

Stereocontrolled asymmetric synthesis of *syn-E*-1,4-diol-2-enes using allyl boronates and its application in the total synthesis of solandelactone F†

Anna Robinson and Varinder K. Aggarwal*

Received 23rd November 2011, Accepted 2nd December 2011

DOI: 10.1039/c2ob06975j

The solandelactones A–H comprise a novel class of oxygenated fatty acids bearing an eight-membered lactone, *trans* cyclopropane, and a 2-ene-1,4-diol subunit. The relative stereochemistry of the 1,4-diol subunit is *anti* in solandelactones A, C, E & G, and *syn* in solandelactones B, D, F & H. Having prepared one member of the solandelactones bearing *anti* stereochemistry (solan-delactone E), we have targeted the *syn* series and developed methodology for the synthesis of enantioenriched *syn*-2-ene-1,4-diols. The methodology comprises asymmetric deprotonation of an alkyl 2,4,6-triisopropylbenzoate using *s*BuLi/sparteine, followed by addition of the α -lithiobenzoate to β -silyl vinyl boronic acid ethylene glycol ester. The boron-ate complex generated undergoes a 1,2-metallate rearrangement furnishing an intermediate allyl boronic ester which is trapped by an aldehyde in the presence of MgBr₂ to furnish *anti*- β -hydroxy *E*-allylsilanes in good yields, high diastereoselectivity and high enantioselectivity. These sensitive products were oxidized using *m*CPBA to the corresponding epoxides and subsequently treated with acid to furnish *syn-E*-2-ene-1,4-diols (~4 : 1 d.r.). Application of the methodology to appropriately functionalized aldehyde and ω -alkenyl 2,4,6-triisopropylbenzoate coupling partners, led to a short, highly selective route to solandelactone F (bearing a *syn-E*-2-ene-1,4-diol).

Introduction

The solandelactones comprise a novel class of oxygenated fatty acids first isolated and characterised by Shin in 1996.¹ (Fig. 1) Their general structure features an eight-membered lactone, *trans* cyclopropane, a 2-ene-1,4-diol subunit, and numerous stereogenic centers, making them challenging synthetic targets. Their correct structure, however, has only recently been validated by

Martin through total synthesis, the original assignment having incorrect stereochemistry at C11.²

The syntheses of all solandelactones A–H have been reported.^{2–5} Martin completed the first synthesis of solandelactone E in 2007, which was highly stereoselective, but linear and therefore somewhat lengthy.² Syntheses of the remaining solandelactones were subsequently reported by White³ and Pietruszka,⁴ who both opted for disconnections at C11–C12 and utilized a Nozaki–Hiyama–Kishi (NHK) reaction to complete the syntheses. However, the NHK reaction between the required vinyl organometallic reagent and cyclopropyl aldehyde (Scheme 1) proceeded with poor stereocontrol, leading to a ~2 : 1 mixture of epimers at C11, in favour of the *anti* diol.^{3,4} Thus, solandelactones A, C, E & G were prepared as the major products but solandelactones B, D, F & H were only isolated as

School of Chemistry, University of Bristol, Cantock's Close, Bristol, UK, BS8 1TS. E-mail: V.Aggarwal@Bristol.ac.uk

† Electronic supplementary information (ESI) available: Materials including experimental procedures, NMR spectra of all new products. See DOI: 10.1039/c2ob06975j

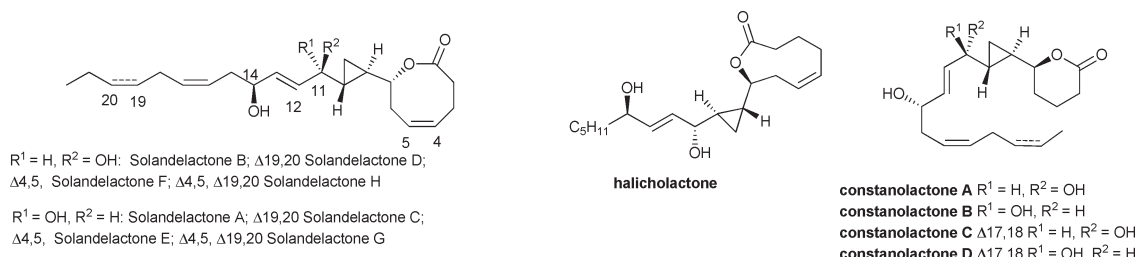
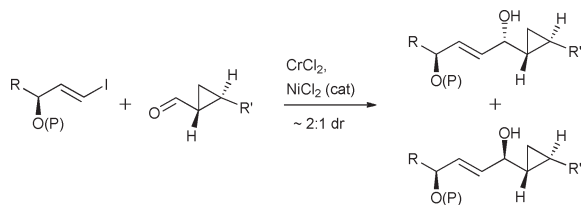
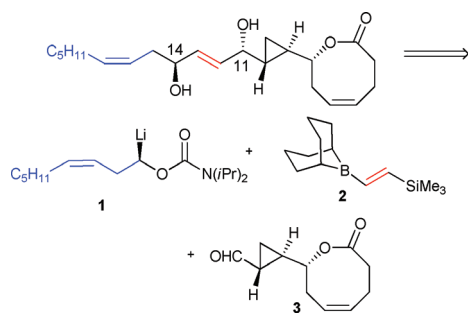


Fig. 1 Structure of the solandelactones, halicholactone and constanolactones.



Scheme 1 Common bond construction (NHK reaction) in the syntheses of solandelactones, halicholactone and constanolactones.



