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A New Facile Preparation of a Bifunctionalized C6 Homologating Agent from 1,4-Cyclohexadiene

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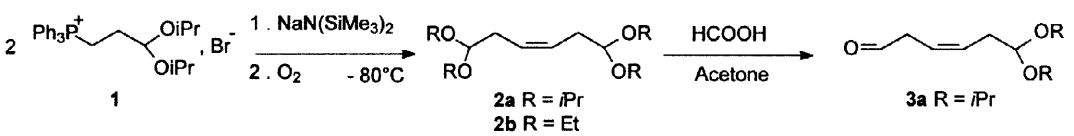
Abstract:
a new preparation of the bifunctionalized unsaturated C6 homologating agent **2b** which is an efficient synthetic tool is described. This method is atom economic, very efficient on grams scale and easy to handle from cheap commercially available 1,4-cyclohexadiene. Synthetic applications by using a mild and selective monohydrolysis of acetal catalysed by $FeCl_3$ are described.

Keywords: acetals, homologation, hydrolysis, Wittig olefination.

Our interest in the stereoselective *cis*-Wittig olefination has led to the proposal of a new strategy for the synthesis of polyunsaturated fatty acids (PUFAs) which are featured by methylene-interrupted *cis* double bonds. Our approach is based on the oxidative coupling of the ylid derived from the previously described C3 homologating agent **1**,[1] which gives a rapid access to the symmetrical *cis*-1,6-diacetal **2a** precursor of the C6 homologating agent **3a** after selective monohydrolysis.[2,3] They were used for the syntheses of several PUFAs incorporating two double bonds.[4]



However the main drawback of our approach was a reproducible preparation of large quantities of the very useful C6 *bis*-acetal **2a**. Although the yield was very high, the method was not an atom economic process, since it needed 2 equivalents of the C3 homologating agent **1** and resulted with the loss of 2 equivalents of triphenylphosphine oxide. Moreover, work up of the reaction, elimination of large quantities of phosphorus derivatives and the anhydrous conditions of the reaction associated with the control of oxygen flow rate are difficult to manage and cause problems of reproducibility of the yields.

We present here a practical access to compounds **2a** and **2b** and we show some new properties of compound **2b**.

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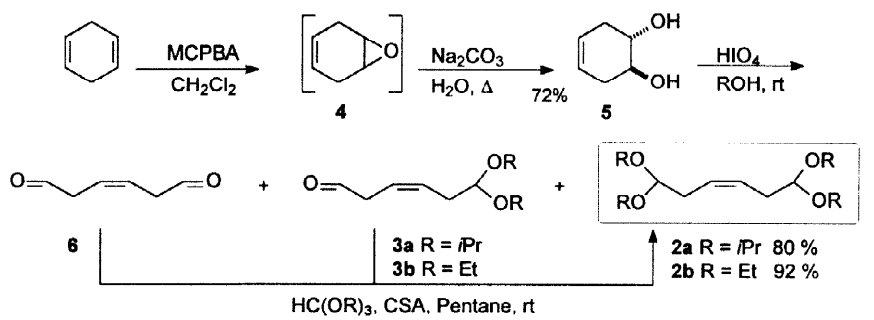
The C6 synthon must bear a *(Z)* double bond which could originate from a ring system: the commercially available 1,4-cyclohexadiene presents the required structure. Literature reported that 1,4-cyclohexadiene may undergo a non selective ozonolysis cleavage leading to a mixture of *(Z)* 1,6-diester, 1,6-esteracetal and 1,6-*bis*-acetal-hex-3-enes **2** (R = CH_3) derivatives together with 1,3-bifunctionalized derivatives, arising from double ozonolysis, in ratios depending on the reaction conditions.[5] Alternatively Mori and *Coll.* reported the direct hydrolytic oxidative cleavage with periodic acid of monoepoxide **4** giving the unstable dialdehyde **6**, which was rapidly reduced into the corresponding diol in 21% overall yield from 1,4-cyclohexadiene.[6]

