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Click Azide-Alkyne Cycloaddition for the Synthesis of D-(–)-1,4-Disubstituted Triazolo-Carbanucleosides

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Dedicated to Professor J. M. Robins on the occasion of his 70th birthday

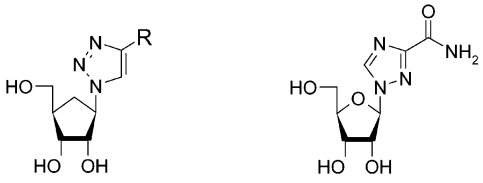
Keywords: Nucleosides / Carbanucleosides / Antiviral agents / Olefin metathesis / Huisgen cycloaddition / Ribavirin / Poxvirus

A revisited and improved synthesis of an optically active azido-carbanucleoside is reported. This azido precursor is used in the successful and versatile synthesis of enantiomerically pure D-(–)-1,4-disubstituted 1,2,3-triazolo-carbanucleosides via copper(I)-catalyzed and microwave-assisted Huisgen 1,3-dipolar cycloaddition.

Introduction

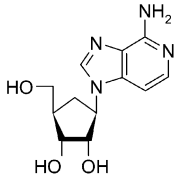
Natural D-nucleosides and their L-counterparts usually exhibit different antiviral activities and toxicities.[1] Regarding carbocyclic nucleosides,[2,3] enantiomers with a β-D-configuration exhibited significantly better antiviral effects than their L-analogues as they appear to be better candidate for enzyme targeting and enzyme activation (phosphorylation). In the search for less toxic and more potent inhibitors of the *S*-adenosylhomocysteine SAH *hydrolase*, an enzyme involved in methyl transfer reactions,[4] many D-carbocyclic analogues have emerged as effective inhibitors of vaccinia virus.[5,6] Therefore, the enantiospecific syntheses of carbanucleosides are crucial for further exploration of this class of compounds.[7] The synthetic approach deals principally with access to the enantiomerically pure highly oxygenated cyclopentane skeleton. However, the overall availability of optically active derivatives remains limited due to the lack of convenient methodologies for large-scale and stereospecific preparation of key intermediates. Thus, new synthetic intermediates for enantiomerically pure carbocyclic nucleosides are of significant interest.

We report here the revisited and improved large-scale synthesis of an optically active azido-carbanucleoside as a flexible building block for further synthetic elaboration[8] This azido-precursor was used in the successful and versatile synthesis of 1,4-disubstituted D-(–)-1,2,3-triazolo-carbanucleosides via copper(I)-catalyzed and microwave-assisted Huisgen 1,3-dipolar cycloaddition.[9] Previously, we and others had reported the synthesis of diverse carbanucleosides bearing a 1,2,3-triazole moiety, structurally related to ribavirin,[10,11] with interesting antiviral activities against HIV-1,[12] varicella-zoster virus,[13] or vaccinia virus.[14] In



D-2',3'-Dihydroxy-4'-hydroxymethyl-carbanucleosides

Ribavirin



Carbocyclic 3-deazaadenosine

Figure 1. Structure–activity relationship.

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order to examine structure-activity relationships and include former results, we opted to study a 2′,3′-dihydroxy-4′-hydroxymethyl-substituted carbocyclic moiety structurally related to the anti-pox agent ribavirin and to carbocyclic 3-deazaadenosine (Figure 1).

