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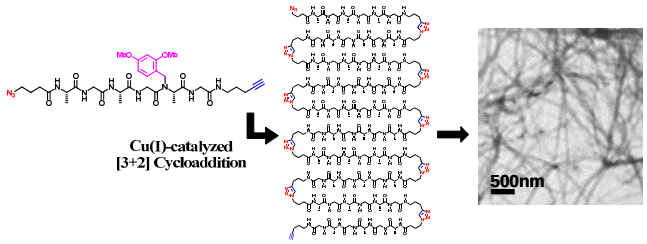


Cu(I)-catalyzed azide–alkyne cycloaddition polymerization of a peptide monomer induced folding of the formed polymer into well-defined β-sheets which further self assemble into hierarchical nanofibrils. The antiparallel β-sheet structure was confirmed by FTIR, CD and powder X-ray diffraction. TEM and AFM micrographs prove the formation of hierarchical amyloid-like nanofibrils.

"Click" to Fold: Cycloaddition-Promoted Self-Assembly of a Polymer into Well-Defined β-Sheets and Hierarchical Nanofibrils

*Ting-Bin Yu, Jane Z. Bai, Zhibin Guan**

Department of Chemistry, University of California, 1102 Natural Sciences 2,

Irvine, California 92697-2025

Supporting Information

I. General Information.

^{1}H NMR spectra were taken on 500MHz and 600MHz Bruker instruments. NMR chemical shifts were reported as δ values in ppm relative to TMS or deuterated solvent: $CDCl_3$ (7.27), DMSO-*d6* (2.50), D_2O (4.80), CD_3OD (4.78, 3.31). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant(s) in Hz. Multiplets were reported over the range (in ppm) it appeared. ^{13}C NMR spectra were taken on 125MHz and 150MHz Bruker instruments. Carbon NMR data were recorded relative to the following solvent signals: $CDCl_3$ (77.0), DMSO-d_6 (39.51), CD_3OD (49.15). All solvents used in reactions were from alumina filtration system. Moisture sensitive reactions were performed under nitrogen atmosphere using flame-dried glassware and standard syringe/septa techniques. Extraction solvents were commercial grade. Flash Chromatography was performed using forced flow of the indicated solvent systems over Fisher silica gel (230 - 400 mesh). All glassware was flame dried before use, and reactions were carried out under nitrogen atmosphere. All buffer solutions were corrected by pH-meter. Infrared (IR) spectra were recorded on a MIDAC Grams/Prospect FT-IR spectrometer using a KBr pellet. Circular dichroism spectroscopy was performed on a Jasco J-810 spectropolarimeter (band width: 1nm, response: 1sec., sensitivity: standard, l range: 250-190 nm, data pitch: 0.5 nm, scanning speed: 20 nm/min., accumulation: 5). Mass spectral data (both ES/MS and HRMS) was obtained on a Micromass auto spec spectrometer. MALDI-TOF data was obtained on Applied Biosystems Voyage-DE STR. Gel Permeation Chromatography (GPC) was carried out using an Agilent 1100 Series GPC-SEC Analysis System along with a mixed bed Plgel Mixed-C column from Polymer Labs. The eluent was DMF with 0.1% LiBr and a flow rate of 1.0 mL / min was used. The calibration was performed using poly(ethylene glycol) (PEG)-based molecular weight standards. HPLC analysis was performed using Rainin SD-200 solvent delivery system, UV-1 detector unit and Zobax-80SB C18 reversed phase analytical column (manufactured by Agilent n Varian). The typical flow rate for the analytical analysis was 1 mL/min. In all cases, water and acetonitrile buffers were used with 0.1% TFA. All other chemicals were purchased from Aldrich, ACROS, Novabiochem, or TCI and used without further purification.

II. Synthesis and Characterization

Experimental details of the solid phase synthesis:

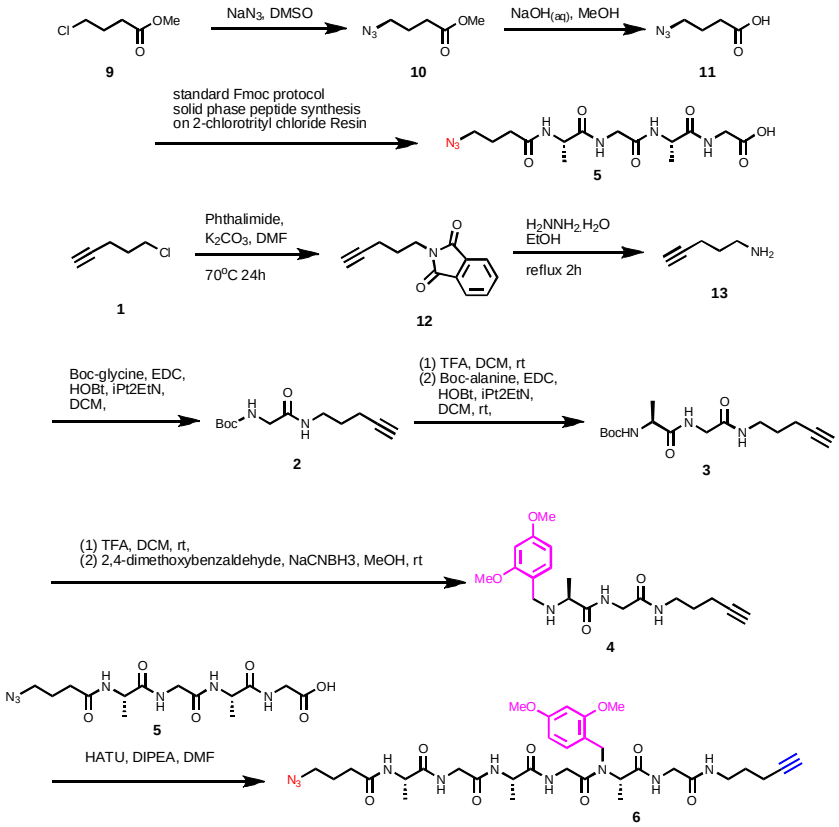
The peptides **5** (Scheme S1) were synthesized by solid phase peptide synthesis (SPPS) following standard Fmoc protocol[1] on 2-chlorotrityl chloride resin using 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and/or O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) as coupling reagents. All the peptides were characterized by analytical HPLC method: 5 - 100% CH_3CN in H_2O gradient over 20 min at 214 nm, 1 mL/min on Agilent Zobax-80SB C18 column.

Standard protocol for SPPS on 2-chlorotrityl chloride resin:[1]

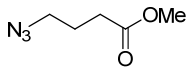
In a 250mL round bottom flask, a suspension of 5.00g 2-chlorotrityl chloride resin (loading: 1.27 mmol/g) and 3.0 equiv of Fmoc-Gly-OH (11.33g, 38.1 mmol) in 50 mL DCM were stirred for 1 hour, followed by addition of 5.0 equiv of *N*,*N*-diisopropylethylamine (DIPEA). The mixture was stirred for 3 hours at room temperature. The resin was filtered in a solid-phase synthesis reaction vessel and washed with DMF (5 x 50 mL), DCM (5 x 50 mL) and NMP (5 x 50 mL). The resin was then added with capping reagent (DIPEA/MeOH/DCM = 1/2/17) and agitated with N_2 gas for 1 hour. the solution was drained and the resin was washed with DMF (5 x 50 mL), DCM (5 x 50 mL). A preactivated solution of Fmoc-amino acid (50.8 mmol), HBTU (50.8 mmol) and DIPEA (76.2 mmol) in 20 ml NMP was added into the resin for the subsequent couplings. The reaction mixture was agitated with N_2 for 2 hours. The solution was drained and the resin was then washed with DMF (5 x 50 mL), DCM (5 x 50 mL). All the reactions were monitored by the Kaiser test. The Fmoc protecting group was removed with 50 mL of 20% piperidine in NMP twice. The mixture was agitated for 30 minutes, the solution was drained, and the resin was washed with 3 x 50 mL of DMF and 3 x 50 mL of CH_2Cl_2.

After all amino acids were coupled, the resin was treated with a solution containing 10% TFE, 10% AcOH, and 80% DCM for 3 hours at room temperature. The cleavage solution was then transferred to a round bottle flask with hexane and then concentrated in vacuo. Cold ether was added subsequently and white powder precipitated out immediately. The peptide was used without any purification.

Scheme S1. The Synthesis of monomer **6**.

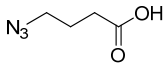


Compounds **10, 11, 12, 13** were prepared according to the literature procedure.[2,3] Their structures were confirmed by ^{1}H, ^{13}C NMR and mass spectrometry, respectively.



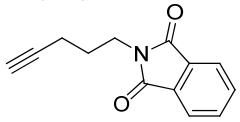
10

(10) Methyl 4-azidobutyrate. Methyl 4-chlorobutyrate (34.25g, 250 mmole) and sodium azide (22.5g, 346 mmole) were dissolved in DMSO (115 mL) in a 500mL round bottom flask. The mixture solution was heated to 45ºC and stirred for 24h. After the mixture was cooled down to room temperature, 200 mL water was added and the mixture was extracted with Et_2O (3 x 100 ml). The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated on a rotary evaporator to give **10** as colorless liquid (35.34g , 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.60 (s, 2H), 3.36 (t, *J* = 6.8, 2H), 2.38 (t, *J* = 7.2, 2H), 1.81-1.75 (m, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ 172.7. 51.4, 49.9, 30.4, 23.8; MS (ESI), *m/z* calcd for $[C_5H_9N_3O_2 + H]^+$ = 144.1; found 144.1.



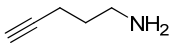
11

(11) 4-Azidobutyric acid. In a in a 500 mL flask compound **10** (33.1g 231 mmol) was dissolved in 2N NaOH (461 mL, 2.0eq) solution. A small amount of MeOH was added slowly to make it a homogeneous solution. The mixture was stirred at room temperature for 48 hours, then MeOH was removed under vacuo. The aqueous layer was washed with Et_2O (4 x 50 mL), then acidified with conc. HCl to pH 1. The compound was extracted with Et_2O (4 x 100 ml), and the combined organic fractions were dried over anhydrous $MgSO_4$, filtered, and concentrated on a rotary evaporator to give **11** as transparent colorless liquid (28.74g,96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.72 (s, 1H), 3.36 (t, *J* = 6.4, 2H), 2.4 (t, *J* = 7.2, 2H), 1.92-1.86 (m, 2H);^{13}C NMR (125MHz, $CDCl_3$) δ 179.2. 50.4, 30.8, 23.8; MS (ESI), *m/z* calcd for $[C_4H_7N_3O_2 + H]^+$ = 130.1; found 130.1.



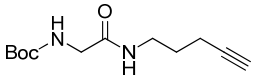
12

(12) 1-Phthalimido-4-pentyne. In a 250 mL flask, 5-chloro-1-pentyne (5.13g, 50 mmol), phthalimide (8.83g, 60 mmol), K_2CO_3(5.13g, 50 mmol) and KI (100mg) were suspended in DMF (50 mL). The mixture solution was heated at 70ºC for 16 hours. Then the solution was cooled down to room temperature and 50mL H_2O was added into solution. The mixture was extracted by Et_2O (200 mL x 4) and the combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated on a rotary evaporator. The crude residue was further purified by flash chromatography (DCM) to give **12** as white solid (10.24g, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.84 (m, 2H), 7.74-7.71 (m, 2H), 3.81 (t, *J* = 7.5, 2H), 2.28 (td, *J* = 7.0, 2.5, 2H), 1.97-1.92 (m, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 168.3. 133.9, 132.1, 82.9, 69.0, 37.1, 27.2, 16.2; MS (ESI), *m/z* calcd for $[C_{13}H_{11}NO_2 + H]^+$ = 214.1; found 214.1.



13

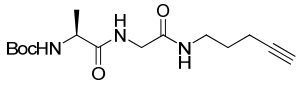
(13) 1-Amino-4-pentyne. In a 250 mL flask was added **12** (7.40g, 34.7 mmol) in EtOH (70 ml) to give a white suspension. Then hydrazine monohydrate was added into solution to give a clean solution. The reaction mixture was heated at 70ºC under stirring for 2 hours, during which time much white solid precipitated. After the mixture solution was cooled down to room temperature, 50 mL H_2O was added into solution followed by addition of 2N HCl to adjust its pH to 3.5. The precipitate was filtered and the filtrate was concentrated using a rotary evaporator. The residue was cooled down to 0ºC and treated with aq. NaOH (10N, 30 mL). Then the aqueous solution was extracted with DCM (3 x 100 mL). The combined organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated on a rotary evaporator to give **13** as green oil (2.16g, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.77 (t, *J* = 7.0, 2H), 2.22 (td, *J* = 7.0, 2.7, 2H), 1.92 (t, *J* = 2.7, 1H), 1.83 (s, 2H), 1.66-1.62 (m, 2H); ^{13}C NMR (125MHz, $CDCl_3$) δ 83.7, 68.6, 40.7, 31.6, 15.7.



2

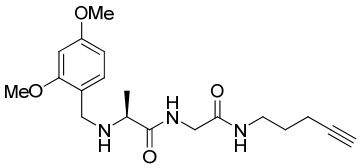
(2) *Tert*-butyl [2-oxo-2-(pent-4-yn-1-ylamino)ethyl]carbamate. Compound **13** (1.58g, 19.0 mmol) and Boc-Gly-OH (2.28g, 13.0 mmol) were dissolved in 100 mL DCM containing 4.56 mL DIPEA, into which EDC (3.64g, 19.0 mmol) and HOBt (2.57g, 19.0 mmol) were added. The mixture was stirred at room temperature for 12 hours. Then 100 mL of H_2O and 250 mL of EtOAc were added into mixture solution. The combined organic layer was washed with H_2O (100 mL × 1), 1M HCl (100

mL × 1), sat. $NaHCO_3$ (100 mL × 1), and brine, and then dried over anhydrous $MgSO_4$, filtered, and concentrated on a rotary evaporator to give **2** as white solid (3.06g, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.51 (s, 1H), 5.27 (s, 1H), 3.77 (d, *J* = 6.3, 2H), 3.39 (q, *J* = 6.3, 2H), 2.26-2.23 (m, 2H), 1.99 (s, 1H), 1.76-1.73 (m, 2H), 1.45 (s, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 169.5, 156.1, 83.4, 80.3, 69.2, 44.4, 38.6, 28.3, 27.9, 16.0; HRMS (ESI), *m/z* calcd for $[C_{12}H_{20}N_2O_3 + Na]^+$ = 263.1372; found 263.1363.



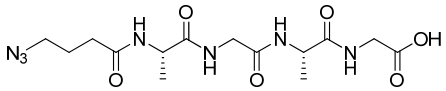
3

(3) *Tert*-butyl [(2*S*)-1-oxo-1-{[2-oxo-2-(pent-4-yn-1-ylamino)ethyl]amino}propan-2-yl]carbamate. In a 250 mL flask was added **2** (4.90g, 20.39 mmol) in a TFA/DCM solution (15 mL/10 mL). After stirring the solution at room temperatire for 3 hours, TFA/DCM was removed under vacuum. The residue was dissvoled in DCM and further evaporated in vacuo. The residue was dried under vacumn for 1 hour. Then the residue and Boc-Alanine were dissolved in DCM (50 mL) and cooled down in a ice bath. DIPEA was added into solution. EDC and HOBt were added into solution subsequently. The mixture was stirred at room temperature for 12 hours. Then 100 mL of H_2O and 250 mL of EtOAc were added into mixture solution. The combined organic layer was washed with H_2O (100 mL × 1), 1M HCl (100 mL × 1), sat. $NaHCO_3$ (100 mL × 1), and brine, and then dried over anhydrous $MgSO_4$, filtered, and concentrated on a rotary evaporator. The residue was purified by flash chromatography (MeOH/DCM=1:9) to give **3** as white solid (5.70g, 90%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.10 (s, 1H), 7.67 (s, 1H), 7.11 (d, *J* = 6.5, 1H), 6.51 (s, 1H), 6.47 (d, *J* = 8.5, 1H), 3.92-3.90 (m, 1H), 3.68-3.58 (qd, *J* = 16.4, 5.9, 2H), 3.18-3.06 (m, 2H), 2.78 (s, 1H), 2.17-2.13 (m, 2H), 1.60-1.56 (p, *J* = 7.0, 2H), 1.39 (s, 9H), 1.16 (d, *J* = 7.0, 3H); ^{13}C NMR (125MHz, $CDCl_3$) δ 173.2, 168.9, 155.9, 83.4, 80.6, 69.0, 50.94, 43.2, 28.3, 28.0, 17.9, 16.0; HRMS (ESI), *m/z* calcd for $[C_{15}H_{25}N_3O_4 + Na]^+$ = 334.1743; found 334.1742.



