Supporting information

An Efficient Synthesis of Epoxydiynes and a Key Fragment of Neocarzinostatin Chromophore

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General procedures:

Melting points were obtained using a Gallenkamp variable heater. Optical rotations were measured on a PolaAr 2000 polarimeter. Infrared spectra were recorded on a SHIMADZU FT-IR 8700 spectrometer. Data were presented as frequency of absorption (cm^{-1}). Proton and carbon NMR were measured on Bruker AMX300 spectrometer, or a Bruker AMX400 spectrometer or a Bruker AVANCE500 spectrometer. Chemical shifts were expressed in parts per million (δ) and are referenced to the residual solvent peak (CHCl_3 , 7.26 and $\text{C}_6\text{D}_5\text{H}$, 7.15). The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet and br, broad. Coupling constants are recorded in Hertz. ^{13}C NMR chemical shift were referenced to resonances of the NMR solvent. Low and high resolution mass spectra were obtained from the mass spectroscopy service at Swansea. Flash chromatography was carried out on silica gel (32-70 μm). Thin layer chromatography was performed on aluminium plates pre-coated with Merck silica gel 60 F₂₅₄ and was visualised by exposure to UV and/or exposure to potassium permanganate followed by heating. All reactions were performed in flame-dried round bottom flasks and under positive pressure of argon unless otherwise noted. Commercial reagents and solvents were used as received with some exceptions. THF, Et₂O and DCM were distilled through alumina column from an anhydrous engineering apparatus. ZnBr_2 99.999% was purchased from Aldrich and prepared from Chemla procedure.¹ Hexamethyldisilazane was distilled from calcium hydride at 760 torr. Lithium Hexamethyldisilazide (1M in THF/Hexanes) was freshly prepared by the addition of n-Butyllithium (2.06 M in hexanes) to a solution of Hexamethyldisilazide in THF. The molarity of n-butyllithium was determined by titration using dry [(1S)-endo]-(-)-Borneol and fluorene as indicator.

(3-chloroprop-1-ynyl)trimethylsilane 5²

To propargyl chloride (5.0 ml, 69 mmol) in THF (200 mL) at -78°C was added a 1.4 M solution of n-BuLi in hexane (25 mL, 35 mmol) dropwise over 2 h. TMSCl (8.8 mL, 69 mmol) was then added dropwise and the solution allowed to warm to rt and stirred for 1 h. The reaction mixture was quenched by adding it to water (200 mL), then Et₂O (200 mL) was added and the layers separated. The aqueous layer was then washed with Et₂O (2 × 200 mL) and the combined organic extracts washed with water (100 mL), brine (100 mL), and dried over magnesium sulfate. Concentration *in vacuo*, followed by purification *via* distillation (bp 135 °C) gave **5** (4.8 g, 48%) as a colourless oil.

$\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 2962, 2183, 1269, 1029; ¹H NMR (300 MHz; CDCl₃) δ_{H} 4.13 (s, 2H), 0.18 (s, 9H); ¹³C NMR (75 MHz; CDCl₃) δ_{C} 99.6 (C), 91.8 (C), 30.7 (CH₂), -0.4 (CH₃).

(3-chloroprop-1-ynyl)triethylsilane 17³

To propargyl chloride (2.5 mL, 34.6 mmol) in THF (100 mL) at -78°C was added a 1.4 M solution of n-BuLi in hexane (12.5 mL, 17.5 mmol) dropwise over 2 h. TESCl (5.8 mL, 34.6 mmol) was then added dropwise and the solution allowed to warm to rt and stirred for 1 h. The reaction mixture was quenched by adding it to water (100 mL), then Et₂O (100 mL) was added and the layers separated. The aqueous layer was then washed with Et₂O (2 × 100 mL) and the combined organic extracts washed with water (50 mL), brine (50 mL), and dried over magnesium sulphate. Concentration *in vacuo* and subsequent column chromatography [PE] gave **17** (2.4 g, 37%) as a colourless oil.

