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A synthesis of (−)-ebelactones A and B

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ABSTRACT

A synthesis of the β-lactone esterase inhibitors (−)-ebelactones A and B is described. The synthesis features the use of a Hoppe homoaldol reaction and a Cu(I)-mediated 1,2-metallate rearrangement of a metallated enol carbamate as key fragment linkage reactions.

1. Introduction

(−)-Ebelactones A and B were isolated from a soil Actinomycete closely related to *Streptomyces aburaviensis* by Umezawa et al.[1] during a screen for esterase activity. The structure of ebelactone A was secured by X-ray analysis of its *p*-bromobenzoate while ebelactone B was identified by spectroscopic comparison.[2] The ebelactones display a wide range of biological activity consequent to the irreversible acylation of various serine hydrolases by the strained β-lactone moiety.[3,4] Examples together with their protein targets include suppressed fat absorption (intestinal lipase),[5] suppression of platelet aggregation (cathepsin A/deamidase),[6] antihypertension (urinary kininase)[7,8] and immunostimulation (*N*-formylmethionine aminopeptidase).[1] In addition, the ebelactones inhibit cutinases produced by fungal plant pathogens thereby blocking the initial step of plant infection,[9,10] and they reduce the destruction of human epidermal and epithelial tissue by pathogenic yeast.[11] They also inhibit prenylated methylated protein methyl esterase (PMPMEase) involved in the regulation of prenylated protein function.[12,13]

The first synthesis of (−)-ebelactone A and (−)-ebelactone B by Paterson and Hulme used three boron-mediated aldol reactions to create six of the seven stereogenic centres and an Ireland–Claisen rearrangement to create the trisubstituted alkene.[14,15] A noteworthy feature of this synthesis is the preservation of the ketone function at C9 with its two flanking stereogenic centres throughout the synthesis without recourse to protection. A synthesis of (−)-ebelactone A by Mandal[16] used Evans aldol, crotylation, hydroxyl-directed reduction and substrate-controlled hydroboration reactions to generate the requisite stereogenic centres, the trisubstituted alkene being generated by a Suzuki–Miyaura coupling of an iodoalkene with an alkylborane. Fleming et al.[17] described the synthesis of an advanced intermediate en route to ebelactone A, in which all of the stereochemical relationships were controlled by silicon-based methods. We now report syntheses of (−)-ebelactones A and B from a common intermediate, which features the use of a 1,2-metallate rearrangement to construct the trisubstituted alkene. Scheme 1 indicates the provenance of five of the strategic bonds.

2. Results and discussion

Our synthesis of (−)-ebelactones A and B began with the construction of the C9–C14 fragment **3** (Scheme 2). The 1,2-*anti*-2,3-*syn* stereochemical relationship between the three contiguous stereogenic centres was created via a reagent-controlled crotylmetallation reaction on the aldehyde **8** generated in two conventional steps from methyl (*R*)-(−)-3-hydroxy-2-methylpropanoate (**6**).[18] As crotylmetallation reagent we chose Roush's[19] diisopropyl-2-crotyl-1,3,2-dioxaboralane-

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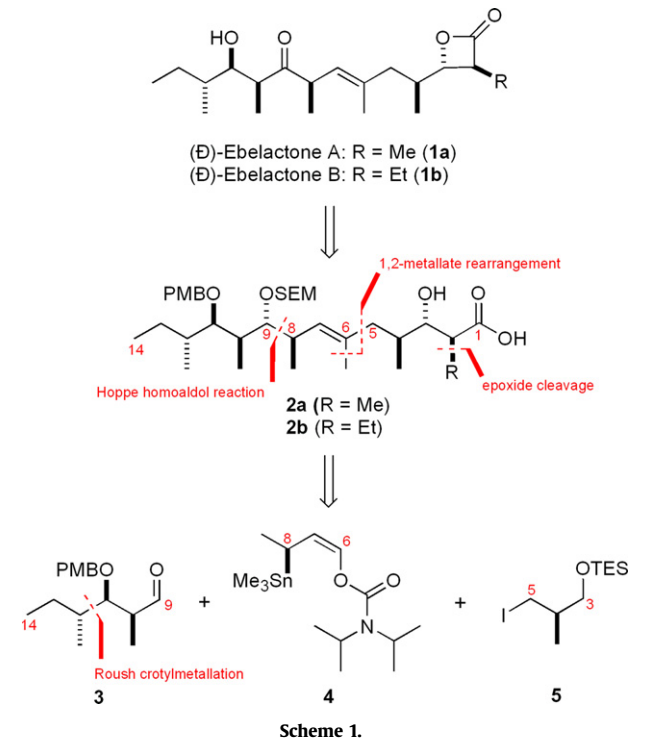
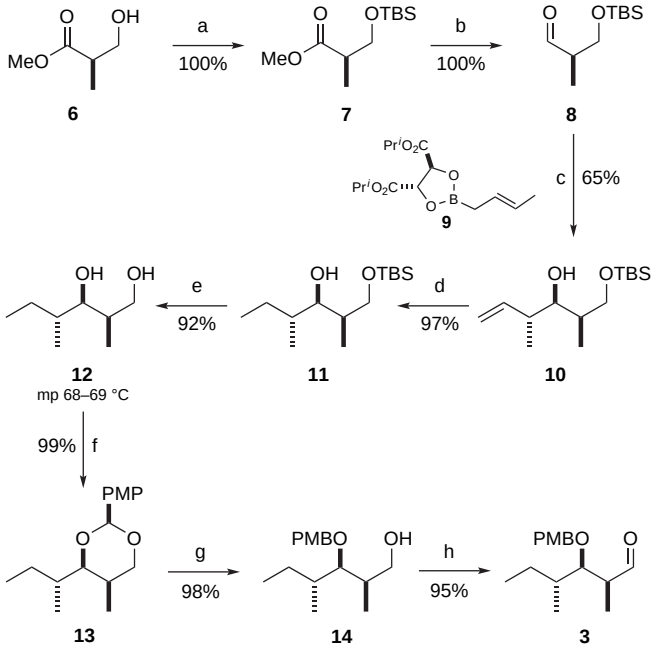


