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The enantioselective total synthesis of nemotin†

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The allene–diyne natural product nemotin was synthesized for the first time through an enantioselective route with the stereogenic center at the lactone moiety derived from L-glutamic acid and the allene axis constructed from the corresponding propargylic tosylate, and the absolute configuration was thus established as (4*S*,5a*S*).

Introduction

Nemotin (**1**) and the closely related nemotinic acid (**2**) were first isolated from fungi by Robbins[1] and co-workers in the 1940s. The preliminary biotesting showed that these two natural products possessed significant activity against a range of microorganisms. In 1955, Jones[2] and co-workers finished determination of the "planar" structure (Fig. 1) based on UV, IR, hydrogenation and elemental analysis data.

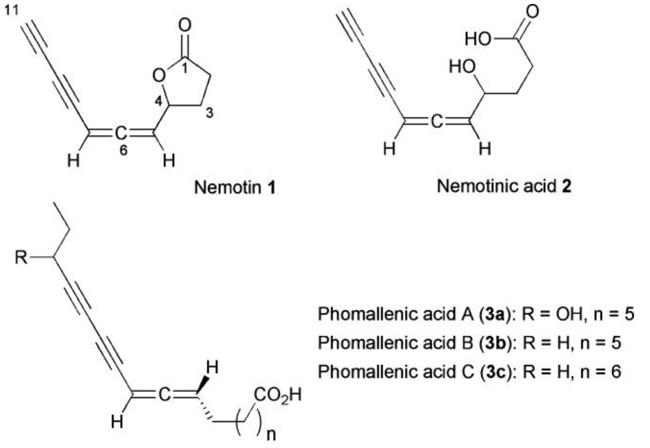

Fig. 1 The structure of nemotin, nemotic acid and phomallenic acids.

More detailed structural information, including the optical rotations of **1** and **2**, were disclosed later in 1966.[3] However, to the best of our knowledge, the relative as well as absolute configurations of these two compounds has never been assigned.

Recently, phomallenic acids (**3**) were identified[4] as potent inhibitors for FabF, an essential enzyme in the bacterial type II fatty acid synthesis pathway (FAS II). As such a mode of action is entirely different from that of all previous antibacterial agents, the high antibacterial activity reported for phomallenic acids, nemotin and cepacin seems to imply that the allene–diyne unit shared by these compounds might be a pharmacophore for the antibacterial activity, making these types of molecules worthy targets for synthesis. Besides, as all the investigations on nemotin (**1**) were performed before NMR spectroscopy became a routine structural analysis tool, neither ^{1}H nor ^{13}C NMR data of **1** and **2** are available to date. All these factors prompted us to carry out the work described below.

Results and discussion

Our strategy for the synthesis of **1** is depicted in Fig. 2. The allene axis was planned to be derived from the propargylic tosylate **6**, either directly or *via* the bromoallene **5**, through a coupling reaction with a proper diyne species. The configuration of the allene axis in either case is governed by that of the propargylic stereogenic center. Consequently, the relative configuration of the end product, nemotin **1**, is decided by that of the hidden vicinal diol unit embedded in the propargylic tosylate.

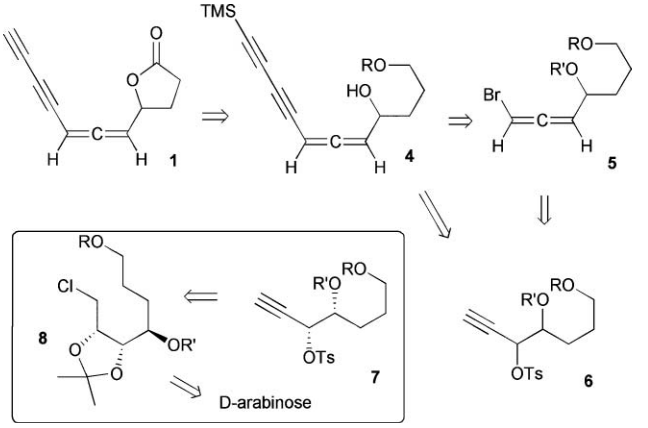

Fig. 2 Outline of our retrosynthetic analysis of nemotin.

Because both the relative and absolute configuration of **1** was unknown at the outset, we arbitrarily chose one of the four possible isomers in the initial trial. The hidden diol motif carried in **7** can be derived from D-arabinose, an inexpensive and readily available chiral pool, and was therefore selected. The alkyne functionality was planned to be built up from the chloride **8** by treatment with LDA (lithium diisopropylamide) as similar[5] transformations had been documented in the literature.

The synthetic endeavor was directed towards **8**. As shown in Scheme 1, starting from D-arabinose *via* diol protection and chain

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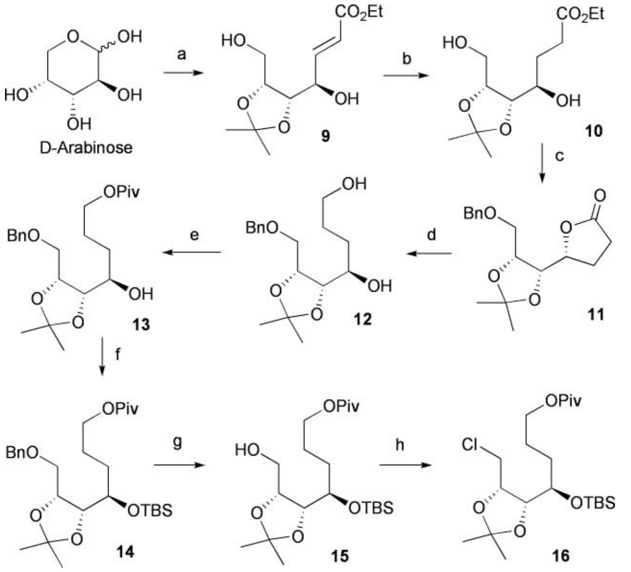
† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR spectra of all new compounds, and HPLC spectra of **48** and **51**. See DOI: 10.1039/b923123d



Scheme 1 *Reagents and conditions*: (a) (i) $Me_2C(OMe)_2$, DMF, *p*-TsOH; (ii) $Ph_3P{=}CHCO_2Et$, toluene, $PhCO_2H$ (cat.), 90 °C, 62% from D-arabinose; (b) Pd–C, H_2, EtOAc, 89%; (c) NaH, BnBr, DMF, 53%, (d) $LiAlH_4$, THF, 89%; (e) PivCl, Et_3N, DMAP (cat.), 66%; (f) TBSOTf (1.5 eq.), 2,6-lutidine (2.0 eq.), 99%; (g) $Pd(OH)_2$, H_2 (1 atm), EtOH, 81%; (h) PPh_3, CCl_4, K_2CO_3, reflux, 69%.

extension, α,β-unsaturated ester **9** was obtained in 62% yield. The C–C double bond was subsequently saturated by hydrogenation over 10% Pd–C to deliver diol **10**. Further treatment with NaH and BnBr in DMF led to lactonisation of the secondary OH, while the primary one was masked as a benzyl ether.

The lactone was then reduced with $LiAlH_4$ to afford diol **12**, which was elaborated into **14** by selective protection of the primary OH as a Piv (pivaloyl) ester and TBS (*tert*-butyldimethylsilyl) protection of the secondary one. The Bn group was cleaved by hydrogenolysis over Pearlman's[6] catalyst, providing alcohol **15**. Finally, replacement of the terminal OH group with a Cl by treatment with Ph_3P and CCl_4 gave desired **16** (which corresponds to **8** with R and R′ being Piv and TBS, respectively) in 69% yield.

With chloride **16** in hand, we proceeded with the planned elimination. Unexpectedly, treatment of **16** with LDA did not lead to the corresponding alkyne **17**, but the methyl ketone **18** (Fig. 3). Close inspection of the molecular structure suggested that because of the relative configuration of the hidden diol motif, the one on the chlorinated methylene group may be more hindered than those at the 1,3-dioxolane (Fig. 3).‡ As a consequence, the LDA-mediated deprotonation occurred through pathway b rather than the usual one a, leading to the enol ether **20** instead of **19**. Further hydrolysis of the acid-sensitive enol ether/acetonide during work-up gave the unexpected product **18**.

Under the given circumstances, it seemed to us that using a smaller sized protecting group such as MOM (methoxymethyl) might increase the chance for the desired deprotonation to occur at the chlorinated methylene group. By then, all **16** had been consumed. To find a shorter route to **23**, the substrate needed for testing the elimination, instead of replacing the TBS group in **16** with a MOM, the synthesis took a bypass from alcohol **13** (Scheme 2). After masking the hydroxyl group as a MOM ether, the benzyl group was cleaved to free the terminal OH for transformation into a chloride. Unexpectedly, under the same conditions that were successful for converting **15** into **16** no discernible amount of chloride **23** was formed at all. The THF species **24** turned out to be the only isolable product. Conversion of **22** into **25** was possible (90%), but further transformation of the tosylate **25** into chloride **23** by treatment with LiCl and DMSO at rt again led to **24** (20%) as the only identifiable product in the complex product mixture.

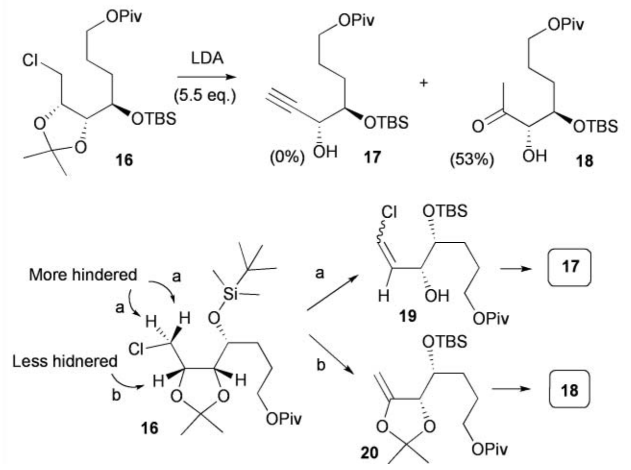
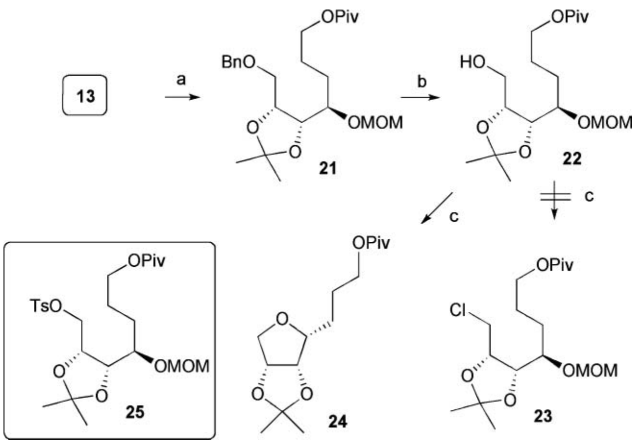


Fig. 3 The possible cause for the formation of methyl ketone **18**.



