Synthetic strategies to epoxydiynes and a key synthon of the neocarzinostatin chromophore†

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We present herein our recent efforts towards the synthesis of epoxydiynes which represent an unusual structural feature of the neocarzinostatin chromophore. A number of different routes to these epoxydiynes have been explored with varying success. Ultimately a concise and convergent approach was developed, which involved the addition of an allenyl zinc bromide to propargylic ketones/aldehydes followed by epoxide formation. This new protocol enabled us to synthesise a fully elaborated epoxydiyne which will find application for our studies towards the total synthesis of the NCS chromophore.

Introduction

The chromoprotein neocarzinostatin (NCS) was the first isolated member of the so-called 'enediyne' class of antibiotics, and was found to exhibit broad-spectrum antitumor activity (Fig. 1). NCS was isolated in 1965 by Ishida *et al.* from the bacterium *Streptomyces carzinostaticus*.[1] NCS is made up of a 1 : 1 non-covalent complex of an extraordinary reactive nine-membered ring epoxydiyne chromophore[2] (NCS chrom) tightly bound to a protein known as apo-NCS (K_D = 0.1 nM).[3] The antitumour activity solely arises from the chromophore[4] which acts as a DNA-cleaving agent initiated by radical hydrogen abstraction of a deoxyribose residue.[5] The apoprotein protects, carries and delivers the chromophore.[6] SMANCS, a polymer-conjugated NCS variant has been approved for a variety of cancers in Japan and has shown some impressive results against solid tumours.[7] Since the disclosure of its structure in 1985,[8] NCS has been the subject of intensive synthetic investigations[9] and to date two successful total syntheses have been reported by Myers and Hirama.[10] The aim of this paper is to report our current efforts to establish a general method for the synthesis of epoxydiynes and towards the total synthesis of the NCS chromophore.

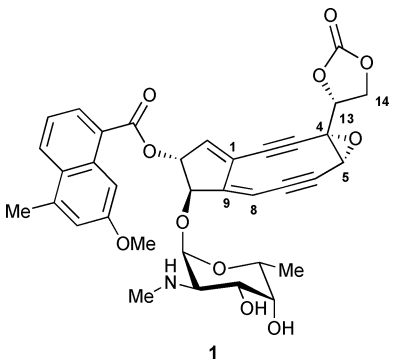

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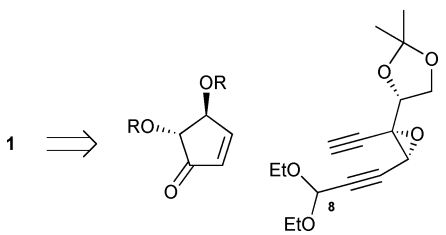
Fig. 1 Neocarzinostatin chromophore.



Scheme 1 Our retrosynthetic approach.

Results and discussion

Our strategy towards the NCS chrom has been to consider two fragments, a cyclopentenone and an epoxydiyne, with the aim of joining the two by an initial Michael addition of the free alkyne followed by an aldol cyclisation to form the 9-membered ring (Scheme 1).[11] We have previously reported a route to the cyclopentenone[9f] and also on model studies of the Michael–aldol sequence.[11] We report here on our efforts towards the challenging epoxydiyne fragment, discuss the different approaches we took, the problems we encountered and ultimately the solution we found which crucially enabled the incorporation of the key C-8 acetal.

Our preliminary approach relied on the preparation of enediynes with the correct stereochemistry ready for the introduction of the epoxide ring using a Sharpless asymmetric epoxidation (SAE). The first investigated and most convenient route to such enediynes involved a dehydration strategy. The alcohol **2** was thus prepared using the protocol developed by Hirama *et al.*[12] Dehydration of **2** *via* base-mediated elimination of the mesylate led to **3** in a disappointing 38% yield with an $E : Z$ ratio of 2 : 1. Alternatively, dehydration of **2** and concomitant introduction of the acetal functionality *via* a zinc-mediated acetalisation at high temperature led to the separable enediynes **4** in poor yield but with good diastereoselectivity ($E : Z$/10 : 1) (Scheme 2).

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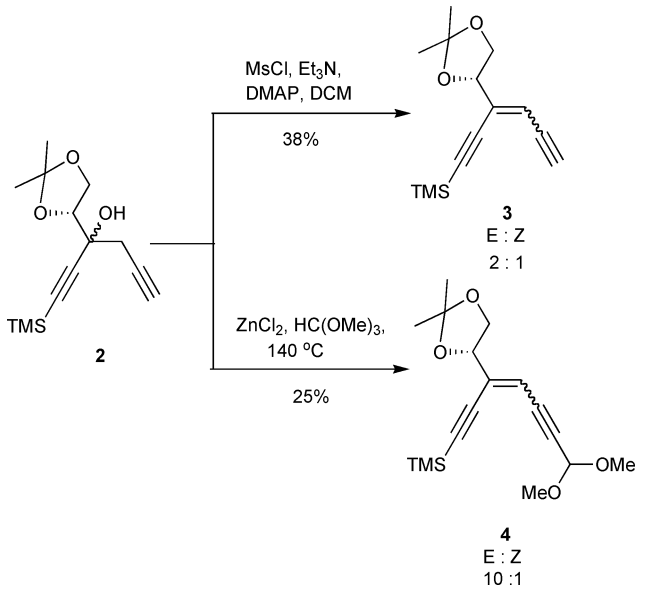
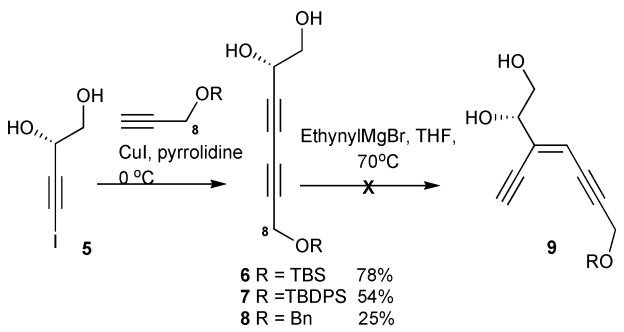


Scheme 2 Enediyne synthesis *via* dehydration.

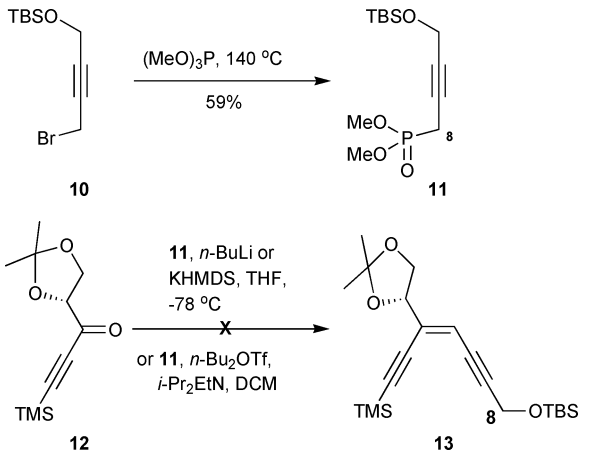
Despite many efforts to optimise the conditions of the dehydration reaction, we were unable to increase the yield and the selectivity and hence sought an alternative route. Hirama *et al.* have reported an efficient synthesis of an enediyne and ultimately an epoxydiyne involving a magnesium-mediated carbometalation.[13] We decided to try to use this approach toward our key fragment which would crucially incorporate the *C*-8 carbon. Copper-mediated coupling of the iodo-alkyne **5** was achieved using protected propargyl alcohols affording **6**, **7**, and **8** in yields ranging from 25% to 78% (Scheme 3). Unfortunately, the addition of ethynyl Grignard failed to give the corresponding *E*-enediyne **9** in each case and only starting material was recovered, revealing this reaction to be highly substrate dependent.



