Iterative Synthesis of Oligo-1,4-diols via Catalytic Anti-Markovnikov Hydration of Terminal Alkynes

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Dedicated to Prof. Dr. Hans-Joachim Gais on the occasion of his 65th birthday

Abstract: A sequential, iterative synthesis of oligo-1,4-diol building blocks has been realized via (a) propargylation of an aldehyde with allenylzinc bromide, (b) alcohol protection and (c) ruthenium-catalyzed anti-Markovnikov hydration of the terminal alkyne to release an aldehyde for the next iteration. Linear chains with 1,4-, 1,4,7- 1,4,7,10- and 1,4,7,10,13- functionalization patterns have been obtained by consecutive sequential iterations.

Key words: addition reactions, aldehydes, alkynes, homogeneous catalysis, ruthenium

The catalytic hydration of alkynes[1] is a promising tool for sustainable synthesis since it generates synthetically versatile carbonyl compounds from alkyne hydrocarbons by a waste-free addition of water, whereas many conventional syntheses involve energy-intensive redox processes and generate by-products.[2] The catalytic anti-Markovnikov[3] hydration of terminal alkynes, which generates aldehydes (Figure 1) is a potentially powerful synthetic tool. The reaction was first described in 1998[4a] and more active catalysts have since been reported,[1,4,5] but this remarkable conversion has not found applications in synthesis so far. We have recently developed an in situ catalyst based on complex **C** and ligands **L** (Figure 1), which combines the advantages of previous catalysts in terms of activity, handling and availability of the components.[5]

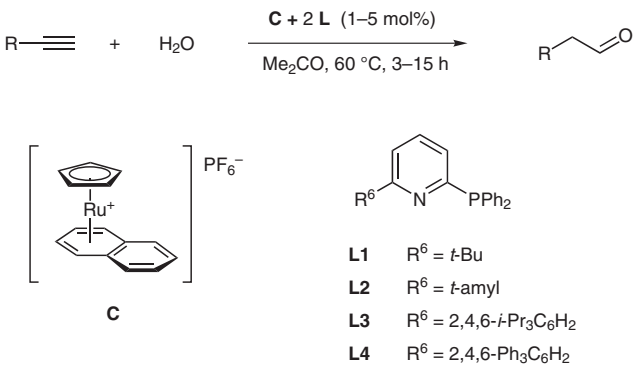

Figure 1 Catalytic anti-Markovnikov hydration of terminal alkynes

Our current studies center on developing applications of the catalytic anti-Markovnikov hydration. Using this waste-free methodology, we want to realize synthetic strategies which give access to structurally complex substrates from simple precursors with high atom-economy.[6]

Here we present the first example of such a synthetic strategy, namely, an iterative synthesis[7] of oligo-1,4-diol fragments by the sequential C–C coupling and anti-Markovnikov hydration outlined in Figure 2. Starting with an anchoring aldehyde RCHO (**I**), propargylation leads to the homopropargylic alcohol **II**. The latter is then protected and catalytically and regioselectively hydrated to aldehyde **III**. The conversion **I**→**III** corresponds to the addition of an umpoled[8] homo-enolate,[9] leading to a 1,4-functionalized product. Indeed, this represents a very efficient synthetic realization of an aldehyde homo-enolate addition. Additional iterations, with aldehyde **III** as starting material, should give oligo-1,4-diol fragments of any desired chain-length.

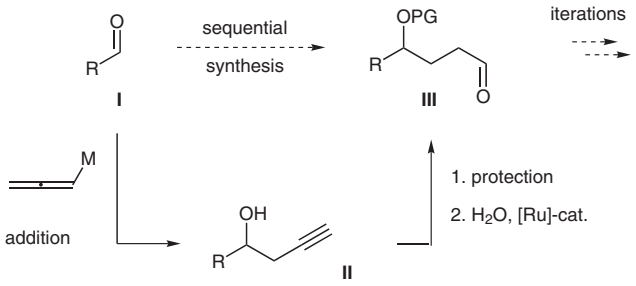

Figure 2 An iterative sequential synthetic strategy for oligo-1,4-diols

Oligo-1,4-diol fragments have, for example, been synthesized non-stereoselectively by hydrogenolysis of furfurylidene aldehydes or ketones.[10] An iterative synthesis was achieved by allylation of an anchoring aldehyde, followed by hydroboration/oxidation to a 1,4-diol; Swern oxidation of the terminal alcohol then liberates the aldehyde for another iteration.[11] Just as in the iterative synthesis of oligo-1,3-diol fragments by allylation or crotylation and ozonolysis,[12] the use of reduction and oxidation steps leads to reliable results, but also produces waste and is energy-consuming.

In contrast, our approach (Figure 2) is designed to use readily available bulk chemicals and to generate the growing chain of the homologation product without using ad-

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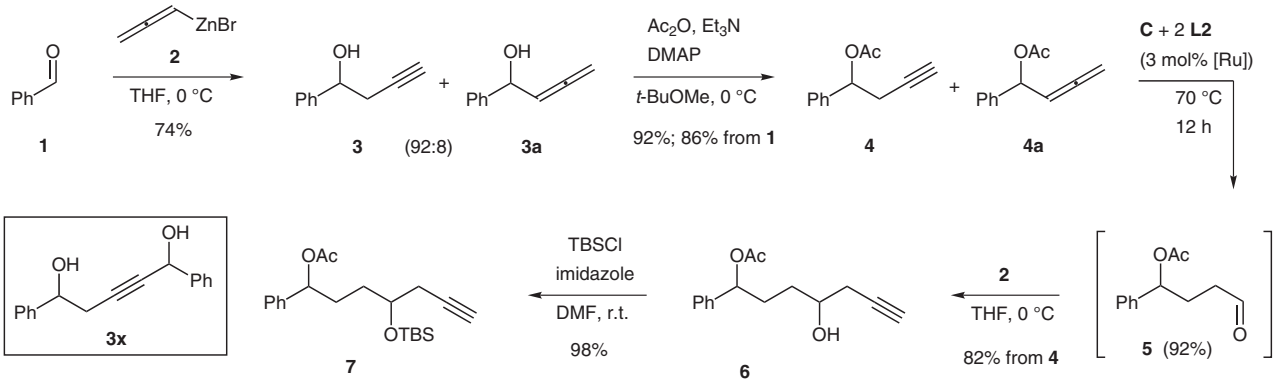


Scheme 1 First iteration steps from benzaldehyde

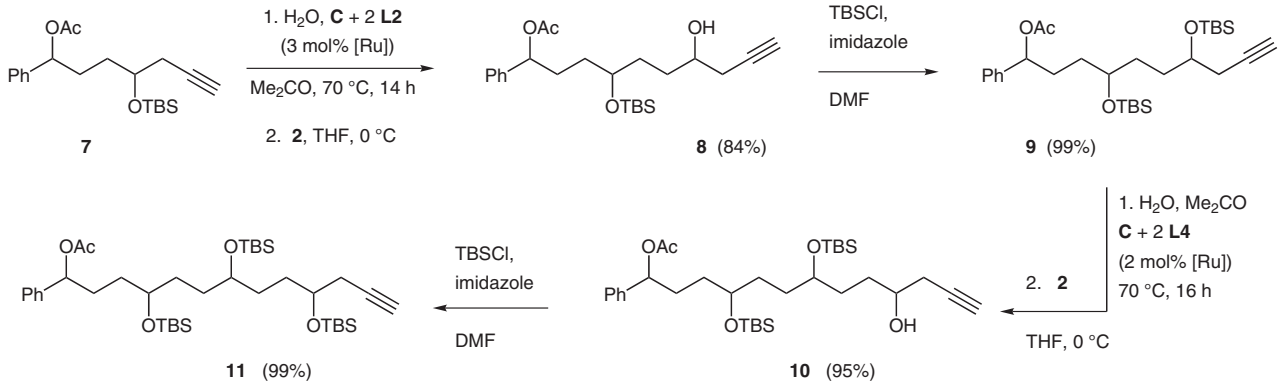
ditional reagents such as oxidants, reductants or temporary protecting groups, in stoichiometric quantities.

