Synthesis of the 2-Alkenyl-4-alkylidenebut-2-eno-4-lactone (= α-Alkenyl-γ-alkylidenebutenolide) Core Structure of the Carotenoid Pyrrhoxanthin *via* the Regioselective Dihydroxylation of Hepta-2,4-diene-5-ynoic Acid Esters

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Dedicated to Professor *Rolf Huisgen* on the occasion of his 85th birthday

A new strategy for the stereoselective synthesis of 4-alkylidenebut-2-eno-4-lactones (= γ-alkylidenebutenolides) with (*Z*)-configuration of the exocyclic C=C bond at C(4) was developed. It is exemplified by the synthesis of 4-alkylidenebutenolactone **31** (*Scheme 4*), which constitutes a substructure of the carotenoids pyrrhoxanthin (**1**) and peridinin. The formation of the precursor 4-(1-hydroxyalkyl)butenolactone **29** was accomplished either by cyclocarbonylation of the prop-2-yn-1-ol moiety of **27** (→**29**) or by hydrostannylation of the isopropylidene-protected alkynoic acid ester **26** (→**28**) followed by transacetalization/transesterification (→**30**). The 4-alkylidenebutenolactone was formed by the *anti*-selective *Mitsunobu* dehydration **29** → **31**.

Introduction. – Carotenoids have attracted and continue to attract the interest of organic chemists, biochemists, and medicinal chemists alike [1]. This is due to the diversity of their functions which include their being colorants, anti-oxidants, progenitors of secondary metabolites (vitamin A, odorants), antitumor agents, or light-harvesting agents [2]. Usually, carotenoids are C_{40} entities. However, a few carotenoids possess a skeleton of no more than 37 C-atoms. One of the latter is pyrrhoxanthin (**1**; *Scheme 1*), a mono-acetate of pyrrhoxanthinol ($C_{37}H_{48}O_6$). Pyrrhoxanthin was first isolated from *Gyrodinium resplendens* [3]. Its structure was elucidated by *Liaaen-Jense*n and co-workers [4][1]). Pyrrhoxanthin features seven conjugated C=C bonds. One of these double bonds is conjugated with a C≡C−C=C moiety. Another C=C bond of pyrrhoxanthin is incorporated into a but-2-enolactone ring. This makes up a 2-alkenyl-4-alkylidenebut-2-enolactone substructure (in which the exocyclic C=C bond at C(4) displays a (*Z*)-configuration). A single total synthesis of pyrrhoxanthin has been accomplished to date, namely in 1993 by *Yamano* and *Ito* [5][2]). Concomitantly, these workers reported the total synthesis of the structurally related [6][3]) carotenoid butenolactone peridinin [7][4]). In fact, several C_{37} carotenoids

[1]) For the second isolation (two-dimensional structure), see [4a]; for the re-isolation (three-dimensional structure), see [4b].

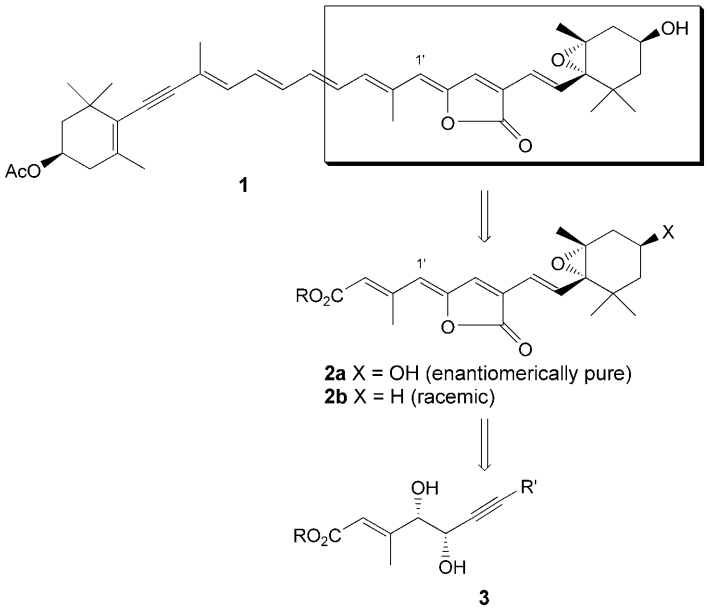
[2]) For the total syntheses of pyrrhoxanthin and enantiomerically pure peridinin, see [5]; continued previous studies which were reported in [7].

[3]) For the two-dimensional structure, see [6a]; for the three-dimensional structure, see [6b,c].

[4]) Synthesis of a racemic mixture of peridinin and diastereoisomers.

containing a 2-alkenyl-4-alkylidenebut-2-eno-4-lactone moiety are known[5]). Synthetic efforts towards such compounds have been resumed recently, culminating in the second total synthesis of peridinin [9] and a total synthesis of epiperidinin [10].

Scheme 1. *Synthetic Strategy for the Butenolactone Core of Pyrrhoxanthin* (**1**)



Given the general [11] and our group's specific [11c] interests in carotenoid (*vide supra*) and noncarotenoid[6]) 4-alkylidenebut-2-eno-4-lactone syntheses, we now report a new access to the 4-(1-hydroxyalkyl)but-2-eno-4-lactone → 4-alkylidenebut-2-eno-4-lactone route towards such target structures. It allows for the first time to prepare the desired 4-(1-hydroxyalkyl)butenolactones from 4,5-dihydroxyhept-2-ene-6-ynates **3**, as demonstrated by a stereoselective synthesis of a 4-alkylidenebutenolactone **2b** (*Scheme 1*; $R = CF_3CH_2$, $X = H$). It is likely that the same strategy could lead to the hydroxy-containing but otherwise analogous 4-alkylidenebutenolactone **2a** ($X = OH$). Conceivably, compound **2a** is a novel building block for the total synthesis of pyrrhoxanthin (**1**).

Scheme 2 juxtaposes the current study's C_1 extension of 4,5-dihydroxyhept-2-ene-6-ynoates **3** to 4-(1-hydroxyalkyl)butenolactones **7** with our previous accesses to this key intermediate *en route* to type-**10** 4-alkylidenebutenolactones. These included the elaboration of sugar lactones **4** [13], the diastereoselective vinylogous *Mukaiyama* aldol addition **5** + **6** → **7** [14], successive manipulation of the three C–Hal bonds of the trihalodienediol **8** [15], and most recently, the desymmetrization of tartrate **9** [16]. The

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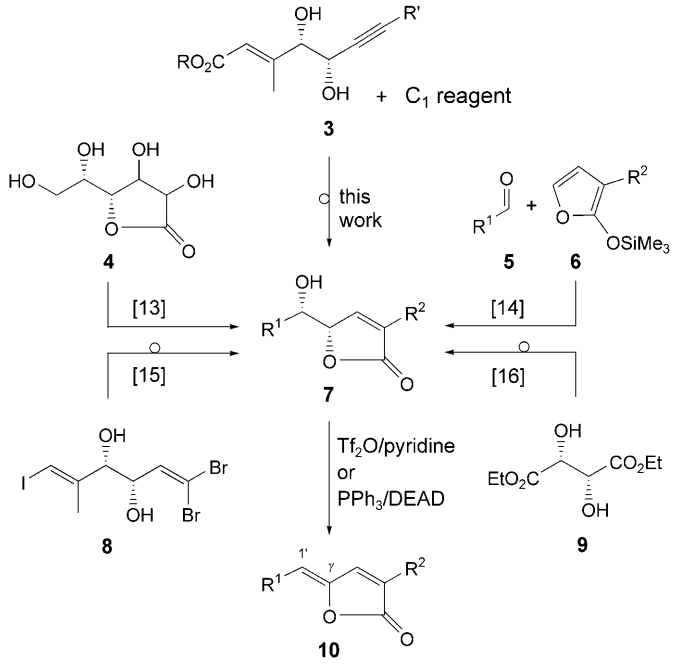
[5]) Peridinol [4], anhydroperidinol [8a], pyrrhoxanthinol [4], hydratopyrrhoxanthinol [8b], uriolide [8c], deepoxyuriolide [8d], anhydrouriolide [8d], 3′-dehydrouriolide [8d], and unnamed carotenoids [8e,f].

[6]) See, *e.g.*, freelingyne (revised structure) [12a,b], lissoclinolide [12c], and xerulinic acid, xerulin, and dihydroxerulin [12d].

diversity and complementariness of these approaches underlines the versatility of our β-elimination strategy 4-(1-hydroxyalkyl)butenolactone **7** → 4-alkylidenebutenolactone **10** [11c].

Scheme 2. *Ways to the 4-(1-Hydroxyalkyl)butenolactone Precursor* **7**



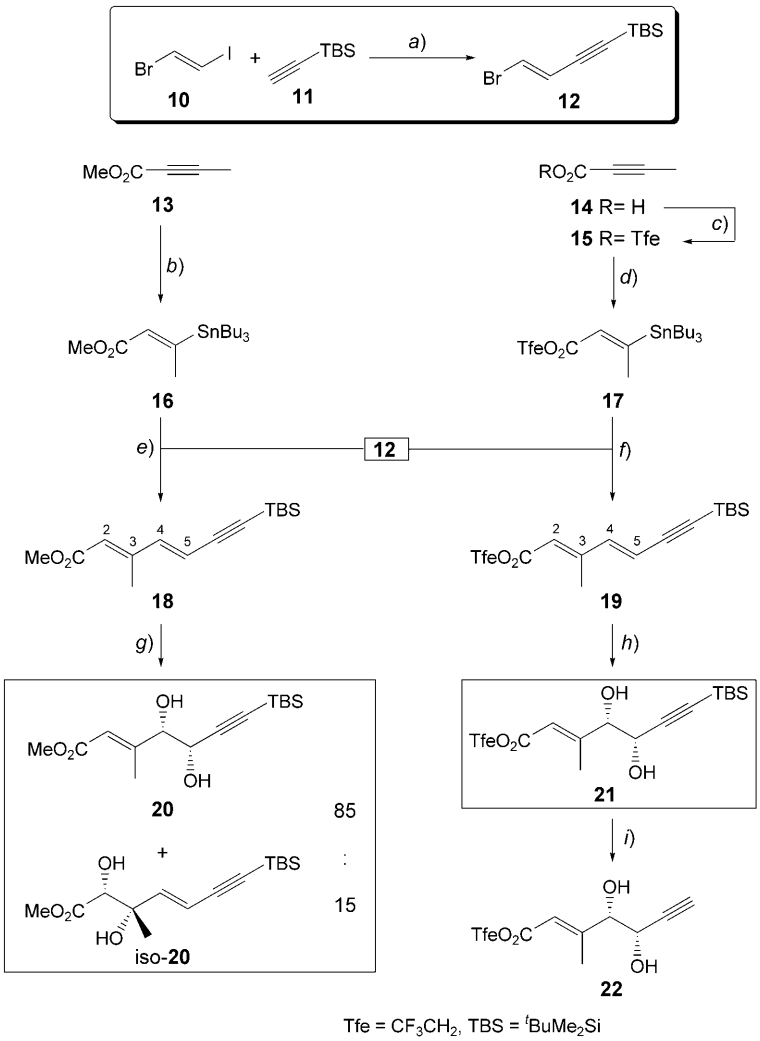
Results and Discussions. – Methyl heptadienynoate **18** and the analogous trifluoroethyl ester **19** were precursors of choice for the desired type-**3** esters **20** and **21**, respectively (*Scheme 3*). Heptadienynoates **18** and **19** were obtained by *Stille* couplings [17] between the (2*E*)-3-stannylbut-2-enoates **16** (methyl ester) or **17** (trifluoroethyl ester) and bromoenyne **12**. This bromoenyne, in turn, resulted from the chemoselective C,C-coupling between bromoiodoethene **10** [18] and the (*tert*-butyl)dimethylsilylated ethyne **11** [19], following the procedure of *Negishi et al.* [18]. The 3-(tributylstannyl)butenoates **16** and **17** were obtained as pure (*E*)-isomers by the (tributylstannyl)cupration [20] of methyl but-2-yonate (**13**)[7]) and trifluoroethyl but-2-ynoate (**15**)[8]), respectively; optimizing yields and stereoselectivies, we found $(Bu_3Sn)BuCu(CN)Li_2$ [23] the best reagent for effecting the conversion of ester **13** (100% yield) and $(Bu_3Sn)Cu \cdot SMe_2 \cdot LiBr$[9]) the best reagent for transforming ester **15**

[7]) Ester **13** was prepared by treating prop-1-ynyllithium (generated *in situ* [21a,b]) with methyl carbonochloridate [21c].

[8]) Ester **15** was prepared from but-2-yonic acid (**14**), which was obtained by the *Jones* oxidation of but-2-yn-1-ol [22].

[9]) For the reagent and stannylcupration of ethyl pentynoate with it, see [24].