Scheme 3 Attempted enediyne synthesis *via* carbometalation approach.

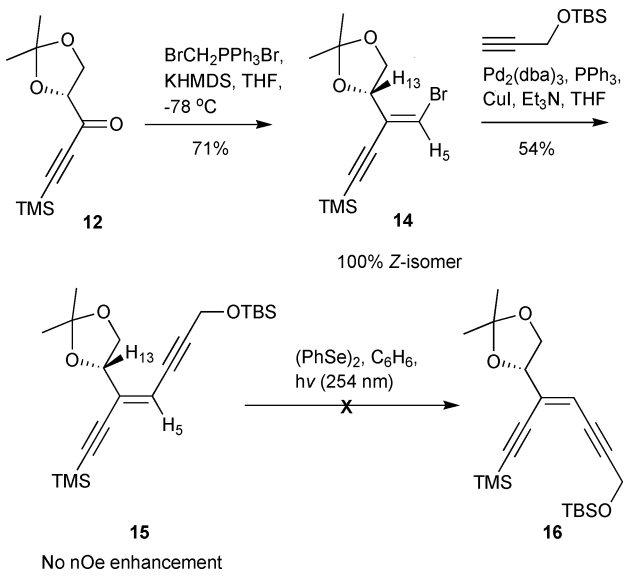
We decided to investigate a variety of other olefination strategies. Initially attempted was the addition of the phosphonate reagent **11** to the propargyl ketone **12** through a Horner–Wadsworth–Emmons (HWE) reaction (Scheme 4).[14] **11** was prepared in one step from **10** and subjected to **12**[10b] under HWE conditions. Unfortunately none of the product **13** could be isolated and only degradation of the starting material was observed. We attributed these results to the instability of the deprotonated phosphonate perhaps *via* cumulene formation.

A second olefination strategy was examined and involved the reaction of alkynyl ketone **12** with the commercially available



Scheme 4 Attempted enediyne synthesis *via* Horner–Wadsworth–Emmons methodology.

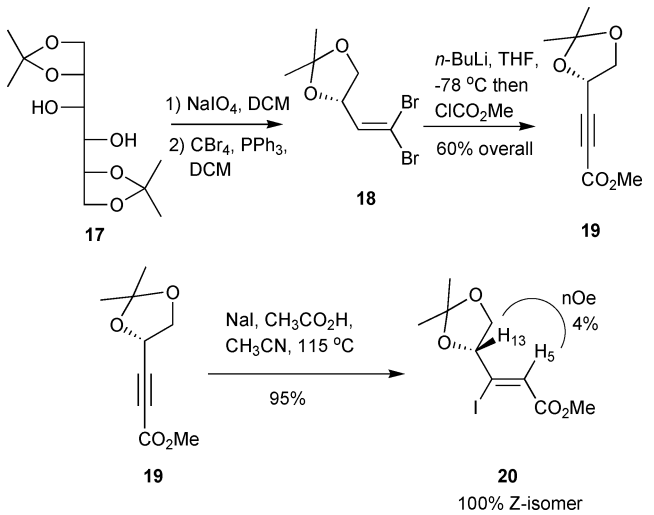
bromomethyltriphenylphosphonium salt (Scheme 5). This reaction proceeded in good yield but unfortunately gave exclusively the *Z*-vinyl bromide **14**. The stereochemistry of this process was confirmed by ^{1}H NMR studies in which no NOE enhancement between *H*-5 and *H*-13 was observed. This is in contrast to the enynes reported below in which these hydrogens are on the same side of the double bond and do result in an NOE enhancement. Despite this we decided to examine a possible isomerisation strategy and hence installed the second acetylenic moiety *via* a Sonogashira coupling which led to the isolation of the *Z*-enediyne **15** in 54% yield. This methodology provides an expeditious access to *Z*-enediynes including *C*-8. We then attempted a photochemical isomerisation of **15** under the conditions reported by Trost *et al.*[15] Unfortunately, no isomerisation to generate **16** was observed and the starting material was recovered in good yield.



Scheme 5 Attempted enediyne synthesis *via* Wittig–Sonogashira approach.

Although the aforementioned strategy failed to deliver the *E*-diyne stereochemical relationship, it did highlight the potential utility of the vinyl halides. Motivated by the pioneering studies

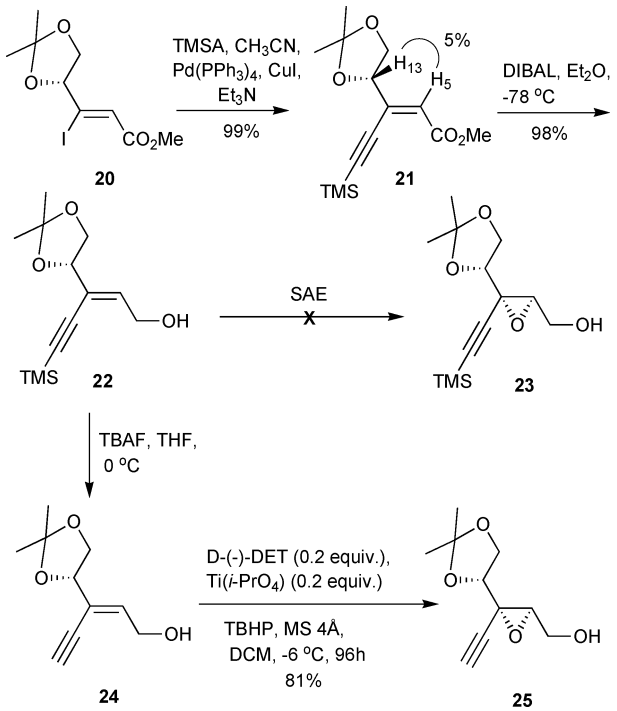
of Piers *et al.*[16] in which stereocontrolled conjugate addition of sodium iodide to alkynes was achieved we devised a related strategy. Thus we conceived that it may be possible to make appropriate functionalised *Z*-iodo-alkenes *via* acid-catalysed addition of iodide to an appropriately substituted acetylenic ester. If successful this strategy would complement the approach described by Bruckner *et al.*[17] who made the enol-triflate ester as key intermediate through the use of the chlorinated Comins' reagent. The acetylenic ester **19** was thus made to apply this methodology. This was prepared from the commercially available D-mannitol derivative **17** in 60% overall yield *via* oxidative cleavage of the diol, Corey–Fuchs homologation *via* dibromoalkene **18** and finally *in situ* methyl chloroformate trapping (Scheme 6).[18] After extensive optimisation studies, we found that treatment of **19** with sodium iodide (1.5 equiv.) and acetic acid (1.6 equiv.) in acetonitrile at high temperature led exclusively to the desired iodo-alkenyloate **20** in excellent yield. The stereochemistry was confirmed by NOE enhancement between *H*-5 and *H*-13.



Scheme 6 *Z*-Iodo-alkenyloate ester synthesis *via* stereocontrolled halide addition.