Scheme 1.

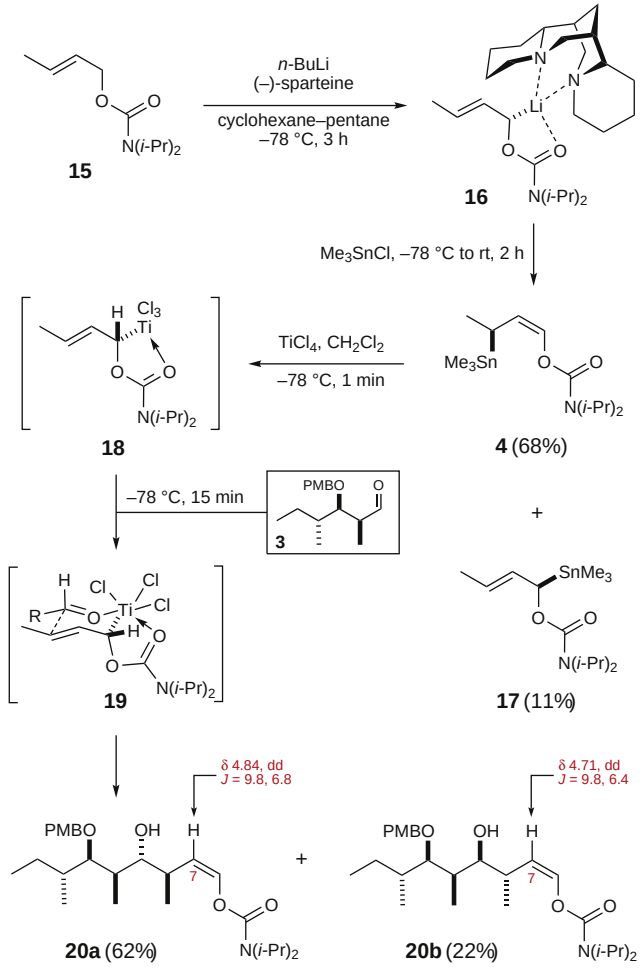


Scheme 2. Reagents and conditions: (a) TBSCl (1.05 equiv), imidazole (1.6 equiv), DMAP (1.0 mol %), CH_2Cl_2, 0 °C to rt, 2 h, ca. 100%; (b) DIBAL-H (1.05 equiv), CH_2Cl_2, −78 to −30 °C, 75 min, ca. 100%; (c) 9 (1.75 equiv), 4 Å MS, PhMe, −78 °C to rt, 5 h, 65%; (d) H_2, $[Ph_3P]_3RhCl$ (2 mol %), PhH, rt, 30 h, 97%; (e) TFA (10 equiv), THF/H_2O (2:1), 0 °C to rt, 3 h, 92%; (f) $PMP/CH(OMe)_2$ (5 equiv), *p*-TsOH·H_2O (5 mol %), CH_2Cl_2, rt, 3 h, 99% (dr≥97:3); (g) DIBAL-H (3.5 equiv), CH_2Cl_2, −78 °C to rt, 2 h, 98%; (h) Dess–Martin periodinane (1.2 equiv), CH_2Cl_2, rt, 1 h, 95%.

4,5-dicarboxylate reagent **9** because it was cheap and easy to prepare from *trans*-2-butene on a 200 mmol scale and it could be stored for weeks at 0 °C in the absence of moisture. The modest yield of the crotylmetallation adduct **10** (65%) was compensated by the excellent dr (≥97:3) consistent with the complementary operation of reagent control and substrate control (matched pair) in accordance with the Felkin–Anh model.[20] Catalytic homogeneous hydrogenation[21] of alkene **10** using freshly prepared Wilkinson's catalyst[22] gave the saturated alcohol **11** with none of the epimerization of the C12 stereogenic centre observed when Pd/C was used as catalyst. Deprotection of the TBS ether **11** using trifluoroacetic acid gave the crystalline diol **12** (mp 68–69 °C). Selective PMB-protection of the secondary alcohol in **12** was accomplished by regioselective reductive cleavage of the PMP acetal **13** with DIBAL-H according to the procedure of Takano et al..[23,24] Finally, Dess–Martin oxidation of the primary alcohol **14** gave the target C9–C14 fragment **3** in 53% overall yield for the eight steps from **6**.

