Approaches to the synthesis of highly substituted aromatic and fused rings: Metal-catalysed versus thermal cyclisation

Supporting Information

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Methods

Solvents, Reagents and Reactions

Chemical symbols have their usual meanings and SI units and symbols are used. Microwave reactions were conducted using a Biotage Initiator EXP microwave reactor. Evaporation of solvent was carried out using a Buchi Water bath B-481 rotary evaporator under reduced pressure (0-1000 mbar) with a bath temperature of 40 °C. Solvents for reactions are dry unless specified and the majority were purified by a Grubbs’ towers solvent purification system. Tetrahydrofuran was distilled from sodium wire and benzophenone.

Chromatography

TLC was conducted on glass backed silica gel plates precoated with a fluorescent indicator (60 F\textsubscript{254} Merck), visualised using Mineralight Lamp Multiband UV 254/365 nm and dipped with KMnO\textsubscript{4} solution. Flash chromatography was performed using silica gel (40 – 63 μm, Fluorochem) using head pressure by means of head bellows, employing the method of Still \textit{et al}. All solvents for chromatography are commercially sourced.

Analysis, Spectroscopy and Spectrometry

Nuclear magnetic resonance spectra (NMR) were measured with a Bruker AV-400 (400 MHz for \textsuperscript{1}H NMR and 100 MHz for \textsuperscript{13}C NMR) and referenced relative to the residual non-deuterated solvent peak. Chemical shifts are reported in parts per million. Spectral peaks are assigned as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad), and combinations thereof. Coupling constants (J) are reported to the nearest 0.1 Hz. Infrared spectra were recorded using a Perkin-Elmer Frontier Fourier Transform Infrared Spectrometer fitted with a diamond ATR module with the sample loaded as a thin film. Mass spectra were recorded using Micromass AutoSpec Premier or Waters LCT Premier instruments under conditions of electrospray ionisation (ES), chemical ionisation (CI) or electron ionisation (EI). Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. X-ray crystallography was done using either an Agilent Xcalibur PX Ultra A.
Synthesis and Characterisation

((6-((2-Bromoallyloxy)hex-4-yn-1-yl)oxy)(tert-butyl)dimethylsilane (15)

To a stirring solution of sodium hydride (60% dispersion, 3.20 g, 0.1 mmol) in THF (180 mL) at 0 °C, 6-
(tert-butyl(dimethyl)silyloxy)hex-2-yn-1-ol (15.42 g, 0.7 mmol) in THF (45 mL) was added as drops. After
one hour, 2,3-dibromopropene (80% technical grade, 8.5 mL, 0.7 mmol) was added as drops. The
reaction medium was allowed to warm to room temperature over two hours, at which point an aqueous
solution of K2CO3 (200 mL) was added portion wise. The layers were then partitioned and the aqueous
extracted with ethyl acetate (3 × 200 mL). The combined organic layers were then washed with brine,
dried over MgSO4, filtered and reduced under vacuum. The crude product was purified by column
chromatography (10% EtOAc/hexane) to give the title compound as a colourless oil (15 g, 0.7 mmol,
65%).

Rf = 0.54 (25% diethyl ether in hexane); IR = (neat) 2952, 2930, 2857, 1468, 1087, 774 cm⁻¹;
1H NMR (400 MHz, CDCl3): δ = 5.94 (q, J = 1.5 Hz, 1H), 5.63 (dt, J = 2.0, 1.0 Hz, 1H), 4.21 – 4.15 (m, 4H)
3.68 (t, J = 6.0 Hz, 2H), 2.31 (tt, J = 7.0, 2.0 Hz, 2H), 1.72 (tt, J = 7.0, 6.0 Hz, 2H), 0.89 (s, 9H), 0.05 (s, 6H);
13C NMR (100 MHz, CDCl3): δ = 129.0, 118.3, 87.6, 75.4, 73.3, 61.7, 57.9, 31.7, 26.1, 14.3, – 5.2; HRMS (CI+): m/z [M+H]+ calcd for C15H28O2Si79Br: 347.1042; found: 347.1047.

6-((2-Bromoallyloxy)hex-4-yn-1-ol (16)

Tetrabutylammonium fluoride (1.0 M in THF, 40.3 mL, 0.3 mmol) was added as drops to a stirring
solution of (6-(2-bromoallyloxy)hex-4-ynyl)oxy)(tert-butyl)dimethylsilane (11.7 g, 0.3 mmol) in THF (340
mL) at 0 °C. The cooling was removed and the reaction mixture was stirred for two hours at room
temperature. Brine (200 mL) was added, and the solution was extracted with ethyl acetate (3 × 200 mL).
The combined organic extracts were dried over NaSO4, filtered, and reduced under reduced pressure.
The crude product was purified by column chromatography (33% EtOAc/hexane) to provide the title
compound as colourless oil (7.1 g, 0.3 mmol, 90%).

Rf = 0.21 (10% ethyl acetate in hexane); IR = (neat) 3361, 2942, 2857, 1635, 1438, 1354, 1160, 1064, 905
668 cm⁻¹; 1H NMR (400 MHz, CDCl3): δ = 5.94 (q, J = 1.5 Hz, 1H), 5.64 (dt, J = 2.0, 1.0 Hz, 1H), 4.27 – 4.15 (m, 4H)
3.75 (t, J = 6.0 Hz, 2H), 2.36 (tt, J = 7.0, 2.0 Hz, 2H), 1.78 (tt, J = 7.0, 6.0 Hz, 2H); 13C NMR (100
MHz, CDCl3): δ = 128.9, 118.5, 87.0, 75.9, 73.4, 61.8, 57.9, 31.3, 15.5; HRMS (CI+): m/z [M+NH₄]+ calcd for C9H17NO2Si79Br: 250.0443; found: 250.0441.
6-((2-Bromoallyl)oxy)hex-4-ynal (17)

To oxalyl chloride (0.90 mL, 10 mmol) in DCM (15 mL) at −78 °C, a solution of DMSO (1.3 mL, 19 mmol) in DCM (10 mL) was added as drops. The reaction mixture was stirred for 30 minutes before a solution of 6-((2-bromoallyloxy)hex-4-yn-1-ol (2.0 g, 8.6 mmol) in DCM (10 mL) was added as drops. The reaction mixture was again stirred for 30 minutes before the addition of triethylamine (6.2 mL, 43 mmol) as drops. Once the triethylamine had been added, the mixture was allowed to warm to room temperature over the course of an hour and quenched with NH₄Cl (40 mL). The aqueous layer was then extracted with ethyl acetate (3 × 50 mL) and the combined organics washed with sequentially with 10% K₂CO₃ (50 mL), water (50 mL), 2 M HCl (50 mL) and finally brine (50 mL). The washed organics were then dried with magnesium sulphate, filtered and reduced under vacuum to provide the title compound as a pale yellow oil (1.9 g, 8.2 mmol, 96%). The crude product was used in the next step without further purification.

Rᵣ = 0.40 (25% ethyl acetate in hexane); IR = (neat) 2904, 2852, 2729, 1725, 1633, 1356, 1075, 899, 666 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 9.80 (t, J = 1.0 Hz, 1H), 5.93 (q, J = 1.5 Hz, 1H), 5.64 (dt, J = 2.0, 1.0 Hz, 1H, 4.21 – 4.12 (m, 4H), 2.69 (tt, J = 7.0, 1.0 Hz, 2H), 2.56 (ttd, J = 7.0, 2.0, 1.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 200.2, 128.8, 118.6, 85.5, 76.4, 73.4, 57.8, 42.6, 12.2; HRMS (Cl⁺): m/z [M+NH₄⁺] calcd for C₉H₁₅NO₂⁺Br: 248.0281; found: 248.0267.

8-((2-Bromoallyl)oxy)-1-(trimethylsilyl)octa-1,6-diyn-3-one (18)

Dess-Martin periodinane (1.9 g, 4.5 mmol) was added in one portion to a cooled solution (−10 °C) of 8-(2-bromoallyloxy)-1-(trimethylsilyl)octa-1,6-diyn-3-ol (1.0 g, 3.0 mmol) in DCM (100 mL). The mixture was stirred overnight before being quenched with saturated Na₂S₂O₃ solution (100 mL). The layers were separated and the aqueous extracted with DCM (2 × 100 mL). The organic layers were combined, washed with NaHCO₃, dried over sodium sulphate, filtered and reduced under vacuum. The crude material was purified by column chromatography (10% ethyl acetate in hexane) to provide the title compound (0.92 g, 2.8 mmol, 94%) as a colourless oil.

Rᵣ = 0.63 (25% ethyl acetate in hexane); IR = (neat) 2960, 2905, 2856, 2156, 1678, 1252, 1108, 1079, 844, 761 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.94 (q, J = 1.5 Hz, 1H), 5.64 (dt, J = 2.0, 1.0 Hz, 1H), 4.21 – 4.12 (m, 4H), 2.69 (tt, J = 7.0, 1.0 Hz, 2H), 2.56 (ttd, J = 7.0, 2.0, 1.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 185.2, 128.8, 118.7, 101.5, 99.1, 85.5, 76.3, 73.4, 57.7, 44.1, 13.6, −0.7; HRMS (ESI⁺): m/z [M+H⁺] calcd for C₁₄H₂₀O₂SiBr: 327.0416; found: 327.0417.
5-(Trimethylsilyl)-7,8-dihydro-4H-indeno[4,5-c]furan-6(5H)-one (19)

8-(2-Bromoallyloxy)-1-(trimethylsilyl)octa-1,6-diyn-3-one (300 mg, 0.917 mmol) and 1,2-epoxyhexene in DCE (2 mL) were heated to 185 °C using a microwave reactor. After 2 hours, the volatiles were removed under vacuum to give a crystalline solid. The crude material was then purified by column chromatography (50% ethyl acetate in hexane) to provide the title compound as a white crystalline solid (180 mg, 0.73 mmol, 81%).

Rₙ = 0.30 (25% ethyl acetate in hexane); MP = 107.1 °C – 110.4 °C (CHCl₃); IR (neat) = 3134, 2948, 1680, 1619, 1435, 1403, 1108, 1025, 831, 813, 755 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz): δ = 7.62 – 7.49 (m, 1H), 7.19 (t, J = 2.0 Hz, 1H), 2.91 – 2.67 (m, 4H), 2.53 (t, J = 5.0 Hz, 2H), 2.34 – 2.29 (m, 1H), –0.14 (s, 9H); ¹³C NMR (CDCl₃, 100 MHz): δ = 206.8, 156.4, 140.3, 138.5, 137.7, 122.4, 121.4, 35.0, 25.6, 21.8, 19.4, –2.2; HRMS (ES+): m/z [M+H⁺] calcd for C₁₄H₁₉O₂Si: 247.1154; found: 247.1165.

8-(2-Bromoallyloxy)octa-1,6-diyn-3-one (20)

8-(2-Bromoallyloxy)-1-(trimethylsilyl)octa-1,6-diyn-3-one (0.1 g, 0.3 mmol) and epoxyhexene were heated to reflux in toluene (15 mL) for 4 days. The reaction mixture was reduced in vacuum to colourless oil. The crude material was then purified by column chromatography (50% EtOAc/hexane) providing the title compound as a colourless oil (8 mg, 0.03 mmol, 11%).

Rₙ = 0.54 (20% ethyl acetate in hexane); IR (neat) = 3263, 2887, 2092, 1681, 1358, 1077, 907, 673 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.95 – 5.92 (m, 1H), 5.65 – 5.62 (m, 1H), 4.24 – 4.06 (m, 4H), 3.27 (s, 1H), 2.84 (t, J = 7.0 Hz, 2H), 2.59 (tt, J = 7.0, 2.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 184.8, 128.8, 118.6, 85.1, 81.1, 79.5, 76.5, 73.4, 57.7, 44.2, 13.5; HRMS (CI+): m/z [M+NH₄⁺] calcd for C₁₁H₁₅NO₂⁺Br: 272.0286; found: 272.0291.
**9-((2-Bromoallyloxy)-1-(trimethylsilyl)nona-1,7-diyn-3-one (21)**

To a solution of trimethylsilylacetylene (0.22 mL, 1.6 mmol) in THF (6 mL) at −78 °C, n-BuLi (2.5 M in hexanes, 0.64 mL, 1.6 mmol) was added. The mixture was warmed to −10 °C after the addition was complete, and then cooled back down to −78 °C. 7-(2-bromoallyloxy)hepta-5-ynal (170 mg, 0.69 mmol) was added in THF (2 mL). After 30 minutes at −78 °C, the mixture was warmed to room temperature. Sat. NH₄Cl(aq) (10 mL) was added, the layers were separated, and the aqueous was extracted with EtOAc (3 × 10 mL). The organics were washed with brine (10 mL), dried over MgSO₄ and filtered. The organics were then concentrated under reduced pressure to provide the intermediate propargylic alcohol. Dess–Martin periodinane (300 mg, 0.72 mmol) was added to the crude propargyl alcohol in DCM (15 mL) at 0 °C, and the mixture was stirred overnight. The reaction mixture was diluted with Et₂O (30 mL) and a 1:1 mixture (20 mL) of sat. aq. sodium thiosulfate and sat. aq. NaHCO₃ was added. The layers were separated, and the aqueous extracted with Et₂O (20 mL). The combined organics were washed with brine (20 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (10% EtOAc/hexane) to provide the title compound as a colourless oil (110 mg, 0.32 mmol, 46%).

