Supplementary Material

Dihydropyrimidinones and -thiones with improved activity against human polyomavirus family members

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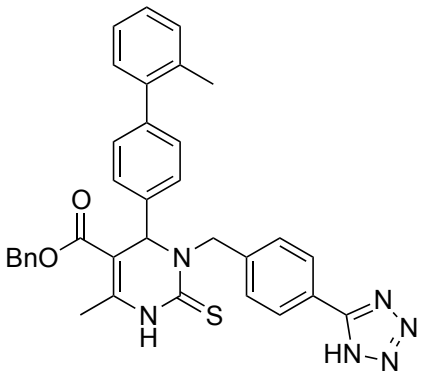
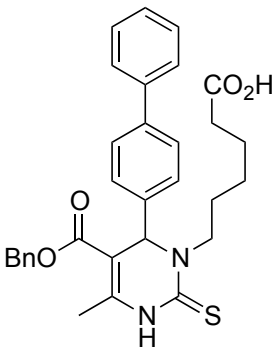
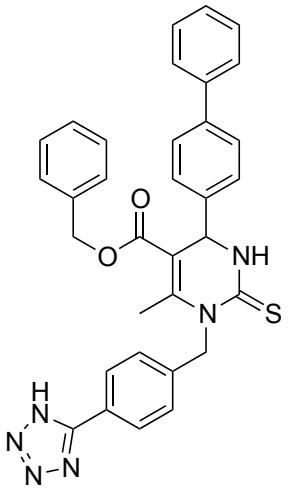
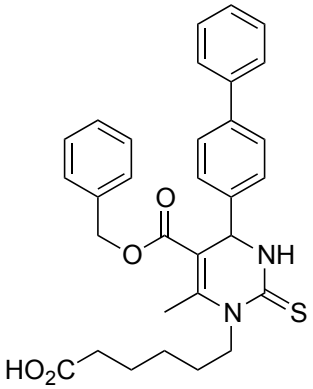
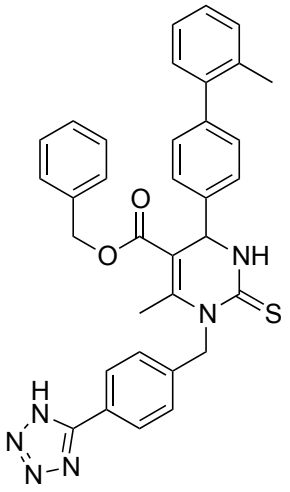
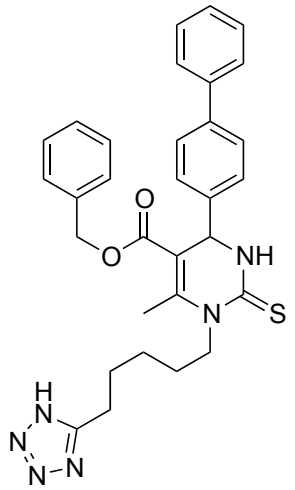
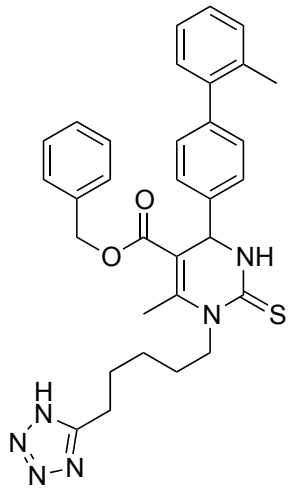
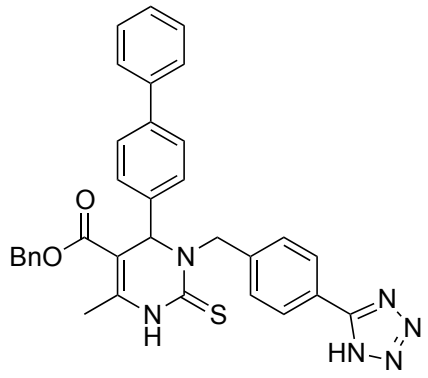
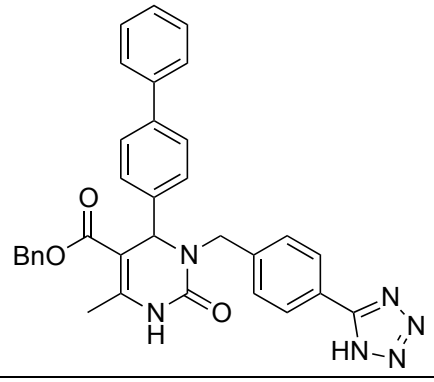
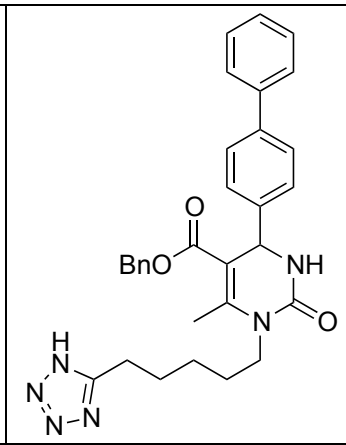
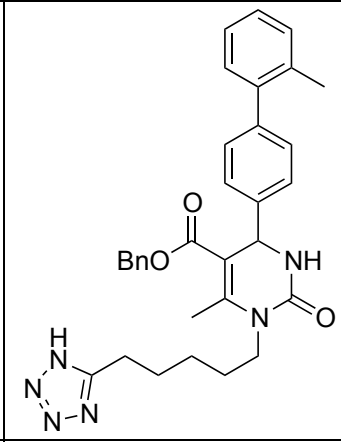
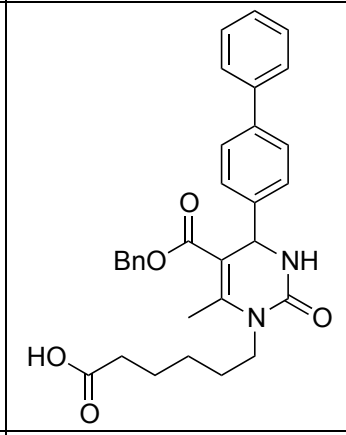
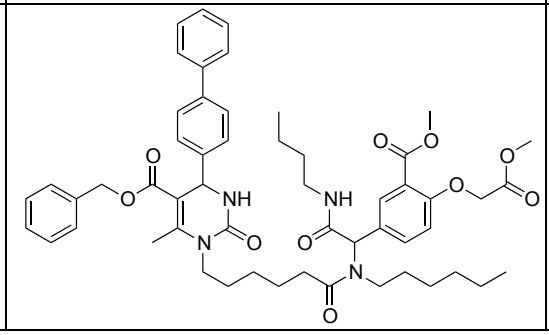
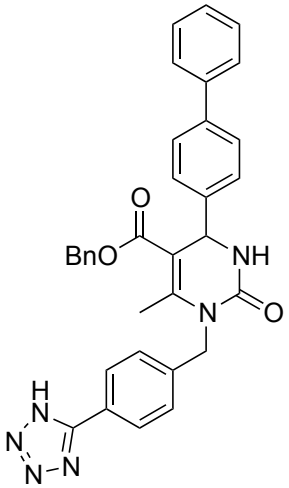
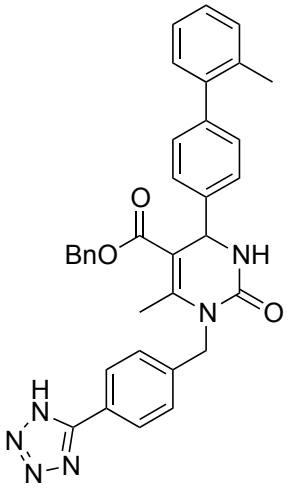
Alphabetical Index of Tested Samples, Incl. Reference Compounds, Used in Biological Assays

Compound Code	Structure	Number in Synthetic Schemes	UPCMLD Code
AMT551-058		8b	UPCMLD40AAMT055158
AMT551-071		8c	UPCMLD40AAMT055171

AMT551-078		**3a**	**UPMCLD40AAMT055178**
AMT551-090		**3e**	**UPCMLD40AAMT055190**
AMT551-093		**3b**	**UPCMLD40AAMT055193**

AMT580-027		**3c**	**UPCMLD40AAMT058027**
AMT580-033		**3d**	**UPCMLD40AAMT058033**
AMT580-043		**8a**	**UPCMLD40AAMT058043**
AMT628-003		**12**	**UPCMLD40AAMT062803**

BQU015242		-	**UPCMLD18BBQU015254**
LR340-006		-	**UPCMLD40ALR340-06**
MAL2-11B		-	**UPCMLD00WMAL2-11B**
MAL3-101		-	-

ML282-56		-	**UPCMLD40AML282-056**
SMAL (ML282-86		-	**UPCMLD40AML282-086**

Protein Purification

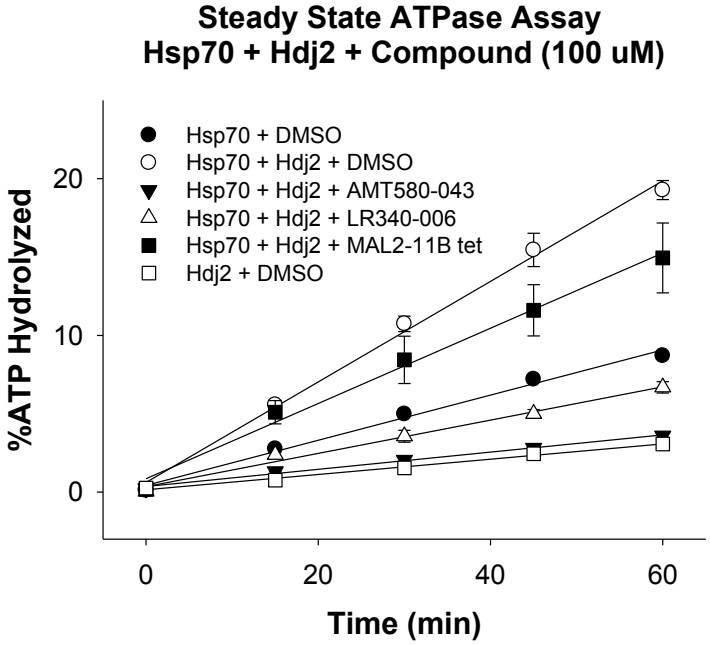
Human hsp70 protein was purified as previously described using a bacterial expression plasmid pMSHSP70 BL21(DE3) kindly provided by R. Morimoto (Northwestern University).[1] Hdj2 was purified as previously described using a bacterial expression plasmid kindly provided by D. Cyr (University of North Carolina School of Medicine).[2]

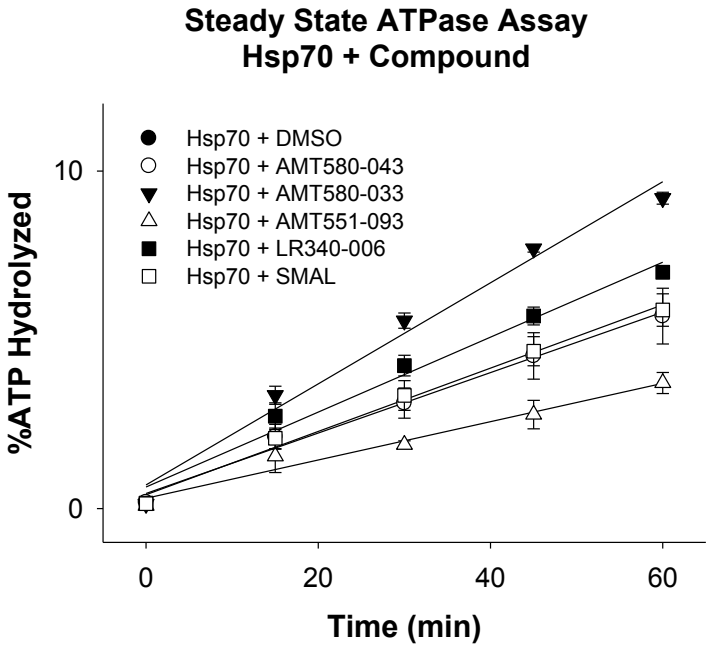
Biochemical Assays

Chemical derivatives were screened for their effects on Hsp40 stimulated ATPase activity and Hsp70 ATPase activity using a steady state ATPase assay. This assay was performed as previously published.[3, 4] In brief, purified Hsp70 (2 μg) and/or Hdj2 (0.65 μg, 0.5:1 molar ratio of the J-domain to Hsp70) and/or either a compound dissolved in dimethyl sulfoxide (DMSO) or an equivalent volume of DMSO in 50 mM HEPES pH 7.4, 50 mM NaCl, 2 mM $MgCl_2$, and 10 mM DTT. The solution of Hsp70 and Hdj2 was preincubated on ice for 15 min prior to compound addition to ensure solubility. In a separate tube, 1 nmol ATP and 0.2 μCi [α^{32}P]ATP were combined on ice. The ATPase reaction was started by adding the Hsp70 solution to the ATP mixture and placing the tube in a 30 °C water bath.

Over a 60-min time course, 3 µL aliquots were removed at 0, 15, 30, 45, and 60 min and quenched with 1 µL of 2 M LiCl, 4 M formic acid, and 36 mM ATP. The quenched reactions were spotted in duplicate on a thin layer chromatography plate (TLC PEI Cellulose F, EMD Chemicals). Chromatography was performed on plates for 15 min in a 0.5 M LiCl/1 M formic acid solution to resolve the ATP and hydrolyzed ADP species. TLC plates were exposed to phosphorimager plates and data was analyzed on a Fuji- film BAS-2500 phosphorimager and quantified using ImageGuage software (Fuji Film Science Lab). All reactions were performed in triplicate and established statistical methods were used. Where indicated, results are shown as percent activity, relative to the DMSO control, which is calculated as 100%. Normalization to this standard was used to ensure assay consistency.

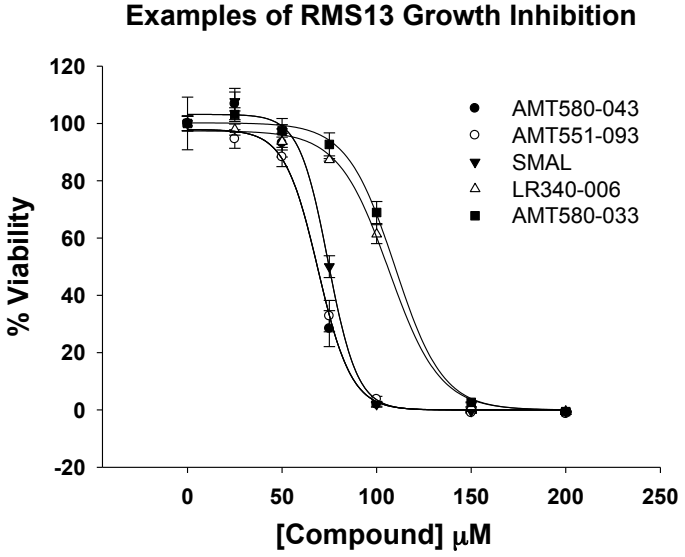
Examples of results in terms of %ATP hydrolysis



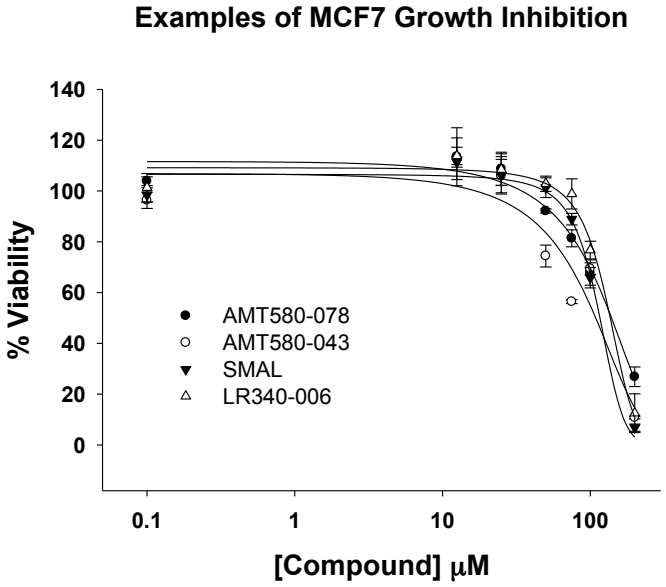


RMS13 and MCF7 Cell Toxicity Assays

To assay for the cytotoxic effect of compounds on MAL3-101 susceptible cancer cell viability, rhabdomyosarcoma RMS13 cells were cultured in RPMI-1640 media with 2 mM L-glutamine, 10 mM HEPES, 1 mM pyruvate, 1 500 mg/L $NaHCO_3$, 4500 mg/L glucose and 10% FBS at 37 °C in 5% CO_2. RMS13 cells (100 µL of 2.5×10^4 cells) were seeded into 96-well plates and grown for 6 h at 37 °C in 5% CO_2 prior to addition of compounds (33 µL) to reach final concentrations of 200, 150, 100, 75, 50 and 25 µM or 100, 30, 10, 5, 1 and 0.1 µM for MAL3-101 (as a positive control). The final DMSO concentration is all experiments was 1.0%. The plates were then incubated for a further 24 h prior to room temperature equilibration for 30 min, addition of Cell Titer-Glo (67 µL; Promega, Madison, WI, USA), and assessment of cell viability according to the manufacturer's protocol. Data represent the means of two independent experiments each run in triplicate. A sigmoidal, 3-parameter line regression of the resulting data was performed using SigmaPlot (v. 11.0, Systat Software, San Jose, CA).



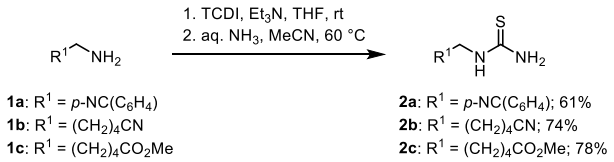
To assay for the cytotoxic effect of compounds on cell viability, breast cancer MCF7 cells were cultured in DMEM with 10% FBS at 37 °C in 5% CO_2. MCF7 cells (100 µL of 2×10^4 cells) were seeded into 96-well plates and grown for 24 h at 37 °C in 5% CO_2 prior to addition of compounds (33 µL) to reach final concentrations of 200, 100, 75, 50, 25 and 12.5 µM or 100, 30, 10, 5, 1 and 0.1 µM for MAL3-101 (as a positive control). The plates were then incubated for a further 48 h prior to room temperature equilibration for 30 min, addition of Cell Titer-Glo (67 µL; Promega, Madison, WI, USA), and assessment of cell viability according to the manufacturer's protocol. Data represent the means of two independent experiments each run in triplicate. A sigmoidal, 3-parameter line regression of the resulting data was performed using SigmaPlot (v. 12.0, Systat Software, San Jose, CA).



Viruses and Cells Used: BK polyomavirus (BKPyV) strain Gardner and JC polyomavirus (JCPyV) strain MAD-4 were obtained from American Type Culture Collection (ATCC, Manassas, VA). The cell line COS7 was also obtained from ATCC. Primary human foreskin fibroblast (HFF) cells were derived routinely from tissue obtained from the University of Alabama at Birmingham tissue procurement facility with approval from its institutional review board by methods we have reported previously .[5]

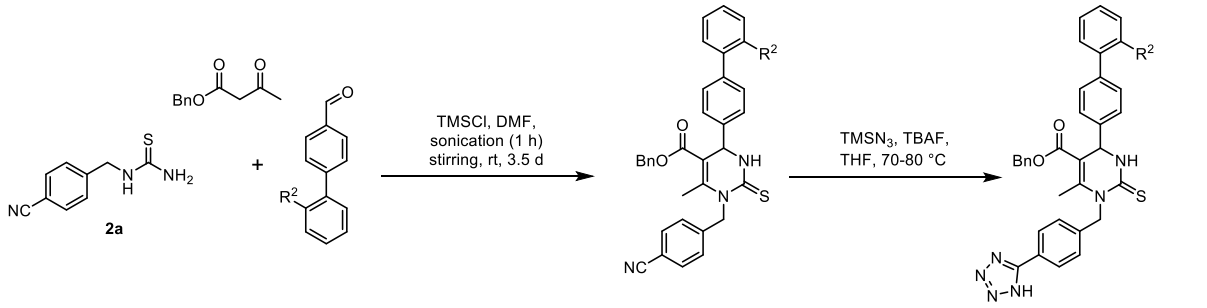
Antiviral assays against BKPyV and JCPyV. Antiviral assays against BKPyV were performed in 96-well plates containing monolayers of HFF cells. Compound dilutions were prepared directly in plates containing cells which were subsequently infected at an MOI of 0.001 PFU/cell. Three-fold dilutions of the compounds were performed and twelve concentrations were tested at a range from 100 uM to 0.5 nM against both the BK and JC virus. Concentrations of DMSO were below 0.5% in all assays and is well tolerated by both cell lines. Cytotoxicity was determined in parallel with the antiviral assays and used the same plate format, the same cell lines, the same drug exposure, and the same incubation times. After a 7 d incubation, total DNA was prepared with a Wizard SV 96 well purification kit and genome copy number was quantified by real time qPCR using the primers 5'- AGT GGA TGG GCA GCC TAT GTA-3', 5'- TCA TAT CTG GGT CCC CTG GA-3' and probe 5'-6-FAM AGG TAG AAG AGG TTA GGG TGT TTG ATG GCA CAG TAMRA-3'.[6] Plasmid pMP526 serves as the DNA standard for quantification purposes. Evaluation of compounds against JCPyV virus were also performed by methods similar to those for BKPyV but were done in 96-well plates containing monolayers of COS7 cells. Viral DNA was quantified using primers 5'-CTG GTC ATG TGG ATG CTG TCA-3' and 5'-GCC AGC AGG CTG TTG ATA CTG-3' and probe 5'-6-FAM-CCC TTT GTT TGG CTG CT-TAMRA-3 together with the plasmid pMP508 to provide a standard curve for absolute quantification. Uninfected cells were evaluated in 96-well plates with equal drug exposure and cytotoxicity was Determined with CellTiter-Glo reagent according to the manufacturer's suggested protocol. Concentrations of compounds sufficient to reduce the DNA copy number by 50% (EC_{50}) and sufficient to reduce cell viability by 50% (CC_{50}) were interpolated from the experimental data.

N1 Substituted Product Synthetic Schemes



1a: R^1 = *p*-NC(C_6H_4)
1b: R^1 = $(CH_2)_4CN$
1c: R^1 = $(CH_2)_4CO_2Me$

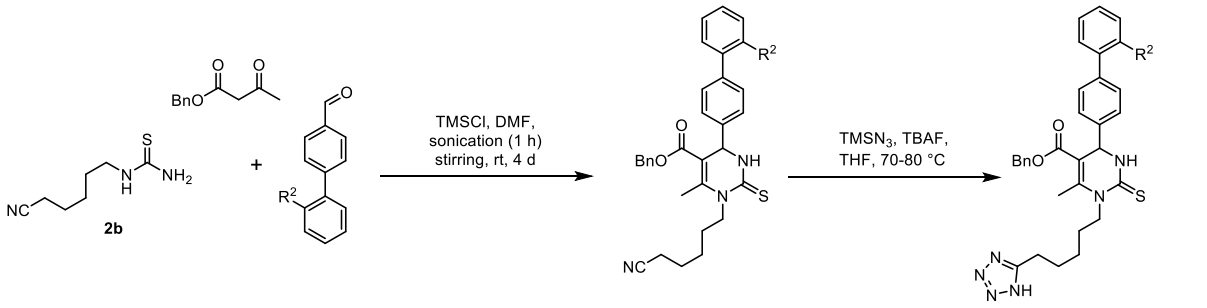
2a: R^1 = *p*-NC(C_6H_4); 61%
2b: R^1 = $(CH_2)_4CN$; 74%
2c: R^1 = $(CH_2)_4CO_2Me$; 78%



2a

13a: R^2 = H, 42%
13b: R^2 = Me, 43%

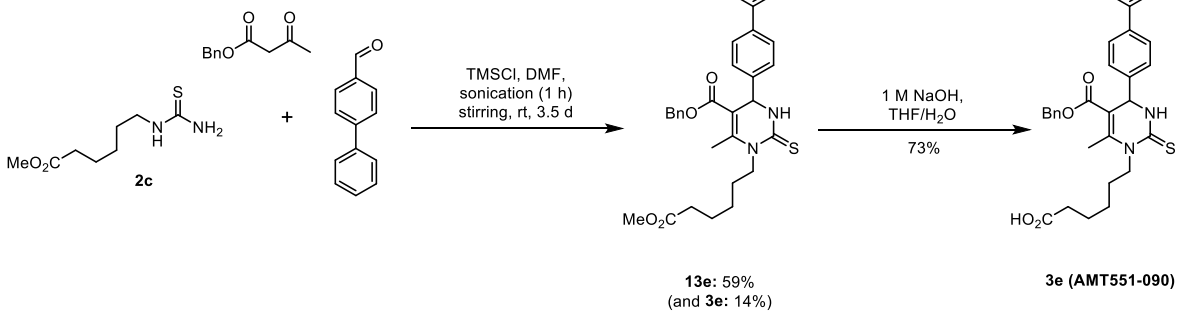
3a (AMT551-078): R^2 = H, 67%
3b (AMT551-093): R^2 = Me, 64%



2b

13c: R^2 = H, 60%
13d: R^2 = Me, 90%

3c (AMT580-027): R^2 = H, 56%
3d (AMT580-033): R^2 = Me, 39%

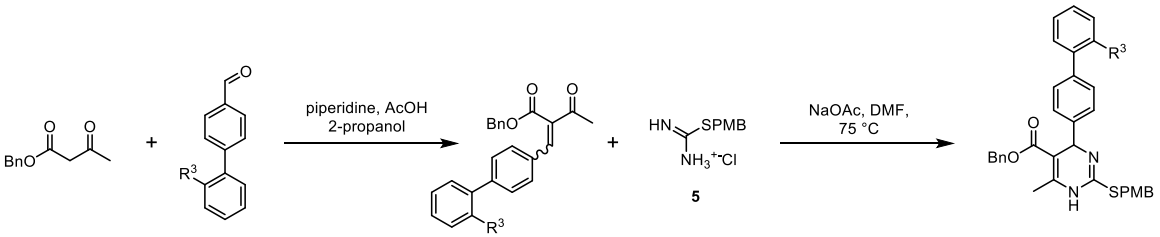


2c

13e: 59%
(and **3e:** 14%)

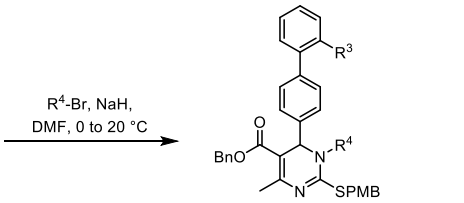
3e (AMT551-090)

N3 Substituted Product Synthetic Schemes

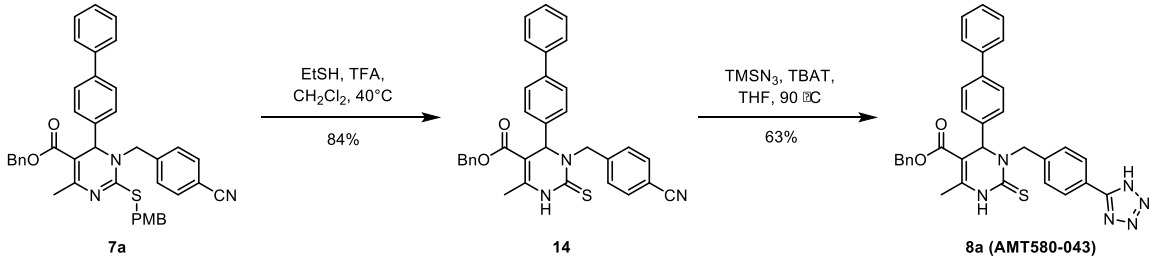


4a: R^3 = H, 77%
4b: R^3 = Me, 72%

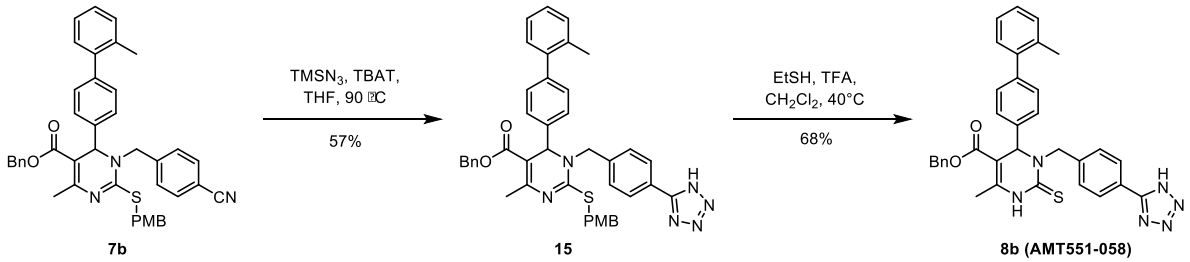
6a: R^1 = H, 64%
6b: R^1 = Me, 81%



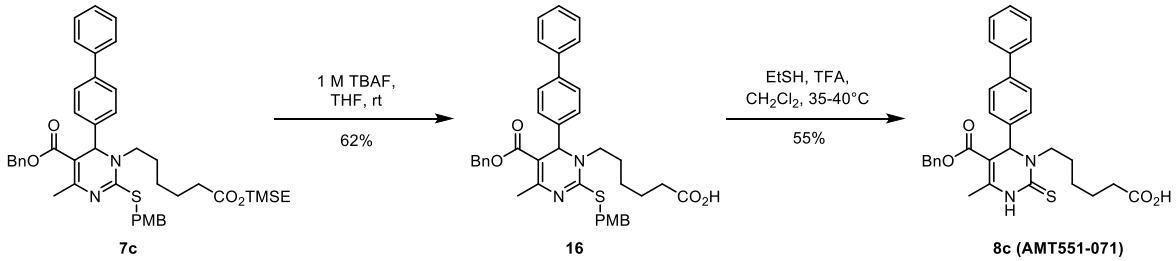
7a: R^3 = H, R^4 = $CH_2(C_6H_4)CN$, 62%
7b: R^3 = Me, R^4 = $CH_2(C_6H_4)CN$, 61%
7c: R^3 = Me, R^4 = $(CH_2)_5CO_2TMSE$, 54%



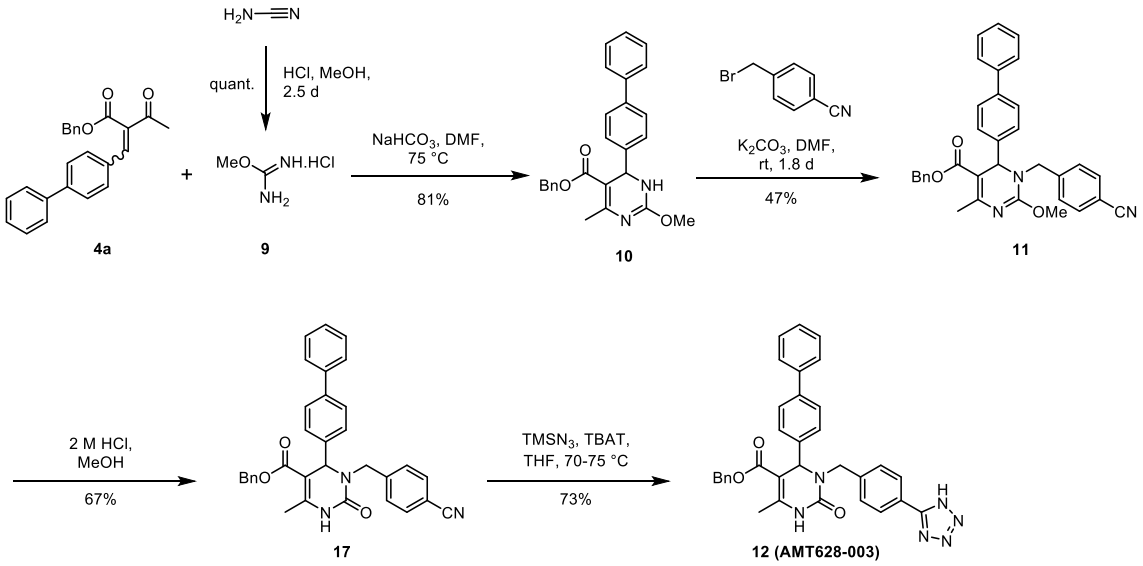
7a **14** **8a (AMT580-043)**



7b **15** **8b (AMT551-058)**



7c **16** **8c (AMT551-071)**


H2N—≡N
quant.
HCl, MeOH,
2.5 d
NaHCO3, DMF,
75 °C
81%
K2CO3, DMF,
rt, 1.8 d
47%
2 M HCl,
MeOH
67%
TMSN3, TBAT,
THF, 70-75 °C
73%
4a
9
10
11
17
12 (AMT628-003)

Experimental

Table of Contents

General Methods **13**
N-1 substituted 3,4-dihydropyrimidine-2(1H)-thione syntheses **13**
1-(4-Cyanobenzyl)thiourea (2a).[9] 13
1-(6-Cyanohexyl)thiourea (2b).[9] 14
Methyl 6-thioureidohexanoate (2c).[9] 14
Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13a) 15
Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3a: AMT580-052). 15
Benzyl 1-(4-cyanobenzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13b). 16
Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3b: AMT551-093). 17
Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(5-cyanopentyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13c). 17
Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3c: AMT580-027). 18
Benzyl 1-(5-cyanopentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13d). 19
Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3d: AMT580-033). 19
Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(6-methoxy-6-oxohexyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13e). 20
6-(4-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-6-methyl-2-thioxo-3,4-dihydropyrimidin-1(2H)-yl)hexanoic acid (3e: AMT551-090). 21
N-3 substituted 3,4-dihydropyrimidine-2(1H)-thione syntheses **21**
Benzyl 2-([1,1'-biphenyl]-4-ylmethylene)-3-oxobutanoate (4a). 21
Benzyl 2-((2'-methyl-[1,1'-biphenyl]-4-yl)methylene)-3-oxobutanoate (4b). 22
2-(4-Methoxybenzyl)isothiouronium chloride (5).[10] 22
Benzyl 4-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-6-methyl-1,4-dihydropyrimidine-5-carboxylate (6a). 23
Benzyl 6-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-1,6-dihydropyrimidine-5-carboxylate (7a). 23
Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14). 24
Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8a: AMT580-043). 25
Benzyl 2-((4-methoxybenzyl)thio)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,4-dihydropyrimidine-5-carboxylate (6b). 25
Benzyl 1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate (7b). 26
Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate (15). 27
Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8b: AMT551-058). 27
2-(Trimethylsilyl)ethyl 6-bromohexanoate (18). 28
Benzyl 6-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-4-methyl-1-(6-oxo-6-(2-(trimethylsilyl)ethoxy)hexyl)-1,6-dihydropyrimidine-5-carboxylate (7c). 28
6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-2-((4-methoxybenzyl)thio)-4-methylpyrimidin-1(6H)-yl)hexanoic acid (16). 29
6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-4-methyl-2-thioxo-3,6-dihydropyrimidin-1(2H)-yl)hexanoic acid (8c: AMT551-071). 30
N-3 substituted dihydropyrimidone 12 synthesis **30**
Methyl carbamimidate hydrochloride (9).[11] 30
Benzyl 4-([1,1'-biphenyl]-4-yl)-2-methoxy-6-methyl-1,4-dihydropyrimidine-5-carboxylate (10). 31
Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-2-methoxy-6-methyl-1,4-dihydro-3λ4-pyrimidine-5-carboxylate (11). 31
Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (17). 32
Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (12: AMT628-003). 32

General Methods

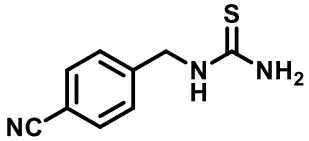
All non-aqueous reactions were carried out under a nitrogen atmosphere in oven- or flame-dried glassware unless otherwise noted. Anhydrous tetrahydrofuran and diethyl ether were distilled from sodium benzophenone ketyl; anhydrous dichloromethane and toluene were distilled from CaH_2; alternatively, the same solvents were obtained from a solvent purification system using alumina columns. Anhydrous DMF was stirred over CaH_2 (5% w/v) overnight, filtered, then distilled and stored over 4Å molecular sieves. All other solvents and reagents were used as obtained from commercial sources without further purification unless noted.

Reactions were monitored by LCMS (see HRMS below) or TLC using 250 µm pre-coated silica gel 60 F_{254} plates, which were visualized with 254 nm and/or 365 nm UV light and by staining with $KMnO_4$ (1.5 g $KMnO_4$, 10 g K_2CO_3, and 1.25 mL 10% NaOH in 200 mL water), cerium molybdate (0.5 g $Ce(NH_4)_2(NO_3)_6$, 12 g $(NH_4)_6Mo_7O_{24}\bullet 4H_2O$, and 28 mL conc. H_2SO_4 in 235 mL water), or vanillin (6 g vanillin and 1.5 mL conc. H_2SO_4 in 100 mL EtOH). Flash chromatography was performed with SiliCycle silica gel 60 (230-400 mesh) or by ISCO MPLC.

^1H and ^{13}C NMR spectra were recorded on Bruker Avance 300, 400, or 500 MHz spectrometers, using the residual solvent as an internal standard.[7, 8] IR spectra were obtained on a Smiths IdentifyIR or PerkinElmer Spectrum 100. HRMS data were obtained on a Thermo Scientific Exactive HRMS coupled to a Thermo Scientific Accela HPLC system using a 2.1 x 50 mm 3.5 µm Waters XTerra C_{18} column eluting with $MeCN/H_2O$ containing 0.1% formic acid. Purity of compounds was assessed using the same HPLC system with either the PDA or an Agilent 385 ELSD.

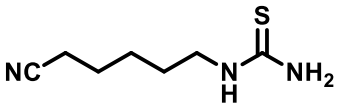
N-1 substituted 3,4-dihydropyrimidine-2(1H)-thione syntheses

1-(4-Cyanobenzyl)thiourea (2a).[9]



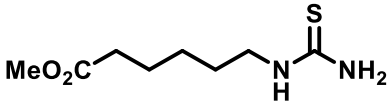
To a suspension of 4-cyanobenzylamine hydrochloride (**1a**, 1.00 g, 5.82 mmol) and 1,1'-thiocarbonyldiimidazole (1.73 g, 8.72 mmol, 1.5 eq) in THF (26.1 mL) stirring under argon, was added Et_3N (2.48 mL, 17.4 mmol, 3 eq) and the reaction mixture was left to stir at rt for 18 h. The mixture was concentrated before addition of MeCN (12.8 mL, 2.2 mL/mmol) and NH_4OH (6.39 mL, 1.1 mL/mmol). The reaction mixture was stirred at 60 °C for 3 h, before being concentrated. The residue was dissolved in EtOAc and washed with sat. aq. NH_4Cl (x 2), dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to provide 1-(4-cyanobenzyl)thiourea (**2a**, 0.753 mg, 3.54 mmol, 61%) as a yellow oil which solidified to a white solid upon freezing: Mp 42-44 °C; ATR IR (neat) 3293, 3180, 2229, 1608, 1546, 1447, 1414, 1347, 1232, 1156, 936, 817, 717 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 7.95 (bs, 1 H), 7.74 (d, 2 H, *J* = 7.5 Hz), 7.48 (d, 2 H, *J* = 7.5 Hz), 6.94 (bs, 2 H), 4.70 (d, 2 H, *J* = 5.5 Hz); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 183.7, 144.7, 131.5, 127.6, 118.1, 109.3, 46.6; HRMS (ESI) *m/z* calcd for $C_9H_{10}N_3S$ $(M+H)^+$ 192.0590, found 192.0590.

1-(6-Cyanohexyl)thiourea (2b).[9]



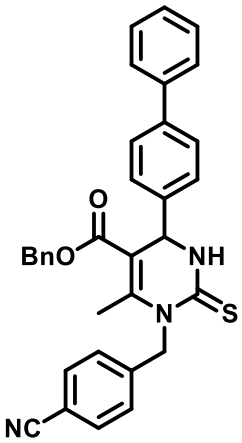
To a suspension of 6-amino capronitrile (**1b**, 1.1 mL, 8.7 mmol) and 1,1'-thiocarbonyldiimidazole (2.60 g, 13.1 mmol, 1.5 eq) in THF (39.2 mL) stirring under argon, was added Et_3N (3.72 mL, 26.2 mmol, 3 eq) and the reaction mixture was left to stir at rt for 16 h. The mixture was concentrated before addition of MeCN (19.1 mL, 2.2 mL/mmol) and NH_4OH (9.57 mL, 1.1 mL/mmol). The reaction mixture was stirred at 60 °C for 3 h, before being concentrated. The residue was dissolved in EtOAc and washed with H_2O. The aqueous layer was extracted with EtOAc and the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The brown oil was purified by chromatography on SiO_2 (MeOH:CH_2Cl_2, 0:100 to 10:90) to provide 1-(6-cyanohexyl)thiourea (**2b**, 1.31 g, 6.49 mmol, 74%) as an orange solid that was carried on without further purification: ATR IR (neat) 3458, 3334, 3312, 3176, 2938, 2865, 2237, 1605, 1591, 1549, 1460, 1425, 1363, 1340, 1263, 1148, 1060, 986, 736 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 7.38 (bs, 1 H), 6.68 (bs, 2 H), 3.30 (app d, 2 H, *J* = 5.0 Hz), 2.45 (t, 2 H, *J* = 7.0 Hz), 1.61 (quin, 2 H, *J* = 7.1 Hz), 1.53 (quin, 2 H, *J* = 7.0 Hz), 1.41 (quin, 2 H, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 182.9, 119.7, 43.1, 27.4, 25.0, 24.1, 15.6; HRMS (ESI) *m/z* calcd for $C_7H_{14}N_3S$ $(M+H)^+$ 172.0903, found 172.0903.

