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Stereoselective total synthesis of (3*Z*)- and (3*E*)-elatenynes†

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We describe here the highly stereoselective total synthesis of the *Laurencia* C₁₅ acetogenins (3*Z*)- and (3*E*)-elatenynes having a 7,12-dibromo-6,9-*cis*-10,13-*cis* adjacent bis-tetrahydrofuran (THF) core. The present synthesis features a highly stereoselective, protecting group-dependent, chelate-controlled intramolecular amide enolate alkylation (IAEA) for the synthesis of key intermediate 7-hydroxy-6,7-*cis*-6,9-*cis*-THF intermediate **10**, deployment of the sequential ate complex (*n*-BuLi/DIBAL-H) reduction/Keck allylation/cross metathesis (CM) protocol for the stereoselective introduction of the C(10)–C(15) unit, a sequential Sharpless asymmetric dihydroxylation (SAD)/intramolecular Williamson etherification for the construction of the 10,13-*cis*-THF ring, and a modified Nakata chloromethanesulfonate-mediated S_N2 displacement for the 7,12-dibromo functionality. Furthermore, our strategy based on chelate-controlled IAEA methodology would provide access to any member of the C₁₅ adjacent bis-THF acetogenin class.

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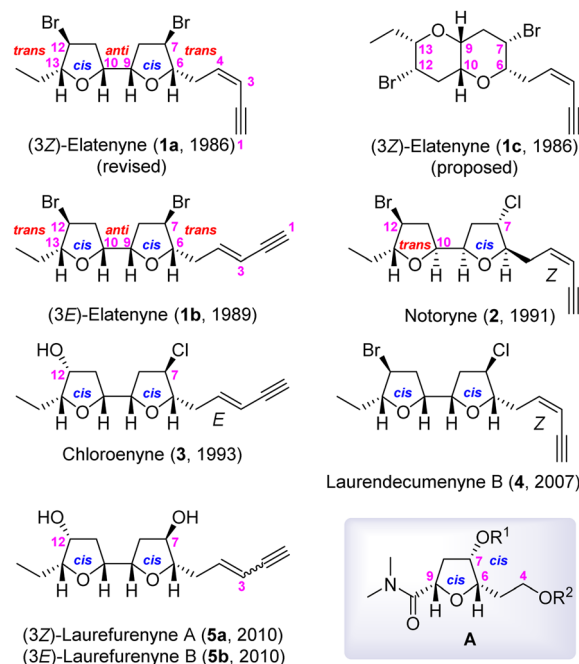
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Marine algae produce a diverse set of oxacyclic C₁₅ acetogenins, among which some, as shown in Fig. 1, have a 2,2'-bifuranyl (adjacent bis-THF) core structure.¹ (3*Z*)-Elatenyne (**1a**) was first isolated from the marine alga *Laurencia elata* by Hall and Reiss in 1986,^{2a} and Erickson reported isolating (3*E*)-elatenyne (**1b**) from the marine alga *Laurencia majuscula* in 1989.^{2b} Later, **1a** was re-isolated from *Laurencia decumbens* by Wang in 2007 (ref. 2c) and from *Laurencia elata* by Urban in 2011.^{2d} The isolation of several closely related *Laurencia* C₁₅ acetogenins has been reported, including notoryne (**2**),³ chloroenyne (**3**) from *L. majuscula*,⁴ laurendecumenyne B (**4**),⁵ and laurefurenynes A (**5a**) and B (**5b**).⁶ It is worth mentioning at this point that the structures depicted in Fig. 1 have been revised or confirmed by total synthesis.^{2h,3c-e,6b,c}

Based on extensive ¹H and ¹³C NMR spectroscopic analyses, the structure of (3*Z*)-elatenyne (**1a**) was initially proposed by Hall and Reiss to have a pyrano[3,2-*b*]pyran core (fused bis-THP), as depicted in **1c**.^{2a} However, the **1c** structure was shown by Burton, *et al.*, to be incorrect through the total synthesis thereof.^{2e,f} The Burton and the Goodman groups collaborated to predict the correct 2,2'-bifuranyl skeleton (adjacent bis-THF) structure and relative stereochemistry of **1a** through comparison of the ¹³C NMR chemical shifts of **1a** with

the Boltzmann-weighted GIAO ¹³C NMR chemical shifts determined through DFT methods.^{2g} Later, a collaborative effort by the Kim and Burton groups achieved the total synthesis of **1a** and *ent*-**1a** utilizing a modular and biomimetic approach, respectively.^{2h} Despite the collaborative effort, the unequivocal


 Fig. 1 *Laurencia* adjacent bis-tetrahydrofuranoid natural products.

