40 °C, 17 h (73%); (ii) NaH, DMF, 0-20 °C, 2.5 h (70%); (iii) PPh_3, aq dioxane, 12-20 °C, 1 d (**38**: 48%, **39**: 32%); (iv) 4-OCF_3PhCHO, $NaBH_3CN$, AcOH, DMF, 0-20 °C, 21 h (50%); (v) PPh_3, DEAD, DPPA, DMF, 0-20 °C, 45 h (83%); (vi) PPh_3, ArCOCl (or 4-OCF_3PhOCH_2COCl), CH_2Cl_2, 20 °C, 1.5-2.2 h (51-84%); (vii) $HS(CH_2)_3SH$, Et_3N, MeOH, CH_2Cl_2, 15-20 °C, 12 h (83%); (viii) 3-OCF_3PhCOCl or $RPhSO_2Cl$, DIPEA, DMF, 0-20 °C, 3-19 h (46-81%); (ix) PPh_3, 4-OCF_3PhNH_2, 2 M TEAB, dioxane, 12-20 °C, 35 h (14-17%); (x) 4-OCF_3BnNCO, DIPEA, $Bu_2Sn(OAc)_2$, DMF, 20 °C, 16 h (93%); (xi) 4-NO_2PhOCOCl, pyridine, CH_2Cl_2, 0-20 °C, 20 h (98%); (xii) **38**, DMAP, DIPEA, DMF, 20 °C, 44 h (71%); (xiii) PPh_3, Boc-ON, CH_2Cl_2, 0-20 °C, 1 d (67%); (xiv) TFA, CH_2Cl_2, 20 °C, 7 h (100%).

Scheme S3[a]



[a]Reagents and conditions: (i) NaI, acetone, 56 °C, 2 h, then 20 °C, 15 h (96%); (ii) **62**, NaH, DMF, 0-20 °C, 80 min (4%); (iii) ArNCO, CuCl, DMF, 20 °C, 32-52 h (44-98%).

Experimental Section

Combustion analyses were executed by the Campbell Microanalytical Laboratory, University of Otago, Dunedin, New Zealand. Melting points were measured using an Electrothermal IA9100 melting point apparatus and are as read. NMR spectra were recorded on a Bruker Avance 400 spectrometer at 400 MHz for ^{1}H and 100 MHz for ^{13}C and were referenced to Me_4Si or solvent resonances. Chemical shifts and coupling constants were listed in units of ppm and hertz, respectively. High-resolution electrospray ionisation mass spectrometry (HRESIMS) was performed on a Bruker micrOTOF-Q II mass spectrometer or an Agilent 6530 Q-TOF mass spectrometer coupled to an Agilent 1200 series HPLC system. Low-resolution atmospheric pressure chemical ionisation (APCI) mass spectra were determined for organic solutions using either a ThermoFinnigan Surveyor MSQ mass spectrometer coupled to a Gilson autosampler or an Agilent 6120 Quadrupole LC/MS connected to an Agilent 1260 Infinity autosampler and quaternary pump. Optical rotations were measured on a Schmidt + Haensch Polartronic NH8 polarimeter. Column chromatography was carried out on silica gel (Merck 230-400 mesh) and thin-layer chromatography was completed on aluminum-backed silica gel plates (Merck 60 F_{254}), with visualization of components by UV light (254 nm), I_2, or $KMnO_4$ staining. Tested compounds (including batches screened *in vivo*) were ≥95% pure, as verified by combustion analysis and/or by HPLC performed on an Agilent 1100 system with diode array detection, using a 150 mm x 3.2 mm Altima 5 µm reversed phase C8 or C18 column. Combustion analyses indicated by the symbols of the elements were within ± 0.4% of the theoretical values.

General Procedure A: Synthesis of arylamino alcohols from epoxides (intermediates 14, 17, 19, 21, 23, 25, 27, 29 and 34)

A mixture of the epoxide (**13** or **16**, 600 mg, 1.0 equiv), aryl amine (1.2-2.4 equiv) and anhydrous cobalt(II) chloride (0.2-0.9 equiv) in anhydrous acetonitrile (10 mL) was stirred at 70 °C for 48 h. The resulting cooled mixture was added to ice-water (100 mL) and extracted with CH_2Cl_2 (5 x 100 mL). The combined extracts were evaporated to dryness under reduced pressure and the residue was chromatographed on silica gel (0-2% MeOH/CH_2Cl_2) to afford the required products.

General Procedure B: Ring closure of arylamino alcohols (target compounds 15, 18, 20, 22, 24, 26, 28, 30 and 35)

Sodium hydride (60% in mineral oil, 1.5 equiv) was added to a solution of the alcohol (**14**, **17**, **19**, **21**, **23**, **25**, **27**, **29**, or **34**, 1.0 equiv) in anhydrous DMF (1 mL/60 mg of alcohol) under N_2 at 0 °C. The mixture was quickly degassed and resealed under N_2 and then stirred at 20 °C for 4.3 h. The resulting mixture was rapidly cooled (CO_2/acetone), quenched with ice/aqueous $NaHCO_3$ (10 mL), added to brine (100 mL), and extracted with CH_2Cl_2 (6 x 100 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was repeatedly chromatographed on silica gel (CH_2Cl_2 or 0-2% MeOH/CH_2Cl_2 or 33-67% Et_2O/petroleum ether and Et_2O or 0-50% EtOAc/petroleum ether) as necessary to afford the required products.

General Procedure C: Direct synthesis of amides from azides (target compounds 43, 44, and 46-48)

A solution of triphenylphosphine (1.2 equiv) in anhydrous CH_2Cl_2 (2 x 0.5 mL) was added dropwise to a stirred mixture of the azide (**37** or **42**, 120 mg, 1.0 equiv) and the acid chloride (2.0 equiv) in anhydrous CH_2Cl_2 (3 mL) under N_2. The mixture was stirred at 20 °C for 100

min, then added to ice/aq $NaHCO_3$ (50 mL), and extracted with CH_2Cl_2 (4 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel (0-75% EtOAc/petroleum ether and EtOAc) to afford the required products.

General Procedure D: Direct synthesis of ureas from azides (target compounds 49 and 51)

A fresh solution of triethylammonium bicarbonate (~2 M, 3.3 equiv) and triphenylphosphine (1.8 equiv) were successively added to a mixture of the azide (**37** or **42**, 1.0 equiv) and 4-(trifluoromethoxy)aniline (1.3-3.0 equiv) in dioxane (1 mL/14 mg of azide) at 12 °C. The mixture was stirred at 20 °C for 35 h in a sealed vial, then transferred to a flask (in $MeOH/CH_2Cl_2$) and evaporated to dryness under reduced pressure (at 30 °C). The residue was chromatographed on silica gel (0-10% $MeOH/CH_2Cl_2$) to afford the required products.

General Procedure E: Synthesis of sulfonamides from the Boc-protected amine (target compounds 57 and 58)

Trifluoroacetic acid (1.2 mL) was added to a stirred suspension of Boc derivative **56** (58 mg, 1.0 equiv) in anhydrous CH_2Cl_2 (1.2 mL). The resulting solution was stirred at 20 °C for 7 h in a sealed vial and then the solvents were removed under a stream of N_2 gas. The oily residue was treated with sodium carbonate (10 equiv) in MeOH (3 mL), stirring at 20 °C for 3 min, then transferred to a flask (in $MeOH/CH_2Cl_2$) and evaporated to dryness under reduced pressure (at 30 °C). The residue was chromatographed on silica gel (0-8% $MeOH/CH_2Cl_2$) to afford amine **38** as a hygroscopic yellow oil. This oil was evaporated twice from toluene, then dissolved in anhydrous DMF (2 mL), sealed under N_2, and cooled in ice. *N*,*N*-Diisopropylethylamine (5.3 equiv) and the required arylsulfonyl chloride (3.2 equiv) were successively added (dropwise with stirring), and the mixture was stirred at 20 °C for 3 h, then quenched with ice/aqueous $NaHCO_3$ (50 mL) and extracted with CH_2Cl_2 (5 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel (0-0.5% $MeOH/CH_2Cl_2$) to afford the required products.

General Procedure F: Synthesis of O-carbamates from alcohols (target compounds 65, 66 and 68-74)

The aryl isocyanate (1.6 equiv) was added to a solution of the alcohol (**41**, **63**, **67**, or *ent*-**67**, 1.0 equiv) in anhydrous DMF (1 mL/80 mg of alcohol) under N_2. Copper(I) chloride (0.1-0.2 equiv) was added and the mixture was quickly degassed and resealed under N_2 and then stirred at 20 °C for 33 h. The resulting mixture was diluted with ice-water (5 mL) and then added to brine (50 mL) and extracted with CH_2Cl_2 (6 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel (0-10% $EtOAc/CH_2Cl_2$) to afford the required products.

Syntheses of arylamino derivatives 15-35 (Scheme 1)

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-1-{[4-(trifluoromethoxy)phenyl]amino}butan-2-ol (14). Reaction of 2-chloro-4-nitro-1-[2-(oxiran-2-yl)ethyl]-1*H*-imidazole[S1] (**13**) (216 mg, 0.992 mmol), 4-(trifluoromethoxy)aniline (316 mg, 1.78 mmol) and anhydrous cobalt(II) chloride (100 mg, 0.770 mmol), using General Procedure A, gave **14** (303 mg, 77%) as a yellow oil; ^{1}H NMR [$(CD_3)_2SO$] δ 8.55 (s, 1 H), 7.03 (br d, J = 8.5 Hz, 2 H), 6.61 (br d, J =

9.0 Hz, 2 H), 5.83 (br t, *J* = 5.7 Hz, 1 H), 5.04 (d, *J* = 5.3 Hz, 1 H), 4.25-4.10 (m, 2 H), 3.72-3.55 (m, 1 H), 3.04 (ddd, *J* = 13.6, 6.3, 6.0 Hz, 1 H), 2.99 (ddd, *J* = 13.7, 6.5, 6.0 Hz, 1 H), 2.09-1.97 (m, 1 H), 1.89-1.73 (m, 1 H); APCI MS calcd for $C_{14}H_{14}Cl_2F_3N_4O_4$ *m*/*z* $[M + Cl]^-$ 431, 429, found 431, 429.

***N*-[(2-Nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-4-(trifluoromethoxy)aniline (15).** Reaction of alcohol **14** (302 mg, 0.765 mmol) and NaH (48 mg, 1.20 mmol), using General Procedure B at 20 °C for 2 h, gave **15** (26 mg, 9%) as a pale yellow solid: mp 181-183 °C; ^{1}H NMR $[(CD_3)_2SO]$ δ 8.06 (s, 1 H), 7.07 (br d, *J* = 8.3 Hz, 2 H), 6.71 (br d, *J* = 9.0 Hz, 2 H), 6.23 (br t, *J* = 6.2 Hz, 1 H), 4.69-4.60 (m, 1 H), 4.15 (ddd, *J* = 12.6, 5.8, 2.6 Hz, 1 H), 4.05 (ddd, *J* = 12.5, 11.3, 5.0 Hz, 1 H), 3.49-3.35 (m, 2 H), 2.33-2.23 (m, 1 H), 2.12-1.99 (m, 1 H). Anal. ($C_{14}H_{13}F_3N_4O_4$) C, H, N (see Table S4).

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-2-methyl-1-{[4-(trifluoromethoxy)phenyl]-amino}butan-2-ol (17). Reaction of 2-chloro-1-[2-(2-methyloxiran-2-yl)ethyl]-4-nitro-1*H*-imidazole[S1] (**16**) (600 mg, 2.59 mmol), 4-(trifluoromethoxy)aniline (460 µL, 3.43 mmol), and anhydrous cobalt(II) chloride (70.7 mg, 0.545 mmol), using General Procedure A at 68 °C, gave **17** (887 mg, 84%) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.79 (s, 1 H), 7.06 (br d, *J* = 8.9 Hz, 2 H), 6.66 (br d, *J* = 9.0 Hz, 2 H), 4.32-4.16 (m, 2 H), 3.98 (br t, *J* = 6.7 Hz, 1 H), 3.19 (dd, *J* = 13.2, 7.3 Hz, 1 H), 3.13 (dd, *J* = 13.1, 6.0 Hz, 1 H), 2.13 (ddd, *J* = 13.8, 9.7, 6.2 Hz, 1 H), 1.98 (ddd, *J* = 13.5, 10.0, 6.2 Hz, 1 H), 1.88 (br s, 1 H), 1.37 (s, 3 H); HRESIMS calcd for $C_{15}H_{16}ClF_3N_4NaO_4$ *m*/*z* $[M + Na]^+$ 433.0680, 431.0704, found 433.0668, 431.0691.

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-4-(trifluoromethoxy)aniline (18).** Reaction of alcohol **17** (886 mg, 2.17 mmol) and NaH (131 mg, 3.28 mmol), using General Procedure B, gave **18** (143 mg, 18%) as a light yellow solid: mp (CH_2Cl_2/pentane) 149-150 °C; ^{1}H NMR $[(CD_3)_2SO]$ δ 8.06 (s, 1 H), 7.04 (br d, *J* = 8.3 Hz, 2 H), 6.75 (br d, *J* = 9.1 Hz, 2 H), 6.11 (br t, *J* = 6.5 Hz, 1 H), 4.16 (ddd, *J* = 13.0, 5.9, 4.7 Hz, 1 H), 4.08 (ddd, *J* = 13.1, 9.7, 5.3 Hz, 1 H), 3.38 (d, *J* = 6.5 Hz, 2 H), 2.26 (ddd, *J* = 14.4, 9.7, 6.1 Hz, 1 H), 2.08 (dt, *J* = 14.2, 4.9 Hz, 1 H), 1.40 (s, 3 H); ^{13}C NMR $[(CD_3)_2SO]$ δ 148.2, 147.4, 142.2, 138.4 (q, $J_{C\text{-}F}$ = 1.9 Hz), 121.9 (2 C), 120.3 (q, $J_{C\text{-}F}$ = 254.0 Hz), 117.7, 112.5 (2 C), 82.5, 50.6, 39.5, 27.2, 21.6. Anal. ($C_{15}H_{15}F_3N_4O_4$) C, H, N (see Table S4).

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-1-[(4-chlorophenyl)amino]-2-methylbutan-2-ol (19). Reaction of epoxide **16** (152 mg, 0.656 mmol), 4-chloroaniline (110 mg, 0.862 mmol), and anhydrous cobalt(II) chloride (58.3 mg, 0.449 mmol), using General Procedure A at 65 °C for 33 h, gave **19** (186 mg, 79%) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.78 (s, 1 H), 7.15 (br d, *J* = 8.9 Hz, 2 H), 6.61 (br d, *J* = 8.9 Hz, 2 H), 4.32-4.16 (m, 2 H), 3.92 (br t, *J* = 5.9 Hz, 1 H), 3.17 (dd, *J* = 13.4, 7.2 Hz, 1 H), 3.12 (dd, *J* = 13.3, 5.7 Hz, 1 H), 2.12 (ddd, *J* = 13.8, 9.6, 6.1 Hz, 1 H), 1.98 (ddd, *J* = 13.7, 9.8, 6.5 Hz, 1 H), 1.88 (s, 1 H), 1.36 (s, 3 H); HRESIMS calcd for $C_{14}H_{16}Cl_2N_4NaO_3$ *m*/*z* $[M + Na]^+$ 385.0441, 383.0465, 381.0492, found 385.0429, 383.0453, 381.0482.

4-Chloro-*N*-[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]aniline (20). Reaction of alcohol **19** (184 mg, 0.512 mmol) and NaH (32.0 mg, 0.800 mmol), using General Procedure B at 20 °C for 3.5 h, gave **20** (25 mg, 15%) as a yellow-orange solid: mp (CH_2Cl_2/pentane) 179-182 °C; ^{1}H NMR $[(CD_3)_2SO]$ δ 8.06 (s, 1 H), 7.07 (br d, *J* = 8.9 Hz, 2 H), 6.71 (br d, *J* = 8.9 Hz, 2 H), 6.03 (br t, *J* = 6.5 Hz, 1 H), 4.15 (ddd, *J* = 13.1, 5.9, 4.7 Hz, 1 H), 4.07 (ddd, *J* = 13.0, 9.7, 5.4 Hz, 1 H), 3.36 (d, *J* = 6.5 Hz, 2 H), 2.24 (ddd, *J* = 14.2, 9.8, 6.0 Hz, 1 H), 2.07 (dt, *J* = 14.4, 4.9 Hz, 1 H), 1.39 (s, 3 H). Anal. ($C_{14}H_{15}ClN_4O_3$) C, H, N (see Table S4).

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-1-[(4-fluorophenyl)amino]-2-methylbutan-2-ol (21). Reaction of epoxide **16** (150 mg, 0.648 mmol), 4-fluoroaniline (85 µL, 0.897 mmol), and anhydrous cobalt(II) chloride (49.3 mg, 0.380 mmol), using General Procedure A at 67 °C for 37 h, gave **21** (189 mg, 85%) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.79 (s, 1 H), 6.91 (br dd, *J* = 8.9, 8.5 Hz, 2 H), 6.64 (br dd, *J* = 9.0, 4.3 Hz, 2 H), 4.32-4.16 (m, 2 H), 3.79 (br s, 1 H), 3.15 (d, *J* = 13.0 Hz, 1 H), 3.11 (d, *J* = 13.1 Hz, 1 H), 2.12 (ddd, *J* = 13.7, 9.9, 5.9 Hz, 1 H), 2.02 (br s, 1 H), 1.98 (ddd, *J* = 13.7, 10.0, 6.3 Hz, 1 H), 1.36 (s, 3 H); HRESIMS calcd for $C_{14}H_{17}ClFN_4O_3$ *m*/*z* $[M + H]^+$ 345.0943, 343.0968, found 345.0942, 343.0967.

4-Fluoro-*N*-[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]aniline (22). Reaction of alcohol **21** (187 mg, 0.546 mmol) and NaH (30.0 mg, 0.750 mmol), using General Procedure B at 20 °C for 200 min, gave **22** (35 mg, 21%) as a yellow-orange solid: mp (CH_2Cl_2/pentane) 193 °C (dec); ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 1 H), 6.90 (br t, *J* = 8.9 Hz, 2 H), 6.69 (br dd, *J* = 9.1, 4.6 Hz, 2 H), 5.73 (br t, *J* = 6.6 Hz, 1 H), 4.15 (ddd, *J* = 13.0, 5.9, 4.8 Hz, 1 H), 4.07 (ddd, *J* = 13.1, 9.6, 5.4 Hz, 1 H), 3.33 (d, *J* = 6.6 Hz, 2 H), 2.26 (ddd, *J* = 14.4, 9.5, 6.1 Hz, 1 H), 2.07 (dt, *J* = 14.3, 5.0 Hz, 1 H), 1.40 (s, 3 H). Anal. ($C_{14}H_{15}FN_4O_3$) C, H, N (see Table S4).

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-1-{methyl[4-(trifluoromethoxy)phenyl]amino}-butan-2-ol (23). Reaction of epoxide **13** (192 mg, 0.882 mmol), *N*-methyl-4-(trifluoromethoxy)aniline (253 mg, 1.32 mmol), and anhydrous cobalt(II) chloride (98 mg, 0.755 mmol), using General Procedure A at 65 °C for 64 h, gave **23** (170 mg, 47%) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.83 (s, 1 H), 7.11 (br d, *J* = 9.2 Hz, 2 H), 6.78 (br d, *J* = 9.2 Hz, 2 H), 4.34-4.24 (m, 2 H), 3.91-3.82 (m, 1 H), 3.28 (dd, *J* = 14.6, 9.0 Hz, 1 H), 3.21 (dd, *J* = 14.5, 3.9 Hz, 1 H), 2.93 (s, 3 H), 2.46 (dd, *J* = 2.3, 1.7 Hz, 1 H), 2.07-1.95 (m, 1 H), 1.95-1.83 (m, 1 H); APCI MS calcd for $C_{15}H_{17}ClF_3N_4O_4$ *m*/*z* $[M + H]^+$ 411, 409, found 411, 409.

***N*-Methyl-*N*-[(2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-4-(trifluoromethoxy)aniline (24).** Reaction of alcohol **23** (169 mg, 0.413 mmol) and NaH (108 mg, 2.70 mmol), using General Procedure B at 20 °C for 2 h, gave **24** (98 mg, 63%) as a pale yellow solid: mp 141-143 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 1 H), 7.16 (br d, *J* = 8.5 Hz, 2 H), 6.82 (br d, *J* = 9.3 Hz, 2 H), 4.81-4.71 (m, 1 H), 4.14 (ddd, *J* = 12.6, 5.8, 2.4 Hz, 1 H), 4.03 (ddd, *J* = 12.4, 11.5, 5.0 Hz, 1 H), 3.77 (dd, *J* = 15.6, 4.0 Hz, 1 H), 3.67 (dd, *J* = 15.6, 7.6 Hz, 1 H), 3.01 (s, 3 H), 2.31-2.23 (m, 1 H), 2.10-1.97 (m, 1 H). Anal. ($C_{15}H_{15}F_3N_4O_4$) C, H, N (see Table S4).

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-2-methyl-1-{methyl[4-(trifluoromethoxy)phenyl]-amino}butan-2-ol (25). Reaction of epoxide **16** (400 mg, 1.73 mmol), *N*-methyl-4-(trifluoromethoxy)aniline (305 µL, 2.07 mmol), and anhydrous cobalt(II) chloride (50.3 mg, 0.387 mmol), using General Procedure A at 67 °C for 45 h, gave **25** (589 mg, 81%) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.78 (s, 1 H), 7.10 (br d, *J* = 9.2 Hz, 2 H), 6.83 (br d, *J* = 9.3 Hz, 2 H), 4.29 (ddd, *J* = 14.3, 9.9, 6.3 Hz, 1 H), 4.24 (ddd, *J* = 14.2, 9.6, 6.5 Hz, 1 H), 3.39 (d, *J* = 15.2 Hz, 1 H), 3.28 (d, *J* = 15.3 Hz, 1 H), 3.04 (s, 3 H), 2.07 (ddd, *J* = 13.6, 9.8, 6.1 Hz, 1 H), 1.97 (ddd, *J* = 13.6, 9.8, 6.4 Hz, 1 H), 1.89 (s, 1 H), 1.35 (s, 3 H); HRESIMS calcd for $C_{16}H_{18}ClF_3N_4NaO_4$ *m*/*z* $[M + Na]^+$ 447.0837, 445.0861, found 447.0829, 445.0851.

***N*-Methyl-*N*-[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-4-(trifluoromethoxy)aniline (26).** Reaction of alcohol **25** (585 mg, 1.38 mmol) and NaH (87 mg, 2.18 mmol), using General Procedure B for 4 h, gave **26** (247 mg, 46%) as a light yellow solid: mp (Et_2O/pentane triturate) 157-158 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 1 H), 7.14 (br d, *J* = 8.6 Hz, 2 H), 6.87 (br d, *J* = 9.3 Hz, 2 H), 4.14 (ddd, *J* = 13.0, 5.4, 4.6 Hz, 1 H), 4.06

(ddd, *J* = 13.1, 8.9, 6.6 Hz, 1 H), 3.71 (d, *J* = 16.2 Hz, 1 H), 3.67 (d, *J* = 16.3 Hz, 1 H), 2.98 (s, 3 H), 2.22-2.09 (m, 2 H), 1.36 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 148.9, 147.2, 142.2, 138.7 (q, J_{C-F} = 1.8 Hz), 121.8 (2 C), 120.3 (q, J_{C-F} = 254.0 Hz), 117.7, 112.5 (2 C), 84.4, 59.2, 40.2, 39.4, 27.3, 21.2. Anal. ($C_{16}H_{17}F_3N_4O_4$) C, H, N (see Table S4).

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-1-[(4-chlorophenyl)(methyl)amino]-2-methylbutan-2-ol (27). Reaction of epoxide **16** (281 mg, 1.21 mmol), 4-chloro-*N*-methylaniline (240 mg, 1.69 mmol), and anhydrous cobalt(II) chloride (101 mg, 0.778 mmol), using General Procedure A at 75 °C for 24 h, gave **27** (427 mg, 94%) as a yellow oil; ^{1}H NMR [$(CD_3)_2SO$] δ 8.55 (s, 1 H), 7.13 (br d, *J* = 9.1 Hz, 2 H), 6.78 (br d, *J* = 9.2 Hz, 2 H), 4.71 (s, 1 H), 4.23-4.13 (m, 2 H), 3.35-3.24 (m, 2 H), 2.95 (s, 3 H), 2.02-1.84 (m, 2 H), 1.13 (s, 3 H); APCI MS calcd for $C_{15}H_{18}Cl_3N_4O_3$ *m*/*z* $[M + Cl]^-$ 411, 409, 407, found 411, 409, 407.

4-Chloro-*N*-methyl-*N*-[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]aniline (28). Reaction of alcohol **27** (267 mg, 0.715 mmol) and NaH (57 mg, 1.43 mmol), using General Procedure B at 55 °C for 2 h, gave **28** (102 mg, 42%) as a yellow solid: mp 183-185 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 1 H), 7.17 (br d, *J* = 9.0 Hz, 2 H), 6.83 (br d, *J* = 9.1 Hz, 2 H), 4.13 (ddd, *J* = 12.9, 5.3, 4.8 Hz, 1 H), 4.06 (ddd, *J* = 13.1, 8.8, 6.7 Hz, 1 H), 3.73-3.62 (m, 2 H), 2.96 (s, 3 H), 2.20-2.05 (m, 2 H), 1.35 (s, 3 H). Anal. ($C_{15}H_{17}ClN_4O_3$) C, H, N (see Table S4).

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-1-[(4-fluorophenyl)(methyl)amino]-2-methylbutan-2-ol (29). Reaction of epoxide **16** (378 mg, 1.63 mmol), 4-fluoro-*N*-methylaniline (285 mg, 2.28 mmol), and anhydrous cobalt(II) chloride (111 mg, 0.855 mmol), using General Procedure A at 75 °C for 24 h, gave **29** (565 mg, 97%) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.77 (s, 1 H), 6.96 (br dd, *J* = 9.3, 8.2 Hz, 2 H), 6.82 (br dd, *J* = 9.3, 4.3 Hz, 2 H), 4.33-4.18 (m, 2 H), 3.32 (d, *J* = 15.2 Hz, 1 H), 3.23 (d, *J* = 15.1 Hz, 1 H), 2.99 (s, 3 H), 2.11-2.01 (m, 2 H), 2.01-1.91 (m, 1 H), 1.34 (s, 3 H); APCI MS calcd for $C_{15}H_{19}ClFN_4O_3$ *m*/*z* $[M + H]^+$ 359, 357, found 359, 357.

4-Fluoro-*N*-methyl-*N*-[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]aniline (30). Reaction of alcohol **29** (563 mg, 1.58 mmol) and NaH (101 mg, 2.53 mmol), using General Procedure B at 50 °C for 3 h, gave **30** (137 mg, 27%) as a yellow solid: mp 149-151 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 1 H), 7.00 (br dd, *J* = 9.1, 8.7 Hz, 2 H), 6.82 (br dd, *J* = 9.3, 4.4 Hz, 2 H), 4.14 (ddd, *J* = 13.0, 5.7, 4.3 Hz, 1 H), 4.06 (ddd, *J* = 13.0, 9.6, 5.9 Hz, 1 H), 3.65 (d, *J* = 16.1 Hz, 1 H), 3.60 (d, *J* = 16.2 Hz, 1 H), 2.94 (s, 3 H), 2.23-2.07 (m, 2 H), 1.36 (s, 3 H). Anal. ($C_{15}H_{17}FN_4O_3$) C, H, N (see Table S4).