Methyl 6-thioureidohexanoate (2c).[9]



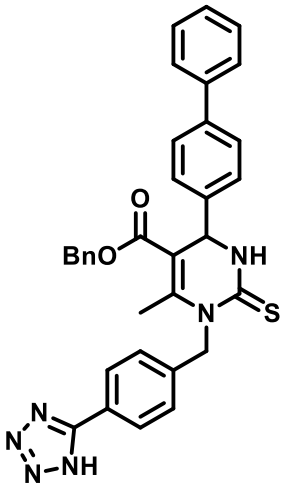
To a suspension of methyl 6-aminohexanoate (**1c**, 0.10 g, 0.69 mmol) and 1,1'-thiocarbonyldiimidazole (0.23 g, 1.2 mmol, 1.7 eq) in THF (2.75 mL) stirring under argon, was added Et_3N (0.29 mL, 2.1 mmol, 3 eq) and the reaction mixture was left to stir at rt for 12 h. The mixture was concentrated before addition of MeCN (1.38 mL, 2.2 mL/mmol) and NH_4OH (0.69 mL, 1.1 mL/mmol). The reaction mixture was stirred at 60 °C for 3 h, before being concentrated. The residue was dissolved in EtOAc and washed with sat. aq. NH_4Cl. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with NH_4Cl (x 2), dried (Na_2SO_4), filtered and concentrated to provide methyl 6-thioureidohexanoate (**2c**, 0.110 mg, 0.537 mmol, 78%) as an orange solid that was carried on without further purification: Mp 73-75 °C; ATR IR (neat) 3281, 3193, 2944, 2866, 1732, 1614, 1559, 1456, 1437, 1350, 1254, 1199, 1167 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 7.33 (bs, 1 H), 6.65 (bs, 2 H), 3.61 (s, 3 H), 3.30 (app d, 2 H, *J* = 6 Hz), 2.30 (t, 2 H, *J* = 7.5 Hz), 1.58 (quin, 2 H, *J* = 7.5 Hz), 1.50 (quin, 2 H, *J* = 7.5 Hz), 1.32 (quin, 2 H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 182.9, 172.6, 50.4, 43.2, 32.9, 27.8, 25.3, 23.7; HRMS (ESI) *m/z* calcd for $C_8H_{17}O_2N_2S$ $(M+H)^+$ 205.1005, found 205.1005.

Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13a).



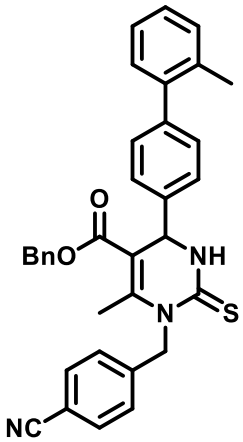
To a mixture of thiourea **2a** (0.23 g, 1.20 mmol, 1.2 eq), 4-biphenylcarboxaldehyde (0.183 g, 1.00 mmol, 1 eq), and benzyl acetoacetate (0.179 mL, 1.00 mmol, 1 eq) in DMF (3 mL) in a 25 mL microwave vial, was added TMSCl (0.519 mL, 4.01 mmol, 4 eq) dropwise. The vial was sealed and the reaction mixture was sonicated for 1 h at rt before being left to stir at rt for 3.5 days, before the addition of H_2O (6 mL). After stirring for 5 min, the reaction mixture was extracted with EtOAc (x 3) and the combined organic layers were washed with sat. aq. LiCl (x 2), dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 55:45) to provide benzyl 4-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13a**, 0.237 g, 0.426 mmol, 42%) as a yellow foam: Mp 64-66 °C; ATR IR (neat) 3316, 3187, 3031, 2935, 2230, 1706, 1630, 1609, 1506, 1382, 1357, 1153, 1133, 1046, 987, 948, 911, 764, 734, 698 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-*d6*, 360 K) δ 9.82 (d, 1 H, *J* = 4.3 Hz), 7.66-7.62 (m, 4 H), 7.59 (d, 2 H, *J* = 8.5 Hz), 7.48 (t, 2 H, *J* = 7.8 Hz), 7.38 (t, 1 H, *J* = 7.5 Hz), 7.31-7.23 (m, 9 H), 6.03 (d, 1 H, *J* = 16.5 Hz), 5.41 (partially hidden d, 1 H, *J* = 16.5 Hz, confirmed by HSQC), 5.39 (d, 1 H, *J* = 4.3 Hz), 5.20, 5.16 (ABq, 2 H, J_{AB} = 12.8 Hz), 2.42 (s, 3 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 178.3, 164.6, 146.3, 143.1, 140.7, 139.3, 135.5, 131.6, 128.3, 127.8, 127.4, 127.3, 126.9, 126.8, 126.3, 126.1, 117.9, 109.5, 106.4, 65.4, 51.8, 50.1, 16.0; HRMS (ESI) *m/z* calcd for $C_{33}H_{28}O_2N_3S$ $(M+H)^+$ 530.1897, found 530.1897.

Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3a: AMT580-052).



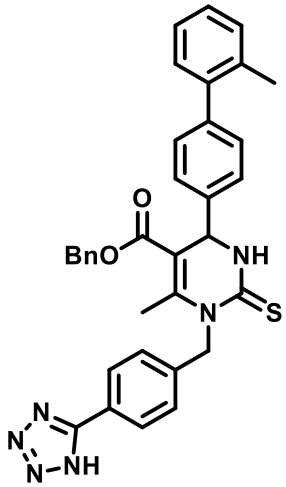
To a solution of **13a** (0.100 g, 0.189) in 1 M TBAF in THF (0.25 mL, 0.25 mmol, 1.3 eq) in a 2 mL microwave vial was added trimethylsilyl azide (0.11 mL, 0.76 mmol, 4 eq). The vial was flushed with Ar and sealed before heating at 70-75 °C for 14 h. The solution was loaded directly onto a column and purified by chromatography on SiO_2 ($MeOH:CH_2Cl_2$, 0:100 to 5:95 with 0.1% formic acid) to provide **AMT580-052** (**3a**, 0.072 g, 0.126 mmol, 67%) as an off-white solid: Mp 127-129 °C; ATR IR (neat) 3170, 3031, 2935, 2866, 2744, 1703, 1619, 1498, 1487, 1381, 1355, 1267, 1252, 1152, 1131, 1044, 987, 733, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-*d6*, 360 K) δ 9.84 (d, 1 H, *J* = 4.0 Hz), 7.90 (d, 2 H, *J* = 8.0 Hz), 7.62 (app d, 2 H, *J* = 8.0 Hz), 7.58 (d, 2 H, *J* = 8.0 Hz), 7.46 (t, 2 H, *J* = 7.6 Hz), 7.37 (t, 1 H, *J* = 7.2 Hz), 7.33-7.27 (m, 7 H), 7.26-7.21 (m, 2 H), 6.10 (d, 1 H, *J* = 17.2 Hz), 5.40 (d, 1 H, *J* = 4.0 Hz), 5.38 (partially hidden d, 1 H, *J* = 17.2 Hz, confirmed by HMQC), 5.19, 5.15 (ABq, 2 H, J_{AB} = 12.6 Hz), 2.47 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-*d6*, 360 K) δ 178.3, 164.6, 146.6, 140.8, 139.5, 139.4, 135.6, 128.4, 127.8, 127.5, 127.4, 126.9, 126.8, 126.6, 126.4, 126.3, 126.2, 106.3, 65.4, 51.8, 50.2, 16.1; HRMS (ESI) *m/z* calcd for $C_{33}H_{29}O_2N_6S$ $(M+H)^+$ 573.2067, found 573.2068; LCMS (ELSD) purity 99.9%.

Benzyl 1-(4-cyanobenzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13b).



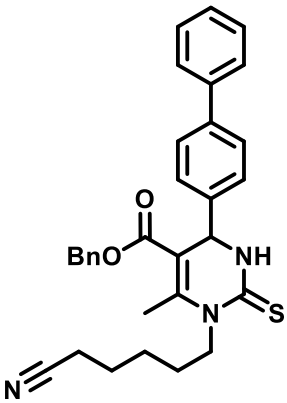
To a mixture of thiourea **2a** (0.24 g, 1.25 mmol, 1.2 eq), 2'-methyl-biphenyl-4-carbaldehyde (0.205 g, 1.05 mmol, 1 eq), and benzyl acetoacetate (0.186 mL, 1.05 mmol, 1 eq) in DMF (2.6 mL) in a 5 mL microwave vial, was added TMSCl (0.542 mL, 4.18 mmol, 4 eq) dropwise. The vial was sealed and the reaction mixture was sonicated for 1 h at rt before being left to stir at rt for 3.5 days, before the addition of H_2O (4 mL). After stirring for 10 min, the reaction mixture was extracted with EtOAc (x 3) and the combined organic layers were washed with sat. aq. LiCl (x 3), dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 55:45) to provide benzyl 1-(4-cyanobenzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13b**, 0.244 g, 0.449 mmol, 43%) as a yellow foam: Mp 69-71 °C; ATR IR (neat) 3301, 3186, 3030, 2935, 2228, 1704, 1626, 1608, 1505, 1380, 1354, 1150, 1129, 1043, 986, 947, 813, 761, 743, 697 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 9.83 (d, 1 H, *J* = 4.0 Hz), 7.64 (d, 2 H, *J* = 7.5 Hz), 7.32-7.18 (m, 15 H), 6.05 (d, 1 H, *J* = 17.5 Hz), 5.41 (partially hidden d, 1 H, *J* = 17.5 Hz, confirmed by HSQC), 5.41 (d, 1 H, *J* = 4.0 Hz), 5.22, 5.15 (ABq, 2 H, J_{AB} = 11.8 Hz), 2.43 (s, 3 H), 2.23 (s, 3 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 178.3, 164.6, 146.3, 143.1, 140.5, 140.2, 135.6, 134.2, 131.6, 129.8, 128.9, 128.5, 127.8, 127.4, 127.3, 126.9, 125.6, 125.3, 117.9, 109.5, 106.4, 65.4, 51.9, 50.1, 19.4, 16.0; HRMS (ESI) *m/z* calcd for $C_{34}H_{30}O_2N_3S$ $(M+H)^+$ 554.2053, found 554.2053.

Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3b: AMT551-093).



To a solution of **13b** (0.100 g, 0.184) in 1 M TBAF in THF (0.24 mL, 0.24 mmol, 1.3 eq) in a 2 mL microwave vial was added trimethylsilyl azide (0.10 mL, 0.74 mmol, 4 eq). The vial was flushed with Ar and sealed before heating at 70-75 °C for 14 h. The solution was diluted with EtOAc and washed with H_2O (1 x 2 mL) before the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (MeOH:CH_2Cl_2, 0:100 to 5:95 with 0.1% formic acid) to provide **AMT551-093** (**3b**, 0.069 g, 0.118 mmol, 64%) as a yellow foam: Mp 129-131 °C; ATR IR (neat) 3180, 3032, 2941, 2871, 2719, 1706, 1620, 1499, 1381, 1356, 1153, 1132, 736, 698 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 9.82 (d, 1 H, *J* = 4.5 Hz), 7.90 (d, 2 H, *J* = 8.5 Hz), 7.32-7.16 (m, 13 H), 6.14 (d, 1 H, *J* = 17.5 Hz), 5.42 (d, 1 H, *J* = 4.5 Hz), 5.37 (d, 1 H, *J* = 17.5 Hz), 5.22, 5.15 (ABq, 2 H, J_{AB} = 12.5 Hz), 2.47 (s, 3 H), 2.22 (s, 3 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 178.4, 164.6, 146.5, 140.5, 140.2, 135.6, 134.2, 129.7, 128.9, 128.5, 127.8, 127.4, 127.3, 126.7, 126.5, 125.6, 125.3, 106.4, 65.4, 51.8, 50.1, 19.4, 16.0; HRMS (ESI) *m/z* calcd for $C_{34}H_{31}O_2N_6S$ $(M+H)^+$ 587.2224, found 587.2226; LCMS (ELSD) purity 100%.

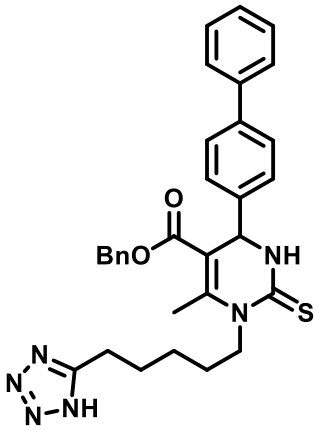
Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(5-cyanopentyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13c).



To a mixture of thiourea **2b** (0.53 g, 2.6 mmol, 1.2 eq), 4-biphenylcarboxaldehyde (0.40 g, 2.2 mmol, 1 eq), and benzyl acetoacetate (0.39 mL, 2.2 mmol, 1 eq) in DMF (5.4 mL) in a 25 mL microwave vial, was added TMSCl (1.13 mL, 8.69 mmol, 4 eq) dropwise. The vial was sealed and the reaction mixture was sonicated for 1 h at rt before being left to stir at rt for 4

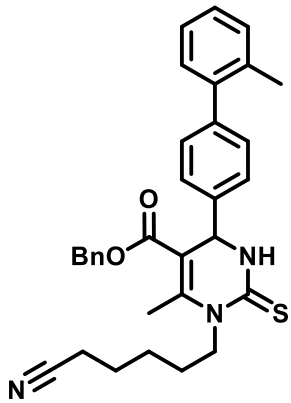
days, before the addition of H_2O (10 mL). After stirring for 10 min, the reaction mixture was extracted with EtOAc (x 3) and the combined organic layers were washed with sat. aq. LiCl (x 2), dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 55:45) to provide benzyl 4-([1,1'-biphenyl]-4-yl)-1-(5-cyanopentyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13c**, 0.669 g, 1.31 mmol, 60%) as an orange foam: Mp 67-69 °C; ATR IR (neat) 3327, 3198, 3031, 2935, 2864, 2245, 1702, 1624, 1382, 1355, 1150, 1127, 1091, 1076, 762, 736, 698 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 9.54 (d, 1 H, *J* = 3.0 Hz), 7.63 (app. d, 2 H, *J* = 7.5 Hz), 7.59 (app. d, 2 H, *J* = 8.0 Hz), 7.46 (app. t, 2 H, *J* = 7.3 Hz), 7.38-7.24 (m, 8 H), 5.33 (d, 1 H, *J* = 4.0 Hz), 5.22, 5.18 (ABq, 2 H, J_{AB} = 12.5 Hz), 4.75-4.68 (m, 1 H), 3.91 (ddd, 1 H, *J* = 14.0, 9.0, 5.5 Hz), 2.57 (s, 3 H), 2.36 (t, 2 H, *J* = 7.0 Hz), 1.72-1.64 (m, 1 H), 1.57-1.45 (m, 3 H), 1.32-1.25 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 177.7, 164.7, 146.5, 140.9, 139.3, 139.2, 135.6, 128.2, 127.7, 127.3, 127.2, 126.8, 126.2, 126.0, 119.4, 106.2, 65.3, 51.7, 46.4, 27.6, 24.6, 24.0, 15.6, 15.5; HRMS (ESI) *m/z* calcd for $C_{31}H_{32}O_2N_3S$ $(M+H)^+$ 510.2210, found 510.2209.

Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3c: AMT580-027).



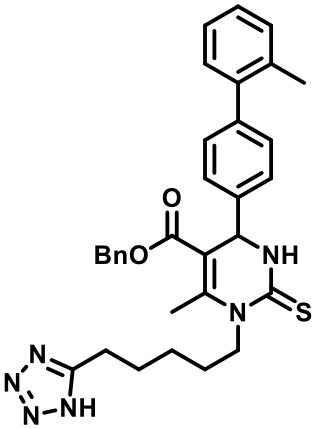
To a solution of **13c** (0.100 g, 0.177) in 1 M TBAF in THF (0.23 mL, 0.23 mmol, 1.3 eq) in a 2 mL microwave vial was added trimethylsilyl azide (0.10 mL, 0.10 mmol, 4 eq). The vial was flushed with Ar and sealed before heating at 70-75 °C for 20 h. As the reaction was incomplete, the mixture was heated at 80 °C for 22 h before further trimethylsilyl azide (0.10 mL, 0.10 mmol, 4 eq) was added and the reaction heated at 80 °C for 2 days. After 75% conversion, and the reaction mixture was loaded directly onto a column and purified by chromatography on SiO_2 (MeOH:CH_2Cl_2, 0:100 to 5:95 with 0.1% formic acid) to provide **AMT580-027** (**3c**, 0.054 g, 0.098 mmol, 56%) as a light yellow foam: Mp 81-83 °C; ATR IR (neat) 3119, 3031, 2936, 2856, 2744, 1702, 1625, 1383, 1151, 1125, 1088, 1049, 736, 698 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 15.66 (bs, 1 H), 9.51 (d, 1 H, *J* = 4.0 Hz), 7.61-7.55 (m, 4 H), 7.43 (app. t, 2 H, *J* = 7.5 Hz), 7.36-7.24 (m, 7 H), 5.30 (d, 1 H, *J* = 4.5 Hz), 5.21, 5.17 (ABq, 2 H, J_{AB} = 12.3 Hz), 4.68 (ddd, 1 H, *J* = 14.7, 9.3, 6.3 Hz), 3.88 (ddd, 1 H, *J* = 14.5, 9.5, 5.3 Hz), 2.80 (t, 2 H, *J* = 7.5 Hz), 2.56 (s, 3 H), 1.72-1.64 (m, 3 H), 1.53-1.45 (m, 1 H), 1.28-1.20 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 177.7, 164.7, 146.5, 140.9, 139.3, 139.3, 135.7, 128.3, 127.8, 127.4, 127.3, 126.8, 126.2, 126.1, 106.1, 65.3, 51.7, 48.1, 46.6, 27.9, 26.0, 24.9, 22.2, 15.6; HRMS (ESI) *m/z* calcd for $C_{31}H_{33}O_2N_6S$ $(M+H)^+$ 553.2380, found 553.2380; LCMS (ELSD) purity 100%.

Benzyl 1-(5-cyanopentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13d).



To a mixture of thiourea **2b** (0.28 g, 1.4 mmol, 1.2 eq), 2'-methyl-biphenyl-4-carbaldehyde (0.229 g, 1.17 mmol, 1 eq), and benzyl acetoacetate (0.23 mL, 1.17 mmol, 1 eq) in DMF (3.5 mL) in a 25 mL microwave vial, was added TMSCl (0.61 mL, 4.67 mmol, 4 eq) dropwise. The vial was sealed and the reaction mixture was sonicated for 1 h at rt before being left to stir at rt for 4 days, before the addition of H_2O (10 mL). After stirring for 10 min, the reaction mixture was extracted with EtOAc (x 3) and the combined organic layers were washed with sat. aq. LiCl (x 2), dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 55:45) to provide benzyl 1-(5-cyanopentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13d**, 0.551 g, 1.05 mmol, 90%) as a yellow foam: Mp 49-51 °C; ATR IR (neat) 3311, 3189, 3029, 2935, 2863, 2244, 1702, 1622, 1381, 1353, 1148, 1125, 1090, 1076, 1044, 760, 741, 697 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 9.56 (d, 1 H, *J* = 4.0 Hz), 7.34-7.16 (m, 13 H), 5.33 (d, 1 H, *J* = 4.5 Hz), 5.24, 5.17 (ABq, 2 H, J_{AB} = 12.5 Hz), 4.72 (ddd, 1 H, *J* = 14.8, 9.0, 6.3 Hz), 3.90 (ddd, 1 H, *J* = 14.3, 9.0, 5.3 Hz), 2.57 (s, 3 H), 2.38 (t, 2 H, *J* = 7.0 Hz), 2.21 (s, 3 H), 1.70-1.62 (m, 1 H), 1.58-1.44 (m, 3 H), 1.33-1.27 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 177.7, 164.7, 146.5, 140.5, 140.3, 135.7, 128.8, 128.4, 127.8, 127.4, 127.3, 126.7, 125.5, 125.2, 119.5, 106.2, 65.3, 51.8, 46.4, 27.6, 24.6, 23.9, 19.4, 15.6, 15.5; HRMS (ESI) *m/z* calcd for $C_{32}H_{34}O_2N_3S$ $(M+H)^+$ 524.2372, found 524.2378.

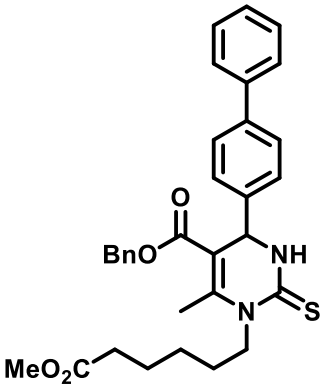
Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3d: AMT580-033).



To a solution of **13d** (0.200 g, 0.382) in 1 M TBAF in THF (0.50 mL, 0.50 mmol, 1.3 eq) in a 5 mL microwave vial was added trimethylsilyl azide (0.21 mL, 1.53 mmol, 4 eq). The vial was flushed with Ar and sealed before heating at 80 °C for 2 days. The reaction was incomplete

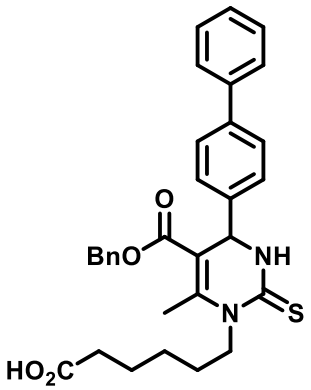
and further trimethylsilyl azide (0.21 mL, 1.53 mmol, 4 eq) was added and the reaction heated at 80 °C for 36 h. At 70% conversion, the reaction mixture was loaded directly onto a column and purified by chromatography on SiO_2 ($MeOH:CH_2Cl_2$, 0:100 to 5:95 with 0.1% formic acid) to provide **AMT580-033** (**3d**, 0.086 g, 0.150 mmol, 39%) as a light yellow foam: Mp 74-76 °C; ATR IR (neat) 3151, 3028, 2934, 2861, 2734, 2613, 1703, 1625, 1382, 1356, 1265, 1151, 1124, 1088, 1050, 762, 736, 699 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 15.63 (bs, 1 H), 9.52 (d, 1 H, *J* = 4.5 Hz), 7.34-7.19 (m, 12 H), 7.14 (d, 1 H, *J* = 7.5 Hz), 5.32 (d, 1 H, *J* = 4.5 Hz), 5.24, 5.17 (ABq, 2 H, J_{AB} = 12.5 Hz), 4.69 (ddd, 1 H, *J* = 15.0, 9.5, 6.0 Hz), 3.89 (ddd, 1 H, *J* = 14.3, 9.3, 5.0 Hz), 2.82 (t, 2 H, *J* = 7.5 Hz), 2.56 (s, 3 H), 2.19 (s, 3 H), 1.73-1.62 (m, 3 H), 1.52-1.45 (m, 1 H), 1.30-1.22 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 177.7, 164.7, 146.5, 140.5, 140.3, 140.3, 135.7, 134.2, 129.7, 128.8, 128.4, 127.8, 127.4, 127.3, 126.7, 125.5, 125.2, 106.2, 65.3, 51.8, 48.1, 46.6, 27.9, 26.0, 24.9, 22.2, 19.4, 15.6; HRMS (ESI) *m/z* calcd for $C_{32}H_{35}O_2N_6S$ $(M+H)^+$ 567.2537, found 567.2538; LCMS (ELSD) purity 99.5%.

Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(6-methoxy-6-oxohexyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (13e).



To a mixture of thiourea **2c** (0.470 g, 2.30 mmol, 1.2 eq), 4-biphenylcarboxaldehyde (0.349 g, 1.92 mmol, 1 eq), and benzyl acetoacetate (0.34 mL, 1.9 mmol, 1 eq) in DMF (4.9 mL) in a 25 mL microwave vial, was added TMSCl (0.99 mL, 7.7 mmol, 4 eq) dropwise. The vial was sealed and the reaction mixture was sonicated for 1 h at rt before being left to stir at rt for 3.5 days, before the addition of H_2O (10 mL). After stirring for 10 min, the reaction mixture was extracted with EtOAc (x 3) and the combined organic layers were washed with sat. aq. LiCl (x 3), dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 55:45) to provide benzyl 4-([1,1'-biphenyl]-4-yl)-1-(6-methoxy-6-oxohexyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**13e**, 0.612 g, 1.13 mmol, 59%) and the saponified product (**3e**, 0.140 g, 0.264 mmol, 14%), both as yellow foams, **13e**: Mp 59-61 °C; ATR IR (neat) 3307, 3191, 3029, 2945, 2859, 1733, 1702, 1622, 1381, 1355, 1241, 1186, 1149, 1121, 1090, 1044, 759, 735, 696 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*, 360 K) δ 9.53 (d, 1 H, *J* = 3.5 Hz), 7.62 (app. d, 2 H, *J* = 8.5 Hz), 7.58 (app. d, 2 H, *J* = 8.0 Hz), 7.45 (app. t, 2 H, *J* = 7.5 Hz), 7.37-7.26 (m, 8 H), 5.31 (d, 1 H, *J* = 4.5 Hz), 5.21, 5.17 (ABq, 2 H, J_{AB} = 12.5 Hz), 4.74-4.68 (m, 1 H), 3.86 (ddd, 1 H, *J* = 14.0, 8.5, 5.5 Hz), 3.55 (s, 3 H), 2.55 (s, 3 H), 2.19 (t, 2 H, *J* = 7.5 Hz), 1.66-1.60 (m, 1 H), 1.53-1.42 (m, 3 H), 1.20-1.14 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 177.8, 172.4, 164.7, 146.6, 140.9, 139.4, 139.2, 135.7, 128.3, 127.8, 127.4, 127.3, 126.8, 126.2, 126.1, 106.2, 65.3, 51.6, 50.3, 46.6, 32.7, 28.1, 25.0, 23.5, 15.6; HRMS (ESI) *m/z* calcd for $C_{32}H_{35}O_4N_2S$ $(M+H)^+$ 543.2312, found 543.2313.

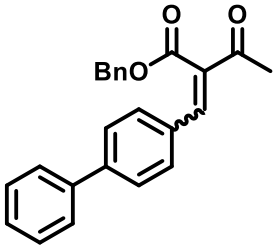
6-(4-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-6-methyl-2-thioxo-3,4-dihydropyrimidin-1(2H)-yl)hexanoic acid (3e: AMT551-090).



To a solution of **13e** (0.053 mg, 0.879 mmol) in THF/H_2O (22 mL, 3:1, 0.04 M) was added 1 M NaOH (1.06 mL, 1.06 mmol, 1.2 eq). The reaction mixture was stirred at rt for 11 h, before addition of more 1 M NaOH (1.06 mL, 1.06 mmol, 1.2 eq). The reaction mixture was then left to stir for 3.5 h before being acidifed to pH 3 with 1 M HCl and extracted with EtOAc (x 3). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. This residual foam was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to give the desired product **AMT551-090** (**3e**, 0.340 g, 0.639 mmol, 73%) as a light yellow foam: Mp 68-70 °C; ATR IR (neat) 3199, 3031, 2938, 1703, 1625, 1383, 1247, 1152, 1125, 1092, 829, 762, 736, 698 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-*d6*, 360 K) δ 9.56 (d, 1 H, *J* = 4.8 Hz), 7.63 (app. d, 2 H, *J* = 7.2 Hz), 7.58 (app. d, 2 H, *J* = 8.4 Hz), 7.45 (app. t, 2 H, *J* = 7.8 Hz), 7.37-7.24 (m, 8 H), 5.32 (d, 1 H, *J* = 4.4 Hz), 5.22, 5.17 (ABq, 2 H, J_{AB} = 12.6 Hz), 4.71 (ddd, 1 H, *J* = 14.8, 9.2, 6.0 Hz), 3.88 (ddd, 1 H, *J* = 14.6, 9.2, 5.6 Hz), 2.56 (s, 3 H), 2.14 (t, 2 H, *J* = 7.4 Hz), 1.69-1.61 (m, 1 H), 1.53-1.42 (m, 3 H), 1.24-1.16 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-*d6*, 360 K) δ 177.7, 173.5, 164.8, 146.7, 140.9, 139.4, 139.3, 135.7, 128.4, 127.9, 127.4, 127.3, 126.9, 126.3, 126.2, 126.2, 106.1, 65.3, 51.7, 46.7, 33.2, 28.2, 25.2, 23.7, 15.7; HRMS (ESI) *m/z* calcd for $C_{31}H_{33}O_4N_2S$ $(M+H)^+$ 529.2156, found 529.2156; LCMS (ELSD) purity 100%.

N-3 substituted 3,4-dihydropyrimidine-2(1H)-thione syntheses

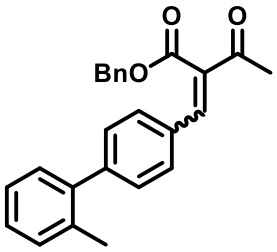
Benzyl 2-([1,1'-biphenyl]-4-ylmethylene)-3-oxobutanoate (4a).



To a solution of 4-biphenylcarboxaldehyde (2.00 g, 10.8 mmol) and benzyl acetoacetate (1.91 mL, 10.8 mmol, 1 eq) in 2-propanol (10.9 mL) was added piperidine (44 uL, 0.44 mmol, 0.04 eq) and AcOH (25 uL, 0.44 mmol, 0.04 eq). The reaction mixture was stirred at rt for 18 h and the resultant precipitate was filtered and washed with cold EtOAc to reveal the desired product benzyl 2-([1,1'-biphenyl]-4-ylmethylene)-3-oxobutanoate (**4a**, 3.01 g, 8.46 mmol, 77%) as a light yellow solid, as a mixture of isomers (1:2): Mp 93-95 °C; ATR IR (neat) 3063, 3031, 3003, 2950, 1726, 1660, 1218, 1200, 1188, 1033, 953, 766, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 0.33 H), 7.56-7.27 (m, 14.33 H), 7.20 (s, 0.33 H), 5.28 (s, 1.33 H),

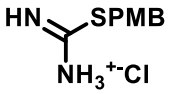
5.24 (s, 0.67 H), 2.35 (s, 2H), 2.33 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 194.6, 167.8, 164.5, 143.6, 143.4, 141.3, 140.8, 140.0, 140.0, 135.6, 134.9, 134.1, 133.6, 131.8, 131.7, 130.5, 130.3, 129.2, 129.1, 128.8, 128.7, 128.7, 128.5, 128.3, 128.2, 127.7, 127.5, 127.2, 127.2, 67.7, 67.3, 31.5, 26.7; HRMS (ESI) *m/z* calcd for $C_{24}H_{20}O_3Na$ $[M+Na]^+$ 379.1305, found 379.1304.

Benzyl 2-((2'-methyl-[1,1'-biphenyl]-4-yl)methylene)-3-oxobutanoate (4b).



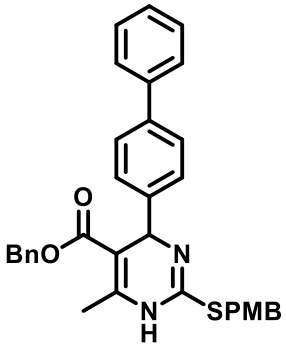
To a solution of 2'-methyl-biphenyl-4-carbaldehyde (0.50 g, 2.50 mmol) and benzyl acetoacetate (0.44 mL, 2.5 mmol, 1 eq) in 2-propanol (2.5 mL) was added piperidine (10 uL, 0.10 mmol, 0.04 eq) and AcOH (6 uL, 0.10 mmol, 0.04 eq). The reaction mixture was stirred at rt for 38 h and the resultant precipitate was isolated by filtration and washed with cold EtOAc to provide initial product. The filtrate was concentrated and purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) and combined with the original filter cake solid to afford benzyl 2-((2'-methyl-[1,1'-biphenyl]-4-yl)methylene)-3-oxobutanoate as a mixture of isomers (**4b**, 0.667 g, 1.80 mmol, 72%) as a yellow semi-solid: Mp 64-66 °C; ATR IR (neat) 3058, 3032, 2957, 2916, 1730, 1663, 1602, 1390, 1242, 1188, 1176, 1037, 760, 737, 697 cm^{-1}; Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1 H), 7.34-7.07 (m, 13 H), 5.20 (s, 2 H), 2.32 (s, 3 H), 2.16 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 167.8, 144.7, 141.4, 140.8, 135.3, 134.9, 134.1, 131.3, 130.6, 129.8, 129.6, 129.6, 129.1, 128.7, 127.9, 126.0, 67.7, 26.6, 20.5; HRMS (ESI) *m/z* calcd for $C_{25}H_{21}O_3Na$ $[M+Na]^+$ 393.1461, found 393.1460.

2-(4-Methoxybenzyl)isothiouronium chloride (5).[10]



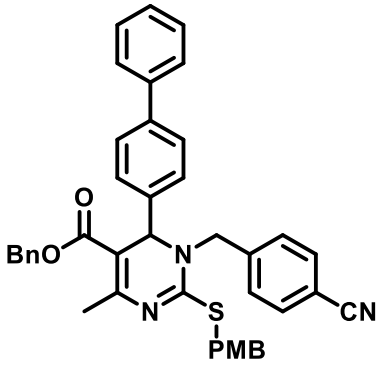
To a mixture of thiourea (1.50 g, 19.7 mmol) in THF (9.9 mL, 2.0 M, dry) at 0 °C was added 4-methoxybenzyl chloride (2.73 mL, 19.7 mmol, 1 eq) over ~2 min. The reaction mixture was allowed to warm to rt, stirred for 2 h, and then heated at 65 °C for 5 h. The resulting white solid was filtered and washed with ether to afford 2-(4-methoxybenzyl)isothiouronium chloride (**5**, 4.34 g, 18.7 mmol, 95%) as a white powder. NMR spectra of **5** match the previously reported data: ^{1}H NMR (300 MHz, DMSO-*d6*) δ 9.28 (s, 4 H), 7.36 (d, 2 H, *J* = 8.7 Hz), 6.93 (d, 2 H, *J* = 8.7 Hz), 4.47 (s, 2 H), 3.75 (s, 3 H).

Benzyl 4-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-6-methyl-1,4-dihydropyrimidine-5-carboxylate (6a).



To a solution of Knoevenagel product **4a** (1.00 g, 2.81 mmol) and protected thiourea **5** (0.652 g, 2.81 mmol, 1 eq) in DMF (7.0 mL, dry, 0.4 M) was added NaOAc (0.230 g, 2.81 mmol, 1 eq). The reaction mixture was heated at 75 °C for 5 h, cooled and quenched with water (6 mL) and extracted using EtOAc (3 x 20 mL). The combined organic layers were washed with LiCl (2 x), dried ($MgSO_4$), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to provide benzyl 4-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-6-methyl-1,4-dihydropyrimidine-5-carboxylate (**6a**, 0.974 g, 1.79 mmol, 64%), as a light yellow foam: Mp 59-61 °C; ATR IR (neat) 3053, 3029, 2926, 2830, 1694, 1679, 1647, 1609, 1510, 1485, 1243, 1201, 1154, 1087, 1030, 832, 766, 733, 696 cm^{-1}; ^1H NMR (300 MHz, MeOD) δ 7.63-7.60 (m, 2 H), 7.50 (d, 2 H, *J* = 8.1 Hz), 7.45-7.41 (m, 2 H), 7.35-7.30 (m, 2 H), 7.27-7.21 (m, 4 H), 7.16-7.13 (m, 2 H), 7.05 (d, 2 H, *J* = 8.4 Hz), 6.63 (d, 2 H, *J* = 8.1 Hz), 5.62 (s, 1 H), 5.15, 5.03 (ABq, 2 H, J_{AB} = 12.6 Hz), 4.29, 3.96 (ABq, 2 H, J_{AB} = 13.7 Hz), 3.60 (s, 3 H), 2.35 (s, 3 H); ^{13}C NMR (100 MHz, MeOD) δ 167.7, 160.3, 155.8, 149.4, 144.5, 142.0, 141.5, 137.7, 131.1, 130.2, 129.9, 129.4, 128.9, 128.9, 128.7, 128.3. 128.1, 127.9, 114.8, 101.8, 66.7, 59.3, 55.5, 35.6, 18.7; HRMS (ESI) *m/z* calcd for $C_{33}H_{31}O_3N_2S$ $(M+H)^+$ 535.2050, found 535.2049.

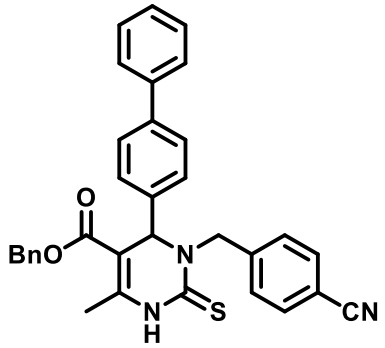
Benzyl 6-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-1,6-dihydropyrimidine-5-carboxylate (7a).



To a solution of **6a** (0.160 g, 0.266 mmol) in DMF (0.89 mL, dry, 0.3 M) under an Ar atmosphere at 0 °C was added NaH (0.021 g, 0.533 mmol, 2 eq) as a 60% dispersion in mineral oil. The reaction mixture was stirred at 0 °C for 1 h before 4-(bromomethyl)benzonitrile (0.117 g, 0.586 mmol, 1.2 eq) was added dropwise as a DMF (0.45 mL, dry, 1.3 M) solution. The reaction mixture was allowed to warm to rt and stirred for 17 h. The reaction was quenched with sat. aq. LiCl (4 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with sat. aq. LiCl (x 2), dried (Na_2SO_4), filtered and concentrated. The residue was purified by chromatography on SiO_2

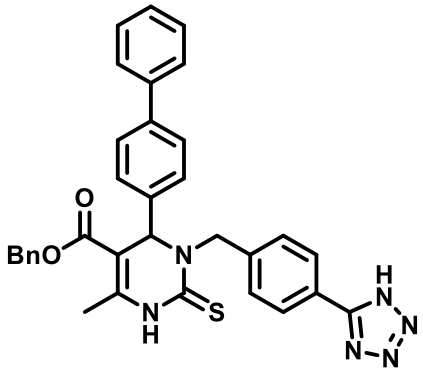
(EtOAc:Hexanes, 0:100 to 100:0) to provide benzyl 6-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-1,6-dihydropyrimidine-5-carboxylate (**7a**, 0.114 g, 0.165 mmol, 62%) as a yellow semi-solid: ATR IR (neat) 3031, 2957, 2932, 2228, 1698, 1677, 1608, 1596, 1511, 1488, 1398, 1374, 1229, 1175, 1068, 829, 734, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59-7.54 (m, 5 H), 7.48-7.42 (m, 4 H), 7.38-7.35 (m, 2 H), 7.29-7.23 (m, 7 H), 7.14-7.11 (m, 2 H), 6.84 (d, 2 H, *J* = 8.7 Hz), 5.18 (s, 1 H), 5.09, 5.01 (ABq, 2 H, J_{AB} = 12.6 Hz), 4.91 (d, 1 H, *J* = 16.8 Hz), 4.48, 4.32 (ABq, 2 H, J_{AB} = 13.4 Hz), 4.24 (d, 1 H, *J* = 16.8 Hz), 3.81 (s, 3 H), 2.47 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 161.8, 159.2, 155.2, 141.4, 141.2, 140.8, 140.7, 136.4, 132.8, 130.5, 129.2, 129.0, 128.5, 128.1, 128.0, 128.0, 127.6, 127.2, 118.7, 114.1, 112.0, 104.3, 65.9, 60.4, 55.5, 52.0, 36.1, 23.4; HRMS (ESI) *m/z* calcd for $C_{41}H_{36}O_3N_3S$ $(M+H)^+$ 650.2472, found 650.2471.

Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14).



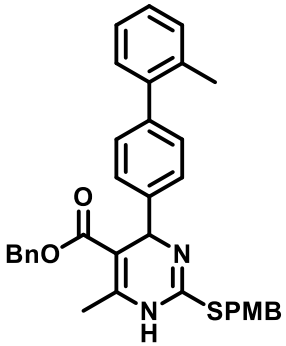
To a solution of **7a** (0.100 g, 0.145 mmol) in CH_2Cl_2 (1.70 mL, dry, 0.085 M) was added TFA (56 µL, 0.73 mmol, 5 eq) and ethanethiol (26 µL, 0.36 mmol, 2.5 eq). The reaction mixture was stirred at 40 °C in a sealed vial for 4 h. The reaction mixture was cooled and concentrated, redissolved in CH_2Cl_2 and washed with sat.'d aq. $NaHCO_3$. The aq. layer was extracted with CH_2Cl_2 (x 2) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residual foam was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to provide benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**14**, 0.068 mg, 0.121 mmol, 84%) as a slightly yellow foam: Mp 77-79 °C; ATR IR (neat) 3216, 3165, 3053, 3032, 2952, 2229, 1708, 1685, 1649, 1526, 1455, 1242, 1206, 1112, 1078, 735, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, 1 H), 7.63 (d, 2 H, *J* = 8.0 Hz), 7.56-7.53 (m, 2 H), 7.50 (d, 2 H, *J* = 8.0 Hz), 7.46 (app. t, 2 H, *J* = 7.5 Hz), 7.42 (d, 2 H, *J* = 8.0 Hz), 7.40-7.36 (m, 1 H), 7.32-7.26 (m, 4 H), 7.16-7.13 (m, 2 H), 6.05 (d, 1 H, *J* = 15.5 Hz), 5.34 (s, 1 H), 5.12, 5.05 (ABq, 2 H, J_{AB} = 12.0 Hz), 4.25 (d, 1 H, *J* = 15.5 Hz), 2.38 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.5, 164.8, 143.0, 141.9, 140.9, 140.4, 138.9, 135.7, 132.7, 129.0, 128.7, 128.5, 128.5, 128.3, 127.9, 127.8, 127.7, 127.2, 118.7, 112.0, 102.7, 66.6, 60.1, 54.3, 18.7; HRMS (ESI) *m/z* calcd for $C_{33}H_{28}O_2N_3S$ $(M+H)^+$ 530.1897, found 530.1896.

Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8a: AMT580-043).



