SHORT PAPER

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Short and stereoselective synthesis of (*E*)-3-alkenyl acetates, insect sex pheromone constituents of Lepidoptera; Gelechidae†

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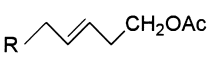
(E)-3-alkenyl acetates, which are insect sex pheromone constituents, have been prepared from linear saturated aldehydes, by a short three steps process, via the *(E)*-3-alkenoic acids and the corresponding *(E)*-3-alkenols, in good overall yield (60–65%) and high stereochemical purity (>99%).

Keywords: pheromones, *(E)*-3-alkenyl acetates, *(E)*-3-alkenols.

Tetra-, tri- and dodecenyl alcohols or acetates, with unsaturation at the C3 position, have been described as sex pheromone constituents from Lepidoptera, Gelechidae. The *(E)*-3-dodecenyl acetate **1** is the main component of the female sex pheromone of the sugar beet moth *Scrobipalpa ocellatella* (Boyd)[1]. Some other male lepidoptera, in particular Metzneria spp. Gelechidae, were also strongly attracted to this compound.[1] The *(E)*-3-tridecenyl acetate **2** is the major volatile component in the extract of the female sex pheromone gland of the tobacco stem borer *Scrobipalpa heliopa* (Lower), a serious pest of tobacco in India, Africa, Australia and in some regions of Asia.[2] The *(E)*-3-tetradecenyl acetate **3**, is a component of the female gland extract of the South American potato tuber moth *Symmetrichema tangolias* (Gyen), a great pest in Peru.[3] It has also been found to attract a close relative, the lesser bud moth of the orchard pest *Recuvraria nanella* (Hubner) as well as *Chionides perpetuella* (H.Sch.)[4].



1 R = C_7H_{15} (E)-3-C_{12}OAc

2 R = C_8H_{17} (E)-3-C_{13}OAc

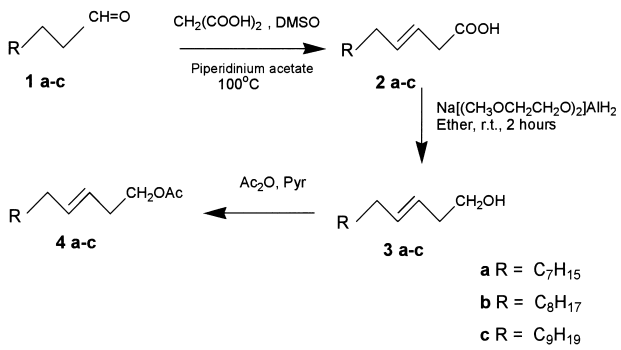
3 R = C_9H_{19} (E)-3-C_{14}OAc

These linear unsaturated acetates have been used to attract native male moths to traps and to provide potent sex lures for monitoring populations in the field. They may also be useful for pest control in storehouses. The development of a practical chemical synthesis will allow further biological research or trials to be carried out, in order to help in successful pest control.

The structure of the above Lepidopterous sex attractants are deceptively simple, but their efficient synthesis in high stereochemical purity offers a considerable synthetic challenge. The previously reported syntheses of the *(E)*-3-alkenyl acetates **1, 2** and **3** are based either on the acetylenic route, starting from the appropriate terminal alkyne, via the addition of ethyleneoxide and partial reduction of the triple bond[1,2] or by the rearrangement of the suitably substituted cyclopropylcarbinol to the *(E)*-3-alkenyl halide and subsequent reaction with sodium or potassium acetate.[5,6]

Although these methods gave the required products in high stereoselectivity, they offer only a partial solution to the availability of these compounds, because of the specialised reagents, labile intermediates and reaction conditions which are unsuitable for a large scale and low cost production of *(E)*-3-alkenyl acetates.

