Supporting information

Synthesis and cycloaddition reactions of strained alkynes derived from 2,2'-dihydroxy-1,1'-biaryls.

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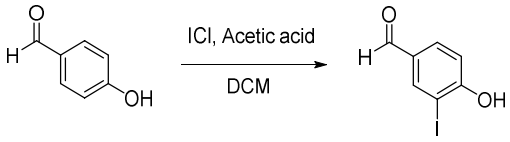
Contents:

Experimental data for compounds not listed in paper.

General experimental section.

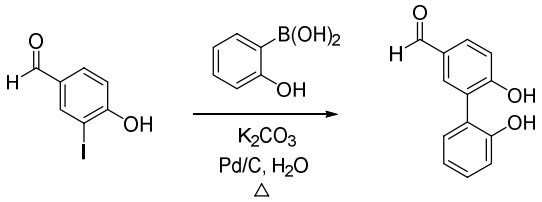
Solvents and reagents were degassed before use and all reactions were carried out under either a nitrogen atmosphere using vacuum line apparatus. Reactions were monitored by TLC using aluminium backed silica gel 60 (F254) plates, visualized using UV 254 nm and phosphomolybdic acid or potassium permanganate as appropriate. Flash column chromatography was carried out routinely on silica gel. Reagents were used as received from commercial sources unless otherwise stated. Dry solvents were purchased and used as received. ^{1}H NMR spectra were recorded on a Bruker DPX (300, 400 or 500 MHz) spectrometer. Chemical shifts are reported in δ units, parts per million relative to the singlet at 7.26 ppm for chloroform and 0.00 ppm for TMS. Coupling constants (*J*) are measured in Hertz. Mass spectra for analysis of synthetic products were recorded on a Bruker Esquire 2000 or a Bruker MicroTOF mass spectrometer. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR Golden Gate. Melting points were recorded on a Stuart Scientific SMP 1 instrument and are uncorrected. GPC was carried out on an Agilent 390LC MDS instrument equipped with differential refractive index (DRI), viscometry (VS) and dual angle light scatter (LS) detectors. The system was equipped with 2 x PLgel Mixed C columns (300 x 7.5 mm) and a PLgel 5 µm guard column. The eluent was $CHCl_3$ with 2 % TEA (triethylamine) additive. Samples were run at 1ml/min at 30'C and narrow Poly(methyl methacrylate) standards were used to create a third order calibration between 1,568,000 – 550 $gmol^{-1}$. Analyte samples were filtered through a GVHP membrane with 0.22 μm pore size before injection. Respectively, experimental molar mass and dispersity values of synthesized polymers were determined by conventional calibration using Agilent GPC/SEC software. TGA measurements were performed on Mettler-Toledo DSC1 equipped with an autosampler. Samples were heated in 40 ul aluminium pans from 25-600 ^{o}C at a rate of 10 ^{o}C min under a nitrogen atmosphere. Samples were analysed used Mettler-Toledo STARe software. X-ray crystallography was carried out on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector or an Xcalibur Gemini diffractometer with a Ruby CCD area detector.

3-Iodo-4-hydroxybenzaldehyde 7.



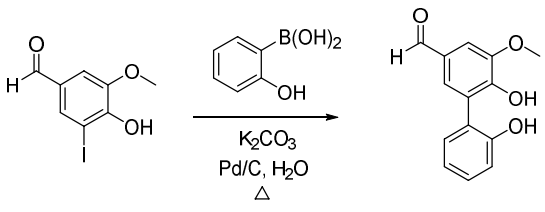
To a solution of 4-hydroxybenzaldehyde (1.22 g, 10 mmol, 1.0 eq.) in DCM (10 mL) was added to a solution of 1M iodine monochloride in DCM (21 mL, 21 mmol, 2.1 eq.) and acetic acid (1 mL) and left to stir for 2 days at rt. The solution was washed with $Na_2S_2O_3$ (3 x 35 mL) thoroughly and the solvent collected dried with Na_2SO_4 and the organics removed under vacuum to produce the product **7** as a white solid (1.95 g, 7.86 mmol, 79%). δ_H (300 MHz, $CDCl_3$) 9.79 (1 H, s, CHO), 8.22 (1 H, d, *J* 1.8, ArH), 7.79 (1 H, dd, *J* 8.4, 1.8, ArH), 7.11 (1 H, d, *J* 8.4, ArH), 6.37 (1 H, br. s, OH). The data matched that reported; R. S. Harapanhalli, L. W. McLaughlin, R. W. Howell, D. V. Rao, S. J. Adelstein and A. I. Kassis, *J. Med. Chem.* 1996, **39**, 4804-4809.

2',6-Dihydroxybiphenyl-3-carbaldehyde 11.



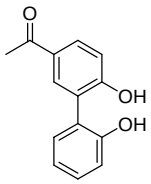
3-Iodo-4-hydroxybenzaldehyde **7** (0.49 g, 1.98 mmol, 1.0 eq.), 2-hydroxyphenyl boronic acid **10** (0.35 g, 2.57 mmol, 1.3 eq), potassium carbonate (1.09 g, 7.92 mmol, 4.0 eq.) and 10% Pd/C (39.0 mg, 2 mol%) were added together and water (20 mL) added and left to stir at 80 ^oC. After 3 hours the mixture cooled and carefully acidified with 1M HCl, which was then extracted with ethyl acetate (3 x 35 mL). The organic layer combined and dried with Na_2SO_4, filtered and concentrated under vacuum. The crude solid was purified by column chromatography (1:1 hexane : diethyl ether) to afford **11** as an off-white solid (0.27 g, 1.26 mmol, 64 %). δ_H (400 MHz, $CDCl_3$) 9.91 (1 H, s, CHO), 7.87 (1 H, dd, *J* 8.3, 2.0, 1H, ArH), 7.86 (1 H, d, *J* 2.0, ArH), 7.39-7.34 (1 H, m, ArH), 7.30 (1 H, dd, *J* 7.6, 1.4, ArH), 7.17 (1 H, d, *J* 8.3, ArH), 7.10 (1 H, td, *J* 7.6, 0.7, ArH), 7.04 (1 H, d, *J* 8.2, ArH), 6.63 (1 H, s, OH), 5.87 (1 H, s, OH). Data matched that reported; B. Schmidt. M. Riemer and M. Karras, *J. Org. Chem*. 2013, **78**, 8680-8688.

2',6-Dihydroxy-5-methoxybiphenyl-3-carbaldehyde 12.



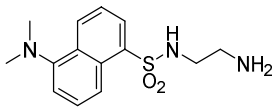
5-Iodovanillin **8** (2.50 g, 8.99 mmol, 1.0 eq.), 2-hydroxyphenyl boronic acid **10** (1.61 g, 11.7 mmol, 1.3 eq), potassium carbonate (4.97 g, 3.6 mmol, 4.0 eq.) and 10% Pd/C (0.18 g, 2 mol%) were added together, water (90 mL) was added and the reaction was stirred at 80 ºC. After 3 hours the mixture was cooled and carefully acidified with 1M HCl, then extracted with ethyl acetate (3 x 90 mL). The organic layers were combined and dried with Na_2SO_4, filtered and concentrated under vacuum. The crude solid was purified by column chromatography (1:1 hexane : diethyl ether) to afford **12** as an off-white solid (1.90 g, 7.78 mmol, 87 %). δ_H (300 MHz, $CDCl_3$) 9.89 (1 H, s, CHO), 7.50-7.47 (2 H, m, ArH), 7.35-7.30 (2 H, m, ArH), 7.10-7.04 (2 H, m, ArH), 6.77 (1 H, s, OH), 5.85 (1 H, s, OH), 4.05 (3 H, s, OCH_3). The data matched that reported; B. Schmidt. M. Riemer and M. Karras, *J. Org. Chem*. 2013, **78**, 8680-8688.

3-Acetyl-2',6-Dihydroxy-biphenyl 13.



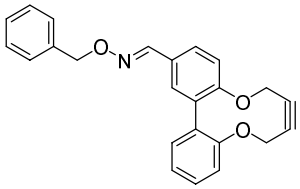
4-Hydroxy-3'-iodoacetophenone **9** (1.00 g, 3.82 mmol, 1.0 eq.), 2-hydroxyphenyl boronic acid **10** (646 mg, 5.08 mmol, 1.3 equiv), K_2CO_3 (2.1 g, 15.2 mmol), and 10 wt% Pd/C (80 mg, 2 mol %) were added to a RBF and suspended in water (40 mL). The mixture was immersed in an oil bath preheated at 80 °C and heated at reflux for 2.5 hrs. The mixture was cooled to rt then, dropwise, was acidified to pH 5 with addition of HCl (aq, 1.0 M) and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried with $MgSO_4$, filtered and solvent removed via rotary evaporation. The residue was purified by column chromatography on silica, using hexane/EtOAc mixtures of increasing polarity until an equal gradient was attained (hexane/EtOAc 1:1), to give compound **13** (685 mg, 3.0 mmol, 78 %) as a white solid. Mp 130 °C; δ_H (400 MHz, $CDCl_3$) 7.94 (2 H, brs, ArH), 7.35 (1 H, t, *J* 7.5, ArH), 7.30−7.26 (1 H, m, ArH), 7.10-7.03 (3 H, m, ArH), 6.38 (2 H, brs, OH), 2.58 (3 H, s, CH_3); *m/z* (ESI) 228.2 $[M]^+$, 251.2 ($[M+Na]^+$). The data matched that reported; J. P. Bachelet, P. Demerseman and R. Royer, *J. Heterocyclic Chem.* 1977, **14**, 1409-1411.

N-(2-Aminoethyl)-5-(dimethylamino)naphthalene-1-sulfonamide 34.



(5-(Dimethylamino)naphthalene-1-sulfonyl chloride (3.0 g, 11.1 mmol) was dissolved in 1,2-diaminoethane (50 mL) and stirred for 18 h at ambient temperature. The solvent was removed under reduced pressure, redissolved in EtOAc (20 mL) and washed with sat. $NaHCO_{3(aq)}$ (2 × 20 mL) and H_2O (20 mL). The organic layer was dried over $MgSO_4$. Purification by column chromatography (silica; MeOH/H_2O; 100:0→90:10) afforded the product **34** as a yellow solid (0.94 g, 3.20 mmol, 29%). δ_H (500 MHz, $CDCl_3$) 8.53 (1 H, d, *J* 8.6, ArH), 8.32 (1 H, d, *J* 8.6, ArH), 8.24 (1H, d, *J* 7.3, ArH), 7.54 (1H, t, *J* 8.0, ArH), 7.50 (1H, t, *J* 8.0, ArH), 7.16 (1H, d, *J* 7.5, ArH), 2.92 (2H, t, *J* 5.8, NCH_2), 2.88 (6H, s, $N(CH_3)_2$), 2.72 (2H, d, *J* 5.8, CH_2NH_2). δ_C (126 MHz, $CDCl_3$) 152.0, 134.8, 130.5, 130.0, 129.7, 129.6, 128.5, 123.3, 118.9, 45.5, 45.4, 41.0. The data matched that reported; R. C. Knighton, M. R. Sambrook, J. C. Vincent, S. A. Smith, C. J. Serpell, J. Cookson, M. S. Vickers and P. D. Beer, *Chem. Commun*. 2013, **49**, 2293-2295. .

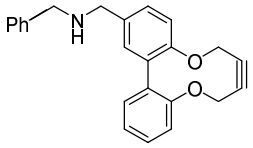
Oxime ether 29.



To a solution of aldehyde alkyne **15** (50 mg, 0.17 mmol, 1.0 eq) in MeOH (1 mL) was added NaOAc (35 mg, 0.43 mmol, 2.5 eq) and benzylhydroxylamine (32 mg, 0.2 mmol, 1.2 eq). The mixture was stirred at 45 ^oC overnight. The mixture was cooled to rt and the MeOH removed under vacuum. Saturated $NaHCO_3$ solution (20 mL) was added and the product extracted with DCM (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuum to give the crude product, which was purified by flash column chromatography (eluent = DCM) to give the product **29** as a thick colourless oil (45 mg, 0.11 mmol, 66 %). Rf = 0.70 (DCM); (Found(ESI)) $[M + Na]^+$ 392.1257 $C_{24}H_{19}NNaO_3$ requires 392.1257 (no molecular ion found by LRMS); ν_{max} 3028, 2962, 2916, 2864, 1497, 1475, 1452, 1346, 1194 and 970 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.15 (1 H, s, N=CH), 7.68 (1 H, dd, *J* 8.4, 1.9, ArH), 7.36 – 7.46 (6 H, m, ArH), 7.31 – 7.35 (1 H, m, ArH), 1.17 – 7.24 (4 H, m, ArH), 5.21 (2 H, s, PhCH_2O), 4.56 (2 H, d, *J* 16.2, 2 x C*H*H), 4.36 (2 H, d, *J* 12.5 , 2 x CH*H*)

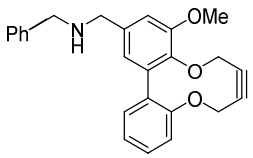
; δ_C (125 MHz, $CDCl_3$) 155.8, 154.4, 148.3, 137.5, 136.3, 135.3, 131.9, 131.2, 129.3, 128.4, 128.3, 128.3, 127.9, 127.4, 124.3, 123.1, 122.6, 86.9, 86.4, 76.4, 63.6 and 63.5.

Benzyl amine derivative 30.



Aldehyde **15** (100 mg, 0.378 mmol) and benzylamine (40 mg, 0.378 mmol) in EtOH (2 mL) were refluxed for 1 h. The mixture was cooled to 0 ^oC and $NaBH_4$ (35.7 mg, 0.945 mmol) was added. The reaction was stirred for 24 h and at the end of this time the solvent was removed under vacuum. DCM (10 mL) and water (10 mL) were added and the organic layer was separated. The water layer was extracted with further DCM (2 x 10 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and the solvent removed to leave 125 mg of crude product. The product was purified by flash chromatography (EtOAc:hexane 7:3, silica) to give the product **30** as a clear oil (60 mg, 0.169 mmol, 45%) (40 mg of impure product was also isolated). TLC EtOAc:hexane 7:3, silica, Rf 0.30; (Found (ESI+): $[M+H]^+$ 356.1648. $C_{24}H_{22}NO_2$ requires 356.1645); υ_{max} 2860, 1497, 1474, 1449, 1251, 1119, 968, 759, 731 cm^{-1}; δ_H (500 MHz, $CHCl_3$) 7.45-7.15 (12 H, m, ArH, 4.56 (2 H, d, *J* 14.0, OC*H*H), 4.36 (2 H, d, *J* 14.0, CH*H*), 3.86 (2 H, s, CH_3), 3.82 (2 H, s, CH_3), 1.75 (1 H, brs, NH); δ_C (125 MHz, $CDCl_3$) 154.5 (C), 153.4 (C), 140.3 (C), 138.8 (C), 136.1 (C), 132.7 (CH), 132.0 (CH), 131.8 (CH), 131.1 (CH), 128.9 (CH), 128.4 (CH), 127.0 (CH). 124.2 (CH), 122.6 (CH), 122.5 (CH), 86.8 (C), 86.7 (C), 62.55 (CH_2). 53.3 (CH_2), 52.7 (CH_2); *m/z* (ES-API+) 355.9 ($[M+H]^+$).

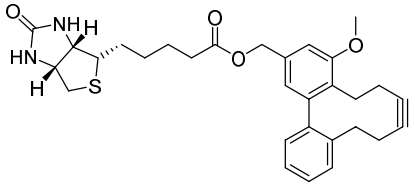
Benzyl amine derivative 31.



Aldehyde **16** (50 mg, 0.17 mmol) and benzylamine (18 mg, 0.17 mmol) in EtOH (1 mL) were refluxed for 1 h. The mixture was cooled to 0 ^oC and $NaBH_4$ (32 mg, 0.86 mmol) was added. The reaction was stirred for 24 h and at the end of this time the solvent was removed under vacuum. DCM (10 mL) and water (10 mL) were added and the organic layer was separated. The water layer was extracted with further DCM (2 x 10 mL) and the combined organic

extracts were dried ($MgSO_4$), filtered and the solvent removed to leave 64 mg of crude product. The product was purified by flash chromatography (EtOAc:hexane 7:3, silica) to give the product **31** as a clear oil (53 mg, 0.138 mmol, 81%). TLC EtOAc:hexane 7:3, silica, Rf 0.3; (Found (ESI+): $[M+H]^+$ 386.1751. $C_{25}H_{24}NO_3$ requires 386.1751); υ_{max} 2926, 2836, 1584, 1450, 1194, 1134, 906, 730, 698 cm^{-1}; δ_H (500 MHz, $CHCl_3$) 7.40-7.15 (9 H, m, ArH), 7.03 (1 H, s, ArH), 6.77 (1 H, s, ArH), 4.65 (1 H, d, *J* 15.0, OCH), 4.58 (1 H, d, *J* 16.0, OCH), 4.40 (1 H, d, *J* 16.0, OCH), 4.37 (1 H, d, *J* 15.0, OCH), 3.95 (3 H, s, OCH_3), 3.86 (2 H, s, CH_2), 3.83 (2 H, s, CH_2) 1.90 (1 H, brs, NH); δ_C (125 MHz, $CDCl_3$) 154.6 (C), 154.4 (C), 153.1 (C), 146.4 (C), 141.3 (C), 132.9 (CH), 128.8 (CH), 128.3 (CH), 128.0 (CH), 127.3 (CH). 125.5 (CH), 124.4 (CH), 124.2 (CH), 111.4 (CH), 87.6 (C), 86.1 (C), 63.6 (CH_2), 60.3 (CH_2), 60.3 (CH_3), 53.5 (CH_2), 53.3 (CH_2). *m/z* (ES-API+) 386.0 ($[M+H]^+$). The cyclisation reaction of **32** with benzyl azide **20** was followed over time and full details are given in the Supporting Information.

Biotin functionalised alkyne 41.

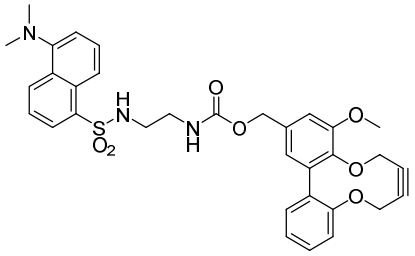


To a solution of alcohol **19** (50 mg, 0.17 mmol, 1.2 eq) in DCM (5 mL), EDC.HCl (32.6 mg, 0.17 mmol, 1.2 eq), biotin (35 mg, 0.14 mmol, 1.0 eq) and DMAP (1 mg, catalytic, 0.01 eq) were added and stirred at rt for 3 days. After this time the reaction was diluted with DCM (20 mL) and washed with water (3 x 20 mL). The organic layer was then dried over $MgSO_4$ and concentrated under vacuum. The crude product was then purified by flash column chromatography (eluent gradient of EtOAc – Pet. Ether 8:2 to EtOAc – MeOH 9:1) to give the pure product **41** as a white solid (31.6 mg, 0.06 mmol, 43 %).

Rf = 0.35 (EtOAc – MeOH 95:5), (Found(ESI)) $[M + Na]^+$ 545.1718. $C_{28}H_{30}N_2NaO_6S$ requires 545.1717); ν_{max} 3243, 3013, 2927, 2862, 1698, 1494, 1337, 1135, 966 and 746 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.35 – 7.41 (1 H, m, ArH), 7.15 – 7.21 (3 H, m, ArH), 6.95 (1 H, s, ArH), 6.79 (1 H, s, ArH), 5.77 (1 H, brs, NH), 5.21 (1 H, brs, NH), 5.09 (2 H, s, C*H*$_2$OCO), 4.61 (1 H, d, *J* 15.3, C*H*H), 4.55 (1 H, d, *J* 15.5, C*H*H), 4.44 – 4.49 (1 H, m, NHC*H*), 4.41 (1 H, d, *J* 15.5, CH*H*), 4.35 (1 H, d, *J* 15.3, CH*H*), 4.25 – 4.30 (1 H, m, NHC*H*), 3.93 (3 H, s, OCH_3), 3.09 – 3.15 (1 H, m, SC*H*), 2.88 (1 H, dd, *J* 4.9, 12.8, SC*H*H), 2.69 (1 H, d, *J* 12.8, SCH*H*), 2.40 (2 H, t, *J* 7.5, CH_2), 1.60 – 1.76 (4 H, m, 2 x), 1.36 – 1.52 (2H, m, CH_2); δ_c

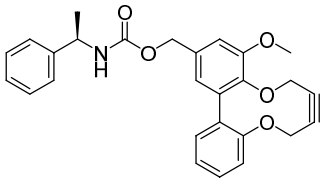
(125 MHz, $CDCl_3$) 173.4, 163.4, 154.3, 153.2, 142.32, 137.1, 135.6, 131.9, 131.9, 129.2, 124.2, 123.8, 122.5, 111.1, 87.4, 86.2, 66.1, 63.6, 61.7, 60.3, 60.0, 55.8, 55.3, 40.5, 33.8, 28.2, 28.1 and 24.7; *m/z* (ESI) 545 ($[M+Na]^+$).

Dansyl carbamate derivative 42.



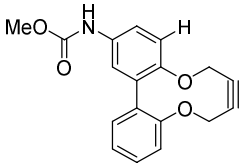
To a solution of **19** (50 mg, 0.17 mmol, 1.0 eq) in MeCN (0.5 mL) was added TEA (68.5 mg, 0.68 mmol, 4.0 eq) and DSC (65 mg, 0.25 mmol, 1.5 eq) and the reaction was stirred for 3 h at rt. The MeCN was removed under vacuum and the resulting residue dissolved in DMF (0.2 mL). The solution was then added to a separate solution of DIPEA (54.8 mg, 0.07 mL, 0.43 mmol, 2.5 eq)) and dansyl amine (100 mg, 0.34 mmol, 2 eq) in DMF (0.5 mL) and the reaction stirred overnight. The mixture was diluted with DCM (20 mL), washed with water (3 x 20 mL) and dried over $MgSO_4$ before being concentrated under vacuum to give the crude product. The product was then purified by flash column chromatography to give the pure product **42** as a thick light green oil (55.6 mg, 0.090 mmol, 53 %). Rf = 0.3 (DCM – EtOAc 9:1) (Found(ESI)) $[M + Na]^+$ 638.1931. $C_{33}H_{33}N_3NaO_7S$ requires 638.1931); υ_{max} 3301, 2927, 2868, 2789, 1699, 1453, 1136 and 788 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.53 (1 H, d, *J* 8.5, ArH) 8.19 – 8.27 (2 H, m, ArH), 7.50 (1 H, t, *J* 7.9, ArH), 7.36 – 7.42 (1 H, m, ArH), 7.13 – 7.22 (4 H, m, ArH), 6.91 (1 H, s, ArH), 6.74 (1 H, s, ArH), 5.26 – 5.31 (1 H, brs, NH), 5.02 (2 H, s, $PhCH_2O$) 4.84 – 4.93 (1 H, brs, NH), 4.60 (1 H, d, *J* 15.4, CH*H*), 4.55 (1 H, d, *J* 15.6, CH*H*), 4.40 (1 H, d, *J* 15.6, C*H*H), 4.34 (1 H, d, *J* 15.3, CH*H*), 3.91 (3 H, s, OCH_3), 3.12 - 3.27 (2 H, m, $NHCH_2$), 2.98 – 3.09 (2 H, m, $NHCH_2$), 2.87 (6 H, s, $N(CH_3)_2$); δ_C (125 MHz, $CDCl_3$) 156.7, 154.3, 153.3, 152.1, 142.2, 137.04, 135.7, 134.5, 132.4, 132.0, 130.7, 129.9, 129.7, 129.5, 129.2, 128.5, 124.3, 123.3, 122.6, 118.5, 115.3, 110.8, 87.5, 86.2, 66.6, 63.7, 60.4, 55.9, 45.4, 43.4 and 40.8; *m/z* (ESI) 638 ($[M+Na]^+$). Fluorescence (MeCN; λ_{ex} = 259 nm); λ_{em} = 519 nm; UV-Vis (MeCN) λ_{max} (ε/M^{-1} cm^{-1}): 342 (3057) nm.

Carbamate alkyne 43.



Alkyne methoxy alcohol **19** (60 mg, 0.202 mmol) and DMAP (one crystal, catalytic) were dissolved in CH_2Cl_2 (2 mL). (*R*)-(1-isocyanatoethyl)benzene (34 µL, 0.242 mmol) was added and the reaction was stirred under N_2 at rt for 18 hours. The solvent was removed in vacuo and the crude mixture was purified by column chromatography (SiO_2; EtOAc/Hex; 20:80→50:50) to afford product **43** as a white solid (79 mg, 0.18 mmol, 89%). Mp 82-84 °C; (found (ESI) [M + Na]$^+$, 466.1630. $C_{27}H_{25}NNaO_5$ requires 466.1625). ν_{max} 3324, 2968, 3934, 1701, 1450, 1135, 964 and 699 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.40 – 7.35 (1 H, m, ArH), 7.31 (3 H, brs, ArH), 7.25 (2 H, brs, ArH), 7.22 – 7.11 (4 H, m, ArH), 6.93 (1 H, s, ArH), 6.79 (1 H, s, ArH), 5.12 – 5.01 (2 H, m, $ArCH_2O$), 4.91 – 4.81 (1 H, m, Ar*C*HCH_3), 4.71 – 4.50 (2 H, m, OCH_2), 4.44 – 4.27 (2 H, m, OCH_2), 3.89 (3 H, s, OCH_3), 1.48 (3 H, d, *J* 6.9, ArCHC*H*$_3$). δ_C (126 MHz, $CDCl_3$) 154.5, 153.3, 137.1, 135.8, 132.6, 132.2, 129.3, 128.8, 127.5, 126.1, 124.3, 123.7, 122.6, 111.1, 87.6, 86.3, 66.7, 63.7, 60.5, 55.9, 50.9, 22.6; *m*/*z* (ESI) 466 ([M+Na]$^+$, 100%) and 482 ([M+K]$^+$ 40).

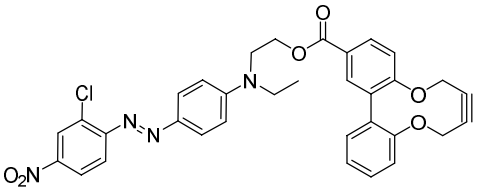
Carbamate 44.



To a solution of acid **5** (74 mg, 0.264 mmol) in DCM (4 mL) at 0 ^{o}C was added trimethylamine (0.029 mL, 0.28 mmol). A solution of diphenylphosphoryl azide (95 mg, 0.074 mL) in DCM (4 mL) was then added dropwise over 30 min. The reaction was stirred at 0 ^{o}C for 5 h then the solvent was evaporated, methanol (5 mL) was added and the reaction was heated overnight at 65 ^{o}C. At the end of this time, the solvent was removed and the product was purified by chromatography on silica get (hexane:EtOAc 8:2) to give the crude product as a white solid (30 mg). TLC showed the presence of a side product at similar Rf therefore the product was washed with hexane (10 x 2 mL) to leave the product **44** as a white solid (25 mg, 0.0809 mmol, 31%). TLC hexane: EtOAc 1:1, silica, Rf 0.75; M.p. 119-121 ^{o}C; (Found (ESI+): [M+Na] $^+$ 332.0888. $C_{18}H_{15}NNaO_4$ requires 332.0893); υ_{max} 3301, 1731, 1614, 1536, 1503, 1476, 1227, 1187, 941, 700, 518 cm^{-1}; δ_H (500 MHz, $CHCl_3$) 7.62 (1 H,

brs, ArH), 7.40-7.34 (1 H, m, ArH), 7.22-7.10 (4 H, m, ArH), 7.03 (1 H, d, *J* 2.0, ArH), 6.62 (1 H, brs, NH), 4.61-4.52 (2 H, m, OCH), 4.38-4.30 (2 H, m, OCH), 3.76 (3 H, s, CH_3); δ_C (125 MHz, $CDCl_3$) 154.3 (C), 150.3 (C), 136.3 (C), 135.5 (C), 133.8 (C), 131.9 (CH), 129.3 (CH), 125.4 (CH), 124.3 (CH), 122.6 (CH), 86.7 (C), 86.6 (C), 63.6 (CH_2), 63.5 (CH_2), 52.4 (CH_3); *m/z* (ES-API+) 331.8 ($[M+Na]^+$).

Ester linked to disperse red 45.

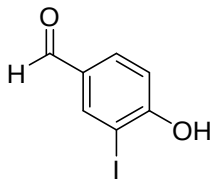


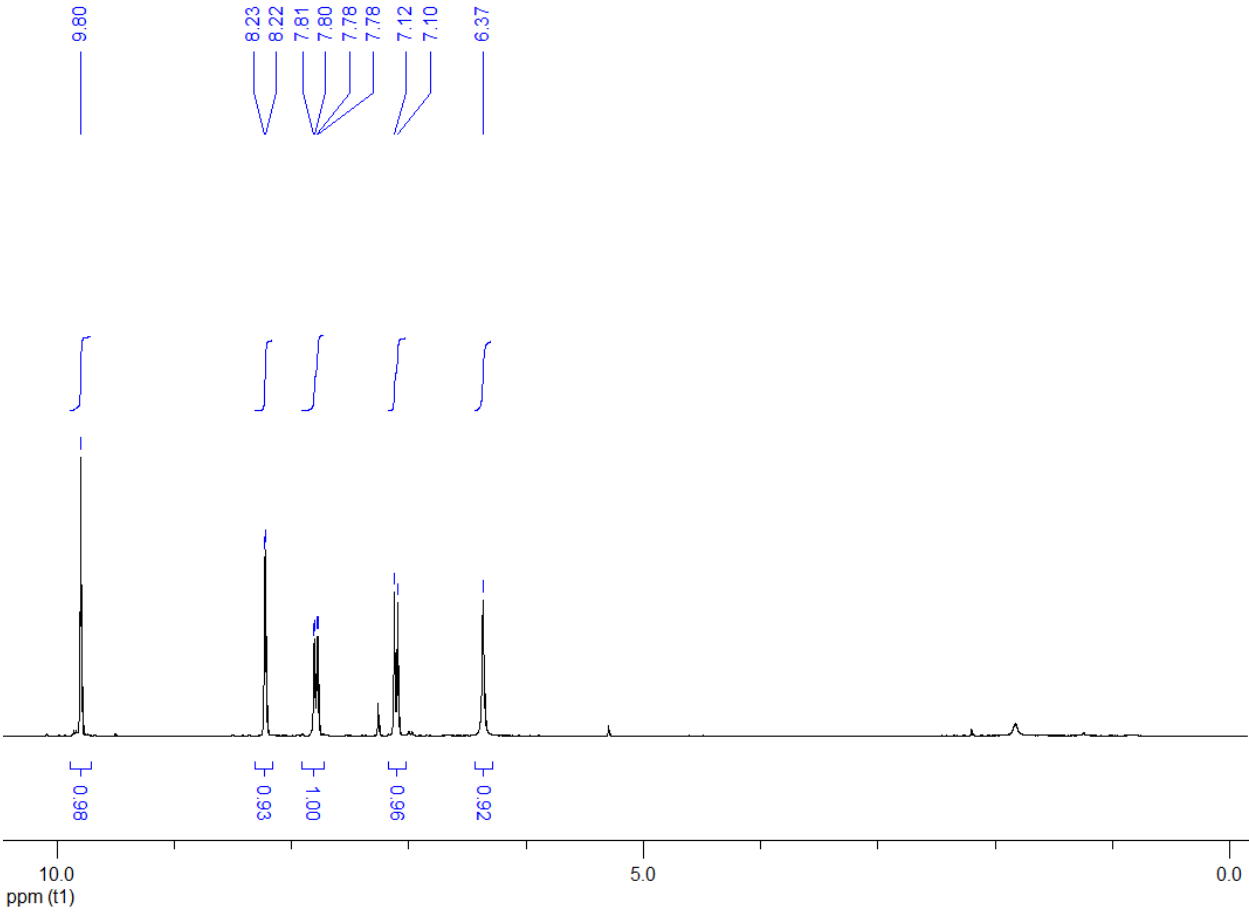
A solution of acid **5** (45 mg, 0.161 mmol), disperse red 13 (67 mg, 0.193 mmol), DMAP (1 mg) and EDC.HCl (37 mg, 0.193 mmol) in DCM (5.0 mL) was stirred at rt overnight. At the end of this time, EtOAc (20 mL) was added and the solution was washed with water (3 x 20 mL). The organic phase was dried with Na_2SO_4, filtered and the solvent removed under vacuum to give the crude product. Product **45** was purified by chromatography on silica gel (100% DCM) and was isolated as a red solid (60 mg, 0.098 mmol, 61%). TLC DCM, silica, Rf 0.60; M.p. 120-123 ^oC; (Found (ESI+): $[M+H]^+$ 611.1687. $C_{33}H_{28}{}^{35}ClN_4NaO_6$ requires 611.1692); υ_{max} 2971, 1713, 1597, 1513, 1332, 1227, 1137, 665 cm^{-1}; δ_H (500 MHz, $CHCl_3$) 8.28 (1 H, brs, ArH), 8.07 (1 H, dd, *J* 7.0, 2.0, ArH), 7.45 (1 H, dd, *J* 8.0, 2.0, ArH), 7.85-7.81 (3 H, m, ArH), 7.69 (1 H, d, *J* 8.0, ArH), 7.32-7.28 (1 H, m, ArH), 7.15-7.05 (4 H,m, ArH), 6.77 (2 H, d, *J* 10.0, ArH), 4.55-4.45 (4 H, m, OCH_2), 4.30-4.20 (2 H, m, OCH_2), 3.73 (2 H, t, *J* 6.5, NCH_2), 3.52 (2 H, q, *J* 6.5, C*H*$_2$$CH_3$), 1.15 (3 H, t, *J* 7.0, CH_3); δ_C (125 MHz, $CDCl_3$) 170.9 (C), 158.9 (C), 154.5 (C), 153.1 (C), 151.8 (C), 147.2 (C), 144.5 (C), 136.3 (C), 134.8 (C), 133.9 (C), 133.0 (CH), 131.7 (CH), 130.8 (CH), 129.4 (CH), 127.0 (CH), 126.0 (CH), 125.6 (C), 124.3 (CH), 122.7 (CH), 122.6 (CH), 118.0 (CH), 111.6 (CH), 87.3 (C), 86.1 (C), 63.8 (CH_2), 63.4 (CH_2), 61.8 (CH_2), 48.9 (CH_2), 45.8 (CH_2), 12.4 (CH_3); *m/z* (ES-API+) 611.0 ($[M+H]^+$).

NMR and fluorescence Spectra and X-ray crystallographic data.

3-Iodo-4-Hydroxybenzaldehyde 7.

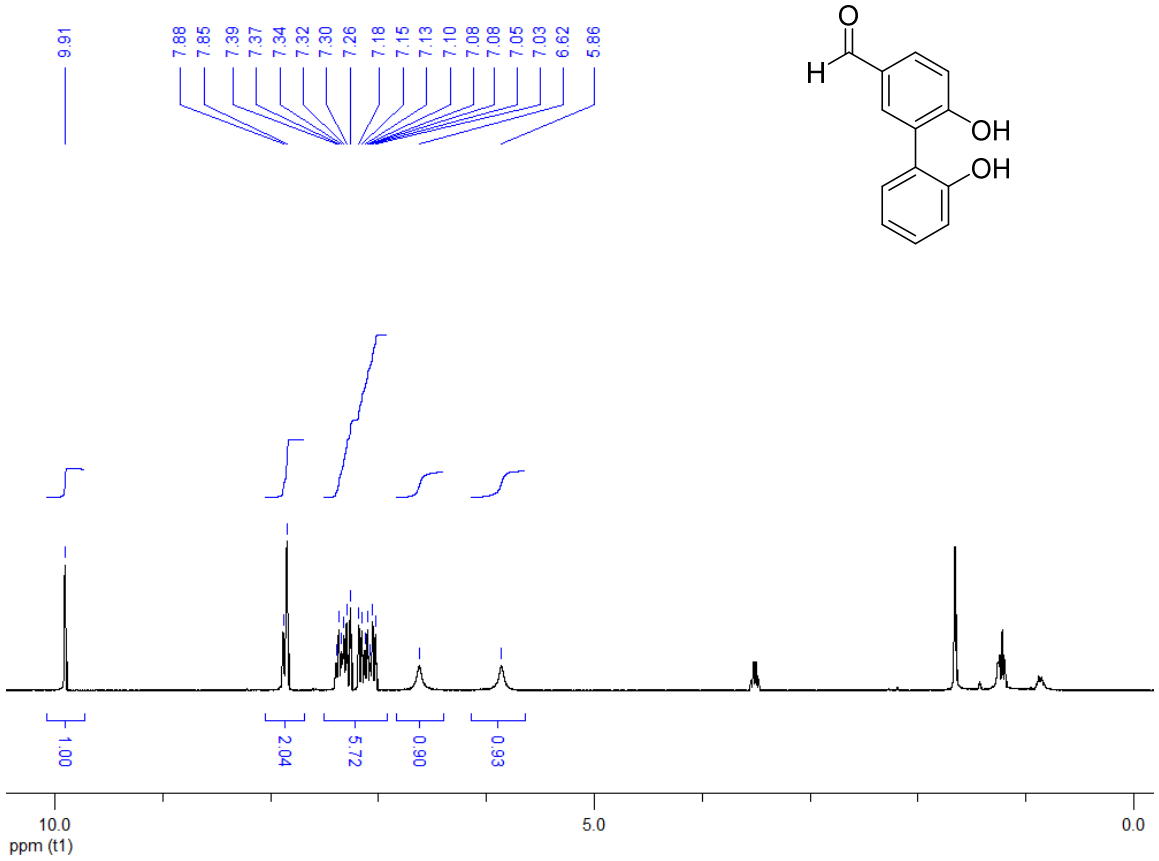
δ_H (300 MHz, $CDCl_3$).





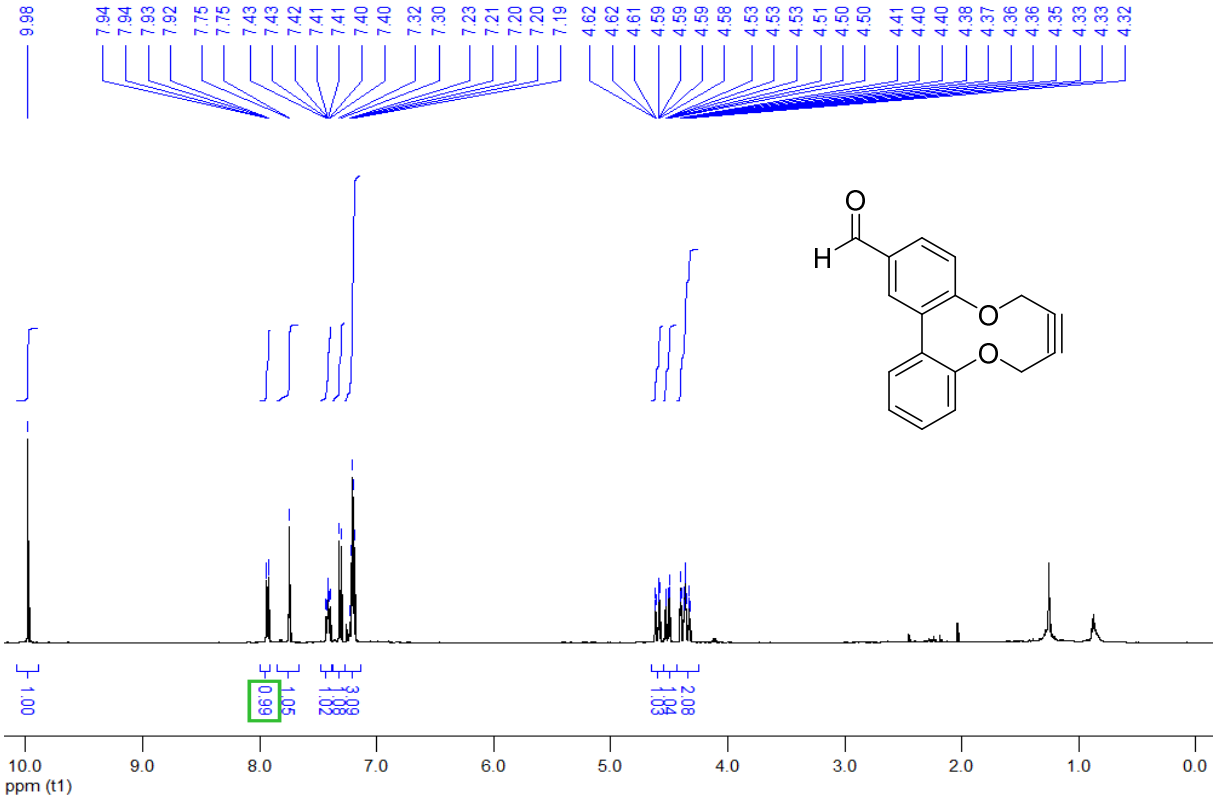
2',6-Dihydroxybiphenyl-3-carbaldehyde 11.

δ_H (300 MHz, $CDCl_3$)

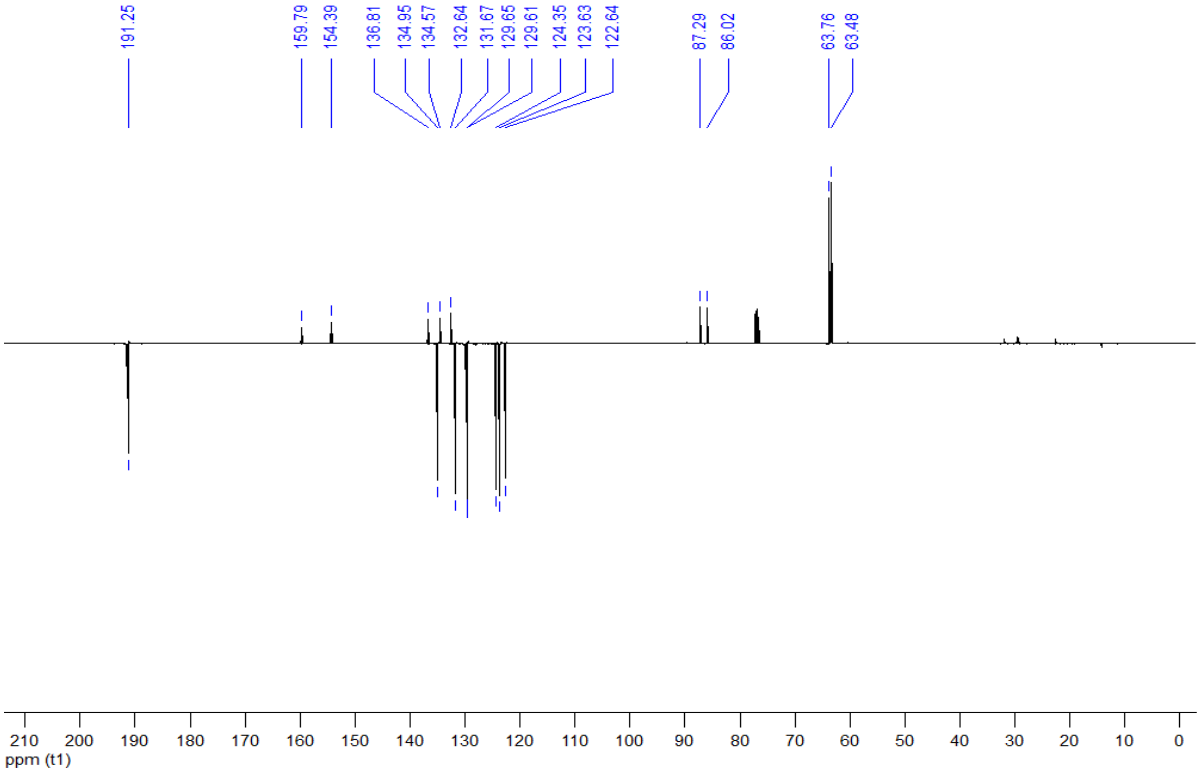


Alkyne 15

δ_H (500 MHz, $CDCl_3$)

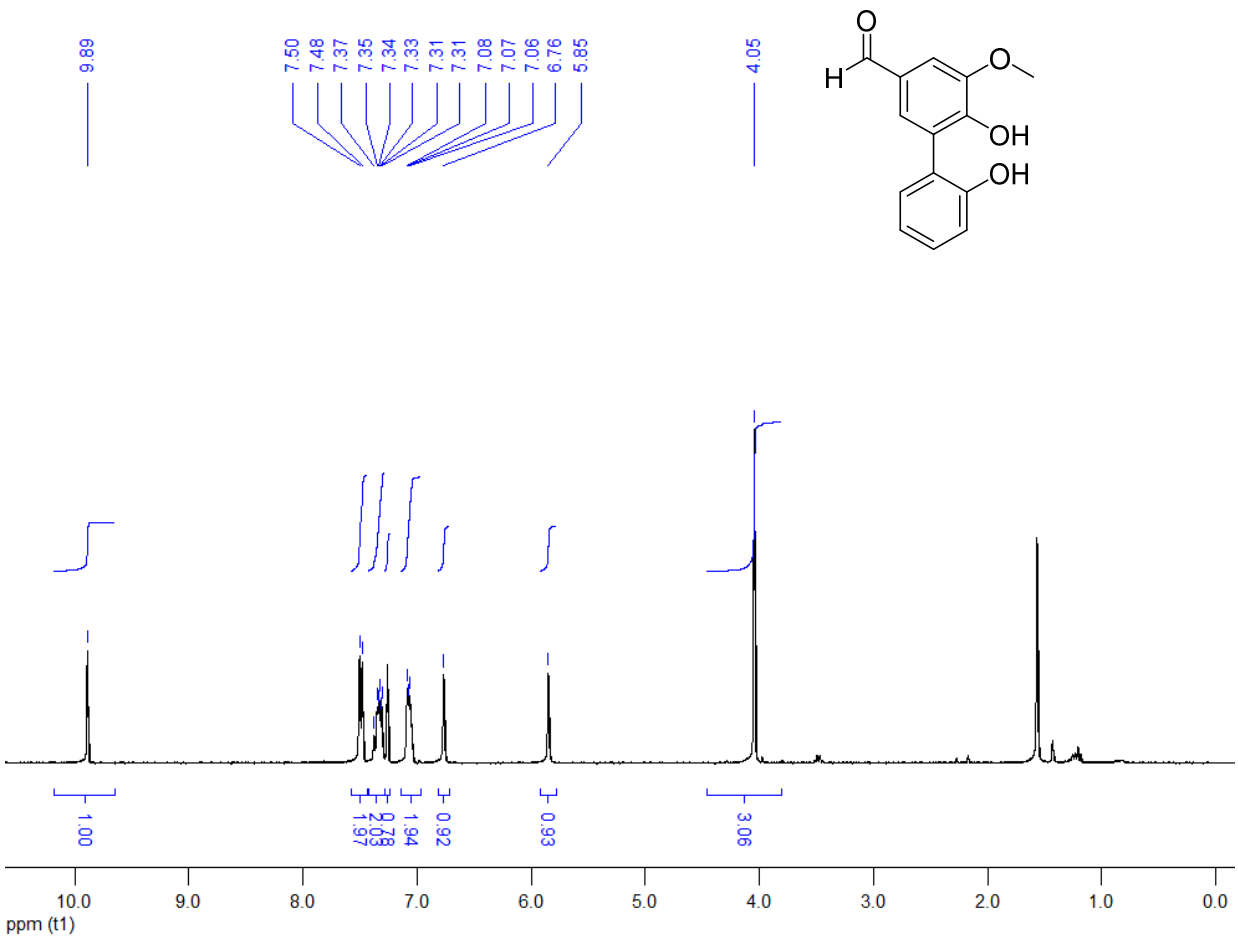


δ_C (126 MHz, $CDCl_3$)



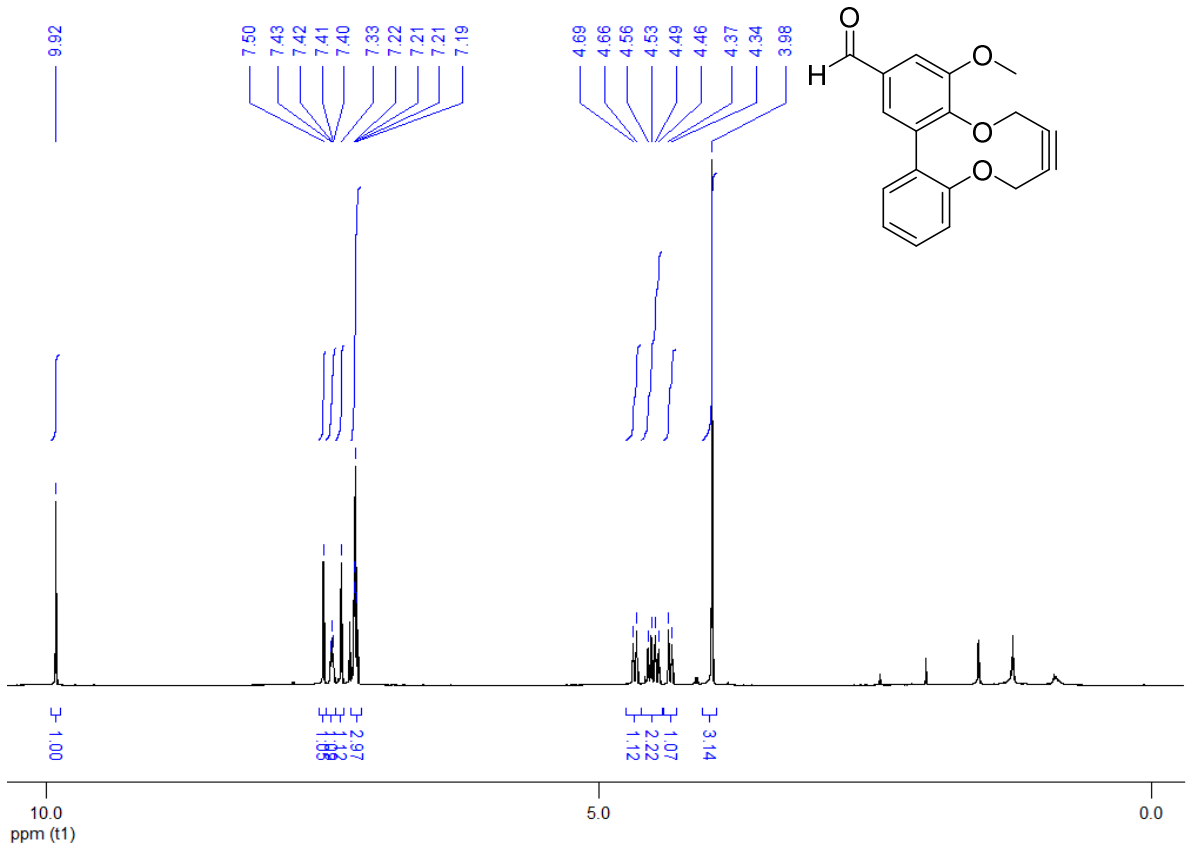
2',6-Dihydroxy-5-methoxybiphenyl-3-carbaldehyde 12.

δ_H (300 MHz, $CDCl_3$)

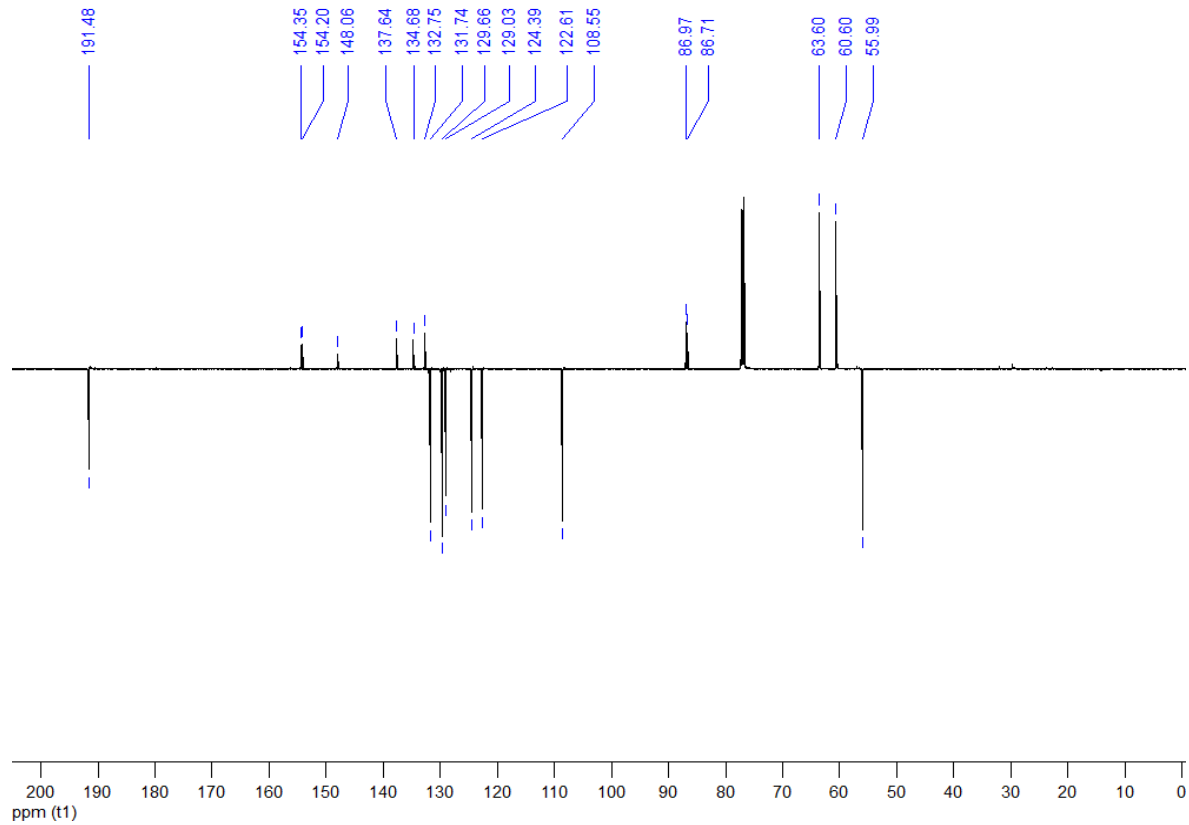


Alkyne 16

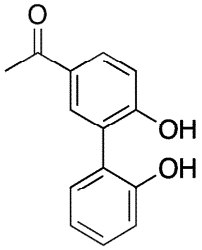
δ_H (500 MHz, $CDCl_3$)



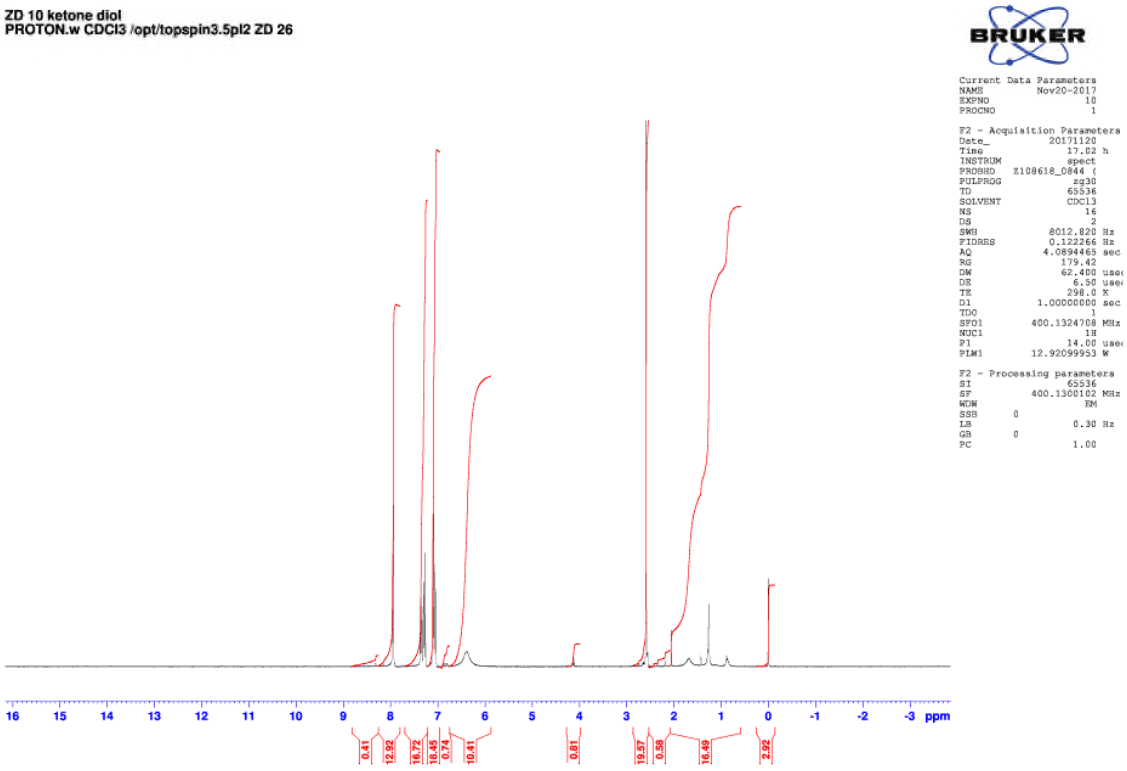
δ_C (126 MHz, $CDCl_3$)



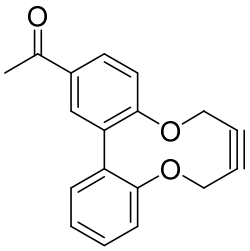
Diol 13. (ZD10).