We started by using benzaldehyde (**1**) as the anchoring unit, to which we added Gaudemar's allenylzinc bromide (**2**),[13] giving homoallyl alcohol **3** (as a 92:8 mixture with allene **3a**) in high yields (Scheme 1).[13b] The generation of the reagent and the mode of reaction deserve some comment. Allenylzinc bromide (**2**) was prepared from zinc dust and propargyl bromide in THF solution according to a literature procedure,[13c] but for convenience, the reaction temperature was held at 0 °C rather than –10 °C.[13c] As reported, reagent **2** could not be stored in solution and was prepared immediately prior to use.[13b] Zinc-mediated propargylations of aldehydes have been realized either with preformed reagent[13a,b,14] or under Barbier conditions in DMF,[15a] THF[15b,c] or water.[15d,e] We found the Barbier conditions to be less suitable for large scale reactions because temperature control was difficult and dangerous; thermal overruns sometimes occurred. The use of pre-formed Gaudemar reagent **2** is a safer procedure for large scale propargylations. An excess of the reagent was necessary to suppress formation of side-products by two-fold addition of benzaldehyde (→**3x**;[15c] Scheme 1) or pinacol coupling of benzaldehyde.

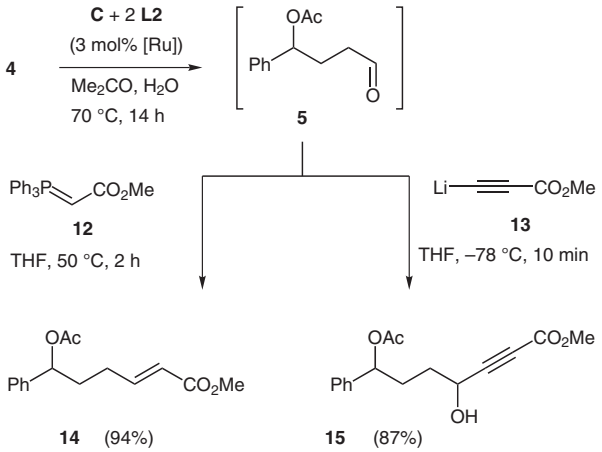
Alcohol **3** was acetylated under standard conditions to give acetate **4**, accompanied by some allene (ratio of **4**/**4a** = 10:1 to 25:1, depending on the purification method). Alternatively, crude preparations of **3** were acetylated directly to give **4** in higher overall yield. Allene **4a** could, in principle, be removed either by careful distillation or by freezing out **4** from the isomer mixture at 4 °C, but this turned out to be unnecessary for our purposes. Hydration of ester **4** with an in situ catalyst (**C** + 2 × **L2**; Figure 1) gave aldehyde **5** in high yield. The allene **4a**, which is present in the starting material, did not react under the hydration catalysis conditions and was easily removed by chromatography of either the reaction product **5** or after the next reaction. In all upcoming hydration experiments, we found it more convenient to immediately use the products from the catalysis in follow-up reactions without isolation of the aldehydes.

Thus, **4** was hydrated and the crude product, after evaporation of solvents and dissolution in THF, was propargylated with **2** to give the elongated homopropargyl alcohol **6**, in good overall yield, as a 1:1 mixture of diastereomers, accompanied by only small amounts (<1/15) of allene.

Alcohol **6** was then protected as its *tert*-butyldimethylsilyl (TBS) ether, to give alkyne **7** as a building block with orthogonally transformable protecting groups. Catalytic anti-Markovnikov hydration of this substrate (Scheme 2) proceeded smoothly and the crude aldehyde was again propargylated with **2** to give alcohol **8**. For further elongations, we continued using TBS protecting groups (**8**→**9**). Compound **9** was hydrated and the intermediary aldehyde



Scheme 2 Continuation of the iterative hydration–propargylation sequence



Scheme 3 Model studies for chain-termination reactions

was directly propargylated to alcohol **10**, which was again TBS-protected to form the tris-silyl ether **11** as the product of four consecutive propargylations and three hydrations, starting from benzaldehyde.

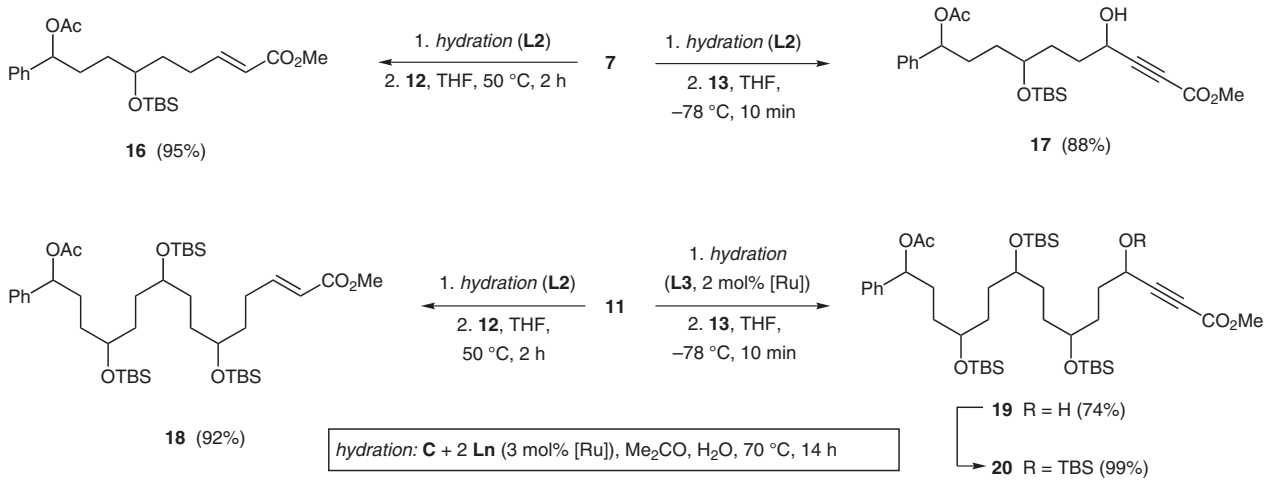
As a next aim, we wished to find how the fully protected oligo-1,4-diol building blocks **7**, **9** and **11** could be further modified and incorporated into synthetic schemes, composed of iterative sequences, and finished by specific chain-termination reactions.

In the first approach, the following chain-terminating reactions were considered: (a) the Wittig reaction with a stabilized phosphonium ylide (**12**), and (b) the addition of lithium methyl propiolate (**13**) (Scheme 3). Both terminations led to carboxylic acid derivatives (see below for reasons why such terminating sequences were chosen). The reactions were first tested with the simple ester **4** (Scheme 3). Catalytic hydration gave aldehyde **5**, which was used in the chain termination steps without purification. Reaction with excess ylide **12** generated the unsaturated ester **14** in high yield and stereoselectivity (*E*/*Z* = 25:1). This product constitutes another interesting building block with a 1,2/3,6-functionalization pattern. Addition of crude aldehyde **5** to a solution of **13** (generated from LDA and methyl propiolate), gave γ-hydroxypropiolic ester **15**, in good yield. It was necessary to quench the reaction at low temperature, otherwise the product decomposed upon warming of the reaction mixture, undoubtedly because of reactions at the sensitive propiolate triple bond.

The chain termination reactions were next applied to some of the higher building blocks (Scheme 4). Alkyne **7** was hydrated and converted into alkenoate **16** or γ-hydroxypropiolate **17** in high yields. Alkyne **11** was likewise hydrated to the corresponding aldehyde (not isolated) and converted into either alkenoate **18** or propiolate **19** by the chain-termination sequences established above. The latter product was TBS-protected to afford hexadecynoic ester derivative **20** as the product of a linear sequence including four catalytic anti-Markovnikov hydrations and four propargylations, followed by a chain termination sequence.

All of the propargylation reactions in the present study were carried out using the achiral allenyl zinc reagent **2**, which leads to the homopropargyl alcohol **3** as a racemic mixture, whereas the iteration to **6** gave a 1:1 mixture of diastereomers. Since this lack of diastereoselectivity was characteristic of most additions of **2** to 4-acetoxy or 4-*tert*-butyldimethylsilyloxy aldehydes under our conditions (THF, 0 °C), building blocks **8/9** therefore must exist as four diastereomeric pairs of enantiomers. As a consequence, building blocks **10/11** form as mixture of eight diastereomers, and the four-fold iteration products **19/20** must consist of 16 diastereomers in equal amounts.

