β-Alkoxycarbonyl Enol Triflates as Precursors of Stereopure 3-Ene-1,5-diyne Building Blocks for the Chromophores of Neocarzinostatin, C-1027, Kedarcidin, Maduropeptin, and N1999A2

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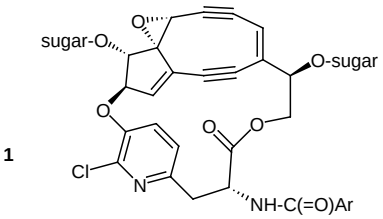
Abstract: A 5-step synthesis of α-alkoxymethyl-, α-siloxymethyl- and α-(carbamoyloxy)methyl-substituted enediynes **7** from type **23** β-oxo esters was developed following the strategy of Scheme 2. Specifically, the β-oxo esters **33**, **36** and **38** (prepared as shown in Scheme 4) and NaH (or *t*-BuLi) gave *Z*-enolates in THF and *E*-enolates in DMF which were scavenged as enol triflates *Z*-**27a**−**c** and *E*-**27a**−**c**, respectively, upon treatment with triflimides **40** or **41** (Scheme 5). The *Z*-configurated enol triflates underwent Cacchi couplings with (trimethylsilyl)acetylene to give the pent-2-en-4-yne-1-carboxylates *E*-**42a**−**c** (Scheme 5). These were reduced to the corresponding aldehydes *E*-**44a**−**c** (Scheme 6) which were homologated with lithio(trimethylsilyl)diazomethane to furnish the desired enediynes **45a**−**c** as pure *E*-isomers.

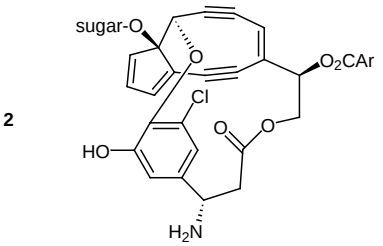
Key words: C−C couplings, enediynes, enynes, β-oxo esters, stereoselective enolate formation

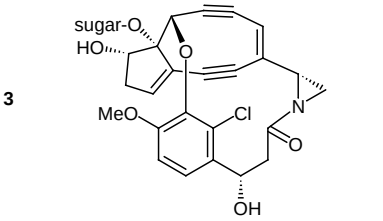
The enediyne antiobiotics are highly cytotoxic natural products.[1] One of their important common structural features is either a *cis*-configured hex-3-ene-1,5-diyne subunit or the corresponding epoxide. According to the substitution pattern of this hex-3-ene-1,5-diyne or its epoxide, the enediyne antibiotics can be subdivided into two groups. In the first group there is no substituent at C-3 of the substructure in question − i. e., the hexenediyne is of type **6** and the epoxide is derived from **6** − while in the second group there is such a 3-substituent − which means that the hexenediyne looks like compound **7** (FG is for functional group) and the epoxide is derived therefrom (Figure). The first group of enediyne antibiotics consists of esperamycin,[2] calicheamicin[3] and dynemicin.[4] The second group comprises the kedarcidin chromophore (**1**),[5] the C-1027 chromophore (**2**),[6] the maduropeptine chromophore (**3**),[7] the neocarzinostatin chromophore (**4**)[8] and a compound named N1999A2 (**5**);[9] of the latter compounds, **1**−**3** are 3-substituted hexenediynes while **4** and **5** are 3-substituted 3,4-epoxyhexenediynes.

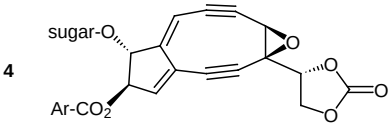
Syntheses of natural products **1**−**5** or derivatives thereof may entail or do entail the use of end-group-differentiated enediynes of the already mentioned structure **7** as key intermediates. Accordingly, routes to such hexenediynes were developed by several groups (Scheme 1).

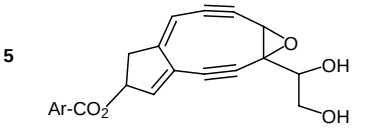
The first approaches depicted stem from Myers´ laboratory. One is based on a double Sonogashira−Tohda−Hagi-

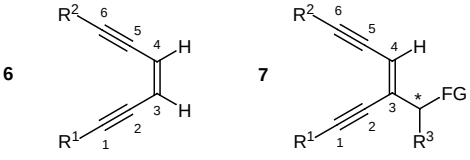












Figure

hara coupling of the stereoselectively accessible dibromoacrylate **8** providing the ester **10**.[10] This can be reduced to the underlying alcohol in which a regioselective desilylation of that Me_3Si group is possible which is closer to the OH group. Myers´ other approach to a *cis*-hex-3-ene-1,5-diyne of type **7** was the Wittig reaction between ylide **11** and ketone **12**; however, compound **13** was produced with a *cis,trans* selectivity no greater than 3:1.[11] Another synthesis of such enediynes was realized by Dai and Meyer.[12] Starting from aldehyde **14**, they prepared allyl alcohol **15**, which underwent an acid-catalyzed nucleophilic substitution with close-to-perfect $S_N1´$ vs S_N1 regioselectivity and perfect stereocontrol at the crucial C=C bond. Recently, Trost et al. developed an elegant approach to type-**7** enediynes through the Pd-catalyzed stereo- and chemoselective addition of electron-rich alkynes like compound **18** to acceptor-substituted alkynes such as compound **17**.[13] The initial C=C bond configuration (in addition product **19**) was subsequently inverted to a considerable extent by a light-induced radical chain isomerization.[14] Thus the isomer **21** was obtained, which was converted via the corresponding aldehyde and the Corey–Fuchs sequence to the desired hexenediyne **20**.

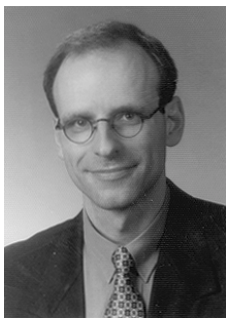
Scheme 2 outlines the strategy which *we* pursued in the quest of stereopure enediynes with the substitution pattern **7**: we desired to elaborate them from stereodefined enol triflates[15] of structure *Z*-**22**. The $R^1-C\equiv C$ moiety of our targets was intended to be introduced via the Cacchi coupling[16] with a suitable terminal alkyne $R^1-C\equiv C-H$ while the $R^2-C\equiv C$ moiety would result from the kind of C_1 elongation used by Trost et al. for the conversion **21**→**20**. The substituents CHR^3(FG) of the key triflates *Z*-**22** were functionalized in such a way that they themselves or derivatives thereof would be suitable for synthesizing the (epoxy)enediyne portions of the enediyne antibiotics **1**–**5**.

The strategy of Scheme 2 suggested the feasability of stereocontrol because of the following literature observations: Weiler et al. had shown a while ago that the deprotonation of β-oxo esters with NaH in THF (or, as one now knows, in diethyl ether[17]) gives a single sodium enolate which is scavenged by diethyl chlorophosphate to give an enol phosphate with >99% *Z* configuration; conversely, the same β-oxo esters and the same phosphorylating agent furnish enol phosphates with 98% *E*-configuration in the presence of triethylamine and HMPA.[18,19] Similarly, *N*-phenyltriflimide[20] reacts in THF with the *Z*-configured potassium enolates **25** of β-oxo esters **24** to give *Z*-enol triflates *Z*-**27**, while triflic anhydride reacts in CH_2Cl_2 with the *E*-configured ethyldiisopropyl(column[2])ammonium enolates **26** of the same β-oxo esters **24** to give the isomeric *E*-triflates *E*-**27** (Scheme 3).[21] Also, *N*-phenyltriflimide[20] transforms the *Z*-configured sodium enolates **28** obtained from β-oxo esters **24** and NaH in THF into enol triflates *Z*-**27** and the *E*-configured sodium enolates **29** obtained from β-oxo esters **24** and NaH in DMF into the isomeric enol triflates *E*-**27**.[22]

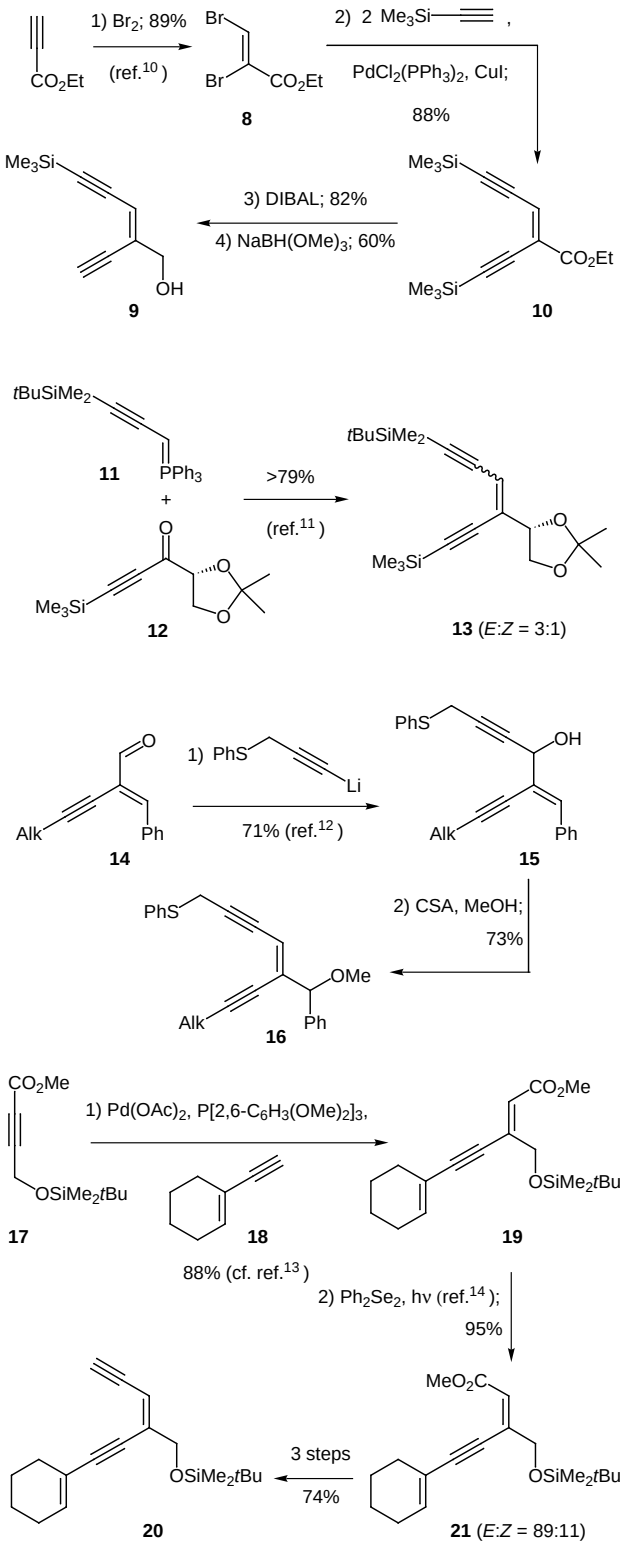
The β-oxo ester substrates of the present study, namely compounds **33**, **36** and **38** (Scheme 4), differ from all previously used β-oxo ester precursors **24** of stereo*pure* enol triflates by the presence of at least one heteroatom in the substituent R^3. The presence of these heteroatoms makes the target enediynes *Z*-**44a**–**c** (Scheme 6) into building

Biographical Sketches

Reinhard Brückner (born in 1955) prepared his doctoral thesis at the Ludwig-Maximilians-Universität München under the supervision of Professor Rolf Huisgen (1984) and was a postdoctoral fellow with Professor Paul A. Wender at Stanford University. After habilitating with Professor Reinhard W. Hoffmann at the Philipps-Universität Marburg he became an associate professor at the Julius-Maximilians-Universität Würzburg (1990). He was a full professor at the Georg-August-Universität Göttingen (1992) and moved to Freiburg six years later. Being a dedicated teacher, he was a visiting professor at the Universities of Wisconsin / Madison and Santiago de Compostela / Spain. His research interests include rearrangements of organolithium compounds and the synthetic chemistry of dienediynes, polyols, butyrolactones and butenolides.

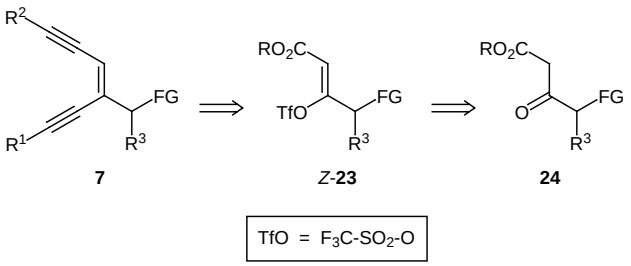


Olaf Gebauer was born in Kiel in 1967. He studied chemistry at the universities of Kiel, Braunschweig and Göttingen and received his Dr. rer. nat. in 1999 (Prof. R. Brückner) synthesizing models of the dienediyne antibiotic neocarzinostatin chromophore. In July 1999, he joined the BAYER company´s crop-protection research center in Monheim. There he is currently synthesizing and developing fungicides.



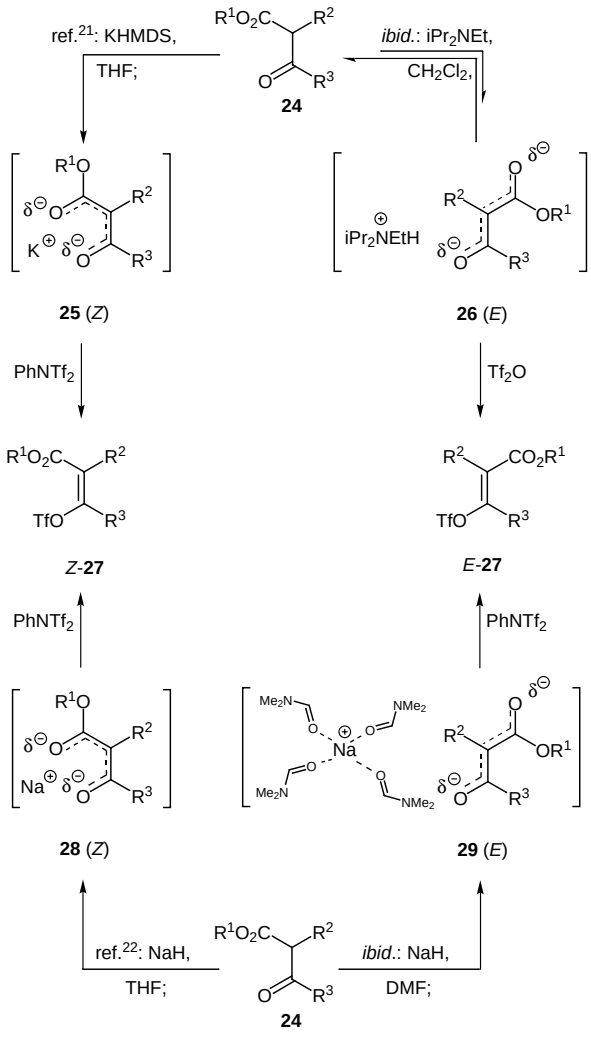
Scheme 1

blocks for the synthesis of enediynes like compounds **1**–**5**. Hence, it remained to be seen how these heteroatoms affect the delicate bias between *Z*- and *E*-selective ester enolate formation.