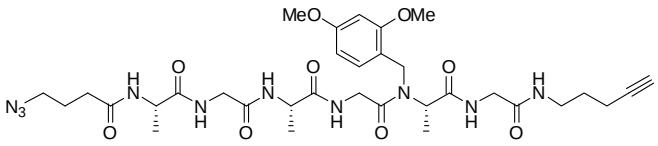
4

(4) (S)-2-(2,4-dimethoxybenzylamino)-N-(2-oxo-2-(pent-4-ynylamino)ethyl) propanamide. In a 100 mL flask, **3** (0.62g, 2.0 mmol) was dissolved in 20 mL TFA/DCM (1:1). The mixture was stirred at room temperature for 2 hours and then the solution concentrated on a rotary evaporator. The residue was added with 2,4-dimethoxybenzylaldehyde (0.33g, 2.0 mmol), 0.35mL Et_3N and 10 mL MeOH. Then the mixture was added with $NaCNBH_3$ (0.15g, 2.4 mmol). The mixture was stirred at room temperature for 48 hours. Then the solution was concentrated on a rotary evaporator. The residue was purified by flash chromatography with EtOAc to give yellow gel-like product 0.60g (1.66 mmol, 83 %) of **4.** ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.07 (s, 1H), 7.87 (s, 1H), 7.18 (d, *J* = 8.5, 1H), 6.51 (s, 1H), 6.47 (d, *J* = 8.5, 1H), 3.74 (d, *J* = 7.0, 4H), 3.70 (d, *J* = 5.5, 2H), 3.55 (q, *J* = 16.4, 2H), 3.13-3.10 (m, 3H), 2.78 (s, 1H), 2.17-2.15 (m, 2H), 1.59-1.56 (m, 2H), 1.14 (d, *J* = 7.0, 3H); ^{13}C NMR (125MHz, DMSO-d_6) δ 168.5, 160.0, 159.2, 130.3, 104.3, 98.2, 84.0, 71.4, 56.3, 55.4, 55.2, 45.2, 41.8, 28.1, 18.6, 15.3; HRMS (ESI), *m/z* calcd for $[C_{19}H_{27}N_3O_4 + H]^+$ = 362.2080; found 362.2074.



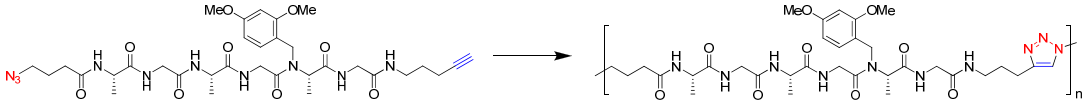
5

(5) (5S,11S)-16-azido-5,11-dimethyl-4,7,10,13-tetraoxo-3,6,9,12-tetraazahexadecan-1-oic acid. Peptide **5** was synthesized according to the standard solid phase peptide synthesis procedure as described earlier on 2-chlorotrityl chloride resin[1]. Following cleavage from resin, the final product was purified by precipitation in Et_2O. The yield is 64% according to the initial loading on the resin. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.15 (t, *J* = 6.6, 3H), 7.92 (d, *J* = 7.0, 1H), 4.31-4.20 (m, 2H), 3.76-3.65 (m, 4H), 3.33-3.30 (t, *J* = 6.8, 2H), 2.20 (t, *J* = 7.0, 2H), 1.76-1.70 (m, 2H), 1.20 (t, *J* = 8.8, 6H); ^{13}C NMR (125MHz, DMSO-d_6) δ 172.8,172.4, 171.4, 171.1, 168.4, 50.3, 48.5, 48.0, 42.0, 40.7, 31.9, 31.0, 24.4, 22.1, 18.3, 17.8, 14.0; HRMS (ESI), *m/z* calcd for $[C_{14}H_{23}N_7O_6 + Na]^+$ = 408.1608; found 408.1601.



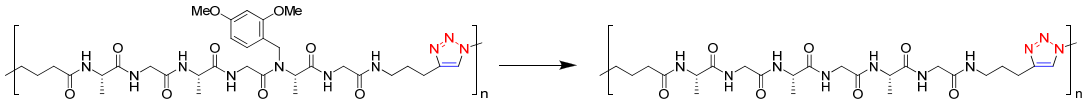
6

(6) 4-azido-N-((2S,8S,14S)-13-(2,4-dimethoxybenzyl)-8,14-dimethyl-3,6,9,12,15,18-hexaoxo-4,7,10,13,16,19-hexaazatetracos-23-yn-2-yl)butanamide. In a 250 mL round bottom flask, **4** (0.365g, 1.01 mmol) and peptide **5** (0.39g, 1.01 mmol) were dissolved in 15 mL a DMF:DMSO (95:5) mixed solvent containing 0.265 mL DIPEA. Following addition of HATU (0.461g, 1.2 mmol), the mixture was stirred at room temperature for 48 hours. After addition of 100 mL of H_2O to the completed reaction solution, the mixture was extracted with EtOAc (50 mL × 2). The combined organic layer was washed with H_2O (100 mL × 1), 1M HCl (100 mL × 1), sat. $NaHCO_3$ (100 mL × 1), and brine, then dried over anhydrous $MgSO_4$, filtered, and finally concentrated on a rotary evaporator. The residue was purified by flash chromatography with MeOH/DCM (1:9) to give **6** as white solid (349mg, 46%).^{1}H NMR (500 MHz, MeOD-d_4) δ 7.16 (d, J = 8.3, 1H), 6.53 (s, 1H), 6.48 (d, J = 8.3, 1H), 4.62 (d, J = 15.7, 1H), 4.40–4.37 (m, 2H), 4.22 (s, 2H), 4.17 (d, J = 7.2, 1H), 4.05 (d, J = 7.2, 1H), 3.89-3.58 (m, 10H), 3.43 (q, J = 7.0, 1H), 3.32-3.27 (m, 2H), 3.19-3.14 (m, 1H), 2.28 (t, J = 7.2, 2H), 2.16-2.10 (m, 3H), 1.86-1.81 (m, 2H), 1.72-1.70 (m, 2H), 1.36–1.10 (m, 9H); ^{13}C NMR (125MHz, DMSO-d_6) δ 173.3, 172.7,172.4, 172.0, 171.5, 171.1, 169.9, 169.2, 168.9, 168.6, 161.8, 160.6, 159.2, 158.2, 132.8, 129.3, 117.4, 105,2, 104.9, 98.8, 98.7, 84.6, 84.5, 71.9, 71.8, 56.1, 55.9, 55.8, 55.7, 55.3, 50.7, 39.0, 48.5, 48.5, 45.6, 44.0, 43.0, 42.4, 41.5, 38.1, 32.4, 31.2, 28.5, 24.8, 18.7, 18.2, 17.1, 15.83, 15.77, 15.0; HRMS (ESI), *m/z* calcd for $[C_{33}H_{48}N_{10}O_9 + Na]^+$ = 751.3503; found 751.3494.



6 **7**

Procedure for [2+3] cycloaddition polymerization:
7 was prepared according to a modified literature procedure.[5] Peptide monomer **6** (182mg, 0.25 mmol), copper acetate (4mg, 0.03 mmol), and 0.25 mL of N_2-degassed DMF were introduced into a small vial. Under stirring the mixture was heated at 80° C in an oil bath for 2 hours. The initial clear solution was transformed into a dark green gel. After cooling down the polymerization mixture with an ice bath, the gel was dissolved with additional DMF and then polymer was precipitated into 0.1 N HCl (20 mL). The precipitate was purified by consecutive three times of centrifugation and redispersion with 0.1 N HCl. A white solid precipitate was finally isolated and dried under vacuum to give 155mg product **7** (yield: 85%). The number average molecular weight (Mn) of polymer is 11500 and weight number average molecular weight (Mw) is 21750 based on GPC characterization. ^{1}H NMR (500 MHz, d_6-DMSO and *d*-TFA) δ 8.37-8.26 (m, 1H), 7.02 (s, 1H), 6.39-6.33(m, 2H), 4.42-4.07 (m, 7H), 3.83–3.20 (m, 11H), 2.73 (s, 2H), 2.17-2.08 (m, 4H), 1.80 (s, 4H), 1.19-1.10 (m, 9H).



7 **8**

Procedure for cleavage of 2,4-dimethoxybenzyl group:
In a 20 mL sample vial, polymer **7** (5mg) was dissolved in 1 mL TFA mixed solution (TFA/TIPS/H_2O=95:2.5:2.5). After stirring at room temperature for 60min, 9 mL of MeOH was introduced slowly into the vial. Cotton-like precipitate appeared overnight which was purified by three Times of centrifugation and redispersion with MeOH to give 3mg of polymer **8**. ^{1}H NMR (500 MHz, d_6-DMSO and *d*-TFA) δ 8.05 (s, 1H), 4.41 (s, 2H), 4.19–4.13 (m, 3H), 4.97-4.70 (m, 6H), 3.12 (s, 2H), 2.69-2.67 (m, 2H), 2.24-2.10 (m, 4H), 1.74 (s, 1H), 1.08-0.82 (m, 9H).

III. ^{1}H NMR spectra of polymer 7 and 8

After TFA/DCM deprotection, the proton peaks attributed to 2,4-dimethoxybenzyl group completely disappeared (spectra were taken in 50% *d*-TFA and DMSO-*d*6) (Fig. S1).

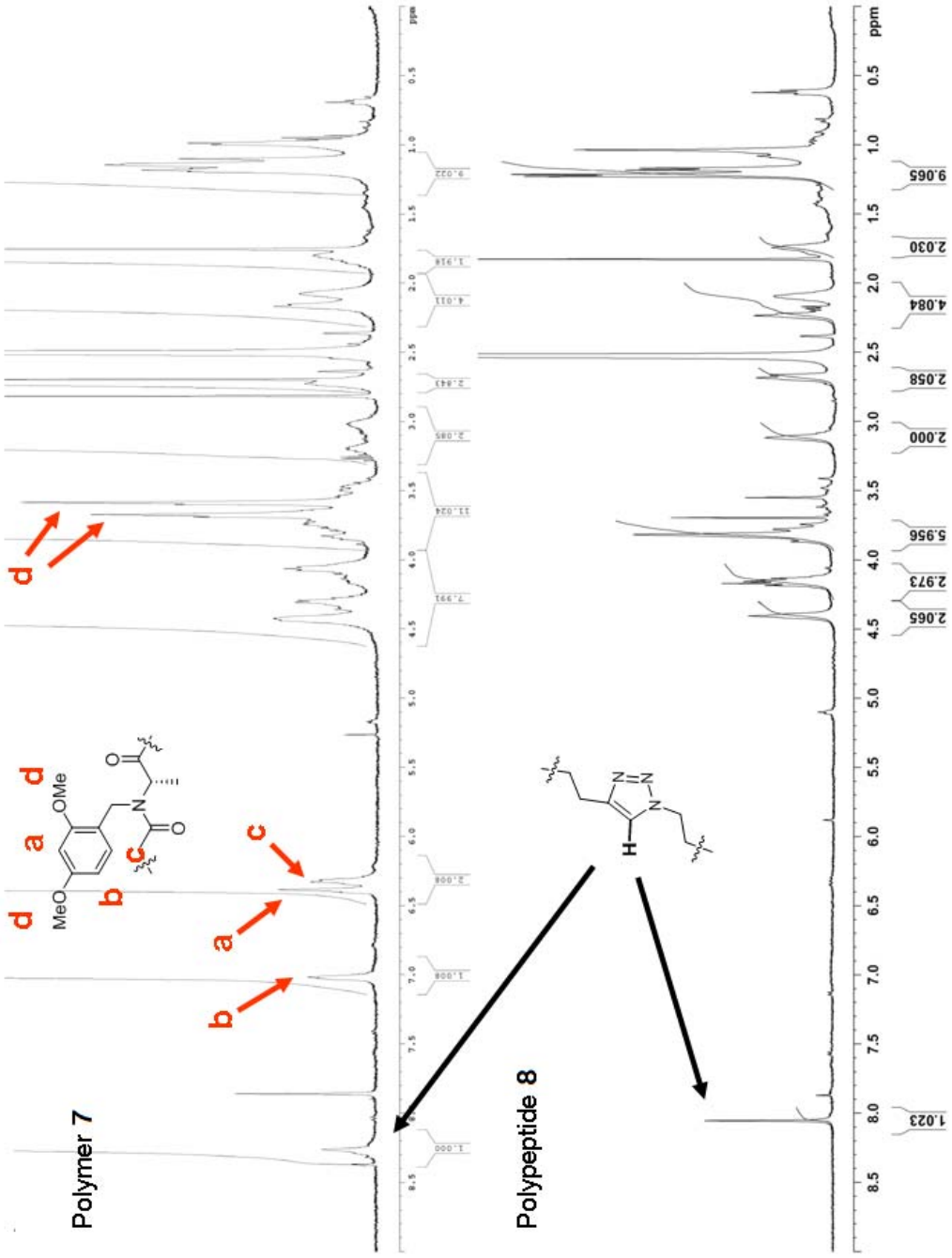


Figure S1. NMR spectra of polymer **7** and **8**.

IV. Circular Dichroism (CD) measurement

Following literature procedure, we utilized CD to identify secondary structure for polymer **8**. 250 μL of peptide **8** solution (~2 mg/mL in hexafluoroisopropanol (HFIP)) was added in a 1.0-mm length UV cell. Far-UV CD spectra were measured at room temperature on a Jasco J-810 spectropolarimeter (band width: 1nm, response: 1sec., sensitivity: standard, l range: 250-190 nm, data pitch: 0.5 nm, scanning speed: 20 nm/min., accumulation: 5). A representative CD spectrum for **8** is shown in Fig. S2. The CD spectra obtained in hexafluoroisopropanol (HFIP) solution exhibit a minima around 206 nm and maxima around 195 nm, which has also been observed in biosynthetic poly$(AG)_3$YG or poly$(AG)_3$HG systems.[6] The unusual shape of spectrum could result from either the formation of π-π stacking in the 1,2,3-triazole ring turn mimics or regular arrangement of β-turn, which might facilitate coupling of the dipole transition moments.[6a]

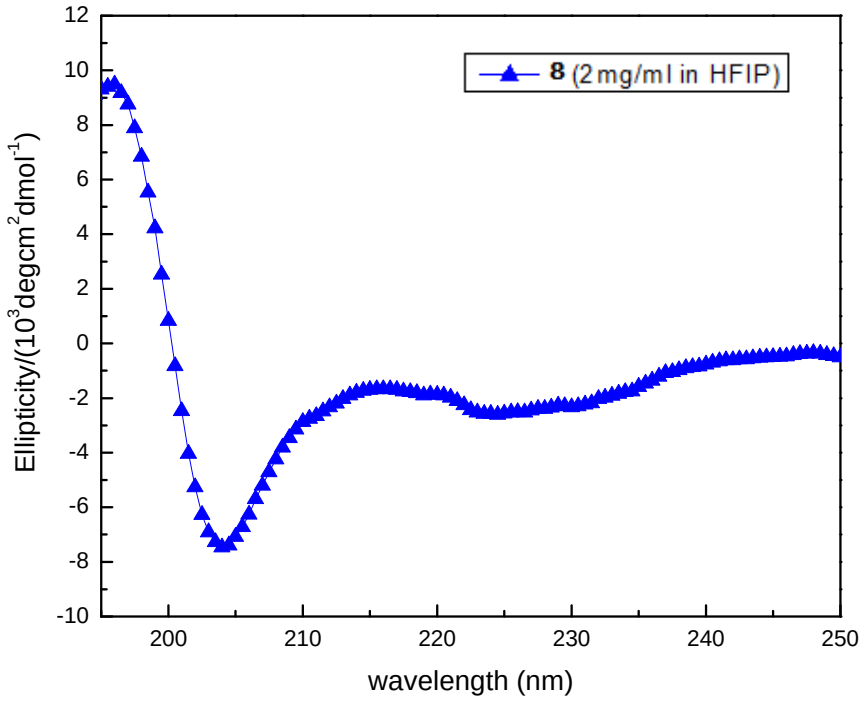


Figure S2. Circular dichroism spectrum of polypeptide **8**.

V. FTIR characterization of polymer 7 and polymer 8

Infrared (IR) spectra were recorded on a MIDAC Grams/Prospect FT-IR spectrometer using a KBr pellet. All powder samples and KBr were ground to reduce the particle size. Then the mixture powder was pressed into a pellet. The IR spectra of polymer **7** revealed a major strong amide I vibration band at ~1655, indicating random coil secondary conformation in peptide (Figure S3a).[7] The IR spectra of polymer **8**, on the other hand, exhibited strong amide I and II vibrational bands at ~1628 cm^{-1} and ~1533 cm^{-1}, characteristic of the β-sheet conformation.[6] In addition, the weak amide I component observed at ~1697 cm^{-1} indicates its antiparallel nature (Figure S3b).[7] The amide I band ~1650 cm^{-1} indicates that some fraction of polymer chain has adopted a secondary structure other than that of the antiparallel β-sheet, where may result from breaking of the crystalline structure while physically mixing sample with KBr salt in the sample preparation.

