A comparative study of the synthetic paths from 1-butyne to 2*E*,4*Z*-heptadien-1-ol

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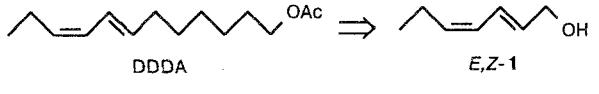
2*E*,4*Z*-Heptadien-1-ol (**1**), the key intermediate in the synthesis of the grapevine moth sex pheromone, was obtained from 1-butyne by a number of alternative procedures, including various variants of the stereocontrolled building of the conjugated *E,Z*-diene system (Cadiot—Chodkiewicz cross-coupling, alkyne—vinyl halide cross-coupling catalyzed by palladium complexes, anionotropic allylic rearrangement, partial *cis*- and *trans*-reduction of the triple bond). None of them could provide for configurational uniformity of **1**. The most acceptable path to obtain **1** in multigram amounts appears to be that which proceeds via the conjugated diynol and enynol intermediates with subsequent catalytic *cis*-hydrogenation.

Key words: 2,4-heptadiyn-1-ol, reduction; 2-hepten-4-yn-1-ol, reduction; 3-acetoxy-1,4-heptadiene, rearrangement; 2,4-heptadien-1-ol, configurational uniformity.

7*E*,9*Z*-Dodeca-7,9-dienyl acetate (DDDA) is the sex pheromone of the grapevine moth *Lobesia botrana* (Schiff). A number of synthetic paths to DDDA have been described; among these, there are methods based on the organocuprate coupling of Grignard reagents obtained from a linear α,ω-bifunctional C_5-fragment, with iodide[1] or acetate[2—4] prepared from 2*E*,4*Z*-hepta-2,4-dien-1-ol (*E,Z*-**1**). Dienol *E,Z*-**1**, which is the key intermediate in these methods used for the synthesis of DDDA, is obtained with a configurational purity of 93—96 % and contains 4—7 % of the 2*E*,4*E*-stereoisomeric alcohol (*E,E*-**1**).[4,5] Although in the case of organocuprate coupling of the electrophiles obtained from *E,Z*-**1** with the complementary Grignard reagents, the C_{12}-block thus obtained contains up to 20—25 % of the 7*E*,9*E*-stereoisomer (i.e., the reaction brings about a partial loss of the *cis*-configurational uniformity of the electrophile),[1—4] this method is considered as suitable for larger scale preparation of DDDA, because field trials have shown[6,7] that the attractive activity of mixtures of DDDA with its 7*E*,9*E*-stereoisomer in ~9:1—6:4 ratios is almost as high as that for geometrically pure DDDA; hence, the above mixtures are quite acceptable for practical application in the struggle against vermin.*



DDDA *E,Z*-**1**

* A similar conclusion was drawn from the field trials of a sample of *E,Z*-DDDA prepared according to the method described in the literature;[4] the trials were carried out in 1990—1991 by the Institute of Plant Protection (Georgia).

Taking this into account, we continued the earlier study[4] of the optimization of the laboratory procedure for the synthesis of dienol *E,Z*-**1** with the idea of using the most readily available starting compounds. In the present study we chose 1-butyne (**2**), which is easily produced by alkylation of acetylene,[8] as such a starting compound. The construction of the intermediate C_7-blocks necessary for the synthesis of *E,Z*-**1** was carried out in various ways (Scheme 1).

Path 2→3→4→1. The coupling of **2** with 3-bromo-2-propyn-1-ol under the Cadiot—Chodkiewicz reaction conditions[9] gives the known diacetylenic alcohol **3** in 50—55 % yield. Diynol **3** is obtained in higher yield by reacting propargyl alcohol (PA) with 1-bromobut-1-yne (BB) under similar conditions; however, in total, this variant is less preferable, since it requires more operations, and the yield of BB does not exceed 40 % as this volatile bromide is partially lost upon purification.