Scheme 2 Retrosynthetic analysis of solandelactone E.

the minor components from the NHK reaction. Indeed, the same selectivity issue has been observed in numerous syntheses of related natural products including halicholactone⁶ and the constanolactones.⁷ For example, there are currently five published syntheses of halicholactone, four of which use the poorly selective NHK coupling reaction. The alternative route by Takemoto, avoids this strategy, but is also the longest synthesis to date.⁸ Three of the four syntheses of constanolactones A–D also involve a poorly selective NHK reaction as the key step.⁷

Our strategy for the synthesis of solandelactone E addressed both the issue of stereocontrol and convergence simultaneously. Through disconnection of solandelactone E at the C11–C12 and

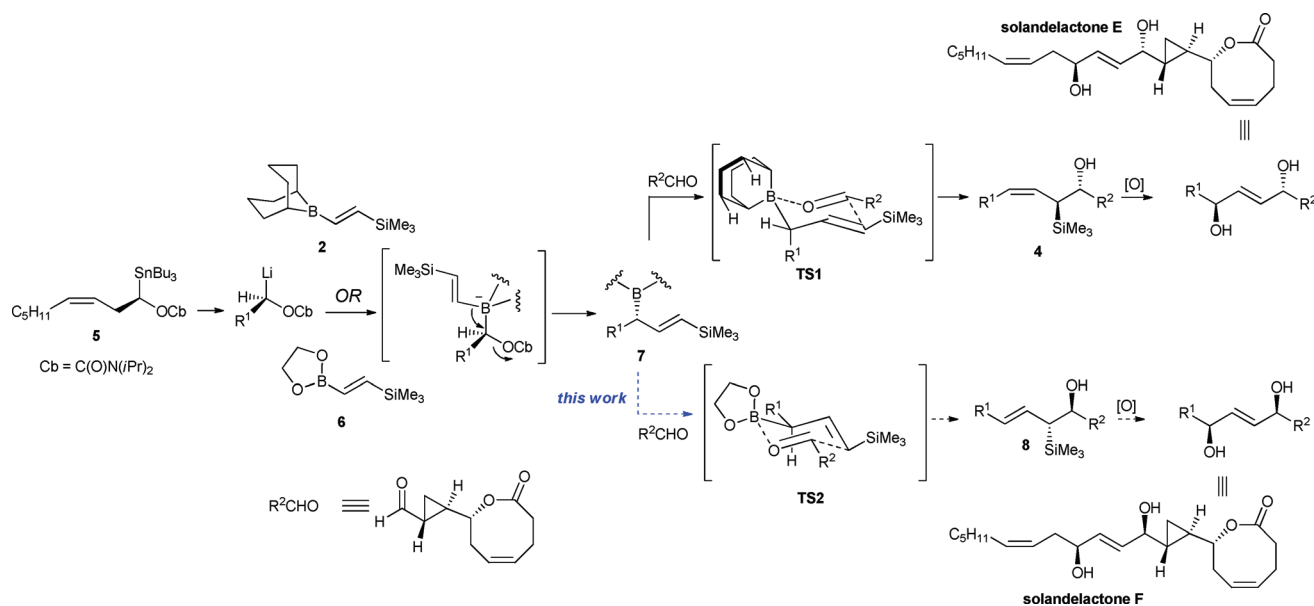
C13–C14 bonds we were able to use our novel stereocontrolled methodology for the synthesis of *anti*-2-ene-1,4-diols (Scheme 2).⁹ Thus, treatment of lithiated carbamate **1** with vinyl borane **2** and aldehyde **3** led to *anti*- β -hydroxy *Z*-allylsilane **4** via 6-membered chair TS1 with high stereoselectivity, which was subsequently converted into the required *anti*-1,4-diol (Scheme 3).⁵

In order to specifically target the other series of solandelactones we needed a method that would deliver *syn*-1,4-diols. These could possibly be prepared from oxidation of either *syn*- β -hydroxy *Z*-allylsilanes or *anti*- β -hydroxy *E*-allylsilanes, compounds which are potentially accessible from the allylboration reaction.¹⁰ Stereocontrol in the allylboration reaction is ultimately dictated by the geometry of the allyl boron reagent and by the nature of the ligands on boron.¹¹ However, all the possible isomers of *syn*- β -hydroxy *Z*-allylsilanes are not accessible from any boron reagent, but *anti*- β -hydroxy *E*-allylsilanes are.^{9d,12} These could potentially be obtained from the reaction of the allylboron reagent **7** bearing small substituents on boron,^{9d} so that upon reaction with an aldehyde, the R¹ substituent would occupy a pseudoequatorial position in the 6-membered chair TS2 (Scheme 3). Allylboron reagent **7** could in turn be obtained from reaction of the same lithiated carbamate **1** with vinyl boronic ester **6**. Although this appears to represent a small modification, there were a number of major challenges inherent in the realization of this plan. Ultimately, we were able to overcome these hurdles and thus develop a new protocol for the synthesis of *syn* 2-ene-1,4-diols which enabled us to craft a stereocontrolled synthesis of solandelactone F.