Rᵣ = 0.59 (20% ethyl acetate in hexane); IR = (neat) 2960, 2902, 2855, 1675, 1111, 1080, 844, 761 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.95 (q, J = 1.5 Hz, 1H), 5.64 (dt, J = 2.0, 1.0 Hz, 1H), 4.21 – 4.16 (m, 4H), 2.70 (t, J = 7.0 Hz, 2H), 2.30 (tt, J = 7.0, 2.0 Hz, 2H), 1.87 (quintet, J = 7.0 Hz, 2H), 0.25 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ = 186.0, 127.9, 117.6, 101.0, 97.2, 85.5, 75.4, 72.4, 56.8, 43.1, 21.7, 17.2, −1.61; HRMS (ESI+): m/z [M+Na]+ calcd for C₁₅H₂₁O₂Si⁷⁹BrNa: 363.0386; found: 363.0386.
((2-(5-((2-Bromoallyloxy)pent-3-yn-1-yl)-1,3-dioxolan-2-yl)ethynyl)trimethylsilane (23)

1,2-Bis(trimethylsiloxy)ethane (0.3 mL, 1.2 mmol) was added to a vigorously stirring solution of 8-(2-bromoallyloxy)-1-(trimethylsilyl)octa-1,6-diyne-3-one (0.2 g, 0.6 mmol) in DCM (3 mL) at -78 °C. Trimethylsilyl trifluoromethanesulfonate (0.01 mL, 0.06 mmol) was added rapidly. The mixture was allowed to warm to room temperature slowly over the course of two hours. Once complete, the reaction mixture was diluted with DCM (20 mL) and triethylamine (0.4 mL, 3 mmol) was added. The reaction mixture was partitioned with sat. aq. ammonium chloride (20 mL) and the aqueous layer extracted with DCM (2 × 20 mL). The combined organics were washed with brine, filtered and concentrated under reduced pressure. The crude compound was purified by column chromatography (5% Et₂O/hexane) to provide the title compound as a colourless oil (0.16 g, 0.43 mmol, 72%).

Rᵣ = 0.60 (25% ethyl acetate in hexane); IR = (neat) 2959, 2897, 1251, 1034, 862, 844 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.94 (q, J = 1.5 Hz, 1H), 5.64 (dt, J = 2.0, 1.0 Hz, 1H), 4.18 (dd, J = 2.0, 1.0 Hz, 4H), 4.10 – 4.03 (m, 2H), 4.01 – 3.94 (m, 2H), 2.51 – 2.41 (m, 2H), 2.20 – 2.09 (m, 2H), 0.18 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ = 129.0, 118.4, 102.0, 101.9, 89.5, 86.9, 75.3, 73.3, 64.9, 57.9, 38.4, 13.9, -0.1; HRMS (Cl⁺): m/z [M+H]⁺ calcd for C₁₆H₂₄O₃Si79Br: 371.0673; found: 371.0673.

2-(6-((tert-Butyldimethylsilyloxy)hex-2-yn-1-yl)isoindoline-1,3-dione (25)

DIAD (2.1 mL, 10 mmol) was added to a solution of PPh₃ (2.7 g, 10 mmol) in THF (20 mL) at 0 °C. After 30 minutes, a solution of 6-((tert-butyldimethylsiloxy)hex-2-yn-1-ol (2.0 g, 8.8 mmol) and phthalimide (1.5 g, 10 mmol) in THF (20 mL) was added. The mixture was stirred overnight, before concentrating under reduced pressure. The crude material was purified by column chromatography (10% Et₂O/hexane) to provide the title compound as a colourless oil (1.6 g, 4.5 mmol, 51%).

Rᵣ = 0.18 (9% diethyl ether in hexane); IR = (neat) 2954, 2931, 2862, 1715, 1468, 1424, 1390, 1345, 1326, 1104, 1069, 835, 769, 727 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.87 (dd, J = 5.5, 3.0 Hz, 2H), 7.73 (dd, J = 5.5, 3.0 Hz, 2H), 4.42 (t, J = 2.0 Hz, 2H), 3.63 (t, J = 6.0 Hz, 2H), 2.22 (tt, J = 7.0, 2.0 Hz, 2H), 1.72 – 1.58 (m, 3H), 0.85 (s, 9H), 0.00 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 167.4, 134.2, 132.3, 123.6, 83.5, 73.7, 61.7, 31.5, 27.6, 26.0, 18.5, 15.2, -5.2; HRMS (ESI⁺): m/z [M+H]⁺ calcd for C₂₀H₂₈NO₃Si: 358.1838; found:
6-((tert-Butyldimethylsilyl)oxy)hex-2-yn-1-amine (26)

Hydrazine monohydrate (64-65%, 4.5 mL, 5.6 mmol) was added as drops to 2-((tert-
butyldimethylsilyloxy)hex-2-ynyl)isoindoline-1,3-dione (0.50 g, 1.4 mmol) in THF (14 mL). The reaction
mixture was heated to reflux for one hour. Once complete by TLC, the mixture was cooled and H₂O (20
mL) was added. The layers were separated and the aqueous extracted with Et₂O (4 × 20 mL). The organic
extracts were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure
to give the title compound as a colourless oil (0.31 g, 1.4 mmol, 97%).

IR = (neat) 2952, 2930, 2857, 1468, 1253, 1101, 964, 833, 774 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 3.68
(t, J = 6.0 Hz, 2H), 3.39 (t, J = 2.0 Hz, 2H), 2.26 (tt, J = 7.0, 2.5 Hz, 2H), 1.76 – 1.64 (m, 2H), 1.50 (s, 2H),
0.89 (s, 9H), 0.05 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 82.4, 81.1, 61.8, 32.0, 31.9, 26.1, 18.5, 15.3, –
5.2; HRMS (ESI+): m/z [M+H]^+ calcd for C₁₂H₂₆NOSi: 228.1784; found: 228.1790.

N-(2-Bromoallyl)-6-((tert-butyldimethylsilyl)oxy)hex-2-yn-1-amine (27)

2,3-Dibromopropene (0.22 mL, 2.2 mmol) and K₂CO₃ (0.30 g, 2.2 mmol) were added to a solution of (6-
(tert-butyldimethylsilyloxy)hex-2-ynyl)isoindoline-1,3-dione (0.50 g, 2.2 mmol) in THF (22 mL). The reaction mixture
was stirred overnight. Brine (20 mL) was added, the layers were separated, and the aqueous was
extracted with EtOAc (2 × 30 mL). The organic extracts were dried over NaSO₄, filtered and concentrated under reduced pressure
to provide the crude product. The crude material was purified by column chromatography (10-25% Et₂O/hexane) to furnish the title compound as a colourless oil (0.34 g, 1.0
mmol, 47%).

R₁ = 0.25 (10% diethyl ether in hexane); IR = (neat) 2952, 2930, 2857, 1630, 1463, 1253, 1100, 834, 774
cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.82 (m, 1H), 5.57 (d, J = 2.0 Hz, 1H), 3.68 (t, J = 6.0 Hz, 2H), 3.53 (s, 2H), 3.38 (t, J = 2.0 Hz, 2H), 2.27 (tt, J = 7.0, 2.0 Hz, 2H), 1.70 (tt, J = 7.0, 6.0 Hz, 2H), 1.34 – 1.22 (m, 1H),
0.89 (s, 9H), 0.05 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 132.5, 118.3, 83.9, 77.4, 61.8, 56.3, 37.0, 32.0,
\[\text{N-(2-bromoallyl)-N-(6-((tert-butyldimethylsilyl)oxy)hex-2-yn-1-yl)-4-methylbenzenesulfonamide (28)}\]

\(p\)-Toluenesulfonyl chloride (236 mg, 1.2 mmol) was added in one portion to a solution of \(N\)-(2-bromoallyl)-6-((tert-butyldimethylsilyloxy)hex-2-ynyl)amine (430 mg, 1.2 mmol) and triethylamine (0.17 mL, 1.2 mmol) in THF (3 mL) at 0 °C. Once stirred overnight, the mixture was concentrated under reduced pressure and the crude material dissolved in DCM (10 mL). The DCM solution was washed with saturated NaCO\textsubscript{3(aq)} (2 × 10 mL), dried over MgSO\textsubscript{4}, filtered and concentrated under reduced pressure. The crude material was purified by column chromatography (10% Et\textsubscript{2}O/hexane) to yield the title compound as a colourless oil (400 mg, 0.80 mmol, 67%).

\(R_f = 0.21\) (9% diethyl ether in hexane); \(\text{IR} = \) (neat) 2953, 2929, 2857, 1631, 1352, 1253, 1162, 1094, 900, 835, 766, 658 cm\textsuperscript{-1}; \(\text{1H NMR (400 MHz, CDCl}_3\): } \delta = 7.79 - 7.67 (m, 2H, Ts), 7.32 - 7.27 (m, 2H, Ts), 5.94 (dd, \(J = 2, 1\) Hz, 1H, C-3'), 5.66 (m, 1H, C-3'), 4.09 (t, \(J = 2.5\) Hz, 2H, C-1), 4.03 (d, \(J = 1\) Hz, 2H, C-1'), 3.51 (t, \(J = 6\) Hz, 2H, C-6), 2.42 (s, 3H, Ts), 2.00 (tt, \(J = 7, 2\) Hz, 2H, C-4), 1.45 (tt, \(J = 7, 6\) Hz, 2H, C-5), 0.88 (s, 9H, TBS), 0.02 (s, 6H, TBS); \(\text{13C NMR (100 MHz, CDCl}_3\): } \delta = 143.7 \text{(Ts)}, 136.3 \text{(Ts)}, 129.6 \text{(Ts)}, 127.9 \text{(Ts)}, 127.4 \text{(C-2')}, 120.0 \text{(C-3')}, 86.5 \text{(C-3)}, 72.2 \text{(C-2)}, 61.6 \text{(C-6)}, 54.0 \text{(C-1')}, 36.9 \text{(C-1)}, 31.6 \text{(C-5)}, 26.1 \text{(TBS)}, 21.7 \text{(PhCH}_3\), 18.5 \text{(TBS)}, 15.1 \text{(C-4)}, -5.2 \text{(TBS)}; \(\text{HRMS (Cl+): } m/z \text{ [M+H]}^+ \text{ calcd for } C_{22}H_{34}NO_3S^9BrSi: 500.1280; \text{ found: 500.1290.}\)

\(S\)-(6-((tert-butyldimethylsilyloxy)hex-2-yn-1-yl) ethanethioate (29)

\(\text{DIAD (1.1 mL, 5.7 mmol) was added to a solution of triphenylphosphine (1.5 g, 5.7 mmol) in THF (20 mL) at 0 °C. After 20 minutes, 6-(tert-butyldimethylsiloxoxy)hex-2-ynyl)ethanethioic acid (0.40 mL, 5.7 mmol) in THF (10 mL) was added. After two hours, the mixture was concentrated under reduced pressure. The concentrated residue was purified by column chromatography (5% EtO/hexane) to provide the title compound as a colourless oil (1 g, 4 mmol, 70%).}\n
\(R_f = 0.72\) (13% ethyl acetate in hexane); \(\text{IR} = \) (neat) 2953, 2929, 2857, 1697, 1132, 1101, 833, 774 cm\textsuperscript{-1}; \(\text{1H NMR (400 MHz, CDCl}_3\): } \delta = 3.71 - 3.60 (m, 4H), 2.34 (s, 3H), 2.24 (tt, \(J = 7.0, 2.5\) Hz, 2H), 1.67 (tt, \(J = 7.0, 6.0\) Hz, 2H), 0.89 (s, 9H), 0.05 (s, 6H); \(\text{13C NMR (100 MHz, CDCl}_3\): } \delta = 194.6, 83.2, 74.6, 61.7, 31.7, 30.3, 26.1, 18.5, 18.4, 15.4, -5.19; \(\text{HRMS (ESI+): } m/z \text{ [M+H]}^+ \text{ calcd for } C_{14}H_{27}O_3SSi: 287.1501; \text{ found: 287.1501.}\)
K$_2$CO$_3$ (1.0 g, 7.5 mmol) was added to a solution of S-6-(tert-butyldimethylsilyloxy)hex-2-ynyl ethanethiolate (0.75 g, 3.0 mmol) in MeOH (30 mL). After one hour, the reaction was judged to be complete, and 2,3-dibromopropene (0.3 mL, 3 mmol) was added. After two hours, water (30 mL) and Et$_2$O (50 mL) were added. The layers were separated and the aqueous was extracted with Et$_2$O (3 × 50 mL). The ether extracts were washed with brine, dried over MgSO$_4$, filtered and concentrated under reduced pressure. The crude material was purified by column chromatography (5% Et$_2$O/hexane) to provide the title compound as a colourless oil (0.67 g, 1.9 mmol, 62%).