The reduction of **3** with lithium aluminum hydride in boiling Et_2O or THF (cf. ref. 10) affords the configurationally uniform *E*-2-hepten-4-yn-1-ol (**4**) in high yield. In addition, the reaction gives (yield 2—12 %) a by-product, 3,4-heptadien-1-ol (**5**), which was identified by IR and ^1H NMR spectral data (ν 1960 cm^{-1} and a multiplet at δ 5.2—5.4 corresponding to the —CH=C=CH— moiety); obviously, the formation of **5** is due to the hydride 1,4-reduction of the enyne system in **4** (cf. ref. 11). The use of excess $LiAlH_4$ (1.5—2 mol) and lowering the reaction temperature to 10—15°C almost suppress the reduction of **4** to **5**. The overall yield of enynol **4** from **2** is ~47 % for the first variant of oxidative coupling and almost 33 % for the second variant.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 4, pp. 769—772, April, 1993.

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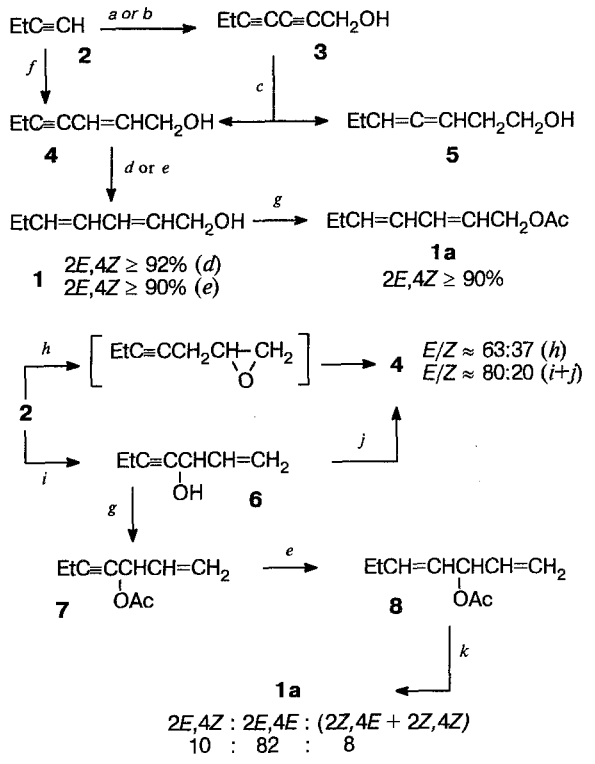
Scheme 1



Reagents and conditions:

a. *1)* $EtMgBr/Et_2O$; *2)* Br_2, −40°C;
3) $HC{\equiv}CCH_2OH/CuCl–t\text{-}BuNH_2$;
b. *1)* $CuCl–t\text{-}BuNH_2$; *2)* $BrC{\equiv}CCH_2OH$;
c. $LiAlH_4/Et_2O$; *d.* $Zn(Cu)/i\text{-}PrOH$ aq;
e. H_2—$Pd/CaCO_3$—PbO (Quin), 0°C;
f. $E\text{-}BrCH{=}CHCH_2OH/CuI–Et_2NH–PdCl_2(PPh_3)_2$;
g. $Ac_2O–NEt_3$—DMAP;
h. *1)* $LiNH_2/NH_3$—THF; *2)* $ClCH_2CH\text{–}CH_2$ (O);
i. *1)* $n\text{-}BuLi/C_6H_{14}$—THF; *2)* $H_2C{=}CHCHO$;
j. 10 % H_2SO_4 aq, 20°C;
k. $PdCl_2(MeCN)_2$/THF, 20°C.

The chemoselective *cis*-hydrogenation of the triple bond in enynol **4** is one of the critical stages in the synthesis of dienol **1** and DDDA. Upon action of the zinc-copper pair[12] on **4** in 2-propanol at 50—60°C, the yield of the reduction products exceeds 70 %, and the configurational uniformity of the 2*E*-double bond existing in enynol **4** and that of the 4*E*-double bond formed upon its reduction are close to 95 %.