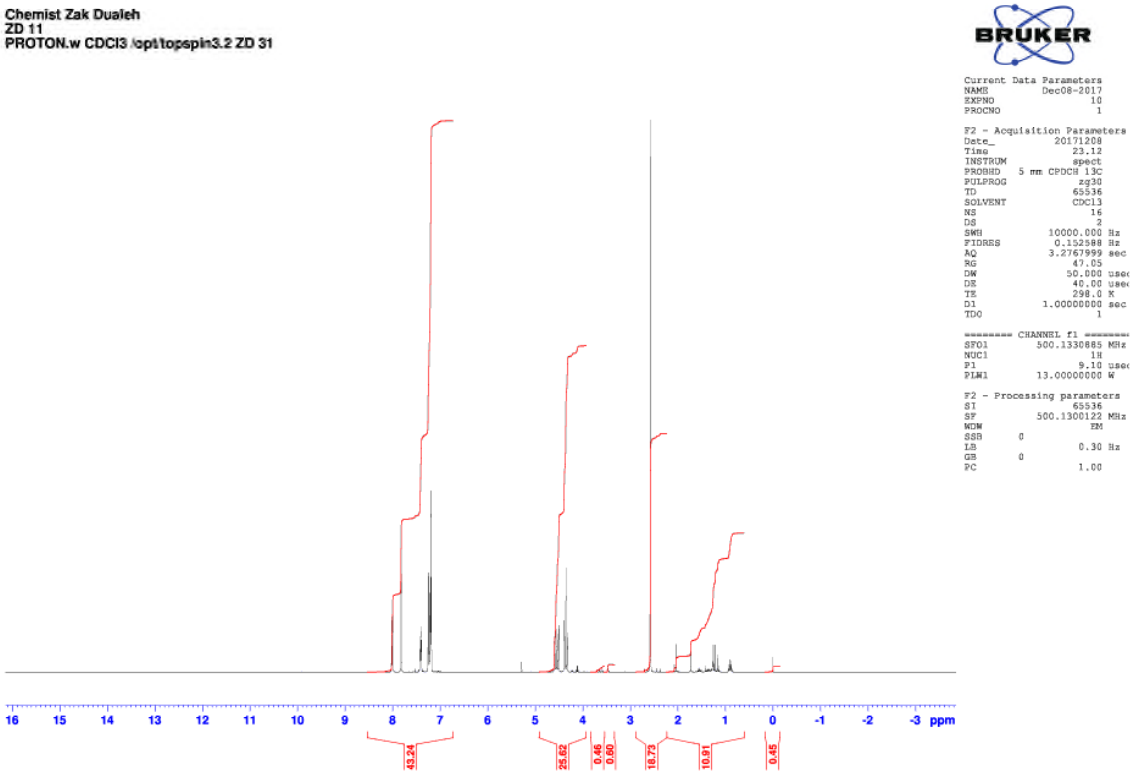
δ_H (400 MHz, $CDCl_3$).



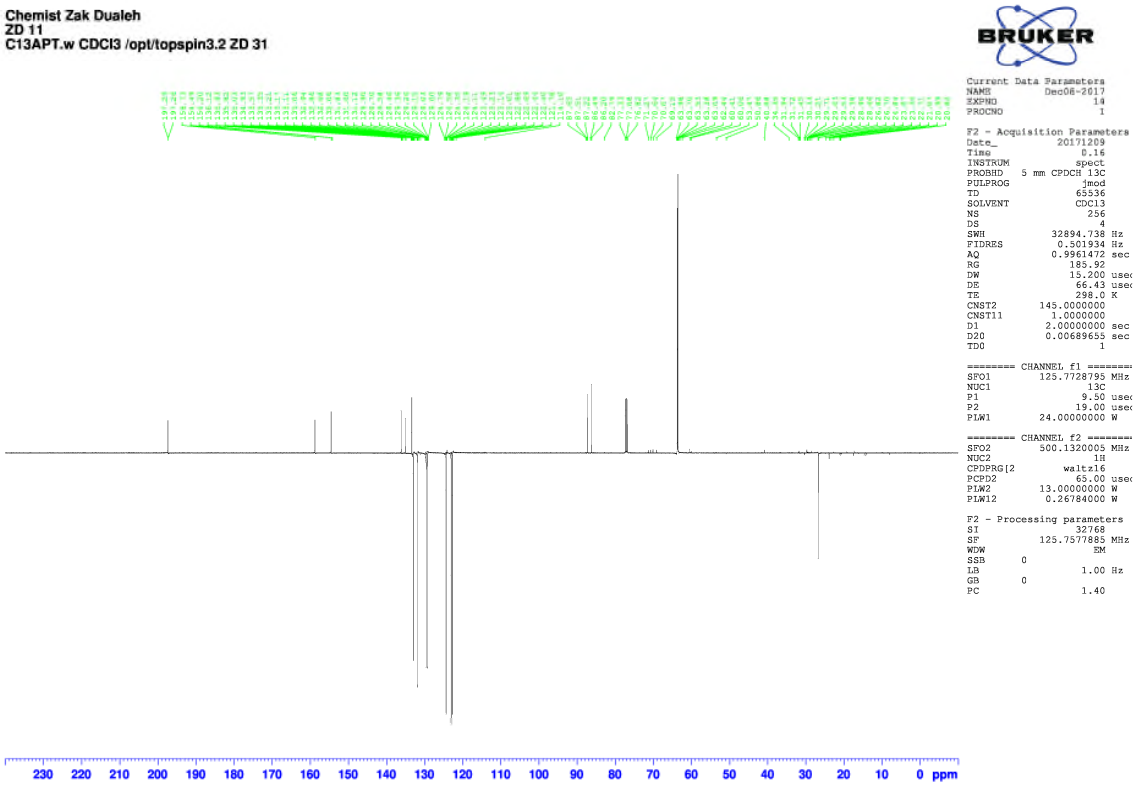
Strained alkyne 17. ZD11.



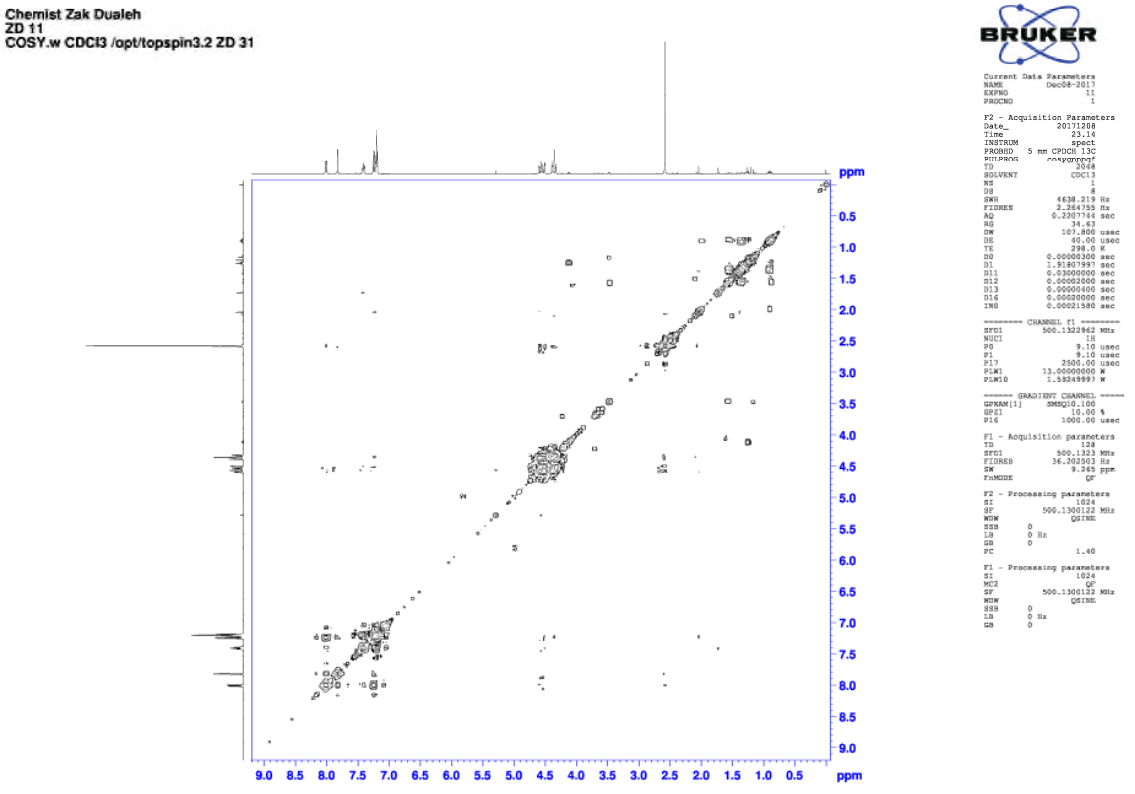
δ_H (500 MHz, $CDCl_3$).



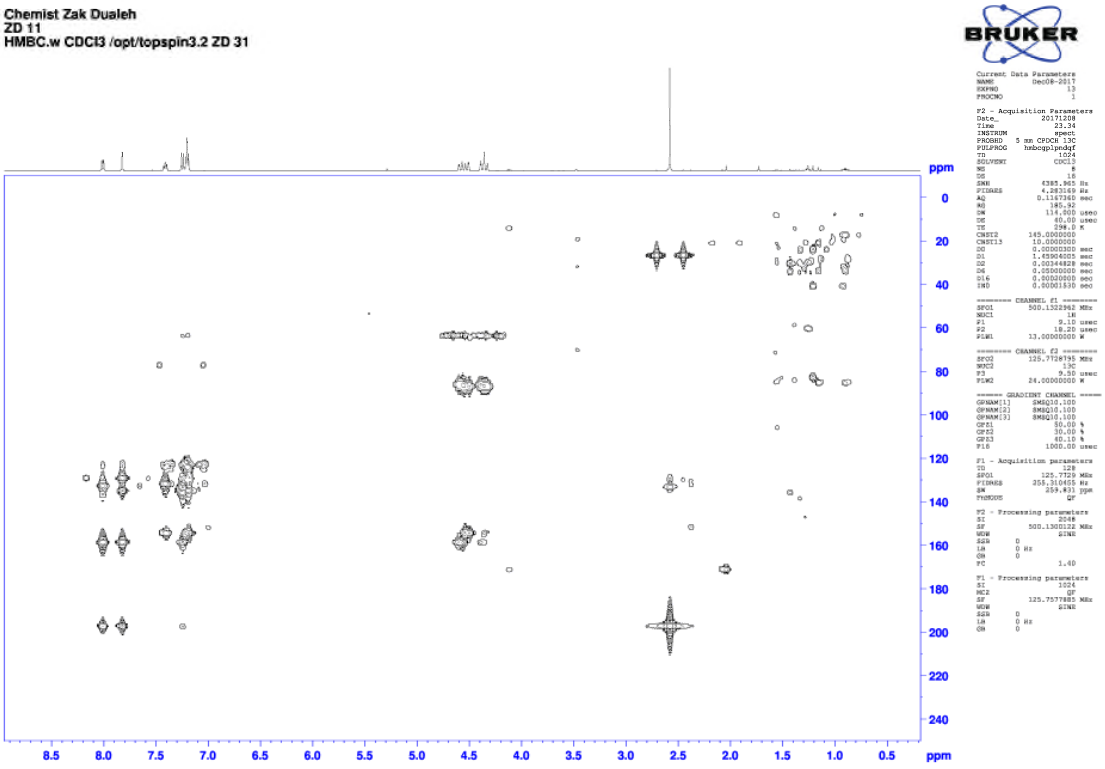
δ_C (126 MHz, $CDCl_3$).



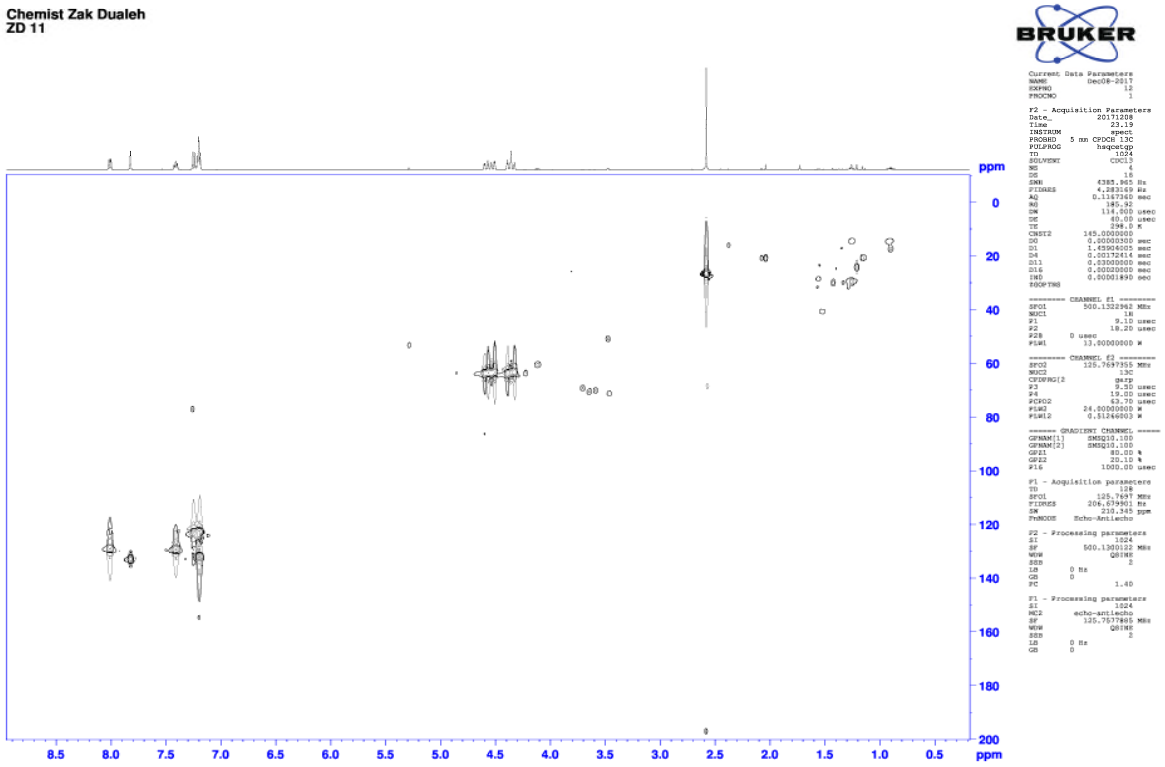
COSY:



HMBC:


Chemist Zak Dualeh
ZD 11
HMBC.w CDCl3 /opt/topspin3.2 ZD 31
BRUKER
ppm
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 ppm
0 20 40 60 80 100 120 140 160 180 200 220 240

HSQC:


Chemist Zak Dualeh
ZD 11
BRUKER
ppm
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 ppm
0 20 40 60 80 100 120 140 160 180 200

Single crystal X-ray crystallographic structure of 16

CCDC 1852221.

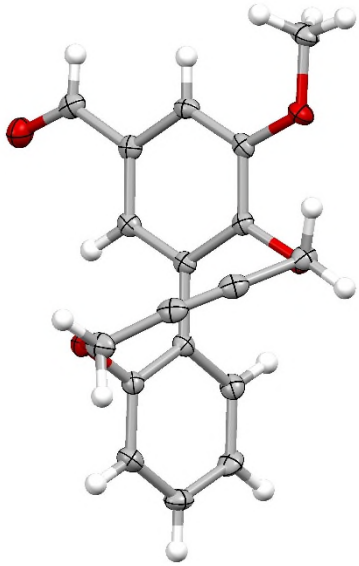


Figure 1: Single crystal X-ray structure of **16** (ellipsoids are plotted at the 50% probability level)

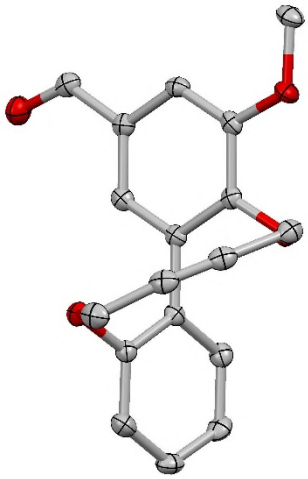


Figure 2: Single crystal X-ray structure of **16** (ellipsoids are plotted at the 50% probability level)

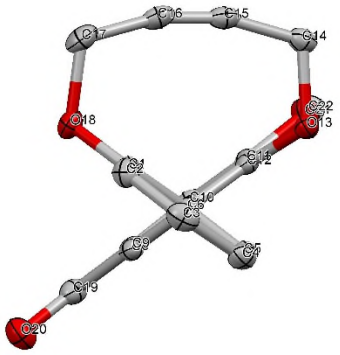


Figure 3: Single crystal X-ray structure of **16** (ellipsoids are plotted at the 50% probability level, hydrogen atoms are omitted for clarity)

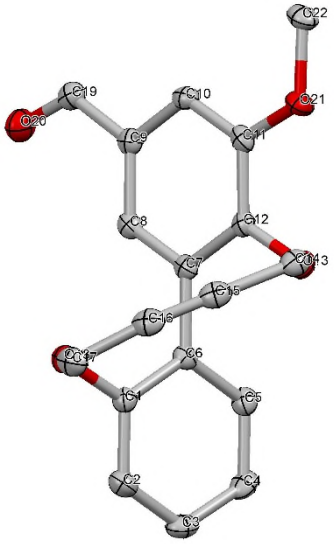


Figure 4: Single crystal X-ray structure of **16** (ellipsoids are plotted at the 50% probability level, hydrogen atoms are omitted for clarity)

CCDC 1852221 contains the supplementary crystallographic data for this paper. These can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Single crystals of **16** were grown from vapour diffusion of *n*-hexane into a chloroform solution of the compound over several days. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector at 150(2) K. The structure was solved using Olex2[1] and the ShelXT[2] structure solution program using Direct Methods and refined with the ShelXL[3] refinement package using Least Squares refinement.

The asymmetric unit contains one crystallographically distinct molecule, with Z = 4. The crystal packing indicates aromatic donor-acceptor (π-π) interactions of the biphenyl moieties of adjacent molecules. The alkyne group displays significant deviation from linearity, the C14-C15-C16 and C15-C16-C17 bond angles are 165.23(13)° and 165.32(13)° respectively. This is accompanied by a large biphenyl torsion angle (C5-C6-C7-C8) of 72.24(15)°.

Table 1: Single-crystal X-ray data for compound **16.**

Compound Reference	**Compound 16**
Chemical Formula	$C_{18}H_{14}O_4$
Formula Mass	294.29
Crystal system	Monoclinic
a/ Å	10.80656(8)
b/ Å	17.94783(10)
c/ Å	7.75427(6)
α/ °	90
β/ °	110.5855(8)
γ/ °	90
Unit cell volume/ Å	1407.942(18)
Temperature/ K	150(2) K
Space group	*-P 2ybc*
Crystal size/ mm	0.12 × 0.40 × 0.40
Radiation	Cu K\a
Goodness-of-fit on F^2	1.052
No. of formula units per unit cell, Z	4
No. of reflections measured	27406
No. of independent reflections	2829
Final R_1 vaules ($I > 2\sigma(I)$)	0.0451
Final *wR*(F^2) values ($I > 2\sigma(I)$)	0.1206
Final R_1 values (all data)	0.0459
Final *wR*(F^2) (all data)	0.1219

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8

X-ray crystallographic structure of ketone 17.

CCDC 1852222

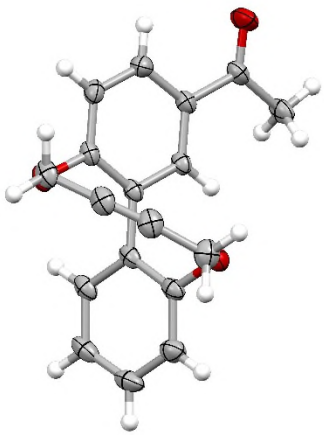


Figure 1: Single crystal X-ray structure of **17** (ellipsoids are plotted at the 50% probability level)

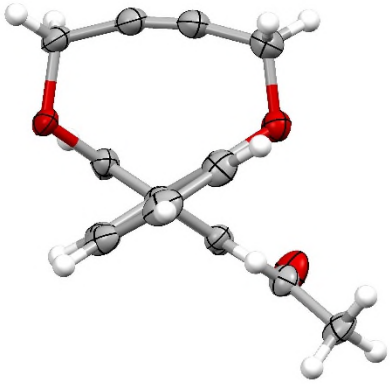


Figure 2: Single crystal X-ray structure of **17** (ellipsoids are plotted at the 50% probability level)

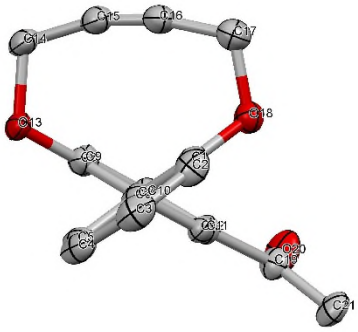


Figure 3: Single crystal X-ray structure of **17** (hydrogen atoms are omitted for clarity; ellipsoids are plotted at the 50% probability level)

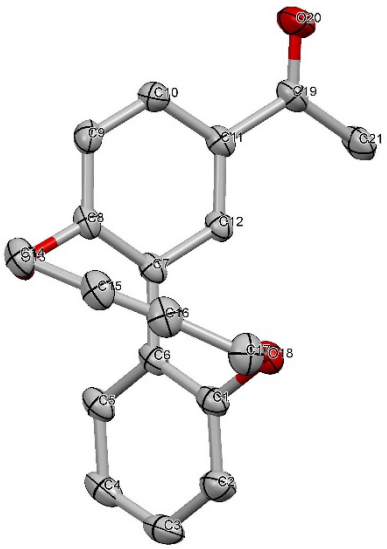


Figure 4: Single crystal X-ray structure of **17** (ellipsoids are plotted at the 50% probability level, hydrogen atoms are omitted for clarity)

CCDC 1852222 contains the supplementary crystallographic data for this paper. These can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Single crystals of X were grown from vapour diffusion of *n*-hexane into a chloroform solution of the compound over several days. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector at 150(2) K. The structure was solved using Olex2[1] and the ShelXT[2] structure solution program using Direct Methods and refined with the ShelXL[3] refinement package using Least Squares refinement.

The asymmetric unit contains one crystallographically distinct molecules, with Z = 8. The crystal packing indicates aromatic donor-acceptor (π-π) interactions of the biphenyl moieties of adjacent molecules. The alkyne group displays significant deviation from linearity, the C14-C15-C16 and C15-C16-C17 bond angles are 165.1298(6)° and 168.5519(3)° respectively. This is accompanied by a large biphenyl torsion angle (C5-C6-C7-C8) of 66.378(2) °.

Table 1: single-crystal X-ray data for compound **17**.

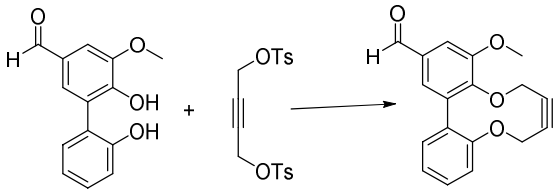
Compound Reference	**Compound 17**
Chemical Formula	$C_{18}H_{14}O_3$
Formula Mass	278.31
Crystal system	Monoclinic
a/ Å	18.8350(8
b/ Å	7.1072(3)
c/ Å	21.7952(9)
α/ °	90
β/ °	105.284(4)
γ/ °	90
Unit cell volume/ Å	2814.4(2)
Temperature/ K	150(2) K
Space group	*I 1 2/a 1*
Crystal size/ mm	0.12 × 0.15 × 0.20
Radiation	Cu K\a
Goodness-of-fit on F^2	1.0443
No. of formula units per unit cell, Z	8
No. of reflections measured	14083
No. of independent reflections	2812
Final R_1 vaules ($I > 2\sigma(I)$)	0.0508
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1342
Final R_1 values (all data)	0.0559
Final $wR(F^2)$ (all data)	0.1432

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

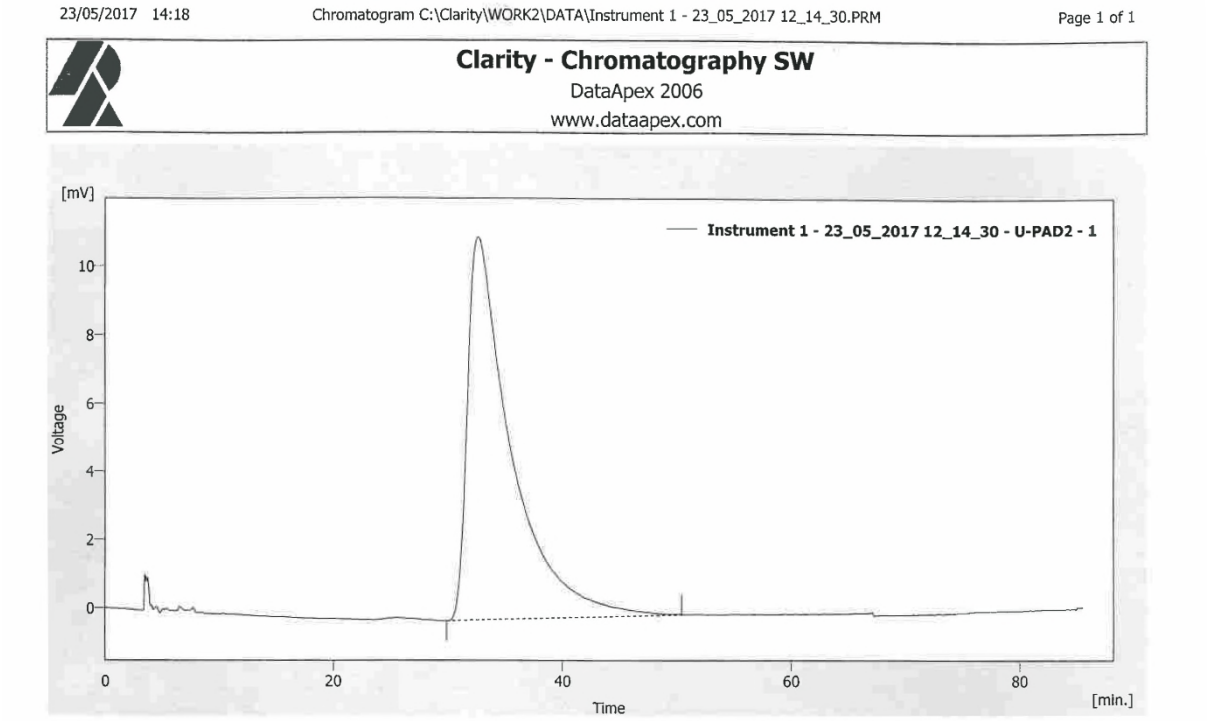
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8

Conversion /time for cyclisation to form aldehyde strained alkyne **16**:



Conditions for HPLC: This reaction was also monitored by HPLC over 14 days, using a Chiralcel IB column, 15:85 IPA:Hexane, 1ml/min.

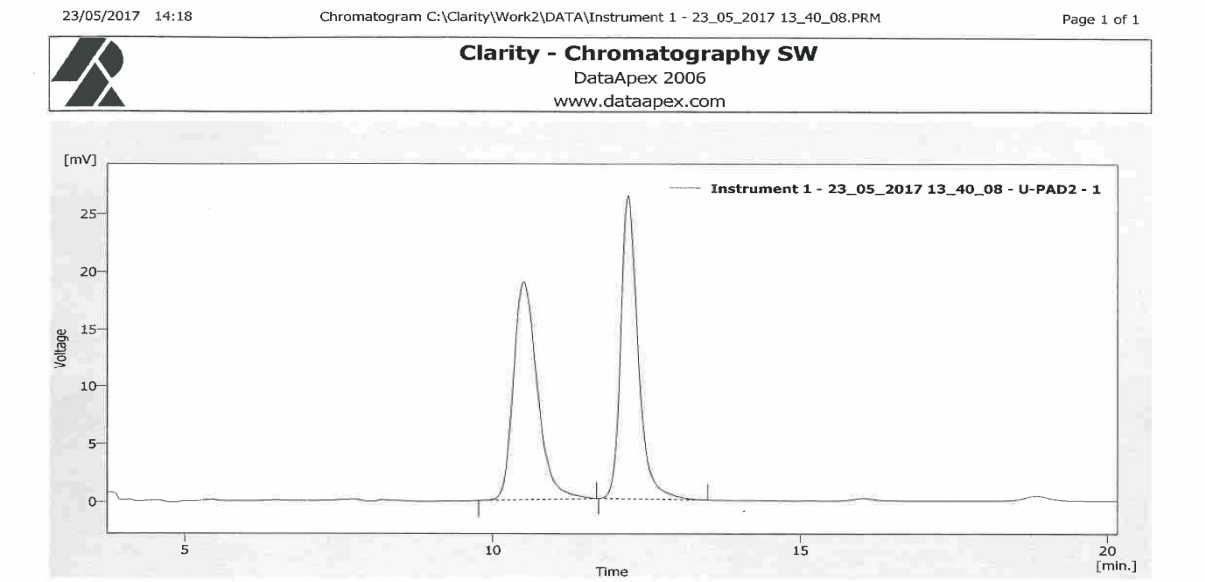
Starting material:



Result Table (Uncal - Instrument 1 - 23_05_2017 12_14_30 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	32.576	2973.594	11.191	100.0	100.0	3.55	
	Total	2973.594	11.191	100.0	100.0		

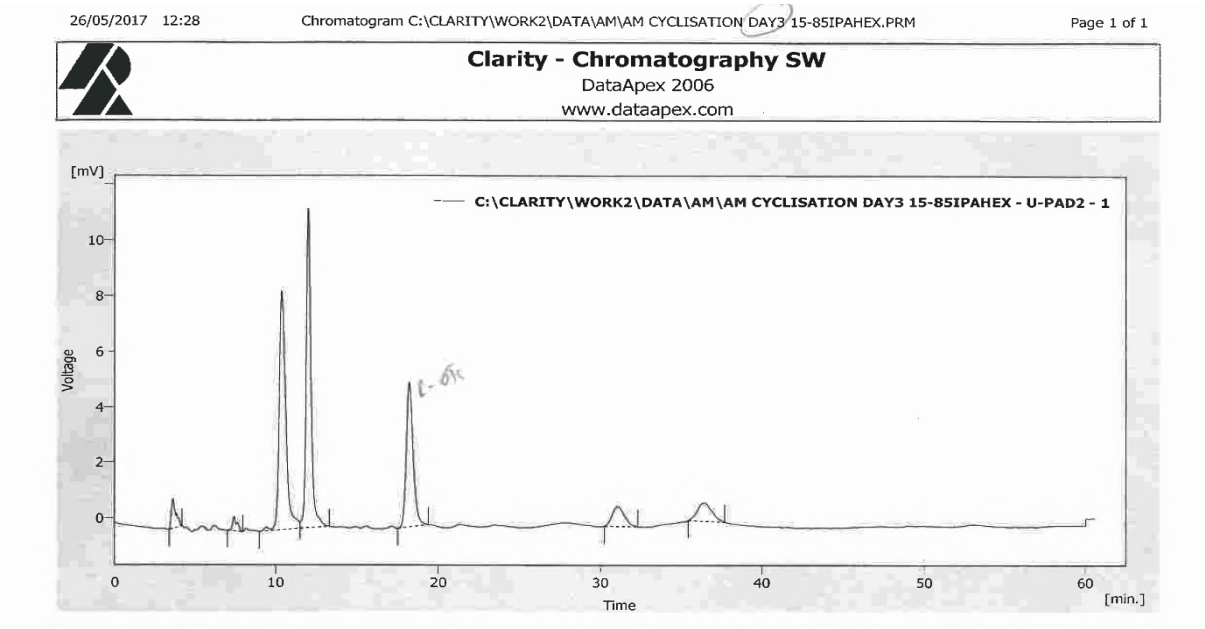
Racemic product (purified):



Result Table (Uncal - Instrument 1 - 23_05_2017 13_40_08 - U-PAD2 - 1)

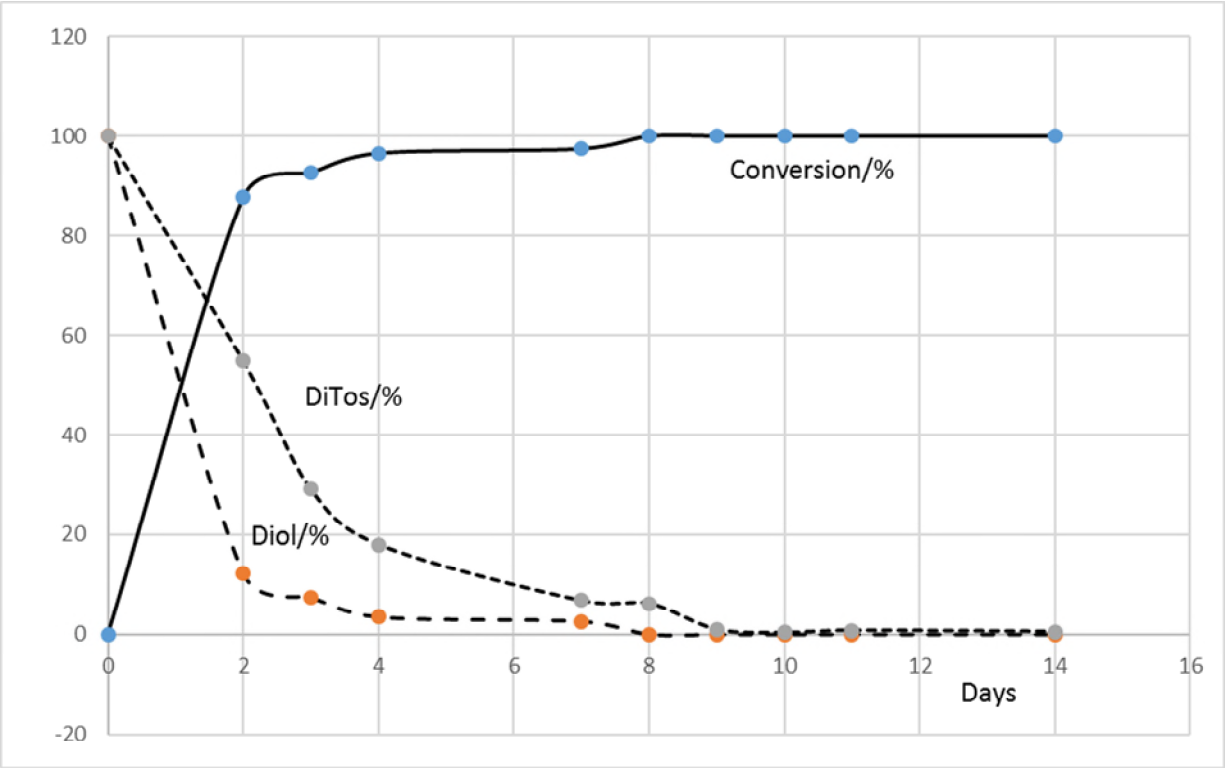
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10.496	511.238	18.969	49.9	41.8	0.41	
2	12.200	513.296	26.392	50.1	58.2	0.28	
	Total	1024.534	45.360	100.0	100.0		

Cyclisation on day 3 (crude mixture; miniworkup using EtOAc/$NaHCO_3$): Products are at 10.4 and 12.0 min., peak at 18.2 min is ditosylate. Uncyclised is at 31.1 min. Unknown impurity at 36.4 min. uv detector and therefore non-quantitative.



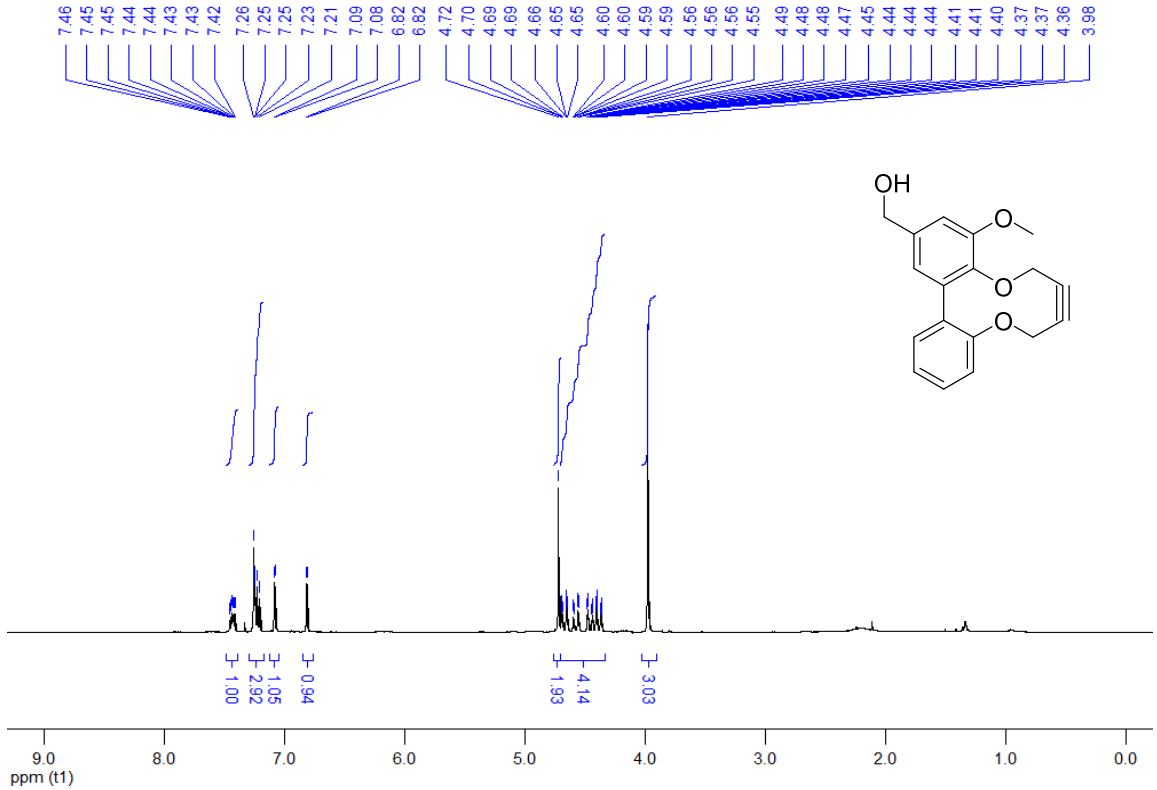
Result Table (Uncal - C:\CLARITY\WORK2\DATA\AM\AM CYCLISATION DAY3 15-85IPAHEX - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	3.620	20.778	1.056	2.8	3.7	0.28	
2	7.428	10.141	0.513	1.4	1.8	0.20	
3	10.376	245.835	8.574	33.2	30.4	0.41	
4	12.012	232.705	11.484	31.5	40.7	0.29	
5	18.216	150.888	5.216	20.4	18.5	0.44	
6	31.096	38.174	0.720	5.2	2.6	0.83	
7	36.404	41.106	0.650	5.6	2.3	1.01	
	Total	739.627	28.214	100.0	100.0		

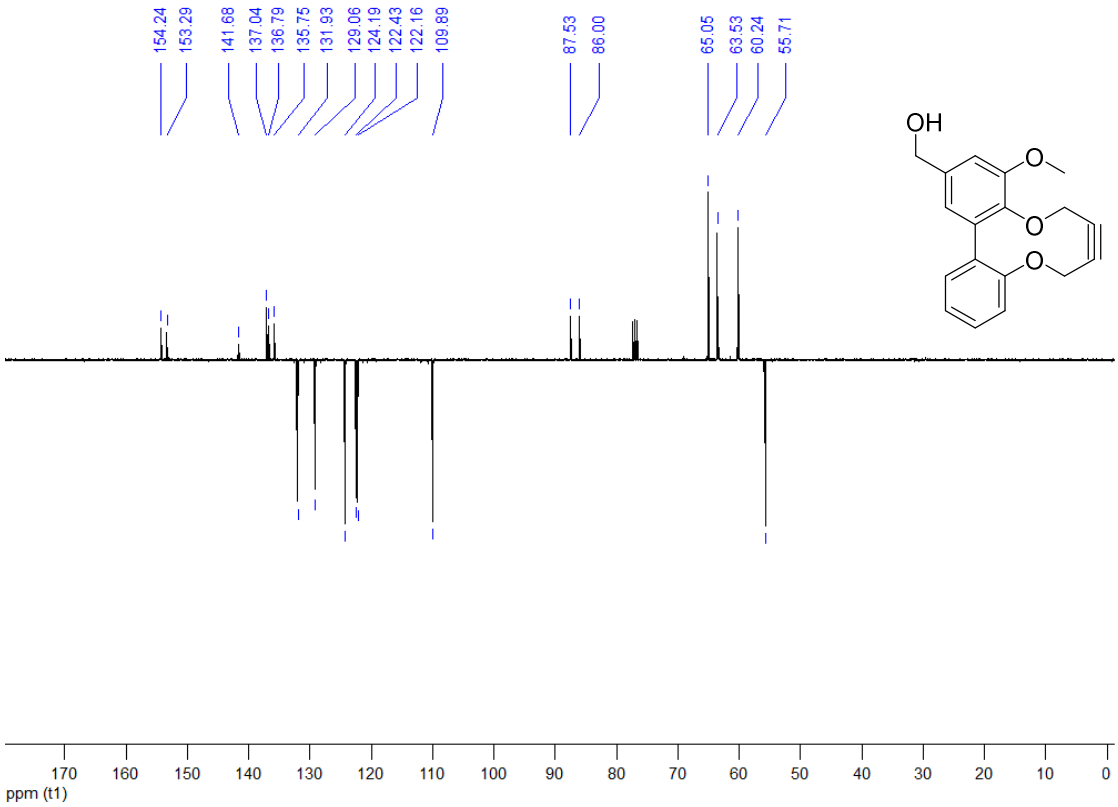

120
100
80
60
40
20
0
-20
0
2
4
6
8
10
12
14
16
Days
Conversion/%
DiTos/%
Diol/%

Alkyne alcohol 19

δ_H (400 MHz, $CDCl_3$)

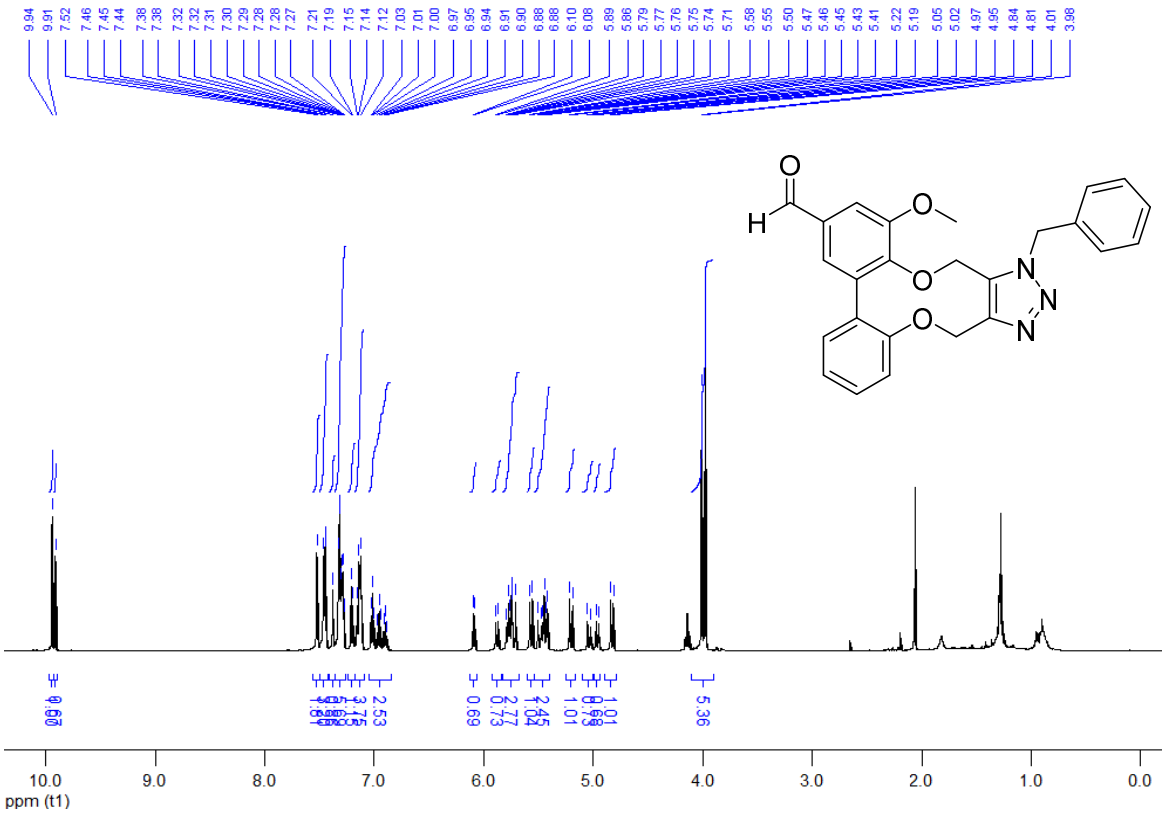


δ_C (100 MHz, $CDCl_3$)

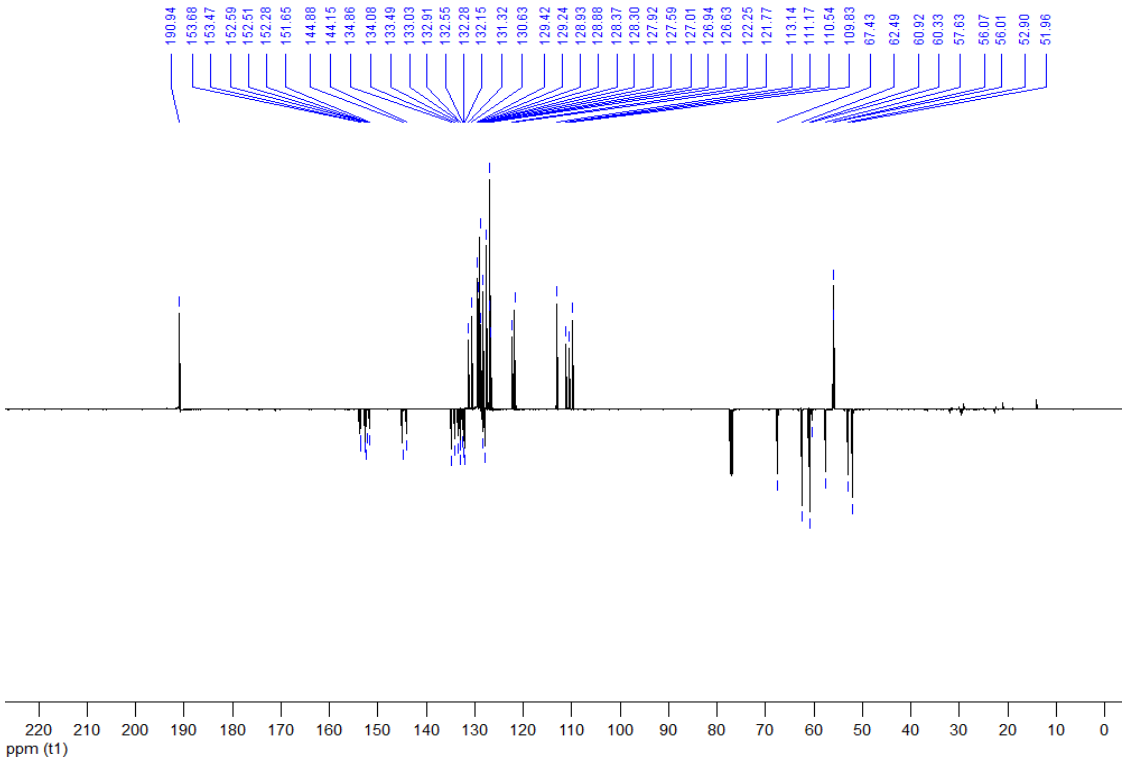


Product of benzylazide addition to aldehyde 21. AM63.

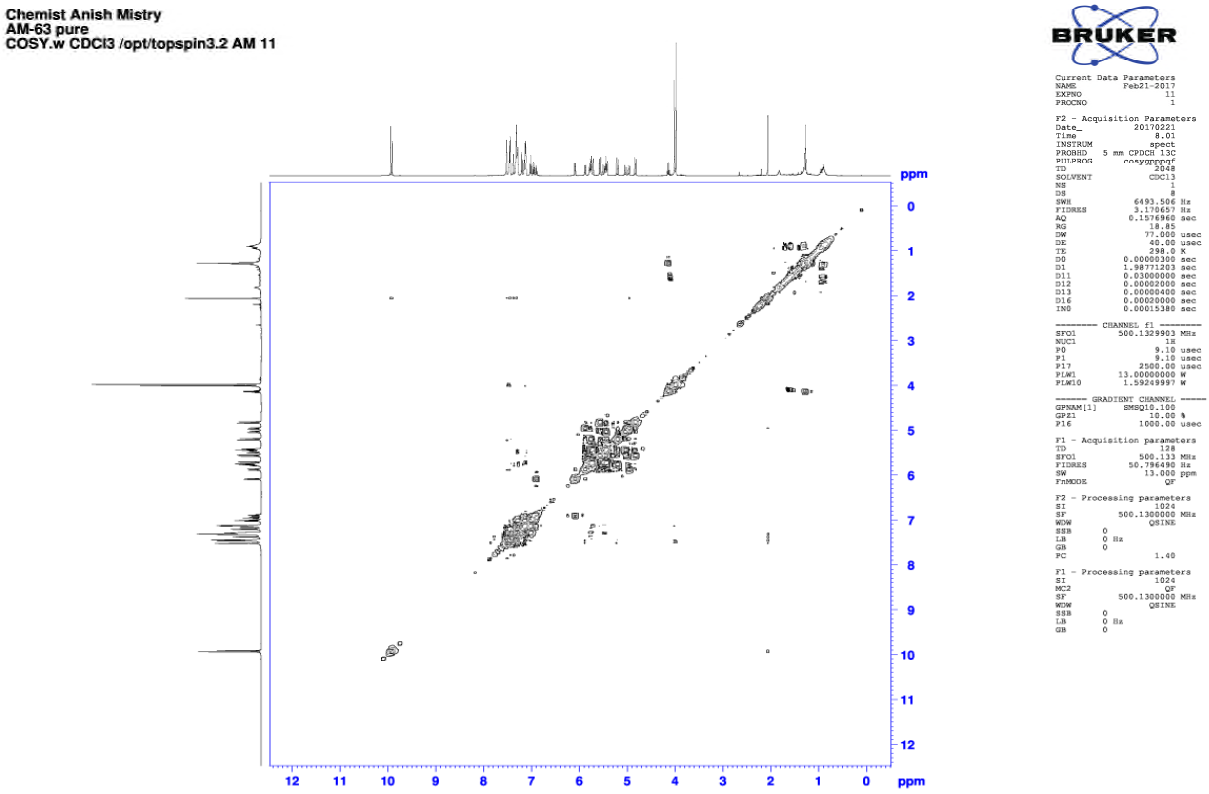
δ_H (500 MHz, $CDCl_3$).



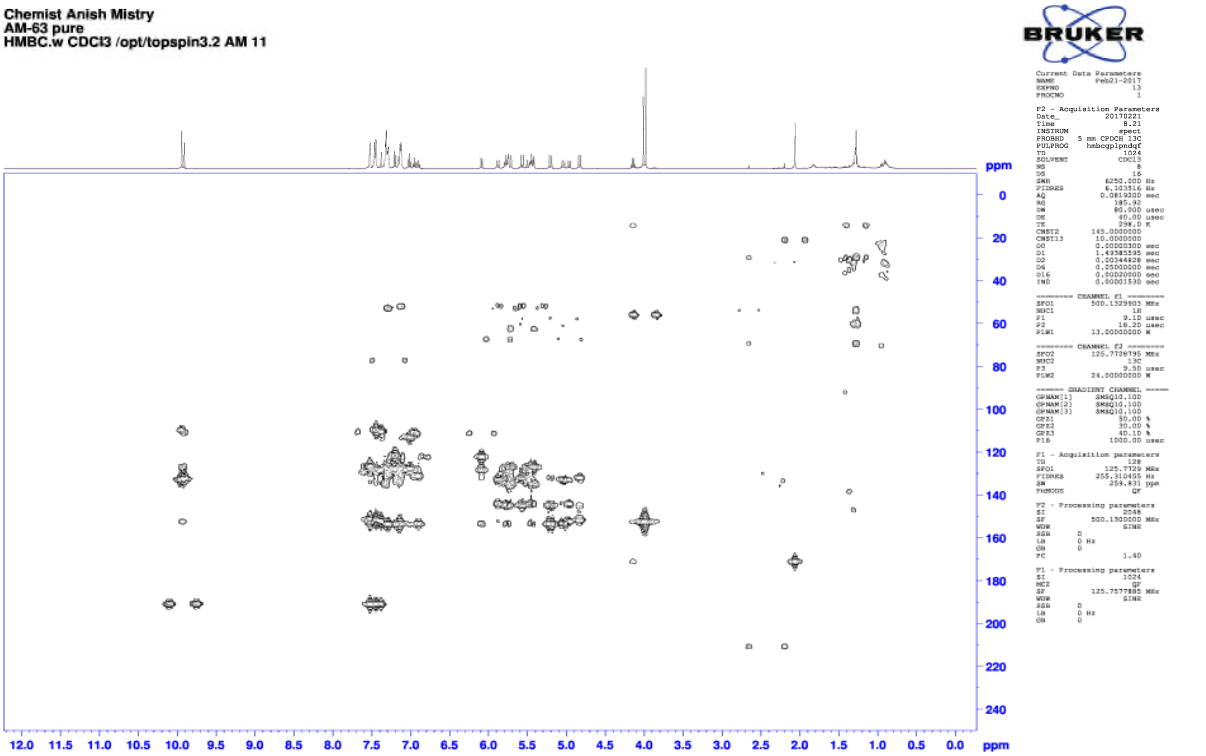
δ_C (126 MHz $CDCl_3$).