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(*vide infra*). Based on our previous work,⁷ we were confident that key 6,7-*cis*-6,9-*cis*-THF intermediate **10** could be accessed by subjecting 6,7-*syn*- ω -bromo- α -alkoxy amide **11** to our stereoselective chelate-controlled IAEA reaction. Finally, we imagined that IAEA substrate **11** could be prepared in a straightforward manner from the known 6,7-*syn* epoxy alcohol **12**.

Our synthesis began with the preparation of IAEA substrate **11**, as outlined in Scheme 2. Thus, known epoxy alcohol **12** (ref. 9) was subjected to *O*-alkylation with *N,N*-dimethyl chloroacetamide to afford the desired epoxy α -alkoxy amide **13** in 94% yield. The regioselective opening of the terminal epoxide **13** was achieved through the action of (*n*-Bu)₄NBr in the presence of Mg(NO₃)₂·6H₂O to furnish the 6,7-*syn*-bromoamide **14** with an excellent 96% yield.¹⁰ Protection of the hydroxyl group in **14** as the PMB ether with 4-methoxybenzyl 2,2,2-trichloroacetimidate in the presence of a catalytic amount of *p*-toluenesulfonic acid (PTSA)¹¹ gave rise to key IAEA substrate **11** in good yield (88%).

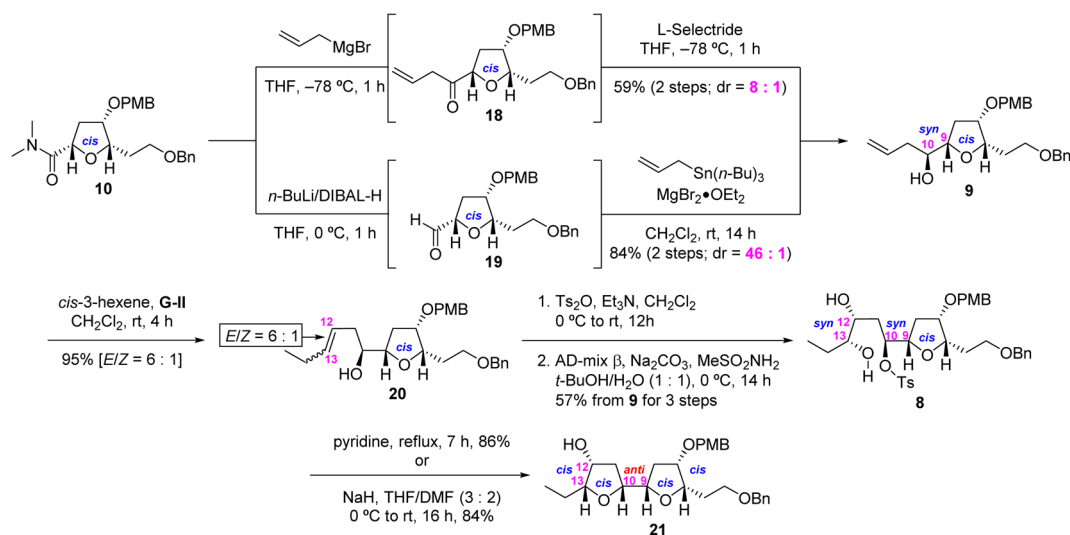
With IAEA substrate **11** in hand, we proceeded to address the pivotal stereoselective IAEA reaction of PMB-protected bromo α -alkoxy amide **11** for the construction of key intermediate **10**. Treatment of **11** with LiHMDS in THF at -78 °C for 1 h led to the desired 6,7-*cis*-6,9-*cis*-THF **10** in 97% yield as a single stereoisomer (by ¹H NMR analysis, see ESI† for details), presumably *via* chelated transition state geometry **B**. The NOE interaction between protons on [C(6) and C(7)] and [C(6) and C(9)] in **10** was supportive of the assigned *cis* relative stereochemistry.