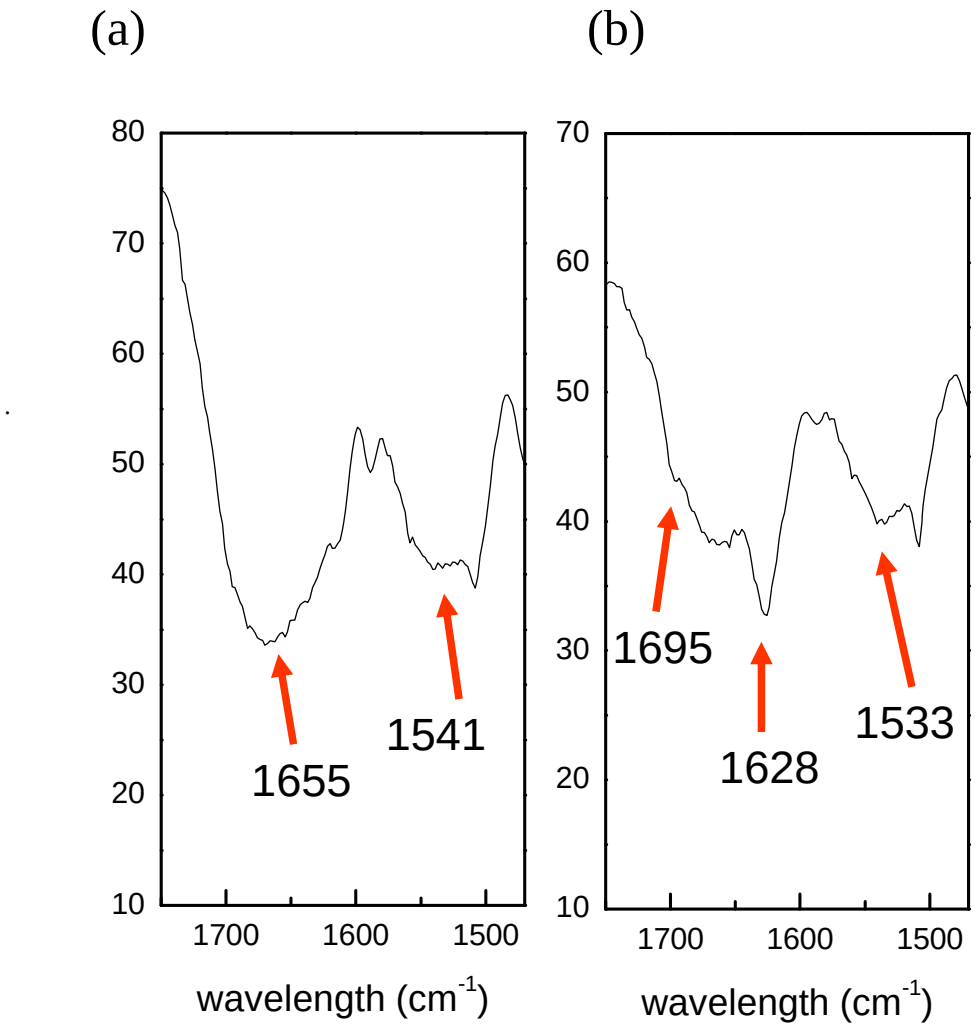
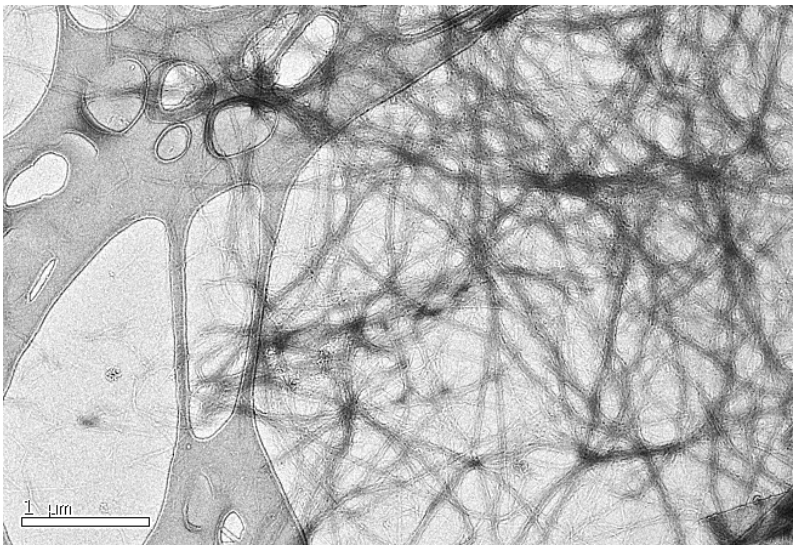


Figure S3. Infrared (IR) spectra of (a) **7** (b) **8**.

VI. Transmission Electron Microscopy (TEM) Analysis

Sample Preparation of Transmission Electron Microscopy: A drop of polymer **8** solutions which crystallized in MeOH/TFA solution with concentrations of 0.5 mg/mL was incubated onto a carbon-coated TEM grid for 1 min, then blotted with filter paper. The grid was floated with 2% uranyl acetate solution. After 60sec incubation, the excess uranyl acetate solution was blotted with filter paper. The sample grid was then dried in vacuo overnight. The investigations were performed on a FEI/Philips CM-20 conventional TEM equipped with an EDAX EDS system operated at an acceleration voltage of 200 kV. Images were recorded either on a CCD camera for bright field imaging. Representative images and histogram of fibril width are shown in Fig. S4 &5, respectively.

A.



B.

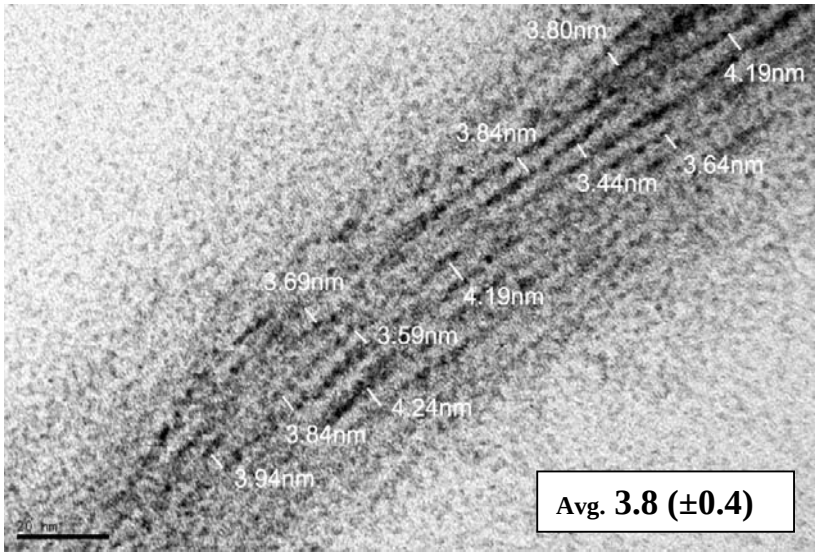


Figure S4. TEM images of fibril formed by polypeptide **8.** (A) Nanofibrils on TEM grid; (B) A zoom up view of one nanofibril. Scale bar on top image: 1μm, scale on bottom image: 20nm.

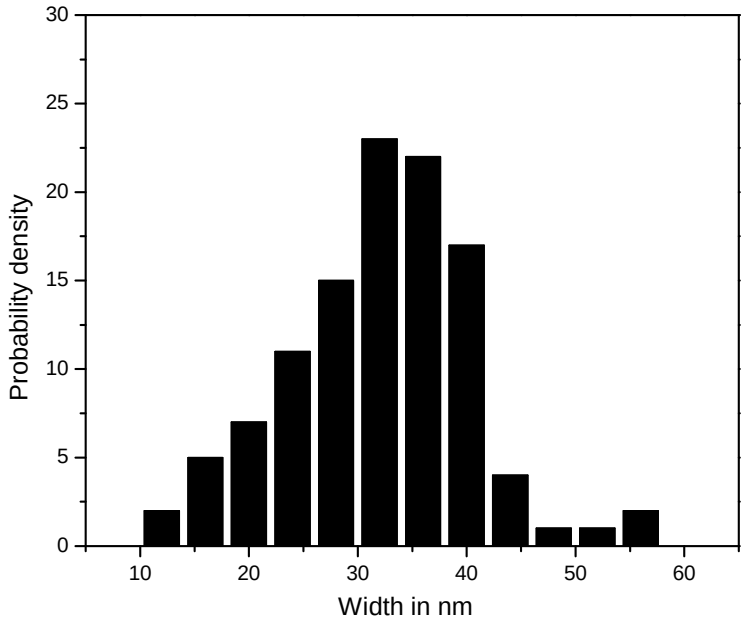


Figure S5. Probability density plot of nanofibril width measured from TEM images of **8**. A total of 110 samplings data were employed in constructing this distribution profile.

VII. Atomic Force Microscopy (AFM) Analysis

Polymer solutions with concentrations of 0.5 mg/mL were spin-coated onto a freshly cleaved mica surface. The morphologies of the samples were analyzed by means of tapping-mode AFM with a Veeco Multimode instrument with a NanoScope IV controller operating in air at room temperature. Height (Figure S6) and phase images were recorded with microfabricated silicon cantilevers (FESP probes, Veeco, Santa Babara). Set point was chosen at attractive regime. Representative images, height profiles and histogram of height for nanofibrils are shown in Fig. S6-8.

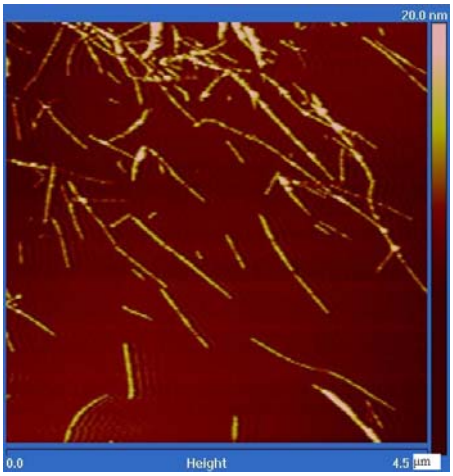


Figure S6. AFM micrograph of fibril formed by polypeptide **8**.

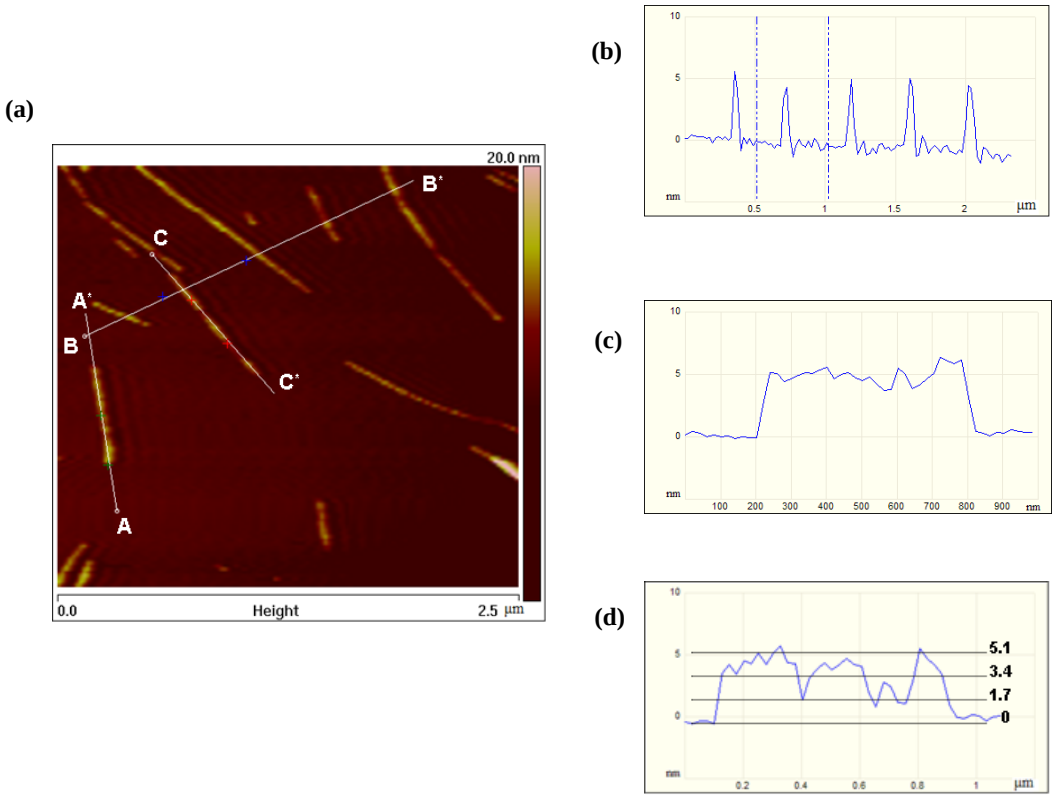


Figure S7. (a) AFM micrograph of fibril formed by polymer **8.** (b) height along A to A* on the fibril. (c) height along B to B* on the fibril. (d) height along C to C* on the fibril.

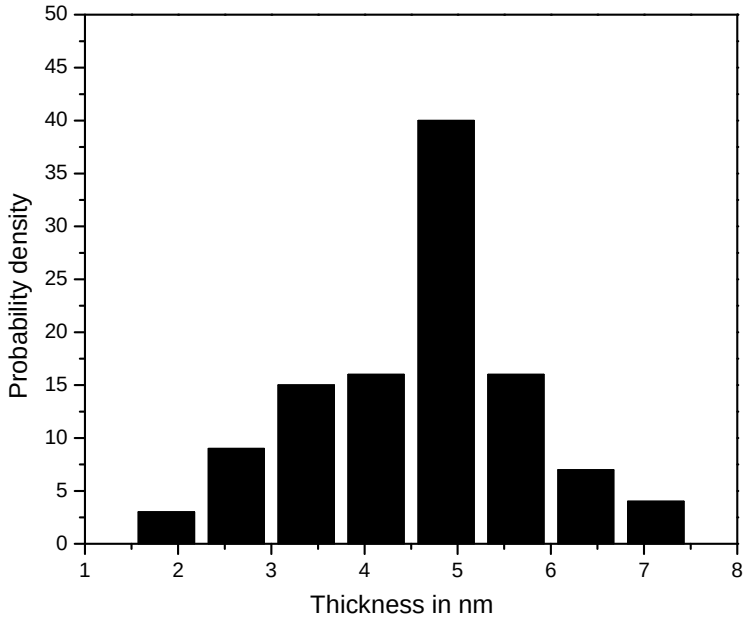


Figure S8. Probability density plot of nanofibril height measured from AFM topographic data of **8**. A total of 110 samplings data were employed in this distribution profile.

VIII. Wide Angle X-Ray Diffraction (WXRD) analysis of 8

The powder of sample was prepared by removing the solvent from the crystallized fibril solution. The crystalline powder sample was packed into a thin-walled glass tube. The powder of the samples were analyzed by means of Four Circle Wide Angle X-ray Spectrometer (WAXS) equipped with an OSMIC double focusing multiplayer monochromator and a MAR 345 mm diameter image plate detector. The X-ray source: 18 kW Rigaku rotating anode x-ray generator (Cu anode, λ = 1.54 Å). The major reflections at d spacings of 4.57, 4.22, and 3.64 Å (Fig. S9), which are consistent with the antiparallel β-sheet d spacings reported for the unoriented fibroin film[8] and the polymer $(AG)_n$ made by genetic engineering.[9]

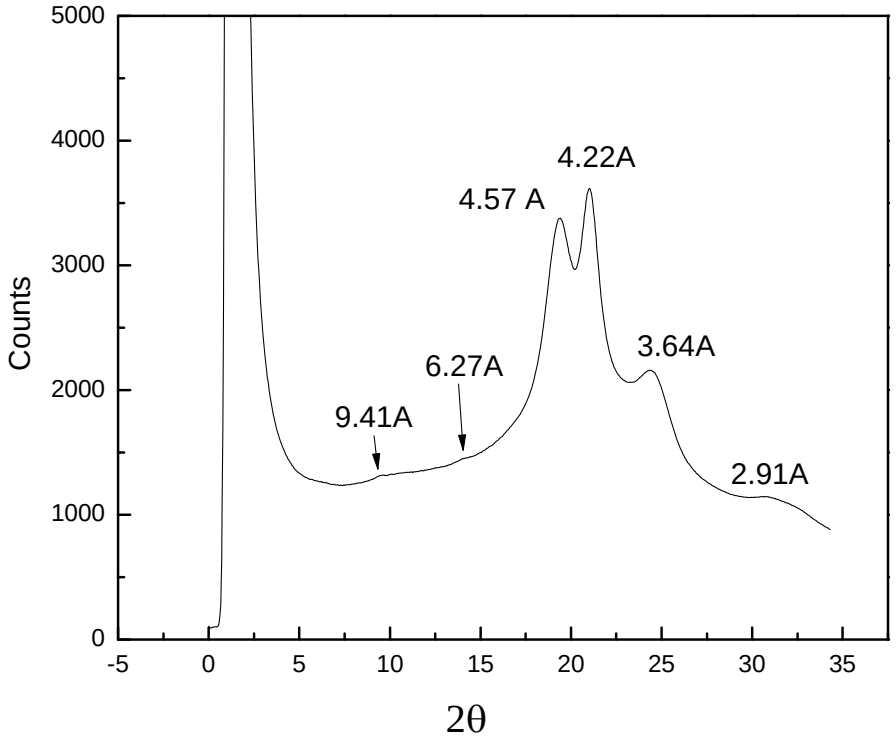


Figure S9. Wide angle X-ray diffraction of solid Polypeptide **8**.

