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Note

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Intramolecular Diels-Alder Reactions of Tethered Enoate Substituted Furans Induced by Dialkylaluminium Chloride

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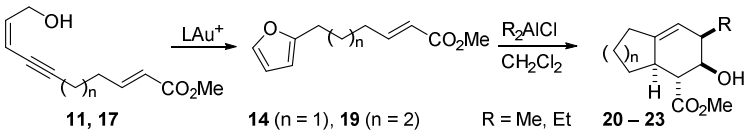
TOC graphic



ABSTRACT: Gold(I) catalyzed cycloisomerization of enynols **11** and **17**, obtained by Sonogashira coupling, led to the tethered enoate substituted furans **14** and **19**. While attempts of thermal and several Lewis acid induced intramolecular Diels-Alder reactions remained fruitless, dialkylaluminium chloride led to the formation of hexahydroindene and octahydronaphthalene derivatives **20** – **23**. Their formation can be explained by Lewis acid induced opening of the epoxy bridge with transfer of one alkyl group to the intermediate cycloadduct.

The importance of furan in chemistry is undisputed. Thus, a furan ring is part of many natural products (Figure 1), where it can be annulated to another ring, like in auxofuran[1,2] (**1**), a fungal-growth-promoting substance produced by a Streptomyces species or cafestol[3] (**2**), a diterpene contained in coffee, or be a substituent as in salvinorin A[4] (**3**). Frequently, a furan ring serves as a functional group or a vehicle that is transformed into some other polyfunctionalized subunit.[5] For example, furan can function as heterodiene in inter- and intramolecular Diels-Alder reactions. In connection with the synthesis of polycyclic natural products intramolecular Diels-Alder reactions of furans have found growing interest.[6]

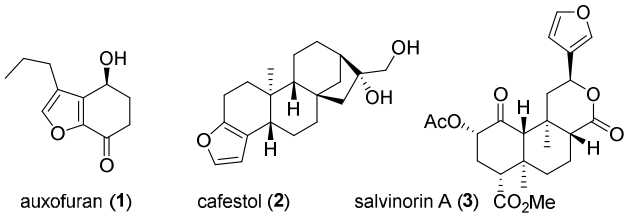
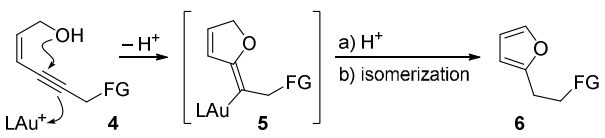


Figure 1. Examples of natural products that contain a furan ring.

As is generally the case for intramolecular cycloadditions the synthesis of the substrate can be challenging. With tethered dienophile substituted furans, substrate synthesis typically involves functionalization of an existing furan ring.[6] However, with the possibility of synthesizing substituted furans by transition metal catalysis from acyclic precursors,[7] the synthesis of substrates for intramolecular Diels-Alder reactions might become more efficient (Scheme 1). For example, cycloisomerization of a terminally functionalized enynol **4** via vinylgold intermediate **5** would lead to furan derivative **6**.

Scheme 1. Cycloisomerization of enynol **4** to functionalized furan derivative **6**.



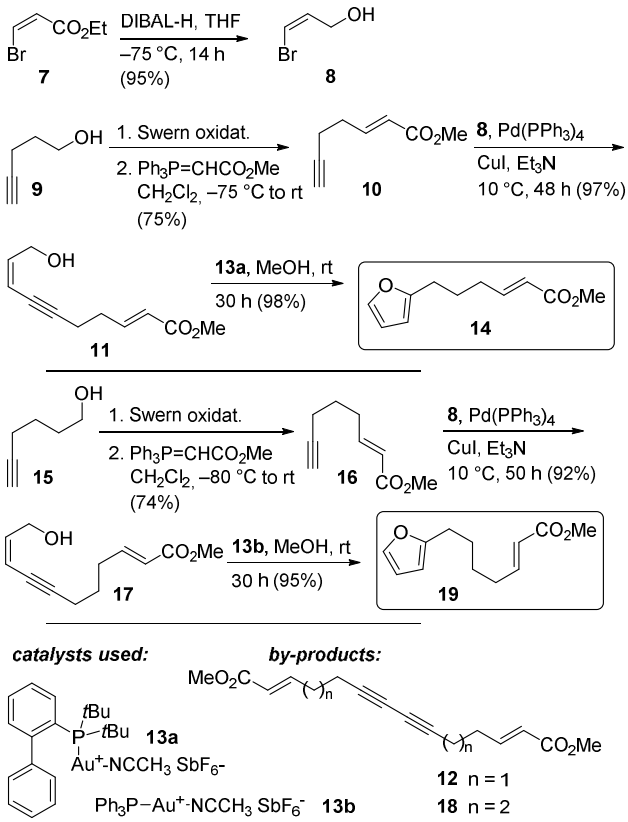
In this paper we describe the synthesis of the two tethered acrylate substituted furans **14** and **19** from conjugated enynols **11** and **17** by gold (I) catalysis and studies of their intramolecular Diels-Alder reactions.

While many examples of intramolecular Diels-Alder reactions of furans are known, frequently there are heteroatoms in the tether or the aliphatic sector of the tether is substituted. The latter can favor the cycloaddition due to the Thorpe-Ingold effect.[8] With substrates like 6-(furan-2-yl)hex-1-en-3-one, where an activating group is on the tether, intramolecular Diels-Alder reactions of furans are also known. Such reactions with internally activated IMDAF substrates are promoted by high pressure,[9] Lewis acids[10] or by simple heating.[11] In addition, substituents like heteroatoms on the furan[12] or as part of the tether[13] affect the IMDAF. As we aimed at substrates **14** and **19** featuring an unsubstituted tether we hoped that we can isolate the primary cycloadducts, which are actually not known in the literature. For the furan synthesis we chose the method of Liu et al. which is based on the gold(I) catalyzed cycloisomerization of enynols (Scheme 1).[14,15,16] Thus, intramolecular hydroalkoxylation is followed by isomerization to the furan ring. The required (*Z*)-enynols should be easily available by Sonogashira cross-coupling.[17]

First, ethyl propiolate[18] was converted to (*Z*)-3-bromoacrylate[19] (**7**) which upon reduction with DIBAL-H gave 3-bromopropenol[20] (**8**). In parallel, 4-pentynol[21] (**9**) was subjected to an one pot Swern oxidation/Wittig reaction[22] using the ylide methyl (triphenylphosphoranylidene) acetate.[23] This furnished enoate **10** in 75% yield (Scheme 2).[24] The seemingly straightforward Sonogashira coupling between vinyl bromide **8** and alkyne **10** was hampered by the formation of the Glaser product, diyne **12**. However, if the reaction was run in Et_3N at 10 °C, an almost quantitative yield of enynol **11** could be secured. The crucial cyclization of enynol **11** to furan **14** was best performed in methanol using 2 mol% of Echavarren catalyst (acetonitrile) [(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoroantimonate[25] (**13a**). These conditions led to a 98% yield of furan derivative **14**. With the simple gold catalyst **13b** (2 mol%) furan **14**

was formed in 66% yield. Using a similar strategy 5-hexynol[26] (**15**) was transformed to homolog **17**. Thus, the domino Swern oxidation/Wittig olefination sequence on hexynol **15** led to enyne[27] **16** in reasonable yield. This was followed by the Sonogashira coupling with vinyl bromide **8** which provided enynol **17** in high yield. Again, the gold (I) catalyzed cycloisomerization of the enynol went smoothly furnishing the substituted furan **19** in almost quantitative yield. Surprisingly, in this case the simple catalyst **13b** performed better (95% yield) than catalyst **13a** (77% yield). As before, the formation of diyne **18** could be suppressed by running the coupling reaction at 10 °C.

Scheme 2. Synthesis of 6-(furan-2-yl)hex-2-enoate (**14**) and the 7-(furan-2-yl)hept-2-enoate (**19**) via cycloisomerization of enynols **11** and **17**.