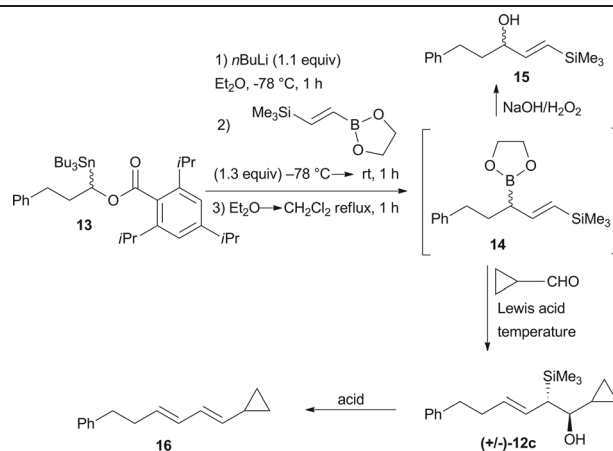
Results & Discussion

Synthesis of *anti* *E/Z*-alkyl-substituted β -hydroxy allylsilanes

The synthesis of *syn* or *anti* *E/Z*-alkyl-substituted β -hydroxy allylsilanes, key components in our targeted synthesis of



Scheme 3 Synthesis of solandelactone E and proposed synthesis of solandelactone F.

Table 1 Optimization of the allylboration reaction

Entry	Lewis acid (equiv.)	T/°C	Time/h	Yield 15 (%)	Yield 16 (%)	Yield 12c (%)
1 ^a	MgBr ₂ ·Et ₂ O (1 equiv.)	-20	18	50	—	29
2	MgBr ₂ ·Et ₂ O (1 equiv.)	-20	18	—	75	—
3	MgBr₂·Et₂O (1 equiv.)	-30	24	—	12	75
4	MgBr ₂ ·Et ₂ O (1 equiv.)	-40	18	26	—	43
5	MgBr ₂ ·Et ₂ O (1 equiv.)	-40	36	28	—	58
6	MgBr ₂ ·Et ₂ O (2 equiv.)	-60	19	46	9	30

^a Complete reaction conducted in Et₂O, without solvent exchange

solandelactone F, is not straightforward and usually requires multiple steps.¹³ Whilst routes have been developed for the synthesis of β-hydroxy allylsilanes bearing terminal alkenes,^{13a-d,f,k} those bearing substituted alkenes have scarcely been documented.^{13e,f,h}

In our synthesis of solandelactone E, the key step in the formation of the *anti*-β-hydroxy *Z*-allylsilane was achieved by reaction of the required Hoppe-type lithiated carbamate¹⁴ with vinyl borane **2** followed by addition of an aldehyde (Scheme 3). The key allylborane intermediate was formed after 1,2-metallate rearrangement of the intermediate boron-ate complex, a reaction pioneered by Matteson¹⁵ and subsequently developed by Kocienski,¹⁶ Blakemore¹⁷ and ourselves.^{9b} This furnished the *anti*-β-hydroxy *Z*-allylsilane **4** in high yield and very high diastereo- and enantioselectivity. Subsequent epoxidation and acid catalyzed rearrangement gave the *anti*-1,4-diol, again with very high selectivity. In order to target the *syn*-1,4-diol, we needed the *anti*-β-hydroxy *E*-allylsilane which could potentially be obtained from reaction of allylboronic ester **7** with a suitable aldehyde. In turn, allylboronic ester **7** could be obtained from reaction of a lithiated carbamate with vinyl boronic ester **6**.²⁴ However, compared to the *anti*-1,4-diols, the preparation of the *syn*-1,4-diol series suffers from the following significant challenges:

(i) The diastereoselectivity in epoxidation of *E*-allylsilanes is considerably lower than for *Z*-allylsilanes.^{18,19}

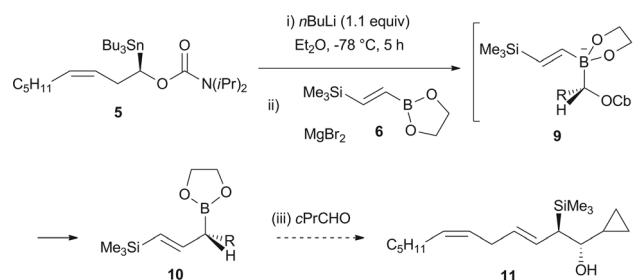
(ii) The 1,2-metallate rearrangement is much slower with boronic esters compared to boranes.²⁰

(iii) The allylic boronic ester is also much slower at allylboration compared to the allyl borane.^{21,9d}

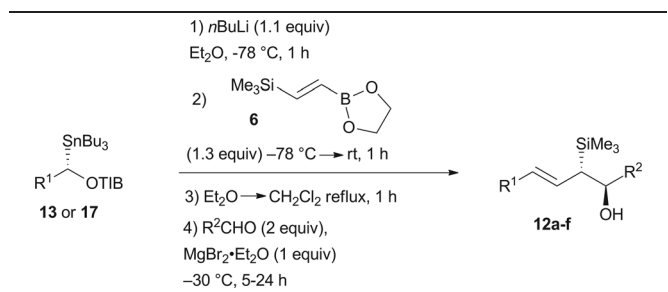
(iv) Although both the 1,2-metallate rearrangement^{9b,22} and allylboration reaction²³ can both be accelerated by Lewis acids,

Lewis acids can also promote Peterson elimination of β-hydroxy allylsilanes to give dienes.

