Stereoselective synthesis of freelingyne and related γ-alkylidenebutenolides *via* vinylogous Mukaiyama aldol additions§

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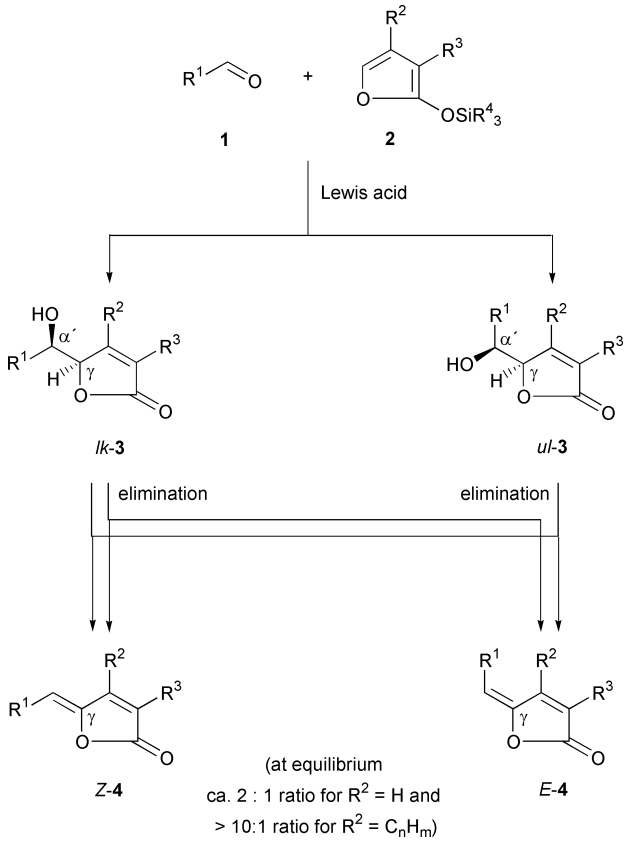
Following the strategy of Scheme 1, a Mukaiyama aldol addition/*anti*-elimination route to stereopure γ-alkylidenebutenolides **4** was established. The addition giving **27** was only moderately diastereoselective but the products *lk*- and *ul*-**27** were chromatographically separable (Scheme 4). They underwent highly selective *anti*-eliminations in the presence of triflic anhydride–pyridine or Burgess' reagent, furnishing the thiophene-containing butenolides *Z*- and *E*-**28**, respectively (Scheme 5). The Mukaiyama aldol addition leading to compound **29** was 100% *lk*-selective when mediated by BF_3 etherate and 87 : 13 *ul*-selective in the presence of $ZnBr_2$ (Scheme 6). Stephens–Castro couplings of the resulting butenolides *lk*- and *ul*-**29** with 3-ethynylfuran proceeded with complete conservation of the stereochemical integrity (Scheme 7). The subsequent *anti*-eliminations of water were best realized by treatment with DEAD–PPh_3. They provided freelingyne (*Z*-**9**) with *ds* = 92 : 8 and its isomer *E*-**9** with *ds* = 98 : 2 (Scheme 8). Analogously, the differently substituted (trimethylsiloxy)furans **15** or **16** provided the freelingyne analogs *Z*-**10**, *E*-**10** and *Z*-**11** (Schemes 6–8).

Background

γ-Lactones constitute the core of many natural and unnatural products.[1] Some of them contain alkylidene substituents—for example, the γ-alkylidene-α,β-unsaturated γ-lactones *Z*- and *E*-**4** (Scheme 1; "γ-alkylidenebutenolides"). We developed a stereoselective synthesis for such compounds that is based upon the *anti*-selective dehydration of type **3** γ-(αhydroxyalkyl)butenolides.[2–6] Ideally, diastereomers *lk*-**3** lead to stereopure γ-alkylidenebutenolides *Z*-**4** and their epimers *ul*-**3** to stereopure γ-alkylidenebutenolides *E*-**4**. Effecting such eliminations with a mixture of triflic anhydride and pyridine, we synthesized unnatural γ-alkylidenebutenolides[2] **4** as well as dihydroxerulin,[3] xerulin[4] and lissoclinolide (≡tetrenolin).[5]

As described in the following, we have now extended this strategy to stereoselective syntheses of the γ-alkylidenebutenolides freelingyne (*Z*-**9**[7] in Scheme 2; constituent of wood oil from *Eremophila freelingii*), *E*-freelingyne (*E*-**9**), "norfreelingyne" (*Z*-**10**), "*E*-norfreelingyne" (*E*-**10**) and "*Z*-isofreelingyne" (*Z*-**11**).[6] A part of this study involves the unexpectedly stereoselective Mukaiyama aldol additions of type-**2** siloxyfurans to aldehydes **1**,[8] which constitute a concise preparation of type-**3** elimination substrates. Our elimination protocol for the dehydrations *lk*-**32** → *Z*-**9** and *ul*-**32** → *E*-**9**[6] has already been found useful by Takayama *et al.*[9] for the penultimate step of their synthesis of the γ-alkylidenebutenolide pandamarilactam-3y. Last but not least, the reactions used here should be adaptable for synthesizing the carotinoid γ-alkylidenebutenolides peridinin (**5**)[10] and pyrrhoxanthin (**8**)[11] (Scheme 2) in a more efficient way than presently known.[12]

The early approaches to freelingyne suffered from the absence of stereocontrol.[13,14] In 1997, two independently



Scheme 1

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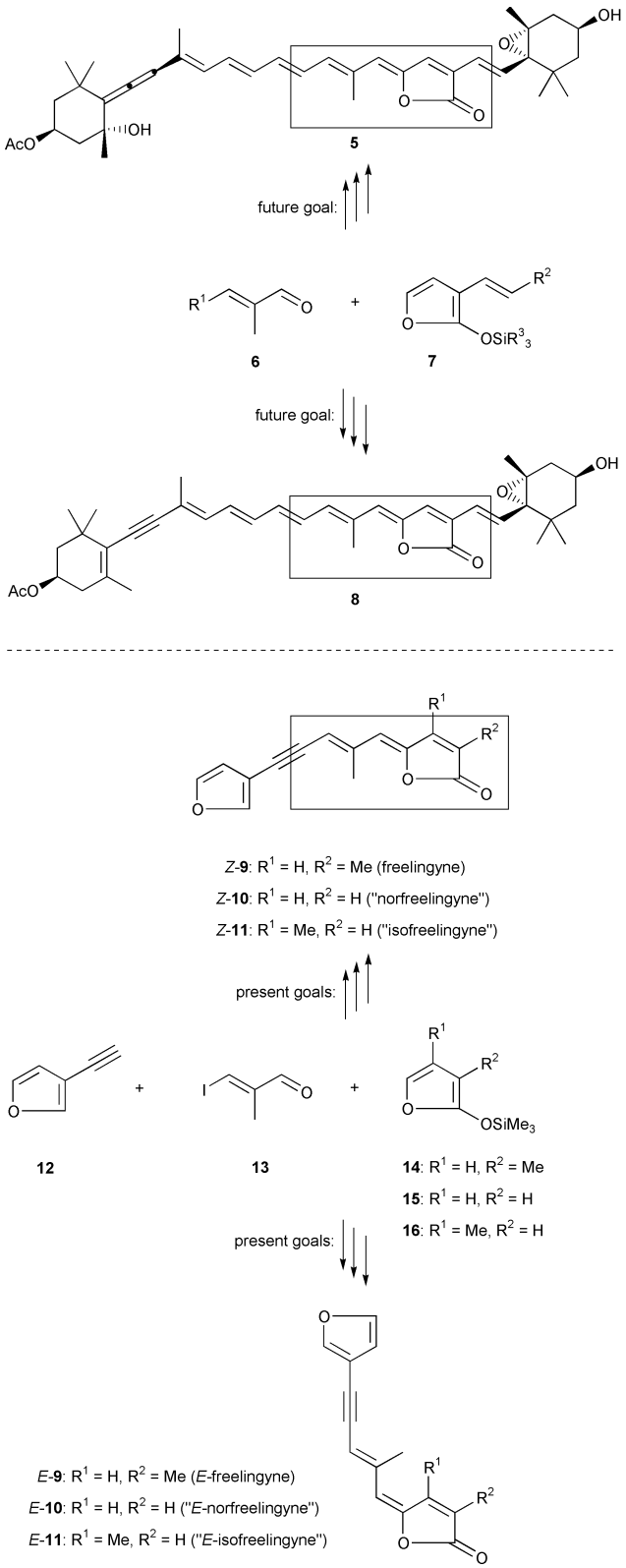
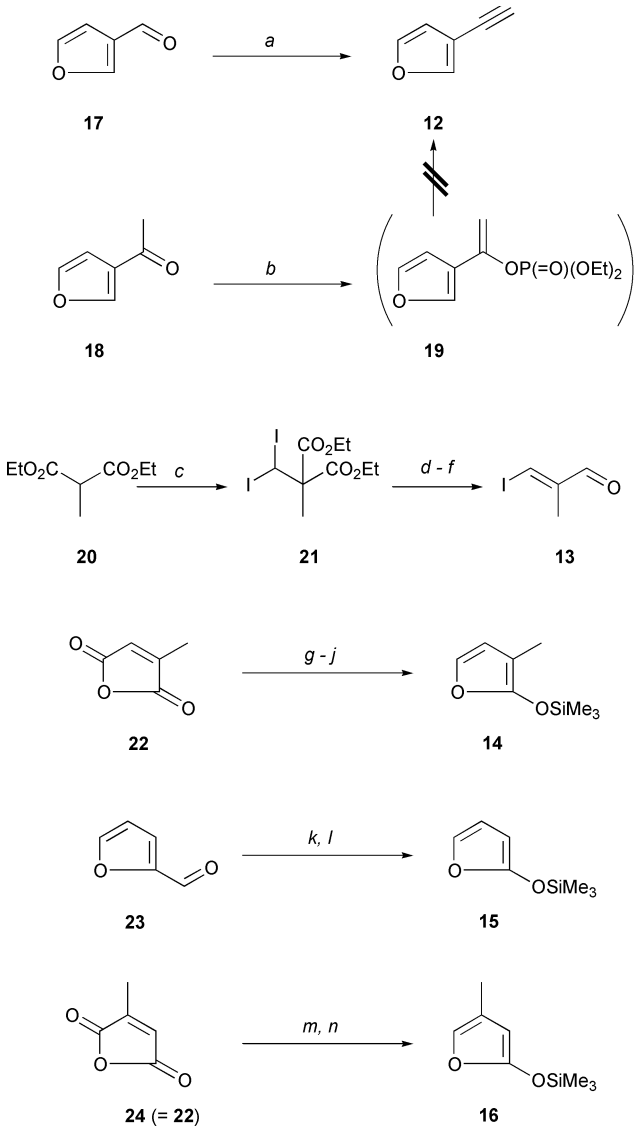
‡ Dedicated to R.B.'s academic teacher, Professor Rolf Huisgen (Ludwig-Maximilians-Universität München), on the occasion of his 80th birthday.

§ Electronic supplementary information (ESI) available: selected detailed NMR data for some of the compounds synthesized. See http://www.rsc.org/suppdata/nj/b0/b002903n/

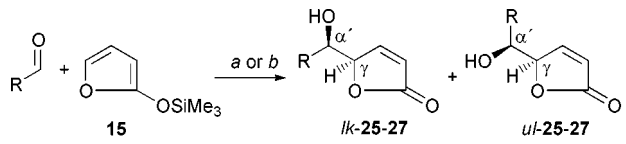


Scheme 2



Scheme 3 (*a*) LDA (1.2 equiv.), Me_3SiCHN_2 (1.2 equiv.), THF, −78 °C, 30 min; **17** (1.0 equiv.), −78 °C, 1 h; room temp., 30 min; *ca.* 48%. (*b*) LDA (1.0 equiv.), −78 °C, 1 h; diethylchlorophosphate (1.0 equiv.) → room temp.; 77%. (*c*) NaH (1.0 equiv.), Et_2O, reflux, 2.5 h; CHI_3 (1.0 equiv.), reflux, 20 h; 74% (lit.[23]: 65%). (*d*) KOH (3.1 equiv.), EtOH–H_2O (3 : 1), reflux, 24 h; 80% (lit.[23]: 89%). (*e*) $LiAlH_4$ (1.0 equiv.), THF, 0 °C, 1 h; 53% (lit.[23]: 70%). (*f*) MnO_2 (10 equiv.), CH_2Cl_2, room temp., 4.5 h; 81% (lit.[23]: >65%). (*g*) Dicyclohexylamine (1.1 equiv.), MeOH, −15 °C, 30 min; room temp., 3 h; 77% (lit.[24]: 80–85%). (*h*) $ClCO_2Bu$ (1.0 equiv.), CH_2Cl_2, −12 °C, 12 h (lit.[24]. with $ClCO_2Bu^i$). (*i*) $NaBH_4$ (2.0 equiv.), THF, 0 °C, 3 h; 65% over the two steps (lit.[24]: 80% over the two steps). (*j*) LDA (1.05 equiv.), Me_3SiCl (1.2 equiv.), −78 °C, 10 min; 0 °C, 1 h; 56% (lit.[27]: yield not specified). (*k*) HCO_2H (2.0 equiv.), 2-(dimethylamino)ethanol (0.4 equiv.), H_2O_2 (35%; 1.6 equiv.), CH_2Cl_2, first reflux temp. because reaction is exothermic, then room temp. overnight, 12 h; 41% (lit.[28]: 41%). (*l*) Me_3SiCl (1.3 equiv.), NEt_3 (1.3 equiv.), Et_2O, −15 °C → room temp., 20 h; 36% (lit.[29]: 38%). (*m*) $NaBH_4$ (1.0 equiv.), THF, 0 °C, 45 min; room temp. 1.5 h; 40% (lit.[30]: 43%). (*n*) LDA (1.05 equiv.), Et_2O, 30 min; Me_3SiCl (1.2 equiv.), 2 h; room temp.; 67%.

