

A stereoselective synthesis of 1,6-diphenyl-1,3,5-hexatrienes utilising 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane as a two-carbon alkenyl building block

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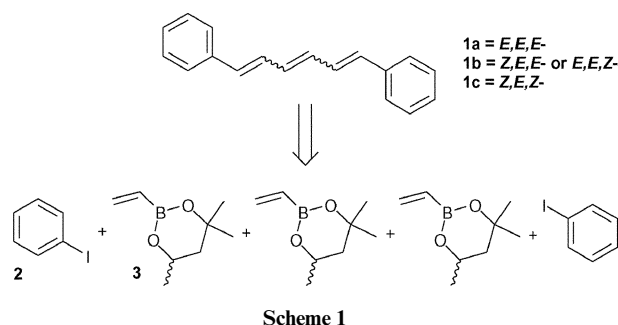
A number of 1,6-diphenyl-1,3,5-hexatrienes of varying alkene geometries were stereoselectively prepared from just two starting materials: iodobenzene and 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane *via* a series of Heck, Suzuki–Miyaura and stereocontrolled iododeboronation reactions. These results demonstrate how 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane can be used as a genuine two-carbon vinyl-dianion building block in stereocontrolled polyene synthesis.

Introduction

The development of efficient strategies for the stereoselective synthesis of polyenes which can be applied to complex natural product synthesis is an important goal.¹ Indeed, this has been the subject of ongoing investigations within our group, resulting in the development of methodology employing a pinacol vinylboronate ester to act as an alkenyl building block,² and the process showed some early success culminating in the synthesis of the natural product and selective herbicide phthoxazolin A.³ Further development in the application to the synthesis of a further natural product, viridenomycin,⁴ was hampered by a number of practicality issues involving the use of the pinacol vinylboronate ester.

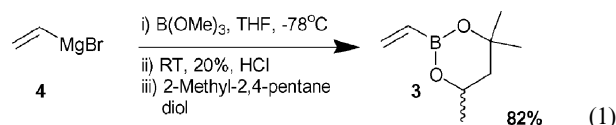
Recently we reported the development of an alternative vinylboronate ester, 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane **3**,⁵ which was free of a number of preparatory and physical problems associated with the pinacol form. Under palladium catalysed coupling conditions the ester **3** can undergo Heck coupling reactions with a range of substrates generating the desired products with greater selectivity and in increased yields.⁵ The substituted alkenylboronate ester can also undergo stereocontrolled iododeboronation reactions to generate *E*- or *Z*-iodoalkenes.⁶ Again, the ester of 2-methyl-2,4-pentanediol has been shown to give superior yields of the desired product albeit with the same high selectivity.⁷ Most recently we have reported the selective use of 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane in Suzuki–Miyaura reactions to prepare a number of styrenes and dienes.⁸ These reported results demonstrate that we have developed procedures where the vinylboronate ester can act as a vinyl-dianion equivalent being able to react exclusively at either end along the Heck or Suzuki–Miyaura pathways, dependent on the conditions employed to perform the reaction. This is further exemplified by results presented in this paper.

Herein we demonstrate how the three reactions discussed can be used in combination to prepare polyene systems; in the present case, the diphenylhexatriene model systems. The products are prepared from just two starting materials: iodobenzene, of which there are two units providing each aryl fragment, and three 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane **3** units which provide each alkene unit of the triene proving how the vinylboronate ester can be genuinely be regarded as a two-carbon alkenyl building block (see Scheme 1).



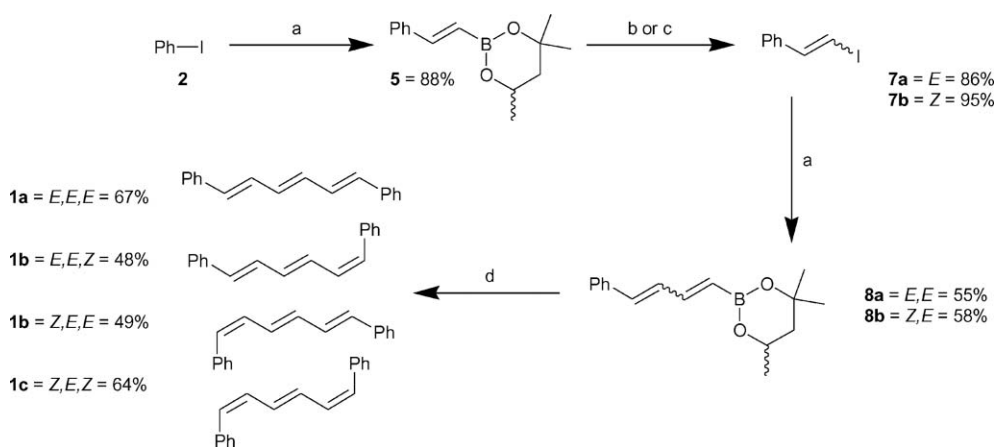
Results and discussion

The first part of the synthesis required the preparation of our key building block reagent, 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinane **3**. This is effected following the procedure outlined in eqn. (1) which is robust and can be performed easily on multi-gram scale to give the desired product **3** in consistently high yields after distillation.



