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ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

A New Synthetic Route to 1,3,5-Undecatrienes and Fucoserratene

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Abstract—A new procedure for preparing natural alkatrienes, fucoserratene and 1,3,5-undecatrienes, was developed. The key step of both syntheses is stereoselective formation of double bonds by the Wittig reaction starting from (*E*)-4,4-dimethoxy-2-butenal.

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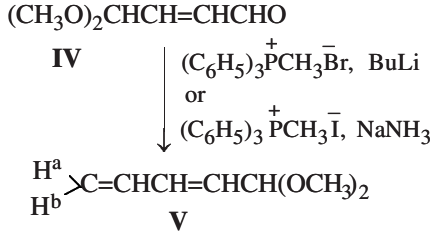
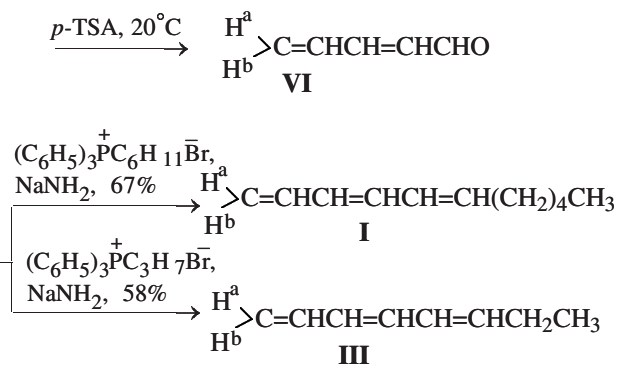
Conjugated trienes containing terminal vinyl group widely occur in the nature. *trans,cis*- and *trans,trans*-1,3,5-undecatrienes **I** and **II** were isolated from essential oils of *Galbanum* gum of various origins [1]. They were also found in essential oils of various algae [2, 3] and are components of various perfume compounds. In addition, triene **I** is one of the components of the odor of parsley, mandarins, apples, and pears [4]; it acts as sex pheromone on gametes of Australian kelps [5]. (3*E*,5*Z*)-1,3,5-Octatriene **III** (fucoserratene) is a pheromone isolated from fertilized ovums of some insect species [6]. These compounds are a subject of numerous studies. They are synthesized by heterolytic fragmentation of unsaturated 1,5-diols [6], stereo- and regioselective palladium-catalyzed synthesis [7], alkylation of terminal acetylene compounds [8], Wittig reation [9, 10], and also using α-haloalkylsulfonyl bromides [11], pentadienyl dithiocarbamates [12], and pyridazine *N*-oxides [13].

Here we suggest two alternative routes to the target products, (3*E*,5*Z*)-1,3,5-undecatriene **I** and fucoserratene **III**, starting from (*E*)-4,4-dimethoxy-2-butenal **IV**. The first route is the sequence of two Wittig reactions: first with triphenylmethylidenephosphorane and then with triphenylpropylidenephosphorane or triphenylhexylidenephosphorane (Scheme 1).

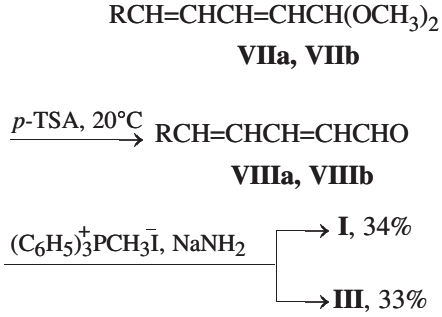
Scheme 1.





In the second route, the same reactions are performed in the reverse order (Scheme 2).

Scheme 2.



where R = Et (**VIIa**, **VIIIa**), Am (**VIIb**, **VIIIb**).

Olefination with triphenylmethylidenephosphorane (Scheme 1) was performed at 0°C in tetrahydrofuran (THF) in the presence of butyllithium. Since the yield of (3*E*)-5,5-dimethoxy-1,1-pentadiene **V** did not exceed 30%, butyllithium was replaced by sodium amide. By so doing, the yield of acetal **V** was in-

creased to 62%. After deprotection of the carbonyl group (20°C, acetone–water, 2 : 1) in the presence of catalytic amounts of *p*-toluenesulfonic acid (*p*-TSA), (2*E*)-penta-2,4-dienal **VI** was prepared in 93% yield. The second Wittig reaction with dienal **VI** was also performed in THF at 0°C. The phosphonium salts were deprotonated with sodium amide. Mixtures of stereoisomers of 1,3,5-undecatriene **I** and fucoserratene **III** were obtained in 67 and 58% yields, respectively. The content of the (3*E*,5*Z*) isomers in the isomeric mixtures exceeded 80%.

