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Concise Preparation of the (3*E*,5*Z*)-Alkadienyl System. New Approach to the Synthesis of Principal Insect Sex Pheromone Constituents

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A new rapid and low-cost preparation of the (3*E*,5*Z*)-3,5-alkadienyl system, encountered in several insect pheromone constituents, was developed. Knoevenagel condensation of (*E*)-2-alkenals with ethyl hydrogen malonate in dimethyl sulfoxide, in the presence of a catalytic amount of piperidinium acetate, led to a mixture of geometrical isomers of ethyl 3,5-alkadienoates and ethyl 2,4-alkadienoates, from which the (3*E*,5*Z*)-3,5-alkadienoate was conveniently separated, by the use of urea inclusion complex formation. The importance of this procedure has been illustrated by the preparation of the (3*E*,5*Z*)-3,5-tetradecadienoic acid (megatomoic acid) **1**, the (3*E*,5*Z*)-3,5-dodecadienyl acetate **2**, and the (3*E*,5*Z*)-3,5-tetradecadienyl acetate **3**. These compounds are the main components of insect sex pheromones and constitute synthetic targets of considerable interest for the semiochemical community.

KEYWORDS: Knoevenagel condensation; pheromone synthesis; semiochemicals; megatomoic acid; *Attagenus megatoma*; *Bonagota cranaodes*; *Recurvaria leucatella*

INTRODUCTION

Conjugated diene compounds, with a 3,5-alkadienoic acid or 3,5-alkadienyl ester moiety, are important insect sex attractants. Among the existing four geometrical isomers, the (3*E*,5*Z*) configuration has already been encountered in certain insect sex pheromone constituents. For example, the dienoic acid (3*E*,5*Z*)-3,5-tetradecadienoic acid **1** (**Figure 1**), to which the trivial name megatomoic acid was assigned, is the principal component of the sex pheromone of the female black carpet beetle *Attagenus megatoma* Fabricius (Coleoptera: Dermestidae) (*1*). This insect is a destructive pest in stored grain and flour and also attacks fabrics in clothing, rugs, and padding of furniture. The (3*E*,5*Z*)-3,5-dodecadienyl acetate **2** is the main female sex pheromone component of the leafroller moth, *Bonagota cranaodes* Meyrick (Lepidoptera: Tortricidae), the most economically important insect pest on apples in southern Brasil (*2*). The (3*E*,5*Z*)-3,5-tetradecadienyl acetate **3** is a male sex attractant for orchard pests of the white-barred groundling moth *Recurvaria leucatella* Clerck (Lepidoptera: Gelechidae) (*3*), found by a screening process.

The above compounds (**Figure 1**), synthetically produced, were found to attract large numbers of insect males in field tests, and therefore they can be applied in integrated pest management programs, for the monitoring or the control of the above noxious insects (*1*−*3*). Therefore, the development of a simple and efficient synthetic preparation should make possible the application of these chemicals on large-scale field investigations.

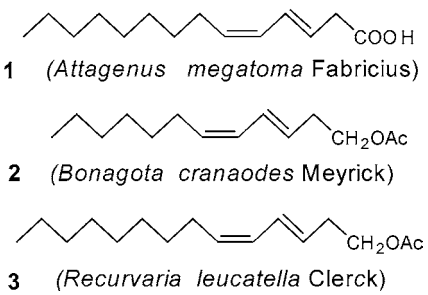

Figure 1. Structures of sex pheromone constituents with the (3*E*,5*Z*)-3,5-alkadienyl fragment.

Different approaches have been reported for the synthesis of (3*E*,5*Z*)-3,5-alkadienoic acids and alkadienoates. Most of these procedures involve partial reduction or isomerization of acetylenes as the steps to introduce the conjugated diene system (*1*, *4*−*9*). They also use, as starting material, an adequate 2,4-dienoate, applying a one carbon homologation (*10*) or a deconjugative protonation in basic medium (*11*, *12*). None of the above-reported methods is practical for a routine synthesis of the conjugated (3*E*,5*Z*)-3,5-alkadienoates. They suffer from insufficient isomeric purity of the final product, or they require precursors not readily available. Furthermore, very often they use reaction conditions and chromatographic separations that

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are unsuitable for large-scale low-cost preparations. A prerequisite for the practical use of these attractants, in pest management programs, will be the availability of relatively large quantities of the pure geometric isomers at a reasonable cost.

