THE HYDROALUMINATION-IODINATION OF ENYNE α-ALCOHOLS: SYNTHESIS OF 3-METHYL-2,4-ALKADIEN-1-OLS

Ashot P. KHRIMYAN[a], Oganes A. GHARIBYAN[a], Ludvík STREINZ[b], Zdeněk WIMMER[b], Miroslav ROMAŇUK[b] and Shaliko O. BADANYAN[a]

[a] *Institute of Organic Chemistry, Armenian Academy of Sciences, 375 094 Yerevan, U.S.S.R. and*
[b] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6, Czechoslovakia*

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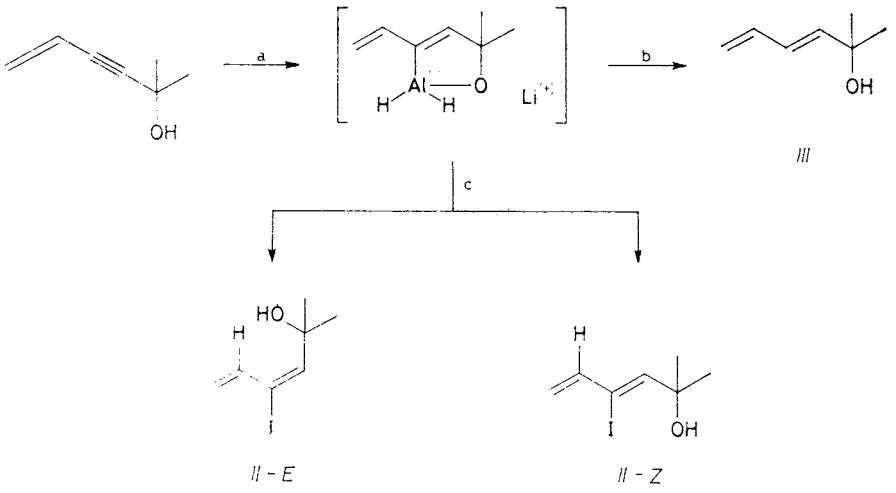
It has been found that the reaction course of hydroalumination-iodination using 2-methyl-5-hexen-3-yn-2-ol and (6*E*)-9,13-dimethyl-6,12-tetradecadien-4-yn-3-ol as substrates is ambiguous. The subsequent reaction of lithium dimethyl cuprate with iodo dienols unlike that of iodo alkenols is non-stereoselective. These reactions have been used for the synthesis of a juvenile hormone mimic (4*E*, 6*E*)-5,9,13-trimethyl-4,6,12-tetradecatrien-3-ol.

The hydroalumination-iodination of propargylic alcohols with subsequent methylation has been used several times for the stereoselective preparation of trisubstituted (*E*)-olefines[1-6]. It has been found that this reaction according to reducing agent used ($LiAlH_4/CH_3ONa$ or $LiAlH_4/AlCl_3$) can be utilised for the synthesis of both 3- or 2-substituted allylic alcohols[1], e.g. stereospecific syntheses of (*E*,*E*)-farnesol (ref.[1]), juvenile hormone JH-I (refs[2,3]), α-santanol (ref.[6]), (2*E*,6*Z*)-7-methyl-3-propyl-2,6-decadien-1-ol (ref.[5]), and sirenin (ref.[6]). In all these papers good stereoselectivity is emphasized.

In order to find out the scope of the above mentioned method for the synthesis of compounds with conjugated unsaturated bonds we have been studying hydroalumination-iodination of conjugated enyne α-alcohols. Hydroalumination-iodination of 2-methyl-5-hexen-3-yn-2-ol (*I*, Scheme 1) using lithium aluminium hydride at −5°C in diethyl ether followed by subsequent decomposition of the excess of $LiAlH_4$ with ethyl acetate led to the intermediate which has been treated with iodine at −70°C. This procedure gave the mixture of *E*- and *Z*-isomers of 4-iodo-2-methyl-3,5-hexadien-2-ol (*II*) in ratio 58 : 42. When tetrahydrofuran instead of diethyl ether has been used as a solvent, the ratio of isomers did not change. The above mentioned geometrical iodo isomers have been separated using column chromatography (silica gel) and compounds were identified by ^1H NMR spectroscopy. The ratio of isomers was determined by comparison of signals H_c of both isomers where the signal cor-

responding to the *E*-isomer is more downfield shifted than that of *Z*-isomer. This interpretation is often used in the chemistry of vitamin A and its analogs[7].



