Bull Soc Chim Fr (1997) 134, 937-946

Vinyltin acetals in terpenic and nor-terpenic synthesis

Valérie Launay, Isabelle Beaudet, Jean-Paul Quintard*

Laboratoire de Synthèse Organique, UMR 6513 du CNRS, Faculté des Sciences et des Techniques, 2 rue de la Houssinière, BP 92208, 44322 Nantes cedex 3, France

(Received 5 November 1997; accepted 15 December 1997)

Summary — Vinyltin acetals obtained by stannylmetallation of homopropargyl acetals with $Bu_3SnMgMe/CuCN$ (*E* configuration) or by titanation of the corresponding alkynyltin acetals (*Z* configuration) have been proved to be efficient storable precursors for the stereoselective synthesis of terpenoids, under mild experimental conditions. Due to the presence of a nucleophilic centre (C^2_{sp}–Sn bond) and of a protected electrophilic centre, they are also useful intermediates for an iterative synthesis of retinal and nor-retinoids.

vinyltin / acetal / vinyllithium / monoterpenoid / retinal / nor-retinoid

Résumé — Synthèse de terpénoïdes et nor-terpénoïdes à l'aide de vinylétains porteurs d'une fonction acétal en position homopropargylique. Les vinylétains porteurs d'une fonction acétal, obtenus par stannylmétallation des acétals homopropargyliques avec $Bu_3SnMgMe/CuCN$ (configuration *E*) ou par titanation des alcynylétains en dérivant (configuration *Z*), constituent d'excellents précurseurs (facilement stockables) pour la synthèse de dérivés terpéniques dans des conditions expérimentales douces. Du fait de la présence d'un site nucléophile (liaison C^2_{sp}–Sn) et d'un site électrophile protégé (fonction acétal), ces vinylétains sont aussi des intermédiaires utiles pour la synthèse itérative de composés tels que le rétinal et ses homologues déméthylés en position 9 ou 13.

vinylétain / acétal / vinyllithium / monoterpénoïde / rétinal / nor-rétinoïde

Introduction

Organotin chemistry has become a useful methodology in modern organic synthesis, especially for carbon-carbon bond forming reactions [1–3]. Indeed, the mildness of the required experimental conditions as well as the high level of chemoselectivity allow the synthesis of highly functionalized products [2–7]. Among them, well known terpenoids [8] and retinoids [9] constitute interesting targets due to the involvement of these last in a wide variety of biological processes, including vision, cellular proliferation and differentiation (anticancer activity) [9–11]. Modified retinoids have been shown to be also of clinical interest and useful for bioorganic studies [12] while more simple monoterpenoids remain compounds of interest as components of flavours, fragrances and aroma or as precursors of compounds having potential pharmacological interest [13–15].

In connection with our investigations related to the regio- and stereoselective synthesis of di- and trisubstituted vinyltin acetals [16, 17], we report herein a convenient synthesis of terpenoids and nor-terpenoids using alternatively the nucleophile site (Sn–C bond) and the electrophilic site (acetal function) contained in the same molecule. The potential of the vinyltin moiety, both as precursor of vinyllithium reagent [2] and in cross coupling reactions [4], has been first used for the synthesis of several hemi- and monoterpenoids. Subsequently, the masked aldehyde function was exploited for extending the carbon chain to provide retinoids and nor-retinoids in an iterative fashion.

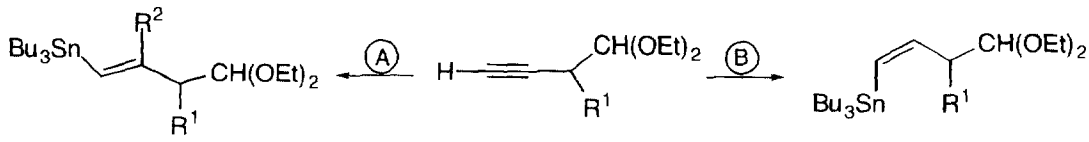
Results and discussion

Preparation of the organotin precursors

Depending on the desired configuration of the vinyltins **1a–c**, two different reactions were used for their preparation (scheme 1). The *E*-vinyltins **1a–c,*E*** were obtained by stannylmetallation of homopropargyl acetals with tributylstannylmethylmagnesium in the presence of cuprous cyanide [16, 18] while titanation of alkynyltin acetals was used to obtain the corresponding *Z*-disubstituted vinyltins **1a–b,*Z*** [17].

In both cases, the title vinyltins were obtained in acceptable to good yields (65–91%) as pure products after distillation or liquid chromatography. The preparations were performed on 20 to 100 mmol scale and the obtained vinyltins are stable and easily storable under nitrogen, at room temperature (**1a–c,*E***) or in an ice-cold freezer (**1a–b,*Z***), for several months.

* Correspondence and reprints



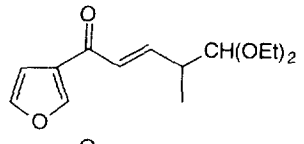
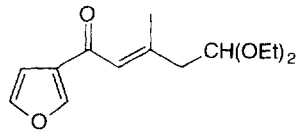
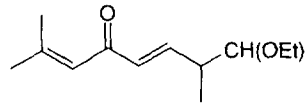
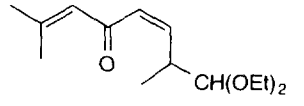
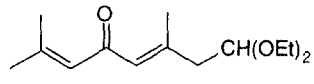
1a-E $R^1 = R^2 = H$ (65%)
1b-E $R^1 = Me$, $R^2 = H$ (75%)
1c-E $R^1 = H$, $R^2 = Me$ (91%)

1a-Z $R^1 = H$ (70%)
1b-Z $R^1 = Me$ (65%)

Experimental conditions:
A 1) $Bu_3SnMgMe$, 15% CuCN, THF, −10 °C, 15 min; 2) H_2O or MeI (3 equiv), −10 °C, 30 min.
B 1) *n*BuLi, ether, −78 °C, 1 h; 2) Bu_3SnCl, −78 to 25 °C; 3) $Ti(OiPr)_4$, ether, −78 °C; 4) iPrMgCl (2 equiv), −78 to −30 °C; 5) H_2O/NH_4Cl.

Scheme 1

Table I. Cross-coupling of vinyltin acetals **1b–c,*E*** and **1b–*Z*** with C_5 acyl chlorides.

Vinyltins +	*Acyl chlorides*	$\xrightarrow[DMF,\ 25\ °C,\ 3\ h]{PdCl_2(CH_3CN)_2}$	*Oxoacetals* **4, 5**
1b-*E*	**2**		**4b-*E*** (64%)
1c-*E*	**2**		**4c-*E*** (58%)
1b-*E*	**3**		**5b-*E*** (59%)
1b-*Z*	**3**		**5b-*Z*** (58%)
1c-*E*	**3**		**5c-*E*** (59%)

Stereoselective synthesis of terpenoids

In a first step, we have explored the potential of C_5 vinyltins **1b-*E***, **1b-*Z*** and **1c-*E*** in terpenic synthesis opposing them to appropriate C_5 partners. The synthesis of C_{10} oxoacetals **4** and **5** was achieved in about 60% isolated yields using a Stille cross-coupling of these vinyltins with C_5 acyl chlorides (3-furoyl chloride **2** and senecioyl chloride **3**). As expected in this case [19], using DMF as solvent, the reaction of the acyl chloride at the acetal function did not interfere and the initial *E* or *Z* configuration of the vinyltin acetal was maintained in the cross coupling products (table I).

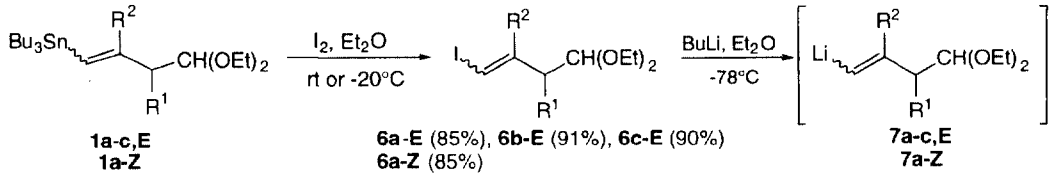
Similarly, vinyltins **1a–c,*E*** and **1a-*Z*** were converted into vinyl iodides without isomerization of the double bond, using a slight excess of iodine at 20 °C for **1a–c,*E*** or at −20 °C for **1a-*Z*** (scheme 2).

These vinyl iodides **6a–c** are convenient precursors for the corresponding vinyllithium reagents **7a–c** (halogen-metal exchange with *n*-BuLi) which, after quenching with 2-ethylacrolein **8** or senecialdehyde **9**, afford bis-allylic alcohols like **10b,c–*E*** or **11b,c–*E*** in good yields (scheme 2, table II).

It is worth noticing that poor yields in vinyllithium reagents were obtained (≈ 30%) when direct transmetallation of trisubstituted vinyltins like **1c-*E*** with *n*-butyllithium was attempted in ether at 0 °C because transmetallation equilibrium is poorly shifted towards vinyllithium reagent [18].

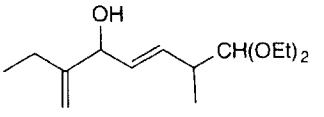
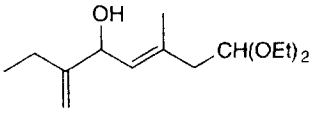
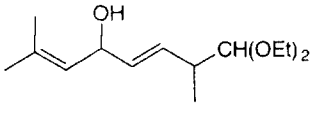
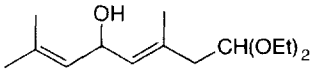
The above results underline the remarkable versatility of vinyltins **1b,c-*E*** and **1b-*Z*** to reach usual or unusual monoterpenoids, since it is possible to obtain *head-to-head, head-to-tail, tail-to-head* or *tail-to-tail* monoterpenic skeletons.

On the basis of these few examples, one can conclude that the above mentionned vinyltin acetals react in cross coupling reactions or as precursors of vinyllithiums like usual vinyltins in terms of chemio-, regio- and stereoselectivity, opening an interesting route to reach functionalized C_{10} monoterpenoids.



Scheme 2

Table II. Reactivity of vinyllithium **7b,c-*E*** derived from **6b,c-*E*** with C_5 aldehydes.

Vinyllithiums + *Aldehydes*		*ether, −78 to 0°C, then H_2O/NH_4Cl*	*Bis-allylic alcohols* **10, 11**
7b-*E*	**8**		**10b-*E*** (76%)
7c-*E*	**8**		**10c-*E*** (74%)
7b-*E*	**9**		**11b-*E*** (71%)
7c-*E*	**9**		**11c-*E*** (93%)

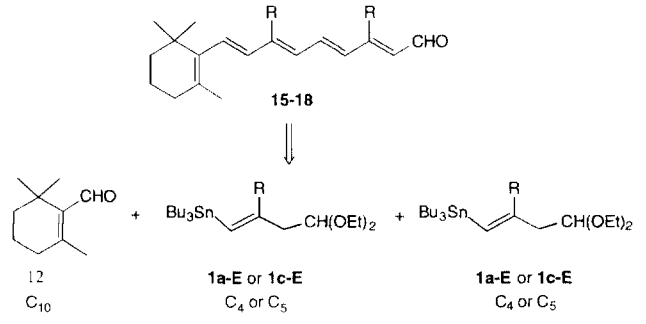
From vinyltin acetals to retinoids and nor-retinoids

Since described vinyltin acetals have been shown to have usual behaviour of vinyltins, we have now to examine their potential in an iterative synthesis of larger branched chains using the possibility to regenerate an aldehyde from the acetal function. For this purpose, we decided to achieve the synthesis of retinoids and C_9 or C_{13} nor-retinoids[1] even if the initial control of the stereochemistry of the vinyltin double bond is not required in this case.

The retrosynthetic analysis of retinal and nor-retinoids is shown in scheme 3. Starting from β-cyclocitral **12** [23], an iterative synthesis seems likely to obtain these compounds according to a C_{10} + (C_4 or C_5) + (C_4 or C_5) reaction sequences.

According to this route, vinyllithium reagents **7a,c** obtained from **1a-*E*** or **1c-*E*** were first quenched by commercial β-cyclocitral giving an adduct of β-ionylidene acetaldehyde type able to react similarly after regeneration of the aldehyde function and dehydration (scheme 4).

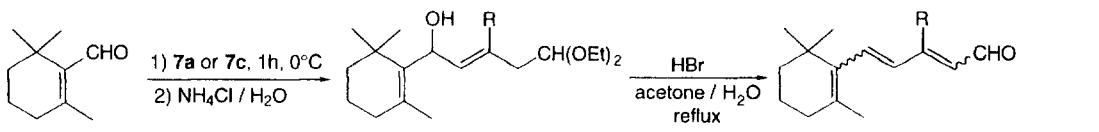
Generation of the vinyllithiums **7a** and **7c**, according to the iododestannylation/halogen-metal exchange sequence, followed by addition of commercial β-cyclocitral provides *E*-hydroxyacetals **13a** and **13c** in good yields, mixed with 15% of their α-isomer, reflecting the rate of



Scheme 3. Retrosynthetic analysis.

α-isomer contained in the starting aldehyde. The dehydration reaction (aqueous HBr/acetone, reflux) allowed the simultaneous acetal hydrolysis and gave directly a 85:15 mixture of (7*E*,9*E*/7*E*,9*Z*) β-ionylidene acetaldehyde **14c** or a 80:20 mixture of (7*E*,9*E*/7*Z*,9*E*) 9-demethylated analogue **14a**, depending on the nature of the vinyllithium which was used. It is worth noticing that the intracyclic double bond isomerization of the minor regioisomer avoids previous purification of **13a** and **13c**. For the elongation of the carbon chain with four or five additional carbon atoms, the same methodology has been applied. However, to avoid polymerization reactions, hydroquinone (0.5 equiv/aldehyde **15–18**) must be added to the crude intermediate hydroxyacetals in order to obtain complexes. In such experimental conditions, moderate (50% for **15**) to good yields (70–90% for **16–18**) in retinal and nor-retinals were obtained. However, while retinal **18** was

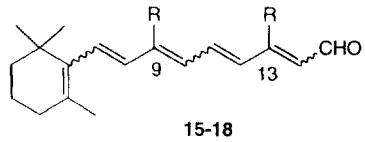
[1] Numerous approaches have already been developped for the synthesis of retinoids [11, 20] or modified retinoids [10b, 12, 21] including C_9 and C_{13} nor-derivatives [22].



12 — 13a (75%), 13c (73%) — 14a R=H (7E,9E / 7Z,9E = 80/20) 88%; 14c R=Me (7E,9E / 7E,9Z = 85/15) 90%

N°	R-C_9	R-C_{13}	Yield (%)	isomeric distribution[a] A/B/C/D/E
15	H	H	50	51/14/28/7/0
16	H	Me	70	A/E=75/25[b]
17	Me	H	85	69/0/26/5/0
18	Me	Me	90	A/E=95/5[c] (72/0/5/0/22)[d]

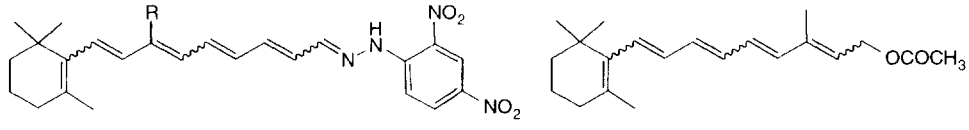
1) 7a or 7c, 1h, 0°C
2) Hydroquinone (0.5eq)
3) HBr, acetone / H_2O, reflux



15-18

(a) Evaluated from ^1H and ^{13}C NMR spectra on the basis of previous studies [11, 22d, 22e]. **A** is the all-*E* isomer, **B** the 7*Z*,9*E*,11*E*,13*E*-isomer, **C** the 7*E*,9*Z*,11*E*,13*E*-isomer, **D** the 7*E*,9*E*,11*Z*,13*E*-isomer and **E** the 7*E*,9*E*,11*E*,13*Z*-isomer.
(b) Only two isomers (>95% of the mixture) were identified at the level of the aldehyde **16** (**A**/**E** = 75:25) and after reduction and derivatization into acetate (isomeric ratio = 90:10).
(c) Isomeric distribution of the recovered products after crystallization as hydroquinone complexes.
(d) Isomeric distribution after flash chromatography (eluent: hexane/ethyl acetate = 80:20) without addition of hydroquinone. The 9*Z*,13*Z*-isomer was also detected (1%) using HPLC by comparison of its relative retention time with that of the all-*E* isomer [24].

Scheme 4



19 (87%, all E / minors = 82/18) from **15** (R = H)

20 (91%, all E / minors = 81/19) from **17** (R = Me)

21 (71%, all E / minor = 90/10) from **16**

Scheme 5

easily crystallized in the presence of hydroquinone, the demethylated analogues were obtained as highly slimy oils. These compounds **15–17** were derivatized into hydrazones **19, 20** or in nor-retinol acetate **21** [22d] in order to increase their stabilities in view of further characterization (scheme 5).

The similarity of ^1H NMR spectra of compounds **19–21** with those of their corresponding nor-retinals is in agreement with an *E* configuration for the major isomer. However, the experimental conditions used for the derivatization appear to modify the isomeric distribution if one compare the obtained results with those reported in scheme 4. Therefore, we do not try to assign the configuration of each minor isomer since our goal was just to demonstrate the efficiency of our method in achieving an iterative synthesis of retinoids and nor-retinoids.

Conclusion

C_5 vinyltins bearing an acetal function have been proved to be useful reagents for terpenic synthesis opening a route to the selective synthesis of monoterpenoids and allowing an iterative synthesis of retinoids and nor-retinoids under mild experimental conditions. Several transformations can be subsequently achieved allowing an easy access to vitamine A derivatives and demethylated analogues. Due to the crucial importance of the substituents borne by the polyenic chain, this strategy opens exciting perspectives for the preparation of modified retinoids because vinyltin acetals are expected to be obtainable in a versatile fashion with appropriate substituents according to our methodology.

Experimental section

General methods

All reactions were carried out under inert atmosphere (Ar or N_2). THF and ether were freshly distilled over sodium/benzophenone and DMF over calcium hydride. Tributyltin hydride was obtained by exchange reaction between bis-(tributyltin)oxide and hydrofugeant H68 (Rhône Poulenc) [25] and homopropargylic acetals according to Miginiac [26]. Alkyllithium reagents were commercially available compounds (Chemetall gmbh) as well as acyl chlorides and aldehydes (Aldrich, Sigma). Flash chromatographies were performed on silica gel 230–400 mesh. GLC analyses were performed on a Carlo-Erba 4200 instrument (FID detector, fitted with a 25 m × 0.32 mm SE 52 capillary column). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200 or a Bruker ARX 400 spectrometer. Chemical shifts are given in ppm relative to Me_4Si used as internal standard for ^1H and ^{13}C NMR spectra (solvent = $CDCl_3$),

while ^{119}Sn chemical shifts are given referring to Me_4Sn used as external standard (solvent = $CDCl_3$). Coupling constants are given in hertz. Mass spectra were obtained in EI mode (70 eV) using a Hewlett Packard apparatus (engine 5989A) in direct introduction mode or in GC/MS mode. The isotopic patterns were given for ^{120}Sn in organotin fragments; this means that the reported abundances (values in brackets) for organotin fragments are roughly one third of the real abundance if compared with organic fragments. IR spectra were recorded on a Bruker IFS 85 apparatus.

Preparation and characterization of vinyltin acetals

• *E-vinyltin acetals* **1a–c**

$Bu_3SnMgMe$ [27] was obtained at −10 °C by addition of MeMgI (78 mmol, 3.2 M in ether) to Bu_3SnLi (78 mmol, in 40 mL THF) previously prepared by deprotonation of Bu_3SnH with iPr$_2$NLi [28]. The $Bu_3SnMgMe$ solution was subsequently stirred at −10 °C with CuCN (15% mol) before dropwise addition of alkyne (0.4 eq) and quenching with water or methyl iodide (2.3 equiv, −10 °C). After usual workup, vinyltins were isolated by distillation ($Eb_{0.06}$ = 114 °C for **1a-*E***) or purified by flash chromatography on silica gel for **1b-*E*** and **1c-*E*** (eluent: hexane/ether/triethylamine = 98:1:1).

• *Z-vinyltin acetals* **1a,b**

We have already described the experimental procedure and the physicochemical data for these compounds [17].

The *E* or *Z* configuration were assigned on the basis of the values of $^3J_{HH}$, $^3J_{SnH}$ and $^3J_{SnC}$ accross the double bond [29–31].

• *(E)-1-Tributylstannyl-4,4-diethoxybut-1-ene* **1a-*E***

IR (film): 2 956, 2 925, 2 872, 1 653 (C=C), 1 465, 1 376, 1 125, 1 062, 1 019 cm^{-1}.

^{1}H NMR δ (ppm): 0.86 (9H, t, $^3J_{2H}$ = 7.1), 1.17 (6H, t, $^3J_{2H}$ = 7.1), 1.20–1.62 (18H, m), 2.45 (2H, dd, $^3J_{1H}$ = 5.9, $^3J_{1H}$ = 5.4), 3.51 and 4.50 (2 × 2H, qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = −9.5), 4.50 (1H, t, $^3J_{2H}$ = 5.9), 5.87 (1H, td, $^3J_{2H}$ = 5.4, $^3J_{1H}$ = 19.0, $^3J_{SnH}$ = 63.7-66.6)[2] , 6.01 (1H, d, $^3J_{1H}$ = 19.0, $^2J_{SnH}$ = 72.4–76.2).

^{13}C NMR δ (ppm): 9.6 (3C, $^1J_{SnC}$ = 327–343), 13.9 (3C), 15.5 (2C), 27.4 (3C, $^3J_{SnC}$ = 52–55), 29.3 (3C, $^2J_{SnC}$ = 21), 42.7 ($^3J_{SnC}$ = 63)[2], 61.3 (2C), 102.8, 131.4 ($^1J_{SnC}$ = 372–389), 143.9 ($^2J_{SnC}$ = 7).

^{119}Sn NMR δ (ppm): −51.3.

MS organotin fragments: m/z = 377 (40), 333 (82), 331 (66), 303 (24), 291 (13), 279 (57), 277 (66), 275 (49), 247 (17), 235 (87), 191 (15), 189 (17), 179 (61), 177 (61), 123 (10), 121 (42); organic fragments: m/z = 103 (54), 75 (72), 47 (100), 41 (15), 29 (38), 27 (10).

Anal calc for $C_{20}H_{42}O_2Sn$: C, 55.27; H, 9.75. Found: C, 55.01; H, 9.85.

• *(E)-1-Tributylstannyl-4,4-diethoxy-3-methylbut-1-ene* **1b-*E***

IR (film): 2 957, 2 925, 2 872, 1 600 (C=C), 1 465, 1 420, 1 376, 1 125, 1 065, 1 020 cm^{-1}.

^{1}H NMR δ (ppm) : 0.95 (9H, t, $^3J_{2H}$ = 7.2), 0.97 (6H, m), 1.12 (3H, t, $^3J_{2H}$ = 7.0), 1.14 (3H, t, $^3J_{2H}$ = 7.0), 1.21 (3H, d, $^3J_{1H}$ = 6.8), 1.30–1.71 (12H, m), 2.67 (1H, m), 3.37 and 3.39 and 3.57 and 3.59 (4 × 1H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.4), 4.25 (1H, d, $^3J_{1H}$ = 6.8), 6.15 (1H, dd, $^4J_{1H}$ = 0.5, $^3J_{1H}$ = 19.1, $^2J_{SnH}$ = 76.3–80.0), 6.32 (1H, dd, $^3J_{1H}$ = 6.1, $^3J_{1H}$ = 19.1, $^3J_{SnH}$ = 65.9–69.0)[2].

^{13}C NMR δ (ppm): 9.4 (3C, $^1J_{SnC}$ = 326–341), 13.7 (3C), 14.7, 15.2 and 15.3 (2C), 27.2 (3C, $^3J_{SnC}$ = 52–54), 29.1 (3C, $^2J_{SnC}$ = 20), 44.5 ($^3J_{SnC}$ = 60)[2], 61.8 and 61.9 (2C), 106.1, 127.3 ($^1J_{SnC}$ = 376–394), 150.2 ($^2J_{SnC}$ = 6).

^{119}Sn NMR δ (ppm): −49.5.

MS organotin fragments: m/z = 391 (15), 347 (28), 345 (57), 291 (10), 279 (45), 277 (32), 235 (100), 179 (48), 177 (45), 165 (17), 121 (24); organic fragments: m/z = 157 (22), 103 (56), 83 (11), 75 (66), 55 (14), 47 (92), 41 (11), 29 (28).

Anal calc for $C_{21}H_{44}O_2Sn$: C, 56.22; H, 9.89. Found: C, 56.34; H, 9.89.

• *(E)-1-Tributylstannyl-4,4-diethoxy-2-methylbut-1-ene* **1c-*E***

IR (film): 2 956, 2 872, 2 854, 1 606 (C=C), 1 465, 1 457, 1 375, 1 116, 1 063, 1 004 cm^{-1}.

^{1}H NMR δ (ppm): 0.86 (9H, t, $^3J_{2H}$ = 7.2), 1.17 (6H, t, $^3J_{2H}$ = 7.0), 1.22–1.58 (18H, m), 1.82 (3H, s, $^4J_{SnH}$ = 10.0), 2.46 (2H, d, $^3J_{1H}$ = 5.9), 3.50 and 3.65 (2 × 2H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.3), 4.62 (1H, t, $^3J_{2H}$ = 5.9), 5.57 (1H, s, $^2J_{SnH}$ = 71.6).

^{13}C NMR δ (ppm): 10.3 (3C, $^1J_{SnC}$ = 324–340), 13.9 (3C), 15.5 (2C), 25.5 ($^3J_{SnC}$ = 35–37), 27.5 (3C, $^3J_{SnC}$ = 53–57), 29.4 (3C, $^2J_{SnC}$ = 20),46.4 ($^3J_{SnC}$ = 56–59)[2], 61.3 (2C), 102.8, 125.5 ($^1J_{SnC}$ = 389–407), 150.6.

^{119}Sn NMR δ (ppm): −61.4.

MS organotin fragments: m/z = 391 (17), 345 (20), 291 (16), 289 (13), 279 (89), 277 (65), 235 (48), 233 (36), 179 (32), 177 (35), 175 (30), 121 (24); organic fragments: m/z = 103 (43), 75 (59), 55 (6), 47 (98), 41 (17), 29 (100), 27 (22).

Anal calc for $C_{21}H_{44}O_2Sn$: C, 56.22; H, 9.89. Found: C, 56.09; H, 9.81.

Cross-coupling reaction of C_5 vinyltin acetals with C_5 acyl chlorides

A DMF solution of acid chloride (1.1 mmol in 5 mL of dry DMF) was placed in a Schlenk tube and degassed before addition of **1b,c-*E*** or **1b-*Z*** (1.1 mmol) and $PdCl_2(MeCN)_2$ (12 mg). The pale yellow mixture turned progressively to brown-red after 3 h at room temperature. At this time, 10 mL of an aqueous solution of sodium fluoride and 10 mL of acetone were added in order to remove tributyltin chloride as tributyltin fluoride. After the extraction and usual treatments, compounds **4b,c-*E***, **5b,c-*E*** and **5b-*Z*** were purified on silica gel (hexane/ether/triethylamine = 80:18:2).

• *(E)-5,5-Diethoxy-1-(3-furanyl)-4-methylpent-2-en-1-one* **4b-*E***

IR (film): 3 120, 2 970–2 880, 1 670, 1 620, 1 555, 1 500, 1 445, 1 376, 1 150, 1 120, 1 050, 870 cm^{-1}.

^{1}H NMR δ (ppm) : 1.08 (3H, d, $^3J_{1H}$ = 6.8), 1.13 (3H, t, $^3J_{2H}$ = 7.0), 1.14 (3H, t, $^3J_{2H}$ = 7.0), 2.63 (1H, m, $^3J_{3H}$ = 6.8, $^3J_{1H}$ = 6.4, $^3J_{1H}$ = 7.6, $^4J_{1H}$ = 1.1), 3.43 and 3.61 (2 × 2H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.3), 4.26 (1H, d, $^3J_{1H}$ = 6.4), 6.48 (1H, dd, $^3J_{1H}$ = 15.6, $^4J_{1H}$ = 1.1), 6.75 (1H, dd, $^4J_{1H}$ = 0.9, $^3J_{1H}$ = 1.8), 6.96 (1H, dd, $^3J_{1H}$ = 7.6, $^3J_{1H}$ = 15.6), 7.38 (1H, dd, $^4J_{1H}$ = 1.5, $^3J_{1H}$ = 1.8), 7.97 (1H, dd, $^4J_{1H}$ = 1.5, $^3J_{1H}$ = 0.9).

[2] The values of these coupling constants accross the double bond must be compared with those of **1a-*Z*** and **1b-*Z*** which are near 140 Hz for $^3J_{SnH}$ and near 36 Hz for $^3J_{SnC}$ as already described [17].

^{13}C NMR δ (ppm): 14.7, 15.3 (2C), 40.8, 62.3 and 62.8 (2C), 105.3, 109.2, 127.1, 128.0, 144.2 and 147.4 (2C), 148.7, 184.9 (C=O).

MS: m/z = 207 (4), 121 (10), 103 (156), 95 (26), 75 (61), 55 (6), 47 (100), 39 (19), 29 (33), 27 (11).

• *(E)-5,5-Diethoxy-1-(3-furanyl)-3-methylpent-2-en-1-one* ***4c-E***

IR (film): 3 125, 2 970–2 880, 1 655, 1 610, 1 555, 1 505, 1 445, 1 376, 1 295, 1 200, 1 050, 965, 870 cm^{-1}.

^{1}H NMR δ (ppm): 1.21 (6H, t, $^3J_{2H}$ = 7.2), 2.26 (3H, d, $^4J_{1H}$ = 1.3), 2.52 (2H, dd, $^3J_{1H}$ = 5.7, $^4J_{1H}$ = 0.8), 3.58 and 3.69 (2 × 2H, qd, $^3J_{3H}$ = 7.2, $^2J_{1H}$ = −9.4), 4.69 (1H, t, $^3J_{2H}$ = 5.7), 6.50 (1H, m, $^4J_{3H}$ = 1.3, $^4J_{2H}$ = 0.8), 6.80 (1H, dd, $^4J_{1H}$ = 0.9, $^3J_{1H}$ = 1.9), 7.42 (1H, dd, $^4J_{1H}$ = 1.5, $^3J_{1H}$ = 1.9), 7.99 (1H, dd, $^4J_{1H}$ = 1.5, $^3J_{1H}$ = 0.9).

^{13}C NMR δ (ppm): 15.3 (2C), 20.4, 45.6, 61.7 (2C), 101.5, 109.1, 123.7, 129.6, 144.1 and 146.7 (2C), 154.5, 185.4 (C=O).

MS: m/z = 207 (3), 103 (35), 95 (28), 75 (45), 47 (100), 39 (27), 29 (53).

• *(5E)-8,8-Diethoxy-2,7-dimethylocta-2,5-dien-4-one* ***5b-E***

IR (film): 2 980–2 880, 1 679, 1 662, 1 633, 1 616, 1 445, 1 376, 1 116, 1 062, 981, 823 cm^{-1}.

^{1}H NMR δ (ppm): 1.05 (3H, d, $^3J_{1H}$ = 6.8), 1.15 (3H, t, $^3J_{2H}$ = 7.0), 1.17 (3H, t, $^3J_{2H}$ = 7.0), 1.88 (3H, d, $^4J_{1H}$ = 1.2), 2.11 (3H, d, $^4J_{1H}$ = 1.2), 2.59 (1H, m, $^3J_{3H}$ = 6.8, $^3J_{1H}$ = 6.2, $^3J_{1H}$ = 7.5, $^4J_{1H}$ = 1.2), 3.44 and 3.49 and 3.61 and 3.66 (4 × 1H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.4), 4.25 (1H, d, $^3J_{1H}$ = 6.2), 6.11 (1H, dd, $^3J_{1H}$ = 16.0, $^4J_{1H}$ = 1.2), 6.21 (1H, m, $^4J_{3H}$ = 1.2, $^4J_{3H}$ = 1.2), 6.78 (1H, dd, $^3J_{1H}$ = 7.5, $^3J_{1H}$ = 16.0).

^{13}C NMR δ (ppm): 14.8, 15.4 (2C), 21.1, 27.9, 40.8, 62.5 and 62.8 (2C), 105.6, 122.9 and 132.2 (2C), 147.0, 155.6, 190.8 (C=O).

MS: m/z = 195 (4), 167 (2), 149 (20), 137 (1), 123 (5), 109 (6), 103 (100), 83 (23), 75 (92), 55 (13), 47 (88), 29 (17), 27 (7), 18 (11).

Anal calc for $C_{14}H_{24}O_3$: C, 69.95; H, 10.07. Found: C, 69.57; H, 10.10.

• *(5Z)-8,8-Diethoxy-2,7-dimethylocta-2,5-dien-4-one* ***5b-Z***

IR (film): 2 980–2 880, 1 723, 1 679, 1 624, 1 445, 1 376, 1 107, 1 062, 859 cm^{-1}.

^{1}H NMR δ (ppm): 1.06 (3H, d, $^3J_{1H}$ = 6.9), 1.17 (3H, t, $^3J_{2H}$ = 7.0), 1.18 (3H, t, $^3J_{2H}$ = 7.0), 1.90 (3H, d, $^4J_{1H}$ = 1.1), 2.17 (3H, d, $^4J_{1H}$ = 1.1), 3.48 and 3.52 and 3.65 and 3.66 (4 × 1H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.5), 3.83 (1H, qdd, $^3J_{3H}$ = 6.9, $^3J_{1H}$ = 5.3, $^3J_{1H}$ = 9.0), 4.32 (1H, d, $^3J_{1H}$ = 5.3), 6.02 (1H, dd, $^3J_{1H}$ = 11.6, $^3J_{1H}$ = 9.0), 6.10 (1H, bs), 6.13 (1H, d, $^3J_{1H}$ = 11.6).

^{13}C NMR δ (ppm): 14.8, 15.1 (2C), 20.6 and 27.7 (2C), 36.3, 62.0 and 62.2 (2C), 105.5, 125.6 and 128.7 and 147.8 (3C), 155.4, 191.5 (C=O).

MS: m/z = 195 (37), 194 (13), 149 (41), 137 (5), 123 (15), 121 (11), 109 (15), 103 (100), 83 (46), 75 (83), 55 (33), 53 (11), 47 (75), 43 (22), 41 (12), 39 (15), 29 (40), 27 (15).

• *(5E)-8,8-Diethoxy-2,6-dimethylocta-2,5-dien-4-one* ***5c-E***

IR (film): 2 970–2 880, 1 670, 1 625, 1 440, 1 375, 1 110, 1 065, 1 040, 870 cm^{-1}.

^{1}H NMR δ (ppm): 1.20 (6H, t, $^3J_{2H}$ = 7.0), 1.89 (3H, bd, $^4J_{1H}$ = 1.1), 2.17 (3H, bd, $^4J_{1H}$ = 1.3), 2.21 (3H, d, $^4J_{1H}$ = 1.3), 2.43 (2H, dd, $^3J_{1H}$ = 5.8, $^4J_{1H}$ = 0.6), 3.44 and 3.70 (2 × 2H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.4), 4.65 (1H, t, $^3J_{2H}$ = 5.8), 6.14–6.20 (2H, m).

^{13}C NMR δ (ppm): 15.2 (2C), 19.7 and 20.6 (2C), 27.8, 45.5, 61.5 (2C), 101.5, 126.2 and 128.0 (2C), 152.5 and 154.7 (2C), 191.5 (C=O).

MS: m/z = 195 (6), 167 (1), 149 (3), 123 (7), 103 (100), 83 (38), 75 (90), 55 (14), 47 (80), 39 (6), 29 (14).

Anal calc for $C_{14}H_{24}O_3$: C, 69.95; H, 10.07. Found: C, 70.25; H, 9.69.

Iododestannylation of vinyltin acetals

To a solution of 2.13 g (8.4 mmol) of iodine in 50 mL of ether was added the vinyltin **1a–c** (7 mmol) at room temperature (for *E*-isomers) or −20 °C (for *Z*-isomer). After 2 h, 20 mL of an aqueous solution of sodium fluoride and acetone were added. After the extraction and usual treatments, compounds **6a–c** were purified on silica gel (hexane/ether/triethylamine = 90:8:2) and used immediately.

• *(E)-4,4-Diethoxy-1-iodobut-1-ene* ***6a-E***

IR (film): 2 980–2 880, 1 609 (C=C), 1 481, 1 443, 1 372, 1 124, 1 061, 1 027, 947, 668 cm^{-1}.

^{1}H NMR δ (ppm): 1.20 (6H, t, $^3J_{2H}$ = 7.1), 2.37 (2H, ddd, $^4J_{1H}$ = 1.3, $^3J_{1H}$ = 5.6, $^3J_{1H}$ = 7.3), 3.48 and 3.65 (2 × 2H, qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = −9.3), 4.50 (1H, t, $^3J_{2H}$ = 5.6), 6.13 (1H, td, $^4J_{2H}$ = 1.3, $^3J_{1H}$ = 14.5), 6.51 (1H, td, $^3J_{1H}$ = 14.5, $^3J_{2H}$ = 7.3).

^{13}C NMR δ (ppm): 15.2 (2C), 40.4, 61.5 (2C), 77.2, 101.2, 141.3.

MS: m/z = 225 (16), 197 (3), 169 (6), 167 (6), 103 (77), 98 (3), 75 (48), 69 (11), 47 (100), 44 (8), 41 (37), 39 (16), 29 (35), 27 (12).

Anal calc for $C_8H_{15}O_2I$: C, 35.55; H, 5.60; I, 47.00. Found: C, 35.47; H, 5.53; I, 47.35.

• *(E)-4,4-Diethoxy-1-iodobut-1-ene* ***6a-Z***

This compound has been already described [17].

• *(E)-4,4-Diethoxy-1-iodo-3-methylbut-1-ene* ***6b-E***

IR (film): 3 060, 3 040, 2 980–2 880, 1 600 (weak), 1 480, 1 440, 1 375, 1 120, 1 060, 1 000, 710, 670 cm^{-1}.

^{1}H NMR δ (ppm): 0.96 (3H, d, $^3J_{1H}$ = 6.9), 1.13 (6H, t, $^3J_{2H}$ = 7.0), 2.42 (1H, m, $^3J_{3H}$ = 6.9, $^3J_{1H}$ = 6.2, $^3J_{1H}$ = 7.6, $^4J_{1H}$ = 1.0), 3.43 and 3.60 (2 × 2H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.4), 4.14 (1H, d, $^3J_{1H}$ = 6.2), 6.01 (1H, dd, $^3J_{1H}$ = 14.5, $^4J_{1H}$ = 1.0), 6.49 (1H, dd, $^3J_{1H}$ = 14.5, $^3J_{1H}$ = 7.6).

^{13}C NMR δ (ppm): 14.2, 15.3 (2C), 44.0, 62.2 (2C), 75.5, 104.9, 147.2.

MS: m/z = 239 (14), 211 (4), 181 (6), 103 (82), 75 (61), 55 (10), 54 (9), 53 (9), 47 (100), 43 (33), 29 (29), 27 (13).

• *(E)-4,4-Diethoxy-1-iodo-2-methylbut-1-ene* ***6c-E***

IR (film): 3 057, 2 980–2 880, 1 616 (weak), 1 481, 1 443, 1 373, 1 118, 1 058, 1 008, 735, 673 cm^{-1}.

^{1}H NMR δ (ppm): 1.20 (6H, t, $^3J_{2H}$ = 7.0), 1.89 (3H, d, $^4J_{1H}$ = 1.1), 2.51 (2H, dd, $^3J_{1H}$ = 5.6, $^4J_{1H}$ = 1.1), 3.51 and 3.63 (2 × 2H, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.3), 4.58 (1H, t, $^3J_{2H}$ = 5.6), 6.02 (1H, dd, $^4J_{2H}$ = 1.1, $^4J_{3H}$ = 1.1).

^{13}C NMR δ (ppm): 15.2 (2C), 24.5, 43.4, 61.3 (2C), 77.5, 101.3, 143.6.

MS: m/z = 239 (14), 183 (3), 181 (3), 112 (18), 103 (89), 83 (10), 75 (53), 55 (34), 54 (10), 53 (12), 47 (100), 44 (10), 39 (13), 29 (34), 27 (20).

Anal calc for $C_9H_{17}O_2I$: C, 38.02; H, 6.03; I, 44.68. Found: C, 38.41; H, 5.99; I, 44.50.

Reactivity of vinyllithium **7b,c-E** *derived from* **6b,c-E** *with* C_5 *aldehydes*

To a stirred solution of **6b,c-E** (1.8 mmol) in dry ether (10 mL), at −78 °C, was added dropwise 1.3 mL of *n*BuLi (2 mmol, 1.5 M in hexanes). After 1 h at −70 to −60 °C, C_5 aldehyde (1.44 mmol) was added and the mixture was allowed to warm up to 0 °C before hydrolysis (H_2O/NH_4Cl). After usual work-up, the residue was chromatographed on silica gel (eluent: hexane/ethyl acetate/triethylamine = 80:18:2), affording the bis-allylic alcohols **10**–**11** in 71–93% isolated yields.

• *(4E)-7,7-Diethoxy-2-ethyl-6-methylhepta-1,4-dien-3-ol* **10b-E** *(2 diastereoisomers A/B ≈ 50:50)*

IR (film): 3 420, 2 980–2 860, 1 665, 1 440, 1 370, 1 120, 1 060, 970 cm^{-1}.

^1H NMR δ (ppm): 0.96 (3H, d, $^3J_{1H}$ = 6.8), 0.99 (3H, t, $^3J_{2H}$ = 7.3), 1.11 and 1.12 (3H, t, $^3J_{2H}$ = 7.1), 1.13 (3H, t, $^3J_{2H}$ = 7.1), 1.75 (OH, d, $^3J_{1H}$ = 3.9), 1.76 (OH, m), 1.97 (2H, bq, $^3J_{3H}$ = 7.3), 1.99 (2H, bq, $^3J_{3H}$ = 7.3), 2.42 (1H, m, $^3J_{1H}$ = 6.9, $^3J_{1H}$ = 6.5, $^3J_{1H}$ = 6.8, $^4J_{1H}$ = 1.0), 3.42 (2H, m), 3.57 (2H, m), 4.14 (1H, d, $^3J_{1H}$ = 6.5), 4.46 (1H, m, $^3J_{1H}$ = 6.9, $^3J_{1H}$ = 3.8, $^4J_{1H}$ = 1.0), 4.79 (1H, m), 4.80 (1H, m), 5.02 (1H, m), 5.41 (1H, ddd, $^3J_{1H}$ = 15.5, $^3J_{1H}$ = 6.9, $^4J_{1H}$ = 1.0), 5.42 (1H, ddd, $^3J_{1H}$ = 15.5, $^3J_{1H}$ = 6.9, $^4J_{1H}$ = 1.0), 5.64 (1H, ddd, $^3J_{1H}$ = 15.5, $^3J_{1H}$ = 6.9, $^4J_{1H}$ = 1.0), 5.67 (1H, ddd, $^3J_{1H}$ = 15.5, $^3J_{1H}$ = 6.9, $^4J_{1H}$ = 1.0).

^{13}C NMR δ (ppm): 12.1, 12.2, 15.1, 15.2 and 15.3 (2C), 24.7, 39.9, 40.0, 61.8 and 62.0 (2C), 62.1 and 62.2 (2C), 75.9, 76.0, 105.9, 106.0, 107.9, 108.1, 131.6 and 133.4 (2C), 152.4, 152.5.

MS: *m/z* = 151 (2), 123 (3), 103 (100), 83 (16), 75 (76), 55 (11), 47 (78), 29 (16).

• *(4E)-7,7-Diethoxy-2-ethyl-5-methylhepta-1,4-dien-3-ol* **10c-E**

IR (film): 3 400, 3 060, 2 950–2 860, 1 630, 1 430, 1 360, 1 335, 1 105, 1 050, 990, 885 cm^{-1}.

^1H NMR δ (ppm) : 0.99 (3H, t, $^3J_{2H}$ = 7.4), 1.10 (3H, t, $^3J_{2H}$ = 7.1), 1.12 (3H, t, $^3J_{2H}$ = 7.1), 1.70 (3H, d, $^4J_{1H}$ = 1.2), 1.80 (OH, m), 1.97 (2H, bq, $^3J_{3H}$ = 7.4), 2.27 (1H, dd, $^3J_{1H}$ = 5.9, $^4J_{1H}$ = 0.8), 2.28 (1H, dd, $^3J_{1H}$ = 5.9, $^4J_{1H}$ = 0.8), 3.41 and 3.57 (2 × 2H, qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = −9.4), 4.54 (1H, t, $^3J_{2H}$ = 5.9), 4.76 (1H, bd, $^3J_{1H}$ = 8.8), 4.77 (1H, m), 5.03 (1H, m), 5.19 (1H, m, $^3J_{1H}$ = 8.8, $^4J_{3H}$ = 1.2, $^4J_{2H}$ = 0.8).

^{13}C NMR δ (ppm): 12.1, 15.2 (2C), 17.2, 24.6, 43.6, 60.8 and 61.1 (2C), 71.4, 101.7, 107.3, 129.2, 134.6 and 152.9 (2C).

MS: *m/z* = 197 (2), 151 (1), 123 (2), 103 (100), 83 (9), 75 (69), 55 (8), 47 (67), 41 (8), 29 (16).

Anal calc for $C_{14}H_{26}O_3$: C, 69.37; H, 10.82. Found: C, 69.57; H, 10.89.

• *(5E)-8,8-Diethoxy-2,7-dimethylocta-2,5-dien-4-ol* **11b-E** *(2 diastereoisomers A/B = 50:50)*

IR (film): 3 420, 2 970–2 860, 1 665, 1 440, 1 370, 1 120, 1 060, 970 cm^{-1}.

^1H NMR δ (ppm): 0.99 and 1.00 (3H, d, $^3J_{1H}$ = 6.7), 1.14 and 1.16 (3H, t, $^3J_{2H}$ = 7.2), 1.17 (3H, 3H, t, $^3J_{2H}$ = 7.2), 1.59 (OH, m), 1.67 (3H, d, $^4J_{1H}$ = 1.3), 1.71 (3H, d, $^4J_{1H}$ = 1.3), 2.47 (1H, m, $^3J_{3H}$ = $^3J_{1H}$ = $^3J_{1H}$ = 6.7), 3.30–3.86 (2H, 2H, m), 4.20 (1H, d, $^3J_{1H}$ = 6.7), 4.72–4.96 (1H, m), 5.23 (1H, m, $^3J_{1H}$ = 8.5, $^4J_{3H}$ = $^4J_{3H}$ = 1.3), 5.49 and 5.52 (1H, m), 5.73 and 5.77 (1H, m).

^{13}C NMR δ (ppm): 14.8 (3C), 17.8 and 25.4 (2C), 39.5, 61.5 and 61.9 (2C), 69.3, 105.8, 126.6, 131.3 and 132.2 (2C), 133.7.

MS: *m/z* = 197 (1), 151 (4), 123 (4), 107 (4), 103 (100), 83 (12), 75 (67), 55 (10), 47 (55), 43 (10), 41 (11), 29 (26).

• *(5E)-8,8-Diethoxy-2,6-dimethylocta-2,5-dien-4-ol* **11c-E**

IR (film): 3 400 (strong), 2 970–2 880, 1 670 (strong), 1 625, 1 440, 1 375, 1 110, 1 065, 1 040, 845 cm^{-1}.

^1H NMR δ (C_6D_6) (ppm): 1.07 (3H, t, $^3J_{2H}$ = 7.0), 1.08 (3H, t, $^3J_{2H}$ = 7.0), 1.57 (3H, 3H, d, $^4J_{1H}$ = 1.2), 1.72 (3H, d, $^4J_{1H}$ = 1.4), 2.14 (OH, m), 2.36 (2H, dd, $^3J_{1H}$ = 5.8, $^4J_{1H}$ = 0.9), 3.33 (2H, m), 3.52 (2H, m), 4.57 (1H, t, $^3J_{2H}$ = 5.8), 5.13 (1H, dd, $^3J_{1H}$ ≈ $^3J_{1H}$ ≈ 8.3), 5.35 (1H, m, $^4J_{3H}$ = 1.4, $^4J_{3H}$ = 1.2, $^3J_{1H}$ = 8.3), 5.46 (1H, m, $^3J_{1H}$ = 8.3, $^4J_{3H}$ = 1.2, $^4J_{2H}$ = 0.9).

^{13}C NMR δ (ppm): 15.2 (2C), 17.2 and 18.2 (2C), 25.8, 43.7, 61.0 (2C), 65.3, 102.0, 127.8 and 130.7 (2C), 132.1 and 132.9 (2C).

MS: *m/z* = 197 (1), 123 (3), 109 (6), 103 (100), 75 (83), 47 (71), 43 (18), 41 (11), 29 (20).

Anal calc for $C_{14}H_{26}O_3$: C, 69.37; H, 10.82. Found: C, 69.16; H, 10.63.

Retinal and nor-retinoids syntheses

• *General procedure for the preparation of aldehydes* **14a,c** *from β-cyclocitral*

The procedure described for **10b,c-E** and **11b,c-E** was employed with β-cyclocitral as electrophile to obtain **13a,c**. The residue were purified by flash-chromatography (eluent: hexane/ethyl acetate/triethylamine = 90:9:1). Crude acetals **13a,c** and 20 mL of aqueous acetone (0.5%) were charged in a 100 mL flask equiped with a reflux condenser. The solution was heated to reflux before adding 0.36 mL of dilute hydrobromic acid (5 mL acetone + 0.1 mL 48% HBr). Reflux was maintained during 40 min before hydrolysis (NH_4Cl/H_2O). After usual work-up, the residue was diluted with hexane to eliminate heavy by-products, washed with brine, dried over $MgSO_4$ and evaporated under vacuum to afford aldehydes **14a** and **14c**.

• *(E)-5,5-Diethoxy-1-(2,6,6-trimethylcyclohex-1-enyl)pent-2-en-1-ol* **13a**

IR (film): 3 447 (strong), 2 970–2 880, 1 685, 1 650, 1 457, 1 374, 1 120, 1 060, 1 020, 970 (strong).

^1H NMR δ (C_6D_6) (ppm): 0.97 (C_1-CH_3, s), 1.08 (2 OCH$_2$CH_3, t, $^3J_{2H}$ = 7.1), 1.09 (C_1-CH_3, s), 1.34–1.50 ($2H_2$, $2H_3$, m), 1.81 (C_5-CH_3, s), 1.84 ($2H_4$, t, $^3J_{2H}$ = 6.2), 1.94 (OH, bs, $^3J_{1H}$ = 5.3), 2.42 ($2H_{10}$, dd, $^3J_{1H}$ = 5.8, $^3J_{1H}$ = 6.7), 3.34 (2 OCH*H*CH$_3$, qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = −9.1), 3.50 and 3.51 (2 × OCH*H*CH$_3$, qd, $^3J_{3H}$ = 7.1, $^2J_{1H}$ = -8.8), 4.46 (H_{11}, t, $^3J_{2H}$ = 5.8), 4.79 (H_7, bd, $^3J_{1H}$ = 4.6), 5.75 (H_9, tdd, $^3J_{1H}$ = 15.5, $^3J_{2H}$ = 6.7, $^4J_{1H}$ = 1.4), 5.83 (H_8, dd, $^3J_{1H}$ = 15.5, $^3J_{1H}$ = 4.6).

^{13}C NMR δ (C_6D_6) (ppm): 15.5 (2 OCH$_2$*C*H$_3$), 19.8 (C_3), 21.2 (C_5-*C*H$_3$), 28.2 and 28.8 (C_1-2*C*H$_3$), 34.1 (C_4), 34.9 (C_1), 37.3 (C_2), 40.3 (C_{10}), 60.8 (2 O*C*H$_2$CH$_3$), 70.7 (C_7), 102.8 (C_{11}), 124.9 (C_9), 131.9 (C_5), 135.9 (C_8), 139.5 (C_6).

MS: *m/z* = 251 (1), 205 (1), 151 (8), 123 (8), 105 (4), 103 (100), 95 (4), 93 (4), 81 (10), 75 (60), 55 (8), 47 (49), 43 (12), 41 (14), 29 (21).

• *(E)-5,5-Diethoxy-3-methyl-1-(2,6,6-trimethylcyclohex-1-enyl)pent-2-en-1-ol* **13c**

IR (film): 3 457 (strong), 2 980–2 830, 1 653, 1 456, 1 373, 1 120, 1 062, 1 004, 970 (strong) cm^{-1}.

^1H NMR δ (C_6D_6) (ppm): 0.99 (C_1-CH_3, s), 1.08 and 1.09 (2 OCH_2CH_3, t, $^3J_{2H}$ = 7.0), 1.15 (C_1-CH_3, s), 1.37–1.50 ($2H_2$, OH and $2H_3$, m), 1.81 (C_9-CH_3, d, $^4J_{1H}$ = 1.4), 1.85 ($2H_4$, m), 1.88 (C_5-CH_3, s), 2.38 ($2H_{10}$, dd, $^3J_{1H}$ = 5.8, $^4J_{1H}$ = 0.8), 3.31 and 3.34 and 3.51 and 3.53 (4 × OCH_2CH_3, qd, $^3J_{3H}$ = 7.0, $^2J_{1H}$ = −9.3), 4.59 (H_{11}, t, $^3J_{2H}$ = 5.8), 5.07 (H_7, bd, $^3J_{1H}$ = 8.2), 5.80 (H_8, m, $^3J_{1H}$ = 8.2, $^4J_{3H}$ = 1.4, $^4J_{2H}$ = 0.8).

^{13}C NMR δ (C_6D_6) (ppm): 15.5 (2 OCH_2CH_3), 17.2 (C_9-CH_3), 19.8 (C_3), 21.4 (C_5-CH_3), 28.3 and 28.9 (C_1-$2CH_3$), 34.1 (C_4), 34.8 (C_1), 40.5 (C_2), 44.2 (C_{10}), 60.8 (2 OCH_2CH_3), 67.1 (C_7), 102.2 (C_{11}), 131.0 (C_5), 131.8 (C_8), 134.7 (C_9), 141.1 (C_6).

MS: *m/z* = 293 (1), 221 (4), 205 (6), 151 (4), 123 (5), 103 (100), 75 (72), 47 (49), 41 (10), 29 (17).

• *(9-Demethyl-β-ionylidene)acetaldehyde* **14a**

IR (film): 3 420, 3 100–2 871 (strong), 1 718, 1 700, 1 636, 1 457, 1 384, 1 004, 788, 764 (strong), 668 cm^{-1}.

Isomer 7E, 9E: ^1H NMR δ (ppm): 1.00 (C_1-$2CH_3$, s), 1.38–1.58 ($2H_2$, $2H_3$, m), 1.70 (C_5-CH_3, bd, $^4J_{1H}$ = 0.8), 2.00 ($2H_4$, bt, $^3J_{2H}$ = 6.5), 6.05 (H_{10}, dd, $^3J_{1H}$ = 8.0, $^3J_{1H}$ = 15.1), 6.30 (H_8, dd, $^3J_{1H}$ = 10.8, $^3J_{1H}$ = 15.6), 6.66 (H_7, bd, $^3J_{1H}$ = 15.6), 7.10 (H_9, dd, $^3J_{1H}$ = 15.1, $^3J_{1H}$ = 10.8), 9.49 (H_{11}, d, $^3J_{1H}$ = 8.0).

^{13}C NMR δ (ppm): 19.1 (C_3), 21.9 (C_5-CH_3), 29.0 (C_1-$2CH_3$), 33.7 (C_4), 34.3 (C_1), 39.9 (C_2), 130.1 (C_{10}), 130.6 (C_8), 135.2 and 137.1 (C_5, C_6), 142.8 (C_7), 153.7 (C_9), 193.8 (C_{11}).

MS: *m/z* = 204 (26), 189 (35), 175 (20), 161 (14), 148 (10), 147 (8), 133 (32), 107 (24), 105 (100), 95 (13), 91 (58), 81 (21), 79 (33), 77 (31), 69 (15), 65 (20), 55 (35), 41 (64), 39 (31), 29 (26), 27 (25).

Isomer 7Z, 9E: ^1H NMR δ (ppm): 1.00 (C_1-$2CH_3$, s), 1.43–1.71 ($2H_2$ + $2H_3$, m), 1.52 (C_5-CH_3, bd, $^4J_{1H}$ = 0.8), 2.05 ($2H_4$, bt, $^3J_{2H}$ = 5.8), 6.18 (H_{10}, dd, $^3J_{1H}$ = 8.0, $^3J_{1H}$ = 15.5), 6.40 (H_8, dd, $^3J_{1H}$ = 10.8, $^3J_{1H}$ = 10.2), 6.49 (H_7, bd, $^3J_{1H}$ = 10.8), 7.07 (H_9, dd, $^3J_{1H}$ = 15.5, $^3J_{1H}$ = 10.2), 9.55 (H_{11}, d, $^3J_{1H}$ = 8.0).

^{13}C NMR δ (ppm): 19.1 (C_3), 21.5 (C_5-CH_3), 28.5 (C_1-$2CH_3$), 32.2 (C_4), 34.5 (C_1), 38.9 (C_2), 128.8 (C_{10}), 132.0 (C_8), 135.2 and 137.1 (C_5, C_6), 141.1 (C_7), 149.3 (C_9), 194.1 (C_{11}).

MS: *m/z* = 204 (24), 189 (49), 175 (20), 161 (17), 148 (11), 147 (8), 133 (36), 105 (100), 95 (14), 91 (44), 81 (31), 79 (19), 77 (28), 69 (22), 65 (29), 55 (20), 41 (52), 39 (37), 29 (22), 27 (18).

• *β-Ionylidene acetaldehyde* **14c**

This compound has been obtained as a mixture of 7*E*,9*E* and 7*E*,9*Z* isomers (85:15) which have been already described [11, 32].

• *Preparation of aldehydes* **15–18** *from aldehydes* **14a,c**

The same experimental procedure was applied reacting the crude β-ionylidene acetaldehydes **14a,c** (1.8 mmol) with vinyllithiums **7a** or **7c** obtained at −78 °C in ether from vinyl iodides **6a-*E*** or **6c-*E*** (2 mmol) and *n*-butyllithium (2.2 mmol, 1.5 M in hexanes). After hydrolysis and usual work-up, the dehydration reaction was carried out on the crude hydroxyacetals as previously reported for **13a,c**. During this step, hydroquinone (0.9 mmol) was added to obtain complexes with retinal and its demethylated analogues. After 10 min, the mixture was extracted with ether, washed with brine and dried over $MgSO_4$. After evaporation of the solvents, the purification was carried out by precipitation in an ether/hexane mixture.

While retinal **18** [11, 33], 9-demethylretinal **16** [22b, 22d] and 13-demethylretinal **17** [22b,22d,34] have been perfectly described, only ^1H NMR spectra were reported for the nor-derivatives **15** [22d].

• *9,13-Bis(demethyl)retinal* **15** *(complementary data)*

Isomer 'all trans': ^{13}C NMR δ (ppm): 19.0 (C_3), 21.7 (C_5-CH_3), 28.8 (C_1-$2CH_3$), 33.3 (C_4), 34.0 (C_1), 39.6 (C_2), 128.8–151.9 (C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13} and C_{14}), 191.2 (C_{15}).

MS: *m/z* = 256 (8), 203 (7), 201 (8), 181 (13), 177 (11), 175 (12), 173 (11), 165 (29), 163 (22), 161 (17), 159 (20), 151 (15), 149 (25), 145 (26), 137 (23), 135 (20), 133 (29), 131 (24), 125 (27), 123 (42), 121 (43), 119 (22), 109 (100), 107 (60), 105 (56), 99 (10), 95 (73), 93 (56), 91 (89).

Concerning retinal and its isomers, when the reaction was performed without hydroquinone, the HPLC analysis in LC/MS mode (HP 1050 coupled with an Engine HP 5989A apparatus via an HP 59980B particle beam interface) was achieved using an Hypersil 5 μ column (20 cm × 4.6 mm, eluent: hexane/ether = 9:1, 0.5 mL/min). A rough evaluation of the isomeric distribution was done on the basis of the abundance of the radical cation *m/z* = 284 (t_R **A** = 24.6 min, t_R **C** = 18.9 min, t_R **E** = 14.6 min, t_R (9*Z*,13*Z*) = 15.4 min).

Synthesis of 2,4-dinitrophenylhydrazones **19** *and* **20**

2,4-Dinitrophenylhydrazine (223 mg, 1.1 mmol) was dissolved in 2 mL of water, 4 mL of 95% ethanol and 1 mL of concentrated sulfuric acid. To this solution was added the aldehyde **15** or **17** (0.94 mmol) dissolved in ethanol (2 mL). After 30 min at room temperature, the reaction mixture was filtered and the product collected. Recrystallization from ethanol gave red crystals of **19** or **20** as fairly stable compounds.

• *9,13-Bis(demethyl)retinal 2,4-dinitrophenylhydrazone* **19**

Isomer 'all trans': ^1H NMR δ (ppm): 1.04 (C_1-$2CH_3$, s), 1.37–1.69 ($2H_2$ and $2H_3$, m), 1.72 (C_5-CH_3, bs), 2.02 ($2H_4$, m), 6.02–6.84 (H_7, H_8, H_9, H_{10}, H_{11}, H_{12}, H_{13} and H_{14}, m), 7.77 (H_{15}, bd, $^3J_{1H}$ = 9.8), 7.91 (1H, d, $^3J_{1H}$ = 9.5), 8.27 (1H, dd, $^3J_{1H}$ = 9.5, $^4J_{1H}$ = 2.6), 9.05 (1H, d, $^4J_{1H}$ = 2.6), 11.15 (NH, bs).

^{13}C NMR δ (ppm): 19.1 (C_3), 21.8 (C_5-CH_3), 28.9 (C_1-$2CH_3$), 33.4 (C_4), 34.2 (C_1), 39.8 (C_2), 116.7–148.9 (C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15} and 6C).

MS: *m/z* = 212 (18), 211 (90), 196 (100), 168 (46), 167 (23), 153 (15), 141 (36), 115 (27), 77 (21), 63 (13), 51 (16), 43 (33), 39 (13).

• *13-Demethylretinal 2,4-dinitrophenylhydrazone* **20**

Isomer 'all trans': ^1H NMR δ (ppm) : 1.04 (C_1-$2CH_3$, s), 1.40–1.60 ($2H_2$-$2H_3$, m), 1.72 (C_5-CH_3, bs), 2.00 (C_9-CH_3, bs), 2.03 ($2H_4$, m), 6.00–7.10 (H_7, H_8, H_{10}, H_{11}, H_{12}, H_{13} and H_{14}, m), 7.82 (H_{15}, bd, $^3J_{1H}$ = 9.8), 7.93 (1H, d, $^3J_{1H}$ = 9.5), 8.29 (1H, dd, $^3J_{1H}$ = 9.5, $^4J_{1H}$ = 2.6), 9.10 (1H, d, $^4J_{1H}$ = 2.6), 11.18 (NH, bs).

^{13}C NMR δ (ppm): 12.8 (C_9-CH_3), 19.2 (C_3), 21.7 (C_5-CH_3), 28.9 (C_1-$2CH_3$), 33.1 (C_4), 34.2 (C_1), 39.6 (C_2), 116.4–150.0 (C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15} and 6C).

MS: m/z = 450 (69), 388 (20), 268 (48), 267 (24), 261 (19), 255 (11), 235 (14), 215 (13), 210 (18), 209 (13), 197 (21), 183 (46), 168 (18), 167 (25), 142 (27), 141 (23), 123 (24), 121 (29), 119 (67), 95 (38), 91 (100), 79 (58), 77 (54), 69 (52), 65 (28), 55 (61), 51 (10), 41 (69), 39 (10).

• *Reduction and acetylation of the nor-retinoid* **16**

The reduction of the aldehyde function was achieved, at room temperature, by adding $NaBH_4$ (1.1 mmol) to a solution of **16** (270 mg) in 5 mL of THF. After usual work-up, the crude alcohol was dissolved in triethylamine (1.5 mmol) and acetic anhydride (1 mmol) in the presence of DMAP (10% mol). After completion of the acetylation (monitored by TLC), the reaction mixture was filtered on neutral alumina. After evaporation, the residue was chromatographed on silica gel (eluent: hexane/ethyl acetate = 90:10) to give 223 mg of a red oil (71%).

• *9-Demethylretinol acetate* **21**

Isomer 'all trans': ^{1}H NMR δ (ppm): 1.02 (C_1-2CH_3, s), 1.41–1.67 ($2H_2$ and $2H_3$, m), 1.72 (C_5-CH_3, bs), 1.85 (C_{13}-CH_3, bs), 2.02 ($2H_4$, tb, $^3J_{2H}$ = 6.3), 2.05 (CH_3CO_2, s), 4.71 ($2H_{15}$, d, $^3J_{1H}$ = 7.2), 5.60 (H_{14}, bt, $^3J_{1H} \approx {}^3J_{2H}$ = 7.2), 6.10–6.64 (H_7, H_8, H_9, H_{10}, H_{11} and H_{12}, m).

^{13}C NMR δ (ppm): 12.5 (C_{13}-CH_3), 19.1 (C_3), 20.9 (CH_3CO_2), 21.7 (C_5-CH_3), 28.8 (C_1-2CH_3), 33.2 (C_4), 34.1 (C_1), 39.7 (C_2), 61.2 (C_{15}), 120.9–138.8 (C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13} and C_{14}), 170.9 (ester).

MS: m/z = 314 (10), 255 (3), 254 (2), 241 (2), 239 (6), 181 (12), 180 (11), 149 (58), 137 (11), 123 (15), 121 (13), 119 (12), 111 (37), 109 (30), 107 (19), 105 (20), 95 (26), 91 (30), 85 (24), 83 (32), 71 (28), 55 (24), 43 (100), 41 (83), 39 (52), 29 (28), 27 (24).

Minor isomer (meaningful signals): ^{1}H NMR δ (ppm): 4.60 ($2H_{15}$, d, $^3J_{1H}$ = 6.4); ^{13}C NMR δ (ppm): 60.2 (C_{15}), 170.2 (ester).

Acknowledgments

The authors are grateful to Chemetall GmbH, Continentale Parker, Schering and Rhône-Poulenc Companies for the gift of organometallic starting materials, to the GIS Medicaments and to the Conseil Général de Loire Atlantique (VL) for financial support.

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