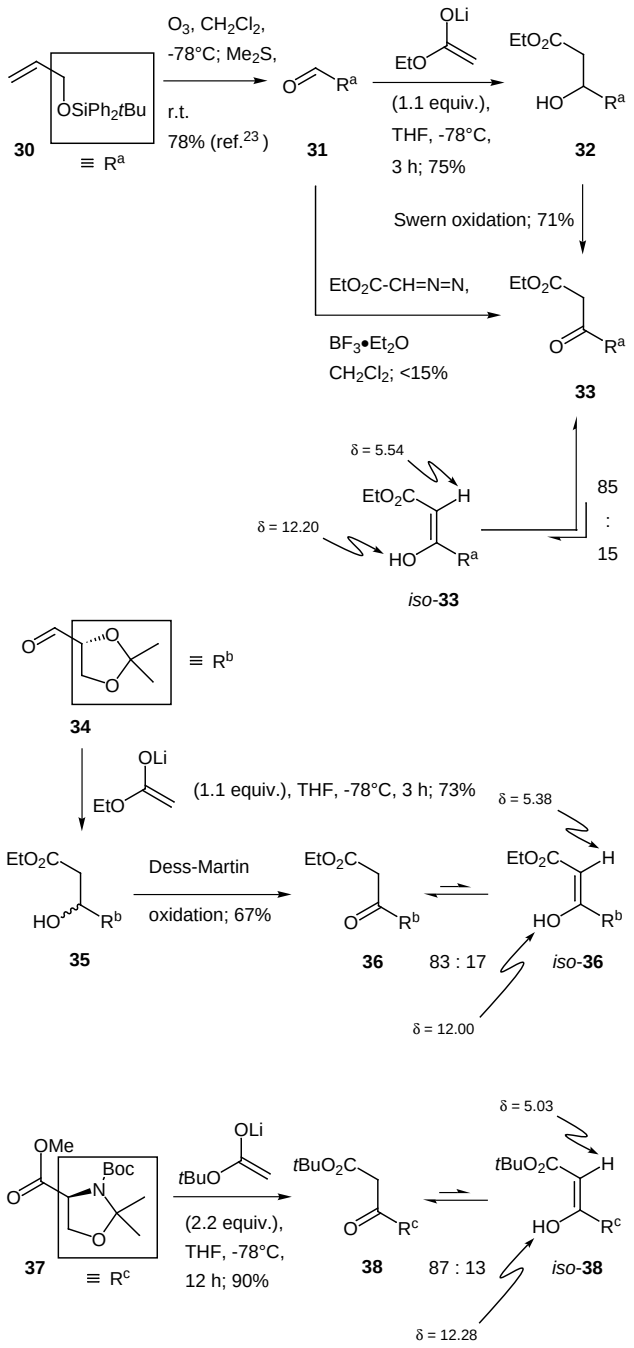


Scheme 2

Scheme 4 shows how the properly functionalized β-oxo esters **33**, **36** and **38** were prepared. The aldehyde precursor **31** of β-oxo esters **33** was obtained in 78% overall yield through the *tert*-butyldiphenylsilylation of allyl alcohol and the ozonolysis of the resulting silyl ether **30**.[23] An aldol addition of the lithium enolate of ethyl acetate transformed this aldehyde into the β-hydroxy ester **32** which was carried on to the β-oxo ester **33** by a Swern oxidation.[24] This 2-step sequence totalled 53% yield. Hence,



Scheme 3



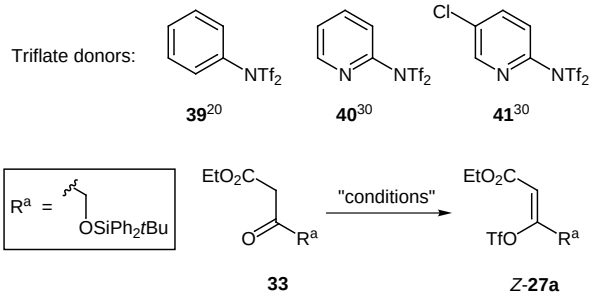
Scheme 4

it was superior to a 1-step conversion of aldehyde **31** into β-oxo ester **33** which we attempted following a general procedure from Roskamp´s group, i. e., by treating aldehyde **31** with ethyl diazoacetate and BF_3−diethyl ether complex:[25] On a reasonably large scale we could not advance to reproducible yields >15%. D-Glyceraldehyde acetonide (**34**) was prepared by the usual sodium periodate cleavage[26] of D−mannitol bisacetonide.[27] Adding ethyl lithioacetate to this aldehyde led to the β-hydroxy ester **35** as a 89:11 mixture of unassigned diastereomers (73% yield). Oxidation with the Dess−Martin periodinane[28] delivered 67% of the acetonide-containing β-oxo ester **36**.

Last, but not least, a Claisen condensation of the lithium enolate derived from *tert*-butyl acetate with Garner´s ester **37**[29] furnished 90% of β-oxo ester **38**. As expected, the ^{1}H NMR spectra of the oxo esters **33**, **36** and **38** of Scheme 4 displayed the (O=)CCH_2C(=O) protons as a singlet at δ = 3.63 (**33**) or as AB spectra δ_A = 3.60 / δ_B = 3.66 (**36**, **38**). In addition, there were the less intense singlets of the C=C−H (δ ≈ 5.0−5.5 ppm) and C=C−OH substructures (δ ≈ 12.0−12.3 ppm) of the tautomeric enols *iso*-**33**, *iso*-**36** and *iso*-**38** as which 13−17% of the material was present.

The stereoselective conversion of the β-oxo esters **33**, **36** and **38** into ester-containing *Z*-configured enol triflates required generating the respective β-oxo ester enolates *Z*-selectively. According to Scheme 3, this is tantamount to generating *cation-bridged* β-oxo ester enolates. For preliminary tests we deprotonated the β-oxo ester **33** (Table 1). Using KHMDS in dry-ice cooled THF for that purpose, i. e. the *Z*-favoring conditions of reference 21, and sulfonylating with McMurry´s phenyl triflimide **39**,[20] we isolated just 27% of the desired triflate **27a** (entry 1). It was the pure *Z*-isomer as was the crude product according to the ^{1}H NMR spectrum. Deprotonating the β-oxo ester **33** with NaH [22,30] in THF and now at 0 °C → room temperature increased the yield of *Z*-**27a** to 43% (entry 2). Replacing the phenyl triflimide **39**[20] by Comins´ pyridyl triflimide **40**[31] under the otherwise unchanged deprotonation conditions, the desired enol triflate ***Z*−27a** became available in 53% yield (entry 3). Finally, by heating the last-mentiond sulfonylating mixture at 55 °C for extended times − 6 h in the case of entry 4 of Table 1 − the yield of ***Z*−27a** rose to 83% (taking 21% of recovered β-oxo ester **33** into account). That *this* temperature turned out to be so beneficial is remarkable because there are ester-containing enol triflates which undergo a β-elimination of triflic acid under much milder conditions − i. e., in the presence of triethylamine within 3 h at room temperature[32] − and

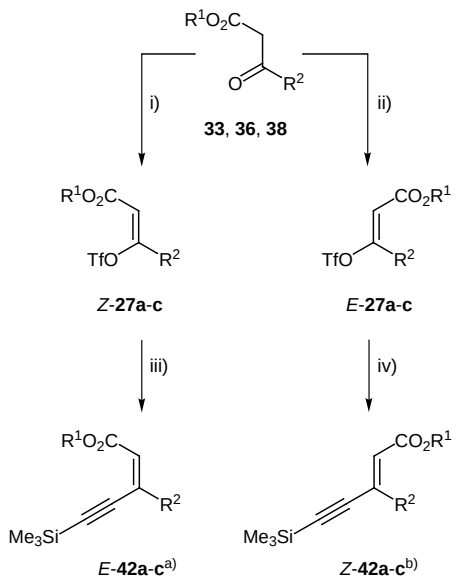
Table 1



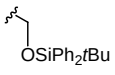
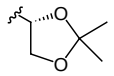
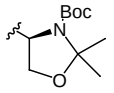
entry	base	triflate donor	conditions	yield[a]
1	KHMDS	**39**	-78°C → room temp.; overnight	27%
2	NaH	**39**	0°C → room temp.; overnight	43%
3	NaH	**40**	0°C, 20 min; room temp., 6 h	53%
4	NaH	**40**	0°C, 20 min; room temp., 30 min; 55°C, 6 h	83%[b]

[a] Small amounts of *E*-**27** were separated by flash chromatography.
[b] Taking into account that 21% of the starting material were recovered; isolated yield: 65%.

give an allenic ester thereby. The ^{1}H NMR spectra of the crude enol triflate revealed that even when the sulfonylating agent was triflimide **40** there was at most 1% of *E*-**27a** formed. In contrast to that, Gibbs et al. had found in a related sulfonylation that the use of **40** vs. **39** tends to increase the proportion of the *E*-product to >5%.[33] It should be noted that we could not use Comins´ pyridyl triflimide **41**[31] for preparing the enol triflate *Z*-**27a** since both compounds co-chromatographed.



a) This is not a *Z*-isomer because of the hetero-substituent at C-α of R^2.
b) This is not an *E*-isomer because of the hetero-substituent at C-α of R^2.

	a (and **33**)	**b** (and **36**)	**c** (and **38**)
R^1	Et	Et	*t*Bu
R^2	= R^a = 	= R^b = 	= R^c = 

i) For **a**: **33**, NaH, THF, r.t., 20 min; **40** (1.2 equiv.), 30 min; 55 °C, 6 h; 83% based on recovered starting material (65% isolated).−For **b**: **36**, NaH, THF, r.t., 20 min; **41** (1.2 equiv.), 30 min, 70 °C, 3.5 h; 62%.− For **c**: **38**, *t*-BuLi (1.0 equiv.), THF, −78 °C, 30 min; **40** (1.2 equiv.), r.t., 30 min; 55 °C, 14 h; 71%. ii) NaH, DMF, r.t., 20 min; **40** (1.2 equiv.), 4 h; **a**: 52%; **b**: 67%; **c**: 72%. iii) $Me_3Si-C\equiv C-H$ (1.2 equiv.), $PdCl_2(PPh_3)_2$ (5 mol-%), CuI (15 mol-%), 3:1 i-Pr_2NH/THF, r.t.; **a** (16 h): 72%; **b** (2 h): 82%; **c** (2 h): 85%. iv) Same as (iii), 2 h; **a**: 67%; **b**: 82%; **c**: 88%.

Scheme 5

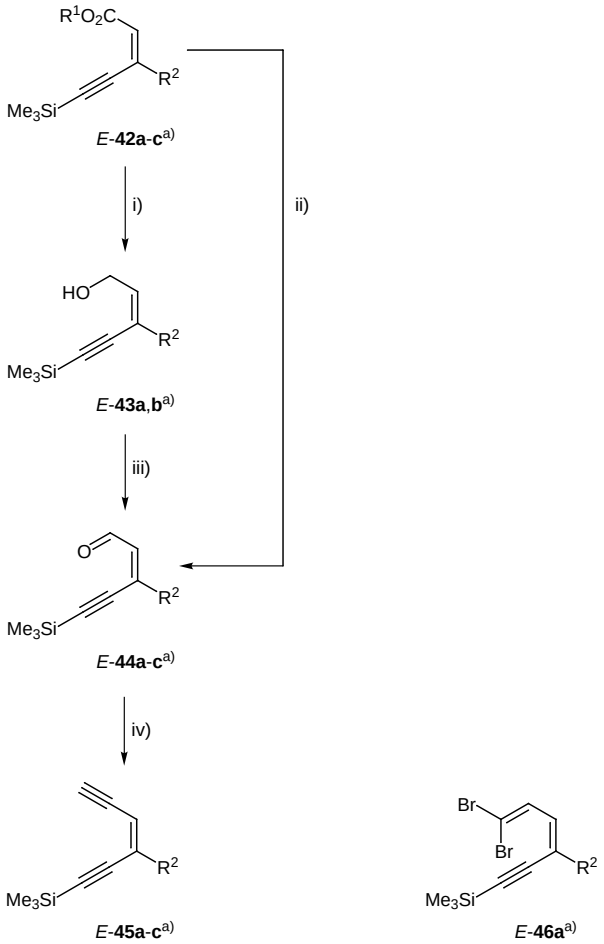
The ester-containing enol triflates *Z*-**27b** and **c** were similarly prepared (Scheme 5) as enol triflate *Z*-**27a** (Table 1) and were likewise isolated as pure *Z*-isomers, now, however, after flash chromatographic separation from 96:4 *Z*:*E* mixures initially obtained. Yield optimization required considerable fine-tuning of the reaction parameters. The triflation of the acetonide-containing β-oxo ester **36** worked best with NaH and the chlorinated pyridyl triflimide **41**. The Boc−containing β-oxo ester **38** was best deprotonated with *t*-BuLi.

In order to assess the stereoselectivity of the trifluoromethanesulfonylations of Table 1 and Scheme 5 (upper left), we needed to know, besides the ^{1}H NMR shifts of the desired *Z*-isomers, the ^{1}H NMR shifts of the *E*-isomers. Therefore, we were pleased to find that we could − as did Keenan et al.[22] − prepare the *E*−triflates *E*-**27a**−**c** from the β-oxo esters **33**, **36** and **38**, NaH and a suitable triflimide (vide infra) *in DMF* (Scheme 5, upper right). These compounds were isolated as a 95:5 mixture in the case of *Z*- and *E*-**27a** or isomerically pure − after the initially obtained 99:1 *E*:*Z* mixtures had been chromatographed − in the case of *Z*-**27b** and **c**.

The alkenic nuclei 2-H and C-2 of the ester-containing enol triflates *Z*- and *E*-**27a**−**c** reveal configuration-dependent δ-values: (1) In triflates *Z*−**27a** and *Z*−**27b**, $\delta_{2\text{-H}}$ = 6.23 ppm (2 ×) is at *lower* field than in the isomeric triflates *E*−**27a** (5.89 ppm) and *E*−**27b** (6.04 ppm). In contrast, there is a *high*-field shift of 2-H in triflate *Z*−**27c** (δ_{2-H} = 5.84) compared with the isomeric triflate *E*−**27c** (δ_{2-H} = 5.98). Yet, the configurational assignment of compound *Z*-**27c** is safe since it is based on the occurrence of a cross-peak between the alkenic and the allylic proton in the NOESY spectrum. (2) The alkenic δ_{C-2} value in triflates *Z*−**27a** and *Z*−**27b** is *high*field with respect to δ_{C-2} in the respective *E* isomer, while it appears at *lower* field in triflate *Z*-**27c** compared with *E*-**27c**. Thus, the configurational assignment of ester-substituted enol triflates of type **7** cannot be based on the sign of $\Delta\delta_{2\text{-H}}$ or $\Delta\delta_{C\text{-}2}$ values.

Next, enol triflates **27a**−**c** and (trimethylsilyl)acetylene as a particularly reactive and synthetically widely manipulable acetylene were subjected to the Cacchi couplings[16] shown in Scheme 5.[33b] Using 5 mol-% of $PdCl_2(PPh_3)_2$ as a catalyst, 15 mol-% CuI as a co-catalyst and 3:1 THF/iPr_2NH as the solvent, i. e., the conditions from reference 19, these couplings occurred at room temperature within 2 h and in yields of 67−88%. They proceeded with complete retention of the double bond configuration, no matter whether we started from the *Z*-configured enol triflates − as our synthetic objective demands − or from the *E*-configured enol triflates − in order to acquire NMR reference data for analyzing the isomer composition of the coupling products. Accordingly, the Cacchi couplings of the 100% stereopure enol triflates *Z*-**27a**−**c**, *E*-**27b** and *E*-**27c** furnished the coupling products *E*-**42a**−**c**, *Z*-**42b** and *Z*-**42c**, respectively, 100% stereopure (note that in these reactions the conversion of *Z*- into *E*-isomers and *vice versa* corresponds to the *retention* of configuration). Similarly, the 95:5 mixture of enol triflates *E*- and *Z*-**27a** reacted with (trimethylsilyl)acetylene to provide the crude coupling product **42a** as a 95:5 *Z*:*E* mixture as evidenced by ^{1}H NMR analysis. Since the minor isomer could be separated by flash chromatography, the major coupling product *Z*-**42a** was isolable 100% stereopure, too. In pairs of isomer-

ic coupling products **42** the ^1H and ^{13}C NMR shifts of the alkenic CH group are ordered as in the corresponding isomer pairs of their respective enol triflate precursor **27**: The alkenic $\delta_{C\text{-}^1H}$ values in *E*−**42a** and *E*−**42b** − but not in *E*−**42c** − are *low*field compared with the respective *Z*-isomer while the alkenic $\delta_{^{13}C-H}$ values in *E*−**42a** and *E*−**42b** − but not in *E*−**42c** − are *high*field compared with the respective *Z*-isomer. Thus, there is again no 1:1 correspondence between the configuration of these compounds and the relative magnitude of the C_{sp^2}-H shifts.



a) This is not a *Z*-isomer because of the hetero-substituent at C-α of R^2.