IX. Reference

[1] *NovaBiochem Catalog*, **2003**.
[2] K. Oh, Z. Guan, *Chem. Comm.* **2006**, 3069.
[3] (a) T. E. Muller, A. -K. Pleier, *J. Chem. Soc., Dalton Trans.* **1999**, 583.
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[6] (a) N. I. Topilina, S. Higashiya, N. Rana, V. V. Ermolenkov, C. Kossow, A. A. Carlsen, S. C. Ngo, C. C. Wells, E. T. Eisenbraun, K. A. Dunn, I. K. Lednev, R. E. Geer, A. E. Kaloyeros, J. T. Welch, *Biomacromolecules* **2006**, *7*, 1104.
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(c) S. Higashiya, N. I. Topilina, S. C. Ngo, D. Zagorevskii, J. T. Welch, *Biomacromolecules* **2007**, *8*, 1487.
(d) M. W. T. Werten, A. P. H. A. Moers, T, Vong, H. Zuilhof, J. C. M. van Hest, F. A. de Wolf, *Biomacromolecule* **2008**, *9*, 1705.
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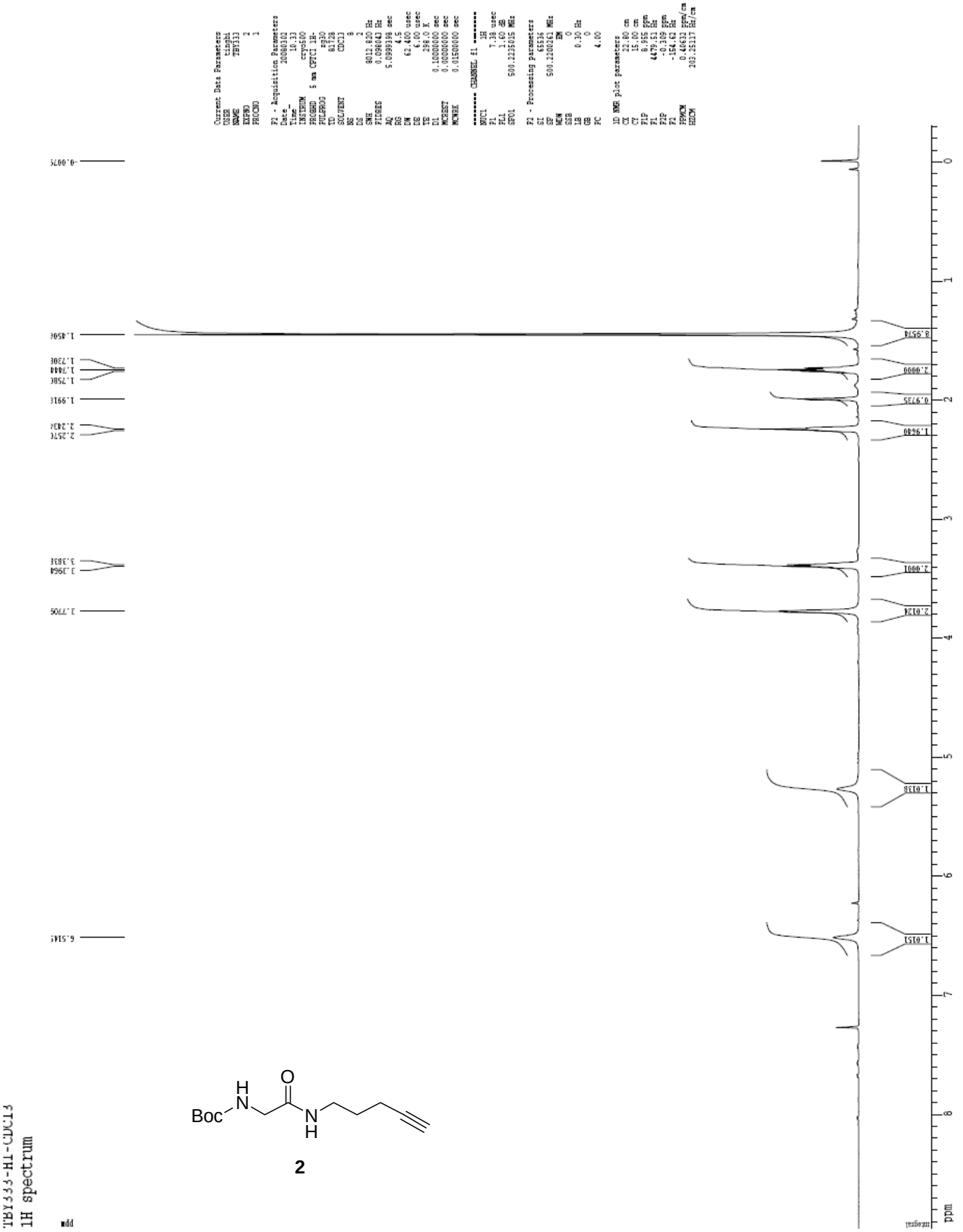
[7] (a) T, Miyazawa, E. R. Blout, *J. Am. Chem. Soc.* **1961**, *83*, 712.
(b) P. I. Haris, D. Chapman, *Biopolymers* **1995**, *37*, 251.

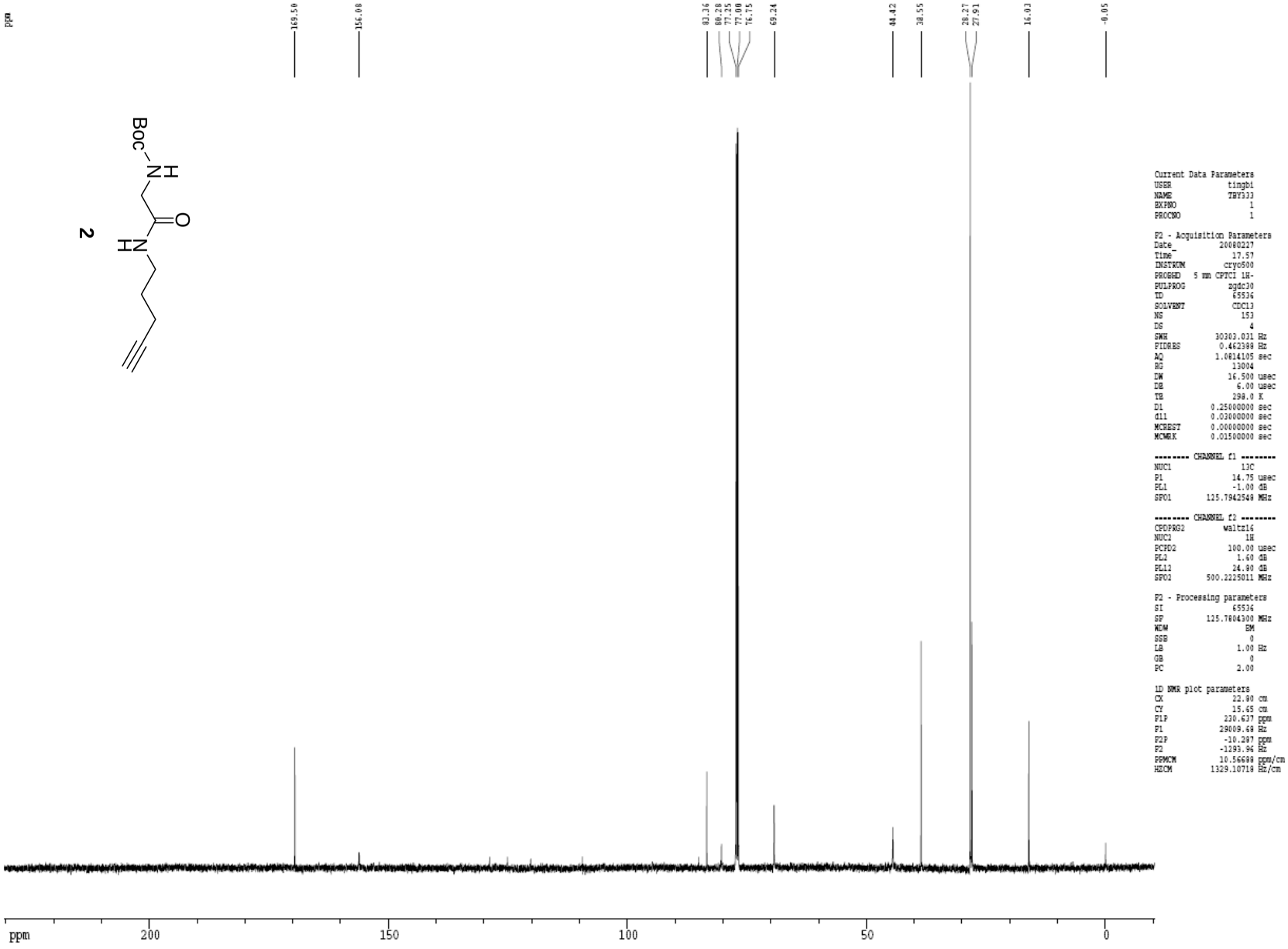
X. NMR and FTIR spectra

^{1}H NMR and ^{13}C NMR spectra of **2**



TBY333-C13-CDCl3

13C spectrum with 1H decoupling



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PL1	-1.00 dB
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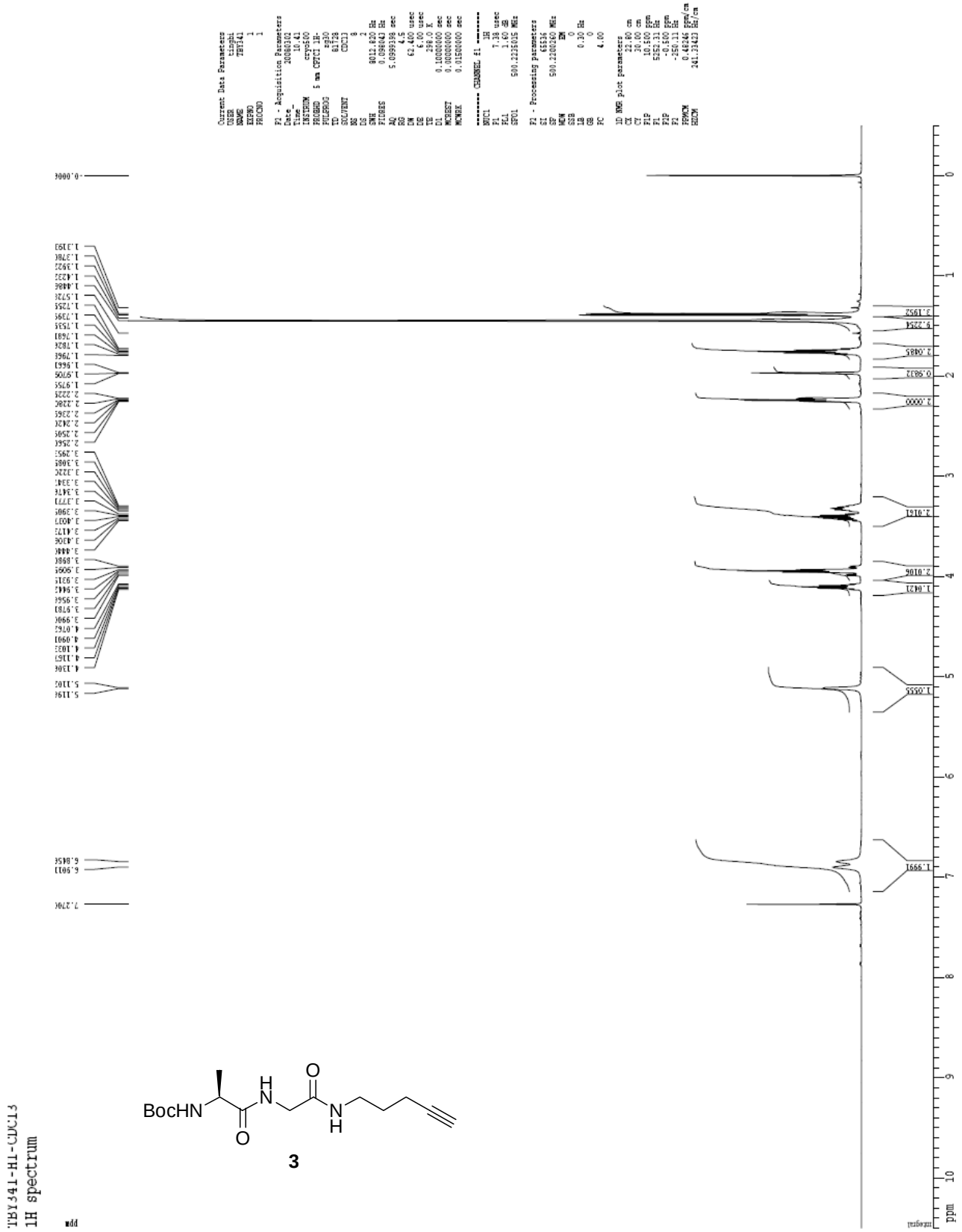
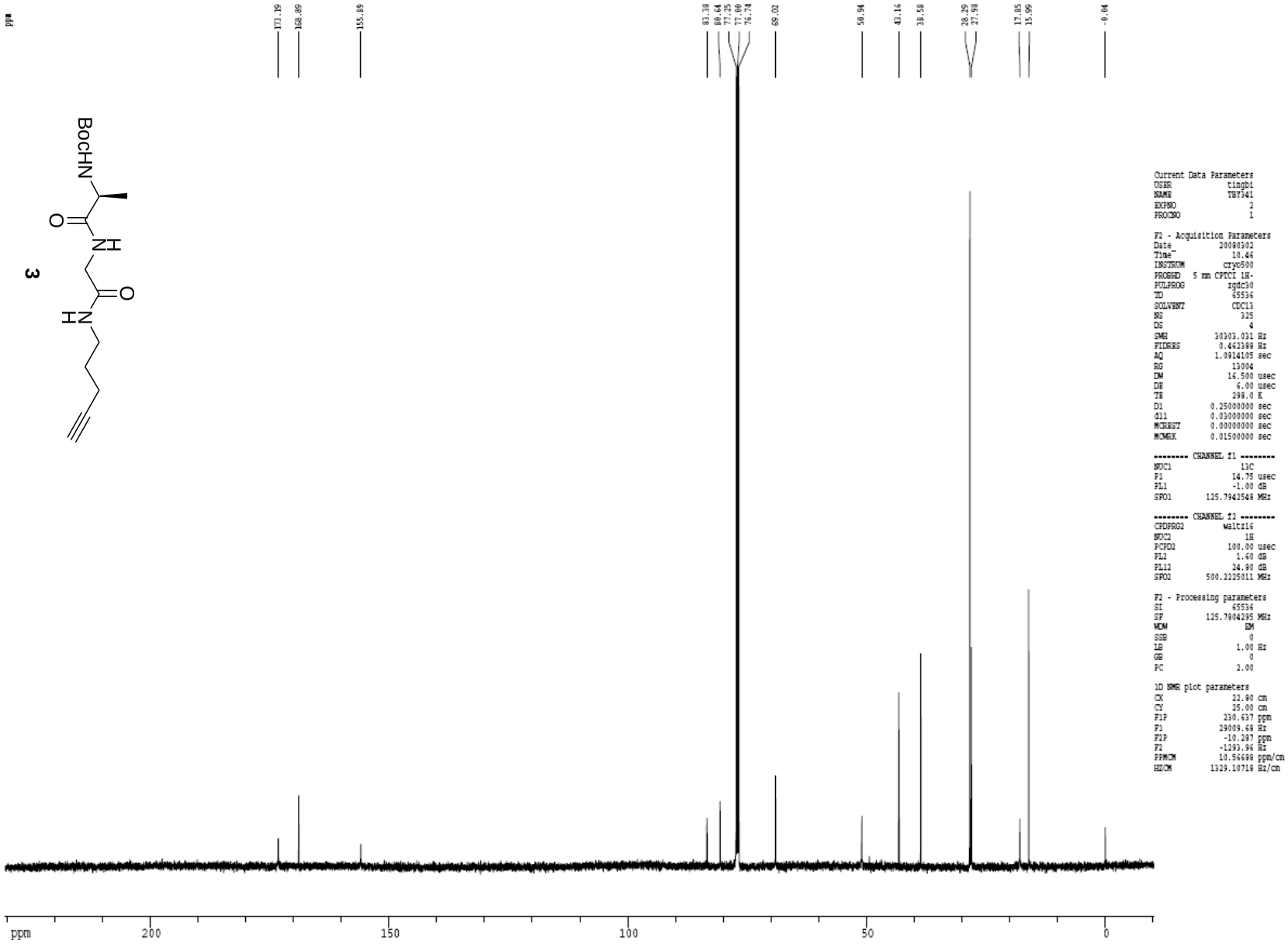
HZCM	1329.10718 Hz/cm

[1]H NMR and [13]C NMR spectra of **3**



TBY341-C13-CDCl3

13C spectrum with 1H decoupling

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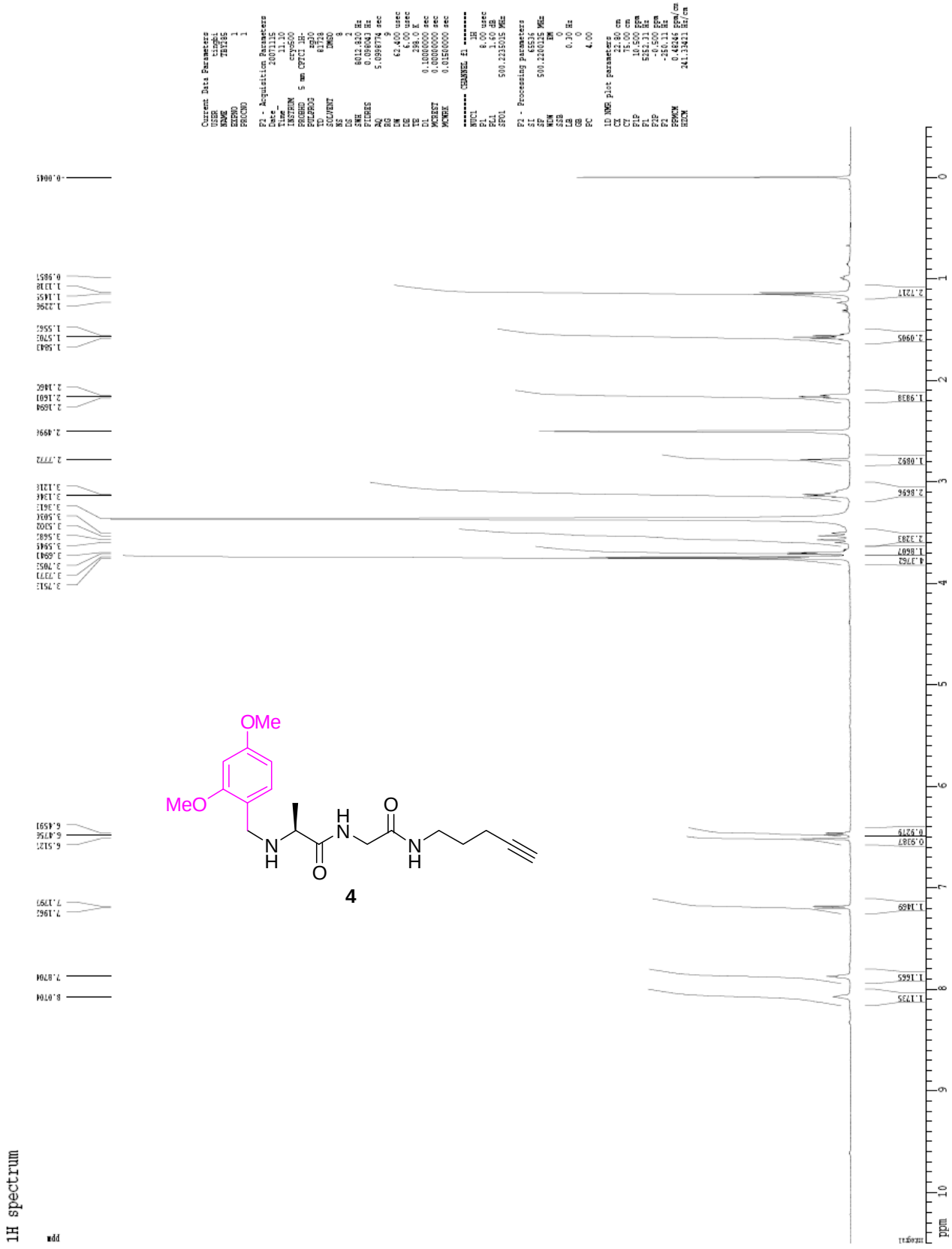
^{1}H NMR and ^{13}C NMR spectra of **4**