Scheme 3. *Synthesis of 2,2,2-Trifluoroethyl Dihydroxyenynoate* **22**



Tfe = CF_3CH_2, TBS = ^{t}BuMe$_2$Si

a) **11**, MeMgBr (1.1 equiv.), THF, r.t., 3 h; $ZnBr_2$ (1.3 equiv.), 0°, 30 min; **10** (1.1 equiv.), [Pd(PPh_3)$_4$] (2 mol-%), r.t., 18 h; 83%; ([14]: 70%). *b*) BuLi (2.4 equiv.), CuCN (1.2 equiv.), THF, −78°, 15 min; Bu_3SnH (2.4 equiv.), −78°, 10 min; MeOH (1.2 equiv.), −78°, 3 min; addition of **13**, −78°, 90 min; 100%. *c*) CF_3CH_2OH (10 equiv.), H_2SO_4 (cat.), benzene, *Dean–Stark* trap filled with $MgSO_4$, reflux, 24 h; 81%. *d*) $Bu_3SnSnBu_3$ (1.3 equiv.), BuLi (1.3 equiv.), THF, −20°, 20 min; addition of CuBr·SMe_2 (1.3 equiv.), −78°, 25 min; addition of **15**, −78°, 12 h; 96% (separated from 4% of the (*Z*)-isomer). *e*) CuI (1.5 equiv.), [Pd(PPh_3)$_4$] (5 mol-%), DMF, 60°, 1 h; 84%. *f*) CuI (1.5 equiv.), [Pd(PPh_3)$_4$] (3 mol-%), DMF, 25°, 8 h; 100%. *g*) $K_2OsO_2(OH)_4$ (1 mol-%), $K_3Fe(CN)_6$ (3.0 equiv.), $(DHQ)_2PHAL$ (5 mol-%), K_2CO_3 (3.0 equiv.), $MeSO_2NH_2$ (1.0 equiv.), ^{t}BuOH/H_2O 1:1, 25°, 24 h; 65% (inseparable mixture of regioisomers **20** and iso-**20**). *h*) $K_2OsO_2(OH)_4$ (1 mol-%), $K_3Fe(CN)_6$ (3.0 equiv.), $(DHQ)_2PHAL$ (5 mol-%), K_2CO_3 (3.0 equiv.), $MeSO_2NH_2$ (1.0 equiv.), ^{t}BuOH/H_2O 1:1, 25°, 24 h; 76%. *i*) Bu_4NF (1.5 equiv.), THF, 4 h, 0°; 76%.

(96% yield)[10]). We noticed an interesting additive effect upon the stereochemical outcome of the stannylcupration of the trifluoroethyl ester **15**: Modifying $(Bu_3Sn)BuCu(CN)Li_2$ with an equimolar amount of *methanol* – which is the general procedure given in [20] –, we obtained 65% of a 97:3 (mol ratio) mixture of **17** and its methanolysis product **16**, plus separately 4% of the (*Z*)-isomer of **17**. However, when we added an equimolar amount of *trifluoroethanol* to the $(Bu_3Sn)BuCu(CN)Li_2$ before combining the resulting mixture with ester **15**, we isolated *only* the (*Z*)-isomer **17** (60%) of the resulting trifluoroethyl ester. This is a remarkable observation in its own right because in [20], solely 'clean *cis*-additions of the stannylcuprate' are reported.

Cu-Assisted [26] $[Pd(PPh_3)_4]$-catalyzed *Stille* couplings between (tributylstannyl)-butenoates **16** and **17** on the one side and bromoenyne **12** on the other side – under conditions gleaned from [27] – furnished methyl heptadienynoate **18** in 83% and trifluoroethyl heptadienynoate **19** in 100% yield. Next, we required a vicinal *cis*-dihydroxylation of the C(4)=C(5) bond of these compounds which left their respective C(2)=C(3) bond unaffected. Yet, starting from methyl ester **18**, such a regioselectivity remained elusive. Adopting *Sharpless*' 'improved' asymmetric dihydroxylation protocol [28][11]) because it gave the best yield (65%), we obtained an 85:15 mixture of diols **20** (desired) and *iso*-**20** (undesired and inseparable by flash chromatography on silica gel [29]). In contrast, *Sharpless*' standard asymmetric dihydroxylation procedure (for the first description, see [30a]; for a review, see [30b]) allowed only a very sluggish dihydroxylation **18** → **20**/*iso*-**20**. From these observations we concluded that a C≡C substituent deactivates C=C bonds towards attack by $[OsO_4L]$. Accordingly, the undesired attack of $[OsO_4L]$ upon the C(2)=C(3) bond should be suppressed if we dihydroxylated trifluoroethyl dienynoate **19** rather than methyl dienynoate **18**. This is because the stronger electron demand of the $CF_3CH_2O_2C$ *vs.* CH_3O_2C substituent was expected to slow down osmylation of the C(2)=C(3) bond in the former substrate compared to the latter. Indeed, our adaptation of the 'improved' asymmetric dihydroxylation protocol [28], when applied to trifluoroethyl ester **19**, provided a single dihydroxyenynoate, namely compound **21** (76% yield). Desilylation with Bu_4NF in THF gave the unprotected dihydroxyenynoate **22** also with 76% yield.

The right-hand moiety of model butenolactone **2b** (*Scheme 1*) was introduced by means of building block **25** (*Scheme 4*). The preparation of **25** began with known well-yielding (83–98%) transformations: *1*) Ozonolysis of β-ionone (**23**) gave the α,β-unsaturated aldehyde [31]; *2*) C_1 extension of the CH=O function led to the homologated enyne [32][12]); *3*) epoxidation of the C=C bond provided epoxyalkyne **24** [33][13]); *4*) Pd-catalyzed regio- and stereoselective hydrostannylation of the C≡C bond delivered a *trans*-configured alkenylstannane [16]. In the terminating new reaction, the stannane, treated with I_2[14]), rendered the (epoxycyclohexyl) alkenyl iodide **25**.

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[10]) For an analogous preparation of the *tert*-butyl analog of ester **16**, see [25].

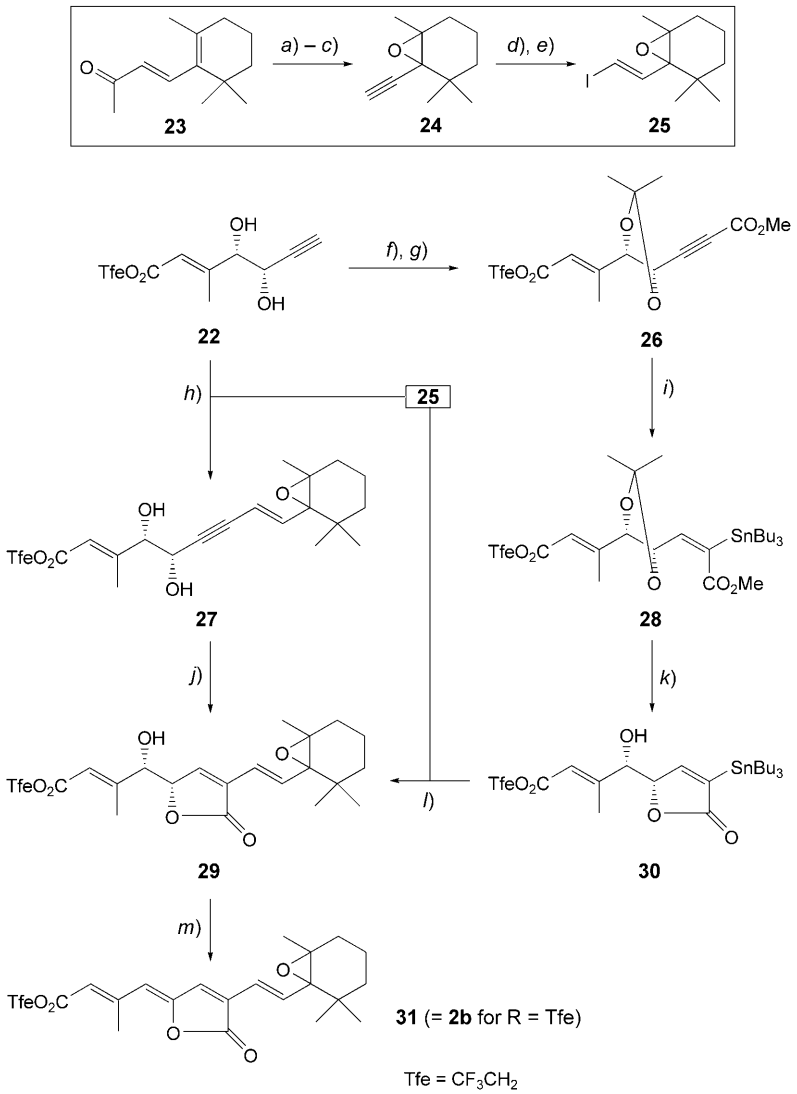
[11]) *Bennani* and *Sharpless* [28a] increased the normal amounts of $K_2OsO_2(OH)_4$ and $(DHQ)_2PHAL$ by a factor of 5 (as we did), while *Blundell et al.* [28b] increased them by a factor of 10.

[12]) The alkynylation method is described in [32b].

[13]) Epoxidation of 1-chloro-2-(2,6,6-trimethylcyclohex-1-enyl)ethene leads in 99% yield to 1-chloro-2-(1,2-epoxy-2,6,6-trimethylcyclohexyl)ethene [33b].

[14]) We followed a protocol published for a related transformation [34].

Scheme 4. *Synthesis of 2-Alkenyl-4-alkylidenebut-2-eno-4-lactone* **31**



a) O_3, MeOH, $-78°$, 2.5 h; Zn (1.5 equiv.), AcOH/H_2O 1:1; 93% ([31a]: 90%; [31b]: 64% combined yield for this step and an ensuing acetalization). *b*) Lithium diisopropylamide (1.2 equiv.), Me_3SiCHN_2 (1.2 equiv.), THF, $-78°$, 90 min; 89% ([32a]: 74%). *c*) 3-Chloroperbenzoic acid (1.2 equiv.), CH_2Cl_2, 16 h, 25°; 98% ([33a]: 64%). *d*) [$Pd(PPh_3)_4$] (5 mol-%), Bu_3SnH (1.2 equiv.), THF, 3 h, 25°; 73% ([16]: 83%). *e*) I_2 (1.0 equiv.), CH_2Cl_2, 3 h, 0°; 91%. *f*) TsOH (10 mol-%), $Me_2C(OMe)_2$ (1.5 equiv.), CH_2Cl_2, 3 h, r.t.; 97%. *g*) Lithium hexamethyldisilazanide (1.3 equiv.), THF, $-78°$, 30 min; $ClCO_2Me$ (4.0 equiv.), 45 min; 85%. *h*) **25** (1.05 equiv.), [$Pd(PPh_3)_2Cl_2$] (5 mol-%), CuI (15 mol-%), THF, Et_3N (21 equiv.), 25°, 50 min; 76%. *i*) Bu_3SnH (1.05 equiv.), [$Pd(PPh_3)_4$] (5 mol-%), THF, 0°, 60 min; 88%. *j*) CO (42 bar), H_2 (8 bar), [Pd_2dba_3]·$CHCl_3$ (10 mol-%), $Ph_2P(CH_2)_4PPh_2$ (20 mol-%), CH_2Cl_2, 50°, 24 h; 32% including the subsequent step. *k*) TsOH (20 mol-%), MeOH, reflux, 8 h; 64%. *l*) **25** (1.1 equiv.), [$Pd(PPh_3)_4$] (5 mol-%), CuI (1.2 equiv.), DMF, 3 h, r.t.; 96% of a presumed 86:14 mixture **29**/epi-**29**. *m*) PPh_3 (6.0 equiv.), diethyl diazenenedicarboxylate (DEAD; 6.0 equiv.), THF, $-30°$, 1 h; 70% of an inseparable 97.3:2.7 (*Z*)/(*E*)-mixture **31**.

Proceeding towards the target butenolactone, we initially combined building block **25** and the unsaturated dihydroxy ester **22** – by virtue of its H–C≡C moiety – *via* a *Sonogashira–Hagihara* coupling (for the original report, see [35a]; reviews in [35b–d]) (*Scheme 4*, left side). It yielded 76% of the (8*E*)-enynoate **27**. The latter, we hoped, would lend itself to butenolactone formation through incorporation of carbon monoxide and lactonization. This transformation has been described for simple primary and secondary alcohols of the prop-2-yn-1-ol type [36][15]) but none of which, however, was functionalized nearly as much as our substrate. Nonetheless, following descriptions by *Alper*, co-workers, and others [36a,b], the one-step carbonylative lactonization of the prop-2-yn-1-ol type alcohol **27** was achieved in the presence of 10 mol-% $[Pd_2(dba)_3]\cdot CHCl_3$ (dba = dibenzylideneacetone = 1,5-diphenylpenta-1,4-dien-3-one) and 20 mol-% $Ph_2P(CH)_4PPh_2$ (dppb) under 50 atmospheres of CO and H_2 (*ca.* 5:1). Workup after 24 h at 50° yielded a mixture of the butenolactone **29** and unreacted starting material **27**. These constituents could neither be separated nor completely liberated from impurities. Accordingly, the mixture was directly dehydrated under *Mitsunobu* conditions [37][16]), *i.e.*, by treatment with 6 equiv. each of triphenylphosphine and diethyl diazenedicarboxylate at −30°. To avoid loss of configurational integrity at the stereogenic C=C bonds of the desired product, we applied the same protective measures which had preserved the C=C geometries in the analogous methyl ester [16]: *1*) We excluded light during reaction and chromatography, *2*) employed degassed THF as a solvent and degassed cyclohexane/AcOEt as an eluent, and *3*) added 2,6-di(*tert*-butyl)cresol to the solvent as a radical scavenger. This completed the generation of 4-alkylidenebutenolactone **31** in 32% overall yield from alcohol **27**[17]).