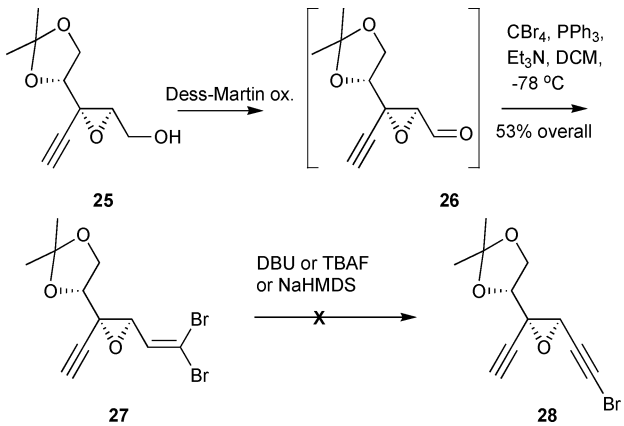
From this iodide **20**, the first acetylenic moiety was installed *via* Sonogashira coupling[19] to afford the known enyne **21** (Scheme 7). NOE experiments (enhancement between *H*-5 and *H*-13, 5%) confirmed that no isomerisation of the double bond occurred under the conditions of the reaction. Subsequent ester reduction with DIBAL gave the allylic alcohol **22** in a quantitative yield. **22** was treated under SAE conditions[20] and despite extensive investigation of the parameters we were unable to isolate the epoxy-alcohol **23**. In order to examine the impact of the trimethylsilyl group, we effected desilylation of **22** with TBAF to the allylic alcohol **24**. Attempted epoxidation of **24** under SAE conditions at −6 °C using sub-stoichiometric amount of titanium–tartrate catalyst (0.2 equiv.)[21] provided the epoxy-alcohol **25** in good yield. Thus it was clear that the silyl group was hindering the epoxidation.

We then turned our efforts towards the introduction of the second acetylenic moiety. Oxidation of **25** with Dess–Martin periodinane[22] led to the highly silica-sensitive epoxy-aldehyde **26**. The dibromoalkene **27** was then prepared by an optimised modification of the Corey–Fuchs procedure[23] and using this approach we could avoid bromination of the terminal alkyne



Scheme 7 Synthesis of alkynyl epoxy-alcohol *via* SAE.

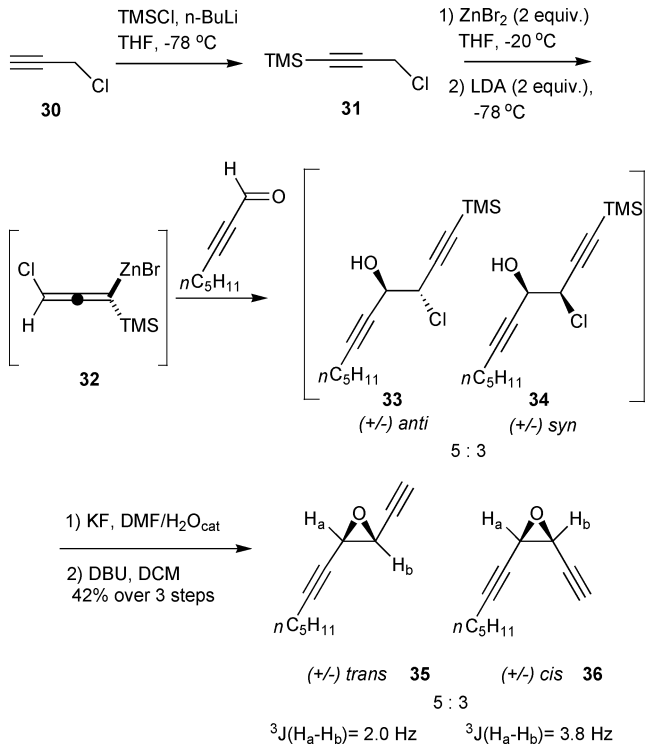
or epoxide opening (Scheme 8). The conversion of **27** to the epoxydiyne **28** turned out to be problematic and despite our best efforts, **28** could not be cleanly isolated. We also attempted to use other methods to generate the second alkyne *via* Shioiri homologation,[24] Seyferth–Gilbert[25] or Ohira[26] methodologies but none of them afforded **28**. We reasoned that the nucleophilic reagents may be causing epoxide ring opening of **27**.



Scheme 8 Attempted synthesis of diyne epoxide *via* Corey–Fuchs or related methodology.

As these attempts to synthesise epoxydiynes had failed to deliver an effective strategy we decided to examine approaches circumventing an SAE approach. It has been recently reported that allenyl zinc bromide **32** can condense with selected aldehydes and ketones *via* a Darzens-like sequence to yield halohydrin intermediates which readily cyclise to propargylic epoxides in good overall yield.[27] We decided to attempt to extend this method to the synthesis of epoxydiynes and investigate the stereochemical

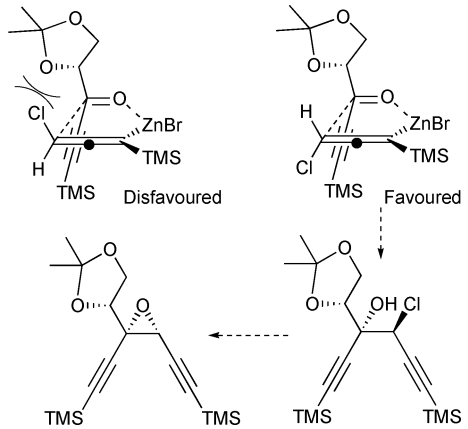
outcome.[28] Treatment of the propargyl chloride **31** with zinc bromide (2 equiv.) followed by LDA (2 equiv.) at low temperature was assumed to afford the organozinc reagent **32**. Addition of 2-octynal gave two chlorohydrin diastereoisomers **33** and **34** whose isolation could not be achieved due to their instability. Subsequent desilylation of the crude mixture with KF in DMF followed by cyclisation with DBU led to the diastereoisomeric epoxydiynes **35** and **36** as a mixture in a 5 : 3 ratio (Scheme 9). The major product was confirmed as *trans* due to its smaller coupling constant (2.0 Hz).[29] This methodology constitutes a convenient route to epoxydiynes.



Scheme 9 Synthesis of epoxydiynes *via* addition of allenyl zinc bromide.

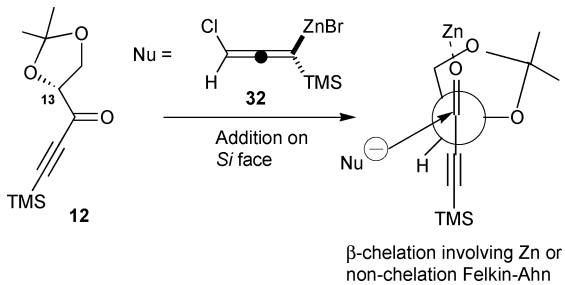
The stereochemical outcome is in agreement with a model in which the major stereoisomer is generated from a transition state minimising the steric interaction between the alkyne and the chlorine atom.[27,28] The stereospecific cyclisation *via* a S_N2 mechanism then leads to the epoxide products. With this early success we decided to examine the application of this methodology to more elaborate epoxydiynes, especially those relevant to the synthesis of NCS chrom. Such studies would require the extension of the method to include a ketone as the electrophile. We postulated that propargylic ketone **12** should preferentially lead to an epoxydiyne with a *trans* configuration due to the increase steric demand at the α-position. Thus the favoured transition state in this case avoids the steric clash between the chloride and the acetal group (Scheme 10).

Also from literature precedent,[30] we anticipated that the chiral centre (*R C*-13) at the α-position would guide the addition of the allenyl zinc reagent **32** to the *Si* face of **12** to favour the formation of the alcohol with the required *R*-stereochemistry (as drawn in Scheme 11). This can be rationalised by proceeding *via*



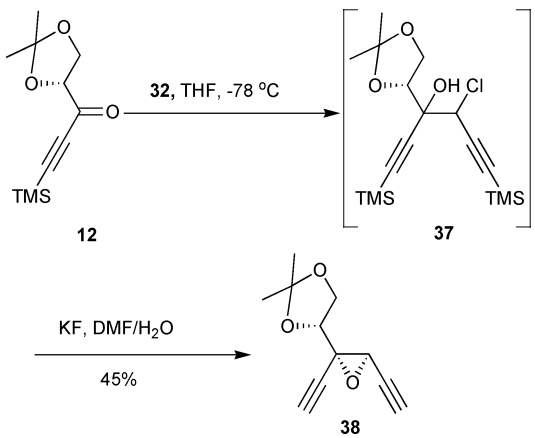
Scheme 10 Chelate-type transition state for diastereoselectivity.

a β-chelation transition state involving the zinc or non-chelation Felkin–Anh transition state (Scheme 11).