Results and Discussion

To the best of our knowledge, the only synthesis of the D-azido-carbanucleoside **8** was reported in 1988 by Tadano et al.[15] and it was used as precursor for the synthesis of carbocyclic nucleoside antibiotics. The synthetic approach used consisted in targeting the optically active carbocyclic skeleton using carbohydrates as starting materials. However, the enantioselectivity across numerous steps could not be controlled and tedious purifications by repeated column chromatography were necessary to separate the different epimers. Herein, we present an enantiomerically controlled synthesis of **8** in 16 steps (Scheme 1). To access the key optically active azide intermediate **8**, we selected the D-2-cyclopentenone **3** known as a versatile synthon for various D-carbocyclic nucleosides.[16] The first practical procedures to obtain **3** were reported by Jeong et al.[17] starting from inexpensive D-isoascorbic acid and then by Chu et al.[19] from D-ribose. The first method was problematic in large-scale preparation due to the extreme sensitivity of many intermediates as well as difficulties in controlling the stereoselective oxidation and reduction steps. Hence in spite of some variations brought to the approach, we chose to follow the second procedure[19] for the larger-scale synthesis of **3** taking advantage of the existing stereogenic centers of D-ribose (Scheme 1).

In both Jeong's and Chu's procedures, the ring-closing metathesis (RCM)[18] reaction of the diene **1** was performed using Grubbs' catalyst.[20] In our case, the RCM reaction to afford the D-cyclopentenol **2** was carried out using 1.5 mol-% of the Ru catalyst **9** developed by Nolan et al.[21] (Figure 2). Diene **1** was completely converted to **2** within 1 h of reaction at 25 °C. However, since the ring-closed cyclopentenol **2** is highly volatile, the desired D-2-cyclopentenone **3** was directly obtained in 79% overall yield from **1** by oxidation of the secondary alcohol under PCC oxidation conditions without isolation of cyclopentenol **2**.

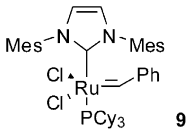

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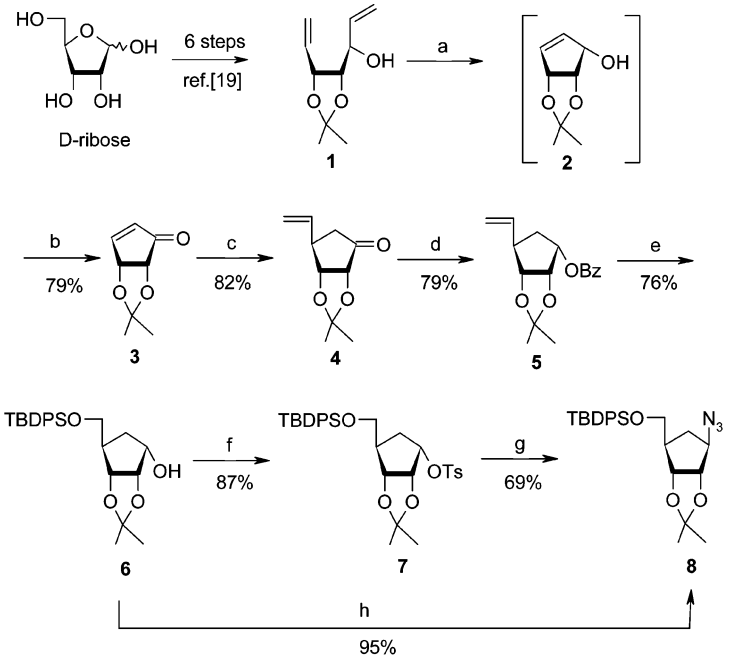
Figure 2. Ruthenium catalyst **9**.

Compound **3** was then easily converted to unstable *exo*-olefin **4** following Schneller's method (Scheme 1).[22] This synthetic approach consists in using a vinyl group as a mask for the hydroxymethyl group of carbocyclic nucleosides.