R^1 and R^2 as in Scheme 5

i) For **a**: DIBAL (2.7 equiv.), CH_2Cl_2, −78 °C → r.t., 3 h; 81%. For **b**: DIBAL (2.7 equiv.), EtO_2/toluene, −78 °C, 3 h; r.t., 30 min; 88%. ii) For **c**: DIBAL (1.3 equiv., toluene, −78 °C, 30 min; MeOH; 81%. iii) Dess−Martin periodinane (1.2 equiv.), CH_2Cl_2, r.t., 1 h (**a**) or 20 min (**b**); for **a**: 81%; for **b**: 82%. iv) LDA (1.2 equiv.), Me_3Si−CH=N=N, THF, −78 °C, 30 min; addition of respective aldehyde **44**; 1.5 h (**a**, **b**) or 3 h (**c**); r.t., 4 h (**a**) or 20 min (**b**, **c**); for **a**: 49%; for **b**: 39%; for **c**: 41%.

Scheme 6

The final goal was to transform the CO_2R^1 groups of the coupling products *E*-**42** into the C≡C−H groups of the target enediynes *E*-**45**. To this end, the esters *E*-**42** were first converted into the corresponding aldehydes *E*-**44** (Scheme 6). In the case of the esters *E*-**42a** and **b** this was done in two steps. We reduced them with 2.7 equiv. of DIBAL to give the allyl alcohols *E*-**43a** and **b** and oxidized those with the Dess−Martin reagent[28] to provide the aldehydes *E*-**44a** and **b** in 66% and 71% yields, respectively. The Boc-containing ester *E*−**42c** could be reduced one-step to the aldehyde *E*-**44c** at −78 °C by treatment with 1.1 equiv. of DIBAH in toluene (81% yield).

For the remaining conversion of the aldehydes **44** into the enediynes **45** we envisioned the Corey−Fuchs sequence.[34] Accordingly, we dibromomethylenated aldehyde *E*-**44a** with CBr_4 (2.0 equiv.), PPh_3 (4.0 equiv.) and Et_3N (1.0 equiv.) and obtained the dibromodienyne *E*-**46a** in 72% yield. However, treatment of this compound with MeLi or BuLi led to a rapid decomposition and not to the desired enediyne *E*-**45a**. In principle, a one-step alternative for alkyne formation from the aldehydes **44** could have been their Horner-Wadsworth-Emmons reaction with a deprotonated dimethyl diazomethanephosphonate[35] but the easier-to-perform Ohira modification of this reaction[36] was not applicable: Instead of the desired transformation −C=C−CH=O → −C=C−C≡C−H it is reported to effect −C=C−CH=O → −C(OMe)C−CH−C≡C−H.[37] Thus, we took recourse to the method of Shioiri et al. from which it was known that it does effect the particular conversion −C=C−CH=O → −C=C−C≡C−H.[38] Accordingly, we treated the aldehydes *E*-**44a**−**c** with lithio(trimethylsilyl)diazomethane − prepared at −78 °C from freshly prepared LDA and the commercially available solution of (trimethylsilyl)diazomethane in THF − as described, i. e., for 1 h at −78 °C and for 3 h at reflux temperature. What occurred was nothing but decomposition. However, when we warmed the reaction mixtures from −78 °C slowly to no more than room temperature, the desired alkynes *E*-**45a**−**c** formed. The feasability of synthesizing functionalized 3-substituted *cis*-configured hex-3-ene-1,5-diynes from β-oxo esters − in a total of 4−5 steps − has hereby been demonstrated. The modest yields of the last step − 49%, 39% and 41%, respectively − seems to reflect the inherent instability of the enediynes and not so much a weakness of their formation reactions since the latter were spot-to-spot conversions as judged by TLC.

All reactions were performed in oven-dried (100 °C) glassware under anhyd N_2. THF, Et_2O and toluene were freshly distilled from K before use, CH_2Cl_2, DMSO, DMF and amines from CaH_2; MeOH was dried with Mg. Titration of RLi according to Suffert.[39] Products purified by flash chromatography[40] on Macherey&Nagel silica gel 60 (particle size 0.040−0.063 mm, 230−240 mesh ASTM; column diameter, eluents and product-containing fractions given in brackets; fraction volumes chosen as a function of the diameter of the used column: 1.0 cm ⇒ 5 mL, 1.5 cm ⇒ 10 mL, 2.0 cm ⇒ 15 mL, 2.5 cm ⇒ 20 mL, 4.0 cm ⇒ 50 mL, 6.0 cm ⇒ 100 mL). Yields refer to analytically pure samples. Optical rotations: Perkin-Elmer polarimeter 241 MC, Na lamp, 589 nm. ^1H NMR spectra (unless speci-

fied differently: TMS or $CHCl_3$ as internal standard working in $CDCl_3$; occasionally: MeOH as internal standard working in CD_3OD): VXL-200 (Varian), AMX300 (Bruker) and VXR-500S (Varian). Integrals in accord with assignments; coupling constants in Hz; AB spectra: H_A refers to high- and H_B to low-field resonance; all signals except AB signals evaluated by first-order splitting. APT ^{13}C NMR spectra: same instruments, "+" for CH or CH_3, "-" for CH_2 or $C_{quaternary}$. IR spectra (film or solution in $CDCl_3$; selected bands only are listed in the following): Perkin Elmer FT-IR 1600. MS and HRMS were registered by Dr. G. Remberg, Institut für Organische Chemie der Universität Göttingen, on a Finnigan MAT 95 spectrometer. Combustion analyses: M. Beller and F. Hambloch, Institut für Organische Chemie der Universität Göttingen.

Ethyl (*Z*)-4-[*tert*-Butyl(diphenyl)siloxy]-3-{[(trifluoromethyl)-sulfonyl]oxy}but-2-enoate (*Z*-27a)

At 0 °C a solution of β-oxo ester **33** (0.970 g, 2.52 mmol) in THF (4 mL) was added carefully to a suspension of NaH (0.079 g, 3.3 mmol, 1.3 equiv.) in THF (4 mL). Stirring was continued at r. t. for 20 min whereupon triflimide **40** was added (1.08 g, 3.02 mmol, 1.2 equiv.). After stirring for 30 min at r. t. and for 6 h at 55 °C the heating bath was removed and Et_2O (20 mL) added. Successive extractions with H_2O (3 × 5 mL), sat. NH_4Cl (5 mL), sat. $NaHCO_3$ (5 mL) and finally brine (5 mL) ensued. After drying (Na_2SO_4) the solvent was removed in vacuo. Purification by flash chromatography gave the title compound >99% isomer-free from *E*-**27a** [1.5 cm, petroleum ether/*t*-BuOMe 20:1, F7−12, 0.849 g, 65%]. Some of the starting oxo ester **33** was re-isolated (F15-22; 0.206 g, 21%) so that the yield of *Z*-**27a** based on recovered starting material measures 83%.

^1H NMR (300 MHz): δ = 1.09 (s, *t*-Bu), 1.34 (t, $J_{2''',1'''}$ = 7.2, 2'''-H_3), 4.23 (d, $J_{1'',2'}$ = 1.5, 1''-H_2), in touch with 4.28 (q, $J_{1''',2'''}$ = 7.1, 1'''-H_2), 6.23 (t, $J_{2',1''}$ = 1.7, 2'-H), 7.38−7.48 (m, 6 *meta*- and *para*-H_{Ar}), 7.63 (dd, J_{ortho} = 7.9, J_{meta} = 1.5, 4 *ortho*-H_{Ar}).

^{13}C NMR (APT spectrum at 50 MHz, contains unidentified peak at δ = "+" 127.98): δ = "+" 14.06 (C-2'''), "-" 19.16 [*C*$(CH_3)_3$], "+" 26.62 [C(*C*$H_3)_3$], "-" 61.40 and "-" 61.81 (C-1'', C-1'''), "+" 111.03 (C-2'), "-" 118.19 (only the innermost lines of q, $J_{C,F}$ = 319.6, CF_3), "+" 128.03 (4 *meta*-C), "+" 130.27 (2 *para*-C, because the intensity of this resonance is only half that of the 4 *meta*- and the 4 *ortho*-C's), "-" 131.72 (2 *ipso*-C), "+" 135.29 (4 *ortho*-C), "-" 156.37 (C-1'), "-" 162.55 (C=O).

MS (EI/70 eV): *m*/*z* = 559 (22%), 516 (2%, M^+), 501 (8%, M^+ − Me), 471 (9%, M^+ −EtOH), 459 (100%, M^+ −*tert*-butyl), 431 (7%), 357 (7%), 309 (8%), 271 (90%), 238 (32%), 199 (70%), 127 (12%), 105 (40%), 91 (12%).− MS (DCI/pos., NH_4^+): *m*/*z* = 534 (100%, $M^+ + NH_4^+$), 475 (10%), 402 (18%), 384 (38%), 356 (10%).

IR ($CDCl_3$): ν = 1725 and 1690 (C=O and C=C st), 1385 and 1185 cm^{-1} (S=O st).

Anal. Calcd for $C_{23}H_{27}O_6F_3SSi$ (516.6): C 53.48; H 5.28. Found C 54.48; H 5.24; a better combustion analysis could not be obtained.

Ethyl (*E*)-4-[*tert*-Butyl(diphenyl)siloxy]-3-{[(trifluoromethyl)-sulfonyl]oxy}but-2-enoate (*E*-27a) in a 94:6 Mixture with *Z*-27a

At 0 °C a solution of the β-oxo ester **33** (0.174 g, 0.450 mmol) in DMF (1 mL) was added carefully to a suspension of NaH (0.014 g, 0.590 mmol, 1.3 equiv.) in DMF (1 mL). After stirring at r. t. for 20 min, the triflimide **40** (0.194 g, 0.540 mmol, 1.2 equiv.) was added and stirring continued for 4 h. Diluting with Et_2O (20 mL), washing successively with H_2O (3 × 5 mL), sat. NH_4Cl (5 mL), sat. $NaHCO_3$ (5 mL) and brine (5 mL), drying (Na_2SO_4), removing the solvent in vacuo and purifying by flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 30:1, F8-12) gave the title compound (0.122 g, 52%); it was a 94:6 *E*:*Z* mixture according to the ^1H NMR integral ratio over the 2´-H resonances.

***E*-27a**

^1H NMR (300 MHz): δ = 1.08 (s, *t*-Bu), 1.17 (t, $J_{2''',1''}$ = 7.2, 2'''-H_3), 4.06 (q, $J_{1'',2'''}$ = 7.2, 1'''-H_2), 4.81 (s, 1''-H_2), 5.89 (s, 2'-H), 7.36−7.47 (m, 6 *meta*- and *para*-H_{Ar}), 7.69 (dd, J_{meta} = 7.7, J_{ortho} = 1.7, 4 *ortho*-H_{Ar}).

^{13}C NMR (APT spectrum at 50 MHz, contains unidentified peak at "+" 135.54): δ = "+" 13.90 (C-2'''), "-" 19.15 [*C*$(CH_3)_3$], "+" 26.52 [C(*C*$H_3)_3$], "-" 59.87 and "-" 61.34 (C-1'', C-1'''), "+" 113.16 (C-2'), "-" 118.49 (three lines of q, $J_{C,F}$ = 320.5, CF_3), "+" 127.79 (4 *meta*-C), "+" 129.95 (2 *para*-C, because the intensity of this resonance is only half that of the 4 *meta*- and the 4 *ortho*-C's), "-" 132.30 (2 *ipso*-C), "+" 135.60 (4 *ortho*-C), "-" 161.55 and "-" 163.17 (C-1', C=O).

***Z*-27a**

^1H NMR (300 MHz): δ = 1.34 (t, $J_{2''',1''}$ = 7.2, 2'''-H_3), 4.23 (d, $J_{1'',2'}$ = 1.5, 1''-H_2), 4.28 (q, $J_{1''',2'''}$ = 7.2, 1'''-H_2), 6.23 (t, $J_{2',1''}$ = 1.7, 2'-H), 7.64 (dd, J_{meta} = 7.7, J_{ortho} = 1.7, 4 *ortho*-H_{Ar}); the residual resonances are superimposed by those of *E*-**27a**.

^{13}C NMR (APT spectrum at 50 MHz, contains unidentified peak at "+" 135.54): δ = "+" 15.18 (C-2'''), "+" 26.61 [C(*C*$H_3)_3$], "-" 60.76 and "-" 61.95 (C-1'', C-1'''), "+" 111.05 (C-2'), "+" 128.05 (4 *meta*-C), "+" 130.30 (2 *para*-C, because the intensity of this resonance is only half that of the 4 *meta*- and the 4 *ortho*-C's ist), "+" 135.31 (4 *ortho*-C); the residual resonances are superimposed by those of *E*-**27a**.

IR ($CDCl_3$): ν = 1725 and 1665 (C=O and C=C st), 1380 and 1225 cm^{-1} (S=O st).

No satisfactory combustion analysis could be obtained.

Ethyl (*Z*)-3-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-{[(trifluoromethyl)sulfonyl]oxy}prop-2-enoate (*Z*-27b)

Prepared as described for *Z*-**27a** from the β-oxo ester **36** (7.39 g, 34.2 mmol) in THF (74 mL), a suspension of NaH (0.813 g, 33.9 mmol, 1.0 equiv.) in THF (74 mL) and the triflimide **41** (16.1 g, 41.1 mmol, 1.2 equiv.) except that the latter was allowed to react 30 min at r. t. and 3.5 h at 70 °C. Extractive workup and flash chromatography (6 cm, petroleum ether/*t*-BuOMe 12:1, F23−38) provided the title compound (7.32 g, 62%). According to the extremely weak 2'-H ^{1}NMR signal it was >99% isomer-free from *E*-**27b**.

$[\alpha]_D^{26}$ = −41.1 (*c* = 1.82 in $CHCl_3$).

^1H NMR (300 MHz): δ = 1.32 (t, $J_{2',1'}$ = 7.2, 2'-H_3), 1.41 and 1.51 [2 s, 2''-$(CH_3)_2$], AB signal (δ_A = 4.02, δ_B = 4.31, J_{AB} = 9.0, in addition split by $J_{A,4''}$ = 5.3, $J_{B,4''}$ = 7.0, 5''-H_2), 4.20 (m_c, 1'''-H_2), 4.63 (poorly resolved ddd, $J_{4'',5''\text{-}H(B)}$ = 6.8, $J_{4'',5''\text{-}H(A)}$ = 5.3, $^4J_{4'',2'}$ = 1.1, 4''-H), 6.23 (d, $^4J_{2',4''}$ = 1.5, 2'-H).

NOESY spectrum for configurational assignment: The resonances at δ = 4.63 (4''-H) and 6.23 (2'-H) exhibit a cross-peak, which proves the *cis*-configuration of the C=C bond.

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 13.97 (C-2'''), "+" 25.01 and "+" 26.11 [2''-$(CH_3)_2$], "-" 61.48 (C-1'''), "-" 67.62 (C-5''), "+" 73.48 (C-4''), "+" 111.60 (C-2'' and C-2'), "-" 118.30 (q, $J_{C,F}$ = 320, CF_3), "-" 155.94 (C-1'), "-" 162.29 (C=O).

IR ($CDCl_3$): ν = 1725 and 1685 (C=O and C=C st), 1380 and 1300 cm^{-1} (S=O st).

Anal. Calcd for $C_{11}H_{15}O_7F_3S$ (348.3): C 37.93; H 4.35. Found C 38.03; H 4.38.