We wish to report a fast and efficient procedure for the synthesis of *(E)*-3-alkenyl acetates, from linear saturated aldehydes. These are condensed with malonic acid in DMSO at 100°C to give the *(E)*-3-alkenoic acids. Subsequent reduction of the latter to the *(E)*-3-alkenols and acetylation under standard conditions gave the required acetates (Scheme 1).



Scheme 1

The synthesis of *(E)*-3-alkenoic acids from aldehydes in high stereoselectivity, by a modified Knoevenagel condensation with malonic acid, has been reported[7].

The *(E)*-3-dodecenoic acid **2a**, as a model, was reduced by a series of reagents, in order to find the most suitable conditions for the selective and high yield production of the corresponding *(E)*-3-alkenol **3a**. The experimental conditions that were studied were: direct reduction of the acid by $LiAlH_4$ in ether or by Red-Al^R [sodium bis(2-methoxyethoxy) aluminum hydride] in toluene or ether[8] or chemoselective reduction by $NaBH_4$ in THF of the corresponding mixed anhydride of the acid **2a** with formic acid.[9] The results of the reductions are summarised on Table 1.

Although all the reductions gave the corresponding *(E)*-3-alkenol without affecting the double bond, the best yield was obtained by the direct reduction of the acid with Red-Al in ether. Thus the other two acids were reduced under the same conditions and finally the resultant *(E)*-3-alkenols were acetylated under standard conditions in pyridine solution by acetic anhydride. The *(E)*-3-alkenyl acetates that were obtained by the present method, were free of other isomers as shown by their ^{1}H NMR and IR spectra. They were purified by a simple distillation and in the final product the *(E)*-2-alkenyl acetate and the *(Z)*-3-alkenyl acetate were present in a quantity less than 1,0 % as it is revealed by their GC analysis. The

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Reduction of (*E*)-3-dodecenoic acid **2a** to (*E*)-3-dodecenol **3a**

	Substrate	Reagent	Solvent	Temp./time °C /h	Yield/%
1	C12-Acid	$LiAlH^4$	Diethylether	40/2	69
2	C12-Acid	$Na[(OCH_3OCH_2CH_2)_2]AlH_2$	Diethylether	25/2	82
3	C12-Acid	$Na[(OCH_3OCH_2CH_2)_2]AlH_2$	Toluene	25/4	79
4	Mixed anhydride	$NaBH_4$	THF/MeOH	15/1	45

spectroscopic properties of the synthetic acetates **4a–c** were identical with those reported for the isolated natural or the synthetic products.

In conclusion the herein described synthesis of the *(E)*-3-alkenyl acetates is chemically very simple, from cheap and commercially available starting materials and the high yield and high stereoselectivity (>99%) which were obtained, are suitable for a large scale production of these biologically active compounds.

Experimental

All starting materials and reagents were commercially available and they were used without any special purification. The Red-Al was purchased from Aldrich and it was 65% in toluene. IR spectra were obtained on a Perkin Elmer 7200 spectrophotometer in 5% CCl_4 solutions. ^{1}H NMR spectra were recorded on a Varian Mercury 200 MHz spectrometer, using $CDCl_3$ as solvent and TMS as internal standard. Mass spectra were taken on a GC-MS Hewlett-Packard 5890-5970 system. GC analyses were performed on a carbowax 20M 50m or a SE30 50m fused silica capillary columns.

Synthesis of (E)-3-alkenoic acids **(2):** The acids **2a, 2b** and **2c** were prepared in one mol scale, according to the typical procedure described in the literature.[7]

(E)-3-dodecenoic acid **(2a):** yield 87%; b.p. 119–123°C/0.8mmHg (lit.,[7] 123–125°C/1 mmHg); ν_{max}/cm^{-1} 1716, 970; σ_H 0.88 (3H, t, *J*=6.9), 1.26 (12H, brs), 1.98-2.08 (2H, m), 3.05 (2H, d, *J*=5.5), 5.37 (1H, dt, J_1= 15.6, J_2=5.4), 5.43 (1H, dt, J_1= 15.6, J_2=5.6); *m/z* 180 (M-18, 8%), 138 (11), 110 (13), 96 (24), 69 (42), 55 (80), 43 (98), 41 (100).

