Asymmetric Induction in the [2,3] Wittig Rearrangement The Stereoselective Synthesis of Unsaturated Alcohols with Three Contiguous Stereogenic Centers

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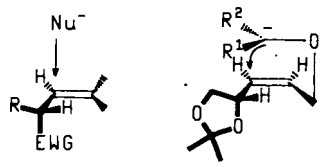
The [2,3] Wittig rearrangements of the lithio anions of the allyl propargyl ethers **7** are diastereoselective. A chiral dioxolane in the allyl moiety of **7** controls the configuration of the vinyl group at one of the newly formed stereogenic centers through asymmetric induction. Proper choice of *cis*- or *trans*-configurated starting material generates *anti* (**12**) or *syn* (**13**) 1,3-dioxygenated systems, respectively, in high selectivity. – It is suggested that the magnitude of the vicinal coupling constant $^3J_{OH,H}$ of the hydroxylic proton can be used to assign the stereochemistry in epimeric *syn* and *anti* γ-alkoxy alcohols.

Asymmetrische Induktion bei der [2,3]-Wittig-Umlagerung. – Stereoselektive Synthese von ungesättigten Alkoholen mit drei zusammenhängenden stereogenen Zentren

Die [2,3]-Wittig-Umlagerungen der lithiierten Allylpropargylether **7** erfolgen diastereoselektiv. Ein chiraler Dioxolanring im Allylteil von **7** bestimmt die Konfiguration der Vinylgruppe an dem einen der neu entstehenden stereogenen Zentren durch asymmetrische Induktion. Der Übergang von *cis*- zu *trans*-konfiguriertem Ausgangsmaterial gestattet, die Hydroxygruppe an dem anderen neuen Stereozentrum des Umlagerungsprodukts selektiv *syn* (**12**) bzw. *anti* (**11**) zu der C–O-Bindung am ursprünglich vorhandenen Stereozentrum zu plazieren. – Es wird vorgeschlagen, daß die Größe der vicinalen Kopplungskonstante $^3J_{OH,H}$ des alkoholischen Protons gestattet, epimeren γ-Alkoxyalkoholen die *syn*- oder *anti*-Konfiguration zuzuweisen.

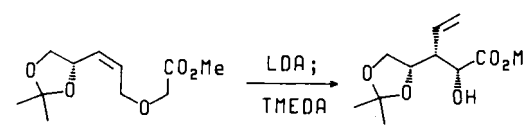
The two faces of a C=C bond bearing allylic asymmetry are rendered diastereotopic. Hence, reactions with this double bond may exhibit facial selectivity. In recent years, diastereofacial control of olefin reactivity by allylic stereogenic centers ("stereocenters") has been studied in a wide variety of reactions. The observed stereoselectivity in many cases can be rationalized by a transition state model related to Felkin Anh's, which was developed and popularized by Houk[1]. According to Houk, in the preferred transition state, *one* allylic σ-bond is oriented *antiperiplanar* with respect to the trajectory of the approaching reagent. *Which* allylic bond it is follows from the requirements to (1) minimize steric hindrance in the transition state and (2) maximize stabilization by overlap with properly disposed allylic σ or σ* orbitals in the transition state. The favored mode of attack of a nucleophile on an olefin with an allylic electron withdrawing group (≡ EWG) for instance may be depicted as shown in **1**.



1

2a $R^1 = CO_2Me$, $R^2 = H$
b $R^1 = H$, $R^2 = CO_2Me$

We reasoned that a transition state akin to **1** would be expected also if the nucleophile and the double bond were incorporated into the *same* molecule such as in the carbanion intermediates of [2,3] Wittig rearrangements. Indeed, when we deprotonated the ester **3**, its enolate rearranged cleanly to *one* hydroxy ester (**4**)[2] thus establishing a new method for configurational control of a Wittig rearrangement product: Asymmetric induction by a stereocenter in the *allylic moiety* of the anion[3]. Transition state **2b** is proposed to rationalize the resulting stereochemistry of the rearranged ester **4**. **2b** is an intramolecular version of Houk's bimolecular transition state **1**.



3 **4**
(1 diastereomer)

The "simple diastereoselectivity" – the preponderance for the *syn* orientation of hydroxy and vinyl groups in the rearranged ester **4** – was contrary to literature precedent[4]. Moreover, it hampered a synthetic project for which we required a Wittig rearrangement product with *anti* configuration. It was reasoned that the oversized methoxycar-

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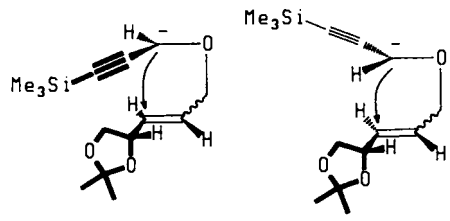
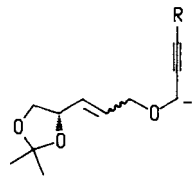
bonyl group prefers the *exo* transition state **2b** yielding the undesired *syn* epimer of **4**. If one wants to accomodate a substituent R^1 in the sterically congested *endo* position "*above*" the heterocycle as in **2a**, R^1 must be small, e.g. $-C\equiv C-R$ with the compact (conformational *A* value[5] 0.41 kcal mol^{-1}) $C\equiv C$ bond (vs. A = 1.20 kcal mol^{-1} for CO_2Me[5]). Specifically, if in the [2,3] Wittig rearrangement of a metalated alkyne like **5** an *endo* transition state **5a** is preferred over **5b** – as expected[6] – the resulting product would be the desired *anti* isomer. The present study brought this hypothesis into practice.