Scheme 2 *Reagents and conditions*: (a) NaI (3.0 eq.), MOMCl (4.0 eq.), DIPEA (4.4 eq.), $MeO(CH_2)_2OMe$, 68%; (b) $Pd(OH)_2$ (20%), H_2, 100%; (c) PPh_3, CCl_4–CH_2Cl_2 (4 : 1), K_2CO_3, 78.6%.

The difficulties with the elimination and the length of the synthesis urged us to redirect our efforts to a more efficient approach, the one shown in Scheme 3. Thus, the known[7] D-tartrate-derived acetonide **26** was reduced with DIBAL-H (di-isobutylaluminium hydride) to give an intermediate dialdehyde, which upon further reaction with Ohira–Bestmann[8] reagent, afforded diyne **27**. Introduction of only one ester group into **27** was troublesome. Use of commonly employed conditions[9] (*n*-BuLi (1.5 eq.), −78 → −40 °C, 1.5 h; then $ClCO_2Et$ (1.3 eq.), −78 °C, 2 h, and then warmed to rt) led to **28** in only 30% yield, along with 21% of the undesired bis-ester. However, deprotonation with *n*-BuLi

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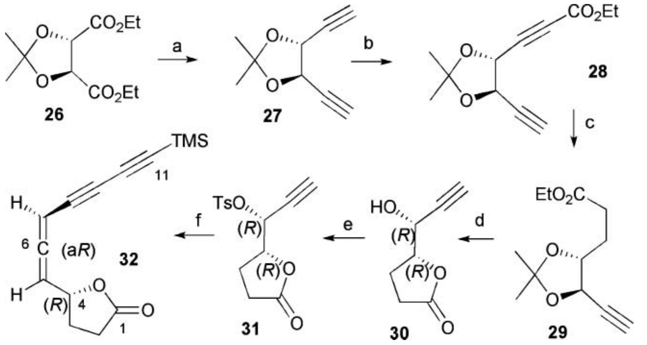
‡ One of the referees suggested that coordination of LDA may also contribute to this unexpected outcome.



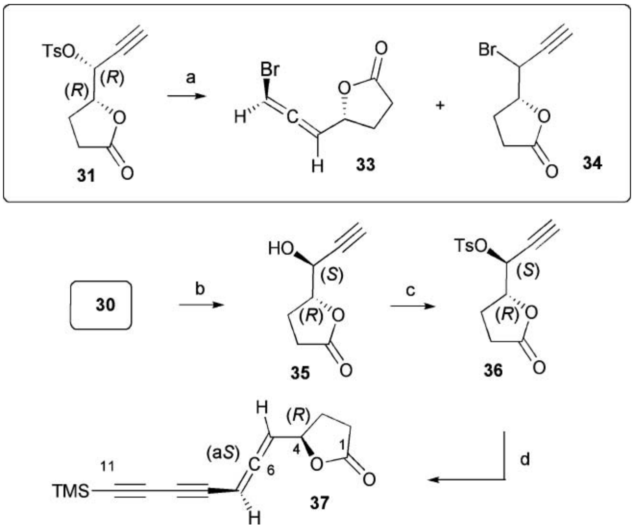
Scheme 3 *Reagents and conditions*: (a) (i) DIBAL-H (2.0 eq.), toluene, −78 °C, 2 h, (ii) $CH_3COC(N_2)PO(OMe)_2$ (3.0 eq.), K_2CO_3 (4.0 eq.), MeOH, 54% from **26**; (b) (i) *n*-BuLi (1.0 eq.), THF, −78 → 0 °C, 2 h, (ii) $ClCO_2Et$ (0.8 eq.), −78 °C, 4 h, 49% (along with 48% of recovered **27**); (c) CuCl (0.5 eq.), $NaBH_4$ (4.0 eq.), MeOH, 60–90%; (d) (i) 50% aq. CF_3CO_2H, CH_2Cl_2, (ii) *p*-TsOH, CH_2Cl_2, 74% from **29**; (e) *p*-TsCl, NEt_3, DMAP, CH_2Cl_2, 79%; (f) (i) TMSC≡C–C≡CTMS, MeLi·LiBr, THF, −78 °C, 1.5 h, then rt, 2 h, (ii) $ZnBr_2$, $Pd(Ph_3P)_4$, −78 → −20 °C, 3 h, 64%.

under more forcing conditions (−78 → 0 °C, 2 h) and introduction of less $ClCO_2Et$ (0.8 eq.) resulted in a substantially increased yield (49%), together with 48% of recovered recyclable starting **27**. We also tried the *t*-BuOK (1.0 eq.), DMSO, $ClCO_2Et$ (0.8 eq.) conditions,[10] but the product mixture was very complicated.

As we were not aware of any literature precedents of selective saturation of a conjugated C–C triple bond without affecting a co-existing isolated one, reduction of **28** to **29** was achieved under the CuCl/$NaBH_4$[11] conditions, which had been developed for similar reduction of conjugated C–C double bonds. The desired **29** was indeed formed; however, the yield fluctuated considerably and the over reduction product (with both triple bonds reduced) was very close to **29** on TLC, making the separation rather difficult. Mg/MeOH[12] conditions were also tested, but only the fully reduced product was observed.

Removal of the acetonide protecting group and formation of the lactone ring were then achieved by sequential treatment with 50% aq. CF_3CO_2H and *p*-TsOH in CH_2Cl_2, resulting in the propargylic alcohol **30**, which, on further reaction with *p*-TsCl, yielded the corresponding tosylate **31**. The coupling with the diyne unit was carried out under conditions similar to those in Negishi[13] couplings, affording the (4*R*,5a*R*)-allenediyne **32** in 64% yield. This compound, like nemotin, is rather unstable. On removal of the solvent, it deteriorated rapidly. Using usual techniques to acquire its spectroscopic data was therefore very difficult (*vide infra*).

To measure the diastereomeric ratio of **32**, we needed the other allene axial isomer (**37**) for comparison. One of the possible approaches would be conversion of **31** into bromoallene **33** (Scheme 4) because the coupling of bromoallenes with alkynes/diynes is known[4c,14] to proceed with conversion of the allene axial configuration. However, the polarity of bromo-allene **33** and the concurrently formed **34** turned out to be very similar to each other, which made isolation of pure **33** unfeasible. Fortunately, Mitsunobu conversion of **30** led smoothly to **35**. These two diastereomers turned out to readily separable from each other on silica gel, ensuring us of the enantiopurity for each. Alcohol **35** was then tosylated to give **36**, which was further converted into **37** under the same conditions as employed for transformation of **31** to **32**. It is noteworthy that the (4*R*,5a*S*) isomer **37** is even more unstable than **32**; it deteriorated almost instantly on removal of the last drop of solvent. The sample of **37** for HPLC analyses thus had to be kept in solution all the time.



Scheme 4 *Reagents and conditions*: (a) CuBr, LiBr, THF, (b) (i) Ph_3P, DEAD, *p*-NO_2-benzoic acid, (ii) NaOH, H_2O, 76%; (c) *p*-TsCl, Et_3N, DMAP, CH_2Cl_2, 68%; (d) (i) TMSC≡C–C≡CTMS, MeLi·LiBr, THF, −78 °C, 1.5 h, then rt, 2 h, (ii) $ZnBr_2$, $Pd(Ph_3P)_4$, −78 → −20 °C, 3 h, *cf.* the text.

Another problem we encountered then was that **32** and **37** were inseparable by HPLC on several different types of columns, which made direct measurement of the d.e. values of these compounds impossible. Further derivatization of **32**/**37** was hence inevitable. However, the modified route (Schemes 3 and 4) leading to **32**/**37** was still rather lengthy. Accumulation of adequate amounts of the allenediynes for derivatization was still difficult—a better alternative had to be found. Then, we noticed a small detail that Jones[1b] *et al.* had reported the specific rotation for the γ-lactone **38** (Fig. 4). Through literature searching, we also found the rotation data[15] for such a lactone of an (*S*) configuration (**39**, Fig. 4). Judging from the sign of the specific rotations, the configuration of natural nemotin at C-4 should be opposite to that in **39** and those intermediates we synthesized above. The subsequent efforts were therefore directed to the lactone of the opposite configuration.

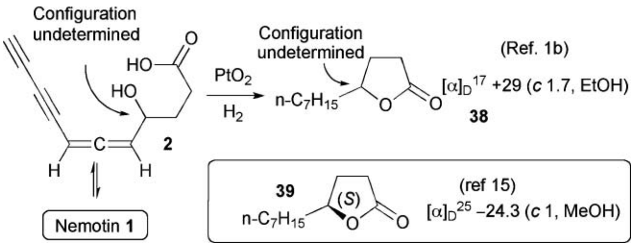
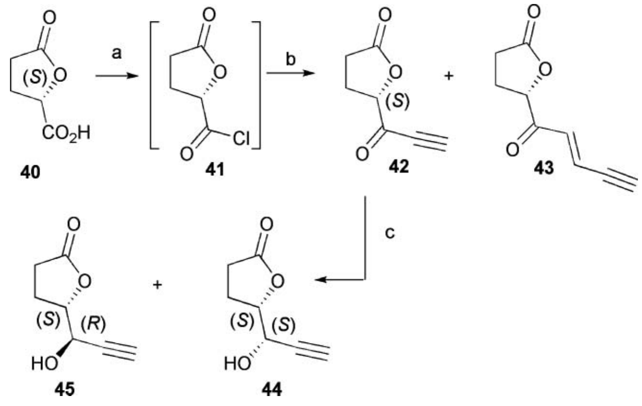


Fig. 4 Comparison of the two γ-lactones (**38** and **39**) reveals the C-4 configuration of **1** and **2**. Note that saturation of the allene changes the substituent priority at the C-4: The (*S*)-isomer after saturation corresponds to the (*R*)-isomer in nemotin.

