Supporting information

Towards taxane analogues synthesis by dienyne ring closing metathesis

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Structural characterization

The relative stereochemistry of taxadiene analogues **19a** and **20a** was established by NOESY experiments (Fig 1SI and Fig 2SI), where the cross peak between protons H2 and H8 confirmed the *trans* configuration of the cyclohexanone C ring in both taxadiene analogues **19a** and **20a**. The observation of the H2-H15 cross peak in compound **19a** established the *cis* orientation of the C15 bridge with H2, therefore it can be inferred that the benzoate group is *cis* to H3 (Fig 2SI). On the other hand, the relative stereochemistry of **20a**, where H2 is *anti* to the C15 bridge was established by the observation of the H2-H14 cross peak (Fig 2SI).

Figure 1SI. NOESY experiment on taxadiene analogue **19a.**

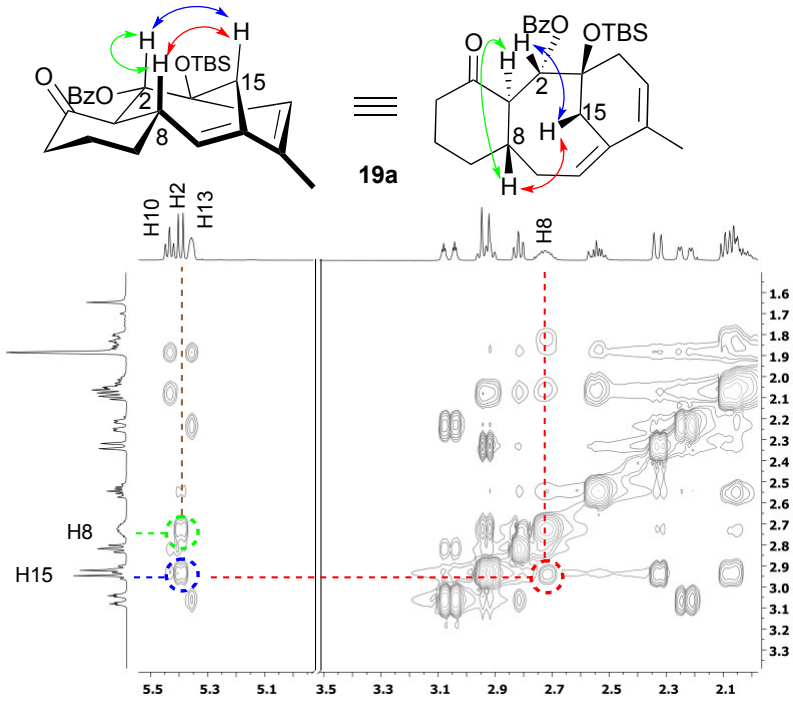
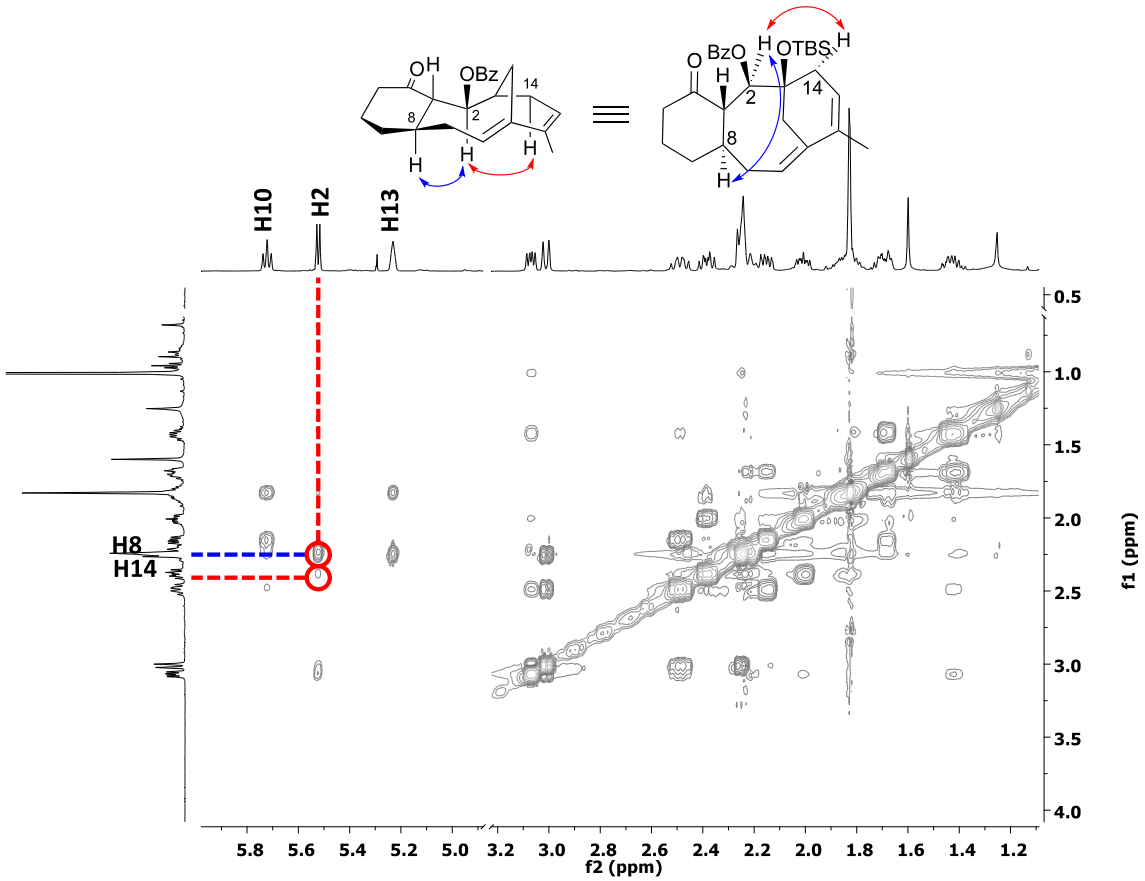


Figure 2SI. NOESY experiment on taxadiene analogue **20a.**

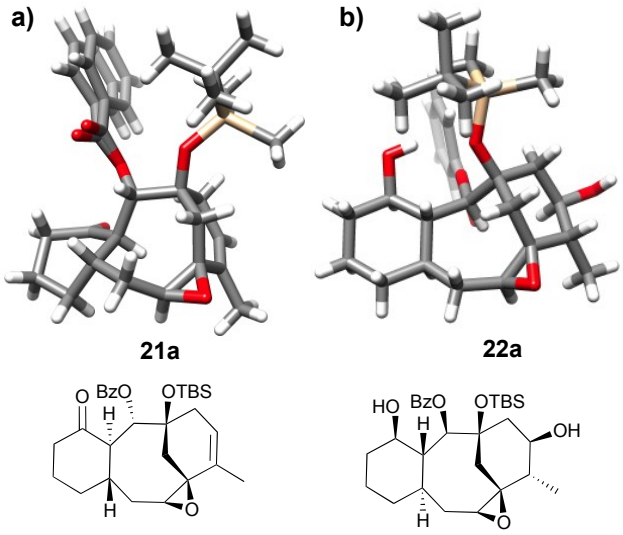


Additionally, the relative and absolute stereochemistry of compounds and **20a** was confirmed by X-ray crystallography, using anomalous scattering and silicon as the heavy atom, the Flack parameters[1] found were close to zero as an indication of the high confidence of the assignation. To this end, we prepared crystalline derivatives of **19a** and **20a**. Monoepoxide **21a**, derived from taxadiene **19a**, was crystallized as a hexane solvate by slow evaporation from a solution of hexanes. The diffraction was carried out at 110 K, and the crystal structure solved in the monoclinic space group *C2*. The molecular structure features a highly congested tricyclic structure, the *trans* substitution of the cyclohexanone, which is found in a twisted boat conformation (Fig 3SIa). It also shows H3 and the benzoate as well as H2 and the C15 bridge *cis* oriented (Fig 3SIa). As shown below, the intermediate **22a**, synthesized from taxadiene **20a**, was crystallized from dichloromethane to give solvent free crystals. Data collection was carried out at 110 K, and the crystal structure was solved in the orthorhombic space group $P2_12_12_1$. Similarly, the molecular structure of **22a** confirms the *trans* stereochemistry of cyclohexane C ring,

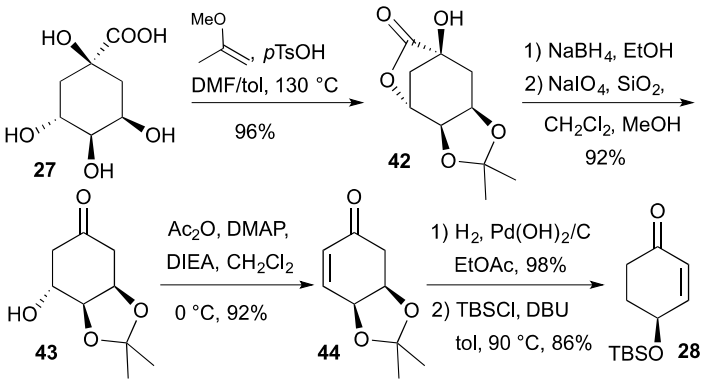
[1] a) H. D. Flack *Acta Cryst.* 1983, **A39**, 876; b) H. D. Flack, G. Bernardinelli *J. Appl. Cryst.* 2000, **33**, 1143.

it also features the *syn* orientation of H3 and the benzoate group (Fig 3SIb). Unlike taxadiene analogue **19b**, in H2 and H8 are oriented *anti* to the C15 bridge (Fig 3SIb).

Figure 3SI. Molecular structures of a) epoxide **21a** and b) compound **22a** obtained by single crystal X-ray diffraction that confirmed the relative and absolute configuration of taxadienes **19a** and **20a**, respectively.



Scheme 1SI. Synthetic strategy for the preparation of ketone 28.



General methods

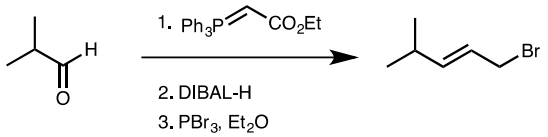
All reactions were carried out under argon atmosphere in oven or flame-dried glassware, unless otherwise stated. All chemicals were purchased from commercial suppliers and used as received. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were dried by continuous distillation from sodium-benzophenone under argon atmosphere. Dichloromethane, triethylamine, pyridine and 2,6-lutidine were dried by distillation from calcium hydride under argon atmosphere. Reactions at room temperature were carried out between 20-25 °C, reactions at 0 °C were performed on a water-ice bath and reactions at -78 °C were performed using an acetone-dry ice bath. All reactions were monitored by thin layer chromatography (TLC) using TLC plates pre-coated with Silica Gel 60 F254 and visualized using a combination of UV, potassium permanganate ($KMnO_4$) and cerium ammonium molybdate (CAM) staining. Column chromatography was performed with silica gel (200-400 mesh) as the stationary phase. Characterization by nuclear magnetic resonance (NMR) was performed at 250 MHz, 300 MHz and 500 MHz for proton and 63 MHz, 75MHz and 126 MHz for carbon-13. Chemical shifts are reported in ppm relative to TMS (δ, 0 ppm) using the residual solvent peaks as reference ($CDCl_3$ 7.26 and 77.16 ppm for ^1H and ^{13}C, respectively). Coupling constants *J* are reported in Hz. Multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q), quintet (qnt), sextet (sxt), septet (spt) and multiplet (m). Optical rotations were measured in solutions of $CHCl_3$ using the sodium D line (589 nm). Mass spectrometry data were collected on a Electrospray Ionization mass spectrometer with a Time-of-Flight detector (ESI-TOF).

X-ray single crystal analysis

Colorless prisms of the epoxide **21a** were grown from a hexanes solution while the colorless plates of compound **22a** were grown from slow evaporation of a dichloromethane solution. Single crystals of these compounds were used for data collection. The diffraction data were measured at 110 K on an X-ray diffractometer system equipped with Mo-Kα radiation (λ = 0.71073 Å) and area detector. The structures were solved and refined using the SHELXTL software package. All atoms were refined anisotropically, and hydrogen atoms were placed at calculated positions.

Synthetic procedures

Synthesis of (E)-1-bromo-4-methylpent-2-ene



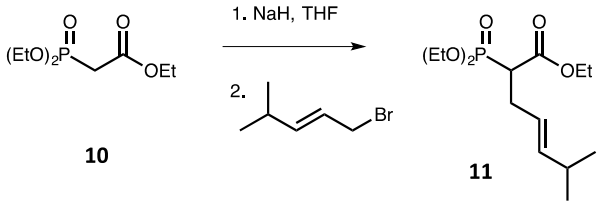
To a solution of ethyl 2-triphenylphosphanylideneacetate (25 g, 71.80 mmol) in dichloromethane (250 mL) at 0 °C was added dropwise isobutyraldehyde (7.5 mL, 82.57 mmol) over 15 min. The mixture was stirred at this temperature for 5 min and then overnight at r.t. The solvent was removed by rotary evaporation (700 mbar, 40 °C) and pentane was added to the resulting residue to precipitate out the triphenylphosphine oxide that was removed by filtration. This process was repeated until all the triphenylphosphine oxide was eliminated. The mixture was dried over Na_2SO_4, filtered and concentrated. The resulting residue was used in the next step without further purification [R_f=0.6 (60% acetone/hexanes), pale yellow oil, volatile].[2]

The residue of the previous reaction was dissolved in dichloromethane (200 mL) and cooled to -78 °C. DIBAL-H (1M solution in dichloromethane, 165 mL, 165 mmol) was added over 30 min. The mixture was stirred at -78 °C for 1 hand then quenched with the addition of aqueous saturated solution of potassium sodium tartrate (150 mL). The aqueous layer was extracted with dichloromethane (2 x 100 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The residue was taken over the next step without further purification [R_f=0.4 (20% EtOAc/hexanes), pale yellow oil, volatile].[3]

The resulting residue was dissolved in diethyl ether (30 mL), cooled to 0 °C and pyridine (0.70 mL, 8.62 mmol) was added. The mixture was stirred at this temperature for 5 min and then a solution of phosphorus tribromide (8.172 g, 30.16 mmol) in diethyl ether (8 mL) was added. The mixture was stirred at room temperature for 2 h, washed with aqueous saturated solution of NH_4Cl (2 x 15 mL) and brine (15 mL). After drying over $MgSO_4$ and filtering the solution was concentrated and the resulting residue was distilled at reduced pressure on a Kugelrohr distillation apparatus (0.3 mbar, r.t.. to 40 °C) to obtain (*E*)-1-bromo-4-methylpent-2-ene as volatile colorless oil [8.65 g, 74% over three steps, R_f = 0.85 (20% EtOAc/hexanes)].[4] **^{1}H RMN** (250 MHz, $CDCl_3$, δ): 5.78-5.56 (m, 2H), 3.94 (d, J = 7.1 Hz, 2H), 2.32 (oct, J = 6.7 Hz, 1H) H-4, 0.99 (d, J = 6.7 Hz, 6H). **^{13}C RMN** (63 MHz, $CDCl_3$, δ): 143.2 (CH), 123.5 (CH), 33.8 (CH_2), 30.6 (CH), 21.9 (CH_3).

[2] Hale, K.; Manamizar, S.; Delisser, V. *Tetrahedron* **1994**, *50*, 9181.
[3] Baker, R.; Swain, C.; Head, J. *J. Chem. Soc., Chem. Commun*. **1985**, *6*, 309.
[4] van der Klei, A.; de Jong, R.; Lugtenburg, J.; Tielens, A. *Eur. J. Org. Chem.* **2002**, *17*, 3015.

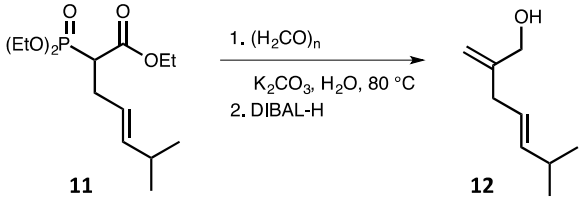
Synthesis of compound 11



10 **11**

A suspension of NaH (60% in mineral oil, 3.585 g, 89.62 mmol) in THF (300 mL) was cooled to 0 °C and ethyl 2-(diethoxyphosphoryl)acetate (**10**, 16.1 mL, 81.47 mmol) was added dropwise. The mixture was stirred at that temperature for 2 h and then a solution of (*E*)-1-bromo-4-methylpent-2-ene (6.640 g, 40.74 mmol) in THF (60 mL) was added. The mixture was stirred at room temperature for 7 h, washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated. The obtained residue was purified by flash column chromatography (30% Et_2O/hexanes) to obtain **11** as a pale yellow oil.[5] [8.98 g, 76%, R_f =0.3 (30% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.27 (ddt, *J* = 15.3, 6.6, 1.1 Hz, 1H), 5.07 (dtd, *J* = 15.2, 6.6, 1.2 Hz, 3H), 4.05 – 3.94 (m, 6H), 2.76 (ddd, *J* = 21.7, 10.8, 4.2 Hz, 1H), 2.52 – 2.20 (m, 2H), 1.97 (o, *J* = 6.8 Hz, 1H), 1.11 (tdd, *J* = 7.0, 1.5, 0.6 Hz, 6H), 1.05 (t, *J* = 7.1 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H), 0.71 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 168.6, 140.4, 122.6, 62.6, 61.0, 46.9, 44.9, 30.7, 29.8, 22.1, 16.2, 14.0. **HRMS-ESI**: calculated for $C_{14}H_{28}O_5P$+H: 307.1669, found: 307.1666.

Synthesis of (E)-6-methyl-2-methylenehept-4-en-1-ol (12)



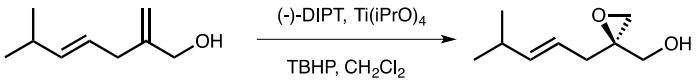
11 **12**

Phosphonate **11** (14.36 g, 46,9 mmol) was suspended in water (94 mL) at room temperate and potassium carbonate (18.31 g, 140.6 mmol) and *p*-formaldehyde (18.31 g, 281.3 mmol) were added. The suspension was heated at 80 °C and stirred at this temperature for 36 h. The reaction mixture was extracted with diethyl ether (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. An analytical sample was prepared by column chromatography (3% Et_2O/pentene) to obtain the corresponding vinylidene product as a volatile pale yellow oil[5] [R_f =0.3 (15% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.96 (s, 1H), 5.34 (s, 1H), 5.29 – 5.09 (m, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 2.79 (d, *J* = 5.2 Hz, 2H), 2.09 (o, *J* = 6.6 Hz, 1H), 1.11 (t, *J* = 7.1 Hz, 5H), 0.79 (s, 3H), 0.77 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 166.9, 140.1, 124.3, 123.2, 60.4, 34.5, 30.9, 22.4, 14.1. **MS-ESI**: M+Na: 205.0634 (100), 206.0713 (6).

[5] Schomaker, J. M.; Borham, B. *Org. Biomol. Chem*. **2004**, *2*, 621.

A solution of the vinylidene product obtained in the previous step in THF (110 mL) was cooled to -78 °C and then treated with DIBAL-H (1M solution in dichloromethane, 108 mL, 108 mmol). The reaction mixture was stirred at -78 °C for 40 min. The reaction was quenched with water (15 mL) and the mixture was poured into aqueous saturated solution of potassium sodium tartrate (150 mL). The mixture was stirred until two layers were formed. The organic layer was separated and the aqueous solution was extracted with dichloromethane (2 x 200 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated and the resulting crude mixture was purified by vacuum distillation using a Kugelrohr distillation apparatus to obtain the alcohol **12** as colorless viscous liquid. [6.03 g, 92% over two steps, R_f = 0.5 (20% EtOAc/hexanes)].[5] **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.50 – 5.24 (m, 2H), 4.99 (s, 1H), 4.83 (s, 1H), 4.00 (s, 2H), 2.69 (d, *J* = 6.4 Hz, 2H), 2.54 (bs, 1H), 2.23 (o, *J* = 6.7 Hz, 1H), 0.96 (s, 3H), 0.93 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 148.1, 139.8, 123.8, 109.6, 65.3, 36.3, 30.9, 22.4. **MS-ESI**: M+Na: 163.1305 (100), 163.1303 (20).

Synthesis of (R,E)-(2-(4-methylpent-2-en-1-yl)oxiran-2-yl)methanol (13)



12 **13**

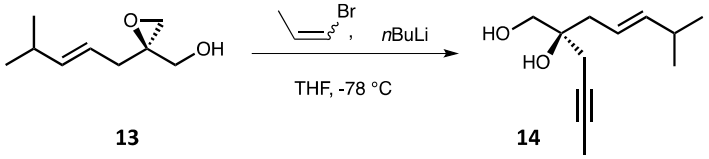
A solution of (-)-diisopropyl tartrate (1.83 g, 7.82 mmol) in dichloromethane (400 mL) containing 4Å molecular sieves (4 g) was cooled to 0 °C and titanium isopropoxide (1.9 mL, 5.21 mmol) was added dropwise. The resulting solution was stirred at this temperature for 30 min and then cooled to -30 °C. A solution of *t*-butyl hydroperoxide in decane (5M, 31 mL, 156.34 mmol) was added and the mixture stirred at this temperature for 30 min. Then a solution of **12** (7.30 g, 52.11 mmol) in dichloromethane (100 mL) was added, and stirred at this temperature for 4 h. The reaction mixture was filtered through a celite path and washed with an aqueous solution NaOH (30%, 100 mL) and brine (sat sol, 100 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by flash column chromatography (5% AcOEt/hexanes) to obtain **13**[5] [7.530 g, 93%, 90% e.e., R_f=0.6 (40% AcOEt/hexanes), pale yellow oil]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.45 (dd, *J* = 15.4, 6.5 Hz, 1H), 5.24 (dddd, *J* = 15.3, 7.7, 6.6, 1.2 Hz, 1H), 3.69 (AB, *J* = 12.4, 4.4 Hz, 1H), 3.54 (AB, *J* = 12.4, 7.6 Hz, 1H), 2.80 (AB, *J* = 4.8 Hz, 1H), 2.61 (AB, *J* = 4.8 Hz, 1H), 2.38 (ddd, *J* = 13.9, 7.1, 1.0 Hz, 1H), 2.20 (ddt, *J* = 13.5, 6.5, 1.0 Hz, 1H) 2.18 (ddt, *J* = 14.0, 6.5, 1.1 Hz, 1H), 0.93 (s, 3H), 0.88 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 142.0, 120.5, 62.9, 60.0, 49.6, 35.2, 31.2, 22.6. **HRMS-ESI**: calculated for $C_9H_{16}O_2$+Na: 179.1048, found: 179.01042.

Synthesis of ester 39

13 **39**

EDC.HCl (19 mg, 0.13 mmol), HOBT (16 mg, 0.13 mmol) and (*S*)-MPA (24 mg, 0.15 mmol) were dissolved in dichloromethane (2 mL) at room temperate and then diisopropiletilamine (0.021 mL, 0.12 mmol) and a solution of **13** (14 mg, 0.10 mmol) in dichloromethane (1 mL) were subsequently added. After 1 h of stirring at this temperature, the reaction mixture was washed with a saturated aqueous solution of NH_4Cl (2 x 1 mL), dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography (8% EtOAc/hexanes) to obtain **39** as a pale yellow oil [14 mg, 38%, R_f=0.7 (40% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 7.51 – 7.29 (m, 5H), 5.40 – 5.15 (m, 2H), 4.81 (s, 1H), 4.20 (AB, *J* = 11.3 Hz, 1H), 4.03 (AB, *J* = 11.3 Hz, 1H), 3.43 (s, 3H), 3.36 (s, 1H), 3.35 (s, 1H), 2.30 – 1.99 (m, 3H), 0.95 (s, 3H), 0.91 (s, 3H). ^{1}H NMR analysis of the resulting diasterotopic misture allowed estimating the stereoisomers mixture.

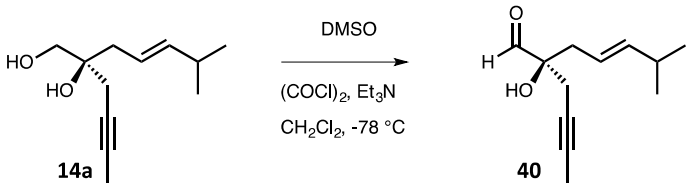
Synthesis of diol 14



13 **14**

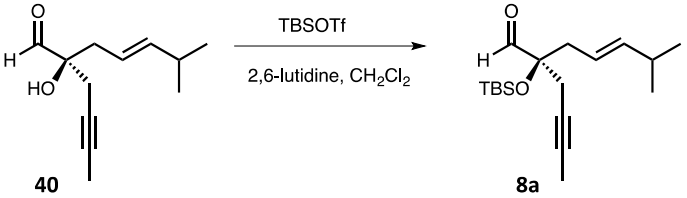
A solution of *cis/trans*-1-bromopropene (3.3 g, 17.3 mmol) in dry THF (21 mL) was treated with *n*BuLi (2.5 M in hexanes, 16.4 mL 40.9 mmol) at -78 °C. The reaction mixture was stirred at -78 °C under argon atmosphere for 2.5 h and then a solution of epoxyde **13** (1.06 g, 6.8 mmol) in dry THF (21 mL) was added and the resulting colorless solution was stirred for additional 5.5 h. The reaction was quenched with aqueous saturated solution of NH_4Cl (50 mL) and brine (50 mL) and extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$, filtered and the solvent evaporated under vacuum. The crude mixture was purified by column chromatography (26% EtOAc/hexanes) to afford diol **14** as a yellowish oil. [1.25 g, 94%, R_f = 0.28 (30% EtOAc/hexanes)]. $[\alpha]_{21}^{D}$ = +2.02 (c = 0.04, $CHCl_3$). **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.51 (dd, *J* = 15.3, 6.2 Hz, 1H), 5.37 (dt, *J* = 15.3, 7.3 Hz, 1H), 3.53 (AB, *J* = 11.3 Hz, 1H), 3.47 (AB, *J* = 11.2 Hz, 1H) 2.45 (bs, 2H), 2.33 (AB, *J* = 2.5 Hz, 1H), 2.32 (AB, *J* = 2.6 Hz, 1H), 2.30 – 2.21 (m, 3H, H-3), 1.78 (t, *J* = 2.5 Hz, 3H), 0.97 (s, 3H), 0.93 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 142.6, 120.8, 78.8, 74.6, 73.6, 67.3, 39.4, 31.1, 22.4, 3.5. **HRMS-ESI**: calculated for $C_{12}H_{20}O_2$+Na: 219.1361, found: 219.1349. **HRMS-ESI**: calculated for $C_{12}H_{20}O_2$+Na: 219.1361, found: 219.1349.

Synthesis of aldehyde 40



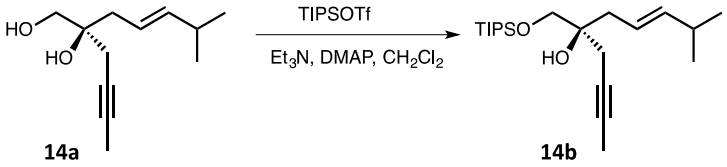
Oxalyl chloride (1.77 g, 14.0 mmol) was added dropwise to a solution of dry DMSO (1.17 g, 15.0 mmol) in dichloromethane (38 mL) at -78 °C. The reaction mixture was stirred under argon atmosphere at this temperature for 10 min and then a solution of diol **14a** (2.11 g, 10.7 mmol) in dry dichloromethane (5.0 mL) was added dropwise. After stirring for 70 min, dry triethylamine (6.53 g, 64.5 mmol) was added and allowed to slowly warm up 0 °C and stirred for 1h at this temperature. The reaction mixture was poured into aqueous HCl solution (5%, 80 mL) and the organic layers were extracted with dichloromethane (3 x 80 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and the solvent was evaporated under vacuum. The crude mixture was purified by column chromatography (15% EtOAc/hexanes) to afford aldehyde **40** as a yellowish viscous liquid. [1.52 g, 73%, R_f = 0.62 (30% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 9.54 (s, 1H), 5.57 (dd, *J* = 15.4, 6.7 Hz, 1H), 5.26 (dt, *J* = 15.9, 7.7 Hz, 1H), 3.23 (bs, 1H), 2.63 – 2.14 (m, 5H), 1.72 (t, *J* = 2.6 Hz, 3H), 0.93 (s, 3H), 0.90 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 203.3, 143.3, 118.9, 79.6, 78.6, 72.5, 38.5, 31.0, 26.6, 22.3, 3.4

Synthesis of aldehyde 8a



A solution of **40** (865 mg, 4.5 mmol) and 2,6-lutidine (2.41 g, 22.5 mmol) in dry dichloromethane (18 mL) was cooled to 0 °C, then *tert*-butyldimethylsilyl triflate (3.57 g, 13.5 mmol) was added and stirred at this temperature for 1 h. The reaction mixture was diluted with dichloromethane (100 mL), washed with aqueous saturated solution of NH_4Cl (1 x 100 mL), dried over $MgSO_4$, filtered and concentrated to dryness. The crude product was purified by flash column chromatography (5% AcOEt/hexanes) to afford the protected aldehyde **125** (942 mg, 68%) as a yellow oil. R_f = 0.8 (15% EtOAC/hexanes). **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.47 – 5.16 (m, 2H), 2.41 – 2.02 (m, 5H), 1.61 (t, *J* = 2.7 Hz, 3H), 0.83 (s, 3H), 0.80 (s, 3H), 0.76 (s, 9H), -0.01 (dd, *J* = 5.4, 2.1 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 142.2, 121.5, 77.9, 75.4, 73.5, 38.6, 31.5, 25.6, 23.5, 22.9, 18.5, 4.0, -4.0, -4.9. **HRMS-ESI**: calculated for $C_{21}H_{40}O_2Si$+Na: 331.2069, found: 331.2023.

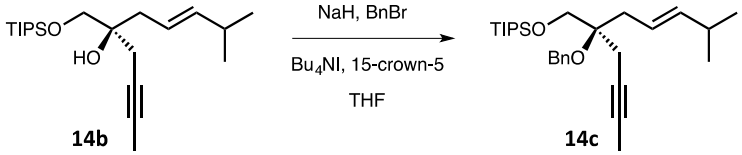
Synthesis of compound 14b



14a **14b**

A solution of **14a** (923 mg, 4.71 mmol) in dichloromethane (50 mL) was cooled to -78 °C was treated with triethylamine (0.60 mL, 5.18 mmol) and dimethylaminopyridine (26 mg, 0.235 mmol). The resulting solution was stirred at this temperature for 15 min and then triisopropylsilyl triflate (1.5 mL, 5.65 mmol) was added. After stirring at this temperature for 2h, the mixture was washed with aqueous saturated solution of NH_4Cl (2 x 25 mL). The aqueous layer was extracted with dichloromethane (2 x 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified with a flash chromatography (5% AcOEt/hexanes) to afford **14a** as a yellow oil [1.253 g, 76%, R_f = 0.8 (20% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.42 – 5.21 (m, 2H), 3.51 (AB, *J* = 9.4 Hz, 1H), 3.43 (AB, *J* = 9.3 Hz, 1H), 2.34 (bs, 1H), 2.24 – 2.09 (m, 5H), 1.66 (t, *J* = 2.5 Hz, 3H), 0.95 (m, 21H), 0.85 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 142.1, 121.8, 78.2, 75.6, 74.1, 67.9, 39.4, 31.5, 27.6, 22.9, 22.9, 18.3, 12.3, 3.9. **HRMS-ESI**: calculated for $C_{21}H_{40}O_2Si$+Na: 375.2695, found: 375.2683.

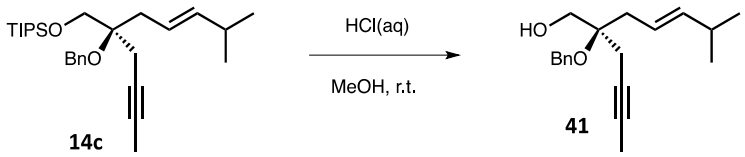
Synthesis of compound 14c



14b **14c**

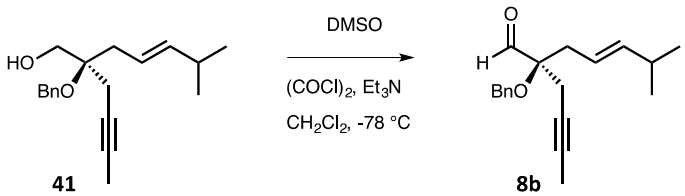
Alcohol **14b** (1.253 g, 3.560 mmol) was dissolved in THF (36 mL) at room temperature and sodium hydride (60% suspension in mineral oil, 712 mg, 10.68 mmol) and 15-crown-5 ether (470 mg, 1.78 mmol) were added. After stirring at this temperature for 15 min, benzyl bromide (2.1 mL, 17.80 mmol) and tetrabutylammonium iodide (396 mg, 1.068 mmol) were added. The mixture was stirred at this temperature overnight and then washed with an aqueous solution of NH_4Cl (sat., 10 mL), dried over Na_2SO_4, filtered and concentrated to dryness. The resulting residue was purified by flash column chromatography (1% EtOAc/hexanes) to afford the protected diol **14c** as a yellow oil [1.271 g, 81%, R_f =0.6 (2% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 7.38 – 7.11 (m, 5H), 5.48 – 5.34 (m, 2H), 4.55 (AB, *J* = 10.8 Hz, 1H), 4.50 (AB, *J* = 10.8 Hz, 1H), 3.73 (AB, *J* = 9.8 Hz, 1H), 3.63 (AB, *J* = 9.8 Hz, 1H), 2.44 (AB, *J* = 2.8 Hz, 1H), 2.42 (AB, *J* = 2.8 Hz, 1H) 2.31 (dd, *J* = 5.1, 1.8 Hz, 2H), 2.20 (o, *J* = 6.8 Hz, 1H), 1.71 (t, *J* = 2.5 Hz, 3H), 1.01 (m, 21H), 0.90 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 141.5, 139.7, 128.6, 128.2, 127.6, 121.9, 79.7, 76.0, 65.8, 64.8, 35.9, 31.6, 24.6, 23.0, 22.9, 18.8, 12.4, 4.0.