4

TBY352-C13-DMSO

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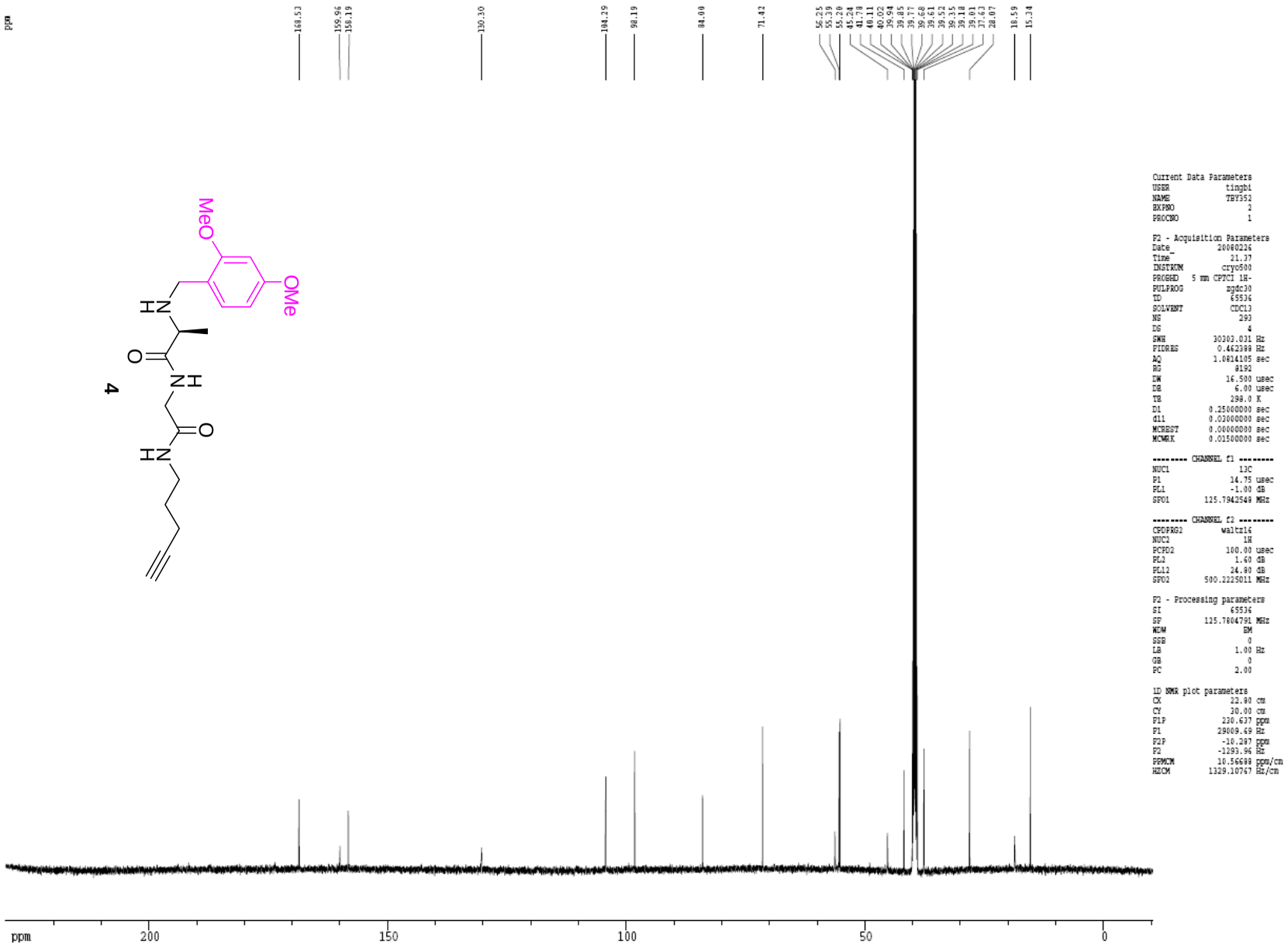
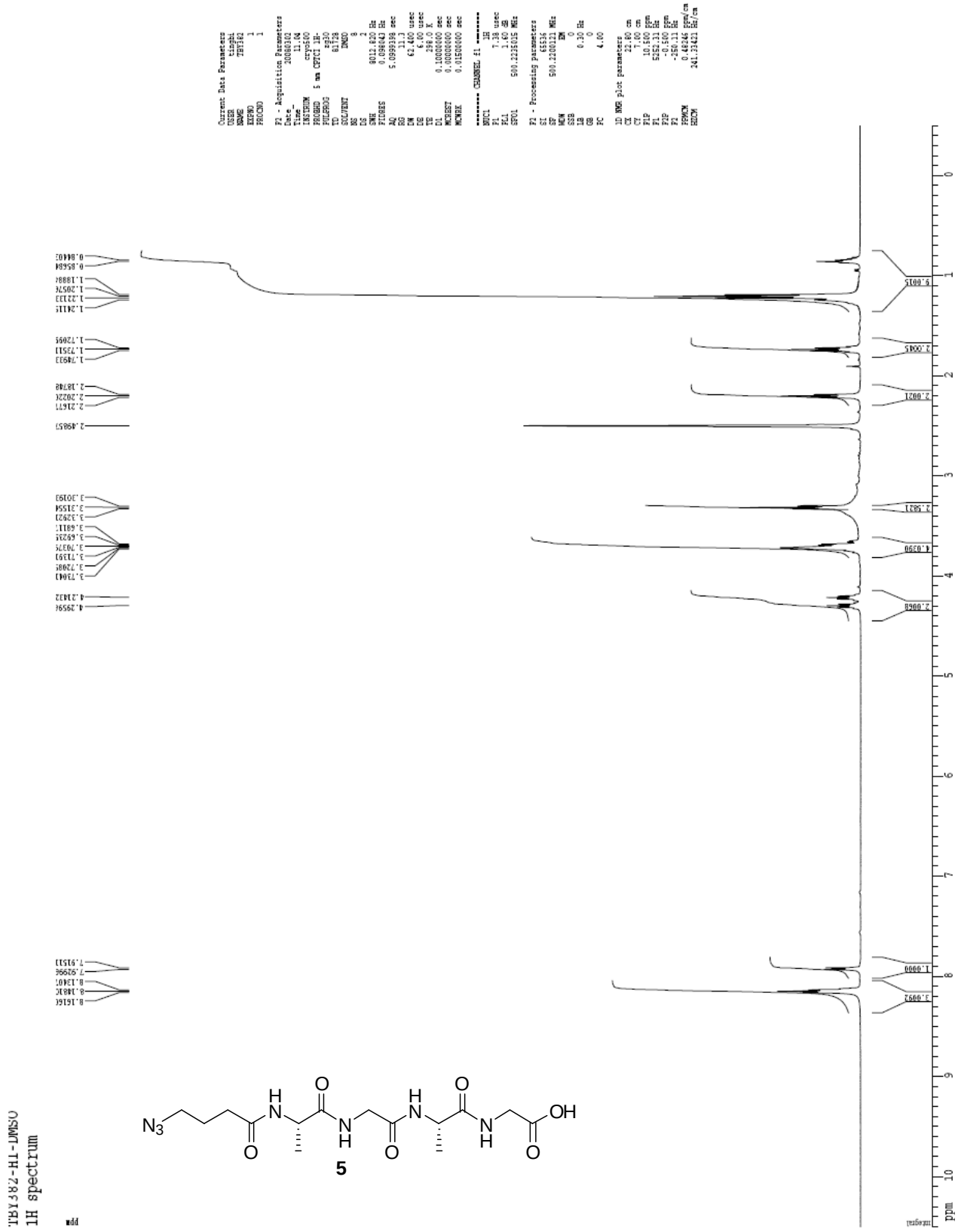
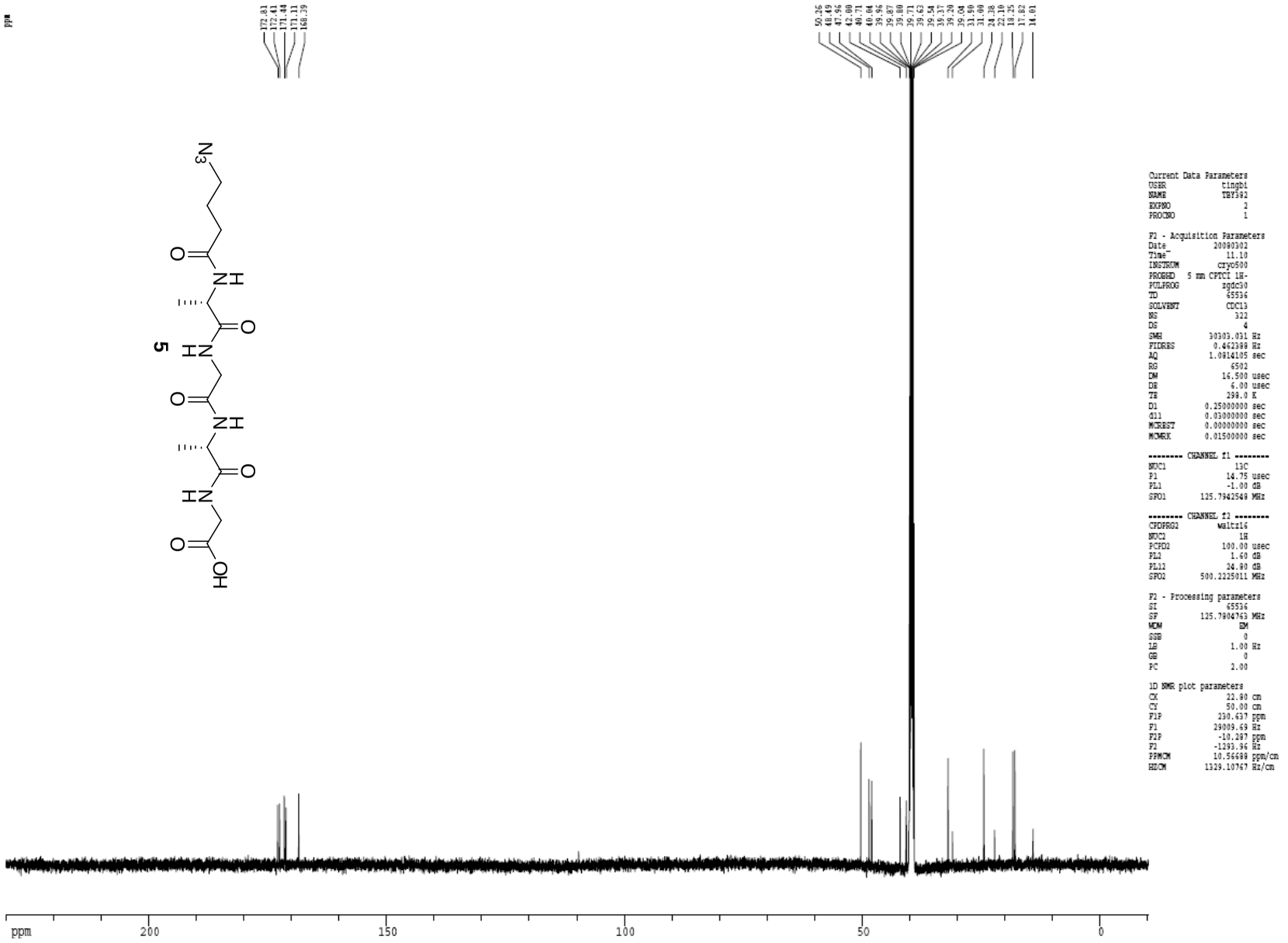


^{1}H NMR and ^{13}C NMR spectra of **5**



TBY382-C13-DMSO

13C spectrum with 1H decoupling



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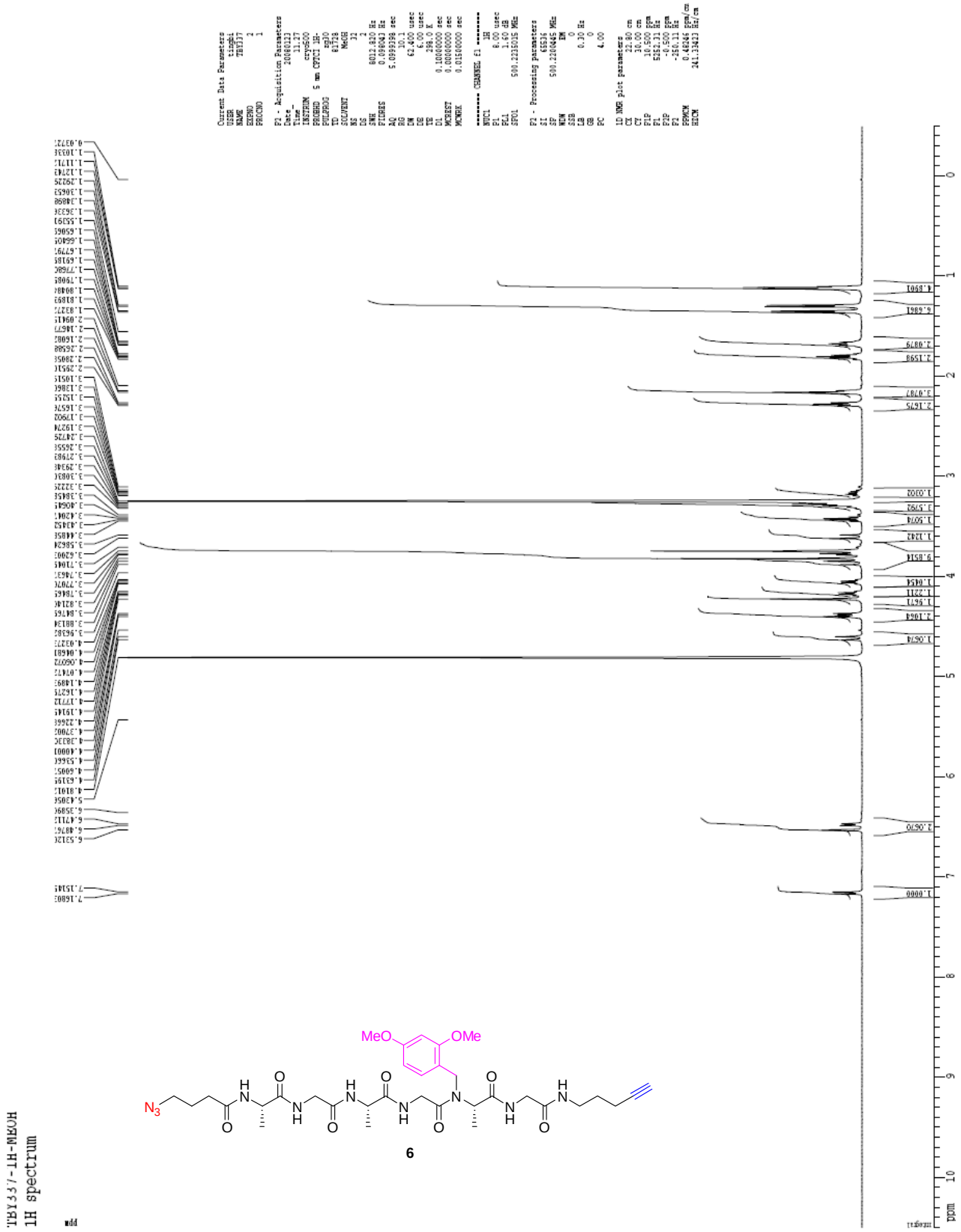
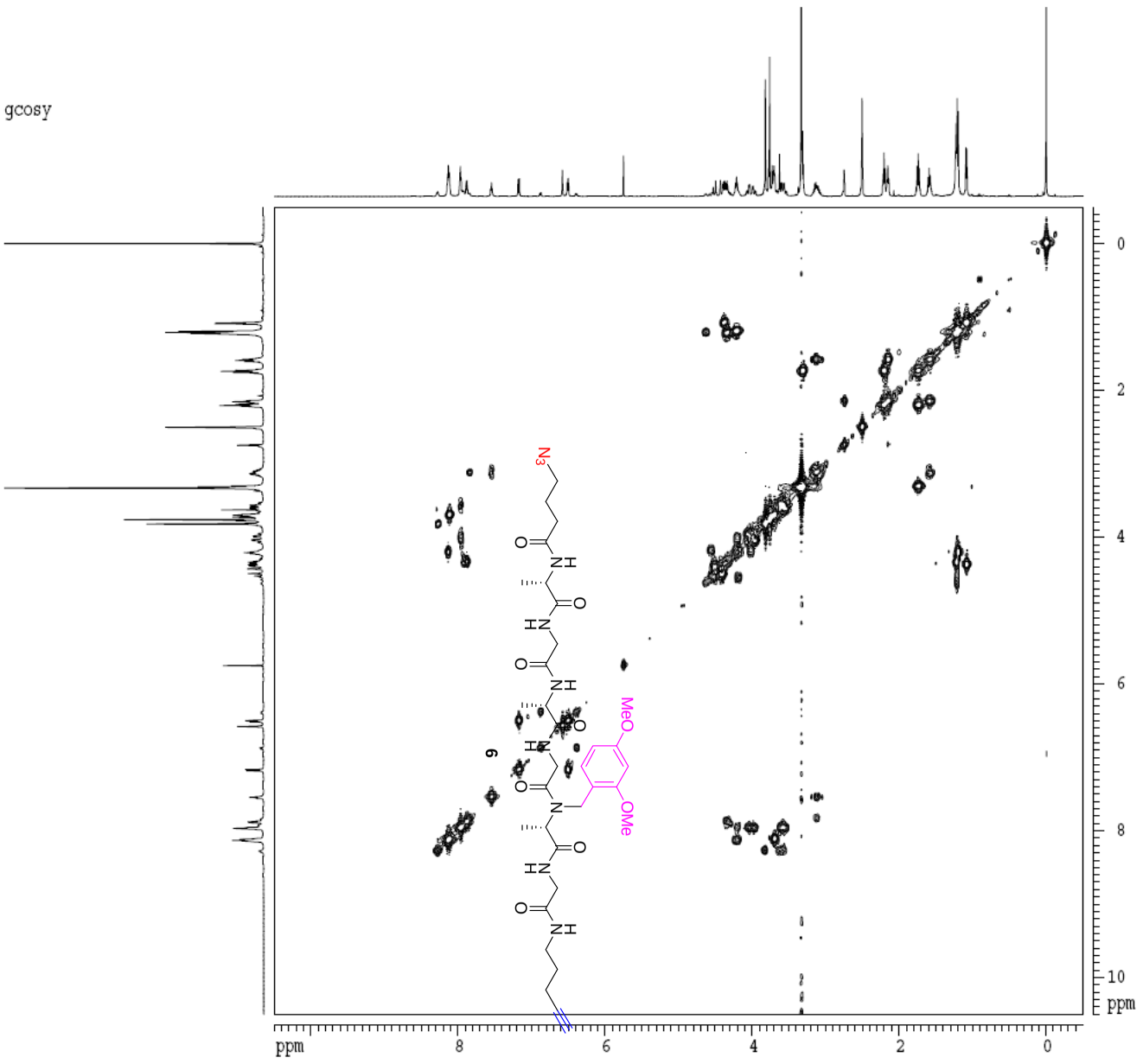
[1]H NMR, COSY, [13]C NMR spectra of **6**





