Efficient Ruthenium-Catalysed Synthesis of 3-Hydroxy-1-propen-1-yl Benzoates: En Route to an Improved Isomerization of 2-Propyn-1-ols into α,β-Unsaturated Aldehydes

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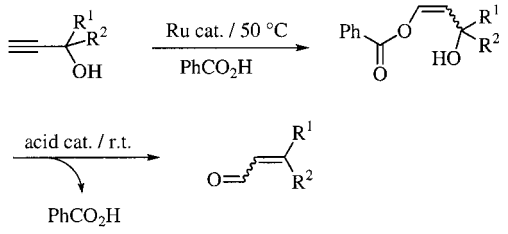
Keywords: Ruthenium / *anti*-Markovnikov addition / Alkynes / Alcohols / 3-Hydroxy enol esters / Aldehydes

A two-step ruthenium(II) and acid-catalysed one-pot selective transformation of 2-propyn-1-ols into α,β-unsaturated aldehydes has been developed. The complex [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$] (dppe = $Ph_2PCH_2CH_2PPh_2$) is an efficient precatalyst for the *anti*-Markovnikov addition of benzoic acid to 2-propyn-1-ols with the formation of 3-hydroxy-1-propen-1-yl benzoates in good yields. The latter readily undergo rapid transformation into α,β-unsaturated aldehydes on treatment with a catalytic amount of an acid such as PTSA or HBF_4 at room temperature.

Introduction

In the field of activation of simple or elaborated molecules, ruthenium derivatives have a tremendous potential in organic synthesis to promote catalytic reactions under mild conditions and with high selectivity.[1] The selective formation of C−O bonds *via* electrophilic activation of alkynes by ruthenium(II) catalysts[2] has been used as a powerful tool for the preparation of enol esters,[3] furans[4] and saturated aldehydes[5] from simple alkynes, whereas β-oxopropyl esters can be obtained from 2-propyn-1-ols.[6] We have recently pointed out that slight modifications of the catalyst precursor allow the control of the regio- and stereoselective *anti*-Markovnikov addition of carboxylic acids to terminal alkynes with the formation of (*Z*)-1-alken-1-yl carboxylates.[7] Advantage of the latter reaction has been taken for the selective isomerization of propargylic alcohols to α,β-unsaturated aldehydes in two steps.[8]

We now report a new one pot, two step catalytic transformation of propargylic alcohols into α,β-unsaturated aldehydes based on: i) the *anti*-Markovnikov addition of benzoic acid to a variety of 2-propyn-1-ols at low temperature in the presence of (dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$ as ruthenium catalyst to afford novel 3-hydroxy-1-propen-1-yl benzoates, and ii) the treatment of these functional esters with a catalytic amount of acid (HBF_4 or *p*-$MeC_6H_4SO_3H$) which leads to total conversion into α,β-unsaturated aldehydes according to Equation 1.



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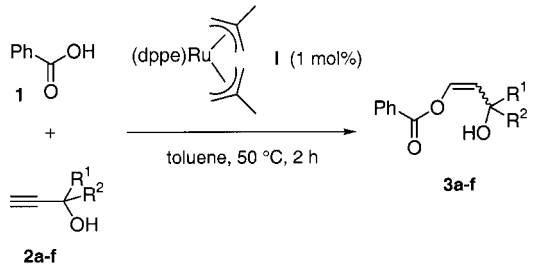
The present paper brings novelty and improvement with respect to our initial results[8] in the search for methods for the isomerization of 2-propyn-1-ols into α,β-unsaturated aldehydes, since our current method not only permits the isolation and characterization of the intermediate enol esters but also allows the acid-catalysed transformation to be conducted at room temperature in contrast to the thermal method which requires a reaction temperature of 110 °C.

Results and Discussions

Catalytic Synthesis of 3-Hydroxy-1-propen-1-yl Benzoates

The reaction of 5 mmol of benzoic acid **1** with 5 mmol of 2-methylbut-3-yn-2-ol **(2a)** ($R^1 = R^2 = Me$) in toluene at 50 °C for 2 h in the presence of 0.05 mmol of [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$] **(I)** led to the complete conversion of the starting propynylic alcohol with the selective formation of 3-hydroxy-1-propen-1-yl benzoate **3a** which was subsequently isolated in 51% yield with a *Z*/*E* ratio of 81:19 (Scheme 1).



Scheme 1. Catalytic addition of benzoic acid to propynols

Similarly, more sterically hindered propargylic alcohols **2b−f** (Table 1) were treated with benzoic acid **1** in the presence of 1 mol-% of **I** at 50 °C to produce the corresponding 3-hydroxy enol esters **3b−f**. Thus, the reaction of 5 mmol of the dialkyl disubstituted 2-propyn-1-ol **2b**, or 5 mmol of the propynylic alcohols **2c** and **2d** containing a carbon-car-

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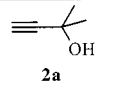
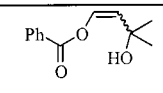
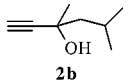
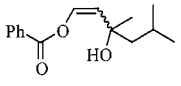
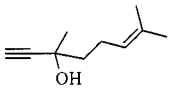
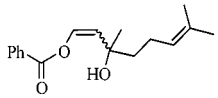
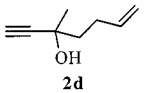
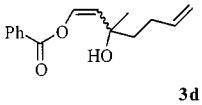
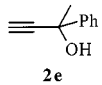
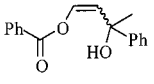
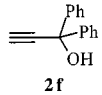
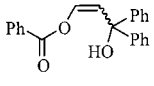
Table 1. Anti-Markovnikov addition of benzoic acid to 2-propyn-1-ols **2a**−**f** catalysed by complex **I**[a]