Ethyl (*E*)-3-[(4*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-{[(trifluoromethyl)sulfonyl]oxy}prop-2-enoate (*E*-27b)

Prepared as described for *E*-**27a** from the β-oxo ester **36** (0.100 g, 0.460 mmol) in DMF (1 mL), NaH (0.011 g, 0.46 mmol, 1.0 equiv.) in DMF (1 mL) and triflimide **40** (0.197 g, 0.550 mmol, 1.2 equiv.). Flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 10:1, F4-

6) provided the title compound (0.108 g, 67%); the *E*:*Z* ratio was >99:1 according to the integrals of the 2'-H´s.

$[\alpha]_D^{25}$ = +40.4 (*c* = 1.55 in $CHCl_3$).

^{1}H NMR (300 MHz): δ = 1.32 (t, $J_{2''',1'''}$ = 7.2, 2'''-H_3), 1.42 and 1.52 [2 s, 2''-$(CH_3)_2$], AB signal (δ_A = 3.90, δ_B = 4.37, J_{AB} = 8.6, in addition split by $J_{A,4''}$ = 6.4, $J_{B,4''}$ = 7.3, 5''-H_2), 4.23 (q, $J_{1''',2'''}$ = 7.2, 1'''-H_2), 5.69 (incompletely resolved ddd, $J_{4'',5''\text{-H(A)}} \approx J_{4'',5''\text{-H(B)}} \approx$ 7.7, $^4J_{4'',2'}$ = 0.8, 4''-H), 6.04 (d, $^4J_{2',4''}$ = 0.8, 2'-H).

NOESY spectrum for configurational assignment: The absence of a cross-peak between the resonances at δ = 5.69 (4''-H) and 6.04 (2'-H) proves the *trans* configuration of the C=C bond.

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 14.01 (C-2'''), "+" 25.19 and "+" 25.40 [2''-$(CH_3)_2$], "-" 61.69 (C-1'''), "-" 68.01 (C-5''), "+" 76.36 (C-4''), "-" 111.83 (C-2''), "+" 114.43 (C-2'), "-" 118.34 (q, $J_{C,F}$ = 319.4, CF_3), "-" 161.10 (C-1'*), "-" 163.49 (C=O*); *assignments interchangeable.

IR ($CDCl_3$): ν = 1720 and 1655 (C=O and C=C st), 1380 and 1215 cm^{-1} (S=O st).

Anal. Calcd for $C_{11}H_{15}O_7F_3S$ (348.3): C 37.93; H 4.34. Found C 37.81; H 4.40.

tert-Butyl (4*S*)-4-((*Z*)-3-Butoxy-3-oxo-1-{[(trifluoromethyl)sulfonyl]oxy}prop-1-enyl)-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (*Z*-27c)

At −78 °C *t*-BuLi (1.18 M; 375 µl, 0.443 mmol, 1.0 equiv.) was added within 40 min dropwise and under continued stirring to a solution of the β-oxo ester **38** (0.152 g, 0.443 mmol) in THF (2.0 mL). After 30 min, triflimide **40** (0.192 g, 0.535 mmol, 1.2 equiv.) was added, and the mixture was allowed to warm to r. t. within 30 min. Thereafter, it was heated at 55 °C for 14 h. Workup through diluting with *t*-BuOMe (30 mL), washing with H_2O (4 × 6 mL), sat. NH_4Cl (6 mL), sat. $NaHCO_3$ (6 mL) and finally brine (6 mL), drying (Na_2SO_4), removing the solvent in vacuo and flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 10:1, F12-21) gave the title compound (0.150 g, 71%). The *Z*:*E* ratio was >99:1 according to the 4''-H ^{1}H NMR signals.

$[\alpha]_D^{26}$ = −4.67 (*c* = 1.30 in $CHCl_3$).

^{1}H NMR (300 MHz; contains an extra peak at δ = 4.57 which is supposed to stem from a rotamer): δ = 1.45 and 1.53 [2 s, 2''-$(CH_3)_2$], 1.51 (s, 2 × t-Bu), AB signal (δ_A = 4.07, δ_B = 4.13, J_{AB} = 9.4, in addition split by $J_{A,4''}$ = 1.9, $J_{B,4''}$ = 6.4, 5''-H_2), 4.42 (br d, $J_{4'',5''\text{-H(B)}}$ = 5.7, 4''-H), 5.84 (s, 2'-H).

NOESY spectrum for configurational assignment: The resonances at δ = 4.42 (4''-H) and 5.84 (2'-H) exhibit a cross-peak which proves the *cis*-configuration of the C=C bond.

^{13}C NMR [APT spectrum at 50 MHz; contains unidentified peak at δ = "+" 28.13 which might be due to 2 × C(CH_3)$_3$ of a rotamer]: δ = "+" 22.74 and "+" 26.48 [2''-$(CH_3)_2$], "+" 27.92 [2 × C(CH_3)$_3$], "+" 58.69 (C-4''), "-" 65.79 (C-5''), "-" 81.62 and "-" 82.85 [2 × *C*(CH_3)$_3$], "-" 95.24 (C-2''), "+" 113.18 (C-2'), "-" 118.33 (q, $J_{C,F}$ = 320.7, CF_3), "-" 151.11 and "-" 155.14 (C-1', C-1'''), "-" 161.55 (*C*CO_2t-Bu).

IR ($CDCl_3$): ν = 1710 (C=O st), 1370 and 1215 cm^{-1} (S=O st).

Anal. Calcd for $C_{18}H_{28}NO_8F_3S$ (475.5): C 45.47; H 5.94. Found C 45.70; H 5.86.

tert-Butyl (4*S*)-4-((*E*)-3-Butoxy-3-oxo-1-{[(trifluoromethyl)sulfonyl]oxy}prop-1-enyl)-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (*E*-27c) in a 65:35 Mixture with a Rotamer (*iso*-*E*-27c)

Prepared as described for *E*-**27a** from the β-oxo ester **38** (0.237 g, 0.690 mmol) in DMF (1.5 mL), NaH (0.016 g, 0.69 mmol, 1.0 equiv.) in DMF (1.5 mL) and the triflimide **40** (0.294 g, 0.820 mmol, 1.2 equiv.). Flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 10:1, F16-22) gave the title compound (0.236 g, 72%). According to the ^{1}H NMR integrals over the 4´´-H signals it constitutes a 65:35 mixture of rotamers *E*-**27c** and *iso*-*E*-**27c**; the integrals over the 2'-H resonances prove that it was >99% isomer-free from *Z*-**27c**.

$[\alpha]_D^{26}$ = +12.6 (*c* = 1.30 in $CHCl_3$).

***E*-27c**

^{1}H NMR (300 MHz): δ = 1.49 (s, 2 × *t*-Bu), 1.53 and 1.65 [2''-$(CH_3)_2$], AB signal (δ_A = 3.97, δ_B = 4.30, J_{AB} = 9.4, in addition split by $J_{A,4''}$ = 2.9, $J_{B,4''}$ = 7.7, 5''-H_2), 5.72 (dd, $J_{4'',5''\text{-H(B)}}$ = 7.4, $J_{4'',5''\text{-H(A)}}$ = 2.9, 4''-H), 5.98 (s, 2'-H).

NOESY spectrum for configurational assignment: The absence of a cross-peak between the resonances at δ = 5.72 (4''-H) and 5.98 (2'-H) is in accord with the *trans* configuration of the C=C bond.

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 23.41 and "+" 24.78 [2''-$(CH_3)_2$], "+" 28.00 [2 × C(CH_3)$_3$], "+" 55.15 (C-4''), "-" 67.07 (C-5''), "-" 80.88 and "-" 82.49 [2 × *C*(CH_3)$_3$], "-" 95.48 (C-2''), "+" 112.45 (C-2'), "-" 118.16 (q, $J_{C,F}$ = 320.1, CF_3), "-" 151.21 (carbamate C=O), "-" 161.65 and "-" 163.07 (C-1', C-3').

iso-*E*-**27c**: ^{1}H NMR (300 MHz): δ = 1.41 (s, 2 × t-Bu), 1.60 and 1.61 [2''-$(CH_3)_2$], 5.65 (poorly resolved dd, $J_{4'',5''\text{-H(B)}}$ = 6.4, $J_{4'',5''\text{-H(A)}}$ = 3.6, 4''-H); the other resonances are superimposed by those of *E*-**27c**.– ^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 24.68 and "+" 25.56 [2''-$(CH_3)_2$], "+" 28.00 (which superimposes − as can be inferred from its greater intensity in comparison to the peak at δ = 28.33 − an analogous resonance of *E*-**27c**) and "+" 28.23 [2 × C(CH_3)$_3$], "+" 56.24 (C-4''), "-" 67.39 (C-5''), "-" 80.19 [*C*(CH_3)$_3$], "-" 94.78 (C-2''), "+" 112.81 (C-2'), "-" 152.00 (carbamate C=O); the residual resonances are superimposed by those of *E*-**27c**.

IR ($CDCl_3$): ν = 1710 and 1655 (C=O and C=C st), 1370 and 1215 cm^{-1} (S=O st).

Anal. Calcd for $C_{18}H_{28}NO_8F_3S$ (475.5): C 45.47; H 5.94. Found C 45.87; H 5.94.

2-(*tert*-Butyldiphenylsiloxy)acetaldehyde (31)

16.6 g, 78%; Prepared by the ozonolysis of allyl ether **30** (21.1 g, 71.3 mmol) in CH_2Cl_2 (250 mL) followed by reductive workup with Me_2S (16.0 mL, 225 mmol, 3 equiv.) and flash chromatography [6 cm, petroleum ether/*t*-*Bu*OMe 5:1, F12-24].[23]

Ethyl 4-(*tert*-Butyldiphenylsiloxy)-3-hydroxybutanoate (32)

At −20 °C BuLi (2.18 M in hexane; 7.00 mL, 15.3 mmol, 1.05 equiv. with respect to **31**) was added dropwise to a solution of i-Pr_2NH (2.11 mL, 1.52 g, 16.1 mmol, 1.10 equiv. with respect to **31**) in THF (14 mL). Stirring at that temperature was continued for 40 min. At −78 °C a solution of EtOAc (1.45 mL, 14.6 mmol, 1.0 equiv. with respect to **31**) in THF (7.8 mL) was added whereupon stirring was continued for 1 h. Aldehyde **31** (4.35 g, 14.6 mmol) in THF (10 mL) was added and stirring at −78 °C continued for another 3 h. The reaction was quenched by adding sat. NH_4Cl (11 mL). Extraction with Et_2O (3 × 100 mL), washing the combined extracts with brine (10 mL), drying over Na_2SO_4, removing the solvent in vacuo and flash chromatography (4 cm, petroleum ether/*t*-BuOMe 5:1, F7-15) led to the title compound (4.24 g, 75%).

^{1}H NMR (300 MHz): δ = 1.06 (s, *t*-Bu), 1.24 (t, $J_{2',1'}$ = 7.2, 2'-H_3), extreme AB signal (δ_A = 2.51, δ_B = 2.57, J_{AB} = 15.8, in addition split by $J_{A,3}$ = 7.4, $J_{B,3}$ = 5.1, 2-H_2), 2.94 (br d, $J_{OH,3}$ = 4.6, exchangeable with D_2O, OH), extreme AB signal (δ_A = 3.63, δ_B = 3.67, J_{AB} = 10.2, in addition split by $J_{A,3}$ = 6.0, $J_{B,3}$ = 5.1, 4-H_2), 4.14 (q, $J_{1',2'}$ = 7.1, 1'-H_2), superimposed by ca. 4.15 (m_c, 3-H), 7.35−7.45 (m, 6 *meta*- and *para*-H_{Ar}), 7.63−7.67 (m, 4 *ortho*-H_{Ar}).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 14.15 (C-2'), "-" 19.22 [*C*(CH_3)$_3$], "+" 26.80 [C(*C*H_3)$_3$], "-" 38.05 (C-2), "-" 60.64 (C-1'), "-" 66.85 (C-4), "+" 68.60 (C-3), "+" 127.73 (4 *meta*-C), "+" 129.79 (2 *para*-C because this resonance is half as intense as for *ortho*- and *meta*-C), "-" 132.95 and "-" 132.98 (2 × 1 *ipso*-C), "+" 135.48 (4 *ortho*-C), "-" 172.02 (C-1).

MS (EI/70 eV): *m*/*z* = 341 (24%, M^+ −EtOH), 329 (21%, M^+ −*t*-butyl), 283 (12%, 341 −*t*-butyl-H), 251 (100%, 329 −PhH), 241 (60%, 329 −EtOAc), 223 (48%), 199 (88%, 241 −C_2H_2O), 181 (50%), 163 (29%).

MS (DCI/pos., NH_3): *m*/*z* = 404 (100%, M^++NH_4^+), 358 (12%, 404 −EtOH), 326 (44%, 358 −MeOH), 309 (10%), 291 (5%), 274 (28%), 231 (8%).

IR ($CDCl_3$): ν = 3575 (O−H st), 1725 (C=O st) cm^{-1}.

Anal. Calcd for $C_{22}H_{30}O_4Si$ (386.6): C 68.34; H 7.82. Found C 68.30; H 7.72.

Ethyl [4-(*tert*-Butyldiphenylsiloxy)-3-oxobutanoate] (33) in a 85:15 Mixture with the Tautomeric Enol Ethyl *(Z)*-[4-(*tert*-Butyldiphenylsiloxy)-3-hydroxybut-2-enoate] (*iso*-33)

At −65 °C a solution of trifluoroacetic anhydride (7.90 mL, 11.7 g, 54.3 mmol, 1.5 equiv. with respect to **32**) in CH_2Cl_2 (19 mL) was added within 10 min to a solution of DMSO (5.25 mL, 72.4 mmol, 2.0 equiv. with respect to **32**) in the same solvent (37 mL). After another 10 min a solution of the β-hydroxy ester **32** (14.0 g, 36.2 mmol) in CH_2Cl_2 (26 mL) was added. 10 min later the cooling bath was removed so that the mixture warmed to r. t. over 40 min. Et_3N (8.40 mL, 106 mmol, 2.9 equiv. with respect to **32**) was added and another 10 min later H_2O (158 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 300 mL). The combined extracts were washed with HCl (1%, 175 mL), sat. $NaHCO_3$ (175 mL) and brine (175 mL). After drying (Na_2SO_4) the solvent was removed in vacuo. Flash chromatography (6 cm, petroleum ether/*t*-BuOMe 8:1, F7-15) furnished the title compound (9.87 g, 71%).

33

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (s, *t*-Bu), 1.26 (t, $J_{2',1'}$ = 7.2, 2'-H_3), 3.63 (s, 2-H_2), 4.18 (q, $J_{1',2'}$ = 7.2, 1'-H_2), in touch with 4.23 (s, 4-H_2), 7.37−7.45 (m, 6 *meta*- and *para*-H_{Ar}), 7.63 (dd, J_{ortho} = 7.9, J_{meta} = 1.5, 4 *ortho*-H_{Ar}).

^{13}C NMR (APT spectrum at 50 MHz; contained unidentified peaks at δ = "-" 77.82 and "+" 130.23): δ = "+" 14.06 (C-2'), "-" 19.16 [*C*(CH_3)$_3$], "+" 26.68 [C(*C*H_3)$_3$], "-" 45.83 (C-2), "-" 61.37 (C-1'), "-" 69.43 (C-4), "+" 127.91 (4 *meta*-C), "+" 130.08 (2 *para*-C), "-" 132.13 (2 *ipso*-C), "+" 135.44 (4 *ortho*-C), "-" 167.14 (C-1),"-" 203.41 (C-3).

***iso*-33**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (t, $J_{2',1'}$ = 7.2, 2'-H_3), 4.20 (d, $^4J_{4,2}$ = 1.1, 4-H_2), superimposed by 4.21 (q, $J_{2',1'}$ = 7.9, 1'-H_2), 5.54 (t, $J_{2,4}$ = 1.1, 2-H); the residual resonances are superimposed by those of **33**.– ^{13}C NMR (APT spectrum at 50 MHz): δ = "-" 60.16 (C-1'), "-" 62.73 (C-4), "+" 87.50 (C-2), "+" 127.83 (4 *meta*-C), "+" 129.93 (2 *para*-C); the residual resonances are superimposed by those of **33**.