5a cis **5b**
6a trans **6b**

7 **8**



9 R = Li
10 R = $SiMe_3$

Initial experiments showed that the terminal alkynes **7** did not undergo [2,3] Wittig rearrangements via the dilithio anions **9**. Upon treatment of **7** with 4 equivalents of *n*-BuLi at −78 °C[7], the starting material was consumed. However, the ^1H NMR spectrum indicated the disappearance of the acetonide and the presence of conjugated double bonds (multiplets between δ = 6.0 and 6.5 ppm) suggesting that prior to the presumably *slow* second metalation the acetylides **8** underwent a base-induced elimination/fragmentation reaction. In this light, we felt that the propargylic *monoanions* **10** would be better suited for the [2,3] Wittig rearrangement than their *dianion* counterparts **9**.

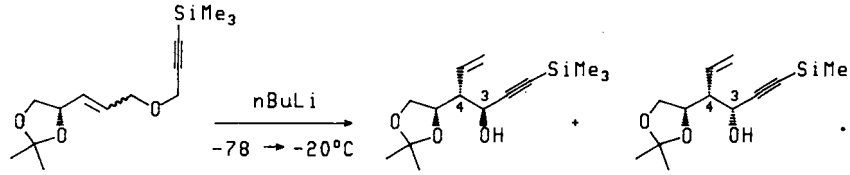
The monoanion *Z*-**10** was formed from the silylalkyne *cis*-**11** under the usual conditions[7]. It rearranged cleanly, chromatographic workup yielding 87% of *one* pure product **12** without indication of any accompanying diastereoisomers. In other words, in the rearrangement product **12**, we had succeeded in controlling the configuration of C-4 by asymmetric induction and the configuration of C-3 by "simple diastereoselectivity".

The configurations of the newly formed stereocenters C-3 and C-4 of **12** were determined by conversion into the saturated alcohol **16** (Scheme 1). No epimerization at the stereocenters in question should have occurred during these transformations. Compound **16** obtained in this way was identical – as judged by 300-MHz ^1H- and 75-MHz ^{13}C-NMR spectroscopy – with a sample of **16** prepared by the catalytic hydrogenation of the dienol **17**. Since the stereochemistry of **17** had been unambiguously assigned[9], the configuration of the alcohol **16** and hence that of the rearrangement product **12** were proven.

The stereoselective rearrangements *cis*-**11** → **12** and **3** → **4** demonstrate that "simple diastereoselectivity" (*syn*: *anti*) *can be controlled while maintaining the sense of the asymmetric induction.* Transition state **5a**, as discussed at the beginning of this paper, rationalizes the stereocontrolled formation of **12** from metalated *cis*-**11**.

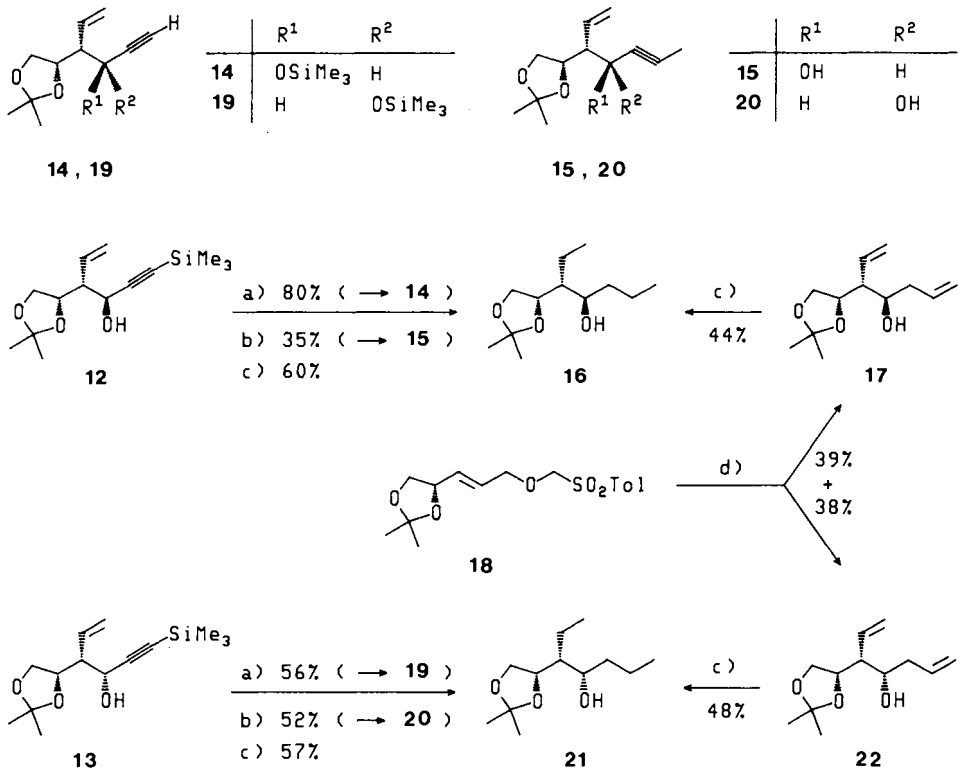
Next, we investigated stereocontrol in the rearrangement of the *E* isomer of **11**. Previously, there had not been an occasion to establish which of the isomeric ethers, *cis* or *trans*, would yield higher asymmetric induction in the [2,3] Wittig rearrangement. *trans*-**11** rearranged as smoothly as *cis*-**11** when treated with a slight excess of *n*-butyllithium at −20 °C. However, this time, *two* rearranged alcohols were isolated in a combined yield of 84%. The mixture contained 83% of **13** – as determined by ^1H-NMR spectroscopy – along with 17% of the epimeric **12**. In addition, we isolated trace amounts of a third diastereomer.