***N*-[6-(Trifluoromethyl)pyridin-3-yl]formamide (32).** A mixture of formic acid (1.25 mL, 33.1 mmol) and acetic anhydride (2.5 mL, 26.5 mmol) was stirred at 50 °C for 2 h, then cooled to 20 °C and added to a solution of 6-(trifluoromethyl)pyridin-3-amine (**31**) (821 mg, 5.06 mmol) in anhydrous THF (2 mL) under N_2, rinsing in residues with additional anhydrous THF (2 mL). The mixture was stirred at 20 °C for 23 h and then added to ice/aq $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (6 x 100 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with 0-0.5% MeOH/CH_2Cl_2 first gave foreruns, and then further elution with 0.5-1% MeOH/CH_2Cl_2 gave **32** (930 mg, 97%) as a white solid: mp (CH_2Cl_2/hexane) 110-113 °C; ^{1}H NMR ($CDCl_3$) δ 8.67 (d, *J* = 2.4 Hz, 1 H), 8.51 (d, *J* = 0.9 Hz, 1 H), 8.44 (dd, *J* = 8.6, 2.3 Hz, 1 H), 7.70 (d, *J* = 8.6 Hz, 1 H), 7.45 (br s, 1 H). Anal. ($C_7H_5F_3N_2O$) C, H, N (see Table S4).

***N*-Methyl-6-(trifluoromethyl)pyridin-3-amine (33).** Borane-dimethyl sulfide complex (5.4 mL of 2 M solution in THF, 10.8 mmol) was added dropwise to a stirred solution of formamide **32** (800 mg, 4.21 mmol) in anhydrous THF (3 mL) under N_2 at 0 °C. The mixture was stirred at 20 °C for 30 min and then at 65 °C for 3.5 h, before being recooled to 0 °C. MeOH (2.2 mL) was added, and the mixture was stirred at 0-20 °C for 22 h, then saturated with anhydrous HCl gas and stirred at 65 °C for 1 h. After cooling to 20 °C, MeOH (20 mL) was added, and the solvents were removed under reduced pressure (at 30 °C). The oily residue was treated with 2 M NaOH (30 mL) and water (20 mL) and extracted with CH_2Cl_2 (4 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with CH_2Cl_2 first gave foreruns and then **33**[S6] (533 mg, 72%) as a colourless oil; ^{1}H NMR ($CDCl_3$) δ 8.06 (d, *J* = 2.8 Hz, 1 H), 7.47 (d, *J* = 8.6 Hz, 1 H), 6.88 (dd, *J* = 8.6, 2.8 Hz, 1 H), 4.16 (br s, 1 H), 2.91 (d, *J* = 5.2 Hz, 3 H); HRESIMS calcd for $C_7H_8F_3N_2$ *m/z* $[M + H]^+$ 177.0634, found 177.0631.

4-(2-Chloro-4-nitro-1*H*-imidazol-1-yl)-2-methyl-1-{methyl[6-(trifluoromethyl)pyridin-3-yl]amino}butan-2-ol (34). Reaction of epoxide **16** (293 mg, 1.26 mmol), methylaminopyridine **33** (536 mg, 3.04 mmol), and anhydrous cobalt(II) chloride (125 mg, 0.963 mmol), using General Procedure A at 70 °C for 3 d, gave **34** (89 mg, 17%) as a yellow oil; ^{1}H NMR ($CDCl_3$) δ 8.31 (d, *J* = 3.0 Hz, 1 H), 7.80 (s, 1 H), 7.49 (d, *J* = 8.9 Hz, 1 H), 7.16 (dd, *J* = 8.8, 2.9 Hz, 1 H), 4.35-4.19 (m, 2 H), 3.52 (d, *J* = 15.4 Hz, 1 H), 3.39 (d, *J* = 15.4 Hz, 1 H), 3.14 (s, 3 H), 2.15-2.05 (m, 1 H), 2.04-1.93 (m, 1 H), 1.86 (s, 1 H), 1.38 (s, 3 H); APCI MS calcd for $C_{15}H_{17}Cl_2F_3N_5O_3$ *m/z* $[M + Cl]^-$ 444, 442, found 444, 442.

***N*-Methyl-*N*-[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-6-(trifluoromethyl)pyridin-3-amine (35).** Reaction of alcohol **34** (103 mg, 0.253 mmol) and NaH (15 mg, 0.375 mmol), using General Procedure B at 70 °C for 2 h, gave **35** (44 mg, 47%) as a pale yellow solid: mp (Et_2O/CH_2Cl_2/pentane triturate) 106-109 °C; ^{1}H NMR ($CDCl_3$) δ 8.22 (d, *J* = 3.0 Hz, 1 H), 7.52 (d, *J* = 8.8 Hz, 1 H), 7.45 (s, 1 H), 7.11 (dd, *J* = 8.9, 3.0 Hz, 1 H), 4.19-4.06 (m, 2 H), 3.79 (d, *J* = 16.1 Hz, 1 H), 3.74 (d, *J* = 16.1 Hz, 1 H), 3.18 (s, 3 H), 2.30 (ddd, *J* = 14.2, 9.9, 8.1 Hz, 1 H), 2.05 (ddd, *J* = 14.2, 4.3, 3.3 Hz, 1 H), 1.48 (s, 3 H); HRESIMS calcd for $C_{15}H_{17}F_3N_5O_3$ *m/z* $[M + H]^+$ 372.1278, found 372.1271; HPLC purity: 97.8%.

Synthesis of benzylamine 40 (Scheme 2A)

1-Azido-4-(2-chloro-4-nitro-1*H*-imidazol-1-yl)-2-methylbutan-2-ol (36). A mixture of epoxide **16** (281 mg, 1.21 mmol), sodium azide (332 mg, 5.11 mmol), and *N*-cetyl-*N*,*N*,*N*-trimethylammonium bromide (446 mg, 1.22 mmol) in MeOH (10 mL) was stirred at 20 °C for 45 min and then at 40 °C for 17 h. The resulting cooled mixture was treated with excess $NaHCO_3$ (0.15 g, 1.79 mmol), then added to brine (50 mL), and extracted with CH_2Cl_2 (5 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with 0-0.25% MeOH/CH_2Cl_2 first gave foreruns and then further elution with 0.25% MeOH/CH_2Cl_2 gave **36** (242 mg, 73%) as a colourless oil; ^{1}H NMR ($CDCl_3$) δ 7.80 (s, 1 H), 4.28-4.13 (m, 2 H), 3.39 (d, *J* = 12.2 Hz, 1 H), 3.34 (d, *J* = 12.2 Hz, 1 H), 2.06 (ddd, *J* = 13.7, 9.5, 6.4 Hz, 1 H), 1.94 (s, 1 H), 1.92 (ddd, *J* = 13.8, 9.5, 6.7 Hz, 1 H), 1.32 (s, 3 H); HRESIMS calcd for $C_8H_{12}ClN_6O_3$ *m/z* $[M + H]^+$ 277.0627, 275.0654, found 277.0632, 275.0648.

7-(Azidomethyl)-7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazine (37). Reaction of alcohol **36** (2.42 g, 8.81 mmol) and NaH (508 mg, 12.7 mmol), using General Procedure B for 2.5 h, gave **37** (1.48 g, 70%) as a cream solid: mp (CH_2Cl_2/pentane) 138-139

°C; ^{1}H NMR ($CDCl_3$) δ 7.45 (s, 1 H), 4.15 (ddd, *J* = 12.7, 6.2, 4.9 Hz, 1 H), 4.09 (ddd, *J* = 12.8, 9.3, 5.5 Hz, 1 H), 3.59 (d, *J* = 12.9 Hz, 1 H), 3.47 (d, *J* = 12.9 Hz, 1 H), 2.39 (ddd, *J* = 14.4, 9.2, 6.2 Hz, 1 H), 2.05 (dt, *J* = 14.4, 5.1 Hz, 1 H), 1.49 (s, 3 H). Anal. ($C_8H_{10}N_6O_3$) C, H, N (see Table S4).

1-(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methanamine (38) and *N*-[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-1,1,1-triphenyl-λ^5-phosphanimine (39). Triphenylphosphine (605 mg, 2.31 mmol) was added to a suspension of azide **37** (181 mg, 0.760 mmol) in dioxane (13.5 mL) and water (1.5 mL) at 12 °C. The mixture was stirred at 20 °C for 24 h in a sealed vial, then transferred to a flask (in $MeOH/CH_2Cl_2$) and evaporated to dryness under reduced pressure (at 30 °C), and the residue was chromatographed on silica gel. Elution with 0-5% $MeOH/CH_2Cl_2$ first gave foreruns, and then further elution with 5-6% $MeOH/CH_2Cl_2$ gave **38** (78 mg, 48%) as a light yellow solid (following Et_2O trituration): mp 118-120 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.05 (s, 1 H), 4.11 (dt, *J* = 13.0, 5.9 Hz, 1 H), 4.04 (ddd, *J* = 13.1, 8.4, 5.5 Hz, 1 H), 2.76 (d, *J* = 13.5 Hz, 1 H), 2.71 (d, *J* = 13.5 Hz, 1 H), 2.22 (ddd, *J* = 14.4, 8.4, 6.0 Hz, 1 H), 1.97 (dt, *J* = 14.4, 5.6 Hz, 1 H), 1.79 (br s, 2 H), 1.32 (s, 3 H); HRESIMS calcd for $C_8H_{12}N_4NaO_3$ *m/z* $[M + Na]^+$ 235.0802, found 235.0791.

Further elution of the above column with 6-7% $MeOH/CH_2Cl_2$ gave a mixture of **38** and **39** (24 mg) and then elution with 10% $MeOH/CH_2Cl_2$ containing 1% concd NH_3 gave crude **39** (114 mg, 32%) as a light orange solid (following Et_2O/pentane trituration): mp 135 °C (dec); ^{1}H NMR [$(CD_3)_2SO$] δ 8.03 (s, 1 H), 7.92-7.71 (m, 15 H), 4.08 (dt, *J* = 13.1, 5.6 Hz, 1 H), 4.00 (ddd, *J* = 13.2, 8.8, 5.4 Hz, 1 H), 3.27 (d, $^3J_{H\text{-}P}$ = 10.9 Hz, 2 H), 2.20 (ddd, *J* = 14.4, 8.6, 6.1 Hz, 1 H), 1.93 (dt, *J* = 14.4, 5.2 Hz, 1 H), 1.20 (s, 3 H); HRESIMS calcd for $C_{26}H_{26}N_4O_3P$ *m/z* $[M + H]^+$ 473.1737, found 473.1735.

1-(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)-*N*-[4-(trifluoromethoxy)benzyl]methanamine (40). 4-(Trifluoromethoxy)benzaldehyde (60 µL, 0.420 mmol) was added to a mixture of amine **38** (26.5 mg, 0.125 mmol) and AcOH (25 µL, 0.437 mmol) in anhydrous DMF (1.8 mL) under N_2. The mixture was stirred at 20 °C for 20 min and then cooled to 0 °C. Sodium cyanoborohydride (30 mg, 0.477 mmol) was added and the mixture was quickly degassed and resealed under N_2, and then stirred at 20 °C for 21 h. The resulting mixture was rapidly cooled (CO_2/acetone), quenched with ice/aqueous sodium carbonate (10 mL), added to brine (40 mL), and extracted with CH_2Cl_2 (5 x 50 mL) and EtOAc (50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with 0-0.4% $MeOH/CH_2Cl_2$ first gave foreruns, and then further elution with 0.5-0.6% $MeOH/CH_2Cl_2$ gave **40** (24 mg, 50%) as a light yellow solid: mp (CH_2Cl_2/pentane) 70-71 °C; ^{1}H NMR ($CDCl_3$) δ 7.42 (s, 1 H), 7.33 (br d, *J* = 8.6 Hz, 2 H), 7.17 (br d, *J* = 7.9 Hz, 2 H), 4.06 (dd, *J* = 8.1, 4.9 Hz, 2 H), 3.84 (s, 2 H), 2.90 (d, *J* = 12.7 Hz, 1 H), 2.78 (d, *J* = 12.7 Hz, 1 H), 2.55 (dt, *J* = 14.6, 8.0 Hz, 1 H), 1.95 (dt, *J* = 14.4, 4.9 Hz, 1 H), 1.45 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 148.5, 147.9, 144.0, 138.8, 129.5 (2 C), 121.2 (2 C), 120.7 (q, $J_{C\text{-}F}$ = 257.3 Hz), 114.5, 81.9, 56.8, 53.3, 40.0, 28.4, 22.7; HRESIMS calcd for $C_{16}H_{18}F_3N_4O_4$ *m/z* $[M + H]^+$ 387.1275, found 387.1276; HPLC purity: 97.4%.

Syntheses of amides 43-48 (Scheme 2B)

7-(Azidomethyl)-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazine (42). Diethyl azodicarboxylate (0.175 mL, 1.13 mmol) was added dropwise to a stirred solution of (2-nitro-

6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methanol[S1] (**41**) (200 mg, 1.00 mmol) and triphenylphosphine (291 mg, 1.11 mmol) in anhydrous DMF (2 mL) under N_2 at 0 °C. The mixture was stirred at 0 °C for 30 min and then diphenylphosphoryl azide (0.250 mL, 1.16 mmol) was added dropwise. After being stirred at 0 °C for 1 h and then at 20 °C for 44 h, the mixture was concentrated under reduced pressure (at 30 °C) to give an oil, which was chromatographed on silica gel. Elution with 0-50% EtOAc/petroleum ether first gave foreruns, and then further elution with 50-75% EtOAc/petroleum ether gave the crude product, which was further purified by chromatography on silica gel. Elution with 0-1% EtOAc/CH_2Cl_2 first gave foreruns, and then further elution with 1-3% EtOAc/CH_2Cl_2 gave **42** (187 mg, 83%) as a white solid: mp (CH_2Cl_2/hexane) 98-101 °C; ^{1}H NMR ($CDCl_3$) δ 7.44 (s, 1 H), 4.59-4.49 (m, 1 H), 4.18 (ddd, *J* = 12.5, 5.4, 3.2 Hz, 1 H), 4.10 (ddd, *J* = 12.5, 10.5, 6.0 Hz, 1 H), 3.68 (dd, *J* = 13.3, 4.9 Hz, 1 H), 3.64 (dd, *J* = 13.2, 4.9 Hz, 1 H), 2.37-2.22 (m, 2 H). Anal. ($C_7H_8N_6O_3$) C, H, N (see Table S4).

***N*-[(2-Nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-4-(trifluoromethoxy)benzamide (43).** Reaction of azide **42** (40.7 mg, 0.182 mmol) with 4-(trifluoromethoxy)benzoyl chloride (60 µL, 0.381 mmol) and triphenylphosphine (61.0 mg, 0.233 mmol), using General Procedure C for 130 min, gave **43** (35.5 mg, 51%) as a cream solid: mp (Et_2O/pentane triturate) 89-91 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.85 (br d, *J* = 8.8 Hz, 2 H), 7.44 (s, 1 H), 7.29 (br d, *J* = 8.8 Hz, 2 H), 6.82 (br t, *J* = 5.9 Hz, 1 H), 4.70-4.60 (m, 1 H), 4.22-4.01 (m, 3 H), 3.69 (ddd, *J* = 14.5, 7.1, 5.6 Hz, 1 H), 2.42-2.32 (m, 1 H), 2.27-2.12 (m, 1 H). Anal. ($C_{15}H_{13}F_3N_4O_5\cdot0.5H_2O$) C, H, N (see Table S4). HPLC purity: 99.8%.

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-4-(trifluoromethoxy)benzamide (44).** Reaction of azide **37** (120 mg, 0.504 mmol) with 4-(trifluoromethoxy)benzoyl chloride (160 µL, 1.02 mmol) and triphenylphosphine (161 mg, 0.614 mmol), using General Procedure C, gave **44** (148 mg, 73%) as a pale yellow solid: mp (Et_2O/pentane triturate) 99-100 °C (dec); ^{1}H NMR [$(CD_3)_2SO$] δ 8.85 (br t, *J* = 6.0 Hz, 1 H), 8.08 (s, 1 H), 8.01 (br d, *J* = 8.6 Hz, 2 H), 7.47 (br d, *J* = 8.3 Hz, 2 H), 4.21 (dt, *J* = 13.1, 5.3 Hz, 1 H), 4.07 (ddd, *J* = 13.0, 8.1, 5.4 Hz, 1 H), 3.64 (dd, *J* = 14.1, 5.9 Hz, 1 H), 3.59 (dd, *J* = 14.1, 6.2 Hz, 1 H), 2.18 (ddd, *J* = 14.3, 8.2, 6.1 Hz, 1 H), 2.08 (dt, *J* = 14.3, 5.2 Hz, 1 H), 1.39 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 165.9, 150.3, 147.3, 142.2, 133.3, 129.8 (2 C), 120.6 (2 C), 119.9 (q, $J_{C\text{-}F}$ = 257.1 Hz), 117.7, 81.8, 46.0, 39.5, 27.4, 22.1. Anal. ($C_{16}H_{15}F_3N_4O_5\cdot0.5H_2O$) C, H, N (see Table S4). HPLC purity: 98.7%.

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-3-(trifluoromethoxy)benzamide (45).** Propane-1,3-dithiol (106 µL, 1.06 mmol) was added to a mixture of azide **37** (126 mg, 0.529 mmol) and triethylamine (150 µL, 1.08 mmol) in anhydrous MeOH (2.5 mL) under N_2 at 15 °C. After being stirred at 20 °C for 45 min, the mixture was diluted with anhydrous CH_2Cl_2 (2 mL), and stirring was continued for 7 h. Further triethylamine (230 µL, 1.65 mmol) and propane-1,3-dithiol (160 µL, 1.59 mmol) were added, and the mixture was stirred at 20 °C for 4 h. The resulting mixture was then added to excess petroleum ether (100 mL) above the top of a silica gel column (20 g packed in petroleum ether), rinsing on with minimal 10% MeOH/CH_2Cl_2. Elution with 0-75% CH_2Cl_2/petroleum ether and 0-3% MeOH/CH_2Cl_2 first gave foreruns, and then further elution with 3-5% MeOH/CH_2Cl_2 gave crude amine **38** (93 mg, 83%) as a yellow solid, which was dissolved in anhydrous DMF (2 mL), sealed under N_2, and cooled in an ice bath. *N*,*N*-Diisopropylethylamine (185 µL, 1.06 mmol) and 3-(trifluoromethoxy)benzoyl chloride (105 mg, 0.468 mmol) were added, and the mixture was stirred at 20 °C for 19 h. The reaction was quenched with ice (5 mL), then added to brine (40 mL) and extracted with CH_2Cl_2 (5 x 50

mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with 0-0.5% MeOH/CH_2Cl_2 first gave foreruns, and then further elution with 0.5-0.67% MeOH/CH_2Cl_2 gave **45** (80 mg, 46%) as a cream solid: mp (Et_2O/pentane triturate) 160-161 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.91 (br t, *J* = 6.2 Hz, 1 H), 8.08 (s, 1 H), 7.94 (dt, *J* = 7.7, 1.2 Hz, 1 H), 7.86-7.82 (m, 1 H), 7.63 (t, *J* = 7.9 Hz, 1 H), 7.59-7.54 (m, 1 H), 4.21 (dt, *J* = 13.0, 5.6 Hz, 1 H), 4.07 (ddd, *J* = 13.1, 8.7, 5.6 Hz, 1 H), 3.65 (dd, *J* = 14.0, 6.4 Hz, 1 H), 3.60 (dd, *J* = 14.0, 6.2 Hz, 1 H), 2.18 (ddd, *J* = 14.5, 8.6, 5.9 Hz, 1 H), 2.09 (dt, *J* = 14.4, 5.4 Hz, 1 H), 1.40 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 165.5, 148.2 (q, J_{C-F} = 1.9 Hz), 147.3, 142.2, 136.3, 130.5, 126.6, 123.9, 120.04 (q, J_{C-F} = 256.8 Hz), 119.97, 117.7, 81.8, 46.1, 39.5, 27.4, 22.1. Anal. ($C_{16}H_{15}F_3N_4O_5$) C, H, N (see Table S4).

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-2-(trifluoromethoxy)benzamide (46).** Reaction of azide **37** (119 mg, 0.500 mmol) with 2-(trifluoromethoxy)benzoyl chloride (230 mg, 1.02 mmol) and triphenylphosphine (161 mg, 0.614 mmol), using General Procedure C for 90 min, gave **46** (163 mg, 82%) as a cream foam (after trituration in Et_2O/pentane and drying under vacuum); ^{1}H NMR ($CDCl_3$) δ 7.89 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.54 (ddd, *J* = 8.2, 7.6, 1.7 Hz, 1 H), 7.45 (s, 1 H), 7.41 (td, *J* = 7.6, 1.0 Hz, 1 H), 7.33 (br dd, *J* = 8.3, 1.2 Hz, 1 H), 6.85 (br t, *J* = 5.9 Hz, 1 H), 4.21 (ddd, *J* = 12.8, 6.2, 3.8 Hz, 1 H), 4.11 (ddd, *J* = 12.7, 10.4, 5.4 Hz, 1 H), 3.86 (dd, *J* = 14.3, 6.7 Hz, 1 H), 3.81 (dd, *J* = 14.4, 6.2 Hz, 1 H), 2.33 (ddd, *J* = 14.6, 10.3, 6.2 Hz, 1 H), 2.12 (ddd, *J* = 14.6, 5.3, 3.8 Hz, 1 H), 1.51 (s, 3 H). Anal. ($C_{16}H_{15}F_3N_4O_5 \cdot 0.25Et_2O$) C, H, N (see Table S4). HPLC purity: 99.7%.

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-2-[4-(trifluoromethoxy)phenyl]acetamide (47).** Reaction of azide **37** (121 mg, 0.508 mmol) with [4-(trifluoromethoxy)phenyl]acetyl chloride[S7] (252 mg, 1.06 mmol) and triphenylphosphine (159 mg, 0.606 mmol), using General Procedure C, gave **47** (176 mg, 84%) as a cream solid: mp (CH_2Cl_2/pentane) 139-141 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.43 (br t, *J* = 6.1 Hz, 1 H), 8.06 (s, 1 H), 7.38 (br d, *J* = 8.7 Hz, 2 H), 7.28 (br d, *J* = 7.9 Hz, 2 H), 4.14 (dt, *J* = 13.1, 5.5 Hz, 1 H), 4.04 (ddd, *J* = 13.1, 8.6, 5.6 Hz, 1 H), 3.56 (d, *J* = 14.6 Hz, 1 H), 3.52 (d, *J* = 14.5 Hz, 1 H), 3.43 (dd, *J* = 14.1, 6.2 Hz, 1 H), 3.38 (dd, *J* = 14.2, 6.2 Hz, 1 H), 2.07 (ddd, *J* = 14.5, 8.6, 5.9 Hz, 1 H), 1.99 (dt, *J* = 14.4, 5.5 Hz, 1 H), 1.30 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 170.5, 147.2, 147.0 (q, J_{C-F} = 1.6 Hz), 142.2, 135.8, 130.8 (2 C), 120.8 (2 C), 120.1 (q, J_{C-F} = 255.8 Hz), 117.7, 81.6, 45.5, 41.2, 39.5, 27.2, 21.8; HRESIMS calcd for $C_{17}H_{18}F_3N_4O_5$ *m/z* $[M + H]^+$ 415.1224, found 415.1232; HPLC purity: 100%.

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-2-[4-(trifluoromethoxy)phenoxy]acetamide (48).** Reaction of azide **37** (139 mg, 0.584 mmol) with [4-(trifluoromethoxy)phenoxy]acetyl chloride (312 mg, 1.23 mmol) and triphenylphosphine (186 mg, 0.709 mmol), using General Procedure C for 95 min, gave **48** (200 mg, 80%) as a cream solid: mp (MeOH/CH_2Cl_2/hexane) 198-200 °C; ^{1}H NMR ($CDCl_3$) δ 7.44 (s, 1 H), 7.18 (br d, *J* = 9.1 Hz, 2 H), 6.99 (br t, *J* = 6.3 Hz, 1 H), 6.95 (br d, *J* = 9.2 Hz, 2 H), 4.56 (d, *J* = 15.2 Hz, 1 H), 4.52 (d, *J* = 15.2 Hz, 1 H), 4.14 (ddd, *J* = 12.8, 6.5, 3.5 Hz, 1 H), 4.08 (ddd, *J* = 12.8, 10.5, 5.3 Hz, 1 H), 3.73 (dd, *J* = 14.4, 6.7 Hz, 1 H), 3.68 (dd, *J* = 14.4, 6.5 Hz, 1 H), 2.17 (ddd, *J* = 14.5, 10.3, 6.5 Hz, 1 H), 2.05 (ddd, *J* = 14.5, 5.2, 3.5 Hz, 1 H), 1.43 (s, 3 H); HRESIMS calcd for $C_{17}H_{18}F_3N_4O_6$ *m/z* $[M + H]^+$ 431.1173, found 431.1186; HPLC purity: 100%.

Syntheses of ureas 49-53 (Scheme 2C and 2D)

1-[(2-Nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-3-[4-(trifluoromethoxy)phenyl]urea (49) and 1,3-bis[(2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]urea (50). Reaction of azide **42** (137 mg, 0.611 mmol) with 4-(trifluoromethoxy)aniline (250 µL, 1.86 mmol), triphenylphosphine (282 mg, 1.08 mmol) and triethylammonium bicarbonate (1 mL of ~2 M, ~2.0 mmol), using General Procedure D, gave (via chromatography on silica gel, eluting with 1% MeOH/CH_2Cl_2) **49** (41 mg, 17%) as a light yellow solid: mp (Et_2O/pentane triturate) 126 °C (dec); ^{1}H NMR [$(CD_3)_2SO$] δ 8.82 (br s, 1 H), 8.07 (s, 1 H), 7.49 (br d, *J* = 9.1 Hz, 2 H), 7.23 (br d, *J* = 8.4 Hz, 2 H), 6.55 (br t, *J* = 5.9 Hz, 1 H), 4.63-4.53 (m, 1 H), 4.14 (ddd, *J* = 12.5, 5.8, 2.6 Hz, 1 H), 4.05 (ddd, *J* = 12.5, 11.3, 5.0 Hz, 1 H), 3.52 (ddd, *J* = 14.3, 6.0, 4.5 Hz, 1 H), 3.43 (dt, *J* = 14.3, 6.2 Hz, 1 H), 2.28-2.14 (m, 1 H), 2.07-1.90 (m, 1 H); ^{13}C NMR [$(CD_3)_2SO$] δ 155.1, 147.9, 142.1 (q, J_{C-F} = 1.6 Hz), 142.0, 139.6, 121.6 (2 C), 120.2 (q, J_{C-F} = 254.8 Hz), 118.7 (2 C), 117.8, 77.3, 42.1, 41.7, 23.4. Anal. ($C_{15}H_{14}F_3N_5O_5$) C, H, N (see Table S4).

Further elution of the silica gel column with 10% MeOH/CH_2Cl_2 gave **50** (39 mg, 15%) as a yellow solid: mp (Et_2O/pentane triturate) 172 °C (dec); ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 2 H), 6.40 (br t, *J* = 6.0 Hz, 2 H), 4.55-4.44 (m, 2 H), 4.13 (ddd, *J* = 12.6, 5.7, 2.5 Hz, 2 H), 4.03 (ddd, *J* = 12.4, 11.3, 5.0 Hz, 2 H), 3.43 (ddd, *J* = 14.4, 5.9, 4.9 Hz, 2 H), 3.37 (ddd, *J* = 14.5, 8.6, 6.1 Hz, 2 H), 2.23-2.11 (m, 2 H), 2.02-1.87 (m, 2 H); HRESIMS calcd for $C_{15}H_{18}N_8NaO_7$ *m*/*z* $[M + Na]^+$ 445.1191, found 445.1182.

