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An Improved Synthesis of (2*E*,4*Z*)-6-(benzyloxy)-4-bromohexa-2,4-dien-1-ol.

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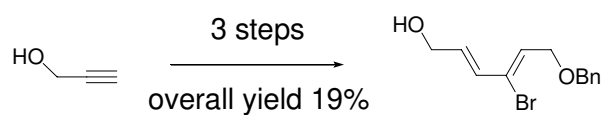
Improved Route

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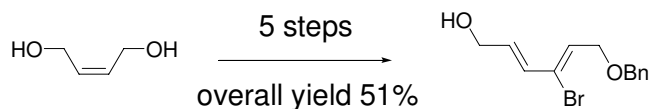
An Improved Synthesis of (2*E*,4*Z*)-6-(benzyloxy)-4-bromohexa-2,4-dien-1-ol.[§]

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Abstract. An improved synthesis of (2*E*,4*Z*)-6-(benzyloxy)-4-bromohexa-2,4-dien-1-ol has been devised. This new route increases the through put and yield of the diene product by circumventing a low yielding preparation of a boronic acid intermediate as well as removing the need to use multi-gram quantities of highly toxic thallium salts. In the process of developing this new route, a higher yielding preparation of (*E*)-3-hydroxyprop-1-enylboronic acid was also achieved.

Introduction

The efficient synthesis of functionalized dienes with defined double bond geometries (Figure 1) is an important goal in organic synthesis,[1] as they are frequently used as intermediates in the construction of natural products. Such dienes are usually desired as precursors to Diels-Alder cyclisations, or as substrates for other stereocentre generating reactions like dihydroxylations and epoxidations. In all of these instances the geometries of the double bonds is of paramount importance, as it translates generally into the stereochemistry present in the product.
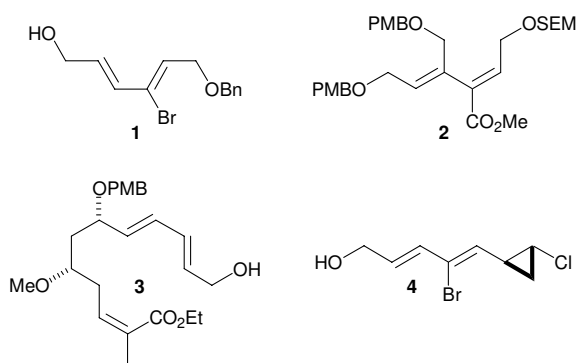
Figure 1

We and others have had cause to synthesise such dienes *en route* to a number of natural products. For example, several groups have reported strategies towards fragments of hexacyclinic acid[2] or the related FR182877[3] *via* Diels-Alder reactions of systems similar to those in Figure 1. We on the other hand, required significant quantities of diene **1** for our approach to the AB-rings of hexacyclinic acid.[4] Similarly, Nicolaou required diene **2** for his synthesis of zaragozic acid A,[5] while Roush needed triene **3** for the synthesis of the superstolides[6] and Evans synthesised diene **4** *en route* to the callipeltoside A side chain[7] (Figure 1).

In the cases of dienes **1**, **3** and **4** a synthetic strategy was adopted which involved formation of the diene's C2-C3 single bond, by use of a Suzuki reaction of a vinyl halide with boronic acid **5**[4, 6, 7] (Scheme 1). Roush has shown that regioselective cross-couplings are possible between boronic acids and 1,1-dibromoalkenes, since the rates of palladium(0) catalysed cross-coupling reactions of *E*-1-bromoalkenes are substantially greater than for those reactions with *Z*-1-bromoalkenes. Roush also

found that standard Suzuki cross-coupling conditions (cat. Pd(PPh$_3$)$_4$, aq. NaOH, PhH, reflux) gave low yields, but the use of Kishi's modification (replacing NaOH with TlOH) led to an increased rate of reaction, such that sluggish Suzuki couplings often reached completion rapidly when TlOH was used.[8] More recently, Roush demonstrated that the unstable TlOH can be substituted for TlOEt with retention of reactivity and selectivity.[9] The high yield and convergence of this coupling are attractive, and as such this was our preferred route to the **1**. While on paper this looks an attractive disconnection, in practice it suffers from a number of attributes which make it less desirable.
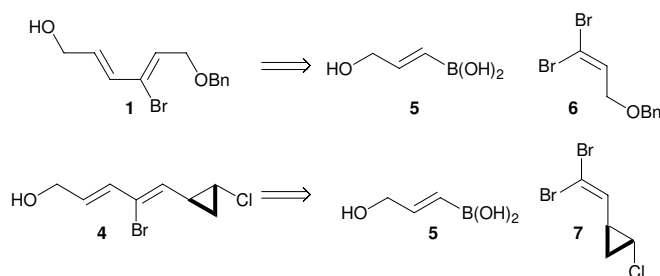
Scheme 1