In our previous work (*13*), it was well documented that the reaction of saturated linear aldehydes with malonic acid or its derivatives in dimethyl sulfoxide (DMSO) leads stereoselectively to (*E*)-3-unsaturated acids, with a regio-selectivity higher than 97%. However, this reaction has not been studied with (*E*)-2-alkenals, which seemed to be good precursors for the synthesis of 3,5-unsaturated acids. So, we sought to extend the use of this reaction to (*E*)-2-alkenals, anticipating that a problem with mixtures of geometrical isomers of 3,5-dienoic acids should be encountered.

Herein, a fast and experimentally simple procedure for the preparation of (3*E*,5*Z*)-3,5-alkadienoates from (*E*)-2-alkenals is reported. The method merely involves Knoevenagel condensation of an (*E*)-2-alkenal with ethyl hydrogen malonate in DMSO, in the presence of piperidinium acetate as a catalyst, to give a mixture of ethyl alkadienoates. The (3*E*,5*Z*)-3,5-alkadienoate was selectively separated from the mixture of isomers, in high isomeric purity (95−98%), by formation of urea inclusion complexes.

MATERIALS AND METHODS

Materials. All commercial reagents and solvents were used as supplied. All (*E*)-2-alkenals were a gift from Vioryl S.A. (Athens, Greece) and were distilled before use. Ethyl hydrogen malonate was prepared according to the literature (*14*). Red-AL is a solution of sodium bis(2-methoxyethoxy)aluminum hydride in toluene 65%, from Sigma-Aldrich Chemie GmbH (Taufkirchen, Germany). Piperidinium acetate was prepared in situ, by mixing equivalent quantities of piperidine and acetic acid in 5 mL of DMSO. Thin-layer chromatography (TLC) was performed on 0.25 mm precoated silica gel 60 F_{254} aluminum sheets and column chromatography on silica gel 60 (0.063−0.2 mm), products of Merck & Co. (Darmstadt, Germany). 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, in $CDCl_3$ (with TMS as the internal standard). Gas chromatography−mass spectrometry (GC−MS) analyses were carried out with a GC−MS system Shimadzu QP 5050 equipped with a 30 m × 0.25 mm i.d. SPB-1 fused silica capillary column (carrier gas, helium 1 mL/min; injector temperature, 230 °C; oven temperature, 50 °C (5 min isothermal) raised at 4 °C/min up to 250 °C; ion source temperature, 220 °C; interface temperature, 250 °C; mass range, 40−500 amu; EI, 70 eV).

Representative Procedure for the Condensation of (*E*)-2-Alkenals with Ethyl Hydrogen Malonate: Synthesis of Ethyl (3*E*,5*Z*)-3,5-Tetradecadienoate (5d). In a round-bottom flask, equipped with a condenser and a bubbler at the exit of the condenser, a solution of ethyl hydrogen malonate (11.88 g, 0.09 mol) and piperidinium acetate (85 mg, 0.6 mmol) in DMSO (60 mL) was stirred at room temperature for 15 min, and (*E*)-2-dodecenal (10.92 g, 0.06 mol) was added at once. Stirring was continued for 30 min, and then the reaction mixture was heated gently at 85 °C, until the evolution of carbon dioxide ceased (3 h). Heating was continued at the same temperature, for 1 more hour. After cooling to room temperature, the reaction mixture was poured into cold water (150 mL) and extracted with diethyl ether (3 × 50 mL). The combined extracts were washed with water (50 mL) and dried over anhydrous Na_2SO_4, and the solvent was removed under a vacuum. The crude product (16.8 g) was distilled, to give a mixture of ethyl (3*E*,5*Z*)-3,5-tetradecadienoate **5d**, ethyl (3*E*,5*E*)-3,5-tetradecadienoate **6d**, and ethyl (2*E*,4*E*)-2,4-tetradecadienoate **7d** (10.58 g, 70%) as a colorless oil: bp 104−115 °C/0.5 mmHg.