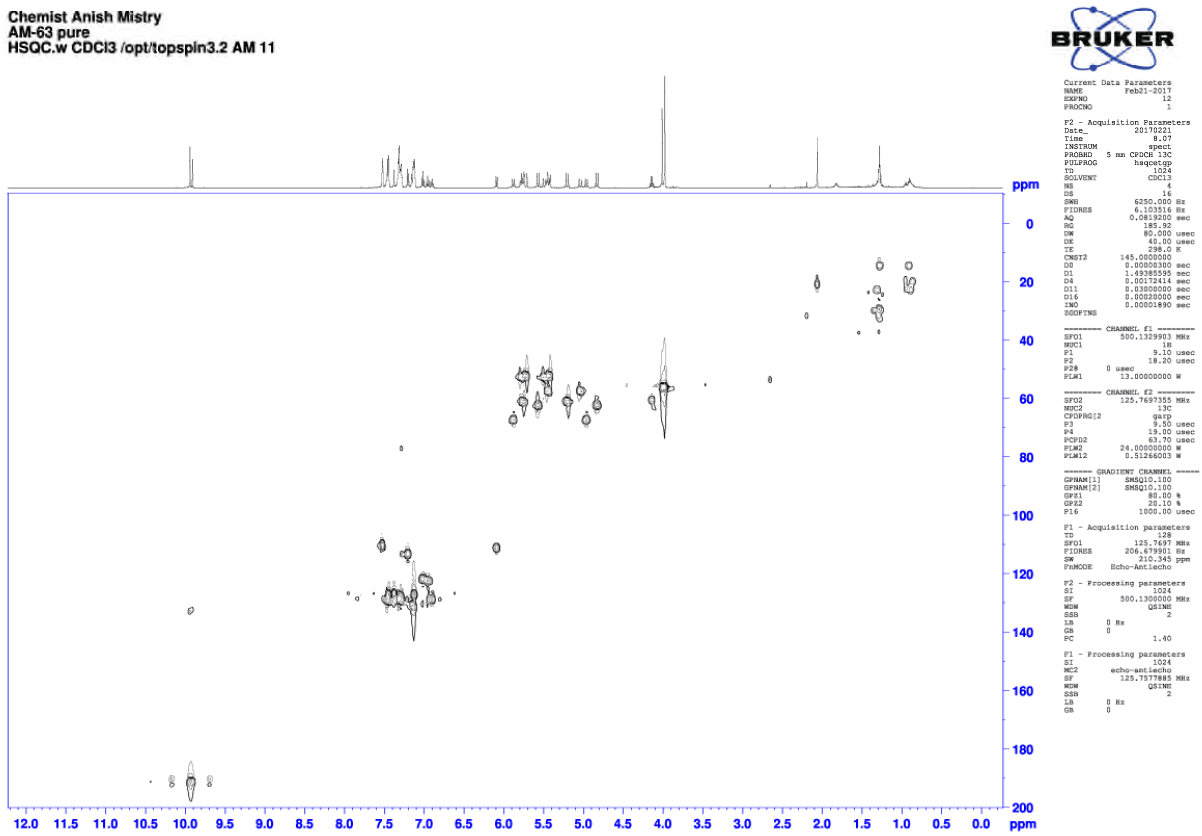
COSY:


Chemist Anish Mistry
AM-63 pure
COSY.w CDCl3 /opt/topspin3.2 AM 11
BRUKER
ppm
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

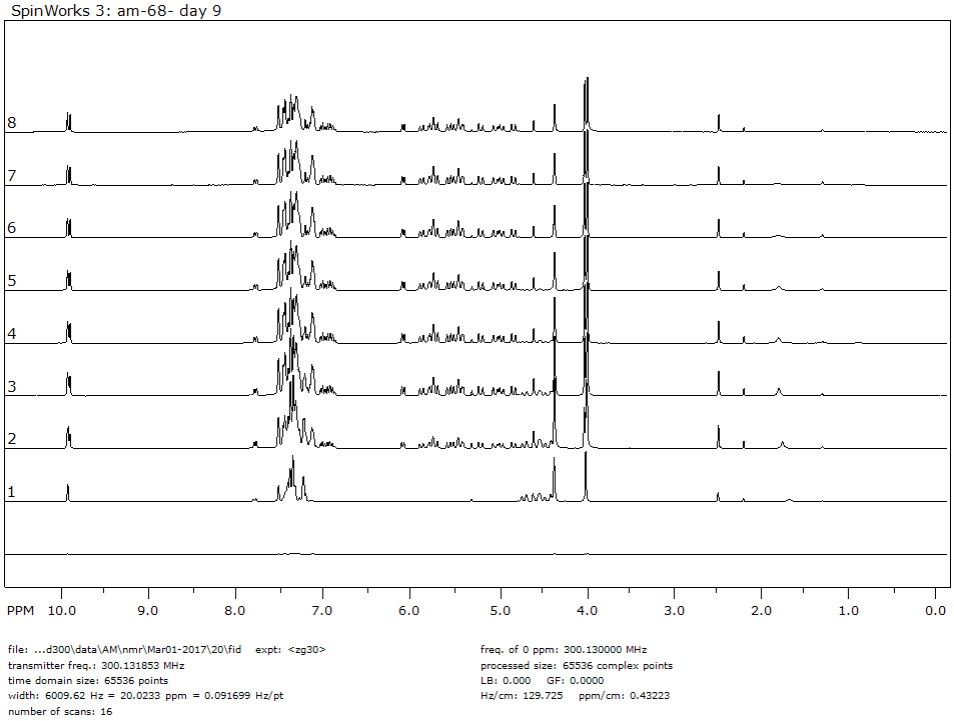
HMBC:


Chemist Anish Mistry
AM-63 pure
HMBC.w CDCl3 /opt/topspin3.2 AM 11
BRUKER
ppm
12.0 11.5 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 ppm

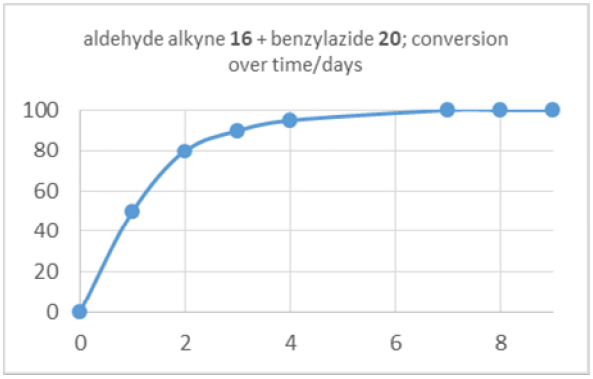
HSQC:



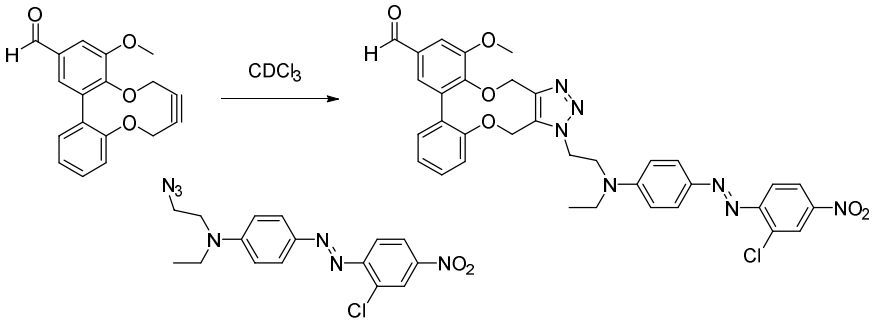
Conversion over time (AM68): Alkyne **16** (15 mg, 51.0 µmol) and benzyl azide **20** (6.4 mg, 51.0 µmol) were added together in deuterated chloroform (0.4 mL) and the reaction left at r.t.. The progression of the reaction was monitored daily by ^{1}H-NMR. (0.128 M in both reagents).



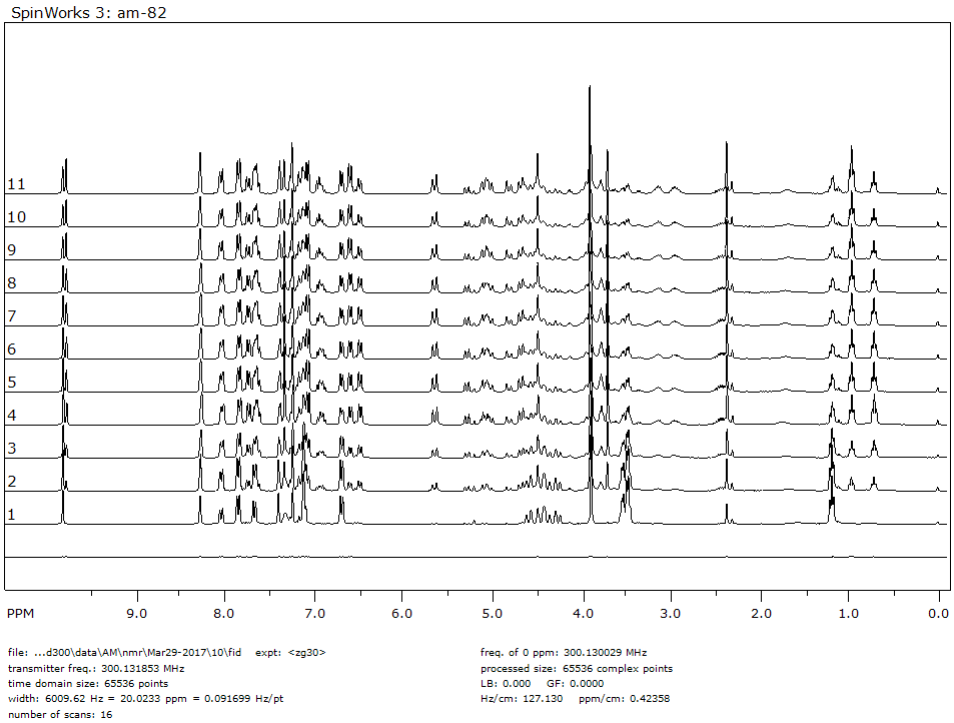
Characteristic peaks in the NMR used to define conversion; δ_H (300 MHz, $CDCl_3$) 9.82 (1H, s, *CHO*), 7.10-6.90 (1H, m, ArH), 6.20-4.90 (6H, 6xAB systems for 6 CH_2 groups), 3.98 (s, 3H, isomer 1 OCH_3), 3.94 (s, 3H, isomer 2 OCH_3). The spectrum contains $PhCH_2N_3$ peak at ca. δ 4.45. Conv approx.; 1) start, 0%, 2) day 1, 50%, 3) day 2, 80%, 4) day 3, 90%, 5) day 4, 95%, 6) day 7, 100%, 7) day 8, 100%, 8) day 9, 100%.



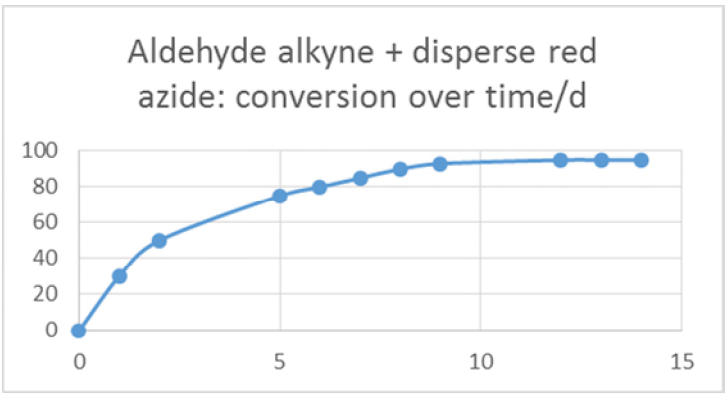
Disperse red cycloadduct 23 (AM82).



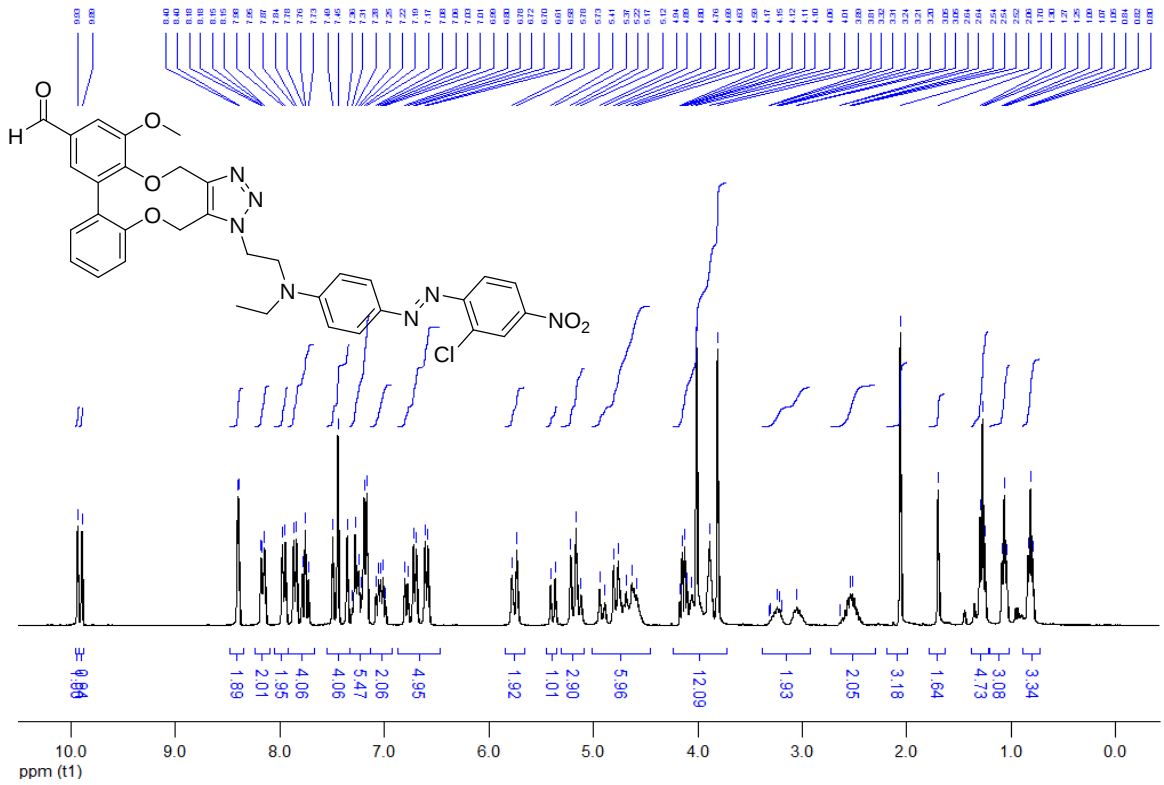
Stacked spectra over time intervals (defined below):



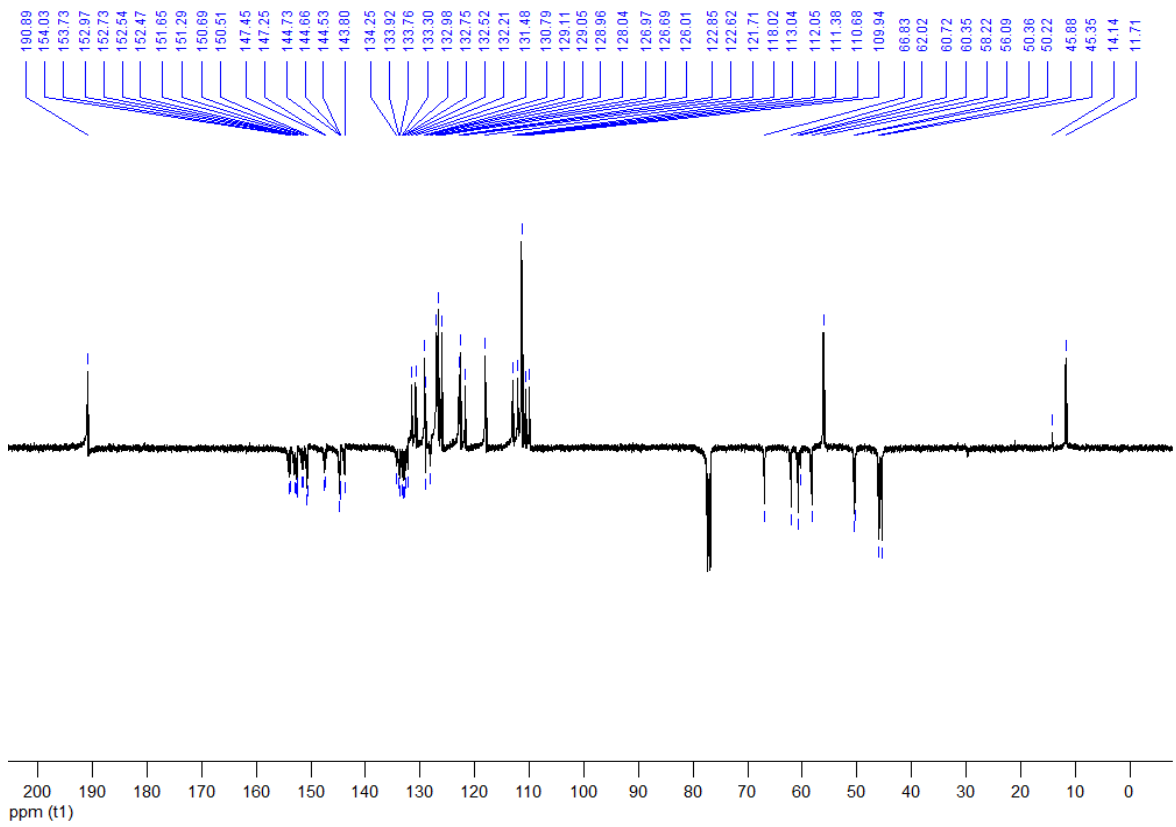
Characteristic peaks in the NMR used to define conversion: δ_H (300 MHz, $CDCl_3$); starting material OCH_2 peaks (4 H) at 4.60-4.15, product OCH_2 peaks (4 H) at 5.70-4.70. Conv approx.; 1) start, 0%, 2) day, 30%, 3) day 2, 50%, 4) day 5, 75%, 5) day 6, 80%, 6) day 7, 85%, 7) day 8, 90%, 8) day 9, 93%, 9-11), days 12,13,14, all 95%.



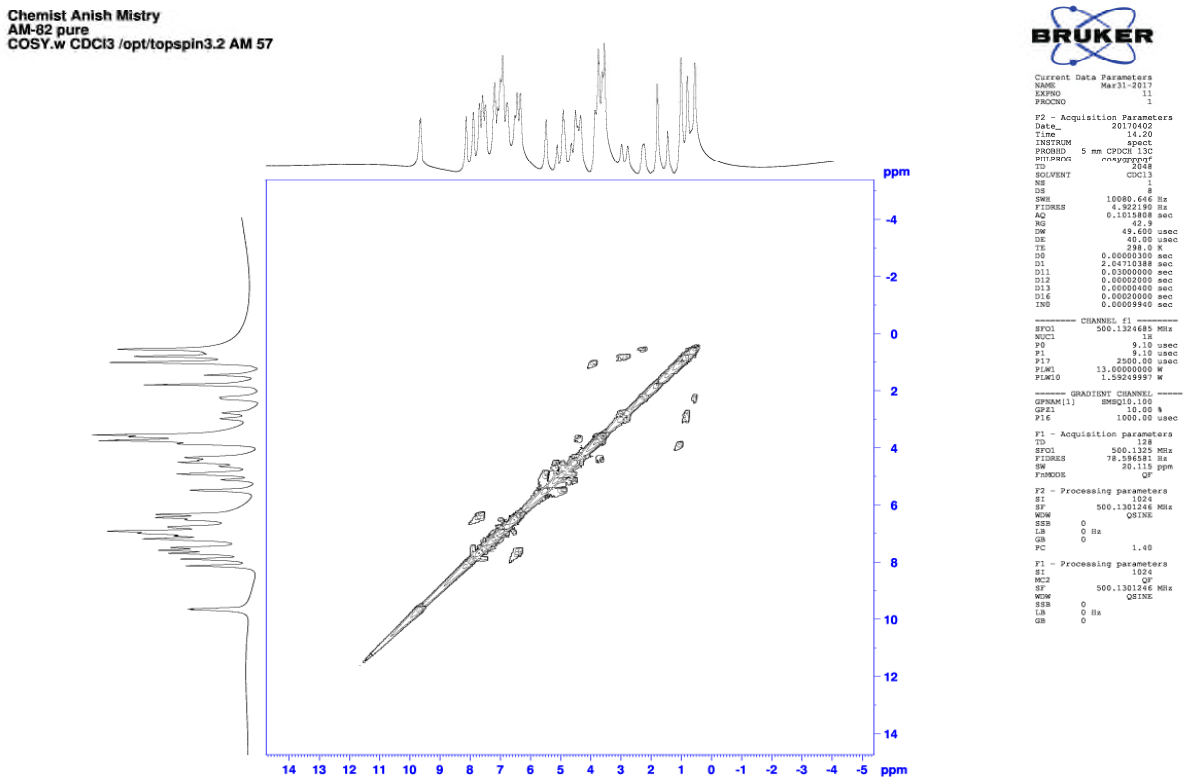
δ_H (300 MHz, $CDCl_3$)..



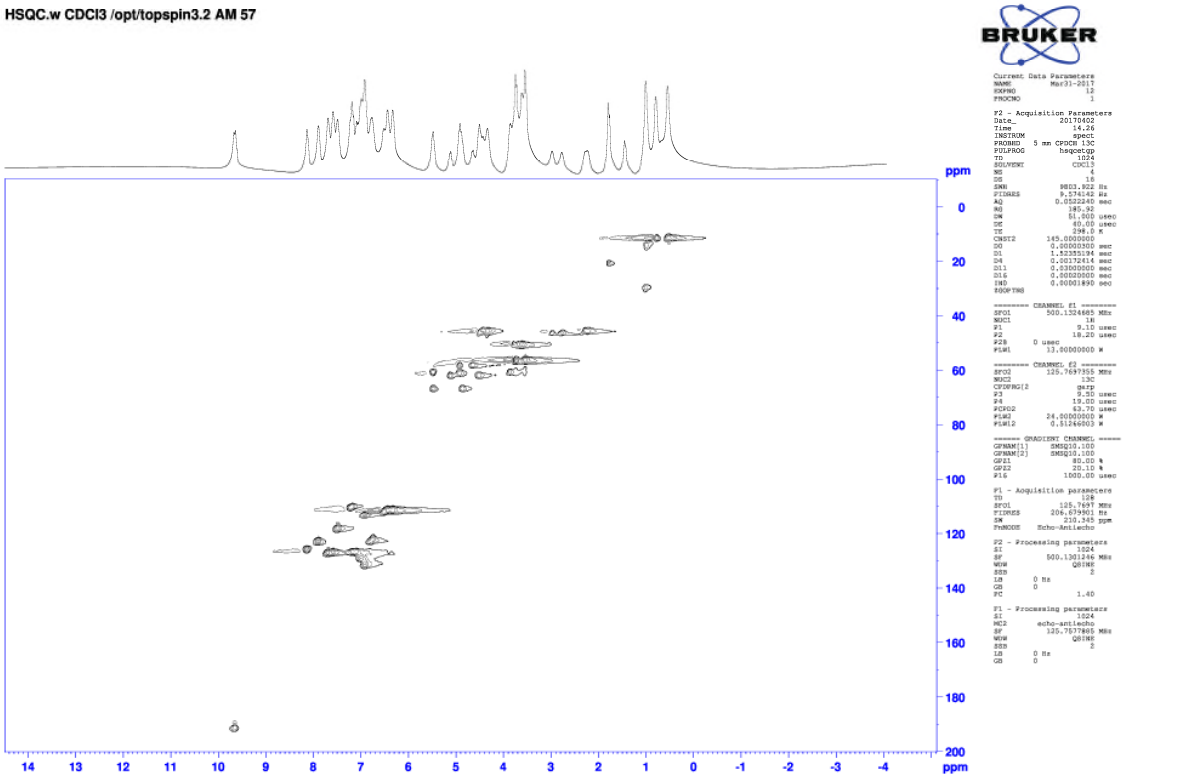
δ_C (126 MHz, $CDCl_3$).



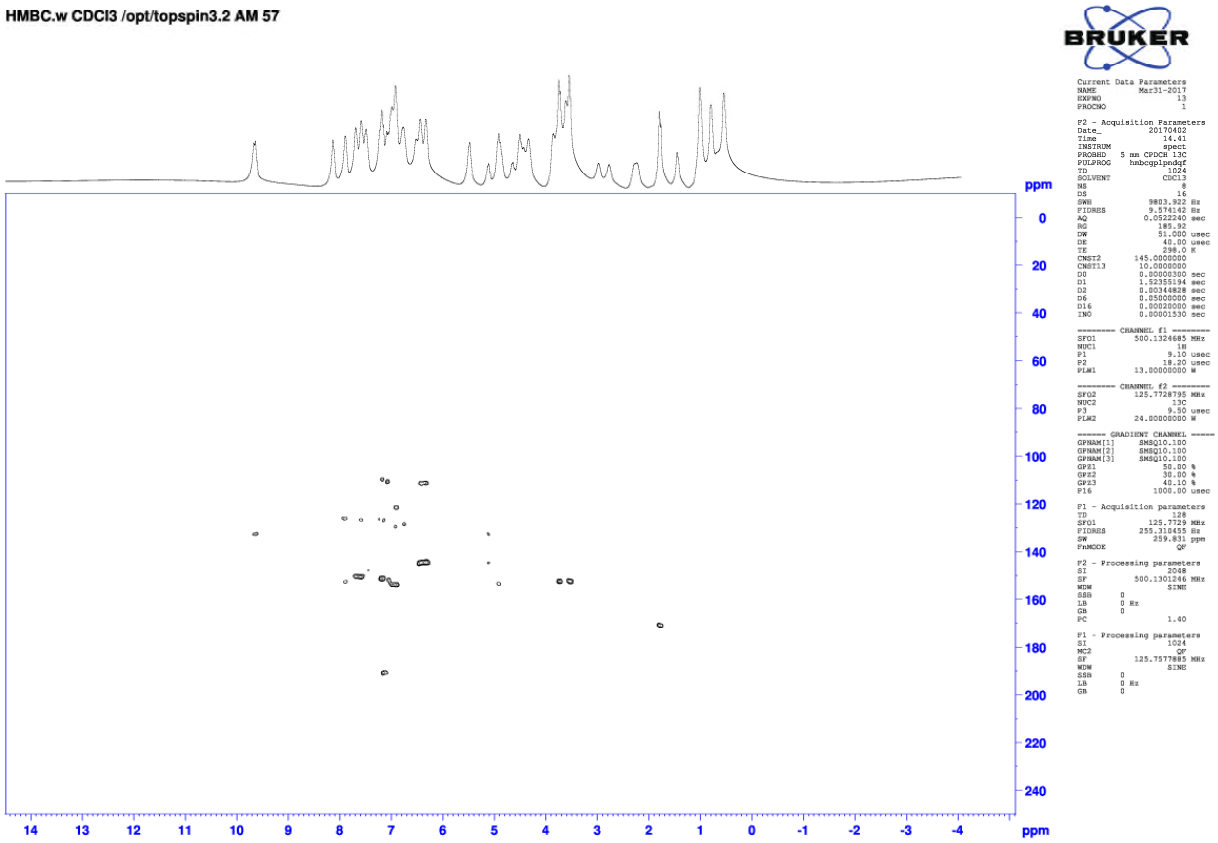
COSY:


Chemist Anish Mistry
AM-82 pure
COSY.w CDCl3 /opt/topspin3.2 AM 57
BRUKER
Current Data Parameters
NAME Mar31-2017
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170402
Time 14.20
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 8
SWH 10080.646 Hz
FIDRES 4.922190 Hz
AQ 0.1015808 sec
RG 42.9
DW 49.600 usec
DE 40.00 usec
TE 298.0 K
D0 0.00000300 sec
D1 2.04710388 sec
D11 0.03000000 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00009940 sec
======== CHANNEL f1 ========
SFO1 500.1324685 MHz
NUC1 1H
P0 9.10 usec
P1 9.10 usec
P17 2500.00 usec
PLW1 13.00000000 W
PLW10 1.59249997 W
======= GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPZ1 10.00 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 128
SFO1 500.1325 MHz
FIDRES 78.596581 Hz
SW 20.115 ppm
FnMODE QF
F2 - Processing parameters
SI 1024
SF 500.1301246 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2
SF 500.1301246 MHz
WDW QSINE
SSB 0
LB 0 Hz
GB 0
ppm
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4 -5 ppm

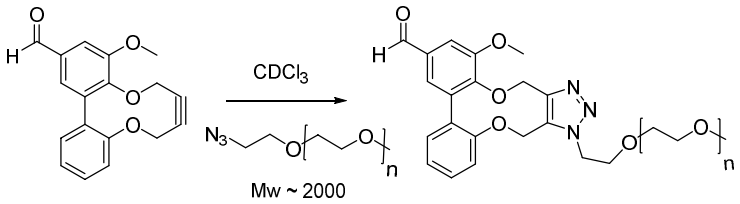
HSQC:


HSQC.w CDCl3 /opt/topspin3.2 AM 57
BRUKER
Current Data Parameters
NAME Mar31-2017
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170402
Time 14.26
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG hsqcetgp
TD 1024
SOLVENT CDCl3
NS 2
DS 16
SWH 9803.922 Hz
FIDRES 9.574142 Hz
AQ 0.0522240 sec
RG 185.92
DW 51.000 usec
DE 60.00 usec
TE 298.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.52355194 sec
D4 0.00172414 sec
D11 0.03000000 sec
D16 0.00020000 sec
IN0 0.00001890 sec
ZGOPTNS
======== CHANNEL f1 ========
SFO1 500.1324685 MHz
NUC1 1H
P1 9.10 usec
P2 18.20 usec
P28 0 usec
PLW1 13.00000000 W
======== CHANNEL f2 ========
SFO2 125.7697355 MHz
NUC2 13C
CPDPRG[2 garp
P3 9.50 usec
P4 19.00 usec
PCPD2 63.70 usec
PLW2 24.60000000 W
PLW12 0.51246803 W
======= GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPNAM[2] SMSQ10.100
GPZ1 80.00 %
GPZ2 20.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 128
SFO1 125.7697 MHz
FIDRES 206.679901 Hz
SW 230.345 ppm
FnMODE Echo-Antiecho
F2 - Processing parameters
SI 1024
SF 500.1301246 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 echo-antiecho
SF 125.7577805 MHz
WDW QSINE
SSB 2
LB 0 Hz
GB 0
ppm
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4 ppm

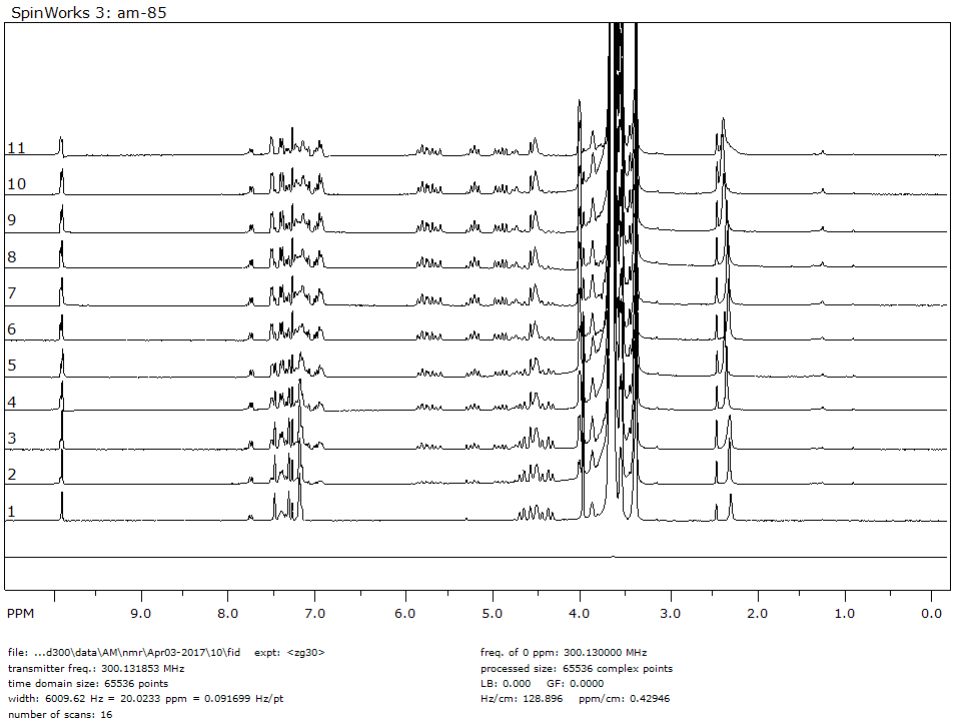
HMBC:


HMBC.w CDCl3 /opt/topspin3.2 AM 57
BRUKER
Current Data Parameters
NAME Mar31-2017
EXPNO 13
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170402
Time 14.41
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG hmbcgplpndqf
TD 1024
SOLVENT CDCl3
NS 8
DS 16
SWH 9803.922 Hz
FIDRES 9.576162 Hz
AQ 0.0522240 sec
RG 185.92
DW 51.000 usec
DE 40.00 usec
TE 298.0 K
CNST2 145.0000000
CNST13 10.0000000
D0 0.00000300 sec
D1 1.52355194 sec
D2 0.00344828 sec
D6 0.05000000 sec
D16 0.00020000 sec
IN0 0.00001530 sec
======== CHANNEL f1 ========
SFO1 500.1324685 MHz
NUC1 1H
P1 9.10 usec
P2 18.20 usec
PLW1 13.00000000 W
======== CHANNEL f2 ========
SFO2 125.7728795 MHz
NUC2 13C
P3 9.50 usec
PLW2 24.80000000 W
====== GRADIENT CHANNEL =====
GPNAM[1] SMSQ10.100
GPNAM[2] SMSQ10.100
GPNAM[3] SMSQ10.100
GPZ1 50.00 %
GPZ2 30.00 %
GPZ3 40.10 %
P16 1000.00 usec
F1 - Acquisition parameters
TD 128
SFO1 125.7729 MHz
FIDRES 255.318455 Hz
SW 259.831 ppm
FnMODE QF
F2 - Processing parameters
SI 2048
SF 500.1301246 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
PC 1.40
F1 - Processing parameters
SI 1024
MC2 QF
SF 125.7577885 MHz
WDW SINE
SSB 0
LB 0 Hz
GB 0
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
ppm

Cycloadduct of PEG-2000 23. AM85.

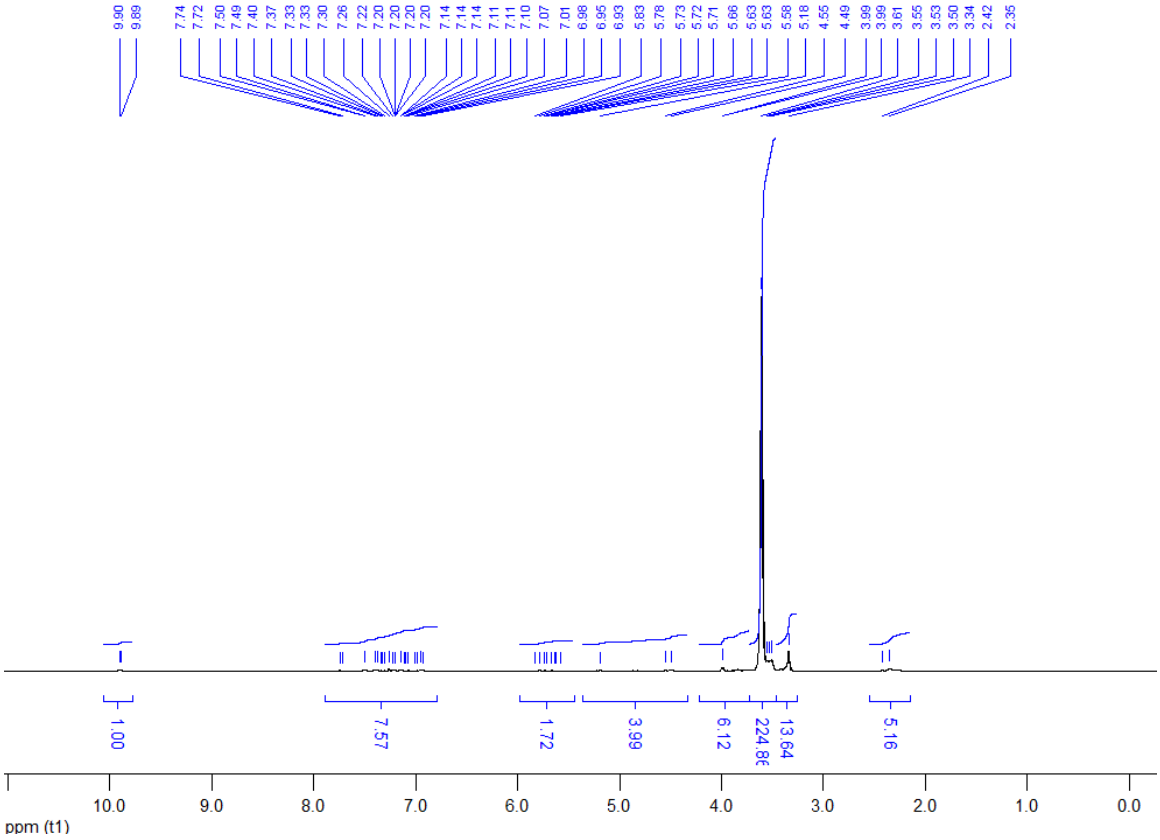


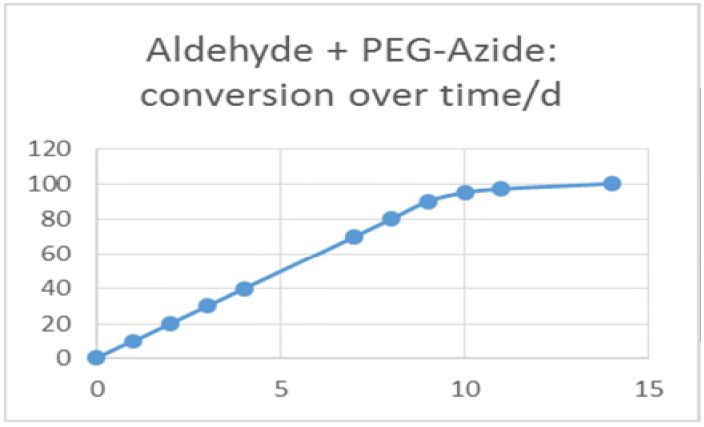
^{1}H NMR followed over time:



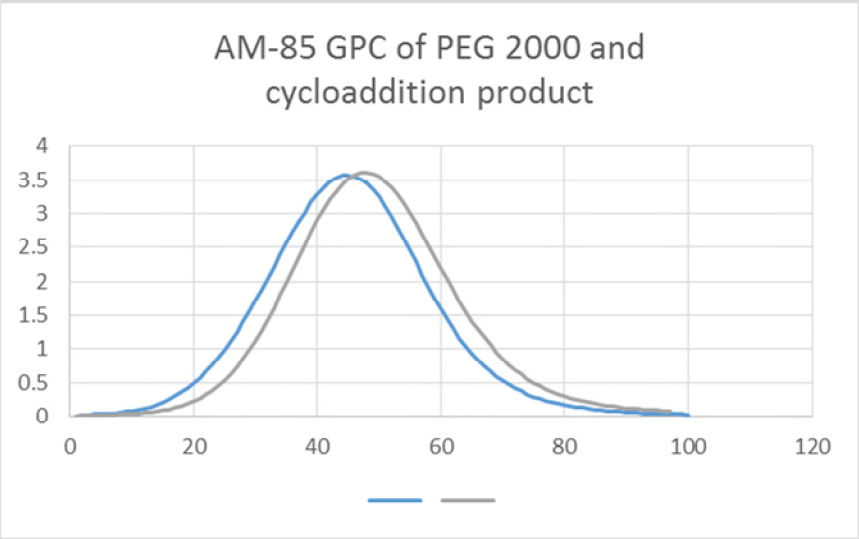
Conv approx.; 1) start, 0%, 2) day 1, 10%, 3) day 2, 20%, 4), day 3, 30%, 5) day 4, 40%, 6) day 7, 70%, 7) day 8, 80%, 8) day 9, 90%, 9) day 10, 95%, 10) day 11, 97%, 11) day 14, 100%.

Day 14, full NMR spectrum:





GPC data is from the reaction above.



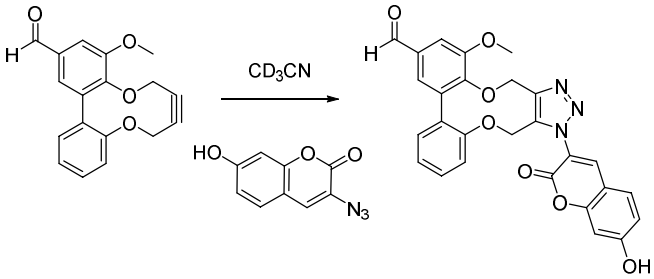
Blue is the starting material PEG-azide. Grey is AM-85 product of cycloaddition.

Agilent 390LC MDS instrument equipped with differential refractive index (DRI), viscometry (VS) and dual angle light scatter (LS) detectors, with full details in main paper.

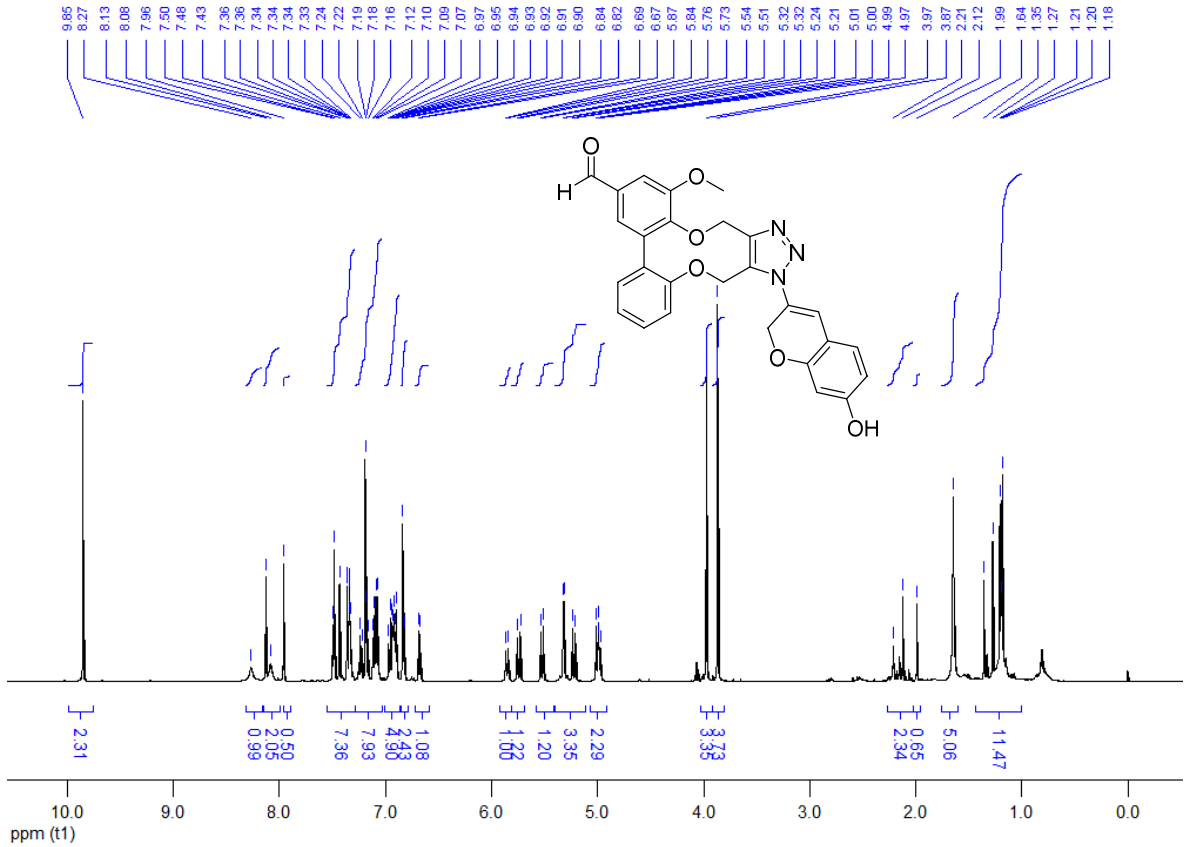
M_n (g/mol)	M_w (g/mol)	PDi
2100	2300	1.08

The PDi is near to 1 which is ideal (sharper peak). The molecular weight is 2305 which is very close to that of which we require (2294).

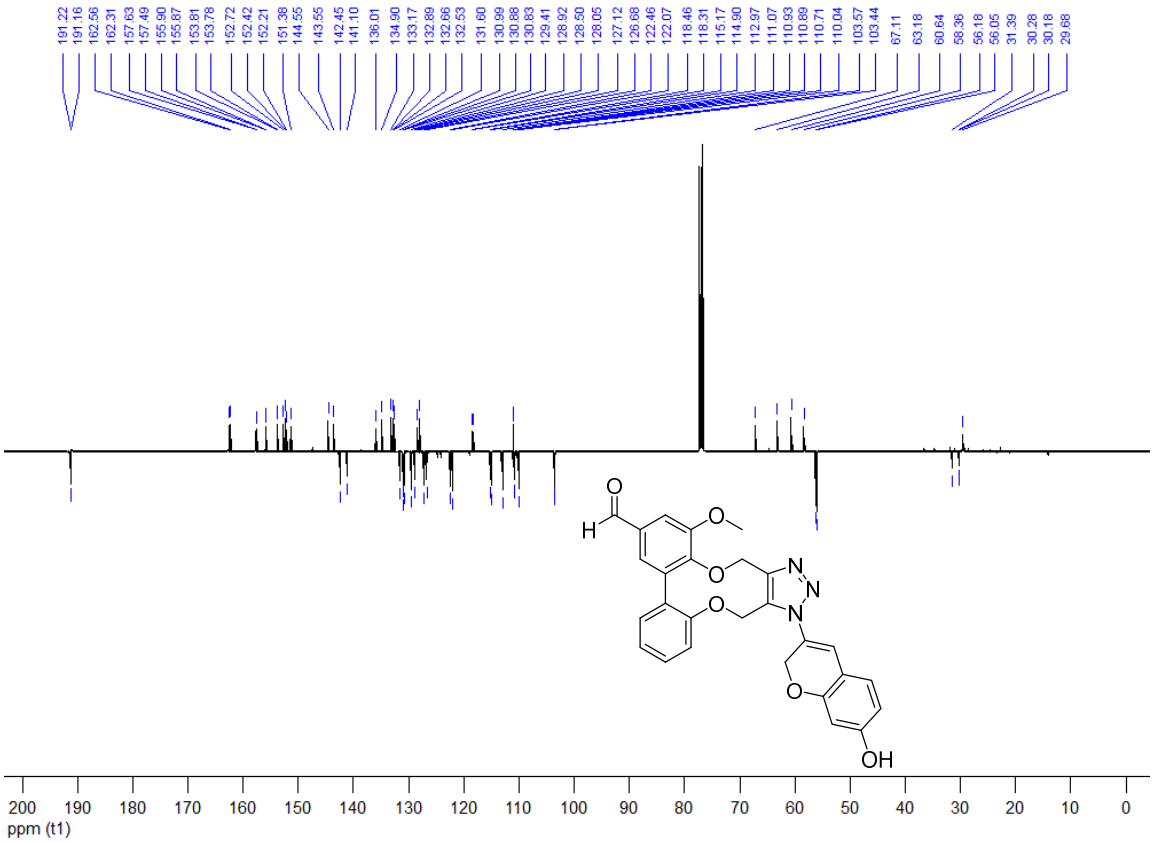
Fluorescent coumarin dye cycloadduct 27. AM86.



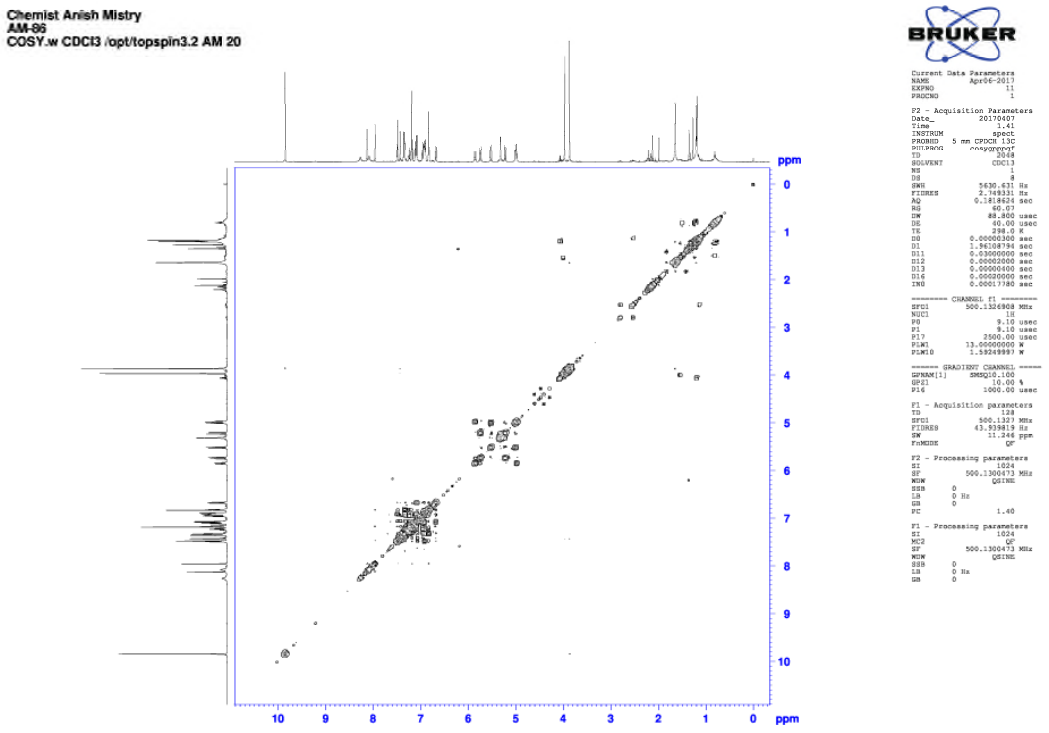
δ_H (500 MHz, $CDCl_3$).



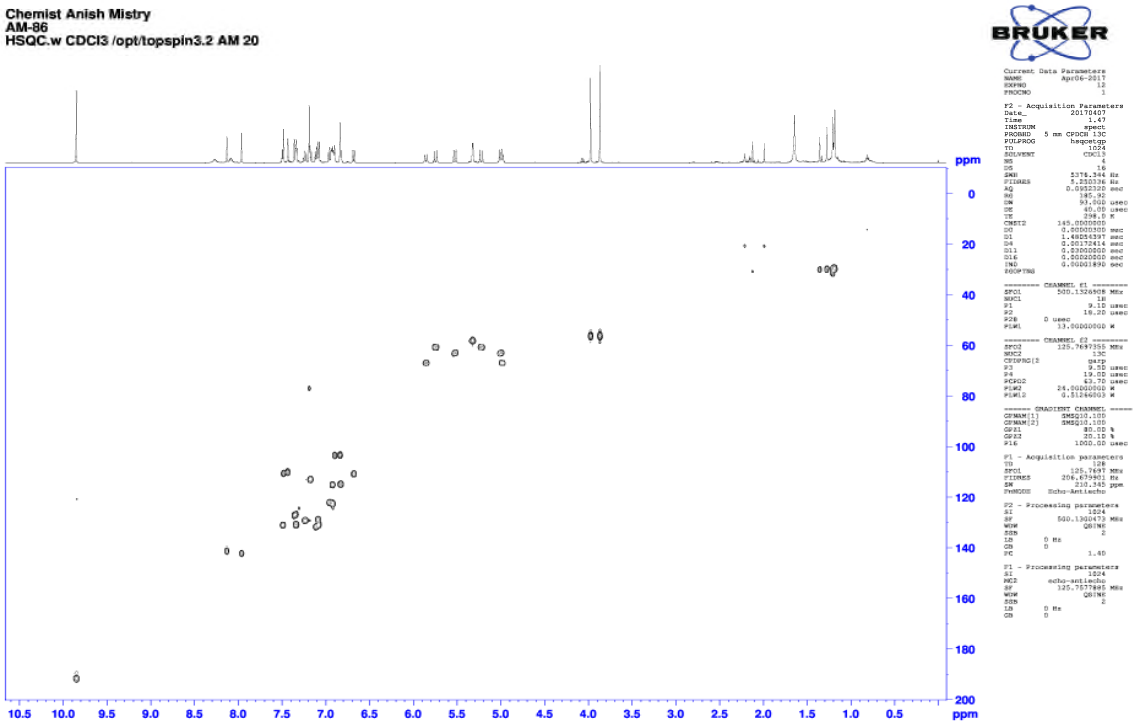
δ_C (126 MHz, $CDCl_3$).