$\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 2959, 2179, 1029; ¹H NMR (300 MHz; CDCl₃) δ_{H} 4.15 (s, 2H) 0.99 (t, 9H, *J* 7.9), 0.61 (q, 6H, *J* 7.8); ¹³C NMR (75 MHz; CDCl₃) δ_{C} 100.8 (C), 89.5 (C), 30.8 (CH₂), 7.3 (CH₃), 4.1 (CH₂).

tert-Butyl-(3-Chloro-prop-1-ynyl)-dimethylsilane 18

To propargyl chloride (5.0 mL, 69 mmol) in THF (200 mL) at -78°C was added a 2.18 M solution of n-BuLi (16 mL, 35 mmol) dropwise over 2 h. A 2 M solution of TBSCl in THF (34.5 mL, 69 mmol) was then added dropwise *via* cannula and the reaction was allowed to warm to rt and stirred for 1 h. The reaction was quenched with water (200 mL), extracted with ether (2 x 200 mL), washed with brine (100 mL), dried over magnesium sulphate, filtered and concentrated *in vacuo*. Column chromatography eluting with 100% PE gave **18** (5.48 g, 42%) as a colourless oil.

ν_{max} (cm^{-1}) 2916, 2198 1450, 1257, 1033, 817; ^1H NMR (300 MHz; CDCl_3) δ_{H} (300 MHz, CDCl_3) 4.14 (s, 2H), 0.94 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (75 MHz; CDCl_3) δ_{C} 100.3 (C), 90.2 (C), 30.7 (CH_2), 25.9 (C), 16.4 (CH_3), -4.8 (CH_3).

4-Hydroxy-but-2-ynal diethyl acetal **14**⁴

To a solution of (propargyloxy)trimethylsilane (30 g, 234 mmol) in THF (150 mL) was added a 1 M THF-solution of ethylmagnesium bromide (234 mL, 234 mmol). The reaction was stirred for 30 min and a solution of phenyl orthoformate (41.8 g, 212 mmol) in THF (110 mL) was added. Stirring was continued for 16 h then the reaction quenched with a saturated solution of ammonium chloride (200 mL) and water (200 mL), extracted with ether (2 x 200 mL), washed with NaOH (4 M solution, 3 x 100 mL) dried over magnesium sulphate and concentrated *in vacuo*. The residue was then dissolved in methanol (530 mL) and potassium carbonate (29.3 g, 212 mmol) was added at 0°C and the mixture stirred for 10 min. The solution was concentrated *in vacuo* then water (200 mL) was added. The mixture was extracted with ethyl acetate (3 x 150 mL), dried over magnesium sulphate and concentrated *in vacuo*. Distillation of the residue under vacuum (bp 88°C; 1 mmHg) gave **14** (23.7 g, 70%) as a colourless oil.

ν_{max} (cm⁻¹) 3424, 1120; ¹H NMR (300 MHz, CDCl₃) δ_{H} 5.26 (s, 1H), 4.28 (dd, 2H, *J* 6.2, 1.3), 3.70 (dq, 2H, *J* 7.2, 9.4), 3.55 (dq, 2H, *J* 7.2, 9.4), 2.30 (br s, 1H), 1.19 (t, 6H, *J* 7.2); ¹³C NMR (300 MHz; CDCl₃) δ_{C} (75 MHz, CDCl₃) 91.6, 84.2, 81.1, 61.3, 51.1, 15.4.

4-Chloro-1,1-diethoxy-but-2-yne **15**⁵

To a solution of the alcohol **14** (10 g, 63 mmol) and triethylamine (26.4 mL, 190 mmol) in ether (320 mL) was added dropwise methanesulfonyl chloride (5.5 mL, 70 mmol) at 0°C. Stirring was continued for 1 h and then the reaction quenched with a saturated aqueous solution of NaHCO₃ (120 mL), extracted with ether (2 x 60 mL), dried over magnesium sulphate, filtered and concentrated *in vacuo*. The residue was dissolved in chloroform (310 mL) with tetra-n-butylammonium chloride (41 g, 126 mmol). The reaction was refluxed for 1 h. Concentration of the mixture *in vacuo* gave the crude residue to which ether (200 mL) was added. The solution was washed with water (100 mL), then brine (2 x 100 mL), dried over magnesium sulphate and concentrated *in vacuo* to furnish the pure propargylic chloride **15** as a yellow oil (8.9 g, 80%).