The new route (Scheme 5) started with the lactone-carboxylic acid **40**, which was readily derived from L-glutamic acid following the well-established literature[16] procedure. Treatment with $SOCl_2$ at reflux for 3 h gave the crude acid chloride **41** in 99% yield.[17]



Scheme 5 *Reagents and conditions*: (a) $SOCl_2$, reflux, 3 h, 99% (crude); (b) HC≡CMgCl, CuCl, −78 °C, 4 h, then −20 °C, 10 h, 31% for **42**; *cf.* also the text and Table 1; (c) $BH_3 \cdot SMe_2$ (1.0 eq.), THF, −40 °C, (*R*)- or (*S*)-2-methyl-CBS-oxaza-borolidine (2 eq.), 92% (**44**/**45** = 7 : 4) or 95% (**44**/**45** = 4 : 17) with (*R*)- or (*S*)-2-methyl-CBS-oxaza-borolidine, respectively, or $NaBH_4$, $CeCl_3$, MeOH, 1 h, 34% (**44**/**45** = 1.7 : 1).

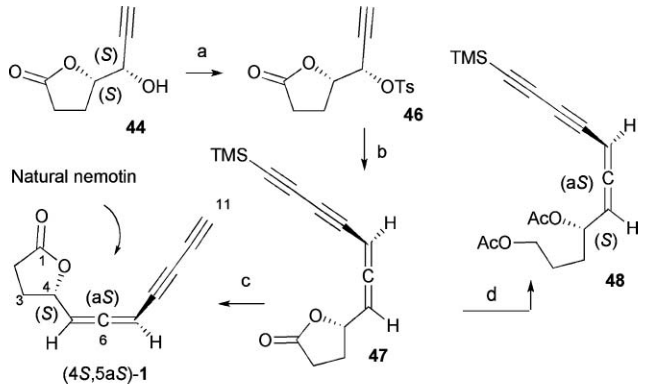
Subsequent addition of an acetylene moiety to **41** was not as facile as expected in the beginning. Under the simplest conditions[18] (TMSC≡C–Li, −78 °C, 4 h), the product mixture was rather complex (Table 1, entry 1). Addition of a catalytic amount of CuCl[19] to this system did not lead to any discernible improvements (entry 2). Use of TMSC≡CTMS and $AlCl_3$[20] to generate the corresponding aluminium species *in situ* also failed to afford the desired **42** (entry 3). The depressing situation then took a favaorable turn when attempts were made to use the corresponding magnesium reagents. With HC≡CMgCl[19] as the nucleophile, the desired **42** was obtained, though the yield was only 7% (entry 4). The introduction of 0.1 molar equivalents of CuCl increased the yield of **42** to 14% (entry 5). However, further reaction at higher temperatures did not lead to more **42**. Instead, the undesired **43** became the only isolable product (entry 6). Therefore, in the end we decided to use only a small amount of CuCl and keep the reaction at temperatures below −20 °C.

The ketone **42** was reduced to corresponding alcohols **44** and **45**. Under Luche[21] conditions ($NaBH_4$, $CeCl_3$, MeOH, 0 °C) the total yield was 45%, with a **44**/**45** (which were readily separable from each other on silica gel) ratio of 7 : 4. CBS[22] (Corey–Bakshi–Shibata) reduction (BH_3, (*R*)- or (*S*)-2-methyl-CBS-oxaza-borolidine, 0 °C) gave better total yields (92% or 95% with the (*R*)- or (*S*)-oxazaborolidine catalyst, respectively).

The (*S*,*S*) propargyl alcohol **44** was then converted to the corresponding tosylate **46** under the conventional conditions (Scheme 6). The latter was treated with TMSC≡C–C≡C–Zn in the presence of $Pd(PPh_3)_4$ to give the (4*S*,5a*S*)-allenediyne **47**. Similar to its diastereomers **32** and **37**, **47** is also very unstable. However, because this isomer is of the same configuration as natural nemotin, and hence is more important than the other ones, extra efforts were made to estimate the yield of the coupling step (*cf.* the Experimental).

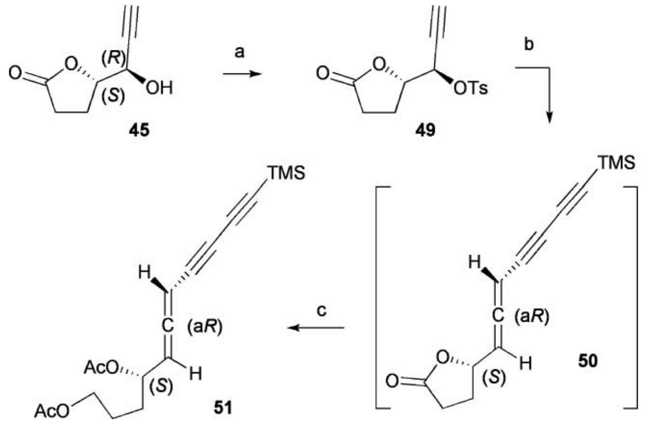
Table 1 Addition of various acetylene species to acid chloride **41**

Entry	Conditions	Outcome
1	TMSC≡CLi, −78 °C, 4 h	Complex
2	TMSC≡CLi, CuCl (0.1 eq.), −78 °C, 4 h	Complex
3	TMSC≡CTMS, $AlCl_3$, rt	Complex
4	HC≡CMgCl, −78 °C, 4 h	**42** (7%)
5	HC≡CMgCl, CuCl (0.1 eq.), −78 °C, 4 h	**42** (14%)
6	HC≡CMgCl, CuCl (0.1 eq.), −78 °C, 4 h, then slowly to rt	**43** (26%)
7	HC≡CMgCl, CuCl (0.04 eq.), −78 °C, 4 h, then −20 °C, 10 h	**42** (31%)



Scheme 6 *Reagents and conditions*: (a) *p*-TsCl, Et_3N, DMAP, CH_2Cl_2, 90%; (b) (i) TMSC≡C–C≡CTMS, MeLi·LiBr, THF, −78 °C, 1.5 h, then rt, 2 h, (ii) $ZnBr_2$, $Pd(Ph_3P)_4$, −78 → −20 °C, 3 h, 64%; (c) (i) $AgNO_3$, MeOH, (ii) NaCN, sat. NH_4Cl, 71% from **47**; (d) (i) DIBAL-H (5.0 eq.), CH_2Cl_2, (ii) Ac_2O, py, DMAP, CH_2Cl_2, rt, 73% from **47**.

Because we had already encountered difficulty in the HPLC separation of **32**/**37** (*vide supra*), a pair of isomers similar to **47**/**50**, no efforts were made on direct measurement of the d.e. value of **47** and/or **50**. Instead, **47** was reduced with DIBAL-H (diisobutylaluminium hydride) and acylated with Ac_2O to afford diacetate **48**. For comparison, the other diastereomer **51** was also prepared in a similar fashion from **50** (which was even more unstable than **47**) as shown in Scheme 7. The d.e. values of **48** and **51** (and consequently **47** and **50**) were then successfully determined on a CHFT-IRALPAK IC column to be 88.7% and 49.1%, respectively. Finally, the isomer (**47**) of the desired configuration was desilyated with $AgNO_3$[23] in MeOH to give the end product (4*S*,5a*S*)-**1**.



Scheme 7 *Reagents and conditions*: (a) *p*-TsCl, Et_3N, DMAP, CH_2Cl_2, 90%; (b) (i) TMSC≡C–C≡CTMS, MeLi·LiBr, THF, −78 °C, 1.5 h, then rt, 2 h, (ii) $ZnBr_2$, $Pd(Ph_3P)_4$, −78 → −20 °C, 3 h; (c) (i) DIBAL-H (5.0 eq.), CH_2Cl_2, (ii) Ac_2O, py, DMAP, CH_2Cl_2, rt, 15% from **49**.

As mentioned for the natural nemotin earlier by the previous investigators, the (4*S*,5a*S*)-**1** we obtained is also very unstable. Near the end of rotary evaporation, an insoluble brown precipitate formed suddenly, and essentially (4*S*,5a*S*)-**1** no longer could be detected by TLC in the remaining supernatant. To acquire the yield as well as optical rotation data, low-boiling point solvents (CH_2Cl_2–pentane) were utilized in the column chromatography, which could be removed gradually by repeated dilution with CH_2Cl_2 followed by partial concentration on a rotary evaporator until the signals for pentane could no longer be detected on ^1H NMR. The (4*S*,5a*S*)-**1** in the solution was quantitized by ^1H NMR in CD_2Cl_2 with methyl 4-iodobenzoate as the internal reference. The optical rotation was then measured to be +356.10 (*c* 0.20, CH_2Cl_2), which is in excellent agreement with the value reported in the literature for the natural nemotin ($[\alpha]_D^{20}$ +350 (*c* 0.20, CH_2Cl_2).

The specific rotation data also indicate that the natural nemotin must be a mixture of allene axial isomers similar to our synthetic (4*S*,5a*S*)-**1**, which was approximately a 16.7 : 1 mixture as estimated from the 88.7% d.e. value (determined on **48**). As phomallenic acid C, another natural allendiyne, has also been shown[4c] to be a mixture instead of a single enantiomer, perhaps co-existence of the allene axial isomers is a common phenomenon for natural allenediynes.

Conclusions

Nemotin, an allenediyne lactone isolated nearly 60 years ago, has been synthesized through an efficient route. The relative as well as absolute configuration of this natural product is thus established to be (4*S*,5a*S*). The ^1H and ^{13}C NMR data for the given structure are also available for the first time. En route to the total synthesis of natural nemotin, some interesting results were also obtained, including the abnormal formation of methyl ketone **18** in the LDA-mediated elimination of **16**, selective reduction of conjugated triple bond in the presence of an isolated one (reduction of **28** to **29**), and direct coupling of a diyne unit with an optically-active propargylic tosylate mediated by zinc salt to yield the allenediyne motif. The new observations with the allenediyne species also help to accumulate the essential knowledge about this unstable and so far underinvestigated structural motif.

Experimental

General

^1H and ^{13}C NMR were recorded on either a Varian Mercury 300 or a Bruker Avance 300 or a Bruker Avance 500 NMR Spectrometer. FT-IR spectra were taken on an FT-IR 440 or a Perkin Elmer 983 or a Nicolet Avatar 360 Infrared Spectrometer. EI-MS and EI-HRMS data were recorded on a HP5989A and a Waters Micromass GCT instrument, respectively. ESI-MS were measured on a PE Mariner API-TOF or an Agilent Technologies LC/MSD SL or a Shimadzu LCMS-2010EV Mass Spectrometer. ESI-HRMS and MALDI-HRMS were collected on a Bruker APEXIII 7.0 Tesla FT-MS and an IonSpec 4.7 Tesla FTMS spectrometer, respectively. Optical rotations were recorded on a Perkin-Elmer Polarimeter 341or an Agilent Technologies P-1030 Polarimeter. Melting points were taken on a micro melting point apparatus equipped with a microscope and were uncorrected. Elemental analyses were performed on an Elementar VarioEL III instrument. Dry solvents were obtained as follows: THF, Et_2O, $MeO(CH_2)_2OMe$ and toluene were refluxed and distilled over Na/PhCOPh under argon prior to use. CH_2Cl_2, DMF, Et_3N, pyridine, *i*-Pr_2NEt and *i*-Pr_2NH were distilled over CaH_2 prior to use. PE (chromatography solvent) stands for petroleum ether (b.p. 60–90 °C). Other chemicals were all commercially available and were used as received.