Separation of Pure Ethyl (3*E*,5*Z*)-3,5-Tetradecadienoate (5d) by Urea Inclusion Complexes. The obtained mixture of ethyl tetradecadienoates (10.5 g) was added, under vigorous stirring, into a hot (50 °C) solution of urea (30.0 g, 0.50 mol) in methanol (150 mL). The resulting clear solution was allowed to cool slowly to room temperature, and a fine white precipitate began to separate. Then the mixture was left overnight at 4 °C. The precipitate was filtered rapidly and washed with cold hexane. The crystalline urea clathrates were treated as usual (*17*), to give a mixture of ethyl (3*E*,5*E*)-3,5-tetradecadienoate and ethyl (2*E*,4*E*)-2,4-tetradecadienoate as a pale yellow oil (6.5 g). The washing hexane and the filtrates were partially concentrated under a vacuum, and the resulting mixture was treated with hot (50 °C) water (100 mL) for 15 min. The mixture was cooled to room temperature and extracted with diethyl ether. The organic phase was washed with water and dried over anhydrous Na_2SO_4, and the solvent was removed under a vacuum, to give a pale yellow oil (4.6 g) enriched in ethyl (3*E*,5*Z*)-3,5-tetradecadienoate.

The obtained product was subjected to urea treatment one more time, as previously, to give an oil, which was purified by distillation to give finally pure ethyl (3*E*,5*Z*)-3,5-tetradecadienoate **5d** (3.2 g, 21% yield based on the alkenal used): bp 112−115 °C/0.1 mmHg; IR ν_{max}/cm^{-1} 1741, 983, 950; ^{1}H NMR δ 0.87 (3H, t, J = 6.8 Hz), 1.22−1.30 (15H, m), 2.15 (2H, q, J = 6.8 Hz), 3.12 (2H, d, J = 6.8 Hz), 4.10 (2H, q, J = 6.8 Hz), 5.41 (1H, dt, J_1 = 10.8 Hz, J_2 = 7.7 Hz), 5.72 (1H, dt, J_1 = 15.0 Hz, J_2 = 7.7 Hz), 5.98 (1H, dd, J_1 = 11.0 Hz, J_2 = 10.8 Hz), 6.41 (1H, ddd J_1 = 15.4 Hz, J_2 = 11.2 Hz, J_3 = 1.3 Hz); MS *m*/*z* 252 (M$^+$, 12), 178 (8), 164 (15), 95 (20), 79 (68), 67 (100). Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.05; H, 11.10.

The IR spectrum matched that of the literature (*12*).

Ethyl (3*E*,5*Z*)-3,5-Dodecadienoate (5c). This compound was obtained from ethyl hydrogen malonate (11.88 g, 0.09 mol) and (*E*)-2-decenal (9.24 g, 0.06 mol) by the typical procedure. The distilled mixture of esters was subjected to the urea inclusion treatment twice, to give finally pure ethyl (3*E*,5*Z*)-3,5-dodecadienoate **5c** (3.4 g, 25%) as a viscous oil: bp 105−108 °C/0.1 mmHg; IR ν_{max}/cm^{-1} 1741, 983, 950; ^{1}H NMR δ 0.88 (3H, t, J = 6.8), 1.17−1.30 (11H, m), 2.16 (2H, q, J = 6.8 Hz), 3.13 (2H, d, J = 6.8 Hz), 4.10 (2H, q, J = 6.8 Hz), 5.42 (1H, dt J_1 = 11.0 Hz, J_2 = 7.7 Hz), 5.73 (1H, dt J_1 = 15.0 Hz, J_2 = 7.7 Hz), 5.98 (1H, dd J_1 = 11.0 Hz, J_2 = 10.8 Hz), 6.42 (1H, ddd J_1 = 15.2 Hz, J_2 = 11.2 Hz, J_3 = 1.3 Hz); MS *m*/*z* 224 (M$^+$, 15), 150 (10), 136 (22), 95 (17), 79 (64), 67 (100). Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78. Found: C, 74.86; H, 10.76.

