Brief Communications

A simple synthesis of 4*E*,7*Z*-tridecadien-1-yl acetate, a component of the sex pheromone of the potato moth *Phtorimaea operculella* (Lepidoptera: *Gelehiidae*)

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A simple, five-step synthesis of the title compound was developed starting from commercially available 2,4-nonadienal. The overall yield of the pheromone is 29%, and the geometric purity of the Δ^4 and Δ^7 double bonds is ≥95%. The *Z* configuration of the Δ^7 bond results from the 1,4-*cis*-hydrogenation of the intermediate 1,4,6-undecatrien-3-ol in the presence of an (arene)chromium tricarbonyl complex, while the *E* configuration of the Δ^4 bond arises in the Claisen—Johnson rearrangement occuring in the reaction of 1,5*Z*-undecadien-3-ol with trimethyl orthoacetate.

Key words: 4*E*,7*Z*-tridecadien-1-yl acetate, synthesis; 1,4,6-undecatrien-3-ol, 1,4-*cis*-hydrogenation; (methyl benzoate)chromium tricarbonyl; 1,5*Z*-undecadien-3-ol, Claisen—Johnson rearrangement.

4*E*,7*Z*-Tridecadien-1-yl acetate (**1**) is one of the two components of the sex pheromone of the potato moth *Phtorimaea operculella*.[1—3] Its molecular structure represents a relatively rare case of natural 1,4-dienes with two differently configured double bonds. The synthesis of compound **1** involves two stereochemical problems: the formation of a *Z*-configured bond in position Δ^7, and the introduction of an *E*-configured double bond at Δ^4 separated from the former by only one CH_2 group.

In previous syntheses of ester **1** the first of these problems was solved by partial hydrogenation of the acetylenic precursors,[3—7] by the *cis* addition of an organocopper reagent and a C-electrophile to acetylene,[8,9] by stereocontrolled condensation of aldehydes with alkyl phenyl sulfones followed by reductive desulfonation,[10] or else by employing olefinic building blocks with a known *Z* configuration of the double bond.[11—14] The methods used to provide the *E* configuration of the Δ^4 bond involved various procedures for partial reduction of acetylenic systems,[11—13] the addition of transiently formed *Z*-alkenyl cuprates to the complementary vinylic derivatives,[8,9] the fragmentation of cyclic oximes under the conditions of the Beckmann rearrangement,[5] a low-temperature modification of the sigmatropic [3,3] rearrangement of appropriately substituted allyl vinyl ethers,[6] as well as the use of olefinic building blocks with an established *E* configuration.[3,4,7,10,14] Most of the aforesaid ways to synthesize **1** involve many steps and employ expensive reagents.

Here we report a simple approach to pheromone **1** starting from commercially available 2,4-nonadienal (**2**) (Scheme 1). The pivotal step of the synthesis consists in

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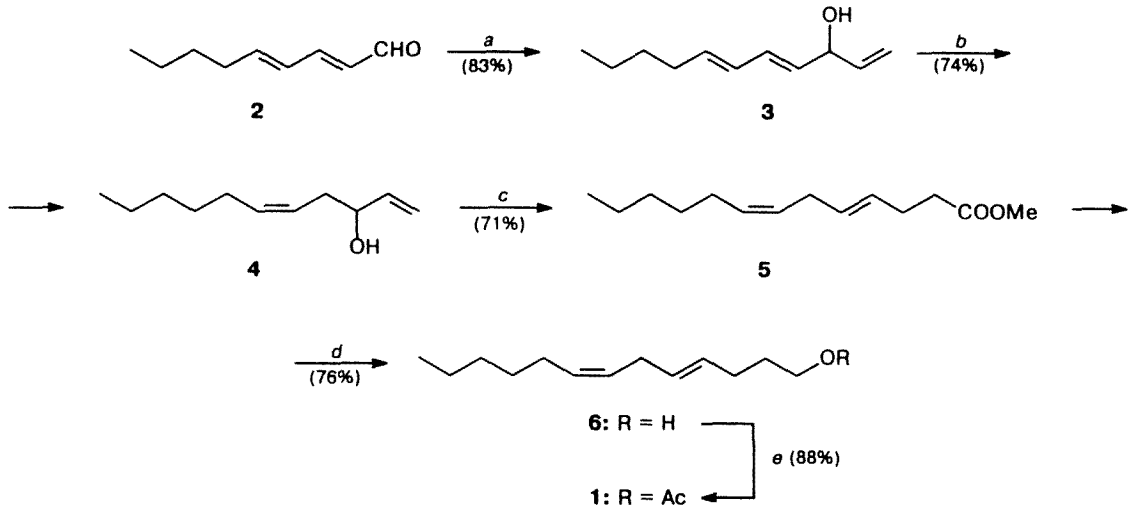
Scheme 1