Results and Discussion

The two 3-carbon fragments required for the Suzuki strategy are both known compounds synthesised in one step from commercially available starting materials. 1,1-Dibromo-3-benzyloxyprop-1-ene **6** was produced in good yield from (benzyloxy)acetaldehyde using Corey–Fuchs methodology (Scheme 2).[10] However, the primary problem with this approach to the synthesis of **1** (Scheme 2) is the synthesis of boronic acid **5**, which was originally reported by Roush, although no experimental details were given in that or subsequent reports.[6] Our initial attempts at the hydroboration of propargyl alcohol were met with failure, but a more thorough experimental procedure, obtained *via* personal correspondence with the original author,[11] did permit its synthesis. The synthesis of **5** can be achieved by the slow addition of catecholborane to neat propargyl alcohol at 0 °C under argon to give the catecholborane ester. Hydrolysis with water produced a white foam which was saturated with NaCl and exhaustively extracted with EtOAc followed by flash column chromatography.[11] This generated **5** in an abysmal 7% yield. Removal of the extraction conditions and direct application of the aqueous mixture to flash silica

resulted in an increase in the isolated yield of **5** to 10-12%. However, it proved apparent that the extended purification times were detrimental to the yield of the product, and addressing this problem directly was difficult. In our highest yielding procedure two solvent systems were required for chromatography: EtOAc–petrol ether (40-60) (1:1) to remove the catechol, followed by CH_2Cl_2–MeOH (9:1) to remove the boronic acid **5**. On a large scale this resulted to the product being exposed to silica for up to four hours. It was reasoned that using a larger grain of silica could speed up the purification procedure and prevent excessive decomposition of the product. Thus, when the two-solvent system of chromotographic purification was run using Kieselgel 60 (0.2–0.5 mm) the chromatography time required was reduced and the yield of **5** increased to 25-30%.[12] The subsequent Suzuki reaction proceeded well and in 77% yield. However, this yield was only obtainable when Tl_2CO_3 was used as the base in order to suppress formation of the triene by reaction of a further equivalent of **5** with the bromodiene **1**.[3c] Use of less toxic $Ba(OH)_2$[13] or Cs_2CO_3 led to much longer reaction times and reduced yields of 37% and 39% respectively. Even Roush's reported conditions utilizing TlOEt[9] only delivered the product in 42% yield. However, as we desired to generate multi-gram quantities of **1** for our synthesis this required the use of large amounts of toxic Tl_2CO_3. For example generating 13 g of diene **1** necessitated the use of 50 g of Tl_2CO_3. This coupled with the crippling yields for the formation of **5** forced us to re-evaluate our synthesis. We now wish to disclose our improved synthesis of diene **1** which increased the overall yield of **1**, and removed the need to synthesise boronic acid **5** and the large quantities of highly toxic thallium salts.
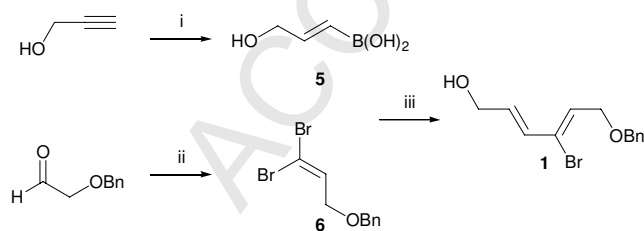
Scheme 2. *Reagents and conditions:* (i) catecholborane, 25-30%; (ii) PPh_3, CBr_4, CH_2Cl_2, 0°C, 87%; (iii) 10 mol% $Pd(PPh_3)_4$, THF, water, Tl_2CO_3, 77%.