The initial reaction along the proposed synthetic route to the trienes was the Heck coupling of iodobenzene **2** with the vinylboronate ester **3** (Scheme 2). This first reaction links the aryl group and one of the three alkenyl units and use of the standard coupling conditions generally gives a small amount of Suzuki–Miyaura product (Table 1, entry 1), although on occasion complete selectivity can be obtained. The styrene side-product **6** can be easily separated from the desired boronate **5**; however, its presence reduces the control over the system and the yield of the desired product **5**. Other reaction conditions were therefore investigated to develop a procedure that consistently gave complete Heck selectivity.

A number of examples exist in the literature in which metal additives have been used in Heck coupling reactions. Thallium(I) salts, particularly TIOAc, have been shown to induce a rate accelerating effect on the Heck coupling process over a range of organic electrophiles.⁹ In addition, silver(I) salts have been



Scheme 2 Reagents and conditions: a) Pd(OAc)₂ (5 mol%), PPh₃ (15 mol%), *n*Bu₃N (1.2 equiv.), AgOAc (1.2 equiv.), **3** (1.2 equiv.), toluene, 110 °C, 24 h; b) (i) NaOMe/MeOH (1.2 equiv.), THF, -78 °C, 30 min, (ii) ICl/DCM (1.2 equiv.), -78 °C to rt, 2 h; c) (i) ICl/DCM (1.2 equiv.), DCM, -78 °C, 4 h, (ii) NaOMe/MeOH (1.2 equiv.), -78 °C to rt, 30 min; d) Pd(PPh₃)₄ (5 mol%), Ag₂O (2 equiv.), **7a** or **7b** (1 equiv.), THF, 65 °C, 24 h.

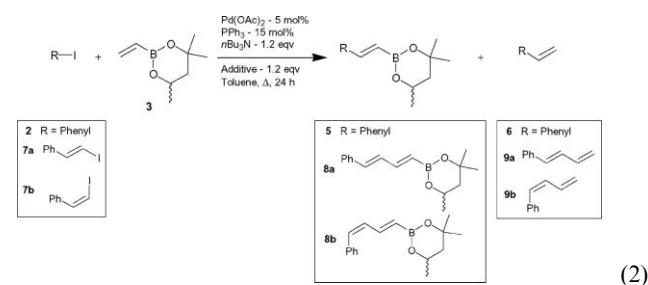
Table 1 Optimised Heck coupling of vinylboronate **3** with iodobenzene **2** and styryl iodides **7**

Entry	Iodide	Additive	H : S-M ^a	Yield (%) ^b
1	2	—	91 : 9	73
2	2	TIOAc	100 : 0	86
3	2	AgOAc	100 : 0	88
4	7a	TIOAc	84 : 16	51
5	7a	AgOAc	88 : 12	55
6	7b	TIOAc	65 : 35	46
7	7b	AgOAc	100 : 0	58

^a The product ratio was derived from the ¹H NMR of the crude reaction material. ^b The yield quoted is the isolated yield after purification by silica gel chromatography.

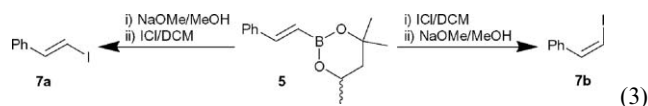
shown to have a similar effect, and of particular relevance, allowing the preparation of dienes from the coupling of *E*- or *Z*-alkenyl iodides with allylic alcohols whilst retaining the alkene geometries.¹⁰ A comparative study of the use of TIOAc and AgOAc in the Heck reaction was performed for the preparation of conjugated dienylic aromatics from aromatic iodides and dienes.¹¹ Both additives gave impressive yields, with TIOAc giving slightly higher values; however, in every case isomerisation of the starting alkene occurred and, as a consequence, only the *E,E*-dienes were obtained, showing that this strategy for the preparation of such systems is unfortunately flawed.

We therefore examined both thallium(I) and silver(I) acetates as additives to determine their effect on this Heck reaction [eqn. (2)], paying particular attention to the ratio of the Heck : Suzuki–Miyaura products formed. As is shown in Table 1 (entries 2 and 3), the use of both metal acetate additives resulted in complete selectivity of the reaction for the desired Heck product, the styrylboronate **5** from the reaction of the vinylboronate ester **3** with iodobenzene **2**, which allows the isolation of the desired styrylboronate **5** in greater yields than without the metal salt additive.