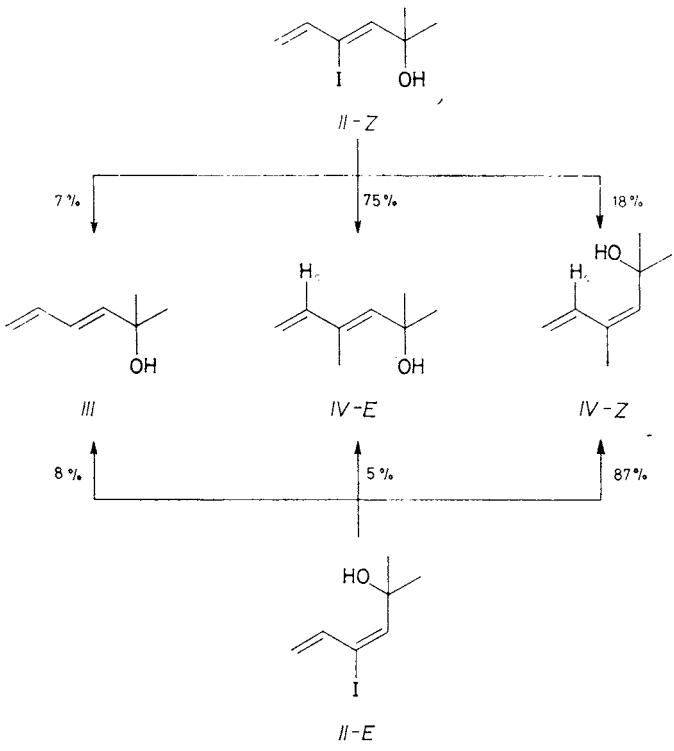
a: $LiAlH_4$, b: H_2O, c: I_2

SCHEME 1

In formulas *II-E* and *II-Z* for H read H_c

There is an interesting fact that the hydrolysis of alanate intermediate led to the *E*-dienol *III* (Scheme 1) indicating *trans* selectivity[8] of hydroalumination step, and therefore decrease of selectivity occurs during the iodination. Thus 2-methyl-5--hexen-3-yn-2-ol is a substrate giving unexpectably under above mentioned reaction conditions a mixture of *E* and *Z* isomers but the reaction course is regioselective because expected[9,10] 3-iodo-2-methyl-3,5-hexadien-2-ol has not been found.

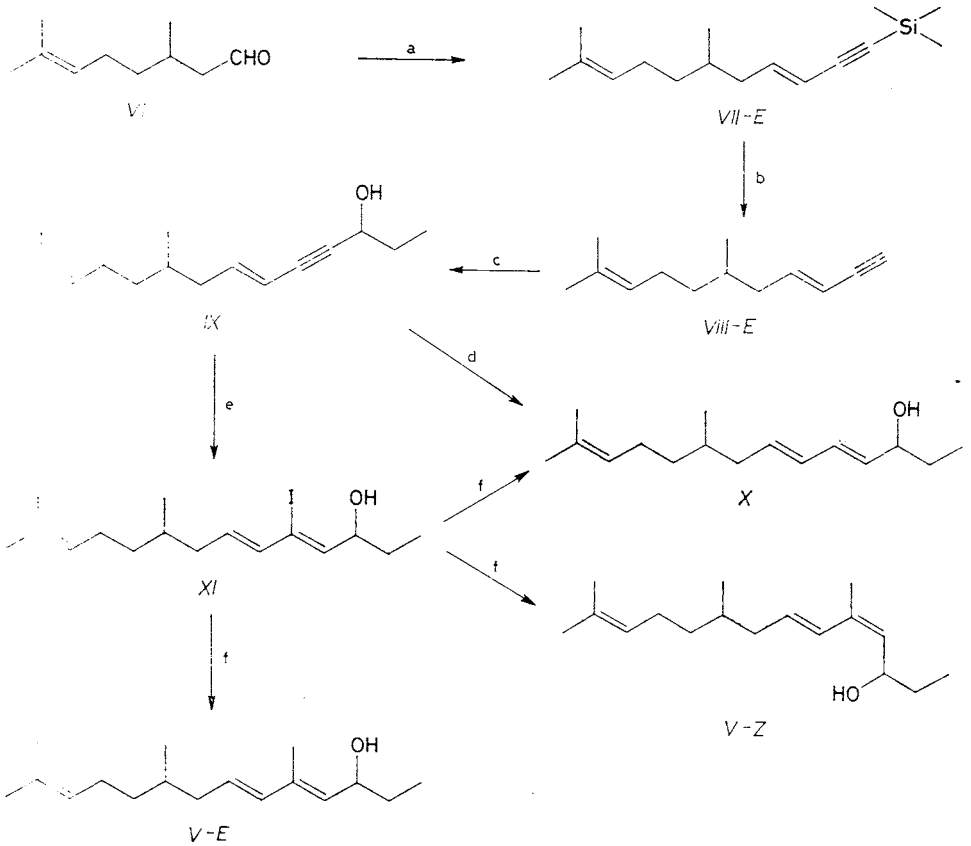
The pure *II-E* and *II-Z* were chosen as model substrates for the methylation. It has been shown that the reaction of *II-Z* and *II-E* iodo derivatives with lithium dimethyl cuprate in diethyl ether at −10°C leads to the mixture of geometrical isomers of 2,4-dimethyl-3,5-hexadien-2-ol (*IV*, Scheme 2) and decrease of stereoselectivity is in the case of the *Z*-isomer bigger than that of the *E*-isomer. Along with expected *IV-E* and *IV-Z* dienols, *E*-dienol *III* has been also identified in the reaction mixture by comparison with an authentic sample. Both *II-E* and *II-Z* iodo dienols afforded a mixture of dienols *IV-E* and *IV-Z* and *III* in ratio 5 : 87 : 8 and 75 : 18 : 7, respectively. Pure *IV-E* and *IV-Z* dienols were separated by column chromatography, and the identification has been done by ^1H NMR spectroscopy. The ratio of isomers was determined by the comparison of chemical shifts of H_c protons[7].