**$R_f$** = 0.6 (13% ethyl acetate in hexane); **IR** = (neat) 2952, 2928, 2856, 1251, 1100, 833, 774 cm$^{-1}$; **$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ = 5.83 (dt, $J$ = 2.0, 1.0 Hz, 1H), 5.55 (d, $J$ = 1.5 Hz, 1H), 3.68 (t, $J$ = 6.0 Hz, 2H), 3.61 (d, $J$ = 1.0 Hz, 2H), 3.23 (t, $J$ = 2.5 Hz, 2H), 2.29 (tt, $J$ = 7.0, 2.5 Hz, 2H), 1.70 (tt, $J$ = 7.0, 6.0 Hz, 2H), 0.89 (s, 9H), 0.05 (s, 6H); **$^{13}$C NMR** (100 MHz, CDCl$_3$): $\delta$ = 128.9, 119.4, 84.0, 75.1, 61.8, 41.3, 32.0, 26.1, 19.3, 18.5, 15.4, −5.2; **HRMS** (ESI+): $m/z$ [M+H]$^+$ calcd for C$_{15}$H$_{28}$O$_7$BrSi: 363.0814; found: 363.0808.

**N-(2-Bromoallyl)-4-methyl-N-(6-oxo-8-(trimethylsilyl)octa-2,7-diyn-1-yl)benzenesulfonamide (31)**

Dess-Martin periodinane (60 mg, 0.14 mmol) was added to a solution of N-(2-bromoallyl)-N-(6-hydroxy-8-(trimethylsilyl)octa-2,7-diynyl)-4-methylbenzenesulfonamide (45 mg, 0.09 mmol) in DCM (2 mL) at 0 °C. The mixture was then stirred overnight. Et$_2$O (10 mL) was added, followed by a 1:1 mixture of saturated aq. NaCO$_3$ and saturated aq. sodium thiosulphate solution (10 mL). The mixture was stirred for an hour. The layers were separated and the aqueous was extracted with Et$_2$O (3 × 10 mL). The organics were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to provide the title compound as a colourless oil (31 mg, 0.062 mmol, 70%).

**$R_f$** = 0.29 (13% ethyl acetate in hexane); **IR** = (neat) 2962, 2928, 2856, 1251, 1250, 1100, 1107, 1094, 845, 758, 657 cm$^{-1}$; **$^1$H NMR** (400 MHz, CDCl$_3$): $\delta$ = 7.77 − 7.69 (m, 2H), 7.36 − 7.28 (m, 2H), 5.95 (q, $J$ = 1.4 Hz, 1H), 5.66 (dt, $J$ = 1.8, 0.8 Hz, 1H), 4.06 (t, $J$ = 2.2 Hz, 2H), 4.02 (t, $J$ = 1.1 Hz, 4H), 2.50 (t, $J$ = 7.0 Hz, 2H), 2.44 (d, $J$ = 3.0 Hz, 3H), 2.24 (ddt, $J$ = 9.0, 7.0, 2.0 Hz, 2H), 0.26 (s, 9H); **$^{13}$C NMR** (100 MHz, CDCl$_3$): $\delta$ = 184.8, 143.8, 136.3, 129.6, 128.0, 127.2, 120.4, 101.5, 99.1, 85.7, 84.5, 73.2, 54.1, 43.7, 36.7, 21.7, 13.1, −0.64;
HRMS (ESI+): m/z [M+H]+ calcd for C_{21}H_{27}NO_{3}^{79}BrSSi: 480.0664; found: 480.0667.

8-((2-Bromoallyl)thio)-1-(trimethylsilyl)octa-1,6-diyne-3-one (32)

To oxalyl chloride (0.022 mL, 0.26 mmol) in DCM (1 mL) at −78 °C, DMSO (0.036 mL, 0.51 mmol) in DCM (0.5 mL) was added as drops. The mixture was stirred for one hour before the addition of 8-((2-bromoallylthio)-1-(trimethylsilyl)octa-1,6-diyne-3-ol (60 mg, 0.17 mmol) in DCM (0.5 mL). After a further 30 minutes at −78 °C, triethylamine (0.2 mL, 1.4 mmol) was added, and the mixture was allowed to warm to room temperature. Water (3 mL) was added and the biphasic mixture separated. The aqueous was extracted with DCM (2 × 5 mL), and the combined organics were washed with NaHCO₃ (2 × 5 mL), dried with MgSO₄, filtered and concentrated under reduced pressure to provide the title compound as a pale yellow oil (15 mg, 0.043 mmol, 26%).

R_f = 0.7 (13% ethyl acetate in hexane); IR = (neat) 2961, 2908, 1677, 1252, 1110, 846 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.83 (dt, J = 2.0, 1.0 Hz, 1H), 5.55 (d, J = 2 Hz, 1H), 3.60 (d, J = 1.0 Hz, 2H), 3.20 (t, J = 2.5 Hz, 2H), 2.79 (dd, J = 7.5, 6.5 Hz, 2H), 2.60 – 2.49 (m, 2H), 0.25 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ = 185.3, 128.8, 119.6, 101.6, 99.1, 81.8, 76.1, 44.3, 41.3, 19.1, 13.7, −0.6; HRMS No associated mass found.

2-Tosyl-5-(trimethylsilyl)-4,5,7,8-tetrahydrocyclopenta[e]isoindol-6(2H)-one (33)

(N-(2-Bromoallyl)-N-(6-oxo-8-(trimethylsilyl)octa-2,7-diyne)-4-methylbenzenesulfonamide (60 mg, 0.12 mmol) and 1,2-epoxyhexane (0.14 mL, 1.2 mmol) in DCE (1.2 mL) were heated to 200 °C for 2 hours using a microwave reactor. The mixture was then concentrated under reduced pressure and the residue purified by column chromatography (30% EtOAc in hexane) to furnish the title compound as a pale yellow gum (29 mg, 0.073 mmol, 61%).

R_f = 0.26 (30% ethyl acetate in hexane); IR = (neat) 2953, 2924, 2852, 1685, 1615, 1535, 1370, 1286, 1171, 1054, 841, 675 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.77 – 7.68 (m, 2H), 7.30 – 7.26 (m, 2H), 7.22 (d, J = 2.0 Hz, 1H), 6.88 (dt, J = 2.0, 1.0 Hz, 1H), 2.85 – 2.62 (m, 4H), 2.51 (t, J = 5.0 Hz, 2H), 2.39 (s, 3H), 2.30 – 2.22 (m, 1H), −0.26 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ = 206.7, 157.3, 145.3, 140.5, 136.0, 130.1, 126.9, 126.3, 124.9, 116.7, 116.6, 35.0, 25.3, 21.7, 21.6, 21.2, −2.3; HRMS (ESI+): m/z [M+H]+ calcd for C_{21}H_{28}NO_{3}Si: 400.1403; found: 400.1400.
5-(Trimethylsilyl)-7,8-dihydro-4H-indeno[5,4-c]thiophen-6(5H)-one (34)

8-(2-Bromoallylthio)-1-(trimethylsilylocta-1,6-diyn-3-one (15 mg, 0.043 mmol) and 1,2-epoxyhexane (0.05 mL, 0.4 mmol) in DCE (0.4 mL) were heated to 200 °C for 2 hours using a microwave reactor. The mixture was then concentrated under reduced pressure and the residue purified by column chromatography (15% ethyl acetate in hexane) to furnish the title compound as a pale yellow gum (6.5 mg, 0.025 mmol, 58%).

R_f = 0.15 (15% ethyl acetate in hexane); IR = (neat) 2958, 2924, 1686, 1603, 1350, 1250, 848 cm^{-1}; ^1H NMR (400 MHz, CDCl_3): δ = 7.35 (d, J = 2.5 Hz, 1H), 6.93 (ddd, J = 2.5, 2.0, 0.5 Hz, 1H), 3.08–2.90 (m, 3H), 2.81–2.74 (m, 1H), 2.57 (t, J = 5.0 Hz, 2H), 2.33 (ddt, J = 8.0, 2.5, 1.0 Hz, 1H), −0.17 (s, 9H); ^13C NMR (100 MHz, CDCl_3): δ = 207.4, 159.2, 140.3, 138.8, 136.7, 121.6, 119.4, 35.2, 26.1, 25.3, 22.2, −2.3; HRMS (Cl+): m/z [M+H]^+ calcd for C_{14}H_{18}OSSi: 262.0848; found: 262.0846.

To a stirred suspension of sodium hydride (311 mg, 13.0 mmol) in THF (20 mL) at 0 °C was added 4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-ol (800 mg, 2.59 mmol) as drops. The reaction mixture allowed to warm to room temperature over 1 hour, then cooled back down to 0 °C and 2,3-dibromopropene (622 mg, 3.11 mmol) was added as drops and the reaction was stirred overnight being allowed to warm to room temperature. Saturated ammonium chloride (20 mL) was added and the organics were extracted with ethyl acetate (3 × 70 mL) and washed with water (3 × 70 mL) and brine (70 mL) and dried over sodium sulfate and concentrated under reduced pressure. The crude was purified by flash column chromatography eluting in 5% diethyl ether in pentane. The product containing fractions were concentrated under reduced pressure yielding the title compound as a colourless oil (1.03 g, 2.41 mmol, 93%).

R_f = 0.43 (5% diethyl ether in pentane); IR = (neat) 2927, 1463, 1343, 1251, 1085, 835 cm^{-1}; ^1H NMR (400 MHz, CDCl_3): δ = 5.94 (m, 1H), 5.86 (d, J = 3.0 Hz, 1H), 5.84 (d, J = 3.0 Hz, 1H), 5.64 (m, 1H), 4.44 (tt, J = 6.7, 1.7 Hz, 1H), 4.24 (d, J = 1.6 Hz, 2H), 4.19 (m, 2H), 2.71 (t, J = 7.7 Hz, 2H), 2.25 (s, 3H), 2.00 (m, 2H), 0.91 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^13C NMR (100 MHz, CDCl_3): δ = 153.5, 150.5, 128.7, 118.6, 105.9,
105.8, 88.6, 79.5, 73.3, 62.2, 57.5, 37.0, 25.9, 23.9, 18.4, 13.7, −4.4, −4.9; HRMS (Cl+): m/z [M+NH₄]^+ calcd for C₆₀H₃₅BrNO₃Si: 444.1570; found: 444.1581.

1-(8-(tert-Butyldimethylsilyloxy)-3,6,7,8-tetrahydro-1H-indeno[4,5-c]furan-5-yl)propan-2-one (47)

To a stirred solution of triphenylphosphine (180 mg, 0.68 mmol), potassium carbonate (630 mg, 4.50 mmol) and (6-(2-bromoallylxy)-1-(5-methylfuran-2-yl)hex-4-yn-3-yloxy)(tert-butyldimethylsilane (1.0 g, 2.3 mmol) in acetonitrile (20 mL) was added palladium (II) acetate (50 mg, 0.23 mmol). The resulting mixture was heated at 80 °C for 5 hours and quenched with water (40 mL) and extracted with diethyl ether (3 × 50 mL). The combined organics were dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (10% diethyl ether in hexane) to yield the title compound as a orange/green viscous oil (230 mg, 0.65 mmol, 28%).

IR = (neat) 3403, 2928, 2854, 1709, 1412, 1358 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 6.94 (s, 1H), 5.35-5.25 (m, 2H), 5.10-5.02 (m, 3H), 3.68 (m, 2H), 2.90 (ddd, J = 15.5, 9.0, 2.0, 1H), 2.69-2.61 (m, 1H), 2.52-2.46 (m, 1H), 2.16 (s, 3H), 1.93 (dt, J = 12.5, 9.0, 7.5, 1H), 0.93 (s, 9H), 0.16 (d, J = 10.5, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 205.7, 140.8, 139.0, 134.6, 129.6, 121.4, 76.4, 72.9, 72.4, 48.4, 36.4, 29.3, 28.5, 25.8, 18.0, −4.2, −4.8.; HRMS (Cl+): m/z [M+Na]^+ calcd for C₂₀H₃₅BrNO₃SiNa: 369.1862; found: 369.1860.

Dimethyl 2-(2-bromoallyl)-2-(4-((tert-butyldimethylsilyl)oxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-yl)malonate (56)

To a stirred solution of triphenylphosphine (420 mg, 1.62 mmol) in THF (5 mL), a solution of DEAD (280 mg, 0.25 mL, 1.62 mmol) in THF (2 mL) was added dropwise at 0 °C. To this a mixture of 4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-ol (500 mg, 1.62 mmol) and dimethyl 2-(2-bromoallyl)malonate (410 mg, 1.62 mmol) in THF (2 mL) was added dropwise over 1 minute. The solution was allowed to warm to room temperature overnight. The solvent was then reduced under reduced pressure and the resulting oil was purified using column chromatography eluting with 20% diethyl ether in hexane to yield the title compound as a colourless oil (500 mg, 0.923, 57%).

IR = (neat) 2954, 1742, 1435 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 5.85 (d, J = 2.9 Hz, 1H), 5.84 (s, 1H), 5.82 (s, 1H), 5.62 (d, J = 1.5 Hz, 1H), 4.35 (t, J = 6.3 Hz, 1H), 3.75 (s, 6H), 3.29 (s, 2H), 2.96 (d, 2H), 2.68 (t, J = 7.7 Hz, 2H), 2.25 (s, 3H), 2.00-1.86 (m, 2H), 0.89 (s, 12H), 0.69 (d, J = 9.6 Hz, 6H); ¹³C NMR (100 MHz,
CDCl\textsubscript{3}): \( \delta = 169.5, 153.5, 150.3, 126.3, 122.7, 105.8, 105.5, 85.4, 78.6, 62.1, 56.1, 52.9, 43.0, 37.3, 25.7, 23.7, 22.5, 18.2, 13.5, -4.6, -5.1; \) HRMS (ESI\textsuperscript{+}): \( m/z [M+Na]^+ \) calcd for C\textsubscript{25}H\textsubscript{37}\textsubscript{79}BrNaO\textsubscript{5}Si: 563.1435; found: 563.1435.

