Synthesis of Unsymmetrical 1,1’-Disubstituted Bis(1,2,3-triazoles) using Monosilylbutadiynes

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SUPPORTING INFORMATION

1. General experimental

^{1}H NMR were recorded either at 300 MHz or 400 MHz on a Bruker Avance 300 MHz or 400 MHz NMR spectrometer respectively. ^{13}C NMR were recorded either at 75 MHz or 100 MHz on a Bruker Avance 300 MHz or 400 MHz NMR spectrometer respectively. Data acquisition was managed using TOPSPIN/ICONNMR (Bruker) and plotting was managed using MestReNova 6.0.2 software. ^{1}H NMR were measured in parts per million (ppm) referenced to an internal standard of relevant solvent signals, δ 4.79 for deuterium oxide, δ 7.26 for chloroform, δ 2.50 for DMSO and δ 3.31 for methanol.[1] ^{13}C NMR were measured in parts per million (ppm) referenced to the relevant solvent signals, δ 77.16 for chloroform, δ 39.52 for DMSO and δ 49.00 for methanol. High Resolution Mass Spectrometry were collected on a Waters Micromass LCT Premier XE time-of-flight mass spectrometer fitted with an electrospray (ESI) ion source and controlled with MassLynx software version 4.5. Low Resolution Mass Spectrometry were performed using a Micromass Platform II single quadrupole mass spectrometer equipped with an atmospheric pressure (ESI/APCI) ion source. Sample management was facilitated by an Agilent 1100 series HPLC system and the instrument was controlled using MassLynx software version 3.5. Analytical High Performance Liquid Chromatography (HPLC) was conducted on the Waters 2690 Separation Module coupled with a Waters 996 Photodiode Array Detector with a Phenomenex Luna 5u C8 (2) 100A (150 × 4.60 mm ID) column. Buffer A: 99.9% Water, 0.1% TFA, Buffer B: 80% Methanol, 19.9% Water, 0.1% TFA. Compounds were analysed using a gradient of 0-100% buffer B in buffer A over 12 mins followed by isocratic 100% buffer B for a further 6 mins followed by isocratic 100% buffer A for 2 mins at a flow rate of 1.0 mL/min. Melting points were recorded on a Mettler Toledo MP50 according to manufacturer's instructions and are uncorrected. Optical rotations were recorded on a Jasco P-2000 Polarimeter according to manufacturer's instructions. Thin layer chromatography was performed on aluminium-backed Merck silica gel 60 F_{254} plates. TLC plates were visualised by UV illumination or with the aid of phosphomolybdic acid (PMA), vanillin, *p*-anisaldehyde, iodine or potassium permanganate solutions. Column chromatography was conducted using Davisil silica gel LC60A (40-63 micron). All commercially available chemicals were purchased from Aldrich/Fluka, Merck or Alfa-Aesar. Hexane and ethyl acetate was distilled before use. HPLC-grade MeCN was dried using MBraun solvent purification system (SPS-800) according to manufacturer's instructions. All other solvents were reagent grade and used as received.

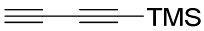
2. Preparation of Azides

Caution: While synthesis of azides has become ubiquitous in the literature some are explosive and care should be taken when synthesizing and handling them.

Azides were synthesised according to literature procedures of Alvarez *et al.*[2] or Goddard-Borger *et al.*[3] The analytical data were in agreement with literature values for benzyl azide[4]; azido acetic acid and (*S*)-azidobenzylacetic acid[5]; adamantylazide[6]; 1-azidodecane[7]; 1-(azidomethyl)napthalene[8]; 4-methoxybenzyl azide[9]; (azidomethyl)cyclohexane, 2-(azidomethyl)pyridine and 4-nitrobenzyl azide [10]; benzyl 2-azidoacetate [11].

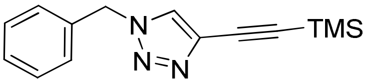
3. Preparation of bis-(1,2,3-triazoles) using TMS-butadiyne

Buta-1,3-diynyltrimethylsilane (**1**)[12-14]



Methyl lithium as the lithium bromide complex in ether (1.75 mL, 2.63 mmol, 1 eq.) was added dropwise over two minutes to a solution of bis-TMS butadiyne (496 mg, 2.55 mmol, 1 eq.) in dry THF (25 mL) during which time an orange colour developed. The solution was left stirring for 3.5 hours at room temperature then quenched with saturated ammonium chloride (15 mL). The solution was then extracted with hexane (2 × 20 mL) and the combined organic extracts washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered and concentrated to a volume of 2 mL. The resulting red solution was diluted to 10 mL with *t*-butanol and used immediately or stored under a nitrogen atmosphere at -4 to -20 °C effectively for up to five days. ^{1}H-NMR analysis of an evaporated sample showed 64 % product conversion on comparison of TMS signals of starting material and product at δ 0.19 ppm and 0.20 ppm respectively, consistent with literature reports.[12-14] The reagent was used in solution assuming a yield of 50 % for reactions as outlined.

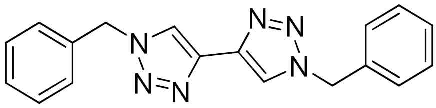
*1-Benzyl-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole* (**2**)[15]



To a solution of benzyl azide (100 mg, 0.751 mmol, 1 eq.), freshly prepared buta-1,3-diynyltrimethylsilane (**1**) (0.46 M in *t*-BuOH, 1.95 mL, 0.90 mmol, 1.2 eq.) and diisopropylethylamine (640 µL, 3.76 mmol, 5 eq.) in acetonitrile (10 mL) was added copper (I) iodide (29 mg, 0.2 eq.). The solution was left stirring at room temperature for 16 hours, then diluted with water (20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, filtered and evaporated to give a crude residue. Purification by flash chromatography in a gradient of hexane to 60:40 hexane : ethyl acetate gave the product as a white solid (101 mg, 51%), with physical and spectroscopic data in agreement with those previously reported.[15]

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.36-7.40 (m, 3H), 7.24-7.26 (m, 2H), 5.51 (s, 2H), 0.20 (s, 9H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 134.1, 131.2, 129.1, 128.8, 128.1, 126.4, 98.7, 93.6, 54.2, -0.3. MS (ESI) *m/z*= 256.4 $(M+H)^+$. HRMS (ESI) found 256.1254, calculated 256.1265 for $(M+H)^+$. RP-HPLC R_t=16.07 min, 96%.

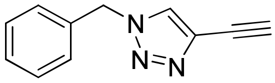
*1,1'-Dibenzyl-1*H,*1*H*'-4,4'-bi(1,2,3-triazole)* (**4**) [16]



Also isolated from above procedure as a white solid (12 mg, 5%). The spectroscopic data were in agreement with literature values.[16]

^{1}H-NMR (400 MHz, d_6-DMSO) δ 8.55 (s, 2H), 7.41 – 7.29 (m, 10H), 5.65 (s, 4H). ^{13}C-NMR (100 MHz, d_6-DMSO) δ 139.3, 136.0, 128.8, 128.2, 128.0, 121.9, 53.0. MS (ESI) *m/z*= 317.5 $(M+H)^+$. RP-HPLC R_t=10.05 min, 95%.

*1-Benzyl-4-ethynyl-1*H*-1,2,3-triazole* (**3**)[17]



Method 1:

1-Benzyl-4-((trimethylsilyl)ethynyl)-1*H*-1,2,3-triazole (**2**) (103 mg, 0.40 mmol, 1 eq.) and potassium fluoride (116 mg, 2.00 mmol, 5 eq.) were added to methanol (5 mL) and heated to 50 °C for 90 minutes followed by evaporation. The resultant solid was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine (1 × 10 mL), dried over anhydrous magnesium sulfate, filtered and evaporated to give the product as a white solid (65 mg, 89%).

Method 2, General procedure A:

1-Benzyl-4-((triisopropylsilyl)ethynyl)-1*H*-1,2,3-triazole (**9b**) (72 mg, 0.21 mmol, 1 eq.) and tetrabutylammonium fluoride (255 μL, 1M in THF, 1.2 eq.) were added to acetonitrile (10 mL) and left stirring at room temperature for 15 mins. The solution was then diluted with water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give a yellow oil. Purification by flash chromatography in a gradient of 80:20 hexane : ethyl acetate to 70:30 hexane : ethyl acetate gave the product as a white solid (38 mg, 98%).

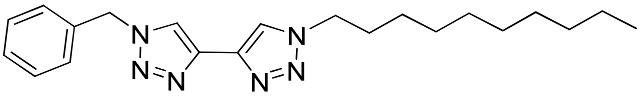
Method 3, General procedure B:

To a solution of benzyl azide (94 mg, 0.71 mmol, 1 eq.) in acetonitrile (15 mL) was added buta-1,3-diynyltriisopropylsilane (**6**) (175 mg, 0.85 mmol, 1.2 eq.), copper iodide (27 mg, 0.14 mmol, 20 mol%) and TBTA (1 mg, cat.), the solution was then sealed under nitrogen and diisopropylethylamine (615 µL, 3.53 mmol, 5 eq.) was added. The solution was stirred at room temperature for 16 hours under nitrogen. Tetrabutylammonium fluoride (847 µL, 1M in THF, 0.85 mmol, 1.2 eq.) was then added and continued stirring for a further 20 mins at room temperature under nitrogen. The reaction was then diluted with water (20 mL) and extracted with ethyl acetate (3 × 20 mL) and the combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give a brown oil.

Purification by flash chromatography in a gradient of 80:20 hexane : ethyl acetate to 50:50 hexane : ethyl acetate gave the product as a white solid (92 mg, 71%), with physical and spectroscopic data in agreement with those previously reported.[17]

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.37-7.39 (m, 3H), 7.26-7.28 (m, 2H), 5.53 (s, 2H), 3.21 (s, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 134.0, 130.3, 129.3, 128.9, 128.1, 126.8, 81.2, 73.1, 54.3. MS (ESI) *m/z*= 206.1 $(M+Na)^+$. HRMS (ESI) found 184.0865, calculated 184.0869 for $(M+H)^+$. RP-HPLC R_t=9.22 min, 99%.

*1-Benzyl-1'-decyl-1*H,*1'*H*-4,4'-bi(1,2,3-triazole)* (**5a**)[15]



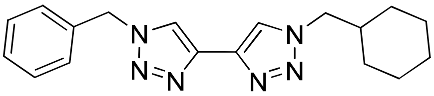
General procedure C:

1-Benzyl-4-ethynyl-1*H*-1,2,3-triazole (**3**) (25 mg, 0.14 mmol, 1 eq.), decylazide (25 mg, 0.14 mmol, 1eq.), copper (II) sulfate pentahydrate (5 mg, cat.), sodium ascorbate (10 mg, cat.) and TBTA (1 mg, cat.) were added to *t*-BuOH : water (2:1, 5 mL) and stirred at room temperature for 16 hours. The solution was then diluted with water (10 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to give the crude product.

Purification by flash chromatography in a gradient of DCM to 95:5 DCM : methanol gave the desired product as a white solid (32 mg, 65%), with physical and spectroscopic data in agreement with those previously reported.[15]

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.96 (s, 1H), 7.29-7.40 (m, 5H), 5.57 (s, 2H), 4.39 (t, *J* = 7 Hz, 2H), 1.85-1.93 (m, 2H), 1.23-1.31 (m, 14H), 0.86 (t, *J* = 7 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 140.6, 140.1, 134.3, 129.2, 128.9, 128.3, 120.6, 120.4, 54.4, 50.6, 31.9, 30.3, 29.5, 29.4, 29.3, 29.0, 26.5, 22.7, 14.2. MS (ESI) *m/z*= 367.5 $(M+H)^+$. HRMS (ESI) found 367.2614, calculated 367.2605 for $(M+H)^+$. RP-HPLC R_t=9.67 min, 96%.

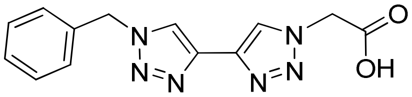
*1-Benzyl-1'-(cyclohexylmethyl)-1*H*,1'*H*-4,4'-bi(1,2,3-triazole)* (**5b**)



Prepared according to general procedure C with 1-benzyl-4-ethynyl-1*H*-1,2,3-triazole (**3**) (25 mg, 0.14 mmol, 1 eq.), (azidomethyl)cyclohexane (19 mg, 0.14 mmol, 1 eq.), copper (II) sulfate pentahydrate (10 mg, cat.), sodium ascorbate (20 mg, cat.) and TBTA (1 mg, cat.) and purified in a gradient of 67:33 hexane : ethyl acetate to 33:67 hexane : ethyl acetate to give the desired product as a white solid (23 mg, 52 %).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.95 (s, 1H), 7.41 – 7.35 (m, 3H), 7.35 – 7.29 (m, 2H), 5.58 (s, 2H), 4.23 (d, *J* = 7.2 Hz, 2H), 1.98 – 1.84 (m, 1H), 1.75 – 1.60 (m, 6H), 1.27 – 1.13 (m, 2H), 1.10 – 0.93 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 141.1, 140.0, 134.4, 129.3, 129.0, 128.4, 121.1, 120.6, 56.8, 54.5, 38.9, 30.6, 26.2, 25.6. MS (ESI) *m/z*= 323.7 (100%) $(M+H)^+$, 645.1 (70%) $(2M+H)^+$. HRMS (ESI) found 323.1975, calculated 323.1979 for $(M+H)^+$. RP-HPLC R_t=14.75 min, 97%.

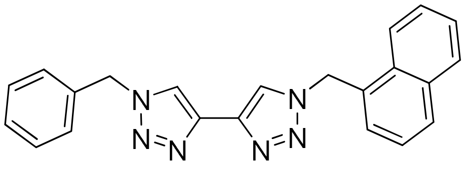
*2-(1'-Benzyl-1*H,*1'*H-*4,4'-bi(1,2,3-triazol)-1-yl)acetic acid* (**5c**)



Prepared according to general procedure C with 1-benzyl-4-ethynyl-1*H*-1,2,3-triazole (**3**) (65 mg, 0.36 mol, 1 eq.), azidoacetic acid (36 mg, 0.36 mmol, 1 eq.), copper (II) sulfate pentahydrate (10 mg, cat.), sodium ascorbate (20 mg, cat.) and TBTA (2 mg, cat.) and purified in a gradient of 90:10:1 ethyl acetate : methanol : acetic acid to 80:20:1 ethyl acetate : methanol : acetic acid to give the product as a white solid (41 mg, 40 %), which was only slightly soluble in D_2O in the presence of $NaHCO_3$ (1 eq.).

^{1}H-NMR (400 MHz, D_2O & $NaHCO_3$) δ 8.40 (s, 1H), 8.32 (s, 1H), 7.43-7.51 (m, 5H), 5.74 (s, 2H), 5.16 (s, 2H). ^{13}C-NMR (100 MHz, D_2O & $NaHCO_3$) δ 173.1, 138.9, 138.4, 134.7, 129.2, 128.8, 128.1, 123.9, 123.0, 54.1, 53.2. MS (ESI) *m/z*= 283.4 $(M-H)^-$. HRMS (ESI) found 283.0960, calculated 283.0949 for $(M-H)^-$. RP-HPLC R_t=7.42 min, 95%.

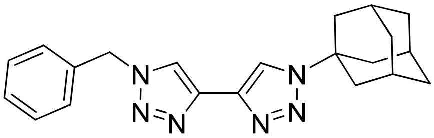
*1-Benzyl-1'-(napthyl-1-ylmethyl)-1*H,*1'*H-*4,4'-bi(1,2,3-triazole)* (**5d**)



Prepared according to general procedure C with 1-benzyl-4-ethynyl-1*H*-1,2,3-triazole (**3**) (28 mg, 0.15 mmol, 1 eq.), 1-(azidomethyl)napthalene (28 mg, 0.15 mmol, 1 eq.), copper (II) sulfate pentahydrate (10 mg, cat.), sodium ascorbate (20 mg, cat.) and TBTA (1 mg, cat.) and purified in a gradient of 50:50 ethyl acetate : hexane to 67:33 ethyl acetate : hexane to give the desired product as a white solid (15 mg, 34%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.87 – 7.97 (m, 4H), 7.80 (s, 1H), 7.48 – 7.52 (m, 4H), 7.35 – 7.38 (m, 3H), 7.26 – 7.29 (m, 2H), 6.02 (s, 2H), 5.53 (s, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 140.5, 140.3, 134.4, 134.2, 131.3, 130.4, 129.6, 129.3, 129.2, 129.0, 128.3 (2 carbons), 127.5, 126.6, 125.5, 122.9, 120.7, 120.6, 54.5, 52.7. MS (ESI) *m/z*= 733.3 (100%) $(2M+H)^+$, 367.1 (50%) $(M+H)^+$. HRMS (ESI) found 367.1673, calculated 367.1666 for $(M+H)^+$. RP-HPLC R_t=6.76 min, 95%.

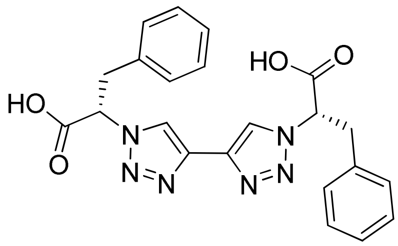
*1-Adamantyl-1'-benzyl-1*H*,1'*H*-4,4'-bi(1,2,3-triazole)* (**5e**)



Prepared according to general procedure C with 1-benzyl-4-ethynyl-1*H*-1,2,3-triazole (**3**) (102 mg, 0.56 mol, 1 eq.), azidoadamantane (100 mg, 0.56 mmol, 1 eq.), copper (II) sulfate pentahydrate (10 mg, cat.), sodium ascorbate (20 mg, cat.) and TBTA (2 mg, cat.) and purified in a gradient of 50:50 ethyl acetate : hexane to ethyl acetate to give the desired product as a white solid (30 mg, 19%).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.96 (s, 1H), 7.27-7.38 (m, 5H), 5.56 (s, 2H), 2.20-2.30 (m, 9H), 1.74-1.80 (m, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$, JMOD) δ 140.9 (C), 139.1 (C), 134.5 (C), 129.2 (CH), 128.9 (CH), 128.2 (CH), 120.5 (CH), 117.3 (CH), 59.9 (C), 54.4 (CH_2), 43.0 (CH_2), 35.9 (CH), 29.5 (CH_2). MS (ESI) *m/z*= 361.7 $(M+H)^+$. HRMS (ESI) found 361.2126, calculated 361.2135 for $(M+H)^+$. RP-HPLC R_t=15.42 min, 95%.

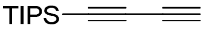
*(S,S)-2,2’-(1*H,*1’*H*-4,4’-Bi(1,2,3-triazole)-1,1’-diyl)bis(3-phenylpropanoic acid)* (**7**)



To a solution of *t*-BuOH : water (10 mL, 2:1) was added 2-azido-3-phenylpropanoic acid (**6**) (107 mg, 0.56 mmol, 1 eq.), freshly prepared buta-1,3-diynyltrimethylsilane (**1**) (0.84 mmol in *t*-BuOH, 1.5 eq.), copper (II) sulfate pentahydrate (20 mg, cat.) and sodium ascorbate (40 mg, cat.). The solution was left stirring at room temperature for 16 hours, then diluted with HCl (1M, 20 mL) and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give a brown solid. Purification by flash chromatography in a gradient of 100:1 ethyl acetate : acetic acid to 80:20:1 ethyl acetate : methanol : acetic acid gave the product as a white solid (48 mg, 40%). ^{1}H-NMR (300 MHz, CD_3OD) δ 8.35 (s, 2H), 7.12-7.18 (m, 10H), 5.73 (s, 2H), 3.67-3.72 (m, 2H), 3.54-3.58 (m, 2H). ^{13}C-NMR (75 MHz, CD_3OD) δ 171.4, 137.3, 130.0, 129.6, 128.1, 140.2, 123.8, 66.6, 39.0. MS (ESI) *m/z*= 433.4 $(M+H)^+$. HRMS (ESI) found 431.1467, calculated 431.1473 for $(M-H)^-$. $[\alpha]^{22}_D = -0.15$, (c 0.20, $CHCl_3$). RP-HPLC R_t=11.95 min, 95%.

4. Preparation of bis-(1,2,3-triazoles) using TIPS-butadiyne

Buta-1,3-diynyltriisopropylsilane (**8**)[18]



N-Bromosuccinimide (5.15 g, 29.0 mmol, 1.15 eq.), silver nitrate (4.28 g, 25.2 mmol, 1 eq.) and triisopropylsilylacetylene (5.6 mL, 25.2 mmol, 1 eq.) were added to acetone (200 mL) and left stirring at room temperature for 2 hours. The solution was then diluted with water (150 mL) and extracted with hexane (3 × 125 mL). The combined organic layers were washed with water (1 × 50 mL) and brine (1 × 50 mL), dried over anhydrous magnesium sulfate, filtered and evaporated to give (bromoethynyl)triisopropylsilane as a clear oil (6.61 g, 99 %), with physical and spectroscopic data in agreement with those previously reported.[19]

^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 21H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 83.7, 61.9, 18.7, 11.5.

n-Butylamine (4.47 mL, 45.2 mmol, 3 eq.), 2-methylbut-3-yn-2-ol (2.95 mL, 30.2 mmol, 2 eq.), copper (I) chloride (30 mg, cat.) and hydroxylamine hydrochloride (314 mg, 4.52 mmol, 0.3 eq.) were added in order to a solution of methanol : water (2:1, 80 mL). (Bromoethynyl)triisopropylsilane (4.00 g, 15.1 mmol, 1 eq.) was diluted with methanol (40 mL) and added dropwise over 30 mins. The solution was left stirring at room temperature for 24 hours. The solution was then diluted with water (100 mL) and extracted with diethylether (3 × 75 mL). The combined organic layers were washed with water (1 × 50 mL) and brine (2 × 50 mL), dried over anhydrous magnesium sulfate, filtered and evaporated. Purification by flash chromatography in a gradient of hexane to 90:10 hexane : ethyl acetate gave 2-methyl-6-(triisopropylsilyl)hexa-3,5-diyn-2-ol as a white solid (1.55 g, 78%), with physical and spectroscopic data in agreement with those previously reported. [18,19]

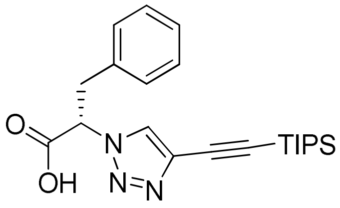
M.P. 50-51 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 1H), 1.52 (s, 6H), 1.06 (s, 21H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 89.0, 84.9, 80.8, 67.8, 65.7, 31.2, 18.6, 11.4.

2-Methyl-6-(triisopropylsilyl)hexa-3,5-diyn-2-ol (504 mg, 1.86 mmol, 1 eq.) was added to a solution of crushed potassium hydroxide (210 mg, 3.73 mmol, 2 eq.) in benzene (15 mL) and the solution heated to 80 °C for 2.5 hours. The solution was then cooled and diluted with water (20 mL) and extracted with hexane (3 × 15 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give an orange oil.

Purification by filtration through silica, eluting with hexane gave the product as an orange/red oil (360 mg, 91%), with physical and spectroscopic data in agreement with those previously reported.[18] The product was stored at -10 °C, at which temperature it has been reported to be stable for months.[20]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.07 (s, 1H), 1.09 (s, 21H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 89.2, 82.2, 68.8, 65.7, 18.6, 11.3

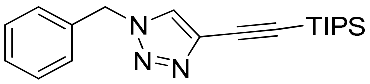
*(S)-3-Phenyl-2-(4-((triisopropylsilyl)ethynyl)-1*H*-1,2,3-triazol-1-yl)propanoic acid* (**9a**)



To a solution of (*S*)-azidobenzylacetic acid (200 mg, 1.05 mmol, 1 eq.), buta-1,3-diynyltriisopropylsilane (**8**) (238 mg, 1.15 mmol, 1.1 eq.) and diisopropylethylamine (911 µL, 5.23 mmol, 5 eq.) in acetonitrile (10 mL) was added copper (I) iodide (40 mg, 0.21 mmol, 0.2 eq.). The solution was then left stirring at room temperature for 16 hours under nitrogen. The solution was then diluted with HCl (1 M, 20 mL) and extracted with ethyl acetate (3 × 20 mL), the combined organic layers were then dried over magnesium sulfate, filtered and evaporated to give the crude which was purification by flash chromatography in a gradient of 70:30:1 hexane : ethyl acetate : acetic acid to 100:1 ethyl acetate : acetic acid to give the product as a yellow solid (226 mg, 54 %).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.18-7.20 (m, 3H), 6.97-6.99 (m, 2H), 5.49 (aq, *J* = 3.0, 6.0 Hz, 1H), 3.49 (m, 2H) 1.08 (s, 21H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 173.3, 136.0, 130.2, 128.8 (2 carbons), 128.1, 127.1, 95.7, 95.0, 66.8, 38.8, 18.7, 11.2. MS (ESI) *m/z*= 398.4 $(M+H)^+$. HRMS (ESI) found 398.2271, calculated 398.2258 for $(M+H)^+$. $[\alpha]^{22}_D$ = -0.27, (c 0.50, $CHCl_3$). RP-HPLC R_t=12.68 min, >99%.

*1-Benzyl-4-((triisopropylsilyl)ethynyl)-1*H-*1,2,3-triazole* (**9b**) [21]



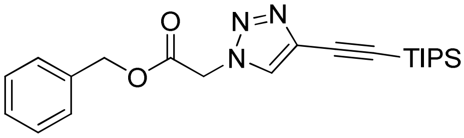
General procedure D:

Benzyl azide (104 mg, 0.782 mmol, 1 eq.), buta-1,3-diynyltriisopropylsilane (**8**) (194 mg, 0.94 mmol, 1.2 eq.), copper iodide (30 mg, 0.16 mmol, 20 mol%), diisopropylethylamine (680 µL, 3.91 mmol, 5 eq.) and TBTA (1 mg, cat.) were added to acetonitrile (15 mL) and sealed under a nitrogen atmosphere and left stirring at room temperature for 16 hours. The solution was then evaporated and taken up in water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give the crude product.

Purified by flash chromatography in a gradient of hexane to 85:15 hexane : ethyl acetate gave the product as a white solid (186 mg, 70%), with physical and spectroscopic data in agreement with those previously reported.[21]

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.36-7.38 (m, 3H), 7.26-7.28 (m, 2H), 5.51 (s, 2H), 1.12 (s, 21H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ 134.2, 131.6, 129.2, 129.0, 128.2, 126.4, 95.4, 95.2, 54.3, 18.6, 11.2. MS (ESI) *m/z*= 340.6 $(M+H)^+$. RP-HPLC R_t=12.12 min, 95%

*Benzyl 2-(4-((triisopropylsilyl)ethynyl)-1*H-*1,2,3-triazol-1-yl)acetate* (**9c**)

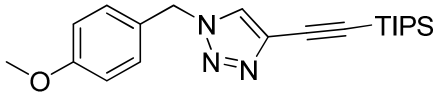


As per general procedure D with benzyl 2-azidoacetate (167 mg, 0.87 mmol, 1 eq.) buta-1,3-diynyltriisopropylsilane (**8**) (216 mg, 1.05 mmol, 1.2 eq.), copper iodide (33 mg, 0.18 mmol, 20 mol%), diisopropylethylamine (760 µL, 4.36 mmol, 5 eq.) and TBTA (1 mg, cat.).

Purification by flash chromatography in a gradient of hexane to 70:30 hexane : ethyl acetate gave the product as a white solid (280 mg, 81 %).

^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.79 (s, 1H), 7.40 – 7.32 (m, 5H), 5.23 (s, 2H), 5.18 (s, 2H), 1.14 – 1.10 (m, 21H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ 165.9, 134.5, 131.9, 129.1, 128.9, 128.8, 127.8, 95.8, 95.1, 68.3, 51.0, 18.7, 11.3. MS (ESI) *m/z*= 795.6 (100%) (2M+H)$^+$, 398.7 (80%) (M+H)$^+$. HRMS (ESI) found 298.2269, calculated 298.2258 for (M+H)$^+$. RP-HPLC R$_t$=14.76 min, >99%.

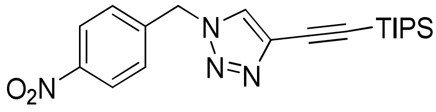
*1-(4-methoxybenzyl)-4-((triisopropylsilyl)ethynyl)-1*H*-1,2,3-triazole* (**9d**)



Prepared according to general procedure D with 4-methoxybenzyl azide (85 mg, 0.52 mmol, 1 eq.) buta-1,3-diynyltriisopropylsilane (**8**) (118 mg, 0.57 mmol, 1.1 eq.), copper iodide (20 mg, 0.10 mmol, 20 mol%), diisopropylethylamine (450 µL, 2.60 mmol, 5 eq.) and TBTA (1 mg, cat.). Purification by flash chromatography in a gradient of hexane to 80:20 hexane : ethyl acetate to give the product as a yellow oil (109 mg, 57 %).

^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.50 (s, 1H), 7.24 – 7.20 (m, 2H), 6.92 – 6.89 (m, 2H), 5.44 (s, 2H), 3.81 (s, 3H), 1.13 – 1.05 (m, 21H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ 160.1, 131.5, 129.8, 129.4, 126.1, 114.6, 95.5, 95.1, 55.4, 53.9, 18.6, 11.2. MS (ESI) *m/z*= 739.5 (2M+H)$^+$. HRMS (ESI) found 370.2313, calculated 370.2309 for (M+H)$^+$. RP-HPLC R$_t$=14.96 min, 99%.

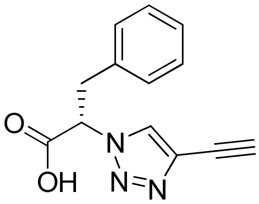
*1-(4-nitrobenzyl)-4-((triisopropylsilyl)ethynyl)-1*H*-1,2,3-triazole* (**9e**)



Prepared according to general procedure D with 4-nitrobenzyl azide (103 mg, 0.58 mmol, 1 eq.) buta-1,3-diynyltriisopropylsilane (**8**) (144 mg, 0.70 mmol, 1.2 eq.), copper iodide (22 mg, 0.11 mmol, 20 mol%), diisopropylethylamine (490 µL, 2.81 mmol, 5 eq.) and TBTA (1 mg, cat.). Purification by flash chromatography in a gradient of hexane to 70:30 hexane : ethyl acetate to give the product as a white solid (175 mg, 78 %).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.23 – 8.18 (m, 2H), 7.66 (s, 1H), 7.43 – 7.39 (m, 2H), 5.64 (s, 2H), 1.13 – 1.07 (m, 21H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.2, 141.3, 132.2, 128.8, 126.6, 124.4, 96.1, 94.9, 53.2, 18.7, 11.3. MS (ESI) *m/z*= 769.5 (100%) $(2M+H)^+$, 385.5 (60%) $(M+H)^+$. HRMS (ESI) found 385.2050, calculated 385.2054 for $(M+H)^+$. RP-HPLC R_t=14.67 min, >99%.

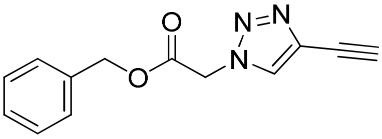
*(S)-2-(4-Ethynyl-1*H*-1,2,3-triazol-1-yl)-3-phenylpropanoic acid* (**10a**)



To 3-phenyl-2-(4-((triisopropylsilyl)ethynyl)-1H-1,2,3-triazol-1-yl)propanoic acid (**9a**) (195 mg, 0.49 mmol) in acetonitrile (10 mL) was added tetrabutylammonium fluoride (2.45 mL, 1 M, 2.45 mmol, 5 eq.) and the solution was left stirring for 30 mins. The solution was then diluted with HCl (1 M, 15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give a crude brown oil which was purified by flash chromatography in a gradient of 100:1 ethyl acetate : acetic acid to 80:20:1 ethyl acetate : methanol : acetic acid to give the product as a yellow oil (31 mg, 26 %).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.11 (bs, 1H), 7.70 (s, 1H), 7.24 (m, 3H), 7.06 – 6.98 (m, 2H), 5.64 (dd, *J* = 8.9, 5.3 Hz, 1H), 3.58 (dd, *J* = 14.4, 5.3 Hz, 1H), 3.49 (dd, *J* = 14.4, 9.2 Hz, 1H), 3.23 (s, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.5, 134.5, 129.7, 129.1, 129.0, 127.9, 127.6, 81.8, 72.5, 64.5, 38.6. MS (ESI) *m/z*= 242.4 $(M+H)^+$. HRMS (ESI) found 242.0922, calculated 242.0924 for $(M+H)^+$. $[\alpha]^{22}_D$ = -0.66, (c 1.00, $CHCl_3$). RP-HPLC R_t=7.54 min, 95%.

*Benzyl 2-(4-ethynyl)-1*H-*1,2,3-triazol-1-yl)acetate* (**10c**)[17]



Method 1:

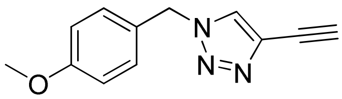
Was prepared according to general procedure A with benzyl 2-(4-((triisopropylsilyl)ethynyl)-*1H*-1,2,3-triazol-1-yl)acetate (**9c**) (74 mg, 0.19 mmol, 1 eq.) and tetrabutylammonium fluoride (226 µL, 0.23 mmol, 1M in THF, 1.2 eq.). Purification by flash chromatography in a gradient of 90:10 hexane : ethyl acetate to 60:40 hexane : ethyl acetate gave the product as a white solid (30 mg, 67 %).

Method 2:

Was prepared according to general procedure B with benzyl 2-azidoacetate (100 mg, 0.52 mmol, 1 eq.), buta-1,3-diynyltriisopropylsilane (**8**) (130 mg, 0.63 mmol, 1.2 eq.), copper iodide (20 mg, 0.11 mmol, 20 mol%), TBTA (1 mg, cat.), diisopropylethylamine (456 µL, 2.62 mmol, 5 eq.) and tetrabutylammonium fluoride (628 µL, 1M in THF, 0.63 mmol, 1.2 eq.). Purification by flash chromatography in a gradient of 90:10 hexane : ethyl acetate to 60:40 hexane : ethyl acetate gave the product as a white solid (89 mg, 70 %), with physical and spectroscopic data in agreement with those previously reported.[17]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.41 – 7.31 (m, 5H), 5.23 (s, 2H), 5.20 (s, 2H), 3.25 (s, 1H). MS (ESI) *m/z*= 242.1 $(M+H)^+$. RP-HPLC R_t=7.92 min, 96%.

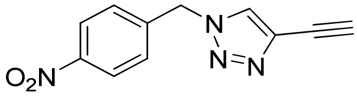
*1-(4-Methoxybenzyl)-4-ethynyl-1*H*-1,2,3-triazole* (**10d**)



Prepared according to general procedure A with 1-(4-methoxybenzyl)-4-((triisopropylsilyl)ethynyl)-*1H*-1,2,3-triazole (**9d**) (52 mg, 0.41 mmol, 1 eq.) and tetrabutylammonium fluoride (169 µL, 0.17 mmol, 1M in THF, 1.2 eq.). Purification by flash chromatography in a gradient of 80:20 hexane : ethyl acetate to 50:50 hexane : ethyl acetate gave the product as a white solid (20 mg, 67 %).

