Synthesis of Highly Functionalized Propargylic Alcohols: Direct Addition of Epoxy Acetylides to Aldehydes and Ketones

by **Anja Hoffmann-Röder** and **Norbert Krause***

Organic Chemistry II, Dortmund University, D-44221 Dortmund
(e-mail: norbert.krause@uni-dortmund.de)

Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday

Direct nucleophilic addition of terminal alkynes comprising an epoxy group to aldehydes and ketones is reported with BuLi or lithium diisopropylamide for the generation of the corresponding lithium acetylides. This alkynylation reaction tolerates a wide variety of different functional groups (*e.g.*, alcohols, silyl ethers, halides, double bonds) in the carbonyl compound, as well as in the acetylenic nucleophile, and furnishes highly functionalized propargylic alcohols in good-to-excellent yields. The method is particularly useful for the regioselective introduction of an epoxide function into multiply unsaturated target molecules.

Introduction. – The addition of C nucleophiles to aldehydes and ketones belongs to the most important C,C-bond-forming processes in organic synthesis [1]. In this respect, acetylides represent a particularly versatile class of C nucleophiles, since the resulting propargylic alcohols are prone to undergo further transformations and, thus, constitute important building blocks for an abundance of natural products (for some selected examples, see [2]), pharmacologically active compounds (for some selected examples, see [3]), and structurally interesting molecules [4]. Consequently, several synthetic strategies for the incorporation of acetylenic entities into carbonyl compounds have been established [5].

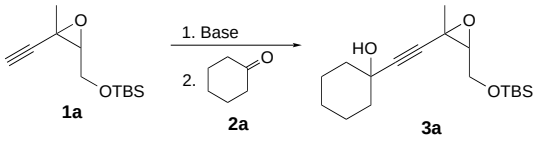
Complex molecules, *e.g.*, natural products, often require in their synthesis the assembly of highly functionalized precursors, resulting from multistep transformations. Thus, from an economic point of view, the development of convergent synthetic strategies, which allow an early introduction of all necessary functionalities into the molecule, is highly rewarding. In the course of our work on the synthesis of 2,5-dihydrofurans from propargylic oxiranes *via* α-hydroxyallenes [6], we became interested in the synthesis of propargylic alcohols comprising an epoxide moiety through direct addition of an epoxy acetylide to an aldehyde or ketone. This reaction would be particularly useful for the regioselective introduction of an oxirane ring into multiply unsaturated target molecules where a direct alkene epoxidation is expected to furnish a mixture of regioisomers.

To the best of our knowledge, there is only scattered precedence for the formation of metal acetylides bearing an epoxide ring [7], and only one example for the direct deprotonation of an epoxy alkyne and the subsequent addition to a carbonyl compound [8]. This is not surprising, since nucleophiles containing an electrophilic moiety are involved, and for a successful transformation of this kind, two requirements have to be met: *i*) the base used for the deprotonation of the epoxy alkyne should not undergo

direct nucleophilic attack at the oxirane ring, and *ii*) the acetylide formed should react with the carbonyl group and not with another epoxide. In this account, we report our findings on the formation and addition of epoxy acetylides to aldehydes and ketones, as well as the application to the synthesis of versatile multifunctionalized propargylic building blocks in only one step.

Results and Discussion. – First, the addition of epoxy acetylides to carbonyl compounds was investigated with oxirane **1a**, which is easily accessible from (*Z*)-pent-2-en-4-yn-1-ol [9], and cyclohexanone (**2a**) as test substrates (*Scheme 1*). To avoid nucleophilic attack at the epoxide ring, non-nucleophilic bases like lithium diisopropylamide (LDA), lithium hexamethyldisilazide (LHMDS), and its potassium counterpart (KHMDS) were used for the acetylide formation in THF, giving the addition product **3a** in 86, 76, and 72% yield, respectively. Strikingly, even the use of the more nucleophilic BuLi as a base resulted in the clean formation of product **3a**, which was obtained in 86% yield in THF as solvent (83% in Et_2O). No side products formed by the undesired reactions mentioned above or by enolization of the ketone were observed.

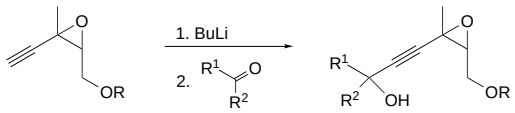
Scheme 1



By contrast, transmetallation of the Li-acetylide of **1a** with $(i\text{-PrO})_3TiCl$ to the corresponding Ti-acetylide [10] furnished only small amounts of the desired addition product. Here, as in the case of *Carreira*'s protocol (with $Zn(OTf)_2$/*N*-methylephedrine) [5d], complex reaction products were obtained, probably because of the *Lewis* acidity of $(i\text{-PrO})_3TiCl$ and $Zn(OTf)_2$, respectively. Moreover, application of *Knochel*'s method (with $CsOH \cdot H_2O$) [5b] furnished, as a result of its low reactivity, only 26% of the desired propargylic alcohol **3a**.

Subsequently, we investigated the scope and limitations of the alkynylation reaction with BuLi as a base. Thus, a variety of different aldehydes and ketones, which cover saturated, unsaturated, and aromatic representatives, were reacted with alkyne **1a** and the corresponding free alcohol **1b** (*Scheme 2* and *Table*).

