A Facile Synthesis of the Sex Pheromone of the Red Bollworm Moth from 10-Undecen-1-ol

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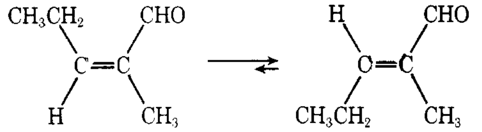
Considerable attention has been focused in recent years on the possibility of utilizing noninsecticidal means of insect control. One particular development in this area has been the examination of the use of insect sex pheromones[2] as a means of controlling insect behavior. Among the pests for which a sex pheromone has been identified is the red bollworm moth, *Diparopsis castanea* Hmps., which does substantial damage to the cotton crop in southeastern Africa. The most potent of the sex pheromones produced by the virgin female of this species was recently shown[3] by Nesbitt and co-workers to be *trans*-9,11-dodecadien-1-ol acetate (**13**). A nonstereoselective synthesis of the latter compound by this same group[4] was followed shortly by an alternate approach[5] that involved the coupling of a Grignard reagent with an allylic halide. In this note we report a convenient method for the synthesis of this diolefinic pheromone (**13**) from 10-undecen-1-ol (**4**), obtained by reduction of undecylenic acid (**3**) with lithium aluminum hydride.

In planning the route to diene **13**, *trans*-11-hydroxy-2-undecenal (**11**) seemed to be the most attractive intermediate. It not only possesses the requisite functionality for further elaboration into the pheromone, but it also offers the potential for a stereoselective synthesis since the double bond in such α,β-unsaturated aldehydes is susceptible to facile isomerization with the equilibrium heavily favoring the E (trans) configuration. As an illustration of the ease with which this and similar isomerizations occur, Rapoport and co-workers have reported[6] that the cis aldehyde **1** is unstable and, after standing for 48 h at room temperature, afforded about 35% of the corresponding trans stereoisomer (**2**) in a sample of **1** which was initially free of the trans isomer.

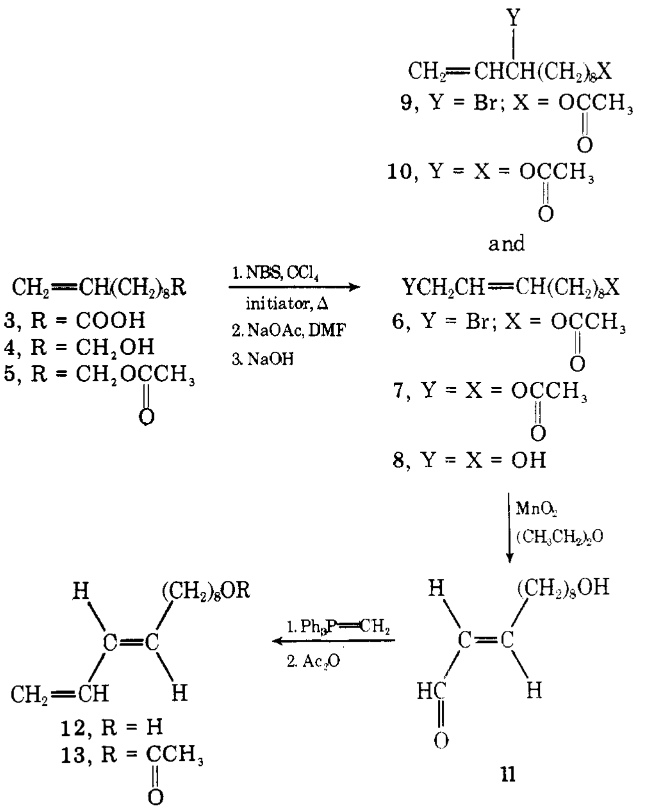


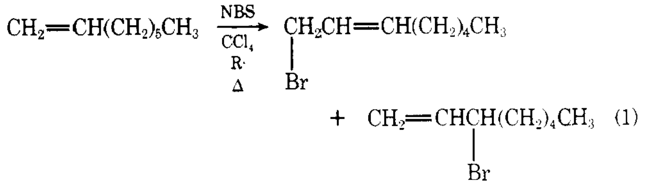
1 2

Aldehyde **11** had previously been prepared[7] by a process involving allylic oxidation of 10-undecen-1-ol acetate (**5**) with selenium dioxide in acetic anhydride as the key step. Unfortunately, the latter reaction proceeded to give a mixture of the desired rearranged allylic acetate (**7**) and the corresponding unrearranged isomer (**10**) in only 27.5% yield after fractional distillation.