The second phase of the synthesis entailed the construction of the stannane **4** and its union with the aldehyde **3** via a Hoppe homoaldol reaction[25] (Scheme 3). Thus, deprotonation of the (*E*)-crotyl carbamate **15**[26] with *n*-BuLi in the presence of (−)-sparteine in a 9:1 mixture of anhydrous pentane/cyclohexane at −78 °C initially generated a pair of configurationally labile diastereoisomeric organolithium·(−)-sparteine complexes, but after ca. 3 h of vigorous mechanical stirring at −78 °C, crystallisation-induced diastereoselection resulted in a thick, white suspension of diastereoisomer **16** whose structure has been rigorously defined by X-ray crystallography.[27] Treating the organolithium·(−)-sparteine complex **16** with trimethylstannyl chloride in pentane then gave an easily separable mixture of enantiomerically enriched stannanes **4** (68%, er=83:17) and **17** (11%), both reactions having taken place by *anti*-S_E' and *anti*-S_E mechanisms, respectively.[28] Stannane **4** could be stored for up to three months at −20 °C under an inert atmosphere with no observable decomposition.

A Hoppe homoaldol reaction between stannane **4** and aldehyde **3** accomplished formation of the C8–C9 bond and installation of

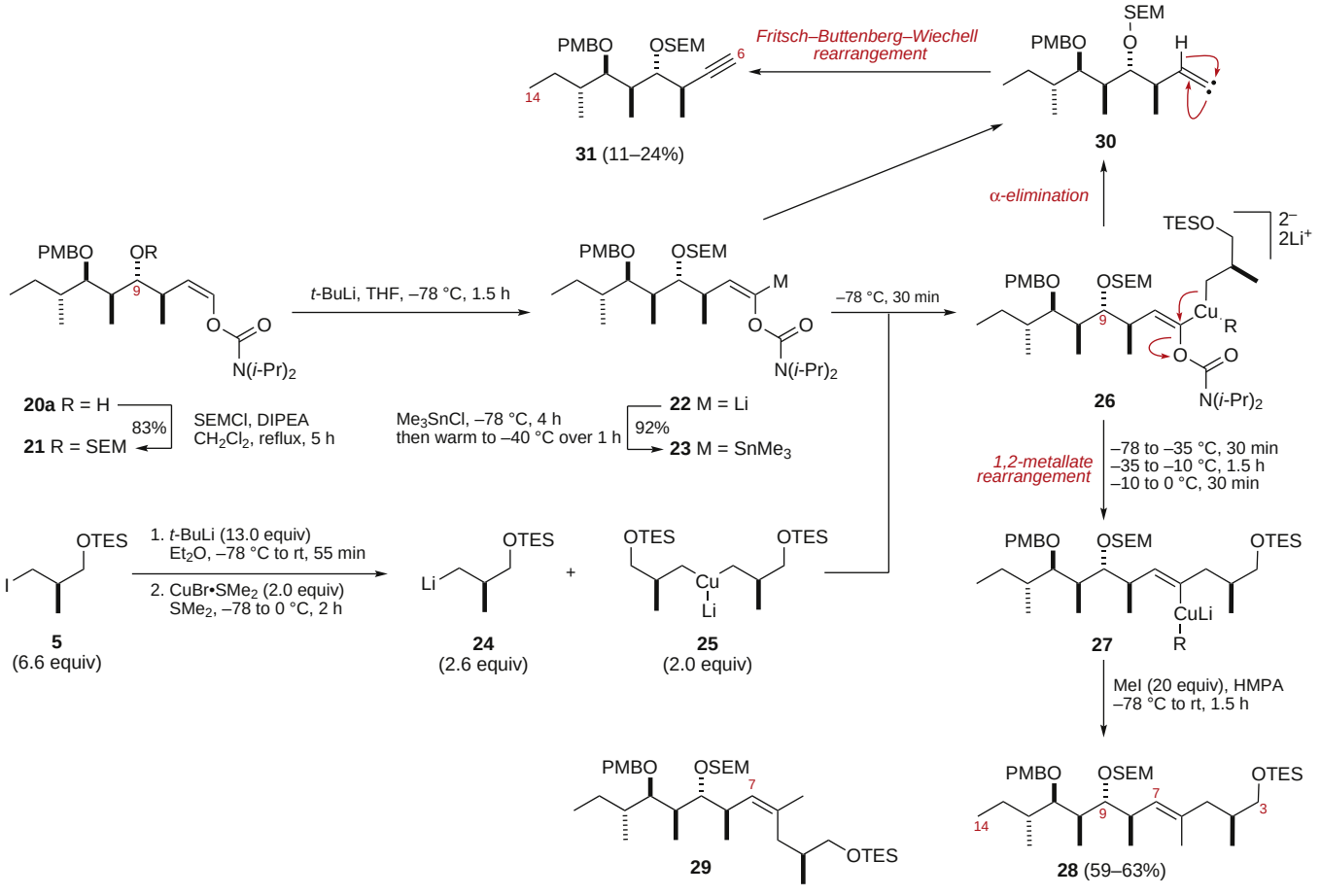


Scheme 3.