ν_{max} (cm⁻¹) 2971, 2901, 2888, 2238; ¹H NMR (300 MHz, CDCl₃) δ_{H} 5.23 (m, 1H, *J* 1.3), 4.13 (d, 2H, *J* 1.3), 3.69 (dq, 2H, *J* 7.2, 9.3), 3.53 (dq, 2H, *J* 7.2, 9.3), 1.18 (t, 6H, *J* 7.2); ¹³C NMR (75 MHz, CDCl₃) δ_{C} 91.1 (CH), 81.6 (C), 79.9 (C), 60.9 (CH₂), 29.7 (CH₂), 14.9 (CH₃); HRMS (M+H)⁺ cald. for C₈H₁₃O₂Cl 175.0520, found *m/z* 175.0518.

2,2-Dimethyl-[1,3]dioxolane-4-yl)-3-trimethylsilanyl-prop-2-yn-1-ol 19⁶

To a solution of 1,2-5,6-diisopropylidene-D-mannitol **3** (25 g, 95 mmol) in DCM (350 mL) and aqueous sodium bicarbonate (4mL) was added portionwise sodium periodate (190 mmol) over 20 min. Then the reaction mixture was stirred for 2 h and filtered through a pad of magnesium sulfate. DCM was then evaporated under vacuum in a cold bath (28°C) to give the D-glyceraldehyde acetonide.

Meanwhile to a solution of trimethylsilylacetylene (31.8 mL, 228 mmol) in THF (900 mL) was added freshly made lithium hexamethyldisilazide (209 mL, 209 mmol) at –78°C. The reaction mixture was stirred for 30 min and a solution of D-glyceraldehyde

acetone (24.7 g, 190 mmol) in THF (250 mL) was added over a period of 30 min. The reaction was stirred for 30 min and quenched by the addition of saturated aqueous ammonium chloride (150 mL). The reaction mixture was concentrated *in vacuo* to a volume of approximately 300 mL and diluted with ethyl acetate (300 mL). The mixture was washed with water (250 mL), saturated aqueous ammonium chloride (250 mL), extracted with ethyl acetate (150 mL), dried over magnesium sulphate, filtered and concentrated *in vacuo*. Flash column chromatography in EtOAc (20%)/PE afforded the inseparable diastereomeric propargylic alcohols **19** (1.2:1, 35 g, 81%) as a pale yellow oil.

ν_{max} (cm^{-1}) 3434, 2990, 2962, 2252, 1456, 1374; ^1H NMR (300 MHz, CDCl_3) δ_{H} 4.33-3.71 (m, 4H), 2.64 (s br, 1H, **major**), 2.50 (s br, 1H, **minor**), 1.28 (3H, s), 1.21 (s, 3H), 0.00 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} 110.8 (C), 110.4 (C), 102.7 (C), 102.6 (C), 91.7 (C), 91.6 (C), 79.1 (CH), 78.1 (CH), 66.5 (CH_2), 65.4 (CH_2), 65.1 (CH), 63.0 (CH), 27.1 (CH_3), 26.6 (CH_3), 25.6 (CH_3), 25.6 (CH_3), 0.4 (CH_3), 0.4 (CH_3). HRMS ($\text{M}+\text{NH}_4$) $^+$ calcd. for $\text{C}_{11}\text{H}_{24}\text{O}_3\text{Si}$ 246.1520, found m/z 246.1517.

