Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Enantioselective Synthesis of *C*-Linked Spiroacetal-Triazoles as Privileged Natural Product-Like Scaffolds

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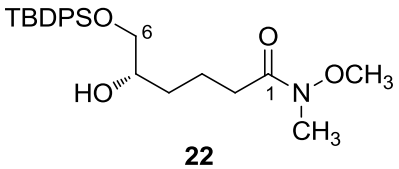
Supporting Information

General Experimental

Experiments requiring anhydrous conditions were performed under a dry nitrogen or argon atmosphere using apparatus heated and dried under vacuum and standard techniques in handling air- and/or moisture-sensitive materials unless otherwise stated. Solvents used for reactions and chromatographic purifications were distilled, unless otherwise stated. Commercial reagents were analytical grade or were purified by standard procedures prior to use.[1] Reactions were monitored by thin layer chromatography (TLC) carried out on 0.2 mm Kieselgel F254 (Merck) silica gel plates using UV light as a visualising agent and then stained and developed with heat using either vanillin in ethanolic sulfuric acid, ammonium heptamolybdate and cerium sulfate in aqueous sulfuric acid or potassium permanganate and potassium carbonate in aqueous sodium hydroxide. Separation of mixtures was performed by flash chromatography using 0.063–0.1 mm silica gel with the indicated eluent. Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Optical rotations were measured using a Perkin-Elmer 341 polarimeter at a wavelength of 598 nm and are reported in 10^{-1} °C cm^2 g^{-1}. Infrared spectra were obtained using a Perkin Elmer Spectrum 100 Fourier Transform Infrared spectrometer on a film ATR sampling accessory. Absorption peaks are reported as wavenumbers (ν, cm^{-1}). NMR spectra were recorded on either a Bruker DRX 300 spectrophotometer operating at 300 MHz for ^{1}H nuclei and 75 MHz for ^{13}C nuclei, or a Bruker DRX400 or a Bruker UltraShield Plus 400 spectrophotometer operating at 400 MHz for ^{1}H nuclei and 100 MHz for ^{13}C nuclei at ambient temperature. ^{1}H NMR chemical shifts are reported in parts per million (ppm) relative to the chloroform peak (δ 7.26). ^{1}H NMR values are reported as chemical shifts δ, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; dd, doublet of doublets; dt, doublet of triplets; td, triplet of doublets; m, multiplet), coupling constant (J, Hz) and assignment. Coupling constants were taken directly from the spectra. ^{13}C NMR chemical shifts are reported in ppm relative to the chloroform peak (δ 77.0). ^{13}C NMR values are reported as chemical shifts δ and assignment. Assignments were made with the aid of DEPT, COSY, HSQC, HMBC and NOESY experiments. Mass spectra were recorded on a VG-70SE mass spectrometer at a nominal accelerating voltage of 70 eV or on a Bruker micrOTOF-Q II mass spectrophotometer by electrospray ionisation in positive mode. Major and significant fragments are quoted in the form x (y), where x is the mass to charge ratio (m/z) and y is the percentage abundance relative to the base peak (100%). High-resolution mass spectra (HRMS) were obtained with a nominal resolution of 5,000 to 10,000.

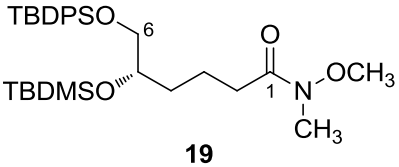
Experimental and Characterization data of the intermediates in the synthesis of of acetylenic spiroacetal **11**



22

6-(*tert*-Butyldiphenylsilyloxy)-(5*S*)-5-hydroxyl-*N*-methoxy-*N*-methylhexanamide (22)

To a stirred suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (2.24 g, 23.0 mmol) in anhydrous CH_2Cl_2 (80 mL) at 0 °C, was added dropwise a solution of $(CH_3)_3Al$ (2.0 M in toluene, 11.5 mL, 23.0 mmol). The mixture was stirred at 0 °C whereupon all of the solids dissolved to give a colourless solution. Whilst maintaining the mixture at 0 °C, a solution of (*S*)-valerolactone **13** (3.98 g, 10.8 mmol) in anhydrous CH_2Cl_2 (40 mL) was added dropwise to give a pale yellow solution that was allowed to warm to RT. After 3.5 h of vigourous stirring, the reaction mixture was carefully poured into a 1:1 ice-cold mixture of saturated NH_4Cl:Rochelle's salt (80 mL) to afford a colourless suspension. Et_2O (60 mL) was added and the suspension stirred vigourously with warming to RT over 45 mins. The layers were separated and the aqueous phase was extracted with Et_2O (2 x 60 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude *title compound* **22** as a yellow oil (4.64 g, 100%) that was used without further purification. Purification by flash chromatography (30% to 70% EtOAc/*n*-hexane) afforded the *title compound* **22** as a faint yellow oil. $[\alpha]_D^{20}$ -2.0 (c 1.00 in $CHCl_3$); R_f (30% EtOAc/*n*-hexane) 0.20, (70% EtOAc/*n*-hexane) 0.55; δ_H (300 MHz, $CDCl_3$) 1.07 (9H, s, $OSiPh_2{}^tBu$), 1.43–1.49 (2H, m, 4–H), 1.64–1.81 (2H, m, 3–H), 2.43 (2H, t, $^3J_{2,3}$ 7.3 Hz, 2–H), 2.65 (1H, br s, OH), 3.16 (3H, s, NCH_3), 3.51 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{6A,5}$ 7.5, 6–H_A), 3.66 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{6B,5}$ 3.5 Hz, 6–H_B), 3.66 (3H, s, OCH_3), 3.70–3.78 (1H, m, 5–H) 7.36–7.43 (6H, m, Ph), 7.64–7.67 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) 19.2 (C, $OSiPh_2{}^tBu$), 20.5 (CH_2, C–3), 26.8 (CH_3, $OSiPh_2{}^tBu$), 31.6 (CH_2, C–2), 32.1 (CH_3, NCH_3), 32.4 (CH_2, C–4), 61.1 (CH_3, OCH_3), 68.0 (CH_2, C–6), 71.6 (CH, C–5), 127.7 (CH, Ph), 129.7 (CH, Ph), 133.2 (C, Ph), 135.5 (CH, Ph), 135.5 (CH, Ph), 174.3 (C, C–1). The ^1H and ^{13}C NMR data obtained was in agreement with that reported in the literature.[2]

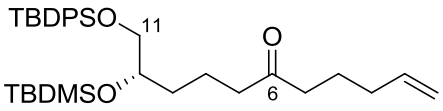


19

(5*S*)-5-(*tert*-Butyl-dimethylsilyloxy)-6-(*tert*-butyldiphenylsilyloxy)-*N*-methoxy-*N*-methylhexanamide (19)

To a stirred solution of crude Weinreb alcohol **22** (*ca.* 7.09 g, 16.5 mmol) in anhydrous CH_2Cl_2 (45 mL) in a nitrogen flushed 2-necked round bottom flask, was added imidazole (2.63 g, 38.64 mmol), DMAP (449.0 mg, 3.68 mmol) and TBDMSCl (2.86 g, 19.0 mmol) at RT and the mixture was heated to 45 ºC. After 13 h, the reaction mixture was cooled to RT and quenched with saturated $NaHCO_3$ (35 mL). The aqueous phase was extracted with Et_2O (50 mL, then 2 x 25 mL) and the

combined organic extracts were washed with saturated NaCl (100 mL). The aqueous washing was extracted with Et_2O (2 x 50 mL) and the organic phases were dried over $MgSO_4$. Concentration of the combined organic phases *in vacuo* gave a thick yellow oil. Purification by flash chromatography twice (5%, 9% to 17% EtOAc/*n*-hexane) gave the *title compound* **19** as a thick pale yellow oil (7.04 g, 78%). $[\alpha]_D^{23}$ -12.6 (c 1.01 in $CHCl_3$); R_f (17% EtOAc/*n*-hexane) 0.48; δ_H (300 MHz, $CDCl_3$) –0.07 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.01 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.84 (9H, s, OSiPh$_2$$^t\underline{Bu}$), 1.04 (9H, s, OSiPh$_2$$^t\underline{Bu}$), 1.43–1.59 (1H, m, 4–$H_A$), 1.61–1.76 (3H, m, 3–H and 4–H_B), 2.43 (2H, t, $^3J_{2,3}$ 7.5, 2–H), 3.18 (3H, s, NC$\underline{H_3}$), 3.48 (1H, dd, $^2J_{AB}$ 10.5 and $^3J_{6A,7}$ 7.5, 6–H_A), 3.59 (1H, dd, $^2J_{AB}$ 10.5 and $^3J_{6A,7}$ 4.5, 6–H_B), 3.67 (3H, s, OC$\underline{H_3}$), 3.71–3.74 (1H, m, 5–H), 7.34–7.45 (6H, m, Ph), 7.65–7.69 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) –4.8 (CH_3, OSi(C$\underline{H_3}$)$_2$^{t}Bu), –4.5 (CH_3, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 18.0 (C, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 19.2 (C, OSiPh$_2$$^t\underline{Bu}$), 20.4 ($CH_2$, C–3), 25.9 ($CH_3$, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 26.9 ($CH_3$, OSiPh$_2$$^t\underline{Bu}$), 32.3 ($CH_3$ and CH_2, NC$\underline{H_3}$ and C–2), 34.1 (CH_2, C–4), 61.2 (CH_3, OCH_3), 67.6 (CH_2, C–6), 72.7 (CH, C–5), 127.6 (CH, Ph), 129.6 (CH, Ph), 133.7 (C, Ph), 133.7 (C, Ph), 135.6 (CH, Ph), 174.6 (C, C–1). The ^{1}H and ^{13}C NMR data obtained was in agreement with that reported in the literature.[2]

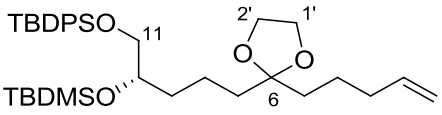


23

(10*S*)-10-(*tert*-Butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)undec-1-en-6-one (23)

Magnesium turnings (467 mg, 19.21 mmol) were stirred vigourously under an argon atmosphere overnight. To this was added anhydrous Et_2O (2 mL) and a single crystal of I_2. The mixture was heated gently and stirred until the orange colour faded. 5-Bromo-1-pentene (1.1 mL, 9.30 mmol) was added dropwise with gentle heating whereupon the reaction was initiated. The reaction mixture went bright opaque yellow to a white cloudy suspension with the evolution of gas. Upon cessation of gaseous evolution (0.5 h), the Grignard reagent was cooled to 0 °C and a solution of Weinreb amide **19** (2.09 g, 3.84 mmol) in anhydrous Et_2O (4 mL, then 2 x 2 mL) were added by cannula. The resulting dark grey suspension was stirred at 0 °C for 3 h. Saturated NH_4Cl (6 mL) was carefully added at 0 °C and the mixture allowed to warm to RT with vigourous stirring. The organic layer was separated and the aqueous phase extracted with EtOAc (4 x 30 mL). The combined organic extracts were washed with saturated NaCl (50 mL), and the aqueous washing extracted with EtOAc (30 mL). The organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to give a yellow oil. Purification by flash chromatography (0%, 5% EtOAc/*n*-hexane) gave the *title compound* **23** as a pale yellow oil (1.67 g, 79%). $[\alpha]_D^{20}$ -12.0 (c 1.02 in $CHCl_3$); R_f (5% EtOAc/*n*-hexane) 0.27; IR (film) ν_{max}/cm^{-1} 2929 (C–H), 2857 (C–H), 1715 (C=O), 1641 (C=C), 1428, 1253, 1111, 824, 774, 701; δ_H (400 MHz, $CDCl_3$) –0.08 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.00 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.84 (9H, s, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 1.04 (9H, s, OSiPh$_2$$^t\underline{Bu}$), 1.40–1.46 (2H, m, 8–$H_A$ and 9–H_A), 1.55–1.72 (4H, m, 4–H, 8–H_B and 9–H_B), 2.03–2.08 (2H, m, 3–H), 2.37–2.42 (4H, m, 5–H and 7–H), 3.45 (1H, dd, $^2J_{AB}$ 10.1 and $^3J_{11A,10}$ 6.9, 11–H_A), 3.57 (1H, dd, $^2J_{AB}$ 10.1 and $^3J_{11B,10}$ 5.0, 11–H_B), 3.66–3.72 (1H, m, 10–H), 4.92–5.04 (2H, m, 1–H), 5.72–5.83 (1H, m, 2–H), 7.36–7.45 (6H, m, Ph), 7.65–7.68 (4H, m, Ph); δ_C (100 MHz, $CDCl_3$) –4.8 (CH_3, OSi(C$\underline{H_3}$)$_2$^{t}Bu), –4.5 (CH_3, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 18.0 (C, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 19.2 (C, OSiPh$_2$$^t\underline{Bu}$), 19.6 ($CH_2$, C–8), 22.8 ($CH_2$, C-4), 25.8 ($CH_3$, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 26.9 ($CH_3$, OSiPh$_2$$^t\underline{Bu}$), 33.1 ($CH_2$, C–3), 33.9 ($CH_2$, C–9), 41.8 ($CH_2$, C–5), 43.2 ($CH_2$, C–7), 67.5 ($CH_2$, C–11), 72.5 (CH, C–10), 115.2 (CH, C–1), 127.6 (CH, Ph), 129.6 (CH, Ph), 133.6 (C, Ph), 133.6 (C, Ph) 135.6 (CH, Ph), 138.0 (CH, C–2) 210.9 (C, C–6); MS *m/z* (ESI+) 575 ([M + Na]$^+$, 100%), 553

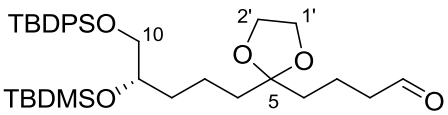
(M + H^+, 12), 475 (4), 421 (15); HRMS (ESI+): $[M + H]^+$, found 553.3535. $C_{33}H_{53}O_3Si_2^+$ requires 553.3528.



18

(10*S*)-10-(*tert*-Butyldimethylsilyloxy)-11-(*tert*-butyldiphenylsilyloxy)-6-(1,3-dioxolan-2-yl)undec-1-ene (18)[3]

A mixture of ketone **23** (932 mg, 1.69 mmol) and ethylene glycol (190 µL, 3.41 mmol) were azeotrophically dried with toluene (3 x 1 mL). Triethyl orthoformate (820 µL, 4.93 mmol) and $Bi(OTf)_3$ (39 mg, 0.059 mmol) were then added at RT. After stirring at RT for 1.75 h, the mixture turned homogeneous. Saturated $NaHCO_3$ (20 mL) and a few drops of aqueous NaOH (1 M) were added at RT and the aqueous phase extracted with EtOAc (3 x 20 mL). The organic extracts were washed with saturated NaCl (20 mL) and the aqueous washing extracted with EtOAc (20 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo* to afford an opaque yellow oil. Purification by flash chromatography (0%, 5% EtOAc/*n*-hexanes) gave the *title compound* **18** as a pale yellow oil (871 mg, 86%). R_f (5% EtOAc/n-hexane) 0.27; $[\alpha]_D^{23}$ -15.5 (c 1.08 in $CHCl_3$); IR (film) ν_{max}/cm^{-1} 2930 (C–H), 2857 (C–H), 1641 (C=C), 1428 (=C–H), 1253, 1112 (C–O–C), 824, 774, 702; δ_H (400 MHz, $CDCl_3$) –0.06 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.01 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.84 (9H, s, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 1.05 (9H, s, OSiPh$_2$$^t\underline{Bu}$), 1.20–1.52 (6H, m, 4–$H_A$, 5–$H_A$, H–$7_A$, 8–H, and 9–$H_A$) 1.55–1.70 (4H, m, 4–$H_B$, 5–$H_B$, H–$7_B$, and 9–$H_B$), 2.03–2.08 (2H, m, 3–H), 3.46 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{11A,10}$ 6.7, 11–H_A), 3.58 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{11B,10}$ 5.0, 11–H_B), 3.67–3.71 (1H, m, 10–H), 3.92 (4H, s, 1'–H and 2'–H), 4.93–5.03 (2H, m, 1–H), 5.75–5.85 (1H, m, 2–H), 7.35–7.44 (6H, m, Ph), 7.66–7.69 (4H, m, Ph); δ_C (100 MHz, $CDCl_3$) –4.8 (CH_3, OSi(C$\underline{H_3}$)$_2$^{t}Bu), –4.4 (CH_3, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 18.1 (C, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 19.2 (C, OSiPh$_2$$^t\underline{Bu}$), 19.5 ($CH_2$, C–8), 23.1 ($CH_2$, C–4), 25.9 ($CH_3$, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 26.9 ($CH_3$, OSiPh$_2$$^t\underline{Bu}$), 33.9 ($CH_2$, C–3), 34.7 ($CH_2$, C–9), 36.7 ($CH_2$, C–5), 37.5 ($CH_2$, C–7), 64.9 (2 x CH_2, C–1' and C–2'), 67.8 (CH_2, C–11), 72.9 (CH, C–10), 111.7 (C, C–6), 114.6 (CH_2, C–1) 127.6 (CH, Ph), 129.6 (CH, Ph), 133.7 (C, Ph), 133.7 (C, Ph), 135.6 (CH, Ph), 138.7 (CH, C–2); MS *m/z* (ESI+, MS_2+ (597)) 597 (17%), 519 ($[M – Ph]^+$, 23), 465 ($[M – OTDBMS]^+$, 69), 403 (36), 383 (100), 329 (57), 279 (21); HRMS (ESI+): $[M + H]^+$, found 597.3791. $C_{35}H_{57}O_4Si_2$ requires 597.3790.

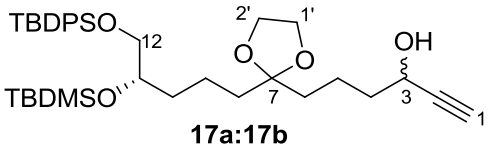


24

(9*S*)-9-(*tert*-Butyl-dimethylsilyloxy)-10-(*tert*-butyldiphenylsilyloxy)-5-(1,3-dioxolan-2-yl) decanal (24)[4]

To a solution of acetal **18** (738 mg, 1.24 mmol) in anhydrous CH_2Cl_2 (46 mL) was added a few drops of Sudan III indicator (0.1% in CH_2Cl_2). The bright red solution was cooled to -78 ºC and O_3 was bubbled through the solution for 1 h (O_3 generator settings, flow rate: 50 L/h, discharge: 100 V,

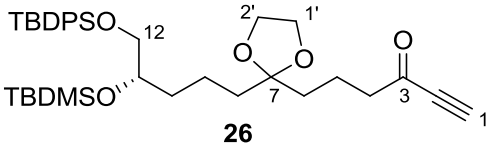
O_2 pressure: 15 psi) until complete discolouration was observed. While maintaining the reaction mixture at -78 ºC, the reaction vessel was flushed with nitrogen for 0.5 h whereupon the reaction mixture turned pale orange. NEt_3 (860 µL, 1.65 mmol) was slowly added at -78 ºC, stirred for 5 mins, then warmed to RT. The organic phase was dried over Na_2SO_4, passed through a glass sinter and the filtrate concentrated *in vacuo* to obtain pale red oil. Purification by flash chromatography (0%, 20% EtOAc/*n*-hexane) afforded the *title compound* **24** as a yellow oil (518 mg, 69%). $[\alpha]_D^{22}$ -13.5 (c 1.04 in $CHCl_3$); R_f (20% EtOAc/n-hexane) 0.33, (33% EtOAc/n-hexane) 0.55; IR (film) ν_{max}/cm^{-1} 2929 (C–H), 2857 (C–H), 1726 (C=O), 1428 (C–H), 1389, 1111 (C–O–C), 701; δ_H (300 MHz, $CDCl_3$) –0.06 (3H, s, OSi(C<u>H</u>$_3$)$_2$^{t}Bu), 0.01 (3H, s, OSi(C<u>H</u>$_3$)$_2$^{t}Bu), 0.84 (9H, s, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 1.05 (9H, s, OSiPh$_2$^{t}<u>Bu</u>), 1.32–1.55 (3H, m, 7–H, and 8–H$_A$), 1.58–1.75 (7H, m, 3–H, 4–H, 6–H, and 8–H$_B$), 2.44 (2H, td, $J_{2,1}$ 1.7 and $J_{2,3}$ 7.2, 2–H), 3.46 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{10A,9}$ 6.7, 10–H$_A$), 3.58 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{10B,9}$ 5.0, 10–H$_B$), 3.66–3.71 (1H, m, 9–H), 3.92 (4H, s, 1'–H and 2'–H), 7.34–7.45 (6H, m, Ph), 7.65–7.70 (4H, m, Ph), 9.76 (1H, t, $J_{1,2}$ 1.7, 1–H); δ_C (75 MHz, $CDCl_3$) –4.8 (CH$_3$, OSi(<u>C</u>H$_3$)$_2$^{t}Bu), –4.4 (CH$_3$, OSi(<u>C</u>H$_3$)$_2$^{t}Bu), 16.5 (CH$_2$, C–3), 18.1 (C, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 19.2 (C, OSiPh$_2$^{t}<u>Bu</u>), 19.5 (CH$_2$, C–7), 25.8 (CH$_3$, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 26.9 (CH$_3$, OSiPh$_2$^{t}<u>Bu</u>), 34.7 (CH$_2$, C–8), 36.4 (CH$_2$, C–4), 37.5 (CH$_2$, C–6), 43.9 (CH$_2$, C–2), 65.0 (2 x CH$_2$, C–1' and C–2'), 67.8 (CH$_2$, C–10), 72.8 (CH, C–9), 111.3 (C, C–5), 127.6 (CH, Ph), 129.6 (CH, Ph), 129.6 (CH, Ph), 133.7 (C, Ph), 133.7 (C, Ph), 135.6 (CH, Ph), 135.6 (CH, Ph), 202.3 (CH, C–1); MS *m/z* (ESI+) 669 (19%), 653 (100), 637 ([M + K]$^+$, 26), 621 ([M + Na]$^+$, 68), 599 ([M + H]$^+$, 4), (7); HRMS (ESI+): [M + H]$^+$, found 599.3583. $C_{34}H_{55}O_5Si_2^+$ requires 599.3583.



17a:17b

(3*S*,11*S*)- and (3*R*,11*S*)-11-(*tert*-Butyldimethylsilyloxy)-12-(*tert*-butyldiphenylsilyloxy)-7-(1,3-dioxolan-2-yl)dodec-1-yn-(3)-ol (17a:17b)

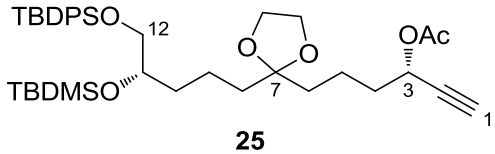
To a solution of aldehyde **24** (1.27 g, 2.12 mmol) in anhydrous THF (20 mL) at 0 ºC under an argon atmosphere was added a solution of ethynylmagnesium bromide (0.5 M in THF, 34 mL, 17 mmol). After stirring at 0 ºC for 3 h, saturated NH_4Cl (10 mL) and distilled H_2O (5 mL) were added and the mixture stirred vigourously. The phases were separated and the aqueous phase extracted with EtOAc (3 x 20 mL). The organic extracts were washed with saturated NaCl (50 mL) and the aqueous washing extracted with EtOAc (40 mL). The combined organic extracts were then dried over Na_2SO_4 and the solvent removed *in vacuo*. The resulting dark brown oil was purified by flash chromatography (0%, 20% to 33% EtOAc/*n*-hexane) to afford an inseparable diastereomeric mixture of the *title compound* **17a:17b** as a thick golden oil (963 mg, 73%). The characterisation data of compound **17** is provided in the procedure describing the hydrolysis of acetate **25** to alkynol **17a**.



26

(11*S*)-11-(*tert*-Butyldimethylsilyloxy)-12-(*tert*-butyldiphenylsilyloxy)-7-(1,3-dioxolan-2-yl)dodec-1-yn-3-one (26)

IBX (87.3 mg, 0.312 mmol) was dissolved in DMSO (600 μL) and stirred at RT for 15 mins. A solution of alkynol **17a:17b** (83 mg, 0.133 mmol) in anhydrous DMSO (3 x 900 μL) was added and the reaction mixture heated to 40 °C. After 2.5 h, the reaction mixture was allowed to cool to RT and saturated $Na_2S_2O_3$ (3 mL) and EtOAc (3 mL) were added. The aqueous phase was extracted with EtOAc (4 x 15 mL) and the organic extracts washed with saturated NaCl (50 mL). The aqueous washing was back extracted with EtOAc (50 mL) and the combined organic extracts dried over Na_2SO_4 and the EtOAc removed *in vacuo* to give an orange solution. Purification by flash chromatography (0%, 17% EtOAc/*n*-hexane) afforded the *title compound* **26** as a pale yellow oil (80 mg, 96%). $[\alpha]_D^{22}$ -11.8 (c 1.07 in $CHCl_3$); R_f (17% EtOAc/*n*-hexane) 0.30; IR (film) ν_{max}/cm^{-1} 3309 (≡C–H), 2929 (C–H), 2858 (C–H), 2091 (C≡C), 1734 (C=O), 1683, 1472, 1187, 1106 (C–O–C), 835, 701; δ_H (400 MHz, $CDCl_3$) –0.07 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.00 (3H, s, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 0.84 (9H, s, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 1.04 (9H, s, OSiPh$_2$$^t\underline{Bu}$), 1.29–1.52 (4H, m, 8–H, 9–H$_A$ and 10–H$_A$), 1.54–1.69 (4H, m, 6–H, 9–H$_B$, and 10–H$_B$), 1.72–1.80 (2H, m, 5–H), 2.60 (2H, t, $^3J_{4,5}$ 7.3, 4–H), 3.18 (1H, s, 1–H), 3.46 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{12A,11}$ 6.7, 12–H$_A$), 3.57 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{12B,11}$ 5.0, 12–H$_B$), 3.66–3.72 (1H, m, 11–H), 3.92 (4H, s, 1'–H and 2'–H), 7.35–7.44 (6H, m, Ph), 7.65–7.69 (4H, m, Ph); δ_C (100 MHz, $CDCl_3$) –4.8 (CH$_3$, OSi(C$\underline{H_3}$)$_2$^{t}Bu), –4.4 (CH$_3$, OSi(C$\underline{H_3}$)$_2$^{t}Bu), 18.1 (C, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 18.1 (CH$_2$, C–5), 19.2 (C, OSiPh$_2$$^t\underline{Bu}$), 19.4 (CH$_2$, C–9), 25.9 (CH$_3$, OSi(CH$_3$)$_2$$^t\underline{Bu}$), 26.9 (CH$_3$, OSiPh$_2$$^t\underline{Bu}$), 34.7 (CH$_2$, C–8), 36.1 (CH$_2$, C–10), 37.5 (CH$_2$, C–6), 45.4 (CH$_2$, C–4), 65.0 (2 x CH$_2$, C–1' and C–2'), 67.8 (CH$_2$, C–12), 72.8 (CH, C–11), 78.3 (CH, C–1), 81.4 (C, C–2) 111.3 (C, C–7), 127.6 (CH, Ph), 129.6 (CH, Ph), 133.7 (C, Ph), 133.7 (C, Ph), 135.6 (CH, Ph), 187.1 (C, C–3); MS *m/z* (ESI+) 661 ([M + K]$^+$, 6%), 645 ([M + Na]$^+$, 24), 640 ([M + H$_2$O]$^+$, 100), 623 ([M + H]$^+$, 14), 605 (30), 545 (15), 527 (7), 491 (16); HRMS (ESI+): [M + H]$^+$, found 623.3571. $C_{36}H_{55}O_5Si_2^+$ requires 623.3583.

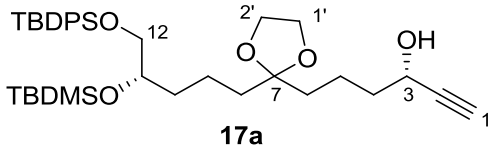


25

(3*S*,11*S*)-11-(*tert*-Butyldimethylsilyloxy)-12-(*tert*-butyldiphenylsilyloxy)-7-(1,3-dioxolan-2-yl)dodec-1-yn-3-yl acetate (25)

To a solution of alkynol **17a:17b** (1.12 g, 1.79 mmol) in distilled hexanes (48 mL) in a 80 mL microwave reaction tube, was added vinyl acetate (300 μL, 3.25 mmol) and Novozyme 435 lipase acrylic resin (252 mg, derived from *Candida antarctica*, 141 mg/mmol). The mixture was heated in a microwave reactor (CEM Discover, 50W) to a maximum of 50 °C for 1 h. The reaction mixture was filtered through a glass sinter, washed with EtOAc (20 mL) and concentrated *in vacuo* to get a pale yellow oil. Purification by flash chromatography (0%, 14% to 25% EtOAc/*n*-hexane) gave the *title compound* **25** as a pale yellow oil (214 mg, 18%) and alkynols **17a:17b** as a yellow oil (799 mg,

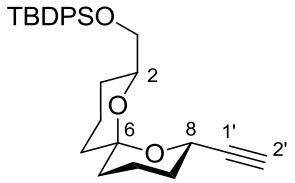
72%). The alkynol fractions were concentrated and resubjected to the enzymatic kinetic resolution as described above to afford a second portion of the *title compound* **25** as a pale yellow oil (155 mg, 13%) and alkynols **17a:17b** (617 mg, 55%). $[\alpha]_D^{20}$ -28.4 (c 1.07 in $CHCl_3$); R_f (17% EtOAc/ *n*-hexane) 0.35; IR (film) ν_{max}/cm^{-1} 3293 (≡C–H), 2956 (C–H), 2859 (C–H), 1744 (C=O), 1473, 1429, 1372 (≡C–H), 1233 (C–C(=O)–O), 1112 (C–O–C), 703; δ_H (400 MHz, $CDCl_3$) –0.07 (3H, s, OSi($C\underline{H}_3$)$_2$^{t}Bu), 0.00 (3H, s, OSi($C\underline{H}_3$)$_2$^{t}Bu), 0.84 (9H, s, OSi(CH_3)$_2$$^t\underline{Bu}$), 1.04 (9H, s, OSiPh$_2$$^t\underline{Bu}$), 1.30–1.69 (10H, m , 5–H, 6–H, 8–H, 9–H and 10–H), 1.75–1.80 (2H, m, 4–H), 2.08 (3H, s, CO$C\underline{H}_3$), 2.44 (1H, d, $^4J_{1,3}$ 2.0, 1–H), 3.46 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{12A,11}$ 6.5, 12–H_A), 3.57 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{12B,11}$ 5.0, 12–H_B), 3.66–3.70 (1H, m, 11–H), 3.90–3.94 (4H, m, 1'–H and 2'–H), 5.34 (1H, td, $^3J_{3,4}$ 6.5 and $^4J_{3,1}$ 2.0, 3–H), 7.35–7.44 (6H, m, Ph), 7.65–7.68 (4H, m, Ph); δ_C (100 MHz, $CDCl_3$) –4.8 (CH_3, OSi($\underline{C}H_3$)$_2$^{t}Bu), –4.4 (CH_3, OSi($\underline{C}H_3$)$_2$^{t}Bu), 18.1 (C, OSi(CH_3)$_2$$^t\underline{Bu}$), 19.2 (C, OSiPh$_2$$^t\underline{Bu}$), 19.3 ($CH_2$, C–5), 19.5 ($CH_2$, C–9), 21.0 ($CH_3$, CO$\underline{C}H_3$), 25.8 ($CH_3$, OSi($CH_3$)$_2$$^t\underline{Bu}$), 26.8 ($CH_3$, OSiPh$_2$$^t\underline{Bu}$), 34.7 (2 x CH_2, C–4 and C–10), 36.7 (CH_2, C–6), 37.5 (CH_2, C–8), 63.7 (CH_2, C–3), 65.0 (2 x CH_2, C–1' and C–2'), 67.8 (CH_2, C–12), 72.8 (CH, C–11), 73.6 (CH, C–1), 81.1 (C, C–2) 111.4 (C, C–7), 127.6 (CH, Ph), 129.6 (CH, Ph), 133.6 (C, Ph), 133.7 (C, Ph), 135.6 (CH, Ph), 169.9 (C, $\underline{C}OCH_3$); MS *m/z* (ESI+) 705 ($[M + K]^+$, 7%), 689 ($[M + Na]^+$, 100), 684 ($[M + H_2O]^+$, 26), 667 ($[M + H]^+$, 6), 645 (25), 589 (13), 535 (7); HRMS (ESI+): $[M + H]^+$, found 667.3846. $C_{38}H_{59}O_6Si_2^+$ requires 667.3845.



17a

Hydrolysis of (3*S*,11*S*)-11-(*tert*-Butyldimethylsilyloxy)-12-(*tert*-butyldiphenylsilyloxy)-7-(1,3-dioxolan-2-yl)dodec-1-yn-3-yl acetate (25) to (3*S*,11*S*)-11-(*tert*-butyldimethylsilyloxy)-12-(*tert*-butyldiphenylsilyloxy)-7-(1,3-dioxolan-2-yl)dodec-1-yn-3-ol (17a)

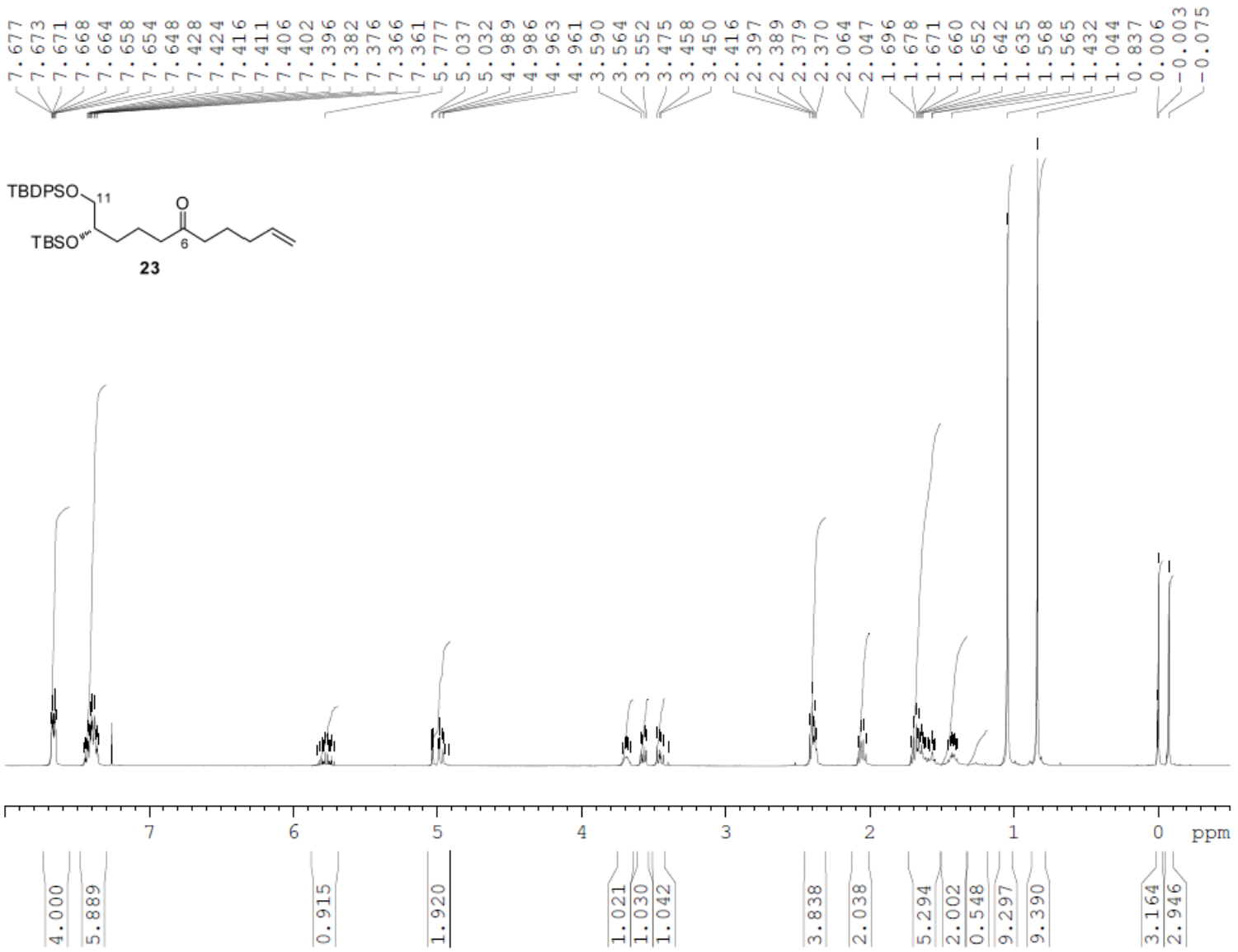
To a solution of acetate **25** (369 mg, 0.553 mmol) in CH_3OH (11 mL) at RT was added solid K_2CO_3 (160 mg, 1.16 mmol). After stirring for 20 mins the mixture was filtered and washed with EtOAc (20 mL) and the filtrate concentrated *in vacuo* to afford a thick yellow oil. Purification by flash chromatography (0%, 20% to 25% EtOAc/*n*-hexanes) gave (3*S*,11*S*)-alkynol **17a** as a colourless oil (337 mg, 97%, 90–96% d.e.).[5] $[\alpha]_D^{21}$ -14.0 (c 1.03 in $CHCl_3$); R_f (20% EtOAc/ n-hexane) 0.11, R_f (50% EtOAc/n-hexane) 0.58; IR (film) ν_{max}/cm^{-1} 3411 (br, O–H), 3309 (≡C–H), 2929 (C–H), 2857 (C–H), 1472, 1428 (C–H), 1253, 1111 (C–O–C), 824, 775, 701; δ_H (400 MHz, $CDCl_3$) –0.06 (3H, s, OSi($C\underline{H}_3$)$_2$^{t}Bu), 0.00 (3H, s, OSi($C\underline{H}_3$)$_2$^{t}Bu), 0.84 (9H, s, OSi(CH_3)$_2$$^t\underline{Bu}$), 1.05 (9H, s, OSiPh$_2$$^t\underline{Bu}$), 1.33–1.49 (3H, m, 5–$H_A$, 9–$H_A$ and 10–H_A), 1.51–1.87 (9H, m, 4–H, 5–H_B, 6–H, 8–H, 9–H_B and 10–H_B), 2.45 (1H, d, $^4J_{1,3}$ 2.0, 1–H), 3.46 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{12A,11}$ 6.6, 12–H_A), 3.58 (1H, dd, $^2J_{AB}$ 10.0 and $^3J_{12B,11}$ 5.0, 12–H_B), 3.66–3.73 (1H, m, 11–H), 3.90–3.95 (4H, m, 1'–H and 2'–H), 4.33–4.39 (1H, m, 3–H), 7.35–7.45 (6H, m, Ph), 7.66–7.68 (4H, m, Ph); δ_C (100 MHz, $CDCl_3$) –4.8 (CH_3, OSi($\underline{C}H_3$)$_2$^{t}Bu), –4.4 (CH_3, OSi($\underline{C}H_3$)$_2$^{t}Bu), 18.1 (C, OSi(CH_3)$_2$$^t\underline{Bu}$), 19.2 (C, OSiPh$_2$$^t\underline{Bu}$), 19.4 ($CH_2$, C–5), 19.5 ($CH_2$, C–9), 25.8 ($CH_3$, OSi($CH_3$)$_2$$^t\underline{Bu}$), 26.8 ($CH_3$, OSiPh$_2$$^t\underline{Bu}$), 34.7 ($CH_2$, C–10), 36.7 ($CH_2$, C–6), 37.5 ($CH_2$, C–8), 37.8 ($CH_2$, C–4) 62.2 (CH, C–3), 65.0 (2 x CH_2, C–1' and C–2'), 67.8 (CH_2, C–12), 72.8 (CH, C–11), 72.9 (CH, C–1), 84.9 (C, C–2) 111.6 (C, C–7), 127.6 (CH, Ph), 129.6 (CH, Ph), 129.6 (CH, Ph), 133.7 (C, Ph), 133.7 (C, Ph), 135.6 (CH, Ph); MS *m/z* (ESI+) 647 ($[M + Na]^+$, 48%), 563 (100), 431 (4), 307 (10); HRMS (ESI+): $[M + Na]^+$, found 647.3574. $C_{36}H_{56}NaO_5Si_2^+$ requires 647.3558.