MS (EI/70 eV): *m*/*z* = 384 (1%, M^+), 353 (4%), 339 (6%), 327 (100%, M^+ − *tert*-butyl), 281 (22%, 327 −EtOH), 253 (72%, 281 − CO), 221 (14%), 199 (86%), 181 (12%), 177 (12%), 135 (10%), 115 (8%).

HRMS (EI/70 eV): *m*/*z* = 384.1756 (M^+) confirms the molecular formula $C_{22}H_{28}O_4Si$ with a precision of ± 2 mDa.

MS (DCI/pos., NH_4^+): *m*/*z* = 402 (100%, M^+ +NH_4^+).

IR ($CDCl_3$): ν = 1740 and 1720 cm^{-1} (C=O st).

Anal. Calcd for $C_{22}H_{28}O_4Si$ (384.6): C 68.70; H 7.34. Found C 68.74; H 7.30.

(4*R*)-2,2-Dimethyl-1,3-dioxolane-4-carbaldehyde (34)

Compound **34** was obtained by known protocols[26] from D-diisopropylidenemannitol[27] (39.3 g, 150 mmol) and $NaIO_4$ (48.0 g, 215 mmol, 1.5 equiv.) as a colorless liquid (25.9 g, 67%; lit. 67%) after distillation (bp. 47 °C$_{20\ mbar}$; lit. 72−74 °C$_{30\ Torr}$).

Ethyl (3*R,4"*R*)-(2,2-Dimethyl-1,3-dioxolan-4-yl)-3-hydroxypropionate (35) in a 83:17 Mixture with the Diastereomer Ethyl (3*S**,4"*R*)-(2,2-Dimethyl-1,3-dioxolan-4-yl]-3-hydroxypropionate (*epi*-35)**

*configurational assignments interchangeable

At −20 °C BuLi (2.18 M in hexane; 55.0 mL, 120 mmol, 1.05 equiv.) was added dropwise to a solution of i-Pr_2NH (17.0 mL, 12.3 g, 121 mmol, 1.10 equiv.) in THF (112 mL). After stirring for 40 min the temperature was lowered to −78 °C. EtOAc (12.0 mL, 123 mmol, 1.1 equiv.), dissolved in THF (55 mL), was added and 1 h later aldehyde **34** (15.1 g, 116 mmol), equally dissolved in THF (88 mL). After stirring for another 3 h at −78 °C the reaction was quenched by the addition of sat. NH_4Cl (100 mL). Extractive work-up as described for **32** and flash chromatography (6 cm, petroleum ether/*t*-BuOMe 1.5:1, F13−36) rendered the title compound (18.5 g, 73%). As determined by the ^{1}H NMR integrals over the 2"-methyl groups, it was a 83:17 mixture of unassigned diastereomers.

$[\alpha]_D^{26}$ = −8.53 (*c* = 1.50 in $CHCl_3$).

35

^{1}H NMR (300 MHz): δ = 1.28 (t, $J_{2',1'}$ = 7.2, 2'-H_3), 1.35 and 1.41 [2 s, 2"-(CH_3)$_2$], AB signal (δ_A = 2.47, δ_B = 2.70, J_{AB} = 16.4, in addition split by $J_{A,3}$ = 8.1, $J_{B,3}$ = 2.4, 2-H_2), 3.32 (br d, $J_{OH,3}$ = 3.0, exchangeable with D_2O, OH), 3.85−4.13 (m, 3-H, 4"-H and 5"-H_2), in touch with 4.18 (q, $J_{1',2'}$ = 7.2, 1'-H_2).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 14.11 (C-2'), "+" 25.10 and "+" 26.60 [2"-(CH_3)$_2$], "-" 37.65 (C-2), "-" 60.80 (C-1'), "-" 66.59 (C-5"), "+" 69.14 (C-3), "+" 77.51 (C-4"), "-" 109.44 (C-2"), "-" 172.65 (C-1).−***epi*-35**^{1}H NMR (300 MHz): δ = 1.37 and 1.45 [2 s, 2"-(CH_3)], AB signal (evaluable speculatively in the following way: δ_A = 2.47, δ_B = 2.55, J_{AB} = 16.6, in addition split by $J_{B,3}$ = 7.9, 2-H_2), 2.99 (br d, $J_{OH,3}$ = 5.6, exchangeable with D_2O, OH); the residual resonances are superimposed by those of **35**.

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 26.32 (2"-CH_3), "-" 38.17 (C-2), "-" 65.54 (C-5"), "+" 68.25 (C-3), "-" 103.71 (C-2"), "-" 171.76 (C-1); the residual resonances are superimposed by those of **35**.

IR ($CDCl_3$): ν = 3575 (O−H st), 1720 cm^{-1} (C=O st).

No satisfactory combustion analysis could be obtained.

Ethyl (4"*R*)-(2,2-Dimethyl-1,3-dioxolan-4-yl)-3-oxopropionate (36) in a 83:17 Mixture with the Tautomeric Enol Ethyl (4"*R*)-*(Z)*-(2,2-Dimethyl-1,3-dioxolan-4-yl)-3-hydroxyprop-2-enoate (*iso*-36)

At 0 °C Dess−Martin reagent[28] (19.2 g, 45.4 mmol, 1.1 equiv.) was added to a solution of β-hydroxy ester **35** (9.00 g, 41.2 mmol) in CH_2Cl_2 (380 mL). After stirring for 1.5 h at r. t. the reaction was quenched by the addition of sat. $NaHCO_3$ (250 mL) and sat. $Na_2S_2O_3$ (10%, 250 mL). After 10 min, the resulting mixture was extacted with CH_2Cl_2 (2 × 200 mL). Washing with (55 mL), drying (Na_2SO_4), evaporating the solvent in vacuo and purifying by flash chromatography (6 cm, petroleum ether/*t*-BuOMe 7:1, F9-24) led to the title compound (5.94 g, 67%); as determined by the ^{1}H NMR integrals over the 2"-methyl resonances, it was a 83:17 mixture of ketone **36** and enol *iso*-**36**. $[\alpha]_D^{26}$ = +73.7 (*c* = 1.50 in $CHCl_3$).

36

^{1}H NMR (300 MHz): δ = 1.28 (t, $J_{2',1'}$ = 7.1, 2'-H_3), 1.38 and 1.49 [2 s, 2"-$(CH_3)_2$], AB signal (δ_A = 3.60, δ_B = 3.66, J_{AB} = 16.2, 2-H_2), 4.10 (dd, J_{gem} = 9.0, $J_{5"\text{-H}(1),4"}$ = 5.2, 5"-H^1), 4.17 - ca. 4.25 (m, 5"-H_2, 1'-H_2), 4.53 (dd, $J_{4",5"\text{-H}(2)}$ = 7.8, $J_{4",5"\text{-H}(1)}$ = 5.5, 4"-H). ^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 14.02 (C-2'), "+" 24.71 and "+" 25.88 [2"-$(CH_3)_2$], "-" 45.66 (C-2), "-" 61.36 (C-1'), "-" 66.44 (C-5"), "+" 79.85 (C-4"), "-" 111.14 (C-2"), "-" 166.90 (C-1), "-" 203.85 (C-3).

***iso*-36**

^{1}H NMR (300 MHz): δ = 1.31 (t of which only the low-field peak is not superimposed, $J_{2',1'}$ = 6.9, 2'-H_3), 1.41 (s, 2"-CH_3), 3.99 (dd, J_{gem} = 8.9, in addition split by $J_{5"\text{-H}(1),4"}$ = 9.0, 5"-H^{1}11111111 $_1$), ca. 4.17 - 4.30 (m, 5"-H^2, 1'-H_2), 5.38 (s, 4"-H), 12.00 (s, OH); the residual resonances are superimposed by those of **36**.

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 14.17 (C-2'), "+" 25.29 and "+" 25.99 [2"-$CH_3)_2$], "-" 60.28 (C-1'), "-" 68.03 (C-5"), "+" 74.39 (C-4"), "+" 88.23 (C-2), "-" 110.59 (C-2"), "-" 175.20 (C-1); the residual resonances are superimposed by those of **36**.

IR ($CDCl_3$): ν = 1740 and 1720 cm^{-1} (C=O st).

Anal. Calcd for $C_{10}H_{16}O_5$ (216.2): C 55.55; H 7.47. Found C 55.44; H 7.61.

3-(*tert*-Butyl) 4-Methyl (4*S*)-2,2-Dimethyl-1,3-oxazolidine-3,4-dicarboxylate (*iso*-37)

Prepared by a published procedure[29] from the methyl ester of *N*-Boc-L-serine[29] (52.6 g, 240 mmol) and 2,2-dimethoxypropane (60.1 mL, 493 mmol, 2.0 equiv.) and purified by distillation (bp. 83−85 °C$_{0.40\ mbar}$; lit. 102 °C$_{2\ Torr}$) to give the title compound (51.2 g, 83%; lit. 70−89%) which solidified in the refrigerator.

***tert*-Butyl (4*S*)-4-[3-(*tert*-Butoxy)-3-oxopropanoyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (38; 63:37 Mixture* of Rotamers 38a and 38b) in a 87:13 Mixture** with the Tautomeric Enol *tert*-Butyl (4*S*)-4-[(*Z*)-3-(*tert*-Butoxy)-1-hydroxy-3-oxoprop-1-enyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate [*iso*-38; Unspecified Mixture of Rotamers *iso*-38a and *iso*-38b]**

*****determined ^{1}H NMR spectroscopically by the integral ratio over the 4´´-H resonances

**determined ^{1}H NMR spectroscopically by the integral ratio over the 2-H resonances

At −20 °C BuLi (2.35 M in hexane; 51.7 mL, 121 mmol, 2.10 equiv.) was added dropwise to a solution of i-Pr_2NH (16.1 mL, 11.6 g, 121 mmol, 2.10 equiv.) in THF (100 mL). After stirring for 40 min the temperature was decreased to −78 °C. *tert*-BuOAc (16.4 mL, 121 mmol, 2.10 equiv.), dissolved in THF (50 mL), was added, stirring at −78 °C continued for 1 h, and ester **37** (15.0 g, 57.9 mmol), also dissolved in THF (51 mL) was added. After stirring for another 12 h at −78 °C, the reaction was quenched by the addition of sat. NH_4Cl (300 mL). Extractive workup with *t*-BuOMe (3 × 500 mL), washing with brine (200 mL) and flash chromatography (6 cm, petroleum ether/*t*-BuOMe 6:1, F12-32) gave the title compound (17.9 g, 90%) as a colorless solid (mp. 78 °C).

$[\alpha]_D^{26}$ = −61.7 (*c* = 1.30 in $CHCl_3$)

38a

^{1}H NMR (300 MHz): δ = 1.47 and 1.48 (2 s, 2 × *t*-Bu), 1.51 and 1.69 [2 s, 2"-$(CH_3)_2$], 3.45 (br s, 2-H_2), AB signal (δ_A = 4.01, δ_B = 4.18, J_{AB} = 9.0, in addition split by $J_{A,4"}$ = 3.0, $J_{B,4"}$ = 8.5, 5"-H_2), 4.40 (dd, $J_{4",5"\text{-H}(B)}$ = 7.6, $J_{4",5"\text{-H}(A)}$ = 3.0, 4"-H).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 23.54 and "+" 25.22 [2"-$(CH_3)_2$], "+" 27.84 [2 × C(CH_3)$_3$], "-" 46.76 (C-2), "+" 65.16 (C-4"), "-" 65.42 (C-5"), "+" 81.03 and "+" 82.01 [2 × *C*(CH_3)$_3$], "-" 95.19 (C-2"), "-" 151.18 (N-*C*O_2t-Bu), "-" 166.10 (C-1), "-" 201.76 (C-3).

38b

^{1}H NMR (300 MHz): δ = 1.43 (s, t-Bu), 1.63 (s, 2"-CH_3), AB signal (δ_A = 3.47, δ_B = 3.58, J_{AB} = 15.9, 2-H_2), AB signal (δ_A = 4.06, δ_B = 4.13, J_{AB} = 8.3, in addition split by $J_{A,4"}$ = 2.2, $J_{B,4"}$ = 5.6, 5"-H_2), 4.55 (dd, $J_{4",5"\text{-H}(B)}$ = 6.4, $J_{4",5"\text{-H}(A)}$ = 3.4, 4"-H); the residual resonances are superimposed by those of **38a**.

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 24.84 "+" 25.90 [2"-$(CH_3)_2$], "+" 28.09 and "+" 28.17 [2 × C(CH_3)$_3$], "-" 47.71 (C-2), "+" 64.74 (C-4"), "-" 65.23 (C-5"), "-" 94.49 (C-2"), "-" 152.41 (N-*C*O_2t-Bu), "-" 166.41 (C-1), "-" 201.47 (C-3); the residual resonances are superimposed by those of **38a**.

***iso*-38a and *iso*-38b:**

^{1}H NMR (300 MHz): δ = 5.03 (s, 2-H), 12.28 and 12.33 (2 br s, OH*); the residual resonances are superimposed by those of **38a** and **38b**.

IR ($CDCl_3$): ν = 1795 and 1700 cm^{-1} (C=O st).

Anal. Calcd for $C_{17}H_{29}NO_6$ (343.4): C 59.46; H 8.51. Found C 59.30; H 8.37.

Ethyl *(E)*-(3-*tert*-Butyldiphenylsiloxymethyl)-5-(trimethylsilyl)pent-2-en-4-ynoate (*E*-42a)

Prepared as described for *E*-**42c** from $PdCl_2(PPh_3)_2$ (0.122 g, 0.170 mmol, 0.06 equiv.) and CuI (0.102 g, 0.540 mmol, 0.16 equiv.) in degassed THF (46 mL), triflate *Z*-**27a** (1.59 g, 3.08 mmol), (trimethylsilyl)acetylene (601 µL, 0.418 g, 4.24 mmol, 1.4 equiv.) and degassed i-Pr_2NH (15.3 mL, 11.1 g, 110 mmol, 36 equiv. with respect to *Z*-**27a**) except that the reaction lasted 16 h. Purification by flash chromatography (2.5 cm, petroleum ether/*t*-BuOMe 20:1, F8-13) gave the title compound (1.03 g, 72%) which − according to the ^{1}H NMR integrals over the 2-H resonances − was >99% isomer-free from *Z*-**42a**.

^{1}H NMR (300 MHz): δ = 0.19 [s, $Si(CH_3)_3$], 1.09 (s, *t*-Bu), 1.34 (t, $J_{2',1'}$ = 7.2, 2'-H_3), 4.26 (q, $J_{1',2'}$ = 7.1, 1'-H_2), low-field part superimposed by 4.27 (d, $^4J_{1",2}$ = 2.2, 1"-H_2), 6.54 (t, $^4J_{2,1"}$ = 2.1, 2-H), 7.37−7.48 (m, 6 *meta*- and *para*-H_{Ar}), 7.65−7.69 (m, 4 *ortho*-H_{Ar}).

^{13}C NMR (APT spectrum at 75 MHz): δ = "+" −0.43 [$Si(CH_3)_3$], "+" 14.24 (C-2'), "-" 19.19 [*C*(CH_3)$_3$], "+" 26.68 [C(*C*H_3)$_3$], "-" 60.34 (C-1'), "-" 65.99 (C-1"), "-" 99.52 and "-" 107.34 (C-4, C-5), "+" 122.81 (C-2), "+" 127.91 (4 *meta*-C), "+" 129.96 (2 *para*-C), "-" 132.76 (2 *ipso*-C), "+" 135.47 (4 *ortho*-C), "-" 137.21 (C-3), "-" 165.41 (C-1).

IR ($CDCl_3$): ν = 2255 (C≡C st), 1705 and 1620 cm^{-1} (C=O and C=C st).