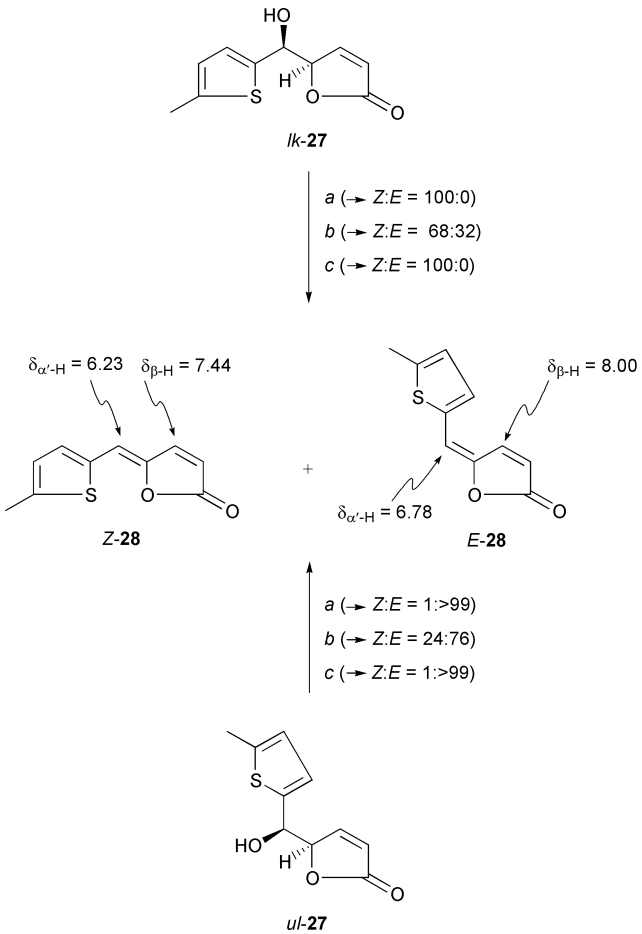
developed, yet strategically identical syntheses of freelingyne were published by Katsumura *et al.*[15] and by Liu and Negishi;[16] they are based upon the palladolactonization of a C≡C-containing carboxylic acid, followed by protonolysis of the resulting palladium–carbon bond. *Our* synthesis transforms the 4-step molecules **13** (25% overall yield) and **14** (28% overall yield) and compound **12** (prepared in a single step in *ca.* 48% yield) in 3 steps (37% yield) into the 92 : 8 mixture of freelingyne (*Z*-**9**) and its *E*-isomer. This corresponds to a 9–10% overall yield of the longest linear sequence. The Katsumura synthesis of freelingyne is 9 steps long (6% overall yield) but requires additional steps for preparing the starting materials ethyl *E*-β-bromomethacrylate and *Z*-γ-iodomethallyl alcohol. The Negishi synthesis is 9 steps long (14% overall yield) but needs another 3 steps for accessing ethyl *E*-β-iodomethacrylate. Accordingly, with respect to *Z*-**9**, our route ranks first in terms of step requirement and second in terms of overall yield. Moreover, distinct from its predecessors, it can be forged either selectively towards the natural *Z*- or selectively towards the unnatural *E*-isomer.



Aldehyde	Conditions	Product	Yield	Diastereomeric ratio
	a	**25***	69%	78 : 22
	b		65%	68 : 32
	a	**26***	45%	59 : 41
	b		44%	82 : 18
	a	-	-	other reactions occurred
	b		-	other reactions occurred
	a	**28**	40%	72 : 28
	b		38%	69 : 31

*Configurational assignments interchangeable.

Scheme 4 Mukaiyama aldol addition reactions between a representative siloxyfuran and α,β-unsaturated aldehydes. (*a*) $BF_3 \cdot OEt_2$ (1.0 equiv.), aldehyde (1.0 equiv.), CH_2Cl_2, −78 °C, 2.5 h; 69% **25**, 45% **26**, 40% **27**. (*b*) $ZnBr_2$ (1.0 equiv.), aldehyde (1.0 equiv.), CH_2Cl_2, −78 °C, 2.5 h; 65% **25**, 44% **26**, 38% **27**.



Scheme 5 Model eliminations leading to γ-alkylidenebutenolides (^1H NMR shifts in $CDCl_3$). (*a*) Pyridine (2.0 equiv.), CH_2Cl_2, −30 °C, 10 min; Tf_2O (3.0 equiv.) → room temp.; 67% from *lk*-**27**; 70% from *ul*-**27**. (*b*) MsCl (2.0 equiv.), CH_2Cl_2, 0 °C, 20 min; NEt_3 (4.0 equiv.), 30 min; 73% from *lk*-**27**, 68% from *ul*-**27**. (*c*) Burgess reagent (1.1 equiv.), benzene, 50 °C, 1 h; 43% from *lk*-**27**, 35% from *ul*-**27**.

Reactants

The preparatory steps of our route comprised syntheses of the furylacetylene **12**, *E*-3-iodomethacrolein (**13**) and the trimethylsiloxylated furans **14**–**16** (Scheme 3).

Furylacetylene **12** was generated in THF solution by a Peterson olefination of 2-furancarbaldehyde (**17**) with lithio(trimethylsilyl)diazomethane, followed by the expulsion of nitrogen and a vinylidene → acetylene rearrangement.[17] Since the yield of **12** did not exceed 48%, we checked several alternatives [dibromomethylenation or dichloromethylenation of **17** followed by treatment with excess *n*-BuLi[18] or MeLi,[19] respectively; conversion of acetylfuran **18** into enol phosphate **19** (77%) and treatment of the latter with excess LDA;[20] Diels–Alder reaction between 4-phenyl-1,3-oxazole and 1,4-bis(trimethylsilyl-1,3-butydiyne), followed by 4 + 2 cycloreversion[21] and desilylation with Bu_4NF;[21,22] $Pd(PPh_3)_4$ catalyzed coupling of 3-bromofuran with bis(tributylstannyl)acetylene] but discarded them as inferior.

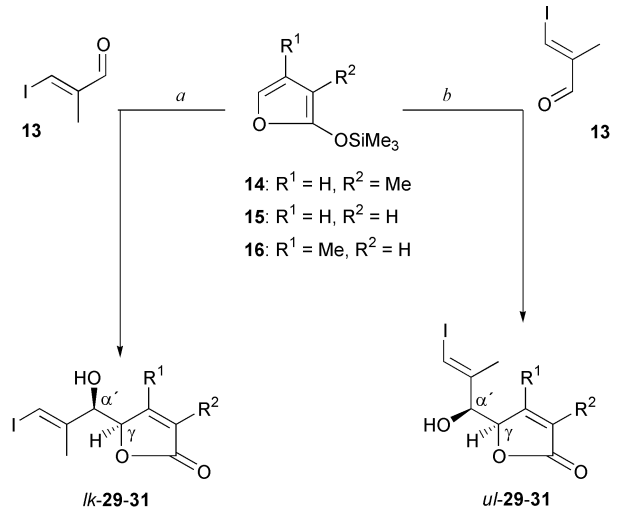
E-3-Iodomethacrolein (**13**) was prepared by the procedure of Baker and Castro,[23] starting with the diiodomethylenation of diethyl methylmalonate (**20**).

For preparation of the 3-methylated siloxyfuran **14** we used Zwanenburg *et al.*'s synthesis of the underlying α-methyl-Δ^3-butenolide.[24] This route was easier to perform than the alternative sequence γ-butyrolactone → α-(hydroxymethylene)-γ-butyrolactone[25] → α-methylene-γ-butyrolactone[25] → α-methyl-Δ^3-butenolide.[26] The α-methyl-Δ^3-butenolide was then trimethylsilylated as described by Morimoto *et al.*[27] The Me_3Si group introduced thereby enabled the resulting siloxyfuran **14** to undergo the intended Mukaiyama aldol addition to aldehyde **13** (*vide infra*), while no such addition could be observed with the *tert*-$BuMe_2Si$ analog[26] of **14**. The non-methylated (trimethylsiloxy)furan **15** was obtained in two steps from furfural (**23**) as described in the literature.[28,29] β-Methyl-Δ^3-butenolide resulted from the $NaBH_4$ reduction of anhydride **24** (which had already been the progenitor of α-methyl-Δ^3-butenolide *en route* to siloxyfuran **14**) following a procedure of Johnson *et al.*[30] It was trimethylsilylated by successive treatment with LDA and Me_3SiCl, rendering compound **16** in 67% yield.

Results

In our previous syntheses of γ-alkylidenebutenolides, their type-**3** precursors stemmed from sugar lactones.[2–5] In the present study, we prepared them by Mukaiyama aldol additions between the siloxyfurans **14**–**16** and suitable aldehydes. A high degree of simple diastereoselectivity in such aldol additions had been limited to the use of α-*chiral* aldehydes; there, considerable *lk*-selectivity occurred.[10] In contrast, Mukaiyama aldol additions of siloxyfuran **15** to achiral aldehydes[31] such as R_{prim}–CH=O, R_{sec}–CH=O and R_{tert}–CH=O were only moderately *lk*-selective [*ds* = 66 : 34–81 : 18; promotion by $SnCl_4$,[32,33] $TiCl_4$,[33] $Ti(BINOL)(OiPr)_2$,[33] $Sc(ClO_4)_3$,[33] $ZnCl_2$,[34] $ZnBr_2$,[34] $BF_3 \cdot OEt_2$,[33,34] $TritClO_4$,[33,34] Me_3SiOTf[34] or Et_3SiOTf[34]]. Just once, in the presence of $SnCl_2$ and towards octanal, an almost satisfactory 90 : 10 *lk* : *ul* selectivity was found.[33] Interestingly, using CsF[34] or Bu_4NF[33,34] as catalysts, the same aldehydes and siloxyfuran **15** reacted to give moderate *ul*-selectivity (*ds* = 67 : 33–70 : 30 for R_{prim}–CH=O[33,34] and Pr^i–CH=O,[34] 88 : 12 for Bu^t–CH=O[33]).

Clearly, for making freelingyne (*Z*-**9**), its analogs (*E*-**9**, **10**, **11**) or the long-term targets peridinin (**5**) and pyrrhoxanthin (**8**) *via* a Mukaiyama aldol addition, the most suitable substrates are α,β-unsaturated aldehydes. Therefore, several of them were subjected to such additions of siloxyfuran **15** and the simple diastereoselectivity determined (Scheme 4). However, the *lk*-selectivities observed (69 : 31–72 : 28 starting



	R^1	R^2	Yield	*ds*	$\delta_{\alpha'\text{-H}}$	$\delta_{\gamma\text{-H}}$	$\delta_{\text{C-}\alpha'}$	$\delta_{\text{C-}\gamma}$
lk-**29**	H	Me	56%	>99:<1	4.26	5.05	74.84	82.81
ul-**29**	H	Me	61%	13:87	4.16	4.99	75.38	81.73
lk-**30**	H	H	54%	>99:<1	4.27	5.10	76.89	84.40[1)]
ul-**30**	H	H	51%	18:82	4.43	5.09	75.03	83.54[2)]
lk-**31**	Me	H	46%	>99:<1	4.39	4.97	73.90	85.19[3)]
ul-**31**	Me	H	55%	20:80	4.47	4.99	75.38	84.56[4)]

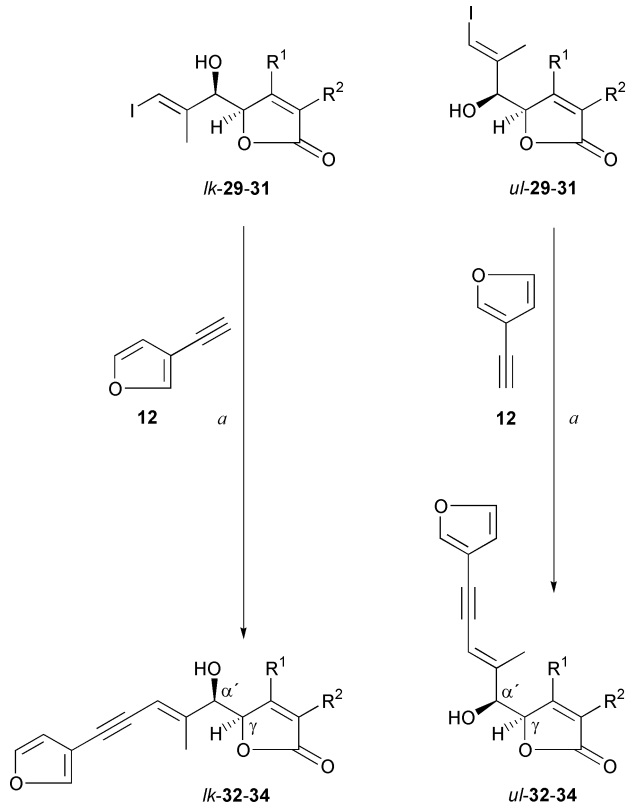
[1)]Or 82.30 (which is tentatively assigned to C-γ′).- [2)]Or 81.72 (which is tentatively assigned to C-γ′).- [3)]Or 81.19 (which is tentatively assigned to C-γ′).- [4)]Or 81.95 (which is tentatively assigned to C-γ′).