^{1}H-NMR (400 MHz, CDCl$_3$) δ 7.54 (s, 1H), 7.24 – 7.19 (m, 2H), 6.92 – 6.86 (m, 2H), 5.45 (s, 2H), 3.80 (s, 3H), 3.19 (s, 1H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ 160.2, 130.4, 129.9, 126.5, 126.0, 114.7, 81.2, 73.2, 55.5, 54.0. MS (ESI) *m/z*= 214.2 (M+H)$^+$. HRMS (ESI) found 214.0984, calculated 214.0975 for (M+H)$^+$. RP-HPLC R$_t$=7.81 min, 96%.

*1-(4-nitrobenzyl)-4-ethynyl-1*H*-1,2,3-triazole* (**10e**)



Method 1:

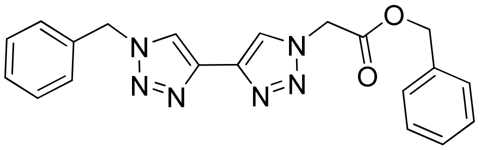
Prepared according to general procedure B with 4-nitrobenzyl azide (100 mg, 0.52 mmol, 1 eq.), buta-1,3-diynyltriisopropylsilane (**8**) (129 mg, 0.63 mmol, 1.2 eq.), copper iodide (20 mg, 0.11 mmol, 20 mol%), TBTA (1 mg, cat.), diisopropylethylamine (456 µL, 2.62 mmol, 5 eq.) and tetrabutylammonium fluoride (628 µL, 1M in THF, 0.63 mmol, 1.2 eq.). Purification by flash chromatography in a gradient of chloroform to 80:20 chloroform : ethyl acetate gave the product as a white solid (89 mg, 70 %).

Method 2:

Was prepared according to general procedure A with 1-(4-nitrobenzyl)-4-((triisopropylsilyl)ethynyl)-1*H*-1,2,3-triazole (**9e**) (75 mg, 0.19 mmol, 1 eq.) and tetrabutylammonium fluoride (226 µL, 0.23 mmol, 1M in THF, 1.2 eq.). Purification by flash chromatography in a gradient of chloroform to 80:20 chloroform : ethyl acetate gave the product as a white solid (29 mg, 66 %).

^{1}H-NMR (400 MHz, d_6-DMSO) δ 8.61 (s, 1H), 8.32 – 8.17 (m, 2H), 7.61 – 7.46 (m, 2H), 5.80 (s, 2H), 4.43 (s, 1H). ^{13}C-NMR (100 MHz, d_6-DMSO) δ 147.3, 142.9, 129.1, 129.1, 128.9, 124.0, 84.1, 73.6, 52.1. MS (ESI) *m/z*= 229.2 $(M+H)^+$. HRMS (ESI) found 229.0716, calculated 229.0720 for $(M+H)^+$. RP-HPLC R_t=7.23 min, 98%.

*Benzyl 2-(1'-benzyl-1*H*,1'*H*-4,4'-bi(1,2,3-triazol)-1-yl)acetate* (**11b**)[17]



Method 1, General procedure E:

To a solution of 1-benzyl-4-(ethynyl)-1*H*-1,2,3-triazole (**3**) (50 mg, 0.27 mmol, 1 eq.) in acetonitrile (15mL) was added benzyl 2-azidoacetate (57 mg, 0.30 mmol, 1.1 eq.), copper iodide (10 mg, 0.06 mmol, 20 mol%) and TBTA (1 mg, cat.), the solution was then sealed under nitrogen and diisopropylethylamine (240 µL, 1.36 mmol, 5 eq.) was added. The solution was left stirring at room temperature for 16 hours, then diluted with water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give a crude residue.

Purification by flash chromatography in a gradient of chloroform to 50:50 chloroform : ethyl acetate gave the product as a white solid (64 mg, 63 %).

Method 2:

To a solution of 1-benzyl-4-((triisopropylsilyl)ethynyl)-1*H*-1,2,3-triazole (**9b**) (50 mg, 0.15 mmol, 1 eq.) in acetonitrile (15mL) was added TBAF (162 µL, 0.16 mmol, 1.1 eq.) and the solution was stirred at room temperature for 15 mins. Acetic acid (17 µL, 0.30 mmol, 2 eq.), benzyl 2-azidoacetate (31 mg, 0.16 mmol, 1.1 eq.), copper iodide (6 mg, 0.03 mmol, 20 mol%) and TBTA (1 mg, cat.) and diisopropylethylamine (130 µL, 0.74 mmol, 5 eq.) were then added in order. The solution was left stirring at room temperature under nitrogen for 14 hours. The solution was then diluted with water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give an off white solid. Purification by flash chromatography in a gradient of chloroform to 50:50 chloroform : ethyl acetate gave the product as a white solid (35 mg, 64 %).

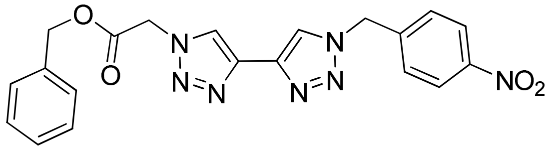
Method 3, General procedure F:

To a solution of benzyl azide (50 mg ,0.38 mmol, 1 eq.) in acetonitrile (10 mL) was added buta-1,3-diynyltriisopropylsilane (**8**) (93 mg, 0.45 mmol, 1.2 eq.), copper iodide (14 mg, 0.08 mmol, 20 mol%) and TBTA (1 mg, cat.), the solution was then sealed under nitrogen and diisopropylethylamine (327 µL, 1.88 mmol, 5 eq.) was added. The solution was left stirring at room temperature for 20 hours. Tetrabutylammonium fluoride (451 µL, 1M in THF, 0.45 mmol, 1.2 eq.) was added and the solution left stirring at room temperature for 20 mins followed by addition of acetic acid (47 µL, 0.75 mmol, 2 eq.). Benzyl 2-azidoacetate (86 mg, 0.45 mmol, 1.2 eq.) in acetonitrile (1 mL) was then added and the reaction left at room temperature for a further 16 hours. The reaction was then diluted with water (20 mL) and extracted with ethyl acetate (3 × 20 mL) and the combined organic layers were dried over anhydrous magnesium sulfate, filtered and evaporated to give a brown solid.

Purification by flash chromatography in a gradient of 80:20 hexane : ethyl acetate to 80:20 ethyl acetate : hexane gave a white solid, which was recrystallised in ethyl acetate/hexane to give the product as a white crystalline solid (69 mg, 49 %), with physical and spectroscopic data in agreement with those previously reported.[17]

M.P. 163 °C (decomp.). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.96 (s, 1H), 7.41 – 7.30 (m, 10H), 5.58 (s, 2H), 5.24 (as, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.0, 140.7, 140.3, 134.6, 134.4, 129.4, 129.1, 129.0, 128.9, 128.8, 128.4, 122.1, 120.9, 68.3, 54.5, 51.1. MS (ESI) *m/z*= 375.2 $(M+H)^+$. RP-HPLC R_t= 8.87 min, 95 %.

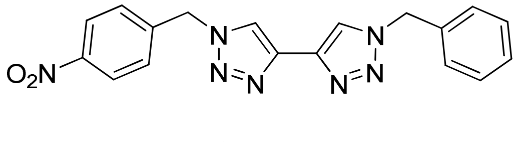
*Benzyl 2-(1'-(4-nitrobenzyl)-1*H*,1'*H*-4,4'-bi(1,2,3-triazol)-1-yl)acetate* (**11c**) [17]



Prepared according to general procedure E with benzyl(2-(4-ethynyl)-1*H*-1,2,3-triazol-1-yl) acetate (**9c**) (41 mg, 0.17 mmol, 1 eq.), 4-nitrobenzyl azide (36 mg, 0.20 mmol, 1.2 eq.), copper iodide (6 mg, 0.03 mmol, 20 mol%), TBTA (1 mg, cat.) and diisopropylethylamine (147 µL, 0.84 mmol, 5 eq.). Purification by flash chromatography in a gradient of 50:50 ethyl acetate : chloroform to 90:10 ethyl acetate : chloroform gave the product as a white solid (36 mg, 50 %)., with physical and spectroscopic data in agreement with those previously reported.[17]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.23 (m, 2H), 8.18 (s, 1H), 8.06 (s, 1H), 7.49 – 7.43 (m, 2H), 7.42 – 7.32 (m, 5H), 5.71 (s, 2H), 5.26 (s, 2H), 5.25 (s, 2H). MS (ESI) *m/z*= 420.2 $(M+H)^+$. RP-HPLC R_t= 9.71 min, 95 %

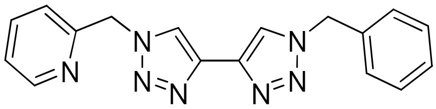
*1-Benzyl-1'-(4-nitrobenzyl)-1*H*,1'*H*-4,4'-bi(1,2,3-triazole)* (**11e**)[17]



Prepared according to general procedure E with 1-(4-nitrobenzyl)-4-(ethynyl)-1*H*-1,2,3-triazole (**9e**) (24 mg, 0.10 mmol, 1 eq.), benzyl azide (14 mg, 0.10 mmol, 1 eq.), copper iodide (4 mg, 0.02 mmol, 20 mol%), TBTA (0.5 mg, cat.) and diisopropylethylamine (90 µL, 0.52 mmol, 5 eq.). Purification by flash chromatography in a gradient of 50:50 ethyl acetate : hexane to 80:20 ethyl acetate : hexane gave the product as a white solid (25 mg, 68 %), with physical and spectroscopic data in agreement with those previously reported.[17]

^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.22 (m, 2H), 8.03 (s, 1H), 7.96 (s, 1H), 7.43 (ad, *J* = 8.8 Hz, 2H), 7.41 – 7.29 (m, 5H), 5.69 (s, 2H), 5.58 (s, 2H). MS (ESI) *m/z*= 362.2 $(M+H)^+$. RP-HPLC R_t= 9.61 min, 98 %.

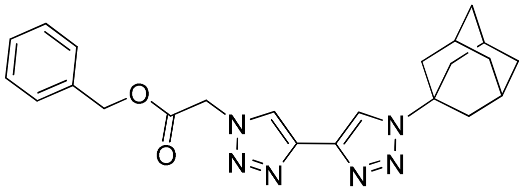
*1-Benzyl-1'-(pyridin-2-ylmethyl)-1*H*,1'*H*-4,4'-bi(1,2,3-triazole)* (**11f**)



Prepared according to general procedure F with benzyl 2-azidomethylpyridine (110 mg, 0.82 mmol, 1 eq.), buta-1,3-diynyltriisopropylsilane (**8**) (203 mg, 0.98 mmol, 1.2 eq.), copper iodide (31 mg, 0.16 mmol, 20 mol%), TBTA (1 mg, cat.), diisopropylethylamine (715 µL, 4.10 mmol, 5 eq.), tetrabutylammonium fluoride (985 µL, 1M in THF, 0.98 mmol, 1.2 eq.), acetic acid (102 µL, 1.64 mmol, 2 eq.) and benzyl azide (131 mg, 0.98 mmol, 1.2 eq.). Purification by flash chromatography in a gradient of 50:50:1 hexane : ethyl acetate : triethylamine to 100:1 ethyl acetate : triethylamine followed by recrystallisation from ethyl acetate gave the product as a brown solid (120 mg, 42 %).

M.P. 182-184 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.60 (ddd, *J* = 4.9, 1.7, 0.9 Hz, 1H), 8.17 (s, 1H), 7.94 (s, 1H), 7.68 (td, *J* = 7.7, 1.8 Hz, 1H), 7.42 – 7.24 (m, 6H), 7.18 (ad, *J* = 7.8 Hz, 1H), 5.70 (s, 2H), 5.57 (s, 2H).^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.4, 150.1, 140.6, 140.6, 137.5, 134.4, 129.3, 129.1, 128.4, 123.6, 122.5, 121.4, 120.7, 55.9, 54.5. MS (ESI) *m/z*= 318.2 $(M+H)^+$. HRMS (ESI) found 318.1477, calculated 318.1462 for $(M+H)^+$. RP-HPLC R_t= 7.90 min, >99 %.

*Benzyl 2-(1'-adamantyl-1*H*,1'*H*-4,4'-bi(1,2,3-triazol)-1-yl)acetate* (**11g**)



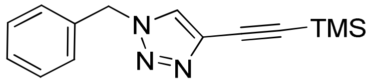
Prepared according to general procedure F with benzyl 2-azidoacetate (100 mg, 0.52 mmol, 1 eq.), buta-1,3-diynyltriisopropylsilane (**8**) (130 mg, 0.63 mmol, 1.2 eq.), copper iodide (20 mg, 0.11 mmol, 20 mol%) and TBTA (1 mg, cat.), diisopropylethylamine (458 µL, 2.63 mmol, 5 eq.), tetrabutylammonium fluoride (628 µL, 1M in THF, 0.63 mmol, 1.2 eq.), acetic acid (65 µL, 1.05 mmol, 2 eq.) and adamantyl azide (111 mg, 0.63 mmol, 1.2 eq.). Purification by flash chromatography in a gradient of 80:20 hexane : ethyl acetate to 30:70 hexane : ethyl acetate gave the product as a white solid (75 mg, 34 %). A portion was recrystallised from ethyl acetate/hexane to give a white crystalline product.

M.P. 224 – 226 °C. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.14 (s, 1H), 7.40 – 7.32 (m, 5H), 5.250 (s, 2H), 5.245 (s, 2H), 2.29 (as, 9H), 1.82 (as, 6H).^{13}C-NMR (100 MHz, $CDCl_3$) δ 166.1, 141.2, 139.0, 134.7, 129.0, 128.9, 128.8, 122.0, 117.6, 68.2, 60.0, 51.1, 43.1, 36.0, 29.6. MS (ESI) *m/z*= 419.6 $(M+H)^+$. HRMS (ESI) found 419.2205, calculated 419.2190 for $(M+H)^+$. RP-HPLC R_t= 11.61 min, 97 %.

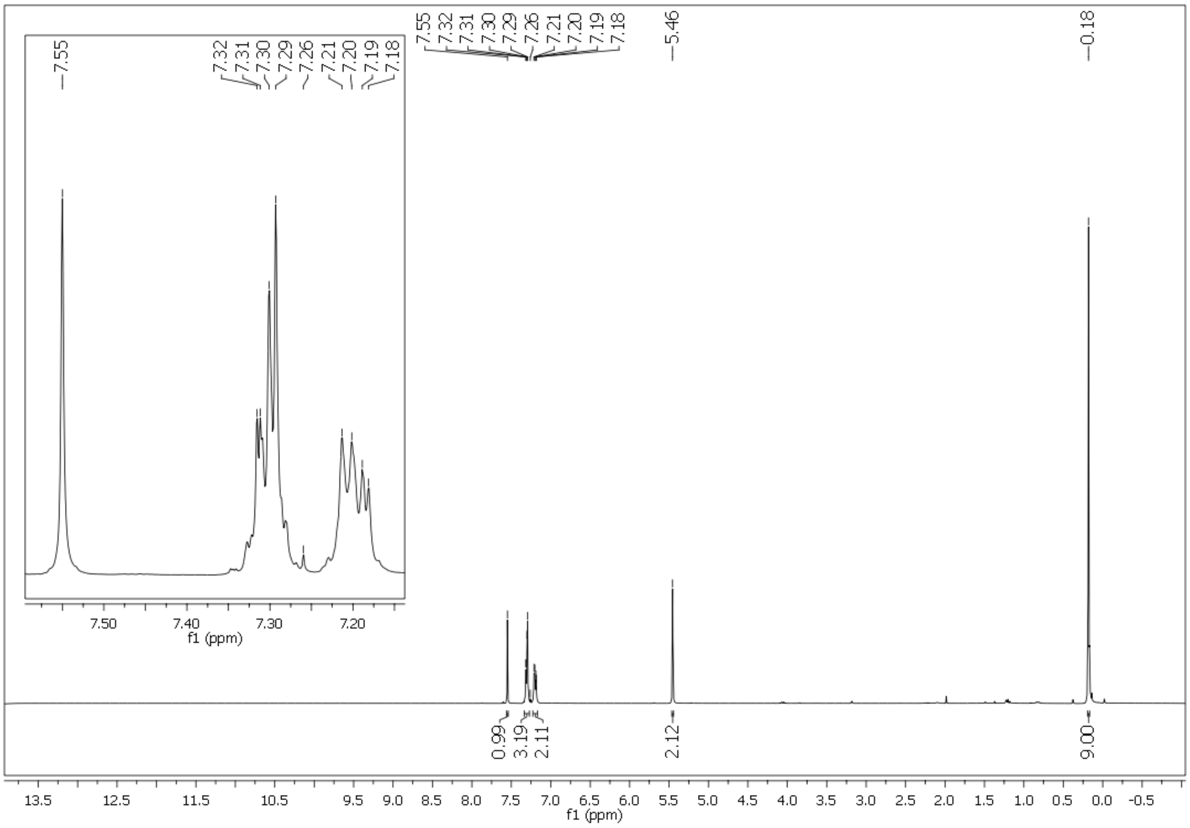
5. Bibliography

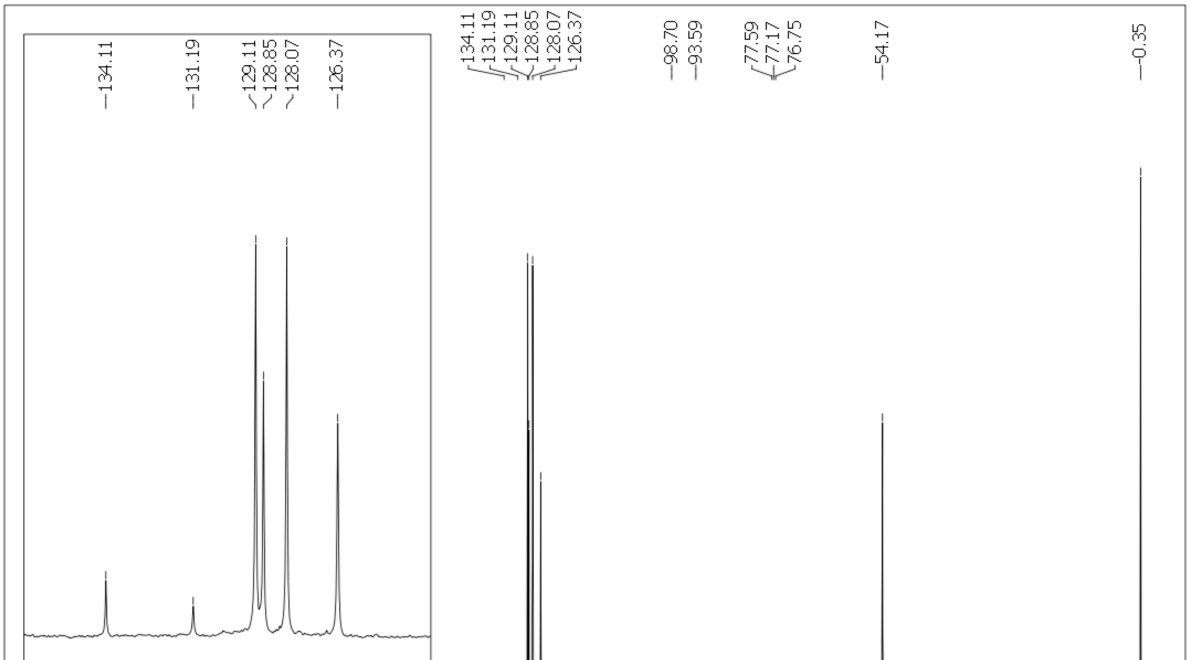
1. Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. NMR chemical shifts of common laboratory solvents as trace impurities. *J. Org. Chem.* **1997,** 62, 7512-7515.
2. Alvarez, S. G.; Alvarez, M. T. A practical procedure for the synthesis of alkyl azides at ambient temperature in dimethyl sulfoxide in high purity and yield. *Synthesis* **1997**, 413-414.
3. Goddard-Borger, E. D.; Stick, R. V. An Efficient, Inexpensive, and Shelf-Stable Diazotransfer Reagent: Imidazole-1-sulfonyl Azide Hydrochloride. *Org. Lett.* **2007,** 9, 3797-3800.
4. Ju, Y. H.; Kumar, D.; Varma, R. S. Revisiting nucleophilic substitution reactions: Microwave-assisted synthesis of azides, thiocyanates, and sulfones in an aqueous medium. *J. Org. Chem.* **2006,** 71, 6697-6700.
5. Lundquist, J. T.; Pelletier, J. C. Improved solid-phase peptide synthesis method utilizing alpha-azide-protected amino acids. *Org. Lett.* **2001,** 3, 781-3.
6. Nyfeler, E.; Renaud, P. Decarboxylative radical azidation using MPDOC and MMDOC esters. *Org. Lett.* **2008,** 10, 985-988.
7. Le Droumaguet, B.; Mantovani, G.; Haddleton, D. M.; Velonia, K. Formation of giant amphiphiles by post-functionalization of hydrophilic protein-polymer conjugates. *J. Mat. Chem.* **2007,** 17, 1916-1922.
8. Ohba, Y.; Kubo, K.; Sakurai, T. Sensitized ring-opening reactions of 3-(1-naphthyl)-2-(1-naphthalenemethyl)oxaziridine. *J. Photoch. Photobi. A.* **1998,** 113, 45-51.
9. Sirion, U.; Kim, H. J.; Lee, J. H.; Seo, J. W.; Lee, B. S.; Lee, S. J.; Oh, S. J.; Chi, D. Y. An efficient F-18 labeling method for PET study: Huisgen 1,3-dipolar cycloaddition of bioactive substances and F-18-labeled compounds. *Tetrahedron Lett.* **2007,** 48, 3953-3957.
10. Pardin, C.; Roy, I.; Lubell, W. D.; Keillor, J. W. Reversible and competitive cinnamoyl triazole inhibitors of tissue transglutaminase. *Chem. Biol. Drug Des.* **2008,** 72, 189-196.
11. Pokorski, J. K.; Jenkins, L. M. M.; Feng, H.; Durell, S. R.; Bai, Y.; Appella, D. H. Introduction of a triazole amino acid into a peptoid oligomer induces turn formation in aqueous solution. *Org. Lett.* **2007,** 9, 2381-3.
12. Bruce, M. I.; Low, P. J.; Werth, A.; Skelton, B. W.; White, A. H. Some transition-metal complexes derived from silylated 1,3 diynes. *Dalton Trans.* **1996**, 1551-1566.
13. Akintomide, T. Synthesis, characterisation and properties of rigid macromolecules with extended conjugation, using palladium catalysed, alkynlated polyhaloarenes. M. Sc. University of North Texas, 2007.
14. Holmes, A. B.; Jennings-White, C. L. D.; Schulthess, A. H. Selective Desilylation of Bis(trimethylsily1)acetylenes. *Chem. Commun.* **1979**, 840-842.
15. Fiandanese, V.; Bottalico, D.; Marchese, G.; Punzi, A.; Capuzzolo, F. An easy access to unsymmetrically substituted 4,4'-bi-1,2,3-triazoles. *Tetrahedron* **2009,** 65, 10573-10580.
16. Monkowius, U.; Ritter, S.; König, B.; Zabel, M.; Yersin, H. Synthesis, Characterisation and Ligand Properties of Novel Bi-1,2,3-triazole Ligands. *Eur. J. Inorg. Chem.* **2007,** 29, 4597-4606.
17. Aizpurua, J. M.; Azcune, I.; Fratila, R. M.; Balentova, E.; Sagartzazu-Aizpurua, M.; Miranda, J. I. "Click" Synthesis of Nonsymmetrical Bis(1,2,3-triazoles). *Org. Lett.* **2010,** 12, 1584-1587.
18. Blanco, L.; Heison, H. E.; Hirthammer, M.; Mestdagh, H.; Spyroudis, S.; Vollhardt, K. P. C. 2,3,9,1O-Tetrakis(trimethylsilyl)[5]phenylene Synthesis via Regiospecific Cobalt-Catalyzed Cocyclization of 1,6-Bis(triisopropylsilyl)-1,3,5-hexatriyne. *Angew. Chem. Int. Ed.* **1987,** 26, 1246-1247.
19. Jiang, M. X.-W.; Rawat, M.; Wulff, W. D. Contingency and Serendipity in the Reactions of Fischer Carbene Complexes with Conjugated Triynes. *J Am. Chem. Soc.* **2004,** 126, 5970-5971.
20. Trost, B. M.; Chan, V. S.; Yamamoto, D. Enantioselective ProPhenol-Catalyzed Addition of 1,3-Diynes to Aldehydes to Generate Synthetically Versatile Building Blocks and Diyne Natural Products. *J. Am. Chem. Soc.* **2010,** 132, 5186-5192.
21. Luu, T.; McDonald, R.; Tykwinski, R. R. Regioselective trapping of terminal di-, tri-, and tetraynes with benzyl azide. *Org. Lett.* **2006,** 8, 6035-6038.

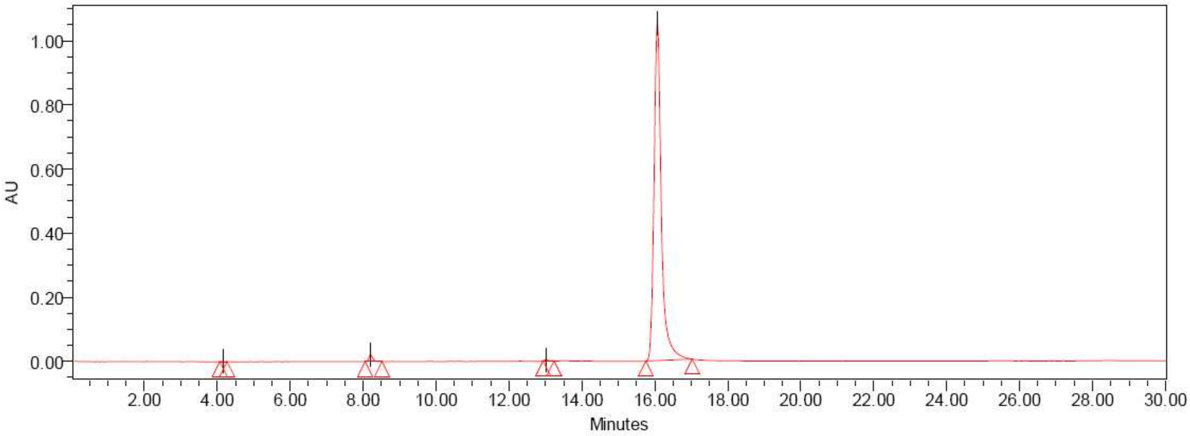
6. ^{1}H-NMR, ^{13}C-NMR and HPLC of selected compounds



(**2**)







Processed Channel: PDA 254.0 nm

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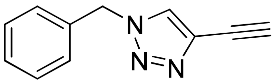
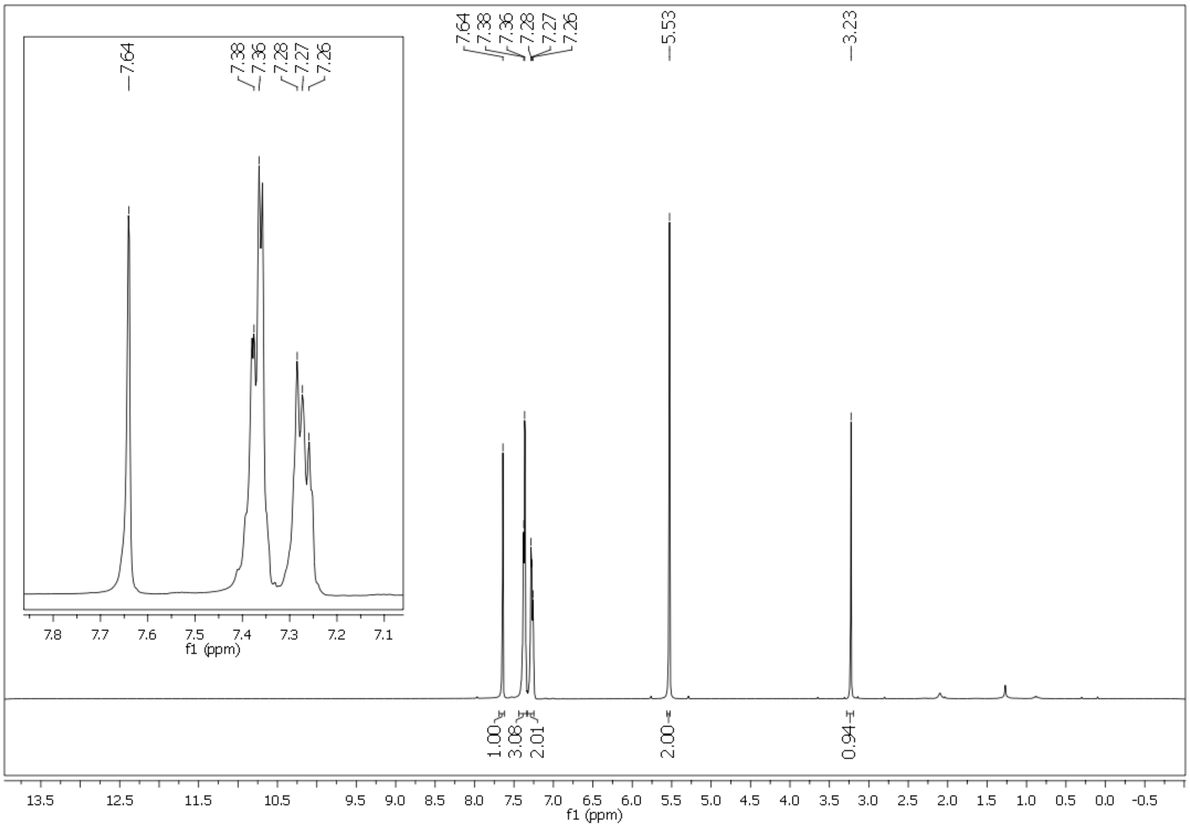
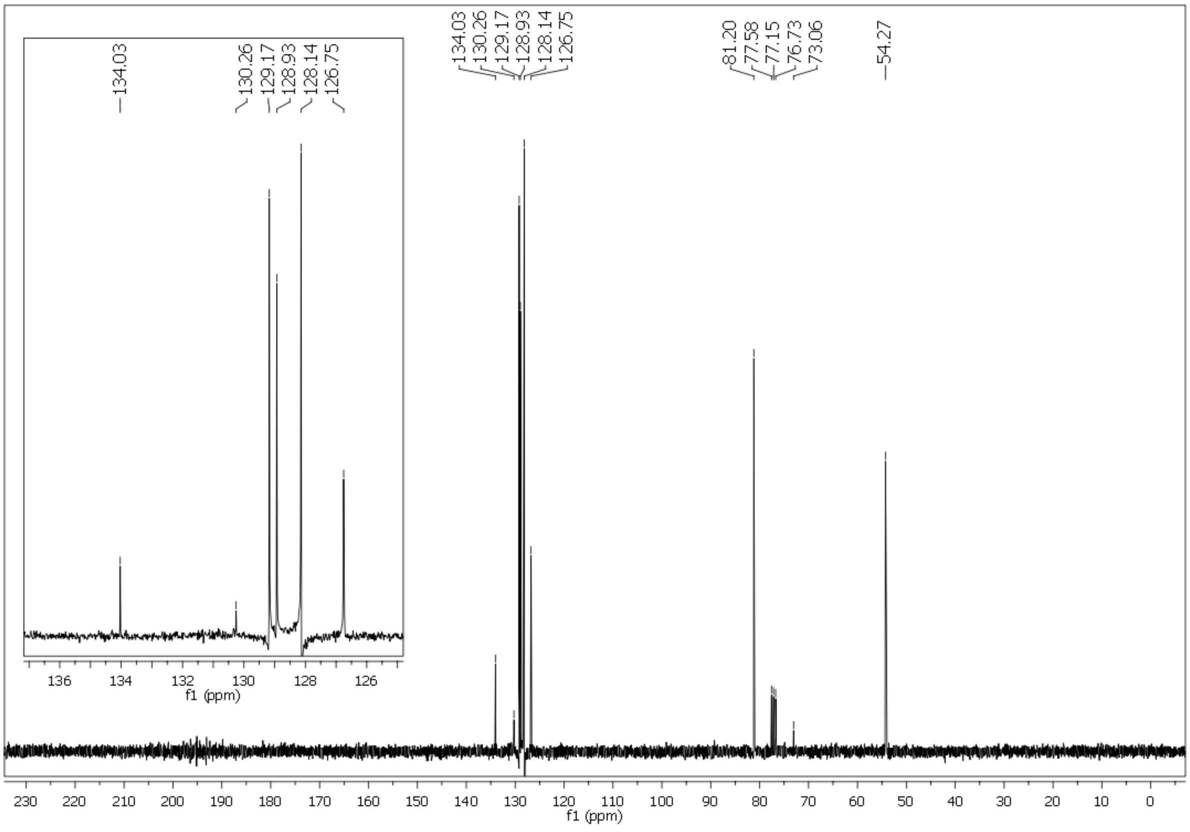
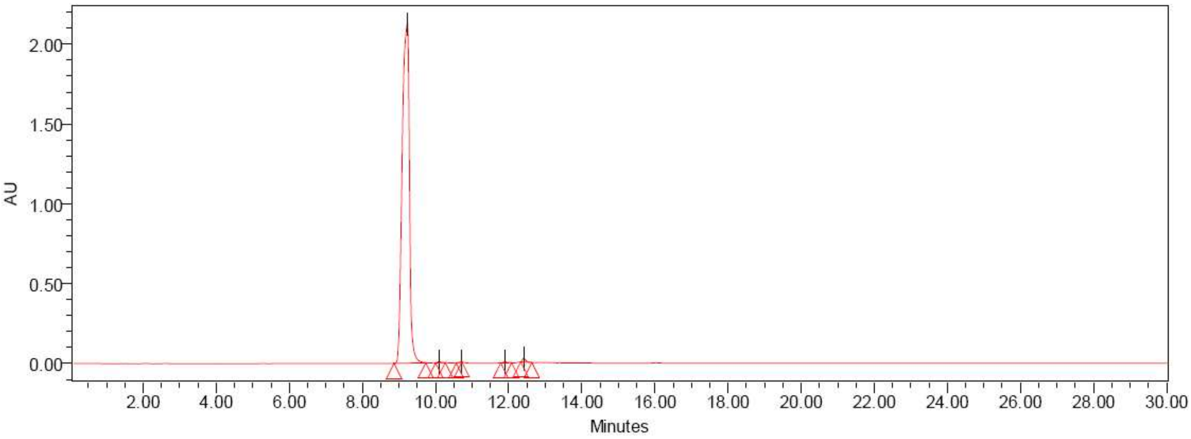
1	PDA 254.0 nm	4.152	6793	0.05	1092
2	PDA 254.0 nm	8.205	161053	1.08	21613
3	PDA 254.0 nm	13.018	24032	0.16	3335
4	PDA 254.0 nm	16.067	14728207	98.71	1054676