Ethyl (2*E*,4*R*,5*S*,6*R*)-4,7-dihydroxy-5,6-(isopropylidendioxy)-hept-2-enoate (9). A solution of D-arabinose (8.000 g, 53.29 mmol), $Me_2C(OMe)_2$ (20 cm^3), and *p*-TsOH (monohydrate, 120 mg, 0.63 mmol) in dry DMF (100 cm^3) was stirred at ambient temperature for 4 h. Powdered Na_2CO_3 (74 mg, 0.63 mmol) was added in portions with stirring. The solids were filtered off. The filtrate was concentrated on a rotary evaporator. The residue was chromatographed on silica gel (20 : 1 CH_2Cl_2–MeOH) to give the known[24] intermediate acetonide-hemiacetal as a white solid (9.509 g, 50 mmol, 93.8%). A portion of this solid (2.982 g, 15.7 mmol) was dissolved in toluene (70 cm^3) and treated with $Ph_3P{=}CHCO_2Et$ (8.187 g, 23.5 mmol) and $PhCO_2H$ (96 mg, 0.79 mmol) at 90 °C with stirring for 10 h. The solvent was removed on a rotary evaporator. The residue was chromatographed (1 : 2 PE : Et_2O) on silica gel to afford ester **9** (2.534 g, 9.73 mmol, 62% from the intermediate hemiacetal or 58.2% from arabinose) as a colorless oil: $[\alpha]_D^{26}$ −8.90 (*c* 2.40, $CHCl_3$). FT-IR (film) ν_{max}: 3456, 2985, 2937, 1717, 1659, 1460, 1371, 1307, 1270, 1217, 1040, 869 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.98 (dd, J = 4.6, 15.4 Hz, 1H), 6.16 (dd, J = 1.7, 16.0 Hz, 1 H), 4.52-4.45 (m, 1H), 4.30 (dt, J = 6.7, 5.0 Hz, 1H), 4.25-4.15 (m, 3H), 3.95-3.77 (m, 2H), 3.47 (d, J = 6.2 Hz, OH, 1H), 2.98 (t, J = 5.7 Hz, OH, 1H), 1.51 (s, 3H), 1.36 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.3, 146.4, 122.2, 108.7, 78.4, 76.9, 68.8, 60.7, 60.5, 26.9, 24.7, 14.2; ESI-MS *m/z*: 283.0 ([M + Na]$^+$); ESI-HRMS calcd for $C_{12}H_{20}O_6Na$ ([M + Na]$^+$): 283.11521; found 283.11392.

Ethyl (4*R*,5*S*,6*R*)-4,7-dihydroxy-5,6-(isopropylidendioxy)-heptanoate (10). A mixture of **9** (3.924 g, 15.1 mmol) and 10% Pd–C (400 mg) in EtOAc (75 cm^3) was stirred under H_2 (1 atm) for 5 h. The catalyst was filtered off. The filtrate was concentrated on a rotary evaporator and the residue was chromatographed (1 : 2 PE : Et_2O) on silica gel to afford **10** (3.500 g, 13.35 mmol, 89.1%) as a colorless oil: $[\alpha]_D^{23}$ +18.68 (*c* 1.70, $CHCl_3$). FT-IR (film) ν_{max}: 3450, 2985, 2936, 1732, 1456, 1381, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.32 (dt, J = 6.9, 5.3 Hz, 1 H), 4.11 (q, J = 7.1 Hz, 2H), 4.02 (dd, J = 3.6, 6.8 Hz, 1H), 3.86-3.66 (m, 3 H), 3.10 (t, J = 6.2 Hz, 1 H, OH), 2.99 (d, J = 6.2 Hz, 1H, OH), 2.50 (t, J = 7.2 Hz, 2H), 1.84 (q, J = 7.0 Hz, 2H), 1.47 (s, 3H), 1.34 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.9, 108.2, 79.4, 77.2, 68.0, 60.8, 60.5, 30.2, 29.6, 27.1, 24.9, 14.1; ESI-MS *m/z* 285.1 ([M + Na]$^+$); ESI-HRMS calcd for $C_{12}H_{22}O_6Na$ ([M + Na]$^+$): 285.13086; found 285.1317.

(4*R*,5*S*,6*R*)-4-Hydroxy-5,6-(isopropylidendioxy)-7-benzyloxy-heptanoic acid-1,4-lactone (11). A solution of **10** (279 mg, 1.07 mmol) in dry DMF (3 cm^3) was added to a suspension of NaH (60% in mineral oil, 128 mg, 3.21 mmol) and BnBr (1.830 g, 1.3 mL, 10.70 mmol) in dry DMF (2 cm^3) stirred at −40 °C. After completion of the addition, the bath temperature was allowed to warm naturally to ambient temperature. The mixture was stirred at the same temperature for 4 h before being diluted with EtOAc, washed with aq. sat. NH_4Cl, water, and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (1 : 1 PE : Et_2O) on silica gel afforded **11** (172 mg, 0.56 mmol, 53%) as a colorless oil: $[\alpha]_D^{24}$ –91.23 (*c* 1.10, $CHCl_3$). FT-IR (film) ν_{max}: 3030, 2984, 2924, 1775, 1455, 1381, 1261, 1215, 1171, 1085, 739, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.42-7.24 (m, 5H), 4.69-4.38 (m, 4H), 4.15 (d, J = 7.0 Hz, 1H), 3.77 (d, J = 6.5 Hz, 2H), 2.71-2.55 (m, 1H), 2.49-2.09 (m, 3H), 1.44 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.5, 137.6, 128.4, 127.89, 127.85, 109.3, 79.0, 77.1, 75.2, 73.6, 68.7, 27.9, 26.5, 25.0, 24.9; ESI-MS *m/z* 329.1 ([M + Na]$^+$); ESI-HRMS calcd for $C_{17}H_{22}O_5Na$ ([M + Na]$^+$): 329.13594; found 329.13595.

(4*R*,5*S*,6*R*)-4-Hydroxy-5,6-(isopropylidendioxy)-7-bezyloxy-heptanol (12). $LiAlH_4$ (285 mg, 7.5 mmol) was added to a solution of **11** (1.173 g, 3.83 mmol) in dry THF (15 cm^3) stirred at 0 °C. The mixture was stirred at ambient temperature over night. $Na_2SO_4{\cdot}10H_2O$ was added. The mixture was stirred for 2 h. Solids were filtered off. The filtrate was washed with water and brine before being dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (2 : 3 PE : Et_2O) on silica gel gave **12** (1.058 g, 3.41 mmol, 89%) as a colorless oil: $[\alpha]_D^{23}$ –2.36 (*c* 0.92, $CHCl_3$). FT-IR (film) ν_{max}: 3431, 2984, 2926, 2869, 1454, 1380, 1246, 1217, 1166, 1089, 1028, 737, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.40-7.28 (m, 5H), 4.57 (s, 2H), 4.33 (dd, J = 5.6, 11.7 Hz, 1H), 4.03 (dd, J = 4.1, 6.3 Hz, 1H), 3.76-3.60 (m, 5H), 2.89 (broad, OH, 1H), 2.31 (broad, OH, 1H), 1.76-1.52 (m, 4H), 1.49 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.4, 128.4, 127.94, 127.87, 108.3, 79.7, 75.8, 73.6, 69.2, 68.5, 62.6, 31.5, 29.4, 27.2, 25.0; ESI-MS *m/z* 333.2 ([M + Na]$^+$); ESI-HRMS calcd for $C_{17}H_{26}O_5Na$ ([M + Na]$^+$): 333.16725; found 333.16704.

(4*R*,5*S*,6*R*)-4-Hydroxy-5,6-(isopropylidendioxy)-7-bezyloxy-heptanyl 2,2-dimethylpropionate (13). To a solution of **12** (1.010 g, 3.26 mmol) in dry CH_2Cl_2 (15 cm^3) stirred at 0 °C were added in turn Et_3N (1.36 cm^3, 9.78 mmol), PivCl (0.52 cm^3, 4.24 mmol), and DMAP (40 mg, 0.33 mmol). The mixture was stirred at ambient temperature overnight before being diluted with EtOAc, washed with aq. sat. NH_4Cl, water, and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : Et_2O) on silica gel gave **13** (847 mg, 2.15 mmol, 66%) as a colorless oil: $[\alpha]_D^{23}$ –2.24 (*c* 0.60, $CHCl_3$). FT-IR (film) ν_{max}: 3505, 2959, 2932, 2872, 1727, 1480, 1285, 1160, 1092, 737, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.40-7.28 (m, 5 H), 4.60 (d, J = 12.4 Hz, 1H), 4.56 (d, J = 12.8 Hz, 1H), 4.35 (dd, J = 5.6, 12.1 Hz, 1H), 4.10-3.98 (m, 3H), 3.77-3.58 (m, 3H), 2.51 (d, J = 6.7 Hz, OH, 1H), 1.94-1.77 (m, 1H), 1.73-1.52 (m, 3H), 1.50 (s, 3H), 1.37 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.6, 137.5, 128.5, 127.94, 127.89, 108.3, 79.3, 75.9, 73.7, 68.8, 68.6, 64.2, 38.7, 31.2, 27.2, 27.1, 25.1, 24.9; ESI-MS *m/z* 417.2 ([M + Na]$^+$). Anal. calcd. for $C_{22}H_{34}O_6$: C, 66.98, H, 8.69; found C, 67.00, H, 8.86.