SCHEME 2

Decrease of stereoselectivity during the methylation of iodo dienols has not been observed in the case of published syntheses[1-6]. There are known examples of non-stereospecific crosscoupling of lithium vinyl cuprates with vinyl halogenides[11,12]. There are also several papers[3,13,14] where the possibility of exchange of halogen atom for a metalic one during the reaction of lithium dimethyl cuprate with alkyl halogenides is outlined. On the basis of that fact one can easily explain the presence of dienol *III* in the reaction mixture. Along with nucleophilic substitution giving *IV-E* and *IV-Z* derivatives a new organo copper compound is formed, hydrolysis of which leads to the dienol *III*. We used these reactions for the synthesis of (4*E*,6*E*)-5,9,13-trimethyl-4,6,12-tetradecatrien-3-ol (*V*), compound having juvenile hormone activity against the yellow mealworm, *Tenebrio molitor*[15]. Synthesis of this compound is outlined in Scheme 3. The reaction of citronellal with triphenyl trimethyl silyl-2-propynyl phosphorane[16,17] according to Wittig procedure leads to the trimethyl silyl derivative *VII-E* (yield 61%, content of *VII-Z* isomer approx. 15%). Desilylation by means of tetrabutyl ammonium fluoride gave rise to the mixture of *VIII-E* and *VIII-Z* from which the pure *VIII-E* isomer could be separated by the

column chromatography on silica gel. This separation is also possible in the case of above mentioned trimethyl silyl derivatives in 55% yield. When comparing the degree of stereoselectivity of the Wittig reaction with aldehydic substrates other than citronellal, one can see that the stereoselectivity is somewhat higher[16]. On the other hand the separation of requested isomer is without any problem and this fact makes the reaction very comfortable. Metalation of *VIII-E* with butyl lithium with subsequent reaction with propanal leads to the compound *IX* in 66% yield.



a: $Ph_3P{=}CHC{\equiv}CSi(CH_3)_3$/THF, b: $(C_4H_9)_4NF.3\,H_2O$/DMF, c: 1. BuLi, 2. CH_3CH_2CHO, d: 1. $LiAlH_4$, 2. H_2O, e: 1. $LiAlH_4/CH_3ONa$, 2. I_2, f: $(CH_3)_2CuLi$

SCHEME 3

The key step was the reaction of compound *IX* with $LiAlH_4/CH_3ONa$ in ratio 1 : 2 : 4 in THF at 40–50°C. The hydrolysis of the aluminate led to the (4*E*,6*E*)-9,13-dimethyl-4,6-tetradecadien-3-ol (*VII*). The *E*,*E* configuration has been proven using NMR data where C_6–H proton of *IV-E* differs from that of *IV-Z* (*IV-E* isomer:

δ 6·01 dd (J_1 = 10·2, J_2 = 14·6); *IV-Z* isomer: δ 7·01)[18]. Electrophilic iodination of alanate intermediate is slower than that of enynol *I*. This fact could be explained by steric reasons. ^{1}H NMR spectrum of iodo trienol *XI* shows a typical ABX_2 spectrum (C_6–H, C_7–H and the neighbouring CH_2 groups) where $J_{6,7}$ = 14·4 Hz and chemical shift of C_6–H proton is δ 5·69. On the basis of these data and comparing those of *II-Z* isomer we can consider above mentioned compound *XI* to be a (4*Z*, 6*E*)-derivative. We can identify in the ^{1}H NMR spectrum of compound *XI*, besides the other, the doublet at δ 6·27 (J = 8·8 Hz) as a signal of C_5–H proton of iodo derivative containing the iodine atom at C_4 position.

The hydroalumination-iodination procedure is reffered to be of high regioselectivity[1]. On the other hand there are several papers[2,5] where the authors observed 6–15% of regioisomer in the reaction mixture which is in good agreement with our results. Our results also indicate that the reaction course of hydroalumination-iodination of enynols *I* and *IX* is quite different. Concerning the compound *I*, the reaction is regioselective, but non-stereoselective, while the compound *IX* afforded product by a non-regioselective but stereoselective way.

It should be noted here that when the column chromatography is used for purification of compound *XI*, the yield is about 35% because the polymerization of desired product takes place. We have performed therefore the reaction step without purification in 74% yield.

