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Synthesis of (3*Z*)-Dodecenyl-(*E*)-2-butenoate, the Pheromone of Sweet Potato Weevil

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Abstract: A practical synthesis of the title pheromone has been developed. The key feature of the synthesis was the fixation of the required olefin geometry *via* a *cis*-selective Wittig reaction and use of commercially available starting materials to prepare the required synthons.

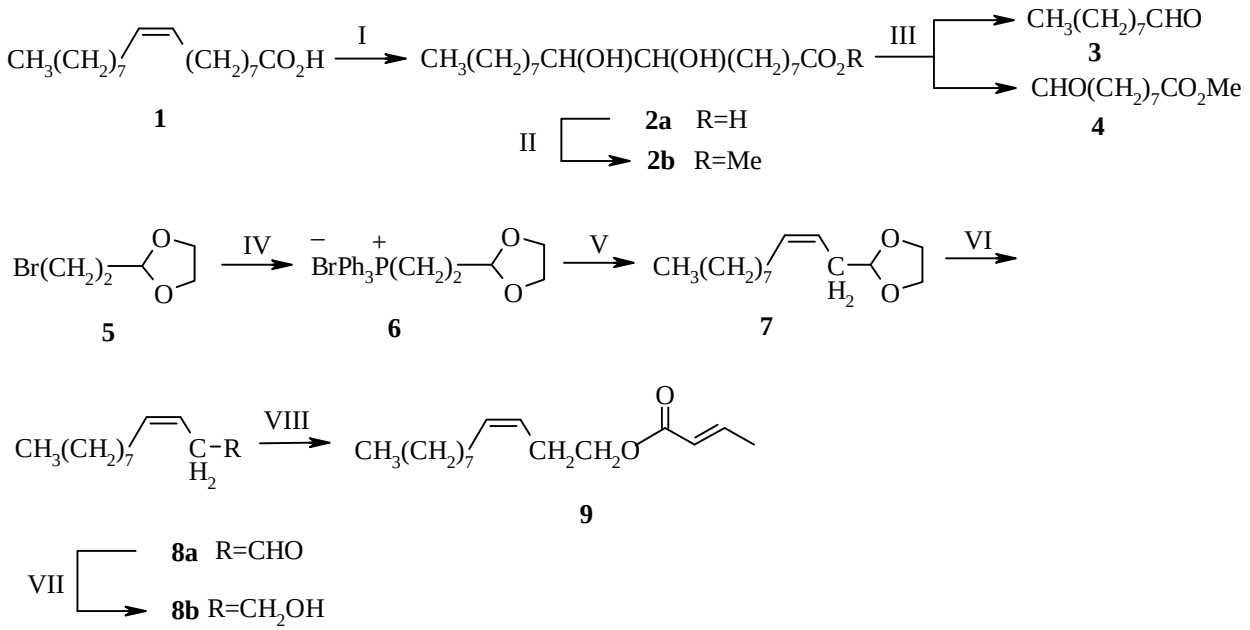
Keywords: sweet potato weevil, insect pheromone, synthesis.

Introduction

Sweet potato, primarily grown in the tropics, is one of the most important root crops in the world, surpassed only by potato. Its production and storage are strongly hampered [1] by the weevil, *Cylas formicarius elegantulus* which is a serious insect pest prevalent in India. The virgin female weevils secrete [2] (3*Z*)-dodecenyl (*E*)-2-butenoate (**9**) as the pheromone. Some other agriculturally important insects *viz*. the potato and sugar beet moths, *Scrobipalpopsis solanivora* [3] and *Scrobipalpa ocetuatella* [4] respectively secrete analogous compounds *viz*. the corresponding (3*E*)-acetate as their pheromone components. In addition, these C_{12}-esters also constitute [5] synthetic attractants for the *Reticulitermes* termites. Our interest for the field control of the weevil has led to a novel preparation of **9**, whose synthesis has already been described [2,6-8]. Amongst these, Heath *et al*. [2] have used the potential carcinogenic compounds like HMPA and ethylene oxide in their synthesis. The Wittig-based

synthesis by a Chinese group [6] has been published with no technical detail. Another synthesis [8] on the other hand, employed expensive 3-butyn-1-ol as the starting material. Moreover, preparation of the alkynol in the laboratory often leads to poor yield in view of its high water solubility. In contrast, the present route does not involve any hazardous and /or expensive chemicals and furnishes the target pheromone in yield comparable with the earlier routes.