To pyridinium dichromate (66 g, 175 mmol) and crushed 3 Å molecular sieves (40 g) in DCM (150 mL) was added dropwise a solution of propargylic alcohol **19** (20 g, 87.6 mmol) in DCM (75 mL) and the reaction mixture was stirred for 4 h. Celite (40 g) was added and the suspension was stirred for 30 min. The reaction mixture was then filtered and washed with ether. The filtrate was washed with saturated aqueous potassium hydrogen sulphate (3 x 100 mL), saturated aqueous sodium hydrogen carbonate (100 mL). The organic layer was washed with brine (2 x 50 mL), filtered through a plug of magnesium sulphate and concentrated *in vacuo*. Flash column chromatography eluting with Et₂O (25%)/PE afforded the ynone **9** (16.25 g, 82%).

ν_{max} (cm⁻¹) 2989, 2963, 2902, 2153, 1677, 1373; ¹H NMR (300 MHz, CDCl₃) δ_{H} 4.28 (1H, dd, *J* 7.4, 5.0), 4.0 (1H, dd, *J* 8.8, 7.4), 3.91 (1H, dd, *J* 8.8, 5.0), 1.27 (3H, s), 1.15 (3H, s), 0.00 (9H, s); ¹³C NMR (75 MHz, CDCl₃) δ_{C} 187.5 (C) 112.8 (C), 104.6 (C), 100.7 (C), 81.8 (CH), 67.8 (CH₂), 27.0 (CH₃), 26.3 (CH₃), 0.0 (CH₃); HRMS (M+NH₄)⁺ calcd. for C₁₁H₂₂O₃Si 244.1363, found *m/z* 244.1363.

2-Ethynyl-3-hept-1-ynyl-oxirane

To ZnBr_2 (0.306 g, 1.36 mmol) in THF (1 mL) at -20°C was added **5** (0.100 g, 0.68 mmol), then the mixture cooled to -78°C and freshly prepared LDA (1.36 mmol) in THF (3 mL) was added. The mixture was stirred for 1 h then 2-Octynal (0.093 g, 0.75 mmol) was added. The stirring was continued for 1 h at -78°C and the reaction was warm to -30°C and stirred for 45 min then $(\text{NH}_4)_{\text{aq}}$ was added to quench and the reaction mixture was partitioned between H_2O (20 mL) and Et_2O (50 mL). The aqueous layer was then washed with Et_2O (2×50 mL) and the combined organic extracts washed with water (20 mL), brine (20 mL), dried over magnesium sulphate. Concentration *in vacuo* gave the crude chlorohydrin **6** to which DMF (3.5 mL) was added followed by addition of KF (2.73 mmol, 0.158 g) in one portion. The reaction mixture was stirred for 1 h then water (1 mL) was added to quench. The mixture was extracted with ether (20 mL), washed with brine (2×10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Column chromatography eluting with CHCl_3 (50%)/PE afforded the crude desilylated chlorohydrin.

To the crude chlorohydrin in DCM (2.5 mL) was added DBU (3.4 mmol, 0.519 g) and the reaction mixture was stirred for 2 h. The mixture was poured on silica gel previously neutralised with DBU (0.1%) in petroleum ether. Column chromatography eluting with CHCl_3 (30%)/PE resulted in the inseparable diastereoisomeric epoxydienes **8** and **7** (42 %, *trans* / *cis*: 5 / 3). Repeated column chromatography allowed a small amount of each diastereoisomer to be isolated for analysis.

$\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3298, 2956, 2933, 2871, 2860, 2237, 2171, 1460, 1398, 1315;

***trans*-Epoxydiyne (major) 8** ^1H NMR (300 MHz, CDCl_3) δ_{H} 3.50 (dt, 1H, J 2.0, 1.7), 3.43 (dd, 1H, J 2.0, 1.7), 2.33 (d, 1H, J 1.7), 2.19 (dt, 2H, J 7.1, 1.7), 1.50 (m, 2H), 1.32 (m, 4H), 0.89 (t, 3H, J 7.3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} 86.0 (C), 79.0 (C), 74.9 (C), 72.4 (C), 47.3 (CH), 46.7 (CH), 30.9 (CH_2), 27.8 (CH_2), 22.1 (CH_2), 18.6 (CH_2), 13.9 (CH_3); ***cis*-Epoxydiyne (minor) 7** ^1H NMR (300 MHz, CDCl_3) δ_{H} 3.54 (dt, 1H, J 3.8, 1.7), 3.50 (dd, 1H, J 3.8, 1.7), 2.43 (d, 1H, J 1.7), 2.26 (dt, 2H, J 7.1,