Ethyl (3*E*,5*Z*)-3,5-Decadienoate (5b). This compound was obtained from ethyl hydrogen malonate (11.88 g, 0.09 mol) and (*E*)-2-octenal (7.56 g, 0.06 mol) by the typical procedure. The distilled mixture of esters was subjected to the urea inclusion treatment, three consecutive times, to give finally pure ethyl (3*E*,5*Z*)-3,5-decadienoate **5b** (3.3 g, 28%) as a viscous oil: bp 98−101 °C/0.1 mmHg; IR ν_{max}/cm^{-1} 1740, 984, 951; ^{1}H NMR δ 0.89 (3H, t, J = 6.8 Hz), 1.17−1.43 (7H, m), 2.15 (2H, q, J = 6.8 Hz), 3.13 (2H, d, J = 6.8 Hz), 4.10 (2H, q, J = 6.8 Hz), 5.42 (1H, dt J_1 = 11.0 Hz, J_2 = 7.7 Hz), 5.73 (1H, dt J_1 = 15.0 Hz, J_2 = 7.7 Hz), 5.98 (1H, dd J_1 = 11.0 Hz, J_2 = 10.8 Hz), 6.42 (1H, ddd J_1 = 15.2 Hz, J_2 = 11.0 Hz, J_3 = 1.3 Hz); MS *m*/*z* 196 (M$^+$, 20), 150 (7), 122 (14), 108 (22), 79 (25), 67 (100). Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.54; H, 10.28.

Ethyl (3*E*,5*Z*)-3,5-Octadienoate (5a) (Mixture with Ethyl (3*E*,5*E*)-3,5-Octadienoate). This compound was obtained from ethyl hydrogen malonate (11.88 g, 0.09 mol) and (*E*)-2-hexenal (5.88 g, 0.06 mol) by the typical procedure. The distilled mixture of esters was subjected to the urea inclusion treatment, four consecutive times, to give finally a product enriched in ethyl (3*E*,5*Z*)-3,5-octadienoate as a viscous oil (3.5 g, 35%), containing a mixture of ethyl (3*E*,5*Z*)-3,5-octadienoate and ethyl (3*E*,5*E*)-3,5-octadienoate in a ratio of 3/2: bp 76−90 °C/0.1 mmHg; MS *m*/*z* less polar compound ethyl (3*E*,5*Z*)-3,5-octadienoate 168 (M$^+$, 44), 122 (5), 98 (4), 79 (42), 67 (100), 55(50); more polar compound ethyl (3*E*,5*E*)-3,5-octadienoate 168 (M$^+$, 33), 122 (2), 95 (100), 79 (28), 67 (80), 55 (40).

(3*E*,5*Z*)-3,5-Tetradecadienoic Acid (1) (Megatomoic Acid). To a cold (0−4 °C) stirred solution of aqueous KOH 1 N (5.6 mL, 5.6 mmol), a solution of ethyl (3*E*,5*Z*)-3,5-tetradecadienoate (140 mg, 0.56 mmol) in ethanol (2 mL) was added. Stirring was continued at the same temperature for 4 h, and the reaction was monitored by TLC. When the starting material was exhausted, the mixture was poured into a cold solution of HCl 1 N (10 mL) and then was extracted with diethyl ether (3 × 5 mL). The organic phase was dried over anhydrous Na_2SO_4 and

the solvent was evaporated under a vacuum, to give pure (3*E*,5*Z*)-3,5-tetradecadienoic acid (megatomoic acid) **1** (113 mg, 90%) as a viscous oil: IR ν_{max}/cm^{-1} 1712, 983, 950, 827; ^{1}H NMR δ 0.88 (3H, t, J = 6.8 Hz), 1.26−1.43 (12, m), 2.16 (2H, q, J = 6.8 Hz), 3.18 (2H, d, J = 10.8 Hz), 5.42 (1H, dt J_1 = 10.8 Hz, J_2 = 7.7 Hz), 5.69 (1H, dt J_1 = 15.3 Hz, J_2 = 7.7 Hz), 5.94 (1H, dd J_1 = 11.3 Hz, J_2 = 10.8 Hz), 6.46 (1H, ddd J_1 = 15.3 Hz, J_2 = 11.0 Hz, J_3 = 1.3 Hz). The IR and ^{1}H NMR spectra matched those of the literature (*8*).