(4*R*,5*S*,6*R*)-4-(Dimethyl-*tert*-butylsilyloxy)-5,6-(isopropyliden-dioxy)-7-bezyloxy-heptanyl 2,2-dimethylpropionate (14). 2,6-Lutidine (0.49 cm^3, 4.16 mmol) was added to a solution of **13** (821 mg, 2.08 mmol) in dry CH_2Cl_2 (10 cm^3) stirred at 0 °C, followed by TBSOTf (0.72 cm^3, 3.12 mmol). The mixture was stirred at the same temperature for 1 h before being diluted with EtOAc, washed with water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (8 : 1 PE : Et_2O) on silica gel gave **14** (1.048 g, 2.07 mmol, 99%) as a colorless oil: $[\alpha]_D^{23}$ +21.03 (*c* 2.10, $CHCl_3$). FT-IR (film) ν_{max}: 3064, 3030, 2954, 2928, 2856, 1731, 1479, 1461, 1379, 1251, 1154, 1101, 834, 777, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.39-7.22 (m, 5H), 4.57 (d, J = 12.0 Hz, 1H), 4.48 (d, J = 11.9 Hz, 1 H), 4.22 (dd, J = 5.8, 11.2 Hz, 1H), 4.05-3.89 (m, 3H), 3.71 (dt, J = 2.4, 7.9 Hz, 1H), 3.57 (dd, J = 5.7, 9.7 Hz, 1H), 3.43 (dd, J = 6.0, 9.8 Hz, 1H), 1.86-1.71 (m, 1H), 1.73-1.52 (m, 3H), 1.41 (s, 3H), 1.32 (s, 3H), 1.18 (s, 9H), 0.85 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5, 137.8, 128.4, 127.8, 108.1, 80.3, 76.0, 73.4, 70.8, 69.1, 64.3, 38.7, 30.7, 27.9, 27.2, 26.0, 25.4, 25.1, 18.3, –4.0, –4.6; ESI-MS *m/z* 531.4 ([M + Na]$^+$); MALDI-HRMS calcd for $C_{28}H_{48}O_6SiNa$ ([M + Na]$^+$): 531.31124; found 531.3125.

(4*R*,5*S*,6*R*)-4-(Dimethyl-*tert*-butylsilyloxy)-5,6-(isopropyliden-dioxy)-7-hydroxy-heptanyl 2,2-dimethylpropionate (15). A mixture of **14** (852 mg, 1.67 mmol) and $Pd(OH)_2$ (320 mg) in EtOH (10 cm^3) was stirred under H_2 (1 atm) for 7 h. The solids were filtered off. The filtrate was concentrated on a rotary evaporator. The residue was chromatographed (7 : 1 PE : EtOAc) on silica gel to afford **15** (564 mg, 1.35 mmol, 81%) as a colorless oil: M.p. 63–65 °C. $[\alpha]_D^{24}$ +45.28 (*c* 3.20, $CHCl_3$). FT-IR (film) ν_{max}: 3277, 2855, 1724, 1481, 1370, 1291, 1003, 721, 661 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.14 (dt, J = 6.2, 11.9 Hz, 1H), 4.11-4.01 (m, 3H), 3.79 (dt, J = 3.0, 8.0 Hz, 1H), 3.61 (t, J = 5.9 Hz, 2H), 2.28 (t, J = 6.0 Hz, 1H), 1.93-1.51 (m, 4H), 1.47 (s, 3H), 1.35 (s, 3H), 1.18 (s, 9H), 0.88 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5, 108.3, 80.0, 77.5, 70.6, 64.0, 61.4, 38.7, 30.4, 28.0, 27.1, 25.9, 25.8, 25.3, 18.3, –4.1, –4.7; ESI-MS *m/z* 441.3 ([M + Na]$^+$); MALDI-HRMS calcd for $C_{21}H_{42}O_6SiNa$ ([M + Na]$^+$): 441.26429; found 441.2645.

(4*R*,5*S*,6*S*)-4-(Dimethyl-*tert*-butylsilyloxy)-5,6-(isopropyliden-dioxy)-7-chloro-heptanyl 2,2-dimethylpropionate (16). A mixture of **15** (64 mg, 0.15 mmol), Ph_3P (100 mg, 0.38 mmol) and K_2CO_3 (42 mg, 0.31 mmol) in CCl_4 (1.5 cm^3) was refluxed with stirring overnight. The solvent was removed by rotary evaporation. The residue was chromatographed (25 : 1 PE : EtOAc) on silica gel to give **16** (46 mg, 0.11 mmol, 69%) as a colorless oil: $[\alpha]_D^{27}$ +38.93 (*c* 0.65, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.22 (dt, J = 8.0, 5.2 Hz, 1 H), 4.12-4.00 (m, 3 H), 3.79 (dt, J = 2.9, 8.2 Hz, 1H), 3.61 (dd, J = 4.6, 11.4 Hz, 1H), 3.50 (dd, J = 8.2, 11.5 Hz, 1H), 1.94-1.39 (m, 4H), 1.49 (s, 3H), 1.36 (s, 3H), 1.20 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.5, 108.7, 80.4, 77.4, 70.3, 63.9, 43.4, 38.7, 30.7, 27.9, 27.2, 25.9, 25.3, 25.0, 18.3, –4.0, –4.5; FT-IR (film) ν_{max}: 2958, 2930, 2857, 1731, 1480, 1381, 1284, 1254, 1222, 1157, 836, 778 cm^{-1}; ESI-MS *m/z* 459.3 ([M + Na]$^+$); ESI-HRMS calcd for $C_{21}H_{41}O_5SiNaCl$ ([M + Na]$^+$) 459.23040; found 459.23056.

(4*R*,5*S*)-4-(Dimethyl-*tert*-butylsilyloxy)-6-oxo-heptanyl 2,2-dimethylpropionate (18). *n*-BuLi (1.6 M in hexanes, 0.69 cm^3, 1.10 mmol) was added to a solution of *i*-Pr_2NH (0.15 cm^3, 1.10 mmol) in dry THF (2 cm^3) and stirred at –78 °C under argon. The mixture was stirred at the same temperature for 1 h. A solution of **16** (87 mg, 0.20 mmol) in dry THF (1 cm^3) was introduced. The bath was allowed to warm slowly (over *ca.* 6 h) to 0 °C before being re-cooled to −78 °C. The mixture was partitioned between EtOAc and aq. sat. NH_4Cl. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (20 : 1 PE : Et_2O) on silica gel gave **18** (38 mg, 0.105 mmol, 53%) as a colorless oil: $[\alpha]_D^{28}$ +49.94 (*c* 0.90, $CHCl_3$). FT-IR (film) ν_{max}: 3477, 2958, 2931, 2859, 1728, 1481, 1463, 1362, 1285, 1256, 1158, 1088, 837, 777 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.13-3.94 (m, 4 H), 3.51 (d, J = 6.3 Hz, OH, 1 H), 2.28 (s, 3H), 1.78-1.52 (m, 3H), 1.41-1.28 (m, 1H), 1.19 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.6, 178.5, 79.2, 73.1, 63.9, 38.7, 29.4 (2′C), 27.2, 25.8, 25.2, 18.0, −4.4, −4.6; ESI-MS *m/z* 383.2 ([M + Na]$^+$); ESI-HRMS calcd for $C_{18}H_{37}O_5Si$ ([M + H]$^+$): 361.24048; found 361.24033.

(4*R*,5*S*,6*R*)-4-(Methoxymethyloxy)-5,6-(isopropylidendioxy)-7-benzyloxy-heptanyl 2,2-dimethylpropionate (21). MOMCl (0.18 cm^3, 2.37 mmol) was added to a solution of NaI (267 mg, 1.78 mmol) in dry $MeO(CH_2)_2OMe$ (1 cm^3) stirred at ambient temperature. The stirring was continued for 10 min before *i*-Pr_2NEt (0.45 cm^3, 2.61 mmol) was introduced. A solution of **13** (234 mg, 0.59 mmol) in dry $MeO(CH_2)_2OMe$ (2 cm^3) was then added. The mixture was heated to reflux overnight. After being cooled to ambient temperature, the mixture was diluted with EtOAc, washed with aq. sat. NH_4Cl, water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (20 : 1 PE : EtOAc) on silica gel gave **21** (176 mg, 0.40 mmol, 68%) as a colorless oil: $[\alpha]_D^{23}$ +59.63 (*c* 0.90, $CHCl_3$). FT-IR (film) ν_{max}: 3031, 2980, 2934, 1727, 1496, 1480, 1455, 1398, 1380, 1369, 1284, 1249, 1220, 1159, 1100, 1031, 738, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39-7.24 (m, 5H), 4.85 (d, J = 7.0 Hz, 1H), 4.63 (d, J = 6.6 Hz, 1H), 4.53 (s, 2H), 4.23 (dd, J = 5.8, 11.6 Hz, 1H), 4.14 (dd, J = 5.6, 8.4 Hz, 1H), 4.05-3.86 (m, 2 H), 3.66 (dt, J = 2.6, 7.8 Hz, 1 H), 3.56 (dd, J = 6.4, 9.7 Hz, 1H), 3.44 (dd, J = 5.8, 10.0 Hz, 1H), 3.38 (s, 3H), 1.91-1.70 (m, 1H), 1.68-1.44 (m, 3H), 1.42 (s, 3H), 1.35 (s, 3H), 1.18 (s, 9H). ESI-MS *m/z* 461.4 ([M + Na]$^+$); MALDI-HRMS calcd for $C_{24}H_{38}O_7Na$ ([M + Na]$^+$): 461.25098; found 461.2514.

(4*R*,5*S*,6*R*)-4-(Methoxymethyloxy)-5,6-(isopropylidendioxy)-7-hydroxy-heptanyl 2,2-dimethylpropionate (22). A mixture of **21** (128 mg, 0.29 mmol) and $Pd(OH)_2$ (25 mg) in EtOH (4 cm^3) was stirred under H_2 (1 atm) for 7 h. The catalyst was filtered off. The filtrate was concentrated on a rotary evaporator and the residue was chromatographed (3 : 1 PE : EtOAc) on silica gel to afford **22** (105 mg, 0.29 mmol, 100%) as a colorless oil: $[\alpha]_D^{22}$ +65.83 (*c* 1.40, $CHCl_3$). FT-IR (film) ν_{max}: 3488, 2961, 2936, 1728, 1481, 1460, 1380, 1370, 1286, 1249, 1221, 1161, 1034 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.86 (d, J = 7.0 Hz, 1H), 4.66 (d, J = 6.5 Hz, 1H), 4.23-4.04 (m, 4H), 3.73 (dt, J = 3.6, 7.6 Hz, 1H), 3.62 (t, J = 5.9 Hz, 2H), 3.40 (s, 3H), 2.24 (t, J = 6.2 Hz, OH, 1H), 1.92-1.50 (m, 4H), 1.48 (s, 3H), 1.36 (s, 3H), 1.19 (s, 9H); ESI-MS *m/z* 371.3 ([M + Na]$^+$); MALDI-HRMS calcd for $C_{17}H_{32}O_7Na$ ([M + Na]$^+$): 371.20403; found 371.2049.