Scheme 6 Diastereoselective vinylogous Mukaiyama aldol addition reactions [NMR shifts in DMSO-d_6 for **29** and in $CDCl_3$ for **30** and **31**, at 300 MHz for ^{1}H and at 50 MHz (75 MHz for *lk*-**29**) for ^{13}C]. (*a*) $BF_3 \cdot OEt_2$ (1.0 equiv.), **13** (1.0 equiv.), CH_2Cl_2, −78 °C, 2.5 h; 56% *lk*-**29**, 54% *lk*-**30**, 46% *lk*-**31**. (*b*) $ZnBr_2$ (1.0 equiv.), **13** (1.0 equiv.), CH_2Cl_2, −78 °C, 2.5 h; 61% *ul*-**29**, 51% *ul*-**30**, 55% *ul*-**31**.

from 5-methylthiophene-2-carbaldehyde, ⩽82 : 18 starting from acetaldehyde or *trans*-crotonaldehyde) remained below our needs. Our distinction of *lk*- *vs.* *ul*-**25**–**27** is partly tentative. On the one hand, it is based upon the assumption that the *lk*-isomer is the major and the *ul*-isomer the minor product because this would be analogous to the preferred course of the **15**-additions to the saturated achiral aldehydes cited above. These assignments would mean that a small high-field shift of the γ- and α′-^{1}H-NMR resonances[35] occurs in some of the *lk*- *vs.* *ul*-isomers.¶ On the other hand, *lk*- and *ul*-**27** were distinguished unambiguously after separation by flash chromatography on silica gel,[36] namely by the steric course of the elimination reactions shown in Scheme 5.

Treatment of the thiophene-containing type-**3** hydroxybutenolides *lk*-**27** and *ul*-**27** under well-tested conditions[2–5]—triflation with Tf_2O in the presence of pyridine in dichloromethane at −30 °C, followed by β-elimination upon warming to room temperature—led to the alkylidenebutenolides *Z*- and *E*-**28** as single isomers in 67 and 70% yield, respectively (Scheme 5). The configuration of the newly established $C^{\alpha'}=C^{\gamma}$ bond was inferred from NOESY spectra, depending on whether the β-H correlated with α′-H (*Z*-**28**) or not (*E*-**28**). *Z*-**27** had been isolated from the roots of *Chamaelum nobile* L. and synthesized non-stereoselectively twice.[37] Dehydrations of

¶ The NMR resonances for the lk- and ul-isomers are respectively [$\delta_{\gamma\text{-H, lk-25}} = 7.45$, $\delta_{\gamma\text{-H, lk-26}} = 7.47$, $\delta_{\gamma\text{-H, lk-27}} = 7.60$; $\delta_{\alpha'\text{-H, lk-25}} = 3.93$, $\delta_{\alpha'\text{-H, lk-26}} = 4.22$, $\delta_{\alpha'\text{-H, lk-27}} = 5.04$ (exception!)] and [$\delta_{\gamma\text{-H, ul-25}} = 7.56$, $\delta_{\gamma\text{-H, ul-26}} = 7.54$, $\delta_{\gamma\text{-H, ul-27}} = 7.64$; $\delta_{\alpha'\text{-H,ul-25}} = 4.05$, $\delta_{\alpha'\text{-H,ul-26}} = 4.39$, $\delta_{\alpha'\text{-H,ul-27}} = 5.00$ (exception!)]



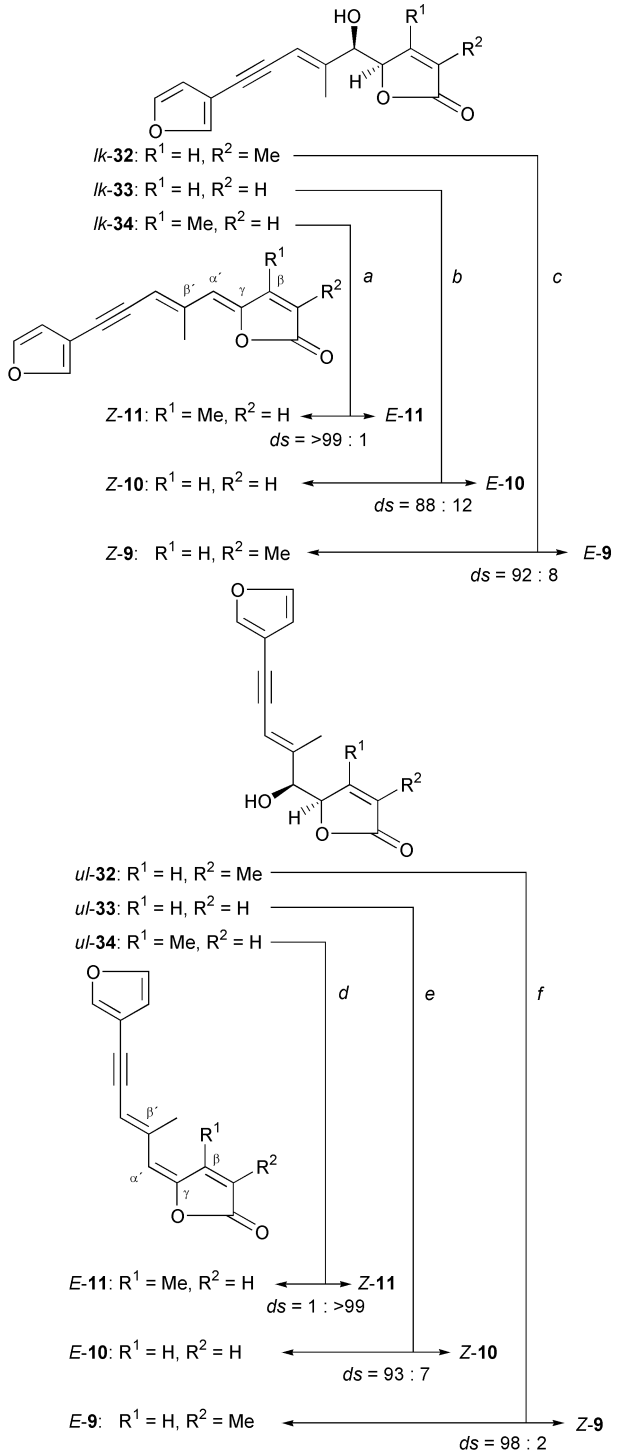
	R^1	R^2	Yield	*ds*	$\delta_{\alpha'\text{-H}}$	$\delta_{\gamma\text{-H}}$	$\delta_{\text{C-}\alpha'}$	$\delta_{\text{C-}\gamma}$
lk-**32**	H	Me	70%	>99:1	4.12	4.97	77.06	82.80
ul-**32**	H	Me	76%	>99:1	4.44	4.99	74.60	81.64
lk-**33**	H	H	68%	>99:1	4.22	5.13	76.39	84.99
ul-**33**	H	H	73%	>99:1	4.47	5.13	76.37	84.03
lk-**34**	Me	H	71%	>99:1	4.39	5.00	[1)]	[1)]
ul-**34**	Me	H	76%	>99:1	4.50	5.03	74.98	84.90

[1)]Not measured.

Scheme 7 (*a*) **12** (1.2 equiv.), $Pd(PPh_3)_4$ (5 mol%), CuI (0.1 equiv.), THF–$(Pr^i)_2NEt$ (4 : 1), room temp., 30 min. ^{1}H NMR shifts (in $CDCl_3$) at 300 MHz (**32** at 400 MHz); ^{13}C NMR shifts (in $CDCl_3$) at 50 (**32**, *lk*-**33**) or at 126 (*ul*-**33**, *ul*-**34**) MHz.

lk- and *ul*-**27** with MsCl–NEt_3 proceeded with comparable yields to compounds *Z*- and *E*-**28** but suffered from 32% and 24% loss of configurational homogeneity, respectively. When treated with Burgess' reagent,[38] *lk*- and *ul*-**27** underwent perfectly *anti*-selective β-eliminations but yields were lower (43% *Z*-**28** and 35% *E*-**28**).

The successful eliminations *lk*-**27** → *Z*-**28** and *ul*-**27** → *E*-**28** of Scheme 5 suggested that if we were able to synthesize (trimethylsiloxy)furan-based Mukaiyama aldol addition products of *appropriate* α,β-unsaturated aldehydes diastereopure, we ought to be able to dehydrate them *anti*-selectively, too, thus gaining the desired access to freelingyne and its congeners. Fortunately, according to Scheme 6 various (trimethylsiloxy)furans and β-iodomethacrolein (**13**) underwent such Mukaiyama additions with much more diastereocontrol than the α,β-unsaturated aldehydes examined in Scheme 4. Performing the said reactions in the presence of BF_3 etherate, all of the (trimethylsiloxy)furans **14**–**16** reacted with >99% *lk*-selectivity to furnish compounds *lk*-**29**–**31** in 49 ± 5% yield. When the same Mukaiyama additions were induced by $ZnBr_2$ we observed the opposite diastereoselectivities, namely 87 : 13, 81 : 18 and 80 : 20 *ul*-preferences, respectively. In these instances, hydrolysis of the reaction



	R^1	R^2	$\delta_{\alpha'\text{-H}}$	$\delta_{\beta\text{-H}}$	$\delta_{\text{C-}\beta'}$	$\delta_{\text{C-}\alpha'}$	$\delta_{\text{C-}\gamma}$	$\delta_{\text{C-}\beta}$
Z-**9**	H	Me	5.64	7.03	143.86	114.38	147.34	138.90
E-**9**	H	Me	6.31	7.50	142.38	116.63	148.97	134.40
Z-**10**	H	H	5.76	7.38	143.57	112.28*	148.33	143.05*
E-**10**	H	H	6.43	7.83	142.04	112.26*	149.98	139.81*
Z-**11**	Me	H	5.77	-	144.12	111.20	154.71	149.75

*Assignment ambiguous.

Scheme 8 (*a*) DEAD (2.0 equiv.), PPh_3 (2.0 equiv.), THF, 0 °C, 2 h; 91% *Z*-**11**. (*b*) Same as (*a*); 83% of a *Z*-**10**/*E*-**10** mixture. (*c*) Same as (*a*) except −40 °C, 5 h; 0 °C, 30 min; 94% of a *Z*-**9**/*E*-**9** mixture. (*d*) Same as (*a*); 24% *Z*-**11**. (*e*) Same as (*a*); 98% of a *E*-**10**/*Z*-**10** mixture. (*f*) Same as (*a*); 87% of a *E*-**9**/*Z*-**9** mixture. δ values in $CDCl_3$ (*Z*-**11**: in C_6D_6) at 300 MHz (δ^1_H), 50 MHz (δ^1_C; *Z*-**9**, *E*-**9**, *E*-**10**) or 125 MHz (δ^{13}_C; *Z*-**10**, *Z*-**11**).

mixture and flash chromatography[36] furnished the previously unformed aldol adducts *ul*-**29**–**31** (56 ± 5% yield) from the early fractions and their diastereomers *lk*-**29**–**31** from the late fractions.

The resonances of the protons at the stereocenters of compounds **29**–**31** (α′-H and γ-H in Scheme 6), as well as those of the ^{13}C nuclei attached to them (C-α′ and C-γ), exhibit inconspicuous and non-uniform dependences on the *lk- vs. ul*-configuration. Therefore, no configurational assignment could be based upon them. The stereostructures of compounds *lk*-**29**, *ul*-**29**, *lk*-**30** and *ul*-**30** were inferred in hindsight. This is because these compounds were carried on *via* *lk*-**32**, *ul*-**32**, *lk*-**33** and *ul*-**33** (Scheme 7) *stereoselectively* towards *Z*-**9**, *E*-**9**, *Z*-**10** and *E*-**10** (Scheme 8). The configurations of the latter compounds followed from ^{1}H-NMR criteria (*vide infra*). The stereostructures of compounds *lk*-**31** *vs. ul*-**31**—and, by consequence, also the stereostructures of their coupling products *lk*-**34** *vs. ul*-**34** in Scheme 8—were assigned by analogy of the preparation and diastereoselectivity: As with the unambiguously assignable compounds **29** and **30**, the BF_3-mediated access should have delivered exclusively the *lk*-isomer and the $ZnBr_2$-mediated access preponderantly the *ul*-isomer.