The configurations of the stereocenters at C-3 and C-4 of the major product **13** were determined by chemical correlation with the independently accessible alcohol **21** (Scheme 1). To this end, the same protocol as in the structure determination of the previously described **12** was applied. Here,



11		12		13
cis-11	87%	100	:	0
trans-11	84%	17	:	83

Scheme 1



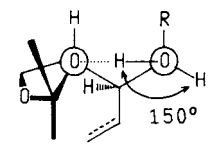
a)Bu_4NF; 1-Trimethylsilylimidazole/DMAP.- b)EtMgBr; MeI/HMPA; HF.- c)H_2, 5% Pd-C.- d)C_3H_5Li; HMPA (method: ref. 8)

the stereocenters C-3 and C-4 of the relay compound **21** originated from the unsaturated alcohol **22** with its unequivocally established configuration[9].

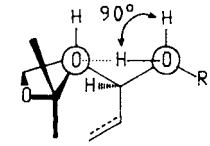
The chiral dioxolane in the *cis/trans* isomeric alkynes **11** effects an equally high asymmetric induction in the Wittig rearrangements of the corresponding anions, *irrespective* of their configurations. Therefore, C-4 of both rearranged products **12** and **13**, respectively, has the *same* absolute configuration. This finding supports our postulated transition states **5** *and* **6**.

On the other hand, as would be predicted, the "simple diastereoselectivity" of the [2,3] rearrangement of metalated **11** *depends* on the geometry of its double bond. The *cis* isomer gives pure *anti* product **12** via **5a**. The isomeric *trans*-**11** leads preferentially to the *syn* product **13** via transition state **6b**. In the *trans* case, however, competition from transition state **6a** gives rise to a stereochemical leak to the minor product **12**. *This* time, i.e. for the Wittig rearrangements of *cis*- and *trans*-**11** (recall **3**→**4**!), the sense and amount of "simple diastereoselectivity" is in agreement with literature precedents[5].

An observation made in our laboratories could be applied in assigning the relative configuration of the oxygen-bearing stereocenters in γ-alkoxy alcohols. Hoffmann deduced from ^{13}C-NMR spectra that such compounds exist in hydrogen-bonded conformations[10]. This should hold true for the dioxolane alcohols described here, too. Hence, the *anti*-γ-alkoxy alcohols **12**, **15**, **16**, and **17** presumably prefer conformations of type *anti*-**23**. The *syn* epimers **13**, **20**, **21**, and **22** are likely to prefer cyclic conformations of type *syn*-**23**. Hoffmann's observation[10] that the sum of the ^{13}C chemical shifts of the oxygen-bearing carbon atoms is smaller in *anti*- vs. *syn*-γ-alkoxy alcohols supports H-bridging for the *anti/syn* pairs **16**/**21** and **17**/**22**, respectively[11].



anti-**23**



syn-**23**

	$J_{OH,H}$	$\Sigma\delta(^{13}C)$
12	8.3 Hz	139.5
15	8.4 Hz	
16	6.0 Hz	147.6
17	4.5 Hz	145.9

	$J_{OH,H}$	$\Sigma\delta(^{13}C)$
13	3.8 Hz	140.2
20	3.5 Hz	
21	2.9 Hz	151.3
22	1.8 Hz	150.8

It is noteworthy that the magnitude of the vicinal coupling constant $^3J_{OH,H}$ of the hydroxyl proton in each pair of these

syn/anti epimers varies uniformly: In the *anti* isomers the value of $J_{OH,H}$ is by 3.7–4.9 Hz larger than in the corresponding *syn* epimers. We take this as *independent* evidence for the existence of the preferred hydrogen-bridged conformations **23**. One may reasonably assume, that the magnitude of $^3J_{OH,H}$ is essentially a function of the dihedral angle between the protons which couple. The Newman projections *syn*- and *anti*-**23** (view along the two O–C σ bonds) in conjunction with a Karplus type dependence of $^3J_{OH,H}$ from the dihedral angle *imply* the observed ranking of the $^3J_{OH,H}$ values. It is therefore suggested that in a pair of γ-alkoxy alcohols the compound with the larger value of $^3J_{OH,H}$ is the *anti* diastereomer. Note, that this novel criterion distinguishes unambiguously alcohol **12** as *anti* and **13** as *syn* diastereomer. These configurations could *not* be distinguished by ^{13}C-NMR spectroscopy (cf. ref.[11]).