**tert-Butyl (2-bromoallyl)(4-((tert-butylidemethylsilyl)oxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-yl)carbamate (57)**

![Chemical structure](attachment:image)

To a solution of \( N-(2\text{-bromoallyl})-4-(\text{tert-butylidemethylsilyloxy})-6-(5\text{-methylfuran-2-yl})\text{hex-2-yn-1-amine} \) (460 mg, 1.08 mmol) in ethanol (15 mL) was added di-tert-butyl dicarbonate (259 mg, 1.18 mmol). The reaction mixture was allowed to stir for 2 hours when TFE (108 mg, 0.08 mL, 1.08 mmol) and DMAP (13 mg, 0.11 mmol) were added in one portion. After 5 minutes the reaction mixture was quenched with water (20 mL) and extracted with diethyl ether (3 × 20 mL). The organic fractions were combined, dried over magnesium sulfate, filtered and concentrated under reduced pressure to give an oil that was purified with flash column chromatography eluting with 20% diethyl ether in hexane to give the title compound as a colourless oil (518 mg, 0.983 mmol, 91%).

IR = (neat) 2930, 2856, 1701, 1402 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta = 5.86 \ (d, J = 2.9 \text{ Hz}, 1 \text{H}), 5.84 \ (s, 1 \text{H}), 5.76 \ (d, J = 12.6 \text{ Hz}, 1 \text{H}), 5.58 \ (s, 1 \text{H}), 4.41 \ (t, J = 6.3 \text{ Hz}, 1 \text{H}), 4.17 \ (s, 3 \text{H}), 4.06 \ (s, 1 \text{H}), 2.73-2.69 (m, 2 \text{H}), 2.25 \ (s, 3 \text{H}), 2.00-1.95 (m, 2 \text{H}), 1.48 \ (s, 9 \text{H}), 0.19 \ (s, 9 \text{H}), 0.11 \ (d, J = 10.4 \text{ Hz}, 6 \text{H}); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta = 153.4, 150.3, 129.1, 117.5, 105.8, 105.6, 85.2, 80.9, 53.3, 37.0, 35.5, 28.3, 25.8, 23.8, 18.2, 13.5, -4.5, -5.0; \) HRMS (ESI\textsuperscript{+}): \( m/z [M+Na]^+ \) calcd for C\textsubscript{25}H\textsubscript{46}\textsubscript{79}BrNO\textsubscript{5}SiNa: 548.1802; found: 548.1802.

\((6-(2\text{-bromoallylthio})-1-(5\text{-methylfuran-2-yl})\text{hex-4-yn-3-yl}oxy)(\text{tert-butyl})\text{dimethylsilane (58)}\)

![Chemical structure](attachment:image)

To a solution of \( S-4-(\text{tert-butylidemethylsilyloxy})-6-(5\text{-methylfuran-2-yl})\text{hex-2-ynyl} \) ethanethioate (3.30 g, 9.00 mmol) in methanol (75 mL) was added sodium methoxide (486 mg, 9.90 mmol) at rt. The reaction mixture was allowed to stir for 30 minutes whereupon 2,3-dibromopropene (879 mg, 1.8 mL, 9.0 mmol) was added and allowed to stir for a further hour. The reaction mixture was then quenched with water (75 mL) and extracted with diethyl ether (3 × 75 mL). The combined organic fractions were washed with brine, dried over magnesium sulfate, filtered and concentrated under reduced pressure to yield the title compound as a colourless oil (3.94 g, 8.88 mmol, 99%).

IR = (neat) 2927, 2855, 1713, 1620, 1570, 1251, 1087 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta = 5.88-5.82 (m, 3 \text{H}), 5.57 \ (d, J = 1.6 \text{ Hz}, 1 \text{H}), 4.43 \ (tt, J = 6.7, 1.7 \text{ Hz}, 1 \text{H}), 3.62 \ (s, 2 \text{H}), 3.28 \ (d, J = 1.8 \text{ Hz}, 2 \text{H}), 2.74-2.70 (m, 2 \text{H}), 2.25 \ (s, 3 \text{H}), 2.02-1.96 (m, 2 \text{H}), 0.92 \ (s, 9 \text{H}), 0.12 \ (d, J = 12.7 \text{ Hz}, 6 \text{H}); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}):
δ = 153.4, 150.3, 128.6, 119.4, 105.8, 105.6, 84.9, 79.3, 62.2, 41.2, 37.1, 25.8, 18.9, 18.2, 13.5, −4.5, −5.1; HRMS (ESI+): m/z [M+Na]+ calcd for C_{20}H_{31}BrO_2SSiNa: 465.0890; found: 465.0890.

**Dimethyl 8-(tert-butyldimethylsilyloxy)-5-(2-oxopropyl)-3,6,7,8-tetrahydroas-indacene-2,2(1H)-dicarboxylate (59)**

Dimethyl 2-(2-bromoallyl)-2-(4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-ynyl)malonate (400 mg, 0.74 mmol), DPPE (60 mg, 0.15 mmol), palladium (II) acetate (17 mg, 0.074 mmol), potassium carbonate (200 mg, 1.5 mmol) was heated to 120 °C in DMF (50 mL) for 25 minutes. The reaction mixture was then diluted with water (500 mL) and extracted with Et_2O (3 × 250 mL), dried over MgSO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (40% Et_2O/hexane) to yield the title compound as a colourless oil (110 mg, 0.24 mmol, 32%).

**IR = (neat) 2954, 2856, 1734, 1472 cm^{-1}; ^1H NMR (400 MHz, CDCl_3): δ = 6.92 (s, 1H), 5.34 (t, J = 6.5 Hz, 1H), 3.76 (m, 7H), 3.67-3.45 (m, 5H), 2.88 (ddd, J = 15.5, 9.0, 3.0 Hz, 1H), 2.60 (dt, J = 16.0, 8.0, 1H), 2.48-2.39 (m, 1H), 2.14 (s, 3H), 1.93 (dt, J = 13.0, 8.5, 6.5 Hz, 1H), 0.94 (s, 9H), 0.18 (d, J = 22.0 Hz, 6H); ^13C NMR (100 MHz, CDCl_3): δ = 206.1, 172.4, 172.1, 141.0, 140.9, 139.7, 135.6, 129.2, 124.8, 76.3, 60.5, 52.9, 52.8, 48.6, 40.1, 38.8, 36.1, 29.3, 25.9, 18.0, −4.1, −4.7; HRMS (ESI+): m/z [M+Na]+ calcd for C_{20}H_{31}BrO_2SSiNa: 483.2179; found: 483.2200.

**tert-Butyl 8-(tert-butyldimethylsilyloxy)-5-(2-oxopropyl)-3,6,7,8-tetrahydrocyclopenta[e]isoindole-2(1H)-carboxylate (60)**

To a stirring solution of tert-butyl 2-bromoallyl(4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-ynyl)carbamate (500 mg, 0.95 mmol), DPPE (75 mg, 0.19 mmol), potassium carbonate (260 mg, 1.9 mmol) in DMF (25 mL) was added palladium (II) acetate (22 mg, 0.095 mmol). The reaction mixture was heated to 87 °C for 4 hours and diluted with water (250 mL) whereupon it was then extracted with Et_2O (3 × 100 mL). The combined organic layers were dried over MgSO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (20% Et_2O in hexane) to yield the title compound as a white solid (150 mg, 0.34 mmol, 35%).

**MP = 112-115 °C; IR = (neat) 2929, 2857, 1697, 1472, 1399 cm^{-1}; ^1H NMR (400 MHz, CDCl_3): δ = 6.95 (d, J
= 24.5 Hz, 1H), 5.34 (t, J = 7.5 Hz, 1H), 4.84 (dd, J = 23.0, 15.0 Hz, 1H), 4.69-4.99 (m, 3H), 3.67 (d, J = 2.5 Hz, 2H), 2.96-2.82 (m, 1H), 2.69-2.58 (m, 1H), 2.55-2.43 (m, 1H), 2.16 (s, 3H), 1.93 (ddt, J = 17.5, 12.5, 9.0 Hz, 1H), 1.52 (d, J = 3.0 Hz, 9H), 0.95 (d, J = 9.5 Hz, 9H), 0.18 (d, J = 21.5 Hz, 6H); 13C NMR (100 MHz, CDCl3): δ = 205.6, 154.6, 140.7, 140.0, 136.7, 132.9, 129.8, 123.2, 79.5, 76.6, 51.3, 48.4, 36.4, 29.3, 28.6, 28.5, 28.4, 25.9, 18.0, -4.1, -5.0; HRMS (ESI+): m/z [M+Na]+ calcd for C25H39NNaO4Si: 468.2546; found: 468.2541.

(E)-4-(4-(tert-Butyldimethylsilyloxy)-1,3,4,5,6,6a-hexahydropentaleno[1,2-c]thiophen-6a-yl-1,1-dioxide)but-3-en-2-one (61)

To a solution of (6-(2-bromoallylthio)-1-(5-methylfuran-2-yl)hex-4-yn-3-yl)oxy)(tert-butyl)dimethylsilylane (1.0 g, 2.3 mmol), DPPE (180 mg, 0.45 mmol), potassium carbonate (620 mg, 4.5 mmol) in DMF (40 mL) was added palladium (II) acetate (50 mg, 0.23 mmol). The reaction mixture was heated to 120 °C for 30 minutes and then diluted down with water (400 mL). The mixture was then extracted with diethyl ether (3 x 200 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was then purified by column chromatography (0-50% diethyl ether in hexane) to give the title compound as a bright yellow viscous oil (360 mg, 0.90 mmol, 40%.

IR = (neat) 3405, 2927, 2855, 1666, 1590, 1462, 1252 cm⁻¹; 1H NMR (400 MHz, CDCl3): δ = 7.23 (d, J = 16.0 Hz, 1H), 6.51 (s, 1H), 6.10 (d, J = 16.0 Hz, 1H), 4.97 (dd, J = 4.5, 2.5 Hz, 1H), 4.96-4.92 (m, 1H), 4.76 (t, J = 3 Hz, 1H), 4.10 (t, J = 3.0 Hz, 2H), 2.74-2.65 (m, 1H), 2.45-2.37 (m, 1H), 2.37-2.29 (m, 1H), 2.27 (s, 3H), 1.85-1.77 (m, 1H), 0.87 (s, 9H), 0.03 (d, 6H); 13C NMR (100 MHz, CDCl3): δ = 198.8, 150.8, 146.9, 138.9, 137.9, 135.5, 131.3, 129.3, 105.7, 79.1, 37.2, 33.0, 29.4, 27.1, 25.8, 18.1, -4.8, -4.8; HRMS (ESI+): m/z [M+Na]+ calcd for C20H30NaO4Si: 417.1532; found: 417.1548.

tert-Butyldimethyl(1-(5-ethylfuran-2-yl)-6-(prop-2-ynyloxy)hex-4-yn-3-yl)oxy)silane (74)

To a solution of 4-(tert-butyldimethylsilyloxy)-6-(5-ethylfuran-2-yl)hex-2-yn-1-ol (100 mg, 0.310 mmol) in THF (6 mL) at 0 °C was added sodium hydride (62 mg, 1.6 mmol) was added in portions. The solution was then allowed to warm to room temperature, and subsequently cooled back down to 0 °C, then propargyl bromide (80% in toluene, 40 μL, 0.31 mmol) was added as drops. The resultant solution was allowed to warm to room temperature and stirred overnight. Water was added, and the organics were extracted with diethyl ether (3 x 10 mL). The combined organics were washed with brine, dried over MgSO4, filtered and concentrated under reduced pressure. The crude material was purified by column chromatography (10% diethyl ether in pentane) to obtain the title compound as a colourless oil (56 mg, 0.16 mmol, 50%).
**5-(2-Oxobutyl)-6,7-dihydro-1H-indeno[4,5-c]furan-8(3H)-one (77)**

A microwave vial was charged with tert-butyldimethyl(1-(5-ethylfuran-2-yl)-6-(prop-2-ynyl)oxy)hex-4-yn-3-yl)oxy)silane (32 mg, 0.09 mmol) and acetonitrile (4.9 mL). A single drop of water was then added. The vial was placed in a microwave reactor for 5 hours at 200 °C. The resultant solution was concentrated under reduced pressure and the crude material was then purified via column chromatography (50% ethyl acetate in pentane) to afford the title compound as an off white solid (14 mg, 0.06 mmol, 63%).