two new stereocentres in the required *anti*-relationship.[28] The reaction involved an *anti*-S_E' reaction of stannane **4** with titanium tetrachloride to give a crotyltitanium intermediate **18**. Addition of aldehyde **3** to the solution of intermediate **18** at −78 °C gave a separable 75:25 mixture of the (*Z*)-*anti*-adducts **20a** and **20b**, respectively, in an overall 84% yield. The dr of the reaction was assigned by integration of the signals corresponding to C7H recorded in the ^{1}H NMR spectrum of the crude mixture of **20a**,**b**.

The nexus of our synthesis of (−)-ebelactones A and B was the construction of the C6–C7 trisubstituted alkene via a 1,2-metallate rearrangement of the metallated enol carbamate **26** (Scheme 4).[29] A range of factors including the nature of the protecting group at C9, the solvent, temperature, time, scale and stoichiometry affected the course of the reaction. The sequence began with protection of the alcohol in **20a** as its 2-(trimethylsilyl)ethoxymethoxy (SEM) ether[30] (see below). The resultant enol carbamate **21** was then metallated with *t*-BuLi in THF at −78 °C and stannylated to afford **23**. A major consideration in the choice of metallation conditions was the instability of the lithiated carbamate **22**, which underwent easy α-elimination and thence Fritsch–Buttenberg–Wiechell rearrangement[31] to the alkyne **31**. For example, when the enol carbamate **21** was metallated with *t*-BuLi in Et_2O at −78 °C and Me_3SnCl added at −78 °C and the reaction mixture allowed to warm slowly over 6 h to −20 °C, the alkyne **31** was formed in 94% yield. This vexatious α-elimination reaction could be suppressed by using THF as the solvent whilst maintaining the temperature at −78 °C until the stannylation was completed.

Under the optimum conditions depicted in Scheme 4, the stannane **23** transmetallated to the lithium **22** and thence to the higher order cuprate **26** both of which are stable at low temperature. Best results were obtained when the transmetallation reactions were performed with a mixture of lithium reagent **24** (2.6 equiv) and the homocuprate **25** (2.0 equiv). On gradual warming, the higher order cuprate **26** underwent a stereospecific 1,2-metallate rearrangement with clean inversion of configuration[32] to give the alkenylcuprate **27**. In the final step of the sequence, the alkenylcuprate **27** reacted with a large excess of MeI in the presence of HMPA with retention of configuration to give the trisubstituted alkene **28** (*E*/*Z*≥97:3) in 59–63% yield.[33] The (*E*)- and (*Z*)-isomers are inseparable at this stage but easily distinguished in the ^{1}H NMR spectrum (500 MHz) by integration of the C7H signals at δ=5.24 (d, *J*=9.3 Hz) for the (*E*)-isomer **28** and δ=5.29 (d, *J*=8.8 Hz) for the (*Z*)-isomer **29**. Unfortunately, the temperature required for the 1,2-metallate rearrangement (−35 to −20 °C) coincides with the temperature at which α-elimination to the vinylidene carbene **30** occurs. Consequently, a competing Fritsch–Buttenberg–Wiechell rearrangement gave the alkyne **31** in 11–24% yield. Hence success depends on stabilizing the higher order cuprate **26** sufficiently to attain the requisite temperature for 1,2-metallate rearrangement to compete favourably with the α-elimination pathway. To that end stabilization of the higher order cuprate **26** is favoured by weakly coordinating solvents (Et_2O/pentane, 5:1) and further augmented by the presence of Me_2S.[34] Addition of even small amounts of THF diminished the yield of the alkene **28**, the *E*/*Z* ratio worsened (10:1) and several additional unidentified minor products were generated. An attempt to improve the ligand economy of the sequence by deploying CuCN as the Cu(I) source instead of $CuBr{\cdot}SMe_2$ failed to deliver improvements in yield and the reproducibility was poor.