In quest for an improved yield, we established a second set of reactions from the dihydroxy ester **22** to the target structure **31** (*Scheme 4*, right side). They started with acetonide formation (97% yield) and continued with consecutive treatments by lithium hexamethyldisilazanide and methyl carbonochloridate. This provided ester **26** with a but-2-ynoate moiety in 85% yield. Its C≡C bond was hydrostannylated with Bu_3SnH/cat. $[Pd(PPh_3)_4]$ [39][18]). Because of the presence of the neighboring isopropylidenedioxy group (see below), this reaction was completely regio- and stereoselective. Consequently, it gave the (2*E*)-2-stannylprop-2-enoate **28** (88% yield) and none of the isomers. Ester derivative **28** was subjected to a one-pot transacetalization/trans-

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15) Conditions: Prop-2-yn-1-ol, CO/H_2, and cat. $[PdL_x]$ (for the original report, see [36a]; for applications, see [36b,c]). A variant for tertiary 3-(trimethylsilyl)prop-2-yn-1-ols, with CO/H_2 and cat. $[Rh_4(CO)_{12}]$ has been described in [36d].

16) For related applications in our group, see [10][13b][14][16].

17) It should be noted that other methods for the conversion of prop-2-yn-1-ol type alcohols into butenolactones are known (for hydromagnesation followed by carboxylation, see [38a,b]; for *i*) hydroalumination followed by iodinolysis, *ii*) CO, cat. $[PdL_x]$, see [38c–i]; for *i*) hydrozirconation, *ii*) CO, see [38j]; for *i*) mesylation, *ii*) CO, H_2O, cat. PdL_x, *iii*) cat. $AgNO_3$, see [38k–p]). Whether they are or are not applicable to 4-alkylidenebutenolactone syntheses as exemplified by our two-step sequence **27** → **29** → **31** has not yet been studied in depth. At least, *Stille*'s method [39b] – reduction by *RedAl*®, iodinolysis, carbonylation of the resulting 3-iodoallyl alcohol – failed when tried with **27**. Of course, this may be less an inherent problem than due to the reducible $CO_2CH_2CF_3$ group.

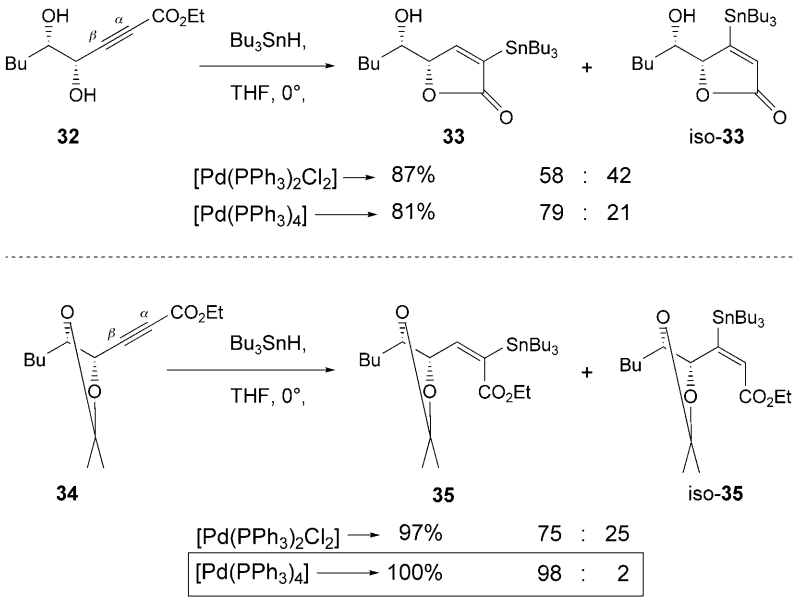
18) For $[Pd(PPh_3)_4]$ as a catalyst, see [39a,b]; for $[Mo(CO)_3(NC{-}tBu)_3]$ as a catalyst, see [39c].

esterification reaction in refluxing MeOH in the presence of 20 mol-% TsOH. This treatment – copied from a similar transformation by *Hanisch* in our group [15] – gave rise to the formation of the 2-(tributylstannyl)-4-(1-hydroxyalkyl)butenolactone **30** in 64% yield. The latter compound and ethenyl iodide **25** containing the epoxycyclohexane moiety then were *Stille*-coupled under the conditions of [27]. This provided the 2-substituted 4-(1-hydroxyalkyl)butenolactone **29** as the major constituent of what we interpreted as a 86 : 14 mixture with the 4-epimer epi-**29**, the yield of **29** thus being 83%. In any event, the presumed **29** epi-**29** mixture was converted into the 2-substituted 4-alkylidenebutenolactone **31** (inseparable 97 : 3 (*E*)/(*Z*)-mixture with respect to the exocyclic C=C bond) in 70% yield when we applied the *Mitsunobu* elimination protocol already described above.

Comparing the three-step synthesis of butenolactone **31** from ester **22** (*via* intermediates **27** and **29**) with the six-step route from **22** (*via* a non-depicted intermediate followed by compounds **26** and **28**–**29**), the overall yields of 24 and 31%, respectively, make the second access the more recommendable. It is somewhat more laborious, yet – which is again a benefit – does not necessitate handling CO at high pressure.

Scheme 5 depicts the model hydrostannylations, which led us to choose to hydrostannylate the acetonide-protected diester **26** containing a prop-2-ynoate moiety (see *Scheme 4*) and not the corresponding unprotected dihydroxy diester. The presence of hydroxy groups in alkyl alk-2-ynoates may lower the regio-selectivity of the $[Pd(PPh_3)_4]$-catalyzed hydro(tributylstannylation) reaction: While being completely α-selective in the absence of such OH groups [39] and exhibiting a 86 : 14 α *vs.* β preference for Sn–C bond-formation in the presence of a 4-OH group (under slightly

Scheme 5. *Regioselective Hydrostannylation of 4,5-Dioxygenated Alk-2-ynoic Acid Esters*



different conditions [40][19]), the α/β bias of the hydrostannylation of ethyl 4,5-dihydroxyalk-2-ynoate **32** was only 79:21 with $[Pd(PPh_3)_4]$ as the catalyst (*Scheme 5*); with $[PdCl_2(PPh_3)_2]$, the α/β ratio decreased to 58:42. In contrast, the analogous acetonide-protected ethyl alk-2-ynoate **34** was hydrostannylated with nearly perfect – namely 98:2 – α-selectivity in the presence of $[Pd(PPh_3)_4]$. Catalysis by $[PdCl_2(PPh_3)_2]$ gave rise to a 75:25 mixture of α- ($\rightarrow$ **35**) and β-tributylstannylated ($\rightarrow$ iso-**35**) products.

In summary, we turned a novel route to 4-(1-hydroxyalkyl)but-2-eno-4-lactones **2** into practice as exemplified by two variants of synthesizing compound **29**. Through an *anti*-selective *Mitsunobu* elimination, we completed the 4-alkylidenebutenolactone core **31** of the carotenoid pyrrhoxanthin with good control of the stereochemistry. Besides, we noticed that the stannylcupration of but-2-ynoate **15** with $(Bu_3Sn)BuCu(CN)Li_2$ switches from *cis*- to *trans*-addition upon modification of the reagent with CF_3CH_2OH rather than MeOH. In addition, we could make a $C{=}CCO_2R$ group inert towards osmylation by exchanging a $C{=}CCO_2Me$ for a $C{=}CCO_2CH_2CF_3$ group.

Experimental Part

General. All reactions were performed in oven-dried (80°) glassware under Ar or N_2. Reactions with light-sensitive compounds were performed in brown glassware or in ordinary glassware in a fume hood lined with a UV protection foil. THF was freshly distilled from K, CH_2Cl_2 was distilled from CaH_2. Flash chromatography (FC) [29]: *Merck* silica gel *60*. Yields refer to anal. pure samples. Isomer ratios were derived from suitable ^{1}H-NMR integrals. M.p.: *Tottoli* apparatus (*Büchi*); uncorrected. IR Spectra: *Perkin-Elmer Paragon-1000*; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Varian Mercury VX-300*, *Bruker AM-400*, and *Bruker DRX-500*; δ in ppm, coupling constants J in Hz, integrals in accordance with assignments; $CHCl_3$ (δ 7.26) as internal standard in $CDCl_3$, C_6HD_5 (δ 7.16) as internal standard in C_6D_6, or $(HD_2C)(D_3C)S{=}O$ (δ 2.49) as internal standard in (D_6)DMSO for ^{1}H; $CDCl_3$ (center peak of t at δ 77.0 ppm) as internal standard in $CDCl_3$ or C_6D_6 (δ 128.0) as internal standard in C_6D_6 for ^{13}C. MS: performed by Dr. *J. Wörth* and *C. Warth*, Institut für Organische Chemie and Biochemie, Universität Freiburg; in m/z (rel. int.). Combustion analyses: performed by *E. Hickl*, Institut für Organische Chemie and Biochemie, Universität Freiburg.

2,2,2-Trifluoroethyl But-2-ynoate (**15**). To a soln. of but-2-ynoic acid (**14**; 1.86 g, 20.0 mmol) in benzene (20 ml), CF_3CH_2OH (14.6 ml, 20.0 g, 200 mmol, 10 equiv.) and H_2SO_4 (conc., 0.2 ml) were added. The soln. was heated under reflux for 36 h in a *Soxhlet* extractor charged with $MgSO_4$. Benzene and CF_3CH_2OH were removed by distillation under atmospheric pressure. The residue was washed with aq. $NaHCO_3$ soln. (3×30 ml) and dried (Na_2SO_4). Distillation (b.p. 60–67°/50 mbar) afforded **15** (2.79 g, 84%). Colorless liquid. n_D^{20} 1.3815. IR (film): 2980, 2320, 2250, 1735, 1440, 1410, 1290, 1235, 1170, 1090, 990, 965, 885. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 2.04 (*s*, Me(4)); 4.52 (*q*, J(H,F) = 8.3, CF_3CH_2). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 3.91 (C(4)), 60.96 (*q*, ^2J(C,F) = 37.0, CF_3CH_2); 70.97 (C(2)); 88.84 (C(3)); 122.56 (*q*, ^1J(C,F) = 277.3, CF_3CH_2); 151.70 (C(1)). ^{13}C-NMR (125.7 MHz, $CDCl_3$; gated-decoupled): 3.91 (*q*, ^1J(C,H) = 133.1, C(4)); 60.96 (*tq*, ^1J(C,H) = 151.4, ^2J(C,F) = 37.0, CF_3CH_2); 70.97 (*q*, ^3J(C,CH_3(4)) = 4.7, C(2)); 88.84 (*q*, ^2J(C,CH_3(4) = 10.8, C(3)); 122.56 (*qt*, ^2J(C,H) = 4.7, ^1J(C,F) = 277.3, CF_3CH_2); 151.70 (C(1)). HR-EI-MS (70 eV): 166.0242 (M^+), $C_6H_5F_3O_2^+$; calc. 166.0242).

*2,2,2-Trifluoroethyl (2*E*)-3-(Tributylstannyl)but-2-enoate* (**17**). At −20°, 2.4M BuLi (13.5 ml, 32.5 mmol, 1.3 equiv.) was added to a soln. of hexabutyldistannane (16.4 ml, 18.6 g, 32.5 mmol, 1.3 equiv.) in THF (100 ml). After 20 min, the soln. was cooled to −78°, and $CuBr \cdot SMe_2$ (6.68 g, 32.5 mmol, 1.3 equiv.) was added in one portion. After 30 min, **15** (4.19 g, 25.0 mmol) was added. The mixture was stirred at −78° for 8 h. The reaction was terminated by the addition of aq. NH_4Cl soln. (100 ml) and brine (100 ml). After warming gradually to r.t., the aq. phase was extracted with Et_2O (5×100 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the obtained colorless liquid purified by FC (11-cm column, cyclohexane/AcOEt 30:1): **17** (10.7 g, 94%) and (*Z*)-isomer (0.8 g, 6%).

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[19]) With $[PdCl_2(PPh_3)_2]$ as the catalyst.