To a solution of **14** (0.053 g, 0.098 mmol) in THF (0.5 mL) in a 2 mL microwave vial was added 1 M TBAF in THF (0.127 mL, 0.127 mmol, 1.3 eq) and trimethylsilyl azide (0.054 mL, 0.392 mmol, 4 eq). The vial was flushed with Ar and sealed before heating at 70-75 °C for 12 h. As the reaction was incomplete, the reaction mixture was concentrated and further trimethylsilyl azide (0.054 mL, 0.392 mmol, 4 eq) was added before stirring at 70-75 °C for 23 h. The reaction mixture was then cooled and loaded directly onto a column for purification on SiO_2 ($MeOH:CH_2Cl_2$, 0:100 to 5:95 with 0.1% formic acid) to provide **AMT580-043** (**8a**, 0.030 mg, 0.052 mmol, 63%) as a white solid: Mp 130-133 °C; ATR IR (neat) 3159, 3031, 2977, 2871, 1707, 1686, 1652, 1529, 1487, 1242, 1203, 1113, 1079, 838, 763, 733, 696 cm^{-1}; ^1H NMR (500 MHz, DMSO-*d6*) δ 10.82 (s, 1 H), 8.03 (d, 2 H, *J* = 8.0 Hz), 7.63 (d, 4 H, *J* = 8.0 Hz), 7.54 (d, 2 H, *J* = 8.5 Hz), 7.46 (t, 2 H, *J* = 7.8 Hz), 7.37 (t, 1 H, *J* = 7.5 Hz), 7.31 (d, 2 H, *J* = 8.0 Hz), 7.24-7.18 (m, 3 H), 7.10 (dd, 2 H, *J* = 6.5, 3.0 Hz), 5.98 (d, 1 H, *J* = 15.5 Hz), 5.42 (s, 1 H), 5.06, 5.03 (ABq, 2 H, J_{AB} = 12.8 Hz), 4.37 (d, 1 H, *J* = 15.5 Hz), 2.34 (s, 3 H); ^{13}C NMR (100 MHz, DMSO-*d6*) δ 176.0, 164.5, 145.2, 140.3, 139.8, 139.6, 136.1, 129.0, 128.3, 128.2, 127.8, 127.6, 127.5, 127.4, 127.3, 126.3, 100.8, 65.2, 58.6, 53.1, 17.1; HRMS (ESI) *m/z* calcd for $C_{33}H_{29}O_2N_6S$ $(M+H)^+$ 573.2067, found 573.2068; LCMS (ELSD) purity 99.4%.

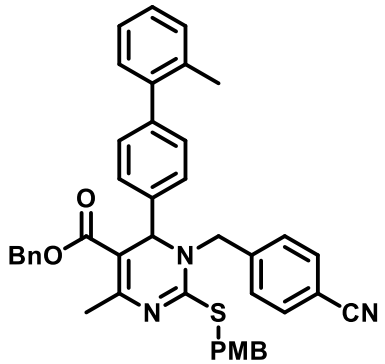
Benzyl 2-((4-methoxybenzyl)thio)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,4-dihydropyrimidine-5-carboxylate (6b).



To a solution of Knoevenagel product **4b** (1.00 g, 2.81 mmol) and protected thiourea **5** (0.652 g, 2.81 mmol, 1 eq) in DMF (7.0 mL dry, 0.4 M) was added NaOAc (0.230 g, 2.81 mmol, 1 eq). The reaction mixture was heated at 75 °C for 5 h, cooled to rt, quenched with H_2O (6 mL), and extracted using EtOAc (3 x 20 mL). The combined organic layers were washed with sat. aq. LiCl solution (x 2) before being dried (MgSO4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to provide benzyl 2-((4-methoxybenzyl)thio)-6-methyl-4-(2'-methyl-[1,1'-

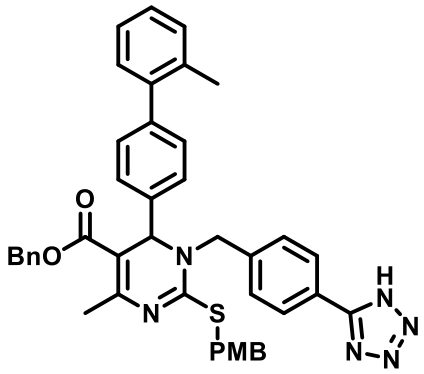
biphenyl]-4-yl)-1,4-dihydropyrimidine-5-carboxylate (**6b**, 0.246 g, 0.438 mmol, 81%) as white crystals (precipitated from MeOH): Mp 148-150 °C; ATR IR (neat) 3028, 2952, 2895, 2830, 1698, 1648, 1601, 1505, 1482, 1240, 1179, 1072, 1033, 830, 760, 702 cm^{-1}; ^{1}H NMR (300 MHz, MeOD) δ 7.33-7.14 (m, 13 H), 7.09 (d, 2 H, *J* = 8.7 Hz), 6.67 (d, 2 H, *J* = 8.7 Hz), 5.63 (s, 1 H), 5.14, 5.01 (ABq, 2 H, J_{AB} = 12.5 Hz), 4.29, 4.05 (ABq, 2 H, J_{AB} = 13.5 Hz), 3.64 (s, 3 H), 2.32 (s, 3 H), 2.21 (s, 3 H); ^{13}C NMR (75 MHz, MeOD) δ 168.1, 160.3, 144.5, 142.9, 142.3, 137.9, 136.2, 131.3, 131.1, 130.7, 130.7, 130.2, 129.4, 129.3, 128.9, 128.9, 128.3, 128.2, 128.0, 127.9, 126.8, 114.8, 66.6, 55.6, 35.4, 20.8; HRMS (ESI) *m/z* calcd for $C_{34}H_{33}O_3N_2S$ $(M+H)^+$ 549.2206, found 549.2210.

Benzyl 1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate (7b).



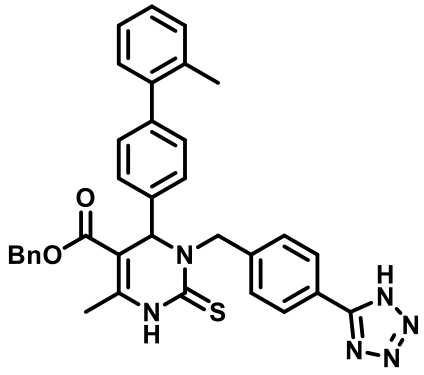
To a solution of **6b** (0.100 g, 0.128 mmol) in DMF (0.43 mL, dry, 0.3 M) under an Ar atomsphere at 0 °C was added NaH (0.010 g, 0.255 mmol, 2 eq) as a 60% dispersion in mineral oil. The reaction mixture was stirred at 0 °C for 1 h before 4-(bromomethyl)benzonitrile (0.043 g, 0.219 mmol, 1.7 eq) was added dropwise as a DMF (0.17 mL, dry, 1.3 M) solution. The reaction mixture was allowed to warm to rt and stirred for 13 h. The reaction was quenched with sat. aq. NH_4Cl (1 mL) and H_2O (3 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with sat. aq. LiCl (x 2), dried (Na_2SO_4), filtered and concentrated. The residue was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to provide benzyl 1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate (**7b**, 0.055 g, 0.078 mmol, 61%) as a light yellow foam: Mp 54-56 °C; ATR IR (neat) 3033, 2957, 2922, 2835, 2228, 1697, 1671, 1608, 1510, 1487, 1396, 1373, 1226, 1173, 1065, 824, 728 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, 2 H, *J* = 8.1 Hz), 7.40-7.18 (m, 17 H), 6.88 (d, 2 H, *J* = 8.4 Hz), 5.26 (s, 1 H), 5.22, 5.02 (ABq, 2 H, J_{AB} = 12.6 Hz), 4.95 (d, 1 H, *J* = 16.8 Hz), 4.55, 4.38 (ABq, 2 H, J_{AB} = 13.2 Hz), 4.38 (partially hidden d, 1 H, *J* = 16.8 Hz), 3.84 (s, 3 H), 2.55 (s, 3 H), 2.32 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 161.7, 159.1, 155.1, 142.1, 141.4, 141.2, 140.2, 136.4, 135.3, 132.6, 130.5, 130.4, 129.8, 129.6, 129.2, 128.5, 128.0, 128.0, 127.5, 127.1, 125.9, 118.6, 114.0, 111.9, 104.3, 65.8, 60.6, 55.3, 52.3, 36.0, 23.2, 20.6; HRMS (ESI) *m/z* calcd for $C_{42}H_{38}O_3N_3S$ $(M+H)^+$ 664.2628, found 664.2629.

Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate (15).



To a solution of **7b** (0.045 g, 0.065 mmol) in THF (108 µL, 0.6 M) in a 1 mL microwave vial was added trimethylsilyl azide (36 µL, 0.26 mmol, 4 eq) and TBAT (0.035 g, 0.064 mmol, 1 eq). The vial was sealed and the reaction mixture was heated at 90 °C for 16 h. The reaction mixture was then allowed to cool before addition of H_2O (2 mL) and extraction with EtOAc (3 x 3 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (MeOH:CH_2Cl_2, 0:100 to 5:95 with 0.1% formic acid) to provide benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate (**15**, 0.029 mg, 0.037 mmol, 57%) as an orange oil: ATR IR (neat) 2997, 2933, 2835, 2770, 1709, 1609, 1512, 1486, 1361, 1221, 1174, 1067, 1031, 837, 763, 742, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.90 (bs, 1 H), 8.00 (d, 2 H, *J* = 8.1 Hz), 7.22-6.98 (m, 17 H), 6.73 (d, 2 H, *J* = 8.7 Hz), 5.24 (s, 1 H), 5.02, 4.90 (ABq, 2 H, J_{AB} = 12.5 Hz), 4.88 (partially hidden d, 1 H, *J* = 16.2 Hz), 4.43, 4.28 (ABq, 2 H, J_{AB} = 13.5 Hz), 4.25 (partially hidden d, 1 H, *J* = 16.2 Hz), 3.68 (s, 3 H), 2.43 (s, 3 H), 2.14 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 162.5, 159.2, 157.5, 154.2, 142.3, 141.3, 139.7, 138.2, 136.1, 135.4, 130.5, 129.9, 129.8, 128.8, 128.5, 128.3, 128.1, 128.0, 128.0, 127.6, 127.3, 126.0, 124.9, 114.3, 104.5, 66.2, 60.5, 55.5, 52.8, 36.6, 22.7, 20.6; HRMS (ESI) *m/z* calcd for $C_{42}H_{39}O_3N_6S$ $(M+H)^+$ 707.2799, found 707.2793.

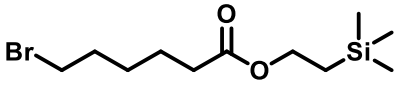
Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8b: AMT551-058).



To a solution of **15** (0.027 g, 0.034 mmol) in CH_2Cl_2 (0.40 mL, dry, 0.085 M) was added TFA (13 µL, 0.174 mmol, 5 eq) and ethanethiol (6 µL, 0.086 mmol, 2.5 eq). The reaction mixture was stirred at 40 °C in a sealed vial for 4 h. The reaction mixture was cooled and concentrated, redissolved in EtOAc and washed with sat.'d aq. $NaHCO_3$. The aq. layer was extracted with EtOAc (x 2) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residual solid was purified by reverse phase HPLC (H_2O:MeCN, 55:45

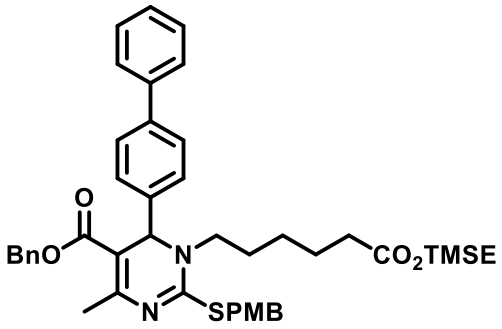
to 30:70 with 0.1% formic acid, over 15 min, 40 mL/min) to provide **AMT551-058** (**8b**, 14 mg, 0.023 mmol, 68%) as a white solid: Mp 129-131 °C; ATR IR (neat) 3210, 3164, 3058, 3033, 2924, 2856, 1707, 1685, 1651, 1530, 1456. 1244, 1206, 1111, 1085, 909, 763, 730, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, 2 H, *J* = 8.0 Hz), 7.99 (bs, 1 H), 7.49 (d, 2 H, *J* = 8.0 Hz), 7.29-7.21 (m, 10 H), 7.18-7.10 (m, 3 H), 6.07 (d, 2 H, *J* = 15.2 Hz), 5.43 (s, 1 H), 5.14, 5.03 (ABq, 2 H, J_{AB} = 12.4 Hz), 4.31 (d, 2 H, *J* = 15.2 Hz), 2.40 (s, 3 H), 2.24 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 165.4, 156.7, 143.6, 142.6, 141.2, 139.3, 138.6, 135.5, 135.4, 130.6, 130.0, 129.8, 128.9, 128.7, 128.4, 128.2, 128.1, 127.7, 127.2, 126.0, 123.6, 102.7, 66.7, 60.1, 54.4, 20.6, 18.6; HRMS (ESI) *m/z* calcd for $C_{34}H_{31}O_2N_6S$ $(M+H)^+$ 587.2224, found 587.2226; LCMS (ELSD) purity 98.4%.

2-(Trimethylsilyl)ethyl 6-bromohexanoate (18).



To a suspension of 6-bromohexanoic acid (1.00 g, 4.97 mmol), DIC (0.770 mL, 4.97 mmol, 1 eq) and DMAP (0.061 g, 0.50 mmol, 0.1 eq) in CH_2Cl_2 (30 mL) at 0 °C was added 2-(trimethylsilyl)ethanol (0.66 g, 5.47 mmol, 1.1 eq). The resulting mixture was stirred at rt for 1.5 d before being filtered through celite. The filtrate was concentrated and purified by chromatography on SiO_2 (EtOAc:Hexanes, 1:4) to provide 2-(trimethylsilyl)ethyl 6-bromohexanoate (**18**, 1.32 g, 4.48 mmol, 90%) as a colourless oil: ATR IR (neat) 2953, 2896, 2866, 1732, 1250, 1173, 1062, 1047, 937, 859, 837, 761, 695 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16, 0.98 (AA'XX', 4 H, $J_{AA'}$ = 7.4 Hz, J_{AX} = 11.5 Hz, $J_{XX'}$ = 4.6 Hz, $J_{AX'}$ = 5.7 Hz), 3.40 (t, 2 H, *J* = 6.8 Hz), 2.29 (t, 2 H, *J* = 7.4 Hz), 2.17 (s, 3 H), 1.91-1.83 (m, 2 H), 1.68-1.60 (m, 2 H), 1.51-1.44 (m, 2 H), 0.04 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 62.7, 34.4, 33.7, 27.8, 24.2, 17.5, -1.3; HRMS (ESI) *m/z* calcd for $C_9H_{20}O_2BrSi$ $(M-C_2H_4+H)^+$ 267.0410, found 267.0409.

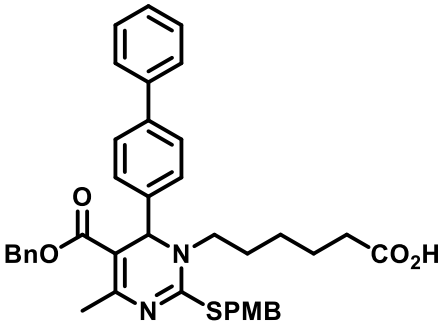
Benzyl 6-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-4-methyl-1-(6-oxo-6-(2-(trimethylsilyl)ethoxy)hexyl)-1,6-dihydropyrimidine-5-carboxylate (7c).



To a solution of **6a** (0.100 g, 0.187 mmol) in DMF (0.623 mL, dry, 0.3 M) under an Ar atomsphere at 0 °C was added NaH (0.015 g, 0.374 mmol, 2 eq) as a 60% dispersion in mineral oil. The reaction mixture was stirred at 0 °C for 30 min before 2-(trimethylsilyl)ethyl 6-bromohexanoate bromide (**18**, 0.066 mL, 0.224 mmol, 1.2 eq) was added dropwise as a DMF (173 uL, dry, 1.3 M) solution. The reaction mixture was allowed to warm to rt and stirred for 13 h The reaction was quenched with sat.'d aq. NH_4Cl (4 mL) and H_2O (6 mL), and extracted using EtOAc (3 x 7 mL). The combined organic layers were washed with sat. aq. LiCl sol (x 2), dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to provide benzyl 6-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-4-methyl-1-(6-oxo-6-(2-

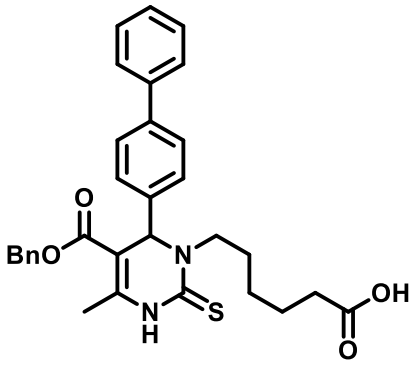
(trimethylsilyl)ethoxy)hexyl)-1,6-dihydropyrimidine-5-carboxylate (**7c**, 0.079 g, 0.100 mmol, 54%) as a yellow oil: ATR IR (neat) 3028, 2951, 2861, 1729, 1697, 1674, 1610, 1512, 1490, 1401, 1373, 1247, 1229, 1173, 1097, 1061, 857, 835, 697 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2 H), 7.47-7.41 (m, 4 H), 7.36-7.25 (m, 10 H), 6.85 (d, 2 H, *J* = 8.8 Hz), 5.35 (s, 1 H), 5.21, 5.08 (ABq, 2 H, J_{AB} = 12.6 Hz), 4.47, 4.31 (ABq, 2 H, J_{AB} = 13.6 Hz), 4.14, 0.96 (AA'XX', 4 H, $J_{AA'}$ = 9.4 Hz, J_{AX} = 11.1 Hz, $J_{XX'}$ = 6.6 Hz, $J_{AX'}$ = 5.8 Hz), 3.80 (s, 3 H), 3.45 (ddd, 1 H, *J* = 14.8, 9.2, 6.0 Hz), 3.18 (ddd, 1 H, *J* = 14.8, 9.2, 5.6 Hz), 2.42 (s, 3 H), 2.20 (t, 2 H, *J* = 5.7 Hz), 1.65-1.51 (m, 4 H), 1.30-1.22 (m, 2 H), 0.05-0.03 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 166.8, 162.0, 159.0, 155.7, 142.0, 141.0, 140.9, 136.7, 130.5, 129.5, 128.9, 128.6, 128.2, 128.0, 127.6, 127.4, 127.2, 114.1, 103.5, 65.9, 62.6, 60.6, 55.4, 49.9, 35.6, 34.3, 27.9, 26.3, 24.6, 23.5, 17.4, -1.3; HRMS (ESI) *m/z* calcd for $C_{44}H_{53}O_5N_2SSi$ $(M+H)^+$ 749.3439, found 749.3442.

6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-2-((4-methoxybenzyl)thio)-4-methylpyrimidin-1(6H)-yl)hexanoic acid (16).



To a solution of **7c** (0.115 g, 0.142 mmol) in THF (1.26 mL) was added 1M TBAF in THF (0.283 mL, 0.283 mmol, 2 eq). The resulting mixture was stirred at rt for 2 h before diluting with sat. aq. NH_4Cl (3 mL) and EtOAc (3 mL). The aqueous layer was extracted with EtOAc (x 2) and the combined organic layers were washed with 0.1 M HCl, dried (Na_2SO_4), filtered, and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to give 6-(6-([1,1'-biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-2-((4-methoxybenzyl)thio)-4-methylpyrimidin-1(6H)-yl)hexanoic acid (**16**, 0.054 g, 0.083 mmol, 62%) as a yellow foam (SM was also collected, so reaction had not reached completion): Mp 45-47 °C; ATR IR (neat) 3031, 2932, 2861, 1702, 1673, 1609, 1598, 1511, 1488, 1399, 1373, 1227, 1096, 1061, 906, 727, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2 H), 7.47-7.41 (m, 4 H), 7.36-7.25 (m, 10 H), 6.85 (d, 2 H, *J* = 8.8 Hz), 5.35 (s, 1 H), 5.21, 5.08 (ABq, 2 H, J_{AB} = 12.4 Hz), 4.48, 4.30 (ABq, 2 H, J_{AB} = 13.6 Hz), 3.79 (s, 3H), 3.47 (ddd, 1 H, *J* = 14.4, 8.4, 6.0 Hz), 3.20 (ddd, 1 H, *J* = 14.4, 8.8, 5.6 Hz), 2.42 (s, 3 H), 2.27 (app. t, 2 H, *J* = 7.4 Hz), 1.62-1.53 (m, 4 H), 1.32-1.24 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.7, 166.9, 162.0, 159.0, 155.7, 141.9, 141.0, 140.9, 136.7, 130.5, 129.5, 128.9, 128.5, 128.2, 128.0, 127.6, 127.4, 127.2, 114.1, 103.6, 65.9, 60.6, 55.4, 49.7, 35.6, 33.7, 27.8, 26.1, 24.3, 23.5; HRMS (ESI) *m/z* calcd for $C_{39}H_{41}O_5N_2S$ $(M+H)^+$ 649.2731, found 649.2731.

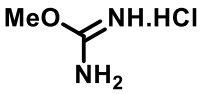
6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-4-methyl-2-thioxo-3,6-dihydropyrimidin-1(2H)-yl)hexanoic acid (8c: AMT551-071).



To a solution of **16** (0.026 g, 0.040 mmol) in CH_2Cl_2 (0.47 mL, dry, 0.085 M) was added TFA (16 µL, 0.20 mmol, 5 eq) and ethanethiol (7 µL, 0.1 mmol, 2.5 eq). The reaction mixture was stirred at 40 °C in a sealed vial for 4 h before further TFA (16 µL, 0.20 mmol, 5 eq) and ethanethiol (7 µL, 0.1 mmol, 2.5 eq) were added and the reaction stirred at 35 °C for 23 h. The reaction mixture was concentrated, redissolved in EtOAc and washed with sat.'d aq. $NaHCO_3$. The aq. layer was extracted with EtOAc (x 2) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) however some SM co-eluted with the product. Purification by reverse phase HPLC (H_2O: MeCN, 55:45 to 30:70 with 0.1% formic acid, over 15 min, 40 mL/min) provided **AMT551-071** (**8c**, 11.6 mg, 0.022 mmol, 55%) as a white solid: Mp 210-212 °C; ATR IR (neat) 3225, 3183, 3068, 3030, 2939, 2866, 1706, 1687, 1649, 1538, 1466, 1321, 1222, 1155, 1103, 910, 733, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (bs, 1 H), 7.56-7.54 (m, 2 H), 7.47-7.41 (m, 4 H), 7.36-7.25 (m, 10 H), 6.85 (d, 2 H, *J* = 8.8 Hz), 5.49 (s, 1 H), 5.23, 5.11 (ABq, 2 H, J_{AB} = 12.4 Hz), 4.34 (ddd, 1 H, *J* = 13.6, 9.0, 6.4 Hz), 3.23 (ddd, 1 H, *J* = 14.0, 8.8, 5.6 Hz), 2.33 (partially hidden t, 2 H, *J* = 7.4 Hz), 2.32 (s, 3 H), 1.76-1.61 (m, 4 H), 1.41-1.32 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.9, 175.2, 165.4, 143.4, 141.5, 140.6, 139.9, 136.0, 129.0, 128.8, 128.5, 127.7, 127.7, 127.5, 127.2, 102.4, 66.6, 60.7, 52.3, 33.6, 26.4, 26.2, 24.4, 18.7; HRMS (ESI) *m/z* calcd for $C_{31}H_{33}O_4N_2S$ $(M+H)^+$ 529.2156, found 529.2156; LCMS (ELSD) purity 100%.

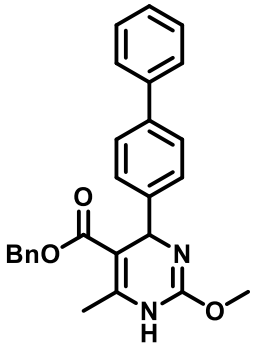
N-3 substituted dihydropyrimidone 12 synthesis

Methyl carbamimidate hydrochloride (9).[11]



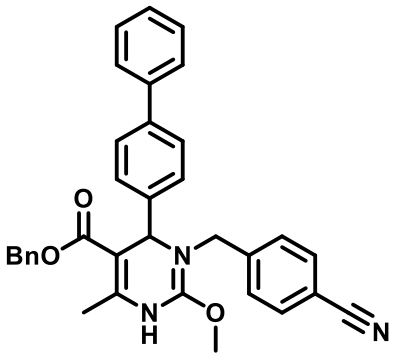
A methanolic HCl solution was prepared at 0 °C by addition of acetyl chloride (1.98 mL, 27.5 mmol, 1.18 eq) to 5 mL of MeOH. This was slowly added to a mixture of cyanamide (1.00 g, 23.3 mmol) in MeOH (3 mL) at 0 °C, maintaining the reaction mixture at rt during the addition. The reaction was warmed to rt and stirred for 2.5 d, to reveal a white solid. The reaction mixture was then concentrated, and the white solid obtained dried under vacuum overnight in the presence of P_2O_5 and KOH to provide methyl carbamimidate hydrochloride (**9**, 2.95 g, 24.0 mmol, quant) as an off-white solid. Data match those previously reported: Mp 114-115 °C; ATR IR (neat) 3198, 3069, 2761, 1681, 1663, 1632, 1578, 1530, 1418, 1210, 1145, 1068, 886, 733 cm^{-1}; ^1H NMR (300 MHz, D_2O) δ 4.04 (s, 3 H); ^{13}C NMR (100 MHz, D_2O) δ 162.9, 57.4.

Benzyl 4-([1,1'-biphenyl]-4-yl)-2-methoxy-6-methyl-1,4-dihydropyrimidine-5-carboxylate (10).



To a solution of Knoevenagel product **4a** (1.00 g, 2.81 mmol) and protected urea **9** (0.403 g, 3.64 mmol, 1.3 eq) in DMF (2.8 mL) was added $NaHCO_3$ (0.943 g, 11.2 mmol, 4 eq). The reaction mixture was heated at 75 °C for 24 h, cooled, diluted with ether (15 mL) and washed with H_2O (20 mL), $NaHCO_3$ (20 mL), brine (20 mL) and LiCl (10 mL). The organic layer was then dried ($MgSO_4$), filtered and concentrated. The obtained orange solid was washed with cooled ether to provide benzyl 4-([1,1'-biphenyl]-4-yl)-2-methoxy-6-methyl-1,4-dihydropyrimidine-5-carboxylate (**10**, 1.08 g, 2.26 mmol, 81%), as a white solid (first crop) and with minor orange impurities (second crop). This fraction was taken to the next step without further purification: Mp 123-125 °C; ATR IR (neat) 3300, 3029, 2948, 1685, 1614, 1548, 1486, 1222, 1104, 1075, 985, 907, 835, 753, /727, 695 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 7.59-7.55 (m, 2 H), 7.49 (d, 2 H, *J* = 8.4 Hz), 7.41 (t, 2 H, *J* = 7.6 Hz), 7.36-7.29 (m, 3 H), 7.25-7.19 (m, 3 H) 7.13-7.07 (m, 2 H), 5.54 (bs, 1 H), 5.12, 4.99 (ABq, 2 H, J_{AB} = 12.4 Hz), 3.72 (s, 3 H), 2.33 (s, 3 H); ^{13}C NMR (100 MHz, MeOD) δ 168.0, 153.8, 149.1, 146.4, 142.2, 142.0, 141.2, 137.9, 129.8, 129.4, 129.0, 128.9, 128.6, 128.6, 128.2, 127.9, 66.5, 59.7, 54.5, 17.9; HRMS (ESI) *m/z* calcd for $C_{26}H_{25}O_3N_2$ $(M+H)^+$ 413.1860, found 413.1861.

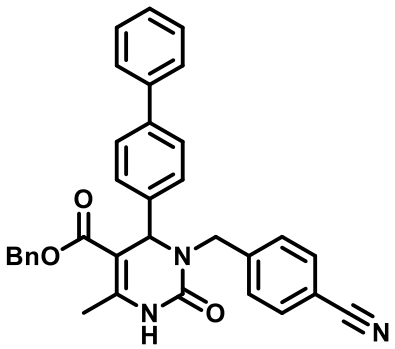
Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-2-methoxy-6-methyl-1,4-dihydro-3λ4-pyrimidine-5-carboxylate (11).



Dihydropyrimidine 5-carboxylate **10** (0.200 g, 0.484 mmol), 4-(bromomethyl)benzonitrile (0.223 g, 1.12 mmol, 2.3 eq) and finely ground K_2CO_3 (0.268 g, 1.94 mmol, 4 eq) were suspended in DMF (2 mL) and stirred at rt for 1.8 d. The reaction mixture was filtered, and the filtrate was diluted with EtOAc, washed with H_2O, brine, and sat. aq. LiCl. The organic layer was then dried ($MgSO_4$), filtered and concentrated. The residual oil was purified by chromatography on SiO_2 (EtOAc:Hexanes, 0:100 to 100:0) to provide benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-2-methoxy-6-methyl-1,4-dihydro-3λ^4-pyrimidine-5-carboxylate (**11**, 0.121 g, 0.226 mmol, 47%) as a white foam ($CHCl_3$)/viscous oil (CH_2Cl_2): ATR IR (neat) 3030, 2953, 2922, 2866, 2229, 1698, 1676, 1609, 1520, 1487, 1404, 1376, 1230,

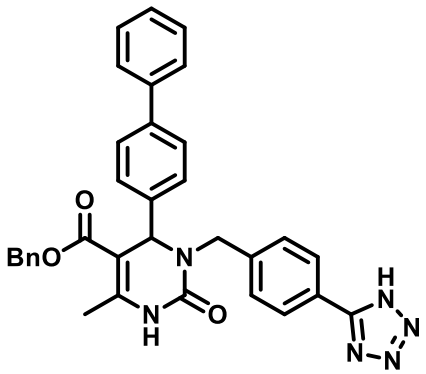
1102, 1064, 989, 908, 830, 728, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, 2 H, *J* = 8.0 Hz), 7.58-7.54 (m, 2 H), 7.50-7.43 (m, 4 H), 7.38-7.33 (m, 1 H), 7.32-7.23 (m, 7 H), 7.14-7.08 (m, 2 H), 5.26 (s, 1 H), 5.10, 4.89 (ABq, 2 H, J_{AB} = 12.4 Hz), 4.87 (d, 1 H, *J* = 16.4 Hz), 4.10 (d, 1 H, *J* = 16.0 Hz), 3.92 (s, 3 H), 2.46 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 158.3, 156.7, 142.0, 141.2, 140.9, 140.7, 136.5, 132.6, 128.9, 128.4, 128.0, 128.0, 127.9, 127.5, 127.4, 127.1, 118.7, 111.5, 103.3, 65.6, 60.9, 55.1, 48.9, 23.6; HRMS (ESI) *m/z* calcd for $C_{34}H_{30}O_3N_3$ $(M+H)^+$ 528.2282, found 528.2281.

Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (17).



Nitrile **11** (0.090 g, 0.171 mmol) was dissolved in MeOH (0.81 mL) and stirred with 1 M HCl (0.144 mL). After stirring for 16 h, a white precipitate had formed and the reaction was concentrated. The residual solid was purified by chromatography on SiO_2 (CH_2Cl_2:MeOH, 0:100 to 90:10) to provide benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (**17**, 0.059 g, 0.115 mmol, 67%) as a white solid: Mp 91-93 ºC; ATR IR (neat) 3220, 3089, 2953, 2229, 1675, 1639, 1463, 1233, 1111, 1074, 762, 734, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.05 (s, 1 H), 7.63 (d, 2 H, *J* = 8.0 Hz), 7.57 (d, 2 H, *J* = 7.5 Hz), 7.51 (d, 2 H, *J* = 8.0 Hz), 7.47 (t, 2 H, *J* = 7.8 Hz), 7.41.7.35 (m, 3 H), 7.33-7.25 (m, 5 H), 7.15-7.11 (m, 2 H), 5.22 (s, 1 H), 5.21 (partially hidden d, 1 H, *J* = 16.5 Hz), 5.12, 5.02 (ABq, 2 H, J_{AB} = 12.5 Hz), 3.93 (d, 1 H, *J* = 16.0 Hz), 2.39 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 153.6, 147.2, 142.2, 141.4, 140.6, 139.9, 136.0, 132.6, 129.0, 128.6, 128.5, 128.2, 128.1, 128.0, 127.6, 127.6, 127.1, 118.7, 111.6, 101.2, 66.1, 59.8, 47.7, 18.8; HRMS (ESI) *m/z* calcd for $C_{33}H_{28}O_3N_3$ $(M+H)^+$ 514.2125, found 514.2126.

Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (12: AMT628-003).



To a solution of nitrile **17** (0.039 g, 0.076 mmol) in THF (0.099 mL) in a 2 mL microwave vial was added TBAT (0.053 g, 0.099 mmol, 1.3 eq, conc. 1 M) and trimethylsilyl azide (0.042 mL,

0.304 mmol, 4 eq). The vial was flushed with Ar and sealed before heating at 70-75 °C for 19 h. As the reaction was incomplete, the reaction mixture was concentrated and further trimethylsilyl azide (0.042 mL, 0.304 mmol, 4 eq) was added before stirring at 70-75 °C for 21 h. The reaction mixture was then cooled and loaded directly onto a column for purification by chromatography on SiO_2 ($MeOH:CH_2Cl_2$, 0:100 to 10:90 with 0.1% formic acid) to provide **AMT628-003** (**12**, 0.032 g, 0.056 mmol, 73%) as a white foam/film: ATR IR (neat) 3030, 2927, 2856, 2770, 2430, 1638, 1463, 1390, 1309, 1237, 1115, 1064, 975, 843, 752, 735, 697 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 7.97 (d, 2 H, *J* = 8.0 Hz), 7.56-7.35 (m, 8 H), 7.34-7.25 (m, 3 H), 7.19-7.12 (m, 3 H), 7.08-7.00 (m, 2 H), 5.26 (s, 1 H), 5.10 (d, 1 H, *J* = 15.6 Hz), 5.03, 4.95 (ABq, 2 H, J_{AB} = 12.2 Hz), 4.02 (d, 1 H, *J* = 16.0 Hz), 2.37 (s, 3 H); ^{13}C NMR (100 MHz, MeOD) δ 166.6, 157.5, 154.4, 149.2, 142.4, 141.8, 141.8, 141.7, 137.5, 129.9, 129.8, 129.3, 129.1, 129.0, 128.9, 128.5, 128.3, 127.9, 124.9, 102.0, 66.7, 60.6, 18.0; HRMS (ESI) *m/z* calcd for $C_{33}H_{29}O_3N_6$ $(M+H)^+$ 557.2296, found 557.2296; LCMS (ELSD) purity 96.0%.

References

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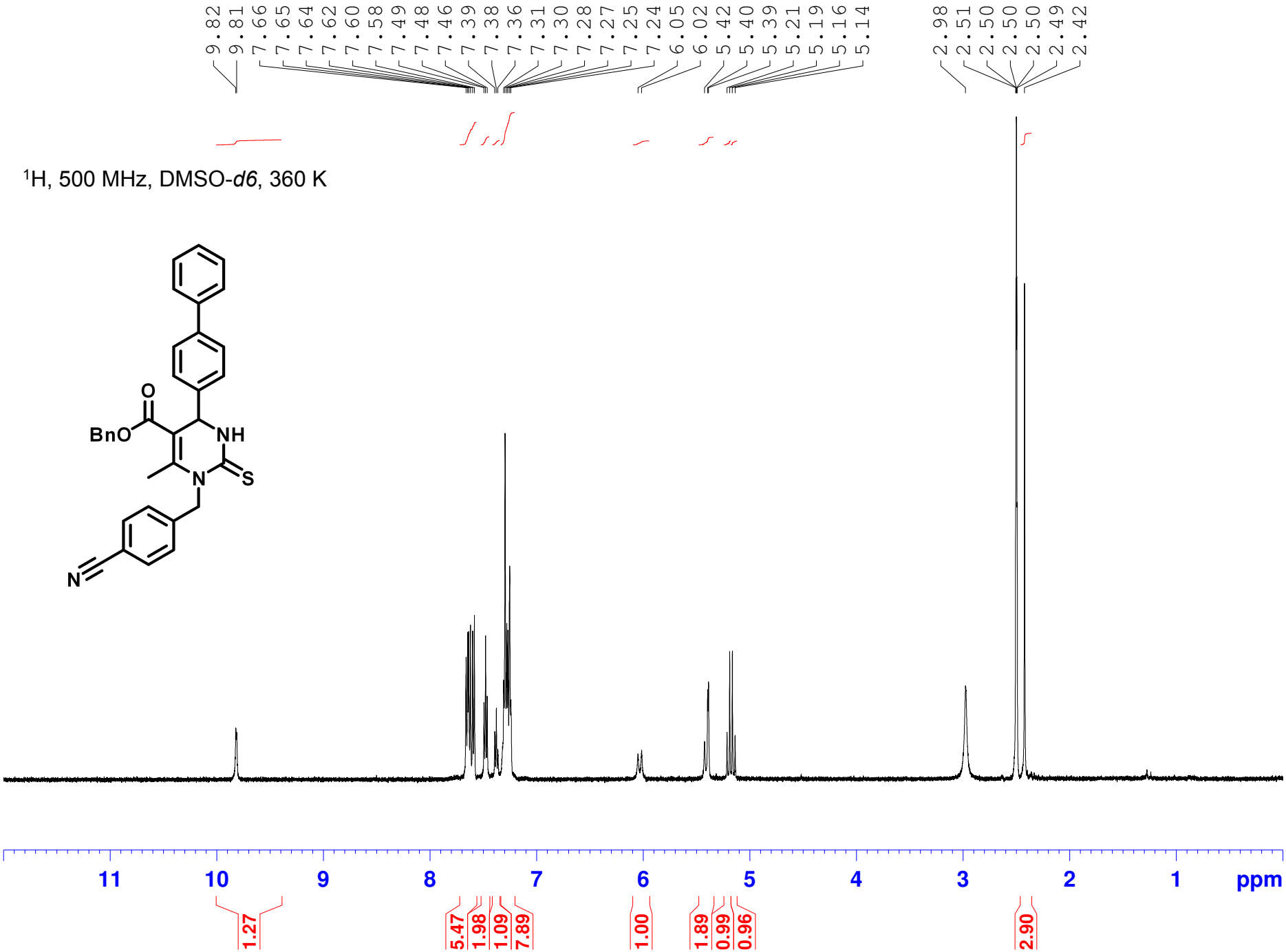
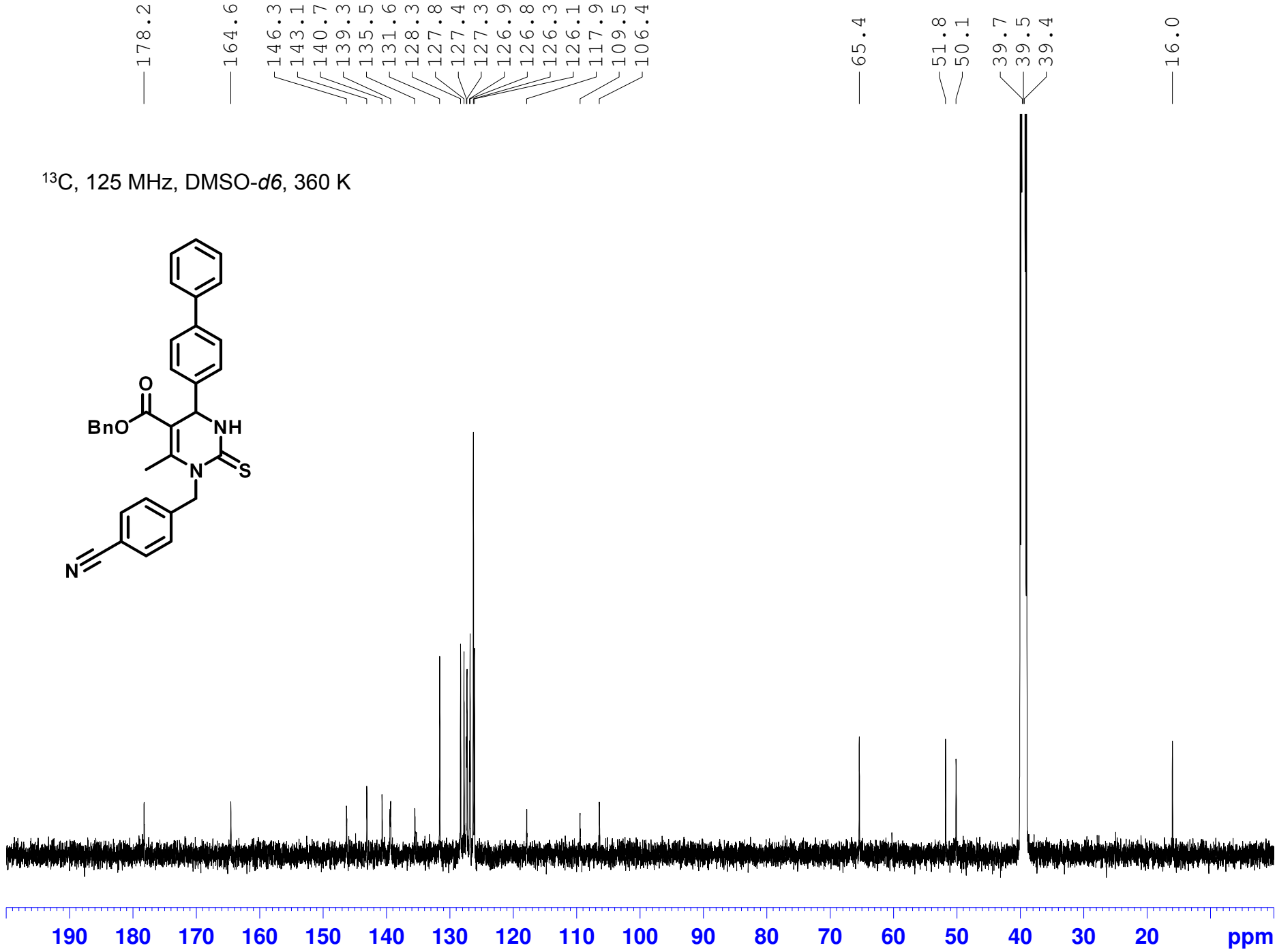
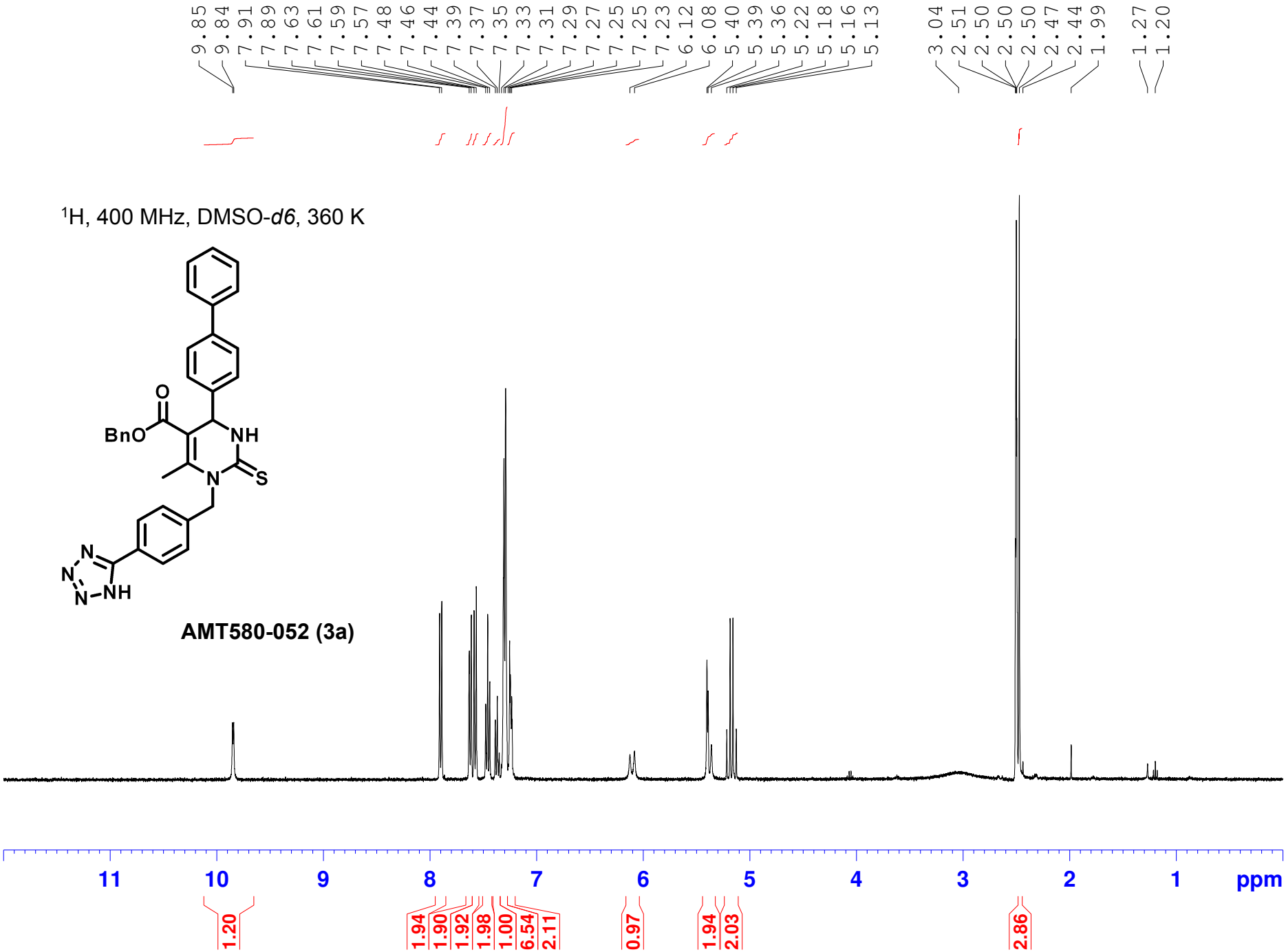
Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13a)**