1-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-3-[4-(trifluoromethoxy)phenyl]urea (51) and 1,3-bis[(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]urea (52). Reaction of azide **37** (180 mg, 0.756 mmol) with 4-(trifluoromethoxy)aniline (135 µL, 1.01 mmol), triphenylphosphine (350 mg, 1.33 mmol) and triethylammonium bicarbonate (1 mL of ~2 M, ~2.0 mmol), using General Procedure D, gave (via chromatography on silica gel, eluting with 1.5% MeOH/CH_2Cl_2) **51** (45 mg, 14%) as a pale yellow solid: mp (Et_2O/pentane) 161-163 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.78 (br s, 1 H), 8.08 (s, 1 H), 7.48 (br d, *J* = 9.1 Hz, 2 H), 7.23 (br d, *J* = 8.3 Hz, 2 H), 6.55 (br t, *J* = 6.2 Hz, 1 H), 4.19 (dt, *J* = 13.0, 5.4 Hz, 1 H), 4.07 (ddd, *J* = 13.1, 9.1, 5.6 Hz, 1 H), 3.45 (d, *J* = 6.2 Hz, 2 H), 2.14 (ddd, *J* = 14.5, 9.0, 5.9 Hz, 1 H), 2.05 (dt, *J* = 14.5, 5.3 Hz, 1 H), 1.36 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 155.2, 147.2, 142.2, 142.1 (q, J_{C-F} = 1.6 Hz), 139.5, 121.7 (2 C), 120.2 (q, J_{C-F} = 255.3 Hz), 118.7 (2 C), 117.7, 82.0, 46.1, 39.5, 27.2, 21.5. Anal. ($C_{16}H_{16}F_3N_5O_5$) C, H, N (see Table S4).

Further elution of the silica gel column with 10% MeOH/CH_2Cl_2 gave **52** (57 mg, 17%) as a light yellow solid: mp (MeOH/CH_2Cl_2/hexane) 217 °C (dec); ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 2 H), 6.36 (br t, *J* = 6.2 Hz, 2 H), 4.17 (dt, *J* = 13.0, 5.5 Hz, 2 H), 4.05 (ddd, *J* = 13.1, 8.9, 5.6 Hz, 2 H), 3.36 (br d, *J* = 6.3 Hz, 4 H), 2.09 (ddd, *J* = 14.4, 8.8, 5.9 Hz, 2 H), 2.00 (dt, *J* = 14.4, 5.3 Hz, 2 H), 1.31 (s, 6 H); HRESIMS calcd for $C_{17}H_{22}N_8NaO_7$ *m*/*z* $[M + Na]^+$ 473.1504, found 473.1488.

1-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-3-[4-(trifluoromethoxy)benzyl]urea (53). 1-(Isocyanatomethyl)-4-(trifluoromethoxy)benzene[S8] (0.11 mL, 0.66 mmol) and dibutyltin diacetate (9.3 mg, 0.026 mmol) were successively added to a stirred solution of amine **38** (40.0 mg, 0.188 mmol) and DIPEA (0.10 mL, 0.574 mmol) in anhydrous DMF (2 mL) under N_2. The mixture was stirred at 20 °C for 16 h and then treated with ice-water (5 mL), added to brine (40 mL), and extracted with CH_2Cl_2 (5 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with 0-1% MeOH/CH_2Cl_2 first

gave foreruns, and then further elution with 1-1.5% MeOH/CH_2Cl_2 gave **53** (75 mg, 93%) as a light yellow solid: mp (Et_2O/pentane triturate) 111-114 °C (dec); ^{1}H NMR ($CDCl_3$) δ 7.43 (s, 1 H), 7.34 (br d, *J* = 8.7 Hz, 2 H), 7.12 (br d, *J* = 7.9 Hz, 2 H), 6.36 (br t, *J* = 5.8 Hz, 1 H), 6.11 (br dd, *J* = 6.6, 5.8 Hz, 1 H), 4.44 (dd, *J* = 15.2, 6.4 Hz, 1 H), 4.38 (dd, *J* = 15.3, 6.1 Hz, 1 H), 4.15 (ddd, *J* = 12.7, 6.2, 3.9 Hz, 1 H), 4.03 (ddd, *J* = 12.7, 10.5, 5.4 Hz, 1 H), 3.85 (dd, *J* = 14.8, 7.7 Hz, 1 H), 3.36 (dd, *J* = 14.9, 5.3 Hz, 1 H), 2.40 (ddd, *J* = 14.7, 10.5, 6.3 Hz, 1 H), 2.09 (ddd, *J* = 14.7, 5.3, 3.9 Hz, 1 H), 1.43 (s, 3 H); HRESIMS calcd for $C_{17}H_{19}F_3N_5O_5$ *m*/*z* $[M + H]^+$ 430.1333, found 430.1336; HPLC purity: 97.2%.

Synthesis of N-carbamate 55 (Scheme 2D)

4-Nitrophenyl [4-(trifluoromethoxy)benzyl] carbonate (54). 4-(Trifluoromethoxy)benzyl alcohol (0.25 mL, 1.73 mmol) was added to a solution of 4-nitrophenyl chloroformate (354 mg, 1.76 mmol) in anhydrous CH_2Cl_2 (8 mL) under N_2. The mixture was cooled to 0 °C and a solution of anhydrous pyridine (0.15 mL, 1.85 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was added dropwise, with stirring. The resulting mixture was stirred at 0-20 °C for 20 h and then concentrated under reduced pressure. The residue was dissolved in EtOAc (15 mL) and washed successively with 10% citric acid (2 x 6 mL), water (15 mL), saturated aq $NaHCO_3$ (2 x 10 mL), and brine (10 mL). The organic phase was evaporated to dryness under reduced pressure (at 25 °C), and then the residue was diluted with benzene (20 mL) and again evaporated to dryness under reduced pressure, to give crude **54** (605 mg, 98%) as a pale yellow solid, which was used directly; ^{1}H NMR ($CDCl_3$) δ 8.28 (br d, *J* = 9.3 Hz, 2 H), 7.49 (br d, *J* = 8.7 Hz, 2 H), 7.39 (br d, *J* = 9.2 Hz, 2 H), 7.27 (br d, *J* = 7.9 Hz, 2 H), 5.30 (s, 2 H).

4-(Trifluoromethoxy)benzyl [(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]carbamate (55). Carbonate **54** (93.5 mg crude, <0.262 mmol) was added to a mixture of amine **38** (35.2 mg, 0.166 mmol), DIPEA (30 μL, 0.172 mmol), and DMAP (7.3 mg, 0.060 mmol) in anhydrous DMF (1 mL) under N_2. The mixture was quickly degassed and resealed under N_2 and stirred at 20 °C for 44 h, then treated with ice/aq $NaHCO_3$ (10 mL), added to brine (40 mL), and extracted with CH_2Cl_2 (5 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with 25-60% EtOAc/petroleum ether first gave foreruns, and then further elution with 60-75% EtOAc/petroleum ether gave **55** (51 mg, 71%) as a pale yellow solid: mp (CH_2Cl_2/pentane) 100-103 °C; ^{1}H NMR [$(CD_3)_2SO$] 8.06 (s, 1 H), 7.71 (br t, *J* = 6.4 Hz, 1 H), 7.49 (br d, *J* = 8.7 Hz, 2 H), 7.37 (br d, *J* = 8.1 Hz, 2 H), 5.09 (d, *J* = 13.0 Hz, 1 H), 5.06 (d, *J* = 13.0 Hz, 1 H), 4.15 (dt, *J* = 13.0, 5.5 Hz, 1 H), 4.04 (ddd, *J* = 13.1, 8.7, 5.6 Hz, 1 H), 3.38-3.27 (m, 2 H), 2.11 (ddd, *J* = 14.5, 8.5, 6.0 Hz, 1 H), 2.02 (dt, *J* = 14.4, 5.4 Hz, 1 H), 1.32 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 156.6, 147.8, 147.2, 142.2, 136.6, 129.6 (2 C), 121.0 (2 C), 120.0 (q, J_{C-F} = 255.0 Hz), 117.7, 81.4, 64.6, 47.5, 39.4, 27.2, 21.8; HRESIMS calcd for $C_{17}H_{18}F_3N_4O_6$ *m*/*z* $[M + H]^+$ 431.1173, found 431.1163; HPLC purity: 98.9%.

Syntheses of sulfonamides 57 and 58 (Scheme 2E)

***tert*-Butyl [(7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]carbamate (56).** A solution of triphenylphosphine (262 mg, 0.999 mmol) in anhydrous CH_2Cl_2 (2 x 0.75 mL) was added dropwise to a stirred mixture of azide **37** (201 mg, 0.844 mmol) and Boc-ON (246 mg, 0.999 mmol) in anhydrous CH_2Cl_2 (4 mL) under N_2 at 0 °C. The mixture was stirred at 20 °C for 24 h, then added to ice/aq $NaHCO_3$ (50 mL), and extracted with 10% MeOH/CH_2Cl_2 (50 mL) and CH_2Cl_2 (3 x 50 mL). The combined

extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with CH_2Cl_2 first gave foreruns and then further elution with 2% MeOH/CH_2Cl_2 gave a mixture (0.48 g), which was dried onto silica gel and chromatographed again on silica gel. Elution with 20-40% EtOAc/petroleum ether gave foreruns, and then further elution with 45% EtOAc/petroleum ether first gave a product-containing mixture (28 mg). Further elution with 45-50% EtOAc/petroleum ether gave **56** (53 mg, 20%) as a cream solid: mp (MeOH/CH_2Cl_2/hexane) 217-219 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.06 (s, 1 H), 7.20 (br t, *J* = 6.3 Hz, 1 H), 4.15 (dt, *J* = 13.1, 5.6 Hz, 1 H), 4.03 (ddd, *J* = 13.1, 8.3, 5.8 Hz, 1 H), 3.23 (d, *J* = 6.4 Hz, 2 H), 2.15-1.94 (m, 2 H), 1.39 (s, 9 H), 1.30 (s, 3 H); HRESIMS calcd for $C_{13}H_{21}N_4O_5$ *m*/*z* $[M + H]^+$ 313.1506, found 313.1499.

Further elution of the above column with 55% EtOAc/petroleum ether and EtOAc gave a product-containing mixture (142 mg). Repeat chromatography of the mixed fractions and fractional crystallization (MeOH/CH_2Cl_2/pentane) gave additional **56** (123 mg, 47%).

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-4-(trifluoromethoxy)benzene-1-sulfonamide (57).** Deprotection of Boc derivative **56** (58 mg, 0.186 mmol) with 1:1 TFA/CH_2Cl_2 and then reaction of the chromatographed crude amine **38** with 4-(trifluoromethoxy)benzenesulfonyl chloride (0.10 mL, 0.589 mmol) and DIPEA (0.17 mL, 0.976 mmol), using General Procedure E, gave **57** (54 mg, 67%) as a cream solid: mp (MeOH/CH_2Cl_2/hexane) 200-201 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.24 (br s, 1 H), 8.05 (s, 1 H), 7.96 (br d, *J* = 8.9 Hz, 2 H), 7.59 (br d, *J* = 8.9 Hz, 2 H), 4.14 (dt, *J* = 13.0, 5.6 Hz, 1 H), 4.05 (ddd, *J* = 13.1, 9.0, 5.4 Hz, 1 H), 3.13 (d, *J* = 14.0 Hz, 1 H), 3.06 (d, *J* = 14.0 Hz, 1 H), 2.20 (ddd, *J* = 14.5, 8.9, 6.0 Hz, 1 H), 2.02 (dt, *J* = 14.4, 5.3 Hz, 1 H), 1.34 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 150.8 (q, J_{C-F} = 1.6 Hz), 147.0, 142.2, 139.7, 129.1 (2 C), 121.5 (2 C), 119.9 (q, J_{C-F} = 257.4 Hz), 117.7, 80.9, 49.4, 39.3, 27.0, 21.7; HRESIMS calcd for $C_{15}H_{16}F_3N_4O_6S$ *m*/*z* $[M + H]^+$ 437.0737, found 437.0736; HPLC purity: 99.9%.

***N*-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl]-3-(trifluoromethoxy)benzene-1-sulfonamide (58).** Deprotection of Boc derivative **56** (57.4 mg, 0.184 mmol) with 1:1 TFA/CH_2Cl_2 and then reaction of the chromatographed crude amine **38** with 3-(trifluoromethoxy)benzenesulfonyl chloride (0.10 mL, 0.587 mmol) and DIPEA (0.17 mL, 0.976 mmol), using General Procedure E, gave **58** (65 mg, 81%) as a pale yellow solid: mp (MeOH/CH_2Cl_2/pentane) 162-163 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.32 (br s, 1 H), 8.06 (s, 1 H), 7.87 (br d, *J* = 7.8 Hz, 1 H), 7.77 (br s, 1 H), 7.75 (t, *J* = 8.0 Hz, 1 H), 7.68 (br d, *J* = 8.2 Hz, 1 H), 4.14 (dt, *J* = 13.0, 5.5 Hz, 1 H), 4.05 (ddd, *J* = 13.1, 9.1, 5.5 Hz, 1 H), 3.14 (d, *J* = 14.0 Hz, 1 H), 3.08 (d, *J* = 14.0 Hz, 1 H), 2.19 (ddd, *J* = 14.4, 9.0, 6.0 Hz, 1 H), 2.02 (dt, *J* = 14.4, 5.3 Hz, 1 H), 1.34 (s, 3 H); HRESIMS calcd for $C_{15}H_{16}F_3N_4O_6S$ *m*/*z* $[M + H]^+$ 437.0737, found 437.0740; HPLC purity: 99.9%.

Synthesis of ether-linked amide 64 (Scheme 3A)

2-Iodo-*N*-[4-(trifluoromethoxy)phenyl]acetamide (62). A mixture of 2-chloro-*N*-[4-(trifluoromethoxy)phenyl]acetamide (**61**) (801 mg, 3.16 mmol) and sodium iodide (5.00 g, 33.4 mmol) in acetone (20 mL) under N_2 was stirred at 56 °C for 2 h and then at 20 °C for 15 h. The resulting mixture was evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with CH_2Cl_2 first gave foreruns and then **62**[S9] (1.05 g, 96%) as a white solid: mp (CH_2Cl_2/hexane) 140-142 °C (lit.[S9] mp 140 °C); ^{1}H NMR ($CDCl_3$) δ 7.66 (br s, 1 H), 7.54 (br d, *J* = 9.0 Hz, 2 H), 7.21 (br d, *J* = 8.5 Hz, 2 H), 3.86 (s, 2 H); HRESIMS calcd for $C_9H_8F_3INO_2$ *m*/*z* $[M + H]^+$ 345.9546, found 345.9548.

2-[(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methoxy]-*N*-[4-(trifluoromethoxy)phenyl]acetamide (64). Sodium hydride (60% in mineral oil, 70 mg, 1.75 mmol) was added to a mixture of 7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methanol[S1] (**63**) (150 mg, 0.704 mmol) and iodide **62** (320 mg, 0.927 mmol) in anhydrous DMF (3 mL) under N_2 at 0 °C. The mixture was immediately degassed and resealed under N_2, and then stirred at 20 °C for 80 min. The resulting mixture was rapidly cooled (CO_2/acetone), quenched with ice/aqueous $NaHCO_3$ (10 mL), added to brine (40 mL), and extracted with 10% MeOH/CH_2Cl_2 (2 x 50 mL) and CH_2Cl_2 (6 x 50 mL). The combined extracts were evaporated to dryness under reduced pressure (at 30 °C) and the residue was chromatographed on silica gel. Elution with 0-0.5% MeOH/CH_2Cl_2 first gave foreruns, and then further elution with 0.75% MeOH/CH_2Cl_2 gave the crude product, which was further purified by chromatography on silica gel. Elution with 75% EtOAc/petroleum ether first gave foreruns, and then further elution with EtOAc gave **64** (13 mg, 4%) as a cream solid: mp (CH_2Cl_2/pentane) 122-124 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 9.91 (br s, 1 H), 8.08 (s, 1 H), 7.73 (br d, *J* = 9.1 Hz, 2 H), 7.32 (br d, *J* = 8.3 Hz, 2 H), 4.20 (d, *J* = 15.3 Hz, 1 H), 4.19 (dt, *J* = 12.8, 5.9 Hz, 1 H), 4.15 (d, *J* = 15.3 Hz, 1 H), 4.09 (ddd, *J* = 13.0, 8.1, 5.6 Hz, 1 H), 3.74 (d, *J* = 10.7 Hz, 1 H), 3.70 (d, *J* = 10.7 Hz, 1 H), 2.34 (ddd, *J* = 14.5, 8.0, 5.8 Hz, 1 H), 2.09 (dt, *J* = 14.4, 5.8 Hz, 1 H), 1.41 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 168.1, 147.4, 143.7 (q, $J_{C\text{-}F}$ = 1.5 Hz), 142.2, 137.6, 121.5 (2 C), 121.0 (2 C), 120.1 (q, $J_{C\text{-}F}$ = 255.6 Hz), 117.7, 81.2, 75.3, 70.5, 39.6, 26.9, 21.5; HRESIMS calcd for $C_{17}H_{18}F_3N_4O_6$ *m*/*z* $[M + H]^+$ 431.1173, found 431.1174; HPLC purity: 99.5%.

Syntheses of O-carbamates 65, 66, and 68-74 (Scheme 3B)

(2-Nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl [4-(trifluoromethoxy)-phenyl]carbamate (65). Reaction of alcohol **41**[S1] (80.3 mg, 0.403 mmol), 1-isocyanato-4-(trifluoromethoxy)benzene (95 µL, 0.630 mmol), and copper(I) chloride (6.5 mg, 0.066 mmol), using General Procedure F, gave **65** (159 mg, 98%) as a cream solid: mp (MeOH/CH_2Cl_2/hexane) 156-158 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 10.07 (br s, 1 H), 8.08 (s, 1 H), 7.57 (br d, *J* = 9.1 Hz, 2 H), 7.31 (br d, *J* = 8.5 Hz, 2 H), 4.87-4.78 (m, 1 H), 4.45 (dd, *J* = 12.3, 2.9 Hz, 1 H), 4.37 (dd, *J* = 12.3, 6.2 Hz, 1 H), 4.17 (ddd, *J* = 12.5, 5.7, 2.5 Hz, 1 H), 4.08 (ddd, *J* = 12.4, 11.4, 5.0 Hz, 1 H), 2.32-2.21 (m, 1 H), 2.18-2.04 (m, 1 H); ^{13}C NMR [$(CD_3)_2SO$] δ 153.1, 147.7, 143.2 (q, $J_{C\text{-}F}$ = 1.8 Hz), 142.1, 138.2, 121.8 (2 C), 120.1 (q, $J_{C\text{-}F}$ = 255.5 Hz), 119.5 (2 C), 117.8, 75.9, 64.9, 41.6, 22.3. Anal. ($C_{15}H_{13}F_3N_4O_6$) C, H, N (see Table S4).

(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl [4-(trifluoromethoxy)phenyl]carbamate (66). Reaction of alcohol **63**[S1] (100 mg, 0.469 mmol), 1-isocyanato-4-(trifluoromethoxy)benzene (110 µL, 0.729 mmol), and copper(I) chloride (8.0 mg, 0.081 mmol), using General Procedure F for 32 h, gave **66** (192 mg, 98%) as a cream solid: mp (CH_2Cl_2/pentane) 97-100 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 10.03 (br s, 1 H), 8.08 (s, 1 H), 7.56 (br d, *J* = 9.0 Hz, 2 H), 7.30 (br d, *J* = 8.4 Hz, 2 H), 4.32 (s, 2 H), 4.19 (dt, *J* = 13.1, 5.5 Hz, 1 H), 4.12 (ddd, *J* = 13.1, 9.1, 5.5 Hz, 1 H), 2.27 (ddd, *J* = 14.4, 9.0, 6.0 Hz, 1 H), 2.14 (dt, *J* = 14.3, 5.2 Hz, 1 H), 1.44 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 153.0, 147.0, 143.2, 142.2, 138.1, 121.7 (2 C), 120.1 (q, $J_{C\text{-}F}$ = 255.3 Hz), 119.5 (2 C), 117.8, 80.4, 67.7, 39.3, 26.6, 20.7. Anal. ($C_{16}H_{15}F_3N_4O_6$) C, H, N (see Table S4).

[(7*R*)-7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl]methyl [4-(trifluoromethoxy)phenyl]carbamate (68). Reaction of [(7*R*)-7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl]methanol[S2] (**67**) (220 mg, 1.03 mmol), 1-isocyanato-4-

(trifluoromethoxy)benzene (260 µL, 1.72 mmol), and copper(I) chloride (19 mg, 0.19 mmol), using General Procedure F for 43 h, gave **68** (420 mg, 98%) as a cream solid: mp (CH_2Cl_2/pentane) 140-142 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 10.03 (br s, 1 H), 8.09 (s, 1 H), 7.56 (br d, *J* = 9.0 Hz, 2 H), 7.31 (br d, *J* = 8.4 Hz, 2 H), 4.32 (s, 2 H), 4.19 (dt, *J* = 13.1, 5.5 Hz, 1 H), 4.12 (ddd, *J* = 13.1, 9.2, 5.5 Hz, 1 H), 2.27 (ddd, *J* = 14.5, 8.9, 6.0 Hz, 1 H), 2.14 (dt, *J* = 14.4, 5.2 Hz, 1 H), 1.44 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 153.0, 147.0, 143.2 (q, J_{C-F} = 1.4 Hz), 142.2, 138.1, 121.7 (2 C), 120.1 (q, J_{C-F} = 255.4 Hz), 119.5 (2 C), 117.8, 80.4, 67.7, 39.3, 26.6, 20.7; $[\alpha]_D^{25}$ 32.9 (*c* 2.007, $CHCl_3$); Anal. ($C_{16}H_{15}F_3N_4O_6$) C, H, N (see Table S4).

[(7*S*)-7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl]methyl [4-(trifluoromethoxy)phenyl]carbamate (69). Reaction of [(7*S*)-7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl]methanol[S2] (*ent*-**67**) (220 mg, 1.03 mmol), 1-isocyanato-4-(trifluoromethoxy)benzene (260 µL, 1.72 mmol), and copper(I) chloride (15 mg, 0.15 mmol), using General Procedure F for 42 h, gave **69** (421 mg, 98%) as a cream solid: mp (CH_2Cl_2/pentane) 141-143 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 10.03 (br s, 1 H), 8.09 (s, 1 H), 7.56 (br d, *J* = 9.0 Hz, 2 H), 7.31 (br d, *J* = 8.4 Hz, 2 H), 4.32 (s, 2 H), 4.19 (dt, *J* = 13.0, 5.5 Hz, 1 H), 4.12 (ddd, *J* = 13.1, 9.1, 5.5 Hz, 1 H), 2.27 (ddd, *J* = 14.4, 9.0, 5.9 Hz, 1 H), 2.14 (dt, *J* = 14.4, 5.2 Hz, 1 H), 1.44 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 153.0, 147.0, 143.2 (q, J_{C-F} = 1.5 Hz), 142.2, 138.1, 121.7 (2 C), 120.1 (q, J_{C-F} = 255.4 Hz), 119.5 (2 C), 117.8, 80.4, 67.7, 39.3, 26.6, 20.7; $[\alpha]_D^{25}$ -32.4 (*c* 2.004, $CHCl_3$). Anal. ($C_{16}H_{15}F_3N_4O_6 \cdot 0.5H_2O$) C, H, N (see Table S4). HPLC purity: 99.9%.

(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl [2-(trifluoromethoxy)phenyl]carbamate (70). Reaction of alcohol **63** (100 mg, 0.469 mmol), 1-isocyanato-2-(trifluoromethoxy)benzene (110 µL, 0.731 mmol), and copper(I) chloride (5.0 mg, 0.051 mmol), using General Procedure F for 52 h, gave **70** (179 mg, 91%) as a cream solid: mp (CH_2Cl_2/pentane) 107-109 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 9.56 (br s, 1 H), 8.07 (s, 1 H), 7.68 (br d, *J* = 8.0 Hz, 1 H), 7.41-7.32 (m, 2 H), 7.25 (td, *J* = 7.8, 1.7 Hz, 1 H), 4.34 (d, *J* = 12.0 Hz, 1 H), 4.29 (d, *J* = 12.0 Hz, 1 H), 4.18 (dt, *J* = 13.1, 5.7 Hz, 1 H), 4.11 (ddd, *J* = 13.1, 8.8, 5.5 Hz, 1 H), 2.28 (ddd, *J* = 14.5, 8.7, 6.1 Hz, 1 H), 2.12 (dt, *J* = 14.3, 5.4 Hz, 1 H), 1.43 (s, 3 H). Anal. ($C_{16}H_{15}F_3N_4O_6$) C, H, N (see Table S4).

(2-Nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl [4-(trifluoromethoxy)-benzyl]carbamate (71) and (2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl [4-(trifluoromethoxy)benzyl]{[4-(trifluoromethoxy)benzyl]carbamoyl}-carbamate (73). Reaction of alcohol **41** (80.1 mg, 0.402 mmol), 1-(isocyanatomethyl)-4-(trifluoromethoxy)benzene[S8] (160 µL, ~0.96 mmol), and copper(I) chloride (7.1 mg, 0.072 mmol), using General Procedure F for 40 h, followed by chromatography of the product mixture on silica gel, eluting with 0-3% EtOAc/CH_2Cl_2 (foreruns) and then with 4-6% EtOAc/CH_2Cl_2, first gave crude **73**, which was chromatographed again on silica gel. Elution with 20-50% EtOAc/petroleum ether gave foreruns, and then further elution with EtOAc gave **73** (131 mg, 51%) as a pale yellow solid: mp (pentane triturate) 77-80 °C; ^{1}H NMR ($CDCl_3$) δ 8.89 (br t, *J* = 5.4 Hz, 1 H), 7.40 (s, 1 H), 7.36 (br d, *J* = 8.7 Hz, 2 H), 7.32 (br d, *J* = 8.7 Hz, 2 H), 7.20 (br d, *J* = 7.9 Hz, 2 H), 7.08 (br d, *J* = 7.9 Hz, 2 H), 5.10 (d, *J* = 15.5 Hz, 1 H), 4.93 (d, *J* = 15.5 Hz, 1 H), 4.54 (d, *J* = 5.7 Hz, 2 H), 4.53-4.43 (m, 3 H), 4.02-3.91 (m, 2 H), 1.99-1.90 (m, 1 H), 1.79-1.64 (m, 1 H); HRESIMS calcd for $C_{25}H_{22}F_6N_5O_8$ *m*/*z* $[M + H]^+$ 634.1367, found 634.1374; HPLC purity: 98.2%.