Nevertheless, this reduction method has a significant drawback from the preparative viewpoint, because it requires a more that tenfold excess of the zinc-copper pair. The chemical purity of the dienol thus prepared is only 84—86 %, as the reaction products contain 4—8 % of the unreacted enynol **4** and 8—10 % of a mixture of two monoolefinic alcohols, the structure of which was not defined more accurately (the latter were assumed to result from the reduction of the allene system in alcohol **5**). Thus, the actual yield of 2*E*,4*Z*-**1** at this stage is 54—60 %. The overall yield of 2*E*,4*Z*-**1** with respect to the original alkyne **2** is 18—28 % for this route (depending on the chosen method of oxidative coupling).

The efficiency of the synthesis of 2*E*,4*Z*-**1** by this route increases if the selective reduction of the triple bond in enynol **4** is carried out by selective hydrogenation over the Lindlar catalyst in the presence of quinoline at 0—2°C. In this case the *Z*-stereoselectivity of hydrogenation is 90—92 %. Taking into account the chemical purity of the sample thus obtained, the yield of the target dienol 2*E*,4*Z*-**1** is 72—75 %. Correspondingly, the overall yield of 2*E*,4*Z*-**1** from **2** increases to 22—32.5 %, depending on the method of oxidative coupling, which makes this modification of the **2**→**3**→**4**→**1** route more favorable than the previous variant.

Path 2→4→1. Variant A. A modification of the above route, which consists in the coupling of copper(I) 1-butynide with 3-bromo-2*E*-propen-1-ol (BP) catalyzed by a Pd(II) phosphine complex, the procedure suggested by Sonogashira *et al.*,[13] allows a one-stage transformation of **2** to enynol **4** with nearly 100 % configurational uniformity. The yield of **4** obtained in this way is 76 %. The overall yield of 2*E*,4*Z*-**1** obtained using this path is 50—52 % with respect to the starting **2**, if selective hydrogenation of the triple bond (see above) is used; this makes the route described one of the most preferable. However, its use for the large-scale production of 2*E*,4*Z*-**1** is restricted by the necessity of using rather difficult to obtain BP (see ref. 14) and $PdCl_2 \cdot 2PPh_3$.

Path 2→4→1. Variant B. An attempt at a one-stage synthesis of enynol **4** from alkyne **2** by coupling the latter with epichlorohydrin in the system $LiNH_2/NH_3$—THF (−70→−23°C) afforded a binary mixture of *E*- and *Z*-isomers of enynol **4** in the ratio *E*/*Z* = 63:37 (data of capillary GLC and ^1H NMR spectra) in 63 % yield. The low stereoselectivity of anionotropic rearrangement of the intermediate propargyloxirane makes this variant unsuitable for subsequent preparation of dienol 2*E*,4*Z*-**1**.

Path 2→6→4→1. An alternative path to the synthesis of enynol **4** is based upon the allylic rearrangement of 1-hepten-4-yn-3-ol (**6**) prepared by the condensation of lithium 1-butynide with acrolein in the mixture hexane—THF (−60°→20°C).* The action of 10 % H_2SO_4 (20°C, 60 h) on alcohol **6** affords (yield 86 %) a binary mixture of the *E*- and *Z*-isomers of enynol **4** with the ratio *E*/*Z* = 80:20. From the preparative viewpoint, this method is simple and efficient (the yield of **4** from **2** is 65 %); however, the rather low content of the required

* The yield of alcohol **6** is 76 % under the conditions described, whereas the reaction of $EtC{\equiv}CMgBr$ with $H_2C{=}CH–CHO$ in THF affords **6** in 64 % yield (see ref. 15).

E-isomer means even lower stereochemical uniformity of dienol **1** prepared by selective hydrogenation of this isomer and hence its further decrease upon the transformation of 2*E*,4*Z*-**1** thus obtained to DDDA.