Each of the aldol adducts depicted in Scheme 7 was coupled under Pd(0) catalysis with the ethynylfuran **12** as summarized in Scheme 8. Coupling products *lk*- and *ul*-**32**–**34** were formed in yields of 72 ± 4% and diastereomerically pure. Their stereostructures were based upon the *lk vs. ul* distinction of their precursor iodides **29**–**31**. Based on that, the α′-^{1}H NMR resonances of coupling products **32**–**34** are shifted towards higher field in each *lk vs. ul*-isomer, while the γ-^{1}H NMR shift was invariant.

The ultimate step of our syntheses were the dehydrations of Scheme 8. To our consternation, the *anti*-eliminations *lk*-**32** → *Z*-**9** and *ul*-**32** → *E*-**9** did not yield even trace amounts of product when tried with the elsewhere successful[2–5] triflic anhydride–pyridine mixture. On the other hand, eliminations with excess DEAD–excess PPh_3[39] were high-yielding (94% *Z*-**9**, 87% *E*-**9**) and *anti*-selective. Thus, natural freelingyne (*Z*-**9**) resulted as a 92 : 8 *Z* : *E*- and the unnatural isomer *E*-**9** as a 98 : 2 *E* : *Z*-mixture. The Mitsunobu dehydrations *lk*-**33** → *Z*-**10**, *ul*-**33** → *E*-**10** and *ul*-**34** → *E*-**11** were similarly successful: yields were 83%, 98% and 87%, respectively, and stereoselectivities 88 : 12, 93 : 7 and >99 : 1. A notable exception was the Mitsunobu dehydration of compound *ul*-**34**, which gave 24% of only *Z*-**11** (*ds* > 99 : 1), thus representing a clean *syn*-elimination. One reason for this could be product-development control: formation of *E*-**11** through a one-step *anti*-elimination would be hindered through the arisal of allyl[1,3] strain. Alternatively, *E*-**11** may have been the kinetically preferred elimination product, which would have then undergone a thermodynamically controlled *E* → *Z* isomerization.

The configuration of the $C^{\alpha'}$=C^{γ} bond of freelingyne and *E*-freelingyne followed unambiguously from NOESY spectra, depending on whether the β-H correlated with α′-H (*Z*-**9**) or not (*E*-**9**). In addition, the high-field shifts that $\delta_{\alpha'\text{-H}}$ and $\delta_{\beta\text{-H}}$ experience in *Z- vs. E*-configurated γ-alkylidenebutenolides according to our previous experience[2–5] underline the stereochemical assignments of *Z- vs. E*-**9** and -**10** (Scheme 8). Since $\delta_{\alpha'\text{-H}}$ is 5.77 in the only isomer of γ-alkylidenebutenolide **11** that we obtained, and thereby resembles $\delta_{\alpha'\text{-H, }Z\text{-9}} = 5.64$ and $\delta_{\alpha'\text{-H, }Z\text{-10}} = 5.76$ while being distinct from $\delta_{\alpha'\text{-H, }E\text{-9}} = 6.31$ and $\delta_{\alpha'\text{-H, }E\text{-10}} = 6.43$, the *Z*-configuration can be assigned to compound **11**, too.

Experimental

General

All reactions were performed in oven-dried (100 °C) glassware under N_2. THF was freshly distilled from K and CH_2Cl_2

from CaH_2. Products were purified by flash chromatography[36] on Merck silica gel 60 (eluents given in brackets). Yields refer to analytically pure samples. ^1H [$CHCl_3$ (7.26 ppm) as internal standard in $CDCl_3$ or C_6HD_5 (7.16 ppm) as internal standard in C_6D_6 or DMSO-d_5 (2.49 ppm) as internal standard in DMSO-d_6] and ^{13}C NMR [$CDCl_3$ (77.00 ppm) as internal standard in $CDCl_3$ or C_6D_6 (128.00 ppm) as internal standard in C_6D_6 or DMSO-d_6 (39.70 ppm) as internal standard in DMSO-d_6] spectra were acquired on Varian VXR 200, Bruker AMX 300, Varian Inova 500 and Varian Unity 300 instruments. In ^1H NMR spectra the integrals are in accord with assignments and coupling constants are given in Hz; APT ^{13}C NMR spectra have peak orientations in accord with asssignments. The assignments of ^1H- and ^{13}C NMR resonances refer to the IUPAC nomenclature; primed numbers belong to the side-chain(s) in the order of their appearance in the IUPAC name. Ample use was made of H,H COSY spectra, delayed H,H COSY spectra, HMQC spectra as well as HMBC spectra for corroborating individual ^1H and ^{13}C assignments; the corresponding data are specified in the supplementary material to this article. Combustion analyses (Micro V/D, Heraeus) were performed by M. Beller and F. Hambloch (Institute of Organic Chemistry, University of Göttingen; mass spectra (MAT 95, Finnigan) were taken by Dr. G. Remberg (Institute of Organic Chemistry, University of Göttingen; IR spectra were acquired on a Perkin–Elmer 1600 Series FTIR.

Syntheses

5*Z*-5-[*E*-5-(3-Furanyl)-2-methyl-2-penten-4-yn-1-ylidene]-3-methyl-2(5*H*)-furanone. Freelingyne (*Z*-**9**; 24.9 mg, 94%) was obtained as a solid (mp 154–156 °C; lit.[7] 157–159 °C) 92 : 8 *Z* : *E*-mixture (according to the averaged ^1H-NMR integrals over the 1′-H's and 4-H's) from the diastereopure alcohol *lk*-**32** (28.4 mg, 0.112 mmol, 1.0 equiv.), DEAD (0.10 ml, 0.11 g, 0.66 mmol, 6.0 equiv.) and PPh_3 (0.18 g, 0.66 mmol, 6.0 equiv.) as described for the synthesis of compound *Z*-**10** except that we stirred at −40 °C for 5 h and at 0 °C for 30 min. ^1H NMR* (300 MHz): $\delta = 2.04$ (d, $^4J_{3\text{-Me},\,4} = 1.1$, 3-$CH_3$), 2.35 (d, $^4J_{2'\text{-Me},\,3'} = 0.8$, 2′-$CH_3$), 5.64 (s, 1′-H), 5.90 (br s, 3′-H), 6.47 (dd, $J_{4'',\,5''} = 1.9$, $^4J_{4'',\,2''} = 0.7$, 4″-H), 7.03 (hardly resolved q, $^4J_{4,\,3\text{-Me}} = 1.5$, 4-H), 7.40 (dd, $J_{5'',\,4''} = {}^4J_{5'',\,2''} = 1.7$, 5″-H), 7.66 (br s, 2″-H); *assignment analogous to ref. 40. $\{^1H\}$ decoupled ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 10.65$ (3-CH_3), 18.23 (2′-CH_3), 89.87 (C-5′), 90.58 (C-4′), 107.79 (C-3″), 112.31 (C-4″), 114.38 (C-1′), 114.99 (C-3′), 128.84 (C-3), 138.90 (C-4), 142.99 (C-5″), 143.86 (C-2′), 145.44 (C-2″), 147.34 (C-5), 170.82 (C-2). The *Z*-configuration of the $C^5{=}C^{1'}$ double bond was deduced from a 300 MHz NOESY spectrum where 4-H ($\delta = 7.03$) correlates with 1′-H ($\delta = 5.64$) [and with 3-CH_3 ($\delta = 2.04$)] but not with 2′-CH_3 ($\delta = 2.35$).

5*E*-5-[*E*-5-(3-Furanyl)-2-methyl-2-penten-4-yn-1-ylidene]-3-methyl-2(5*H*)-furanone. *E*-Freelingyne (*E*-**9**; 23.0 mg, 87%) was obtained as a solid (mp 156–157 °C; lit.[7] 158–159 °C) 98 : 2 *E* : *Z*-mixture (according to the averaged ^1H NMR integrals over the 1′-H's and 4-H's) from alcohol *ul*-**32** (28.4 mg, 0.112 mmol, 1.0 equiv.), DEAD (0.10 ml, 0.11 g, 0.66 mmol, 6.0 equiv.) and PPh_3 (0.18 g, 0.66 mmol, 6.0 equiv.) as described for compound *Z*-**10**. ^1H NMR (300 MHz)*: $\delta = 2.07$ (s, 3-CH_3), 2.24 (s, 2′-CH_3), 5.89 (br s, 3′-H), 6.31 (br s, 1′-H), 6.48 (dd, $J_{4'',\,5''} = 1.9$, $^4J_{4'',\,2''} = 0.8$, 4″-H), 7.41 (dd, $J_{5'',\,4''} = {}^4J_{5'',\,2''} = 1.7$, 5″-H), 7.50 (br s, 4-H), 7.66 (br s, 2″-H); *assignment analogous to *Z*-**9**. ^{13}C NMR (APT, 50 MHz, $CDCl_3$): $\delta = 11.04$ (3-CH_3), 18.19 (2′-CH_3), 89.54 (C-5′), 90.77 (C-4′), 107.67 (C-3″), 112.28 (C-4″), 115.97 (C-3′), 116.63 (C-1′), 131.49 (C-3), 134.40 (C-4), 142.38 (C-2′), 143.07 (C-5″), 145.53 (C-2″), 148.97 (C-5), 169.80 (C-2). The *E*-configuration of the $C^5{=}C^{1'}$ double bond was deduced from a NOESY spectrum where 4-H ($\delta = 7.50$) exhibits a cross-peak with 2′-CH_3 ($\delta = 2.24$) [and with 3 CH_3 ($\delta = 2.07$)] but not with 1′-H ($\delta = 6.31$).

5*Z*-5-[*E*-5-(3-Furanyl)-2-methyl-2-penten-4-yn-1-ylidene]-2(5*H*)-furanone. The synthesis of norfreelingyne (*Z*-**10**) began by adding, at 0 °C, PPh_3 (57.7 mg, 0.220 mmol, 2.0 equiv.) and 10 min later DEAD (40% in toluene, 0.10 ml, 0.22 mmol, 2.0 equiv.) to a solution of alcohol *lk*-**33** (26.7 mg, 0.109 mmol, 1.0 equiv.) in THF (4 ml). After stirring for 2 h a saturated aqueous solution of NH_4Cl (2 ml) was added. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 × 5 ml). The combined organic layers were dried over $MgSO_4$. After removal of the solvent flash chromatography (2 cm, light petroleum–*tert*-BuOMe 10 : 1) provided **10** (20.4 mg, 83%) as a solid (mp 144–145 °C) 88 : 12 *Z* : *E*-mixture (as determined by the ^1H NMR integrals over the 3-H's). IR (KBr; accidentally, only peaks with $\nu < 2000$ cm^{-1} were registered): $\nu = 1770$, 1755, 1340, 1165, 1110, 1070, 945, 920, 885, 870, 805, 785, 770, 675 cm^{-1}. ^1H NMR (300 MHz): $\delta = 2.37$ (d, $^4J_{2'\text{-Me},\,3'} = 1.1$, 2′-$CH_3$), 5.76 (s, 1′-H)*, 5.97 (br s, 3′-H)*, 6.19 (dd, $J_{3,\,4} = 5.3$, $^5J_{3,\,1'} = 0.8$, 3-H), 6.48 (dd, $J_{4'',\,5''} = 1.9$, $^4J_{4'',\,2''} = 0.8$, 4″-H), 7.38 (d, $J_{4,\,3} = 5.3$, 4-H), 7.41 (dd, $J_{5'',\,4''} = {}^4J_{5'',\,2''} = 2.1$, 5″-H)#, 7.66 (br s, 2″-H)#; *assignment analogous to *Z*-**9** where δ(1′-H) = 5.64 < δ(3′-H) = 5.90; #assignment analogous to *Z*-**9** where δ(2″-H) = 7.66 > δ(5″-H) = 7.40. ^{13}C NMR (APT spectrum at 125 HHz, $CDCl_3$): $\delta = 18.10$ (2′-CH_3), 89.82 and 91.50 (C-4′, C-5′), 107.67 (C-3″), 112.28, 116.56, 116.72 and 118.28 (C-3, C-1′, C-3′, C-4″), 143.57 (C-2′)*, 143.05, 144.70 and 145.60 (C-4, C-2″, C-5″), 148.33 (C-5)*, 169.90 (C-2); *assignment analogous to *Z*-**9** where δ (C-2′) = 143.86 and δ (C-5) = 147.34; in addition, 11 less intense ^{13}C-NMR resonances of *E*-**10** were observed. $C_{14}H_{10}O_3$ (226.2) calcd. C 74.33, H 4.46; found C 74.44, H 4.39.