(**3**)


7.64
7.38
7.36
7.28
7.27
7.26
5.53
3.23
1.00
3.08
2.01
2.00
0.94
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

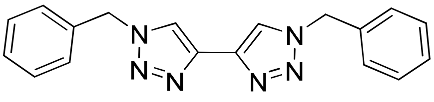

134.03
130.26
129.17
128.93
128.14
126.75
81.20
77.58
77.15
76.73
73.06
54.27
136 134 132 130 128 126
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



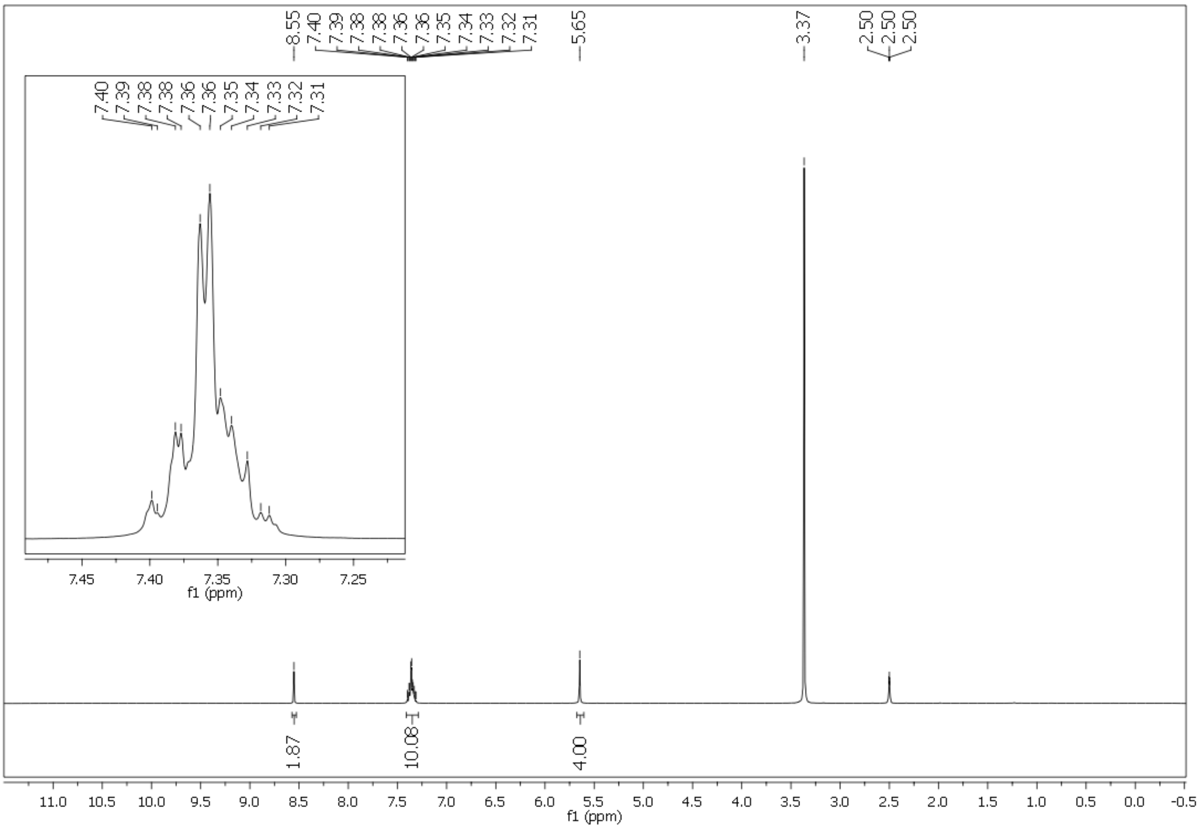
Processed Channel: PDA 254.0 nm

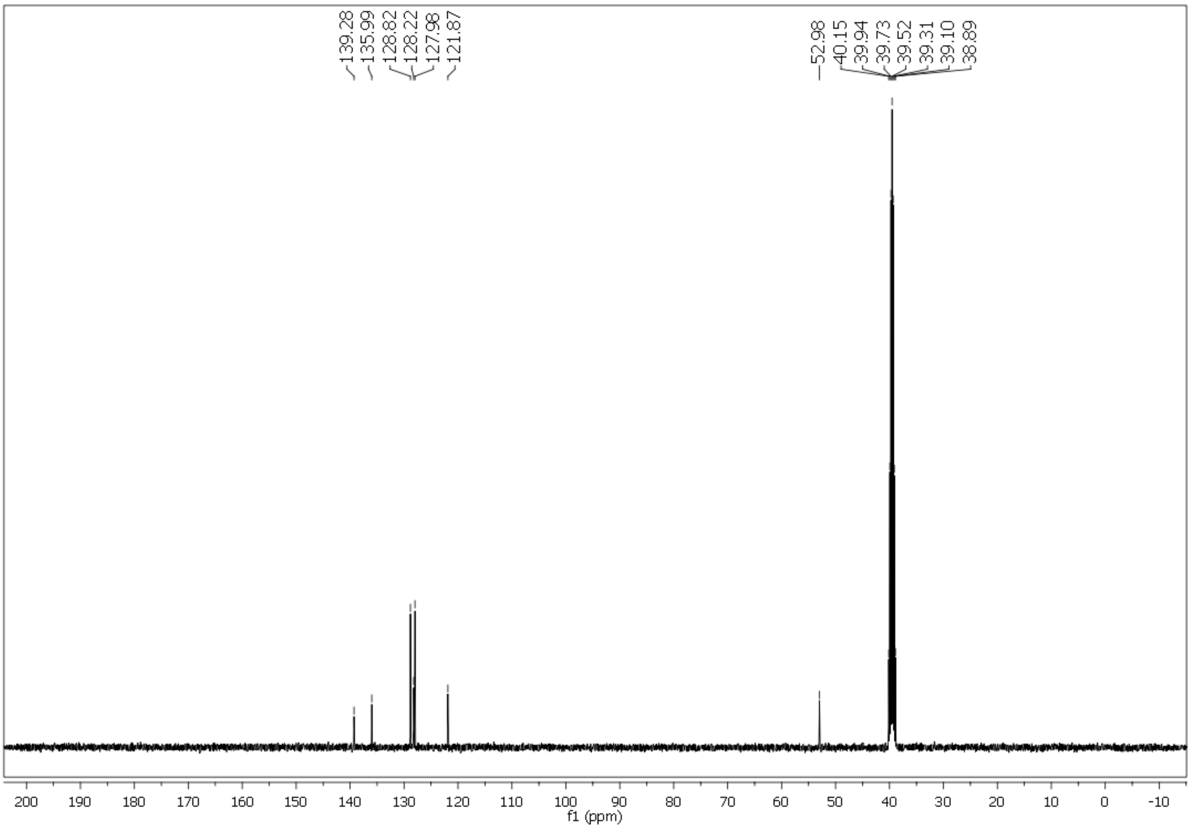
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	9.220	29482686	99.16	2159008
2	PDA 254.0 nm	10.098	49581	0.17	7118
3	PDA 254.0 nm	10.704	7198	0.02	735
4	PDA 254.0 nm	11.899	52280	0.18	6867

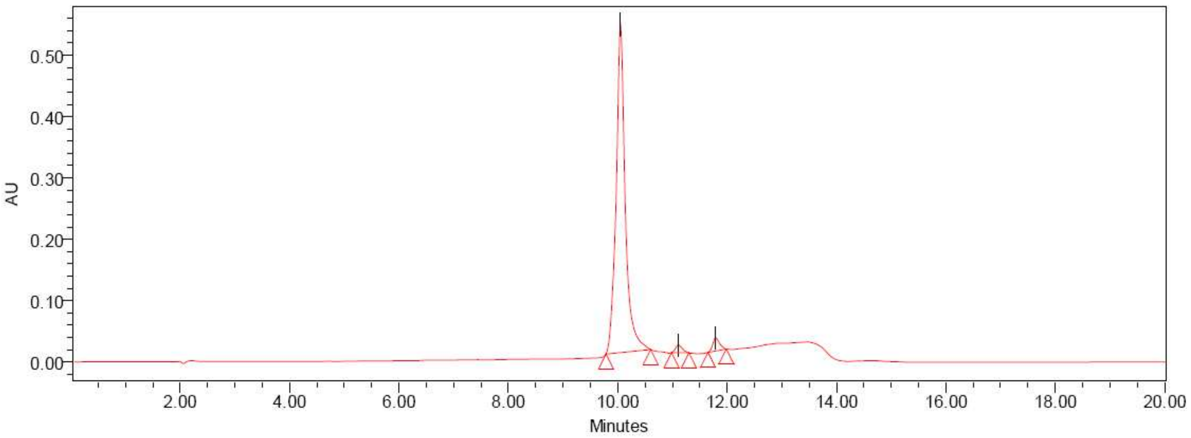
	Processed Channel	Retention Time (min)	Area	% Area	Height
5	PDA 254.0 nm	12.413	139271	0.47	21596



(**4**)

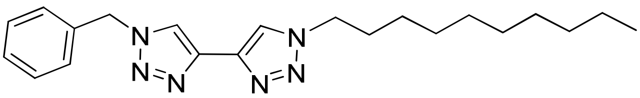

8.55
7.40
7.39
7.38
7.38
7.36
7.36
7.35
7.34
7.33
7.32
7.31
5.65
3.37
2.50
2.50
2.50
1.87
10.08
4.00
7.45
7.40
7.35
7.30
7.25
f1 (ppm)
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


139.28
135.99
128.82
128.22
127.98
121.87
52.98
40.15
39.94
39.73
39.52
39.31
39.10
38.89
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

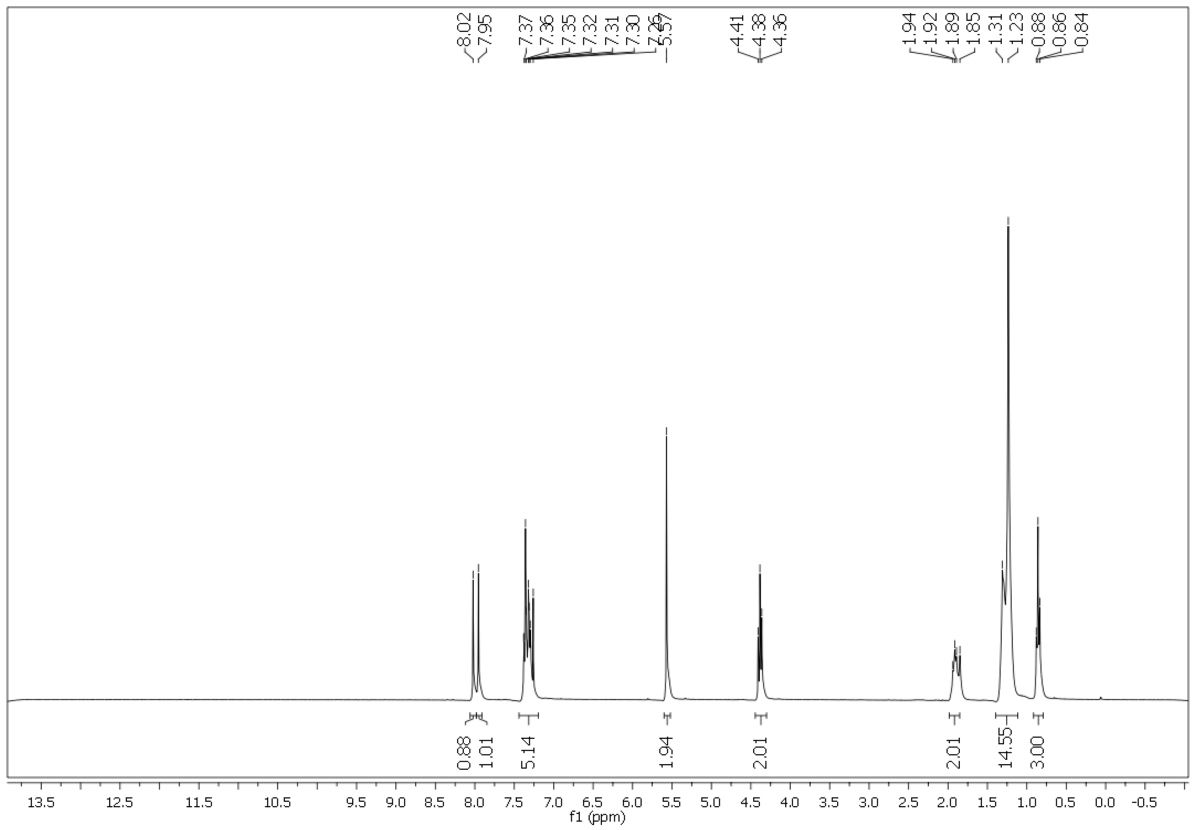


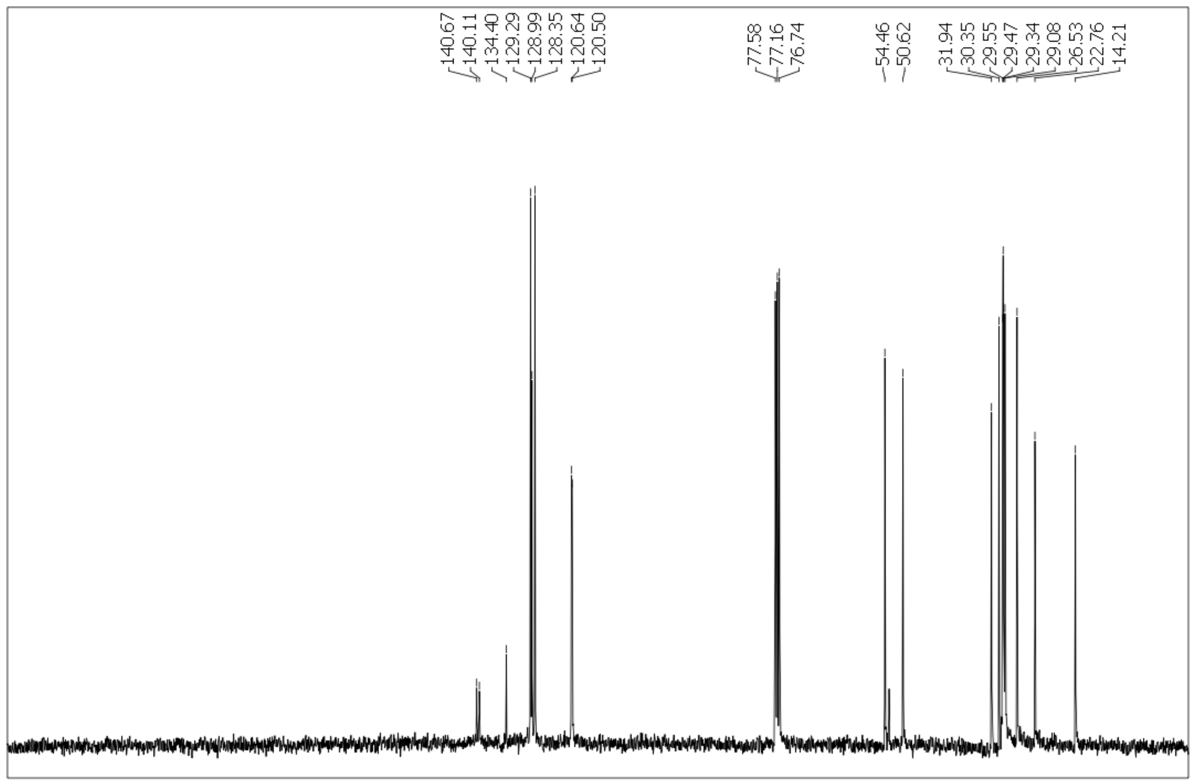
Processed Channel: PDA 254.0 nm

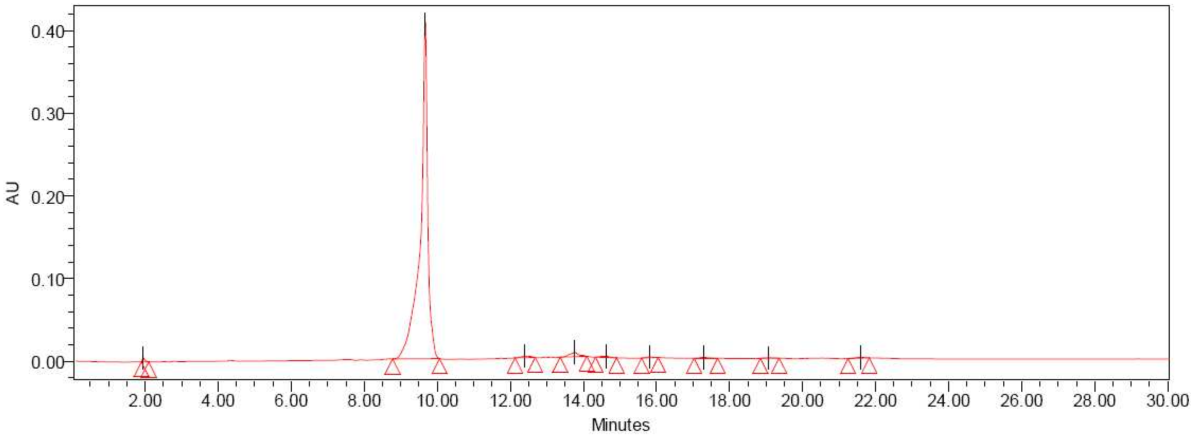
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	10.051	6170757	95.45	534407
2	PDA 254.0 nm	11.112	108429	1.68	12485
3	PDA 254.0 nm	11.791	185951	2.88	21338


N
N
N
N
N
N

(**5a**)


8.02
7.95
7.37
7.36
7.35
7.32
7.31
7.30
7.26
5.57
4.41
4.38
4.36
1.94
1.92
1.89
1.85
1.31
1.23
0.88
0.86
0.84
0.88
1.01
5.14
1.94
2.01
2.01
14.55
3.00
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

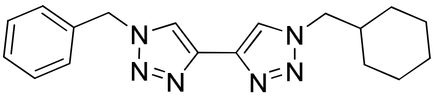

140.67
140.11
134.40
129.29
128.99
128.35
120.64
120.50
77.58
77.16
76.74
54.46
50.62
31.94
30.35
29.55
29.47
29.34
29.08
26.53
22.76
14.21
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



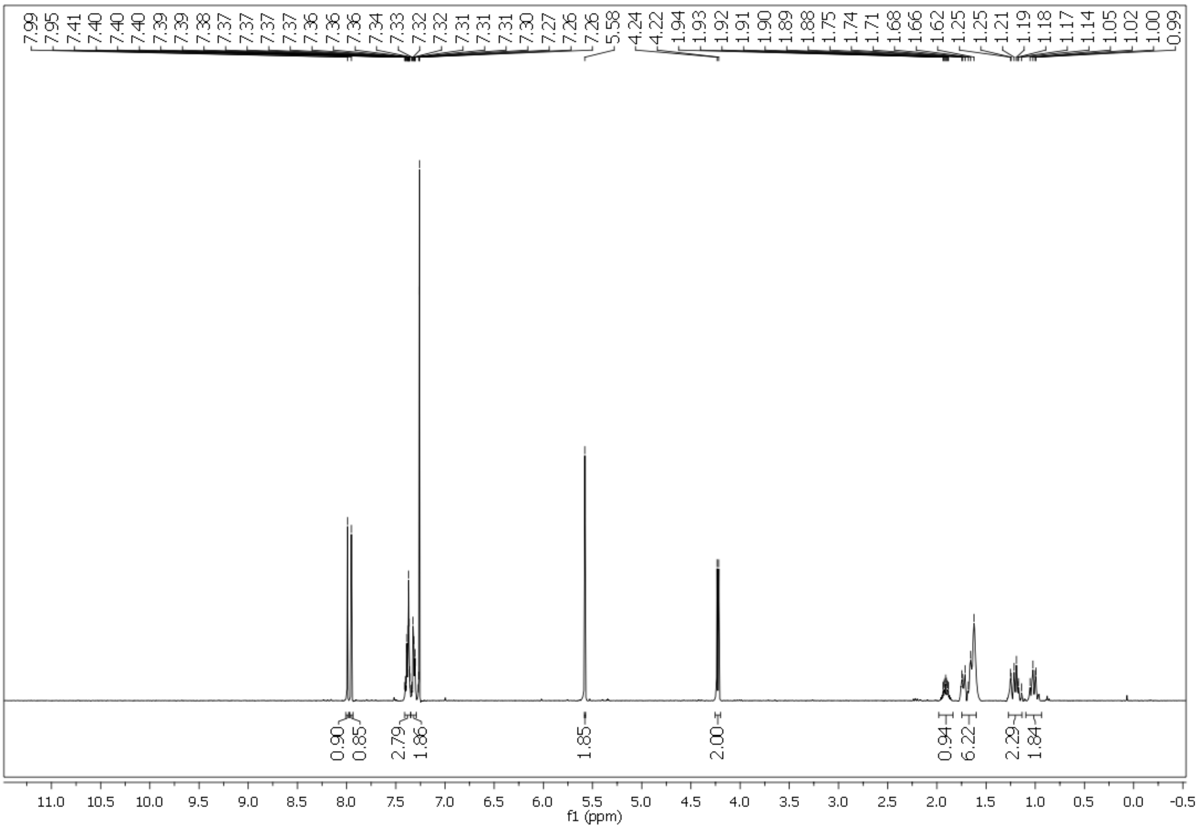
Processed Channel: PDA 254.0 nm

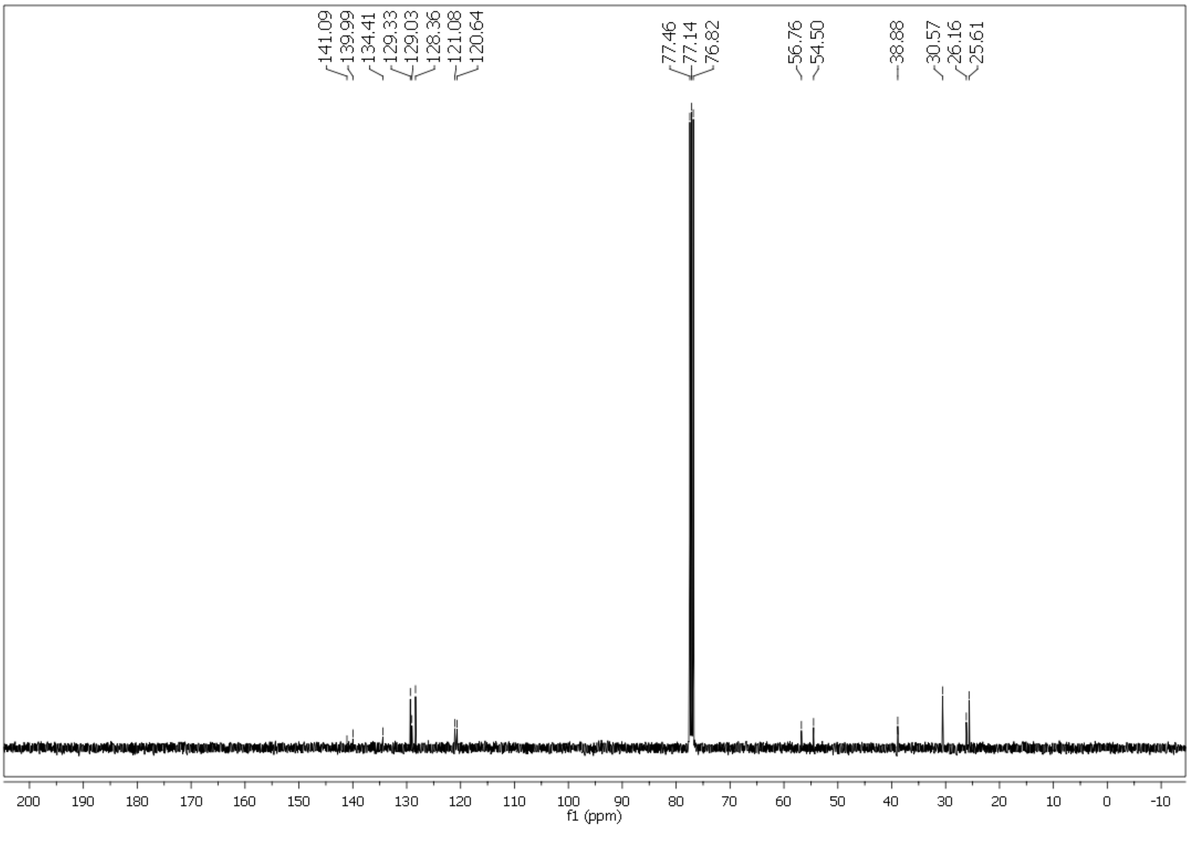
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	1.948	23943	0.40	5065
2	PDA 254.0 nm	9.671	5740945	96.19	408428
3	PDA 254.0 nm	12.383	31695	0.53	1936
4	PDA 254.0 nm	13.761	88721	1.49	5278

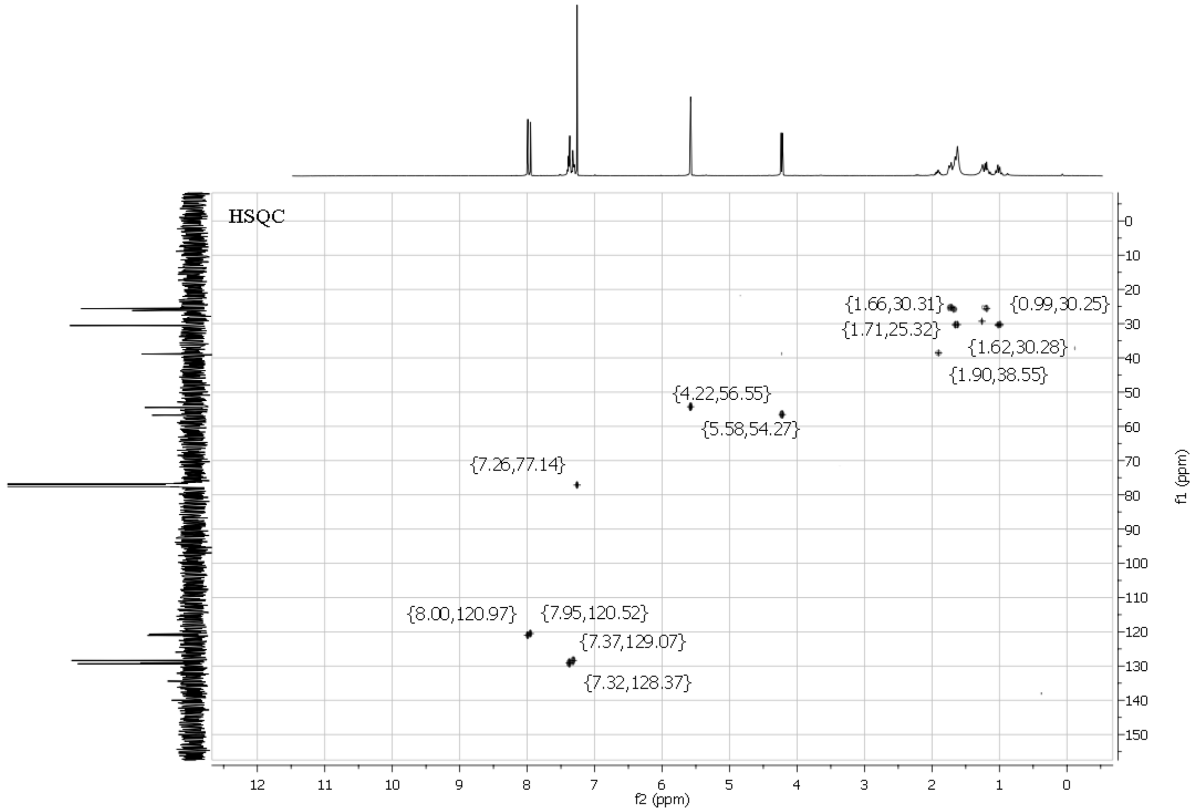
	Processed Channel	Retention Time (min)	Area	% Area	Height
5	PDA 254.0 nm	14.630	23979	0.40	1432
6	PDA 254.0 nm	15.814	9931	0.17	849
7	PDA 254.0 nm	17.299	19925	0.33	1103
8	PDA 254.0 nm	19.072	11161	0.19	705

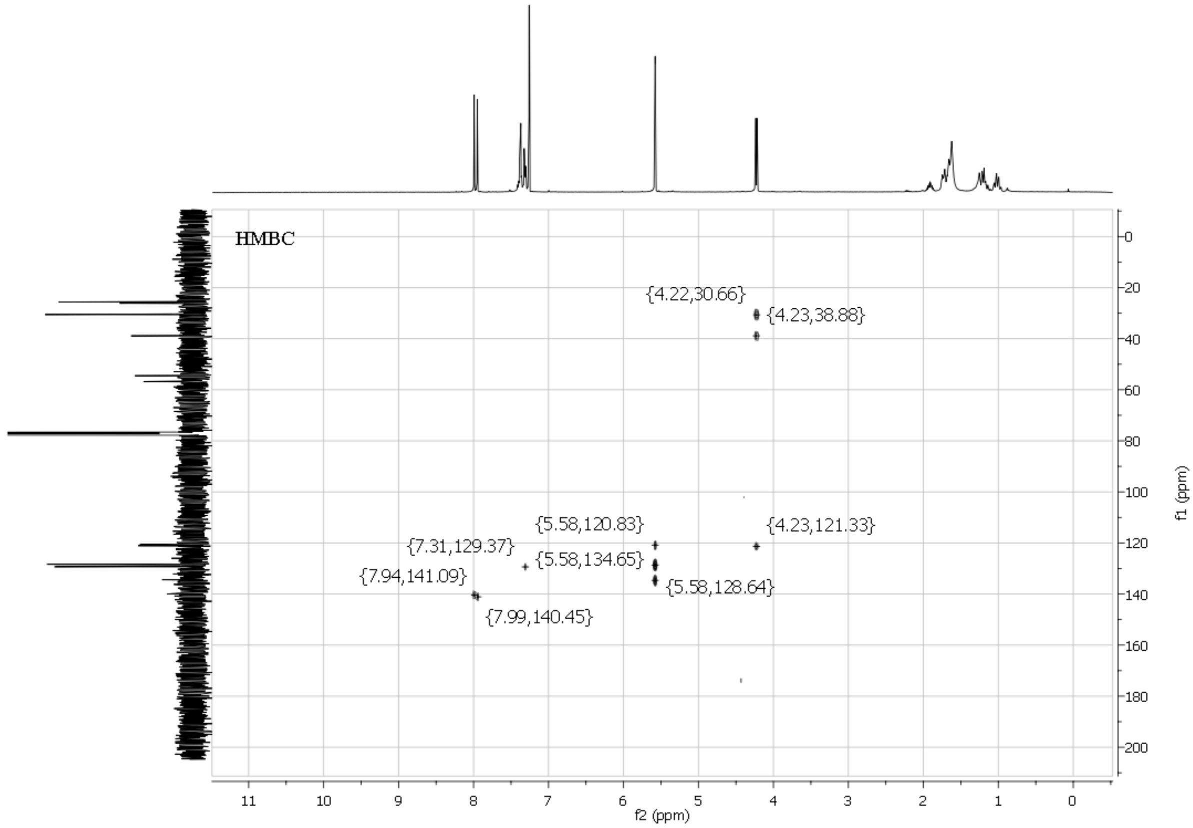

N
N
N
N
N
N

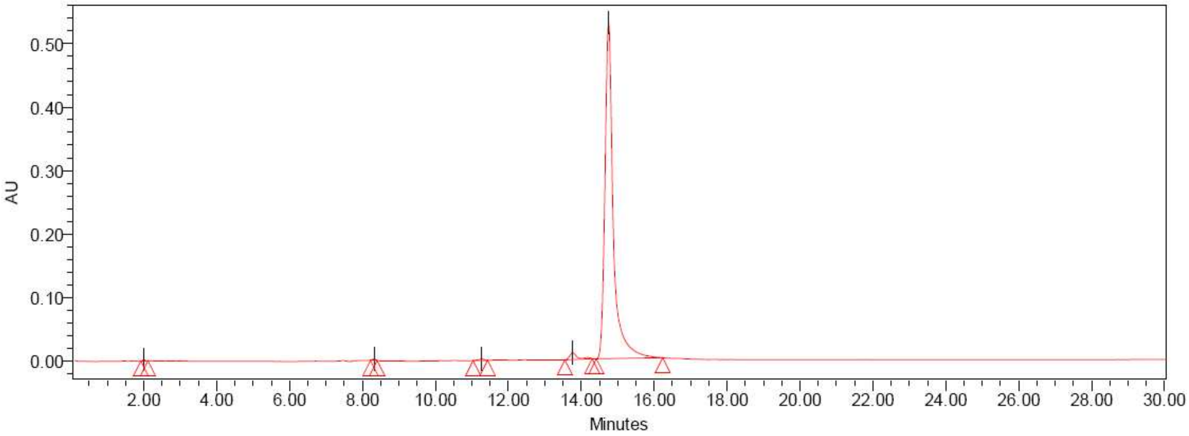
(**5b**)


7.99
7.95
7.41
7.40
7.40
7.39
7.39
7.38
7.37
7.37
7.37
7.37
7.36
7.36
7.36
7.34
7.33
7.32
7.32
7.31
7.31
7.31
7.30
7.27
7.26
7.26
5.58
4.24
4.22
1.94
1.93
1.92
1.91
1.90
1.89
1.88
1.75
1.74
1.71
1.68
1.66
1.62
1.25
1.25
1.21
1.19
1.18
1.17
1.14
1.05
1.02
1.00
0.99
0.90
0.85
2.79
1.86
1.85
2.00
0.94
6.22
2.29
1.84
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


141.09
139.99
134.41
129.33
129.03
128.36
121.08
120.64
77.46
77.14
76.82
56.76
54.50
38.88
30.57
26.16
25.61
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

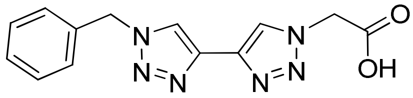

HSQC
{1.66,30.31}
{0.99,30.25}
{1.71,25.32}
{1.62,30.28}
{1.90,38.55}
{4.22,56.55}
{5.58,54.27}
{7.26,77.14}
{8.00,120.97}
{7.95,120.52}
{7.37,129.07}
{7.32,128.37}
f1 (ppm)
f2 (ppm)


HMBC
{4.22,30.66}
{4.23,38.88}
{5.58,120.83}
{4.23,121.33}
{7.31,129.37}
{5.58,134.65}
{7.94,141.09}
{5.58,128.64}
{7.99,140.45}
f1 (ppm)
f2 (ppm)