Further elution of the first column above with 10% EtOAc/CH_2Cl_2 gave **71** (74 mg, 44%) as a cream solid: mp (CH_2Cl_2/pentane) 94-97 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.07 (s, 1 H), 7.97 (br t,

J = 6.1 Hz, 1 H), 7.38 (br d, *J* = 8.7 Hz, 2 H), 7.33 (br d, *J* = 8.4 Hz, 2 H), 4.79-4.70 (m, 1 H), 4.33 (dd, *J* = 12.3, 3.0 Hz, 1 H), 4.24 (dd, *J* = 12.0, 6.2 Hz, 1 H), 4.23 (d, *J* = 6.2 Hz, 2 H), 4.15 (ddd, *J* = 12.4, 5.6, 2.5 Hz, 1 H), 4.06 (ddd, *J* = 12.3, 11.3, 4.9 Hz, 1 H), 2.26-2.16 (m, 1 H), 2.13-1.98 (m, 1 H); HRESIMS calcd for $C_{16}H_{16}F_3N_4O_6$ *m*/*z* $[M + H]^+$ 417.1016, found 417.1021; HPLC purity: 98.7%.

(7-Methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl [4-(trifluoromethoxy)benzyl]carbamate (72) and (7-methyl-2-nitro-6,7-dihydro-5*H*-imidazo[2,1-*b*][1,3]oxazin-7-yl)methyl [4-(trifluoromethoxy)benzyl]-{[4-(trifluoromethoxy)benzyl]carbamoyl}carbamate (74). Reaction of alcohol **63** (80.2 mg, 0.376 mmol), 1-(isocyanatomethyl)-4-(trifluoromethoxy)benzene[S8] (160 µL, ~0.96 mmol), and copper(I) chloride (8.0 mg, 0.081 mmol), using General Procedure F for 36 h, followed by chromatography of the product mixture on silica gel, eluting with 0-4% EtOAc/CH_2Cl_2 (foreruns) and then with 4-6% EtOAc/CH_2Cl_2, first gave crude **74**, which was chromatographed again on silica gel. Elution with 20-50% EtOAc/petroleum ether gave foreruns, and then further elution with EtOAc gave **74** (112 mg, 46%) as a pale yellow solid: mp (pentane triturate) 77-80 °C; ^{1}H NMR ($CDCl_3$) δ 8.90 (br t, *J* = 5.5 Hz, 1 H), 7.40 (s, 1 H), 7.37 (br d, *J* = 8.7 Hz, 2 H), 7.30-7.24 (m, 2 H), 7.20 (br d, *J* = 8.7 Hz, 2 H), 7.06 (br d, *J* = 7.9 Hz, 2 H), 5.07 (d, *J* = 15.7 Hz, 1 H), 4.96 (d, *J* = 15.7 Hz, 1 H), 4.54 (d, *J* = 5.7 Hz, 2 H), 4.30 (s, 2 H), 3.94 (ddd, *J* = 12.8, 9.9, 5.7 Hz, 1 H), 3.84 (ddd, *J* = 12.8, 5.9 Hz, 1 H), 1.74 (ddd, *J* = 14.3, 5.6, 4.1 Hz, 1 H), 1.67 (ddd, *J* = 14.3, 9.8, 6.1 Hz, 1 H), 1.29 (s, 3 H); HRESIMS calcd for $C_{26}H_{24}F_6N_5O_8$ *m*/*z* $[M + H]^+$ 648.1524, found 648.1538; HPLC purity: 99.9%.

Further elution of the first column above with 8-10% EtOAc/CH_2Cl_2 gave **72** (80 mg, 49%) as a cream solid: mp (Et_2O/pentane triturate) 76-79 °C; ^{1}H NMR [$(CD_3)_2SO$] δ 8.07 (s, 1 H), 7.94 (br t, *J* = 6.2 Hz, 1 H), 7.36 (br d, *J* = 8.7 Hz, 2 H), 7.32 (br d, *J* = 8.5 Hz, 2 H), 4.27-4.03 (m, 6 H), 2.22 (ddd, *J* = 14.5, 8.5, 5.9 Hz, 1 H), 2.09 (dt, *J* = 14.4, 5.4 Hz, 1 H), 1.39 (s, 3 H); ^{13}C NMR [$(CD_3)_2SO$] δ 156.0, 147.1 (2 C), 142.2, 139.1, 128.8 (2 C), 120.9 (2 C), 120.1 (q, J_{C-F} = 255.8 Hz), 117.7, 80.5, 67.6, 43.1, 39.4, 26.7, 20.9; HRESIMS calcd for $C_{17}H_{18}F_3N_4O_6$ *m*/*z* $[M + H]^+$ 431.1173, found 431.1176; HPLC purity: 97.3%.

Minimum Inhibitory Concentration Assays (MABA and LORA). MIC_{90} data against *Mycobacterium tuberculosis* (*M. tb*, strain H37Rv), representing the lowest concentration values to effect at least 90% growth inhibition, were determined using the standard MABA[S10] and LORA[S11] assays, which were conducted at the Institute for Tuberculosis Research (UIC).

***In Vitro* Parasite Growth Inhibition and Cytotoxicity Assays.** All test compounds were screened against the intracellular amastigote stages of *L. inf* and *Trypanosoma cruzi*, and the bloodstream form of *Trypanosoma brucei*, as well as for cytotoxicity toward human MRC-5 cells. These assays were carried out at the University of Antwerp in accordance with the published protocols.[S12]

Solubility Assessments. The previously reported method was employed.[S2] Briefly, the solid sample was suspended in water or 0.1 M HCl, sonicated for 15 min, and then centrifuged for 6 min; the clear supernatant was diluted with the same solvent (2-fold) and the solubility was quantified by HPLC (comparing against the peak area recorded from a standard solution).

Microsomal Stability Assays. These metabolism studies were performed by WuXi AppTec (Shanghai) Co., Ltd., Shanghai, China, in line with the recorded procedure,[S4] in which the compound concentration was 1 µM and the incubation time was 1 h.

***In Vivo* Experiments.** All animal experiments were conducted according to institutional ethical guidelines for animal care. The LSHTM animal work was performed under a UK Home Office project licence according to the Animal (Scientific Procedures) Act 1986 and the new European Directive 2010/63/EU. The project licence (70/8427) was reviewed by the LSHTM Animal Welfare and Ethical Review Board prior to submission and consequent approval by the UK Home Office.

Acute VL Infection Model (LSHTM). The original protocols were followed.[S13] Briefly, groups of five female BALB/c mice were infected with 2 x 10^7 *L. don* amastigotes and, after 7 days, were orally dosed with test compounds (or vehicle alone) once daily for five consecutive days. Parasite load in mouse livers (or spleens) was assessed by microscopic examination of impression smears. Two standard VL drugs, AmBisome and miltefosine (**1**), were also included in each experiment as positive controls.

Mouse Pharmacokinetics. Compounds **65** and **66** were evaluated by WuXi AppTec (Shanghai) Co., Ltd. Each compound was administered to two different groups of three female BALB/c mice (4 groups in total of fasted animals); intravenous dosing (at 1 mg/kg) employed a solution vehicle comprising 20% NMP and 40% PEG-400 in water, whereas oral dosing (at 25 mg/kg) used 7% Tween 80 and 3% EtOH in water. Blood samples collected at various time points post-dose (iv: 0.083, 0.25, 1, 2, 4, 7, 12, and 24 h; oral: 0.25, 1, 2, 4, 6, 8, and 24 h) were transferred into prechilled K2-EDTA tubes and kept on ice until being processed for plasma by centrifugation at 4 °C. Plasma samples were stored at -70 °C prior to analysis by LC-MS/MS, and the PK parameters were determined using Phoenix WinNonlin software (version 6.3).

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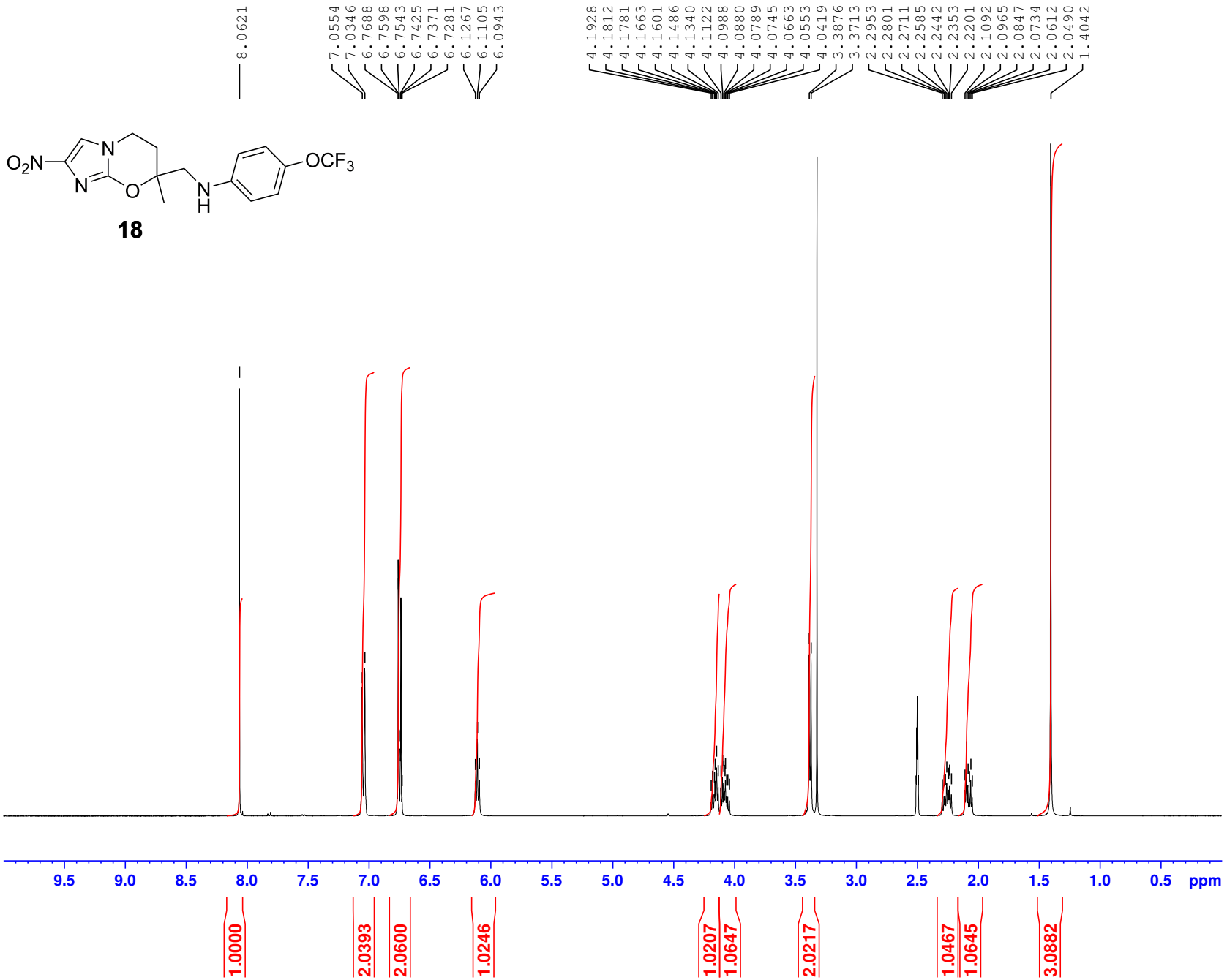
Table S4. Combustion analyses for the new compounds of Table 1 and intermediates.

No.	Formula	Calculated			Found		
		C	H	N	C	H	N
15	$C_{14}H_{13}F_3N_4O_4$	46.93	3.66	15.64	46.89	3.58	15.61
18	$C_{15}H_{15}F_3N_4O_4$	48.39	4.06	15.05	48.21	4.02	14.98
20	$C_{14}H_{15}ClN_4O_3$	52.10	4.68	17.36	52.08	4.69	17.25
22	$C_{14}H_{15}FN_4O_3$	54.90	4.94	18.29	54.94	4.92	18.30
24	$C_{15}H_{15}F_3N_4O_4$	48.39	4.06	15.05	48.38	3.93	15.04
26	$C_{16}H_{17}F_3N_4O_4$	49.74	4.44	14.50	49.80	4.40	14.57
28	$C_{15}H_{17}ClN_4O_3$	53.50	5.09	16.64	53.19	5.10	16.52
30	$C_{15}H_{17}FN_4O_3$	56.24	5.35	17.49	56.20	5.27	17.50
32	$C_7H_5F_3N_2O$	44.22	2.65	14.73	44.38	2.54	14.80
37	$C_8H_{10}N_6O_3$	40.34	4.23	35.28	40.54	4.26	35.46
42	$C_7H_8N_6O_3$	37.50	3.60	37.49	37.80	3.54	37.40
43	$C_{15}H_{13}F_3N_4O_5 \cdot 0.5H_2O$	45.58	3.57	14.17	45.59	3.55	14.04
44	$C_{16}H_{15}F_3N_4O_5 \cdot 0.5H_2O$	46.95	3.94	13.69	47.00	3.95	13.58
45	$C_{16}H_{15}F_3N_4O_5$	48.01	3.78	14.00	47.97	3.79	13.84
46	$C_{16}H_{15}F_3N_4O_5 \cdot 0.25Et_2O$	48.75	4.21	13.38	48.54	3.84	13.72
49	$C_{15}H_{14}F_3N_5O_5$	44.90	3.52	17.45	45.06	3.68	17.18
51	$C_{16}H_{16}F_3N_5O_5$	46.27	3.88	16.86	46.35	3.88	16.63
65	$C_{15}H_{13}F_3N_4O_6$	44.79	3.26	13.93	45.02	3.20	13.97
66	$C_{16}H_{15}F_3N_4O_6$	46.16	3.63	13.46	46.44	3.65	13.37
68	$C_{16}H_{15}F_3N_4O_6$	46.16	3.63	13.46	45.96	3.51	13.20
69	$C_{16}H_{15}F_3N_4O_6 \cdot 0.5H_2O$	45.18	3.79	13.17	45.25	3.63	13.15
70	$C_{16}H_{15}F_3N_4O_6$	46.16	3.63	13.46	46.20	3.64	13.48

18 (in D_6-DMSO)

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NUC1                    1H
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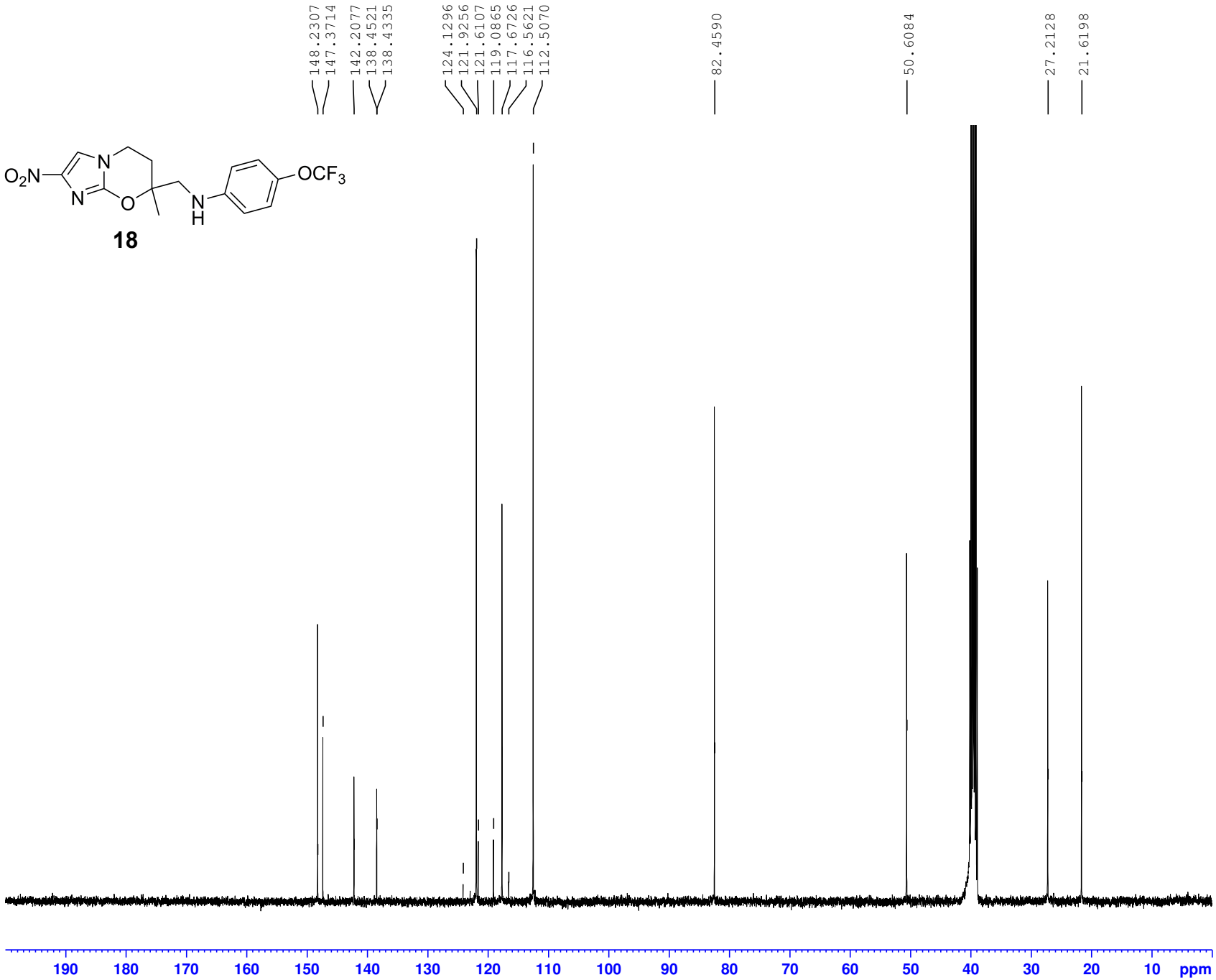
18 (in D_6-DMSO)

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TE               298.0 K
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PCPD2             100.00 usec

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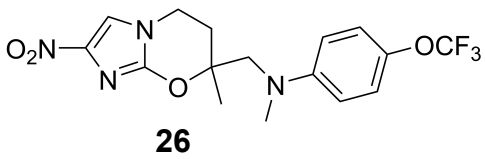
GB        0
PC                 1.40
```

26 (in D_6-DMSO)



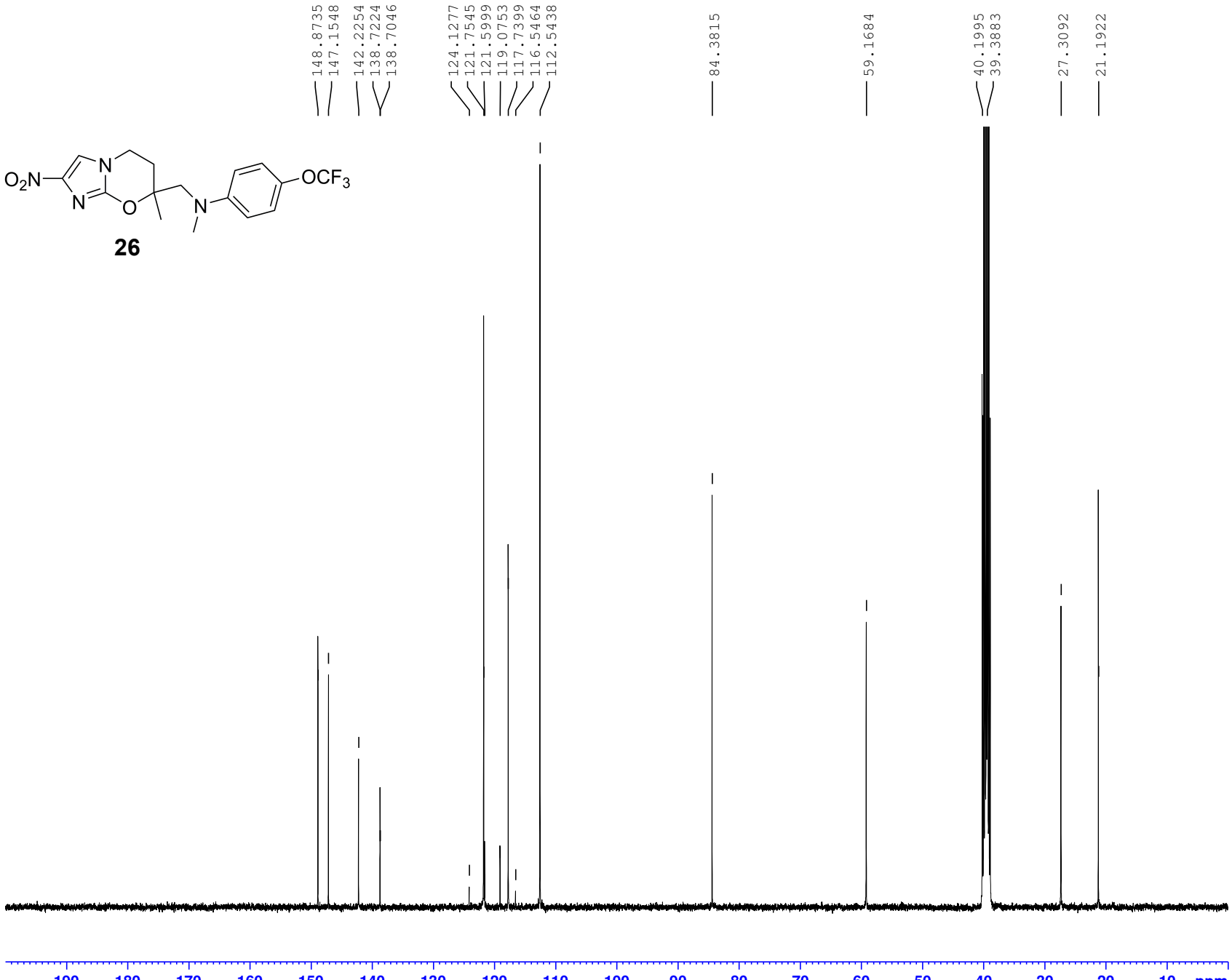
26


```
Current Data Parameters
NAME          Jan11-2016
EXPNO                 16
PROCNO                 1

F2 - Acquisition Parameters
Date_           20160111
Time              16.16 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                156.54
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF           400.1300027 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

26 (in D_6-DMSO)

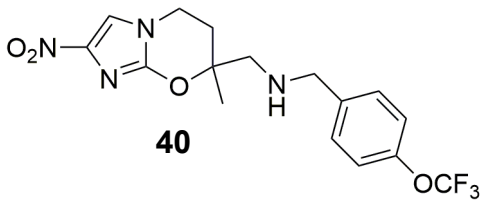



```
Current Data Parameters
NAME          Jan11-2016
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20160111
Time              21.31 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG           zgpg50
TD                 65536
SOLVENT             DMSO
NS                  9000
DS                     4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ            1.3631488 sec
RG               198.55
DW               20.800 usec
DE                6.50 usec
TE               298.0 K
D1           0.63999999 sec
D11          0.03000000 sec
TD0                    1
SFO1        100.6228298 MHz
NUC1                13C
P1               10.00 usec
PLW1        48.17399979 W
SFO2        400.1316005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2            90.00 usec
PLW2        13.19999981 W
PLW12        0.30142000 W
PLW13        0.15161000 W

F2 - Processing parameters
SI                 32768
SF          100.6128171 MHz
WDW                   EM
SSB      0
LB                1.00 Hz
GB       0
PC                1.40
```

40 (in $CDCl_3$)



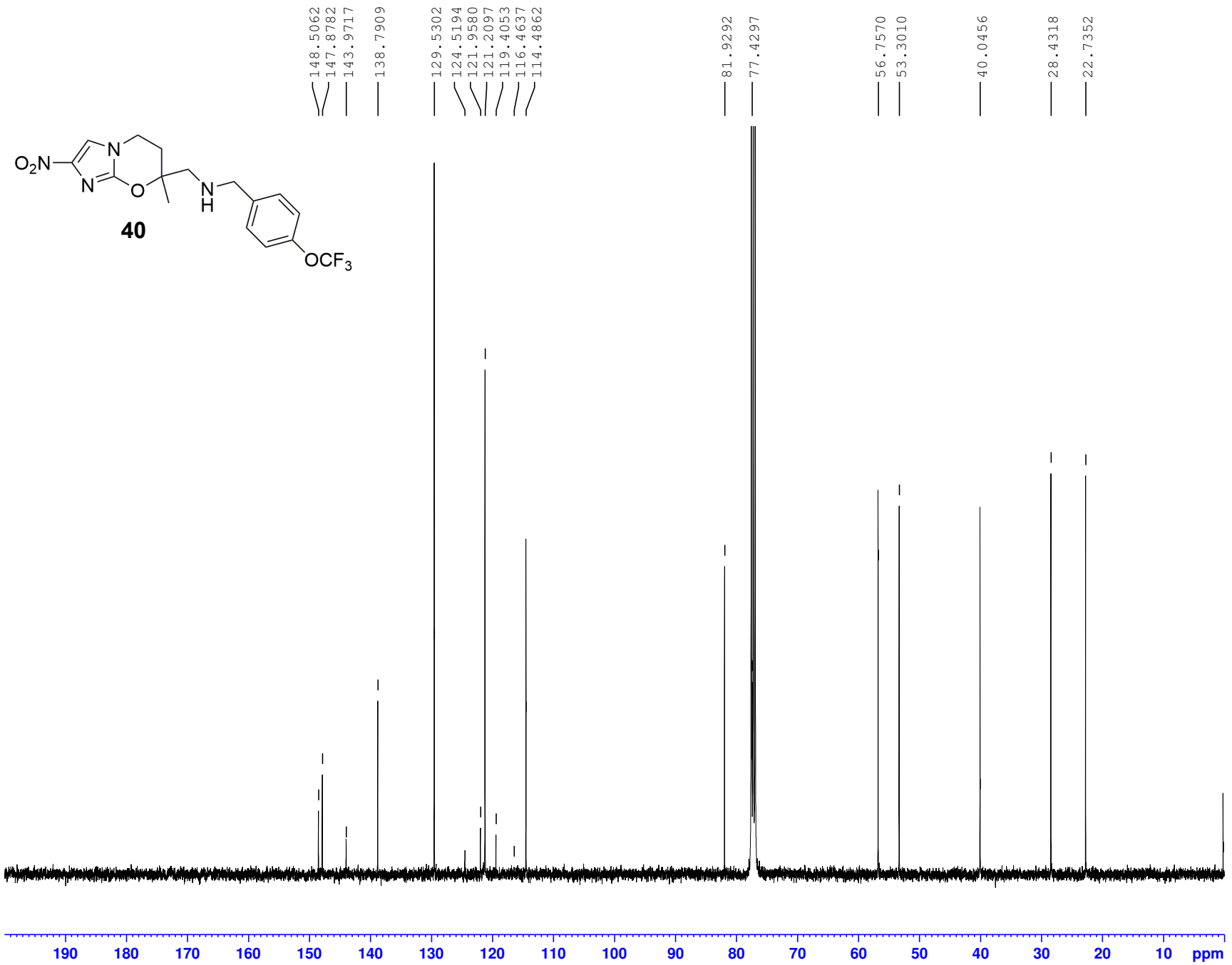
40


```
Current Data Parameters
NAME          Aug15-2019
EXPNO                 16
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190815
Time              16.39 h
INSTRUM            spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                176.55
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF           400.1300082 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

40 (in $CDCl_3$)

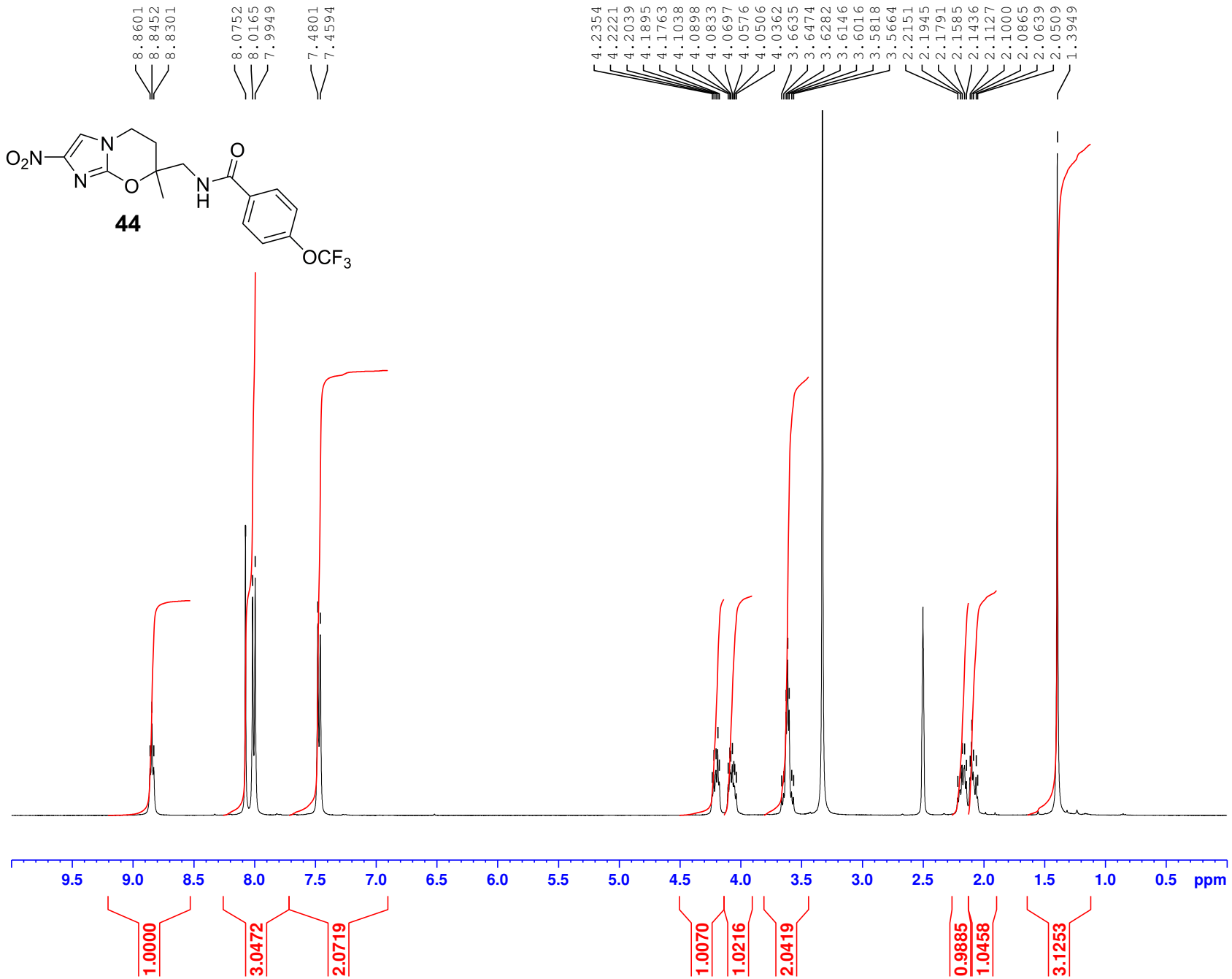