With the tethered enoate substituted furans **14** and **19** in hand, we could examine the intramolecular Diels-Alder reaction. Initial studies were performed with enoate **14**. Attempts at a thermal cycloaddition (60 – 110 °C, toluene, 140 °C, xylenes) were unsuccessful. Below 110 °C, the substrate **14** remained,

whereas above this temperature prolonged reaction times caused decomposition. We then looked at Lewis acid catalysis. Unfortunately, most of them either left the substrate unchanged or produced a complex mixture (Table 1).

Table 1. Intramolecular Cycloaddition of Furanylenoates **14** and **19**.

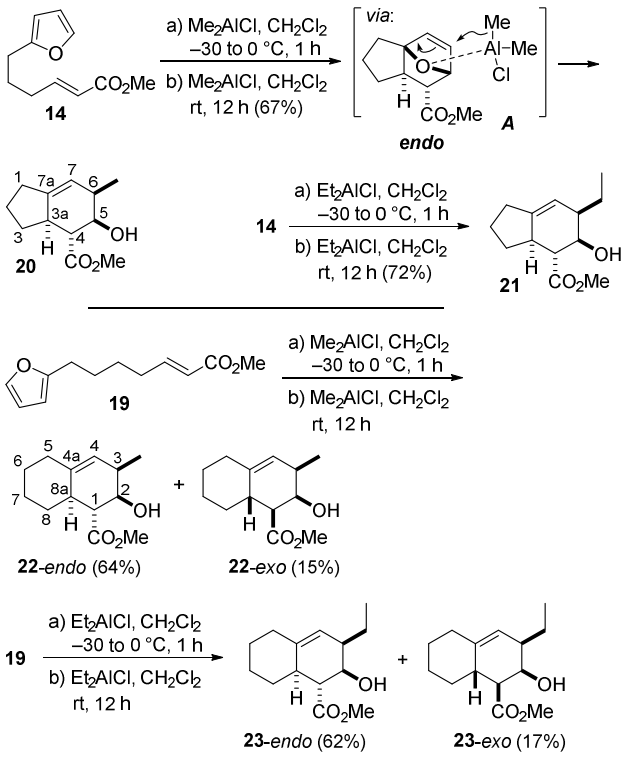
entry	substrate, molarity [mol/L]	solvent	Lewis Acid, equiv	t [°C]	result, yield [%]
1	**14** or **19**, 0.035	toluene	–	60 to 110	NR[a]
2	**14** or **19**, 0.035	xylene	–	140	–[b]
3	**14**, 0.04	CH_2Cl_2	$BF_3{\cdot}Et_2O$, 0.05 – 1	–20	NR[a]
4	**14**, 0.04	CH_2Cl_2	$BF_3{\cdot}Et_2O$, 0.05 – 3	–20 to 40	–[b]
5	**14**, 0.02	CH_2Cl_2	$AlCl_3$, 3	–20 to rt	–[b]
6	**14** or **19**, 0.05	CH_2Cl_2	$EtAlCl_2$, 2	–20 to 0	–[c]
7	**14**, 0.05	CH_2Cl_2	Me_3Al, 2	–80 to rt	–[b]
8	**14**, 0.05	CH_2Cl_2	$Sc(OTf)_3$, 0.5	0 to rt	–[d]
9	**14**, 0.2	CH_2Cl_2	Me_2AlCl, 2	–30 to rt	**20**, 42
10	**14**, 0.048	CH_2Cl_2	Me_2AlCl, 2	–30 to rt	**20**, 67
11	**14**, 0.06	CH_2Cl_2	Et_2AlCl, 2	–30 to rt	**21**, 72

[a]No reaction, starting material remained. [b]Decomposition of starting material. In presence of butylated hydroxytoluene (BHT, 8 mol%) no reaction was observed and the starting material could be re-isolated. [c]Possibly bimolecular cycloadditions. [d]Complex mixture.

But with the Lewis acid dimethylaluminium chloride (Me_2AlCl, 2 equiv, sequential addition of the Lewis acid) in CH_2Cl_2 as solvent and a substrate concentration of 0.044M, a new product could be isolated. This

compound only showed one olefinic proton in the ^{1}H NMR spectrum. The presence of a methyl doublet at δ = 0.96 ppm made it clear that the product had incorporated a methyl group from the Lewis acid. Further spectroscopic analysis suggested hexahydroindene derivative **20** as the structure. The coupling constants observed for 4-H (J = 10.8 Hz) and 5-H (10.8, 6.2 Hz) were indicative of the *trans-trans* arrangement of the protons 3a, 4 and 5. An ultimate prove of the structure **20** came from the X-ray analysis (Scheme 3).

Scheme 3. Domino intramolecular Diels-Alder reactions and nucleophilic opening of the ether bridge of Furanylenoates **14** and **19**.



The formation of the hexahydroindene **20** can be explained by an intramolecular Diels-Alder reaction followed by transfer of a methyl group from the Lewis acid, complexed to the ether bridge. Examples of allylic substitution of bridged ether furan Diels-Alder adducts have been reported, employing organolithium nucleophiles.[28] Related ring opening reactions of strained oxa/azabicyclic alkenes are well known in the literature.[29,30]

In initial runs we only obtained moderate yields for hydroxyester **20**. Analysis of the reaction mixture indicated that bimolecular Diels-Alder reactions must have taken place. The yield for the hexahydroindene derivative **20** substantially increased if the reaction was run under higher dilution. In a similar manner the reaction of furanylhexenoate **14** in presence of diethylaluminium chloride gave the ethyl derivative **21** in 72% yield.

With the substrate **19** having four methylene groups in the tether, the domino Diels-Alder reaction/epoxy bridge opening worked as well. In this case however, two diastereomers namely, the major octahydronaphthalene derivative **22**-*endo* and the minor isomer **22**-*exo* were observed. Compound **22**-*endo* results from the intermediate *endo*-cycloadduct, whereas the minor isomer **22**-*exo* was formed from the *exo*-cycloadduct. In contrast to the *endo*-product **22**-*endo*, where 1-H and 2-H show large coupling constants (J = 11.0 Hz), among the corresponding protons of the *exo*-product **22**-*exo* only 1-H shows a large coupling constant (J = 10.3 Hz) indicating the *trans*-arrangement of 8a-H and 1-H and the *cis*-arrangement of 1-H and 2-H.

The same reaction in presence of Et_2AlCl gave comparable results. Thus, we isolated 62% of **23**-*endo* and 17% of *exo*-product **23**-*exo*. The structure of **23**-*exo* was unambiguously confirmed by an X-ray analysis. It clearly showed the all *cis* arrangement of the C1-C3 substituents. Thus, in all cases the alkyl group from the Lewis acid was introduced *syn* to the epoxy bridge. ORTEPs for compounds **20**, **21**, **22**-*endo*, **23**-*endo*, **23**-*exo,* and **24** (vide infra) are included in the SI.