5*E*-5-[*E*-5-(3-Furanyl)-2-methyl-2-penten-4-yn-1-ylidene]-2(5*H*)-furanone. *E*-Norfreelingyne (*E*-**10**; 33.3 mg, 98%) was prepared as a solid (mp 146–147 °C) 93 : 7 *E* : *Z*-mixture (as evidenced by the ^1H NMR integrals over the 2′-Me's) from alcohol *ul*-**33** (36.6 mg, 0.150 mmol, 1.0 equiv.), PPh_3 (78.7 mg, 0.300 mmol, 2.0 equiv.) and DEAD (40% in toluene, 0.14 ml, 0.30 mmol, 2.0 equiv.) as described for compound *Z*-**10**. IR (accidentally, only peaks with $\lambda < 2000$ cm^{-1} were registered): $\nu = 1770$, 1755, 1340, 1185, 1165, 1110, 1070, 1025, 1010, 945, 920, 885, 870, 825, 805, 785, 770, 675 cm^{-1}. ^1H NMR (300 MHz): $\delta = 2.25$ (d, $^4J_{2'\text{-Me},\,3'} = 0.9$, 2′-$CH_3$), 5.95 (br s, 3′-H), 6.30 (dd, $J_{3,\,4} = 5.4$, $^5J_{3,\,1'} = 1.6$, 3-H), 6.43 (ddd, $^5J_{1',\,3} = 1.7$, $^4J_{1',\,3'} = {}^4J_{4,\,1} = 0.8$, 1′-H), 6.48 (dd, $J_{4'',\,5''} = 1.8$, $^4J_{4'',\,2''} =$ 0.9, 4″-H), 7.41 (dd, $J_{5'',\,4''} = {}^4J_{5'',\,2''} = 1.8$, 5″-H)*, 7.67 (br s, 2″-H)*, 7.83 (dd, $J_{4,\,3} = 5.7$, $^4J_{4,\,1'} = 0.6$, 4-H); *assignment analogous to *Z*-**9** where δ (2″-H) = 7.66 > δ (5″-H) = 7.40. ^{13}C NMR (APT spectrum at 50 MHz, $CDCl_3$):$\delta = 18.12$ (2′-CH_3), 89.47 and 91.71 (C-4′, C-5′), 107.55 (C-3″), 112.26, 117.56, 119.04 and 120.77 (C-3, C-1′, C-3′, C-4″), 142.04 (C-2′) *, 139.81, 143.13 and 145.69 (C-4, C-2″, C-5″), 149.98 (C-5)*, 168.86 (C-2); *assignment analogous to *E*-**9** where δ (C-2′) = 142.38 and δ (C-5) = 148.97; in addition, 6 less intense ^{13}C-NMR resonances of *Z*-**10** were observed. $C_{14}H_{10}O_3$ (226.2) calcd. C 74.33, H 4.46; found C 74.30, H 4.20.

5*Z*-5-[*E*-5-(3-Furanyl)-2-methyl-2-penten-4-yn-1-ylidene]-4-methyl-2(5*H*)-furanone. Isofreelingyne (*Z*-**11**) was prepared as a pure isomer by either of two methods. Method A (22.6 mg *Z*-**11**, 91%; mp 141–143 °C) started from alcohol *lk*-**34** (26.7 mg, 0.109 mmol, 1.0 equiv.), PPh_3 (57.7 mg, 0.220 mmol, 2.0 equiv.) and DEAD (40% in toluene, 0.10 ml, 0.22 mmol, 2.0 equiv.) as described for compound *Z*-**10**. Method B (13.3 mg *Z*-**11**, 24%) started from alcohol *ul*-**34** (!; 59.4 mg, 0.229

mmol, 1.0 equiv.), PPh_3 (0.121 g, 0.460 mmol, 2.0 equiv.) and DEAD (40% in toluene, 0.21 ml, 0.46 mmol, 2.0 equiv.) as described for compound *Z*-**10**. IR (accidentally, only peaks with $\nu < 2000$ cm^{-1} were registered): $\nu = 1765$, 1540, 1505, 1340, 1185, 1165, 1110, 1070, 1025, 1010, 945, 920, 885, 870, 805, 785, 770, 730, 675 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): $\delta = 1.21$ (d, $^4J_{4\text{-Me},3'} = 1.5$, 4-$CH_3$), 2.46 (d, $^4J_{2'\text{-Me},3''} = 1.1$, 2′-$CH_3$), 5.14 (s, 1′-H), 5.29 (br s, 3-H), 5.82 (br s, 3′-H), 6.20 (dd, $J_{4'',5''} = 1.9$, $^4J_{4'',2''} = 0.8$, 4″-H)*, 6.83 (dd, $J_{5'',4''} = {}^4J_{5'',2''} = 1.7$, 5″-H)*, 7.28 (br s, 2″-H)*; *the furan protons were assigned on the grounds of their coupling patterns and analogy with the corresponding assignments in compound *Z*-**9**. The *Z*-configuration of the exocyclic double bond is fixed through a 300 MHz NOESY spectrum, in which the 1′-H ($\delta = 5.14$) shows a cross-peak with 4-Me ($\delta = 1.21$). ^{13}C NMR (APT spectrum plus $\{^1H\}$ decoupled ^{13}C-NMR spectrum, both 125 MHz, C_6D_6 as internal standard in C_6D_6): $\delta = 11.00$ (4-CH_3), 18.34 (2′-CH_3)*, 90.43 (C-5′), 91.23 (C-4′), 108.41 (C-3″), 111.20 (C-1′), 112.54 (C-4″), 115.38 (C-3′), 116.07 (C-3), 143.27 (C-5″), 144.12 (C-2′), 145.85 (C-2″), 149.75 (C-4), 154.71 (C-5), 168.08 (C-2); *assignment analogous to *Z*-**9** where δ (2′-CH_3) = 18.23 (albeit in $CDCl_3$). $C_{15}H_{12}O_3$ (240.3) calcd. C 74.99, H 5.03; found C 74.79, H 5.19.

3-Ethynylfuran (12). At −78 °C freshly prepared LDA [from Pr^i_2NH (0.84 ml, 0.61 g, 6.0 mmol) and n-BuLi (2.54 M solution in hexane, 2.36 ml, 6.0 mmol, 1.2 equiv.)] was added to a solution of Me_3SiCHN_2 (2.0 M in toluene, 3.0 ml, 6.0 mmol, 1.2 equiv.) in THF (5 ml). After stirring for 30 min furan-3-carbaldehyde (**17**; 0.42 ml, 0.48 g, 5.0 mmol, 1.0 equiv.) in THF (5 ml) was added and stirring continued for 1 h. After warming up to room temperature and stirring for another 30 min brine (10 ml) was added. After extraction with pentane the organic layer was dried over $MgSO_4$. The solvent was removed and distillation of the residue gave a solution of the title compound (0.22 g, 48%) in THF (0.24 g). ^{1}H NMR (300 MHz): $\delta = 3.06$ (s, 2′-H), 6.49 (br d, $J_{5,4} = 1.5$, 4-H), 7.39 (dd, $J_{4,5} \approx {}^4J_{4,2} \approx 1.7$, 5-H), 7.67 (incompletely resolved d, $^4J_{2,4} = 1.9$, 2-H).

***E*-3-Iodo-2-methyl-2-propen-1-al. 13** (34% over 3 steps) was prepared from compound **21** according to a literature procedure (40% overall yield[23]). 1st steps: **21** (70.6 g, 160 mmol, 1.0 equiv.) and KOH (27.4 g, 488 mmol, 3.05 equiv.) (gaves 27.1 g, 80%; lit.[23] 89%); 2nd steps: *E*-3-iodo-2-methyl-2-propenoic acid (18.7 g, 88 mmol, 1.0 equiv.) and $LiAlH_4$ (3.42 g, 90 mmol, 1.0 equiv.) (gaves 9.23 g, 53%; lit.[23] 70%) and 3rd step: *E*-3-iodo-2-methyl-2-propen-1-ol (0.99 g, 5.0 mmol, 1.0 equiv.) and MnO_2 (4.35 g, 50 mmol, 10 equiv.) (gaves 0.79 g, 81%; lit.[23] >65%).

3-Methyl-2-(trimethylsiloxy)furan. 14 was prepared according to literature procedures[24,25] (*a*) Citraconic anhydride (45.2 ml, 56.0 g, 500 mmol, 1.0 equiv.), dicyclohexylamine (110 ml, 99.7 g, 550 mmol, 1.1 equiv.) (gaves 125 g, 77%, lit.[24] 80–85%); (*b*) $ClCO_2Bu$ (43.1 ml, 45.3 g, 332 mmol, 1.0 equiv.); (*c*) $NaBH_4$ (25.2 g, 664 mmol, 2.0 equiv.) (gave 21.2 g, 65% over two steps; lit.[24] 80% over two steps); (*d*) 3-methyl-2(5*H*)-furanone (4.43 ml, 5.00 g, 51.0 mmol, 1.0 equiv.), LDA [from diisopropylamine (7.57 ml, 5.46 g, 54.0 mmol, 1.1 equiv.) and BuLi (2.37 M solution in hexane, 22.8 ml, 54.0 mmol, 1.1 equiv.], Me_3SiCl (7.74 ml, 6.63 g, 61.0 mmol, 1.2 equiv.) (gave 4.86 g, 56%, lit.[25] no yield specified).

2-(Trimethylsiloxy)furan. 15 was prepared according to a literature procedure[28,29] from (*a*) furfural (16.6 ml, 19.2 g, 200 mmol, 1.0 equiv.), Na_2SO_4 (10 g), *N*,*N*-dimethylethanolamine (7.9 ml, 7.0 g, 79 mmol, 0.4 equiv.), formic acid (15.1 ml, 18.4 g, 400 mmol, 2.0 equiv.) and H_2O_2 (35% in H_2O, 31.0 ml, 320 mmol, 1.6 equiv.) (gave 6.89 g, 41%; lit.[28] 41%); (*b*) 2(5*H*)-furanone (6.31 g, 75.0 mmol, 1.0 equiv.), Me_3SiCl (12.1 ml, 10.3 g, 94.8 mmol, 1.3 equiv.), NEt_3 (13.2 ml, 9.61 g, 94.9 mmol, 1.3 equiv.) (gave 4.22 g, 36%; lit.[29] 38%).

4-Methyl-2-(trimethylsiloxy)furan. 16 was prepared by a known reduction[30] [citraconic anhydride (16.0 ml, 20.0 g, 178 mmol), $NaBH_4$ (6.80 g, 178 mmol, 1.0 equiv.); treatment by HCl (6 N, 80 ml); gave 6.87 g, 40%; lit.[30] 43%] followed by formation of the title compound (gave 7.99 g, 67%) from the resulting 4-methyl-2(5*H*)-furanone (6.87 g, 70.0 mmol), LDA [from diisopropylamine (10.3 ml, 7.42 g, 73.3 mmol, 1.05 equiv.) and MeLi (1.65 M solution in Et_2O, 44.4 ml, 73.3 mmol, 1.05 equiv.)] and Me_3SiCl (10.6 ml, 9.10 g, 83.8 mmol, 1.2 equiv.).

Diethyl [1-(3-furyl)ethenyl]phosphate 19. At −78 °C 3-acetylfuran **18** (55 mg, 0.50 mmol, 1.0 equiv.) was added to a solution of freshly prepared LDA (0.50 mmol, 1.0 equiv.) in THF (2 ml). After stirring for 1 h diethyl chlorophosphate (72 µl, 86 mg, 0.5 mmol, 1.0 equiv.) was added and the solution allowed to warm up to room temperature After adding H_2O (4 ml) the aqueous layer was extracted with *tert*-BuOMe. The combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure. Flash chromatography of the residue (light petroleum–*tert*-BuOMe, 10 : 1) afforded **19** (94.8 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$: $\delta = 1.36$ (td, $J_{2,1} = 7.2$, $^4J_{H,P} = 0.9$, 2 × 2-H_3), 4.21 (m_c, 2 × 1-H_2), 4.98 (dd, $J_{gem} = {}^4J_{2'\text{-H(A)},P} = 2.6$, 2′-$H^A$), 5.08 (dd, $J_{gem} = {}^4J_{2'\text{-H(B)},P} = 2.3$, 2′-$H^B$), 6.49 (dd, $J_{4'',5''} = 1.9$, $^4J_{4'',2''} = 0.7$, 4″-H), 7.38 (dd, $J_{5'',4''} = {}^4J_{5'',2''} = 1.9$,5″-H), 7.60 (br s, 2″-H).

Diethyl (diiodomethyl)methylmalonate. 21 (88.5 g, 74%; lit.[23] 65%) was prepared according to a literature procedure[23] from diethyl methylmalonate (47.03 g, 270 mmol, 1.0 equiv.), NaH (6.58 g, 270 mmol, 1.0 equiv.) and iodoform (81.7 g, 270 mmol, 1.0 equiv.).

General procedure for the Mukaiyama aldol additions (preparation of compounds 25–27). At −78 °C the Lewis acid (1.0 equiv.) indicated in Scheme 4 was added to a solution of the trimethylsiloxylated furan (10 mmol) and the aldehyde (1.0 equiv.) in CH_2Cl_2 (10 ml). After stirring for 2.5 h at this temperature an aqueous solution of $NaHCO_3$ (4 ml) was added. Then the mixture was warmed to room temperature. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 × 10 ml). The combined organic layers were dried over $MgSO_4$. After removal of the solvent flash chromatography provided the addition product. It was isolated as a diastereomeric mixture in the case of **25**, as a diastereomeric mixture containing Δ^3-butenolide in the case of **26** and separately as the *lk*- and the *ul*-diastereomers through crystallization in the case of **27**, respectively.