All of the samples of dienol **1** prepared using the above paths were acetylated in the system Ac_2O—NEt_3—4-dimethylaminopyridine (DMAP) to give (in 92—95 % yield) the corresponding 1-acetoxyhepta-2*E*,4*Z*-diene **1a**; this reaction proceeded with the retention of the configurational uniformity of the original alcohol (data of capillary GLC and ^{1}H NMR spectra). In a similar way, acetate **7** was prepared in 92 % yield from alcohol **6**.

Path 2→6→7→8→1a. We also studied a new variant that transforms alcohol **6** directly into acetate **1a** without the stage of preparing 2*E*,4*Z*-**1**. For this purpose enynol **6** was transformed to acetate **7**, which was then partially hydrogenated over $Pd/CaCO_3/PbO$ in the presence of quinoline. However, the reduction selectivity of the triple bond proved to be low. The hydrogenation yielded a multicomponent mixture comprising ~30 % of 3-acetoxy-1,4*Z*-heptadiene **8** (GLC and ^{1}H NMR spectral data). The remaining components may correspond to more saturated acetates, judging by the retention times (R_t). Isolation of **8** from the mixture of components with close boiling points by distillation or by chromatography showed little efficiency.

Under the conditions of allylic rearrangement catalyzed by the $PdCl_2 \cdot 2MeCN$ complex, the nonpurified acetate **8** affords a mixture of 2*E*,4*Z*-**1a** and 2*E*,4*E*-**1a**, where the latter predominates (GLC data). Thus, the new variant studied by us is not appropriate for the preparation of the target 2*E*,4*Z*-**1a**.

The above comparison of several variants for the synthesis of 2*E*,4*Z*-**1** and/or its acetate indicates that paths **2→3→4→1** and **2→4→1** (variant A), involving the partial catalytic hydrogenation of the triple bond in enynol **4**, are the most acceptable methods for obtaining these intermediates in multigram amounts.

Experimental

The GLC analysis of the compounds and reaction products was carried out on a glass capillary column (l = 55 m, d = 0.27 mm), with PEG 40 M as the liquid phase, on a Biokhrom chromatograph equipped with a flame ionization detector. Helium was used as the carrier gas.

IR spectra were recorded with a UR-20 spectrometer in thin layers; ^{1}H NMR spectra were taken with a Bruker WM-250 instrument (250 MHz) in $CDCl_3$. The qualitative analysis of the mixtures was carried out by means of TLC on Silufol plates, with a hexane—ether mixture (25—50 %) as the eluent. In the isolation of the reaction products, solvent removal was carried out on a rotary evaporator at a bath temperature not above 40°C.

The starting compounds: acrolein, b.p. 52—53°C, and **epichlorohydrin**, bp 115—116°C, were used as technical-grade products; **1-butyne** was prepared by alkylation of lithium acetylenide with EtI;[8] **1-bromo-1-butyne**, b.p. 90—91°C, was obtained in a 40 % yield by treating butynylmagnesium bromide with Br_2 in ether at −40°C according to the procedure in ref. 8; **3-bromo-2-propyn-1-ol**, b.p. 60°C (11 Torr), n_D^{20} 1.5164, was obtained in 52 % yield by the hypobromite method[8] using the reverse sequence of addition. **3-Bromo-2*E*-propen-1-ol**, bp 70—72°C (12 Torr), n_D^{21} 1.5092, was prepared[14] in 74 % yield by reduction of 3-bromo-2-propyn-1-ol with the $LiAlH_4$—$AlCl_3$ complex (4:3) in ether after boiling for 3 h. **1-Hepten-4-yn-3-ol (6)** was prepared in a 64 % yield by condensation of 1-butynylmagnesium bromide with acrolein in THF at −25°C;[15] it was also prepared in a higher yield by the following procedure: 1.6 mol *n*-butyllithium (34 mL) in hexane was added to THF (30 mL) cooled to −60°C; the mixture was treated with 1-butyne (3.5 g, 50 mmol) and 5 min later with a solution of freshly distilled acrolein (2.8 g, 50 mmol) in 5 mL of THF. The reaction mixture was stirred until it reached room temperature, and treated with 100 mL of ether and 50 mL of water. Compound **6** (4.2 g, 76 %) was isolated from the organic phase by the usual work-up; bp 72—73°C (12 Torr), n_D^{20} 1.4652; ^{1}H NMR, δ: 1.12 (t, 3 H, CH_3, J = 7 Hz), 2.24 (q.d, 2 H, $CH_2C\equiv$, J = 7 and 2 Hz), 4.83 (br.d, 1 H, H-3), 5.18 (d, 1 H, H-1, J = 11 Hz), 5.41 (d, 1 H, H-1, J = 16 Hz), 5.94 (d.d.d, 1 H, H-2, J = 16, 11, and 6 Hz).