Data of **17**: IR (film): 2930, 2855, 1740, 1725, 1595, 1465, 1410, 1375, 1345, 1290, 1250, 1165, 1105, 1050, 980, 860. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 0.90 (*t*, $^3J = 7.3$, 3 *Me*$CH_2CH_2CH_2$); 0.99 (*m*, 3 $MeCH_2CH_2CH_2$, flanked by Sn-isotope satellites as *dm*, $^2J(H,^{119}Sn) = 52.1$, $^2J(H,^{117}Sn) = 49.8$); 1.32 (*qt*, $^3J = 7.8$, 7.8, 3 $MeCH_2CH_2CH_2$); 1.43–1.59 (*m*, 3 $MeCH_2CH_2CH_2$); 2.43 (*d*, $^4J(4,2) = 1.9$, each peak flanked by Sn-isotope satellites as 2 *d*, $^3J(4,^{119}Sn) = 43.8$, $^3J(4,^{117}Sn) = 42.0$, Me(4)); 4.48 (*q*, $^3J(H,F) = 8.6$, CF_3CH_2); 6.03 (*q*, $^4J(2,4) = 1.9$, each peak flanked by Sn-isotope satellites as interlocked *q*, $^3J(2,^{119}Sn) = 64.0$, $^3J(2,^{117}Sn) = 57.3$, H–C(2)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 9.53 (flanked by Sn-isotope satellites as 2 *d*, $^1J(C,^{119}Sn) = 336.7$, $^1J(C,^{117}Sn) = 321.8$, 3 $MeCH_2CH_2CH_2$); 13.62 (3 *Me*$CH_2CH_2CH_2$); 22.76 (C(4)); 27.29 (flanked by Sn-isotope satellites as *d*, $^3J(C,Sn) = 56.6$, 3 $MeCH_2CH_2CH_2$); 28.94 (flanked by Sn-isotope satellites as *d*, $^2J(C,Sn) = 20.6$, 3 $MeCH_2CH_2CH_2$); 59.59 (*q*, $^2J(C,F) = 36.4$, CF_3CH_2); 123.39 (incompletely resolved *q*, $^1J(C,F) = 148.5$, CF_3CH_2); 125.71 (flanked by Sn-isotope satellites as *d*, $^2J(C,Sn) = 35.4$, C(2)); 161.77 (C(3)); 174.79 (C(1)). edHSQC (C,H-COSY, 125.7/499.9 MHz, $CDCl_3$): 9.53 ($CH_3CH_2CH_2CH_2$) ↔ 0.99 ($CH_3CH_2CH_2CH_2$); 13.62 ($CH_3CH_2CH_2CH_2$) ↔ 0.90 ($CH_3CH_2CH_2CH_2$); 22.76 (C(4)) ↔ 2.43 (CH_3(4)); 27.29 ($MeCH_2CH_2CH_2$) ↔ 1.32 ($MeCH_2CH_2CH_2$); 28.94 ($MeCH_2CH_2CH_2$) ↔ 1.43–1.59 ($MeCH_2CH_2CH_2$); 59.59 (CF_3CH_2) ↔ 4.48 (CF_3CH_2); 125.71 (C(2)) ↔ 6.03 (*H*–(2)). HR-EI-MS (70 eV): 401.0750 ($[M-Bu]^+$, $C_{14}H_{24}F_3O_2Sn^+$; calc. 458.1455). Anal. calc. for $C_{18}H_{33}F_3O_2Sn$ (457.2): C 47.29, H 7.28; found: C 47.37, H 7.10.

Data of (Z)-Isomer of **17**: ^{1}H-NMR (300.1 MHz, $CDCl_3$): 0.88 (*t*, $^3J = 7.2$, 3 *Me*$CH_2CH_2CH_2$); 0.98 (*m*, 3 $MeCH_2CH_2CH_2$, flanked by Sn-isotope satellites as *m*, $^2J(H,Sn) = 51.9$); 1.32 (*qt*, $^3J = 7.2$, 7.2, 3 $MeCH_2CH_2CH_2$); 1.42–1.52 (*m*, 3 $MeCH_2CH_2CH_2$); 2.18 (*d*, $^4J(4,2) = 1.8$, each peak flanked by Sn-isotope satellites as 2 *d*, $^3J(4,Sn) = 38.0$, Me(4)); 4.51 (*q*, $^3J(H,F) = 8.5$, CF_3CH_2); 6.48 (*q*, $^4J(2,4) = 1.6$, each peak flanked by Sn-isotope satellites as interlocked *q*, $^3J(2,^{119}Sn) = 101.7$, $^3J(2,^{117}Sn) = 97.9$, H–C(2)).

*2,2,2-Trifluoroethyl (2*E*,4*E*)-7-[(*tert*-Butyl)dimethylsilyl]-3-methylhepta-2,4-dien-6-ynoate* (**19**). To a soln. of $[Pd(PPh_3)_4]$ (241 mg, 209 μmol, 3 mol-%) in degassed DMF (50 ml) were added first bromoenyne **12** (1.88 g, 7.65 mmol, 1.1 equiv.), then CuI (1.99 g, 10.4 mmol, 1.6 equiv.), and finally dropwise **17** (3.18 g, 6.96 mmol). After stirring at r.t. for 90 min, the soln. was diluted with ^{t}BuOMe (20 ml), aq. NH_4Cl soln. (50 ml), and aq. NaCl soln. (50 ml). The aq. phase was extracted with Et_2O (4 × 100 ml), the extract concentrated to 50 ml, and 20% aq. KF soln. (50 ml) added. After stirring for 30 min at r.t., the aq. phase was extracted with Et_2O (3 × 50 ml) once more. The combined org. phase was dried (Na_2SO_4) and evaporated, and the residue purified by FC (11.0-cm column, cyclohexane, cyclohexane/AcOEt 20:1): **19** (2.31 g, 100%). IR (film): 2955, 2930, 2890, 2860, 1735, 1610, 1470, 1465, 1440, 1410, 1360, 1285, 1250, 1230, 1170, 1140, 1095, 1060, 980, 955. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 0.15 (*s*, Me_2Si); 0.96 (*s*, ^{t}BuSi); 2.27 (*d*, $^4J(Me,2) = 1.2$, Me–C(3)); 4.50 (*q*, $^3J(H,F) = 8.5$, CF_3CH_2); 5.87 (*m*, presumably a partly unresolved *qdd*, $^4J(2,Me) \approx {}^4J(2,4) \approx {}^5J(2,5) \approx 0.9$, H–C(2)); 6.09 (*dd*, $J(5,4) = 16.1$, $^5J(5,2) = 0.5$, H–C(5) (see edHSQC)); 6.67 (*dd*, $J(4,5) = 16.0$, $^4J(4,2) = 0.8$, H–C(4) (see edHSQC)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): −4.75 (flanked by ^{29}Si-isotope satellites as *d*, $^1J(C,Si) = 55.1$, (Me_2Si); 13.38 (*Me*–C(3)); 16.66 (lower intensity than preceding signal, Me_3CSi); 26.07 (Me_3CSi); 59.91 (*q*, $^2J(C,F) = 36.5$, CF_3CH_2); 100.21, 103.94 (C(6), C(7)); 115.39 (C(5)[20]); 118.57 (C(2)); 123.11 (*q*, $^1J(C,F) = 277.2$, CF_3CH_2); 144.32 (C(4)[20])); 153.60 (C(3)); 164.52 (C(1)). edHSQC (C,H-COSY, 125.7/499.9 MHz, $CDCl_3$): −4.75 (($CH_3)_2Si$) ↔ 0.15 (($CH_3)_2Si$); 13.38 (CH_3–C(3) ↔ 2.27 (CH_3–C(3)); 26.07 (($CH_3)_3CSi$) ↔ 0.96 (($CH_3)_3CSi$); 59.91 (CF_3CH_2) ↔ 4.50 (CF_3CH_2); 115.39 (C(5)) ↔ 6.09 (*H*–C(5)); 118.57 (C(2)) ↔ 5.87 (*H*–C(2)); 144.32 (C(4)) ↔ 6.67 (*H*–C(4)). HR-EI-MS (70 eV): 332.1417 (M^+, $C_{16}H_{23}F_3O_2Si^+$; calc. 332.1419). Anal. calc. for $C_{16}H_{23}F_3O_2Si$ (332.4): C 57.81, H 6.97; found: C 57.99, H 6.88.

*2,2,2-Trifluoroethyl (2*E*,4*S*,5*S*)-7-[(*tert*-Butyl)dimethylsilyl]-4,5-dihydroxy-3-methylhept-2-en-6-ynoate* (**21**). To a soln. of **19** (332 mg, 1.00 mmol) in ^{t}BuOH/H_2O 1:1 (2 ml), K_2CO_3 (414 mg, 3.00 mmol, 3.0 equiv.), $K_3[Fe(CN)_6]$ (988 mg, 3.00 mmol, 3.0 equiv.), $MeSO_2NH_2$ (95 g, 1.0 mmol, 1.0 equiv.), and $(DHQ)_2PHAL$ (39 mg, 50 μmol, 5 mol-%) were added. The mixture was cooled to 0° and $K_2OsO_2(OH)_4$ (3.7 mg, 10 μmol, 1 mol-%) was added. After stirring for 20 h, aq. $Na_2S_2O_3$ soln. (10 ml) was added and stirring continued at r.t. for 1 h. The aq. phase was extracted with AcOEt (4 × 25 ml), the combined org. phase dried (Na_2SO_4), and evaporated, and the residue purified by FC (4.5-cm column, cyclohexane/AcOEt 2:1): **21** (0.265 g, 72%). IR (film): 3320, 2955, 2935, 2890, 2860, 1745, 1650, 1470, 1465, 1445, 1410, 1395, 1365, 1285, 1255, 1210, 1170, 1140, 1060, 1005, 980. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 0.11 (*s*, Me_2Si); 0.92 (*s*, ^{t}BuSi); 2.22 (*d*, $^4J(Me,2) = 1.4$, Me–C(3)); 2.31–2.34 (*m*, OH–C(5) (see DQF-COSY)); 2.76 (*m*, (='*dd*' with a strong 'roof-effect' towards higher field), $J(OH,4) = J(OH,?) = 2.7$, OH–C(4) (see DQF-COSY)); 4.17 (br. *dd*, $J(4,5) = 6.2$, $^3J(4,OH) =$

[20]) Assignments analogous to those given in [41] for ethyl 8,8-dimethylnona-2,4-dien-6-ynoate (δ(C) 137.4 (C(4)) and 120.4 (C(5))).

2.1, broadened by unresolved $^4J(4,2)$, H–C(4); 4.37 (*dd*, $J(5,4) = {}^3J(5,OH) = 6.2$, no broadening (*cf.* H–(4)), H–(5)); 4.47, 4.50 (*AB*, $J_{AB} = 12.8$, *A* and *B* in addition split to *q*, $^3J(A,F) = {}^3J(B,F) = 8.5$, CF_3CH_2); 6.12 (*qd*, $^4J(2,Me) = {}^4J(2,4) = 1.3$, H–C(2)). DQF-COSY (' H,H-COSY', 499.9 MHz, $CDCl_3$; only selected signals): 2.33 (OH–C(5)) ↔ 4.37 (H–C(5)); 2.76 (OH–C(4)) ↔ 4.17 (H–C(4), extremely weak); 4.17 (H–C(4) ↔ 2.76 (OH–C(4)), 4.37 (H–C(5)); 4.37 (H–C(5) ↔ 2.33 (OH–C(5)), 4.17 (H–C(4)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): −4.89 (Me_2Si); 15.71 (*Me*–C(3)); 16.35 (lower intensity than δ 15.71, Me_3CSi); 25.92 (much lower intensity than δ 15.71, Me_3CSi); 59.88 (*q*, $^2J(C,F) = 36.5$, CF_3CH_2); 64.99 (C(5) (see edHSQC)); 79.32 (C(4) (see edHSQC)); 91.60 (calc. 97.16, C(7)[21]); 102.89 (calc. 108.64, C(6)[21])); 116.48 (C(2)); 123.10 (incompletely visible *q*, $^1J(C,F) = 276.7$, CF_3CH_2); 157.88 (C(3)); 164.17 (C(1)). edHSQC ('C,H-COSY', 125.7/499.7 MHz, $CDCl_3$): −4.89 ($(CH_3)_2Si$) ↔ 0.11 ($(CH_3)_2Si$); 15.71 (CH_3–C(3) ↔ 2.22 (CH_3–C(3)); 25.92 ($(CH_3)_3CSi$) ↔ 0.92 ($(CH_3)_3CSi$); 59.88 (CF_3CH_2) ↔ 4.47 and 4.50 (CF_3CH_2); 64.99 (C(5)) ↔ 4.37 (H–C(5)); 79.32 (C(4)) ↔ 4.17 (H–C(4)); 116.48 (C(2)) ↔ 6.12 (H–C(2)). HR-EI-MS (70 eV): 309.0778 ($[M - {}^t\text{Bu}]^+$, $C_{12}H_{16}F_3O_4Si^+$; calc. 309.0770). Anal. calc. for $C_{16}H_{25}F_3O_4Si$ (366.5): C 52.44, H 6.88; found: C 52.14, H 6.52.