5-(1-Hydroxyethyl)-2(5*H*)-furanone (**25**, mixture of diastereomers). No IR spectrum was recorded and no correct combustion analysis obtained. *lk*-5-(1-Hydroxyethyl)-2(5*H*)-furanone (*lk*-**25**): ^{1}H NMR (300 MHz): $\delta = 1.31$ (d, $J_{2',1} = 6.4$, 2′-Me), 2.32 (br s, OH), 3.93 (dq, $J_{1',2} \approx J_{1',5} \approx 6.5$, 1′-H), 4.90–4.95 ($m_c$, 5-H), 6.14 (dd, $J_{3,4} = 6.1$, $^4J_{3,5} = 2.3$, 3-H), 7.45 (dd, $J_{4,3} = 5.7$, $J_{4,5} = 1.5$,4-H). *ul*-5-(1-Hydroxyethyl)-2(5*H*)-furanone (*ul*-**25**): ^{1}H NMR (300 MHz): $\delta = 1.32$ (d, $J_{2',1} = 6.4$, 2′-Me), 2.32 (br s, OH), 4.05 (dq, $J_{1',5} = 6.5$, $J_{1',2'} = 4.6$, 1′-H), 4.90–4.95 (m_c, 5-H), 6.19 (dd, $J_{3,4} = 6.1$, $^4J_{3,5} = 2.3$, 3-H), 7.56 (dd, $J_{4,3} = 6.0$, $J_{4,5} = 1.5$, 4-H).

5-(*trans*-1-Hydroxy-2-butenyl)-2(5*H*) furanone (**26**) obtained as a mixture of diastereomers contaminated with Δ^3-butenolide (a hydrolysis product of siloxyfuran **14**) could not be analyzed fully by ^{1}H-NMR spectroscopy because of severe signal overlap; the presence of diastereomers *lk*-**26** and *ul*-**26** was inferred from appropriate ^{1}H NMR resonances (*lk*-**26**: $\delta_{1'\text{-H}} = 4.22$, $\delta_{4\text{-H}} = 7.47$; *ul*-**26**: $\delta_{1'\text{-H}} = 4.39$, $\delta_{4\text{-H}} = 7.54$) and their ratio determined by integrating the 4-H resonances.

lk-5-[1-Hydroxy-1-(5-methyl-2-thiophenyl)methyl]-2(5*H*)-furanone [(*lk*-**27**; 285.2 mg, 29%; separated through crystallization from dichloromethane (2 ml) and hexane (5 ml); mp 121–122 °C] along with *ul*-**27** (111.9 mg, 11%) was prepared from siloxyfuran **15** (736 mg, 4.71 mmol), 5-methylthiophene-2-carbaldehyde (594 mg, 4.71 mmol, 1.0 equiv.) and $BF_3 \cdot OEt_2$ (592 µl, 668 mg, 4.71 mmol, 1.0 equiv.) as described for the synthesis of *lk*-**30**. IR (KBr): $\nu = 3155, 2985, 2360, 2255, 1710, 1640, 1605, 1480, 1385, 1310, 1290, 1215, 1180, 1145, 1095, 1060\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 2.38$ (d, $^4J_{5''\text{-Me},\,4''} = 0.8$, 5″-Me), 5.04 (dd, $J_{1',\,OH} \approx J_{1',\,5} \approx 4.9$, 1′-H), 5.25–5.29 (m, 5-H), 6.12 (d, $J_{OH,\,1'\text{-H}} = 5.3$, OH), 6.19 (dd, $J_{3,\,4} = 5.6$, $^4J_{3,\,5} = 1.8$, 3-H), 6.64 (dq, $J_{4'',\,3''} = 3.4$, $^4J_{4'',\,5''\text{-Me}} = 1.1$, 4″-H), 6.76 (d, $J_{3'',\,4''} = 3.4$, 3″-H), 7.60 (dd, $J_{4,\,3} = 5.7$, $J_{4,\,5} = 1.5$, 4-H). $C_{10}H_{10}O_3S$ (210.3) calcd. C 57.13, H 4.79; found C 57.32, H 4.87.

ul-5-[1-Hydroxy-1-(5-methyl-2-thiophenyl)methyl]-2(5*H*)-furanone (*ul*-**27**; 116.7 mg, 12%) along with *lk*-**27** [259.7 mg, 26%; separated through crystallization from dichloromethane (2 ml) and hexane (5 ml); mp. *vide supra*] was prepared from siloxyfuranon **15** (736 mg, 4.71 mmol), 5-methylthiophene-2-carbaldehyde (594 mg, 4.71 mmol, 1.0 equiv.) and $ZnBr_2$ (1.06 g, 4.71 mmol, 1.0 equiv.) as described for the synthesis of *ul*-**30**. IR (KBr): $\nu = 3155, 2985, 2360, 2255, 1710, 1640, 1605, 1480, 1385, 1310, 1290, 1215, 1180, 1145, 1095, 1060\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 2.40$ (d, $^4J_{5''\text{-Me},\,4''} = 0.7$, 5″-Me), 5.00 (dd, $J_{1',\,OH} \approx J_{1',\,5} \approx 4.9$, 1′-H), 5.25–5.29 (m, 5-H), 6.15 (d, $J_{OH,\,1'\text{-H}} = 5.2$, OH), 6.22 (dd, $J_{3,\,4} = 5.6$, $^4J_{3,\,5} = 1.9$, 3-H), 6.64 (dq, $J_{4'',\,3''} = 3.4$, $^4J_{4'',\,5''\text{-Me}} = 1.1$, 4″-H), 6.82 (d, $J_{3'',\,4''} = 3.4$, 3″-H), 7.64 (dd, $J_{4,\,3} = 5.7$, $J_{4,\,5} = 1.5$, 4-H). $C_{10}H_{10}O_3S$ (210.3) calcd. C 57.13, H 4.79; found C 57.32, H 4.87.

Dehydration of 27 to give 28. Method A. At −30 °C pyridine (19.8 µl, 19.4 mg, 0.240 mmol, 2.0 equiv.) was added to a solution of alcohol *lk*-**27** (25.2 mg, 0.120 mmol, 1.0 equiv.) in CH_2Cl_2 (3 ml). After 10 min triflic anhydride (61 µl, 0.10 g, 0.36 mmol, 3.0 equiv.) was added and the reaction mixture allowed to warm to room temperature. After 30 min H_2O (10 ml) was added. The organic layer was separated and the aqueous layer extracted with *tert*-BuOMe (3 × 10 ml). The combined organic layers were dried over $MgSO_4$. After removal of the solvent flash chromatography provided *Z*-**28** (15.5 mg, 67%). A similar experiment starting from alcohol *ul*-**27** furnished *E*-**28** (16.1 mg, 70%).

Method B. At 0 °C MsCl (37 µl, 55 mg, 0.48 mmol, 2.0 equiv.) was added to a solution of the alcohol *lk*-**27** (51 mg, 0.24 mmol, 1.0 equiv.) in CH_2Cl_2 (5 ml). After stirring for 20 min NEt_3 (0.13 ml, 97 mg, 0.96 mmol, 4.0 equiv.) was added. Stirring was continued for 30 min, H_2O (10 ml) added, the organic layer separated and the aqueous layer extracted with *tert*-BuOMe (3 × 15 ml). The combined organic layers were dried over $MgSO_4$. After removal of the solvent flash chromatography (1 cm, light petroleum–*tert*-BuOMe 1.5 : 1) provided **28** (33.8 mg, 73%) as a 68 : 32 *Z*–*E*-mixture as determined by the ^1H-NMR integrals over the 4-H's. A similar experiment starting from alcohol *ul*-**27** furnished **28** (15.7 mg, 68%) as a 24 : 76 *Z*,*E*-mixture as determined by the ^1H-NMR integrals over the 4-H's.

Method C. A solution of the alcohol *lk*-**27** (25 mg, 0.12 mmol, 1.0 equiv.) in benzene (2 ml) was added to freshly prepared Burgess reagent (31 mg, 0.13 mmol, 1.1 equiv.). After heating for 1 h at 50 °C H_2O (5 ml) was added. The organic layer was separated and the aqueous. layer extracted with CH_2Cl_2 (3 × 10 ml). The combined organic layers were dried over $MgSO_4$. After removal of the solvent flash chromatography (1 cm, light petroleum–*tert*-BuOMe 1 : 1) provided *Z*-**28** (9.9 mg, 43%). A similar experiment starting from alcohol *ul*-**27** furnished a 35% yield of *E*-**28**.

5*Z*-5-[(5-Methyl-2-thiophenyl)methylene]-2(5*H*)-furanone (*Z*-**28**). ^1H NMR (300 MHz): $\delta = 2.53$ (s, 5″-Me), 6.14 (dd, $J_{3,\,4} = 5.3$, $^5J_{3,\,1'} = 0.8$, 3-H), 6.23 (s, 1′-H), 6.74 (dq, $J_{4'',\,3''} = 3.8$, $^4J_{4'',\,5''\text{-Me}} = 0.8$, 4″-H), 7.18 (d, $J_{3'',\,4''} = 3.4$, 3″-H), 7.44 (d, $J_{4,\,3} = 5.3$, 4-H). ^{13}C NMR (APT spectrum at 75 MHz, $CDCl_3$): $\delta = 15.67$ (5″-Me), 108.10 (C-1′); 117.24 (C-3), 131.87 (C-3″), 134.08 (C-2″), 143.65 (C-4), 145.85 (C-5), 146.69 (C-5″), 169.83 (C-2). The *Z*-configuration of the C=C bond was inferred from a 300 MHz NOESY spectrum in which 4-H correlates with 1′-H (as well as with 3-H).

5*E*-5-[(5-Methyl-2-thiophenyl)methylene]-2(5*H*)-furanone (*E*-**28**). ^1HNMR (500 MHz): $\delta = 2.52$ (s, 5‴-Me), 6.29 (dd, $J_{3,\,4} = 5.5$, $^5J_{3,\,1'} = 1.8$, 3-H), 6.72 (dq, $J_{4',\,3'} = 3.4$, $^4J_{4',\,5''\text{-Me}} = 1.0$, 4′-H), 6.78 (br s, 1′-H), 6.98 (d, $J_{3',\,4'} = 3.4$, 3′-H), 8.00 (dd, $J_{4,\,3} = 5.5$, $^4J_{4,\,1'} = 0.7$, 4-H). The *E*-configuration of the C=C bond was inferred from 300 MHz NOESY spectrum win which 4-H does not correlate with 1′-H (but correlates with 3-H).

***lk*-5-(*E*-1-Hydroxy-3-iodo-2-methyl-2-propenyl)-3-methyl-2(5*H*)-furanone.** *lk*-**29** (504 mg, 56%; mp 123–124 °C) was prepared from siloxyfuran **14** (0.60 g, 3.5 mmol), aldehyde **13** (0.69 g, 3.5 mmol, 1.0 equiv.) and $BF_3 \cdot OEt_2$ (0.44 ml, 0.50 g, 3.5 mmol, 1.0 equiv.) as described for the synthesis of *lk*-**30**. IR (KBr): $\nu = 3380, 3135, 2360, 1730, 1650, 1400, 1350, 1260, 1210, 1105, 1065, 1025, 905, 880, 795, 750, 695\ cm^{-1}$. ^1H NMR (300 MHz, DMSO-d_6, DMSO-d_5 as internal standard): $\delta = 1.79$ (m_c, 2′-CH_3), 4.26 (br dd, $J_{1',\,OH} = J_{1',\,5} = 4.7$, 1′-H), 5.05 (dqd, $J_{5,\,1'} = 4.3$, $^5J_{5,\,3\text{-Me}} \approx J_{5,\,4} \approx 1.9$, 5-H), 5.61 (d, $J_{OH,\,1'} = 5.3$, OH), 6.39 (hardly resolved qd, $^4J_{3',\,2'\text{-Me}}$ $^4J_{3',\,1'} \approx 1.5$, 3′-H), 7.19 (qd, $^4J_{4,\,3\text{-Me}} \approx J_{4,\,5} \approx 1.0$, 4-H). ^{13}C NMR (75 MHz, DMSO-d_6 as internal standard in DMSO-d_6): $\delta = 10.91$ and 21.30 (3-CH_3, 2′-CH_3), 74.84 (C-1′), 81.44 (C-3′), 82.81 (C-5), 129.71 (C-3), 147.65 (C-2′), 148.34 (C-4), 174.39 (C-2). $C_9H_{11}IO_3$ (294.1) calcd. C 36.76, H 3.77; found C 36.80, H 3.98. HRMS (EI, 70 eV) $m/z = 293.9752 \pm 2$ mDa $[M]^+$.