The isomer ratio was determined by ^{1}H NMR spectroscopy from the chemical shift of the H^6 atom. In the (*E*,*Z*) isomer, the H^6 signal is shifted upfield (5.50 ppm) relative to the (*E*,*E*) isomer (5.75 ppm) [8]. In the case of undecatriene **I**, the isomer ratio was also determined by GLC on a capillary column coated with SE-30.

By Wittig olefination of butenal **IV** with triphenylpropylidenephosphorane and triphenylhexylidenephosphorane, we previously prepared mixtures of isomers of acetals **VIIa** and **VIIb**, respectively, with more than 95% content of (2*E*,4*Z*) isomers. The acetal protection was removed at 0°C in acetone–water (2 : 1) in the presence of catalytic amount of *p*-toluenesulfonic acid to obtain the corresponding dienals **VIIIa** and **VIIIb**, with the configuration of (4*Z*) double bond being almost fully retained [14]. Then, by the Wittig reaction, we prepared the desired trienes: (3*E*,5*Z*)-1,3,5-undecatriene **I** and fucoserratene **III** (Scheme 2).

By choosing appropriate deprotection conditions, from acetal **VIIb** we prepared (*E*,*Z*)- and (*E*,*E*)-decadienals **IX** with the prevalence of the (*E*,*E*) isomer. For example, at 20°C in the presence of catalytic amounts of *p*-toluenesulfonic acid and equimolar amounts of water in acetone, we prepared decadienal **IX** with 81% content of the (*E*,*E*) isomer [14], which was converted by the Wittig reaction into (3*E*,5*E*)-1,3,5-undecatriene **II** with 34% yield:

$$\underset{\textbf{IX}}{CH_3(CH_2)_4CH{=}CHCH{=}CHCHO} \xrightarrow{(C_6H_5)_3^+PCH_3\bar{I},\ NaNH_2} \underset{\textbf{II}}{CH_3(CH_2)_4CH{=}CHCH{=}CHCH{=}C\begin{matrix}H^a\\H^b\end{matrix}}$$

Undecatriene **II** was also synthesized by the Schlosser reaction. (2*E*,4*E*)-1,1-Dimethoxy-2,4-decadiene **V** was prepared in 57% yield form butenal **IV** and hexyltriphenylphosphonium bromide; the product contained 90% (*E*,*E*) isomer [14]. Deacetalization of **V** followed by the Wittig reaction yielded undecatriene **II** containing 87% (*E*,*E*) isomer.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian VXR-300 spectrometer (300 MHz) in $(CD_3)_2CO$ or $CDCl_3$. The chemical shifts (δ, ppm) are given relative to TMS. The IR spectra were recorded on a UR-20 spectrophotometer from thin films. GLC analysis was performed with a Chrom-5 chromatograph (flame ionization detector, 25 m × 0.25 mm glass capillary column, liquid phase SE-30, carrier gas nitrogen, flow rate 3 ml min^{-1}). Column chromatography was performed on silica gel L 40/100. Thin-layer chromatography was performed on Silufol UV-254 plates; the chromatograms were developed by treatment with iodine vapor or $KMnO_4$ solution. Compound **IV** was prepared as described in [15], and phosphonium salts, as described in [16].

(3*E*)-5,5-Dimethoxy-1,3-pentadiene V. *a.* A 1.45 N solution of butyllithium (16.8 ml) was added dropwise at room temperature to 8.9 g of methyltriphenylphosphonium bromide in 35 ml of THF. Then the mixture was cooled to a temperature from 0 to –5°C, and a solution of 3.0 g of butenal **IV** in 5 ml of THF was added dropwise. The mixture was allowed to stand for 1 h, after which it was poured onto ice and extracted with ether. The extract was dried over sodium sulfate. The solvent was distilled off, and the residue was distilled in a vacuum to obtain 1.3 g (30%) of (3*E*)-5,5-dimethoxy-1,3-pentadiene **V**, bp 72–73°C (12 mm Hg). IR spectrum, ν, cm^{-1}: 1116 (CH_3O–C–OCH_3), 1600 (C=C). ^{1}H NMR spectrum [$(CD_3)_2CO$], δ, ppm (*J*, Hz): 3.2 s (6H, OCH_3), 4.8 d (1H, H^5, $J_{5,4}$ 5.0), 5.12 d (1H, H^{1a}, $J_{1a,2}$ 10.5), 5.28 d (1H, H^{1b}, $J_{1b,2}$ 16.0), 5.61 d.d (1H, H^4, $J_{4,3}$ 15.5, $J_{4,5}$ 5.0), 6.07 d.d.d (1H, H^2, $J_{2,1a}$ 10.5, $J_{2,1b}$ 16.0, $J_{2,3}$ 11.2), 6.67 d.d (1H, H^3, $J_{3,2}$ 11.2, $J_{3,4}$ 15.5).