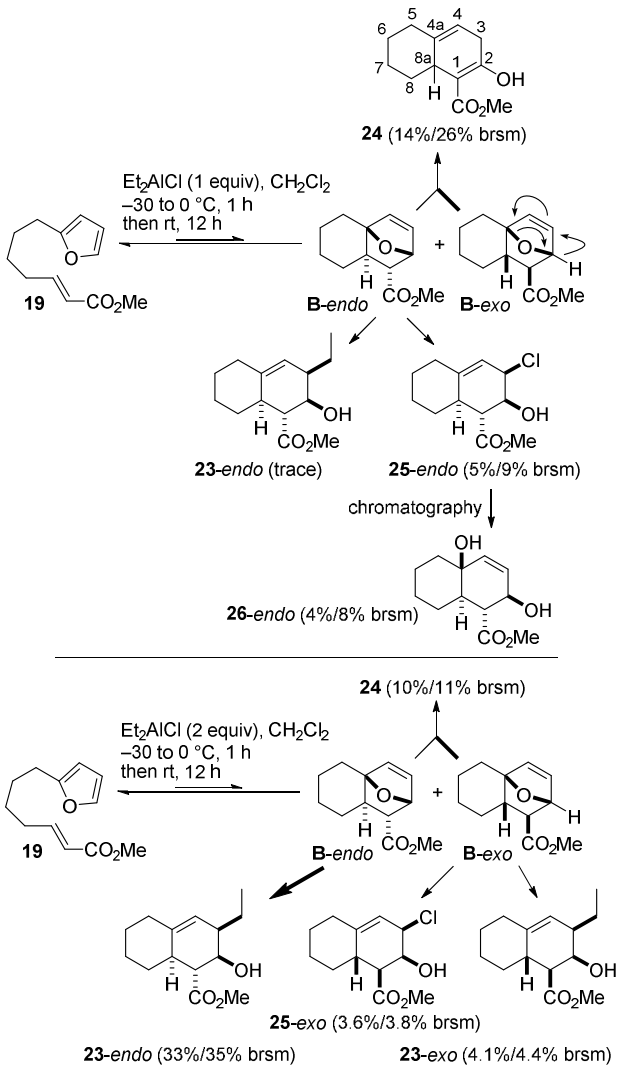
By running the reaction of furanylenoate **19** with only one equivalent of the Lewis acid Et_2AlCl we hoped to isolate the primary cycloadduct **B** (Scheme 4). Keeping the reaction conditions as before (–30 to 0 °C, 1 h, then rt, 12 h) we observed the formation of several products that are derivatives of the initial cycloadducts **B**-*endo* and **B**-*exo*. It can be assumed that the initial cycloadducts **B**-*endo* and **B**-*exo* are in equilibrium with the starting furanylenoate **19**. Thus, enol **24** was formed as the major product (14% / 26% brsm). The formation of this enol can be explained by opening of the epoxy bridge and subsequent

semipinacol rearrangement of both **B**-*endo* and **B**-*exo*[31]. Its structure was proven by NMR and an X-ray analysis. In addition, a lot of starting material **19** (48%) was recovered under these conditions. Further elution of the column gave a fraction containing a small amount of octahydronaphthalene **23**-*endo* (about 1%) and the chlorohydrin **25**-*endo* (5% / 9% brsm). Attempts to separate **25**-*endo* from **23**-*endo* yielded only pure **23**-*endo* (about 0.8%) and the diol **26**-*endo* (4% / 8% brsm) resulting from solvolysis of the unstable chlorohydrin **25**-*endo*. Attack of water takes place at C-4a of **25**-*endo*, so that the two rings are *trans* fused. It can be assumed that cycloadduct **B**-*exo* is even more unstable than **B**-*endo*. Most likely, the latter completely reacted to enol **24**. The formation of the chlorohydrin **25**-*endo* arises from transfer of a chloride ion of the Lewis acid causing opening of the epoxy bridge of **B**-*endo*. A change in the reaction conditions (Et_2AlCl, –30 to 15 °C, 72 h) gave similar results (16% of **24**). The largest coupling constant of 3-H to its neighbors is around 4 Hz, indicating the pseudoaxial orientation of the chlorine atom.

We also performed the same experiment on substrate **19** where we added two equivalents of Et_2AlCl in one portion and kept the reaction conditions the same as before. Here **23**-*endo* was the major product (33% / 35% brsm). Enol **24** was also isolated (10% / 11% brsm). In addition, a small amount of octahydronaphthalene **23**-*exo* (4.1% / 4.4% brsm) was formed. Finally, we were able to detect the chlorohydrin **25**-*exo* (3.6% / 3.8%) and some starting **19** (6%). These results can be interpreted as follows: Clearly, the additional Lewis acid promotes the transfer of the ethyl group from the aluminium center to the initial cycloadducts more efficiently. Since the ratio **23**-*endo*/**23**-*exo* (8:1) is significantly different from the one observed in the sequential addition of the Lewis acid (3.75:1, Scheme 3) one can conclude that cycloadduct **B**-*exo* is less stable and either reacts to enol **24** or the chlorohydrin **25**-*exo*. Under the conditions chlorohydrin **25**-*endo* cannot form since cycloadduct **B**-*endo* must react faster to give **23**-*endo*.

The reason why the sequential addition of the two equivalents of Et_2AlCl gives **23**-*endo* and **23**-*exo* in high combined yield (79%) is difficult to explain and to clarify this issue would require additional experiments. As has been noted by Snider et al.[32] with two equivalents of Me_2AlCl a more reactive substrate·$(Me_2AlCl)_2$ complex is formed. Moreover, it was claimed that alkylaluminium halides can also function as proton scavengers.

Scheme 4. Domino intramolecular Diels-Alder reaction and semipinacol rearrangement of **19** to give enol **24**; reaction of **19** with Et_2AlCl under two different conditions; brsm = based on recovered starting material.



In conclusion, we demonstrated the usefulness of the Liu strategy for the synthesis of functionalized furans. Thus, starting with a terminal alkyne, a Sonogashira coupling with (*Z*)-bromopropenol **8** gave conjugated (*Z*)-enynols **11** and **17**. Through a gold-catalyzed cycloisomerization the tethered enoate substituted furans **14** and **19** were obtained. Probably due to the lack of substituents on the tether and the facile retro Diels-Alder reaction, the subsequent intramolecular cycloaddition only worked in presence of a Lewis acid, here R_2AlCl, R = Me, Et, that not only catalyzes the cycloaddition but also is able to trap the unstable cycloadducts. With the aluminium based Lewis acids R_2AlCl, R = Me, Et, the intramolecular cycloaddition was followed by a transfer of an alkyl group to the cycloadducts with concomitant opening of the epoxy bridge. This way hexahydroindene and octahydronaphthalene derivatives were obtained. As it turned out, the outcome of the experiments depends on the amount and order of addition of the Lewis acid.

Experimental Section

General. Reactions were generally run under nitrogen atmosphere in oven dried glassware. Progress of the reactions was followed using TLC plates "POLYGRAM SIL G/UV254", petroleum ether, ethyl acetate (EtOAc), dichloromethane, methanol and mixtures of them as an eluent. Dry diethyl ether (Et_2O) and tetrahydrofuran were distilled from sodium and benzophenone, whereas dry CH_2Cl_2, methanol and EtOAc were distilled from CaH_2. Distilled petroleum ether with a boiling range of 40–60 °C was used. ^1H NMR (400.160 MHz) and ^{13}C NMR (100.620 MHz) spectra were measured on a "Bruker Avance 400" spectrometer using $CDCl_3$ or C_6D_6 as solvent at room temperature. Some of the spectra were acquired on a Bruker Avance 600 spectrometer, (^1H NMR at 600.13 MHz, ^{13}C NMR at 150.90 MHz) or Bruker Avance 700 spectrometer, (^1H NMR at 700.29 MHz, ^{13}C NMR at 176.09 MHz). Peak assignments were done by NMR spectroscopy (^1H, ^{13}C, DEPT-135, H,H-COSY, HSQC, and HMBC). Infrared spectra were recorded on a

single-reflection diamond ATR spectrometer as thin films. In the IR spectra only the strongest/structurally most important peaks (ν, cm^{-1}) are listed. High-resolution mass spectra (HRMS) were recorded on a "Bruker maXis 4G" instrument with electron spray ionization (ESI) and TOF mass detector.

Methyl (*E*)-hept-2-en-6-ynoate (**10**). Under nitrogen-atmosphere dry CH_2Cl_2 (130 mL) was brought to –75 °C, then oxalyl chloride (5.40 mL, 8.05 g, 63.4 mmol, 1.2 equiv) was added. Thereafter, dry DMSO (8.90 mL, 9.79 g, 125 mmol, 2.3 equiv) was added dropwise over 10 min. The solution was stirred for 10 min and after that a solution of 4-pentyn-1-ol[21] (4.52 g, 53.7 mmol, 1 equiv) in dry CH_2Cl_2 (43 mL) was added dropwise within 10 min. The mixture was stirred for 15 min and subsequently dry triethylamine (37.0 mL, 27.0 g, 267 mmol, 5 equiv) was added over 25 min. The resulting yellow mixture was brought to 0 °C and under vigorous stirring methyl (triphenylphosphoranylidene)acetate[23] (21.2 g, 63.4 mmol, 1.2 equiv) was added in one portion. The reaction mixture was stirred at rt for 1 h and then quenched with water (200 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified first by flash chromatography (petroleum ether/EtOAc 15:1) to remove the unpreferred *cis*-isomer and then the obtained yellow liquid was distilled (107 °C, 25 mbar). Ester[24] **10** (5.57 g, 40.3 mmol, 75%) was obtained as a colorless liquid. R_f = 0.26 (petroleum ether/EtOAc, 15:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.98 (t, ^4J = 2.6 Hz, 1H, 7-H), 2.31-2.36 (m, 2H, 5-H), 2.39-2.45 (m, 2H, 4-H), 3.72 (s, 3H, OCH_3), 5.88 (dt, ^3J = 15.7 Hz, ^4J = 1.5 Hz, 1H, 2-H), 6.96 (dt, ^3J = 15.7 Hz, ^3J = 6.6 Hz, 1H, 3-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.4 (C-5), 31.0 (C-4), 51.5 (OCH_3), 69.4 (C-7), 82.6 (C-6), 122.1 (C-2), 146.6 (C-3), 166.8 (C-1).