***ul*-5-(*E*-1-Hydroxy-3-iodo-2-methyl-2-propenyl)-3-methyl-2(5*H*)-furanone.** *ul*-**29** 1.53 g, 52%), along with *lk*-**29** (0.27 g, 9%; separated as the late fractions of the flash chromatography), was prepared from siloxyfuran **14** (1.70 g, 10.0 mmol), aldehyde **13** (1.96 g, 10.0 mmol, 1.0 equiv.) and $ZnBr_2$ (2.25 g, 10.0 mmol, 1.0 equiv.) as described for the synthesis of *ul*-**30**. IR (KBr): $\nu = 3440, 3020, 2925, 1755, 1660, 1620, 1385, 1330, 1215, 1060, 870, 760, 670\ cm^{-1}$. ^1H NMR (300 MHz, DMSO-d_5 as internal standard in DMSO-d_6): $\delta = 1.80$ (dd, $^4J_{3\text{-Me},\,4'} = {}^5J_{3\text{-Me},\,5} = 1.9$, 3-Me), 1.81 (d, $^4J_{2'\text{-Me},\,3'} = 1.1$, 2′-Me), 4.16 (br dd, $J_{1',\,OH} \approx J_{1',\,5} \approx 5.1$, 1′-H), 4.99 (dqd, $J_{5,\,1'*} = 6.1$, $^5J_{5,\,3\text{-Me}} \approx J_{5,\,4} \approx 1.9$, 5-H), 5.76 (d, $J_{OH,\,1'} = 4.9$, OH), 6.43 (qd, $^4J_{3',\,2'\text{-Me}} \approx {}^4J_{3',\,1'} \approx 1.6$, 3′-H), 7.29 (qd, $^4J_{4.3\text{-Me}} \approx J_{4,\,5} \approx 1.1$, 4-H). ^{13}C NMR (APT spectrum at 50 MHz, DMSO-d_6 as internal standard in DMSO-d_6): $\delta = 10.81$ (3-Me), 20.80 (2′-Me), 75.38 (C-1′), 81.73 (C-5), 81.88 (C-3′), 129.78 (C-3)*, 147.48 (C-2′)*, 148.32 (C-4), 173.99 (C-2); *assignment of C-3 (high-field) *vs.* C-2′ (low-field) made because of shift analogy to *lk*-**29** ($\delta_{C\text{-}3} = 129.71$, $\delta_{C\text{-}2'} = 147.65$). $C_8H_9IO_3$ (294.1) calcd. C 36.76, H 3.77; found C 36.41, H 3.83.

***lk*-5-(*E*-1-Hydroxy-3-iodo-2-methyl-2-propenyl)-2(5*H*)-furanone (lk-30).** At 78 °C $BF_3 \cdot OEt_2$ (1.27 ml, 1.42 g, 10.0 mmol, 1.0 equiv.) was added to a solution of siloxyfuran **15** (1.56 g, 10.0 mmol) and aldehyde **13** (1.96 g, 10.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 ml). After stirring for 2.5 h at this temperature aqueous $NaHCO_3$ solution (4 ml) was added and the reaction mixture allowed to warm to room temperature. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 ml). The combined organic layers were dried over $MgSO_4$. The solvent was removed and flash chromatography of the residue (2.5 cm, light petroleum–*tert*-BuOMe 2 : 1 until F21, then 1 : 1) afforded *lk*-**30** (1.51 g,

54%; mp 134–136 °C). IR (KBr): $\nu = 3415, 3230, 1735, 1635, 1620, 1400, 1255, 1175, 1120, 1050, 1020, 920, 835, 800\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.93$ (d, $^4J_{2'\text{-Me},\,3'} = 1.1$, 2′-Me), 2.58 (d, $J_{OH,\,1'} = 4.5$, OH), 4.27 (dd, $J_{1',\,OH} = J_{1',\,5} = 5.1$, 1′-H), 5.10 (ddd, $J_{5,\,1'} = 6.0$, $J_{5,\,4} = {}^4J_{5,\,3} = 1.9$, 5-H), 6.20 (dd, $J_{3,\,4} = 5.7$, $^4J_{3,\,5} = 1.9$, 3-H), 6.49 (br s, 3′-H), 7.35 (dd, $J_{4,\,3} = 5.9$, $J_{4,\,5} = 1.7$, 4-H). ^{13}C NMR (APT spectrum at 50 MHz, $CDCl_3$): $\delta = 20.83$ (2′-Me), 76.89 (C-1′), 82.30 (C-3′)*, 84.40 (C-5)*, 123.06 (C-3), 144.70 (C-2′), 152.71 (C-4), 171.74 (C-2); *assignments interchangeable. $C_8H_9IO_3$ (280.1) calcd. C 34.31, H 3.24; found C 34.13, H 3.18.

***ul*-5-(*E*-1-Hydroxy-3-iodo-2-methyl-2-propenyl)-2(5*H*)-furanone (*ul*-30).** At −78 °C $ZnBr_2$ (2.25 g, 10.0 mmol, 1.0 equiv.) was added to a solution of siloxyfuran **15** (1.56 g, 10.0 mmol) and aldehyde **13** (1.96 g, 10.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 ml). After stirring for 2.5 h at this temperature, aqueous $NaHCO_3$ solution (4 ml) was added and the reaction mixture allowed to warm to room temperature. Work-up as described for *lk*-**30** including flash chromatography (2.5 cm, light petroleum–*tert*-BuOMe 2 : 1 until F18, then 1 : 1) afforded *ul*-**30** (1.174 g, 42%; mp 104–106 °C) in the early fractions and *lk*-**30** (258 mg, 9%) in the late fractions. IR (KBr): $\nu = 3415, 3095, 2915, 1765, 1620, 1600, 1335, 1270, 1170, 1105, 1045, 910, 890, 815, 725, 710\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.92$ (d, $^4J_{2'\text{-Me},\,3'} = 0.7$, 2′-Me), 3.16 (br s, OH), 4.43 (d, $J_{1',\,5} = 4.9$, 1′-H), 5.09 (ddd, $J_{5,\,1'} = 5.3$, $J_{5,\,4} = {}^4J_{5,\,3} = 1.7$, 5-H), 6.18 (dd, $J_{3,\,4} = 5.6$, $^4J_{3,\,5} = 1.9$, 3-H), 6.51 (qd of which only the three central tips are visible, $^4J_{3',\,2'\text{-Me}} \approx {}^4J_{5',\,1'} \approx 1.1$, 3′-H), 7.47 (dd, $J_{4,\,3} = 5.7$, $J_{4,\,5} = 1.6$, 4-H). ^{13}C NMR (APT spectrum at 50 MHz, $CDCl_3$): $\delta = 21.15$ (2′-Me), 75.03 (C-1′), 81.72 (C-3′)*, 83.54 (C-5)*, 122.93 (C-3), 144.50 (C-2′), 153.50 (C-4), 173.07 (C-2); *assignments interchangeable. $C_8H_9IO_3$ (280.1) calcd. C 34.31, H 3.24; found C 34.10, H 3.02.

***lk*-5-(*E*-1-Hydroxy-3-iodo-2-methyl-2-propenyl)-4-methyl-2(5*H*)-furanone.** *lk*-31 (1.36 g, 46%; mp 102–103 °C) was prepared from siloxyfuran **16** (1.70 g, 10.0 mmol), aldehyde **13** (1.96 g, 10.0 mmol, 1.0 equiv.) and $BF_3 \cdot OEt_2$ (1.27 ml, 1.42 g, 10.0 mmol, 1.0 equiv.) as described for *lk*-**29**. IR (KBr): $\nu = 3415, 1845, 1745, 1645, 1435, 1395, 1325, 1260, 1185, 1160, 1110, 1055, 980, 925, 870, 760, 665\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.96$ and 2.13 (2 d which were hardly resolved, $^4J = 0.8$ and 0.7, respectively, 4-Me, 2′-Me), 2.72 (d, $J_{OH,\,1'} = 7.9$, OH), 4.39 (br dd, $J_{1',\,OH} = 7.8$, $J_{1',\,5} = 2.5$, 1′-H), 4.97 (m_c, 5-H), 5.89 (qd, $^4J_{3,\,4\text{-Me}} = {}^4J_{3,\,5} = 1.5$, 3-H), 6.53 (hardly resolved qd, $^4J_{3',\,2'\text{-Me}} = {}^4J_{3',\,1'} = 1.1$, 3′-H). ^{13}C NMR (APT spectrum at 50 MHz, $CDCl_3$; spectrum contained artifacts): $\delta = 14.26$ and 21.55 (4-Me, 2′-Me), 73.90 (C-1′)*, 81.19 (C-3′)**, 85.19 (C-5)**, 118.20 (C-3), 145.28 (C-2′), 166.58 (C-4), 173.14 (C-2); *assignment made because of shift analogy to *lk*-**29** ($\delta_{C-1'} = 74.84$); **assignments interchangeable. $C_9H_{11}IO_3$ (294.1) calcd. C 36.76, H 3.77 found C 36.74, H 3.79.

***ul*-5-(*E*-1-Hydroxy-3-iodo-2-methyl-2-propenyl)-4-methyl-2(5*H*)-furanone.** *ul*-**31** (1.27 g, 44%, mp 114–115 °C), along with *lk*-30 (318 mg, 11%; separated as the late fractions of the flash chromatography), was prepared from siloxyfuran **16** (1.70 g, 10.0 mmol), aldehyde **13** (1.96 g, 10.0 mmol, 1.0 equiv.) and $ZnBr_2$ (2.25 g, 10.0 mmol, 1.0 equiv.) as described for the synthesis of *ul*-**30**. IR (KBr): $\nu = 3410, 3100, 1845, 1780, 1650, 1435, 1395, 1380, 1330, 1260, 1185, 1160, 1110, 1055, 980, 925, 870, 760, 665\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.93$ and 2.10 (2 br s, 4-Me, 2′-Me), 2.85 (d, $J_{OH,\,1'} = 4.5$, OH), 4.47 (br dd, $J_{1',\,5} = J_{1',\,OH} = 4.4$, 1′-H), 4.99 (br d, $J_{5,\,1'} = 4.2$, 5-H), 5.86 (qd of which only the three central tips are visible, $^4J_{3,\,4\text{-Me}} = {}^4J_{3,\,5} = 1.5$, 3-H), 6.56 (qd of which only the three central tips are visible, $^4J_{3',\,2'\text{-Me}} = {}^4J_{3',\,1'} = 1.2$, 3′-H). ^{13}C NMR (APT spectrum at 50 MHz, $CDCl_3$, spectrum contains artifacts): $\delta = 15.37$ and 21.23 (4-Me, 2′-Me), 75.38 (C-1′)*, 81.95 (C-3′)**, 84.56 (C-5)**, 118.23 (C-3), 144.28 (C-2′), 167.47 (C-4), 173.20 (C-2); *assignment analogous to compound *ul*-**29** ($\delta_{C\text{-}1'} = 75.38$); **assignments interchangeable. $C_9H_{11}IO_3$ (294.1) calcd. C 36.76, H 3.77; found C 36.68, H 3.84.

***lk*-5-[*E*-5-(3-Furanyl)-1-hydroxy-2-methyl-2-penten-4-ynyl]-3-methyl-2(5*H*)-furanone.** *lk*-**32** (72.3 mg, 70%) was prepared from iodide *lk*-**29** (117.6 mg, 0.400 mmol), CuI (9.5 mg, 0.050 mmol, 0.10 equiv.), $Pd(PPh_3)_4$ (28.9 mg, 0.0250 mmol, 5 mol%), alkyne **12** (5.63 wt% in THF, 785 mg, 0.481 mmol, 1.2 equiv.) and $(Pr^i)_2NEt$ (1 ml) as described for the synthesis of *lk*-**33**. IR (KBr): $\nu = 3440, 3020, 1755, 1215, 1165, 1065, 870, 760, 670\ cm^{-1}$. ^1H NMR (400 MHz): $\delta = 1.96$ (dd, $^4J_{3\text{-Me},\,4} = {}^5J_{3\text{-Me},\,5} = 1.8$, 3-Me), 2.04 (d, $^4J_{2'\text{-Me},\,3'} = 1.1$, 2′-Me), 2.40 (d, $J_{OH,\,1'} = 3.9$, OH), 4.12 (dd, $J_{1',\,5} = 6.4$, $J_{1',\,OH} = 4.2$, , 1′-H), 4.97 (dqd, $J_{5,\,1'} = 6.6$, $^5J_{5,\,3\text{-Me}} \approx J_{5,\,4} \approx 2.0$, 5-H), 5.78 (br s, 3′-H), 6.46 (d, $J_{4'',\,5''} = 1.4$, 4″-H), 6.96 (hardly resolved qd, $^4J_{4,\,3\text{-Me}} \approx J_{4,\,5} \approx 1.5$, 4-H), 7.40 (dd, $J_{5'',\,4''} = {}^4J_{5'',\,2''} = 1.7$, 5″-H), 7.63 (br s, 2″-H). ^{13}C NMR (100 MHz gated-decoupled and 100 MHz DEPT spectrum, respectively; DEPT-CH_2 and CH_3 signals in italics, $CDCl_3$): $\delta = \textit{10.78}, \textit{15.88}$ (2′-CH_3 and 3-CH_3), *77.06* (C-1′)*, *82.80* (C-5)*, 86.21, 87.42 (C-4′ and C-5′), 107.59 (C-3″), *109.25*, *112.38* (C-4″ and C-3′), 131.72 (C-3)**, *142.94*, *145.11*, *145.34* (C-2″, C-4 and C-5″), 146.61 (C-2′), 173.54 (C-2); *assignments interchangeable; **assignment analogous to compound *lk*-**29** ($\delta_{C\text{-}3} = 129.71$). $C_{15}H_{14}O_4$ (258.3) calcd. C 69.76, H 5.46; found C 69.69, H 5.71.