(3*E*,5*Z*)-3,5-Tetradecadienyl Acetate (3). (a) To a cold (0−4 °C) stirred solution of Red-AL (2.1 mL, 6 mmol) in anhydrous diethyl ether (5 mL), a solution of ethyl (3*E*,5*Z*)-3,5-tetradecadienoate (252 mg, 1 mmol) in diethyl ether (2 mL) was added dropwise under nitrogen. Stirring was continued for 1 h at the same temperature, and then the solution was left overnight at room temperature. The end of the reaction was checked by TLC. The reaction mixture was poured carefully into a cold 5% solution of HCl (20 mL) and then was extracted with diethyl ether (3 × 5 mL). The organic phase was dried over anhydrous Na_2SO_4, and the solvent was evaporated under a vacuum. The residue was purified by column chromatography, over silica gel, to give pure (3*E*,5*Z*)-3,5-tetradecadienol (186 mg, 88%) as a viscous oil: IR ν_{max}/cm^{-1} 3625, 3390, 2990, 985, 952; ^{1}H NMR δ 0.88 (3H, t, J = 6.8 Hz), 1.26−1.40 (12H, m), 2.15 (2H, q, J = 6.8 Hz), 2.37 (2H, q, J = 6.8 Hz), 3.68 (2H, t, J = 6.8 Hz), 5.39 (1H, dt J_1 = 10.8 Hz, J_2 = 7.7 Hz), 5.62 (1H, dt J_1 = 15.0 Hz, J_2 = 7.7 Hz), 5.96 (1H, dd J_1 = 11.0 Hz, J_2 = 10.8 Hz), 6.42 (1H, ddd J_1 = 15.4 Hz, J_2 = 11.0 Hz, J_3 = 1.3 Hz). The ^{1}H NMR spectrum matched that of the literature (*8*).

(b) To a solution of acetic anhydride (1.0 mL, 10 mmol) in pyridine (4.0 mL) at 0−4 °C, (3*E*,5*Z*)-3,5-tetradecadienol (160 mg, 0.76 mmol) was added under stirring. The reaction was maintained at the same temperature for 1 h and then was brought to room temperature and monitored by TLC. When the reaction was finished (5 h), the mixture was poured in cold water (20 mL) and was extracted with diethyl ether. The organic phase was washed by dilute (5%) HCl and then by saturated $NaHCO_3$ and dried over anhydrous Na_2SO_4, and the solvent was removed under a vacuum. The crude product was purified by column chromatography over silica gel, to give pure (3*E*,5*Z*)-3,5-tetradecadienyl acetate **3** (160 mg, 84%) as a viscous liquid: IR ν_{max}/cm^{-1} 2990, 1744, 984, 950; ^{1}H NMR δ 0.87 (3H, t, J = 6.8 Hz), 1.27−1.43 (12H, m), 2.05 (3H, s), 2.16 (2H, q, J = 6.8 Hz), 2.43 (2H, q, J = 6.8 Hz), 4.10 (2H, t, J = 6.8 Hz), 5.39 (1H, dt J_1 = 10.8 Hz, J_2 = 7.7 Hz), 5.60 (1H, dt J_1 = 15.3 Hz, J_2 = 7.7 Hz), 5.96 (1H, dd J_1 = 11.3 Hz, J_2 = 10.8 Hz), 6.38 (1H, ddd J_1 = 15.2 Hz, J_2 = 11.0 Hz, J_3 = 1.3 Hz); MS *m*/*z* 192 (M^+ − 60, 26), 138 (3), 93 (23), 80 (100), 79 (92), 67 (28). The IR and ^{1}H NMR spectra matched those of the literature (*4*).