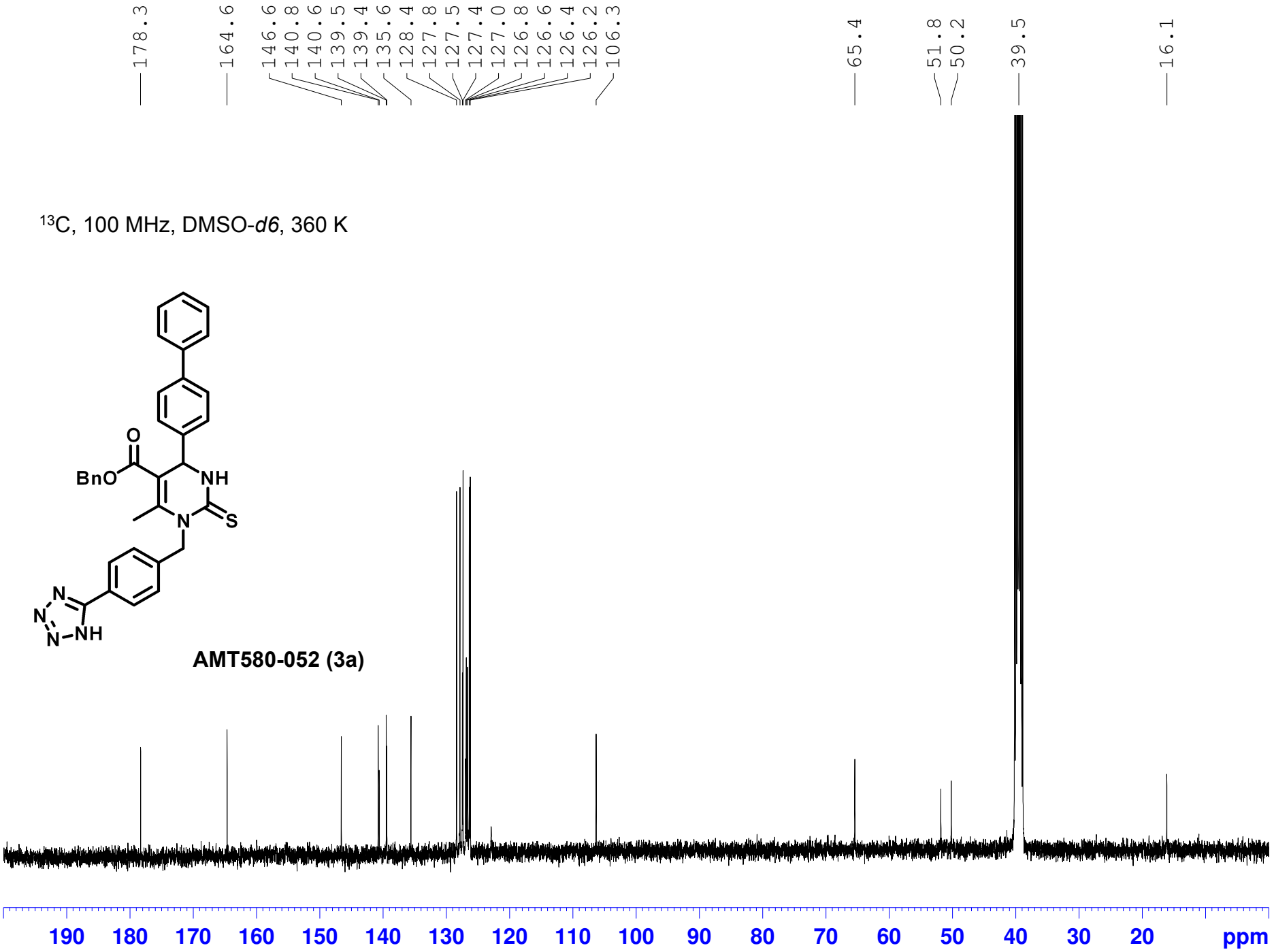
Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13a)**



Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



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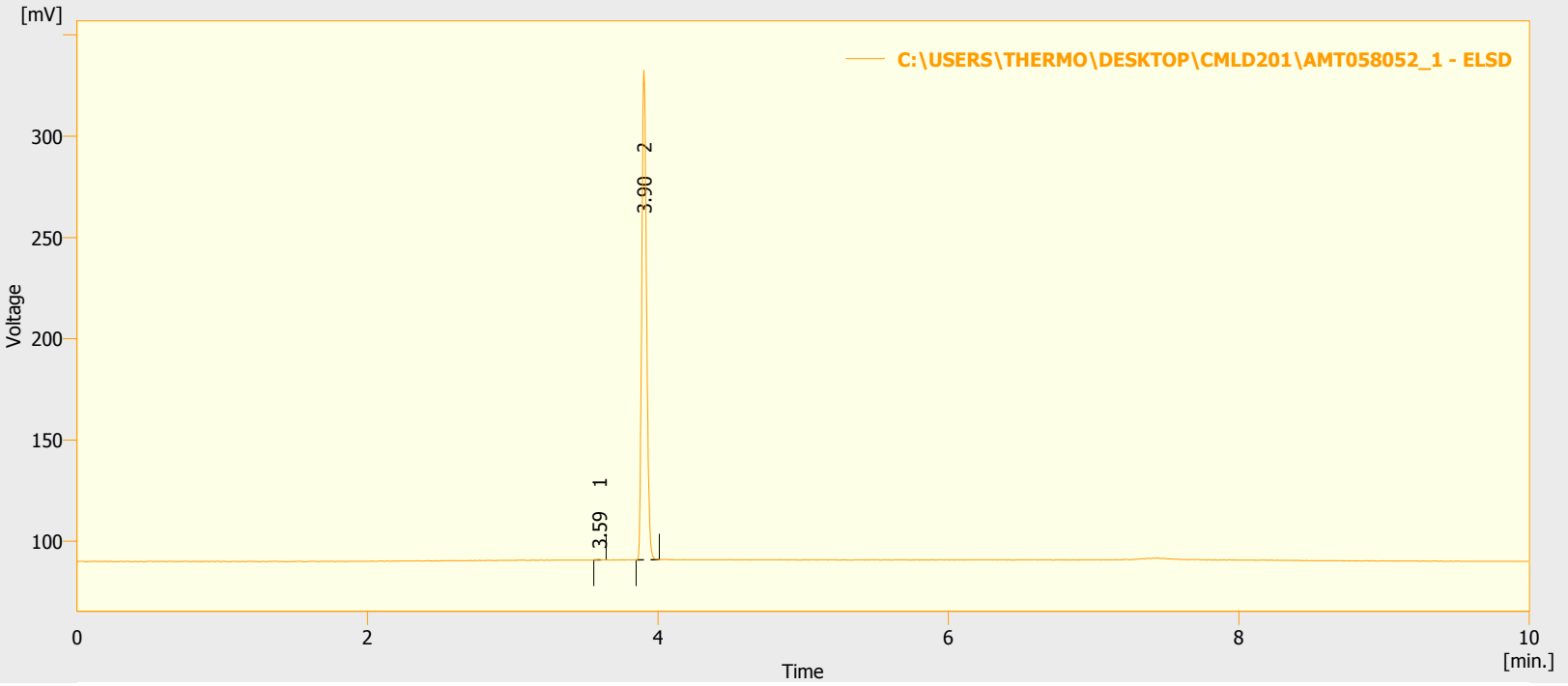
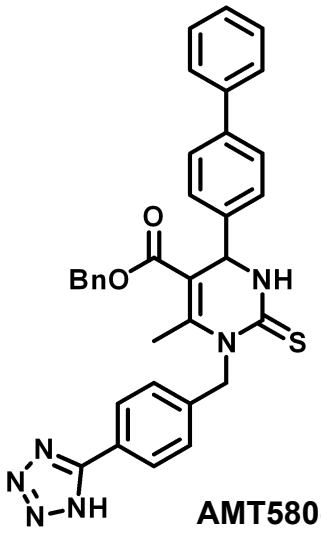
Project	: c:\Clarity\Projects\Work1.PRJ	By	: None



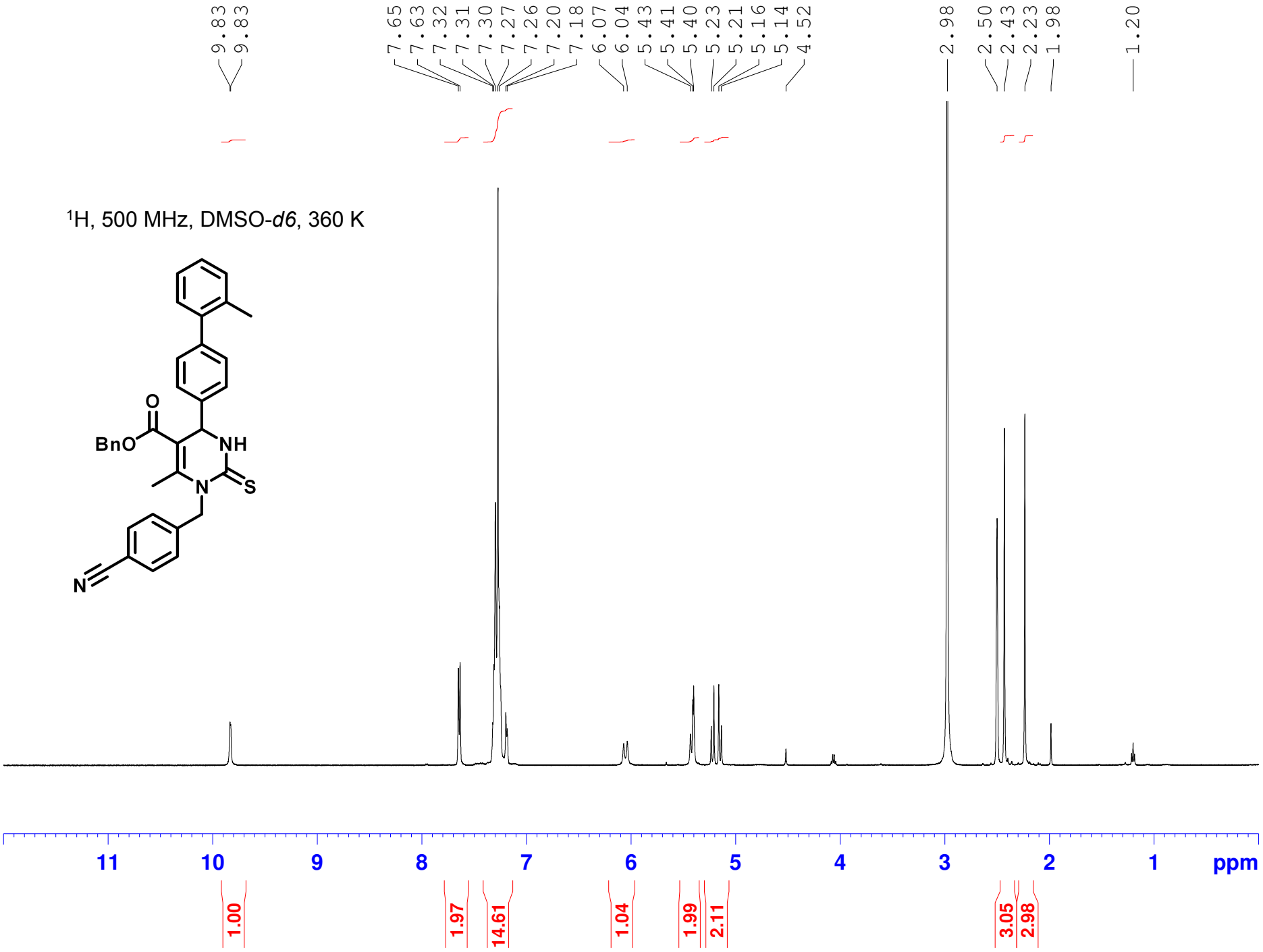
Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD201\AMT058052_1 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	3.593	0.505	0.274	0.1	0.1	0.02	
2	3.903	555.434	241.678	99.9	99.9	0.04	
	Total	555.939	241.952	100.0	100.0		

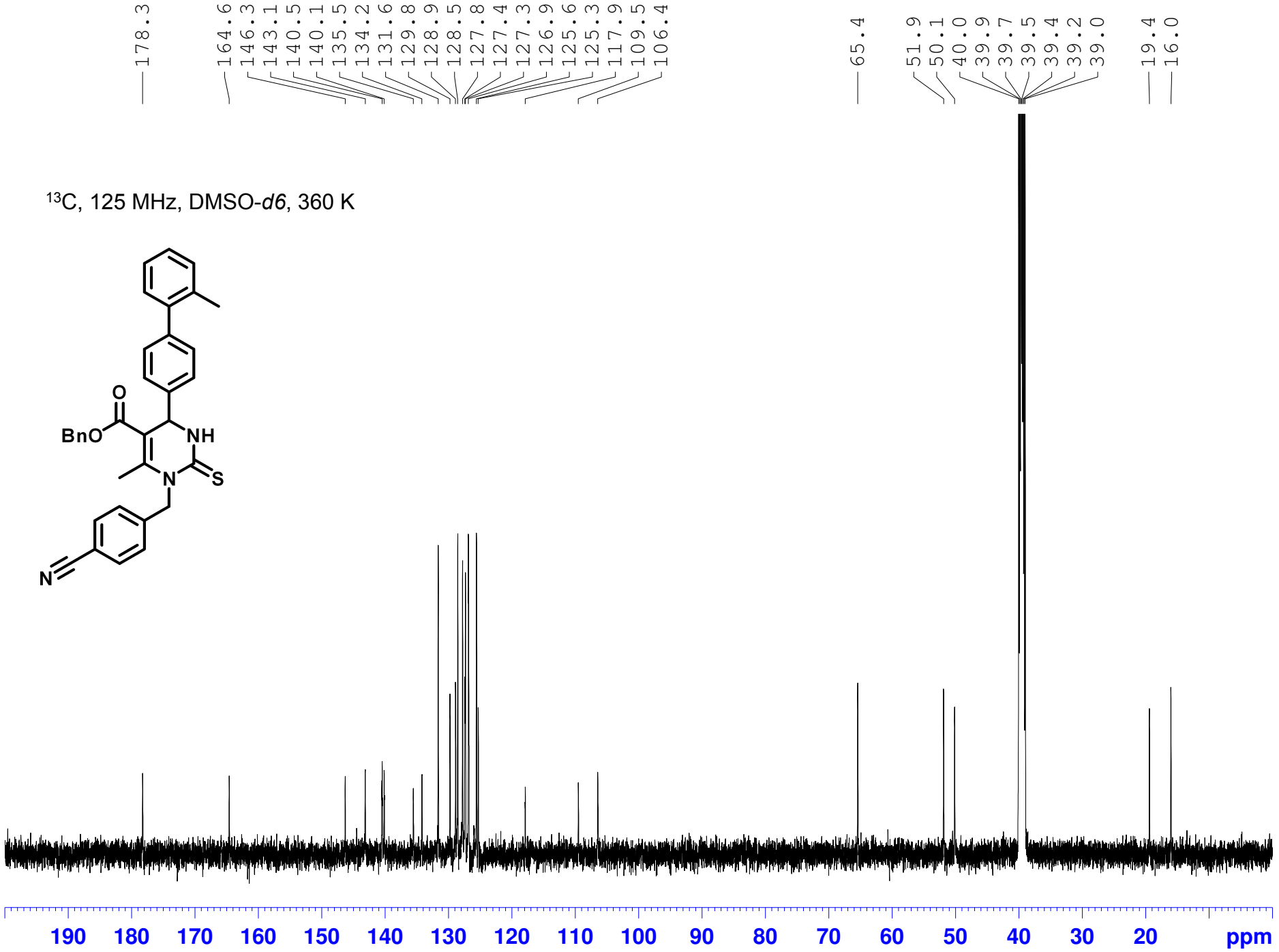


AMT580-052 (3a)

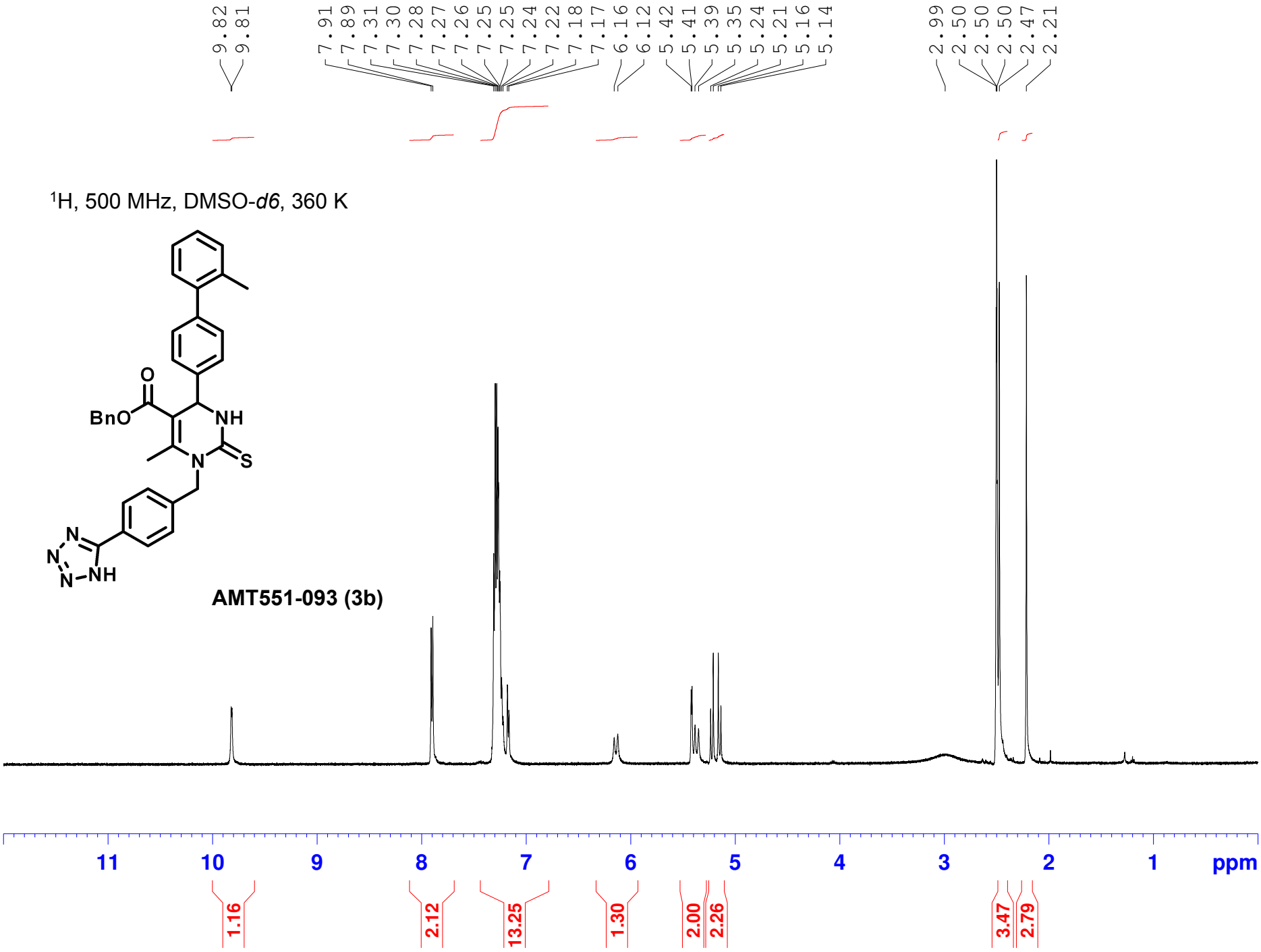
Benzyl 1-(4-cyanobenzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13b)**



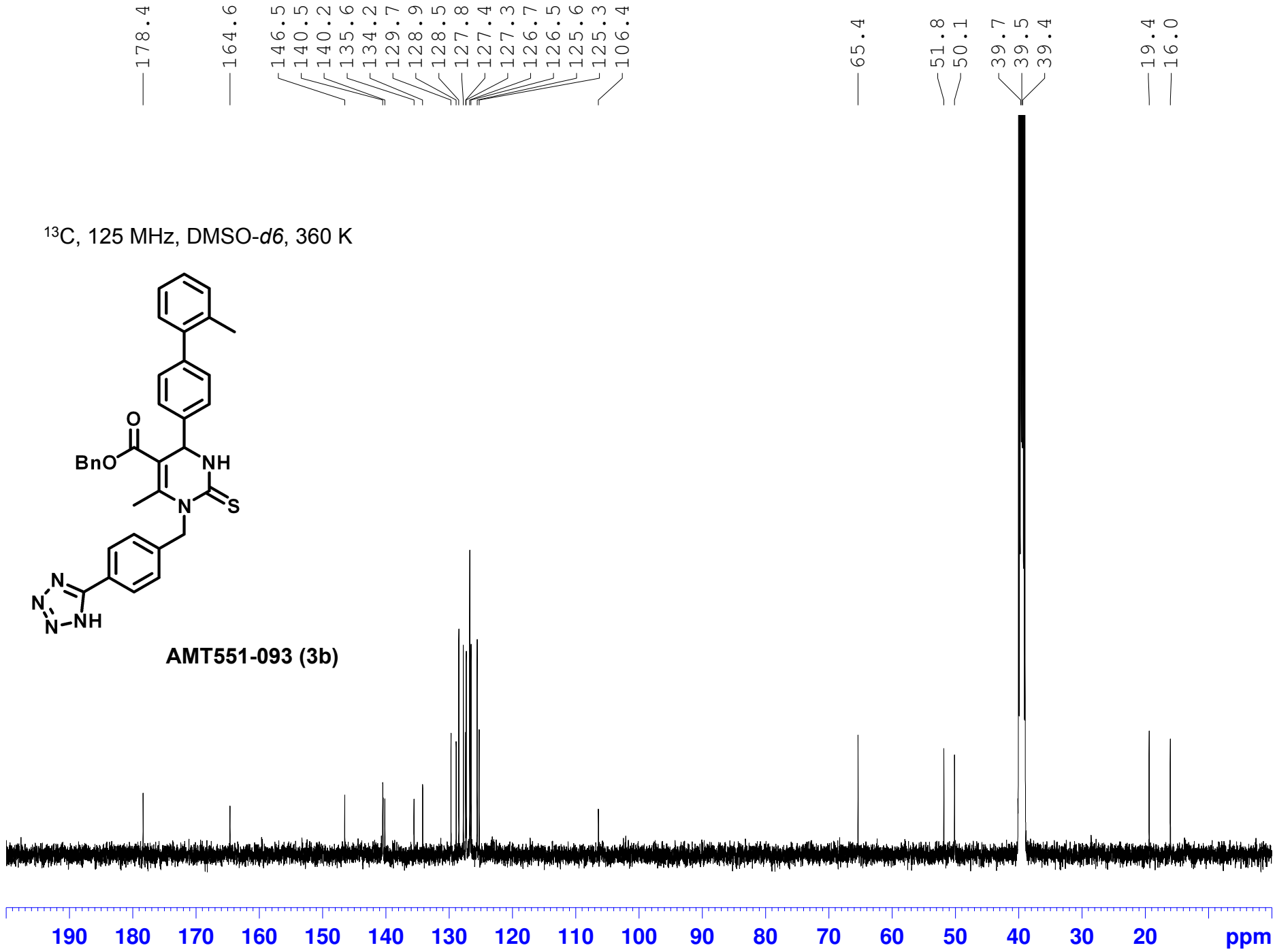
Benzyl 1-(4-cyanobenzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13b)**



Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



^{13}C, 125 MHz, DMSO-*d6*, 360 K

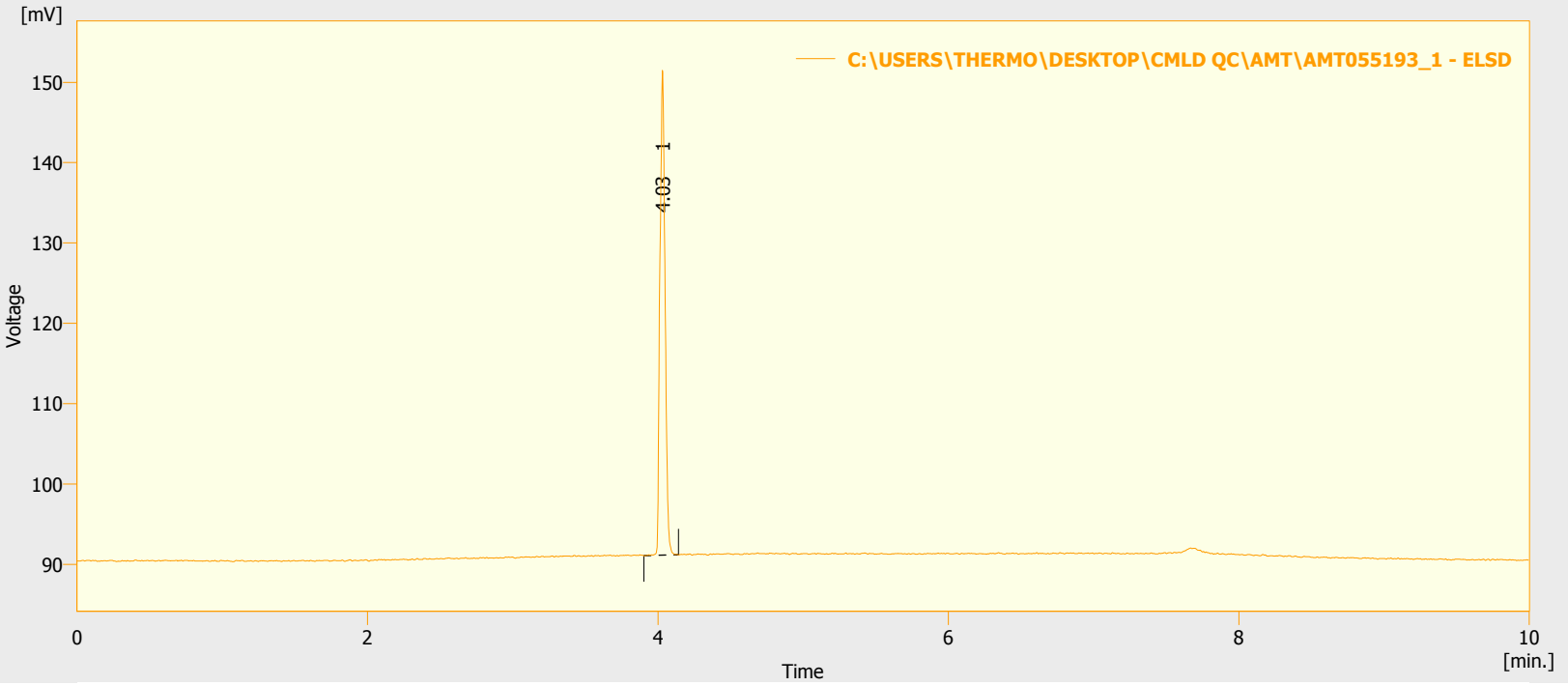
AMT551-093 (3b)

Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

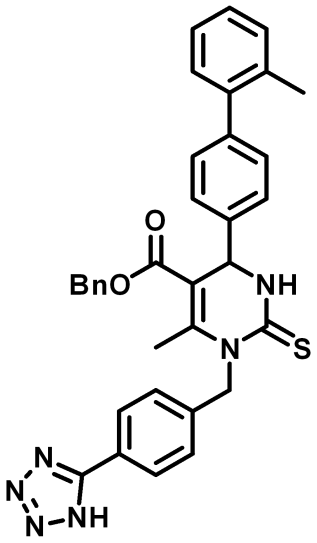
Chromatogram Info:

File Name	: C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055193_1.PRM	File Created	: 4/9/2014 5:23:42 PM
Origin	: Acquired, Acquisition started 4/9/2014 5:13:42 PM	Acquired Date	: 4/9/2014 5:23:42 PM
Project	: c:\Clarity\Projects\Work1.PRJ	By	: None



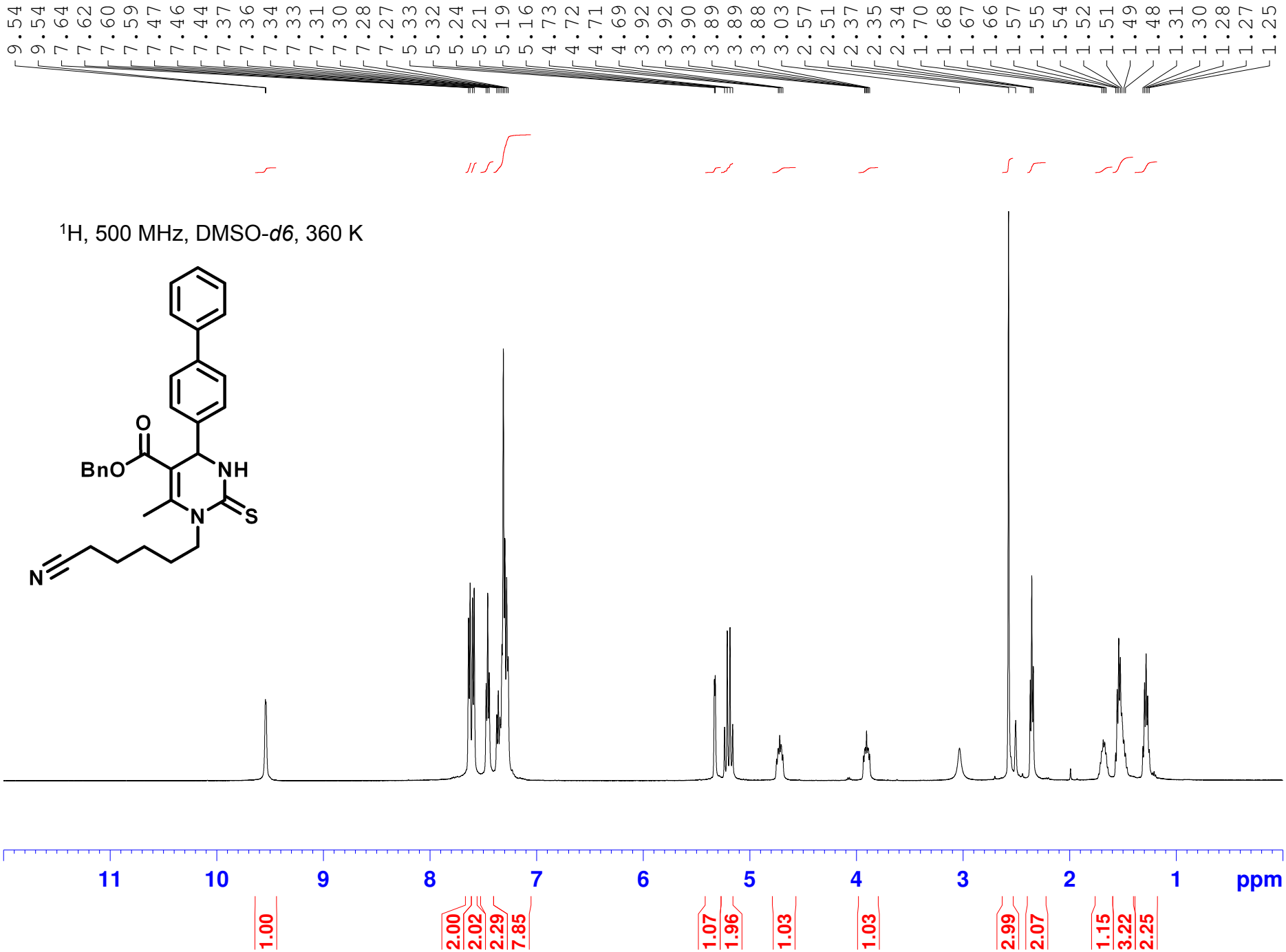
Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055193_1 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.030	148.135	60.349	100.0	100.0	0.05	
	Total	148.135	60.349	100.0	100.0		



AMT551-093 (3b)

Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(5-cyanopentyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13c)**

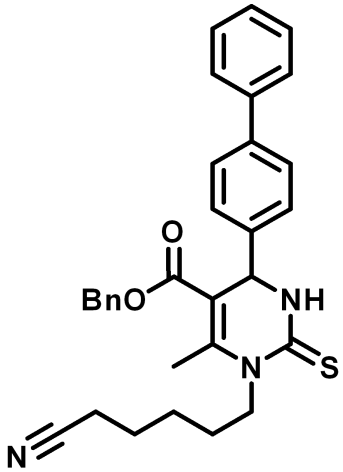


Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(5-cyanopentyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13c)**

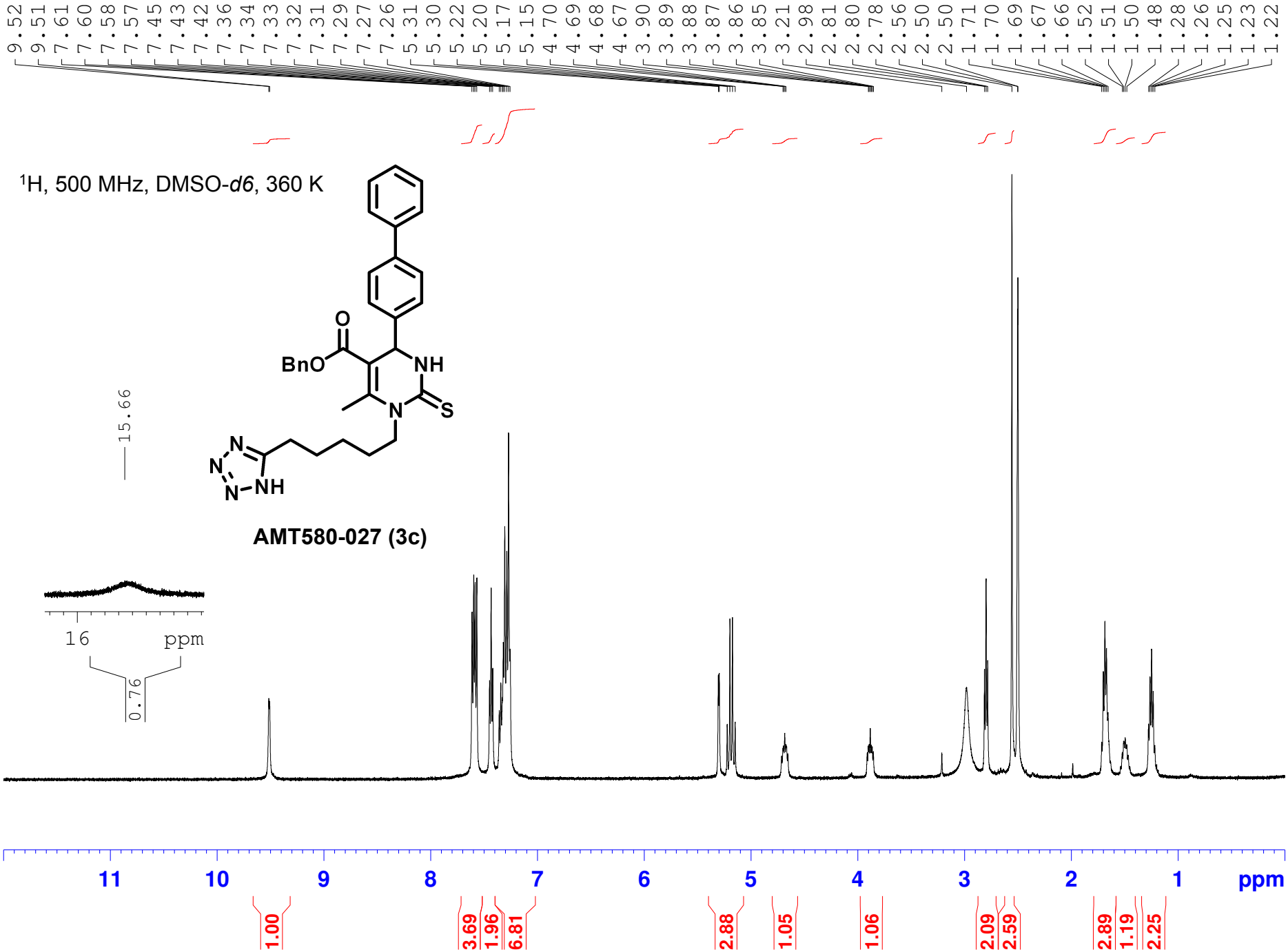
177.7 164.7 146.5 140.9 139.3 139.2 135.6 128.2 127.7 127.3 127.2 126.8 126.2 126.0 119.4 106.2