With the desired Heck product **5** in hand, the next step was to convert it into both the alkenyl iodides **7**. Conditions for the iododeboronation reactions have been developed in

our group giving either the *E*- or *Z*-alkenyl iodide with very high geometrical purity using iodine monochloride and sodium methoxide.⁶ The order of reagent addition determines the stereochemical outcome: initial treatment with sodium methoxide before addition of the ICl affords the *E*-styryl iodide **7a**, whereas reaction with ICl followed by sodium methoxide generates the *Z*-styryl iodide **7b** [eqn. (3)]. The ester of 2-methyl-2,4-pentanediol again gives improved yields over the pinacol form albeit with the same level of selectivity. Using these reaction conditions both styryl iodides were prepared in high yields (**7a** = 86%, **7b** = 95%) and with what is of greater significance very high geometrical purity (**7a** = 98%, **7b** = 96%). It is noteworthy that the quality of the ICl reagent is of extreme importance, particularly with regard to the level of conversion of the starting material and hence the yield of the reaction.



After the successful iododeboronation reactions, the second alkenyl unit was introduced through another Heck coupling reaction of the vinylboronate **3**, but on this occasion, with the *E*- and *Z*-alkenyl iodides **7a** and **7b** respectively. To date, the coupling of aryl systems had been predominantly explored using the 2-methyl-2,4-pentanediol boronate ester derivatives, rather than alkenyl; however, the conditions for these couplings were based on those developed for the aryl systems.

A series of screening reactions was therefore carried out to determine what the preferred coupling conditions for the preparation of dienylic boronates **8** from styryl iodides **7** and vinylboronate **3** were; the results are shown in Table 2. The first thing to note is the very poor Heck selectivity shown for both iodides **7a** and **7b** under the standard conditions (Table 2, entries 2 and 9), which in the case of the *E*-iodide **7a** favours the formation of the Suzuki–Miyaura product. This contrasts dramatically with the results obtained for iodobenzene and a number of other aryl substrates where the by-product formation was minimal.⁵ This surprising result led us to investigate a further range of reaction variables to assess their impact upon the Heck : Suzuki–Miyaura selectivity of the coupling reaction (Table 2).

The standard coupling conditions (Table 2, entries 2 and 9) established the 'natural' selectivities of the coupling of each iodide, and the effect of other variables on this ratio was then investigated. Initially, and most obviously, the choice of palladium ligand was examined; however, variations of the phosphine ligands had a minimal effect on the product ratio (Table 2, entries 2–5), and there was very little variation in the selectivity. It was also expected that the use of bulky bidentate ligands would have a dramatic effect on the selectivity of the

Table 2 Heck coupling of the vinylboronate **3** with styryl iodides **7**: variables and their influence on the Heck : Suzuki–Miyaura product ratio

Entry	Iodide	Ligand	Base	Solvent	Additive	<i>T</i> /°C	Conversion (%) ^a	H : S–M ^b ratio
1	7b	—	<i>n</i> Bu ₃ N	Toluene	—	110	100	58 : 42 ^c
2	7b	PPh ₃	<i>n</i> Bu ₃ N	Toluene	—	110	100	53 : 47
3	7b	P(<i>o</i> -tolyl) ₃	<i>n</i> Bu ₃ N	Toluene	—	110	100	32 : 68
4	7b	P ^{<i>t</i>} Bu ₃	<i>n</i> Bu ₃ N	Toluene	—	110	100	58 : 42
5	7b	P(2-furyl) ₃	<i>n</i> Bu ₃ N	Toluene	—	110	100	54 : 46
6	7b	1,10-Phenanthroline	<i>n</i> Bu ₃ N	Toluene	—	110	13	100 : 0
7	7b	PPh ₃	<i>n</i> Bu ₃ N	Toluene	TIOAc	110	100	65 : 35
8	7b	PPh ₃	<i>n</i> Bu ₃ N	Toluene	AgOAc	110	100	100 : 0
9	7a	PPh ₃	<i>n</i> Bu ₃ N	Toluene	—	110	100	34 : 66
10	7a	BINAP ^d	<i>n</i> Bu ₃ N	Toluene	—	110	63	29 : 71
11	7a	DUPHOS ^e	<i>n</i> Bu ₃ N	Toluene	—	110	0	—
12	7a	XANTHPHOS ^f	<i>n</i> Bu ₃ N	Toluene	—	110	36	43 : 57
13	7a	PPh ₃	<i>n</i> Bu ₃ N	Toluene	—	78	15	30 : 70
14	7a	PPh ₃	<i>n</i> Bu ₃ N	Acetonitrile	—	78	49	35 : 65
15	7a	PPh ₃	<i>n</i> Bu ₂ NH	Acetonitrile	—	78	37	35 : 65
16	7a	PPh ₃	<i>n</i> BuNH ₂	Acetonitrile	—	78	84	26 : 74
17	7a	PPh ₃	<i>n</i> Bu ₃ N	Toluene	TIOAc	110	100	84 : 16
18	7a	PPh ₃	<i>n</i> Bu ₃ N	Toluene	AgOAc	110	100	88 : 12