The methylation of derivative *XI* was performed by means of lithium dimethyl cuprate at 20°C in diethyl ether where the ratio of reagents was 1 : 5. In contrast to iodo dienols *II-Z* and *II-E* the reaction proceeds very slowly at 0°C and we obtained the mixture of *V-E* and *V-Z* isomers and the product of reduction *X* in ratio 2 : 2 : 1. The yield was 51%. (4*E*, 6*E*)-5,9,13-Trimethyl-4,6,12-tetradecatrien-3-ol (*V-E*) was separated from the reaction mixture using chromatography. Trienols *V-E* and *V-Z* were identified by comparison with authetic samples (GLC). Both isomers exhibit differences in ^{1}H NMR spectra. One can observe the signal of C_6–H proton of *V-E* and *V-Z* isomers at δ 6·05 and δ 6·43, resp. From these results follows that the methylation of compound *IX* is less stereoselective than that of alcohol *I*.

We can conclude that the hydroalumination-iodination with subsequent methylation by lithium dimethyl cuprate as described, is strongly dependent on the type of starting compound used.

EXPERIMENTAL

^{1}H NMR spectra of compounds *II*—*IV* were taken on a Perkin–Elmer R-12B (60 MHz) spectrometer, while those of *V*—*X* on a Varian XL-200 (200 MHz) spectrometer. The chemical shifts are expressed in δ units. IR spectra were taken on a UR-20 spectrometer and mass spectra on an AEI MS-906 spectrometer. For GLC of compounds *II*—*IV*, an LCHM-80 apparatus has been used (metalic column 2 m × 3 mm (i.d.) filled with Chromaton N-Super (0·125—0·160) DMCS with 5% XE-60, helium, v = 40 ml/min) and for *V*—*X*, an HP 5890 apparatus has been used

(capilary column 25 m × 0·3 mm (i.d.), phase HP-5, nitrogen, $v = 3$ ml/min). For column chromatography silica gel Gebr. Herrmann was used (60—120 μm) and for TLC experiments Silufol foils coated with silica gel (Kavalier, Sázava, Czechoslovakia) were used. The iodine vapors or $KMnO_4$ solution has been used for detection. (+)-Citronellal was supplied by Fluka with 85% announced optical purity and was purified by column chromatography just before the use. Solution of BuLi (1·78 mol/l) in hexane has been obtained by dissolving of commercial 4·5 mol/l product (Alpha). Triphenyl trimethyl silyl-2-propynyl phosphorane (TTPB) was prepared according to papers[16,17]. Tetrahydrofuran (THF) was freshly distilled from benzophenone sodium ketyl. The solution of lithium dimethyl cuprate was prepared according to the known procedure[13].

Hydroalumination-iodination of Enynol *I*

To a mixture of 2·3 g (0·06 mol) of lithium aluminium hydride in 50 ml of abs. diethyl ether at 0°C and under nitrogen a solution of 5·5 g (0·05 mol) of compound *I* in 10 ml of abs. diethyl ether was added dropwise. The mixture was stirred for additional 4 h at RT and then 1 ml of total reaction mixture was decomposed (0°C) by cold water and dienol *III* has been identified by GLC (ref.[18]). Excess of lithium aluminium hydride has been decomposed by 5·3 g (0·06 mol) of ethyl acetate at 0°C. The reaction mixture after staying at 0°C for 1 h was cooled to −70°C and 25·4 g (0·1 mol) of iodine was added in small portions during 0·5 h. The reaction was stirred at −70°—(−50)°C for 1 h and then finally decomposed by sodium thiosulfate solution. The solid was filtered off and extracted three times with diethyl ether. The organic layer was washed three times by sodium thiosulfate solution, then brine and dried over magnesium sulfate. After removing the solvent the product was obtained by distillation. Yield 7·5 g (63%) of a mixture *II-E* and *II-Z* iodo dienols in ratio 58 : 42 (GLC, NMR). B.p. 80—82°C/133 Pa; n_D^{20} 1·5645. For $C_7H_{11}IO$ (238·1) calculated: 53·36% I; found: 53·67% I. In order to obtain pure isomers we subjected 1 g of *II-E* and *II-Z* mixture to a chromatographic separation on 50 g of silica gel. A mixture of petroleum ether–diethyl ether (19 : 1) as a mobile phase was used. We obtained 0·347 g of (3*E*)-4-iodo-2-methyl-3,5-hexadien-2-ol (*II-E*). R_F 0·32 in hexane–diethyl ether(2 : 1). IR (neat): 940, 980, 1 590, 1 630, 3 110, 3 300 cm^{-1}. ^1H NMR (CCl_4): 1·30 s, 6 H ($(CH_3)_2$); 3·40 (OH); 5·35 dd, 1 H (J = 11·0 and 1·5, C_6–H); 5·40 dd, 1 H (J = 16·0 and 1·0, C_6–H); 6·57 m, 1 H (C_3–H); 6·73 ddd, 1 H (J = 16·0, 11·0 and 1·0, H_c). Mass spectrum (*m/z*): 238 (M^+), 223, 111 (bp), 96.