65.2 51.7 46.4 40.0 39.8 39.7 39.5 39.3 39.2 39.0 27.6 24.6 24.0 15.6 15.5

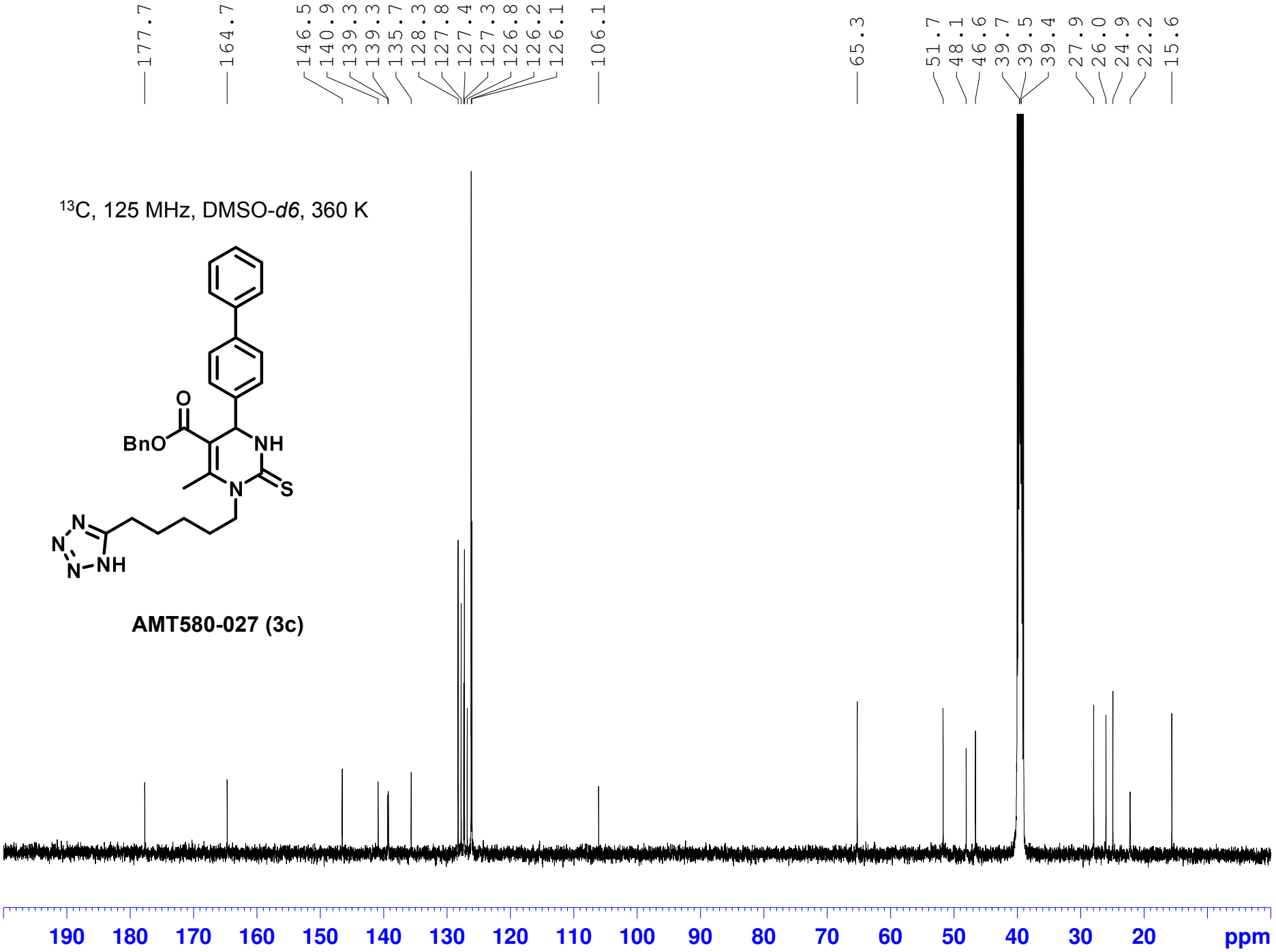
^{13}C, 125 MHz, DMSO-*d6*, 360 K



Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



^{13}C, 125 MHz, DMSO-*d6*, 360 K

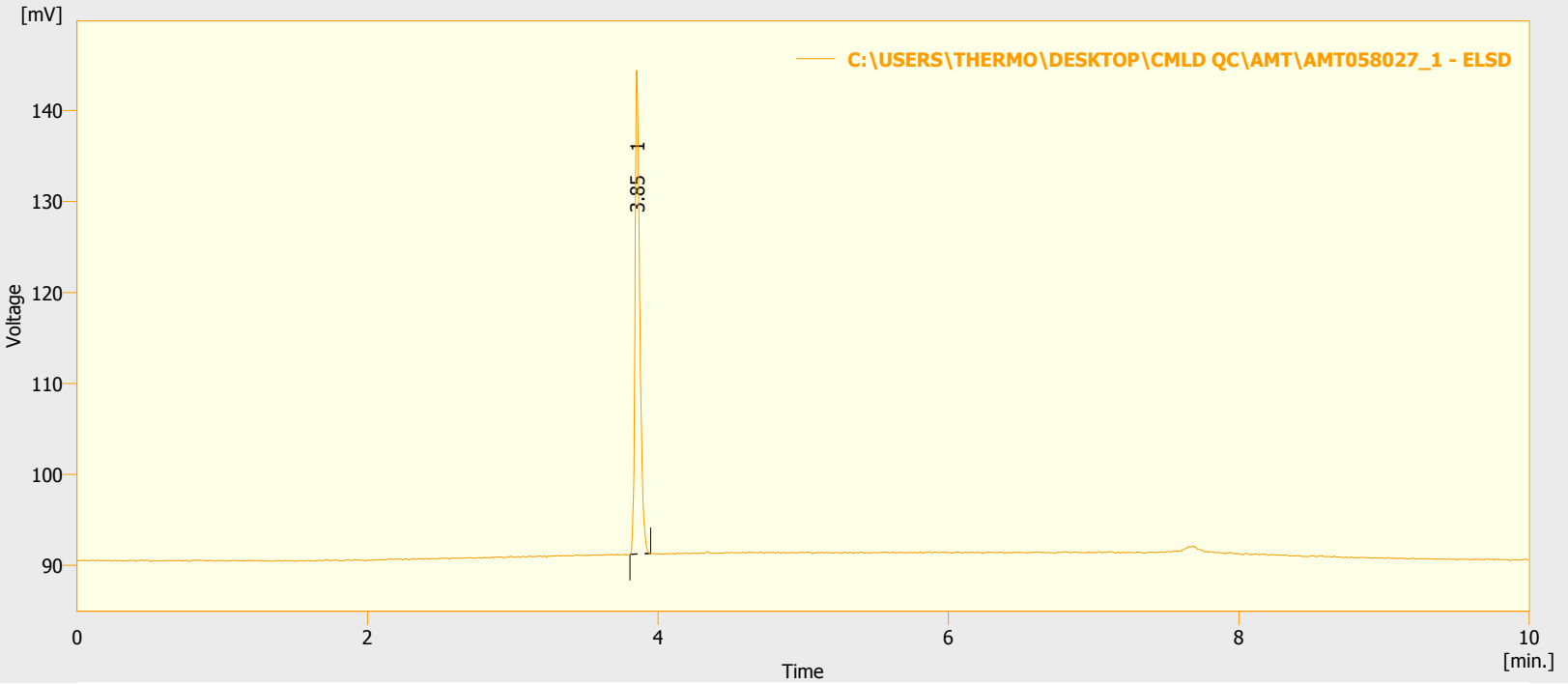
AMT580-027 (3c)

Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

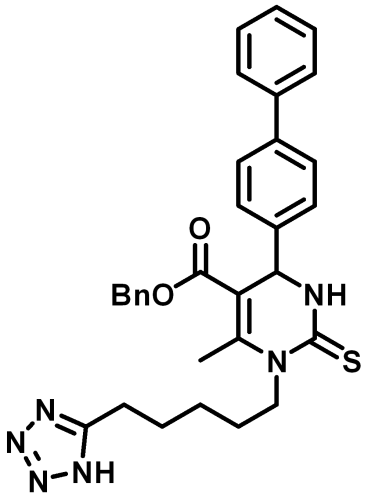
Chromatogram Info:

File Name	: C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT058027_1.PRM	File Created	: 4/9/2014 5:45:48 PM
Origin	: Acquired, Acquisition started 4/9/2014 5:35:48 PM	Acquired Date	: 4/9/2014 5:45:48 PM
Project	: c:\Clarity\Projects\Work1.PRJ	By	: None



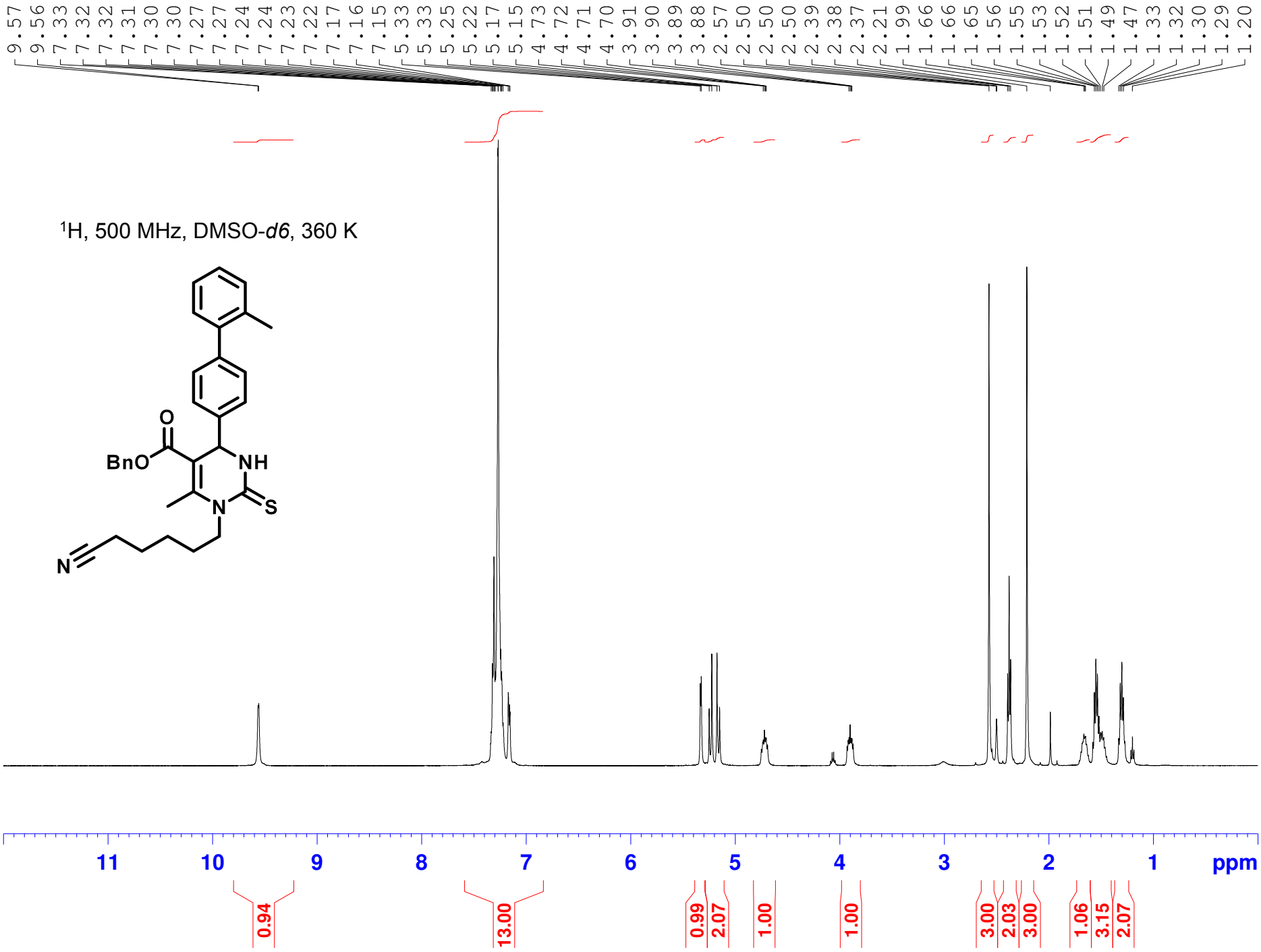
Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT058027_1 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	3.853	121.795	53.219	100.0	100.0	0.04	
	Total	121.795	53.219	100.0	100.0		

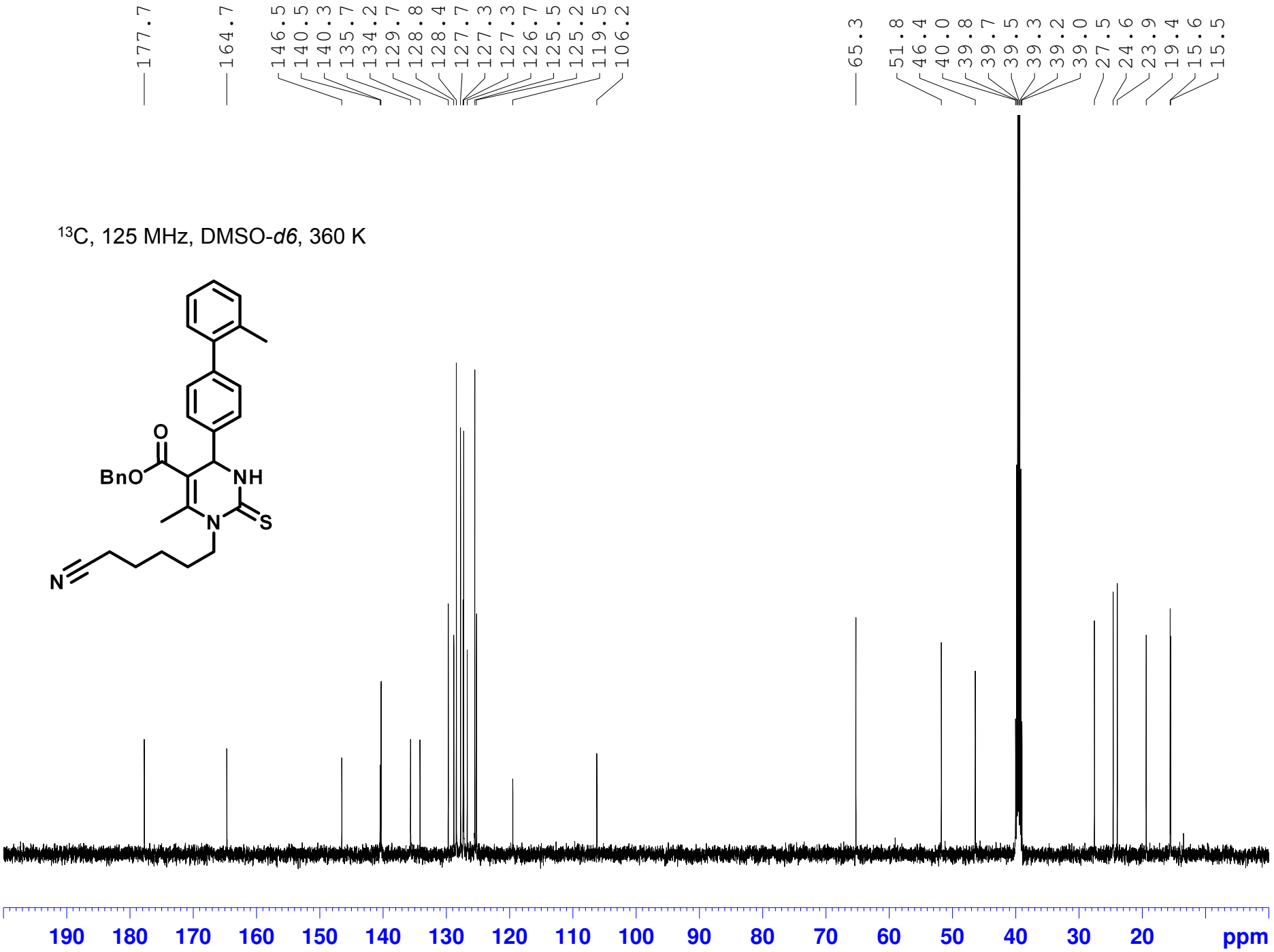


AMT580-027 (3c)

Benzyl 1-(5-cyanopentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13d)**



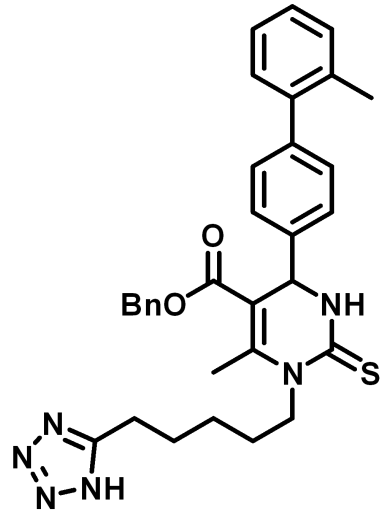
Benzyl 1-(5-cyanopentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13d)**



Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

9.52 9.51 7.34 7.32 7.31 7.30 7.28 7.27 7.25 7.23 7.21 7.20 7.15 7.13 5.32 5.31 5.24 5.22 5.17 5.15 4.70 4.69 4.68 4.68 4.66 3.91 3.90 3.89 3.88 3.87 3.86 3.22 2.83 2.82 2.80 2.56 2.50 2.19 1.73 1.71 1.70 1.68 1.67 1.66 1.65 1.64 1.63 1.50 1.49 1.47 1.30 1.28 1.27 1.25 1.24

^{1}H, 500 MHz, DMSO-*d6*, 360 K



15.63

AMT580-033 (3d)

ppm

0.78

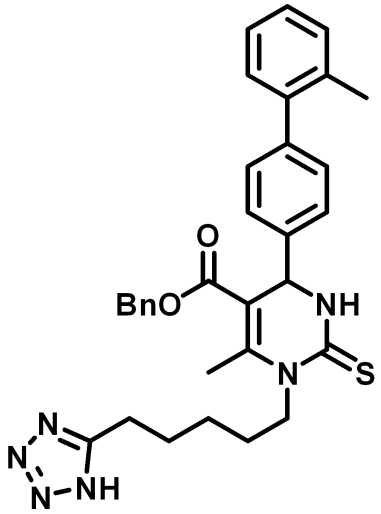
11 10 9 8 7 6 5 4 3 2 1 ppm

1.00 12.38 3.00 1.07 1.06 0.42 2.21 2.87 3.02 3.08 1.25 2.51

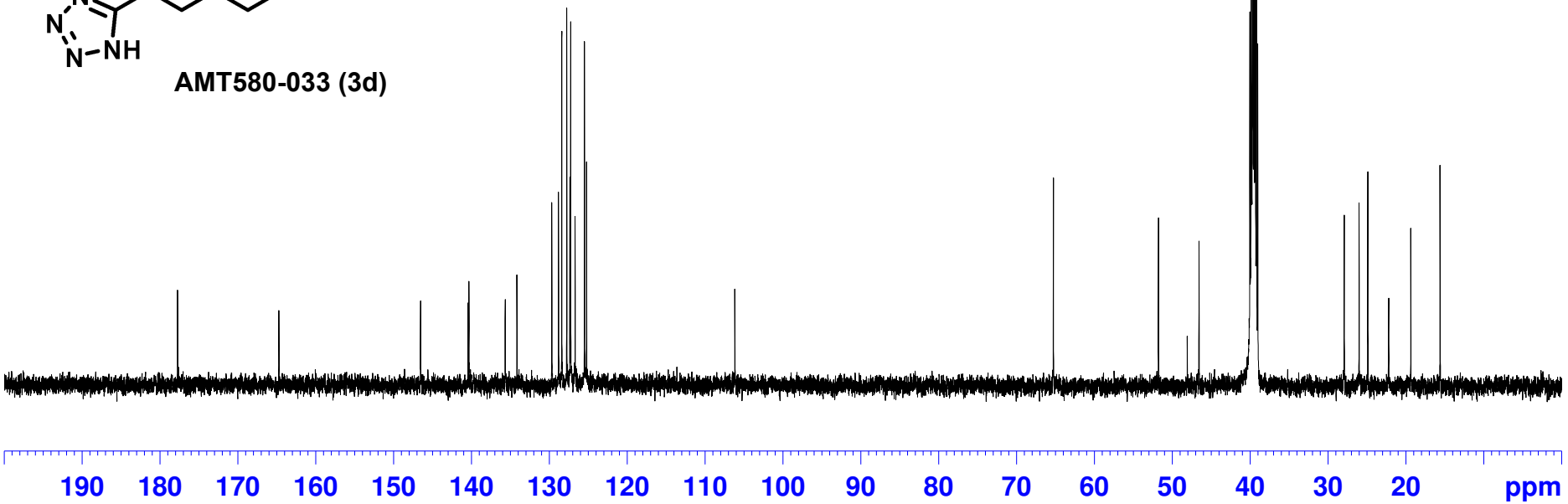
Benzyl 1-(5-(1H-tetrazol-5-yl)pentyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

177.7 164.7 146.5 140.5 140.3 140.3 135.7 134.2 129.7 128.8 128.4 127.8 127.4 127.3 126.7 125.5 125.2 106.2 65.3 51.8 48.1 46.6 39.7 39.5 39.4 27.9 26.0 24.9 22.2 19.4 15.6

^{13}C, 125 MHz, DMSO-*d6*, 360 K



AMT580-033 (3d)



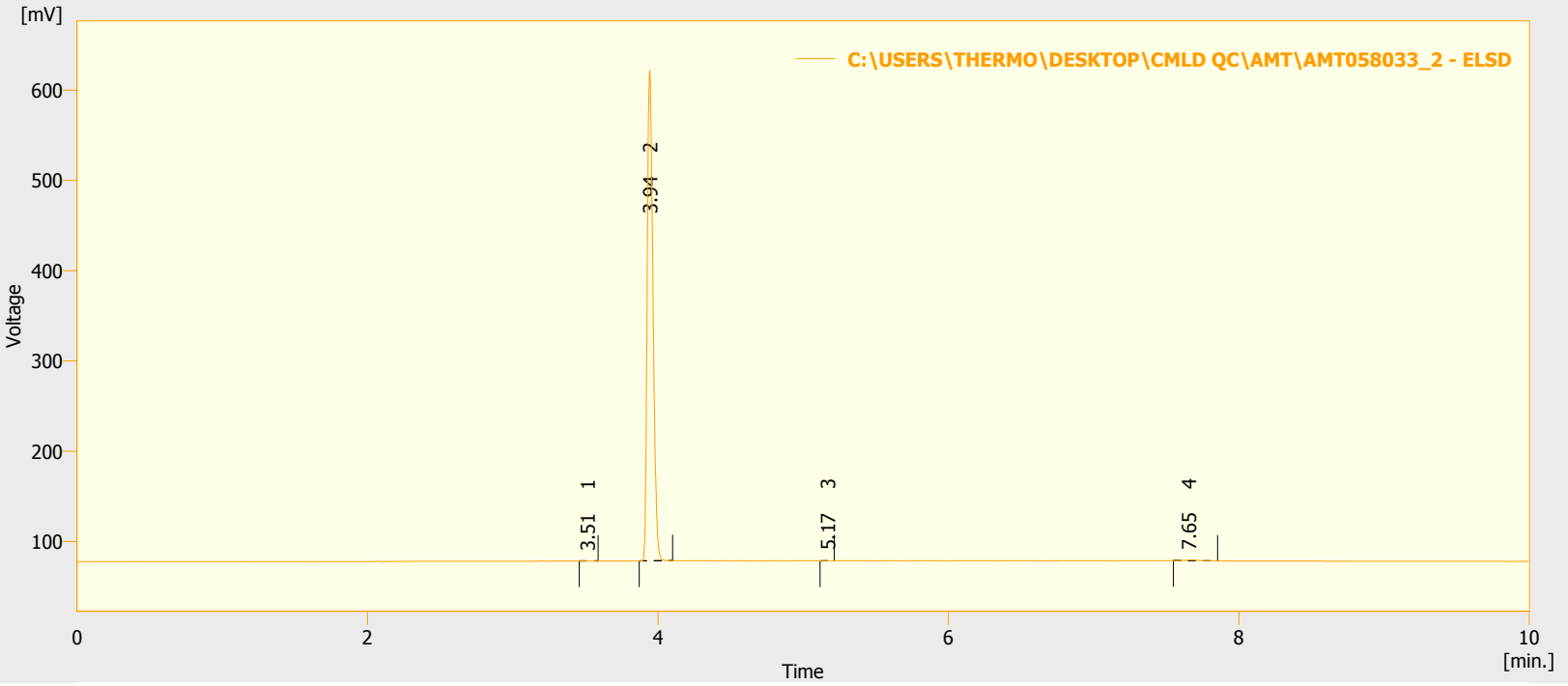
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

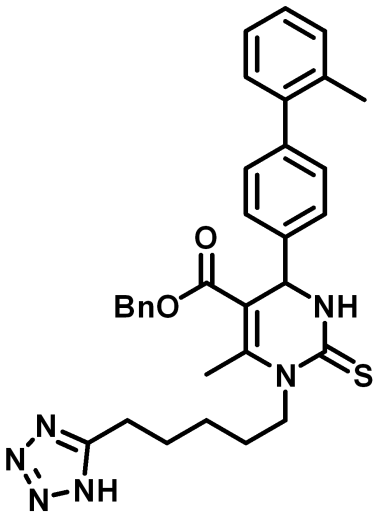
Chromatogram Info:

File Name	: C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT058033_2.PRM	File Created	: 4/16/2014 5:45:39 PM
Origin	: Acquired, Acquisition started 4/16/2014 5:35:39 PM	Acquired Date	: 4/16/2014 5:45:39 PM
Project	: c:\Clarity\Projects\Work1.PRJ	By	: None



Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT058033_2 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	3.513	0.895	0.247	0.1	0.0	0.06	
2	3.943	1497.050	543.527	99.5	99.8	0.05	
3	5.167	0.540	0.216	0.0	0.0	0.03	
4	7.653	5.411	0.740	0.4	0.1	0.10	
	Total	1503.896	544.730	100.0	100.0		

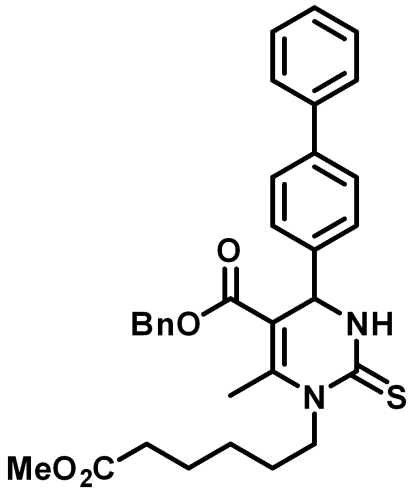


AMT580-033 (3d)

Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(6-methoxy-6-oxohexyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13e)**

9.53 9.52 7.63 7.61 7.59 7.57 7.46 7.45 7.43 7.37 7.37 7.35 7.34 7.32 7.31 7.30 7.28 7.26 5.32 5.31 5.23 5.20 5.18 5.15 4.73 4.71 4.70 3.88 3.87 3.86 3.85 3.85 3.55 2.99 2.55 2.50 2.50 2.20 2.19 2.17 1.64 1.63 1.62 1.52 1.51 1.49 1.48 1.46 1.45 1.44 1.20 1.19 1.17 1.16 1.14

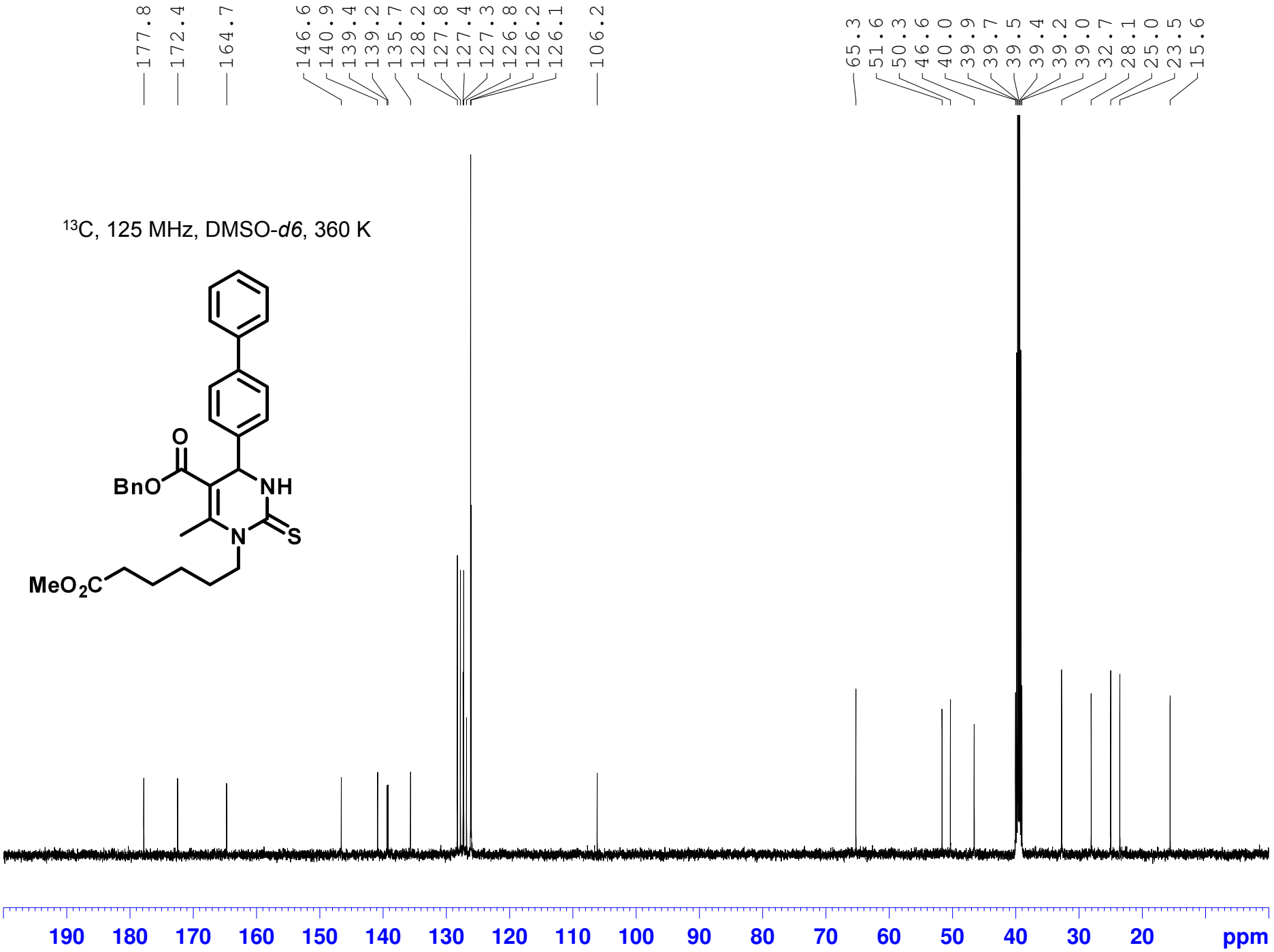
^{1}H, 500 MHz, DMSO-*d6*, 360 K



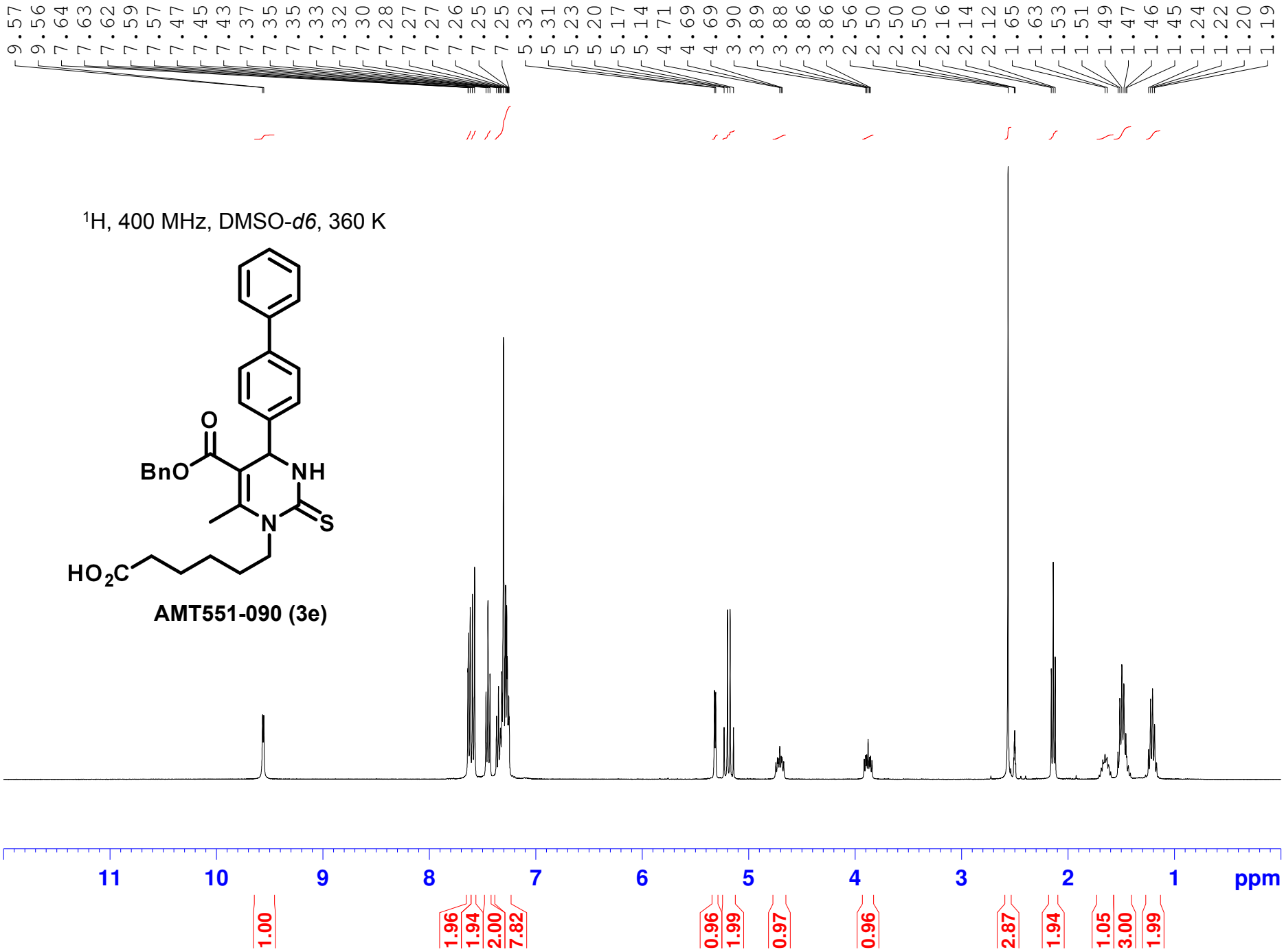
11 10 9 8 7 6 5 4 3 2 1 ppm

0.98 4.05 2.09 7.98 1.00 2.08 1.01 1.02 3.00 2.93 2.04 1.09 3.12 2.18

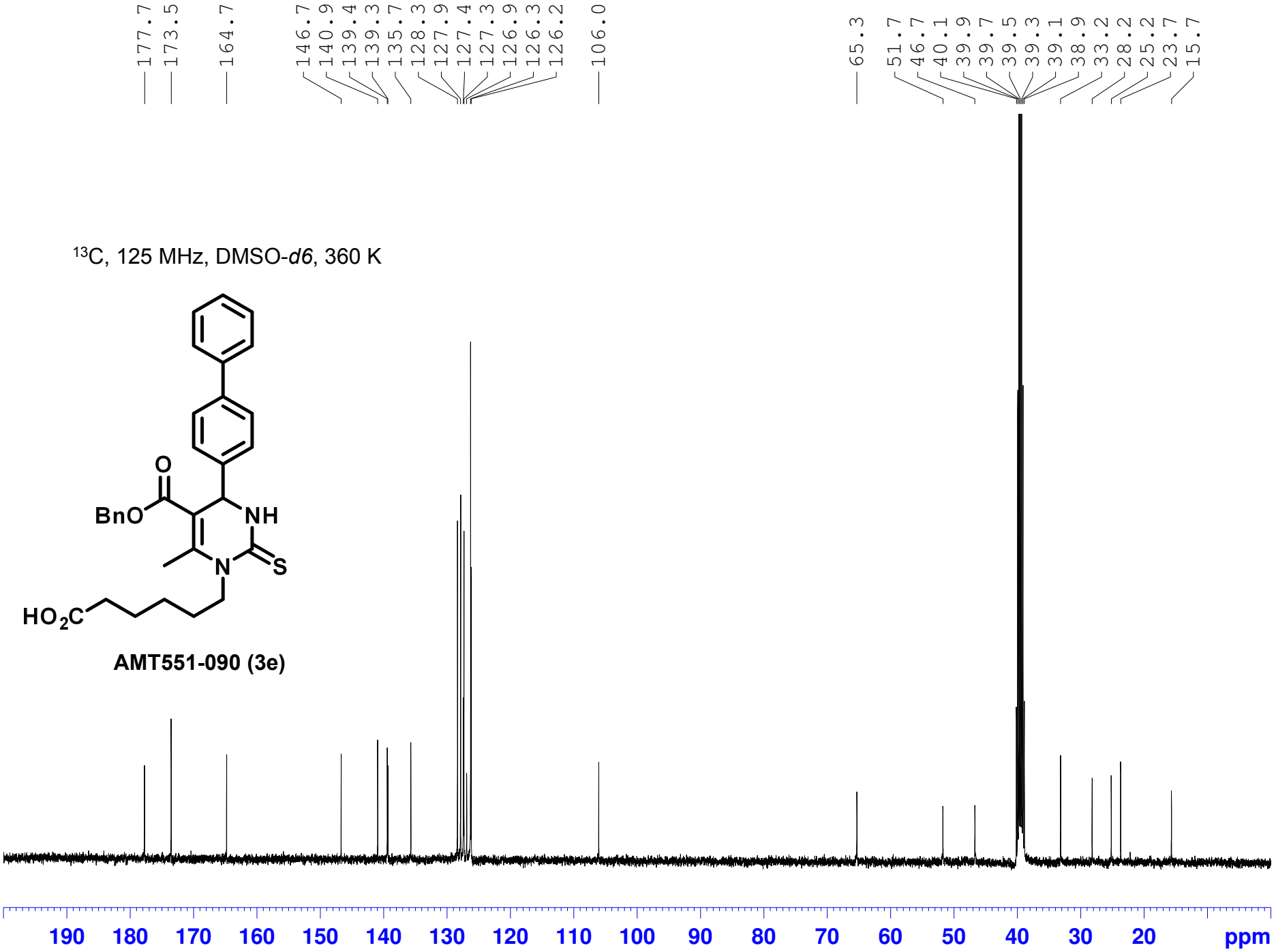
Benzyl 4-([1,1'-biphenyl]-4-yl)-1-(6-methoxy-6-oxohexyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(13e)**



6-(4-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-6-methyl-2-thioxo-3,4-dihydropyrimidin-1(2H)-yl)hexanoic acid



6-(4-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-6-methyl-2-thioxo-3,4-dihydropyrimidin-1(2H)-yl)hexanoic acid



^{13}C, 125 MHz, DMSO-*d6*, 360 K

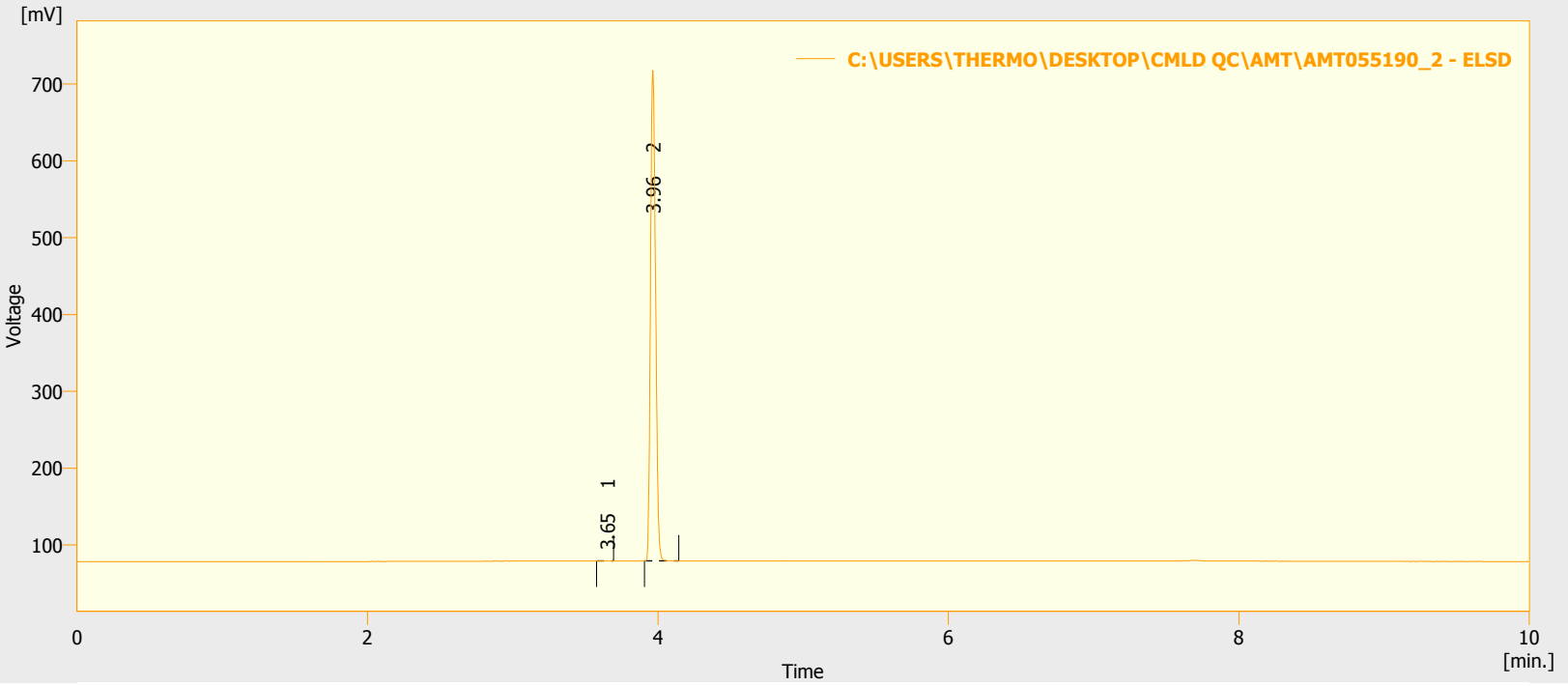
AMT551-090 (3e)

Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

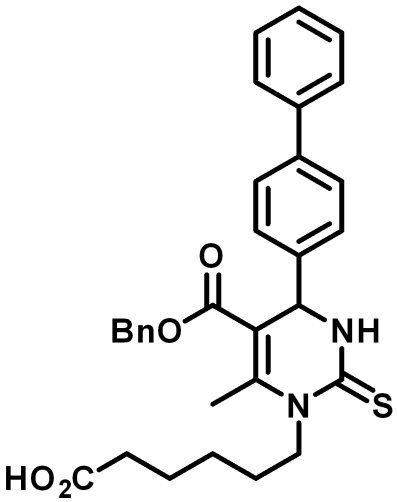
Chromatogram Info:

File Name	: C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055190_2.PRM	File Created	: 4/3/2014 5:48:17 PM
Origin	: Acquired, Acquisition started 4/3/2014 5:38:17 PM	Acquired Date	: 4/3/2014 5:48:17 PM
Project	: c:\Clarity\Projects\Work1.PRJ	By	: None



