The half-sandwich titanocene $CpTi^{III}Cl_2$ as efficient system for the preparation of 2,5-dihydrofurans *via* α-allenols

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ABSTRACT: The half-sandwich titanocene reagent $CpTi^{III}Cl_2$, obtained by in situ reduction of commercial $CpTiCl_3$ with manganese, is an excellent system for the Barbier-type reaction between aldehydes and propargylic halides, leading to homopropargylic alcohols and α-allenols. An efficient and straightforward methodology for the conversion of aldehydes into 2,5-dihydrofurans involving a two-step sequence (Ti^{III} addition-Ag^{I} cyclization) is presented. The usefulness of the method is proved by the preparation of a Natural Product: a dihydrofuranic labdane, isolated from the leaves of *Mikania* sp. nov.

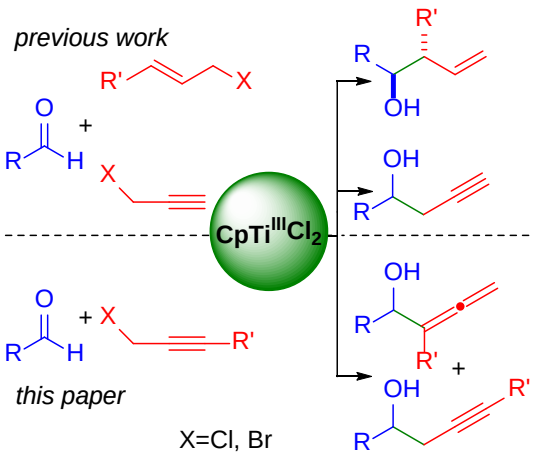
INTRODUCTION

Titanium complexes in low oxidation state are important reagents due to their magnificent reducing power of organic compounds and their ability to activate small molecules.[1] In particular, the use of Nugent−RajanBabu reagent $[Ti(\eta^5\text{-}C_5H_5)_2Cl]$ is increasingly common, given its ability to promote a wide range of organic synthetic transformations.[2] Cp_2TiCl_2 has proved to be very useful in the synthesis of natural products,[3] because it can act as a single electron transfer agent which can be used to open epoxides (triggering radical cascade cyclizations), as promoter of carbonyl pinacol couplings, umpolung reactions, Barbier-type allylations[4] and propargylations,[5] hydrogen atom transfer reactions, and also as catalyst in polymerization processes.[6] However, the ability of half-sandwich titanium(III) species as catalysts in organic synthesis remains almost

unexplored, despite the fact that these compounds have been known for almost half a century.[7] In fact, with the exception of the Duthaler-Hafner reagent,[8] which is used in stoichiometric amounts in the asymmetric allylation of aldehydes,[9] half-sandwich titanocenes and their derivatives have found, so far, limited applications, mainly to the preparation of polymers from alkenes and lactides.[10] However, in recent years they are emerging as new catalysts in organic synthesis,[11] possibly, because removing a Cp ligand could decrease their steric profile and at the same time maintain their redox properties, giving them an advantageous position as catalysts. In other words, the loss of a Cp could increase their coordination ability, leaving extra-coordination sites for the substrate and allowing more compact "Zimmerman–Traxler"-like transition states.

Recently, it has been published that the titanium (III) complex $CpTiCl_2$ prepared by reduction of $CpTiCl_3$ with Mn, is a good catalyst in Barbier-type inter- and intramolecular allylation and propargylation reactions with aldehydes[12] and ketones.[13] This reaction has shown high regio- and stereoselectivities and can be carried out in the presence of different functional groups (Scheme 1).

Scheme 1. $CpTi^{III}Cl_2$ in C-C bond formation



Now we are interested in the synthesis of α-hydroxyallenes *via* the coupling between aldehydes and substituted propargylic halides in the presence of $CpTi^{III}Cl_2$. The metal-mediated cyclization of functionalized allenes is an excellent technique for the rapid increase in structural complexity, which paves the way for the preparation of heterocyclic systems. Having this in mind, we have also focused our attention towards the use of α-hydroxyallenes as substrates for the synthesis of 2,5-dihydrofurans, prompted by the great diversity of natural products which include this structural motif. In this way, we have

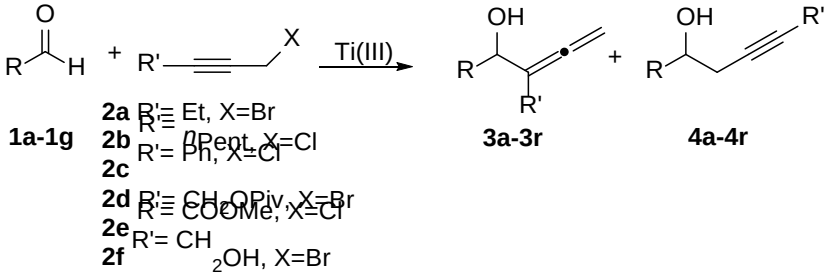
explored two different synthetic approaches. In the first one the new dihydrofuran ring is prepared by Ag(I) catalyzed intramolecular addition of the hydroxyl group to the allene.[14] The second approach increases the structural diversity through a Pd(II) catalyzed cyclization followed by a C-C coupling with an allyl halide.[15]

Terpenoids with labdane skeleton are a type of natural products with many notorious representatives for their biological activities or their applications in the perfumery industry.[16] The present work shows the synthesis of a natural dihydrofuranic labdane previously isolated from *Mikania* sp. nov.[17] using as raw material a mixture of communic acids, which are diterpenes readily available from commercial juniper's berries.[18]

RESULTS AND DISCUSSION

In order to optimize the preparation of α-hydroxyallenes, we chose undec-10-enal (**1a**) as a convenient model aldehyde. In this way, we first attempted the coupling between **1a** and substituted propargylic halides (**2a**-**2c**) under the catalytic conditions previously described for propargyl chloride[12] (Scheme 2, Table 1).

Scheme 2. $CpTi^{III}Cl_2$ induced coupling between aldehydes and substituted propargylic halides



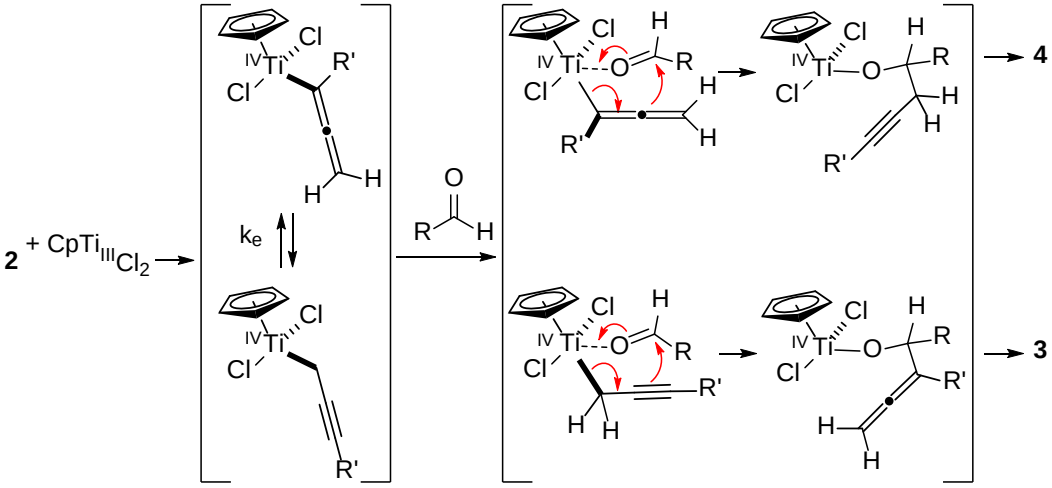
In all three cases, both allene (**3a-c**) and alkyne (**4a-c**) were formed, being the alkynes slightly favoured (Table 1, entries 1-3). The highest allene ratio appeared with the phenyl substituted propargyl chloride, although in a 1:1 ratio (Table 1, entry 3). A similar result was obtained with the aldehyde **1b** (Table 1, entry 4). Finally, the products ratios observed in the reactions of 1-bromopent-2-yne (**2a**) with hexanal (**1c**) (Table 1, entry 5) and undec-10-enal (**1a**) (Table 1, entry 1) are very similar, suggesting that the nature of the alkyne has a strong influence in the outcome of the reaction.

It has been published that, in the case of Cp_2TiCl_2 derived titanium intermediates, the relative ratio of products depends both on the nature of the propargyl halide and the carbonyl substrate[19]. In the examples in table 1, the alkyne ratio is slightly higher for

propargylic chlorides than for propargylic bromides. However, the presence of a phenyl group conjugated with the alkyne, increases the ratio of allene.

The hypothetical metallotropic allenyl–propargyl equilibrium in the intermediates, similarly to what we reported for Cp_2TiCl,[20] should be faster than their reaction with the aldehyde (Scheme 3). This would lead, through a dynamic kinetic resolution, to a reaction mixture in which the product ratio is determined by the activation energy of the C-C bond formation step.

Scheme 3. Proposed pathway to homopropargylic alcohols and α-allenols



In an attempt to improve the ratio of allene, we also performed the reaction using stoichiometric amounts of $CpTiCl_2$. A wide range of aldehydes and alkynes gave satisfactory yields under these reaction conditions (Scheme 2, Table 2), proving the synthetic versatility of the method.

Again, 1-bromopent-2-yne (**2a**) and undec-10-enal (**1a**) were chosen for the reaction optimization. With these substrates, a preferential formation of the α-allenol (**3a**) towards the homopropargylic alcohol (**4a**) is observed, in an 83:17 ratio (Table 2, entry 1), substantially improved if compared with the catalytic procedure (Table 1, entry 1). The reaction temperature also affects the product ratio. A decrease in the temperature increases the homopropargylic alcohol ratio (44:56) (Table 2, entry 2). On the other hand, an increase in the temperature results in a lower yield, while the allene/alkyne ratio remains similar.

In addition, the result with the chloride derivative **2b** (Table 2, entry 3) is very similar to that of the catalytic version (Table 1, entry 2), although now the yield is significantly

higher (92%). Also, very high α-allenol ratios are obtained when a phenyl ring is conjugated with the alkyne, even if a chloride derivative as **2c** is used (Table 2, entries 4 and 5). Moreover, in the case of the propargylic chloride **2e**, which carries another conjugated function, only the α-allenol **3g** is detected, although in a moderate yield.