Methyl (*E*)-oct-2-en-7-ynoate (**16**). Under nitrogen-atmosphere dry CH_2Cl_2 (112 mL) was brought to –80 °C, then oxalyl chloride (4.70 mL, 6.94 g, 54.7 mmol, 1.2 equiv) was added. Thereafter, dry DMSO (7.70 mL, 108 mmol, 2.3 equiv) was added dropwise over 10 min. The solution was stirred for 10 min and after

that a solution of 5-hexyn-1-ol[26] (**15**) (4.55 g, 46.4 mmol, 1 equiv) in dry CH_2Cl_2 (37 mL) was added dropwise within 10 min. The mixture was stirred for 1 h before dry triethylamine (33.0 mL, 23.3 g, 230 mmol, 5 equiv) was added within 20 min. The resulting yellow mixture was brought to 0 °C and under vigorous stirring methyl (triphenylphosphoranylidene)acetate (31.0 g, 92.7 mmol, 2.0 equiv) was added in one portion. The reaction mixture was stirred at rt for 1 h and then quenched with water (200 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified first by flash chromatography (petroleum ether/EtOAc, 20:1) to remove the unpreferred *cis*-isomer and then the yellow liquid was distilled (105 °C, 12 mbar). Enoate[27] **16** (5.23 g, 34.2 mmol, 74%) was obtained as a colorless liquid. R_f = 0.53 (petroleum ether/EtOAc, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.66 (tt (app. quin), ^3J = 7.2 Hz, 2H, 5-H), 1.95 (t, ^4J = 2.7 Hz, 1H, 8-H), 2.19 (td, ^3J = 7.0 Hz, ^4J = 2.7 Hz, 2H, 6-H), 2.30 (dtd (app. qd), ^3J = 7.2 Hz, ^4J = 1.6 Hz, 2H, 4-H), 3.69 (s, 3H, OCH_3), 5.83 (dt, ^3J = 15.7 Hz, ^4J = 1.6 Hz, 1H, 2-H), 6.86 (dt, ^3J = 15.7 Hz, ^3J = 7.0 Hz, 1H, 3-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8 (C-6), 26.6 (C-5), 30.9 (C-4), 51.4 (OCH_3), 69.0 (C-8), 83.4 (C-7), 121.6 (C-2), 148.1 (C-3), 166.9 (C-1).

Methyl (2*E*,8*Z*)-10-hydroxydeca-2,8-dien-6-ynoate (**11**). Under argon-atmosphere dry triethylamine (127 mL) was brought in a water bath to 10 °C. Under stirring, alcohol[20] **8** (2.00 g, 14.6 mmol, 1 equiv), alkyne **10** (2.82 g, 20.4 mmol, 1.4 equiv), $Pd(PPh_3)_4$ (844 mg, 0.730 mmol, 0.05 equiv) and CuI (556 mg, 2.92 mmol, 0.22 equiv) were added consecutively. Then the yellow mixture was slowly allowed to come to rt in the water bath, initially having a temperature of 10 °C. After 48 h the olive-brown mixture was diluted with hexane (50 mL), filtered (repeatedly rinsed) and evaporated. The olive-brown oil was purified by flash chromatography (CH_2Cl_2/EtOAc, 20:1, 0.1% triethylamine) to obtain enynol **11** (2.75 g, 14.2 mmol, 97%) as a yellow oil. R_f: 0.26 (CH_2Cl_2/EtOAc, 20:1); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.70 (bs, 1H, OH), 2.42-2.45 (m, 2H, 4-H), 2.49-2.52 (m, 2H, 5-H), 3.73 (s, 3H, OCH_3), 4.35 (dd, ^3J = 6.6 Hz, ^4J = 1.5 Hz, 2H, 10-H), 5.53 (dt, ^3J = 10.7 Hz, ^4J = 1.5 Hz, 1H, 8-H), 5.90 (dt, ^3J = 15.8 Hz, ^4J = 1.5 Hz, 1H, 2-H), 6.02 (dt, ^3J = 11.0 Hz,

^3J = 6.3 Hz, 1H, 9-H), 6.98 (dt, ^3J = 15.8 Hz, ^3J = 6.6 Hz, 1H, 3-H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 18.5 (C-5), 31.2 (C-4), 51.6 (OCH_3), 60.9 (C-10), 77.5 (C-7), 94.3 (C-6), 110.9 (C-8), 122.2 (C-2), 140.6 (C-9), 146.9 (C-3), 166.9 (C-1); IR: 3436, 2951, 2919, 2850, 2361, 2341, 1721, 1659, 1539, 1508, 1436, 1320, 1263, 1205, 1158, 1087, 1021, 801, 726; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{11}H_{14}O_3Na$ 217.0835; found 217.0835.

If the reaction was carried out at rt, or the palladium catalyst was not good enough or there was oxygen present, one observed a significant amount of the dimeric side product **12** as a light amorphous yellow solid and conversely the yield of the enynol **11** decreased.

Dimethyl (2*E*,12*E*)-tetradeca-2,12-dien-6,8-diynedioate (**12**). R_f = 0.51 (CH_2Cl_2/EtOAc, 20:1); ^{1}H NMR (700 MHz, $CDCl_3$): δ = 2.41-2.44 (m, 8H, 4-H, 5-H, 10-H, 11-H), 3.73 (s, 6H, OCH_3), 5.88 (d, ^3J = 15.6 Hz, 2H, 2-H, 13-H), 6.94 (dt, ^3J = 15.7 Hz, ^3J = 6.3 Hz, 2H, 3-H, 12-H); ^{13}C NMR (175 MHz, $CDCl_3$): δ = 18.2 (C-5, C-10), 30.8 (C-4, C-11), 51.6 (OCH_3), 66.1 (C-7, C-8), 76.0 (C-6, C-9), 122.3 (C-2, C-13), 146.3 (C-3, C-12), 166.7 (C-1, C-14); IR: 3375, 2953, 2361, 1717, 1658, 1434, 1320, 1265, 1204, 1174, 1157, 1085, 1019, 971, 851, 737, 721, 703, 668; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{18}O_4Na$ 297.1097; found 297.1102.