Two comments should be made. First, we anticipate that the use of asymmetric reagents[16] or catalysts[17] for the propargylation of aldehydes should convert the current synthesis into an asymmetric version, whereby the configuration of each stereocenter would be controlled by the asymmetric reagent (or catalyst) for propargylation. The lack of diastereoselectivity in the propargylation steps implies that double stereo-differentiation will be of minor importance.[18]



Scheme 4 Chain terminations applied to long-chain building blocks

As a second observation, the generation of diastereomeric mixtures in these initial studies on the application of anti-Markovnikov hydration of alkynes in synthesis, offers opportunities which do not arise in a highly selective asymmetric synthesis. Thus, the resulting 1,4-diol building blocks may be incorporated into the syntheses of libraries of stereodivergent targets, i.e. in the sense of a diversity-oriented synthesis (DOS).[19] A direct consequence of non-stereoselective synthesis is that NMR spectra of the synthesis products represent an overlay of the spectra of individual diastereomers and that diastereomer-specific differences of the spectra, caused by conformational preferences, are directly visible in the overlay spectrum.

This aspect of detecting conformational preferences became evident from analysis of the ^{1}H NMR spectra of building blocks containing a single non-protected alcoholic function (compounds **6**, **8**, **10**, **15**, **17**, **19**). Even though these samples consist of mixtures of up to 16 diastereomers, the spectrum could usually be interpreted as if it were that of a single compound. For example, Figure 3 shows an expansion of the proton NMR spectrum of **10**, which shows that the signal due to the H-1 (Figure 3, b) appears as a pseudo-triplet and does not indicate the presence of a mixture of eight diastereomers. However, two curious multiplets (δ = 2.79 and 2.23 ppm), with an integral value of 0.5 H each, were observed; exchange experiments with D_2O showed that these corresponded to hydroxylic protons. Comparison with reference spectra of shorter building blocks showed that the well-structured multiplet at δ = 2.79 ppm (Figure 3, c), actually represents a (coincidental) regular arrangement of four doublets, each with a coupling constant of $^3J_{H–H}$ = ~7.7 Hz.

The multiplet centered at δ = 2.23 ppm (Figure 3, d) is also a superimposition of four doublets ($^3J_{H–H}$ = 3.8–4.4 Hz) arising from four diastereomers in an irregular arrangement. Thus, it is only the signals of the OH group which indicate the presence of eight diastereomers. Three arguments imply that there is an intramolecular hydrogen bond from the OH to the TBS-protected oxygen, which fixes the diastereomers into distinct conformations, namely: (a) the separation of the OH signals into two distinct spectral regions; (b) their high frequency shift, and (c) the well-defined signals for the OH-proton with their $^3J_{HO–CH}$ coupling.

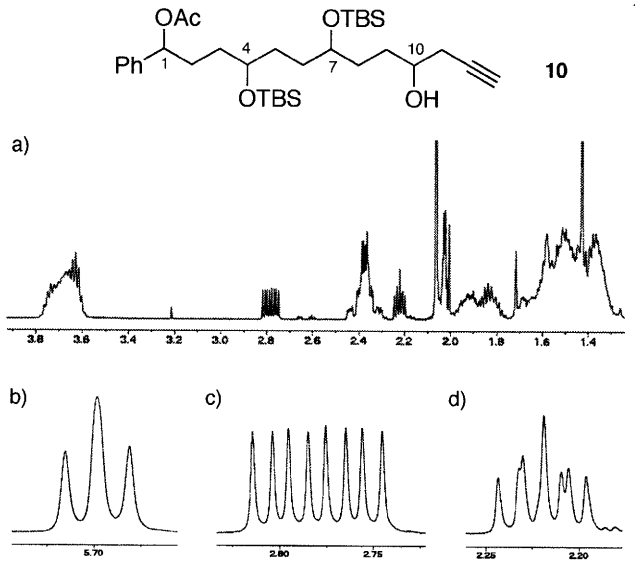
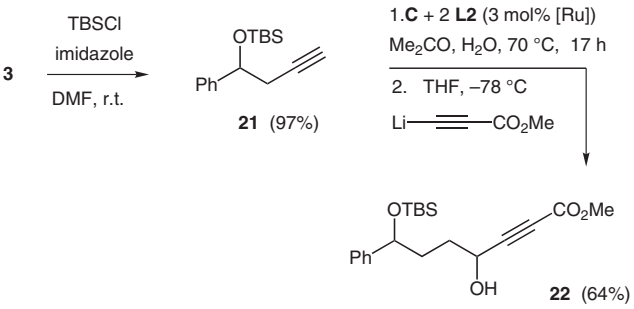


Figure 3 Expansions of the ^{1}H NMR spectrum (400 MHz) of **10**. a) Aliphatic region from δ = 1.2–3.9 ppm; b) Signal arising from H-1; c) OH signals centered at δ = 2.79 ppm; d) OH signals centered at δ = 2.23 ppm

Whereas a range of conformationally restricted 1,4-diols, namely the TADDOLs,[20] are known to form stable hydrogen-bonded chelates,[20] little information is available on hydrogen bonding in simple mono-protected 1,4-diol fragments with high conformational flexibility. A search in the Cambridge structural database gave us one clear-cut example of an intramolecular hydrogen bond from OH to OTBS within a 1,4-functionalized compound.[21] In most other cases, hydrogen bridges form to acceptors such as carbonyl groups or in an intermolecular fashion.



Scheme 5 Synthesis of a test compound for studying intramolecular hydrogen bonding in a mono-protected 1,4-diol

Using the methodology developed in this work, a model compound was synthesized with which to investigate hydrogen bonding in a simple substrate that consists of only two diastereomers (Scheme 5). Alcohol **3** was TBS-protected and the alkyne unit was catalytically hydrated with anti-Markovnikov selectivity. Addition of lithium methyl propiolate gave alcohol **22** as a mixture of diastereoisomers (**22-A**/**22-B** = 60:40). This compound contains an electron-rich hydrogen-bond acceptor and an electron-poor alcohol as hydrogen-bond donor. Indeed, **22** displayed well-resolved signals for the alcoholic function at δ = 2.45 ppm (doublet, ^3J = 5.5 Hz, 0.6 H) and δ = 3.07 ppm (doublet, ^3J = 7.2 Hz, 0.4 H) in the proton NMR spectrum.

If we assume the conformations depicted in Figure 4 for the two diastereomers to be prevalent, then the spectral data, including the size of the coupling constant ($^3J_{HC–OH}$)[22] and the results of a 2D NOESY spectrum, indicate that the relative configurations of diastereomers **22-A** and **22-B** should be as depicted (Figure 4), though this assignment must currently be considered as tentative. The different values for δ (OH) of the two diastereomers probably arises as a consequence of the deshielding effect perpendicular to the alkyne unit,[23] which affects the hydroxyl

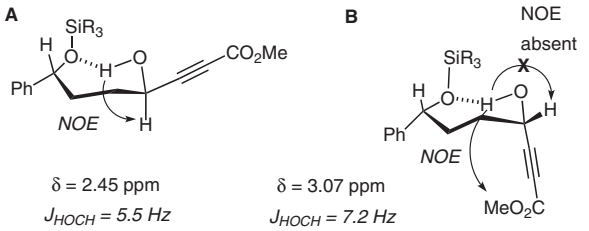


Figure 4 Tentative assignments for the relative configurations of the diastereomers **22-A** and **22-B**, based on NMR data

proton of diastereomer **22-B** far more than that of **22-A** (and presumably likewise in alkynols **6**, **8**, **10**, **17**, **19**).

The primary aim of the current investigation was to show that catalytic anti-Markovnikov hydration of terminal alkynes is a synthetically valuable technique that can be applied in multistep reaction sequences. Due to the efficiency and availability of our new in situ catalysts,[5] we have been able to realize a successful first application of the reaction towards an iterative, sequential synthesis of oligo-1,4-diol fragments and derived products. The linear sequence leading to **18**–**20** involves four anti-Markovnikov hydrations in series.