Using petroleum ether–diethyl ether (9 : 1) we have obtained 0·23 g of a mixture of *II-E* and *II-Z* isomers and 0·289 g of pure *II-Z* isomer. R_F 0·2 (hexane–diethyl ether (2 : 1)). IR (neat): 930, 1 010, 1 640, 3 110, 3 400 cm^{-1}. ^1H NMR (CCl_4): 1·30 s, 6 H ($(CH_3)_2$)); 3·15 (OH); 5·10 d, 1 H (J = 11, C_6–H); 5·42 d, 1 H (J = 16, C_6–H); 5·90 dd. 1 H (J = 16·0 and 11·0, H_c); 6·47 br s, 1 H (C_3–H). Mass spectrum (*m/z*): 238 (M^+) 223, 111 (bp), 96.

Methylation of Iodo Dienols *II-E* and *II-Z*

A) To a suspension of 17·87 g (93·6 mmol) cuprous iodide in 60 ml of diethyl ether at −30°C and under argon, a solution of 187·2 mmol CH_3Li in diethyl ether (100 ml, 0·184 mol/l) has been added dropwise. The yellow solid which appeared in the very beginning was then fully dissolved. The reaction mixture was warmed up to −10°C and the solution of 5·57 g of the mixture of iodo dienols *II-Z* and *II-E* was added (48 : 52). The mixture has been stirred for 1 h at −5°C and then worked up (decomposed by saturated solution of NH_4Cl at 0°C and extracted with diethyl ether). The yield was 1·7 g (58·8%) of mixture of *IV-E*, *IV-Z*, and *III* in ratio 53 : : 42 : 5, resp. B.p. 59—66°C/1·7 kPa. The above mentioned mixture (1·6 g) has been separated

by means of chromatography using hexane–diethyl ether (19 : 1) as a mobile phase. The yield was: 0·296 g of (3*Z*)-2,4-dimethyl-3,5-hexadien-2-ol (*IV-Z*); m.p. 35–38°C; R_F 0·42 (hexane–diethyl ether (2 : 1)). ^{1}H NMR (CD_3OD): 1·31 s, 6 H ($(CH_3)_2$); 1·80 br s, 3 H (C_4–CH_3); 4·80 br s, 1 H (OH); 5·10 d, 1 H (J = 12, C_6–H); 5·17 d, 1 H (J = 17, C_6–H); 5·55 m, 1 H (C_3–H); 7·45 dd, 1 H (J = 17·0 and 12·0, C_5–H). IR (neat): 900, 1 000, 1 600, 1 620, 3 100, 3 350 cm^{-1}. For $C_8H_{14}O$ (126·2) calculated: 76·26% C, 11·11% H; found: 76·13% C, 11·02% H. Using hexane–diethyl ether (9 : 1) as a mobile phase 0·20 g (3*E*)-2,4-dimethyl-3,5-hexadien-2-ol (*IV-E*), R_F 0·36 (hexane–diethyl ether (2 : 1)) was obtained. ^{1}H NMR (CD_3OD): 0·93 s,6 H ($(CH_3)_2$); 1·52 br s, 3 H (C_4–CH_3); 3·60 br s, 1 H (OH); 4·52 d, 1 H (J = 12·0, C_6–H); 4·75 d, 1 H (J = 17, C_6–H); 5·25 m, 1 H (C_3–H); 5·95 dd, 1 H (C_5–H); IR (neat): 900, 990, 1 610, 1 630, 3 100, 3 340 cm^{-1}. For $C_8H_{14}O$ (126·2) calculated: 76·26% C, 11·11% H; found: 76·31% C, 11·08% H. By comparison with an authentic sample (NMR, GLC) also 20 mg of dienol *III* has been identified.

B) By analogy with the procedure *A*) 0·289 g (1·2 mmol) of iodo dienol *II-Z* and 5 mmol of lithium dimethyl cuprate (prepared from 0·95 g of cuprous iodide and 5·5 ml of 0·184 mol/l methyl lithium) were mixed. The yield was 0·158 g of dienols *IV-E*, *IV-Z*, and *III* in ratio 75 : 18 : : 7, resp. (GLC, NMR) and by the way described for the methylation in the example *A*) dienols *IV-E*, *IV-Z*, and *III* from the dienol *II-E* have been gained in ratio 5 : 87 : 8.

(3*E*)-1-Trimethylsillyl-6,10-dimethyl-3,9-undecadien-1-yne (*VII-E*)