Methyl (2*E*,9*Z*)-11-hydroxyundeca-2,9-dien-7-ynoate (**17**). Under argon-atmosphere dry triethylamine (95 mL) was brought in a water bath to 10 °C. Under stirring, alcohol **8** (1.50 g, 11.0 mmol, 1 equiv), alkyne **15** (2.50 g, 16.4 mmol, 1.5 equiv), $Pd(PPh_3)_4$ (633 mg, 0.55 mmol, 0.05 equiv) and CuI (417 mg, 2.19 mmol, 0.2 equiv) were added consecutively. Then the yellow mixture was slowly allowed to reach rt, while keeping the flask in the water bath. After 50 h the olive-brown mixture was diluted with hexane (40 mL), filtered (repeatedly rinsed) and evaporated. The olive-brown oil was purified by flash chromatography (petroleum ether/EtOAc, 3.5:1, 0.1% triethylamine) to obtain enynol **17** (2.10 g, 10.1 mmol, 92%) as a yellow oil. R_f = 0.26 (petroleum ether/EtOAc, 2:1); ^{1}H NMR (700 MHz, C_6D_6): δ = 1.20 (tt (app. quin), ^3J = 7.3 Hz, 2H, 5-H), 1.34 (bs, 1H, -OH), 1.82 (dtd (app. qd), ^3J = 7.1 Hz, ^4J = 1.5 Hz, 2H, 4-H), 1.92 (tt (app. td) ^3J = 7.1 Hz, ^4J = 2.2 Hz, 2H, 6-H), 3.41 (s, 3H, OCH_3), 4.31 (dd, ^3J = 6.2 Hz, ^4J = 1.1 Hz, 2H,

11-H), 5.43 (dt, ^3J = 11.0 Hz, ^4J = 1.5 Hz, 1H, 9-H), 5.80 (dt, ^3J = 15.7 Hz, ^4J = 1.5 Hz, 1H, 2-H), 5.80 (dt, ^3J = 10.8 Hz, ^3J = 6.5 Hz, 1H, 10-H), 6.91 (dt, ^3J = 15.7 Hz, ^3J = 7.1 Hz, 1H, 3-H); ^{13}C NMR (175 MHz, C_6D_6): δ = 19.4 (C-6), 27.4 (C-5), 31.6 (C-4), 51.4 (OCH_3), 61.4 (C-11), 78.1 (C-6), 95.7 (C-7), 110.7 (C-9), 122.3 (C-2), 142.0 (C-10), 148.6 (C-3), 166.9 (C-1); IR: 3423, 2950, 2360, 2343, 1721, 1658, 1436, 1325, 1269, 1203, 1153, 1094, 1024, 798; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{16}O_3Na$ 231.0992; found 231.0990.

If the reaction was carried out at rt, or the palladium catalyst was not good enough or there was oxygen present, one observed a significant amount of the dimeric side product **18** as a yellow oil and conversely the yield of enynol **17** decreased.

Dimethyl (2*E*,14*E*)-hexadeca-2,14-dien-7,9-diynedioate (**18**). R_f = 0.57 (petroleum ether/EtOAc, 7:2); ^{1}H NMR (400 MHz, C_6D_6): δ = 1.13 (tt (app. sept), ^3J = 7.3 Hz, 4H, 5-H, 12-H), 1.73-1.78 (m, 8H, 4-H, 6-H, 11-H, 13-H), 3.42 (s, 6H, OCH_3), 5.72 (dt, ^3J = 15.7 Hz, ^4J = 1.5 Hz, 2H, 2-H, 15-H), 6.79 (dt, ^3J = 15.7 Hz, ^3J = 6.97 Hz, 2H, 3-H, 14-H); ^{13}C NMR (100 MHz, C_6D_6): δ = 19.0 (C-6, C-11), 27.0 (C-5, C-12), 31.3 (C-4, C-13), 51.3 (OCH_3), 67.4 (C-8, C-9), 77.3 (C-7, C-10), 122.4 (C-2, C-15), 148.1 (C-3, C-14), 166.7 (C-1, C-16); IR: 2951, 2850, 2359, 2341, 1720, 1658, 1435, 1324, 1262, 1198, 1150, 1094, 1027, 976, 801; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{18}H_{22}O_4Na$ 325.1410; found 325.1410.

Methyl (*E*)-6-(furan-2-yl)hex-2-enoate (**14**). Under nitrogen-atmosphere enynol **11** (2.06 g, 10.6 mmol, 1 equiv) was dissolved in dry methanol (195 mL) and (acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I)hexafluoro-antimonate (**13a**) (164 mg, 0.212 mmol, 0.02 equiv) was added to the light yellow solution. The reaction mixture was stirred for 30 h at rt and then quenched with tetra-*n*-butylammonium bromide (TBAB)-solution (1M, 200 mL). Then diethyl ether to reach phase separation was added, followed by extraction of the aqueous phase with diethyl ether (4 × 200 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. The light yellow oil was purified by flash chromatography (petroleum ether/EtOAc, 30:1) to obtain furan derivative **14** (2.02 g, 10.4 mmol, 98%) as a colorless liquid. R_f = 0.22 (petroleum ether/EtOAc, 30:1); ^{1}H NMR (400 MHz, $CDCl_3$):

δ = 1.80 (tt (app. quin), ^3J = 7.3 Hz, 2H, 5-H), 2.32 (dtd (app qd), ^3J = 7.3 Hz, ^4J = 1.6 Hz, 2H, 4-H), 2.64 (t, ^3J = 7.5 Hz, 2H, 6-H), 3.72 (s, 3H, OCH_3), 5.83 (dt, ^3J = 15.7 Hz, ^4J = 1.6 Hz, 1H, 2-H), 5.97 (dd, ^3J = 3.1 Hz, ^4J = 0.8 Hz, 1H, 3'-H), 6.26 (dd, ^3J = 3.1 Hz, ^3J = 1.8 Hz, 1H, 4'-H), 6.95 (dt, ^3J = 15.7 Hz, ^3J = 7.0 Hz, 1H, 3-H), 7.29 (dd, ^3J = 1.8 Hz, ^4J = 0.8 Hz, 1H, 5'-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (C-5), 27.2 (C-6), 31.4 (C-4), 51.4 (OCH_3), 105.2 (C-3'), 110.1 (C-4'), 121.4 (C-2), 141.0 (C-5'), 148.7 (C-3), 155.3 (C-2'), 167.0 (C-1); IR: 3700, 2950, 2359, 2337, 1722, 1658, 1652, 1435, 1271, 1199, 1149, 1008, 864, 732; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{11}H_{14}O_3Na$ 217.0835; found 217.0835.

Methyl (*E*)-7-(furan-2-yl)hept-2-enoate (**19**). Under nitrogen-atmosphere enynol **17** (2.00 g, 9.60 mmol, 1 equiv) was dissolved in dry methanol (96 mL) and (acetonitrile)[triphenylphosphine]gold(I) hexafluoroantimonate (**13b**) (141 mg, 0.192 mmol, 0.02 equiv) was added to the light yellow solution. The reaction mixture was stirred for 30 h at rt and then quenched with TBAB-solution (1M, 100 mL). Then diethyl ether was added to reach phase separation and after separation of the layers, the aqueous phase was extracted with diethyl ether (4 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The light yellow oil was purified by flash chromatography (petroleum ether/EtOAc, 20:1) to obtain furan **19** (1.89 g, 9.08 mmol, 95%) as a colorless liquid. R_f = 0.56 (petroleum ether/EtOAc, 5:1); ^{1}H NMR (400 MHz, C_6D_6): δ = 1.06 (tt (app. quin), ^3J = 7.5 Hz, 2H, 5-H), 1,34 (tt (app. quin), ^3J = 7.5 Hz, 2H, 6-H), 1.69 (dtd (app. qd), ^3J = 7.3 Hz, ^4J = 1.5 Hz, 2H, 4-H), 2.34 (t, ^3J = 7.3 Hz, 2H, 7-H), 3.43 (s, 3H, OCH_3), 5.79 (dt, ^3J = 15.7 Hz, ^4J = 1.6 Hz, 1H, 2-H), 5.81 (dd, ^3J = 3.3 Hz, ^4J = 0.9 Hz, 1H, 3'-H), 6.12 (dd, ^3J = 3.1 Hz, ^3J = 1.8 Hz, 1H, 4'-H), 6.93 (dt, ^3J = 15.7 Hz, ^3J = 7.0 Hz, 1H, 3-H), 7.12 (dd, ^3J = 1.8 Hz, ^4J = 0.9 Hz, 1H, 5'-H); ^{13}C NMR (100 MHz, C_6D_6): δ = 27.9 (C-5), 28.1 (C-6), 28.2 (C-7), 32.2 (C-4), 51.3 (OCH_3), 105.6 (C-3'), 110.8 (C-4'), 121.9 (C-2), 141.4 (C-5'), 149.3 (C-3), 156.5 (C-2'), 166.9 (C-1); IR: 3733, 2935, 2861, 2359, 2343, 1723, 1657, 1596, 1508, 1436, 1315, 1272, 1199, 1176, 1148, 1095, 1038, 1008, 808, 739, 670, 601; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{16}O_3Na$ 231.0992; found 231.0995.