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Experimental

^{1}H- and ^{13}C-NMR spectra: Bruker AC 300; tetramethylsilane as internal standard in $CDCl_3$; integrals in accord with assignments; coupling constants in Hz. – All reactions were performed in oven-dried (100°C) glassware under an atmosphere of dry nitrogen. Compounds were purified by flash chromatography[12] on Merck silica gel 60 (particle size 0.040–0.063 mm, 230–400 mesh ASTM); eluents given in brackets. Yields refer to analytically pure samples.

cis-(4′S)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-propen-1-ol ⟨$[\alpha]_D^{18}$ = +20.5 (*c* = 5.4, CH_2Cl_2); ref.[13] $[\alpha]_D$ = +17.1 (*c* = 0.34, $CHCl_3$); ref.[14] $[\alpha]_D$ = +14.0 (*c* = 4.5, $CHCl_3$)⟩ was prepared in 92% yield by DIBAL reduction of methyl [*cis*-(4′*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propenoate]. The latter compound was prepared via 1,2:5,6-di-*O*-isopropylidene-D-mannitol[15] and (4*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde[16] by the method of Mulzer[17].

trans-(4′S)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-propen-1-ol ⟨$[\alpha]_D^{18}$ = +30.2 (*c* = 7.2, CH_2Cl_2); ref.[13] $[\alpha]_D$ = +26.7 (*c* = 0.21, $CHCl_3$); ref.[14] $[\alpha]_D$ = +33.9 (*c* = 3.6, $CHCl_3$)⟩ was prepared in 95% yield by DIBAL reduction of methyl [*trans*-(4′*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propenoate], which was obtained via (4*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (vide supra) according to ref.[18].

cis-(4″S)-3-[{3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-propen-1-yl}oxy]-1-propyne (*cis*-**7**): *cis*-(4′*S*)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-propen-1-ol (0.500 g, 3.16 mol) was vigorously stirred under reflux with CH_2Cl_2 (8 ml), 50% KOH (8 ml), 3-chloropropyne (2.0 ml), and benzyltriethylammonium chloride (0.029 g, 0.158 mmol). After 25 min, H_2O (30 ml) was added, and the mixture was extracted with ether (50 + 30 ml). Flash chromatography (petroleum ether/diethyl ether, 5:1) gave a volatile liquid (0.452 g, 73%). – $[\alpha]_D^{20}$ = +2.7 ($CHCl_3$, *c* = 5.9). – ^{1}H NMR: δ = 1.40 and 1.43 [2 s; 2″-$(CH_3)_2$], 2.45 (t, *J* = 2.4; 1-H), 3.56 (dd, J_{gem} = $J_{5'-H^1,4'}$ = 8.0; 5″-H^1), 4.11 (dd, J_{gem} = 8.1, $J_{5'-H^2,4'}$ = 6.1; 5″-H^2), 4.15 (d, *J* = 2.4; 3-H_2), 4.17–4.22 (m; 1′-H_2), 4.87 (bddd, all *J* values ca. 7; 4″-H), 5.63–5.80 (m; 2′-H, 3′-H).

$C_{11}H_{16}O_3$ (196.3) Calcd. C 67.32 H 8.22
Found C 67.14 H 8.31

trans-**7**: *trans*-(4′*S*)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-propen-1-ol (1.000 g, 6.322 mmol) gave *trans*-**7** (0.905 g, 73%) when treated as described for the preparation of *cis*-**7**. – $[\alpha]_D^{20}$ = +35.7 ($CHCl_3$, *c* = 4.5). – ^{1}H NMR: δ = 1.39 and 1.43 [2 s; 2″-$(CH_3)_2$], 2.43 (t, *J* = 2.4; 1-H), 3.61 (dd, J_{gem} = $J_{5'-H^1,4'}$ = 7.9; 5″-H^1), 4.09 (d, *J* = 6.1; 1′-H_2), 4.10 (dd, J_{gem} = 8.2, $J_{5'-H^2,4'}$ = 6.2; 5″-H^2), 4.15 (d, *J* = 2.5; 3-H_2), 4.53 (ddd, all *J* values ca. 7; 4″-H), 5.71–5.93 (m; 2′-H, 3′-H).