These challenges proved insurmountable when we employed vinyl boronic ester **6** in the lithiation–borylation reaction with carbamate **5** (Scheme 4).²⁵ Although the boronate complex **9** easily formed, we were unable to effect both the 1,2-migration and subsequent allylboration reactions cleanly. The use of Lewis acids (e.g. MgBr₂) to promote 1,2-migration resulted in Peterson elimination of the β-hydroxy *E*-allylsilane **11**. In contrast, the use of thermal conditions to promote the 1,2-migration resulted in a subsequent 1,3-borotropic shift of the intermediate allyl boronic ester **10** (for a full discussion of this investigation see ESI†).²⁶ We therefore sought a better leaving group than the carbamate for the 1,2-metallate rearrangement and focused on the 2,4,6-triisopropyl benzoyl group, which we had found to be effective in lithiation–borylation reactions involving slow migrating substituents.²⁷

**Scheme 4** Attempted synthesis of *anti*-*E*-allylsilanes.

Beak first showed that the position α to an alkyl 2,4,6-triisopropylbenzoate could be deprotonated and trapped with

Table 2 Synthesis of *E*-allyl silanes

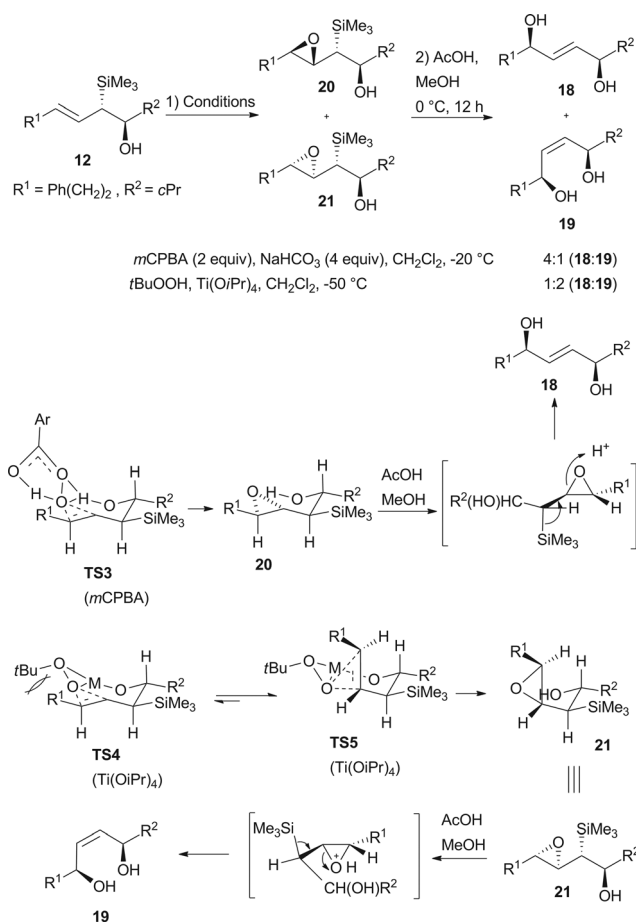
Entry	R ¹	R ²	Product	Yield (%) ^a	d.r.	e.r. ^b
1	Ph(CH ₂) ₂ (13)	Ph	12a	61	>20 : 1	95 : 5
2	Ph(CH ₂) ₂ (13)	<i>n</i> Bu	12b	70	>20 : 1	95 : 5
3	Ph(CH ₂) ₂ (13)	<i>c</i> Pr	12c	75	>20 : 1	95 : 5
4	Me (17)	Ph	12d	88	20 : 1	91 : 9
5	Me (17)	<i>n</i> Bu	12e	64	19 : 1	91 : 9
6	Me (17)	<i>c</i> Pr	12f	64	10 : 1	91 : 9

^a Isolated yield. ^b The e.r. of the product was identical to the e.r. of the starting stannane. *c*Pr = cyclopropyl

electrophiles.²⁸ Hammerschmidt demonstrated that this reaction could be performed enantioselectively, through a tin-lithium exchange and that the lithiated benzoate was configurationally stable at -78 °C.²⁹ Work within our group has shown that this lithiated species, formed by transmetalation of the stannane with *n*-BuLi, or by deprotonation with *s*-BuLi/sparteine, undergoes a lithiation-borylation reaction with a broad range of especially challenging boronic esters.²⁷

Thus, the benzoate ester **13** was prepared, lithiated and reacted with boronic ester **6** at -78 °C. Heating the ate complex for just 1 h at 40 °C effected a much more rapid 1,2-metallate rearrangement. Subsequent addition of cyclopropylaldehyde and MgBr₂·OEt₂ at -20 °C gave the *anti*-β-hydroxy *E*-allylsilane **12c** as a single diastereoisomer in 29% yield. However, large amounts of alcohol **15** were also isolated indicating that the allylboration step had not gone to completion (Table 1, entry 1). We therefore decided to carry out a solvent exchange from Et₂O to the less coordinating CH₂Cl₂ in order to maximize the effect of the Lewis acid.^{9d} Thus, after the boron-ate complex formation, Et₂O was removed and CH₂Cl₂ added, the reaction was heated at reflux for 1 h, followed by the aldehyde and MgBr₂·OEt₂ at -20 °C, but this now led to the Peterson elimination product **16** in 75% yield (Table 1, Entry 2). This indicated that essentially complete conversion of **13**→**14**→**12c** had been achieved, but that under the reaction conditions the Lewis acid was also promoting elimination. Careful control of temperature and time was required to produce optimum results (Table 1). Lower temperatures reduced the amount of the elimination side-product **16** but also led to increased amounts of alcohol **15**. Optimum conditions were the use of just one equivalent of MgBr₂·Et₂O at -30 °C which gave the *anti* β-hydroxy *E*-allylsilane **12c** in excellent yield and with complete diastereoselectivity (Entry 3).

These conditions were applied to a range of aliphatic and aromatic aldehydes and to several unhindered benzoates to explore the generality and selectivity of the reaction (Table 2). In general, the *anti* β-hydroxy *E*-allylsilanes **12** were formed in excellent yield and high diastereoselectivity (*via* TS2, Scheme 3)

**Scheme 5** Selectivity in the epoxidation/elimination reaction of β-hydroxy *E*-allylsilanes.

even when a small Me group (R¹) was present (entries 4–6). The enantiomeric excess of the product reflected the e.r. of the starting stannane, which in turn was a reflection of the selectivity in deprotonation by *s*-BuLi/sparteine.