With these informations in hands, we prepared the epoxide **4**, which did not react with HIO_4 in organic solvents such as CH_2Cl_2 or CH_2Cl_2/*i*PrOH. Reaction of **4** with Na_2CO_3 in water gave the diol **5** in 72% yield from 1,4-cyclohexadiene.[7] The oxidative cleavage of **5** with periodic acid could then be done in dry THF or CH_2Cl_2 in the presence of isopropanol and triisopropylorthoformiate leading to the expected *bis*-acetal **2a** as major product together with *bis*-aldehyde **6** and monoacetal **3a**. Oxidation of **5** in *i*PrOH gave the same mixture which, when treated with triisopropylorthoformiate in pentane in the presence of a catalytic amount of camphorsulfonic acid (CSA) was transformed into the pure *bis*-acetal **2a** in 80% yield from diol **5**. Unfortunately, the diisopropyl acetal is very sensitive to the reaction conditions, and scaling up the reaction to 1 or 2 grams gave a complex mixture of unsaturated compounds including **2a**. This problem was resolved by switching from iPrOH to EtOH. The bis-acetal **2b** became the major product of the mixture which upon treatment with triethylorthoformate in pentane gave pure **2b** in 92% overall yield on a 10 g scale (Scheme 1).



Scheme 1

The next step was the selective conversion of *bis*-acetal **2b** to the corresponding monoaldehyde **3b**, the direct precursor of various C6 homologating agents. Unfortunately, the reaction conditions used for the hydrolysis of diisopropyl *bis*-acetal **2a** failed: formic acid was not strong enough to hydrolyse the diethyl acetal and TsOH in THF rapidly gave the unwanted *bis*-aldehyde **6** together with **3b** and **2b**.

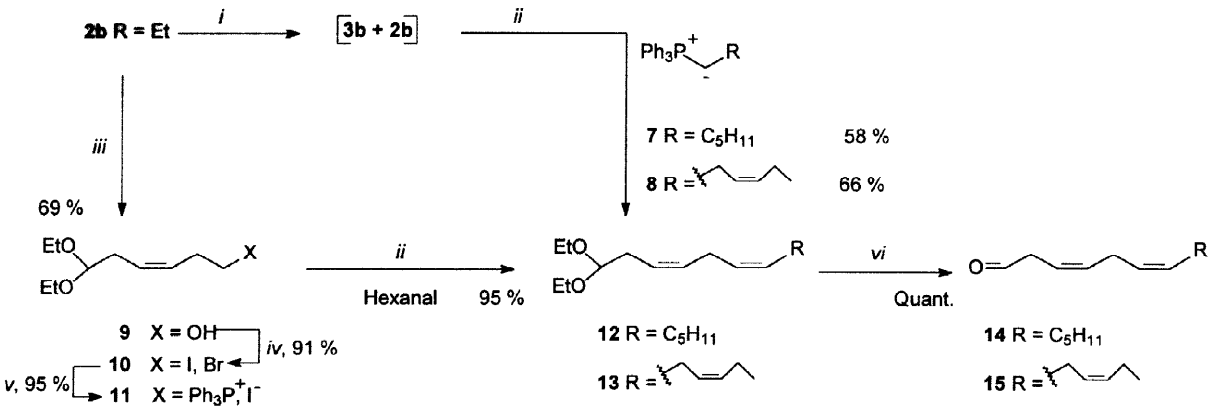
There are alternative methods for the cleavage of acetals.[8,9,10,11,12]

Ferric chloride adsorbed on silica gel[11] has been shown to hydrolyse the very stable cyclic dioxane or dioxolane acetals. In our case best results for the monohydrolysis of *bis*-acetal **2b** were obtained under very mild conditions: in acetone at 40°C only using 0.2% of $FeCl_3$ and 5 equivalents of H_2O. The reaction is completed in 30 to 50 minutes and a very easy and rapid work up leads to a 95% yield of a 1/2.3 mixture of **2b** and **3b** (66% yield) ready to be used for the next step without further purification (scheme 2).