2,4-Heptadiyn-1-ol (3). ***A.*** To a mixture of propargyl alcohol (0.1 mol), CuCl (0.2 g), 40 % aqueous *tert*-butylamine (0.18 mol), and $NH_2OH \cdot HCl$ (0.2 g) in 200 mL of methanol, a solution of 1-bromo-1-butyne (0.1 mol) in 50 mL of methanol was added with stirring under Ar at 10°C (water bath) over 1.5—2 h; the temperature of the reaction mixture slowly increased to 36°C. The blue coloration typical of Cu(II) ions that appeared was removed by the addition of $NH_2OH \cdot HCl$ (0.1 g). The mixture was kept for 2 h at 40°C, then concentrated to a small volume, diluted with an equal volume of 0.1 *N* HCl, and thoroughly extracted with ether. The ethereal layer was washed with saturated NaCl and dried with $MgSO_4$, and the resulting product was distilled *in vacuo* to give **3** in 72 % yield, b.p. 105°C (10 Torr), n_D^{18} 1.5125. IR, ν (cm^{-1}): 3370 (OH), 2260 (C≡C), 1040 (C—O). UV (heptane), λ_{max} (nm): 214 (ε 480), 226 (ε 410), 241 (ε 420), 254 (ε 275). ^{1}H NMR, δ: 1.15 (t, 3 H, CH_3, J = 7.5 Hz), 1.8 (br.s, OH), 2.25 (q.t, 2 H, $CH_2C\equiv$, J = 7.5 and 1.0 Hz), 4.31 (t, 2 H, CH_2O, J = 1.0 Hz); cf. ref. 17.

B. To a yellow solution of 1-butyne (0.1 mol), CuCl (0.2 g), $NH_2OH \cdot HCl$ (0.2 g), and 40 % *tert*-butylamine (34 mL) in methanol, stirred at 10°C under Ar, 3-bromo-2-butyn-1-ol (0.1 mol) was added dropwise, and the mixture was heated at 40°C for 3 h with continuous stirring; after that, the mixture was decomposed with 0.1 *N* HCl. The further workup was carried out as described above to give **3** in 45 % yield.

2-Hepten-4-yn-1-ol (4). ***A.*** To a stirred suspension of lithium aluminum hydride (2.28 g, 60 mmol) in 100 mL of abs. ether, compound **3** (5.5 g, 50 mmol) in 40 mL of abs. ether was added dropwise at 20°C under an Ar atmosphere. Then the reaction mixture was boiled for 2.5 h, and water (25 mL) and 10 % H_2SO_4 (25 mL) were successively added; thereafter the product was extracted with ether and the extract was dried with $MgSO_4$. Distillation of the residue yielded *E*-**4** (4.7 g, 85 %), bp 100°C (13 Torr), n_D^{18} 1.4970. IR, ν (cm^{-1}): 3350, 2220, 1630, 1010, 980, 960. ^{1}H NMR, δ: 1.15 (t, 3 H, CH_3, J = 7.5 Hz), 2.17 (br.s, OH), 2.30 (q.d, 2 H, $CH_2C\equiv$, J = 7.5 and 2.2 Hz), 4.16 (d.d, 2 H, CH_2O, J = 2 and 6 Hz), 5.70 (d. of quint., 1 H, =CHC≡, J = 16 and 2.2 Hz), 6.14 (d.t, 1 H, =CH—, J = 16 and 6 Hz). Judging from the IR and ^{1}H NMR spectra, the compounds thus prepared contained an ~8 % admixture of 3,4-heptadien-1-ol **5**, ν 1960 cm^{-1} and δ 5.07—5.26 m (the —CH=C=CH— group).