Our second generation synthesis of **1** (Scheme 3) began with the mono-benzylation of *cis*-buten-1,4-diol with NaH, BnCl, *n*-Bu₄NI in THF/DMSO in 78% yield.[14] Parikh-Doering oxidation generated aldehyde **9** quantitatively in which isomerisation of the double bond had taken place. Treatment of **9** with bromine followed by the addition of pyridine generated α-bromoaldehyde **10** in 70% yield.[15, 16] Wittig olefination installed the second double bond as a single (*E*)-geometric isomer in a yield of 64%. Further enhancement of the yield of this oxidation-bromination-Wittig sequence could be achieved by the addition of (triphenylphosphoranylidene)acetate to the bromination reaction 1 hr after the addition of pyridine.[15, 16] This generated **11** in an improved yield of 70% over the bromination-Wittig steps. Reduction of ester **11** with DIBAL-H gave diene **1** in 92% yield. Spectroscopic analysis of **1** showed it to be identical to the compound produced by our procedure reported previously.[4] Furthermore we found that it was possible to telescope several of the steps in this second generation synthesis together. Bromination was achieved by the direct addition of bromine and pyridine to aldehyde **9**. This was followed by addition of the ylide for the Wittig reaction when the bromination was seen to be complete by analysis of an aliquot of the reaction mixture by ^{1}H NMR. Ester **11** was isolated from the reaction by precipitation of the triphenylphosphine oxide with Et₂O-petrol ether (40-60) 3:1. Crude **11** was then treated with DIBAL-H and the resultant desired bromodiene **1** was isolated by filtration through a plug of silica in 64% yield over 3 steps.
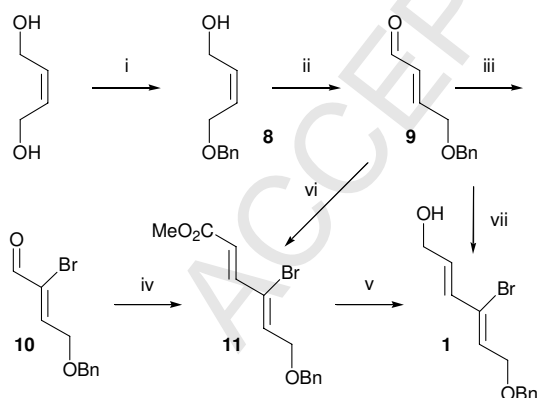
Scheme 3. *Reagents and conditions:* (i) NaH, BnCl, *n*-Bu₄NI, THF/DMSO, 60 °C, 78%; (ii) SO₃.py, DIPEA, CH₂Cl₂, RT, 100%; (iii) Br₂, 30 min, py, CH₂Cl₂, 0°C, 62%; (iv) MeO₂CCHPPh₃, CH₂Cl₂, 64%; (v) DIBAL-H/hexane, THF, -78°C, 92%; (vi) Br₂, 30 min, py, CH₂Cl₂, 0°C, 1 h then

MeO$_2$CCHPPh$_3$ 70% (2 steps); (vii) Br$_2$, 30 min, py, CH$_2$Cl$_2$, 0°C, 1 h then MeO$_2$CCHPPh$_3$, DIBAL-H/hexane, THF, -78°C, 64% (3 steps).

Conclusions

We have developed an improved procedure for the synthesis and isolation of boronic acid **5**, although for our purposes even this improved procedure was insufficient to solve our supply problem of diene **1**. Therefore we had to develop a second generation synthesis of **1**, which takes 5 steps and can provide over 50 g of **1**, without the use of toxic thallium salts. The improved second generation route provides **1** in an overall yield of 51% compared to our original synthesis which supplied it in only a 19% yield.

Experimental

General

All melting points are uncorrected. Reaction progress was monitored using glass-backed TLC plates pre-coated with silica UV$_{254}$ and visualized by using either UV radiation (254 nm), ceric ammonium molybdate or anisaldehyde stains. Column chromatography was performed using silica gel 60 (220-240 mesh), with the solvent systems indicated in the relevant experimental procedures. Dichloromethane was distilled from calcium hydride; tetrahydrofuran and diethyl ether were distilled from sodium / benzophenone ketyl, DMSO was distilled from calcium hydride prior to use. Hexane was distilled prior to use. All other reagents were used as received from commercial suppliers unless stated otherwise in the appropriate text.