(E)-3-tridecenoic acid **(2b):** yield 85%; m.p. 32–34°C (hexane); b.p. 128–130°C/0,5 mmHg (lit.,[10] 137–139°C/0.3 mmHg); ν_{max}/cm^{-1} 1712, 970; σ_H 0.88 (3H, t, *J*=7.0), 1.26 (14H, brs), 2.02 (2H, m), 3.08 (2H, d, *J*=5.6), 5.45 (1H, dt, J_1 = 15.6, J2=5.0), 5.55 (1H, dt, J_1=15.6, J_2=5.2); *m/z* 194 (m-18, 6), 152(8), 110(13), 97(26), 83(32), 69(45), 55(76), 41(100).

(E)-3-tetradecenoic acid **(2c):** yield 87%; m.p. 40–42°C (hexane); ν_{max}/cm^{-1} 1712, 969; σ_H 0.87 (3H, t, *J*=6.9), 1.24 (16H, brs), 2.02 (2H, m), 3.06 (2H, d, *J*=5.6), 5.47 (1H, dt, J_1= 15.8, J2=6.0), 5.54 (1H, dt, J_1= 15.8, J_2=5.8); *m/z* 208 (M-18, 5), 166 (7), 110 (13), 97 (28), 83 (33), 69 (47), 55 (65), 41 (100).

General procedure for the synthesis of (E)-3-alkenols **(3):** *(E)*-3-Alkenoic acid (0.1 mol), dissolved in ether (50 ml), was added dropwise into a cold (5°C) solution of Red-Al (52 ml, 0.15 mol) in ether (150 ml) under nitrogen, over 30 min and the mixture was stirred at the same temperature for one hour and then overnight at room temperature. The reaction mixture and the excess of Red-Al were hydrolysed by a drop wise addition of dilute HCl 10% (100 ml). The organic phase was separated and the aqueous phase was extracted by ether (2 × 50 ml). The combined extracts are dried over anhydrous Na_2SO_4 and the solvents were evaporated under vacuum. The resultant crude *(E)*-3-alkenols were purified by distillation under vacuum.

(E)-3-Dodecenol **(3a):** yield 73%; b.p. 102–105°C/1.0 mmHg (lit.,[11] 95-97°C/0.8 mmHg); ν_{max}/cm^{-1}3636, 970; σ_H 0.88 (3H, t, *J*=6.6), 1.26 (12H, s), 2.00 (2H, dt, J_1= J_2= 6.6), 2.28 (2H, dt, J_1= J_2= 6.6), 3.62 (2H, t, *J*=6.6), 5.40 (1H, dt, J_1= 15.5, J_2=7.0), 5.52 (1H, dt, J_1= 15.5, J_2=7.0); *m/z* 184 (M, 1%), 166 (6), 109 (12), 96 (31), 82 (54), 68 (68), 55 (92), 41 (100).

(E)-3-Tridecenol **(3b):** yield 75%; b.p. 113–115°C/0.5 mmHg (lit.,[12] m.p. 16–17°C from hexane); ν_{max}/cm^{-1} 3636, 971; σ_H 0.88 (3H, t, *J*=6.6), 1.26 (14H, s), 2.00 (2H, dt, J_1= J_2= 6.6), 2.26 (2H, dt, J_1= 6.2, J_2= 6.6), 3.62 (2H, t, *J*=6.0), 5.40 (1H, dt, J_1= 15.4, J_2=7.0), 5.52 (1H, dt, J_1= 15.4, J_2=7.0); *m/z* 198 (M, 0.5%0, 180 (4), 109 (10), 96 (25), 82 (48), 68 (70), 55 (90), 41 (100).