Methyl (rel 3a*S*,4*S*,5*S*,6*S*)-5-hydroxy-6-methyl-2,3,3a,4,5,6-hexahydro-1*H*-indene-4-carboxylate (**20**). Under argon-atmosphere furan **14** (119 mg, 0.613 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (13 mL) and brought to –30 °C. Me_2AlCl (0.9M in heptane, 0.75 mL, 0.68 mmol, 1.1 equiv) was added dropwise. The light-yellow solution was allowed to warm to 0 °C within 1 h. Then additional Me_2AlCl (0.9M in heptane, 0.75 mL, 0.68 mmol, 1.1 equiv) was added dropwise again. The yellow solution was stirred at rt overnight and then poured on ice-cooled sodium potassium tartrate solution (1M, 13 mL) and stirred at rt until phase-separation. The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to obtain hexahydroindene **20** (87.0 mg, 0.414 mmol, 67%) as colorless needles. mp 97.8-98.0 °C (petroleum ether/EtOAc, 5:1); R_f = 0.24 (petroleum ether/EtOAc, 5:1); ^{1}H NMR (700 MHz, $CDCl_3$): δ = 0.96 (d, ^3J = 6.9 Hz, 3H, CH_3), 1.16-1.24 (m, 1H, 3-H), 1.53-1.60 (m, 1H, 2-H), 1.72-1.77 (m, 1H, 2-H), 1.88-1.92 (m, 1H, 3-H), 2.15-2.20 (m, 1H, 1-H), 2.30 (dd (app. t), ^3J = 10.8 Hz, 3H, 1-H, 4-H, OH), 2.41-2.45 (m, 1H, 3a-H), 2.49-2.54 (m, 1H, 6-H), 3.74 (s, 3H, OCH_3), 4.15 (dd, ^3J = 10.8 Hz, ^3J = 6.2 Hz, 1H, 5-H), 5.34-5.35 (m, 1H, 7-H); ^{13}C NMR (175 MHz, $CDCl_3$): δ = 15.1 (CH_3), 23.4 (C-2), 29.1 (C-1), 31.9 (C-3), 35.1 (C-6), 45.1 (C-3a), 48.8 (C-4), 51.8 (OCH_3), 71.4 (C-5), 122.0 (C-7), 141.4 (C-7a), 175.7 (CO_2CH_3); IR: 3448, 2960, 2931, 2865, 2360, 2341, 1730, 1436, 1314, 1283, 1197, 1170, 1077, 1044, 857, 669; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{18}O_3Na$ 233.1148; found 233.1150.

Methyl (rel 3a*R*,4*R*,5*R*,6*R*)-6-ethyl-5-hydroxy-2,3,3a,4,5,6-hexahydro-1*H*-indene-4-carboxylate (**21**). Under argon-atmosphere furan **14** (119 mg, 0.613 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (10 mL) and brought to –30 °C. Then Et_2AlCl (0.9M in toluene, 0.75 mL, 0.68 mmol, 1.1 equiv) was added dropwise. The light-yellow solution was allowed to warm to 0 °C over 1 h. Then additional Et_2AlCl (0.9M in toluene, 0.75 mL, 0.68 mmol, 1.1 equiv) was added dropwise. The yellow solution was stirred at rt overnight and then poured on ice-cooled sodium potassium tartrate solution (1M, 10 mL) and the

mixture stirred at rt until phase-separation. The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to obtain hexahydroindene **21** (99.0 mg, 0.440mmol, 72%) as colorless needles. R_f = 0.28 (petroleum ether/EtOAc, 5:1); mp 107.1-108.2 °C (petroleum ether/EtOAc, 5:1); ^{1}H NMR (700 MHz, $CDCl_3$): δ = 0.96 (t, ^3J = 7.4 Hz, 3H, CH_2CH_3), 1.04-1.11 (m, 1H, CH_2CH_3), 1.17-1.24 (m, 1H, 3-H), 1.54-1.62 (m, 1H, 2-H), 1.73-1.78 (m, 1H, 2-H), 1.79-1.84 (m, 1H, CH_2CH_3), 1.89-1.93 (m, 1H, 3-H), 2.17-2.22 (m, 1H, 1-H), 2.23-2.27 (m, 1H, 6-H), 2.28 (d, ^3J = 4.9 Hz, 1H, OH), 2.29-2.31 (m, 1H, 1-H), 2.33 (dd (app t), ^3J = 10.5 Hz, 1H, 4-H), 2.39-2.44 (m, 1H, 3a-H), 3.74 (s, 3H, OCH_3), 4.17 (ddd (app. quin), ^3J = 10.5 Hz, ^3J = 6.3 Hz, ^3J = 4.9 Hz, 1H, 5-H), 5.50-5.52 (m, 1H, 7-H); ^{13}C NMR (175 MHz, $CDCl_3$): δ = 12.0 (CH_2CH_3), 22.8 (CH_2CH_3), 23.4 (C-2), 29.2 (C-1), 32.0 (C-3), 41.5 (C-6), 44.9 (C-3a), 49.5 (C-4), 51.8 (OCH_3), 71.6 (C-5), 119.7 (C-7), 142.2 (C-7a), 175.8 (CO_2CH_3); IR: 3447, 2957, 2864, 2361, 2341, 1732, 1660, 1438, 1378, 1316, 1281, 1199, 1171, 1080, 1051, 866, 796, 671; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{20}O_3Na$ 247.1305; found 247.1308.

Methyl (rel 1*R*,2*R*,3*R*,8a*R*)-2-hydroxy-3-methyl-1,2,3,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (**22-***endo*) and methyl (rel 1*S*,2*R*,3*R*,8a*S*)-2-hydroxy-3-methyl-1,2,3,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (**22-***exo*). Under argon-atmosphere a solution of furan **19** (82.0 mg, 0.390 mmol, 1 equiv) in dry CH_2Cl_2 (49 mL) was treated dropwise at –30 °C with Me_2AlCl (0.9M in heptane, 0.48 mL, 0.43 mmol, 1.1 equiv). The light-yellow solution was allowed to warm to 0 °C over 1 h. Then, further Me_2AlCl (0.9M in heptane, 0.48 mL, 0.43 mmol, 1.1 equiv) was added dropwise. The yellow solution was stirred at rt overnight and then poured on ice-cooled sodium potassium tartrate solution (1M, 50 mL) and stirred at rt until phase-separation. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to obtain octahydronaphthalenes

22-*endo* (57.0 mg, 0.254 mmol, 64%) and **22**-*exo* (13.0 mg, 0.058 mmol, 15%) as colorless needles. dr **22**-*endo* / **22**-*exo* = 3.75 / 1.0.

Octahydronaphthalene **22**-*endo*: R_f = 0.19 (petroleum ether/EtOAc, 5:1); mp 106.9-107.8 °C (petroleum ether/EtOAc, 5:1); ^{1}H NMR (700 MHz, $CDCl_3$): δ = 0.96 (d, ^3J = 6.9 Hz, 3H, CH_3), 0.99-1.03 (m, 1H, 8-H), 1.16-1.22 (m, 1H, 6-H), 1.26-1.32 (m, 1H, 7-H), 1.66 (bs, 1H, -OH), 1.69-1.73 (m, 2H, 6-H, 7-H), 1.82-1.84 (m, 1H, 8-H), 1.90-1.94 (m, 1H, 5-H), 2.19-2.22 (m, 1H, 5-H), 2.29-2.32 (m, 1H, 8a-H), 2.37-2.39 (m, 1H, 3-H), 2.40 (dd (app. t), ^3J = 11.0 Hz, 1H, 1-H), 3.74 (s, 3H, OCH_3), 4.05 (dd, ^3J = 11.0 Hz, ^3J = 5.6 Hz, 1H, 2-H), 5.30-5.31 (m, 1H, 4-H); ^{13}C NMR (175 MHz, $CDCl_3$): δ = 14.5 (CH_3), 25.6 (C-7), 27.1 (C-6), 33.7 (C-8), 34.6 (C-5), 34.7 (C-3), 41.3 (C-8a), 50.5 (C-1), 51.9 (OCH_3), 70.8 (C-2), 123.3 (C-4), 137.6 (C-4a), 175.9 (CO_2CH_3); IR: 3459, 2923, 2858, 2361, 2343, 1737, 1437, 1332, 1294, 1199, 1169, 1092, 1050, 1042, 845, 689; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{20}O_3Na$ 247.1305; found 247.1305.