***ul*-5-[*E*-5-(3-Furanyl)-1-hydroxy-2-methyl-2-penten-4-ynyl]-3-methyl-2(5*H*)-furanone.** *ul*-**32** (78.4 mg, 76%) was prepared from iodide *ul*-**29** (117.6 mg, 0.40 mmol, 1.0 equiv.), CuI (9.5 mg, 0.050 mmol, 0.1 equiv.), $Pd(PPh_3)_4$ (28.9 mg, 0.0250 mmol, 5 mol%), alkyne **12** (5.63 wt% in THF, 785.2 mg, 0.480 mmol, 1.2 equiv.) and $(Pr^i)_2NEt$ (1 ml) as described for compound *lk*-**33** (mp 125–126 °C). IR (KBr): $\nu = 3375, 3145, 1730, 1400, 1160, 1110, 1065, 875, 785\ cm^{-1}$. ^1H NMR (400.13 MHz): $\delta = 1.95$ (qd of which only the central tips are resolved, $^4J_{3\text{-Me},\,4} \approx {}^5J_{3\text{-Me},\,5} \approx 1.5$, 3-Me), 2.04 (br s, 2′-$CH_3$), 2.44 (d, $J_{OH,\,1'} = 3.9$, OH), 4.44 (hardly resolved dd, $J_{1',\,OH} \approx J_{1',\,5} \approx 3.3$, 1′-H), 4.99 (dqd, $J_{5,\,1'} = 4.4$, $^5J_{5,\,3\text{-Me}} \approx J_{5,\,4} \approx 1.8$, 5-H), 5.90 (br s, 3′-H), 6.46 (d, $J_{4'',\,5''} = 1.5$, 4″-H), 7.06 (hardly resolved qd, $^4J_{4,\,3\text{-Me}} \approx J_{4,\,5} \approx 1.3$, 4-H), 7.40 (dd, $J_{5'',\,4''} = {}^4J_{5'',\,2''} = 1.4$, 5″-H), 7.63 (br s, 2″-H). ^{13}C NMR (100 MHz gated-decoupled and 100 MHz DEPT spectrum, respectively; DEPT-CH_2 and CH_3 signals in italics, $CDCl_3$): $\delta = \textit{10.74}, \textit{16.39}$ (2′-CH_3 and 3-CH_3), *74.60* (C-1′)*, *81.64* (C-5)*, 86.15, 87.64 (C-4′ and C-5′), 107.71 (C-3″), *108.22*, *112.43* (C-4″ and C-3′), 131.89 (C-3)**, *142.98*, *145.21*, *145.31* (C-2″, C-5″ and C-4), 146.60 (C-2′), 174.05 (C-2); *assignments interchangeable; **assignment analogous to *lk*-**29** ($\delta_{C\text{-}3} = 129.71$). $C_{15}H_{14}O_4$ (258.3) calcd. C 69.76, H 5.46; found C 69.88, H 5.64.

***lk*-5-[*E*-5-(3-Furanyl)-1-hydroxy-2-methyl-2-penten-4-ynyl]-2(5H)-furanone (*lk*-33).** A solution of alkyne **12** (27.8 wt% in THF, 16.6 mg, 0.500 mmol, 1.25 equiv.) in $(Pr^i)_2NEt$ (1 ml) was added dropwise to a suspension of iodide *lk*-**30** (112.0 mg, 0.3999 mmol, 1.0 equiv.), CuI (9.5 mg, 0.050 mmol, 0.1 equiv.) and $PdCl_2(PPh_3)_2$ (17.5 mg, 0.0249 mmol, 5 mol%) in THF (4 ml). After stirring for 30 min a saturated aqueous solution of NH_4Cl (5 ml) was added. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (4 × 10 ml). The combined organic layers were dried over $MgSO_4$. After removal of the solvent *in vacuo*, flash chromatography (1.5 cm, light petroleum–*tert*-BuOMe 4 : 1 until F13, then 1 : 3, #14–24) provided *lk*-**33** (66.4 mg, 68%; mp 132–134 °C). IR (film): $\nu = 3435, 1755, 1345, 1185, 1165, 1115, 1085, 1045, 1010, 940, 920, 870, 840, 790, 780, 725\ cm^{-1}$. ^1H

NMR (300 MHz): $\delta = 2.04$ (hardly resolved d, $^4J_{2'\text{-Me},3'} =$ 0.8. 2′-Me), 2.38 (d, $J_{\text{OH},1'} = 4.1$, OH), 4.22 (badly resolved dd, $J_{1',5} = 5.8$, $J_{1',\text{OH}} = 4.7$, 1′-H), 5.13 (ddd, $J_{5,1'} = 6.2$, $J_{5,4} = {}^4J_{5,3} = 1.7$, 5-H), 5.79 (br s, 3′-H), 6.22 (dd, $J_{3,4} = 5.7$, $^4J_{3,5} = 1.9$, 3-H), 6.45 (d, $J_{4'',5''} = 1.2$, 4″-H), 7.38–7.41 (m, 4-H, 5″-H)*, 7.63 (br s, 2″-H)*; *assignments analogous to *Z*-**9** where δ (2″-H) = 7.66 is low-field from δ (5″-H) = 7.40. ^{13}C NMR (APT spectrum at 50 MHz, $CDCl_3$): $\delta = 16.03$ (2′-Me), 76.39 (C-1′)*, 84.99 (C-5)*, 86.43 and 87.44 (C-4′, C-5′), 107.70 (C-3″), 109.24 and 112.39 (C-4″, C-3′), 122.92 (C-3), 142.92 and 145.33 (C-2″, C-5″), 146.59 (C-2′), 153.02 (C-4), 172.35 (C-2); *assignments interchangeable. $C_{14}H_{12}O_4$ (244.3) calcd. C 68.85, H 4.95; found C 68.93 H 4.81.

***ul*-5-[*E*-5-(3-Furanyl)-1-hydroxy-2-methyl-2-pent-2-en-4-ynyl]-2(5*H*)-furanone.** *ul*-**33** (71.3 mg, 73%) was prepared from iodide *ul*-**30** (112.0 mg, 0.3999 mmol), CuI (9.5 mg, 0.040 mmol, 0.1 equiv.), $PdCl_2(PPh_3)_2$ (17.5 mg, 0.0249 mmol, 5 mol%), alkyne **12** (27.8 wt% in THF, 16.6 mg, 0.500 mmol, 1.25 equiv.) and $(Pr^i)_2NEt$ (1 ml) as described for compound *lk*-**33** (mp 124–125 °C). IR (film): $\nu = 3430$, 1755, 1725, 1345, 1185, 1165, 1115, 1085, 1045, 1010, 940, 920, 870, 840, 790, 780, 725 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 2.05$ (br s, 2′-Me), 2.18 (d, $J_{\text{OH},1'} = 3.8$, OH), 4.47 (br dd, $J_{1',\text{OH}} = J_{1',5} = 4.4$, 1′-H), 5.13 (ddd, $J_{5,1'} = 4.9$, $J_{5,4} = {}^4J_{5,3} = 1.7$, 5-H), 5.90 (br s, 3′-H), 6.22 (dd, $J_{3,4} = 5.8$, $^4J_{3,5} = 2.1$, 3-H), 6.46 (d, $J_{4'',5''} = 1.8$, 4″-H), 7.39 (dd, $J_{5'',4''} = {}^4J_{5'',2''} = 1.5$, 5″-H)*, 7.48 (dd, $J_{4,3} = 5.7$, $J_{4,5} = 1.5$, 4-H), 7.63 (br s, 2″-H)*; *assignment analogous to *Z*-**9** where δ(2″-H) = 7.66 is low-field from δ(5″-H) = 7.40. ^{13}C NMR (APT spectrum at 125 MHz, $CDCl_3$): $\delta = 16.27$ (2′-Me), 76.37 (C-1′)*, 84.03 (C-5)*, 86.39 and 87.60 (C-4′, C-5′), 107.77 (C-3″), 108.56 and 112.40 (C-3′, C-4″), 123.07 (C-3), 142.92 and 145.27 (C-2″, C-5″), 146.49 (C-2′), 153.16 (C-4), 172.73 (C-2); *assignments interchangeable. $C_{14}H_{12}O_4$ (244.3) calcd. C 68.85, H 4.95; found C 68.99, H 4.88.

***lk*-5-[*E*-5-(3-Furanyl)-1-hydroxy-2-methyl-2-penten-4-ynyl]-4-methyl-2(5*H*)-furanone.** *lk*-**34** (36.7 mg, 71%) was prepared from iodide *lk*-**31** (58.8 mg, 0.199 mmol), CuI (4.8 mg, 0.025 mmol, 0.13 equiv.), $PdCl_2(PPh_3)_2$ (8.8 mg, 0.010 mmol, 5 mol%), alkyne **12** (27.8 wt% in THF, 82.8 mg, 0.250 mmol, 1.25 equiv.) and $(Pr^i)_2NEt$ (1 ml) as described for compound *lk*-**30** (mp 138–139 °C). IR (film): $\nu = 3375$, 1745, 1440, 1380, 1340, 1320, 1185, 1165, 1110, 990, 870, 780, 705 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 2.05$ and 2.14 (2 br s, 4-Me, 2′-Me), 2.84 (d, $J_{\text{OH},1'} = 7.6$, OH), 4.39 (br d, $J_{1',\text{OH}} = 5.3$, 1′-H), 5.00 [br s ($J_{1',5}$ does not lead to a resolved splitting as in the case of compound *lk*-**33**), 5-H], 5.88 (m_c, 3-H, 3′-H), 6.45 (d, $J_{4'',5''} =$ 1.5, 4″-H), 7.38 (dd, $J_{5'',4''} = {}^4J_{5'',2''} = 1.7$, 5″-H)*, 7.61 (br s, 2″-H)*; *assignment analogous to *Z*-**9** where δ(2″-H) = 7.66 is low-field from δ(5″-H) = 7.40. $C_{15}H_{14}O_4$ (258.3) calcd. C 69.76, H 5.46; found C 69.89, H 5.61.

***ul*-5-[*E*-5-(3-Furanyl)-1-hydroxy-2-methyl-2-penten-4-ynyl]-4-methyl-2(5*H*)-furanone.** *ul*-**34** (58.9 mg, 76%) was prepared from iodide *ul*-**31** (88.2 mg, 0.299 mmol), CuI (7.2 mg, 0.030 mmol, 0.1 equiv.), $PdCl_2(PPh_3)_2$ (13.2 mg, 0.0150 mmol, 5 mol%), alkyne **12** (27.8 wt% in THF, 0.124 g, 0.374 mmol, 1.25 equiv.) and $(Pr^i)_2NEt$ (1.5 ml) as described for compound *lk*-**33** (mp 132–133 °C). IR (film): $\nu = 3375$, 1740, 1635, 1440, 1340, 1320, 1185, 1165, 1110, 990, 870, 780, 705 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 2.04$ and 2.12 (2 s, 4-Me, 2′-Me), 2.31 (d, $J_{\text{OH},1'} = 4.5$, OH), 4.50 (br dd, $J_{1',\text{OH}} = J_{1',5} = 4.3$, 1′-H), 5.03 (br d, $J_{5,1'} = 4.1$, 5-H), 5.87 and 5.92 (m_c and brs respectively br s, 3-H, 3′-H), 6.45 (d, $J_{4'',5''} = 1.5$, 4″-H), 7.39 (dd, $J_{5'',4''} = {}^4J_{5'',2''} = 1.7$, 5″-H)*, 7.62 (br s, 2″-H)*; *assignment analogous to *Z*-**9** where δ(2″-H) = 7.66 is low-field from δ(5″-H) = 7.40. ^{13}C NMR (APT spectrum at 125 MHz, $CDCl_3$): $\delta = 15.37$ and 16.40 (4-Me, 2′-Me), 74.98 (C-1′)*, 84.90 (C-5)*, 86.24 and 87.66 (C-4′, C-5′), 107.69 (C-3″), 108.60, 112.40 and 118.46 (C-3, C-3′, C-4″), 142.91 and 145.27 (C-2″, C-5″), 146.09 (C-2′), 167.01 (C-4), 172.91 (C-2); *assignments interchangeable. $C_{15}H_{14}O_4$ (258.3) calcd. C 69.76, H 5.46; found C 70.04, H 5.71.

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