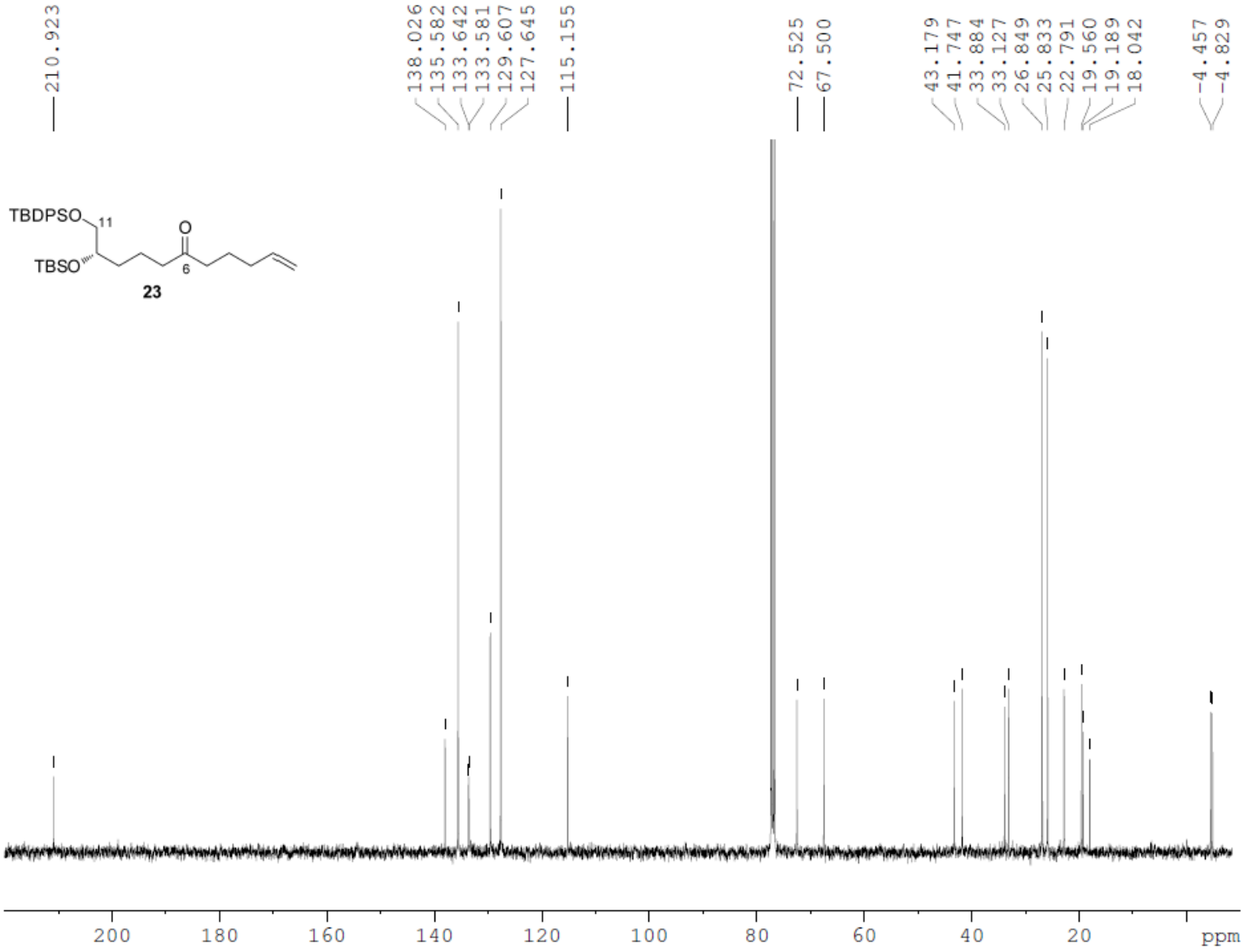


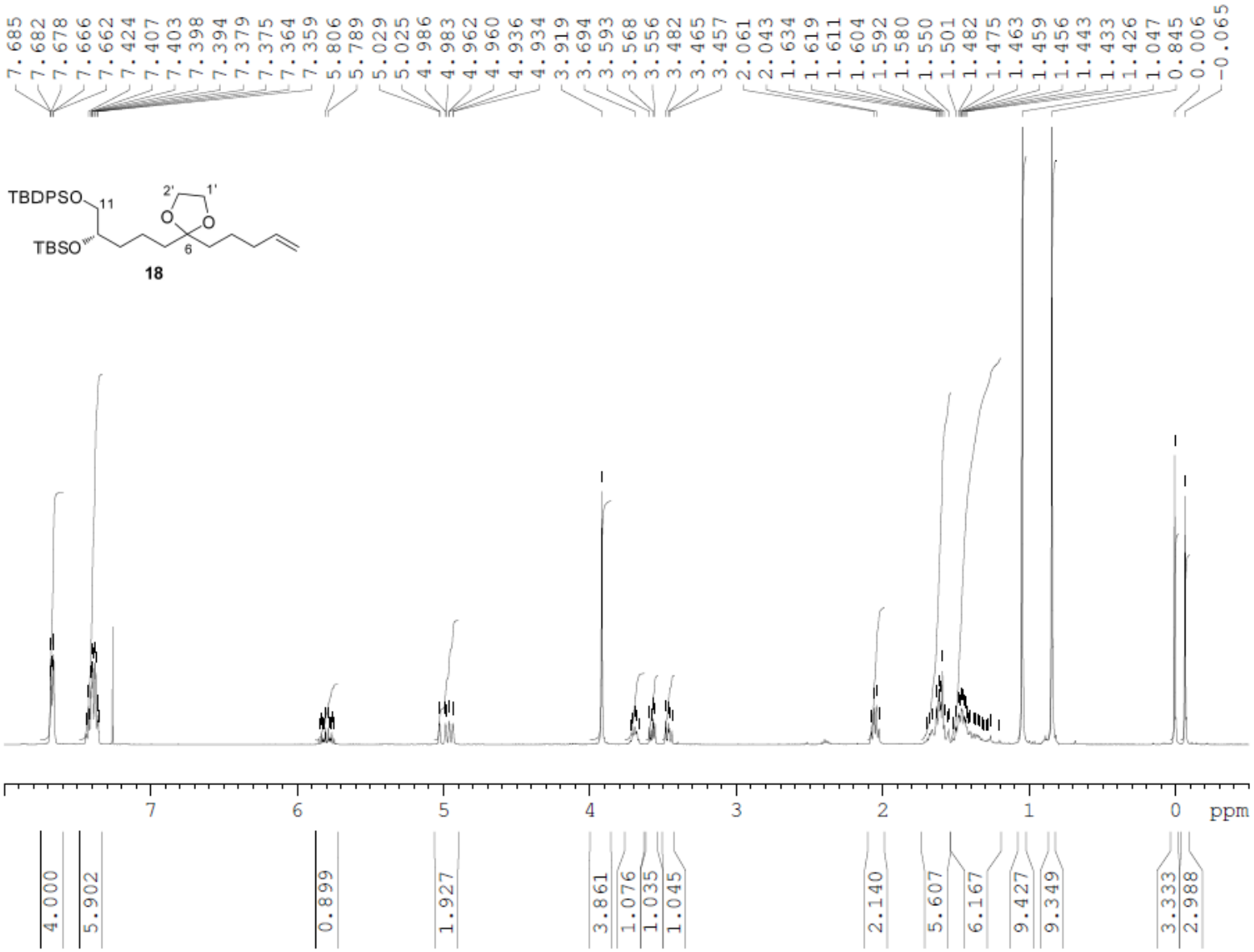
11

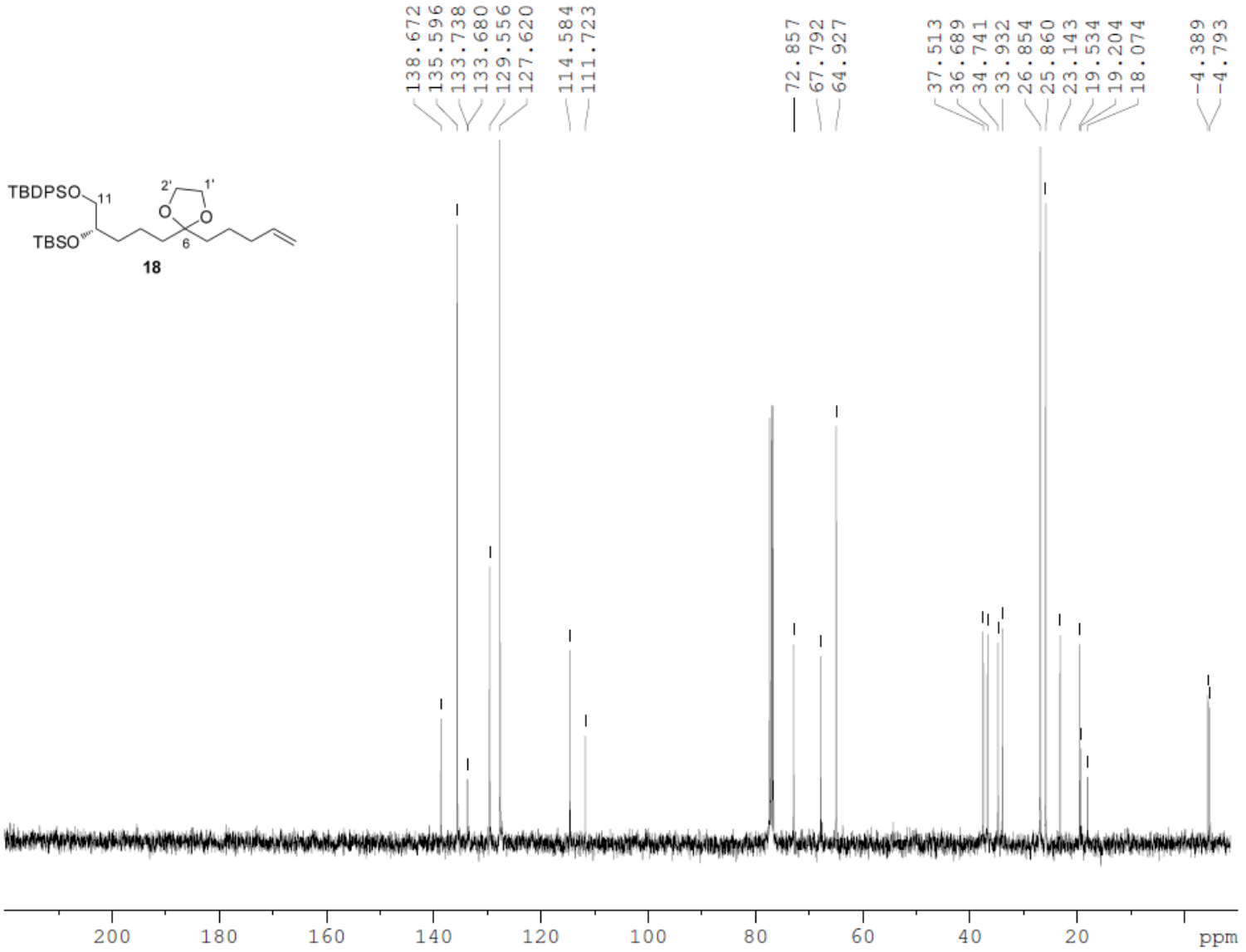
8-Ethynyl-2-(*tert*-butyldiphenylsilyloxymethyl)-1,7-dioxaspiro[5.5]undecane (11)

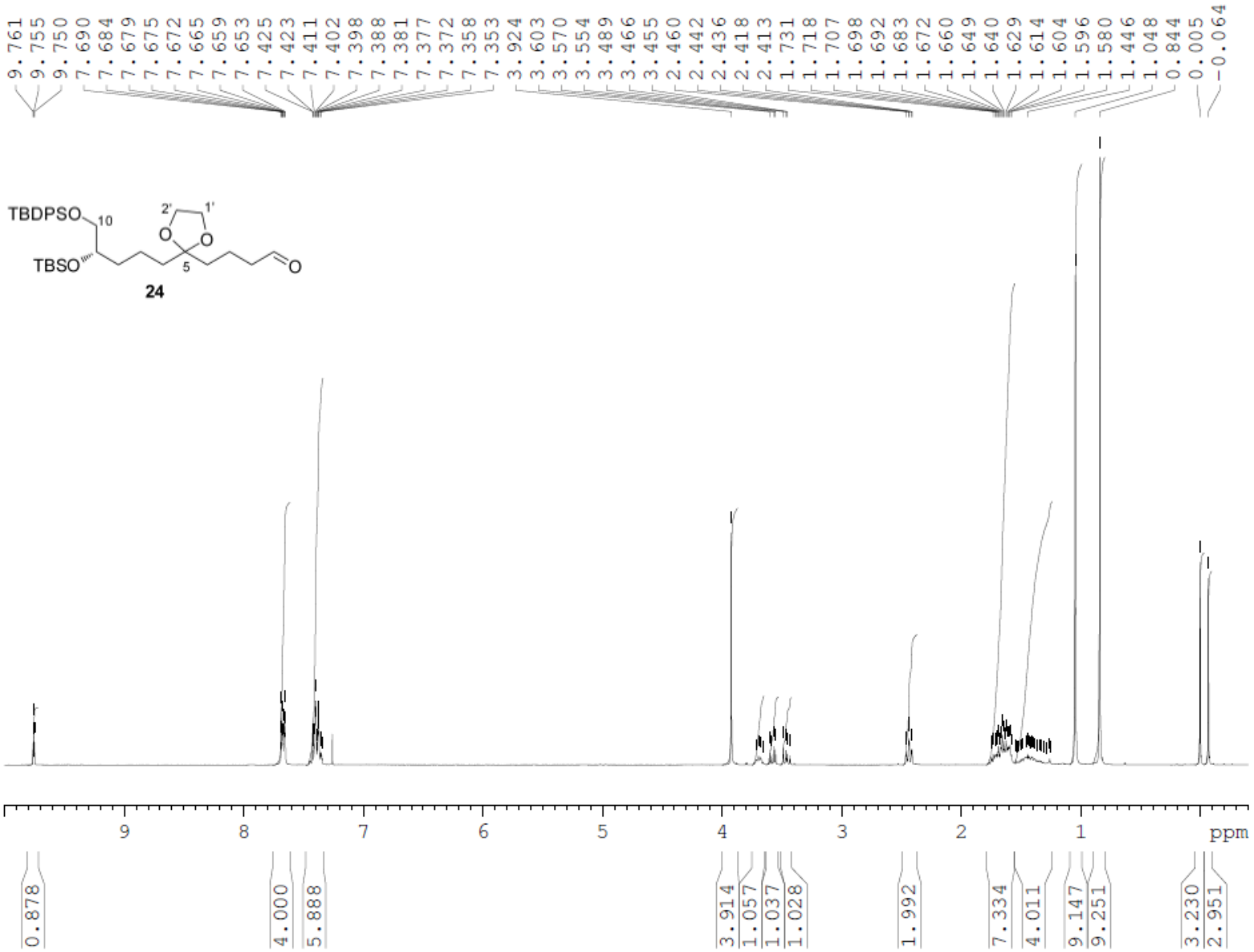
To a stirred solution of alkynol **17a** (337 mg, 0.539 mmol) in EtOH:H_2O (99:1 mixture, 5.8 mL) was added (+)-CSA (272 mg, 1.17 mmol) in three equal portions at RT. After stirring for 3 h, solid $NaHCO_3$ (104 mg, 0.33 mmol) was added directly and the solvent was removed *in vacuo* to afford a yellow oil. The yellow oil was dissolved in saturated $NaHCO_3$ (10 mL) and the aqueous phase extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to afford an orange oil. Purification by flash chromatography (0%, 9% EtOAc/*n*-hexane) gave the *title compound* **11** as a yellow oil (181 mg, 75%). $[\alpha]_D^{21}$ -9.3 (c 1.05 in $CHCl_3$); R_f (9% EtOAc/n-hexane) 0.30; IR (film) ν_{max}/cm^{-1} 3292 (≡C–H), 2932 (C–H), 2858 (C–H), 1473 (CH_2), 1428 (C–H), 1219, 1112 (C–O–C), 1072 (C–O–C), 980; δ_H (300 MHz, $CDCl_3$) 1.06 (9H, s, $OSiPh_2{}^tBu$), 1.14–1.28 (1H, m, 3–H_A), 1.34–1.64 (6H, m, 3–H_B, 4–H, 5–H_A, 9–H_A, and 10–H_A), 1.66–1.81 (3H, m, 9–H_B and 11–H), 1.88–2.03 (2H, m, 5–H_B and 10–H_B), 2.43 (1H, d, $^4J_{2',8}$ 2.3, 2'–H), 3.58 (1H, dd, $^3J_{AB}$ 10.3 and $^3J_{2\text{-}CH_2,2}$ 4.4, 2–CH_AH_BO), 3.68 (1H, dd, $^3J_{AB}$ 10.3 and $^3J_{2\text{-}CH_2,2}$ 6.5, 2–CH_AH_BO), 3.77–3.87 (1H, m, 2–H), 4.53 (1H, dt, $^3J_{8,9ax}$ 11.4, $^3J_{8,9eq}$ 2.6, and $^4J_{8,2'}$ 2.3, 8–H), 7.35–7.45 (6H, m, Ph), 7.68–7.76 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) 18.35, 18.4 (2 x CH_2, C–4 and C–10), 19.2 (C, $OSiPh_2{}^tBu$), 26.75 (CH_3, $OSiPh_2{}^tBu$), 26.8 (CH_2, C–3), 31.8 (CH_2, C–9), 34.7, 35.0 (2 x CH_2, C–5 and C–11), 59.8 (CH, C–8), 67.3 (CH_2, 2–CH_2O), 70.6 (CH, C–2), 71.7 (CH, C–2'), 84.1 (C, C–1'), 96.6 (C, C–6), 127.6 (CH, Ph), 127.6 (CH, Ph) 129.5 (CH, Ph), 129.6 (CH, Ph), 133.8 (C, Ph), 135.7 (C, Ph); MS *m/z* (ESI+) 487 ($[M + K]^+$, 100%), 471 ($[M + Na]^+$, 11), 429 (22), 371 ($[M – Ph]^+$, 12); HRMS (ESI+): $[M + K]^+$, found 487.2084. $C_{28}H_{36}KO_3Si^+$ requires 487.2065.