B. A solution of 1-butyne (11.02 g, 0.204 mol) in 40 mL of dry THF was added over 40 min at −70°C to a vigorously stirred solution of lithium amide prepared from Li (1.42 g) and 300 mL of liquid ammonia; after the addition, the solution turned gray. The solution was further stirred for 0.5 h (acetone — solid CO_2); then epichlorohydrin (16.7 g, 0.18 mol) in 40 mL of THF was added over 15 min, and the mixture was slowly boiled at −23°C (CCl_4 — solid CO_2) for 8 h. The reaction mixture was kept for 12 h in order to let the ammonia evaporate; then the residue was diluted with stirring with 200 mL of saturated NH_4Cl and extracted with ether (3×200 mL). The ethereal solution was washed with 0.1 *N* HCl, solutions of $NaHCO_3$ and NaCl, and dried with $MgSO_4$. Distillation yielded 12.5 g (63 %) of **4**, bp 90—100°C (12 Torr), as a mixture of *E*/*Z*-isomers in the ratio of ~5:3. The quantitative composition of the mixture was established from the GLC data [150°C, the pressure of He at the inlet was 1.2 atm; the retention times were 11.2 min (the *Z*-isomer) and 11.4 min (the *E*-isomer)] as well as from the ^{1}H NMR spectra, in particular from the ratio of the integral intensities of the signals from the two protons at C-1. ^{1}H NMR, δ: 1.17 (t, 3 H, CH_3, J = 7 Hz), 2.2—2.4 (2 H, overlapped by the signal from the *E*-isomer, $CH_2C\equiv$); 4.37 (d.d, 2 H, CH_2O, J = 2 and 6 Hz), 5.57 (d. of quintets, 1 H, $=CHC\equiv$, J = 11 and 6 Hz).

C. A mixture of alcohol **6** (4.4 g) and 10 % H_2SO_4 (80 mL) was stirred for 60 h at ~20°C, diluted with water, extracted with ether (3×100 mL), and dried with $MgSO_4$ to afford 3.8 g (86 %) of a sample of **4**; as in the previous case, the latter was obtained as a mixture of *E*/*Z*-isomers in the ratio of ~4:1 (the GLC and ^{1}H NMR data).

D. To a stirred suspension of *E*-3-bromo-2-propen-1-ol (3.5 g, 26 mmol), $PdCl_2(PPh_3)_2$ (140 mg, 0.2 mmol), and CuI (76 mg, 0.4 mmol) in 70 mL of diethylamine, 1.08 g (20 mmol) of 1-butyne was added under Ar; the mixture was warmed to 40°C and kept at this temperature for 3 h. The reaction mixture was concentrated *in vacuo*, treated with ether, washed to a neutral pH, and the residue was subjected to flash-chromatography on SiO_2, using gradient elution with a hexane—ether mixture (0→40 %) to give dimeric 3,5-octadiyne and pure *E*-**4** in 1.67 g (76 %) yield. The configurational and chemical purities were >99 %, as judged by the spectral data and the GLC analysis.

2,4-Heptadien-1-ol (1). ***A.*** Preparation of active zinc.[12] To a suspension of Zn dust (27.4 g, 0.42 mol) in 10 mL of water heated to boiling, a solution of $CuCl_2 \cdot 2H_2O$ (7.2 g, 0.042 mol) in 36 mL of water was added. The dark-brown precipitate was washed with water (2×50 mL), and then a solution of KOH (40.0 g) in 250 mL of water was added; the mixture was heated for 40 min at 60°C and the reducing agent thus prepared was washed with water to a neutral pH.