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F1LO	5248.16 Hz
F1PHI	-0.500 ppm
F1HI	-249.91 Hz
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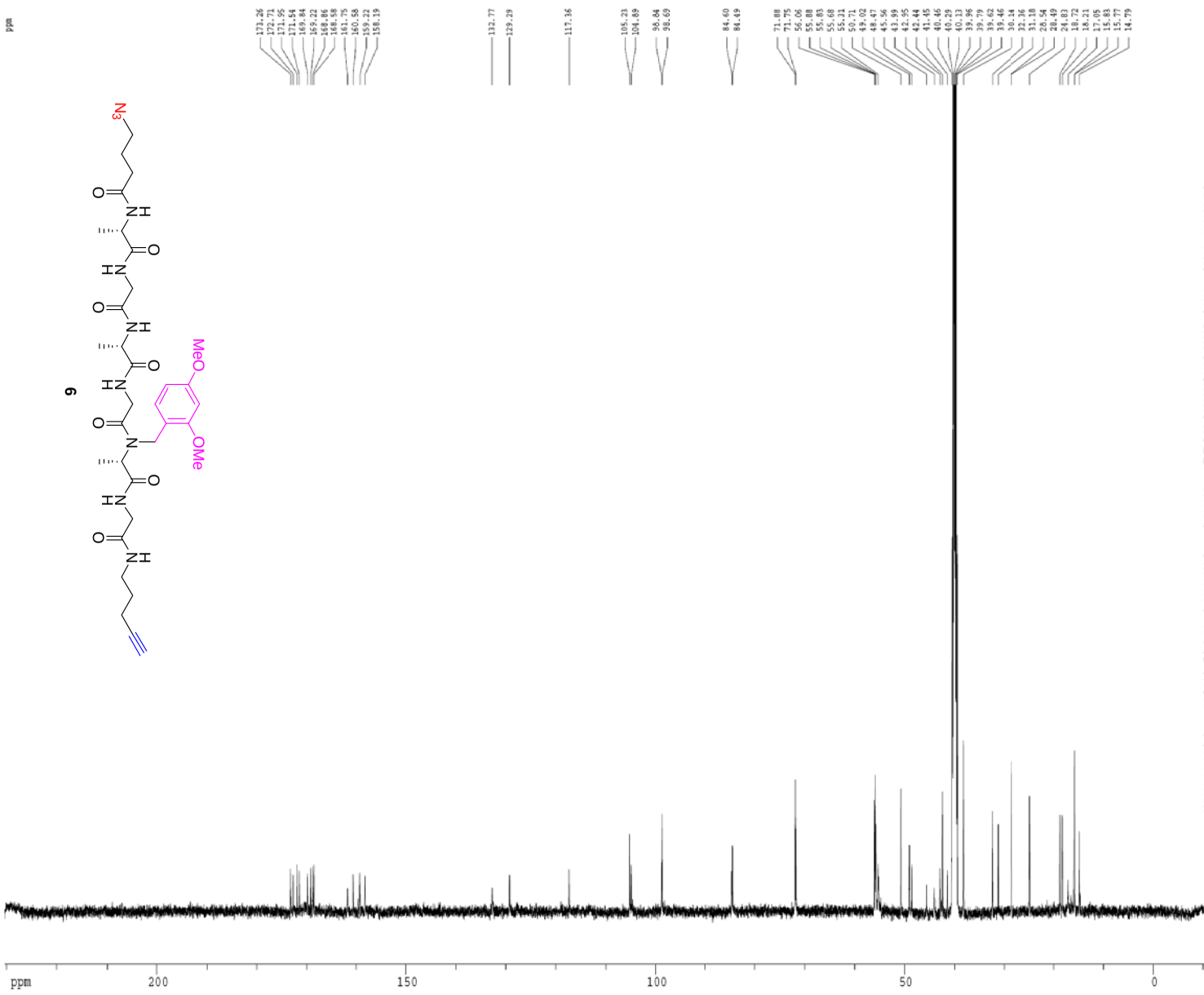
TBY337-C13-DMSO

13C spectrum with 1H decoupling



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MCWRK	0.01500000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	14.75 usec
PL1	-1.00 dB
SFO1	125.7942548 MHz

======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	1.60 dB
PL12	24.80 dB
SFO2	500.2225011 MHz

F2 - Processing parameters

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WDW	EM
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1D NMR plot parameters

CX	22.80 cm
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F1	29009.68 Hz
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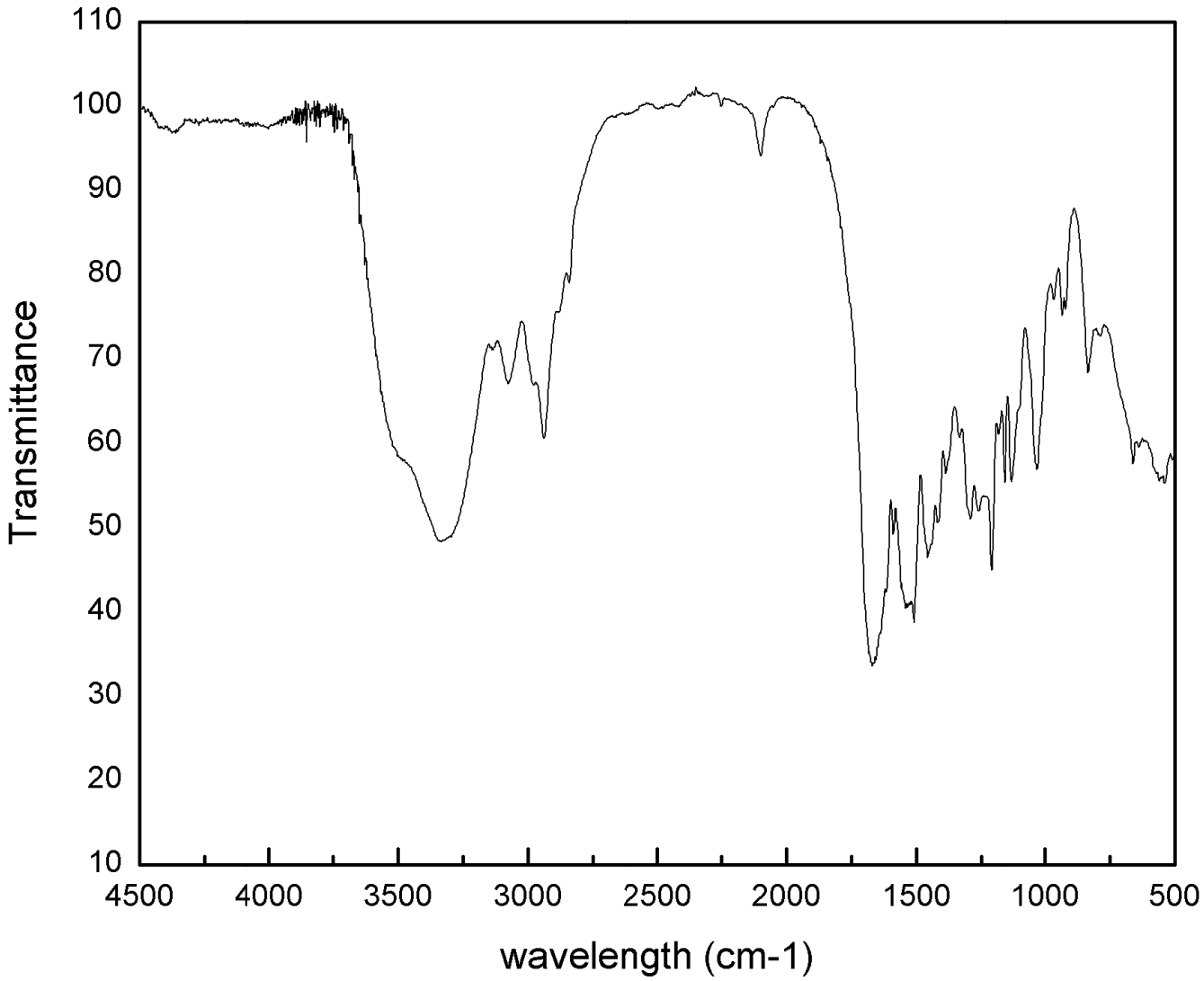
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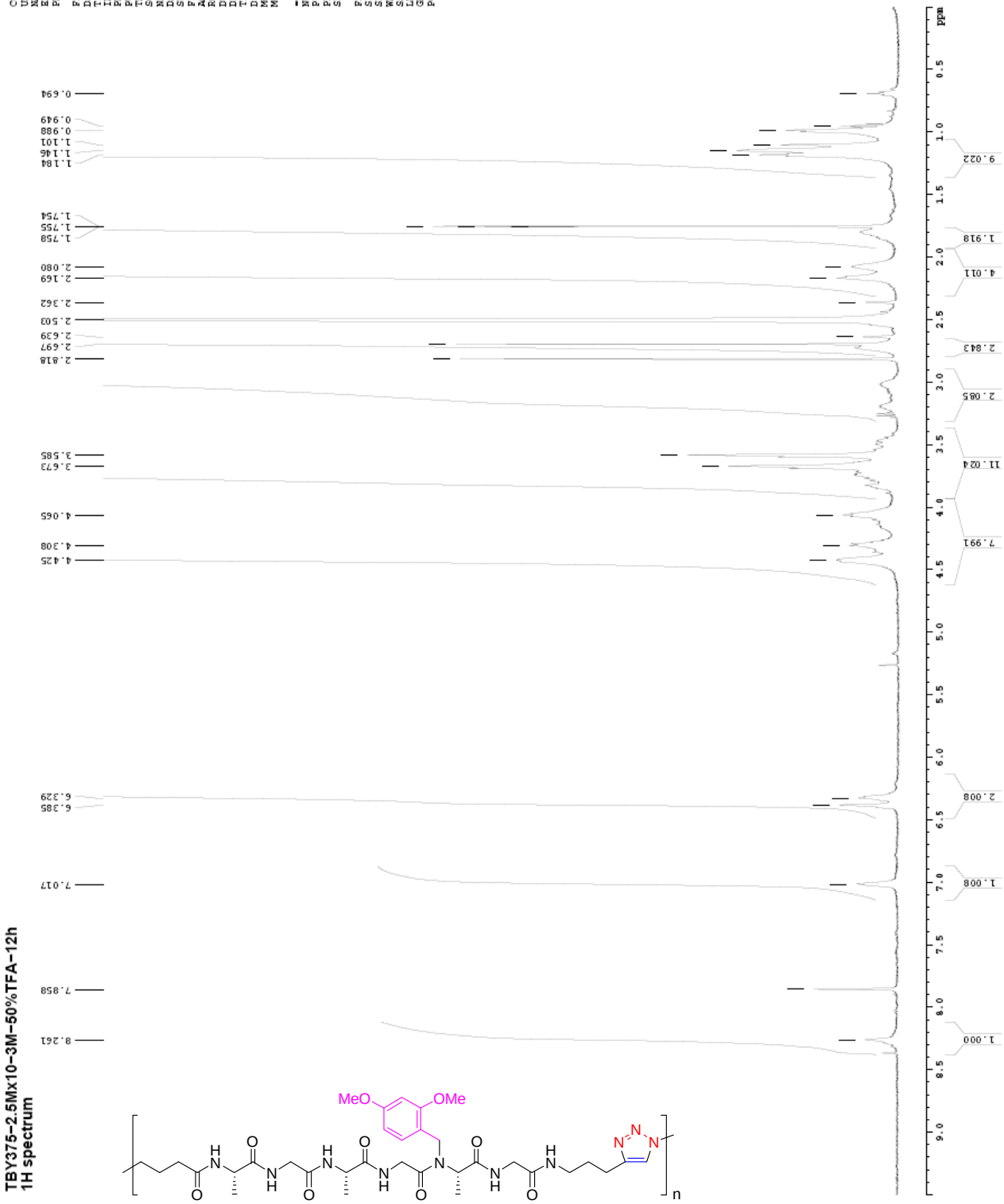