$C_{11}H_{16}O_3$ (196.3) Calcd. C 67.32 H 8.22
Found C 67.33 H 8.27

cis-(4″S)-3-[{3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-propen-1-yl}oxy]-1-(trimethylsilyl)-1-propyne (*cis*-**11**): At dry-ice temperature *n*-BuLi (1.65 mol/l in hexane, 1.14 ml, 1.88 mmol, 1.0 equiv.) was added dropwise to *cis*-(4″*S*)-3-[{3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propen-1-yl}oxy]-1-propyne (0.370 g, 1.88 mmol) in THF (5 ml). After 18 min, the solution was warmed briefly to –15°C and cooled to –78°C again. After addition of chlorotrimethylsilane (0.311 ml, 2.45 mmol, 1.3 equiv.) the dry-ice bath was removed. 30 min later, NEt_3 was added as acid scavenger. The resulting suspension was filtered through silica gel. Purification by flash chromatography (petroleum ether/ether, 25:1 → 13:1) gave an oil (0.447 g, 88%). – $[\alpha]_D^{19}$ = +4.9 (*c* = 4.2, CH_2Cl_2). – ^{1}H NMR: δ = 0.19 (s; $SiMe_3$), 1.40 and 1.43 [2 s; 2″-$(CH_3)_2$], 3.56 (dd, $J_{5'-H^1,4'}$ = J_{gem} = 8.0; 5″-H^1), 4.13 (s; 3-H_2), in part superimposed by 4.09–4.18 (m; 1′-H_2, 5″-H^2), 4.88 (ddd, all *J* values ca. 7; 4″-H), 5.62–5.80 (m; 2′-H, 3′-H).

$C_{14}H_{24}O_3Si$ (268.4) Calcd. C 62.64 H 9.01
Found C 62.42 H 8.92

trans-**11** (1.035 g, 84%) was prepared from *trans*-(4″*S*)-3-[{3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propen-1-yl}oxy]-1-propyne (0.905 g, 4.61 mmol) as detailed above for the synthesis of *cis*-**11**. – $[\alpha]_D^{18}$ = +24.0 (*c* = 4.6, CH_2Cl_2). – ^{1}H NMR: δ = 0.18 (s; $SiMe_3$), 1.39 and 1.43 [2 s; 2″-$(CH_3)_2$], 3.60 (dd, J_{gem} = $J_{5'-H^1,4'}$ = 7.9; 5″-H^1), 4.06–4.14 (m; 3-H_2, 1′-H_2, 5″-H^2), 4.53 (ddd, all *J* values ca. 7; 4″-H), 5.70–5.79 (m; 3′-H), 5.84–5.93 (m; 2′-H).

$C_{14}H_{24}O_3Si$ (268.4) Calcd. C 62.64 H 9.01
Found C 62.43 H 9.17

(3S,4R,4′S)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1-(trimethylsilyl)-5-hexen-1-yn-3-ol (**12**): *n*-BuLi (1.65 mol/l in hexane, 1.15 ml, 1.90 mmol, 1.2 equiv.) was added at –78°C to *cis*-**11** (0.425 g, 1.58 mmol) in THF (9.8 ml). The solution was kept in a freezer (ca. –20°C) for about 12 h, quenched with saturated aqueous NH_4Cl (15 ml), diluted with H_2O (10 ml), and extracted three times with ether (40, 20, 20 ml). Flash chromatography (petroleum ether/ether, 4:1) led to **12** (0.370 g, 87%). – $[\alpha]_D^{21}$ = –1.53 (*c* = 5.6, CH_2Cl_2). – ^{1}H NMR: δ = 0.18 (s; $SiMe_3$), 1.38 and 1.41 [2 s; 2′-$(CH_3)_2$], 2.39 (ddd, $J_{4,5}$ = 10, $J_{4,4'}$ = $J_{4,3}$ = 5; 4-H), 2.73 (d, $J_{OH,3}$ = 8.3; OH), 3.73 (dd, J_{gem} = 8.1, $J_{5'-H^1,4'}$ = 7.4; 5′-H^1), 4.07 (dd, J_{gem} = 8.1, $J_{5'-H^2,4'}$ = 6.4; 5′-H^2), 4.41 (dd, $J_{3,OH}$ = 8.3, $J_{3,4}$ = 5.3; 3-H), 4.56 (ddd, $J_{4',5'-H^1}$ = $J_{4',5'-H^2}$ ≈ 7, $J_{4',4}$ = 4.7; 4′-H), 5.23 (dm, J_{trans} = 17.4; *Z*-6-H), 5.33 (dd, J_{cis} = 10.3, J_{gem} = 1.8; *E*-6-H), 5.93 (ddd, J_{trans} = 17.2, J_{cis} ≈ $J_{5,4}$ ≈ 10; 5-H). – ^{13}C NMR: δ = –0.21 ($SiMe_3$), 25.33 and 26.25 [2′-$(CH_3)_2$], 52.16 (C-4), 64.52 (C-3), 67.28 (C-5′), 75.00 (C-4′), 91.31 (C-1), 104.82 (C-2), 109.22 (C-2′), 120.26 (C-6), 133.26 (C-5).