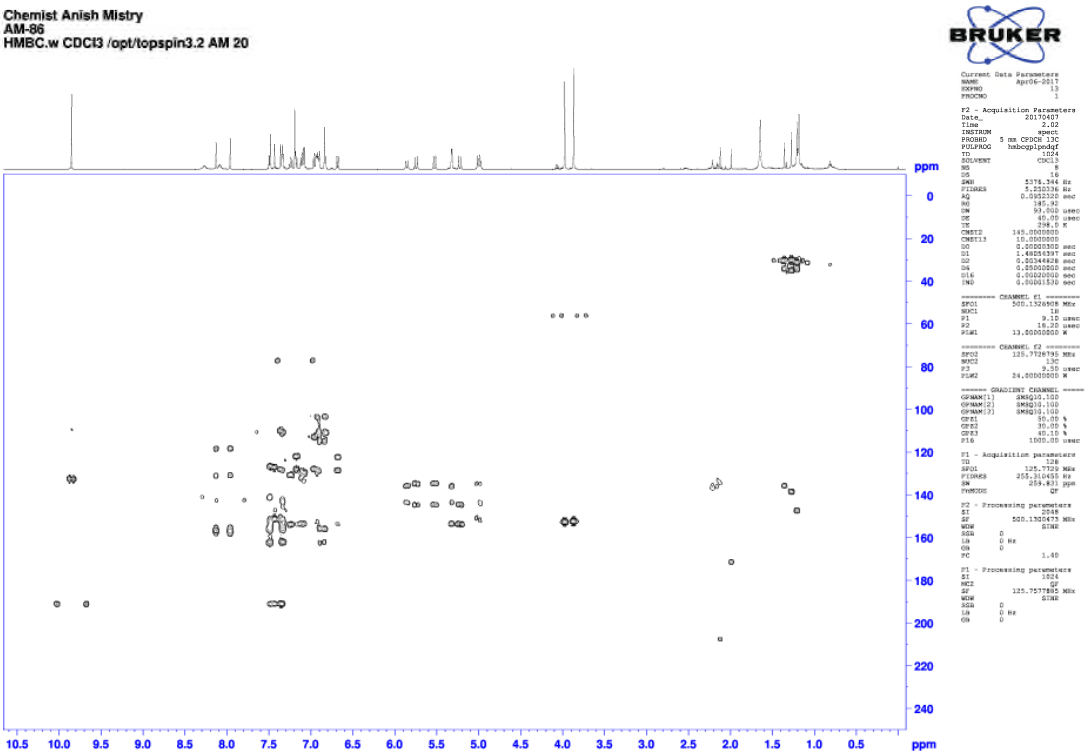
COSY:



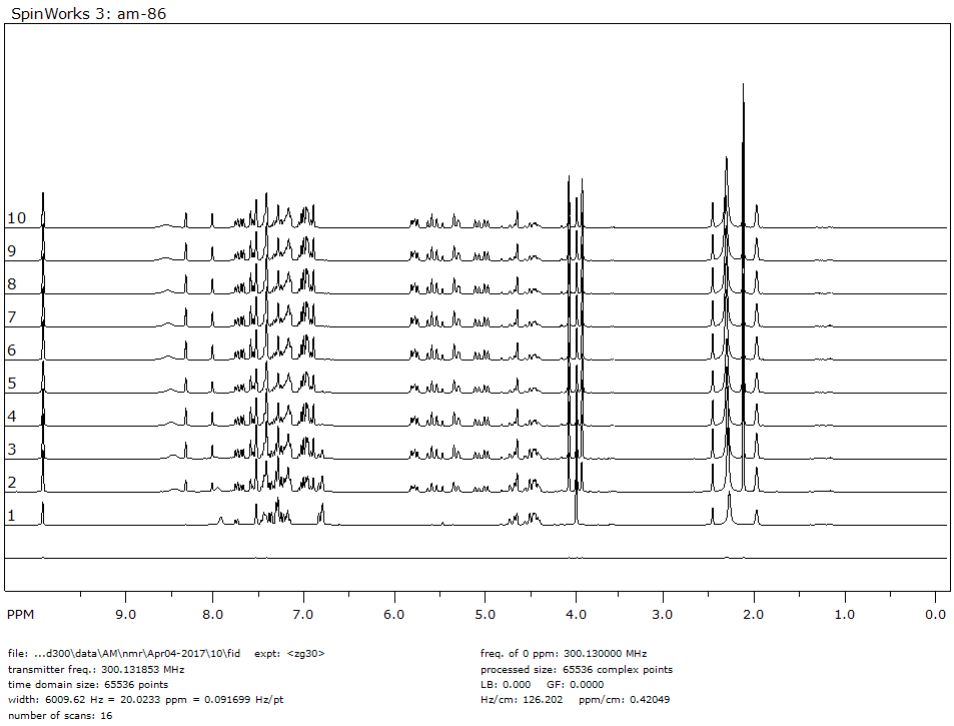
HSQC:


Chemist Anish Mistry
AM-86
HSQC.w CDCl3 /opt/topspin3.2 AM 20
BRUKER
ppm
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 ppm

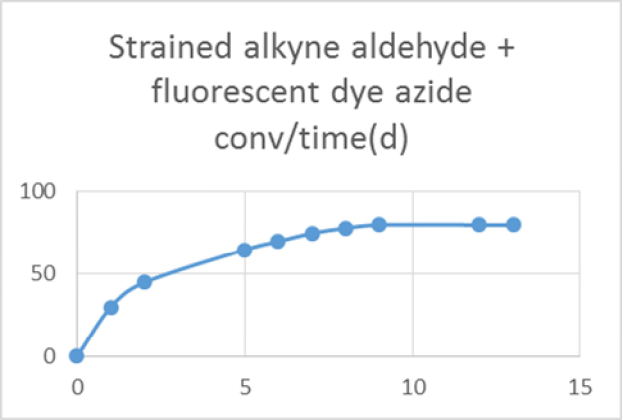
HMBC:


Chemist Anish Mistry
AM-86
HMBC.w CDCl3 /opt/topspin3.2 AM 20
BRUKER
ppm
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 ppm

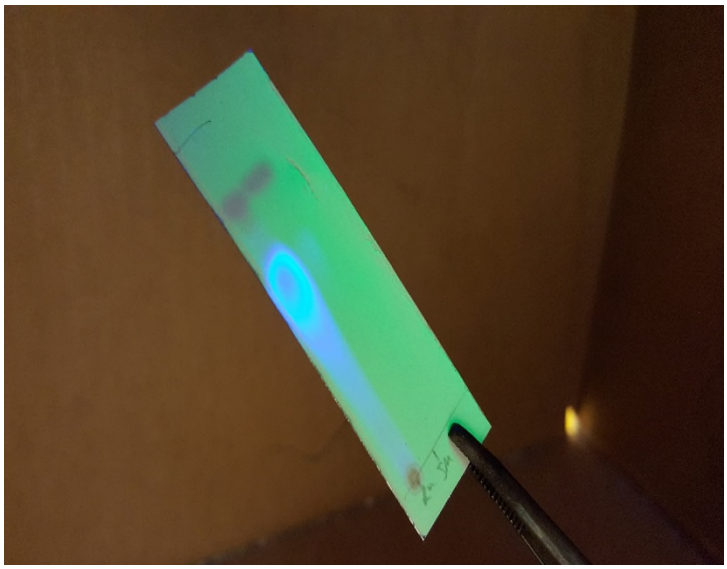
The conversion was followed over time during the reaction. Characteristic peaks of product were observed as follows:



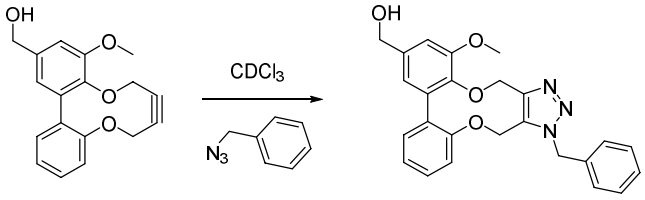
δ_H (400 MHz, $CDCl_3$) 9.84+9.82 (1H, s x 2, *CHO*), 8.40-6.80 (m, ArHs..several distinctive, from Dye), 5.80-5.00 (4H, 2 x OCH_2 in product), 4.65-4.35 ((4H, 2 x OCH_2 in strained alkyne), 4.10 (3H, s, OCH_3 - shifts). Conv approx.; 1) start, 0%, 2) day 1, 30%, 3) day 2, 45%, 4), day 5, 65%, 5) day 6, 70%, 6) day 7, 75%, 7) day 8, 75%, 8) day 9, 78%, 9) day 12, 80%, 10) day 13, 80%.



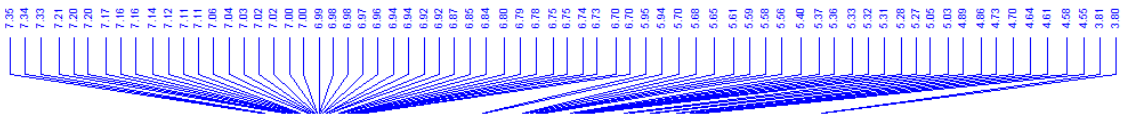
TLC of the fluorescent product, irradiated at 254 nm:

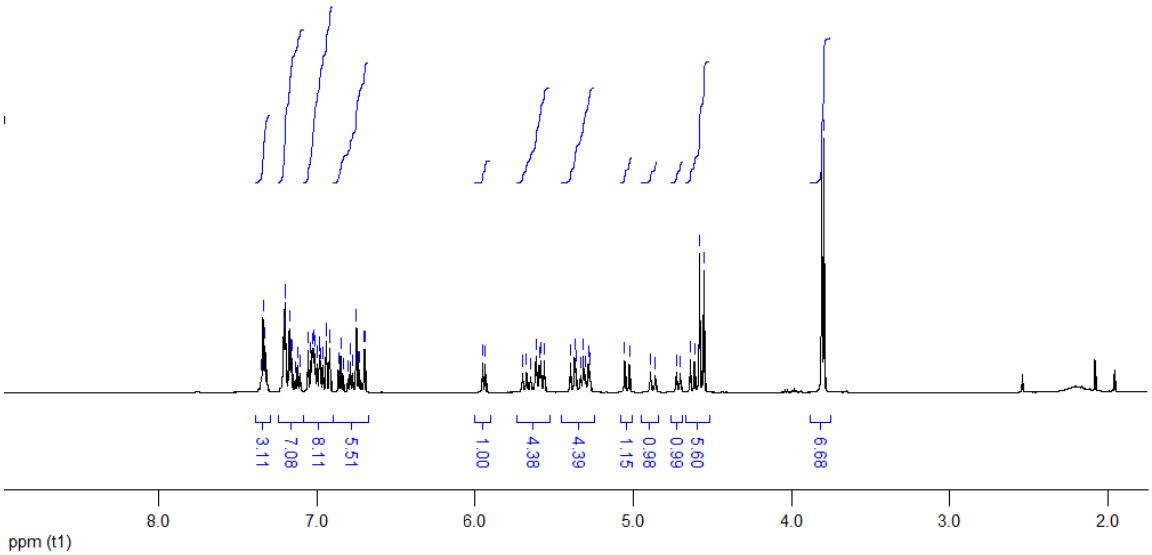


Alcohol 19/benzyl azide Cycloadduct 28. AM60.

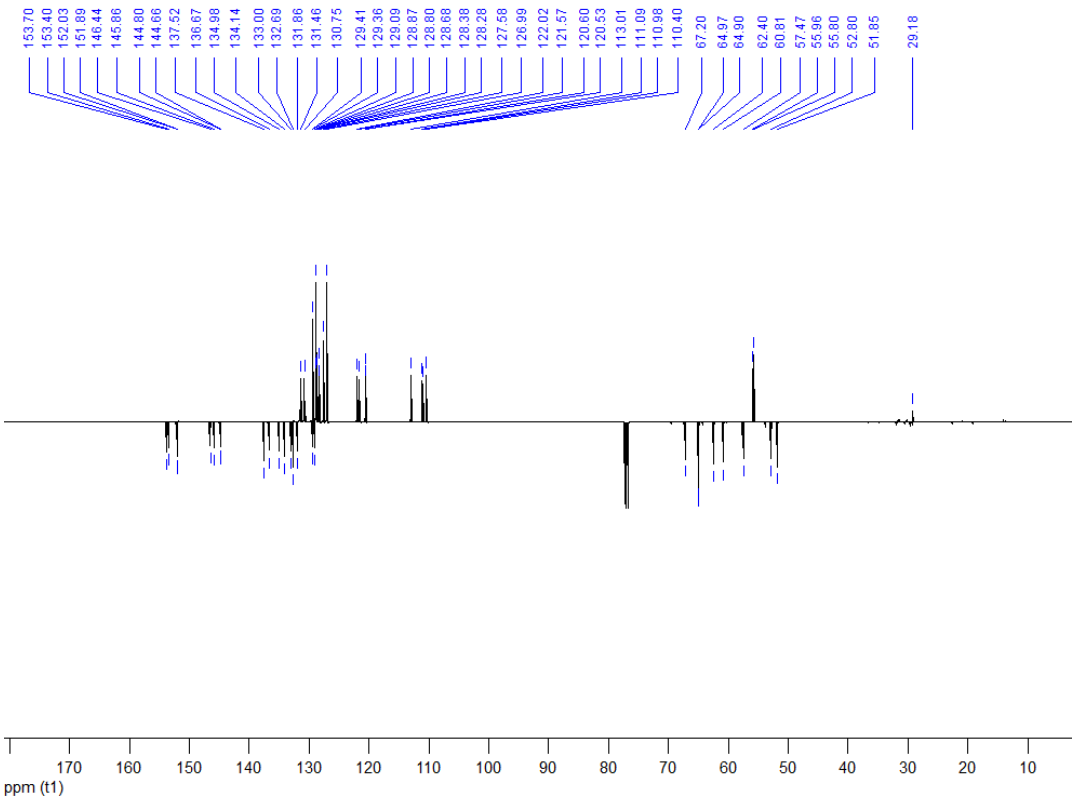


δ_H (500 MHz, $CDCl_3$).

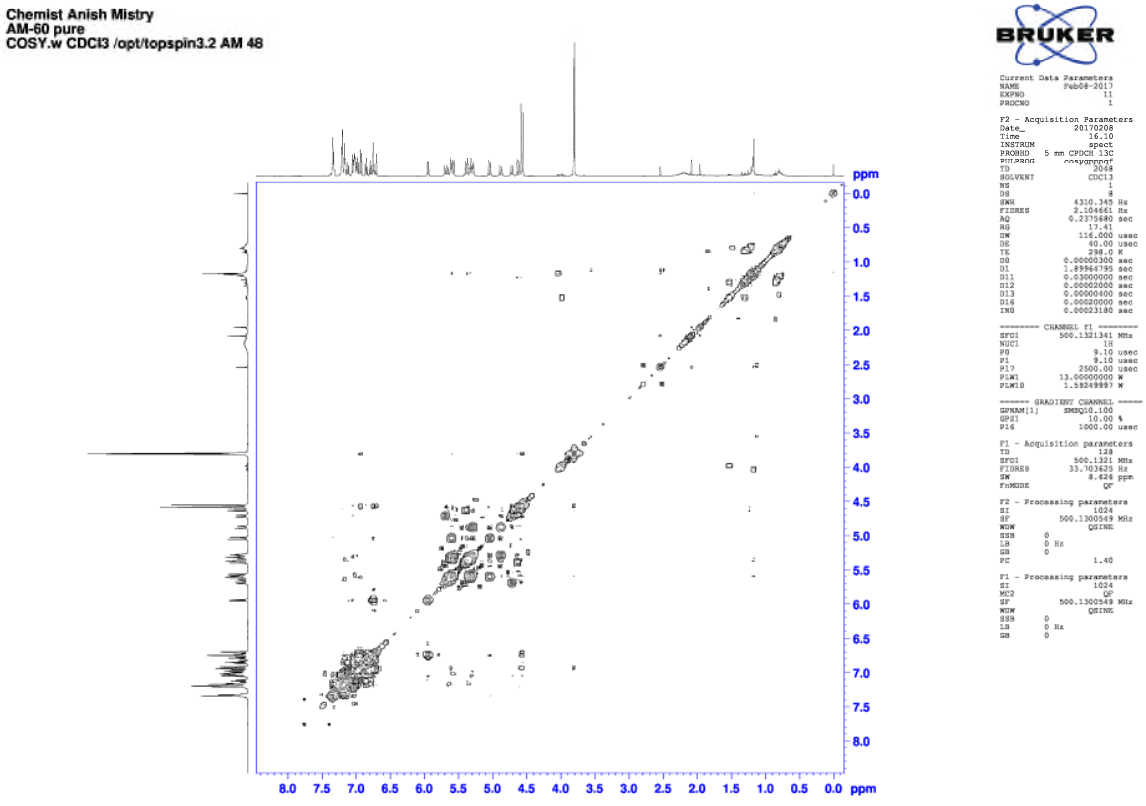




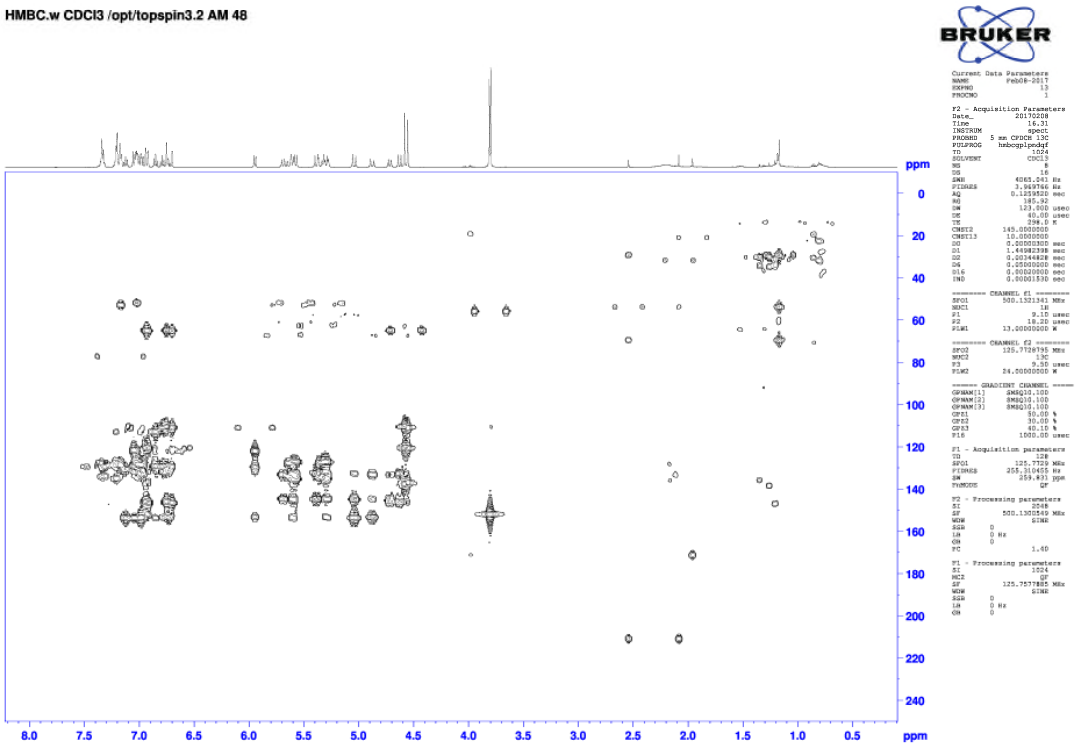
δ_C (126 MHz, $CDCl_3$).



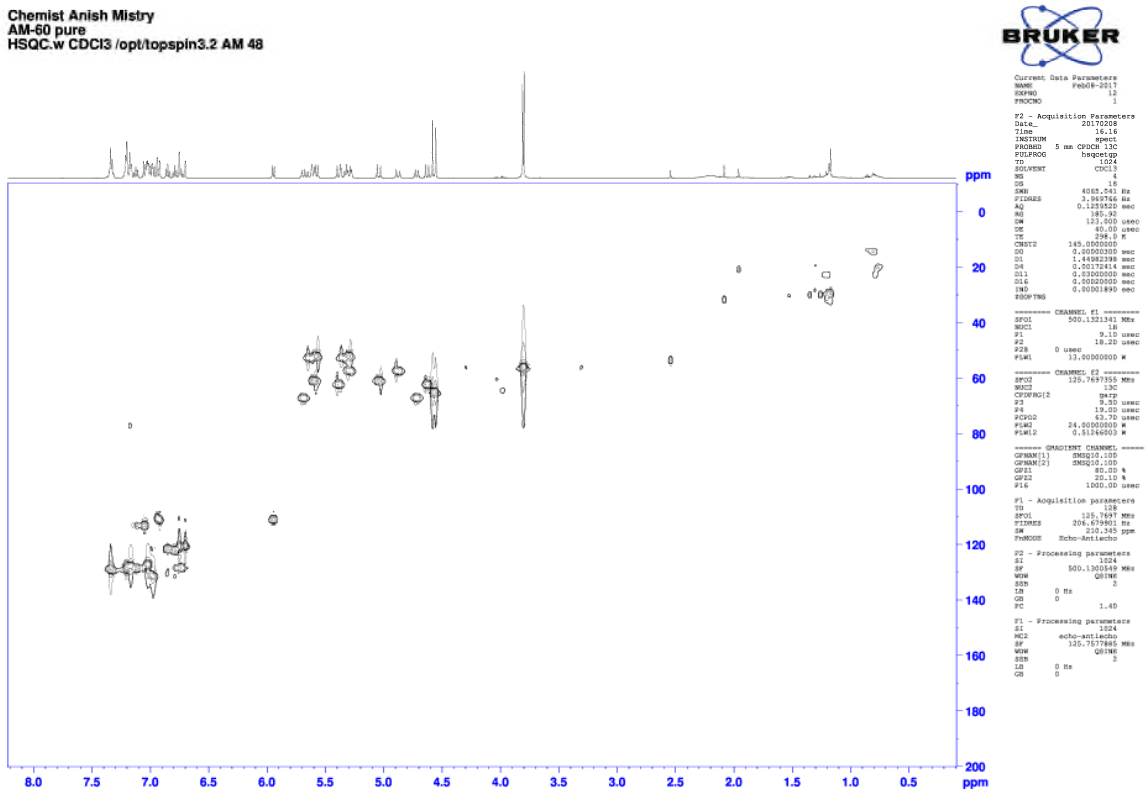
COSY:



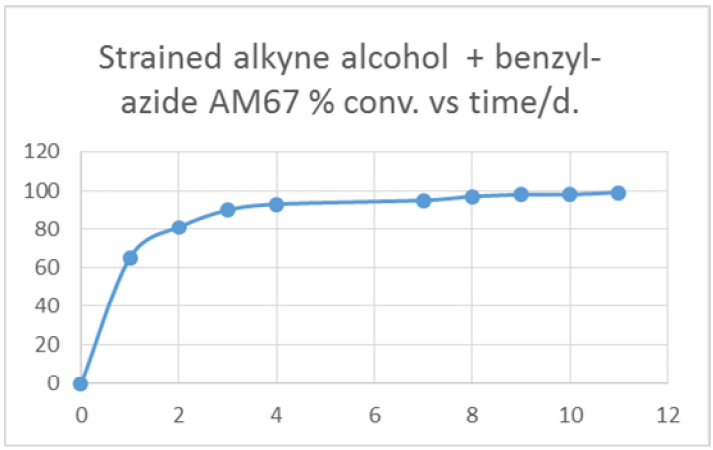
HMBC:


HMBC.w CDCl3 /opt/topspin3.2 AM 48
BRUKER
ppm
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
ppm

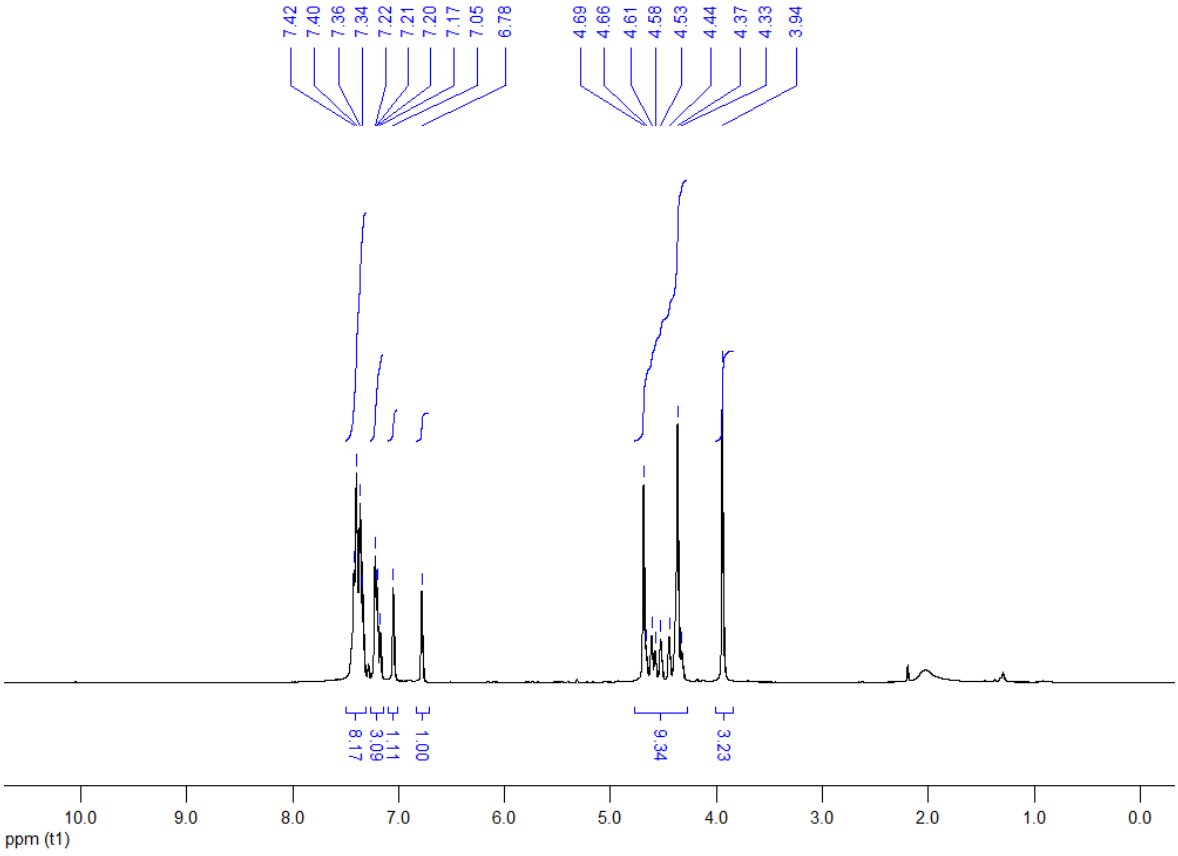
HSQC:


Chemist Anish Mistry
AM-60 pure
HSQC.w CDCl3 /opt/topspin3.2 AM 48
BRUKER
ppm
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
ppm

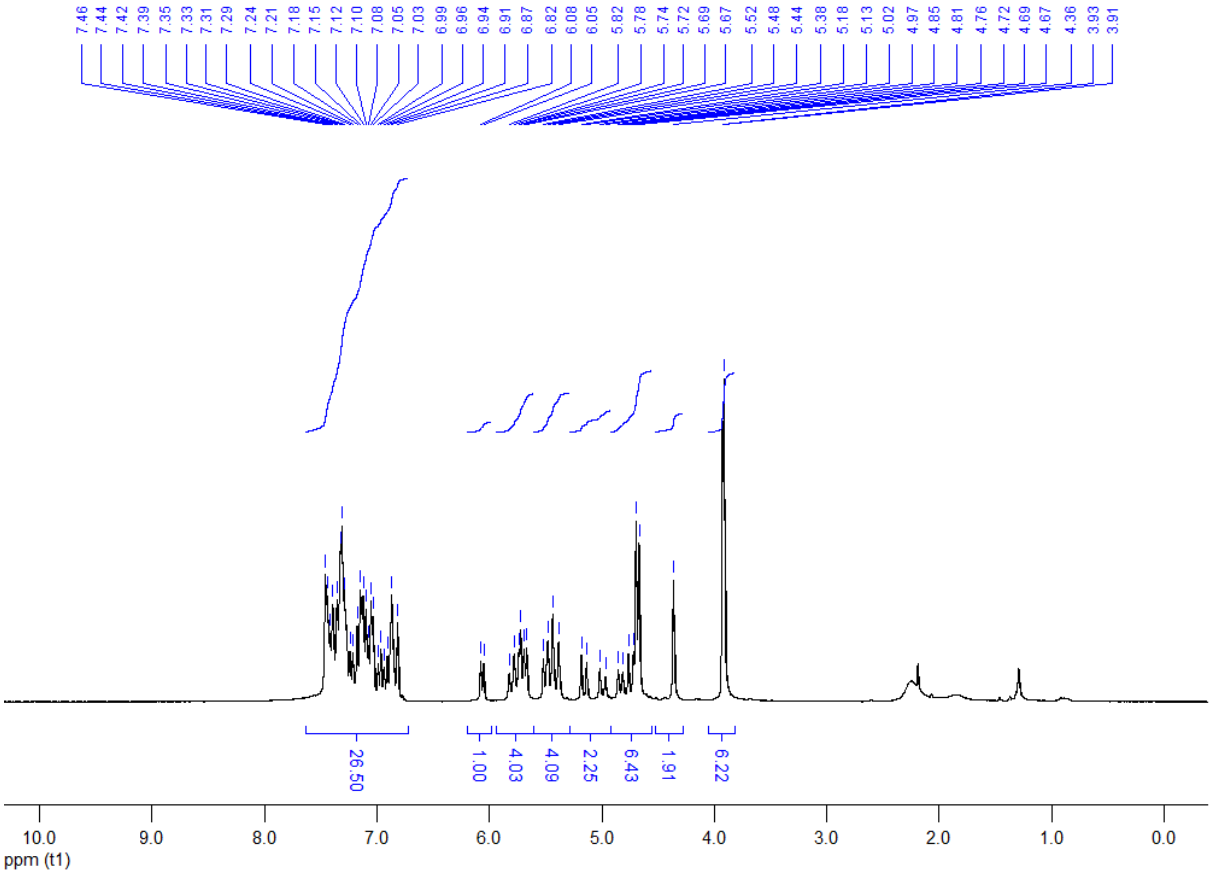
AM67 Is conversion over time; some error likely due to overlaps but start and finish NMRs show extent of conversion. Characteristic peaks were the OCH_2 and NCH_2 peaks of the product and the OCH_2 peaks of the strained alkyne. Day 1; 65%, day 2; 81%, day 3; 90%, dau 4; 93%, day 7; 95%, day 8; 97%, day 9; 98%, day 10; 98%, day 11; 99% conversion.



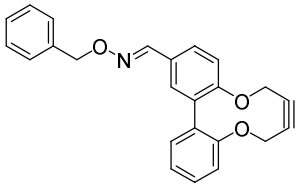
NMR at start (day 0): δ_H (300 MHz, $CDCl_3$).



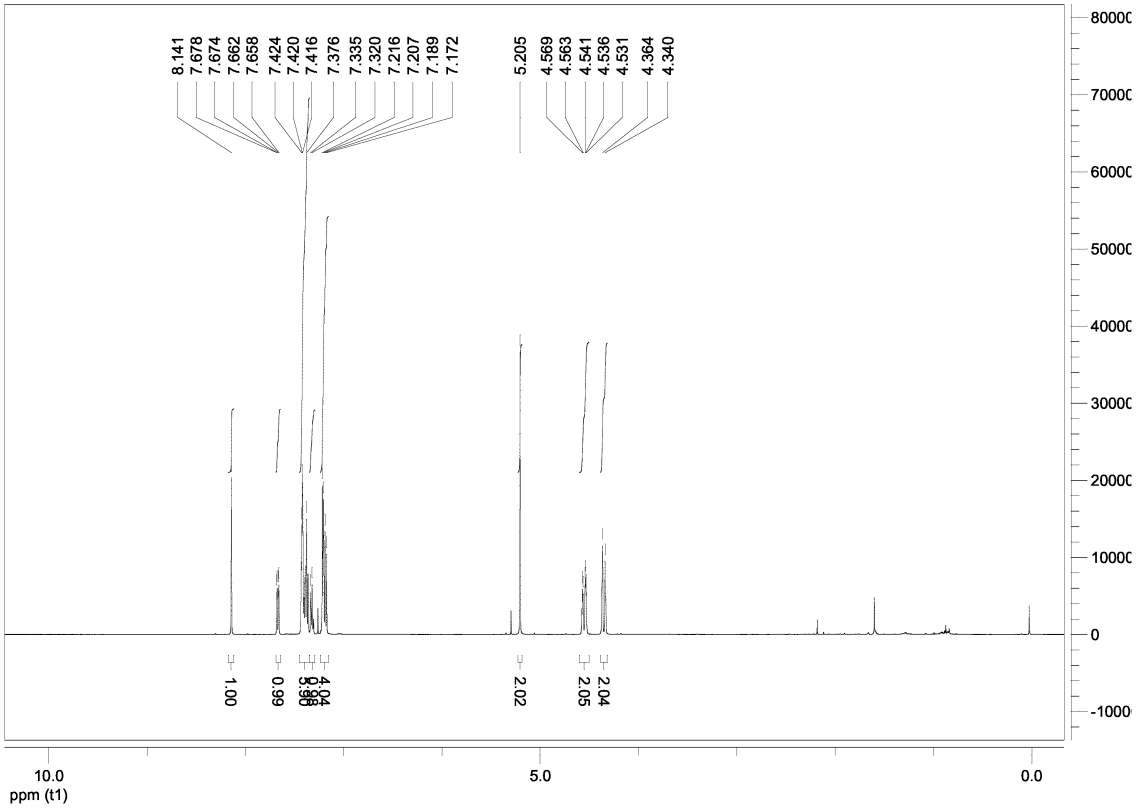
NMR at end (day 11); ca. 99% conversion: δ_H (300 MHz, $CDCl_3$).



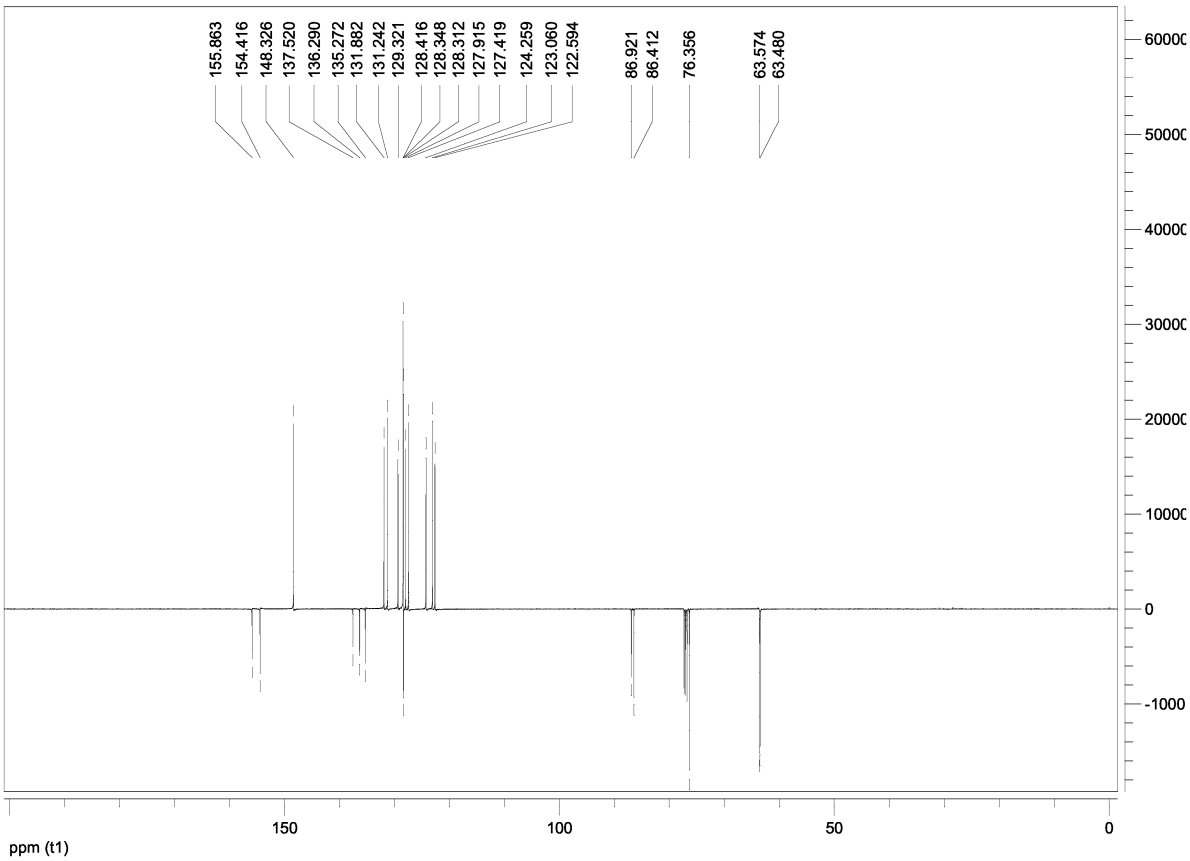
Oxime ether 29 SF271.



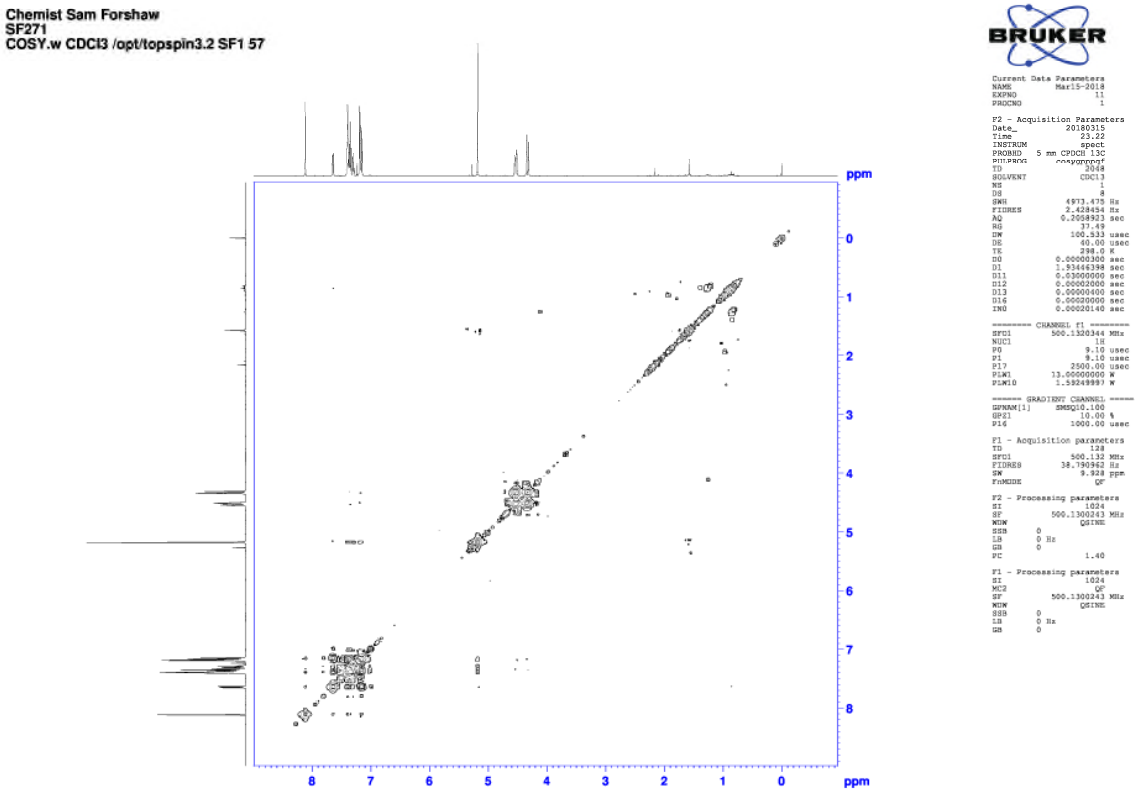
δ_H (500 MHz, $CDCl_3$).



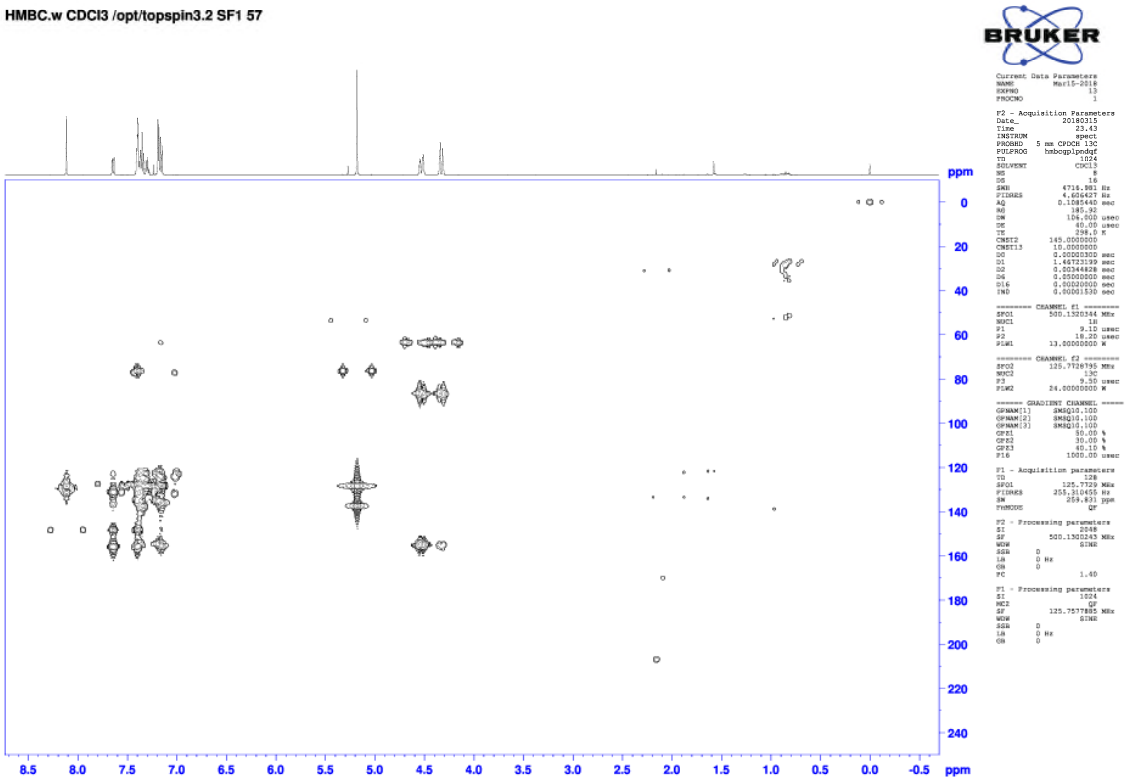
δ_C (126 MHz, $CDCl_3$).



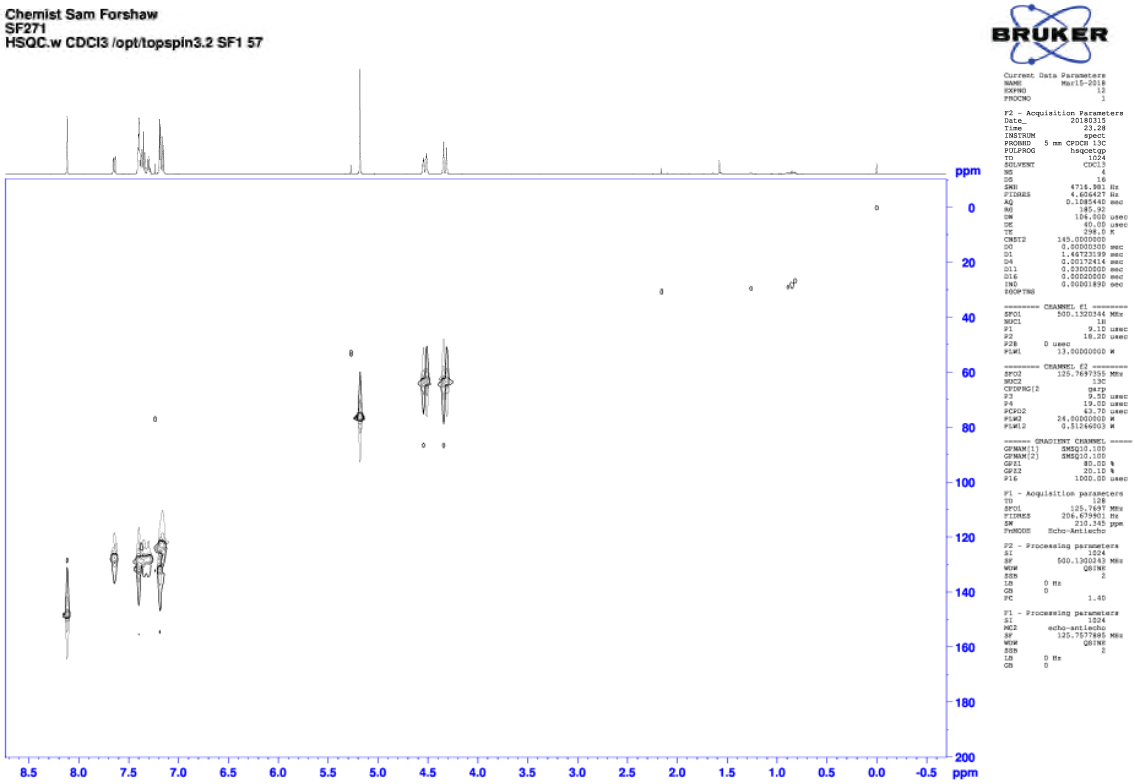
COSY.



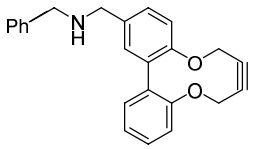
HMBC.


HMBC.w CDCl3 /opt/topspin3.2 SF1 57
BRUKER
ppm
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 ppm
0 20 40 60 80 100 120 140 160 180 200 220 240

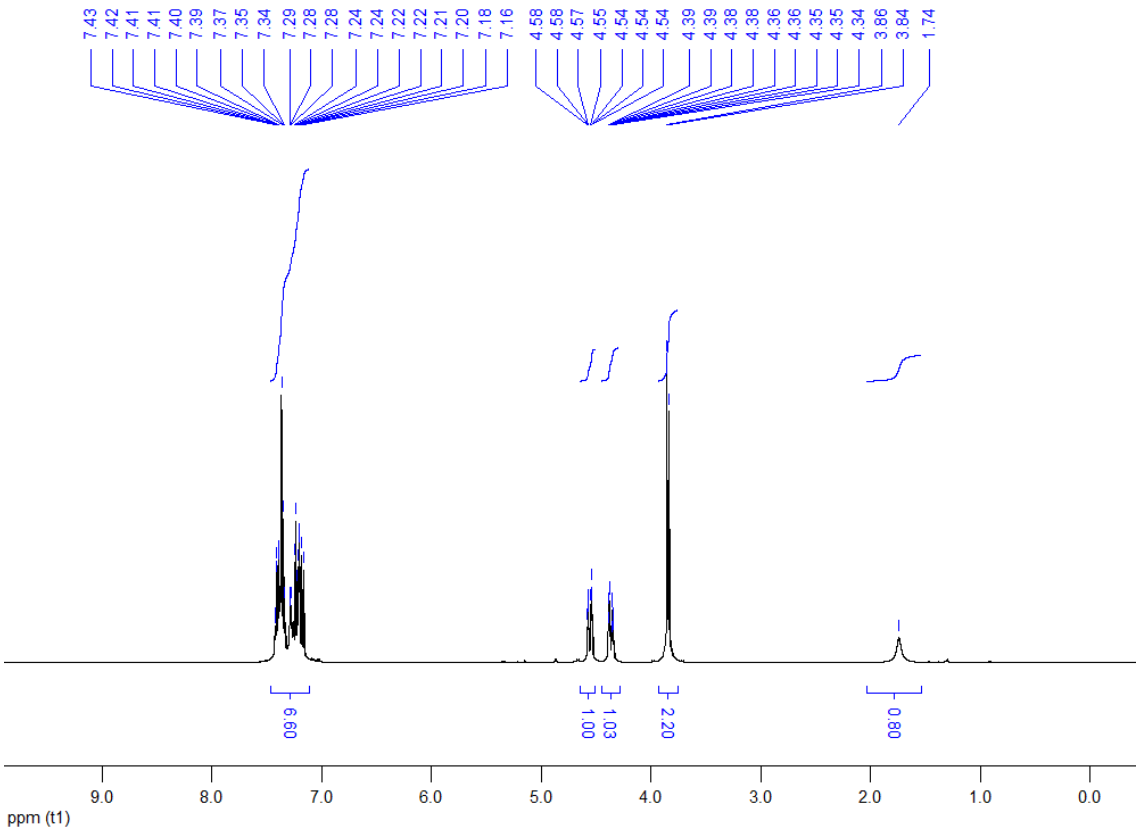
HMQC.


Chemist Sam Forshaw
SF271
HSQC.w CDCl3 /opt/topspin3.2 SF1 57
BRUKER
ppm
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 ppm
0 20 40 60 80 100 120 140 160 180 200

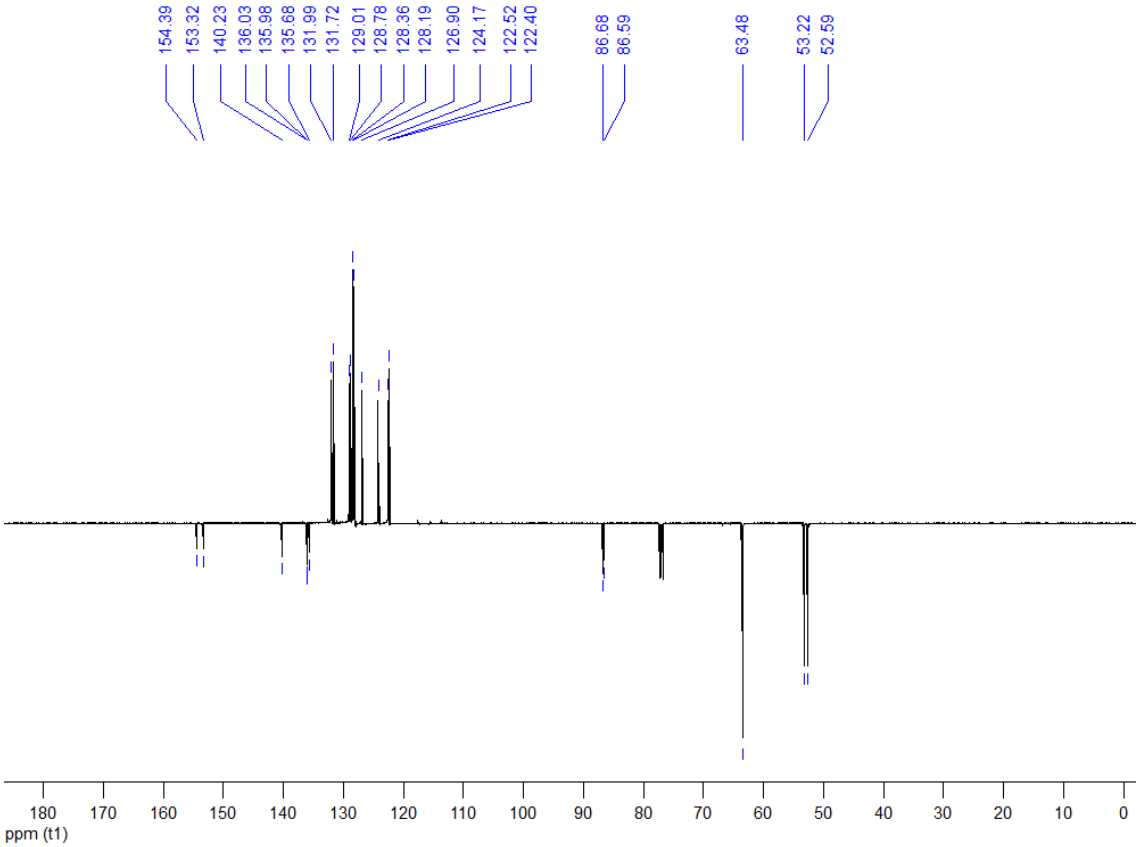
Benzyl amine derivative 30. AM66.



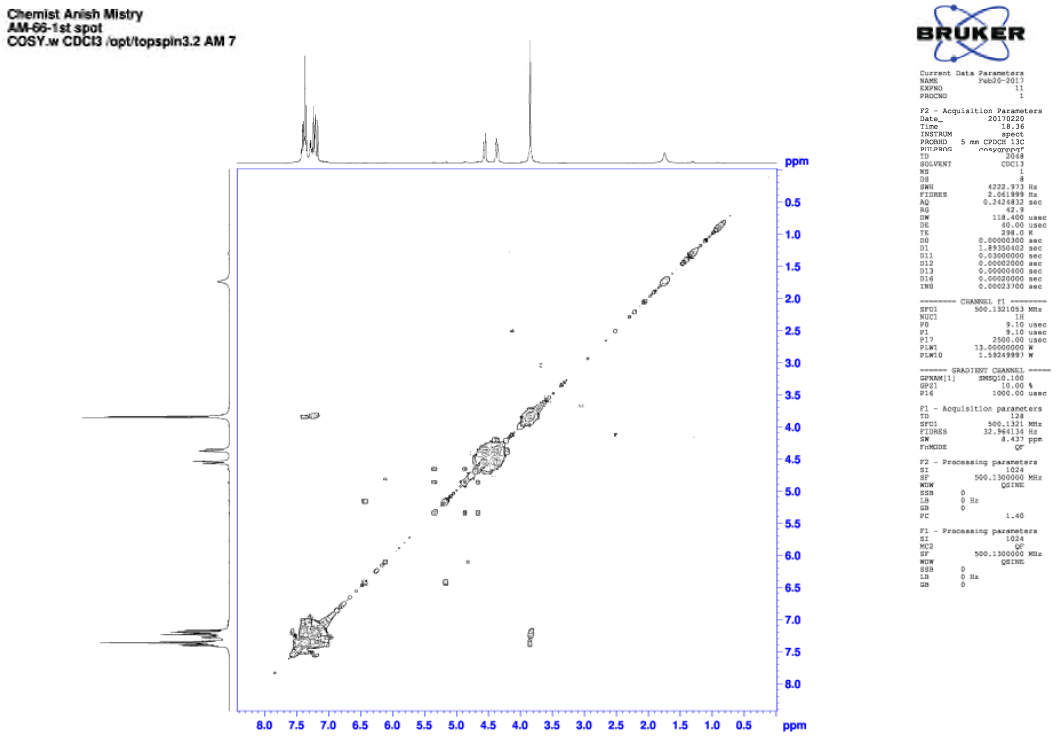
δ_H (500 MHz, $CDCl_3$).