Scheme 2



1a (R = TBS) **2** **3**
1b (R = H)

Table. *Nucleophilic Addition of Epoxy Alkynes* **1** *to Carbonyl Compounds* **2**

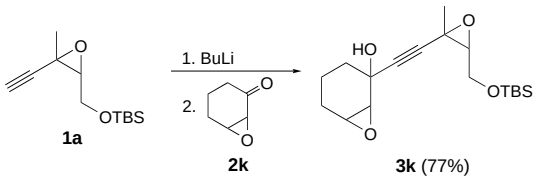
Entry	Alkyne	Carbonyl compound		Product (yield [%])
		R^1	R^2	
1	**1a**	$-(CH_2)_5-$		**3a** (86)
2	**1b**	$-(CH_2)_5-$		**3b** (91)
3	**1a**	$-Me_2C(CH_2)_4-$		**3c** (75)
4	**1a**	$-CH=CH(CH_2)_3-$		**3d** (78)
5	**1a**	Me	Me	**3e** (94)
6	**1b**	cyclopropyl	Me	**3f** (31)
7	**1b**	$C_5H_{11}CH=CH$	H	**3g** (65)
8	**1a**	Ph	H	**3h** (57)
9	**1a**	Ph	Me	**3i** (28)
10	**1a**	4-BrC_6H_4	H	**3j** (83)

As can be seen from the *Table*, both aldehydes and ketones can be transformed smoothly into the corresponding propargylic derivatives **3** in good-to-excellent yields. In particular, cyclohexanone derivatives proved to be profitable substrates even in the presence of an adjacent quaternary center (*Entry 3*). By contrast, the addition of **1a**/**1b** to acyclic ketones gave mixed results: whereas the reaction with acetone proceeded uneventfully to give the expected adduct **3e** in 94% yield (*Entry 5*), the analogous reaction with cyclopropyl methyl ketone was not satisfactory, most probably due to the high ring strain. As a consequence, a complex product mixture was obtained with only 31% yield of the cyclopropyl-substituted propargylic alcohol **3f** (*Entry 6*).

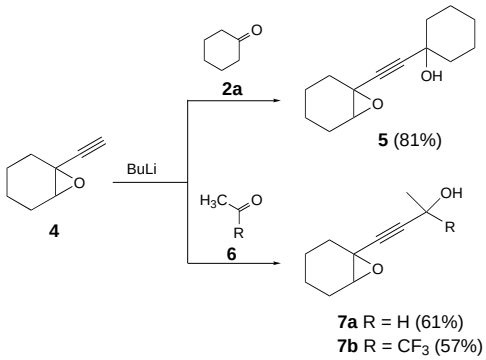
Nonetheless, the addition of epoxy-substituted alkynes to aldehydes and ketones, as outlined above, appears to be a generally applicable method. Hence, this reaction tolerates besides simple alkyl-substituted electrophiles even those comprising further functionalities in the molecule, *e.g.*, C=C bonds (even in conjugation to the C=O group), aromatic substituents, and halides. In this respect, the resulting propargylic derivatives containing a reactive C=C bond (*Entries 4* and *7*) are particularly interesting, since they are not accessible *via* the conventional addition–epoxidation sequence (see below). In both cases, the addition takes place regioselectively to furnish the 1,2-addition products only. In the case of the less reactive PhCHO (*Entry 8*) and acetophenone (*Entry 9*), however, the reaction proceeded sluggishly, furnishing the desired addition products in only moderate yields (in the case of acetophenone, enolization may also contribute to the low yield). Here, as expected, introduction of an electron-withdrawing group in *para*-position activated the substrate and improved the yield (*Entry 10*), notably without any halogen/metal exchange. A particularly interesting example is the reaction of the lithium acetylide formed from **1a** and BuLi with the ambident electrophile 2,3-epoxycyclohexanone (**2k**); again, the addition takes place regioselectively to give the product **3k** comprising two different epoxide moieties (77% yield; *Scheme 3*).

Even cyclic epoxides containing a terminal triple bond, *e.g.*, **4** [11], can be applied in the addition to cyclohexanone (**2a**; *Scheme 4*). As before, the reaction proceeded smoothly leading to propargylic alcohol **5** as the sole product in 81% yield. The corresponding addition to acetaldehyde (**6a**) and 1,1,1-trifluoroacetone (**6b**) gave also the desired alcohols **7a**/**b** with reasonable 61 and 57% yield, respectively.