As discussed earlier, our main objective was to develop a multi-gram synthesis for the pheromone **9**. To this end, we have already reported [7] two independent approaches *via* acetylenic route and Doebner condensation respectively. While the former led to a modest yield, the latter was primarily targeted to the corresponding (3*E*)-compound and its elaboration to **9** involved too many steps to be suitable for a practical synthesis. For the synthesis, a stereoselective Wittig route involving C_9 + C_3 combination seemed ideal, especially as the required C_9-aldehyde moiety is amenable from many natural fatty acids *viz*. oleic acid (**1**). The bifunctional C_3-unit can also be easily prepared from acrolein, another commercially available material. (Scheme 1.). Thus, the acid **1** was first dihydroxylated [9] with HCO_3H to the diol acid **2a**. After esterification to **2b**, the diol function was cleaved with $NaIO_4$. The required aldehyde **3** was easily separated from the ester component **4** by distillation.



Scheme 1. I) HCO_3H; KOH, II) MeOH/ H^+, III) $NaIO_4$/ CH_3CN-H_2O, IV) Ph_3P/ CH_3CN/ , V) Dimsyl ion/ **3**, VI) THF/ HOAc/ H_2O, VII) $NaBH_4$/ MeOH, VIII)Crotonyl chloride/ Py.

Conversion of the Wittig salt **6** of the bromoacetal **5** [10] to the corresponding ylide with dimsyl ion as the base [10], followed by reaction with **3** gave the olefinic acetal **7**. Hydrolysis of **7** proved difficult. The best result was obtained by refluxing its solution in THF-HOAc-H_2O. Upon reduction of the resultant aldehyde **8a** with $NaBH_4$, the known [5,6,11] alcohol **8b** was obtained. Acylation with cro-

tonyl chloride *via* a conventional procedure [7,8] gave the title pheromone **9** whose properties (IR, NMR, BP) were in agreement with those reported previously. [7,8,11].

Experimental

All the boiling points were uncorrected. The IR spectra were scanned with a Perkin-Elmer spectrophotometer model 837. The ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ (unless specified otherwise) with a Bruker AC-200 (200 MHz) instrument. The GLC analyses were carried out using Shimadzu GC-7A chromatograph fitted with stainless steel column (2 Mt. x 0.5 mm 3% OV-17 column) and flame ionization detector. The mass spectrum was recorded with a Shimadzu QP-1000 mass spectrograph at 70 eV. Anhydrous reactions were carried out under Ar using freshly dried solvents. The organic extracts were dried over anhydrous Na_2SO_4.

Methyl 9,10-Dihydroxyoctadecanoate (**2b**)

Dihydroxylation of oleic acid **1** (25.0 g, 0.88 mol) was carried out by the slow addition of HCO_3H [prepared from 40% H_2O_2 (20 mL) and HCO_2H (125 mL) at 0 ^{0}C] followed by stirring for 8 h at 40 ^{0}C and at room temperature overnight. The mixture was distilled *in vacuo* (10 mm) and the residue was diluted with water and extracted with ether. The ethereal layer was washed with water, dried ($MgSO_4$) and concentrated. The residue was hydrolyzed with 5% aqueous KOH (200 mL) on a steam bath for 1 h, cooled and poured into excess cold dil. HCl (1N) under vigorous stirring (maintaining the temperature ~20 ^{0}C). The product was isolated by extraction with ether followed by washing with water, drying and concentration of the extract. The crude diol acid **2a** was recrystallized from EtOAc. yield: 22.3 g (80%); mp 91 ^{0}C, (lit. [12] mp 95 ^{0}C); IR: 3600-3400, 3340, 2660, 1700 cm^{-1}; ^{1}H-NMR (DMSO): δ 0.9 (distorted t, 3H), 1.3 (br. s, 26H), 1.9-2.1 (m, 2H), 2.61 (br. s, D_2O exchangeable, 2H), 3.6-3.9 (m, 2H), 8.1 (br. s, D_2O exchangeable, 1H).