^a Determined from the ratio of starting iodide to products in the ¹H NMR of the crude reaction material. ^b The product ratio was derived from the ¹H NMR of the crude reaction material. ^c Isomerisation of the *Z*-alkene to the *E*-form occurred for both products. ^d 2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene. ^e (–)-1,2-Bis[(2*R*,5*R*)-2,5-dimethylphospholano]benzene. ^f 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene.

reaction (Table 2, entries 10–12). However, there was a small degree of change in selectivity but a dramatic reduction in the conversion of the reaction. Indeed, in the case of the DUPHOS ligand, the reaction failed altogether. The use of the amine ligand 1,10-phenanthroline (Table 2, entry 6) resulted in a dramatic increase in Heck selectivity; however, the conversion under these conditions is very low at just 13%. This led to testing the reaction in the absence of any ligand (Table 2, entry 1). Surprisingly, this gave full conversion and a product ratio comparable with those obtained previously; however, isomerisation of the *Z*-alkene occurred, so that both of the products possessed an internal *E*-alkene. The isomerisation of the *Z*-alkene most likely occurs in the coupled products rather than during the reaction. The lack of an added ligand would result in stabilisation of the palladium(0) species through π -coordination of the products, and any allylation formation, however, would lead to the isomerisation to give the all *E*-alkenyl product.

Changing the solvent from toluene to acetonitrile, both at reflux, resulted in a reduction in conversion (Table 2, entries 9 and 14); however, this can most likely be attributed to the lower temperature of the reaction, rather than any significant solvent effect. Indeed, using toluene at a lower temperature induces a lower conversion (Table 2, entry 13).

Three different bases were also used for this reaction (Table 2, entries 14–16), tri-*n*-butylamine, di-*n*-butylamine and *n*-butylamine. It was hoped the different steric and basicity effects would perhaps perturb the Heck selectivity obtained using tri-*n*-butylamine, but no significant changes in product selectivity were obtained and as identified above the low levels of conversion obtained can be attributed to performing the reaction in refluxing acetonitrile.

The use of the metal additives, *i.e.* thallium(i) and silver(i) acetates (Table 2, entries 7, 8, 17 and 18) was the only variable that resulted in a dramatic change in product selectivity. The Heck selectivity of the *E*-styryl iodide **7a** coupling swung dramatically in favour of the Heck product when using both additives (Table 2, entries 17 and 18). There was little difference between using either thallium or silver, both additives being suitable for scale up and isolation of the product diene **8a** in good yields. The optimised reactions are shown in Table 1 (entries 4 and 5).

There was a more marked difference in using the two different metal additives when coupling the *Z*-styryl iodide **7b** to the vinylboronate **3** (Table 2, entries 7 and 8). Although both thallium(i) and silver(i) acetate increased the Heck selectivity compared to that without additive (Table 2, entry 2), the increase in selectivity was more modest using the thallium salt compared

to silver, which gave complete Heck selectivity. This was further demonstrated by reaction scale up and isolation of the desired *Z,E*-dienylboronate **8b** (Table 1, entries 6 and 7). In all cases, the expected retention of alkenyl iodide geometry was observed, with no isomerisation under these reaction conditions.

Hence, an overall survey of Table 2 shows that the only really significant factor in boosting Heck selectivity is the presence of the metal additives, thallium(i) or silver(i) acetate, and that these should be used (if required), and to achieve high conversions the reactions should be performed in refluxing toluene. Also, the preferable base and palladium ligand (Table 2) are triphenylphosphine and tri-*n*-butylamine respectively. These conditions were scaled up and applied to the synthesis of the desired triene **1** syntheses, *via* formation of the dienylboronates **8**, as shown in Table 1. Completion of the syntheses of trienes **1** required Suzuki–Miyaura couplings of the dienylboronates **8a** and **8b** to be performed with the *E*- and *Z*-alkenyl iodides **7a** and **7b** [eqn. (4)], which in turn were prepared as outlined previously [eqn. (3)] with high geometric purity from the styrylboronate **5**. The conditions used were the same as those that had proved to be successful in our study involving the reactivity of the vinylboronate ester **3** in Suzuki–Miyaura reactions.⁸ For the coupling of **7a** and **7b**, the choice of base was of vital importance: the use of 'hard' alkoxide and hydroxide bases led to the elimination of HI from the substrates resulting in phenylacetylene formation and reduced amounts, if any, of the desired coupled product. This led to the use of silver(i) oxide as the base.^{8,12} This proved to be successful allowing the coupling reactions [eqn. (4)] to generate the desired trienes **1** with no side-product formation. These key coupling steps were consequently performed in the presence of silver(i) oxide, the results of which are shown in Table 3.