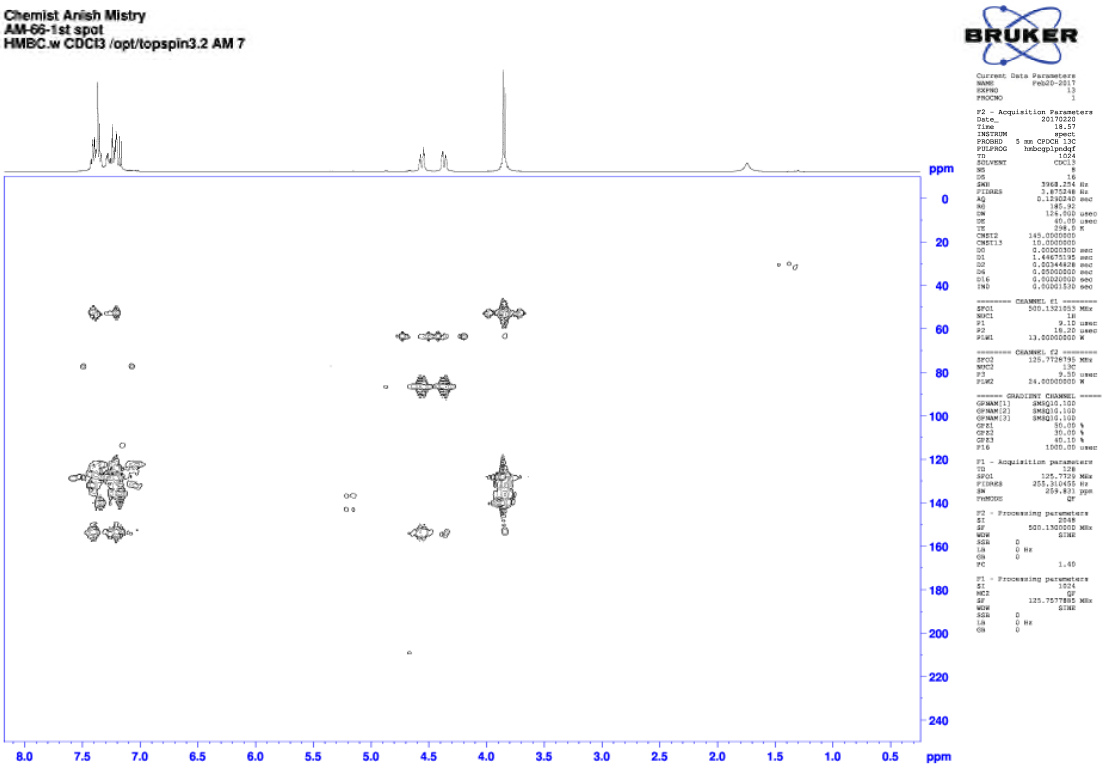
δ_C (126 MHz, $CDCl_3$).



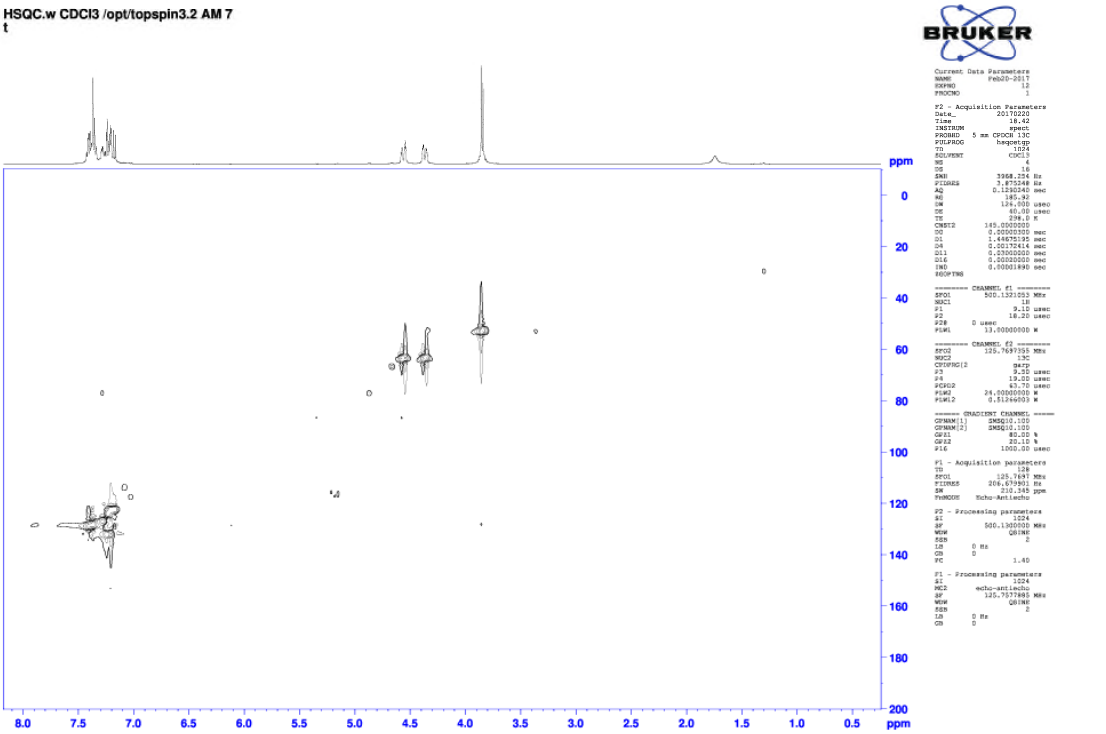
COSY:



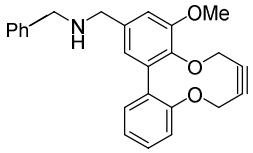
HMBC:


Chemist Anish Mistry
AM-66-1st spot
HMBC.w CDCl3 /opt/topspin3.2 AM 7
BRUKER
ppm
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
20
40
60
80
100
120
140
160
180
200
220
240

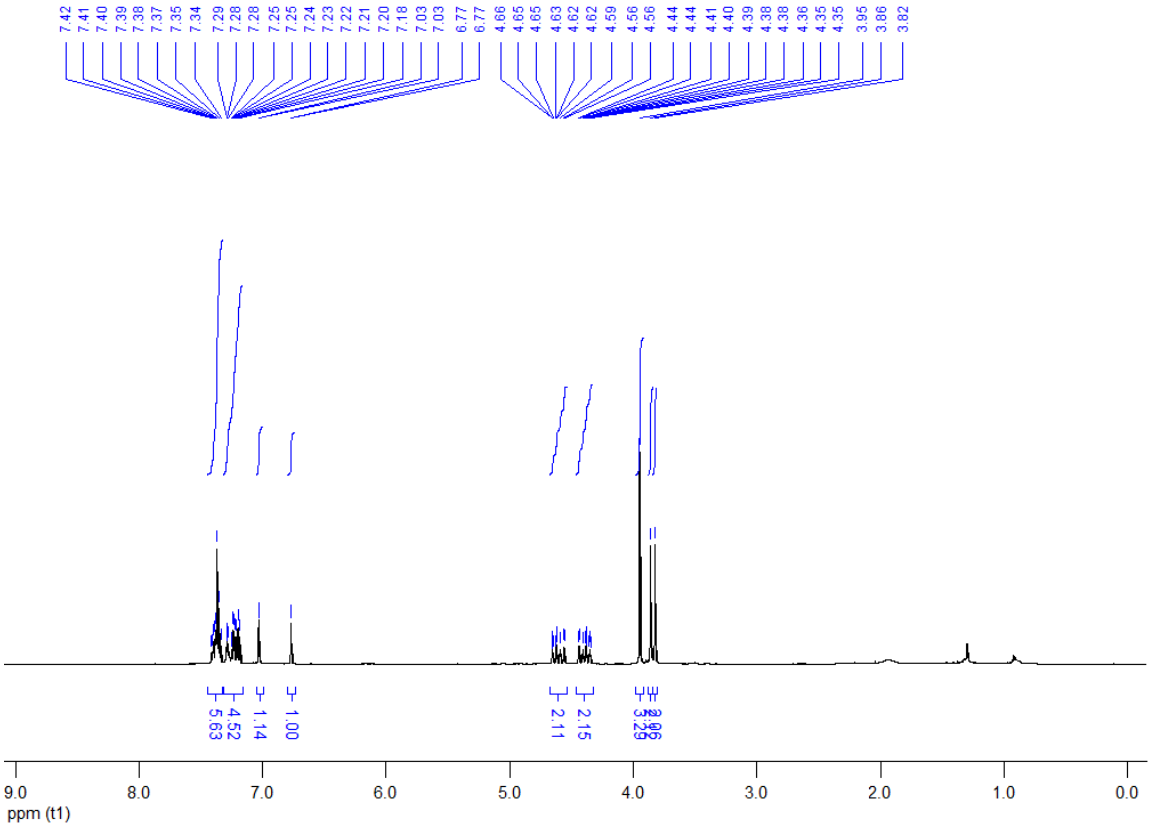
HSQC:


HSQC.w CDCl3 /opt/topspin3.2 AM 7
t
BRUKER
ppm
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
20
40
60
80
100
120
140
160
180
200

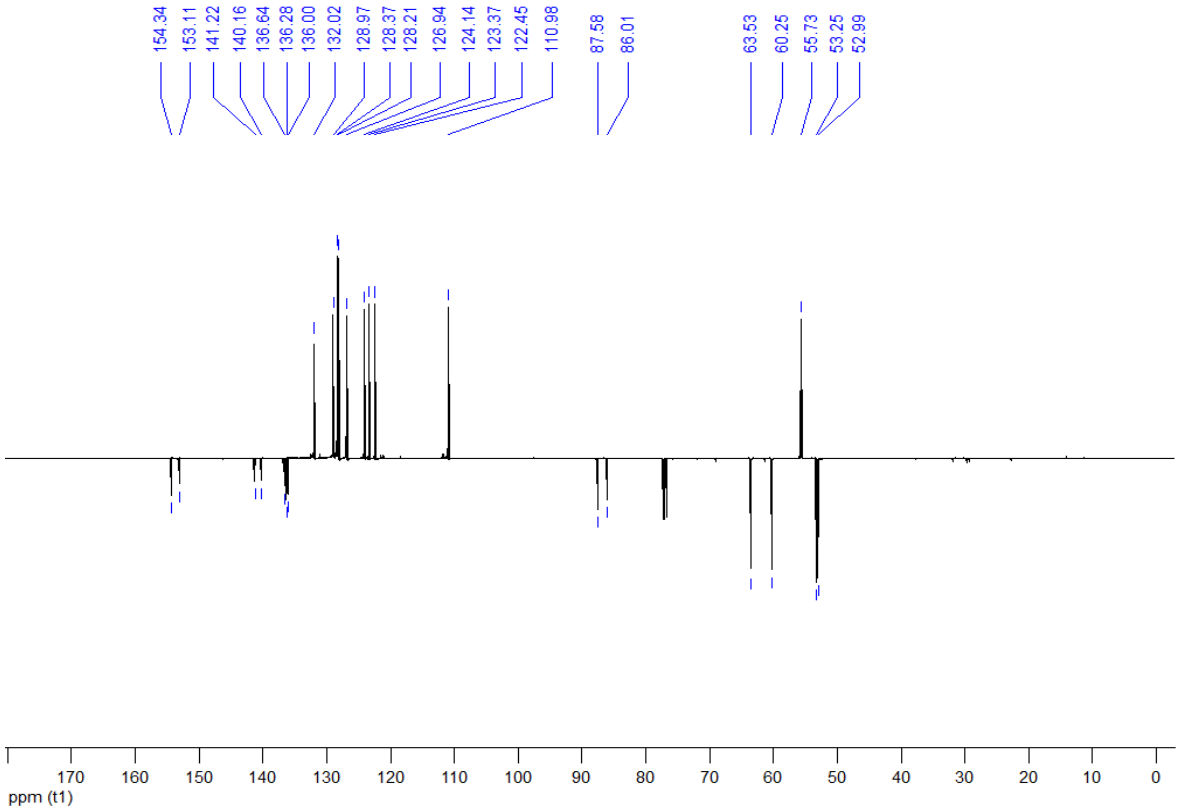
Benzyl amine derivative 31. AM70



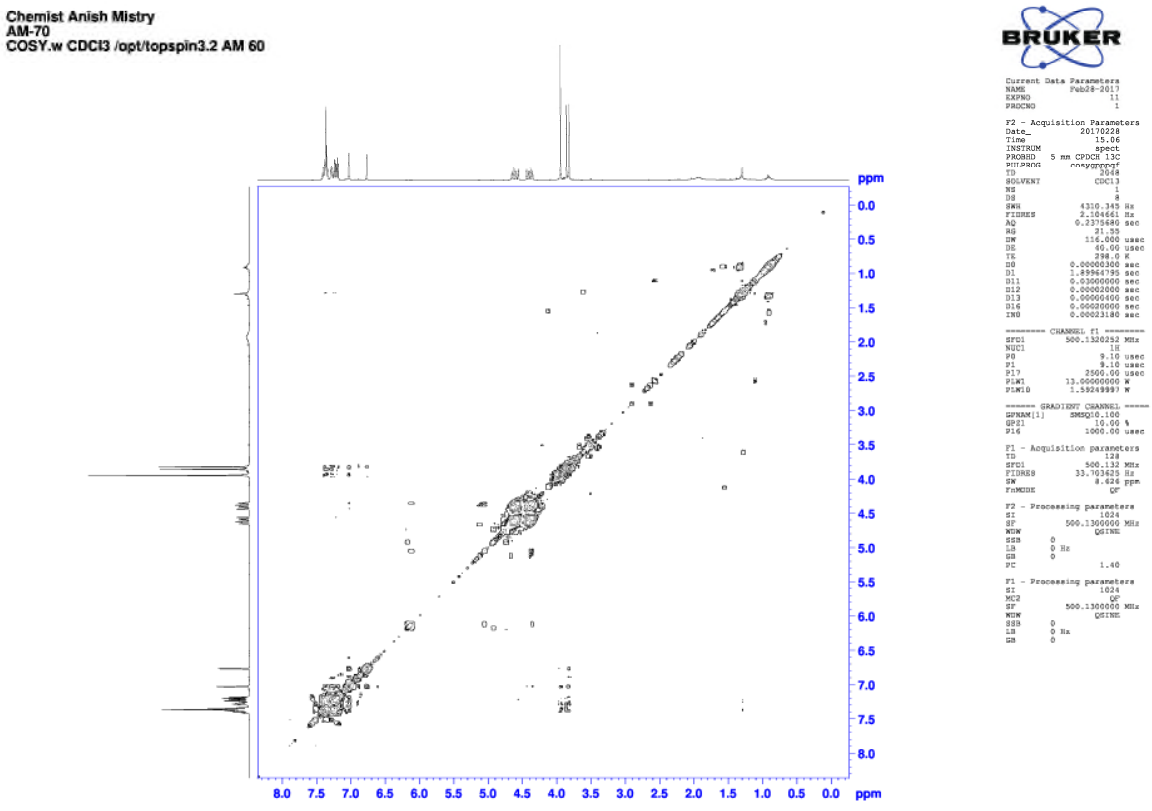
δ_H (500 MHz, $CDCl_3$).



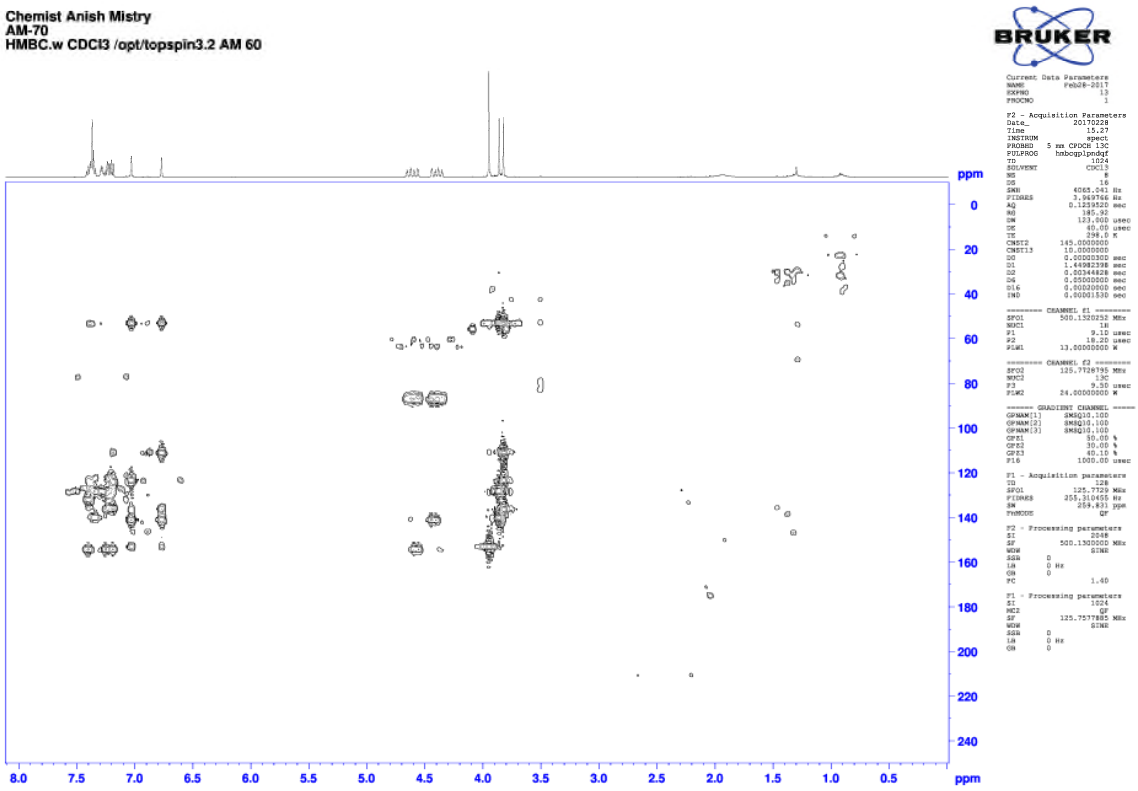
δ_C (126 MHz, $CDCl_3$).



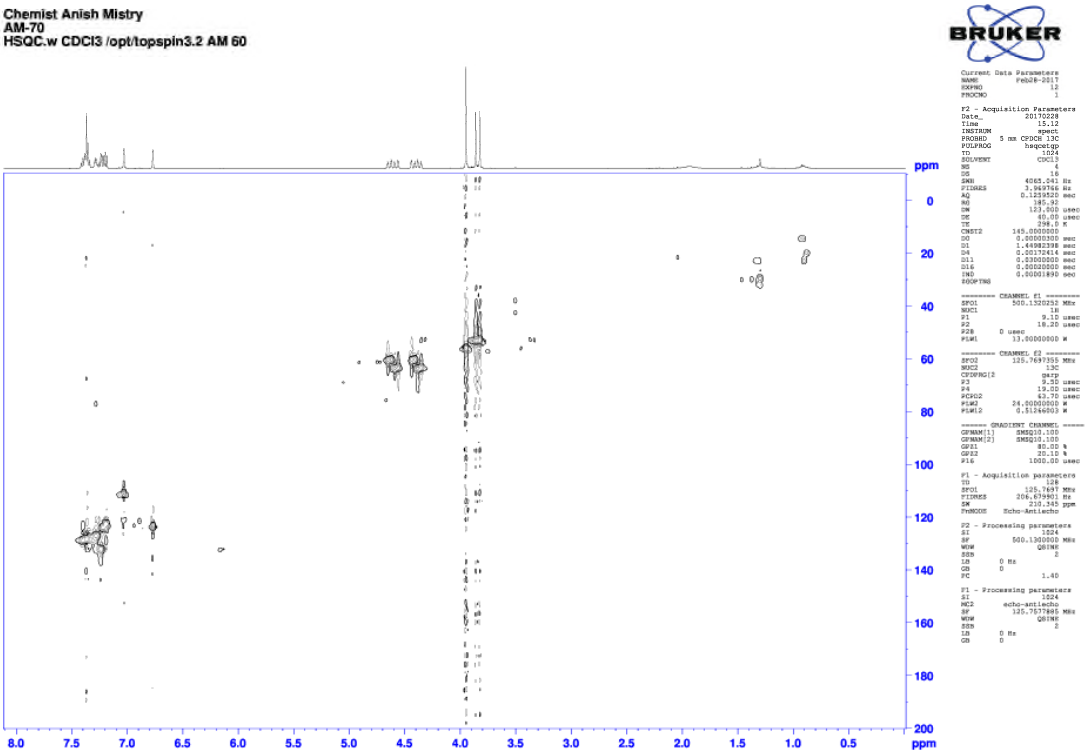
COSY:



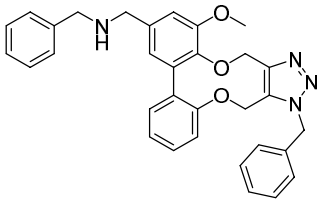
HMBC:


Chemist Anish Mistry
AM-70
HMBC.w CDCl3 /opt/topspin3.2 AM 60
BRUKER
ppm
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

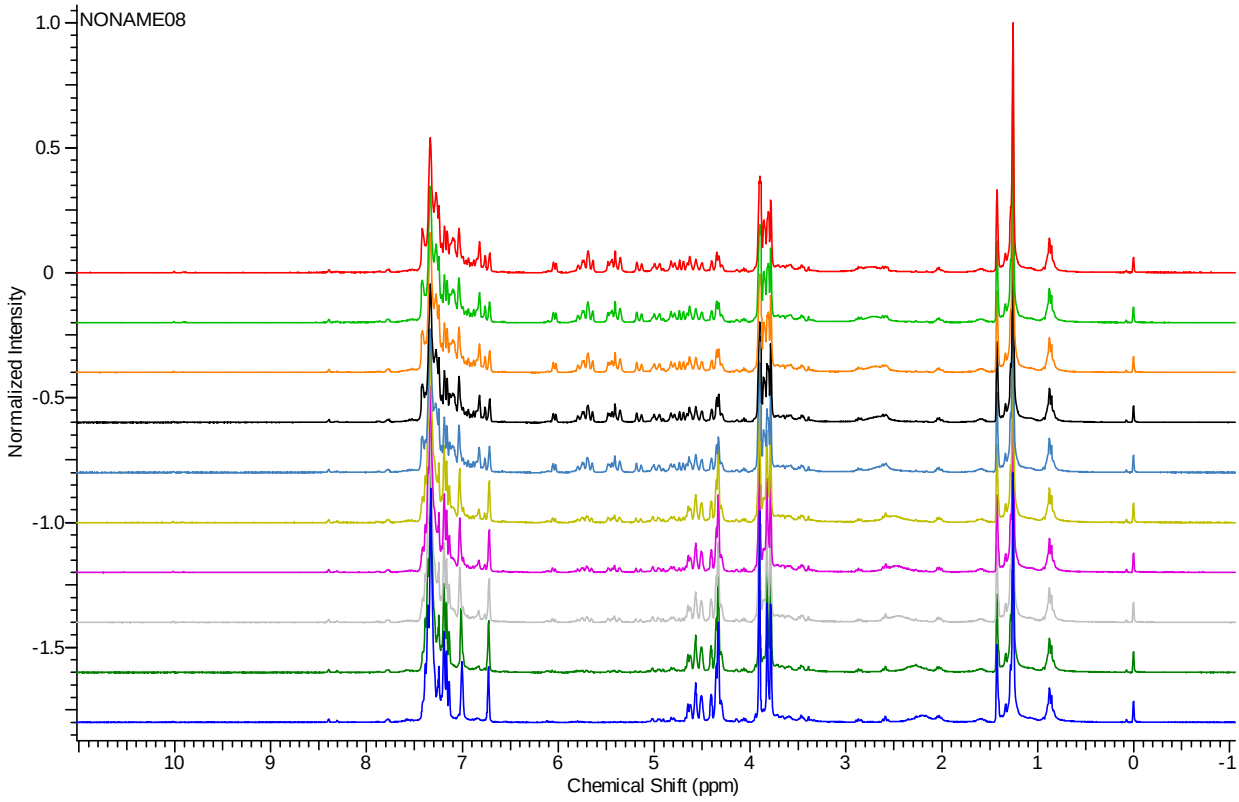
HSQC:


Chemist Anish Mistry
AM-70
HSQC.w CDCl3 /opt/topspin3.2 AM 60
BRUKER
ppm
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

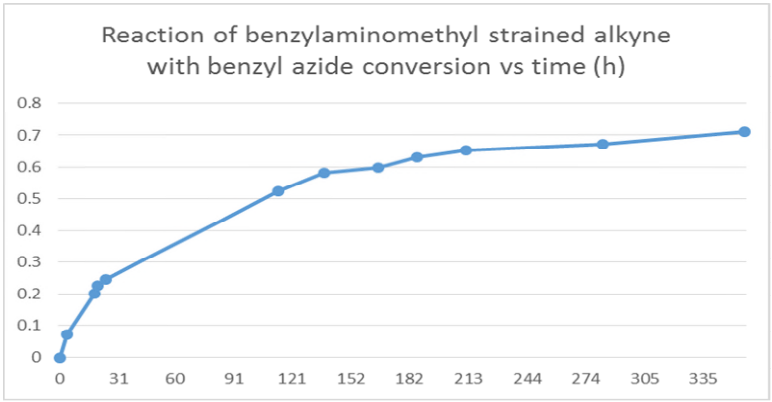
Cycloaddition to give the compound below (mixture of isomers) SF224.



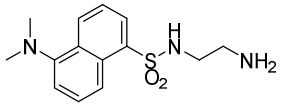
To a solution of alkyne **16** (16 mg, 0.041mmol, 1 eq) in $CDCl_3$ (0.5 mL), benzylazide **20** (5.8 mg, 5.4 µL, 0.051 mmol, 1.2 eq) was added and the reaction was followed by NMR. The product was not isolated.



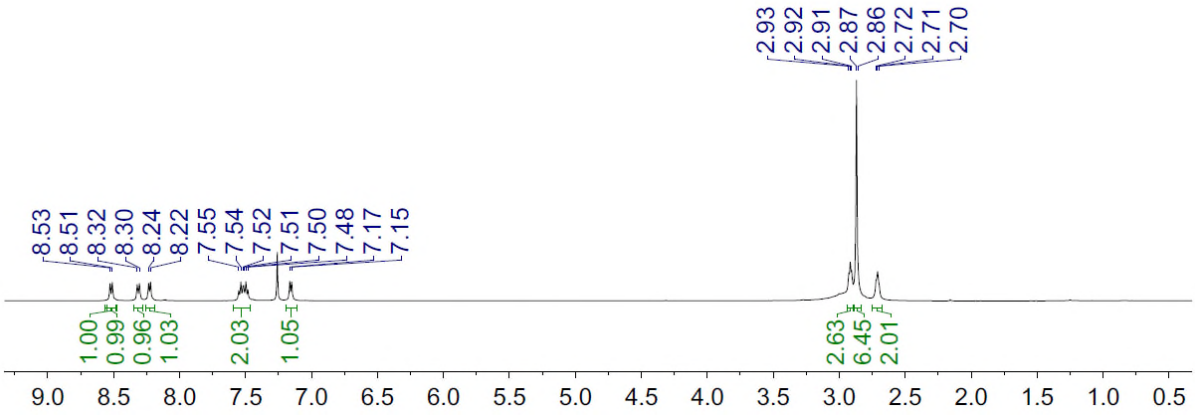
Times are 1) 0 h, 2) 4h , 3) 18 h, 4) 20.75 h, 5) 24 h, 6) 114.5 h, 7) 138.5 h, 8) 166.5 h, 9) 186.5 h, 10) 212 h, 13) 283 h.



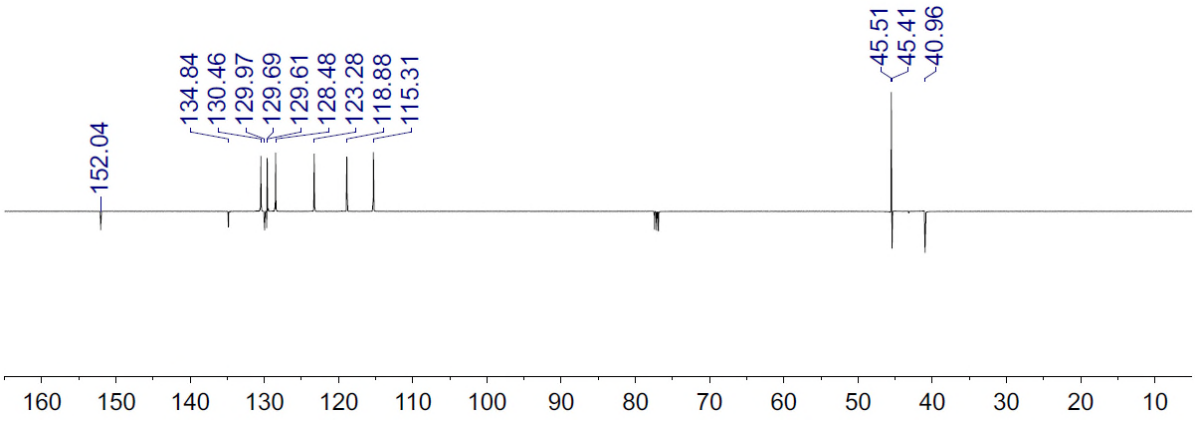
Dansyl amine precursor 34 (RK-2-182):



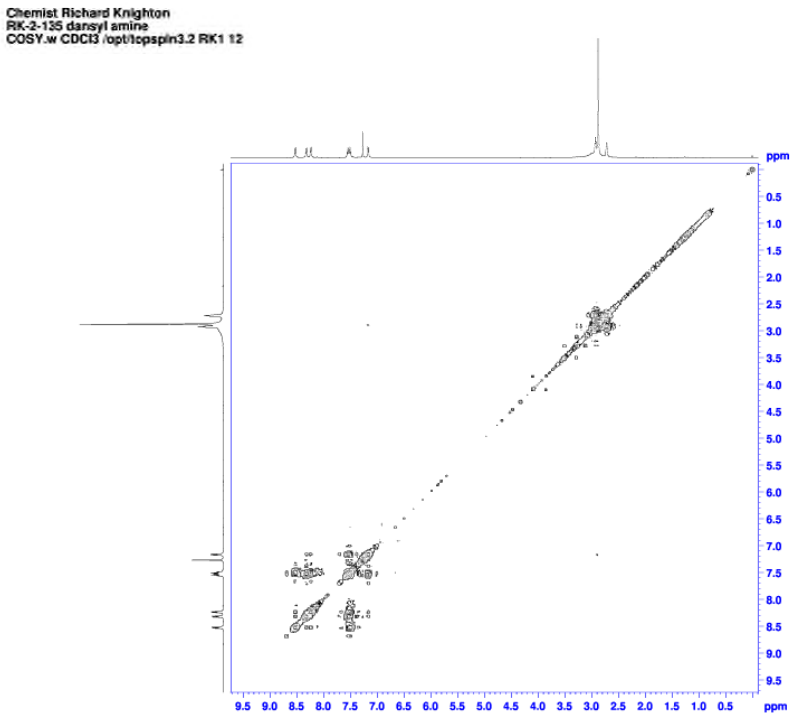
δ_H (500 MHz, $CDCl_3$).



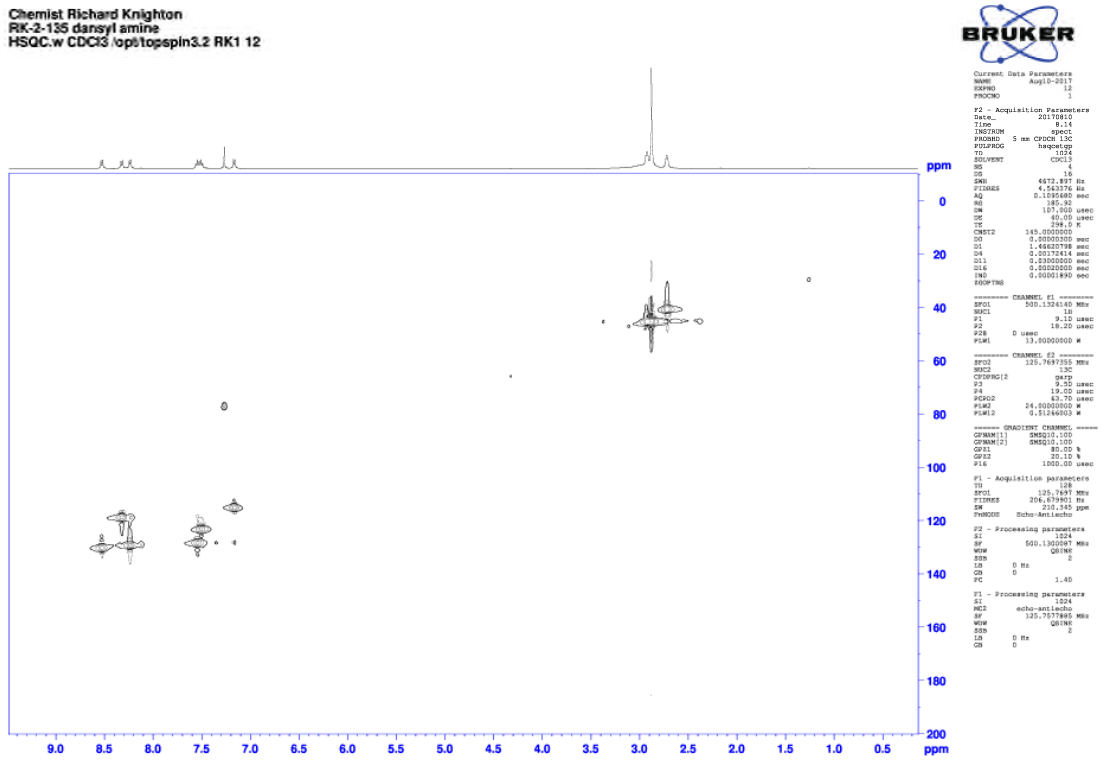
δ_C (126 MHz, $CDCl_3$).



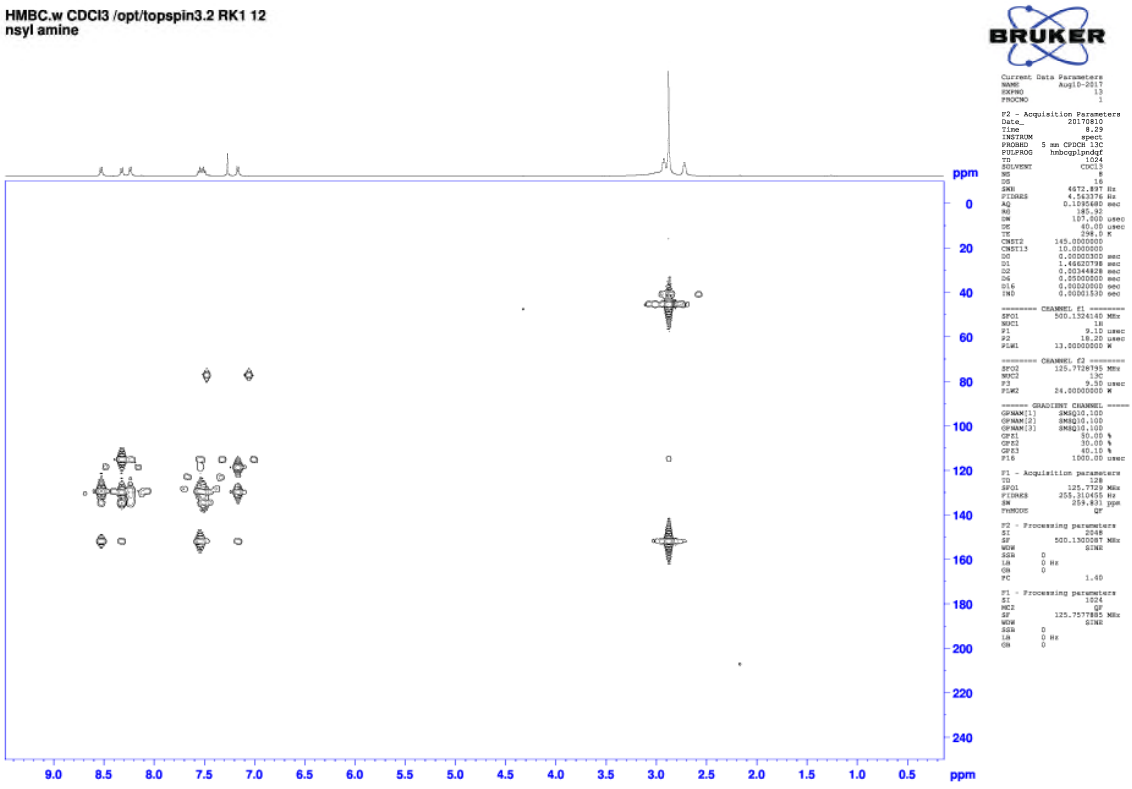
COSY.


Chemist Richard Knighton
RK-2-135 dansyl amine
COSY.w CDCl3 /opt/topspin3.2 RK1 12
BRUKER
ppm
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
ppm

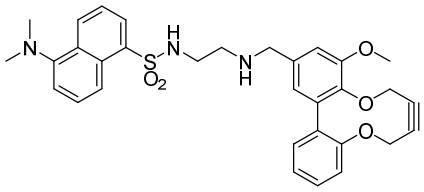
HMQC.


Chemist Richard Knighton
RK-2-135 dansyl amine
HSQC.w CDCl3 /opt/topspin3.2 RK1 12
BRUKER
ppm
0
20
40
60
80
100
120
140
160
180
200
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
ppm

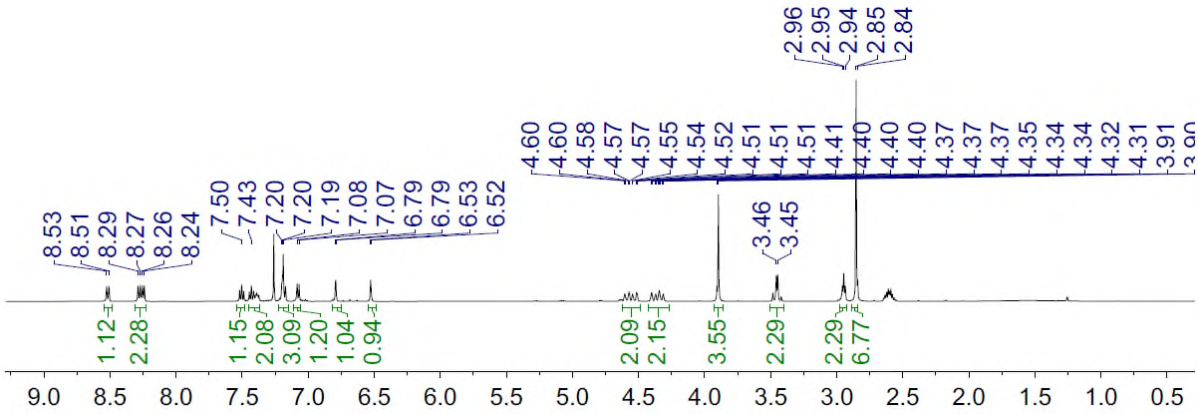
HMBC.



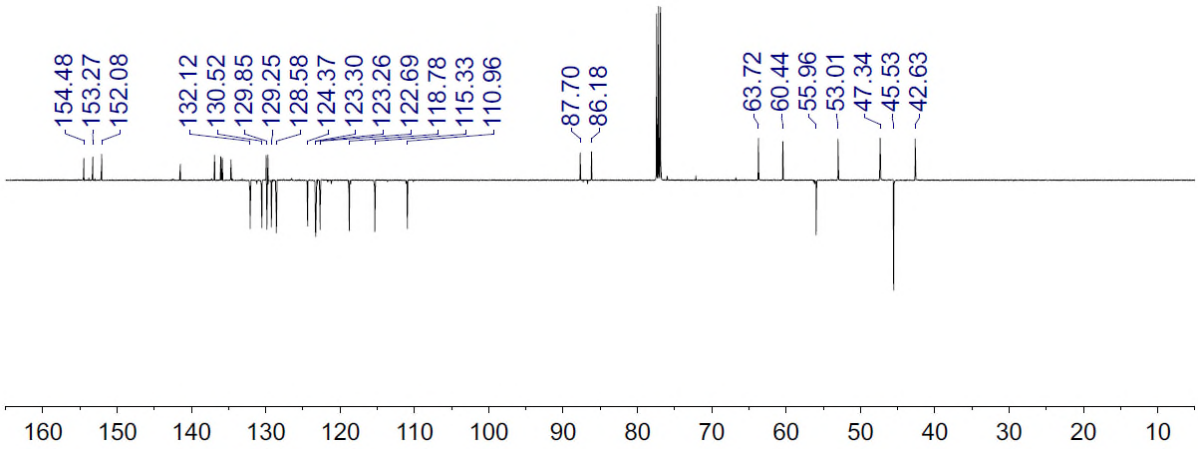
Dansyl strained alkyne 35 (RK-2-184):



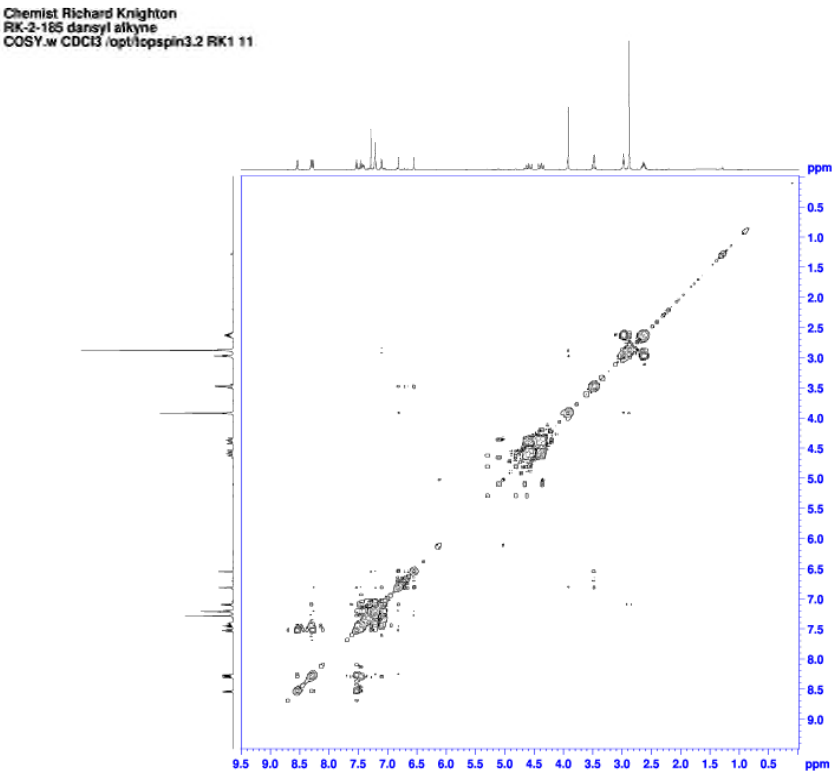
δ_H (500 MHz, $CDCl_3$).



δ_c (126 MHz, $CDCl_3$).


154.48
153.27
152.08
132.12
130.52
129.85
129.25
128.58
124.37
123.30
123.26
122.69
118.78
115.33
110.96
87.70
86.18
63.72
60.44
55.96
53.01
47.34
45.53
42.63
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

COSY.


Chemist Richard Knighton
RK-2-185 dansyl alkyne
COSY.w CDCl3 /opt/topspin3.2 RK1 11
BRUKER
ppm
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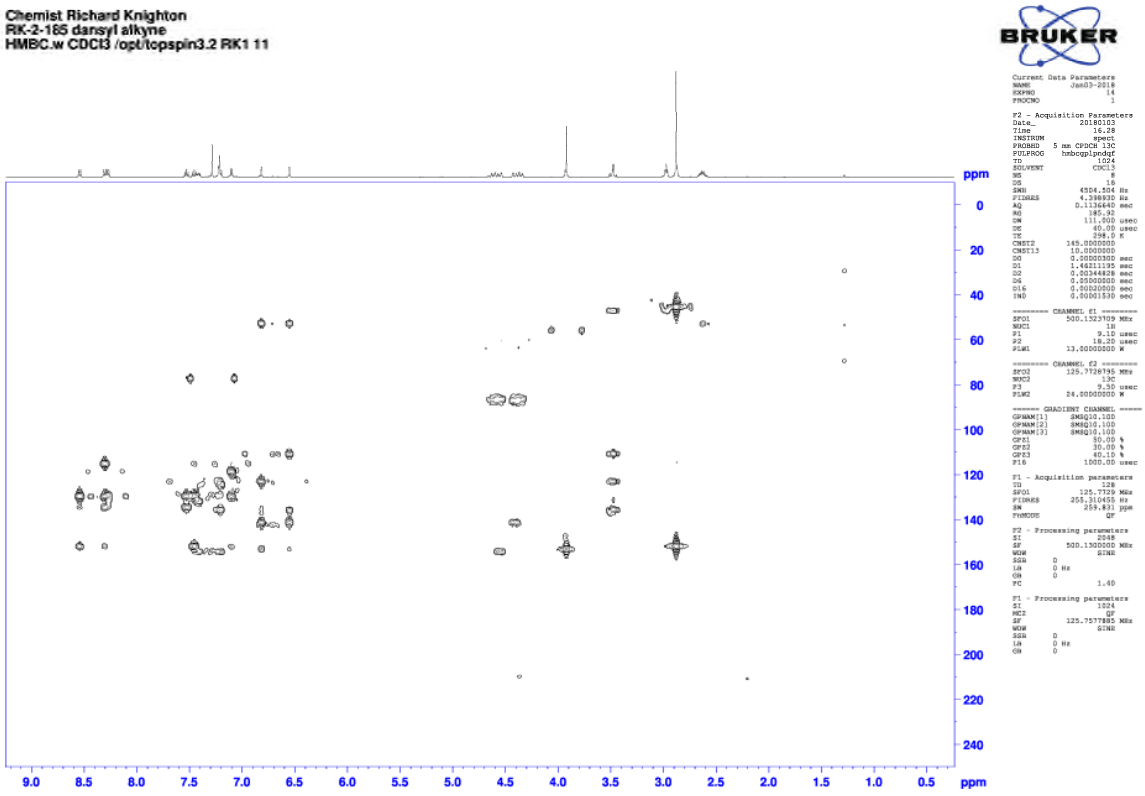
HMBC.


Chemist Richard Knighton
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BRUKER
ppm
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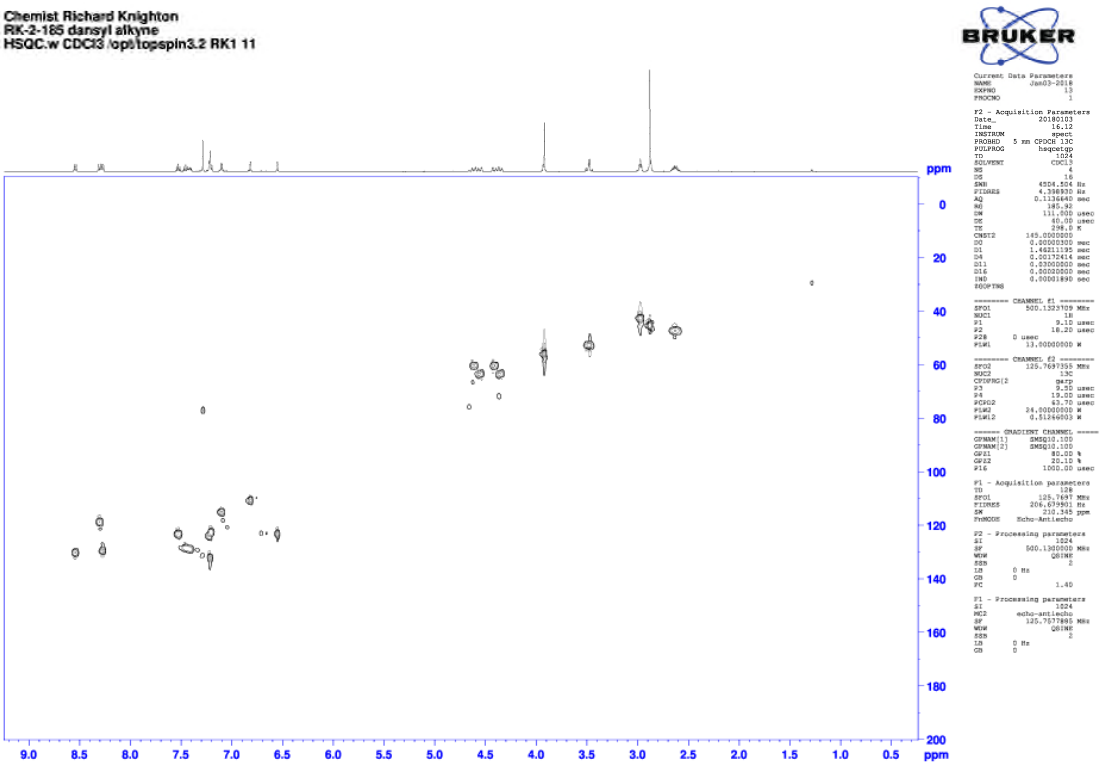
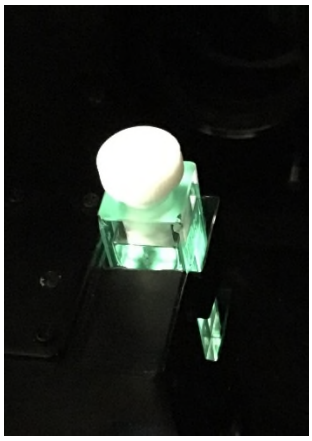
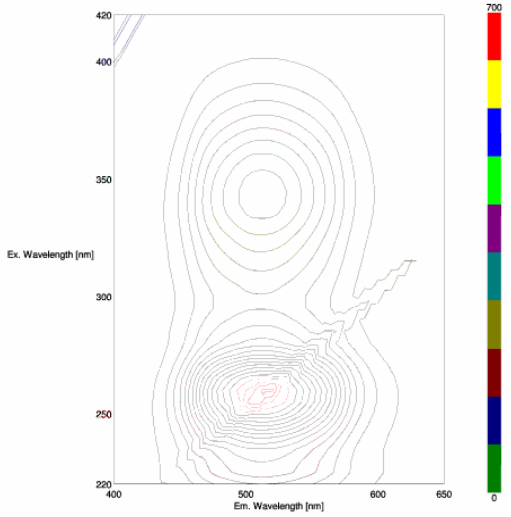
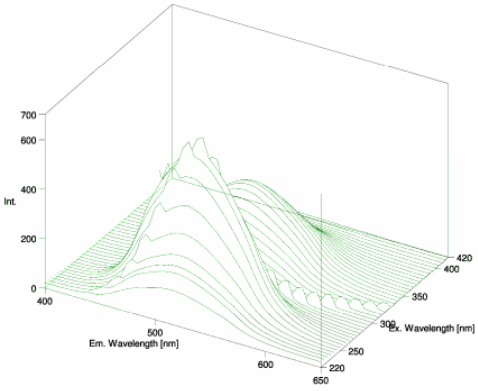


Fluorescence spectra and images.







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Serial No.	C377660822
Measurement Mode	Emission Spectrum
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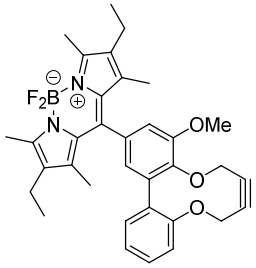
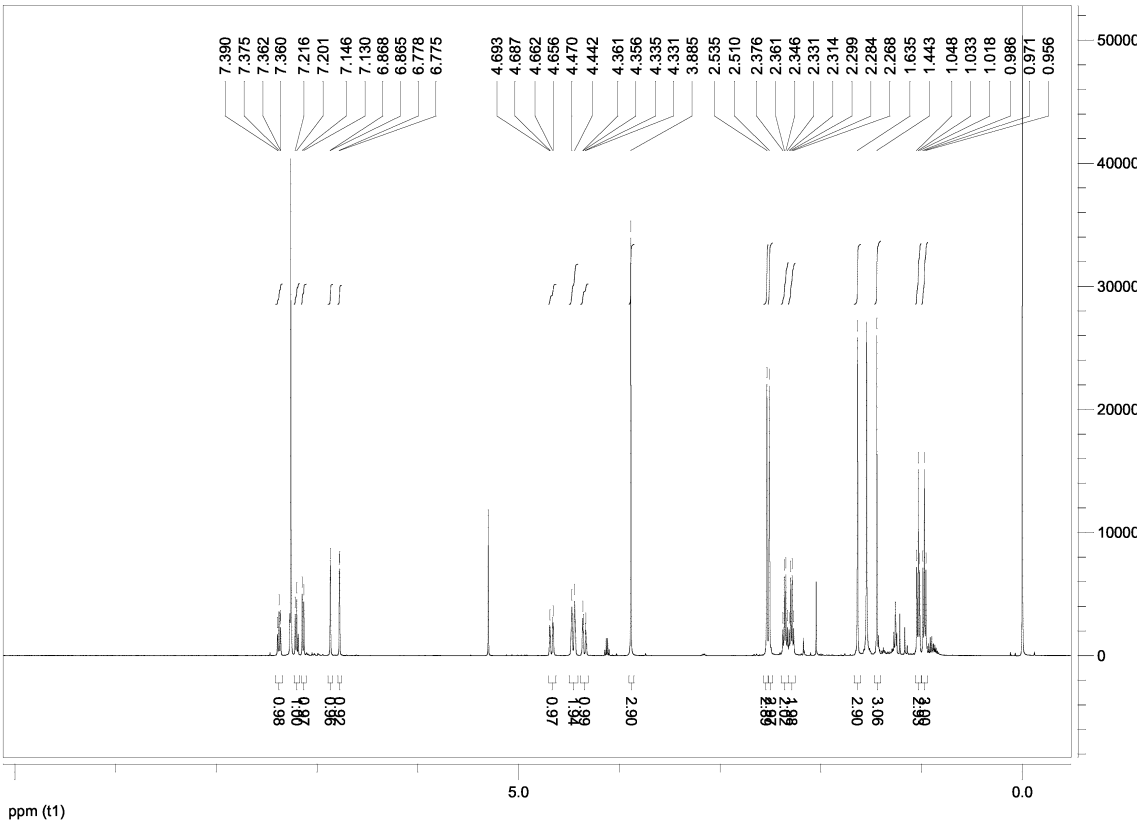
Band width(Em)	3 nm
Response	1 sec
Sensitivity	Medium
Measurement range	400 - 650 nm
Data pitch	5nm
Excitation Wavelength	355.0 nm
Scanning speed	200 nm/min
Sample ID	17
No. of cycle	1
Sample name	
Operator	Chemistry - JCEPS
Comment	

Date	17/11/2017 14:37
File name	RCK TEST DANSYL ALKYNE TEST#017.jwb
Model	FP-6500
Serial No.	C377660822
Measurement Mode	Emission Spectrum
Band width(Ex)	3 nm
Band width(Em)	3 nm
Response	1 sec
Sensitivity	Medium
Measurement range	400 - 650 nm
Data pitch	5nm
Excitation Wavelength	355.0 nm
Scanning speed	200 nm/min
Sample ID	17
No. of cycle	1
Sample name	
Operator	Chemistry - JCEPS
Comment	

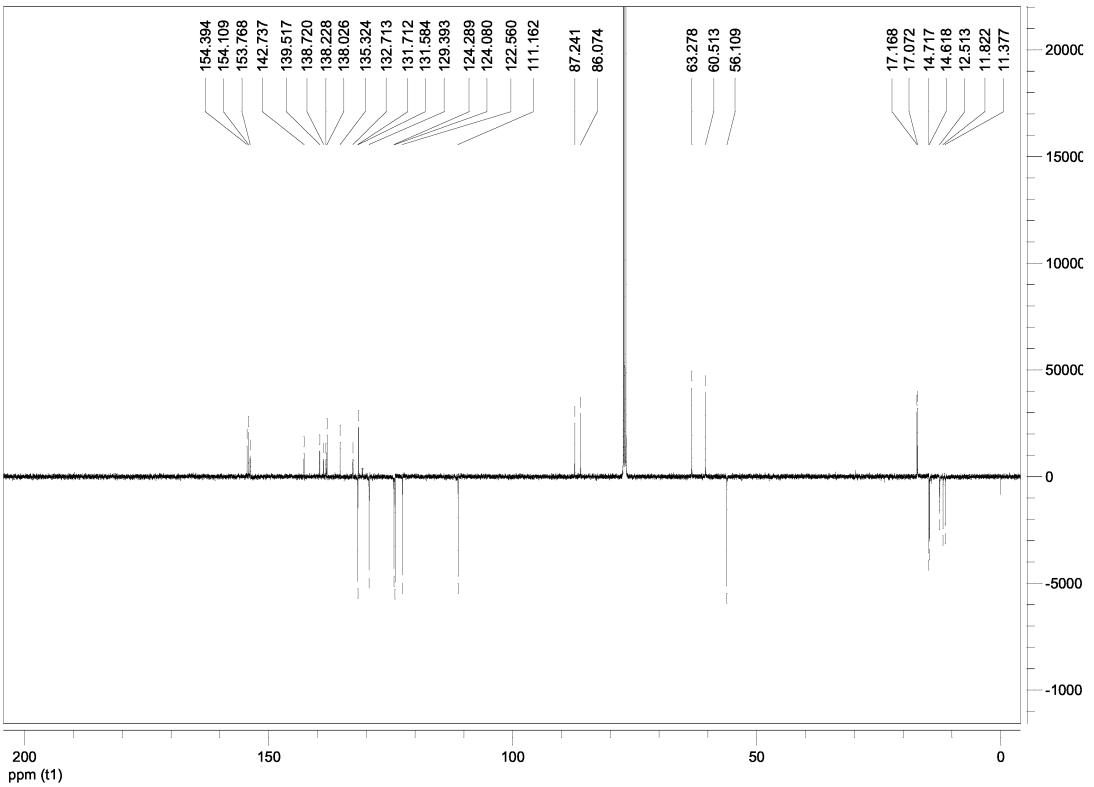
2,4-Dimethyl-3-ethyl BoDIPY Strained alkyne 36. SF232.