2-propyn-1-ol	3-hydroxy-1-propen-1-yl benzoate	isolated yield (%)	isomer ratio *Z*/*E*
 **2a**	 **3a**	51	81/19 86/14[b]
 **2b**	 **3b**	82	82/18
 **2c**	 **3c**	83	87/13 85/15[b]
 **2d**	 **3d**	71	100/0
 **2e**	 **3e**	90	67/33 70/30[b]
 **2f**	 **3f**	79	60/40 63/37[b]

[a] General conditions: 2-propyn-1-ol 2 (5 mmol), benzoic acid (5 mmol), (dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$ **I** (1 mol-%, 0.05 mmol), toluene (3 mL), 50 °C, 2 h; *Z*/*E* ratio determined by ^{1}H NMR spectroscopy. − [b] *Z*/*E* ratio for experiments carried out at 70 °C.

bon double bond, with 5 mmol of benzoic acid **1** under the same conditions afforded 82, 83 and 71% of **3b**, **3c** and **3d**, respectively. The propynols **2e** and **2f**, with at least one phenyl group at the propargylic position, led to the isolation of 90 and 79% of the corresponding 3-hydroxy-1-propen-1-yl esters **3e** and **3f**. These experiments show that the *anti*-Markovnikov addition of benzoic acid to various 2-propyn-1-ols can be selectively performed and controlled at 50 °C in the presence of [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$] as catalyst. These results contrast directly with our previous results with [(dppb)Ru(η^3-$CH_2C(Me)CH_2)_2$] (dppb = $Ph_2P(CH_2)_4PPh_2$) as precatalyst, which led to the addition of the carboxylate at C(2) of the triple bond and the formation of β-oxopropyl esters.[2c,7]

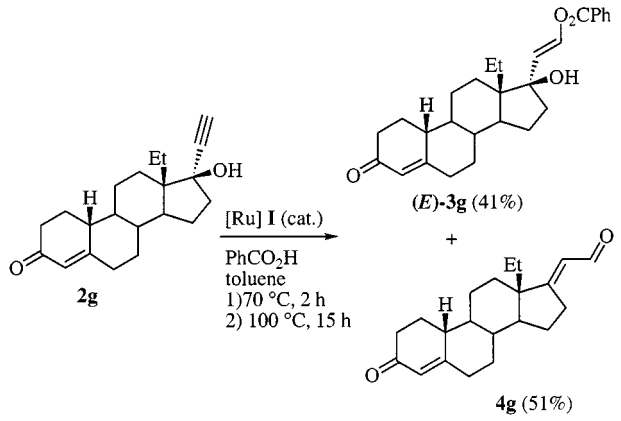
It is noteworthy that the (*Z*)-stereoisomer was always obtained as the major ester. However, the *Z*/*E* ratio was strongly dependent on the nature of the substituents at the propargylic position: substitution by alkyl groups afforded good *Z*/*E* ratios of 81:19, 82:18, 87:13, and 100:0 for **3a** (R^1 = R^2 = Me), **3b** [R^1 = Me, R^2 = $CH_2CH(Me)_2$], **3c** (R^1 = Me, R^2 = $CH_2CH_2CH{=}CMe_2$) and **3d** (R^1 = Me, R^2 = $CH_2CH_2CH{=}CH_2$), respectively, whereas the presence of phenyl groups dramatically decreased the selectivity with *Z*/*E* ratios of 67:33 for **3e** (R^1 = Me, R^2 = Ph) and 60:40 for **3f** (R^1 = R^2 = Ph) (Table 1).

It should be noted that in a previous communication we reported the presence of 3-hydroxy-1-propen-1-yl benzoates as intermediates, which were detected during the two-step ruthenium-catalysed isomerization of 2-propyn-1-ols into α,β-unsaturated aldehydes at elevated temperature.[8] These benzoates were not isolated, but ^{1}H NMR spectroscopic examination of the crude mixture after treatment of various propynylic alcohols **2** with benzoic acid **1** and [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$] **(I)** as catalyst in toluene at 70 °C made possible the determination of the *Z*/*E* ratios of the 3-hydroxy-1-propen-1-yl benzoates formed as intermediates (Table 1).

An increase of the reaction temperature from 50 °C to 70 °C did not significantly modify the *Z*/*E* ratio. In addition, we have also found that the *anti*-Markovnikov addition of benzoic acid to 2-phenyl-3-butyn-2-ol **(2e)** catalysed by 1 mol-% of the ruthenium complex **I** was also efficient at room temperature and led to complete conversion of **2e** to 3-hydroxy-3-phenyl-1-propen-1-yl benzoate **(3e)** after 2 h with a similar stereoselectivity (*Z*/E = 66:34). These results strongly suggest that the stereoselectivity of the addition of the carboxylic acid to the triple bond of propargylic alcohols is probably not a result of thermodynamic control.

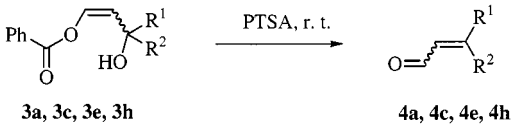
Transformation of 3-Hydroxy-1-propen-1-yl Benzoates into α,β-Unsaturated Aldehydes

The synthesis of simple α,β-unsaturated aldehydes has potential in the preparation of a variety of terpenoids, e.g. vitamin A and derivatives, as well as perfume and cosmetic components,[11,12] or can be used to obtain biologically active derivatives.[13] We recently reported that such enals could be obtained from **3** by thermal transformation at 100 °C. However, ^{1}H NMR spectroscopic monitoring revealed that only the (*Z*)-esters of **3** were converted into α,β-enals **4**.[8] For example, treatment of the steroid derivative **2g** (levonorgestrel) at 70 °C for 2 h in the presence of 1 equivalent of benzoic acid and **I** as catalyst afforded the corresponding enol ester **3g** with low stereoselectivity. Further heating of the reaction mixture at 100 °C for 15 h led to the total conversion of (*Z*)-**3g** into the α,β-unsaturated aldehyde **4g** (51% yield), whereas the (*E*)-isomer remained unchanged and was recovered in 41% yield (Scheme 2).[9]