```
Current Data Parameters
NAME          Aug15-2019
EXPNO                 17
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190816
Time                4.09 h
INSTRUM            spect
PROBHD   Z108618_0860 (
PULPROG          zgpg50
TD                65536
SOLVENT           CDC13
NS                20000
DS                    4
SWH           24038.461 Hz
FIDRES         0.733596 Hz
AQ             1.3631488 sec
RG                198.55
DW                20.800 usec
DE                 6.50 usec
TE                298.0 K
D1             0.63999999 sec
D11            0.03000000 sec
TD0                    1
SFO1          100.6228298 MHz
NUC1                 13C
P1                10.00 usec
PLW1          48.17399979 W
SFO2          400.1316005 MHz
NUC2                 1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2          13.19999981 W
PLW12          0.30142000 W
PLW13          0.15161000 W

F2 - Processing parameters
SI                 32768
SF            100.6127480 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

44 (in D_6-DMSO)

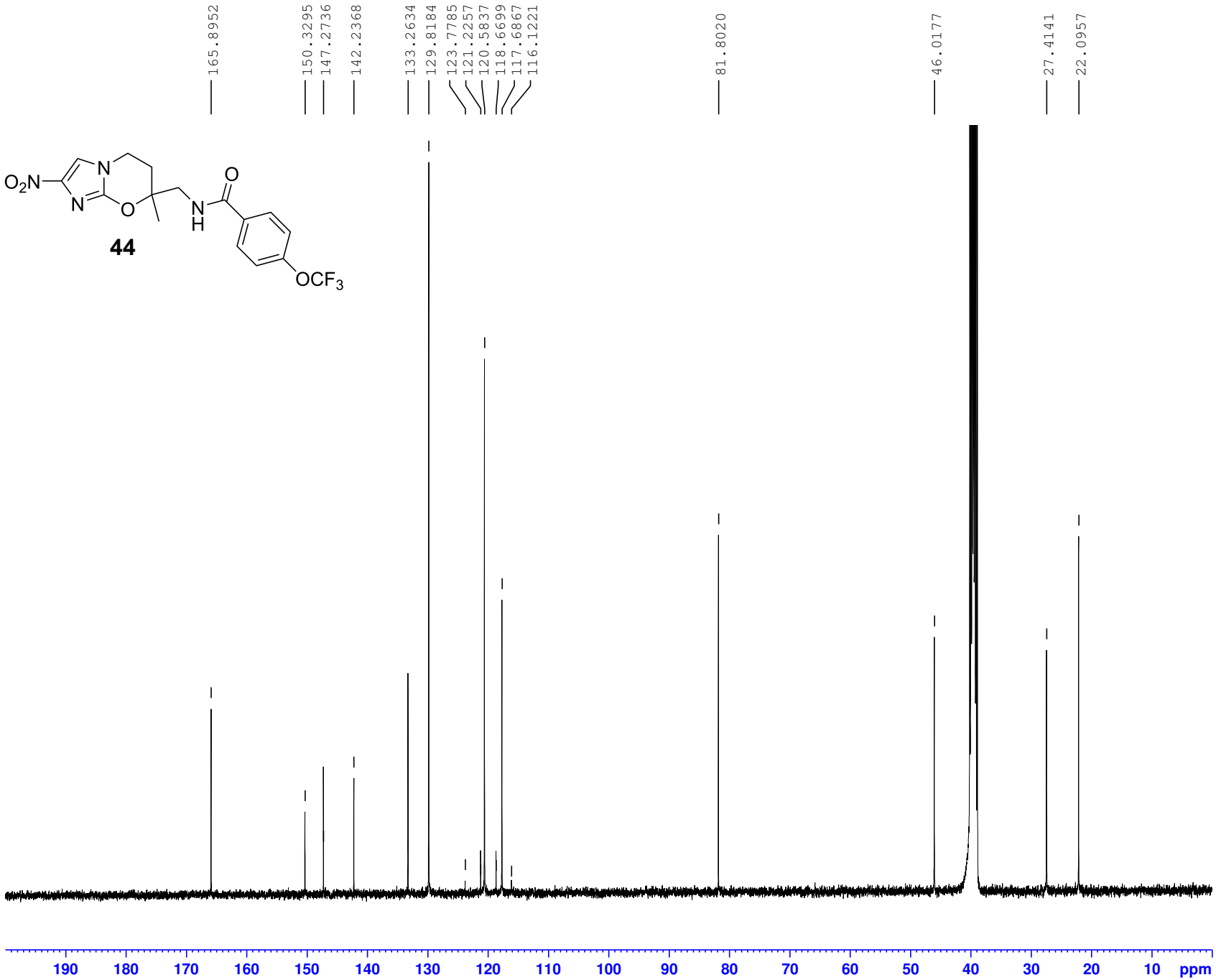



```
Current Data Parameters
NAME      Aug07-2015-FMHSacsr
EXPNO                   50
PROCNO                   1

F2 - Acquisition Parameters
Date_              20150810
Time                  1.20 h
INSTRUM               spect
PROBHD   5 mm BBO BB-1H
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       64
DS                        2
SWH                8389.262 Hz
FIDRES             0.256020 Hz
AQ                 3.9059455 sec
RG                     161.3
DW                    59.600 usec
DE                    10.00 usec
TE                    298.0 K
D1              2.00000000 sec
TD0                       1
SFO1           400.1334011 MHz
NUC1                    1H
P1                    11.00 usec

F2 - Processing parameters
SI                    32768
SF             400.1300021 MHz
WDW                      EM
SSB       0
LB                     0.30 Hz
GB        0
PC                    1.00
```

44 (in D_6-DMSO)

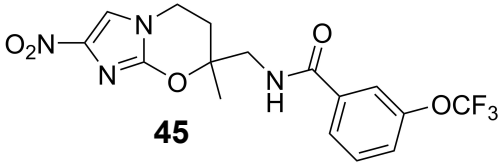



```
Current Data Parameters
NAME      Aug07-2015-FMHSacsrcnmr
EXPNO                 51
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150810
Time                6.32 h
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg50
TD                 65536
SOLVENT              DMSO
NS                    9000
DS                       4
SWH            26178.010 Hz
FIDRES             0.798889 Hz
AQ             1.2517376 sec
RG                 11585.2
DW                19.100 usec
DE                10.00 usec
TE                298.0 K
D1            0.75000000 sec
d11           0.03000000 sec
DELTA         0.64999998 sec
TD0                      1
SFO1         100.6248425 MHz
NUC1                  13C
P1                11.80 usec
SFO2         400.1316005 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              100.00 usec

F2 - Processing parameters
SI                   32768
SF           100.6128170 MHz
WDW                     EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

45 (in D_6-DMSO)



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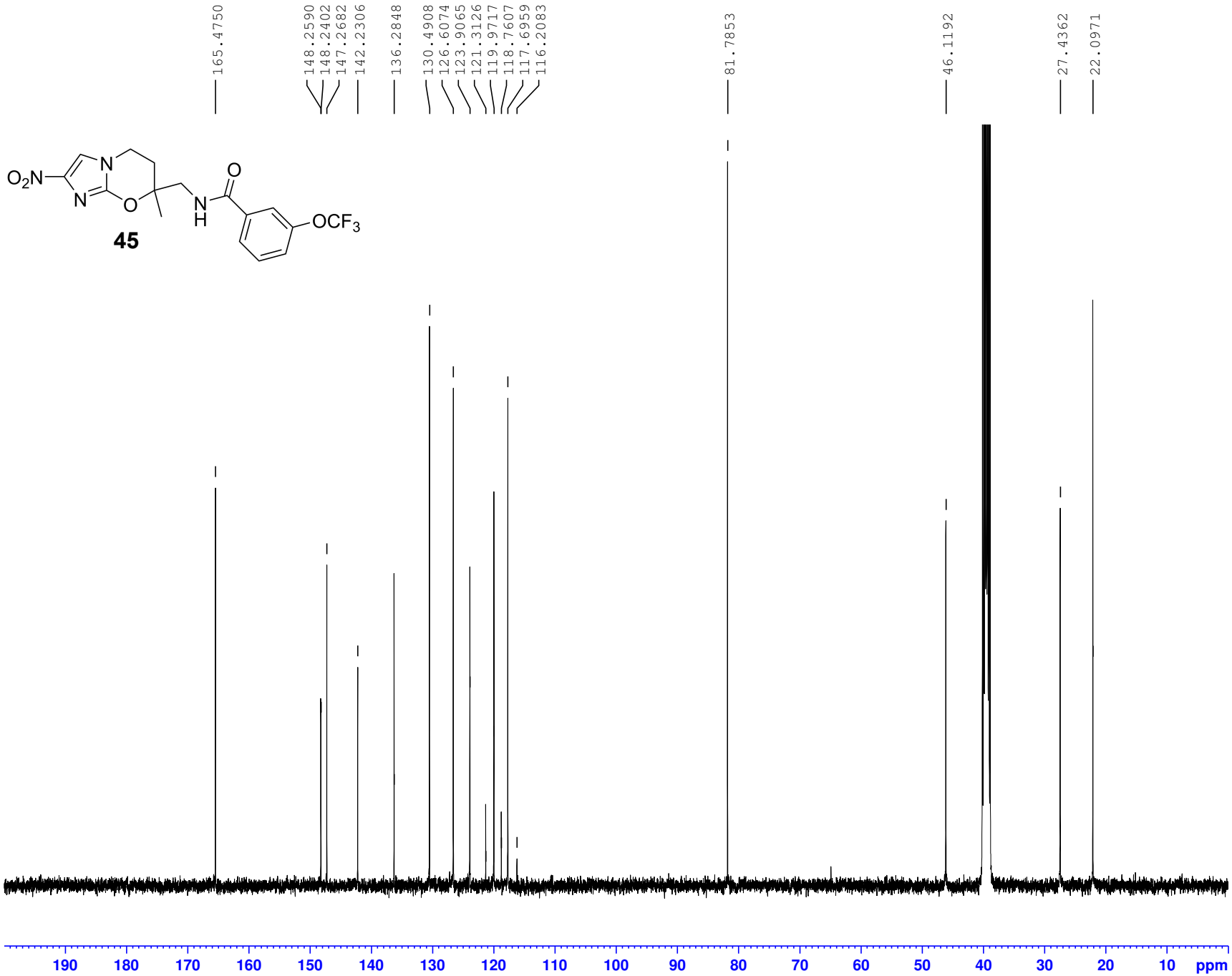
```
Current Data Parameters
NAME          Dec04-2020
EXPNO                  5
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201205
Time              14.55 h
INSTRUM            spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                176.55
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF          400.1300026 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

45 (in D_6-DMSO)

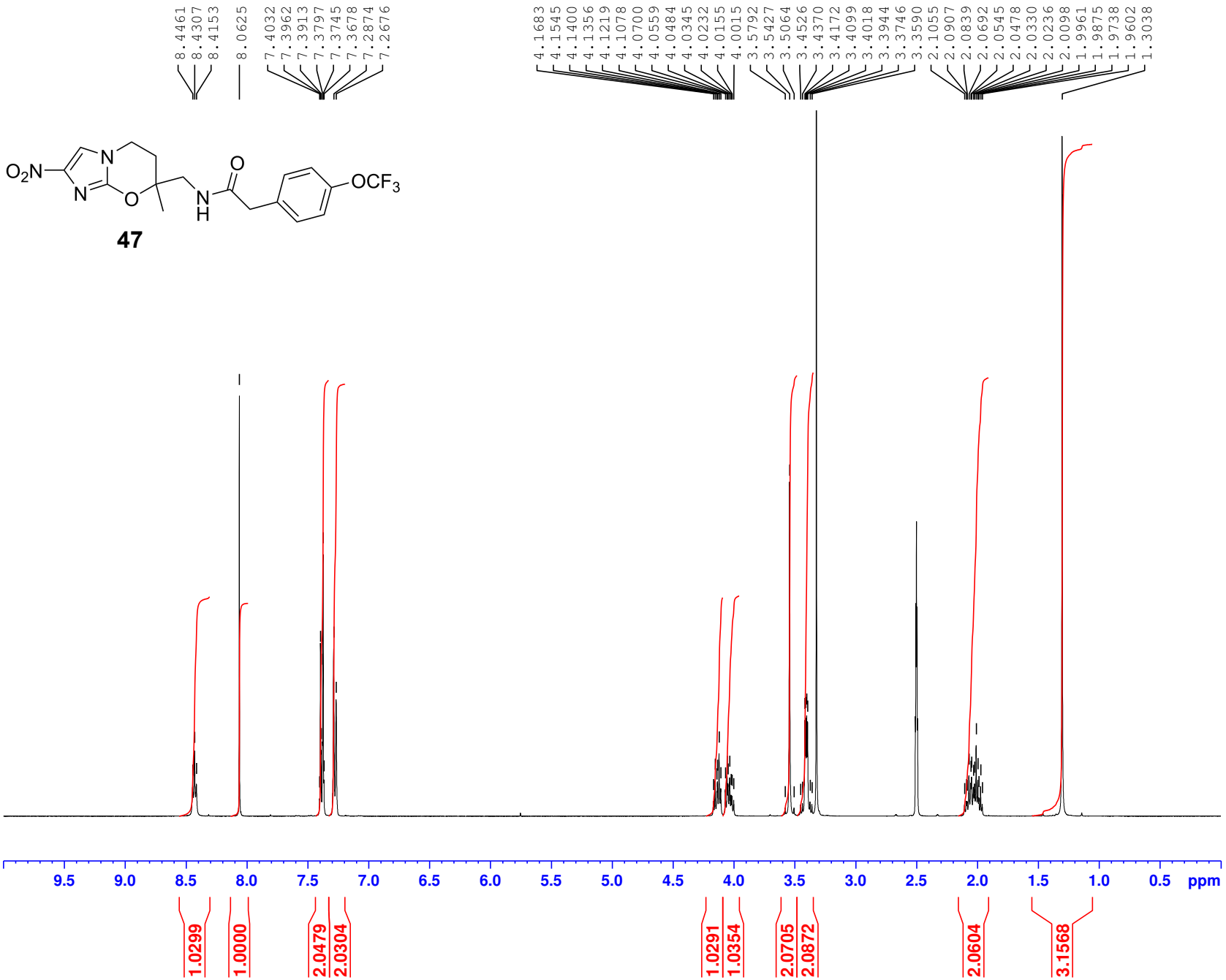



```
Current Data Parameters
NAME          Dec04-2020
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201205
Time               21.49 h
INSTRUM             spect
PROBHD    Z108618_0860 (
PULPROG           zgpg50
TD                 65536
SOLVENT             DMSO
NS                 12000
DS                     4
SWH            24038.461 Hz
FIDRES         0.733596 Hz
AQ             1.3631488 sec
RG                198.55
DW                20.800 usec
DE                 6.50 usec
TE                298.0 K
D1             0.63999999 sec
D11            0.03000000 sec
TD0                    1
SFO1          100.6228298 MHz
NUC1                  13C
P1                 10.00 usec
PLW1          48.17399979 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2              90.00 usec
PLW2          13.19999981 W
PLW12          0.30142000 W
PLW13          0.15161000 W

F2 - Processing parameters
SI                 32768
SF            100.6128174 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```

47 (in D_6-DMSO)

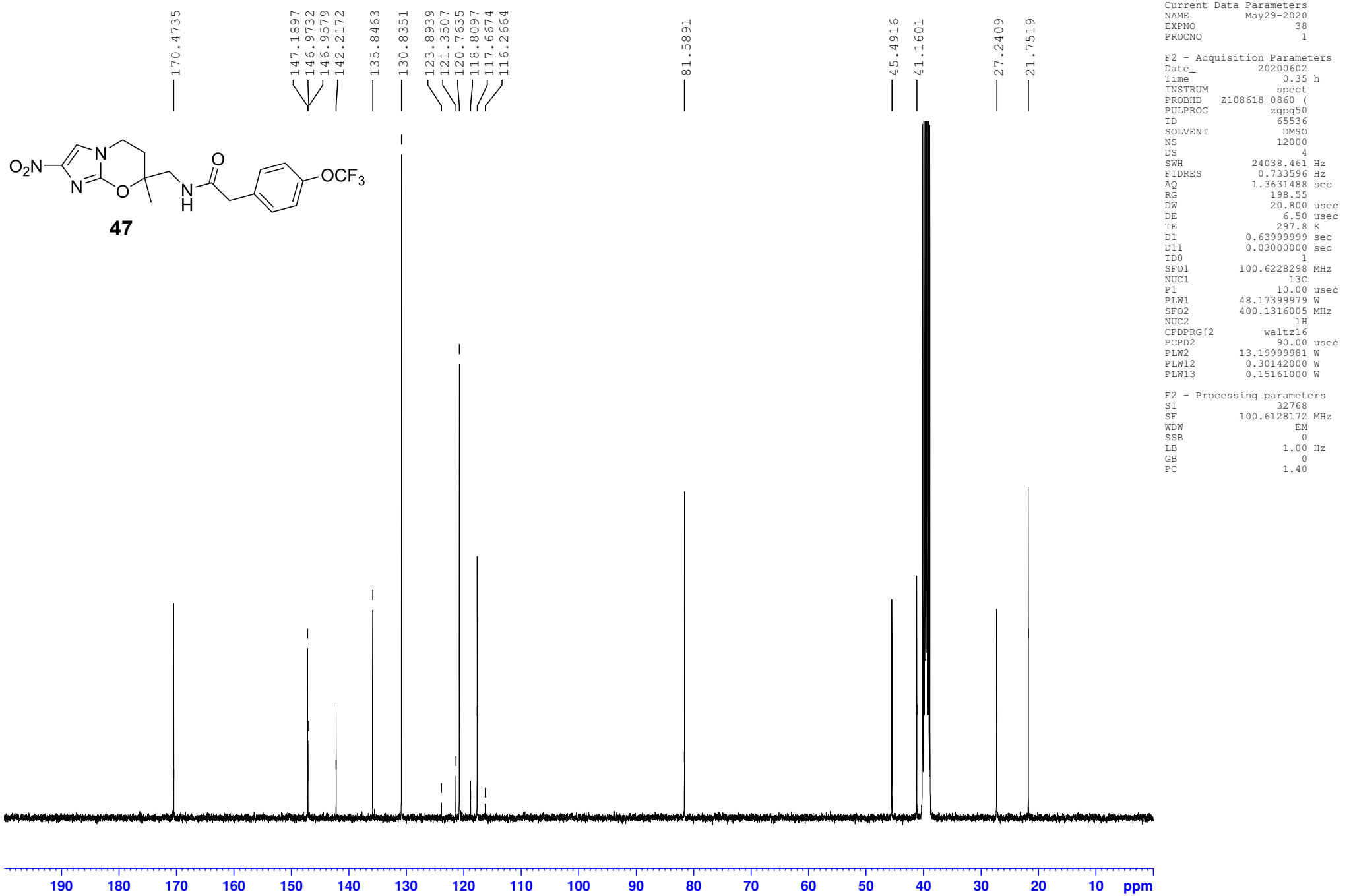



```
Current Data Parameters
NAME          May29-2020
EXPNO                 37
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200601
Time              17.40 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                156.54
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1        13.19999981 W

F2 - Processing parameters
SI                 65536
SF          400.1300026 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

47 (in D_6-DMSO)

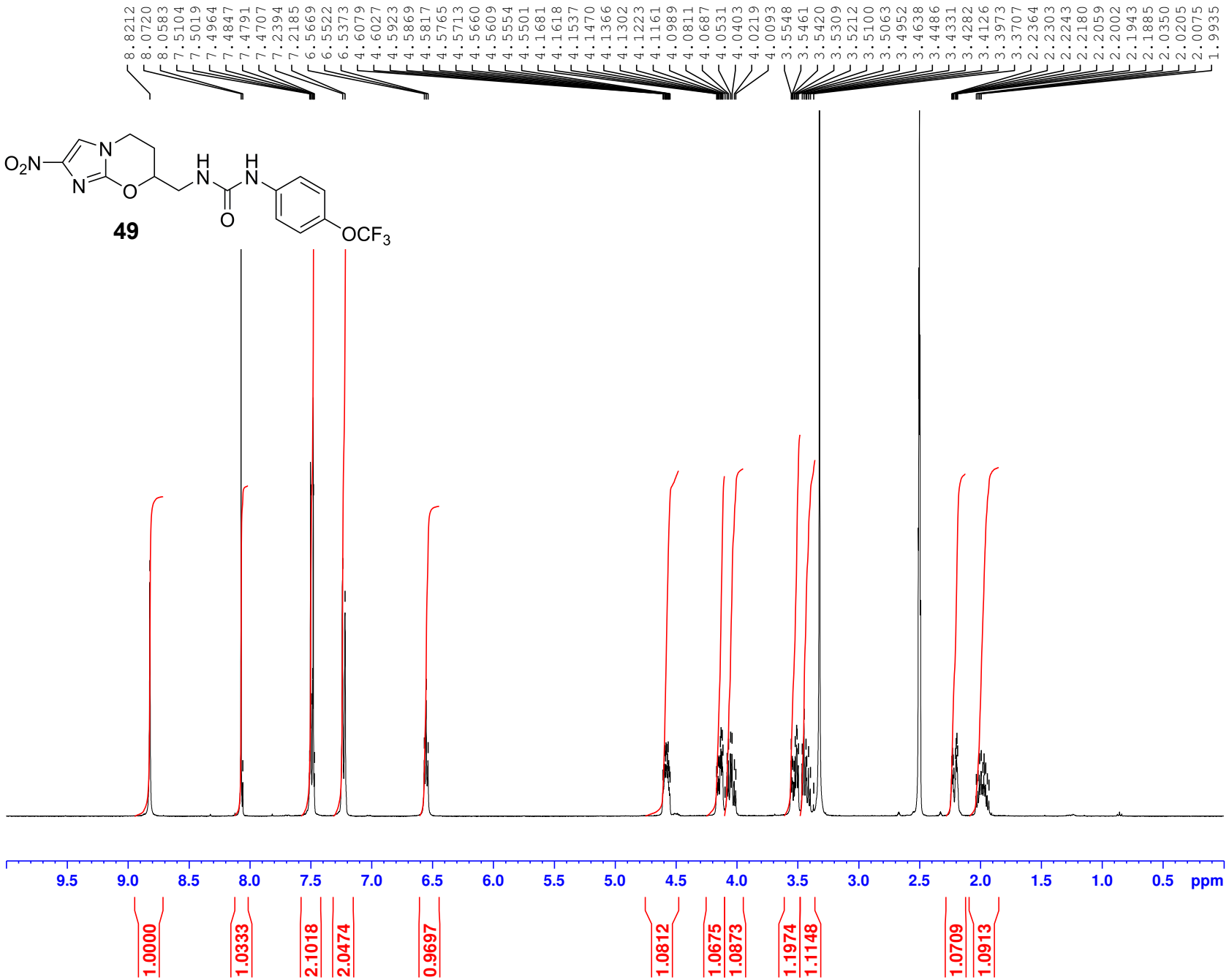



```
Current Data Parameters
NAME          May29-2020
EXPNO                 38
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200602
Time               0.35 h
INSTRUM           spect
PROBHD   Z108618_0860 (
PULPROG          zgpg50
TD                65536
SOLVENT            DMSO
NS                12000
DS                    4
SWH           24038.461 Hz
FIDRES         0.733596 Hz
AQ             1.3631488 sec
RG                198.55
DW                20.800 usec
DE                 6.50 usec
TE                297.8 K
D1             0.63999999 sec
D11            0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                13C
P1                10.00 usec
PLW1         48.17399979 W
SFO2         400.1316005 MHz
NUC2                1H
CPDPRG[2        waltz16
PCPD2             90.00 usec
PLW2         13.19999981 W
PLW12         0.30142000 W
PLW13         0.15161000 W

F2 - Processing parameters
SI                32768
SF           100.6128172 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

49 (in D_6-DMSO)

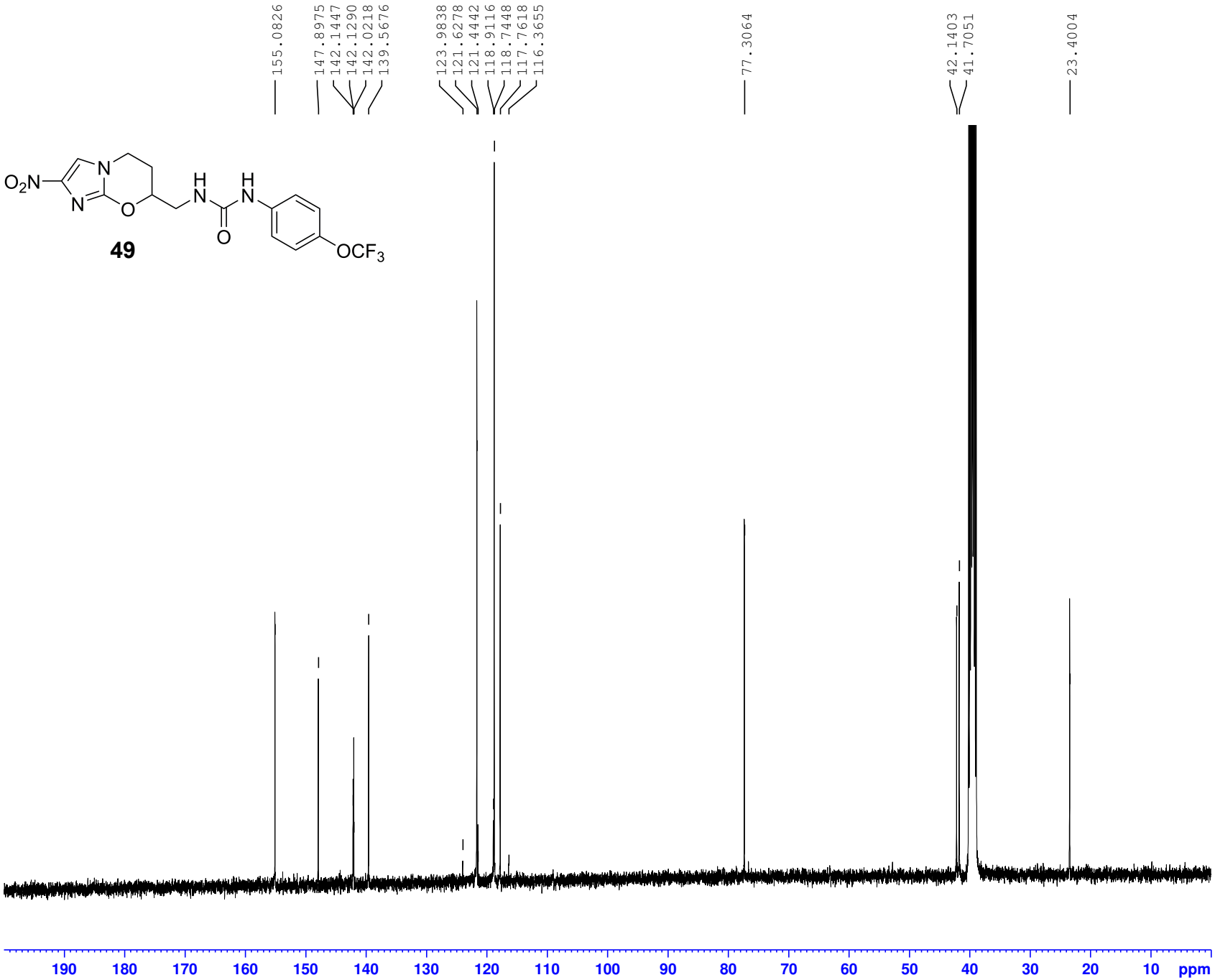