Scheme 3



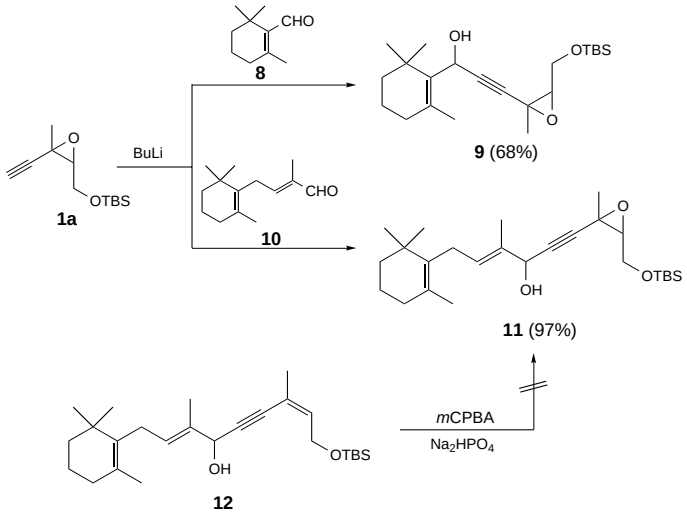
Scheme 4



Finally, to demonstrate the applicability of the method to the assembly of complex, multiply unsaturated target molecules, the epoxy acetylide formed from **1a** and BuLi was added to vitamin A building blocks. Reaction with the sterically hindered aldehyde β-cyclocitral (**8**) gave the addition product **9** in 68% yield, whereas the corresponding addition to the β-C_{14}-aldehyde **10** [12] furnished the expected adduct **11** with an exceptionally high 97% yield (*Scheme 5*). The latter is an intermediate in the projected synthesis of a vitamin A metabolite comprising a 2,5-dihydrofuran unit [13]. As expected, epoxypropargylic alcohol **11** cannot be directly obtained by epoxidation of the trienyne **12** (prepared in analogy to the corresponding diol [14]); treatment of the latter with *m*-chloroperbenzoic acid (*m*CPBA) provided a complex mixture of several oxiranes and other by-products.

Conclusions. – We reported the direct addition of lithium acetylides bearing an epoxy group to aldehydes and ketones. This alkynylation reaction not only leads to the generation of the corresponding functionalized propargylic alcohols in good-to-excellent yields, but is also compatible with a variety of different functional groups (*e.g.*, alcohols, silyl ethers, halides, C=C bonds) in both reaction partners. Moreover, the reaction can be conducted in a very simple manner with LDA or BuLi as a base. The method is particularly useful for the regioselective introduction of an epoxide functionality into multiply unsaturated target molecules.

Scheme 5



Experimental Part

General. The reactions were carried out in thoroughly dried glassware under Ar. Et_2O and THF were distilled from Na/benzophenone prior to use. BuLi was titrated with diphenylacetic acid according to the procedure of *Kofron* and *Baclawski* [15]. GC Analyses were carried out with a *Carlo-Erba GC-8000* gas chromatograph with He as carrier gas and an *OV-1701* cap. column. IR Spectra: *Bruker IFS66 FT-IR* spectrometer. FAB-MS: *Jeol SX102A* spectrometer. NMR Spectra: *Bruker DRX-400* or *DRX-500* spectrometer, in $CDCl_3$ or C_6D_6 as solvent and internal standard; abbreviations for ^{13}C-NMR DEPT spectra: +: CH_3, CH, −: CH_2, x: C(quart.).

General Procedure for the Addition of Epoxy Acetylides to Aldehydes and Ketones. To a soln. of the epoxy acetylene **1** or **4** (2.2 mmol) in *ca.* 25 ml of dry THF (or Et_2O) under Ar, 2.2 mmol (4.4 mmol in the case of **1b**) of BuLi were added at −80°. The resulting soln. was stirred for 15 min at this temp., and 2.2 mmol of the carbonyl compound, dissolved in *ca.* 5 ml of THF (or Et_2O), were added. The mixture was allowed to warm to r.t. and was stirred for additional 30 min. After hydrolysis with 15 ml of a sat. NH_4Cl soln., the aq. phase was washed with Et_2O (3 × 10 ml). The combined org. layers were washed with brine, dried, and the solvent was evaporated *in vacuo*. Flash column chromatography (FC) (SiO_2; cyclohexane/AcOEt 10:1) afforded the propargylic alcohol.

*1-[2-(*cis*-3-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)ethynyl]cyclohexan-1-ol* (**3a**). From 500 mg (2.2 mmol) of **1a** in 25 ml of THF, 1.4 ml (2.2 mmol) of BuLi (1.6M in hexane) and 217 mg (2.2 mmol) of cyclohexanone in 5 ml of THF; yield: 620 mg (86%) of **3a**. Slightly yellow liquid. IR (neat): 3415*s*, 2933*s*, 2858*s*. ^{1}H-NMR (500 MHz, C_6D_6): 4.01 (*dd*, ^2J(H,H) = 11.5, ^3J(H,H) = 5.0, 1 H, CH_2O); 3.94 (*dd*, ^2J(H,H) = 11.5, ^3J(H,H) = 5.5, 1 H, CH_2O); 2.96 (ψt, CH−O); 1.93 (*s*, OH); 1.88–1.77 (*m*, CH_2); 1.56–1.49 (*m*, 3 CH_2); 1.41–1.27 (*m*, 1 H, CH_2); 1.35 (*s*, MeCO); 1.11–1.00 (*m*, 1 H, CH_2); 0.99 (*s*, *t*-Bu); 0.14, 0.12 (2*s*, Me_2Si). ^{13}C-NMR (125 MHz, C_6D_6): 89.0 (x, C(1′)); 81.7 (x, C(2′)); 68.2 (x, C(1)); 64.4 (+, C(3″)); 63.8 (−, CH_2O); 51.7 (x, C(2″)); 40.1 (−, C(2), C(6)); 26.1 (+, Me_3C); 25.4, 23.5 (2−, C(3), C(4), C(5)); 23.4 (+, Me−C(2″)); 18.5 (x, Me_3C), −5.0, −5.2 (2+, Me_2Si). FAB-MS: 347 (8, $[M+Na]^+$), 323 (14, $[M-H]^+$), 277 (60), 249 (48), 163 (95), 133 (88), 73 (100). HR-FAB-MS: calc. for $C_{18}H_{32}O_3Si$ (324.53): 347.2018 ($[M+Na]^+$); found: 347.2025.