To establish the diastereoselectivity of the IAEA reaction in a rigorous manner, we decided to synthesize the corresponding 6,9-*trans* isomer **17** for comparison purposes as shown at the bottom of Scheme 2. To this end, subjection of TIPS-protected bromo α -alkoxy amide **15** (prepared by TIPS protection of alcohol **14**) to KHMDS in THF at -78 °C for 1 h gave rise to the desired 6,9-*trans*-THF **16** in 80% yield as the major isomer (dr > 41 : 1 by ¹H NMR analysis), presumably *via* transition state **C**. Deprotection of the TIPS protecting group in **16** by exposure to TBAF and subsequent protection of the resultant alcohol as the

PMB ether provided the 6,9-*trans*-THF **17** in 59% yield (two steps).

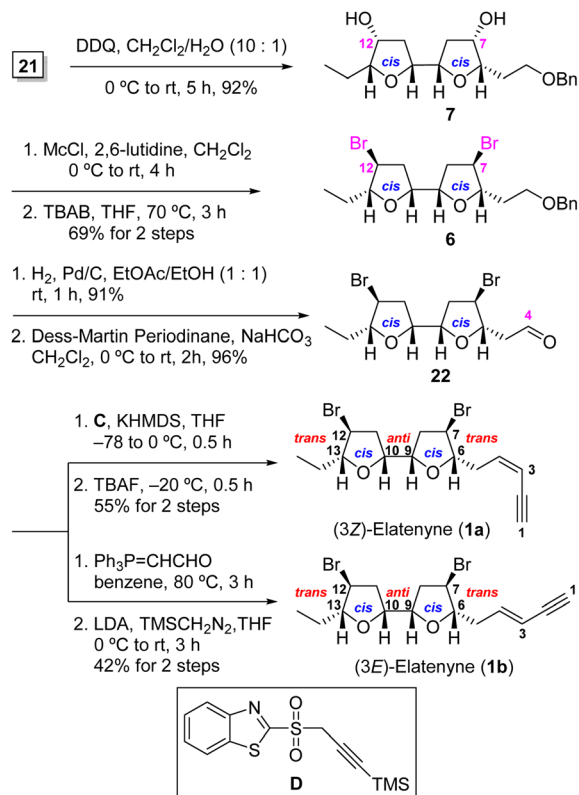
Having accomplished a highly stereoselective synthesis of the desired 6,9-*cis*-THF **10**, we turned our attention to the construction of the crucial adjacent bis-THF **21** as shown in Scheme 3. This requires the stereoselective synthesis of 9,10-*syn* homoallylic alcohol **9** from α -alkoxy amide **10** through application of our direct ketone synthesis/*L*-Selectride protocol.⁷ Thus, the Grignard reaction of **10** with CH₂=CHCH₂MgBr, and the subsequent *L*-Selectride reduction of the resulting ketone **18**, afforded the desired 9,10-*syn*-homoallylic alcohol **9** in moderate yield (59% for two steps) and good selectivity (dr = 8 : 1 by ¹H NMR analysis). In an alternative approach, **10** was reduced using the ate complex derived from *n*-BuLi and DIBAL-H¹² and subjected to Keck allylation¹³ to afford homoallylic alcohol **9** in improved yield (75% for two steps) and improved selectivity (dr = 46 : 1 by ¹H NMR analysis)¹⁴ CM reaction of the alcohol **9** with *cis*-3-hexene in the presence of Grubbs second-generation catalyst [G-II, (H₂IMes)(Cy₃P)Cl₂Ru=CHPh]¹⁵ afforded alkene **20** as an inseparable mixture of stereoisomers (95% total yield, *E/Z* = 6 : 1 by ¹H NMR analysis). Tosylation of alkene **20** (*E/Z* = 6 : 1) and subsequent AD-mix β -mediated SAD reaction¹⁶ of the resulting tosylate afforded the pure *syn*-diol **8** in 57% overall yield from **9** (three steps) after separation. Internal Williamson cyclization of **8** in refluxing pyridine or NaH in THF/DMF (3 : 2) furnished the desired adjacent bis-THF **21** in 86% or 84% yield, respectively.