$C_{14}H_{24}O_3Si$ (268.4) Calcd. C 62.64 H 9.01
Found C 62.57 H 8.98

(3R,4R,4′S)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1-(trimethylsilyl)-5-hexen-1-yn-3-ol (**13**): This compound was obtained as a 83:17 mixture (0.934 g, 83%) with **12** when *trans*-**11** (1.111 g, 4.138 mmol) was treated as described for the preparation of **12**. – $[\alpha]_D^{19}$ = +9.1 (for the mixture!; CH_2Cl_2, *c* = 3.9). – ^{1}H NMR: δ = 0.17 (s; $SiMe_3$), 1.36 and 1.41 [2 s; 2′-$(CH_3)_2$], 2.32 (d, $J_{OH,3}$ = 3.7; OH), 2.40 (m$_c$;

4-H), 3.79 (dd, J_{gem} = 8.1, $J_{5'\text{-}H^1,4'}$ = 7.5; 5'-H^1), 4.07 (dd, J_{gem} = 8.2, $J_{5'\text{-}H^2,4'}$ = 6.3; 5'-H^2), 4.40–4.46 (m; 4'-H), 4.50 (dd, $J_{3,4}$ = 6.1, $J_{3,OH}$ = 3.8; 3-H), 5.26 (dm, $J_{trans} \approx 17$; Z-6-H), 5.38 (dd, J_{cis} = 10.4, J_{gem} = 1.8; E-6-H), 5.90 (ddd, J_{trans} = 17.2, J_{cis} = 10.3, $J_{5,4}$ = 9.3; 5-H). – ^{13}C NMR: δ = –0.20 ($SiMe_3$), 25.29 und 26.23 [2'-(CH_3)$_2$], 52.84 (C-4), 64.24 (C-3), 67.48 (C-5'), 75.91 (C-4'), 91.31 (C-1), 104.32 (C-2), 109.08 (C-2'), 121.00 (C-6), 132.77 (C-5).

$C_{14}H_{24}O_3Si$ (268.4) Calcd. C 62.64 H 9.01
Found C 62.95 H 8.73

(3S,4S,4'S)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-3-[(trimethylsilyl)oxy]-5-hexen-1-yne (**14**): At 0°C, a mixture of (3S,4R,4'S)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-1-(trimethylsilyl)-5-hexen-1-yn-3-ol (**12**) (0.370 g, 1.38 mmol) in THF (5 ml) and Bu_4NF (5.52 ml of the 1 mol/l solution in THF, 5.52 mmol, 4.0 equiv.) was left standing for 5 min; then 4-(dimethylamino)pyridine (0.0169 g, 0.138 mmol, 0.1 equiv.) and trimethylsilylimidazole (3.00 ml, 20.5 mmol, 15 equiv.) were added. After 6 h, the reaction mixture was diluted with saturated aqueous NH_4Cl (50 ml) and extracted four times with ether (60, 25, 25, 25 ml). Flash chromatography (petroleum ether/ether, 100:1 → 25:1) furnished **14** as an oil (0.294 g, 80%). – $[\alpha]_D^{23}$ = –42.5 (*c* = 4.3, CH_2Cl_2). – ^{1}H NMR: δ = 0.19 (s; $SiMe_3$), 1.34 and 1.38 [2 s; 2'-(CH_3)$_2$], 2.34 (ddd, $J_{4,5}$ = $J_{4,3}$ = 9.0, $J_{4,4'}$ = 4.5; 4-H), 2.42 (d, $J_{1,3}$ = 2.2; 1-H), 3.70 (dd, J_{gem} = $J_{5'\text{-}H^1,4'}$ = 7.9; 5'-H^1), 4.02 (dd, J_{gem} = 8.0, $J_{5'\text{-}H^2,4'}$ = 6.4; 5'-H^2), 4.36 (m_c; 4'-H), superimposing 4.38 (dd, $J_{3,4}$ = 8.8, $J_{3,1}$ = 2.1; 3-H), 5.21 (dm, $J_{trans} \approx 17$; Z-6-H), 5.29 (dd, J_{cis} = 10.4, J_{gem} = 1.9; E-6-H), 5.75 (ddd, J_{trans} = 17.2, J_{cis} = 10.3, $J_{5,4}$ = 9.4; 5-H).