(E)-3-Tetradecenol **(3c):** yield 76%; b.p. 129–132°C/0.3 mmHg (lit.,[6] 97°C/0.03 mmHg); ν_{max}/cm^{-1}3637, 971; σ_H 0.88 (3H, t, *J*=6.6), 1.26 (16H, s), 2.01 (2H, dt, J_1= J_2= 6.6), 2.26 (2H, dt, J_1= J_2= 6.6), 3.62 (2H, t, *J*=7.0), 5.36 (1H, dt, J_1= 15.4, J_2=7.0), 5.56 (1H, dt, J_1= 15.4, J_2=7.0); *m/z* 212 (M, 1%), 19 (6), 132 (5), 109 (15), 96 (44), 82 (63), 55 (90), 41 (100).

General procedure for the synthesis of (E)-3-alkenyl acetates **(4):** Acetic anhydride (6.12 g, 0.06 mol) was added dropwise into a cold (5°C) solution of the *(E)*-3-alkenol (0.05 mol) in pyridine (15 ml) and the whole was stirred at the same temperature for 1 hour and then overnight at room temperature. The reaction mixture was poured into a cold aqueous HCl 15% (100 ml) and extracted with ether (3 × 50 ml). The organic phase was washed with HCl 5%, then by saturated $NaHCO_3$ and finally with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated under vacuum. The crude *(E)*-3-alkenyl acetate was purified by distillation under vacuum.

(E)-3-Dodecenyl acetate **(4a):** yield 94%; b.p. 102–104°C/0.8 mmHg (lit.,[5] 95°C/1.0 mmHg); ν_{max}/cm^{-1} 1741, 1238, 969; σ_H 0.88 (3H, t, *J*=7.0), 1.26 (12H, s), 1.99 (2H, dt, J_1= J_2= 6.2), 2.05 (3H, s), 2.30 (2H, dt, J_1= J_2= 6.6), 4.07 (2H, t, *J*=7.0), 5.35 (1H, dt, J_1= 17.0, J_2=6.6), 5.52 (1H, dt, J_1= 17.0, J_2=6.6); *m/z* 166 (M-60, 6%), 138 (6), 124(4), 96 (21), 82 (28), 67 (42), 54 (48), 43 (100).

(E)-3-Tridecenyl acetate **(4b):** yield 93%; b.p. 105–108°C/1.0 mmHg (lit.,[2a] 75–77°C/0.1 mmHg); ν_{max}/cm^{-1} 1741, 1238, 970; σ_H 0.88 (3H, t, *J*=6.8), 1.28 (14H, s), 2.00(2H, dt, J_1= J_2= 6.6), 2.05 (3H, s), 2.30 (2H, dt, J_1= J_2= 6.6), 4.05 (2H, t, *J*=7.0), 5.32 (1H, dt, J_1= 16.5 J_2=6.6), 5.50 (1H, dt, J_1= 16.5, J_2=6.6); *m/z* 180 (M-60, 7%), 152 (4), 124(5), 110 (9), 96 (25), 81 (27), 67 (37), 43 (100).

(E)-3-Tetradecenyl acetate **(4c):** yield 97%; b.p. 122–126°C/0.8 mmHg (lit.,[6] 91°C/0.03 mmHg); ν_{max}/cm^{-1} 1741, 1238, 970; σ_H 0.88 (3H, t, *J*=7.0), 1.26 (16H, s), 2.00 (2H, dt, J_1= J_2= 6.6), 2.05 (3H, s), 2.32 (2H, dt, J_1= J_2= 6.6), 4.05 (2H, t, *J*=7.0), 5.30 (1H, dt, J_1= 16.5, J_2=6.6), 5.50 (1H, dt, J_1= 16.5, J_2=6.6); *m/z* 194 (M-60, 8%), 166(3), 152 (5), 110(12), 96 (26), 82 (32), 67 (38), 54 (36), 43 (100).

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