```
Current Data Parameters
NAME          Jan25-2017
EXPNO                 20
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170126
Time              0.38 h
INSTRUM           spect
PROBHD   Z108618_0860 (
PULPROG           zg30
TD               65536
SOLVENT           DMSO
NS                  64
DS                   2
SWH            8012.820 Hz
FIDRES         0.244532 Hz
AQ             4.0894465 sec
RG               176.55
DW               62.400 usec
DE                6.50 usec
TE               298.0 K
D1            1.00000000 sec
TD0                  1
SFO1         400.1324708 MHz
NUC1                 1H
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI               65536
SF           400.1300025 MHz
WDW                  EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

49 (in D_6-DMSO)

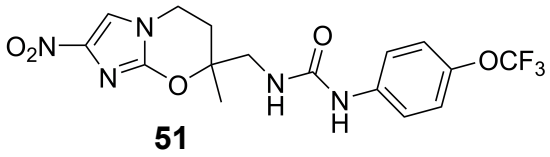



```
Current Data Parameters
NAME          Jan25-2017
EXPNO                 21
PROCNO                 1

F2 - Acquisition Parameters
Date_           20170126
Time               8.42 h
INSTRUM           spect
PROBHD   Z108618_0860 (
PULPROG          zgpg50
TD                65536
SOLVENT             DMSO
NS                14000
DS                    4
SWH           24038.461 Hz
FIDRES         0.733596 Hz
AQ            1.3631488 sec
RG               198.55
DW               20.800 usec
DE                6.50 usec
TE               298.0 K
D1           0.63999999 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6228298 MHz
NUC1               13C
P1               10.00 usec
PLW1        48.17399979 W
SFO2        400.1316005 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2             90.00 usec
PLW2        13.19999981 W
PLW12        0.30142000 W
PLW13        0.15161000 W

F2 - Processing parameters
SI                32768
SF          100.6128174 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.40
```

51 (in D_6-DMSO)



51

8.7824 | 8.0784 | 7.4986 7.4901 7.4846 7.4729 7.4673 7.4588 7.2360 7.2152 | 6.5668 6.5513 6.5358

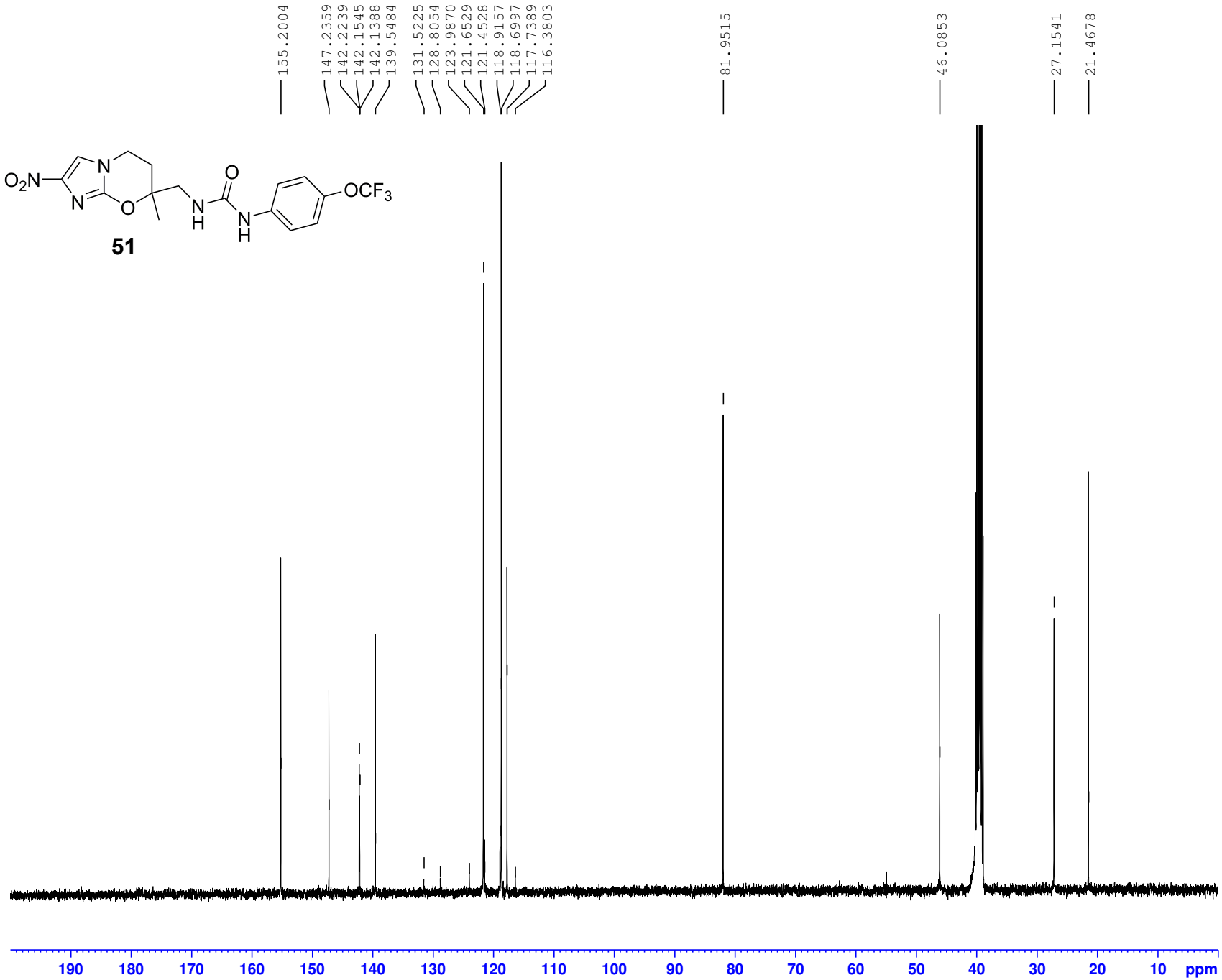
4.2168 4.2036 4.1896 4.1841 4.1713 4.1574 4.1070 4.0931 4.0842 4.0703 4.0605 4.0514 4.0376 3.5510 3.4574 3.4418 3.4264 2.1773 2.1625 2.1545 2.1407 2.1263 2.1185 2.1037 2.0822 2.0680 2.0551 2.0452 2.0323 2.0192 1.3565


```
Current Data Parameters
NAME      Aug07-2015-FMHSacsr
EXPNO                   48
PROCNO                   1

F2 - Acquisition Parameters
Date_              20150809
Time                 19.58 h
INSTRUM              spect
PROBHD   5 mm BBO BB-1H
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     64
DS                      2
SWH             8389.262 Hz
FIDRES             0.256020 Hz
AQ              3.9059455 sec
RG                   161.3
DW                  59.600 usec
DE                  10.00 usec
TE                  298.0 K
D1            2.00000000 sec
TD0                     1
SFO1          400.1334011 MHz
NUC1                   1H
P1                  11.00 usec

F2 - Processing parameters
SI                  32768
SF            400.1300024 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

51 (in D_6-DMSO)

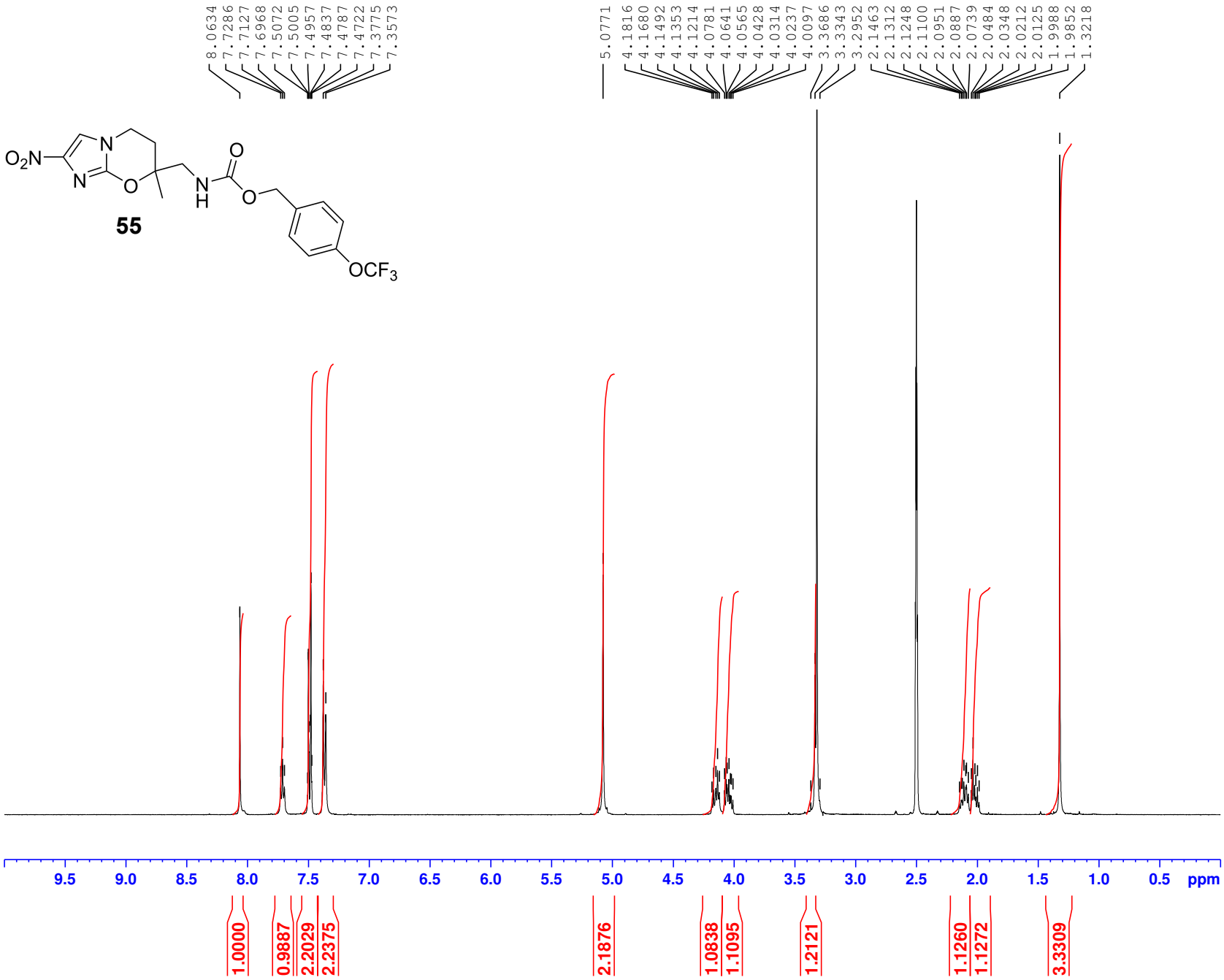



```
Current Data Parameters
NAME      Aug07-2015-FMHSacsrcnmr
EXPNO                 49
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150810
Time                1.10 h
INSTRUM            spect
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg50
TD                65536
SOLVENT             DMSO
NS                  9000
DS                     4
SWH           26178.010 Hz
FIDRES            0.798889 Hz
AQ             1.2517376 sec
RG                11585.2
DW                19.100 usec
DE                10.00 usec
TE                298.0 K
D1             0.75000000 sec
d11            0.03000000 sec
DELTA          0.64999998 sec
TD0                    1
SFO1          100.6248425 MHz
NUC1                  13C
P1                11.80 usec
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2              100.00 usec

F2 - Processing parameters
SI                 32768
SF            100.6128164 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

55 (in D_6-DMSO)

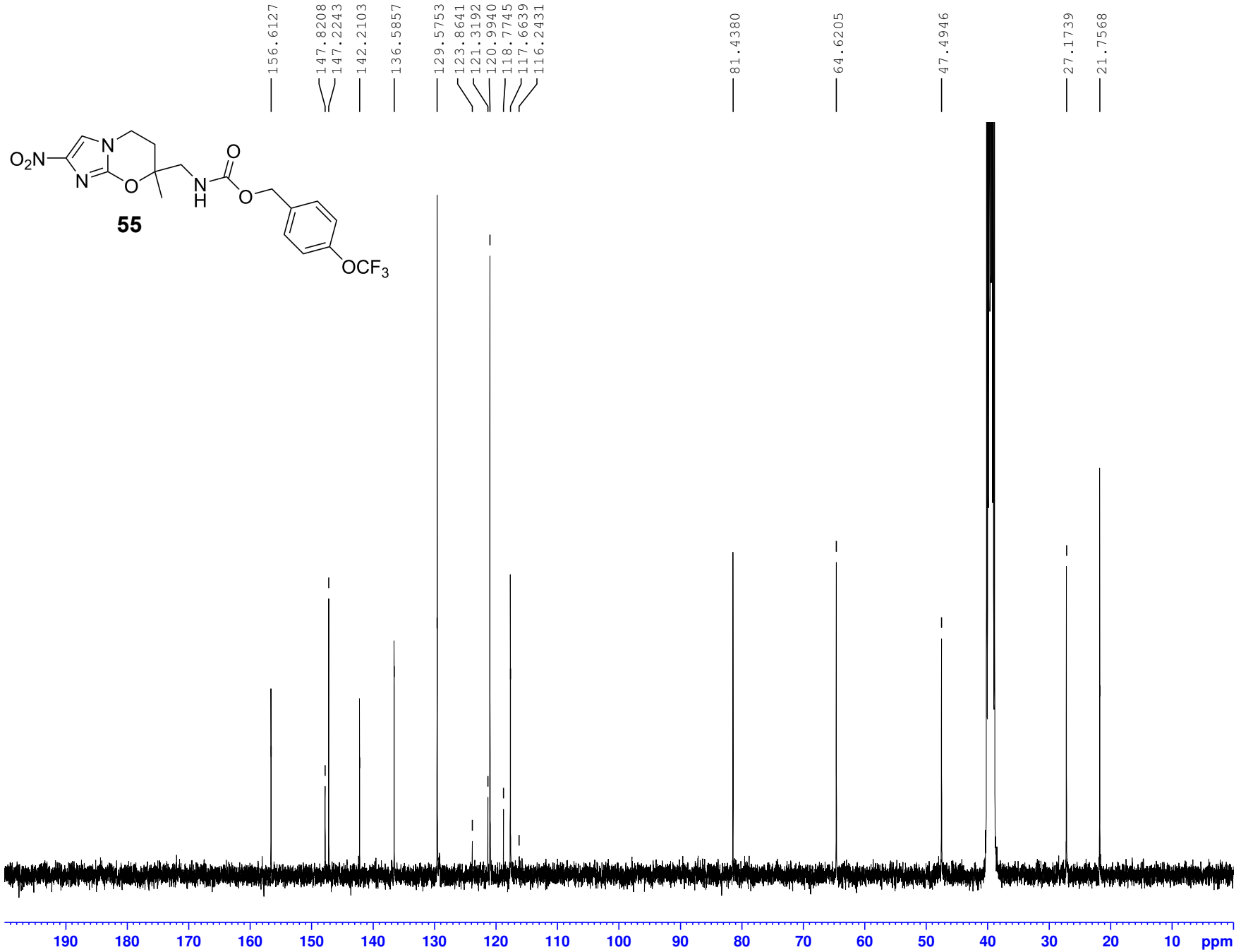



```
Current Data Parameters
NAME          Jun12-2020
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200612
Time              23.20 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                198.55
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1
SFO1          400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1          13.19999981 W

F2 - Processing parameters
SI                 65536
SF            400.1300026 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

55 (in D_6-DMSO)

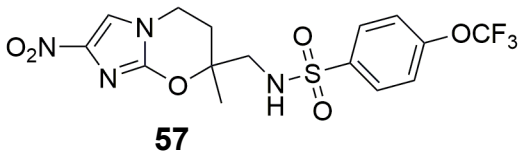



```
Current Data Parameters
NAME          Jun12-2020
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200613
Time               9.41 h
INSTRUM             spect
PROBHD    Z108618_0860 (
PULPROG           zgpg50
TD                 65536
SOLVENT             DMSO
NS                 18000
DS                     4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ              1.3631488 sec
RG                 198.55
DW                20.800 usec
DE                 6.50 usec
TE                298.0 K
D1             0.63999999 sec
D11            0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                13C
P1                10.00 usec
PLW1         48.17399979 W
SFO2         400.1316005 MHz
NUC2                1H
CPDPRG[2        waltz16
PCPD2             90.00 usec
PLW2         13.19999981 W
PLW12         0.30142000 W
PLW13         0.15161000 W

F2 - Processing parameters
SI                 32768
SF           100.6128174 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```

57 (in D_6-DMSO)



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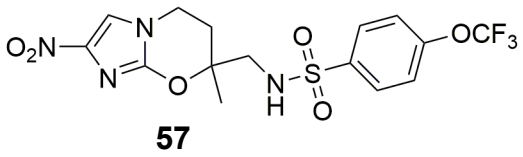
```
Current Data Parameters
NAME          Aug14-2019
EXPNO                 15
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190814
Time              17.19 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                176.55
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF           400.1300026 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

57 (in D_6-DMSO)



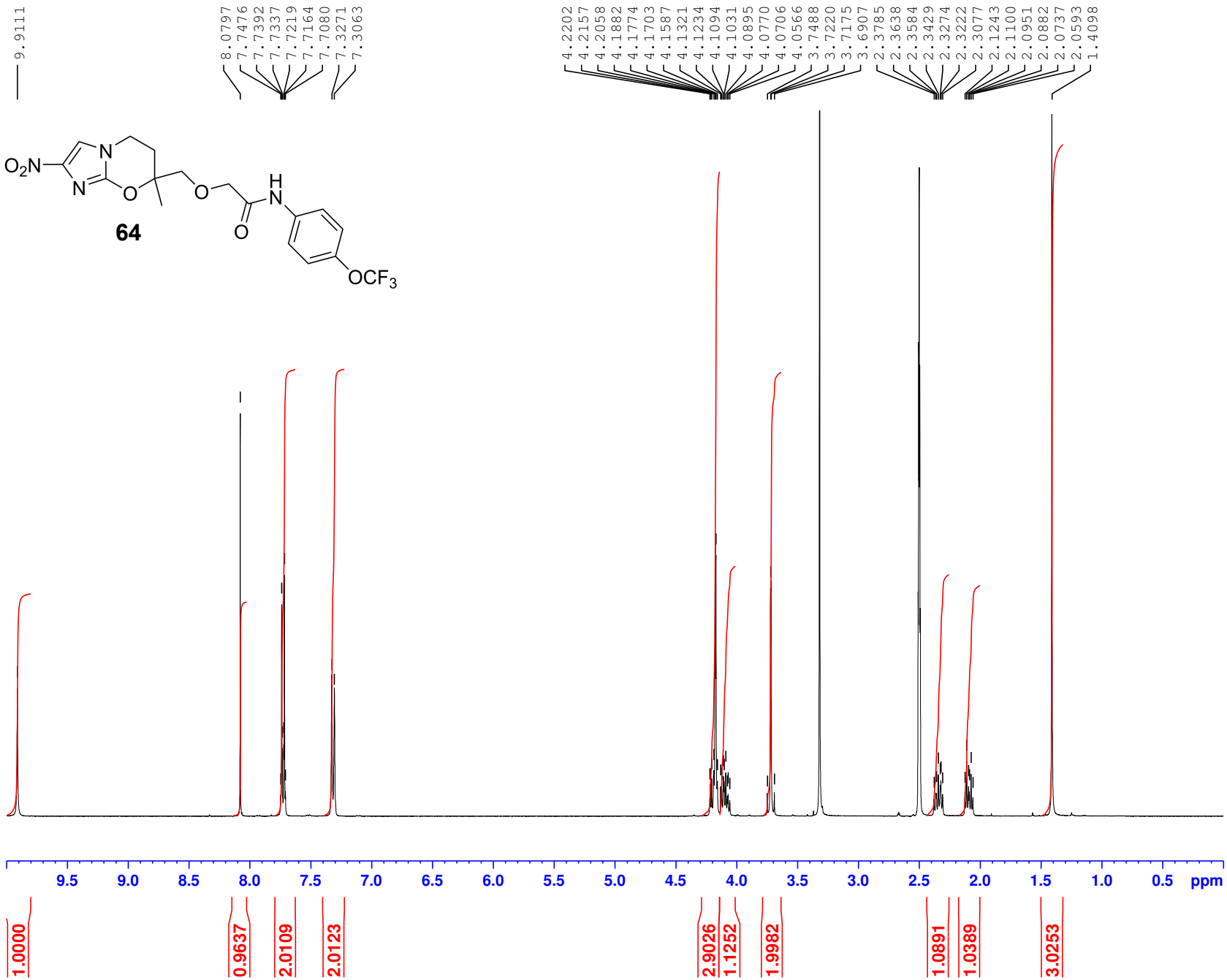
57


```
Current Data Parameters
NAME          Aug14-2019
EXPNO                 16
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190815
Time               4.49 h
INSTRUM            spect
PROBHD   Z108618_0860 (
PULPROG          zgpg50
TD                65536
SOLVENT            DMSO
NS                20000
DS                    4
SWH           24038.461 Hz
FIDRES         0.733596 Hz
AQ            1.3631488 sec
RG               198.55
DW               20.800 usec
DE                6.50 usec
TE               298.0 K
D1            0.63999999 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6228298 MHz
NUC1                13C
P1                10.00 usec
PLW1         48.17399979 W
SFO2         400.1316005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2         13.19999981 W
PLW12         0.30142000 W
PLW13         0.15161000 W

F2 - Processing parameters
SI                32768
SF           100.6128176 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

64 (in D_6-DMSO)