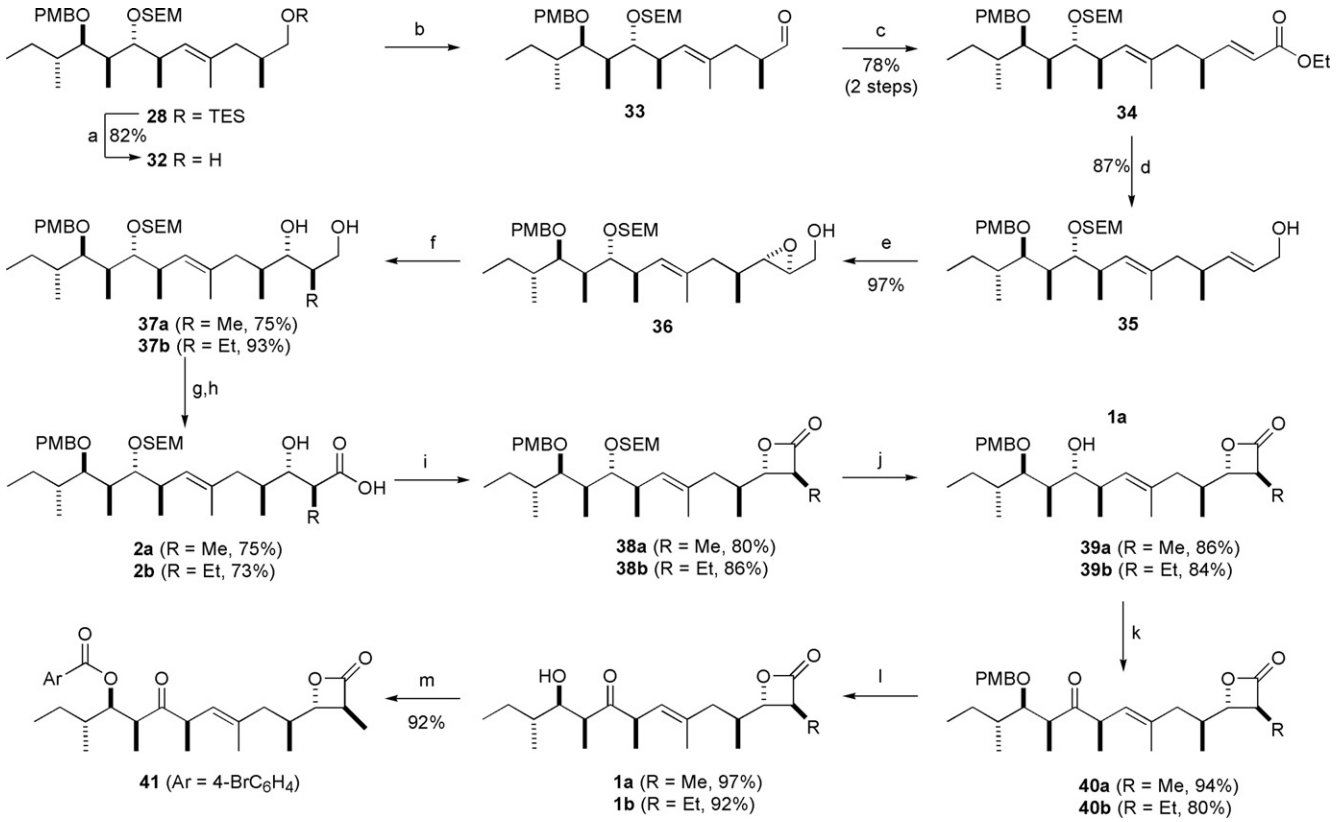


Scheme 4.

Completion of the synthesis of (−)-ebelactone A was accomplished using a series of conventional transformations depicted in Scheme 5 beginning with the deprotection of TES ether **28** using $Bu_4NF{\cdot}3H_2O$. Dess–Martin oxidation of the resulting primary alcohol **32** gave the aldehyde **33** that was used immediately in a Horner–Wadsworth–Emmons olefination. The α,β-unsaturated ester **34** (*E*/*Z*≥97:3) was obtained in 59% yield over two steps from **32**. Subsequent reduction of the ester with DIBAL-H gave the allylic alcohol **35** in 87% yield. At this stage any (*Z*)-trisubstituted alkene formed during the 1,2-metallate rearrangement reaction could now be separated by column chromatography.

benzenesulfonyl chloride at −20 °C using the procedure of Adam et al.[41] and gave the β-lactone **38a** in 80% yield.

A major impediment to the completion of the synthesis was the selective removal of the SEM protecting group in **38a** without detriment to the labile β-lactone ring or PMB protecting group. For example, treatment of **38a** with $Bu_4NF{\cdot}3H_2O$ or TASF $[(Me_2N)_3S^+Me_3SiF_2^-]$[42] in refluxing THF, HF in aqueous MeCN at rt or HF·py in THF at rt resulted in destruction of the substrate. However, SEM-deprotection was eventually accomplished by gently refluxing compound **38a** with pyridinium *p*-toluenesulfonate in *t*-BuOH to give the alcohol **39a** in 86% yield.[43] To



Scheme 5. Reagents and conditions: (a) $Bu_4NF{\cdot}3H_2O$ (1.1 equiv), THF, 0 °C, 2 h, 82%; (b) Dess–Martin periodinane (2.0 equiv, CH_2Cl_2, 0 °C to rt, 2 h; (c) $(EtO)_2P(O)CH_2CO_2Et$ (1.5 equiv), NaH (1.5 equiv), THF, −30 °C to rt, 17 h, 78% (two steps); (d) DIBAL-H (2.1 equiv), CH_2Cl_2, −78 °C to rt, 2.5 h, 87%; (e) (+)-DIPT (1.2 equiv), $Ti(O\text{-}i\text{-}Pr)_4$ (1.0 equiv), *t*-BuOOH (2.0 equiv), 4 Å MS, CH_2Cl_2, −20 °C, 48 h, 97%; (f) R_2CuLi (15 equiv), Et_2O, −40 °C to rt, 7 h then $NaIO_4$ (2.0 equiv), acetone/MeOH/H_2O (1:1:1), rt, 2 h; (g) $PhI(OAc)_2$ (1.5 equiv), TEMPO (0.1 equiv), CH_2Cl_2, rt, 7 h; (h) $NaClO_2$ (2.5 equiv), NaH_2PO_4 (7.7 equiv), 2-methyl-2-butene (5.7 equiv), *t*-BuOH/H_2O, rt, 1 h; (i) $PhSO_2Cl$ (4.0 equiv), py, −20 °C, 48 h; (j) PPTS (5.0 equiv), *t*-BuOH, reflux, 5 h; (k) Dess–Martin periodinane (1.1 equiv), CH_2Cl_2, 0 °C to rt, 1 h; (l) DDQ (1.5 equiv), CH_2Cl_2/H_2O (20:1), rt, 30 min; (m) 4-BrC_6H_4COCl (4.0 equiv), DMAP (4.0 equiv), py, rt, 18 h, 92%.