(2*E*,4*Z*)-6-(Benzyloxy)-4-bromohexa-2,4-dien-1-ol 1

Original synthesis coupling of boronic acid 5 and bromide 6: Nitrogen was bubbled through a solution of dibromoalkene **6** (18.1 g, 59.2 mmol) and boronic acid **5** (6.64 g, 65.2 mmol) in THF–water (3:1, 400 ml) at rt for 2 h. Under a flow of N$_2$, Pd(PPh$_3$)$_4$ (3.42 g, 2.96 mmol) and Tl$_2$CO$_3$ (50.0 g, 107 mmol) were added sequentially and the resulting green-brown solution with pale precipitate was stirred

at rt for 44 h. The suspension was added to a 1M aqueous solution of NaHSO$_4$ (150 ml) and then stirred until gas evolution ceased (1 h). The mixture was filtered through Celite, then extracted with EtOAc (2 × 150 ml). The combined organics were washed with brine (150 ml), dried (MgSO$_4$), filtered and concentrated *in vacuo* to leave a crude brown oil (22.1 g, overweight). Flash chromatography (petrol ether (40-60)–EtOAc, 2:1) afforded an orange oil **1** (13.0 g, 77%).

From ester 11: A 1M solution of DIBAL-H (10.6 ml) in hexane was added to a solution of 6-benzyloxy-4-bromo-hexa-2,4-dienoic acid methyl ester (1.10 g, 3.54 mmol) in THF (15 ml). After 15 min the reaction was quenched with 10% solution of Rochelles' salt (15 ml) and stirred for 8 h. After extraction of the aqueous layer with EtOAc (3 x 15 ml) the combined organic layers were washed with brine (10 ml), 10% solution of Rochelles' salt (15 ml) and brine (10 ml); dried (MgSO$_4$) and concentrated *in vacuo* to give a pale yellow oil (920 mg, 92%).

The telescoped procedure: To a solution of 4-benzyloxy-but-2-enal (50.76 g, 288 mmol) in CH$_2$Cl$_2$ (600 ml) at 0°C was added bromine (15.6 ml, 302 mmol), the mixture was stirred for 15 min at 0 °C then treated with pyridine (93.2 ml, 1.15 mol) and stirred for a further 1 h at 0 °C. Methyl (triphenylphosphoranylidene)acetate (192.7 g, 576 mmol) was then added, and the reaction mixture was stirred for 24 h at rt and concentrated *in vacuo*. The bulk of triphenylphosphineoxide was removed by trituration of the crude solid with Et$_2$O-petroleum ether (40-60) 3:1 followed by filtration and concentrated *in vacuo* which gave a brown solid. The brown solid was then triturated with hot petroleum ether (40-60), filtered and concentrated *in vacuo* which gave a brown solid (84.9 g, crude). A 1M solution of DIBAL-H (543 ml) in hexane was added to a solution of crude 6-benzyloxy-4-bromo-hexa-2,4-dienoic acid methyl ester (84.9 g) in THF (1.1 l) over 2 h. After 30 minutes the reaction was diluted with EtOAc (1 l), quenched with 10% solution of Rochelles' salt (1 l) and stirred for 8 h. The organic layer was washed with 10% Rochelles' salt (2 x 400 ml) and brine (200 ml). The aqueous layer was extracted with EtOAc (3 x 1 l) and the combined organic layers were washed with 10% Rochelles' salt (2 x 400 ml) and brine (400 ml). The combined organic layers were dried (MgSO$_4$) concentrated *in*

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vacuo and subjected to filtration over a plug of silica to give a pale yellow oil (51.4 g, 63% over 4 steps).