Scheme 2. Selective transformations of steroid **2g**

Interestingly, we found that by treating compounds **3** at room temperature in the same pot without isolation, with a catalytic amount of either *para*-toluenesulfonic acid



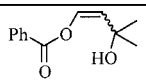
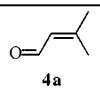
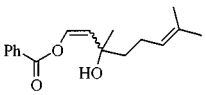
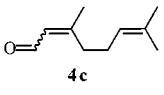
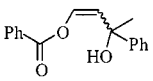
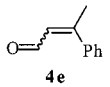
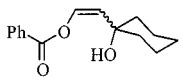
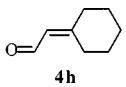
Scheme 3. Acid-catalyzed formation of conjugated enols

(PTSA) or HBF_4, α,β-unsaturated aldehydes were rapidly obtained in good yields according to Scheme 3.[10] Moreover, this method made possible the transformation of both *Z* and *E* isomers of 3-hydroxy-1-propen-1-yl benzoates **3** into the corresponding aldehydes **4**.

Thus, treatment of the hydroxy enol ester **3a** with 1 mol-% of PTSA at room temperature and in the absence of solvent led after 2 h to a complete transformation into prenal **4a** in 88% isolated yield (Table 2). By contrast, thermal rearrangement afforded prenal in a lower yield of 68%.[8]

With toluene as solvent, compound **3c** led to the terpenoid citral **4c** in 57% yield after treatment with a catalytic amount of PTSA, whereas compound **3h** afforded 72% of the aldehyde **4h**. Remarkably, no side products which could arise from possible dehydration of the alkyl-substituted hydroxy enol esters **3** were observed. It is noteworthy that compound **4e** was obtained in 91% yield with PTSA as catalyst, whilst the starting product **3e** contained only 67% of the (*Z*)-isomer, thus indicating that both (*Z*)- and (*E*)-3-hydroxy-1-propen-1-yl benzoates were quantitatively transformed into α,β-unsaturated aldehydes. Moreover, the high selectivity obtained for compound **4e** (*Z*/*E* = 10:90) strongly contrasts with that obtained by thermal rearrangement at 100 °C (*Z*/*E* = 67:33).[8] The use of 10 mol-% of the stronger acid HBF_4 gave the enal **4e** in 79% isolated yield after only 5 min in exothermic reaction but with a lower stereoselectivity.

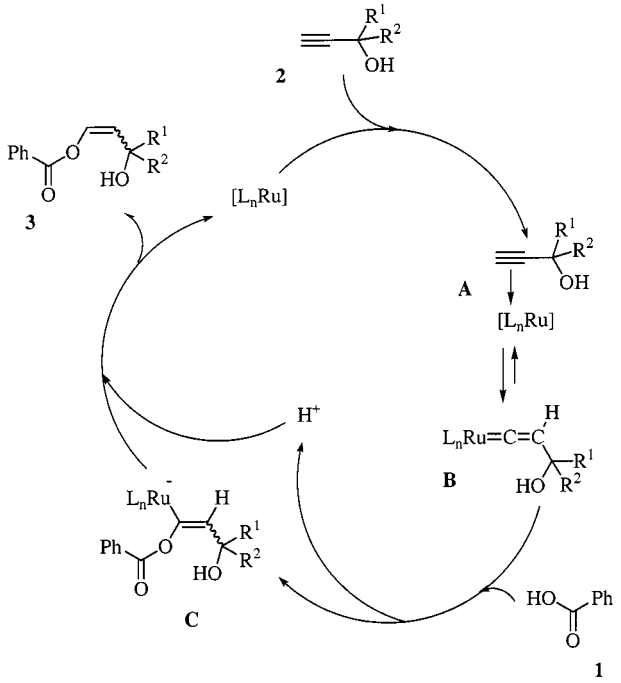
Table 2. Acid-catalysed transformation of in situ generated 3-hydroxy-1-propen-1-yl benzoates **3** into aldehydes 4[a]

3-hydroxy-1-propen-1-yl benzoate	Acid (mol%)	reaction time	α,β-unsaturated aldehyde	yield[b] (%)
 **3a**, *Z*/*E* = 81/19	PTSA (1 mol%)	2 h[c]	 **4a**	88
 **3c**, *Z*/*E* = 87/13	PTSA (1 mol%)	15 h[d]	 **4c**	57
 **3e**, *Z*/*E* = 67/33	PTSA (1 mol%)	1.5 h	 **4e**	91 *Z*/*E* = 10/90
	HBF_4 (10 mol%)	5 min		79 *Z*/*E* = 33/67
 **3h**, *Z*/*E* = 78/22	PTSA (1 mol%)	15 h[d]	 **4h**	72

[a] General conditions: 2-propyn-1-ol **2** (5 mmol), benzoic acid (5 mmol), (dppe)Ru(η³-$CH_2C(Me)CH_2$)$_2$ **I** (1 mol-%, 0.05 mmol), toluene (3 mL), 50 °C, 2 h leading to complete conversion into **3**, followed by addition of a catalytic amount of PTSA or HBF_4 at room temp. – [b] Isolated yields based on the starting propynylic alcohol **2**. – [c] Solvent free reaction. – [d] Reaction performed at 10 °C.

Mechanistic Considerations

The proposed mechanism of the transformation **2** → **3** is depicted in Scheme 4.