Synthesis of compound 41



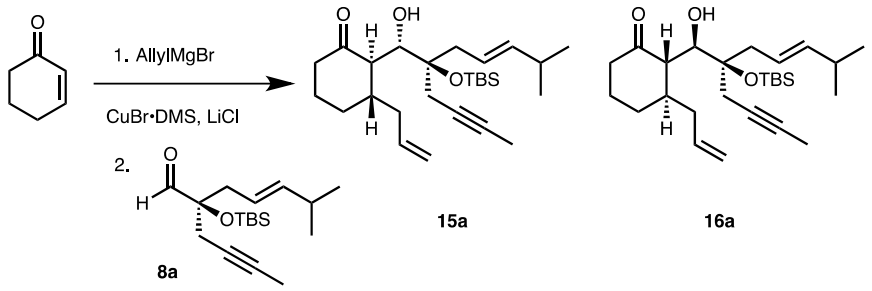
A solution of compound **14c** (1.271 g, 2.875 mg) in methanol (150 mL) was treated with aqueous HCl (2M, 40 mL) and stirred at rt for 48 h. The mixture was quenched with aqueous saturated solution of $NaHCO_3$ (100 mL). The aqueous layer was extracted with dichloromethane (4 x 50 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude mixture was purified by flash column chromatography (10% EtOAc-hexanes) to afford alcohol **41** as a yellow oil [1.229 g, 97%, R_f = 0.2 (10% EtOAc-hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 7.45 – 7.20 (m, 5H), 5.56 (dd, *J* = 15.4, 6.4 Hz, 1H), 5.41 (m, 1H), 4.56 (AB, *J* = 12.5, 11.2 Hz, 2H), 3.70 (ABd, *J* = 11.7, 6.7 Hz, 1H), 3.64 (ABd, *J* = 11.4, 5.9 Hz, 1H) 2.55 – 2.36 (m, 4H), 2.29 (o, *J* = 6.8 Hz, 1H), 1.81 (t, *J* = 2.6 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 141.8, 138.7, 128.3, 127.5, 127.4, 120.9, 79.1, 78.2, 74.8, 65.1, 64.1, 35.8, 31.2, 24.2, 22.5, 3.6. **HRMS-ESI**: calculated for $C_{19}H_{26}O_2$+Na: 307.1674, found: 307.1666.

Synthesis of aldehyde 8b



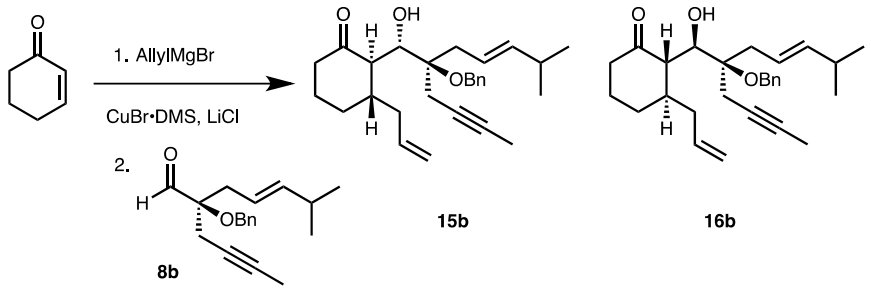
A solution of dimethyl sulfoxide (0.86 mL, 12.09 mmol) in dry dichloromethane (70 mL) was cooled to -78 ^{o}C and oxalyl chloride (0.98 mL, 11.227 mmol) was added dropwise and stirred at this temperature. After 15 min, a solution of alcohol **41** (2.470 g, 8.64 mmol) in dry dichloromethane (20 mL) was added: The resulting solution was stirred at this temperature for 1 h and then treated with triethylamine (7.2 mL, 51.62 mmol). The reaction mixture was stirred at this temperature for 2 h and washed with aqueous saturated solution of NH_4Cl (2 x 20 mL), dried over $MgSO_4$, filtered and concentrated to dryness. The resulting residues were purified by flash column chromatography (4% EtOAc/hexanes) to obtain **8b** as a yellow oil. [2.047 g**,** 83%, R_f = 0.7 (15% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 9.65 (s, 1H), 7.45 – 7.27 (m, 5H), 5.55 (ddt, *J* = 15.3, 6.6, 1.2 Hz, 1H), 5.31 (dtd, *J* = 15.5, 7.2, 1.3 Hz, 1H), 4.54 (AB, *J* = 7.6 Hz, 1H), 2.64 – 2.54 (m, 4H), 2.26 (o, *J* = 6.7 Hz, 1H), 1.79 (t, *J* = 2.6 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 204.1, 143.3, 138.3, 128.8, 128.2, 128.1, 119.5, 83.7, 79.5, 73.2, 66.8, 35.9, 31.6, 23.0, 22.8, 4.0. **HRMS-ESI**: calculated for $C_{19}H_{24}O_2$+Na: 309.1825, found: 309.1833.

Synthesis of dienynes 15a and 16ba



A mixture of anhydrous lithium chloride (197 mg, 4.6 mmol) and CuBr.DMS (956 mg, 4.6 mmol) in dry THF (34 mL) was stirred at rt until a yellowish solution was formed. The resulting solution was cooled to -78 °C and a solution of solution of allylmagnesium bromide (1.0 M in THF, 4.0 mL, 4.0 mmol) was added dropwise, stirred 15 min followed by slow addition of cyclohexenone (339 mg, 4.0 mmol). The reaction mixture was stirred at -78 °C under argon atmosphere for 40 min and then a solution of aldehyde **8a** (624 mg, 2.0 mmol) in dry THF (6 mL) was added. The reaction mixture was stirred during 50 min at -78 °C, quenched with aqueous saturated solution of NH_4Cl (40 mL) and let warm up to r.t. The organic solution was extracted with diethyl ether (2x 50 mL) and the combined organic layers were dried with $MgSO_4$, filtered and the solvent evaporated under vacuum. The residue was purified by column chromatography (10% EtOAc/hexanes) to afford compounds **15a** and **16**a (3:2 ratio) as viscous colorless liquid. [680 mg, 75%, R_f = 0.42 (10% EtOAc/hexanes)]. **^{1}H RMN** (300 MHz, $CDCl_3$, δ): 5.72 (m, 1H), 5.55 – 5.36 (m, 2H), 5.08 – 4.98 (m, 2H), 3.93 – 3.74 (m, 2H), OH, 2.68 (m, 1H), 1.76 (t, *J* = 2.5 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 6H), 0.87 (s, 9H), 0.17 – 0.13 (s, 6H). **^{13}C RMN** (75.4 MHz, $CDCl_3$, δ): 215.9, 215.5, 141.5, 141.4, 135.9, 121.9, 121.8, 116.9, 80.5, 79.1, 78.9, 76.3, 76.1, 74.8, 74.5, 53.8, 53.5, 42.9, 42.8, 42.01, 41.7, 41.0, 40.3, 37.8, 31.1, 28.5, 28.2, 27.8, 27.6, 26.1, 24.9, 24.6, 22.4, 22.3, 18.6, 3.6, -2.0, -2.1, -2.1. **HRMS-ESI**: calculated for: $C_{29}H_{46}O_3Si$+Na: 469.3114, found: 469.3106.

Synthesis of dienynes 15b and 16b

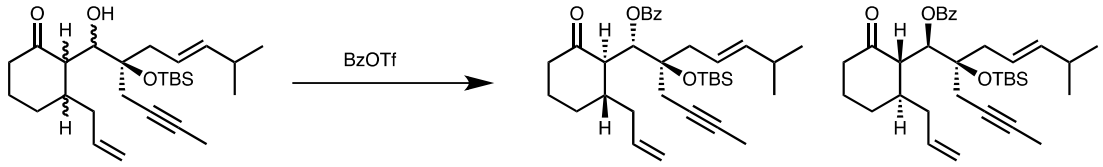


A suspension of CuBr.DMS (1.522 g, 7.39 mmol) and LiCl (310 mg, 7.39 mmol) in THF (40 mL) was stirred at room temperature until a yellowish solution was formed. The mixture was cooled to -78 °C and a solution of AllylMgBr (1M solution in THF, 6.3 mL, 6.3 mmol) was added dropwise and after stirring for 30 min ciclohexenone (0.44 mL, 4.478 mmol) was added. Finally, after another 30 min of stirring at this temperature the resulting solution was treated with a solution of aldehyde **8b** (636 mg, 2.24 mmol) in THF (10 mL). The reaction mixture was stirred at this temperature for 90 min and then quenched with aqueous saturated solution of NH_4Cl. The mixture was poured in a separation funnel and washed with NH_4Cl (2 x 20 mL), dried over Na_2SO_4, filtered and concentrated. The residues were purified by flash column chromatography (2% EtOAc/hexanes) to obtain a mixture of **15b** and **16b** in a 5:3 ratio as a yellow oil. [747 mg, 79%, R_f = 0.27 (10% EtOAc/hexanes)]. **HRMS-ESI**: calculated for $C_{28}H_{28}O_3$+Na: 445.2738, found: 445.2719.

Spectroscopic data for **15b**: **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 7.36 – 7.22 (m, 5H), 5.73 (dddd, *J* = 16.9, 10.2, 7.4, 6.6 Hz, 1H), 5.60 – 5.39 (m, 2H), 5.02 (m, 2H), 4.59 (AB, *J* = 10.8 Hz, 2H), 4.10 (dd, *J* = 9.4, 2.8 Hz, 1H), 2.73 (dd, *J* = 7.0, 2.8 Hz, 1H), 2.61 – 2.43 (m, 4H), 2.39 – 2.15 (m, 5H), 2.12 – 1.88 (m, 3H), 1.78 (t, *J* = 2.5 Hz, 3H), 1.72 (m, 1H), 1.49 (m, 1H), 0.97 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 216.6, 141.6, 139.0, 135.9, 128.1, 127.5, 127.2, 121.7, 116.9, 80.9, 78.7, 75.4, 75.1, 64.9, 53.5, 43.1, 42.0, 38.0, 36.5, 31.2, 28.6, 25.1, 24.6, 22.4, 3.6.

Spectroscopic data for **16b**: **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 7.37 – 7.23 (m, 5H), 5.71 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.56 (dd, *J* = 15.4, 6.5 Hz, 1H), 5.42 (dt, *J* = 15.3, 7.0 Hz, 1H), 4.99 (m, 2H), 4.60 (AB, *J* = 10.7 Hz, 1H), 3.97 (dd, *J* = 9.8, 2.3 Hz, 1H), 2.90 (dd, *J* = 8.5, 2.4 Hz, 1H), 2.62 – 2.48 (m, 3H), 2.48 – 1.87 (m, 10H), 1.75 (t, *J* = 2.6 Hz, 3H), 1.69 (m, 1H), 1.49 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 217.9, 141.7, 139.1, 135.6, 128.1, 127.5, 127.4, 127.2, 127.1, 121.3, 117.0, 80.4, 78.7, 76.2, 73.5, 64.4, 52.4, 43.2, 42.4, 37.8, 36.6, 31.2, 29.6, 26.0, 23.8, 22.6, 22.4, 3.8.

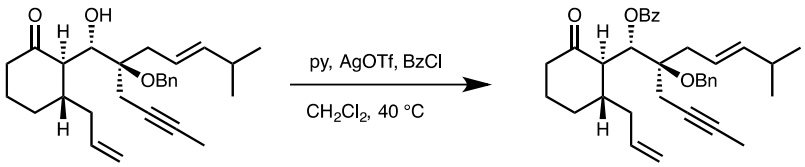
Synthesis of dienynes 17a and 18a



15a, 16a **17a** **18a**

A solution of dienynes **15a** and **16a** (180 mg, 0.4 mmol) in dry dichloromethane (5.3 mL) in a sealed tube was cooled to 0 °C and successively treated with dry pyridine (1.28 g, 16.1 mmol) and freshly prepared benzoyl triflate (2.05 g, 8.1 mmol). The reaction mixture was heated at 60 °C for 12 h. The reaction mixture was cooled down to rt and quenched with water (10 mL). The resulting mixture was poured into a separation funnel and diluted with dichloromethane (40 mL). The organic layer was washed with saturated aqueous solution of $NaHCO_3$ (2x30 mL), dried over $MgSO_4$ and filtered. After concentration to dryness under vacuum, the residue was purified by flash chromatography (4% EtOAC/hexanes) to yield dienynes **17a** and **18a** as a viscous colorless liquid [170 mg, 77%, R_f = 0.40 (10% EtOAc/hexanes)]. **^{1}H NMR** (300 MHz, $CDCl_3$, δ): 8.01 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 5.71 (m, 1H), 5.61 (d, *J* = 5.7 Hz, 1H), 5.50 - 5.37 (m, 2H), 5.11 - 4.98 (m, 2H), 3.04 - 2.93 (m, 1H), 1.69 (m, 3H), 0.96 - 0.88 (m, 6H), 0.86 (s, 9H), 0.21 - 0.14 (s, 6H). **^{13}C NMR** (75.4 MHz, $CDCl_3$, □): 211.2, 211.1, 165.6, 165.5, 141.7, 141.5, 135.9, 135.9, 133.1, 133.0, 130.0, 129.9, 129.8, 128.4, 121.3, 120.9, 117.1, 80.3, 80.1, 79.5, 79.4, 77.1 76.9, 75.7, 75.1, 54.6, 54.5, 41.2, 41.0, 40.9, 40.6, 39.7, 39.3, 37.3, 37.1, 31.2, 31.1, 28.6, 28.1, 26.1, 26.0, 24.7, 24.4, 22.3, 22.3, 22.3, 22.2, 21.8, 21.6, 18.6, 3.6, 3.5, -1.8, -2.0, -2.0, -2.1. **HRMS-ESI:** calculated for: $C_{34}H_{50}O_4Si$+Na: 573.3376, found: 573.3379.

Synthesis of dienyne 17b

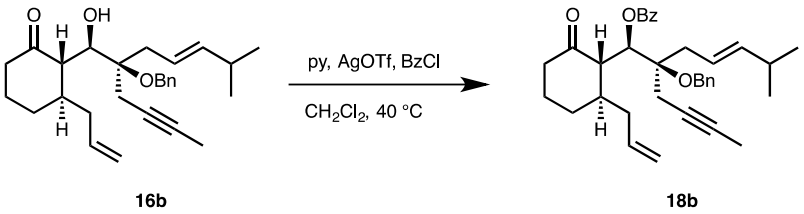


15b **17b**

A suspension of silver triflate (339 mg, 1.32 mmol) in dichloromethane (1 mL) at room temperature was treated with benzoyl chloride (0.15 mL, 1.32 mmol) and the resulting mixture was stirred at this temperature for 5 min. The supernatant was transferred via cannula to a falsk containing the solution of **15b** (374 mg, 0.44 mmol) and pyridine (0.38 mL, 2.21 mmol) in

dichloromethane (5 mL). The resulting solution was refluxed during 3 h and then washed with aqueous saturated solution of NH_4Cl (2 x 2 mL), dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash column chromatography (3% EtOAc/hexanes) to obtain compound **17b** as a yellow oil [165 mg, 71%, R_f = 0.5 (15% AcOEt/hexane)].[6] **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 8.06 – 8.02 (m, 2H), 7.64 – 7.23 (m, 8H), 5.71 (d, *J* = 6.3 Hz, 1H), 5.61 (m, 1H), 5.53 – 5.36 (m, 2H), 5.01 (dtd, *J* = 13.2, 2.4, 1.0 Hz, 2H), 4.76 (AB, *J* = 10.5 Hz, 1H), 4.56 (AB, *J* = 10.5 Hz, 1H), 3.03 (d, *J* = 6.3 Hz, 1H), 2.67 – 2.36 (m, 8H), 2.33 – 1.85 (m, 5H), 1.79 (m, 1H), 1.72 (t, *J* = 2.5 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 211.8, 165.7, 142.4, 138.7, 136.1, 133.7, 133.3, 130.2, 129.9, 128.6, 128.1, 127.9, 127.3, 120.5, 117.0, 80.7, 79.0, 76.2, 75.0, 65.1, 54.5, 41.1, 39.5, 37.4, 36.8, 31.4, 25.0, 24.1, 22.5, 22.2, 3.6. **HRMS-ESI**: calculated for $C_{35}H_{42}O_4$+Na: 549.2975, found: 549.2966.

Synthesis of dienyne 18b

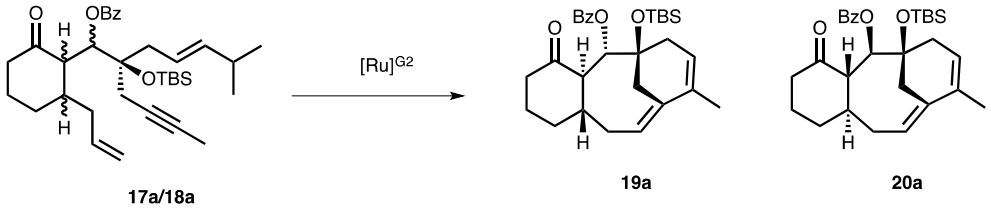


16b **18b**

Compound **18b** was obtained employing the same method used to obtain **16b** as yellow oil (74%, R_f = 0.5 (15% EtOAc/hexanes).[6] **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 8.07 – 8.02 (m, 2H), 7.67 – 7.28 (m, 8H), 6.04 (d, *J* = 7.1 Hz, 1H), 5.69 (ddt, *J* = 17.2, 10.2, 7.0 Hz, 1H), 5.60 – 5.40 (m, 2H), 5.05 (m, 2H), 4.77 (d, *J* = 10.3 Hz, 1H), 4.55 (d, *J* = 10.3 Hz, 1H), 3.21 (d, *J* = 6.9 Hz, 1H), 2.68 – 2.54 (m, 2H), 2.51 – 1.97 (m, 10H), 1.72 (t, *J* = 2.5 Hz, 3H), 1.76 (m, 1H), 1.31 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 211.6, 165.9, 142.0, 138.6, 136.0, 133.8, 133.5, 130.2, 129.9, 129.6, 129.4, 128.8, 128.6, 128.2, 127.5, 120.5, 117.1, 81.1, 79.3, 76.5, 74.4, 65.6, 54.0, 41.0, 39.2, 37.2, 34.7, 31.3, 25.7, 24.7, 22.3, 21.7, 3.6. **HRMS-ESI**: calculated for $C_{35}H_{42}O_4$+Na: 549.2975, found: 549.2966.

[6] Brown, L.; Koreeda, M. *J. Org. Chem.* **1984**, *49*, 3875.

Synthesis of taxadienes 19a and 20a



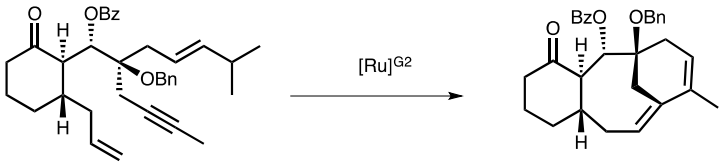
17a/18a 19a 20a

A solution of dienynes **17a** and **18a** (766 mg, 1.4 mmol) and second generation Grubbs catalyst **[Ru]^{G2}** (71 mg, 83 μmol) in dry dichloromethane (278 mL) was refluxed under Ar for 2h. The reaction mixture was cooled to r.t. and the solvent was evaporated under vacuum. The residue was filtered through a short plug of alumina (20% diethyl ether/hexanes). The crude mixture was purified by column chromatography (4% EtOAc/hexanes) to obtain taxadienes **19a** [254 mg, 38%, R_f = 0.38 (10% EtOAc/hexanes)] and **20a** [200 mg, 30%, R_f = 0.45 (10% EtOAc/hexanes)] in the form of colorless viscous liquids.

Spectroscopic data for **19a**: **^{1}H NMR** (500 MHz, $CDCl_3$, δ): 7.95 (d, J = 7.6 Hz, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.39 (t, J = 7.6 Hz, 2H), 5.41 (t, J = 7.2 Hz, 1H), 5.37 (d, J = 8.3 Hz, 1H), 5.33 (m, 1H), 3.03 (dq, J = 19.2, 2.7 Hz, 1H), 2.91 (d, J = 12.5 Hz, 1H), 2.90 (m, 1H), 2.79 (t, J = 8.3 Hz, 1H), 2.70 (m, 1H), 2.52 (m, 1H), 2.30 (d, J = 12.5 Hz, 1H), 2.21 (dd, J = 19.2, 4.6 Hz, 1H), 2.05 (m, 1H), 2.01 (m, 1H), 2.01 (m, 1H), 1.86 (m, 3H), 1.84 (m, 1H), 1.78 (m, 1H), 1.19 (m, 1H), 0.68 (s, 9H), 0.06 (s, 3H), -0.07 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$, δ): 211.8, 165.9, 141.0, 138.2, 132.7, 130.5, 129.8, 128.2, 120.6, 119.7, 83.1, 77.2, 54.2, 42.0, 40.2, 37.7, 35.1, 32.9, 31.7, 25.4, 21.8, 18.1, 17.7, -2.4, -2.6. **HRMS-ESI:** Calculated for $C_{29}H_{40}O_4Si$+Na: 503.2594, found: 503.2585.

Spectroscopic data for **20b: ^{1}H NMR** (500 MHz, $CDCl_3$, δ): 7.99 (d, J = 7.7 Hz, 2H), 7.52 (t, J = 7.7 Hz, 1H), 7.39 (t, J = 7.7 Hz, 2H), 5.72 (t, J = 7.9 Hz, 1H), 5.52 (d, J = 5.7 Hz, 1H), 5.23 (m, 1H), 3.07 (dd, J = 1.0 Hz, 1H), 3.01 (d, J = 11.5 Hz, 1H), 2.55-2.44 (m, 1H), 2.43-2.33 (m, 1H), 2.31-2.10 (m, 5H), 2.06-1.95 (m, 1H), 1.94-1.77 (m, 5H), 1.75-1.64 (m, 1H), 1.48-1.36 (m, 1H), 1.01 (s, 9H), 0.16 (s, 3H), 0.11 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$, δ): 210.4, 166.9, 140.3, 135.4, 132.9, 130.1, 129.8, 128.2, 122.2, 121.1, 77.9, 75.2, 58.0, 46.1, 38.3, 37.6, 37.6, 35.1, 30.7, 25.8, 22.2, 18.3, 17.8, -1.9, -2.1. **HRMS-ESI:** calculated for $C_{29}H_{40}O_4Si$+Na: 503.2594, found: 503.2589.

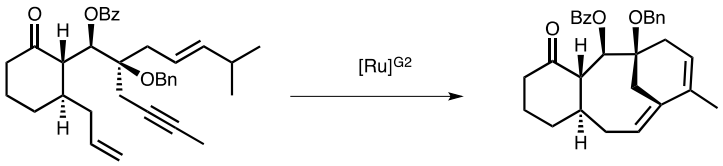
Synthesis of taxadiene 19b



17b 19b

A solution of compound **17b** (153 mg, 0.29 mmol) and second generation Grubbs catalyst (25 mg, 0.03 mmol) in dichloromethane (58 mL) was refluxed for 2 h under Ar. After this time the mixture was filtered through a celita path and concentrated to dryness. The residue was purified by flash column chromatography (5% EtOAc/hexanes) to obtain **19b** as yellow oil [75 mg, 53%, R_f=0.5 (15% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 500 MHz, δ): 7.96 (d, *J* = 1.4 Hz, 1H), 7.95 (d, *J* = 1.6 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.18 – 7.12 (m, 5H), 5.81 (d, *J* = 9.1 Hz, 1H), 5.45 (dd, *J* = 8.1, 5.4 Hz, 1H), 5.35 (dt, *J* = 4.6, 2.2 Hz, 1H), 4.62 (AB, *J* = 11.7 Hz, 1H), 4.46 (AB, *J* = 11.6 Hz, 1H), 3.08 – 2.96 (m, 2H), 2.93 – 2.85 (m, 2H), 2.79 (m, 1H), 2.54 (ddd, *J* = 15.0, 9.1, 3.7 Hz, 1H), 2.37 (AB, *J* = 12.5 Hz, 1H), 2.25 (dd, *J* =19.2, 5.0 Hz, 1H), 2.18 – 1.98 (m, 3H), 1.92 (ddt, *J* = 13.2, 9.5, 4.4 Hz, 1H), 1.87 (s, 3H), 1.87 – 1.84 (m, 3H), 1.83 (dt, *J* = 11.7, 3.9 Hz, 1H), 1.20 (dt, *J* = 12.9, 4.4 Hz, 1H). **^{13}C NMR** ($CDCl_3$, 126 MHz, δ): 211.8, 165.9, 140.4, 139.1, 139.1, 132.9, 130.3, 129.8, 128.3, 128.1, 127.0, 126.9, 120.2, 119.8, 80.7, 78.5, 64.0, 54.5, 42.3, 37.7, 35.5, 33.6, 32.3, 29.5, 22.2, 18.2. **HRMS-ESI**: calculated for $C_{30}H_{32}O_4$+Na: 479.2193, found: 479.2199.

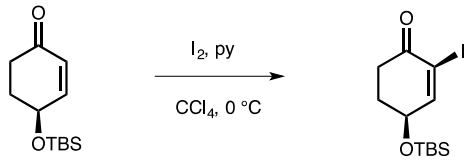
Synthesis of taxadiene 20b



18b 20b

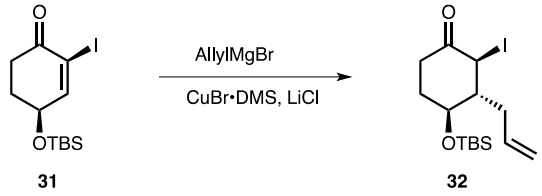
Compound **20b** was prepared using similar conditions to obtaine **19b** as yellow oil. [57%, R_f = 0.4 (15% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 500 MHz, δ): 7.99 (d, *J* = 1.2 Hz, 1H), 7.97 (d, *J* = 1.5 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.39 (dt, *J* = 23.8, 7.8 Hz, 4H), 7.32 – 7.25 (m, 2H), 5.77 (t, *J* = 7.9 Hz, 1H), 5.51 (d, *J* = 4.3 Hz, 1H), 5.27 (dt, *J* = 3.1, 1.4 Hz, 1H), 5.20 (d, *J* = 10.9 Hz, 1H), 4.70 (d, *J* = 10.9 Hz, 1H), 3.13 (dd, *J* = 10.3, 4.4 Hz, 1H), 3.01 (AB, *J* = 11.7 Hz, 1H), 2.57 (ddd, *J* = 17.5, 3.0, 1.7 Hz, 1H), 2.52 – 2.36 (m, 4H), 2.32 (AB, *J* = 11.9 Hz, 1H), 2.19 (dd, *J* = 13.3, 7.3 Hz, 1H), 2.06 (ddd, *J* = 13.2, 7.0, 5.7 Hz, 1H), 1.94 (dddd, *J* = 18.8, 12.3, 9.3, 6.2 Hz, 1H), 1.85 (s, 3H), 1.81 (dddd, *J* =10.1, 8.2, 6.5, 4.7 Hz, 1H), 1.74 (ddd, *J* = 13.9, 4.0, 2.6 Hz, 1H), 1.39 (ddt, *J* = 18.7, 12.1, 6.5 Hz, 1H). **^{13}C NMR** ($CDCl_3$, 126 MHz, δ): 210.2, 167.1, 140.8, 139.9, 135.9, 133.2, 129.9, 129.7, 128.6, 128.3, 127.9, 127.3, 122.8, 120.5, 78.7, 78.0, 66.3, 57.1, 44.6, 37.7, 37.0, 35.3, 33.1, 30.7, 21.0, 17.8. **HRMS-ESI**: calculated for $C_{30}H_{32}O_4$+Na: 479.2193, found: 479.2193.

Synthesis of (S)-4-((tert-butyldimethylsilyl)oxy)-2-iodocyclohex-2-en-1-one (31)



A solution of I_2 (425 mg, 1.67 mmol) in pyridine-carbon tetrachloride (1:1, 6 mL) was cooled to 0 °C and then added over a solution of **28** (126 mg, 0.26 mmol) in pyridine-carbon tetrachloride (1:1, 6 mL) at the same temperature. The resulting mixture was stirred at room temperature for 2 h, poured into a separatory funnel and washed with an aqueous saturated solution of NH_4Cl (2 x 15 mL). The resulting organic solution was dried over Na_2SO_4, filtered, concentrated under vacuum and the resulting residue was purified by flash column chromatography (6% EtOAc/hexanes) to obtain **31** as a yellow oil [154 mg, 78%, R_f =0.7 (20% EtOAc/hexanes)].[7] **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 7.59 (dd, *J* = 2.8, 1.3 Hz, 1H), 4.50 (ddd, *J* = 8.8, 4.9, 2.8 Hz, 1H), 2.82 (dt, *J* = 16.7, 4.7 Hz, 1H), 2.49 (ddd, *J* = 16.9, 12.5, 4.6 Hz, 1H), 2.24 (dddd, *J* = 9.7, 8.2, 5.6, 4.1 Hz, 1H), 2.04 (tdd, *J* = 13.1, 8.8, 4.3 Hz, 1H), 0.90 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 191.5, 162.1, 104.1, 69.3, 33.5, 32.9, 25.7, 18.1, -4.7, -4.8. **HRMS-ESI**: calculated for $C_{12}H_{21}IO_2Si$+Na: 375.0253, found: 375.0242.

Synthesis of compound 32

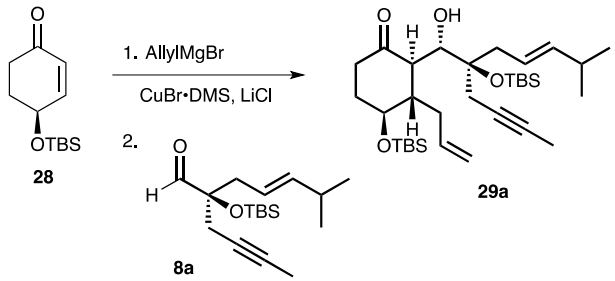


CuBr.DMS (224 mg, 1.09 mmol) and lithium chloride (46 mg, 1.09 mmol) were suspended in THF (3 mL) at room temperature and stirred for 15 min and mixture was cooled to -78 °C. A solution of allylmagnesium bromide (1M solution in THF, 0.87 mL, 0.87 mmol) was added dropwise and the resulting mixture stirred at this temperature for 30 min. Finally, a solution of **31** (154 mg, 0.436 mmol) in THF (1 mL) was added and the mixture was additionally stirred at this temperature for 1 h. The reaction was quenched by addition of an aqueous saturated solution of NH_4Cl (1 mL) and the resulting organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (2%

[7] William, A. D.; Kobayashi, Y. *J. Org. Chem*. **2002**, *67*, 8771.

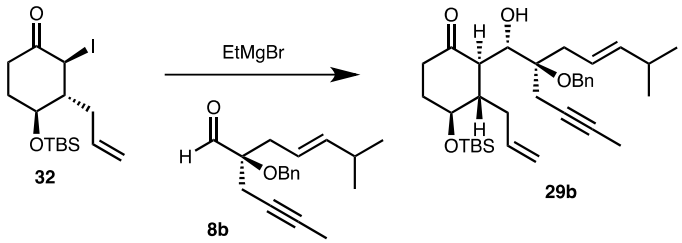
EtOAc/hexanes) to obtain **32** as a yellow oil [121 mg, 76%, R_f = 0.6 (5% EtOAc/hexanes)]. **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 5.69 (ddt, *J* = 16.8, 10.1, 7.0 Hz, 1H), 5.23 – 5.12 (m, 2H), 4.48 (dd, *J* = 7.4, 1.3 Hz, 1H), 3.89 (ddd, *J* = 7.4, 5.8, 3.4 Hz, 1H), 3.06 (ddd, *J* = 14.2, 8.4, 5.4 Hz, 1H), 2.41 (dddd, *J* = 12.9, 6.5, 3.1, 1.2 Hz, 1H), 2.34 – 2.13 (m, 3H), 2.03 (dddd, *J* = 13.5, 8.6, 5.1, 3.2 Hz, 1H), 1.83 (dtd, *J* = 13.5, 8.3, 5.4 Hz, 1H), 0.90 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 203.5, 132.9, 119.2, 69.1, 52.5, 37.0, 33.3, 33.1, 31.5, 25.8, 18.0, -4.3, -4.7. **HRMS-ESI**: calculated for $C_{15}H_{29}IO_2Si$+Na: 417.0717, found: 417.0726.

Synthesis of dienyine 29a



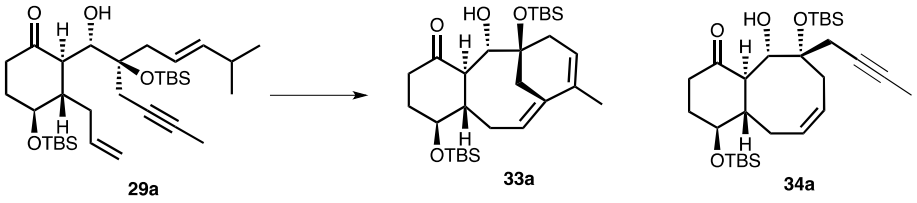
A mixture of LiCl (16 mg, 375 μmol) and CuBr.DMS (77 mg, 375 μmol) in dry THF (4 mL) was stirred at room temperature until a yellowish solution was formed. The solution was cooled down to -78 °C and then treated with a solution of allylmagnesium bromide (1.0 M in THF, 0.32 mL, 326 μmol). After stirring for 15 min at this temperature, a solution of cyclohexenone **28** (74 mg, 326 μmol) in dry THF (1 mL) was added. The resulting mixture was stirred for 30 min and a solution of aldehyde **8a** (67 mg, 217 μmol) in dry THF (1 mL) was added. After stirring the solution at this temperature for 4.5 h, the reaction was quenched with saturated solution of NH_4Cl (5 mL). The mixture was allowed to warm up to rt and extracted with diethy ether (3x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated to dryness. The residue was purified by column chromatography (5% EtOAc/hexanes) to afford the dienyne **29a** as a colorless oil [25 mg, 40% based on 50% of consumed aldehyde, Rf =0.52 (10% EtOAc/hexanes)]. **^{1}H RMN** (300 MHz, $CDCl_3$, δ): 5.72 (m, 1H), 5.46 (m, 1H), 5.46 (m, 1H), 5.08 (m, 1H), 5.03 (m, 1H), 4.66 (d, *J* = 5.7 Hz, 1H), 3.94 (m, 1H), 3.84 (dd, *J* = 5.7, 1.7 Hz, 1H), 2.82 (ddd, *J* = 14.0, 12.1, 7.2 Hz, 1H), 1.77 (t, *J* = 2.5 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.92 (s, 9H), 0.87 (s, 9H), 0.19 (s, 3H), 0.17 (s, 3H), 0.125 (s, 3H), 0.118 (s, 3H). **^{13}C RMN** (75.4 MHz, $CDCl_3$, δ): 214.5, 140.8, 135.5, 122.3, 117.5, 80.2, 78.4, 77.5, 76.7, 69.2, 52.6, 50.5, 39.6, 37.7, 37.6, 31.1, 30.1, 27.1, 26.2, 25.8, 22.6, 22.4, 18.7, 18.1, 3.7, -2.2, -2.4, -4.8. **HRMS-ESI:** calculated for $C_{33}H_{33}O_4Si$+Na: 599.3928, found: 599.3927.