*2,2,2-Trifluorethyl (*2E,*4*S,5S*)-4,5-Dihydroxy-3-methylhept-2-en-6-ynoate* (**22**). At 0°, 1.0M Bu_4NF in THF (1.49 ml, 1.49 mmol, 1.5 equiv.) was added to a soln. of **21** (0.25 g, 0.99 mmol) in THF (10 ml). After 50 min stirring at 0°, more 1.0M Bu_4NF in THF (1.49 ml, 1.49 mmol, 1.5 equiv.) was added. After another 3 h at 0°, H_2O (10 ml) was added. The aq. phase was extracted with AcOEt (4 × 10 ml), the combined org. layer dried (Na_2SO_4) and evaporated, and the residue purified by FC (4.5-cm column, cyclohexane/AcOEt 2:1, cyclohexane/AcOEt 1:1): **22** (139 mg, 76%). IR (film): 3400, 3305, 2975, 1730, 1650, 1410, 1285, 1210, 1170, 1145, 1060, 980, 870, 840. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 2.22 (*d*, $^4J(Me,2) = 1.4$, Me–C(3)); 2.45 (br. *s*, OH–C(5) (*cf.* **21**)); 2.57 (*d*, $^4J(7,5) = 2.2$, H–C(7) (see DQF-COSY)); 2.75 (br. *s*, OH–C(4) (*cf.* **21**)); 4.22 (br. *d*, $J(4,5) = 5.2$, H–C(4) (see DQF-COSY)); 4.41 (br. *s*, surprising, *cf.* H–C(4)), H–C(5) (see DQF-COSY); 4.49, 4.50 (*AB*, $J_{AB} = 12.8$, *A* and *B* in addition split to *q*, $^3J(H,F) = 8.5$, CF_3CH_2); 6.15 (*qd*, $^4J(2,Me) = {}^4J(2,4) = 1.4$, H–C(2)). DQF-COSY ('H,H-COSY', 499.9 MHz, $CDCl_3$): 2.22 (Me–C(3)) ↔ 6.15 (H–C(2)); 2.45 (OH–C(5)) ↔ 4.41 (H–C(5)); 2.57 (H–C(7)) ↔ 4.41 (H–C(5)); 2.75 (OH–C(4)) ↔ 4.22 (H–C(4), weak); 4.22 (H–C(4)) ↔ 2.75 (OH–C(4), weak), 4.41 (H–C(5)); 4.41 (H–C(5)) ↔ 2.45 (OH–C(5)); 4.22 (H–C(4)); 6.15 (H–C(2)) ↔ 2.22 (Me–C(3)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 16.00 (*Me*–C(3)); 59.92 (*q*, $^2J(C,F) = 36.5$, CF_3CH_2); 64.13 (C(5)); 75.57 (C(7)); 78.66 (C(4)); 81.19 (weaker than the two preceding signals, C(6)); 116.31 (C(2)); 123.09 (*q*, $^1J(C,F) = 277.2$, CF_3CH_2); 157.57 (C(3)); 164.23 (C(1)). edHSQC ('C,H-COSY', 125.7/499.9 MHz, $CDCl_3$): 16.00 (CH_3–C(3)) ↔ 2.22 (CH_3–C(3)); 59.92 (CF_3CH_2) ↔ 4.49 and 4.50 (CF_3CH_2); 64.13 (C(5)) ↔ 4.41 (H–C(5)); 75.57 (C(7)) ↔ 2.57 (H–C(7)); 78.66 (C(4)) ↔ 4.22 (H–C(4)); 116.31 (C(2)) ↔ 6.15 (H–C(2)). HR-EI-MS (70 eV): 197.0420 ($[M - HC{\equiv}CH(OH)]^+$, $C_7H_8F_3O_3^+$; calc. 197.0425). Anal. calc. for $C_{10}H_{11}F_3O_4$ (252.2): C 47.63, H 4.40; found: C 47.90, H 4.52.

*(1*E*)-1-(1,2-Epoxy-2,6,6-trimethylcyclohexyl)-2-iodoethene* (*=1-[(1*E*)-2-Iodoethenyl]-2,2,6-trimethyl-7-oxabicyclo[4.1.0]heptane;* **25**). At 0°, a soln. of I_2 (0.79 g, 3.13 mmol, 1.0 equiv.) in CH_2Cl_2 (30 ml) was added *via* cannula to a soln. of the ethenylstannane (1.42 g, 3.13 mmol; prepared from alkyne **24**) in CH_2Cl_2 (30 ml). After stirring at 0° for 3 h, the solvent was evaporated. A conc. aq. KF soln. was added to the residue. After stirring for 30 min at r.t., the suspension was diluted with Et_2O (40 ml) and filtered through a pad of *Celite*. The aq. phase was extracted with Et_2O (3 × 100 ml), the combined org. phase was dried (Na_2SO_4) and evaporated, and the residue purified by FC (6.0-cm column, cyclohexane/AcOEt 50:1): **25** (0.83 g, 91%). IR (film): 2960, 2930, 2870, 1605, 1460, 1455, 1380, 1365, 1285, 1265, 1235, 1175, 1145, 1115, 1080, 1065, 1045, 975, 950, 910. ^{1}H-NMR (499.9 MHz, $CDCl_3$; *s* of unknown contamination at δ 0.17): 0.94, 1.08, 1.18 (3 *s*, Me–C(2), 2 Me–C(6)); 1.03–1.08 (*m*, H_a–C(5)); 1.35–1.43 (*m*, CH_2(4), H_b–C(5)); 1.73 (*ddd*, $J_{gem} = 15.2$, $J(3,4) = 5.7$, H_a–C(3)), 1.83–1.90 (*m*, H_b–C(3)); 6.22 (*d*, $^3J = 14.3$, (IC*H*=CH (see edHSQC)); 6.75 (*d*, $^3J = 14.3$, ICH=C*H* (see edHSQC)). DQF-COSY (' H,H-COSY', 499.9 MHz, $CDCl_3$): 1.03–1.08 (H_a–C(5)) ↔ 1.35–1.43 (CH_2(4), H_b–C(5)); 1.35–1.43 (*inter alia* CH_2(4)) ↔ 1.03–1.08 (H_a–C(5)), 1.73 (H_a–C(3)), 1.83–1.90 (H_b–C(3)); 1.73 (H_a–C(3)) ↔ 1.35–1.43 (*inter alia* CH_2(4)), 1.83–1.90 (H_b–C(3)); 1.83–1.90 (H_b–C(3)) ↔ 1.35–1.43 (*inter alia* CH_2(4)), 1.73 (H_a–C(3)); 6.22 (IC*H*=CH) ↔ 6.75 (ICH=C*H*); 6.75 (ICH=C*H*) ↔ 6.22 (IC*H*=CH). ^{13}C-NMR (125.7 MHz, $CDCl_3$; contamination present as specified below): 16.86 (C(4)); 20.88 25.65, 25.69 (*Me*–C(2), 2 *Me*–C(6)); 29.86 (C(3)); 35.61 (C(5)); 64.95 (calc. 64.29, C(2)[21]); 73.51 (calc. 67.52, C(1)[21])); 78.94 (calc. 71.92, I*C*H=CH[21])); 141.95 (calc. 148.13, ICH=*C*H[21])); C(6) could not be identified unambiguously among the 'extra peaks' – all but one due to the unknown contaminant(s) – at δ 16.75, 18.49, 22.76, 25.54, 26.23, 28.99, 33.27, and

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[21]) Tentative assignment based on increment calculation by ACD/Chem Sketch, Vs. 4.04 (1999); Vs. 4.07 for **26** and **29**.

33.82. edHSQC ('C,H-COSY', 125.7/499.7 MHz, $CDCl_3$): 16.86 (C(4)) ↔ 1.35–1.43 (*inter alia* CH_2(4)); 20.88, 25.65, 25.69 (3 CH_3) ↔ 0.94, 1.08, 1.18 (3 CH_3); 29.86 (C(3)) ↔ 1.73 (H_a–C(3)), 1.83–1.90 (H_b–C(3)); 35.61 (C(5)) ↔ 1.03–1.08 (H_a–C(5)), 1.35–1.43 (*inter alia* H_b–C(5)); 78.94 (ICH=CH) ↔ 6.22 (ICH=CH); 141.95 (ICH=CH) ↔ 6.75 (ICH=CH). HR-EI-MS (70 eV): 292.0322 (M^+, $C_{11}H_{17}IO^+$; calc. 292.0324).

*2,2,2-Trifluoroethyl (2*E*,4*S*,5*S*)-4,5-(Isopropylidenedioxy)-3-methylhept-2-en-6-ynoate* (=*2,2,2-Trifluoroethyl (2*E*)-3-[(4*S*,5*S*)-5-Ethynyl-2,2-dimethyl-1,3-dioxolan-4-yl]but-2-enoate*). TsOH (7.5 mg, 40 µmol, 0.1 equiv.) and 2,2-dimethoxypropane (74.0 µl, 62.0 mg, 595 µmol, 1.5 equiv.) were added to a soln. of **22** (100 mg, 397 µmol) in CH_2Cl_2 (5 ml). After stirring for 3 h at r.t., aq. $NaHCO_3$ soln. (10 ml) was added. The aq. phase was extracted with CH_2Cl_2 (4 × 8 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the crude product purified by FC (3.0-cm column, cyclohexane/AcOEt 1.5:1): title compound (113 mg, 97%). IR (film): 3460, 3305, 2990, 1740, 1655, 1415, 1385, 1285, 1245, 1220, 1170, 1090, 1060, 980. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.49, 1.53 (2 incompletely resolved *q*, ^4J(within Me_2C) = 0.5, Me_2C); 2.23 (*d*, ^4J(Me,2) = 1.3, Me–C(3)); 2.63 (*d*, ^4J(7,5) = 2.1, H–C(7)); 4.34 (*dd*, *J*(5,4) = 7.7, ^4J(5,7) = 2.1, (>^4J(4,2)), H–C(5)); 4.51 (*q*, ^3J(C,F) = 8.5, CF_3CH_2); 4.53 (*dd*, *J*(4,5) = 7.7, ^4J(4,2) = 1.0, (<^4J(5,7)), H–C(4)); 6.17 (*dq*, ^4J(2,4) = ^4J(2,Me) = 1.4, H–C(2)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 15.28 (*Me*–C(3)); 26.15, 26.48 (*Me*$_2$C); 59.92 (*q*, ^2J(C,F) = 36.5, CF_3CH_2); 69.82 (C(5) (see edHSQC)); 75.73 (C(7)); 80.16 (lower intensity than the preceding signal, C(6)); 84.65 (C(4) (see edHSQC)); 111.48 (Me_2C); 114.51 (C(2)); 123.08 (*q*, ^1J(C,F) = 277.2, CF_3CH_2); 156.20 (C(3)); 164.21 (C(1)). edHSQC ('C,H-COSY', 125.7/499.9 MHz, $CDCl_3$): 15.28 (CH_3–C(3)) ↔ 2.23 (CH_3–C(3)); 26.15, 26.48 ((CH_3)C) ↔ 1.49 and 1.53 ((CH_3)C); 59.92 (CF_3CH_2) ↔ 4.51 (CF_3CH_2); 69.82 (C(5)) ↔ 4.34 (H–C(5)); 84.65 (C(4)) ↔ 4.53 (H–C(4)); 114.51 (C(2)) ↔ 6.17 (H–C(2)). Anal. calc. for $C_{13}H_{15}F_3O_4$ (292.3): C 53.43, H 5.17; found: C 53.61, H 5.11.

*2,2,2-Trifluoroethyl (2*E*,4*S*,5*S*)-4,5-(Isopropylidenedioxy)-7-(methoxycarbonyl)-3-methyloct-2-en-6-ynoate* (=*2,2,2-Trifluoroethyl (2*E*)-3-[(4*S*,5*S*)-5-(3-Methoxy-3-oxoprop-1-ynyl)-2,2-dimethyl-1,3-dioxolan-4-yl]but-2-enoate*; **26**). At −78°, 1.0M LiHMDS in THF (0.22 mmol, 0.22 ml, 1.3 equiv.) was added dropwise to a soln. of 2,2,2-trifluoroethyl (2*E*,4*S*,5*S*)-4,5-(isopropylidenedioxy)-3-methylhept-2-en-6-ynoate (50.0 mg, 0.17 mmol) in THF (5 ml). The resulting soln. was stirred for 30 min before $ClCO_2Me$ (0.053 ml, 64.3 mg, 680 µmol, 4.0 equiv.) was added all at once. After stirring for 45 min at −78°, H_2O (10 ml) was added. After warming to r.t., the aq. phase was extracted with Et_2O (4 × 15 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue purified by FC (3.0-cm column, cyclohexane/AcOEt 3.5:1): **26** (53.0 mg, 89%). IR (film): 2995, 2245, 1725, 1655, 1440, 1410, 1385, 1375, 1325, 1280, 1260, 1220, 1165, 1145, 1085, 1060, 980, 965. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 1.50, 1.53 (*s* and incompletely resolved *q*, resp., ^4J(within Me_2C) = 0.5, Me_2C); 2.21 (*d*, ^4J(Me,4) = 1.4, Me–C(3)); 3.81 (*s*, MeO); 4.45 (*d*, *J*(5,4) = 7.4, H–C(5)); 4.51 (*q*, ^3J(H,F) = 8.5, CF_3CH_2); 4.61 (br. *dd*, *J*(4,5) = 7.4, ^4J(4,2) = 0.8, H–C(4)); 6.17 (*qd*, ^4J(2,Me) = ^4J(2,4) = 1.4, H–C(2)). DQF-TPPI-COSY ('H,H-COSY', 499.9 MHz, $CDCl_3$): 2.21 (Me–C(3)) ↔ 4.61 (H–C(4)), 6.17 (H–C(2)); 4.45 (H–C(5)) ↔ 4.61 (H–C(4)); 4.61 (H–C(4)) ↔ 2.21 (Me–C(3)), 4.45 (H–C(5)), 6.17 (H–C(2)); 6.17 (H–C(2)) ↔ 2.21 (Me–C(3)), 4.61 (H–C(4)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 15.21 (*Me*–C(3)); 25.84, 26.43 (*Me*$_2$C); 52.98 (MeO); 59.98 (*q*, ^2J(C,F) = 36.6, CF_3CH_2); 69.38 (C(4) (see edHSQC)); 78.17 (calc. 88.34, C(6)[21]); 83.06 (calc. 91.89, C(7)[21]); 84.22 (C(5) (see edHSQC)); 112.35 (Me_2C); 114.99 (C(2)); 123.04 (incompletely visible *q*, ^1J(C,F) = 277.3, CF_3CH_2); 153.18 (CO_2Me[22]); 155.38 (C(3)[22])); 164.05 (C(1)[22])). edHSQC ('C,H-COSY', 125.7/499.9 MHz, $CDCl_3$): 15.21 (CH_3–C(3)) ↔ 2.21 (CH_3–C(3)); 25.84, 26.43 ((CH_3)$_2$C) ↔ 1.50, 1.53 ((CH_3)$_2$C); 52.98 (CH_3O) ↔ 3.81 (CH_3O); 59.98 (CF_3CH_2) ↔ 4.51 (CF_3CH_2); 69.38 (C(4)) ↔ 4.61 (H–C(4)); 84.22 (C(5)) ↔ 4.45 (H–C(5)); 114.99 (C(2)) ↔ 6.17 (H–C(2)). HR-EI-MS (70 eV): 335.0745 ($[M - CH_3]^+$, $C_{14}H_{14}F_3O_6^+$; calc. 335.0742). Anal. calc. for $C_{15}H_{17}F_3O_6$ (350.3): C 51.43, H 4.89; found: C 51.37, H 4.75.