Since N-bromosuccinimide (NBS) can be used to brominate olefins at the allylic position (the Wohl–Ziegler bromination) and allylic shifts can occur when the radical intermediate is unsymmetrical,[8] we decided to investigate this reaction using 10-undecen-1-ol acetate (**5**). Reaction of the latter olefinic ester with 1 equiv of NBS in refluxing carbon tetrachloride in the presence of 2,2′-azobis(2-methylpropionitrile) as an initiator, followed by treatment of the crude allylic bromide (**6** and perhaps **9**) with sodium acetate in N,N-dimethylformamide, afforded 2-undecen-1,11-diol diacetate (**7**) as an undetermined mixture[9] of stereoisomers in 32% overall yield (51%, based on recovered starting material) from 10-undecen-1-ol (**4**). The failure to detect significant amounts (>2%) of the unrearranged allylic isomer (**10**) by VPC and NMR analysis was surprising in view of previous work[10] that demonstrated conversion of 1-octene under similar reaction conditions to a 5:1 mixture of 1-bromo-2-octene and unrearranged 3-bromo-1-octene (eq 1).

Scheme I





$$CH_2{=}CH(CH_2)_5CH_3 \xrightarrow[\Delta]{\text{NBS},\ CCl_4,\ R\cdot} \underset{Br}{CH_2}CH{=}CH(CH_2)_4CH_3 + CH_2{=}CH\underset{Br}{CH}(CH_2)_4CH_3 \quad (1)$$

After saponification of diacetate **7** the corresponding diol (**8**) was selectively oxidized using manganese dioxide[11] to afford the known[7] aldehyde **11** as an 85:15 mixture[12] of E:Z stereoisomers in 75% yield. The total synthesis of the desired pheromone (**13**) was formally completed by a Wittig reaction between methylenetriphenylphosphorane and aldehyde **11** to give 9,11-dodecadien-1-ol (**12**) in 78% yield [28% conversion overall from 10-undecen-1-ol (**4**)] and 97% purity by VPC analysis. The physical and spectral properties of the latter compound (**12**) were consistent with those previously reported[5] for this same compound.

Since the E and Z stereoisomers of alcohol **12** and its acetate derivative (**13**) have been reported[4] to be difficult to resolve by chromatographic methods, a procedure devised by Nesbitt and co-workers[4] was utilized to elucidate the stereoisomeric purity of compound **12**. The E:Z ratio as determined by this method[13] was 7:1, indicating that no appreciable isomerization of the α,β-unsaturated carbonyl system had occurred in the strongly basic medium necessary for effecting the Wittig reaction used to convert aldehyde **11** into diene **12**.

Experimental Section[14]

2-Undecen-1,11-diol Diacetate (7). A mixture of 7.88 g (37.06 mmol) of 10-undecen-1-ol acetate (**5**),[15] 6.61 g (37.1 mmol) of N-

bromosuccinimide,[16] and 40 mg of 2,2′-azobis(2-methylpropionitrile) in 30 mL of carbon tetrachloride was refluxed for 60 min. After cooling this mixture to room temperature, it was diluted with 120 mL of pentane and the product was isolated in the usual manner.[14] Owing to the instability of allylic bromide **6**, the crude product (10.70 g) was immediately dissolved in 60 mL of *N,N*-dimethylformamide containing 11.5 g (140 mmol) of anhydrous sodium acetate and this mixture was subsequently stirred at room temperature for 20 h. Dilution of this mixture with 450 mL of water followed by extraction with ether[14] afforded 8.39 g of crude diacetate **7**, contaminated with a substantial amount of unreacted starting material (**5**) among other impurities. Chromatography on 400 mL of silica gel (elution with hexane–4% ether) afforded 2.97 g (13.99 mmol, 38% recovery of starting material) of 10-undecen-1-ol acetate (**5**).[17] Subsequent elution with hexane–40% ether afforded 3.15 g (32% overall yield; 51% based on recovered starting material) of diacetate **7**: bp 140–155 °C (bath temperature, 0.1 mm) [lit.[7] bp 136–138 °C (0.8 mm)]; $\nu_{\max}$ (film) 1750 ($C{=}O$), 1245, 1172, 1030, 970 cm^{-1}; δ Me_4Si (CCl_4) 5.60 (m, $CH{=}CH$), 4.42 (doublet, J = 5.5 Hz, $CH{=}CHCH_2OAc$), 3.98 (triplet, J = 6 Hz, CH_2OAc), 1.98 [s, 2 $OC({=}O)CH_3$], 1.33 ppm (broad s, 12 H).