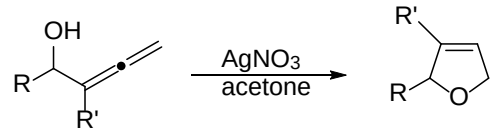
The opposite result is obtained with the propargylic bromide **2d**. The presence of the bulky pivaloyloxy group favors the formation of the homopropargylic alcohol **4f** rather than the α-allenol **3f** (Table 2, entry 6). The reaction with the same substrate but at lower temperature leads to the exclusive formation of the homopropargylic alcohol (Table 2, entry 7). Reaction of **2d** with a different aldehyde (**1b**) leads again to the prevalent formation of alkyne over the allene (Table 2, entry 17).

Some other aldehydes were tested in addition to **1a**. In this way, we found that aldehydes **1d-f** show a similar reactivity pattern than **1a**. Their reactions with propargylic halides **2a-d** lead to α-allenol/homopropargylic alcohol ratios in accordance with those above mentioned. However, aldehyde **1g** affords only α-allenol **3n** (entry 15). In this case, the higher steric hindrance in the carbonyl neighborhood due to the α-methyl could be the reason for this behavior. It was also satisfying to find that the free hydroxy group present in propargylic halide **2f** was not an obstacle for the reaction. In the same way, when a pivaloyl group was present, the homopropargylic alcohol was the major product (**3q**:**4q** 28:72). However, two side products could be also detected, formed by reductive deoxygenation of the hydroxy group (**3r**:**4r**).[21]

At this point we thought that the α-allenols just prepared could be excellent building blocks for the synthesis of the 2,5-dihydrofuranic subunits present in many natural products. In this sense, we explored the cyclization of our α-allenols through Ag(I) mediated intramolecular addition of the hydroxy group to the allene, which should lead to the formation of the target 2,5-dihydrofurans. In our hands, the best results were achieved with $AgNO_3$, using acetone as solvent[14] (Scheme 4).

It is worth pointing out that this reaction can be carried out with the mixture of α-allenol/homopropargylic alcohol in the cases were their similar polarity do not allow chromatographic separation. In this way, the dihydrofuran product can be separated from the unaltered homopropargylic alcohol substrate.

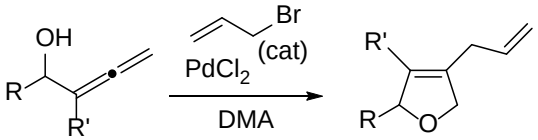
Scheme 4. Preparation of 2,5-dihydrofurans



3a: R'= Et, R= -$(CH_2)_8CH=CH_2$ **6a** 84%
3d: R'= Ph, R= -CH_2CH_2Ph **6d** 95%
3l: R'= Et, R= cyclohex-2-en-1-yl **6l** 73%
3m: R'= Ph, R= cyclohex-2-en-1-yl **6m** 93%
3o: R'= Et, R= -CH_2CH_2Ph **6o** 87%

We have also explored a different approach for the conversion of α-allenols into 2,5-dihydrofurans. It has been reported that Pd(II) complexes can induce the cyclization of α-allenols through a process which can also involve a coupling with an allyl derivative.[15] In this way, the structural complexity is increased as the Pd(II) catalyzed cyclization of the α-allenol is followed by a *C-C* coupling with an allyl halide. Scheme 5 shows some examples of this methodology, using a selection of the α-allenols we had previously prepared.

Scheme 5. Preparation of allyldihydrofurans



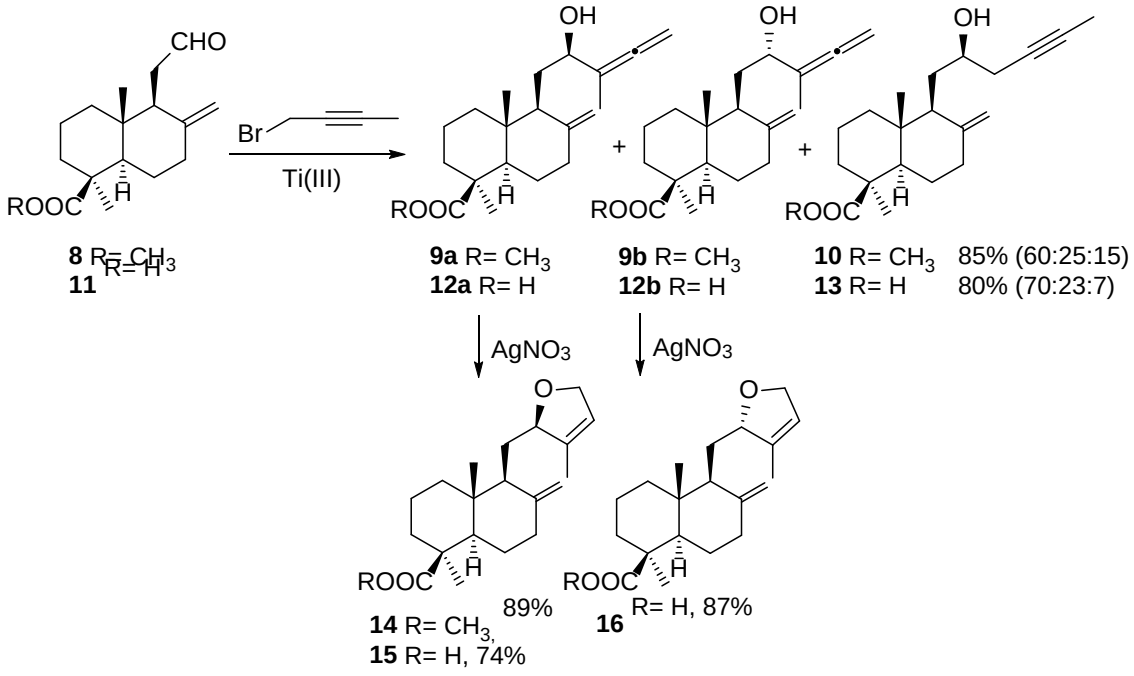
3i: R= hexyl, R'= pentyl **7i** 79%
3m: R= cyclohex-2-en-1-yl, R'= Ph **7m** 85%
3o: R= -CH_2CH_2Ph, R'= Et **7o** 93%

At this point we had optimized a two step methodology which can convert aldehydes into 2,5-dihydrofurans through a $CpTi^{III}Cl_2$ Barbier type allenylation followed by a Ag(I) cyclization. We though that this straightforward strategy could be useful in the preparation of natural products containing this type of ring. As an example, we selected compound **14**, the precursor of natural dihydrofuranic labdane **15**, isolated from the leaves of *Mikania* sp. nov.[17], whose structure was confirmed by Mack *et al* by synthesis.[22] In this way, aldehyde **8**, a communic acid derivative previously described[23] which is readily available from juniper berries, was coupled with 1-bromobut-2-yne. The reaction led to the formation of both epimers **9a** and **9b**, and also the alkyne **10** in a relative ratio 6:3:1 respectively (global yield 85%) (Scheme 6). This Ti(III) reaction, in which the extra chiral center present in **14** is formed, shows high diastereoselectivity, being the major product that required for the preparation of the target natural product. Ag(I) catalyzed

intramolecular isomerization of compound **9a** readily afforded the 2,5-dihydrofuran **14**, which can be transformed into the natural product **15** by saponification of the methyl ester. However, we thought that our methodology could also avoid this final step if the Ti(III) addition could be performed in the presence of a carboxylic acid functional group. To the best of our knowledge, it has not been described the compatibility of Ti(III) chemistry with COOH groups, but, if achieved, this would reduce another step in the global process. In fact, the addition of 1-bromobut-2-yne to the aldehyde **11** led to the mixture of **12a**, **12b** and **13** with even higher selectivity in favor of the required **12a**. Its cyclization with Ag(I) led to the natural product. In this way, we have achieved the synthesis of **15** in two key steps: Silver (I) catalyzed cyclization of the allenol **12a** and $CpTi^{III}Cl_2$ mediated allenylation of aldehyde **11**[24] through Barbier type reaction with a propagyl halide.

As we have just shown, the synthesis can be performed in good yields either with the ester derivatives or the free acids, and the Ti(III) system is compatible with both functional groups. In addition, the process is stereoselective in both cases. In conclusion, the new strategy here described allows for the preparation of the natural product **15** in only 3 steps.[25]

Scheme 6. Synthesis of the labdane diterpenoid 15



CONCLUSIONS

We have proved that the half-sandwich titanocene reagent $CpTi^{III}Cl_2$ can be successfully used in the Barbier-type allenylation and propargylation of aldehydes, in a product ratio which depends on the reaction conditions and substrate nature. The substituents on the alkyne have a greater impact on the allene ratio, and the reaction can be performed in the presence of several functional groups. This process can be used in the preparation of natural products through a straightforward methodology which involves a two step sequence: Ti(III) addition-Ag(I) isomerization.

EXPERIMENTAL SECTION

General Remarks.

NMR spectra were recorded on Bruker Nanobay Avance III HD 300 MHz. Proton-decoupled $^{13}C\{1H\}$ NMR spectra and DEPT-135 were measured in all cases. Chemical shifts (δ) are expressed in ppm and coupling constants (*J*) in hertzs (Hz). Chemical shifts are reported using $CDCl_3$ as internal reference. IR Spectra were recorded with a Bruker Alpha spectrometer. Mass spectra were recorded in a Waters Xevo by LC-QTof-MS by electrospray ionization. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.2 mm DC-Fertigfolien Alugram® XtraSil G/UV254 silica gel plates. The TLC plates were visualized with UV light and 7% phosphomolybdic acid or $KMnO_4$ in water/heat. Flash chromatography was performed on silicagel 60 (0.04 - 0.06 mm).Commercially available chemicals were obtained from Aldrich Chemical Co., Acros, Alfa Aesar, TCI and used as received. In all experiments involving Ti(III), reactions were performed under argon atmosphere, using oven-dried glassware in all cases. THF was distilled from Na/benzophenone under argon, and was deoxygenated prior to use.

4-Bromobut-2-yn-1-yl pivalate (2d)

Under N_2 atmosphere, pyridine (8 mL, 99.34 mmol) is added to a solution of but-2-yne-1,4-diol (4.35 g, 50.52 mmol) in CH_2Cl_2 (150 mL). Pivaloyl chloride (4.98 mL, 40.45 mmol) is slowly added dropwise over a period of 30 min, and the mixture is stirred overnight at room temperature. The mix is washed with water and HCl 3%. The organic phase is dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography (hexane/AcOEt 6:4) provided 4-hydroxybut-2-yn-1-yl pivalate (3.95 g, 57%) as a yellow oil. IR (film) *v* (cm^{-1}) 3417, 2974, 2874, 1729,

1480, 1279, 1136, 1019, 964, 735. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.69 (br s, 2H), 4.30 (br s, 2H), 1.21 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 178.1 (C), 84.8 (C), 79.8 (C), 52.4 (CH_2), 50.8 (CH_2), 38.7 (C), 27.0 (CH_3).