Octahydronaphthalene **22**-*exo*: R_f = 0.28 (petroleum ether/EtOAc, 5:1); mp 71.1-72.3 °C (petroleum ether/EtOAc, 5:1); ^{1}H NMR (700 MHz, C_6D_6): δ = 0.86-0.92 (m, 1H, 8-H), 1.04 (d, ^3J = 7.3 Hz, 3H, CH_3), 1.12-1.18 (m, 1H, 6-H), 1.21-1.28 (m, 1H, 7-H), 1.56-1.61 (m, 2H, 6-H, 7-H), 1.85-1.89 (m, 1H, 5-H), 1.98-2.01 (m, 1H, 8-H), 2.08-2.09 (m, 1H, 3-H), 2.09-2.12 (m, 1H, 5-H), 2.18-2.19 (m, 1H, OH), 2.25 (dd, ^3J = 10.3 Hz, ^4J = 1.7 Hz, 1H, 1-H), 2.62-2.66 (m, 1H, 8a-H), 3.35 (s, 3H, OCH_3), 3.93-3.95 (m, 1H, 2-H), 4.91-4.93 (m, 1H, 4-H); ^{13}C NMR (175 MHz, C_6D_6): δ = 17.5 (CH_3), 26.7 (C-7), 28.2 (C-6), 34.3 (C-8), 35.6 (C-8a), 35.7 (C-5), 36.1 (C-3), 51.7 (OCH_3), 53.4 (C-1), 70.4 (C-2), 122.2 (C-4), 138.7 (C-4a), 175.5 (CO_2CH_3); IR: 3531, 2926, 2852, 2360, 2341, 1734, 1684, 1436, 1260, 1195, 1161, 1124, 1062, 1014, 671; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{13}H_{20}O_3Na$ 247.1305; found 247.1307.

Methyl (rel 1*R*,2*R*,3*R*,8a*R*)-3-ethyl-2-hydroxy-1,2,3,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (**23**-*endo*) and methyl (rel 1*S*,2*R*,3*R*,8a*S*)-3-ethyl-2-hydroxy-1,2,3,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (**23**-*exo*). Under argon atmosphere furan **19** (103 mg, 0.495 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (19 mL) and brought to –30 °C. Et_2AlCl (0.9M in toluene, 0.60 mL, 0.54 mmol, 1.1 equiv) was

added dropwise. The light-yellow solution was allowed to warm to 0 °C over 1 h. Then, further Et_2AlCl (0.9M in toluene, 0.60 mL, 0.54 mmol, 1.1 equiv) was added dropwise. The yellow solution was stirred at rt overnight and then poured on ice-cooled sodium potassium tartrate-solution (1M, 20 mL) and stirred at rt until phase-separation. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give octahydronaphthalenes **23**-*endo* (73.0 mg, 0.306 mmol, 62%) and **23**-*exo* (20.0 mg, 0.084 mmol, 17%) as colorless needles. dr **23**-*endo* / **23**-*exo* = 3.75 / 1.0.

Octahydronaphthalene **23**-*endo*: R_f = 0.21 (petroleum ether/EtOAc, 5:1); mp 115.0-116.8 °C (petroleum ether/EtOAc, 5:1); ^{1}H NMR (700 MHz, $CDCl_3$): δ = 0.98 (t, ^3J = 7.3 Hz, 3H, CH_2CH_3), 0.99-1.05 (m, 1H, 8-H), 1.06-1.13 (m, 1H, CH_2CH_3), 1.17-1.25 (m, 1H, 6-H), 1.27-1.34 (m, 1H, 7-H), 1.70-1.75 (m, 3H, 6-H, 7-H, OH), 1.76-1.82 (m, 1H, CH_2CH_3), 1.83-1.86 (m, 1H, 8-H), 1.92-1.96 (m, 1H, 5-H), 2.11-2.15 (m, 1H, 3-H), 2.21-2.23 (m, 1H, 5-H), 2.28-2.32 (m, 1H, 8a-H), 2.43 (dd (app. t), ^3J = 11.0 Hz, 1H, 1-H), 3.73 (s, 3H, OCH_3), 4.07 (dd, ^3J = 11.0 Hz, ^3J = 5.4 Hz, 1H, 2-H), 5.42-5.43 (m, 1H, 4-H); ^{13}C NMR (175 MHz, $CDCl_3$): δ = 12.0 (CH_2CH_3), 22.8 (CH_2CH_3), 25.7 (C-7), 27.3 (C-6), 33.9 (C-8), 34.9 (C-5), 41.2 (C-8a), 41.5 (C-3), 51.1 (C-1), 51.9 (OCH_3), 71.0 (C-2), 121.2 (C-4), 138.3 (C-4a), 175.9 (CO_2CH_3); IR: 3451, 2927, 2855, 2359, 2342, 1732, 1660, 1437, 1378, 1286, 1197, 1169, 1101, 1052, 995, 860, 671; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{22}O_3Na$ 261.1461; found 261.1462.

Octahydronaphthalene **23**-*exo*: R_f = 0.32 (petroleum ether/EtOAc, 5:1); mp 74.2-75.4 °C (petroleum ether/EtOAc, 5:1); ^{1}H NMR (700 MHz, $CDCl_3$): δ = 0.95-1.01 (m, 1H, 8-H), 0.98 (t, ^3J = 7.5 Hz, 3H, CH_2CH_3), 1.19-1.27 (m, 1H, 6-H), 1.35-1.43 (m, 2H, CH_2CH_3, 7-H), 1.49-1.56 (m, 1H, CH_2CH_3), 1.74-1.78 (m, 2H, 6-H, 7-H), 1.89-1.91 (m, 1H, 8-H), 2.01-2.09 (m, 2H, 3-H, 5-H), 2.21-2.24 (m, 1H, 5-H), 2.26 (d, ^3J = 5.4 Hz, 1H, OH), 2.32 (dd, ^3J = 10.5 Hz, ^4J = 1.7 Hz, 1H, 1-H), 2.47-2.50 (m, 1H, 8a-H), 3.74 (s, 3H, OCH_3), 4.10-4.13 (m, 1H, 2-H), 5.06-5.08 (m, 1H, 4-H); ^{13}C NMR (175 MHz, $CDCl_3$): δ = 11.6 (CH_2CH_3), 24.3 (C-6), 26.0 (C-7), 27.5

(*C*H_2CH_3), 33.6 (C-8), 35.1 (C-5), 35.5 (C-8a), 42.3 (C-3), 51.9 (OCH_3), 52.5 (C-1), 67.9 (C-2), 120.0 (C-4), 138.8 (C-4a), 175.7 (*C*O_2CH_3); IR: 3504, 2926, 2854, 2361, 2342, 1724, 1659, 1507, 1435, 1261, 1195, 1171, 1093, 1020, 797; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{14}H_{22}O_3Na$ 261.1461; found 261.1464.

Reaction of furanylenoate **19** with one equivalent of Et_2AlCl: Under argon-atmosphere furan **19** (161 mg, 0.773 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (30 mL) and cooled to –30 °C before Et_2AlCl (0.9M in toluene, 0.860 mL, 0.773 mmol, 1 equiv) was added dropwise. The light-yellow solution was allowed to warm up to 0 °C over 1 h. Then the solution was stirred at rt overnight. The reaction mixture was quenched with ice-cooled sodium-potassium-tartrate-solution (1M, 30 mL) and stirred at room temperature until phase-separation. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 30:1) to obtain enol **24** (22.0 mg, 0.106 mmol, 14%, 26% brsm) as a white solid. Some starting material could be recovered (77.1 mg, 0.370 mmol). R_f (enol) = 0.51 (petroleum ether/EtOAc, 5:1); R_f (ketone) 0.84 (petroleum ether/EtOAc, 5:1), they are not separable.