Reagents and conditions: *a*. CH_2=CHMgBr/THF; *b*. H_2—(PhCOOMe)$Cr(CO)_3$/Me_2CO, ~80 atm, 120—125 °C, 3 h; *c*. $MeC(OMe)_3$—EtCOOH (Cat.)/PhMe, Δ; *d*. $LiAlH_4/Et_2O$; *e*. Ac_2O—Py.

the chemo- and stereoselective 1,4-*cis* hydrogenation of the conjugated diene system in trienol **3** in the presence of an (arene)chromium tricarbonyl complex; this reaction gives rise to the *Z* olefin **4** of 96—99% geometrical purity (g.p.).

Normally,[15,16] 1,4-*cis* hydrogenation of 1,3-dienes over an (arene)chromium tricarbonyl catalyst proceeds smoothly when the molar substrate/catalyst ratio is within (10 : 1) to (5 : 1). However, in the case of trienol **3** it was observed that a good yield of the *Z*-olefinic alcohol **4** could be obtained only when the substrate **3** and (methyl benzoate)chromium tricarbonyl catalyst were taken in more comparable amounts, *i.e.*, at molar ratios ~10 : 3. At lower molar proportions of the catalyst the resultant alcohol **4** contained up to 50% of other secondary alcohols (as could be deduced from the GC and NMR data). One can assume that under these conditions the target reaction is decelerated; as a consequence, at the required reaction temperature (120 °C) the labile trienol **3** may undergo competitive transformations such as allylic rearrangement (with subsequent cyclization of the resultant conjugated trienes) and/or a Diels—Alder reaction. Similar cases were observed recently in our synthesis of the sex pheromones of the California red scale and the white peach scale.[17]

It is known[6] that vinyl carbinol **4** can be transformed into the target compound **1** *via* the respective vinyl ether and subsequent sigmatropic [3,3] rearrangement of the latter in the presence of organoaluminum compounds; this procedure provides 95% configurational purity of the olefinic 4*E* bond. We employed the essentially similar, but preparatively more convenient protocol of extending the carbon chain by a C_2-fragment using trimethyl orthoacetate and trace amounts of propionic acid (Claisen—Johnson rearrangement).[18,19] This transformation afforded the ester **5** which was reduced with lithium aluminum hydride to give dienol **6**. Finally, the latter produced upon acetylation a specimen of pheromone **1** containing no less than 95% of the main component (as follows from the capillary GC data). The structure of the main component and the configuration of its double bonds were unambigously confirmed by the values of the chemical shifts in the ^{13}C NMR spectrum of the parent alcohol **6**, as well as by the full coincidence of the ^1H NMR spectrum data for specimen **1** with those published previously.[5—10]

Thus, 4*E*,7*Z*-tridecadien-1-yl acetate (**1**) was obtained in just five preparatively convenient steps, and in a 29% yield overall with respect to the starting commercially available 2,4-nonadienal. The effectiveness of the proposed synthetic scheme is likely to be substantially improved upon, when the conditions are found under which the 1,4-*cis* hydrogenation of trienol **3** does not require large amounts of the catalyst (*e.g.*, by adopting a low-temperature modification of the process) (see Ref. 15).

Experimental

^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AC-200 spectrometer. Serial GC analyses were performed on an LKhM-8MD gas chromatograph using a 2000×3 mm stainless steel column packed with 5% XE-60 on Chromaton N-AW-DMCS, and a flame ionization detector (N_2 as the carrier gas (40 mL min^{-1}), injector temperature — 225 °C, oven temperature — 100—150 °C). Capillary gas chromatography was performed on a Hewlett Packard 5890 instrument equipped with an Ultra 1 column (25 m), at an oven temperature program of 100 → 230 °C/10 °C min^{-1}.

(Methyl benzoate)chromium tricarbonyl was prepared by treating $Cr(CO)_6$ with $PhCO_2Me$ in a boiling Bu_2O—THF

mixture (*cf.* Ref. 20). Chromatographic separations were carried out on silica gel L 100/160 (Chemapol, Czech Republic).