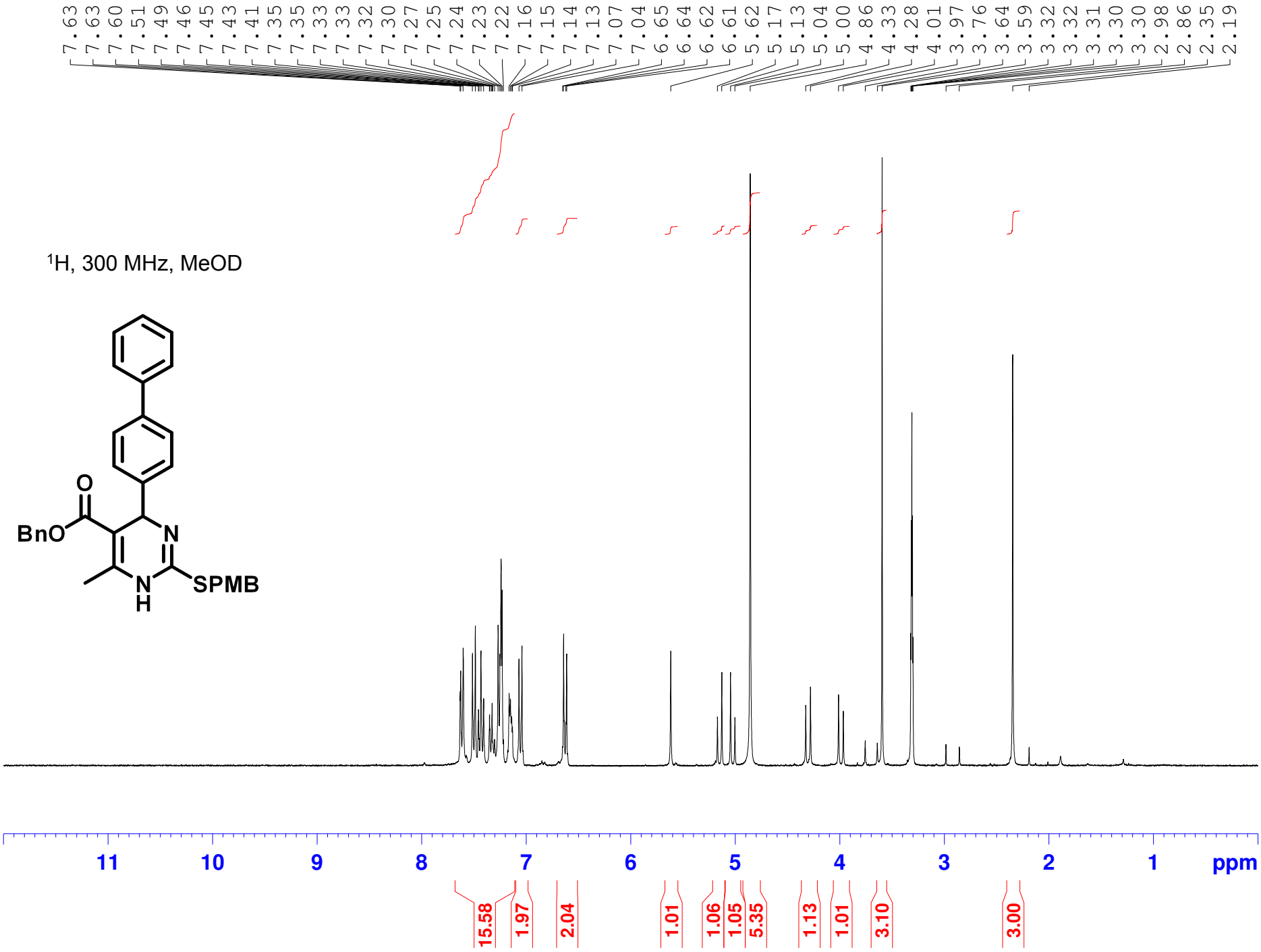
Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055190_2 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	3.650	0.730	0.252	0.0	0.0	0.04	
2	3.963	1556.843	638.588	100.0	100.0	0.04	
	Total	1557.573	638.841	100.0	100.0		

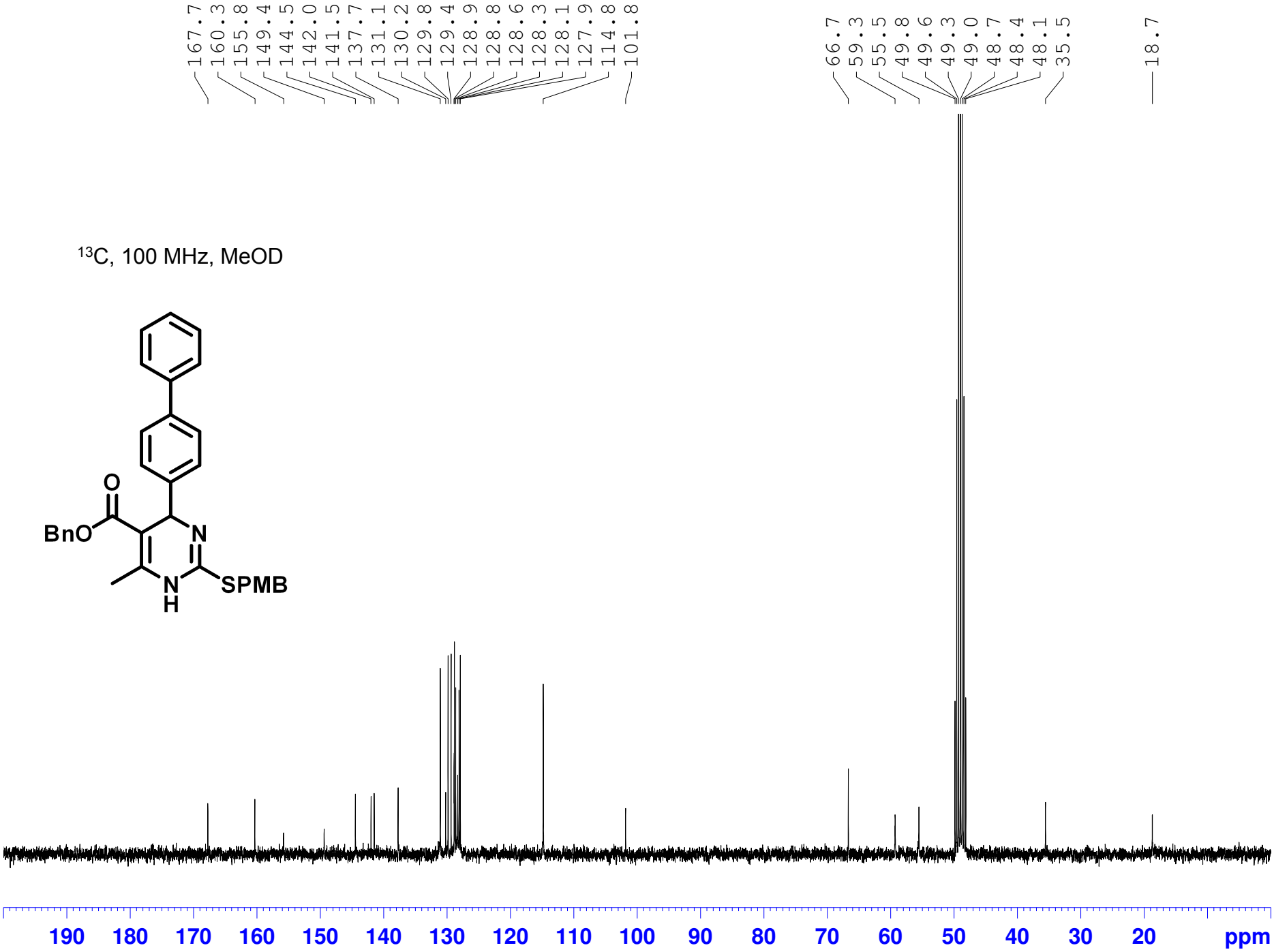


AMT551-090 (3e)

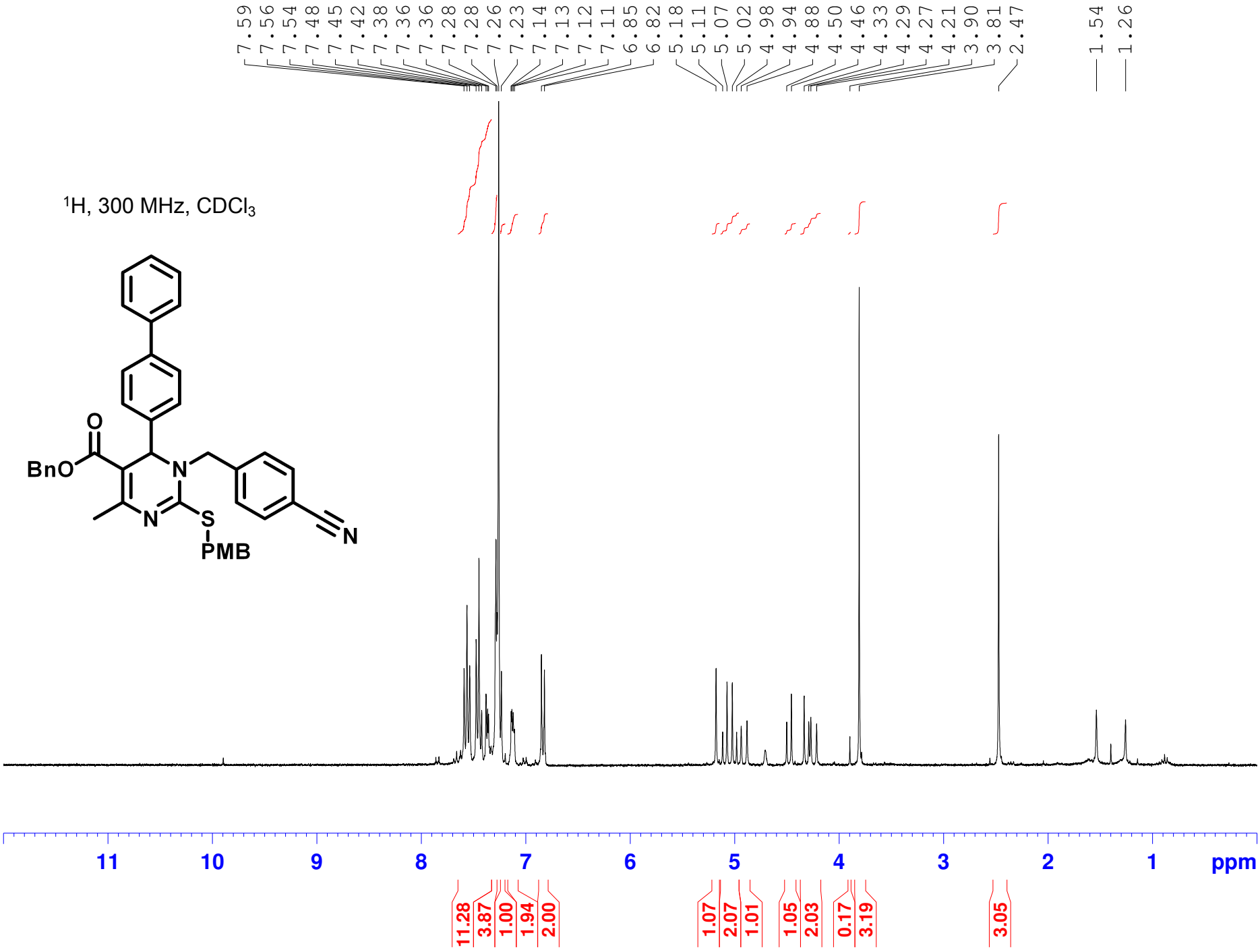
Benzyl 4-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-6-methyl-1,4-dihydropyrimidine-5-carboxylate **(6a)**



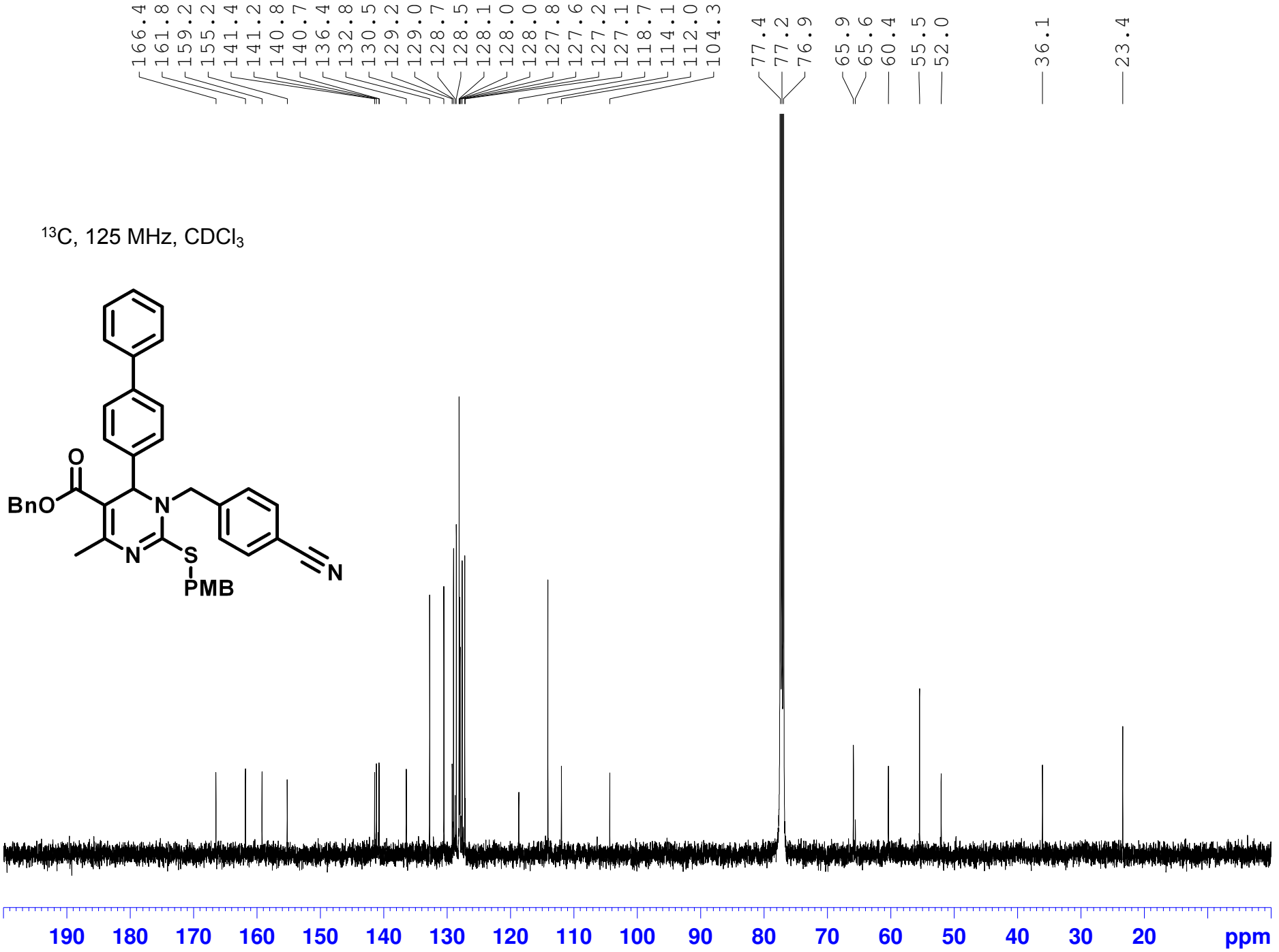
Benzyl 4-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-6-methyl-1,4-dihydropyrimidine-5-carboxylate **(6a)**



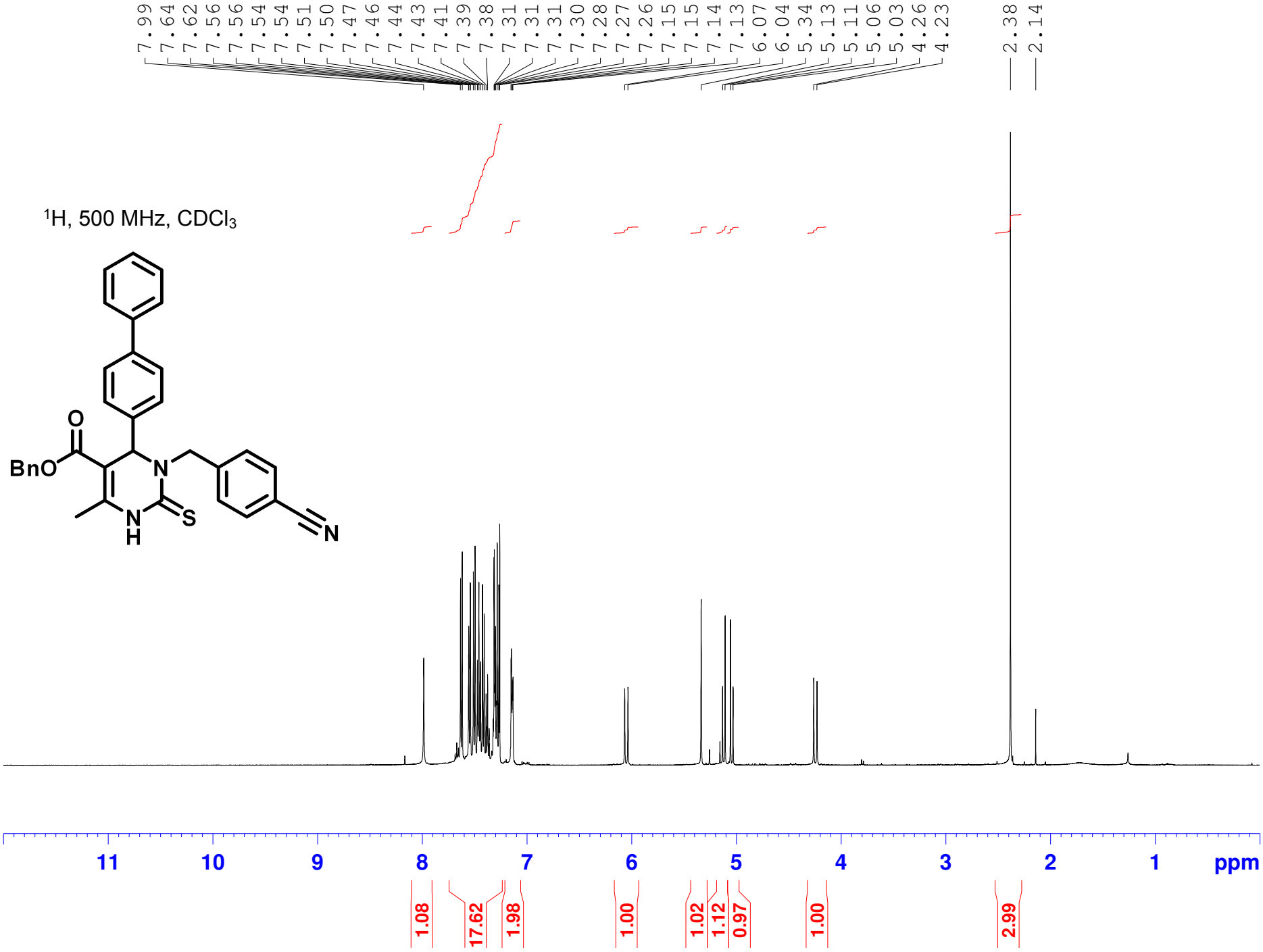
Benzyl 6-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-1,6-dihydropyrimidine-5-carboxylate **(7a)**



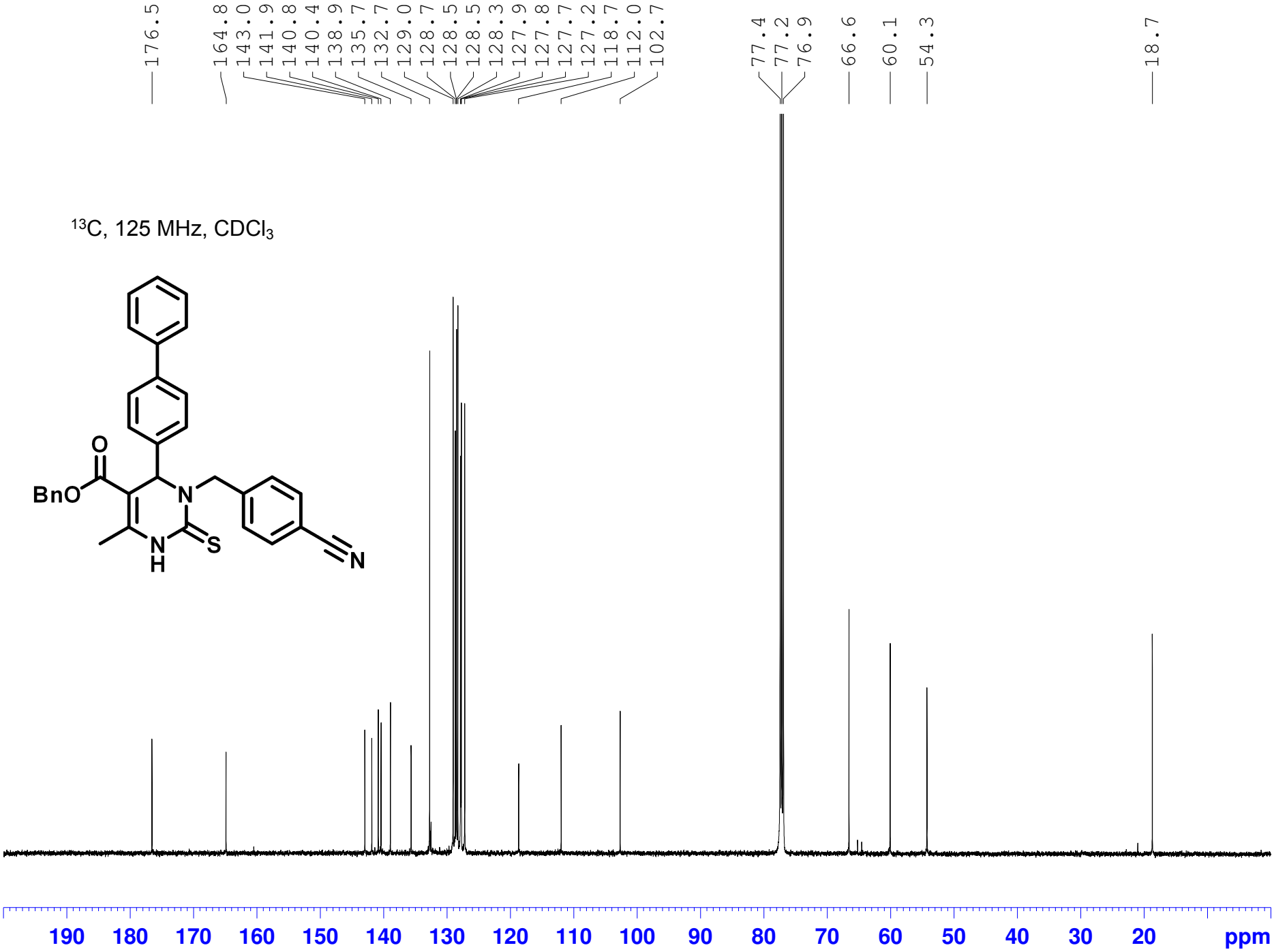
Benzyl 6-([1,1'-biphenyl]-4-yl)-1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-1,6-dihydropyrimidine-5-carboxylate **(7a)**



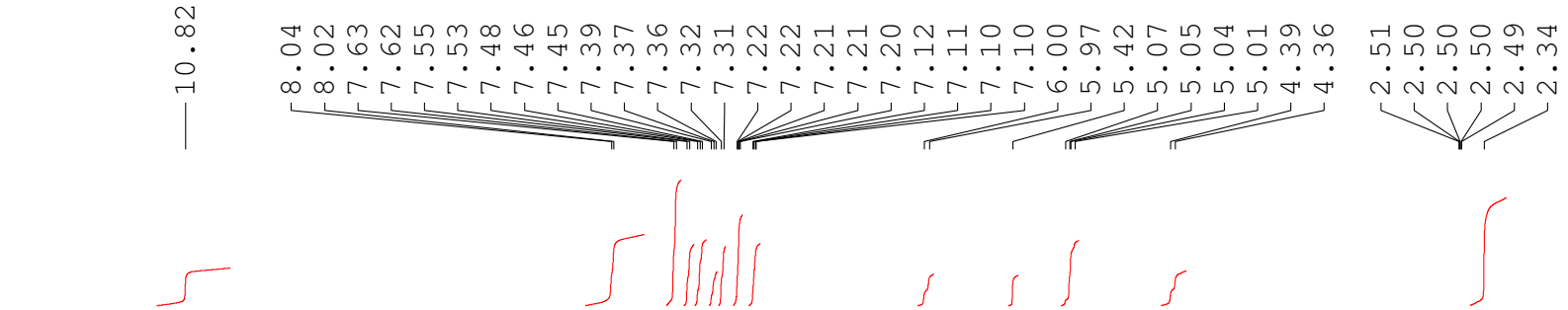
Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(14)**



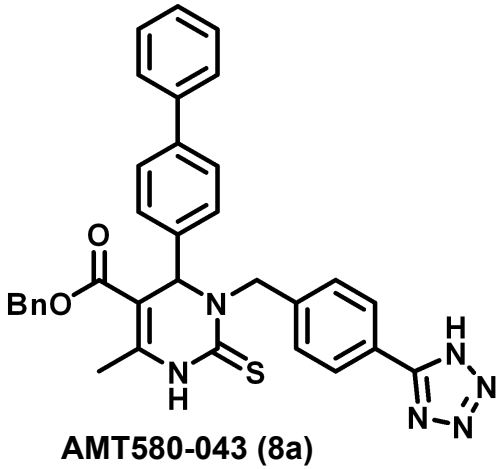
Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(14)**



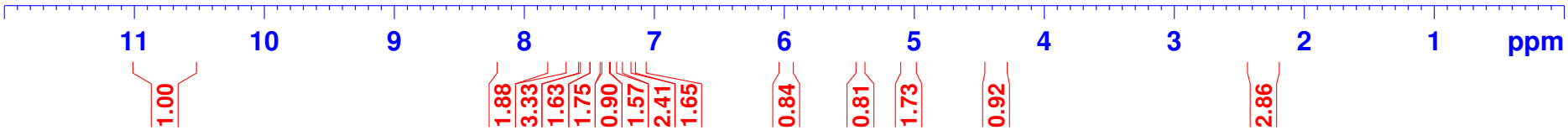
Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



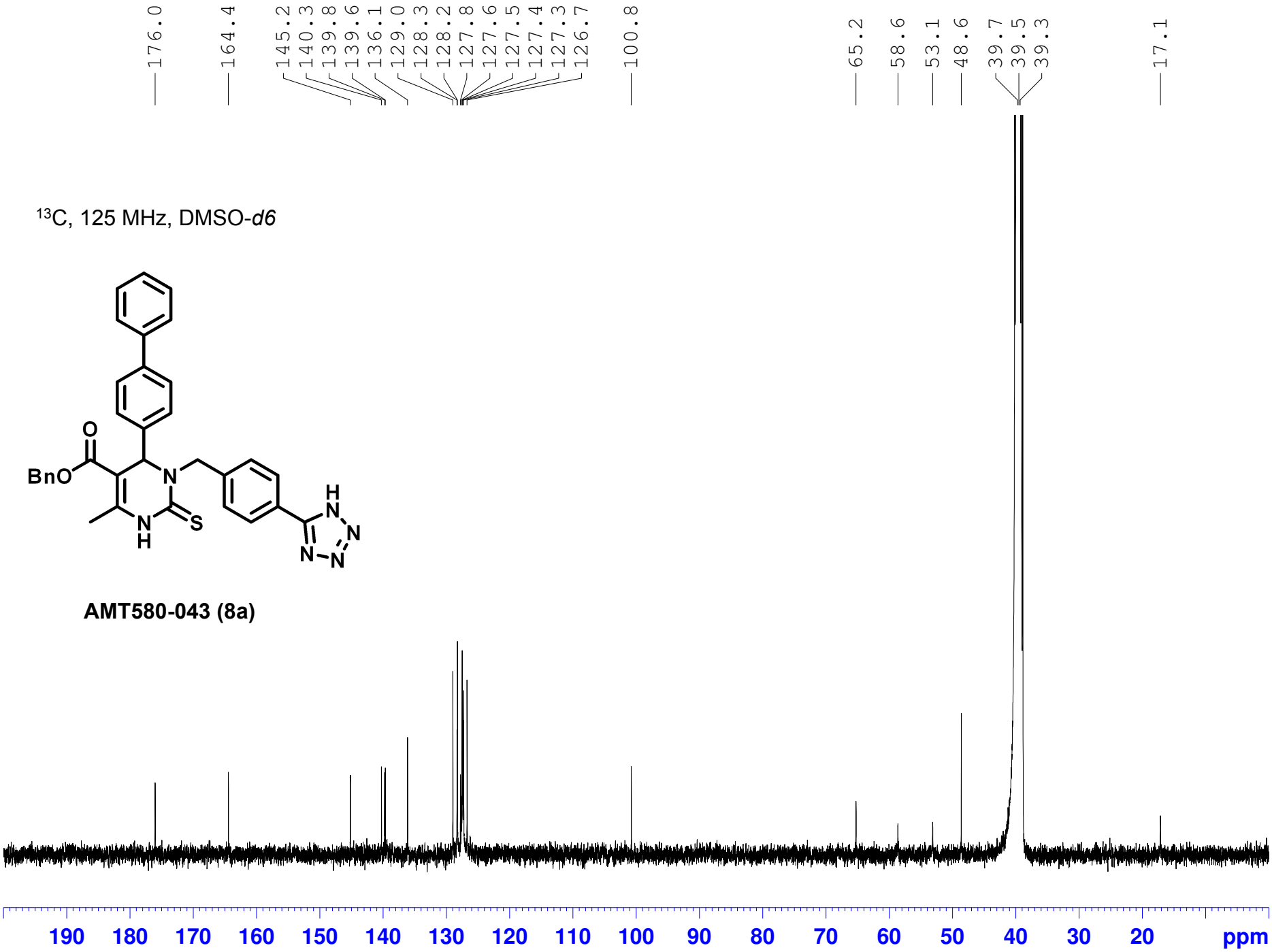
^{1}H, 500 MHz, DMSO-*d6*



AMT580-043 (8a)



Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

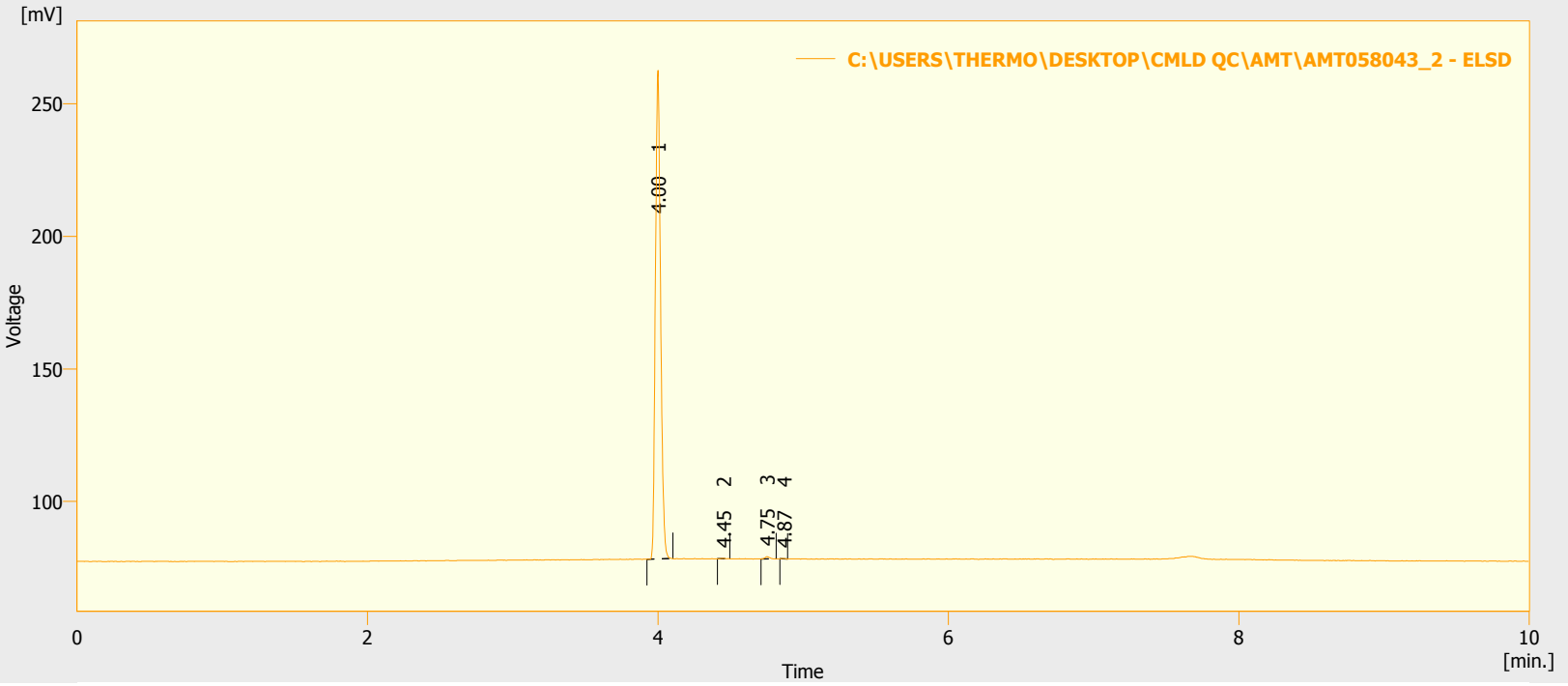


Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

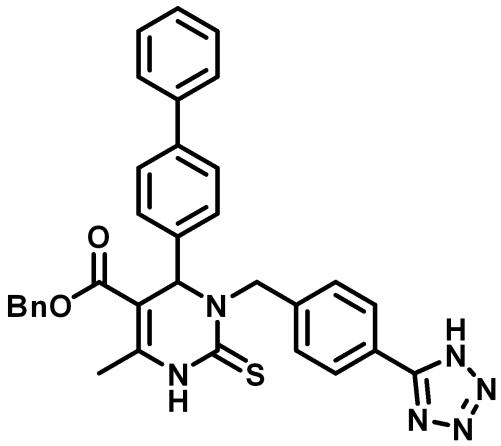
Chromatogram Info:

File Name	: C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT058043_2.PRM	File Created	: 4/24/2014 5:22:54 PM
Origin	: Acquired, Acquisition started 4/24/2014 5:12:54 PM	Acquired Date	: 4/24/2014 5:22:54 PM
Project	: C:\Clarity\Projects\Work1.PRJ	By	: None



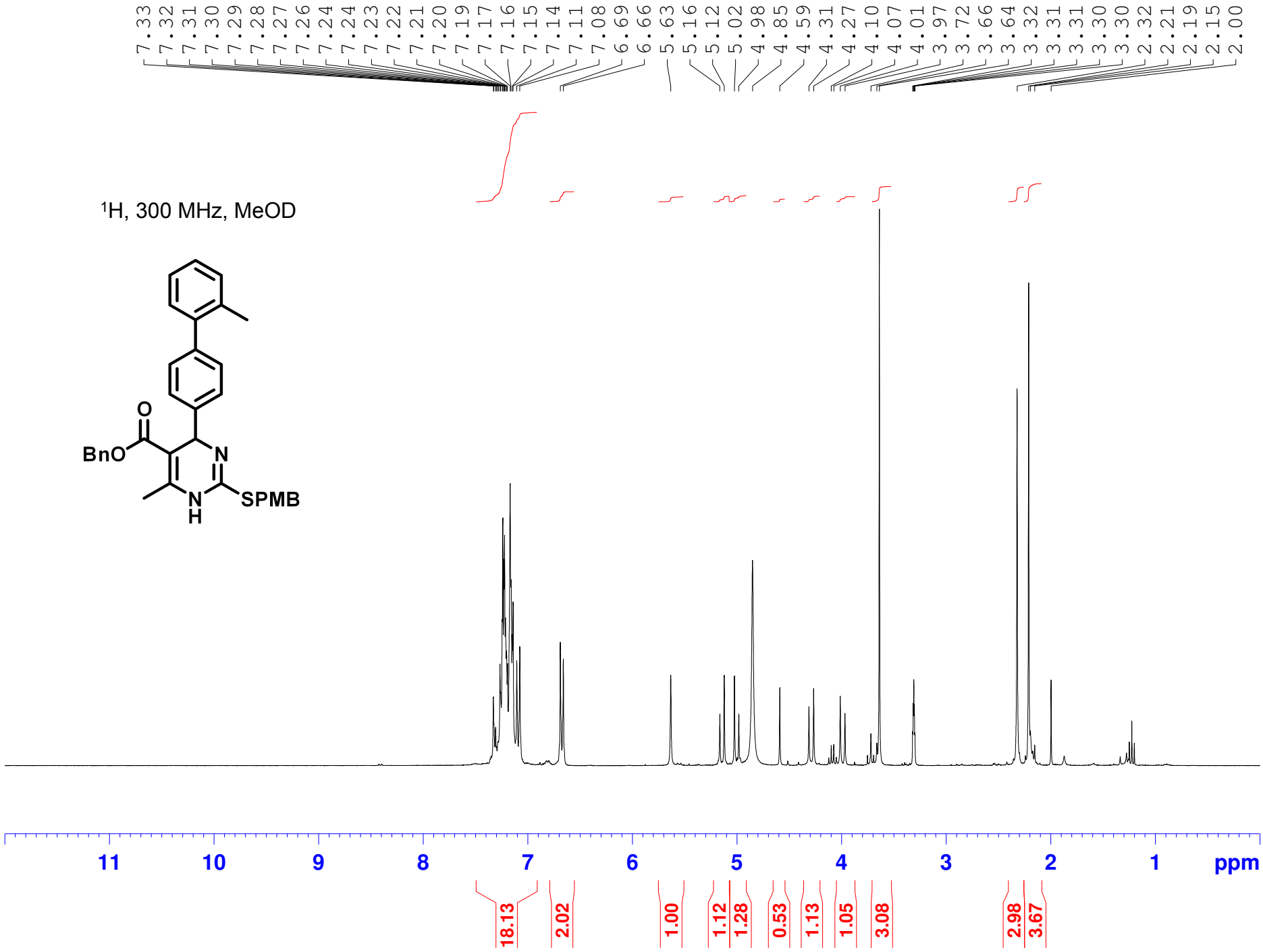
Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT058043_2 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.000	459.196	184.305	99.4	99.3	0.04	
2	4.450	0.487	0.204	0.1	0.1	0.03	
3	4.750	2.006	0.876	0.4	0.5	0.04	
4	4.867	0.324	0.182	0.1	0.1	0.03	
	Total	462.013	185.568	100.0	100.0		

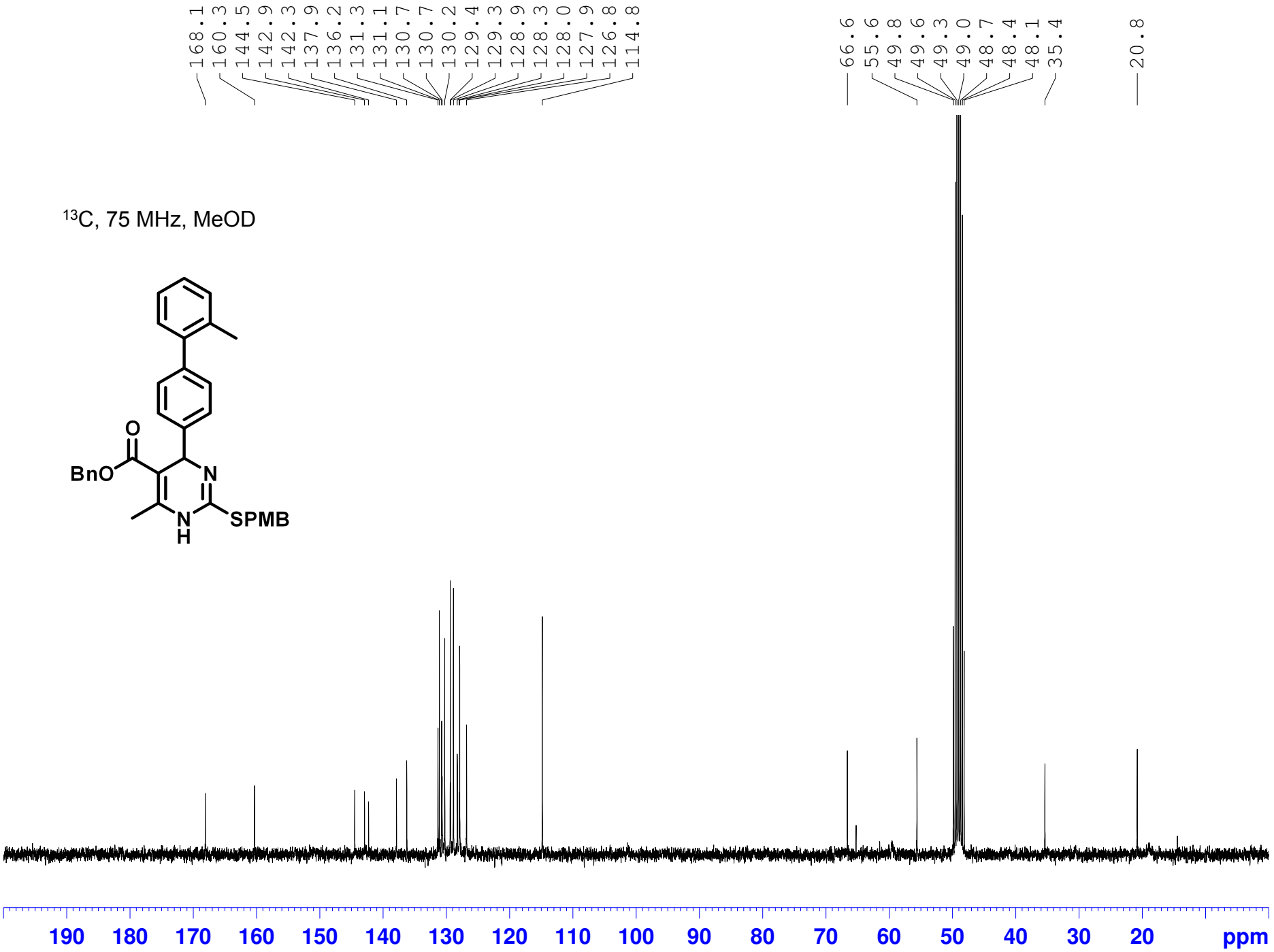


AMT580-043 (8a)