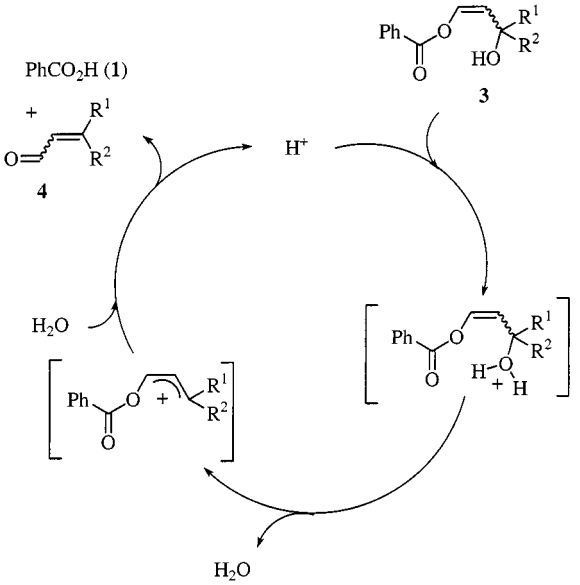


Scheme 4. Proposed mechanism for the addition of acid to propynol

As the electrophilic precatalyst **I** is known to favour the *trans-anti*-Markovnikov addition of carboxylic acids to terminal alkynes either *via* an initial η²-alkyne (**A**) or η¹-vinylidene (**B**) coordination of the alkynol[2,7] with the probable formation of intermediate **C**. On protonolysis of the electron-rich Ru–C bond, the (*Z*)-3-hydroxy-1-propen-1-yl benzoate **3** is expected to be formed and the catalytic species regenerated.

Whereas a concerted mechanism was proposed to explain the selective thermal transformation of the hydroxylated enol esters **3**,[8] the reaction promoted by strong acids probably involves a cationic species. The protonation of 3-hydroxy-1-propen-1-yl benzoate **3** by a catalytic amount of a strong acid would give a cationic intermediate which readily undergoes transformation into the α,β-unsaturated aldehyde **4** with the release of benzoic acid (Scheme 5).

This process is an efficient alternative to the direct isomerization of 2-propyn-1-ols into α,β-unsaturated aldehydes, either conducted in strong acidic medium as initially described in the Meyer–Schuster reaction[14] or with metal-oxo catalysts,[15] which lead to partial dehydration of the



Scheme 5. Acid-catalyzed cleavage of enol esters **3**

starting propynylic alcohol or the formation of α,β-unsaturated ketones by the Rupe rearrangement.[14b]

With our catalytic systems, attempts to carry out this transformation in one step were unsuccessful because the presence of PTSA or HBF_4 inhibited the crucial catalytic addition of benzoic acid to the alkynol, probably as a consequence of destruction the active catalyst.

Conclusion

The *anti*-Markovnikov addition of benzoic acid to 2-propyn-1-ols takes place in toluene at 50 °C and even at room temperature in the presence of [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$] as catalyst. The regio- and stereoselectivity of the reaction is closely related to the steric hindrance of the starting 2-propyn-1-ol and does not depend on the reaction temperature. Both the (*Z*)- and (*E*)-3-hydroxy-1-propen-1-yl benzoates obtained were easily and cleanly converted into α,β-unsaturated aldehydes in the presence of a catalytic amount of an acid such as PTSA or HBF_4 with regeneration of benzoic acid. The two steps can be performed in the same pot without isolation of the intermediate **3** and benzoic acid can be recycled, thus providing an environmentally friendly process.

Experimental Section

General: All experiments were carried out using classical Schlenk techniques under an inert atmosphere of nitrogen. All chemicals were used as received. Complex **I** was synthesised according to a literature procedure.[7] Toluene and diethyl ether were distilled over sodium/benzophenone, pentane was distilled over calcium hydride. Flash column chromatography was performed over Merck silica gel 30−60 mesh. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 200 at 200.131 MHz and 50.32 MHz, respectively. − IR spectra were recorded on a Nicolet 205 FTIR-spectrometer. Elemental analyses were obtained from "Le Service de Microanalyses du CNRS", Vernaison, France.

Typical Experiment for the *anti*-Markovnikov Addition Catalysed by [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$]: 2-Propyn-1-ol (5 mmol) was added to a mixture of benzoic acid (5 mmol), [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$] (0.05 mmol) and toluene (3 mL). The mixture was stirred and heated at 50 °C for 2 h, then evaporated and purified by flash column chromatography over silica gel.

3-Hydroxy-3-methyl-1-buten-1-yl Benzoate (3a): Obtained from 2-methyl-3-butyn-2-ol **(2a)** (5 mmol), benzoic acid (5 mmol) and [(dppe)Ru(η^3-$CH_2C(Me)CH_2)_2$] **(I)** (1 mol-%, 0.05 mmol) in toluene (3 mL) as a colourless liquid (0.531 g, 51%, *Z*/*E* = 81:19) after column chromatography with ether/pentane (1:1) as eluent. − IR: $\tilde{\nu}$ = 3480 (OH), 3150, 3100 (arom. CH), 2975 (CH_3), 1731 (C=O), 1671 (C=C), 1265 (C−O) cm^{-1}. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = (*Z*) 8.10−8.00 (m, 2 H, C_6H_5), 7.65−7.35 (m, 3 H, C_6H_5), 7.19 (d, *J* = 7.2 Hz, 1 H, −O−C*H*=C), 5.14 (d, *J* = 7.2 Hz, 1 H, −O−C=C*H*), 3.20 (broad s, 1 H, OH), 1.51 (s, 6 H, 2 Me); (*E*) 8.10−8.00 (m, 2 H, C_6H_5), 7.65−7.35 (m, 4 H, C_6H_5 + −O−C*H*=C), 5.79 (d, *J* = 12.4 Hz, 1 H, −O−C=C*H*), 3.20 (broad s, 1 H, OH), 1.60 (s, 6 H, 2 Me). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = (*Z*) 163.1 (C=O), 133.6−128.4 (C_6H_5), 133.8 (−O−*C*H=C), 121.7 (−O−C=*C*H), 70.5 (C), 30.5 (2 Me); (*E*) 168.0 (C=O), 133.6−128.4 (C_6H_5), 135.3 (−O−*C*H=C), 123.7 (−O−C=*C*H), 69.4 (C), 30.0 (2 Me).