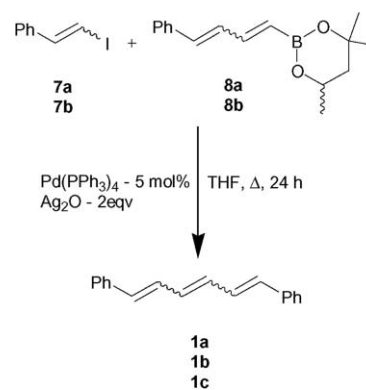


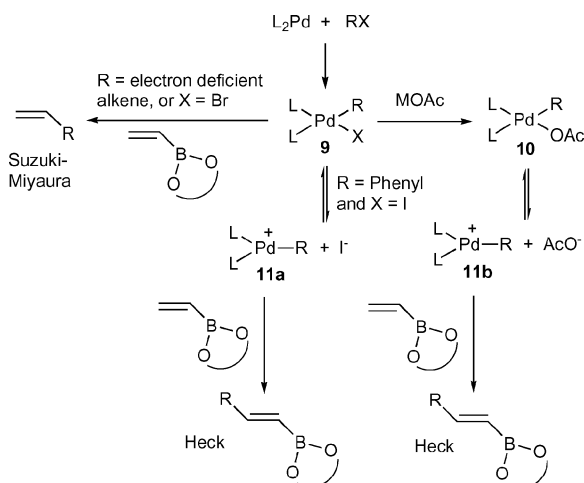
Table 3 Suzuki–Miyaura coupling reactions of the dienylboronate esters

Entry	Iodide	Boronate	Product	Yield (%) ^a
1	7a	8a	1a	67
2	7a	8b	1b	48
3	7b	8a	1b	49
4	7b	8b	1c	64

^a Isolated yield after silica gel chromatography.

Overall, the reactions proceeded in good yields and as with the Suzuki–Miyaura couplings of the boronate **3** the use of silver(I) oxide allowed coupling with no phenylacetylene formation. The dienylboronate esters **5** show similar levels of reactivity to the vinylboronate systems and, importantly, no alkene isomerisation was observed under the reaction conditions developed. However, the triene products **1** are susceptible to isomerisation to the all-*E*-form **1a**, either under heating above the reaction temperature of 65 °C, as reinforced by identical melting points, or even upon storage at room temperature over a few months which was observed in the cases of **1b** and **1c**.

Having demonstrated the overall strategy for efficiently and stereoselectively producing trienes **1**, we are left to consider exactly why thallium(I) and silver(I) salts are necessary in order to avoid the unwanted production of Suzuki–Miyaura products in the approaches to products **8** [see eqn. (2), and Tables 1 and 2]. These results augment our previous work in the area, coupling aryl halides with vinylboronate esters,² which does not require the co-addition of metal salts, except when using heteroaromatic halides.¹³ Iodides certainly perform better than bromides, as is the case with alkenyl halides, with alkenyl bromides proving unreactive under Heck coupling conditions.⁶ Electron deficient iodoalkenes (*e.g.* iodo acrylate) fail to undergo Heck coupling at all with hindered vinylboronate esters¹⁴ even with the co-addition of thallium or silver salts, though they react efficiently to give the Suzuki–Miyaura products. Although further detailed mechanistic studies are required, we believe that all the current evidence points in the direction of the need to have a cationic palladium species in order to drive the Heck coupling pathway and avoid the formation of Suzuki–Miyaura products, *i.e.* as outlined in Scheme 3.



Scheme 3

Thus, use of aryl halide substrates favours the formation of a cationic palladium intermediate **11a** by dissociation of iodide ion from palladium(II) complex **9**, as does the better leaving characteristics of iodide *versus* bromide. Electron deficient alkenes favour destabilisation of any cationic palladium species such as **11a**, hence forcing the reaction down the Suzuki–Miyaura route from complex **9**. The major impact of either thallium

or silver is to force halide decomplexation of palladium¹⁵ (*i.e.* decomplexation of **9** *via* acetoxy complex **10**) in less stabilised situations, *i.e.* when coupling medium and electron-rich alkenyl iodides. Addition of these salts not only results in a less coordinatively saturated (kinetically more reactive) palladium complex,¹⁶ but also promotes the formation of cationic palladium complex¹⁷ **11b** *via* halide–acetate ligand exchange and acetate decomplexation; a process which is known to have profound effects on the regiocontrol of Heck reactions with vinyl ethers.¹⁵ Overall, kinetically reactive cationic palladium complexes **11** produce chemoselective coupling to provide the Heck coupled products observed.

