Synthesis of *cis*-12-Nonadecen-9-one, *cis*-13-Icosen-10-one, the Pheromone of Peach Fruit Moth, and *cis*-15-Henicosen-11-one, the Pheromone of Douglas Fir Tussock Moth

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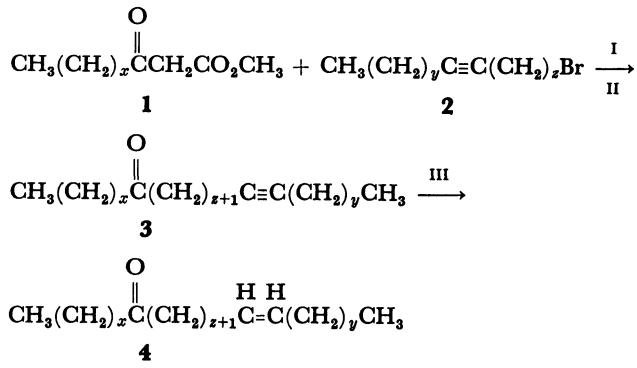
Synopsis. A convenient synthesis of *cis*-12-nonadecen-9-one (**4a**), *cis*-13-icosen-10-one (**4b**), the pheromone of peach fruit moth, and *cis*-15-henicosen-11-one (**4c**), the pheromone of Douglas fir tussock moth, is described. **4a** was synthesized from methyl 3-oxoundecanoate and 1-bromo-2-nonyne (**2a**) *via* 12-nonadecyn-9-one. The higher homolog **4b** could be obtained from methyl-3-oxododecanoate and **2a**. Similarly, **4c** was prepared from methyl 3-oxotridecanoate and 1-bromo-3-nonyne (**2b**).

cis-12-Nonadecen-9-one (**4a**) and *cis*-13-icosen-10-one (**4b**) have been recognized as the principles of sex pheromone of Japanese peach fruit moth (*Carposina niponensis* Walsingham), a major economic pest of peach, apple and other fruits in Japan.[1] It is pointed out that a mixture of **4a** and **4b** in a ratio 1:20 shows the strongest biological activity.[1,2] On the other hand, *cis*-15-henicosen-11-one (**4c**) is known as the sex pheromone of Douglas fir tussock moth (*Orgyia pseudotsugata* McDunnough), a severe defoliator of Douglas fir and other fir forests in western North America.[3] These three compounds are unusual in that most lepidopterous sex pheromones are characterized as unsaturated fatty alcohols, acetates or aldehydes of C_{12}, C_{14}, or C_{16} chain length.[4]

Since above mentioned pheromones are potent male attractants, and might be of practical interests, a variety of synthetic methods of **4a**, **4b**,[1,5] and **4c**[6] have been reported. However no example for the preparation of these unsaturated ketones by the same technique has been explored.

Recently general and practical methods for the synthesis of arbitrary β-keto esters, versatile intermediates in organic synthesis, have been developed.[7] Thus we wish to report here a convenient synthesis of **4a**, **4b**, and **4c** starting from β-keto esters (**1**) which could be obtained easily accoding to Yonemitsu *et al.*[7a]



1 a: $x=7$, b: $x=8$, c: $x=9$; **2** a: $y=5$, $z=1$, b: $y=4$, $z=2$; **3**,**4** a: $x=7$, $y=5$, $z=1$, b: $x=8$, $y=5$, $z=1$, c: $x=9$, $y=4$, $z=2$
I: NaH in Toluene; II: wet DMSO; III: H_2/Pd-$BaSO_4$

Scheme 1.

The high stereoselectivity and chemical yield anticipated for the reduction of acetylenic bond to corresponding *cis*-olefin suggested 12-nonadecyn-9-one (**3a**), 13-icosyn-10-one (**3b**) and 15-henicosyn-11-one (**3c**) as the primary synthetic goal.[8] Thus the synthesis of title compounds **4a**, **4b**, and **4c** was carried out according to Scheme 1.

Methyl 3-oxoundecanoate (**1a**) was alkylated with 1-brom-2-nonyne (**2a**) in toluene in the presence of sodium hydride. The porduct, without isolation, was then heated in wet dimethyl sulfoxide (DMSO)[9] to be demethoxycarbonylated to 12-nonadecyn-9-one (**3a**) in a good yield (80%). **3b** was also prepared in the same manner from methyl 3-oxododecanoate (**1b**). **3c** could be obtained by the same procedure from methyl 3-oxotridecanoate (**1c**) and 1-bromo-3-nonyne (**2b**) in a low yield (≈40%). However, the yield of **3c** was improved upon (78%) by carrying out the alkylation in the presence of *N*,*N*-dimethylformamide (DMF). These acetylenic ketones were partially hydrogenated over palladium/barium sulfate catalyst to give desired compounds in 89—91% yields. The resulting products, **4a**, **4b**, and **4c** showed no infrared absorption band in the neighborhood of 970 cm^{-1} due to disubstituted *trans*-alkene. The structure of these products were identified by comparing IR and NMR spectra with those of reported data.[5,6]

Experimental

The IR and NMR spectra were recorded on Hitachi 285 and JEOL/FX-100 spectrometer respectively.