Under N_2 atmosphere, pyridine (0.33 mL, 4.14 mmol) is added to a solution of 4-hydroxybut-2-yn-1-yl pivalate (3.90 g, 23.00 mmol) in $CHCl_3$ (150 mL). PBr_3 (1.10 mL, 11.5 mmol) is added at 0ºC and the mixture is stirred at room temperature for 1h. Then, the reaction is heated to 40ºC for 45 min. After this time, water is added, and the mixture is extracted with CH_2Cl_2 (x3). The combined organic layers are washed with a saturated solution of $NaHCO_3$, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography (hexane/Et_2O 6:4) provided **2d** (3.89 g, 73%) as a colorless oil. IR (film) *v* (cm^{-1}) 2974, 2874, 1731, 1480, 1367, 1271, 1138, 1031, 969, 734. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.72 (t, *J* = 2.1 Hz, 2H), 3.95 (t, *J* = 2.1 Hz, 2H), 1.23 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 177.7 (C), 81.3 (C), 81.0 (C), 52.2 (C), 38.8 (C), 27.1 (CH_3), 14.0 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_9H_{14}BrO_2$ 233.0177, 235.0157; found 233.0162, 235.0045.

Ti-catalyzed coupling between aldehydes and substituted propargyl halides (general procedure A)

Under an Ar atmosphere, dry deoxygenated THF (7 mL) is added to a miscellany of $CpTiCl_3$ (0.12 mmol), Mn dust (2.4 mmol) and $Et_3N{\cdot}HBr$ (2.4 mmol). To this dark blue suspension, Me_3SiBr (3.6 mmol) is added and the mixture turned turquoise. A solution of the aldehyde (**1**) (1.2 mmol) and substituted propargyl halide (**2**) (2.4 mmol) in THF (2 mL) is dripped and the mixture is stirred (4 h). The mixture filtered, diluted with AcOEt, washed with HCl 3% and brine, dried (anhydrous $MgSO_4$) and the solvent removed. Products are purified by silica gel flash column chromatography (hexane/Et_2O mixtures).

3-Ethyltetradeca-1,2,13-trien-4-ol (3a) and hexadec-15-en-3-yn-6-ol (4a)

Reaction of undec-10-enal (**1a**) (0.24 mL, 1.2 mmol) and 1-bromopent-2-yne (**2a**) (0.25 mL, 2.4 mmol), according to general procedure A, afforded compounds **3a** (74 mg, 26%) and **4a** (127 mg, 45%). Compound **3a:** isolated as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.83 (ddt, *J* = 16.8, 10.2, 6.6 Hz, 1H), 5.04-4.93 (m, 2H), 4.90 (m, 2H), 4.07-4.04 (m, 1H), 2.09-1.99 (m, 4H), 1.65-1.50 (m, 3H), 1.31 (m, 12H), 1.06 (t, *J* = 7.5 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.2 (C), 139.2 (CH), 114.1 (CH_2), 109.4 (C), 79.0 (CH_2), 72.0 (CH), 35.6 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 29.4 (CH_2),

29.1 (CH_2), 28.9 (CH_2), 25.5 (CH_2), 20.9 (CH_2), 12.2 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{29}O$ 237.2218; found 237.2237.

Compound **4a**: light yellow oil. IR (film) *v* (cm^{-1}) 3383, 2975, 2926, 2854, 1640, 1461, 1320, 995, 910. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.03-4.91 (m, 2H), 3.68 (tt, *J* = 4.7, 6.6 Hz, 1H), 2.40 (ddt, *J* = 14.0, 4.6, 2.4 Hz, 1H), 2.31-2.14 (m, 3H), 2.08-2.01 (m, 3H), 2.05 (m, 2H), 1.35 (m, 12H), 1.13 (t, *J* = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 139.2 (CH), 114.1 (CH_2), 84.5 (C), 75.5 (C), 70.2 (CH), 36.2 (CH_2), 33.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 27.7 (CH_2), 14.2 (CH_3), 12.4 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{29}O$ 237.2218; found 237.2236.

6-Ethenylideneheptadec-16-en-7-ol (3b) and nonadec-18-en-6-yn-9-ol (4b)

Reaction of undec-10-enal (**1a**) (0.24 mL, 1.2 mmol) and 1-chlorooct-2-yne (**2b**) (0.38 mL, 2.4 mmol), according to general procedure A, afforded compounds **3b** (57 mg, 17%) and **4b** (160 mg, 48%). Compound **3b**: colorless oil, IR (film) *v* (cm^{-1}) 3347, 2927, 2855, 1955, 1641, 1463, 994, 909, 843. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.83 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.04-4.92 (m, 2H), 4.87-4.84 (m, 2H), 4.03 (m, 1H), 2.09-1.95 (m, 4H), 1.68 (br s, 1H), 1.61-1.30 (m, 20H), 0.91 (m, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.4 (C), 139.2 (CH), 114.1 (CH_2), 107.7 (C), 78.5 (CH_2), 72.0 (CH), 35.6 (CH_2), 33.8 (CH_2), 31.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 27.8 (CH_2), 27.4 (CH_2), 25.5 (CH_2), 22.5 (CH_2), 14.1 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{35}O$ 279.2688; found 279.2644.

Compound **4b**: light yellow oil. IR (film) *v* (cm^{-1}) 3376, 2927, 2855, 1641, 1463, 1081, 994, 909. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.82 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.04-4.92 (m, 2H), 3.69 (m, 1H), 2.41 (ddt, *J* = 16.4, 4.6, 2.4 Hz, 1H), 2.27 (ddt, *J* = 16.4, 6.8, 2.4 Hz, 1H), 2.18 (m, 2H), 2.05 (m, 2H), 1.97 (br s, 1H), 1.51 (m, 4H), 1.30 (m, 16H), 0.91 (t, *J* = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 139.2 (CH), 114.1 (CH_2), 83.3 (C), 76.1 (C), 70.2 (CH), 36.2 (CH_2), 33.8 (CH_2), 31.1 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 28.7 (CH_2), 27.8 (CH_2), 25.7 (CH_2), 22.2 (CH_2), 18.7 (CH_2), 14.0 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{35}O$ 279.2688; found 279.2664.

3-Phenyltetradeca-1,2,13-trien-4-ol (3c) and 1-phenyltetradec-13-en-1-yn-4-ol (4c)

Reaction of undec-10-enal (**1a**) (0.24 mL, 1.19 mmol) and (3-chloroprop-1-yn-1-yl)benzene (**2c**) (0.33 mL, 2.38 mmol), according to general procedure A, afforded

compounds **3d** and **4d** (1:1, 63% overall yield after CC). Compound **3c** was isolated as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.50-7.46 (m, 2H), 7.40-7.34 (m, 2H), 7.29-7.24 (m, 1H), 5.84 (ddt, *J* = 17.1, 10.2, 6.6 Hz, 1H), 5.27 (br s, 2H), 5.02 (ddt, *J* = 17.3, 2.2, 1.6 Hz, 1H), 4.96 (ddt, *J* = 10.2, 2.2, 1.1 Hz, 1H), 4.66 (m, 1H), 2.12-2.05 (m, 2H), 1.93 (br s, 1H), 1.80-1.67 (m, 2H), 1.44-1.32 (m, 12H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 207.1 (C), 139.2 (CH), 134.7 (C), 128.6 (CH), 127.1 (CH), 126.8 (CH), 114.2 (CH_2), 110.1 (C), 80.6 (CH_2), 69.8 (CH), 36.3 (CH_2), 33.9 (CH_2), 31.2 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.0 (CH_2), 25.8 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{29}O$ 285.2218; found 285.2230. Compound **4c** could not be isolated and an inseparable mixture of **3c** and **4c** was obtained. Signals due to **4c**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.86 (m, 1H), 2.69 (dd, *J* = 16.7, 4.8 Hz, 1H), 2.57 (dd, *J* = 16.7, 6.7 Hz, 1H).

1,4-Diphenylhexa-4,5-dien-3-ol (3d) and 1,6-diphenylhex-5-yn-3-ol (4d)

Reaction of 3-phenylpropanal (**1b**) (0.30 mL, 2.24 mmol) and (3-chloroprop-1-yn-1-yl)benzene (**2c**) (0.61 mL, 4.47 mmol), according to general procedure A, afforded compounds **3d** and **4d** (47:53, 60% overall yield after CC). Compound **3d** was isolated as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.48-7.24 (m, 10H), 5.31 (d, *J* = 2.3 Hz, 2H), 4.72 (ddt, *J* = 7.2, 4.8, 2.3 Hz, 1H), 2.96-2.76 (m, 2H), 2.21-1.97 (m, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 207.1 (C), 141.9 (C), 134.5 (C), 128.7 (CH), 128.6 (CH), 128.4 (CH), 127.2 (CH), 126.8 (CH), 125.9 (CH), 109.0 (C), 81.0 (CH_2), 69.0 (CH), 37.9 (CH_2), 32.1 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{19}O$ 251.1436; found 251.1421. Compound **4d**[26] could not be isolated and an inseparable mixture of **3d** and **4d** was obtained. Signals due to **4d**: ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 141.8 (C), 131.7 (CH), 128.5 (CH), 128.36 (CH), 128.33 (CH), 128.0 (CH), 126.0 (CH), 123.4 (C), 86.1 (C), 83.3 (C), 69.5 (CH), 38.0 (CH_2), 32.0 (CH_2), 28.6 (CH_2).

3-Ethylnona-1,2-dien-4-ol (3e) and undec-3-yn-6-ol (4e)

Reaction of hexanal (**1c**) (0.25 mL, 2 mmol) and 1-bromopent-2-yne (**2a**) (0.45 mL, 4 mmol), according to general procedure A, afforded compounds **3e** and **4e** (67% overall yield after CC). Compound **3e** was isolated as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.90 (br s, 2H), 4.06 (br s, 1H), 2.02 (m, 2H), 1.64 (m, 2H), 1.32 (m, 6H), 1.06 (t, *J* = 7.3 Hz, 3H), 0.91 (m, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.2 (C), 109.4 (C), 79.0 (CH_2), 72.0 (CH), 35.6 (CH_2), 31.8 (CH_2), 25.2 (CH_2), 22.6 (CH_2),

20.9 (CH_2), 14.1 (CH_3), 12.2 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{21}O$ 169.1592; found 169.1567. Compound **4e** could not be isolated and an inseparable mixture of **3e** and **4e** was obtained. Signals due to **4e**: 3.69 (m, 1H), 2.40 (br d, *J* = 18.6 Hz, 1H), 2.23 (m, 3H), $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 84.6 (C), 75.5 (C), 70.2 (CH), 36.2 (CH_2), 31.8 (CH_2), 27.7 (CH_2), 25.3 (CH_2), 22.6 (CH_2), 14.2 (CH_2), 14.0 (CH_3), 12.4 (CH_3).