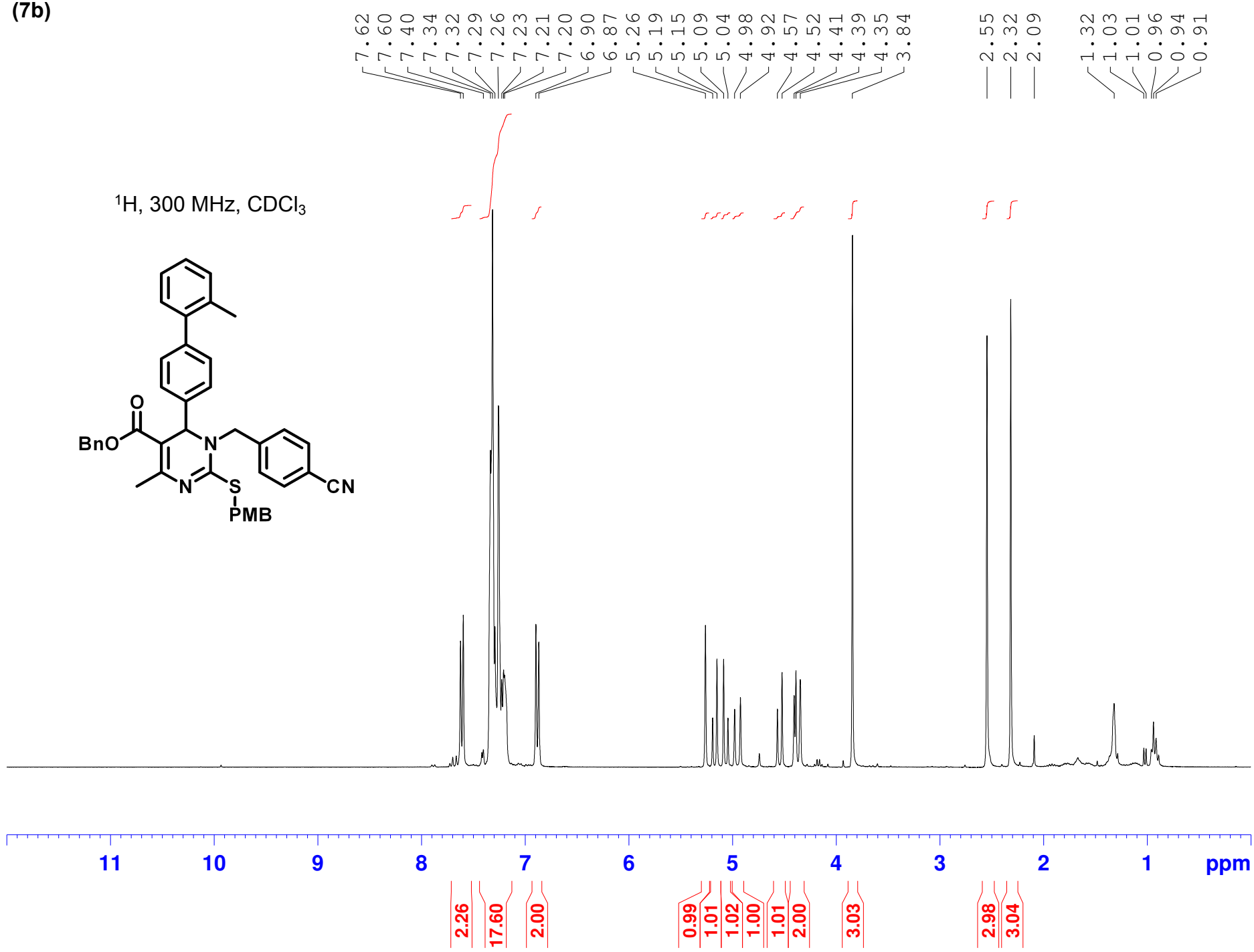
Benzyl 2-((4-methoxybenzyl)thio)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,4-dihydropyrimidine-5-carboxylate **(6b)**



Benzyl 2-((4-methoxybenzyl)thio)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,4-dihydropyrimidine-5-carboxylate **(6b)**



Benzyl 1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate
(7b)



Benzyl 1-(4-cyanobenzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate **(7b)**

166.4
161.7
159.1
155.1
142.1
141.4
141.2
140.2
136.4
135.3
132.6
130.5
130.4
129.8
129.6
129.2
128.5
128.0
128.0
127.5
127.1
125.9
118.6
114.0
111.9
104.3

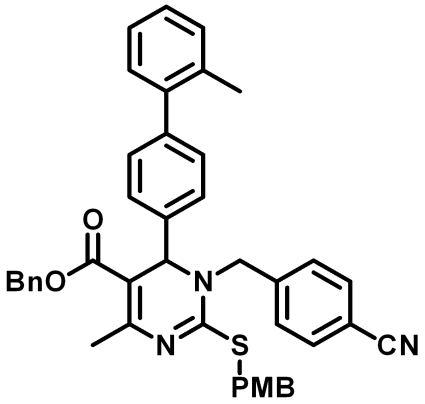
77.5
77.1
76.7

65.8
60.6
55.3
52.3

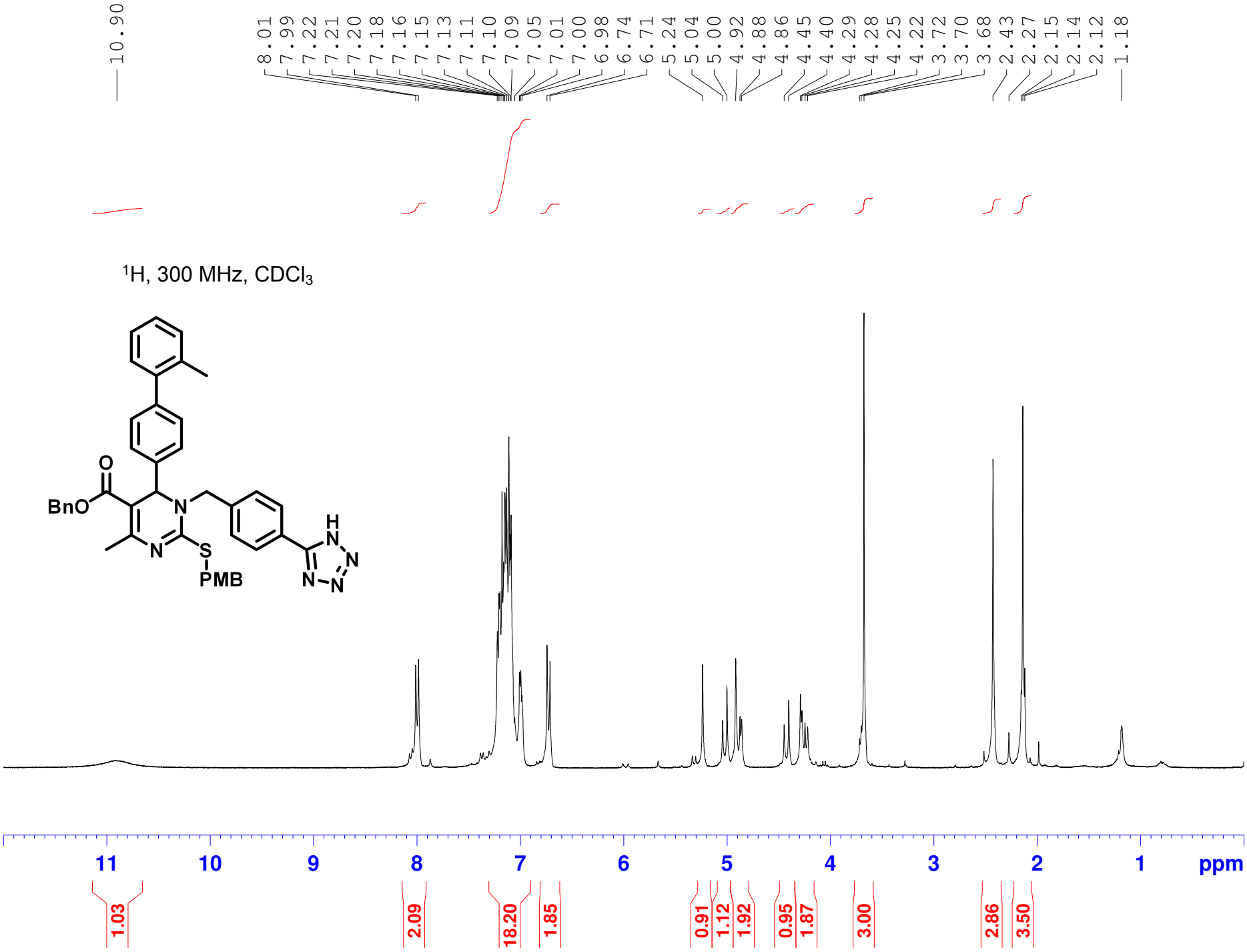
36.0

23.2
20.6

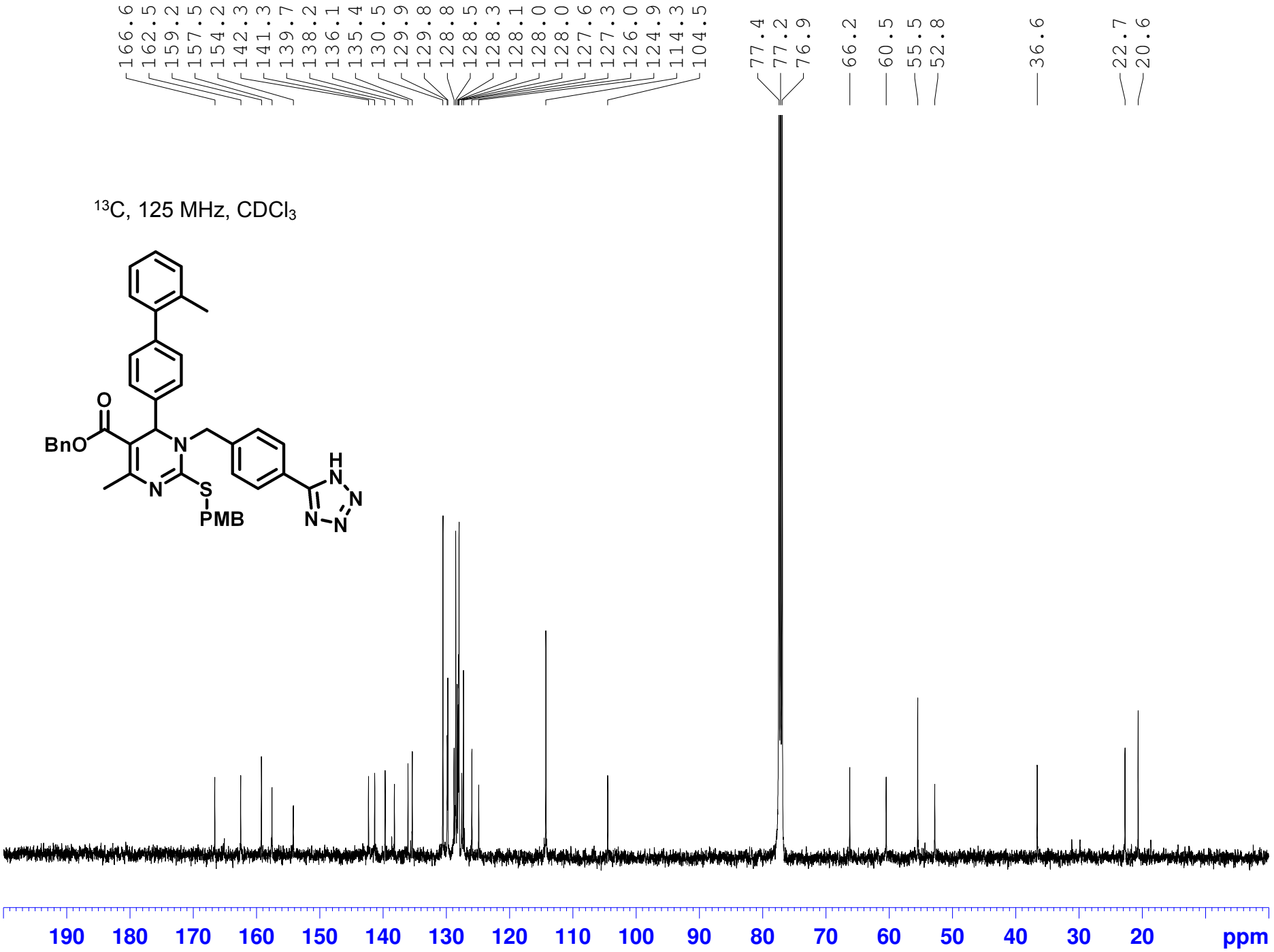
^{13}C, 75 MHz, $CDCl_3$



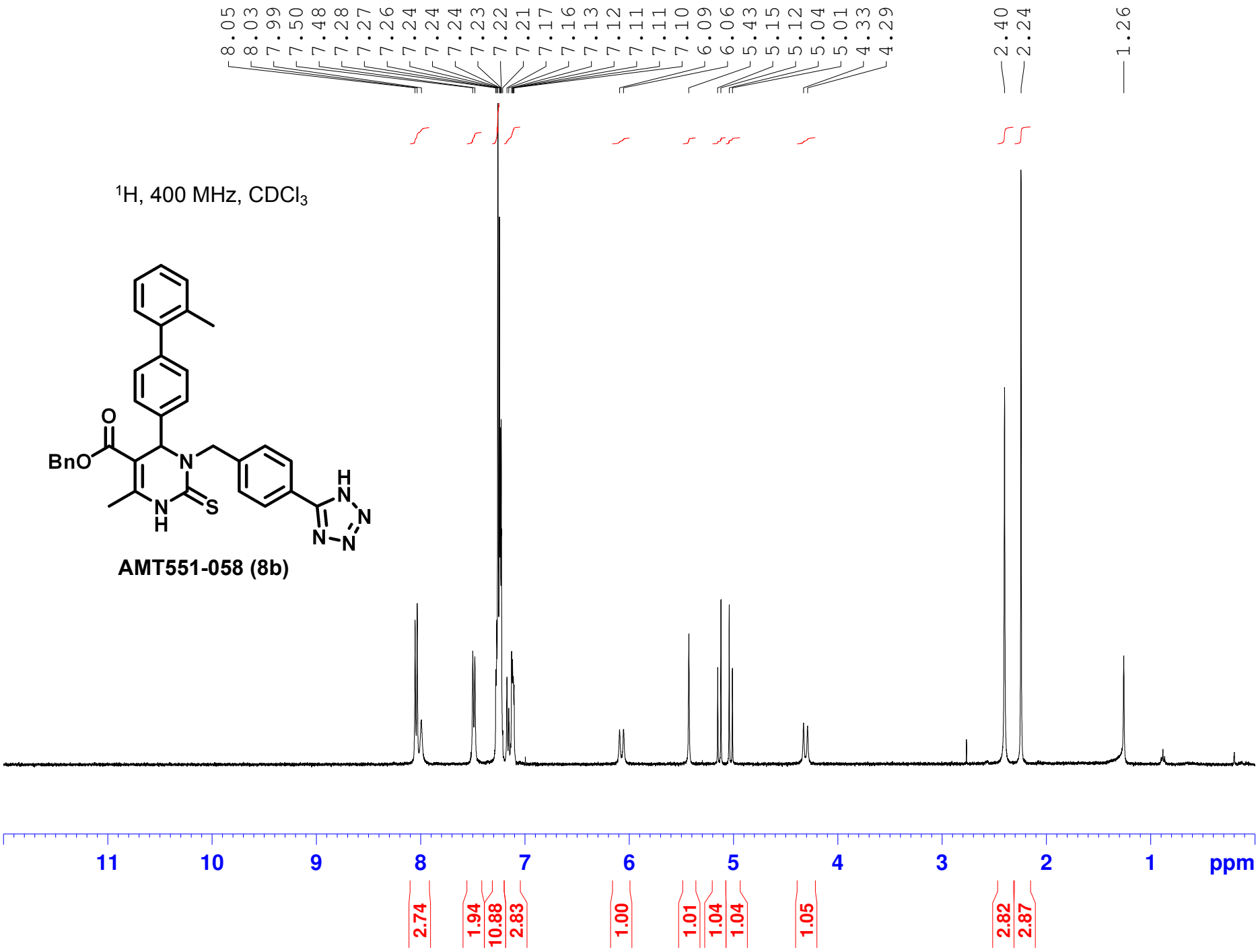
Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate **(15)**



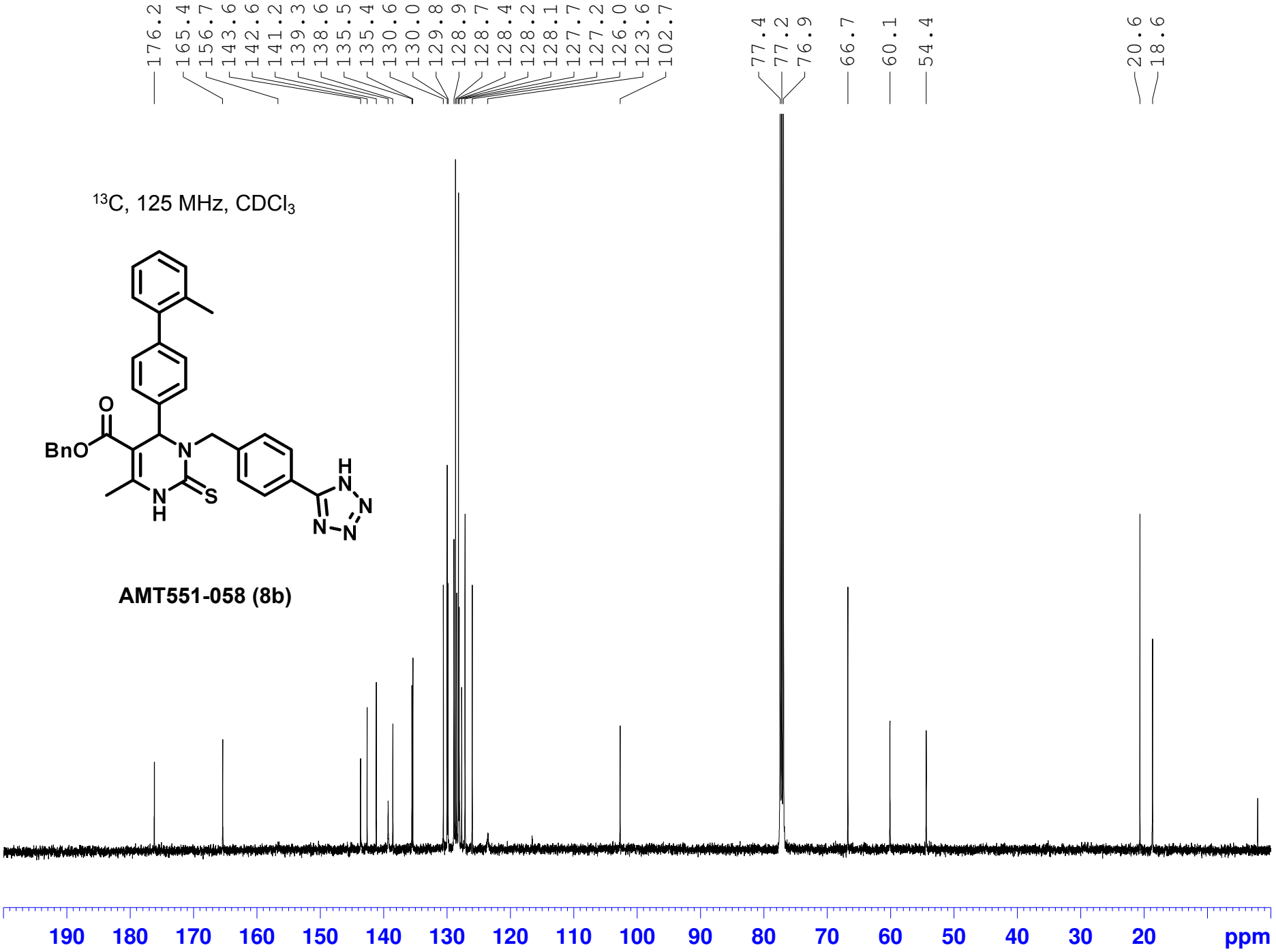
Benzyl 1-(4-(1H-tetrazol-5-yl)benzyl)-2-((4-methoxybenzyl)thio)-4-methyl-6-(2'-methyl-[1,1'-biphenyl]-4-yl)-1,6-dihydropyrimidine-5-carboxylate **(15)**



Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate



Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-6-methyl-4-(2'-methyl-[1,1'-biphenyl]-4-yl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

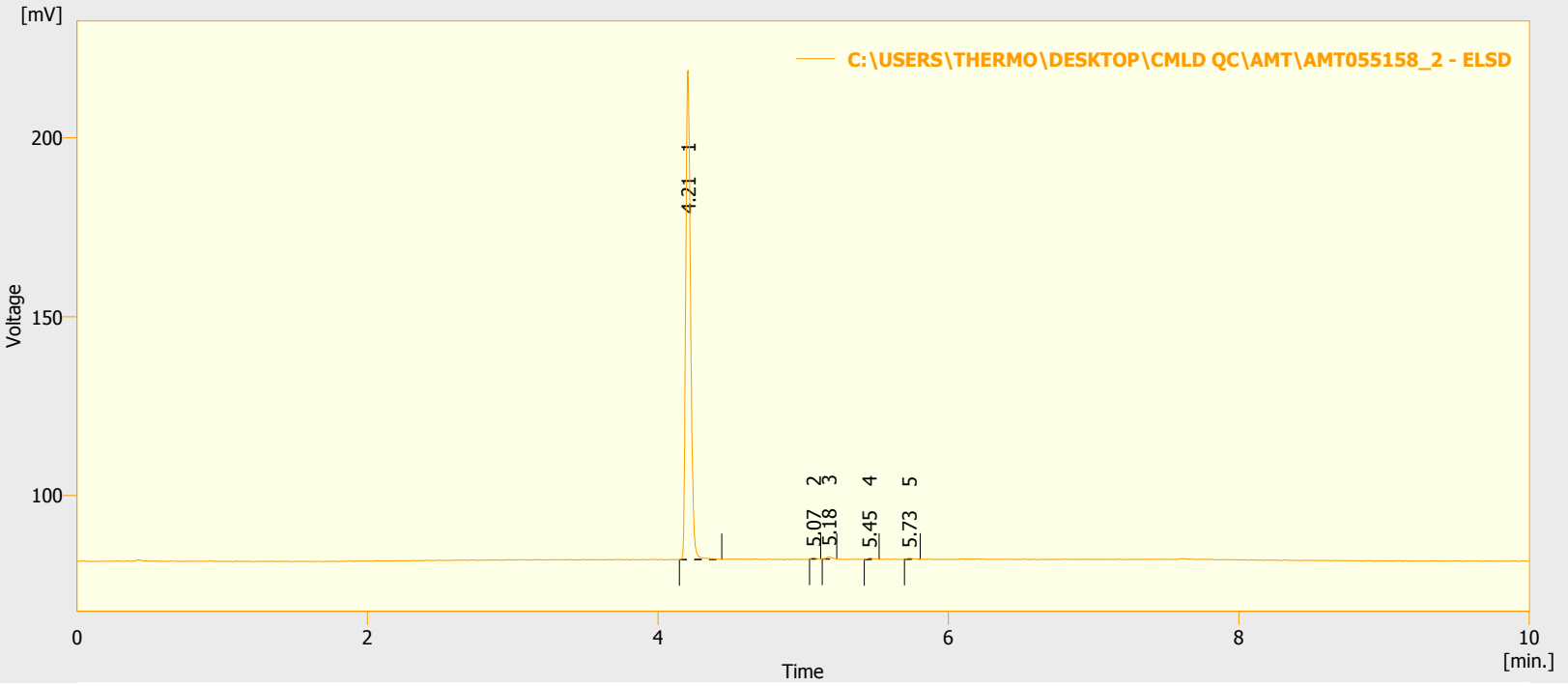


Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

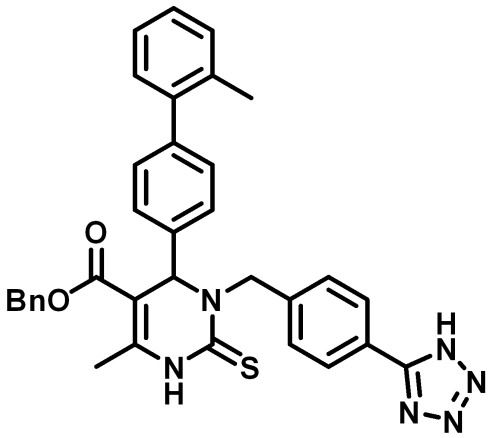
Chromatogram Info:

File Name	: C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055158_2.PRM	File Created	: 2/21/2014 5:00:13 AM
Origin	: Acquired, Acquisition started 2/21/2014 4:50:13 AM	Acquired Date	: 2/21/2014 5:00:13 AM
Project	: c:\Clarity\Projects\Work1.PRJ	By	: None



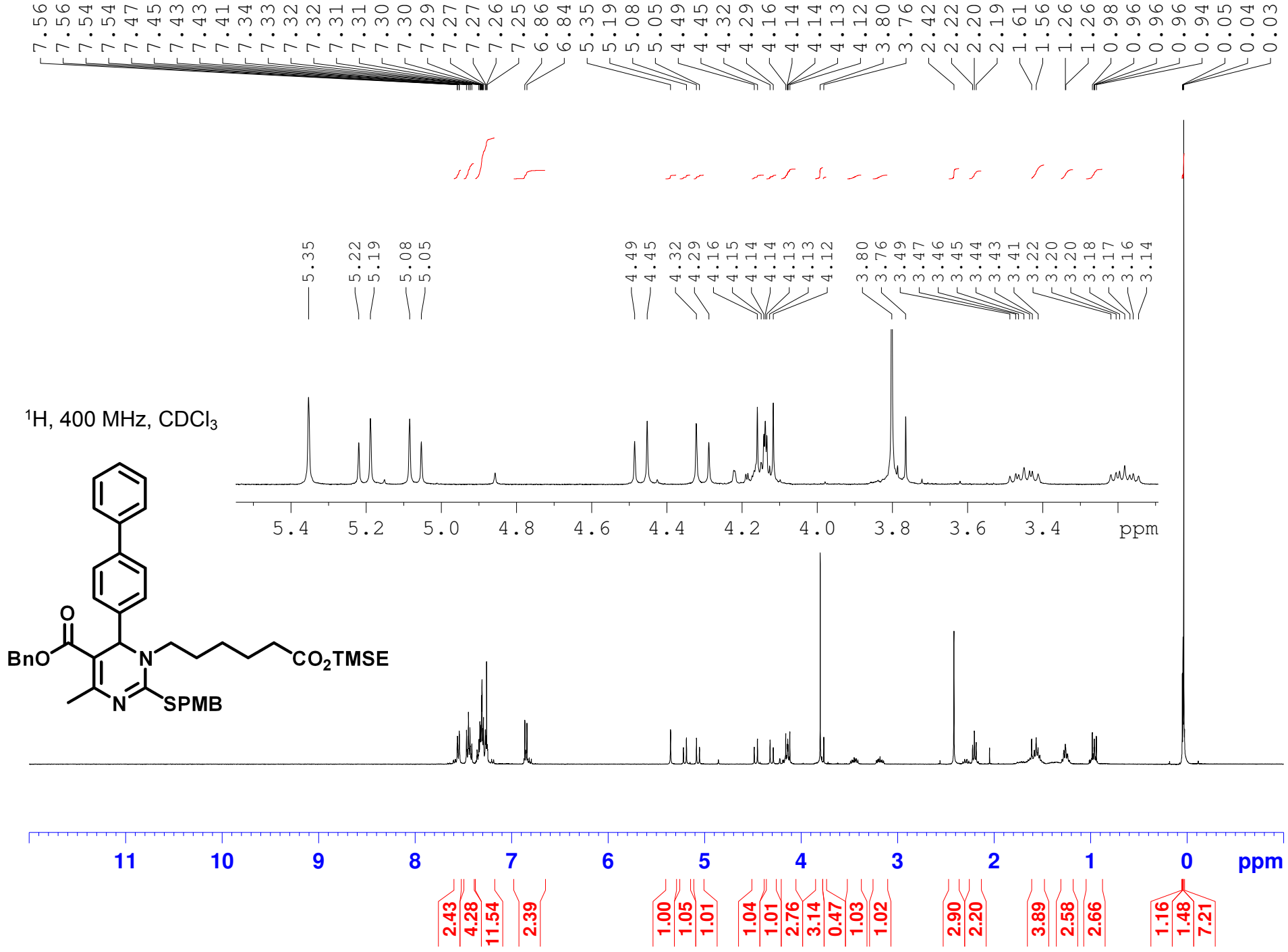
Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055158_2 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.207	316.799	136.779	98.4	98.6	0.04	
2	5.070	0.977	0.448	0.3	0.3	0.03	
3	5.177	1.986	0.699	0.6	0.5	0.05	
4	5.453	1.126	0.406	0.3	0.3	0.05	
5	5.730	1.053	0.342	0.3	0.2	0.05	
	Total	321.940	138.674	100.0	100.0		

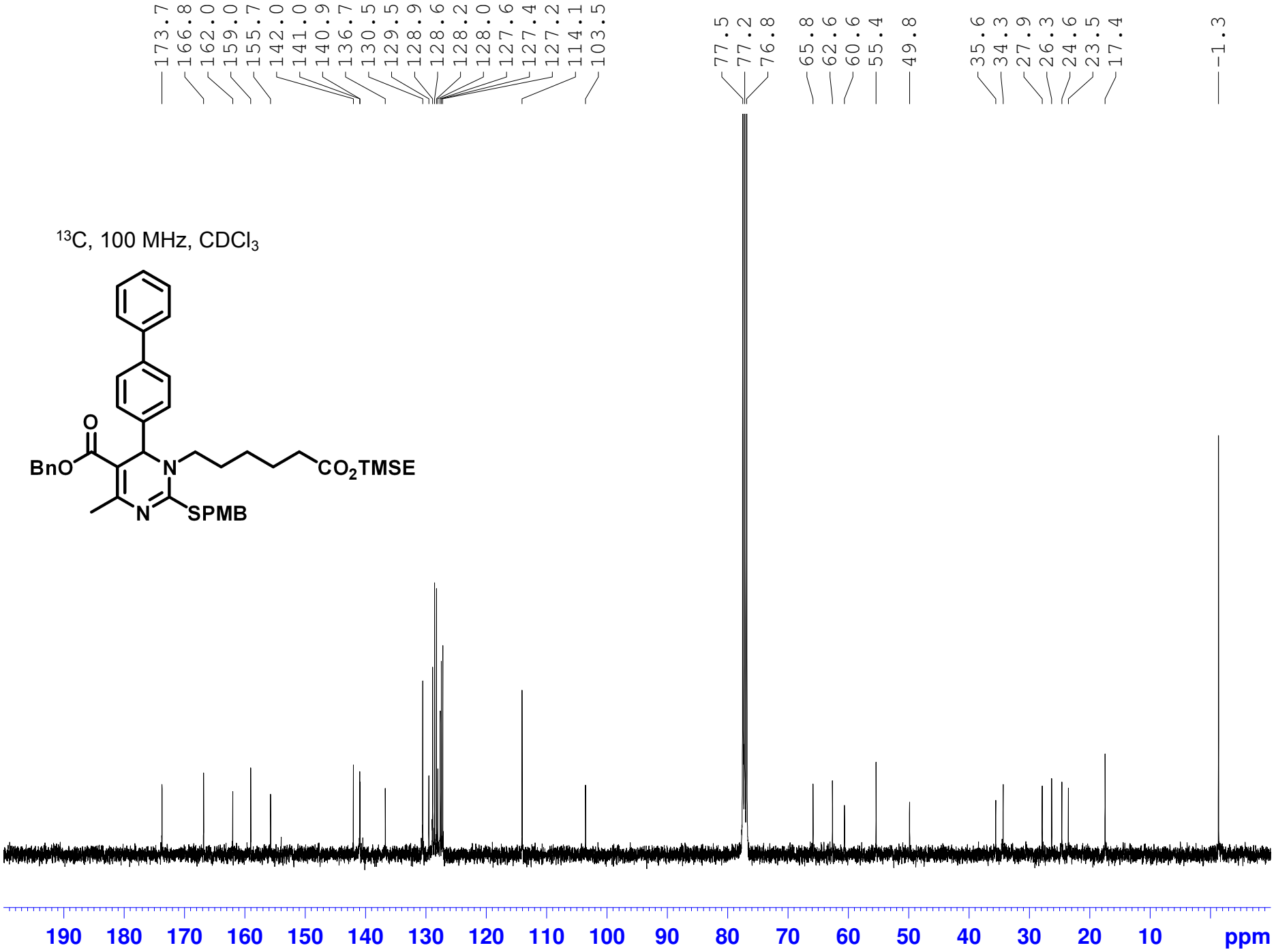


AMT551-058 (8b)

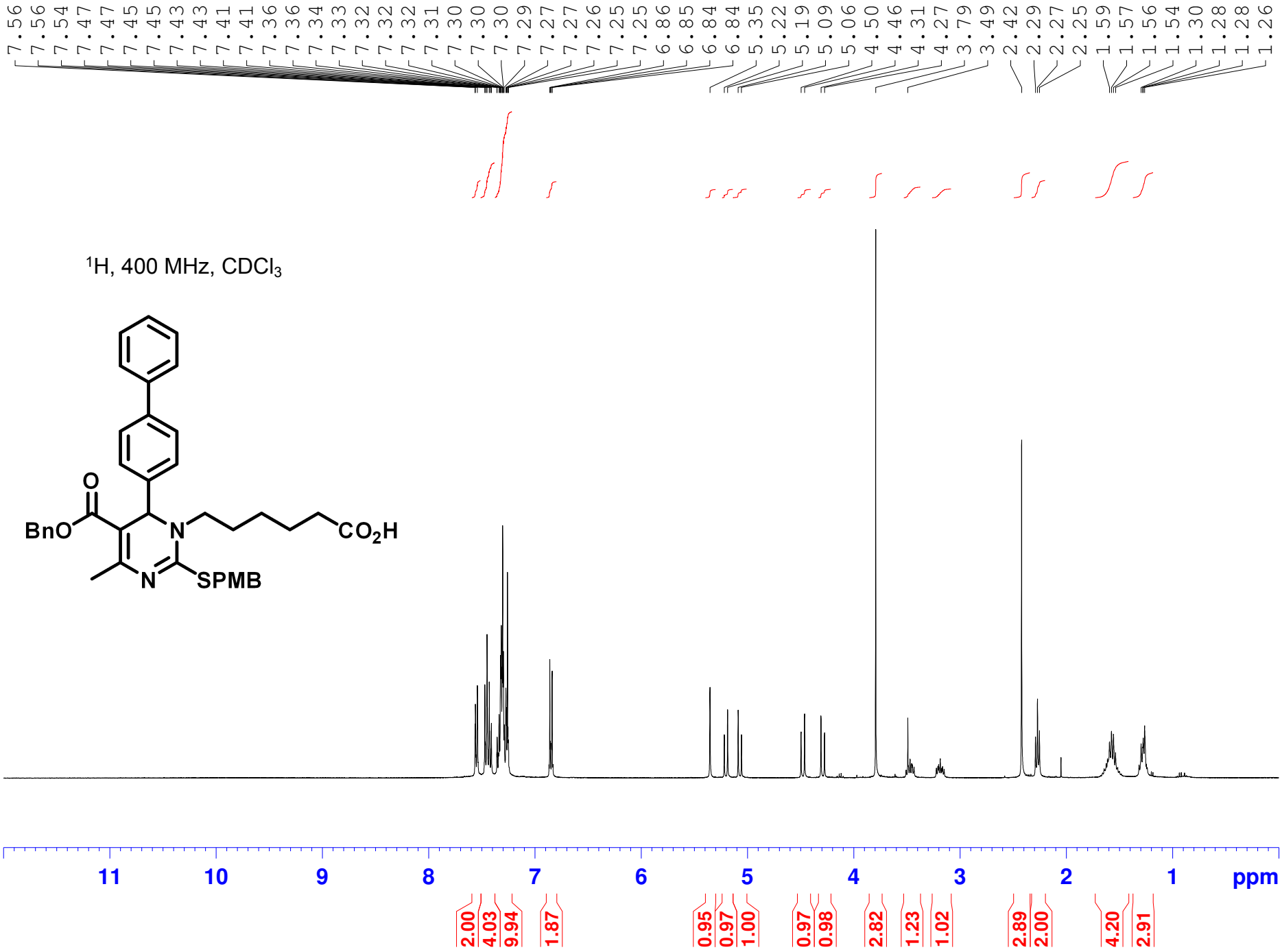
Benzyl 6-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-4-methyl-1-(6-oxo-6-(2-(trimethylsilyl)ethoxy)hexyl)-1,6-dihydropyrimidine-5-carboxylate **(7c)**



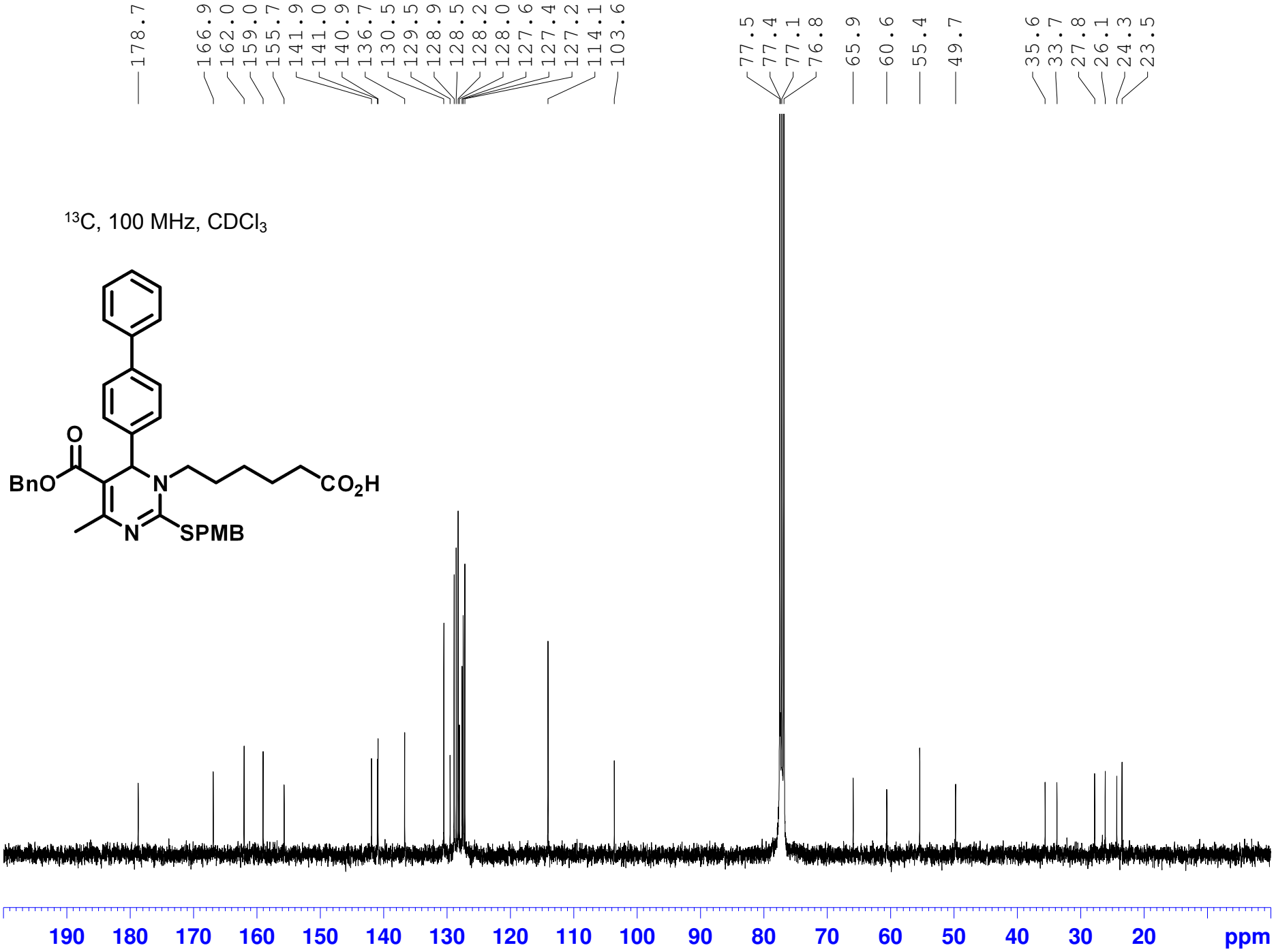
Benzyl 6-([1,1'-biphenyl]-4-yl)-2-((4-methoxybenzyl)thio)-4-methyl-1-(6-oxo-6-(2-(trimethylsilyl)ethoxy)hexyl)-1,6-dihydropyrimidine-5-carboxylate **(7c)**



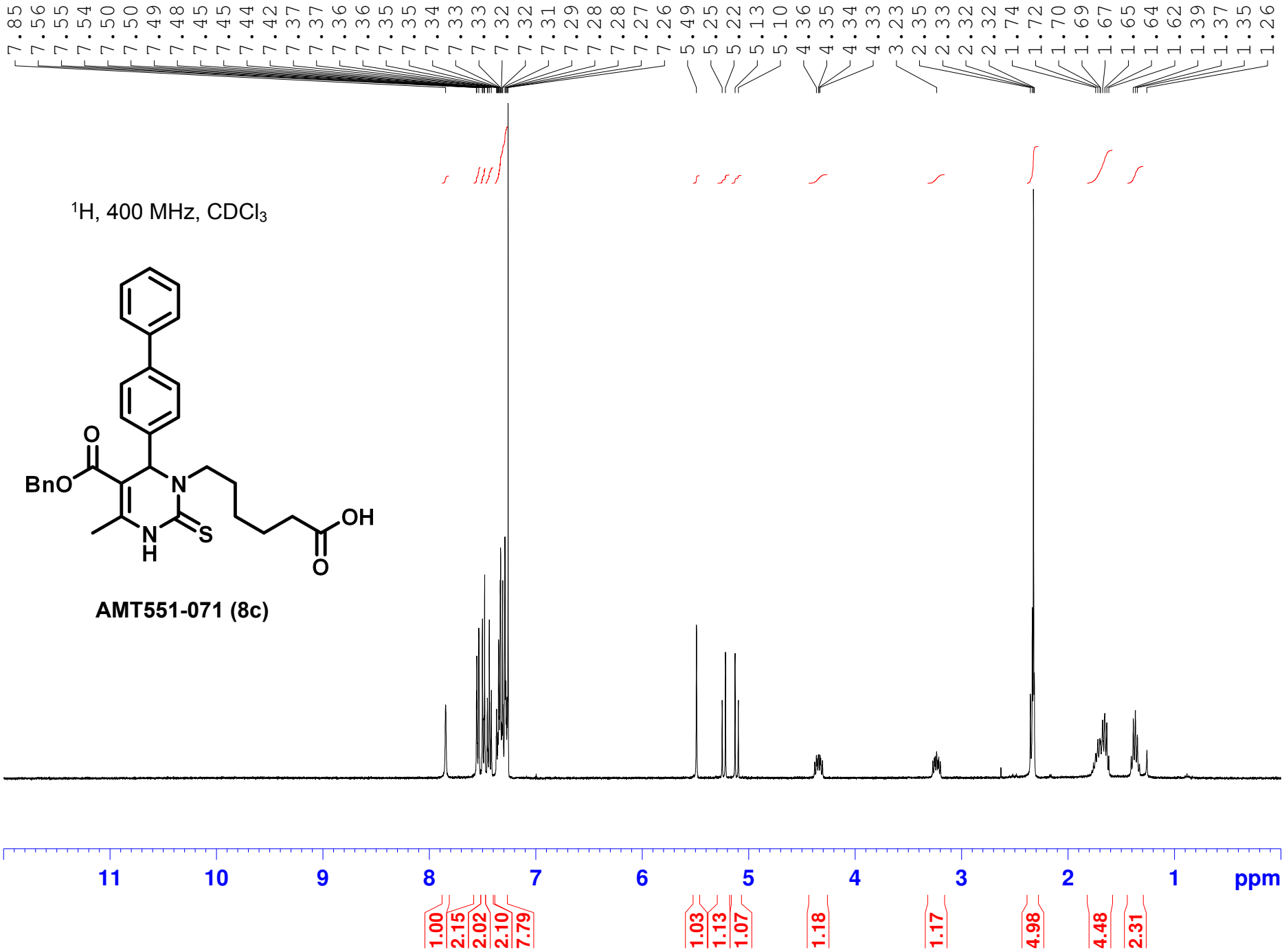
6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-2-((4-methoxybenzyl)thio)-4-methylpyrimidin-1(6H)-yl)hexanoic acid **(16)**