A solution of **2a** (20.0 g, 0.063 mol) in MeOH (150 mL) containing *para*-toluenesulfonic acid (PTS) (0.2 g) was refluxed for 6 h. Most of the solvent was removed in *vacuo*. The residue was dissolved in ether and the ether layer was washed with water and brine and dried. Removal of solvent furnished the pure diol-ester **2b** as a low melting solid. yield: 20.6 g (~ quantitative); IR: 3360, 1750 cm^{-1}; ^{1}H-NMR: δ 0.9 (distorted t, 3H), 1.33 (m, 26H), 2.1-2.5 (m, 2H), 2.7 (br. s, D_2O exchangeable, 2H), 3.2-3.6 (m, 2H), 3.65 (s, 3H).

Nonanal (**3**)

To a stirred solution of the diol **2b** (16.5 g, 0.05 mol) in CH_3CN (50 mL)-CH_2Cl_2 (50 mL)-H_2O (10 mL) at 25 ^{0}C was added $NaIO_4$ (11.0 g, 0.05 mol) in portions. After stirring for 2 h, the reaction mixture was filtered, the filtrate concentrated in *vacuo* and the residue extracted with ether. The ethereal

extract was washed successively with aqueous 10% Na_2SO_3, water, aqueous 10% $Na_2S_2O_3$, water and brine. After drying, the organic extract was concentrated and the crude product mixture was fractionally distilled to afford the aldehyde **3** and the ester aldehyde **4**.

3: yield: 5.7 g (79.2%); bp. 80-85 ^{0}C/10 mm; IR: 2930, 2860, 2710, 1730 cm^{-1}; ^{1}H-NMR: δ 0.9 (distorted t, 3H), 1.4-1.8 (m, 12H), 2.0-2.3 (m, 2H), 9.1 (t, *J* = 1.5 Hz, 1H).

4: yield: 5.85 g (63%); bp 70-75 ^{0}C/2.5 mm.

3-Bromopropanal Ethyleneglycol Acetal (**5**)

HBr gas [generated from Br_2 (51.5 mL, 1.0 mol) to tetralin (37.5 mL, 0.275 mol)] was bubbled through a stirred and cooled (0 ^{0}C) solution of acrolein (67.5 mL, 1.0 mol) in CH_2Cl_2 (500 mL). Ethylene glycol (66.6 mL, 1.2 mol) was then added to it and the mixture stirred at room temperature overnight. It was cooled to 0 ^{0}C, made basic with 10% aqueous $NaHCO_3$ and extracted with ether. The organic layer was washed with water, dried, concentrated and distilled to give **5** as a colourless liquid. yield: 94.3 g (52%); bp 68-70 ^{0}C/5 mm, (lit. [10] bp.68-70 ^{0}C/5 mm); IR: 1410, 1360, 1265, 1210, 1030, 880, 820 cm^{-1}. ^{1}H-NMR: δ 1.95-2.35 (m, 2H), 3.4 (t, *J* = 6 Hz, 2H), 3.7-4.0 (m, 4H), 4.93 (t, *J* = 4 Hz, 1H).

1,3-Dioxolan-2-yl-methyltriphenylphosphonium Bromide (**6**)

A solution of triphenylphosphine (28.4 g, 0.11 mol) and the bromide **5** (18.1 g, 0.1 mol) in CH_3CN (200 mL) was refluxed for 24 h. After removing most of the solvent, the mixture was diluted with benzene (300 mL) and refluxed for 3 h. After cooling the upper solvent layer was decanted to give **6** as a yellow-brown thick mass which was used as such for the next step. yield: 27.2 g (61.4%).