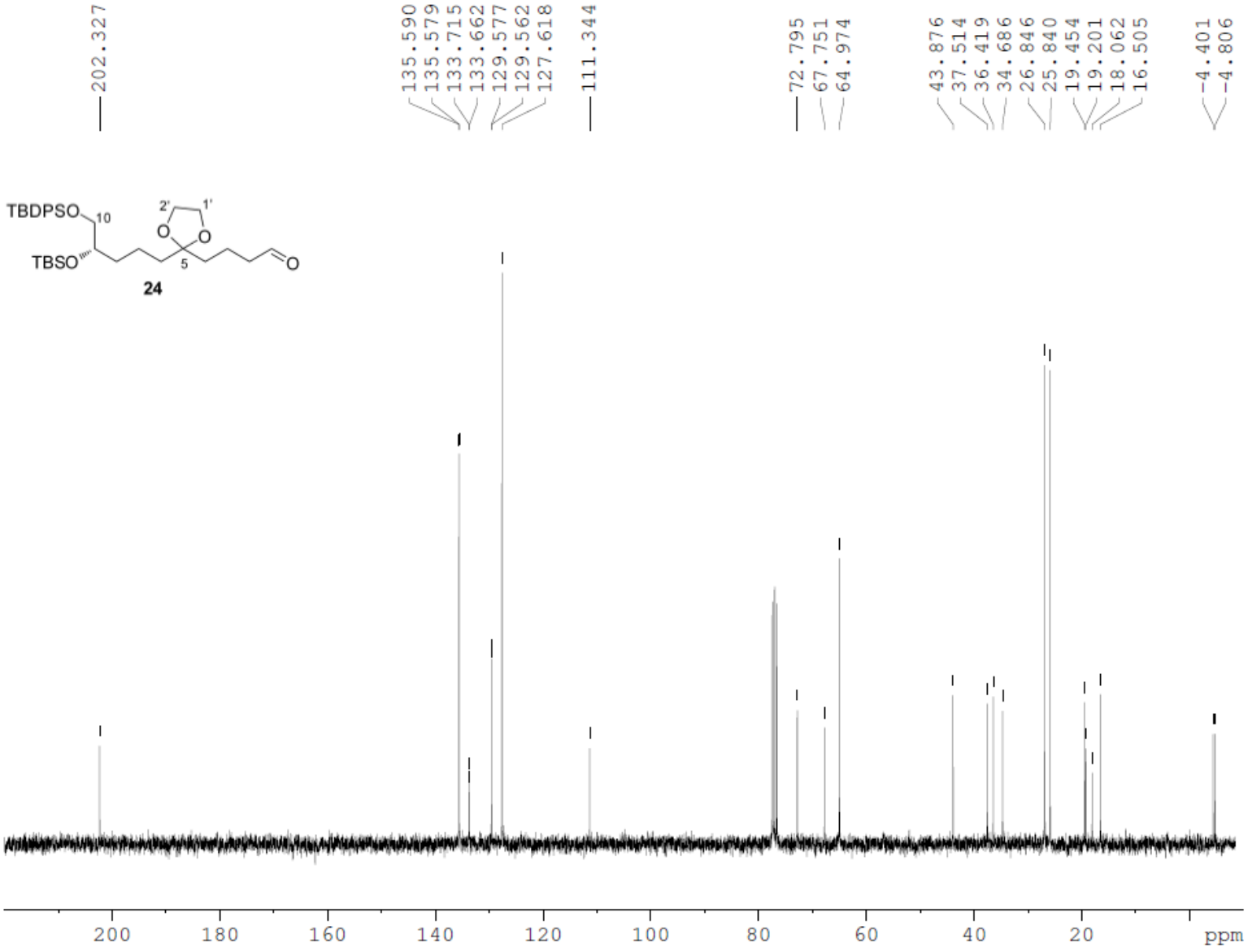


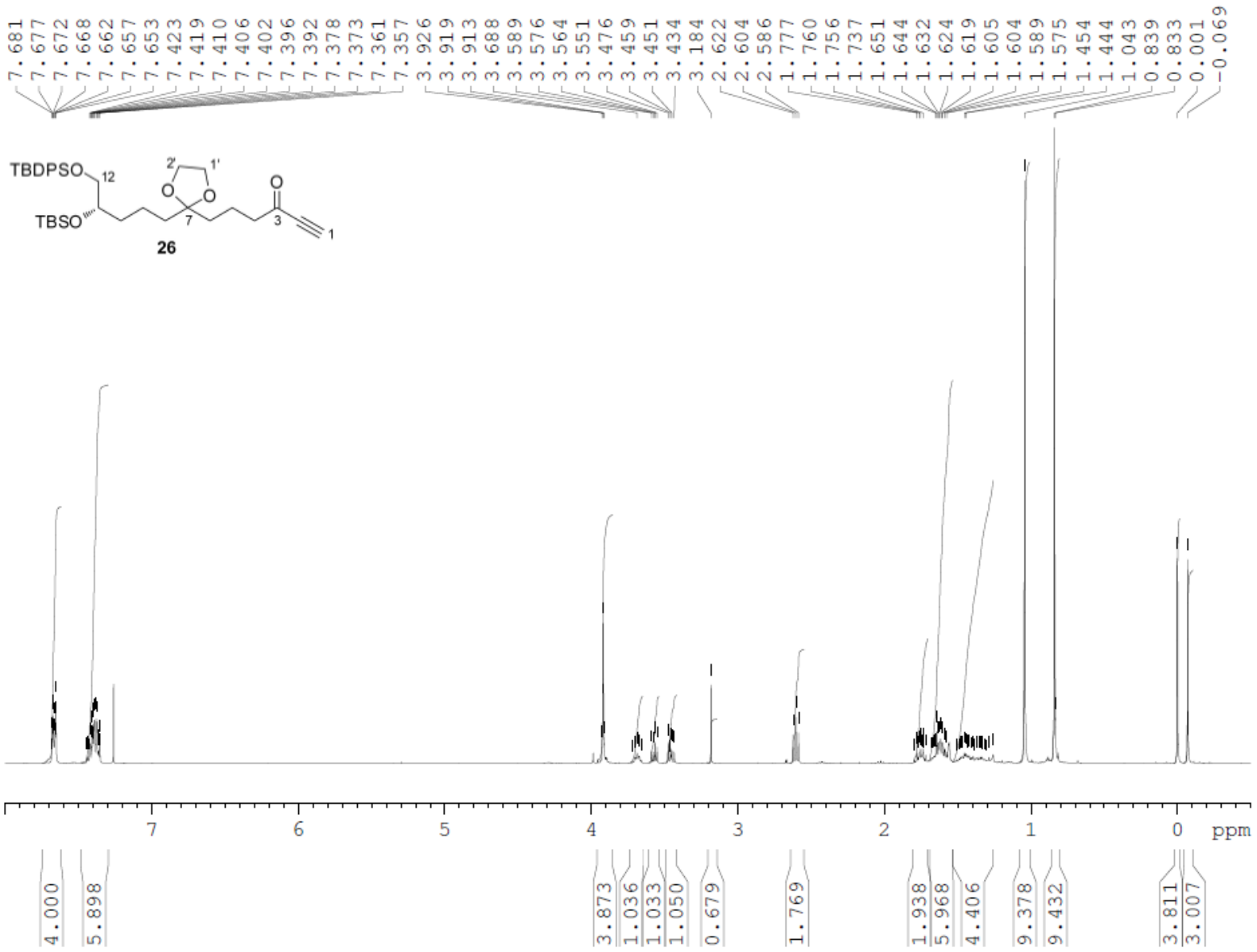


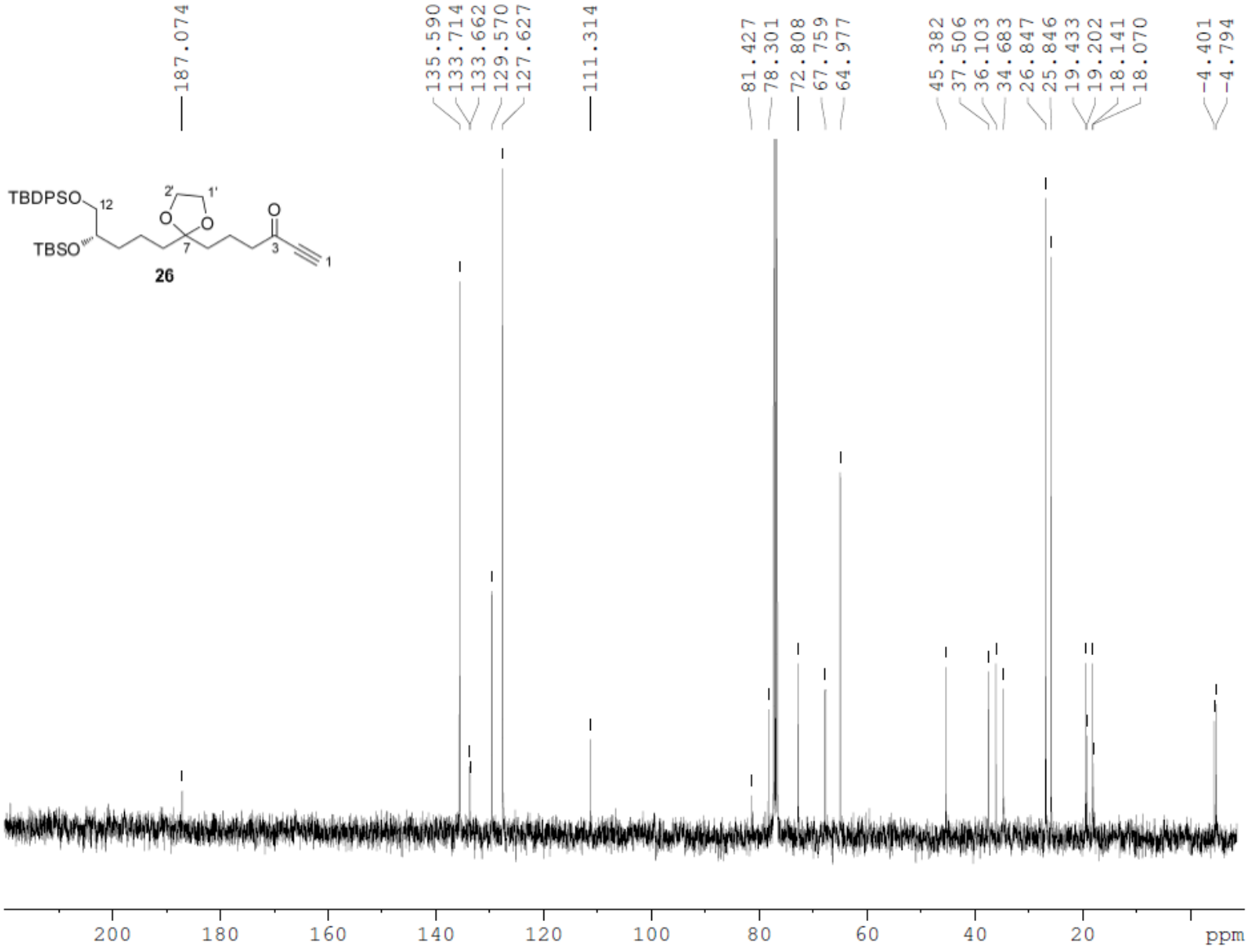


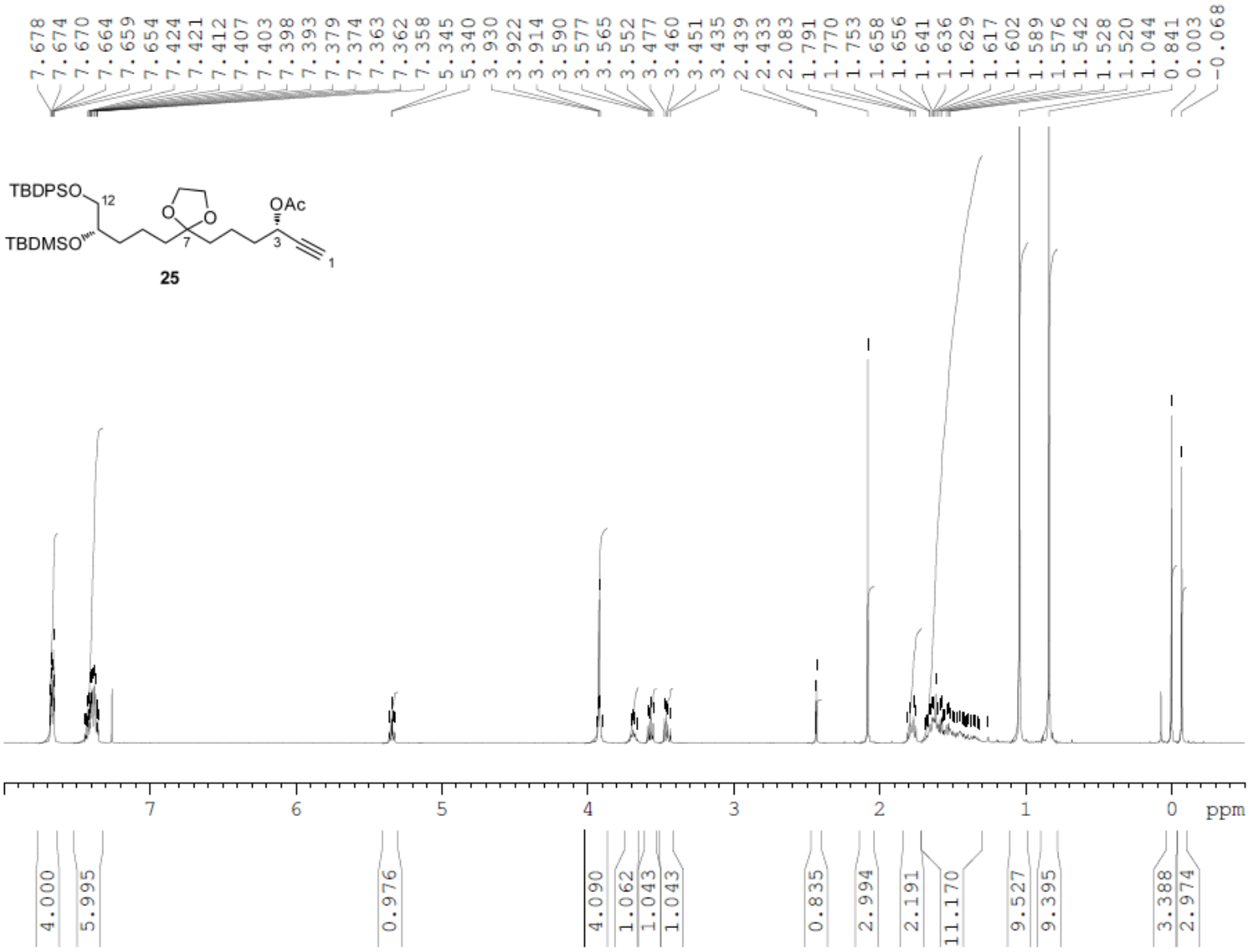


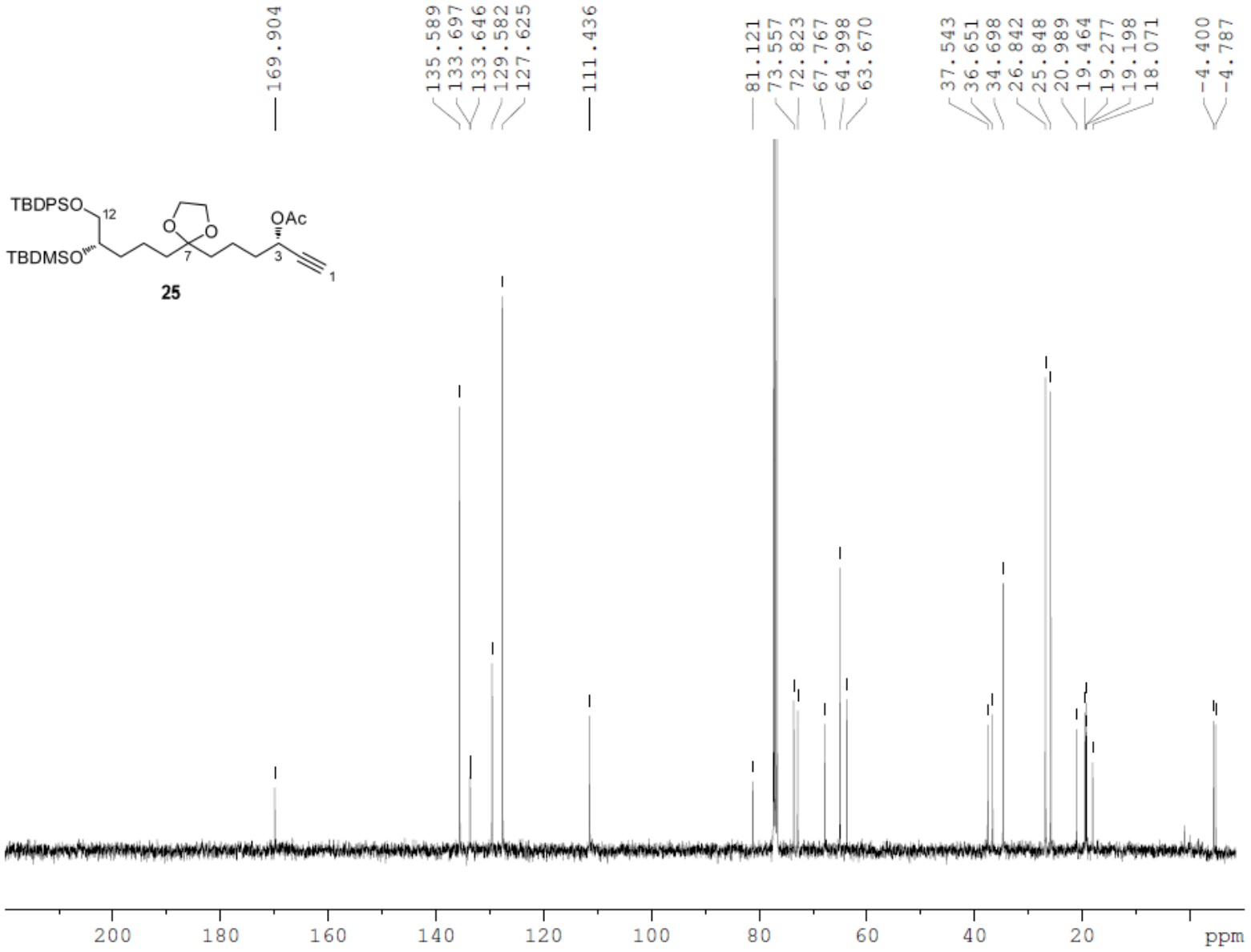


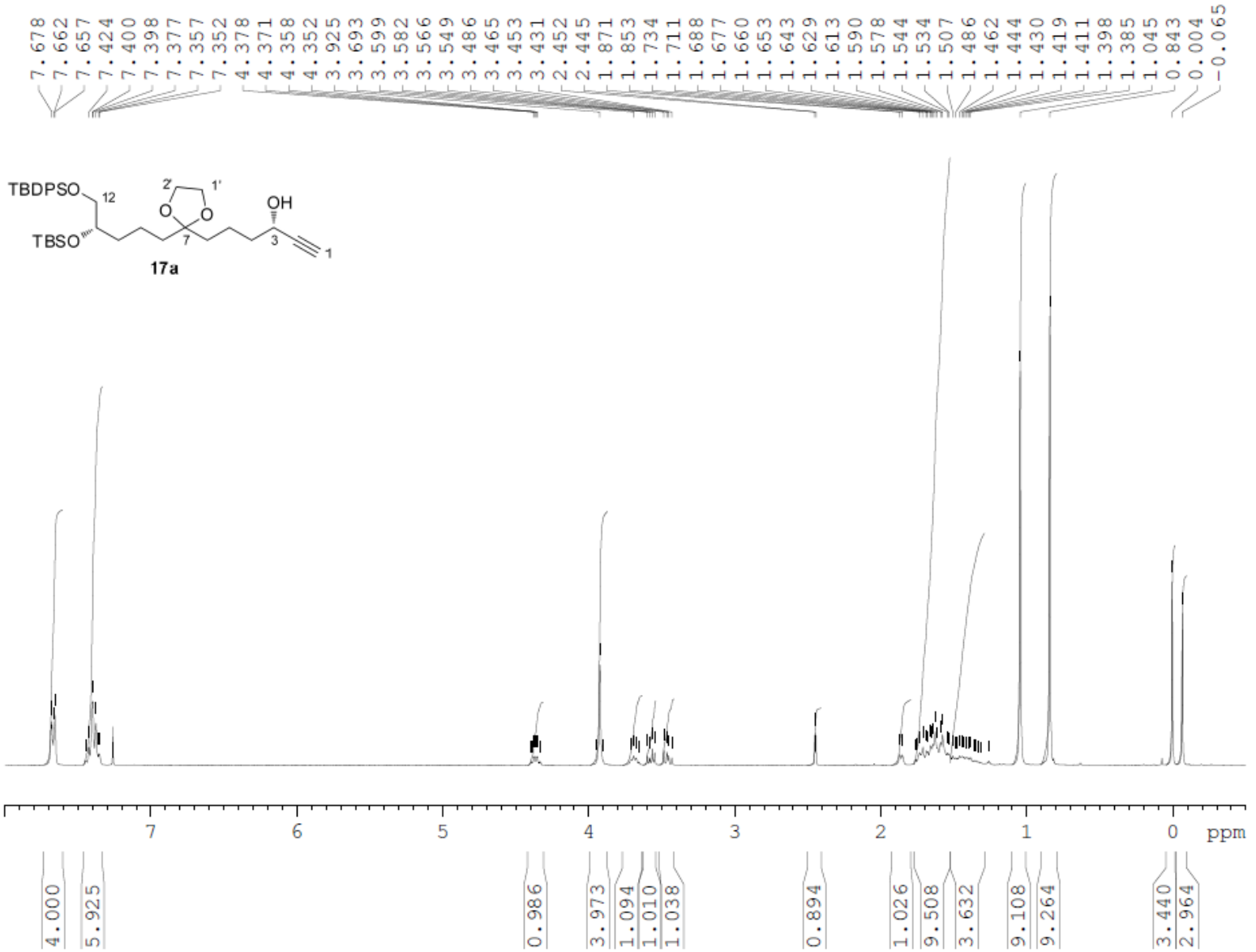


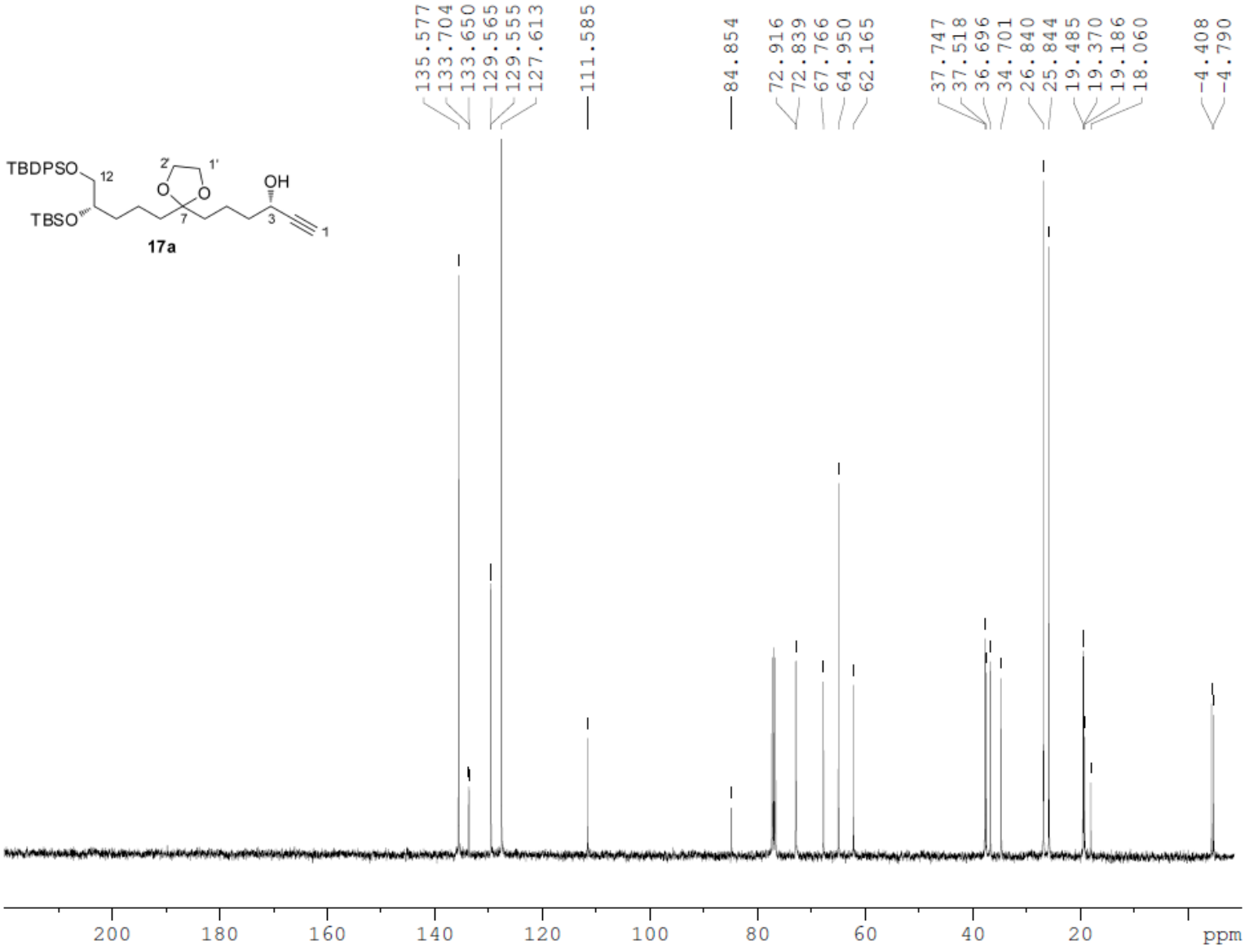


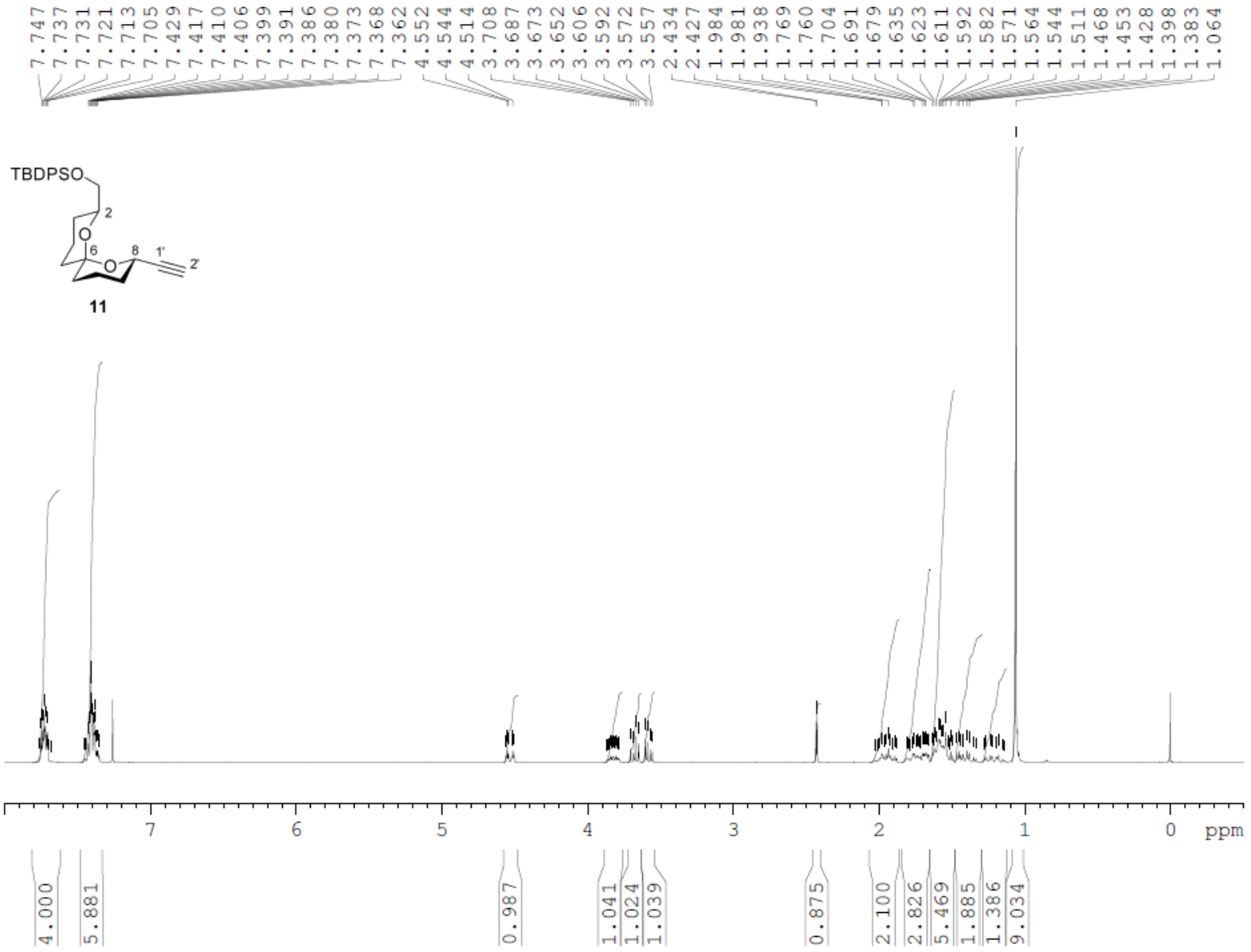


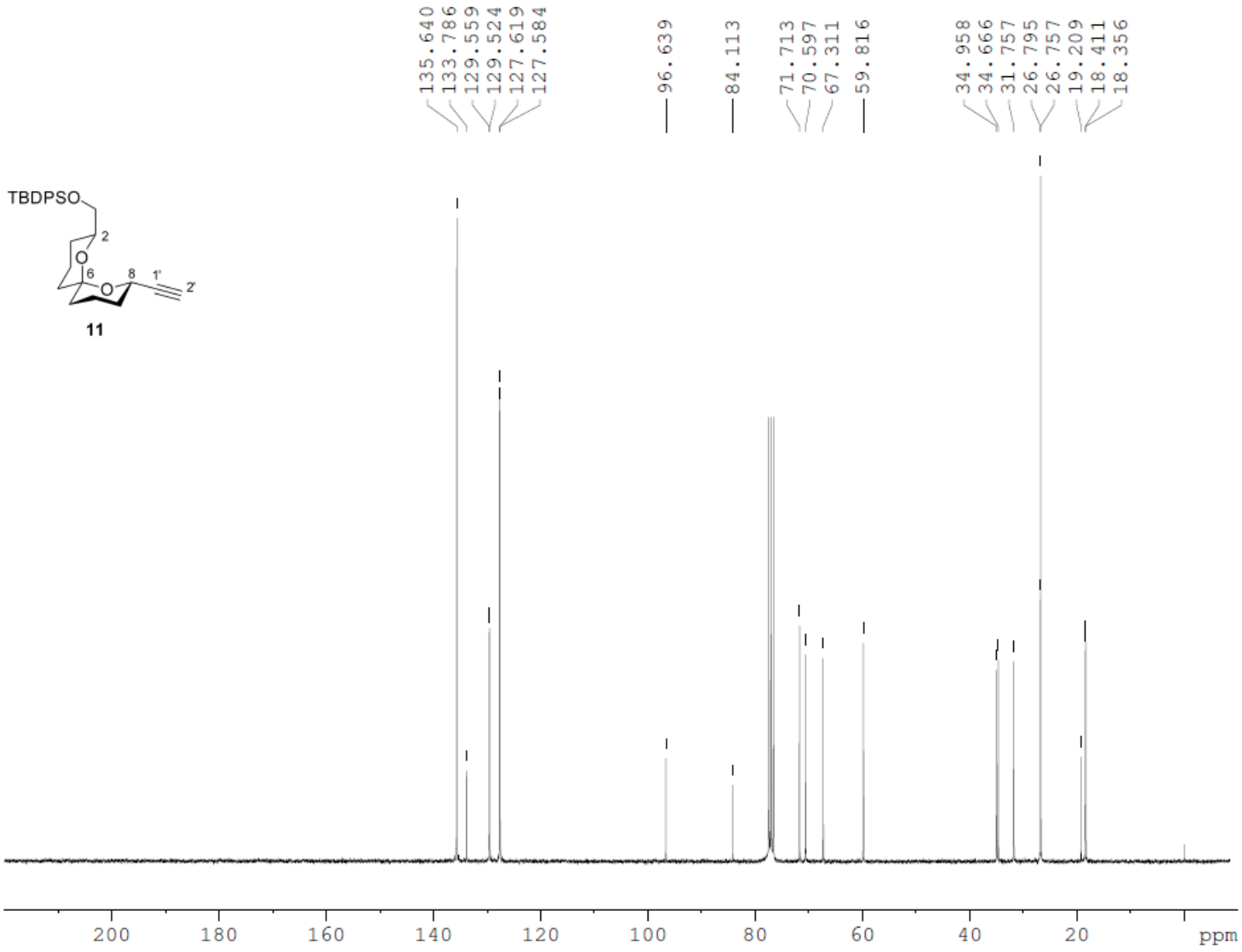




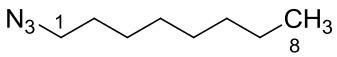








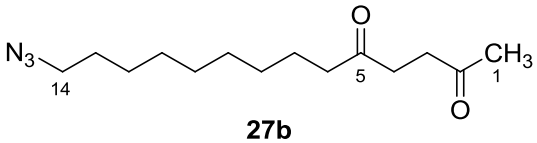
Experimental and Characterization data for azides **27a-h** and intermediates involved in the synthesis of **27a-h**.



27a

1-Azidooctane (27a)

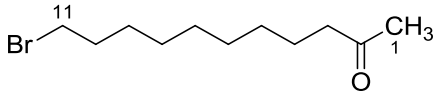
To a solution of 1-bromooctane (60 μL, 0.347 mmol) in anhydrous DMF (2 mL) was added NaN_3 (62 mg, 0.95 mmol). The reaction mixture was heated to 80 °C for 21 h. Upon cooling to RT, H_2O (5 mL) was added and the aqueous phase extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to get a yellow oil. Purification by flash chromatography (0%, 0.5% Et_2O/*n*-hexane) afforded the *title compound* **27a** as a colourless oil (53 mg, 98%). R_f (0.5% Et_2O/*n*-hexanes) 0.40; δ_H (400 MHz, $CDCl_3$) 0.89 (3H, t, $^3J_{8,7}$ 7.0, 8–H), 1.28–1.38 (10H, m, 3–H, 4–H, 5–H, 6–H and 7–H), 1.56–1.63 (2H, m, 2–H), 3.25 (2H, t, $^3J_{1,2}$ 6.8, 1–H); δ_C (100 MHz, $CDCl_3$) 14.0 (CH_3, C–8), 22.6 (CH_2, C–7), 26.7 (CH_2, C–3), 28.8 (CH_2, C–4), 29.1, 29.1 (2 x CH_2, C–2 and C–5), 31.7 (CH_2, C–6), 51.5 (CH_2, C–1). ^{1}H and ^{13}C NMR spectra were in agreement with that from literature sources.[6]



27b

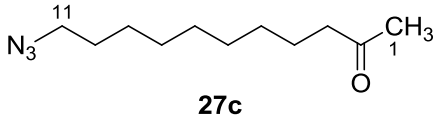
14-Azidotetradecane-2,5-dione (27b)

To a stirred solution of the corresponding tosylate (70.0 mg, 0.177 mmol) dissolved in DMF (5.0 mL) was added NaN_3 (13.0 mg, 0.2 mmol) and the yellow solution was left to stir at RT for 4 h. Addition NaN_3 (35.0 mg, 0.53 mmol) was added and the reaction mixture was left to stir at RT for a further 20 h. The mixture was then diluted with EtOAc (5 mL) and filtered through a silica plug that was washed with EtOAc (50 mL). Concentration of the filtrate *in vacuo* gave an orange oil that was purified by flash chromatography (0%, 25% to 33% EtOAc/*n*-hexane) to afford the *title compound* **27b** as a colourless solid (44.1 mg, 93%). Mp. 24–26 °C; R_f (25% EtOAc/ n-hexane) 0.29, (33% EtOAc/n-hexane) 0.52; δ_H NMR (300 MHz, $CDCl_3$) 1.27-1.38 (10H, m, 8–H, 9–H, 10–H, 11–H and H–12), 1.54–1.62 (4H, m, 7–H and 13–H), 2.19 (3H, s, 1–H), 2.44 (2H, t, $^3J_{6,7}$ 7.5, 6–H), 2.65-2.72 (4H, m, 3–H and 4–H), 3.25 (2H, t, $^3J_{14,13}$ 6.0, 14–H); δ_C NMR (100 MHz, $CDCl_3$) 23.8 (CH_2, C–7), 26.7 (CH_2, C–12), 28.8, 29.05, 29.1, 29.2, 29.2 (5 x CH_2, C–8, C–9, C–10, C–11 and C–13), 30.0 (CH_3, C–1), 36.0 (CH_2, C–3), 36.9 (CH_2, C–4), 42.8 (CH_2, C–6), 51.5 (CH_2, C–14), 207.3 (C, C–2), 209.6 (C, C–5). The ^{1}H and ^{13}C NMR spectroscopic data obtained were in agreement with literature values.[7]



11-Bromoundecan-2-one[8]

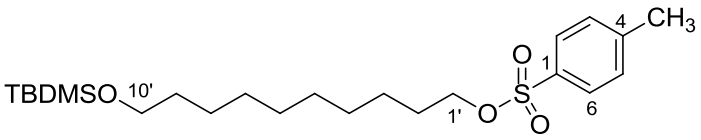
A 2-necked round bottom flask flushed with argon was charged with CuCl (73 mg, 0.74 mmol), $PdCl_2$ (62 mg, 0.35 mmol), and 11-bromoundecene (159 mg, 0.68 mmol). The reagents were suspended in a mixture of DMF and distilled H_2O (3:1, 4 mL) and cooled to 0 °C. *tert*-Butylhydroperoxide (5.5M in decane, 140 µL, 0.77 mmol), was then added dropwise and the stirred reaction mixture allowed to warm to RT. After 20 h, saturated Na_2SO_3 (2 mL) was added and after vigourous stirring, the black mixture was washed through a silica plug with EtOAc (100 mL) and the filtrate concentrated *in vacuo* to afford an orange oil. Purification by flash chromatography (0%, 9% EtOAc/*n*-hexane) yielded the *title compound* as a pale orange oil (144 mg, 67%). R_f (9% EtOAc/n-hexane) 0.25; IR (film) ν_{max}/cm^{-1} 2926 (C–H), 2854 (C–H), 1715 (C=O), 1464, 1357, 1164, 720, 643 (C–Br); δ_H (400 MHz, $CDCl_3$) 1.12–1.18 (8H, m, 5–H, 6–H, 7–H, and 8–H), 1.26–1.30 (2H, m, 9–H), 1.42 (2H, m, 4–H), 1.71 (2H, m, 10–H), 1.99 (3H, s, 1–H), 2.28 (2H, t, $^3J_{3,4}$ 7.4, 3–H), 3.26 (2H, t, $^3J_{11,10}$ 6.9, 11–H); δ_C (100 MHz, $CDCl_3$) 23.4 (CH_2, C–4), 27.8 (CH_2, C–9), 28.3, 28.7, 28.9, 28.9 (4 x CH_2, C–5, C–6, C–7, and C–8), 29.5 (CH_3, C–1), 32.4 (CH_2, C–10), 35.6 (CH_2, C–11), 43.3 (CH_2, C–3), 208.5 (C, C–2); MS *m/z* (ESI+) 271 ($[M + Na]^+$, Br isotope, 100%), 251 ($[M + H]^+$, Br isotope, 19), 191 ($[M – C_3H_5O]^+$, 36); HRMS (ESI+): $[M + Na]^+$, found 271.0671. $C_{11}H_{21}BrNaO$ requires 271.0668.



27c

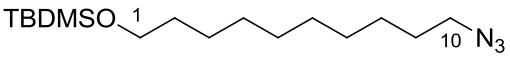
11-Azidoundecan-2-one (27c)

To a solution of *11-bromoundecan-2-one* (84.3 mg, 0.34 mmol) in anhydrous DMF (6.5 mL) was added NaN_3 (45 mg, 0.69 mmol). The colourless mixture was stirred at RT for 17 h whereupon the reaction mixture had turned a pale yellow colour. EtOAc (5 mL) was added and the reaction mixture passed through a silica plug with EtOAc (100 mL). The filtrate was concentrated *in vacuo* to give an orange oil that was purified by flash chromatography (0%, 9% EtOAc/*n*-hexane) to yield the *title compound* **27c** as a pale yellow oil (52 mg, 72%). R_f (9% EtOAc/n-hexane) 0.24; IR (film) ν_{max}/cm^{-1} 2927 (C–H), 2855 (C–H), 2092 (C–N=N^+=N^-), 1715 (C=O), 1457, 1355, 1256, 1164, 720; δ_H (400 MHz, $CDCl_3$) 1.25–1.34 (10H, m, 5–H, 6–H, 7–H, 8–H, and 9–H), 1.51–1.59 (4H, m, 4–H and 10–H), 2.10 (3H, s, 1–H), 2.38 (2H, t, $^3J_{3,4}$ 7.4, 3–H), 3.22 (2H, t, $^3J_{11,10}$ 6.9, 11–H); δ_C (100 MHz, $CDCl_3$) 23.7 (CH_2, C–4), 26.6 (CH_2, C–9), 28.7 (CH_2, C–10), 29.0, 29.0, 29.2 (4 x CH_2, C–5, C–6, C–7, and C–8), 29.7 (CH_3, C–1), 43.6 (CH_2, C–3), 51.4 (CH_2, C–11), 209.1 (C, C–2); MS *m/z* (ESI+) 234 ($[M + Na]^+$, 100%), 184 ($[M + H – N_2]^+$, 7); HRMS (ESI+): $[M + Na]^+$, found 234.1582. $C_{11}H_{21}N_3NaO$ requires 234.1577.



10-(*tert*-Butyldimethylsilyloxy)decyl-4-methylbenzenesulfonate

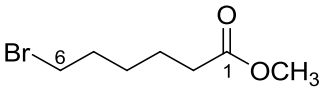
To a solution of mono-TBMDS protected decanol (150.0 mg, 0.52 mmol) in anhydrous CH_2Cl_2 (1.3 mL) was added NEt_3 (220 µL, 1.56 mmol), DMAP (32.5 mg, 0.27 mmol) and 4-toluenesulfonyl chloride (186.6 mg, 0.98 mmol). The mixture was stirred at RT for 18 h and then passed through a plug of celite with EtOAc (50 mL). The filtrate was concentrated *in vacuo* to get an orange residue. Purification by flash chromatography (0%, 5% to 17% EtOAc/*n*-hexane) gave the *title compound* as a yellow oil (195.4 mg, 85%). R_f (5% EtOAc/n-hexane) 0.24; IR (film) ν_{max}/cm^{-1} 2928 (C–H), 2856 (C–H), 1362 (S=O), 1189 (S=O), 1177 (S=O), 1098 (C–O), 834; δ_H (400 MHz, $CDCl_3$) 0.04 (6H, s, OSi(C<u>H</u>$_3$)$_2$^{t}Bu), 0.89 (9H, s, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 1.22–1.28 (12H, m, 3'–H, 4'–H, 5'–H, 6'–H, 7'–H and 8'–H), 1.47–1.51 (2H, m, 2'–H), 1.59–1.64 (2H, m, 9'–H), 2.45 (3H, s, PhC<u>H</u>$_3$), 3.59 (2H, t, $^3J_{1',2'}$ 6.6, 1'–H), 4.01 (2H, t, $^3J_{10',9'}$ 6.6, 10'–H), 7.34 (2H, d, $^3J_{2,3\text{ and }6,5}$ 8.2, 2–H and 6–H), 7.79 (2H, d, $^3J_{3,2\text{ and }5,6}$ 8.2, 3–H and 5–H); δ_C (100 MHz, $CDCl_3$) –5.3 (2 x CH_3, OSi(<u>C</u>H$_3$)$_2$^{t}Bu), 18.4 (C, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 21.6 (CH_3, Ph<u>C</u>H$_3$), 25.3 (CH_2, C–3'), 25.8 (CH_2, C–8'), 26.0 (CH_3, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 28.8 (CH_2, C–7'), 28.9 (CH_2, C–9'), 29.3, 29.4, 29.4 (3 x CH_2, C–4', C–5' and C–6'), 32.8 (CH_2, C–2'), 63.3 (CH_2, C–1'), 70.7 (CH_2, C–10'), 127.9 (2 x CH, C–2 and C–6), 129.8 (2 x CH, C–3 and C–5), 133.2 (C, C–1), 144.6 (C, C–4); MS *m/z* (ESI+) 907 ($[M_2 + Na]^+$, 3%), 465 ($[M + Na]^+$, 100), 443 ($[M + H]^+$, 70), 351 ($[M – PhCH_3]^+$, 3), 287 ($[M – S(O)_2PhCH_3]^+$, 68); HRMS (ESI+): $[M + H]^+$, found 443.2650. $C_{23}H_{43}O_4SSi$ requires 443.2646.



27d

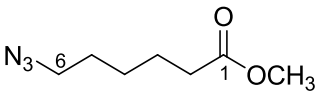
10-(Azidodecyloxy)-1-*tert*-butyldimethylsilane (27d)

To a solution of *10-(tert-butyldimethylsilyloxy)decyl 4-methylbenzenesulfonate* (52 mg, 0.12 mmol) in anhydrous DMF (390 µL) was added NaN_3 (26.7 mg, 0.41 mmol) at RT. After stirring at RT for 17 h, the reaction mixture was passed through a plug of silica and washed through with EtOAc (40 mL). The filtrate was concentrated *in vacuo* to get an orange oil. Purification by flash chromatography (0%, 2.5% EtOAc/*n*-hexane) gave the *title compound* **27d** as a pale yellow oil (32.3 mg, 88%). R_f (2.5% EtOAc/n-hexane) 0.29; IR (film) ν_{max}/cm^{-1} 2928 (C–H), 2856 (C–H), 2095 (C–N=N$^+$=N$^-$), 1471, 1361, 1256, 1098 (C–O), 835, 775; δ_H (300 MHz, $CDCl_3$) 0.04 (6H, s, OSi(C<u>H</u>$_3$)$_2$^{t}Bu), 0.89 (9H, s, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 1.28–1.45 (12H, m, 3–H, 4–H, 5–H, 6–H, 7–H and 8–H), 1.48–1.55 (2H, m, 2–H), 1.57–1.62 (2H, m, 9–H), 3.25 (2H, t, $^3J_{10,9}$ 6.9, 10–H), 3.59 (2H, t, $^3J_{1,2}$ 6.6, 1–H); δ_C (75 MHz, $CDCl_3$) –5.3 (2 x CH_3, OSi(<u>C</u>H$_3$)$_2$^{t}Bu), 18.4 (C, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 25.8 (CH_2, C–3), 26.0 (CH_3, OSi(CH$_3$)$_2$^{t}<u>Bu</u>), 26.7 (CH_2, C–8), 28.8 (CH_2, C–7), 29.1 (CH_2, C–9), 29.4, 29.4, 29.5 (3 x CH_2, C–4, C–5 and C–6), 32.8 (CH_2, C–2), 51.5 (CH_2, C–10), 63.3 (CH_2, C–1); MS *m/z* (ESI+) 336 ($[M + Na]^+$, 29%), 314 ($[M + H]^+$, 63), 286 ($[M + H – N_2]^+$, 69), 270 ($[M – HN_3]^+$, 11), 154 ($[M – CH_2CH_2OTBDMS]^+$, 100), 133 (24); HRMS (ESI+): $[M + H]^+$, found 314.2624. $C_{16}H_{36}N_3OSi$ requires 314.2622.



Methyl 6-bromohexanoate

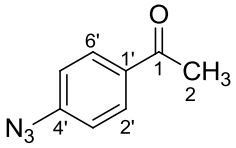
DMAP (40 mg, 0.328 mmol) and EDCI•HCl (436 mg, 2.27 mmol) were added to a solution of 6-bromohexanoic acid (300 mg, 1.538 mmol) in CH_3OH (320 μL, 12.6 mmol) at RT. After stirring for 5 h, the reaction mixture was quenched with H_2O (5 mL) and the organic phase separated. The aqueous phase was extracted with EtOAc (2 x 10 mL) and the combined organic extracts washed with saturated NaCl (20 mL). The aqueous washing was extracted with EtOAc (20 mL) and the organic extracts dried over $MgSO_4$ and then concentrated *in vacuo* to get a yellow oil. Purification by flash chromatography (0%, 14% EtOAc/*n*-hexane) gave *methyl 6-bromohexanoate* as a pale yellow liquid (261 mg, 81%). R_f (14% EtOAc/*n*-hexane) 0.27; δ_H (400 MHz, $CDCl_3$) 1.43–1.51 (2H, m, 4–H), 1.61–1.69 (2H, m, 3–H), 1.83–1.91 (2H, m, 5–H) 2.33 (2H, t, $^3J_{2,3}$ 7.4, 2–H), 3.40 (2H, t, $^3J_{6,5}$ 6.8 Hz, 6-H), 3.67 (3H, s, OC<u>H</u>$_3$); δ_C (100 MHz, $CDCl_3$) 24.0 (CH_2, C–3), 27.6 (CH_2, C–4), 32.3 (CH_2, C–5), 33.5 (CH_2, C–2), 33.8 (CH_2, C–6), 51.5 (CH_3, O<u>C</u>H$_3$), 173.9 (C, C–1). The ^{1}H and ^{13}C NMR spectra obtained was in agreement with that reported in the literature.[9]



27e

Methyl 6-azidohexanoate (27e)

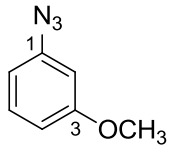
NaN_3 (65 mg, 1.00 mmol) and TBAI (199 mg, 0.59 mmol) were added to a solution of methyl 6-bromohexanoate (56 mg, 0.27 mmol) in DMF (900 μL) at RT. The red mixture was heated to 70 °C for 20.5 h where the mixture went colourless. After cooling to RT, H_2O (2 mL) and EtOAc (2 mL) were added and the organic phase separated. The aqueous phase was extracted with EtOAc (3 x 10 mL) and the combined organic extracts dried over $MgSO_4$. Concentration of the organic extracts *in vacuo* gave a pale red oil that was purified by flash chromatography (0%, 14% EtOAc/ *n*-hexane) to afford the *title compound* **27e** as a pale yellow oil (41 mg, 89%). R_f (14% EtOAc/ *n*-hexane) 0.28; δ_H (300 MHz, $CDCl_3$) 1.35–1.46 (2H, m, 4–H), 1.57–1.71 (4H, m, 3–H and 5–H), 2.33 (2H, t, $^3J_{2,3}$ 7.4, 2–H), 3.27 (2H, t, $^3J_{6,5}$ 6.8 Hz, 6-H), 3.67 (3H, s, OC<u>H</u>$_3$); δ_C (75 MHz, $CDCl_3$) 24.4 (CH_2, C–3), 26.2 (CH_2, C–4), 28.5 (CH_2, C–5), 33.8 (CH_2, C–2), 51.2 (CH_2, C–6), 51.5 (CH_3, O<u>C</u>H$_3$), 173.9 (C, C–1). The ^{1}H and ^{13}C NMR spectra obtained was in agreement with that reported in the literature.[9]



27f

1-(4-Azidophenyl)ethanone (27f)

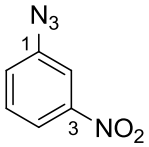
To a suspension of 4-amino-acetophenone (150 mg, 1.11 mmol) in H_2O (2.2 mL) at 0 °C, was added concentrated HCl (12 M, 240 μL). A solution of $NaNO_2$ (86.0 mg, 1.25 mmol) in H_2O (2.8 mL) was added dropwise at a rate to maintain a reaction temperature < 5 °C, whereupon completion of addition, the off-white suspension had dissolved to a bright yellow solution. The reaction was stirred at 0 °C for 0.5 h, and then NaN_3 (88.9 mg, 1.37 mmol) was added slowly to maintain a reaction temperature of < 5 °C. The reaction mixture was wrapped in aluminium foil and allowed to warm to RT. After 2 h, the resulting pink precipitate was dissolved in EtOAc (5 mL) and the aqueous phase extracted with EtOAc (3 x 5 mL). The organic extracts were washed with saturated NaCl (10 mL) and the aqueous washing extracted with EtOAc (10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to obtain a dark orange oil. Purification by flash chromatography (0%, 17% EtOAc/*n*-hexane) afforded the *title compound* **27f** as a beige solid (176.6 mg, 99%). Mp. 42–44 °C. (Lit.[10] 43-45 °C); R_f (17% EtOAc/*n*-hexane) 0.32; δ_H (400 MHz, $CDCl_3$) 2.58 (3H, s, 2–H), 7.09 (2H, dt, $^3J_{3',2' \text{ and } 5',6'}$ 8.6 and $^4J_{3',5'}$ 2.2, 3'–H and 5'–H), 7.97 (2H, dt, $^3J_{2',3' \text{ and } 6',5'}$ 8.6 and $^4J_{2',6'}$ 2.2, 2'–H and 6'–H); δ_C (100 MHz, $CDCl_3$) 26.5 (CH_3, C–1), 119.0 (2 x CH, C–3' and C–5'), 130.3 (2 x CH, C–2' and C–6'), 133.9 (C, C–1'), 144.9 (C, C–4'), 196.5 (C, C–1). The ^1H and ^{13}C NMR spectra obtained was in agreement with that reported in the literature.[11]



27g

1-Azido-3-methoxybenzene (27g)

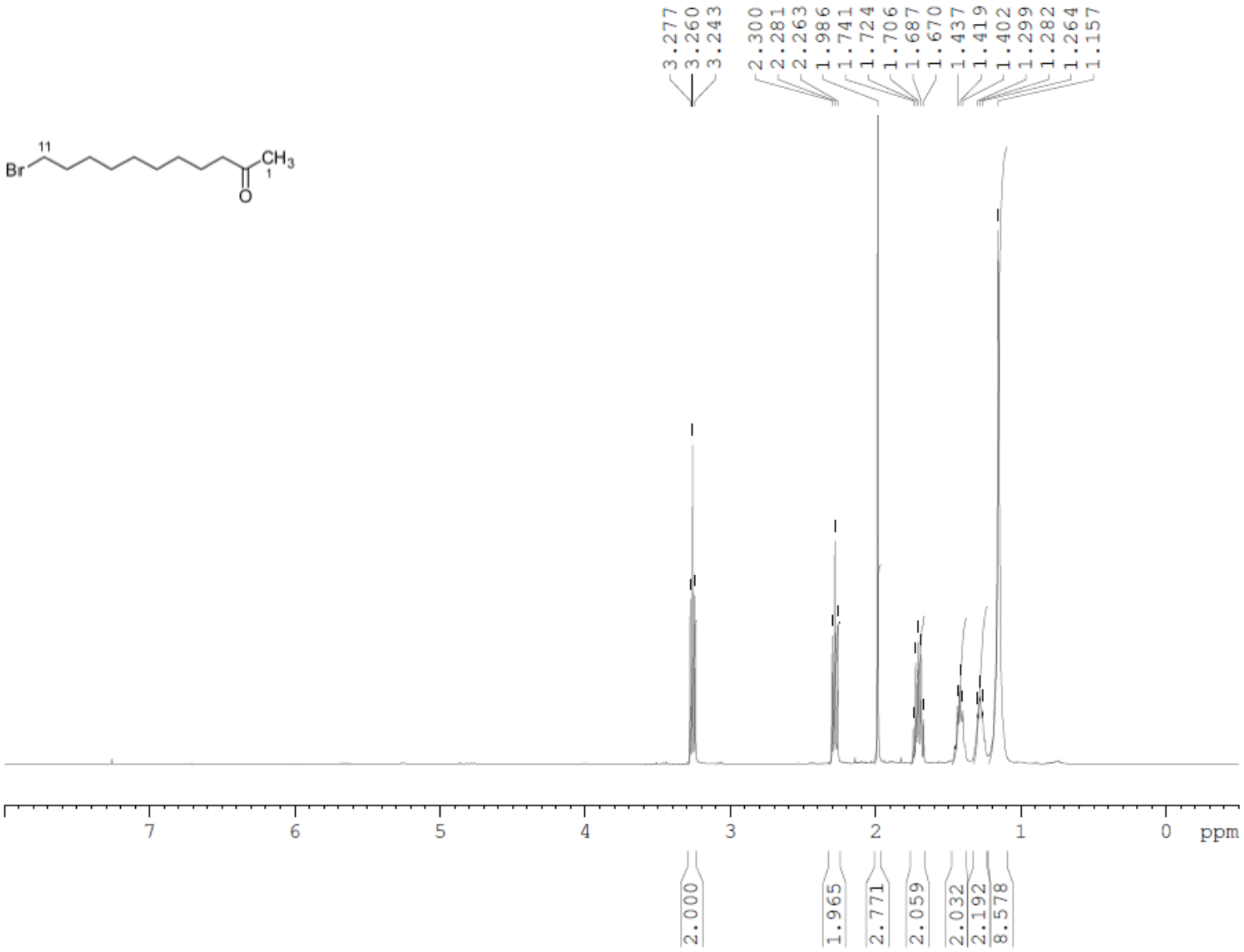
A suspension of 3-methoxyaniline (164 mg, 1.34 mmol) in H_2O (2.4 mL) was dissolved with concentrated HCl (12 M, 290 μL) at RT. The solution was cooled to 0 °C and a solution of $NaNO_2$ (93 mg, 1.35 mmol) in H_2O (2.9 mL) was added at a rate to maintain a reaction temperature < 5 °C. The light brown mixture was stirred for 15 minutes at 0 °C whereupon NaN_3 (104 mg, 1.60 mmol) was added slowly at 0 °C. The reaction mixture was allowed to warm to RT over 2 h. The aqueous phase was extracted with EtOAc (4 x 20 mL) and the combined organic extracts dried over Na_2SO_4 and concentrated *in vacuo* to get a brown oil. Purification by flash chromatography (0%, 9% to 20% EtOAc/*n*-hexane) afforded the *title compound* **27g** as a yellow oil (102 mg, 68%). R_f (9% EtOAc/*n*-hexane) 0.51; δ_H (300 MHz, $CDCl_3$) 3.80 (3H, s, $OC\underline{H}_3$), 6.56 (1H, t, $^4J_{2,4 \text{ and } 2,6}$ 2.2, 2–H), 6.63–6.71 (2H, m, 4–H and 6–H), 7.26 (1H, t, $^3J_{5,4 \text{ and } 5,6}$ 8.1, 5–H); δ_C (75 MHz, $CDCl_3$) 55.3 (CH_3, $O\underline{C}H_3$), 104.9 (CH, C–2), 110.7 (CH, C–4), 111.3 (CH, C–6), 130.4 (CH, C–5), 141.3 (C, C–1), 160.8 (C, C–3). The ^1H and ^{13}C NMR spectra obtained was in agreement with that reported in the literature.[11]

