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Stereospecific synthesis of all four isomeric 6,8-heneicosadien-11-ones: sex pheromone components of the painted apple moth *Teia anartoides*

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Abstract—The stereospecific synthesis of all four isomeric 6,8-heneicosadien-11-ones, sex pheromone components of the painted apple moth, *Teia anartoides*, is reported using the Suzuki-coupling of vinyl boronic acid and vinyl iodide intermediates.

The painted apple moth *Teia anartoides*[1] occurs naturally in the south-eastern States of Australia but was accidentally introduced to New Zealand in 1999 where it poses a significant threat to the native fauna as well as to commercial plant species. The potential economic cost of this pest prompted the New Zealand government to initiate a spray campaign to eradicate the insect. As part of an ongoing study into the monitoring the population and spread of this pest, we became interested in identifying its sex pheromone. Previously, 6*Z*,8*E*-heneicosadien-11-one **1** has been reported as one component of a complex pheromone blend.[2,3] In an effort to identify further unknown components, we decided to synthesise the other possible isomers of 6,8-heneicosadien-11-ones.

To prepare all four isomers of 6,8-heneicosadien-11-one (**1**, **2**, **3** and **4**), we needed a route that was diastereospecific and gave swift access to reasonable quantities of material for wind-tunnel and field testing. We decided on a Suzuki-coupling[4] strategy as one, which would utilise some common intermediates and thus be more efficient in cost and time. This required access to C7 iodides **7** and **8** and boronic acids **9** and **10**, as well as the C14 boronic acid **5** and C14 iodide **6**. The proposed syntheses of all the isomers by this method are illustrated in Scheme 1.

Catecholborane was reacted with 1-heptyne at 70 °C to give boronic acid **9** in 55% yield as an off-white solid.[5] Boronic acid **9** was readily converted to *E*-1-iodohept-1-ene **8** by reaction with iodine in the presence of base,[6] while *Z*-1-iodohept-1-ene **7** was obtained by addition of iodine to a solution of boronic acid **9** in a mixture of THF and Et_2O[7] (Scheme 2). Both these iodides were somewhat light sensitive.

Preparation of 6*Z*,8*Z*-heneicosadien-11-one **4** requires access to *Z*-heptenylboronic acid **10**. Thus, 1-heptyne was converted to 1-bromo-1-heptyne using NBS and catalytic $AgNO_3$ in acetone.[8] Subsequent treatment with $HBBr_2$ DMS complex followed by potassium triisopropoxyborohydride and then methanol (Scheme 3) afforded the *Z*-heptenylboronic acid **10** as a viscous oil.[9]

Starting from epoxydodecane, ring opening with lithium acetylide–EDA complex afforded tetradec-1-yn-4-ol **11**.[2,10] Treatment of tetradec-1-yn-4-ol **11** with catecholborane gave *E*-tetradec-1-en-4-ol-1-boronic acid **12**, which in turn could be readily converted to *Z*-1-iodotetradec-1-en-4-ol **13** by reaction with I_2 in THF and Et_2O (Scheme 4).

With access to all intermediates needed to prepare the target dienes, we now investigated the Suzuki-coupling reaction. Treatment of a mixture of the boronic acid **12** with each of the iodides **7** and **8** with *tetrakis*-triphenylphosphine palladium(0) followed by 2 equiv of base (NaOEt) and heating to 70 °C in benzene, gave reasonably clean conversion to the dienes **14** and **15**. GCMS and

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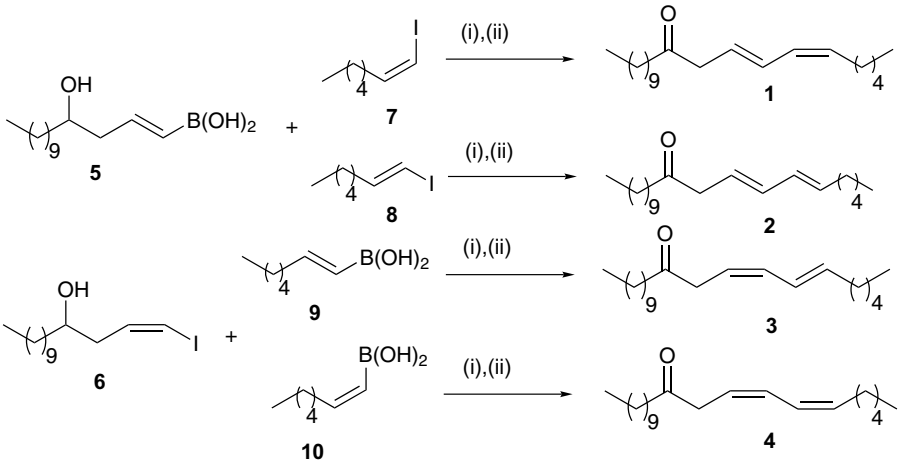
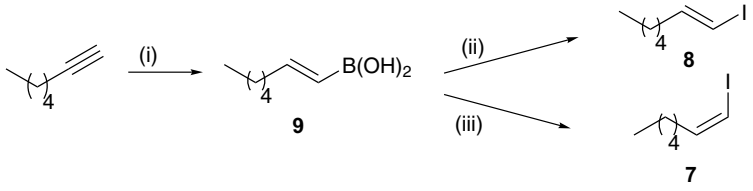
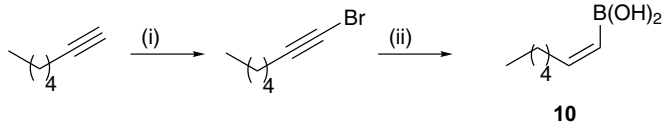