Scheme 1. Reagents and conditions: (a) [Ru] = **9** (1.5 mol-%), anhydrous CH_2Cl_2, 24 °C, 1 h; (b) pyridinium chlorochromate, CH_2Cl_2, room temp., 12 h; (c) vinylmagnesium bromide, CuBr·Me_2S, TMSCl, HMPA, THF, –78 °C, 3 h; (d) *(i)* $LiAlH_4$, THF, 0 °C to room temp., 2 h; *(ii)* BzCl, DMAP, *i*Pr_2NEt, CH_3CN, 0 °C to room temp., 2 h; (e) *(i)* OsO_4, $NaIO_4$, MeOH/acetone/H_2O, room temp., 30 min; *(ii)* $NaBH_4$, MeOH, –78 °C to room temp., 40 min; *(iii)* *tert*-butylchlorodiphenylsilane, imidazole, DMAP, CH_3CN, room temp., 1 h; *(iv)* NaOMe, MeOH, 0 °C to room temp., 15 h; (f) TsCl, *i*Pr_2NEt, DMAP, CH_3CN, 0 °C to room temp., 24 h; (g) NaN_3, 18-crown-6, DMF, 140 °C, 2 h; (h) DIAD, DPPA, PPh_3, THF, 0 °C to room temp., 7 h.

The incorporation of a vinyl group onto a cyclopentyl ring by 1,4-enone addition is known to be a high-yielding reaction.[23]

Copper(I) bromide–dimethyl sulfide complex induces the formation of an organocuprate via transmetallation with vinylmagnesium bromide.[24] This less reactive organocuprate leads to a regioselective 1,4-addition of the vinyl group to α,β-unsaturated ketones. On the other hand, addition of TMSCl-HMPA promotes the conjugate addition by trapping the magnesium enolate intermediate with TMSCl.[25] The role of HMPA may be to cleave the dimer frequently engendered by cuprates.[26] Thus, 1,4-addition of vinylmagnesium bromide to **3** cleanly afforded ketone **4** in 82% yield. Freshly opened vinylmagnesium bromide (*not* chloride!) is essential to successfully carry out this reaction. After stereoselective reduction of ketone **4** and subsequent benzoylation, benzoate **5** was afforded in moderate yield. The silyl ether **6** was obtained in good yield from **5** by i) oxidative glycol cleavage of *exo*-olefin using osmium tetroxide/sodium periodate, ii) sodium borohydride reduction of the resulting aldehyde, iii) protection of primary alcohol, and iv) debenzoylation sequence. Finally, we first tried to introduce an azide function by simple tosylation and S_N2 azidation. However, the overall yield of the desired **8** was only 60% for two steps. On the other hand, the application of Mitsunobu azidation[27] appeared to be more convenient for the synthesis of **8**. Alcohol **6** was treated with diisopropyl azodicarboxylate (DIAD) and diphenyl phosphoryl azide (DPPA) in the presence of PPh_3. Azide **8** was obtained in 95% yield as the single stereoisomer. The enantioselective addition of azide function with inversion of configuration was confirmed by NOESY spectroscopy (Figure 3). Unlike the correlation observed between $H^{1'}$ and $H^{2'}$ in the α-cyclopentanol **6**, only correlations between $H^{1'}$ and the two $H^{6'}$ were detected in the β-oriented azido carbocycle **8**.

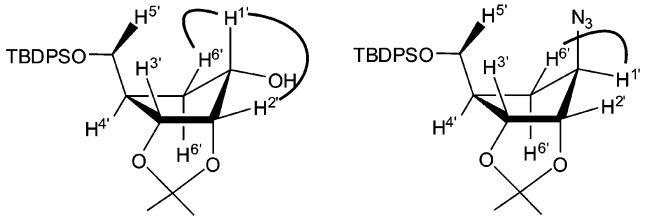
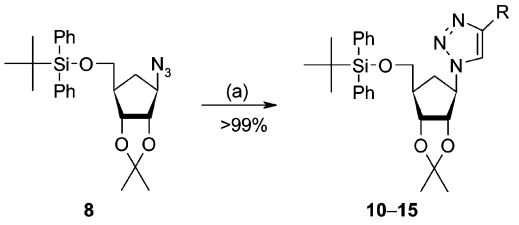


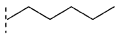
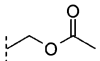
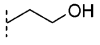
Figure 3. NOESY correlations of **6** and **8**.