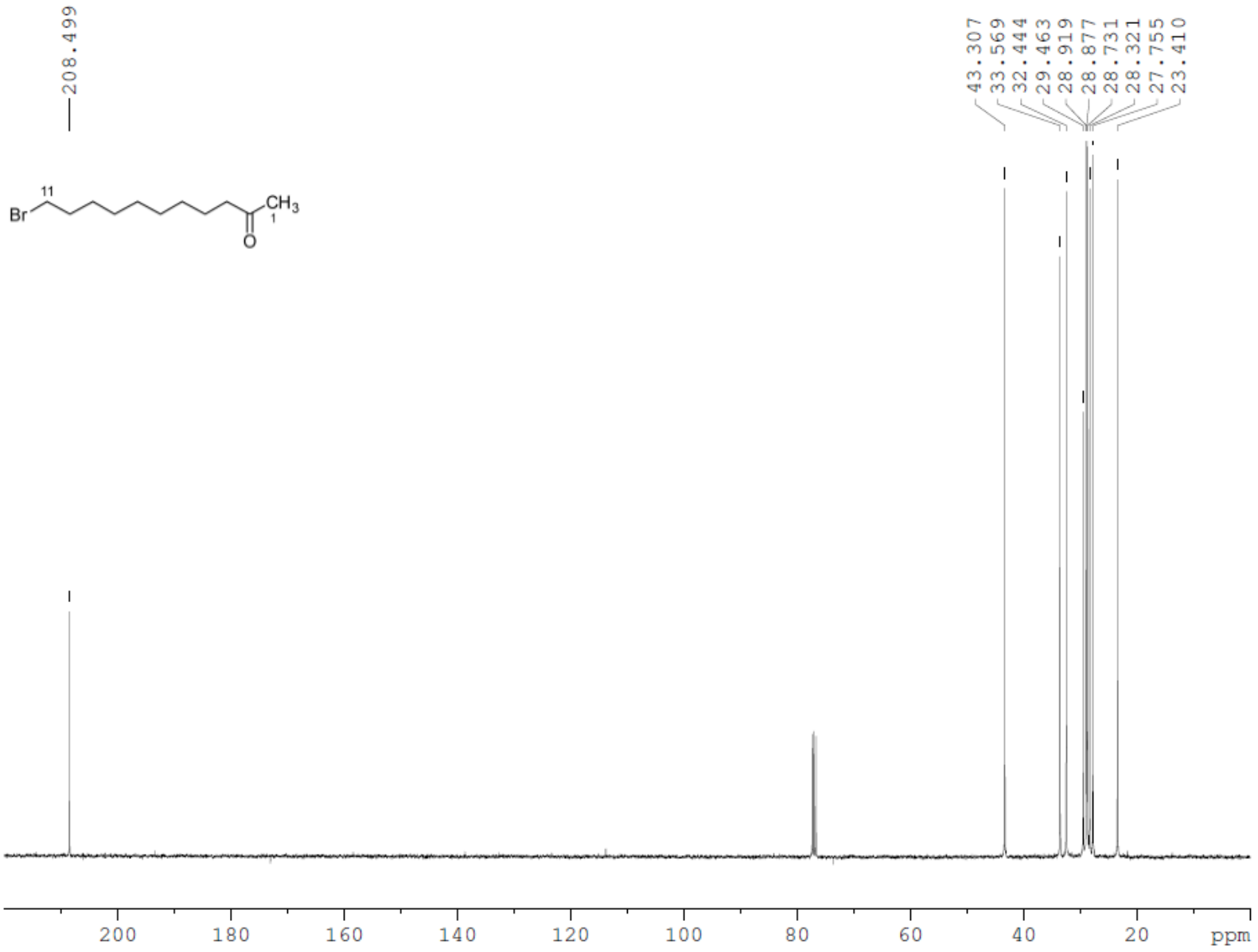


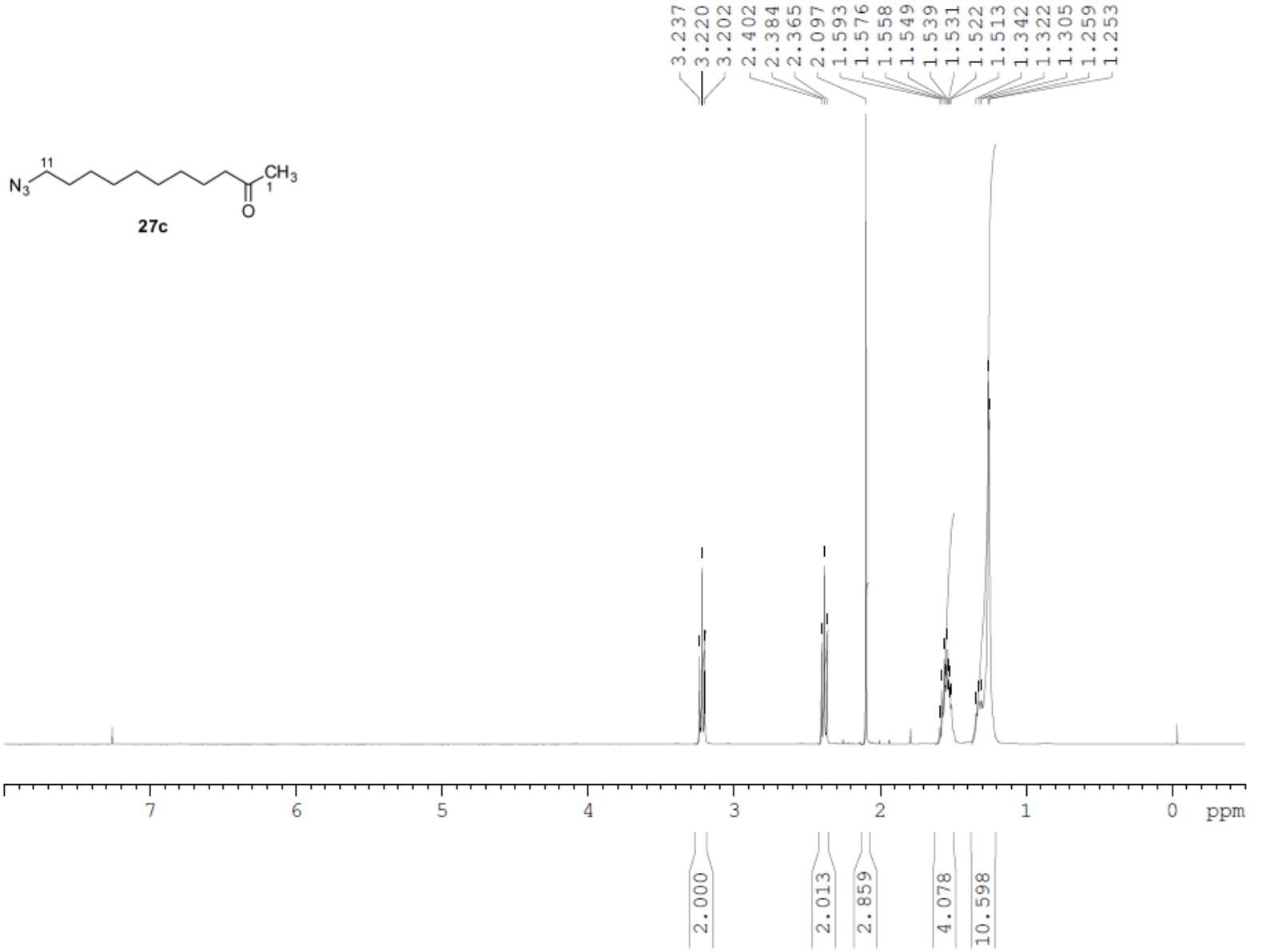
27h

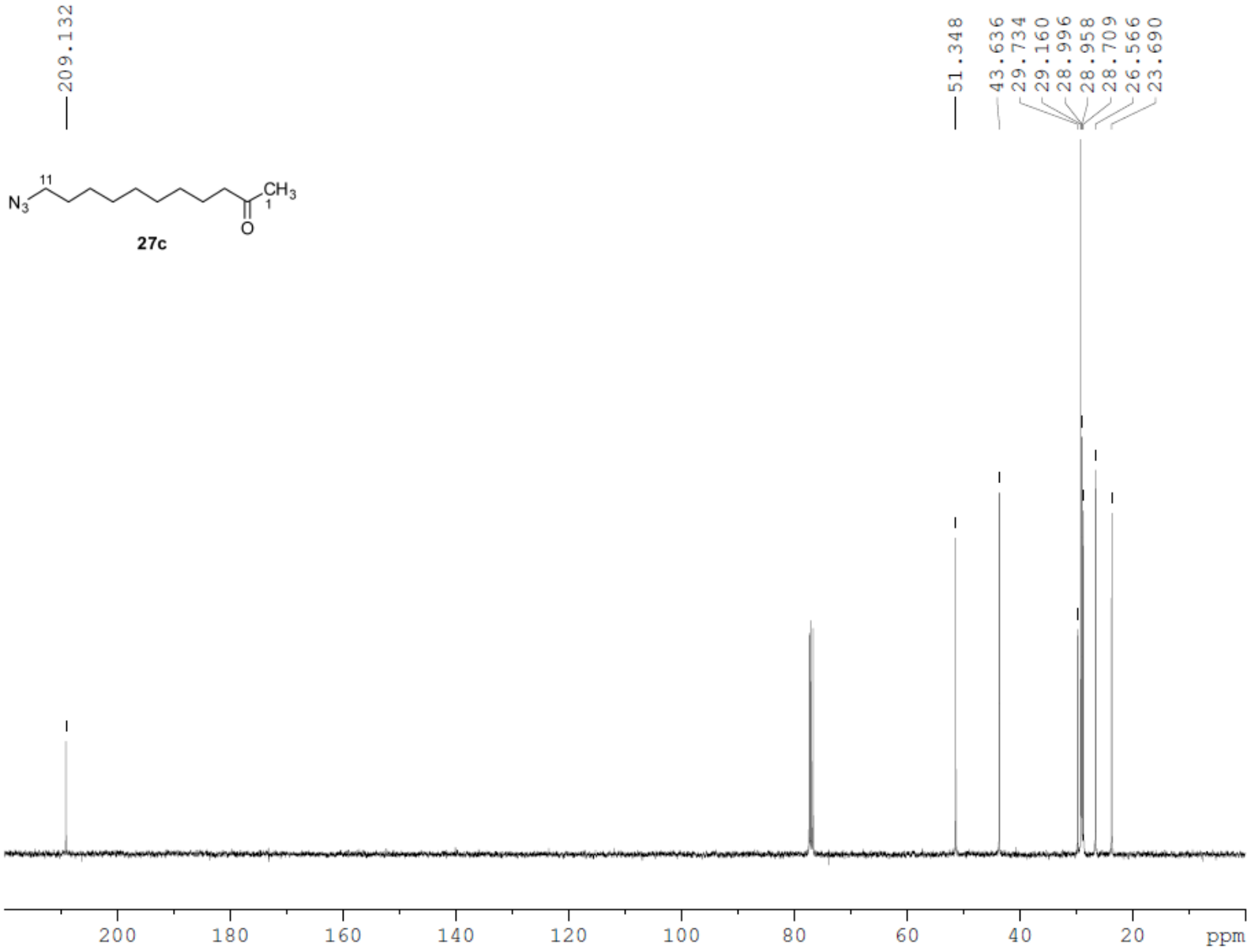
1-Azido-3-nitrobenzene (27h)

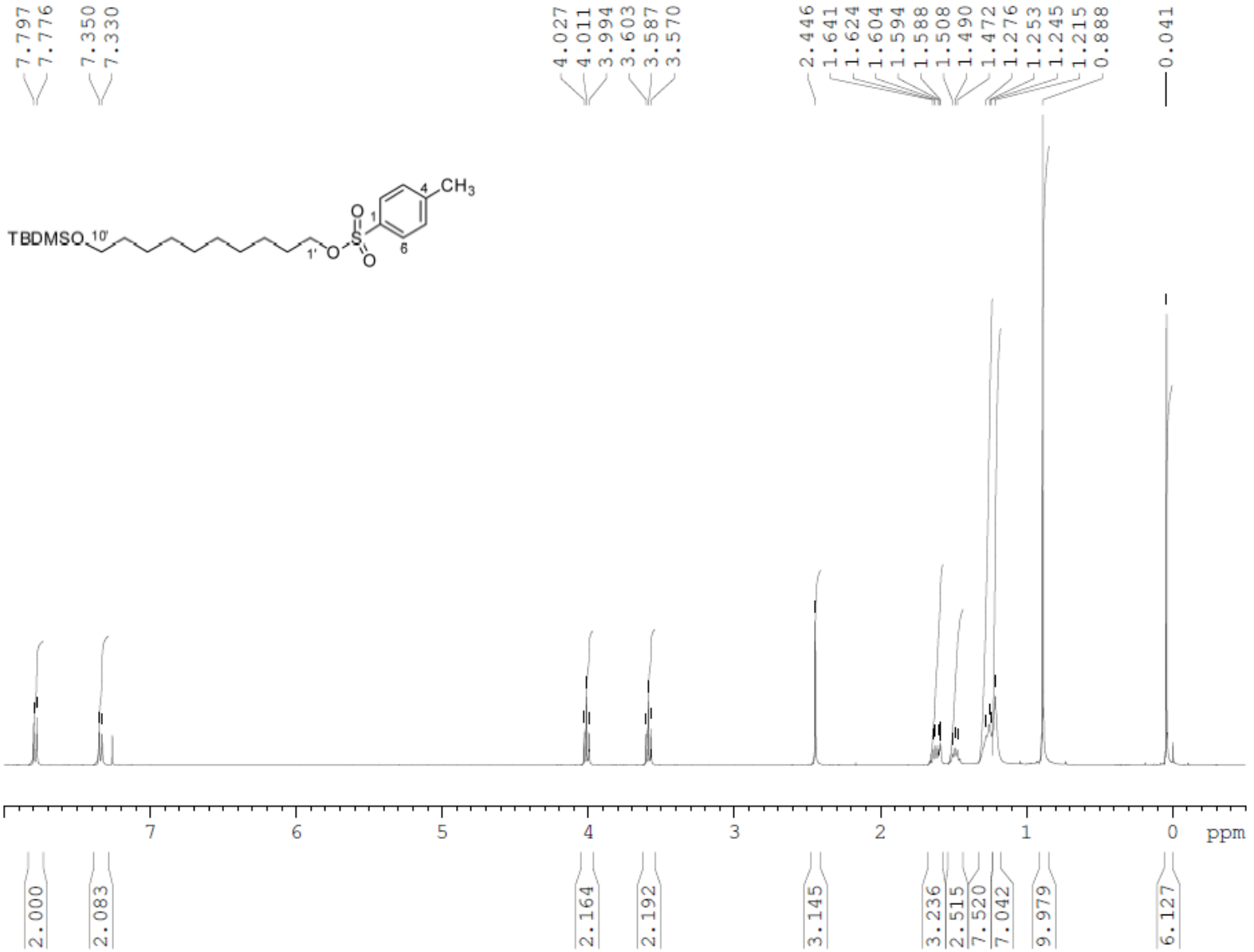
A suspension of 3-nitroaniline (172 mg, 1.25 mmol) in H_2O (2.4 mL) was dissolved with HCl (12 M, 270 μL) at RT. The yellow solution was cooled to 0 °C and a solution of $NaNO_2$ (98 mg, 1.42 mmol) in H_2O (3 mL) was added at a rate to maintain a reaction temperature < 5 °C and the reaction mixture stirred for 15 minutes at 0 °C. NaN_3 (104 mg, 1.60 mmol) was then added slowly at 0 °C and the reaction allowed to warm to RT over 2.5 h. The aqueous phase was extracted with EtOAc (4 x 10 mL) and the combined organic extracts dried over Na_2SO_4 and concentrated *in vacuo* to get an orange oil. Purification by flash chromatography (0%, 9% EtOAc/*n*-hexane) afforded the *title compound* **27h** as a yellow crystalline solid (139 mg, 68%). Mp. 44-47 °C. (Lit.[12] 59-60 °C); R_f (9% EtOAc/*n*-hexane) 0.31; δ_H (400 MHz, $CDCl_3$) 7.33–7.36 (1H, m, 6–H), 7.54 (1H, t, $^3J_{5,4 \text{ and } 5,6}$ 8.0, 5–H) 7.89 (1H, t, $^4J_{2,4 \text{ and } 2,6}$ 2.2, 2–H), 7.99–8.02 (1H, m, 4–H); δ_C (100 MHz, $CDCl_3$) 114.1 (CH_3, C–2), 119.7 (CH, C–4), 124.9 (CH, C–6), 130.6 (CH, C–5), 142.0 (C, C–1), 149.3 (C, C–3). The ^1H and ^{13}C NMR spectra obtained was in agreement with that reported in the literature.[12]

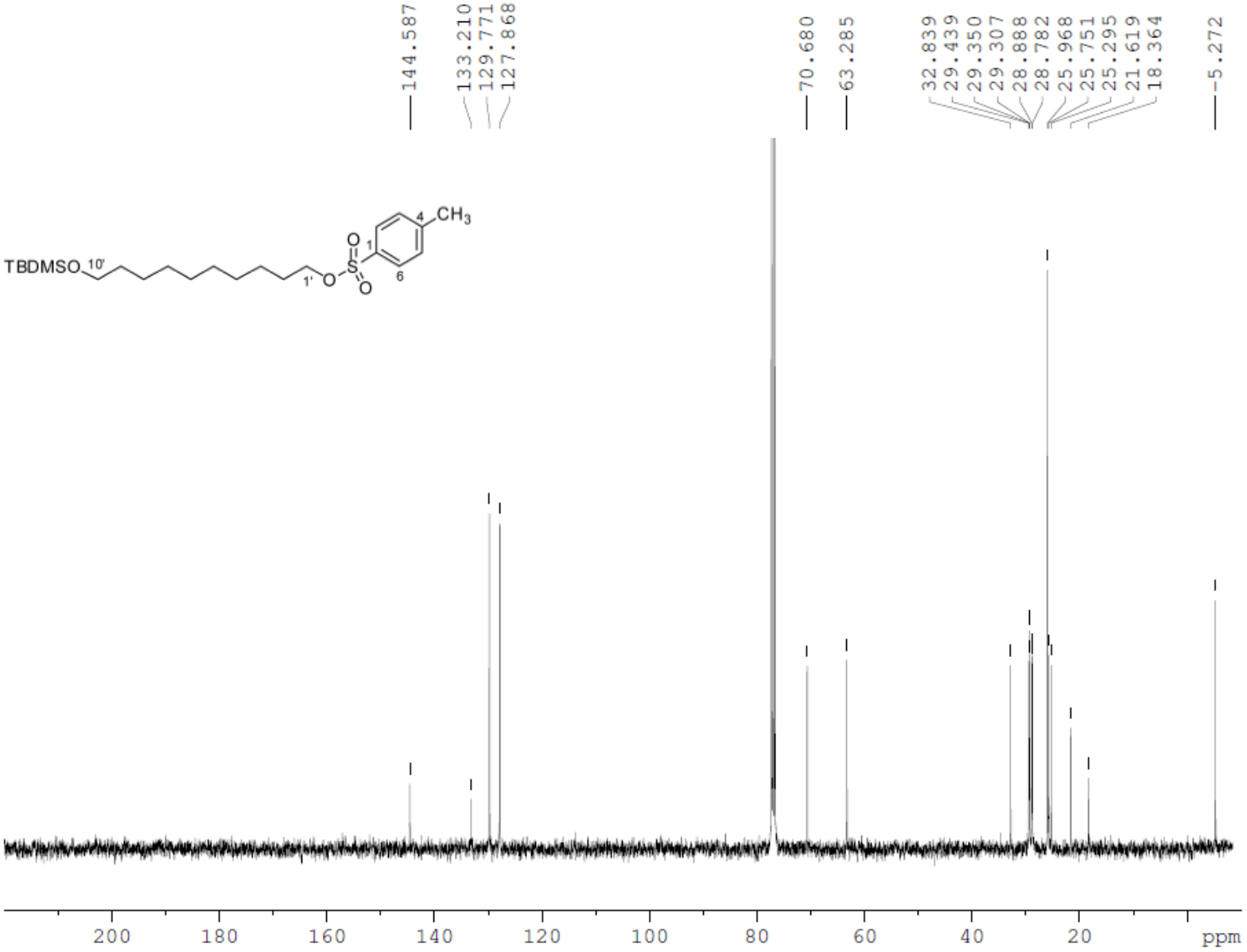


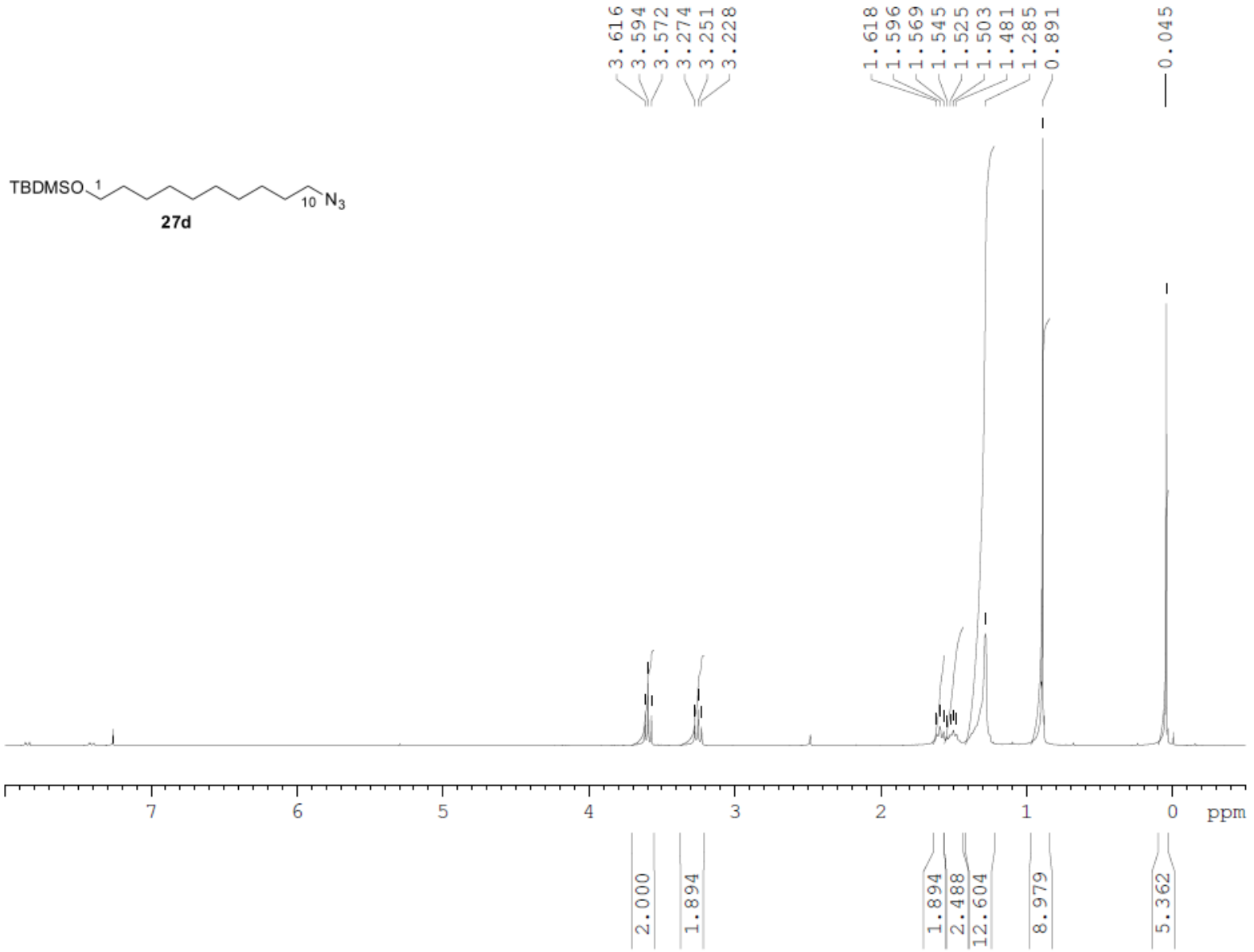


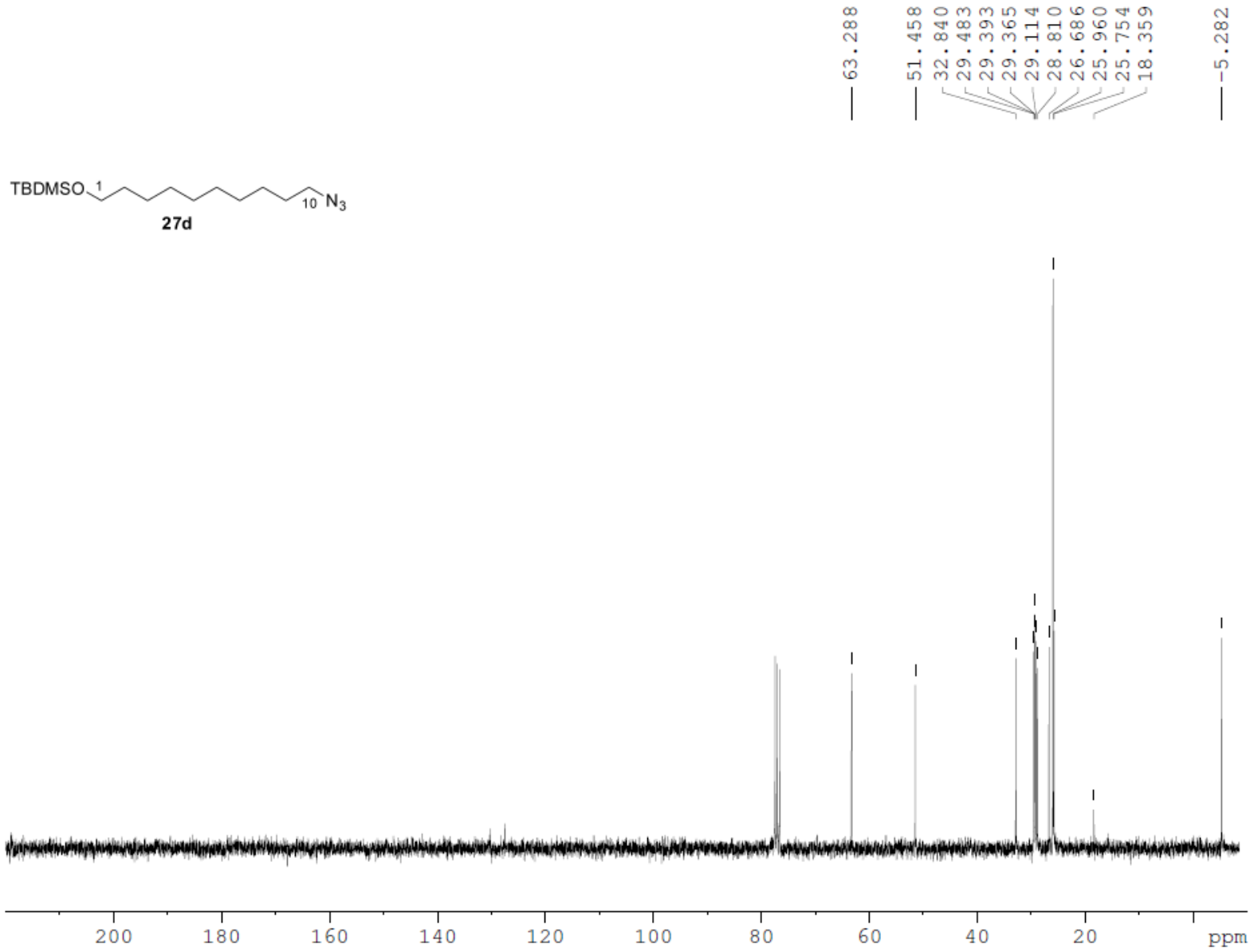








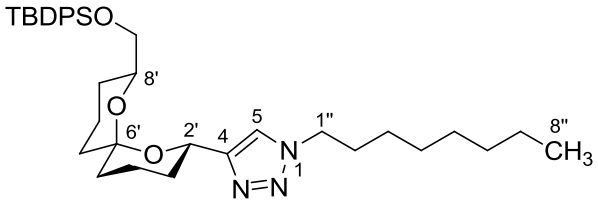




Experimental and Characterization data for silyl-protected spiroacetal-triazoles **28a-h**

General Procedure for the Copper-Catalysed Azide-Alkyne Cycloaddition (CuAAC) of Acetylenic Spiroacetal 11 to Azides 27 (Procedure A)

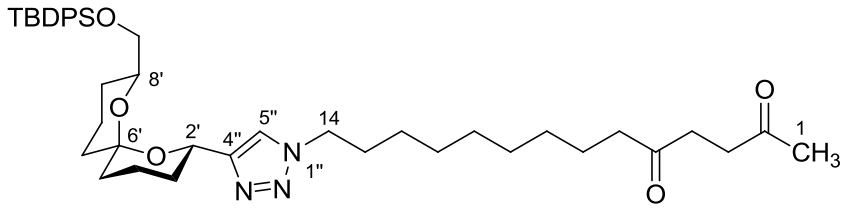
To a mixture of acetylenic spiroacetal **11** (1.0 equiv.) and azide **27** (1.1-1.4 equiv.) in anhydrous toluene (0.050-0.086 M) under an argon atmosphere was added a catalytic quantity (a single crystal) of CuI•P(OEt)$_3$ and the reaction mixture heated to reflux for 1.0–1.5 h. Upon reaction completion by TLC analysis, the product was purified directly by flash chromatography (EtOAc–*n*-hexane) to yield only the 1,4-disubstituted regioisomer of the desired spiroacetal-triazole analogue **28**.



28a

4-((2S,6S,8S)-8-((*tert*-Butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1-octyl-1H-1,2,3-triazole (28a)

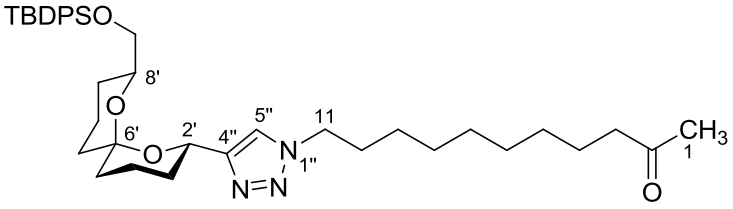
The *title compound* **28a** (22.7 mg, 99%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (17.0 mg, 37.9 µmol), 1-azidooctane **(27a)** (8.1 mg, 52.2 µmol) and a single crystal of CuI•P(OEt)$_3$ in anhydrous toluene (750 µL) using Procedure A. The reaction mixture was purified by flash chromatography using EtOAc–*n*-hexane (0%, 9% to 17% EtOAc/*n*-hexane). $[\alpha]_D^{25}$ -15.0 (c 1.18 in $CHCl_3$); R_f (17% EtOAc/*n*-hexane) 0.29; IR (film) ν_{max}/cm^{-1} 2929 (C–H), 2857 (C–H), 1429 (C–H), 1113 (C–O–C), 982, 702 (C–H); δ_H (300 MHz, $CDCl_3$) 0.88 (3H, t, $^3J_{8'',7''}$ 6.7, 8''–H), 1.06 (9H, s, OSiPh$_2$^{t}Bu), 1.27–1.34 (11H, m, 3''–H, 4''–H, 5''–H, 6''–H, 7''–H and 9'–H$_A$), 1.44–1.72 (8H, m, 3'–H$_A$, 4'–H, 5'–H, 9'–H$_B$, 10'–H$_A$ and 11'–H$_A$), 1.85–1.94 (3H, m, 2''–H and 10'–H$_B$), 2.02–2.14 (2H, m, 3'–H$_B$ and 11'–H$_B$), 3.62 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 4.7, 8'–C$\underline{H}_A$H$_B$O), 3.73 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 5.9, 8'–CH$_A\underline{H}_B$O), 3.81–3.88 (1H, m, 8'–H), 4.32 (2H, t, $^3J_{1'',2''}$ 7.5, 1''–H), 4.98 (1H, dd, $^3J_{2',3'ax}$ 11.6 and $^3J_{2',3'eq}$ 1.8, 2'–H), 7.34–7.43 (7H, m, 5–H and Ph), 7.70–7.74 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) 14.0 (CH_3, C–11''), 18.5, 18.7 (2 x CH_2, C–4' and C–10'), 19.2 (C, OSiPh$_2$^{t}Bu), 22.6 (CH_2, C–7''), 26.6 (CH_2, C–3''), 26.8 (CH_3, OSiPh$_2$^{t}Bu), 27.0 (CH_2, C–9'), 28.9, 29.0 (2 x CH_2, C–4'' and C–5''), 30.3 (CH_2, C–2''), 30.8 (CH_2, C–3'), 31.7 (CH_2, C–6''), 35.1, 35.2 (2 x CH_2, C–5' and C–11'), 50.2 (CH_2, C–1''), 64.8 (CH, C–2'), 67.4 (CH_2, 8'–$\underline{C}H_2$O), 70.3 (CH, C–8'), 96.6 (C, C–6'), 120.2 (CH, C–5), 127.5 (CH, Ph), 129.5 (CH, Ph), 133.8 (C, Ph), 135.6 (CH, Ph), 135.6 (CH, Ph), 150.2 (C, C–4); MS *m/z* (ESI+, MS_2+ (604)) 604 ([M + H]$^+$, 40%), 586 (100), 568 ([M + H – ^{t}Bu]$^+$, 38), 526 ([M – Ph]$^+$, 61), 508 ([M – Ph – H_2O]$^+$, 87), 448 ([M – 2Ph – H]$^+$, 73), 348 ([M – OTBDPS]$^+$, 6), 330 (71), 312 (70), 302 (45), 284 (22); HRMS (ESI+): [M + H]$^+$, found 604.3925. $C_{36}H_{54}N_3O_3Si$ requires 604.3929.



28b

14-(4-(8-((*tert*-Butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl)tetradecane-2,5-dione (28b).

The *title compound* **28b** (10.1 mg, 58%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (10.5 mg, 24.3 µmol), diketo-azide **27b** (9.8 mg, 37.0 µmol) and a single crystal of CuI•P(OEt)$_3$ in anhydrous toluene (280 µL) using Procedure A. The reaction mixture was purified by flash chromatography using EtOAc–*n*-hexane (0 %, 25% to 33% EtOAc/*n*-hexane). $[\alpha]_D^{21}$ -19.5 (c 0.93 in $CHCl_3$); R_f (33% EtOAc/n-hexane) 0.15; IR (film) ν_{max}/cm^{-1} 2932 (C–H), 2857 (C–H), 1714 (C=O), 1428 (C–H), 1364, 1225, 1112 (C–O–C), 1086 (C–O–C), 982, 704; δ_H (300 MHz, $CDCl_3$) 1.05 (9H, s, OSiPh$_2$^{t}Bu), 1.24–1.33 (11H, m, 8–H, 9–H, 10–H, 11–H, 12–H, and 9'–H$_A$), 1.43–1.72 (10H, m, 7–H, 3'–H$_A$, 4'–H, 5'–H, 9'–H$_B$, 10'–H$_A$, and 11'–H$_A$), 1.89–1.93 (3H, m, 13–H and 10'–H$_B$), 2.06–2.12 (2H, 3'–H$_B$ and 11'–H$_B$), 2.18 (3H, s, 1–H), 2.44 (2H, t, $^3J_{6,7}$ 7.4, 6–H), 2.63–2.73 (4H, m, 3–H and 4–H), 3.61 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 4.7, 8'–C$\underline{H_A}$H$_B$O), 3.72 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 5.9, 8'–CH$_A$$\underline{H_B}$O), 3.80–3.87 (1H, m, 8'–H), 4.32 (2H, t, $^3J_{14,13}$ 7.4, 14–H), 4.97 (1H, dd, $^3J_{2',3'ax}$ 11.5 and $^3J_{2',3'eq}$ 2.0, 2'–H), 7.32–7.40 (7H, m, 5''–H and Ph), 7.69–7.73 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) 18.5, 18.7 (2 x CH_2, C–4' and C–10'), 19.3 (C, OSiPh$_2$^{t}Bu), 23.8 (CH_2, C–7), 26.5 (CH_2, C–12), 26.8 (CH_3, OSiPh$_2$^{t}Bu), 27.1 (CH_2,C–9'), 28.9, 29.1, 29.2, 29.2 (4 x CH_2, C–8, C–9, C–10 and C–11), 29.9 (CH, C–1), 30.3 (CH_2, C–13), 30.8 (CH_2, C–3'), 35.1, 35.3 (2 x CH_2, C–5' and C–11'), 36.0 (CH_2, C–4), 36.9 (CH_2, C–3), 42.8 (CH_2, C–6), 50.2 (CH_2, C–14), 64.8 (CH, C–2'), 67.4 (CH_2, 8'–$\underline{C}H_2$O), 70.3 (CH, C–8'), 96.6 (C, C–6'), 120.3 (CH, C–5''), 127.6 (CH, Ph), 129.5 (CH, Ph), 129.5 (CH, Ph), 133.9 (C, Ph), 135.6 (CH, Ph), 135.7 (CH, Ph), 150.2 (C, C–4''), 207.3 (C, C–2), 209.6 (C, C–5); MS *m/z* (ESI+, MS$_2$+ (716)) 716 ([M + H]$^+$, 14%), 698 (53), 639 ([M – Ph]$^+$, 23), 620 (34), 542 (18), 442 (99), 424 (100); HRMS (ESI+): [M + H]$^+$, found 716.4464. $C_{42}H_{62}N_3O_5Si$ requires 716.4453.

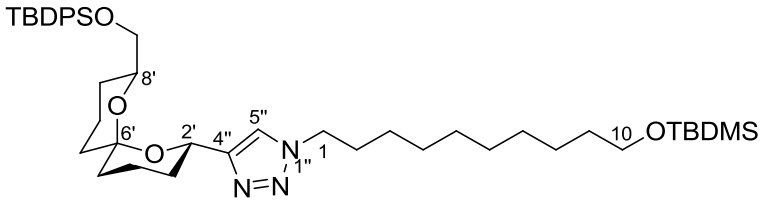


28c

11-(4-(8-((*tert*-Butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl)undecan-2-one (28c)

The *title compound* **28c** (10.6 mg, 55%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (13.1 mg, 29.0 µmol), keto-azide **27c** (6.7 mg, 32.0 µmol) and a single crystal of CuI•P(OEt)$_3$ in anhydrous toluene (340 µL) using Procedure A. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (0 %, 9% to 25% EtOAc/*n*-hexane). $[\alpha]_D^{21}$ -30.3 (c 1.06 in $CHCl_3$); R_f (25% EtOAc/n-hexane) 0.21; IR (film) ν_{max}/cm^{-1} 2930 (C–H), 2856 (C–H), 1715 (C=O), 1428

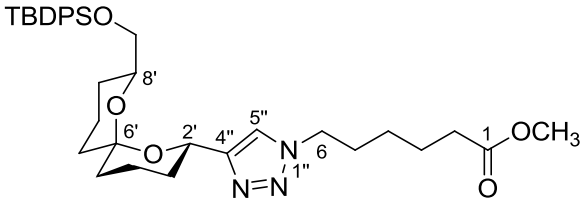
(C–H), 1361, 1112 (C–O–C), 1086 (C–O–C), 981, 702; δ_H (300 MHz, $CDCl_3$) 1.05 (9H, s, $OSiPh_2{}^tBu$), 1.26–1.47 (11H, m, 5–H, 6–H, 7–H, 8–H, 9–H, and 9'–H_A), 1.49–1.77 (10H, m, 4–H, 3'–H_A, 4'–H, 5'–H, 9'–H_B, 10'–H_A, and 11'–H_A), 1.89–1.99 (3H, m, 10–H and 10'–H_B), 2.01–2.07 (2H, m, 3'–H_B and 11'–H_B), 2.13 (3H, s, 1–H), 2.41 (2H, t, $^3J_{3,4}$ 7.4, 3–H), 3.61 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 4.7, 8'–CH_AH_BO), 3.73 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 5.9, 8'–CH_AH_BO), 3.80–3.88 (1H, m, 8'–H), 4.32 (2H, t, $^3J_{11,10}$ 7.4, 11–H), 4.97 (1H, dd, $^3J_{2',3'ax}$ 11.6 and $^3J_{2',3'eq}$ 1.9, 2'–H), 7.32–7.40 (7H, m, 5''–H and Ph), 7.69–7.73 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) 18.5, 18.7 (2 x CH_2, C–4' and C–10'), 19.3 (C, $OSiPh_2{}^tBu$), 23.8 (CH_2, C–4), 26.5 (CH_2, C–9), 26.8 (CH_3, $OSiPh_2{}^tBu$), 27.0 (CH_2, C–9'), 28.9, 29.1, 29.2, 29.2 (4 x CH_2, C–5, C–6, C–7 and C–8), 29.8 (CH_3, C–1), 30.3 (CH_2, C–10), 30.8 (CH_2, C–3'), 35.1, 35.2 (2 x CH_2, C–5' and C–11'), 43.7 (CH_2, C–3), 50.2 (CH_2, C–11), 64.8 (CH, C–2'), 67.4 (CH_2, 8–CH_2O), 70.3 (CH, C–8'), 96.6 (C, C–6'), 120.3 (CH, C–5''), 127.6 (CH, Ph), 129.5 (CH, Ph), 133.9 (C, Ph), 135.6 (CH, Ph), 135.7 (CH, Ph), 150.2 (C, C–4''), 209.2 (C, C–2); MS *m/z* (ESI+, MS_2+ (660)) 660 ($[M + H]^+$, 61%), 642 (100), 582 ($[M – Ph]^+$, 59), 564 (41), 504 (39), 386 (62), 358 (51); HRMS (ESI+): $[M + H]^+$, found 660.4182. $C_{39}H_{58}N_3O_4Si$ requires 660.4191.



28d

1-(10-(*tert*-Butyldimethylsilyloxy)decyl)-4-((2S,6S,8S)-8-((tert-butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazole (28d)

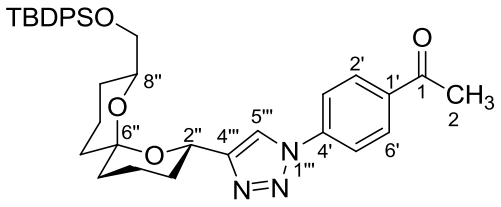
The *title compound* **28d** (11.9 mg, 57%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (12.2 mg, 27.2 µmol), TBDMS-protected-azide **27d** (9.4 mg, 30.0 µmol) and a single crystal of CuI•$P(OEt)_3$ in anhydrous toluene (420 µL) using Procedure A. The reaction mixture was purified by flash chromatography using EtOAc–*n*-hexane (0%, 11% to 17% EtOAc/*n*-hexane). $[\alpha]_D^{20}$ -15.9 (c 1.19 in $CHCl_3$); R_f (17% EtOAc/*n*-hexanes) 0.19; IR (film) ν_{max}/cm^{-1} 2930 (C–H), 2856 (C–H), 1428, 1113 (C–O–C), 983, 835, 702; δ_H (400 MHz, $CDCl_3$) 0.05 (6H, s, $OSi(CH_3)_2{}^tBu$), 0.89 (9H, s, $OSi(CH_3)_2{}^tBu$), 1.05 (9H, s, $OSiPh_2{}^tBu$), 1.26–1.33 (12H, m, 3–H, 4–H, 5–H, 6–H, 8–H, 9'–H_A, and 11'–H_A), 1.40–1.72 (11H, m, 7–H, 9–H, 3'–H_A, 4'–H, 5'–H, 9'–H_B and 10'–H_A), 1.87–1.93 (3H, m, 2–H and 10'–H_B), 2.02–2.17 (2H, m, 3'–H_B and 11'–H_B), 3.59 (2H, t, $^3J_{10,9}$ 6.6, 10–H), 3.59–3.64 (1H, m, 8'–CH_AH_BO), 3.72 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 5.9, 8'–CH_AH_BO), 3.81–3.87 (1H, m, 8'–H), 4.32 (2H, t, $^3J_{1,2}$ 7.4, 1–H), 4.97 (1H, dd, $^3J_{2',3'ax}$ 11.5 and $^3J_{2',3'eq}$ 2.2, 2'–H), 7.32–7.42 (7H, m, 5''–H and Ph), 7.69–7.73 (4H, m, Ph); δ_C (100 MHz, $CDCl_3$) –5.3 (2 x CH_3, $OSi(CH_3)_2{}^tBu$), 18.4 (C, $OSi(CH_3)_2{}^tBu$), 18.5, 18.7 (2 x CH_2, C–4' and C–10'), 19.3 (C, $OSiPh_2{}^tBu$), 25.8 (CH_2, C–3), 26.0 (CH_3, $OSi(CH_3)_2{}^tBu$), 26.6 (CH_2, C–7), 26.8 (CH_3, $OSiPh_2{}^tBu$), 27.0 (CH_2, C–9'), 29.0, 29.3, 29.4, 29.5 (4 x CH_2, C–4, C–5, C–6 and C–8), 30.3 (CH_2, C–2), 30.8 (CH_2, C–3') 32.9 (CH_2, C–9), 35.1, 35.2 (2 x CH_2, C–5' and C–11'), 50.3 (CH_2, C–1), 63.3 (CH_2, C–10), 64.8 (CH, C–2'), 67.4 (CH_2, 8'–CH_2O), 70.3 (CH, C–8'), 96.6 (C, C–6'), 120.3 (CH, C–5''), 127.6 (CH, Ph), 129.5 (CH, Ph), 133.9 (C, Ph), 135.6 (CH, Ph), 135.7 (CH, Ph), 150.2 (C, C–4''); MS *m/z* (ESI+, MS_2+ (762)) 762 ($[M + H]^+$, 59%), 744 (100), 684 ($[M – Ph]^+$, 86), 666 (55), 606 ($[M – OTBDPS + H_2O]^+$, 46), 506 ($[M – OTBDPS]^+$, 3), 488 (25), 470 (23), 442 (16); HRMS (ESI+): $[M + H]^+$, found 762.5057. $C_{44}H_{72}N_3O_4Si_2$ requires 762.5056.