(3Z)-Dodecenal (**8a**)

To a stirred solution of dimsyl anion [prepared by heating NaH (2.22 g, 0.042 mol, 50% dispersion in oil) in DMSO (75 mL) at 65 ^{0}C for 1 h] was added the phosphonium salt **6** (18.58 g, 0.042 mol) at room temperature. After stirring for 1 h, the aldehyde **3** (5.4 g, 0.038 mol) in DMSO (15 mL) was added to the resulting orange ylide solution. Stirring was continued for 16 h at the same temperature, the mixture poured in large excess ice-water and extracted with ether. The ethereal layer was washed with water and brine and dried. Removal of solvent gave a residue which was thoroughly extracted with hexane and the extract after concentration subjected to column chromatography (silicagel, 0-10% EtOAc/hexane) to furnish the acetal **7**. yield: 4.17 g (48.5%); bp 100 ^{0}C (bath)/0.5 mm; IR: 3010, 1460, 1030 cm^{-1}; ^{1}H-NMR: δ 0.9 (distorted t, 3H), 1.2-1.7 (m, 12H), 2.0-2.1 (m, 4H), 3.8-4.0 (m, 4H), 4.8 (distorted t, 1H), 5.3-5.5 (m, 2H).

A solution of **7** (3.84 g, 0.017 mol) in THF (35 mL), HAc (8.5 mL) and H_2O (8.5 mL) was heated

on a water bath for 3 h. Most of the solvent was removed, water added and the residue extracted with ether. The ether layer was washed with water and brine and dried. Removal of solvent gave the aldehyde **8a**. yield: 2.38 g (77.1%); IR: 2720, 1715 cm^{-1}.

(3Z)-Dodecen-1-ol (**8b**)

To a cooled (0 ^{0}C) and stirred solution of compound **8a** (2.3 g, 0.013 mol) in MeOH (20 mL) was added $NaBH_4$ (0.5 g, 0.013 mol) in portions. After 1.5 h, when the reaction was complete (*cf.* TLC), it was quenched with NH_4Cl (s), concentrated and extracted with ether. The ether layer was washed with water, brine and dried. After concentration, the residue was distilled to afford **8b**. yield: 1.95 g (81.5%); bp 90-110 ^{0}C/0.1 mm, (lit.[11] bp 67-70 ^{0}C/0.05 mm; IR: 3350, 1460, 1050 cm^{-1}; ^{1}H-NMR: δ 0.9 (t, *J* = 6 Hz, 3H), 1.30 (br. s, 12H), 2.0-2.6 (m, 4H), 2.9 (s, 1H, D_2O exchangeable), 3.63 (t, *J* = 7 Hz, 2H), 5.2-5.7 (m, 2H).

(3Z)-Dodec-3-enyl-(E)-2-butenoate (**9**)

A mixture of **8b** (1.84 g, 0.01 mol), crotonyl chloride (2.09 g, 0.02 mol) and pyridine (4 mL) in CH_2Cl_2 (15 mL) was stirred at room temperature for 12 h. Water (20 mL) was added and the mixture was extracted with ether. The extract was washed with aqueous $NaHCO_3$ (10%), water, aqueous HCl (2N), water and brine and finally dried. Usual isolation followed by column chromatography (silica gel, hexane) afforded pure **9**. yield: 1.81 g (72%); bp 135-140 ^{0}C (bath)/2 mm, (lit. [11] bp105-109 ^{0}C/0.1 mm); GLC (temp. prog. 100-250 ^{0}C @ 8 ^{0}C/min): R_t = 14.21 (94.1%); IR: 3010, 1740, 1680 and 980 cm^{-1}; ^{1}H-NMR: δ 0.9 (t, 3H), 1.24 (br. s, 12H), 1.6-2.5 (m, 7H), 4.1 (t, *J* = 6 Hz, 2H), 5.3-5.9 (m, 3H), 6.8-7.1 (m, 1H); ^{13}C NMR: δ 14.02, 17.82, 22.61, 25.9, 26.86, 27.27, 28.65, 29.59, 31.84, 32.18, 36.58, 39.01, 62.24, 64.23, 64.88, 122.8, 123.82, 124.28, 132.84, 136.33, 144.13, 166.53; MS (rel. int.): m/z 43 (49), 54 (87), 68 (100), 81 (59), 87 (43), 96 (41), 109 (15.7), 110 (14.9), 124 (10), 138 (11.6), 166 (24.3), 252 (M^+, 2.1), 253 (4.3). Anal. Calcd. for $C_{16}H_{28}O_2$: C 76.1%, H 11.2%; Found: C 76.3%, H 11.3%.

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Samples Availability: Available from the authors.