To a stirred suspension of TTPB (1·836 g, 4·05 mmol) in 20 l of THF at −78°C and under argon 2·3 ml of butyl lithium (1·78M hexane solution, 4·1 mmol) was added dropwise during 3 min. In the same time a deep orange color of ylide appeared. The stirring has been continued for 1 h at −78°C and then 0·616 g (4·0 mmol) of citronellal (*VI*) in 3 ml THF was added. The solution was stirred for 1 h and then the reaction mixture was slowly warmed up to 0°C, and after 20 min stirring at 0°C warmed up to RT. The reaction mixture was poured into 100 ml of cold water, extracted with petroleum ether and organic layer dryied with magnesium sulfate. During the evaporation of solvent some solid (triphenyl phosphine oxide) has appeared. This solid was removed by filtration through a short silica gel column. After evaporation of solvent 0·87 g of mixture of compounds *VII-E* and *VII-Z* (85 : 15, GLC) was obtained. Part of this mixture (100 mg) was subjected to a chromatographic purification (20 g of silica gel, petroleum ether). The yield was: 3·0 mg of trimethyl silyl derivative *VII-Z*. R_F: 0·47 (hexane). IR (CCl_4): 846, 1 248, 2 150, 3 015, 3 050 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0·19 s, 9 H, ($(CH_3)_3Si$); 0·90 d, 3 H (J = 6·7, C_6–CH_3); 1·11–1·45 m, 3 H (C_6–H, C_7–H); 1·61 dt, 3 H (J = 1·2 and 0·8, C_{10}–CH_3); 1·69 dt, 3 H (J = 1·3, C_{11}–H); 2·00 dt, 2 H (J_1 = J_2 = 7·6, C_8–H); 2·10–2·40 m, 2 H (C_5–H); 5·10 m, 1 H (C_9–H); 5·50 dt, 1 H (J = 11·0 and 1·4, C_3–H); 5·98 dt, 1 H (J = 11·0 and 7·6, 1·69 dt, 3 H (J = 1·3, C_{11}–H); 2·00 dt, 2 H (J_1 = J_2 = 7·6, C_8–H); 2·10–2·40 m, 2 H (C_5–H); 5·10 m, 1 H (C_9–H); 5·50 dt, 1 H (J = 11·0 and 1·4, C_3–H); 5·98 dt, 1 H (J = 11·0 and 7·6, C_4–H).

In the next fractions 30·7 mg of a mixture of *VII-Z* and *VII-E* and 37·3 mg of pure *VII-E* have been eluted. R_F: 0·4 (hexane); GLC purity: 98%. IR (CCl_4): 846, 854, 958, 1 249, 1 672, 2 140, 2 175, 3 020, 3 050 cm^{-1}. ^{1}H NMR ($CDCl_3$): 0·18 s, 9 H, ($(CH_3)_3Si$); 0·88 d, 3 H (J = 6·6, C_6–CH_3); 1·04–1·40 m, 3 H (C_6–H, C_7–H); 1·60 dt, 3 H (J = 1·2 and 0·8, C_{10}–CH_3); 1·68 dt, 3 H (J_1 = J_2 = 1·3, C_{11}–H); 1·88–2·20 m, 2 H (C_5–H); 1·95 dtt 2 H (C_5–H); 1·95 dt, 2 H (J_1 = J_2 = 7·6, C_8–H); 5·09 m, 1 H (C_9–H); 5·49 dt, 1 H (J = 16 and 1·5, C_3–H); 6·19 dt, 1 H (J = 16 and 7·4, C_4–H). The total yield of enynes *VII-E* and *VII-Z* after column purification is 61%.

(3*E*)-6,10-Dimethyl-3,9-undecadien-1-yne (*VIII-E*)

A) A mixture of trimethyl silyl derivatives *VII-E* and *VII-Z* (0·204 g, 0·82 mmol) was mixed with solution of 0·634 g (2 mmol) tetrabutyl ammonium fluoride trihydrate in 12 ml of dimethyl formamide. After staying 30 min at RT the mixture was poured in the flask with 40 ml of cold water and then extracted with pentane. The organic layer was dried by sodium sulfate, filtered through a short silica column and then the solvent was removed by distillation. The yield was 0·148 g. Part of this product (0·102 g) was subjected to a chromatographic purification on silica gel using petroleum ether as a mobile phase. The yield was 10·0 mg (10%) of dienyne *VIII-Z*, R_F: 0·53 (hexane); GLC purity was 99%. IR (CCl_4): 1 687, 2 105, 3 315 cm^{-1}. ^1H NMR ($CDCl_3$): 0·85 dt 3 H (J = 6·7, C_6–CH_3); 1·03—1·55 m, 3 H (C_6–H, C_7–H); 1·54 d, 3 H (J = 1·3, C_{13}–H); 1·61 d, 3 H (J = 1·3, C_{10}–CH_3); 1·95 m, 2 H (C_8–H); 2·20 m, 2 H (C_5–H); 2·99 dd, 1 H (J = = 2·3 and 1·0, C_1–H); 5·03 m, 1 H (C_9–H); 5·42 ddt, 1 H (J = 10·9, 2·3, and 1·4, C_3–H); 5·95 ddt, 1 H (J = 10·9, 7·5, and 1·0, C_4–H). As the next a mixture of 14·5 mg *VIII-Z* and *VIII-E* and finally 60 mg (60%) dienyne *VIII-E* has been eluted. R_F: 0·45 (hexane); GLC purity 98·8%. IR (CCl_4): 962, 2 110, 3 025, 3 315 cm^{-1}. ^1H NMR ($CDCl_3$): 0·88 dt 3 H (J = 6·6, C_6–CH_3); 1·06—1·55 m, 3 H (C_6–H, C_7–H); 1·6 dt, 3 H (J = 1·4 and 0·8, C_{11}–H); 1·68 dt, 3 H (J_1 = = J_2 = 1·4, C_{10}–CH_3); 1·87—2·22 m, 2 H (C_5–H); 2·78 dd, 1 H (J = 2·2 and 6·5, C_1–H); 5·08 m, 1 H (C_9–H); 5·45 ddt, 1 H (J = 16, 2·2, and 1·5, C_3–H); 6·23 ddt, 1 H (J = 16, 0·5, and 7·6, C_4–H). Mass spectrum (*m/z*): 176 (M^+), 161, 147, 133, 124, 119, 109, 105, 91, 69 (bp).