Epoxidation of β-hydroxy allylsilanes and conversion to 1,4-diols

β-Hydroxy allylsilanes are versatile building blocks in organic synthesis, undergoing a range of transformations, including Fleming–Tamao oxidation,^{13d,30} fluorination,³¹ addition to acetals,³² [3+2] annulations³³ and [4+2] annulations.³⁴

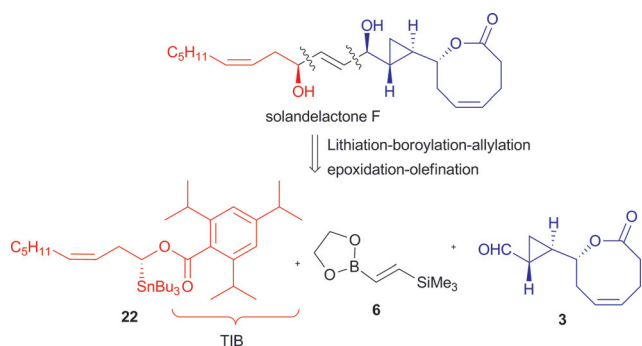
Of particular interest to us was epoxidation followed by acid catalyzed elimination^{13a,b} leading to 1,4-*syn* diols for application in the synthesis of the solandelactones. The facial selectivity of epoxidation of β-hydroxy *E*-allylsilanes can be influenced by the oxidizing reagent employed, but the diastereoselectivity is usually low, in contrast to related *Z*-allylsilanes which invariably lead to very high stereoselectivity.^{15,16,35} As expected, moderate-low diastereoselectivity was observed with **12d**: using *m*CPBA a ~4 : 1 ratio *E*-1,4-diol **18** : *Z*-1,4-diol **19** was obtained, whilst using Ti(O*i*Pr)₄/*t*BuOOH the *Z*-1,4-diol was favored (2 : 1) (Scheme 5).³⁶

Landais¹⁸ has accounted for the stereochemical outcome of this type of reaction by invoking a chair-like transition-state,

with the bulky silyl group adopting a pseudoequatorial position to minimize $A^{1,3}$ strain (Scheme 5). With *m*CPBA there is little steric interaction between R^1 and *m*CPBA, so the reaction goes through the hydrogen bonded **TS3** leading to epoxide **20** as the major product. However, with $Ti(OiPr)_4$ and *t*BuOOH there is significant steric repulsion between R^1 and the bulky oxidizing reagent in **TS4** which is alleviated by placing the olefin in a pseudoaxial position (**TS5**), resulting in epoxidation on the opposite face and leading to **21** as the major product.

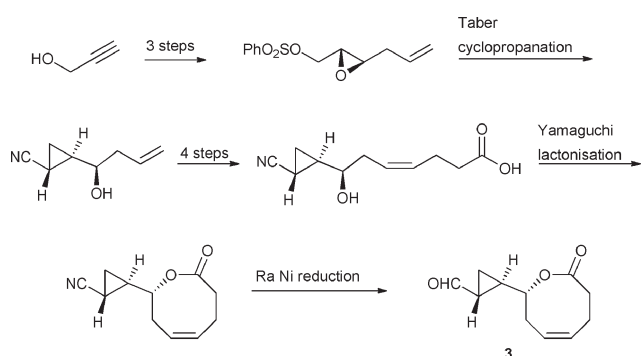
Completion of the synthesis of solandelactone F

Finally, we turned our attention to the application of this methodology to the synthesis of solandelactone F. Disconnection of the *syn*-*E*-2-ene-1,4-diol according to the methodology described above gives aldehyde **3** (as used in the synthesis of solandelactone E⁵), vinyl boronic ester **6** and stannane **22** (Scheme 6).



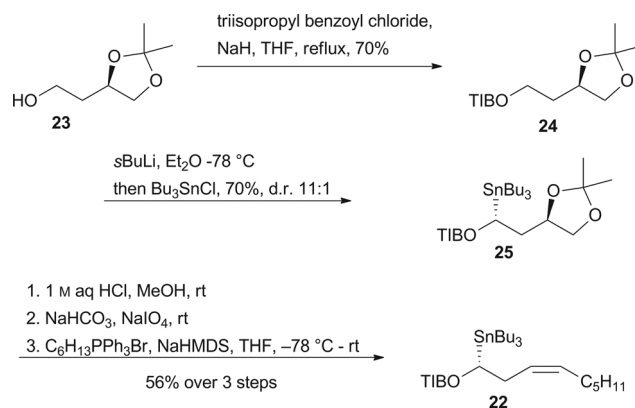
Scheme 6 Retrosynthesis of solandelactone F.