1,4,6-Undecatrien-3-ol (3) was prepared by a standard procedure by reacting vinylmagnesium bromide (25 mmol) with *trans,trans*-2,4-nonadienal **2** (Aldrich, USA) (2.5 g, 18 mmol) in abs. THF (10 mL). The yield of trienol **3** was 2.5 g (83%), b.p. 95—97 °C (3 Torr), n_D^{20} 1.5000. ^{1}H NMR, δ: 0.89 (t, 3 H, 11-H_3, $J \approx 7$ Hz); 1.33 (m, 4 H, 10-H_2, 9-H_2); 1.75 (br.s, 1 H, OH); 2.98 (m, 2 H, 8-H_2); 4.63 (dd, 1 H, three peaks, 3-H, $J = J' = 6.0$ Hz); 5.10 (dd, 1 H, 1-H(a), $J_{ac} = 11.4$ Hz, $J_{ab} = 1.5$ Hz); 5.36 (dd, 1 H, 1-H(b), $J_{bc} = 17.1$ Hz, $J_{ab} = 1.5$ Hz); 5.50—6.30 (m, 5 H, 2-H, 4-H, 5-H, 6-H, 7-H).

1,5*Z*-Undecadien-3-ol (4). A stainless steel autoclave (capacity 50 mL) was loaded under argon with trienol **3** (0.5 g, 3 mmol) and (methyl benzoate)chromium tricarbonyl (0.25 g, 0.92 mmol) in degassed anhydrous acetone (5 mL). The autoclave was closed and filled three times with H_2 (up to 10 atm). Then dry H_2 was delivered at 60 atm (initial pressure), and hydrogenation was carried out at 120—125 °C for 3 h. After cooling to room temperature and decompressing, the autoclave was unloaded, and the acetone was stripped off from the reaction mass. The remainder was chromatographed on a column of SiO_2 using hexane—AcOEt (6 : 1, v/v) as the eluent. Evaporation of the eluate afforded crude dienol **4** (0.46 g), which contained *ca.* 20% methyl benzoate (GC and ^{1}H NMR data). The calculated yield of pure **4** was 74%. ^{1}H NMR, δ: 0.89 (t, 3 H, 11-H_3, $J \approx 7$ Hz); 1.30 (m, 6 H, 8-H_2, 9-H_2, 10-H_2); 1.82 (br.s, 1 H, OH); 2.04 (m, 2 H, 7-H_2); 2.31 (m, 2 H, 4-H_2); 4.14 (m, 1 H, 3-H, $J_{main} = 6.0$ Hz); 5.11 (d, 1 H, 1-H(a), $J_{ac} = 11.4$ Hz); 5.24 (d, 1 H, 1-H(b), $J_{bc} = 17.1$ Hz); 5.38 (m, 1 H, 5-H); 5.56 (m, 1 H, 6-H); 5.89 (ddd, 1 H, 2-H, $J_{2\text{-H}\,:\,3\text{-H}} = 6.0$ Hz, $J_{ac} = 11.4$ Hz, $J_{bc} = 17.1$ Hz). ^{13}C NMR, δ: 14.0 (C(11)); 22.5 (C(10)); 27.3 (C(7)); 29.2 (C(8)); 31.4 (C(9)); 35.0 (C(4)); 72.4 (C(3)); 114.4 (C(1)); 124.4 (C(5)); 133.0 (C(6)); 140.5 (C(2)).

When compound **3** (2 g, 12 mmol) was hydrogenated in the presence of only 0.3 g (methyl benzoate)chromium tricarbonyl (1.1 mmol), the resultant product (~1 g) was a mixture of the target dienol **4** (~50%) and three secondary alcohols with different molecular structures (in total ~50%); the ratio of these side products was about 1 : 1 : 1. Their diagnostic signals in the ^{1}H NMR spectrum of the mixture appeared at δ 3.52 (quint, OCH), 3.61 (br.s, OCH), and 3.95 (q, OCH) ppm.