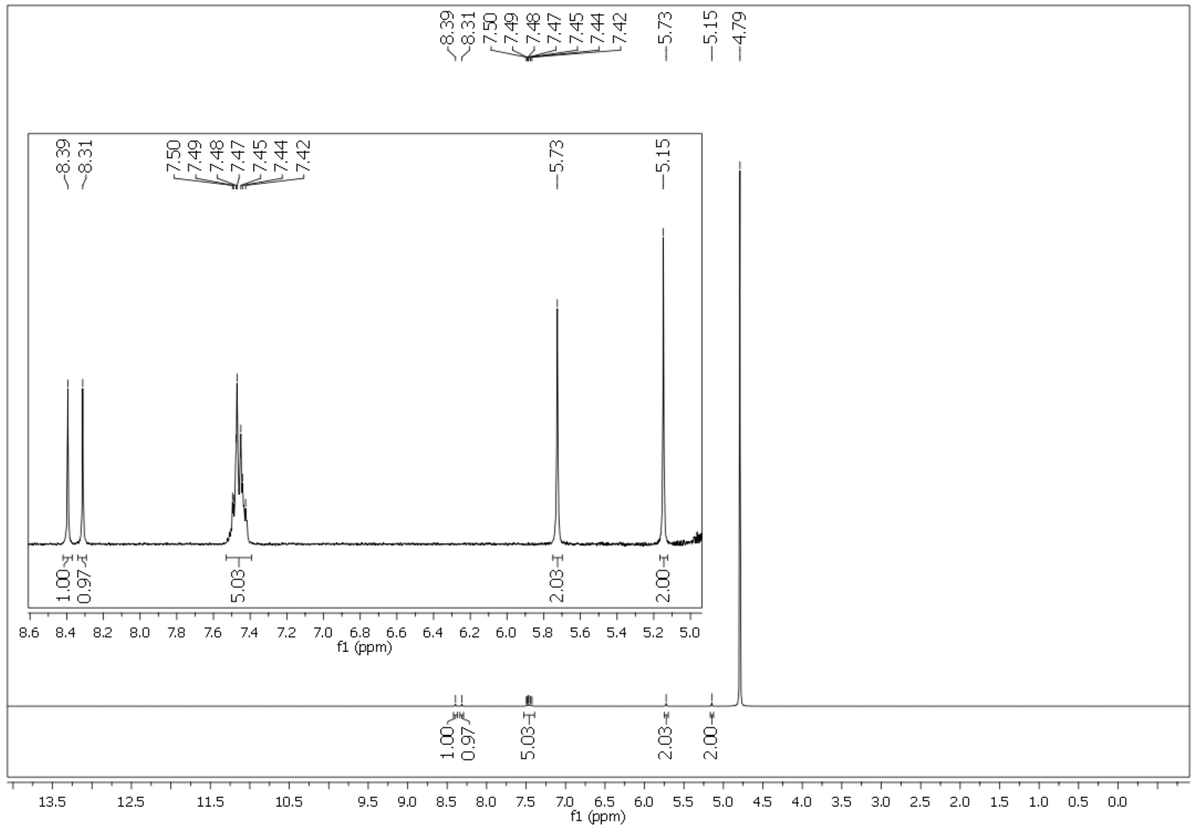


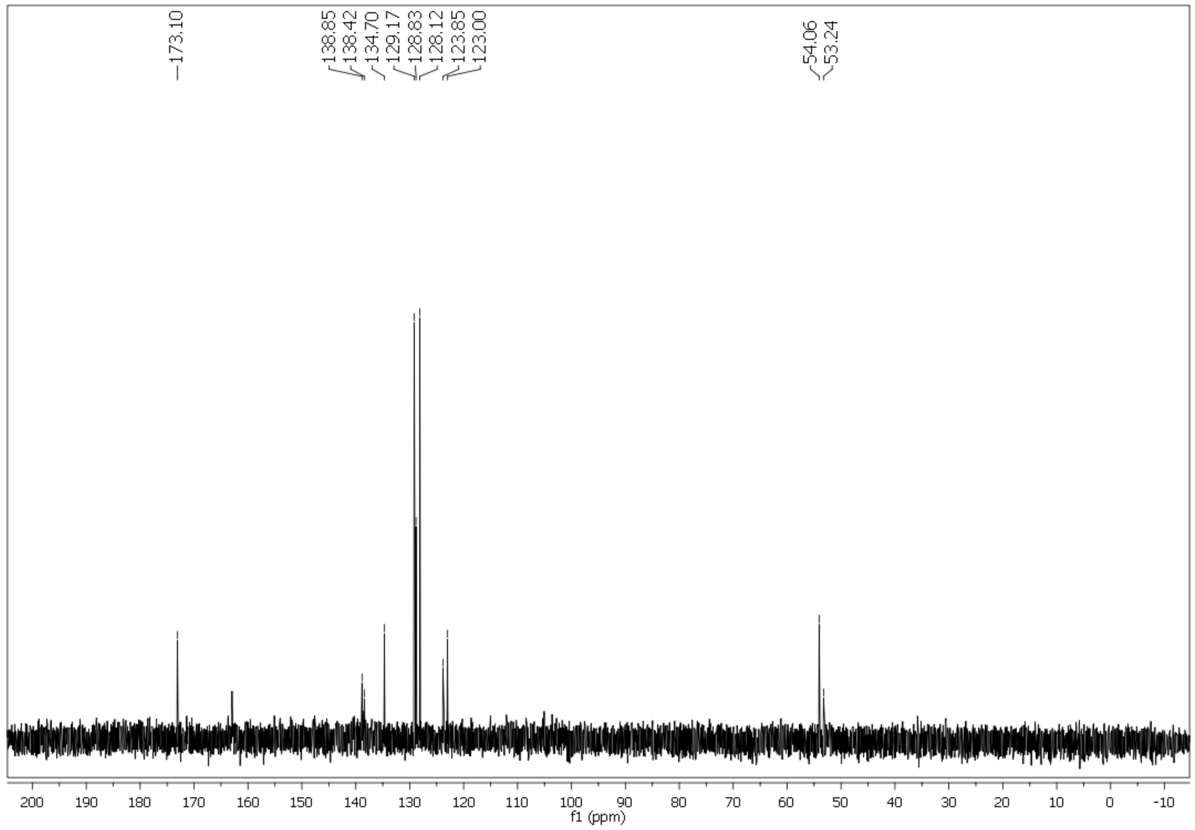
Processed Channel: PDA 254.0 nm

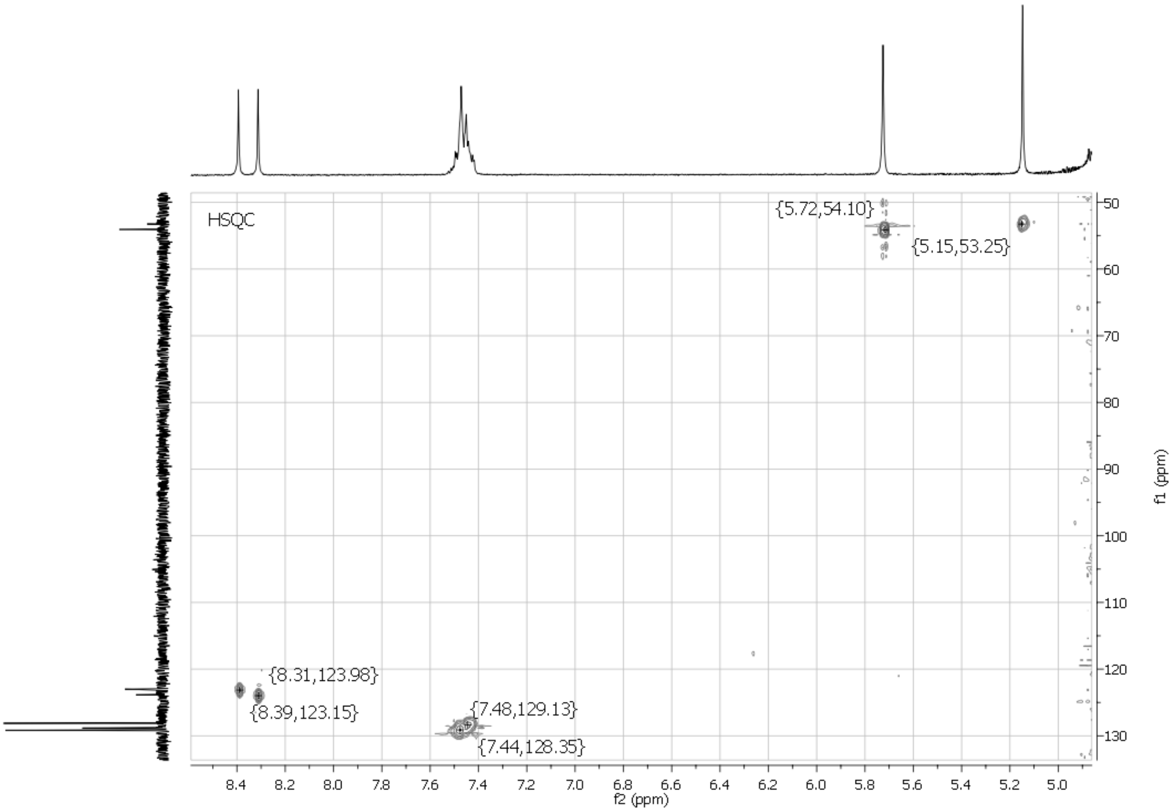
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	2.000	7861	0.09	2113
2	PDA 254.0 nm	8.315	13550	0.16	2383
3	PDA 254.0 nm	11.276	25716	0.30	2375
4	PDA 254.0 nm	13.769	158645	1.83	10768
5	PDA 254.0 nm	14.751	8449137	97.62	529682

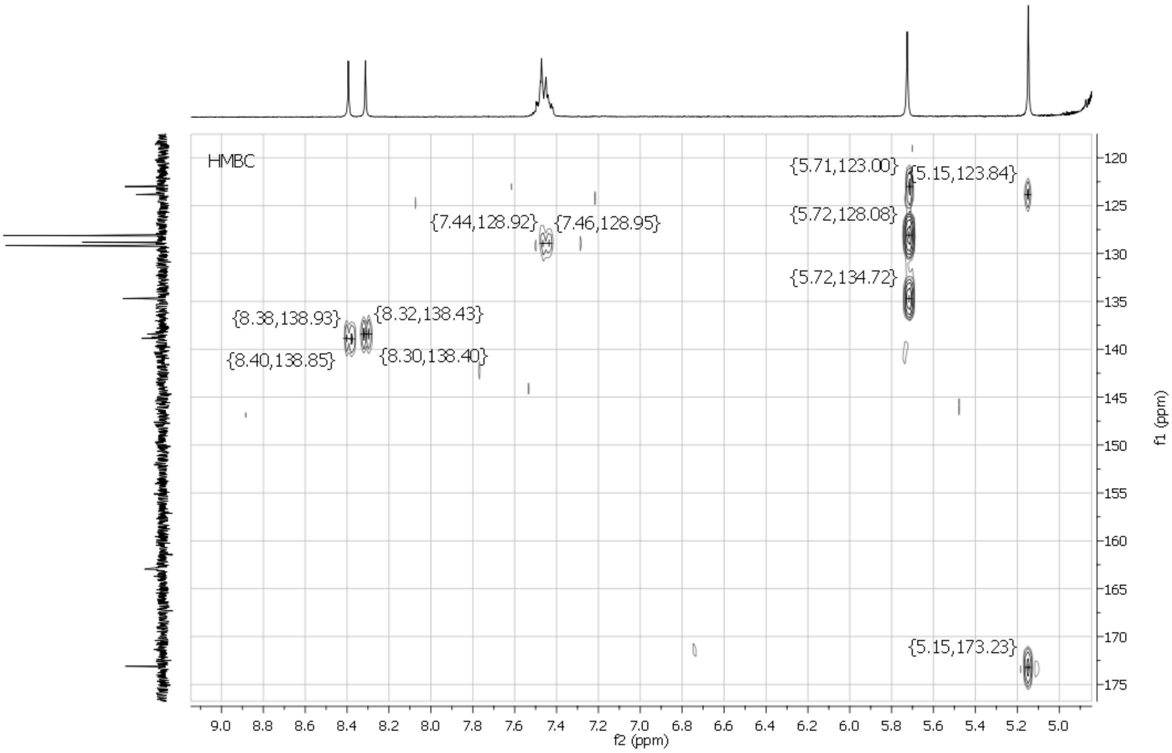

N
N
N
N
N
N
O
OH

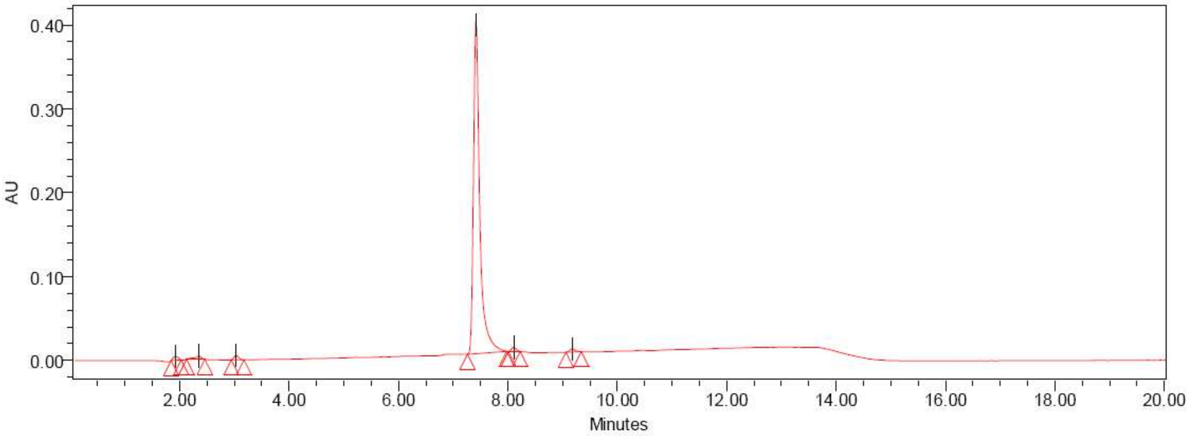
(**5c**)


8.39
8.31
7.50
7.49
7.48
7.47
7.45
7.44
7.42
5.73
5.15
4.79
1.00
0.97
5.03
2.03
2.00
8.6 8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0
f1 (ppm)
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


173.10
138.85
138.42
134.70
129.17
128.83
128.12
123.85
123.00
54.06
53.24
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


HSQC
{5.72,54.10}
{5.15,53.25}
{8.31,123.98}
{8.39,123.15}
{7.48,129.13}
{7.44,128.35}
f2 (ppm)
f1 (ppm)

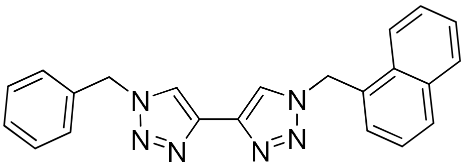

HMBC
{5.71,123.00}
{5.15,123.84}
{7.44,128.92}
{7.46,128.95}
{5.72,128.08}
{5.72,134.72}
{8.38,138.93}
{8.32,138.43}
{8.40,138.85}
{8.30,138.40}
{5.15,173.23}
f2 (ppm)
f1 (ppm)



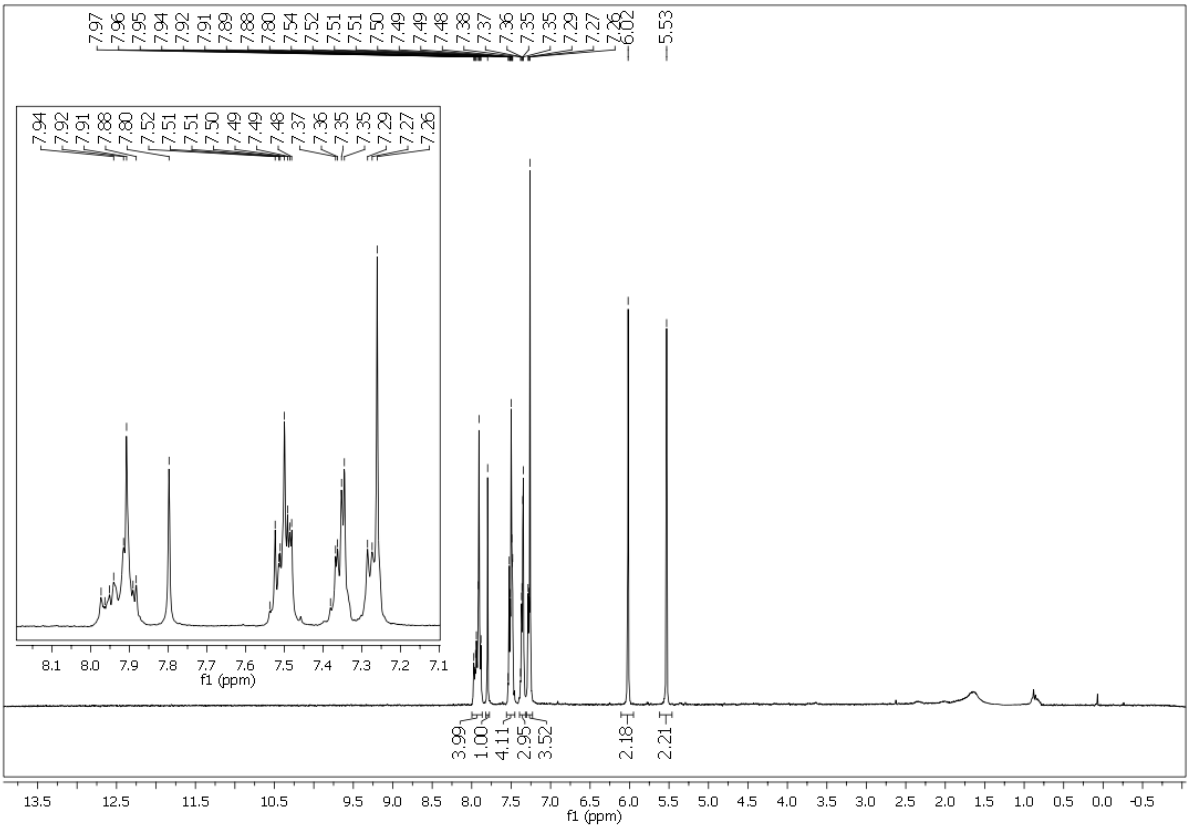
Processed Channel: PDA 254.0 nm

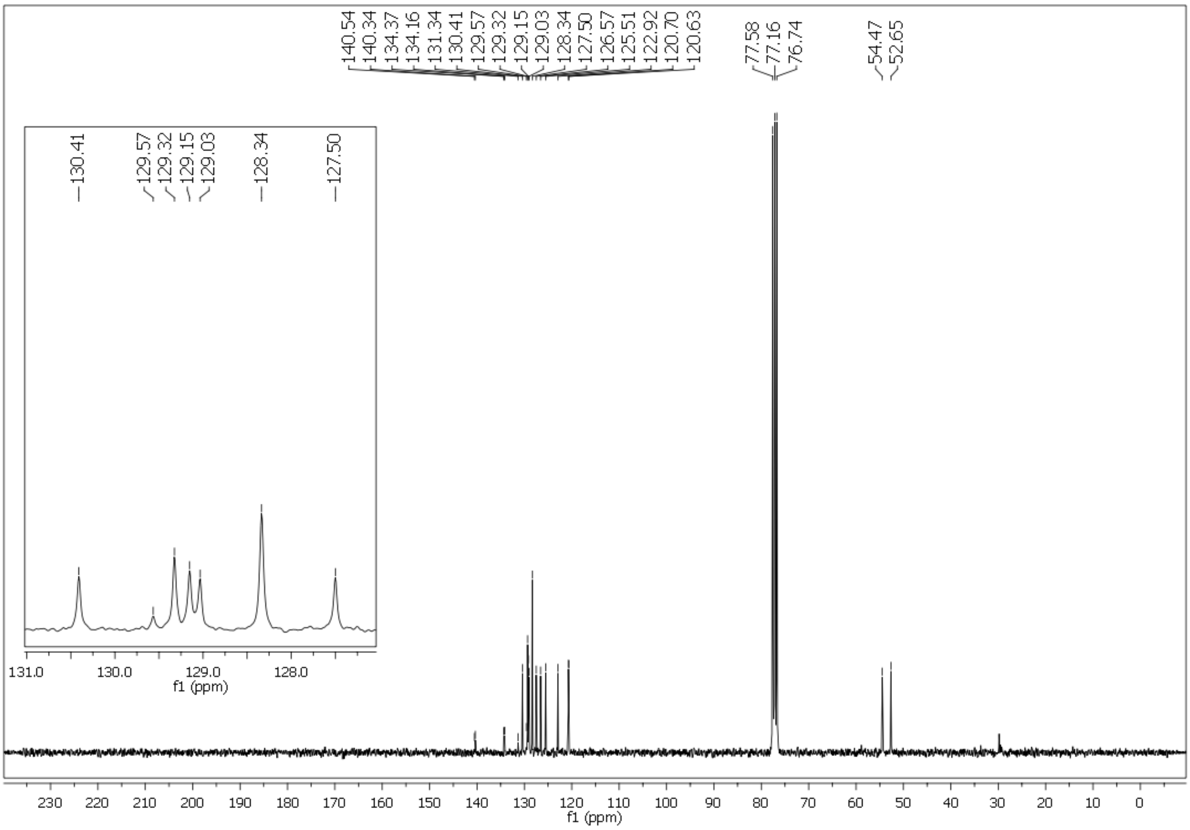
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	1.918	31599	0.94	4833
2	PDA 254.0 nm	2.352	34880	1.04	4047
3	PDA 254.0 nm	3.033	32229	0.96	5460
4	PDA 254.0 nm	7.417	3203425	95.35	397150

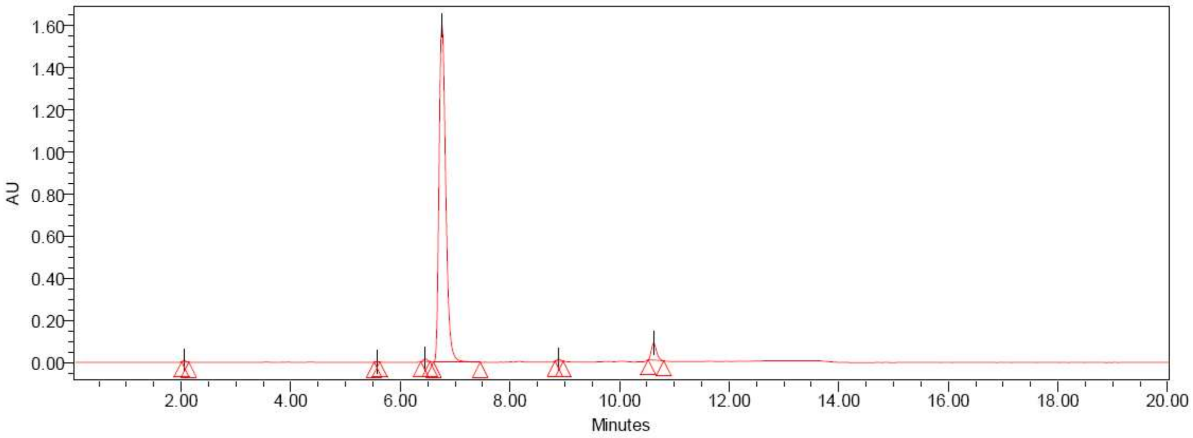
	Processed Channel	Retention Time (min)	Area	% Area	Height
5	PDA 254.0 nm	8.107	30511	0.91	4962
6	PDA 254.0 nm	9.178	26867	0.80	3836



(**5d**)

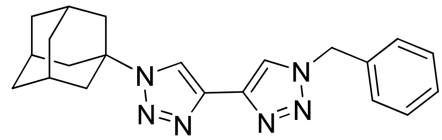

7.97 7.96 7.95 7.94 7.92 7.91 7.89 7.88 7.80 7.54 7.52 7.51 7.51 7.50 7.49 7.49 7.48 7.38 7.37 7.36 7.35 7.35 7.29 7.27 7.26
6.02
5.53
7.94 7.92 7.91 7.88 7.80 7.52 7.51 7.51 7.50 7.49 7.49 7.48 7.37 7.36 7.35 7.35 7.29 7.27 7.26
8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)
3.99
1.00
4.11
2.95
3.52
2.18
2.21
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


140.54 140.34 134.37 134.16 131.34 130.41 129.57 129.32 129.15 129.03 128.34 127.50 126.57 125.51 122.92 120.70 120.63
77.58 77.16 76.74
54.47 52.65
130.41
129.57 129.32 129.15 129.03
128.34
127.50
131.0 130.0 129.0 128.0
f1 (ppm)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

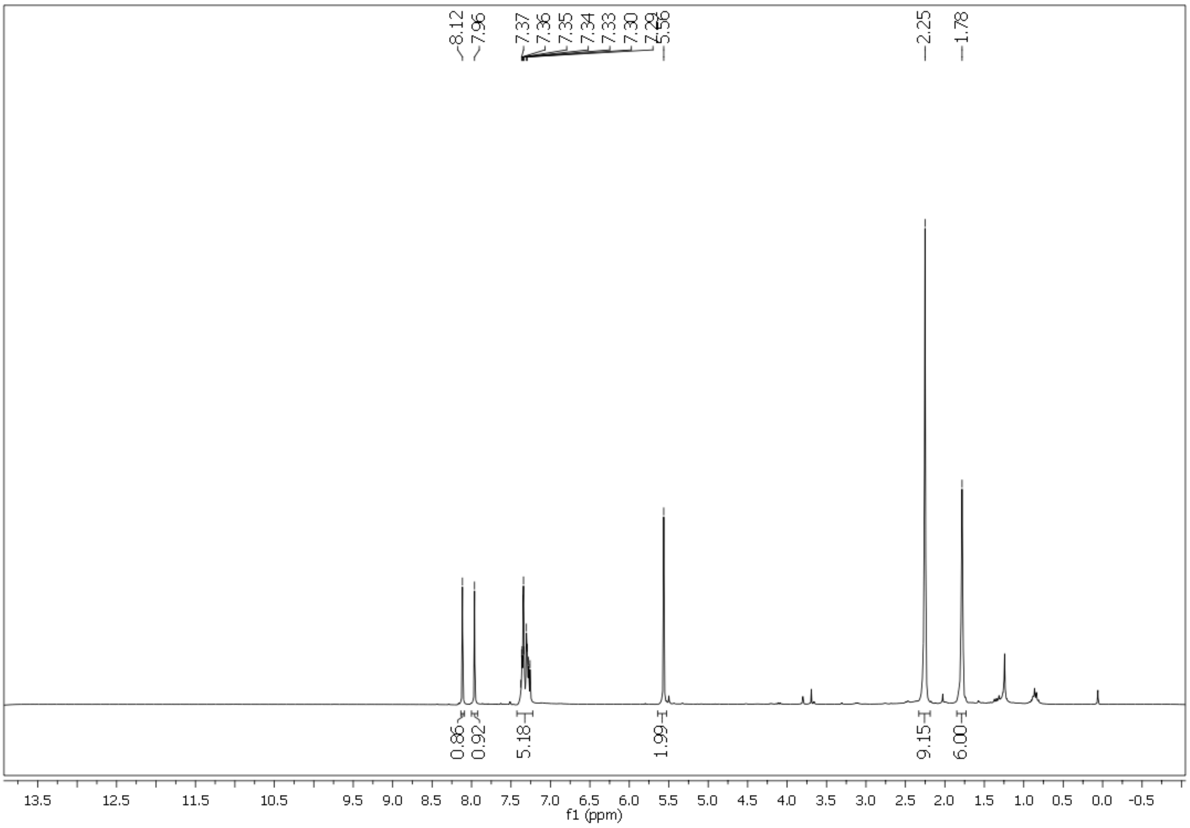


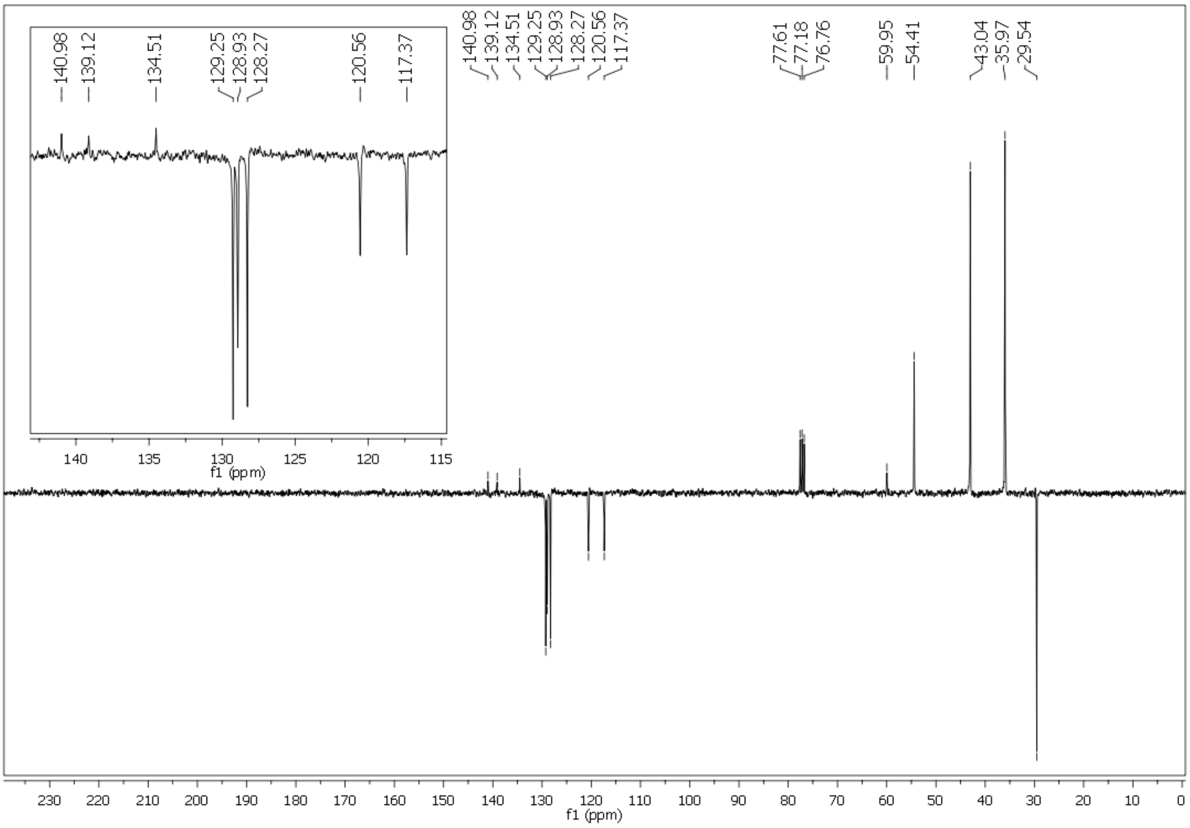
Processed Channel: PDA 254.0 nm

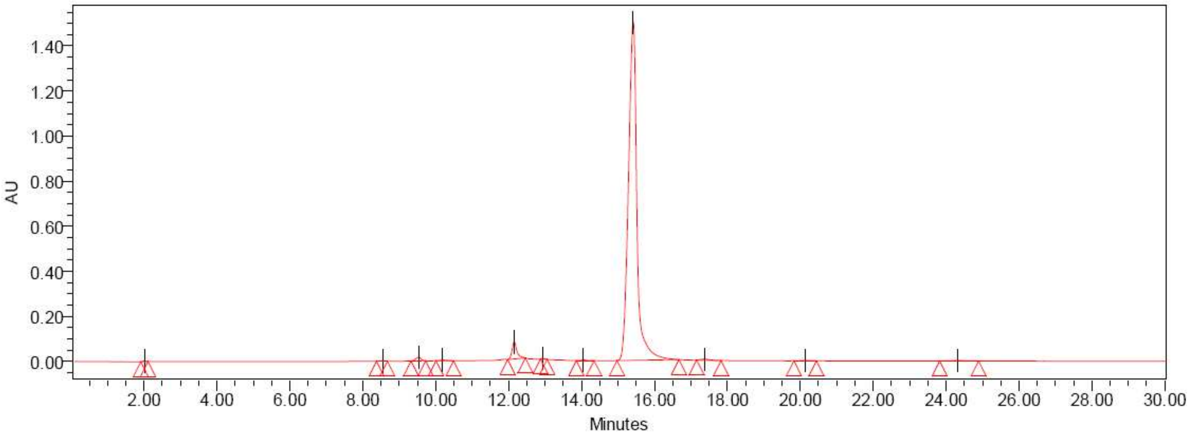
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	2.054	29702	0.21	8162
2	PDA 254.0 nm	5.578	5157	0.04	1418
3	PDA 254.0 nm	6.457	70578	0.49	13213
4	PDA 254.0 nm	6.760	13626205	95.25	1612829
5	PDA 254.0 nm	8.884	45271	0.32	9047
6	PDA 254.0 nm	10.623	528178	3.69	81443


N
N
N
N
N
N

(**5e**)


8.12
7.96
7.37
7.36
7.35
7.34
7.33
7.30
7.29
5.56
2.25
1.78
0.86
0.92
5.18
1.99
9.15
6.00
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

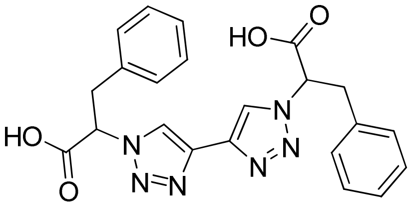

140.98
139.12
134.51
129.25
128.93
128.27
120.56
117.37
140
135
130
125
120
115
f1 (ppm)
140.98
139.12
134.51
129.25
128.93
128.27
120.56
117.37
77.61
77.18
76.76
59.95
54.41
43.04
35.97
29.54
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