The catalytic hydrations were performed as described earlier[5] but with some very practical improvements.[5b] The original protocol required pre-forming the catalytically active complex [CpRu(**Ln**)$_2$(MeCN)]PF$_6$ [4d,5] from **C**+2 **Ln** (cf. Figure 1) in hot acetonitrile, followed by evaporation of the in situ catalyst solution in vacuo, prior to catalytic hydration. We now find that we can simply mix **C**, **L1**–**5** and the alkyne in acetone–water and heat to 70 °C to start the reaction;[5b] this was not expected as NMR studies had indicated that acetonitrile was a necessary solvent for mediating ligand exchanges of complex **C**.[5b] The new procedure saves time and gives results comparable to those obtained using pre-formed catalysts. Most hydration reactions in the present study were carried out using the readily synthesized ligand 6-*tert*-amyl-2-diphenylphosphinopyridine (**L2**), the performance of which was somewhat better than **L1** and comparable to **L3/4**.[5b] A typical catalyst loading was 3 mol% [Ru], but 2 mol% was often sufficient to bring most reactions to complete conversion.

The basic idea behind applying a catalytic heterofunctionalization reaction in synthesis was to increase the atom-economy and efficiency of synthetic routes by reducing the number of energy and waste-intensive redox steps. The efficiency of the current iterative synthesis is nicely illustrated in Figure 5, where it is schematically shown that the hexadecynoic acid derivative **20**, of a certain structural complexity, is assembled from very simple starting materials, which are readily available from base-chemicals; e.g. allenylzinc bromide (**2**) derives from zinc and propargyl bromide, and the latter is industrially produced from acetylene, formaldehyde and HBr. In principle, the oligo-1,4-diol chains are simply built from the components allene ($H_2C{=}C{=}CH_2$) and water.

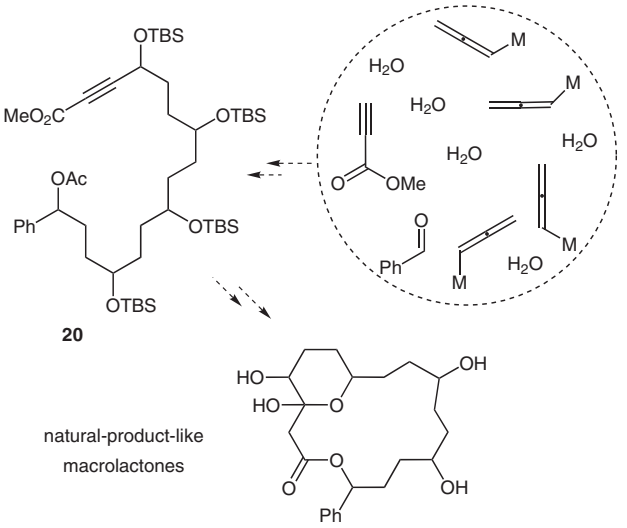


Figure 5 Structurally complex targets from simple precursors via sequential catalytic synthesis with high atom-economy

The synthesis and chemistry of oligo-1,4-diols has not been investigated intensively, probably because these structural fragments, unlike oligo-1,3-diols (poly-acetates), do not widely occur in natural products. It is our current objective to proceed with several oligo-1,4-oxygenated carboxylic acid building blocks towards the synthesis of natural-product-like[24] macrolactones (Figure 5). The observation of conformational preferences in flexible 1,4-diol fragments (Figure 4), implies that oligo-1,4-functionalized compounds may even arrange into preferred secondary structures.

In the current work we have demonstrated the application of catalytic anti-Markovnikov hydration to the sequential synthesis of oligo-1,4-diol fragments, which has resulted in a strategically simple synthesis with high atom-economy from base-chemicals. We plan to extend this chemistry to asymmetric syntheses via asymmetric propargylation reactions,[16,17] and are interested in realizing a synthesis of oligo-1,3-diol fragments by an iterative acetylide addition–hydration sequence.

Complex **C**[25] and ligands **L1**,[26,4d,5b] **L2**[5b] and **L3/4**[5a] were prepared according to literature procedures. Propargyl bromide was a commercial 80% solution in toluene. Reactions were performed in analytically pure solvents under argon. Column chromatography was performed on SiO_2 (40–63 μm), using technical quality distilled solvents. Analyses were carried out by in-house services at the Institute of Organic Chemistry, RWTH Aachen. NMR data are referenced to internal TMS. Spectra of diastereomeric mixtures are interpreted as for a single compound, unless separate signal sets are visible, in which case fractional integral values are given (^{1}H NMR) and δ-values for the corresponding carbons in two or more diastereomers are listed in groups (^{13}C NMR), providing $\Delta\delta \geq 0.1$ ppm.

Anti-Markovnikov Hydration of Terminal Alkynes; General Procedure (GP1)

A Schlenk flask was charged with [CpRu(η^6-naphthalene)]PF$_6$ (**C**; 3 mol%),[25] ligands **L** (6 mol%), alkyne (1 equiv), H_2O (5 equiv) and acetone (2 mL/mmol). The liquid level was marked on the flask and more acetone (0.5 mL/mmol) was added, and the liquid level was

reduced back to the mark in vacuo (this procedure removes O_2). The mixture was heated under argon to 70 °C and the reaction was stirred in the closed vessel (CAUTION: pressure may develop). After completion of the reaction (12–18 h, monitored by TLC), the solution was cooled to r.t. and volatiles were removed in vacuo. The crude aldehydes were dissolved in THF (as a 0.5 M solution) and directly used for further transformations (assuming aldehyde as 1 equiv).

Allenylzinc Bromide (2) Solution in THF[13c]

A Schlenk flask was charged under argon with zinc dust (1.1 equiv), THF (2 mL/mmol) and TMSCl (1–2 drops/mmol zinc dust). The solution was heated to reflux for a short time until the zinc dust clumped together. The mixture was cooled to 0 °C (ice bath) and propargyl bromide (1 equiv) was slowly added dropwise. After completion of the addition, the solution was stirred for another 30 min at 0 °C before use.

Propargylation of Aldehydes; General Procedure (GP2)

A solution of aldehyde (1 equiv) in THF (2 mL/mmol) was added to a solution of allenylzinc bromide (**2**; 1.5 equiv in THF) at 0 °C and the mixture was stirred for 20 min at that temperature. The reaction was quenched by addition of aq NH_4Cl (4 M, 1.5 mL/mmol), aq HCl (2.4 M, 0.1 mL/mmol) and *t*-BuOMe (1.4 mL/mmol). The aqueous phase was extracted with *t*-BuOMe (1.5 mL/mmol) and the combined organic phase was washed with H_2O, aq $NaHCO_3$ (0.9 M) and H_2O (1.5 mL/mmol each). After drying ($MgSO_4$), filtration and evaporation, the residue was purified by column chromatography (*t*-BuOMe–hexanes, typically 1:5→1:3).

TBS Protection; General Procedure (GP3)

The alcohol (1 equiv), TBSCl (2 equiv) and imidazole (3 equiv) were stirred at r.t. in DMF (2 mL/mmol). Upon completion (TLC; 10–48 h), the reaction was quenched by addition of aq HCl (2.4 M, 3 mL/mmol). The aqueous phase was extracted with *t*-BuOMe (2 × 3 mL/mmol) and the combined organic phases were washed with aq $NaHCO_3$ (0.9 M) and H_2O (5 mL/mmol each) then dried over $MgSO_4$. Evaporation in vacuo afforded the crude product, which was purified by column chromatography (*t*-BuOMe–hexanes, typically 1:5→1:3).

Wittig Reaction; General Procedure (GP4)

To the aldehyde (1 equiv) in THF (0.5 M), obtained from GP1, methyl triphenylphosphoranylidene acetate (2.5 equiv) was added and the solution was stirred at 50 °C for 2 h. The reaction was quenched by addition of aq HCl (2.4 M, 2–3 mL/mmol) and *t*-BuOMe (3 mL/mmol). The organic phase was washed with H_2O, aq $NaHCO_3$ (0.9 M) and H_2O (4–5 mL/mmol each) then dried over $MgSO_4$. Filtration and evaporation under vacuo, gave the crude product, which was purified by column chromatography (*t*-BuOMe–hexanes, typically 1:5→1:3).

Addition of Lithium Methylpropiolate to Aldehydes; General Procedure (GP5)

In a Schlenk flask under argon, *n*-BuLi (5 equiv) was added to diisopropylamine (5 equiv) in THF (5 mL/mmol) and the solution was stirred at 0 °C for 15 min then cooled to –78 °C. Methyl propiolate (5 equiv) was slowly added and the solution was stirred for 20 min before the aldehyde (1 equiv, in THF, see GP1) was added dropwise at –78 °C. After 5 min, the reaction was quenched by the addition of aq NH_4Cl (4 M, 4 mL/mmol) and *t*-BuOMe (5 mL/mmol) at –78 °C. The aqueous phase was extracted with *t*-BuOMe (5 mL/mmol) and the combined organic phases were washed with aq $NaHCO_3$ (0.9 M) and H_2O (5–6 mL/mmol each). After drying ($MgSO_4$), filtration and evaporation, the residue was purified by column chromatography (*t*-BuOMe–hexanes; typically 1:4→1:2).