δ_H (500 MHz, $CDCl_3$).



δ_C (126 MHz, $CDCl_3$).



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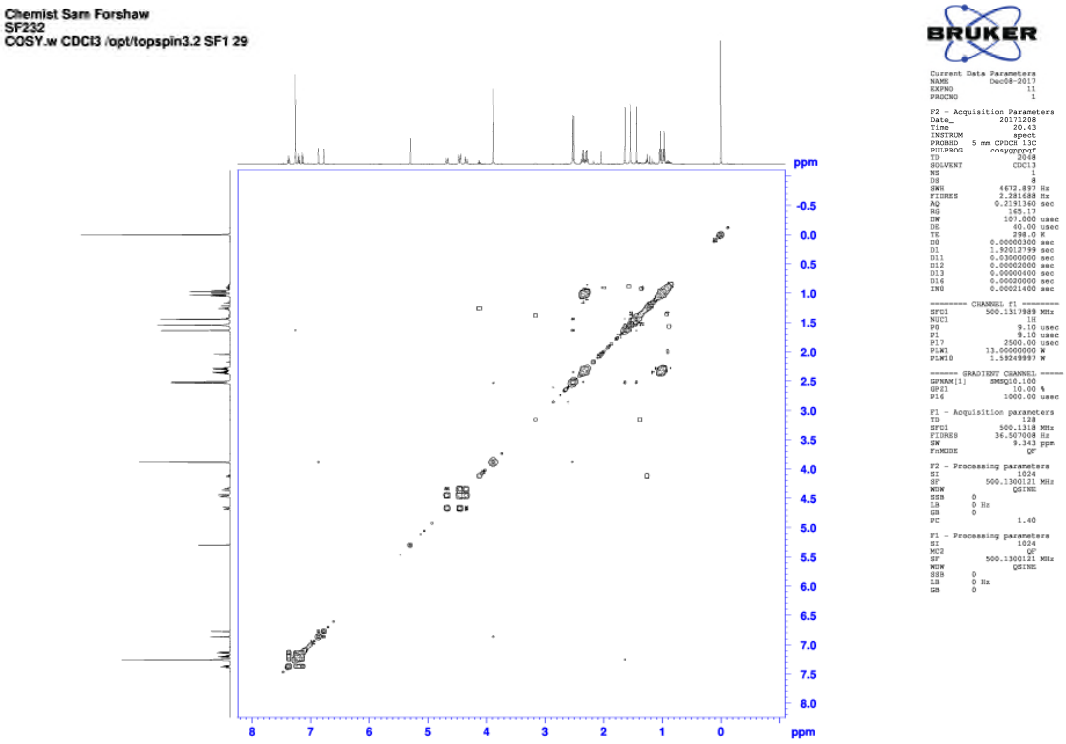
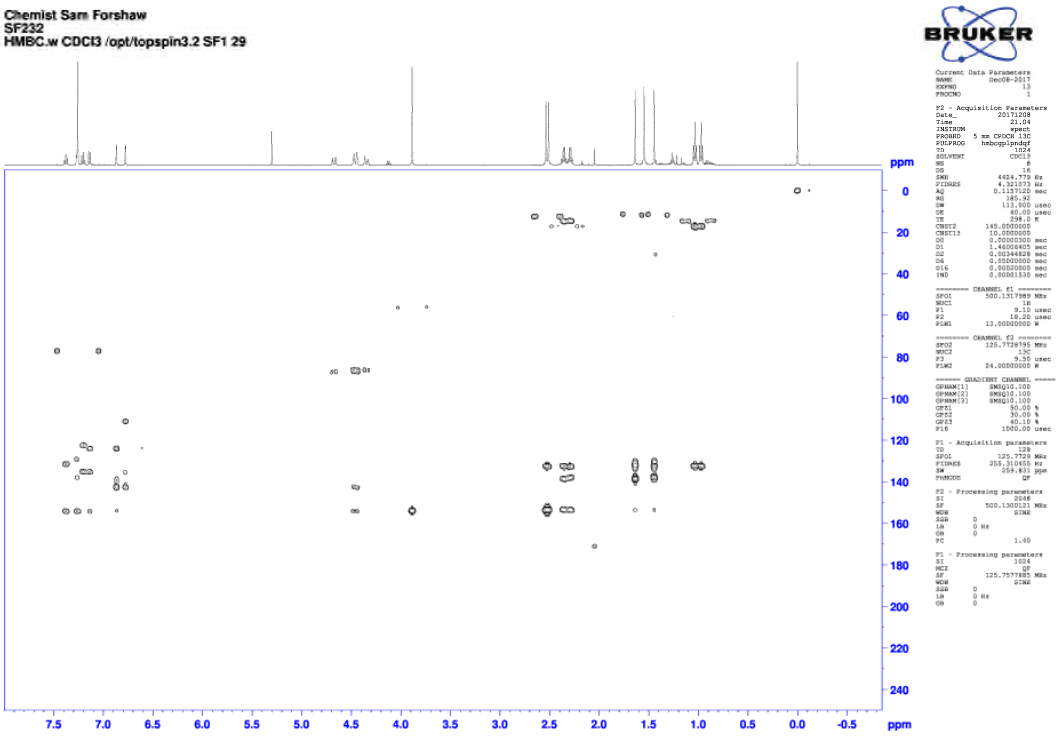


HMBC:


Chemist Sam Forshaw
SF232
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BRUKER
ppm
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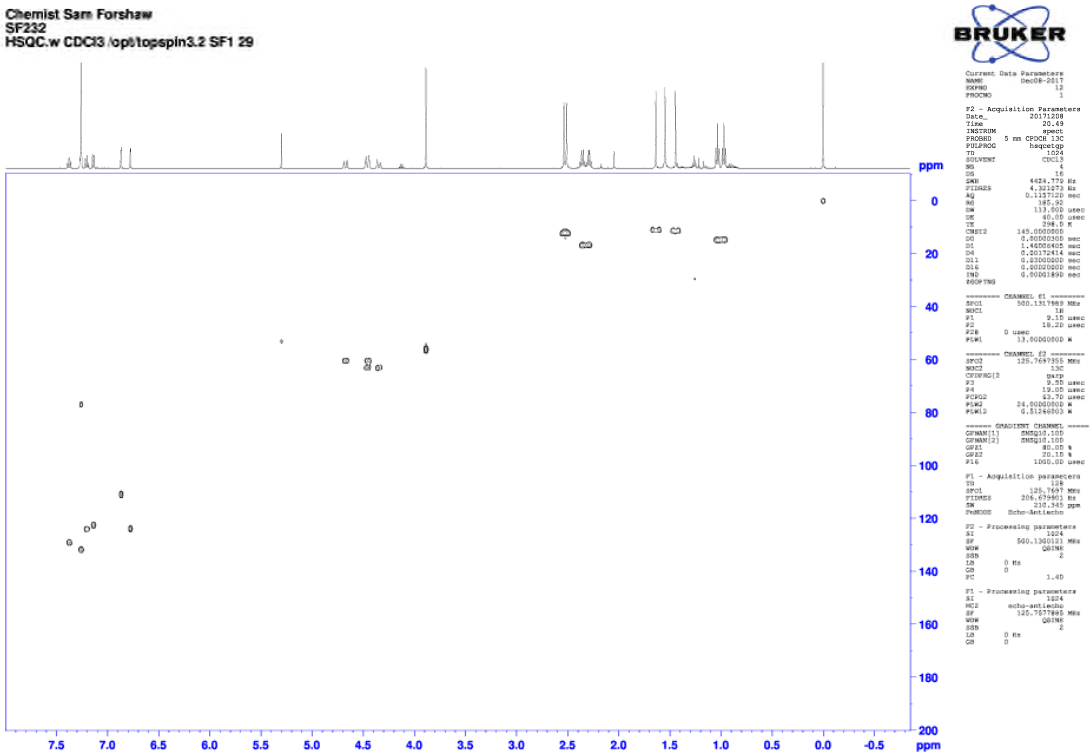
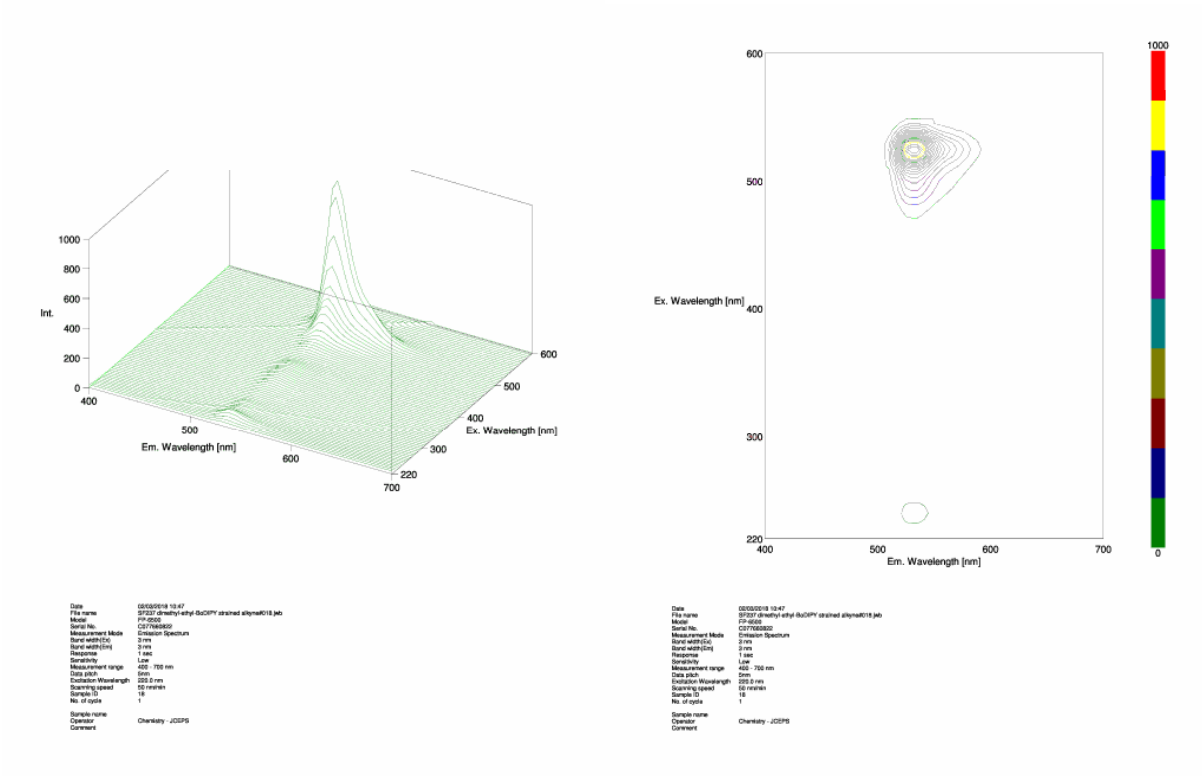
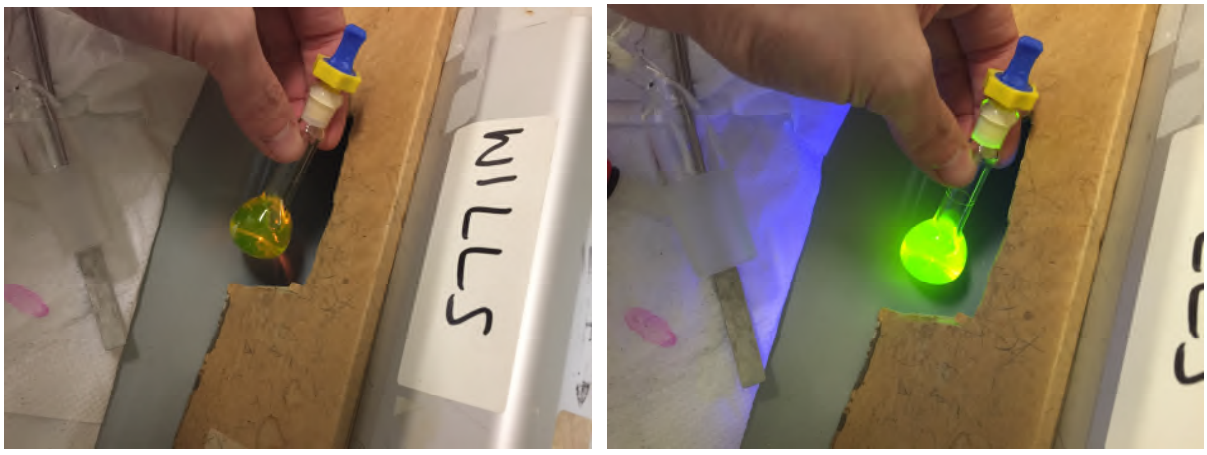
HSQC:


Chemist Sam Forshaw
SF232
HSQC.w CDCl3 /opt/topspin3.2 SF1 29
BRUKER
ppm
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 ppm
0 20 40 60 80 100 120 140 160 180 200

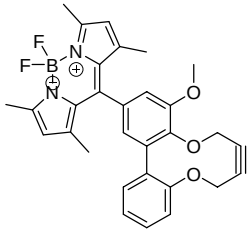
Fluorescence spectra and images.



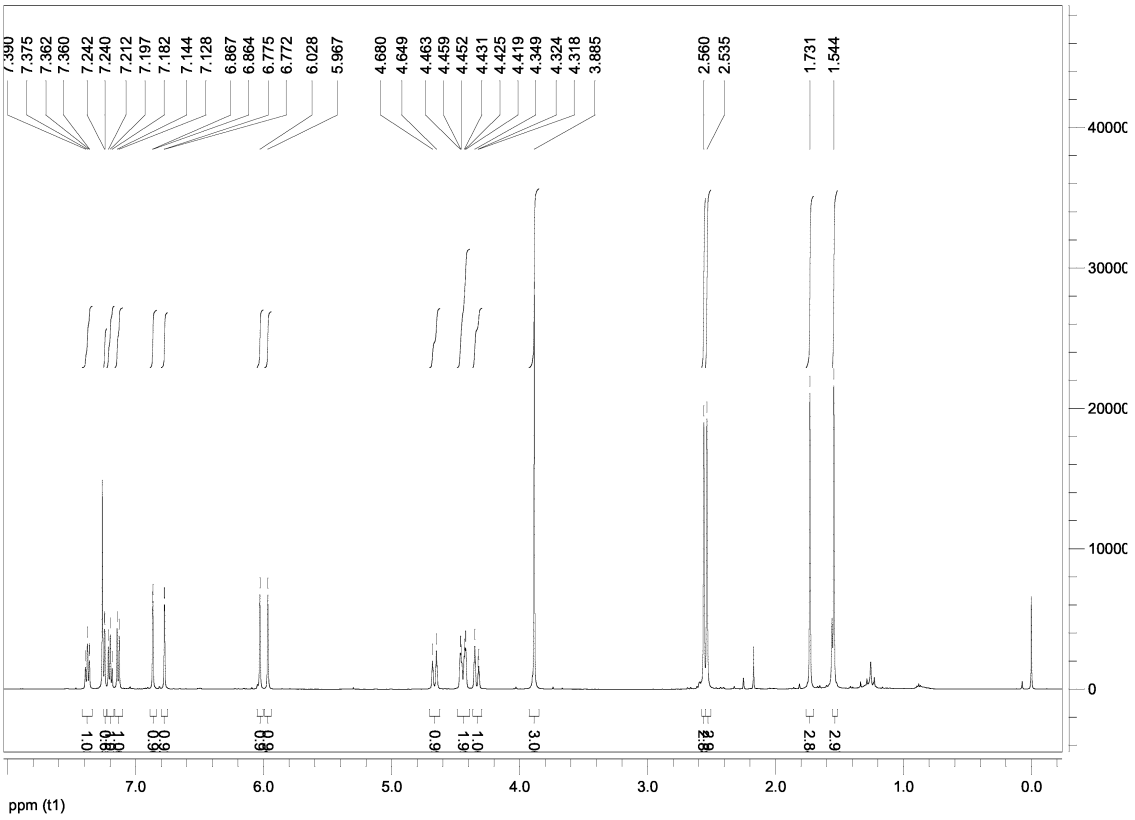


(above) Compound 36 in absence (left) and presence (right) of uv light.

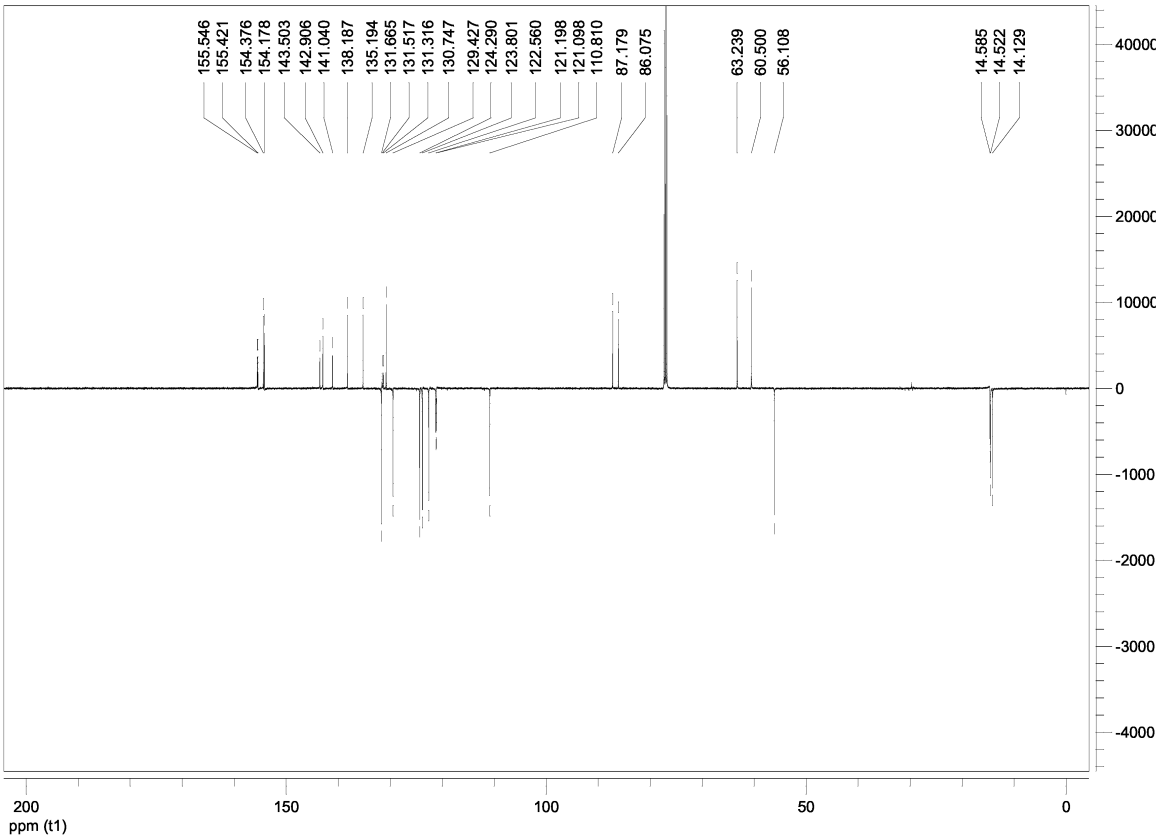
BoDIPY derivative with Me,H,Me substitution 37 (SF261):



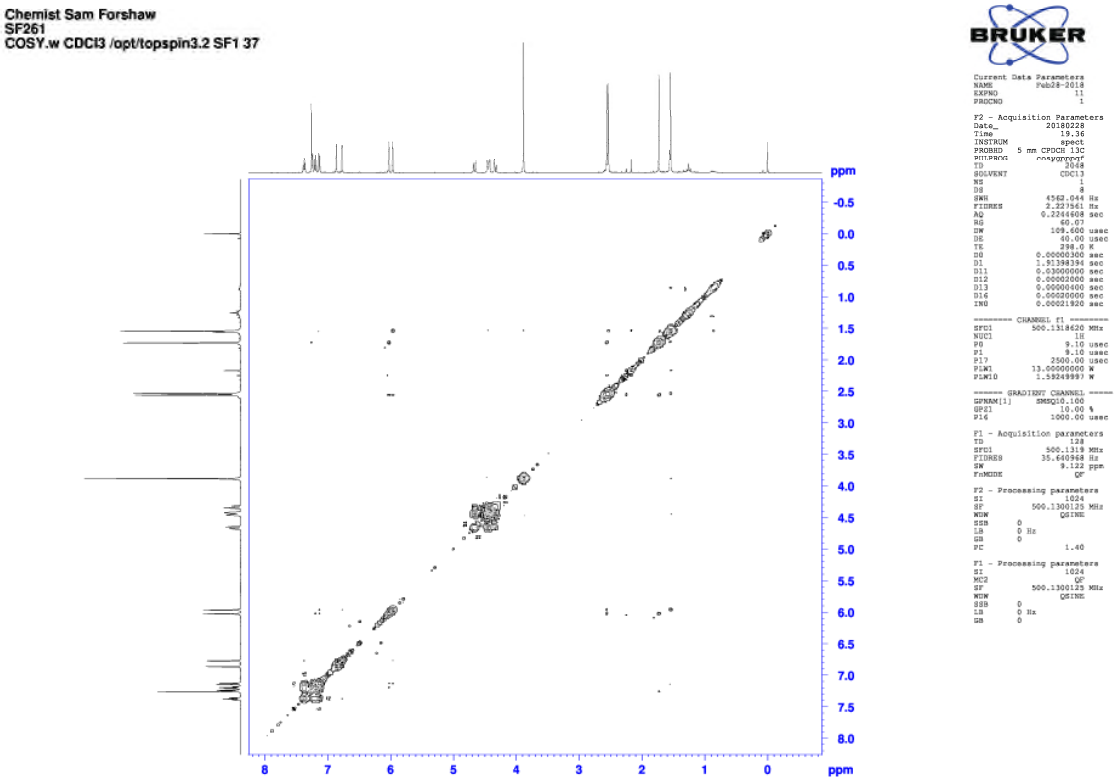
δ_H (500 MHz, $CDCl_3$).



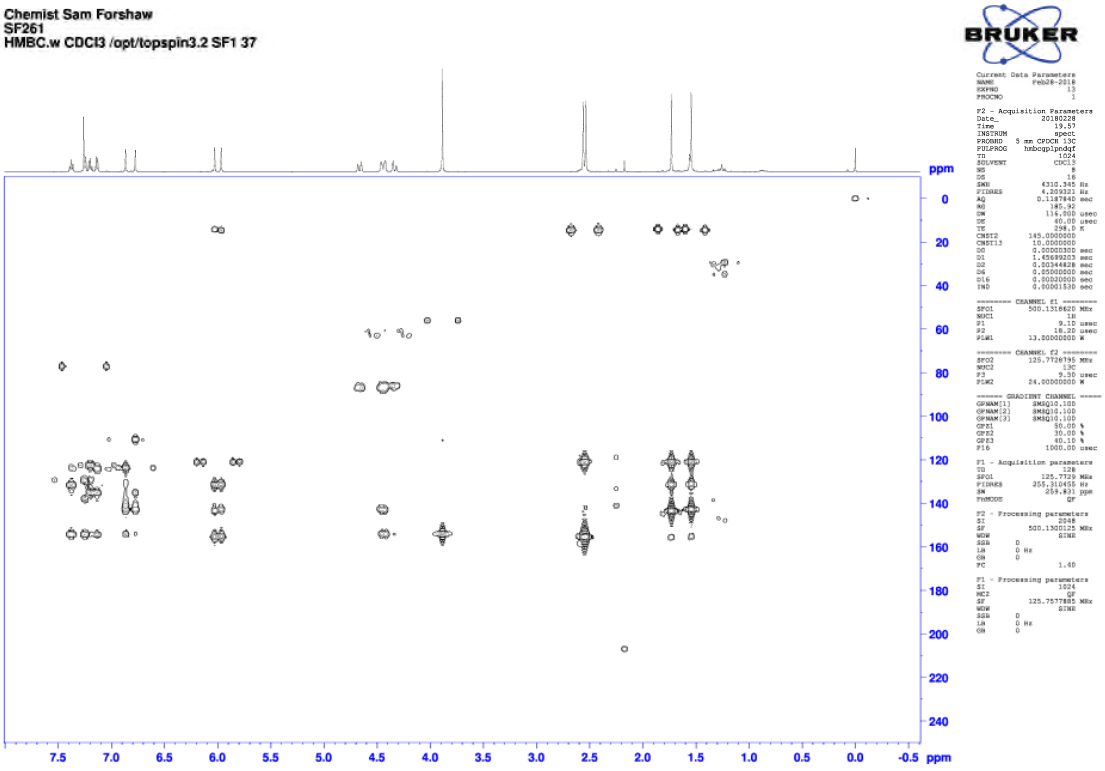
δ_C (126 MHz, $CDCl_3$).



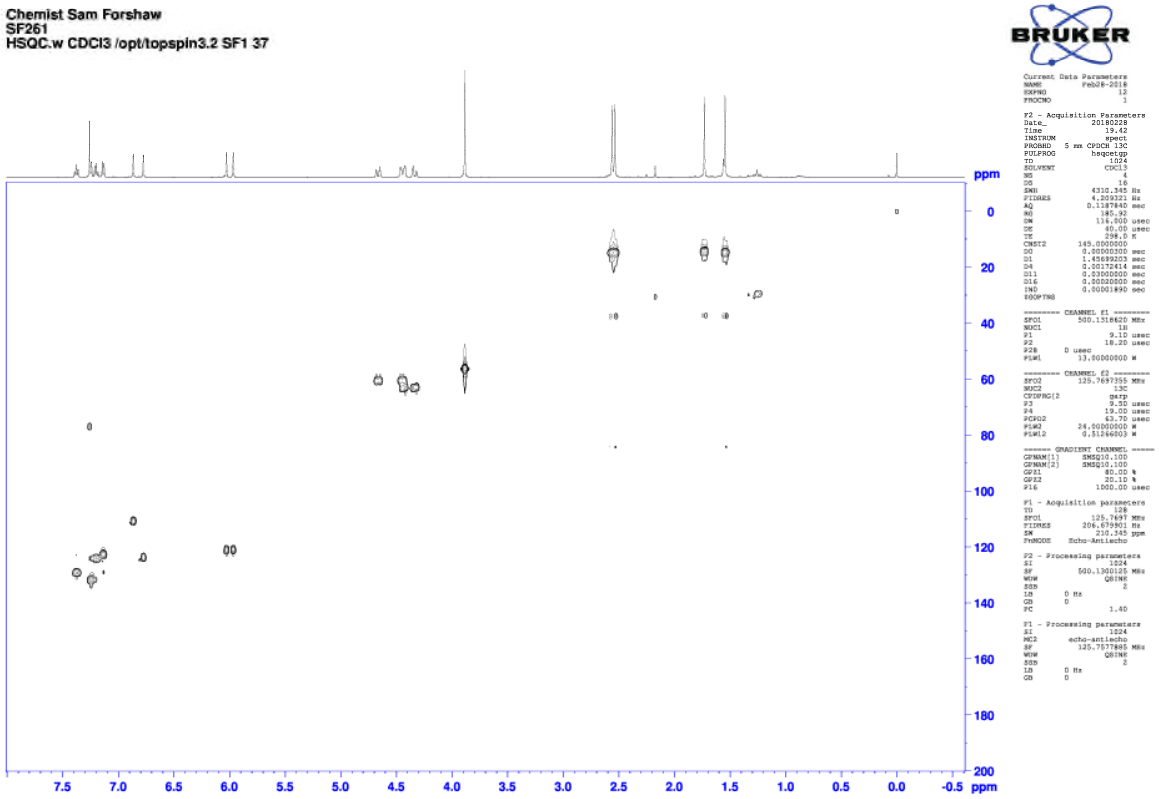
COSY:



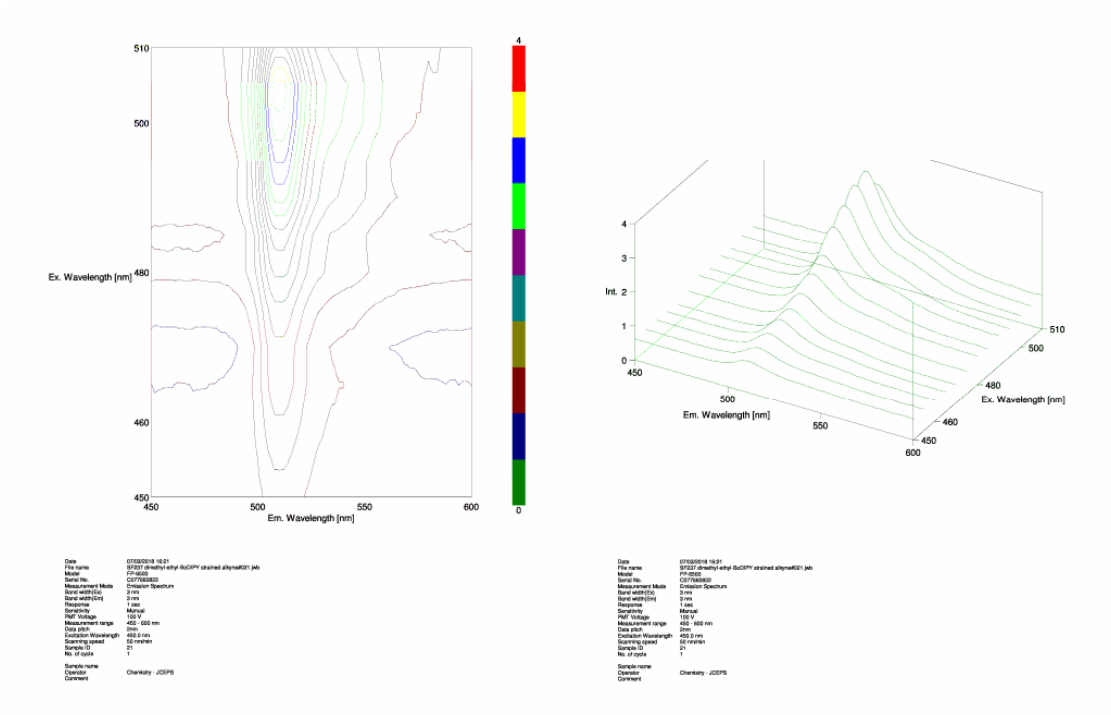
HMBC:


Chemist Sam Forshaw
SF261
HMBC.w CDCl3 /opt/topspin3.2 SF1 37
BRUKER
ppm
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 ppm

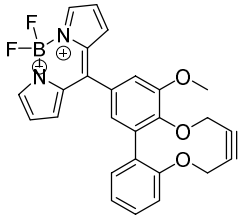
HSQC:


Chemist Sam Forshaw
SF261
HSQC.w CDCl3 /opt/topspin3.2 SF1 37
BRUKER
ppm
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 ppm

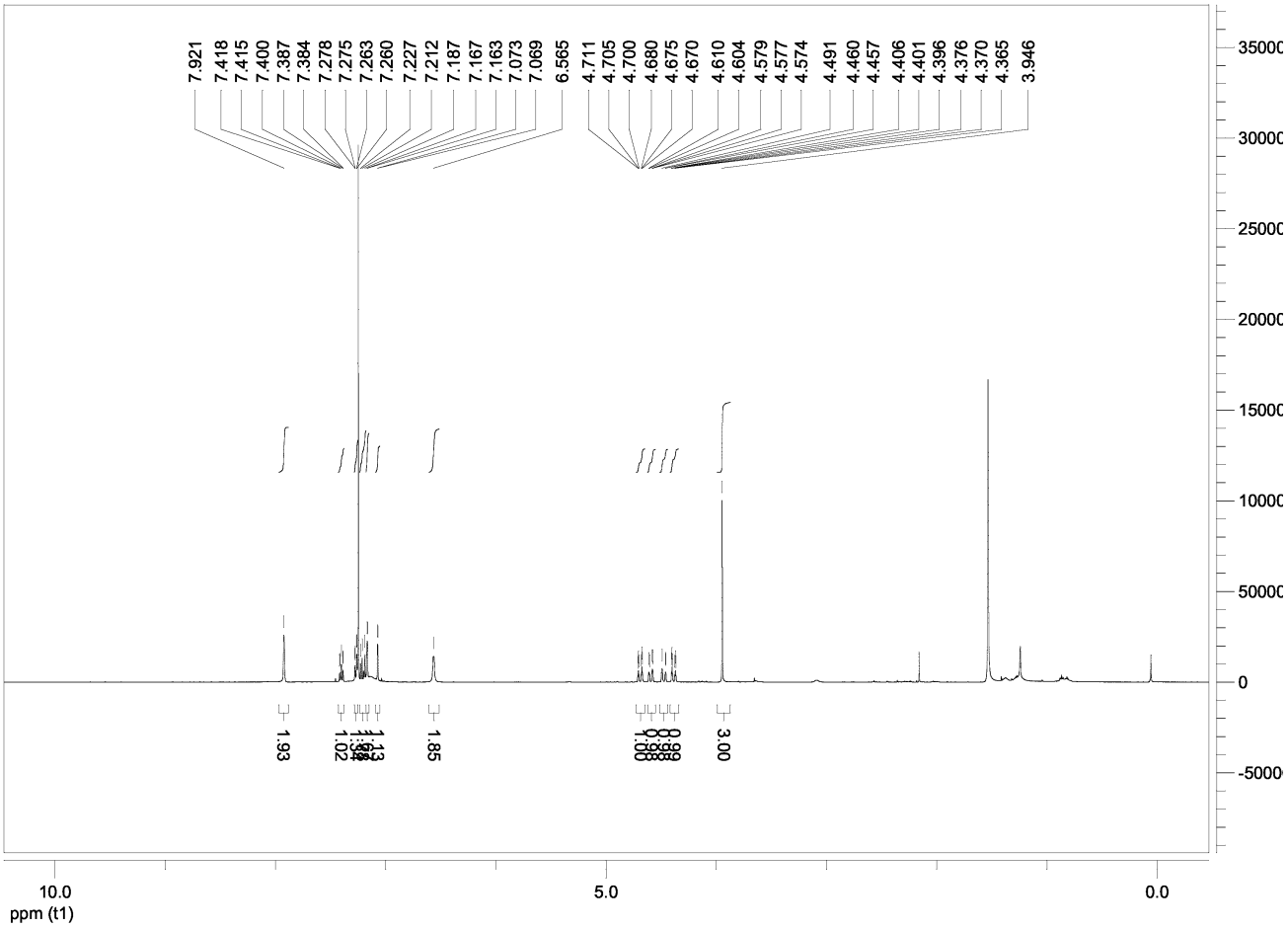
Fluorescence spectra and images.



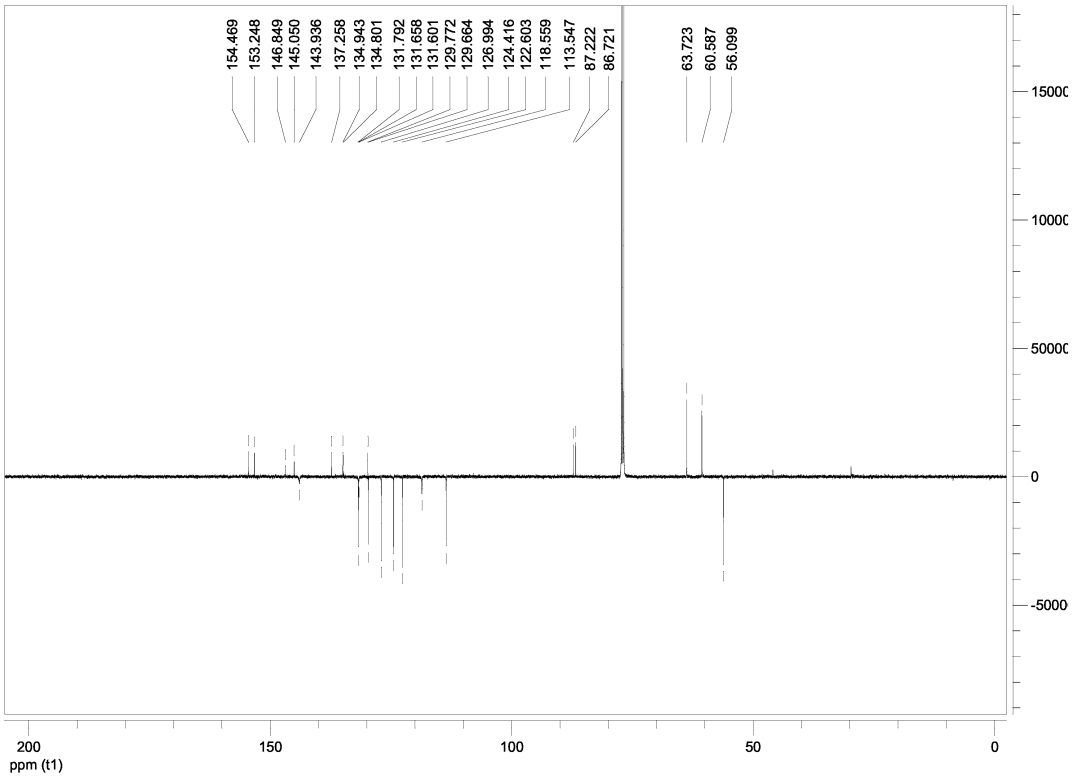
BoDIPY derivative with H,H,H substitution 38 (SF262):



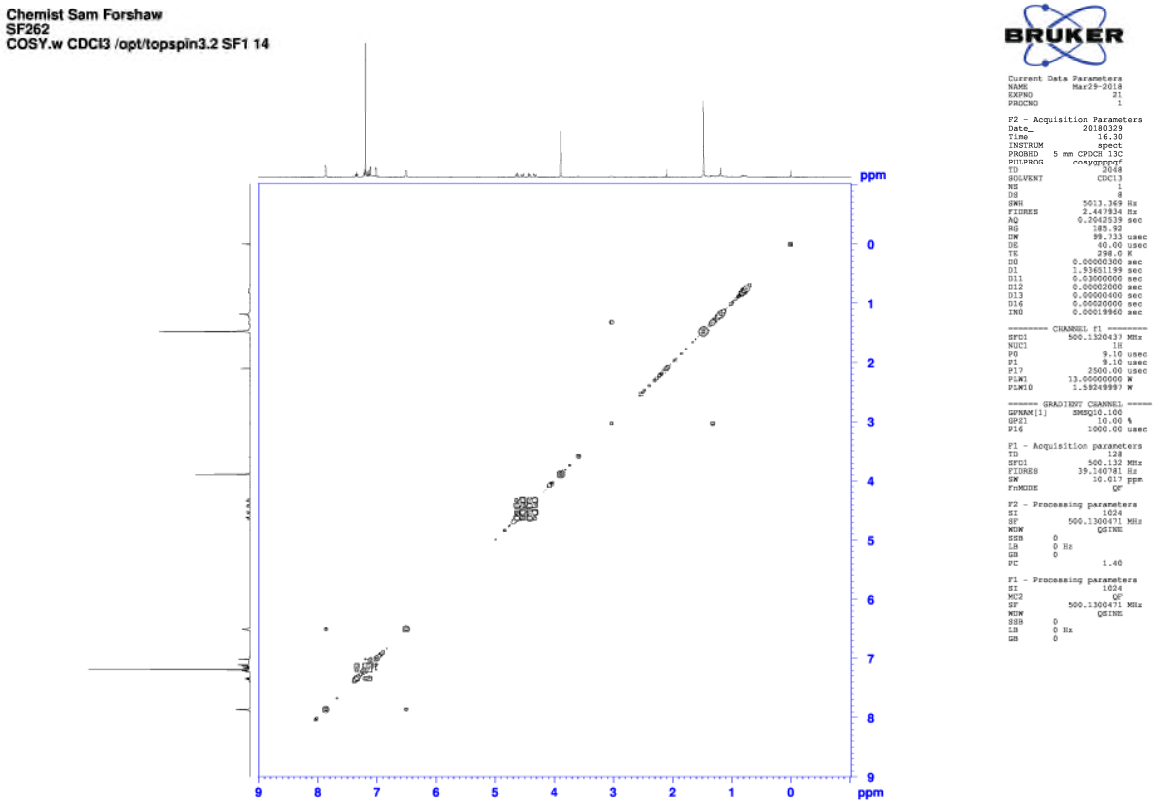
δ_H (500 MHz, $CDCl_3$).



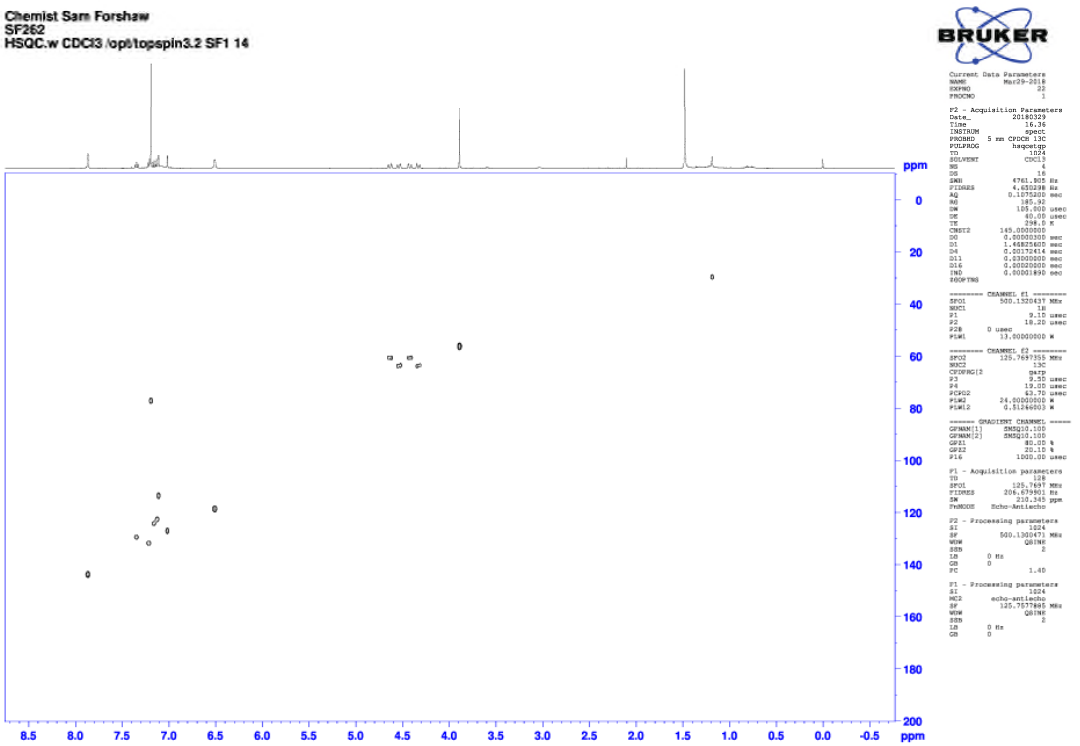
δ_C (126 MHz, $CDCl_3$).



COSY:



HSQC:


Chemist Sam Forshaw
SF262
HSQC.w CDCl3 /opt/topspin3.2 SF1 14
BRUKER
ppm
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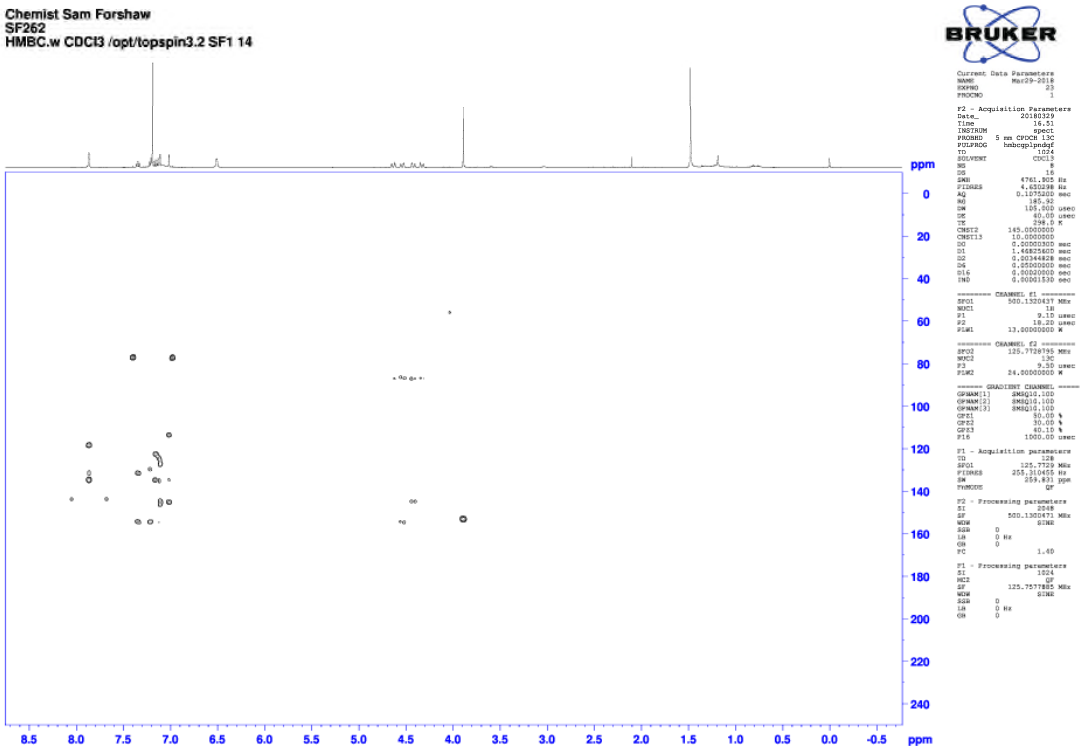
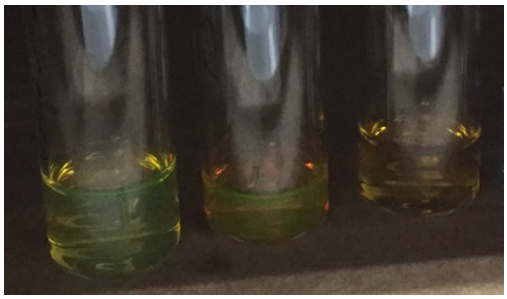
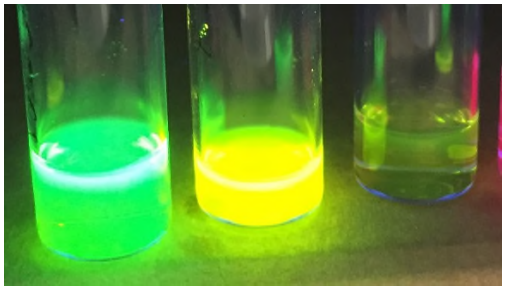
HMBC:


Chemist Sam Forshaw
SF262
HMBC.w CDCl3 /opt/topspin3.2 SF1 14
BRUKER
ppm
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 ppm

(a)  (b) 

Effect of UV irradiation on the fluorescence of compound **37, 36** and **38** (from left to right). (a) in the absence of UV light, (b) upon irradiation at 365 nm.

Single crystal X-ray crystallographic structure of 38 CCDC 1852224

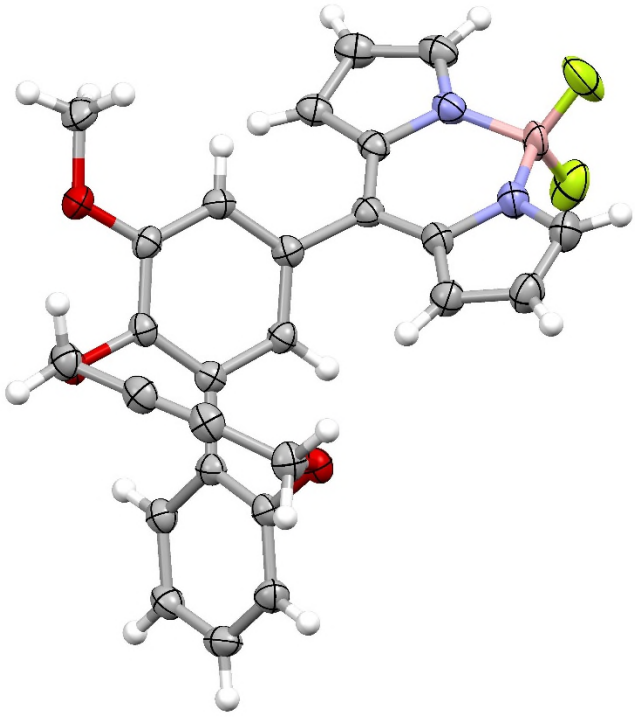


Figure 1: Single crystal X-ray structure of **38** (ellipsoids are plotted at the 50% probability level, disorder omitted for clarity)

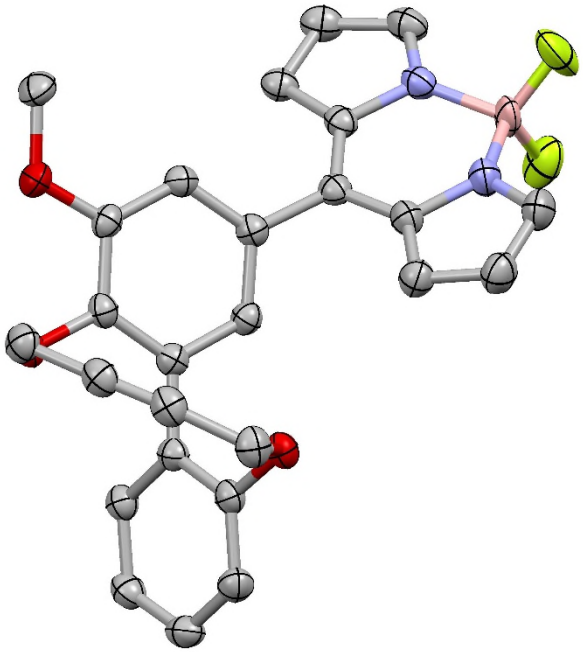


Figure 2: Single crystal X-ray structure of **38** (ellipsoids are plotted at the 50% probability level, disorder and H-atoms omitted for clarity)

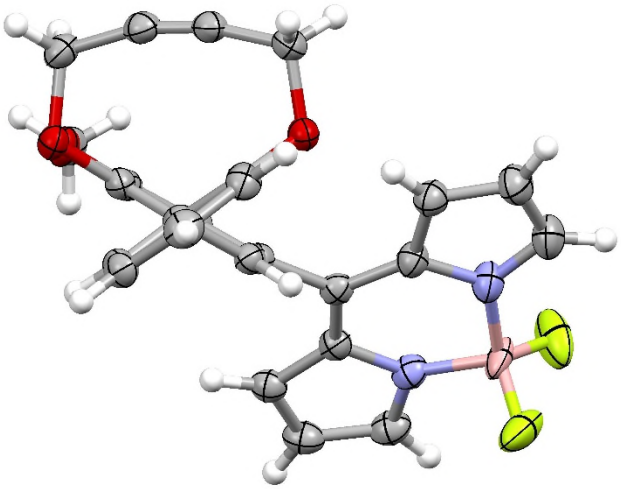


Figure 3: Single crystal X-ray structure of **38** (ellipsoids are plotted at the 50% probability level, disorder omitted for clarity)

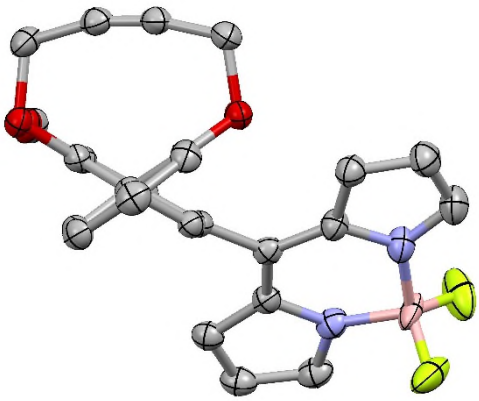


Figure 4: Single crystal X-ray structure of **38** (ellipsoids are plotted at the 50% probability level, disorder and H-atoms omitted for clarity)

CCDC 1852224 contains the supplementary crystallographic data for this paper. These can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Single crystals were grown from slow evaporation of a chloroform solution of the compound over several days. A suitable crystal was mounted on a Mitegen head with Fomblin oil and collected on an Xcalibur Gemini diffractometer with a Ruby CCD area detector at 150(2) K. The structure was solved using Olex2[1] and the ShelXT[2] structure solution program using Direct Methods and refined with the ShelXL[3] refinement package using Least Squares refinement.

The asymmetric unit contains one crystallographically distinct molecule, with Z = 4. The crystal packing indicates aromatic donor-acceptor (π-π) interactions of the biphenyl and BODIPY moieties of adjacent molecules in the crystal lattice.

The alkyne group displays significant deviation from linearity, the C14-C15-C16 and C15-C16-C17 bond angles are 165.7(4)° and 168.1(4)° respectively. This is accompanied by a large biphenyl torsion angle (C5-C6-C7-C8) of 68.6(4)°.