Found, %: C 65.56, H 9.41.

$C_7H_{12}O_2$. Calculated, %: C 65.60, H 9.44.

b. Methyltriphenylphosphonium iodide (28.7 g) was added to 3.6 g of sodium amide in 40 ml of THF under nitrogen. The mixture was refluxed for 1 h, after which it was cooled to a temperature from 0 to –10°C, and a solution of 9.2 g of aldehyde **IV** in 10 ml of THF was added dropwise. The mixture was allowed to stand dor 1 h, after which 50 ml of water was added, and the mixture was extracted with ether. The extract was dried over sodium sulfate, the solv-

ents were removed, and the residue was distilled in a vacuum. Dimethoxy diene **V** was obtained, bp 72–73°C (12 mm Hg); yield 5.6 g (62%).

(2*E*)-2,4-Pentadienal VI. *p*-Toluenesulfonic acid (36 mg) was added to a mixture of 0.9 g of dimethoxy diene **V** in 10 ml of acetone and 5 ml of water. The mixture was stirred for 10 min at 20°C and neutralized with Na_2CO_3, after which acetone was removed and the residue was extracted with ether. The extract was dried over sodium sulfate, and the crude mixture after removing the solvent was purified on a column (silica gel, hexane : ether = 10 : 1). (2*E*)-2,4-Pentadienal **VI** was isolated; yield 534 mg (93%). IR spectrum, ν, cm^{-1}: 1620 (C=C), 1675, 2720 (C=O). ^1H NMR spectrum [$(CD_3)_2CO$], δ, ppm (*J*, Hz): 5.64 d (1H, H^{5a}, $J_{5a,4}$ 10.5), 5.81 d (1H, H^{5b}, $J_{5b,4}$ 16.0), 6.05 d.d (1H, H^2, $J_{2,1}$ 8.5, $J_{2,3}$ 15.3), 6.40 m (1H, H^4), 7.12 d.d (1H, H^3, $J_{3,2}$ 15.3, $J_{3,4}$ 10.3), 9.55 d (1H, H^1, $J_{1,2}$ 8.5) [17].

(3*E*,5*Z*)-1,3,5-Undecatriene I. *a.* Hexyltriphenylphosphonium bromide (1.6 g) was added to 0.185 g of sodium amide in 2 ml of THF. The mixture was refluxed for 1 h and cooled to a temperature from 0 to –10°C, and a solution of 0.3 g of dienal **VI** in 1 ml of THF was added dropwise. After keeping for 1 h, 3 ml of water was added, and the mixture was extracted with ether and dried over sodium sulfate. After removing the solvents, the crude mixture was purified on a column (silica gel, hexane : ether from 19 : 1 to 10 : 1) to obtain 0.37 g (67%) of (3*E*,5*Z*)-1,3,5-undecatriene **I** [relative content of the (3*E*,5*Z*) isomer 86%]. IR spectrum, ν, cm^{-1}: 840 (C=C), 935 [(*E*)-C=C], 1560 (C=C), 3100 (CH_2=CH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.91 t (3H, H^{11}, $J_{11,10}$ 7.0) 1.28–1.46 m (6H, H^8, H^9, H^{10}), 2.20 q (2H, H^7, $J_{7,6} = J_{7,8}$ = 7.2), 5.08 d.d (1H, H^{1a}, $J_{1a,1b}$ 1.2, $J_{1a,2}$ 10.0), 5.22 d.d (1H, H^{1b}, $J_{1b,1a}$ 1.2, $J_{1b,2}$ 16.0), 5.50 d.t (1H, H^6, $J_{6,5}$ 10.0, $J_{6,7}$ 7.0), 5.98–6.56 m (4H, H^2, H^3, H^4, H^5). Signals belonging to (3*E*,5*E*)-1,3,5-undecatriene **II** were also present: 2.14 q (2H, H^7, $J_{7,6} = J_{7,8}$ = 7.4), 5.05 d.d (1H, H^{1a}, $J_{1a,1b}$ 1.2, $J_{1a,2}$ 10.0), 5.19 d.d (1H, H^{1b}, $J_{1b,1a}$ 1.2, $J_{1b,2}$ 16.0), 5.74 d.t (1H, H^6, $J_{6,5}$ 15.0, $J_{6,7}$ 7.0) [9].

b. Methyltriphenylphosphonium iodide (0.94 g) was added to 0.13 g of sodium amide in 4 ml of THF, and the mixture was refluxed for 1 h. After cooling to a temperature from 0 to –10°C, a solution of 0.4 g of aldehyde **VIII** in 1 ml of THF was added. One hour later, 3 ml of water was added, the mixture was extracted with ether, and the extract was dried over sodium sulfate. After removing the solvent, the crude mixture was purified on a column (silica gel, hexane : ether from 19 : 1 to 10 : 1) to obtain 0.13 g (34%) of undecatriene **I** with 84% content of the (3*E*,5*Z*) isomer.