Conclusion

The successful syntheses of these 1,6-diphenyl-1,3,5-hexatriene model systems using just three key reactions demonstrates the strength of this strategy in the preparation of polyenes with full control over the alkene geometries. The ability to control the iododeboronation reactions to give either *E*- or *Z*-iodoalkenes and the coupling of the alkenylboronates to give either the Heck and Suzuki–Miyaura products simply through variation of the reaction conditions has been demonstrated and is the backbone of the strategy. It is important to note that the order in which the polyenes are constructed has little effect on the yields and geometrical purity. This is demonstrated when examining the preparation of the *E,E,Z*- and *Z,E,E*-trienes, the point in the reaction sequence at which the *Z*-alkene unit is introduced has little effect on the end result showing that the sensitive *Z*-alkene is stable to the reaction conditions required to perform each of the key reactions of the strategy.

Further results on the application of this strategy to the synthesis of natural products which contain polyene units and their biological activity will be reported in due course.

Experimental

General experimental

All IR spectra were recorded on a Perkin-Elmer 298 spectrometer employing NaCl plates or KBr discs. All ¹H and ¹³C NMR spectra were recorded on either a Varian Mercury-400, Bruker Avance-400 or Varian Inova-500 spectrometers. ¹¹B NMR spectra were recorded on the Bruker Avance-400 at a frequency of 128 MHz. Chemical shifts are expressed as parts per million downfield from the internal standard TMS with all samples run in CDCl₃. Mass spectrometry was performed on either a Micromass Autospec, Finnigan MAT 95 XP or Finnigan MAT 900 XLT. Column chromatography was performed on Davisil Silica gel, 60 mesh. TLC was performed on Polygram SIL G/UV₂₅₄ plastic-backed silica gel plates with visualization achieved using a UV lamp, or by staining with KMnO₄. All glassware was oven dried (130 °C) before use and cooled under a positive pressure of argon. Solvents were dried by distillation from CaH₂ (DCM, Toluene) or sodium-benzophenone ketyl (THF). All reactions were performed at room temperature unless otherwise stated. All other materials were purchased directly from either Aldrich or Lancaster (as was) and used without further purification, unless stated otherwise.

Warning: All reactions involving thallium salts produce insoluble residues which are collected by Celite filtration. These residues should be treated as hazardous waste.

4,4,6-Trimethyl-2-vinyl-1,3,2-dioxaborolane **3**

Vinylmagnesium bromide **4** (100 cm³ of a 1.0 M solution in THF, 100 mmol) was added dropwise over 1 hour to a stirred solution of anhydrous trimethylborate (10.2 cm³, 18 mmol) in dry THF (100 cm³) at –78 °C under argon. The reaction was left to stir for a further hour before warming to room temperature and allowing the addition of 20% HCl (44 cm³).

After 10 min, a solution of 2-methyl-2,4-pentanediol (11.34 cm³, 90 mmol) in Et₂O (9 cm³) was added and the reaction was stirred for a further hour. The two phases were separated and the aqueous phase extracted with Et₂O (100 cm³), the combined organic extracts were washed with saturated aq. NaHCO₃ (2 × 100 cm³) and water (2 × 100 cm³), dried (MgSO₄) and the solvent evaporated to afford the crude product as a yellow oil. Kugelrohr distillation yielded **3** (11.3 g, 82%) as a clear oil, bp 50–55 °C (0.46 mm Hg) (lit.¹⁸ 57–58 °C, 22 mm Hg); $\nu_{\max}/\text{cm}^{-1}$ 3064, 2975, 1616, 1419 and 1391; δ_{H} (500 MHz) 1.28 (3H, d, $J = 6.0$ Hz, CHMe), 1.31 (6H, s, CMe₂), 1.52 (1H, t, $J = 12.0$, CHH), 1.80 (1H, dd, $J = 14.0$ and 3.0, CHH), 4.23 (1H, m, CHMe), 5.82 (2H, m, olefinic) and 6.05 (1H, dd, $J = 19.0$ and 5.0, olefinic); δ_{C} (125 MHz) 23.4 (CHMe), 28.3 (CMe₂), 31.4 (CMe₂), 46.1 (CH₂), 65.0 (CHMe), 71.0 (CMe₂), 134.1 (olefinic); δ_{B} (128 MHz) 25.7; m/z (EI) 154 (M⁺), 139, 59 (100) and 43; (found: M⁺, 154.1156; C₈H₁₅O₂B⁺ requires 154.1160).