B) According to the above mentioned procedure, 1·84 g of citronellal has been subjected to the reaction with TTPB ylide (generated from 5·53 g TTPB and 7 ml of 1·78M solution of BuLi). After desilylation of the reaction mixture, 1·3 g (55%) of dienyne *VIII-E* has been obtained.

(6*E*)-9,13-Dimethyl-6,12-tetradecadien-4-yn-3-ol (*IX*)

To a solution of 0·292 g (1·66 mmol) of dienyne *VIII-E* in 7 ml of diethyl ether and under the nitrogen atmosphere a solution of 1·78M-BuLi in hexane (1·66 mmol) at −78°C was added dropwise. Then the reaction mixture was stirred for 1 h at −78°C. After this period the solution of 0·103 g (1·78 mmol) propanal in 2 ml of diethyl ether was added and the reaction mixture was stirred for additional 2 h at −78°C. The temperature was slowly increased to 0°C and the reaction mixture was decomposed by pouring into the 20 ml of saturated ammonium chloride solution. This system was several times extracted with a mixture of petroleum ether–diethyl ether (1 : 1). After drying with sodium sulfate and evaporating of solvent the mixture was subjected to the column chromatography. Using pure petroleum ether as a solvent we have obtained 73 mg of dienyne *VIII-E* and then using petroleum ether–diethyl ether (20 : 1) — 0·255 g (66%) of the dienynol *IX*. R_F: 0·30 (petroleum ether–diethyl ether (5 : 1)); GLC purity: 98%. IR (CCl_4): 963, 1 682, 2 215, 2 255, 3 620 cm^{-1}. ^1H NMR ($CDCl_3$): 0·88 d, 3 H (J = 6·6, C_9–CH_3); 1·02 t, 3 H (J = 7·1, C_1–H); 1·08—1·60 m, 3 H (C_9–H, C_{10}–H); 1·60 m, 3 H (C_{14}–H); 1·68 m, 3 H (C_{13}–CH_3); 1·76 m, 2 H (C_2–H); 1·85—2·20 m, 2 H (C_8–H); 1·95 m, 2 H (C_{11}–H); 4·42 td, 1 H (J = 6·5 and 1·6, C_3–H); 5·08 m, 1 H (C_{12}–H); 5·48 dtd, 1 H (J = 15·7, 1·6, and 1·6, C_6–H); 6·13 dt, 1 H (J = 15·7 and 7·4, C_7–H). Mass spectrum (*m/z*): 234 (M^+), 219, 206, 205, 201, 191, 177, 121, 109, 91, 81, 69 (bp), 57.

(4*E*, 6*E*)-9,13-Dimethyl-4,6,12-tetradecatrien-3-ol (*X*)

Compound *IX* (0·117 g, 0·5 mmol) was added dropwise under the nitrogen at 0°C to the mixture of 38 mg (1 mmol) lithium aluminium hydride and 0·108 g (2 mmol) sodium methyl alcoholate in THF. After the addition the reaction mixture was warmed up to 40—45°C. This temperature

was maintained for 2 h and then the mixture was cooled to −20°C and decomposed by adding of 5 ml of water. After the extraction (petroleum ether–diethyl ether (1 : 1)), drying with sodium sulfate and chromatography on silica gel (mobile phase: petroleum ether–diethyl ether from 50 : 1 to 20 : 1) we have obtained 95 mg (80%) of trienol *X*. R_F: 0·26 (petroleum ether–diethyl ether (5 : 1). ^{1}H NMR ($CDCl_3$): 0·87 d, 3 H (J = 6·6, C_9–CH_3); 0·92 t, 3 H (J = 7·1, C_1–H); 1·00–1·65 m, 5 H (C_2–H, C_9–H, C_{10}–H); 1·60 m, 3 H (C_{14}–H); 1·68 m, 3 H (C_{13}–CH_3); 1·80–2·25 m, 4 H (C_8–H, C_{11}–H); 4·04 dtd, 1 H (J = 6·8, 6·8, and 1·0, C_3–H); 5·09 m, 1 H (C_{12}–H); 5·56 dd, 1 H (J = 14·8 and 7·0, C_4–H); 5·67 dt, 1 H (J = 14·6 and 7·2, C_7–H); 6·01 ddt, 1 H (J = 14·6, 10·2, and 1·2, C_6–H); 6·29 ddt, 1 H (J = 14·8, 10·2, and 1·1, C_5–H). Mass spectrum (m/z): 236 (M^+), 234, 218, 175, 149, 109, 69 (bp), 57, 41.