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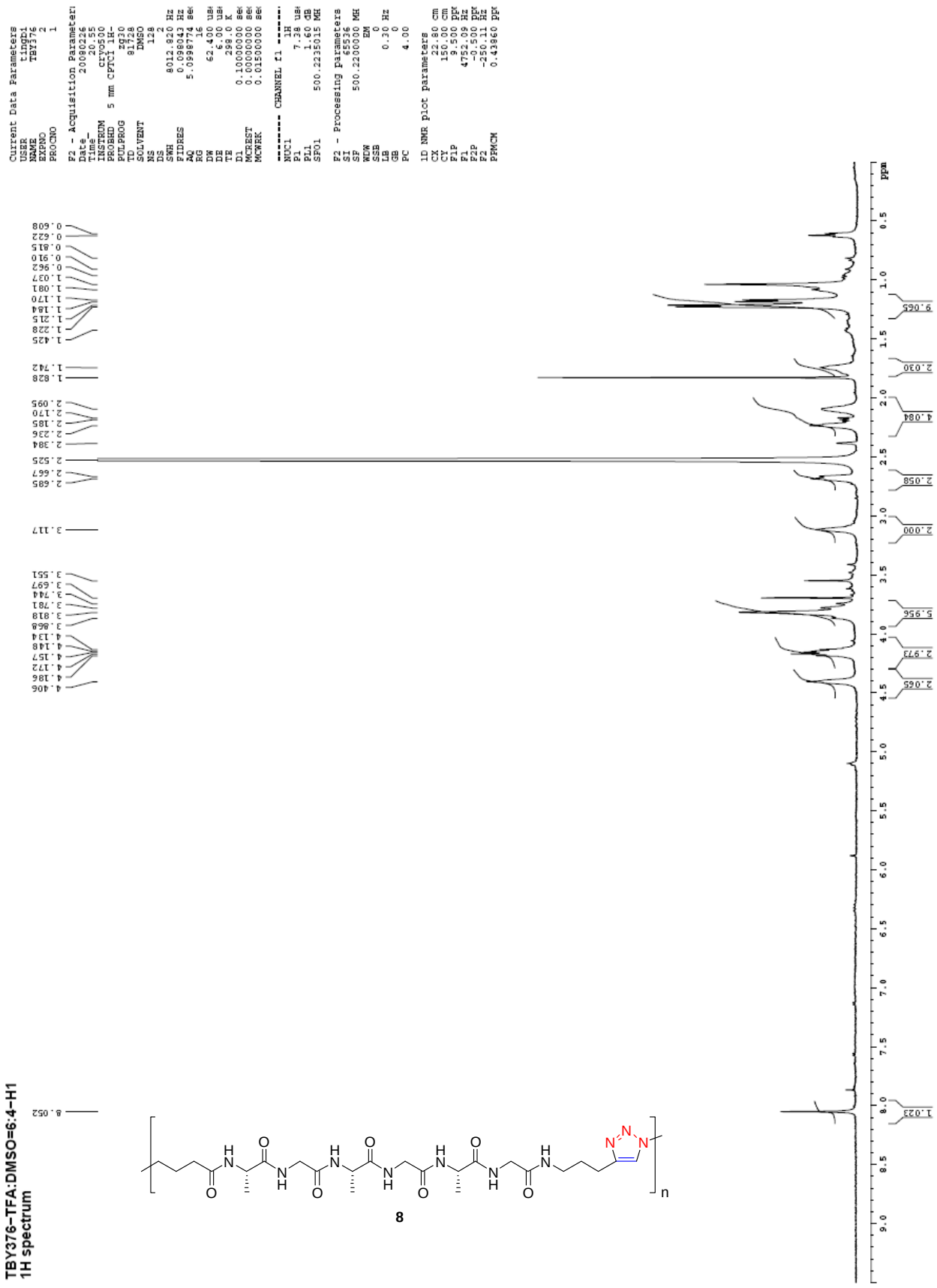
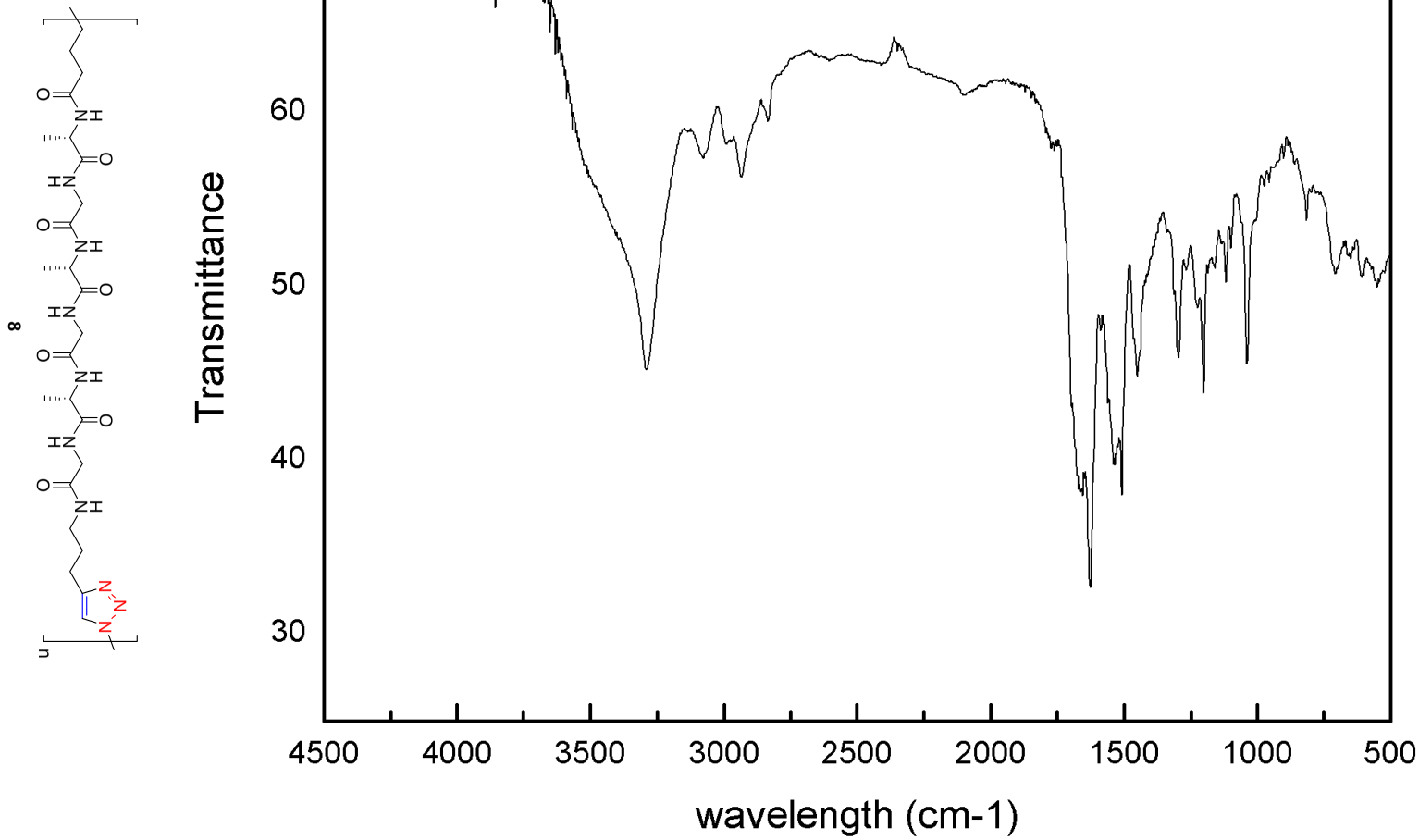
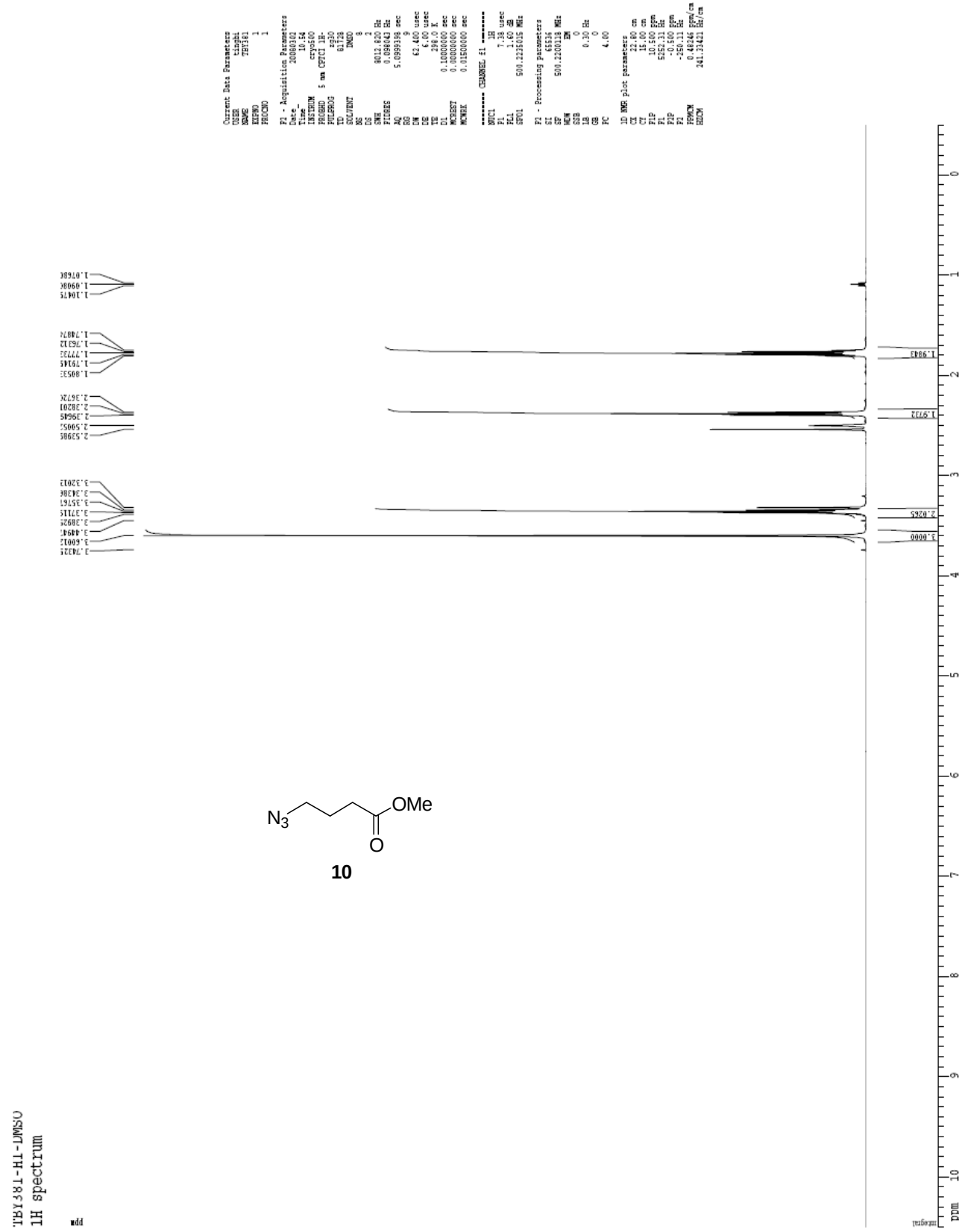
1H spectrum

[1]H NMR and IR spectra of **8**




Transmittance
70
60
50
40
30
4500
4000
3500
3000
2500
2000
1500
1000
500
wavelength (cm-1)

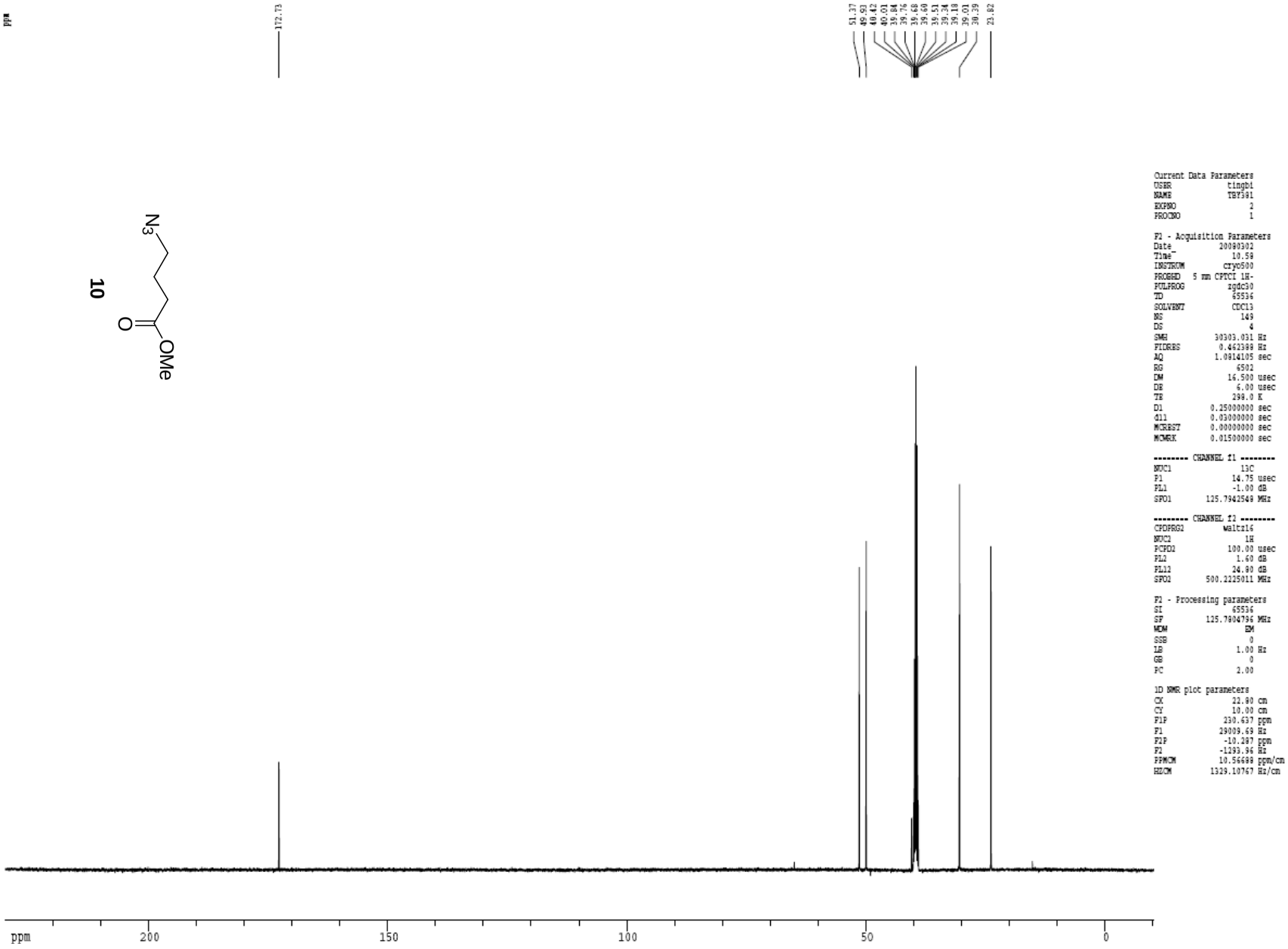
^{1}H NMR and ^{13}C NMR spectra of **10**



10

TBY381-C13-DMSO

13C spectrum with 1H decoupling



Current Data Parameters

USER	tingbi
NAME	TBY381
EXPNO	2
PROCNO	1

F1 - Acquisition Parameters

Date_	20080302
Time	10.59
INSTRUM	cryo500
PROBHD	5 mm CPTCI 1H-
PULPROG	zgdc30
TD	65536
SOLVENT	CDCl3
NS	149
DS	4
SWH	30303.031 Hz
FIDRES	0.462398 Hz
AQ	1.0814105 sec
RG	6502
DW	16.500 usec
DE	6.00 usec
TE	298.0 K
D1	0.25000000 sec
d11	0.03000000 sec
MCREST	0.00000000 sec
MCWRK	0.01500000 sec

-------- CHANNEL f1 --------

NUC1	13C
P1	14.75 usec
PL1	-1.00 dB
SFO1	125.7942549 MHz

-------- CHANNEL f2 --------

CPDPRG2	waltz16
NUC2	1H
PCPD2	100.00 usec
PL2	1.60 dB
PL12	24.80 dB
SFO2	500.2225011 MHz

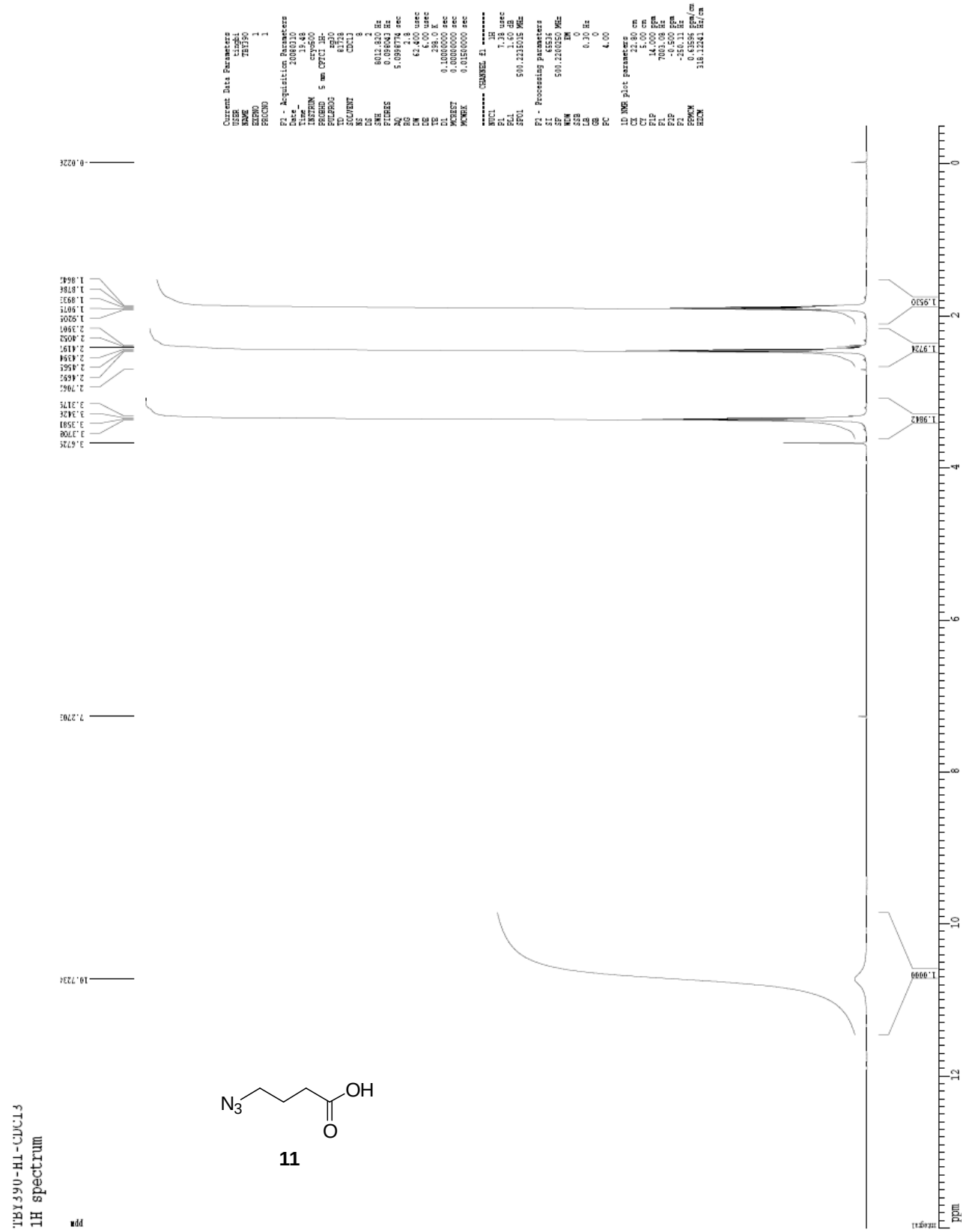
F2 - Processing parameters

SI	65536
SF	125.7804796 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	2.00

