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TETRAHEDRON

Ene Diiodo Acetals : Stereoselective Synthesis of Ene Hydroxy Acetals. Handy Access to Non Conjugated Dienals

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Abstract : After halogen-metal exchange reaction followed by condensation with carbonyl compounds, ene diiodo acetal **1** allow the stereoselective synthesis of ene hydroxy acetals **2** with *Z* configuration, in a two step procedure. Moreover, after dehydration, the intermediate diene acetals **3-4**, *via* an appropriated hydrolysis procedure, lead to pure non conjugated dienals **5**.

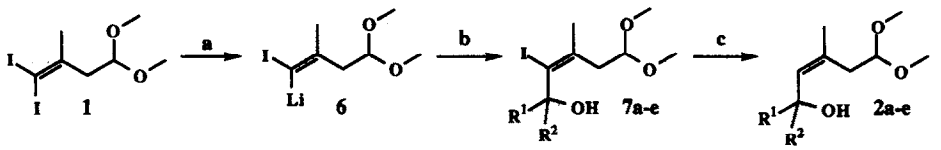
INTRODUCTION

In previous papers we have shown that ene lithio acetals are versatile reagents for the preparation of α -polyunsaturated aldehydes by polyvinylogation of carbonyl compounds.[1] Our interest in this field and to highlight the great reactivity of ene diiodo acetal **1**[2] led us to investigate the stereospecific synthesis of *Z* ene hydroxy acetals **2**. Moreover, the dehydration of these compounds **2**, *via* a mesylate intermediate, leads to diene acetals **3b-e** and **4a-e** ; then a well controlled hydrolysis procedure gives an handy access to non classical non conjugated aldehydes **5**.

RESULTS

Synthesis of ene hydroxy acetals 2 (Z)

The ene diiodo acetal **1** was submitted to a first iodine-lithium exchange reaction by action of *t*-butyllithium in dry diethyl ether at - 70 °C. The intermediate carbenoid **6** was converted into ene hydroxy iodo acetals **7a-e** after condensation with carbonyl compounds **8** and treatment with a mildly basic solution (Scheme 1, Table 1).



a) *t*-BuLi, Et_2O, -70 °C; **b)** R^1R^2CO **8a-e**, 5% Na_2CO_3; **c)** *t*-BuLi, Et_2O, -70 °C, 5% Na_2CO_3.

Scheme 1

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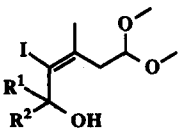
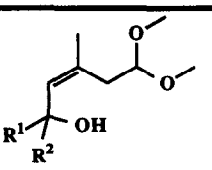
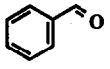
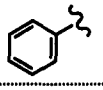
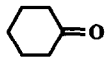
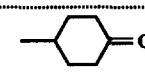
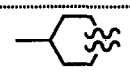
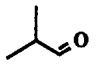
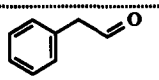
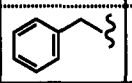
These new compounds **7**, obtained with good yield, offer an exclusive *E* configuration (determined by NMR Overhauser Effect). This stereoselective reaction is governed by an exclusive formation of *E* iodo carbenoid **6**, obtained intermediately by a favourable exchange of the iodine atom nearer the acetal group. This intermediate **6**, with *E* configuration may be stabilized by coordination of the lithium atom with the oxygen atoms of the acetal function.[3]

Table 1 Ene hydroxy iodo acetals *(E)* **7a-e** and Ene hydroxy acetals *(Z)* **2a-e**

 **8**	R^1	R^2	 **7**		 **2**	
			Compound	Yield %	Compound	Yield %[a]
 **8a**		H	**7a**	82	**2a**	82
 **8b**			**7b**	78	**2b**	77
 **8c**			**7c**	84	**2c**	77
 **8d**		H	**7d**	81	**2d**	78
 **8e**		H	**7e**	89	**2e**	89

a : Yield from ene diiodo acetal **1**.

The ene hydroxy iodo acetals **7a-e**, according to a second iodine-lithium exchange reaction, followed by hydrolysis, led to ene hydroxy acetals **2a-e** with *Z* configuration (Scheme 1, Table 1).

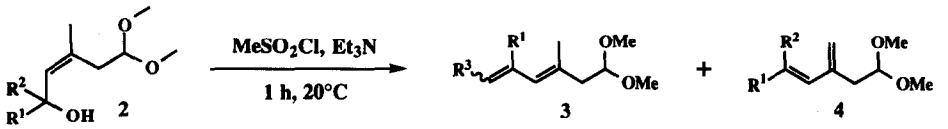
Synthesis of non conjugated dienals 5.