1-Phenylbut-3-yn-1-ol (3)

To allenylzinc (**2**; 1 M in THF, 0.15 mol, 1.5 equiv), prepared as described above, benzaldehyde (10.2 mL, 0.10 mol, 1 equiv) was slowly added at 0 °C. After complete addition, the reaction mixture was stirred another 30 min then quenched by the addition of aq NH_4Cl (4 M, 250 mL), aq HCl (2.4 M, 50 mL) and *t*-BuOMe (300 mL). The aqueous phase was extracted with *t*-BuOMe (100 mL) and the combined organic phases were washed with H_2O, aq $NaHCO_3$ (0.9 M) and H_2O (300 mL each). After drying ($MgSO_4$), filtration and evaporation of the solvent, the crude product was purified by column chromatography (*t*-BuOMe–hexanes, 1:3→1:1) to give a colorless oil (10.8 g, 74%) containing some allene isomer **3a** (**3**/**3a** = 92:8).

Known compound: CAS 1743-36-8.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.06 (t, *J* = 2.7 Hz, 1 H, H-3), 2.56 (d, *J* = 3.1 Hz, 1 H, OH), 2.62 (AB-system, *pseudo*-dd, *J* = 6.4, 2.6 Hz, 2 H, H-2), 4.84 (dt, *J* = 6.4, 2.9 Hz, 1 H, H-1), 7.25–7.41 (m, 5 H). Selected signals for allene **3a**: δ = 2.35 (br d, *J* = 3.9 Hz, 1 H, OH), 4.87–4.96 (m, 2 H), 5.22–5.27 (m, 1 H), 5.43 (q, *J* = 7.1 Hz, 1 H).

1,5-Diphenylbut-2-yne-1,5-diol (3x)

This compound crystallized in variable amounts from the evaporated organic phases of preparations of **3**, when the quantity of **2** was low. Colorless crystals from toluene; 1:1 mixture of diastereomers.

Known compound: CAS 42512-63-0.[15c]

^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.57 (ddd, *J* = 16.6, 6.6, 2.2 Hz, 1 H, H-4), 2.64 (ddd, *J* = 16.5, 6.3, 2.2 Hz, 1 H, H-4), 4.70 (t, *J* = 6.3 Hz, 1 H, H-5), 5.29 (s, 1 H, H-1), 5.52 (br s, 1 H, OH), 5.85 (br s, 1 H, OH), 7.23–7.41 (m, 10 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 29.4 (CH_2), 62.7 (CH), 71.2 (CH), 82.6 (C), 83.2 (C), 126.0 (CH), 126.4 (CH), 126.9 (CH), 127.2 (CH), 127.7 (CH), 127.9 (CH), 142.4 (C), 144.4 (C). Slight splitting of several signals due to diastereomers is observed.

Acetic Acid 1-Phenyl but-3-ynyl Ester (4)

DMAP (0.757 g, 6.2 mmol, 10 mol%) and Et_3N (12.95 mL, 93 mmol, 1.5 equiv) were added to a solution of alcohol **3** (9.086 g, 62 mmol) in *t*-BuOMe (0.5 M) at 0 °C. Acetic anhydride (5.9 mL, 62 mmol, 1 equiv) was slowly added with stirring. When the reaction was complete (~30 min, monitored by TLC), the reaction was quenched by addition of H_2O (150 mL). The aqueous phase was extracted with *t*-BuOMe (25 mL) and the combined organic phases were washed with H_2O, aq $NaHCO_3$ (0.9 M) and H_2O (100 mL each). After drying ($MgSO_4$) and evaporation of the solvent, the residual oil was distilled at 80 °C (0.2 mbar) to give a colorless liquid (10.845 g, 93%) as 92:8 mixture of the product **4**, with the allene isomer **4a**.

In an alternative synthesis, starting from benzaldehyde on a 0.1 mole scale, crude alcohol **3** was acetylated without purification to give **4** (16.18 g, 86%) after distillation.

Known compound: CAS 76698-68-5.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.97 (t, *J* = 2.7 Hz, 1 H, H-4), 2.10 (s, 3 H, Me), 2.69 (ddd, *J* = 16.8, 6.4, 2.7 Hz, 1 H, H-2), 2.78 (ddd, *J* = 16.8, 6.9, 2.6 Hz, 1 H, H-2), 5.89 (t, *J* = 6.6 Hz, 1 H, H-1), 7.27–7.41 (m, 5 H, Ph). Selected signals for allene **4a**: δ = 4.79–4.9 (m, 2 H), 5.42 (q, *J* = 6.7 Hz, 1 H), 6.29 (dt, *J* = 6.7, 2.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1 (CH_3), 26.5 (CH_2), 70.7 (CH), 73.5 (CH), 79.5 (C), 126.5 (CH), 128.4 (CH), 128.5 (CH), 139.0 (C), 170.0 (C).

4-Acetoxy-4-phenylbutanal (5)

Prepared from **4** (250 mg, 1.33 mmol) according to GP1 (with **L2**).

Yield: 252 mg (92%); colorless oil; R_f = 0.24 (*t*-BuOMe–hexane, 1:3).

IR (film): 3034, 2936, 2827, 2727, 1734, 1495, 1451, 1373, 1239, 1025, 763, 702, 546 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.08 (s, 3 H), 2.10–2.28 (m, 2 H, H-2), 2.44–2.50 (m, 2 H, H-3), 5.77 (dd, *J* = 7.6, 5.9 Hz, 1 H, H-4), 7.26–7.38 (m, 5 H, Ph), 9.73 (t, *J* = 1.3 Hz, 1 H, H-1).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 28.8 (CH_2), 40.0 (CH_2), 75.0 (CH), 126.3 (CH), 128.2 (CH), 128.6 (CH), 139.6 (C), 170.1 (C), 200.9 (CH).

MS (EI): *m*/*z* (%) = 206 (1) [M^+], 188 (1), 163 (80), 146 (45), 120 (100), 107 (75), 91 (55), 77 (40).

Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.62; H, 6.91.

Acetic Acid 4-Hydroxy-1-phenylhept-6-ynyl Ester (6)

Prepared from **4** (1.035 g, 5.5 mmol) according to GP1 ([Ru] = 5 mol%; with **L1**) and GP2.

Yield: 1.106 g (82%); colorless oil; R_f = 0.32 (*t*-BuOMe–hexane, 1:3).

IR (film): 3476, 3291, 3033, 2932, 2363, 1735 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.41–1.66 (m, 2 H), 1.79–2.15 (m, 3 H), 2.03–2.06 (m, 1 H), 2.07 (s, 3 H), 2.25–2.45 (m, 2 H), 3.72–3.81 (m, 1 H), 5.72–5.80 (m, 1 H), 7.27–7.37 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.4 (CH_3), 27.6 (CH_2), 32.0/32.2 (CH_2), 32.5/32.6 (CH_2), 69.4/69.6 (CH), 71.1/71.2 (CH), 75.7/76.0 (CH), 80.5 (C), 126.4 (CH), 127.9 (CH), 128.4 (CH), 140.2/140.3 (C), 170.3 (C).

MS (EI): *m*/*z* (%) = 246 (3) [M^+], 203 (97), 186 (25), 185 (35), 147 (100), 129 (43), 120 (64), 107 (99), 91 (61), 79 (43).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.61; H, 7.27.

Acetic Acid 4-(*tert*-Butyldimethylsilanyloxy)-1-phenylhept-6-ynyl Ester (7)

Prepared from **6** (7.66 g, 31.1 mmol) according to GP3.

Yield: 10.947 g (98%); colorless oil; R_f = 0.7 (*t*-BuOMe–hexane, 1:3).

