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# Syntheses of Three New Lithio Hexavinylogation Reagents

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**Abstract :** Syntheses of new lithio hexavinylogation reagents are described starting either from ω-bromo polyenacetal, ω-bromo polyenol ether or ω-bromo non conjugated aldehyde. The reactivity of the lithio reagents has been tested by condensation with benzaldehyde; the resulting hexaenal has been obtained in a one or two steps procedure.


*Keywords*: polyenes; polyenals; hexavinylogation; lithium and compounds.

## INTRODUCTION

The presence of conjugated linear polyenic chains in various natural products prompted us to developp an efficient and very short strategy to introduce the polyunsaturated groups. Polyenals are ideals precursors for the synthesis of polyenes.

In preceding papers, we have described the synthesis of di,[1,2] tri,[2-6] tetra[4,6] and pentaenals[6] using new polyvinylogation reagents. According to a one[1-6] or two steps[3,4] procedure the condensation of ω-lithio polyenol ethers,[1,3-6] ω-lithio polyenacetals[3,4] and phosphonates[2] with enolizable carbonyl compounds like ketones as well as aldehydes aliphatic or aromatic has led to the corresponding polyenals.

Our interest in this field led us to investigate a short synthesis of new hexavinylogation reagents **1a-c**. This challenge has involved different strategies to obtain an efficient synthesis. In this work, we report successively

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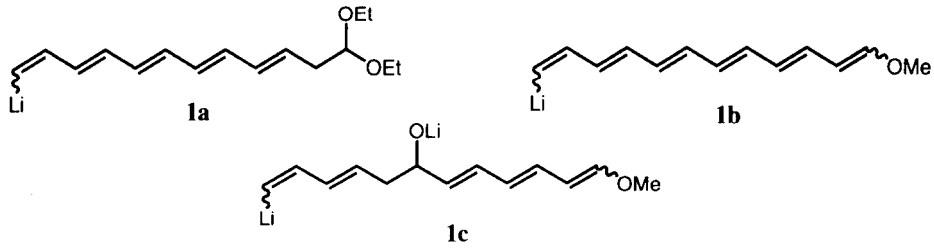
the preparation of an ω-lithio hexaenacetal **1a**, an ω-lithio hexaenol ether **1b** and an ω-lithio polyenol **1c**.



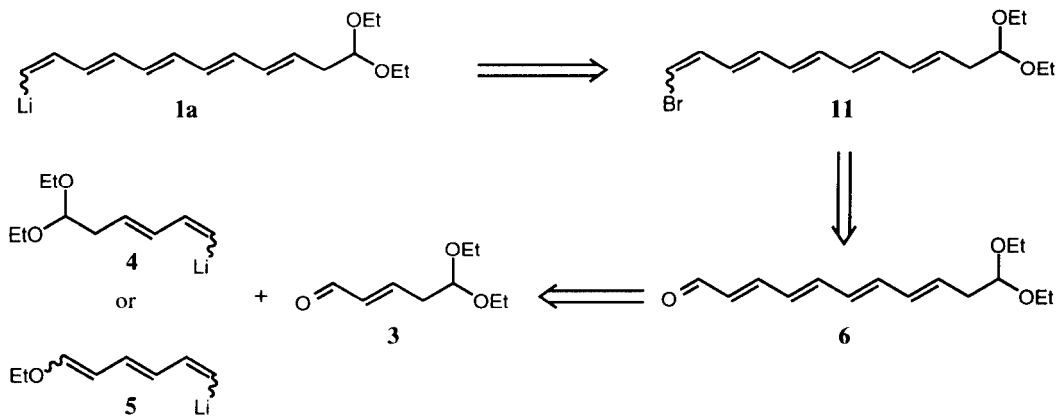

To our knowledge, in the literature only two hexavinylogation reagents have been previously described. In 1985, Masamune and *coll.*[7] have published the synthesis of a pentaenic phosphonoester prepared in five steps from the octa-2,4,6-triendial.[8] Then, in 1998, Lipshutz *et al.*[9] have described the synthesis of an aluminium derivative, with an hexavinyl conjugated group, *via* a bromo trienyne, intermediate, itself prepared from the 5-bromopentadienal **2** previously described by us.[10,11]

## RESULTS AND DISCUSSION

In a first time we have synthesized the 1,1-diethoxy-12-lithiododeca-3,5,7,9,11-pentaene **1a** from the ene oxo acetal[3,4] **3** and lithio acetal[3,4] **4** or lithio enol ether[3,4] **5** as starting materials as shown in the following retrosynthetic scheme (Scheme 1). The oxoacetal **6**, with a conjugated linear polyenic framework, is an ideal intermediate for this synthesis.

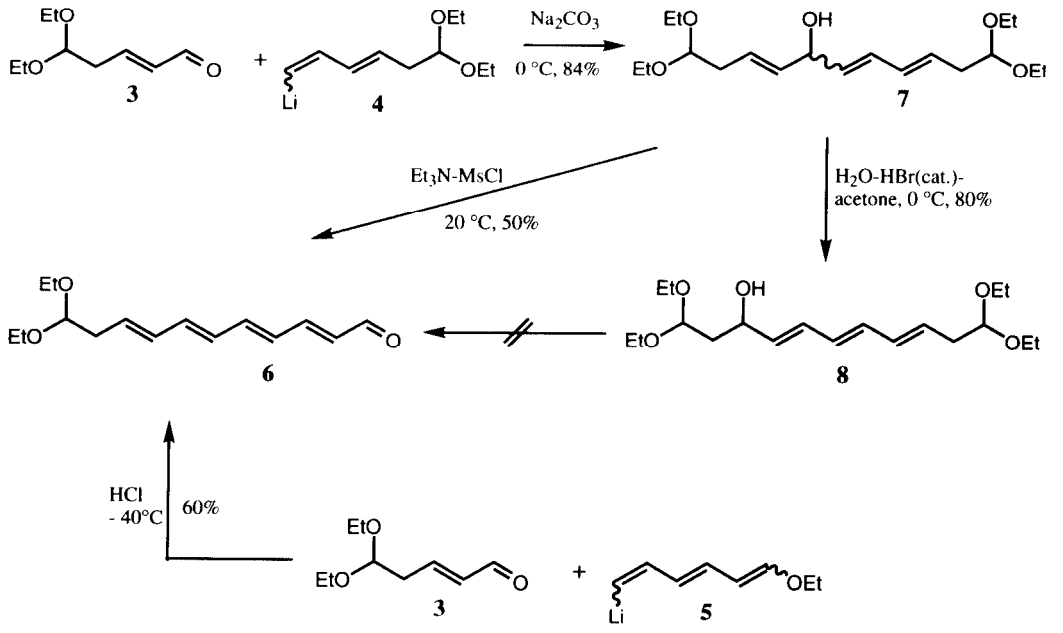
The lithio acetal **4** and lithio enol ether **5** have been prepared by a bromine-lithium exchange reaction, as previously described by us, respectively from ω-bromo dienol acetal[3,4] and ω-bromo trienol ether.[3,4]

Scheme 1



The reaction done with the lithio acetal **4**[3,4] (Scheme 2) afforded after basic hydrolysis the hydroxy diacetal **7**. By treatment of **7** with mesyle chloride, we have realized, in a one pot procedure, the deshydratation[12] and the hydrolysis of only one acetal group, leading to the oxo acetal **6** with 50% yield. This process has avoided a simultaneous hydrolysis of the two acetal groups. To optimise this result, the hydroxy diacetal **7** has been treated by bromhydric acid (in catalytic amount) in acetone at 0 °C. This reaction shows an interesting and original allylic transposition of the hydroxy group. Indeed, in these conditions we have isolated a new hydroxy diacetal **8**, stabilized by a more conjugated polyenic system. Unfortunately, this compound **8** of transposition doesn't lead to the oxo acetal **6** under usual hydrolysis conditions.

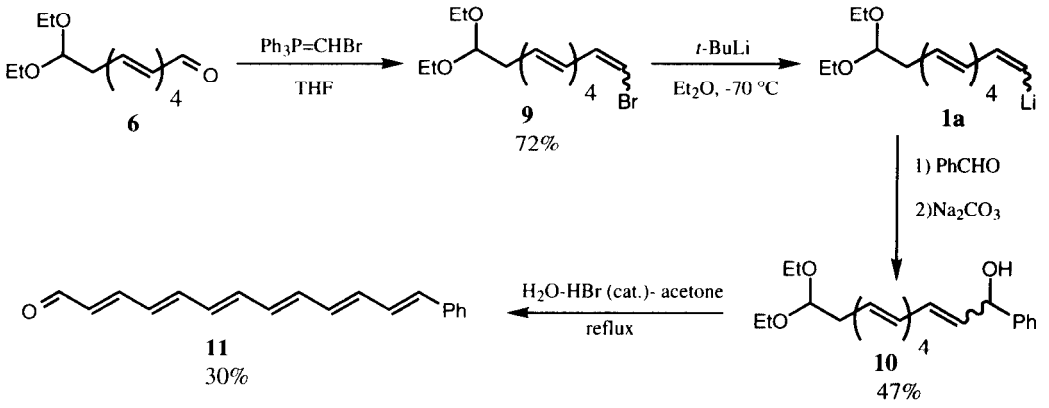
Scheme 2




The second synthesis of the oxo acetal **6** has been performed in one pot by condensation of the lithio enol ether **5** with the oxo acetal **3**, followed by acid hydrolysis (Scheme 2). This last synthesis constitutes the most efficient access to **6** which is obtained in 60% yield as a single product.

The hexavinylogation reagent **1a** has been prepared *via* a bromine-lithium exchange reaction using *t*-butyllithium (*t*-BuLi) in dry diethyl ether ($Et_2O$) at -70 °C on the ω-bromo pentaenic acetal **9**, itself obtained from the oxo acetal **6** using to a Wittig reaction[13] (Scheme 3).

Scheme 3




The reactivity of this new hexavinylogation reagent **1a** has been tested by condensation with benzaldehyde. This reaction leads to the corresponding hydroxy acetal intermediate **10** with 47% yield. Subsequent acidic hydrolysis afforded the expected hexaenal **11** with 30% yield.

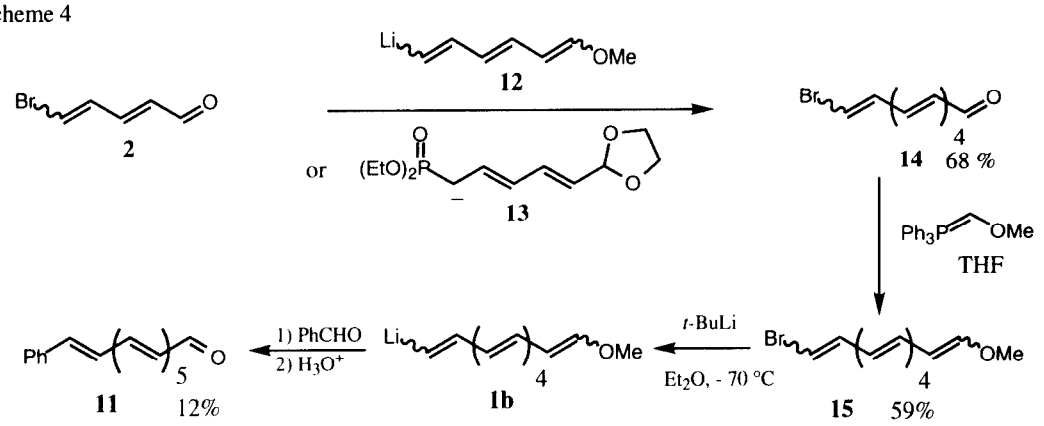
The structure and the stereochemistry of the different compounds **6-11** have been determined by high field NMR spectroscopy (400 MHz). The oxo acetal **6** and the hexaenal **11** is a single stereoisomer with an all *trans*-configuration. This is also the case of the hydroxy diacetal **8**, while in the case of the hydroxy diacetal **7**, the ene bromo acetal **9** and the ene hydroxy acetal **10** a mixture of stereoisomers was obtained (**7** : 6Z / 6E = 80 / 20 ; **9** : 11Z / 11E : 70 / 30 ; **10** : 11Z / 11E : 80 / 20).

Thus, the hexaenal **11** has been obtained in two steps from the ene bromo acetal **9** with an overall yield of 14%. This poor result is due to the poor solubility of the ene bromo acetal **9** in $Et_2O$ and by the difficult hydrolysis of the acetal group of **10** in the subsequent reaction.

To improve the access to an efficient hexavinylogation reagent, we have attempted to prepare an ω-lithio polyenol ether **1b** ; in this case, the hydrolysis step would be easy.

The ω-bromo undecapentaenal[6] **14** has been obtained by condensation of the 5-bromopentadienal **2** with the ω-lithio trienol ether[6] **12** or with the phosphonate acetal[2] **13** followed by acidic hydrolysis, with the same yield of 68% for each of the two different routes (Scheme 4).

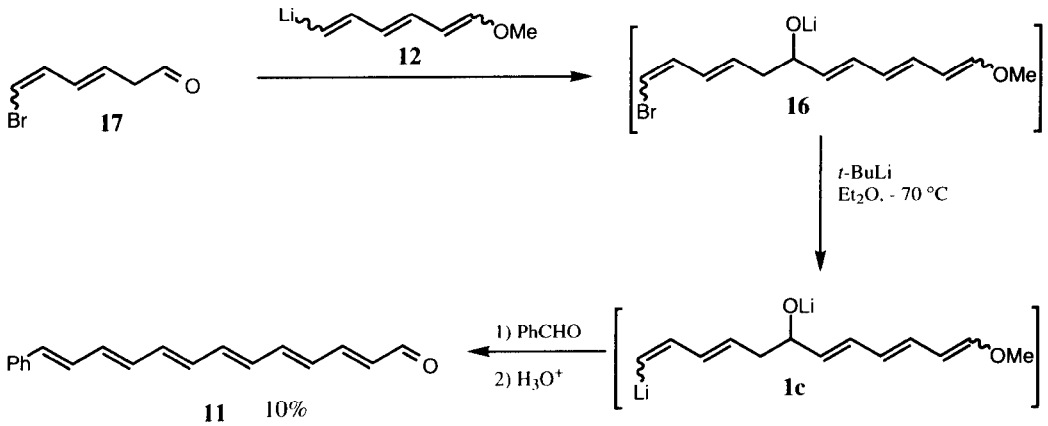
Scheme 4




Reaction of the ω-bromo pentaenal **14** with (methoxymethylene)triphenylphosphorane prepared *in situ* from commercial (methoxymethyl)triphenylphosphonium chloride and potassium tert-butoxide leads to the ω-bromo hexaenol ether **15** (59% yield) after flash chromatography. The bromo enol ether **15** was then transformed into the hexavinylogation reagent **1b** *via* bromine-lithium exchange and condensation at -70 °C in $Et_2O$ with benzaldehyde affords the hexaenal **11** after acid hydrolysis with 12% yield. This second procedure seems to be limited because of the very weak solubility of the ω-bromo enol ether **15** ; therefore the exchange reaction couldn't be performed in good conditions.

So, we decided to built *in situ* the twelve carbon skeleton of a third hexavinylogation reagent, the ω-lithio polyenol ether lithio alkoxy **1c**, from two six carbon starting material having a great solubility in $Et_2O$. The intermediate ω-bromo polyenol ether lithio alkoxy **16** has been formed by condensation of the ω-bromo non conjugated aldehyde **17** with the ω-lithio trienol ether[6] **12** (Scheme 5).

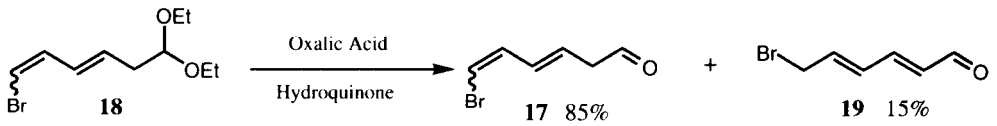
Scheme 5




The intermediate **16** has been submitted, without isolation to bromine-lithium exchange by action of *t*-BuLi in $Et_2O$ at -70 °C and the hexavinylogation reagent **1c** formed *in situ* has been treated by benzaldehyde and an acidic

hydrolysis has led to the hexaenal **11** in one step from the ω-bromo non conjugated aldehyde **17** with an overall yield of 10% after recristallization.

Scheme 6




The starting material **17** has been obtained by hydrolysis of the ω-bromo acetal[4] **18** using oxalic acid with catalytic amount of hydroquinone, as described by M. Winter.[14] In fact, the reaction has led to a mixture of non conjugated aldehyde **17** (85%) and of conjugated aldehyde **19** (15%) with an overall yield of 85% (Scheme 6). **17** was very difficult to purify because of its great instability; this mixture has been used for the further step, leading to **16**.

## CONCLUSION

We have synthesized three new hexavinylogation reagents **1a-c** and we have tested their reactivity by condensation with benzaldehyde. Unfortunately, the resulting hexaenal **11** has been obtained in poor yield and further studies to improve these synthetic routes are in progress.

## EXPERIMENTAL SECTION

**IR** spectra were recorded on a Perkin-Elmer 16 PC FT-IR infrared spectrometer as pure films. **$^1$H NMR** spectra were obtained on a Bruker AC spectrometer operating at 200 MHz or at 400 MHz for proton and at 50 MHz or at 100 MHz for carbon. No TMS was added; shifts were referenced to the solvent line ($CDCl_3$ or $C_6D_6$). δ values are given in ppm and J in Hz. Mass spectra were recorded on JEOL JMS AX 500 mass spectrometer. UV spectra were recorded on a Kontron Uvikon 940. Flash chromatography was performed with Merck Kieselgel 60 (230-400 mesh ASTM) support with light petroleum (boiling point<60 °C) and diethyl ether ($Et_2O$) as eluent. All reagents were of commercial quality or purified before use. Anhydrous tetrahydrofuran (THF) and $Et_2O$ were distilled under argon atmosphere from purple solutions of sodium/benzophenone. *t*-Butyllithium (*t*-BuLi) solutions were titrated before use.[15] All reactions were carried out under dry argon. Microanalyses were performed by INSA laboratories, Rouen.

- **1,1-diethoxy-11,11-diethoxy-5-hydroxyundeca-3,6,8-triene 7.**

To a solution of 6,6-diethoxy-1-bromohexa-3,5-diene[3,4] (0.70 g, 2.8 mmol) in anhydrous $Et_2O$ (10 ml) at - 70 °C was added a solution of *t*-BuLi (3 ml of a 1.7 M solution in pentane; 5.1 mmol). After 90 min at - 70 °C a solution of 5,5-diethoxypenta-2-enal[3,4] **3** (0.38 g, 2.2 mmol) in anhydrous $Et_2O$ (2 ml) was added. The mixture was warmed to 0 °C, stirred for 2 h and hydrolysed by aq. $Na_2CO_3$ (3 ml; 5%) for 2 h. The organic layer was separated and dried ($MgSO_4$). Evaporation gave the crude product which was chromatographed over silica gel (light petroleum/$Et_2O$ : 50/50). The 1,1-diethoxy-11,11-diethoxy-5-hydroxyundeca-3,6,8-triene **7**, yellow oil (0,63 g, 84%), was obtained as a mixture of isomers 3E,6Z,8E/3E,6E,8E : 80/20.

3E,6Z,8E : **$^1$H NMR** ($CDCl_3$) (400 MHz) : δ 6.40 (dd, 1H, H8, J = 15.0; 11.2), 6.02 (dd, 1H, H7, J = 10.9; 10.9), 5.71 (td, 1H, H9, J = 14.9; 7.1), 5.64 (td, 1H, H3, J = 6.7; 12.8), 5.63 (td, 1H, H4, J = 6.8; 12.4), 5.32 (dd, 1H, H6, J = 10.4; 9.1), 5.03 (m, 1H, H5), 4.49 (t, 1H, H11, J = 6.1), 4.47 (t, 1H, H1, J = 5.8), 3.62 (m, 4H, $OCH_2$), 3.48 (m, 4H, $OCH_2$), 2.43 (dd, 2H, H10, J = 6.7; 6.7), 2.36 (dd, 2H, H2, J = 6.1; 6.1), 1.84 (s, 1H, OH), 1.18 (t, 6H, $CH_3$, J = 7.O), 1.17 (t, 6H, $CH_3$, J = 7.O).

**IR** ($cm^{-1}$): 3420; 2980; 1630; 1120. **Anal. Calcd;** for $C_{19}H_{34}O_5$ : C, 66.64 ; H, 10.01. Found : C, 66.62 ; H, 9.92.

- **(2E,4E,6E,8E)-11,11-diethoxyundeca-2,4,6,8-tetraenal 6.**

First procedure :

To a solution of hydroxy diacetal **7** (0.79 g, 2.31 mmol) in $CH_2Cl_2$ (11 ml) was added, at room temperature, $Et_3N$ (0.74g, 7.31 mmol) and then MsCl (0.3 g, 2.62 mmol) in $CH_2Cl_2$ (2 ml). The mixture was stirred for 3 h at room temperature and then treated by aq. HCl (1M, until pH 1). After 40 min the solution was neutralised by saturated aq. $NaHCO_3$ (5 ml) and the aqueous layer was extracted with $CH_2Cl_2$. After the usual treatment, the crude product was chromatographed over silica gel (light petroleum/$Et_2O$ : 50/50). The oxo acetal **6** was obtained as a yellow oil (0.28 g, 50%).

**$^1$H NMR** ($CDCl_3$) (400 MHz) : δ 9.55 (d, 1H, H1, J = 7.9), 7.13 (dd, 1H, H3, J = 15.1; 11.2), 6.68 (dd, 1H, H5, J = 14.7; 11.0), 6.47 (dd, 1H, H7, J = 15.1; 10.9), 6.43 (dd, 1H, H4, J = 10.9; 14.9), 6.26 (dd, 1H, H6, J = 14.9; 11.2), 6.22 (dd, 1H, H8, J = 10.9; 14.9), 6.13 (dd, 1H, H2, J = 15.2; 7.9), 5.87 (dt, 1H, H9, J = 15.2; 7.4), 4;52 (t, 1H, H11, J = 5.5), 3.64 (m, 2H, $OCH_2$), 3.48 (m 2H, $OCH_2$), 2.48 (dd, 2H, H10, J = 6.1; 6.1), 1.20 (t,6H, $CH_3$, J = 7.3). **$^{13}$C NMR** ($CDCl_3$) (100 MHz) : δ 193.37 (C1), 151.85 (C3), 142.71 (C5), 138.70 (C7), 133.37 (C9), 132.40 (C8), 130.62 (C2), 129.96 (C6), 129.31 (C4), 101.90 (C11), 61.22 (2 x $OCH_2$), 37.54 (C10), 15.13 (2 x $CH_3$).

**IR** ($cm^{-1}$) **:** 2980; 1680; 1590; 1120.

Second procedure :

To a solution of 6-bromo-1-ethoxyhexa-1,3,5-triene [3,4] (2.09 g, 10 mmol) in anhydrous $Et_2O$ (40 ml) at - 70 °C was added a solution of *t*-BuLi (11 ml of a 1.7 M solution in pentane; 18 mmol). After 90 min at - 70 °C, a solution of 5,5-diethoxypenta-2-enal[3,4] **3** (1.42 g, 8 mmol) in anhydrous $Et_2O$ (8 ml) was added. The mixture was warmed to 0 °C and stirred for 90 min. The solution was then cooled to - 40 °C and hydrolysed by aq. HCl (23 ml; 1.2 M) for 90 min. After return to room temperature, the mixture was stirred for 2 h. The organic layer was separated and dried ($MgSO_4$). Evaporation gave the crude product which was chromatographed over silica gel (light petroleum/$Et_2O$ : 50/50). The 11,11-diethoxyundeca -2,4,6,8-tetraenal **6** was obtained as a yellow oil (1.2 g, 60%).

- **(4E,6E,8E)-1,1-diethoxy-11,11-diethoxy-3-hydroxyundeca-4,6,8-triene 8.**

To a solution of hydroxy diacetal **7** (0.119 g, 0.35 mmol) in acetone-water (7.5 ml; acetone/water 192 ml / 1 ml) at 0 °C was added a fresh solution of acetone-HBr (47%) (0.05 ml; acetone/HBr : 5/0.1). After 10 min the mixture was treated by saturated aq. $NaHCO_3$ (5 ml). After extraction of the aqueous layer with $Et_2O$, the organic layer was dried ($MgSO_4$). Evaporation gave the crude product which was chromatographed over silica gel (light petroleum/$Et_2O$ : 50/50). The hydroxy diacetal **8** was obtained as an orange oil (0.095 g, 80%).

**$^1$H NMR** ($CDCl_3$) (400 MHz) : δ 6.25 (dd, 1H, H8, J = 15.2; 10.2), 6.18 (dd, 1H, H6, J = 14.5; 10.2), 6.13 (dd, 1H, H5, J = 14.8; 10.2), 6.10 (dd, 1H, H7, J = 10.5; 14.9), 5.65 (m, 2H, H4, H9), 4.67 (t, 1H, H1, J = 5.5), 4.48 (t, 1H, H11, J = 6.1), 4.36 (m, 1H, H3), 3.65 (m, 4H, $OCH_2$), 3.50 (m, 4H, $OCH_2$), 3.17 (s, 1H, *OH*), 2.41 (t, 2H, H10, J = 6.7), 1.84 (t, 2H, H2, J = 5.5), 1.20 (t, 12H, $CH_3$, J = 7.3).

**IR** ($cm^{-1}$): 3470; 2980; 1650; 1600; 1120.

- **12-bromo-1,1-diethoxydodeca-3,5,7,9,11-pentaene 9.**

To a mixture of bromo methyl triphenylphosphonium bromide (3.05 g, 7.0 mmol) in THF (40 ml) at - 70°C was slowly added *t*-BuOK (0.78 g, 7.0 mmol). The mixture was stirred for 90 min to allow the formation of the ylide and the oxo acetal **6** (1.46 g, 5.8 mmol) was added as a solution in THF (8 ml). After 10 min at - 70°C, the mixture was warmed to 0 °C for 1h and then was stirred at room temperature for 2 h. After hydrolysis by water, extraction with $Et_2O$ and usual treatment, the crude product was chromatographed over silica gel (light petroleum/$Et_2O$ : 70/30). The 12-bromo-1,1-diethoxydodeca-3,5,7,9,11-pentaene **9** was obtained (1.37 g, 72 %) as a mixture of isomers 3E,5E,7E,9E,11Z / 3E,5E,7E,9E,11E : 70/30 (yellow solid, mp = 90 °C).

3E,5E,7E,9E,11Z : **$^1$H NMR** ($CDCl_3$) (400 MHz) : δ 6.64 (dd, 1H, H11, J = 9.7; 7.0), 6.51 (dd, 1H, H10, J = 7.8; 14.9), 6.44 (dd, 1H, H9, J = 14.9; 9.7), 6.34-6.13 (m, 6H), 5.73 (dt, 1H, H3, J = 15.1, 7.2), 4.50 (t, 1H, H1, J = 5.7), 3.64 (m, 2H, $OCH_2$), 3.50 (m, 2H, $OCH_2$), 2.45 (t, 2H, H2, J = 6.5), 1.20 (t, 6H, $CH_3$, J = 7.0). **$^{13}$C NMR** ($CDCl_3$) (100 MHz) : δ 136.38, 135.15, 134.24, 132.86, 132.55, 131.99, 131.16, 130.24, 127.58, 107.90, 102.17, 61.17 (2 x $OCH_2$), 37.51, 15.16 (2 x $CH_3$).

3E,5E,7E,9E,11E : **$^1$H NMR** ($CDCl_3$) (400 MHz) : δ 6.72 (dd, 1H, H11, J = 13.4; 10.9), 6.33-6.05 (m, 8H), 5.71 (dt, 1H, H3, J = 15.4, 7.2), 4.48 (t, 1H, H1, J = 5.8), 3.63 (m, 2H, $OCH_2$), 3.48 (m 2H, $OCH_2$), 2.42 (t, 2H, H2, J = 6.4), 1.18 (t, 6H, $CH_3$, J = 7.0). **$^{13}$C NMR** ($CDCl_3$) (100 MHz) : δ 137.60, 134.64, 133.94, 133.79, 132.88, 131.63, 131.17, 130.09, 129.15, 108.31, 102.19, 61.19 (2 x $OCH_2$), 37.54, 15.19 (2 x $CH_3$).

**IR** ($cm^{-1}$): 2960, 1594, 1376, 1140.

**MS (m/z)** : 326-328 ($M^{+\cdot}$, 10%); 103 (100%); 75 (60%).

- **12-bromo-1-methoxydodeca-1,3,5,7,9,11-hexene 15.**

To a solution of (methoxymethyl)triphenylphosphonium chloride (0.79 g, 2.3 mmol) in anhydrous THF (10 ml) at - 50 °C was added *t*-BuOK (0.26 g, 2.3 mmol). The mixture was stirred for 1 h and 11-bromoundeca-2,4,6,8,10-pentaenal [6] **14** (0.48 g, 2.0 mmol) was added as a solution in anhydrous THF (1 ml). The mixture was warmed to room temperature and stirred for 1 h. After treatment with aq. $NaHCO_3$ (5 ml; 5%), the aqueous layer was extracted with pentane. After the usual treatment, the crude product was chromatographed over silica gel (desactivated by triethylamine, pentane as eluent). The bromo enol ether **15** (unstable yellow solid) was obtained (0.31 g, 59%) as a mixture of four isomers observed by NMR spectroscopy.

**$^1$H NMR** ($C_6D_6$) (400 MHz) : δ 6.80-5.85 (m, 11H, H1, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12), 5.60 (2 dd, H2, H2', J = 12.5; 10.2), 5.13 (2 dd, H2'', H2''', J = 11.3; 6.1), 3.69 (s, 3H, $CH_3$), 3.68 (s, 3H, $CH_3$), 3.62 (s, 3H, $CH_3$), 3.60 (s, 3H, $CH_3$).

- **6-bromohexa-3,5-dienal 17.**

To a solution of bromo acetal **18** (0.50 g, 2.0 mmol) and hydroquinone (0.01 g, 0.1 mmol) in mixture of acetone (5 ml) and water (7 ml) heated to 45 °C under argon was added oxalic acid (0.07 g, 0.7 mmol). After 1 h at 45 °C, the mixture was cooled to room temperature and extracted with $Et_2O$ (3 x 15 ml). The organic layers were washed by saturated aq. $NaHCO_3$ (3 x 15 ml) and water (3 x 15 ml) and dried with a mixture of $MgSO_4$ and $Na_2CO_3$ ( 80 / 20). Evaporation gave the crude product, mixture of non conjugated aldehyde **17** and conjugated aldehyde **19** (85 / 15) (0.30 g, 85%).

Non conjugated aldehyde **17** : **$^1$H NMR** ($C_6D_6$) (200 MHz) : δ 9.13 (t, 1H, H1, J = 1.7), 6.80-5.20 (m, 4H, H3, H4, H5, H6), 2.60 (dd, 2H, H2, J = 1.7; 7.2).

Conjugated aldehyde **19** : **$^1$H NMR** ($C_6D_6$) (200 MHz) : δ 9.29 (d, 1H, H1, J = 7.6), 6.19 (dd, 1H, H3, J = 9.6; 15.4), 5.81 (dd, 1H, H2, J = 7.6; 15.4), 5.54-5.62 (m, 2H, H4, H5), 3.33 (d, 2H, H6, J = 6.6).

- **Hexavinylogation reagent 1a.**

- **13-phenyl-13-hydroxy-1,1-diethoxytrideca-3,5,7,9,11-pentaene 10.**

To a solution of ω-bromo pentaene acetal **9** (0.2 g, 0.61 mmol) in anhydrous $Et_2O$ (4 ml) at - 70 °C was added a solution of *t*-BuLi (0.6 ml of a 1.8 M solution in pentane: 1.10 mmol) in 10 min. After 60 min at - 5 °C, a solution of benzaldehyde (0.12 g, 1.10 mmol) in anhydrous $Et_2O$ (1 ml) was added at - 70 °C to this solution of hexavinylogation reagent **1a**. The mixture was warmed to 0 °C and stirred for 2 h. After hydrolysed by aq. $Na_2CO_3$ (1 ml; 5%), extraction with ethyl acetate and the usual treatment, the crude product was chromatographed over silica gel (light petroleum/$Et_2O$ : 70/30). The 13-phenyl-13-hydroxy-1,1-diethoxytrideca-3,5,7,9,11-pentaene **10** was obtained as a yellow oil (0.100 g, 47%).

**$^1$H NMR** ($CDCl_3$) (400 MHz) : δ 7.36-7.28 (m, 5H, H arom), 6.65 (dd, 1H, H5, J = 13.2; 11.2), [6.34-6.17 (m, 7H); 6.34 (1H, H7), 6.31 (1H, H6), 6.29 (1H, H8), 6.25 (1H, H10), 6.21 (1H, H9), 6.18 (1H, H4), 6.17 (1H, H11)], 5.72 (dt, 1H, H3, J = 15.3; 7.3), 5.69 (m, 1H, H13), 5.60 (dd, 1H, H12, J = 10.2; 13.7), 4.51 (t, 1H, H1, J = 5.6), 3.65 (m, 2H, $OCH_2$), 3.48 (m, 2H, $OCH_2$), 2.45 (t, 2H, H2, J = 5.9), 1.20 (t, 6H, $CH_3$, J = 7.2), the $^1$H attribution has been done from the 2D Cosy spectrum.

**IR** ($cm^{-1}$): 3414, 2959, 1640, 1124.

- **13-phenyltrideca-2,4,6,8,10,12-hexaenal 11.**

A solution of hydroxy acetal **10** (0.100 g, 0.28 mmol) in acetone-water (36 ml; acetone/water 192/1) was refluxed and a fresh solution of acetone-HBr (47%) (0.24 ml; acetone/HBr : 5/0.1) was added. The mixture was refluxed 30 min and then treated by aq. $Na_2CO_3$ (10 ml; 5%). After extraction of the aqueous layer with $Et_2O$, the organic layer was dried ($MgSO_4$). Evaporation gave the crude product which was washed with $Et_2O$ (2 x 20 ml). The hexaenal **11** (yellow solid, mp = 208 °C) was obtained (0.022 g, 30%).

**$^1$H NMR** ($CDCl_3$) (400 MHz) : δ 9.55 (d, 1H, H1, J = 8.0), 7.39-7.23 (m, 5H, H arom), 7.13 (dd, 1H, H3, J = 15.1; 11.3), 6.85 (dd, 1H, H12, J = 10.3; 15.4), 6.71 (dd, 1H, H5, J = 14.5; 11.3), 6.60 (d, 1H, H13, J = 15.7), [6.56-6.40 (m, 6H); 6.56 (1H, H7), 6.53 (1H, H9), 6.48 (1H, H11), 6.47 (1H, H4), 6.43 (1H, H10), 6.40 (1H, H6)], 6.36 (dd, 1H, H8, J = 14.1; 10.9), 6.14 (dd, 1H, H2, J = 15.0; 8.0), the $^1$H attribution has been done from the 2D Cosy spectrum. **$^{13}$C NMR** ($CDCl_3$) (100 MHz) : δ 193.28 (C1), 151.58 (C3), 142.57 (C5), 138.79 (C7), 137.05 (C arom), 136.58 (C9), 135.46 (C11), 133.90 (C13), 132.95 (C6), 132.45 (C2), 131.63 (C4), 130.78 (C8), 129.79 (C10), 128.82 (C arom), 128.60 (2 x C arom), 127.76 (C12), 126.42 (2 x C arom).

**IR** ($cm^{-1}$) : 3017, 1667, 1551, 1148. **MS (m/z)** : 262 ($M^{+\cdot}$, 100%); 233 (M-CHO, 10%); 115 (45%); 91 (80%); **HRMS. Calcd.** for $C_{19}H_{18}O$ : 262.1358, Found : 262.1361. **UV** : EtOH λ = 431 nm; (ε = 102450).

- **Hexavinylogation reagent 1b.**

- **13-phenyltrideca-2,4,6,8,10,12-hexaenal 11.**

To a solution of bromo hexaenol ether **15** (0.270 g, 1.0 mmol) in anhydrous $Et_2O$ (4 ml) cooled to - 70 °C, under argon, was added a solution of *t*-BuLi (1 ml of a 1.8 M solution in pentane; 1.8 mmol); the hexavinylogation reagent **1b** is formed. After 90 min at - 70 °C a solution of benzaldehyde (0.085 g, 0.8 mmol) in anhydrous $Et_2O$ (1 ml) was added to this solution of hexavinylogation reagent **1b**. The mixture was warmed to 0 °C and was stirred for 2 h before treatment at -50 °C with aq. HCl (3 ml; 1.5 M). The mixture was warmed to 10 °C and was stirred for 30 min. After return to room temperature, the organic layer was separated, washed with water and dried ($MgSO_4$). After evaporation the crude product was chromatographed over silica gel (light petroleum/$Et_2O$ : 70/30) and the hexaenal **11** was obtained (0.025 g, 12%).

- **Hexavinylogation reagent 1c.**

- **13-phenyltrideca-2,4,6,8,10,12-hexaenal 11.**

To a solution of ω-lithio enol ether **12,** prepared from the corresponding ω-bromo enol ether (0.210 g, 1.1 mmol) and a solution of *t*-BuLi (1.25 ml of a 1.6 M solution in pentane; 2.0 mmol) in anhydrous $Et_2O$ (4 ml) cooled to - 70 °C, under argon, was added a solution of non conjugated aldehyde **17** (0.200 g, 1.1 mmol) in anhydrous $Et_2O$ (1 ml). The mixture was warmed to 0 °C and was stirred for 2 h. After cooling at - 70 °C, the solution of the intermediate **16** was treated by a solution of *t*-BuLi (1.25 ml of a 1.6 M solution in pentane; 2.0 mmol). After 90 min at - 70 °C a solution of benzaldehyde (0.120 g, 1.1 mmol) in anhydrous THF (2 ml) was added to this solution of hexavinylogation reagent **1c**. The mixture was warmed to 0 °C and was stirred for 2 h and then 30 min at room temperature. After return to - 70 °C, the mixture was treated with aq. HCl (4 ml; 3 M). After return to room temperature and stirred one night, the organic layer was separated, washed with water and dried ($MgSO_4$). After evaporation the crude product was purified by recristallization in $Et_2O$ and the hexaenal **11** was obtained (0.028 g, 10%).

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