(3*E*,5*Z*)-3,5-Dodecadienyl Acetate (2). (a) Reduction of ethyl (3*E*,5*Z*)-3,5-dodecadienoate (450 mg, 2 mmol) by Red-AL (3 mL, 8 mmol) in anhydrous diethyl ether (8 mL), as previously described, gave pure (3*E*,5*Z*)-3,5-dodecadienol (332 mg, 91%) as a viscous oil: IR ν_{max}/cm^{-1} 3625, 3350, 2990, 985, 949; ^{1}H NMR δ 0.88 (3H, t, J = 6.8 Hz), 1.28−1.44 (8H, m), 2.17 (2H, q, J = 6.8 Hz), 2.38 (2H, q, J = 6.8 Hz), 3.72 (2H, t, J = 6.8 Hz), 5.37 (1H, dt J_1 = 10.8 Hz, J_2 = 7.7 Hz), 5.63 (1H, dt J_1 = 15.3 Hz, J_2 = 7.7 Hz), 5.96 (1H, dd J_1 = 11.0 Hz, J_2 = 10.8 Hz), 6.42 (1H, ddd J_1 = 15.3 Hz, J_2 = 11.2 Hz, J_3 = 1.3 Hz).

(b) Acetylation of (3*E*,5*Z*)-3,5-dodecadienol (182 mg, 1.0 mmol) by acetic anhydride (1.0 mL, 10 mmol) in pyridine (4.0 mL), as previously described, gave pure (3*E*,5*Z*)-3,5-dodecadienyl acetate **2** (192 mg, 86%) as a viscous oil: IR ν_{max}/cm^{-1} 2990, 1744, 984, 950; ^{1}H NMR δ 0.87 (3H, t, J = 6.8 Hz), 1.27−1.43 (8H, m), 2.05 (3H, s), 2.16 (2H, q, J = 6.8 Hz), 2.43 (2H, q, J = 6.8 Hz), 4.10 (2H, t, J = 6.8 Hz), 5.39 (1H, dt J_1 = 10.8 Hz, J_2 = 7.7 Hz), 5.60 (1H, dt J_1 = 15.3 Hz, J_2 = 7.7 Hz), 5.96 (1H, dd J_1 = 11.3 Hz, J_2 = 10.8 Hz), 6.38 (1H, ddd J_1 = 15.2 Hz, J_2 = 11.0 Hz, J_3 = 1.3 Hz); MS *m*/*z* 164 (M^+ − 60, 41), 110 (6), 93 (28), 80 (100), 79 (94), 67 (30). The ^{1}H NMR and mass spectra matched those of the literature (*2*, *15*, *16*).

RESULTS AND DISCUSSION

In the beginning of this investigation, the condensation of (*E*)-2-octenal with ethyl hydrogen malonate was used as a model study. Ethyl hydrogen malonate was chosen as the condensation agent instead of malonic acid, to obtain directly the corresponding ethyl ester, which could be easier isolated from the reaction mixture by distillation. This condensation was performed in DMSO, for 4 h at 85 °C, in the presence of a catalytic amount of piperidinium acetate and, as was expected, gave a mixture of isomers of ethyl decadienoate, along with other byproducts. Careful distillation, under a vacuum, of the crude reaction product gave the mixture of isomeric esters in good yield (71%). Detailed GC−MS analysis showed the presence of three main components with the same molecular weight (MW = 196). The more polar compound gave a dominant fragment *m*/*z* 125, corresponding to ethyl pyrilium, and also the pyrilium fragments *m*/*z* 97 and *m*/*z* 81, characteristic of ethyl (2*E*,4*E*)-decadienoate (*17*). The two less polar compounds have similar mass spectra, with fragments at *m*/*z* 123 and 122 corresponding to $[M - COOCH_2CH_3]^+$ and $[M - HCOOCH_2CH_3]^+$ and *m*/*z* 108 corresponding to $[M - CH_3COOCH_2CH_3]^+$, characteristic of the ethyl 3,5-alkadienoates (*6*), suggesting that the two compounds are isomeric ethyl 3,5-decadienoates. On the other hand, study of the ^{1}H NMR spectrum of the obtained mixture showed a system of two doublets at 3.07−3.11 and 3.11−3.14 ppm, which can be attributed to the allylic protons on C2 of two isomers of the ethyl 3,5-decadienoates (*1*, *5*). A distinct multiplet at the lower fields 7.11−7.33 ppm can be attributed to the protons on C3 of the ethyl (2*E*,4*E*)-decadienoate (*17*).