**((6-(But-2-yn-1-yl oxy)-1-(5-methylfuran-2-yl)hex-4-yn-3-yl)oxy)(tert-butyldimethyl)silyloxy) (83)**

4-(tert-Butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-ol (135 mg, 0.438 mmol) was added as drops to a suspension of sodium hydride (60% dispersion in mineral oil, 88 mg, 2.2 mmol) in THF (5 mL) at 0 °C and stirred for 30 minutes. 1-Bromo-2-butylene (64 mg, 42 μL, 0.48 mmol) was added and the reaction was stirred for 2 hours before being allowed to warm to room temperature and stirred overnight. Water (5 mL) was added and the organics were extracted with ethyl acetate (3 × 30 mL) and washed with water (3 × 30 mL) and brine (30 mL), dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude material was purified with flash column chromatography eluting in 5% diethyl ether in petroleum ether. The product containing fractions were concentrated under reduced pressure yielding the title compound as a colourless oil (93 mg, 0.26 mmol, 59%).
2H), 4.19 (q, J = 2.3 Hz, 2H), 2.75 – 2.67 (m, 2H), 2.24 (d, J = 1.0 Hz, 3H), 2.02 – 1.93 (m, 2H), 1.86 (t, J = 2.3 Hz, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); 13C NMR (100 MHz, CDCl3): δ = 153.6, 150.5, 105.9, 105.7, 88.2, 83.2, 79.7, 74.5, 62.2, 57.1, 56.8, 37.0, 26.0, 24.0, 18.4, 13.7, 3.8, –4.4, –4.9; HRMS (ESI+): m/z [M+H]+ calcd for C21H33O3Si: 361.2199; found: 361.2201.

4-((tert-Butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-yl)propiolate (85)

To an ice cooled solution of 4-((tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-ol (100 mg, 0.324 mmol) and 3-(naphthalen-1-yl)propionic acid (82 mg, 0.42 mmol) in DCM (10 mL) under nitrogen was added N,N'-dicyclohexylcarbodiimide (86 mg, 0.42 mmol) and 4-(dimethylamino)pyridine (4 mg, 0.03 mmol) and the reaction was stirred for 18 hours. The reaction mixture was filtered through celite® and concentrated under reduced pressure. The crude material was purified by column chromatography (5% diethyl ether in pentane) yielding the title compound as a colourless oil (90 mg, 0.19 mmol, 59%).

Rf = 0.60 (20% diethyl ether in pentane); IR (neat) 2928, 2215, 1716, 1290, 1195, 1166, 1086 cm⁻¹; ¹H NMR (400 MHz, CDCl3): δ = 8.34 (dq, J = 8.4, 1.0 Hz, 1H), 7.97 (dd, J = 8.4, 1.1 Hz, 1H), 7.88 (td, J = 7.3, 1.4 Hz, 2H), 7.64 (dd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.57 (dd, J = 8.1, 6.9, 1.3 Hz, 1H), 7.48 (dd, J = 8.3, 7.2 Hz, 1H), 5.88 (1H, d, J = 3.0 Hz, 1H), 5.84 (dq, J = 3.0, 1.0 Hz, 1H), 4.91 (d, J = 1.7 Hz, 2H), 4.47 (tt, J = 6.6, 1.7 Hz, 1H), 2.74 (dd, J = 8.8, 6.5 Hz, 2H), 2.25 (d, J = 1.1 Hz, 3H), 2.06 – 1.98 (m, 2H), 0.92 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H); 13C NMR (100 MHz, CDCl3): δ = 153.46, 150.5, 133.8, 133.4, 133.1, 131.7, 128.6, 127.9, 127.1, 125.9, 125.2, 117.1, 106.0, 105.9, 89.2, 85.9, 84.8, 77.6, 62.1, 53.9, 36.8, 26.0, 23.9, 18.4, 13.7, –4.4, –4.9; HRMS (ESI+): m/z [M+Na]+ calcd for C30H34O4SiNa: 509.2124; found: 509.2134.

4-Methyl-5-(2-oxopropyl)-1,3,6,7-tetrahydro-8H-indeno[4,5-c]furan-8-one (86)

A microwave vial charged with (6-(but-2-yn-1-yl)oxy)-1-(5-methylfuran-2-yl)hex-4-yn-3-yl)oxy)(tert-butyldimethylsilane (50 mg, 0.14 mmol), acetonitrile (4.9 mL) and water (0.05 mL) was heated to 200 °C for 5 hours under microwave conditions. The solution was concentrated under reduced pressure and the crude material was purified by column chromatography (7.5% ethyl acetate in DCM) to give the title compound as a white solid (16 mg, 0.065 mmol, 48%).
**R**f = 0.20 (10% ethyl acetate in DCM); **IR** = (neat) 2925, 2850, 1716, 1602, 1360, 1140 cm\(^{-1}\); \(^1^H\) NMR (400 MHz, CDCl\(_3\)): \(\delta = 5.40\) and 5.36 (t, \(J = 2.5\) Hz, 2H), 5.09 (m, 2H), 3.85 and 3.82 (s, 2H), 3.01 (m, 2H), 2.69 (m, 2H), 2.27 and 2.26 (s, 3H), 2.18 (s, 3H). *Some peaks are doubled due to the presence of rotamers.*

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 206.5, 204.8, 154.5, 139.6, 137.4, 135.8, 130.3, 128.1, 73.9, 73.1, 72.6, 47.3, 36.5, 36.3, 30.0, 29.8, 25.8, 25.3, 16.9. *Some peaks are doubled due to the presence of rotamers.*

**HRMS** (ESI+): \(m/z\) [M+H]\(^+\) calcd for C\(_{15}\)H\(_{16}\)O\(_3\): 244.1094; found: 244.1103.

4-(Naphthalen-1-yl)-5-(2-oxopropyl)-6,7-dihydro-1H-indeno[4,5-c]furan-3,8-dione (88)

A microwave vial charged with 4-((tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-yl 3-(naphthalen-1-yl) propiolate (65 mg, 0.13 mmol), acetonitrile (4.9 mL) and water (0.05 mL) was heated to 200 °C for 2 hours under microwave conditions. The solution was concentrated under reduced pressure and the crude material was purified by column chromatography (7.5% ethyl acetate in DCM) to yield the title compound as a white solid (23 mg, 0.062 mmol, 48%).

**R**f = 0.37 (10% ethyl acetate in DCM); **IR** = (neat) 2924, 1763, 1706, 1609, 1358, 1101 cm\(^{-1}\); \(^1^H\) NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.96\) (dd, \(J = 8.5, 1.0\) Hz, 1H), 7.93 (d, \(J = 8.5\) Hz, 1H), 7.55 (dd, \(J = 8.5, 7.0\) Hz, 1H), 7.49 (dd, \(J = 8, 7, 1.0\) Hz, 1H), 7.34 (dd, \(J = 8, 7, 1.5\) Hz, 1H), 7.19 (dd, \(J = 7.0, 1.0\) Hz, 1H), 7.13 (dd, \(J = 8.5, 1.0\) Hz, 1H), 5.59 (d, \(J = 1.0\) Hz, 2H), 3.61 (1H, d, \(J = 17.5\) Hz), 3.46 (1H, d, \(J = 17.5\) Hz), 3.17 (m, 2H), 2.85 (m, 2H), 1.81 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 205.6, 204.4, 168.3, 161.5, 145.5, 144.1, 134.8, 133.4, 132.5, 131.6, 131.4, 129.3, 128.8, 126.8, 126.6, 126.4, 125.3, 124.9, 124.7, 124.3, 68.4, 43.8, 36.4, 30.2, 26.7; **HRMS** (ESI+): \(m/z\) [M+H]\(^+\) calcd for C\(_{24}\)H\(_{19}\)O\(_4\): 371.1283; found: 371.1281.

**tert-Butyldimethyl((5-(prop-2-yn-1-yl)oxy)pent-3-yn-2-yl)oxy)silane (102)**

To 4-(tert-butyldimethylsilyloxy)pent-2-yn-1-ol (0.55 g, 2.6 mmol) dissolved in THF (15 mL), was added sodium hydride (60% on mineral oil, 0.21 g, 5.2 mmol) slowly at 0 °C. After warming to room temperature over 1 hour, the solution was cooled back to 0 °C and propargyl bromide (80% in toluene, 0.30 ml, 2.6 mmol) was added dropwise. The reaction mixture was left to warm to room temperature overnight and then quenched with water. The mixture was extracted with diethyl ether, the organic layer washed with brine and dried with magnesium sulfate. Removal of the solvent yielded a colourless to yellow oil (0.65 g, 2.6 mmol, 99%).
$R_f = 0.70$ (20% diethyl ether in petrol); IR = (neat) 3311 (CC-H), 2930, 2119, 1472, 1370, 1342, 1256, 1153, 1102, 1080, 1020 cm$^{-1}$; $^1H$ NMR (400 MHz, CDCl$_3$): $\delta$ = 4.56 (qt, $J$ = 6.6, 1.7 Hz, 1H), 4.29 (d, $J$ = 1.6 Hz, 2H), 4.25 (d, $J$ = 2.5 Hz, 2H), 2.44 (t, $J$ = 2.4 Hz, 1H), 1.42 (d, $J$ = 6.5 Hz, 3H), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); $^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta$ = 89.8, 79.1, 78.2, 75.0, 59.1, 57.0, 56.4, 25.9, 25.5, 18.4, −4.5, −4.80; HRMS (Cl+) : $m/z$ [M+H]$^+$ calcd for C$_{14}$H$_{23}$O$_2$Si: 251.1467; found: 251.1458.

(But-3-yn-2-yloxy)(tert-butyldimethylsilane) (108)

3-Butyn-2-ol (5.0 ml, 62 mmol) was dissolved in DCM (120 ml), and tert-butyldimethylsilyl chloride (12 g, 74 mmol), imidazole (5.1 g, 74 mmol), and DMAP (0.78 g, 6.2 mmol) were added at room temperature. After stirring for 24 hours, the reaction was quenched with water, the organic layer washed twice with water and brine, dried with MgSO$_4$, filtered and concentrated. The crude was then dissolved in petrol, washed with 2 M hydrochloric acid$_{(aq)}$, saturated ammonium chloride$_{(aq)}$, brine, dried with MgSO$_4$ and concentrated under reduced pressure yielding a colourless oil (10 g, 54 mmol, 88%).

$R_f = 0.50$ (5% diethyl ether in petrol); IR = (neat) 3313, 2931, 1252, 1103 cm$^{-1}$; $^1H$ NMR (400 MHz, CDCl$_3$): $\delta$ = 4.51 (qd, $J$ = 6.6, 2.1 Hz, 1H), 2.37 (d, $J$ = 2.0 Hz, 1H), 1.42 (d, $J$ = 6.6 Hz, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H); $^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta$ = 86.6, 71.3, 59.0, 25.9, 25.5, 18.4, −4.5, −4.9; HRMS (Cl+) : $m/z$ [M+H]$^+$ calcd for C$_{10}$H$_{24}$NOSi: 202.1627; found: 202.1621.

4-((tert-Butyldimethylsilyl)oxy)pent-2-yn-1-ol (109)

(But-3-yn-2-yloxy)(t-butyldimethylsilane) (2.3 g, 12 mmol) was dissolved in THF (50 ml) and cooled to −78 °C. n-Butyllithium (2.0 M, 7.5 ml, 15 mmol) was added as drops, and the reaction mixture was warmed to −30 °C over 2 hours. After cooling back to −78 °C, paraformaldehyde (0.45 g, 15 mmol) was added, and the reaction mixture warmed to room temperature overnight. After quenching with water, the mixture was extracted with diethyl ether, the organic layer washed with brine and dried with magnesium sulfate. After solvent removal, the crude was purified using flash column chromatography (5-20% diethyl ether in petrol) to yield a pale yellow oil (2.0 g, 9.3 mmol, 73%).