This new C6 aldehyde-acetal **3b** reacted with ylids **7** and **8** at low temperature giving 1,4-diene **12** or 1,4,7-triene **13** in yields, which are comparable or better than in the previous method.[3]

The synthetic potential of aldehyde-acetal **3b** has been increased with its transformation into the corresponding phosphonium salt. Mono-hydrolysis of **2b** followed by *in situ* reduction with $NaBH_4$ in ethanol led after chromatography to the corresponding alcohol-acetal **9** in 69% yield from *bis*-acetal **2b**. Halogenation with Ph_3P/CBr_4 or PH_3PI_2[13] gave respectively bromide- or iodide-acetals **10** (X = Br, I) in good yields. Phosphorylation of the bromide derivative **10** (X = Br) was a low yield reaction.[14] With the iodide, however, it took place in 95% yield. The reaction time was shorter, and the presence of K_2CO_3 in the reaction mixture

prevents any acid-catalysed transformations (elimination of **ethanol, hydrolysis, addition-elimination on the double bond, ...). Finally,** Wittig reaction with hexanal under the **conditions of *cis*-olefination,[15] gave the pure 1,4-dienic diethylacetal 12 in** 95% yield.



Scheme 2

i: $FeCl_3$ 0.2%, acetone, 40 °C; *ii*: $NaN(SiMe_3)_2$, THF, -80 °C; *iii*: $FeCl_3$ 0.2%, acetone, 40 °C, then, $NaBH_4$, EtOH, 0 °C; *iv*: Ph_3PI_2, pyridine, CH_2Cl_2, 0 °C; *v*: Ph_3P, CH_3CN, K_2CO_3, reflux; *vi*: $FeCl_3$ 5%, acetone, 40°C.

Acetals **12** and **13** have been hydrolysed into their corresponding aldehydes **14** and **15**. The cleavage of the mono acetals needed higher concentration of $FeCl_3$ (5% instead of 0.2%). However, these reaction conditions are very mild compared to those described in the literature for the same substrates.[16] Pure aldehydes were obtained quantitatively, and there was no isomerisation of the double bonds.

The new preparation of (*Z*)-3-hexene *bis*-diethyl acetal **2b** is atom economic, very efficient on grams scale and easy to handle from cheap starting materials. The very mild hydrolysis with ferric chloride allowed us to get monoaldehyde **3b** which has been involved in Wittig olefination either as aldehyde compound **3b** or after transformation into a phosphonium salt **11**. Additional studies on various C6 bifunctionalized 3-hexene derivatives are under investigation.

Experimental

General Methods. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200 spectrometer respectively at 200.13 MHz and 50.32 MHz, in $CDCl_3$ solutions. Chemical shifts are given in ppm relative to the solvent (7.24 ppm ^1H; 77.1 ppm, ^{13}C). Coupling constant are given in Hz. IR spectra were recorded on a Perkin-Elmer Model 1600 (FT) spectrophotometer (neat). Wittig olefinations were carried out under a positive argon atmosphere. THF was distilled over benzophenone/sodium. CH_2Cl_2, EtOH were from technical grade and used without further purification. All reactions were monitored by TLC carried out on E. Merck 60F-254 silica gel plates. Microanalyses were performed with a CHN auto-analyzer Technicon.

Materials: Chemicals were purchased from Aldrich Chemical (MCPBA), Acros (1,4-cyclohexadiene and periodic acid).

***(E)*-cyclohex-4-ene-1,2-diol (5).** To a solution of 1,4-cyclohexadiene (10 mL, 105 mmol) in CH_2Cl_2 (10 mL) at –5°C, was slowly added a solution of MCPBA (70% in water, 27.1 g) in CH_2Cl_2 (200 mL). Then, the reaction mixture was stirred for 20 h at rt. A 2.5 M solution of Na_2CO_3 (105 mL) was added at 0°C to the reaction mixture and stirred for 0.25 h. After extraction with CH_2Cl_2 (3 x 100 mL) and washing with water (50 mL) and brine (2 x 50 mL), the solvent was slowly distilled. Near completion of the distillation, a 0.2 M solution of Na_2CO_3 (105 mL) was added and the temperature was raised until 92-94°C and maintained with stirring for 48 h. After cooling to rt and addition of 2N HCl solution until pH 4-5, H_2O was removed under vacuum. The crude solid was partially dissolved in MeOH (60 mL) at 40°C and silica gel (230-400 mesh, 15 g) was added to this

mixture, then dried under vacuum. The resulting light powder was poured onto the top of a silica gel column prepared with diethyl ether/pentane: 1/1. Elution with a gradient of solvent diethyl ether/pentane:1/1 to diethyl ether/MeOH 2/1, allowed to obtain pure diol **4** which was crystallised from anhydrous benzene, 8.65 g (72%).