IR (film): 3303, 2943, 2363, 1740, 1463, 1369, 1242, 1094, 1034, 838, 779, 698, 635, 541 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.02–0.06 (m, 6 H, 2 × Me), 0.87/0.87 (s, 9 H), 1.40–1.77 (m, 2 H), 1.79–2.05 (m, 3 H), 2.07 (s, 3 H, Me), 2.21–2.47 (m, 2 H), 3.78–3.86 (m, 1 H), 5.70–5.77 (m, 1 H), 7.26–7.38 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.7 (CH_3), –4.5 (CH_3), 18.0 (C), 21.2 (CH_3), 25.8 (CH_3), 27.0/27.1 (CH_2), 31.2/31.4 (CH_2), 32.0/32.2 (CH_2), 70.0 (CH), 70.1/70.3 (CH), 75.7/75.9 (CH), 81.1/81.2 (C), 126.3 (CH), 127.7 (CH), 128.2 (CH), 140.2/140.3 (C), 170.0 (C).

MS (ESI, $CHCl_3$): *m*/*z* = 383.2 [M + Na]$^+$.

Anal. Calcd for $C_{21}H_{32}O_3Si{\cdot}0.2\ H_2O$: C, 69.26; H, 8.97. Found: C, 69.19; H, 9.28.

Acetic Acid 4-(*tert*-Butyldimethylsilanyloxy)-7-hydroxy-1-phenyldec-9-ynyl Ester (8)

Prepared from **7** (1.00 g, 2.77 mmol) according to GP1 ([Ru] = 2 mol%, with **L4**) and GP2.

Yield: 1.15 g (>95%); oil; R_f = 0.30 (*t*-BuOMe–hexane, 1:3).

IR (film): 3503, 3302, 2941, 2363, 1732, 1460, 1371, 1247, 1045, 838, 764, 699, 638, 541 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = –0.02–0.05 (m, 6 H, 2 × Me), 0.87 (s, 9 H), 1.305–2.00 (m, 8 H), 2.00–2.05 (m, 1 H), 2.06 (s, 3 H), 2.09 (d, *J* = 4.7 Hz, 0.5 H, OH), 2.25–2.47 (m, 2 H), 2.48–2.54 (m, 0.5 H, OH), 3.64–3.78 (m, 2 H), 5.70 (t, *J* = ~7 Hz, 1 H), 7.26–7.40 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.5 (CH_3), –4.6 (CH_3), 18.1 (C), 21.3 (CH_3), 25.9 (CH_3), 27.3/27.4 (CH_2), 31.5–32.8 (4 × CH_2), 69.9/70.2/70.7/70.8 (CH), 71.3/71.4/71.5/71.6 (CH), 76.0 (CH), 80.9 (C), 126.4/126.5 (CH), 127.9 (CH), 128.4 (CH), 140.5/140.6 (C), 170.3 (C).

MS (ESI, MeOH): *m*/*z* = 441.3 [M + Na]$^+$.

Anal. Calcd for $C_{24}H_{38}O_4Si$: C, 68.86; H, 9.15. Found: C, 69.35; H, 9.34.

Acetic Acid 4,7-Bis(*tert*-butyldimethylsilanyloxy)-1-phenyldec-9-ynyl Ester (9)

Prepared from **8** (2.26 g, 5.4 mmol) according to GP3.

Yield: 2.855 g (99%); oil; R_f = 0.84 (*t*-BuOMe–hexane, 1:3).

IR (film): 3307, 2943, 1741, 1465, 1369, 1244, 1064, 838, 776, 699, 636, 546 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = –0.03–0.07 (m, 12 H), 0.86/0.87 (s, 9 H), 0.88 (s, 9 H), 1.28–1.75 (m, 6 H), 1.77–1.99 (m, 2 H), 1.94–1.97 (m, 1 H), 2.06 (s, 3 H), 2.22–2.38 (m, 2 H), 3.60–3.70 (m, 1 H), 3.71–3.83 (m, 1 H), 5.71 (t, *J* = ~7 Hz, 1 H), 7.26–7.37 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.5 to –4.3 (4 × CH_3), 18.2 (2 × C), 21.4 (CH_3), 25.9 (CH_3), 26.0 (CH_3), 27.3/27.4 (CH_2), 31.6–32.7 (4 × CH_2), 70.0 (CH), 71.0/71.1 (CH), 71.5/71.7/71.8 (CH), 76.2 (CH), 81.6 (C), 126.4/126.5 (CH), 127.8 (CH), 128.4 (CH), 140.6 (C), 170.2 (C).

MS (ESI, $CHCl_3$): *m*/*z* = 555.5 [M + Na]$^+$.

Anal. Calcd for $C_{30}H_{52}O_4Si_2{\cdot}0.2\ H_2O$: C, 67.16; H, 9.84. Found: C, 66.96; H, 9.74.

Acetic Acid 4,7-Bis(*tert*-butyldimethylsilanyloxy)-10-hydroxy-1-phenyltridec-12-ynyl Ester (10)

Prepared from **9** (1.00 g, 1.88 mmol) according to GP1 (with **L2**) and GP2.

Yield: 0.907 g (82%); oil; R_f = 0.33 (*t*-BuOMe–hexane, 1:3).

IR (film): 3428, 3310, 2952, 2119, 1737, 1465, 1371, 1251, 1065, 836, 775, 701, 633, 544 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = –0.04–0.06 (m, 12 H), 0.86 (s, 9 H), 0.88 (s, 9 H), 1.24–1.74 (m, 10 H), 1.75–1.98 (m, 2 H), 1.99–2.04 (m, 1 H), 2.06 (s, 3 H), 2.19–2.25 (m, 0.5 H, OH), 2.28–2.46 (m, 2 H), 2.73–2.83 (m, 0.5 H, OH), 3.57–3.79 (m, 3 H), 5.70 (t, *J* = ~7 Hz, 1 H), 7.25–7.37 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.5 (4 × CH_3), 18.1 (2 × C), 21.2 (CH_3), 25.8 (2 × CH_3), 26.9/27.3 (CH_2), 31.3–32.9 (6 × CH_2), 69.8/70.1 (CH), 70.4/70.7 (CH), 71.4–72.2 (2 × CH), 76.0 (CH), 80.7/80.9 (C), 126.2/126.3 (CH), 127.7 (CH), 128.2 (CH), 140.3/140.4 (C), 170.1 (C).

MS (ESI, MeOH): *m*/*z* = 613.6 [M + Na]$^+$.

Anal. Calcd for $C_{33}H_{58}O_5Si_2$: C, 67.07; H, 9.89. Found: C, 67.33; H, 10.43.

Acetic Acid 4,7,10-Tris(*tert*-butyldimethylsilanyloxy)-1-phenyltridec-12-ynyl Ester (11)

Prepared from **10** (3.00 g, 5.076 mmol) according to GP3.

Yield: 3.57 g (>99%); oil; R_f = 0.9 (*t*-BuOMe–hexane, 1:3).

IR (film): 3306, 2944, 1740, 1465, 1369, 1247, 1070, 837, 771, 699, 636, 532 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.03–0.07 (m, 18 H), 0.85–0.88 (m, 27 H), 1.27–2.02 (m, 12 H), 1.91–1.95 (m, 1 H), 2.06 (s, 3 H), 2.23–2.38 (m, 2 H), 3.55–3.67 (m, 2 H), 3.73–3.82 (m, 1 H), 5.70 (t, *J* = ~7 Hz, 1 H), 7.25–7.37 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.6 to –4.4 (6 × CH_3), 18.0 (3 × C), 21.2 (CH_3), 25.7–25.9 (3 × CH_3), 27.3 (CH_2), 31.4–32.8 (6 × CH_2), 69.8 (CH), 70.9/71.0 (CH), 71.6/71.7/71.8 (CH), 72.1/72.2 (CH), 76.0 (CH), 81.5 (C), 126.3 (CH), 127.6 (CH), 128.2 (CH), 140.5 (C), 170.1 (C).

MS (ESI, $CHCl_3$): *m*/*z* = 727.8 $[M + Na]^+$.

Anal. Calcd for $C_{39}H_{72}O_5Si_3$: C, 66.42; H, 10.29. Found: C, 65.84; H, 9.98.

(*E*)-6-Acetoxy-6-phenylhex-2-enoic Acid Methyl Ester [(*E*)-14]
Prepared from **4** (160 mg, 0.88 mmol) according to GP1 (with **L2**) and GP4.

Yield: 217 mg (93.6%); oil; R_f = 0.43 (*t*-BuOMe–hexane, 1:3). (*Z*)-**14** (8.5 mg, 3.7%) was also obtained as an oil. Ratio of *E*/*Z* = 25:1.