1.7), 1.54 (m, 2H), 1.38 (m, 2H), 1.31 (m, 2H), 0.89 (t, 3H, J 7.3); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} 87.7 (C), 78.2 (C), 77.2 (C), 73.9 (C), 46.6 (CH), 46.1 (CH), 30.8 (CH_2), 27.9 (CH_2), 22.1 (CH_2), 18.7 (CH_2), 13.9 (CH_3); HRMS ($\text{M}+\text{H}$) $^+$ cald. for $\text{C}_{11}\text{H}_{14}\text{O}$ 163.11228, found m/z 163.11190.

trans-epoxydiyne **8**

cis-epoxydiyne **7**

(R)-4-((2S,3R)-2,3-diethynyloxiran-2-yl)-2,2-dimethyl-1,3-dioxolane 10

Method 1

To ZnBr₂ (0.225 g, 1.0 mmol) in THF (1 mL) at -20°C was added **5** (0.073 g, 0.5 mmol), then the mixture cooled to -78°C and freshly prepared LDA (1 mmol) in THF (2 mL) was added. The mixture was stirred for 1 h then **9** (0.113 g, 0.5 mmol) was added. After stirring for a further 2 h at -78°C, NH₄Cl_(aq) was added to quench, and once the mixture had warmed to rt it was separated between H₂O (20 mL) and Et₂O (50 mL). The aqueous layer was then washed with Et₂O (2 × 50 mL) and the combined organic extracts washed with water (20 mL), brine (20 mL), and dried over magnesium sulphate. Concentration *in vacuo*, followed by purification *via* column chromatography [Et₂O (15%)/PE] gave the crude halohydrin (115 mg).

To the crude halohydrin (0.050 g) in DMF (1.0 mL) was added KF (0.028 g, 0.48 mmol) followed by H₂O (1 drop). The reaction mixture was stirred for 22 h then NH₄Cl_(aq) was added to quench, and it was separated between H₂O (20 mL) and Et₂O (50 mL). The aqueous layer was then washed with Et₂O (2 × 50 mL) and the combined organic extracts washed with water (20 mL), brine (20 mL), and dried over magnesium sulfate. Concentration *in vacuo*, followed by purification *via* column chromatography [Et₂O (20%)/PE] gave **10** (0.018 mg, 45%) as a white solid (mp 78-79°C).

[α]_D²⁰ +16.0 (*c* 0.1, CHCl₃); $\nu_{\max}$ (film)/cm⁻¹ 3300, 2991, 2120, 1383, 1074; ¹H NMR (300 MHz; CDCl₃) δ_{H} 4.26-4.06 (m, 3H), 3.65 (d, 1H, *J* 2.0), 2.51 (s, 1H), 2.47 (d, 1H, *J* 2.0), 1.47 (s, 3H), 1.36 (s, 3H); ¹³C NMR (75 MHz; CDCl₃) δ_{C} 111.1 (C), 77.3 (CH), 76.8 (CH), 75.7 (C), 75.6 (CH), 74.9 (C), 66.4 (CH₂), 57.6 (C), 49.1 (CH), 26.0 (CH₃), 25.1 (CH₃), *m/z* (DCi) 193 (M + H)⁺, 17%, 177 (100), 135 (95).

Method 2: To **11** (0.090g, 0.29 mmol) in THF (1.5 ml) at -78°C was added a 1 M solution of TBAF in THF (0.58 ml, 0.58 mmol). After stirring for 10 min the reaction

¹H NMR spectrum (CDCl₃) of compound 10. The spectrum displays four main signals with the following integrations: a triplet at ~7.2 ppm (1.71), a multiplet between 4.5-5.5 ppm (3.27, 1.52, 4.27), a doublet at ~3.9 ppm (1.96), and a sharp singlet at ~7.8 ppm (5.97). A solvent peak for CDCl₃ is visible at ~7.26 ppm. The x-axis is labeled from 8 to 0 ppm.