R_f: 0.15 (diethyl ether). ^1H NMR: δ = 5.51 (2H, br s), 3.67-3.43 (2H, m), 2.47-2.27 (2H, m), 2.14-1.75 (2H, m). ^{13}C NMR: δ = 124.60 (2CH), 72.17 (2CH), 33.5 ($2CH_2$). IR: 3421, 3054, 1651, 1420, 1271, 1050, 895 cm^{-1}. Anal. calcd. for $C_6H_{10}O_2$: C, 63.14; H, 8.83; found: C, 63.19; H, 8.88.

(*Z*)-1,1,6,6-tetraethoxyhex-3-ene- (2b). To a solution of diol **5** (8.33 g, 73 mmol, 1 eq.) in EtOH (290 mL) at –10°C, was poured solid HIO_4-H_2O (18.34 g, 80 mmol, 1.1 eq.). The mixture was stirred for 0.5 h at –10°C, then diethyl ether/pentane: 1/1 (2 volumes) and water (0.25 volume) were added. After separation, the aqueous layer was extracted twice with diethyl ether/pentane: 1/1 (100 mL). Organic phases were combined, washed with 1/2 brine (50 mL) and 1M $Na_2S_2O_3$ aq. solution (50 mL) and brine (50 mL), dried over $MgSO_4$ and concentrated under vacuum. The crude material was dissolved in pentane (350 mL), then triethylorthoformate (21 mL) and CSA (20 mg) were added. The completion of the acetalization was checked by TLC (about 1 h). Solid KOH (0.25 g in pellets), H_2O (50 mL) were added. After decantation, the organic phase was washed with water (50 mL) and brine (50 mL). Concentration and chromatography on silica gel furnished the pure colourless *bis*-acetal **2b** (17.4 g, 92%). R_f = 0.55 (diethyl ether/pentane: 1/1).

^1H NMR: δ = 5.51-5.46 (2H, br t, *J* = 4.4 Hz), 4.46 (2H, t, *J* = 5.8 Hz), 3.71-3.37 (8H, m), 2.37, (4H, br t, *J* = 5.5 Hz), 1.16 (12H, t, *J* = 7.0 Hz). ^{13}C NMR: δ = 126.32 (2CH), 102.45 (2CH), 61.24 ($4CH_2$), 32.31 ($2CH_2$) 15.30 ($4CH_3$). IR: 3023, 2900, 1653, 1444, 1260, 1216 cm^{-1}. Anal. calcd. for $C_{14}H_{28}O_4$: C, 64.58; H, 10.84; found: C, 64.55; H, 10.89.

(*Z*)-6,6-diethoxyhex-3-en-1-al (3b): To a 0.2 M freshly distilled acetone solution (13.5 mL) of *bis*-acetal **2b** (0.702 g, 2.7 mmol) was added at rt a 0.02M aq. solution of $FeCl_3$ (0.27 mL, 5.4 10^{-3} mmol). The mixture was stirred at 40°C and the reaction was checked by TLC. When the spot of monoaldehyde **3b** became darker than the *bis*-acetal one (30 to 50 min), the reaction mixture was cooled to –20°C and diluted with 3 volumes of petroleum ether. Filtration at –20°C of this mixture over a pad of silica gel (∅ = 2.5 cm, H = 3 cm) and concentration under vacuum gave a colourless liquid (0.515 g, **3b/2b**: 2.3/1) which was directly used in a next step. R_f **3b** = 0.46 (diethyl ether/pentane: 1/1).

^1H NMR: δ = 9.64 (1H, t, *J* = 1.7 Hz), 5.85-5.51 (2H, m), 4.45 (1H, t, *J* = 5.6 Hz), 3.69-3.35 (4H, m), 3.18 (2H, br d, *J* = 1.0 Hz), 2.39-2.33 (2H, br t, *J* = 5.8 Hz), 1.16 (6H, t, *J* = 7.0 Hz). ^{13}C NMR: δ = 199.42 (1CH), 129.13 (1CH), 126.21 (1CH), 102.07 ($1CH_2$), 61.57 ($2CH_2$), 42.59 ($1CH_2$), 32.68 ($1CH_2$), 15.45 ($2CH_3$). IR: 3027, 2726, 1726, 1653, 1120, 1062, 734 cm^{-1}.