Anal. Calcd for $C_{27}H_{36}O_3Si_2$ (464.7): C 69.78; H 7.81. Found C 69.77; H 7.94.

Ethyl *(Z)*-(3-*tert*-Butyldiphenylsiloxymethyl)-5-(trimethylsilyl)-pent-2-en-4-ynoate (*Z*-42a)

Prepared as described for *E*-**42c** from $PdCl_2(PPh_3)_2$ (0.012 g, 0.017 mmol, 0.05 equiv.) and CuI (0.010 g, 0.051 mmol, 0.16 equiv.) in degassed THF (4.5 mL), triflate *E*-**27a** (0.159 g, 0.308 mmol), (trimethylsilyl)acetylene (52 µl, 0.036 g, 0.370 mmol, 1.2 equiv.) and degassed i-Pr_2NH (1.5 mL, 1.1 g, 11 mmol, 36 equiv.). Purification by flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 40:1, F8-16) gave the title compound (0.096 g, 67%) which was − according to the ^{1}H NMR integrals over the 2-H´s − >99% isomer-free from *E*-**42a**.

^{1}H NMR (300 MHz): δ = 0.22 [s, $Si(CH_3)_3$], 1.09 (s, *t*-Bu), 1.17 (t, $J_{2',1'}$ = 7.0, 2'-H_3), 4.04 (q, $J_{1',2'}$ = 7.2, 1'-H_2), 4.78 (d, $^4J_{1",2}$ = 2.3, 1"-

H_2), 6.09 (t, $^4J_{2,1''}$ = 2.1, 2-H), 7.34−7.44 (m, 4 *meta*-H_{Ar} and 2 *para*-H_{Ar}), 7.70−7.74 (m, 4 *ortho*-H_{Ar}).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" - 0.43 [$Si(CH_3)_3$], "+" 14.24 (C-2'), "-" 19.19 [$C(CH_3)_3$], "+" 26.68 [$C(CH_3)_3$], "-" 60.34 (C-1'*), "-" 65.99 (C-1"*), "-" 99.52 and "-" 107.34 (C-4, C-5), "+" 122.81 (C-2), "+" 127.91 (4 *meta*-C), "+" 129.96 (2 *para*-C), "-" 132.76 (2 *ipso*-C), "+" 135.47 (4 *ortho*-C), "-" 137.21 (C-3), "-" 165.41 (C-1); *so assigned because of the similar chemical environment of C-1'here and C-1'in compound **33** and because of the similar chemical environment of C-1" here and C-4 in compound **33**.

IR ($CDCl_3$): ν = 2250 and 2150 (C≡C st), 1705 and 1605 cm^{-1} (C=O and C=C st).

Anal. Calcd for $C_{27}H_{36}O_3Si_2$ (464.7): C 69.78; H 7.81. Found C 69.58; H 7.90.

Ethyl (4"*R*)-*(E)*-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(trimethylsilyl)pent-2-en-4-ynoate (*E*-42b)

Prepared as described for *E*-**42c** from $PdCl_2(PPh_3)_2$ (0.024 g, 0.033 mmol, 0.05 equiv.) and CuI (0.021 g, 0.099 mmol, 0.15 equiv.) in degassed THF (9 mL), triflate *Z*-**27b** (0.226 g, 0.649 mmol), (trimethylsilyl)acetylene (109 µl, 0.076 g, 0.779 mmol, 1.2 equiv.) and degassed i-Pr_2NH (3.00 mL, 2.17 g, 21.6 mmol, 33 equiv.). Purification by flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 20:1, F22-35) gave the title compound (0.158 g, 82%) which was − according to the ^{1}H NMR integrals over the 2-H´s − >99% isomer-free from *Z*-**42b**.

$[\alpha]_D^{25}$ = +32.8 (*c* = 1.83 in $CHCl_3$).

^{1}H NMR (300 MHz): δ = 0.17 [s, $Si(CH_3)_3$], 1.24 (t, $J_{2',1'}$ = 7.2, 2'-H_3), 1.34 and 1.39 [2 s, 2"-$(CH_3)_2$], AB signal (δ_A = 3.87, δ_B = 4.20, J_{AB} = 8.3, in addition split by $J_{A,4''} \approx J_{B,4''} \approx$ 6.8, 5"-H_2), high-field portion of B-part superimposed by 4.13 (q, $J_{1',2'}$ = 7.1, 1'-H_2), 4.54 (dd, $J_{4'',5''\text{-H(A)}} \approx J_{4'',5''\text{-H(B)}} \approx$ 6.8, 4"-H), 6.29 (hardly resolved d, $^4J_{2,4''}$ = 1.1, 2-H).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" −0.40 [$Si(CH_3)_3$], "+" 14.22 (C-2'), "+" 25.76 and "+" 26.17 [2"-$(CH_3)_2$], "-" 60.44 (C-1'), "-" 69.00 (C-5"), "+" 77.67 (C-4"), "-" 99.41 and "-" 108.74 (C-4, C-5), "-" 110.77 (C-2"), "+" 123.96 (C-2), "-" 136.34 (C-3), "-" 164.72 (C-1).

IR ($CDCl_3$): ν = 2250 and 2145 (C≡C st), 1710 and 1625 cm^{-1} (C=O and C=C st).

Anal. Calcd for $C_{15}H_{24}O_4Si$ (296.4): C 60.78; H 8.16. Found C 61.05; H 8.09.

Ethyl (4"*R*)-*(Z)*-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(trimethylsilyl)pent-2-en-4-ynoate (*Z*-42b)

Prepared as described for *E*-**42c** from $PdCl_2(PPh_3)_2$ (0.030 g, 0.042 mmol, 0.05 equiv.) and CuI (0.026 g, 0.13 mmol, 0.15 equiv.) in degassed THF (11 mL), triflate *E*-**27b** (0.288 g, 0.827 mmol), (trimethylsilyl)acetylene (139 µl, 0.097 g, 0.992 mmol, 1.2 equiv.) and degassed i-Pr_2NH (3.80 mL, 2.74 g, 27.4 mmol, 33 equiv.). Purification by flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 20:1, F12-20) gave the title compound (0.202 g, 82%) which was − according to the ^{1}H NMR integrals over the 2-H´s − >99% isomer-free from *E*-**42b**.

$[\alpha]_D^{25}$ = +59.9 (*c* = 1.55 in $CHCl_3$).

^{1}H NMR (300 MHz): δ = 0.19 [s, $Si(CH_3)_3$], 1.25 (t, $J_{2',1'}$ = 7.2, 2'-H_3), 1.39 and 1.49 [2 s, 2"-$(CH_3)_2$], AB signal (δ_A = 3.78, δ_B = 4.32, J_{AB} = 8.5, in addition split by $J_{A,4''}$ = 7.0, $J_{B,4''}$ = 6.8, 5"-H_2), 4.13 (q, $J_{1',2'}$ = 7.1, 1'-H_2), 5.60 (ddd, $J_{4'',5''\text{-H(A)}}$ = 7.0, $J_{4'',5''\text{-H(B)}}$ = 6.8, $^4J_{4'',2}$ = 1.2, 4"-H), 6.18 (d, $^4J_{2,4''}$ = 1.5, 2-H).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" −0.44 [$Si(CH_3)_3$], "+" 14.09 (C-2'), "+" 25.74 and "+" 26.13 [2"-$(CH_3)_2$], "-" 60.55 (C-1'), "-" 69.15 (C-5"), "+" 72.81 (C-4"), "-" 101.59 and "-" 103.40 (C-4, C-5), "-" 110.42 (C-2"), "+" 126.43 (C-2), "-" 141.41 (C-3), "-" 165.00 (C-1).

IR ($CDCl_3$): ν = 2255 and 2150 (C≡C st), 1705 and 1610 cm^{-1} (C=O and C=C st).

Anal. Calcd for $C_{15}H_{24}O_4Si$ (296.4): C 60.78; H 8.16. Found C 60.95; H 8.01.

***tert*-Butyl *E*-(4"*R*)-[3-*N*-(*tert*-Butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl]-5-(trimethylsilyl)pent-2-en-4-ynoate (*E*-42c) in a 68:32 Mixture* with a Rotamer (*iso*-*E*-42c)**

*determined ^{1}H NMR spectroscopically by the integral ratios over the 4"-H´s

At r.t. triflate *Z*-**27c** (0.300 g, 0.631 mmol), (trimethylsilyl)acetylene (106 µl, 0.074 g, 0.757 mmol, 1.2 equiv.) and degassed i-Pr_2NH (2.93 mL, 2.12 g, 21.1 mmol, 33 equiv.) were added in this order to a stirred suspension of $PdCl_2(PPh_3)_2$ (0.023 g, 0.032 mmol, 0.05 equiv.) and CuI (0.020 g, 0.095 mmol, 0.15 equiv.) in degassed THF (8.8 mL). After 2 h *t*-BuOMe (4 mL) was added. Washings with sat. NH_4Cl (3 × 3 mL) and brine (3 mL), drying (Na_2SO_4), evaporation of the solvent in vacuo and flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 10:1, F9-22) gave the title compound (0.227 g, 85%) which − according to the ^{1}H NMR integrals over the 2-H´s − was >99% isomer-free from *Z*-**42c**.

$[\alpha]_D^{24}$ = −68.7 (*c* = 2.53 in $CHCl_3$).

***E*-42c**

^{1}H NMR (300 MHz): δ = 0.20 [s, $Si(CH_3)_3$], 1.49 (2 × t-Bu), 1.54 and 1.64 [2 s, 2"-$(CH_3)_2$], AB signal (δ_A = 3.97, δ_B = 4.09, J_{AB} = 8.8, in addition split by $J_{A,4''}$ = 5.3, $J_{B,4''}$ = 6.8, 5"-H_2), 4.54 (dd, $J_{4'',5''\text{-H(A)}} = J_{4'',5''\text{-H(B)}}$ = 5.7, 4"-H), 5.95 (s, 2-H).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" −0.32 [$Si(CH_3)_3$], "+" 24.31 and "+" 25.44 [2"-$(CH_3)_2$], "+" 28.14 [2 × $C(CH_3)_3$], "+" 62.61 (C-4"), "-" 67.51 (C-5"), "-" 80.38 and "-" 80.97 [2 × $C(CH_3)_3$], "-" 94.90 (C-2"), "-" 99.41 and "-" 108.74 (C-4, C-5), "+" 127.19 (C-2), "-" 135.14 (C-3), "-" 152.21 (N-CO_2t-Bu), "-" 163.96 (C-1).− *iso*-*E*-**42c**: ^{1}H NMR (300 MHz): δ = 1.41 (2 × *t*-Bu), 4.49 (m_c, 4"-H); the residual signals are superimposed by those of *E*-**42c**.

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" 24.85 and "+" 25.88 [2"-$(CH_3)_2$], "+" 28.19 [2 × $C(CH_3)_3$], "-" 67.31 (C-5"), "-" 80.44 and "-" 80.91 [2 × $C(CH_3)_3$], "-" 99.76 (C-2"),"+" 127.26 (C-2); the residual signals are superimposed by those of *E*-**42c**.

IR ($CDCl_3$): ν = 2255 and 2145 (C≡C st), 1695 (C=C st) cm^{-1}.

Anal. Calcd for $C_{22}H_{37}NO_5Si$ (423.6): C 62.38; H 8.82. Found C 62.28; H 8.67.

***tert*-Butyl *(Z)*-(4"*R*)-[3-*N*-(*tert*-Butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl]-5-(trimethylsilyl)pent-2-en-4-ynoate (*Z*-42c) in a 68:32 Mixture* with a Rotamer (*iso*-*Z*-42c)**

*determined ^{1}H NMR spectroscopically by the integral ratios over the 2-H´s**.**

Prepared as described for *E*-42c from $PdCl_2(PPh_3)_2$ (0.011 g, 0.015 mmol, 0.05 equiv.) and CuI (0.010 g, 0.047 mmol, 0.15 equiv.) in degassed THF (4.3 mL), triflate *E*-**27c** (0.146 g, 0.307 mmol), (trimethylsilyl)acetylene (51 µl, 0.035 g, 0.37 mmol, 1.2 equiv.) and degassed i-Pr_2NH (1.43 mL, 1.03 g, 10.3 mmol, 33 equiv.). Flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 12:1, F10-21) afforded the title compound (0.114 g, 88%) which was − according to the ^{1}H NMR integrals over the 2-H´s − >99% isomer-free from *E*-42c).

$[\alpha]_D^{25}$ = −64.5 (*c* = 1.82 in $CHCl_3$).

***Z*-42c** ^{1}H NMR (300 MHz): δ = 0.15 [s, $Si(CH_3)_3$], 1.40 and 1.45 [2 s, 2"-$(CH_3)_2$], 1.67 (2 x *t*-Bu), AB signal (δ_A = 3.79, δ_B = 4.26, J_{AB} = 9.2, in addition split by $J_{A,4''}$ = 4.7, $J_{B,4''}$ = 7.3, 5"-H_2), 5.40

(ddd, $J_{4'',5''\text{-H(B)}} = 7.3$, $J_{4'',5''\text{-H(A)}} = 5.2$, $^4J_{4'',2} = 1.2$, 4''-H), 6.11 (d, $^4J_{2,4''} = 1.2$, 2-H).

^{13}C NMR (APT spectrum at 75 MHz): δ = "+" −0.49 [Si(CH_3)$_3$], "+" 24.35 and "+" 25.03 [2''-(CH_3)$_2$], "+" 28.08 and "+" 28.17 [2 × C(CH_3)$_3$], "+" 56.93 (C-4''), "-" 68.78 (C-5''), "-" 79.76 and "-" 80.91 [2 × C(CH_3)$_3$], "-" 94.73 (C-2''), "-" 102.21 and "-" 102.57 (C-4, C-5), "+" 127.04 (C-2), "-" 142.96 (C-3), "-" 151.40 (N-CO_2*t*-Bu), "-" 164.79 (C-1).

***iso*-*Z*-42c** ^{1}H NMR (300 MHz): δ = 1.42 and 1.48 [2 s, 2''-(CH_3)$_2$], 1.65 (2 × *t*-Bu), AB signal (A part superimposed, $\delta_B = 4.32$, $J_{AB} = 9.4$, in addition split by $J_{B,4''} = 7.1$, 5''-H_2), 6.15 (d, $^4J_{2,4''} = 1.5$, 2-H); the other resonances are superimposed by those of ***Z*-42c**.

^{13}C NMR (APT spectrum at 75 MHz): δ = "+" −0.37 [Si(CH_3)$_3$], "+" 25.14 and "+" 25.83 [2''-(CH_3)$_2$], "+" 28.49 [C(CH_3)$_3$], "+" 57.76 (C-4''), "-" 69.34 (C-5''), "-" 80.17 and "-" 80.73 [2 × C(CH_3)$_3$], "-" 94.19 (C-2''), "-" 101.80 and "-" 102.73 (C-4, C-5), "+" 127.65 (C-2), "-" 143.06 (C-3), "-" 152.08 (N-CO_2t-Bu), "-" 164.69 (C-1); the other resonances are superimposed by those of ***Z*-42c**.

IR ($CDCl_3$): ν = 2255 and 2145 (C≡C st), 1695 cm^{-1} (C=O st).

Anal. Calcd for $C_{22}H_{37}NO_5Si$ (423.6): C 62.38; H 8.82. Found C 62.41; H 8.71.

(E)-3-[(*tert*-Butyldiphenylsiloxy)methyl]-5-(trimethylsilyl)pent-2-en-4-yn-1-ol (*E*-43a)

At −78 °C DIBAL (1.0 M in CH_2Cl_2, 12.0 mL, 12.0 mmol, 2.7 equiv.) was added to a solution of ester *E*-**42a** (2.06 g, 4.43 mmol) in CH_2Cl_2 (12 mL). Within 3 h the temperature was gradually raised to 0 °C. The reaction was quenched by the addition of sat. K,Na tartrate (42 mL). After stirring for 40 min, the phases were separated and the organic phase was extracted with CH_2Cl_2 (3 × 100 mL). Washing with brine (10 mL), drying (Na_2SO_4) removal of the solvent in vacuo and flash chromatography (4 cm, petroleum ether/*t*-BuOMe 30:1, F6-13) furnished the title compound (1.80 g, 81%).