*2,2,2-Trifluoroethyl (2*E*,8*E*,4*S*,5*S*)-9-(1,2-Epoxy-2,6,6-trimethylcyclohexyl)-4,5-dihydroxy-3-methylnona-2,8-dien-6-ynoate* (=*2,2,2-Trifluoroethyl (2*E*,8*E*,4*S*,5*S*)-4,5-Dihydroxy-3-methyl-9-(2,2,6-trimethyl-7-oxabicyclo[4.1.0]hept-1-yl)nona-2,8-dien-6-ynoate*; **27**; 1:1 diastereoisomer mixture if the Me–C(2′) ^{1}H-NMR signal is correctly interpreted and not split by a ^4J(3′,Me–C(2′)) coupling). To a suspension of [$PdCl_2(PPh_3)_2$] (94.9 mg, 0.135 mmol, 5 mol-%) in THF (15 ml), CuI (77.2 mg, 0.405 mmol, 15 mol-%) was added. Then a soln. of **25** (829 mg, 2.84 mmol, 1.05 equiv.) and **22** (681 mg, 2.70 mmol) in THF (10 ml) was added *via* cannula. After the dropwise addition of Et_3N (8.00 ml, 5.81 g, 57.4 mmol, 21.2 equiv.), the mixture was stirred for 90 min at r.t. The reaction was terminated by the addition of aq. NH_4Cl soln. (10 ml). The aq. phase was extracted with Et_2O

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[22]) Assignment of the $C_{quat.}$ based on the similarity to the unequivocally assigned $C_{quat.}$ resonances 156.20 (C(3)) and 164.21 (C(1)) of 2,2,2-trifluoroethyl (2*E*,4*S*,5*S*)-4,5-(isopropylidenedioxy)-3-methylhept-2-en-6-ynoate (see above); this left δ 153.18 (or 179,71 in case of **28**) for CO_2Me.

(4×15 ml), the combined phase dried (Na_2SO_4) and evaporated, and the residue purified by FC (5.5-cm column, cyclohexane/AcOEt 1:1): **27** (0.859 g, 76%). IR (film): 3420, 2965, 2935, 2875, 1735, 1650, 1450, 1440, 1410, 1380, 1365, 1285, 1205, 1170, 1140, 1065, 1045, 980, 960. ^{1}H-NMR (499.9 MHz, $CDCl_3$; most assignments by DQF-TPPI-COSY, see below): 0.92, 1.08 (2 br. *s*, 2 Me–C(6′)); 1.03–1.08 (*m*, H_a–(5′)); 1.151, 1.153 (2 *s*, Me–C(2′)[23]); 1.37–1.47 (*m*, CH_2(4′) (H_b–C(5′)); 1.74 (*ddd*, ^2J = 15.3, J(3′a,4′) = 5.6, 5.6, H_a–C(3′)); 1.89 (*ddd*, ^2J = 15.1, J(3′b,4′) = 7.8, 7.8, H_b–C(3)); 2.23 (*d*, ^4J(Me,2) = 1.4, Me–C(3)); 2.42 (br. *d*, J(OH,5) = 6.3, OH–C(5)); 2.77 (br. *d*, J(OH,4) = 3.1, OH–C(4)); 4.22 (br. *dd*, J(4,5) = 5.2, J(4,OH) = 2.2, H–C(4)); 4.44–4.55 (*m*, CF_3CH_2, H–C(5)); 5.70 (*dd*, J(8,9) = 15.7, ^5J(8,5) = 1.8 (diagnostic for assignment), H–C(8)); 6.16 (*qd*, ^4J(2,Me) = ^4J(2,4) = 1.3, H–C(2)); 6.40 (*d*, J(9,8) = 15.8, H–C(9)). DQF-TPPI-COSY (H,H-COSY, 499.9 MHz, $CDCl_3$): 0.92 (Me_a–C(6′)) ↔ 1.08 (Me_b–C(6′)); 1.08 (Me_b–C(6′)) ↔ 0.92 (Me_a–C(6′)); 1.03–1.08 (H_a–C(5′)) ↔ 1.37–1.47 (CH_2(4′), H_b–C(5′)); 1.37–1.47 (CH_2(4′), H_b–C(5′)) ↔ 1.03–1.08 (H_a–C(5′)), 1.74 (H_a–C(3′)), 1.89 (H_b–C(3′)); 1.74 (H_a–C(3′)) ↔ 1.37–1.47 (*inter alia* CH_2(4′)), 1.89 (H_b–C(3′)); 1.89 (H_b–C(3′)) ↔ 1.37–1.47 (*inter alia* CH_2(4′)), 1.74 (H_a–C(3′)); 2.23 (*Me*–C(3)) ↔ 6.16 (H–C(2)); 2.42 (OH–C(5)) ↔ 4.44–4.55 (*inter alia* H–C(5)); 2.77 (OH–C(4)) ↔ 4.22 (H–C(4)); 4.22 (H–C(4)) ↔ 2.77 (OH–C(4)), 4.44–4.55 (*inter alia* H–C(5)), 6.16 (H–C(2), very low intensity); 4.44–4.55 (*inter alia* H–C(5)) ↔ 2.42 (OH–C(5)), 4.22 (H–C(4)), 6.40 (H–C(9), very low intensity); 5.70 (H–C(8)) ↔ 4.44–4.55 (very low intensity, *inter alia* H–C(5)), 6.40 (H–C(9)); 6.16 (H–C(2)) ↔ 2.23 (Me–C(3)), 4.22 (very low intensity, H–C(4)); 6.40 (H–C(9)) ↔ 5.70 (H–C(8)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 16.12 (*Me*–C(3)); 16.89 (C(4′)); 20.69 (*Me*–C(2′)[24]); 25.68, 25.76 (2 *Me*–C(6′)[24]); 29.90 (C(3′)); 33.45 (low intensity, C(6′)); 35.60 (C(5′)); 59.87 (incompletely resolved *q*, ^2J(C,F) = 36.5, CF_3CH_2); 64.94 (C(5)[24]); 65.90 (C(2′)); 70.97 (C(1′)); 78.88 (C(4)[24]); 85.65, 86.84 (C(6), C(7)); 111.48 (C(8)[24]); 116.05 (C(2)[24]); 123.11 (*q* (only the center signals are visible), ^1J(C,F) = 277.0, CF_3CH_2); 141.00 (C(9)[24]); 158.11 (C(3)); 164.27 (C(1)). edHSQC ('C,H-COSY', 125.7/499.9 MHz, $CDCl_3$): 16.12 (CH_3–C(3)) ↔ 2.23 (CH_3–C(3)); 16.89 (C(4′)) ↔ 1.37–1.47 (*inter alia* CH_2(4′)); 20.69 (CH_3–C(2′)) ↔ 1.151, 1.153 (CH_3–C(2′))); 25.68, 25.76 (2 CH_3–C(6′)) ↔ 0.92, 1.08 (2 CH_3–(6′)); 29.90 (C(3′)) ↔ 1.74 (H_a–C(3′)), 1.89 (H_b–C(3′)); 35.60 (C(5′)) ↔ 1.03–1.08 (H_a–C(5′)), 1.37–1.47 (*inter alia* H_b–C(5′)); 59.87 (CF_3CH_2) ↔ 4.44–4.55 (*inter alia* CF_3CH_2); 64.94 (C(5)) ↔ 4.44–4.55 (*inter alia H*–C(5)); 78.88 (C(4)) ↔ 4.22 (*H*–C(4)); 111.48 (C(8)) ↔ 5.70 (*H*–C(8)); 116.05 (C(2)) ↔ 6.16 (*H*–C(2)); 141.00 (C(9)) ↔ 6.40 (*H*–C(9)). Anal. calc. for $C_{21}H_{27}F_3O_5$ (416.4): C 60.57, H 6.54; found: C 60.86, H 6.79.

*2,2,2-Trifluoroethyl (2*E*,4*S*,5*S*,6*E*)-4,5-(Isopropylidenedioxy)-7-(methoxycarbonyl)-3-methyl-7-(tributylstannyl)hepta-2,6-dienoate* (=*2,2,2-Trifluoroethyl (2*E*)-3-[(4*S*,5*S*)-5-[(1*E*)-3-Methoxy-3-oxo-2-(tributylstannyl)prop-1-enyl]-2,2-dimethyl-1,3-dioxolan-4-yl]but-2-enoate*; **28**). To a degassed soln. of [Pd(PPh_3)$_4$] (57 mg, 50 μmol, 5 mol-%) in THF (10 ml), a degassed soln. of **26** (347 mg, 0.99 mmol) in THF (2 ml) was added. At 0°, Bu_3SnH (0.293 ml, 317 mg, 1.09 mmol, 1.1 equiv.) was added. After stirring for 1 h at 0°, H_2O (10 ml) and aq. NaCl soln. (10 ml) were added. The aq. phase was extracted with Et_2O (4×25 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue purified by FC (4.5-cm column; cyclohexane, cyclohexane/AcOEt 10:1): **28** (558 mg, 88%). IR (film): 2985, 2960, 2930, 2875, 2855, 1740, 1710, 1650, 1615, 1455, 1435, 1415, 1380, 1285, 1240, 1220, 1200, 1170, 1140, 1080, 1065, 980, 960, 865. ^{1}H-NMR (499.9 MHz, $CDCl_3$): 0.89 (*t*, ^3J = 7.3, 3 *Me*$CH_2CH_2CH_2$); 1.00 (*m*, probably each peak flanked by Sn-isotope satellites as 2 *d*, ^2J(H,^{119}Sn) = 53.2, ^2J(H,^{117}Sn) = 51.0, 3 $MeCH_2CH_2CH_2$); 1.31 (*qt*, ^3J = 7.3, 7.3, 3 $MeCH_2CH_2CH_2$); 1.46–1.53 (*m*, 3 $MeCH_2CH_2CH_2$), superimposing 1.479 and 1.483 (2 *s*, Me_2C); 2.16 (*d*, ^4J(Me,2) = 1.4, Me–C(3)); 3.63 (*s*, MeO); 4.10 (*dd*, J(4,5) = 8.2, ^4J(4,2) = 0.8, H–C(4)); 4.46, 4.51 (*AB*, J_{AB} = 12.4, *A* and *B* in addition split to *q*, ^3J(*A*,F) = ^3J(*B*,F) = 8.4, CF_3CH_2); 4.83 (*dd*, J(5,6) = J(5,4) = 8.1, each peak flanked by Sn-isotope satellites as *d*, ^4J(5,Sn) = 5.7, H–C(5)); 5.97 (*d*, J(6,5) = 8.0, each peak flanked by Sn-isotope satellites as 2 *d*, ^3J(6,^{119}Sn) = 55.9, ^3J(6,^{117}Sn) = 53.5, H–C(6)); 6.01 (*dq*, ^4J(2,4) = ^4J(2,Me) = 1.3, H–C(2)). DQF-COSY (H,H-COSY, 499.9 MHz, $CDCl_3$): 0.89 (*Me*$CH_2CH_2CH_2$) ↔ 1.31 ($MeCH_2CH_2CH_2$); 1.00 ($MeCH_2CH_2CH_2$) ↔ 1.46–1.53 ($MeCH_2CH_2CH_2$); 1.31 ($MeCH_2CH_2CH_2$) ↔ 0.89 (*Me*$CH_2CH_2CH_2$), 1.46–1.53 ($MeCH_2CH_2CH_2$); 1.46–1.53 ($MeCH_2CH_2CH_2$) ↔ 1.00 ($MeCH_2CH_2CH_2$), 1.31 ($MeCH_2CH_2CH_2$); 2.16 (Me–C(3)) ↔ 6.01 (H–C(2)); 4.10 (H–C(4)) ↔ 4.83 (H–C(5)); 4.83 (H–C(5)) ↔ 4.10 (H–C(4)), 5.97 (H–C(6)); 5.97 (H–C(6)) ↔ 4.83 (H–C(5)); 6.01 (H–C(2)) ↔ 2.16 (Me–C(3)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): 10.46 (flanked by Sn-isotope satellites as 2 *d*, ^1J(C,^{119}Sn) = 349.4, ^1J(C,^{117}Sn) = 333.9, 3 $MeCH_2CH_2CH_2$); 13.61 (3 *Me*$CH_2CH_2CH_2$), 15.11 (*Me*–C(3)); 26.70 (Me_2C); 27.16 (flanked by Sn-isotope satellites as *d*, ^3J(C,Sn) = 57.8, 3 $MeCH_2CH_2CH_2$);

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[23]) The splitting of this signal could be caused by the existence of a 1:1 mixture of diastereoisomers.