(*Z*)-6-Hydroxy-hex-3-en-1-al diethylacetal (9): *Bis*-diethylacetal **2b** (3.9 g, 15 mmol) was selectively hydrolysed as previously described giving a crude 2.5/1 mixture of **6b/2b** which was diluted with EtOH (35 mL) and added at –15°C to a solution of $NaBH_4$ (0.57 g, 15 mmol) in ethanol (35 mL). The mixture was then stirred at rt for 0.25 h. Excess $NaBH_4$ was neutralised with 2N HCl at 0°C. Addition of silica gel (4 g) to the reaction mixture and concentration under vacuum at 35°C gave a pale yellow powder. The supported substrate was introduced onto a top of pre-coated pad of silica gel and eluted with diethyl ether/pentane: 1/4 to diethyl ether. The *bis*-diethylacetal **2b** (1.124 g) and the alcohol-acetal **9** (1.387 g) were recovered as pure colourless compounds. The yield based on recovered starting material was 69%. R_f = 0.24 (diethyl ether/pentane : 1/1).

^1H NMR δ = 5.58-5.38 (2H, m), 4.45 (1H, t, *J* = 5.5 Hz), 3.68-3.37 (4H, m), 2.40-2.34 (2H, br t, *J* = 5.5), 2.31-2.22 (2H, br q, *J* = 6.2 Hz), 1.14 (6H, t, *J* = 7.0 Hz). ^{13}C NMR: δ = 128.08 (1CH), 126.28 (1CH), 102.18 (1CH), 61.53 ($1CH_2$), 61.35 ($2CH_2$), 31.97 ($1CH_2$), 30.69 ($1CH_2$), 14.99 ($2CH_3$). IR: 3420, 2879, 1653, 1444, 732 cm^{-1}. Anal. calcd. for $C_{10}H_{20}O_3$: C, 63.80; H, 10.71; found: C, 63.78; H, 10.69.

(*Z*)-6-Bromo-hex-3-en-1-al diethylacetal (10, X = Br): To a mixture of alcohol **9** (0.55 mg, 2.93 mmol), Et_3N (0.525 mL, 3.81 mmol) and CBr_4 (1.27 g, 3.81 mmol) in CH_2Cl_2 (3 mL) was added dropwise a solution of Ph_3P (1 g, 3.81 mmol) in CH_2Cl_2 (3 mL). After stirring for 4 h at rt, addition to diethyl ether/pentane 1/1 (50

mL), filtration over a pad of silica gel, concentration and flash chromatography (diethyl ether/pentane 1/10) gave a mixture of bromide **10** and bromoform. Elimination of the later under vacuum at 40°C gave the pure bromide as a colourless oil (0.7 g, 2.79 mmol, 95%). R_f = 0.71 (diethyl ether/pentane1/1).

^{1}H NMR: δ = 5.60-5.39 (2H, m), 4.46 (1H, t, *J* = 5.8 Hz), 3.69-3.38 (4H, m), 3.34 (H, t, *J* = 7.0 Hz), 2.64-2.54 (2H, br q, *J* = 6.6 Hz), 2.38-2.32 (2H, br t, *J* = 7.0 Hz), 1.16 (6H, t, *J* = 7.2 Hz). ^{13}C NMR: δ = 128.43 (1CH), 127.09 (1CH), 102.34 (1CH), 61.54 ($3CH_2$), 32.40 ($1CH_2$), 31.03 ($1CH_2$), 15.35 ($2CH_3$). IR: 2974, 1653, 1442, 1371, 1342, 1123, 1061, 733 cm^{-1}.

(*Z*)-6-Iodo-hex-3-en-1-al diethylacetal (10, X = I): To a solution of iodine (0.895 g, 3.53 mmol) in CH_2Cl_2 (9 mL) was added at –15°C a solution of Ph_3P (0.985 g, 3.76 mmol) in CH_2Cl_2 (9 mL). The yellow solution of Ph_3PI_2 was stirred for 0.25 h and a mixture of alcohol **9** (0.442 g, 2.35 mmol) and pyridine (0.54 mL, 7.05 mmol) in CH_2Cl_2 was added dropwise. The mixture was allowed to warm up to rt and stirred for 24 h. Then it was added to 70 mL of diethyl ether/pentane: 1/2. Filtration over silica gel, concentration and flash chromatography (diethyl ether/pentane : 1/100 to 1/4) gave a colourless liquid (0.638 g, 2.14 mmol, 91%). R_f = 0.70 (diethyl ether/pentane: 1/1).