Scheme 11 Proposed transition state for the stereoselective addition of the allenyl zinc reagent.

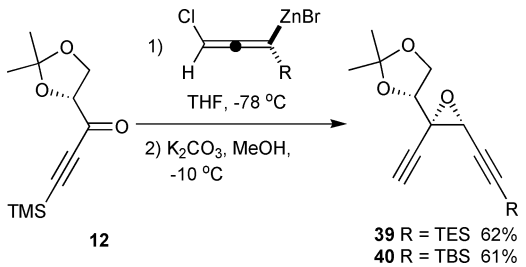
Addition of **12** to **32** clearly led to one major chlorohydrin **37** from crude NMR. Desilylation and concomitant cyclisation were achieved with KF in DMF affording a mixture of diastereoisomeric epoxydiynes from which only **38** was cleanly isolable in moderate yield (Scheme 12). Confirmation of the stereochemical outcome in this reaction is explained below.



Scheme 12 Diastereoselective synthesis of epoxydiynes from propargyl ketones.

We then extended this methodology to the synthesis of epoxydiynes in which one alkyne retained a protecting group. Thus the protocol was applied to the appropriate TES and TBS-protected

propargyl chlorides. In each case, one major chlorohydrin was seen from crude NMR analysis but the isolation of the chlorohydrin could not be achieved due to its instability. Subsequent treatment of the crude mixture in each case with K_2CO_3 in methanol at low temperature led to selective TMS-removal and ring closure affording a mixture of epoxydiynes from which the major product, **39** and **40** respectively, was cleanly isolable in good yield (Scheme 13). The other diastereoisomers were present in complex mixtures thus preventing the determination of reliable diastereoisomeric ratios. However for the major products, the stereochemistry was confirmed as the compounds were correlated with those reported by Hirama[9e] and Myers.[10a] In the latter case the completion of the synthesis of the NCS chrom by Myers from compound **40** unambiguously confirmed the stereochemistry. Furthermore comparison of the α_D of **39** and **40** with the literature values suggested that no racemisation of the ketone **12** occurred under the conditions of the addition. The synthesis of Myers' key NCS chrom intermediate **40** by this method has thus been reduced from 9 steps from the commercially available D-mannitol derivative **17**, to just 5 steps from the same starting material using this new methodology.

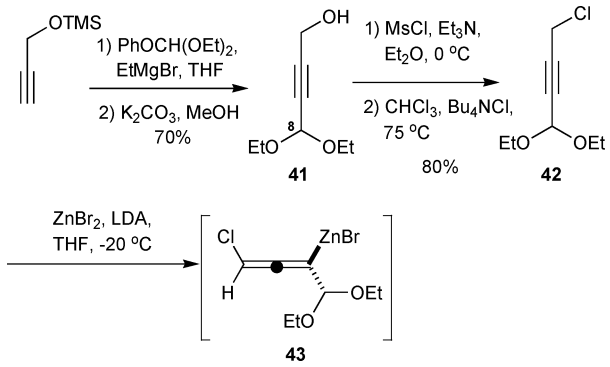


Scheme 13 Diastereoselective synthesis of unsymmetrical epoxydiynes from propargyl ketones.

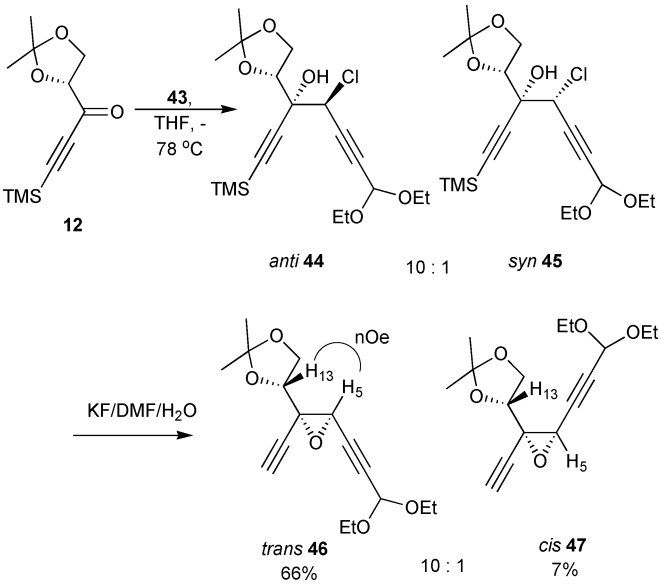
The removal of the TES group from **39** with TBAF gave **38**, providing confirmation of the stereochemical outcome of this initial example.

As mentioned above our general strategy towards the NCS chrom demands the inclusion of *C*-8 on the epoxydiyne synthon. To do this the allenyl zinc methodology required an appropriately substituted propargylic chloride. **42** was thus prepared from the commercially available propargyloxytrimethylsilane. Functionalisation using diethylphenyl orthoformate with ethyl magnesium bromide to include *C*-8 followed by immediate desilylation afforded the propargyl acetal **41** in good yield after distillation.[31] Mesylation immediately followed by substitution with tetrabutylammonium chloride gave the functionalised propargylic chloride **42** in good yield and of sufficient purity after a simple work-up (Scheme 14). We had considerable concerns about the application of the zinc methodology to a substrate containing two leaving groups and considered that decomposition *via* cumulene formation might be problematic.

Gratifyingly however, formation of the allenyl zinc reagent **43** appeared to occur without problem and its addition to **12** led to the chlorohydrins **44** and **45** as a mixture in a 10 : 1 ratio (Scheme 15). In this particular case, the chlorohydrins could be isolated. Traces of the two other diastereoisomers were also visible by NMR but only in negligible quantities. Subsequent treatment of this mixture with KF in DMF led to the separable epoxydiynes **46** and **47** in a *trans* : *cis*/10 : 1 ratio from which our key target **46** was isolated



Scheme 14 Generation of allenyl zinc reagent **43**.



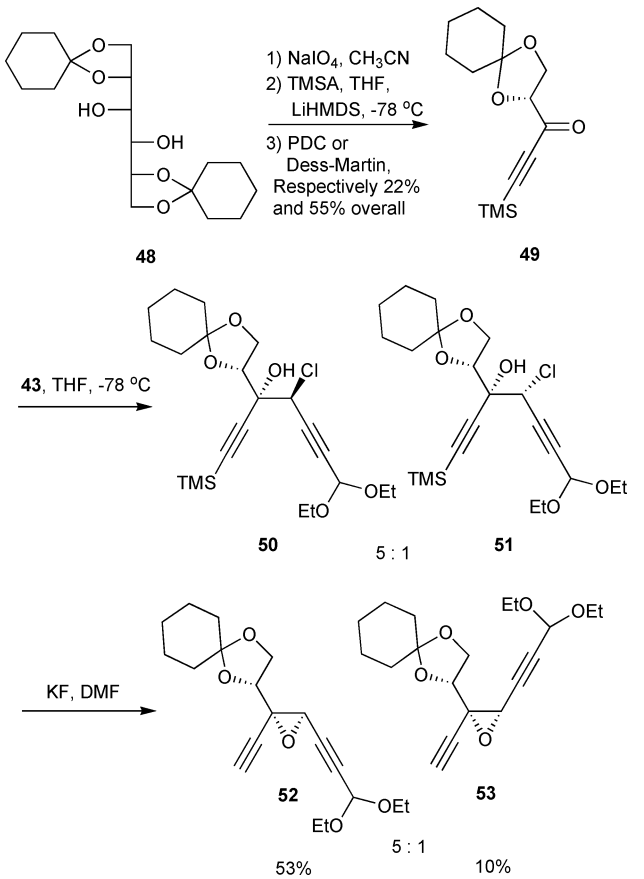
Scheme 15 Diastereoselective synthesis of epoxydiynes including *C*-8.

in 66% over two steps. The *cis*/*trans* geometry of the epoxydiynes was confirmed with a 3% NOE enhancement observed between *H*-5 and *H*-13 in the case of the major compound. These data allowed us to confirm the stereochemistry of the intermediate chlorohydrins.