^{1}H NMR (300 MHz): δ = 0.19 [s, Si(CH_3)$_3$], 1.09 (s, *t*-Bu), 1.68 (br s, OH), 4.20 (br d, $^4J_{1',2} = 1.5$, 1'-H_2), 4.43 (br d, $J_{1,2} = 6.8$, 1-H_2), 6.23 (tt, $J_{2,1} = 6.6$, $^4J_{2,1'} = 1.8$, 2-H), 7.37−7.48 (m, 4 *meta*- and 2 *para*-H_{Ar}), 7.71 (m_c, 4 *ortho*-H_{Ar}).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" −0.15 [Si(CH_3)$_3$], "-" 19.27 [C(CH_3)$_3$], "+" 26.76 [C(CH$_3$)$_3$], "-" 61.15 (C-1*), "-" 65.34 (C-1'*), "-" 100.20 and "-" 101.28 (C-4, C-5), "-" 124.47 (C-3), "+" 127.70 (4 *meta*-C), "+" 129.73 (2 *para*-C), "-" 133.20 (2 *ipso*-C), "+" 135.09 (C-2), "+" 135.51 (4 *ortho*-C); *so assigned because of the similar chemical environment of C-1' here and C-1' in compound *E*-**44a**.

IR ($CDCl_3$): ν = 3610 (O−H st), 2255 and 2145 cm^{-1} (C≡C st).

Anal. Calcd for $C_{25}H_{34}O_2Si_2$ (422.7): C 71.03; H 8.11. Found C 70.80; H 8.39.

(4'*S*)-*(E)*-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(trimethylsilyl)-pent-2-en-4-yn-1-ol (*E*-43b)

At −78 °C DIBAL (1.05 M in toluene, 46.2 mL, 48.5 mmol, 2.5 equiv.) was added to a solution of ester *E*-**42b** (5.85 g, 19.7 mmol) in Et_2O (57 mL). Stirring was continued for 3 h at −78 °C. Then, within 30 min, the temperature was gradually raised to r. t., then the mixture was poured into sat. K,Na tartrate (150 mL). After 20 min a similar workup followed as described for *E*-**43a**, which was teminated by a flash chromatography (4 cm, petroleum ether/*t*-BuOMe 2:1, F13-25) providing the title compound (4.43 g, 88%).

$[\alpha]_D^{25} = +36.7$ (c = 2.07 in $CHCl_3$).

^{1}H NMR (300 MHz): δ = 0.18 [s, Si(CH_3)$_3$], 1.39 and 1.44 [2 s, 2'-(CH_3)$_2$], 2.06 (br s, exchangeable with D_2O, OH), AB signal ($\delta_A = 3.88$, $\delta_B = 4.13$, $J_{AB} = 8.2$, in addition split by $J_{A,4'} = 7.9$, $J_{B,4'} = 6.4$, 5'-H_2), 4.38 (m_c, 1-H_2), 4.47 (dd, $J_{4',5'\text{-H(A)}} = J_{4',5'\text{-H(B)}} = 6.8$, 4'-H), 6.22 (t, $J_{2,1} = 6.4$, 2-H).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" −0.21 [Si(CH_3)$_3$], "+" 26.00 and "+" 26.27 [2'-(CH$_3$)$_2$], "-" 61.00 (C-1), "-" 68.57 (C-5'*), "+" 77.81 (C-4'), "-" 98.97 and "-" 102.63 (C-4, C-5), "-" 109.98 (C-2'), "-" 123.10 (C-3), "+" 138.85 (C-2); *assignment based on the similarity of the chemical environment here with that in compound *E*-**42b**.

IR ($CDCl_3$): ν = 3610 (O−H st), 2250 and 2145 cm^{-1} (C≡C st).

Anal. Calcd for $C_{13}H_{22}O_3Si$ (254.4): C 61.37; H 8.73. Found C 61.35; H 8.82.

(E)-3-[(*tert*-Butyldiphenylsiloxy)methyl]-5-(trimethylsilyl)pent-2-en-4-ynal (*E*-44a)

Dess−Martin reagent[28] (2.35 g, 5.32 mmol, 1.2 equiv.) was added to a solution of alcohol *E*-**43a** (2.02 g, 4.43 mmol) in CH_2Cl_2 (36 mL) at r.t. After stirring for 1 h the mixture was poured into sat. $NaHCO_3$ (42 mL) and sat. $Na_2S_2O_3$ (10%, 42 mL) and stirring continued for 10 min. Extractive workup with CH_2Cl_2 (2 × 40 mL) and brine (10 mL), drying (Na_2SO_4) evaporation of the solvent in vacuo and flash chromatography (4 cm, petroleum ether/*t*-BuOMe 30:1, F6-13) gave the title compound (1.80 g, 81%).

^{1}H NMR [300 MHz; contained aliphatic contaminant(s)]: δ = 0.19 [s, Si(CH_3)$_3$], 1.08 (s, t-Bu), 4.33 (d, $^4J_{1',2} = 1.9$, 1'-H_2), 6.72 (dt, $J_{2,1} = 8.4$, $^4J_{2,1'} = 2.1$, 2-H), 7.38−7.49 (m, 4 *meta*- and 2 *para*-H_{Ar}), 7.66 (m_c, 4 *ortho*-H_{Ar}), 10.17 (d, $J_{1,2} = 8.7$, 1-H).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" −0.45 [Si(CH_3)$_3$], "-" 19.26 [C(CH_3)$_3$], "+" 26.71 [C(CH$_3$)$_3$], "-" 65.43 (C-1'), "-" 99.52 (C-4), "-" 107.34 (C-5), "+" 127.88 (4 *meta*-C), "+" 129.99 (2 *para*-C), "+" 132.34 (C-2), "-" 132.47 (2 *ipso*-C), "+" 135.40 (4 *ortho*-C), "-" 145.64 (C-3), "+" 192.68 (C-1).

IR ($CDCl_3$): ν = 2860 (carbonyl−H st), 2255 (C≡C st), 1670 cm^{-1} (C=O st).

Anal. Calcd for $C_{25}H_{32}O_2Si_2$ (420.7): C 71.37; H 7.67. Found C 71.07; H 7.69.

(4'*S*)-*(E)*-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-5-(trimethylsilyl)-pent-2-en-4-ynal (*E*-44b)

Prepared as described for *E*-**44a** from Dess−Martin reagent[28] (0.519 g, 1.18 mmol, 1.1 equiv.) and alcohol *E*-**43b** (0.272 g, 1.07 mmol) in CH_2Cl_2 (7 mL) except that the reaction was allowed to proceed for 20 min. Purification by flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 10:1, F15-25) furnished the title compound (0.220 g, 82%).

$[\alpha]_D^{23} = +24.6$ (c = 1.99 in $CHCl_3$).

^{1}H NMR (300 MHz): δ = 0.21 [s, Si(CH_3)$_3$], 1.39 and 1.43 [2 s, 2'-(CH_3)$_2$], AB signal ($\delta_A = 3.93$, $\delta_B = 4.27$, $J_{AB} = 8.5$, in addition split by $J_{A,4'} = 6.4$, $J_{B,4'} = 7.0$, 5'-H_2), 4.65 (ddd, $J_{4',5'\text{-H(A)}} = J_{4',5'\text{-H(B)}} = 6.7$, $^4J_{4',2} = 1.2$, 4'-H), 6.48 (dd, $J_{2,1} = 8.3$, $^4J_{2,4'} = 1.5$, 2-H), 10.08 (d, $J_{1,2} = 8.3$, 1-H).

^{13}C NMR (APT spectrum at 50 MHz): δ = "+" −0.59 [Si(CH_3)$_3$], "+" 25.56 and "+" 26.06 [2'-(CH$_3$)$_2$], "-" 68.72 (C-5'), "+" 77.00 (C-4'), "-" 97.32 and "-" 109.29 (C-4*, C-5*), "-" 111.02 (C-2'*), "+" 133.30 (C-2), "-" 144.17 (C-3), "+" 192.19 (C-1); *distinguishable because of the lower intensity of quaternary acetylenic ^{13}C nuclei.

IR ($CDCl_3$): ν = 2845 (carbonyl−H st), 2255 and 2145 (C≡C st), 1680 cm^{-1} (C=O st).

Anal. Calcd for $C_{13}H_{20}O_3Si$ (252.3): C 61.88; H 8.01. Found C 61.61; H 7.74.

(4'*R*)-*(Z)*-3-[*N*-(*tert*-Butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl]-5-(trimethylsilyl)pent-2-en-4-ynal (*E*-44c) in a 68:32 Mix-

ture* with a Rotamer (*iso*-*E*-44c)

*determined ^{1}H NMR spectroscopically by the integral ratio over the 4´-H´s

At −78 °C DIBAL (1.05 M in toluene, 1.14 mL, 1.20 mmol, 1.3 equiv.) was added to a solution of ester *E*-**42c** (0.390 g, 0.921 mmol) in toluene (2.7 mL) within 10 min. Stirring at −78 °C was continued for 30 min. MeOH (300 µl), cooled to −78 °C, was added. The resulting mixture was poured into sat. K,Na tartrate (6 mL). After 20 min, a similar workup followed as described for *E*-**43a** which was terminated by a flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 7:1, F18-28) leading to the title compound (0.261 g, 81%).

$[\alpha]_D^{23} = -76.8$ (c = 2.85 in $CHCl_3$).

***E*-44c**

^{1}H NMR (300 MHz; slightly contaminated in the aliphatic region): δ = 0.21 [s, Si(CH_3)$_3$], 1.37 (s, t-Bu), 1.54 and 1.64 [2 s, 2'-(CH_3)$_2$], AB signal (δ_A = 3.97, δ_B = 4.09, J_{AB} = 8.8, in addition split by $J_{A,4'}$ = 5.3, $J_{B,4'}$ = 6.8, 5'-H$_2$), 4.43 (br dd, $J_{4',5'\text{-}H(B)}$ = 6.4, $J_{4',5'\text{-}H(A)}$ = 4.2, 4'-H), 6.22 (d, $J_{2,1}$ = 8.2, 2-H), 10.09 (d, $J_{1,2}$ = 7.9, 1-H).

^{13}C NMR (APT spectrum at 75 MHz; contained unidentified peaks at δ = "-" 26.84 and δ = "+" 26.91): δ = "+" −0.58 [Si(CH_3)$_3$], "+" 23.92 and "+" 25.40 [2'-(CH_3)$_2$], "+" 28.21 [C(CH_3)$_3$], "+" 61.90 (C-4'), "-" 67.53 (C-5'), "-" 80.61 [C(CH_3)$_3$], "-" 94.63 (C-2'), "-" 98.03 and "-" 109.51 (C-4, C-5), "+" 134.15 (C-2), "-" 145.88 (C-3), "-" 151.26 (N-CO_2t-Bu), "-" 192.35 (C-1).

***iso*-*E*-44c**

^{1}H NMR (300 MHz; slightly contaminated in the aliphatic region): δ = 1.47 (s, *t*-Bu), 1.51 and 1.60 [2 s, 2'-(CH_3)$_2$], 4.57 (br dd, $J_{4',5'\text{-}H(B)}$ = 6.0, $J_{4',5'\text{-}H(A)}$ = 2.3, 4'-H), ca. 10.07 (br d, $J_{1,2} \approx$ 8 Hz, 1-H); the other resonances are superimposed by those of *E*-**44c**.

^{13}C NMR (APT spectrum at 75 MHz; contained unidentified peaks at δ = "-" 26.84 and δ = "+" 26.91): δ = "+" 24.69 and "+" 26.39 [2'-(CH_3)$_2$], "+" 28.29 [C(CH_3)$_3$], "-" 67.16 (C-5'), "-" 81.08 [C(CH_3)$_3$], "-" 95.14 (C-2'), "-" 97.68 and "-" 109.03 (C-4, C-5), "+" 133.74 (C-2), "-" 144.99 (C-3), "-" 151.99 (N-CO_2*t*-Bu), "+" 192.49 (C-1); the other resonances are superimposed by those of *E*-**44c**.

IR ($CDCl_3$): ν = 2850 (carbonyl−H st), 2255 and 2145 (C≡C st), 1700 and 1680 cm^{-1} (C=O st).

Anal. Calcd for $C_{18}H_{29}NO_4Si$ (351.5): C 61.50; H 8.33. Found C 61.70; H 8.57.

***(E)*-3-[(*tert*-Butyldiphenylsiloxy)methyl]-1-(trimethylsilyl)hex-3-ene-1,5-diyne (*E*-45a)**

At −78 °C BuLi (1.49 M in hexane; 154 µl, 0.230 mmol, 1.2 equiv.) was added dropwise to a solution of i-Pr$_2$NH (30.0 µl, 0.021 g, 0.230 mmol, 1.2 equiv.) in THF (1.5 mL). After stirring for 10 min (trimethylsilyl)diazomethane (2.0 M in hexane; 115 µl, 0.230 mmol, 1.2 equiv.) was added dropwise, too. After stirring for another 30 min a pre-cooled (−78 °C) solution of aldehyde *E*-**44a** (0.080 g, 0.190 mmol) in THF (420 µl) was added, again dropwise. After stirring at −78 °C for another 1.5 h, the cooling bath was removed so that r.t. was attained within 4 h. After stirring for another 20 min the reaction was quenched by adding H_2O (2 mL) and *t*-BuOMe (12 mL). Extraction with *t*-BuOMe (3 × 12 mL), washing with brine (5 mL) and drying (Na_2SO_4) led to the title compound (0.039 g, 49%) after flash chromatography (0.8 cm, petroleum ether/*t*-*Bu*OMe 50:1, F7-9).

^{1}H NMR (300 MHz): δ = 0.19 [s, Si(CH_3)$_3$], 1.08 (s, t-Bu), 3.33 (d, $^4J_{6,4}$ = 2.2, 6-H), 4.25 (incompletely resolved dd, $^4J_{1',4}$ = 1.9, $^6J_{1',6}$ = 0.8, 1'-H$_2$), 6.24 (dt, $^4J_{4,1'} = {}^4J_{4,6}$ = 2.3, 4-H), 7.37−7.45 (m, 4 *meta*- and 2 *para*-H$_{Ar}$), 7.66 (m$_c$, 4 *ortho*-H$_{Ar}$).

^{13}C NMR (APT spectrum at 50 MHz, contains unidentified peak at δ = "-" 135.53): δ = „+“ −0.16 [Si(CH_3)$_3$], "-" 19.29 [C(CH_3)$_3$], "+" 26.74 [C(CH_3)$_3$], "-" 64.99 (C-1'), "-" 81.12 (C-5), "+" 83.84 (C-6), "-" 100.43 and "-" 103.57 (C-1, C-2), "+" 112.71 (C-4), "+" 127.80 (4 *meta*-C), "+" 129.84 (2 *para*-C), "-" 132.82 (2 *ipso*-C), "+" 135.41 (4 *ortho*-C), "-" 135.99 (C-3).

IR ($CDCl_3$): ν = 3305 (≡C−H st), 2255 and 2145 cm^{-1} (C≡C st).

HRMS (EI/70 eV): m/z = 401.1756 (M$^+$ −Me): confirms the fragment formula $C_{25}H_{29}OSi_2$ with a precision of ± 2 mDa; m/z = 359.1287 (M$^+$ −t-Bu): confirms the fragment formula $C_{22}H_{23}OSi_2$ with a precision of ± 2 mDa; the mole peak was not intense enough for HRMS.

MS (DCI/pos., NH_4^+): m/z = 434 (100%, M$^+$ +NH_4^+), 391 (8%), 363 (3%), 346 (5%), 302 (10%), 291 (12%), 274 (93%), 254 (5%), 216 (4%), 196 (12%). Because of its lability no correct combustion analysis could be obtained of compound *E*-**45a**.