Aldehyde **3** was synthesized in ten steps from propargylic alcohol as previously described (Scheme 7).⁵ The key steps included a Sharpless epoxidation,³⁷ Taber cyclopropanation,³⁸ Yamaguchi lactonization and chemoselective RANEY® nickel reduction of the nitrile in the presence of the lactone.³⁹



Scheme 7 Synthesis of aldehyde **3**.⁵

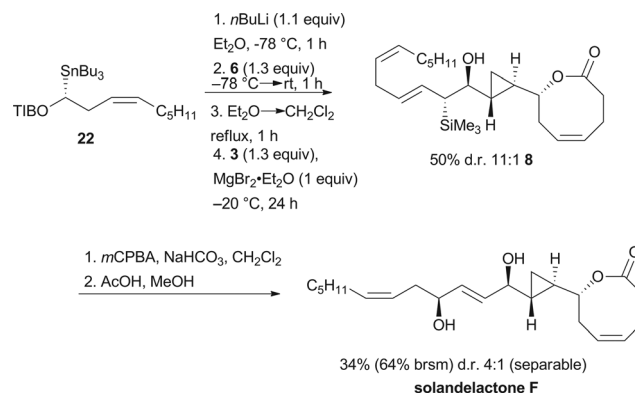
Stannane **22** was prepared as shown in Scheme 8. Following conversion of the commercially available alcohol **23** into benzoate **24**, substrate-directed lithiation and trapping with Bu_3SnCl (as described by Hoppe⁴⁰) furnished stannane **25** with 11 : 1 d.r. (inseparable). Installation of the required aliphatic chain was



Scheme 8 Synthesis of the required stannane for the synthesis of solandelactone F.

achieved by a sequence of acetal deprotection, oxidative cleavage and Wittig olefination to give stannane **22** (Scheme 8).

Application of our optimized conditions for lithiation–borylation–allylation with stannane **22**, aldehyde **3** and β -silyl vinylboronic ester **6**, gave our desired *E*-allylsilane **8** in 50% yield and with the same d.r. as the e.r. of the stannane. It should be noted that stannane **22** was required in this process to ensure specific lithiation α to the benzoate. Direct deprotonation of the corresponding carbamate or benzoate with *s*-BuLi/sparteine resulted in substantial deprotonation at the allylic position followed by elimination. Epoxidation with one equivalent of *m*CPBA effected chemoselective epoxidation and, following acid catalyzed elimination, gave solandelactone F as the major stereoisomer (Scheme 9). Although the epoxidation/rearrangement only occurred in 34% yield, the yield based on recovered SM was 64% as we found it best to ensure that the reaction did not go to completion as otherwise side-products were formed. Synthetic solandelactone F was identical in all respects to the data reported in the literature.^{1,3,4}



Scheme 9 Completion of the synthesis of solandelactone F.

Conclusion

In conclusion, we have developed a selective method for the synthesis of enantioenriched *anti*- β -hydroxy *E*-allylsilanes. The

components used to assemble such motifs comprise an α -alkyl lithiated hindered benzoate, β -silyl vinyl ethylene glycol boronic ester, and an aldehyde. Thus, reaction of the lithiated benzoate with the boronic ester gave an intermediate allyl boronic ester which was trapped with an aldehyde in the presence of the Lewis acid, $MgBr_2$ to give the *anti* β -hydroxy *E*-allylsilane in high yield and high d.r. Key to the success of this one pot transformation is the use of the alkyl 2,4,6-triisopropylbenzoate which enables the 1,2-metallate rearrangement to proceed under milder conditions and leads to the formation of the intermediate allyl boronic ester without interference from side reactions. Through complex-induced proximity effects it also directs the initial lithiation. The use of a small group on boron (ethylene glycol) is key to controlling the relative stereochemistry in the aldehyde-allylboration step. The optimized conditions and reagents employed have now considerably increased the range of both the alkyl benzoates and the aldehydes that can participate in the reaction.

The methodology has enabled us to complete a short, highly selective route to solandelactone F. Previously this compound and the series in general had been isolated as minor components from a mixture. However, now we can target either solandelactones A, C, E & G using our previously described methodology comprising a lithiated carbamate, β -silyl vinyl-9BBN **2** and an aldehyde, or the remaining solandelactones B, D, F, & H using the methodology described herein.

Acknowledgements

We thank the EPSRC for support of this work. VKA thanks the Royal Society for a Wolfson Research Merit Award and the EPSRC for a Senior Research Fellowship. We thank Professor Hisashi Yamamoto for a generous gift of bishydroxamic acid ligands to test reagent controlled epoxidations.