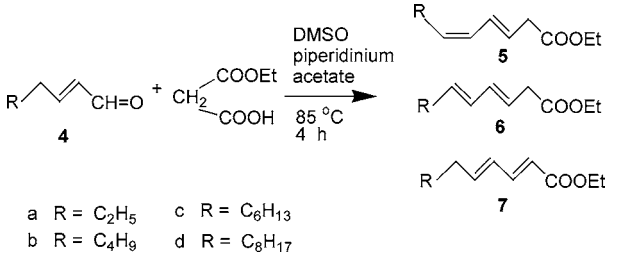

Figure 2. Condensation of (*E*)-2-alkenals with ethyl hydrogen malonate in DMSO, at 85 °C, in the presence of piperidinium acetate.

On the basis of the ^{1}H NMR spectrum and the GC−MS analysis of the obtained mixture, the structures that were attributed to the three main components were ethyl (3*E*,5*Z*)-3,5-decadienoate **5b**, ethyl (3*E*,5*E*)-3,5-decadienoate **6b**, and ethyl (2*E*,4*E*)-2,4-decadienoate **7b**. Other isomers of ethyl decadienoate, if present, were in quantities less than 0.5%. The overall condensation of the (*E*)-2-octenal with ethyl hydrogen malonate, illustrated in **Figure 2**, gave in 71% yield a mixture of ethyl (3*E*,5*Z*)-3,5-decadienoate **5b**, ethyl (3*E*,5*E*)-3,5-decadienoate **6b**, and ethyl (2*E*,4*E*)-2,4-decadienoate **7b**, in a ratio of 44:38:18, according to the GC analysis.

Regarding the reaction conditions, prolongation of the reaction time from 4 to 8 or more hours and increase of the reaction temperature from 85 to 120 °C gave a somewhat higher yield of the mixture of ethyl decadienoates, but the ethyl (3*E*,5*Z*)-3,5-decadienoate **5b** was less than 10% and the main product was the ethyl (2*E*,4*E*)-2,4-decadienoate **7b** (**Table 1**, entry 3). The same reaction conditions were applied to the condensation of the following aldehydes: (*E*)-2-hexenal **4a**, (*E*)-2-decenal **4c**, and (*E*)-2-dodecenal **4d**. Detailed GC−MS analyses of the distilled reaction products from any of the above aldehydes gave similar results to the (*E*)-2-octenal **4b** condensation (**Table 1**).

Separation of geometrical isomers of 3,5-alkadienyl esters by preparative column chromatography on silver nitrate impregnated silica gel has been already reported (*2a*, *18*). To avoid this laborious and expensive procedure, the use of urea inclusion complexes seemed promising. It is known that formation of urea inclusion complexes is a useful method for preparative scale

Table 1. Condensation of (*E*)-2-Alkenals with 50% Excess of Ethyl Hydrogen Malonate, in the Presence of Piperidinium Acetate (1% mol) as Catalyst, in DMSO

entry	substr	product	bp (°C, 0.5 mmHg)	yield[a] **5** + **6** + **7** (%)	ratio[b] **5**:**6**:**7**
1	**4a**	ethyl octadienoates[c]	60–80	78	42:41:17
2	**4b**	ethyl decadienoates[c]	75–90	71	44:38:18
3	**4b**	ethyl decadienoates[d]	75–90	75	8:28:64
4	**4c**	ethyl dodecadienoates[c]	85–100	72	39:43:18
5	**4d**	ethyl tetradecadienoates[c]	104–115	70	37:48:15

[a] Yields refer to the distilled mixture of isomers. [b] Calculated from the integration of the GC analyses. [c] The condensation was performed at 85 °C for 4 h. [d] The condensation was performed at 120 °C for 8 h.