3,5-Dimethyl-3-hydroxy-1-hexen-1-yl Benzoate (3b): Obtained from DL-3,5-dimethyl-1-hexyn-3-ol **2b** (5 mmol), benzoic acid (5 mmol) and **I** (1 mol-%, 0.05 mmol) in toluene (3 mL) as a colourless liquid (1.023 g, 82%, *Z*/*E* = 82:18) after column chromatography with ether/pentane (1:4) as eluent. − IR: $\tilde{\nu}$ = 3452 (OH), 3060 (arom. CH), 2975, 2929, 2872 (alkyl CH), 1734 (C=O), 1669 (C=C), 1260 (C−O) cm^{-1}. − ^{1}H NMR (200 MHz, $CDCl_3$; mixed signals): δ = 8.09−8.04 (m, 2 H, C_6H_5), 2.50−2.20 (broad s, 1 H, OH), 1.90−1.76 [m, 1 H, C*H*$(Me)_2$], 1.74−1.52 (m, 2 H, CH_2), 0.99−0.94 [m, 6 H, CH$(Me)_2$]; (*Z*) 7.63−7.42 (m, 3 H, C_6H_5), 7.24 (d, *J* = 7.3 Hz, 1 H, O−C*H*=C), 5.11 (d, *J* = 7.3 Hz, 1 H, O−C=C*H*), 1.50 (s, 3 H, Me); (*E*) 7.63−7.42 (m, 4 H, C_6H_5 + O−C*H*=C), 5.74 (d, *J* = 12.4 Hz, 1 H, O−C=C*H*), 1.39 (s, 3 H, Me). − ^{13}C NMR (50 MHz, $CDCl_3$) (mixed signals): δ = 133.1−127.8 (C_6H_5), (*Z*) 162.3 (C=O), 132.0 (O−*C*H=C), 120.5 (O−C=*C*H), 71.4 (C), 50.9 (CH_2), 29.0 (Me), 24.0 [*C*H$(Me)_2$], 23.9 [CH$(Me)_2$]; (*E*) 163.3 (C=O), 134.8 (O−*C*H=C), 122.4 (O−C=*C*H), 72.8 (C), 51.0 (CH_2), 28.4 (Me), 23.8 [*C*H$(Me)_2$], 23.7 [CH$(Me)_2$].

3,7-Dimethyl-3-hydroxy-1,6-octadien-1-yl Benzoate (3c): Obtained from DL-3,7-dimethyl-6-octen-1-yn-3-ol **2c** (5 mmol), benzoic acid (5 mmol) and **I** (1 mol-%, 0.05 mmol) in toluene (3 mL) as a colourless liquid (1.14 g, 83%, *Z*/*E* = 87:13) after column chromatography using ether/pentane (1:4) as eluent. − IR: $\tilde{\nu}$ = 3475 (OH), 3100, 3061 (arom. CH), 2969, 2927, 2875, 2856 (alkyl CH), 1719 (C=O), 1671, 1666 (C=C), 1265 (C−O) cm^{-1}. − ^{1}H NMR (200 MHz, $CDCl_3$) (mixed signals): δ = 8.15−8.0 (m, 2 H, C_6H_5), 7.60−7.32 (m, 3 H, C_6H_5), 5.15−5.05 [m, 1 H, C*H*=C$(Me)_2$], 3.35 (broad s, 1 H, OH), 2.25−1.95 (m, 2 H, C=C−CH_2), 1.85−1.55 (m, 2 H, CH_2), 1.63 (s, 3 H, C=C*Me*), 1.56 (s, 3 H, C=C*Me*), 1.48 (s, 3 H, Me); (*Z*) 7.26 (d, *J* = 7.7 Hz, 1 H, O−C*H*=C), 5.06 (d, *J* = 7.7 Hz, 1 H, O−C=C*H*); (*E*) 7.48 (d, *J* = 12.4 Hz, 1 H, O−C*H*=C), 5.71 (d, *J* = 12.4 Hz, 1 H, O−C=C*H*). − ^{13}C NMR (50 MHz, $CDCl_3$) (mixed signals): δ = 163.0 (C=O), 133.5−132.8 (C_6H_5), 131.9 [C=*C*$(Me)_2$], 129.9−128.5 (C_6H_5), 124.2 [*C*=C$(Me)_2$], 122.6 (C_6H_5), 73.1 (C), 25.7 (Me); (*Z*) 133.8 (O−*C*H=C), 120.6 (O−C=*C*H), 42.9 (C=CH−*C*H_2), 28.9 (C=C*Me*), 23.1

(CH_2), 17.7 (C=C*Me*); (*E*) 135.9 (O−*C*H=C), 122.6 (O−C=*C*H), 42.8 (C=CH−*C*H_2), 28.3 (C=C*Me*), 23.0 (CH_2), 17.8 (C=C*Me*). − $C_{17}H_{22}O_3$ (274.4): calcd. C 74.40, H 8.08; found C 74.00, H 8.02.

3-Hydroxy-3-methyl-1,6-heptadien-1-yl Benzoate (3d): Obtained from DL-3-methyl-6-hepten-1-yn-3-ol **(2d)** (5 mmol), benzoic acid (5 mmol) and **I** (1 mol-%, 0.05 mmol) in toluene (3 mL) as a colourless liquid (0.874 g, 71%, *Z*/*E* = 100:0) after column chromatography with ether/pentane (1:4) as eluent. − IR: $\tilde{\nu}$ = 3460 (OH), 3050 (arom. CH), 2976, 2930 (alkyl CH), 1734 (C=O), 1672 (C=C), 1264 (C−O) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = (*Z*) 8.10−7.95 (m, 2 H, C_6H_5), 7.65−7.30 (m, 3 H, C_6H_5), 7.26 (d, *J* = 7.3 Hz, 1 H, O−C*H*=C), 5.80 (m, 2 H, C=CH_2), 5.08 (d, *J* = 7.3 Hz, 1 H, O−C=C*H*), 4.90 (m, 1 H, C*H*=CH_2), 4.60 (broad s, 1 H, OH), 2.25−1.95 (m, 2 H, C=C−CH_2), 1.85−1.55 (m, 2 H, CH_2), 1.48 (s, 3 H, Me).