In order to carry out the reduction, a solution of enynol **4** (5.0 g, 0.045 mol) in 10 mL of aqueous *iso*-PrOH (2:1, v/v) was added to the suspension of active Zn (see above) and stirred at 55—60°C until total conversion of the alkyne took place (GLC control, 3—5 h). The metal was filtered off and washed with aqueous alcohol; the filtrate was diluted with saturated NH_4Cl, and the product was extracted with ether (4×80 mL). The extract was thoroughly washed with brine and dried with $MgSO_4$ to give 3.5—3.8 g (72—76 %) of a fraction of dienols **1**, bp 80—86°C (8 Torr), n_D^{18} 1.4942, containing mainly 2*E*,4*Z*-**1**.

2*E*,4*Z*-**1** (in the mixture): GLC (100°C, pressure of He at the inlet 1.2 atm), retention time 14 min; IR, ν (cm^{-1}): 3340, 1680, 1610, 980, 720. ^{1}H NMR, δ: 1.01 (t, 3 H, CH_3, J = 7 Hz), 1.54 (br.s, OH), 2.14—2.28 (m, 2 H, H-6, J = 6.5 and 7 Hz), 4.24 (br.d, 2 H, H-1, J = 6.5 Hz), 5.48 (d.t, 1 H, H-5, J = 10.5 and 6.5 Hz), 5.82 (d.t, 1 H, H-2, J = 15.5 and 6.5 Hz), 5.96 (d.d, 1 H, H-4, J = 10.5 and 10.5 Hz), 6.59 (d.d, 1 H, H-3, J = 15.5 and 10.5 Hz), cf. ref. 3.

According to the GLC and ^{1}H NMR spectral data, the product obtained contains, in addition to dienols **1** and an admixture of the original alcohol (3—5 %), two more hydroxyl-containing compounds; the total intensity of the ^{1}H NMR signals corresponding to all admixtures amounts to 12—18 % that of the compound **1**.

B. The hydrogenation of a sample of **4** (6.6 g, 60 mmol) in the presence of the Lindlar catalyst (0.38 g) and quinoline (0.18 g, 1.4 mmol) at 0—8°C in 80 mL of heptane until complete disappearance of the starting alcohol (1410 mL of H_2 was consumed) afforded **1** in a 93 % yield. According to the GLC analysis, the stereochemical purity of **1** was ~90 %, while its chemical purity was 80—82 %.

Acetylation. To a mixture of an alcohol (1 mmol), Ac_2O (0.2 mL), and triethylamine (0.8 mL) in 4 mL of dry ether (or CH_2Cl_2) 6 mg of DMAP was added, and the mixture was kept for 24—36 h at 20—25°C. The reaction mixture was diluted with ice water and extracted with ether. The organic layer was washed with saturated solutions of $CuSO_4$, $NaHCO_3$, and NaCl, and dried with $MgSO_4$. The yield was 92—95 %.

1-Acetoxy-2,4-heptadiene (1a). 2*E*,4*Z*-**1a** (in a mixture), bp 106°C (25 Torr), n_D 1.4690. IR, ν (cm^{-1}): 1742, 1240, 1024. ^{1}H NMR, δ: 1.01 (t, 3 H, CH_3, J = 7 Hz), 2.08 (s, 3 H, CH_3CO), 2.12—2.18 (d.q, 2 H, H-6, J = 7 and 1.5 Hz), 4.60 (d.d, 2 H, H-1, J = 6.7 and 1.5 Hz), 5.52 (d.t, 1 H, H-5, J = 10.5 and 1.5 Hz), 5.74 (d.t, 1 H, H-2, J = 15.5 and 6.7 Hz), 5.96 (d.d, 1 H, H-4, J = 10.5 and 10.5 Hz), 6.58 (d.d, 1 H, H-3, J = 15.5 and 10.5 Hz).