4,4,6-Trimethyl-2-styryl-1,3,2-dioxaborinane **5**

Dry toluene (10 cm³) was added to a Schlenk-like tube with stirring under a positive pressure of argon containing Pd(OAc)₂ (9 mg, 0.04 mmol), PPh₃ (31 mg, 0.12 mmol) and AgOAc (0.16 g, 0.96 mmol) forming a suspension. Tri-*n*-butylamine (0.23 cm³, 0.96 mmol), iodobenzene **2** (0.09 cm³, 0.8 mmol) and vinylboronate **3** (0.15 g, 0.96 mmol) were added and the solution was degassed using the freeze–pump–thaw method (3×), before heating to 110 °C. After 24 h, the reaction mixture was diluted with Et₂O (40 cm³) and passed through Celite before washing with 10% HCl (20 cm³), water (20 cm³) and brine (20 cm³). Drying (MgSO₄) and solvent removal provided the crude product as a brown oil. Kugelrohr distillation provided **5** (0.16 g, 88%) as a clear oil, bp 95–100 °C (0.38 mm Hg) (lit.¹⁹ 101–104 °C, 0.2 mm Hg); $\nu_{\max}/\text{cm}^{-1}$ 3023, 2973, 1624, 1576 and 1494; δ_{H} (500 MHz) 1.33 (3H, d, $J = 6.0$ Hz, CHMe), 1.35 (6H, d, $J = 3.0$, CMe₂), 1.57 (1H, t, $J = 12.0$, CHH), 1.83 (1H, dd, $J = 14.0$ and 3.0, CHH), 4.29 (1H, m, CHMe), 6.12 (1H, d, $J = 18.5$, olefinic), 7.31 (4H, m, 3Ar–H and 1 olefinic) and 7.49 (2H, d, $J = 8.0$, Ar–H); δ_{C} (125 MHz) 23.4 (CHMe), 28.4 (CMe₂), 31.5 (CMe₂), 46.2 (CH₂), 65.1 (CHMe), 71.2 (CMe₂), 127.2 (Ar), 128.5 (Ar), 128.7 (Ar), 138.2 (Ar) and 146.7 (olefinic); δ_{B} (128 MHz) 26.9; m/z (EI) 230 (M⁺), 215, 130 (100), 91, 77 and 51; (found: M⁺, 230.1478; C₁₄H₁₉O₂B⁺ requires 230.1482).

E-Styryl iodide **7a**

To a stirred solution of boronate **5** (2.0 g, 8.70 mmol) in dry THF (25 cm³) under argon at –78 °C in the absence of light, was added dropwise NaOMe (20.9 cm³ of a 0.5 M solution in MeOH, 10.44 mmol). ICl (10.4 cm³ of a 1.0 M solution in DCM, 10.4 mmol) was added over 5 min and the reaction was allowed to warm to room temperature. After 2 h, the reaction was diluted with Et₂O (60 cm³) before washing with 5% aq. Na₂S₂O₅ (70 cm³), water (70 cm³) and brine (70 cm³) before drying (MgSO₄) and solvent removal to afford the crude product. Purification by silica gel chromatography (9 : 1, petroleum ether–Et₂O as eluant) provided **7a** (1.7 g, 86%) as a yellow oil. Characterisation data were consistent with the literature.²⁰

Z-Styryl iodide **7b**

To a stirred solution of boronate **5** (1.5 g, 6.52 mmol) in dry DCM (20 cm³) under argon, in the absence of light at –78 °C was added ICl (7.83 cm³ of a 1.0 M solution in DCM, 7.83 mmol) dropwise over a period of 5 min. After stirring for 4 h, NaOMe (15.65 cm³ of a 0.5 M solution in MeOH, 7.83 mol) was added and the reaction left for a further 30 min to warm to room temperature. The reaction mixture was diluted with Et₂O (60 cm³), washed with 5% aq. Na₂S₂O₅ (50 cm³), water (50 cm³) and brine (50 cm³) before drying (MgSO₄) and solvent removal to afford the crude product. Purification by

silica gel chromatography (9 : 1, petroleum ether–Et₂O as eluant) provided **7b** (1.4 g, 95%) as a yellow oil. Characterisation data were consistent with the literature.²¹