^{1}H NMR: δ = 5.60-5.35 (2H, m), 4.46 (1H, t, *J* = 5.6 Hz), 3.70-3.39 (4H, m), 3.15-3.08 (2H, br t, *J* = 7.2 Hz), 2.66-2.56 (2H, br q, *J* = 7.0 Hz), 2.37-2.31 (2H, br t, *J* = 6.2 Hz), 1.17 (6H, t, *J* = 7.0 Hz). ^{13}C NMR: δ = 130.33 (1CH), 126.59 (1CH), 102.29 (1CH), 61.51 ($3CH_2$), 32.40 ($1CH_2$), 31.68 ($1CH_2$), 15.35 ($2CH_3$). IR: 2971, 1652, 1442, 1370, 1340, 1122, 1060, 734. Anal. calcd. for $C_{10}H_{19}IO_2$: C, 40.28; H, 6.42; found: C, 40.25; H, 6.43.

(*Z*)-6,6-Diethoxy-hex-3-enyltriphenylphophonium iodide (11): A mixture of iodide **10** (0.961 g, 3.23 mmol), Ph_3P (1.52 g, 5.81 mmol) and K_2CO_3 (0.89 g, 6.45 mmol) in CH_3CN (15 mL) was refluxed for 4 h. After concentration, the crude material was chromatographied (diethyl ether/pentane : 1/1 to diethyl ether, CH_2Cl_2/MeOH : 1/0 to 10/1) giving the white crystalline phosphonium salt **11** (1.59 g, 3.06 mmol, 95%). R_f = 0.42 (CH_2Cl_2/MeOH: 10/1).

^{1}H NMR: δ = 7.77-7.62 (15H, M), 5.73-5.32 (2H, m), 4.33 (1H, t, *J* = 5.5 Hz), 3.64-3.28 (6H, m), 2.43-2.27 (2H, M), 2.18-2.06 (2H, br t, *J* = 6.3 Hz), 1.03 (6H, t, *J* = 7.0 Hz). ^{13}C NMR: δ = 134.84 (3CH, d, *J* = 3.0 Hz), 133.14 (6CH, d, *J* = 10.4 Hz), 131.47 (1CH, d, *J* = 10.4 Hz), 130.89 (6CH, d, *J* = 12.7 Hz), 127.95 (1CH, d, *J* = 14.9 Hz), 117.26 (3C, d, *J* = 85.6 Hz), 101.74 (1CH), 61.62 ($2CH_2$), 32.17 ($1CH_2$), 22.66 ($1CH_2$, d, *J* = 49.1 Hz), 19.96 ($1CH_2$, d, *J* = 3.7 Hz), 14.85 ($2CH_3$). Anal. calcd. for $C_{28}H_{34}IO_2P$: C, 60.01; H, 6.11; found: C, 59.95; H, 6.02.

(*Z,Z*)-Dodeca-3,6-dien-1-al diethylacetal (12). *Method from 3b*: To a suspension of hexyltriphenylphosphonium bromide (1.95 g, 4.57 mmol) in THF was added $NaN(SiMe_3)_2$ (1M/THF, 4.2 mL). The orange suspension was stirred for 2 h at rt. During this time, *bis*-acetal **2b** (0.78 g, 3 mmol) underwent the selective hydrolysis described above. Then, the ylid solution was cooled at –90°C and the resulting aldehyde **3b**, dissolved in THF (1.5 mL), was added. After classical work-up, flash chromatography (diethyl ether/pentane:1/100 to 1/1) gave **2b** (0.31 g, 1.2 mmol) and 1,4-diene **12** (0.364 g, 1.43 mmol,79% based on recovered material).

Method from 11: Phosphonium salt **11** (0.392 g, 0.7 mmol) was first dried thrice by azeotropic distillation of toluene under vacuum. To a solution of **11** in THF (12 mL) at -10°C was added a 0.6M THF solution of $NaN(SiMe_3)_2$ (1.17 mL, 0.7 mmol). The red solution of phosphorane was stirred for 2 h at rt, cooled to –90°C and hexanal (0.084 mL, 0.7 mmol) was added. After work-up, flash chromatography led to pure 1,4-diene **12** (0.169 g, 95%). R_f = 0.67 (diethyl ether/pentane: 1/4).