Table 2. Separation of Ethyl (3*E*,5*Z*)-3,5-Alkadienoates by Formation of Urea Inclusion Complexes

entry	isolated isomer	no. of treatments	yield[a] (%)	isomeric purity
1	ethyl (3*E*,5*Z*)-3,5 octadienoate	4	35.0	60
2	ethyl (3*E*,5*Z*)-3,5-decadienoate	3	28.0	95
3	ethyl (3*E*,5*Z*)-3,5-dodecadienoate	2	25.3	97
4	ethyl (3*E*,5*Z*)-3,5-tetradecadienoate	2	21.1	98

[a] Yield based on the quantity of the starting (*E*)-2-alkenal.

separation of individual geometrical isomers from their mixtures (*19*). Urea inclusion complexes (clathrates) are formed preferentially with *E*,*E* isomers (*17*), which, as guest molecules, are held in the channel of the helical lattice of hydrogen bonded urea molecules. Indeed, in the present work, the (2*E*,4*E*) and (3*E*,5*E*) isomers are able to form crystalline complexes with urea, while the (3*E*,5*Z*) isomers remained in solution and were isolated from the mother liquid. The complexation process was repeated one or more times, to improve the isomeric purity of the product. The results of the separations are summarized in **Table 2**.

Taking into account the above results, it is concluded that the separation of the (3*E*,5*Z*)-3,5-alkadienoates, by the urea complexation, was more efficient for the products with a longer chain of carbon atoms. The ethyl (3*E*,5*Z*)-3,5-dodecadienoate **5c** and the (3*E*,5*Z*)-3,5-tetradecadienoate **5d** were obtained in high isomeric purity (97−98%), only with two complexations with urea. The ethyl (3*E*,5*Z*)-3,5-decadienoate **5b** was obtained in 95% isomeric purity, after three complexations, and the ethyl (3*E*,5*Z*)-3,5-octadienoate **5a** failed to be isolated in acceptable isomeric purity, even after four urea complexations.

The utility of the herein described preparation of pure ethyl (3*E*,5*Z*)-3,5-alkadienoates was illustrated by their simple transformations to known principal sex pheromone components. Thus, the ethyl (3*E*,5*Z*)-3,5-tetradecadienoate **5d**, by simple hydrolysis in aqueous KOH, gave the corresponding acid, known as megatomoic acid **1** (**Figure 3**). Reduction of the same ethyl ester **5d**, by Red-AL in diethyl ether, gave the corresponding alcohol, which by acetylation gave in 84% yield the (3*E*,5*Z*)-3,5-tetradecadienyl acetate **3**, sex attractant of the *R. leucatella* Clerck (**Figure 3**). Starting from the ethyl (3*E*,5*Z*)-3,5-dodecadienoate **5c**, by the same reduction−acetylation procedure, the (3*E*,5*Z*)-3,5-dodecadienyl acetate **2** was obtained in 86% yield. From all the reported syntheses of the (3*E*,5*Z*)-3,5-dodecadienyl acetate **2**, pheromone of the leafroller *B. cranaodes* Meyrick (*2*, *15*, *16*, *20*), the present synthesis uses the most common and cheap reagents.

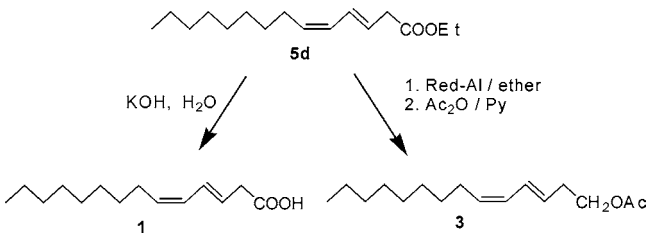

Figure 3. Synthesis of megatomoic acid **1** and (3*E*,5*Z*)-3,5-tetradecadienyl acetate **3**.

In conclusion, the one step preparation of the (3*E*,5*Z*)-3,5-alkadienoates, by the herein described method, is experimentally easy and efficient. The separation of the (3*E*,5*Z*) isomer from the reaction mixture was easily and conveniently accomplished by elimination of the (3*E*,5*E*) and (2*E*,4*E*) isomers by formation of crystalline urea inclusion complexes. This step eliminates the necessity for chromatographic separations, making the technique suitable for large-scale preparation of the biologically active compounds **1**, **2**, and **3**. The simplicity, rapidity, and low cost of this procedure make it useful for the semiochemical community.

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