Table 1: single-crystal X-ray data for compound 38

Compound Reference	**Compound 38**
Chemical Formula	$C_{26}H_{19}BF_2N_2O_3$
Formula Mass	456.24
Crystal system	Monoclinic
a/ Å	11.4282(2)
b/ Å	25.2193(4)
c/ Å	7.59768(13)
α/ °	90
β/ °	104.5629(17)
γ/ °	90
Unit cell volume/ Å	2119.39(6)

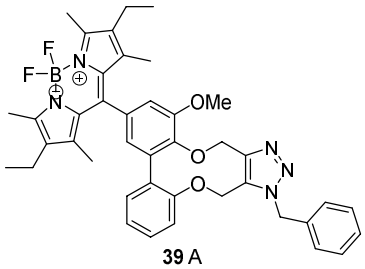
Temperature/ K	150(2) K
Space group	*-P 2ybc*
Crystal size/ mm	0.10 × 0.10 × 0.25
Radiation	CuK\a
Goodness-of-fit on F^2	1.063
No. of formula units per unit cell, Z	4
No. of reflections measured	13289
No. of independent reflections	4488
Final R_1 vaules ($I > 2\sigma(I)$)	0.0424
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1123
Final R_1 values (all data)	0.0449
Final $wR(F^2)$ (all data)	0.1148

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

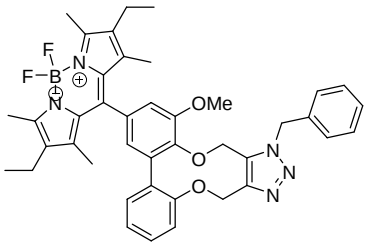
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8

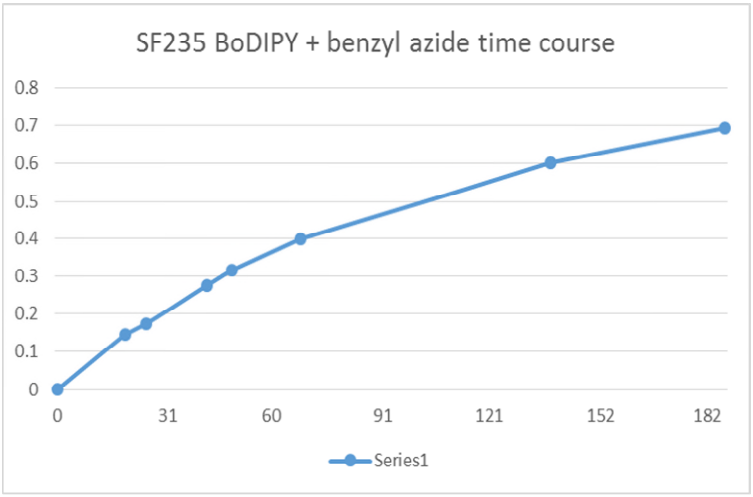
Click reactions using 36 to form two separated regioisomers 39 and 40 (SF235):



39 A



40 B



Conversion / time (in hours) above.

Tentative assignment of regioisomers are shown. It is difficult to establish exactly which regioisomer is which in this case. However there is a distinctive difference in the ^{13}C NMR spectra for the three CH_2 groups (adjacent to heteroatoms) in each molecule. In the case where the pattern corresponds to that in the simpler compound lacking the OMe group (reference 9), and all its previously-reported derivatives, we have assumed that the benzyl group is further away from the OMe and therefore causes no distortion to the shape of the molecule (hence assigned as **39**). In the other regioisomer, we assume that the change is due to the closer proximity of the benzyl to the OMe, causing distortion to the ring and a change in the characteristic ^{13}C NMR positions.

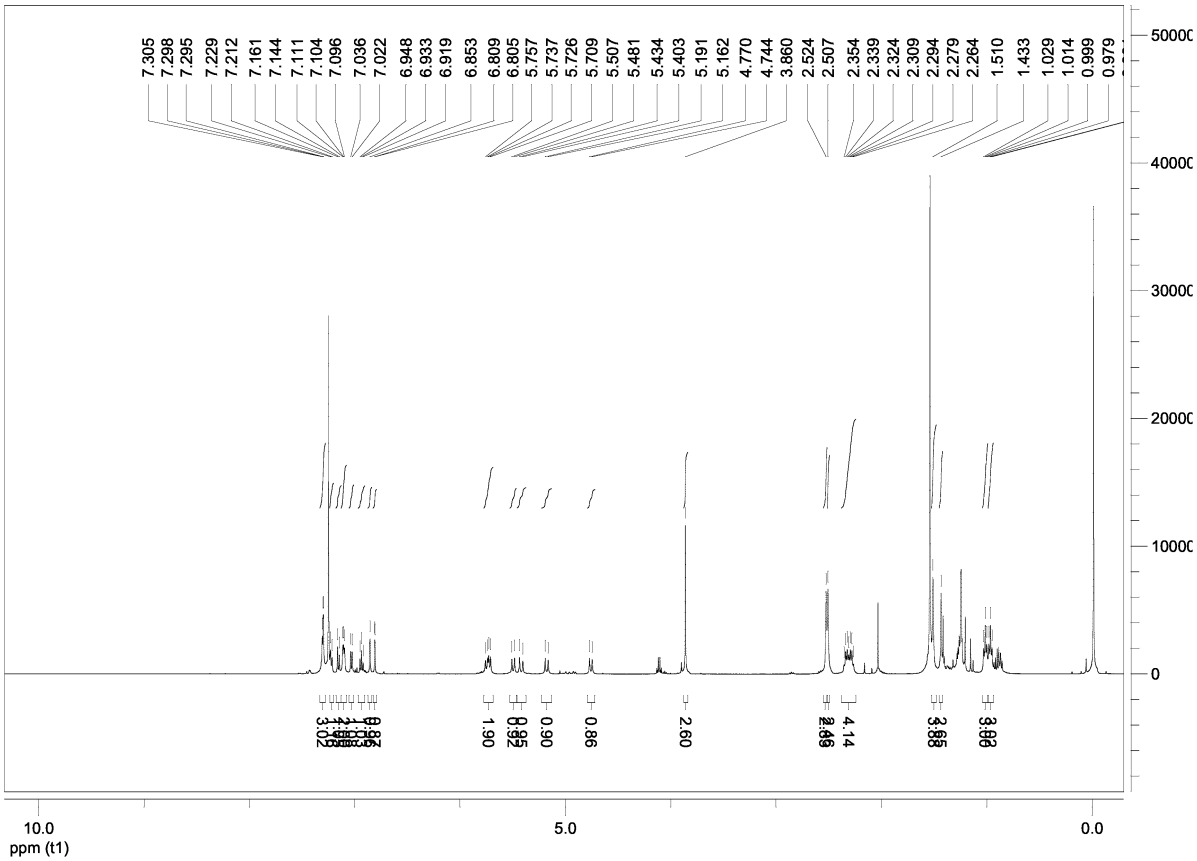
Compound **39**: OCH_2 at 63.0 and 61.4 ppm, NCH_2 at 52.0 ppm.

Compound **40**: OCH_2 at 67.6 and 58.1 ppm, NCH_2 at 52.9 ppm.

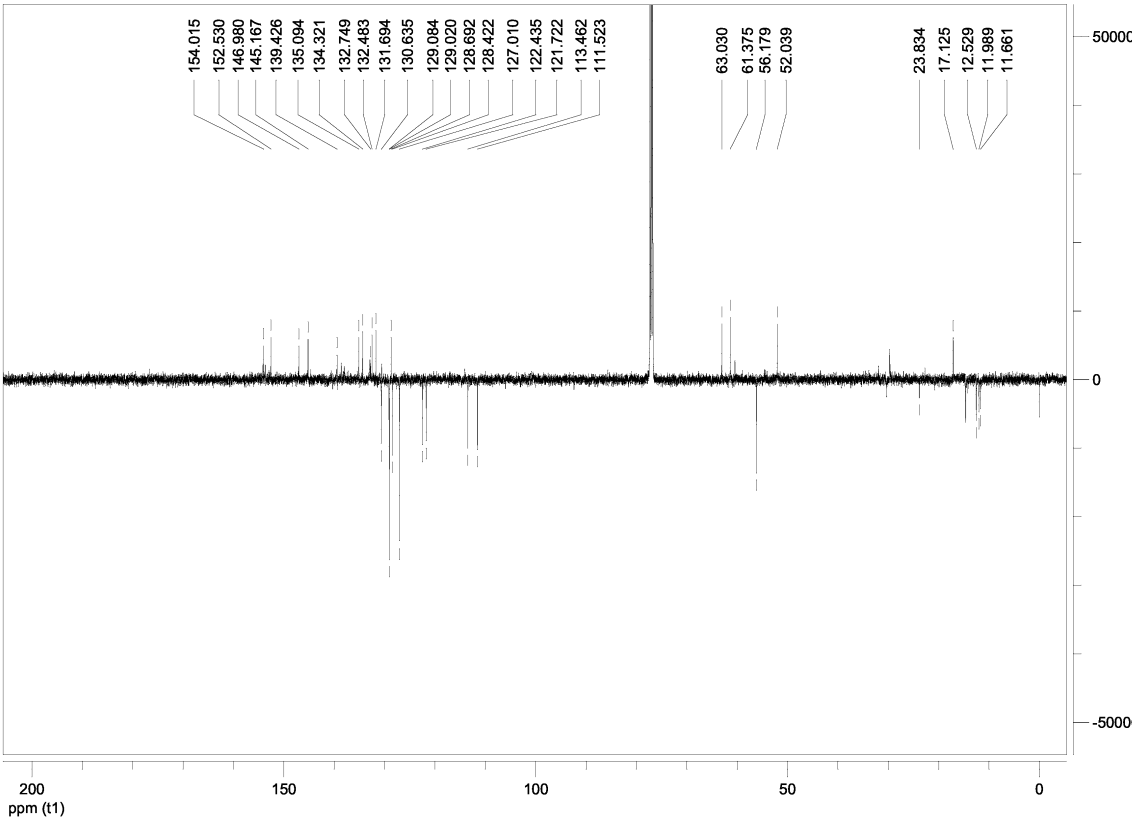
Compound lacking BoDIPY and OMe group (reported in reference 9): OCH_2 at 62.9 and 60.5 ppm, NCH_2 at 52.3 ppm. The two OCH_2 groups are close in chemical shift, as in **39**.

Regioisomer A:

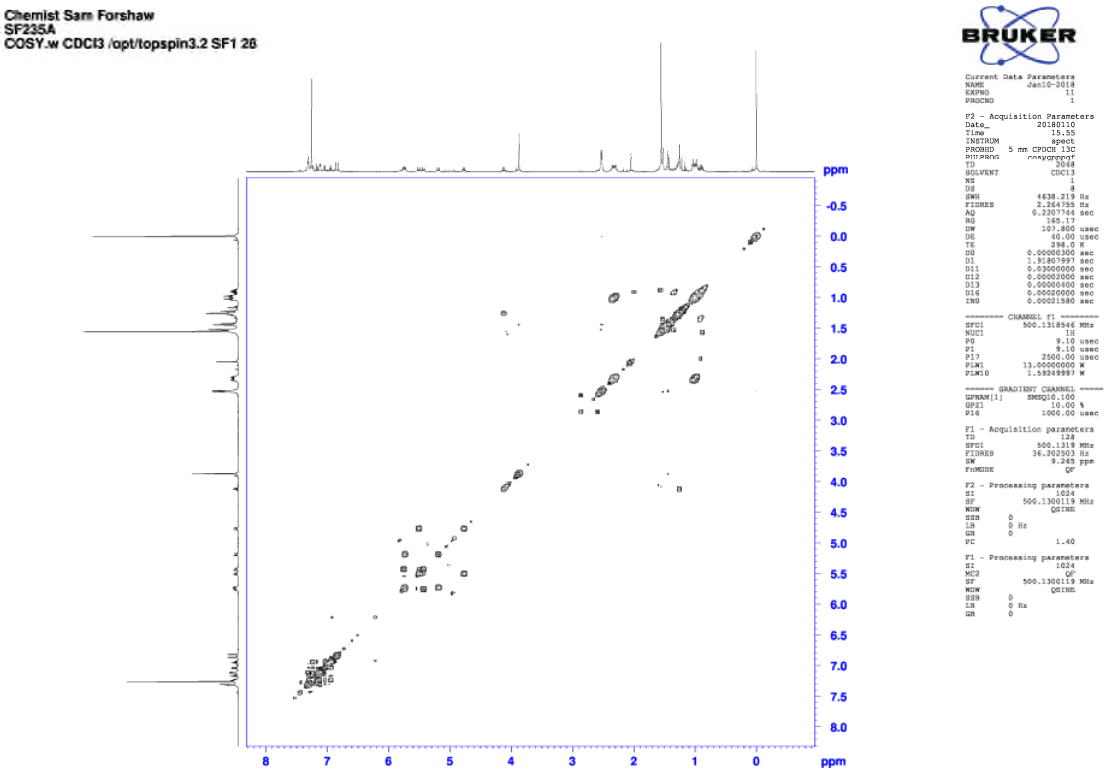
δ_H (500 MHz, $CDCl_3$).



δ_C (126 MHz, $CDCl_3$).



COSY: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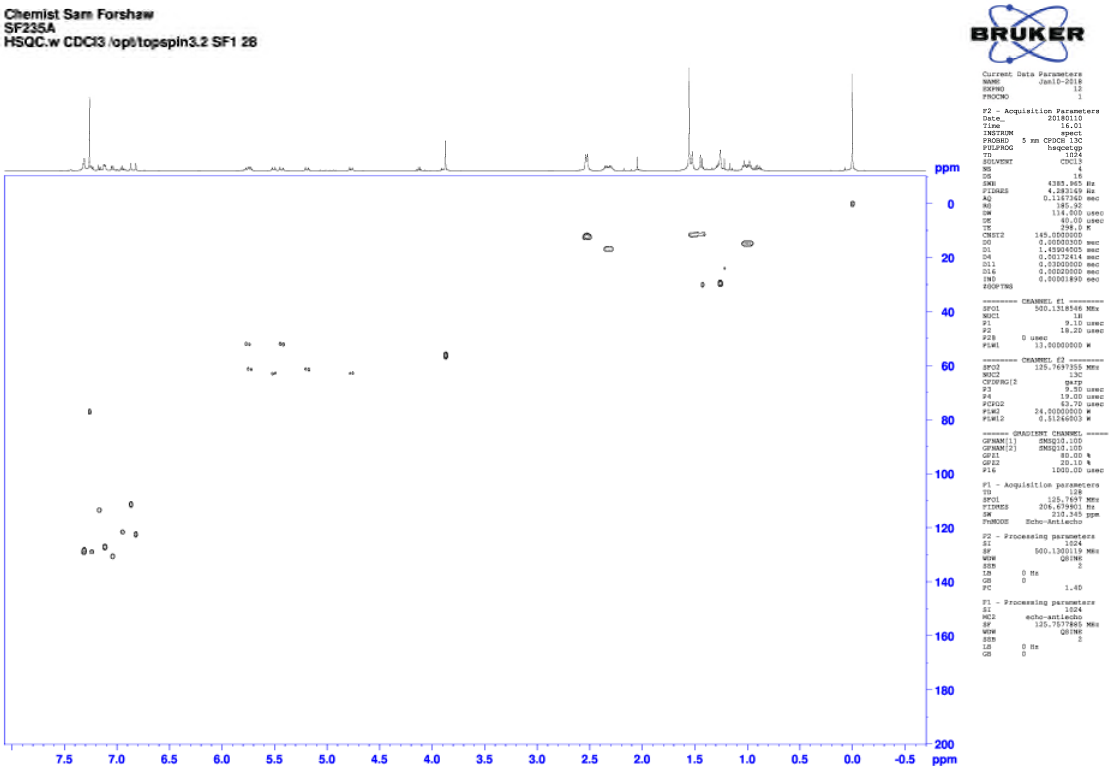
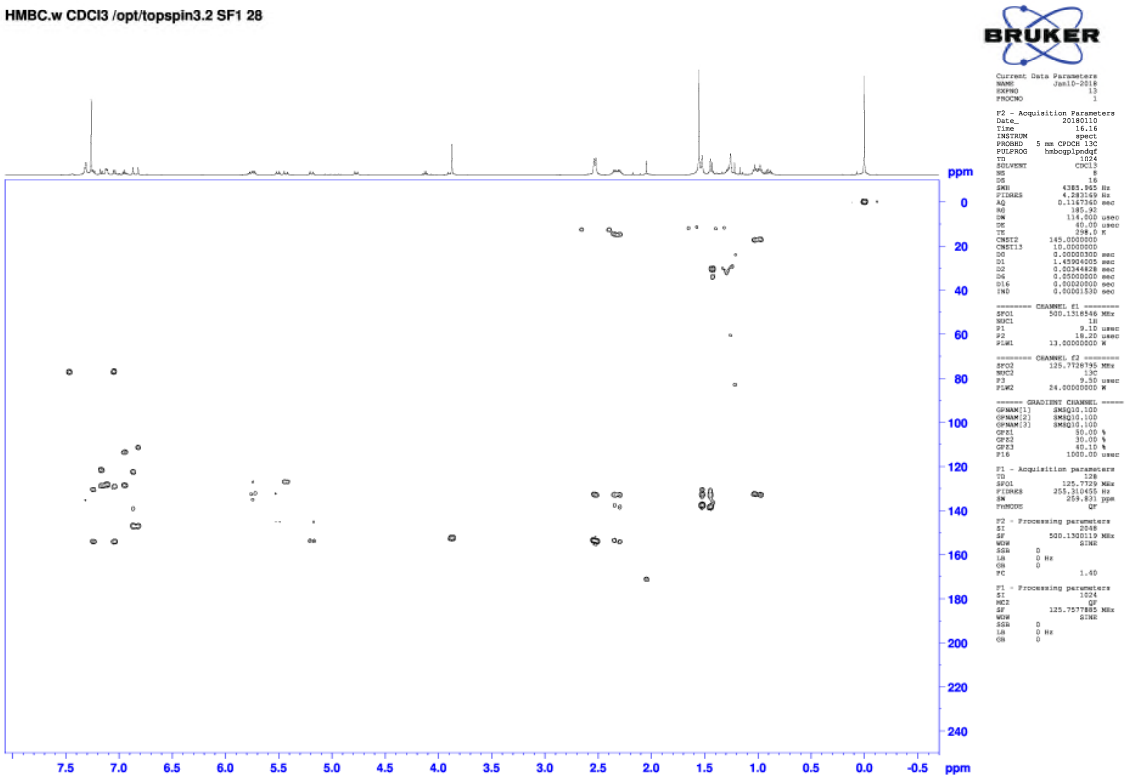
SF235A
COSY.w CDCl3 /opt/topspin3.2 SF1 28
BRUKER
ppm
ppm

HSQC:


Chemist Sam Forshaw
SF235A
HSQC.w CDCl3 /opt/topspin3.2 SF1 28
BRUKER
ppm
ppm

HMBC:


HMBC.w CDCl3 /opt/topspin3.2 SF1 28
BRUKER
ppm
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20
40
60
80
100
120
140
160
180
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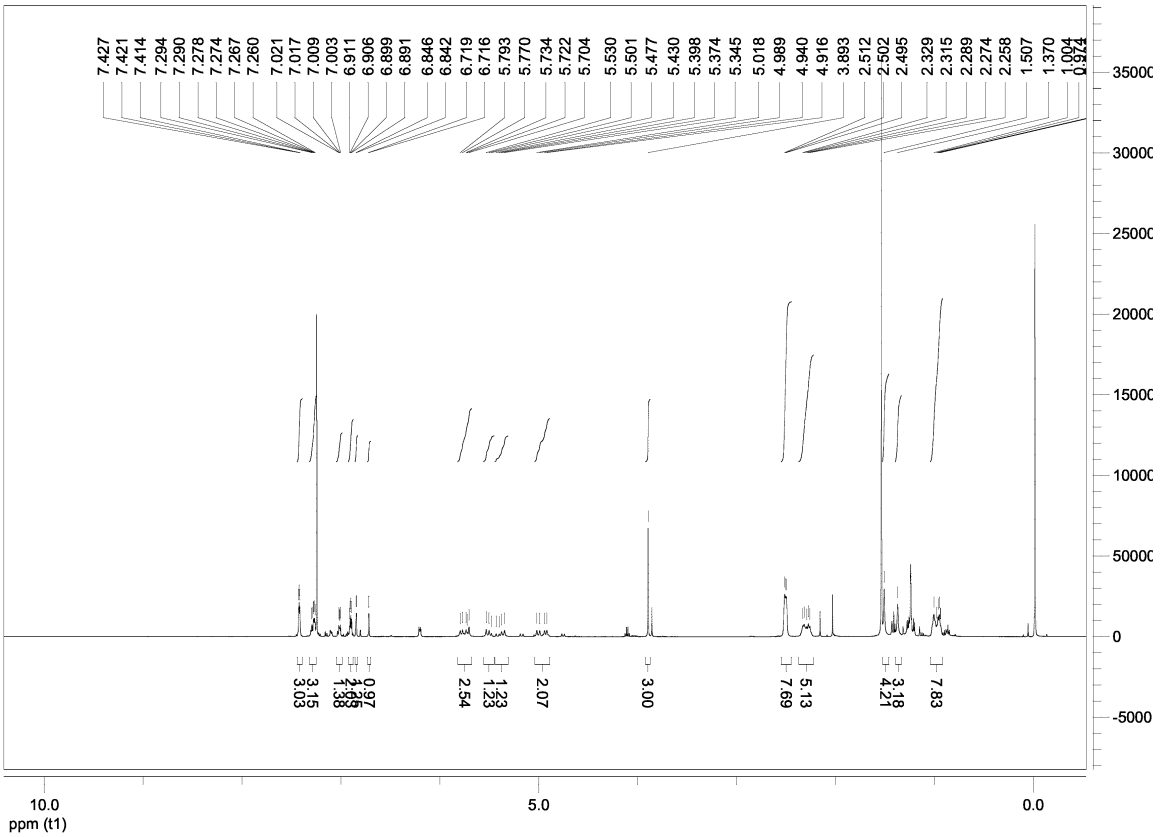
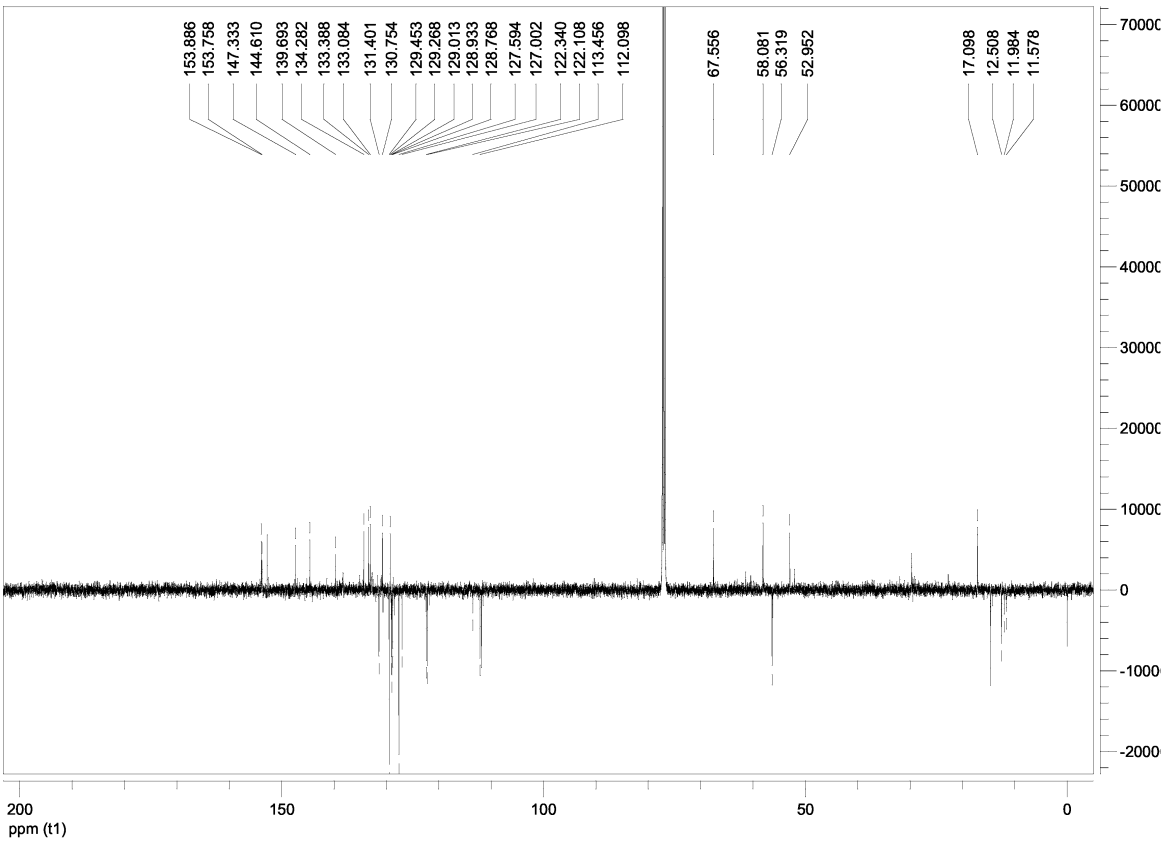
220
240
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

Regioisomer B:

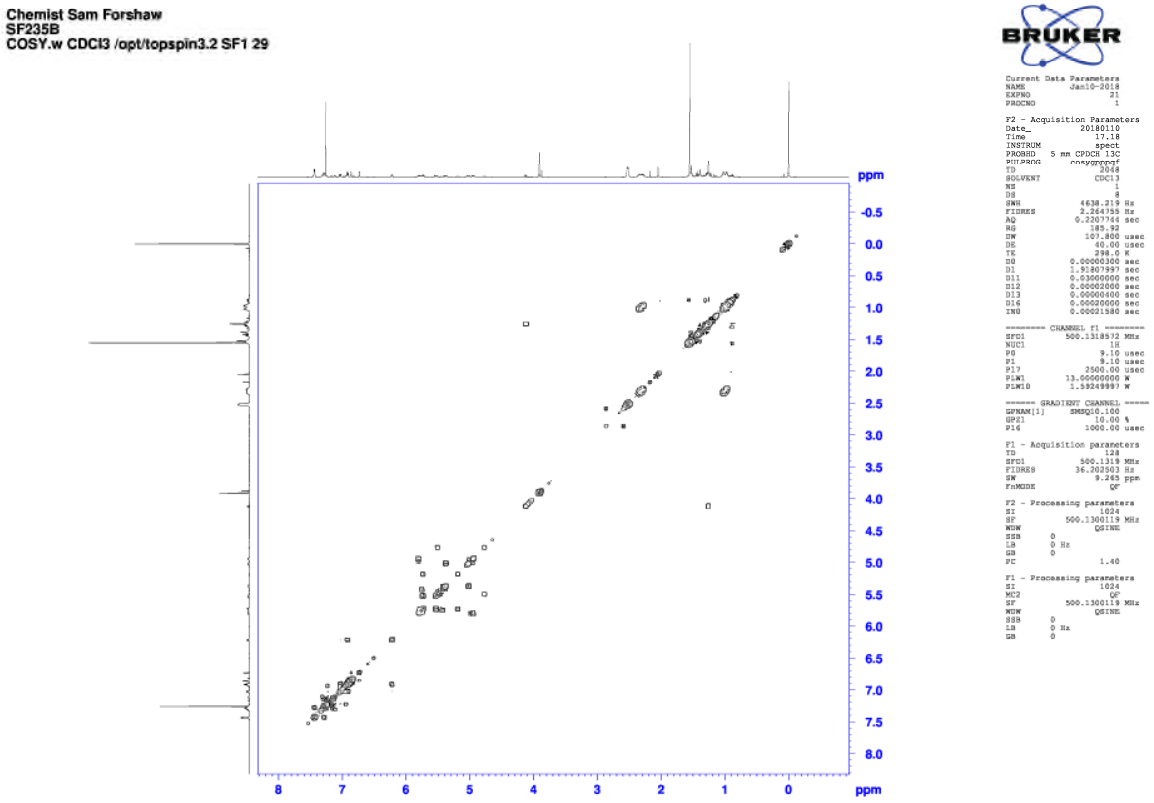
δ_H (500 MHz, $CDCl_3$).



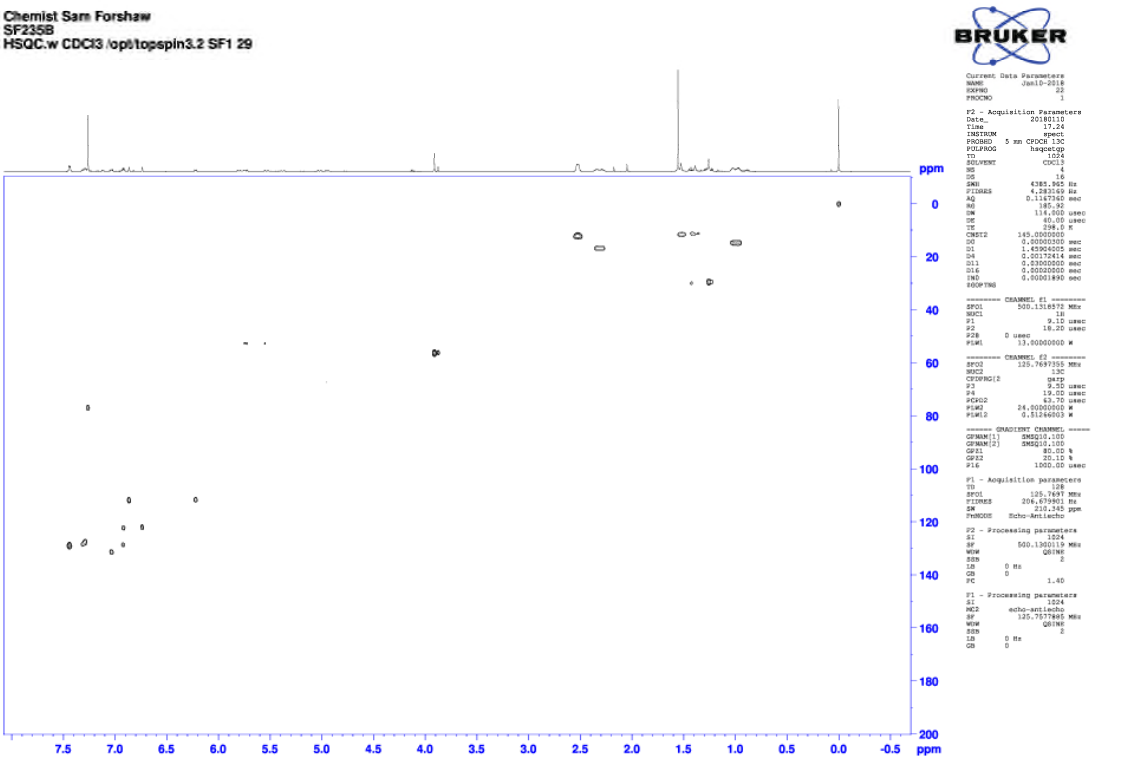
δ_C (126 MHz, $CDCl_3$).



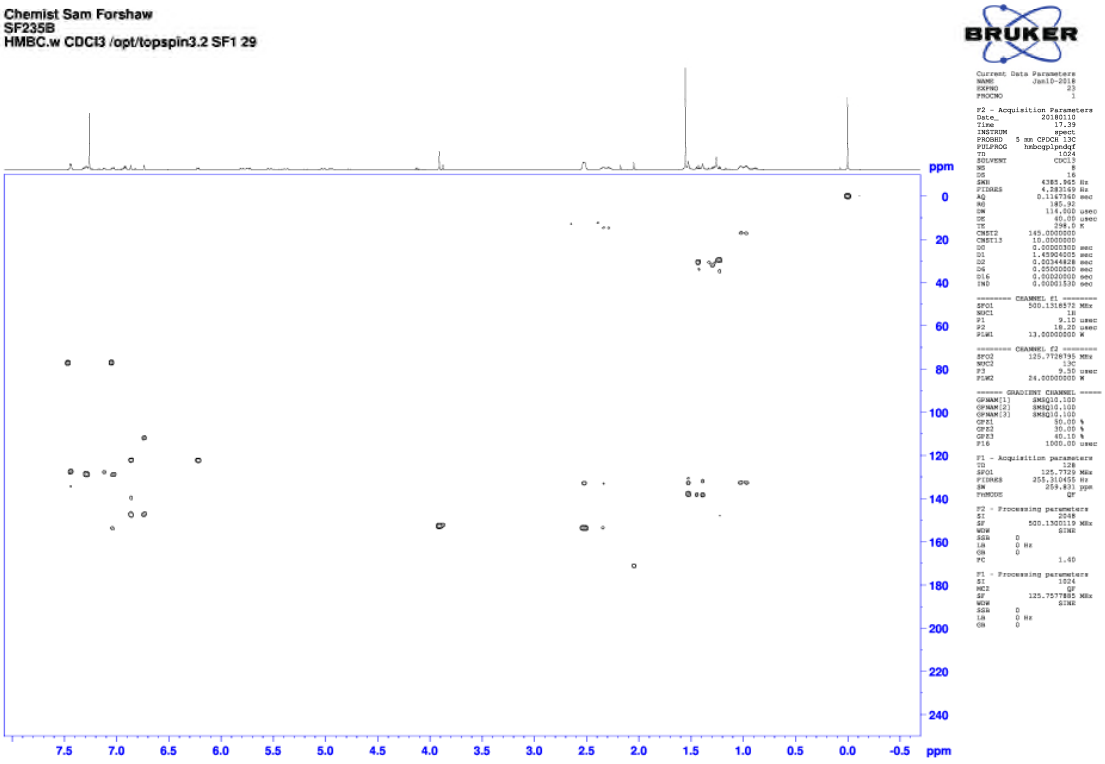
COSY:


Chemist Sam Forshaw
SF235B
COSY.w CDCl3 /opt/topspin3.2 SF1 29
BRUKER
ppm
ppm

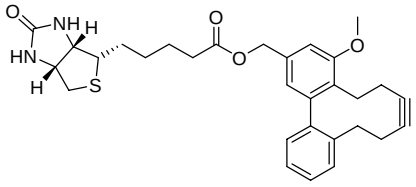
HSQC:


Chemist Sam Forshaw
SF235B
HSQC.w CDCl3 /opt/topspin3.2 SF1 29
BRUKER
ppm
ppm

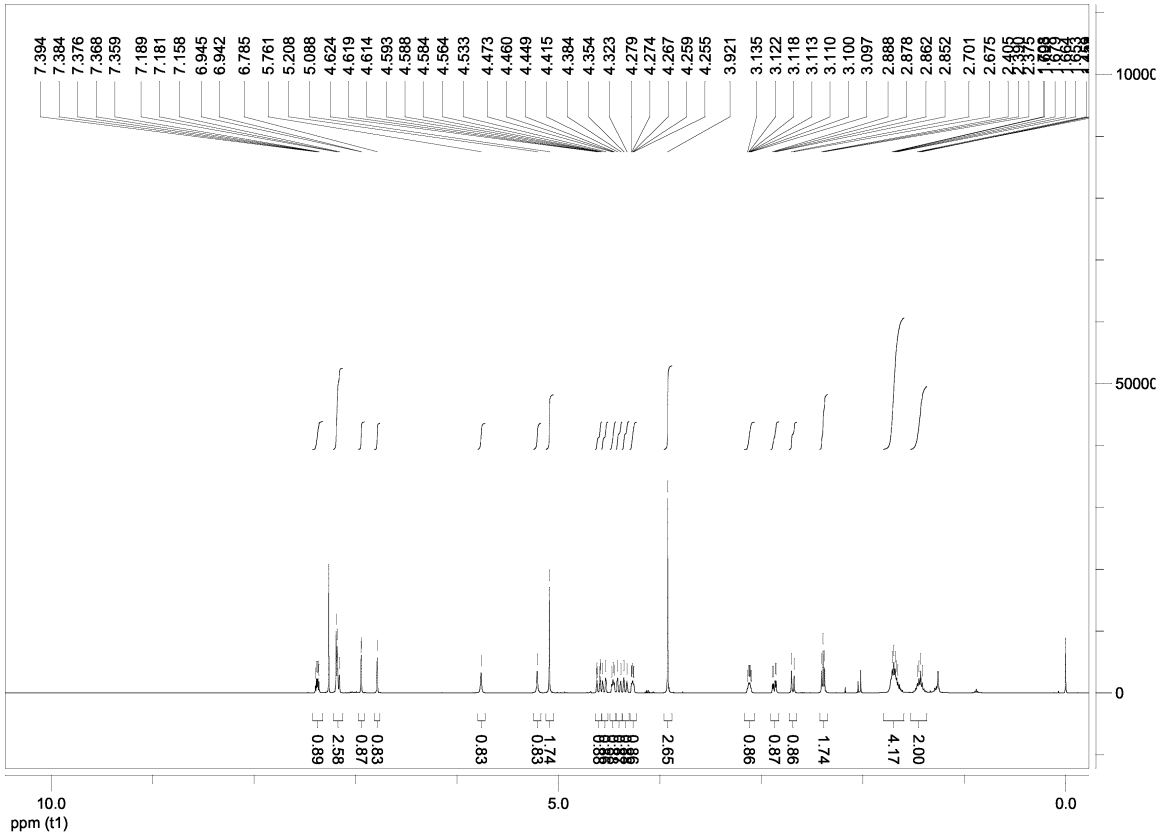
HMBC:


Chemist Sam Forshaw
SF235B
HMBC.w CDCl3 /opt/topspin3.2 SF1 29
BRUKER
ppm
0
20
40
60
80
100
120
140
160
180
200
220
240
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
ppm

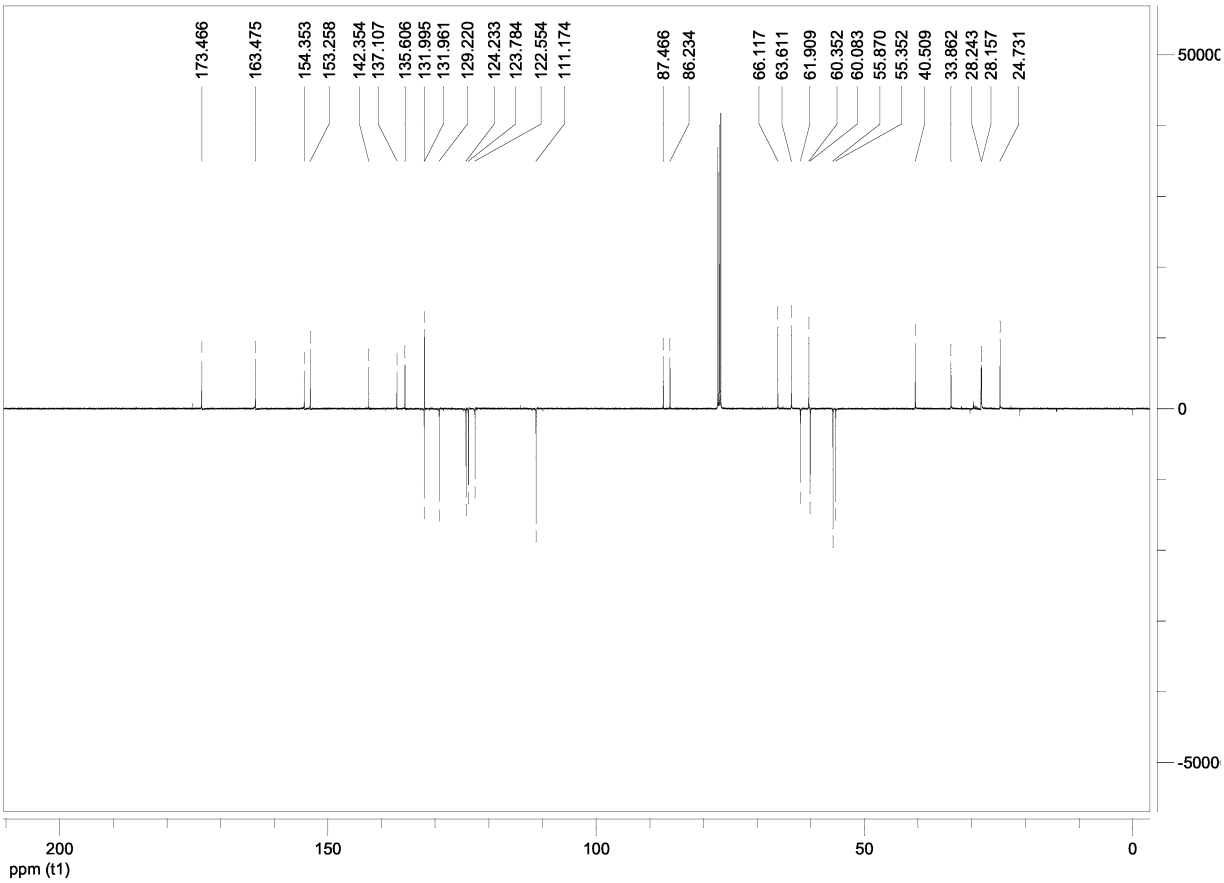
Biotin functionalised alkyne 41. AM89, SF269 (data).



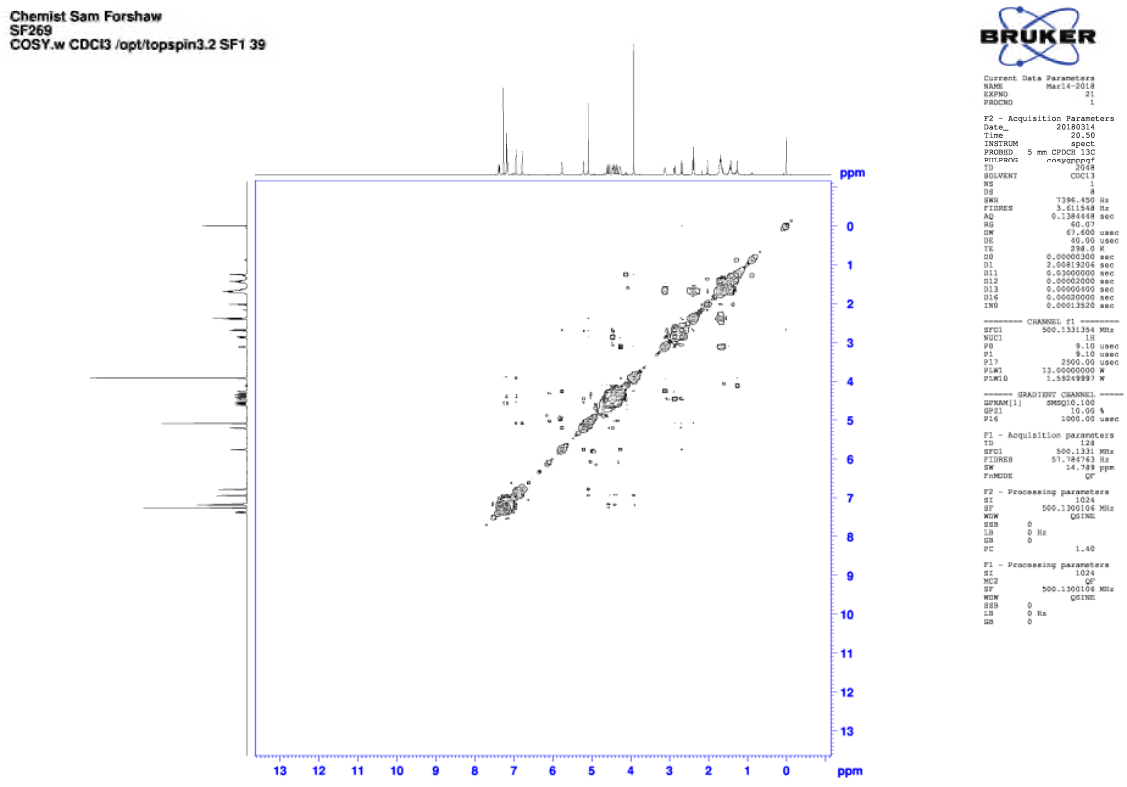
δ_H (500 MHz, $CDCl_3$).



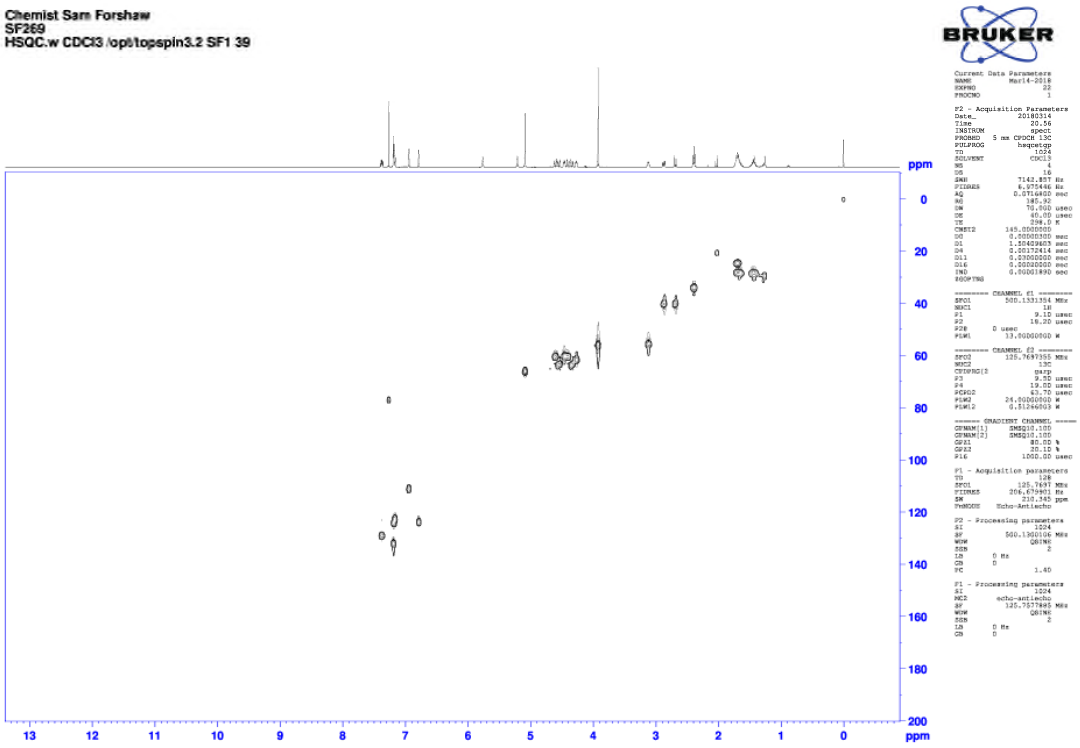
δ_C (126 MHz, $CDCl_3$).



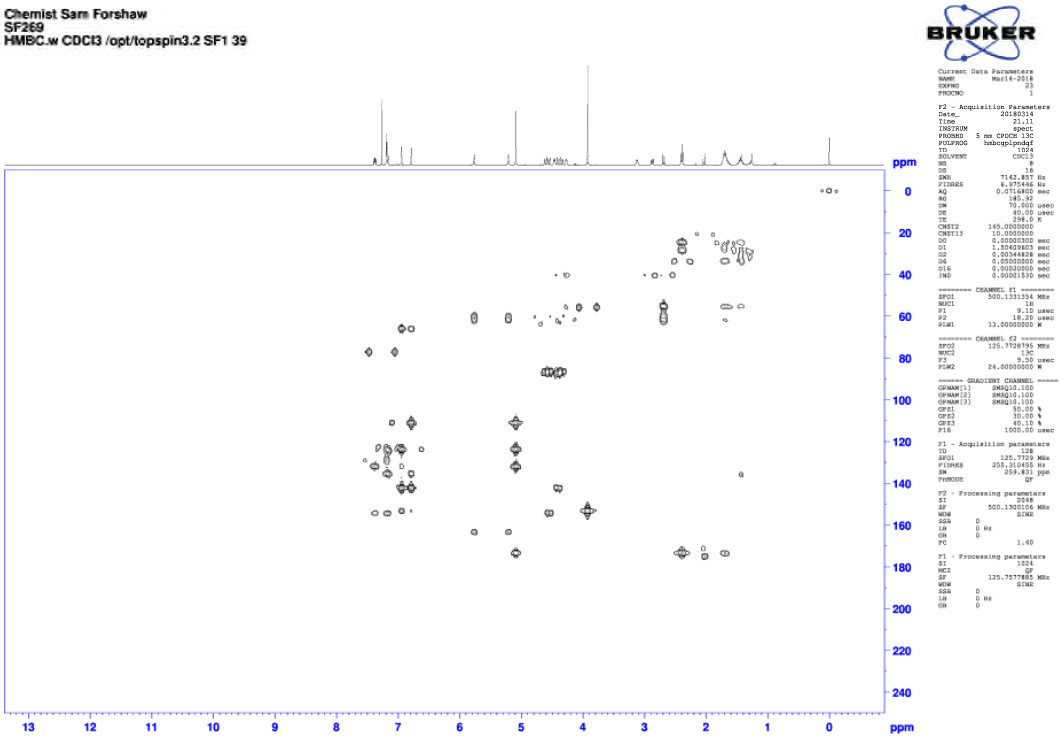
COSY:



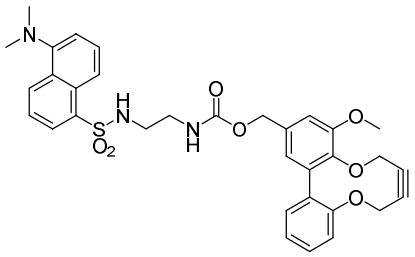
HSQC:


Chemist Sam Forshaw
SF269
HSQC.w CDCl3 /opt/topspin3.2 SF1 39
BRUKER
ppm
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

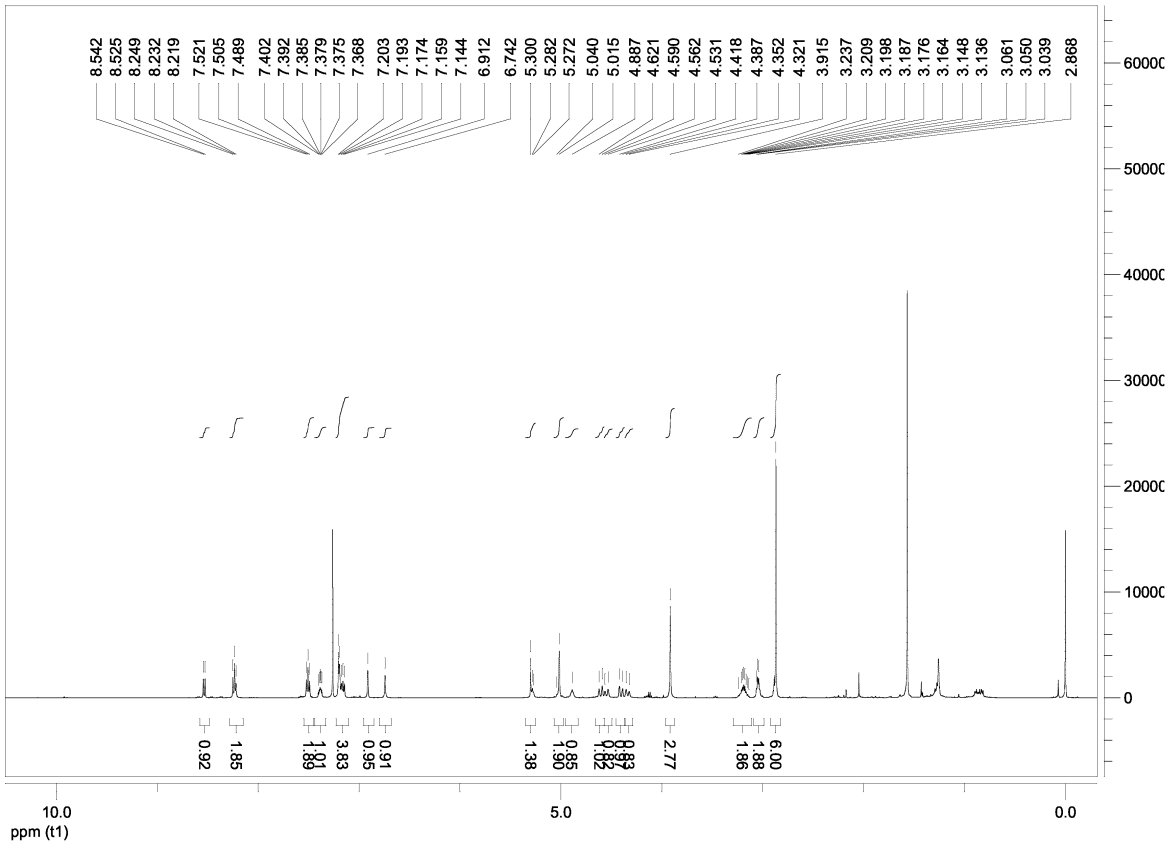
HMBC:


Chemist Sam Forshaw
SF269
HMBC.w CDCl3 /opt/topspin3.2 SF1 39
BRUKER
ppm
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm

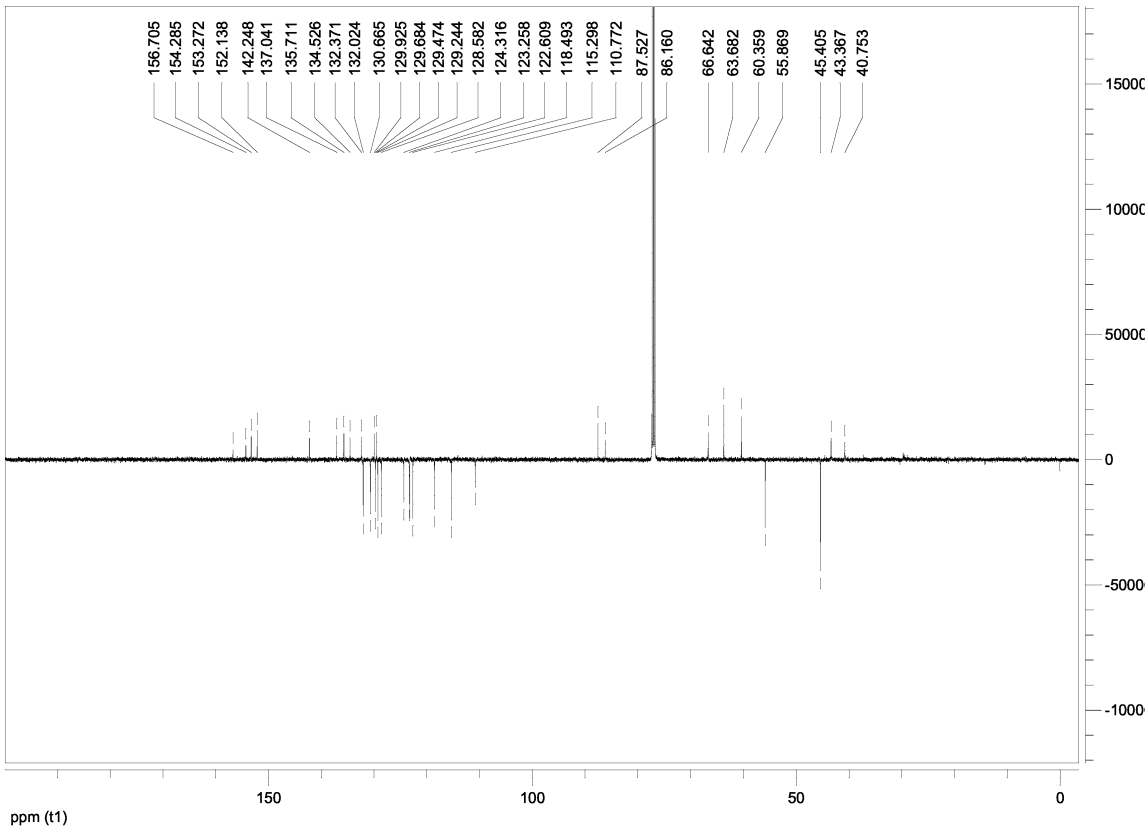
Dansyl carbamate derivative 42 (SF268).