To ZnBr_2 (477 mg, 2.1 mmol) in THF (2 mL) at -20°C was added **17** (200 mg, 1.06 mmol) then the reaction was cooled to -78°C . A freshly prepared 1M solution of LDA in THF (2.12 mL, 2.1 mmol) was added dropwise and the reaction was stirred for 1 h. The ketone **9** (240 mg, 1.06 mmol) was then added quickly. Stirring was continued for 2 h at -78°C and the reaction quenched with saturated aqueous solution of ammonium chloride (10 mL). The resulting mixture was allowed to warm to rt, extracted with ether (20 mL), washed with brine (2 x 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)/PE afforded a crude chlorohydrin.

To the crude chlorohydrin in methanol (5 mL) at -10°C was added K_2CO_3 (585 mg, 4.23 mmol). The stirring was continued for 4 h until completion and then saturated ammonium chloride solution (10 mL) was added. The reaction mixture was extracted with ether (2 x 30 mL), washed with brine (2 x 10 mL), dried over magnesium, filtered and concentrated *in vacuo*. Flash chromatography eluting with Et_2O (10%)/PE resulted in a pure epoxydiyne **11** (201 mg, 62%).

$\alpha_{\text{D}}^{22} +63^\circ$ (*c* 1 in CHCl_3) [*lit*⁷ $+64.5^\circ$ (*c* 1 in CHCl_3)], ^1H NMR (300 MHz, CDCl_3) δ_{H} 4.21 (dd, 1H, *J* 8.6, 6.7), 4.10 (dd, 1H, *J* 8.6, 6.2), 4.05 (t, 1H, *J* 6.4), 3.63 (s, 1H), 2.47 (s, 1H), 1.47 (s, 3H), 1.35 (s, 3H), 0.99 (t, 9H, *J* 7.8), 0.61 (q, 6H, *J* 7.8); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} 110.9 (C), 99.4 (C), 90.2 (C), 77.1 (C), 75.7 (CH), 75.4 (CH), 66.8 (CH_2), 57.8 (C), 49.8 (CH), 26.0 (CH_3), 25.1 (CH_3), 7.3 (CH_3), 4.0 (CH_2); HRMS ($\text{M}+\text{H}$)⁺ calcd. for $\text{C}_{17}\text{H}_{26}\text{O}_3\text{Si}$ 307.1729, found *m/z* 307.1725.

***tert*-Butyl-[3-(2,2-dimethyl-[1,3]dioxolan-4-yl)-3-ethynyl-oxyranylethynyl]dimethyl-silane **12**⁶**

To ZnBr_2 (238 mg, 1.06 mmol) in THF (2 mL) at -20°C was added **18** (100 mg, 0.53 mmol) then the reaction was cooled to -78°C . A freshly prepared 1 M solution of LDA in THF (1.06 mL, 1.06 mmol) was added dropwise and the reaction was stirred for 1 h. The ketone **9** (119 mg, 0.53 mmol) was then added quickly. Stirring was continued for 2 h at -78°C and the reaction quenched with saturated aqueous solution of ammonium chloride (10 mL). The resulting mixture was allowed to warm to rt, extracted with ether (20 mL), washed with brine (2 x 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)/PE afforded a crude chlorohydrin.

To the crude chlorohydrin in methanol (5 mL) at -10°C was added K_2CO_3 (293 mg, 2.12 mmol). The stirring was continued for 4 h until completion and then saturated ammonium chloride solution (10 mL) was added. The reaction mixture was extracted with ether (2 x 30 mL), washed with brine (2 x 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Flash chromatography eluting with Et_2O (5%)/PE resulted in a pure epoxydiyne **12** (99 mg, 61%).