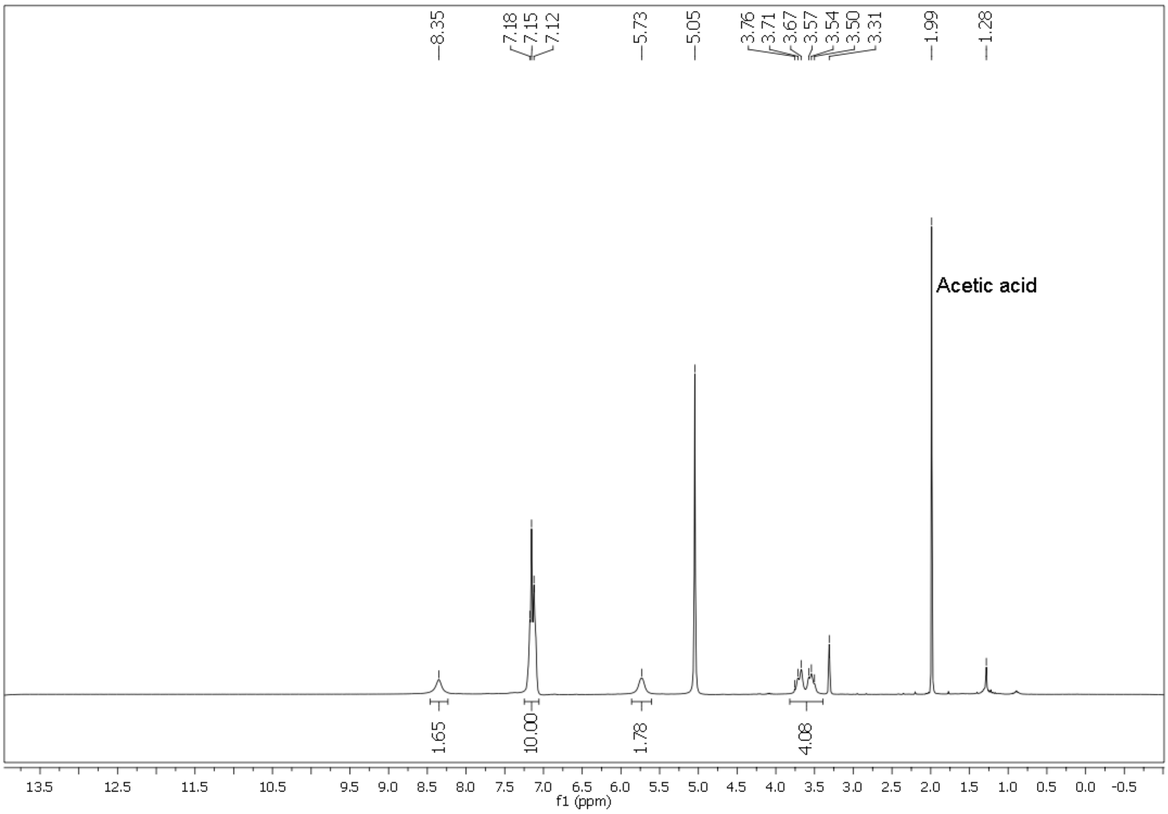
Processed Channel: PDA 254.0 nm

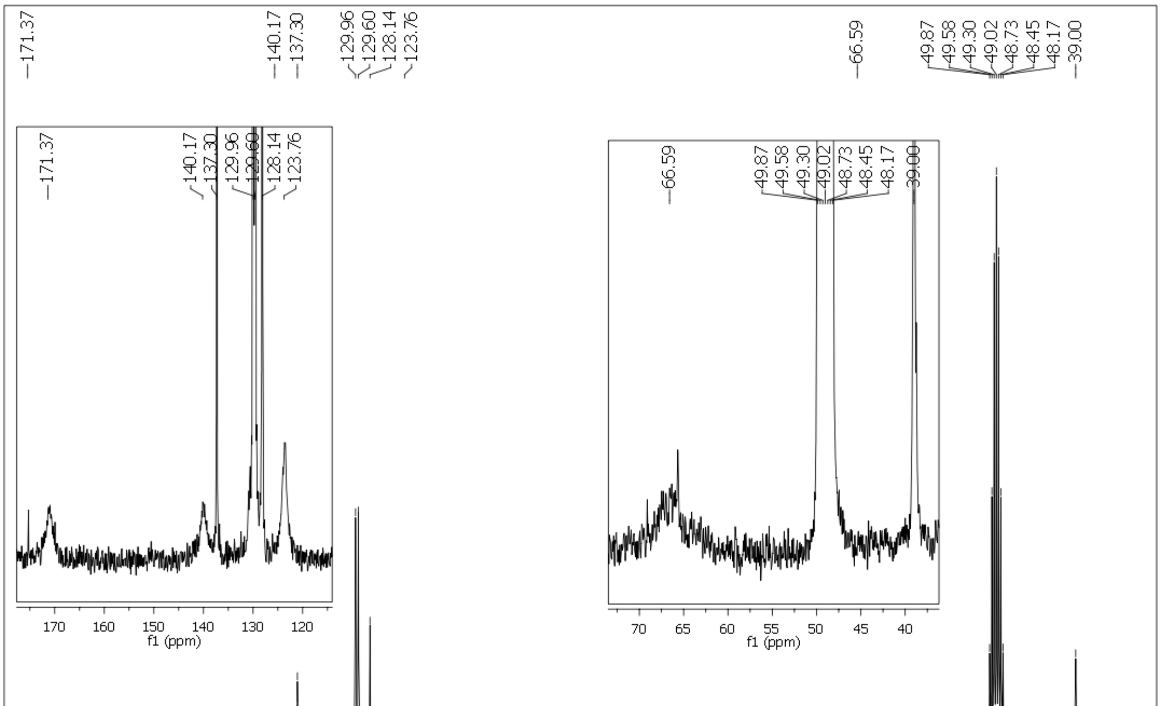
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	2.009	17787	0.07	2903
2	PDA 254.0 nm	8.549	15169	0.06	1483
3	PDA 254.0 nm	9.535	173862	0.68	16795
4	PDA 254.0 nm	10.186	48918	0.19	3223

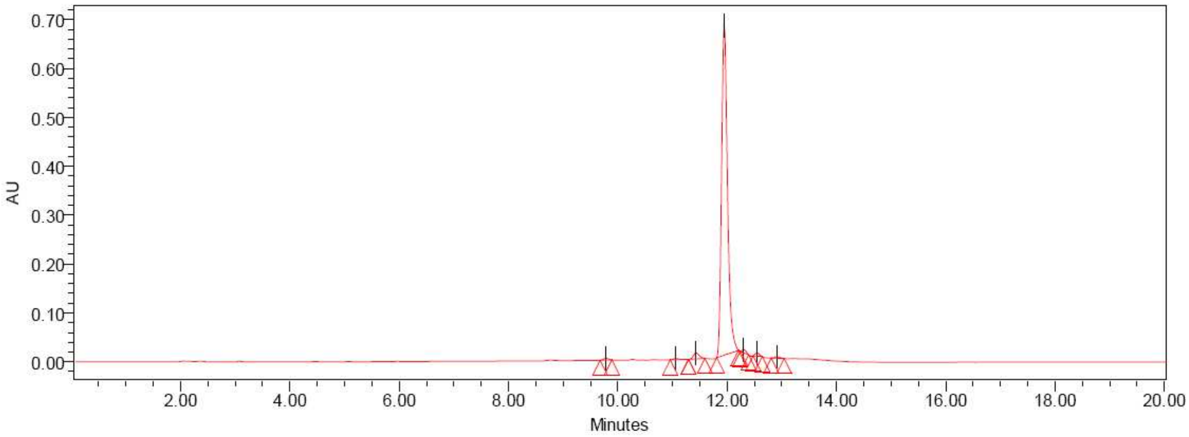
	Processed Channel	Retention Time (min)	Area	% Area	Height
5	PDA 254.0 nm	12.155	709749	2.78	75811
6	PDA 254.0 nm	12.940	20924	0.08	3608
7	PDA 254.0 nm	14.050	21803	0.09	1756
8	PDA 254.0 nm	15.416	24386225	95.39	1506285


HO
O
N
N
N
HO
O
N
N
N

(**7**)


8.35
7.18
7.15
7.12
5.73
5.05
3.76
3.71
3.67
3.57
3.54
3.50
3.31
1.99
1.28
Acetic acid
1.65
10.00
1.78
4.08
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

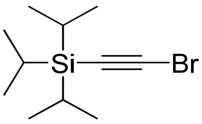

171.37
140.17
137.30
129.96
129.60
128.14
123.76
66.59
49.87
49.58
49.30
49.02
48.73
48.45
48.17
39.00
170
160
150
140
130
120
f1 (ppm)
70
65
60
55
50
45
40
f1 (ppm)
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
f1 (ppm)

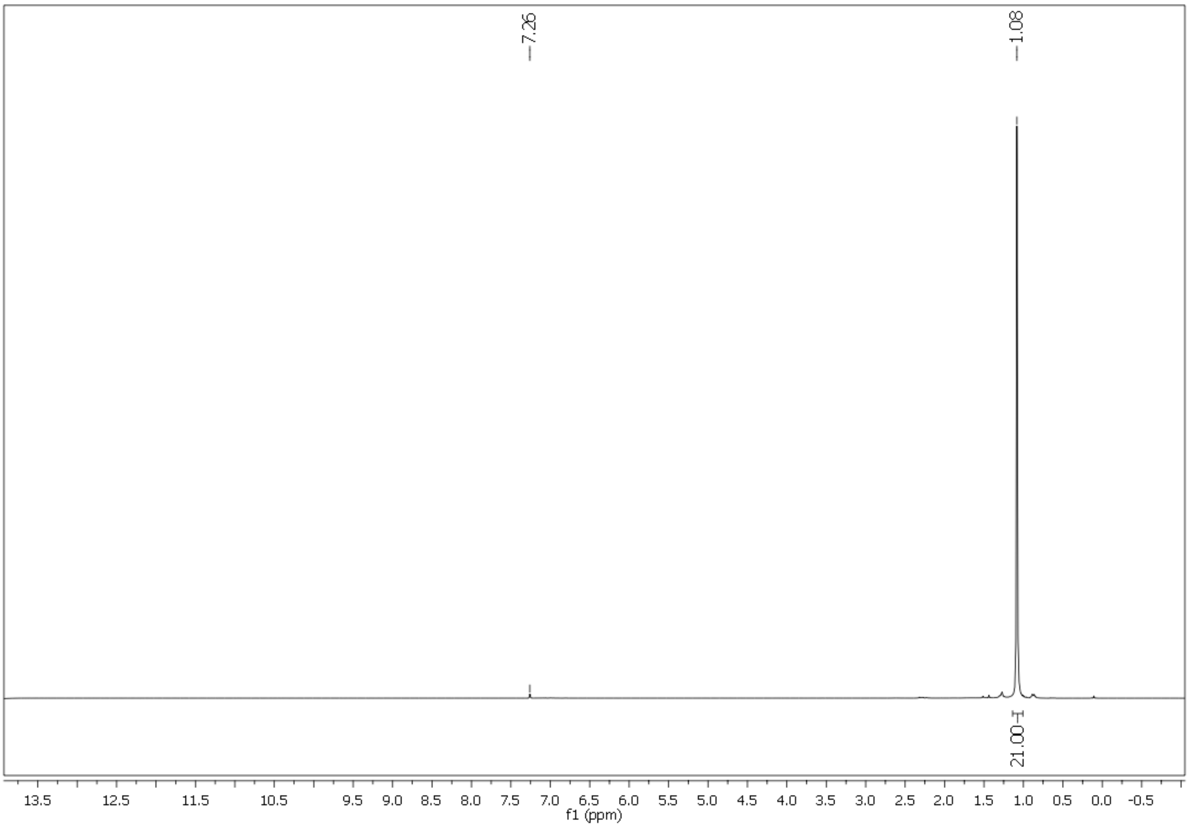


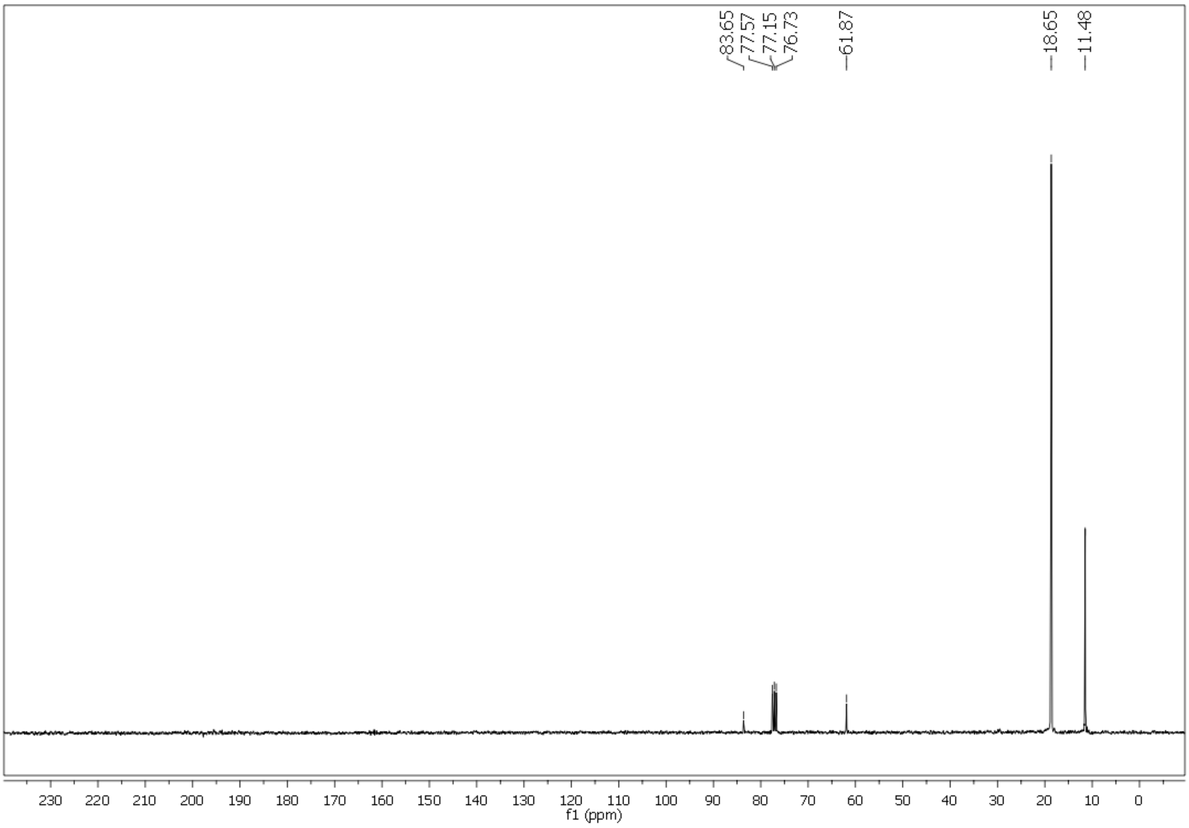
Processed Channel: PDA 254.0 nm

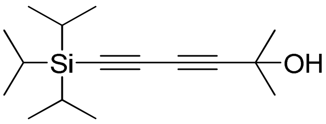
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	9.786	24317	0.45	3721
2	PDA 254.0 nm	11.061	17503	0.33	2591
3	PDA 254.0 nm	11.432	90094	1.69	12289
4	PDA 254.0 nm	11.947	5120488	95.81	679733

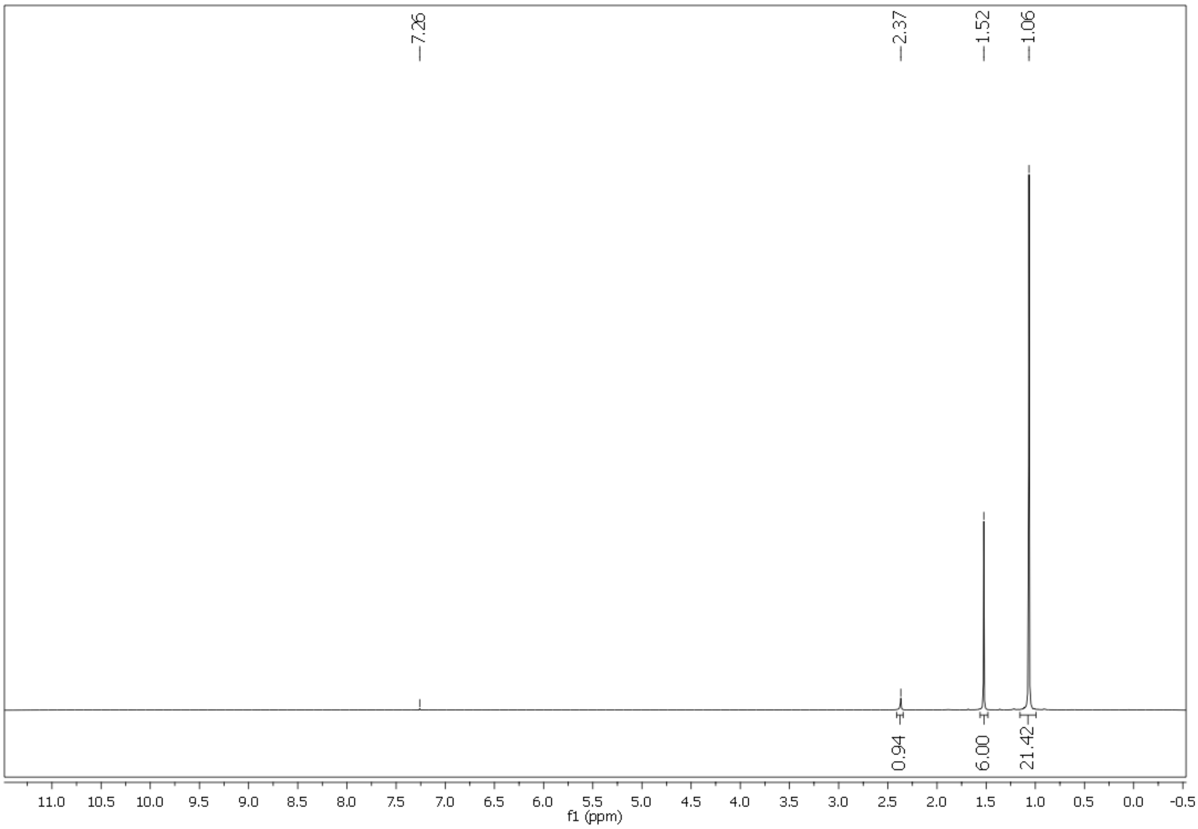
	Processed Channel	Retention Time (min)	Area	% Area	Height
5	PDA 254.0 nm	12.301	32636	0.61	6256
6	PDA 254.0 nm	12.549	36804	0.69	6586
7	PDA 254.0 nm	12.914	22497	0.42	3207

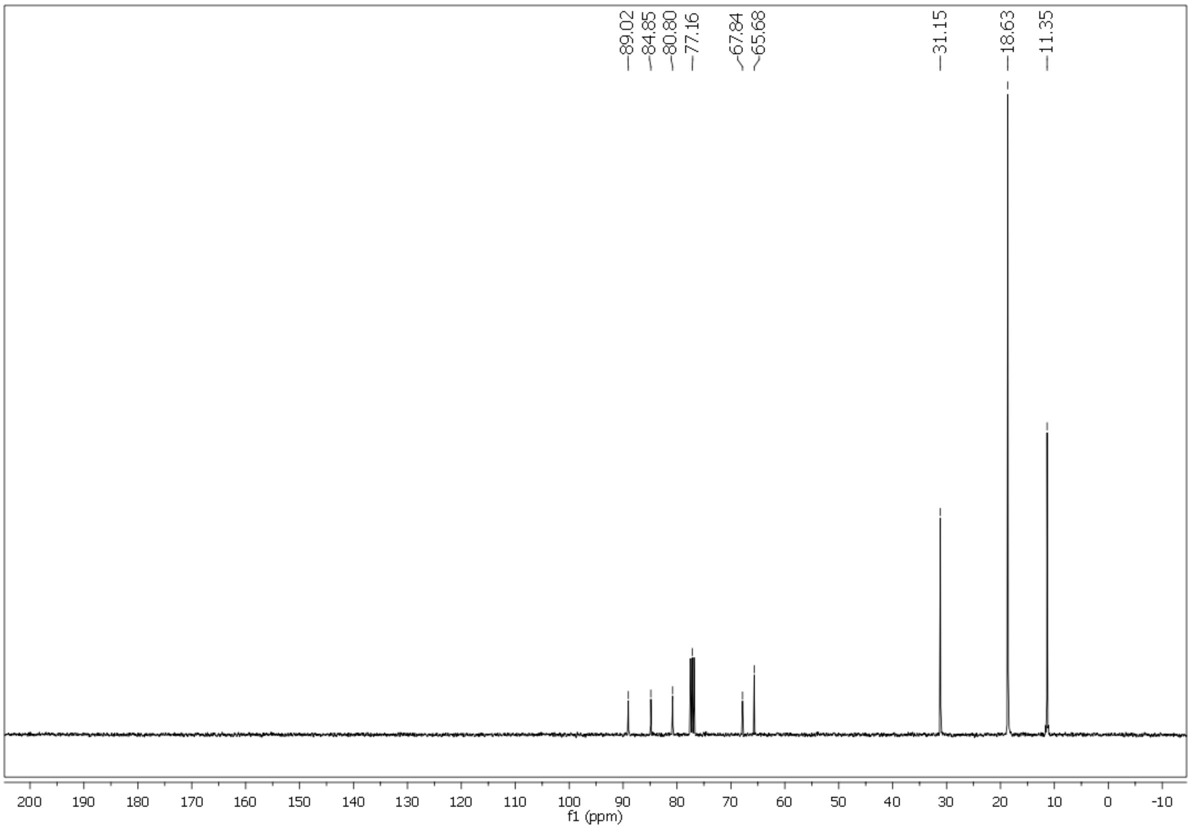

Si
Br

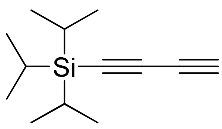

7.26
1.08
21.00
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


83.65
77.57
77.15
76.73
61.87
18.65
11.48
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

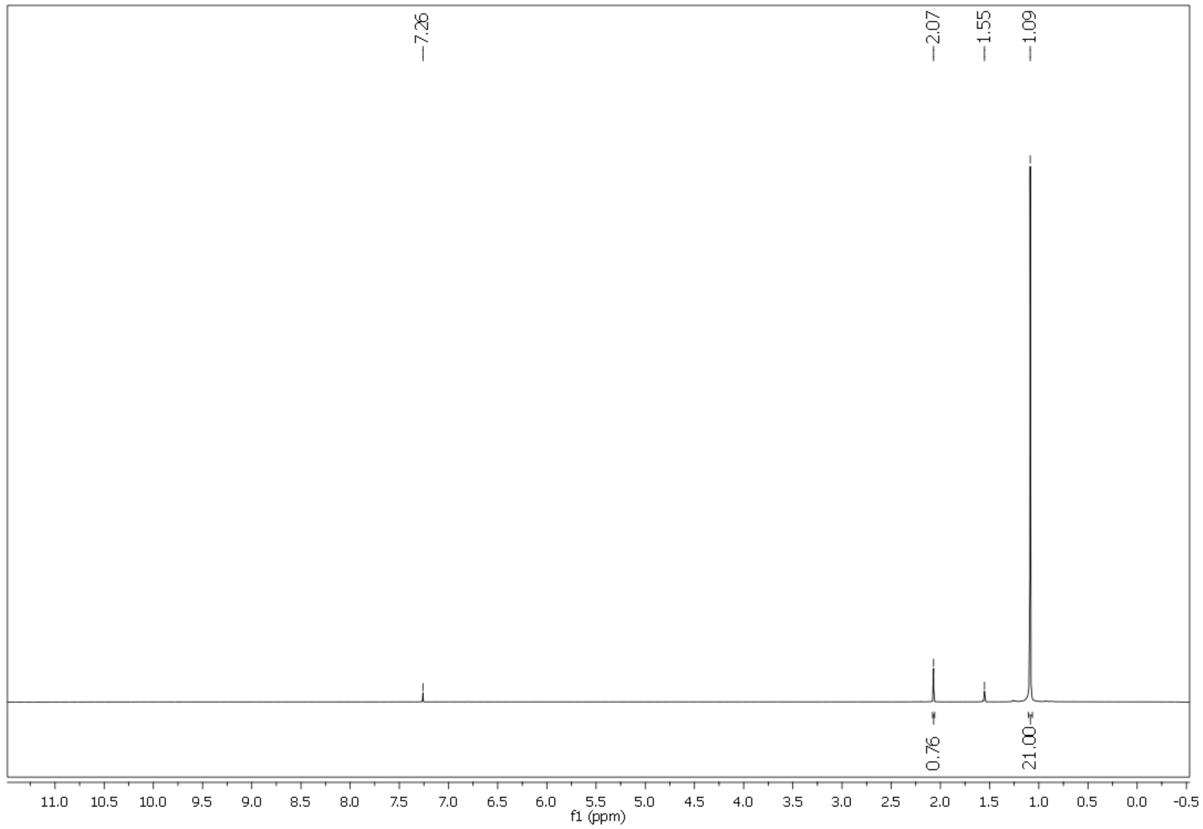

Si
OH

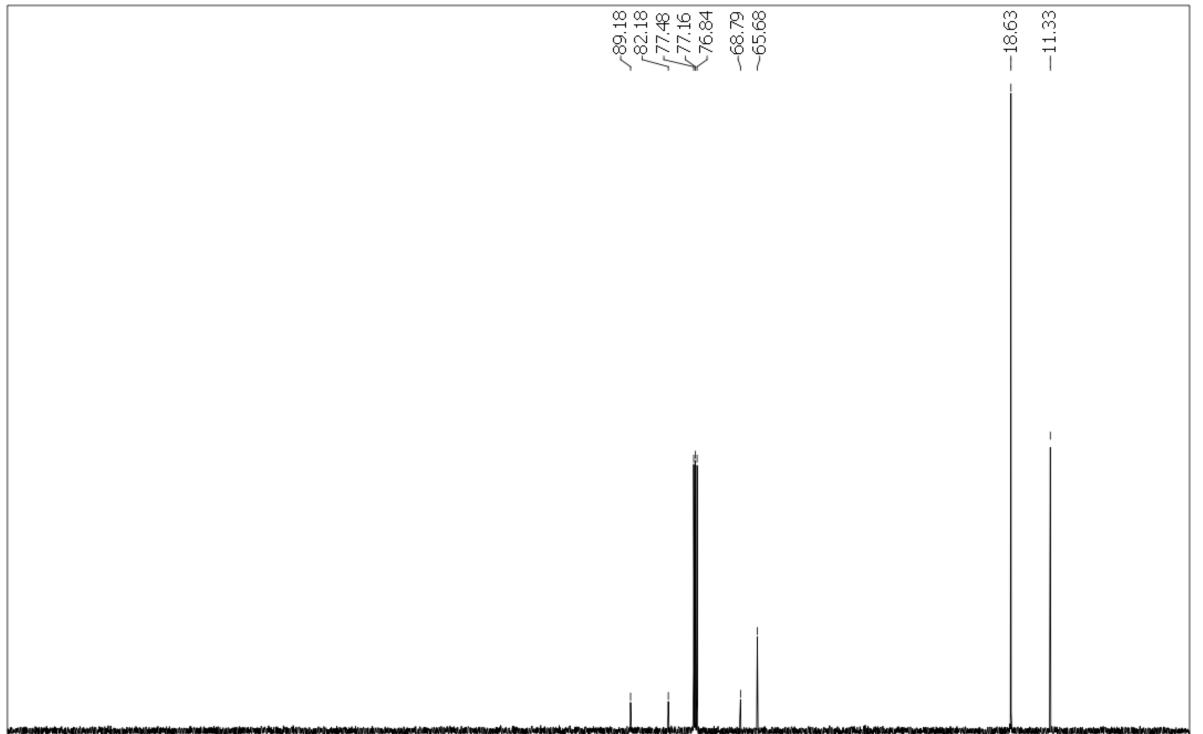

7.26
2.37
1.52
1.06
0.94
6.00
21.42
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

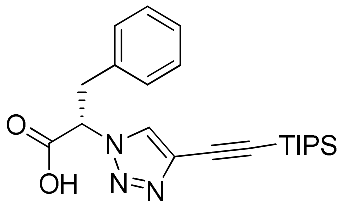

89.02
84.85
80.80
77.16
67.84
65.68
31.15
18.63
11.35
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



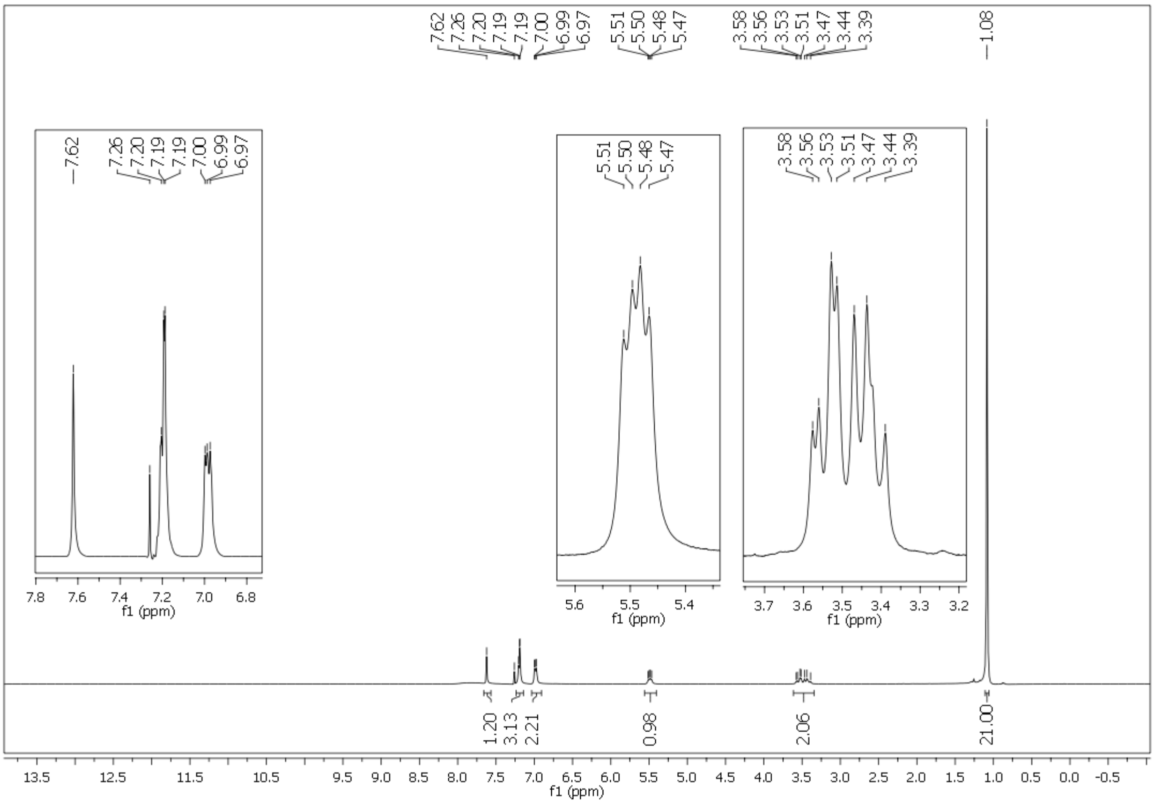
(**8**)

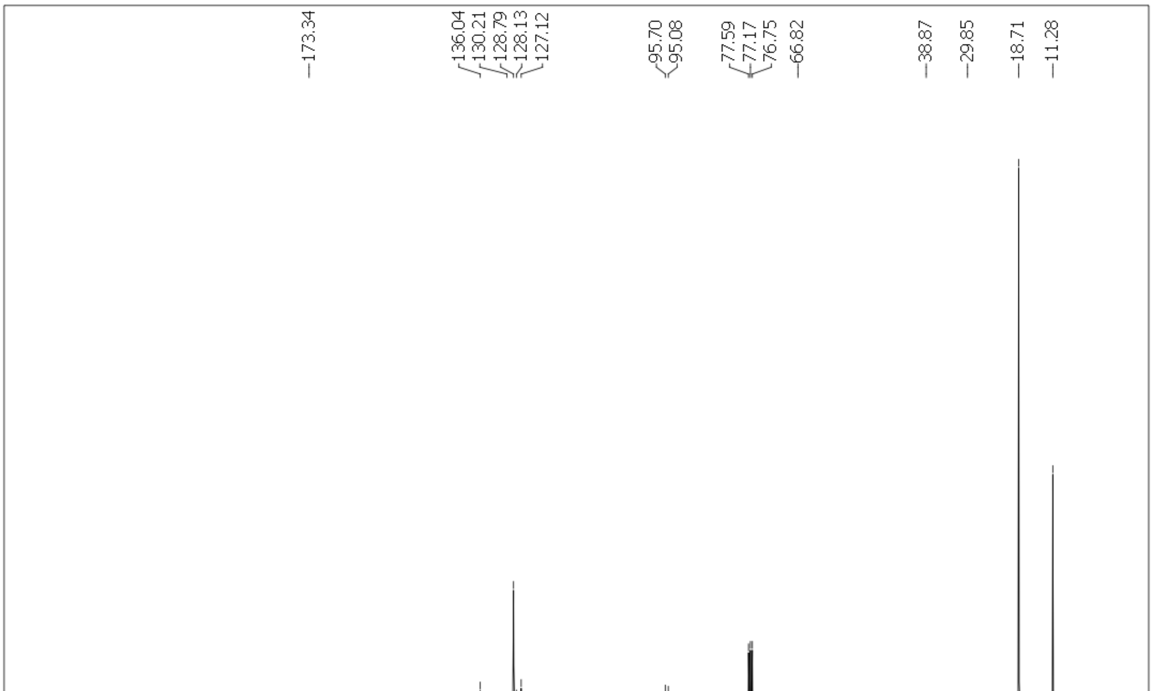

7.26
2.07
1.55
1.09
0.76
21.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

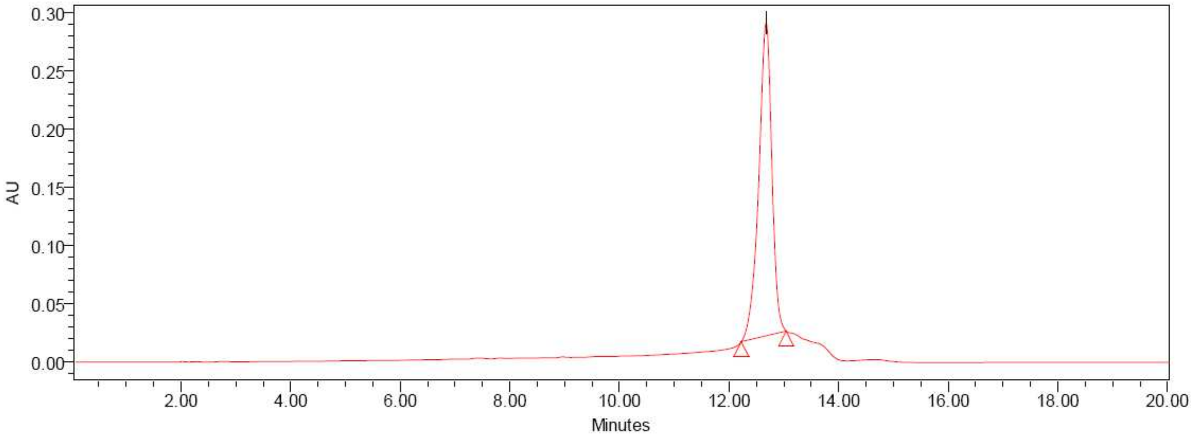

89.18
82.18
77.48
77.16
76.84
68.79
65.68
18.63
11.33
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OH
N
N
N
TIPS

(**9a**)

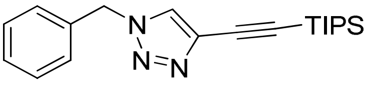

7.62
7.26
7.20
7.19
7.19
7.00
6.99
6.97
5.51
5.50
5.48
5.47
3.58
3.56
3.53
3.51
3.47
3.44
3.39
1.08
1.20
3.13
2.21
0.98
2.06
21.00
f1 (ppm)


173.34
136.04
130.21
128.79
128.13
127.12
95.70
95.08
77.59
77.17
76.75
66.82
38.87
29.85
18.71
11.28
f1 (ppm)