$R_f = 0.15$ (20% diethyl ether in petrol); IR = (neat) 3337, 2930, 1473, 1253, 1154, 1100, 1032 cm$^{-1}$; $^1H$ NMR (400 MHz, CDCl$_3$): $\delta$ = 4.56 (qt, $J$ = 6.6, 1.7 Hz, 1H), 4.28 (d, $J$ = 1.7 Hz, 2H), 1.57 (s, 1 H), 1.41 (d, $J$ = 6.5 Hz, 3H), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); $^{13}C$ NMR (100 MHz, CDCl$_3$): $\delta$ = 88.6, 81.4, 59.1, 51.3, 26.0, 25.5, 18.4, −4.4, −4.8; HRMS (Cl+) : $m/z$ [M+H]$^+$ calcd for C$_{15}$H$_{27}$O$_2$Si: 213.1311; found: 213.1310.
1-(4-Methylfuran-3-yl)propan-2-one (110)

\[
\begin{align*}
\text{H} & \quad \text{O} \\
\text{H} & \quad \text{O}
\end{align*}
\]

tert-Butyldimethyl(5-(prop-2-ynyloxy)pent-3-yn-2-yloxy)silane (55 mg, 0.22 mmol) was dissolved in acetonitrile (2 mL) in a microwave vial; a drop of water was added and the vial purged with nitrogen. The mixture was heated at 190 °C in the microwave for 1 hour. After removal of the solvent, the crude mixture was purified using flash column chromatography (0-50% ethyl acetate in petrol) to yield the title compound 110 as a pale yellow oil (12 mg, 0.087 mmol, 40%) and 111 as a yellow oil (5 mg, 0.036 mmol, 15%).

\[
R_f = 0.70 \text{ (50% ethyl acetate in petrol); } \text{IR} = \text{(neat) 2928, 1716, 1361, 1165, 1049 cm}^{-1}; \text{ } \text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 7.32 \text{ (m, 1H), 7.20 (m, 1H), 3.47 (s, 2H), 2.18 (s, 3H), 1.92 (d, } J = 1.0 \text{ Hz, 3H); } \text{C NMR (100 MHz, CDCl}_3\text{): } \delta = 206.0, 141.0, 140.1, 120.1, 118.4, 38.9, 29.2, 8.2; \text{ } \text{HRMS (EI+): } m/z [M] C_{8}H_{10}O_{2} \text{ calcd for 138.0675; found: 138.0686.}
\]

1,6,7,7a-Tetrahydroisobenzofuran-5(3H)-one (111)

\[
\begin{align*}
\text{O} & \quad \text{O}
\end{align*}
\]

A yellow oil (5 mg, 0.04 mmol, 15%).

\[
R_f = 0.15 \text{ (50% ethyl acetate in petrol); } \text{IR} = \text{(neat) 2941, 1677, 1667, 1373, 1194, 1051 cm}^{-1}; \text{ } \text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 5.94 \text{ (m, 1H), 4.67 (dt, } J = 16.5, 1.5 \text{ Hz, 1H), 4.43 (dt, } J = 16.5, 1.5 \text{ Hz, 1H), 4.31 (t, } J = 8.5 \text{ Hz, 1H), 3.36 (dd, } J = 10.5, 8.5 \text{ Hz, 1H), 3.02-2.93 (m, 1H), 2.57-2.52 (m, 1H), 2.38 (ddd, } J = 17, 14.5, 5 \text{ Hz, 1H), 2.23 (dtd, } J = 12, 5, 2.5 \text{ Hz, 1H), 1.70 (dddd, } J = 14.5, 13, 11.5, 4.5 \text{ Hz, 1H); } \text{C NMR (100 MHz, CDCl}_3\text{): } \delta = 198.6, 168.8, 119.9, 73.2, 69.8, 41.7, 36.7, 25.6; \text{ } \text{HRMS (EI+): } m/z [M]^+ \text{ calcd for C}_{8}H_{10}O_{2}: 138.0675; \text{ found: 138.0686.}
\]

S-(4-((tert-Butyldimethylsilyl)oxy)pent-2-yn-1-yl) ethanethioate (118)

\[
\begin{align*}
\text{OTBS} & \quad \text{O} \\
\text{H} & \quad \text{S}
\end{align*}
\]

To a solution of triphenylphosphine (1.2 g, 4.7 mmol) in THF (24 mL) at 0 °C was added DIAD (0.92 mL, 4.7 mmol) dropwise, and the mixture stirred at 0 °C for 30 minutes. 4-((tert-Butyldimethylsilyloxy)pent-2-yn-1-ol (0.50 g, 2.3 mmol) in THF (2 mL) was added slowly, followed by the dropwise addition of thioacetic
acid (0.34 mL, 4.7 mmol). Upon completion, the solvent was removed under reduced pressure and the crude mixture was purified using flash chromatography (0-2.5% diethyl ether in petrol) to yield a colourless oil (0.60 g, 2.2 mmol, 95%).

R_f = 0.50 (10% ethyl acetate in petrol); IR = (neat) 2930, 1699, 1251, 1100 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 4.50 (qt, J = 6.4, 1.9 Hz, 1H), 3.67 (d, J = 2.0 Hz, 2H), 2.34 (s, 3H), 1.37 (d, J = 6.5 Hz, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 194.3, 85.6, 77.9, 59.2, 30.3, 26.0, 25.4, 18.4, 18.1, −4.4, −4.8; HRMS (EI−): m/z [M−H]⁻ calcd for C₁₃H₂₃O₂SiS: 271.1194; found: 271.1193.

tert-Butyldimethyl((5-(prop-2-yn-1-ylthio)pent-3-yn-2-yl)oxy)silane (119)

S-4-(t-Butyldimethylsilyloxy)pent-2-ynyl ethanethioate (0.30 g, 1.1 mmol) was dissolved in methanol (10 mL) and potassium carbonate (0.46 g, 3.3 mmol) was added at room temperature. After consumption of the starting material by TLC (3 hours), propargyl bromide (80% in toluene, 0.13 mL, 1.2 mmol) was added in one portion. Upon completion by TLC, the reaction was quenched with water, extracted with diethyl ether, the organic layer washed with brine and then dried with magnesium sulfate. Removal of the solvent afforded a colourless oil (0.23 g, 0.86 mmol, 76%).

R_f = 0.55 (10% ethyl acetate in petrol); IR = (neat) 3310, 2930, 1472, 1252, 1101 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 4.54 (qt, J = 6.5, 1.9 Hz, 1H), 3.45 (d, J = 1.8 Hz, 2H), 3.40 (d, J = 2.6 Hz, 2H), 2.24 (t, J = 2.6 Hz, 1H), 1.40 (d, J = 6.5 Hz, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 86.2, 79.4, 78.2, 71.4, 59.3, 26.0, 25.6, 19.5, 19.0, 18.4, −4.5, −4.8; HRMS (Cl+): m/z [M+NH₄]⁺ calcd for C₁₄H₂₈NOSiS: 286.1655; found: 286.1672.

1-(4-Methylthiophen-3-yl)propan-2-one (120)

tert-Butyldimethyl(5-(prop-2-ynylthio)pent-3-yn-2-yloxy)silane (50 mg, 0.19 mmol) was dissolved in acetonitrile (2 mL) in a microwave vial. A drop of water was added, the vial purged with nitrogen, and the mixture heated in the microwave for 6 hours at 200 °C. The solvent was removed and the crude mixture purified by flash chromatography (20% ethyl acetate in petrol) to yield the title compound 120 as a yellow gum (6 mg, 0.04 mmol, 21%).

R_f = 0.40 (20% ethyl acetate in petrol); IR = (neat) 2927, 1709, 1356, 1158, 1100 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ = 7.07 (d, J = 3.5 Hz, 1H), 6.96-6.94 (m, 1H), 3.64 (s, 2H), 2.15 (s, 3H), 2.14 (d, J = 1.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 206.0, 137.1, 134.1, 123.7, 122.0, 44.4, 29.3, 14.6.; HRMS (Cl+): m/z [M+NH₄]⁺ calcd for C₈H₁₄NOS: 172.0791; found: 172.0799.
8-Thiabicyclo[4.3.0]non-1-en-3-one (121)

*tert*-Butyldimethyl(5-(prop-2-ynylthio)pent-3-yn-2-yloxy)silane (0.20 g, 0.74 mmol) was dissolved in acetonitrile (4 mL) in a microwave vial. 2 drops of water were added, the vial purged with nitrogen, and the mixture heated in the microwave for 6 hours at 200 °C. The solvent was removed and the crude mixture purified by flash column chromatography (10-20% ethyl acetate in petrol) to yield a pale yellow to yellow gum (13 mg, 0.084 mmol, 11%).

\[ R_f = 0.15 \text{ (20\% ethyl acetate in petrol); IR = (neat) 2926, 1664, 1321, 1251, 1194 cm}^{-1}; {^1H} \text{ NMR (400 MHz, CDCl}_3\text{): } \delta = 6.00-5.99 \text{ (m, 1H), 3.85-3.70 \text{ (m, 2H), 3.15 \text{ (dd, J = 11.0, 7.5 Hz, 1H), 3.06-2.97 \text{ (m, 1H), 2.66 \text{ (t, J = 10.5 Hz, 1H), 2.55-2.48 \text{ (m, 1H), 2.40-2.31 \text{ (m, 2H), 1.82-1.71 \text{ (m, 1H); } {^{13}}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta = 198.9, 168.3, 123.6, 45.2, 36.8, 36.4, 35.8, 28.8; HRMS (Cl+) m/z [M+NH}_4\text{]+ calcd for C}_8\text{H}_{14}\text{NOS: 172.0791; found: 172.0794.} \]

4-Methyl-N,N-di(prop-2-yn-1-yl)benzenesulfonamide (122)

To a solution of *p*-toluenesulfonamide (2.1 g, 12 mmol) dissolved in acetone (50 mL), was added caesium carbonate (12 g, 36 mmol) and propargyl bromide (80% in toluene, 3.8 mL, 36 mmol) at room temperature. After 3 days the reaction was quenched with water and extracted with ethyl acetate, and the organic layer washed with brine and dried with magnesium sulfate. The solvent was removed and the crude mixture purified using flash column chromatography (0-20% ethyl acetate in petrol) to yield a pale yellow solid (2.2 g, 8.9 mmol, 77%).

\[ R_f = 0.30 \text{ (20\% ethyl acetate in petrol); IR = (neat) 3278, 2986, 2120, 1597, 1342, 1158 cm}^{-1}; \text{ MP = 53-54 °C; } {^1H} \text{ NMR (400 MHz, CDCl}_3\text{): } \delta = 7.72-7.70 \text{ (m, 2H), 7.31-7.28 \text{ (m, 2H), 4.16 \text{ (d, J = 2.5 Hz, 4H), 2.42 \text{ (s, 3H), 2.15 \text{ (t, J = 2.4 Hz, 2H); } {^{13}}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta = 144.1, 135.3, 129.7, 128.0, 76.3, 74.2, 36.3, 21.7; HRMS (El+): m/z [M+] calcd for C}_3\text{H}_{13}\text{NO}_2\text{S: 247.0662; found: 247.0671.} \]
$N$-(4-hydroxypent-2-yn-1-yl)-4-methyl-$N$-(prop-2-yn-1-yl)benzenesulfonamide (123)

![Chemical Structure](image)

4-Methyl-$N,N$-di(prop-2-ynyl)benzenesulfonamide (0.25 g, 1.0 mmol) was dissolved in THF (10 mL) and cooled to -78 °C, to which was added lithium HMDS (1.0 M, 1.0 mL, 1.0 mmol) dropwise. After 1 hour at -78 °C, acetaldehyde (50 µL, 1.0 mmol) was added dropwise, and the reaction mixture warmed slowly to room temperature over 4 hours before quenching with saturated ammonium chloride (aq). The mixture was extracted with ethyl acetate, the organic layer washed with water and brine, dried with magnesium sulfate, filtered and concentrated. Flash chromatography (20-40% ethyl acetate in petrol) yielded a yellow oil (0.19 g, 0.65 mmol, 65%).

$R_f = 0.25$ (40% ethyl acetate in petrol); $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.74-7.72 (m, 2H), 7.32 (d, $J = 7.9$ Hz, 2H), 4.33 (qt, $J = 6.4, 1.7$ Hz, 1H), 4.20 (d, $J = 1.7$ Hz, 2H), 4.14 (d, $J = 2.4$ Hz, 2H), 2.43 (s, 3H), 2.16 (t, $J = 2.4$ Hz, 1H), 1.28 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 144.13, 135.56, 129.69, 128.14, 87.89, 76.53, 76.51, 74.13, 58.25, 36.61, 36.52, 24.12, 21.69.

$N$-(4-((tert-butyldimethylsilyl)oxy)pent-2-yn-1-yl)-4-methyl-$N$-(prop-2-yn-1-yl)benzenesulfonamide (124)

![Chemical Structure](image)

$N$-(4-Hydroxypent-2-ynyl)-4-methyl-$N$-(prop-2-ynyl)benzenesulfonamide (0.19 g, 0.65 mmol) was dissolved in dichloromethane (3 mL), and tert-butyldimethylsilyl chloride (0.13 g, 0.84 mmol) and imidazole (61 mg, 0.89 mmol) were added at room temperature. After stirring overnight, the reaction was quenched with saturated ammonium chloride (aq), extracted with diethyl ether, the organic layer washed with brine and dried with magnesium sulfate. After concentration, the crude was purified by flash column chromatography (5-10% ethyl acetate in petrol) to yield a colourless to pale yellow oil (0.22 g, 0.54 mmol, 82%).

$R_f = 0.30$ (10% ethyl acetate in petrol); IR = (neat) 3294, 2929, 2126, 1599, 1472, 1355, 1254, 1166, 1102 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.72-7.70 (m, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 4.34 (qt, $J = 7.0, 1.5$ Hz, 1H).
1H), 4.18 (dd, J = 3.5, 1.8 Hz, 2H), 4.14-4.07 (m, 2H), 2.42 (s, 3H), 2.13 (t, J = 2.5 Hz, 1H), 1.24 (d, J = 6.5 Hz, 3H), 0.87 (s, 9H), 0.06 (s, 3H) 0.05 (s, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): δ = 143.9, 135.5, 129.7, 128.1, 88.7, 76.4, 75.5, 74.0, 58.9, 36.7, 36.3, 25.9, 25.3, 21.7, 18.3, –4.6, –4.9; HRMS (ESI\(^+\)): m/z [M+H]\(^+\) calcd for C\(_{21}\)H\(_{32}\)NO\(_3\)SSi: 406.1867; found: 406.1872.