2-Undecen-1,11-diol (8). A mixture of 1.57 g (5.81 mmol) of diester **7**, 25 mL of methanol, and 7 mL of 10% aqueous sodium hydroxide solution was stirred at room temperature for 16 h. Dilution of the mixture with 150 mL of saturated brine followed by extraction[14] with ether afforded 1.01 g (93%) of diol **8**: bp 128–143 °C (bath temperature, 0.08 mm) [lit.[7] bp 128 °C (0.45 mm)]; $\nu_{\max}$ (film) 3360 (OH), 1675 ($C{=}C$), 1085, 1055, 1005, 970, 720 cm^{-1} (weak); δ Me_4Si ($CDCl_3$) 5.65 (m, $CH{=}CH$), 4.08 (broad doublet, J = 3.5 Hz, $CH{=}CHCH_2OH$), 3.61 (triplet, J = 6 Hz, CH_2OH), 2.57 (s, 2 OH), 2.04 (broad m, $CH_2CH{=}CH$), 1.32 ppm (broad s, 12 H); mp of bisphenylurethane 106–107 °C [reported[7] mp 108 °C (136 °C)].

Alternatively, diol **8** could be obtained directly from crude diacetate **7** without the necessity of chromatography of the latter (**7**) on silica gel. The crude diacetate **7** contaminated with 10-undecen-1-ol acetate (**5**) and other unidentified impurities was prepared as described earlier with 29.8 mmol of unsaturated ester **5**. The saponification was effected by subsequent treatment of this material with 100 mL of methanol and 25 mL of 10% aqueous sodium hydroxide at room temperature for 16 h. Dilution of this mixture with 75 mL of water and extraction (6 × 50 mL) with carbon tetrachloride permitted separation of 10-undecen-1-ol (**4**) and other impurities from the more polar diol (**8**) which remained in the aqueous methanol layer. Subsequent addition of 650 mL of saturated brine to the aqueous layer followed by extraction[14] with ether afforded 1.44 g (26% uncorrected yield from acetate **5**) of diol **8**, 96% pure by VPC analysis,[18] oven temperature 205 °C, retention time 7.4 min. Two unidentified impurities (retention times 4.7 and 9.5 min), each comprising approximately 2% of the mixture, were shown not to be 10-undecen-1-ol (**4**) by coinjection with an authentic sample of the latter (**4**).

***trans*-11-Hydroxy-2-undecenal (11).** A mixture of 1.691 g (9.09 mmol) of diol **8**, 17.9 g (206 mmol) of activated manganese dioxide,[19] and 85 mL of anhydrous diethyl ether was stirred vigorously at room temperature for 8 h. Removal of the solid by filtration, thorough washing of this material with anhydrous ether, and subsequent removal of the solvent under reduced pressure[14] afforded 1.255 g (75%) of aldehyde **11** as an 85:15 mixture[12] of *E*:*Z* stereoisomers: $\nu_{\max}$ (film) 3410 (OH), 2750 (CHO), 1690 ($C{=}O$), 1640 ($C{=}C$), 1055, 972 cm^{-1}; δ Me_4Si ($CDCl_3$) 10.09 (doublet, J = 7.5 Hz, "*Z*" CHO, 15% of the mixture), 9.52 (doublet, J = 7.5 Hz, "*E*" CHO, 85% of the mixture), 7.06–5.86 (complex pattern, $CH{=}CH$, peaks at 7.06, 6.96, 6.84, 6.79, 6.68, 6.57, 6.23, 6.11, 5.98, and 5.86), 3.52 ppm (triplet, J = 6 Hz, CH_2OH); mp of 2,4-dinitrophenylhydrazone 116–117 °C [reported[7] mp 118 °C].

***trans*-9,11-Dodecadien-1-ol (12).** A mixture of 9.38 mmol of sodium hydride and 10 mL of dimethyl sulfoxide was heated at 65 °C until hydrogen evolution had ceased, after which the reaction flask was placed in a water bath (20 °C) and a solution of 3.68 g (10.3 mmol) of methyltriphenylphosphonium bromide[16] in 15 mL of dimethyl sulfoxide was added dropwise rapidly. This mixture was stirred at room temperature for 20 min and then a solution of 273 mg (1.48 mmol) of aldehyde **11** in 5 mL of dimethyl sulfoxide was added dropwise over a period of 5 min. This mixture was subsequently stirred at room temperature for 2 h, after which it was diluted with 200 mL of water and the product was isolated[14] by extraction with 1:1 (v/v) ether–pentane. The dried extracts were concentrated in vacuo to a volume of 5 mL and triphenylphosphine oxide was removed from the desired product by filtration through a column of 15 mL of Florisil (elution with 1:1 ether–pentane). Removal of the solvent followed by evaporative distillation afforded 213 mg (78%) of dienol **12**: bp 95–105 °C (bath temperature, 0.1 mm) [lit.[5] bp 111.5–112.5 °C (0.3 mm)]; 97% pure[20] by VPC analysis,[18] oven temperature 188 °C, retention time 6.1 min. The IR and NMR spectra of the product were virtually identical[21] with those previously reported[5] for this same alcohol (**12**). Subsequent analysis of dienol **12** using a method[13] devised by Nesbitt and co-workers[4] indicated that the product consisted of a 7:1 mixture of *E*:*Z* stereoisomers.