(4*Z*,6*E*)-9,13-Dimethyl-5-iodo-4,6,12-tetradecatrien-3-ol (*X*)

Compound *IX* (0·234 g, 1 mmol) was added dropwise under nitrogen at 0°C to the mixture of 76 mg (2 mmol) lithium aluminium hydride and 216 mg (2 mmol) sodium methyl alcoholate in 10 ml THF. The reaction mixture was warmed up to 40–45°C and after maintaining this temperature for 2 h the reaction mixture was decomposed by adding of 176 mg (2 mmol) ethyl acetate at 0°C. The reaction mixture was stirred for 2 h at this temperature and then was cooled to −40°C. The solution of 0·508 g (2 mmol) iodine in 2 ml THF was added and the stirring has been continued for additoinal 2 h at the above temperature. The reaction mixture was decomposed. with saturated solution of sodium thiosulfate (until the amount of iodine has not been reduced). After the extraction (diethyl ether) and drying (sodium sulfate) the residue (0·268 g (74%)) was subjected to column chromatography (eluent: petroleum ether–diethyl ether from 25 : 1 to 5 : 1). The yield was 0·127 g (35%) of compound *XI*. R_F: 0·28 hexane–diethyl ether (5 : 1)). ^{1}H NMR ($CDCl_3$): 0·86 d, 3 H (J = 6·5, C_9–CH_3); 0·98 t, 3 H (J = 7·4, C_1–H); 1·20–1·60 m, 5 H (C_2–H, C_9–H, C_{10}–H); 1·60 d, 3 H (J = 1·5, C_{14}–H); 1·85–2·25 m, 4 H (C_8–H, C_{11}–H); 4·46 dtd, 1 H (J = 6·8, 6·8, and 1·0, C_3–H); 5·09 m, 1 H (C_{12}–H); 5·69 dtd, 1 H (J = 14·4, 1·2) and 1·2, C_6–H); 5·79 dd, 1 H (J = 6·8 and 1·2, C_4–H); 6·01 dt, 1 H (J = 14·4 and 7·4, C_7–H).

The Methylation of Iodo Trienol *XI* with Lithium Dimethyl Cuprate

To a suspension of 0·382 g (2 mmol) cuprous iodide in 10 ml of diethyl ether the solution of methyl lithium (4 mmol) in diethyf ether has been added dropwise (under nitrogen, at −30°C). To this solution of lithium dimethyl cuprate at −10°C and under nitrogen 0·144 g (0·4 mmol) of compound *XI* in 2 ml of diethyl ether has been added (during this procedure the yellow solid appeared). The mixture was stirred for 3 h at 0°C, for 10 h at 20°C and finally decomposed by pouring into the saturated solution of ammonium chloride. After extraction with diethyl ether and drying of organic phase we obtained 0·1 g of compound which was subjected to chromatographic separation (15 g of silica gel, petroleum ether–diethyl ether (25 : 1)). The yield was 29 mg of compound *X* and trienol *V-Z* in ratio 1 : 2. R_F: 0·28 (hexane–diethyl ether (5 : 1)). ^{1}H NMR ($CDCl_3$): along with the signals of trienol *X* the signals corresponding to the *V-Z* have also been identified: 0·86 d, 3 H (J = 6·6, C_9–CH_3); 0·91 t, 3 H (J = 7·2, C_1–H); 1·01–1·68 m, 5 H (C_2–H, C_9–H, C_{10}–H); 1·60 br s, 3 H (C_{14}–H); 1·68 br s, 3 H (C_{13}–CH_3); 1·84 d, 3 H (J = 1·3, C_5–CH_3); 1·86–2·21 m, 4 H (C_8–H, C_{11}–H); 4·52 dt, 2 H (J = 8·8 and 6·6, C_3–H); 5·10 m, 1 H (C_{12}–H); 5·23 br d, 1 H (J = 8·8, C_4–H); 5·74 dt, 1 H (J = 15·6 and 7·4, C_7–H); 6·43 dtd, 1 H (J = 15·6, 1·5, and 1·0, C_6–H). The next fractions 15 mg of the mixture of compounds *X*, *V-E*, *V-Z* and 7 mg of pure trienol *V-E* has been eluted. R_F: 0·24 (hexane–diethyl ether (5 : 1)). ^{1}H NMR ($CDCl_3$): 0·89 d, 3 H (J = 6·4, C_9–CH_3); 0·91 t, 3 H (J = 7·4, C_1–H); 1·05–1·68 m, 5 H (C_2–H, C_9–H, C_{10}–H); 1·60 br s, 3 H (C_{14}–H); 1·68 br s, 3 H (C_{13}–CH_3); 1·80 d, 3 H

(C_5-CH_3); 1·70–2·24 m, 4 H C_8-H, C_{11}-H); 4·41 dt, 1 H (J = 8·8 and 6·6, C_3-H); 5·10 m, 1 H (C_{12}-H); 5·34 br d, 1 H (J = 8·8, C_4-H); 5·67 dt, 1 H (J = 15·6, 7·2, and 7·2, C_7-H); 6·05 dtd, 1 H (J = 15·6, 1·5, and 1·5, C_6-H).

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