ν_{max} (solution; CHCl$_3$) 3616, 2922, 2863, 1651, 1614, 1454, 1088 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.37–7.27 (5H, m, Ph), 6.31 (1H, d, J =15.0 Hz, H3), 6.25 (1H, dt, J = 15.0 and 5.0 Hz, H2), 6.19 (1H, t, J = 6.0 Hz, 5-H), 4.54 (2H, s, H7), 4.31 (4H, apparent d, J = 5.0 Hz, H1 and H6); δ_C (100 MHz, CDCl$_3$) 137.9 (C, Ph), 134.2 (CH, C2), 130.8 (CH, C5), 128.9 (CH, C3), 128.4 (CH, Ph), 127.8 (CH, Ph), 127.8 (CH, Ph), 125.1 (C, C4), 72.7 (CH$_2$, C7), 69.6 (CH$_2$, C6), 62.4 (CH$_2$, C1); m/z (CI) 302 and 300 (1:1, [M + NH$_4$]$^+$), 286 and 284 (1:1, [M + H]$^+$), 204 (M + H − Br) $^+$; found M + NH$_4$ 300.0594, C$_{13}$H$_{19}$^{79}BrNO$_2$ requires M + NH$_4$ 300.0594.

(*E*)-3-Hydroxyprop-1-enylboronic acid 5

Catecholborane (113 ml, 833 mol) was added to neat propargyl alcohol (23.6 ml, 407 mmol) at 0 °C under N$_2$ at a rate of 2 ml min^{-1} (CARE: gas evolution) with vigorous stirring. The clear solution was allowed to warm to rt over 1 h during which time it solidified (CARE: exotherm). The solid was held at rt for 20 h. Water (5 × 10 ml) was added at 1 h intervals (CARE: gas evolution) and the mixture allowed to stir for 24 h. The solid did not dissolve completely, so water (20 ml) was added and the mixture stirred for a further 24 h. The resulting white foam was added directly to a column of silica (~750 g; Kieselgel 60 (0.2–0.5 mm)). Elution with EtOAc–petroleum ether (40-60) (1:1, 5 l) removed the catechol byproduct, then MeOH (5–15%) in CH$_2$Cl$_2$ removed the product. Concentration *in vacuo* left a light-brown foam **5** (16.6 g, 40%). ν_{max} (nujol) 3375, 1642, 1334, 1197, 1085, 1001, 916, 775, 737 cm^{-1}. δ_H (400 MHz, CD$_3$OD) 6.57 (1H, dt, J = 18.0 and 4.0 Hz, H2), 5.81 (1H, dt, J = 18.0 and 2.0 Hz, H1), 4.11 (2H, dd, J = 4.0 and 2.0 Hz, H3). δ_C (125 MHz, CD$_3$OD) 153.1 (CH, C2), 66.2 (CH$_2$, C3) ppm. MS m/z (ES-) 100 and 101 (1:4, [M-H]$^-$); found (EI-) M - H, 101.0405 C$_3$H$_7$O$_3$B requires M - H 101.0405.

3-(Benzyloxy)-1,1-dibromoprop-1-ene 6

To a solution of PPh$_3$ (26.5 g, 101 mmol) in CH$_2$Cl$_2$ (150 ml) at 0 °C under Ar was added a solution of CBr$_4$ (14.6 g, 43.9 mmol) in CH$_2$Cl$_2$ (50 ml) at a rate of 1 ml min^{-1}, and the resulting red solution was stirred at 0 °C for 1 h. A solution of benzyloxyacetaldehyde (5.06 g, 33.7 mmol) in CH$_2$Cl$_2$ (100 ml) was added at a rate of 1 ml min^{-1} then the solution was stirred at 0 °C warming to rt over 1 h, and at rt for a further 13 h. A saturated aqueous solution of NH$_4$Cl (150 ml) was added, the organic layers were separated and washed with water (150 ml) and the combined aqueous layers were extracted with CH$_2$Cl$_2$ (3 × 100 ml). The combined organics were washed with brine (200 ml), dried (MgSO$_4$), filtered and concentrated *in vacuo* to give a yellow solid. Hexane (250 ml) was added and the suspension stirred for 14 h. The solvent was decanted, then hexane (100 ml) added to the residue, and the suspension treated with sonication for 30 min. The suspension was filtered, and the combined organics concentrated *in vacuo* to leave a pale yellow oil **6** (9.03 g, 87%). δ_H (270 MHz, CDCl$_3$) 7.37–7.30 (5H, m, Ph), 6.65 (1H, t, J = 6.0 Hz, H2), 4.53 (2H, s, H4), 4.06 (2H, d, J = 6.0 Hz, H3). Data in agreement with the literature.[17]