3-Hydroxy-3-phenyl-1-buten-1-yl Benzoate (3e): Obtained from DL-2-phenyl-3-butyn-2-ol **(2e)** (5 mmol), benzoic acid (5 mmol) and **I** (1 mol-%, 0.05 mmol) in toluene (3 mL) as a colourless liquid (1.21 g, 90%, *Z*/*E* = 67:33) after column chromatography with ether/pentane (1:3) as eluent. − IR: $\tilde{\nu}$ = 3452 (OH), 3050 (arom. CH), 2975, 2945 (alkyl CH), 1737 (C=O), 1602 (C=C), 1265 (C−O) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$) (mixed signals): δ = 8.10−7.0 (m, 11 H, 2 C_6H_5 + O−C*H*=C), 2.60 (broad s, 1 H, OH); (*Z*) 5.46 (d, *J* = 7.1 Hz, 1 H, O−C=C*H*), 1.77 (s, 3 H, Me); (*E*) 5.92 (d, *J* = 12.4 Hz, 1 H, O−C=C*H*), 1.74 (s, 3 H, Me). − ^{13}C NMR (50 MHz, $CDCl_3$) (mixed signals): δ = 133.8−125.2 (2 C_6H_5); (*Z*) 163.1 (C=O), 147.9 (C_6H_5 *ipso*), 133.5 (O−*C*H=C), 121.1 (O−C=*C*H), 73.7 (C), 31.7 (Me); (*E*) 164.0 (C=O), 146.8 (C_6H_5 *ipso*), 136.4 (O−*C*H=C), 123.4 (O−C=*C*H), 73.0 (C), 30.1 (Me). − $C_{17}H_{16}O_3$ (268.3): calcd. C 76.10, H 6.11; found C 76.47, H 6.29.

3,3-Diphenyl-3-hydroxy-1-propen-1-yl Benzoate (3f): Obtained from 1,1-diphenyl-2-propyn-1-ol **(2f)** (5 mmol), benzoic acid (5 mmol) and **I** (1 mol-%, 0.05 mmol) in toluene (3 mL) as a white solid (0.82 g, 79%, *Z*/*E* = 60:40) after column chromatography with ether/pentane (1:6) as eluent; m.p. 73 °C. − IR: $\tilde{\nu}$ = 3472 (OH), 1715 (C=O), 1672 (C=C), 1273 (C−O) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$) (mixed signals): δ = 8.10−8.00 (m, 2 H, C_6H_5), 7.60−7.00 (m, 14 H, 3 C_6H_5 + O−C*H*=C), 3.05 (broad s, 1 H, OH); (*Z*) 5.74 (d, *J* = 7.0 Hz, 1 H, O−C=C*H*), (*E*) 6.30 (d, *J* = 12.3 Hz, 1 H, O−C=C*H*), 1.74 (s, 3 H, Me). − ^{13}C NMR (50 MHz, $CDCl_3$) (mixed signals): δ = 133.8−126.5 (C_6H_5), 77.8 (C); (*Z*) 162.8 (C=O), 146.7 (C_6H_5 *ipso*), 135.5 (O−*C*H=C), 120.4 (O−C=*C*H); (*E*) 163.8 (C=O), 145.8 (C_6H_5 *ipso*), 137.9 (O−*C*H=C), 122.1 (O−C=*C*H). − $C_{22}H_{18}O_3$ (330.4): calcd. C 79.98, H 5.49; found C 79.92, H 5.44.

20,21-Dehydrolevonorgestrel-21-yl Benzoate (3g) and 18,19-Dinor-13-β-ethylpregna-4,17-dien-21-al-3-one (4g): Obtained from levonorgestrel **2g** (1 mmol), benzoic acid (1 mmol) and **I** (1 mol-%, 0.01 mmol) in toluene (2 mL) after 2 h at 70 °C and 15 h at 100 °C as white solids after column chromatography with ether/pentane (3:1) as eluent; (**3g**) (0.176 g, 41%, *Z*/*E* = 0:100). − IR: $\tilde{\nu}$ = 3472 (OH), 1727 (C=O benzoate), 1660 (C=O enone), 1619 (C=C) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 8.12−8.00 (m, 2 H, C_6H_5), 7.65−7.34 (m, 4 H, C_6H_5 + O−C*H*=C), 5.83 (d, *J* = 15.6 Hz, 1 H, O−C=C*H*), 5.81 (s, 1 H, C=C^4−H), 2.56−1.72 and 1.72−0.67 (2 m, 23 H), 1.02 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3); (**4g**) (0.158 g, 51%, *E*-isomer). − IR: $\tilde{\nu}$ = 1667 (C=O), 1615 (C=C) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 3.84 (d, *J* = 7.9 Hz, 1 H, CHO), 5.81 (s, 1 H, C=C^4−H), 5.66 (dt, *J* = 7.9 and 2.3 Hz, 1 H, C=C*H*−CHO), 3.0−2.7 (m, 2 H, CH_2[18]), 2.58−1.98, 1.98−1.75, 1.75−1.37 and 1.37−0.60 (4 m, 20 H), 0.70 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3).