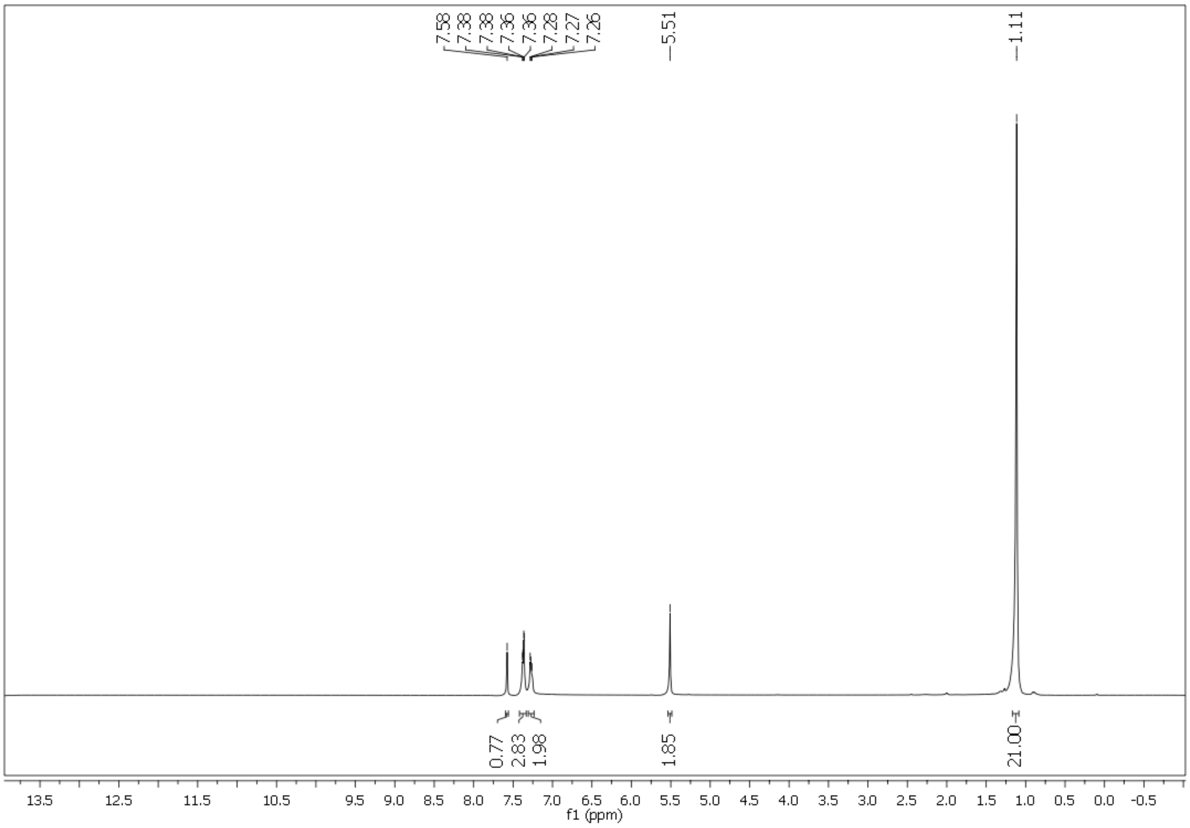


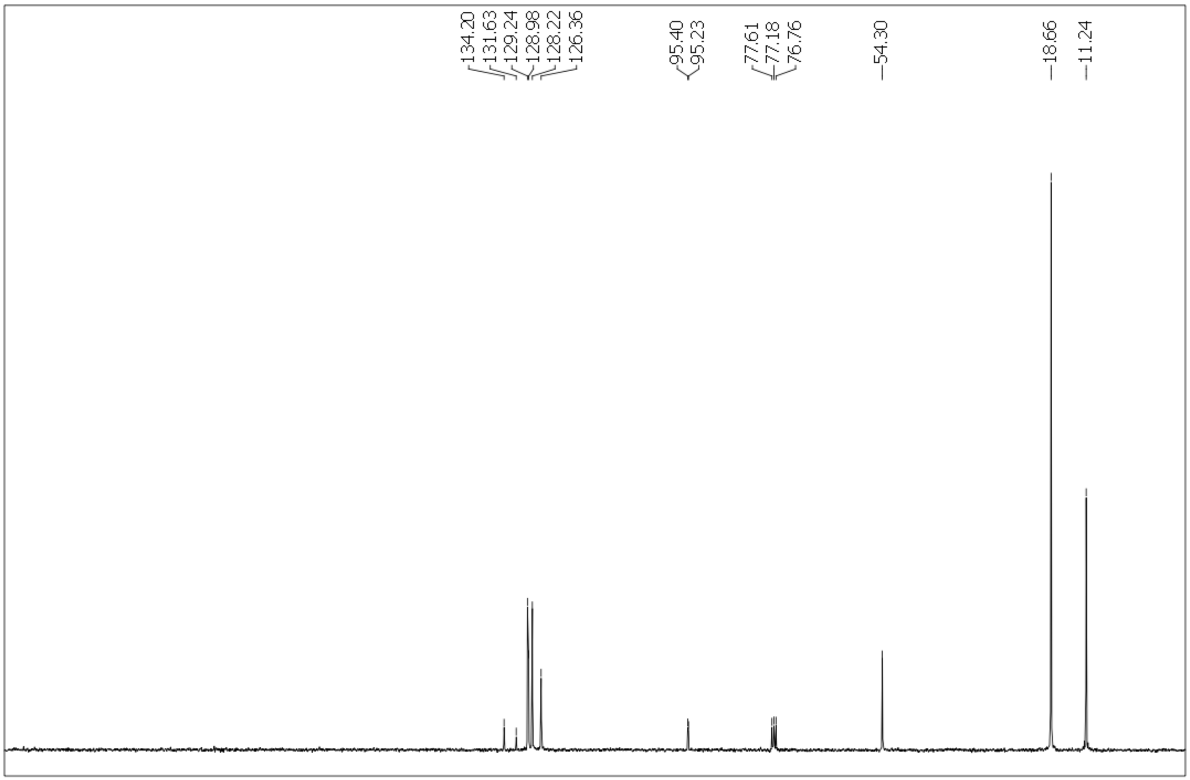
Processed Channel: PDA 254.0 nm

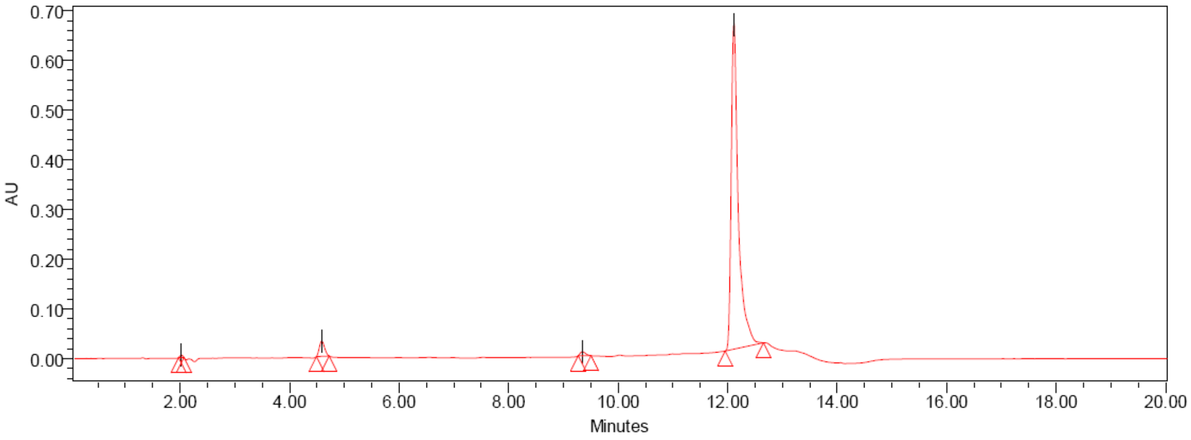
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	12.676	4488297	100.00	269256


N
N
N
TIPS

(**9b**)

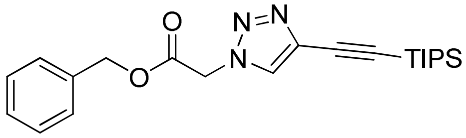

7.58
7.38
7.38
7.36
7.36
7.28
7.27
7.26
5.51
1.11
0.77
2.83
1.98
1.85
21.00
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


134.20
131.63
129.24
128.98
128.22
126.36
95.40
95.23
77.61
77.18
76.76
54.30
18.66
11.24
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

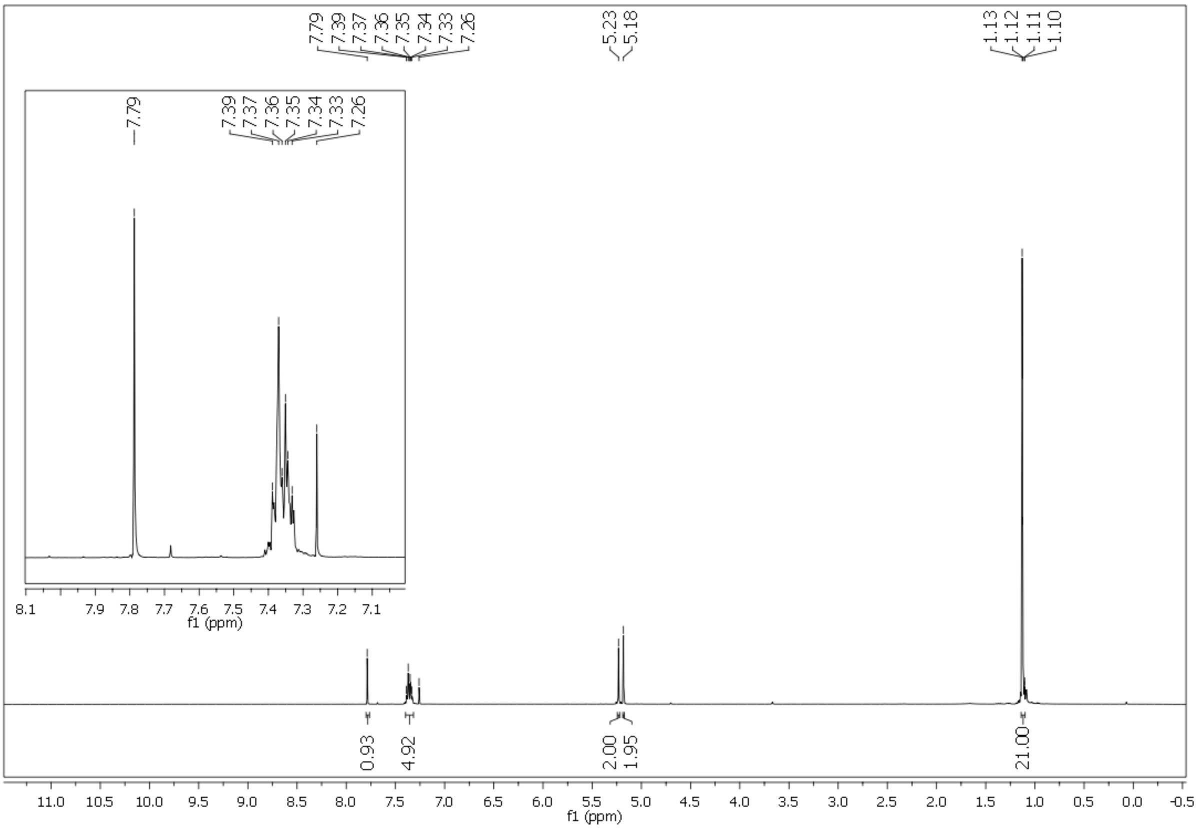


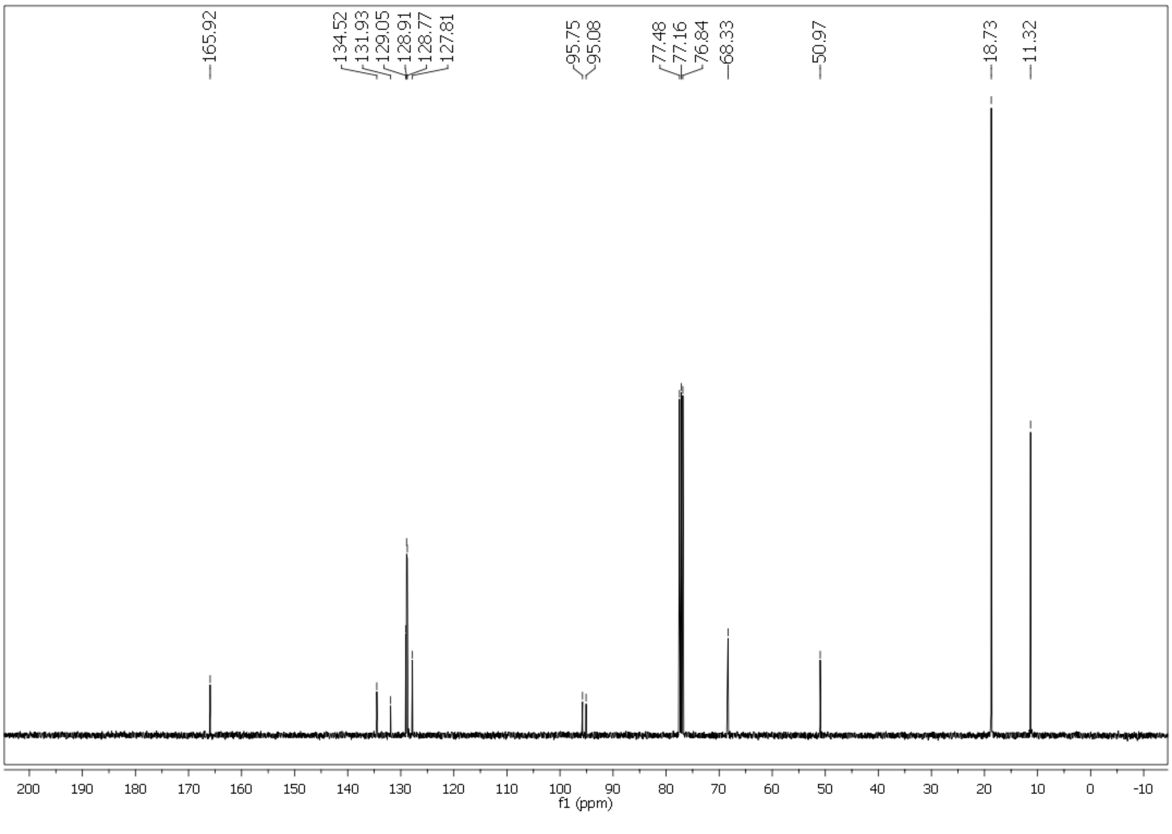
Processed Channel: PDA 226.0 nm

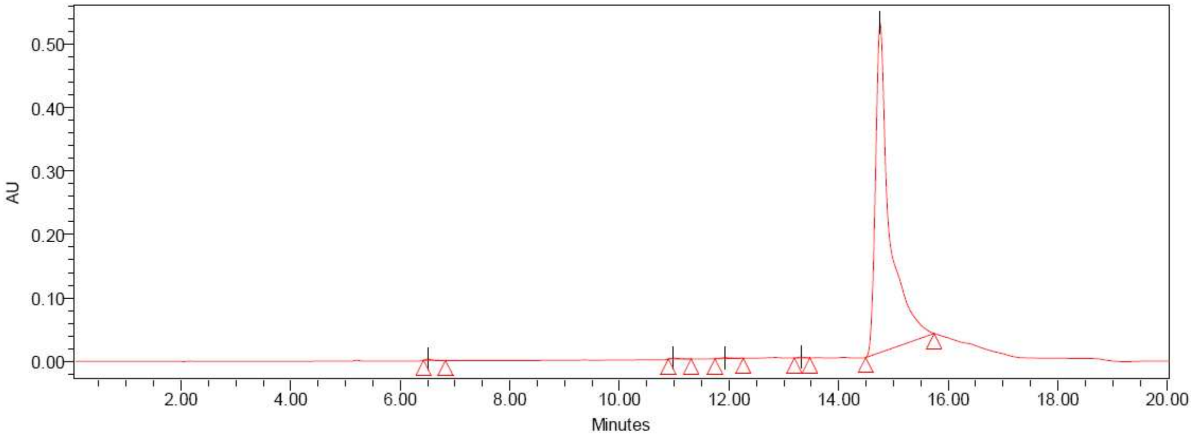
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 226.0 nm	2.024	17985	0.29	4853
2	PDA 226.0 nm	4.588	207471	3.35	30771
3	PDA 226.0 nm	9.352	53885	0.87	7908
4	PDA 226.0 nm	12.117	5912960	95.49	655814


O
N=N
N
O
TIPS

(**9c**)


7.79
7.39
7.37
7.36
7.35
7.34
7.33
7.26
5.23
5.18
1.13
1.12
1.11
1.10
0.93
4.92
2.00
1.95
21.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
8.1 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)

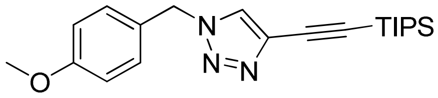

165.92
134.52
131.93
129.05
128.91
128.77
127.81
95.75
95.08
77.48
77.16
76.84
68.33
50.97
18.73
11.32
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



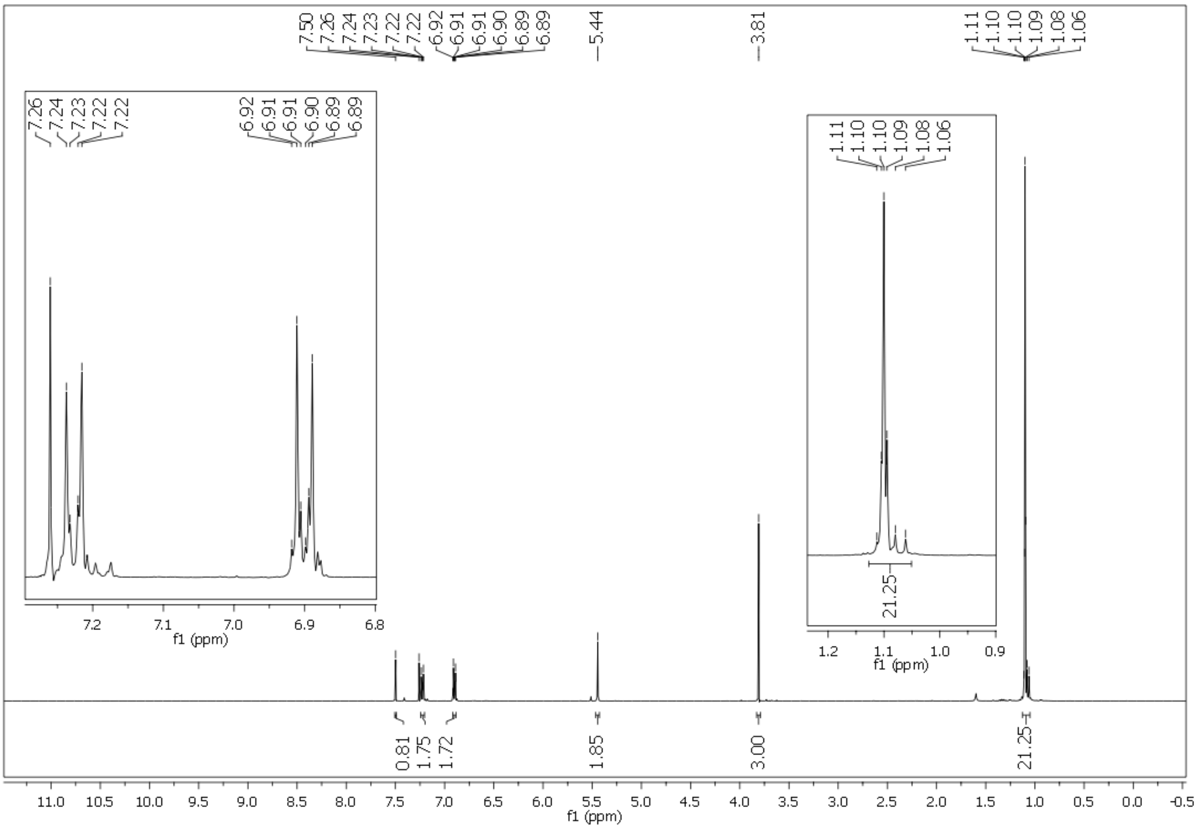
Processed Channel: PDA 254.0 nm

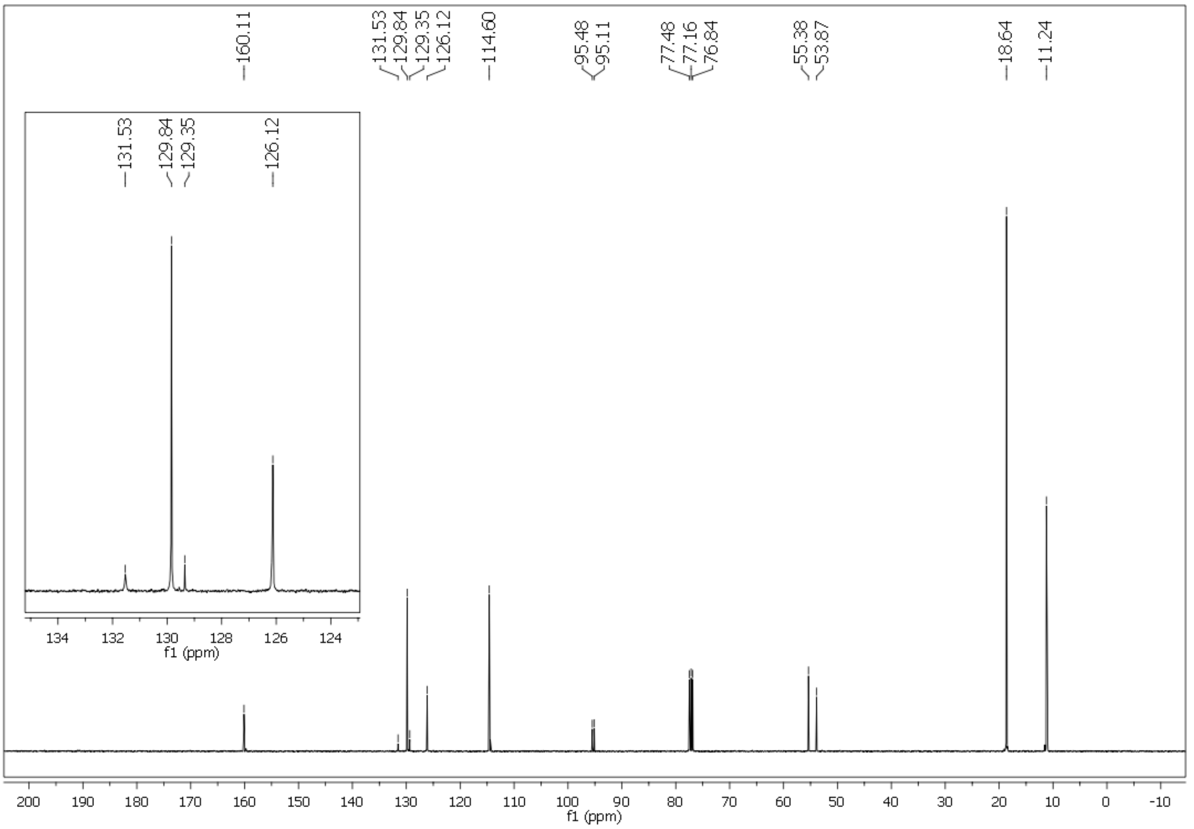
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	6.499	14556	0.16	1743
2	PDA 254.0 nm	10.970	15908	0.17	1377
3	PDA 254.0 nm	11.929	19480	0.21	1487

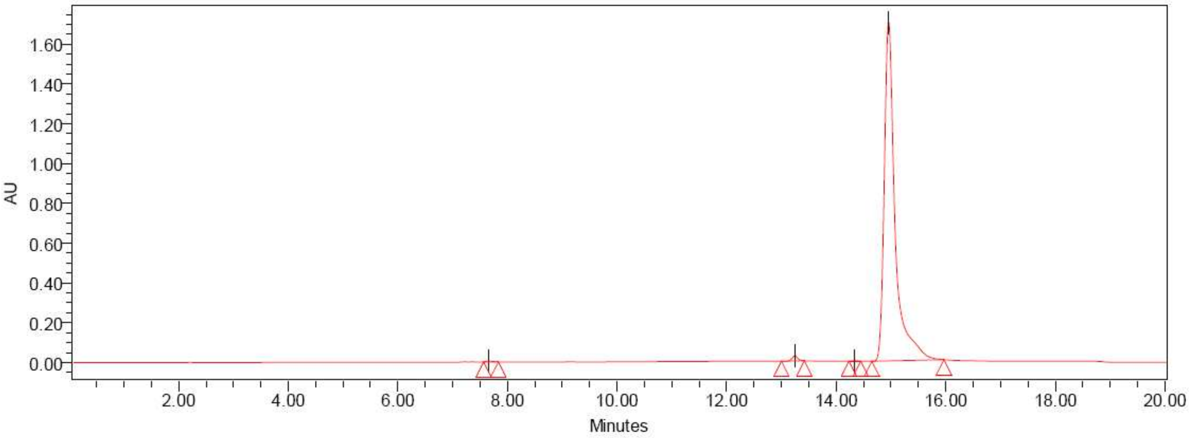
	Processed Channel	Retention Time (min)	Area	% Area	Height
4	PDA 254.0 nm	13.313	10737	0.11	1513
5	PDA 254.0 nm	14.759	9327107	99.35	519255


N
N
N
O
TIPS

(**9d**)


7.50
7.26
7.24
7.23
7.22
7.22
6.92
6.91
6.91
6.90
6.89
6.89
5.44
3.81
1.11
1.10
1.10
1.09
1.08
1.06
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
21.25
1.2
1.1
1.0
0.9
f1 (ppm)
0.81
1.75
1.72
1.85
3.00
21.25
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

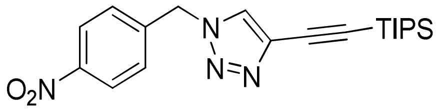

160.11
131.53
129.84
129.35
126.12
114.60
95.48
95.11
77.48
77.16
76.84
55.38
53.87
18.64
11.24
134
132
130
128
126
124
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



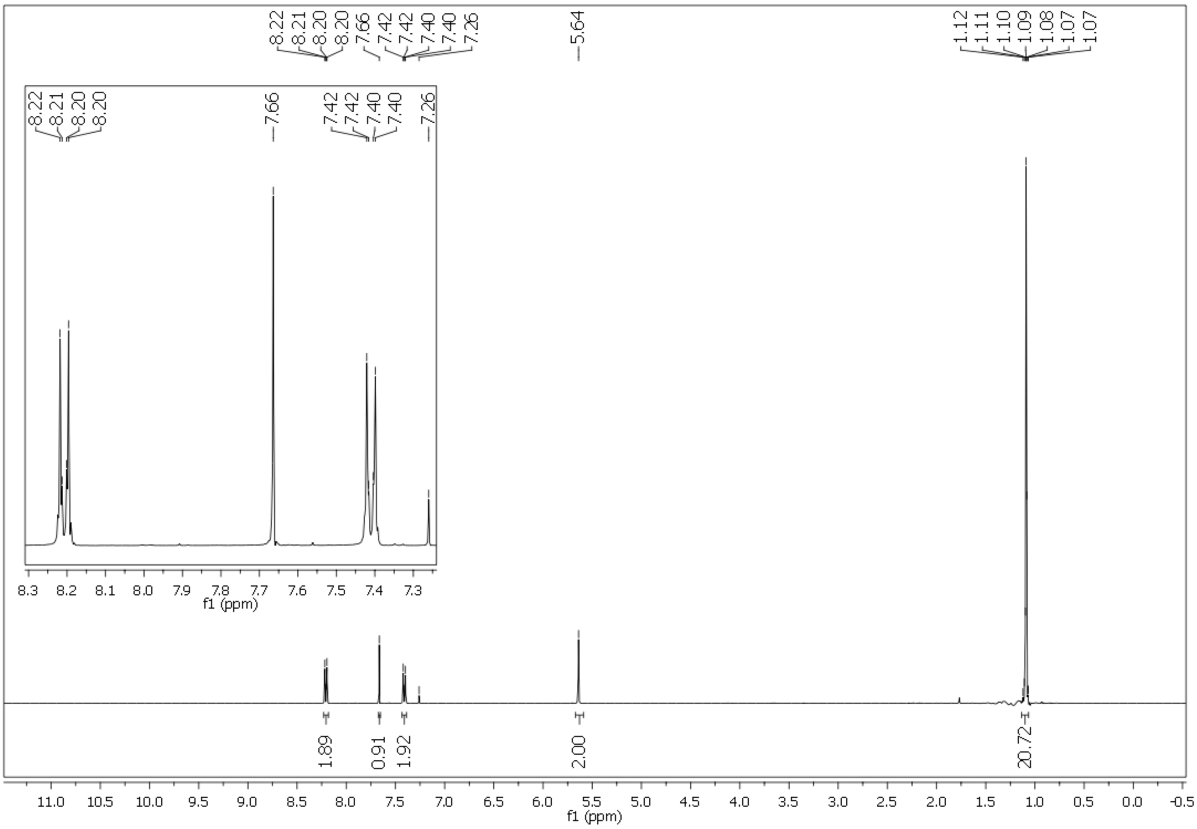
Processed Channel: PDA 254.0 nm

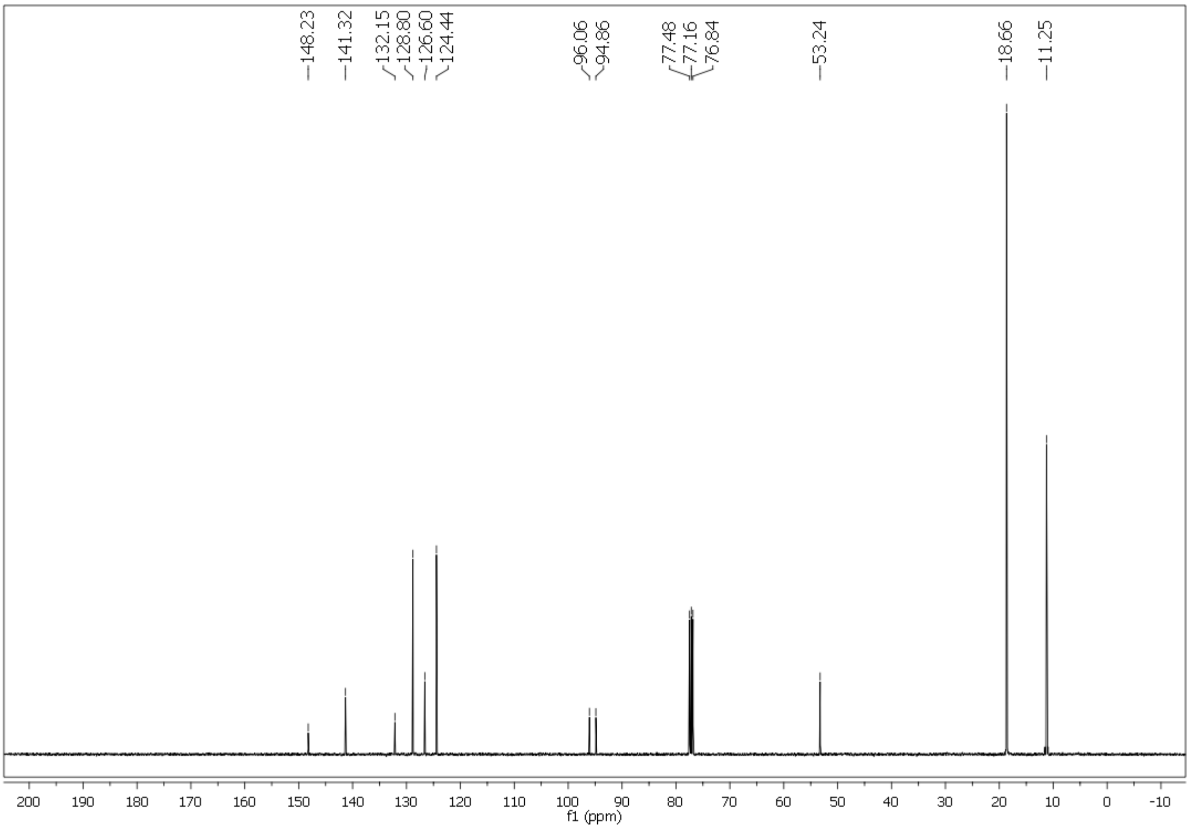
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	7.654	37424	0.16	5041
2	PDA 254.0 nm	13.245	181303	0.77	25374
3	PDA 254.0 nm	14.340	13545	0.06	1886

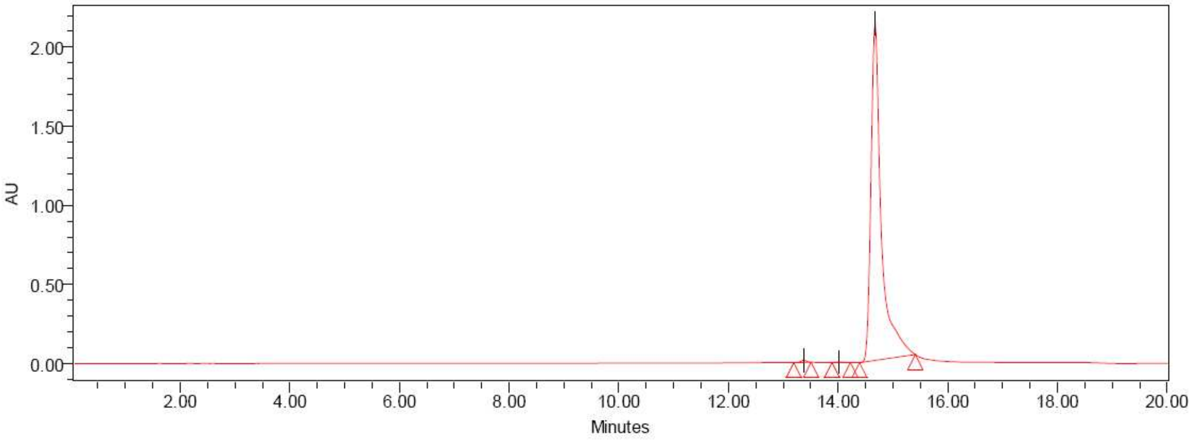
	Processed Channel	Retention Time (min)	Area	% Area	Height
4	PDA 254.0 nm	14.959	23339032	99.01	1705783


TIPS
O_2N
N
N
N

(**9e**)

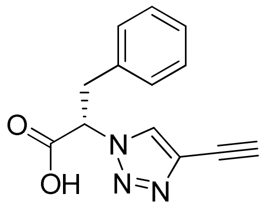

8.22
8.21
8.20
8.20
7.66
7.42
7.42
7.40
7.40
7.26
5.64
1.12
1.11
1.10
1.09
1.08
1.07
1.07
1.89
0.91
1.92
2.00
20.72
8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3
f1 (ppm)
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