28e

Methyl 6-(4-((2S,6S,8S)-8-((*tert*-butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl)hexanoate (28e)

The *title compound* **28e** (19.6 mg, 78%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (18.2 mg, 40.6 µmol), methyl 6-azidohexanoate **(27e)** (6.9 mg, 40.3 µmol) and a single crystal of CuI•P(OEt)$_3$ in anhydrous toluene (800 µL) using Procedure A. The reaction mixture was purified by flash chromatography using EtOAc–*n*-hexane (0%, 17% to 33% EtOAc/*n*-hexane). $[\alpha]_D^{26}$ -19.7 (c 1.12 in $CHCl_3$); R_f (33% EtOAc/*n*-hexanes) 0.28; IR (film) ν_{max}/cm^{-1} 2936 (C–H), 2858 (C–H), 1737 (C=O), 1429, 1112 (C–O–C), 1086, 982, 703; δ_H (300 MHz, $CDCl_3$) 1.05 (9H, s, OSiPh$_2$^{t}Bu), 1.23–1.31 (1H, m, 9'–H$_A$), 1.34–1.52 (4H, m, 4–H, 10'–H$_A$ and 11'–H$_A$), 1.55–1.74 (8H, m, 3–H, 3'–H$_A$, 4'–H, 5'–H, 9'–H$_B$), 1.85–1.99 (3H, m, 5–H and 10'–H$_B$), 2.02–2.17 (2H, m, 3'–H$_B$ and 11'–H$_B$), 2.32 (2H, t, $^3J_{2,3}$ 7.4, 2–H), 3.62 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 4.6, 8'–C$\underline{H_A}$H$_B$O), 3.66 (3H, s, OC$\underline{H_3}$), 3.73 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 5.9, 8'–CH$_A$$\underline{H_B}$O), 3.81–3.88 (1H, m, 8'–H), 4.33 (2H, t, $^3J_{6,5}$ 7.3, 6–H), 4.97 (1H, dd, $^3J_{2',3'ax}$ 11.5 and $^3J_{2',3'eq}$ 1.6, 2'–H), 7.31–7.43 (7H, m, 5''–H and Ph), 7.69–7.74 (4H, m, Ph); δ_C (75 MHz, $CDCl_3$) 18.5, 18.6 (2 x CH_2, C–4' and C–10'), 19.2 (C, OSiPh$_2$^{t}Bu), 24.2 (CH_2, C–3), 26.0 (CH_2, C–4), 26.8 (CH_3, OSiPh$_2$^{t}Bu), 27.0 (CH_2, C–9'), 30.0 (CH_2, C–5), 30.8 (CH_2, C–3'), 33.7 (CH_2, C–2), 35.1, 35.2 (2 x CH_2, C–5' and C–11'), 49.9 (CH_2, C–6), 51.5 (CH_3, O$\underline{C}H_3$), 64.8 (CH, C–2'), 67.4 (CH_2, 8'–$\underline{C}H_2$O), 70.3 (CH, C–8'), 96.6 (C, C–6'), 120.3 (CH, C–5''), 127.5 (CH, Ph), 129.5 (CH, Ph), 129.5 (CH, Ph), 133.8 (C, Ph), 135.6 (CH, Ph), 135.7 (CH, Ph), 150.3 (C, C–4''), 173.8 (C, C–1); MS *m/z* (ESI+, MS_2+ (620)) 620 ([M + H]$^+$, 52%), 602 (100), 542 ([M – Ph]$^+$, 54), 524 ([M – Ph – H$_2$O]$^+$, 61), 464 ([M – 2Ph – H]$^+$, 52), 346 (52), 328 (53), 318 (36), 129 ([$C_7H_{13}O_2$]$^+$, 5); HRMS (ESI+): [M + H]$^+$, found 620.3492. $C_{35}H_{50}N_3O_5Si$ requires 620.3514.

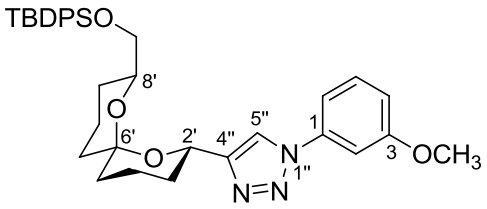


28f

1-(4-(4-((2S,6S,8S)-8-((*tert*-Butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl)phenyl)ethanone (28f)

The *title compound* **28f** (18.8 mg, 81%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (16.9 mg, 38.0 µmol), 1-(4-azidophenyl)ethanone **(27f)** (6.9 mg, 40.3 µmol) and a single crystal of CuI•P(OEt)$_3$ in anhydrous toluene (600 µL) using Procedure A. The reaction mixture was purified by

flash chromatography using EtOAc–*n*-hexane (0 %, 9% to 25% EtOAc/*n*-hexane). $[\alpha]_D^{21}$ -30.0 (c 0.99 in $CHCl_3$); R_f (25% EtOAc/*n*-hexanes) 0.27; IR (film) ν_{max}/cm^{-1} 2933 (C–H), 2857 (C–H), 1689 (C=O), 1605 (C=C), 1429 (C–H), 1264 (C–O), 1113 (C–O–C), 983, 703; δ_H (300 MHz, $CDCl_3$) 1.07 (9H, s, $OSiPh_2{}^tBu$), 1.22–1.36 (1H, m, 9"–H_A), 1.40–1.56 (2H, m, 10"–H_A and 11"–H_A), 1.59–1.75 (6H, m, 3"–H_A, 4"–H, 5"–H and 9"–H_B), 1.85–2.00 (1H, m, 10"–H_B), 2.04–2.17 (2H, m, 3"–H_B and 11"–H_B), 2.66 (3H, s, 2–H), 3.63 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 4.6, 8"–CH_AH_BO), 3.75 (1H, dd, $^2J_{AB}$ 10.3 and $^3J_{8'\text{-}CH_2O,8'}$ 6.1, 8"–CH_AH_BO), 3.82–3.88 (1H, m, 8"–H), 5.08 (1H, dd, $^3J_{2',3'ax}$ 11.5 and $^3J_{2',3'eq}$ 1.7, 2"–H), 7.31–7.42 (6H, m, Ph), 7.69–7.74 (4H, m, Ph), 7.89–7.93 (3H, m, 5'"–H, 3'–H and 5'–H), 8.13 (2H, d, $^3J_{2',3' \text{ and } 6',5'}$ 8.9, 2'–H and 6'–H); δ_C (75 MHz, $CDCl_3$) 18.5, 18.6 (2 x CH_2, C–4" and C–10"), 19.2 (C, $OSiPh_2{}^tBu$), 25.6 (CH_3, C–2), 26.8 (CH_3, $OSiPh_2{}^tBu$), 27.0 (CH_2, C–9"), 30.9 (CH_2, C–3"), 35.1, 35.2 (2 x CH_2, C–5" and C–11"), 64.7 (CH, C–2"), 67.4 (CH_2, 8"–CH_2O), 70.5 (CH, C–8"), 96.7 (C, C–6"), 118.5 (CH, C–5'"), 120.0 (2 x CH, C–3' and C–5'), 127.6 (CH, Ph), 129.5 (CH, Ph), 129.5 (CH, Ph), 130.0 (2 x CH C–2' and C–6'), 133.8 (C, Ph), 135.6 (CH, Ph), 135.7 (CH, Ph), 136.7 (C, C–1'), 140.3 (C, C–4'), 151.6 (C, C–4'"), 196.6 (C, C–1); MS *m/z* (ESI+, MS_2+ (610)) 610 ([M + H]$^+$, 47%), 592 (43), 564 (19), 532 ([M – Ph]$^+$, 52), 514 (63), 504 (48), 486 (34), 454 ([M – 2Ph – H]$^+$, 46), 369 ([M – OTBDPS]$^+$, 10), 336 (54), 318 (33), 308 (100); HRMS (ESI+): [M + H]$^+$, found 610.3100. $C_{36}H_{44}N_3O_4Si$ requires 610.3096.

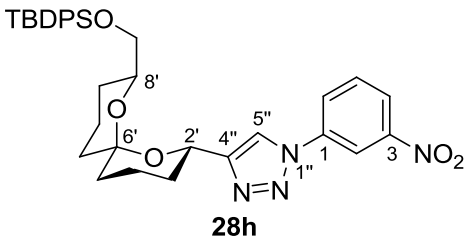


28g

4-((2S,6S,8S)-8-((*tert*-Butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1-(3-methoxyphenyl)-1H-1,2,3-triazole (28g)

The *title compound* **28g** (15.0 mg, 65%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (17.4 mg, 38.7 µmol), 1-azido-3-methoxybenzene **(27g)** (6.8 mg, 46.0 µmol) and a single crystal of CuI•P(OEt)$_3$ in anhydrous toluene (620 µL) using Procedure A. The reaction mixture was purified by flash chromatography using EtOAc–*n*-hexane (0%, 9% to 17% EtOAc/*n*-hexane). $[\alpha]_D^{23}$ -30.5 ° (c 1.27 in $CHCl_3$); R_f (17% EtOAc/*n*-hexanes) 0.30; IR (film) ν_{max}/cm^{-1} 2982 (C–H), 2971 (C–H), 1610 (C=C), 1226 (C–H), 1113 (C–O–C), 1067 (C–O), 1046 (C–O), 982, 702; δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, $OSiPh_2{}^tBu$), 1.22–1.34 (1H, m, 9'–H_A), 1.43–1.55 (2H, m, 10'–H_A and 11'–H_A), 1.57–1.75 (6H, m, 3'–H_A, 4'–H, 5'–H and 9'–H_B), 1.87–1.99 (1H, m, 10'–H_B), 2.10–2.17 (2H, m, 3'–H_B and 11'–H_B), 3.63 (1H, dd, $^2J_{AB}$ 10.4 and $^3J_{8'\text{-}CH_2O,8'}$ 4.6, 8'–CH_AH_BO), 3.75 (1H, dd, $^2J_{AB}$ 10.4 and $^3J_{8'\text{-}CH_2O,8'}$ 6.1, 8'–CH_AH_BO), 3.83–3.87 (1H, m, 8'–H), 3.89 (3H, s, PhOCH_3), 5.06 (1H, dd, $^3J_{2',3'ax}$ 11.6 and $^3J_{2',3'eq}$ 1.9, 2'–H), 6.97 (1H, dd, $^3J_{4,5}$ 8.3 and $^4J_{4,2}$ 2.5, 4–H), 7.27–7.29 (1H, m, 2–H), 7.32–7.43 (8H, m, 5–H, 6–H and Ph), 7.70–7.75 (4H, m, Ph), 7.85 (1H, s, 5"–H); δ_C (100 MHz, $CDCl_3$) 18.5, 18.7 (2 x CH_2, C–4' and C–10'), 19.3 (C, $OSiPh_2{}^tBu$), 26.8 (CH_3, $OSiPh_2{}^tBu$), 27.0 (CH_2, C–9'), 30.9 (CH_2, C–3'), 35.1, 35.2 (2 x CH_2, C–5' and C–11'), 55.6 (CH_3, PhOCH_3), 64.8 (CH, C–2'), 67.4 (CH_2, 8'–CH_2O), 70.4 (CH, C–8'), 96.7 (C, C–6'), 106.4 (CH, C–6), 112.4 (CH, C–2), 114.4 (CH, C–4), 118.9 (CH, C–5"), 127.6 (CH, Ph), 129.5 (CH, Ph), 129.5 (CH, Ph), 130.4 (CH, C–5), 133.8 (C, Ph), 135.6 (CH, Ph), 135.7 (CH, Ph), 138.3 (C, C–1), 151.0 (C, C–4"), 160.6 (C, C–3); MS *m/z* (ESI+, MS_2+ (598)) 598 ([M + H]$^+$, 16%), 580 (50), 552 (21), 520

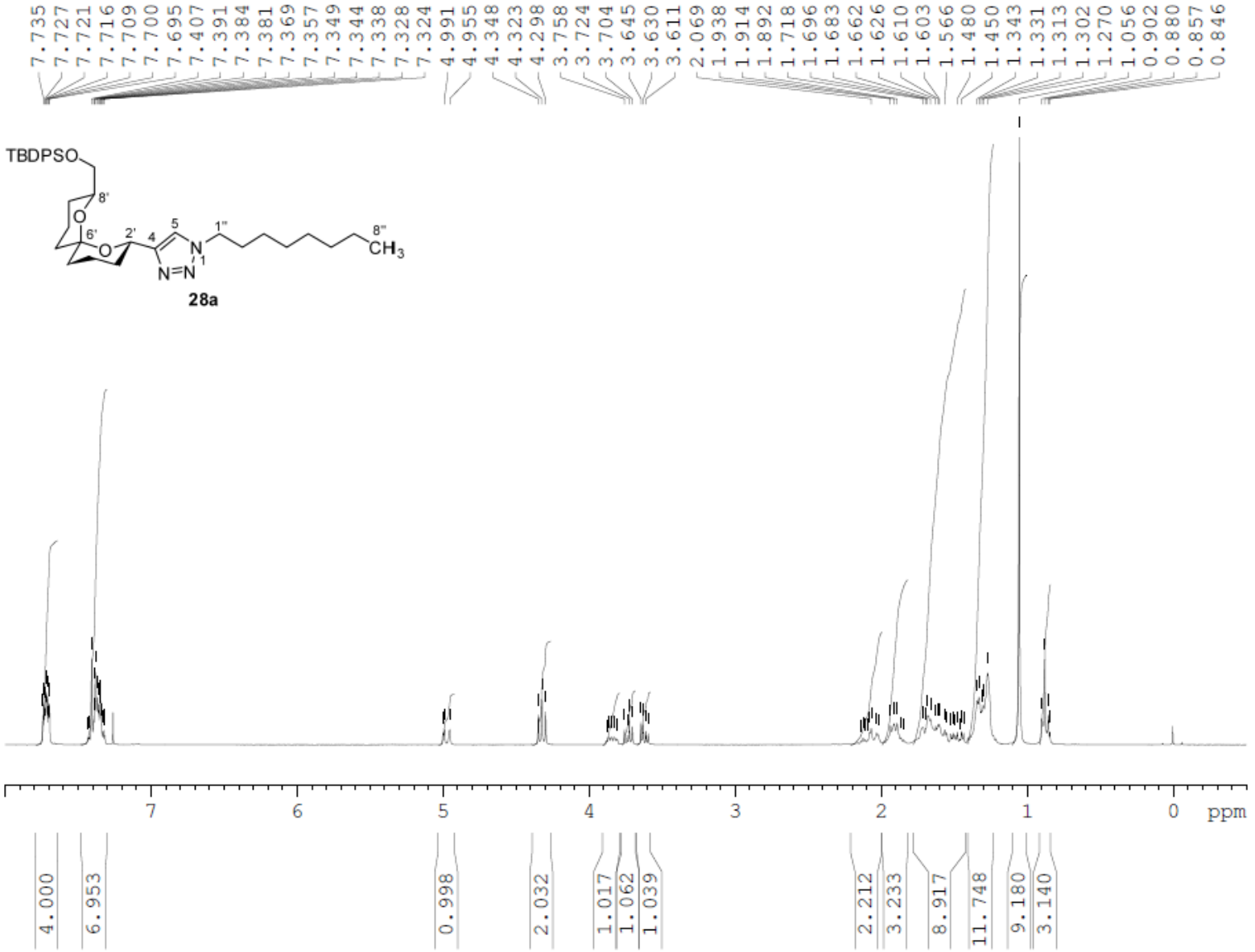
([M – Ph]$^+$, 31), 502 (70), 492 (35), 474 (30), 442 ([M – 2Ph – H]$^+$, 37), 324 (53), 306 (37), 296 (100); HRMS (ESI+): [M + H]$^+$, found 598.3082. $C_{35}H_{44}N_3O_4Si$ requires 598.3096.

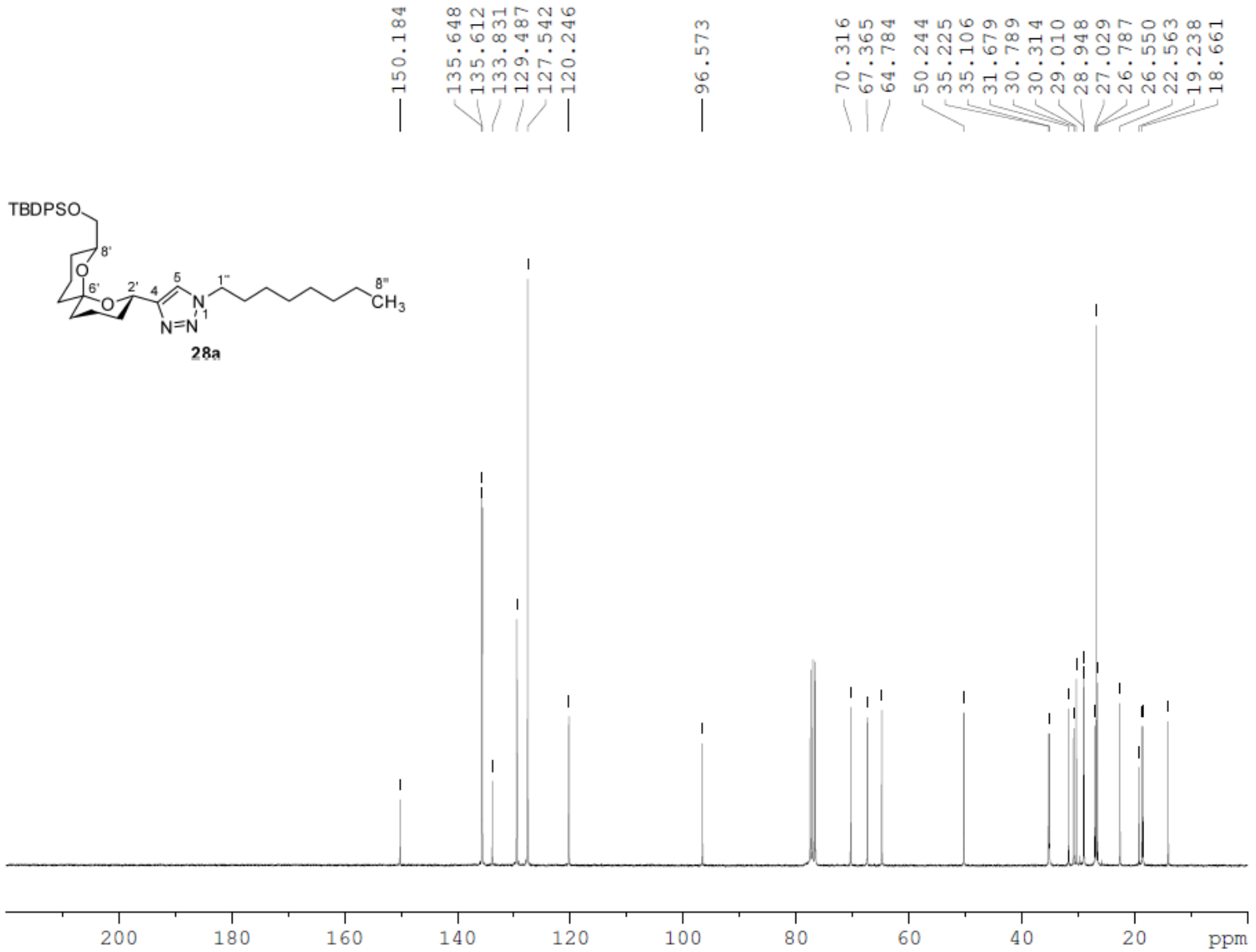


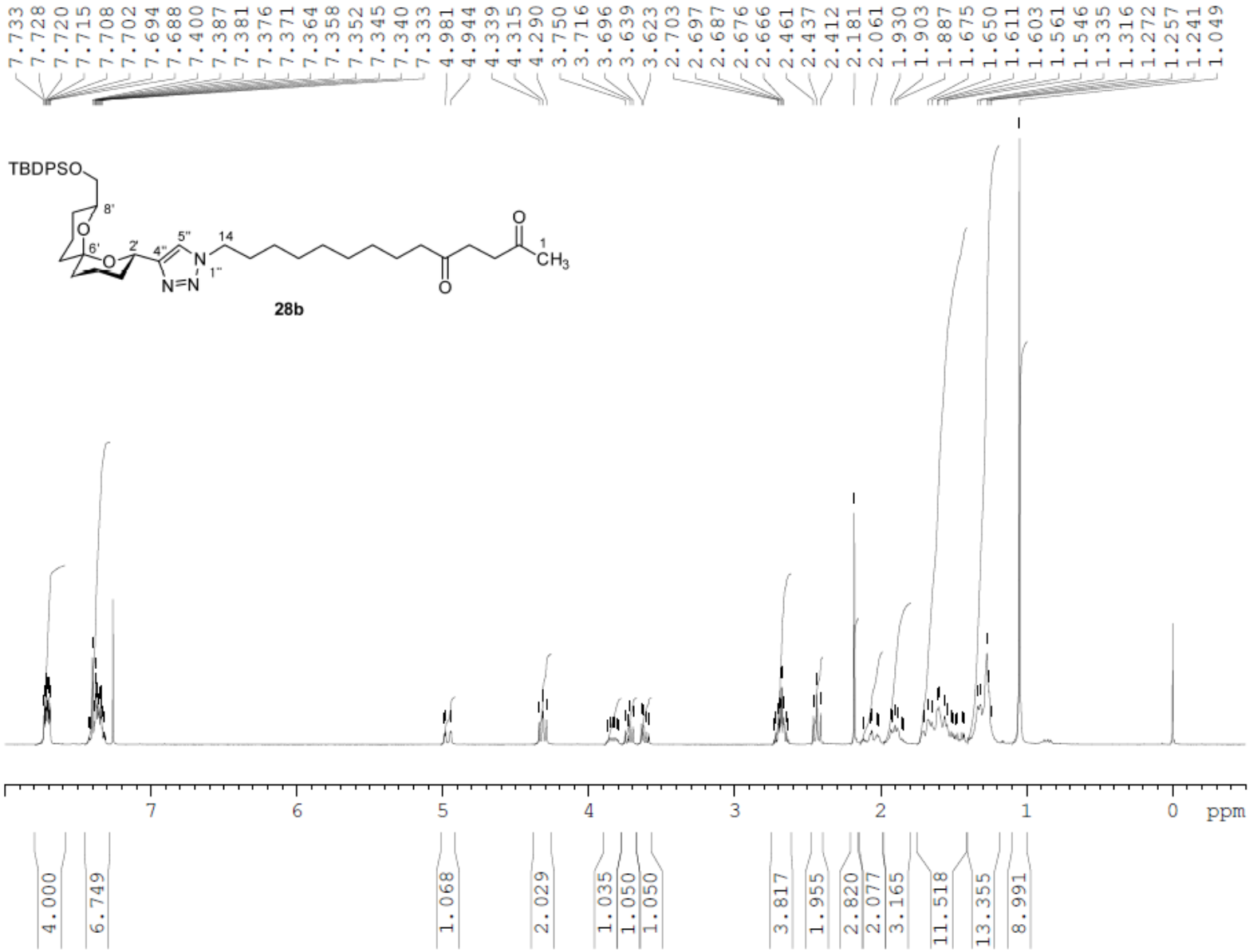
28h

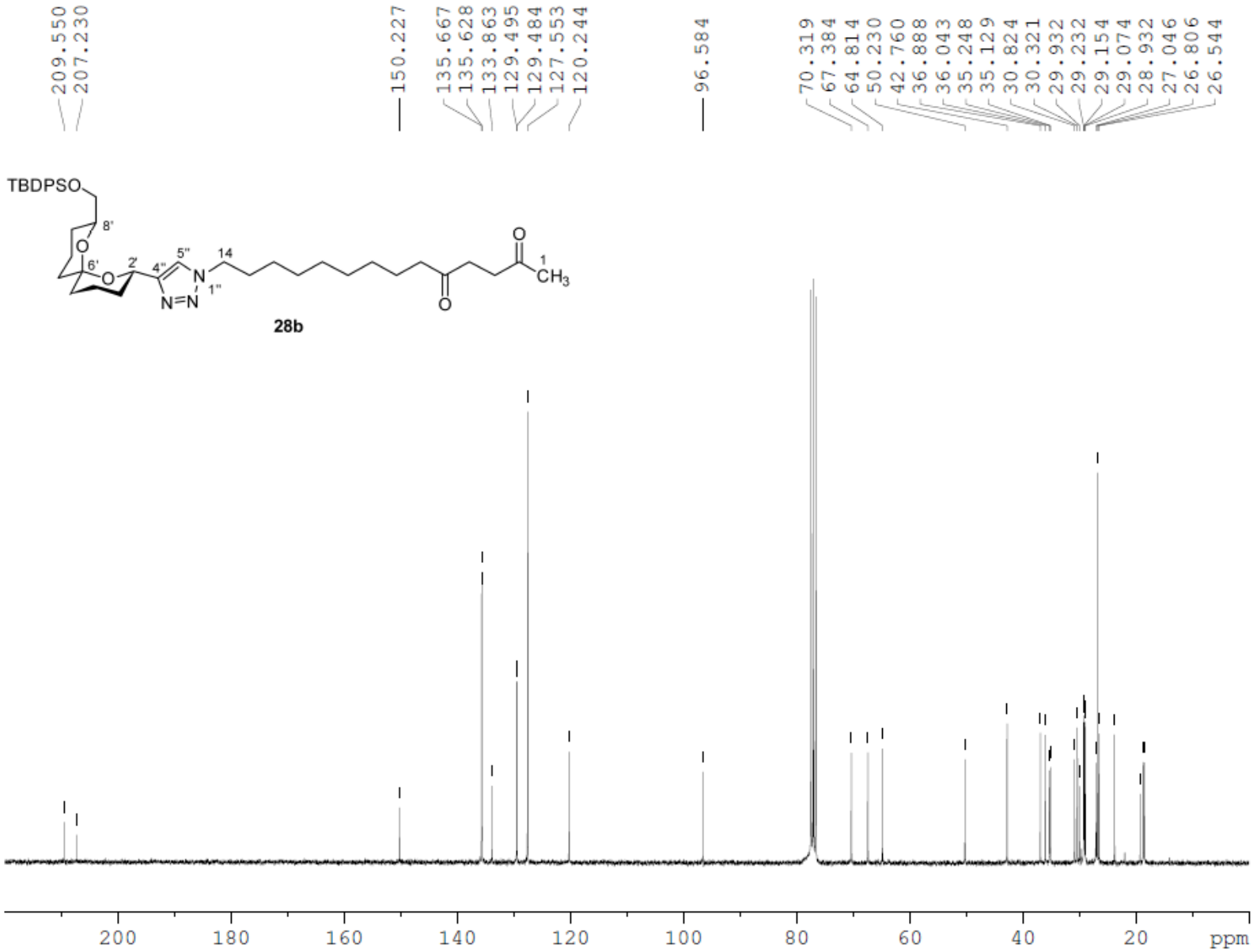
4-((2S,6S,8S)-8-((*tert*-Butyldiphenylsilyloxy)methyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1-(3-nitrophenyl)-1H-1,2,3-triazole (28h)

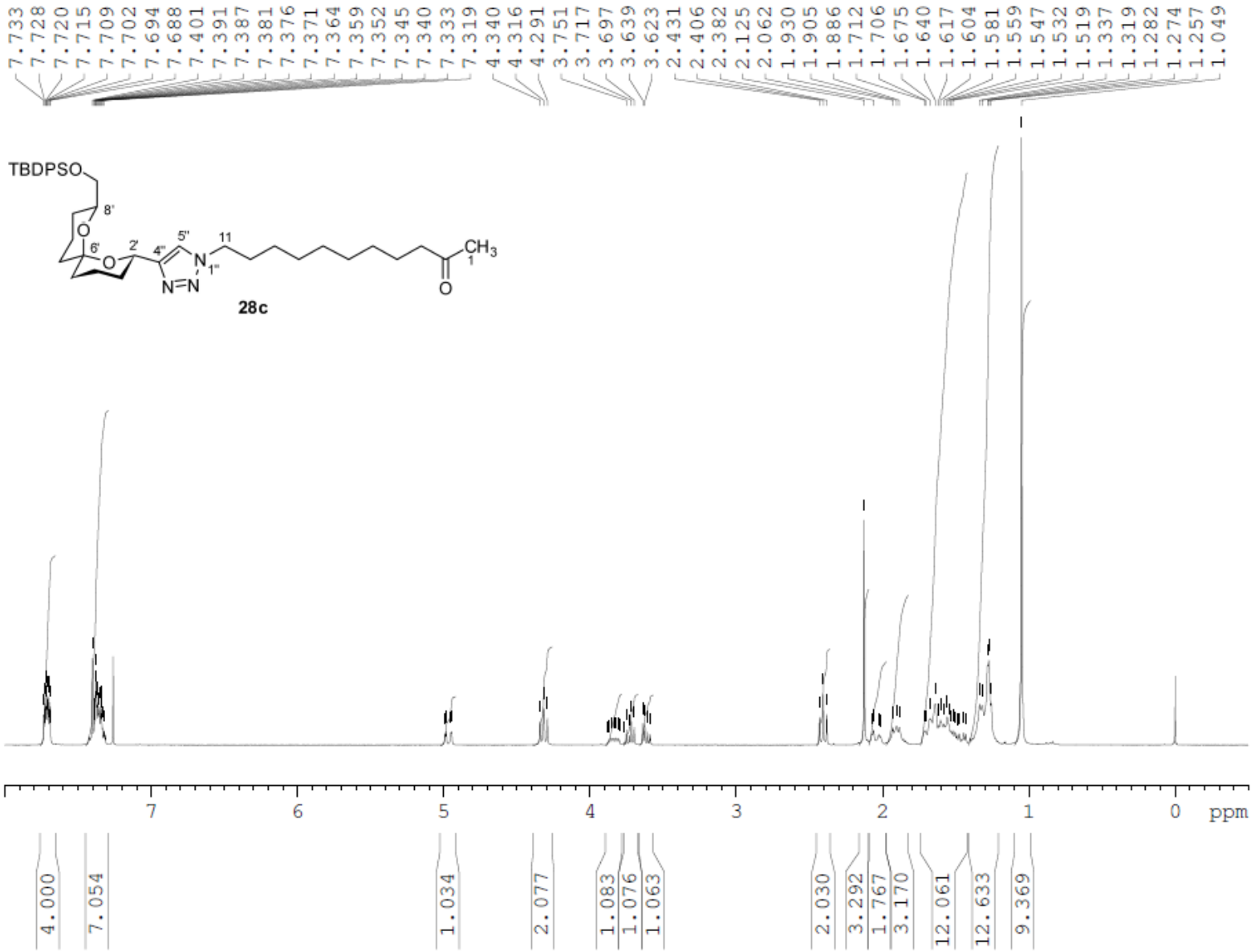
The *title compound* **28h** (18.4 mg, 75%) was prepared as a pale yellow oil from acetylenic spiroacetal **11** (17.9 mg, 39.9 µmol), 3-azido-1-nitrobenzene **(27h)** (7.3 mg, 45.0 µmol) and a single crystal of CuI•P(OEt)$_3$ in anhydrous toluene (640 µL) using Procedure A. The reaction mixture was purified by flash chromatography using EtOAc–*n*-hexane (0%, 9% to 17% EtOAc/*n*-hexane to 33% *n*-hexane/EtOAc). $[\alpha]_D^{24}$ -39.9 (c 0.99 in $CHCl_3$); R_f (33% *n*-hexane/EtOAc) 0.29; IR (film) ν_{max}/cm^{-1} 2931 (C–H), 2857 (C–H), 1537 (N=O), 1428 (C–H), 1350 (N=O), 1112 (C–O–C), 702; δ_H (400 MHz, $CDCl_3$) 1.07 (9H, s, OSiPh$_2$^{t}Bu), 1.22–1.35 (1H, m, 9'–H$_A$), 1.45–1.59 (2H, m, 10'–H$_A$ and 11'–H$_A$), 1.62–1.76 (6H, m, 3'–H$_A$, 4'–H, 5'–H and 9'–H$_B$), 1.89–1.99 (1H, m, 10'–H$_B$), 2.11–2.21 (2H, m, 3'–H$_B$ and 11'–H$_B$), 3.64 (1H, dd, $^2J_{AB}$ 10.4 and $^3J_{8'\text{-}CH_2O,8'}$ 4.5, 8'–CH$_A$H$_B$O), 3.75 (1H, dd, $^2J_{AB}$ 10.4 and $^3J_{8'\text{-}CH_2O,8'}$ 6.2, 8'–CH$_A$H$_B$O), 3.82–3.88 (1H, m, 8'–H), 5.10 (1H, dd, $^3J_{2',3'ax}$ 11.8 and $^3J_{2',3'eq}$ 1.8, 2'–H), 7.33–7.42 (6H, m, Ph), 7.70–7.77 (5H, m, 5–H and Ph), 7.97 (1H, s, 5"–H), 8.21–8.24 (1H, m, 6–H), 8.29–8.31 (1H, m, 4–H), 8.60 (1H, t, $^4J_{2,4\text{ and }2,6}$ 2.1, 2–H); δ_C (100 MHz, $CDCl_3$) 18.5, 18.6 (2 x CH_2, C–4' and C–10'), 19.3 (C, OSiPh$_2$^{t}Bu), 26.8 (CH_3, OSiPh$_2$^{t}Bu), 26.9 (CH_2, C–9'), 30.9 (CH_2, C–3'), 35.1, 35.2 (2 x CH_2, C–5' and C–11'), 64.7 (CH, C–2'), 67.3 (CH_2, 8'–CH_2O), 70.6 (CH, C–8'), 96.7 (C, C–6'), 115.1 (CH, C–2), 118.6 (CH, C–5"), 122.9 (CH, C–4), 126.0 (CH, C–6), 127.6 (CH, Ph), 129.5 (CH, Ph), 129.5 (CH, Ph), 130.9 (CH, C–5), 133.8 (C, Ph), 133.8 (C, Ph), 135.6 (CH, Ph), 135.6 (CH, Ph), 138.0 (C, C–1), 148.9 (C, C–3), 152.0 (C, C–4"); MS *m/z* (ESI+, MS_2+ (613)) 613 ([M + H]$^+$, 67%), 595 (10), 567 ([M – NO_2 + H]$^+$, 4), 535 ([M – Ph]$^+$, 100), 517 (29), 507 (57), 489 ([M – Ph – NO_2]$^+$, 12), 457 ([M – 2Ph – H]$^+$, 55), 357 ([M – OTBDPS]$^+$, 11), 311 ([M – OTBDPS – NO_2]$^+$, 64); HRMS (ESI+): [M + H]$^+$, found 613.2828. $C_{34}H_{41}N_4O_5Si$ requires 613.2841.