We then attempted to further improve the diastereoselectivity of the transformation by increasing the steric bulk at the α-position to the ketone **49**. Therefore the *C*-13/*C*-14 diol moiety of **49** was protected as its cyclohexylidene ketal prior coupling to the organozinc **43** (Scheme 16). The propargylic ketone **49** was prepared from the readily available D-mannitol derivative **48**. In this sequence, the oxidation with PDC proved to be difficult and the use of periodinane turned out to be much more efficient. The formation of chlorohydrins **50** and **51** proceeded with a good diastereoselective ratio although it was surprisingly lower than the dimethylacetal case previously discussed. Subsequent desilylation with concomitant cyclisation afforded the diastereoisomeric epoxydiynes **52** and **53** in a 5 : 1 ratio from which the required product was isolated in 53% overall yield.

Conclusions

The development of a general strategy for a synthesis of epoxydiynes has proven to be extremely difficult due to the formation of



Scheme 16 Diastereoslective synthesis of epoxydiynes from propargyl ketone **49**.

unstable intermediates which could not be processed to the fully elaborated epoxydiyne. After considerable investigations, we finally found that the addition of allenyl zinc bromide to propargylic ketones provides an expeditious entry to stereochemically pure epoxydiynes. For our particular strategy the ability to introduce the *C*-8 portion required for NCS chrom is particularly useful. It is noteworthy that the present protocol provides a very simple synthetic route to other functionalised epoxydiynes which have previously found use in the synthesis of NCS chrom. Studies are underway to complete the total synthesis of the NCS chrom using this methodology.

Experimental Section

General remarks

Optical rotations were measured on a PolaAr 2000 polarimeter at the sodium D line (589 nm) in the solvent and concentration indicated. 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 a Bruker AMX300, a Bruker AMX400 or a Bruker AVANCE500 spectrometer. Chemical shifts are expressed in parts per million (δ) and are referenced to the residual solvent peak ($CHCl_3$, 7.26 and C_6D_5H, 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. 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 F_{254} and was visualised by exposure to UV and/or exposure to potassium permanganate or anisaldehyde 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, Et_2O, CH_3CN and DCM were distilled through an alumina column from an anhydrous engineering apparatus. Triethylamine was distilled from calcium hydride at 760 Torr. Lithium diisopropylamide (1 M in THF–hexanes) was freshly prepared by the addition of n-butyllithium (freshly titrated) respectively to a solution of freshly distilled diisopropylamine in THF. The molarity of n-Butyllithium was determined by titration using dry [(1*S*)-*endo*]-(−)-borneol and fluorene as indicator. $ZnBr_2$ 99.999% was purchased from Aldrich. Trimethyl phosphite was distilled prior to use. Ti(IV) isopropoxide was distilled under reduced pressure at 10^{-3} Mbar and stored in a drybox. D-(−)-diethyl tartrate was distilled under reduced pressure at 10^{-3} Mbar and stored under argon.

2-Ethynyl-3-hept-1-ynyl-oxirane (35 and 36)

To $ZnBr_2$ (0.306 g, 1.36 mmol) in THF (1 mL) at −20 °C was added **31** (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 warmed to −30 °C and stirred for 45 min then a saturated aqueous solution of NH_4Cl 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 H_2O (20 mL), brine (20 mL), dried over magnesium sulfate. Concentration *in vacuo* gave the crude chlorohydrin 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 H_2O (1 mL) was added to quench. The mixture was extracted with Et_2O (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 PE. Column chromatography eluting with $CHCl_3$ (30%)–PE resulted in the inseparable diastereoisomeric epoxydiynes **35** and **36** (42%, *trans* : *cis*: 5 : 3). Repeated column chromatography allowed a small amount of each diastereoisomer to be isolated for analysis. ν_{max}(film)/cm^{-1} 3298, 2956, 2933, 2871, 2860, 2237, 2171, 1460, 1398, 1315; *trans*-epoxydiyne (major): ^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 (td, 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 (CH), 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): ^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

(td, 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 (CH), 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 $(M + H)^+$ calc. for $C_{11}H_{14}O$ 163.11228, found *m*/*z* 163.11190.

(*R*)-4-((2*S*,3*R*)-2,3-Diethynyloxiran-2-yl)-2,2-dimethyl-1,3-dioxolane (38)

Method A: To $ZnBr_2$ (0.225 g, 1.0 mmol) in THF (1 ml) at −20 °C was added **31** (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 **12** (0.113 g, 0.5 mmol) was added. After stirring for a further 2 h at −78 °C, $NH_4Cl_{(aq)}$ was added to quench, and once the mixture had warmed to RT it was separated 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), and dried ($MgSO_4$). Concentration *in vacuo*, followed by purification *via* column chromatography [Et_2O (15%) in 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 H_2O (1 drop). The reaction mixture was stirred for 22 h then $NH_4Cl_{(aq)}$ was added to quench, and it was separated 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), and dried ($MgSO_4$). Concentration *in vacuo*, followed by purification *via* column chromatography [Et_2O (20%) in PE] gave **38** (0.018 mg, 45%) as a white solid (mp 78–79 °C). $[\alpha]_D^{20}$ +16.0 (*c* 0.1, $CHCl_3$); ν_{max}(film)/cm^{-1} 3300 (s), 2991 (m), 2120 (w), 1383 (m), 1074 (s); ^{1}H NMR (300 MHz; $CDCl_3$) δ 1.36 (3 H, s, OCH_3), 1.47 (3 H, s, OCH_3), 2.47 (1 H, d, *J* 2.0, HCCC*H*), 2.51 (1 H, s, CCC*H*), 3.65 (1 H, d, *J* 2.0), 4.06–26 (3 H, m, CH_2CH, CH_2C*H*); ^{13}C NMR (75 MHz; $CDCl_3$) δ 25.1 (CH_3), 26.0 (CH_3), 49.1 (CH), 57.6 (C), 66.4 (CH_2), 74.9 (C), 75.6 (CH), 75.7 (C), 76.8 (CH), 77.3 (CH), 111.1 (C). *m*/*z* (DCi) 193 $(M + H)^+$, 17%), 177 (100), 135 (95).

Method B: To **39** (0.090 g, 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 mixture was quenched with $NH_4Cl_{(aq)}$, then allowed to warm to RT. The aqueous layer was then washed with Et_2O (2 × 10 ml) and the combined organic extracts washed with brine (5 ml), and dried ($MgSO_4$). Concentration *in vacuo*, followed by purification *via* column chromatography [Et_2O (20%) in PE] gave **38** (0.024 g, 55%). Data matched that given above.