Having acquired adjacent bis-THF **21**, we proceeded to introduce the bis-bromide functionality to both the C(7) and C(12) positions utilizing the two-step modified Nakata chloromethanesulfonate-mediated S_N2 displacement protocol^{2h,7b,17} (Scheme 4). To this end, treatment of bis secondary alcohol **7**, obtained from **21** after PMB deprotection (92%), with chloromethanesulfonyl chloride (MsCl) in the presence of 2,6-lutidine and subsequent exposure of the resulting sulfonate to (*n*-Bu)₄NBr in refluxing THF furnished the desired 7,12-dibromo-bis-THF **6** in an overall yield of 63% from **21** in two



Scheme 3 Construction of 7,12-dihydroxy adjacent bis-THF **21**.



Scheme 4 Completion of total synthesis of **1a** and **1b**.

steps. It is of note that the two-step Nakata protocol was superior to Hooz bromination in term of yield and purification in our hands [69% vs. 58%; see ESI† for details].¹⁸

Having successfully installed both the C(7) and C(12) bromide atoms in **1a** and **1b**, the remaining task was attaching the C(4) enyne appendages. Catalytic hydrogenolysis of benzyl ether **6**, followed by Dess–Martin oxidation¹⁹ of the resultant primary alcohol gave rise to aldehyde **22**. The stereoselective Julia–Kocienski olefination²⁰ of aldehyde **22** with benzothiazole sulfone **C** by treatment with KHMDS in THF at -78 to 0°C for 0.5 h gave rise to the (3Z)-TMS-enyne ($Z/E = 31 : 1$ by ^1H NMR analysis), which was desilylated with TBAF to afford (3Z)-elatenyne (**1a**) in 55% overall yield for the two steps from **22**. For the second target, Wittig olefination of aldehyde **22** with $\text{Ph}_3\text{P=CHCHO}$ [(triphenylphosphoranylidene)acetaldehyde] gave exclusively the (*E*)- α,β -unsaturated aldehyde, which was then subjected to the condition of Colvin–Ohira homologation²¹ using trimethylsilyldiazomethane and LDA to afford (3*E*)-elatenyne (**1b**) in 42% overall yield for two steps. The spectral characteristics of our synthetic material **1a** and **1b** were in good agreement with those reported for both the natural and synthetic (3*Z*)-^{2a,d,h} and (3*E*)-^{2b,h}-elatenynes, respectively.

Conclusions

In summary, we have accomplished the total synthesis of both (3*Z*)-elatenyne (**1a**) and (3*E*)-elatenyne (**1b**), featuring the protecting group-dependent chelate-controlled IAEA methodology

for a highly stereoselective construction of key intermediate 6,7-*cis*-6,9-*cis*-THF **10**. Other key features of the synthesis include the sequential ate complex reduction/Keck allylation for stereoselective establishment of 9,10-*syn* configuration, the CM/SAD/Williamson cyclization sequence for the efficient construction of the bis-THF moiety, and the chloromethanesulfonate-mediated $\text{S}_{\text{N}}2$ displacement for installation of the 7,12-dibromo functionality. Application of our strategy on the basis of chelate-controlled IAEA and the Marshall's protocol to the synthesis of other members of the adjacent C₁₅ bis-THF acetogenin class in Fig. 1 is currently under investigation in our laboratories.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- (a) B.-G. Wang, J. B. Gloer, N.-Y. Ji and J.-C. Zhao, Halogenated Organic Molecules of Rhodomeleaceae Origin: Chemistry and Biology, *Chem. Rev.*, 2013, **113**, 3632–3685; (b) T. Wanke, A. C. Philippus, G. A. Zatelli, L. F. O. Vieira, C. Lhullier and M. Falkenberg, C₁₅ Acetogenins from the Laurencia Complex: 50 Years of Research-An Overview, *Rev. Bras. Farmacogn.*, 2015, **25**, 569–587; (c) Z. F. Zhou, M. Menna, Y.-S. Cai and Y. W. Guo, Polyacetylenes of Marine Origin: Chemistry and Bioactivity, *Chem. Rev.*, 2015, **115**, 1543–1596; (d) M. Harizani, E. Ioannou and V. Roussis, The Laurencia paradox: An endless source of chemodiversity, in *Progress in the Chemistry of Organic Natural Products*, ed. A. D. Kinghorn, H. Galk, S. Gibbons and J. Kobayashi, Springer, Berlin, 2016, vol. 102, pp. 91–252.
- (a) J. G. Hall and J. A. Reiss, Elatenyne – a Pyrano[3,2-*B*] Pyranyl Vinyl Acetylene from the Red Alga *Laurencia elata*, *Aust. J. Chem.*, 1986, **39**, 1401–1409; (b) The absolute configuration of natural (*E*)-elatenyne was not determined because no optical rotation data were reported in the original isolation paper; see, K. Kim, M. R. Brennan and K. L. Erickson, Lauroxolanes from the marine alga *Laurencia majuscula*, *Tetrahedron Lett.*, 1989, **30**, 1757–1760; (c) N. Y. Ji, X. M. Li, K. Li and B. G. Wang, Laurendecumallenes A–B and Laurendecumenynes A–B, Halogenated Nonterpenoid C₁₅-Acetogenins from the Marine Red Alga *Laurencia decumbens*, *J. Nat. Prod.*, 2007, **70**, 1499–1502; (d) D. A. Dias and S. Urban, Phytochemical studies of the southern Australian marine alga, *Laurencia elata*, *Phytochemistry*, 2011, **72**, 2081–2089; (e) H. M. Sheldrake, C. Jamieson and J. W. Burton, The Changing Faces of Halogenated Marine Natural Products:



- Total Synthesis of the Reported Structures of Elatenyne and an Enyne from *Laurencia majuscula*, *Angew. Chem., Int. Ed.*, 2006, **45**, 7199–7202; (f) H. M. Sheldrake, C. Jamieson, S. I. Pascu and J. W. Burton, Synthesis of the Originally Proposed Structures of Elatenyne and an Enyne from *Laurencia Majuscula*, *Org. Biomol. Chem.*, 2009, **7**, 238–252; (g) S. G. Smith, R. S. Paton, J. W. Burton and J. M. Goodman, Stereostructure Assignment of Flexible Five-Membered Rings by GIAO ^{13}C NMR Calculations: Prediction of the Stereochemistry of Elatenyne, *J. Org. Chem.*, 2008, **73**, 4053–4062; (h) B. S. Dyson, J. W. Burton, T. I. Sohn, B. Kim, H. Bae and D. Kim, Total Synthesis and Structure Confirmation of Elatenyne: Success of Computational Methods for NMR Prediction with Highly Flexible Diastereomers, *J. Am. Chem. Soc.*, 2012, **134**, 11781–11790; (i) S. Urban, R. Brkljača, M. Hoshino, S. Lee and M. Fujita, Determination of the Absolute Configuration of the Pseudo-Symmetric Natural Product Elatenyne by the Crystalline Sponge Method, *Angew. Chem., Int. Ed.*, 2016, **55**, 2678–2682.
- 3 (a) For the isolation and structure determination of notoryne see: H. Kikuchi, T. Suzuki, E. Kurosawa and M. Suzuki, The Structure of Notoryne, a Halogenated C15 Nonterpinoid with a Novel Carbon Skeleton from the Red Alga *Laurencia Nipponica* Yamada, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 1763–1775; (b) 3(*E*)-Notoryne has also been reported as a natural product, see: A. Fukuzawa, M. Aye, M. Nakamura, M. Tanura and A. Murai, Structure elucidation of laureoxanyne, a new nonisoprenoid C-15-enyne, using lactoperoxidase, *Tetrahedron Lett.*, 1990, **31**, 4895–4898; For total synthesis of **3**, see:; (c) M. Lee, First Asymmetric Total Synthesis of (*Z*)- and (*E*)-Notorynes, *M.S. thesis*, Seoul National University, Seoul, Korea, 2009; (d) S. Senapati, S. Das and C. V. Ramana, Total Synthesis of Notoryne, *J. Org. Chem.*, 2018, **83**, 12863–12868; (e) E. D. Shepherd, B. S. Dyson, W. E. Hak, Q. N. N. Nguyen, M. Lee, M. J. Kim, T. I. Sohn, D. Kim, J. W. Burton and R. S. Paton, Structure Determination of a Chloroenyne from *Laurencia majuscula* Using Computational Methods and Total Synthesis, *J. Org. Chem.*, 2019, **84**, 4971–4991.
- 4 (a) A. D. Wright, G. M. König, R. Denys and O. Sticher, Seven New Metabolites From The Marine Red Alga *Laurencia Majuscula*, *J. Nat. Prod.*, 1993, **56**, 394–401; (b) For total synthesis of **3**, see: S. Senapati, N. A. Unmesh, M. N. Shet, I. Ahmad, N. Ajikumar and C. V. Ramana, Unified Approach for the Total Synthesis of Bis-THF C15 Acetogenins: A Chloroenyne from *Laurencia majuscula*, *Laurendecumenyne B* and *Laurefurenynes A/B*, *Synthesis*, 2021, **53**, 2903–2910; and also see: ref. 3e.
- 5 (a) For isolation of **4**, see: ref. 2c; (b) For total synthesis of **4**, see: ref. 2h and 4b.