*1-{2-[*cis*-3-(Hydroxymethyl)-2-methyloxiran-2-yl]ethynyl}cyclohexan-1-ol* (**3b**). From 500 mg (4.5 mmol) of **1b** in 30 ml of THF, 5.9 ml (8.9 mmol) of BuLi (1.5M in hexane), and 438 mg (4.5 mmol) of cyclohexanone in 5 ml of THF; yield: 855 mg (91%) of **3b**. Slightly yellow oil. IR (neat): 3420*s*, 2933*s*, 2861*s*. ^{1}H-NMR (500 MHz, C_6D_6): 4.33 (*s*, OH); 4.18 (*s*, OH); 3.97 (*m*, CH_2O); 3.05 (*t*, ^3J(H,H) = 5.5, H−C(3″)); 2.02–1.93 (*m*, CH_2); 1.71–1.58 (*m*, 2 CH_2); 1.55–1.47 (*m*, CH_2); 1.40 (*s*, Me); 1.39–1.34 (*m*, 1 H, CH_2); 1.25–1.17 (*m*, 1 H, CH_2).

^{13}C-NMR (125 MHz, C_6D_6): 89.2 (x, C(1′)); 81.5 (x, C(2′)); 68.4 (x, C(1)); 64.3 (+, C(3″)); 62.5 (−, CH_2O); 52.2 (x, C(2″)); 40.0 (−, C(2), C(6)); 25.5, 23.5 (2−, C(3), C(4), C(5)); 23.4 (+, Me). FAB-MS: 193 (20, $[M-OH]^+$), 73 (100).

*1-[2-(*cis*-3-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)ethynyl]-2,2-dimethylcyclohexan-1-ol* (**3c**). From 500 mg (2.2 mmol) of **1a** in 25 ml of THF, 1.5 ml (2.2 mmol) of BuLi (1.5M in hexane), and 279 mg (2.2 mmol) of 2,2-dimethylcyclohexanone in 5 ml of THF; yield: 585 mg (75%) of **3c**. Slightly yellow liquid. IR (neat): 3471*m*, 2931*s*, 2859*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.91 (*dd*, ^2J(H,H) = 11.5, ^3J(H,H) = 4.5, 1 H, CH_2O); 3.75 (*dd*, ^2J(H,H) = 11.5, ^3J(H,H) = 5.7, 1 H, CH_2O); 3.01 (ψt, H−C(3″)); 1.92 (*s*, OH); 1.76–1.73 (*m*, CH_2); 1.63–1.61 (*m*, 1 H, CH_2); 1.53 (*s*, Me−C(2″)); 1.43–1.36 (*m*, 2 CH_2); 1.05 (*s*, Me−C(2)); 0.98 (*s*, Me−C(2)); 0.89 (*s*, *t*-Bu); 0.07, 0.07 (2*s*, Me_2Si). ^{13}C-NMR (125 MHz, $CDCl_3$): 87.8 (x, C(1′)); 82.1 (x, C(2′)); 73.8 (x, C(1)); 64.6, 64.5 (2+, C(3″)); 63.4 (−, CH_2O); 51.6 (x, C(2″)); 37.9, 37.9 (2x, C(2)); 36.2 (−, C(3)); 35.6, 35.5 (2−, C(6)); 25.8 (+, Me_3C); 25.4 (+, Me−C(3)); 23.4 (+, Me−C(2″)); 22.6, 21.0 (2−, C(4), C(5)); 18.3 (x, Me_3C); −5.2, −5.3 (2+, Me_2Si). FAB-MS: 375 (19, $[M+Na]^+$), 351 (16, $[M-H]^+$), 295 (45), 277 (32), 203 (46), 191 (95), 161 (63), 105 (36), 73 (100). HR-FAB-MS: calc. for $C_{20}H_{36}O_3Si$ (352.59): 375.2331 ($[M+Na]^+$); found: 375.2360.

*1-[2-(*cis*-3-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)ethynyl]cyclohex-2-en-1-ol* (**3d**). From 500 mg (2.2 mmol) of **1a** in 25 ml of Et_2O, 1.5 ml (2.2 mmol) of BuLi (1.5M in hexane), and 212 mg (2.2 mmol) of cyclohex-2-enone in 5 ml of Et_2O; yield: 556 mg (78%) of **3d**. Slightly yellow liquid. IR (neat): 3424*m*, 3030*w*, 2931*s*, 2858*s*, 1649*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.80 (*dt*, ^3J(H,H) = 10.0, 3.5, H−C(3)); 5.68 (*d*, ^3J(H,H) = 10.0, H−C(2)); 3.86, 3.86 (2*dd*, ^2J(H,H) = 11.8, ^3J(H,H) = 5.0, 1 H), 3.75 (*dd*, ^2J(H,H) = 11.8, ^3J(H,H) = 5.3, 1 H, CH_2O); 3.01, 3.01 (2ψt, H−C(3″)); 2.23 (*s*, OH); 2.00–1.94 (*m*, 3 H, CH_2(4), CH_2(5), CH_2(6)); 1.90–1.83 (*m*, 1 H, CH_2(4), CH_2(5), CH_2(6)); 1.75–1.72 (*m*, 2 H, CH_2(4), CH_2(5), CH_2(6)); 1.53 (*s*, Me−C(2″)); 0.89 (*s*, *t*-Bu); 0.08, 0.07 (2*s*, Me_2Si). ^{13}C-NMR (100 MHz, $CDCl_3$): 130.0, 130.0, 129.9, 129.9 (4+, C(2), C(3)); 88.0 (x, C(1′)); 80.7 (x, C(2′)); 65.1 (x, C(1)); 64.5, 64.4 (2+, C(3″)); 63.0, 63.0 (2−, CH_2O); 51.8 (x, C(2″)); 37.7, 37.6 (2−, C(6)); 25.8 (+, Me_3C); 24.5, 19.0, 19.0 (3−, C(4), C(5)); 23.2 (+, Me−C(2″)); 18.3 (x, Me_3C), −5.2, −5.3 (2+, Me_2Si). FAB-MS: 321 (4, $[M-H]^+$), 305 (45), 277 (15), 247 (10), 173 (12), 161 (30), 131 (63), 73 (100). HR-FAB-MS: calc. for $C_{18}H_{30}O_3Si$ (322.52): 321.1882 ($[M-H]^+$); found: 321.1878.