[24]) Assignments of Me–C(2′) *vs.* 2 Me–C(6′), C(4) *vs.* C(5), and C(2) *vs.* C(8) *vs.* C(9) based on edHSQC cross-peaks.

28.77 (flanked by Sn-isotope satellites as *d*, ^2J(C,Sn) = 20.6, 3 $MeCH_2CH_2CH_2$); 51.42 (CO_2Me); 59.78 (*q*, ^2J(C,F) = 36.5, CF_3CH_2); 78.03 (flanked by Sn-isotope satellites as *d*, ^3J(C,Sn) = 41.2, C(5) (see edHSQC)); 84.65 (C(4) (see edHSQC)); 110.35 (low intensity, Me_2C); 114.67 (C(2) (see edHSQC)); 123.12 (*q* (only three peaks visible), ^1J(C,F) = 277.2, CF_3CH_2); 143.28 (C(7)); 145.01 (flanked by Sn-isotope satellite as *d*, ^2J(C,Sn) = 13.9, C(6) (see edHSQC)); 157.25 (C(3)[22])); 164.17 (C(1)[22])); 170.71 (CO_2Me[22]). edHSQC (C,H-COSY, 125.7/499.9 MHz, $CDCl_3$): 10.46 ($CH_3CH_2CH_2CH_2$) ↔ 1.00 ($CH_3CH_2CH_2CH_2$); 13.61 ($CH_3CH_2CH_2CH_2$) ↔ 0.89 ($CH_3CH_2CH_2CH_2$); 15.11 (CH_3–C(3)) ↔ 2.16 (CH_3–C(3)); 26.70 (($CH_3)_2$C) ↔ 1.479, 1.483 (($CH_3)_2$ C); 27.16 ($CH_3CH_2CH_2CH_2$) ↔ 1.31 ($CH_3CH_2CH_2CH_2$); 28.77 ($CH_3CH_2CH_2CH_2$) ↔ 1.46–1.53 ($CH_3CH_2CH_2CH_2$); 51.42 (CO_2CH_3) ↔ 3.63 (CO_2CH_3); 59.78 (CF_3CH_2) ↔ 4.46, 4.51 (CF_3CH_2); 78.03 (C(5)) ↔ 4.83 (H–C(5)); 84.65 (C(4)) ↔ 4.10 (H–C(4)); 114.67 (C(2)) ↔ 6.01 (H–C(2)); 145.01 (C(6)) ↔ 5.97 (H–C(6)). HR-EI-MS (70 eV): 585.1500 ($[M - Bu]^+$, $C_{23}H_{36}F_3O_6Sn^+$; calc. 585.1486). Anal. calc. for $C_{27}H_{45}F_3O_6Sn$ (641.4): C 50.56, H 7.07; found: C 51.04, H 7.27.

*(5*S*)-3-[(1*E*)-2-(1,2-Epoxy-2,6,6-trimethylcyclohexyl)ethenyl]-5-{(1*S*,2*E*)-1-hydroxy-2-methyl-3-[(2,2,2-trifluoroethoxy)carbonyl]prop-2-enyl}-furan-2(5*H*)-one* (*=2,2,2-Trifluoroethyl (2*E*,4*S*)-4-{(2*S*)-2,5-Dihydro-5-oxo-4-[(1*E*)-2-(2,2,6-trimethyl-7-oxabicyclo[4.1.0]hept-1-yl)ethenyl]furan-2-yl}-4-hydroxy-3-methylbut-2-enoate*; **29**; should be a 1:1 mixture with respect to the epoxide moiety, but there was no spectral evidence; tentatively assigned to represent a 86:14 mixture with its diastereoisomer epi-**29** (=(5*R*)-isomer)). *Method A:* To a soln. of $[Pd_2dba_3]\cdot CHCl_3$ (7.7 mg, 7.5 μmol, 10 mol-%) in CH_2Cl_2 (40 ml), butane-1,4-diyl-bis[diphenylphosphine] (7.7 mg, 15 μmol, 20 mol-%) was added. The soln. was stirred for 30 min (red → yellow). A soln. of **27** (31 mg, 74 μmol) in CH_2Cl_2 (10 ml) was added *via* cannula. The resulting soln. was transferred into an autoclave, which was pressurized with H_2 (8 bar) and CO (42 bar). Under stirring, the mixture was heated at 50° for 24 h. After cooling and release of the gases, the solvent was evaporated and the residue passed through a short chromatography column (1.5 cm × 15 cm, cyclohexane/AcOEt 2:1): 7:3-mixture (19.9 mg) of **29**/epi-**29** (14.2 mg, 43%) and re-isolated **27** (5.7 mg, 19%).

Method B: A degassed soln. of **30** (347 mg, 610 μmol) in DMF (5 ml) was transferred *via* cannula to a degassed soln. of $[Pd(PPh_3)_4]$ (35 mg, 30 μmol, 5 mol-%) and iodoalkene **25** (196 mg, 0.671 mmol, 1.1 equiv.) in DMF (5 ml). CuI (139 mg, 0.732 mmol, 1.2 equiv.) was then added and the resulting suspension stirred for 3 h at r.t. After dilution with ^{t}BuOMe (5 ml), aq. NH_4Cl soln. (10 ml), and H_2O (10 ml), the aq. phase was extracted with Et_2O (4 × 25 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue purified by FC (6.0-cm column, cyclohexane/AcOEt 2:1): **29**/epi-**29** (260 mg, 96%). IR (film): 3445, 2960, 2930, 2875, 2855, 1740, 1655, 1455, 1410, 1380, 1365, 1350, 1280, 1260, 1205, 1170, 1145, 1100, 1070, 980, 870, 840, 800. ^{1}H-NMR (499.9 MHz, $CDCl_3$; postulated 86:14 mixture **29**/epi-**29**): **29**: 0.93, 1.14, 1.15 (3 *s*, Me–C(2″), (2 Me–C(6″)); 1.06–1.11 (*m*, H_a–C(5″)); 1.40–1.49 (*m*, CH_2(4″), H_b–C(5″)); 1.76 (*m*, (='*ddd*', J_{gem} = 15.0, ^3J(3″a,4″) = 5.5, 5.5, H_a–C(3″)); 1.90 (*m*, ('*ddd*', J_{gem} = 15.2, ^3J(3″b,4″) = 7.8, 7.8), H_b–C(3″)); 2.26 (*d*, ^4J(Me,3‴) = 1.2, Me–C(2‴)); 2.54 (very br. *d*, *J*(OH,1‴) = 2.5, OH); 4.25 (very br. *d*, *J*(1‴,OH) = 3.2, H–C(1‴)); 4.50, 4.52, (*AB*, J_{AB} = 12.7, *A* and *B* in addition split to *q*, ^3J(H,F) = 8.5, CF_3CH_2); 5.04 (*dd*, *J*(5,1″) = 5.4, *J*(5,4) = 2.0, H–C(5)); 6.10 (*qd*, ^4J(3‴,Me) = ^4J(3‴,1‴) = 1.3, H–C(3‴)); 6.31 (*d*, *J*(1′,2′) = 15.7, H–C(1′) (see edHSQC)); 7.00 (*d*, *J*(4,5) = 2.0, H–C(4)); 7.234 (*d*, *J*(2′,1′) = 15.8, H–C(1′) (see edHSQC)); epi-**29**: 0.92, 1.16 (Me–C(2″), 2 Me–C(6″)); 2.25 (*d*, ^4J(Me,3‴) = 1.4, Me–C(2‴)); 6.08 (*qd*, ^4J(3‴,Me) = ^4J(3‴,1‴) = 1.3, H–C(3‴)); 7.228 (*d*, *J*(1′,2′) = 15.7, H–C(1′)). DQF-COSY (H,H-COSY, 499.9 MHz, $CDCl_3$): 1.06–1.11 (H_a–C(5″)) ↔ 1.40–1.49 (CH_2(4″), H_b–C(5″)); 1.40–1.49 (CH_2(4″), H_b–C(5″)) ↔ 1.06–1.11 (H_a–C(5″)), 1.76 (H_a–C(3″)), 1.90 (H_b–C(3″)); 1.76 (H_a–C(3″)) ↔ 1.40–1.49 (*inter alia* CH_2(4″); 1.90 (H_b–C(3″)); 1.90 (H_b–C(3″) ↔ 1.40–1.49 (*inter alia* CH_2(4″)), 1.76 (H_a–C(3″)); 2.26 (Me–C(2‴)) ↔ 6.10 (H–C‴)); 2.54 (br. *s*, OH) ↔ 4.25 (H–C(1‴)); 4.25 (H–C(1‴)) ↔ 2.43 (br. *s*, OH), 5.04 (H–C(5)), 6.10 (H–C(3‴)), very weak); 5.04 (H–C(5)) ↔ 4.24 (H–C(1‴)), 6.99 (H–C(4)); 6.10 (H–C(3‴)) ↔ 2.26 (Me–C(2‴)), 4.24 (H–C(1‴), very weak); 6.31 (H–C(1′)) ↔ 7.234 (H–C(2′)); 7.00 (H–C(4)) ↔ 5.04 (H–C(5)); 7.234 (H–C(2′)) ↔ 6.31 (H–C(1′)). ^{13}C-NMR (125.7 MHz, $CDCl_3$): **29**: 15.97 (*Me*–C(2‴) (see edHSQC)), 16.96 (C(4″) (see edHSQC)); 20.82, 25.82, 25.89 (*Me*–C(2″), 2 *Me*–C(6″)), 29.98 (C(3″)); 33.59 (lower intensity than preceding and following signal, C(6″)); 35.65 (C(5″)); 60.01 (*q*, ^3J(C,F) = 36.6, CF_3CH_2), 65.90 (calc. 66.63, C(2″)[21]); 71.33 (calc. 73.72, C(1″)[21]); 76.79 (C(1‴)); 81.53 (C(5)); 116.60 (C(3‴)); 120.65 (C(1′); *cf.* C(8) of **27**); 123.02 (incompletely visible *q*, ^1J(C,F) = 277.2, CF_3CH_2); 130.29 (C(3); δ(C(3)) < δ(C(2)); 134.63 (C(2′); *cf.* C(9) of **27**); 143.41 (C(4)); 157.35 (C(2‴); *cf.* C(2′) of **30**); 163.94 (CO_2Tfe; *cf.* C(1) of **22**), 170.74 (C(2); δ(C(3)) < δ(C(2))); epi-**29**: 20.89 (*Me*–C(2″)); 29.69 (C(3″)); 33.57 (C(6″)); 35.63 (C(5″)); 143,46 (C(4)). edHSQC (C,H-COSY, 125.7/499.9 MHz, $CDCl_3$): 15.97 (CH_3–C(2‴)) ↔ 2.26 (CH_3–C(2‴)); 16.96 (C(4″)) ↔ 1.40–1.49 (*inter alia* CH_2(4″)); 20.82, 25.82, 25.89 (CH_3–C(2″), 2 CH_3–C(6″)) ↔ 0.93, 1.14, 1.15 (CH_3–C(2″), 2 CH_3–C(6″)); 29.98 (C(3″)) ↔ signal of very low intensity 1.76 (H_a–C(3″)), signal of normal intensity 1.90 (H_b–C(3″)); 35.65 (C(5″)) ↔ signal

of normal intensity 1.06–1.11 (*m*, H_a–C(5″)), signal of very low intensity 1.40–1.49 (*inter alia* CH_2(5″)); 60.01 (CF_3CH_2) ↔ 4.50, 4.52 (CF_3CH_2); 76.79 (C(1‴)) ↔ 4.25 (*H*–C(1‴)); 81.53 (C(5)) ↔ 5.04 (*H*–C(5)); 116.60 (C(3‴)) ↔ 6.10 (*H*–C(3‴)); 120.65 (C(1′)) ↔ 6.31 (*H*–C(1′)); 134.63 (C(2′)) ↔ 7.234 (*H*–C(2′)); 143.42 (C(4)) ↔ 7.00 (*H*–C(4)). HR-EI-MS (70 eV): 444.1750 (M^+, $C_{22}H_{27}F_3O_6^+$, calc. 444.1760). Anal. calc. for $C_{22}H_{27}F_3O_6$ (444.4): C 59.45, H 6.12; found: C 59.76, H 6.89.