On the other hand, we described an original handy access to non conjugated dienals **5**. The synthesis of the non classical dienals **5** is performed from the ene hydroxy acetals **2** *via* the diene acetals **3** and **4**.[4]

In the literature, the dehydration of allylic alcohols has been previously described. This reaction has been done by using thioethers,[6] sulfones,[7] sulfoxides,[7-12] phosphorus derivatives[13] and mesylates.[14]

To carry out the dehydration of the ene hydroxy acetals **2**, we have applied the method described by E.J. Corey and D. Enders[14] using mesylates as intermediates. A methylene chloride solution of mesyl chloride is added at room temperature to a methylene chloride solution of ene hydroxy acetal **2** in the presence of

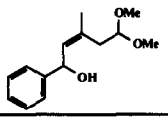
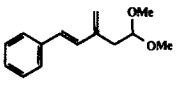
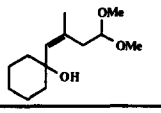
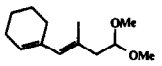
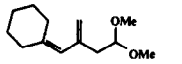
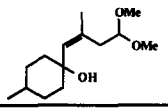
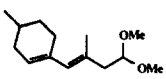
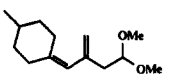
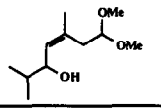
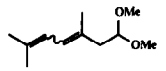
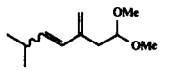
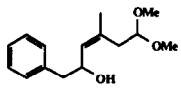
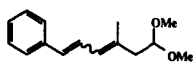
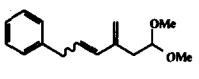
triethylamine. After flash chromatography, the product is isolated as a mixture of diene acetals **3** and **4** in different amounts depending on the starting material structure (Scheme 2, Table 2).



2 3 4

Scheme 2

Table 2 Diene acetals **3** and **4**

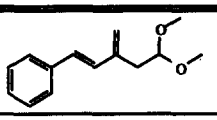
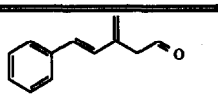
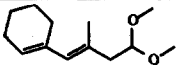
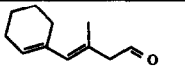
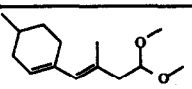
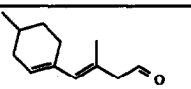
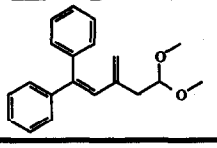
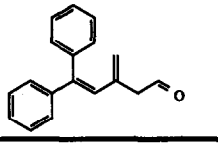
Ene hydroxy acetals **2**	Yield %	Diene acetals **3**			Diene acetals **4**		
		%		Z/E	%		Z/E
 **2a** (Z)	80				100	 **4a**	0/100
 **2b** (Z)	73	90	 **3b**	0/100	10	 **4b**	
 **2c** (Z)	73	90	 **3c**	0/100	10	 **4c**	
 **2d** (Z)	38	20	 **3d**		80	 **4d**	30/70
 **2e** (Z)	40	50	 **3e**	50/50	50	 **4e**	40/60

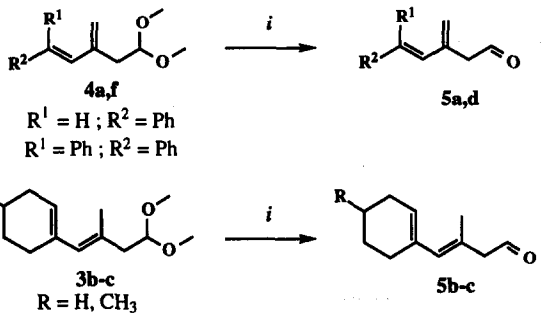
The diene acetals **3b-e** and **4a-e** are formed by dehydration reaction respectively by elimination of an hydrogen atom from the R^2 group (leading to the substituent R^3, Scheme 2) and by elimination of an hydrogen atom from the methyl group (leading to the methylene group). The percentages of **3** and **4** have been determined by NMR spectoscopy (for **3b-e** : by integration of the methyl group in position 3 of the main chain; for **4a-e** : by integration of the methylene group).

Non conjugated aldehydes are not very common and to our knowledge, the first synthesis was described by M. Julia and Coll. in 1966.[15] In the literature only some methods have been more recently described.[16]

For our part, we have applied the conditions described by K. L. Ford and E. J. Roskamp in 1992[17] for the hydrolysis of saturated acetals. This method, never used for the synthesis of non conjugated aldehydes, has been successful for hydrolyzing our diene acetals **3** and **4**, and has given non conjugated dienals **5** (Scheme 3) with good yield (Table 3).

Table 3 Non conjugated dienals **5**

Diene acetals	3-4	Dienals[4]	5	Yield %
	**4a** *(E)*		**5a** *(E)*	72
	**3b** *(E)*		**5b** *(E)*	80
	**3c** *(E)*		**5c** *(E)*	73
	**4f**		**5d**	79



i : $SnCl_2,2H_2O$; CH_2Cl_2; 2 h.

Scheme 3

The structural analysis of the new compounds **2-5** and **7** has been performed using standard methods and the configuration of the double bond has been determined by NMR Overhauser Effect.

CONCLUSION

Results reported in this paper show the great reactivity of ene diiodo acetal **1**, a choice reagent for stereospecific synthesis of ene hydroxy acetals **2** with an exclusive *Z* configuration. These compounds **2**, *via* a mesylate intermediate undergo an elimination reaction leading to diene acetals **3-4** which are good precursors for an original synthesis of non conjugated dienals **5**.

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 360 MHz for proton and at 50 MHz or at 90 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 500 mass spectrometer (CI : Chemical Ionisation with NH_3). Flash chromatography[18] 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 ketyl. *t*-Butyllithium solutions were titrated before use. [19] All reactions were carried out under dry argon. Microanalyses were performed by INSA laboratories, Rouen.

Synthesis of the ene hydroxy acetals 2 (Z)

General Procedure (I). To a solution of ene diiodo acetal **1** (0.80 g, 2.1 mmol) in Et_2O (9 ml) was added at -70 °C, under argon, *t*-butyllithium (1.7 M in pentane, 4.2 ml). The mixture was stirred for 1.5 h at -70 °C, then the carbonyl compound **8** (2.1 mmol) in dry Et_2O (2 ml) was added. After 0.5 h at -70 °C, the reaction mixture was warmed to 0 °C in 1.5 h and 5% Na_2CO_3 (3 ml) was added. After extraction with Et_2O, the organic solution was dried on $MgSO_4$. After evaporation of the solvent, the ene hydroxy iodo acetals **7a-e** were purified by flash chromatography (silica gel, petroleum ether/Et_2O : 70/30). Then, to a solution of compound **7** (1.8 mmol) in Et_2O (9 ml) was added at -70 °C, under argon, *t*-butyllithium (1.7 M in pentane, 5.4 mmol). After the usual treatment, the ene hydroxy acetals **2** (*Z* : 100%) were obtained.

The configuration *Z* (100%) of the double bond in position 3 has been determined by NMR Overhauser effect (by irradiation of methyl group substituting the carbon 3, observation of NOE on H^4).

Ene hydroxy iodo acetals 7

(3E)-1,1-Dimethoxy-5-hydroxy-4-iodo-3-methyl-5-phenyl-pent-3-ene **7a**. Yellow oil. **^{1}H NMR** (200 MHz, C_6D_6) : 1.94 (s, CH_3) ; 2.44 (dd, 1H, CH_2, J = 4.8 ; J = 13.7) ; 2.67 (dd, 1H, CH_2, J = 5.8 ; J = 13.7) ; 2.97 (s, 2xOCH_3) ; 4.22 (dd, CH, J = 4.8 ; J = 5.8) ; 5.44 (s, CH) ; 7.05-7.45 (m, ArH) ; **^{13}C NMR** (50 MHz, C_6D_6) : 31.23 (CH_3) ; 38.77 (CH_2) ; 53.31 and 53.64 (OCH_3) ; 73.60 (CH) ; 103.04 (CH) ; 116.14 (C=) ; 126.60 (C-Ar) ; 127.43 (C-Ar) ; 128.30 (C-Ar) ; 138.44 (C-Ar) ; 143.55 (C=) ; **IR** : 3358 ; 2936 ; 1720 ; 1622 ; 1450 ; 1374 ; 1110 ; 1026 ; **MS (m/z)** : 380 (MNH_4^+, 50%) ; 362 (MNH_4^+-H_2O, 15%) ; 345 (MH^+-H_2O,

100%) ; 75 ($CH(OCH_3)_2^+$, 80%) ; **Anal. Calcd.** for $C_{14}H_{19}IO_3$: C, 46.41 ; H, 5.25. Found : C, 46.74 ; H, 5.52.

(3E)-1,1-Dimethoxy-4-(1-hydroxy-cyclohexyl)-4-iodo-3-methyl-but-3-ene **7b**. Yellow oil. **^{1}H NMR** : 1.45-1.90 (m, 3xCH_2, cyclohexyl) ; 1.98 (s, CH_3) ; 2.50 (m, 2xCH_2, cyclohexyl) ; 2.94 (s, 2xOCH_3) ; 3.13 (d, CH_2, J = 5.7) ; 3.84 (s, OH) ; 4.22 (t, CH, J = 5.7) ; **^{13}C NMR** (50 MHz, C_6D_6) : 22.15 (CH_2, cyclohexyl) ; 25.36 (CH_2, cyclohexyl) ; 35.45 (CH_3) ; 38.29 (CH_2, cyclohexyl) ; 39.31 (CH_2) ; 52.94 (OCH_3) ; 77.79 (C, cyclohexyl) ; 102.29 (CH) ; 121.04 (C=) ; 134.69 (C=) ; **IR** : 3438 ; 2922 ; 1600 ; 1446 ; 1376 ; 1116 ; 1062 ; **MS (m/z)** : 372 (MNH_4^+-, 15%) ; 337 (MH^+-H_2O, 10%) ; 323 (MH^+-CH_3OH, 25%) ; 291 (MH^+-2CH_3OH, 100%) ; 196 (MH^+-CH_3OH-I, 10%) ; 75 ($CH(OCH_3)_2^+$, 60%) ; **Anal. Calcd.** for $C_{13}H_{23}IO_3$: C, 44.07 ; H, 6.50. Found : C, 44.28 ; H, 6.62.

(3E)-1,1-Dimethoxy-4-(1-hydroxy-4-methyl-cyclohexyl)-4-iodo-3-methyl-but-3-ene **7c**. The ^{1}H NMR spectrum has shown the presence of two isomers (A and B) in a 80/20 ratio corresponding to the hydroxy group in an axial or equatorial position. Yellow oil. **^{1}H NMR** : isomer A (80%) : 0.92 (d, CH_3, J = 6.4) ; 1.25-1.80 (m, 4xCH_2, cyclohexyl) ; 1.99 (s, CH_3) ; 2.15-2.25 (m, CH, cyclohexyl) ; 2.95 (s, 2xOCH_3) ; 3.05 (d, CH_2, J = 5.7) ; 3.84 (s, OH) ; 4.23 (t, CH, J = 5.7) ; isomer B (20%) : 1.07 (d, CH_3, J = 7.1) ; 1.25-1.80 (m, 4xCH_2, cyclohexyl) ; 1.99 (s, CH_3) ; 2.15-2.25 (m, CH-cyclohexyl) ; 2.95 (s, 2xOCH_3) ; 3.05 (d, CH_2, J = 5.7) ; 3.84 (s, OH) ; 4.23 (t, CH, J = 5.7) ; **^{13}C NMR** (50 MHz, C_6D_6) : : isomer A (80%) : 22.82 (CH_3) ; 31.01 (CH_2, cyclohexyl) ; 31.97 (CH, cyclohexyl) ; 35.82 (CH_3) ; 38.60 (CH_2, cyclohexyl) ; 39.63 (CH_2) ; 53.23 (OCH_3) ; 77.79 (C, Cyclohexyl) ; 102.59 (CH) ; 121.09 (C=) ; 135.26 (C=) ; isomer B (20%): 22.82 (CH_3) ; 31.01 (CH_2, cyclohexyl) ; 31.97 (CH, cyclohexyl) ; 35.82 (CH_3) ; 38.60 (CH_2, cyclohexyl) ; 39.63 (CH_2) ; 53.23 (OCH_3) ; 78.51 (C, Cyclohexyl) ; 102.59 (CH) ; 121.64 (C=) ; 134.84 (C=) ; **IR** : 3438 ; 2918 ; 1604 ; 1438 ; 1372 ; 1116 ; 1056 ; **MS (m/z)** : 386 (MNH_4^+, 5%) ; 349 (MH^+-H_2O, 5%) ; 336 (MNH_4^+-H_2O-CH_3OH, 30%) ; 319 (MH^+-H_2O-CH_3OH, 10%) ; 304 (MNH_4^+-H_2O-2 CH_3OH, 100%) ; 177 (MNH_4^+-H_2O-2CH_3OH-I, 5%) ; 75 ($CH(OCH_3)_2^+$, 100%). ; **Anal. Calcd.** for $C_{14}H_{25}IO_3$: C, 45.65 ; H, 6.79. Found : C, 45.78 ; H, 6.85.

(3E)-1,1-Dimethoxy-3,6-dimethyl-5-hydroxy-4-iodo-hept-3-ene **7d**. Yellow oil. **^{1}H NMR** (200 MHz, C_6D_6) : 0.87 (d, CH_3, J= 6.7) ; 1.17 (d, CH_3, J = 6.5) ; 1.70 (qd, CH, J = 6.5 ; J = 8.9) ; 1.94 (s, CH_3) ; 2.28 (dd, 1H, CH_2, J = 4.4 ; J = 13.7) ; 2.75 (dd, 1H, CH_2, J = 6.4 ; J = 13.7); 2.98 (s, 2xOCH_3) ; 3.45 (d, CH, J = 8.9) ; 4.19 (dd, CH, J = 4.4 ; J = 6.4) ; **^{13}C NMR** (50 MHz, C_6D_6) : 18.78 (CH) ; 18.96 (CH_3) ; 35.73 (CH_3) ; 39.06 (CH_2) ; 53.74 (OCH_3) ; 77.73 (CH) ; 103.35 (CH) ; 117.33 (C=) ; 137.82 (C=) ; **IR** : 3456 ; 2952 ; 1622 ; 1466 ; 1364 ; 1114 ; 1036 ; **MS (m/z)** : 346 (MNH_4^+, 30%) ; 328 (MNH_4^+-H_2O, 5%) ; 311 (MH^+-H_2O, 15%) ; 75 ($CH(OCH_3)_2^+$, 100%) ; **Anal. Calcd.** for $C_{11}H_{21}IO_3$: C, 40.24 ; H, 6.40. Found : C, 40.38 ; H, 6.55.

(3E)-1,1-Dimethoxy-5-hydroxy-4-iodo-3-methyl-6-phenyl-hex-3-ene **7e**. Yellow oil. **^{1}H NMR** : (200 MHz, C_6D_6) : 1.87 (s, CH_3) ; 2.14 (dd, 1H, CH_2, J = 4.2 ; J = 13.5) ; 2.37 (dd, 1H, CH_2, J = 6.4 ; J = 13.5) ; 2.91 (s, 2xOCH_3) ; 2.98 (d, CH_2, J = 6.5) ; 3.86 (t, CH, J = 6.5) ; 4.17 (dd, CH, J = 4.2 ; J = 6.4) ; 7.05-7.25 (m, ArH) ; **^{13}C NMR** (50 MHz, C_6D_6) : 31.28 (CH_3) ; 38.86 (CH_2) ; 44.99 (CH_2) ; 53.17 and 53.52 (OCH_3) ; 73.42 (CH) ; 103.35 (CH) ; 116.69 (C=) ; 126.65 (C-Ar) ; 128.79 (C-Ar) ; 130.03 (C-Ar) ; 137.98 (C-Ar) ;

138.28 (C=) ; **IR** : 3456 ; 2926 ; 1602 ; 1452 ; 1368 ; 1116 ; 1030 ; **MS (m/z)** : 394 (MNH_4^+, 100%) ; 376 (MNH_4^+-H_2O, 10%) ; 359 (MH^+-H_2O, 15%) ; 344 (MH^+-H_2O- CH_3OH, 10%) ; 267 (MNH_4^+-I, 15%) ; 75 ($CH(OCH_3)_2^+$, 100%) ; **Anal. Calcd.** for $C_{15}H_{21}IO_3$: C, 47.87 ; H, 5.58. Found : C, 47.95 ; H, 5.67.

Ene hydroxy acetals 2 *(Z)*

(3Z)-1,1-Dimethoxy-5-hydroxy-3-methyl-5-phenyl-pent-3-ene **2a**. Yellow oil. **^{1}H NMR** (200 MHz, C_6D_6) : 1.62 (d, CH_3, J = 1.3) ; 2.25 (dd, 1H, CH_2, J = 4.4 ; J = 13.6) ; 2.65 (dd, 1H, CH_2, J = 6.6; J = 13.6) ; 3.05 (s, 2xOCH_3) ; 4.55 (dd, CH, J = 4.4 ; J =6.6) ; 5.45 (d, CH, J = 8.7) ; 5.60 (d, CH=, J = 8.7) ; 7.05-7.45 (m, ArH) ; **^{13}C NMR** (50 MHz, C_6D_6) : 24.36 (CH_3) ; 36.34 (CH_2) ; 52.56 and 53.71 (OCH_3) ; 69.68 (CH) ; 103.32 (CH) ; 126.43 (C-Ar) ; 127.11 (C-Ar) ; 128.47 (C-Ar) ; 132.72 (CH=) ; 133.64 (C-Ar) ; 145.13 (C=) ; **IR** : 3418 ; 2934 ; 1720 ; 1660 ; 1604 ; 1450 ; 1376 ; 1118 ; 1062 ; **MS (m/z)** : 254 (MNH_4^+-, 10%) ; 236 (MNH_4^+-H_2O, 15%) ; 219 (MH^+-H_2O, 30%) ; 75 ($CH(OCH_3)_2^+$, 100%) ; **Anal. Calcd.** for $C_{14}H_{20}O_3$: C, 71.18 ; H, 8.77. Found : C, 71.30 ; H, 8.88.

1,1-Dimethoxy-4-(1-hydroxy-cyclohexyl)-3-methyl-but-3-ene **2b**. Yellow oil. **^{1}H NMR** (200 MHz, C_6D_6) : 1.42-1.60 (m, 2xCH_2, cyclohexyl) ; 1.64 (d, CH_3, J = 1.1) ; 1.75-1.85 (m, 2xCH_2, cyclohexyl) ; 2.83 (d, CH_2, J = 5.7) ; 3.05 (s, 2xOCH_3) ; 3.38 (s, OH) ; 4.36 (t, CH, J = 5.7) ; 5.42 (d, CH=, J = 1.1) ; **^{13}C NMR** (50 MHz, C_6D_6) : 22.48 (CH_2, cyclohexyl) ; 25.72 (CH_3) ; 26.10 (CH_2, cyclohexyl) ; 36.16 (CH_2, cyclohexyl) ; 40.23 (CH_2) ; 53.06 (OCH_3) ; 71.51 (C, cyclohexyl) ; 103.12 (CH) ; 130.08 (C=) ; 135.09 (CH=) ; **IR** : 3474 ; 2928 ; 1658 ; 1444 ; 1372 ; 1116 ; 1066 ; **MS (m/z)** : 246 (MNH_4^+, 5%) ; 228 (MNH_4^+-H_2O, 30%) ; 211 (MH^+-H_2O, 35%) ; 196 (MNH_4^+-H_2O-CH_3OH, 23%) ; 179 (MH^+-H_2O-CH_3OH, 65%) ; 164 (MNH_4^+-H_2O-2CH_3OH, 82%) ; 75 ($CH(OCH_3)_2^+$, 100%) ; **Anal. Calcd.** for $C_{13}H_{24}O_3$: C, 68.42 ; H, 10.53. Found : C, 68.57 ; H, 10.66.

(3Z)-1,1-Dimethoxy-4-(1-hydroxy-4-methyl-cyclohexyl)-3-methyl-but-3-ene **2c**. Yellow oil. **^{1}H NMR** (200 MHz, C_6D_6) : 0.97 (d, CH_3, J = 6.5) ; 1.30-1.50 (m, 2xCH_2 + CH, cyclohexyl) ; 1.63 (d, CH_3, J = 1.4) ; 1.70-1.85 (m, 2xCH_2, cyclohexyl) ; 2.84 (d, CH_2, J = 5.6) ; 3.21 (s, 2xOCH_3) ; 4.35 (t, CH, J = 5.6) ; 5.32 (d, CH=, J = 1.4) ; **^{13}C NMR** (50 MHz, C_6D_6) : 22.88 (CH_3) ; 25.86 (CH_3) ; 30.51 (CH_2, cyclohexyl) ; 32.35 (CH, cyclohexyl) ; 36.00 (CH_2, cyclohexyl) ; 39.65 (CH_2) ; 53.01 (OCH_3) ; 71.09 (C, cyclohexyl) ; 103.03 (CH) ; 129.70 (C=) ; 137.43 (CH=) ; **IR** : 3472 ; 2920 ; 1669 ; 1442 ; 1372 ; 1116 ; 1060 ; **MS (m/z)** : 260 (MNH_4^+, 5%) ; 242 (MNH_4^+-H_2O, 25%) ; 225 (MH^+-H_2O, 30%) ; 193 (MH^+-H_2O-CH_3OH, 45%) ; 178 (MNH_4^+-H_2O-2CH_3OH, 90%) ; 75 ($CH(OCH_3)_2^+$, 100%) ; **Anal. Calcd.** for $C_{14}H_{26}O_3$: C, 69.42 ; H, 10.74. Found : C, 69.55 ; H, 10.90.

(3Z)-1,1-Dimethoxy-3,6-dimethyl-5-hydroxy-hept-3-ene **2d**. Yellow oil. **^{1}H NMR** (200 MHz, C_6D_6) : 1.06 (d, 1H, CH_2, J = 6.7) ; 1.14 (d, 1H, CH_2, J = 6.6) ; 1.65 (d, CH_3, J = 1.4) ; 1.79 (m, CH) ; 2.27 (dd, 1H, CH_2, J = 3.6 ; J = 13.4) ; 2.73 (dd, 1H, CH_2, J = 7.3; J = 13.4) ; 2.64 (s, OH) ; 3.12 (s, 2xOCH_3) ; 4.05 (dd, CH, J = 7.1 ; J = 8.4) ; 4.30 (dd, CH, J = 3.6 ; J = 7.3) ; 5.49 (d, CH=, J = 8.4) ; **^{13}C NMR** (50 MHz, C_6D_6) : 16.74 (CH_3) ; 24.36 (CH_3) ; 34.25 (C=) ; 36.39 (CH_2) ; 52.12 and 53.98 (OCH_3) ; 72.42 (CH) ; 103.18 (CH) ; 131.68 (CH=) ; 134.06 (CH) ; **IR** : 3468 ; 2954 ; 1664 ; 1444 ; 1366 ; 1118 ; 1062 ; **MS (m/z)** :

220 (MNH_4^+, 15%) ; 202 (MNH_4^+-H_2O, 5%) ; 185 (MH^+-H_2O, 20%) ; 153 (MH^+-H_2O-CH_3OH, 55%) ; 75 ($CH(OCH_3)_2^+$, 100%) ; **Anal. Calcd.** for $C_{11}H_{22}O_3$: C, 65.35 ; H, 10.89. Found : C, 65.52 ; H, 11.10.

(3Z)-1,1-Dimethoxy-5-hydroxy-3-methyl-6-phenyl-hex-3-ene **2e**. Yellow oil. **^{1}H NMR** (200 MHz, C_6D_6) : 1.59 (d, CH_3, J = 1.3) ; 2.00 (dd, 1H, CH_2, J = 3.8 ; J = 13.5) ; 2.52 (dd, 1H, CH_2, J = 7.1 ; J = 13.5) ; 2.82 (dd, 1H, CH_2, J = 5.9 ; J = 13.4) ; 2.95 (dd, 1H, CH_2, J = 4.1 ; J = 13.4) ; 3.00 (s, 2xOCH_3) ; 4.15 (dd, CH, J = 3.8 ; J = 7.1) ; 4.59 (m, CH) ; 5.48 (d, CH=, J = 8.4) ; 7.05-7.20 (m, ArH) ; **^{13}C NMR** (50 MHz, C_6D_6) : 24.33 (CH_3) ; 36.40 (CH_2) ; 44.13 (CH_2) ; 52.26 and 53.89 (OCH_3) ; 85.85 (CH) ; 103.26 (CH) ; 126.36 (CH=) ; 128.44 (C-Ar) ; 130.06 (C-Ar) ; 132.16 (C-Ar) ; 133.87 (C-Ar) ; 139.11 (C=) ; **IR** : 3426 ; 2934 ; 1664 ; 1602 ; 1452 ; 1366 ; 1118 ; 1042 ; **MS (m/z)** : 268 (MNH_4^+, 20%) ; 250 (MNH_4^+-H_2O, 15%) ; 233 (MH^+-H_2O, 10%) 201 (MH^+-H_2O-MeOH, 5%) ; 75 ($CH(OCH_3)_2^+$, 100%) ; **Anal. Calcd.** for for $C_{15}H_{22}O_3$: C, 72.00 ; H, 8.81. Found : C, 72.15 ; H, 8.96.

***Synthesis of the non conjugated dienals* 5**

General Procedure (II). To a solution of ene hydroxy acetals **2** (2.2 mmol) in CH_2Cl_2 (5 ml) was added, at room temperature and under argon, triethylamine (0.77 g, 7.6 mmol). Then, mesyl chloride (0.58 g, 5.1 mmol) in CH_2Cl_2 (1 ml) was added. After one hour at room temperature, the reaction mixture is treated by 5% Na_2CO_3. After extraction with CH_2Cl_2, the organic layer was washed with an aqueous saturated solution of $NaHCO_3$. After the usual treatment, the crude product was purified by flash chromatography (florisil, petroleum ether/Et_2O : 95/5). The percentages of acetals **3** and **4** have been determined by ^{1}H NMR spectroscopy. Before the following hydrolysis reaction, the diene acetals **3b-c** were purified from the mixture (**3b-c/4b-c** : 90/10) by flash chromatography (desactivated silica gel, petroleum ether/ether : 98/2).

To a suspension of $SnCl_2$,$2H_2O$ (0.190 g, 0.8 mmol) in CH_2Cl_2 (10 ml) was added, at 0 °C, a solution of diene acetals **3b-c** or **4a,f** in CH_2Cl_2 (5 ml). After 2 h at room temperature, H_2O was added (5 ml). After extraction with CH_2Cl_2 and the usual treatment, the residue was chromatographed on silica gel (petroleum ether/ether : 95/5). For the dienals **5b-c**, the *E* configuration of the double bond in position 3 has been determined by NMR Overhauser effect (by irradiation of H^2, observation of NOE on H^4).

3-Methylene-5-phenyl-pent-4-enal **5a**. Red liquid. **^{1}H NMR** (360 MHz, C_6D_6) : 2.86 (d, 2H, CH_2, J = 1.5) ; 4.82 (s, 1H, CH_2=) ; 5.07 (s, 1H, CH_2=) ; 6.39 (d, 1H, CH=, J = 16.3) ; 6.66 (d, 1H, CH=, J = 16.3) ; 7.05-7.25 (m, 5H, Ar-H) ; 9.29 (t, -CHO, J = 1.5) ; **^{13}C NMR** (90 MHz, C_6D_6) : 47.41 ($\underline{C}H_2$) ; 120.38 ($\underline{C}H_2$=) ; 126.99 ($\underline{C}$-Ar) ; 127.33 ($\underline{C}$-Ar) ; 128.84 ($\underline{C}$-Ar) ; 130.22 ($\underline{C}$H=) ; 130.38 ($\underline{C}$H=) ; 137.03 ($\underline{C}$-Ar) ; 138.00 ($\underline{C}$=) ; 198.26 (-$\underline{C}$HO) ; **IR** : 2918 ; 1722 ; 1602 ; 1448 ; 1332 ; 1044 ; **MS (m/z)** : 172 (M^+, 40%) ; 129 M^+- CH_2CHO, 100%) ; **HRMS Calcd.** for $C_{12}H_{12}O$: 172.0888, Found : 172.0916 ; **Anal. Calcd.** for $C_{12}H_{12}O$: C, 83.72 ; H, 6.97. Found : C, 83.84 ; H, 7.03.

4-(Cyclohex-1-enyl)-3-methyl-but-3-enal **5b**. Red liquid. **^{1}H NMR** (360 MHz, C_6D_6) : 1.40-1.60 (m, 4H, $2CH_2$) ; 1.63 (d, 3H, CH_3, J = 1.1) ; 1.90-2.10 (m, 4H, $2CH_2$) ; 2.60 (d, 2H, CH_2, J = 2.3) ; 5.52 (m, 2H, 2CH=) ; 9.29 (t, 1H, -CHO, J = 2.3) ; **^{13}C NMR** (90 MHz, C_6D_6) : 8.66 ($\underline{C}H_3$) ; 22.42 ($\underline{C}H_2$) ; 23.14 ($\underline{C}H_2$) ; 25.74 ($\underline{C}H_2$) ; 29.29 ($\underline{C}H_2$) 55.16 ($\underline{C}H_2$) ; 126.62 ($\underline{C}$=) ; 127.23 ($\underline{C}$H=) ; 133.22 ($\underline{C}$H=) ; 135.12 ($\underline{C}$=) ;

198.38 (-CHO) ; **IR** : 2924 ; 1722 ; 1648 ; 1436 ; 1132 ; 1052 ; **MS (m/z)** : 164 ($M^{+\cdot}$, 22%) ; 135 (M^{+}-CHO, 11%) ; 121 (M^{+}- CH_2CHO, 100%) ; **HRMS Calcd.** for $C_{11}H_{16}O$: 164.1201, Found : 164.1224 ; **Anal. Calcd.** for $C_{11}H_{16}O$: C, 80.49 ; H, 9.75. Found : C, 80.56 ; H, 9.83.

4-(4-Methyl-cyclohex-1-enyl)-3-methyl-but-3-enal **5c** . Red liquid. **^{1}H NMR** (360 MHz, C_6D_6) : 0.94 (d, 3H, CH_3, J = 6.2) ; 1.10-1.30 (m, 1H, CH) ; 1.50-1.80 (m, 2H, CH_2) ; 1.82 (d, 3H, CH_3, J = 1.2) ; 2.05-2.25 (m, 4H, 2 CH_2) ; 3.05 (d, 2H, CH_2, J = 2.4) ; 5.49 (d, 1H, CH=, J = 1.2) ; 5.69 (m, 1H, CH=) ; 9.29 (t, 1H, -CHO, J = 2.4) ; **^{13}C NMR** (90 MHz, C_6D_6) : 18.72 ($\underline{C}H_3$) ; 21.59 ($\underline{C}H_3$) ; 27,93 ($\underline{C}H$) ; 28.94 ($\underline{C}H_2$) ; 30.97 ($\underline{C}H_2$) ; 34.02 ($\underline{C}H_2$) ; 55.13 ($\underline{C}H_2$) ; 125.89 ($\underline{C}$=) ; 127.01 ($\underline{C}$H=) ; 133.00 ($\underline{C}$H=) ; 134.37 ($\underline{C}$=) ; 200.22 (-$\underline{C}$HO) ; **IR** : 2950 ; 1722 ; 1648 ; 1434 ; 1376 ; 1012 **MS (m/z)** : 178 ($M^{+\cdot}$, 42%) ; 149 (M^{+}-CHO, 27%) ; 135 (M^{+}- CH_2CHO, 100%); **HRMS Calcd.** for $C_{12}H_{18}O$: 178.1358, Found : 178.1356 ; **Anal. Calcd.** for $C_{12}H_{18}O$: C, 80.89 ; H, 10.11. Found : C, 80.95 ; H, 10.23.

5,5-Diphenyl-3-methylene-pent-4-enal **5d**. Red liquid. **^{1}H NMR** (360 MHz, C_6D_6) : 2.57 (d, 2H, CH_2, J = 1.8) ; 4.80 (s, 1H, CH_2=) ; 5.08 (s, 1H, CH_2=) ; 6.55 (s, 1H, CH=) ; 7.05-7.25 (m, 10H, Ar-H) ; 9.16 (t, 1H, -CHO, J = 1.8) ; **^{13}C NMR** (90 MHz, C_6D_6) : 49.68 ($\underline{C}H_2$) ; 122.14 ($\underline{C}H_2$=) ; 126.85 ($\underline{C}$-Ar) ; 127.93 ($\underline{C}$-Ar) ; 128.45 ($\underline{C}$-Ar) ; 130.48 ($\underline{C}$H=) ; 138.10 ($\underline{C}$-Ar) ; 140.43 ($\underline{C}$=) ; 143.14 ($\underline{C}$=) ; 197.55 (-$\underline{C}$HO) ; **IR** : 3024 ; 1722 ; 1598 ; 1444 ; 1384 ; 1074 ; **MS (m/z)** : 248 ($M^{+\cdot}$, 35%) ; 219 (M^{+}-CHO, 22%) ; 205 (M^{+}- CH_2CHO, 100%) ; **HRMS Calcd.** for $C_{17}H_{24}O$: 248.1201, Found : 248.1189 ; **Anal. Calcd.** for $C_{17}H_{24}O$: C, 87.10 ; H, 6.45. Found : C, 87.36 ; H, 6.68.

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