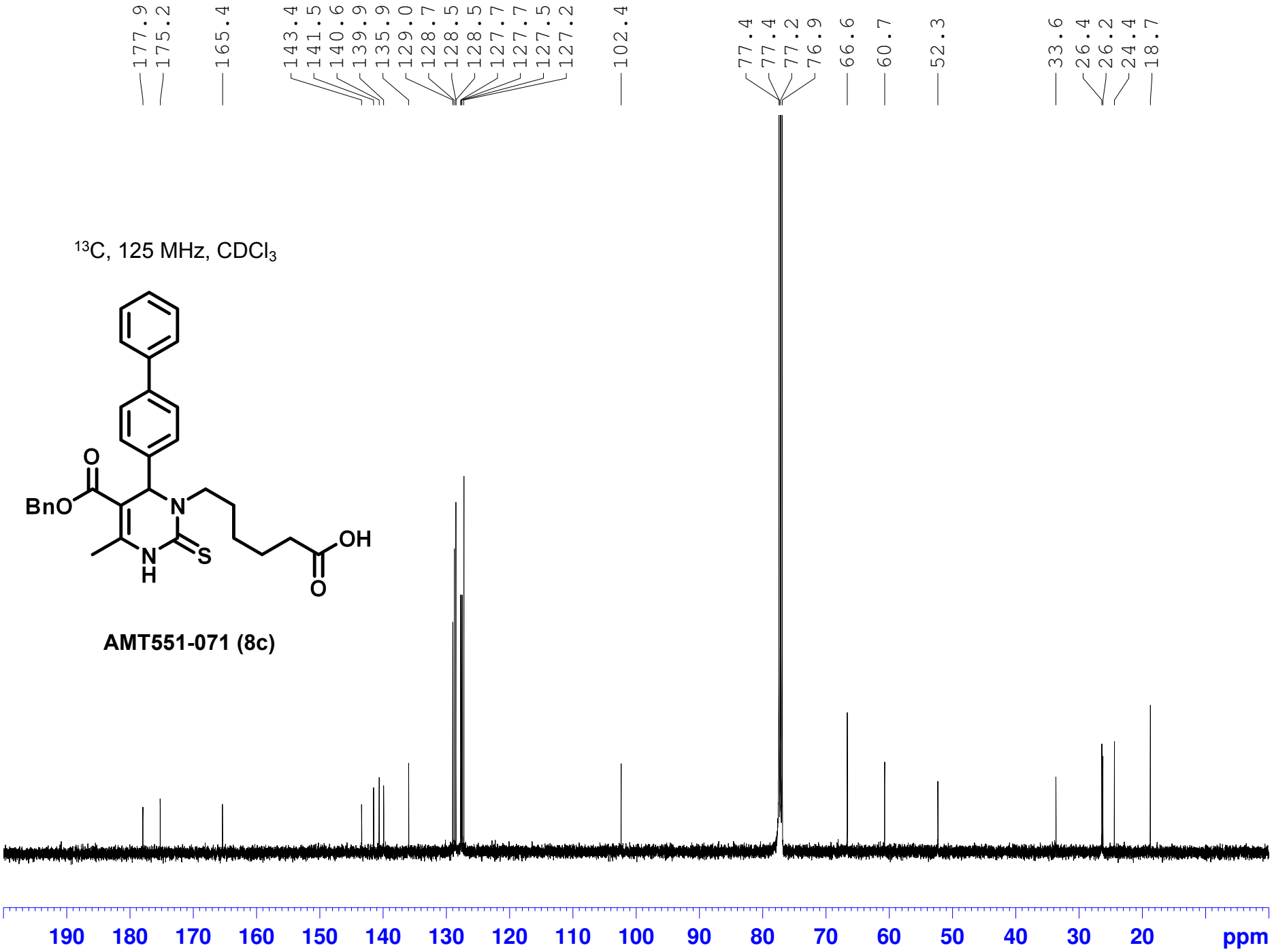
6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-2-((4-methoxybenzyl)thio)-4-methylpyrimidin-1(6H)-yl)hexanoic acid **(16)**



6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-4-methyl-2-thioxo-3,6-dihydropyrimidin-1(2H)-yl)hexanoic acid



6-(6-([1,1'-Biphenyl]-4-yl)-5-((benzyloxy)carbonyl)-4-methyl-2-thioxo-3,6-dihydropyrimidin-1(2H)-yl)hexanoic acid

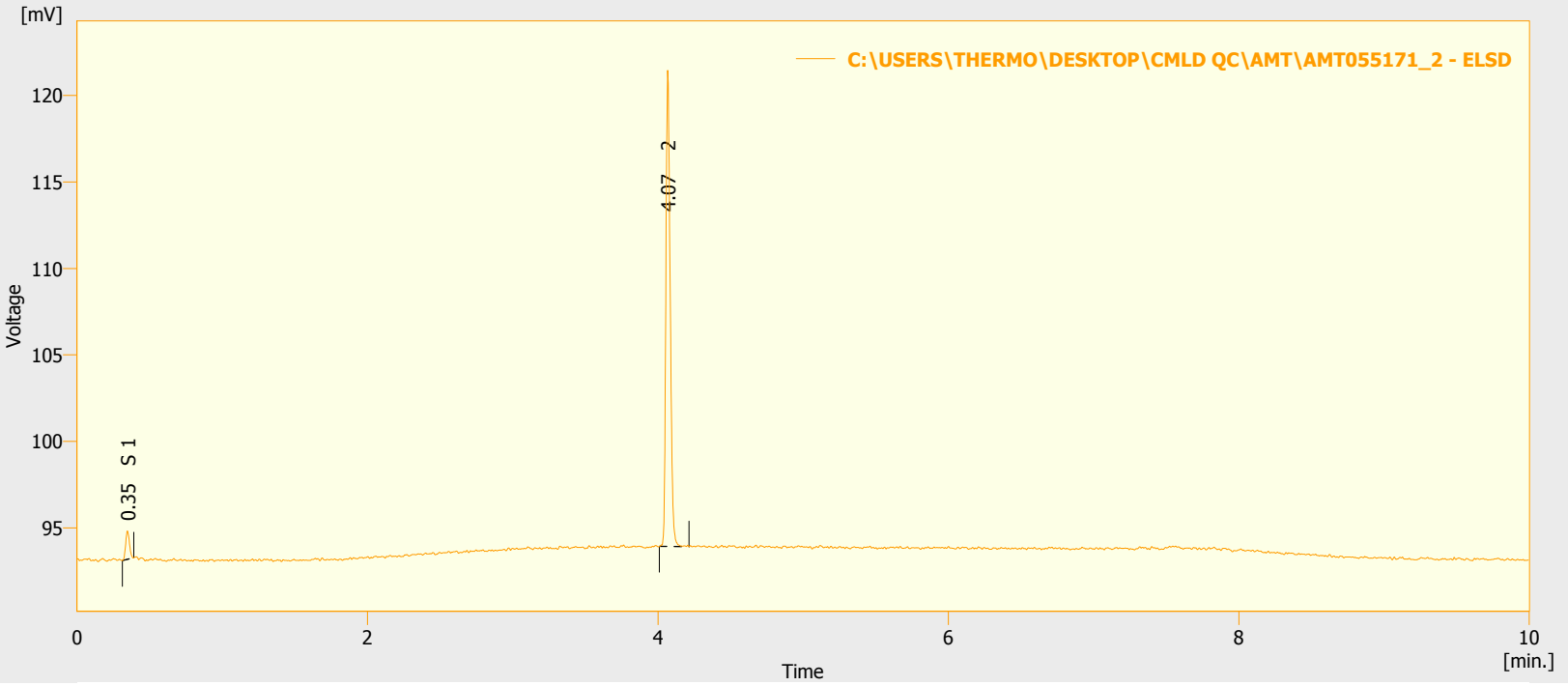


Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

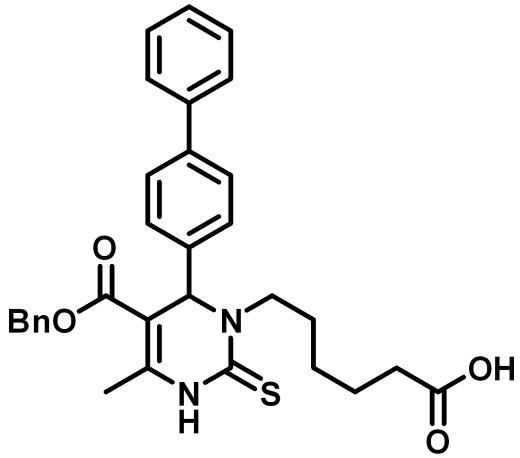
Chromatogram Info:

File Name	: C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055171_2.PRM	File Created	: 3/5/2014 6:25:12 PM
Origin	: Acquired, Acquisition started 3/5/2014 5:15:12 PM	Acquired Date	: 3/5/2014 5:25:12 PM
Project	: c:\Clarity\Projects\Work1.PRJ	By	: None



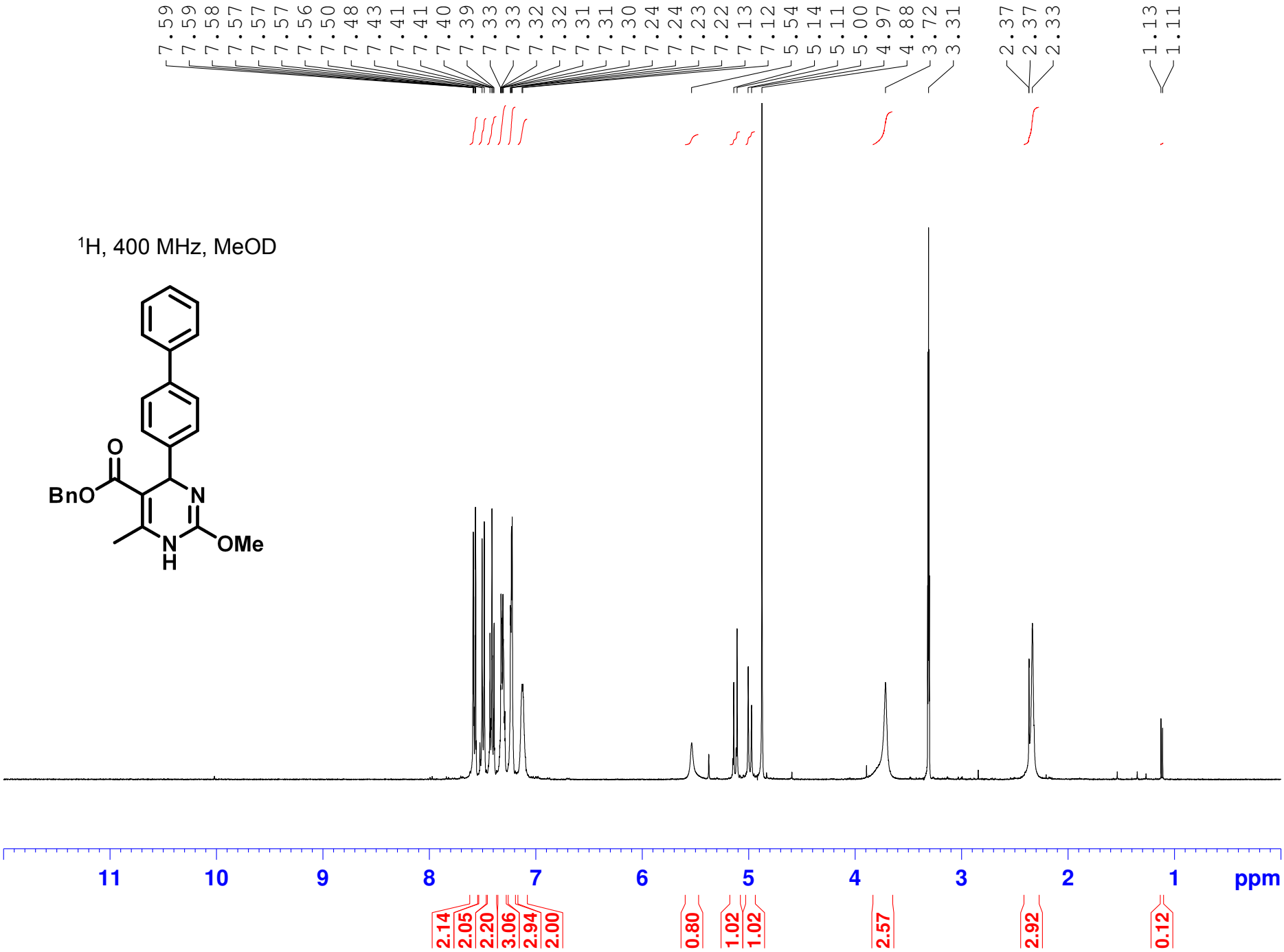
Result Table (Uncal - C:\USERS\THERMO\DESKTOP\CMLD QC\AMT\AMT055171_2 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
2	4.067	56.578	27.513	100.0	100.0	0.04	
	Total	56.578	27.513	100.0	100.0		

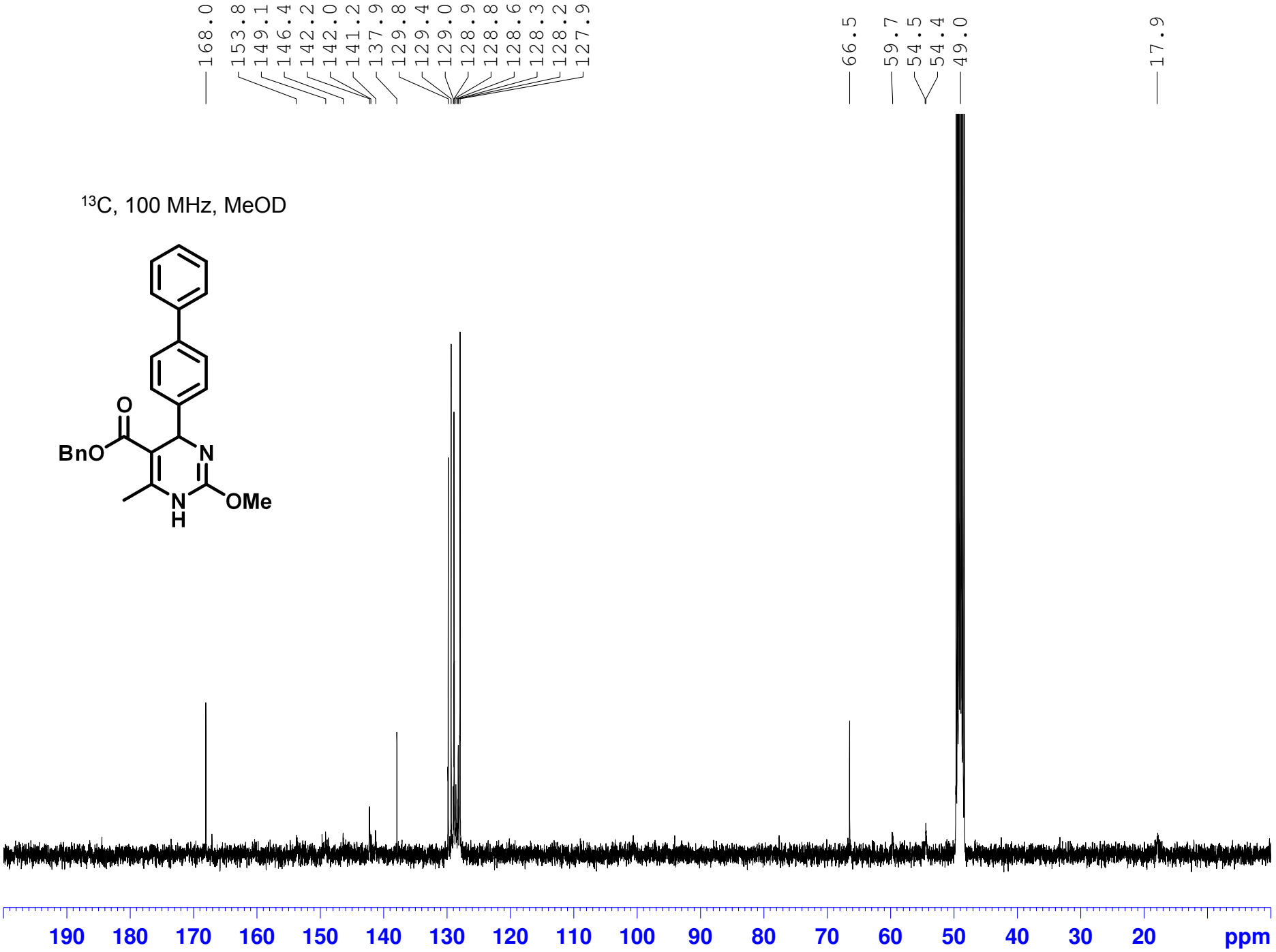


AMT551-071 (8c)

Benzyl 4-([1,1'-biphenyl]-4-yl)-2-methoxy-6-methyl-1,4-dihydropyrimidine-5-carboxylate **(10)**

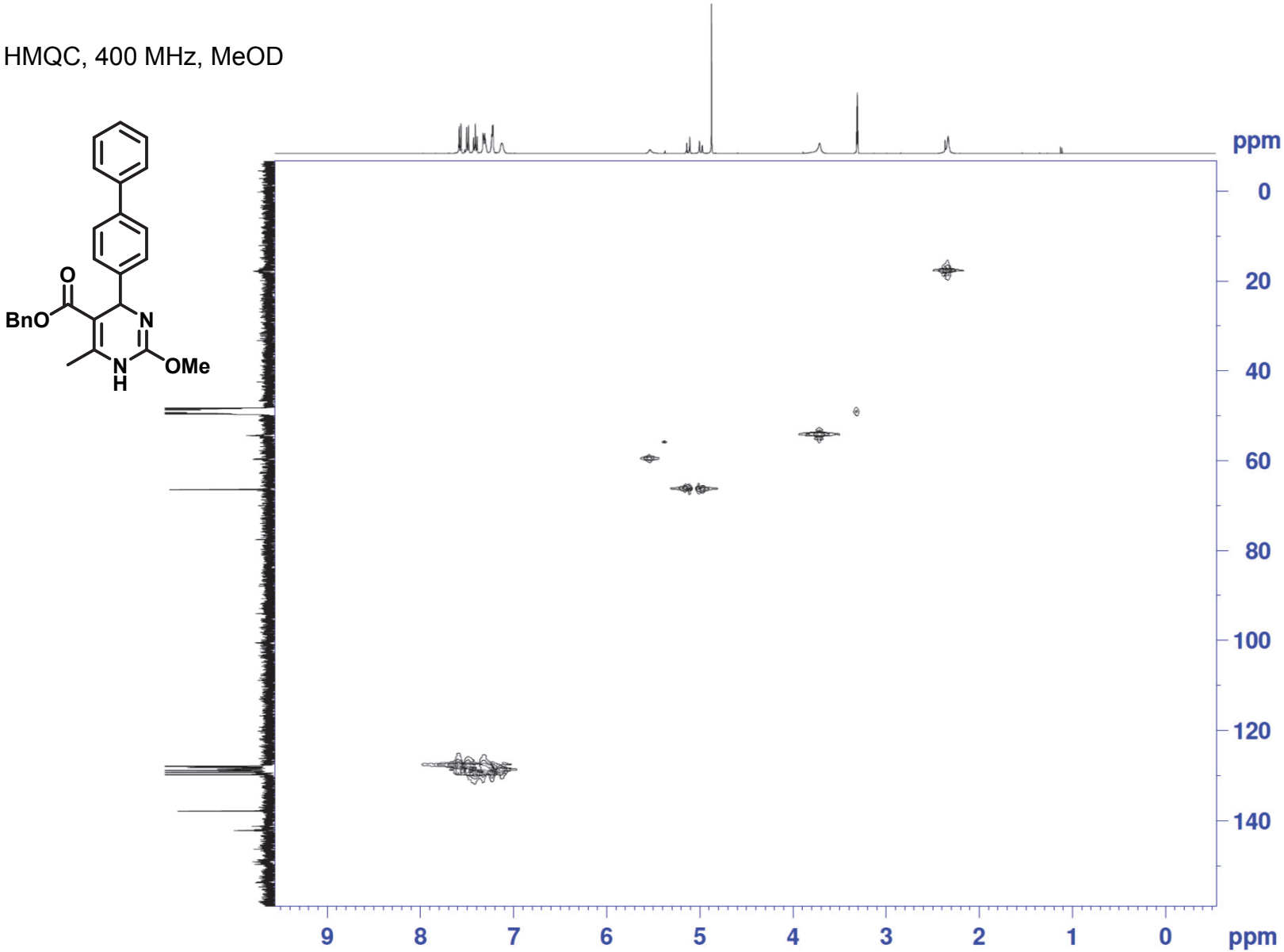


Benzyl 4-([1,1'-biphenyl]-4-yl)-2-methoxy-6-methyl-1,4-dihydropyrimidine-5-carboxylate **(10)**



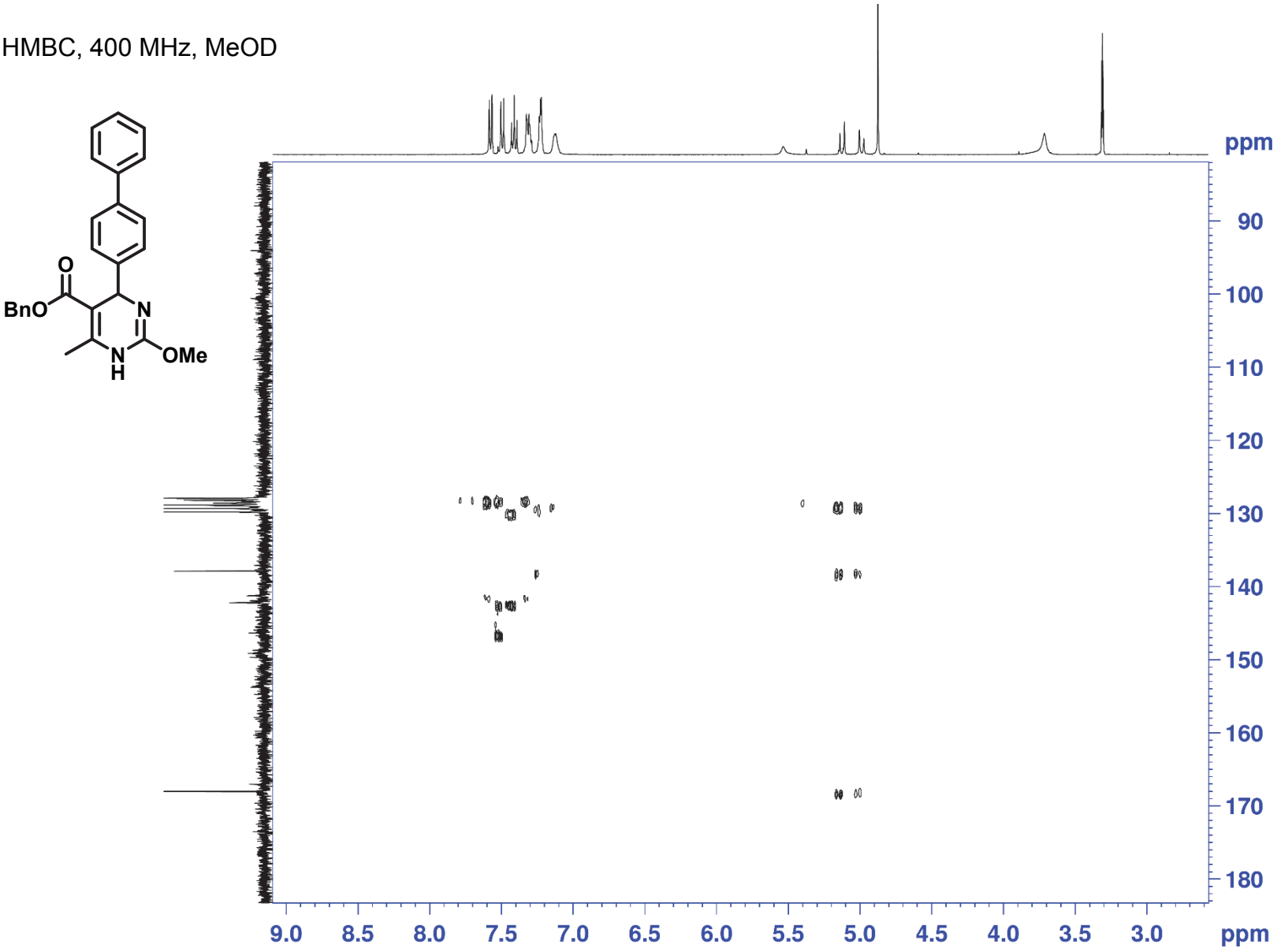
Benzyl 4-([1,1'-biphenyl]-4-yl)-2-methoxy-6-methyl-1,4-dihydropyrimidine-5-carboxylate **(10)**

HMQC, 400 MHz, MeOD

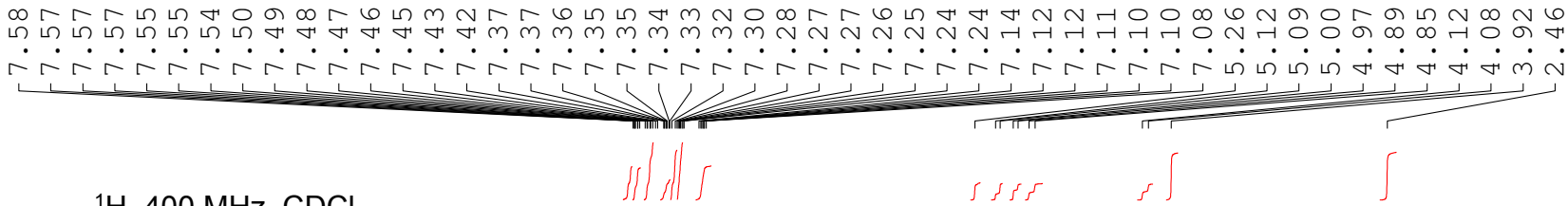


Benzyl 4-([1,1'-biphenyl]-4-yl)-2-methoxy-6-methyl-1,4-dihydropyrimidine-5-carboxylate **(10)**

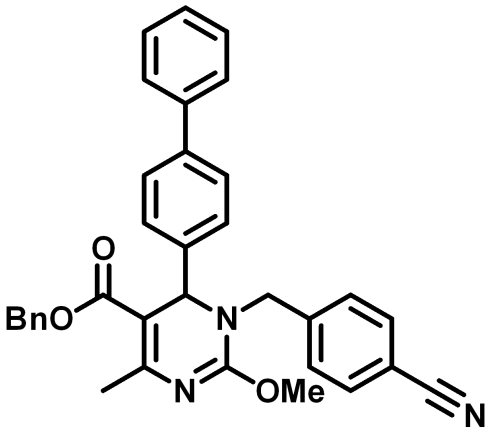
HMBC, 400 MHz, MeOD



Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-2-methoxy-6-methyl-1,4-dihydro-3λ4-pyrimidine-5-carboxylate **(11)**



^{1}H, 400 MHz, $CDCl_3$



Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-2-methoxy-6-methyl-1,4-dihydro-3λ4-pyrimidine-5-carboxylate **(11)**

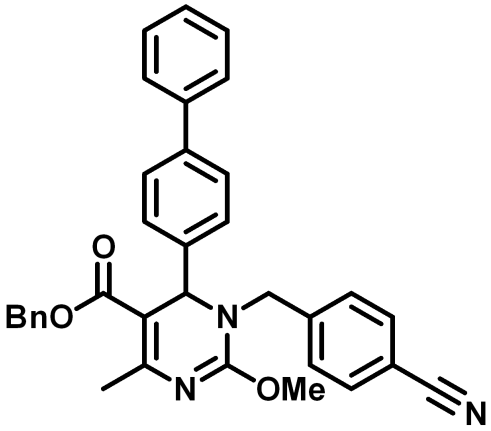
166.1
158.3
156.7
142.0
141.2
140.9
140.7
136.5
132.6
128.9
128.4
128.0
127.9
127.9
127.5
127.4
127.1
118.7
111.5
103.3

77.5
77.1
76.8

65.6
60.9
55.1
48.9

23.6

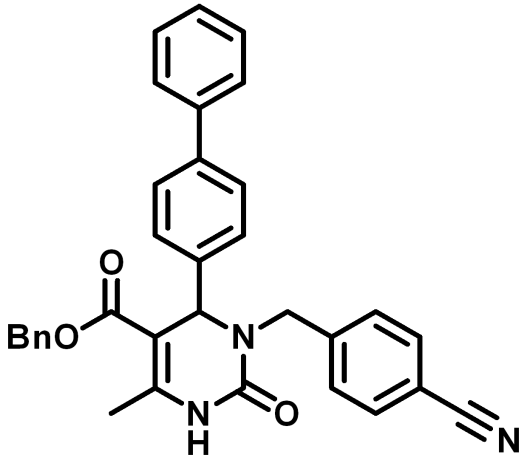
^{13}C, 100 MHz, $CDCl_3$



Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(17)**

9.05 7.64 7.62 7.58 7.57 7.51 7.50 7.49 7.47 7.46 7.41 7.39 7.38 7.38 7.37 7.36 7.34 7.33 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.27 7.27 7.26 7.15 7.14 7.14 7.13 7.12 7.11 5.22 5.19 5.13 5.11 5.03 5.00 3.94 3.91 2.39

^{1}H, 500 MHz, $CDCl_3$



11 10 9 8 7 6 5 4 3 2 1 ppm

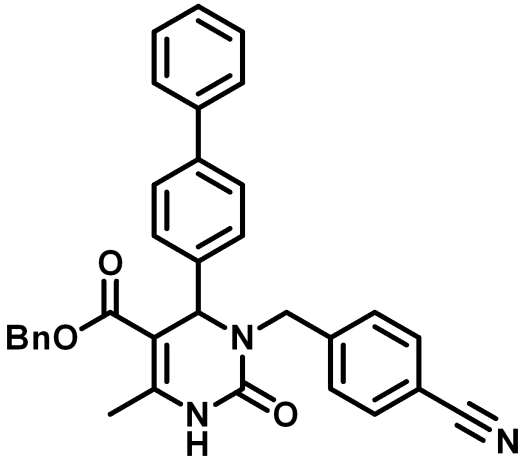
0.98 2.04 2.04 4.15 3.06 5.16 1.97 2.03 1.02 1.00 0.97 3.04

Benzyl 4-([1,1'-biphenyl]-4-yl)-3-(4-cyanobenzyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate **(17)**

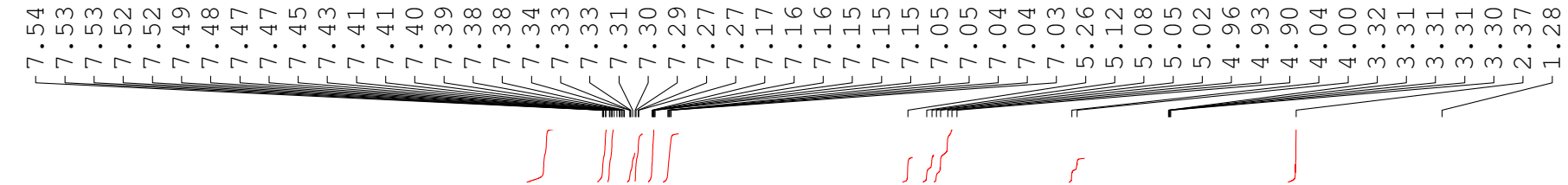
165.2 153.6 147.2 142.2 141.4 140.6 139.9 136.0 132.6 129.0 128.6 128.5 128.2 128.1 128.0 127.6 127.6 127.1 118.7 111.6 101.2

77.4 77.1 76.9 66.1 59.8 47.7 18.8

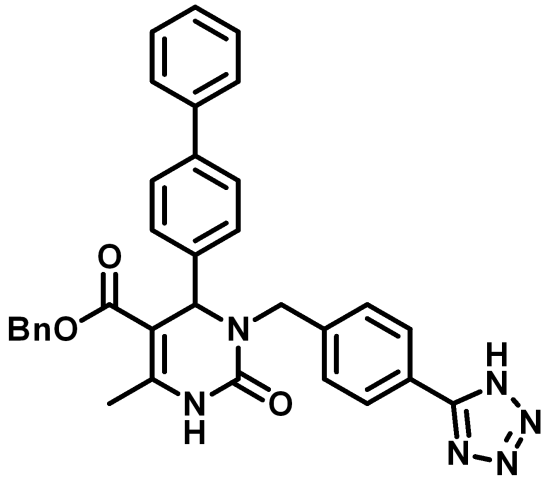
^{13}C, 125 MHz, $CDCl_3$



Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

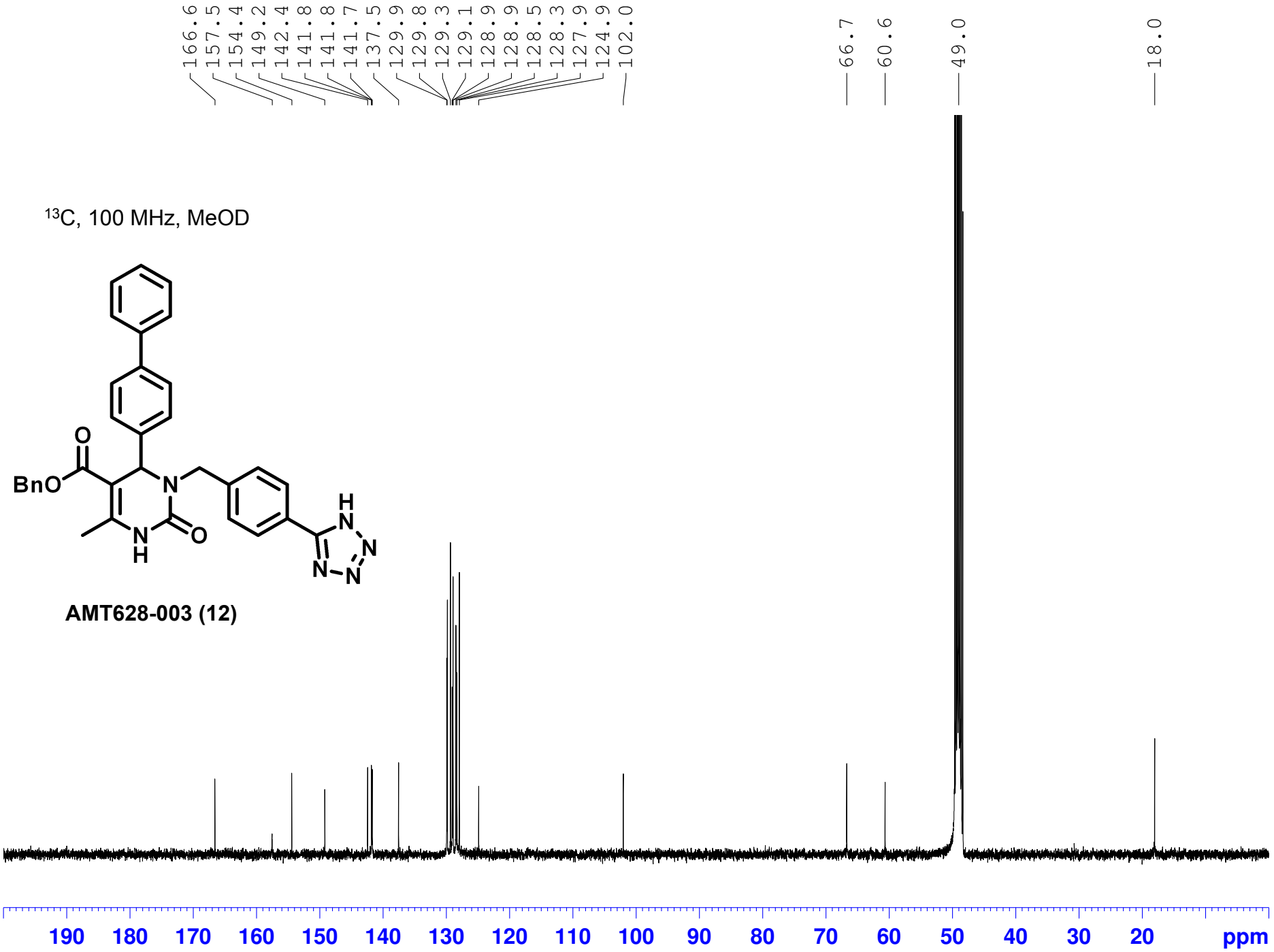


^{1}H, 400 MHz, MeOD



AMT628-003 (12)

Benzyl 3-(4-(1H-tetrazol-5-yl)benzyl)-4-([1,1'-biphenyl]-4-yl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate

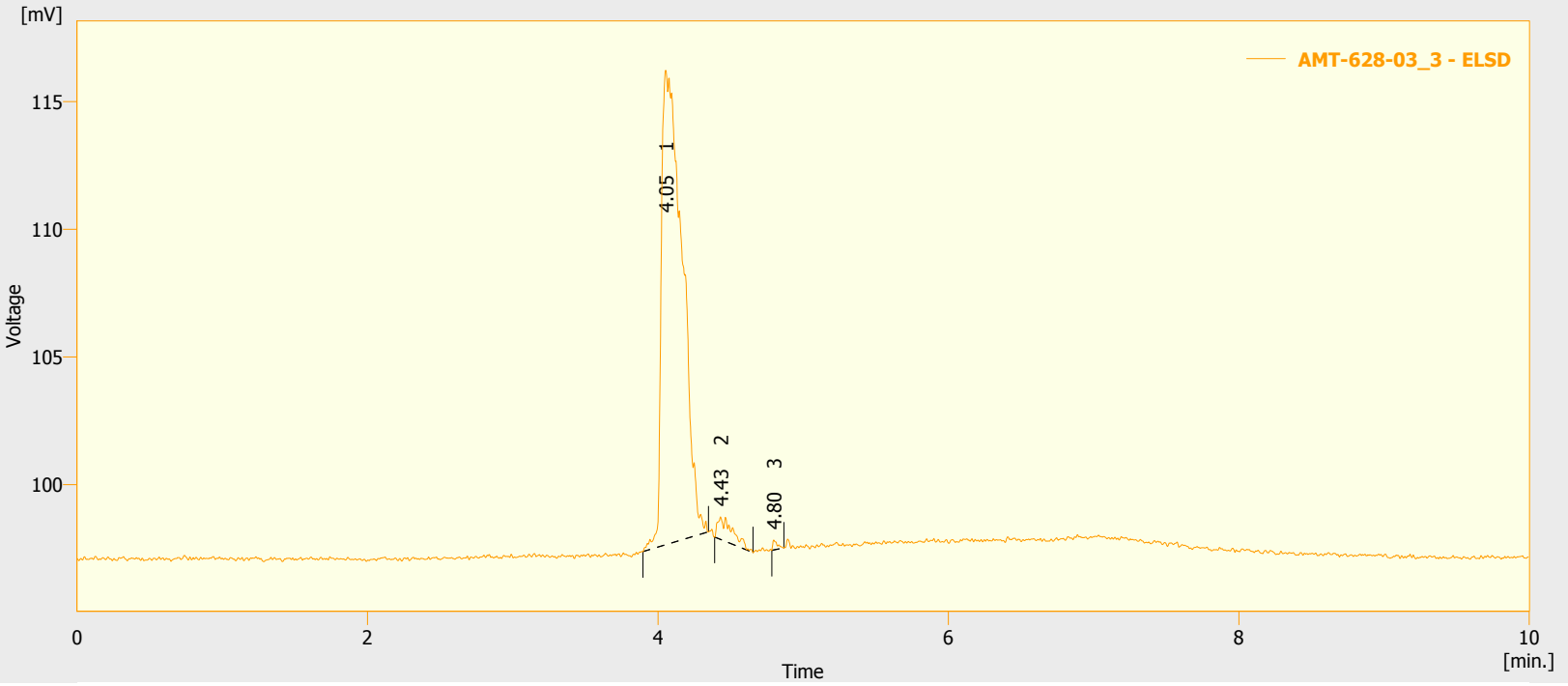


Clarity - Agilent ELSD385

Evap:45 Neb:45 Gas 1.20

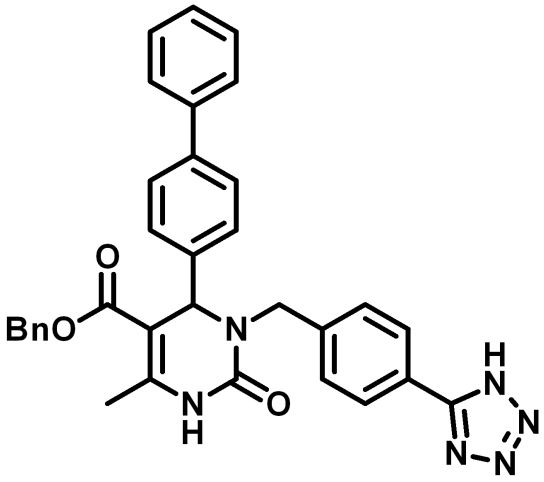
Chromatogram Info:

File Name	: C:\CLARITY\WORK1\DATA\AMT-628-03_3.PRM	File Created	: 11/26/2014 10:13:13 AM
Origin	: Acquired, Acquisition started 11/26/2014 10:03:13 AM	Acquired Date	: 11/26/2014 10:13:13 AM
Project	: C:\Clarity\Projects\Work1.PRJ	By	: None



Result Table (Uncal - AMT-628-03_3 - ELSD)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.053	184.832	18.583	96.0	93.6	0.18	
2	4.430	6.825	0.892	3.5	4.5	0.05	
3	4.797	0.814	0.386	0.4	1.9	0.03	
	Total	192.471	19.862	100.0	100.0		



AMT628-003 (12)