The remaining C2 and C3 stereocentres in (−)-ebelactone A were installed using an epoxidation/ring-opening protocol as reported by Kishi et al..[35,36] Sharpless asymmetric epoxidation[37] of the allylic alcohol **35** gave the epoxy alcohol **36** in 97% yield and dr ≥97:3. Treating epoxy alcohol **36** with a large excess of lithium dimethylcuprate gave an inseparable 8:1 mixture of the 1,3-diol **37a** and a 1,2-diol regioisomer. The regioisomeric ratio was determined by integration of the C7H ^{1}H NMR signals at δ=5.30 (1H, d, J=8.6) for the 1,3-diol **37a** and δ=5.24 (1H, d, J=9.0) for the 1,2-diol. Destruction of the 1,2-diol with sodium periodate gave **37a** in 75% yield from epoxy alcohol **36** after column chromatography. Chemoselective oxidation of the primary alcohol in diol **37a** gave the β-hydroxy acid **2a** in an overall 75% yield.[38–40] Formation of the *β*-lactone was accomplished by treating compound **2a** with freshly distilled

complete the synthesis, Dess–Martin oxidation of compound **39a** gave the labile ketone **40a** (94% yield) from which the PMB group was excised with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[44] to give crystalline (−)-ebelactone A (**1a**, mp 80–81 °C) in 97% yield. Spectroscopic data (^{1}H NMR, ^{13}C NMR and IR) recorded for **1a** prepared using this route agreed with the data reported by Umezawa et al.,[2] Paterson and Hulme[14,15] and Mandal.[16] The structure and stereochemistry of (−)-ebelactone A was confirmed by single crystal X-ray crystallography of the *p*-bromobenzoate derivative **41** (Fig. 1). By an analogous route (Scheme 5), crystalline (−)-ebelactone B (mp 71–72 °C) was prepared in seven steps (39% overall) from epoxy alcohol **37**. Spectroscopic data (^{1}H NMR, ^{13}C NMR and IR) recorded for our synthetic (−)-ebelactone B (**1b**) agreed with the data reported by Umezawa et al.[2] and Paterson and Hulme.[14,15]

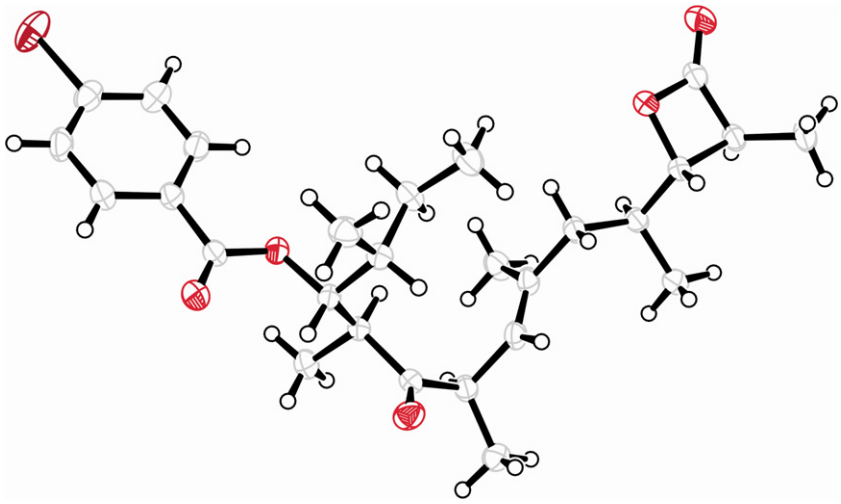


Figure 1. X-ray structure of ebelactone A *p*-bromobenzoate (**41**).

3. Conclusions

In conclusion, we have accomplished the synthesis of (−)-ebelactones A and B in 2.9% and 3.7% overall yields, respectively, for the longest linear sequence (24 steps) from a commercial precursor **6**. The synthesis features the use of a Hoppe homoaldol reaction and a Cu(I)-mediated 1,2-metallate rearrangement as key fragment linkage reactions. We have shown that by careful choice of reaction parameters, such as solvent and temperature, the 1,2-metallate rearrangement of a metallated enol carbamate can prevail over competing α-elimination and the stereochemical integrity of the resultant alkenylcuprate can be preserved during alkylation—both problems, which beset earlier attempts to exploit this chemistry in the construction of trisubstituted alkenes in polyketide natural products.[45–48] Recently Gais et al.[49] described an analogous route to trisubstituted alkenes based on the 1,2-metallate rearrangement of higher order sulfoximine-substituted cuprates, which are more stable than their alkenyl carbamate analogues and therefore potentially more practical.