Synthesis of dienyine 29b



A solution of ketone **32** (46 mg, 0.12 mmol) in THF (1 mL) was treated with a solution of ethylmagnesium bromide (1M solution in THF, 0.14 mL, 0.14 mmol) and the mixture was stirred at this temperature for 30 min. After this time, a solution of **8b** (33 mg, 0.12 mmol) in THF (0. 5 mL) was added. After stirring the mixture for 2 h, the solution was poured into a separatory funnel and washed with aqueous saturated solution of NH_4Cl (2 x 1 mL). The aqueous layers were extracted with diethyl ether (2 x 1 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by flash column chromatography (3% EtOAc/hexanes) to obtain of **29b** as yellow oil [33 mg, 50%, R_f = 0.5 (10% EtOAc/hexanes)].[7] **^{1}H NMR** ($CDCl_3$, 300 MHz, δ): 7.37 – 7.24 (m, 5H), 5.66 (ddd, *J* = 11.7, 11.1, 5.3 Hz, 1H), 5.57 – 5.39 (m, 2H), 5.08 – 4.93 (m, 2H), 4.61 (dd, *J* = 11.1, 7.1 Hz, 2H), 4.07 – 3.77 (m, 1H), 4.07 – 3.77 (m, 1H), 3.65 (ddd, *J* = 10.6, 5.8, 2.1 Hz, 1H), 2.70 – 2.08 (m, 8H), 2.04 – 1.84 (m, 3H), 1.80 (dt, *J* = 4.5, 2.1 Hz, 3H), 1.72 – 1.60 (m, 2H), 1.09 – 0.88 (m, 9H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 7.3 Hz, 3H), 0.12 – 0.06 (m, 6H). **^{13}C NMR** ($CDCl_3$, 75 MHz, δ): 211.1, 141.3, 135.4, 128.3, 128.0, 127.4, 121.8, 117.2, 80.8, 80.2, 78.8, 75.2, 70.1, 64.2, 51.0, 44.2, 42.2, 37.5, 36.9, 31.4, 25.7, 24.2, 24.0, 23.6, 22.5, 3.6, -4.5, -4.8. **HRMS-ESI**: calculated for $C_{34}H_{52}O_4Si$+Na: 575.3533, found: 575.3569.

Synthesis of taxadiene analogue 33a



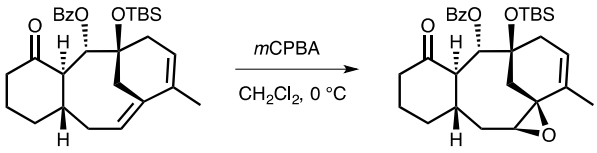
A solution of dienyne **29a** (16 mg, 27 μmol) and second generation Grubbs [Ru]^{G2} catalyst (2 mg, 3 μmol) in dry dichloromethane (8 mL) was refluxed for 2h. The reaction mixture was cooled to rt and the solvent was evaporated under vacuum. The residue was filtered through a plug of alumina (20% diethyl ether/hexanes) and the resulting solution was concentrated to dryness. The residue was purified by flash column chromatography (15% diethyl ether/hexanes) to afford taxadiene analogue **33a [**8 mg, 56%, R_f = 0.43 (10% EtOAc/hexanes)] together with cyclooctane

derivative **34a** [6 mg, 40%, R_f = 0.52 (10% EtOAc/hexanes)] in the form of colorless viscous liquids.

Spectroscopic data for **33a**: **^{1}H NMR** (300 MHz, $CDCl_3$, δ): 5.33 (t, *J* = 7.4 Hz, 1H), 5.29 (m, 1H), 3.81 (dd, *J* = 7.6, 2.0 Hz, 1H), 3.37 (td, *J* = 9.1, 5.0 Hz, 1H), 3.21 (d, *J* = 2.0 Hz, 1H), 1.82 (m, 3H), 0.90 (s, 9H,), 0.86 (s, 9H), 0.13 (s, 6H), 0.07 (s, 3H), 0.06 (s, 3H). **HRMS-ESI**: Calculated for $C_{28}H_{50}O_4Si_4$+Na: 529.3145, found: 529.3140.

Spectroscopic data for **34a**: **^{1}H NMR** (300 MHz, $CDCl_3$, δ): 5.82 (m, 1H), 5.70 (m, 1H), 3.99 (dd, J = 8.9, 3.7 Hz, 1H), 3.53 (td, J = 10.0, 4.9 Hz, 1H), 1.80 (t, J = 2.6 Hz, 3H), 0.91 (s, 9H), 0.86 (s, 9H), 0.18 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$, δ): 215.2, 129.8, 128.9, 81.5, 78.3, 77.3, 76.2, 70.2, 49.3, 38.8, 36.1, 32.7 , 30.1, 29.7, 27.0, 25.9, 25.8, 18.5, 18.0, 3.7, -2.1, -3.9, -4.8. **MS-ESI (m/e, I)**: 529.2 ($M+Na^+$, 100), 335.1 (16), 313.2 (41), 301.1 (82).

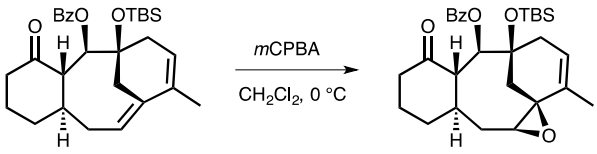
Synthesis of epoxide 21a



19a **21a**

A solution of taxadiene **19a** (31 mg, 64 μmol) in dichloromethane (3 mL) cooled at 0 °C was treated with *m*CPBA (13 mg, 77 μmol). The reaction mixture was stirred under argon atmosphere for 30 min and then saturated solution of $NaHCO_3$ (20 mL) was added and extracted with dichloromethane (3x30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under vacuum. The crude mixture was purified by column chromatography (8% EtOAc/hexanes) to afford epoxide **21a** as a white solid [20 mg, 62%, R_f=0.21 (10% EtOAc/hexanes)]. **^{1}H NMR** (500 MHz, $CDCl_3$, δ): 7.97 (dd, *J* = 7.5, 1.3 Hz, 2H), 7.53 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 2H), 5.00 (dd, *J* = 4.8, 0.8 Hz, 1H), 3.37 (dq, *J* = 19.5, 2.6 Hz, 1H), 2.82 (dd, *J* = 11.3, 3.9 Hz, 1H), 2.73 (m, 1H), 2.63 (1H, ddd, *J* = 11.4, 4.8, 0.5 Hz, 1H), 2.49 (ddd, *J* = 13.9, 10.3, 7.8 Hz, 1H), 2.47 (d, J = 13.0 Hz, 1H), 2.37 (dsa, *J* = 19.5 Hz, 1H), 2.13 (ddd, *J* = 14.2, 3.9, 0.6 Hz, 1H), 2.02 (m, 1H), 1.96 (m, 1H), 1.90 (ddd, *J* = 14.2, 11.3, 7.2 Hz, 1H), 1.81 (d, *J* = 13.0 Hz, 1H), 1.77 (m, 1H) 1.56 (dt, *J* = 3.7, 2.1 Hz, 3H), 1.45 (m, 1H), 0.64 (s, 9H), 0.03 (s, 3H), -0.06 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$, δ): 209.7, 166.4, 134.7, 132.9, 130., 129.7, 128.2, 125.5, 80.9, 76.1, 60.5, 57.5, 53.4, 39.6, 38.2, 36.9, 34.8, 30.8, 29.1, 25.4, 20.5, 17.8, 15.2, - 2.4, -2.4. **HRMS-ESI:** calculated for $C_{29}H_{40}O_5Si$+Na: 519.2443, found: 519.2536.

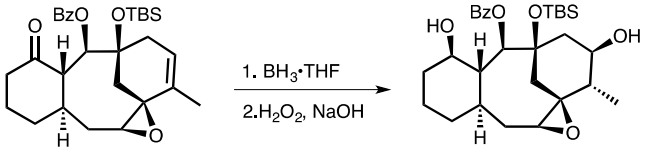
Synthesis of epoxide 36a



20a **36a**

A solution of taxadiene **20a** (41 mg, 85 μmol) in dichloromethane (4 mL) at 0 °C was treated with *m*CPBA (19 mg, 94 μmol). The reaction mixture was stirred under argon atmosphere for 35 min and then a saturated solution of $NaHCO_3$ (20 mL) was added. The mixture was poured into a separation funnel and extracted with dichloromethane (3x30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under vacuum. The residue was purified by flash column chromatography (8% EtOAc/hexanes) to afford epoxide **36a** as a colorless viscous liquid [32 mg, 76%, R_f = 0.33 (10% EtOAc/hexanes)]. **^{1}H NMR** (500 MHz, $CDCl_3$, δ): 8.00 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 5.51 (m, 1H), 5.37 (d, *J* = 4.6 Hz, 1H), 3.06 (dd, *J* = 9.5, 5.1 Hz, 1H), 2.66 (dd, *J* = 10.3, 4.6 Hz, 1H), 1.53 (d, *J* = 1.5 Hz, 3H), 1.00 (s, 9H), 0.15 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$, δ): 209.7, 166.8, 134.5, 133.2, 129.8, 129.7, 128.4, 124.5, 76.9, 76.3, 60.7, 57.9, 56.3, 39.4, 37.7, 37.5, 37.0, 36.8, 30.0, 25.7, 21.3, 18.2, 15.2, -2.0, -2.1. **HRMS-ESI:** calculated for $C_{29}H_{40}O_5Si$+H: 497.2723, found: 497.2719.

Synthesis of taxane 22a

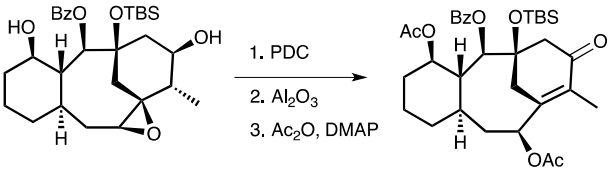


36a **22a**

A solution of BH_3.THF (1.0 M, 0.8 mmol) in THF (0.8 mL) was added to a 0 °C cooled solution of epoxide **36a** (64 mg, 129 μmol) in dry THF (4.8 mL). After stirring for 4 h at 0 °C, the mixture was successively treated with aqueous solutions of NaOH (3.0M, 1.2 mL) and H_2O_2 (30%, 0.6 mL). The reaction mixture was allowed to slowly warm up to rt and stirred for additional 12 h. The reaction mixture was treated with diethy ether (30 mL) and 3.0 M NaOH (20 mL). The organic layer was separated and the aqueous layer was extracted with diethyl (2x30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent evaporated under vacuum. The residue was purified by flash chromatography (16% EtOAc/hexanes) to afford compound **22a** as a white solid [50 mg, 76%, R_f = 0.31 (20% EtOAc/hexanes)]. **^{1}H NMR** (500 MHz, $CDCl_3$, δ): 8.09 (d, *J* = 7.6 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 5.27 (d, *J* = 4.2 Hz, 1H), 3.51 (td, *J* = 10.5, 5.1 Hz, 1H), 3.13 (dt, *J* = 9.8, 4.1 Hz, 1H), 3.05 (dd, *J* = 9.2, 5.1 Hz, 1H), 2.91 (s, 1H), 2.36 (ddd, *J* = 12.3, 5.1, 2.5 Hz, 1H), 2.32 (dd, *J* = 14.3, 5.1 Hz, 1H), 2.13 (d, *J* = 12.4 Hz, 1H), 2.36 (dd, *J*

= 12.4, 2.8 Hz, 1H), 1.92 (m, 1H), 1.90 (m, 1H), 1.82 (m, 1H), 1.69 (m, 1H), 1.68 (m, 1H), 1.66 (m, 1H), 1.61 (m, 1H), 1.25 (s, 1H), 1.22 (m, 1H), 1.18 (m, 1H), 1.14 (m, 1H), 1.00 (m, 1H), 0.96 (s, 9H), 0.89 (d, J = 6.7 Hz, 3H), 0.25 (s, 3H), 0.23 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$, δ): 166. 4, 133.6, 129.8, 129.1, 128.7, 79.2, 76.6, 71.7, 69.8, 60.8, 54.6, 49.8, 44.7, 44.1, 40.0, 39.8, 38.0, 34.7, 33.4, 26.0, 22.3, 18.2, 9.9, - 1.6, -1.7. **EM- ESI** (m/e, I): 539.2 ($M+Na^+$, 100), 517.1 ($M+H^+$, 17.7), 4999.2 (M-OH, 7.7), 395 ($M-C_6H_5CO_2$, 9.7).

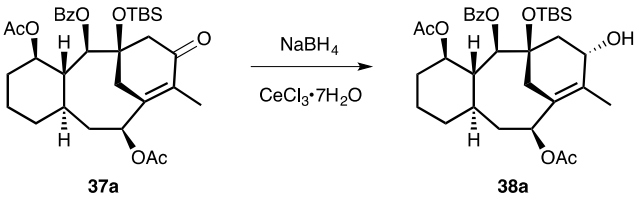
Synthesis of taxane 37a



22a **37a**

A solution of epoxyalcohol **22a** (35 mg, 68 μmol) in dry dichloromethane (2 mL) was treated with PDC (102 mg, 271 μmol) and molecular sieves 4Å (30 mg). The resulting mixture was stirred at room temperature for 2h and then the solids were filtered through a celites pad. The solids were washed with diethyl ether (2x25 mL) and the organic phase was concentrated to dryness. The residue was dissolved with dichloromethane (1.4 mL) and activated alumina (4 mg) was added. The reaction mixture was stirred at room temperature for 15 h and then 4-dimethylaminopyridine (83 mg, 677 μmol) and acetic anhydride (34 mg, 339 mmol) were added. The suspension was stirred at rt for 30 min, diluted with diethyl ether (40 mL) and successively washed with aqueous HCl (10%, 2x30 mL) and brine (30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent evaporated under vacuum. The residue was purified by flash chromatography (12% EtOAc/hexanes) to afford compound **37a** as a colorless viscous liquid [30 mg, 74%, R_f = 0.32 (20% EtOAc/hexanes)]. **^{1}H NMR** (300 MHz, $CDCl_3$, δ): 8.00 (d, *J* = 7.4 Hz, 2H), 7.55 (tt, *J* = 7.4, 1.5 Hz, 1H), 7.41 (t, *J* = 7.4 Hz, 2H), 5.86 (t, *J* = 8.2 Hz, 1H), 5.28 (d, *J* = 5.9 Hz, 1H), 4.96 (m, 1H), 2.84 (dd, *J* = 14.1, 3.1 Hz, 1H), 2.67 (dd, *J* = 17.7, 3.1 Hz, 1H), 2.48 (d, *J* = 17.7 Hz, 1H), 2.46 (d, *J* = 14.1 Hz, 1H), 2.24 – 2.09 (m, 3H), 2.06 (s, 3H), 1.97 (d, *J* = 2.0 Hz, 3H), 1.93 (s, 3H), 0.98 (s, 9H), 0.20 (s, 3H), 0.14 (s, 3H). **^{13}C NMR** (75.4 MHz, $CDCl_3$, δ): 198.7, 169.8, 169.7, 166.7, 147.0, 136.2, 133.3, 129.7, 129.5, 128.3, 78.2, 78.0, 71.9, 71.0, 50.0, 45.6, 42.6, 37.7, 35.8, 32.9, 29.7, 26.1, 25.8, 21.6, 21.1, 19.7, 18.2, 11.1, -1.7, -2.0. **HRMS-ESI:** calculated for $C_{33}H_{46}O_8Si$+H: 599.3040, found: 599.3034.

Synthesis of taxane 38a



37a 38a

A solution of ketone **37a** (29 mg, 48 μmol) in methanol (3 mL) was treated with $CeCl_3.7H_2O$ (18 mg, 48 μmol) and stirred until a clear solution was formed. Afterwards the solution was cooled to 0 °C and $NaBH_4$ (2 mg, 53 μmol) was added. After stirring for 15 min at this temperature, reaction was quenched by addition of a saturated solution of NH_4Cl (3 mL), then diluted with brine (20 mL) and extracted with diethyl ether (3x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed under vacuum. The resulting residue was purified by flash chromatography (18% EtOAc/hexanes) to afford compound **38a** as a white solid [28 mg, 97%, R_f = 0.31 (20 EtOAc/hexanes)]. **^{1}H NMR** (500 MHz, $CDCl_3$, δ): 8.07 (d, *J* = 7.4 Hz, 2H), 7.57 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 5.59 (dd, *J* = 10.6, 6.1 Hz, 1H), 5.48 (m, 1H), 4.78 (m, 1H), 4.50 (m, 1H), 3.06 (m, 1H), 2.27 (m, 1H), 2.15 (m, 4H), 2.08 (s, 3H), 1.95 (s, 3H), 1.81 (m, 2H), 1.66 (m, 1H), 1.56 (dd, *J* = 14.0, 9.2 Hz, 1H), 1.27 (m, 1H), 0.75 (s, 9H), 0.09 (s, 3H), 0.03 (s, 3H). **^{13}C RMN** (126 MHz, $CDCl_3$, δ): 170.6, 165.6, 142.4, 132.9, 130.7, 129.6, 128.4, 126.7, 78.2, 77.4, 73.8, 71.6, 68.9, 53.8, 43.8, 36.2, 35.6, 33.0, 31.2, 25.7, 23.2, 21.3, 17.9, 12.3, -2.0, -2.3. **HRMS-ESI:** calculated for $C_{33}H_{48}O_8Si$+Na: 623.3016, found: 623.3010.

Spectra

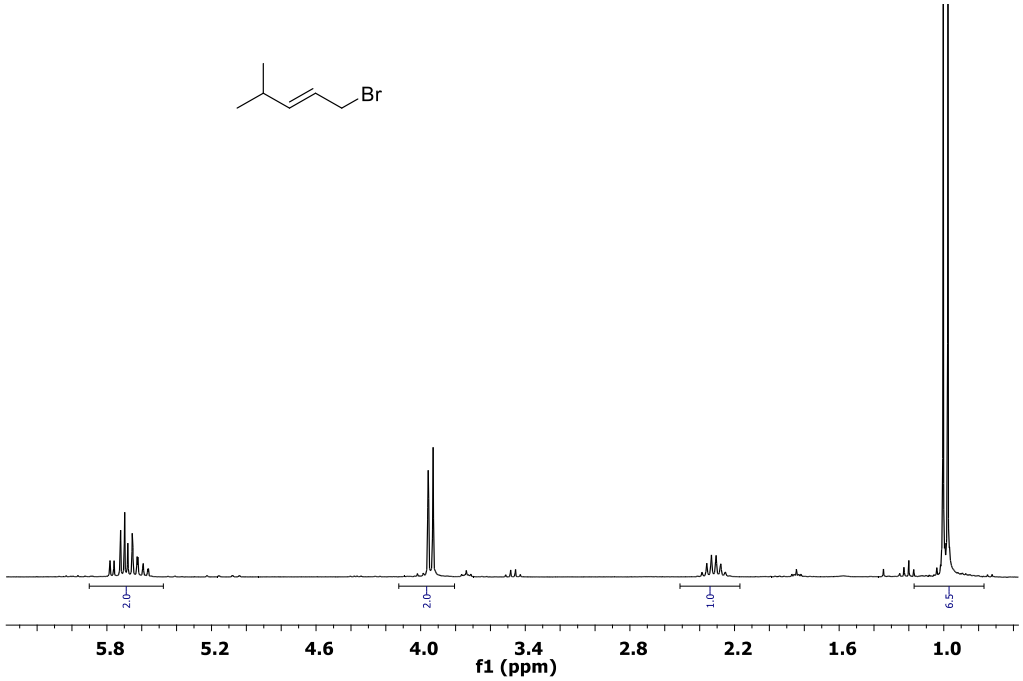


Figure 4SI. ^{1}H NMR spectrum of 1-bromo-4-methylpent-2-ene recorded in $CDDl_3$ at 250 MHz.

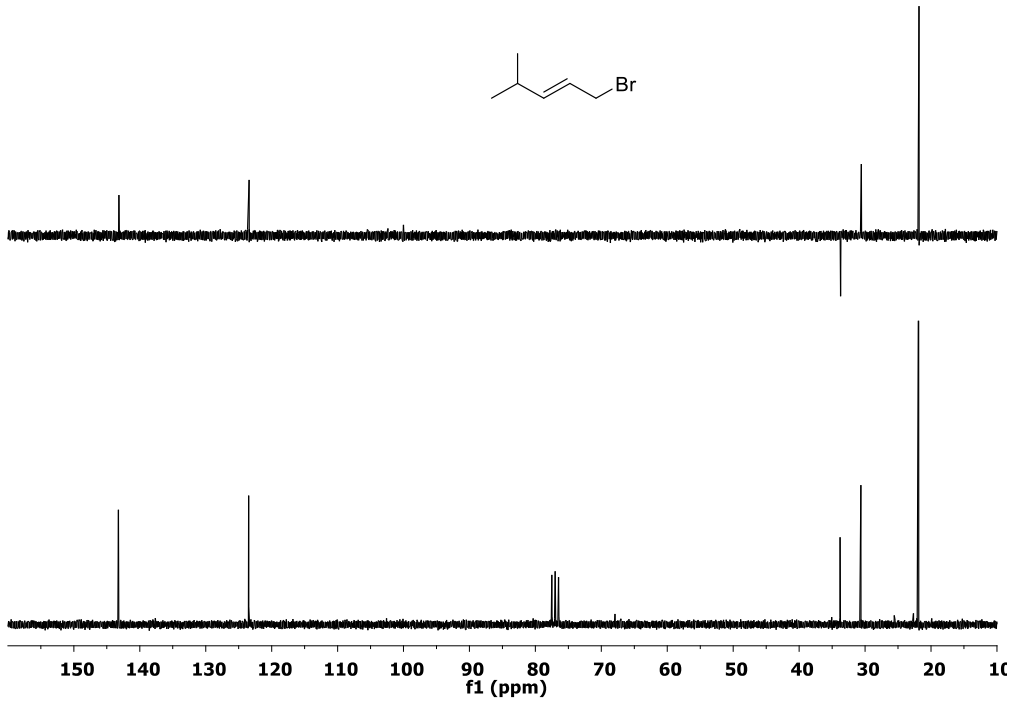


Figure 5SI. DEPT 135 (top) and ^{13}C NMR (bottom) of 1-bromo-4-methylpent-2-ene recorded in $CDCl_3$ at 63 MHz.

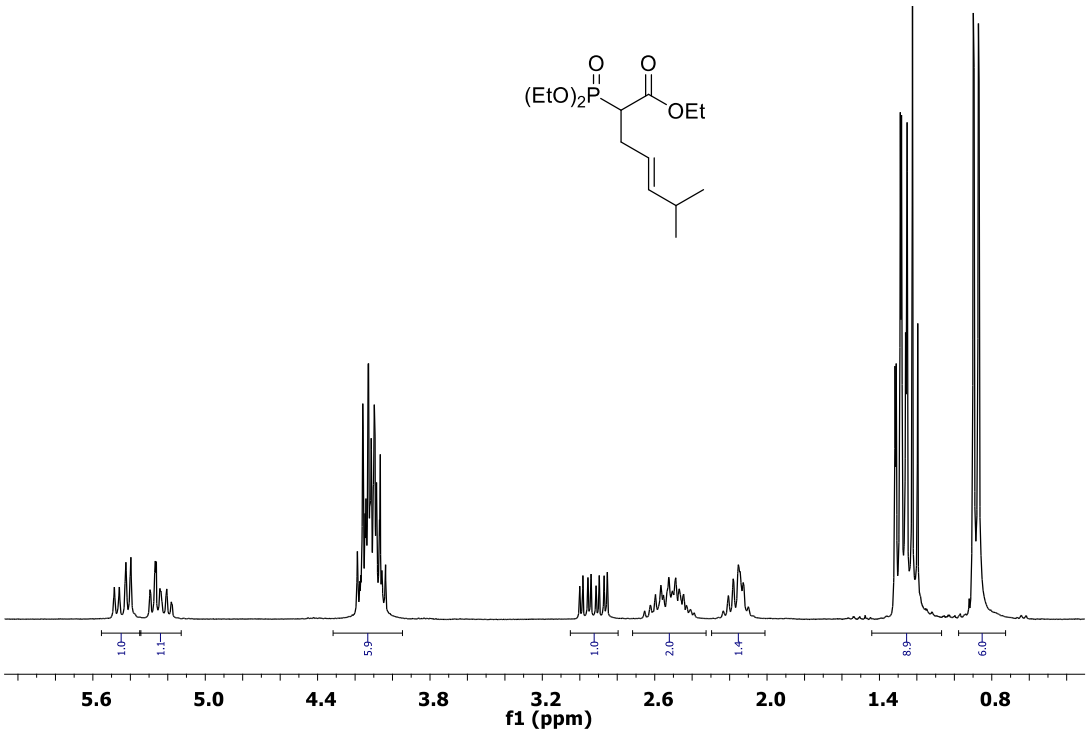


Figure 6SI. ^{1}H NMR spectrum of compound **11** recorded in $CDDl_3$ at 300 MHz.

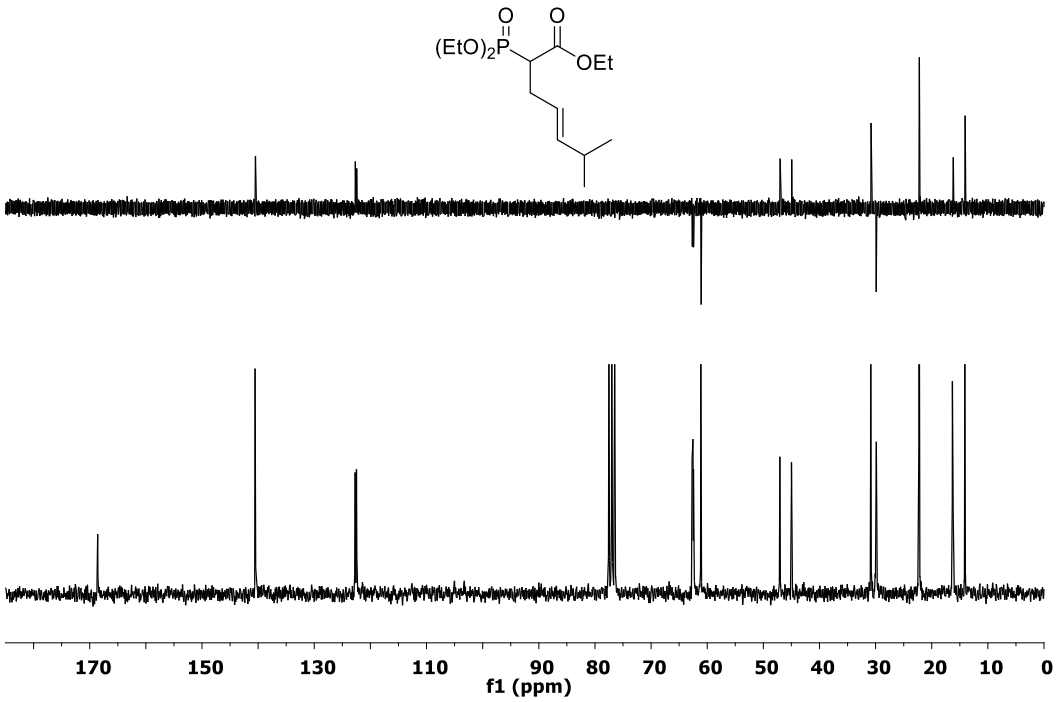


Figure 7SI. DEPT 135 (top) and ^{13}C NMR (bottom) of compound **11** recorded in $CDCl_3$ at 63 MHz.

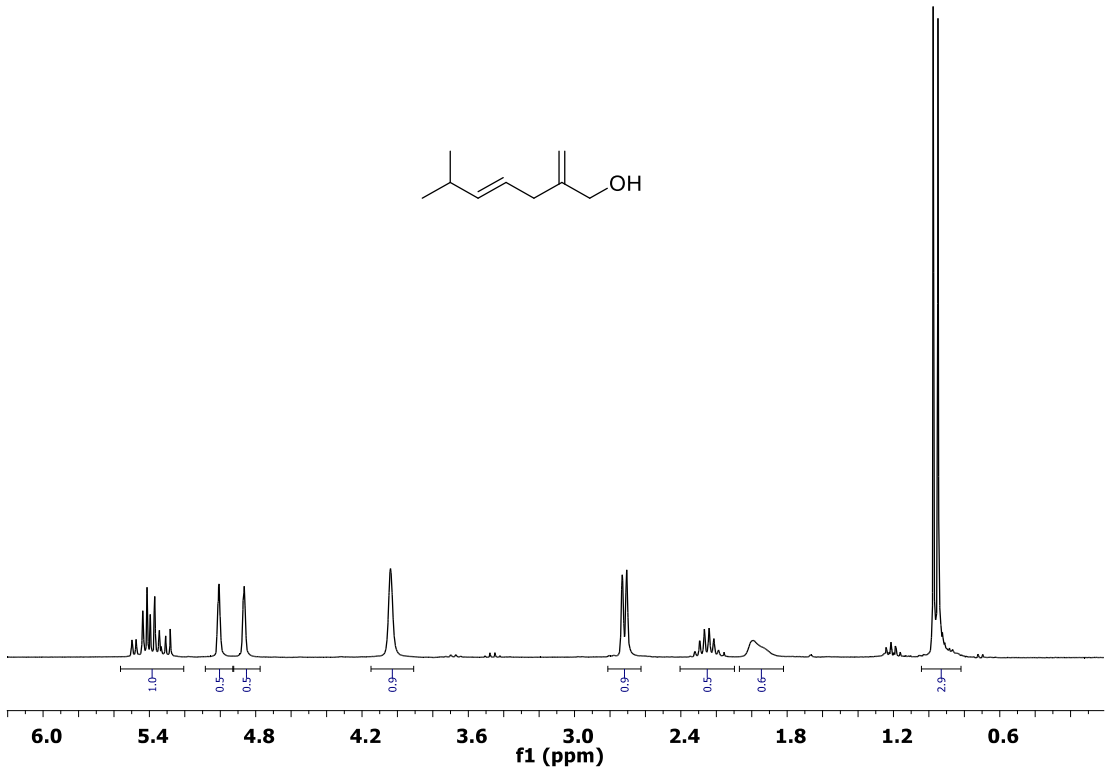


Figure 8SI. ^{1}H NMR spectrum of compound **12** recorded in $CDDl_3$ at 300 MHz.

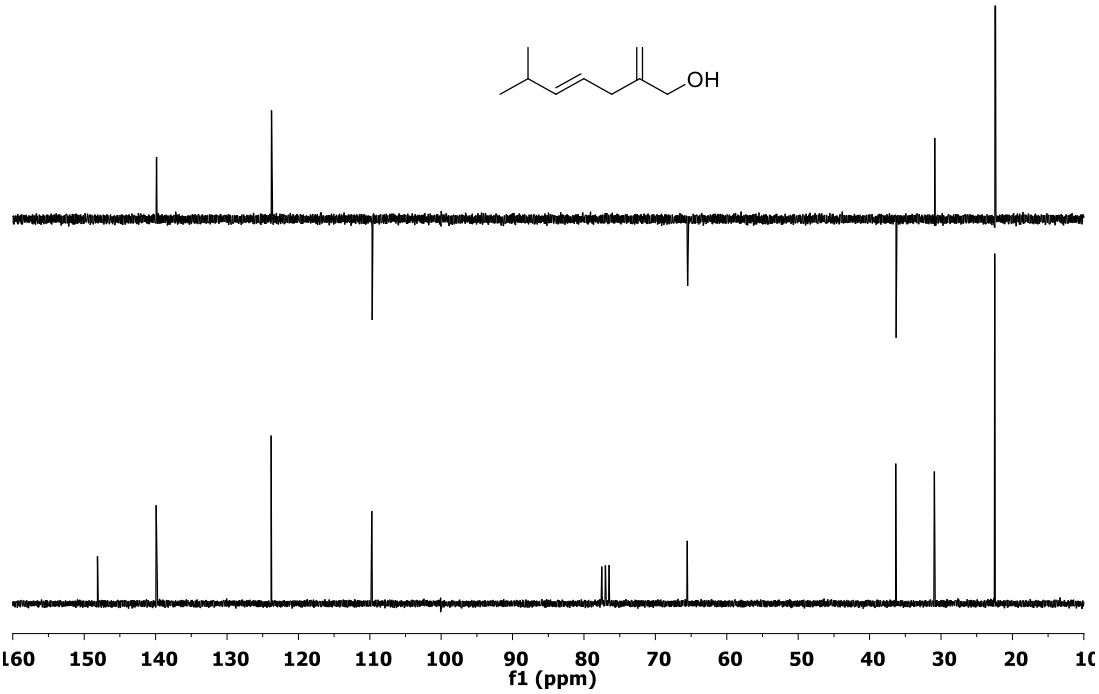


Figure 9SI. DEPT 135 (top) and ^{13}C NMR (bottom) of compound **12** recorded in $CDCl_3$ at 75 MHz.

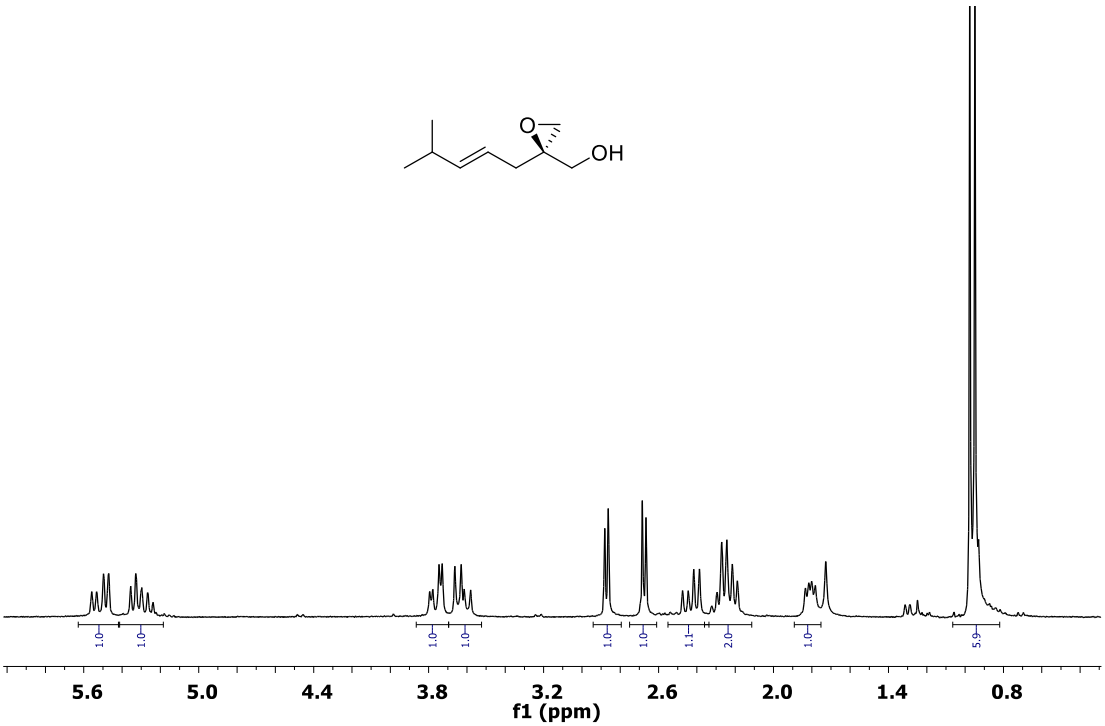


Figure 10SI. ^{1}H NMR spectrum of epoxy-alcohol **13** recorded in $CDDl_3$ at 300 MHz.