148.23
141.32
132.15
128.80
126.60
124.44
96.06
94.86
77.48
77.16
76.84
53.24
18.66
11.25
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

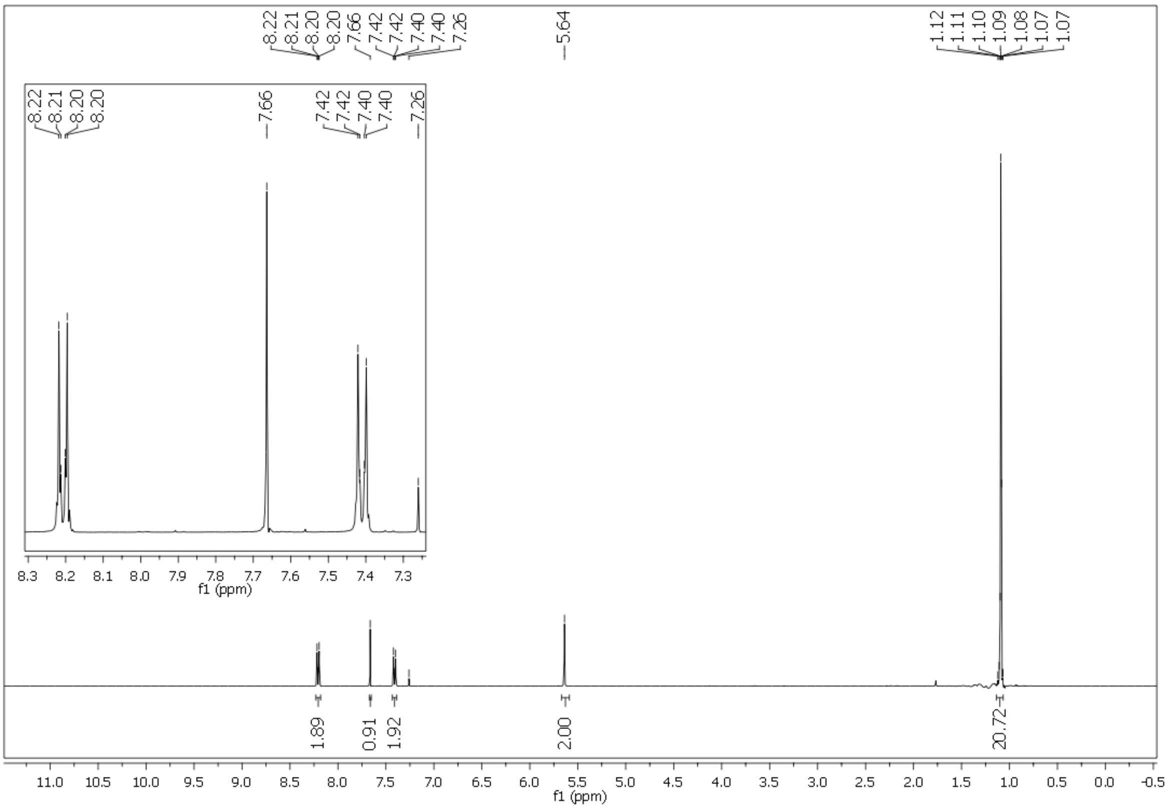


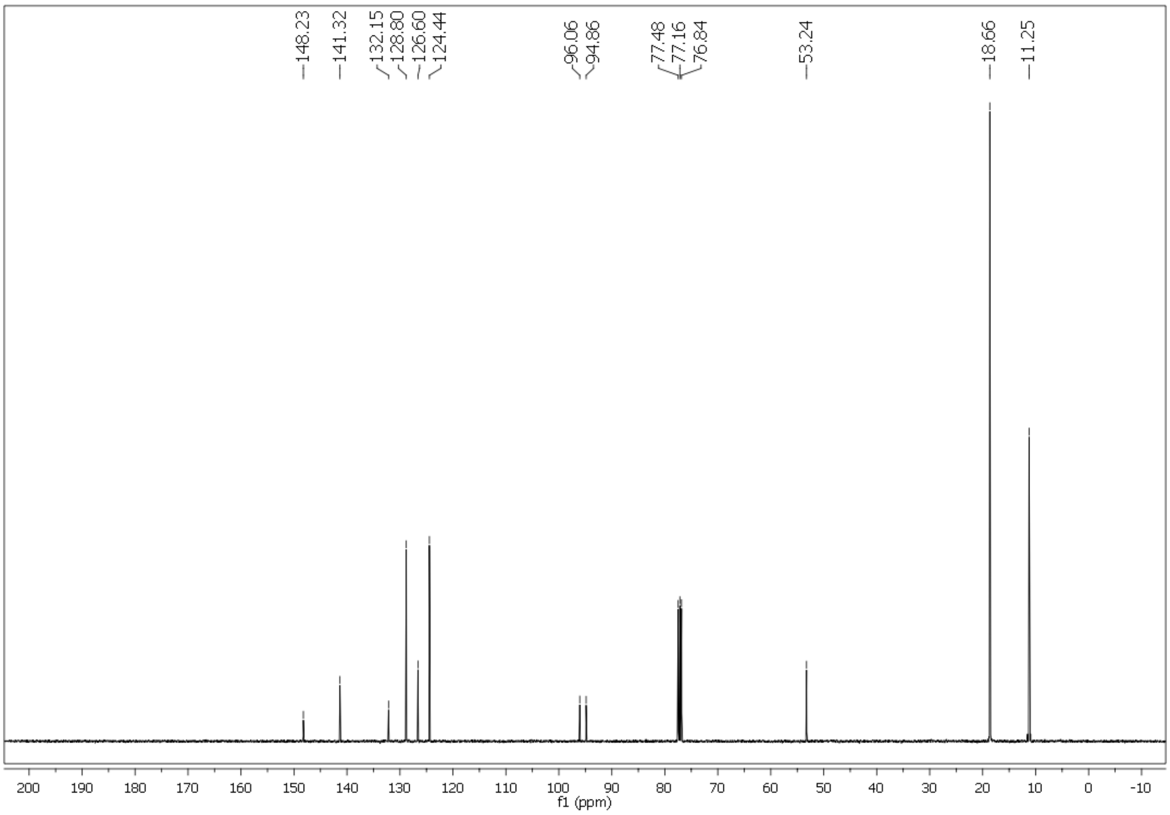
Processed Channel: PDA 254.0 nm

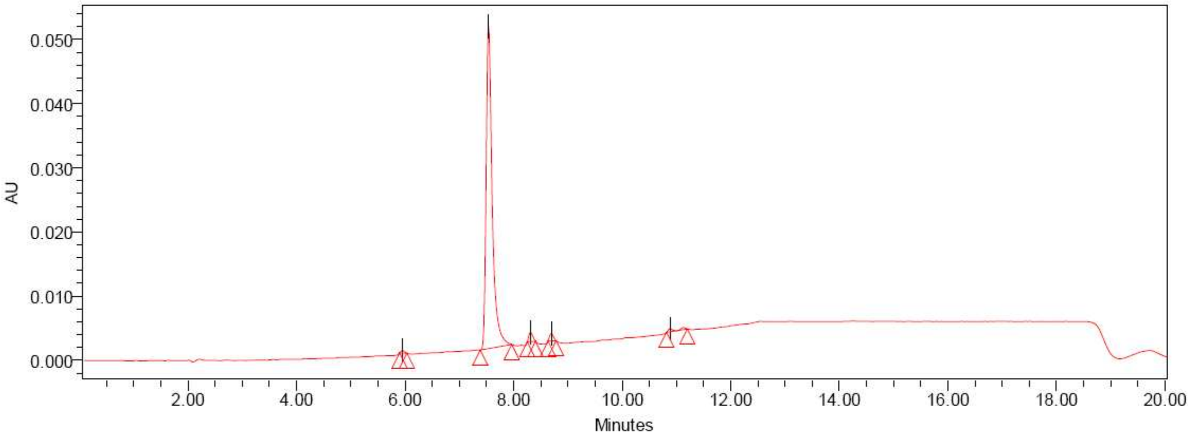
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	13.369	95836	0.34	13046
2	PDA 254.0 nm	14.012	36353	0.13	3954
3	PDA 254.0 nm	14.674	28017498	99.53	2131899



(**10a**)


8.22
8.21
8.20
8.20
7.66
7.42
7.42
7.40
7.40
7.26
5.64
1.12
1.11
1.10
1.09
1.08
1.07
1.07
1.89
0.91
1.92
2.00
20.72
f1 (ppm)

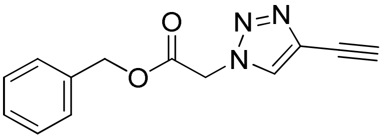

148.23
141.32
132.15
128.80
126.60
124.44
96.06
94.86
77.48
77.16
76.84
53.24
18.66
11.25
f1 (ppm)



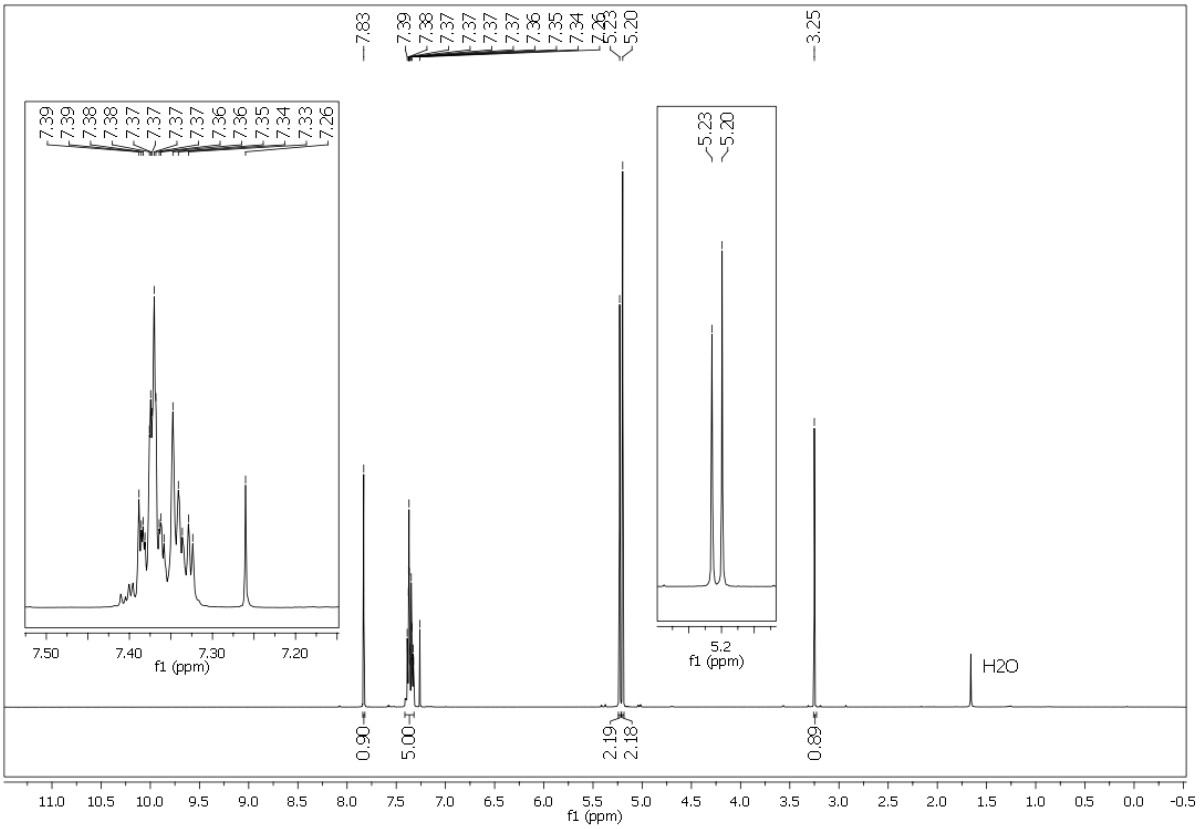
Processed Channel: PDA 254.0 nm

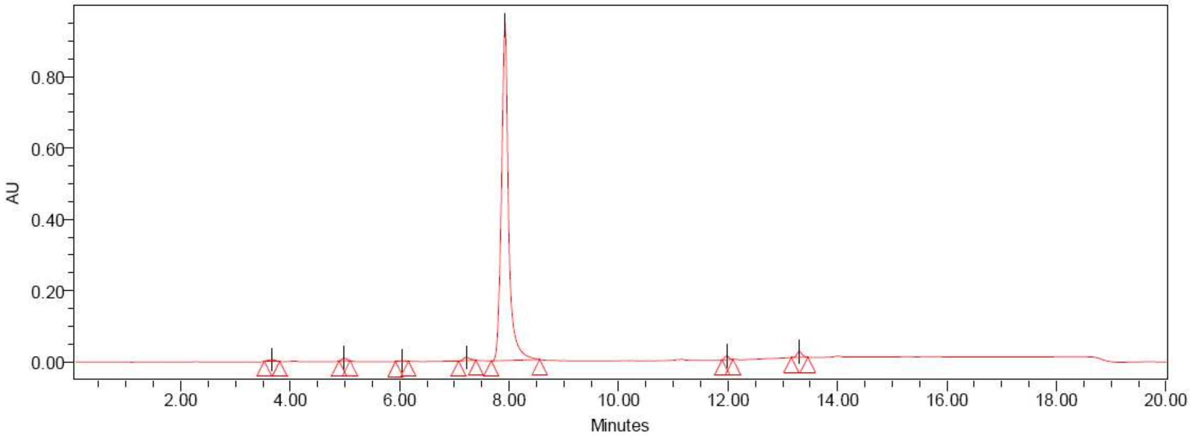
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	5.953	1807	0.44	403
2	PDA 254.0 nm	7.539	388098	95.36	50804
3	PDA 254.0 nm	8.314	7166	1.76	1439

	Processed Channel	Retention Time (min)	Area	% Area	Height
4	PDA 254.0 nm	8.697	5761	1.42	1158
5	PDA 254.0 nm	10.887	4153	1.02	420



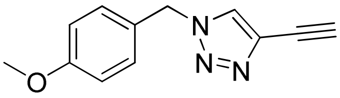
(**10c**)





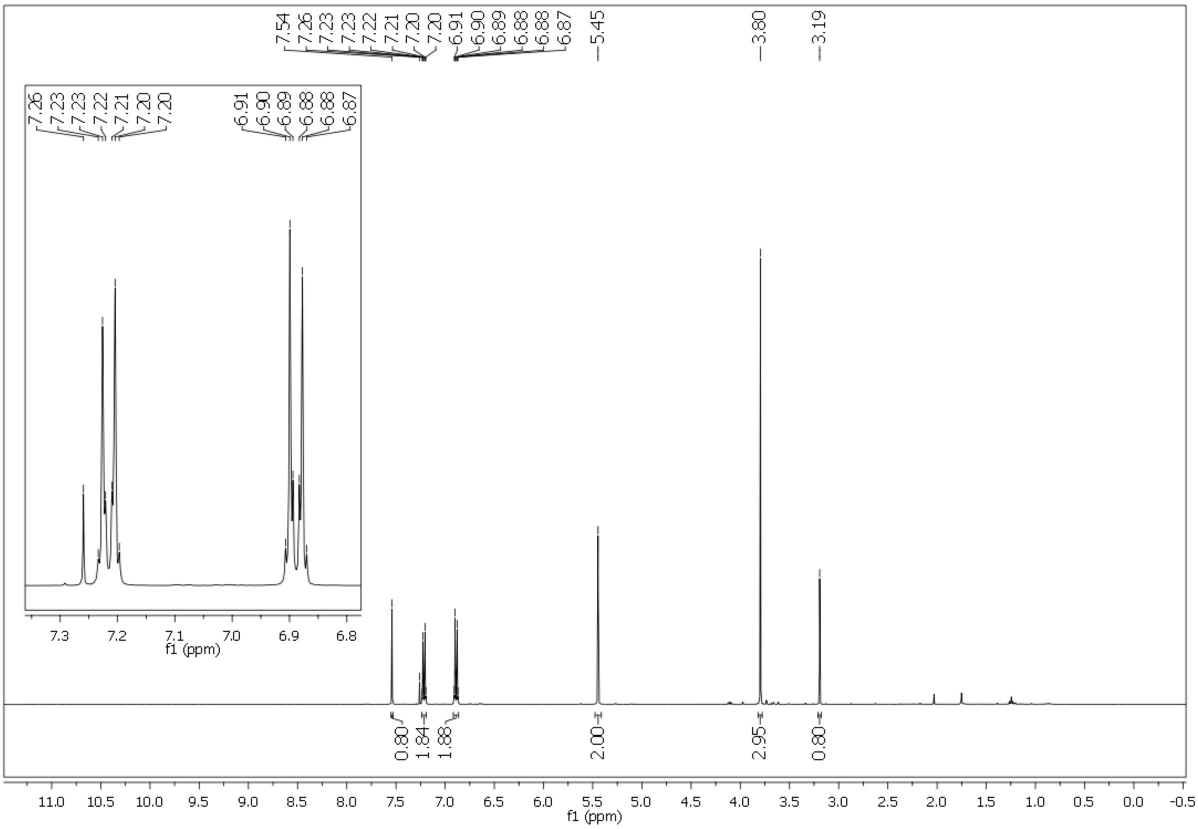
Processed Channel: PDA 254.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	3.659	42944	0.48	4615
2	PDA 254.0 nm	4.989	48686	0.55	7258
3	PDA 254.0 nm	6.048	16832	0.19	2295
4	PDA 254.0 nm	7.218	81104	0.91	9701
5	PDA 254.0 nm	7.923	8556217	96.06	942772
6	PDA 254.0 nm	11.976	55929	0.63	10540

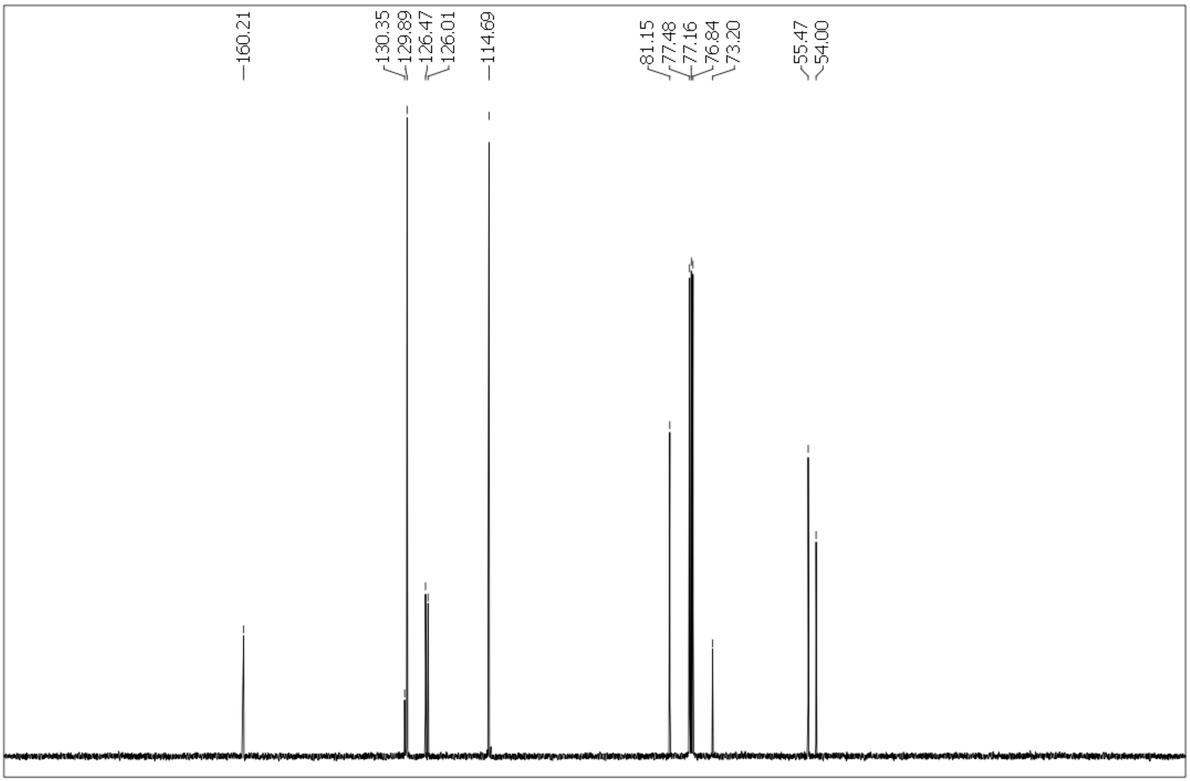


O
N
N
N

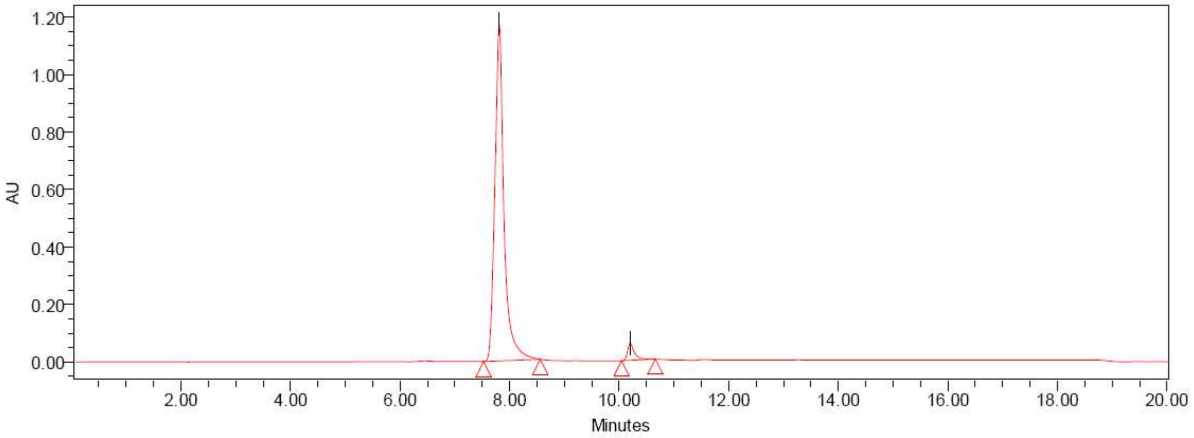
(**10d**)



7.54
7.26
7.23
7.23
7.22
7.21
7.20
7.20
6.91
6.90
6.89
6.88
6.88
6.87
5.45
3.80
3.19
7.26
7.23
7.23
7.22
7.21
7.20
7.20
6.91
6.90
6.89
6.88
6.88
6.87
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
0.80
1.84
1.88
2.00
2.95
0.80
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

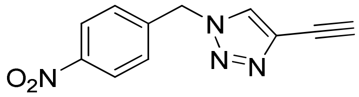


160.21
130.35
129.89
126.47
126.01
114.69
81.15
77.48
77.16
76.84
73.20
55.47
54.00
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

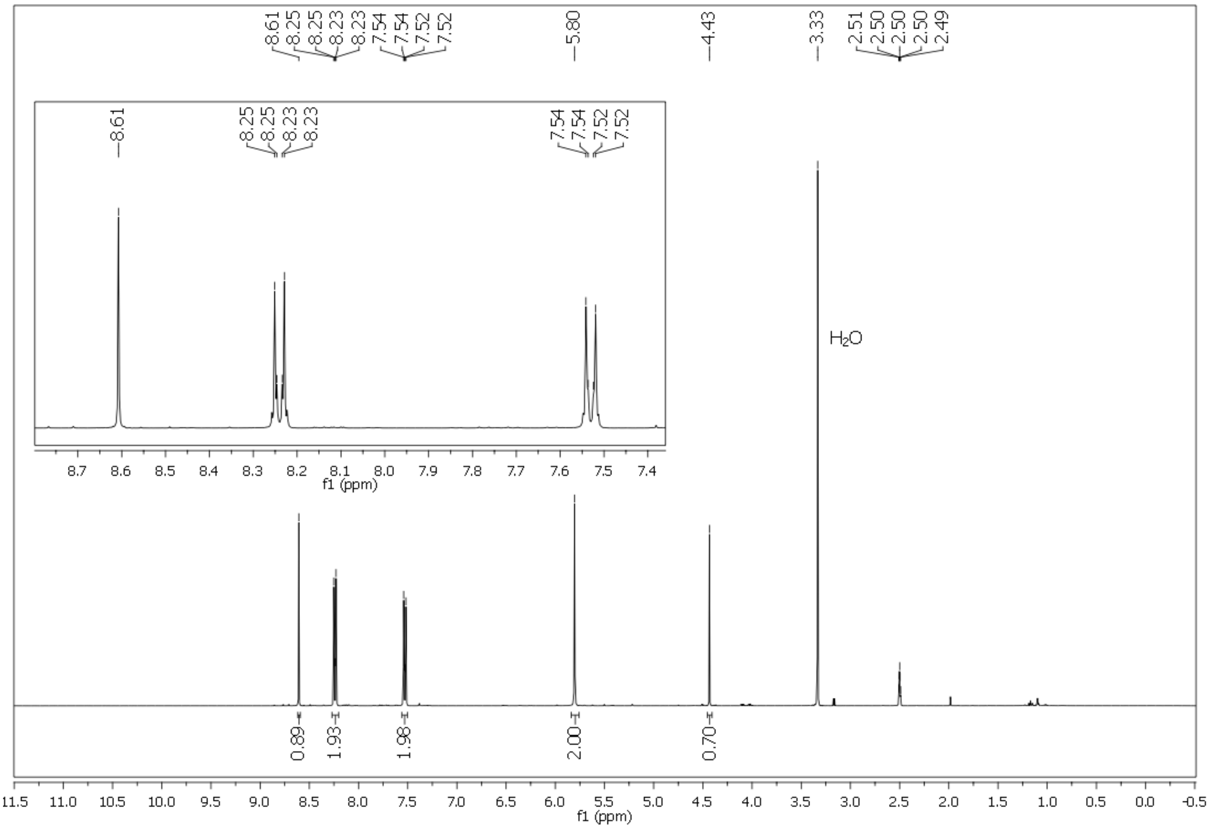


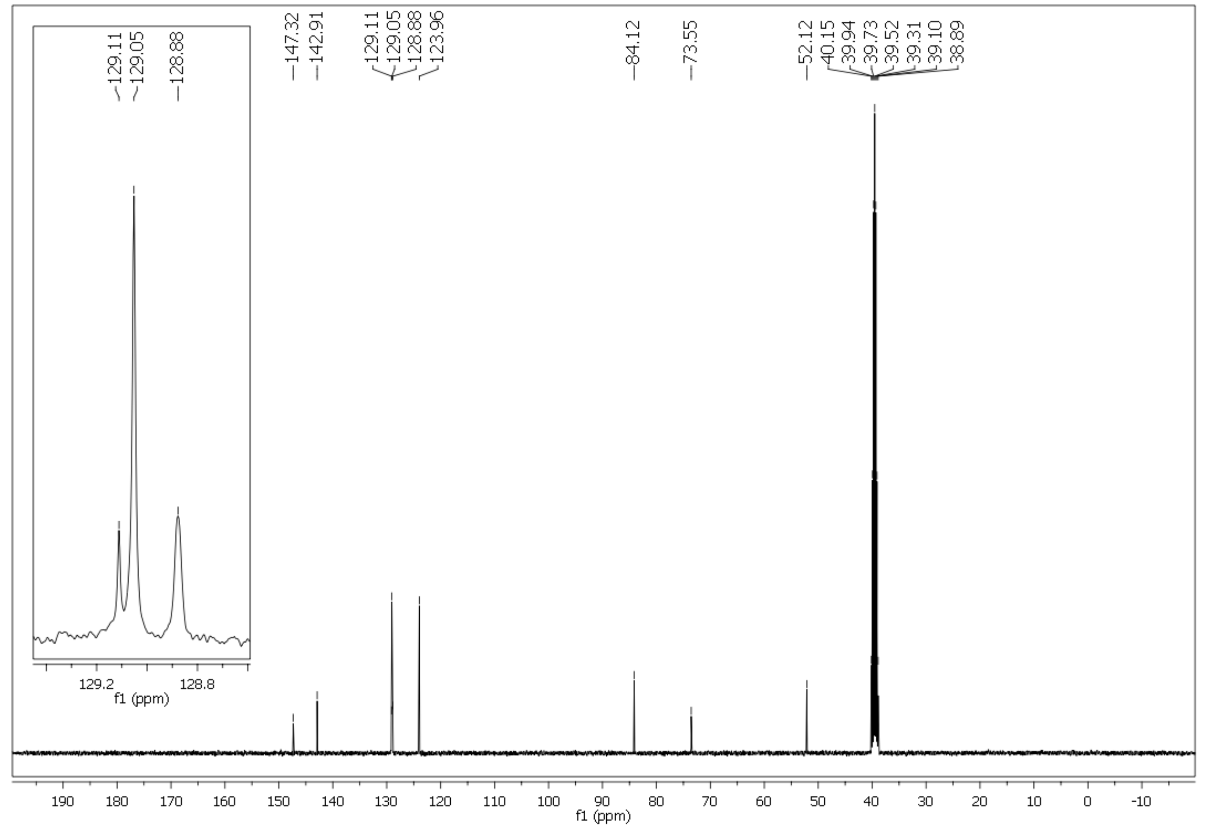
Processed Channel: PDA 254.0 nm

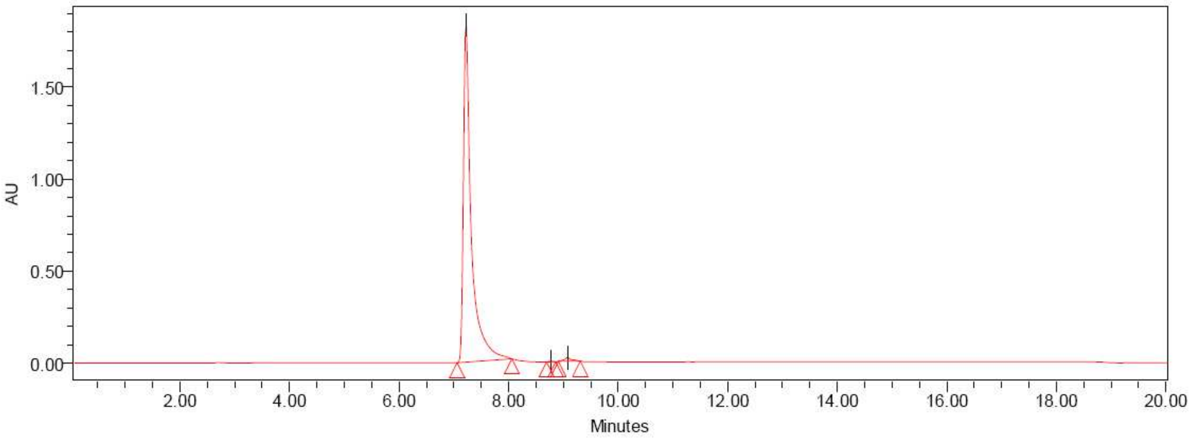
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	7.810	13386124	96.20	1173421
2	PDA 254.0 nm	10.203	528346	3.80	59714



(**10e**)

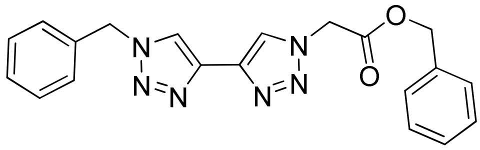

8.61
8.25
8.25
8.23
8.23
7.54
7.54
7.52
7.52
5.80
4.43
3.33
2.51
2.50
2.50
2.50
2.49
H₂O
0.89
1.93
1.98
2.00
0.70
f1 (ppm)


147.32
142.91
129.11
129.05
128.88
123.96
84.12
73.55
52.12
40.15
39.94
39.73
39.52
39.31
39.10
38.89
f1 (ppm)