$C_{14}H_{24}O_3Si$ (268.4) Calcd. C 62.64 H 9.01
Found C 62.72 H 8.95

(3R,4S,4'S)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1-hepten-5-yn-4-ol (**15**): A solution of **14** (0.131 g, 0.490 mmol) and *n*-BuLi (0.356 ml of a 1.65 M solution in hexane, 0.587 mmol, 1.2 equiv.) in THF (3.0 ml) at –78°C was allowed to warm to –16°C, 25 min after mixing the reagents. Recooling to –78°C 25 min later was followed by successive additions of iodomethane (0.091 ml, 1.47 mmol, 3.0 equiv.) and HMPA (0.256 ml, 1.47 mmol, 3.0 equiv.). After 10 min the dry ice bath was removed. Quenching with aqueous HF (0.107 ml of a 40% solution, 2.45 mmol, 5.0 equiv. of HF) was followed – after 45 min of reaction – by basification with Na_2CO_3 (5 ml) and $NaHCO_3$ (15 ml). The crude product was extracted three times with ether (60, 30, 20 ml). Purification by flash chromatography (petroleum ether/ether, 2:1) yielded 0.036 g (35%) of product. – $[\alpha]_D^{20}$ = –12.6 (*c* = 1.0, $CHCl_3$). – ^{1}H NMR: δ = 1.38 and 1.41 [2 s; 2'-(CH_3)$_2$], 1.87 (d, $J_{7,4}$ = 2.2; 7-H_3), 2.37 (ddd, $J_{3,2}$ = 9.8, $J_{3,4}$ = $J_{3,4'}$ = 5.0; 3-H), 2.70 (d, $J_{OH,4}$ = 8.4; OH), 3.72 (dd, J_{gem} = $J_{5'\text{-}H^1,4'}$ = 7.8; 5'-H^1), 4.07 (dd, J_{gem} = 8.1, $J_{5'\text{-}H^2,4'}$ = 6.4; 5'-H^2), 4.37 (m_c; 4-H), 4.55 (m_c; 4'-H), 5.22 (dd, J_{trans} = 17.2, J_{gem} = 1.7; Z-1-H), 5.33 (dd, J_{cis} = 10.3, J_{gem} = 1.8; E-1-H), 5.93 (ddd, J_{trans} = 17.2, J_{cis} = $J_{2,3} \approx 10$; 2-H).

$C_{12}H_{18}O_3$ (210.3) Calcd. C 68.55 H 8.63
Found C 68.10 H 8.64

(3R,4R,4'S)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-heptanol (**16**): Catalytic hydrogenation (5% Pd/C, 1 bar, 2.1 h) of **15** (0.0311 g, 0.148 mmol) in ethyl acetate (2 ml) followed by flash chromatography (petroleum ether/ether, 2:1) gave 0.0192 g (60%) of the saturated alcohol. – The same compound (0.0231 g, 44%) could be prepared by catalytic hydrogenation (5% Pd/C, 6 bar, 13 h) of (3R,4R,4'S)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-1,6-heptadien-4-ol (**17**) (0.0516 g, 0.243 mmol) in ethyl acetate (1.5 ml) and similar chromatographic workup. The latter product could not be distinguished by $[\alpha]_D$, ^{1}H-, and ^{13}C-NMR spectroscopy from the sample of **16** isolated before. – $[\alpha]^{20.5}$ = +6.5 (*c* = 1.0, CH_2Cl_2). – ^{1}H NMR: δ = 0.82–0.98 (m; 1-H_3, 7-H_3), 1.35 and 1.42 [2 s; 2'-(CH_3)$_2$], superimposed by 1.35–1.64 (m; 2-H_2, 3-H, 5-H_2, 6-H_2), 2.71 (d, *J* = 6.0; OH), 3.72 (m_c; 4-H), 3.75 (dd, J_{gem} = $J_{5'\text{-}H,4'}$ = 8.0; 5'-H^1), 4.03 (dd, J_{gem} = 8.1, $J_{5'\text{-}H^2,4'}$ = 6.5; 5'-H^2), 4.42 (ddd, $J_{4',5'\text{-}H^1}$ = 8.5, $J_{4',5'\text{-}H^2}$ = 6.6, $J_{4',3}$ = 3.8; 4'-H). – ^{13}C NMR: δ = 12.24, 14.15, 18.97, 19.14, 25.14, 26.33, 37.76 [C-1, C-2, C-5, C-6, C-7, 2'-(CH_3)$_2$], 45.84 (C-3), 67.12 (C-5'), 71.50 (C-4), 76.14 (C-4'), 108.65 (C-2'). – MS: *m/z* = 201.1492 (M^+ – CH_3) [calculated for ($C_{12}H_{24}O_3$ – CH_3): 201.1491].

(3R,4S,4'S)-4-(2,2-Dimethyl-1,3-dioxolan-4-yl)-3-[(trimethylsilyl)oxy]-5-hexen-1-yne (**19**): **19** was isolated (0.521 g, 56%; mixed with small amounts of **14**) upon submitting **13** (0.928 g, 3.46 mmol, containing small amounts of **12**, vide supra) to the protocol used for the preparation of **14**. – $[\alpha]_D^{23}$ = +12.5 (*c* = 6.0, CH_2Cl_2). – ^{1}H NMR: δ = 0.16 (s; $SiMe_3$), 1.36 and 1.39 [2 s; 2'-(CH_3)$_2$], 2.35 (ddd, $J_{4,5}$ = 9.1, $J_{4,4'}$ = $J_{4,3}$ = 6.1; 4-H), 2.47 (d, $J_{1,3}$ = 2.2; 1-H), 3.74 (dd, J_{gem} = $J_{5'\text{-}H^1,4'}$ = 7.9; 5'-H^1), 4.09 (dd, J_{gem} = 8.3, $J_{5'\text{-}H^2,4'}$ = 6.1; 5'-H^2), 4.39–4.43 (m; 3-H, 4'-H), 5.19 (dm, $J_{trans} \approx 17$; Z-6-H), 5.26 (dd, J_{cis} = 10.3, J_{gem} = 1.8; E-6-H), 5.83 (ddd, J_{trans} = 17.1, J_{cis} = 10.3, $J_{5,4}$ = 9.1; 5-H).