(3*E*,5*Z*)-1,3,5-Octatriene III. *a.* Propyltriphenylphosphonium bromide (1.4 g) was added to 0.185 g of sodium amide in 2 ml of THF. The mixture was refluxed for 1 h, after which it was cooled to a temperature from 0 to –10°C, and a solution of 0.3 g of aldehyde **VI** in 1 ml of THF was added dropwise. One hour later, 3 ml of water was added, and the mixture was extracted with ether. The extract was dried over sodium sulfate. After distilling off the solvents, the crude mixture was purified on a column (silica gel, hexane : ether from 19 : 1 to 10 : 1) to obtain 0.23 g (58%) of octatriene **III** with 85% content of the (3*E*, 5*Z*) isomer. IR spectrum, ν, cm^{-1}: 840 [(*Z*)-C=C], 935 [(*E*)-C=C], 1560 (C=C), 3100 (CH_2=CH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.9 t (3H, H^8, $J_{8,7}$ 7.0), 2.16 m (2H, H^7), 5.10 d.d (1H, H^{1a}, $J_{1a,1b}$ 1.2, $J_{1a,2}$ 10.0), 5.22 d.d (1H, H^{1b}, $J_{1b,1a}$ 1.2, $J_{1b,2}$ 16.0), 5.48 d.t (1H, H^6, $J_{6,5}$ 10.0, $J_{6,7}$ 7.0), 5.96–6.56 m (4H, H^2, H^3, H^4, H^5). Along with these signals, we found a signal at 5.78 d.t (1H, $J_{6,5}$ 15.0, $J_{6,7}$ 7.0), belonging to the H^6 atom of (3*E*,5*E*)-1,3,5-octatriene **III**.

b. Methyltriphenylphosphonium iodide (6.2 g) was added to 0.85 g of sodium amide in 6 ml of THF, and the mixture was refluxed for 1 h. After cooling to a temperature from 0 to –10°C, a solution of 1.7 g of (2*E*,4*Z*)-2,4-heptadienal **VIII** was added dropwise. The mixture was allowed to stand for 1 h, treated with water, and extracted with ether. The extract was dried over sodium sulfate. The residue after removing the solvents was chromatographed on a column (silica gel, hexane : ether = 20 : 1) to obtain 0.55 g (33%) of octatriene **III** with 89% content of the (3*E*,5*Z*) isomer.

(3*E*,5*E*)-1,3,5-Undecatriene II. Methyltriphenylphosphonium iodide was added to 0.13 g of sodium amide in 2 ml of THF. The mixture was refluxed for 1 h. After cooling to a temperature from 0 to –10°C, a solution of 0.4 g of dienal **IX** in 1 ml of THF was added dropwise. One hour later, 3 ml of water was added, and the mixture was extracted with ether. The extract was dried over sodium sulfate. The residue after removing the solvents was chromatographed on a column (silica gel, hexane : ether = 20 : 1) to obtain 0.13 g (34%) of undecatriene **II** with 87% content of the (3*E*,5*E*) isomer. IR spectrum, ν, cm^{-1}: 965 [(*E*)-C=C], 1585 (C=C), 3080 (C=C). ^1H NMR spectrum [$(CD_3)_2CO$], δ, ppm (*J*, Hz): 0.91 t (3H, H^{11}, $J_{11,10}$

7.0), 1.23–1.46 m (6H, H^8, H^9, H^{10}), 2.14 q (2H, H^7, $J_{7,8}$ 7.2), 5.05 d.d (1H, H^{1a}, $J_{1a,1b}$ 1.3, $J_{1a,2}$ 10.0), 5.19 d.d (1H, H^{1b}, $J_{1a,1b}$ 1.3, $J_{1b,2}$ 6.0), 5.74 d.t (1H, H^6, $J_{6,5}$ 14.5, $J_{6,7}$ 7.2), 5.98–6.58 m (4H, H^2, H^3, H^4, H^5).

CONCLUSION

A stereoselective procedure for preparing conjugated alkatrienes by the Wittig reaction with (*E*)-4,4-dimethoxy-2-butenal was developed.

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