4-Benzyloxy-but-2-en-1-ol 8

Neat *cis*-butendiol (15 g, 170 mmol) was added to a suspension of NaH, 60% dispersion in oil, (7.5 g, 187 mmol) in 4:1 THF-DMSO (375 ml) and stirred at 0°C. After 30 min a solution of benzyl chloride (20.5 g, 162 mmol) in THF (200 ml) was added over 15 min followed by the addition of *n*-Bu$_4$NI (6.3 g, 17 mmol). The reaction mixture was stirred at 60 °C for 12 h, cooled to rt, diluted with water (700 ml) and extracted with Et$_2$O (3 x 700 ml). The combined organic layes were washed with brine (200 ml), dried (MgSO$_4$) and concentrated *in vacuo*. Distillation at 0.2 mbar, 110 °C gave a colourless oil (22.5 g, 78%). ν_{max} (film) 3386, 3028, 2923, 2861, 1454, 1387, 1207, 1071, 1028, 738, 699 cm^{-1}. δ_H (400 MHz; CDCl$_3$) 7.38-7.28 (5H, m, Ph), 5.75 (1H, m, H2), 5.73 (1H, m, H3), 5.53 (2H, s, H5), 4.19 (2H, t, J = 5.7 Hz, H1), 4.11 (2H, dd, J = 6.1, 0.6 Hz, H4), 1.78 (1H, t, J = 5.7 Hz, OH) ppm. δ_C (100 MHz; CDCl$_3$) 137.7 (C, Ph), 132.4 (CH, C2), 128.4 (CH, C3), 128.0 (CH, Ph), 127.8 (CH, Ph), 127.7 (CH,

Ph), 72.4 (CH_2, C5), 65.5 (CH_2, C4), 58.5 (CH_2, C1) ppm. MS (ES+) m/z 201 $(M + Na)^+$, 179 $(M + H)^+$ and 161 $(M + H - H_2O)^+$; found M + H 179.1067, $C_{11}H_{15}O_2$ requires M + H 179.1072.

4-Benzyloxy-but-2-enal 9

To a solution of 4-benzyloxy-but-2-en-1-ol (22.5 g, 126 mmol) in CH_2Cl_2 (240 ml) was added DMSO (45 ml) followed by DIPEA (55 ml, 316 mmol). To this mixture SO_3Py (40.2 g, 253 mmol) was added over 10 min in 5 portions. The reaction mixture was stirred for 1 h at rt, diluted with CH_2Cl_2 (300 ml), washed with 0.5M HCl (3 x 150 ml), brine (2 x 100 ml) then dried ($MgSO_4$) and concentrated *in vacuo* to give a orange oil (22.2 g, >99%). ν_{max} (film) 3064, 3031, 2844, 2730, 1690, 1468, 1361, 1113, 1026, 968, 739, 699 cm^{-1}. δ_H (400 MHz; $CDCl_3$) 9.59 (1H, d, J = 8.0 Hz, H1), 7.39-7.30 (1H, m, Ph), 6.85 (1H, dt, J = 15.8, 4.1 Hz, H3), 6.41 (1H, ddt, J = 15.8, 8.0, 1.9 Hz, H2), 4.60 (2H, s, H5), 4.29 (2H, dd, J = 4.1, 1.9 Hz, H4) ppm. δ_C (100 MHz; $CDCl_3$) 193.3 (CH, C1), 153.0 (CH, C3), 137.4 (C, Ph), 131.8 (CH, C2), 128.5 (CH, Ph), 127.9 (CH, Ph), 127.6 (CH, Ph), 73.0 (CH_2, C5), 68.5 (CH_2, C4) ppm. MS (ESI) m/z 199 $(M+Na)^+$, 177 $(M + H)^+$ and 159 $(M + H - H_2O)^+$; found M + H 177.0910, $C_{11}H_{13}O_2$ requires M + H 177.0916.