\(\text{1-(4-Methyl-1-tosyl-1H-pyrrol-3-yl)propan-2-one (125)}\)

\[
\text{N-(4-(tert-Butyldimethylsilyloxy)pent-2-ynyl)-4-methyl-N-(prop-2-ynyl) benzenesulfonamide (60 mg, 0.15 mmol) was dissolved in acetonitrile (2 mL) in a microwave vial. A drop of water was added, the vial purged with nitrogen, and then heated in the microwave at 200 °C for 1.5 hours. The solvent was removed and the crude mixture purified by flash column chromatography (5-50% ethyl acetate in petrol) to yield the title compound 125 as a white to yellow gum (18 mg, 0.062 mmol, 41%), along with 126 and 127.}
\]

\(R_f = 0.20\) (20% ethyl acetate in petrol); IR = (neat) 2919, 1713, 1595, 1364, 1169, 1064 cm\(^{-1}\); \(^{1}H\) NMR (400 MHz, CDCl\(_3\)): δ = 7.72-7.70 (m, 2H), 7.30-7.28 (m, 2H), 7.02-7.02 (d, J = 2 Hz, 1H), 6.89-6.88 (m, 1H), 3.41 (s, 2H), 2.39 (s, 3H), 2.11 (s, 3H), 1.90-1.89 (d, J = 1 Hz, 3H); \(^{13}C\) NMR (100 MHz, CDCl\(_3\)): δ = 205.9, 144.9, 136.3, 130.1, 126.9, 124.3, 121.8, 119.5, 118.5, 40.7, 29.2, 21.8, 10.4; HRMS (ES\(^+\)): m/z [M+H]\(^+\) calcd for C\(_{15}\)H\(_{18}\)NO\(_3\)S: 292.1002; found: 292.1010.

\(\text{2-Tosyl-1,2,3,6,7,7a-hexahydroisoindol-5-one (126)}\)

Pale yellow to yellow gum (7 mg, 0.02 mmol, 16%).

\(R_f = 0.25\) (50% ethyl acetate in petrol); IR = (neat) 2933, 1670, 1595, 1345, 1162, 1094 cm\(^{-1}\); \(^{1}H\) NMR (400 MHz, CDCl\(_3\)): δ = 7.73-7.71 (m, 2H), 7.37-7.35 (d, J = 8 Hz, 2H), 5.88-5.87 (m, 1H), 4.33-4.27 (dt, J = 17, 1.5 Hz, 1H), 3.94-3.90 (m, 1H), 3.83-3.79 (dt, J = 17, 2 Hz, 1H), 2.98-2.89 (m, 1H), 2.66-2.61 (dd, J = 11, 9.5 Hz, 1H), 2.49-2.45 (m, 1H), 2.45 (s, 3H), 2.34-2.25 (ddd, J = 17, 14.5, 5 Hz, 1H), 2.22-2.16 (ddt, J = 12.5, 5, 2.5 Hz, 1H), 1.64-1.53 (dddd, J = 14.5, 13, 11.5, 4.5 Hz, 1H); \(^{13}C\) NMR (125 MHz, CDCl\(_3\)): δ = 197.7, 164.0, 144.3, 132.8, 130.1, 127.9, 122.5, 53.2, 51.3, 40.5, 36.5, 26.7, 21.7.

\(\text{2-Tosyl-2,3,6,7-tetrahydro-1H-isoindol-5(4H)-one (127)}\)
Pale yellow to yellow gum (6 mg, 0.021 mmol, 14%).

\[ R_f = 0.30 \text{ (50\% ethyl acetate in petrol); IR} = \text{(neat) 2921, 1713, 1595, 1341, 1160, 1100 cm}^{-1}; \text{ } ^{1}H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta = 7.74-7.72 \text{ (m, 2H), 7.35-7.33} \text{ (d, } J = 8 \text{ Hz, 2H), 4.08 \text{ (s, 2H), 4.04} \text{ (s, 2H), 2.77 (s, 2H), 2.52-2.49} \text{ (t, } J = 7 \text{ Hz, 2H), 2.44 (s, 3H), 2.40-2.36 (m, 2H); } ^{13}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta = 207.4, 143.8, 134.3, 130.3, 130.0, 128.3, 127.6, 56.6, 56.5, 37.9, 23.1, 21.7. \]

Cyanomethyl 4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-ynoate (130)

To a solution of 4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-ynoic acid (370 mg, 1.15 mmol) and \( N,N \)-disopropylethylamine (222 mg, 300 \( \mu \)L, 1.72 mmol) in DMF (10 mL) at 50 °C was added bromoacetonitrile (413 mg, 0.240 mL, 3.44 mmol) as drops. The resulting solution was stirred for 36 hours and then allowed to cool to room temperature. Saturated ammonium chloride (20 mL) was added and the organics were extracted with ethyl acetate (3 × 50 mL) and washed with water (3 × 50 mL) and brine (50 mL). The organics were dried over sodium sulfate, filtered and concentrated to dryness under reduced pressure. The product was purified by flash column chromatography eluting in 0 to 10% diethyl ether in pentane yielding the title compound as a colourless oil (170 mg, 0.470 mmol, 41%).

\[ R_f = 0.34 \text{ (25\% diethyl ether in pentane); IR} = \text{(neat) 2955, 2931, 2858, 2237, 1731, 1221, 1094, 835, 771 cm}^{-1}; \text{ } ^{1}H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta = 5.88 \text{ (d, } J = 3.0 \text{ Hz, 1H), 5.84 (dd, } J = 3.0 \text{ Hz, 1.0 Hz, 1H), 4.79 (s, 2H), 4.52 \text{ (t, } J = 6.4 \text{ Hz, 1H), 2.75 (t, } J = 7.5 \text{ Hz, 2H), 2.25 (s, 3H), 2.11 - 1.99 (m, 2H), 0.91 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); } ^{13}C \text{ NMR (100 MHz, CDCl}_3\text{): } \delta = 152.6, 151.5, 150.8, 113.6, 106.3, 106.0, 92.3, 74.3, 61.8, 49.2, 36.1, 25.8, 23.6, 18.3, 13.6, -4.5, -5.0; \text{ HRMS (CI+): } m/z [M+H]^+ \text{ calcd for } C_{19}H_{28}NO_4Si: 362.1788; \text{ found: 362.1782.} \]

\((E)-4\text{-Amino-3-(5-oxo-2-(3-oxobut-1-en-1-yl)cyclopent-1-en-1-yl)furan-2(5H)-one (132)}\)

A microwave vial charged with cyanomethyl 4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-ynoate (50 mg, 0.14 mmol), acetonitrile (4.9 mL) and water (0.05 mL) was heated to 200 °C for 5 hours under microwave conditions. The solution was concentrated under reduced pressure and the crude
material was purified by column chromatography (0-50% ethyl acetate in DCM) to give the title compound as a colourless oil (21 mg, 0.086 mmol, 62%).

\[ R_f = 0.27 \text{ (5\% MeOH in DCM)}; \text{ IR } = \text{(neat) 2918, 2850, 1724, 1263, 1098 cm}^{-1}; \text{ }^1\text{H NMR (400 MHz, CDCl}_3): \delta = 7.45 (d, J = 16.0 Hz, 1H), 7.26 (br. s, 2H), 6.57 (d, J = 16.0 Hz, 1H), 4.73 (s, 2H), 2.77 (m, 2H), 2.47 (m, 2H), 2.29 (s, 3H); ^{13}\text{C NMR (100 MHz, CDCl}_3): \delta = 206.6, 198.1, 172.6, 167.1, 161.7, 137.8, 136.8, 130.8, 84.1, 66.6, 33.9, 27.8, 25.6; \text{ HRMS (ESI–): } m/z [M–H]^{-}\text{ calcd for C}_{13}\text{H}_{12}\text{NO}_4: 246.0766; \text{ found: 246.0771.}

Cyanomethyl (syn-1-anti-3,6)-1-((tert-butyldimethylsilyl)oxy)-6-methyl-1,2,3,6-tetrahydro-3a,6-epoxyindene-7-carboxylate (133)

\[
\text{N} = \text{O}
\]

Cyanomethyl 4-(tert-butyldimethylsilyloxy)-6-(5-methylfuran-2-yl)hex-2-ynoate (40 mg, 0.11 mmol) allowed to stand under N\(_2\) for 10 days. The product was obtained as a white crystalline solid (40 mg, 0.11 mmol, 100%).

\[ R_f = 0.17 \text{ (10\% ethyl acetate in pentane); MP = 87 – 90 }^\circ\text{C; Decomposition; IR } = \text{(neat) 2930, 2238, 1720, 1253, 1087, 1057, 838 cm}^{-1}; \text{ }^1\text{H NMR (400 MHz, CDCl}_3): \delta = 6.90 (d, J = 5.0 Hz, 1H), 6.8 (d, J = 5.0 Hz, 1H), 5.0 (m, 1H), 4.8 (s, 2H), 2.5 (m, 1H), 2.2 (m, 2H), 2.0 (m, 1H), 1.9 (s, 3H), 0.8 (s, 9H), 0.1 (s, 3H), –0.1 (s, 3H); ^{13}\text{C NMR (100 MHz, CDCl}_3): \delta = 181.1, 161.8, 146.0, 145.1, 135.7, 114.4, 99.4, 95.6, 67.6, 48.2, 39.0, 25.7, 24.7, 18.2, 17.2, –4.7, –5.0; \text{ HRMS (Cl+): } m/z [M+H]^+ \text{ calcd for C}_{19}\text{H}_{28}\text{NO}_4\text{Si: 362.1788; found: 362.1782.} \]
$^1$H and $^{13}$C NMR Spectra

$$((6-((2\text{-Bromoallyl})\text{oxy})\text{hex-4-yn-1-yl})\text{oxy})(\text{tert-butyl})\text{dimethylsilane (15)}$$

\[ \text{OTBS} \]

Aug 14, 2014
LAD003a

[Chemical structure image]

$^1$H and $^{13}$C NMR Spectra

$$((6-((2\text{-Bromoallyl})\text{oxy})\text{hex-4-yn-1-yl})\text{oxy})(\text{tert-butyl})\text{dimethylsilane (15)}$$

[Chemical structure image]

Aug 14, 2014
LAD003a
6-((2-Bromoallyl)oxy)hex-4-ynal (17)
8-((2-Bromoallyl)oxy)-1-(trimethylsilyl)octa-1,6-diyne-3-one (18)
5-(Trimethylsilyl)-7,8-dihydro-4H-indeno[4,5-c]furan-6(5H)-one (19)
8-((2-Bromoallyl)oxy)octa-1,6-diyne-3-one (20)
9-((2-Bromoallyl)oxy)-1-(trimethylsilyl)nona-1,7-diyn-3-one (21)
((2-((2-Bromoallyloxy)pent-3-yn-1-yl)-1,3-dioxolan-2-yl)ethynyl)trimethylsilane (23)
2-(6-((tert-Butyldimethylsilyl)oxy)hex-2-yn-1-yl)isoindoline-1,3-dione (25)
6-((tert-Butyldimethylsilyl)oxy)hex-2-yn-1-amine (26)
$N$-(2-bromoallyl)-6-((tert-butyldimethylsilyl)oxy)hex-2-yn-1-amine (27)
$N$-(2-bromoallyl)-$N$-(6-((tert-butyldimethylsilyl)oxy)hex-2-yn-1-yl)-4-methylbenzenesulfonamide (28)
S-(6-((tert-butyl(dimethyl)silyl)oxy)hex-2-yn-1-yl) ethanethioate (29)
(6-((2-Bromoallyl)thio)hex-4-yn-1-yl)oxy)(tert-butyl)dimethylsilane (30)
$N$-((2-Bromoallyl)-4-methyl-N-(6-oxo-8-(trimethylsilyl)octa-2,7-diyn-1-yl)benzenesulfonamide (31)

\[
\begin{align*}
\text{Chemical Structure Image}
\end{align*}
\]
2-Tosyl-5-(trimethylsilyl)-4,5,7,8-tetrahydrocyclopenta[e]isoindol-6(2H)-one (33)
5-(Trimethylsilyl)-7,8-dihydro-4H-indeno[5,4-c]thiophen-6(5H)-one (34)
(6-(2-Bromoallyloxy)-1-(5-methylfuran-2-yl)hex-4-yn-3-yl)oxy)(tert-butyl)dimethylsilane (46)
1-(8-(tert-Butyldimethylsilyloxy)-3,6,7,8-tetrahydro-1H-indeno[4,5-c]furan-5-yl)propan-2-one (47)
Dimethyl 2-(2-bromoallyl)-2-(4-((tert-butyldimethylsilyl)oxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-yl)malonate (56)
tert-Butyl (2-bromoallyl)(4-((tert-butyldimethylsilyl)oxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-yl)carbamate (57)
((6-((2-Bromoallyl)thio)-1-(5-methylfuran-2-yl)hex-4-yn-3-yl)oxy)((tert-butyl)dimethylsilane (58)

\[
\begin{align*}
&7^1{H}\text{NMR (500 MHz, CDCl3): } 5.06 (s, 1H), 5.85 - 5.84 (m, 2H), 5.57 (d, J = 6.1 Hz, 1H), 4.43 \\
&\text{Br} \\
&4.36 (t, J = 6.3, 1H), 3.62 (s, 2H), 2.82 (t, J = 4.1 Hz, 2H), 2.79 (m, 2H), 2.27 (t, J = 9.9 Hz, 2H), 2.18 - \\
&1.95 (m, 2H), 2.12 (s, 3H), 1.12 (s, 3H), 0.84 (s, 3H) \\
&\text{OTBS} \\
&3.05 (s, 3H) \\
&4.60 (s, 2H) \\
&6.07 (s, 1H) \\
&1.32 (s, 3H) \\
&1.28 (s, 3H) \\
&1.20 (s, 3H) \\
&1.05 (s, 3H) \\
&0.99 (s, 3H) \\
&0.91 (s, 3H) \\
&0.82 (s, 3H) \\
&0.77 (s, 3H) \\
&0.72 (s, 3H) \\
&0.60 (s, 3H) \\
&0.12 (s, 3H)
\end{align*}
\]

\[
\begin{align*}
&13^C\text{NMR (125 MHz, CDCl3): } 139.92, 130.10, 128.10, 119.31, 106.36, 99.08, 84.09, 79.26, 42.17, 41.28, \\
&37.14, 25.71, 23.81, 18.85, 18.11, 13.45, -7.69, -5.08
\end{align*}
\]
Dimethyl 8-(tert-butyldimethylsilyloxy)-5-(2-oxopropyl)-3,6,7,8-tetrahydroas-indacene-2,2(1H)-dicarboxylate (59)
tert-Butyl 8-(tert-butyldimethylsilyloxy)-5-(2-oxopropyl)-3,6,7,8-tetrahydrocyclopenta[e]isoindole-2(1H)-carboxylate (60)
(E)-4-(4-(tert-Butyldimethylsilyloxy)-1,3,4,5,6,6a-hexahydropentaleno[1,2-c]thiophen-6a-yl-1,1-dioxide)but-3-en-2-one (61)
**tert-Butyldimethyl(1-(5-ethylfuran-2-yl)-6-(prop-2-ynyloxy)hex-4-yn-3-yloxy)silane (74)**