Methyl 4*E*,7*Z*-tridecadienoate (5). A mixture of dienol **4** (0.37 g, 2.2 mmol) and trimethyl orthoacetate (2 g, ~17 mmol) in anhydrous toluene (3 mL) was treated with a catalytical amount of propionic acid (4 droplets) and then boiled for 3 h; the methanol that formed in the reaction was continuously removed using a Dean—Stark trap. When stopped, the conversion of alcohol **4** amounted to ~80% (GC monitoring). The mixture was cooled to 20—25 °C, treated with an 1% aqueous solution of *p*-toluenesulfonic acid, stirred for 30 min to hydrolyze the orthoesters present, neutralized with a saturated aqueous solution of $NaHCO_3$, and washed with brine. The organic layer was separated, dried ($MgSO_4$), and evaporated; the residue was chromatographed on a column of silica gel using hexane—AcOEt (10 : 1, v/v) to elute the product. When monitored by TLC (Silufol sheets, development with the same solvent system), the resultant ester **5** displayed R_f 0.5. Evaporation of the respective fractions of the eluate afforded a pure specimen of ester **5**. Yield 0.35 g (71%). ^{1}H NMR, δ: 0.88 (t, 3 H, 13-H_3, $J \approx 7$ Hz); 1.24 (m, 6 H, 10-H_2, 11-H_2, 12-H_2); 2.00 (m, 2 H, 9-H_2, $J_{main} = 7.1$ Hz); 2.31 (m, 4 H, 2-H_2, 3-H_2); 2.70 (m, 2 H, 6-H_2); 3.63 (s, 3 H, OMe); 5.23—5.43 (m, 4 H, 4 =CH). ^{13}C NMR, δ: 13.9 (C(13)); 22.5 (C(12)); 27.0 (C(3)); 27.8 (C(9)); 29.2 (C(6)); 30.0 (C(10)); 31.4 (C(11)); 33.8 (C(2)); 51.3 (OMe); 127.1, 128.2, 129.8, 130.6 (C(4), C(5), C(7), and C(8)).

4*E*,7*Z*-Tridecadien-1-ol (6) was obtained by reducing ester **5** (0.32 g) with $LiAlH_4$ (twofold excess) according to the standard procedure. The product was purified by column chromatography on SiO_2 using hexane—AcOEt (6 : 1, v/v) as the eluent. TLC-monitoring of the eluates (development with the same solvent mixture) showed that alcohol **6** had R_f 0.2. The respective fractions of the eluate were evaporated to give pure alcohol **6** as a colorless oil with n_D^{16} 1.4741. Yield 0.21 g (76%). ^{1}H NMR, δ: 0.90 (t, 3 H, 13-H_3, $J \approx 7$ Hz); 1.34 (m, 6 H, 10-H_2, 11-H_2, 12-H_2); 1.40 (br.s, 1 H, OH); 1.62 (quint, 2 H, 2-H_2, $J = 6.5$ Hz); 2.04 (m, 4 H, 3-H_2, 9-H_2); 2.73 (m, 2 H, 6-H_2); 3.64 (t, 2 H, 1-H_2, $J = 6.5$ Hz); 5.30—5.48 (m, 4 H, 4 =CH). ^{13}C NMR, δ: 14.0 (C(13)); 22.5 (C(12)); 27.0 (C(9)); 28.8 (C(10)); 29.3 (C(6)); 30.3 (C(3)); 31.4 (C(11)); 32.3 (C(2)); 62.5 (C(1)); 127.1, 129.2, 129.8, 130.7 (C(4), C(5), C(7), and C(8)).

4*E*,7*Z*-Tridecadien-1-yl acetate (1) was prepared by acetylating alcohol **6** (0.2 g) with Ac_2O in pyridine according to the standard procedure. Excess Ac_2O and pyridine were washed out in a conventional manner, and the reaction product was purified by column chromatography on SiO_2 using hexane—AcOEt (12 : 1, v/v) as the eluent. TLC-monitoring of the eluate (silufol sheets, development with the same solvent system) showed that compound **1** had R_f 0.70. Evaporation of the respective fractions of the eluate gave a specimen of the acetate **1** (colorless oil with n_D^{20} 1.4730) that contained more than 95% of the main component (capillary GC data). Yield 0.21 g (88%). Two minor components, detected by capillary GC, displayed considerably shorter retention times. ^{1}H NMR, δ: 0.89 (t, 3 H, 13-H_3, $J \approx 7$ Hz); 1.32 (m, 6 H, 10-H_2, 11-H_2, 12-H_2); 1.67 (quint, 2 H, 2-H_2, $J = 6.5$ Hz); 2.02 (s, 3 H, MeCO); 2.05 (m, 4 H, 3-H_2, 9-H_2); 2.72 (m, 2 H, 6-H_2); 4.06 (t, 2 H, 1-H_2, $J = 6.5$ Hz); 5.28—5.47 (m, 4 H, four =CH); this spectrum is practically identical with those reported for compound **1** earlier.[5—10]

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References

1. T. Ono, R. E. Charlton, and R. D. Cardé, *J. Chem. Ecol.*, 1990, **16**, 531.
2. C. J. Persoons, S. Voerman, P. E. J. Verwiel, F. J. Ritter, W. J. Nooyen, and A. K. Minks, *Entomol. Exp. Appl.*, 1976, 289.
3. W. L. Roelofs, J. P. Kochansky, R. T. Cardé, C. A. Henrick, J. N. Labovitz, and V.-L. Corbin, *Life Sci.*, 1975, **17**, 699.
4. C. A. Henrick, *Tetrahedron*, 1977, **33**, 1845.
5. H. Nishiyama, K. Sakuta, and K. Iton, *Tetrahedron Lett.*, 1984, 233.
6. K. Nonoshita, H. Banno, K. Maruoka, and H. Yamamoto, *J. Am. Chem. Soc.*, 1990, **112**, 316.
7. S. S. Voerman and R. H. Rothschild, *J. Chem. Ecol.*, 1978, **4**, 531.