[3-(2,2-Dimethyl[1,3]dioxolan-4-yl)-3-ethynyloxiranylethynyl]triethylsilane[9e] (39)

To $ZnBr_2$ (477 mg, 2.1 mmol) in THF (2 mL) at −20 °C was added the TES-protected propargyl chloride (see supporting information†) (200 mg, 1.1 mmol) then the reaction was cooled to −78 °C. A freshly prepared 1 M solution of LDA in THF (2.12 mL, 2.1 mmol) was added dropwise and the reaction was stirred for 1 h. The ketone **12** (240 mg, 1.06 mmol) was then added quickly. Stirring was continued for 2 h at −78 °C and the reaction quenched with a saturated aqueous solution of NH_4Cl (10 mL). The resulting mixture was allowed to warm to rt, extracted with ether (20 mL), washed with brine (2 × 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)–PE afforded the crude chlorohydrin.

To the crude chlorohydrin in methanol (5 mL) at −10 °C was added K_2CO_3 (585 mg, 4.2 mmol). The stirring was continued for 4 h until completion and then a saturated aqueous solution of NH_4Cl (10 mL) was added. The reaction mixture was extracted with Et_2O (2 × 30 mL), washed with brine (2 × 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Flash chromatography eluting with Et_2O (10%)–PE resulted in a pure epoxydiyne **39** (201 mg, 62%). $[\alpha]_D^{22}$ +63 (*c* 1.0 in $CHCl_3$), ^{1}H 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 (3 × CH_3), 4.0 (3 × CH_2); HRMS $(M + H)^+$ calc. for $C_{17}H_{26}O_3Si$ 307.1729, found *m*/*z* 307.1725.

tert-Butyl-[3-(2,2-dimethyl[1,3]dioxolan-4-yl)-3-ethynyloxiranylethynyl]dimethylsilane (40)

To $ZnBr_2$ (238 mg, 1.06 mmol) in THF (2 mL) at −20 °C was added the TBS-protected propargyl chloride (see supporting information†) (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 **12** (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 NH_4Cl (10 mL). The resulting mixture was allowed to warm to rt, extracted with Et_2O (20 mL), washed with brine (2 × 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)–PE afforded the 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 a saturated aqueous solution of NH_4Cl (10 mL) was added. The reaction mixture was extracted with Et_2O (2 × 30 mL), washed with brine (2 × 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Flash chromatography eluting with Et_2O (5%)–PE resulted in the pure epoxydiyne **40** (99 mg, 61%). $[\alpha]_D^{22}$ +74 (*c* 1.0 in C_6H_6), ^{1}H 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 (4 × CH_3), 25.4 (CH_3), 16.7 (C), −4.8 (2 × CH_3); HRMS $(M + H)^+$ calc. for $C_{17}H_{26}O_3Si$ 307.1729, found *m*/*z* 307.1729.

4-Chloro-3-(2,2-dimethyl[1,3]dioxolan-4-yl)-7,7-diethoxy-1-trimethylsilanylhepta-1,5-diyn-3-ol (44 and 45)

To $ZnBr_2$ (255 mg, 1.1 mmol) in THF (2 mL) at −20 °C was added **42** (100 mg, 0.6 mmol) then the reaction was cooled to −78 °C. A freshly prepared 1 M solution of LDA in THF (1.1 mL, 1.1 mmol) was added dropwise and the reaction was

stirred for 1 h. The ketone **12** (118 mg, 0.5 mmol) was then added quickly. Stirring was continued for 2 h at −78 °C and the reaction quenched with a saturated aqueous solution of NH_4Cl (5 mL). The resulting mixture was allowed to warm to rt, extracted with Et_2O (20 mL), washed with brine (2 × 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)–PE afforded the inseparable diastereoisomeric chlorohydrins **44** and **45** (363 mg, *anti* : *syn* 10 : 1, 60%) as a clear yellow oil. ν_{max} (cm^{-1}) 3400, 2976, 2929, 2895, 2354, 2173, 1450; ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.34 (d, 1H, *J* 1.3, syn), 5.32 (d, 1H, *J* 1.4, anti), 4.93 (d, 1H, *J* 1.4, syn), 4.90 (d, 1H, *J* 1.4, anti), 4.33 (dd, 1H, *J* 6.8, 5.8, anti), 4.32 (dd, 1H, *J* 6.8, 5.8, syn), 4.21 (dd, 1H, *J* 8.5, 5.8, anti), 4.16 (dd, 1H, *J* 8.5, 6.8, anti), 3.727 (dq, 1H, *J* 9.5, 7.1, anti), 3.722 (dq, 1H, *J* 9.5, 7.1, syn), 3.59 (dq, 1H, *J* 9.5, 7.1, anti), 3.58 (dq, 1H, *J* 9.5, 7.1, syn), 2.86 (s, 1H, anti), 2.84 (s, 1H, syn), 1.44 (s, 3H), 1.32 (s, 3H), 1.22 (t, 3H, *J* 7.2), 1.21 (t, 3H, *J* 7.2), 0.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 110.4 (C_{anti}), 110.3 (C_{syn}), 101.5 (C_{anti}), 101.3 (C_{syn}), 93.6 (C_{syn}), 92.7 (C_{anti}), 90.99 (CH_{anti}), 90.95 (CH_{syn}), 84.1 (C_{anti}), 83.3 (C_{syn}), 80.3 (C_{syn}), 78.9 (C_{anti}), 77.6 (CH_{anti}), 76.3 (CH_{syn}), 74.9 (C_{anti}), 74.3 (C_{syn}), 66.8 (CH_{2anti}), 66.3 (CH_{2syn}), 60.9 (CH_{2anti}), 60.8 (CH_{2syn}), 60.8 (CH_{2syn}), 60.9 (CH_{2anti}), 55.0 (CH_{anti}), 53.7 (C_{syn}), 26.2 (CH_{3anti}), 26.1 (CH_{3syn}), 25.2 (CH_{3anti}), 25.1 (CH_{3syn}), 14.914 (CH_{3anti}), 14.912 (CH_{3syn}), −0.53 (3 × CH_{3anti}), −0.57 (3 × CH_{3syn}); HRMS $(M + NH_4)^+$ calc. for $C_{19}H_{31}O_5Cl$ 420.1968, found *m*/*z* 420.1970.

4-[3-(3,3-Diethoxyprop-1-ynyl)-2-ethynyloxiranyl]-2,2-dimethyl[1,3]dioxolane (46 and 47)

To $ZnBr_2$ (255 mg, 1.1 mmol) in THF (2 mL) at −20 °C was added **42** (100 mg, 0.6 mmol) then the reaction was cooled to −78 °C. A freshly prepared 1 M solution of LDA in THF (1.1 mL, 1.1 mmol) was added dropwise and the reaction was stirred for 1 h. The ketone **12** (118 mg, 0.5 mmol) was then added quickly. Stirring was continued for 2 h at −78 °C and the reaction quenched with a saturated aqueous solution of NH_4Cl (5 mL). The resulting mixture was allowed to warm to rt, extracted with Et_2O (20 mL), washed with brine (2 × 10 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo* to give the crude diastereoisomeric chlorohydrins.