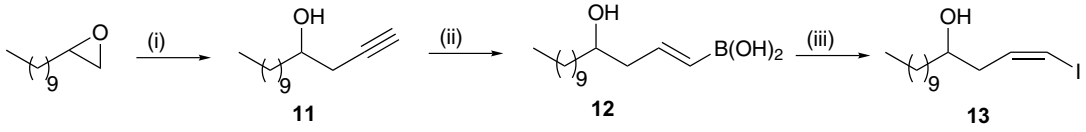
Scheme 1. Proposed syntheses of 6,8-heneicosadien-11-one isomers by Suzuki-coupling. Reagents and conditions: (i) $Pd(PPh_3)_4$, NaOEt; (ii) Dess–Martin periodinane.



Scheme 2. Preparation of *E*-1-iodohept-1-ene, *Z*-1-iodohept-1-ene and *E*-hept-1-enyl-1-boronic acid. Reagents and conditions: (i) catecholborane 70 °C (55%); (ii) Et_2O, NaOH, I_2 (53%); (iii) Et_2O, THF, I_2 (37%).



Scheme 3. Preparation of *Z*-hept-1-enyl-1-boronic acid. Reagents and conditions: (i) $AgNO_3$, acetone, NBS (46%); (ii) $HBBr_2$ then KIPBH (78%).



Scheme 4. Preparation of *E*-tetradec-1-en-4-ol-1-boronic acid and *Z*-1-iodotetradec-1-en-4-ol. Reagents and conditions: (i) lithium acetylide–EDA complex, DMSO (82%); (ii) catecholborane, 70 °C (29%); (iii) Et_2O, THF, I_2 (46%).

NMR analysis of the dienes showed that the stereochemical integrity of the starting materials had been preserved in the product.

The coupling reactions between *Z*-1-iodotetradec-1-en-4-ol **13** and the two C7 boronic acids **9** and **10** did not, however, proceed as cleanly as hoped. In both cases, separation of the product from side-products was troublesome, and in the case of the 6*Z*,8*Z*-isomer the yield was only 8%. The results of all the coupling reactions are summarised in Table 1.[13]

The final step in the synthesis was to oxidise the alcohols to the ketones. Previously, chromium(VI)[9] and the Dess-Martin periodinane[11] have been used to prepare **1**. A typical reaction using chromium(VI) needed several hours for completion, whereas use of the Dess–Martin reagent gave rapid conversion to the ketone in good yield with no side products.[14] In particular, we found the 6*Z*,8*Z*-isomer **4** to be degraded during the course of an oxidation using chromium(VI). We now had a reliable method, which gave access to all four 6,8-heneicosadien-11-ones. Despite the low yields overall, particularly in the case of