4. Experimental

4.1. General

For general experimental details see the Supplementary data.

4.2. Procedure for the synthesis of alkene 28 via a 1,2-metallate rearrangement (Scheme 4)

A flame-dried 250 mL 3-neck round-bottom flask fitted with a magnetic stirring bar, addition funnel, thermometer and nitrogen inlet was charged with a solution of iodoalkane **5** (5.02 g, 16.0 mmol, 6.6 equiv, dried with activated 4 Å MS for 30 min prior to use) in Et_2O (65 mL). The solution was cooled to −78 °C and *tert*-butyllithium (1.55 M solution in pentane; 20.3 mL, 31.4 mmol, 13.0 equiv) was added dropwise at a rate sufficient to keep the internal reaction temperature ≤−75 °C. The resulting white suspension was stirred at −78 °C for 30 min whereupon the cooling bath was removed and the mixture allowed to warm to ambient temperature over 25 min forming a pale yellow solution. The reaction mixture was then re-cooled to −78 °C and a solution of freshly recrystallised Cu(I)Br·SMe_2 complex (994 mg, 4.84 mmol, 2.0 equiv) in SMe_2 (10 mL+8 mL rinse) was added dropwise at −78 °C, again at a rate sufficient to keep the internal reaction temperature ≤−75 °C. The resulting yellow suspension was warmed to −20 °C over 1.5 h and then to 0 °C for 30 min forming a white suspension. A solution of stannane **23** (1.83 g, 2.42 mmol, 1.0 equiv) in Et_2O (20 mL+7 mL rinse, dried with activated 4 Å MS for 30 min prior to use) was added dropwise to the reaction mixture at −78 °C, at a rate sufficient to keep the internal reaction temperature ≤−75 °C. The resulting yellow/orange suspension was stirred at −78 °C for 30 min, warmed to −35 °C over 30 min forming a pale yellow suspension that was warmed to −10 °C over 1.5 h and finally warmed to 0 °C over 30 min. The resulting white suspension containing the alkenylcuprate **27** was stirred at 0 °C for 30 min and then re-cooled to −78 °C whereupon a solution of iodomethane (freshly distilled from $CaCl_2$, 3.0 mL, 48.4 mmol, 20.0 equiv) in HMPA (1.8 mL), dried with activated 4 Å MS for 30 min prior to use, was added dropwise at a rate sufficient to keep the internal reaction temperature ≤−75 °C. The resulting yellow solution was stirred at −78 °C for 1.5 h whereupon the cooling bath was removed and the mixture allowed to warm to ambient temperature over 25 min. The reaction was quenched at rt with a mixture of saturated aqueous NH_4OH (150 mL) and saturated aqueous NH_4Cl (150 mL). The layers were separated and the aqueous layer extracted with Et_2O (3×300 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo. The residual yellow oil was purified by column chromatography on SiO_2 eluting with petrol/Et_2O (15:1) to give in order of elution the title compound **28** (995 mg, 1.53 mmol, 63%) and alkyne **31** (185 mg, 0.41 mmol, 17%) as colourless oils.

*4.2.1. Spectroscopic data for (2S,6R,7R,8S,9R,10R,E)-9-(4-methoxybenzyloxy)-2,4,6,8,10-pentamethyl-7-((2-trimethylsilyl)ethoxymethoxy)-1-(triethylsilyloxy)dodec-4-ene (**28**).* R_f (SiO_2)=0.52 (petrol/Et_2O, 15:1), E/Z ≥97:3. $[\alpha]_D^{21}$ −16.4 (*c* 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ=7.28 (2H, d, *J*=8.6, ArH), 6.87 (2H, d, *J*=8.6, ArH), 5.24 (1H, d, *J*=9.3, C7H), 4.75 (1H, d, *J*=6.9, C16H_AH_B), 4.71 (1H, d, *J*=6.9, C16H_AH_B), 4.58 (2H, s, $C15H_2$), 3.80 (3H, s, OCH_3), 3.77 (1H, apparent q, *J*=8.8, C17H_AH_B), 3.60 (1H, apparent q, *J*=8.8, C17H_AH_B), 3.52 (1H, dd, *J*=7.3, 1.5, C11H), 3.45 (1H, dd, *J*=9.8, 5.6, C3H_AH_B), 3.35 (1H, dd, *J*=8.6, 2.2, C9H), 3.30 (1H, dd, *J*=9.8, 7.5, C3H_AH_B), 2.63 (1H, qdd, *J*=9.3, 7.1, 2.2, C8H), 2.10 (1H, dd, *J*=13.0, 5.4, C5H_AH_B), 1.86–1.72 (1H, m, C4H), 1.78–1.66 (3H, m, C5H_AH_B/C12H/C13H_AH_B), 1.71–1.59 (1H, m, C10H), 1.59 (3H, s, $C6CH_3$), 1.23–1.13 (1H, m, C13H_AH_B), 1.01–0.94 (2H, m, $C18H_2$), 0.98 (3H, d, *J*=7.1, $C8CH_3$), 0.96 (9H, t, *J*=8.0, $Si(CH_2CH_3)_3$), 0.93 (3H, t, *J*=7.5, $C14H_3$), 0.89 (3H, d, *J*=6.9, $C10CH_3$), 0.85 (3H, d, *J*=7.1, $C12CH_3$), 0.83