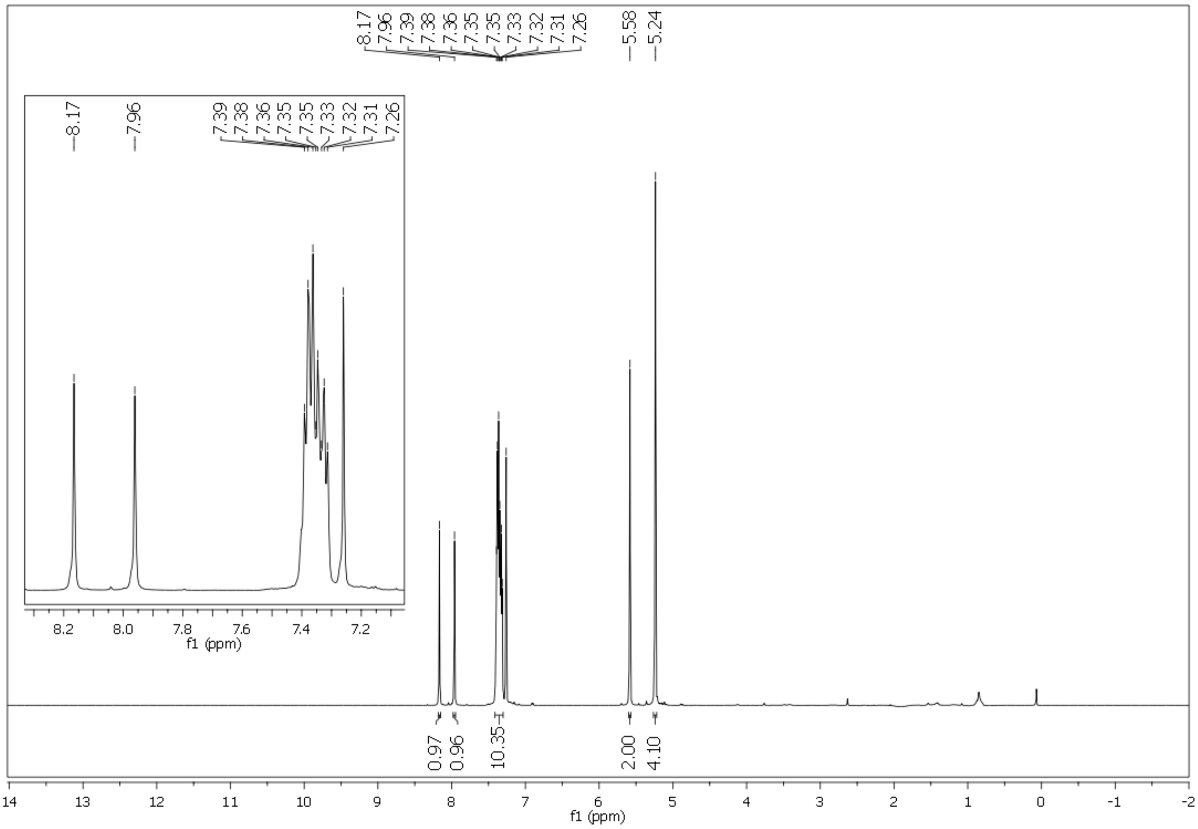


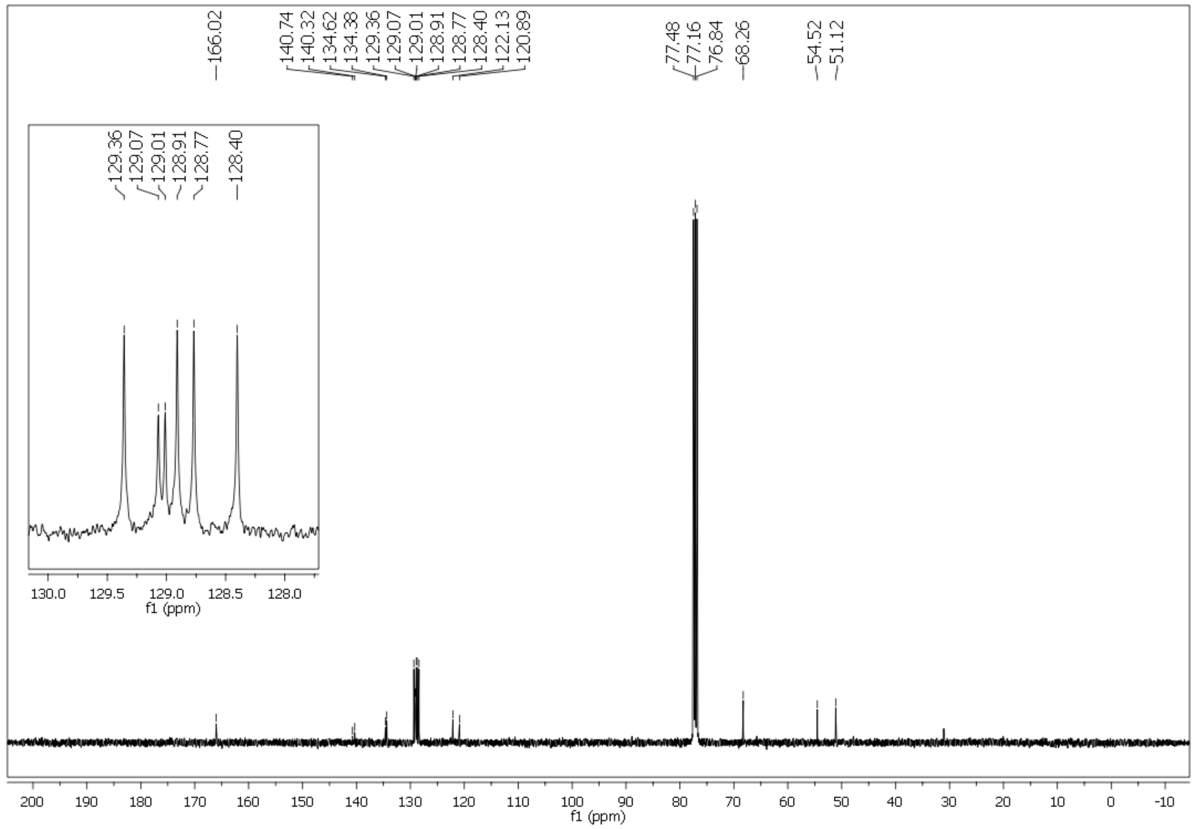
Processed Channel: PDA 254.0 nm

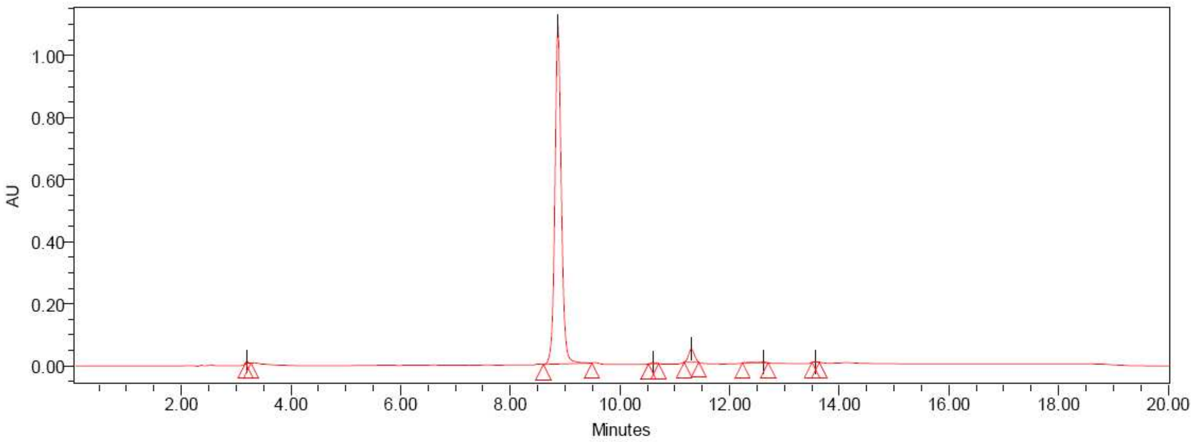
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	7.226	18159554	98.77	1830940
2	PDA 254.0 nm	8.769	23177	0.13	4302
3	PDA 254.0 nm	9.075	203470	1.11	20029



(**11b**)

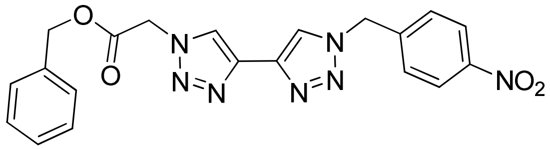

8.17
7.96
7.39
7.38
7.36
7.35
7.35
7.33
7.32
7.31
7.26
5.58
5.24
0.97
0.96
10.35
2.00
4.10
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
f1 (ppm)
8.2
8.0
7.8
7.6
7.4
7.2
f1 (ppm)


166.02
140.74
140.32
134.62
134.38
129.36
129.07
129.01
128.91
128.77
128.40
122.13
120.89
77.48
77.16
76.84
68.26
54.52
51.12
130.0
129.5
129.0
128.5
128.0
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

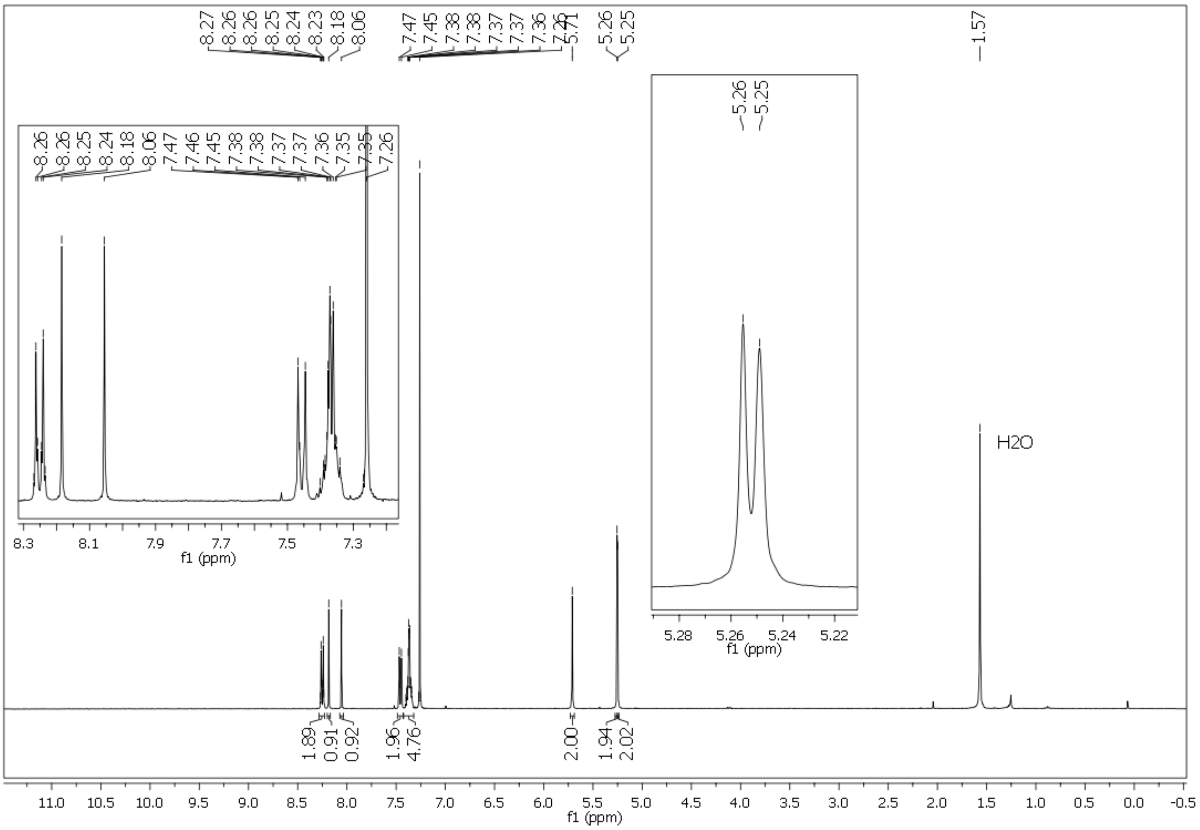


Processed Channel: PDA 254.0 nm

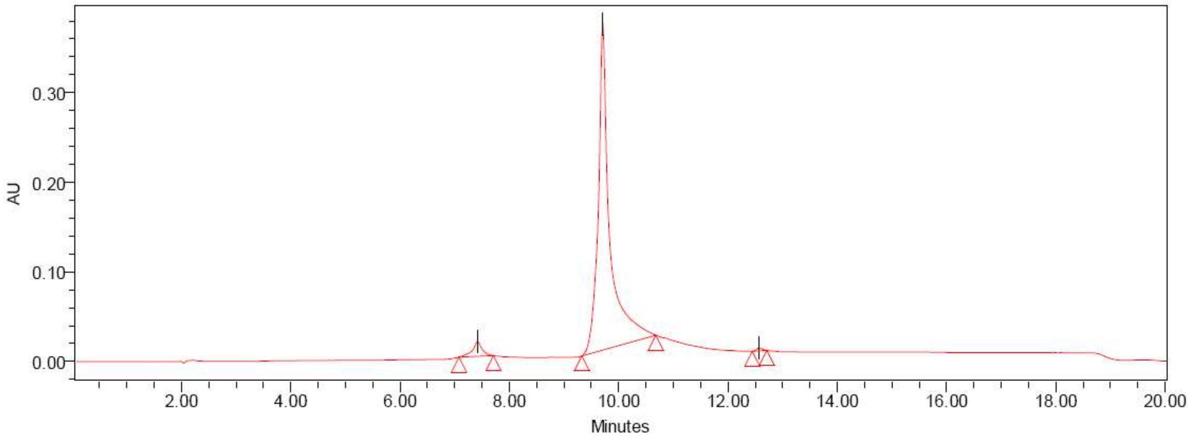
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	3.203	12542	0.14	4993
2	PDA 254.0 nm	8.870	8805954	95.59	1087707
3	PDA 254.0 nm	10.609	24626	0.27	4005
4	PDA 254.0 nm	11.305	313396	3.40	42807
5	PDA 254.0 nm	12.618	47320	0.51	2962
6	PDA 254.0 nm	13.563	8752	0.10	1754



(**11c**)

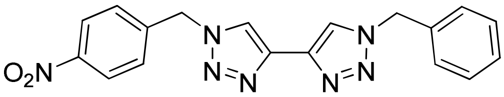


Auto-Scaled Chromatogram

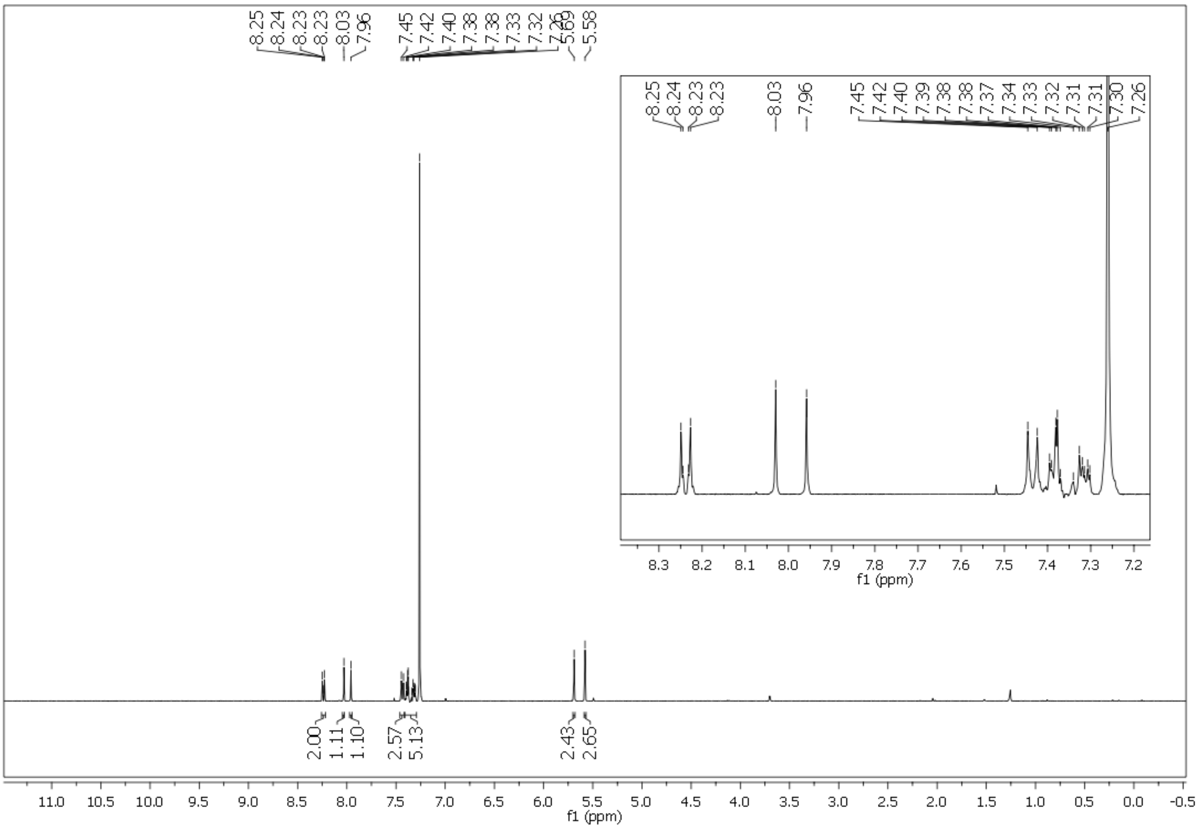


Processed Channel: PDA 254.0 nm

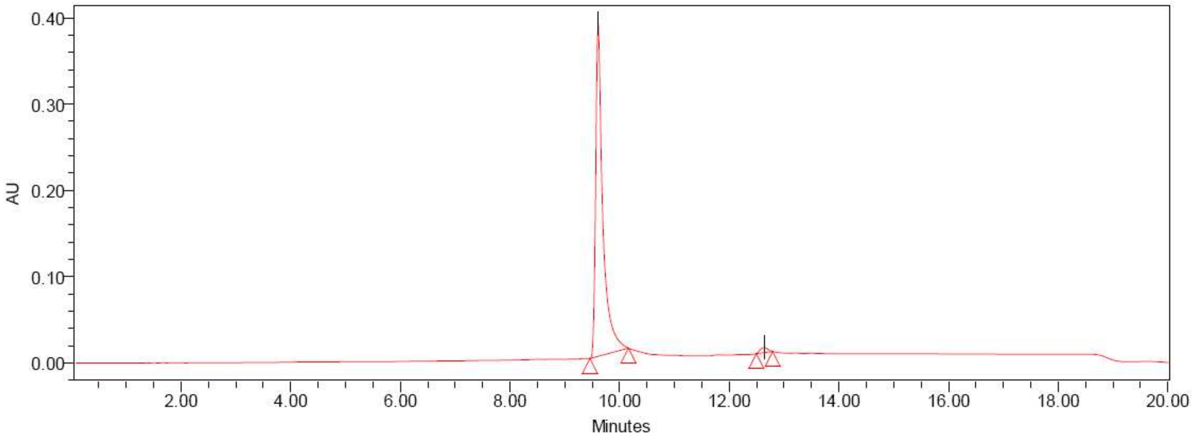
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	7.417	203216	3.64	16325
2	PDA 254.0 nm	9.711	5355634	95.93	363430
3	PDA 254.0 nm	12.573	24270	0.43	3276



(**11e**)

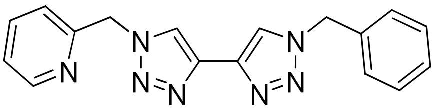


Auto-Scaled Chromatogram

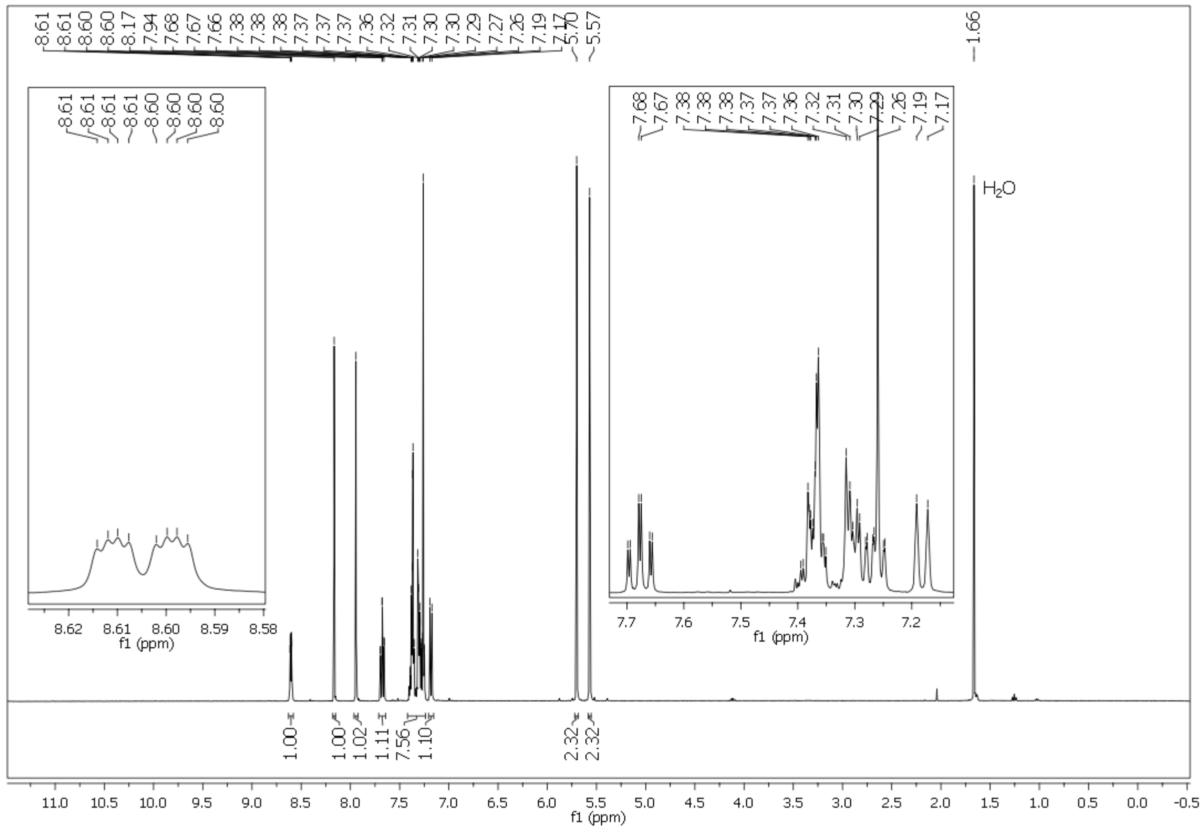


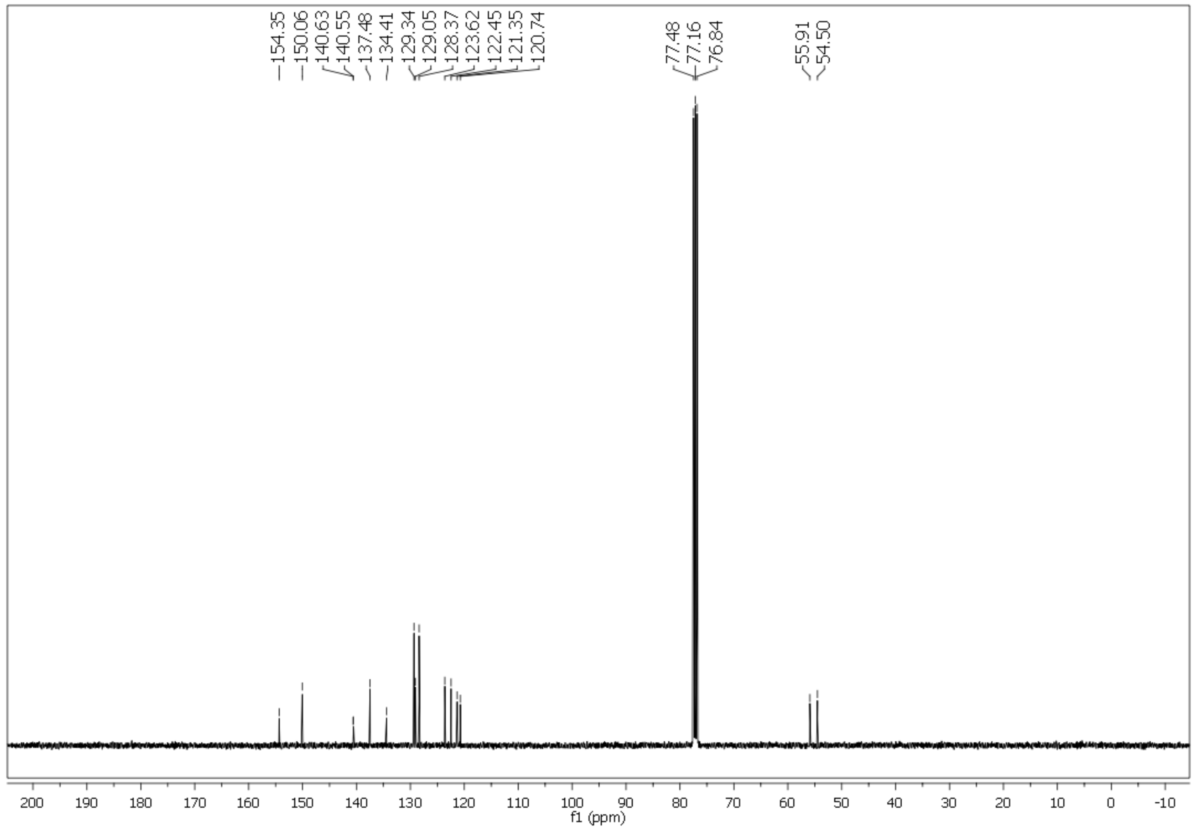
Processed Channel: PDA 254.0 nm

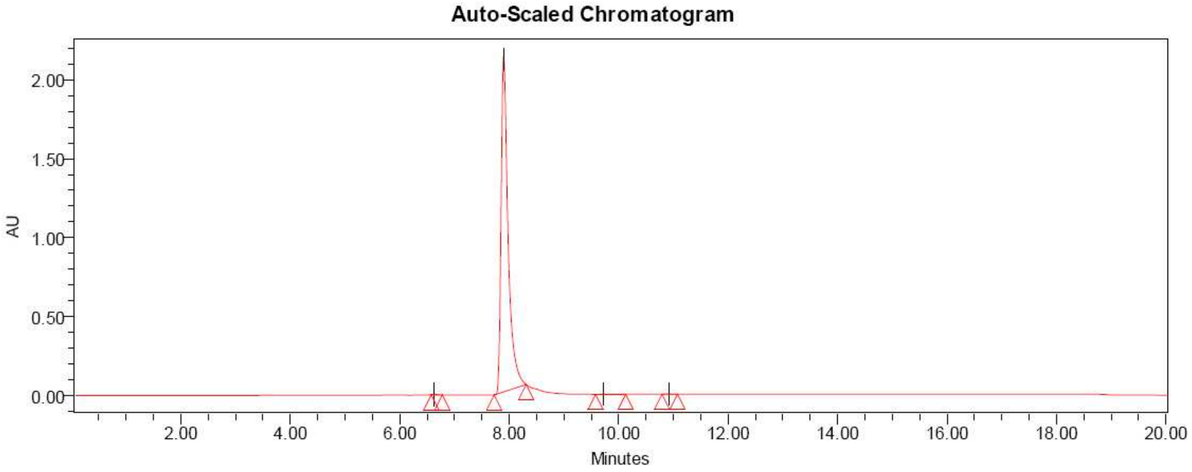
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	9.610	3526035	98.35	384514
2	PDA 254.0 nm	12.641	59233	1.65	6074


N
N
N
N
N
N
N

(**11f**)


8.61
8.61
8.60
8.60
8.17
7.94
7.68
7.67
7.66
7.38
7.38
7.38
7.37
7.37
7.37
7.36
7.32
7.31
7.30
7.30
7.29
7.27
7.26
7.19
7.17
5.70
5.57
1.66
8.61
8.61
8.61
8.61
8.60
8.60
8.60
8.60
8.62
8.61
8.60
8.59
8.58
f1 (ppm)
7.68
7.67
7.38
7.38
7.38
7.37
7.37
7.36
7.32
7.31
7.30
7.29
7.26
7.19
7.17
7.7
7.6
7.5
7.4
7.3
7.2
f1 (ppm)
H$_2$O
1.00
1.00
1.02
1.11
7.56
1.10
2.32
2.32
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

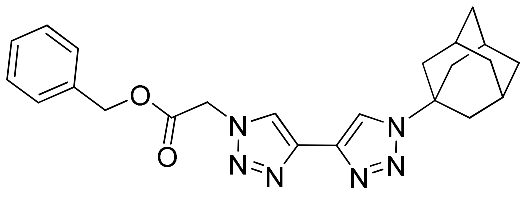

154.35
150.06
140.63
140.55
137.48
134.41
129.34
129.05
128.37
123.62
122.45
121.35
120.74
77.48
77.16
76.84
55.91
54.50
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



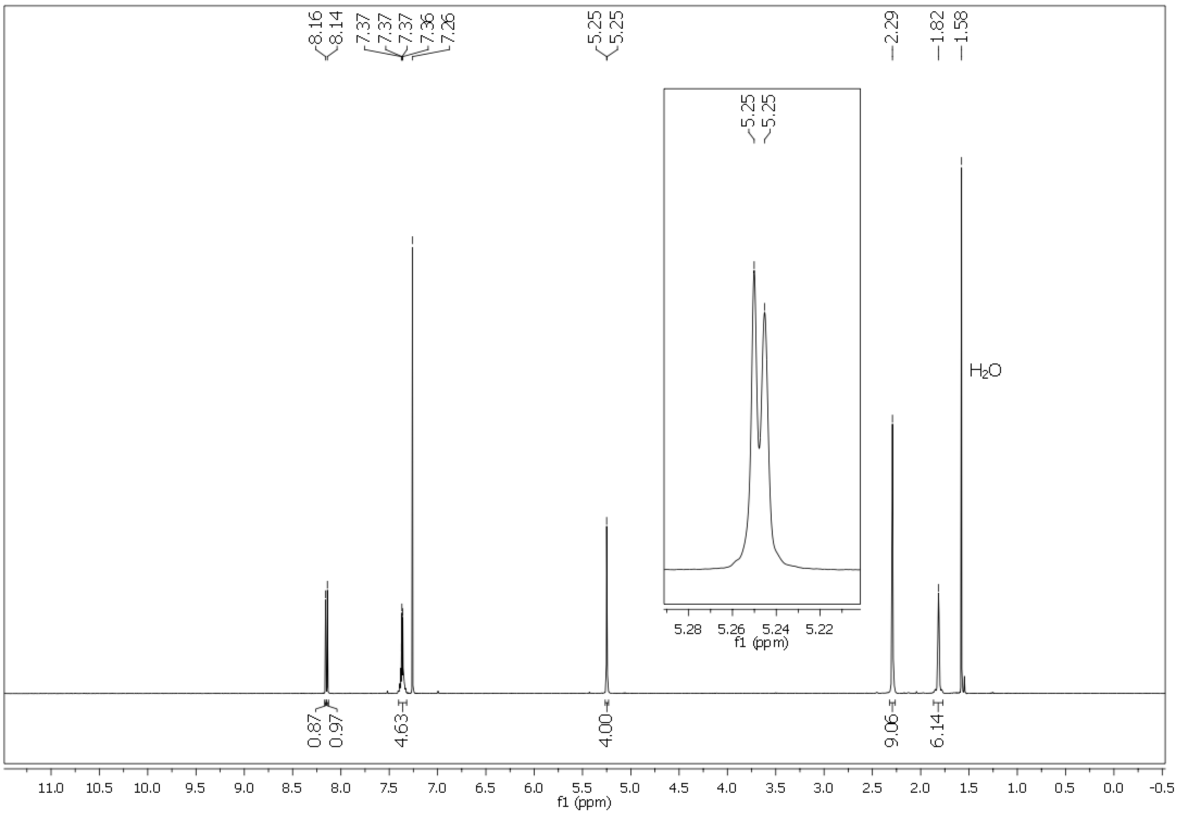
Processed Channel: PDA 254.0 nm

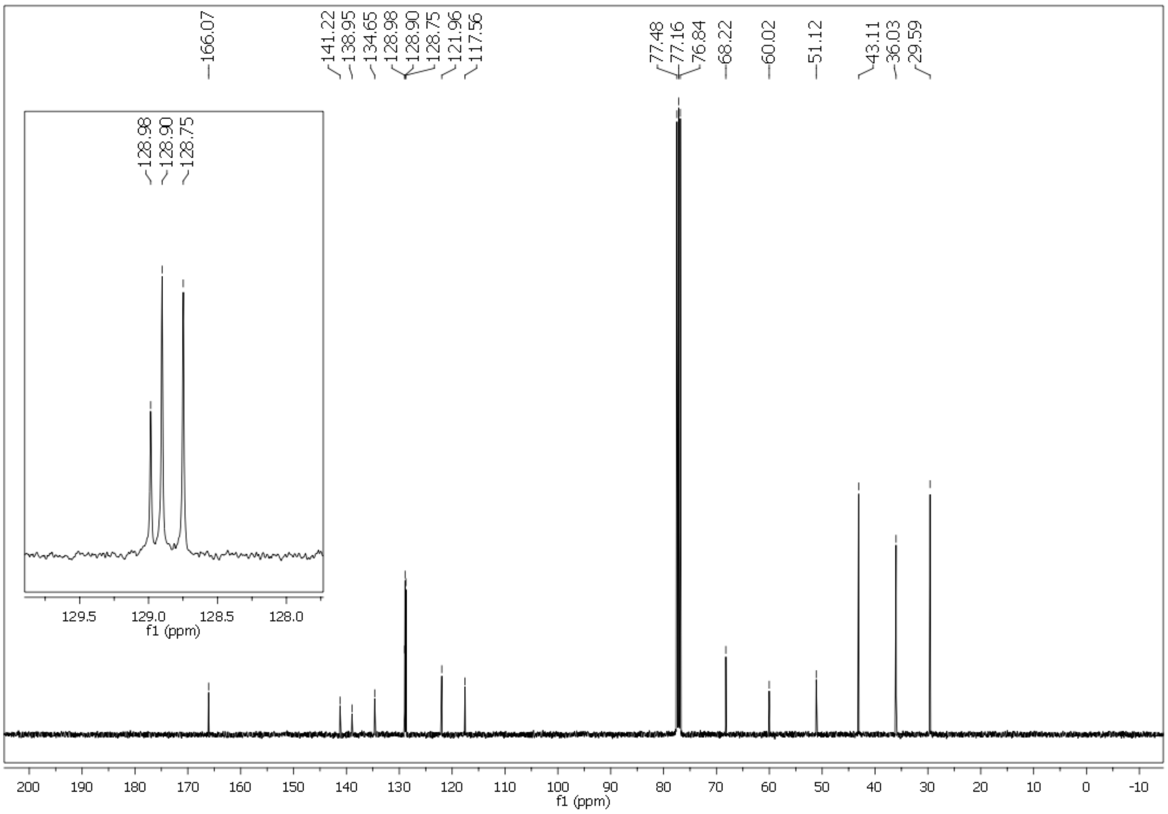
	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	6.630	15720	0.08	3218
2	PDA 254.0 nm	7.900	18909544	99.63	2137905
3	PDA 254.0 nm	9.729	36560	0.19	2602

	Processed Channel	Retention Time (min)	Area	% Area	Height
4	PDA 254.0 nm	10.918	17789	0.09	2388

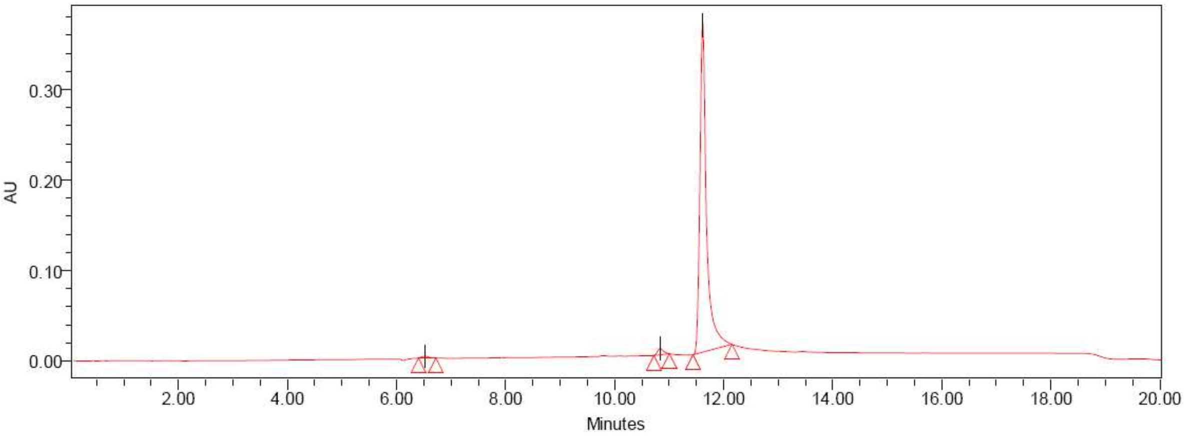


(**11g**)


8.16
8.14
7.37
7.37
7.37
7.36
7.26
5.25
5.25
2.29
1.82
1.58
5.25
5.25
5.28
5.26
5.24
5.22
f1 (ppm)
H₂O
0.87
0.97
4.63
4.00
9.06
6.14
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


166.07
141.22
138.95
134.65
128.98
128.90
128.75
121.96
117.56
77.48
77.16
76.84
68.22
60.02
51.12
43.11
36.03
29.59
128.98
128.90
128.75
129.5
129.0
128.5
128.0
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

Auto-Scaled Chromatogram



Processed Channel: PDA 254.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 254.0 nm	6.525	17756	0.56	2118
2	PDA 254.0 nm	10.837	51851	1.64	6758
3	PDA 254.0 nm	11.616	3082638	97.79	363765