2-((3a*S*,4*R*,6a*R*)-2,2-Dimethyl-tetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)-propyl 2,2-dimethylpropionate (24). A mixture of **22** (72 mg, 0.21 mmol), Ph_3P (136 mg, 0.52 mmol) and K_2CO_3 (58 mg, 0.42 mmol) in CH_2Cl_2–CCl_4 (1 : 4 v/v, 2 cm^3) was refluxed with stirring overnight. The solvent was removed by rotary evaporation. The residue was chromatographed (12 : 1 PE : EtOAc) on silica gel to give **24** (48 mg, 0.17 mmol, 80%) as a colorless oil: $[\alpha]_D^{23}$ −30.82 (*c* 0.82, $CHCl_3$). FT-IR (film) ν_{max}: 2975, 2933, 2853, 1728, 1481, 1459, 1380, 1371, 1284, 1208, 1162, 1101, 1073, 862 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.76 (dd, J = 3.8, 6.1 Hz, 1H), 4.57 (dd, J = 3.7, 6.0 Hz, 1H), 4.17-4.04 (m, 2H), 3.99 (d, J = 10.7 Hz, 1H), 3.44 (dd, J = 3.7, 10.8 Hz, 1H), 3.42-3.37 (m, 1H), 1.86-1.71 (m, 4H), 1.47 (s, 3H), 1.36 (s, 3H), 1.20 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.6, 112.0, 82.2, 81.2, 81.0, 72.6, 64.2, 38.7, 27.2, 26.0, 25.4, 24.9 (2′C); ESI-MS *m/z* 309.2 ([M + Na]$^+$); ESI-HRMS calcd for $C_{15}H_{26}O_5Na$ ([M + Na]$^+$): 309.16725; found 309.1669.

(4*R*,5*S*,6*R*)-4-(Methoxymethyloxy)-5,6-(isopropylidendioxy)-7-(*p*-tosyloxy)-heptanyl 2,2-dimethylpropionate (25). To a solution of alcohol **22** (28 mg, 0.08 mmol) in dry CH_2Cl_2 (1 cm^3) stirred at 0 °C were added in turn Et_3N (0.017 cm^3, 0.12 mmol), *p*-TsCl (18 mg, 0.096 mmol), and DMAP (1 mg, 0.008 mmol). The mixture was stirred at ambient temperature overnight. EtOAc was added, followed by aq. sat. NH_4Cl. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (6 : 1 PE : EtOAc) on silica gel gave tosylate **25** (37 mg, 0.074 mmol, 92%) as a colorless oil: $[\alpha]_D^{27}$ +53.62 (*c* 0.95, $CHCl_3$). FT-IR (film) ν_{max}: 2960, 1728, 1598, 1481, 1368, 1285, 1190, 1178, 1097, 1035, 973, 815, 665 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 4.79 (d, J = 7.0 Hz, 1H), 4.62 (d, J = 7.2 Hz, 1H), 4.24 (dd, J = 5.8, 11.6 Hz, 1H), 4.19-3.99 (m, 4H), 3.95 (dd, J = 6.5, 10.2 Hz, 1H), 3.62 (dt, J = 3.9, 7.4 Hz, 1H), 3.38 (s, 3H), 2.46 (s, 3H), 1.91-1.44 (m, 4H), 1.31 (s, 6H), 1.20 (s, 9H); ESI-MS *m/z* 525.4 ([M + Na]$^+$); ESI-HRMS calcd for $C_{24}H_{38}O_9SNa$ ([M + Na]$^+$): 525.21287; found 525.21305.

(4*R*,5*R*)-4,5-Diethynyl-2,2-dimethyl-[1,3]dioxolane (27). DIBAL-H (1 M in cyclohexane, 13 cm^3, 13 mmol) was added to a solution of **26** (1.418 g, 6.50 mmol) in dry toluene (28 cm^3) and stirred at −78 °C under argon. After completion of the addition, the mixture was stirred at the same temperature for 2 h when a solution (already stirred at 0 °C for 5 min) of $MeC(O)C(N_2)P(O)(OMe)_2$ (3.740 g, 19.5 mmol) and K_2CO_3 (3.588 g, 26 mmol) in anhydrous MeOH (100 cm^3) was introduced dropwise. The cooling bath was allowed to warm naturally while the stirring was continued overnight. The mixture was diluted with EtOAc, washed with aq. sat. NH_4Cl, water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (6 : 1 PE : Et_2O) on silica gel gave **27** (529 mg, 3.53 mmol, 54%) as a white solid: M.p. 51–53 °C. $[\alpha]_D^{26}$ +81.29 (*c* 0.96, $CHCl_3$). FT-IR (film) ν_{max}: 3267, 2989, 2939, 2929, 2857, 2125, 1735, 1457, 1382, 1240, 1055, 870 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.65 (s, 2 H), 2.57 (s, 2 H), 1.47 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 112.0, 79.0, 75.3, 70.8, 26.4; EI-MS *m/z* (%) 135 (M–CH_3^+, 6.18), 96 (9), 53 (12), 43 (100), 41 (17). Anal. calcd. for $C_9H_{10}O_2$: C, 71.98, H, 6.71. Found: C, 71.68, H, 6.93.

Ethyl ((4*R*,5*R*)-5-ethynyl-2,2-dimethyl-[1,3]dioxolan-4-yl)propynoate (28). *n*-BuLi (2.5 M, in hexanes, 1.4 cm^3, 3.45 mmol) was added to a solution of **27** (517 mg, 3.45 mmol) in dry THF (35 cm^3) stirred at −78 °C under argon. The stirring was continued for 30 min. The cooling bath was allowed to warm slowly to 0 °C (*ca.* 2 h) and at that temperature for 1 h. The bath was re-cooled to −78 °C. ClCO$_2$Et (299 mg, 2.76 mmol) was added. The mixture was stirred at the same temperature for 4 h, diluted with EtOAc, washed with aq. sat. NH$_4$Cl, water and brine, and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (40 : 1 PE : Et$_2$O) on silica gel gave **28** (302 mg, 1.35 mmol, 49%) as a colorless oil along with recovered starting **27** (300 mg, 2.00 mmol, 58%). Data for **28**: $[\alpha]_D^{24}$ +116.58 (*c* 1.00, CHCl$_3$). FT-IR (film) ν_{max}: 3285, 2990, 2939, 2245, 2123, 1716, 1455, 1384, 1246, 1160, 1058, 845, 751 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.79 (d, *J* = 5.8 Hz, 2H), 4.76 (dd, *J* = 1.7, 6.0 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 2.60 (d, *J* = 1.3 Hz, 1H), 1.50 (s, 3H), 1.49 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 152.8, 112.8, 81.7, 78.9, 77.9, 75.7, 70.7, 70.4, 62.4, 26.5, 26.4, 13.9. EI-MS *m/z* (%) 222 (M$^+$, 0.01), 207 (100), 168 (19), 165 (34), 123 (26), 119 (32), 96 (41), 53 (28), 43 (97); EI-HRMS calcd for C$_{12}$H$_{14}$O$_4$ (M$^+$) 222.0892; found 222.0894.

Ethyl ((4*R*,5*R*)-5-ethynyl-2,2-dimethyl-[1,3]dioxolan-4-yl)propanoate (29). NaBH$_4$ (247 mg, 6.50 mmol) was added quickly in one portion to a mixture of **28** (288 mg, 1.30 mmol) and CuCl (96 mg, 0.97 mmol) in anhydrous MeOH (26 cm^3) stirred at −50 °C. The mixture was stirred at the same temperature for 3 h. EtOAc was added, followed by aq. sat. NH$_4$Cl. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (20 : 1 PE : EtOAc) on silica gel gave **29** (263 mg, 1.16 mmol, 89%) as a colorless oil: $[\alpha]_D^{25}$ +15.66 (*c* 1.05, CHCl$_3$). FT-IR (film) ν_{max}: 3271, 2987, 2935, 2114, 1736, 1456, 1373, 1248, 1072, 872 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.24 (dd, *J* = 2.1, 7.7 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.07 (ddd, *J* = 4.6, 7.6, 7.6 Hz, 1H), 2.59-2.34 (m, 3H), 2.13-1.99 (m, 1H), 1.98-1.84 (m, 1H), 1.46 (s, 3H), 1.41 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 172.8, 110.2, 80.5, 80.3, 74.9, 70.0, 60.5, 30.3, 27.3, 27.0, 26.1, 14.2. ESI-MS *m/z* 249.1 ([M + Na]$^+$); EI-HRMS calcd for C$_{12}$H$_{18}$O$_4$ (M$^+$): 226.1205; found 226.1203.

(4*R*,5*R*)-4,5-Dihydroxy-hept-6-yne-1,4-lactone (30). A solution of **29** (115 mg, 0.51 mmol) and aq. F$_3$CCO$_2$H (50% v/v, 0.73 cm^3) in CH$_2$Cl$_2$ (8 cm^3) was stirred at ambient temperature overnight. EtOAc was added, followed by aq. sat. NaHCO$_3$. The phases were separated. The organic layer was washed with water and brine, and dried over anhydrous Na$_2$SO$_4$. The solvent was removed on a rotary evaporator. The residue was dissolved in CH$_2$Cl$_2$ (8 cm^3). To the solution was added *p*-TsOH (monohydrate, 5 mg, 0.026 mmol). The solution was stirred at ambient temperature overnight. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : EtOAc) on silica gel gave **30** (62 mg, 0.44 mmol, 87%) as a colorless oil: $[\alpha]_D^{29}$ −30.10 (*c* 0.37, CHCl$_3$). FT-IR (film) ν_{max}: 3407, 3271, 2960, 2927, 2852, 2122, 1743, 1459, 1184, 1047 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.67-4.57 (m, 1H), 4.54-4.45 (m, 1H), 2.93 (d, *J* = 5.0 Hz, 1H), 2.75-2.48 (m, 3H), 2.46-2.14 (m, 2H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 177.0, 81.3, 80.0, 75.2, 64.2, 28.1, 23.2. EI-MS *m/z* (%): 140 (M$^+$, 0.07), 85 (100), 57 (8), 55 (10); EI-HRMS calcd for C$_7$H$_8$O$_3$ (M$^+$): 140.0473; found 140.0472.