$\alpha_D^{22} + 74^\circ$ (*c* 1 in C_6H_6), [lit $+78^\circ$ (*c* 1 in C_6H_6)], ^1H NMR (400 MHz, C_6D_6) δ_{H} 3.99 (dd, 1H, *J* 8.8, 6.2), 3.79 (dd, 1H, *J* 8.8, 6.6) 3.64 (t, 1H, *J* 6.6) 3.47 (s, 1H), 1.98 (s, 1H), 1.37 (s, 3H), 1.19 (s, 3H), 1.03 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ_{C} 110.7 (C), 100.5 (C), 90.6 (C), 78.1 (C), 76.7 (CH), 75.4 (CH), 66.8 (CH_2), 58.1 (C), 50.1 (CH), 26.2 (CH_3), 26.2 (CH_3), 25.4 (CH_3), 16.7 (C), -4.8 (CH_3). HRMS ($\text{M}+\text{H}$)⁺ calcd. for $\text{C}_{17}\text{H}_{26}\text{O}_3\text{Si}$ 307.1729, found *m/z* 307.1729.

**4-[3-(3,3-Diethoxy-prop-1-ynyl)-2-ethynyl-oxyranyl]-2,2-dimethyl-[1,3]dioxolane
16**

To ZnBr_2 (255 mg, 1.13 mmol) in THF (2 mL) at -20°C was added **15** (100 mg, 0.57 mmol) then the reaction was cooled to -78°C . A freshly prepared 1 M solution of LDA in THF (1.13 mL, 1.13 mmol) was added dropwise and the reaction was stirred for 1 h. The ketone **9** (118 mg, 0.52 mmol) was then added quickly. Stirring was continued for 2 h at -78°C and the reaction quenched with saturated aqueous solution of ammonium chloride (10 mL). The resulting mixture was allowed to warm to rt, extracted with ether (20 mL), washed with brine (2 x 10 mL), dried over magnesium sulfate, filtrated and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)/PE afforded a crude chlorohydrin.

To the crude chlorohydrin in DMF (3 mL) was added KF (263 mg, 4.53 mmol). The reaction mixture was stirred overnight and both ether (40 mL) and saturated aqueous solution of ammonium chloride (30 mL) were added. The aqueous layer was extracted with ether (2 x 15 mL) and the combined organic extracts washed with water (2 x 20 mL), brine (20 mL), dried over magnesium sulphate and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)/PE afforded a pure epoxydiyne **16** (109 mg, 66%).

$\alpha_D^{22} +30.2^\circ$ (*c* 0.5 in CHCl_3); ν_{max} (cm^{-1}) 3201, 2926, 2854, 2195, 2160, 1399, 1273, 1210, 1087; ^1H NMR (500 MHz, CDCl_3) δ_{H} 5.29 (d, 1H, *J* 1.1), 4.18 (dd, 1H, *J* 10.8, 8.9), 4.06 (dd, 1H, *J* 10.8, 5.9), 4.06 (dd, 1H, *J* 8.9, 5.9), 3.75 (dq, 1H, *J* 9.6, 7.0), 3.73 (dq, 1H, *J* 9.6, 7.0), 3.68 (d, 1H, *J* 1.1), 3.57 (dq, 2H, *J* 9.4, 7.0), 2.47 (s, 1H), 1.42 (s, 3H), 1.32 (s, 3H), 1.25 (t, 3H, *J* 7.0), 1.20 (t, 3H, *J* 7.0); ^{13}C NMR (125 MHz, CDCl_3) δ_{C} 111.0 (C), 91.0 (CH), 81.8 (C), 78.8 (C), 77.0 (C), 75.6 (CH), 75.4 (CH), 66.7 (CH₂), 61.1 (CH₂), 61.0 (CH₂), 57.7 (C), 49.1 (CH), 25.9 (CH₃), 25.0 (CH₃), 15.2

(CH₃), 15.0 (CH₃); HRMS (M+NH₄)⁺ cald. for C₁₆H₂₂O₅ 312.1805, found *m/z* 312.1805.

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