*(5*S*)-5-{(2*E*,1*S*)-1-Hydroxy-2-methyl-3-[(2,2,2-trifluoroethoxy)carbonyl]prop-2-enyl}-3-(tributylstannyl)-furan-2(5*H*)-one* (*=2,2,2-Trifluoroethyl (2*E*,4*S*)-4-[(2*S*)-2,5-Dihydro-5-oxo-4-(tributylstannyl)furan-2-yl]-4-hydroxy-3-methylbut-2-enoate*; **30**). TsOH (37 mg, 0.19 mmol, 0.2 equiv.) was added to a soln. of **28** (616 mg, 960 μmol) in MeOH (15 ml). The resulting soln. was heated under reflux for 8 h. After dilution with ^{t}BuOMe (10 ml), aq. $NaHCO_3$ soln. (10 ml), and H_2O (5 ml), the aq. phase was extracted with Et_2O (4 × 25 ml), the combined org. phase dried (Na_2SO_4) and evaporated, and the residue purified by FC (3.5-cm column, cyclohexane/AcOEt 5:1): **30** (347 mg, 64%). IR (film): 3410, 2955, 2925, 2855, 1735, 1650, 1580, 1455, 1410, 1285, 1165, 1140, 980, 1065, 870. ^{1}H-NMR (499.9 MHz, $CDCl_3$; unknown contaminant with *s* at δ 0.07): 0.89 (*t*, ^3J = 7.4, 3 *Me*$CH_2CH_2CH_2$); 1.10 (*m*, each peak flanked by Sn-isotope satellites as 2 *d*, ^2J(H,^{119}Sn) = 54.6, ^2J(H,^{117}Sn) = 52.1, 3 Me$CH_2CH_2CH_2$); 1.32 (*qt*, ^3J = 7.4, 7.4, 3 Me$CH_2CH_2CH_2$); 1.43–1.61 (*m*, 3 Me$CH_2CH_2CH_2$); 2.24 (*d*, ^4J(Me,3′) = 1.4, Me–C(2′)); 2.34 (*d*, *J*(OH,1) = 4.9, OH); 4.20 (*dd*, *J*(1′,OH) = *J*(1′,5) = 4.8, H–C(1′)); 4.49, 4.51 (J_{AB} = 12.7, *A* and *B* in addition split to *q*, ^3J(H,F) = 8.5, CF_3CH_2); 5.08 (*dd*, *J*(5,1′) = 5.3, *J*(5,4) = 1.5, each peak flanked by Sn-isotope satellites as *d*, ^4J(5,Sn) = 7.4, H–C(5)); 6.07 (*qd*, ^4J(3′,Me) = ^4J(3′,1′) = 1.2, H–C(3′)); 7.36 (*d*, *J*(4,5) = 1.5, each peak flanked by Sn-isotope satellites as *d*, ^3J(4,Sn) = 21.6, H–C(4)). DQF-COSY (H,H-COSY, 499.9 MHz, $CDCl_3$): 0.89 (*Me*$CH_2CH_2CH_2$) ↔ 1.32 (Me$CH_2CH_2CH_2$); 1.10 (Me$CH_2CH_2CH_2$) ↔ 1.43–1.61 (Me$CH_2CH_2CH_2$); 1.32 (Me$CH_2CH_2CH_2$) ↔ 0.89 (*Me*$CH_2CH_2CH_2$), 1.43–1.61 (Me$CH_2CH_2CH_2$); 1.43–1.61 (Me$CH_2CH_2CH_2$) ↔ 1.10 (Me$CH_2CH_2CH_2$), 1.32 (Me$CH_2CH_2CH_2$); 2.24 (Me–C(2′)) ↔ 6.07 (H–C(3′), low intensity); 2.34 (OH–C(1′)) ↔ 4.20 (H–C(1′)); 4.20 (H–C(1′)) ↔ 2.24 (Me–C(2′)), 5.08 (H–C(5)); 5.08 (H–C(5)) ↔ 4.20 (H–C(1′)); 6.07 (H–C(3′)) ↔ 2.24 (Me–C(2′), low intensity); no cross-peak H–C(4) ↔ H–C(5). ^{13}C-NMR (125.7 MHz, $CDCl_3$; unknown contaminant at δ 29.69): 9.85 (flanked by Sn-isotope satellites as 2 *d*, ^1J(C,^{119}Sn) = 361.5, ^1J(C,^{117}Sn) = 345.1, 3 Me$CH_2CH_2CH_2$); 13.60 (3 *Me*$CH_2CH_2CH_2$); 16.13 (*Me*–C(2′)); 27.13 (flanked by Sn-isotope satellites as *d*, ^3J(C,Sn) = 59.0, 3 Me$CH_2CH_2CH_2$); 28.88 (flanked by Sn-isotope satellites as *d*, ^2J(C,Sn) = 21.8, 3 Me$CH_2CH_2CH_2$); 59.98 (*q*, ^2J(C,F) = 36.5, CF_3CH_2); 76.86 (C(1′) see edHSQC)); 85.62 (flanked by Sn-isotope satellites as *d*, ^3J(5,Sn) = 33.0, C(5) (see edHSQC)); 116.23 (C(3′) (see edHSQC)); 123.03 (incompletely resolved *q*, ^1J(C,F) = 277.0, *C*F_3CH_2); 138.18 (C(3)); 157.83 (C(2′)[22]); 161.07 (more intense than the 2 preceding and the 2 following signals and thus not C_{quat}, flanked by Sn-isotope satellites as *d*, ^2J(C,Sn) = 15.8, C(4); *cf.* C(3′)); 163.98 (*C*O_2Tfe[22])); 176.89 (C(2)[22])). edHSQC (C,H-COSY, 125.7/499.9 MHz, $CDCl_3$): 9.85 ($CH_3CH_2CH_2CH_2$) ↔ 1.10 ($CH_3CH_2CH_2CH_2$); 13.60 (*C*$H_3CH_2CH_2CH_2$) ↔ 0.89 (*CH*$_3$$CH_2CH_2CH_2$); 16.13 (*C*$H_3$–C(2′)) ↔ 2.24 (*CH*$_3$–C(2′)); 27.13 ($CH_3CH_2CH_2CH_2$) ↔ 1.32 ($CH_3CH_2CH_2CH_2$); 28.88 ($CH_3CH_2CH_2CH_2$) ↔ 1.43–1.61 ($CH_3CH_2CH_2CH_2$); 59.98 ($CF_3CH_2$) ↔ 4.49, 4.51 ($CF_3CH_2$); 76.86 (C(1′)) ↔ 4.20 (*H*–C(1′)); 85.62 (C(5)) ↔ 5.08 (*H*–C(5)); 116.23 (C(3′)) ↔ 6.07 (*H*–C(3′)). HR-EI-MS (70 eV): 513.0931 ([*M* – Bu]$^+$, $C_{19}H_{28}F_3O_5Sn^+$; calc. 513.0911).

*(5*Z*)-3-[(1*E*)-2-(1,2-Epoxy-2,6,6-trimethylcyclohexyl)ethenyl]-5-{(2*E*)-3-[(2,2,2-trifluoroethoxy)carbonyl]prop-2-enyliden}furan-2(5*H*)-one* (*=2,2,2-Trifluoroethyl (2*E*,4*Z*)-3-Methyl-4-{5-oxo-4-[(1*E*)-2-(2,2,6-trimethyl-7-oxabicyclo[4.1.0]hept-1-yl)ethenyl]furan-2(5 H)-ylidene}but-2-enoate*; **31**). At –30° and excluding light, DEAD (0.112 ml, 123 mg, 0.707 mmol, 6 equiv.) was added to a soln. of **29** (52.4 mg, 0.118 mmol) in degassed THF (8 ml; containing 250 mg/l of 2,6-di-(*tert*-butyl)cresol). After 10 min of stirring, PPh_3 (186 mg, 0.707 mmol, 6 equiv.) was added in one portion. After 1 h, the solvent was removed at –30° *in vacuo*. The remaining crude product was purified by FC (3.5-cm column, degassed cyclohexane/AcOEt 10:1, with 0.9% Et_3N): **31** (35.3 mg, 70%). Yellow solid. IR (film): 3080, 2960, 2930, 2870, 2855, 1780, 1730, 1600, 1570, 1445, 1410, 1380, 1365, 1285, 1255, 1220, 1170, 1140, 1065, 1045, 980, 955, 940, 890, 845, 815, 765. ^{1}H-NMR (499.9 MHz, C_6D_6; sample containing 2.7 wt.-% of (5*E*)-isomer, determined by its *d* at 7.46 (*J*(2′,1′) = 15.7, H–C(2′))): 0.93 (*ddd*, J_{gem} = 13.2, *J*(5″,4″a) = 7.1, *J*(5″,4″b) = 3.1, H_a–C(5″)); 1.05, 1.08, 1.09 (3 *s*, Me–C(2″), 2 Me–C(6″)); 1.17–1.27 (*m*, H_a–C(4″)); 1.30–1.37 (*m*, H_b–C(4″)); 1.49 (*m*, H_a–C(3″), H_b–C(5″)); 1.81 (*ddd*, J_{gem} = 15.2, *J*(3″,4″a) = 8.6, *J*(3″,4″b) = 6.6, H_b–C(3″)); 2.54 (*d*, ^4J(Me,3‴) = 1.4, Me–C(2‴)); 4.07 (*q*, ^3J(H,F) = 8.7, CF_3CH_2); 4.75 (*s*, H–C(1‴)); 5.76 (*dq*, ^4J(3‴,1‴) = ^4J(3‴,Me) = 1.2, H–C(3‴)); 5.86 (*s*, H–C(4)); 6.49 (*d*, *J*(1′,2′) = 15.5, H–C(1′)); 7.55 (*d*, *J*(2′,1′) = 15.5, H–C(2′)). DQF-COSY (H,H-COSY, 499.9 MHz, C_6D_6): 0.93 (H_a–C(5″)) ↔ 1.30–1.37 (H_b–C(4″)), 1.49 (*inter alia* H_b–C(5″)); 1.17–1.27 (H_a–C(4″)) ↔ 1.30–1.37 (H_b–C(4″)), 1.49 (H_a–C(3″), H_b–C(5″)), 1.81 (H_b–C(3″)); 1.30–1.37 (H_b–C(4″)) ↔ 0.93 (H_a–C(5″)), 1.17–1.27 (H_a–C(4″)), 1.49 (H_a–C(3″), H_b–C(5″)), 1.81 (H_b–C(3″)); 1.49 (H_a–C(3″), H_b–C(5″)) ↔ 0.93

(H_a–C(5″)), 1.17–1.27 (low intensity, H_a–C(4″)), 1.30–1.37 (low intensity, H_b–C(4″)), 1.81 (H_b–C(3″)); 1.81 (H_b–C(3″)) ↔ 1.17–1.27 (H_a–C(4″)), 1.30–1.37 (H_b–C(4″)), 1.49 (H_a–C(3″), H_b–C(5″)); 2.54 (Me–C(2‴)) ↔ 5.76 (H–C(3‴)); 5.76 (H–C(3‴)) ↔ 2.54 (Me–C(2‴)); 6.49 (H–C(1′)) ↔ 7.55 (H–C(2′)); 7.55 (H–C(2′)) ↔ 6.49 (H–C(1′)). ^{13}C-NMR (125.7 MHz, C_6D_6): 17.30 (C(4″) or *Me*–C(2‴)); 17.37 (*Me*–C(2‴) or C(4″)); 20.80, 25.96, 26.17 (*Me*–C(2″), 2 *Me*–C(6″)); 30.32 (C(3″)); 33.88 (lower intensity than preceding and following signal, C(6″)); 36.07 (C(5″)); 59.64 (*q*, ^2J(C,F) = 36.1, CF_3CH_2); 65.96 (C(2″)); 71.31 (C(1″)); 114.42 (C(1‴)); 120.56 (C(3‴)); 121.81 (C(1′)); 123.83 (incompletely visible *q*, ^1J(C,F) = 277.6, CF_3CH_2); 128.06 (C(3), tentative; lower intensity than δ 128.29 of solvent C_6D_5H); 135.98 (C(4)); 137.13 (C(2′)); 151.16, 152.69 (C(5), C(2‴); δ(olef. C) < δ(C(2) and CO_2Tfe)); 163.97, 167.31 (C(2) and CO_2Tfe)). edHSQC (C,H-COSY, 125.7/499.9 MHz, C_6D_6): 17.30, 17.37 (C(4″), CH_3–C(2‴)) ↔ 1.17–1.27 (H_a–C(4″)), 1.30–1.37 (H_b–C(4″)), 2.54 (CH_3–C(2‴)); 20.80, 25.96, 26.17 (CH_3–C(2″), 2 CH_3–C(6″)) ↔ 1.05, 1.08, 1.09 (CH_3–C(2″), 2 CH_3–C(6″)); 30.32 (C(3″)) ↔ 1.49 (*inter alia* H_a–C(3″)), 1.81 (H_b–C(3″)); 36.07 (C(5″)) ↔ 0.93 (H_a–C(5″)), 1.49 (*inter alia* H_b–C(5″)); 59.64 (CF_3CH_2) ↔ 4.07 (CF_3CH_2); 114.42 (C(1‴)) ↔ 4.75 (*H*–C(1‴)); 120.56 (C(3‴)) ↔ 5.76 (*H*–C(3‴)); 121.81 (C(1′)) ↔ 6.49 (*H*–C(1′)); 135.98 (C(4)) ↔ 5.86 (*H*–C(4)); 137.13 (C(2′)) ↔ 7.55 (*H*–C(2′)). ROESY (499.9 MHz, C_6D_6): 4.75 (H–C(1‴)) ↔ 5.76 (H–C(3‴)), 5.86 (H–C(4)); 5.76 (H–C(3‴)) ↔ 4.75 (H–C(1‴)); 5.86 (H–C(4)) ↔ 4.75 (H–C(1‴)), 6.49 (H–C(1′)); 6.49 (H–C(1′)) ↔ 5.86 (H–C(4), 7.55 (H–C(2′)); 7.55 (H–C(2′)) ↔ 6.49 (H–C(1′)). HR-EI-MS (70 eV): 426.1653 (M^+, $C_{22}H_{25}F_3O_5^+$; calc. 426.1654).

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