*4-(*cis*-3-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)-2-methylbut-3-yn-2-ol* (**3e**). From 2.00 g (8.8 mmol) of **1a** in 50 ml of THF, 3.9 ml (8.8 mmol) of BuLi (2.3M in hexane), and 513 mg (8.8 mmol) of acetone; yield: 2.36 g (94%) of **3e**. Slightly yellow liquid. IR (neat): 3403*m*, 2931*s*, 2858*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.85 (*dd*, ^2J(H,H) = 11.7, ^3J(H,H) = 5.2, 1 H, CH_2); 3.76 (*dd*, ^2J(H,H) = 11.7, ^3J(H,H) = 5.2, 1 H, CH_2); 3.00 (*t*, ^3J(H,H) = 5.2, H−C(3′)); 2.18 (*s*, OH); 1.52 (*s*, Me−C(2′)); 1.48 (*s*, Me−C(2)); 0.89 (*s*, *t*-Bu); 0.08, 0.08 (2*s*, Me_2Si). ^{13}C-NMR (125 MHz, $CDCl_3$): 89.3 (x, C(3)); 79.2 (x, C(4)); 65.0 (x, C(2)); 64.4 (−, CH_2); 62.9 (+, C(3′)); 51.8 (x, C(2′)); 31.2, 31.2 (2+, Me−C(2)); 25.8 (+, Me_3C); 23.2 (+, Me−C(2′)); 18.3 (x, Me_3C); −5.2, −5.3 (2+, Me_2Si). FAB-MS: 283 (6, $[M-H]^+$), 267 (32), 237 (25), 209 (22), 123 (30), 73 (100). HR-FAB-MS: calc. for $C_{15}H_{28}O_3Si$ (284.47): 284.1808 (M^+); found: 284.1802.

*1-[*cis*-3-(Hydroxymethyl)-2-methyloxiran-2-yl]dec-4-en-1-yn-3-ol* (**3g**). From 500 mg (4.5 mmol) of **1b** in 25 ml of THF, 5.9 ml (8.9 mmol) of BuLi (1.5M in hexane), and 563 mg (4.5 mmol) of (*E*)-oct-2-enal in 5 ml of THF; yield: 692 mg (65%) of **3g**. Yellow liquid. IR (neat): 3362*m*, 2929*s*, 2857*s*, 1653*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.81 (*m*, H−C(5)); 5.54, 5.54 (2*dd*, ^3J(H,H) = 15.3, 6.3, H−C(4)); 4.81, 4.80 (2*m*, H−C(3)); 3.82 (*d*, ^3J(H,H) = 5.5, CH_2OH); 3.65 (*s*, OH); 3.10 (*t*, ^3J(H,H) = 5.5, H−C(3′)); 2.02 (*q*, ^3J(H,H) = 7.2, CH_2(6)); 1.55 (*s*, Me−C(2′)); 1.38–1.35 (*m*, CH_2(7)); 1.29–1.25 (*m*, CH_2(8), CH_2(9)); 0.86 (*t*, ^3J(H,H) = 7.2, Me(10)). ^{13}C-NMR (100 MHz, $CDCl_3$): 134.4, 134.4 (2+, C(4)); 128.1 (+, C(5)); 84.4, 84.4 (2x, C(2)); 82.4, 82.4 (2x, C(1)); 63.9, 63.8 (2+, C(3′)); 62.5, 62.5 (2+, C(3)); 61.8 (−, CH_2OH); 52.0 (x, C(2′)); 31.9, 31.3, 28.4 (3−, C(6), C(7), C(8)); 26.8 (+, Me−C(2′)); 22.4 (−, C(9)); 14.0 (+, C(10)). FAB-MS: 375 (19, $[M+Na]^+$), 351 (16, $[M-H]^+$), 295 (45), 277 (32), 203 (46), 191 (95), 161 (63), 105 (36), 73 (100). HR-FAB-MS: calc. for $C_{14}H_{22}O_3$ (238.33): 261.1466 ($[M+Na]^+$); found: 261.1477.