$C_{14}H_{24}O_3Si$ (268.4) Calcd. C 62.64 H 9.01
Found C 62.61 H 9.12

(3R,4R,4'S)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-1-hepten-5-yn-4-ol (**20**): This alcohol (0.182 g, 52%) was synthesized from **19** (0.449 g, 1.67 mmol) in a manner analogous to the preparation of **15**. – $[\alpha]_D^{20}$ = +16 (*c* = 3.2, $CHCl_3$). – ^{1}H NMR: δ = 1.37 and 1.41 [2 s; 2'-(CH_3)$_2$], 1.87 (d, $J_{7,4}$ = 2.2; 7-H_3), 2.30 (d, $J_{OH,4}$ = 3.5; OH), 2.34 (m_c; 3-H), 3.75 (dd, J_{gem} = $J_{5'\text{-}H^1,4'}$ = 8.0; 5'-H^1), 4.07 (dd, J_{gem} = 8.2, $J_{5'\text{-}H^2,4'}$ = 6.4; 5'-H^2), 4.40–4.48 (m; 4-H, 4'-H), 5.25 (dd, J_{trans} = 17.3, J_{gem} = 1.7; Z-1-H), 5.37 (dd, J_{cis} = 10.4, J_{gem} = 1.8; E-1-H), 5.88 (ddd, J_{trans} = 17.3, J_{cis} = 10.3, $J_{2,3}$ = 9.3; 2-H).

$C_{12}H_{18}O_3$ (210.3) Calcd. C 68.55 H 8.63
Found C 68.20 H 8.51

(3R,4S,4'S)-3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-heptanol (**21**): Hydrogenation (5% Pd/C, 6 bar, 6.7 h) of **20** (0.0563 g, 0.268 mmol) in ethyl acetate (1.5 ml) led to the title compound (0.0332 g, 57%). 0.0647 g (48%) of **21** was obtained similarly from (3R,4S,4'S)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-1,6-heptadien-4-ol (**22**) (0.133 g, 0.624 mmol). – $[\alpha]_D^{20}$ = –3.2 (*c* = 2.8, CH_2Cl_2). – ^{1}H NMR: δ = 0.92–1.02 (m; 1-H_3, 7-H_3), 1.36 and 1.42 [2 s; 2'-(CH_3)$_2$], superimposes 1.32–1.53 (m; 2-H_2, 3-H, 5-H_2, 6-H_2), 2.06 (bd, $J_{OH,4}$ = 2.9; OH), 3.77 (dd, J_{gem} = $J_{5'\text{-}H^1,4'} \approx 7.7$; 5'-$H^1$), superimposes 3.82 ($m_c$; 4-H), 4.03 (dd, J_{gem} = 8.2, $J_{5'\text{-}H^2,4'}$ = 6.3; 5'-H^2), 4.25 (ddd, $J_{4',5'\text{-}H^1}$ = 7.5, $J_{4',5'\text{-}H^2}$ = 6.4, $J_{4',4}$ = 4.7; 4'-H). – ^{13}C NMR: δ = 14.07, 14.20, 17.41, 19.66, 25.38, 26.51, 36.57 [C-1, C-2, C-5, C-6, C-7, 2'-(CH_3)$_2$], 47.07 (C-3), 67.49 (C-5'), 73.06 (C-4), 78.25 (C-4'), 108.47 (C-2'). – MS: *m/z* = 201.1496 (M^+ – CH_3) [calculated for ($C_{12}H_{24}O_3$ – CH_3): 201.1491].

CAS Registry Numbers

(*cis*)-**7**: 117341-47-6 / (*trans*)-**7**: 117341-48-7 / (*cis*)-**11**: 117341-49-8 / (*trans*)-**11**: 117341-50-1 / **12**: 117341-51-2 / **13**: 117465-39-1 / **14**: 117341-52-3 / **15**: 117341-53-4 / **16**: 117341-54-5 / **17**: 117341-55-6 / **19**: 117465-40-4 / **20**: 117465-41-5 / **21**: 117465-42-6 / **22**: 117465-43-7 / (4*R*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde: 15186-48-8 / 1,2:5,6-di-*O*-isopropylidene-D-mannitol: 1707-77-3 / methyl [*cis*-(4'*S*-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propenoate]: 81703-94-8 / *cis*-(4'*S*-3-(2,2-dimethyl-1,3-dioxolan-4-yl-2-propen-1-ol: 80532-35-0 / *trans*-(4'*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propen-1-ol: 79060-23-4 / methyl [*trans*-(4'*S*)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-propenoate]: 81703-93-7 / 3-chloropropyne: 624-65-7

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