2-Bromo-3-ethylnona-1,3-diene (5). Reaction of hexanal (not freshly distilled) (**1c**) (0.25 mL, 2 mmol) and 1-bromopent-2-yne (**2a**) (0.45 mL, 4 mmol), according to general procedure A, afforded compounds **3e** (7%), **4e** (18%) and **5** (20%) (mixture of isomers *Z:E* 66:34): yellow oil. IR (film) *v* (cm^{-1}) 2927, 2854, 1640, 1462, 1215, 994, 909. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) isomer *Z*: 5.96 (t, *J* = 7.4 Hz, 1H), 5.78 (s, 1H), 5.57 (s, 1H); isomer *E*: 5.66 (s, 1H), 5.52 (s, 1H), 5.35 (t, *J* = 7.4 Hz, 1H); both isomers 2.37-2.10 (m, 4H), 1.44-1.33 (m, 6H), 1.14 (m, 1H), 1.03 (t, *J* = 7.5 Hz, 3H), 0.92 (br s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8 (C), 134.5 (CH), 134.3 (C), 129.3 (CH), 119.3 (CH_2), 115.7 (CH_2), 31.6 (CH_2), 31.5 (CH_2), 29.3 (CH_2), 29.1(CH_2), 28.9 (CH_2), 28.6 (CH_2), 28.4 (CH_2), 22.6 (CH_2), 21.4 (CH_2), 14.0 (CH_3), 13.3 (CH_3), 12.6 (CH_3). HRMS (ESI (HEI-II)) *m/z*: $[M - Br]^+$ calcd for $C_{11}H_{19}$ 151.1481; found 151.1481

Ti-induced coupling between aldehydes and substituted propargyl halides (general procedure B)

Under an Ar atmosphere, dry THF (8 mL/1.4 mmol of aldehyde) previously deoxygenated is added to a mixture of $CpTiCl_3$ (1 eq.), Mn dust (2 eq.) resulting a green suspension. Then, a solution of aldehyde (**1**) (1 eq.) and substituted propargyl halide (**2**) (2 eq.) in THF (2mL/1.4 mmol of aldehyde) is dripped and the mixture is stirred (3-5h). The mix is filtered, diluted with AcOEt, washed with HCl 3% and brine, dried (anhydrous $MgSO_4$) and the solvent removed. Products are purified by silica gel flash column chromatography (CC) (hexane/Et_2O mixtures).

3-Ethyltetradeca-1,2,13-trien-4-ol (3a) and hexadec-15-en-3-yn-6-ol (4a)

Reaction of **1a** (0.24 mL, 1.19 mmol) and **2a** (0.25 mL, 2.38 mmol), according to general procedure B, afforded compounds **3a** (202 mg, 72%) and **4a** (39 mg, 14%).

Reaction of **1a** (0.12 mL, 0.6 mmol) and **2a** (0.13 mL, 1.20 mmol), according to general procedure B but at -10ºC, afforded compounds **3a** (57 mg, 40%) and **4a** (71 mg, 50%).

6-Ethenylideneheptadec-16-en-7-ol (3b) and nonadec-18-en-6-yn-9-ol (4b)

Reaction of **1a** (0.24 mL, 1.19 mmol) and **2b** (0.38 mL, 2.38 mmol), according to general procedure B, afforded compounds **3b** (103 mg, 31%) and **4b** (202 mg, 61%).

3-Phenyltetradeca-1,2,13-trien-4-ol (3c) and 1-phenyltetradec-13-en-1-yn-4-ol (4c)

Reaction of **1a** (0.24 mL, 1.19 mmol) and **2c** (0.33 mL, 2.38 mmol), according to general procedure B, afforded compounds **3d** and **4d** (86:14; 83% overall yield after CC).

1,4-Diphenylhexa-4,5-dien-3-ol (3d) and 1,6-diphenylhex-5-yn-3-ol (4d)

Reaction of **1b** (0.20 mL, 1.49 mmol) and **2c** (0.41 mL, 2.98 mmol), according to general procedure B, afforded compounds **3d** and **4d** (83:17; 67% overall yield after CC).

3-Hydroxy-2-ethenylidenenetridec-12-en-1-yl pivalate (3f) and 5-hydroxypentadec-14-en-2-yn-1-yl pivalate (4f)

Reaction of **1a** (0.19 mL, 0.94 mmol) and 4-bromobut-2-yn-1-yl pivalate (**2d**) (440 mg, 1.89 mmol), according to general procedure B, afforded compounds **3f** (27 mg, 9%) and **4f** (191 mg, 63%). Compound **3f**: isolated as a colorless oil. IR (film) ν (cm^{-1}) 3441, 2927, 2855, 1959, 1732, 1640, 1480, 1461, 1366, 1282, 1151, 1033, 994, 909, 849. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.83 (ddt, *J* = 17.1, 10.2, 6.7 Hz, 1H), 5.05-4.92 (m, 4H), 4.73 (dt, *J* = 12.4, 2.5 Hz, 1H), 4.63 (dt, *J* = 12.4, 2.4 Hz, 1H), 4.14 (m, 1H), 2.05 (m, 3H), 1.65 (m, 2H), 1.30 (m, 10H), 1.23 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 205.9 (C), 178.5 (C), 139.2 (CH), 114.1 (CH_2), 103.4 (C), 78.8 (CH_2), 70.2 (CH), 62.1 (CH_2), 38.9 (C), 35.6 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 27.2 (CH_3), 25.7 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{35}O_3$ 323.2586; found 323.2554. Compound **4f**: isolated as a yellow oil. IR (film) ν (cm^{-1}) 3441, 2927, 2855, 2238, 1735, 1640, 1480, 1461, 1366, 1281, 1150, 1032, 964, 910. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.82 (ddt, *J* = 17.1, 10.2, 6.7 Hz, 1H), 5.00 (ddt, *J* = 17.4, 2.2, 1.6 Hz, 1H), 4.94 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H), 4.67 (t, *J* = 2.1 Hz, 2H), 3.75 (m, 1H), 2.47 (ddt, *J* = 16.7, 4.4, 2.2 Hz, 1H), 2.35 (ddt, *J* = 16.7, 6.7, 2.2 Hz, 1H), 2.03 (m, 3H), 1.54-1.36 (m, 6H), 1.52 (br s, 8H), 1.23 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 177.9 (C),139.2 (CH), 114.1 (CH_2), 83.5 (C), 77.0 (C), 69.9 (CH), 52.7 (CH_2), 38.8 (C), 33.8 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 27.7 (CH_2), 27.1 (CH_3), 25.6 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{35}O_3$ 323.2586; found 153.2602.

Reaction of undec-10-enal (0.19 mL, 0.94 mmol) and 4-bromobut-2-yn-1-yl pivalate (440 mg, 1.89 mmol), according to general procedure B but at -10ºC. Compound **4f** was exclusively formed, quantitative transformation by ^{1}H NMR analysis.

Ethyl 3-hydroxy-2-ethenylidenetridec-12-enoate (3g)

Reaction of **1a** (0.08 mL, 0.41 mmol) and ethyl 4-chlorobut-2-ynoate (**2e**) (119 mg, 0.82 mmol), according to general procedure B, afforded compound **3g** (42 mg, 36%), isolated as a light yellow oil. IR (ATR) *v* (cm^{-1}) 3462, 2925, 2854, 1964, 1939, 1700, 1458, 1253, 1064, 910, 847, 789. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.82 (ddt, *J* = 16.8, 9.9, 6.6 Hz, 1H), 5.26 (d, *J* = 1.8 Hz, 2H), 5.00 (ddt, *J* = 17.4, 1.8, 1.8 Hz, 1H), 4.94 (ddt, *J* = 10.2, 2.4, 1.2 Hz, 1H), 4.42 (t, *J* = 6.6 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 2.28 (br s, 1H), 2.04 (m, 2H), 1.65 (m, 2H), 1.38-1.25 (m, 15H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 212.3 (C), 167.2 (C), 139.2 (CH), 114.1 (CH_2), 103.2 (C), 80.6 (CH_2), 69.4 (CH), 61.2 (CH_2), 35.3 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.8 (CH_2), 14.2 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{29}O_3$ 281.2117; found 281.2103.

3-Ethyl-1,2-decadien-4-ol (3h) and dodec-3-yn-6-ol (4h)

Reaction of heptanal (**1d**) (0.20 mL, 1.43 mmol) and 1-bromopent-2-yne (**2a**) (0.30 mL, 2.86 mmol), according to general procedure B, afforded compounds **3h** and **4h** (83% overall yield after CC). Compound **3h** (64 mg), isolated as a light yellow oil: IR (film) *v* (cm^{-1}) 3418, 2959, 2930, 2858, 1955, 1714, 1460, 1379, 1038, 844, 726. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.86 (m, 2H), 4.06-4.00 (m, 1H), 2.05-1.94 (m, 2H), 1.66-1.46 (m, 2H), 1.28 (br s, 8H), 1.03 (t, *J* = 7.4 Hz, 3H), 0.88 (m, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.3 (C), 109.2 (C), 78.7 (CH_2), 72.17 (CH), 35.6 (CH_2), 31.8 (CH_2), 29.2 (CH_2), 25.5 (CH_2), 22.6 (CH_2), 20.7 (CH_2), 14.0 (CH_3), 12.1 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{23}O$ 183.1749; found 183.1762. Compound **4h** could not be isolated and an inseparable mixture of **3h** and **4h** was obtained. Signals due to **4h**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.71-3.64 (m, 1H), 2.39 (ddt, *J* = 16.4, 4.8, 2.5 Hz, 1H), 2.31-2.21 (m, 1H), 2.17 (m, 2H), 1.15 (t, *J* = 7.5 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 84.5 (C), 75.5 (C), 70.2 (CH_2), 36.2 (CH_2), 31.8 (CH_2), 29.2 (CH_2), 27.7 (CH_2), 25.6 (CH_2), 14.1 (CH_2), 12.4 (CH_3).