IR (film): 3032, 2950, 1729, 1657, 1495, 1437, 1372, 1314, 1237, 1032, 852, 761, 702, 549 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85–2.32 (m, 4 H), 2.08 (s, 3 H, Me), 3.72 (s, 3 H, OMe), 5.74 (dd, *J* = 7.2, 5.9 Hz, 1 H, H-6), 5.82 (dt, *J* = 15.8, 1.4 Hz, 1 H, H-2), 6.94 (dt, *J* = 15.7, 6.8 Hz, 1 H, H-3), 7.26–7.38 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.2 (CH_3), 28.3 (CH_2), 34.5 (CH_2), 51.5 (CH_3), 75.2 (CH), 121.5 (CH), 126.4 (CH), 128.1 (CH), 128.6 (CH), 140.0 (C), 147.9 (CH), 166.9 (C), 170.2 (C).

MS (EI): *m*/*z* = 263.2 (3) $[M^+]$, 219.1 (14), 202.1 (38), 163.0 (63), 143.1 (85), 121.1 (67), 107.1 (87), 100.1 (100), 91.1 (31).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.41; H, 6.70.

(*Z*)-14
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85–2.17 (m, 2 H), 2.08 (s, 3 H), 2.64–2.77 (m, 2 H), 3.68 (s, 3 H), 5.75 (dd, *J* = 8.1, 5.7 Hz, 1 H), 5.79 (dt, *J* = 11.5, 1.7 Hz, 1 H), 6.20 (dt, *J* = 11.5, 7.5 Hz, 1 H), 7.27–7.35 (m, 5 H).

7-Acetoxy-4-hydroxy-7-phenylhept-2-ynoic Acid Methyl Ester (15)
Prepared from **4** (100 mg, 0.531 mmol) according to GP1 (with **L2**) and GP5.

Yield: 135 mg (87%); oil; R_f = 0.14 (*t*-BuOMe–hexane, 1:3).

IR (film): 3416, 3032, 2955, 2855, 2236, 1717, 1496, 1437, 1374, 1251, 1028, 957, 754, 702, 542 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.64–2.15 (m, 4 H), 2.08 (s, 3 H, Me), 3.02/3.04 (d, *J* = 5.7/5.5 Hz, 1 H, OH), 3.76 (s, 3 H, OMe), 4.42–4.50 (m, 1 H, H-4), 5.73–5.78 (m, 1 H, H-7), 7.27–7.37 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (CH_3), 31.5/31.6 (CH_2), 32.6 (CH_2), 52.8 (CH_3), 61.2/61.3 (CH), 75.3/75.4 (C), 76.1 (CH), 87.7 (C), 126.2 (CH), 127.9 (CH), 128.3 (CH), 139.8 (C), 153.5 (C), 170.3 (C).

MS (ESI, MeOH): *m*/*z* = 313.0 $[M + Na]^+$.

Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.13; H, 6.62.

(*E*)-9-Acetoxy-6-(*tert*-butyldimethylsilanyloxy)-9-phenylnon-2-enoic Acid Methyl Ester [(*E*)-16]
Prepared from **7** (166 mg, 0.46 mmol) according to GP1 (with **L2**) and GP4.

Yield: 190 mg (95%); oil; R_f = 0.58 (*t*-BuOMe–hexane, 1:3). (*Z*)-**16** (7.6 mg, 3.8%) was also obtained as an oil. Ratio of *E*/*Z* = 25:1.

IR (film): 3032, 2951, 1730, 1658, 1496, 1438, 1372, 1317, 1239, 1040, 837, 775, 702, 543 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.03/0.00/0.07 (s, 6 H, 2 × Me), 0.86/0.86 (s, 9 H), 1.27–2.00 (m, 6 H), 2.07 (s, 3 H), 2.11–2.27 (m, 2 H), 3.63–3.72 (m, 1 H), 3.72 (s, 3 H), 5.7 (t, *J* = 7.1 Hz, 1 H), 5.79 (dq, *J* = 15.7, 1.6 Hz, 1 H), 6.95 (dtd, *J* = 15.6, 7.1, 1.3 Hz, 1 H), 7.25–7.38 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.4 (CH_3), –4.3 (CH_3), 18.2 (C), 21.4 (CH_3), 26.0 (CH_3), 28.1 (CH_2), 31.6/31.8 (CH_2), 32.7 (CH_2), 35.0/35.1 (CH_2), 51.6 (CH_3), 70.9/71.0 (CH), 76.2 (CH), 121.0 (CH), 126.6 (CH), 128.1 (CH), 128.6 (CH), 140.6/140.7 (C), 149.5 (CH), 167.2 (C), 170.5 (C).

MS (ESI, MeOH): *m*/*z* = 457.1 $[M + Na]^+$.

Anal. Calcd for $C_{24}H_{38}O_5Si$: C, 66.32; H, 8.81. Found: C, 66.06; H, 8.51.

(*Z*)-16
^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00/0.02/0.04 (s, 6 H, 2 × Me), 0.88/0.89 (s, 9 H), 1.32–2.04 (m, 6 H), 2.09 (s, 3 H), 2.55–2.75 (m, 2 H), 3.66–3.77 (m, 1 H), 3.72 (s, 3 H), 5.68–5.83 (m, 2 H), 6.21 (dtd, *J* = 11.4, 7.3, 1.9 Hz, 1 H) 7.25–7.41 (m, 5 H).

10-Acetoxy-7-(*tert*-butyldimethylsilanyloxy)-4-hydroxy-10-phenyldec-2-ynoic Acid Methyl Ester (17)
Prepared from **7** (0.995 g, 2.76 mmol) according to GP1 (with **L2**) and GP5.

Yield: 1.129 g (88%); oil; R_f = 0.19 (*t*-BuOMe–hexane, 1:3).

IR (film): 3398, 3031, 2955, 2858, 2236, 1719, 1496, 1437, 1374, 1254, 1053, 949, 837, 756, 702, 544 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = –0.01–0.06 (several s, 6 H, 2 × Me), 0.86/0.88 (s, 9 H), 1.32–1.99 (m, 8 H), 2.07 (s, 3 H), 2.63/2.66 (d, *J* = 5.2 Hz, 0.5 H, OH), 3.24/3.30 (d, *J* = 7.4 Hz, 0.5 H), 3.69–3.81 (m, 1 H), 3.77 (s, 3 H), 4.42–4.54 (m, 1 H), 5.70 (t, *J* = ~7 Hz, 1 H), 7.24–7.39 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.4 to –4.3 (2 × CH_3), 18.3 (C), 21.5 (CH_3), 26.1 (CH_3), 31.2–32.7 (4 × CH_2), 52.9/53.0 (CH_3), 61.9/62.4 (CH), 71.1/71.3/71.4 (CH), 76.0/76.1 (CH), 76.3/76.5 (C), 88.2/88.3 (C), 126.5/126.6 (CH), 128.0/128.1 (CH), 128.5 (CH), 140.3/140.4/140.5/140.5 (C), 153.8 (C), 170.4 (C).

MS (ESI, MeOH): *m*/*z* = 485.1 $[M + Na]^+$.

Anal. Calcd for $C_{25}H_{38}O_6Si$: C, 64.90; H, 8.28. Found: C, 64.89; H, 8.63.

(*E*)-15-Acetoxy-6,9,12-tris(*tert*-butyldimethylsilanyloxy)-15-phenylpentadec-2-enoic Acid Methyl Ester [(*E*)-18]
Prepared from **11** (250 mg, 0.354 mmol) according to GP1 (with **L2**) and GP4.

Yield: 255 mg (92%); oil; R_f = 0.80 (*t*-BuOMe–hexane, 1:3).