(4*R*,5*R*)-4-Hydroxy-5-(*p*-tosyloxy)-hept-6-yne-1,4-lactone (31). To a solution of alcohol **30** (45 mg, 0.32 mmol) in dry CH$_2$Cl$_2$ (3 cm^3) stirred at 0 °C were added in turn Et$_3$N (0.089 cm^3, 0.64 mmol), *p*-TsCl (91 mg, 0.48 mmol), and DMAP (12 mg, 0.096 mmol). The mixture was stirred at ambient temperature overnight. EtOAc was added, followed by aq. sat. NH$_4$Cl. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : EtOAc) on silica gel gave tosylate **31** (104 mg, 0.32 mmol, 100%) as a white solid: M.p. 116–117 °C. $[\alpha]_D^{26}$ −62.50 (*c* 0.93, CHCl$_3$). FT-IR (KBr) ν_{max}: 3269, 2950, 2130, 1783, 1595, 1369, 1345, 1190, 1178, 938, 833, 810, 699 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 5.19 (dd, *J* = 2.4, 4.4 Hz, 1H), 4.69 (dt, *J* = 7.4, 5.3 Hz, 1H), 2.74-2.20 (m, 8H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 175.8, 145.6, 132.7, 129.9, 128.1, 78.3, 78.0, 74.9, 70.4, 27.5, 22.9, 21.7. ESI-MS *m/z* 316.9 ([M + Na]$^+$); EI-HRMS calcd for C$_{14}$H$_{14}$O$_5$S (M$^+$): 294.0562; found 294.0564.

(4*R*,5*S*)-4,5-Dihydroxy-hept-6-yne-1,4-lactone (35). A solution of **30** (99 mg, 0.71 mmol), Ph$_3$P (741 mg, 2.83 mmol), *p*-NO$_2$PhCO$_2$H (473 mg, 2.83 mmol) in THF (10 cm^3) was stirred at ambient temperature for 10 min. EtO$_2$CN=NCO$_2$Et (0.44 cm^3, 2.83 mmol) was added. The mixture was stirred at ambient temperature overnight. Solvent was removed by rotary evaporation. The residue was chromatographed (3 : 1 PE : EtOAc) on silica gel to give the intermediate ester (205 mg, 0.709 mmol) as a colorless oil. MeOH (12 cm^3) was added to the residue. The resulting solution was cooled to −15 °C. With stirring, aq. NaOH (1 N, 0.7 cm^3) was added. The mixture was stirred at −15 °C for 30 min. EtOAc was added, followed by aq. sat. NH$_4$Cl. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (3 : 1 PE : EtOAc) on silica gel gave **35** (75 mg, 0.54 mmol, 76% from **30**) as a colorless oil: $[\alpha]_D^{27}$ +28.68 (*c* 0.58, CHCl$_3$). FT-IR (film) ν_{max}: 3407, 3290, 2092, 1739, 1471, 1256, 1091 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.72-4.61 (m, 2H), 3.30 (broad, OH, 1H), 2.79-2.62 (m, 1H), 2.60-2.24 (m, 4H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 177.6, 81.3, 79.8, 75.4, 63.7, 28.1, 21.7; EI-MS *m/z* (%): 140 (M$^+$, 0.10), 85 (100); EI-HRMS calcd for C$_7$H$_8$O$_3$ (M$^+$): 140.0473; found 140.0470.

(4*R*,5*S*)-4-Hydroxy-5-(*p*-tosyloxy)-hept-6-yne-1,4-lactone (36). To a solution of alcohol **35** (26 mg, 0.19 mmol) in dry CH$_2$Cl$_2$ (2 cm^3) stirred at 0 °C were added in turn Et$_3$N (0.052 cm^3, 0.37 mmol), *p*-TsCl (53 mg, 0.28 mmol), and DMAP (7 mg, 0.056 mmol). The mixture was stirred at ambient temperature overnight. EtOAc was added, followed by aq. sat. NH$_4$Cl. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : EtOAc) on silica gel gave tosylate **25** (37 mg, 0.13 mmol, 68%) as a white solid: M.p. 103–105 °C. $[\alpha]_D^{23}$ +45.69 (*c* 0.95, CHCl$_3$). FT-IR (KBr) ν_{max}: 3287, 3041, 2990, 2938, 2124, 1774, 1698, 1600, 1533, 1366, 1180, 935, 821, 674 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.80 (d, $J = 8.5$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 5.26-5.19 (m, 1H), 4.73-4.63 (m, 1H), 2.69-2.22 (m, 8H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 175.8, 145.6, 132.6, 129.9, 128.1, 78.6, 78.5, 75.0, 70.7, 27.4, 22.1, 21.7; ESI-MS m/z 316.9 ([M + Na]$^+$); EI-HRMS calcd for $C_{14}H_{14}O_5S$ (M$^+$): 294.0562; found 294.0572.

(*R*)-5-(Hepta-(1a*R*)-1,2-diene-7-trimethylsilyl-4,6-diynyl)-dihydro-furan2-one (32). MeLi·LiBr (*ca.* 1.5 M, 0.67 cm^3, 1.0 mmol) was added to a solution of TMSC≡C–C≡CTMS (194 mg, 1.0 mmol) in dry THF (5 cm^3) stirred at −78 °C under argon. The cooling bath was allowed to warm to ambient temperature slowly. The stirring was then continued at ambient temperature for 2 h before a solution of anhydrous ZnBr$_2$ in dry THF (1.0 M, 1.0 cm^3, 1.0 mmol) was introduced. The resulting mixture was stirred at the same temperature for 10 min to give a THF solution of TMSC≡C–C≡CZnBr (*ca.* 0.14 M).

The above prepared THF solution of TMSC≡C–C≡CZnBr (0.14 M, 1.5 cm^3, 0.21 mmol) was transferred *via* a cannula to a flame-dried flask containing Pd(Ph$_3$P)$_4$ (11 mg, 0.010 mmol) and **31** (30 mg, 0.10 mmol) in dry THF (1 cm^3) stirred at −78 °C under argon. The bath was allowed to warm slowly to −20 °C (*ca.* 3 h). The mixture was diluted with Et$_2$O, washed with aq. sat. NH$_4$Cl, water and brine, before being dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : Et$_2$O) on silica gel gave **32** (16 mg, 0.066 mmol, 64%) as a yellowish oil (which deteriorated quickly on removal of the solvent; from a partially concentrated sample of **32** the following data were acquired: ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.68 (d, $J = 4.0$ Hz, 2H), 5.10-5.00 (m, 1H), 2.69-2.39 (m, 3H), 2.23-2.08 (m, 1H), 0.21 (s, 9H). This sample was mainly used for exploring HPLC separation of the allene axial isomers (*cf.* **37**).

(*R*)-5-(Hepta-(1a*S*)-1,2-diene-7-trimethylsilyl-4,6-diynyl)-dihydro-furan2-one (37). The same procedure for conversion of **31** into **32** given above was adopted. From a partially concentrated sample of **37** the following data were acquired: ^{1}H NMR (300 MHz, CDCl$_3$) δ 5.76-5.63 (m, 2H), 5.10-5.00 (m, 1H), 2.72-2.07 (m, 4H), 0.21 (s, 9H). This sample was mainly used as a reference in HPLC analysis of **32**.

(*S*)-5-(Prop-2-ynoyl)-dihydro-furan2-one (42). A mixture of acid **40** (780 mg, 6 mmol) in SOCl$_2$ (6 cm^3) was heated to reflux for 3 h. The volatiles were removed on a rotary evaporator. The residue was dissolved in dry THF (24 cm^3). To this solution was added CuCl (18 mg, 0.18 mmol). The mixture was cooled to −78 °C. With stirring, a solution of HC≡CMgCl (0.5 M, in THF, 11.5 cm^3, 5.75 mmol) was added over 1 h. The bath was then allowed to warm naturally to −20 °C and the stirring was continued at that temperature for 15 h. The mixture was diluted with EtOAc, washed with aq. sat. NH$_4$Cl, water and brine, and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : Et$_2$O) on silica gel gave **42** (240 mg, 1.74 mmol, 31%): $[\alpha]_D^{25}$ +6.89 (*c* 0.57, CHCl$_3$), 99.0% e.e. as determined by HPLC analysis ($t_{R(Major)} = 22.53$ min, $t_{R(Minor)} = 18.13$ min) on a CHFT-IRALPAK IC column (0.46 cm × 25 cm) eluting with 70 : 30 *n*-hexane : *i*-PrOH at a flow rate of 0.7 cm^3 min^{-1} with the UV detector set to 214 nm. FT-IR (film) ν_{max}: 3255, 2961, 2095, 1804, 1686, 1461, 1420, 997 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 5.01-4.94 (m, 1H), 3.57 (s, 1H), 2.69-2.30 (m, 4H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 183.1, 175.5, 84.6, 81.6, 78.4, 26.6, 24.7; EI-MS m/z (%): 139 (M$^+$ + 1, 5), 85 (100); EI-HRMS calcd for $C_7H_6O_3$ (M$^+$): 138.0317; found 138.0318.

(4*S*,5*S*)-4,5-Dihydroxy-hept-6-yne-1,4-lactone (44) and (4*S*,5*R*)-4,5-dihydroxy-hept-6-yne-1,4-lactone (45).

Method A. (*R*)-2-Me-CBS-oxazaborolidine (1.0 M in toluene, 1.82 cm^3, 1.82 mmol) was added dropwise to a solution of **42** (126 mg, 0.91 mmol) in dry THF (9 cm^3) stirred at −40 °C under argon, followed by BH$_3$·Me$_2$S (2.0 M, in THF, 0.46 cm^3, 0.92 mmol). The mixture was stirred at the same temperature for 1 h. EtOH (2 cm^3) was added. The stirring was continued for 15 min. Water was added, followed by Et$_2$O. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : EtOAc) on silica gel gave (*S*,*S*)-alcohol **44** (74 mg, 0.53 mmol, 58.2%) and (*S*,*R*)-alcohol **45** (42 mg, 0.30 mmol, 33.0%).

Method B. The procedure was the same as in Method A, except that (*S*)-2-Me-CBS-oxazaborolidine was utilized instead of (*R*)-2-Me-CBS-oxazaborolidine. From **42** (91 mg, 0.66 mmol) were obtained (*S*,*S*)-alcohol **44** (17 mg, 0.12 mmol, 18.2%) and (*S*,*R*)-alcohol **45** (71 mg, 0.51 mmol, 77.2%).

Method C. NaBH$_4$ (10 mg, 0.27 mmol) was added in one portion to a solution of **42** (24 mg, 0.174 mmol) and CeCl$_3$ (57 mg, 0.23 mmol) in MeOH (2 cm^3) stirred at ambient temperature. Stirring was continued for 1 h before the mixture was diluted with EtOAc, washed with aq. sat. NH$_4$Cl, water and brine, and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent by rotary evaporation and column chromatography (2 : 1 PE : EtOAc) on silica gel gave (*S*,*S*)-alcohol **44** (7 mg, 0.050 mmol, 21.7%) and (*S*,*R*)- alcohol **45** (4 mg, 0.029 mmol, 12.6%).