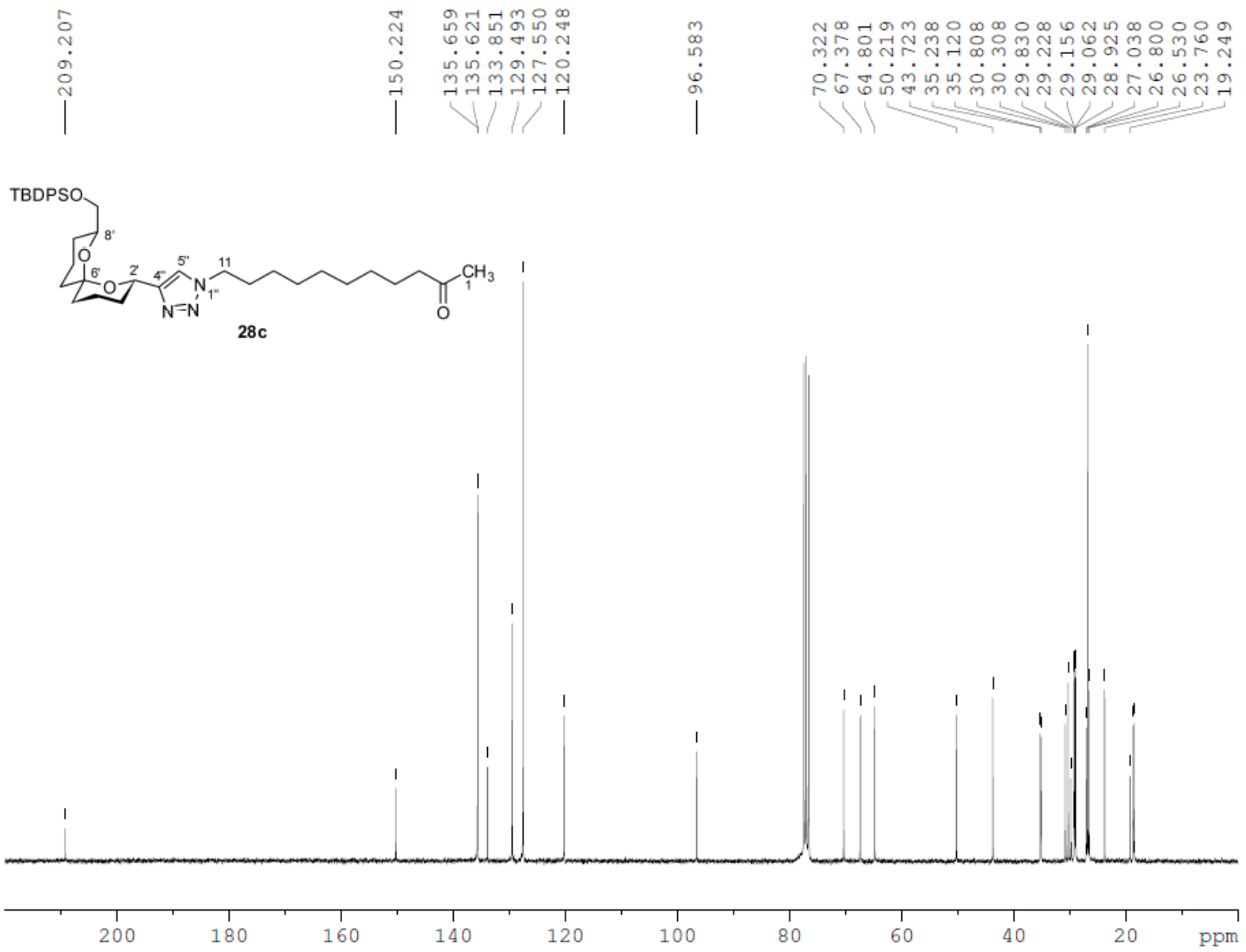


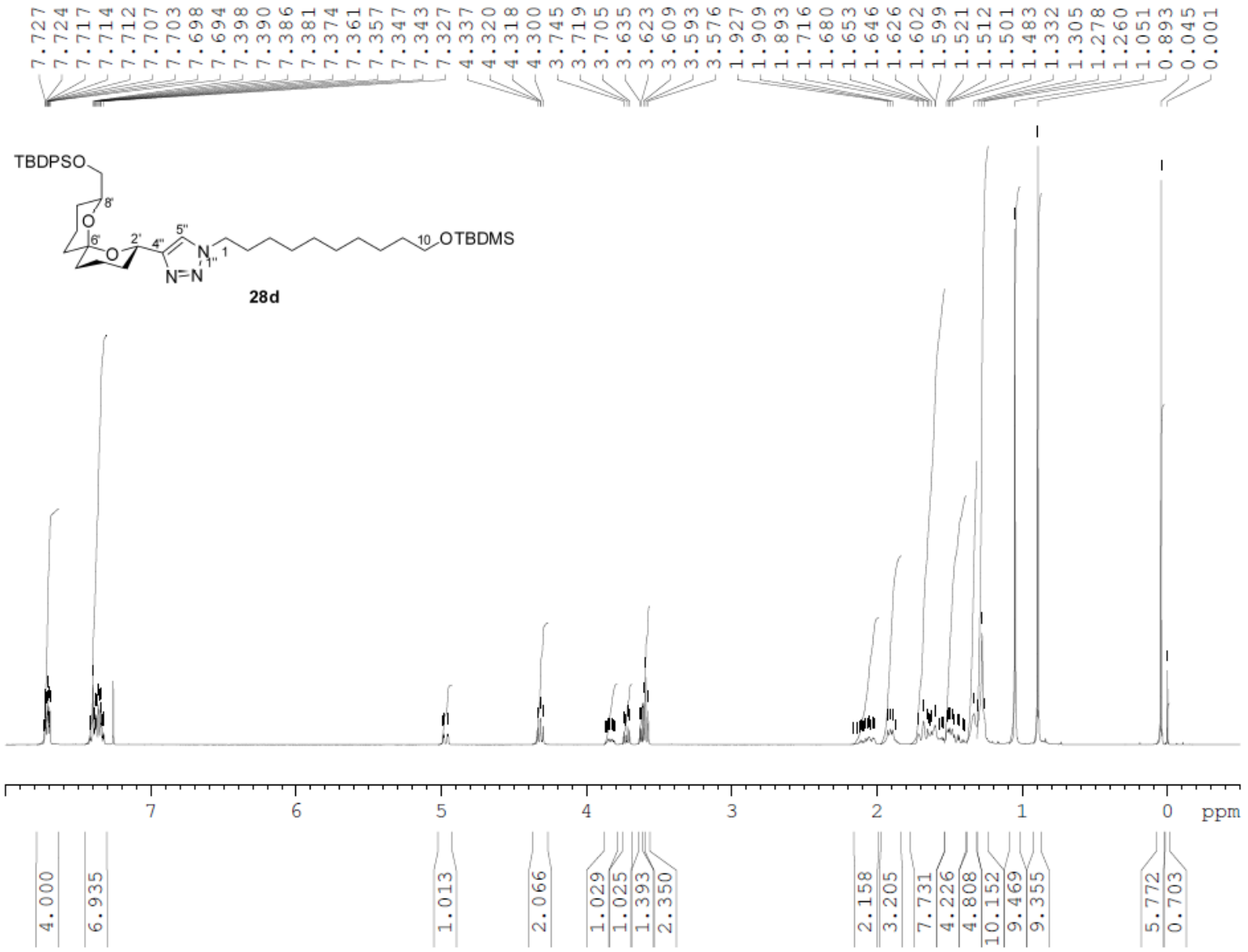


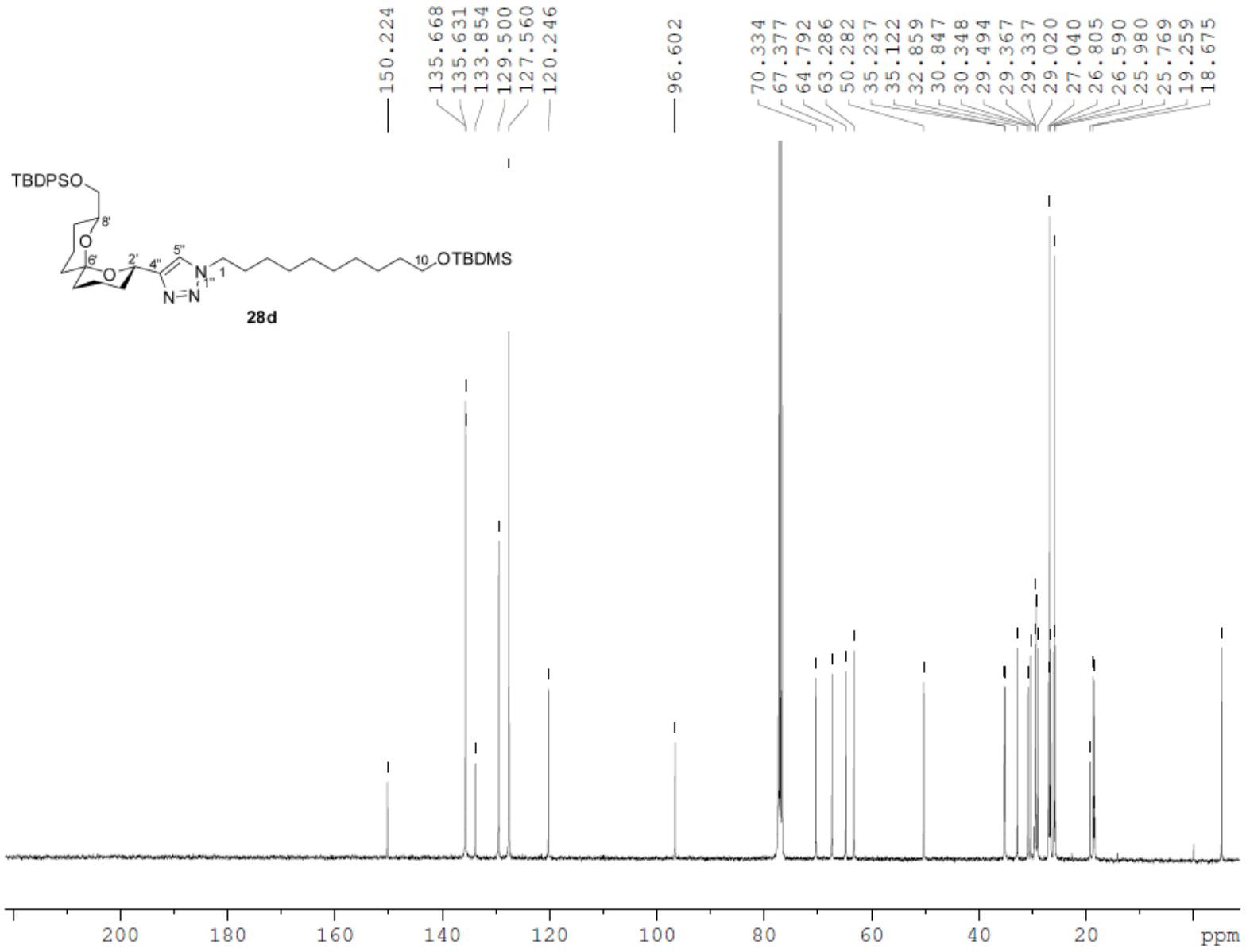


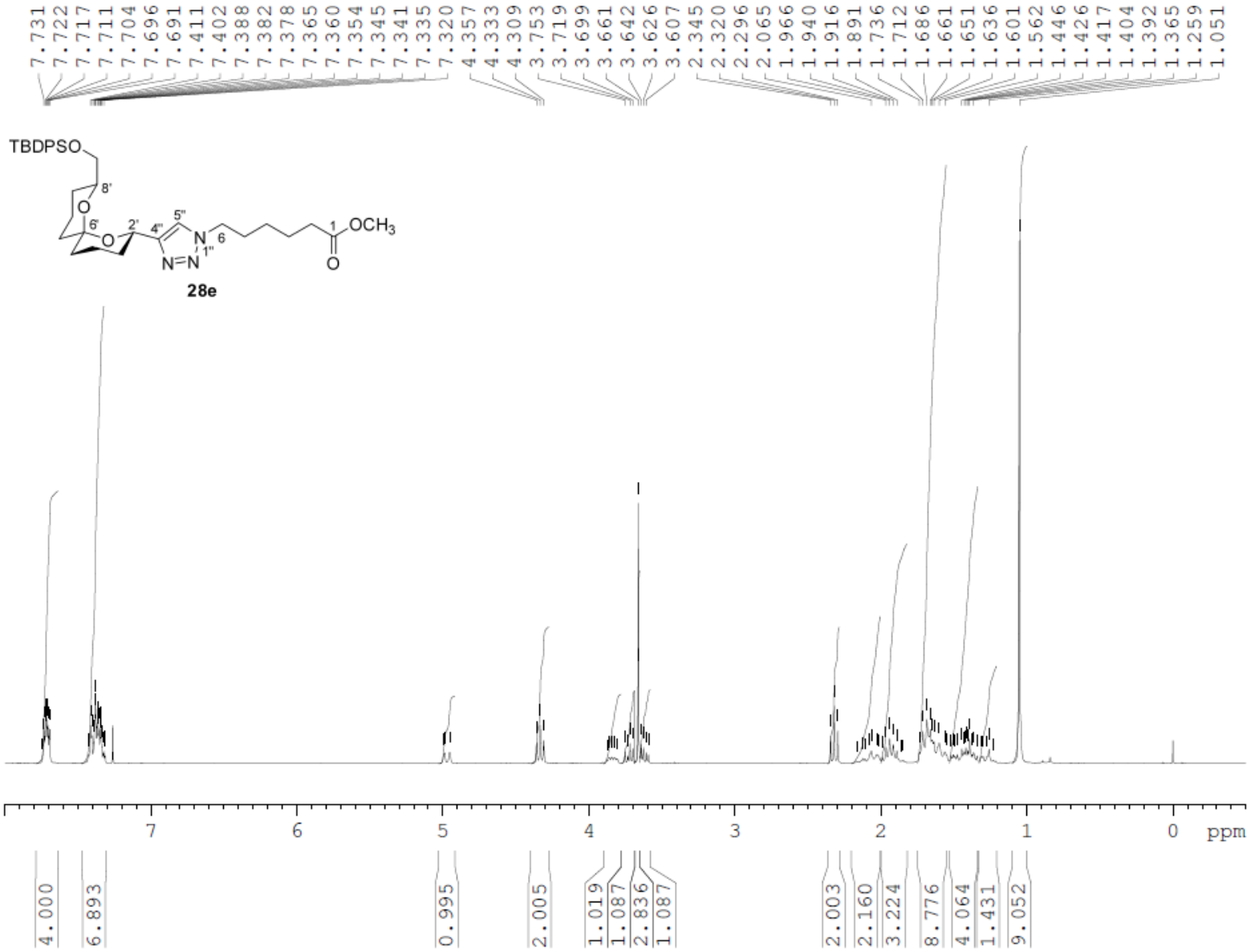


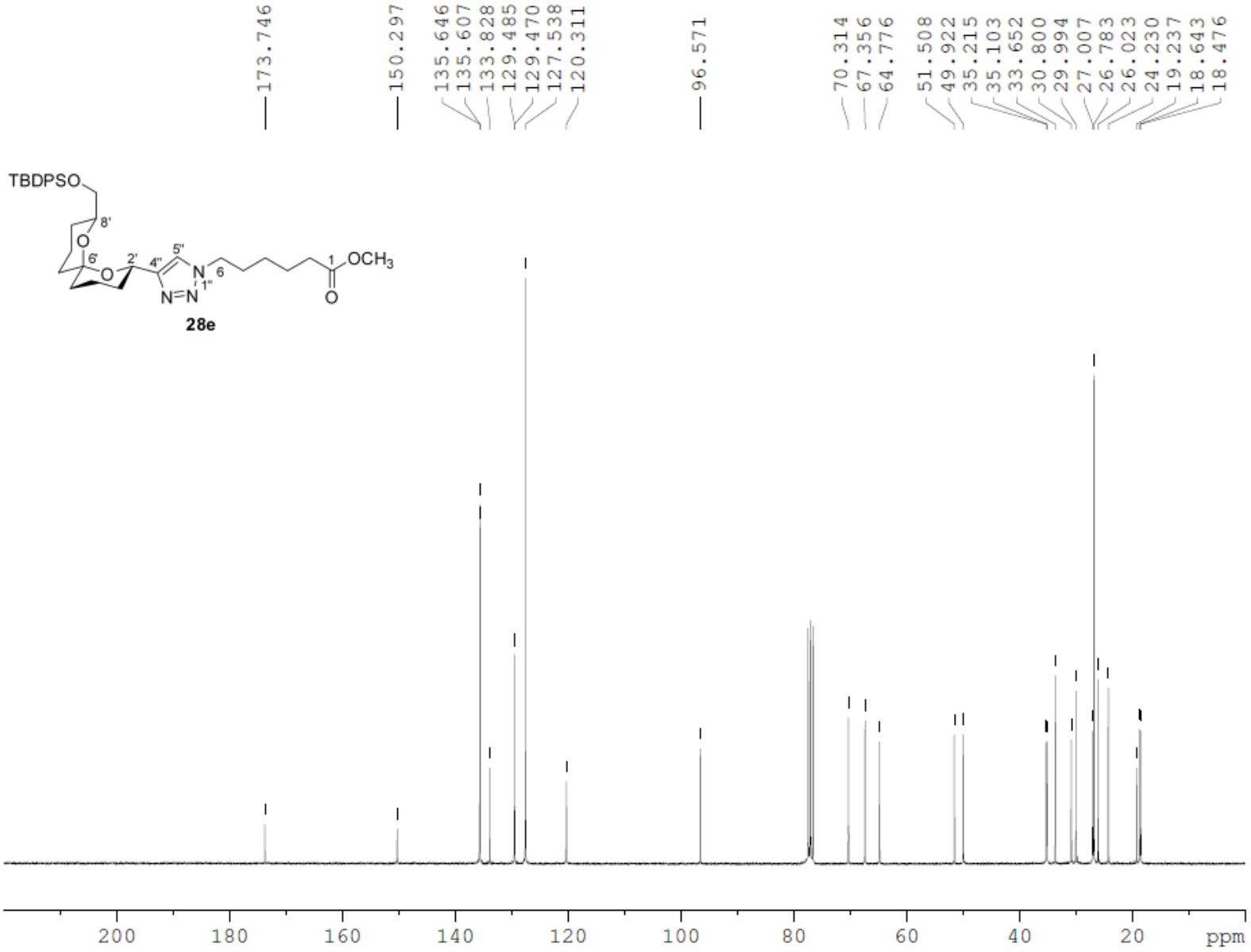


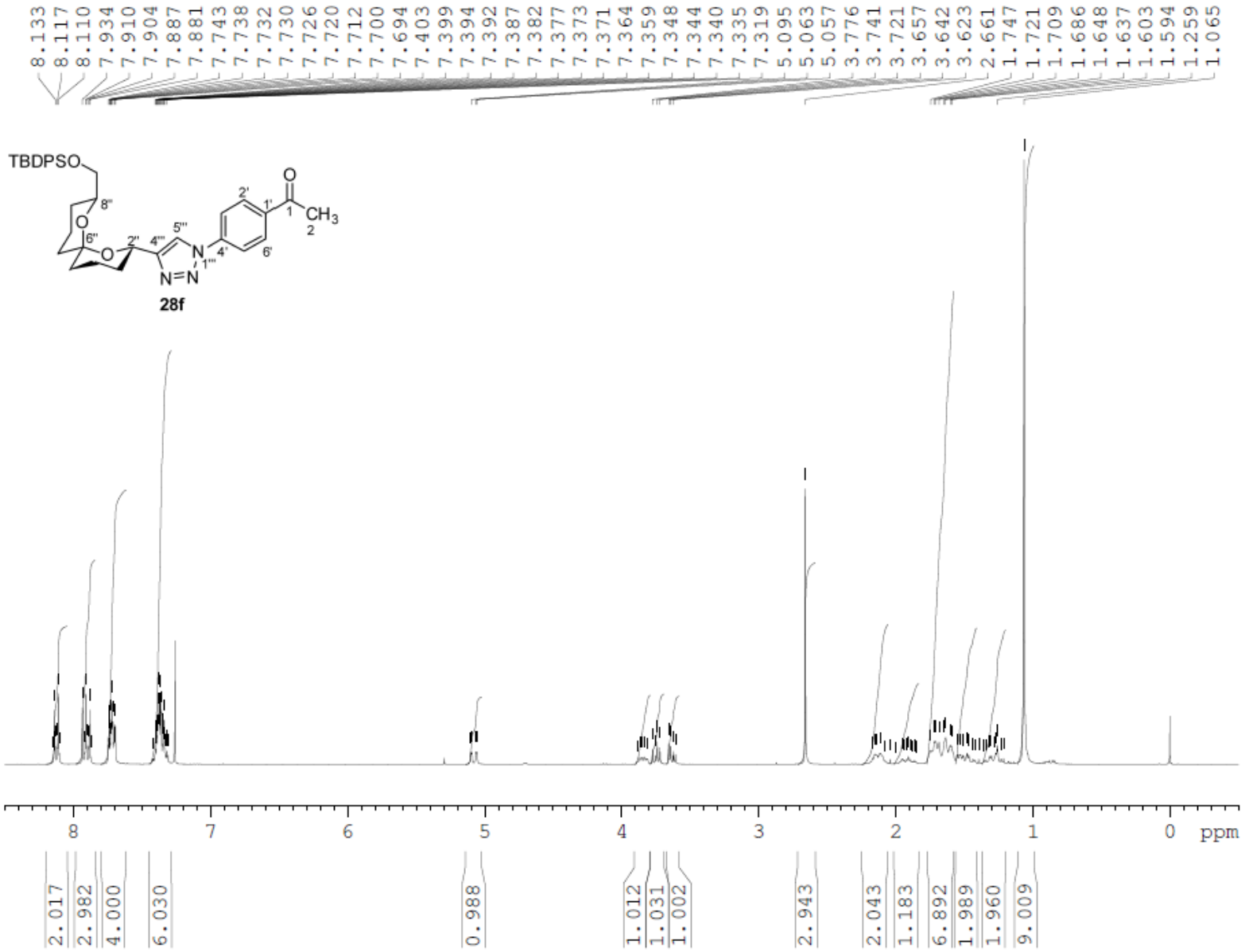


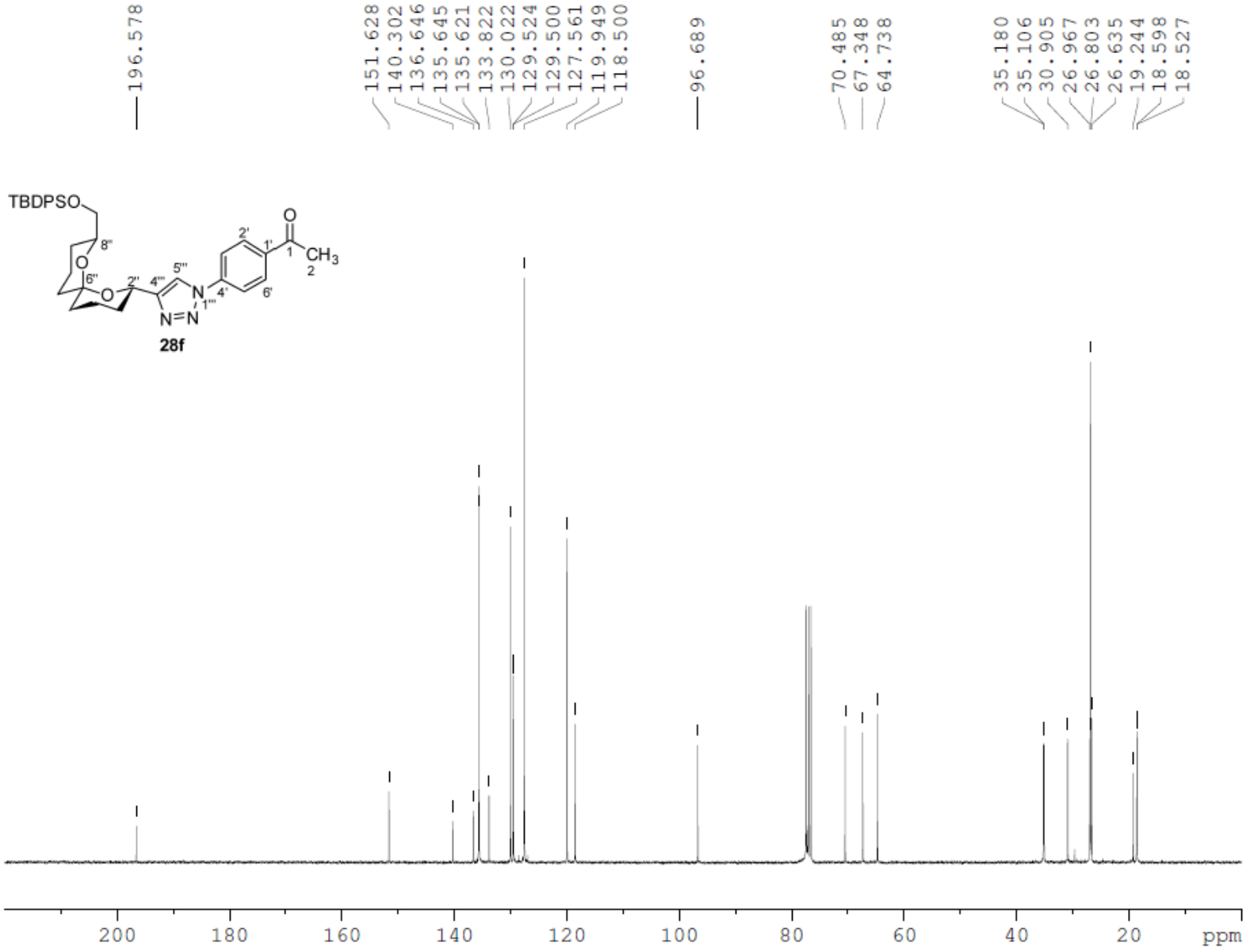


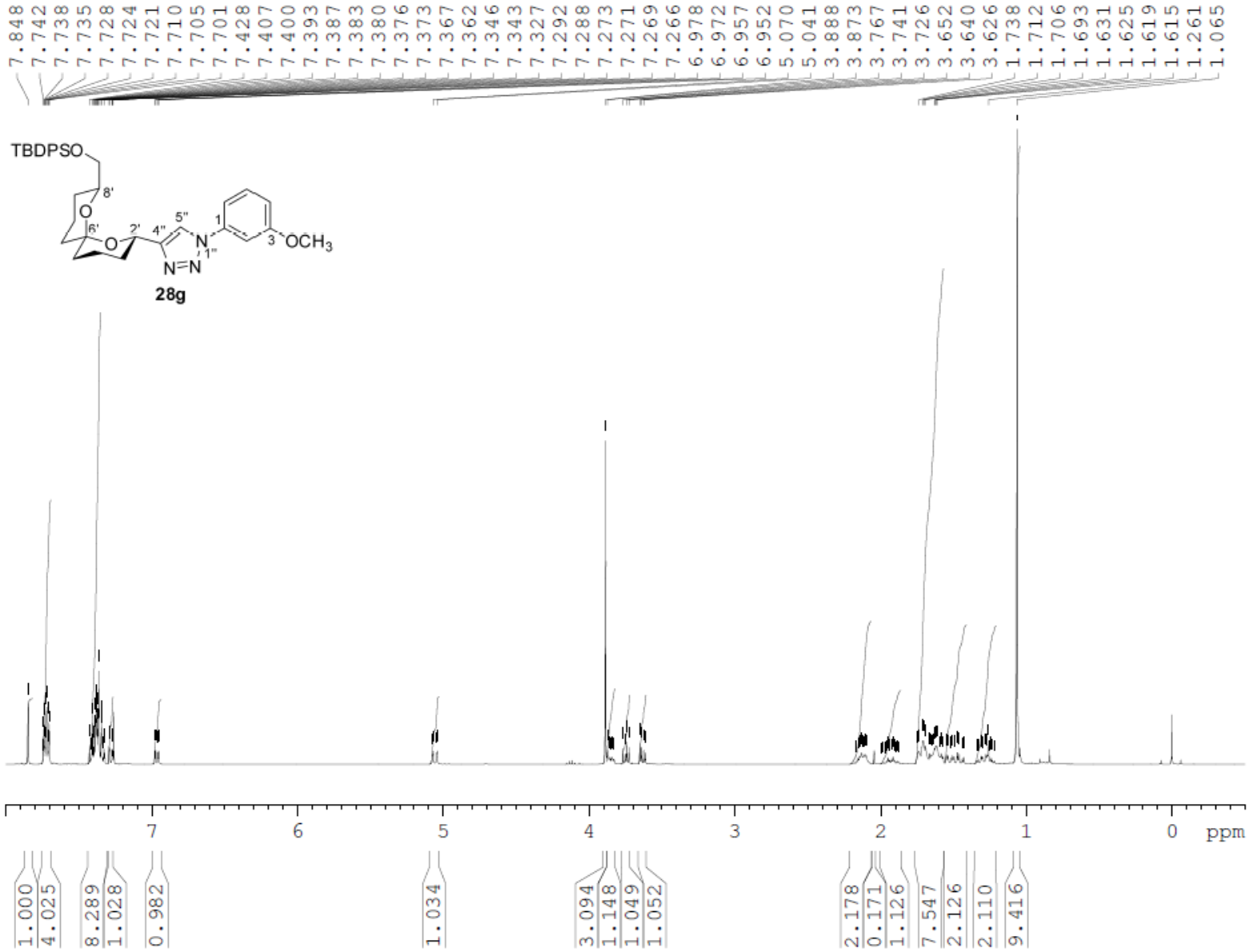


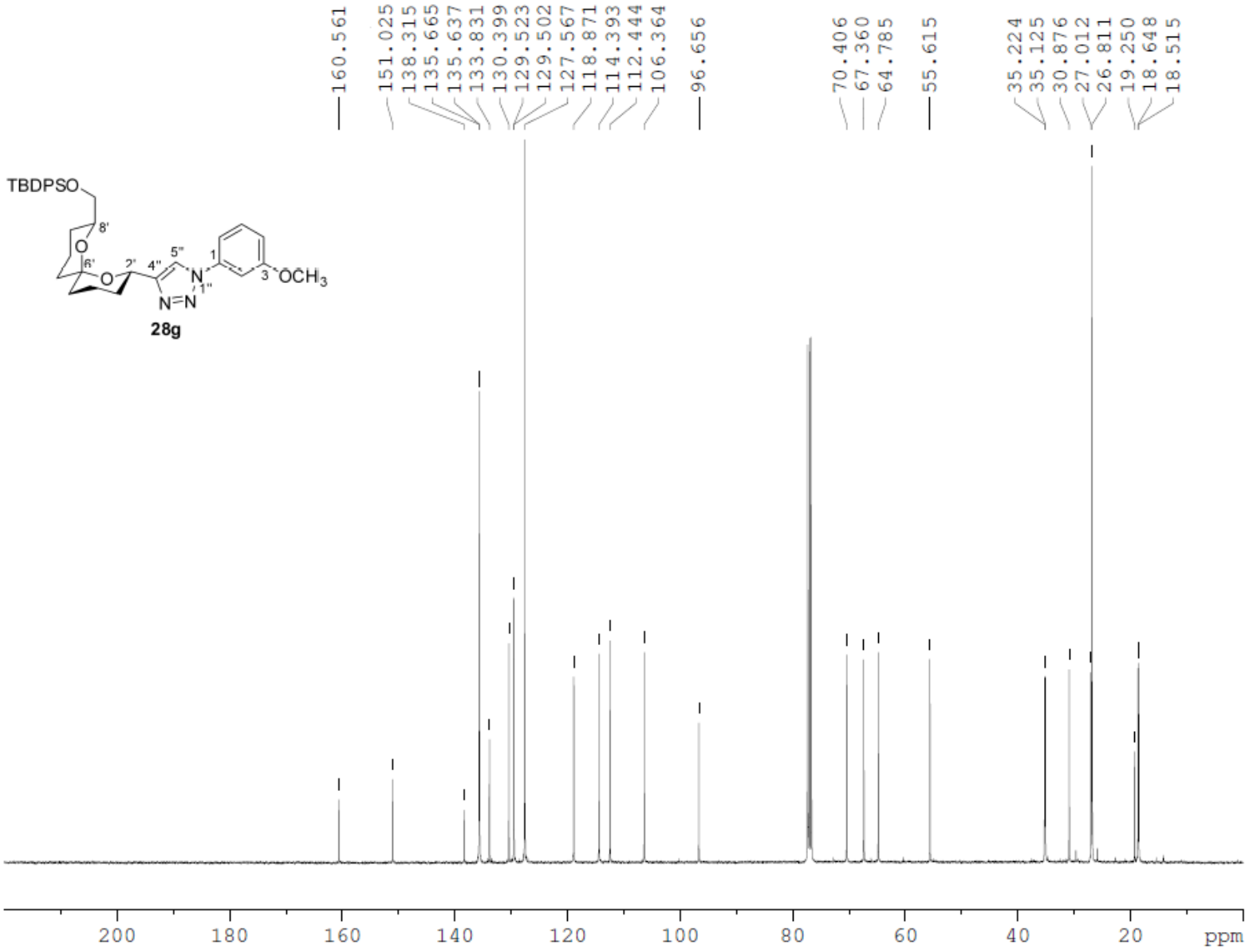


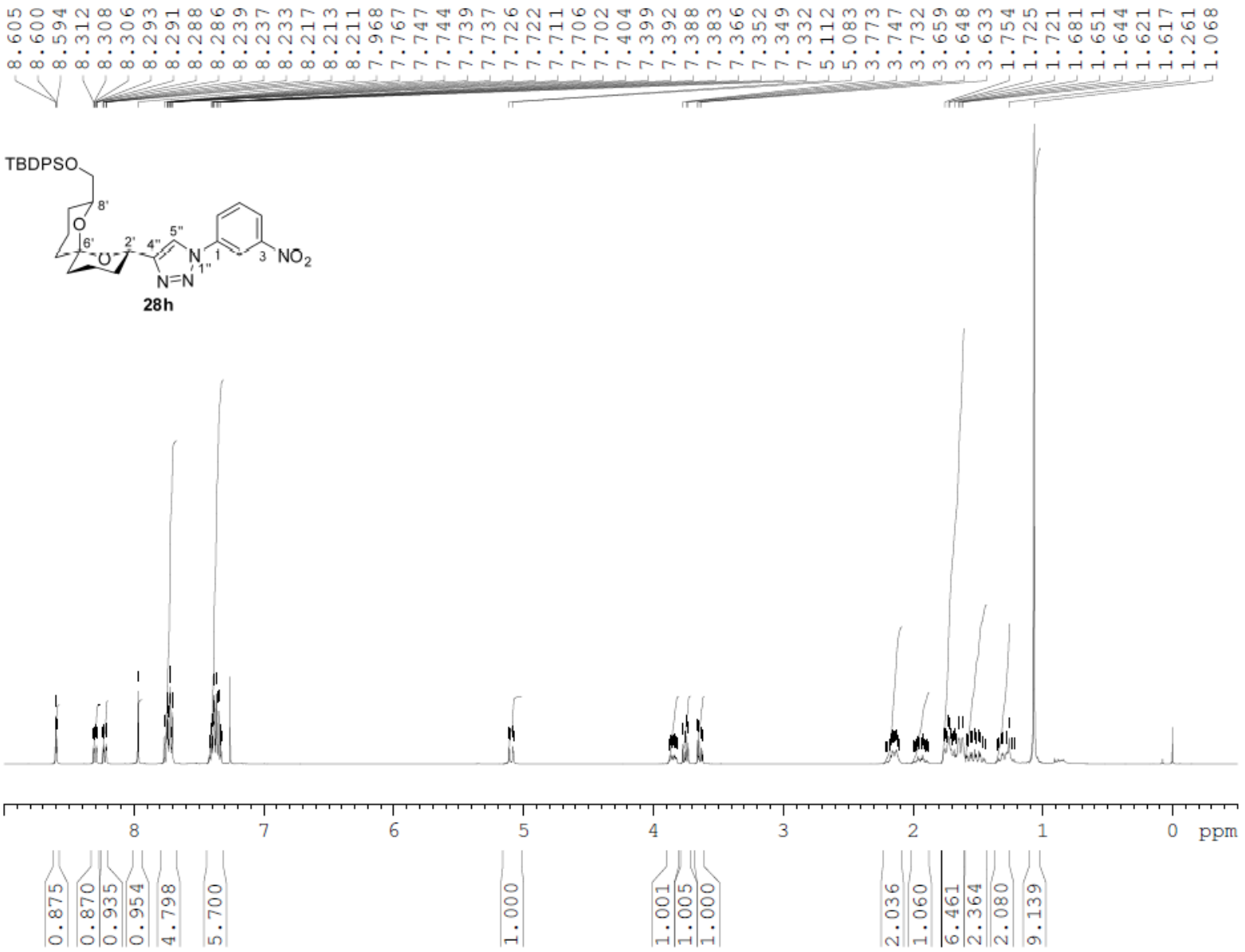


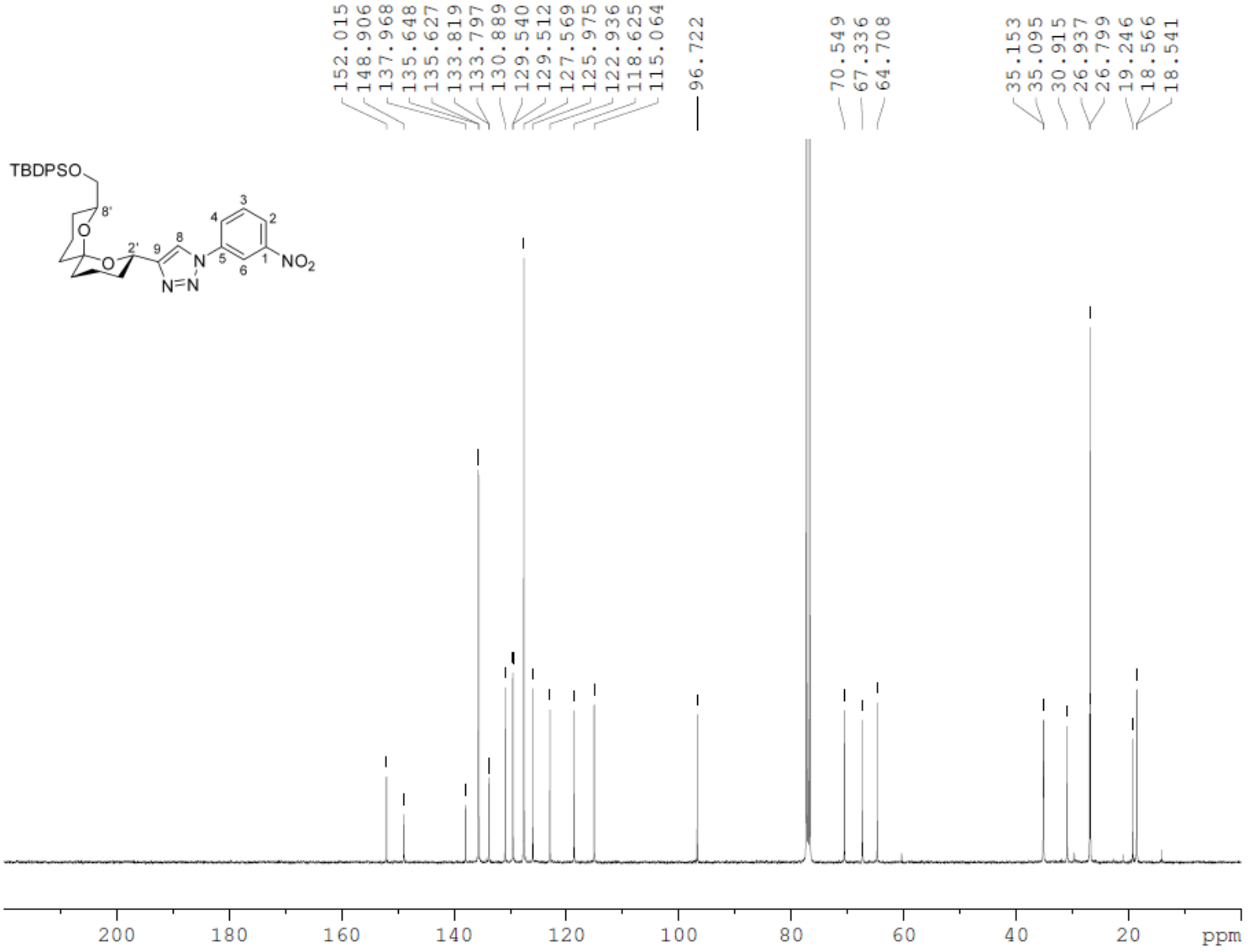








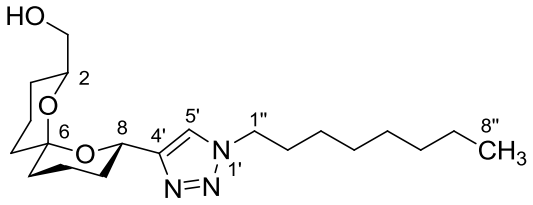




Experimental and Characterization data for hydroxymethyl spiroacetal-triazoles **10a-h**

General Procedure for Deprotection of Silyl Protected Spiroacetal-Triazole Analogues 28 (Procedure B)

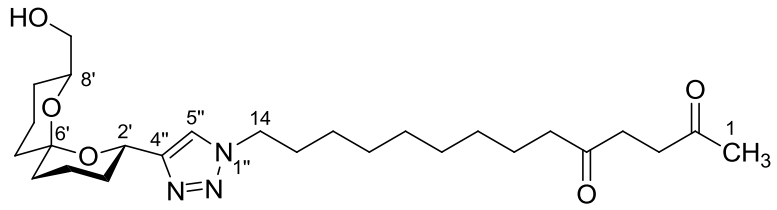
3HF•NEt_3 (2.4-2.8 µL per µmol of spiroacetal-triazole) was added to a solution of silyl-protected spiroacetal-triazole **28** (1.0 equiv.) in anhydrous THF (0.042-0.078 M) under an argon atmosphere. After stirring at RT for 24 h, a second portion of 3HF•NEt_3 (2.1-2.8 µL per µmol of spiroacetal-triazole) was added and the mixture was stirred at RT for an additional 24 h. Saturated $NaHCO_3$ was added dropwise (2 mL) and the aqueous phase extracted with EtOAc (4 x 5-10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (EtOAc–*n*-hexane) afforded the desired hydroxymethyl spiroacetal-triazole analogue **10**.



10a

((2S,6S,8S)-8-(1-Octyl-1H-1,2,3-triazol-4-yl)-1,7-dioxaspiro[5.5]undecan-2-yl)methanol (10a)

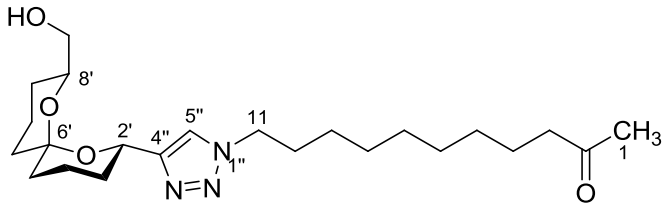
The *title compound* **10a** (11.7 mg, 85%) was prepared as a pale yellow oil from TBDPS-protected triazole **28a** (22.7 mg, 37.6 µmol) and 3HF•NEt_3 (100 µL, 2.66 µL/µmol, then 80 µL, 2.13 µL/µmol) in anhydrous THF (890 µL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (0%, 25% EtOAc/*n*-hexane to 25% *n*-hexane/EtOAc) $[\alpha]_D^{24}$ -0.8 (c 1.17 in $CHCl_3$); R_f (25% *n*-hexane/EtOAc) 0.29; IR (film) ν_{max}/cm^{-1} 3374 (br, O–H), 2930 (C–H), 2857 (C–H), 1438 (C–H), 1224, 1203, 1054 (C–O), 981 (C–O–C); δ_H (300 MHz, $CDCl_3$) 0.87 (3H, t, $^3J_{8",7"}$ 6.8, 8"–H), 1.26–1.36 (11H, m, 3"–H, 4"–H, 5"–H, 6"–H, 7"–H and 3–H_A), 1.38–1.61 (5H, m, 3–H_B, 4–H_A, 5–H_A, and 10–H), 1.64–1.71 (3H, m, 9–H_A and 11–H), 1.83–2.01 (4H, m, OH, 4–H_B and 2"–H), 2.04–2.08 (2H, m, 5–H_B and 9–H_B), 3.53 (1H, dd, $^2J_{AB}$ 11.3 and $^3J_{2\text{-}CH_2O,2}$ 6.5, 2–C$\underline{H}_A$$H_B$O), 3.64 (1H, br d, $^2J_{AB}$ 11.3, 2–C$H_A\underline{H}_B$O), 3.77–3.86 (1H, m, 2–H), 4.31 (2H, t, $^3J_{1",2"}$ 7.3, 1"–H), 4.89 (1H, dd, $^3J_{8,9ax}$ 11.5 and $^3J_{8,9eq}$ 2.0, 8–H), 7.45 (1H, s, 5'–H); δ_C (75 MHz, $CDCl_3$) 14.0 (CH_3, C–8"), 18.2, 18.7 (2 x CH_2, C–4 and C–10), 22.6 (CH_2, C–7"), 26.4 (CH_2, C–3), 26.5 (CH_2, C–3"), 28.9, 29.0 (2 x CH_2, C–4" and C–5"), 30.3 (CH_2, C–2"), 30.8 (CH_2, C–9), 31.7 (CH_2, C–6"), 35.0, 35.3 (2 x CH_2, C–5 and C–11), 50.3 (CH_2, C–1"), 65.0 (CH, C–8), 66.2 (CH_2, 2–$\underline{C}H_2$O), 69.9 (CH, C–2), 96.6 (C, C–6), 120.3 (CH, C–5'), 149.9 (C, C–4'); MS *m/z* (ESI+, MS_2+ (366)) 366 ($[M + H]^+$, 13%), 348 ($[M – OH]^+$, 100), 330 (17), 320 ($[M – OH – Et]^+$, 22), 302 (6), 192 (30); HRMS (ESI+): $[M + H]^+$, found 366.2746. $C_{20}H_{36}N_3O_3$ requires 366.2751.