6-Ethenylidenetridecan-7-ol (3i) and pentadec-9-yn-7-ol (4i)

Reaction of heptanal (0.20 mL, 1.43 mmol) and 1-chlorooct-2-yne (**2b**) (0.44 mL, 2.86 mmol), according to general procedure B, afforded compounds **3i** and **4i** (60% overall

yield after CC). Compound **3i** (55 mg), isolated as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.84 (m, 2H), 4.02 (t, *J* = 6.5 Hz, 1H), 2.04-1.90 (m, 2H), 1.77 (br s, 1H), 1.67-1.56 (m, 2H), 1.51-1.41 (m, 3H), 1.34-1.29 (m, 11H), 0.92-0.87 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.4 (C), 107.7 (C), 78.4 (CH_2), 72.0 (CH), 35.6 (CH_2), 31.8 (CH_2), 31.6 (CH_2), 29.2 (CH_2), 27.8 (CH_2), 27.3 (CH_2), 25.5 (CH_2), 22.6 (CH_2), 22.5 (CH_2), 14.1 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{29}O$ 225.2218; found 225.2237. Compound **4i**[27] could not be isolated and an inseparable mixture of **3i** and **4i** was obtained. Signals due to **4i**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.69 (m, 1H), 2.41 (ddt, *J* = 16.4, 4.8, 2.4 Hz, 1H), 2.27 (ddt, *J* = 16.4, 6.8, 2.4 Hz, 1H), 2.17 (tt, *J* = 7.1, 2.4 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 83.3 (C), 76.1 (C), 70.3 (CH).

3-Phenyl-1,2-decadien-4-ol (3j) and 1-phenyldec-1-yn-4-ol (4j)

Reaction of heptanal (0.20 mL, 1.43 mmol) and (3-chloroprop-1-yn-1-yl)benzene (**2c**) (0.39 mL, 2.86 mmol), according to general procedure B, afforded compounds **3j** and **4j** (69% overall yield after CC). Compound **3j** (156 mg) was isolated as a light yellow oil and its spectral data are in agreement with literature values.[28] Compound **4j** could not be isolated and an inseparable mixture of **3j** and **4j** was obtained. Signals due to **4j**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.89-3.84 (m, 1H), 2.68 (dd, *J* = 16.7, 4.8 Hz, 1H), 2.57 (dd, *J* = 16.7, 6.7 Hz, 1H).

1-Cyclopentyl-2-ethylbuta-2,3-dien-1-ol (3k) and 1-cyclopentylhex-3-yn-1-ol (4k)

Reaction of cyclopentanecarbaldehyde (**1e**) (0.22 mL, 2.04 mmol) and 1-bromopent-2-yne (**2a**) (0.43 mL, 4.08 mmol), according to general procedure B, afforded compounds **3k** and **4k** (94% overall yield after CC). Compound **3k** (124 mg), isolated as a light yellow oil: IR (film) *v* (cm^{-1}) 3421, 2957, 2868, 1955, 1708, 1453, 1023, 843, 631. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.87 (dd, *J* = 3.7, 1.7 Hz, 1H), 4.86 (dd, *J* = 3.7, 1.7 Hz, 1H), 3.87 (br d, *J* = 7.8 Hz, 1H), 2.13 (tt, *J* = 7.9 Hz, 1H), 2.04 (m, 2H), 2.82-1.73 (m, 1H), 1.69-1.53 (m, 5H), 1.46-1.39 (m, 1H), 1.53-1.26 (m, 1H), 1.06 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 205.2 (C), 108.8 (C), 78.3 (CH_2), 76.7 (CH), 44.1 (CH), 29.3 (CH_2), 28.6 (CH_2), 25.8 (CH_2), 25.8 (CH_2), 20.8 (CH_2), 12.2 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{11}H_{19}O$ 167.1436; found 167.1415. Compound **4k** could not be isolated and an inseparable mixture of **3k** and **4k** was obtained. Signals due to **4k**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.47 (dt, *J* = 7.5, 3.8 Hz, 1H), 2.50-2.40 (m, 1H), 2.27 (ddt, *J* = 16.5, 7.5, 2.4 Hz, 1H), 1.14 (t, *J* = 7.5 Hz, 3H).

$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 84.5 (C), 75.7 (C), 74.3 (CH), 45.2 (CH), 29.1 (CH_2), 28.9 (CH_2), 26.8 (CH_2), 25.6 (CH_2), 25.6 (CH_2), 14.2 (CH_3), 12.4 (CH_2).

1-(Cyclohex-3-en-1-yl)-2-ethylbuta-2,3-dien-1-ol (3l) and 1-(cyclohex-3-en-1-yl)hex-3-yn-1-ol (4l)

Reaction of cyclohex-3-ene-1-carbaldehyde (**1f**) (0.21 mL, 1.82 mmol) and 1-bromopent-2-yne (**2a**) (0.38 mL, 3.64 mmol), according to general procedure B, afforded compounds **3l** (217 mg, 67%) and **4l** (49 mg, 15%). Compound **3l** (mixture of diastereoisomers 6:4): light yellow oil; IR (film) *v* (cm^{-1}) 3387, 3022, 2914, 1955, 1436, 1380, 1265, 1011, 846, 735, 655. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) both isomers: 5.69 (m, 2H), 4.92-4.86 (m, 2H), 2.18-1.67 (m, 9H), 1.49-1.29 (m, 1H); major isomer: 3.92 (d, *J* = 6.3 Hz, 1H), 1.06 (t, *J* = 7.5 Hz, 3H); minor isomer: 3.87 (d, *J* = 6.6 Hz, 1H), 1.05 (t, *J* = 7.5 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) both isomers: 205.0 (C), 204.7 (C), 127.1 (CH), 126.9 (CH), 126.4 (CH), 126.3 (CH), 108.2 (C), 107.8 (C), 79.0 (CH_2), 78.6 (CH_2), 76.1 (CH), 76.0 (CH), 37.7 (CH), 37.4 (CH), 28.5 (CH_2), 26.3 (CH_2), 25.9 (CH_2), 25.2 (CH_2), 25.1 (CH_2), 23.7 (CH_2), 20.7(CH_2), 20.7 (CH_2), 12.1 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{19}O$ 179.1436; found 179.1410. Compound **4l** (mixture of diastereoisomers 53:46): light yellow oil; IR (film) *v* (cm^{-1}) 3413, 3023, 2915, 1435, 1264, 1048, 733. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) both isomers: 5.70 (m, 2H), 2.55-2.43 (m, 1H), 2.40-2.28 (m, 1H), 2.18 (qt, *J* = 7.2, 2.1 Hz, 2H), 2.09-1.68 (m, 8H), 1.14 (t, *J* = 7.5 Hz, 3H); major isomer: 3.57 (m, 1H); minor isomer: 3.46 (m, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) both isomers: 127.4 (CH), 126.8 (CH), 126.3 (CH), 125.8 (CH), 84.8 (C), 84.7 (C), 75.6 (C), 75.4 (C), 73.7 (CH), 73.5 (CH), 38.6 (CH), 38.4 (CH), 27.8 (CH_2), 26.8 (CH_2), 25.2 (CH_2), 25.14 (CH_2), 25.09 (CH_2), 23.07 (CH_2), 24.4(CH_2), 14.2 (CH_3), 12.5 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{12}H_{19}O$ 179.1436; found 179.1452.

1-(Cyclohex-2-en-1-yl)-2-phenylbuta-2,3-dien-1-ol (3m) and 1-(cyclohex-2-en-1-yl)-4-phenylbut-3-yn-1-ol (4m)

Reaction of cyclohex-3-ene-1-carbaldehyde (**1f**) (0.21 mL, 1.82 mmol) and (3-chloroprop-1-yn-1-yl)benzene (**2c**) (0.50 mL, 3.64 mmol), according to general procedure B, afforded compounds **3m** and **4m** (56% overall yield after CC). Compound **3m** (24 mg), isolated as a mixture of diastereoisomers 1:1. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) both isomers: 7.50-7.46 (m, 2H), 7.39-7.33 (m, 2H), 7.28-7.23 (m, 1H), 5.69 (m,

2H), 5.31-5.21 (m, 2H), 2.17-1.74 (m, 7H); isomer a: 4.53 (br s, 1H); isomer b: 4.46 (br s, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) both isomers: 207.8 (C), 207.4 (C), 134.84 (C), 134.78 (C), 128.6 (CH), 127.2 (CH), 127.0 (CH), 126.9 (CH), 126.4 (CH), 126.3 (CH), 109.0 (C), 108.8 (C), 80.5 (CH_2), 80.2 (CH_2), 74.1 (CH), 74.0 (CH), 38.3 (CH), 38.1 (CH), 28.7 (CH_2), 26.4 (CH_2), 26.2 (CH_2), 25.3 (CH_2), 25.0 (CH_2), 23.6 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{19}O$ 227.1436; found 227.1458. Compound **4m** could not be isolated and an inseparable mixture of **3m** and **4m** was obtained. Signals due to **4m** (mixture of diastereoisomers 1:1): ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) isomer a: 3.74 (m, 1H); isomer b: 3.64 (m, 1H); common signals: 2.75 (m, 1H), 2.64 (m, 1H).

3-Ethyl-5,9-dimethyldeca-1,2,8-trien-4-ol (3n)

Reaction of 2,6-dimethylhept-5-enal (**1g**) (0.23 mL, 1.43 mmol) and 1-bromopent-2-yne (**2a**) (0.30 mL, 2.86 mmol), according to general procedure B, afforded compound **3n** (217 mg, 73%), isolated as a light yellow oil (mixture of diastereoisomers 35:65). ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) both isomers: 5.12 (br t, *J* = 7.5 Hz, 1H), 4.96-4.89 (m, 2H), 2.14-1.88 (m, 4H), 1.70 (s, 3H), 1.63 (s, 3H), 1.59-1.44 (m, 1H), 1.35-1.10 (m, 2H), 1.06 (t, *J* = 7.5 Hz, 3H); minor isomer: 3.92 (m, 1H), 0.89 (d, *J* = 6.9 Hz, 3H); major isomer: 3.85 (m, 1H), 0.96 (d, *J* = 6.9 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) both isomers: 204.7 (C), 204.2 (C), 131.4 (C), 124.8 (CH), 124.6 (CH), 109.1 (C), 108.6 (C), 79.7 (CH_2), 79.0 (CH_2), 77.0 (CH), 74.6 (CH), 36.3 (CH), 35.8 (CH), 33.8 (CH_2), 31.0 (CH_2), 25.7 (CH_3), 25.7 (CH_2), 25.6 (CH_2), 21.2 (CH_2), 20.9 (CH_2), 17.7 (CH_3), 16.4 (CH_3), 13.4 (CH_3), 12.1 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{25}O$ 209.1095; found 209.1117.