Data for (*S*,*S*)-alcohol **44** (a colorless oil): $[\alpha]_D^{23}$ +37.86 (*c* 1.00, CHCl$_3$); other data the same as its antipode **30**.

Data for (*R*,*S*)-alcohol **45** (a colorless oil): $[\alpha]_D^{23}$ −29.56 (*c* 0.58, CHCl$_3$); other data the same its antipode **35**.

(4*S*,5*S*)-4-Hydroxy-5-(*p*-tosyl)-hept-6-yne-1,4-lactone (46). Using the same procedure for conversion of **30** into **31** given above, tosylate **46** (270 mg, 0.92 mmol, 90%) was obtained as a white solid from alcohol **44** (143 mg, 1.02 mmol); M.p. 116–117 °C. $[\alpha]_D^{22}$ +81.25 (*c* 0.73, CHCl$_3$); other data the same its antipode **31**.

(*S*)-5-(Hepta-(1a*S*)-1,2-diene-7-trimethylsilyl-4,6-diynyl)-dihydrofuran2-one (47). The same procedure for conversion of **31** into **32** given above was employed for converting **46** into **47**, except that chromatography on silica gel was performed using 2 : 1 pentane–Et$_2$O as elutent. The fractions containing **47** were combined and partially concentrated and diluted with CHCl$_3$. The partial concentration and dilution with CHCl$_3$ was repeated several times until no pentane–Et$_2$O could be detected on ^{1}H NMR. The yield of **47** (obtained from **46** (200 mg, 0.68 mmol)) was determined to be 64% by ^{1}H NMR with methyl 4-iodobenzoate as the internal reference. Data for **47**: $[\alpha]_D^{22}$ +262.97 (*c* 0.38, CHCl$_3$). FT-IR (film) ν_{max}: 2956, 2921, 2850, 2200, 2101, 1950, 1775, 1249, 1149, 843 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$): δ 5.68 (d, $J = 4.0$ Hz, 2H), 5.10-5.00 (m, 1H), 2.69-2.39 (m, 3H), 2.23-2.08 (m, 1H), 0.21 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$): δ 214.4, 175.7, 94.3, 91.0, 87.7, 79.0, 77.0, 76.3, 67.9, 28.1, 27.9, −0.4. EI-MS m/z (%): 244

(M^+, 11.31), 162 (13), 85 (100); EI-HRMS calcd for $C_{14}H_{16}O_2Si$ (M^+): 244.0920; found 244.0922.

(*S*)-5-(Hepta-(1a*S*)-1,2-diene-4,6-diynyl)-dihydro-furan-2-one ((4*S*,5a*S*)-1). A solution of $AgNO_3$ (24 mg, 0.14 mmol) in H_2O (0.5 cm^3) was added to a solution of **47** (estimated to be 29 mg, 0.119 mmol, using the partial concentration-dilution technique to change the solvent and ^{1}H NMR to measure the quantity) in MeOH (2 cm^3) stirred at 0 °C with precaution against light. A yellow precipitate formed. The mixture was stirred at the same temperature for 1 h. Et_2O was added, followed by aq. sat. NaCN and aq. sat. NH_4Cl. The phases were separated. The organic layer was washed three times with water and once with brine before being dried over anhydrous Na_2SO_4. Solvent was removed (not to dryness) by rotary evaporation and the residue was chromatographed (2 : 1 pentane–CH_2Cl_2) on silica gel to give (4*S*,5a*S*)-**1**. The fractions containing this compound were combined and partially concentrated by rotary evaporation and diluted with CH_2Cl_2. The concentration-dilution was repeated several times until no more pentane was detected on ^{1}H NMR, giving a solution of (4*S*,5a*S*)-**1** in CH_2Cl_2. The total amount of (4*S*,5a*S*)-**1** formed in this run was estimated to be 14 mg (0.081 mmol, 71% from **47**) by ^{1}H NMR with methyl 4-iodobenzoate as the internal reference. Data for (4*S*,5a*S*)-**1** (same as natural nemotin): UV (MeOH) λ_{max} 208 (shoulder), 235, 249, 263, 278 nm. $[\alpha]_D^{23}$ +356.10 (*c* 0.20, CH_2Cl_2), (lit.[1d] $[\alpha]_D^{20}$ +350 (*c* 0.20, CH_2Cl_2)). FT-IR (film) ν_{max}: 3257, 2960, 2925, 2854, 2204, 2096, 1953, 1774, 1458, 1261, 1097, 1019, 800 cm^{-1}; ^{1}H NMR (300 MHz, CD_2Cl_2): δ 5.68-5.58 (m, 2 H), 5.00-4.90 (m, 1 H), 2.54-2.30 (m, 4 H), 2.12-1.96 (m, 1 H); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 214.6, 175.8, 94.8, 78.5, 76.4, 75.8, 71.7, 67.9, 67.2, 28.2, 28.1. EI-MS *m*/*z* (%): 172 (M^+) (5.72), 142 (15), 107 (9), 90 (23), 85 (100); EI-HRMS calcd. for $C_{11}H_8O_2$ (M^+): 172.0524; found 172.0526.

(8*S*,5a*S*)-Undeca-1-trimethylsilyl-5,6-diene-8,11-diacetoxy-1,3-diyne (48). DIBAL-H (1 M, in cyclohexane, 0.5 cm^3, 0.5 mmol) was added to a solution of **47** (10 mg, 0.041 mmol) in CH_2Cl_2 (1 cm^3) stirred at −78 °C under argon. After completion of the addition, the bath was allowed to warm naturally to ambient temperature (over *ca.* 2 h). MeOH (1 cm^3) was added, followed by Et_2O and aq. sat. potassium sodium tartrate. The mixture was stirred until it became clear. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na_2SO_4. Solvent was removed (not to dryness) by rotary evaporation and the residue was diluted with CH_2Cl_2 (1 cm^3). To this solution were added Ac_2O (0.024 cm^3, 0.25 mmol), pyridine (0.010 cm^3, 0.12 mmol) and DMAP (1 mg). The mixture was stirred at ambient temperature overnight before being diluted with Et_2O, washed with aq. sat. NH_4Cl, water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (4 : 1 PE : Et_2O) on silica gel gave diacetate **48** (10 mg, 0.030 mmol, 73%) as a colorless oil: $[\alpha]_D^{22}$ +55.90 (*c* 0.18, $CHCl_3$), 88.7% d.e. ($t_{R(Major)}$ = 25.10 min, $t_{R(Minor)}$ = 27.15 min) as determined by HPLC on a CHFT-IRALPAK IC column (0.46 cm × 25 cm) eluting with 95 : 5 *n*-hexane/*i*-PrOH at a flow rate of 0.5 cm^3 min^{-1} with the UV detector set to 214 nm. FT-IR (film) ν_{max}: 2957, 2923, 2852, 2200, 2096, 1941, 1741, 1736, 1369, 1232, 1020, 846 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.65-5.51 (m, 2H), 5.36-5.24 (m, 1H), 4.08 (t, $J = 5.7$ Hz, 2H), 2.08 (s, 3H), 2.07 (s, 3H), 1.83-1.61 (m, 4H), 0.20 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 214.4, 171.1, 170.2, 94.3, 90.5, 87.7, 77.9, 75.9, 70.4, 68.8, 63.8, 30.5, 24.4, 21.0, 20.9, −0.5; ESI-MS *m*/*z* 355.1 ([M + Na]$^+$); ESI-HRMS calcd for $C_{18}H_{24}O_4SiNa$ ([M + Na]$^+$): 355.13361; found 355.13318.

(4*S*,5*R*)-4-Hydroxy-5-(*p*-tosyl)-hept-6-yne-1,4-lactone (49). Using the same procedure for conversion of **35** into **36** given above, tosylate **49** (403 mg, 1.37 mmol, 90%) was obtained as a white solid from alcohol **45** (213 mg, 1.52 mmol); M.p. 104–106 °C. $[\alpha]_D^{22}$ −58.72 (*c* 0.95, $CHCl_3$); other data the same as its antipode **36**.

(8*S*,5a*R*)-Undeca-1-trimethylsilyl-5,6-diene-8,11-diacet-oxy-1,3-diyne (51). Using the same procedure for the conversion of **31** into **32** given above (with **49** to replace **31**) starting from **49** (74 mg, 0.25 mmol), (4*S*,5a*R*)-allenediyne **50** was obtained as a solution in $CHCl_3$ and kept at −20 °C. A portion of this solution (2/3) was dissolved in CH_2Cl_2 (1 cm^3). The solution was stirred at −20 °C under argon while DIBAL-H (1 M, in cyclohexane, 0.5 cm^3, 0.5 mmol) was added dropwise. After completion of the addition, the bath was allowed to warm naturally to ambient temperature (over *ca.* 2 h). MeOH (1 cm^3) was added, followed by Et_2O and aq. sat. potassium sodium tartrate. The mixture was stirred until it became clear. The phases were separated. The organic layer was washed with water and brine before being dried over anhydrous Na_2SO_4. The solvent was removed (not to dryness) by rotary evaporation and the residue was diluted with CH_2Cl_2 (1 cm^3). To this solution were added Ac_2O (0.024 cm^3, 0.25 mmol), pyridine (0.010 cm^3, 0.12 mmol) and DMAP (1 mg). The mixture was stirred at ambient temperature overnight before being diluted with Et_2O, washed with aq. sat. NH_4Cl, water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (4 : 1 PE : Et_2O) on silica gel gave **51** (10 mg, 0.024 mmol, 15% from **49**) as a colorless oil: $[\alpha]_D^{22}$ −10.54 (*c* 0.55, $CHCl_3$), 49.2% d.e. (*cf.* the details given above for **48**). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.63-5.53 (m, 2H), 5.35-5.24 (m, 1H), 4.08 (t, $J = 5.9$ Hz, 2H), 2.07 (s, 3H), 2.06 (s, 3H), 1.82-1.62 (m, 4H), 0.20 (s, 9H); FT-IR (film): 2957, 2924, 2853, 2199, 2102, 1945, 1741, 1235; ESI-MS *m*/*z* 355.1 ([M + Na]$^+$); ESI-HRMS calcd for $C_{18}H_{24}O_4SiNa$ ([M + Na]$^+$): 355.13361; found 355.13403.

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