4-Benzyloxy-2-bromo-but-2-enal 10

To a solution of 4-benzyloxy-but-2-enal (23.2 g, 132 mmol) in CH_2Cl_2 (250 ml) was added bromine (7.15 ml, 139 mmol), the mixture was stirred for 10 min at rt and then cooled at 0°C, treated with pyridine (42 ml, 528 mmol) and stirred for a further 30 min at 0 °C. The reaction mixture was diluted with Et_2O (700 ml) then washed with 0.5M HCl (5 x 150 ml), brine (2 x 100 ml) and dried ($MgSO_4$). Concentration *in vacuo* gave a brown oil (20.8 g, 62%). ν_{max} (film) 3063, 3030, 2860, 1701, 1628, 1454, 1349, 1138, 1110, 741, 699 cm^{-1}. δ_H (400 MHz; $CDCl_3$) 9.19 (1H, s, H1), 7.40-7.32 (5H, m, Ph), 7.33 (1H, t, J = 5.0 Hz, H3), 4.61 (2H, s, H5), 4.45 (2H, d, J = 5.0 Hz, H4) ppm. δ_C (100 MHz; $CDCl_3$) 185.0

(CH, C1), 151.9 (CH, C3), 137.0 (C, Ph), 128.6 (CH, Ph), 128.1 (CH, Ph), 127.9 (CH, Ph), 126.7 (C, C2), 73.4 (CH_2, C5), 69.4 (CH_2, C4) ppm. MS (CI) *m/z* 274, 272 (1:1 $[M + H_2O]^+$); found (ES+) M + Na 276.9835, $C_{11}H_{11}{}^{79}BrNaO_2$ requires M + Na 276.9040.

6-Benzyloxy-4-bromo-hexa-2,4-dienoic acid methyl ester 11

To a solution of 4-benzyloxy-2-bromo-but-2-enal (972 mg, 3.81 mmol) in CH_2Cl_2 (1.5 ml) methyl (triphenylphosphoranylidene)acetate (2.55 g, 7.63 mmol) was added. The reaction mixture was stirred for 10 h at rt and concentrated *in vacuo*. Column chromatography (petroleum ether (40-60) -Et_2O 5:1) gave a light yellow semi solid (755 mg, 64%).

The telescoped procedure: To a solution of 4-benzyloxy-but-2-enal (577 mg, 3.27 mmol) in CH_2Cl_2 (6.5 ml) was added bromine (0.177 ml, 3.44 mmol), the mixture was stirred for 10 min at rt and then cooled at 0°C, pyridine (1.1 ml, 13.1 mmol) was then added and the mixture was stirred for 1 h. Methyl (triphenylphosphoranylidene)acetate (2.19 g, 6.55 mmol) was added after this time and the reaction mixture was stirred for a further 24 h at rt and then concentrated *in vacuo*. The bulk of triphenylphosphine oxide was removed triturating the crude solid with hot petroleum ether (40-60) and decanting the solution away from the residue. Concentration of the decanted petroleum ether under reduced pressure gave an orange oil. Column chromatography (petroleum ether (40-60)-Et_2O 5:1) gave a light yellow semi solid (710 mg, 70% over three steps).

ν_{max} (film) 2950, 1717, 1635, 1456, 1436, 1307, 1154, 1105, 734, 698 cm^{-1}. δ_H (400 MHz; $CDCl_3$) 7.39-7.29 (5H, m, Ph), 7.28 (1H, dd, *J* = 14.8, 0.7 Hz, H3), 6.57 (1H, tt, *J* = 5.5, 0.7 Hz, H5), 6.25 (1H, dd, *J* = 14.8, 0.7 Hz, H2), 4.55 (2H, s, benzylic CH_2), 4.33 (2H, d, *J* = 5.5 Hz, H6), 3.78 (3H, s, CH_3) ppm. δ_C (100 MHz; $CDCl_3$) 166.6 (C, C1), 142.4 (CH, C3), 139.3 (CH, C5), 137.4 (C, Ph), 128.5 (CH, Ph), 127.9 (CH, Ph), 127.8 (CH, Ph), 122.9 (CH, C2), 122.5 (C, C4), 73.0 (CH_2, C7), 69.7 (CH_2, C6), 51.8 (CH_3, C11) ppm. MS (ES+) *m/z* 335 and 333 (1:1, $[M + Na]^+$), 313, 311 (1:1, $[M + H]^+$); found M + H 311.0277, $C_{14}H_{16}{}^{79}BrO_3$ requires M + H 311.0283.

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Acknowledgments

References and Notes.

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