8. A. Alexakis, G. Cahier, and J. Normant, *Tetrahedron Lett.*, 1978, 2027.
9. T. Fujisawa, T. Sato, M. Kawashima, K. Naruse, and K. Tamai, *Tetrahedron Lett.*, 1982, 3583.
10. N. M. Ivanova, B. A. Cheskis, A. M. Moiseenkov, and O. M. Nefedov, *Izv. Akad. Nauk, Ser. Khim.*, 1992, 2362 [*Bull. Russ. Acad. Sci., Div. Chem. Sci.*, 1992, **41**, 1853 (Engl. Transl.)].
11. R. I. Ishchenko and B. G. Kovalev, *Zh. Org. Khim.*, 1989, **25**, 291 [*J. Org. Chem. USSR*, 1989, **25**, No. 2 (Engl. Transl.)].
12. O. P. Vig, M. L. Sharma, S. Kumari, and V. Rani, *Ind. J. Chem.*, 1985, **24(B)**, 675.
13. J. S. Yadav and P. S. Reddy, *Synth. Commun.*, 1986, **16**, 1119.
14. H.-J. Bestmann, Th. Zeibig, and O. Vostrowsky, *Synthesis*, 1990, 1039.
15. M. Sodeoka and M. Shibasaki, *Synthesis*, 1993, 643.
16. A. A. Vasil'ev, G. V. Kryshtal, and E. P. Serebryakov, *Mendeleev Commun.*, 1995, 41.
17. A. A. Vasil'ev, A. L. Vlasyuk, G. V. Kryshtal, and E. P. Serebryakov, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 2026 [*Russ. Chem. Bull.*, 1995, **44**, 1946 (Engl. Transl.)].
18. W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, and T. Lee, *J. Am. Chem. Soc.*, 1970, **92**, 741.
19. J. N. Labovitz, C. A. Henrick, and V. L. Corbin, *Tetrahedron Lett.*, 1975, 4209.
20. C. A. L. Mahaffy, P. L. Pauson, M. D. Rausch, and W. Lee, *Inorg. Synth.*, 1979, **19**, 154.

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Ternary condensation of cyclic azomethines, aromatic aldehydes, and barbituric acid: a new approach to the synthesis of 8,15,17-triaza-D-homogonanes

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New fused heterocyclic compounds of the 8,15,17-triaza-D-homogonane series have been obtained by ternary condensation of cyclic azomethines (1-methyl-3,4-dihydroisoquinolines) with aromatic aldehydes and barbituric acid in DMF.

Key words: azomethines, aldehydes, barbituric acid, ternary condensation; azasteroids, 8,15,17-triaza-D-homogonanes; benzo[*a*]pyrimido[4,5-*f*]quinolizines.

The reactions of cyclic azomethines and Schiff's bases with β-dicarbonyl and β-tricarbonyl compounds[1,2] and their enol derivatives[3,4] are widely used in the syntheses of fused nitrogen-containing heterocyclic compounds. They serve as the final stages of synthetic schemes in which the preliminarily built blocks are combined in a target molecular structure.[5] Multicomponent one-pot processes that make it possible to perform a sequence of reactions and to obtain a product with the required structure and stereochemistry over a single synthetic cycle are the most effective.

In a continuation of the studies dealing with the synthesis of fused nitrogen-containing heterocyclic compounds structurally related to steroids,[6—8] we found that heating equimolar mixtures of cyclic azomethines (**1a,b**), aromatic aldehydes (**2a,b**), and barbituric acid (**3**) in DMF (Scheme 1) affords previously unknown 12-aryl-substituted derivatives of 8,15,17-triaza-D-homogonane (**4a—c**).

The compounds obtained are of considerable interest in the search for new biologically active compounds with immunotropic properties.[6] There are grounds to believe that this reaction can be extended to other azomethines, methylene-active compounds, and aldehydes and can be used for the synthesis of quinolizine derivatives including those used in medicine.

Experimental

Melting points of 8,15,17-triaza-D-homogonanes **4a—c** were determined using a Boetius hot-stage apparatus. UV spectra were recorded on a Specord M-400 spectrophotometer,

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