***(E)*-(4*S*)-2,2-Dimethyl-4-{1-[2-(trimethylsilyl)ethynyl]but-1-en-3-ynyl}-1,3-dioxolane (*E*-45b)**

Prepared as described for *E*-**45a** from BuLi (1.49 M in hexane; 255 µl, 0.380 mmol, 1.2 equiv.), i-Pr$_2$NH (50.0 µl, 0.035 g, 0.380 mmol, 1.2 equiv.) in THF (2.5 mL), (trimethylsilyl)diazomethane (2.0 M in hexane; 190 µl, 0.380 mmol, 1.2 equiv.) and aldehyde *E*-**44b** (0.080 g, 0.317 mmol) in THF (650 µl) except that the latter reacted at −78 °C for 1.5 h, during warming to r.t. for 1 h and at r.t. for another 20 min. Flash chromatography (0.8 cm, petroleum ether/*t*-BuOMe 30:1, F4−8) provided the title compound (0.031 g, 39%).

$[\alpha]_D^{22} = +43.5$ (c = 1.32 in $CHCl_3$).

^{1}H NMR (300 MHz; slightly contaminated in the alkyl region): δ = 0.22 [s, Si(CH_3)$_3$], 1.40 and 1.45 [2 s, 2-(CH_3)$_2$], 3.32 (d, $^4J_{4',2'}$ = 2.3, 4'-H), AB signal (δ_A = 3.89, δ_B = 4.19, J_{AB} = 8.3, in addition split by $J_{A,4'}$ = 6.8, $J_{B,4'}$ = 6.4, 5-H$_2$), 4.56 (ddd, $J_{4,5\text{-}H(A)} = J_{4,5\text{-}H(B)}$ = 6.8, $^4J_{4,2'}$ = 1.1, 4-H), 6.04 (dd, $^4J_{2',4'}$ = 2.5, $^4J_{2',4}$ = 1.4, 2'-H).

^{13}C NMR (APT spectrum at 75 MHz): δ = "+" −0.22 [Si(CH_3)$_3$], "+" 25.88 and "+" 26.24 [2-(CH_3)$_2$], "-" 68.98 (C-5), "+" 77.09 (C-4), "-" 80.54 (C-3'), "+" 84.62 (C-4'), "-" 99.98 and "-" 104.88 (C-1", C-2"), "-" 110.46 (C-2), "+" 114.95 (C-2'), "-" 135.12 (C-1').

IR ($CDCl_3$): ν = 3305 (≡C−H st), 2255 and 2145 cm^{-1} (C≡C st).

HRMS (EI/70 eV): m/z = 248.1232 (M$^+$); confirms the molecular formula $C_{14}H_{20}O_2Si$ with a precision of ± 2 mDa. Because of its lability no correct combustion analysis could be obtained of compound *E*-**45b**.

***tert*-Butyl 2,2-Dimethyl-4-{(*E*)-1-[2-(trimethylsilyl)ethynyl]but-1-en-3-ynyl}-1,3-oxazolidine-3-carboxylate (*E*-45c) in a 62:38 Mixture* with a Rotamer (*iso*-*E*-45c)**

*determined ^{1}H NMR spectroscopically by the integral ratios over the 4-H´s

Prepared as described for *E*-**45a** from BuLi (2.35 M in hexane; 146 µl, 0.342 mmol, 1.2 equiv.), i-Pr$_2$NH (45.0 µL, 0.031 g, 0.342 mmol, 1.2 equiv.) in THF (2.2 mL), (trimethylsilyl)diazomethane (2.0 M in hexane; 171 µL, 0.342 mmol, 1.2 equiv.) and aldehyde *E*-**44c** (0.101 g, 0.285 mmol) in THF (600 µL) except that the latter reacted at −78 °C for 3 h, during warming to r.t. for 30 min and at r.t. for another 20 min. Flash chromatography (1.5 cm, petroleum ether/*t*-BuOMe 20:1, F28-38) gave the title compound (0.041 g, 41%).

$[\alpha]_D^{25} = -116$ (c = 1.70 in $CHCl_3$).

***E*-45c**

^{1}H NMR (300 MHz; contaminated in the alkyl region): δ = 0.20 [s, Si(CH_3)$_3$], 1.42 (*t*-Bu), 1.48 oder 1.54 and 1.64 [2 s, 2-(CH_3)$_2$], 3.30 (br d, $^4J_{4',2'}$ = 1.9, 4'-H), AB signal (δ_A = 3.93, δ_B = 4.07, J_{AB} = 9.0, in addition split by $J_{A,4}$ = 5.1, $J_{B,4}$ = 6.8, 5-H$_2$), 4.31 (br dd, $J_{4,5\text{-}H(A)} \approx J_{4,5\text{-}H(B)} \approx$ 5.7, 4-H), 5.76 (br s, 2'-H).

^{13}C NMR (APT spectrum at 75 MHz; contaminated in the alkyl region): δ = "+" −0.27 [Si(CH_3)$_3$], "+" 24.27 and "+" 25.37 [2-(CH_3)$_2$], "+" 28.27 [C(CH_3)$_3$], "+" 61.45 (C-4), "-" 67.67 (C-5), "-" 80.27 and "-" 80.59 [C-3', *C*(CH_3)$_3$], "+" 84.17 (C-4'), "-" 94.81 (C-2), "-" 100.35 and "-" 104.85 (C-1", C-2"), "+" 115.04 (C-2'), "-" 136.69 (C-1'), "-" 151.58 (N-*C*O$_2$t-Bu).

***iso*-*E*-45c**

^{1}H NMR (300 MHz; contaminated in the alkyl region): δ = 4.46 (br s, 4-H), 5.81 (br s, 2'-H); the other resonances are superimposed by those of *E*-**45c**.

^{13}C NMR (APT spectrum at 75 MHz; contaminated in the alkyl region): δ = "+" 24.94 and "+" 26.49 [2-(*C*H$_3$)$_2$], "+" 28.29 [C(*C*H$_3$)$_3$], "+" 61.29 (C-4), "-" 67.37 (C-5), "-" 80.76 and "-" 80.78 [C-3', *C*(CH$_3$)$_3$], "-" 94.33 (C-2), "+" 135.91 (C-1'), "-" 151.94 (N-*C*O$_2$*t*-Bu); the other resonances are superimposed by those of *E*-**45c** IR ($CDCl_3$): ν = 3305 (≡C−H st), 2255 and 2145 (C≡C st), 1695 cm^{-1} (C=O st).

HRMS (EI/70 eV): *m*/*z* = 347.1916 (M^+); confirms the molecular formula $C_{19}H_{29}NO_4Si$ with a precision of ± 2 mDa. Because of its lability no correct combustion analysis could be obtained of compound *E*-**45c**.

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References

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(1) Waldmann, H. *Nachr. Chem. Tech. Lab.* **1991**, *39*, 211.
Nicolaou, K. C.; Dai, W.-M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1387.
Lee, M. D.; Ellestadt, A. G.; Borders, D. B. *Acc. Chem. Res.* **1991**, *24*, 235; Murphy, J. A.; Griffiths, J. *Nat. Prod. Rep.* **1993**, 550.
Maier, M. E. *Kontakte (Merck)* **1994**, *2*, 3; *Synlett* **1995**, 13.
Nicolaou, K. C.; Smith A. L. In *Modern Acetylene Chemistry;* Stang, P. J.; Diederich, F.Eds.; VCH-Verlagsgesellschaft: Weinheim **1995**, 203−283.
Lhermitte, H.; Grierson, D. *Contemp. Org. Synth.* **1996**, *3*, 41; **1996**, *3*, 93.
Wang, K. K. *Chem. Rev.* **1996**, *96*, 207.
Smith, A. L.; Nicolaou, K. C. *J. Med. Chem.* **1996**, *39*, 2103.
Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453.
Brückner, R.; Suffert, J. *Synlett* **1999**, 657.

(2) Golik, J.; Dubay, G.; Groenewold, G.; Kawaguchi, H.; Konishi, M.; Krishnan, B.; Ohkuma, H.; Saitoh, K.-I.; Doyle, T. W. *J. Am. Chem. Soc.* **1987**, *109*, 3462.

(3) Lee, M. D.; Dunne, T.-S.; Chang, C. C.; Ellestad, G. A.; Siegel, M. M.; Morton, G. O.; McGahren, W. J.; Borders, D. B. *J. Am. Chem. Soc.* **1987**, *109*, 3466.

(4) Konishi, M.; Ohkuma, H.; Tsuno, T.; Oki, T.; VanDuyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1990**, *112*, 3715.

(5) Leet, J. E.; Schroeder, D. R.; Hofstead, S. J.; Golik, J.; Colson, K. L.; Huang, S.; Klohr, S. E.; Doyle, T. W.; Matson, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 7946.
Revised structure: Kawata, S.; Ashizawa, S.; Hirama, M. *J. Am. Chem. Soc.* **1997**, *119*, 12012.

(6) Yoshida, K.-i.; Minami, Y.; Azuma, R.; Saeki, M.; Otani, T. *Tetrahedron Lett.* **1993**, *34*, 2637.

(7) Schroeder, D. R.; Colson, K. L.; Klohr, S. E.; Zein, N.; Langley, D. R.; Lee, M. S.; Matson, J. A.; Doyle, T. W. *J. Am. Chem. Soc.* **1994**, *116*, 9351.

(8) Koide, Y.; Ishi, F.; Hasuda, K.; Koyama, Y.; Edo, K.; Katamine, S.; Kitame, F.; Ishida, N. *J. Antibiot.* **1980**, *33*, 342
Edo, K.; Katamine, S.; Kitame, F.; Ishida, N.; Koide, Y.; Kusano, G.; Nozoe, S. *J. Antibiot.* **1980**, *33*, 347 (partially revised in Shibuya, M.; Toyooka, K.; Kubota, S. *Tetrahedron Lett.* **1984**, *25*, 1171).
Edo, K.; Akiyama, Y.; Saito, K.; Mizugaki, M.; Koide, Y.; Ishida, N. *J. Antibiot.* **1986**, *39*, 1615.
Myers, A. G.; Proteau, P. J.; Handel, T. M. *J. Am. Chem. Soc.* **1988**, *110*, 7212.

(9) Ando, T.; Ishii, M.; Kajiura, T.; Kameyama, T.; Miwa, K.; Suguira, Y. *Tetrahedron Lett.* **1998**, *39*, 6495.

(10) Myers, A. G.; Alauddin, M. M.; Fuhry, M. M.; Dragovich, P. S.; Finney, N. S.; Harrington, P. M. *Tetrahedron Lett.* **1989**, *30*, 6997.

(11) Myers, A. G.; Hammond, M.; Wu, Y.; Xiang, J. N.; Harrington, P. M.; Kuo, E. Y. *J. Am. Chem. Soc.* **1996**, *118*, 10006-
Myers, A. G.; Liang, J.; Hammond, M.; Harrington, P. M.; Wu, Y.; Kuo, E. Y. *J. Am. Chem. Soc.* **1998**, *120*, 5319.

(12) Dai, W.-M.; Fong, K. C. *Tetrahedron Lett.* **1996**, *37*, 8413.

(13) Method: Trost, B. M.; Sorum, M. T.; Chan, C.; Harms, A. E.; Rüther, G. *J. Am. Chem. Soc.* **1997**, *119*, 698.
Trost, B. M.; McIntosh, M. C. *Tetrahedron Lett.* **1997**, *38*, 3207.

(14) Trost, B. M.; Hachiya, I.; McIntosh, M. C. *Tetrahedron Lett.* **1998**, *39*, 6445.

(15) Synthesis applications of enol triflates were reviewed by Ritter, K. *Synthesis* **1993**, 735.

(16) Method: Cacchi, S.; Morera, E.; Ortar, G. *Synthesis* **1986**, 320. For related couplings with alkenyl halide cf. Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.

(17) Cf. the reaction **12**→**13** in Eis, K.; Schmalz, H.-G. *Synthesis* **1997**, 202.

(18) Aldercide, M.; Spino, C.; Weiler, L. *Tetrahedron Lett.* **1984**, *25*, 1643.

(19) a) Certain β-oxo aldehydes were converted in a very similar manner into stereopure enol triflates with *Z*-selectivity when a lithium enolate (in THF) was the intermediate or with *E*-selectivity via the 2,6-di-*tert*-butylpyridinium enolate (in dichloromethane): Brückner, R.; Scheuplein, S. W.; Suffert, J. *Tetrahedron Lett.* **1991**, *32*, 1449.
Suffert, J.; Brückner, R. *Tetrahedron Lett.* **1991**, *32*, 1453.
K. Brickmann, F. Hambloch, J. Suffert, R. Brückner, *Liebigs Ann.* **1996**, 457.

(20) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979.

(21) Crisp, G. T.; Meyer, A. G. *J. Org. Chem.* **1992**, *57*, 6972.

(22) Keenan, R. M.; Weinstock, J.; Finkelstein, J. A.; Franz, R. G.; Gaitanopoulos, D. E.; Girard, G. R.; Hill, D. T.; Morgan, T. M.; Samanen, J. M.; Hempel, J.; Eggleston, D. S.; Ayar, N.; Griffin, E.; Ohlstein, E. H.; Stack, E. J.; Weidley, E. F.; Edwards, R. J. *J. Med. Chem.* **1992**, *35*, 3858.

(23) Görth, F. C.; Brückner, R. *Synthesis* **1999**, 1520.

(24) Method: Huang, S. L.; Omura, K.; Swern, D. *J. Org. Chem.* **1976**, *41*, 3329.

(25) Holmquist, C. R.; Roskamp, E. J. *J. Org. Chem.* **1989**, *54*, 3258.

(26) a) Reimnitz, F. *Diplomarbeit*, Universität Göttingen **1996**.
b) Schmid, C. R.; Bryant, J. D.; Dowlatzedah, M.; Phillips, J.

L.; Prather, D. E.; Schantz, R. R.; Sear, N. L.; Vianco, C. S. *J. Org. Chem*. **1991**, *56*, 4056.
(27) Tipson, R. S.; Cohen, A. *Carbohydr. Res.* **1968**, *7*, 237.
(28) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.
(29) Garner, P.; Park, J. M. *Org. Synth*. **1992**, *70*, 18.
(30) Houpis, I. N. *Tetrahedron Lett.* **1991**, *32*, 6675.
(31) Comins, D. A.; Dehghani, A. *Tetrahedron Lett.* **1992**, *33*, 6299.
(32) Kant, J.; Roth, J. A.; Fuller, C. E.; Walker, D. G.; Benigni, D. A.; Farina, V. *J. Org. Chem.* **1994**, *59*, 4956.
(33) a) Gibbs, R. A.; Krishnan, U.; Dolence, J. M.; Poulter, C. D. *J. Org. Chem.* **1995**, *60*, 7821.
b) These authors coupled an ester-substituted *Z*-configured enol triflate with $Bu_3Sn-C\equiv C-H$ under and destannylated thereafter to obtain 31% of the derived *Z*-enyne.
(34) Original procedure: Ramirez, F.; Desai, N. B.; Mc Kelvie, N. *J. Am. Chem. Soc.* **1962**, *84*, 1745. Extension thereof: Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.
(35) Regitz, M.; Anschütz, W. *Liebigs Ann. Chem.* **1969**, *730*, 194. Seyferth, D.; Marmor, R. S. *Tetrahedron Lett.* **1970**, 2493; Seyferth, D.; Marmor, R. S.; Hilbert, P. J. *J. Org. Chem.* **1971**, *36*, 1379.
(36) Ohira, S. *Synth. Comm.* **1989**, *19*, 561 (using a reagent by Grieco, P. A.; Pogonowski, C. S. *J. Am. Chem. Soc.* **1973**, *95*, 3071).
(37) Müller, S.; Liephold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521.
(38) Miwa, K.; Aoyama, T.; Shioiri, T. *Synlett* **1994**, 107.
(39) Suffert, J. *J. Org. Chem.* **1989**, *54*, 509.
(40) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

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