To the crude chlorohydrins in DMF (3 ml) was added KF (263 mg, 4.5 mmol). The reaction mixture was stirred overnight and both ether (40 mL) and a saturated aqueous solution of NH_4Cl (30 mL) were added. The aqueous layer was extracted with Et_2O (2 × 15 mL) and the combined organic extracts washed with water (2 × 20 mL), brine (20 mL), dried over magnesium sulfate and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)–PE afforded the *trans*-epoxydiyne **46** (97 mg, 66%) and the *cis* epoxydiyne **47** (10 mg, 7%). ν_{max} (cm^{-1}) 3201, 2926, 2854, 2195, 2160, 1399, 1273, 1210, 1087; HRMS $(M + NH_4)^+$ calc. for $C_{16}H_{22}O_5$ 312.1805, found *m*/*z* 312.1805; *trans*-epoxydiyne: $[a]_D^{22}$ +30.2 (*c* 0.51 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.29 (1H, d, *J* 1.1), 4.18 (1H, dd, *J* 10.8, 8.9), 4.065 (1H, dd, *J* 10.8, 5.9), 4.062 (1H, dd, *J* 8.9, 5.9), 3.75 (1H, dq, *J* 9.6, 7.0), 3.73 (1H, dq, *J* 9.6, 7.0), 3.68 (1H, dd, *J* 1.1), 3.57 (2H, dq, *J* 9.4, 7.0), 2.47 (1H, s), 1.42 (3H, s), 1.32 (3H, s), 1.25 (3H, t, *J* 7.0), 1.20 (3H, t, *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 (CH_2), 61.1 (CH_2), 61.0 (CH_2), 57.7 (C), 49.1 (CH), 25.9 (CH_3), 25.0 (CH_3), 15.2 (CH_3), 15.0 (CH_3); *cis*-epoxydiyne: $[a]_D^{22}$ −61.2 (*c* 1.0 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.20 (1H, d, *J* 1.1), 4.12 (1H, dd, *J* 8.7, 6.3), 4.11 (1H, dd, *J* 8.75, 6.3), 3.98 (1H, t, *J* 6.2), 3.71 (1H, d, *J* 1.1), 3.64 (1H, dq, *J* 9.5, 7.0), 3.63 (1H, dq, *J* 9.5, 7.0), 3.51 (1H, dq, *J* 9.5, 7.0), 3.50 (1H, dq, *J* 9.5, 7.0), 2.38 (1H, s), 1.42 (3H, s), 1.32 (3H, s), 1.14 (3H, t, *J* 7.0), 1.13 (3H, t, *J* 7.0); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 110.6 (C), 90.8 (CH), 82.4 (C), 77.7 (C), 77.5 (C), 75.1 (CH), 73.8 (CH), 66.5 (CH_2), 60.8 (CH_2), 60.7 (CH_2), 55.6 (C), 51.4 (CH), 25.9 (CH_3), 25.1 (CH_3), 14.8 (2 × CH_3).

1-(1,4-Dioxaspiro[4.5]dec-2-yl)-3-trimethylsilanylprop-2-yn-1-ol

To a solution of 1,2–5,6-di-*O*-cyclohexylidene-D-mannitol **48** (25.0 g, 73 mmol) in MeCN–H_2O (145 mL : 95 mL) was added portionwise sodium periodate (31 g, 146 mmol) over 20 min and the reaction mixture was stirred for 2 h. The reaction mixture was extracted with ether, dried over magnesium sulfate and concentrated *in vacuo* in a cold bath (35 °C). Meanwhile to a solution of trimethylsilylacetylene (24 mL, 175 mmol) in THF (900 mL) was added freshly made lithium hexamethyldisilazide (192 mL, 192 mmol) at −78 °C. The reaction mixture was stirred for 30 min and a solution of D-glyceraldehyde acetonide (24.8 g, 146 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 NH_4Cl (150 mL). The reaction mixture was concentrated *in vacuo* to a volume of approximately 300 mL and diluted with EtOAc (300 mL). The mixture was washed with H_2O (250 mL), saturated aqueous NH_4Cl (250 mL) and the aqueous layer was extracted with EtOAc (150 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Flash column chromatography in EtOAc (20%)–PE afforded the inseparable diastereomeric propargylic alcohols (1 : 1, 22.7 g, 58%) as a pale yellow oil. ν_{max} (cm^{-1}) 3431, 2932, 2903, 2853, 2173; ^1H NMR (300 MHz; $CDCl_3$) δ_H 4.35–3.71 (m, 4H), 2.40 (1H, d, *J* 3.9), 2.25 (1H, d, *J* 4.8, other diastereoisomer), 1.51–1.29 (m, 10H), 0.01 (s, 9H); ^{13}C NMR (75 MHz; $CDCl_3$) δ_C 111.4 (C), 111.0 (C), 102.6 (C), 102.5 (C), 91.8 (C), 91.7 (C), 78.7 (CH), 77.7 (CH), 66.1 (CH_2), 65.3 (CH_2), 65.0 (CH), 63.1 (CH), 36.8 (CH_2), 36.2 (CH_2), 35.1 (CH_2), 35.0 (CH_2), 25.4 (CH_2), 25.3 (CH_2), 24.2 (2 × CH_2), 24.0 (2 × CH_2), 0.0 (6 × (CH_3)); HRMS $(M + H)^+$ calc. for $C_{14}H_{24}O_3Si$ 269.1567, found *m*/*z* 269.1570.

1-(1,4-Dioxaspiro[4.5]dec-2-yl)-3-trimethylsilanylpropynone (49)

Method A: To pyridinium dichromate (2.8 g, 7.5 mmol) and crushed 3 Å molecular sieves (1.7 g) in DCM (7 mL) was added dropwise a solution of the diastereomeric mixture of 1-(1,4-dioxaspiro[4.5]dec-2-yl)-3-trimethylsilanylprop-2-yn-1-ol (1.0 g, 3.7 mmol) in DCM (3.5 mL) and the reaction mixture was stirred for 4 h. Celite (2 g) was added and the suspension was stirred for 30 min. The reaction mixture was then filtered and washed with ether (20 mL). The filtrate was washed with saturated aqueous potassium hydrogen sulfate (3 × 5 mL), saturated aqueous $NaHCO_3$ (5 mL) and brine (2 × 10 mL), then filtered through a plug of magnesium sulfate and concentrated *in vacuo*. Flash column chromatography eluting with Et_2O (10%)–PE afforded the ynone **49** (0.405 g, 38%).

Method B: To a solution of the diastereomeric mixture of 1-(1,4-dioxaspiro[4.5]dec-2-yl)-3-trimethylsilanylprop-2-yn-1-ol (5.0 g, 18.6 mmol) in DCM (93 mL) at 0 °C was added Dess–Martin periodinane (15.5 g, 37.2 mmol) in one portion. The stirring was continued at RT for 12 h and the reaction mixture was poured into a mixture of a saturated aqueous solution of sodium thiosulfate (10 mL) and a saturated aqueous solution of $NaHCO_3$ (10 mL). Then Et_2O (150 mL) was added and the mixture stirred for 30 min. The mixture was extracted with Et_2O, washed with brine, dried over magnesium sulfate and concentrated *in vacuo*. Flash column chromatography eluting with Et_2O (10%)–PE afforded the pure ynone **49** (4.6 g, 94%). ν_{max} (cm^{-1}) 2932, 2862, 2150, 1677, 1399, 1372; ^1H NMR (300 MHz, $CDCl_3$) δ_H 4.33 (1H, dd, *J* 7.3, 4.6), 4.05 (1H, dd, *J* 8.6, 7.3), 3.97 ((1H, dd, *J* 8.6, 4.6), 1.74–1.36 (m, 10H), 0.07 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 187.0 (C=O), 113.4 (C), 104.4 (C), 100.6 (C), 81.5 (CH), 67.5 (CH_2), 36.5 (CH_2), 35.9 (CH_2), 25.9 (CH_2), 24.8 (CH_2), 24.7 (CH_2), 0.0 (3 × CH_3), HRMS (M + H)$^+$ calc. for $C_{14}H_{22}O_3Si$ 267.1411, found *m/z* 267.1413.