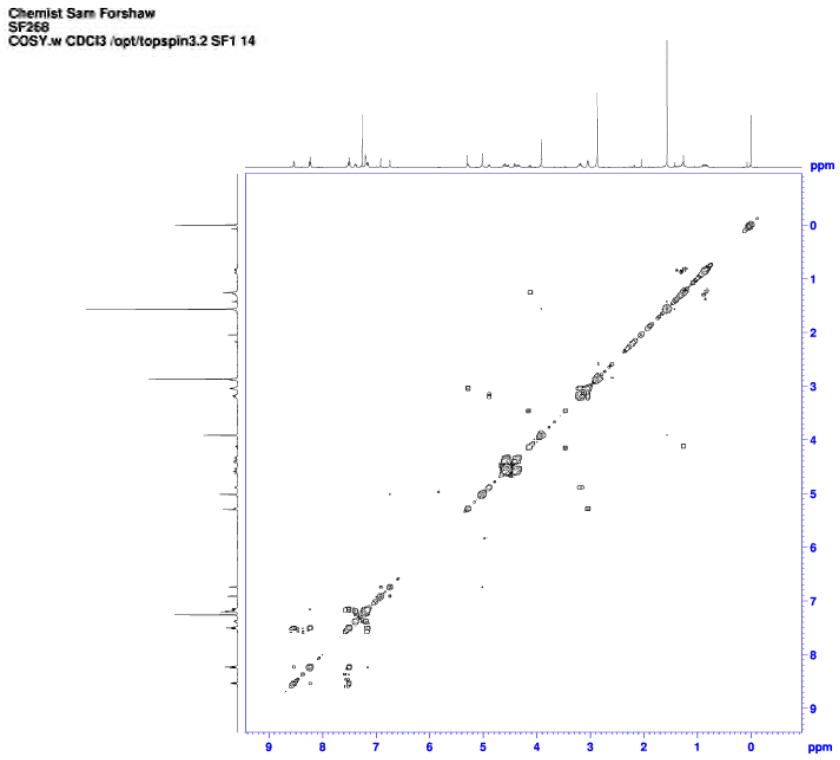
δ_H (500 MHz, $CDCl_3$).



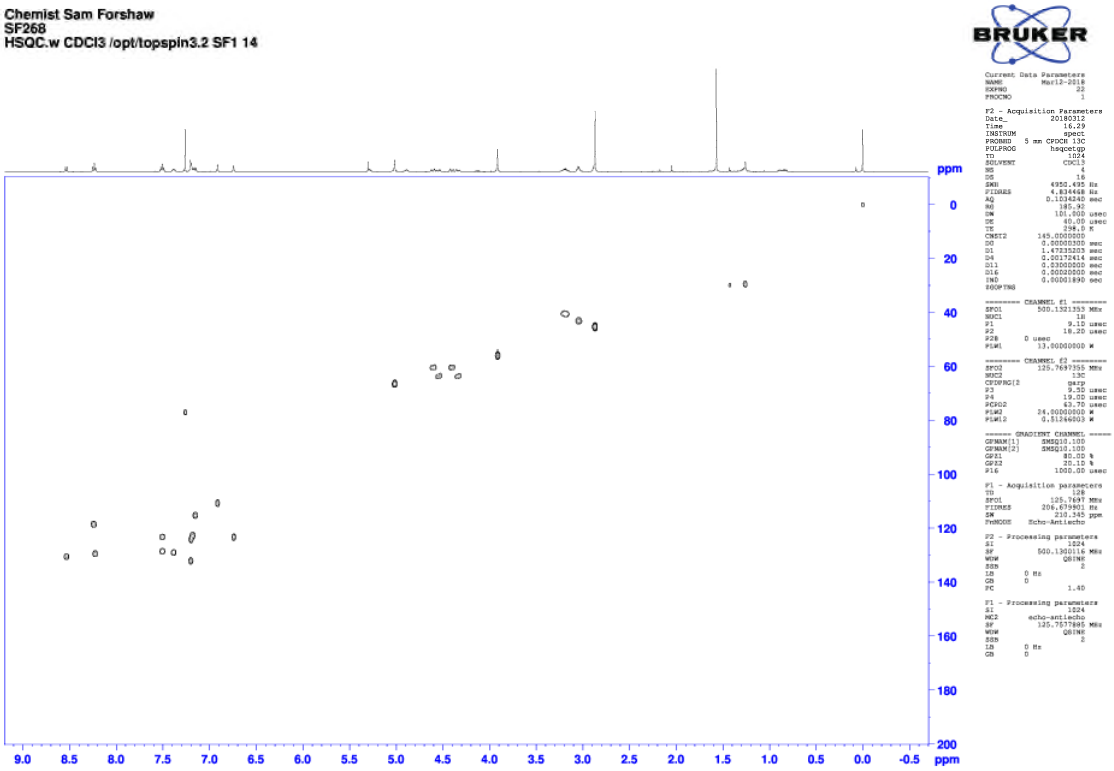
δ_C (126 MHz, $CDCl_3$).



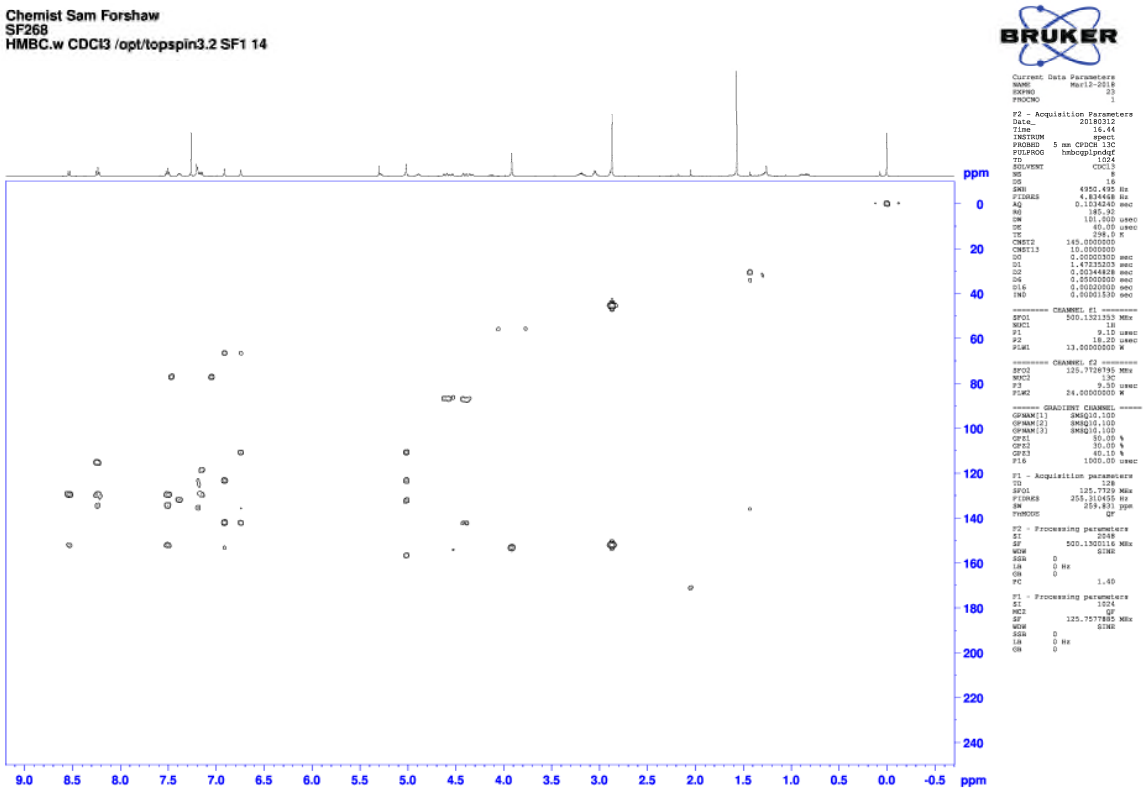
COSY



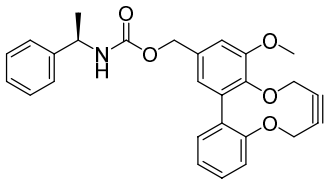
HSQC:


Chemist Sam Forshaw
SF268
HSQC.w CDCl3 /opt/topspin3.2 SF1 14
BRUKER

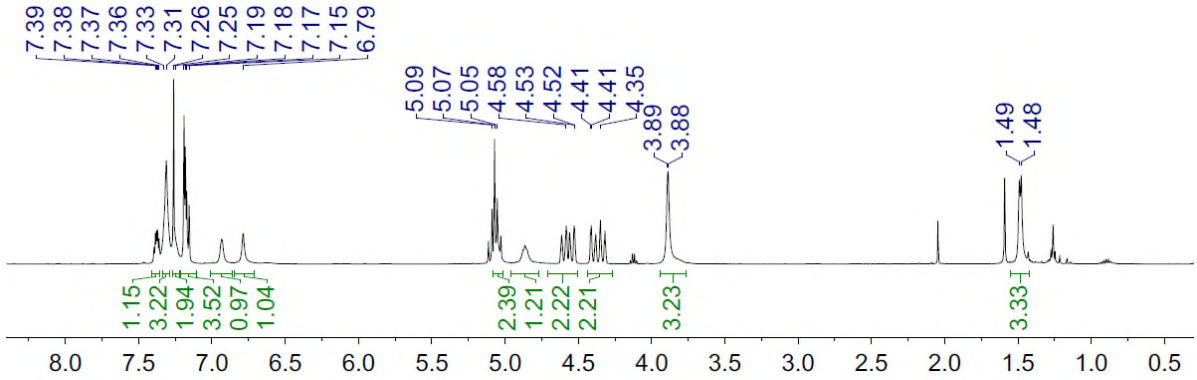
HMBC:


Chemist Sam Forshaw
SF268
HMBC.w CDCl3 /opt/topspin3.2 SF1 14
BRUKER

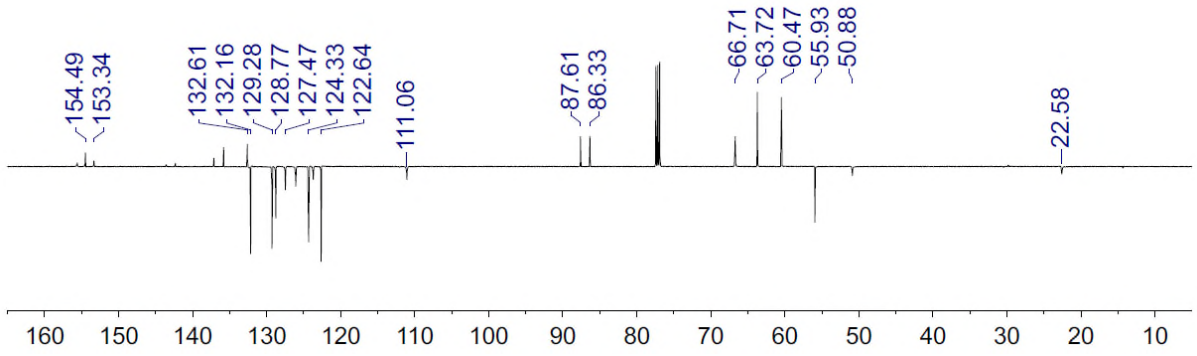
Carbamate alkyne 43 (RK-3-220).



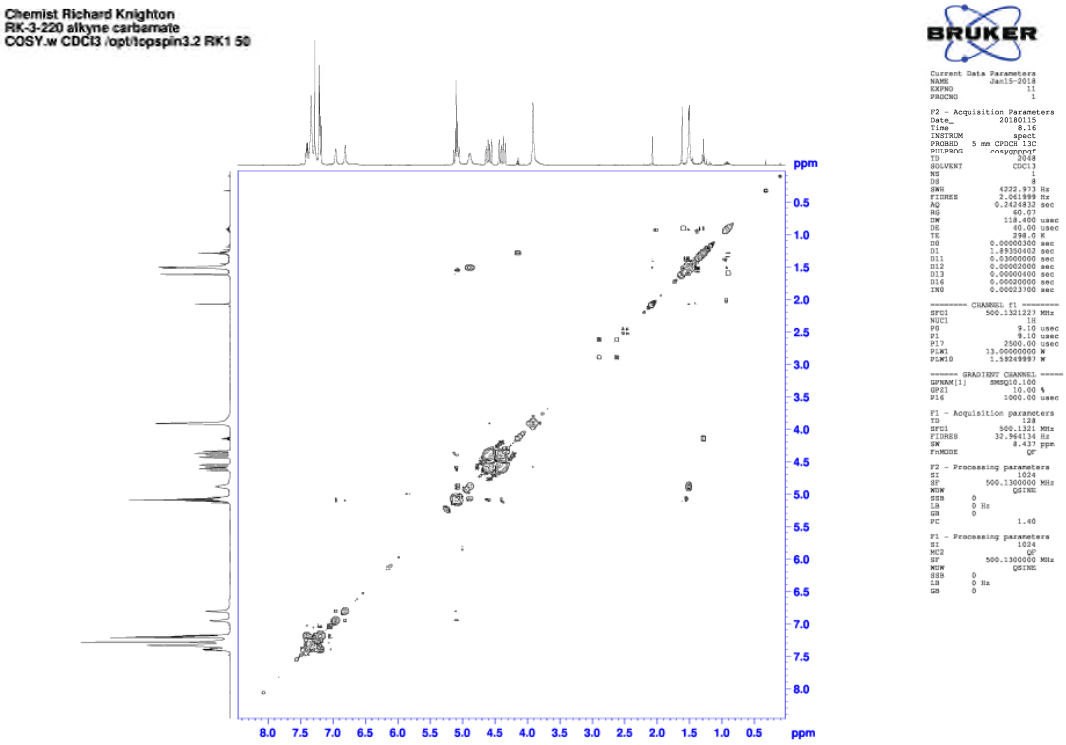
δ_H (500 MHz, $CDCl_3$).



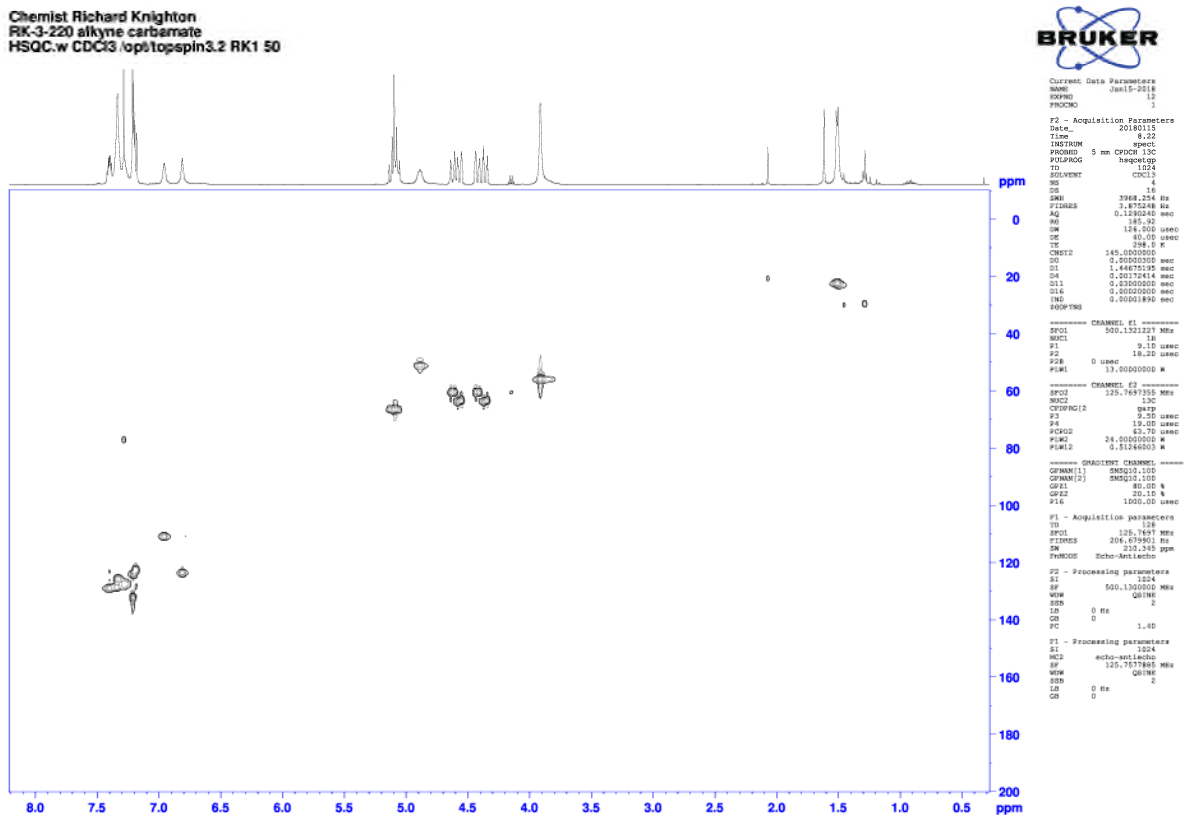
δ_C (126 MHz, $CDCl_3$).



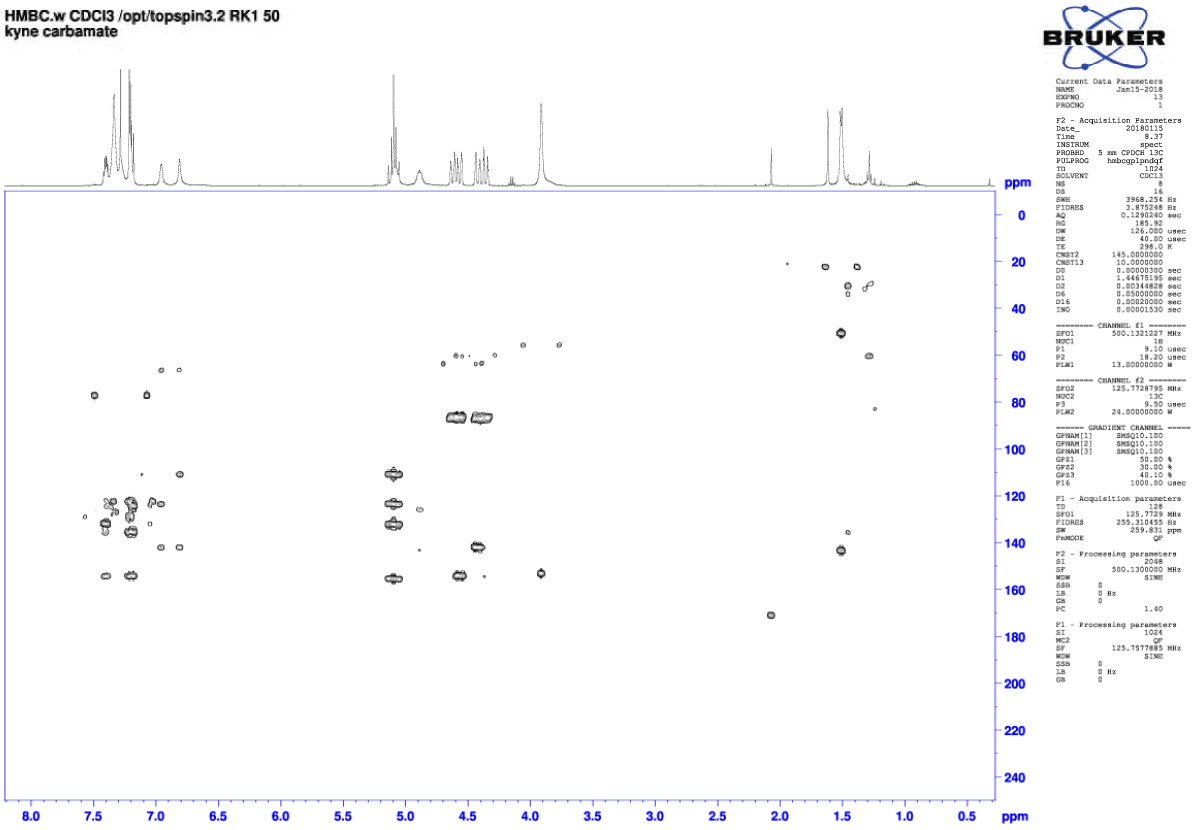
COSY


Chemist Richard Knighton
RK-3-220 alkyne carbamate
COSY.w CDCl3 /opt/topspin3.2 RK1 50
BRUKER
ppm
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 ppm

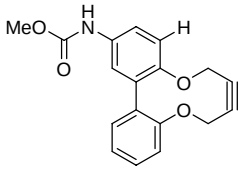
HSQC


Chemist Richard Knighton
RK-3-220 alkyne carbamate
HSQC.w CDCl3 /opt/topspin3.2 RK1 50
BRUKER
ppm
0 20 40 60 80 100 120 140 160 180 200 ppm
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 ppm

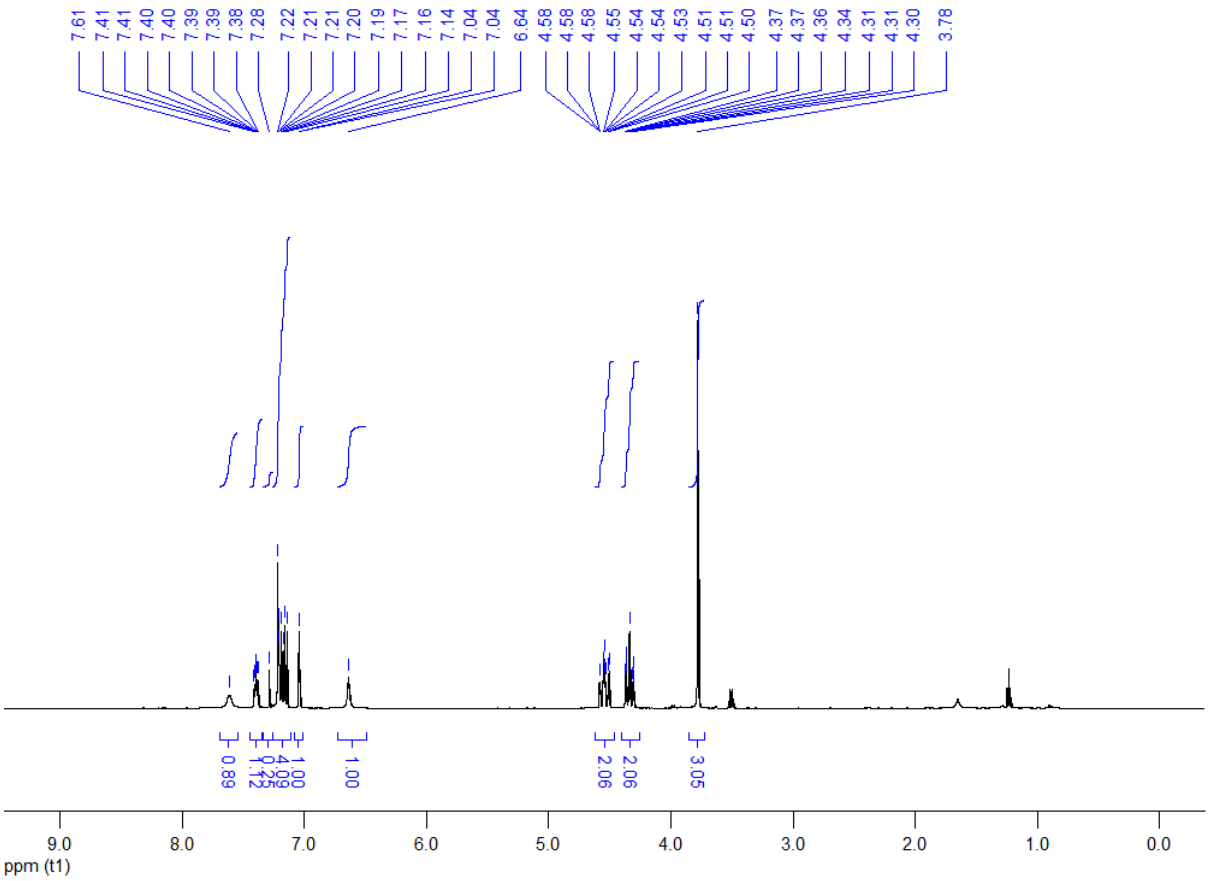
HMBC


HMBC.w CDCl3 /opt/topspin3.2 RK1 50
kyne carbamate
BRUKER
ppm
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
20
40
60
80
100
120
140
160
180
200
220
240

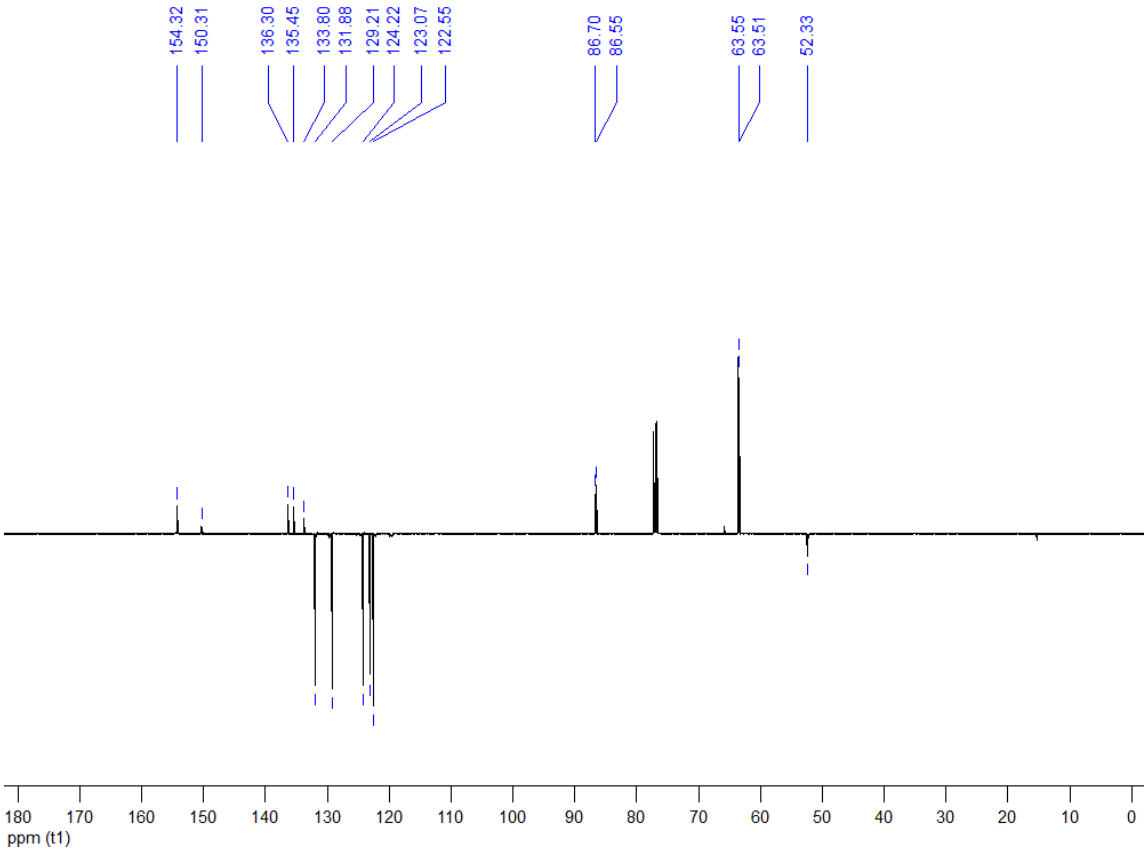
Carbamate 44. (AM102).



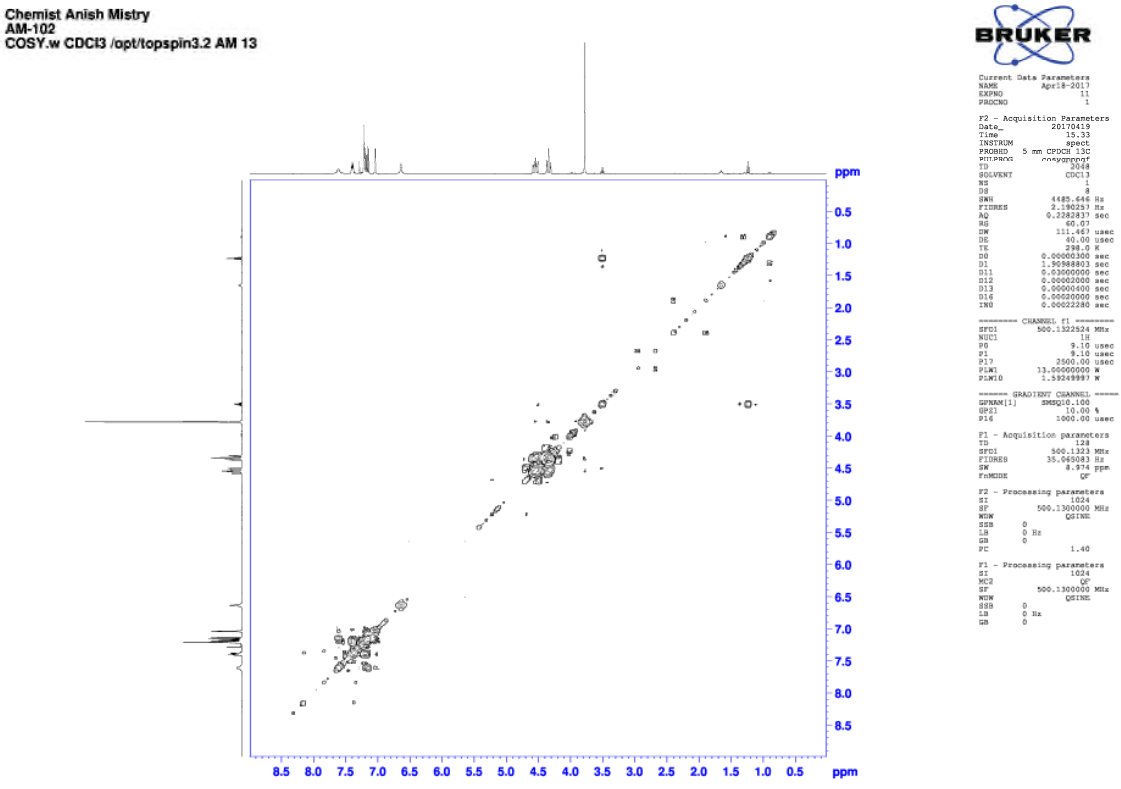
δ_H (500 MHz, $CDCl_3$).



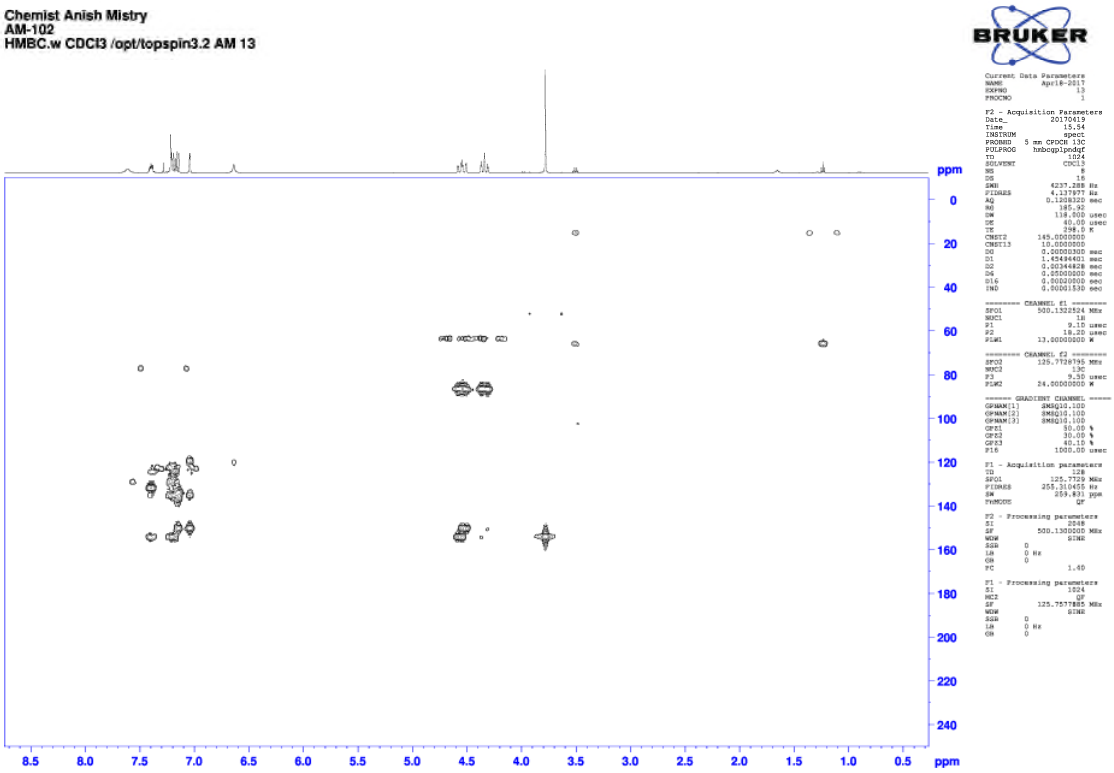
δ_C (126 MHz, $CDCl_3$).



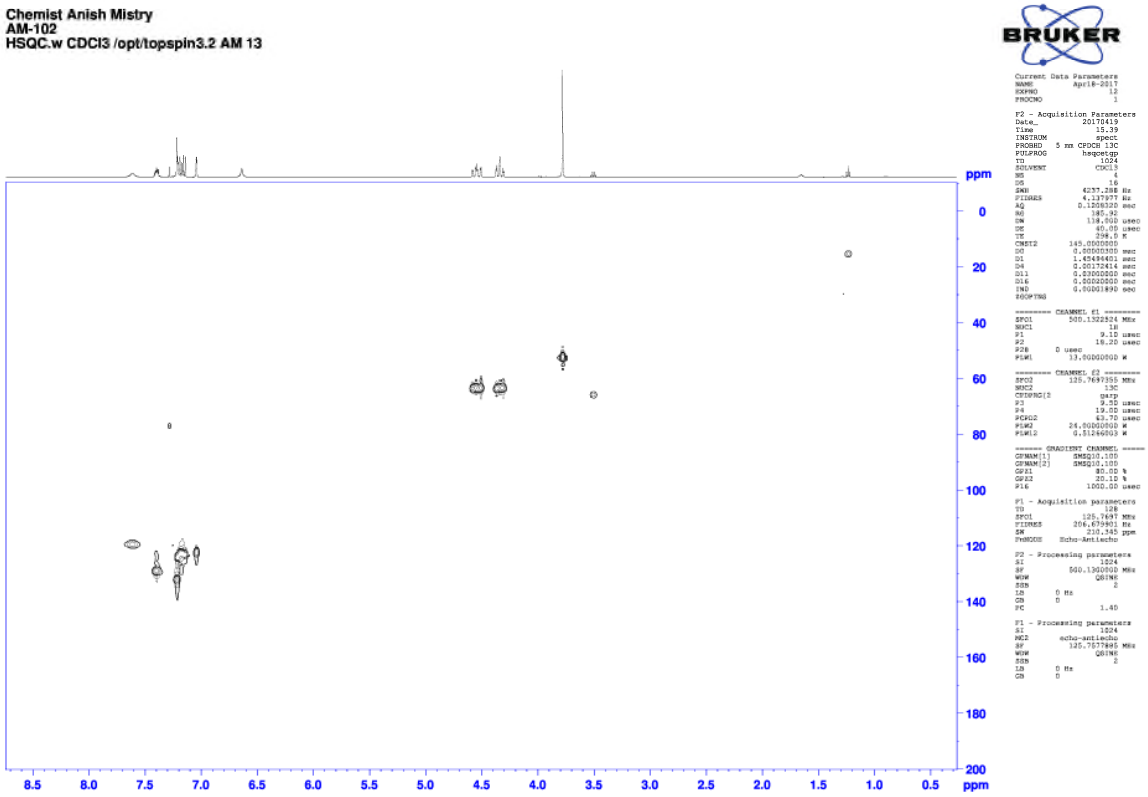
COSY



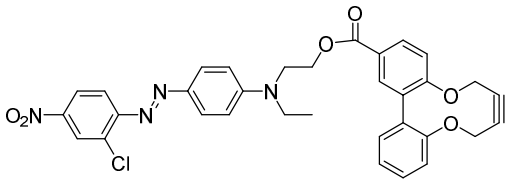
HMBC


Chemist Anish Mistry
AM-102
HMBC.w CDCl3 /opt/topspin3.2 AM 13
BRUKER
ppm
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 ppm

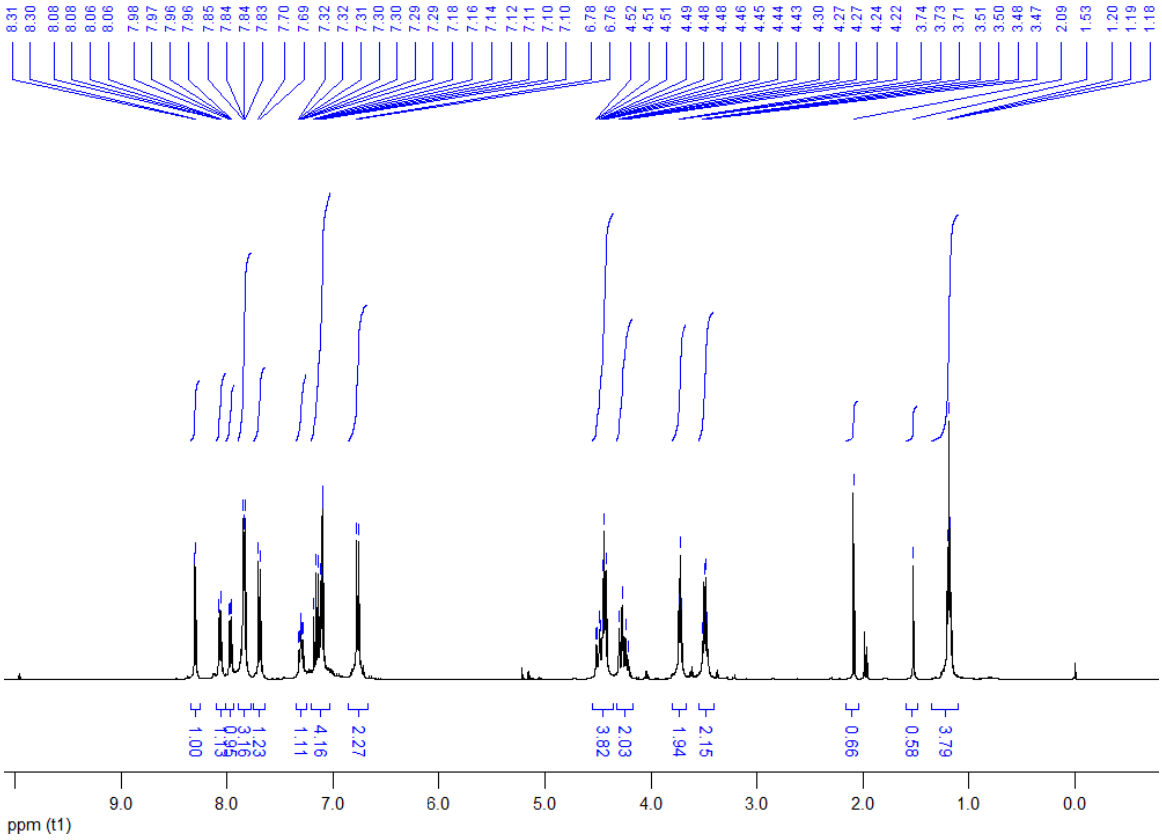
HSQC


Chemist Anish Mistry
AM-102
HSQC.w CDCl3 /opt/topspin3.2 AM 13
BRUKER
ppm
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 ppm

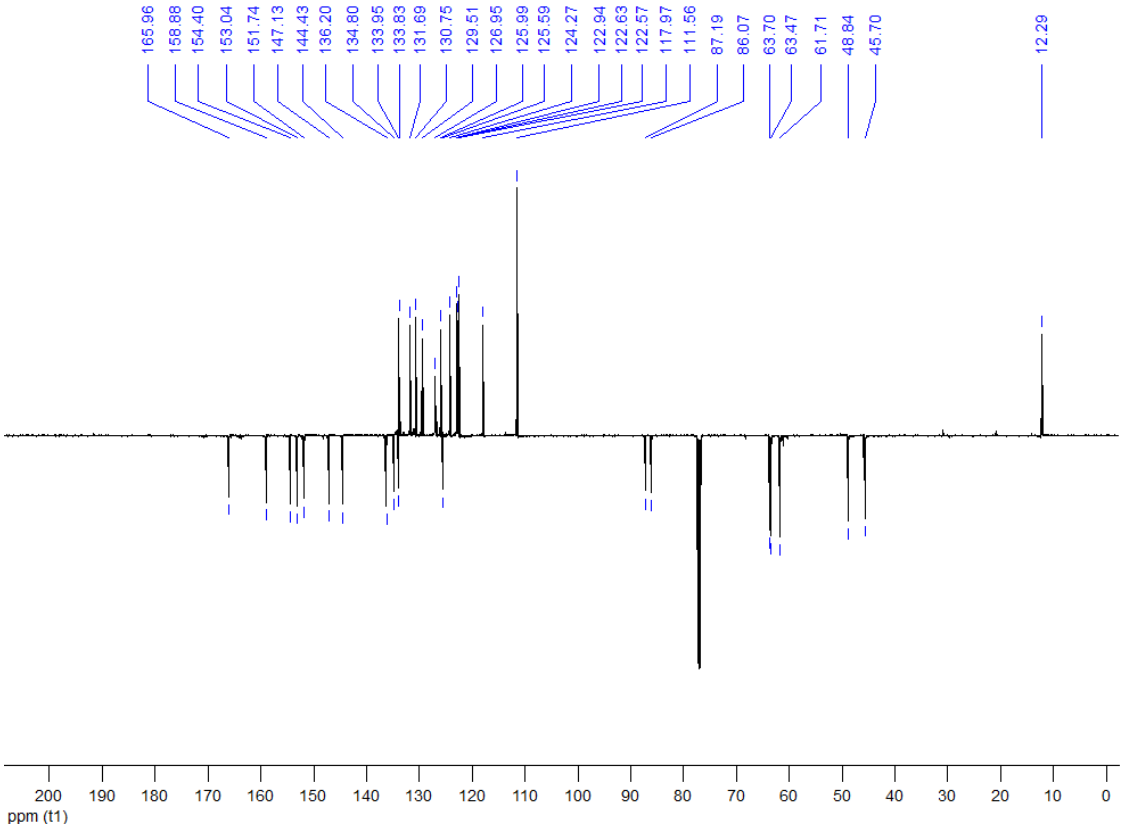
Ester linked to disperse red 45. AM90.



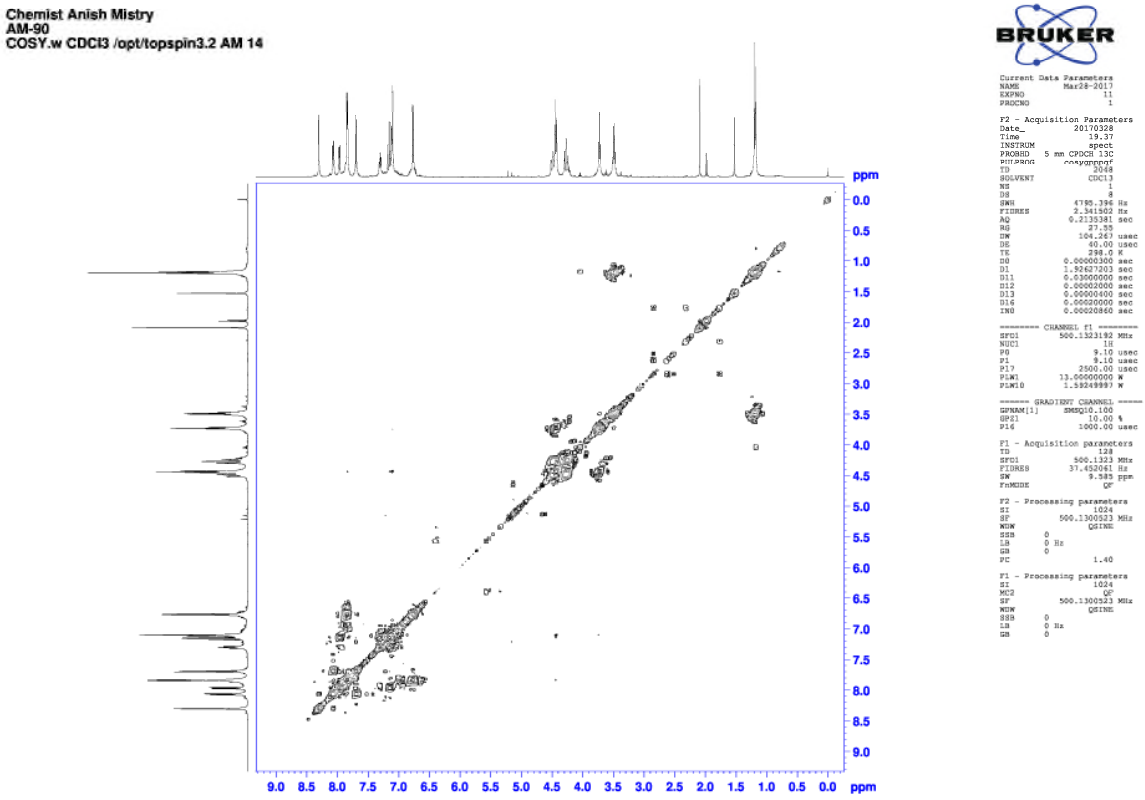
δ_H (500 MHz, $CDCl_3$).



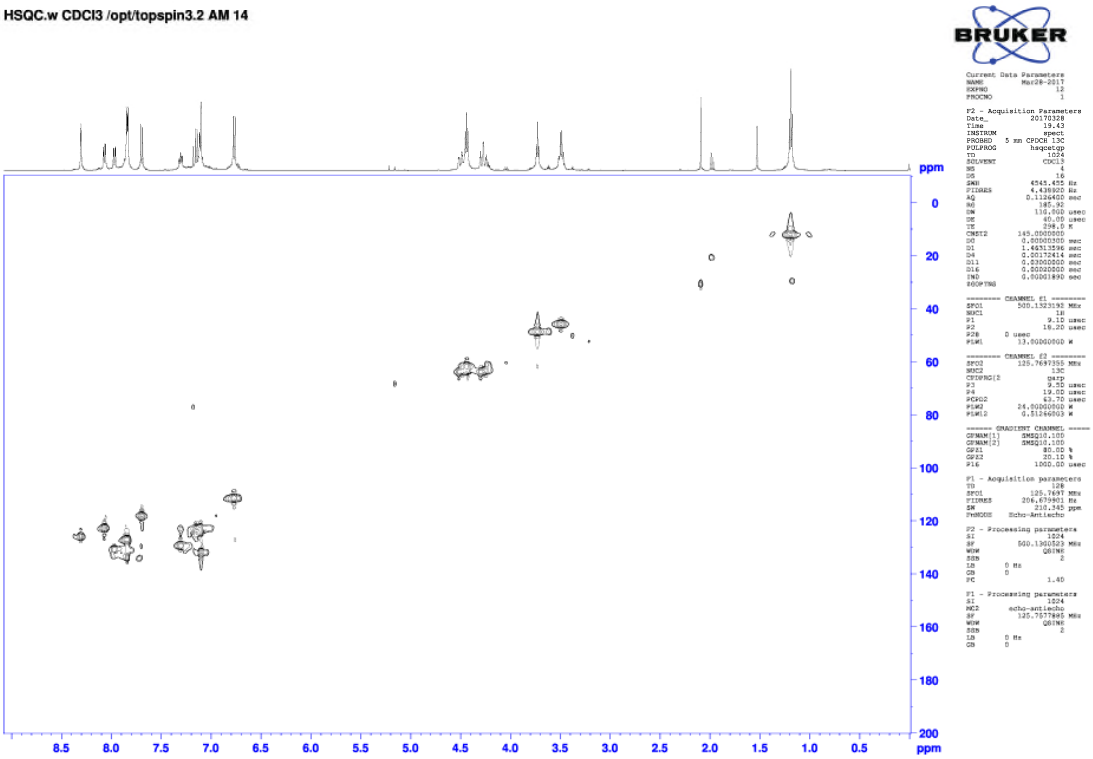
δ_C (126 MHz, $CDCl_3$).



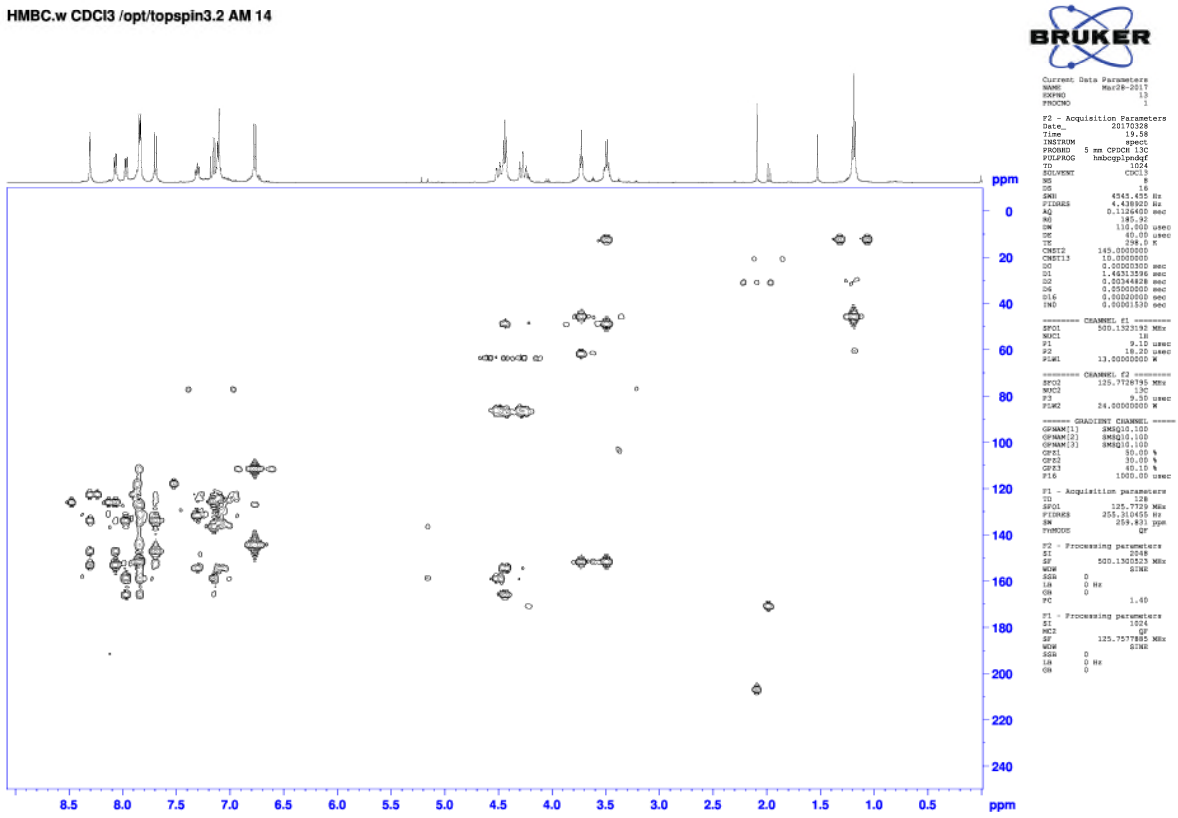
COSY



HSQC

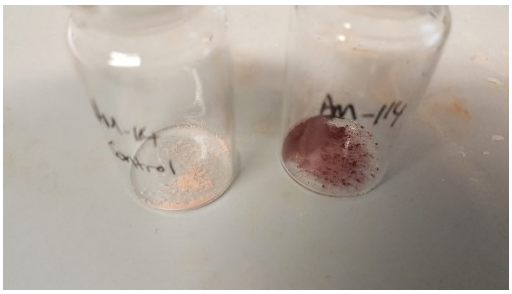

HSQC.w CDCl3 /opt/topspin3.2 AM 14
BRUKER
ppm
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

HMBC.


HMBC.w CDCl3 /opt/topspin3.2 AM 14
BRUKER
ppm
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 ppm

Polystyrene bead functionalisation (AM113,114).

Tris(2-aminoethyl)amine polymer beads (polystyrene based, Aldrich, 3.5-5.0 mmol/g N loading, 1% cross-linked with dibvinylbenzene) (10 mg) and aldehyde **16 (**10 mg, 0.034 mmol) were stirred in MeOH (1.5 mL) and $NaBH_3CN$ (5 mg, 0.131 mmol) was added. The mixture was stirred overnight. At the end of this time the beads were filtered using filter paper and washed with MeOH, then collected and dried. Disperse red azide **22** (7 mg, 0.019 mmol) was dissolved in MeCN (2 mL) and the dried beads were added to this solution. A control reaction was set up containing unfunctionalised beads (5 mg) and **22** (7 mg, 0.019 mmol) in MeCN (2 mL). After stirring for 4 days (left hand picture below) the beads were filtered and washed with acetonitrile until no more colour was washed from the beads (right hand picture below). The beads which had been functionalised with **16** retained the red colour (right hand vial) whereas the colour was washed from the control vial (left) indicating that the bead has become functionalised by **16** and retained the ability to react in 'click' cycloadditions with azides. The control reaction indicated that no non-specific interactions were responsible for the retention of the red colour by the beads.

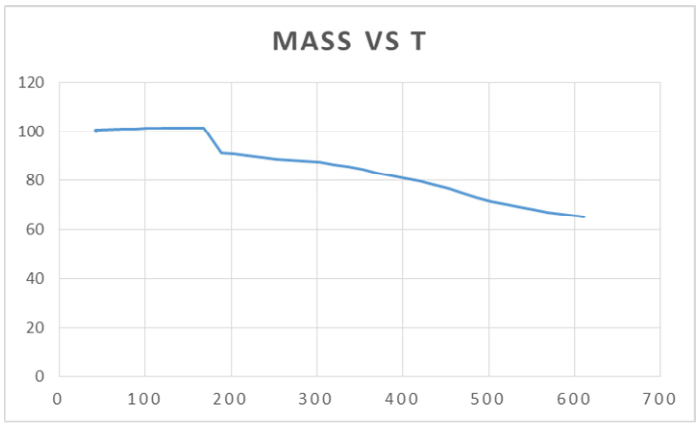


(above) Labelled polystyrene beads – before (left) and after (right) washing with MeCN.

TGA test results:

TGA measurements were performed on Mettler-Toledo DSC1 equipped with an autosampler. Samples were heated in 40 ul aluminium pans from 25-600 ‘C at a rate of 10’C min in a nitrogen atmosphere. Samples were analysed used Mettler-Toledo STARe software.

Aldehyde 16:



Methyl ester of acid 5: