Preparation of C-4 Alkylated Dideoxyribosides: Potential Precursors to a Novel Series of Nucleosides

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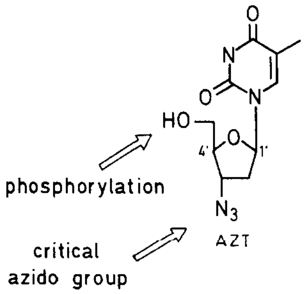
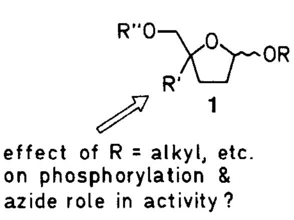
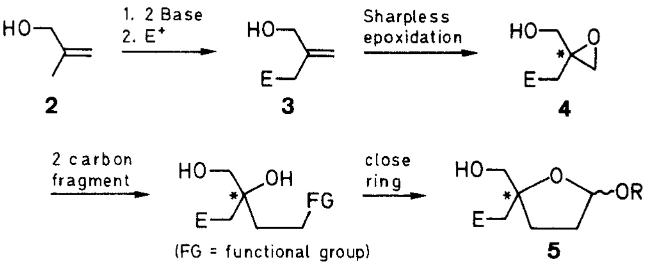
Methallyl alcohol can be converted in five simple operations (alkylation, epoxidation, alkynyl-coupling, hydroboration/oxidation, cyclization) to C-5 protected, chiral, non-racemic dideoxyribosides containing an alkyl appendage at the C-4 site.

Since the discovery of *anti* human immunodeficiency viral (HIV) activity associated with 3′-azido-3′-deoxythymidine (AZT) for the treatment of AIDS,[1] a number of nucleosides have been found to possess similar levels of potency, including, as examples, 2′,3′-dideoxycytidine,[2] ribavirin,[3] 3′-azido-2′,3′-dideoxyuridine,[4] 2′,3′-dideoxyinosine,[5] 3′-deoxy-2′,3′-didehydrothymidine,[6] 2′,3′-dideoxyadenosine,[7] and 1-(2′,3′-dideoxy-β-D-glycero-pent-2-eno-furanosyl)thymine.[8] In light of the importance of the azido moiety at C-3′ and the requirement for phosphorylation at C-5′ in AZT,[9] it seems curious that there are no examples of C-4′ alkylated (di)deoxynucleosides of defined absolute stereochemistry (cf., **1**).[10] This missing link among so many known analogs would seem to be an essential component of any emerging picture relating structure and activity, given the obvious proximity of such a residue to both the C-3′ and C-5′ positions. The explanation behind the lack of C-4′ alkylated cases may, perhaps, derive from limited access to this novel class of (di)deoxyriboses. We now describe a very straightforward route to chiral, non-racemic C-4 alkylated riboses which relies on readily available materials and has potential for large-scale production of intermediates suitable for eventual bioassay.





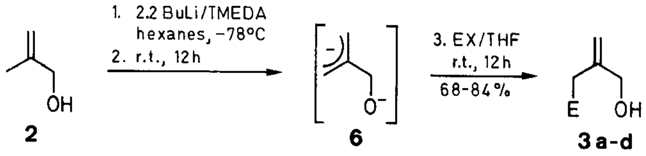
The plan for arriving at riboses of general structure **5**, illustrated in Scheme 1, commenced with methallyl alcohol **2**, which can be *C,O*-dimetalated (cf. **6**, below) and quenched at the carbanionic center with various electrophiles giving **3**.[11] Catalytic Sharpless epoxidation was anticipated to introduce asymmetry in **4** at what is to become the critical C-4 center.[12] Attachment of a two-carbon piece followed by the appropriate functional group manipulation/cyclization was envisioned to provide a four-step route to the targeted riboses **5**.



Scheme 1

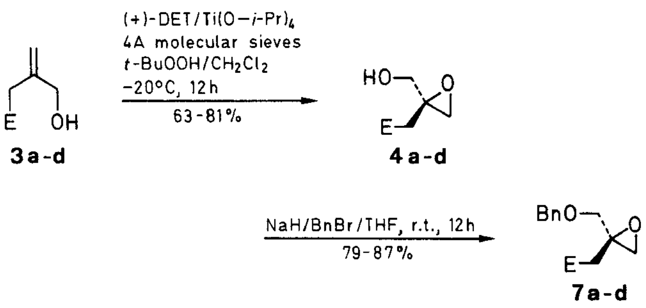
In practice, treatment of alcohol **2** with excess *n*-BuLi overnight followed by reaction of the intermediate dianion **6** with various alkylating agents afforded moderate to good (unoptimized) yields of products **3** (Scheme 2).[11] Obviously the case of methallyl alcohol itself represents, ultimately, one example of an alkylated ribose, **5** (E = H).

Epoxidation of allylic alcohols **3** proceeded smoothly,[12] and prior to the organometallic-based opening of **4**, it was decided to protect the alcohol as its benzyl ether **7** (Scheme 3). Use of silyl ethers derived from $Me_2(t\text{-}Bu)SiCl$ or $Me_2(thexyl)SiCl$ were both unsatisfactory, as the former was not compatible with subsequent steps in the series, while the latter derivative reacted extremely sluggishly with an acetylenic nucleophile (vide infra).



EX	3	R	Yield (%)
n-$C_7H_{15}I$	a	n-C_7H_{15}	68
$PhCH_2Br$	b	$PhCH_2$	84
t-$BuPh_2SiOCH_2CH_2I$	c	t-$BuPh_2SiOCH_2CH_2$	69

Scheme 2



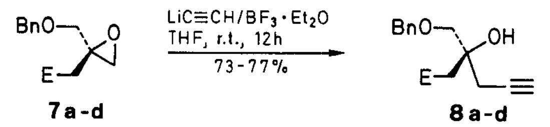
3,4,7	E	4		7
		Yield (%)	ee (%)	Yield (%)
a	n-C_7H_{15}	81	96[a]	82
b	$PhCH_2$	77	87[a]	87
c	t-$BuPh_2SiOCH_2CH_2$	81	98[a]	79
d[b]	H	63	91[c]	84

[a] Determined by NMR analyses on the corresponding Mosher ester.

[b] Compound **3d** ≡ **2** (methylallyl alcohol); cumene hydroperoxide was used in this case.

[c] Determined according to reference 17.

Scheme 3



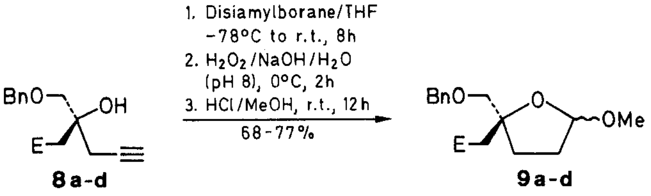
7,8	E	Yield (%) of 8	Recovered 7 (%)
a	n-C_7H_{15}	77	11
b	$PhCH_2$	73	17
c	t-$BuPh_2SiOCH_2CH_2$	73	21
d	H	75	17

Scheme 4

Opening of epoxides **7** with vinyl-, allyl- or alkynyllithium-based cuprate reagents did not proceed to any significant extent. Although the regiochemistry of attack must take place on **7** at its neopentyl-like center, such displacements, especially with higher order cuprates,[13] normally occur without incident. Rather than pursue this line of investigation further, we opted to rely on the Yamaguchi protocol,[14] involving lithiated acetylene in the presence of $BF_3 \cdot Et_2O$. These couplings took place cleanly to provide homopropargylic alcohols **8**, although it was noted that starting epoxides were never fully consumed even under the influence of *pseudo* first-order conditions in organolithium/Lewis acid.

Conversion of acetylenic alcohol **8** to riboses **9** could be effected in a one-pot operation by initial hydroboration/oxidation using disiamylborane,[15] followed by removal of solvent in vacuo and treatment of the remaining material with methanolic HCl at ambient temperatures. The resulting anomeric mix of desired methyl ribosides was isolated by column chromatography in good yields as colorless oils, thereby completing the overall series of transformations (Scheme 5).

In summary, a short sequence has been developed for arriving at C-4 alkylated dideoxyriboses, a new class of nucleoside precursors, in chiral, non-racemic form.[16] Once eventually coupled with various purine/pyrimidine bases, the resulting unprecedented nucleosides should add valuable information regarding structure–activity relationships among antiviral agents of this class. Opportunities now present themselves for studying the impact of a C-4′ residue, from both the steric and stereoelectronic viewpoint, on nucleosides derived from these and related systems, the results of which will be reported in due course.



8,9	E	Yield (%) of 9
a	n-C_7H_{15}	68
b	$PhCH_2$	77
c	t-$BuPh_2SiOCH_2CH_2$	75
d	H	74

Scheme 5

Alkylations of Methallyl Alcohol to give (3a–c): General Procedure:
To a flame dried three-necked flask equipped with an argon inlet, a magnetic stir bar, and a rubber septum, a solution of TMEDA 8.02 g, 69.0 mmol) in hexanes (12.0 mL) was added followed by n-BuLi (30.0 mL, 69.0 mmol) in hexanes, dropwise while maintaining the mixture below − 10 °C. A vigorous reaction occurred resulting in a thick white slurry, which was stirred at this temperature for 30 min. After cooling the reaction to − 78 °C, 2-methyl-2-propen-1-ol (2.38 g, 33.0 mmol) was added dropwise. The reaction was allowed to stir overnight (~ 12 h) while warming to r.t.. A yellowish-

Table. Characteristic Data of Compounds **3a–c**, **4a**, **4c**, **7a–d**, **8a–d** and **9a–d** Prepared[a]

Compound	IR ν (cm^{-1})	^{1}H NMR (CDCl$_3$) δ, J (Hz)	^{13}C NMR (CDCl$_3$) δ	Mass Spec (MS) m/z (rel. int.)	HRMS: found (calcd)
3a	3360, 3006, 2940, 2860, 1450, 1100	5.03 (s, 1H), 4.89 (s, 1H), 4.08 (s, 2H), 3.46 (t, J = 7.1, 2H), 2.07 (p, J = 7.7, 2H), 1.77 (br s, 1H), 1.45 (m, 2H), 1.29 (m, 8H), 0.86 (t, J = 7.1, 3H)	149.2, 108.2, 65.7, 32.9, 31.8, 29.4, 29.2, 27.7, 22.6, 15.2, 14.0	(EI): 170 (3), 95 (15), 81 (21), 57 (100)	for $C_{11}H_{22}O$ (M^+): 170.1680 (170.1681)
3b	3360, 3006, 2940, 2860, 1450, 1040	7.14–7.24 (m, 5H), 5.03 (s, 1H), 4.89 (s, 1H), 4.10 (s, 2H), 2.77 (q, J = 7.7, 2H), 2.37 (t, J = 7.2, 2H), 1.77 (br s, 1H)	148.3, 141.8, 128.3, 125.8, 109.7, 65.9, 60.4, 34.6, 34.2	(EI): 144 (6), 129 (16), 91 (100)	for $C_{11}H_{13}$ ($M^+ - OH$): 145.1043 (145.1046)
3c	3340, 3006, 2920, 2860, 1430, 1110	7.34–7.50 (m, 10H), 5.01 (s, 1H), 4.84 (s, 1H), 4.12 (s, 2H), 3.68 (t, J = 7.7, 1H), 3.56 (t, J = 7.7, 1H), 2.06 (t, J = 7.6, 2H), 1.77 (br s, 1H), 1.07 (s, 9H)	148.8, 135.8, 134.5, 129.4, 127.5, 109.1, 65.7, 65.6, 63.6, 32.1, 27.8, 26.9, 23.8, 19.2, 18.1, 14.0, 6.1	(CI): 369 (1), 351 (6), 311 (9), 291 (12), 199 (25), 95 (100)	
4a	3444, 2940, 2860, 1460, 1380, 1050	3.64–3.59 (dd, J = 12.1, 2H, AB), 2.62–2.83 (dd, J = 4.6, 2H, AB), 2.14 (m, 2H), 1.98 (br s, 1H), 1.76 (m, 2H), 1.46 (m, 2H), 1.29 (m, 8H), 0.83 (t, J = 7.1, 3H)	67.5, 62.7, 59.8, 49.8, 31.8, 31.7, 29.7, 26.2, 24.6, 22.6, 14.0	(CI): 187 (92), 157 (5), 149 (6), 145 (28), 43 (100)	for $C_{11}H_{23}O_2$ ($M^+ + 1$): 187.1674 (187.1676)
4c	3444, 3006, 2920, 2830, 1430, 1380, 1100	7.50–7.34 (m, 10H), 3.64 (t, J = 6.1, 2H), 3.76–3.57 (dd, J = 12.1, 1H, AB), 2.86–2.65 (dd, J = 4.6, 2H, AB), 1.80 (br s, 1H), 1.72 (m, 2H), 1.58 (m, 4H), 1.02 (s, 9H)	135.5, 133.9, 129.4, 127.5, 63.5, 62.7, 60.4, 59.6, 49.7, 31.9, 31.6, 26.9, 22.5, 20.9, 19.2, 14.2	(CI): 368 (6), 350 (7), 309 (16), 111 (97), 93 (100)	
7a	2940, 2860, 1755, 1400, 1100	7.34–7.23 (m, 5H), 4.53 (dd, J = 12.0, 2H, AB), 3.58 (d, J = 11.1, 1H), 3.44 (d, J = 11.1, 1H), 2.69 (d, J = 4.8, 1H), 2.62 (d, J = 4.8, 1H), 1.83–1.74 (m, 1H), 1.57–1.49 (m, 1H), 1.38–1.16 (m, 12H), 0.85 (br t, J = 6.5, 3H)	138.1, 128.3, 127.6, 73.0, 71.8, 58.6, 50.3, 31.9, 31.8, 29.7, 24.6, 24.3, 22.5, 14.1	(CI): 276 (1), 275 (8), 271 (3), 185 (5), 181 (16), 119 (4), 107 (14), 105 (3), 95 (4), 92 (8), 91 (100), 83 (4), 81 (4), 71 (5), 69 (3)	for $C_{18}H_{28}O_2$ (M^+): 276.2095 (276.2096)
7b	2940, 2860, 1755, 1400, 1100	7.37–7.16 (m, 10H), 4.56 (dd, J = 12.0, 2H, AB), 3.63 (d, J = 11.0, 1H), 3.50 (d, J = 11.0, 1H), 2.68 (m, 3H), 2.64 (d, J = 5.0, 1H), 2.18–2.12 (m, 1H), 1.95–1.89 (m, 1H)	141.4, 128.4, 127.7, 125.9, 73.3, 72.0, 58.2, 50.4, 33.7, 30.9	(CI): 233 (3), 181 (8), 180 (2), 159 (3), 147 (2), 145 (2), 144 (3), 143 (7), 131 (9), 130 (3), 129 (10), 119 (4), 117 (3), 107 (3), 105 (5), 104 (3), 92 (12), 91 (100)	for $C_{17}H_{18}O$ ($M^+ - CH_2O$): 238.1358 (238.1360)
7c	2940, 2860, 1710, 1430, 1100	7.66 (d, J = 7.0, 4H), 7.41–7.18 (m, 11H), 4.53 (dd, J = 12.0, 2H), 3.65 (t, J = 6.3, 2H), 3.57 (d, J = 11.0, 1H), 3.44 (d, J = 11.0, 1H), 2.67 (d, J = 4.9, 1H), 2.59 (d, J = 4.9, 1H), 1.83–1.77 (m, 1H), 1.60–1.53 (m, 3H), 1.47–1.41 (m, 2H), 1.04 (s, 9H)	137.9, 135.5, 133.9, 129.6, 128.1, 127.5, 73.2, 71.8, 63.6, 60.3, 58.4, 50.1, 34.6, 32.5, 31.6, 26.8, 25.2, 22.6, 20.9, 19.1, 14.1	(CI): 349 (4), 311 (8), 291 (6), 289 (14), 249 (19), 247 (6), 229 (13), 219 (12), 199 (9), 183 (5), 171 (11), 169 (6), 129 (6), 111 (14), 95 (12), 93 (13), 92 (8), 91 (100), 81 (5)	
7d	3020, 2940, 2860, 1725, 1450, 1100	7.44–7.34 (m, 5H), 4.56 (q, J = 12.0, 2H), 3.57–3.41 (dd, J = 12.1, 2H, AB), 2.73–2.62 (dd, J = 4.8, 2H, AB), 1.39 (s, 3H)	137.9, 128.2, 127.4, 73.2, 72.9, 55.8, 51.3, 46.1, 18.3	(EI): 148 (1), 118 (2), 91 (100)	for $C_{10}H_{12}O$ ($M^+ - CH_2O$): 148.0858 (148.0855)
8a	3460, 3300, 2940, 2860, 1450, 1100	7.37–7.28 (m, 5H), 4.57 (s, 2H), 3.51 (d, J = 9.0, 1H), 3.38 (d, J = 9.0, 1H), 2.46 (d, J = 2.6, 2H), 2.37 (s, 1H), 1.99 (dd, J = 2.6, 1H), 1.67–1.52 (m, 2H), 1.28 (br s, 12H), 0.86 (t, J = 6.9, 3H)	138.00, 128.38, 127.71, 127.59, 115.176, 80.68, 74.44, 73.47, 73.23, 70.56, 36.21, 32.29, 31.85, 30.12, 29.50, 29.24, 27.41, 23.00, 22.65, 22.56, 14.09	(CI): 277 (0.5), 243 (0.1), 107 (10), 91 (100)	for $C_{18}H_{29}O_2$ ($M^+ - C_2H$): 277.2168 (277.2170)
8b	3460, 3300, 2940, 2860, 1450, 1090	7.38–7.15 (m, 10H), 4.57 (s, 2H), 3.55 (d, J = 9.0, 1H), 3.43 (d, J = 9.0, 1H), 2.75–2.65 (m, 2H), 2.54 (d, J = 2.6, 2H), 2.48 (s, 1H), 2.02 (dd, J = 2.7, 1H), 2.00–1.86 (m, 2H)	142.23, 137.85, 128.35, 127.94, 127.88, 127.77, 127.67, 125.77, 80.35, 76.54, 74.29, 73.50, 73.15, 70.86, 38.15, 29.28, 27.47	(EI): 277 (10), 259 (22), 249 (13), 237 (8), 197 (11), 181 (8), 169 (20), 143 (6), 133 (11), 131 (6), 129 (19), 117 (8), 105 (23), 92 (9), 91 (100)	
8c	3440, 3300, 3006, 2920, 2880, 1450, 1375, 1100	7.66 (br d, J = 7.8, 4H), 7.47–7.11 (m, 11H), 4.56 (br s, 2H), 3.66 (td, J = 1.1, 0.4, 2H), 3.49 (dd, J = 9.2, 1.5, 1H), 3.37 (dd, J = 9.1, 1.4, 1H), 2.46 (dd, J = 2.1, 2H), 2.34 (d, J = 4.8, 1H), 1.98 (m, 1H), 1.65–1.53 (m, 4H), 1.47–1.37 (m, 2H), 1.04 (s, 9H)	137.97, 135.56, 134.09, 129.47, 128.38, 127.70, 127.61, 127.56, 80.566, 74.38, 73.50, 73.25, 70.61, 63.76, 36.00, 33.00, 27.44, 26.88, 19.38, 19.21	(CI): 501 (0.9), 235 (8), 227 (10), 215 (8), 199 (10), 139 (8), 137 (7), 123 (12), 119 (27), 117 (7), 115 (7), 92 (9), 91 (100), 79 (6), 77 (6), 75 (6)	for $C_{32}H_{41}O_3Si$ ($M^+ + 1$): 501.2771 (501.2825)

Table. (continued)

Compound	IR ν (cm^{-1})	^{1}H NMR (CDCl$_3$) δ, J (Hz)	^{13}C NMR (CDCl$_3$) δ	Mass Spec (MS) m/z (rel. int.)	HRMS: found (calcd)
8d	3440, 3300, 3060, 2920, 2880, 1450, 1375, 1100	7.50–7.34 (m, 5H), 4.56 (s, 2H), 3.47–3.35 (dd, $J = 9.2$, 2H, AB), 2.45 (d, $J = 2.6$, 2H), 2.00 (t, $J = 2.6$, 1H), 1.28 (s, 3H)	137.79, 128.25, 127.59, 127.46, 80.59, 75.61, 73.29, 71.48, 70.60, 46.09, 29.21, 23.33	(CI): 204 (0.5), 122 (4), 91 (100)	for $C_{13}H_{16}O_2$ (M$^+$): 204.1176 (204.1178)
9a	1739, 1454, 1366, 1210, 1097, 1041, 1009, 953	7.36–7.25 (m, 5H), 4.99 (d, $J = 4.8$, 1H), 4.57 (dd, $J = 12.5$) and 4.54 (br s, 2H), 3.44 (d, $J = 9.2$) and 3.38 (d, $J = 9.2$) with 3.32 (dd, $J = 8.1$, AB) and 3.30 (d, $J = 8.1$, AB, 2H), 3.33 (s) and 3.29 (s, 3H), 2.09–1.97 (m, 1H), 1.97–1.77 (m, 3H), 1.76–1.64 (m, 1H), 1.64–1.53 (m, 1H), 1.26 (br s, 10H), 0.88 (br t, $J = 6.7$)	138.51, 128.26, 128.22, 127.63, 127.51, 127.44, 105.54, 105.45, 86.54, 86.27, 78.59, 74.45, 73.42, 54.34, 54.27, 38.75, 36.98, 32.96, 32.69, 31.89, 30.95, 30.60, 30.22, 30.15, 29.60, 29.53, 29.26, 24.25, 23.90, 22.66, 14.10	(CI): 304 (9), 303 (43), 214 (14), 213 (100), 211 (13), 181 (6), 91 (23)	for $C_{20}H_{31}O_2$ (M$^+$ – CH$_2$O): 303.2328 (303.2324)
9b	1734, 1603, 1497, 1454, 1367, 1211, 1096, 1039, 956	7.37–7.22 (m, 10H), 5.04 (d, $J = 6.2$) and 5.02 (d, $J = 4.8$, 1H), 4.57 (dd, $J = 2.4$, AB) and 4.55 (br s, 2H), 3.52 (d, $J = 9.2$) and 3.43 (d, $J = 9.2$) with 3.39 (dd, $J = 9.4$, AB, 2H), 3.37 (s) and 3.31 (s, 3H), 2.75–2.55 (m, 2H), 2.09–1.77 (m, 4H)	142.65, 138.44, 128.31, 128.08, 127.65, 127.58, 127.50, 125.62, 105.62, 105.53, 99.09, 86.09, 85.76, 76.47, 74.23, 73.47, 54.47, 54.32, 40.47, 38.94, 32.85, 32.70, 31.06, 31.00, 30.71, 30.24, 29.68	(CI): 295 (0.2), 294 (0.3), 206 (6), 205 (41), 173 (10), 105 (12), 92 (9), 91 (100), 81 (5), 65 (10)	for $C_{20}H_{22}O_2$ (M$^+$ – CH$_2$O): 294.1609 (294.1610)
9c	1454, 1429, 1390, 1362, 1210, 1100, 1038, 1007, 954	7.70 (br d, $J = 1.5$, 4H), 7.43–7.20 (m, 11H), 4.98–4.96 (m, 1H), 4.55 (dd, $J = 10.5$) and 4.52 (br s, 2H), 3.65 (t, $J = 6.5$) and 3.66 (t, $J = 6.4$, 2H), 3.43 (d, $J = 9.3$) and 3.36 (d, $J = 9.3$) with 3.30 (d, $J = 9.4$, AB) and 3.27 (d, $J = 9.4$, 2H), 3.30 (s), and 3.27 (s, 3H), 2.06–1.94 (m, 1H), 1.94–1.76 (m, 3H), 1.75–1.51 (m, 4H), 1.44–1.22 (m, 3H), 1.04 (br s, 9H)	135.56, 134.12, 129.47, 128.25, 127.61, 127.56, 127.17, 105.56, 105.49, 76.65, 74.40, 73.44, 63.90, 54.35, 54.26, 38.53, 36.65, 33.06, 32.94, 30.50, 26.85, 20.62, 20.18, 19.21	(CI): 502 (0.2), 501 (0.3), 335 (7), 333 (18), 315 (9), 275 (15), 255 (15), 219 (7), 199 (9), 155 (7), 137 (26), 123 (7), 119 (31), 117 (7), 109 (8), 95 (7), 93 (18), 92 (9), 91 (100), 79 (14), 71 (10)	for $C_{32}H_{41}O_3Si$ (M$^+$ – CH$_3$O): 501.2797 (501.2794)
9d	2960, 2980, 2750, 1450, 1240	7.50–7.34 (m, 5H), 5.06 (t, $J = 4.4$, 1H), 4.56 (s, 2H), 3.66 (m, 2H), 3.35 (s, 3H), 1.97–1.82 (m, 4H), 1.20 (s, 3H)	138.4, 128.2, 127.4, 105.5, 76.5, 73.7, 54.3, 33.3, 32.2, 25.8, 24.3	(EI): 236 (0.5), 115 (100), 91 (92)	for $C_{13}H_{16}O_2$ (M$^+$ – CH$_2$O): 204.1136 (204.1137)