Table 1. Suzuki-coupling reactions between C14 boronic acids and C7 iodides

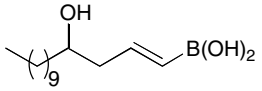
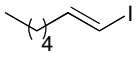
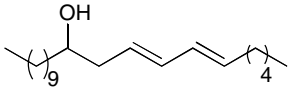
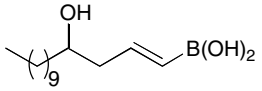
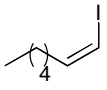
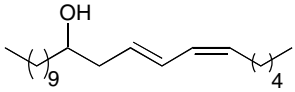
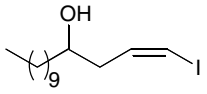
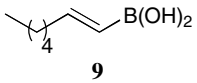
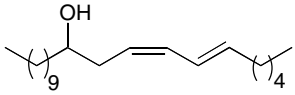
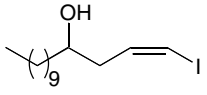
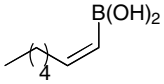
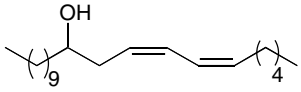
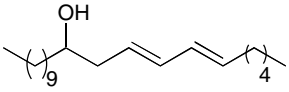
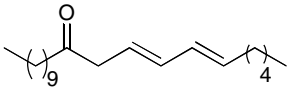
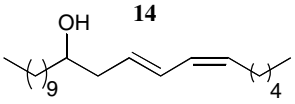
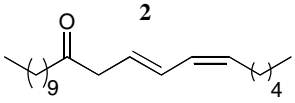
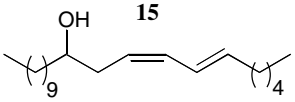
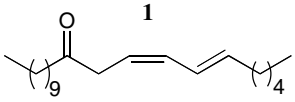
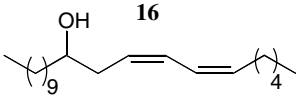
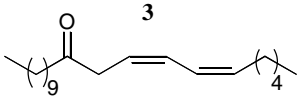
C14 fragment	C7 fragment	Product	Yield/%
 **12**	 **7**	 **14**	36
 **12**	 **8**	 **15**	66
 **13**	 **9**	 **16**	40
 **13**	 **10**	 **17**	8

Table 2. Oxidation of 6,8-heneicosadien-11-ols to 6,8-heneicosadien-11-ones using Dess–Martin periodinane

Dienol	Dienone	Yield/%
 **14**	 **2**	72
 **15**	 **1**	66
 **16**	 **3**	64
 **17**	 **4**	78

the 6*Z*,8*Z*-isomer, we were able to prepare sufficient quantities of all compounds to carry out extensive wind-tunnel and field testing[12] (Table 2).

In summary, we have synthesised all four isomeric 6,8-heneicosadien-11-ones from readily accessible intermediates using 4 Suzuki-coupling reactions.