Notes and references

- 1 Y. Seo, K. W. Cho, J.-R. Rho and J. Shin, *Tetrahedron*, 1996, **52**, 10583–10596.
- 2 (a) J. E. Davoren and S. F. Martin, *J. Am. Chem. Soc.*, 2007, **129**, 510–511; (b) J. E. Davoren, C. Harcken and S. F. Martin, *J. Org. Chem.*, 2008, **73**, 391–402.
- 3 (a) J. D. White, W. H. C. Martin, C. Lincoln and J. Yang, *Org. Lett.*, 2007, **9**, 3481–3483; (b) J. D. White, C. Lincoln, J. Yang, W. H. C. Martin and D. B. Chan, *J. Org. Chem.*, 2008, **73**, 4139–4150.
- 4 J. Pietruszka and A. C. Rieche, *Adv. Synth. Catal.*, 2008, **350**, 1407–1412.
- 5 A. Robinson and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2010, **49**, 6673–6675.
- 6 For syntheses of halicholactone featuring a NHK coupling see: (a) D. J. Critcher, S. Connolly and M. Wills, *J. Org. Chem.*, 1997, **62**, 6638–6657; (b) D. J. Critcher, S. Connolly and M. Wills, *Tetrahedron Lett.*, 1995, **36**, 3763–3766; (c) T. Takahashi, H. Watanabe and T. Kitahara, *Heterocycles*, 2002, **58**, 99–104; (d) C.-Y. Zhan, X.-Y. Cao, B.-H. Zhu, C. Deng, X.-L. Sun, B.-Q. Wang, Q. Shen and Y. Tang, *Chem.-Eur. J.*, 2009, **15**, 11465–11468; (e) M. Bischoff, V. Doum, A. C. M. Nordschild (née Rieche), J. Pietruszka and D. Sandkuhl, *Synthesis*, 2010, **3**, 527–537.
- 7 For syntheses of constanolactone featuring a NHK coupling see: (a) J. Pietruszka and T. Wilhelm, *Synlett*, 2003, 1698–1700; (b) J. Pietruszka, A. C. M. Rieche and N. Schoene, *Synlett*, 2007, 2525–2528; (c) C. B.-D. Silva, A. Benkouider and P. Pale, *Tetrahedron Lett.*, 2000, **41**, 3077–3081; (d) J. D. White and M. S. Jensen, *J. Am. Chem. Soc.*, 1995, **117**, 6224–6233.
- 8 (a) Y. Takemoto, Y. Baba, G. Saha, S. Nakao, C. Iwata, T. Tanaka and T. Ibuka, *Tetrahedron Lett.*, 2000, **41**, 3653–3656; (b) Y. Baba, G. Saha, S. Nakao, C. Iwata, T. Tanaka, T. Ibuka, H. Ohishi and Y. Takemoto, *J. Org. Chem.*, 2001, **66**, 81–88.
- 9 (a) M. Binanzer, G. Y. Fang and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2010, **49**, 4264–4268; . For other related work on lithiated carbamates see: (b) J. L. Stymiest, G. Dutheil, A. Mahmood and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2007, **46**, 7491–7494; (c) G. Dutheil, M. P. Webster, P. A. Worthington and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2009, **48**, 6317–6319; (d) M. Althaus, A. Mahmood, J. Ramón Suárez, S. P. Thomas and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2010, **132**, 4025–4028.
- 10 (a) S. E. Denmark and N. G. Almstead, in *Modern Carbonyl Chemistry*; J. Otera, ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 10, p 299; (b) S. R. Chemler and W. R. Roush, in *Modern Carbonyl Chemistry*; J. Otera, ed.; Wiley-VCH: Weinheim, Germany, 2000; Chapter 11, p 403; (c) H. Lachance and D. G. Hall, in *Organic Reactions*; S. E. Denmark, ed.; John Wiley & Sons: New York, 2008, Vol. 73; (d) S. E. Denmark and J. Fu, *Chem. Rev.*, 2003, **103**, 2763; (e) W. R. Roush, in *Stereo-selective Synthesis*, 4th ed.; G. Helmchen, R. W. Hoffman, J. Muler, E. Schaumann, ed.; Thieme Verlag: Stuttgart, 1996; Vol. 3, p 1410.
- 11 (a) R. W. Hoffmann and H.-J. Zeiss, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 306; (b) R. W. Hoffmann and H.-J. Zeiss, *J. Org. Chem.*, 1981, **46**, 1309; (c) R. W. Hoffmann, *Pure Appl. Chem.*, 1988, **60**, 123; (d) R. W. Hoffmann, G. Niel and A. Schlapbach, *Pure Appl. Chem.*, 1990, **62**, 1993.
- 12 The synthesis of *anti*- β -hydroxy *E*-allylsilanes via allylboration has been reported, however products were not isolated but eliminated on work-up to give dienes: K. K. Wang, Y.-G. Gu and C. Liu, *J. Am. Chem. Soc.*, 1990, **112**, 4424–4431.
- 13 (a) W. R. Roush and P. T. Grover, *Tetrahedron Lett.*, 1990, **52**, 7567–7570; (b) W. R. Roush and P. T. Grover, *Tetrahedron*, 1992, **48**, 1981–1998; (c) W. R. Roush, A. N. Pinchuk and G. C. Micalizio, *Tetrahedron Lett.*, 2000, **41**, 9413–9417; (d) A. G. M. Barrett and J. W. Malecha, *J. Org. Chem.*, 1991, **56**, 5243–5254; (e) M. A. Sparks and J. S. Panek, *J. Org. Chem.*, 1991, **56**, 3431–3438; (f) D. Hodgson and M. C. Wells, *Tetrahedron Lett.*, 1992, **33**, 4761–4762; (g) A. Alexakis and D. Jachiet, *Tetrahedron*, 1989, **45**, 381–389; (h) N. Kishi, T. Maeda, K. Mikami and T. Nakai, *Tetrahedron*, 1992, **48**, 4087–4098; For impressive recent applications see: (i) J. Wu, Y. Chen and J. S. Panek, *Org. Lett.*, 2010, **12**, 2112–2115; (j) J. Lee and J. S. Panek, *Org. Lett.*, 2011, **13**, 502–505; (k) M. Chen and W. R. Roush, *Org. Lett.*, 2011, **13**, 1992–1995.
- 14 For a review of Hoppe's seminal contributions see: (a) D. Hoppe and T. Hense, *Angew. Chem.*, 1997, **109**, 2376–2410; D. Hoppe and T. Hense, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2282–2316; (b) E. Beckmann, V. Desai and D. Hoppe, *Synlett*, 2004, 2275–2280.
- 15 (a) D. S. Matteson and D. Majumdar, *J. Am. Chem. Soc.*, 1980, **102**, 7588–7590; (b) D. S. Matteson, *Chem. Rev.*, 1989, **89**, 1535–1551.
- 16 G. Besong, K. Jarowicki, P. J. Kocienski, E. Sliwinski and F. T. Boyle, *Org. Biomol. Chem.*, 2006, **4**, 2193–2207.
- 17 P. R. Blakemore and M. S. Burge, *J. Am. Chem. Soc.*, 2007, **129**, 3068–3069.
- 18 Y. Landais and L. Parra-Rapado, *Tetrahedron Lett.*, 1996, **37**, 1205–1208.
- 19 (a) I. Fleming, A. K. Sarkar and A. P. Thomas, *J. Chem. Soc., Chem. Commun.*, 1987, 157–159; I. Fleming, N. J. Lawrence, A. K. Sarkar and A. P. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1992, 3303–3308.
- 20 For examples, see: (a) J. M. Stoddard and K. J. Shea, *Chem. Commun.*, 2004, 830; (b) A. Bottoni, M. Lombardo, A. Neri and C. Trombini, *J. Org. Chem.*, 2003, **68**, 3397; (c) G. Y. Fang and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2007, **46**, 359.
- 21 Allylboranes react readily with aldehydes at $-78\text{ }^\circ\text{C}$ (a), whereas allylboronic esters require room temperature or above (b). For examples see: (a) H. C. Brown and P. K. Jadhav, *J. Am. Chem. Soc.*, 1983, **105**, 2092; (b) R. W. Hoffmann and B. Landmann, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 437–438.
- 22 (a) D. J. S. Tsai, P. K. Jesthi and D. S. Matteson, *J. Am. Chem. Soc.*, 1983, **105**, 2077–2078.
- 23 (a) J. W. J. Kennedy and D. G. Hall, *J. Am. Chem. Soc.*, 2002, **124**, 11586; (b) T. Ishiyama, T. Ahiko and N. Miyaura, *J. Am. Chem. Soc.*, 2002, **124**, 12414–12415; . For reviews, see: (c) D. G. Hall, *Synlett*, 2007, **11**, 1644; (d) J. W. J. Kennedy, D. G. Hall, in *Boronic Acids*; D. G. Hall, ed.; Wiley-VCH: Weinheim, Gerandmany, 2005; Chapter 6, p 241.
- 24 The ethylene glycol boronic ester was chosen as this is what we had found to work best with β -silylvinyl boronic esters (ref. 9a). The