^{1}H NMR: δ = 5.51-5.22 (4H, m), 4.47 (1H, t, *J* = 5.8 Hz), 3.70-3.39 (4H, m), 2.79-2.73 (2H, br t, *J* = 5.7 Hz), 2.41-2.35 (2H, br t, *J* = 5.5 Hz), 2.05-1.96 (2H, br q, *J* = 6.5 Hz), 1.26 (6H, br s), 1.17 (6H, t, *J* = 7.2 Hz), 0.85 (3H, t, *J* = 6.7 Hz). ^{13}C NMR: δ = 130.55 (1CH), 130.52 (1CH), 127.51 (1CH), 124.06 (1CH), 102.56 (1CH), 61.25 ($2CH_2$), 32.12 ($1CH_2$), 31.56 ($1CH_2$), 29.37 ($1CH_2$), 27.27 ($1CH_2$), 25.91 ($1CH_2$), 22.62 ($1CH_2$), 15.33 ($2CH_3$), 14.11 ($1CH_3$). IR: 3018, 2927, 1652, 1456,1370, 1342, 1123, 1062 cm^{-1}. Anal. calcd. for $C_{16}H_{30}O_2$: C,

75.54; H, 11.89; found: C, 75.51; H, 11.86.

(*Z,Z,Z*)-Dodeca-3,6,9-trien-1-al diethylacetal (13): to a suspension of phosphonium salt **8**[17] (0.425 g, 4.86 mmol) in THF (48 mL) was added, at –10°C, 1M THF solution of $NaN(SiMe_3)_2$ (4.61 mL). The orange suspension was stirred for 2 h at rt. During this time, the *bis*-acetal **2b** (0.702 g, 2.7 mmol) underwent the selective hydrolysis as described above. Then, the ylid solution was cooled at –90°C and the resulting aldehyde **3b** (0.515 g, **3b/2b**: 2.3/1) diluted in THF (2 mL) was added. Classical work-up and flash chromatography (silica gel, diethyl ether/pentane: 1/100 to 1/2) gave starting *bis*-acetal **2b** (0.13 g, 0.5 mmol) and pure 1,4,7-triene **13** (0.37 g, 1.46 mmol, 66% based on recovered material). R_f = 0.65 (diethyl ether/pentane: 1/4).

^{1}H NMR: δ = 5.47-5.25 (6H, m), 4.47 (1H, t, *J* = 5.8 Hz), 3.71-3.38 (4H, m), 2.82-2.74 (4H, br q, *J* = 5.7 Hz), 2.41-2.36 (br t, *J* = 5.7 Hz), 2.11-1.96 (2H, br quint, *J* = 7.2 Hz), 1.17 (6H, t, *J* = 7.0 Hz), 0.94 (3H, t, *J* = 7.4 Hz). ^{13}C NMR: δ = 132.06 (1CH), 130.26 (1CH), 128.63 (1CH), 127.83 (1CH), 127.06 (1CH), 124.28 (1CH), 102.54 (1CH), 61.30 ($2CH_2$), 32.14 ($1CH_2$), 25.89 ($1CH_2$), 25.60 ($1CH_2$), 20.60 ($1CH_2$), 15.36 ($2CH_3$), 14.30 ($1CH_3$). IR: 3022, 1680, 1653, 1465, 1320, 1184, 1062 cm^{-1}. Anal. calcd. for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18; found: C, 76.10; H, 11.13.

(*Z,Z,Z*)-Dodeca-3,6,9-trien-1-al (15):): To a 0.2 M freshly distilled acetone solution (4.6 mL) of acetal **13** (0.23 g, 0.91 mmol) was added at rt H_2O (0.082 mL, 4.56 mmol) and a 0.1M solution of $FeCl_3$ in acetone (0.456 mL, 5.10^{-2} mmol). The mixture was stirred at 40°C and the reaction was monitored by TLC until completion (about 15'). Then, the mixture was cooled to –20°C and diluted with 3 volumes of petroleum ether. Filtration at –20°C of this mixture over a pad of silica gel (∅ = 1.5 cm, H = 2 cm) and concentration gave the pure aldehyde **15** (0.158 g, 0.88 mmol). Spectroscopic data are identical to those previously described.[4]

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