4-Ethyl-1-phenylhexa-4,5-dien-3-ol (3o) and 1-phenyloct-5-yn-3-ol (4o)

Reaction of 3-phenylpropanal (**1b**) (0.20 mL, 1.49 mmol) and 1-bromopent-2-yne (**2a**) (0.32 mL, 2.98 mmol), according to general procedure B, afforded compounds **3o** and **4o** (74% overall yield after CC). Compound **3o** (62 mg), isolated as a colorless oil. Spectral data are in agreement with literature values[29]. Compound **4o** could not be isolated and an inseparable mixture of **3o** and **4o** was obtained. Signals due to **4o**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 3.74 (m, 1H), 2.45 (ddt, *J* = 16.4, 4.7, 2.4 Hz, 1H), 2.33 (ddt, *J* = 16.4, 6.8, 2.3 Hz, 1H), 2.21 (qt, *J* = 7.5, 2.4 Hz, 2H), 1.16 (t, *J* = 7.5 Hz, 3H).

3-Hydroxy-5-phenyl-2-ethenylidenepentyl pivalate (3p) and 5-hydroxy-7-phenylhept-2-yn-1-yl pivalate (4p)

Reaction of 3-phenylpropanal (**1b**) (0.12 mL, 0.91 mmol) and 4-bromobut-2-yn-1-yl pivalate (**2d**) (422 mg, 1.81 mmol), according to general procedure B, afforded compounds **3p** (34 mg, 13%) and **4p** (170 mg, 65%). Compound **3p**, isolated as a colorless oil. IR (film) *v* (cm^{-1}) 3439, 3027, 2959, 2931, 2869, 1958, 1729, 1603, 1480,1454, 1397, 1366, 1282, 1149, 1033, 854, 748, 700. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.31 (m, 2H), 7.23 (m, 3H), 4.99 (m, 2H), 4.78 (dt, *J* = 12.4, 2.5 Hz, 1H), 4.63 (dt, *J* = 12.4, 2.3 Hz, 1H), 4.14 (m, 1H), 2.78 (m, 2H), 2.30 (br s, 1H), 1.97 (m, 2H), 1.21 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 205.8 (C), 178.7 (C), 141.7 (C), 128.5 (CH), 128.4 (CH), 125.9 (CH), 103.3 (C), 79.1 (CH_2), 69.0 (CH), 62.2 (CH_2), 38.9 (C), 37.1 (CH_2), 31.9 (CH_2), 27.2 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{25}O_3$ 289.1804; found 289.1785. Compound **4p**, isolated as a light yellow oil. IR (film) *v* (cm^{-1}) 3440, 3027, 2973, 2935, 2873, 2237, 1733, 1603, 1480, 1455, 1366, 1281, 1149, 1032, 962, 746, 700. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.31 (m, 2H), 7.23 (m, 3H), 4.68 (t, *J* = 4.7 Hz, 2H), 3.79

(m, 1H), 2.83 (m, 1H), 2.72 (dt, *J* = 13.8, 8.1 Hz, 1H), 2.50 (ddt, *J* = 16.8, 4.5, 2.4 Hz, 1H), 2.40 (ddt, *J* = 16.8, 6.6, 2.4 Hz, 1H), 1.87 (td, *J* = 8.1, 5.4 Hz, 2H), 1.23 (s, 9H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 178.0 (C), 141.7 (C), 128.5 (CH), 125.9 (CH), 83.2 (C), 77.3 (C), 69.1 (CH), 52.6 (CH_2), 38.8 (C), 37.9 (CH_2), 31.9 (CH_2), 27.9 (CH_2), 27.1 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{25}O_3$ 289.1804; found 289.1827.

Ti-induced coupling between 1a and 2f

Reaction of undec-10-enal (**1a**) (0.15 mL, 0.75 mmol) and 4-bromobut-2-yn-1-ol (**2a**) (0.22 g, 1.5 mmol), according to general procedure B (but with $CpTiCl_3$ (2 eq.) and Mn dust (3 eq.)), afforded compounds **3q** and **4q** (28:72) (40% overall yield after CC) and compounds **3r** (9 mg, 5%) and **4r** (57 mg, 34%). Compounds **3q** and **4q** could not be isolated and an inseparable mixture of **3q** and **4q** was obtained. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.80 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.03-4.87 (m, 2H), 4.23 (m, 5H), 3.77-3.59 (m, 3H), 2.52-2.24 (m, 2H), 2.03 (m, 2H), 1.69-1.45 (m, 2H), 1.28 (br s, 12H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 205.2 (C), 139.2 (CH), 114.1 (CH_2), 105.6 (C), 82.7 (C), 80.8 (C), 77.9 (CH_2), 71.4 (CH), 70.1 (CH), 61.9 (CH_2), 50.8 (CH_2), 36.3 (CH_2), 35.6 (CH_2), 33.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 27.5 (CH_2), 25.7 (CH_2), 25.7 (CH_2).

3-Methyltetradeca-1,2,13-trien-4-ol (**3r**). IR (film) ν (cm^{-1}) 3359, 3076, 2924, 2854, 1959, 1641, 1459, 995, 908. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.84 (ddt, J = 16.9, 10.2, 6.7 Hz, 1H), 5.5-4.93 (m, 2H), 4.78 (m, 2H), 4.06 (m, 1H), 2.06 (q, J = 6.8 Hz, 2H), 1.73 (t, J = 3.2 Hz, 3H), 1.59 (s, 3H), 1.37-1.27 (m, 12H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.9 (C), 139.3 (CH), 114.1 (CH_2), 102.0 (C), 76.6 (CH_2), 72.6 (CH), 35.1 (CH_2), 33.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.4 (CH_2), 14.3 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{27}O$ 223.2062; found 223.2048.

Pentadec-14-en-2-yn-5-ol (**4r**). IR (film) ν (cm^{-1}) 3380, 3075, 2923, 2854, 1641, 1458, 1077, 956, 910. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.90-5.76 (m, 1H), 4.96 (m, 2H), 3.70 (m, 1H), 2.24-2.21 (m, 2H), 2.05 (m, 2H), 1.83 (br s, 3H), 1.51 (m, 2H), 1.30 (br s, 13H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 139.2 (CH), 114.1 (CH_2), 78.4 (C), 75.4 (C), 70.2 (CH), 36.3 (CH_2), 33.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 27.7 (CH_2), 25.7 (CH_2), 3.6 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{27}O$ 223.2062; found 223.2067.

Synthesis of compounds 9a, 9b and 10

Reaction of **8** (85 mg, 0.31 mmol) and 1-bromobut-2-yne (0.055 mL, 0.62 mmol), according to general procedure B, but under reflux instead of r.t., afforded compounds **9a** (52 mg, 51%) and an inseparable mixture of **9b** and **10** (63:35) (35 mg, 34%).

(4*S*,5*R*,9*S*,10*R*,12*R*)-Methyl 12-hidroxylabda-8(17),13,14-trien-19-oate (**9a**), isolated as a colorless oil. IR (film) ν (cm^{-1}) 3430, 3077, 2946, 1958, 1724, 1644, 1463, 1443, 1229, 1154, 1031, 891, 845. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.88 (br s, 1H), 4.80 (m, 2H), 4.47 (br s, 1H) 4.03 (m, 1H), 3.64 (s, 3H), 2.43 (m, 1H), 2.19 (m, 1H), 2.09-1.79 (m, 6H), 1.76 (t, J = 3.0 Hz, 3H), 1.72-1.38 (m, 5H), 1.21 (s, 3H), 1.07 (m, 1H), 0.52 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.3 (C), 177.8 (C), 148.5 (C), 106.4 (CH_2), 103.3 (C), 77.0 (CH_2), 70.4 (CH), 56.2 (CH), 51.6 (CH), 51.2 (CH_3), 44.3 (C), 39.9 (C), 39.1 (CH_2), 38.7 (CH_2), 38.2 (CH_2), 30.6 (CH_2), 28.8 (CH_3), 26.2 (CH_2), 19.9 (CH_2), 14.8 (CH_3), 12.7 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{33}O_3$ 333.2430; found 333.2413. $[\alpha]_D^{22}$+51.45 (c 0.013, $CHCl_3$). Compounds **9b** and **10** could not be isolated and an inseparable mixture of **9b** and **10** (1:0.5) was obtained. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) common signals: 4.90 (s, 1H), 4.69 (s, 1H), 3.64 (s, 3H), 2.42 (m, 1H), 2.19 (m, 1H), 1.21 (s, 3H); characteristic signals of **9b**: 4.69 (s, 2H), 4.23 (m,

1H), 1.71 (t, *J* = 3.0 Hz, 3H), 0.54 (s, 3H); characteristic signals of **10**: 3.77 (m, 1H), 0.53 (s, 3H).

Synthesis of compounds 12a, 12b and 13

Reaction of **11** (65 mg, 0.25 mmol) and 1-bromobut-2-yne (0.044 mL, 0.49 mmol), according to general procedure B ($CpTiCl_3$ (2 eq.) and Mn dust (3 eq.) in this case), but under reflux instead of r.t., afforded compounds **12a** (30 mg, 46%), **12b** (16 mg, 20%) and an inseparable mixture of **12b** and **13** (1:0.9) (12 mg, 14%).

(4*S*,5*R*,9*S*,10*R*,12*R*)-12-Hidroxylabda-8(17),13,14-trien-19-oic acid (**12a**), isolated as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.88 (br s, 1H), 4.80 (t, *J* = 3.3 Hz, 2H), 4.48 (br s, 1H), 4.05 (dd, *J* = 9.9, 1.8 Hz, 1H), 2.43 (m, 1H), 2.19 (m, 1H), 2.10-1.85 (m, 6H), 1.76 (t, *J* = 3.3 Hz, 3H), 1.69 (s, 1H), 1.62-1.53 (m, 2H), 1.45-1.41 (m, 1H), 1.26 (s, 3H), 1.17-1.03 (m, 2H), 0.62 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 204.3 (C), 183.6 (C), 148.4 (C), 106.6 (CH_2), 103.2 (C), 77.0 (CH_2), 70.5 (CH), 56.2 (CH), 51.6 (CH), 44.2 (C), 40.1 (C), 39.0 (CH_2), 38.6 (CH_2), 37.9 (CH_2), 30.6 (CH_2), 29.0 (CH_3), 26.0 (CH_2), 19.9 (CH_2), 14.8 (CH_3), 12.9 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{31}O_3$ 319.2273; found 319.2288.