(3H, d, J=6.6, C4CH_3), 0.59 (6H, q, J=8.0, Si(CH_2CH_3)$_3$), 0.02 (9H, s, Si(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.0 (C_{Ar}), 133.1 (C_{Ar}), 132.3 (C6), 128.8 (2C_{Ar}H), 127.5 (C7H), 113.8 (2C_{Ar}H), 97.2 (C16H_2), 86.9 (C9H), 83.0 (C11H), 73.5 (C15H_2), 68.4 (C3H_2), 65.8 (C17H_2), 55.4 (OCH_3), 44.1 (C5H_2), 39.2 (C10H), 38.4 (C12H), 35.3 (C8H), 34.3 (C4H), 25.7 (C13H_2), 19.2 (C8CH_3), 18.4 (C18H_2), 16.7 (C6CH_3), 16.3 (C14H_3), 16.2 (C12CH_3), 12.0 (C10CH_3), 11.1 (C4CH_3), 7.0 (Si(CH_2CH_3)$_3$), 4.7 (Si(CH_2CH_3)$_3$), −1.2 (Si(CH_3)$_3$). IR (neat): ν_{max}=2956s, 2876s, 1514m, 1461m, 1248s, 1092s, 1029s cm^{-1}. HRMS (ES$^+$ mode): found 673.4657 (M$^+$+Na). $C_{37}H_{70}NaO_5Si_2$ requires 673.4659. Anal. calcd for $C_{37}H_{70}O_5Si_2$: C 68.25, H 10.84, found: C 68.50, H 10.90%.

*4.2.2. Spectroscopic data for (3R,4R,5S,6R,7R)-9-(4-methoxybenzyloxy)-3,5,7-trimethyl-4-((2-trimethylsilyl)ethoxymethoxy)non-1-yne (**31**).* R_f (SiO_2)=0.37 (petrol/Et_2O, 15:1). $[\alpha]_D^{21}$ −38.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.27 (2H, d, J=8.3, ArH), 6.87 (2H, d, J=8.3, ArH), 4.80 (1H, d, J=7.1, C16H_AH$_B$), 4.74 (1H, d, J=7.1, C16H$_A$$H_B$), 4.60 (1H, d, J=11.2, C15H_AH$_B$), 4.56 (1H, d, J=11.2, C15H$_A$$H_B$), 3.80 (3H, s, OCH_3), 3.77 (1H, apparent q, J=8.8, C17H_AH$_B$), 3.64 (1H, apparent q, J=8.8, C17H$_A$$H_B$), 3.55 (1H, d, J=7.3, C11H), 3.37 (1H, dd, J=8.6, 2.4, C9H), 2.82–2.75 (1H, m, C8H), 2.09 (1H, d, J=2.1, C6H), 2.06 (1H, qdd, J=7.3, 7.1, 2.4, C10H), 1.77–1.65 (2H, m, C12H/C13H_AH$_B$), 1.25 (3H, d, J=7.1, C8CH_3), 1.27–1.14 (1H, m, C13H$_A$$H_B$), 1.00 (3H, d, J=7.1, C10CH_3), 1.01–0.91 (2H, m, C18H_2), 0.94 (3H, t, J=7.6, C14H_3), 0.91 (3H, d, J=6.6, C12CH_3), 0.02 (9H, s, Si(CH_3)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.0 (C_{Ar}), 132.0 (C_{Ar}), 128.7 (2C_{Ar}H), 113.8 (2C_{Ar}H), 96.8 (C16H_2), 85.8 (C7), 84.7 (C9H), 82.4 (C11H), 73.4 (C15H_2), 70.1 (C6H), 65.9 (C17H_2), 55.3 (OCH_3), 39.1 (C10H), 38.2 (C12H), 29.4 (C8H), 25.8 (C13H_2), 18.3 (2C, C8CH_3/C18H_2), 15.9 (C12CH_3), 12.0 (C14H_3), 11.0 (C10CH_3), −1.3 (Si(CH_3)$_3$). IR (neat): ν_{max}=3310m, 2957s, 2877s, 1613m, 1514s, 1463m, 1248s, 1055s, 1029s cm^{-1}. HRMS (ES$^+$ mode): found 471.2897 (M$^+$+Na). $C_{26}H_{44}NaO_4Si$ requires: 471.2907. Anal. calcd for $C_{26}H_{44}O_4Si$: C, 69.59; H, 9.88. Found: C, 69.60; H, 10.05%.

Supplementary data

Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.05.072.

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