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Registry No.—4, 112-43-6; **5,** 112-19-6, **6,** 61617-98-9; *E*-**7,** 61617-99-0; *Z*-**7,** 61618-03-9; *E*-**8,** 61618-00-6; *Z*-**8,** 61618-04-0; *E*-**11,** 61618-01-7; *Z*-**11,** 61618-02-8; *E*-**12,** 55110-79-7; *Z*-**12,** 61618-05-1; *E*-**13,** 50767-78-7; *Z*-**13,** 51760-35-1.

References and Notes

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(9) The infrared spectrum exhibited a strong absorption band at 970 cm^{-1} (characteristic of a trans disubstituted olefinic linkage), whereas there was only an extremely weak absorption band at 720 cm^{-1}. Hence the olefinic linkage in diacetate **7** has predominantly the *E* configuration.

(10) L. Bateman and J. I. Cunneen, *J. Chem. Soc.*, 941 (1950).

(11) J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J. Chem. Soc.*, 1094 (1952).

(12) The *E*:*Z* ratio was determined by integration of the signals for the aldehydic proton. The *E* (trans) configuration of the major component of the mixture was verified by comparison of the chemical shift of its aldehydic proton (δ 9.52) with the corresponding peak for a pure sample of *trans*-2-hexenal[16] (doublet at δ 9.52).

(13) This method involved acetylation of alcohol **12**, followed by selective epoxidation of the internal double bond in unsaturated ester **13** using 1 equiv of *m*-chloroperbenzoic acid in benzene at 6 °C. The *E*:*Z* ratio was determined by subsequent VPC analysis of the trans and cis internal monoepoxides using a 6 ft × 0.125 in. Carbowax 20M column. The authors would like to thank Mr. Fred Alexander of Loyola University of Chicago for his assistance in this analysis.

(14) Reactions were carried out under a nitrogen atmosphere. Unless indicated otherwise, the isolation of reaction products was accomplished by pouring the mixture into water or saturated brine and extracting thoroughly with the specified solvent. The combined extracts were washed with water and dried over anhydrous magnesium sulfate. The solvent was removed from the dried extracts by using a rotary evaporator under reduced pressure. Evaporative distillation refers to bulb-to-bulb (Kugelrohr) short-path distillation. Melting points were determined on a Fisher-Johns block and are corrected. The NMR spectra were recorded with a Varian A-60 NMR spectrometer and infrared spectra were obtained using a Beckman Acculab 1 spectrophotometer.

(15) A. Grün and T. Wirth, *Ber.*, **55**, 2206 (1922). Ester **5** was prepared in quantitative yield from the commercially available[16] 10-undecen-1-ol (**4**) by treatment of the latter with 1:1 (v/v) benzene–acetic anhydride (2.5 M solution with respect to alcohol **4**) containing anhydrous sodium acetate (1.25 M).

(16) Available from Aldrich Chemical Co., Milwaukee, Wis.

(17) Identified by comparison of its IR and NMR spectra with those of an authentic sample.

(18) A 6 ft × 0.125 in. SE-30 column was used for this analysis.

(19) Available from Sterwin Chemicals, Inc., New York, N.Y.

(20) Two unidentified impurities (retention times 4.3 and 7.2 min, respectively) each comprised approximately 1.5% of the mixture.

(21) The only discrepancy between the spectral data observed for alcohol **12** prepared by the route described in this note and that reported previously[5] for this same compound was the exact number (and location) of signals in the vinyl hydrogen region of the NMR spectrum. The vinyl hydrogen absorption (5 H) consisted of a complex multiplet (4.85–6.40 ppm) with peaks at 4.85, 4.96, 4.99, 5.12, 5.15, 5.22 (weak), 5.61 (weak), 5.72, 5.81, 5.96, 6.06, 6.13, 6.19, 6.24, 6.28, and 6.40 ppm. This discrepancy is perhaps due to the presence of a different amount of the cis stereoisomer of alcohol **12** as a minor component in the product.