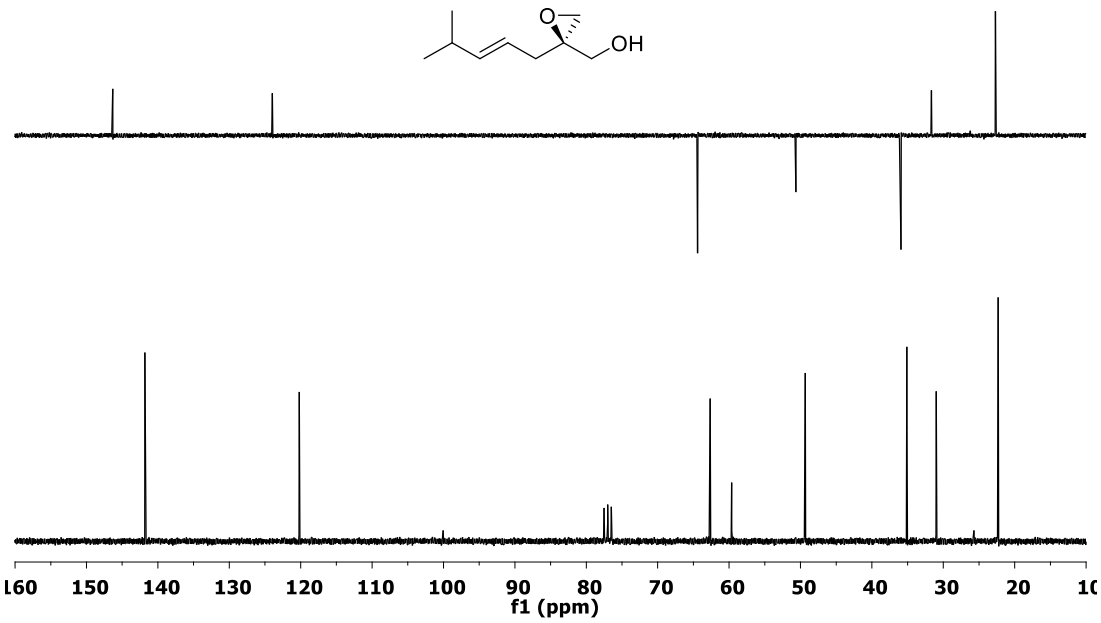


Figure 11SI. DEPT 135 (top) and ^{13}C NMR (bottom) of epoxy-alcohol **13** recorded in $CDCl_3$ at 75 MHz.

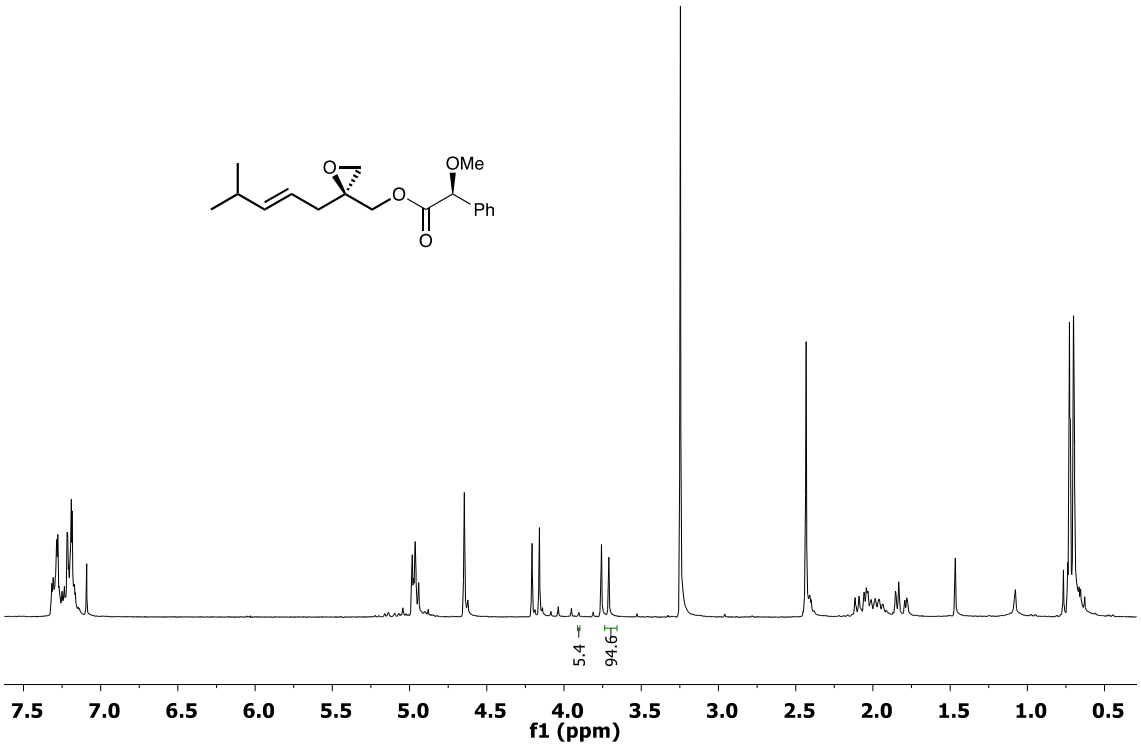


Figure 12SI. ^{1}H NMR spectrum of epoxy-alcohol **39** recorded in $CDDl_3$ at 300 MHz.

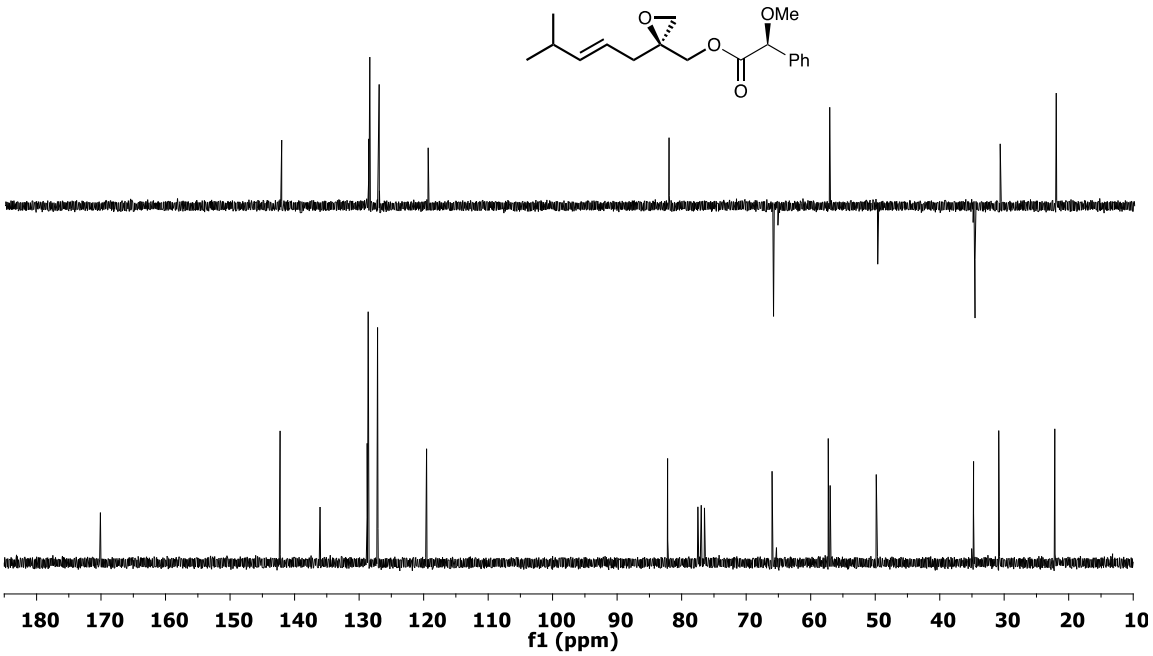


Figure 13SI. DEPT 135 (top) and ^{13}C NMR (bottom) of epoxy-alcohol **39** recorded in $CDCl_3$ at 75 MHz.

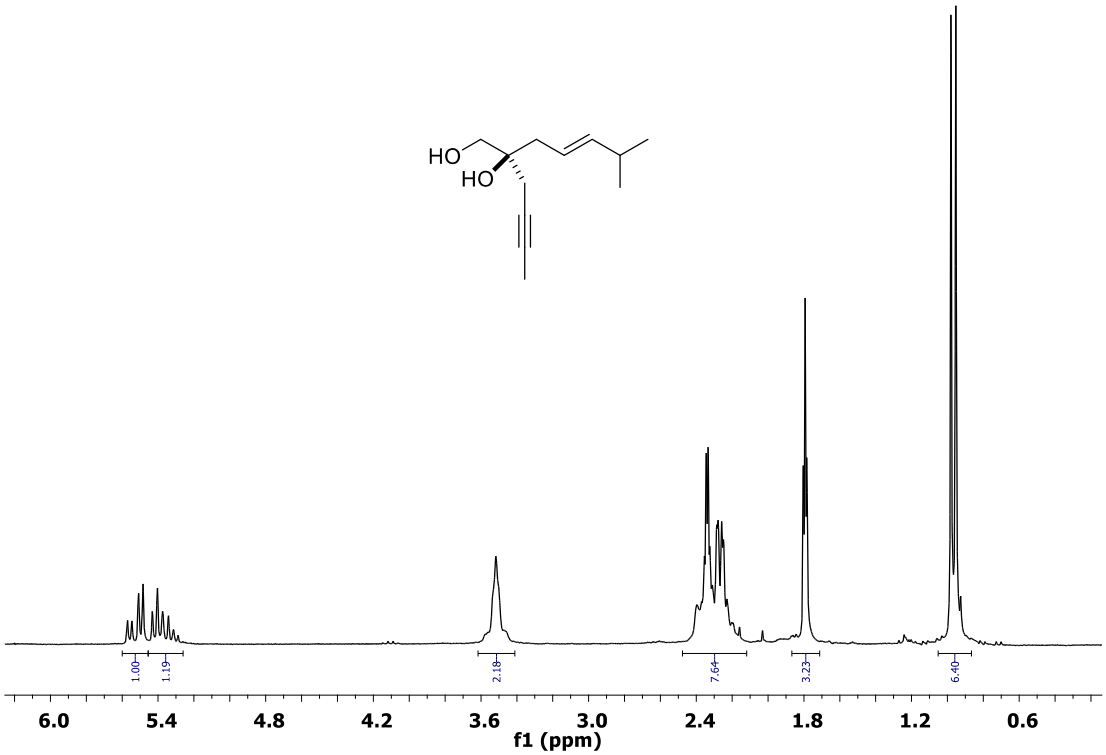


Figure 14SI. ^{1}H NMR spectrum of diol **14a** recorded in $CDDl_3$ at 300 MHz.

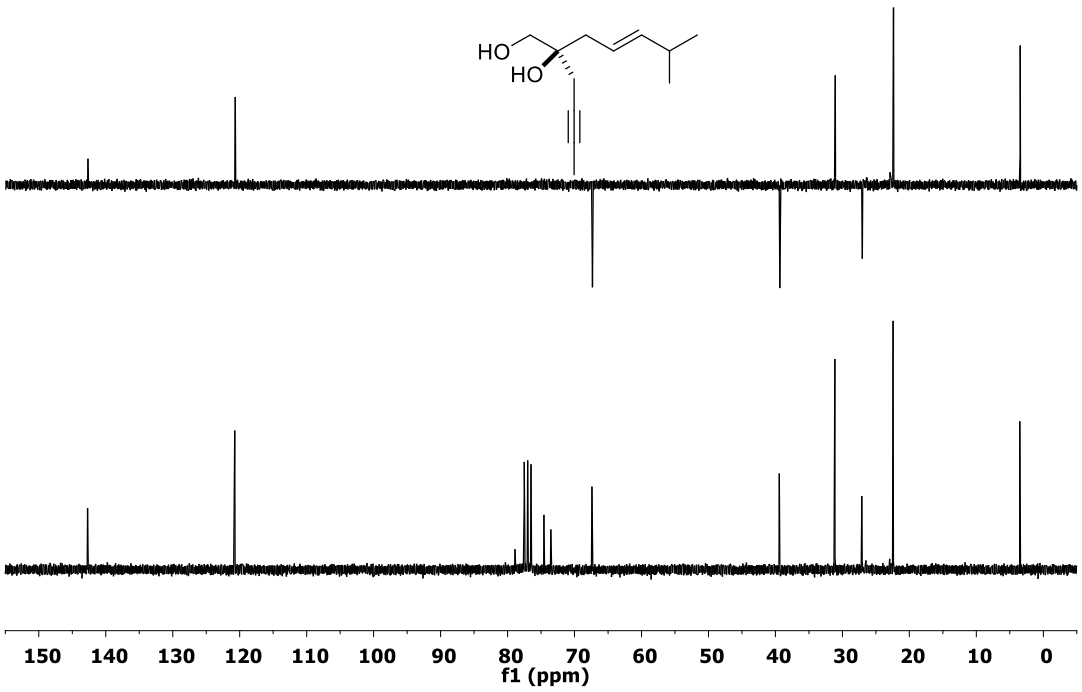


Figure 15SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dio **14a** recorded in $CDCl_3$ at 75 MHz.

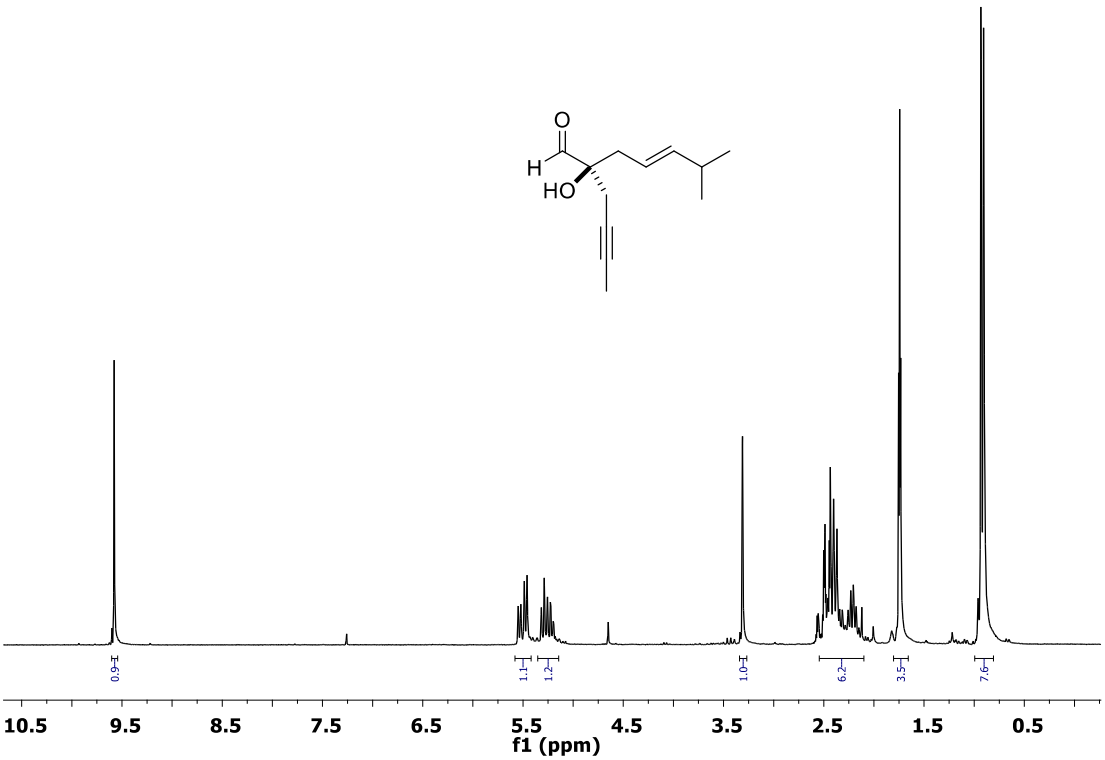


Figure 16SI. ^{1}H NMR spectrum of aldehyde **40** recorded in $CDDl_3$ at 300 MHz.

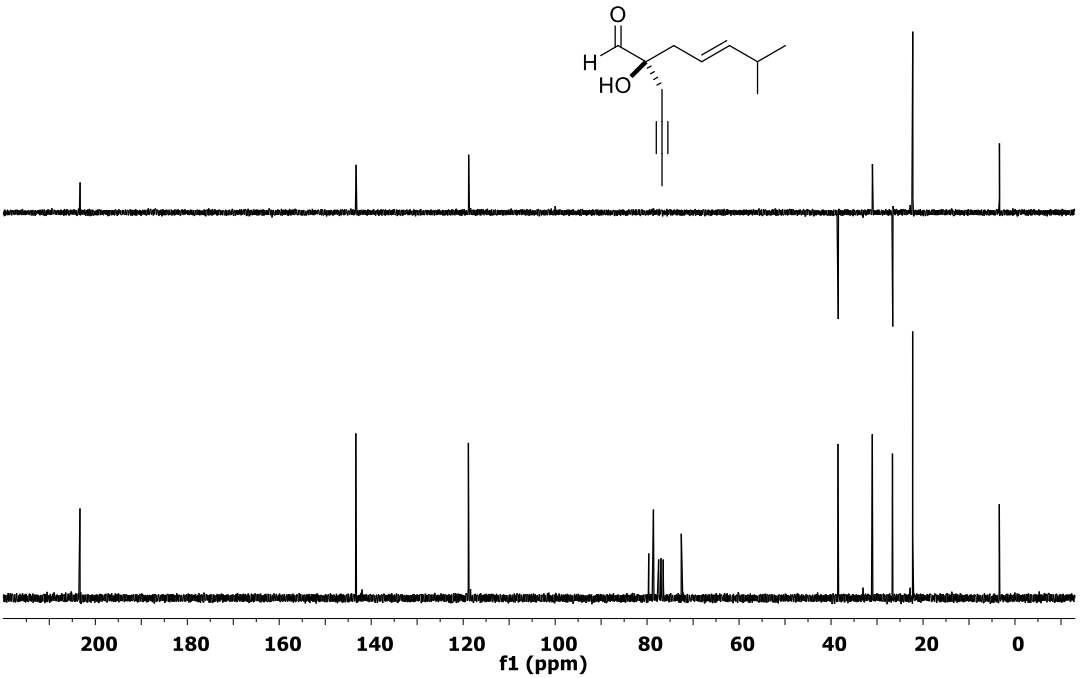


Figure 17SI. DEPT 135 (top) and ^{13}C NMR (bottom) of aldehyde **40** recorded in $CDCl_3$ at 75 MHz.

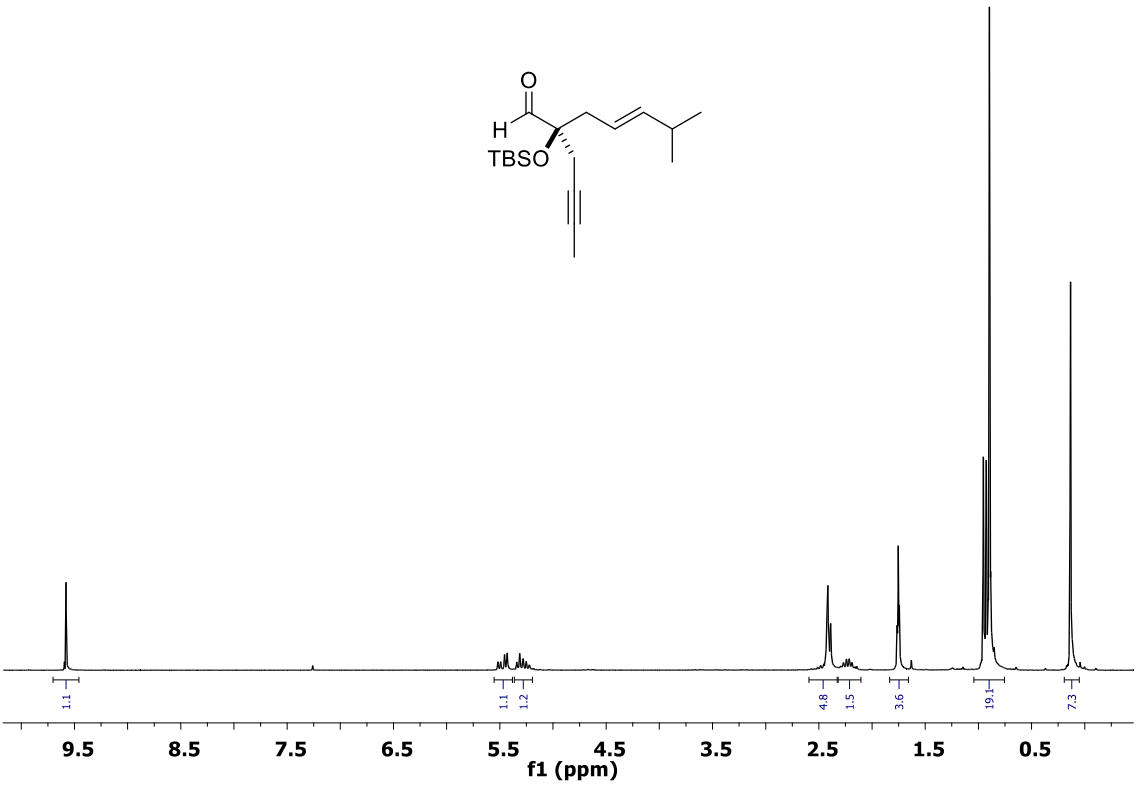


Figure 18SI. ^{1}H NMR spectrum of aldehyde **8a** recorded in $CDDl_3$ at 300 MHz.

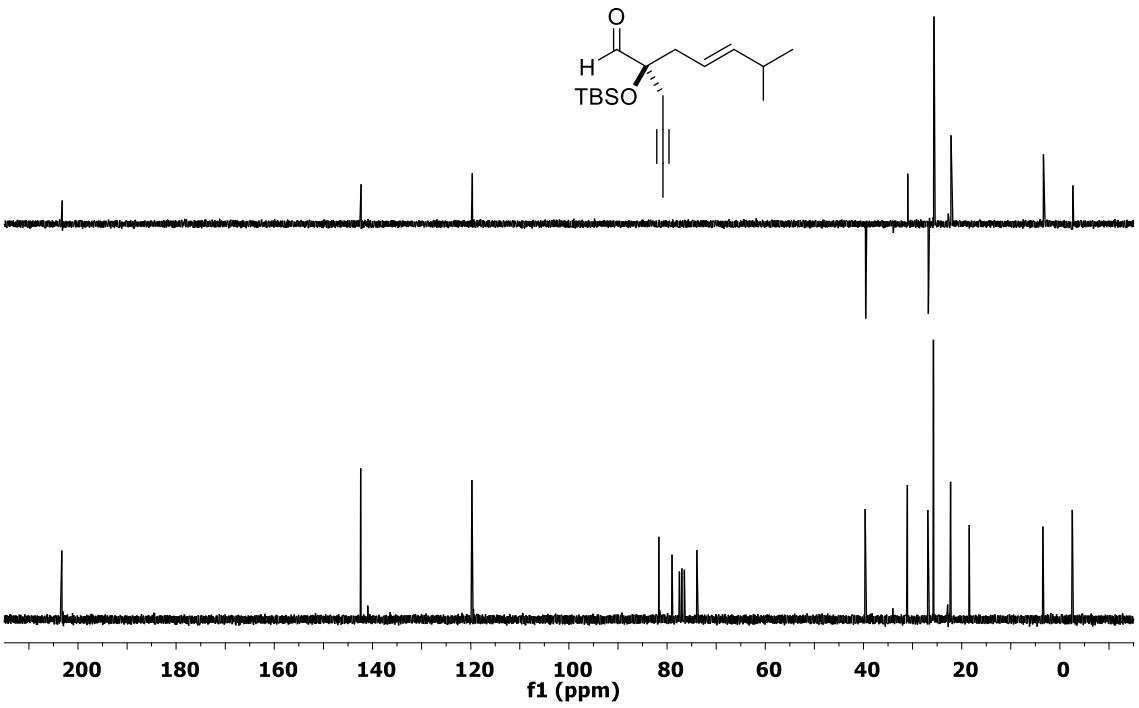


Figure 19SI. DEPT 135 (top) and ^{13}C NMR (bottom) of aldehyde **8a** recorded in $CDCl_3$ at 75 MHz.

Figure 20SI. ^{1}H NMR spectrum of alcohol **14b** recorded in $CDDl_3$ at 300 MHz.

Figure 21SI. DEPT 135 (top) and ^{13}C NMR (bottom) of alcohol **14b** recorded in $CDCl_3$ at 75 MHz.

Figure 22SI. ^{1}H NMR spectrum of compound **14c** recorded in $CDDl_3$ at 300 MHz.

Figure 23SI. DEPT 135 (top) and ^{13}C NMR (bottom) of alcohol **14c** recorded in $CDCl_3$ at 75 MHz.

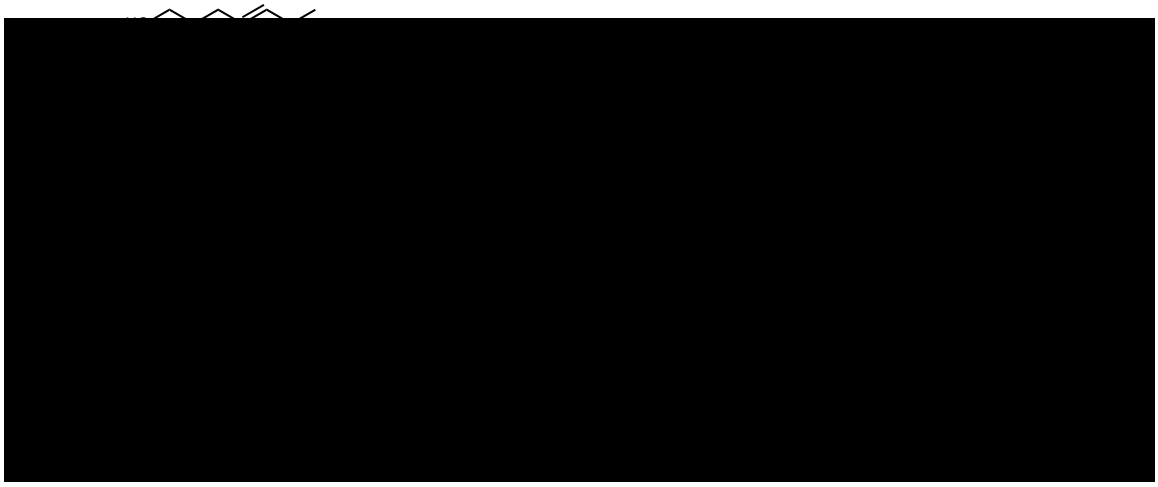


Figure 24SI. ^{1}H NMR spectrum of compound **41** recorded in $CDDl_3$ at 300 MHz.

Figure 25SI. DEPT 135 (top) and ^{13}C NMR (bottom) of alcohol **41** recorded in $CDCl_3$ at 75 MHz.

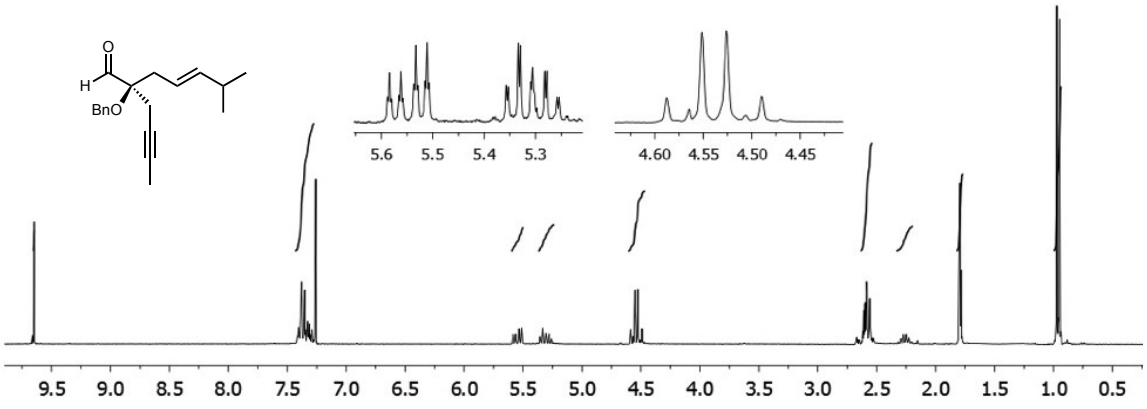


Figure 26SI. ^{1}H NMR spectrum of aldehyde **8b** recorded in $CDDl_3$ at 300 MHz.

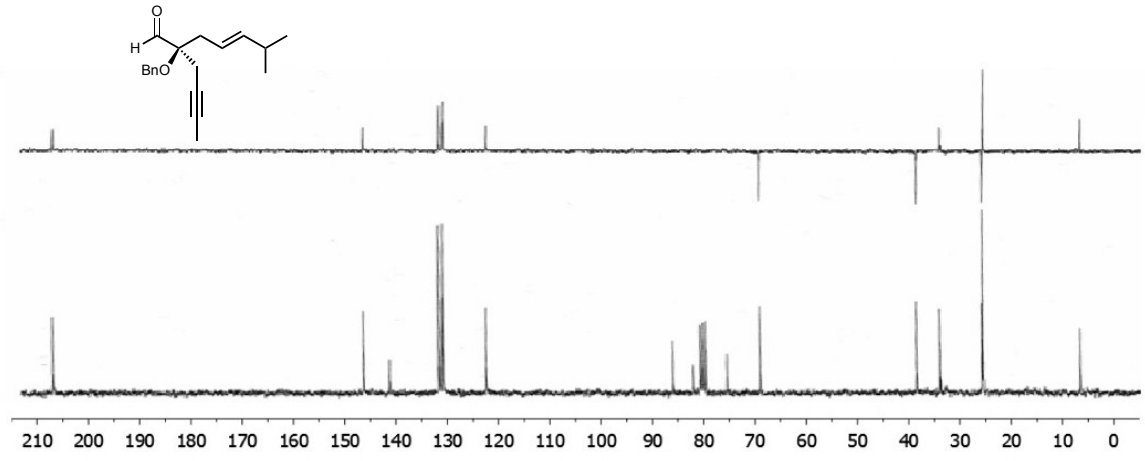


Figure 27SI. DEPT 135 (top) and ^{13}C NMR (bottom) of aldehyde **8b** recorded in $CDCl_3$ at 75 MHz.

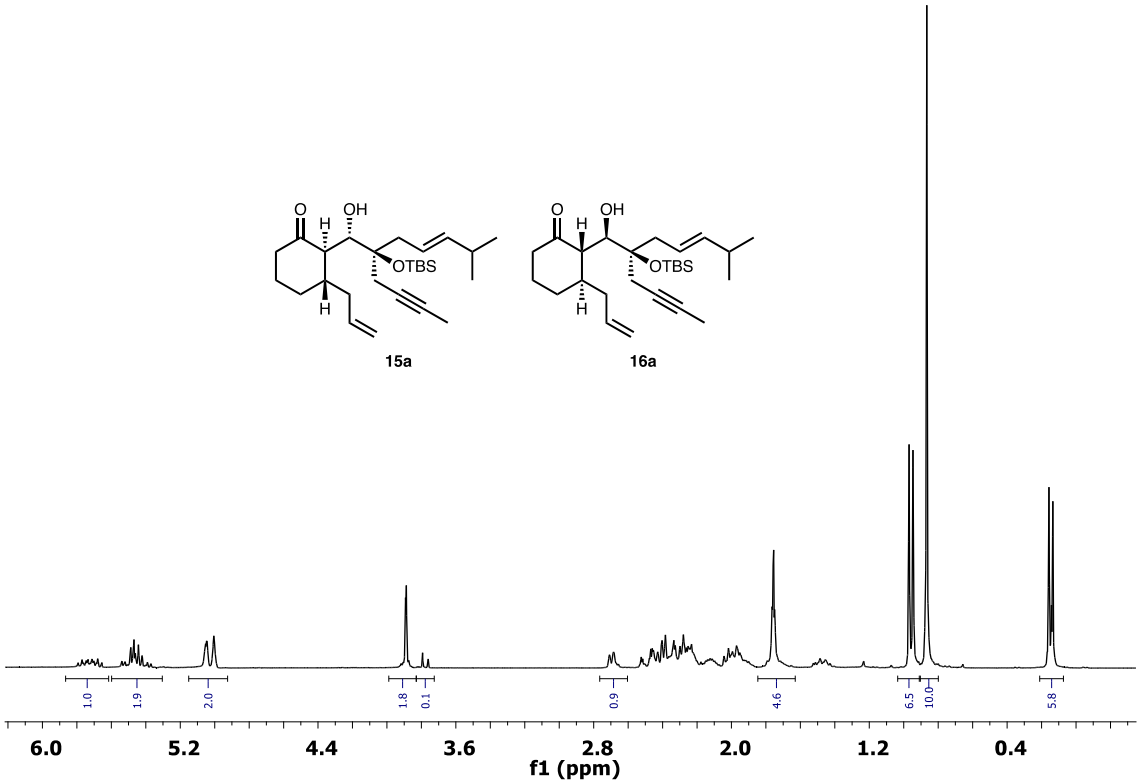


Figure 28SI. ^{1}H NMR spectrum of dienynes **15a/16a** recorded in $CDDl_3$ at 300 MHz.

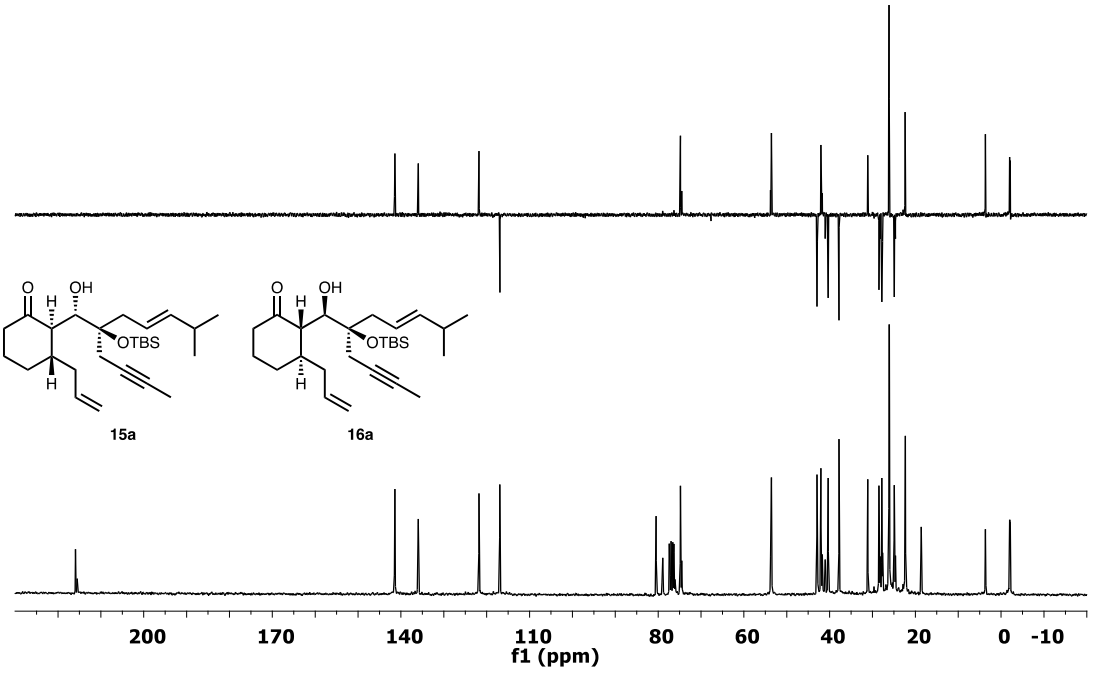


Figure 29SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienynes **15a/16a** recorded in $CDCl_3$ at 75 MHz.