- corresponding β -silylvinyl neopentyl glycol boronic esters gave considerably lower diastereoselectivity ($\sim 80 : 20$). In contrast, β -alkylvinyl neopentyl glycol boronic esters gave $>95 : 5$ d.r. (ref. 9d).
- 25 We had previously described a single example of the synthesis of an *anti*- β -hydroxy *E*-allylsilane, but our only real success was with the aromatic aldehyde, benzaldehyde. See ref. 9a.
- 26 (a) R. W. Hoffmann and H. J. Zeiss, *J. Org. Chem.*, 1981, **46**, 1309–1314; (b) H. C. Brown, M. V. Rangaishenvi and S. Jayaraman, *Organometallics*, 1992, **11**, 1948–1954.
- 27 R. Larouche-Gauthier, C. J. Fletcher, I. Couto and V. K. Aggarwal, *Chem. Commun.*, 2011, **47**, 12592–12594.
- 28 P. Beak, M. Baillargeon and L. G. Carter, *J. Org. Chem.*, 1978, **43**, 4255–4256.
- 29 F. Hammerschmidt, A. Hanninger, B. P. Simov, H. Völlenkle and A. Werner, *Eur. J. Org. Chem.*, 1999, 3511–3518.
- 30 J. A. Hunt and W. R. Roush, *J. Org. Chem.*, 1997, **62**, 1112–1124.
- 31 G. T. Giuffredi, S. Purser, M. Sawicki, A. L. Thompson and V. Gouverneur, *Tetrahedron: Asymmetry*, 2009, **20**, 910–920.
- 32 J. S. Panek and M. Yang, *J. Am. Chem. Soc.*, 1991, **113**, 6594–6600.
- 33 J. S. Panek and M. Yang, *J. Am. Chem. Soc.*, 1991, **113**, 9868–9870.
- 34 H. Huang and J. S. Panek, *J. Am. Chem. Soc.*, 2000, **122**, 9836–9837.
- 35 *Z*-Allylsilanes usually give high diastereoselectivity in epoxidation in contrast to *E*-allylsilanes with either *m*CPBA or metal-mediated reactions. This is because the conformation of *Z*-allylsilanes is far better controlled, and thus epoxidation occurs almost exclusively through a single conformer.
- 36 The substrate scope with *m*CPBA was briefly explored as this was most relevant to our synthesis of solandelactone F. Indeed, this reaction worked well on a range of substrates. See supporting information for further details†.
- 37 For Sharpless epoxidation of this substrate see: (a) Y. E. Raifeld, A. A. Nikitenko, B. M. Arshava, I. E. Mikerin, L. L. Zilberg, G. Y. Vid, S. A. Lang Jr. and V. J. Lee, *Tetrahedron*, 1994, **50**, 8613–8616; (b) X. Ginesta, M. A. Pericas and A. Riera, *Tetrahedron Lett.*, 2002, **43**, 779–782; For Sharpless' seminal work on catalytic asymmetric epoxidation see: (c) Y. Gao, J. M. Klunder, R. M. Hanson, H. Masamune, S. Y. Ko and K. B. Sharpless, *J. Am. Chem. Soc.*, 1987, **109**, 5765–5780; (d) H. C. Kolb, M. S. Van Nieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483–2547.
- 38 D. F. Taber, G. Bui and B. Chen, *J. Org. Chem.*, 2001, **66**, 3423–3426.
- 39 O. G. Backeberg and B. Staskun, *J. Chem. Soc.*, 1962, 3961–3963.
- 40 H. Helmke and D. Hoppe, *Synlett*, 1995, 978–980.