Typical Experiment for the Synthesis of α,β-Unsaturated Aldehydes (4): 2-Propyn-1-ol **(2)** was added to a solution of benzoic acid (1 equiv.) and **I** (1 mol-%) in toluene. The mixture was stirred and heated at 50 °C for 2 h, generating quantitatively compounds **3** as checked by ^1H NMR spectroscopy. Toluene-4-sulfonic acid (1 mol-%) or $HBF_4{\cdot}Et_2O$ solution (10 mol-%) was then added directly to the crude mixture containing the corresponding 3-hydroxy-1-propen-1-yl benzoate **3** at room temperature. The solution was stirred for 5 min to 15 h at room temperature, washed twice with 20 mL of a saturated aqueous $NaHCO_3$ solution, extracted twice with 20 mL of diethyl ether and dried over magnesium sulfate. After filtration and evaporation of the solvent, the α,β-unsaturated aldehydes **4** were purified by bulb-to-bulb distillation (kugelrohr).

3-Methyl-2-butenal (prenal, 4a): Obtained from 2-methyl-3-butyn-2-ol **(2a)** (10 mmol), benzoic acid (10 mmol) and **I** (1 mol-%, 0.1 mmol) without solvent after 2 h at 50 °C, then addition of PTSA (1 mol-%, 0.1 mmol) followed by stirring for 2 h at room temperature. Direct transfer at 20 °C at 1 Torr afforded **4a** as a colourless liquid (0.74 g, 88%). − IR: $\tilde{\nu}$ = 2983, 2942, 2919, 2856 (alkyl C−H), 1676 (C=O), 1640 (C=C) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 9.90 (d, *J* = 8.2 Hz, 1 H, CHO), 5.83 (dm, *J* = 8.2 Hz, 1 H, C=CH), 2.12 (d, *J* = 1.1 Hz, 3 H, Me), 1.93 (d, *J* = 1.1 Hz, 1 H, Me). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 191.6 (CHO), 161.5 [HC=*C*$(Me)_2$], 128.3 [H*C*=C$(Me)_2$], 27.5 (Me), 19.2 (Me).

3,7-Dimethyl-2,6-octadienal (citral, 4c): Obtained from DL-3,7-dimethyl-6-octen-1-yn-3-ol **(2c)** (2.5 mmol), benzoic acid (2.5 mmol) and **I** (1 mol-%, 0.025 mmol) in toluene (3 mL) after 2 h at 50 °C, then addition of PTSA (1 mol-%, 0.025 mmol) followed by stirring at room temperature for 15 h. Bulb-to-bulb distillation (kugelrohr) at 75 °C and 1 Torr afforded **4c** as a colourless liquid (0.217 g, 57%). − IR: $\tilde{\nu}$ = 2925 (alkyl CH), 1672 (C=O), 1636 (C=C) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$) (mixed signals): δ = 5.81 (d, *J* = 8.1 Hz, 1 H, C=C*H*−CHO), 5.08−4.97 (m, 1 H, C*H*=C$(Me)_2$), 1.60 (s, 3 H, *trans*-*Me*−C=C−CH_2), 1.50 (d, *J* = 1.3 Hz, 3 H, *cis*-*Me*−C=C−CH_2); (*Z*) 9.82 (d, *J* = 8.1 Hz, 1 H, CHO), 2.52 (t, *J* = 7.4 Hz, 2 H, CH_2−C=C−CHO), 2.22−2.08 (m, 2 H, Me_2C=CH−CH_2), 1.92 (s, 3 H, *Me*−C=C−CHO); (*E*) 9.92 (d, *J* = 8.1 Hz, 1 H, CHO), 2.22−2.08 (m, 4 H, 2 CH_2), 2.10 (s, 3 H, *Me*−C=C−CHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = (*Z*) 191.2 (CHO), 163.8 (*C*=C−CHO), 132.9 [C=*C*$(Me)_2$], 127.4 [*C*=C$(Me)_2$], 122.6 (C=*C*H−CHO), 40.6 (*C*H_2−C=CH−CHO), 25.7 [*C*H_2−CH=C$(Me)_2$], 25.6 (*Me*−C=C−CHO), 17.7, 17.6 [C=C(*Me*)$_2$]; (*E*) 190.7 (CHO), 163.8 (*C*=C−CHO), 133.6 [C=*C*$(Me)_2$], 128.6 [*C*=C$(Me)_2$], 122.3 (C=*C*H−CHO), 32.6 (*C*H_2−C=CH−CHO), 27.0 [*C*H_2−CH=C$(Me)_2$], 25.0 (*Me*−C=C−CHO), 17.7, 17.6 [C=C(*Me*)$_2$].

3-Phenyl-2-butenal (β-Methylcinnamaldehyde, 4e): Obtained from DL-2-phenyl-3-butyn-2-ol **(2e)** (5 mmol), benzoic acid (5 mmol) and **I** (1 mol-%, 0.05 mmol) in toluene (3 mL) after 2 h at 50 °C, then addition of PTSA (1 mol-%, 0.05 mmol) followed by stirring at room temperature for 1.5 h. Bulb-to-bulb distillation (kugelrohr) at 116 °C and 1 Torr afforded **4e** as a colourless liquid (0.665 g, 91%, *Z*/*E* = 10:90). − IR: $\tilde{\nu}$ = 3060, 3030 (arom. CH), 2852 (alkyl CH), 1663 (C=O), 1617 (C=C) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = (*Z*) 10.09 (d, *J* = 8.2 Hz, 1 H, CHO); (*E*) 9.39 (d, *J* = 8.2 Hz, 1 H, CHO), (mixed signals) 7.48−7.18 (m, 5 H, C_6H_5), 6.31 (dd, *J* = 7.8 and 1.2 Hz, 1 H, C=C*H*), 2.48 (d, *J* = 1.2 Hz, 3 H, Me), 6.05 (dd, *J* = 8.2 and 1.4 Hz, 1 H, C=C*H*), 2.23 (d, *J* = 1.4 Hz,

3 H, Me). – ^{13}C NMR (50 MHz, $CDCl_3$): δ = (*Z*) 191.6 (CHO), 162.5 (Ph−*C*=CH), 140.9 (C_6H_5 *ipso*), 130.5−126.7 (C_6H_5), 127.6 (Ph−C=*C*H), 26.8 (Me); (*E*) 193.7 (CHO), 158.0 (Ph−*C*=CH), 138.8 (C_6H_5 *ipso*), 133.5 (Ph−C=*C*H), 130.5−126.7 (C_6H_5), 16.7 (Me).