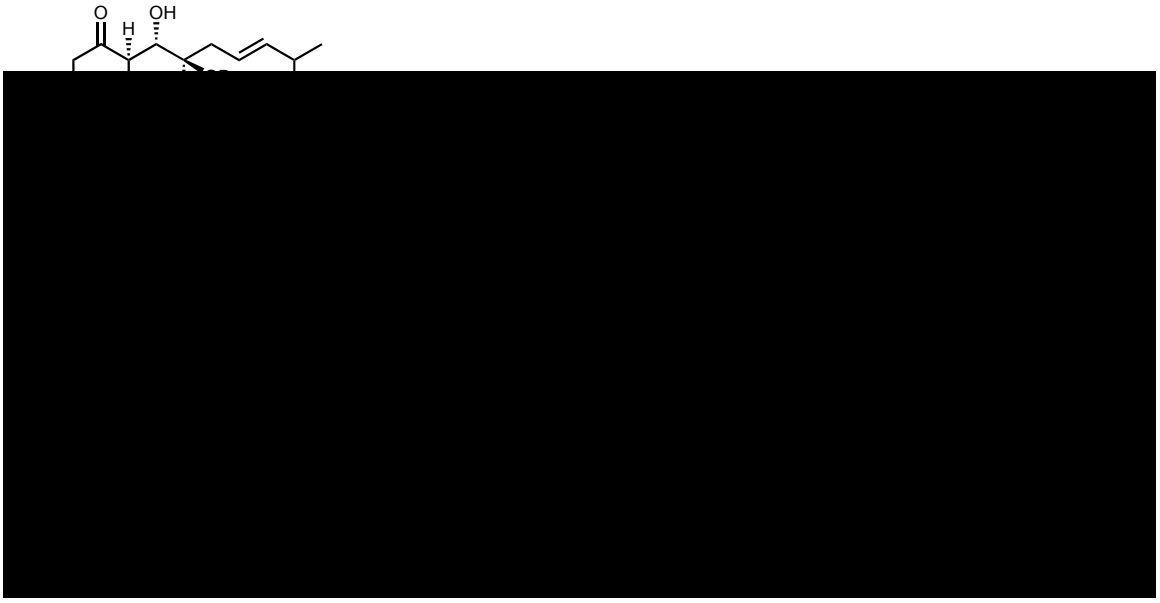


Figure 30SI. ^{1}H NMR spectrum of dienyne **15b** recorded in $CDDl_3$ at 300 MHz.

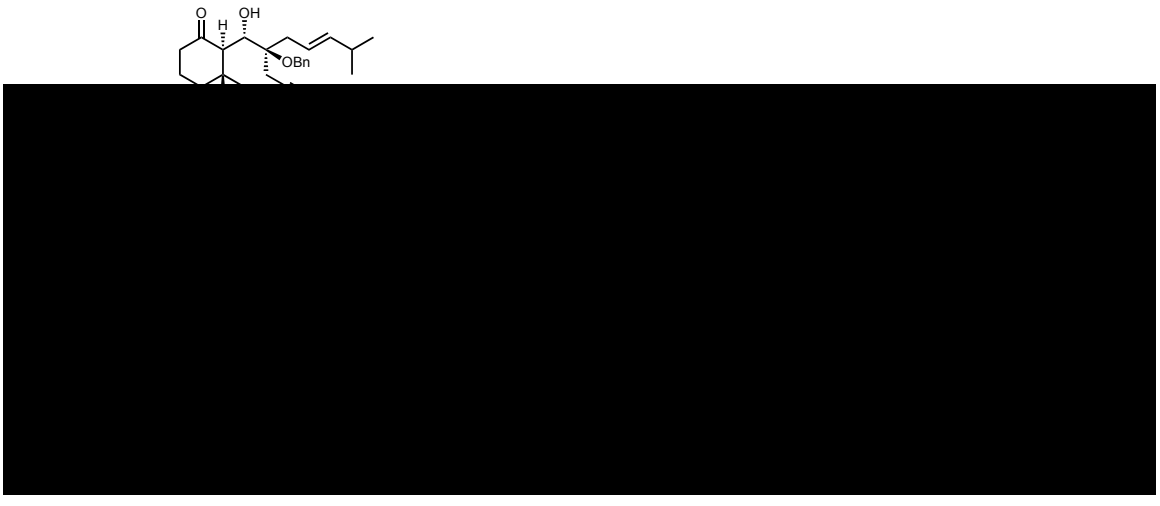


Figure 31SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienyne **15b** recorded in $CDCl_3$ at 75 MHz.

Figure 32SI. ^{1}H NMR spectrum of dienyne **16b** recorded in $CDDl_3$ at 300 MHz.

Figure 33SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienyne **16b** recorded in $CDCl_3$ at 75 MHz.

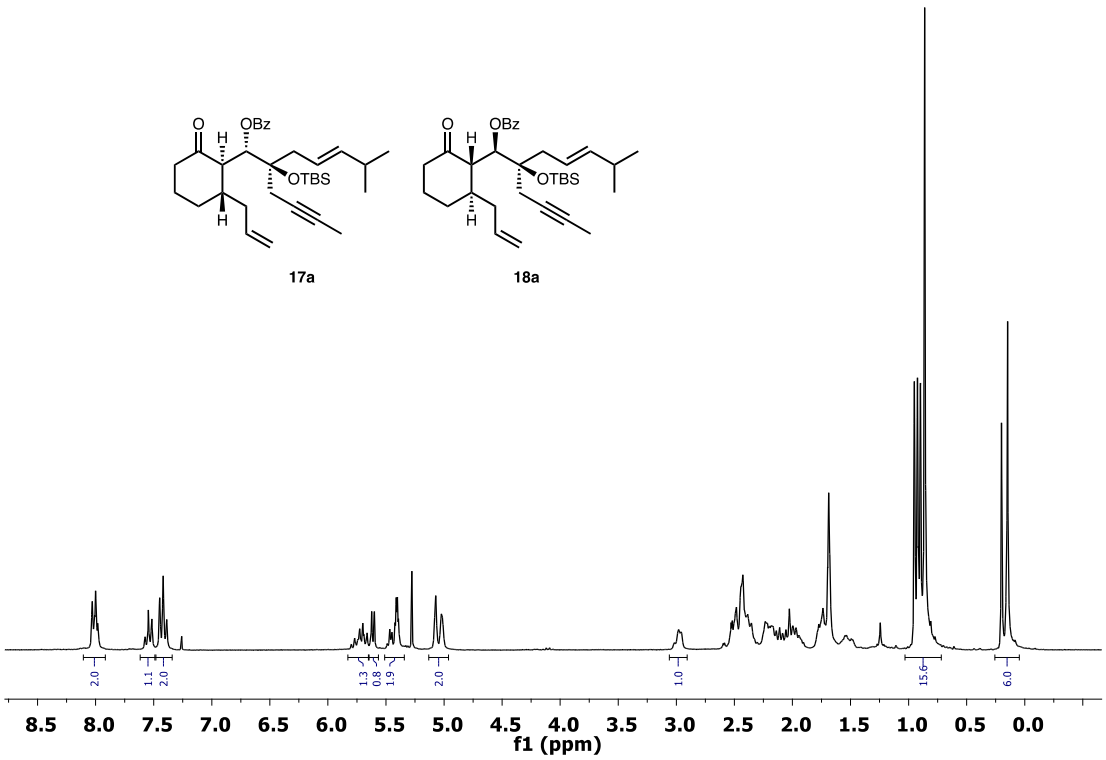


Figure 34SI. ^{1}H NMR spectrum of dienynes **17a/18a** recorded in $CDDl_3$ at 300 MHz.

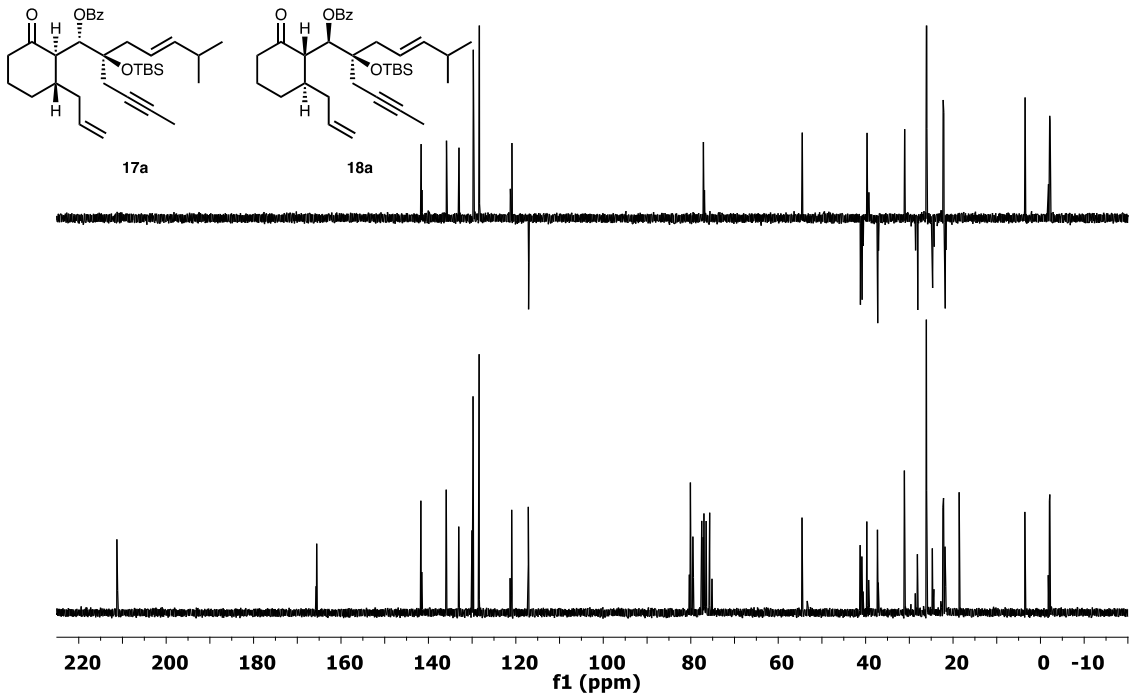


Figure 35SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienynes **17a/18a** recorded in $CDCl_3$ at 75 MHz.

Figure 36SI. ^{1}H NMR spectrum of dienyne **17b** recorded in $CDDl_3$ at 300 MHz.

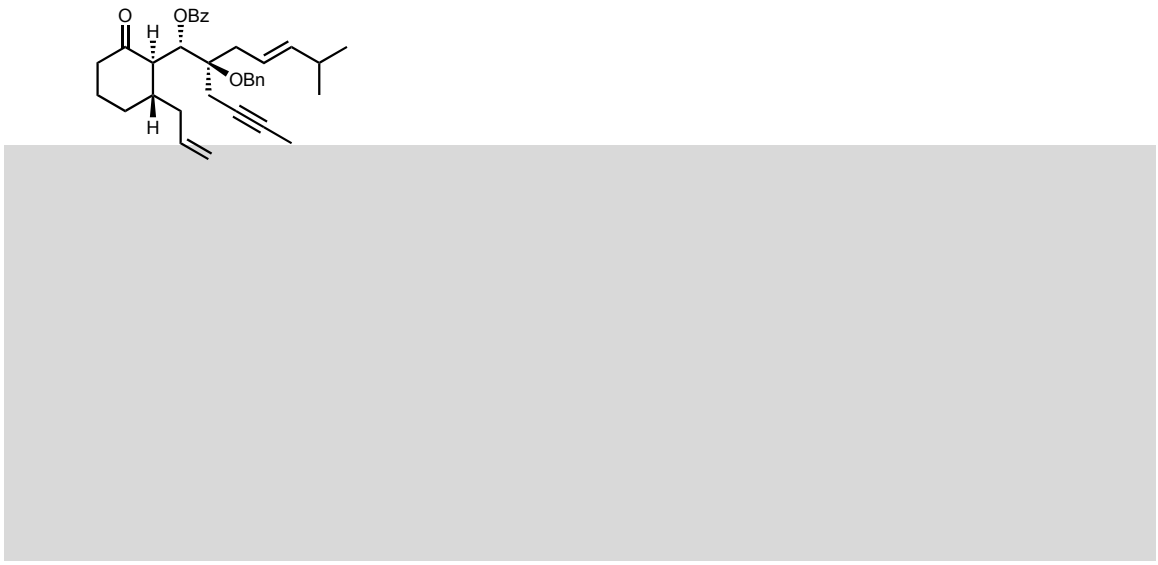


Figure 37SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienyne **17b** recorded in $CDCl_3$ at 75 MHz.

Figure 38SI. ^{1}H NMR spectrum of dienyne **18b** recorded in $CDDl_3$ at 300 MHz.

Figure 39SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienyne **18b** recorded in $CDCl_3$ at 75 MHz.

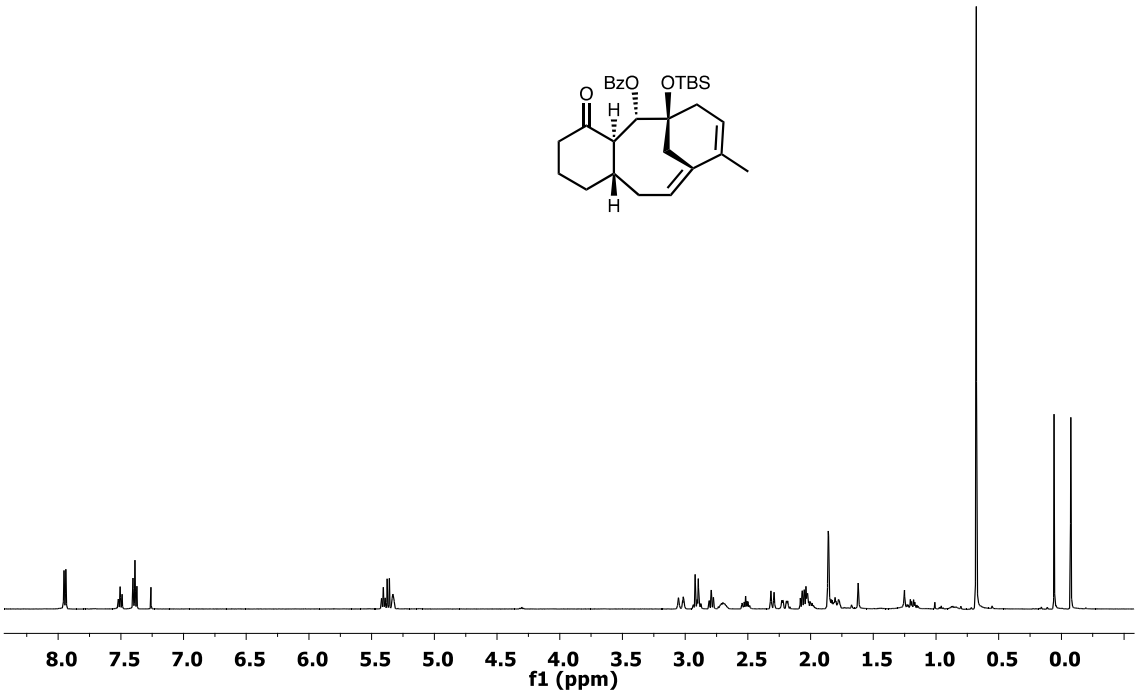


Figure 40SI. ^{1}H NMR spectrum of taxadiene analogue **19a** recorded in $CDDl_3$ at 500 MHz.

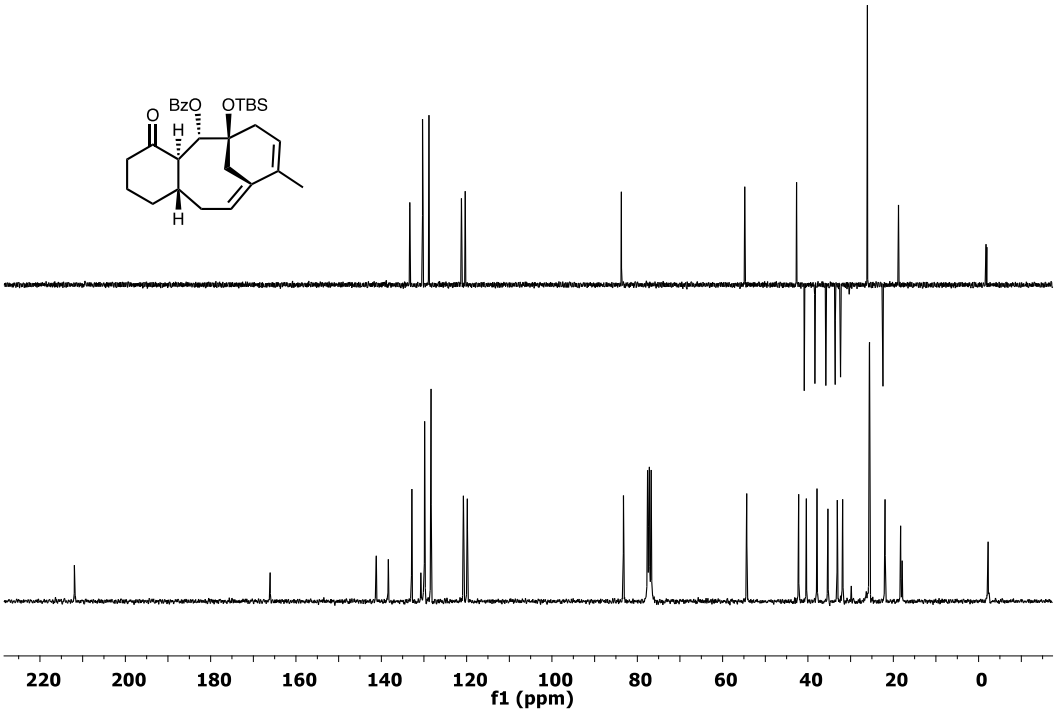


Figure 41SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxadiene analogue **19a** recorded in $CDCl_3$ at 75 MHz.

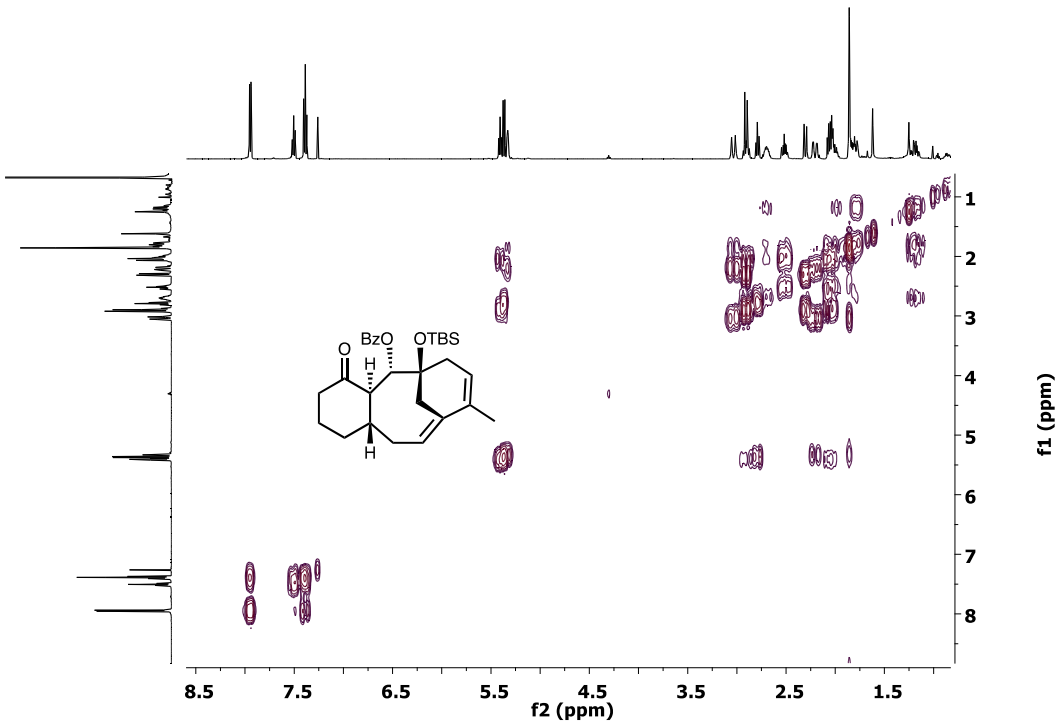


Figure 42SI. COSY spectrum of taxadiene analogue **19a**.

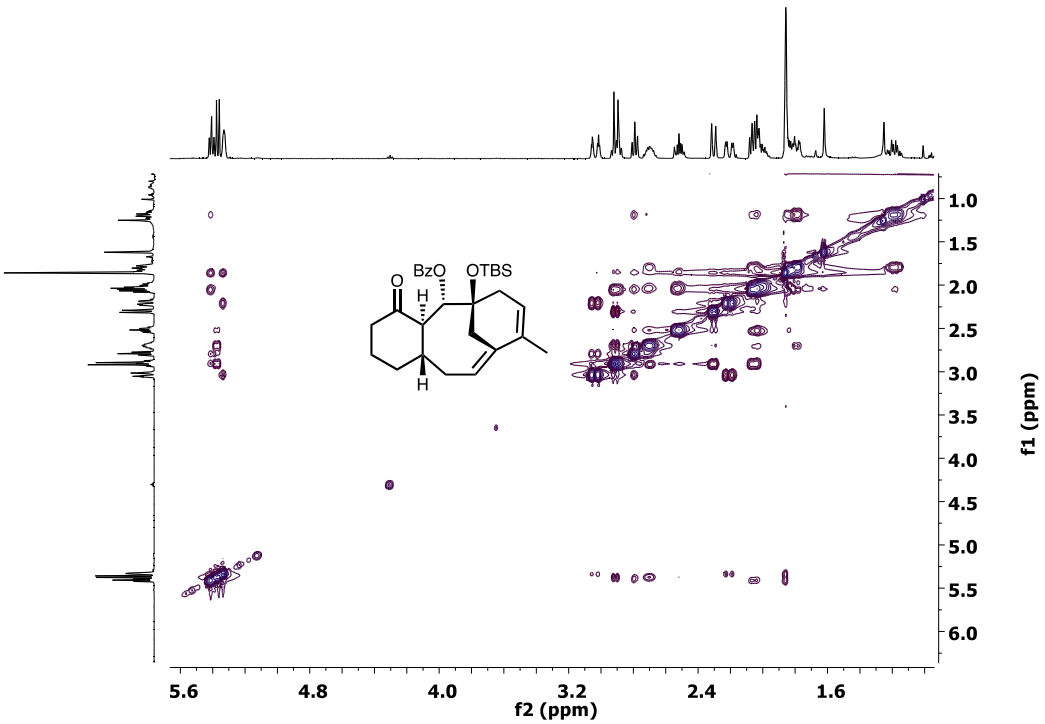


Figure 43SI. NOESY spectrum of taxadiene analogue **19a**.

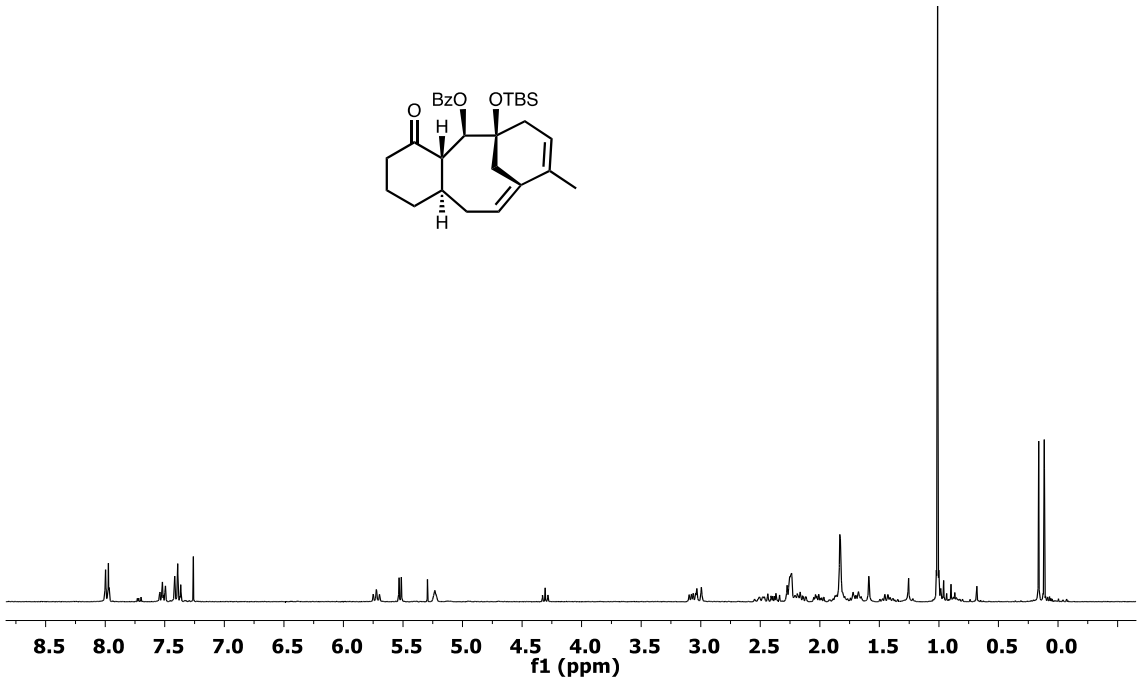


Figure 44SI. ^{1}H NMR spectrum of taxadiene analogue **20a** recorded in $CDDl_3$ at 500 MHz.

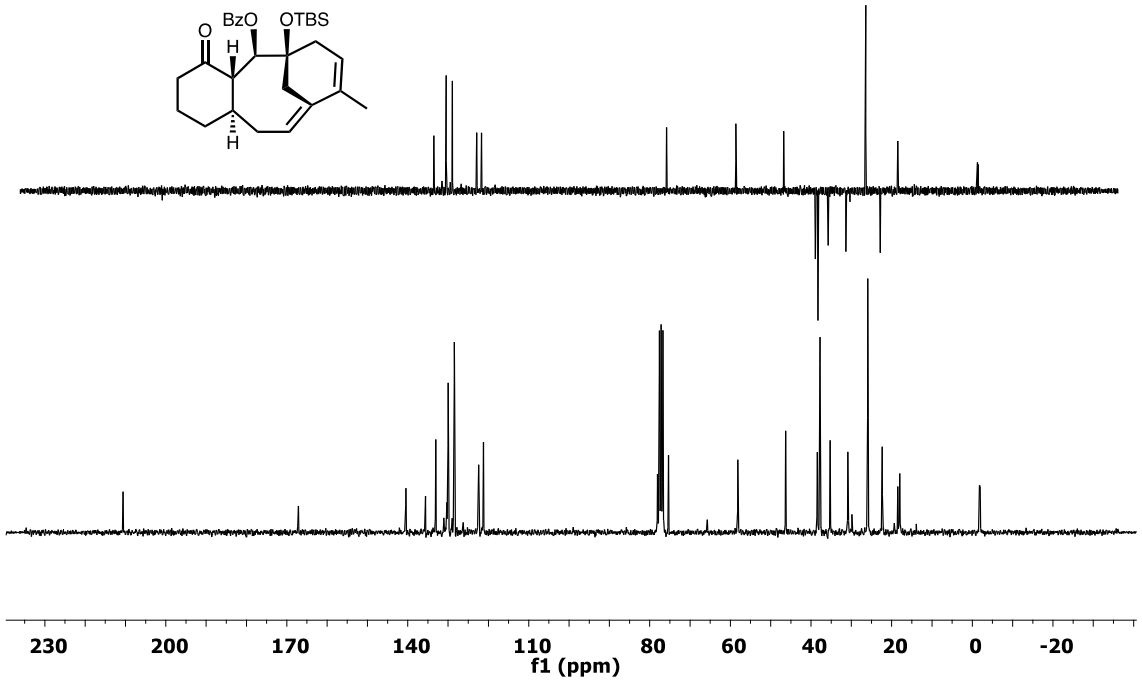


Figure 45SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxadiene analogue **20a** recorded in $CDCl_3$ at 75 MHz.

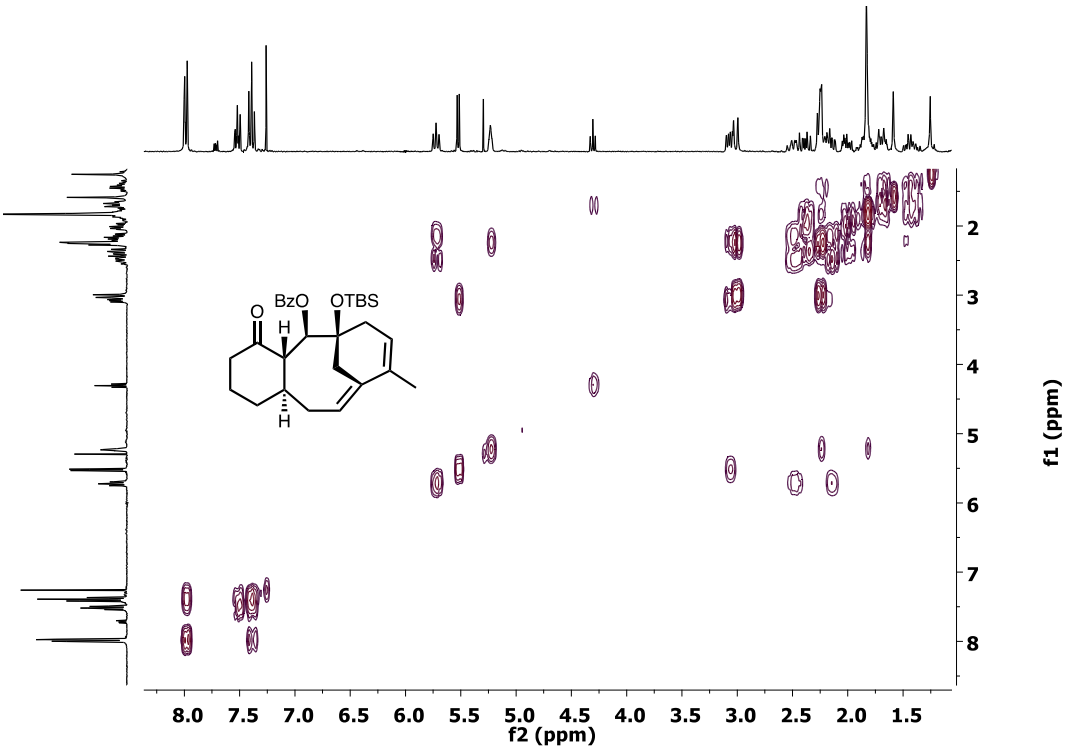


Figure 46SI. COSY spectrum of taxadiene analogue **20a**.

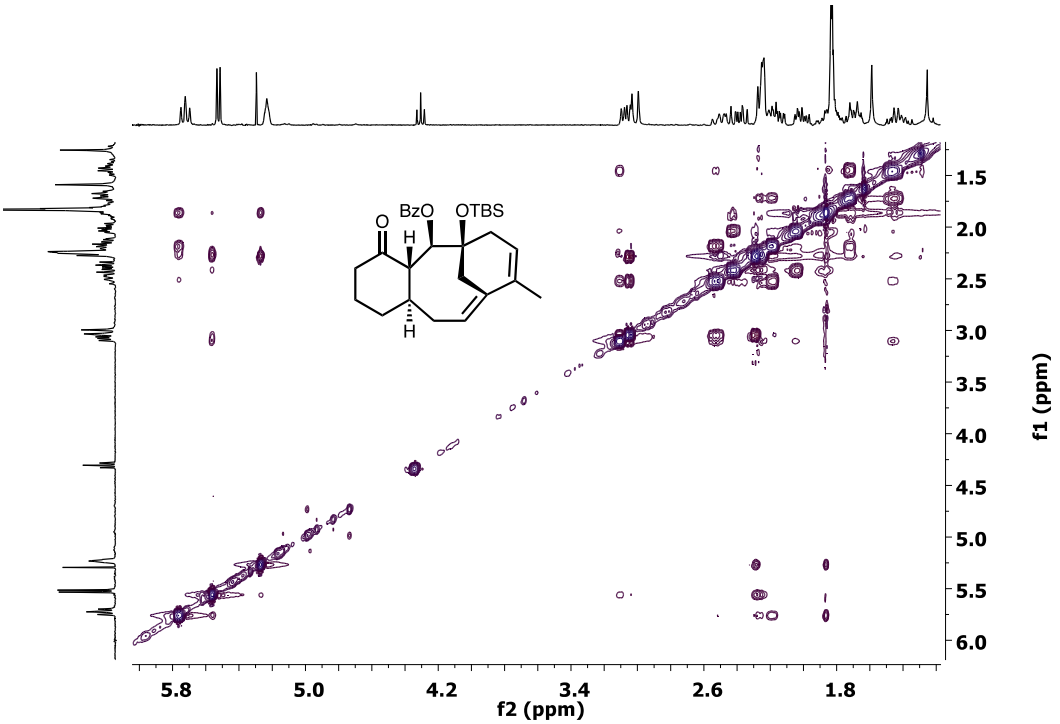


Figure 47SI. NOESY spectrum of taxadiene analogue **20a**.

Figure 48SI. ^{1}H NMR spectrum of taxadiene analogue **19b** recorded in $CDDl_3$ at 500 MHz.