(4*S*,5*R*,9*S*,10*R*,12*S*)-12-Hidroxylabda-8(17),13,14-trien-19-oic acid (**12b**), isolated as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 4.90 (br s, 1H), 4.69 (m, 3H), 4.24 (m, 1H), 2.43 (m, 1H), 2.19 (m, 1H), 2.01-1.79 (m, 7H), 1.71 (t, *J* = 3.0 Hz, 3H), 1.65-1.53 (m, 2H), 1.39-1.34 (m, 1H), 1.26 (s, 3H), 1.08 (m, 2H), 0.64 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 206.3 (C), 183.3 (C), 148.4 (C), 106.8 (CH_2), 100.5 (C), 75.1 (CH_2), 73.1 (CH), 56.3 (CH), 52.4 (CH), 44.2 (C), 40.3 (C), 39.1 (CH_2), 38.7 (CH_2), 37.9 (CH_2), 29.4 (CH_2), 29.0 (CH_3), 26.1 (CH_2), 19.9 (CH_2), 13.2 (CH_3), 12.9 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{31}O_3$ 319.2273; found 319.2254.

Compounds **13** could not be isolated and an inseparable mixture of **12b** and **13** (1:0.9) was obtained. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) common signals: 4.88 (s, 1H), 4.80 (m, 1H), 2.42 (m, 2H), 2.19 (m, 2H), 1.27 (s, 3H), 0.63 (s, 3H); characteristic signals of **13**: 3.75 (m, 1H).

Preparation of 11. Compound **11** was prepared as previously described.[24] IR (film) *v* (cm^{-1}) 3078, 2846, 2722, 1719, 1691, 1446, 1386, 1320, 1262, 947, 891. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 9.65 (br s, 1H), 4.85 (br s, 1H), 4.41 (br, 1H), 2.54-2.34 (m, 4H), 2.21 (d, *J*= 13.5 Hz, 1H), 2.05-1.80 (m, 4H), 1.68-1.43 (m, 4H), 1.28 (s, 3H), 1.16-1.04 (m, 1H), 0.64 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 203.3 (CH), 184.0

(C), 147.9 (C), 108.2 (CH_2), 55.9 (CH), 50.2 (CH), 44.1 (C), 39.8 (C), 39.7 (CH_2), 39.3 (CH_2),, 37.9 (CH_2), 37.8 (CH_2), 28.9 (CH_3), 25.5 (CH_2), 19.8 (CH_2), 13.0 (CH_3).

General procedure C for the synthesis of 2,5-dihydrofurans

A solution of the allenol (1 eq) in acetone (6 mL/mmol) is added to a suspension of $AgNO_3$ (1.5 eq) in acetone (4 mL/mmol) in absence of light, and the mixture is stirred overnight. Brine is added before being extracted with Et_2O. The organic phase is dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Products are purified by silica gel flash column chromatography (hexane/Et_2O mixtures).

2-(Dec-9-en-1-yl)-3-ethyl-2,5-dihydrofuran (6a)

Reaction of allenol **3a** (115 mg, 0.49 mmol), according to general procedure C, afforded compound **6a** (97 mg, 84%), isolated as a yellow oil. IR (film) *v* (cm^{-1}) 3077, 2927, 2853, 1641, 1461, 1093, 1061, 908. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.83 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.47 (m, 1H), 5.05-4.91 (m, 2H), 4.73-4.64 (m, 1H), 4.62-4.56 (m, 2H), 2.08-1.91 (m, 4H), 1.69-1.59 (m, 1H), 1.45-1.30 (m, 13H), 1.12 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 144.6 (C), 139.3 (CH), 118.2 (CH), 114.1 (CH_2), 86.9 (CH), 74.6 (CH_2), 34.2 (CH_2), 33.8 (CH_2), 29.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.2 (CH_2), 28.9 (CH_2), 24.7 (CH_2), 20.1 (CH_2), 11.9 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{29}O$ 237.2218; found 237.2195.

2-Phenethyl-3-phenyl-2,5-dihydrofuran (6d)

Reaction of allenol **3d** (54 mg, 0.22 mmol), according to general procedure C, afforded compound **6d** (52 mg, 95%), isolated as a light yellow oil. IR (film) *v* (cm^{-1}) 3060, 3027, 2924, 2847, 1949, 1879, 1495, 1450, 1157, 1083, 1012, 750, 697. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.35-7.18 (m, 10H), 6.19 (m, 1H), 5.42 (m, 1H), 4.88 (m, 2H), 2.79 (t, *J* = 7.5 Hz, 2H), 2.13 (m, 1H), 1.94 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) δ 142.2 (C), 141.8 (C), 133.4 (C), 128.7 (CH), 128.5 (CH), 128.3 (CH), 127.9 (CH), 126.4 (CH), 125.8 (CH), 122.0 (CH), 85.0 (CH), 75.3 (CH_2), 36.2 (CH_2), 31.2 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{19}O$ 251.1436; found 251.1461.

2-(Cyclohex-3-en-1-yl)-3-ethyl-2,5-dihydrofuran (6l)

Reaction of allenol **3l** (84 mg, 0.47 mmol), according to general procedure C, afforded compound **6l** (61 mg, 73%), as an inseparable mixture of diastereoisomers (6:4), isolated as a light yellow oil. IR (film) *v* (cm^{-1}) 3021, 2837, 1655, 1457, 1256, 1105, 1065, 1026, 808, 673. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) both isomers: 5.68 (m, 2H), 4.68 (br s, 1H), 4.60 (m, 2H), 2.20-1.62 (m, 9H), 1.14 (t, *J* = 7.5 Hz, 3H); minor isomer: 5.56 (m,

1H); major isomer: 5.52 (m, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) major isomer: δ 143.0 (C), 126.9 (CH), 126.7 (CH), 119.0 (CH), 90.8 (CH), 75.6 (CH_2), 37.0 (CH), 26.5 (CH_2), 26.0 (CH_2), 24.0 (CH_2), 20.2 (CH_2), 11.9 (CH_3); minor isomer: 142.9 (C), 127.1 (CH), 119.2 (CH), 90.1 (CH), 75.2 (CH_2), 37.3 (CH), 29.0 (CH_2), 25.6 (CH_2), 21.2 (CH_2), 20.2 (CH_2), 11.9 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{19}O$ 179.1436; found 179.1455.

2-(Cyclohex-3-en-1-yl)-3-phenyl-2,5-dihydrofuran (6m)

Reaction of allenol **3m** (47 mg, 0.21 mmol), according to general procedure C, afforded compound **6m** (44 mg, 93%) as an inseparable mixture of diastereoisomers (1:1), isolated as a light yellow oil. IR (film) *v* (cm^{-1}) 3023, 2838, 1495, 1350, 1264, 1078, 1014, 735, 699. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) both isomers: 7.40-7.29 (m, 5H), 5.76-5.61 (m, 2H), 5.33 (m, 1H), 4.88-4.71 (m, 2H), 2.31-1.60 (m, 7H); isomer a: 6.17 (dt, *J*= 2.1, 1.9 Hz, 1H); isomer b: 6.14 (dt, *J*= 2.1, 1.9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) both isomers: 140.8 (C), 140.6 (C), 133.8 (C), 133.7 (C), 128.6 (CH), 128.0 (CH), 127.8 (CH), 128.7 (CH), 127.0 (CH), 126.9 (CH), 126.8 (CH), 126.6 (CH), 126.5 (CH), 122.7 (CH), 122.6 (CH), 89.6 (CH), 88.8 (CH), 76.4 (CH_2), 76.0 (CH_2), 37.6 (CH), 37.1 (CH), 29.1 (CH_2), 26.6 (CH_2), 25.9 (CH_2), 25.4 (CH_2), 24.1 (CH_2), 21.4 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}O$ 227.1436; found 227.1419.

3-Ethyl-2-phenethyl-2,5-dihydrofuran (6o)

Reaction of allenol **3o** (57 mg, 0.28), according to the general procedure C, afforded compound **6o** (50 mg, 87%), isolated as a yellow oil. IR (film) *v* (cm^{-1}) 3060, 3027, 2966, 2933, 2842, 1603, 1496, 1455, 1351, 1254, 1177, 1091, 1052, 1014, 908, 811, 743, 699. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.33-7.18 (m, 5H), 5.54 (m, 1H), 4.76 (m, 1H), 4.66 (m, 2H), 2.72 (m, 2H), 2.10-1.96 (m, 3H), 1.82-1.70 (m, 1H), 1.14 (t, *J* = 7.5 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) δ 144.2 (C), 142.5 (C), 128.5 (CH), 128.3 (CH), 125.7 (CH), 118.7 (CH), 86.3 (CH), 74.8 (CH_2), 36.2 (CH_2), 31.0 (CH_2), 20.1 (CH_2), 11.9 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{14}H_{19}O$ 203.1436; found 203.1443.

(4*S*,5*R*,9*S*,10*R*,12*R*)-Methyl 12,15-epoxylabda-8(17),13-dien-19-oate (14)

Reaction of **9a** (15 mg, 0.047 mmol) according to general procedure C, afforded compound **14** (14 mg, 89%). Spectral data are in agreement with literature values.[22]

(4*S*,5*R*,9*S*,10*R*,12*R*)-12,15-Epoxylabda-8(17),13-dien-19-oic acid (15)

Reaction of **12a** (15 mg, 0.049 mmol)) according to general procedure C, afforded compound **15** (12 mg, 74%). Spectral data are in agreement with literature values.[22],[17]

(4*S*,5*R*,9*S*,10*R*,12*S*)-12,15-Epoxylabda-8(17),13-dien-19-oic acid (16)

Reaction of **12b** (7 mg, 0.022 mmol) according to the general procedure C, afforded compound **16** (6 mg, 87%). Spectral data are in agreement with literature values.[22]

General procedure D for the synthesis of allyldihydrofurans

The allenol (1 eq), allyl bromide (5 eq) and $PdCl_2$ (0.05 eq) in *N*,*N*-dimethylacetamide (DMA) (2 mL/ 0.25 mmol) are stirred under nitrogen atmosphere at room temperature (2h-4h). Then, Et_2O is added and the resulting mixture was washed with brine (x3). The organic phase is dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Products are purified by silica gel flash column chromatography (hexane/Et_2O mixtures).