*3-(*cis*-3-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)-1-phenylprop-2-yn-1-ol* (**3h**). From 500 mg (2.2 mmol) of **1a** in 25 ml of THF, 1.5 ml (2.2 mmol) of BuLi (1.5M in hexane), and 235 mg (2.2 mmol) of PhCHO in 5 ml of THF; yield: 418 mg (57%) of **3h**. Yellow liquid. IR (neat): 3403*m*, 3032*w*, 2929*s*, 2857*s*, 1472*m*, 1456*m*. ^{1}H-NMR (500 MHz, C_6D_6): 7.51 (*m*, 2 arom. H); 7.23 (*m*, 3 arom. H); 5.33 (*s*, H−C(1)); 4.04–3.95 (*m*, CH_2); 3.03 (ψt, H−C(3′)); 2.28 (*s*, OH); 1.40 (*s*, Me−C(2′)); 1.05 (*s*, *t*-Bu); 0.17, 0.17, 0.15, 0.15 (4*s*, Me_2Si). ^{13}C-NMR (125 MHz, C_6D_6): 141.1 (x, arom. C); 128.7, 128.4, 126.8, 126.8 (4+, arom. C); 85.2 (x, C(2) or C(3)); 84.0, 84.0 (2x, C(2) or C(3)); 64.6, 64.5, 64.5 (3+, C(1), C(3′)); 63.6 (−, CH_2); 51.7 (x, C(2′)); 26.1 (+, Me_3C); 23.1 (+, Me−C(2′)); 18.4 (x, Me_3C), −5.1, −5.2 (2+, Me_2Si). FAB-MS: 355 (6, $[M+Na]^+$), 331

(8, $[M-H]^+$), 315 (35), 285 (28), 245 (22), 141 (100). HR-FAB-MS: calc. for $C_{19}H_{28}O_3Si$ (332.51): 331.1729 ($[M-H]^+$); found: 331.1704.

*1-(4-Bromophenyl)-3-(*cis*-3-{[(*tert*-butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)prop-2-yn-1-ol* (**3j**). From 500 mg (2.2 mmol) of **1a** in 25 ml of Et_2O, 1.5 ml (2.2 mmol) of BuLi (1.5M in hexane), and 409 mg (2.2 mmol) of 4-bromobenzaldehyde in 5 ml of Et_2O; yield: 754 mg (83%) of **3j**. Yellow liquid. IR (neat): 3402*s*, 2930*s*, 2857*s*, 1486*s*, 1472*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.74 (*d*, ^3J(H,H) = 8.3, H–C(3), H–C(5) of 4-BrC_6H_4); 7.35 (*d*, ^3J(H,H) = 8.3, H–C(2), H–C(6) of 4-BrC_6H_4); 5.40 (*s*, H–C(1)); 3.84, 3.83 (2*dd*, ^2J(H,H) = 11.8, ^3J(H,H) = 5.0, 1 H, CH_2); 3.74 (*dd*, ^2J(H,H) = 11.8, H–C(1), ^3J(H,H) = 5.2, 1 H, CH_2); 3.04 (ψt, H–C(3′)); 2.83 (*s*, OH); 1.56 (*s*, Me–C(2′)); 0.88 (*s*, *t*-Bu); 0.05, 0.04 (2*s*, Me_2Si). ^{13}C-NMR (100 MHz, $CDCl_3$): 139.1 (x, arom. C(1)); 131.7, 131.4 (2+, arom. C(3), C(5)); 128.2, 128.1, 127.6 (3+, arom. C(2), C(6)); 122.4 (x, arom. C(4)); 84.0, 83.9 (2x, C(2), C(3)); 64.5, 64.5, 63.6, 63.6 (4+, C(1), C(3′)); 63.0 (–, CH_2); 51.7 (x, C(2′)); 25.8 (+, *Me*$_3$C); 23.0 (+, Me–C(2′)); 18.2 (x, Me$_3$*C*); –5.3, –5.3 (2+, Me_2Si). FAB-MS: 411/409 (2, $[M-H]^+$), 355/353 (8), 325/323 (6), 251/249 (7), 221/219 (9), 185/183 (14), 136 (13), 73 (100). HR-FAB-MS: calc. for $C_{19}H_{27}BrO_3Si$ (411.41): 411.0814 ($[M-H]^+$); found: 411.0815.

*2-[2-(*cis*-3-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)ethynyl]-7-oxabicyclo[4.1.0]-heptan-2-ol* (**3k**). From 500 mg (2.2 mmol) of **1a** in 25 ml of THF, 1.3 ml (2.2 mmol) of BuLi (1.7M in hexane), and 248 mg (2.2 mmol) of 2,3-epoxycyclohexanone in 5 ml of THF; yield: 578 mg (77%) of **3k**. Yellow oil. IR (neat): 3415*s*, 2933*s*, 2858*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.89–3.85 (*m*, 1 H, CH_2O); 3.77–3.73 (*m*, 1 H, CH_2O); 3.32–3.26 (*m*, H–C(1), H–C(6)); 3.02 (*m*, H–C(3″)); 2.78, 2.76 (2*s*, OH); 1.85–1.80 (*m*, CH_2(3)); 1.70–1.63 (*m*, CH_2(4)); 1.54 (*s*, Me–C(2′)); 1.52–1.48 (*m*, CH_2(5)); 0.88 (*s*, *t*-Bu); 0.07, 0.06 (2*s*, Me_2Si). ^{13}C-NMR (100 MHz, $CDCl_3$): 84.9, 84.8 (2x, C(2′)); 82.8 (x, C(1′)); 67.4 (x, C(2)); 64.4, 64.3 (2+, C(3″)); 63.0 (–, CH_2O); 58.0 (+, C(1)); 55.5 (+, C(6)); 51.6 (x, C(2″)); 34.0, 33.9 (2–, C(3)); 25.8 (+, *Me*$_3$C); 23.1 (+, Me–C(2″)); 22.1 (–, C(5)); 18.3 (–, C(4)); 18.3 (x, Me$_3$*C*); –5.2, –5.3 (2+, Me_2Si). FAB-MS: 361 (15, $[M+Na]^+$), 337 (3, $[M-H]^+$), 321 (20), 291 (10), 281 (6), 177 (12), 147 (16), 115 (13), 90 (45), 73 (100).