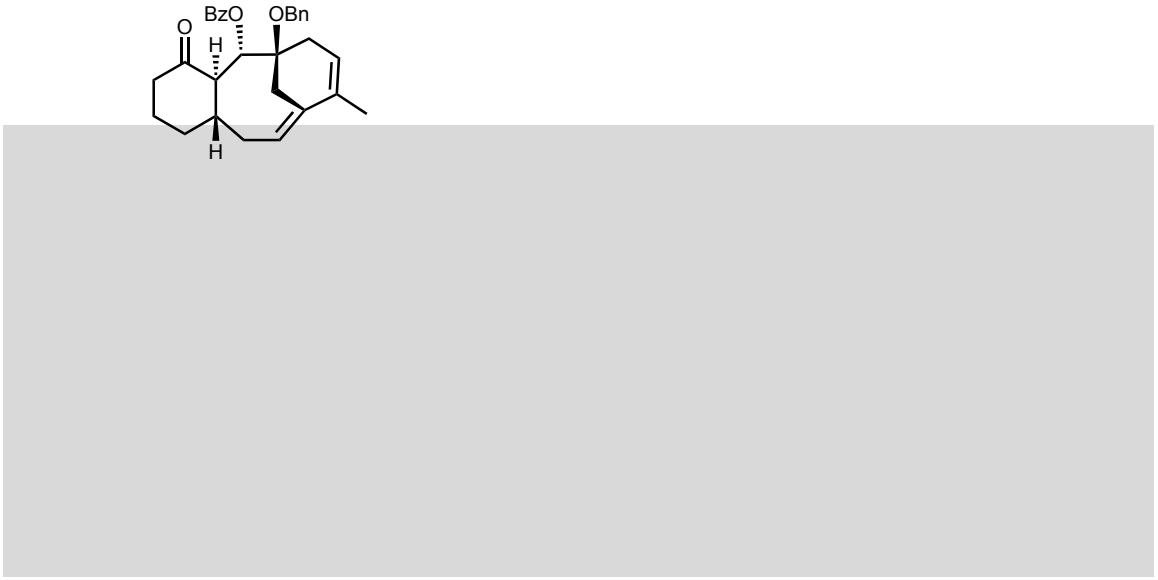


Figure 49SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxadiene analogue **19b** recorded in $CDCl_3$ at 126 MHz.

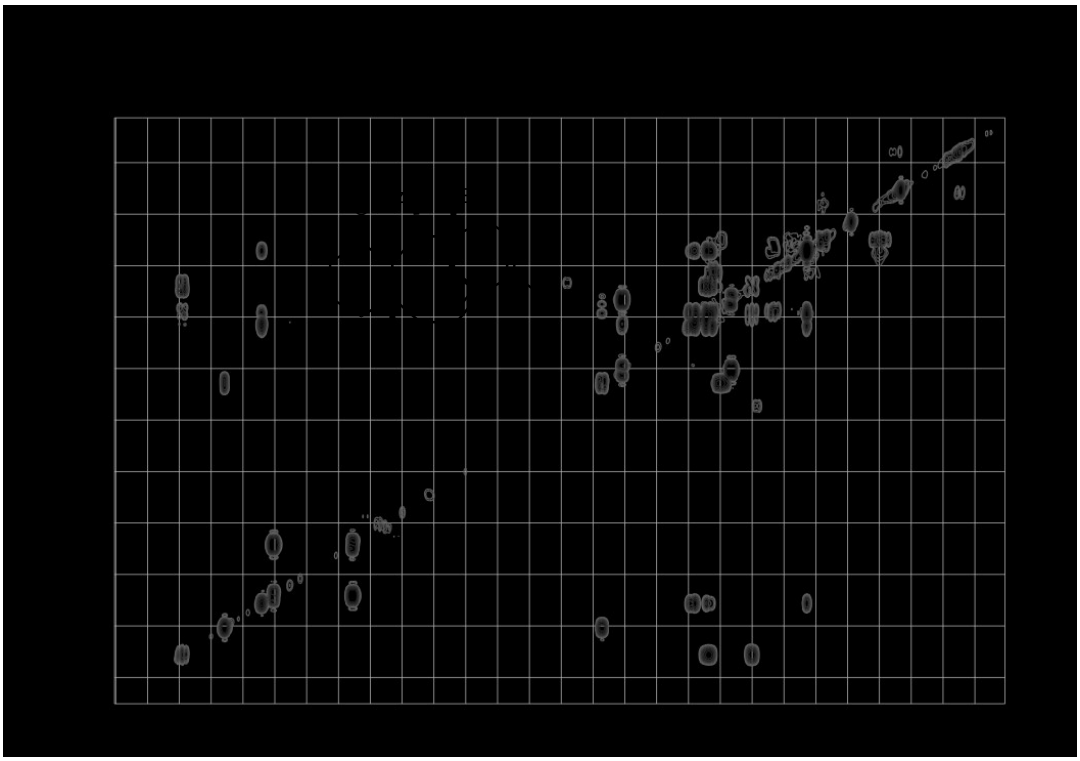


Figure 50SI. COSY spectrum of taxadiene analogue **19b**.

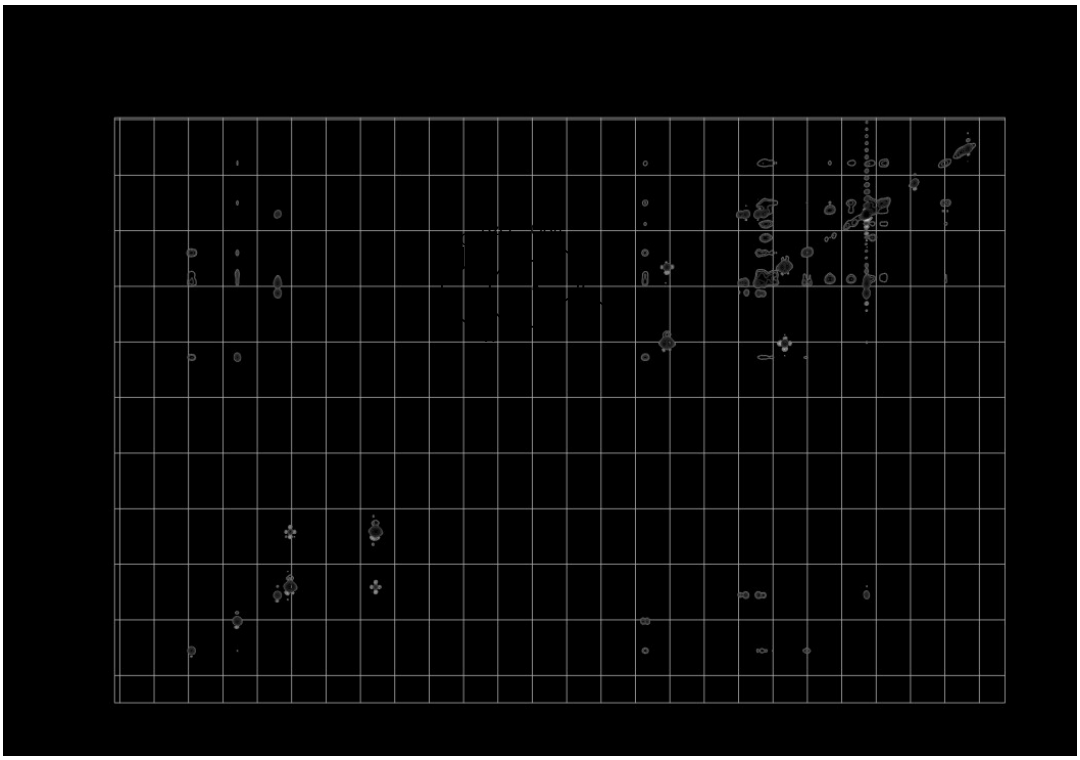


Figure 451SI. TOCSY spectrum of taxadiene analogue **19b**.

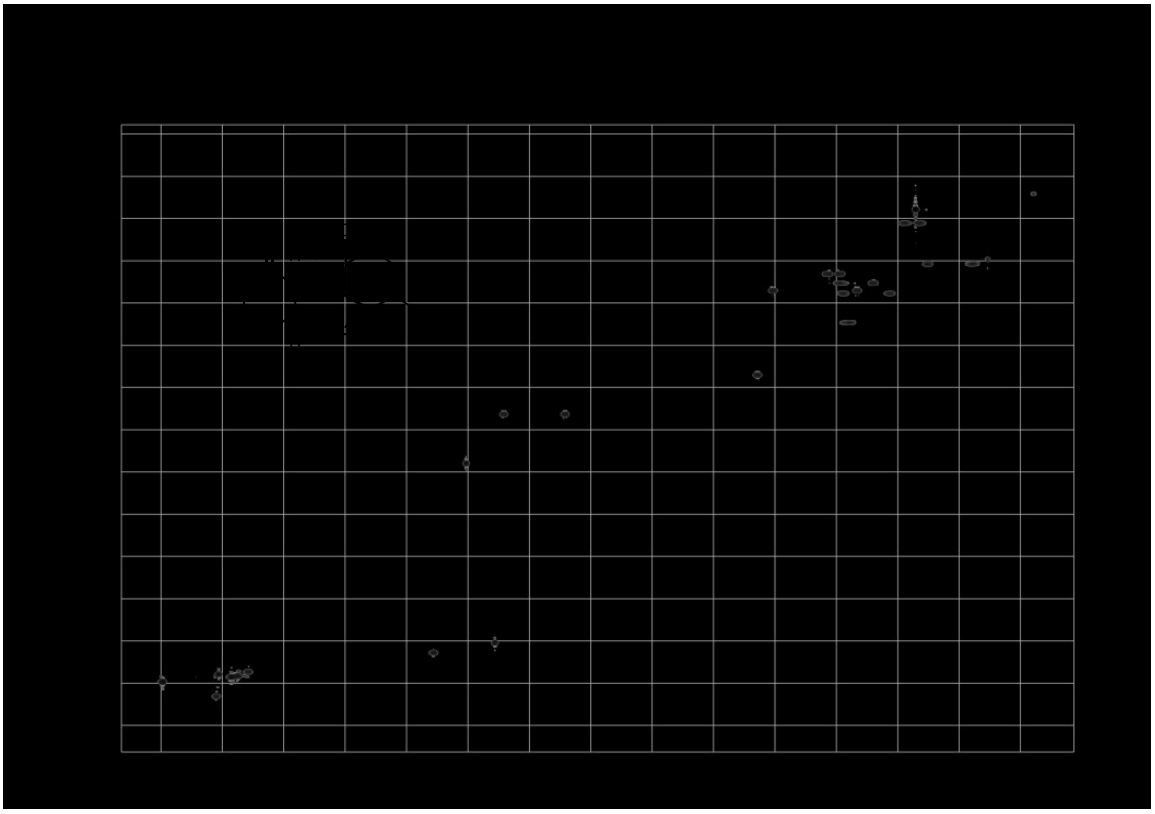


Figure 52SI. HSQC spectrum of taxadiene analogue **19b**.

Figure 53SI. ^{1}H NMR spectrum of taxadiene analogue **20b** recorded in $CDDI_3$ at 500 MHz.

Figure 54SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxadiene analogue **20b** recorded in $CDCl_3$ at 126 MHz.

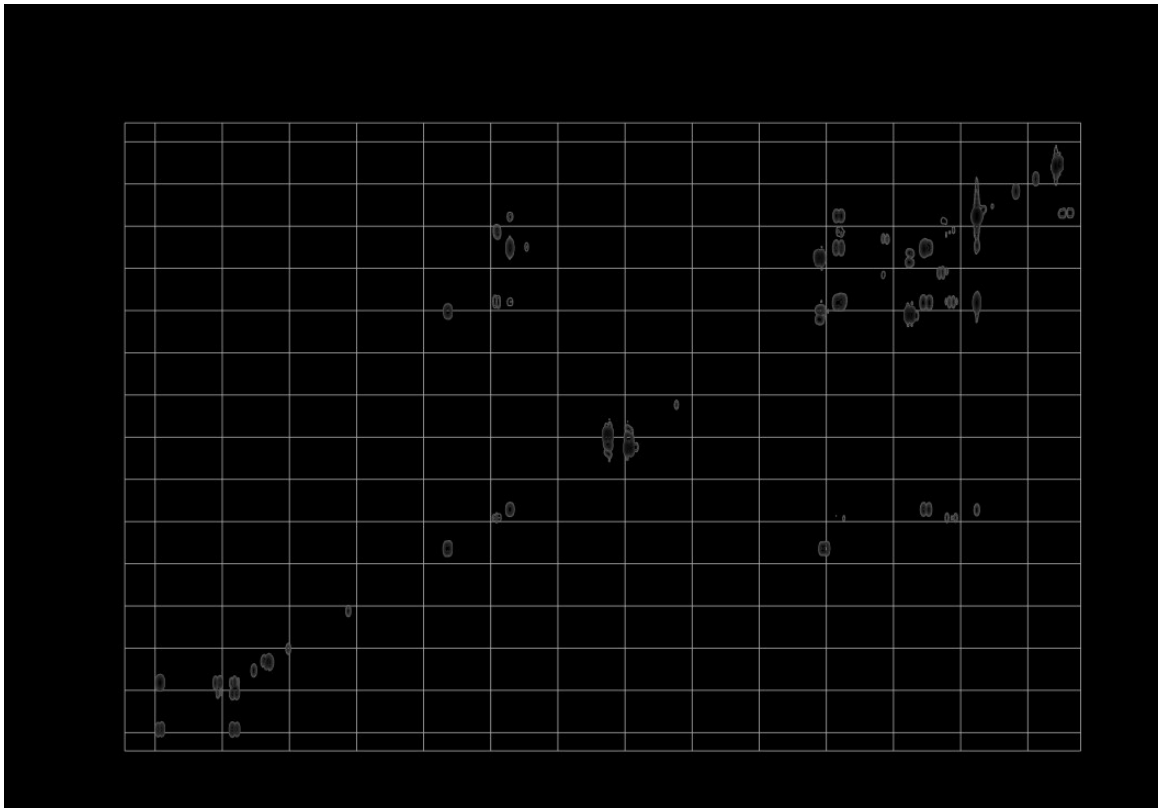


Figure 55SI. COSY spectrum of taxadiene analogue **20b**.

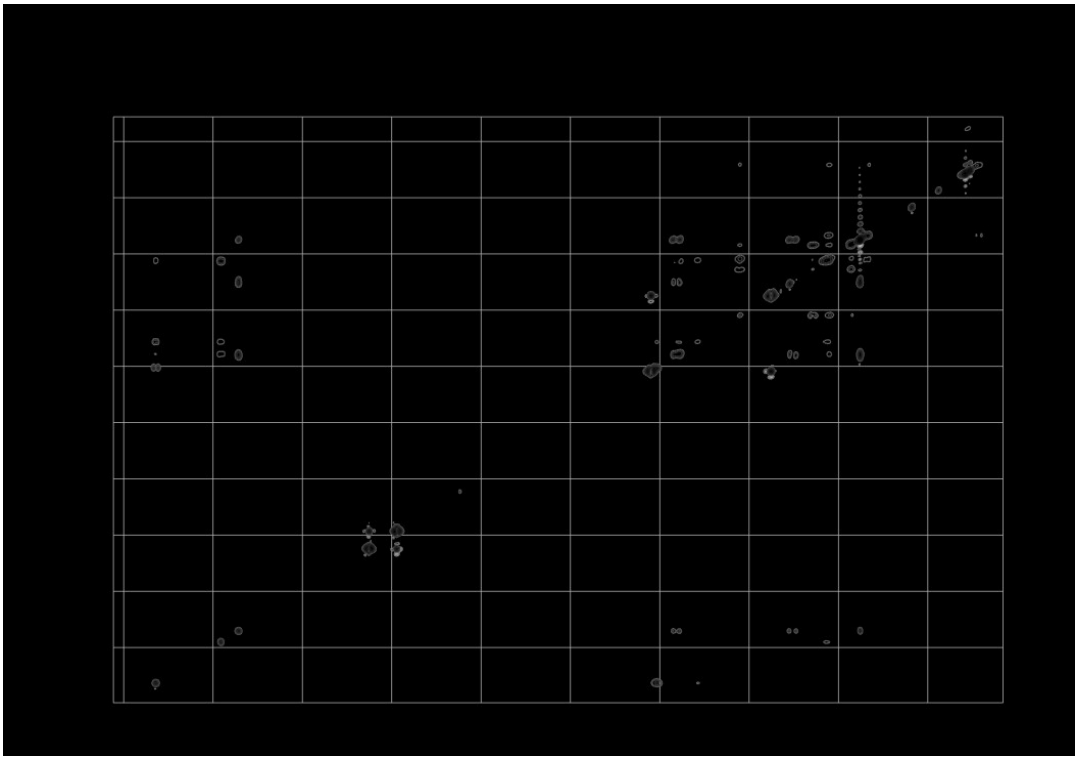


Figure 56SI. TOCSY spectrum of taxadiene analogue **20b**.

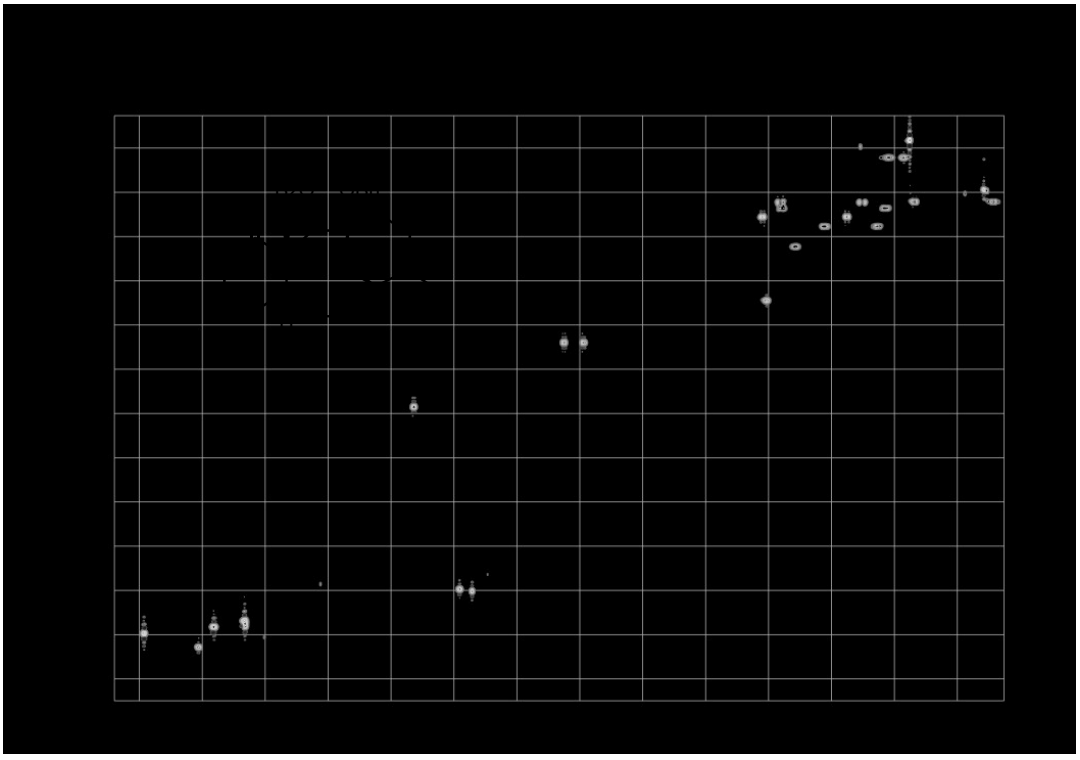


Figure 57SI. HSQC spectrum of taxadiene analogue **20b**.

Figure 58SI. ^{1}H NMR spectrum of compound **31** recorded in $CDDl_3$ at 300 MHz.

Figure 59SI. DEPT 135 (top) and ^{13}C NMR (bottom) of compound **31** recorded in $CDCl_3$ at 75 MHz.

Figure 60SI. ^{1}H NMR spectrum of compound **32** recorded in $CDDl_3$ at 300 MHz.

Figure 61SI. DEPT 135 (top) and ^{13}C NMR (bottom) of compound **32** recorded in $CDCl_3$ at 75 MHz.

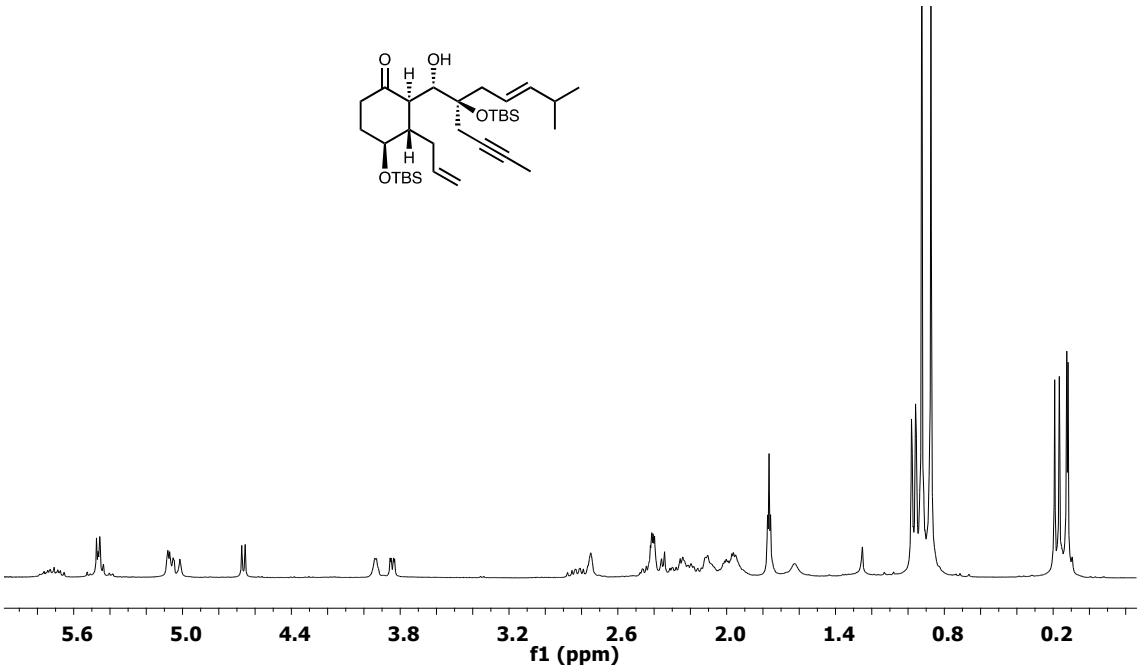


Figure 64SI. ^{1}H NMR spectrum of dienyne **29a** recorded in $CDDl_3$ at 300 MHz.

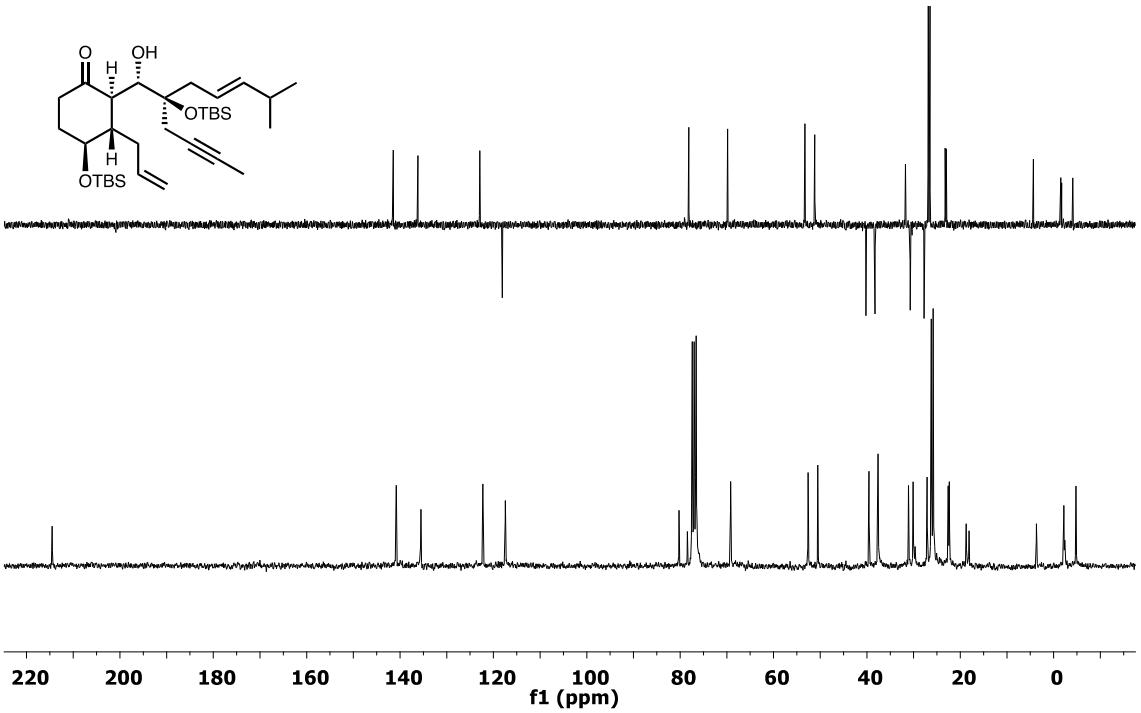


Figure 65SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienyne **29a** recorded in $CDCl_3$ at 75 MHz.

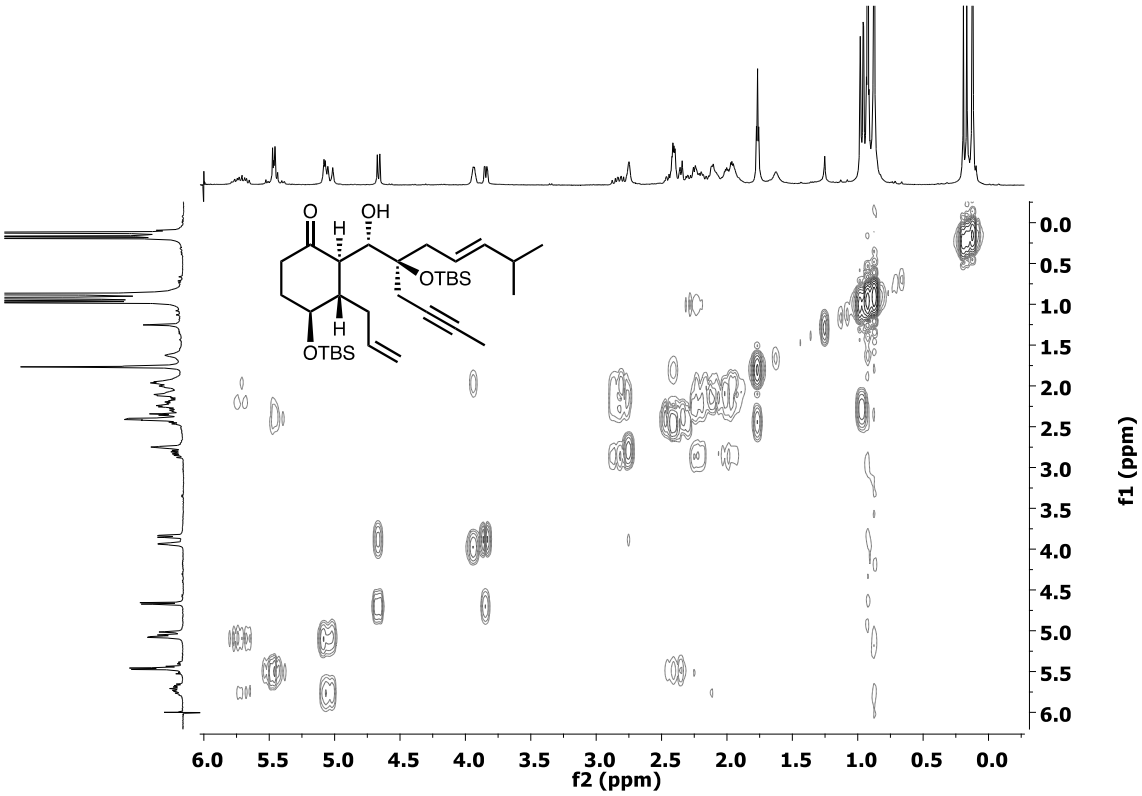


Figure 66SI. COSY spectrum of dienyne **29a**.

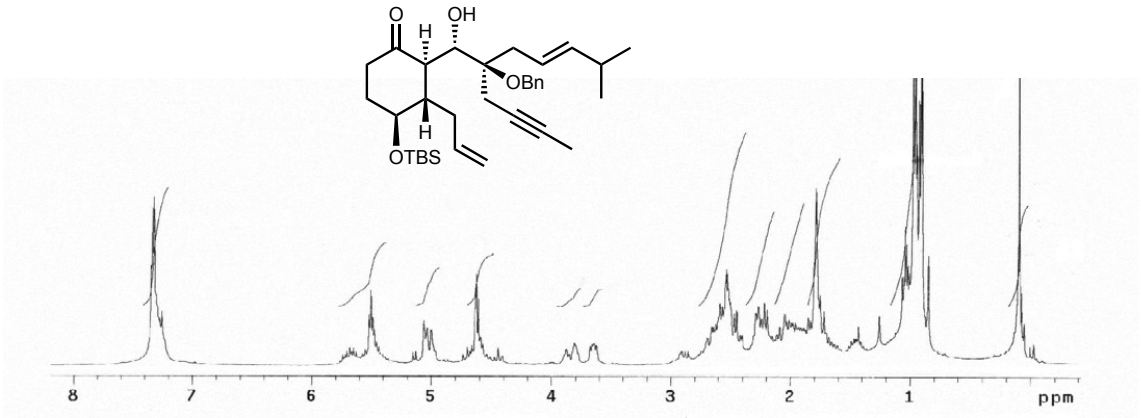


Figure 62SI. ^{1}H NMR spectrum of dienyne **29b** recorded in $CDDl_3$ at 300 MHz.

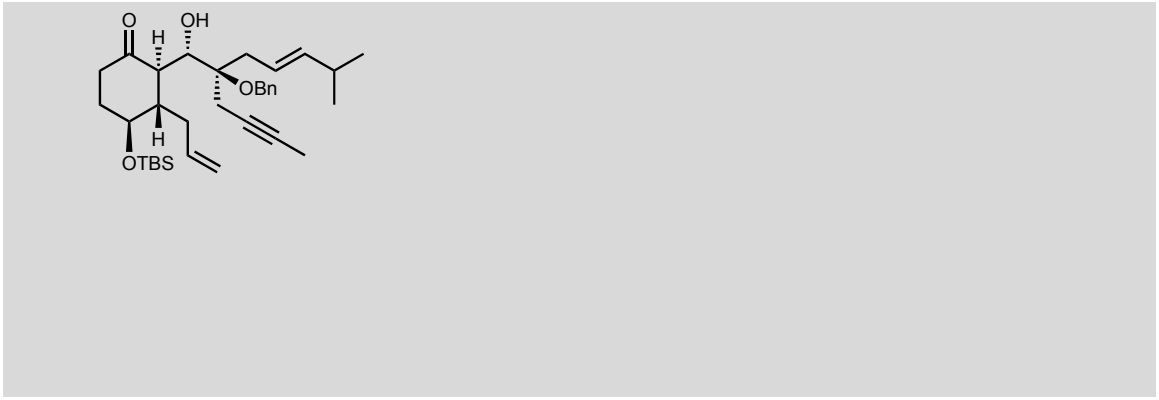


Figure 63SI. DEPT 135 (top) and ^{13}C NMR (bottom) of dienyne **29b** recorded in $CDCl_3$ at 75 MHz.

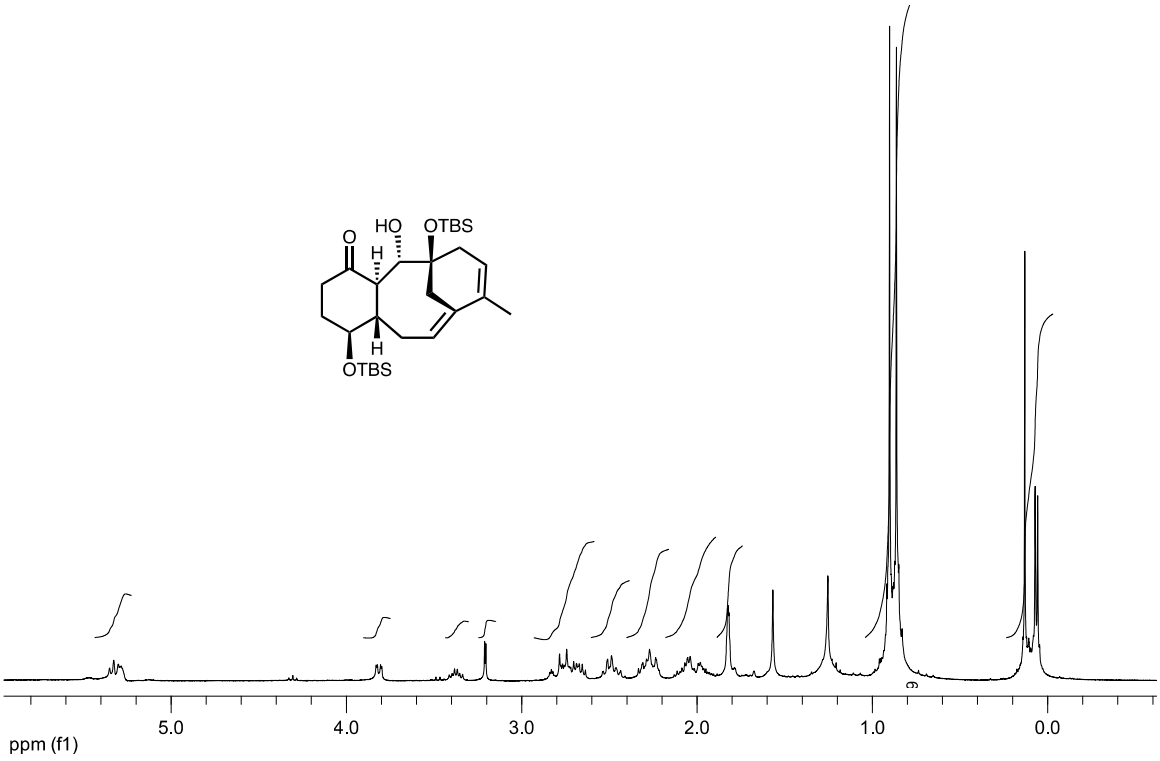


Figure 67SI. ^{1}H NMR spectrum of taxadiene analogue **33a** recorded in $CDDl_3$ at 300 MHz.