Cyclohexylidenacetaldehyde, (4 h): Obtained from 1-ethynylcyclohexanol **(2h)** (5 mmol), benzoic acid (5 mmol) and **I** (1 mol-%, 0.05 mmol) in toluene (3 mL) after 2 h at 25 °C, then addition of PTSA (1 mol-%, 0.05 mmol) followed by stirring at room temperature for 15 h. Bulb-to-bulb distillation (kugelrohr) at 34 °C and 1 Torr afforded **4h** as a colourless liquid (0.445 g, 72%. – IR: $\tilde{\nu}$ = 1670 (C=O), 1635 (C=C) cm^{-1}. – ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.98 (d, *J* = 8.3 Hz, 1 H, CHO), 5.79 (d, *J* = 8.3 Hz, 1 H, C=C*H*), 2.67 (m, 2 H, cyclohexyl), 2.26 (m, 2 H, cyclohexyl), 1.65 (m, 6 H, cyclohexyl).

Acknowledgments

The authors wish to thank Dr. J.-E. Ancel (Rhône-Poulenc Industrialisation) for helpful discussions.

[1] T. Naota, H. Takaya, S.-I. Murahashi, *Chem.Rev.* **1998**, *98*, 2599−2660.
[2] [2a] C. Bruneau, P. H. Dixneuf, *Chem. Commun.* **1997**, 507−512. – [2b] T. Mitsudo, Y. Hori, Y. Yamakawa, Y. Watanabe, *J. Org. Chem*. **1987**, *52*, 2230−2239.
[3] C. Bruneau, M. Neveux, Z. Kabouche, P. H. Dixneuf, *Synlett* **1991**, 755−763.
[4] B. Seiller, C. Bruneau, P. H. Dixneuf, *Tetrahedron* **1995**, *51*, 13089−13102.
[5] M. Tokunaga, Y. Wakatsuki, Y. *Angew. Chem. Int. Ed.* **1998**, *37*, 2867−2869.
[6] [6a] C. Bruneau, Z. Kabouche, M. Neveux, B. Seiller, P. H. Dixneuf, *Inorg. Chim. Acta* **1994**, *22*, 155−163. – [6b] C. Darcel, C. Bruneau, P. H. Dixneuf, *J. Chem. Soc., Chem. Commun.* **1994**, 333−334.
[7] [7a] H. Doucet, B. Martin-Vaca, C. Bruneau, P. H. Dixneuf, *J. Org. Chem.* **1995**, *60*, 7247−7255. – [7b] H. Doucet, J. Höfer, N. Derrien, C. Bruneau, P. H. Dixneuf, *Bull. Soc. Chim. Fr.* **1996**, *133*, 939−944. – [7c] H. Doucet, N. Derrien, Z. Kabouche, C. Bruneau, P. H. Dixneuf, *J. Organomet. Chem.* **1997**, *551*, 151−157.
[8] M. Picquet, C. Bruneau, P. H. Dixneuf, *Chem. Commun*. **1997**, 1201−1202.
[9] Similar observations were made for compound **3d**, see [8] .
[10] For related transformation of enol ethers to α,β-unsaturated aldehydes in 1 M HCl solution, see: H.-X. Wei, M. Schlosser, *Chem. Eur. J.* **1998**, *4*, 1738−1743.
[11] G. Olhoff, *Scent and fragrances*; Springer-Verlag, Berlin, **1994**.
[12] [12a] C. Mercier, P. Chabardès, *Pure Appl. Chem*. **1994**, *66*, 1509−1518. – [12b] T. Mino, S. Fukui, M. Yamashita, *J. Org. Chem*. **1997**, *62*, 734−735.
[13] [13a] N. Balu, J. V. Thomas, S. V. Bhat, *J. Med. Chem*. **1991**, *34*, 2821−2823. – [13b] A. Wada, M. Sakai, Y. Imamoto, Y. Shichida, M. Yamauchi, M. Ito, *J. Chem. Soc., Perkin Trans. 1* **1997**, 1773−1777. – [13c] A. Francesch, R. Alvarez, S. Lopez, A. R. de Lera, *J. Org. Chem*. **1997**, *62*, 310−319.
[14] [14a] K. H. Meyer, K. Schuster, *Chem. Ber*. **1922**, *55*, 819−823. – [14b] For a related review, see: S. Swaminathan, K. V. Narayanan, *Chem. Rev.* **1971**, *71*, 429−438.
[15] [15a] H. Pauling, D. A. Andrews, N. C. Hindley, *Helv. Chim. Acta* **1976**, *59*, 1233−1243. – [15b] M. B. Erman, I. S. Aul′ Chenko, L. A. Kheifits, V. G. Dulova, J. N. Novikov, M. E. Vol′pin, *Tetrahedron Lett*. **1976**, *34*, 2981- 2984. – [15c] P. ChabardÈs, E. Kuntz, J. Varagnat, *Tetrahedron* **1977**, *33*, 1775−1783. – [15d] P. Chabardès, *Tetrahedron Lett.* **1988**, *48*, 6253−6256. – [15e] K. Narasaka, H. Kusama, Y. Hayashi, *Chem. Lett*. **1991**, 1413−1416. – [15f] C. Y. Lorber, J. A. Osborn, *Tetrahedron Lett*. **1996**, *37*, 853−856.

Received October 10, 1999
[O99586]