- 6 (a) W. M. Abdel-Mageed, R. Ebel, F. A. Valeriote and M. Jaspars, Laurefurenynes A–F, new Cyclic Ether Acetogenins from a Marine Red Alga, *Laurencia* sp, *Tetrahedron*, 2010, **66**, 2855–2862; For total synthesis of **5a** and **5b**, see: (b) D. J. Shepherd, P. A. Broadwith, B. S. Dyson, R. S. Paton and J. W. Burton, Structure Reassignment of Laurefurenynes A and B by Computation and Total Synthesis, *Chem. – Eur. J.*, 2013, **19**, 12644–12648; (c) M. T. Holmes and R. A. Britton, Total Synthesis and Structural Revision of Laurefurenynes A and B, *Chem. – Eur. J.*, 2013, **19**, 12649–12652.
- 7 (a) H. Jang, I. Shin, D. Lee, H. Kim and D. Kim, Stereoselective Substrate-Controlled Asymmetric Syntheses of both 2,5-*cis*- and 2,5-*trans*-Tetrahydrofuranoid Oxylipids: Stereodivergent Intramolecular Amide Enolate Alkylation, *Angew. Chem., Int. Ed.*, 2016, **55**, 6497–6501; (b) S. Y. Kwak, Y. Park, S. Lim, H. Jang, D. Lee, H. Kim and D. Kim, Total Synthesis and Structure Confirmation of (–)-Asimitrin, a C₃₇ Annonaceous Acetogenin with a Hydroxylated Adjacent Bis-Tetrahydrofuran Core, *Org. Lett.*, 2023, **25**, 6659–6664; (c) I. Shin, D. Lee and H. Kim, Substrate-Controlled Asymmetric Total Synthesis and Structure Revision of (–)-Bisezakyne A, *Org. Lett.*, 2016, **18**, 4420–4423; (d) I. Shin, H. Jang, S. Y. Kwak, Y. Park, D. Lee, H. Kim and D. Kim, Highly Stereodivergent Construction of C₂-Symmetric *cis,cis*- and *trans,trans*-2,6-dioxabicyclo [3.3.0]octane Framework by Double Intramolecular Amide Enolate Alkylation: Total Synthesis of (+)-Laurenidificin and (+)-Aplysiallene, *Org. Lett.*, 2022, **24**, 8780–8785.
- 8 J. A. Marshall and J. J. Sabatini, Synthesis of *cis*- and *trans*-2,5-Disubstituted Tetrahydrofurans by a Tandem Dihydroxylation-SN2 Cyclization Sequence, *Org. Lett.*, 2005, **7**, 4819–4822.
- 9 (a) H. Lee, H. Kim, S. Baek, S. Kim and D. Kim, Total Synthesis and Determination of the Absolute Configuration of (+)-Neoisoprelaufucin, *Tetrahedron Lett.*, 2003, **44**, 6609–6612; (b) The *ee* value of known epoxy alcohol **12** was determined as >86.9% by analysis of the ^1H NMR spectrum of the corresponding Mosher esters, see the ESI† for the details.
- 10 Y.-G. Suh, B.-A. Koo, J.-A. Ko and Y.-S. Cho, A Facile and Highly Regioselective of Epoxides to Bromohydrins Using Tetrabutylammonium Bromide and Magnesium Nitrate, *Chem. Lett.*, 1993, **22**, 1907–1910.
- 11 T. Iversen and D. R. Bundle, Benzyl trichloroacetimidate, a versatile reagent for acid-catalysed benzylation of hydroxy-groups, *J. Chem. Soc. Chem. Commun.*, 1981, 1240–1241.
- 12 S. Kim and K. H. Ahn, Ate complex from diisobutylaluminum hydride and *n*-butyllithium as a powerful and selective reducing agent for the reduction of selected organic compounds containing various functional groups, *J. Org. Chem.*, 1984, **49**, 1717–1724.
- 13 G. E. Keck and E. P. Boden, Stereocontrolled additions of allyltri(*n*-butyl)stannane to α -hydroxyaldehyde derivatives. A useful route to monoprotected erythro or threo diols, *Tetrahedron Lett.*, 1984, **25**, 265–268.
- 14 The stereochemistry of C(10) in **9** was confirmed unambiguously utilizing Mosher ester analysis. (a) I. Ohtani, T. Kusumi, Y. Kashman and H. Kakisawa, High-Field FT NMR Application of Mosher's Method. The Absolute Configuration of Marine Terpenoids, *J. Am. Chem. Soc.*, 1991, **113**, 4092–4096; (b) J. A. Dale and H. S. Mosher,