1D NMR plot parameters

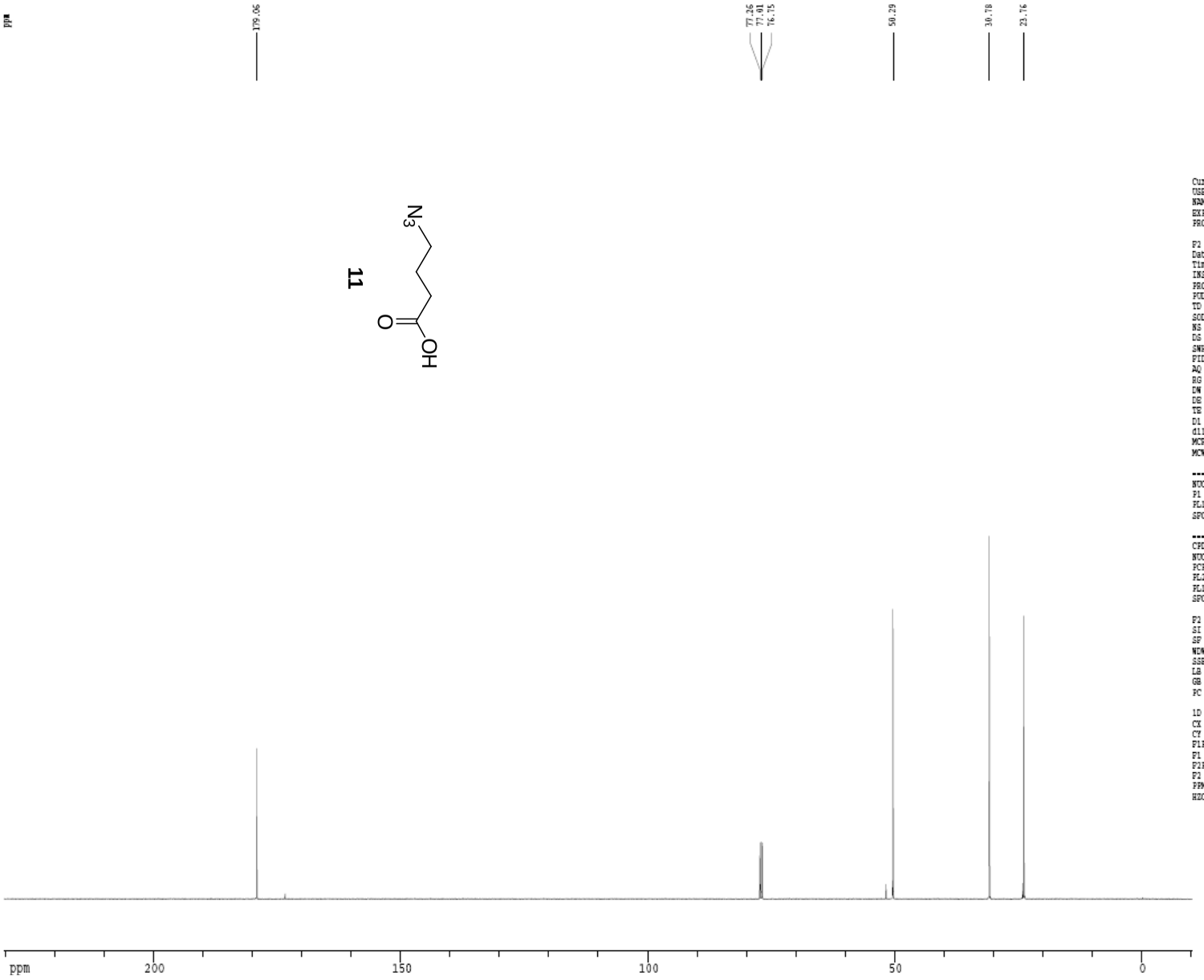
CX	22.80 cm
CY	10.00 cm
F1P	230.637 ppm
F1	29009.69 Hz
F2P	-10.287 ppm
F2	-1293.96 Hz
PPMCM	10.56699 ppm/cm
HZCM	1329.10767 Hz/cm

[1]H NMR and [13]C NMR spectra of **11**



TBY390-C13-CDCl3

13C spectrum with 1H decoupling

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Current Data Parameters
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NAME              TBY390
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_          20080310
Time               19.52
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PROBHD    5 mm CPTCI 1H-
PULPROG          zgdc30
TD                 65536
SOLVENT             CDCl3
NS                    101
DS                      4
SWH           30303.031 Hz
FIDRES            0.462398 Hz
AQ             1.0813940 sec
RG                10321.3
DW                 16.500 usec
DE                  6.00 usec
TE                298.0 K
D1            0.25000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWSK         0.01500000 sec

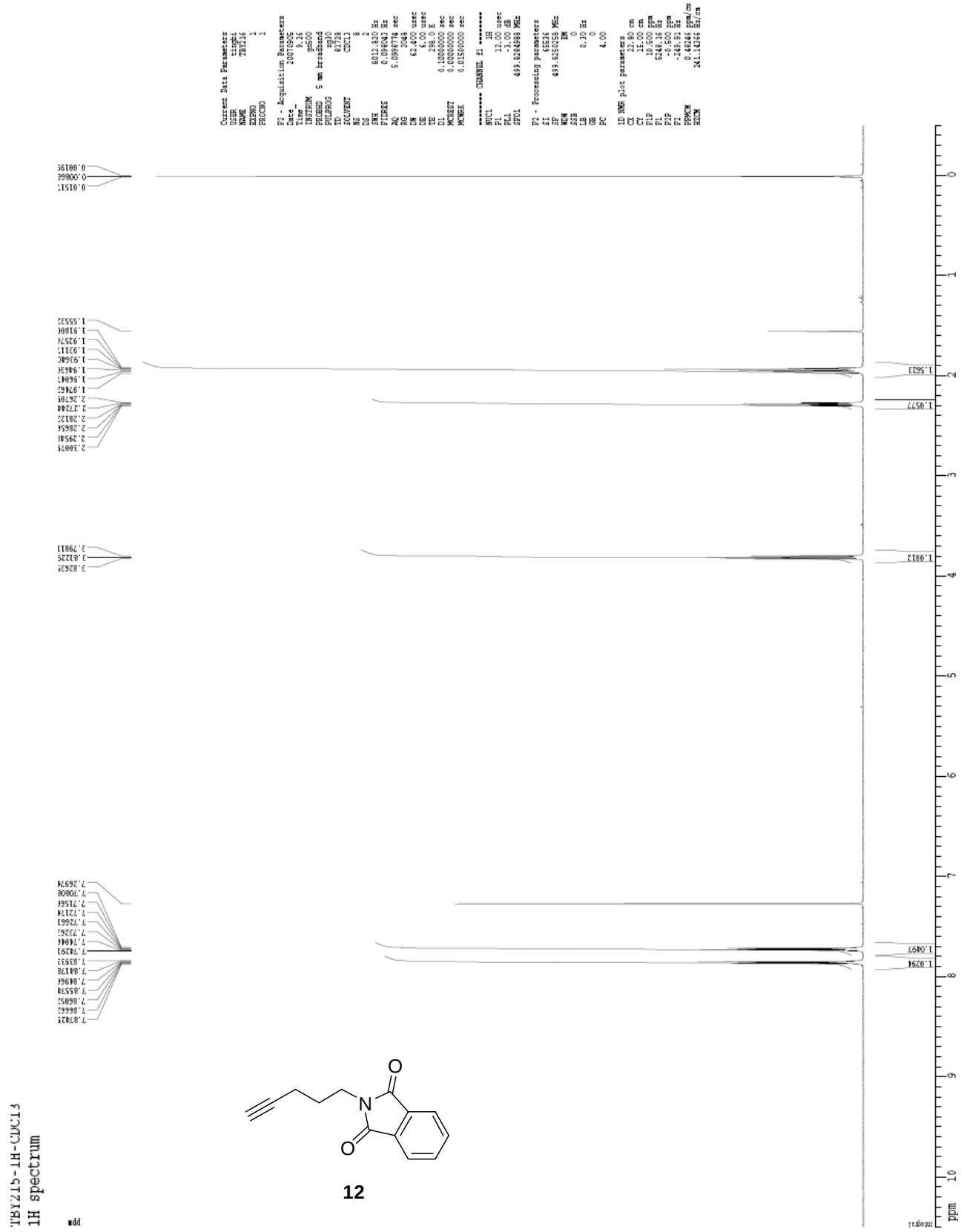
-------- CHANNEL f1 --------
NUC1                 13C
P1                 14.75 usec
PL1                -1.00 dB
SFO1         125.7942548 MHz

-------- CHANNEL f2 --------
CPDPRG2          waltz16
NUC2                  1H
PCPD2              100.00 usec
PL2                 1.60 dB
PL12               24.90 dB
SFO2         500.2225011 MHz

F2 - Processing parameters
SI                 65536
SF           125.7804406 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                  7.00 cm
F1P               230.637 ppm
F1              29009.69 Hz
F2P               -10.287 ppm
F2              -1293.96 Hz
PPMCM           10.56498 ppm/cm
HZCM          1329.10730 Hz/cm
```

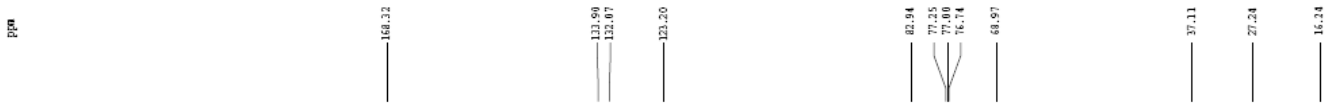
^{1}H NMR and ^{13}C NMR spectra of **12**



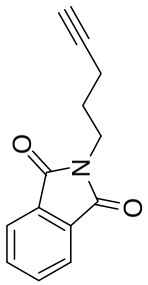
12

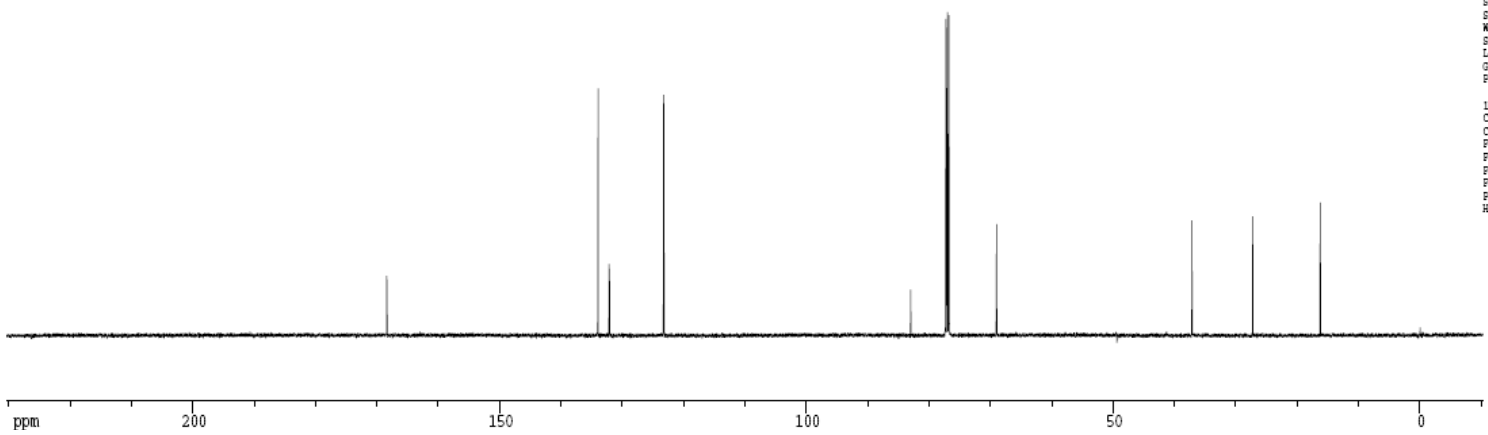
TBY216-C13-CDCl3

13C spectrum with 1H decoupling



12



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Current Data Parameters
USER              tingbi
NAME              TBY216
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_          20080226
Time               20.49
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG          zgdc30
TD                65536
SOLVENT           CDCl3
NS                   69
DS                    4
SWH           30303.031 Hz
FIDRES        0.462398 Hz
AQ            1.0814105 sec
RG                 8192
DW               16.500 usec
DE                6.00 usec
TE               298.0 K
D1          0.25000000 sec
d11         0.03000000 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec

--------- CHANNEL f1 ---------
NUC1              13C
P1               14.75 usec
PL1              -1.00 dB
SFO1        125.7942548 MHz

--------- CHANNEL f2 ---------
CPDPRG2        waltz16
NUC2               1H
PCPD2           100.00 usec
PL2               1.60 dB
PL12             24.80 dB
SFO2        500.2225011 MHz

F2 - Processing parameters
SI                65536
SF          125.7804300 MHz
WDW                  EM
SSB                   0
LB                 1.00 Hz
GB                    0
PC                 2.00

1D NMR plot parameters
CX                22.80 cm
CY                 5.00 cm
F1P              230.637 ppm
F1             29009.68 Hz
F2P              -10.297 ppm
F2             -1293.96 Hz
PPMCM           10.56698 ppm/cm
HZCM         1329.10719 Hz/cm
```
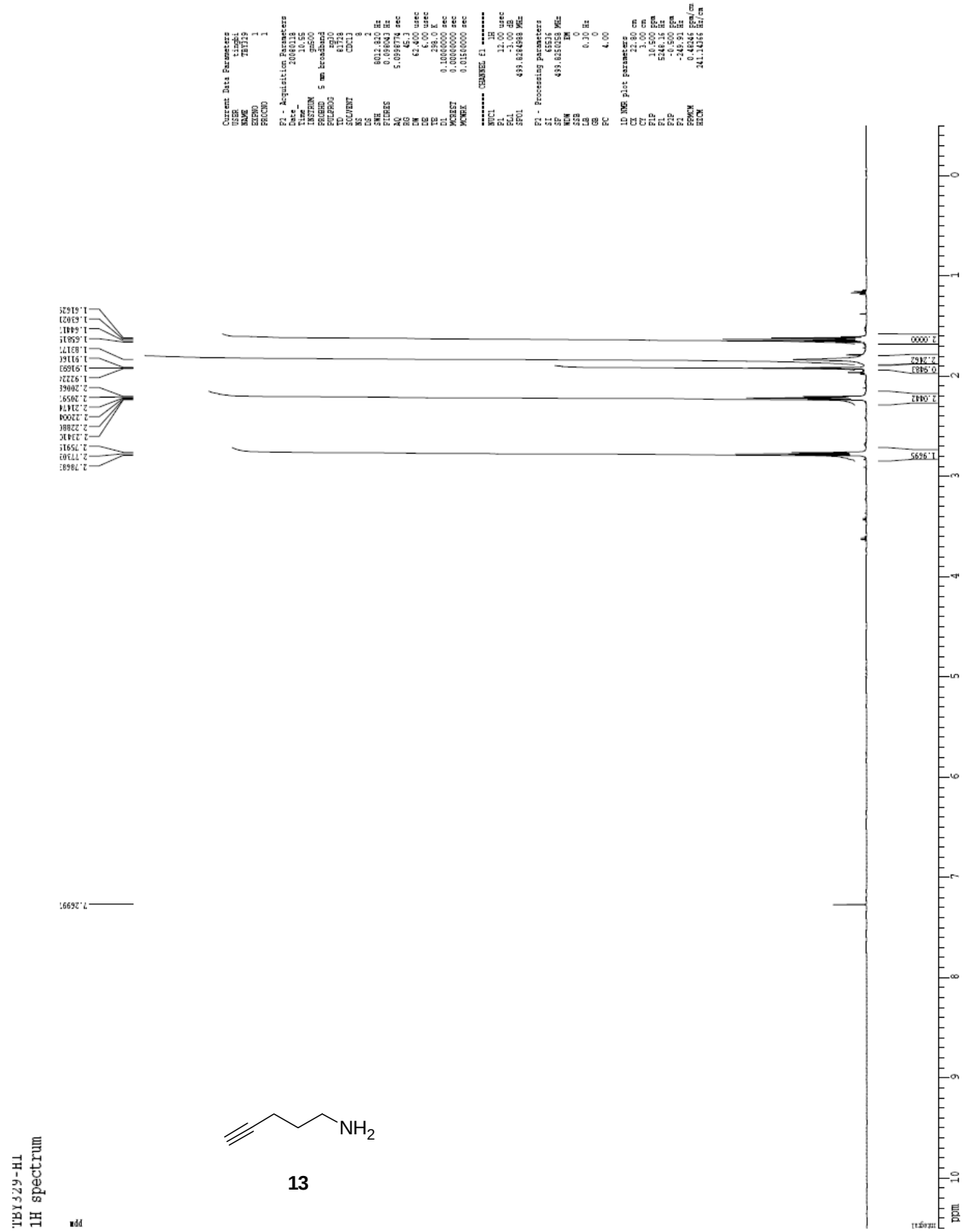

^{1}H NMR and ^{13}C NMR spectra of **13**



13

TBY329-C13-CDCl3

13C spectrum with 1H decoupling