*12-Nonadecyn-9-one (**3a**), 13-Icosyn-10-one (**3b**),* and *15-Henicosyn-11-one (**3c**).* To a stirred suspension of sodium hydride (50% mineral oil dispersion 1.49 g, 31 mmol) in dry toluene (150 ml) a solution of methyl 3-oxoundecanoate (**1a**) (6.42 g, 30 mmol) in dry toluene (20 ml) was added dropwise over a period of 20 min at room temperature. Stirring was continued for 1 h. Then 1-bromo-2-nonyne (**2a**)[10] (6.7 g, 32 mmol) and powdered sodium iodide (2 g) were added. The mixture was refluxed for 11 h and then poured onto cold hydrochloric acid. The toluene layer was separated and the solvent was distilled off *in vacuo*. The residue was dissolved in a mixture of DMSO (50 ml) and water (5 ml) then the solution was heated (150 °C, bath temp) for 3.5 h. The mixture was poured onto ice water and extracted with ether (100 ml×2). The ether solution was washed with brine and dried over anhydrous magnesium sulfate, concentrated *in vacuo* to give crude **3a** as a pale yellow liquid. This crude **3a** was chromatographed over silicagel with hexane-benzene (6:4) as eluent to give 6.66 g (80%) of **3a**. IR (neat): 2940, 2860, 1720, 1460, 1090 cm^{-1}. NMR ($CDCl_3$): δ 0.87 (6H, distored t, J=6 Hz), 1.08—

1.66 (20H, br s), 1.97—2.23 (4H, m), 2.25—2.63 (4H, m). *13-Icosyn-10-one (3b)* was obtained from methyl 3-oxododecanoate (**1b**) and **2a** by the same procedure in 78% yield. IR (neat): 2960, 2860, 1720, 1460, 1090 cm^{-1}. NMR ($CDCl_3$): δ 0.90 (6H, distored t, J=6 Hz), 1.05—1.73 (22H, br s), 1.96—2.22 (4H, m), 2.27—2.63 (4H, m). *15-Henicosyn-11-one (3c)* could be prepared from methyl 3-oxotridecanoate (**1c**) and 1-bromo-3-nonyne (**2b**)[11] in 78% yield by using a mixture of toluene and DMF (10—15% of toluene)[12] as the solvent of the alkylation. IR (neat): 2920, 2840, 1715, 1460, 1090 cm^{-1}. NMR ($CDCl_3$): δ 0.93 (6H, distored t, J=6 Hz), 1.10—1.80 (24H, br s), 1.98—2.23 (4H, m), 2.26—2.60 (4H, m).

cis-*12-Nonadecen-9-one (4a)*, cis-*13-Icosen-10-one (4b)*, and cis-*15-Henicosen-11-one (4c)*. A methanol solution (35 ml) of **3a** (1.60 g, 5.8 mmol) containing two drops of quinoline was hydrogenated over 5% Pd-$BaSO_4$ (120 mg) under atmospheric pressure for 3 h. The solid was filtered off and the filtrate was concentrated *in vacuo*. The residue was dissolved in ether and washed with 5% hydrochloric acid, brine, dried over magnesium sulfate. Concentration of ether gave crude **4a** which was chromatographed over silica gel with hexane-benzene (6:4) as eluent to obtain 1.48 g (91%) of **4a**. IR (neat): 2960, 1710, 1460, 1370 cm^{-1}. NMR ($CDCl_3$): δ 0.88 (6H, distored t, J=6 Hz), 1.10—1.70 (20H, br s), 1.90—2.12 (2H, m), 2.20—2.42 (6H, m), 5.17—5.40 (2H, m). cis-*13-Icosen-10-one (4b)* was obtained by the same manner from **3b** in 89% yield. IR (neat): 2930, 1710, 1470, 1370 cm^{-1}. NMR ($CDCl_3$): δ 0.90 (6H, distored t, J=6 Hz), 1.10—1.70 (22H, br s), 1.90—2.10 (4H, m), 2.20—2.40 (6H, m), 5.15—5.40 (2H, m). cis-*Henicosen-11-one (4c)* was prepared from **3c** by the same procedure in 91% yield. IR (neat): 3000, 1715, 1460, 1370 cm^{-1}. NMR ($CDCl_3$): δ 0.98 (6H, distored t, J=6 Hz), 1.05—1.75 (24H, br s), 1.90—2.15 (4H, m), 2.35 (4H, t, J=7 Hz), 5.26—5.32 (2H, m).

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8) Another reason for choosing **3** as key intermediate for **4** is the fact that *trans*-olefin can also be obtained easily by reduction of acetylene with Na/NH_3. It is known that the trans isomer of **4c** is also biologically active (see Ref. 3).

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12) When a large quantity of DMF was used the yield of **3c** was lower (≈66%).