- Nuclear Magnetic Resonance Enantiomer Regents. Configurational Correlations via Nuclear Magnetic Resonance Chemical Shifts of Diastereomeric Mandelate, O-Methylmandelate, and α -Methoxy- α -trifluoromethylphenylacetate (MTPA) Esters, *J. Am. Chem. Soc.*, 1973, **95**, 512–519.
- 15 A. K. Chatterjee, T. L. Choi, D. P. Sanders and R. H. Grubbs, A General Model for Selectivity in Olefin Cross Metathesis, *J. Am. Chem. Soc.*, 2003, **125**, 11360–11370.
- 16 H. C. Kolb, M. S. VanNieuwenhze and K. B. Sharpless, Catalytic Asymmetric Dihydroxylation, *Chem. Rev.*, 1994, **94**, 2483–2547.
- 17 T. Shimizu, S. Hiranuma and T. Nakata, Efficient Method for Inversion of Secondary Alcohols by Reaction of Chloromethanesulfonates with Cesium Acetate, *Tetrahedron Lett.*, 1996, **37**, 6145–6148.
- 18 The five-step bromination of **21** utilizing modified Nakata chloromethanesulfonate-mediated S_N2 displacement afforded bis-bromide **6** in 41% yield over five steps, see ESI† for details.
- 19 D. B. Dess and J. C. Martin, A useful 12-I-5 triacetoxyperiodinane (the Dess-Martin periodinane) for the selective oxidation of primary or secondary alcohols and a variety of related 12-I-5 species, *J. Am. Chem. Soc.*, 1991, **113**, 7277–7287.
- 20 (a) C. Bonini, L. Chiummiento and V. Videtta, Direct Preparation of Z-1,3-Enyne Systems with a TMS-Propargylic Sulfone: Application of a One-Pot Julia Olefination, *Synlett*, 2006, 2079–2082; (b) G. Kim, T. I. Sohn, D. Kim and R. S. Paton, Asymmetric Total Synthesis of (+)-Bermudenynol, a C15 Laurencia Metabolite with a Vinyl Chloride Containing Oxocene Skeleton, through Intramolecular Amide Enolate Alkylation, *Angew. Chem., Int. Ed.*, 2014, **53**, 272–276.
- 21 (a) E. W. Colvin and B. J. Hamill, One-Step Conversion of Carbonyl Compounds into Acetylenes, *J. Chem. Soc., Chem. Commun.*, 1973, 151–152; (b) E. W. Colvin and B. J. Hamill, A Simple Procedure for the Elaboration of Carbonyl Compounds into Homologous Alkynes, *J. Chem. Soc., Perkin Trans. 1*, 1977, 869–874; (c) S. Ohira, K. Okai and T. Moritani, Generation of Alkylidenecarbenes by the Alkenation of Carbonyl Compounds with Lithiotrimethylsilyldiazomethane, *J. Chem. Soc., Chem. Commun.*, 1992, 721–722; (d) K. Miwa, T. Aoyama and T. Shioiri, Extension of the Colvin rearrangement using trimethylsilyldiazomethane. A new synthesis of alkynes, *Synlett*, 1994, 107–108.