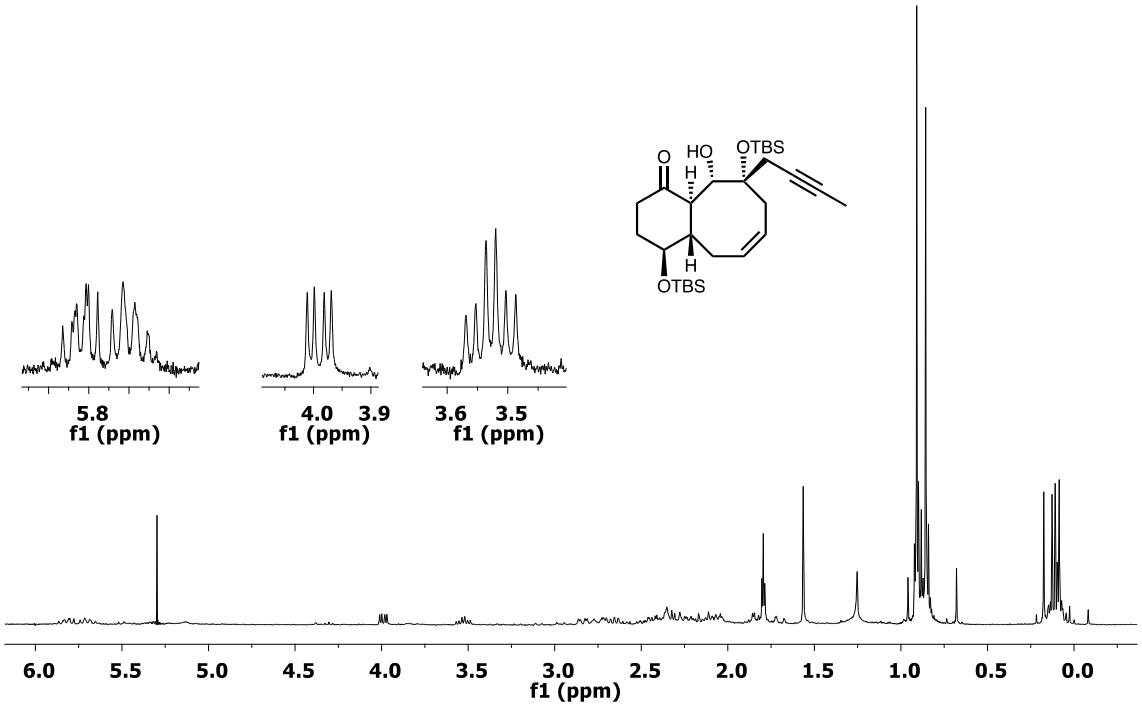


Figure 68SI. ^{1}H NMR spectrum of compound **34a** recorded in $CDDl_3$ at 300 MHz.

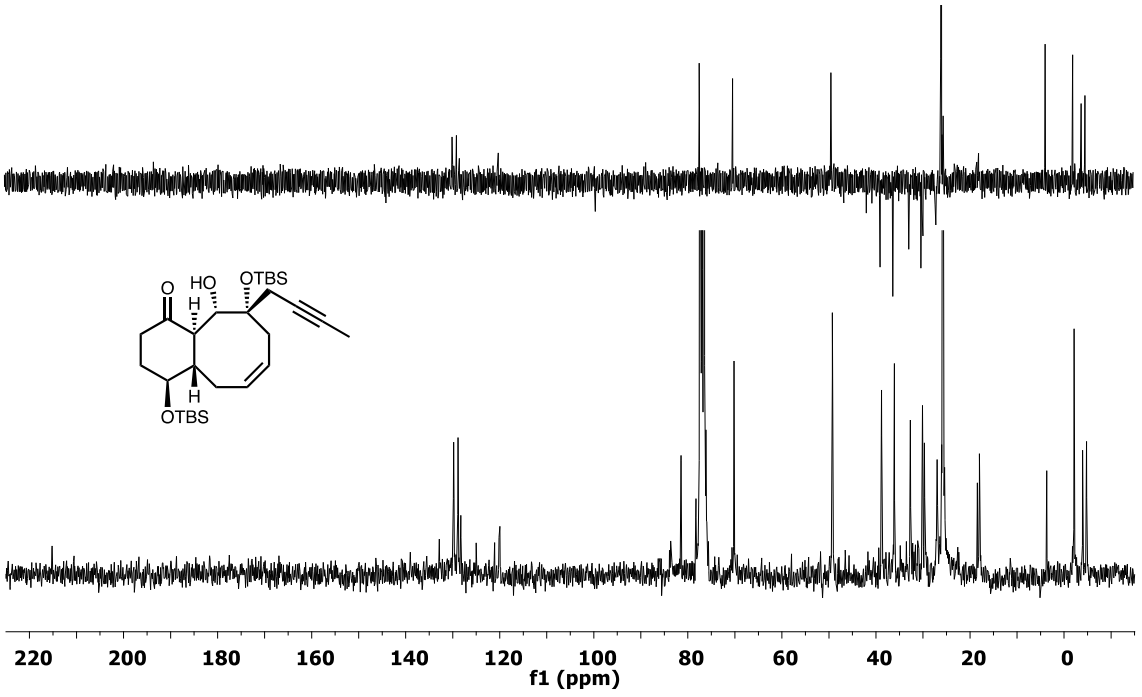


Figure 69SI. DEPT 135 (top) and ^{13}C NMR (bottom) of compound **34a** recorded in $CDCl_3$ at 75 MHz.

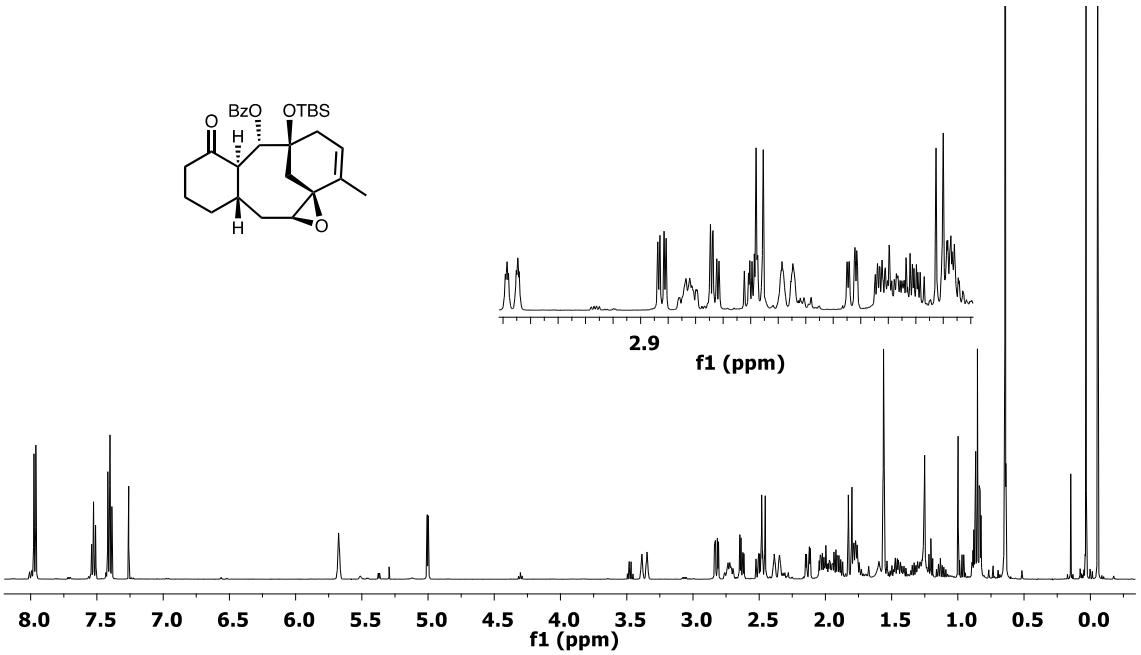


Figure 70SI. ^{1}H NMR spectrum of epoxide **21a** recorded in $CDDl_3$ at 500 MHz.

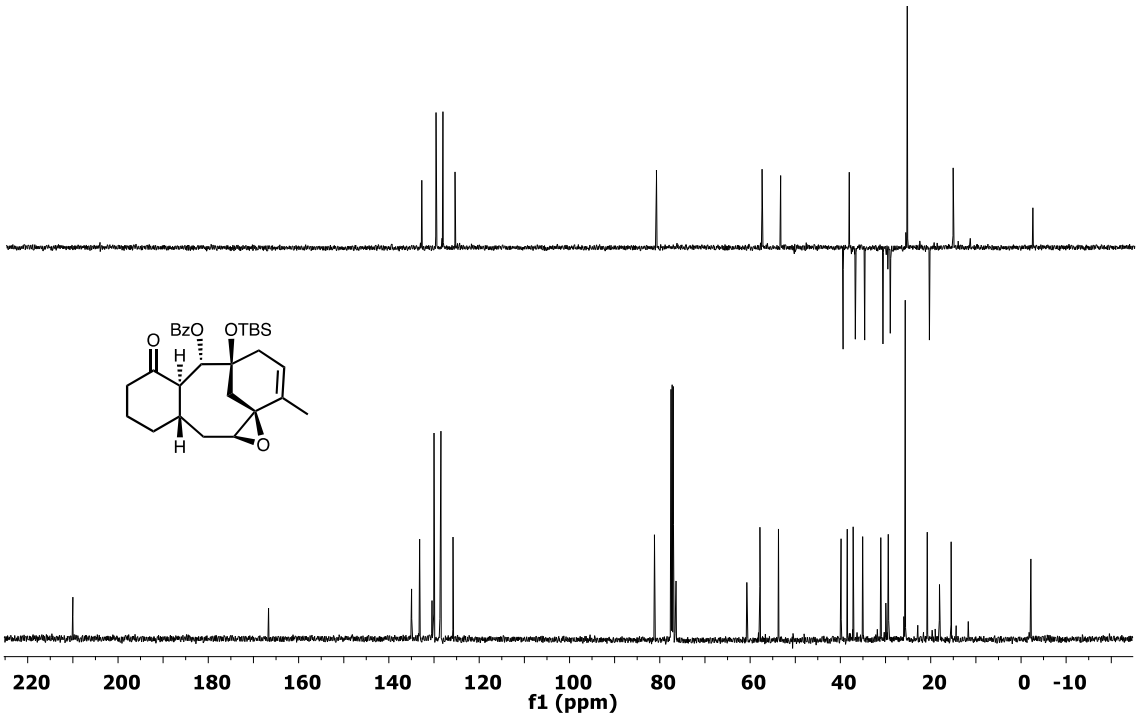


Figure 71SI. DEPT 135 (top) and ^{13}C NMR (bottom) of epoxide **21a** recorded in $CDCl_3$ at 126 MHz.

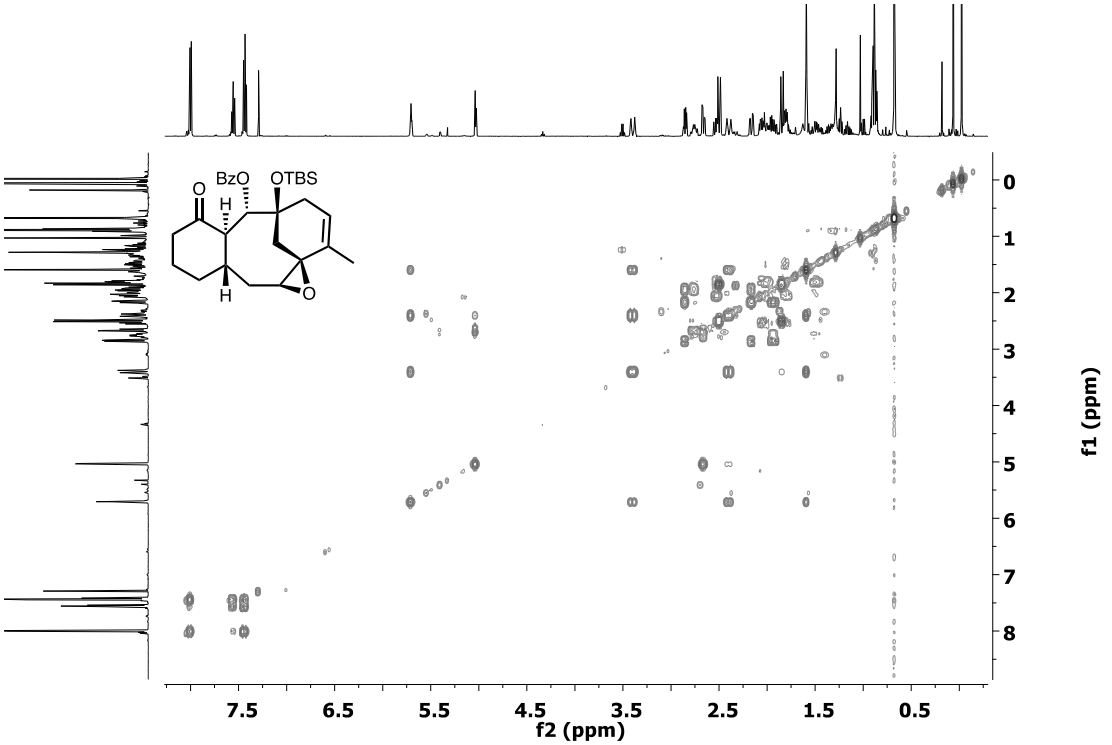


Figure 72SI. COSY spectrum of epoxide **21a**.

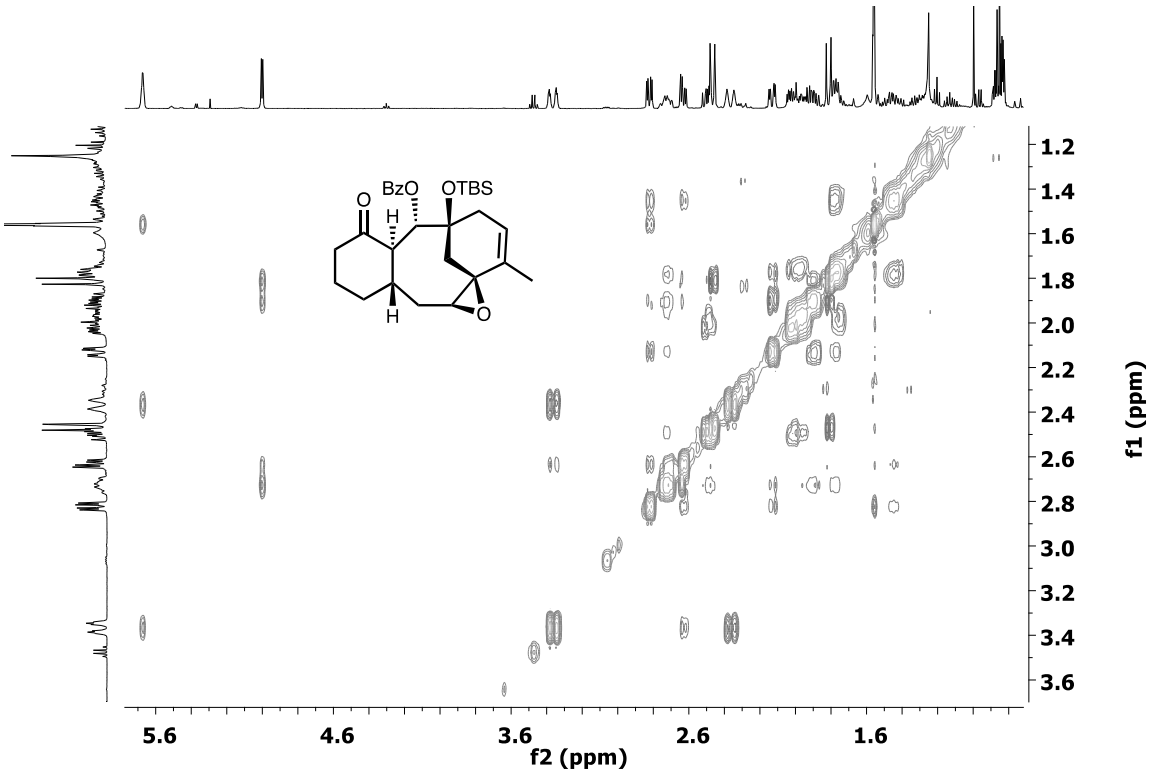


Figure 73SI. NOESY spectrum of epoxide **21a**.

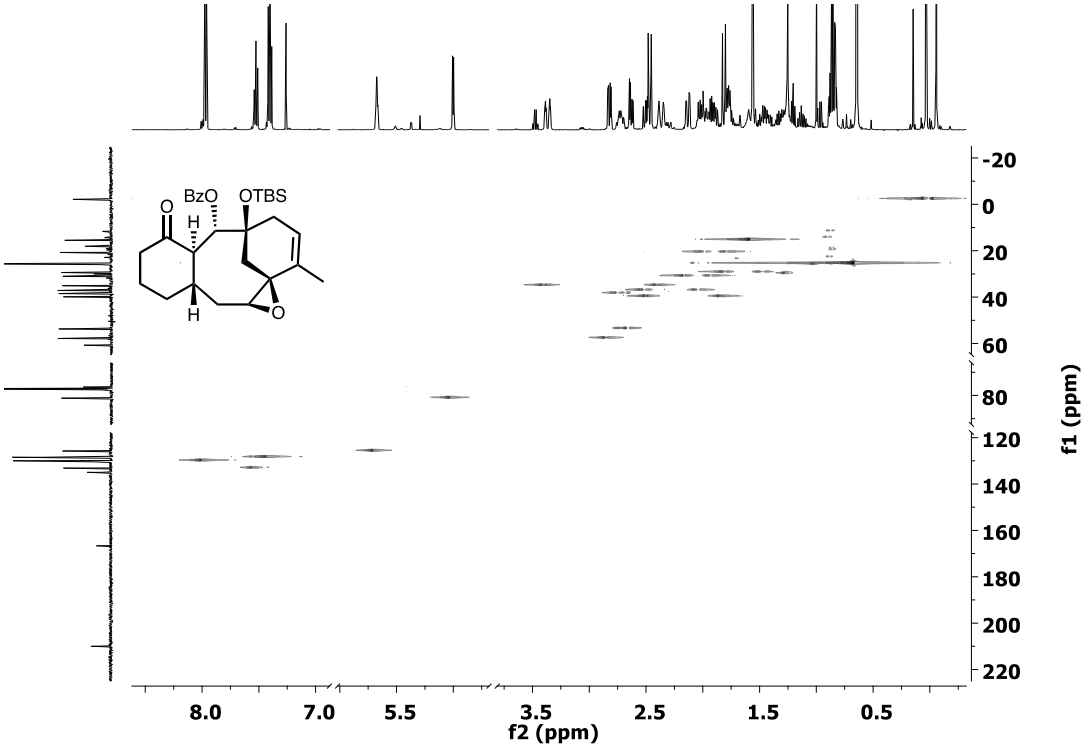


Figure 74SI. HSQC spectrum of epoxide **21a**.

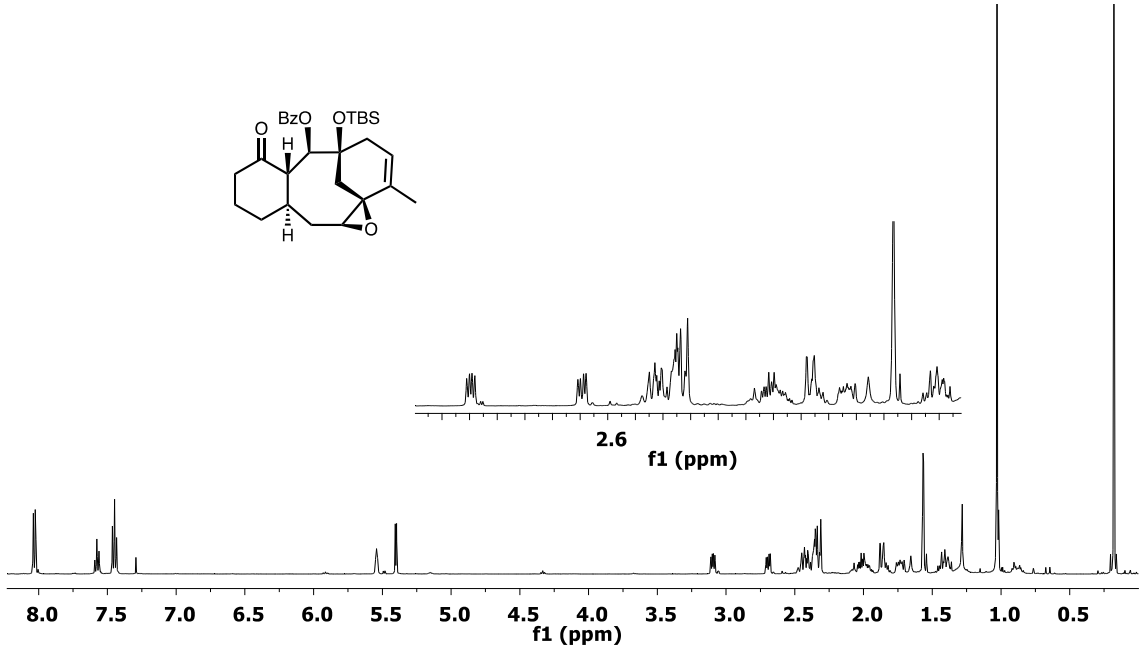


Figure 75SI. ^{1}H NMR spectrum of taxane analogue **36a** recorded in $CDDI_3$ at 500 MHz.

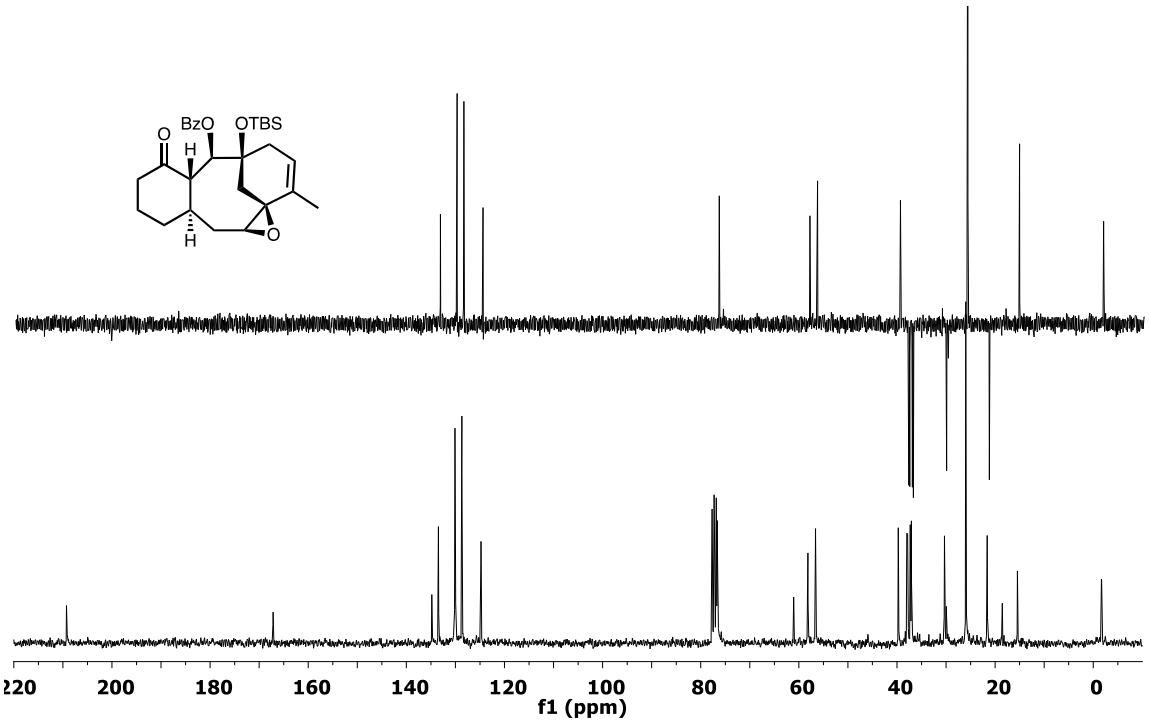


Figure 76SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxane analogue **36a** recorded in $CDCl_3$ at 126 MHz.

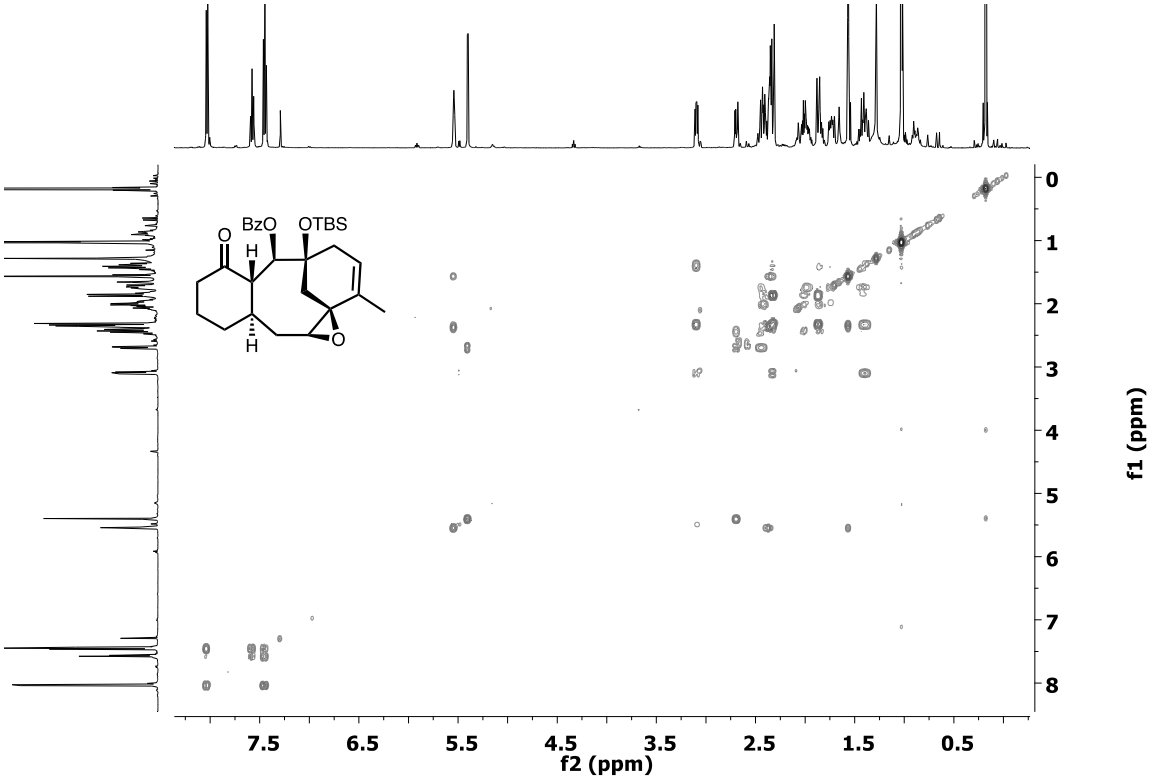


Figure 77SI. COSY spectrum of taxane analogue **36a**.

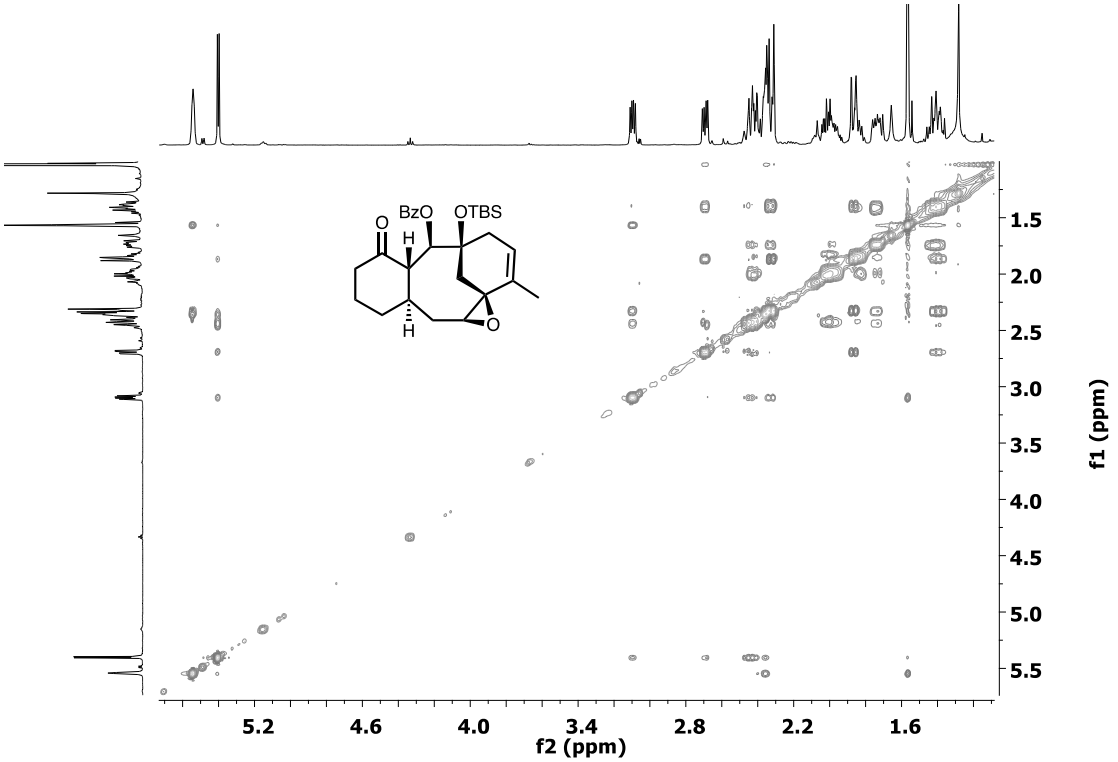


Figure 78SI. NOESY spectrum of taxane analogue **36a**.

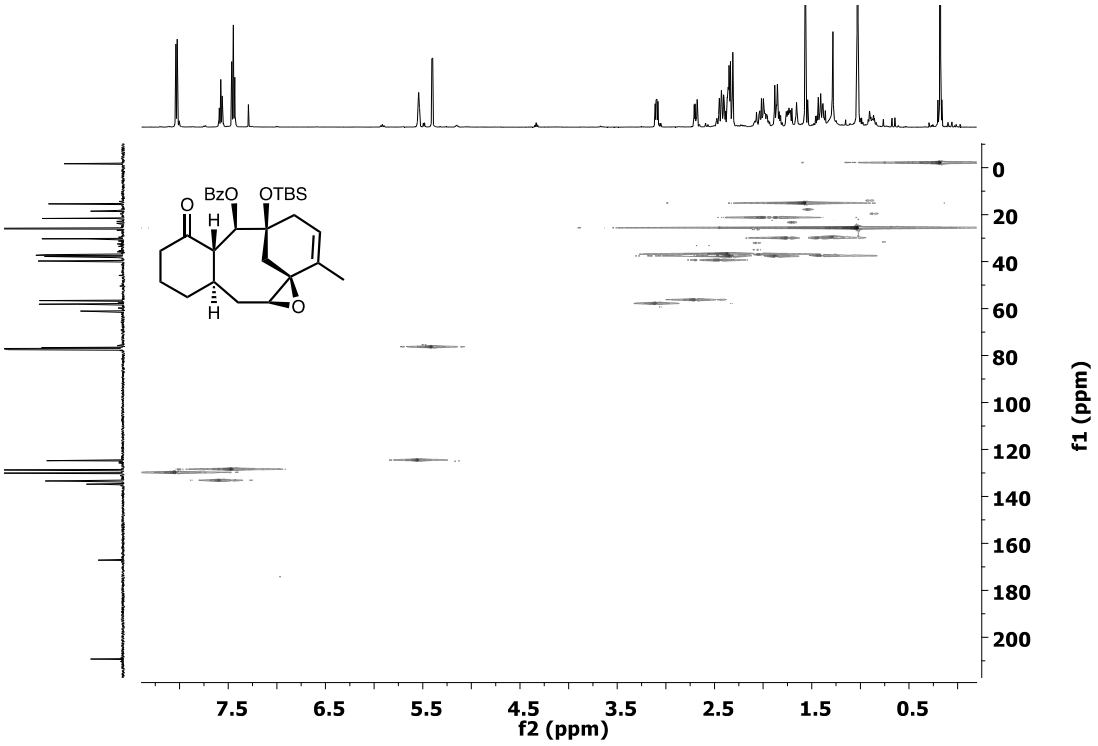


Figure 79SI. HSQC spectrum of taxane analogue **36a**.

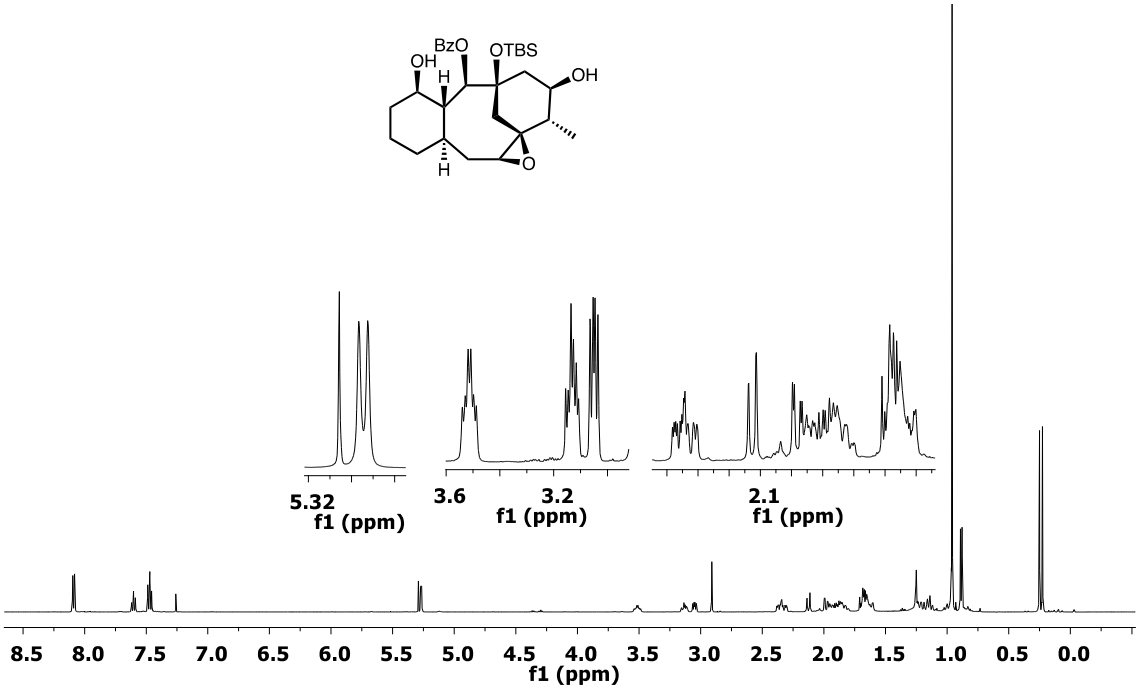


Figure 80SI. ^{1}H NMR spectrum of taxane analogue **22a** recorded in $CDDI_3$ at 500 MHz.