1-[2-(7-Oxabicyclo[4.1.0]hept-1-yl)ethynyl]cyclohexan-1-ol (**5**). From 296 mg (2.4 mmol) of **4** in 25 ml of THF, 1.6 ml (2.4 mmol) of BuLi (1.5M in hexane), and 238 mg (2.4 mmol) of cyclohexanone in 5 ml of THF; yield: 429 mg (81%) of **5**. Yellow liquid. IR (neat): 3403*s*, 2935*s*, 2858*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): 3.30 (ψt, H–C(6″)); 2.19 (*s*, OH); 2.15–2.10 (*m*, 1 H, H–C(2″)/H–C(5″)); 2.00–1.94 (*m*, 1 H, H–C(2″)/H–C(5″)); 1.90–1.86 (*m*, 4 H, H–C(2″), H–C(5″), H–C(2), H–C(6)); 1.67–1.64 (*m*, H–C(2), H–C(6)); 1.54–1.48 (*m*, CH_2(3), CH_2(4), CH_2(5)); 1.47–1.29 (*m*, 2 H, H–C(3″)/H–C(4″)); 1.23–1.20 (*m*, 2 H, H–C(3″)/H–C(4″)). ^{13}C-NMR (125 MHz, $CDCl_3$): 85.7, 84.6 (2x, C(1′), C(2′)); 68.5 (x, C(1)); 60.0 (+, C(6″)); 50.2 (x, C(1″)); 39.7 (–, C(2), C(6)); 29.8 (–, C(2″)/C(5″)); 25.1, 24.1 (2–, C(3), C(4), C(5)); 23.2, 19.4, 18.8 (3–, C(2″)/C(5″), C(3″), C(4″)). FAB-MS: 203 (100, $[M-OH]^+$).

4-(7-Oxabicyclo[4.1.0]hept-1-yl)but-3-yn-2-ol (**7a**). From 670 mg (5.5 mmol) of **4** in 25 ml of THF, 3.7 ml (5.5 mmol) of BuLi (1.5M in hexane), and 242 mg (5.5 mmol) of MeCHO in 5 ml of THF; yield: 555 mg (61%) of **7a**. Yellow liquid. IR (neat): 3403*s*, 2983*s*, 2940*s*, 2864*s*. ^{1}H-NMR (500 MHz, $CDCl_3$): 4.50 (*q*, ^3J(H, H) = 6.7, H–C(2)); 3.30 (*s*, H–C(6′)); 2.52 (*s*, OH); 2.12–2.07 (*m*, 1 H, H–C(2′)/H–C(5′)); 1.98–1.86 (*m*, 3 H, H–C(2′)/H–C(5′)); 1.41–1.20 (*m*, CH_2(3″), CH_2(4″)); 1.40 (*d*, ^3J(H,H) = 6.7, Me(1)). ^{13}C-NMR (100 MHz, $CDCl_3$): 84.1, 84.0 (2x, C(3), C(4)); 60.0 (+, C(6′)); 58.1 (+, C(2)); 50.2 (x, C(1′)); 29.5 (–, C(2′)/C(5′)); 24.0 (+, C(1)); 24.0, 19.3, 18.7 (3–, C(2′)/C(5′), C(3′), C(4′)). FAB-MS: 166 (27, M^+), 149 (100). HR-FAB-MS: calc. for $C_{10}H_{14}O_2$ (166.22): 166.0994 (M^+); found: 166.0975.

1,1,1-Trifluoro-2-methyl-4-(7-oxabicyclo[4.1.0]hept-1-yl)but-3-yn-2-ol (**7b**). From 305 mg (2.5 mmol) of **4** in 25 ml of THF, 1.7 ml (2.5 mmol) of BuLi (1.5M in hexane), and 280 mg (2.5 mmol) of 1,1,1-trifluoroacetone in 5 ml of THF; yield: 335 mg (57%) of **7b**. Yellow liquid. IR (neat): 3404*s*, 2935*s*, 2858*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.39 (*s*, OH); 3.35 (*t*, ^3J(H,H) = 2.0, H–C(2′)); 2.16–2.09 (*m*, 1 H, H–C(2′)/H–C(5′)); 2.01–1.89 (*m*, 3 H, H–C(2′)/H–C(5′)); 1.60 (*q*, ^4J(H,F) = 2.8, Me); 1.41–1.20 (*m*, CH_2(3′), CH_2(4′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 123.8 (x*q*, ^1J(C,F) = 285, CF_3); 86.5 (x, C(4)); 78.0 (x, C(3)); 68.4 (x*q*, ^2J(C,F) = 33, C(2)); 60.0 (+, C(6′)); 49.9 (x, C(1′)); 29.1 (–, C(2′)/C(5′)); 23.9, 19.2, 18.6 (3–, C(2′)/C(5′), C(3′), C(4′)); 22.9 (+, C(1)). FAB-MS: 234 (80, M^+), 217 (100). HR-FAB-MS: calc. for $C_{11}H_{13}F_3O_2$ (234.22): 234.0867 (M^+); found: 234.0868.