3-Acetoxy-1-hepten-4-yne (7), yield 92 %, bp 70°C (13 Torr), n_D^{18} 1.4501. IR, ν (cm^{-1}): 3080, 2245, 2200, 1740, 980, 920. ^{1}H NMR, δ: 1.08 (t, 3 H, CH_3, J = 7 Hz), 1.98 (s, 3 H, CH_3CO), 2.18 (q.d, 2 H, $CH_2C\equiv$, J = 7 and 2 Hz), 5.17 (d, 1 H, H-1, J = 11 Hz), 5.42 (d, 1 H, H-1, J = 16 Hz), 5.7—5.9 (m, 2 H, H-2 and H-3).

An attempt to transform acetate 7 to acetate 1a. A mixture of **7** (0.31 g, 2 mmol), 30 mg of Pd (the Lindlar catalyst), and 10 mg of quinoline was hydrogenated at 0—2°C. Hydrogenation was interrupted after 44 mL of H_2 had been consumed. The GLC analysis indicates that partial reduction of the triple bond occurs by *ca.* 30 %. A signal of one proton at C-3 is distinctly observed in the ^{1}H NMR spectrum: δ 6.00 d.d ($=\overset{|}{C}-CH(OAc)-\overset{|}{C}=$). In order to carry out the isomerization according to the procedures in ref. 16, the non-purified residue (0.3 g) in 1.5 mL of anhydrous THF was stirred at 20°C with 80 mg of the $PdCl_2(MeCN)_2$ catalyst. The GLC analysis showed that the conjugated acetate **1a** is formed as a mixture of isomers (2*E*,4*E*):(2*E*,4*Z*):(2*Z*,4*E*+2*Z*,4*Z*) in the ratio of 40:5:4.

The final composition of the isomerization products was not studied in detail.

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Received July 21, 1992

Pheromones of *Coleoptera*. 12*. Synthesis of (±)-2,6-dimethyloctyl formate, the biologically active analog of the smaller flour beetle aggregation pheromone

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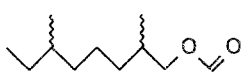
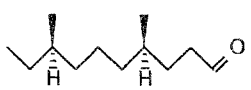
Racemic 2,6-dimethyloctyl formate (**1**), a synthetic analog of the aggregation pheromone of two species of *Tribolium* beetles, has been obtained in six steps and in 28 % overall yield starting from methyl ethyl ketone, vinyl bromide, and 2-methylpropenal. The key step of the synthesis is the sigmatropic [3,3]-rearrangement of 4-ethyl-2,4-dimethyl-1,5-hexadien-3-ol (**5**) to 2,6-dimethyl-5-octenal (**6**).

Key words: 4-ethyl-2,4-dimethyl-1,5-hexadien-3-ol, synthesis and thermal rearrangement; 2,6-dimethyl-5-octenal, hydrogenation; (±)-2,6-dimethyloctyl formate as an attractant for *Tribolium confusum*.

We have shown previously that [3,3]-sigmatropic rearrangement of α,β; β,γ-dienols in its various modifications can serve as a convenient route for constructing the carbon skeleton of a number of insect pheromones.[2,3] In this work this method is used for preparation of racemic 2,6-dimethyloctyl formate (**1**), which is an effective replacement for *R,R*-(−)-4,8-dimethyldecanal (**2**), the aggregation pheromone of the smaller flour beetle (*Tribolium confusum*) and of the flour beetle Rhopalocera (*T. castaneum*), and is more stable to oxidation in air than the natural attractant.[4]



1



2

The known methods for preparation of **1** are based either on malonate methodology,[4,5] or on organocuprate coupling of alkyl and allyl halides.[6] In both cases the

*For Part 11 see Ref. 1.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 4, pp. 773—775, April, 1993.