Methyl 2-hydroxy-3,5,6,7,8,8a-hexahydronaphthalene-1-carboxylate (**24**). mp 59.6-61.0 °C; ^{1}H NMR (400 MHz, C_6D_6): δ = 1.00-1.10 (m, 1H, 8-H), 1.18-1.29 (m, 1H, 6-H), 1.33-1.45 (m, 1H, 7-H), 1.62-1.69 (m, 2H, 6-H, 7-H), 1.81-1.90 (m, 1H, 5-H), 2.08-2.13 (m, 1H, 5-H), 2.24-2.30 (m, 1H, 8-H), 2.79-2.83 (m, 2H, 3-H), 2.87-2.95 (m, 1H, 8a-H), 3.32 (s, 3H, OCH_3), 4.99 (bs, 1H, 4-H), 12.96 (s, 1H, OH); ^{13}C NMR (100 MHz, C_6D_6): δ = 27.4 (C-7), 29.7 (C-6), 30.9 (C-3), 36.6 (C-5), 37.0 (C-8), 39.3 (C-8a), 51.3 (OCH_3), 100.5 (C-1), 112.8 (C-4), 140.6 (C-4a), 171.2 (C-2), 173.3 (*C*O_2CH_3); IR: 2927, 2853, 2361, 1652, 1615, 1441, 1358, 1316, 1286, 1219, 1070, 1057, 1015, 826, 808, 744, 668; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{16}O_3Na$ 231.0992; found 231.0994.

After washing the column with ethyl acetate a mixture (19.3 mg) was obtained. NMR and mass spectra indicated that the mixture contains **23**-*endo*, **25**-*endo* and **26**-*endo*. Separation by flash chromatography

(PE/EtOAc, 10:1 to 1:1) provided a mixture (10.6 mg) of **23**-*endo* and **25**-*endo* (9.01 mg, 0.0368 mmol, 5%, 9% brsm, according to NMR) and pure **26**-*endo* (7.0 mg, 0.0309 mmol, 4%, 8% brsm) as a white solid. A second flash chromatography (CH_2Cl_2/EtOAc, 40:1 to 5:1) of the mixture of **23**-*endo* and **25**-*endo* only provided **23**-*endo* (1.40 mg, 0.00587 mmol, 0.8%, 1% brsm) and **26**-*endo* (8.10 mg, 0.0358 mmol, 5%, 8% brsm). Chlorohydrin **25**-*endo* underwent solvolysis to the diol **26**-*endo* on the column.

Methyl (rel 1*R*,2*S*,3*R*,8a*R*)-3-chloro-2-hydroxy-1,2,3,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (**25**-*endo*). R_f = 0.44 (CH_2Cl_2/EtOAc, 20:1); ^{1}H NMR (700 MHz, C_6D_6): δ = 0.92-0.99 (m, 3H, 6-H, 7-H, 8-H), 1.36-1.37 (m, 2H, 6-H, 7-H), 1.53-1.57 (m, 1H, 5-H), 1.72-1.74 (m, 1H, 8-H), 1.87-1.89 (m, 1H, 5-H), 2.15 (d, ^3J = 10.8 Hz, 1H, OH), 2.39-2.45 (m, 1H, 8a-H), 2.79 (dd, ^3J = 10.3 Hz, ^3J =11.2 Hz, 1H, 1-H), 3.44 (s, 3H, OCH_3), 3.97 (ddd (app. td), ^3J = 3.8 Hz, ^3J = 11.0 Hz, 1H, 2-H), 4.25-4.27 (m, 1H, 3-H), 5.15 (dt, ^4J = 2.0 Hz, ^3J = 5.8 Hz, 1H, 4-H); ^{13}C NMR (175 MHz, C_6D_6): δ = 25.7 (C-6 or C-7), 27.1 (C-6 or C-7), 33.6 (C-8), 34.7 (C-5), 42.1 (C-8a), 51.5 (C-1), 51.9 (OCH_3), 62.5 (C-3), 70.4 (C-2), 119.1 (C-4), 144.9 (C-4a), 174.4 (CO_2CH_3); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{17}ClO_3Na$ 267.0758; found 267.0761.

Methyl (1*R*,2*S*,3*S*,8a*R*)-2,3-dihydroxy-1,2,3,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (**26**-*endo*). R_f = 0.34 (petroleum ether/EtOAc, 1:2); mp 149.3–152.9 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.97-0.99 (m, 1H, 8-H), 1.07-1.28 (m, 2H, 5-H, 6-H), 1.35-1.48 (m, 3H, 7-H, 8-H, 8a-H), 1.56-1.71 (m, 3H, 5-H, 6-H, 7-H), 2.60 (dd, ^3J = 9.7 Hz, ^3J = 11.0 Hz, 1H, 1-H), 3.59 (s, 1H, OCH_3), 4.20-4.24 (m, 1H, 2-H), 4.36 (s, 1H, 4a-OH), 5.03 (d, ^3J = 6.2 Hz, 1H, 2-OH), 5.44-5.52 (m, 2H, 3-H, 4-H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.6 (C-7), 24.3 (C-8), 25.4 (C-6), 37.3 (C-5), 44.3 (C-8a), 50.1 (C-1), 51.0 (OCH_3) 65.7 (C-4a), 69.3 (C-2), 131.3 (C-3), 134.2 (C-4), 174.8 (CO_2CH_3); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{18}O_4Na$ 249.1097; found 249.1101.

Reaction of furanylenoate **19** with two equivalents of Et_2AlCl: Under argon-atmosphere furan **19** (170 mg, 0.816 mmol, 1 equiv) was dissolved in dry CH_2Cl_2 (32 mL) and cooled to –30 °C before Et_2AlCl (0.9M in toluene, 1.81 mL, 1.63 mmol, 2 equiv) was added dropwise. The light-yellow solution was allowed to

warm up to 0 °C over 1 h. Then the solution was stirred at rt overnight. The yellow reaction mixture was quenched with ice-cooled sodium-potassium-tartrate-solution (1M, 35 mL) and stirred at room temperature until phase-separation. The aqueous phase was extracted with CH_2Cl_2 (3 × 40 mL) and the combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/EtOAc, 10:1) to give octahydronaphthalene **23**-*endo* (64.2 mg, 0.269 mmol, 33%, 35% brsm), enol **24** (17.2 mg, 0.0826 mmol, 10%, 11% brsm), a mixture (15.1 mg, white solid) of chlorohydrin **25**-*exo* (7.10 mg calculated by ^{1}H NMR, 0.0290 mmol, 3.6%, 3.8% brsm) and naphthalene **23**-*exo* (8.00 mg, calculated by ^{1}H NMR, 0.0336 mmol, 4.1%, 4.4% brsm) and some recovered starting material **19** (10.2 mg, 0.0490 mmol).

Methyl (rel 1*S*,2*R*,4a*R*,8a*S*)-4a-chloro-2-hydroxy-1,2,4a,5,6,7,8,8a-octahydronaphthalene-1-carboxylate (**25**-*exo*). R_f = 0.32 (petroleum ether/EtOAc, 5:1), same R_f-value as naphthalene **23**-*exo*. ^{1}H NMR (400 MHz, $CDCl_3$): δ =0.78-2.29 (m, 9H, CH_2, OH), 2.40 (dd, ^3J = 2.1 Hz, ^3J = 8.9 Hz, 1H, 1-H), 2.60-2.69 (m, 1H, 8a-H), 3.75 (s, 3H, OCH_3), 4.25-4.27 (m, 1H, 2-H), 4.72-4.75 (m, 1H, 3-H), 4.26-4.28 (m, 1H, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2 (CH_2), 27.5 (CH_2), 33.7 (CH_2), 34.9 (CH_2), 34.7 (C-8a), 50.6 (C-1), 52.2 (OCH_3), 60.7 (C-3), 68.3 (C-2), 117.0 (C-4), 143.6 (C-4a), 172.9 (CO_2CH_3); HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{12}H_{17}ClO_3Na$ 267.0758; found 267.0758.

ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra for all new compounds, cif-files and ORTEP plots for **20**, **21**, **22**-*endo*, **23**-*endo*, **23**-*exo*, and **24**. The Supporting Information is available free of charge on the ACS Publications website.

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The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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