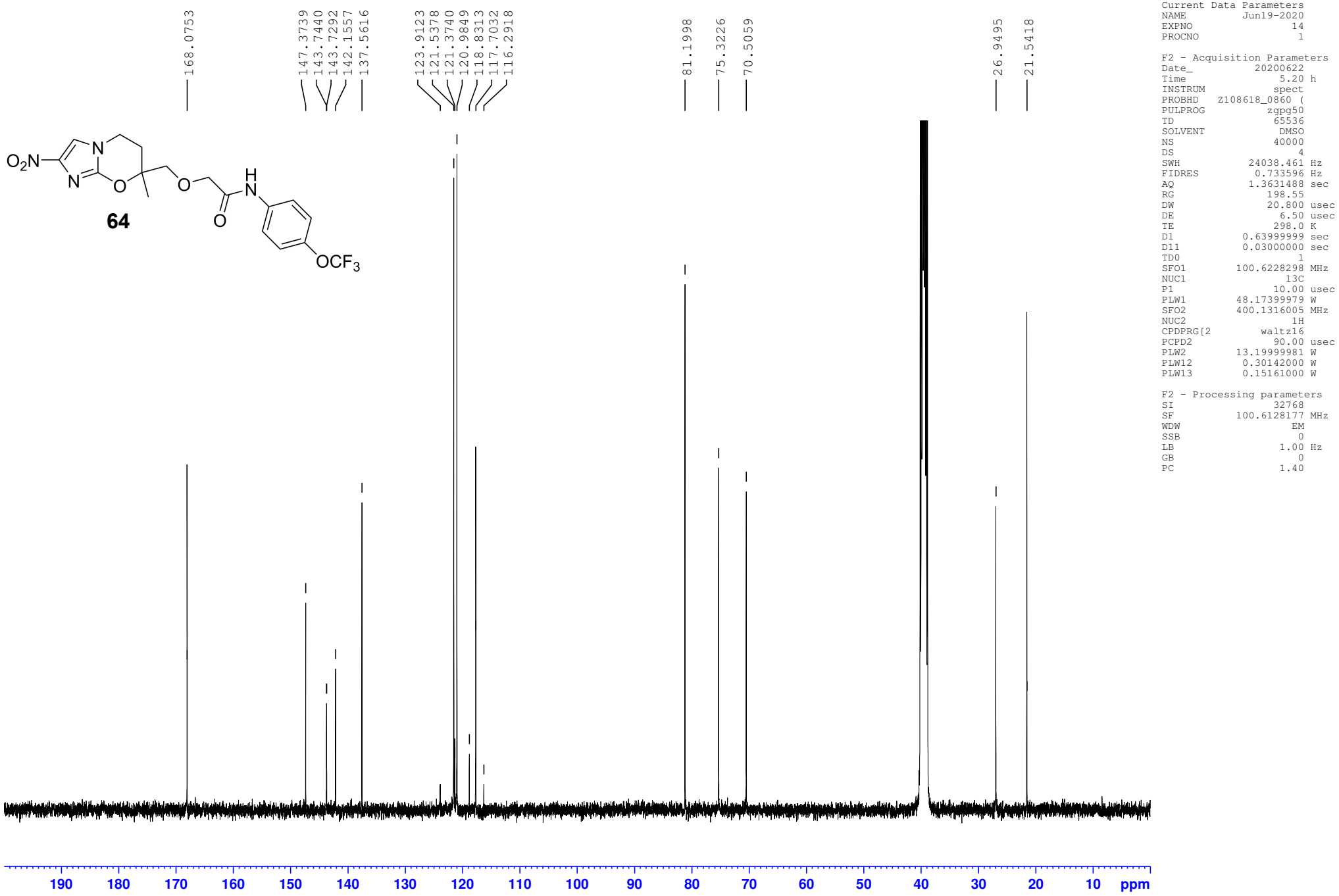



```
Current Data Parameters
NAME          Jun19-2020
EXPNO                 13
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200621
Time               6.22 h
INSTRUM           spect
PROBHD   Z108618_0860 (
PULPROG            zg30
TD                65536
SOLVENT            DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                198.55
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF          400.1300026 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

64 (in D_6-DMSO)

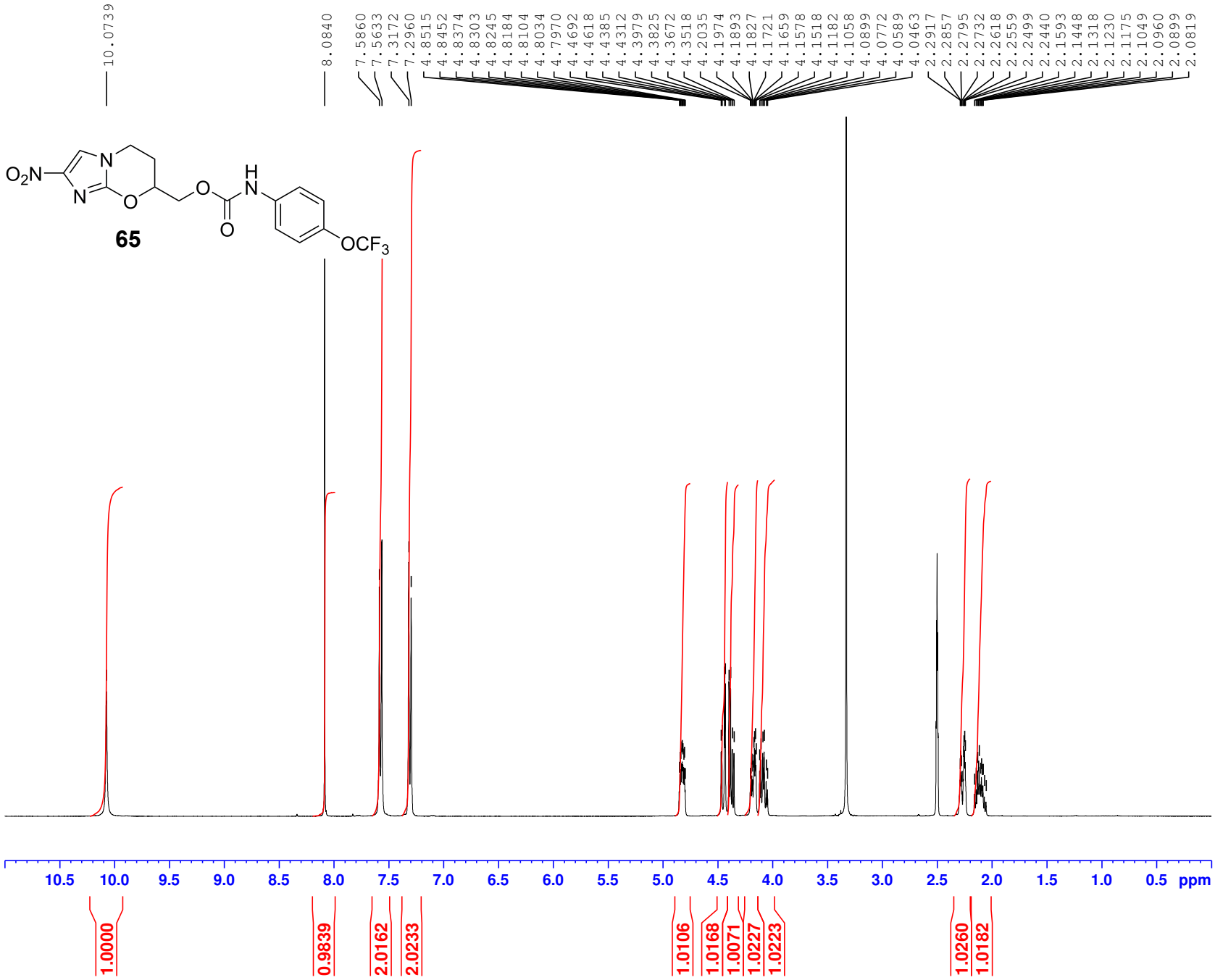



```
Current Data Parameters
NAME          Jun19-2020
EXPNO                 14
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200622
Time               5.20 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG           zgpg50
TD                 65536
SOLVENT             DMSO
NS                 40000
DS                     4
SWH            24038.461 Hz
FIDRES          0.733596 Hz
AQ              1.3631488 sec
RG                198.55
DW                20.800 usec
DE                 6.50 usec
TE                298.0 K
D1             0.63999999 sec
D11            0.03000000 sec
TD0                    1
SFO1          100.6228298 MHz
NUC1                 13C
P1                10.00 usec
PLW1          48.17399979 W
SFO2          400.1316005 MHz
NUC2                 1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2          13.19999981 W
PLW12          0.30142000 W
PLW13          0.15161000 W

F2 - Processing parameters
SI                 32768
SF            100.6128177 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                 1.40
```

65 (in D_6-DMSO)

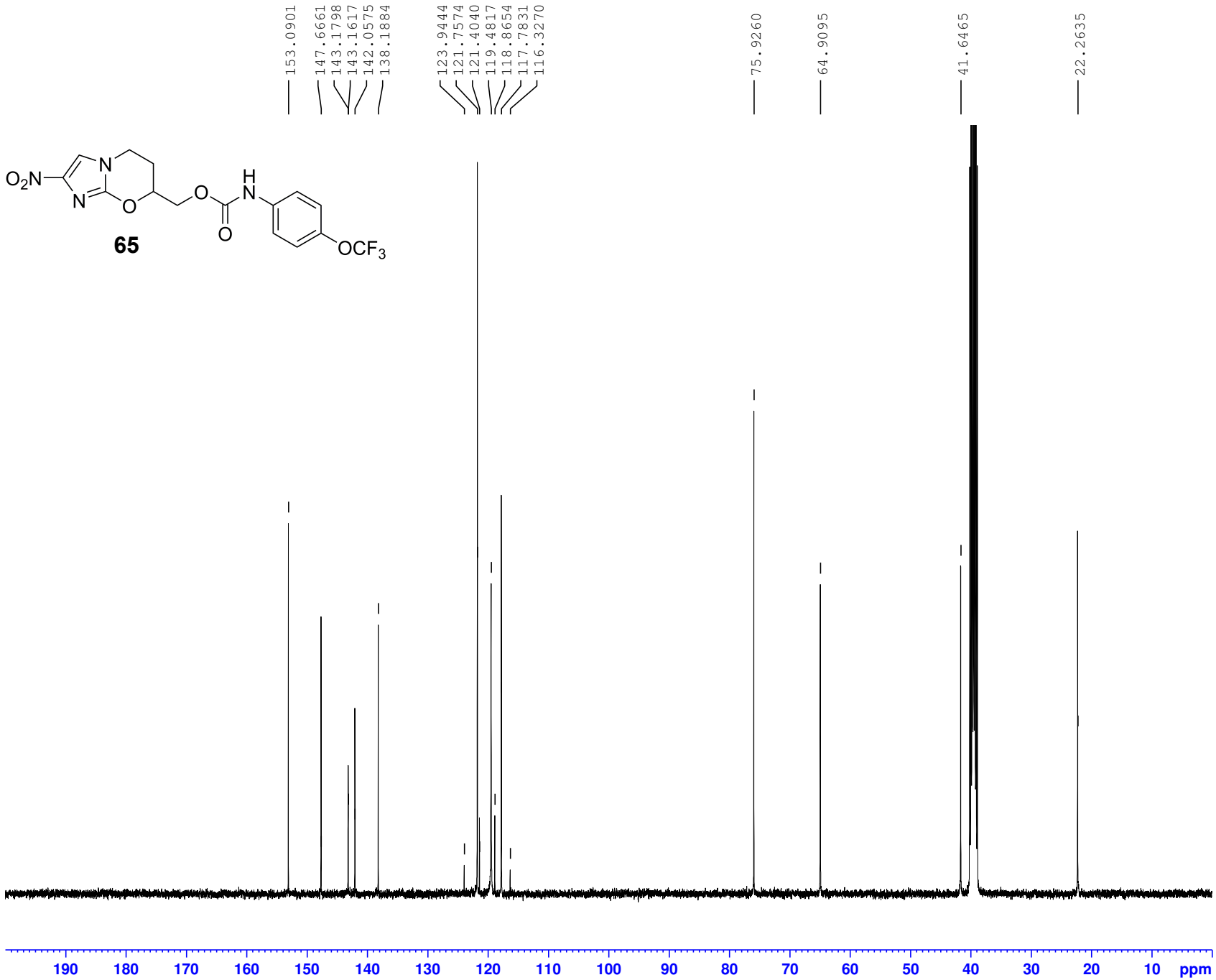



```
Current Data Parameters
NAME          Jan12-2016
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20160112
Time              16.11 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH            8012.820 Hz
FIDRES         0.122266 Hz
AQ             4.0894465 sec
RG                176.55
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P1                13.60 usec
PLW1        13.19999981 W

F2 - Processing parameters
SI                 65536
SF           400.1300026 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

65 (in D_6-DMSO)

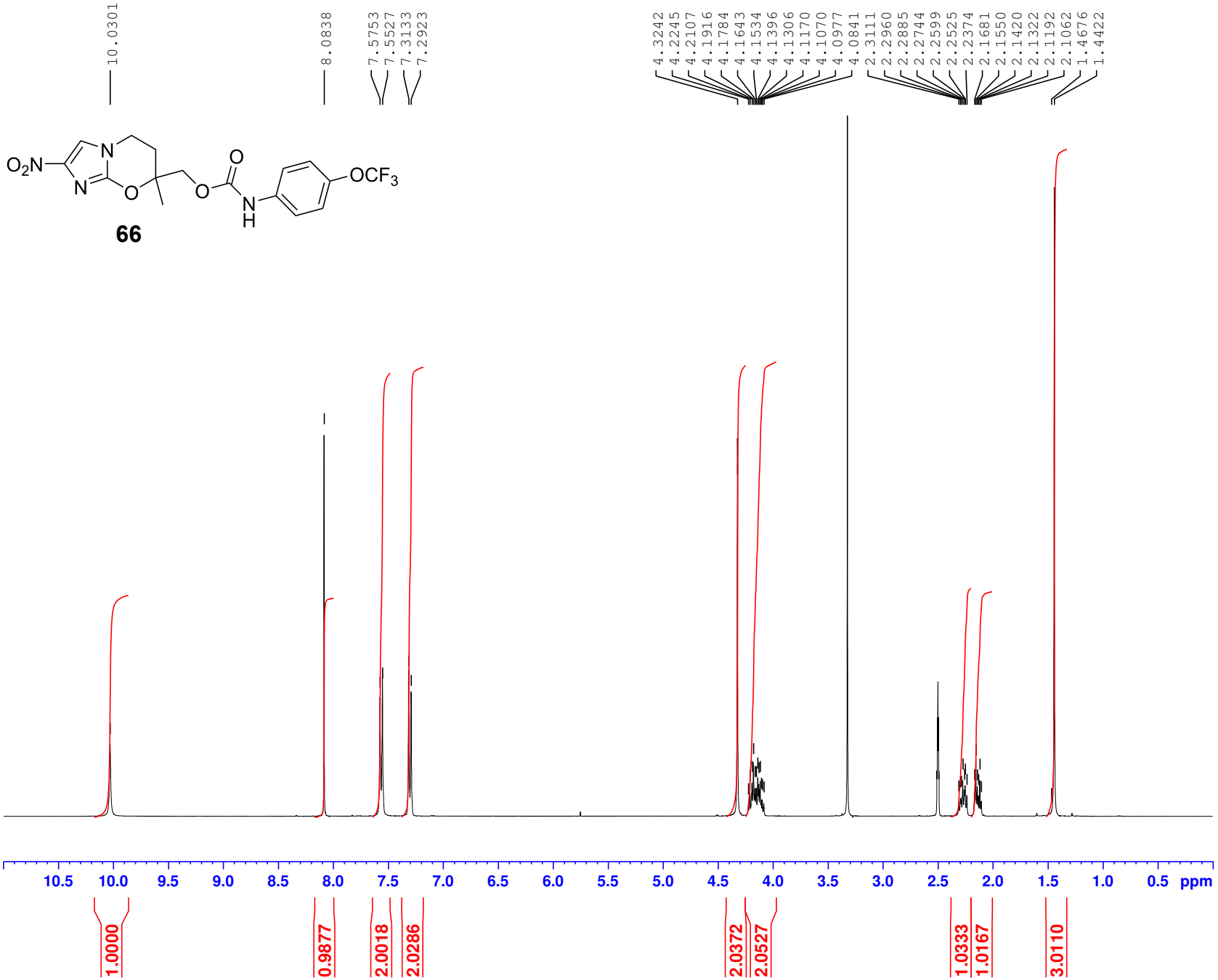



```
Current Data Parameters
NAME          Jan12-2016
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20160112
Time               23.06 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG           zgpg50
TD                 65536
SOLVENT              DMSO
NS                 12000
DS                     4
SWH            24038.461 Hz
FIDRES             0.366798 Hz
AQ              1.3631488 sec
RG                198.55
DW                20.800 usec
DE                 6.50 usec
TE                298.0 K
D1             0.63999999 sec
D11            0.03000000 sec
TD0                    1
SFO1          100.6228298 MHz
NUC1                  13C
P1                10.00 usec
PLW1          48.17399979 W
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2             90.00 usec
PLW2          13.19999981 W
PLW12          0.30142000 W
PLW13          0.15161000 W

F2 - Processing parameters
SI                 32768
SF            100.6128164 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

66 (in D_6-DMSO)

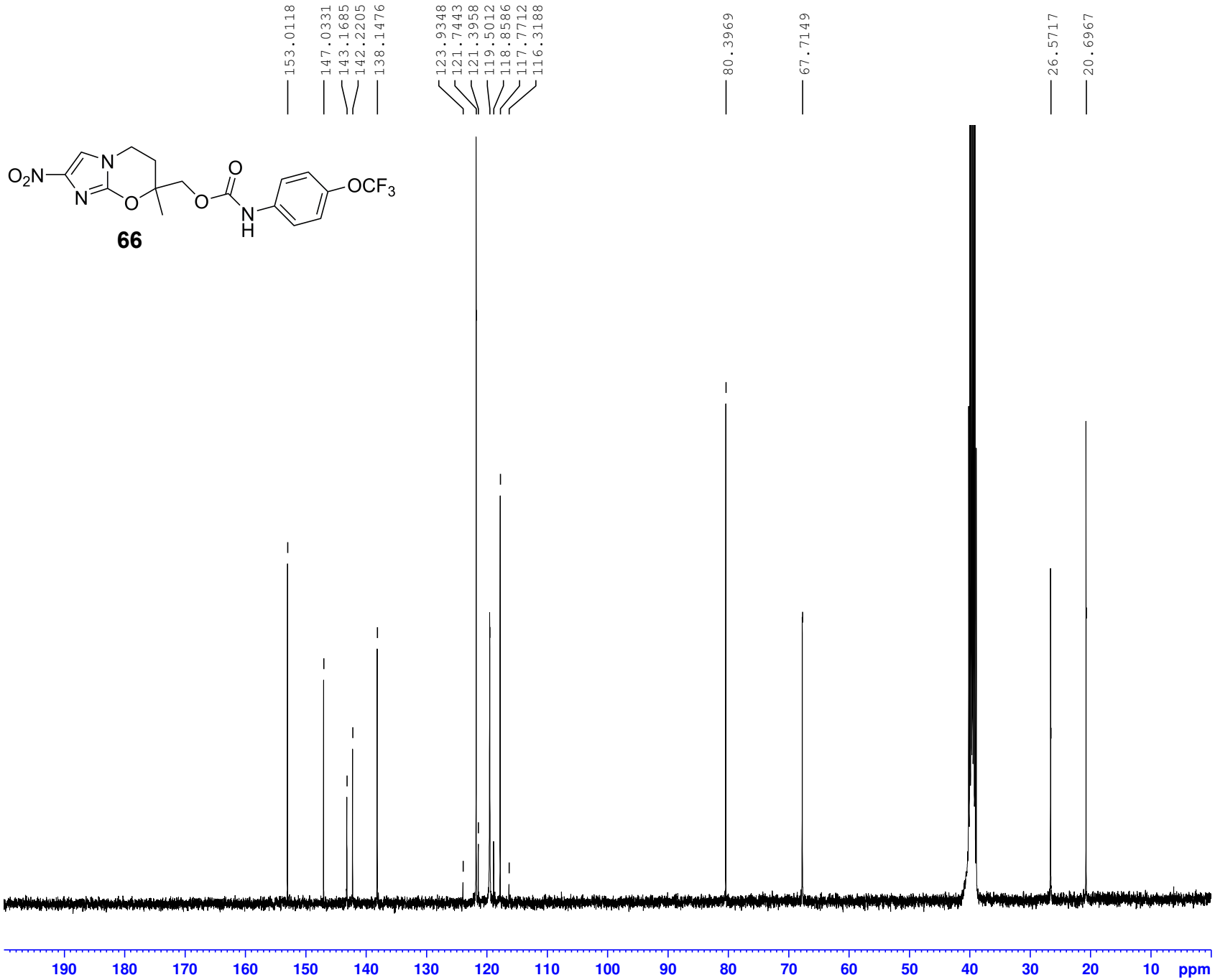



```
Current Data Parameters
NAME      Aug07-2015-FMHSacsr
EXPNO                   46
PROCNO                   1

F2 - Acquisition Parameters
Date_              20150809
Time                 14.36 h
INSTRUM              spect
PROBHD   5 mm BBO BB-1H
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     64
DS                      2
SWH               8389.262 Hz
FIDRES               0.256020 Hz
AQ                3.9059455 sec
RG                   228.1
DW                  59.600 usec
DE                  10.00 usec
TE                  298.0 K
D1             2.00000000 sec
TD0                     1
SFO1           400.1334011 MHz
NUC1                   1H
P1                  11.00 usec

F2 - Processing parameters
SI                  32768
SF             400.1300024 MHz
WDW                    EM
SSB       0
LB                   0.30 Hz
GB        0
PC                   1.00
```

66 (in D_6-DMSO)

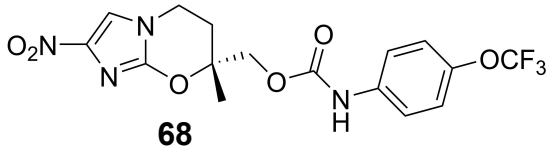



```
Current Data Parameters
NAME      Aug07-2015-FMHSacsrcnmr
EXPNO                 47
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150809
Time              19.48 h
INSTRUM             spect
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg50
TD                65536
SOLVENT             DMSO
NS                  9000
DS                     4
SWH           26178.010 Hz
FIDRES            0.798889 Hz
AQ             1.2517376 sec
RG                11585.2
DW                19.100 usec
DE                10.00 usec
TE                298.0 K
D1             0.75000000 sec
d11            0.03000000 sec
DELTA          0.64999998 sec
TD0                    1
SFO1          100.6248425 MHz
NUC1                  13C
P1                11.80 usec
SFO2          400.1316005 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2             100.00 usec

F2 - Processing parameters
SI                 32768
SF            100.6128169 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

68 (in D_6-DMSO)



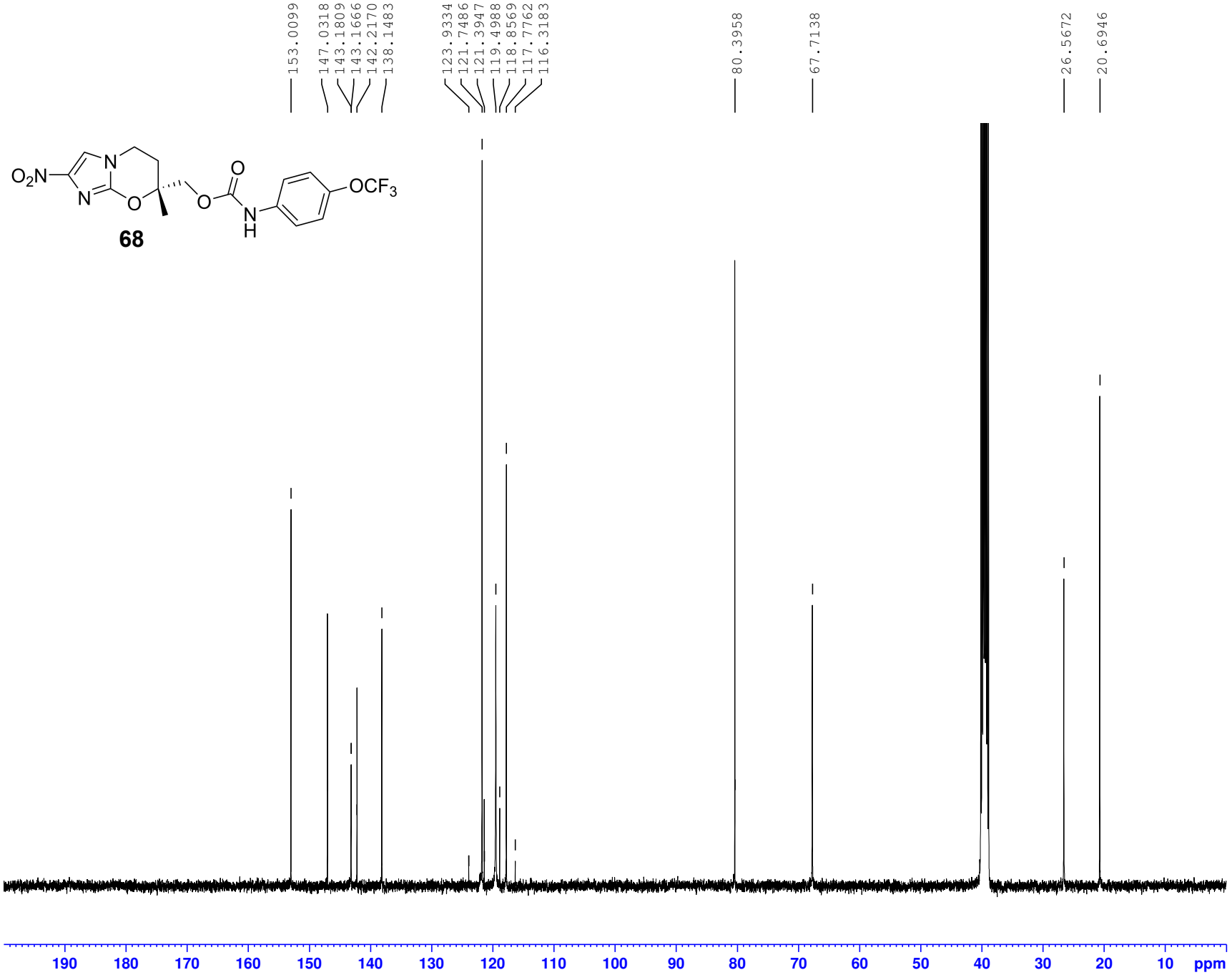
68


```
Current Data Parameters
NAME          Dec04-2020
EXPNO                 11
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201206
Time               9.35 h
INSTRUM            spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                 176.55
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF           400.1300026 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                 1.00
```

68 (in D_6-DMSO)