![Chemical Structure Image]

**NMR Spectra Image**

- Spectra showing various chemical shifts and peaks.
- Peaks labeled with chemical shifts and assignments.

**Notes and Interpretation**

- Detailed analysis of the NMR spectra showing the presence of specific functional groups and their integration.
- Discussion on the implications of these findings in the context of organic chemistry or materials science.

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54
5-(2-Oxobutyl)-6,7-dihydro-1H-indeno[4,5-c]furan-8(3H)-one (77)
((6-(But-2-yn-1-yloxy)-1-(5-methylfuran-2-yl)hex-4-yn-3-yl)oxy)(tert-butyl)dimethylsilane (83)
4-((tert-Butyldimethylsilyl)oxy)-6-(5-methylfuran-2-yl)hex-2-yn-1-yl 3-(naphthalen-1-yl) propiolate (85)
4-Methyl-5-(2-oxopropyl)-1,3,6,7-tetrahydro-8H-indeno[4,5-c]furan-8-one (86)
4-(Naphthalen-1-yl)-5-(2-oxopropyl)-6,7-dihydro-1H-indeno[4,5-c]furan-3,8-dione (88)
*tert*-Butyldimethyl((5-({prop-2-yn-1-yloxy}pent-3-yn-2-yl)oxy)silane (102)
(But-3-yn-2-yl)oxy)(tert-butyl)dimethylsilane (108)
4-((tert-Butyldimethylsilyl)oxy)pent-2-yn-1-ol (109)
1-(4-Methylfuran-3-yl)propan-2-one (110)
$S$-4-((tert-butyldimethylsilyl)oxy)pent-2-yn-1-yl) ethanethioate (118)
**tert-Butyldimethyl(5-(prop-2-yn-1-ylthio)pent-3-yn-2-yl)oxy)silane (119)**

![NMR Spectrogram](image)

**Chemical Structure**

- OTBS

**NMR Data**

- f1 (ppm) values for various peaks are listed, indicating chemical shifts and assignments.

- Peaks are labeled with various chemical elements and their assignments.

- Compounds are identified with their respective chemical shifts and assignments.

**Additional Information**

- Experimental conditions are noted, including the date and the solvent used (CDCl3) for the NMR analysis.

- The images show the detailed NMR spectra, including the 1D and 2D NMR spectra, with annotations for each peak and its corresponding chemical shift.

- The spectra are labeled with chemical names and their respective NMR chemical shifts for clear identification.
1-(4-Methylthiophen-3-yl)propan-2-one (120)
8-Thiabicyclo[4.3.0]non-1-en-3-one (121)
4-Methyl-\(\text{N}_{2}\text{N}_{-}\text{di[prop-2-yn-1-yl]benzenesulfonamide\ (122)}\)
$N$-(4-hydroxypent-2-yn-1-yl)-4-methyl-$N$-(prop-2-yn-1-yl)benzenesulfonamide (123)
$N$-(4-((tert-butyldimethylsilyl)oxy)pent-2-yn-1-yl)-4-methyl-$N$-(prop-2-yn-1-yl)benzenesulfonamide (124)
1-(4-Methyl-1-tosyl-1H-pyrrol-3-yl)propan-2-one (125)
2-Tosyl-2,3,6,7-tetrahydro-1H-isindol-5(4H)-one (127)
Cyanomethyl 4-(tert-butyl(dimethyl)silyloxy)-6-(5-methylfuran-2-yl)hex-2-ynoate (130)
(E)-4-Amino-3-(5-oxo-2-(3-oxobut-1-en-1-yl)cyclopent-1-en-1-yl)furan-2(5H)-one (132)
Cyanomethyl (syn-1-anti-3,6)-1-((tert-butylidemethylsilyl)oxy)-6-methyl-1,2,3,6-tetrahydro-3a,6-epoxyindene-7-carboxylate (133)
X-ray Crystallographic Data for Cyanomethyl (syn-1-anti-3,6)-1-((tert-butyldimethylsilyl)oxy)-6-methyl-1,2,3,6-tetrahydro-3a,6-epoxyindene-7-carboxylate

The X-ray crystal structure of 133

Crystal data for 133: C_{19}H_{27}NO_{4}Si, M = 361.50, monoclinic, P2_{1}/c (no. 14), a = 15.2885(6), b = 11.7798(5), c = 11.3042(4) Å, β = 93.110(3)^°, V = 2032.84(14) Å^3, Z = 4, D_c = 1.181 g cm^{-3}, μ(Mo-Kα) = 0.137 mm^{-1}, T = 173 K, colourless tablets, Agilent Xcalibur 3 E diffractometer; 4071 independent measured reflections (R_{int} = 0.0172), F^2 refinement,[X1,X2] R_I(obs) = 0.0442, wR_{2}(all) = 0.1071, 3135 independent observed absorption-corrected reflections ([F_o] > 4σ([F_o]), 2θ_{max} = 56°), 232 parameters. CCDC 1569441.

References

### Table S1. Crystal data and structure refinement.

<table>
<thead>
<tr>
<th>Crystal Data</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formula</strong></td>
<td>C_{19}H_{27}NO_{4}Si</td>
</tr>
<tr>
<td><strong>Formula weight</strong></td>
<td>361.50</td>
</tr>
<tr>
<td><strong>Temperature</strong></td>
<td>173 K</td>
</tr>
<tr>
<td><strong>Diffractometer, wavelength</strong></td>
<td>Agilent Xcalibur 3 E, 0.71073 Å</td>
</tr>
<tr>
<td><strong>Crystal system, space group</strong></td>
<td>Monoclinic, P2_1/c</td>
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<tr>
<td><strong>Unit cell dimensions</strong></td>
<td></td>
</tr>
<tr>
<td>a = 15.2885(6) Å, α = 90°</td>
<td></td>
</tr>
<tr>
<td>b = 11.7798(5) Å, β = 93.110(3°)</td>
<td></td>
</tr>
<tr>
<td>c = 11.3042(4) Å, γ = 90°</td>
<td></td>
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<tr>
<td><strong>Volume, Z</strong></td>
<td>2032.84(14) Å³, 4</td>
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<tr>
<td><strong>Density (calculated)</strong></td>
<td>1.181 Mg/m³</td>
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<tr>
<td><strong>Absorption coefficient</strong></td>
<td>0.137 mm⁻¹</td>
</tr>
<tr>
<td><strong>F(000)</strong></td>
<td>776</td>
</tr>
<tr>
<td><strong>Crystal colour / morphology</strong></td>
<td>Colourless tablets</td>
</tr>
<tr>
<td><strong>Crystal size</strong></td>
<td>0.64 × 0.46 × 0.09 mm³</td>
</tr>
<tr>
<td><strong>θ range for data collection</strong></td>
<td>2.668 to 28.208°</td>
</tr>
<tr>
<td><strong>Index ranges</strong></td>
<td>-19&lt;=h&lt;=15, -15&lt;=k&lt;=11, -14&lt;=l&lt;=9</td>
</tr>
<tr>
<td><strong>Reflns collected / unique</strong></td>
<td>7040 / 4071 [R(int) = 0.0172]</td>
</tr>
<tr>
<td><strong>Reflns observed [F&gt;4σ(F)]</strong></td>
<td>3135</td>
</tr>
<tr>
<td><strong>Absorption correction</strong></td>
<td>Analytical</td>
</tr>
<tr>
<td><strong>Max. and min. transmission</strong></td>
<td>0.988 and 0.944</td>
</tr>
<tr>
<td><strong>Refinement method</strong></td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td><strong>Data / restraints / parameters</strong></td>
<td>4071 / 0 / 232</td>
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<tr>
<td><strong>Goodness-of-fit on F²</strong></td>
<td>1.030</td>
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<tr>
<td><strong>Final R indices [F&gt;4σ(F)]</strong></td>
<td>R1 = 0.0442, wR2 = 0.0974</td>
</tr>
<tr>
<td><strong>R indices (all data)</strong></td>
<td>R1 = 0.0631, wR2 = 0.1071</td>
</tr>
<tr>
<td><strong>Largest diff. peak, hole</strong></td>
<td>0.257, -0.279 eÅ⁻³</td>
</tr>
<tr>
<td><strong>Mean and maximum shift/error</strong></td>
<td>0.000 and 0.000</td>
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Table S2. Bond lengths [Å] and angles [°].

<table>
<thead>
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<th>Bond</th>
<th>Length [Å]</th>
<th>Bond</th>
<th>Length [Å]</th>
</tr>
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<tbody>
<tr>
<td>C(1)-O(10)</td>
<td>1.447(2)</td>
<td>C(12)-C(5)-C(4)</td>
<td>125.34(15)</td>
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<tr>
<td>C(1)-C(9)</td>
<td>1.512(3)</td>
<td>C(5)-C(6)-C(7)</td>
<td>145.03(17)</td>
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<tr>
<td>C(1)-C(2)</td>
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<td>C(5)-C(6)-C(1)</td>
<td>106.62(14)</td>
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<tr>
<td>C(1)-C(6)</td>
<td>1.534(2)</td>
<td>C(7)-C(6)-C(1)</td>
<td>107.64(14)</td>
</tr>
<tr>
<td>C(2)-C(3)</td>
<td>1.317(3)</td>
<td>O(17)-C(7)-C(6)</td>
<td>105.42(13)</td>
</tr>
<tr>
<td>C(3)-C(4)</td>
<td>1.534(3)</td>
<td>O(17)-C(7)-C(8)</td>
<td>110.02(15)</td>
</tr>
<tr>
<td>C(4)-O(10)</td>
<td>1.458(2)</td>
<td>C(6)-C(7)-C(8)</td>
<td>100.32(14)</td>
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<tr>
<td>C(4)-C(11)</td>
<td>1.498(2)</td>
<td>C(7)-C(8)-C(9)</td>
<td>105.26(15)</td>
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<tr>
<td>C(4)-C(5)</td>
<td>1.572(2)</td>
<td>C(1)-C(9)-C(8)</td>
<td>104.36(15)</td>
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<td>C(5)-C(6)</td>
<td>1.324(2)</td>
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<td>O(12)-C(12)-O(13)</td>
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<td>1.499(2)</td>
<td>O(12)-C(12)-C(5)</td>
<td>126.47(16)</td>
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<td>O(13)-C(12)-C(5)</td>
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<tr>
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<td>1.528(3)</td>
<td>C(12)-O(13)-C(14)</td>
<td>115.47(14)</td>
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<td>1.539(3)</td>
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<td>112.07(15)</td>
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<td>1.6411(13)</td>
<td>O(17)-Si(18)-C(19)</td>
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<td>Si(18)-C(24)</td>
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<td>Si(18)-C(23)</td>
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<td>Si(18)-C(19)</td>
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<td>C(20)-C(19)-C(21)</td>
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<td>C(20)-C(19)-C(22)</td>
<td>108.86(18)</td>
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<td>C(19)-C(21)</td>
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<td>C(21)-C(19)-C(22)</td>
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<td>1.529(3)</td>
<td>C(20)-C(19)-Si(18)</td>
<td>110.00(15)</td>
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<td>O(10)-O(12)</td>
<td>116.61(15)</td>
<td>C(21)-C(19)-Si(18)</td>
<td>109.36(15)</td>
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<td>O(10)-C(1)-C(9)</td>
<td>100.08(14)</td>
<td>C(22)-C(19)-Si(18)</td>
<td>110.58(1)</td>
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</table>