*3-(*cis*-3-{[(*tert*-Butyl)dimethylsilyloxy]methyl}-2-methyloxiran-2-yl)-1-(2,6,6-trimethylcyclohex-1-enyl)-prop-2-yn-1-ol* (**9**). From 500 mg (2.2 mmol) of **1a** in 25 ml of THF, 1.5 ml (2.2 mmol) of BuLi (1.5M in hexane), and 336 mg (2.2 mmol) of β-cyclocitral (**8**) in 5 ml of THF; yield: 569 mg (68%) of **9**. Yellow liquid. IR (neat): 3439*m*, 2955*s*, 2930*s*, 2859*s*. ^{1}H-NMR (400 MHz, C_6D_6): 4.98, 4.97 (2*s*, H–C(1)); 3.95 (*dd*, ^2J(H,H) = 11.5, ^3J(H,H) = 4.5, 1 H, CH_2O); 3.91, 3.90 (2*dd*, ^2J(H,H) = 11.5, ^3J(H,H) = 5.5, 1 H, CH_2O); 2.94 (ψt, H–C(3′));

1.98 (*s*, Me–C(2′)); 1.84–1.79 (*m*, CH_2(3″)); 1.53 (*s*, OH), 1.47–1.40 (*m*, CH_2(4″)); 1.38–1.31 (*m*, CH_2(5″)); 1.34, 1.34 (2*s*, Me–C(4″)); 1.03, 1.01 (2*s*, 2 Me–C(6″)); 0.98 (*s*, *t*-Bu); 0.13, 0.12 (2*s*, Me_2Si). ^{13}C-NMR (100 MHz, C_6D_6): 138.2 (x, C(1″)); 133.9 (x, C(2″)); 86.8, 86.7 (2x, C(3)); 81.5 (x, C(2)); 64.7, 64.6 (2+, C(3′)); 63.9, 63.5 (2−, CH_2O); 59.7 (+, C(1)); 51.7 (x, C(2′)); 39.8 (−, C(3′)); 34.8 (x, C(6″)); 33.7 (−, C(3″)); 27.9 (+, Me–C(6″)); 26.1 (+, Me_3C); 23.3 (+, Me–C(2′)); 23.0 (+, Me–C(2″)); 18.9 (−, C(4″)); 18.5 (x, Me_3C); −5.1, 5.2 (2+, Me_2Si). FAB-MS: 377 (2, $[M-H]^+$), 361 (10), 287 (6), 229 (7), 187 (15), 151 (12), 123 (22), 73 (100). HR-FAB-MS: calc. for $C_{22}H_{38}O_3Si$ (378.63): 378.2590 (M^+); found: 378.2604.

*1-(*cis*-3-[[(*tert*-Butyl)dimethylsilyloxy]methyl]-2-methyloxiran-2-yl)-4-methyl-6-(2,6,6-trimethylcyclohex-1-enyl)hex-4-en-1-yn-3-ol* (**11**). From 500 mg (2.2 mmol) of **1a** in 25 ml of THF, 1.5 ml (2.2 mmol) of BuLi (1.5M in hexane), and 456 mg (2.2 mmol) of β-C_{14}-aldehyde **10** [12] in 5 ml of THF; yield: 928 mg (97%) of **11**. Yellow liquid. IR (neat): 3420*m*, 2955*s*, 2928*s*, 2859*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.39 (*t*, ^3J(H,H) = 6.5, H–C(5)); 4.73 (*s*, H–C(3)); 3.87 (2*dd*, ^2J(H,H) = 11.8, ^3J(H,H) = 4.5, 1 H, CH_2O); 3.75 (*dd*, ^2J(H,H) = 11.8, ^3J(H,H) = 5.3, 1 H, CH_2O); 3.01 (*t*, ^3J(H,H) = 5.0, H–C(3′)); 2.72 (*d*, ^3J(H,H) = 6.5, CH_2(6)); 1.97 (*s*, OH); 1.90 (*t*, ^3J(H,H) = 6.2, CH_2(3″)); 1.77, 1.77 (2*s*, Me–C(2″)); 1.55–1.52 (*m*, CH_2(4″)); 1.54 (*s*, Me–C(2′)); 1.51 (*s*, Me–C(4)); 1.42–1.39 (*m*, CH_2(5″)); 0.95, 0.95 (2*s*, 2 Me–C(6″)); 0.90 (*s*, *t*-Bu); 0.08, 0.08 (2*s*, Me_2Si). ^{13}C-NMR (100 MHz, $CDCl_3$): 135.7 (x, C(1″)); 132.0 (x, C(2″)); 129.7 (+, C(5)); 128.3 (x, C(4)); 84.2, 84.1 (2x, C(1)); 82.7, 82.7 (2x, C(2)); 68.1 (+, C(3)); 64.5, 64.5 (2+, C(3′)); 63.1 (−, CH_2O); 51.7 (x, C(2′)); 39.6 (−, C(5″)); 34.8 (x, C(6″)); 32.8 (−, C(3″)); 28.2 (+, *Me*–C(6″)); 27.0 (−, C(6)); 25.8 (+, Me_3C); 23.2 (+, Me–C(2′)); 19.7 (+, Me–C(2″)); 19.4 (−, C(4″)); 18.2 (x, Me_3C); 12.0 (+, Me–C(4)); −5.2, −5.3 (2+, Me_2Si). FAB-MS: 455 (3, $[M+Na]^+$), 431 (2, $[M-H]^+$), 415 (8), 283 (6), 241 (12), 137 (40), 73 (100). HR-FAB-MS: calc. for $C_{26}H_{44}O_3Si$ (432.72): 455.2957 ($[M+Na]^+$); found: 455.2975.

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