4,4,6-Trimethyl-2-(4-phenylbuta-1E,3E-dienyl)-1,3,2-dioxaborinane **8a**

To a dried Schlenk-like tube under a positive pressure of argon was added Pd(OAc)₂ (9 mg, 0.04 mmol), PPh₃ (31 mg, 0.12 mmol) and AgOAc (0.16 g, 0.96 mmol). Syringe addition of toluene (5 cm³), iodide **7a** (0.18 g, 0.80 mmol) and vinylboronate **3** (0.15 g, 0.96 mmol) was followed by degassing using the freeze–pump–thaw method (3×) before heating to 110 °C. After 24 h the reaction was cooled and diluted with Et₂O (40 cm³) before passing through Celite and washing with 10% HCl (20 cm³) and brine (20 cm³). Drying (MgSO₄) and solvent removal yielded the crude product as a brown oil. Purification by silica gel chromatography (95 : 5, hexane–Et₂O) afforded **8a** (0.11 g, 55%) as a yellow oil; $\nu_{\max}/\text{cm}^{-1}$ 3058, 3023, 2973, 2934, 1622, 1602, 1447, 1417, 1391, 1301 and 1249; δ_{H} (500 MHz) 1.31–1.34 (9H, m, 3 × Me), 1.55 (1H, t, $J = 13.0$ Hz, boronate CHH), 1.82 (1H, dd, $J = 14.0$ and 3.0, boronate CHH), 4.23–4.30 (1H, m, O–CHMe–), 5.64 (1H, d, $J = 17.0$, Ph–CH=CH–CH=CHB), 6.69 (1H, d, $J = 15.5$, Ph–CH=CH–CH=CHB), 6.85 (1H, dd, $J = 15.5$ and 10.5, Ph–CH=CH–CH=CHB), 7.11 (1H, dd, $J = 17.5$ and 10.5, Ph–CH=CH–CH=CHB), 7.25 (1H, t, $J = 7.5$, Ar–H), 7.33 (2H, t, $J = 7.5$, Ar–H) and 7.44 (2H, d, $J = 7.5$, Ar–H); δ_{C} (126 MHz) 23.4 (Me), 28.4 (Me), 31.5 (Me), 46.2 (boronate CHH), 65.0 (O–CHMe–), 71.1 (O–CMe₂–), 126.9 (Ar), 128.1 (Ar), 128.8 (Ar), 131.3 (olefinic), 135.0 (olefinic), 137.4 (Ar) and 147.1 (olefinic); δ_{B} (160 MHz) 26.0; m/z (EI) 256 (M⁺), 241, 185, 156, 128, 84, 77, 69, 55 and 43 (100); (ES⁺ found: MH⁺ 257.1708; C₁₆H₂₂O₂B⁺ requires 257.1707).

4,4,6-Trimethyl-2-(4-phenylbuta-1E,3Z-dienyl)-1,3,2-dioxaborinane **8b**

To a dried Schlenk-like tube under a positive pressure of argon was added Pd(OAc)₂ (74.1 mg, 0.33 mmol), PPh₃ (260 mg, 0.99 mmol) and AgOAc (1.31 g, 1.82 mmol). Syringe addition of toluene (10 cm³), iodide **7b** (1.5 g, 6.52 mmol) and vinylboronate **3** (1.20 g, 7.82 mmol) was followed by degassing using the freeze–pump–thaw method (3×) before heating to 110 °C. After 24 h the reaction was cooled and diluted with EtOAc (50 cm³) before passing through Celite and washing with 10% HCl (50 cm³) and brine (50 cm³). Drying (MgSO₄) and solvent removal yielded the crude product as a brown oil. Purification by silica gel chromatography (98 : 2, hexane–Et₂O) afforded **8b** (0.98 g, 58%) as a thick orange oil; $\nu_{\max}/\text{cm}^{-1}$ 3057, 3023, 2973, 2934, 1623, 1599, 1591, 1492, 1447, 1408, 1390, 1369 and 1305; δ_{H} (500 MHz) 1.27–1.37 (9H, m, 3 × Me), 1.52 (1H, dd, $J = 13.5$ and 12.0 Hz, boronate CHH), 1.80 (1H, dd, $J = 14.0$ and 3.0, boronate CHH), 4.20–4.27 (1H, m, boronate OCHMe), 5.69 (1H, d, $J = 17.0$, =CHB), 6.32 (1H, t, $J = 11.5$, PhCH=CH–CH=CHB), 6.51 (1H, d, $J = 11.5$, PhCH=CH–CH=CHB), 7.30–7.38 (5H, m, Ar–H) and 7.48 (1H, dd, $J = 17.5$ and 12.0, PhCH=CH–CH=CHB); δ_{C} (100 MHz) 23.1, 28.1 and 31.2 (each Me), 46.0 (BCH₂), 65.0 (OCHMe), 70.8 (CMe₂), 127.1 (Ar), 128.2 (Ar), 129.2 (Ar), 131.7 (olefinic), 132.5 (olefinic), 137.5 (Ar), 142.5 (olefinic); δ_{B} (128 MHz) 25.7; m/z (EI) 256 (M⁺), 241, 185, 156, 129, 128 (100), 115, 91, 77, 69, 55 and 43; (ES⁺ found: MH⁺ 257.1705; C₁₆H₂₂O₂B⁺ requires 257.1707).

1,6-Diphenyl-1,3,5-hexatrienes **1a–c**

Pd(PPh₃)₄ (0.36 μmol, 42 mg) and Ag₂O (1.45 mmol, 0.34 g) was dissolved with stirring under argon in freshly distilled THF (8 cm³). To this was added the iodide **7a** or **7b** (0.72 mmol, 0.17 g) and the boronate **8a** or **8b** (0.72 mmol, 0.19 g). The reaction was then heated at reflux for 24 h before cooling

and diluting with diethyl ether followed by washing through Celite. Solvent removal yielded the crude product which could be purified by silica gel chromatography (96 : 4, hexane–Et₂O). The characterisations for all products **1a–c** are consistent with literature values.²²

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