[a] Compounds **4b** and **4d** prepared and used in situ.

orange suspension resulted. The mixture was cooled to – 78 °C and the alkyl halide (28.0 mmol) in THF (12.0 mL) was added. The reaction was slowly allowed to warm to r. t. overnight (~ 12 h), then quenched with aq NH$_4$Cl. The organic layer was extracted with Et$_2$O, washed with brine, and concentrated in vacuo. Column chromatography on silica gel using hexanes/EtOAc gave the desired products as oils of $>$ 98 % purity as judged by capillary GC analyses.

Epoxides 4a–d: General Procedure:

To a slurry of molecular seives (4 A, freshly activated and crushed; 3.0 g) in CH$_2$Cl$_2$ (100 mL) was added diethyl L-tartrate (1.05 g, 5.1 mmol) followed by titanium Ti(O-*i*-Pr)$_4$ (1.108 g, 3.9 mmol) at – 20 °C. The mixture was further stirred for 10 min and then *t*-BuOOH (or cumene hydroperoxide for **3d**) in 2,2,4-trimethylpentane (34.0 mL, 102.0 mmol) was added followed by the alcohol 3 (39.3 mmol) over 30 min. The reaction was stirred overnight (~ 12 h) at – 20 °C, warmed to 0 °C and quenched with water (22 mL). After warming to r. t., stirring was continued for 45–60 min to enhance phase separation. Hydrolysis of tartrates was effected by adding 4.5 mL of a 30 % aq NaOH solution saturated with NaCl. After 30 min of vigorous stirring, the mixture was filtered through a pad of Celite. The organic phase was removed and combined with the extracts from two additional extractions of the aqueous phase using CH$_2$Cl$_2$. Drying (MgSO$_4$) followed by removal of solvent in vacuo and column chromatographic purification on silica gel using hexanes/EtOAc gave the desired products. Compounds **4b** and **4d** were not subjected to purification but used directly in the next step.

Benzyl Ethers 7a–d: General Procedure:

The alcohol 4 (10.0 mmol) was added to a slurry of NaH (0.48 g, 60 % in mineral oil, 12 mmol) in THF (25.0 mL) at 0 °C. The reaction was warmed to r. t. temperature and stirred for 1 h. Benzyl bromide (1.71 g, 10.0 mmol) was added and the reaction allowed to stir overnight (~ 12 h). Column chromatographic purification on silica gel using hexanes/EtOAc gave the desired products.

Homopropargylic Alcohols 8a–d: General Procedure:

Acetylene gas was passed successively through two dry ice-acetone traps and a CaCl$_2$ trap and then bubbled into THF (15.0 mL) at – 78 °C until a saturated solution was formed. *n*-BuLi (6.0 mL, 13.0 mmol) was then added slowly. After 30 min, BF$_3$ · Et$_2$O (1.84 g, 13.0 mmol) was added[18] to this solution followed by the epoxide (1.33 mmol) over 15 min. The reaction was stirred overnight (~ 12 h) at r.t. and then quenched with sat NaHCO$_3$ solution, extracted with Et$_2$O, washed with brine and concentrated in vacuo. Column chromatography on silica gel using hexanes/EtOAc gave the desired products along with varying percentages of the starting material.

Methylribosides 9a–d: General Procedure:

The alkyne (1.0 mmol) was added to a freshly prepared solution of disiamylborane (2.5 mL, 2.0 mmol) in THF at – 20 °C. The reaction was stirred overnight (8 h) at r.t., then cooled to – 20 °C and inversely added dropwise to a pH 8.0 phosphate buffer solution (2.0 mL, 2.0 mmol) containing 30 % H$_2$O$_2$ (0.75 mL) while maintaining the reaction at 0 °C. The mixture was stirred for 2 h at 0 °C, at which point Et_2O was introduced and the phases separated. All volatiles were then removed in vacuo from the organic portion and the residue treated with an excess of a 5% HCl in MeOH solution. Stirring overnight (12 h) at r.t. followed by column chromatography on silica gel using hexanes/EtOAc gave the desired products.

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