Acknowledgements

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12. The pheromone components synthesised in this paper have been utilised in field and wind-tunnel testing. El-Sayed, A. *J. Chem. Ecol.*, in press.
13. Experimental details and selected data for compounds **14**–**17**. *Preparation of 6Z,8E heneicosadien-11-ol*. A mixture of *E*-tetradec-1-en-4-ol-1-boronic acid (250 mg, 0.97 mmol) and *Z*-1-iodohept-1-ene (237 mg, 1.06 mmol) was stirred in dry benzene (3.9 mL) at room temperature under N_2. *Tetrakis*-triphenylphosphine palladium (56 mg, 0.046 mmol) was added, immediately followed by NaOEt (0.97 mL of a 2 M solution in EtOH, 1.94 mmol). The reaction mixture was heated to 70 °C for 45 min. After cooling to room temperature, Et_2O (15 mL) was added followed by water (10 mL). The aqueous phase was extracted with Et_2O (3×10 mL) and the combined organics dried over $MgSO_4$. The solvent was removed in vacuo. Column chromatography using 5% EtOAc/95% petroleum ether as the eluant gave compound **15** as a colourless oil. 158 mg, 53%. NMR data were consistent with those reported in the literature.[2,3] *6E,8E-Heneicosadien-11-ol*: 36%. Found M^+-H_2O 290.2975, requires 290.2974; ^1H NMR ($CDCl_3$, 400 MHz) 6.04–5.98 (2H, m), 5.66–5.53 (2H, m), 3.62 (1H, br), 2.20–2.00 (4H, m), 1.50–1.20 (24H, m), 0.90–0.70 (6H, m) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 134.2, 134.2, 130.2, 127.6, 71.5, 41.1, 37.2, 32.9, 32.2, 31.7, 30.0, 30.0, 30.0, 30.0, 29.3, 26.0, 22.3, 22.8, 14.4, 14.3 ppm. *6Z,8Z-Heneicosadien-11-ol*: 8%. Found M^+-H_2O 290.2983, requires 290.2974; ^1H NMR ($CDCl_3$, 400 MHz) 6.42 (1H, dd, $J = 11.3$, 7.6 Hz), 6.24 (1H, m), 5.52–5.47 (2H, m), 3.65 (1H, d, $J = 6$ Hz), 2.35 (2H, m), 2.17 (2H, m), 1.50–1.20 (24H, m), 0.88 (3H, t, $J = 6.4$ Hz), 0.87 (3H, t, $J = 7.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 133.8, 127.3, 127.0, 123.6, 72.0, 37.3, 35.9, 32.3, 31.9, 30.0, 29.7, 29.6, 29.6, 29.6, 29.6, 27.9, 26.1, 23.0, 22.9, 14.5, 14.4 ppm. *6E,8Z-Heneicosadien-11-ol*: 40%. Found M^+-H_2O 290.2973, requires 290.2974; ^1H NMR ($CDCl_3$, 400 MHz) 6.30 (1H, m), 6.12 (1H, m), 5.71 (1H, m), 5.33 (1H, m), 3.64 (1H, br), 2.33 (2H, m), 2.10 (2H, m), 1.50–1.20 (24H, m), 0.88 (3H, t, $J = 6.8$ Hz), 0.87 (3H, t, $J = 6.8$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) 136.3, 131.9, 125.3, 124.8, 71.6, 36.9, 35.8, 32.9, 31.9, 31.5, 29.7, 29.6, 29.6, 29.6, 29.4, 29.0, 25.8, 22.7, 22.5, 14.1, 14.0 ppm.
14. Experimental details and selected data for compounds **1**–**4**. *Preparation of 6Z,8E-heneicosadien-11-one*. Dess–Martin periodinane (671 mg, 1.63 mmol) was added to solution of 6*Z*,8*E*-heneicosadien-11-ol (180 mg, 0.58 mmol) in CH_2Cl_2 (12 mL) at room temperature. After 1 h, $NaHCO_3$ (10 mL, satd aq) was added. The aqueous phase was extracted with CH_2Cl_2 (3×10 mL) and the combined organics were dried over $MgSO_4$. Column chromatography using 5% EtOAc/95% petroleum ether as the eluant gave compound **1** as a colourless oil. 119 mg, 66%. Spectral data were consistent with those reported in the literature.[2,3] *6E,8E-Heneicosadien-11-one*: 72%. Found M^+ 306.2924, requires 306.2923; ^1H NMR ($CDCl_3$, 400 MHz) 6.10–5.99 (2H, m), 5.74–5.59 (2H, m), 3.15 (2H, d, $J = 7.2$ Hz), 2.42 (2H, t, $J = 7.4$ Hz), 2.06 (2H, m), 1.70–1.60 (2H, m), 1.40–1.20 (20H, m), 0.89 (3H, t, $J = 6.6$ Hz), 0.88 (3H, t, $J = 6.7$ Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) 209.3, 134.7, 134.2, 129.6, 122.8, 46.7, 42.3, 32.5, 31.9, 31.4, 29.5, 29.4, 29.4, 29.3, 29.2, 28.9, 23.7, 22.6, 22.5, 14.1, 14.0 ppm. *6E,8Z-Heneicosadien-11-one*: 64%. Found M^+ 306.2931, requires 306.2923; ^1H NMR ($CDCl_3$, 400 MHz) 6.24–6.09 (2H, m), 5.78–5.71 (1H, m), 5.48–5.42 (1H, m), 3.26 (2H, dd, $J = 7.5$, 1.2 Hz), 2.43 (2H, t, $J = 7.3$ Hz), 2.11 (2H, m), 1.70–1.60 (2H, m), 1.50–1.30 (20H, m), 0.88 (3H, t, $J = 6.8$ Hz), 0.87 (3H, t, $J = 6.8$ Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 208.9, 137.1, 131.7, 124.8, 120.0, 42.3, 42.0, 32.0, 31.9, 31.4, 29.5, 29.4, 29.4, 29.3, 29.2, 28.9, 23.8, 22.7, 22.5, 14.1, 14.0 ppm. *6Z,8Z-Heneicosadien-11-one*: 78%. Found M^+ 306.2920, requires 306.2923; ^1H NMR ($CDCl_3$, 400 MHz) 6.44 (1H, m), 6.17 (1H, m), 5.61–5.54 (2H, m), 3.29 (2H, dd, $J = 7.5$, 1.4 Hz), 2.43 (2H, t, $J = 7.5$ Hz), 2.17 (2H, m), 1.60–1.40 (2H, m), 1.50–1.20 (20H, m), 0.88 (3H, t, $J = 6.8$ Hz), 0.88 (3H, t, $J = 6.2$ Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) 208.8, 134.3, 126.5, 122.8, 122.1, 42.4, 41.7, 31.9, 31.4, 29.5, 29.4, 29.4, 29.3, 29.2, 27.5, 23.8, 22.6, 22.5, 14.1, 14.0 ppm.