4-Allyl-2-hexyl-3-pentyl-2,5-dihydrofuran (7i)

Reaction of allenol **3i** (70 mg, 0.31 mmol), according to the general procedure D, afforded compound **7i** (55 mg, 79%), isolated as a light yellow oil. IR (film) *v* (cm^{-1}) 3080, 2957, 2928, 2856, 1639, 1462, 1377, 1259, 1068, 1047, 991, 913, 719. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 5.74 (ddt, *J* = 16.5, 10.0, 6.4 Hz, 1H), 5.10-5.04 (m, 2H), 4.80 (m, 1H), 4.52 (m, 2H), 2.84 (d, *J* = 6.3 Hz, 2H), 2.33-2.14 (m, 1H), 1.93-1.86 (m, 1H), 1.69-1.62 (m, 1H), 1.30 (m, 15H), 0.90 (m, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 135.2 (CH), 135.1 (C), 129.3 (C), 115.6 (CH_2), 87.7 (CH), 76.6 (CH_2), 34.4 (CH_2), 31.9 (CH_2), 31.8 (CH_2), 29.7 (CH_2), 29.5 (CH_2), 27.6 (CH_2), 24.9 (CH_2), 24.8 (CH_2), 22.7 (CH_2), 22.5 (CH_2), 14.1 (CH_3), 14.0 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{33}O$ 265.2531; found 265.2516.

4-Allyl-2-(cyclohex-3-en-1-yl)-3-phenyl-2,5-dihydrofuran (7m)

Reaction of allenol **3m** (56 mg, 0.25 mmol), according to the general procedure D, afforded compound **7m** (57 mg, 85%), as an inseparable mixture of diastereoisomers (1:1), isolated as a yellow oil. IR (film) *v* (cm^{-1}) 3058, 2834, 1639, 1494, 1436, 1256, 1070, 917, 764, 700. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) both isomers: 7.41-7.23 (m, 5H), 5.94-5.80 (m, 1H), 5.71-5.58 (m, 2H), 5.19-5.10 (m, 2H), 4.86-4.66 (m, 2H), 3.07 (m, 1H), 2.90 (m, 1H), 2.28-1.62 (m, 7H); isomer a: 5.33 (m, 1H); isomer b: 5.27 (m, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) both isomers: 135.1 (CH), 135.0 (CH), 134.8 (C), 134.3 (C), 133.3 (C), 133.1 (C), 128.6 (CH), 128.5 (CH), 128.0 (CH), 127.9 (CH), 127.3 (CH), 127.3 (CH), 126.9 (CH), 126.9 (CH), 126.8 (CH), 126.6 (CH), 116.2 (CH_2), 92.4 (CH), 92.0 (CH), 78.8 (CH_2), 78.3 (CH_2), 37.8 (CH), 37.2 (CH), 30.4

(CH_2), 30.3 (CH_2), 28.8 (CH_2), 26.3 (CH_2), 25.8 (CH_2), 25.4 (CH_2), 24.2 (CH_2), 21.8 (CH_2). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{19}H_{23}O$ 267.1749; found 267.1753.

4-Allyl-3-ethyl-2-phenethyl-2,5-dihydrofuran (7o)

Reaction of allenol **3o** (51 mg, 0.25 mmol), according to the general procedure D, afforded compound **7o** (56 mg, 93%), isolated as a yellow oil. IR (film) *v* (cm^{-1}) 3027, 2967, 2931, 2838, 1948, 1812, 1496, 1455, 1251, 1046, 913, 876, 700. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.26 (m, 5H), 5.79 (ddt, *J* = 16.5, 10.0, 6.5 Hz, 1H), 5.07 (m, 2H), 4.90 (br s, 1H), 4.69-4.54 (m, 2H), 2.88 (d, *J* = 6.3 Hz, 2H), 2.73 (m, 2H), 2.25 (m, 1H), 2.01 (m, 2H), 1.76 (m, 1H), 1.01 (t, *J* = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$, DEPT) δ (ppm) 142.6 (C), 136.1 (C), 135.1 (CH), 129.3 (C), 128.5 (CH), 128.3 (CH), 125.7 (CH), 115.8 (CH_2), 86.9 (CH), 76.9 (CH_2), 36.4 (CH_2), 31.2 (CH_2), 29.6 (CH_2), 18.1 (CH_2), 12.9 (CH_3). HRMS (ESI/Q-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{23}O$ 243.1749; found 243.1761

ASSOCIATED CONTENT

Supporting Information. Copies of IR and NMR spectra (PDF)

ACKNOWLEDGMENTS

We are grateful for the financial support received from the Ministerio de Economía y Competitividad (MINECO) (Project CTQ2015-70724-R).

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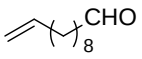
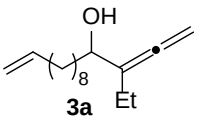
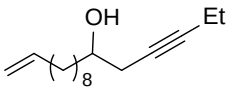
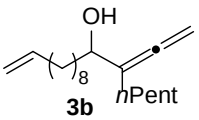
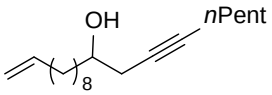
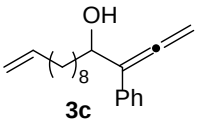
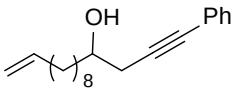
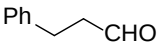
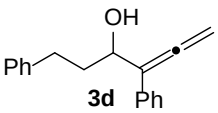
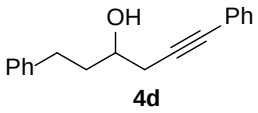
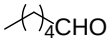
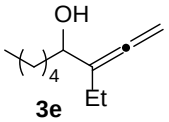
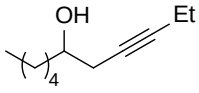
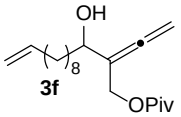
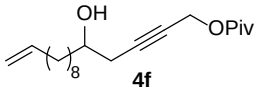
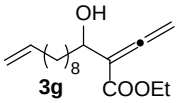
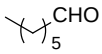
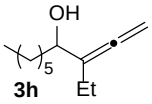
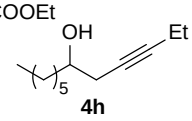
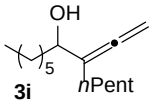
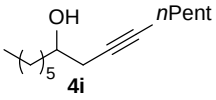
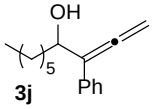
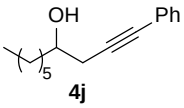
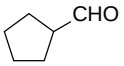
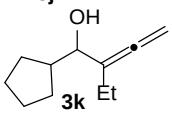
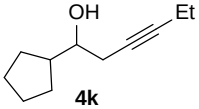
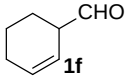
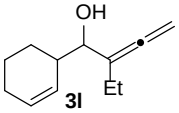
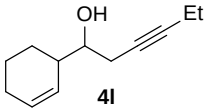
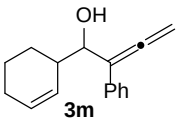
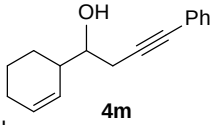
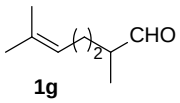
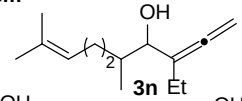
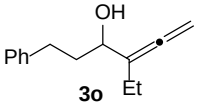
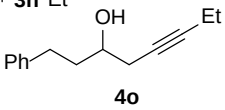
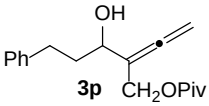
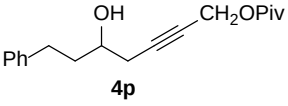
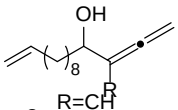
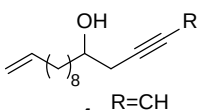
Table 1. Allenylation *versus* propargylation of aldehydes catalyzed by $CpTiCl_2$

entry	aldehyde	alkyne	products	3:4 ratio	yield(%)[a]
1	 **1a**	**2a**	 **3a**	 **4a**	37:63	71
2	**1a**	**2b**	 **3b**	 **4b**	26:74	65
3	**1a**	**2c**	 **3c**	 **4c**	50:50	63
4	 **1b**	**2c**	 **3d**	 **4d**	47:53	60
5	 **1c**	**2a**	 **3e**	 **4e**	33:67	67[b]

Reaction conditions: $CpTiCl_3$ (0.1 eq.), Mn (2 eq.), Et_3N•HBr (2 eq.), Me_3SiBr (3 eq.), THF, r.t. [a] global yield after purification by column chromatography of both compounds. [b] When aldehyde **1c** is not freshly distilled, a brominated diene (**5**) is formed as byproduct, in a similar way as described.[30]

Table 2. Allenylation *versus* propargylation of different aldehydes mediated by $CpTiCl_2$

Entry	Aldehyde	Alkyne	Products	Ratio	Yield(%)[a]
1	**1a**	**2a**	**3a**:**4a**	83:17	86
2[b]	**1a**	**2a**	**3a**:**4a**	44:56	90
3	**1a**	**2b**	**3b**:**4b**	34:66	92
4	**1a**	**2c**	**3c**:**4c**	86:14	83
5	**1b**	**2c**	**3d**:**4d**	83:17	67
6	**1a**	**2d**	 **3f**  **4f**	12:88	72
7[b]	**1a**	**2d**	**4f**	-	c
8	**1a**	**2e**	 **3g**	-	36
9	 **1d**	**2a**	 **3h**  **4h**	77:23	83
10	**1d**	**2b**	 **3i**  **4i**	53:47	60
11	**1d**	**2c**	 **3j**  **4j**	80:20	69
12	 **1e**	**2a**	 **3k**  **4k**	61:39	94
13	 **1f**	**2a**	 **3l**  **4l**	71:29	82
14	**1f**	**2c**	 **3m**  **4m**	67:33	56
15	 **1g**	**2a**	 **3n**	-	73
16	**1b**	**2a**	 **3o**  **4o**	73:27	74
17	**1b**	**2d**	 **3p**  **4p**	17:83	78
18	**1a**	**2f**	 **3q** R=CH$_2$OH **3r** R=CH$_3$  **4q** R=CH$_2$OH **4r** R=CH$_3$	28:72 13:87	40 39

Reaction conditions: $CpTiCl_3$ (1 eq.), Mn (2 eq.), THF, r.t. [a] global yield after purification by column chromatography of both compounds, except in some cases with the similar polarity (see experimental). [b] -10ºC. [c] Compound **4f** was exclusively formed. Quantitative transformation by ^{1}H NMR analysis.