4-Choro-3-(1,4-dioxaspiro[4.5]dec-2-yl)-7,7-diethoxy-1-trimethylsilanylhepta-1,5-diyn-3-ol (50 and 51)

To $ZnBr_2$ (2.2 g, 9.8 mmol) in THF (9 mL) at −20 °C was added **42** (0.8 g, 4.7 mmol) then the reaction was cooled to −78 °C. A freshly prepared 1 M solution of LDA in THF (9.3 mL, 9.3 mmol) was added dropwise and the reaction was stirred for 1 h, thus forming **43** *in situ*. The ketone **49** (1.2 g, 4.6 mmol) was then added quickly. Stirring was continued for 3 h at −78 °C and the reaction was poured into mixture of a solution of saturated aqueous solution of NH_4Cl (4 mL) and H_2O (50 mL), then diluted with Et_2O (150 mL). The resulting mixture was filtered through Celite, extracted with Et_2O (50 mL), washed with brine (2 × 30 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)–PE afforded the inseparable diastereomeric chlorohydrins **50** and **51** (1.4 g, *anti* : *syn*: 5 : 1, 59%) as a clear yellow oil. ν_{max} (cm^{-1}) 3402, 2932, 2895, 2866, 2252, 2173, 1446; ^1H NMR (400 MHz, $CDCl_3$) δ_H 5.34 (d, 1H, *J* 1.3, syn), 5.32 (d, 1H, *J* 1.4, anti), 4.96 (d, 1H, *J* 1.3, syn), 4.93 (d, 1H, *J* 1.4, anti), 4.32 (dd, 1H, *J* 6.8, 5.9, anti), 4.30 (dd, 1H, *J* 6.8, 5.9, syn), 4.20 (dd, 1H, *J* 8.5, 5.9, anti), 4.19 (dd, 1H, *J* 8.5, 5.9, syn), 4.16 (dd, 1H, *J* 8.5, 6.8, anti), 4.14 (dd, 1H, *J* 8.5, 6.8, syn), 3.77–3.67 (m, 2H), 3.53–3.64 (m, 2H, CH_2), 2.94 (s, 1H, syn), 2.86 (s, 1H, anti), 1.72–1.65 (m, 2H), 1.62–1.49 (m, 6H), 1.42–1.32 (m, 2H), 1.23 (t, 3H, *J* 7.0, syn), 1.22 (t, 3H, *J* 7.1, syn), 1.22 (t, 3H, *J* 7.1, anti), 1.21 (t, 3H, *J* 7.1, anti), 0.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 111.0 (C_{anti}), 110.9 (C_{syn}), 101.8 (C_{anti}), 101.5 (C_{syn}), 93.7 (C_{syn}), 92.7 (C_{anti}), 91.1 (CH_{anti}), 91.0 (CH_{syn}) 84.2 (C_{anti}), 83.5 (C_{syn}), 80.4 (C_{syn}), 79.1 (C_{anti}), 77.2 (CH_{anti}), 76.1 (CH_{syn}), 75.2 (C_{anti}), 74.6 (C_{syn}), 66.6 (CH_{2anti}), 66.1 (CH_{2syn}), 61.0 (CH_{2anti}), 60.97 (CH_{2syn}), 60.94 (CH_{2syn}) 60.8 (CH_{2anti}), 55.3 (CH_{anti}), 53.9 (C_{syn}), 35.9 (CH_2), 34.9 (CH_2), 25.10 (CH_2), 23.8 (CH_2), 23.7 (CH_2), 15.0 (2 × $CH_{3anti+syn}$), −0.3 (3 × CH_{3syn}), −0.4 (3 × CH_{3anti}); HRMS (M + NH_4)$^+$ calc. for $C_{22}H_{35}ClO_5Si$ 460.2281, found *m/z* 460.2279.

2-[3-(3,3-Diethoxyprop-1-ynyl)-2-ethynyloxiranyl]-1,4-dioxaspiro[4.5]decane (52 and 53)

To $ZnBr_2$ (2.2 g, 9.8 mmol) in THF (9 mL) at −20 °C was added **42** (0.8 g, 4.7 mmol) then the reaction was cooled to −78 °C. A freshly prepared 1 M solution of LDA in THF (9.3 mL, 9.3 mmol) was added dropwise and the reaction was stirred for 1 h. The ketone **49** (1.2 g, 4.6 mmol) was then added quickly. Stirring was continued for 3 h at −78 °C and the reaction was poured into a solution of saturated aqueous solution of NH_4Cl (4 mL) and H_2O (50 mL) and diluted with Et_2O (150 mL). The resulting mixture was filtered through Celite, extracted with Et_2O (50 mL), washed with brine (2 × 30 mL), dried over magnesium sulfate, filtered and concentrated *in vacuo* to give the crude diastereoisomeric chlorohydrins.

To the crude chlorohydrins in DMF (3 mL) was added KF (263 mg, 4.53 mmol). The reaction mixture was stirred overnight and both Et_2O (40 mL) and saturated aqueous solution of NH_4Cl (30 mL) were added. The aqueous layer was extracted with Et_2O (2 × 15 mL) and the combined organic extracts washed with H_2O (2 × 20 mL), brine (20 mL), dried over magnesium sulfate and concentrated *in vacuo*. Column chromatography eluting with Et_2O (20%)–PE afforded the *trans*-epoxydiyne **52** (814 mg, 53%) and the *cis*-epoxydiyne **53** (153 mg, 10%). ν_{max} (cm^{-1}) 3205, 2940, 2841, 2180, 2160; HRMS (M + NH_4)$^+$ calc. for $C_{19}H_{26}O_5$ 352.2118, found *m/z* 352.2118; *trans*-epoxydiyne: $[\alpha]_D^{22}$ +30.2 (*c* 0.508 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.30 (d, 1H, *J* 0.9), 4.19 (dd, 1H, *J* 11.0, 9.2), 4.065 (dd, 1H, *J* 10.8, 5.9), 4.062 (dd, 1H, *J* 8.9, 5.9), 3.757 (dq, 1H, *J* 9.5, 7.0), 3.750 (dq, 1H, *J* 9.5, 7.0), 3.71 (dd, 1H, *J* 0.9), 3.58 (dq, 2H, *J* 9.4, 7.0), 2.48 (s, 1H), 1.42 (s, 3H), 1.32 (s, 3H), 1.219 (t, 3H, *J* 7.0), 1.214 (t, 3H, *J* 7.0); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 111.6 (C), 91.0 (C), 81.6 (C), 78.8 (C), 77.0 (C), 75.5 (CH), 75.0 (CH), 66.3 (CH_2) 61.0 (CH_2), 60.9 (CH_2), 57.8 (C), 49.0 (*C*H), 35.4 (CH_2), 34.4 (CH_2), 24.8 (CH_2), 23.7 (CH_2), 23.5 (CH_2), 14.932 (CH_3), 14.931 (CH_3); *cis*-epoxydiyne: $[\alpha]_D^{22}$ −61.2 (*c* 1.0 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ_H 5.27 (1H, d, *J* 0.9), 4.17 (1H, dd, *J* 8.7, 6.5), 4.16 (1H, dd, *J* 8.7, 6.5), 4.04 (1H, t, *J* 6.5), 3.78 (1H, d, *J* 0.9), 3.71 (1H, dq, *J* 9.4, 7.1), 3.70 (1H, dq, *J* 9.4, 7.1), 3.57 (1H, dq, *J* 9.4, 7.1), 3.56 (1H, dq, *J* 9.4, 7.1), 2.38 (1H, s), 1.42 (3H, s), 1.32 (3H, s), 1.21 (3H, t, *J* 7.1), 1.20 (3H, t, *J* 7.1); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 111.3 (C), 90.9 (CH), 82.4 (C), 77.9 (C), 77.7 (C), 74.7 (CH), 73.8 (CH), 66.2 (CH_2), 61.0 (CH_2), 60.9 (CH_2), 55.8 (C), 51.6 (CH), 35.5 (CH_2), 34.7 (CH_2), 25.0 (CH_2), 23.7 (CH_2), 23.6 (CH_2), 14.915 (CH_3), 14.914 (CH_3).

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Notes and references

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