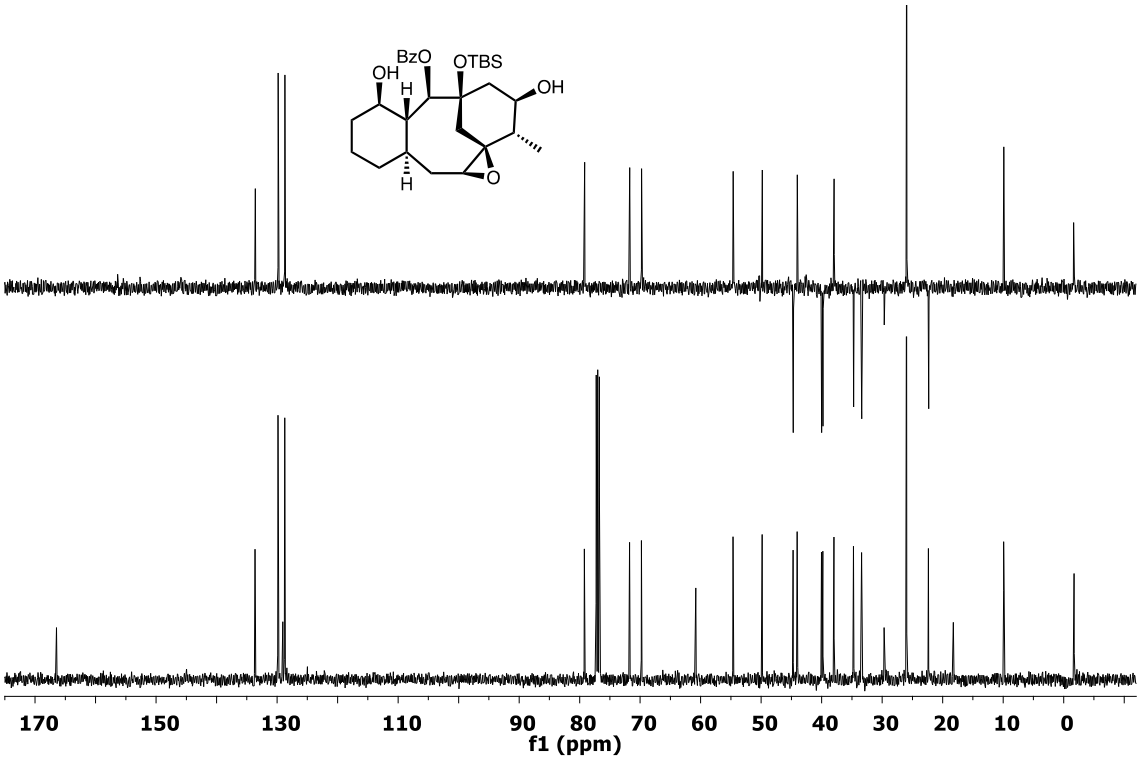


Figure 81SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxane analogue **22a** recorded in $CDCl_3$ at 126 MHz.

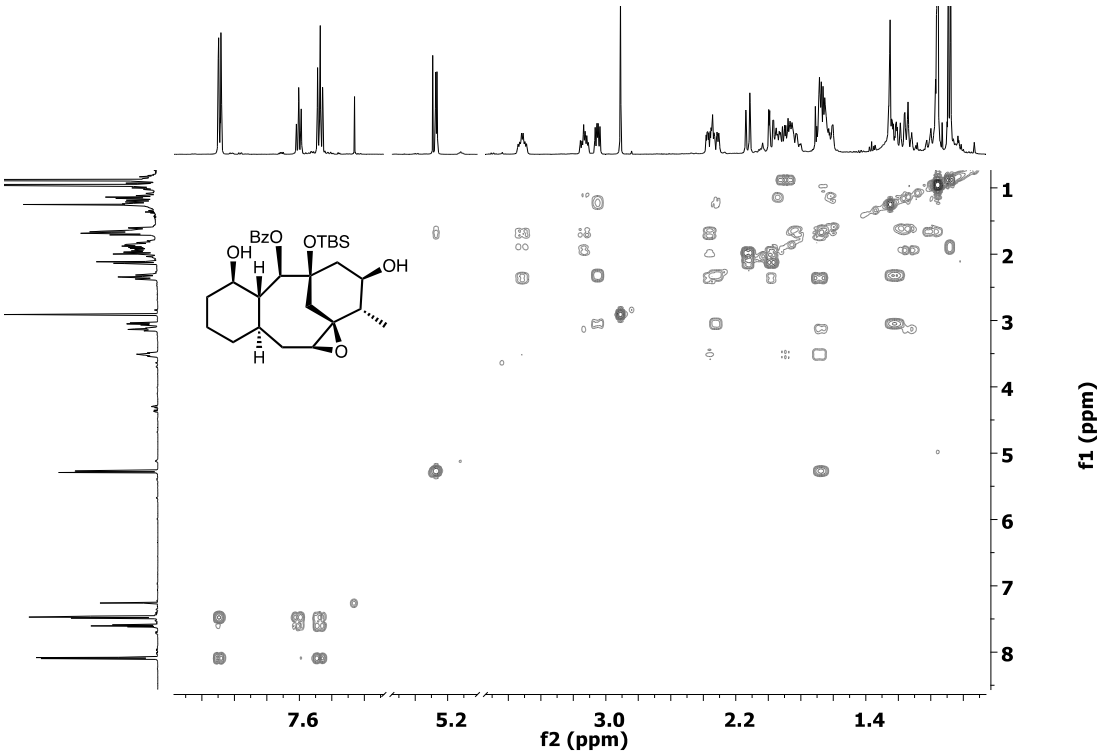


Figure 82SI. COSY spectrum of taxane analogue **22a**.

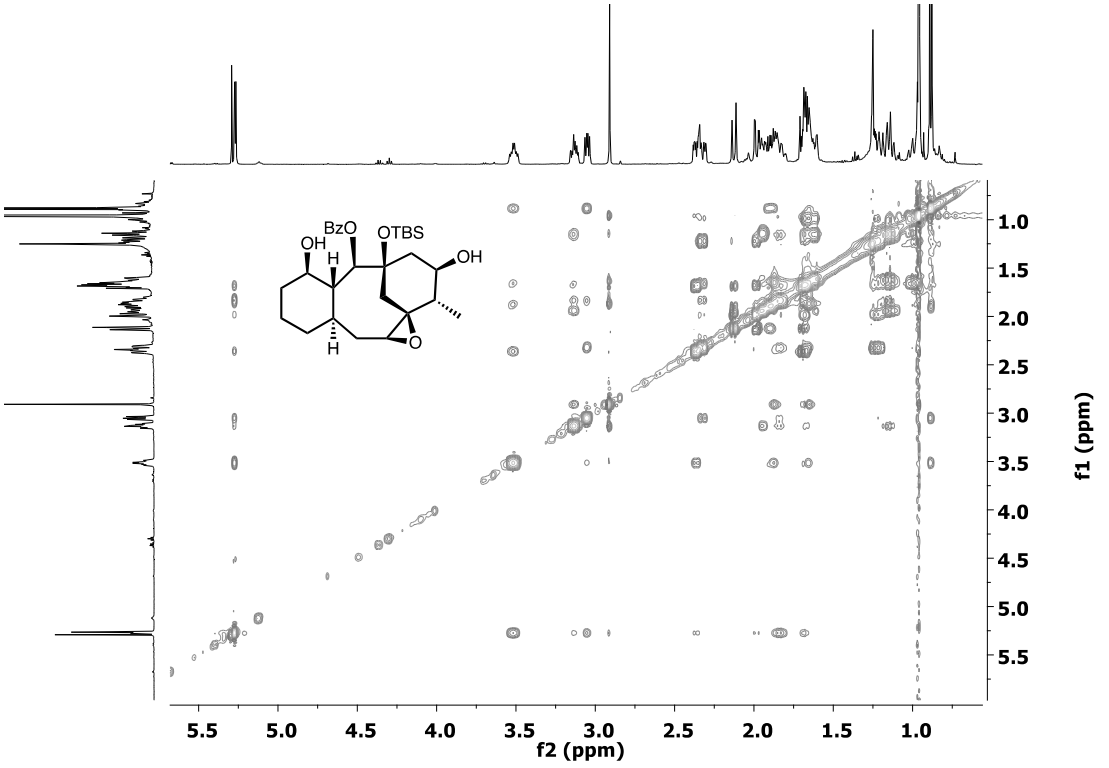


Figure 83SI. NOESY spectrum of taxane analogue **22a**.

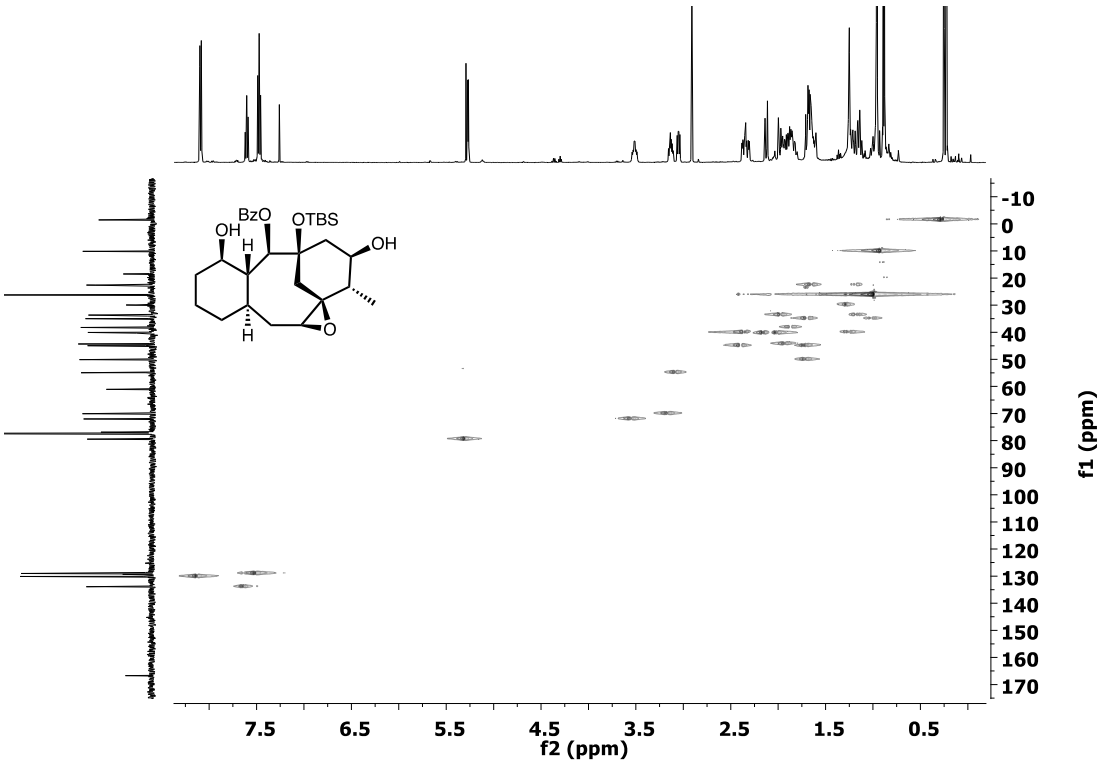


Figure 84SI. HSQC spectrum of taxane analogue **22a**.

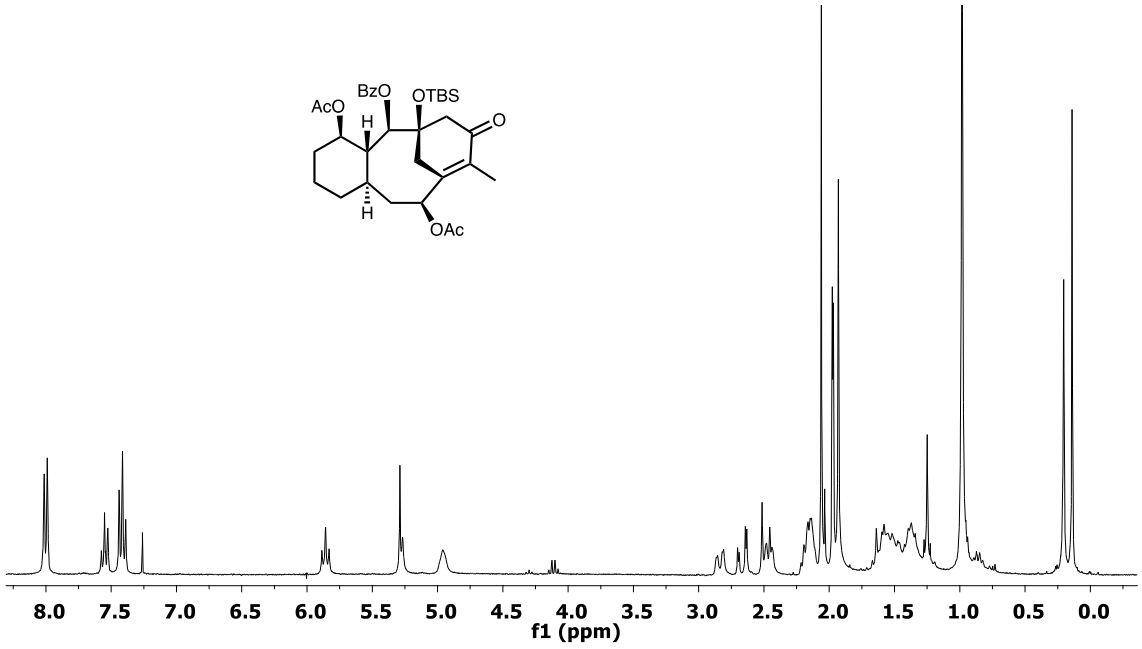


Figure 85SI. ^{1}H NMR spectrum of taxane analogue **37a** recorded in $CDDI_3$ at 300 MHz.

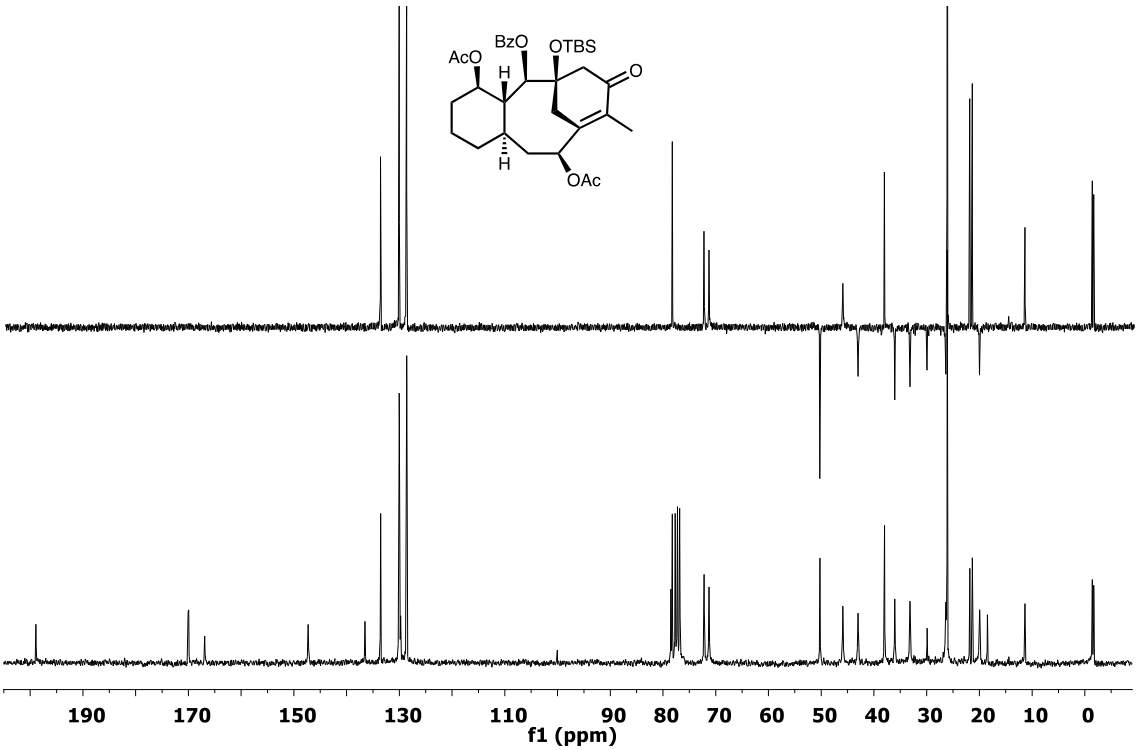


Figure 86SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxane analogue **37a** recorded in $CDCl_3$ at 75 MHz.

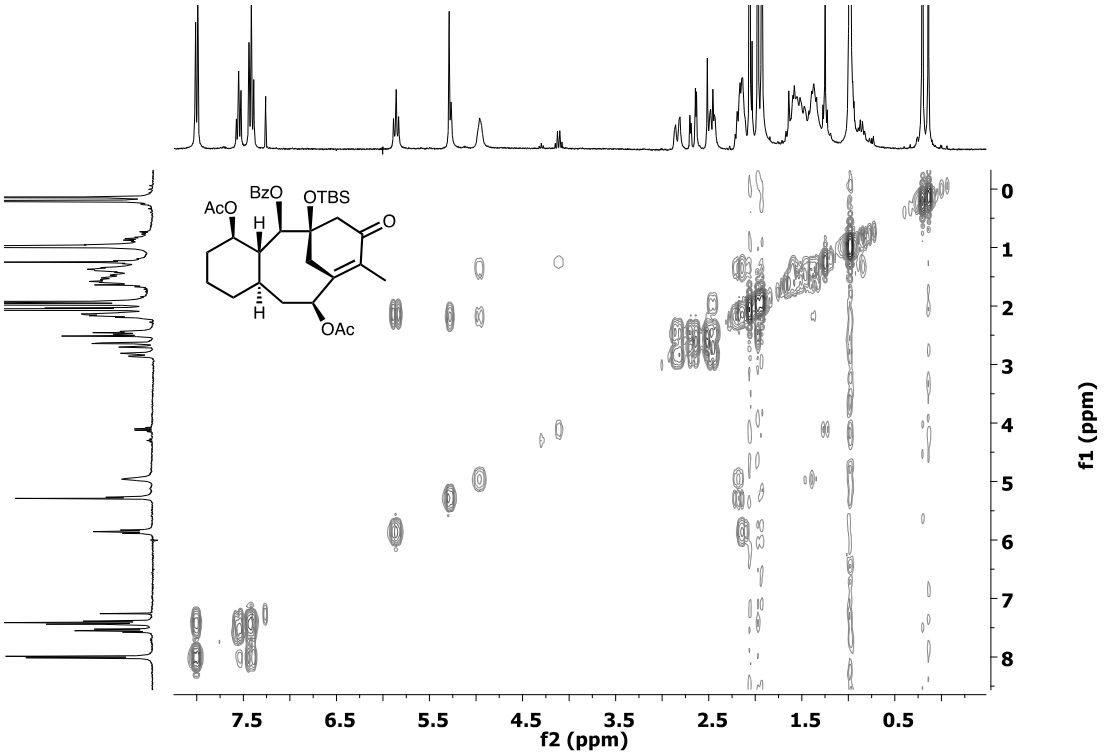


Figure 87SI. COSY spectrum of taxane analogue **37a**.

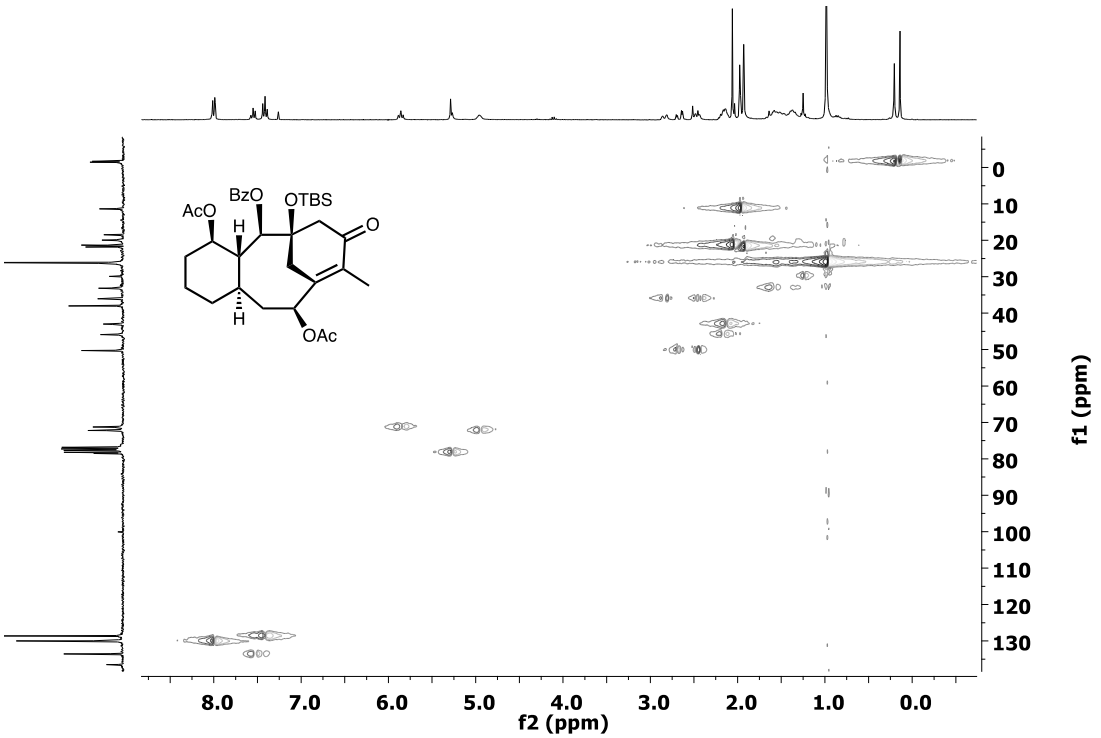


Figure 88SI. HMQC spectrum of taxane analogue **37a**.

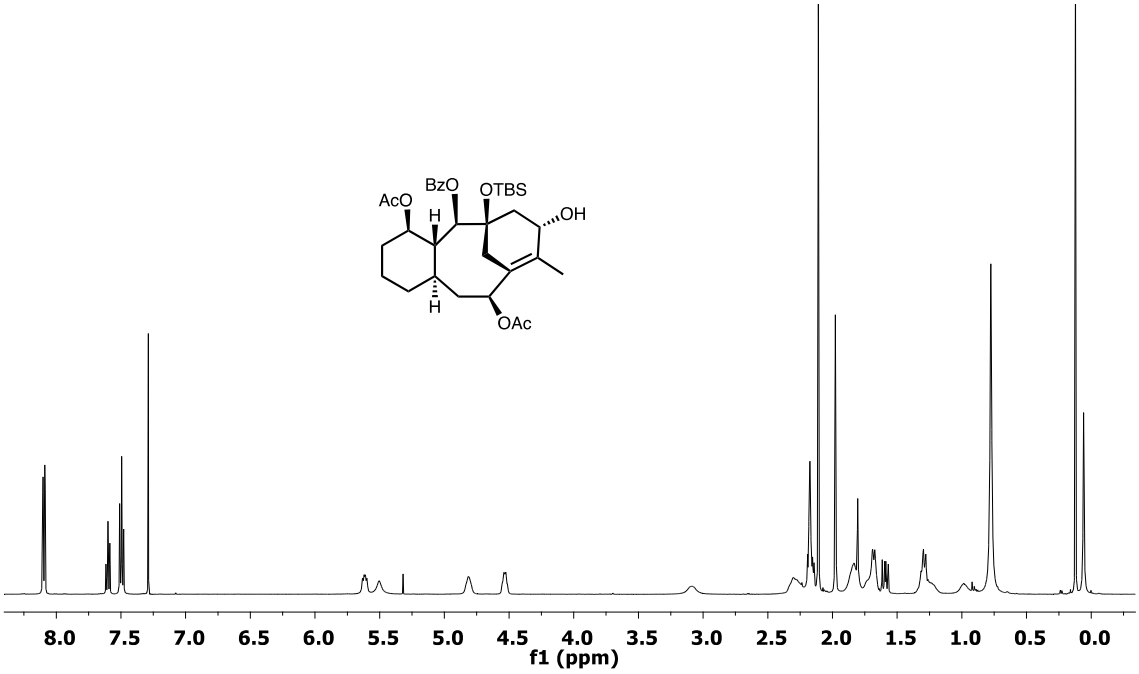


Figure 89SI. ^{1}H NMR spectrum of taxane analogue **38a** recorded in $CDDI_3$ at 500 MHz.

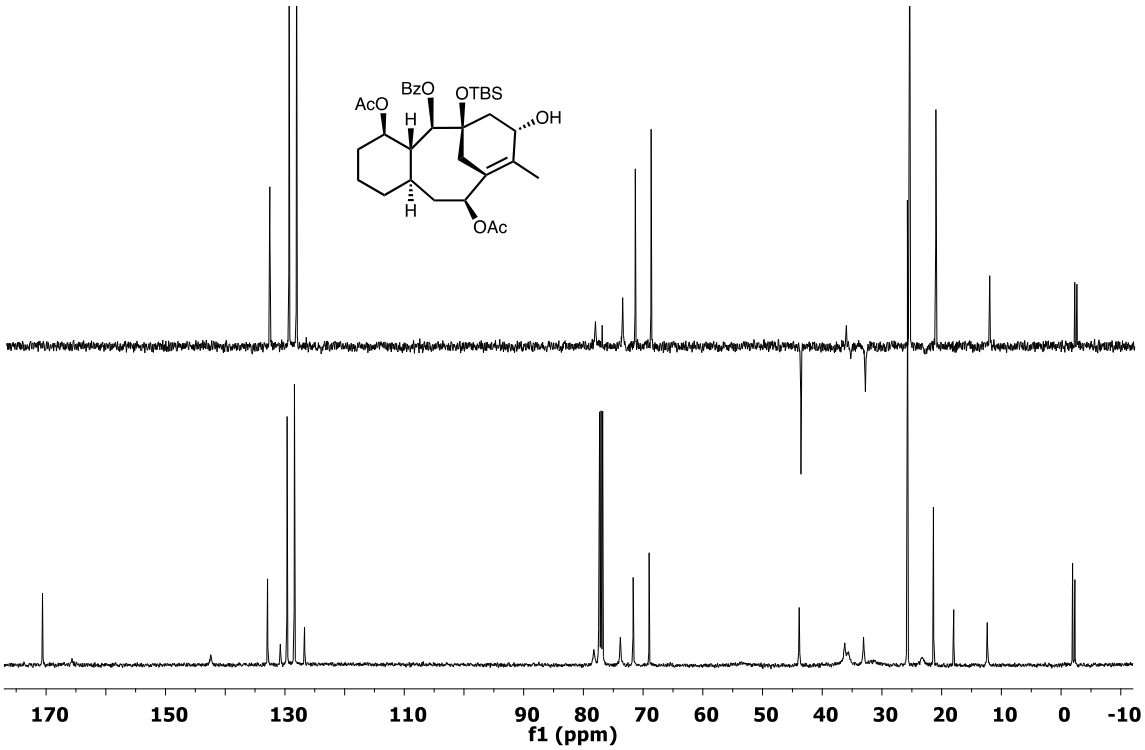


Figure 90SI. DEPT 135 (top) and ^{13}C NMR (bottom) of taxane analogue **38a** recorded in $CDCl_3$ at 126 MHz.

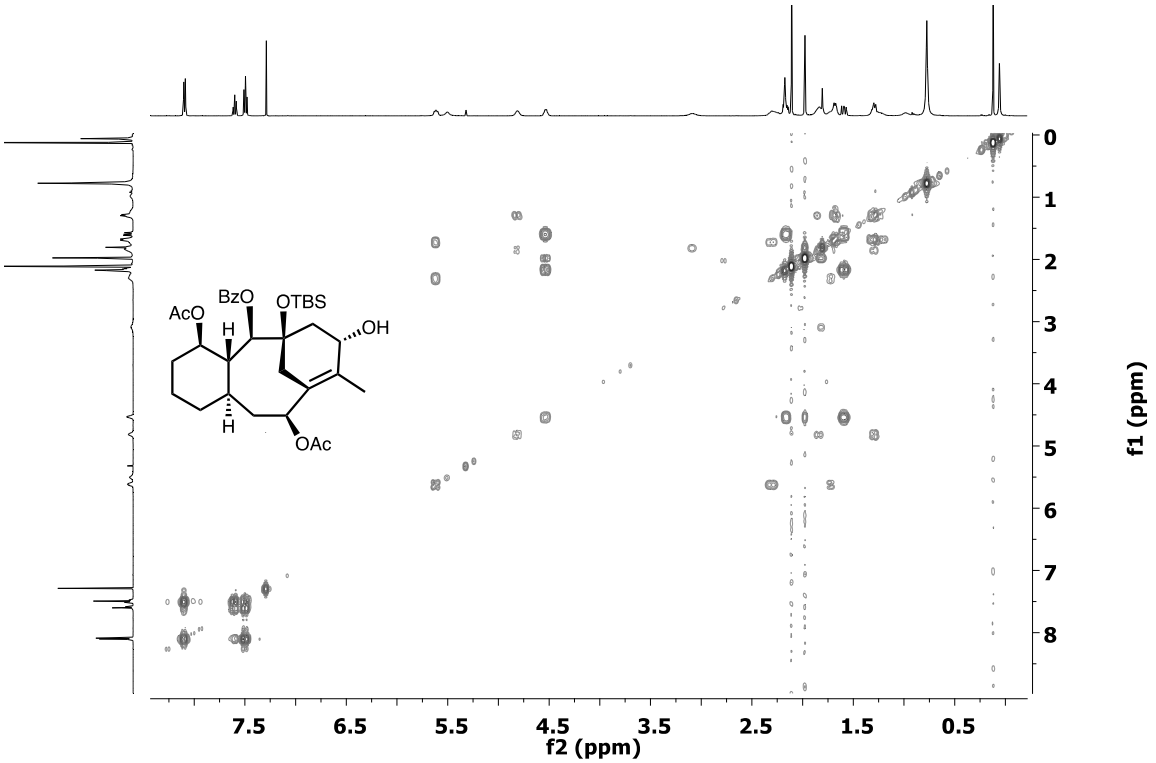


Figure 91SI. COSY spectrum of taxane analogue **38a**.

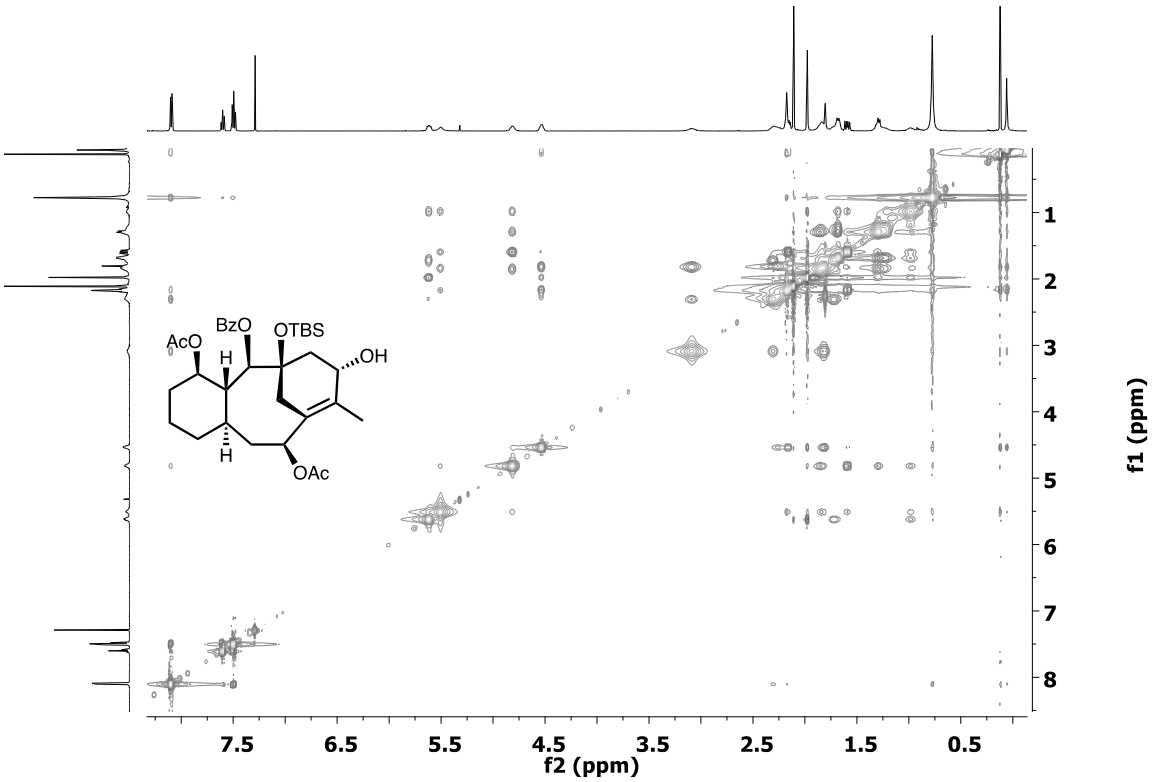


Figure 92SI. NOESY spectrum of taxane analogue **38a**.

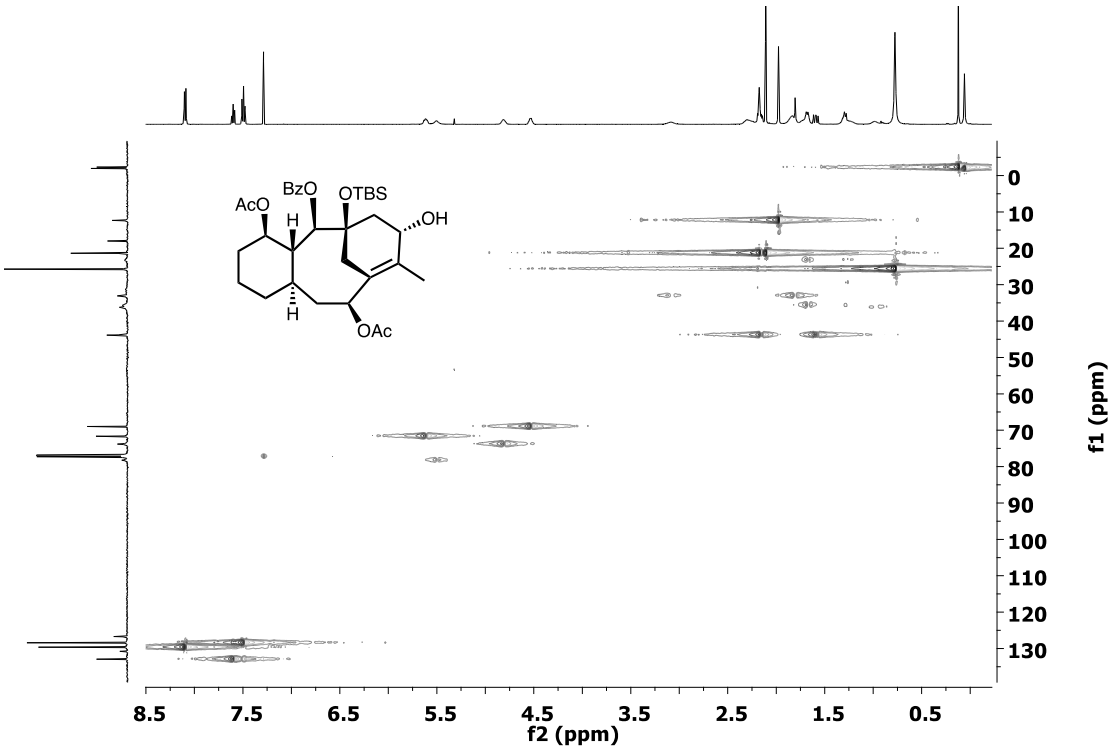


Figure 93SI. HSQC spectrum of taxane analogue **38a**.