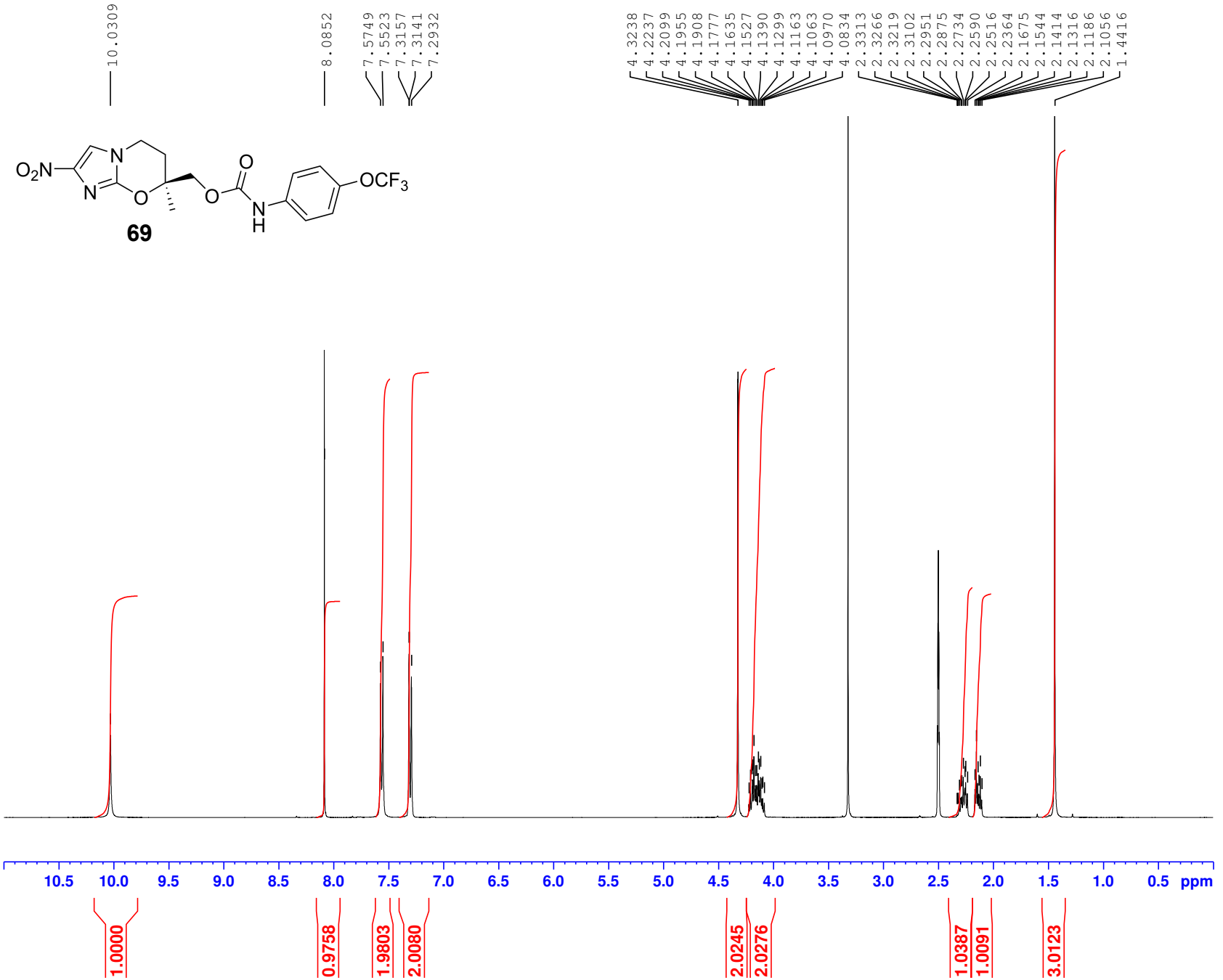



```
Current Data Parameters
NAME          Dec04-2020
EXPNO                 12
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201206
Time               16.30 h
INSTRUM             spect
PROBHD    Z108618_0860 (
PULPROG          zgpg50
TD                65536
SOLVENT            DMSO
NS                12000
DS                    4
SWH           24038.461 Hz
FIDRES         0.733596 Hz
AQ            1.3631488 sec
RG               198.55
DW               20.800 usec
DE                6.50 usec
TE               298.0 K
D1            0.63999999 sec
D11           0.03000000 sec
TD0                   1
SFO1         100.6228298 MHz
NUC1                13C
P1                10.00 usec
PLW1         48.17399979 W
SFO2         400.1316005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2         13.19999981 W
PLW12         0.30142000 W
PLW13         0.15161000 W

F2 - Processing parameters
SI                32768
SF           100.6128171 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```

69 (in D_6-DMSO)

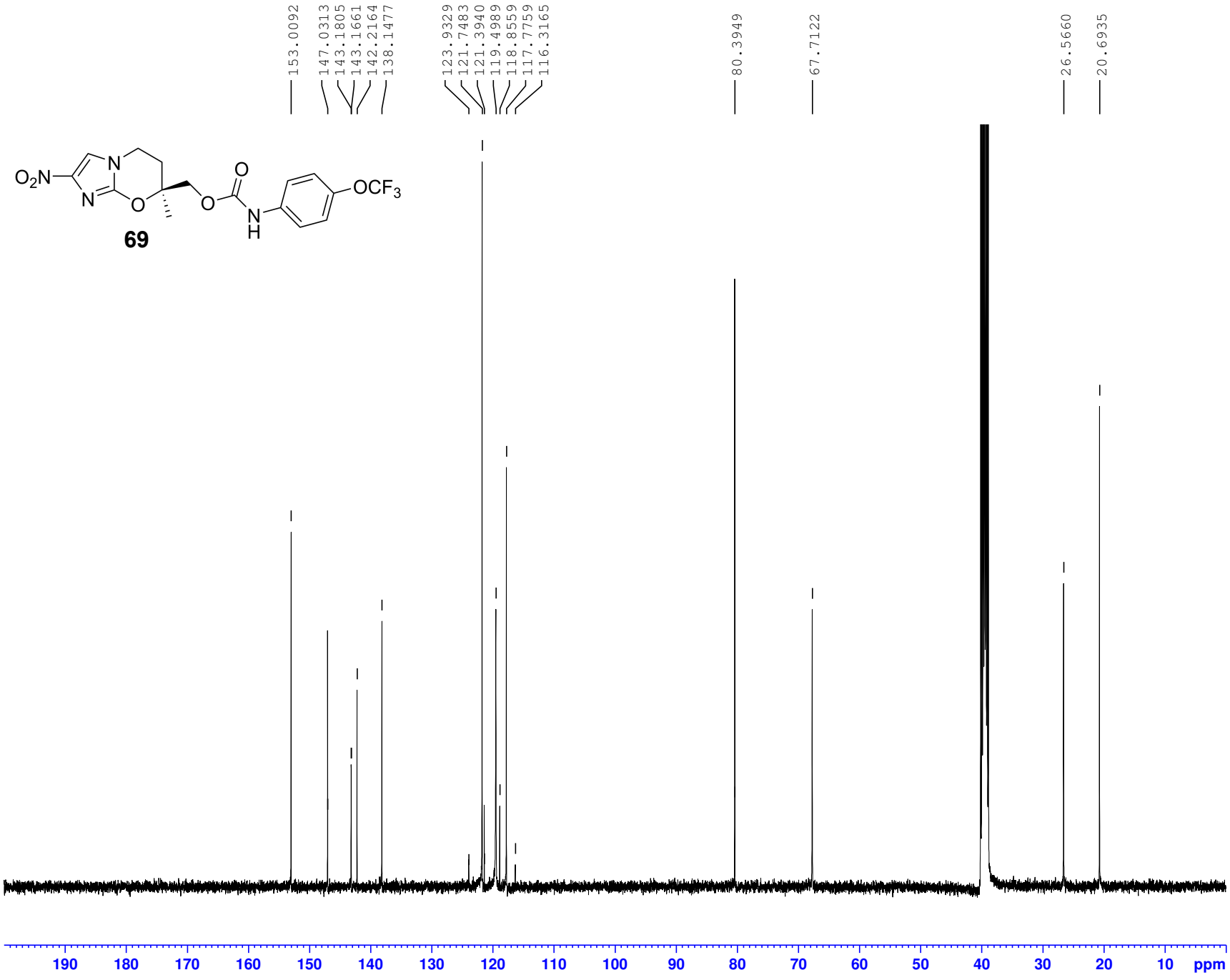



```
Current Data Parameters
NAME          Dec04-2020
EXPNO                 14
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201206
Time              18.56 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                156.54
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1         400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF           400.1300026 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

69 (in D_6-DMSO)

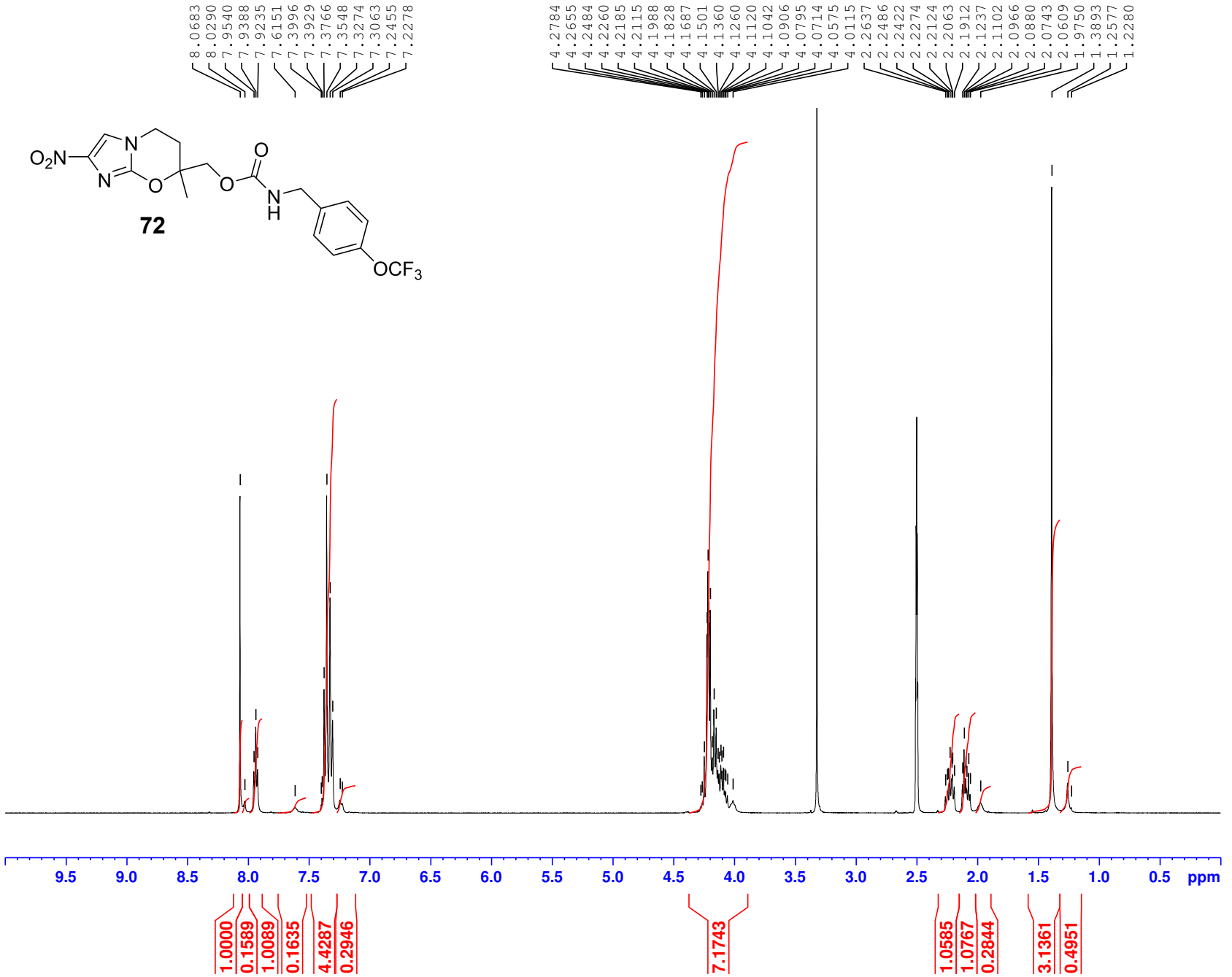



```
Current Data Parameters
NAME          Dec04-2020
EXPNO                 15
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201207
Time                1.50 h
INSTRUM             spect
PROBHD    Z108618_0860 (
PULPROG           zgpg50
TD                 65536
SOLVENT             DMSO
NS                 12000
DS                     4
SWH            24038.461 Hz
FIDRES         0.733596 Hz
AQ             1.3631488 sec
RG                198.55
DW                20.800 usec
DE                 6.50 usec
TE                298.0 K
D1           0.63999999 sec
D11          0.03000000 sec
TD0                    1
SFO1         100.6228298 MHz
NUC1                13C
P1                10.00 usec
PLW1         48.17399979 W
SFO2         400.1316005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2         13.19999981 W
PLW12         0.30142000 W
PLW13         0.15161000 W

F2 - Processing parameters
SI                 32768
SF           100.6128173 MHz
WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                  1.40
```

72 (in D_6-DMSO)

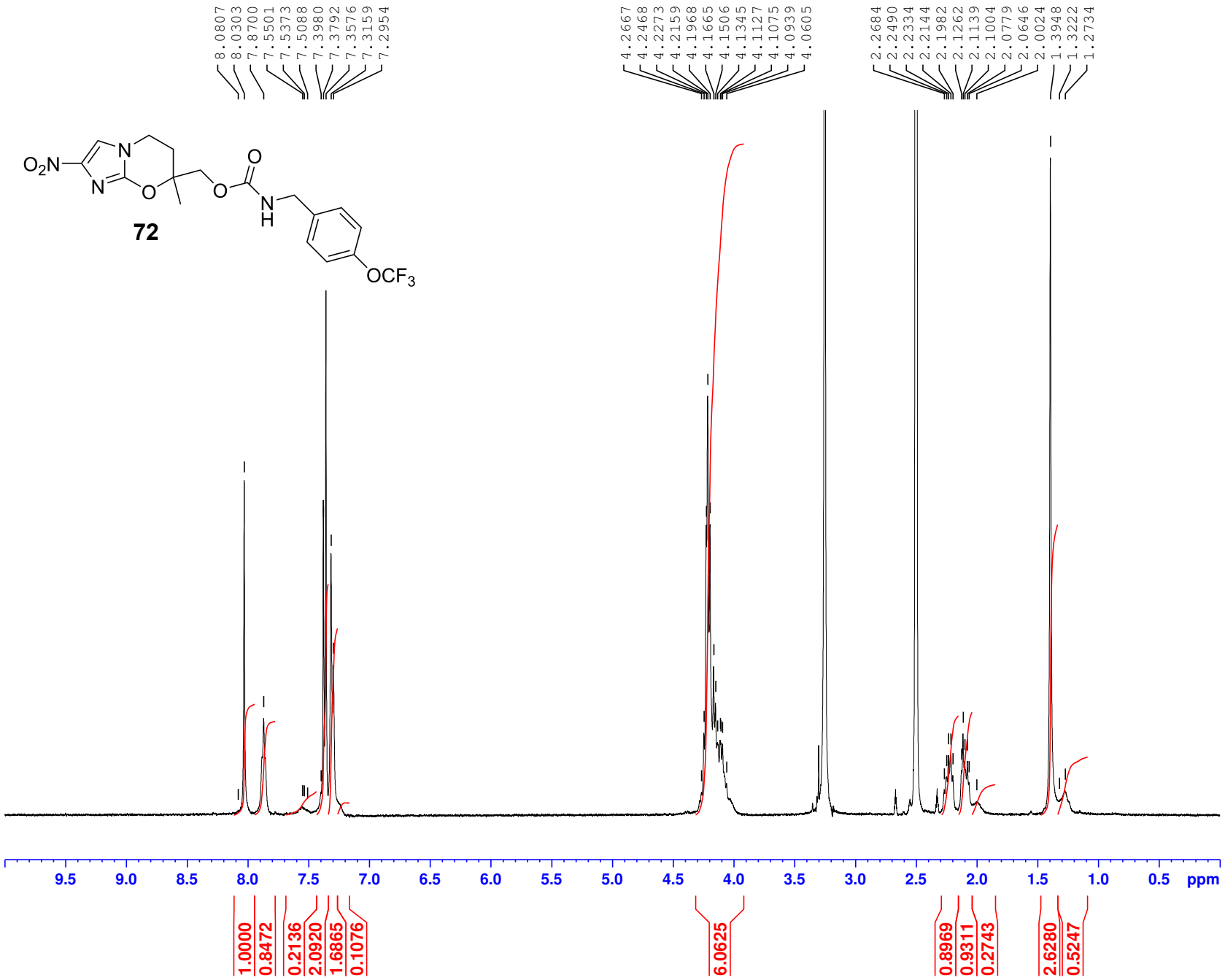



```
Current Data Parameters
NAME          Dec04-2020
EXPNO                  8
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201206
Time               0.15 h
INSTRUM             spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                156.54
DW                62.400 usec
DE                 6.50 usec
TE                298.0 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1        13.19999981 W

F2 - Processing parameters
SI                 65536
SF          400.1300026 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

72 (in D_6-DMSO at 313K)

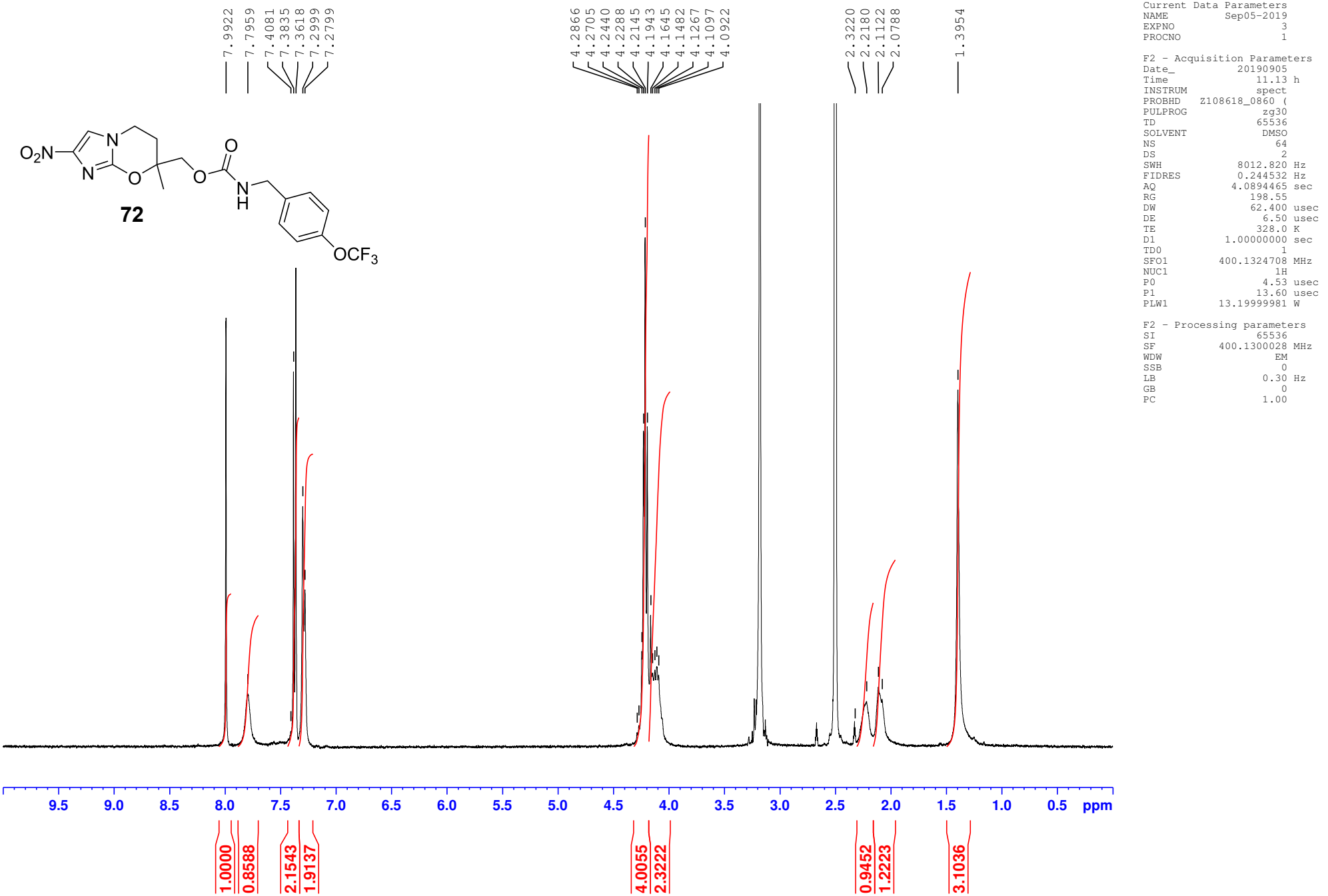



```
Current Data Parameters
NAME          Sep05-2019
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20190905
Time              10.59 h
INSTRUM            spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                198.55
DW                62.400 usec
DE                 6.50 usec
TE                313.3 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1        13.19999981 W

F2 - Processing parameters
SI                 65536
SF          400.1300027 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

72 (in D_6-DMSO at 328K)

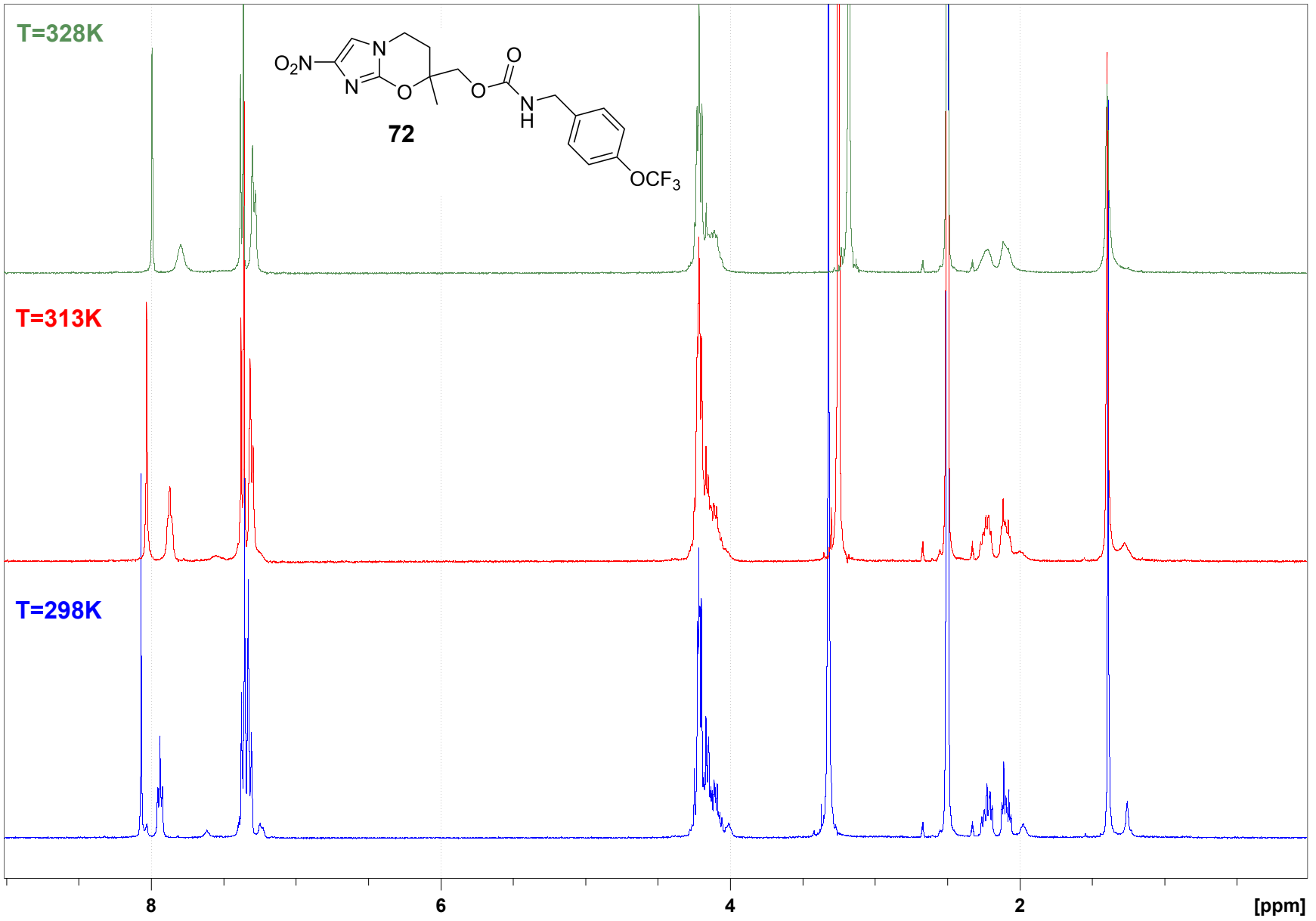



```
Current Data Parameters
NAME          Sep05-2019
EXPNO                  3
PROCNO                 1

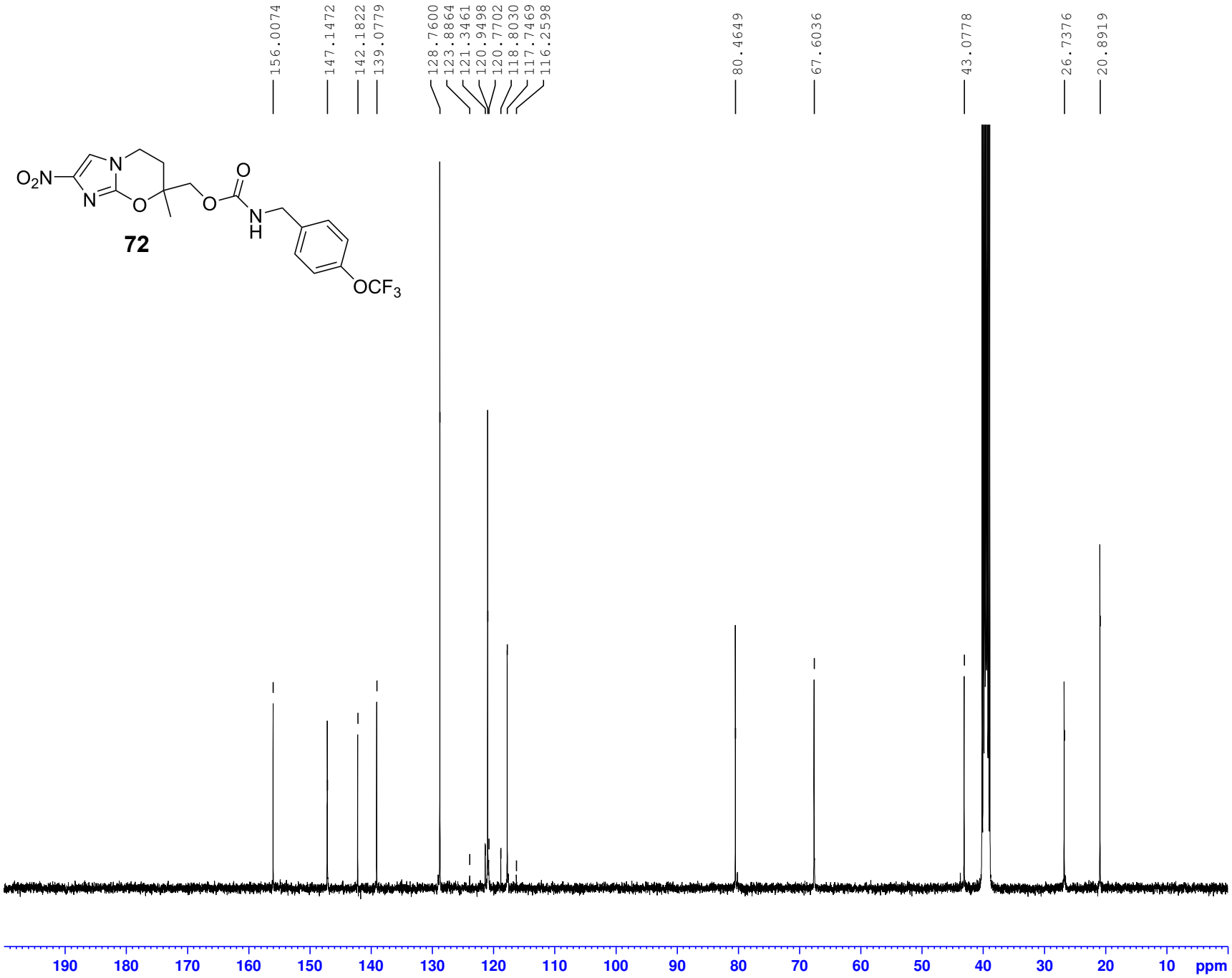
F2 - Acquisition Parameters
Date_           20190905
Time              11.13 h
INSTRUM            spect
PROBHD   Z108618_0860 (
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    64
DS                     2
SWH             8012.820 Hz
FIDRES          0.244532 Hz
AQ              4.0894465 sec
RG                198.55
DW                62.400 usec
DE                 6.50 usec
TE                328.0 K
D1           1.00000000 sec
TD0                    1
SFO1        400.1324708 MHz
NUC1                  1H
P0                 4.53 usec
P1                13.60 usec
PLW1         13.19999981 W

F2 - Processing parameters
SI                 65536
SF          400.1300028 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
```

72 (in D_6-DMSO - variable temperature spectra overlaid)



72 (in D_6-DMSO)




```
Current Data Parameters
NAME          Dec04-2020
EXPNO                  9
PROCNO                 1

F2 - Acquisition Parameters
Date_           20201206
Time                7.09 h
INSTRUM            spect
PROBHD    Z108618_0860 (
PULPROG          zgpg50
TD                65536
SOLVENT            DMSO
NS                12000
DS                    4
SWH           24038.461 Hz
FIDRES         0.733596 Hz
AQ            1.3631488 sec
RG               198.55
DW               20.800 usec
DE                6.50 usec
TE                298.0 K
D1           0.63999999 sec
D11          0.03000000 sec
TD0                   1
SFO1        100.6228298 MHz
NUC1                13C
P1                10.00 usec
PLW1        48.17399979 W
SFO2        400.1316005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             90.00 usec
PLW2        13.19999981 W
PLW12        0.30142000 W
PLW13        0.15161000 W

F2 - Processing parameters
SI                32768
SF          100.6128171 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 1.40
```