10b

14-(4-((2S,6S,8S)-8-(Hydroxymethyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl) tetradecane-2,5-dione (10b)

The *title compound* **10b** (3.2 mg, 54%) was prepared as a pale yellow oil from TBDPS-protected triazole **28b** (9.0 mg, 12.6 μmol) and 3HF•NEt_3 (2 x 30 μL, 2.40 μL/μmol) in anhydrous THF (300 μL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (25% EtOAc/*n*-hexane to 100% EtOAc). $[\alpha]_D^{20}$ -22.4 (c 0.32 in $CHCl_3$); R_f (100% EtOAc) 0.25; IR (film) ν_{max}/cm^{-1} 3416 (br, O–H), 2931 (C–H), 2856 (C–H), 1711 (C=O), 1366, 1224, 1053 (C–O–C), 980; δ_H (400 MHz, $CDCl_3$) 1.25–1.35 (11H, m, 8–H, 9–H, 10–H, 11–H, 12–H and 9'–H_A), 1.37–1.73 (10H, m, 7–H, 3'–H_A, 4'–H, 5'–H, 9'–H_B, 10'–H_A and 11'–H_A), 1.86–1.97 (3H, m, 13–H and 10'–H_B), 1.98–2.10 (3H, m, OH, 3'–H_B, and 11'–H_B), 2.18 (3H, s, 1–H), 2.44 (2H, t, $^3J_{6,7}$ 7.4, 6–H), 2.65–2.72 (4H, m, 3–H and 4–H), 3.53 (1H, dd, $^2J_{AB}$ 11.0 and $^3J_{8'\text{-}CH_2O,8'}$ 6.5, 8'–C$\underline{H_A}H_B$O), 3.63–3.66 (1H, m, 8'–C$H_A\underline{H_B}$O), 3.79–3.85 (1H, m, 8'–H), 4.31 (2H, t, $^3J_{14,13}$ 7.4, 14–H), 4.90 (1H, dd, $^3J_{2',3'ax}$ 11.7 and $^3J_{2',3'eq}$ 2.0, 2'–H), 7.45 (1H, s, 5''–H); δ_C (75 MHz, $CDCl_3$) 18.2, 18.8 (2 x CH_2, C–4' and C–10'), 23.8 (CH_2, C–7), 26.4 (CH_2, C–9'), 26.5 (CH_2, C–12), 28.9, 29.1, 29.1 29.2 (4 x CH_2, C–8, C–9, C–10 and C–11), 29.9 (CH_3, C–1), 30.3 (CH_2, C–13), 30.8 (CH_2, C–3'), 35.0, 35.3 (2 x CH_2, C–5' and C–11'), 36.1 (CH_2, C–4), 36.9 (C–3), 42.8 (CH_2, C–6), 50.3 (CH_2, C–14), 65.1 (CH, C–2'), 66.2 (CH_2, 8–C$\underline{H_2}$O), 69.9 (CH, C–8'), 96.6 (C, C–6'), 120.3 (CH, C–5''), 150.0 (C, C–4''), 207.3 (C, C–2), 209.6 (C, C–5); MS *m/z* (ESI+, MS_2+ (500)) 500 ($[M + Na]^+$, 100%), 472 ($[M - Ac]^+$, 4), 442 (47), 342 (19), 316 (4), 288 (30); HRMS (ESI+): $[M + H]^+$, found 478.3283. $C_{26}H_{44}N_3O_5$ requires 478.3275.

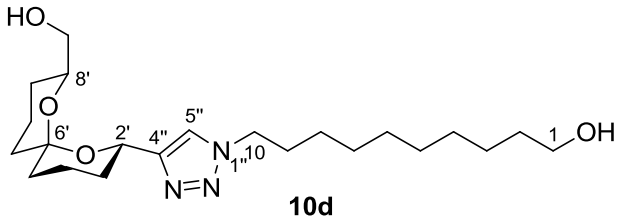


10c

11-(4-((2S,6S,8S)-8-(Hydroxymethyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl)undecan-2-one (10c)

The *title compound* **10c** (3.7 mg, 52%) was prepared as a pale yellow oil from TBDPS-protected triazole **28c** (11.2 mg, 17.0 μmol) and 3HF•NEt_3 (2 x 40 μL, 2.37 μL/μmol) in anhydrous THF (400 μL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (33% EtOAc/*n*-hexane to 100% EtOAc). $[\alpha]_D^{20}$ -7.5 (c 0.41 in $CHCl_3$); R_f (100% EtOAc) 0.33; IR (film) ν_{max}/cm^{-1} 3399 (br, O–H), 2931 (C–H), 2855 (C–H), 1713 (C=O), 1438 (C–H), 1366, 1223, 1053 (C–O–C), 981; δ_H (300 MHz, $CDCl_3$) 1.25–1.43 (12H, m, 5–H, 6–H, 7–H, 8–H, 9–H, 9'–H_A, and 11'–H_A), 1.45–1.73 (9H, m, 4–H, 3'–H_A, 4'–H, 5'–H, 9'–H_B, and 10'–H_A), 1.85–1.98 (3H, m, 10–H, and 10'–H_B), 1.99–2.10 (2H, m, 3'–H_B, and 11'–H_B), 2.13 (3H, s, 1–H),

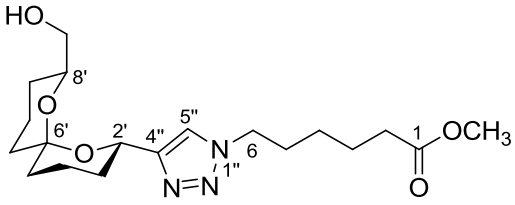
2.41 (2H, t, $^{3}J_{3,4}$ 7.4, 3–H), 3.53 (1H, dd, $^{2}J_{AB}$ 11.1 and $^{3}J_{8'\text{-}CH_2O,8'}$ 6.5, 8'–C$\underline{H}_A$H$_B$O), 3.63–3.67 (1H, m, 8'–CH$_A\underline{H}_B$O), 3.78–3.86 (1H, m, 8'–H), 4.31 (2H, t, $^{3}J_{11,10}$ 7.3, 11–H), 4.90 (1H, dd, $^{3}J_{2',3'ax}$ 11.6 and $^{3}J_{2',3'eq}$ 1.9, 2'–H), 7.45 (1H, s, 5''–H); δ_C (75 MHz, $CDCl_3$) 18.2, 18.8 (2 x CH_2, C–4' and C–10'), 23.8 (CH_2, C–4), 26.4 (CH_2, C–9'), 26.5 (CH_2, C–9), 28.9, 29.1, 29.1 29.2 (4 x CH_2, C–5, C–6, C–7 and C–8), 29.9 (CH_3, C–1), 30.3 (CH_2, C–10), 30.8 (CH_2, C–3'), 35.0, 35.3 (2 x CH_2, C–5' and C–11'), 43.7 (CH_2, C–3), 50.3 (CH_2, C–11), 65.1 (CH, C–2'), 66.2 (CH_2, 8–$\underline{C}H_2$O), 69.9 (CH, C–8'), 96.6 (C, C–6'), 120.3 (CH, C–5''), 150.0 (C, C–4''), 209.2 (C, C–2); MS *m/z* (ESI+, MS_2+ (422)) 422 ($[M + H]^+$, 6%), 404 ($[M – OH]^+$, 100), 394 (5), 386 (21), 376 (24); HRMS (ESI+): $[M + H]^+$, found 422.3012. $C_{23}H_{40}N_3O_4$ requires 422.3013.



10d

10-(4-((2S,6S,8S)-8-(Hydroxymethyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl) decan-1-ol (10d)

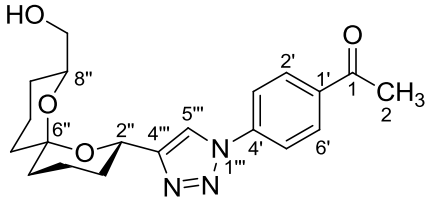
The *title compound* **10d** (5.6 mg, 63%) was prepared as a pale yellow oil from TBDPS-protected triazole **28d** (16.7 mg, 21.9 μmol) and 3HF•NEt_3 (2 x 60 μL, 2.75 μL/μmol) in anhydrous THF (520 μL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (0%, 17% EtOAc/*n*-hexane to 100% EtOAc). $[\alpha]_D^{26}$ -10.7 (c 0.56 in $CHCl_3$); R_f (100% EtOAc) 0.17; IR (film) ν_{max}/cm^{-1} 3377 (O–H), 2927 (C–H), 2855 (C–H), 1456, 1055 (C–O–C), 980; δ_H (400 MHz $CDCl_3$) 1.25–1.37 (11H, m, 4–H, 5–H, 6–H, 7–H, 8–H, 9'–H$_A$), 1.41–1.63 (8H, m, 2–H, 3–H, 3'–H$_A$, 9'–H$_B$, 10'–H$_A$ and 11'–H$_A$), 1.65–1.72 (4H, m, 4'–H and 5'–H), 1.88–1.93 (3H, m, 9–H and 10'–H$_B$), 2.02–2.08 (2H, m, 3'–H$_B$ and 11'–H$_B$), 3.54 (1H, dd, $^{2}J_{AB}$ 11.4 and $^{3}J_{8'\text{-}CH_2O,8'}$ 6.6, 8'–C$\underline{H}_A$H$_B$O), 3.62–3.66 (3H, m, 1–H and 8'–CH$_A\underline{H}_B$O), 3.80–3.86 (1H, m, 8'–H), 4.32 (2H, t, $^{3}J_{10,9}$ 7.3, 10–H), 4.90 (1H, dd, $^{3}J_{2',3'ax}$ 11.8 and $^{3}J_{2',3'eq}$ 1.9, 2'–H), 7.46 (1H, s, 5''–H); δ_C (75 MHz, $CDCl_3$) 18.2, 18.8 (2 x CH_2, C–4' and C–10'), 25.6 (CH_2, C–3), 26.4 (CH_2, C–8), 26.4 (CH_2, C–9'), 28.8 (CH_2, C–7), 29.1, 29.2, 29.3 (3 x CH_2, C–4, C–5 and C–6), 30.2 (CH_2, C–9), 30.7 (CH_2, C–3') 32.7 (CH_2, C–2), 35.0, 35.3 (2 x CH_2, C–5' and C–11'), 50.3 (CH_2, C–10), 62.9 (CH_2, C–1), 65.0 (CH, C–2'), 66.2 (CH_2, 8'–$\underline{C}H_2$O), 70.0 (CH, C–8'), 96.7 (C, C–6'), 120.4 (CH, C–5''), 149.9 (C, C–4''); MS *m/z* (ESI+, MS_2+ (410)) 410 ($[M + H]^+$, 7%), 392 ($[M – OH]^+$, 100), 374 (21), 364 (16), 346 (4), 252 (2), 236 (11); HRMS (ESI+): $[M + H]^+$, found 410.2999. $C_{22}H_{40}N_3O_4$ requires 410.3013.



10e

Methyl 6-(4-((2S,6S,8S)-8-(hydroxymethyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl)hexanoate (10e)

The *title compound* **10e** (3.2 mg, 38%) was prepared as a pale yellow oil from TBDPS-protected triazole **28e** (13.6 mg, 21.9 µmol) and 3HF•NEt_3 (60 µL, 2.74 µL/µmol, then 50 µL, 2.28 µL/µmol) in anhydrous THF (520 µL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (0%, 25% EtOAc/*n*-hexane to 100% EtOAc). $[\alpha]_D^{24}$ -10.8 (c 0.42 in $CHCl_3$); R_f (100% EtOAc) 0.24; IR (film) ν_{max}/cm^{-1} 2936 (C–H), 2872 (C–H), 1730 (C=O), 1543, 1436 (C–H), 1224 (C(=O)-O); δ_H (300 MHz, $CDCl_3$) 1.31–1.62 (7H, m, 4–H, 5'–H, 9'–H and 11'–H_A), 1.63–1.73 (6H, m, 3–H, 3'–H_A, 4'–H and 10'–H_A), 1.86–2.01 (4H, m, OH, 5–H and 10'–H_B), 2.02–2.17 (2H, m, 3'–H_B and 11'–H_B), 2.32 (2H, t, $^3J_{2,3}$ 7.4, 2–H), 3.53 (1H, dd, $^2J_{AB}$ 11.3 and $^3J_{8'\text{-}CH_2O,8'}$ 6.5, 8'–C$\underline{H}_A$$H_B$O), 3.63–3.67 (4H, m, O$\underline{CH_3}$ and 8'–$CH_A\underline{H_B}$O), 3.77–3.85 (1H, m, 8'–H), 4.33 (2H, t, $^3J_{6,5}$ 7.2, 6–H), 4.90 (1H, d, $^3J_{2',3'ax}$ 11.2, 2'–H), 7.46 (1H, s, 5"–H); δ_C (100 MHz, $CDCl_3$) 18.2, 18.7 (2 x CH_2, C–4' and C–10'), 24.2 (CH_2, C–3), 26.0 (CH_2, C–4), 26.4 (CH_2, C–9'), 30.0 (CH_2, C–5), 30.8 (CH_2, C–3'), 33.7 (CH_2, C–2), 35.0, 35.3 (2 x CH_2, C–5' and C–11'), 50.0 (CH_2, C–6), 51.5 (CH_3, O$\underline{C}H_3$), 65.0 (CH, C–2'), 66.2 (CH_2, 8'–$\underline{C}H_2$O), 69.9 (CH, C–8'), 96.7 (C, C–6'), 120.4 (CH, C–5"), 150.1 (C, C–4"), 173.8 (C, C–1); MS *m/z* (ESI+, MS_2+ (382)) 382 ($[M + H]^+$, 13%), 364 ($[M – OH]^+$, 100), 346 (17), 336 (17), 208 (21), 129 (5); HRMS (ESI+): $[M + H]^+$, found 382.2335. $C_{19}H_{32}N_3O_5$ requires 382.2336.

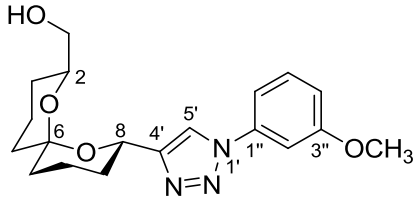


10f

1-(4-(4-((2S,6S,8S)-8-(Hydroxymethyl)-1,7-dioxaspiro[5.5]undecan-2-yl)-1H-1,2,3-triazol-1-yl) phenyl)ethanone (10f)

The *title compound* **10f** (6.8 mg, 59%) was prepared as a pale yellow oil from TBDPS-protected triazole **28f** (18.8 mg, 30.8 µmol) and 3HF•NEt_3 (2 x 80 µL, 2.60 µL/µmol) in anhydrous THF (730 µL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (0%, 25% EtOAc/*n*-hexane to 20% *n*-hexane/EtOAc). $[\alpha]_D^{23}$ -65.2 (c 0.68 in $CHCl_3$); R_f (20% *n*-hexanes/EtOAc) 0.27; IR (film) ν_{max}/cm^{-1} 3411 (O–H), 2939 (C–H), 2868 (C–H), 1684 (C=O), 1605 (C=C), 1265 (C–O), 980; δ_H (300 MHz, $CDCl_3$) 1.30–1.44 (1H, m, 9"–H_A), 1.47–1.58 (2H, m, 9"–H_B and 11"–H_A), 1.59–1.76 (6H, m, 3"–H_A, 4"–H, 5"–H and 10"–H_A), 1.87–2.07 (1H, m, 10"–H_B), 2.09–2.20 (2H, m, 3"–H_B and 11"–H_B), 2.66 (3H, s, 2–H), 3.53–3.58 (1H, m, 8"–C$\underline{H}_A$$H_B$O), 3.65–3.68 (1H, m, 8"–$CH_A\underline{H_B}$O), 3.80–3.88 (1H, m, 8"–H), 5.00 (1H, dd, $^3J_{2",3"ax}$ 11.5

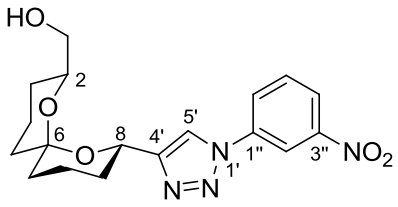
and $^{3}J_{2",3"eq}$ 1.8, 2"–H), 7.89 (2H, d, $^{3}J_{3',2' \text{ and } 5',6'}$ 8.9, 3'–H and 5'–H), 7.99 (1H, s, 5'"–H), 8.12 (2H, d, $^{3}J_{2',3' \text{ and } 6',5'}$ 8.9, 2'–H and 6'–H); δ_C (75 MHz, $CDCl_3$) 18.2, 18.7 (2 x CH_2, C–4" and C–10"), 26.4 (CH_2, C–9"), 26.7 (CH_3, C–2), 30.9 (CH_2, C–3"), 35.0, 35.3 (2 x CH_2, C–5" and C–11"), 65.0 (CH, C–2"), 66.2 (CH_2, 8"–$\underline{C}H_2O$), 70.1 (CH, C–8"), 96.8 (C, C–6"), 118.6 (CH, C–5'"), 120.0 (2 x CH, C–3' and C–5'), 130.0 (2 x CH, C–2' and C–6'), 136.7 (C, C–1'), 140.3 (C, C–4'), 151.4 (C, C–4'"), 196.6 (C, C–1); MS *m/z* (ESI+) 394 ($[M + Na]^+$, 100%), 372 ($[M + H]^+$, 31), 354 ($[M – OH]^+$, 12); HRMS (ESI+): $[M + H]^+$, found 372.1918. $C_{20}H_{26}N_3O_4$ requires 372.1918.



10g

((2S,6S,8S)-8-(1-(3-methoxyphenyl)-1H-1,2,3-triazol-4-yl)-1,7-dioxaspiro[5.5]undecan-2-yl) methanol (10g).

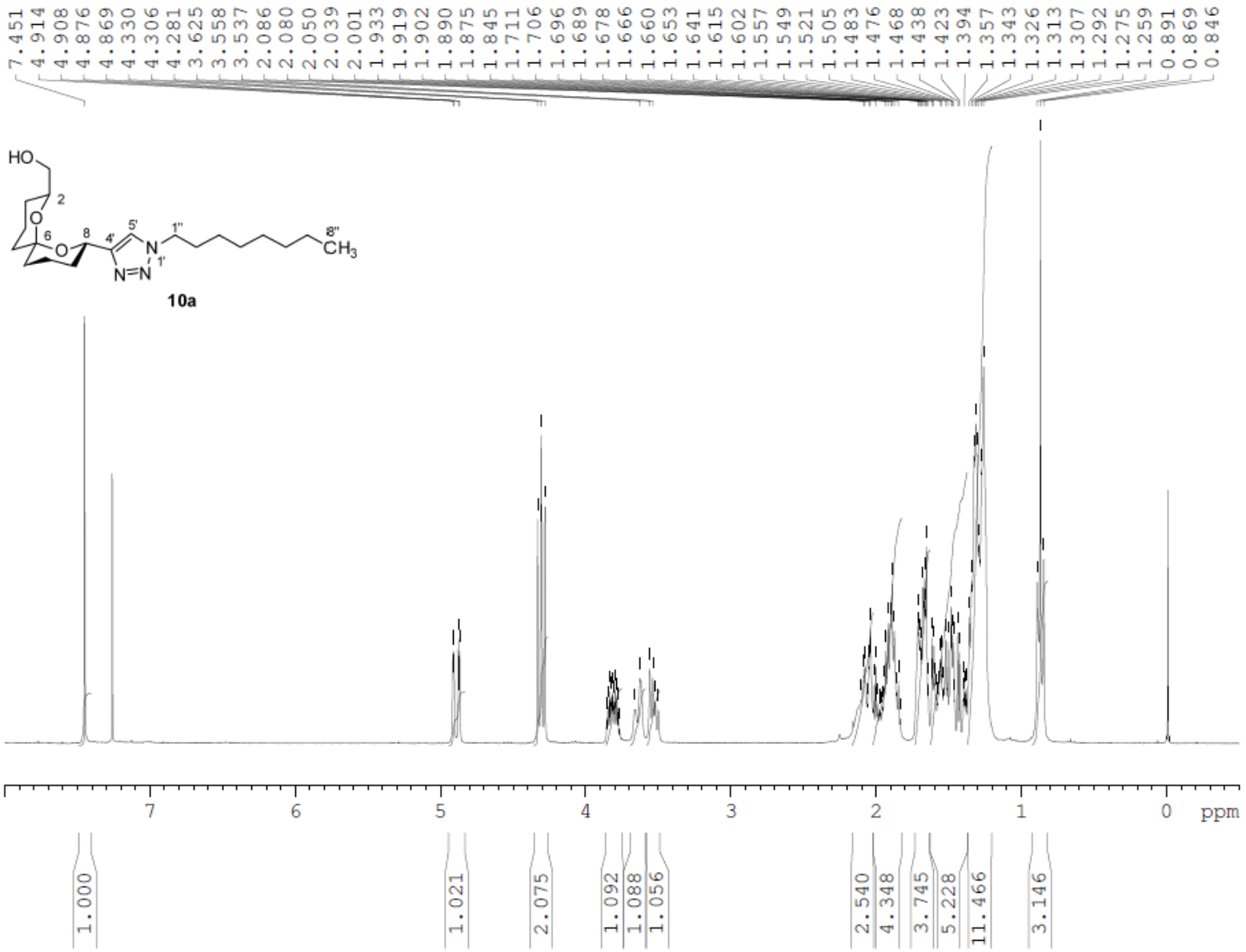
The *title compound* **10g** (8.9 mg, 99%) was prepared as a pale yellow oil from TBDPS-protected triazole **28g** (15.0 mg, 25.1 µmol) and 3HF•NEt_3 (2 x 70 µL, 2.79 µL/µmol) in anhydrous THF (590 µL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (0%, 17% EtOAc/*n*-hexane to 33% *n*-hexane/EtOAc). $[\alpha]_D^{27}$ -29.9 (c 0.89 in $CHCl_3$); R_f (33% *n*-hexanes/EtOAc) 0.29; IR (film) ν_{max}/cm^{-1} 3389 (O–H), 2938 (C–H), 2871 (C–H), 1610 (C=C), 1596 (C=C), 1498 (C=C), 1224 (C–O), 1043 (C–O–C), 977, 755, 686; δ_H (400 MHz, $CDCl_3$) 1.30–1.44 (1H, m, 3–H_A), 1.46–1.74 (8H, m, 3–H_B, 4–H_A, 5–H_A, 9–H_A, 10–H and 11–H), 1.88–2.03 (1H, m, 4–H_B), 2.07–2.12 (3H, m, OH, 5–H_B and 9–H_B), 3.55 (1H, dd, $^{2}J_{AB}$ 11.4 and $^{3}J_{2\text{-}CH_2O,2}$ 6.5, 2–C$\underline{H_A}H_B$O), 3.67 (1H, dd, $^{2}J_{AB}$ 11.4 and $^{3}J_{2\text{-}CH_2O,2}$ 2.9, 2–C$H_A\underline{H_B}$O), 3.82–3.87 (1H, m, 2–H), 3.88 (3H, s, PhOC$\underline{H_3}$), 4.98 (1H, dd, $^{3}J_{8,9ax}$ 11.5 and $^{3}J_{8,9eq}$ 1.9, 8–H), 6.94–6.97 (1H, m, 4"–H), 7.25–7.28 (1H, m, 6"–H), 7.34 (1H, t, $^{4}J_{2",4" \text{ and } 2",6"}$ 2.2, 2"–H), 7.40 (1H, t, $^{3}J_{5",4" \text{ and } 5",6"}$ 8.2, 5"–H), 7.90 (1H, s, 5'–H); δ_C (75 MHz, $CDCl_3$) 18.2, 18.7 (2 x CH_2, C–4 and C–10), 26.4 (CH_3, C–3), 30.8 (CH_2, C–9), 35.0, 35.3 (2 x CH_2, C–5 and C–11), 55.6 (CH_3, PhO$\underline{C}H_3$), 65.0 (CH, C–8), 66.2 (CH_2, 2–$\underline{C}H_2O$), 70.0 (CH, C–2), 96.7 (C, C–6), 106.4 (CH, C–2"), 112.5 (CH, C–6"), 114.5 (CH, C–4"), 119.0 (CH, C–5'), 130.4 (CH, C–5"), 138.4 (C, C–1"), 150.7 (C, C–4'), 160.6 (C, C–3"); MS *m/z* (ESI+, MS_2+ (360)) 360 ($[M + H]^+$, 1%), 342 ($[M – OH]^+$, 9), 314 (8); 256 (6), 204 (6), 186 ($[M + H – C_2HN_3PhOCH_3]^+$, 100), 173 (4); HRMS (ESI+): $[M + H]^+$, found 360.1909. $C_{19}H_{26}N_3O_4$ requires 360.1918.

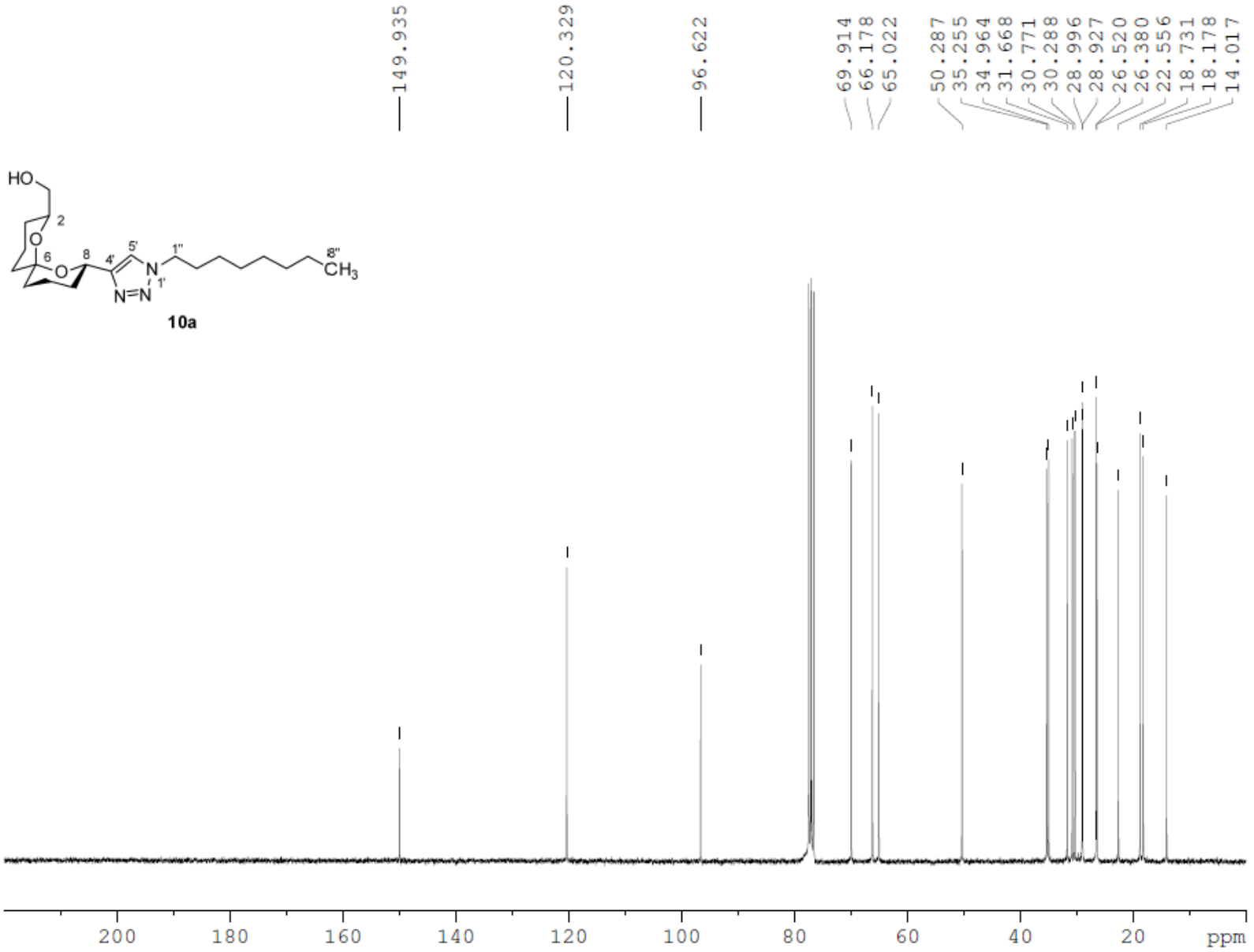


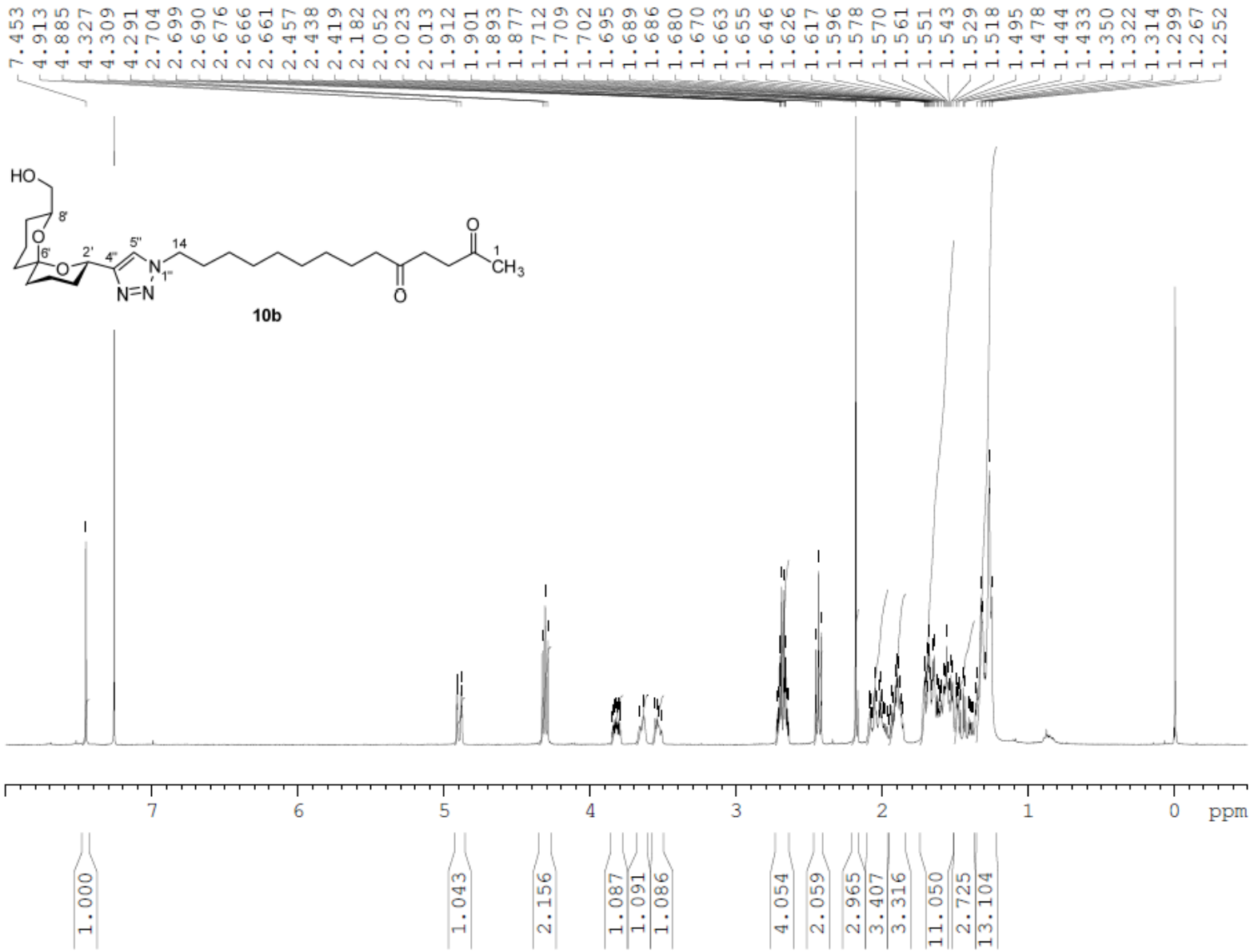
10h

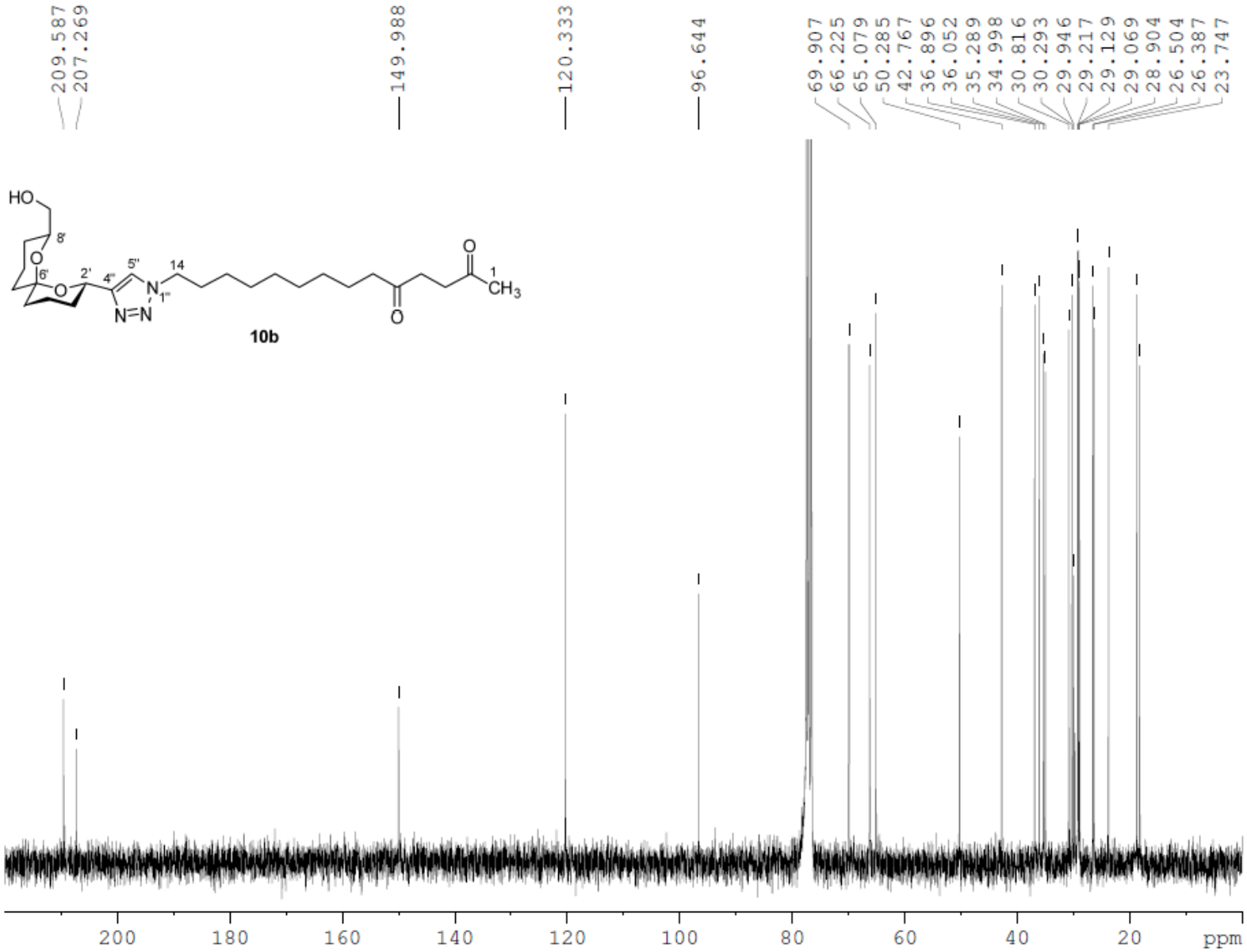
((2S,6S,8S)-8-(1-(3-Nitrophenyl)-1H-1,2,3-triazol-4-yl)-1,7-dioxaspiro[5.5]undecan-2-yl) methanol (10h)

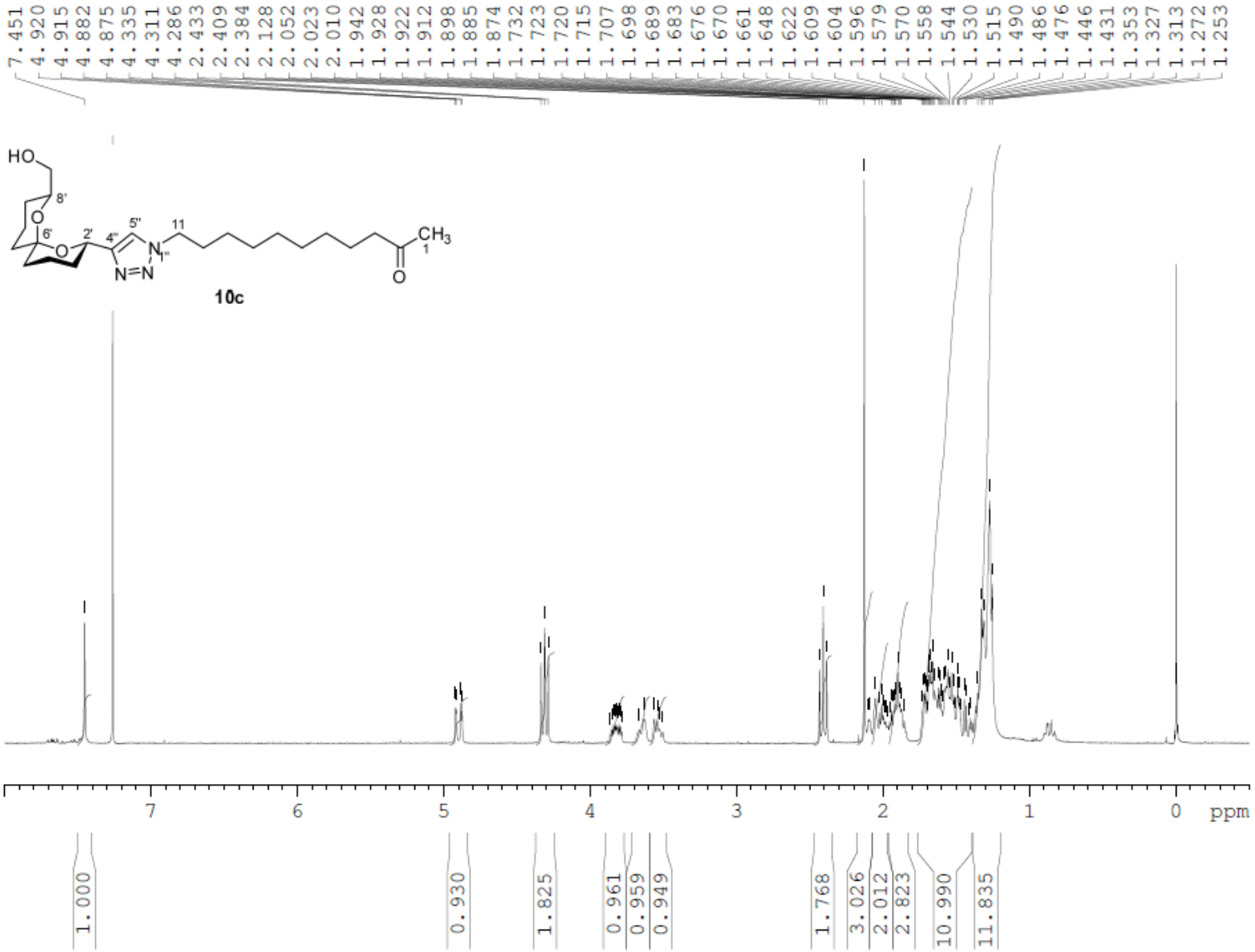
The *title compound* **10h** (7.5 mg, 67%) was prepared as an amorphous, yellow solid from TBDPS-protected triazole **28h** (15.0 mg, 30.0 µmol) and 3HF•NEt_3 (2 x 80 µL, 2.67 µL/µmol) in anhydrous THF (710 µL) using Procedure B. Purification was carried out by flash chromatography using EtOAc–*n*-hexane (0%, 17% EtOAc/*n*-hexane to 40% *n*-hexane/EtOAc). Mp. 110–112 °C; $[\alpha]_D^{26}$ -46.4 (c 0.75 in $CHCl_3$); R_f (40% *n*-hexane/EtOAc) 0.20; IR (film) ν_{max}/cm^{-1} 3403 (O–H), 2942 (C–H), 1536 (N=O), 1351 (N=O), 1042, 980; δ_H (300 MHz, $CDCl_3$) 1.29–1.44 (2H, m, 3–H_A and 5–H_A), 1.47–1.76 (6H, m, 3–H_B, 4–H_A, 9–H_A, 10–H_A and 11–H,), 1.89–2.19 (4H, m, 4–H_B, 5–H_B, 9–H_B and 10–H_B), 3.56 (1H, dd, $^2J_{AB}$ 11.3 and $^3J_{2\text{-}CH_2O,2}$ 6.6, 2–C$\underline{H}_A$$H_B$O), 3.67 (1H, dd, $^2J_{AB}$ 11.3 and $^3J_{2\text{-}CH_2O,2}$ 2.9, 2–C$H_A\underline{H}_B$O), 3.80–3.88 (1H, m, 2–H), 5.01 (1H, dd, $^3J_{8,9ax}$ 11.6 and $^3J_{8,9eq}$ 2.2, 8–H), 7.74 (1H, t, $^3J_{5",4" \text{ and } 5",6"}$ 8.2, 5"–H), 8.04 (1H, s, 5'–H), 8.20–8.23 (1H, m, 4"–H), 8.28–8.31 (1H, m, 6"–H), 8.59 (1H, t, $^4J_{2",4" \text{ and } 2",6"}$ 2.1, 2"–H); δ_C (75 MHz, $CDCl_3$) 18.2, 18.6 (2 x CH_2, C–4 and C–10), 26.3 (CH_2, C–3), 30.9 (CH_2, C–9), 35.0, 35.2 (2 x CH_2, C–5 and C–11), 65.0 (CH, C–8), 66.2 (CH_2, 2–$\underline{C}H_2$O), 70.1 (CH, C–2), 96.8 (C, C–6), 115.1 (CH, C–2"), 118.8 (CH, C–5'), 123.0 (CH, C–6"), 126.0 (CH, C–4"), 130.9 (CH, C–5"), 137.9 (C, C–1"), 148.9 (C, C–3"), 151.7 (C, C–4'); MS *m/z* (ESI+, MS_2+ (375)) 375 ($[M + H]^+$, 62%), 357 ($[M - H_2O]^+$, 100), 329 ($[M - NO_2 + H]^+$, 27), 201, (13); HRMS (ESI+): $[M + H]^+$, found 375.1650. $C_{18}H_{23}N_4O_5$ requires 375.1663.