IR (film): 2946, 1734, 1656, 1464, 1370, 1247, 1065, 837, 775, 702, 665, 538 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = –0.04–0.05 (m, 18 H, Me), 0.86–0.87 (several s, 27 H, *t*-Bu), 1.21–1.62 (m, 12 H), 1.73–2.00 (m, 2 H), 2.06 (s, 3 H, Me), 2.15–2.32 (m, 2 H), 3.51–3.72 (m, 3 H, H-6, H-9, H-12), 3.73 (s, 3 H, OMe), 5.70 (t, *J* = ~7 Hz, 1 H, H-15), 5.82 (d, *J* = 15.7 Hz, 1 H, H-2), 6.98 (dt, *J* = 15.6, 6.9 Hz, 1 H, H-3), 7.25–7.37 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.6 to –4.3 (6 × CH_3), 18.1 (3 × C), 21.3 (CH_3), 25.9 (3 × CH_3), 27.9/28.0 (CH_2), 31.4–32.9 (6 × CH_2), 35.20 (CH_2), 51.4 (CH_3), 71.7–72.4 (3 × CH), 76.2 (CH),

120.8 (CH), 126.5 (CH), 127.8 (CH), 128.4 (CH), 140.7 (C), 149.7 (CH), 167.1 (C), 170.3 (C).

MS (ESI, MeOH): m/z = 801.8 $[M + Na]^+$.

Anal. Calcd for $C_{42}H_{78}O_7Si_3$: C, 64.73; H, 10.09. Found: C, 65.20; H, 10.17.

16-Acetoxy-7,10,13-tris(*tert*-butyldimethylsilanyloxy)-4-hydroxy-16-phenylhexadec-2-ynoic Acid Methyl Ester (19)
Prepared from **11** (500 mg, 0.709 mmol) according to GP1 ([Ru] = 2 mol%, with **L3**) and GP5.

Yield: 423 mg (74%); oil; R_f = 0.46 (*t*-BuOMe–hexane, 1:3).

IR (film): 3415, 3029, 2953, 2857, 2236, 1720, 1466, 1437, 1371, 1253, 1061, 938, 837, 770, 701, 666 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = –0.04–0.07 (several s, 18 H), 0.86–0.90 (several s, 27 H), 1.23–2.00 (m, 16 H and 0.5 OH), 2.06 (s, 3 H, Me), 2.82–2.91 (m, 0.5 H, OH), 3.52–3.72 (m, 3 H), 3.77 (s, 3 H), 4.44–4.57 (m, 1 H, H-4), 5.70 (t, J = ~7 Hz, 1 H, H-16), 7.24–7.39 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.5 to –4.2 (6 × CH_3), 18.2 (3 × C), 21.4 (CH_3), 26.0 (3 × CH_3), 31.1–33.1 (8 × CH_2), 52.8/52.9 (CH_3), 61.8/62.5 (CH), 71.7–72.6 (3 × CH), 76.2 (C), 76.3 (CH), 88.4/88.5 (C), 126.6/126.7 (CH), 128.0 (CH), 128.6 (CH), 140.8 (C), 154.0 (C), 170.5 (C).

MS (ESI, MeOH): m/z = 829.9 $[M + Na]^+$.

Anal. Calcd for $C_{43}H_{78}O_8Si_3$: C, 63.97; H, 9.74. Found: C, 63.79; H, 10.02.

16-Acetoxy-4,7,10,13-tetrakis(*tert*-butyldimethylsilanyloxy)-16-phenylhexadec-2-ynoic Acid Methyl Ester (20)
Prepared from **19** (430 mg, 0.533 mmol) according to GP3.

Yield: 487 mg (99%); oil; R_f = 0.79 (*t*-BuOMe–hexane, 1:3).

IR (film): 2947, 2859, 2237, 1728, 1466, 1368, 1250, 1073, 938, 838, 777, 700, 667 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = –0.06–0.14 (several s, 24 H), 0.82–0.94 (several s, 36 H), 1.20–1.99 (m, 16 H), 2.06 (s, 3 H), 3.48–3.70 (m, 3 H, H-7, H-10, H-13), 3.76 (s, 3 H, OMe), 4.43/4.47 (t, J = 6.2 Hz, 1 H, H-4), 5.70 (t, J = ~7 Hz, 1 H, H-16), 7.23–7.36 (m, 5 H).

^{13}C NMR (100 MHz. $CDCl_3$): δ = –4.4 to –4.2 (8 × CH_3), 18.2–18.3 (4 × C), 21.4 (CH_3), 25.8–26.0 (4 × CH_3), 31.5–33.8 (8 × CH_2), 51.8/51.9/52.7 (CH_3), 62.7/62.9 (CH), 71.7–72.7 (3 × CH), 75.8 (C), 76.2 (CH), 88.9 (C), 126.4/126.5 (CH), 127.8 (CH), 128.4 (CH), 140.6 (C), 153.8 (C), 170.2 (C).

MS (ESI, $CHCl_3$/EtOH): m/z = 990.0 $[M + EtOH + Na]^+$.

Anal. Calcd for $C_{49}H_{92}O_8Si_4 \cdot 1.25\ H_2O$: C, 62.34; H, 10.09. Found: C, 62.34; H, 10.01.

***tert*-Butyldimethyl(1-phenylbut-3ynyloxy)silane (21)**
Prepared from **3** (2.00 g, 13.7 mmol) according to GP3.

Yield: 3.461 g (97%); oil; R_f = 0.94 (*t*-BuOMe–hexane, 1:3); contains 5% of allene isomer.

IR (film): 3306, 3028, 2941, 2363, 1598, 1465, 1362, 1254, 1097, 937, 841, 778, 697, 636, 543 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = –0.08 (s, 3 H, Me), 0.07 (s, 3 H, Me), 0.89 (s, 9 H, *t*-Bu), 1.95 (t, J = 2.7 Hz, 1 H), 2.48 (ddd, J = 16.6, 5.8, 2.7 Hz, 1 H), 2.59 (ddd, J = 16.6, 7.1, 2.6 Hz, 1 H), 4.81 (dd, J = 6.9, 5.9 Hz, 1 H), 7.21–7.38 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.7 (CH_3), –4.6 (CH_3), 18.4 (C), 25.9 (CH_3), 31.1 (CH_2), 70.0 (CH), 73.8 (CH), 81.7 (C), 125.9 (CH), 127.4 (CH), 128.1 (CH), 143.9 (C).

MS (EI): m/z (%) = 245.0 (4) $[M – CH_3]^+$, 221.1 (31), 203.0 (100), 185.0 (4), 128.1 (9), 115.0 (3), 97.1 (22), 75.1 (35).

Anal. Calcd for $C_{16}H_{24}OSi$: C, 73.79; H, 9.29. Found: C, 73.47; H, 8.81.

7-(*tert*-Butyldimethylsilanyloxy)-4-hydroxy-7-phenylhept-2-ynoic Acid Methyl Ester (22)
Prepared from **21** (500 mg, 1.92 mmol) according to GP1 (with **L2**) and GP5.

Yield: 432 mg (62%); oil; R_f = 0.4 (*t*-BuOMe–hexane, 1:3). Mixture of diastereomers (A/B = 60:40).

IR (film): 3401, 3027, 2945, 2862, 2238, 1715, 1444, 1257, 1080, 843, 773, 700, 541 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = –0.13/–0.08 (s, 3 H, Me), 0.04/0.07 (s, 3 H, Me), 0.89/0.91 (s, 9 H), 1.72–2.08 (m, 4 H), 2.45 (d, J = 5.4 Hz, 0.6 H, OH-A), 3.07 (d, J = 7.2 Hz, 0.4 H, OH-B), 3.77/3.78 (s, 3 H, OMe), 4.43–4.53 (m, 1 H, H-4), 4.77 (t, J = 5.6 Hz, 0.6 H, H-7 A), 4.85 (dd, J = 5.7, 4.6 Hz, 0.4 H, H-7 B), 7.19–7.37 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.9 (B, CH_3), –4.9 (A, CH_3), –4.6 (B, CH_3), –4.5 (A, CH_3), 18.3/18.4 (C), 26.0 (CH_3), 31.9 (B, CH_2), 32.6 (A, CH_2), 35.4 (B, CH_2), 36.0 (A, CH_2), 52.8 (CH_3), 61.8 (B, CH), 62.2 (A, CH), 74.2 (B, CH), 74.4 (A, CH), 76.2/76.4 (C), 88.1/88.2 (C), 125.8 (CH), 127.1 (CH), 128.1 (CH), 143.8 (B, C), 144.3 (A, C), 153.7 (C), 170.3 (C).

MS (ESI, $CHCl_3$): m/z = 385.1 $[M + Na]^+$.

Anal. Calcd for $C_{20}H_{30}O_4Si \cdot 0.2\ H_2O$: C, 65.61; H, 8.37. Found: C, 65.55; H, 8.27.

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