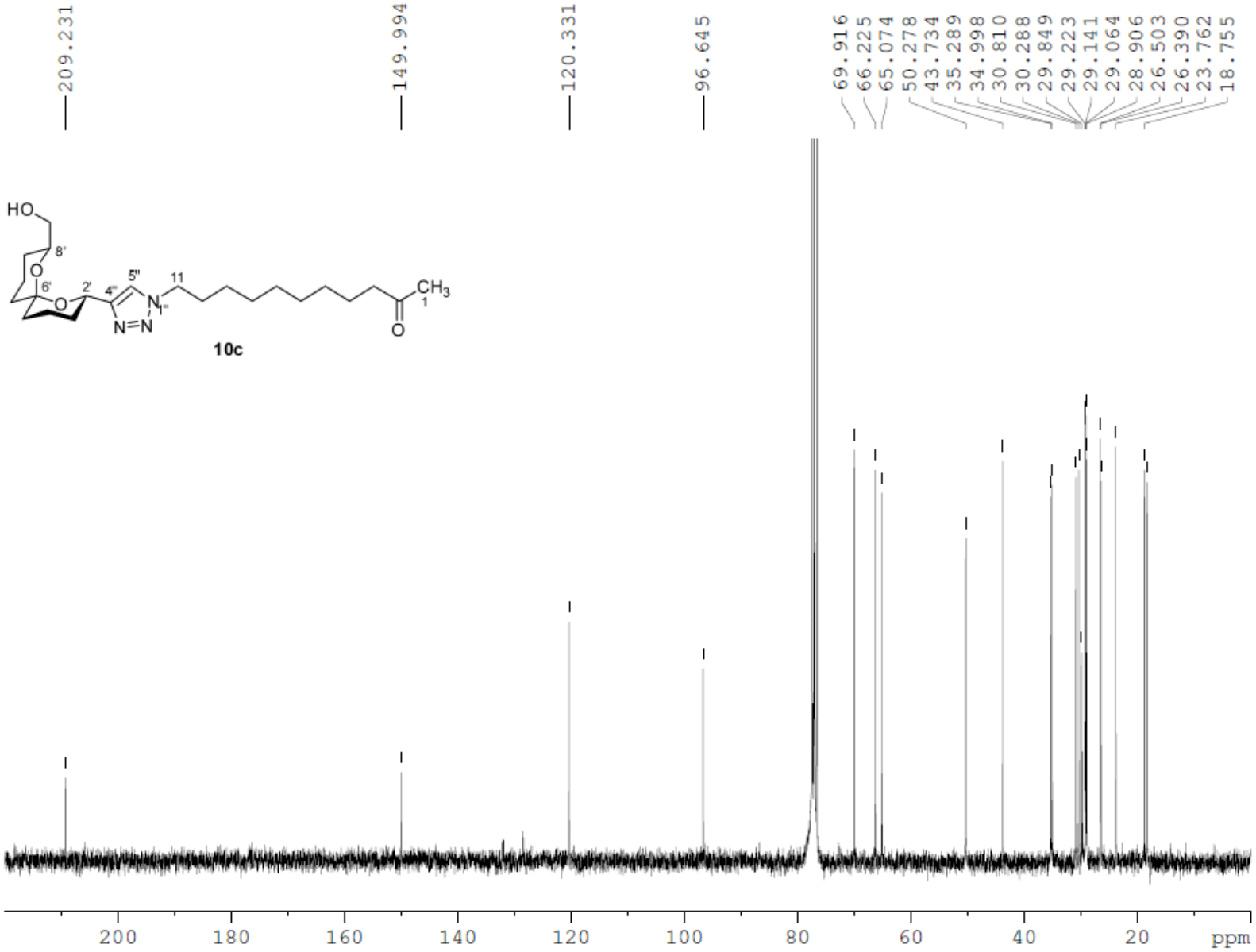












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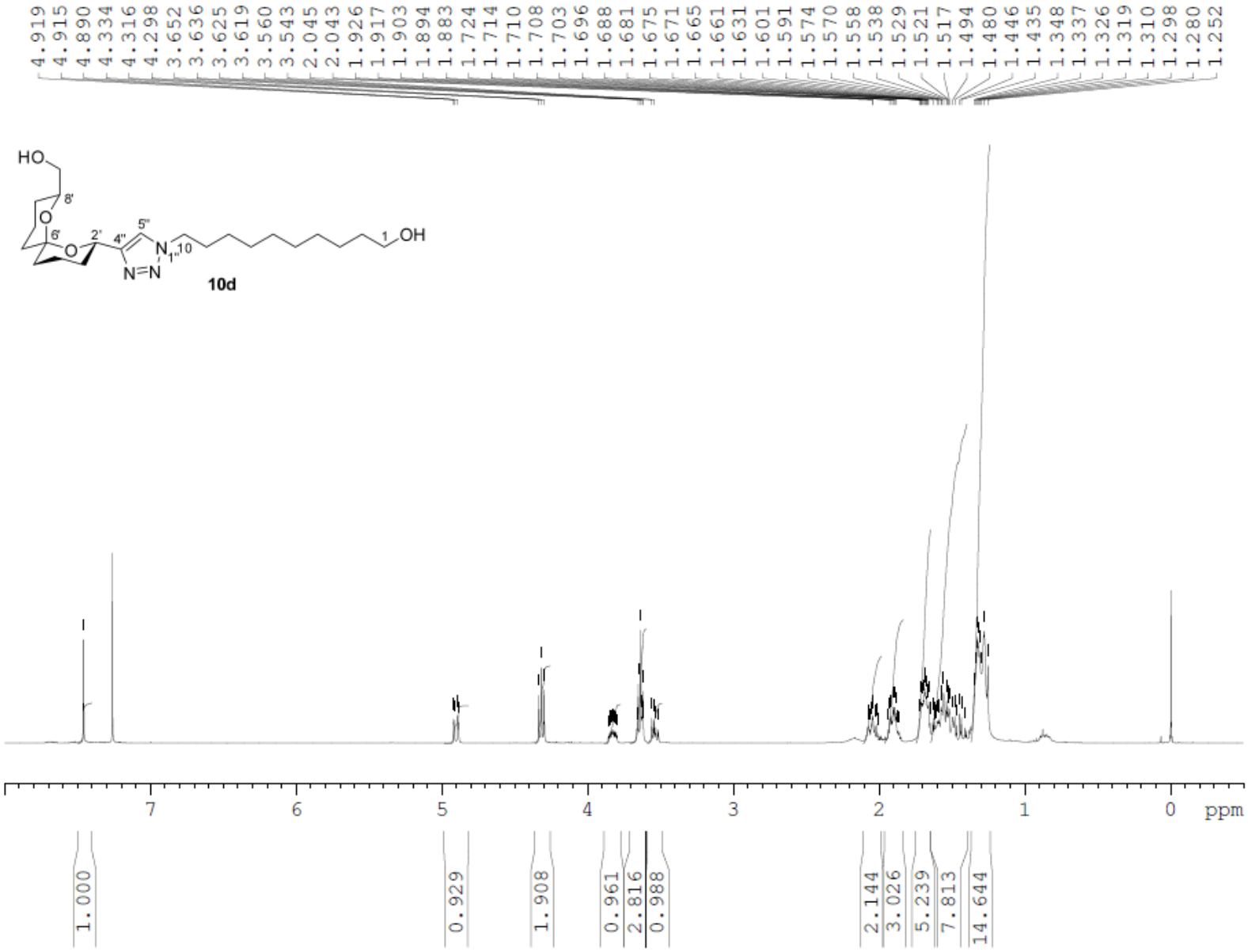

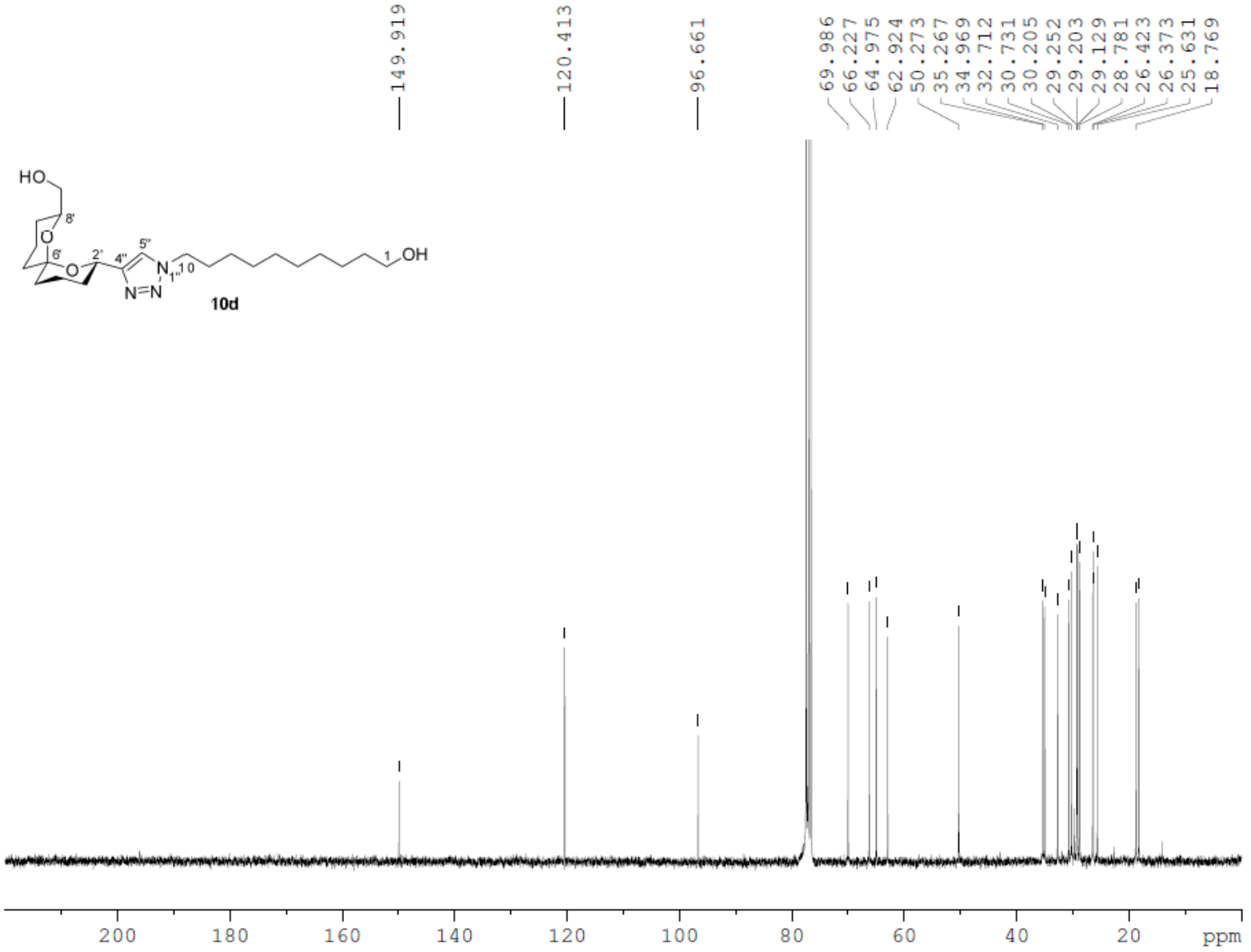

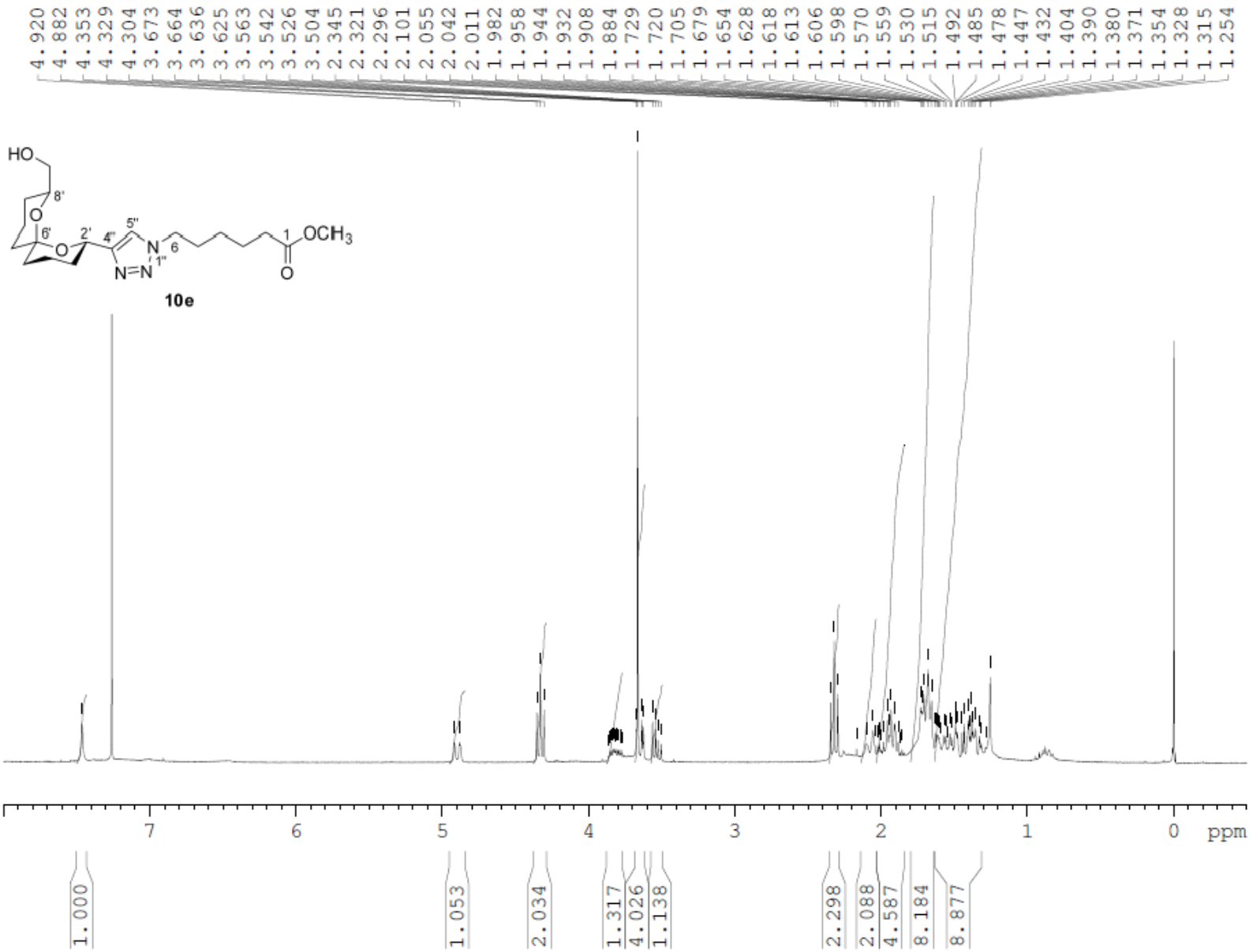

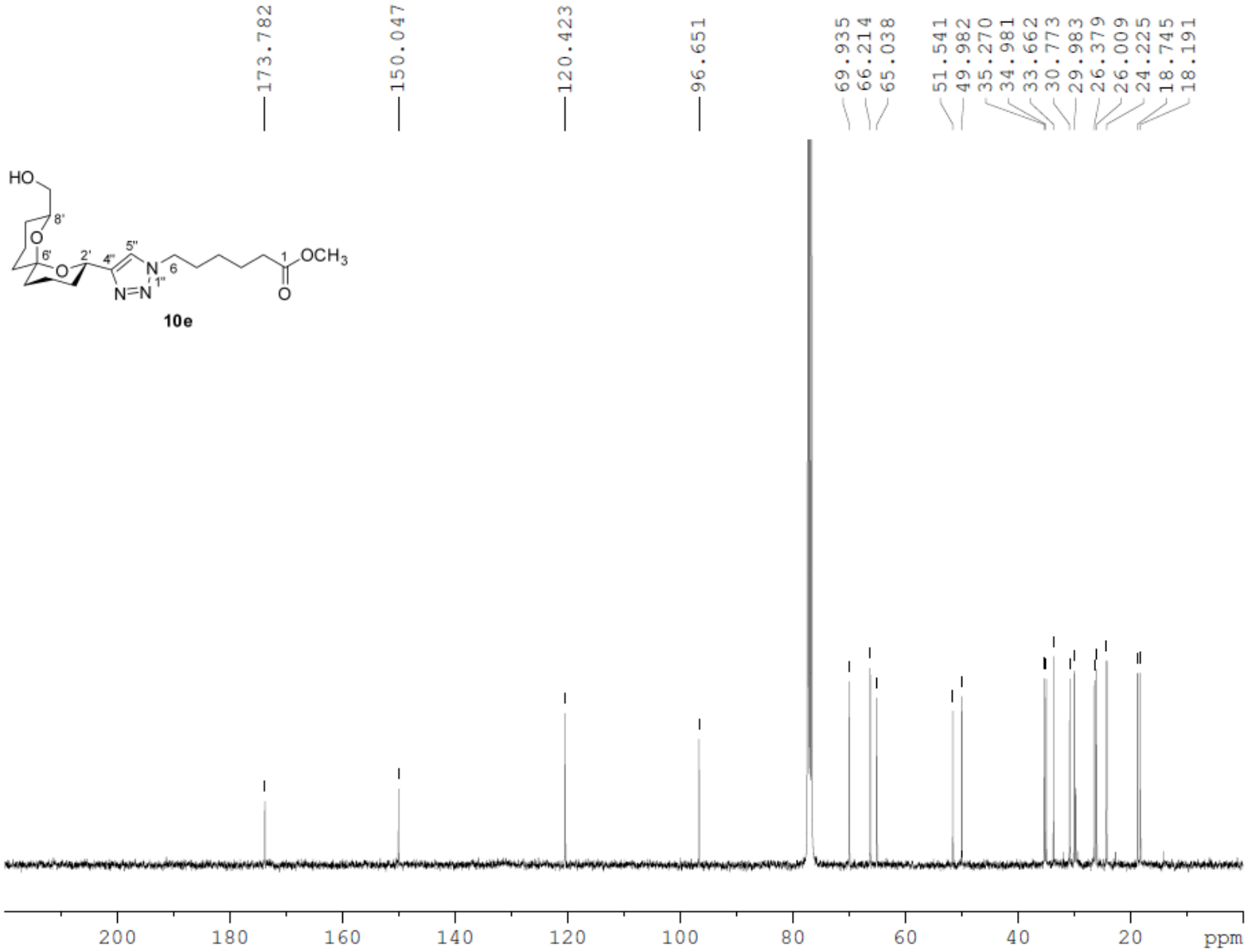

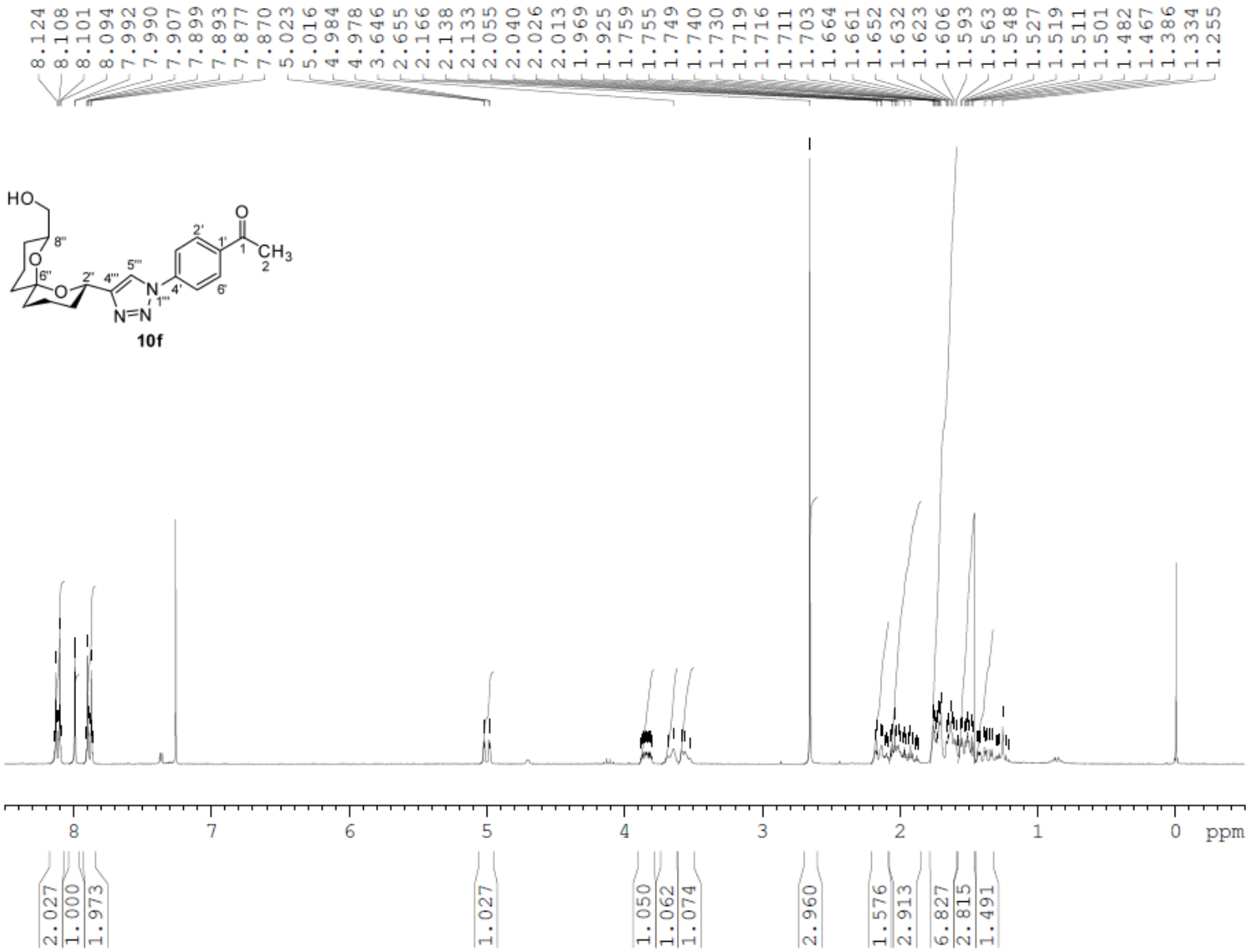

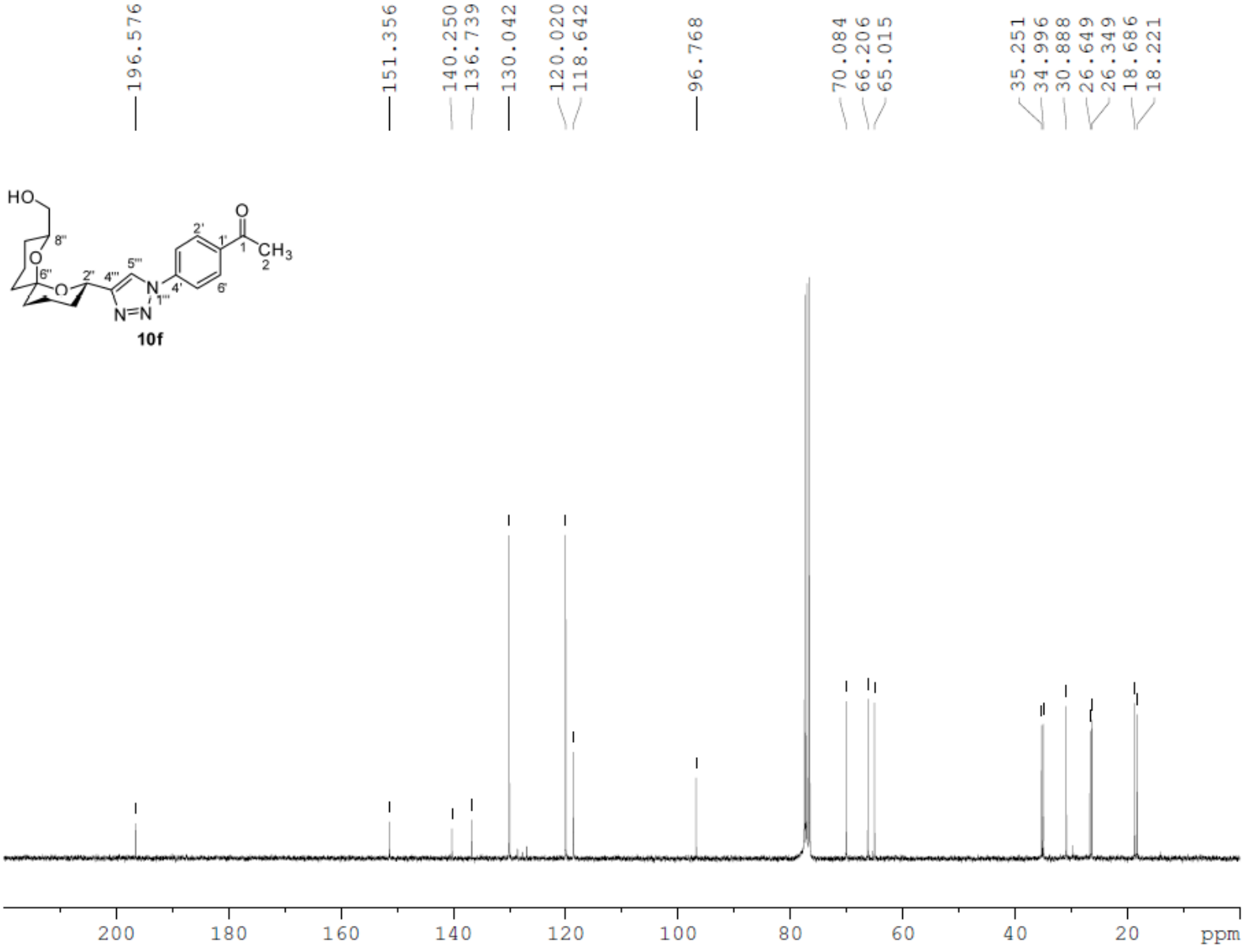

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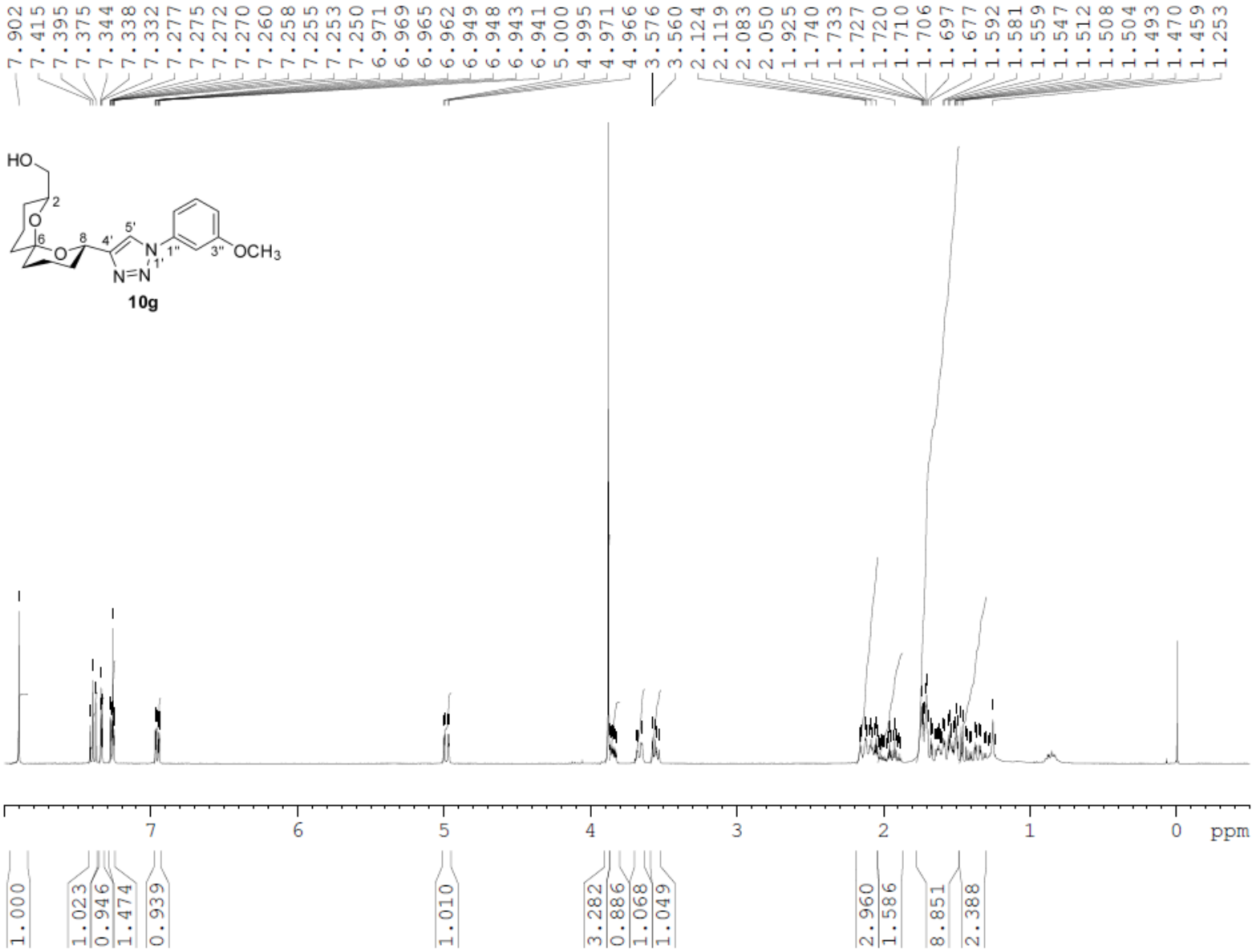

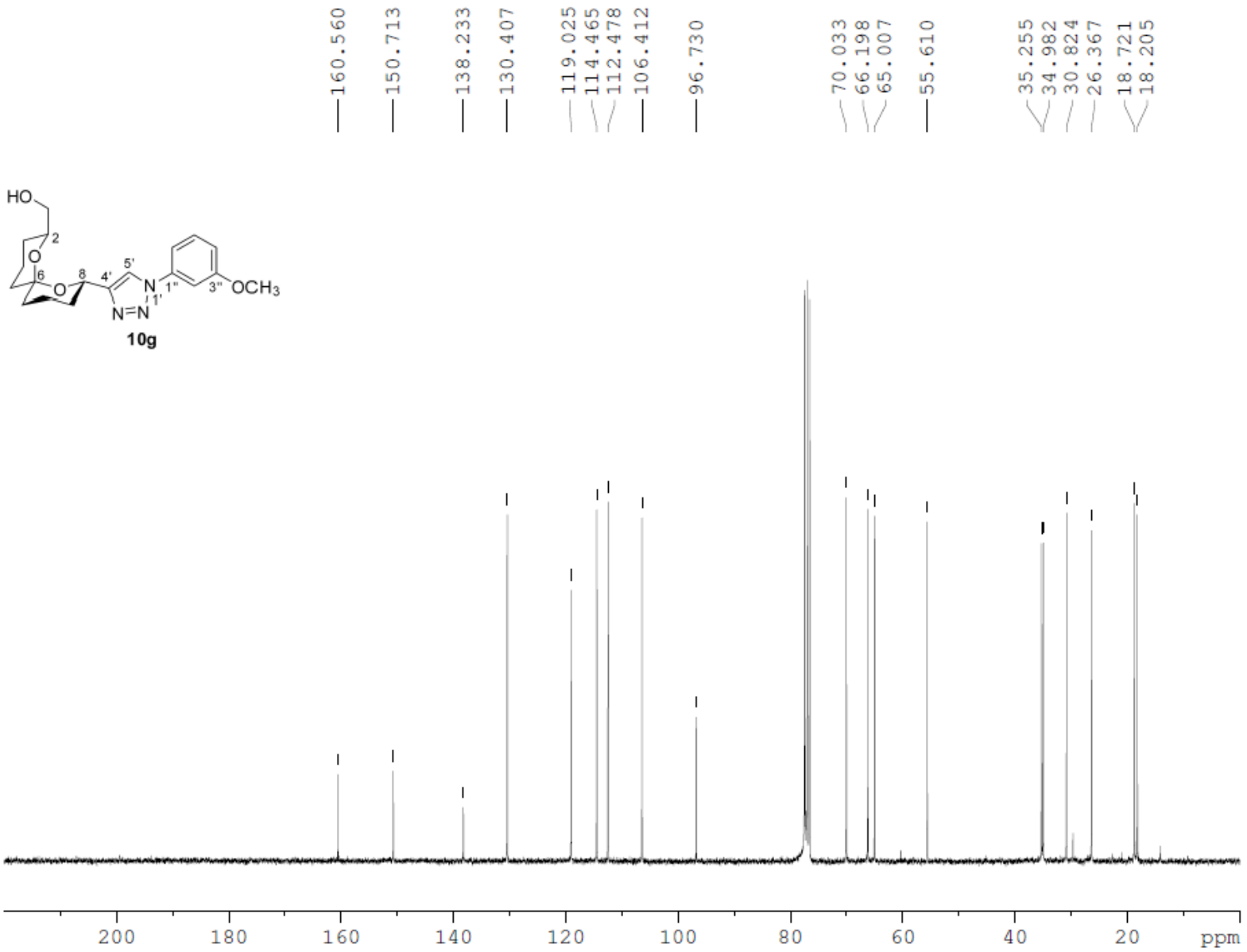

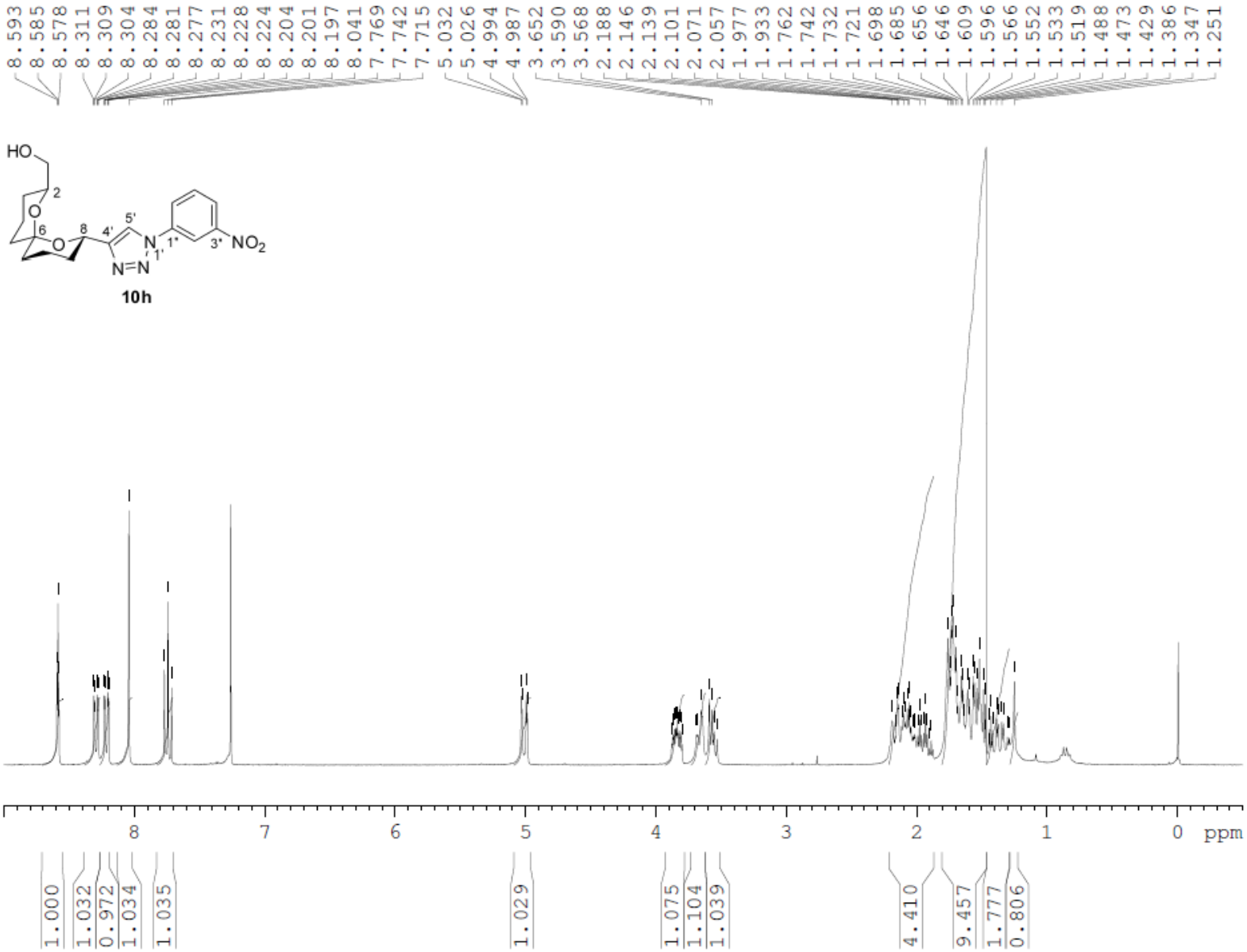

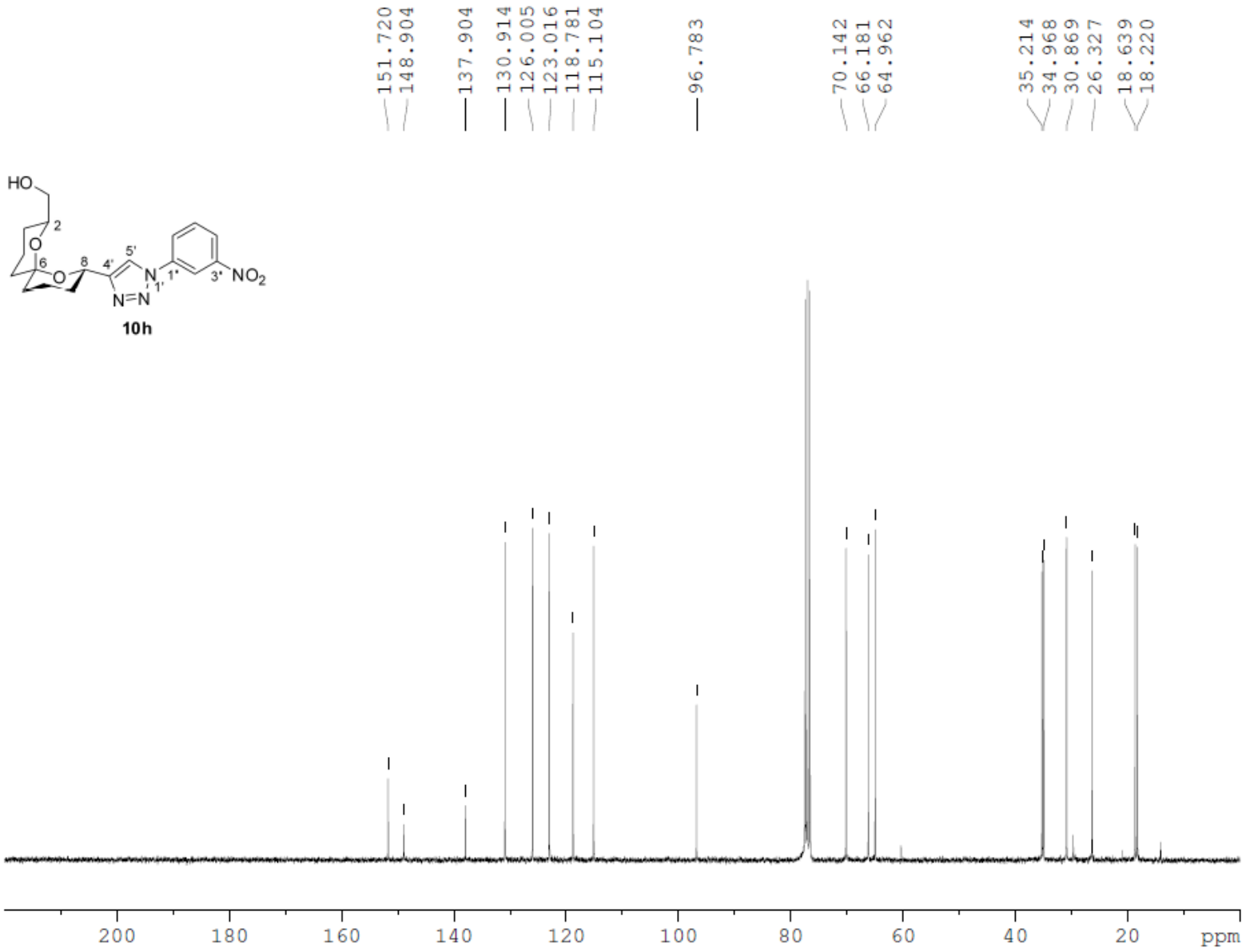

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