Then, we performed the Huisgen 1,3-dipolar cycloaddition[9] between enantiomerically pure azidocarbocycle **8** and various terminal alkynes under the optimized reaction conditions previously reported for racemic series of 1,4-disubstituted (±)-1,2,3-triazolo-4′-hydroxymethyl-carbanucleosides.[28] A mixture copper Cu^0/copper sulfate $Cu^{II}SO_4$,[29] in situ comproportionated to form Cu^I, was used as a water soluble catalyst to obtain selectively the 1,4-disubstituted regioisomer.[30] This option is particularly attractive, as copper metal and copper sulfate are inexpensive. In a mixture water/*tert*-butyl alcohol under microwave irradiation,[31] $Cu^0/CuSO_4$-catalyzed reactions were performed with complete conversion of **8** into the desired 1,4-disubstituted triazoles **10**–**15** in extremely short reaction times (<15 min) and with no observable formation of by-products (Table 1). These results demonstrated that this previously developed method[28] was also applicable to different azido-carbanucleosidic substrates even if the latter contained protecting groups. According to the "click" chemistry prerogatives,[32] the reaction was stereoselective, versatile, and insensitive to oxygen and water. Even, the electron-deficient 1-heptyne reacted within a few minutes (Table 1, entry 3). Compounds **10**–**15** were isolated in high yield and purity by simple liquid-liquid extraction.

Table 1. Microwave assisted 1,3-dipolar cycloaddition of azido derivative **8**.



Reaction conditions: (a) azide **8** (0.1 mmol), alkyne (1.05 equiv.), Cu^0 (80 mol-%)/$CuSO_4$ (20 mol-%), *t*BuOH/H_2O (1:1) (1 mL), microwave (MW): $T = 125$ °C.

Entry	R	Triazole	Time [min]
1		**10**	5
2		**11**	1
3		**12**	15
4		**13**	1
5		**14**	1
6		**15**	1

The regioselectivity of the cycloaddition reaction under microwave irradiation was confirmed by using ^1H and ^{13}C long-range NMR experiments (HMBC). The selective formation of 1,4-disubstituted 1,2,3-triazoles was confirmed by a long-range correlation between the $H^{1'}$ of the sugar and the carbon bearing the 1*H*-triazole H^5 (Figure 4).

Finally, deprotection of the isopropylidene and the silyloxy groups afforded the final optically active compounds **16**–**21** in moderate to quantitative yields (Table 2). According to NOESY experiments, the β-configuration is conserved during the 1,3-dipolar cycloaddition. As for azide **8**, only correlations between $H^{1'}$ and the two $H^{6'}$ were detected in the β-oriented triazolo-carbanucleosides.

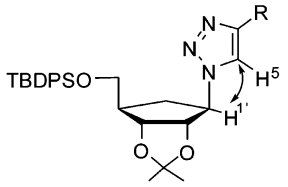
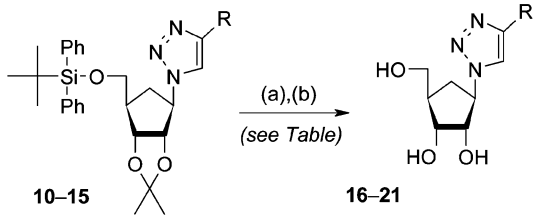
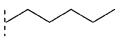


Figure 4. HMBC correlation for 1,4-disubstituted 1,2,3-triazoles **10**–**15**.

Table 2. Deprotection of 1,4-disubstituted 1,2,3-triazolo-carbanucleosides **10**–**15**.[a]



Reaction conditions: (a) triazole **10-15** (0.1 mmol), TFA 60% (2 mL), r.t., 16 h; (b) TBAF (1.05 equiv.), THF (2 mL), r.t., 1 h.

Entry	R	Triazole	Yield (%)
1		**16**	86
2		**17**	98
3		**18**	88
4		**19**	76
5		**20**	80
6		**21**	52

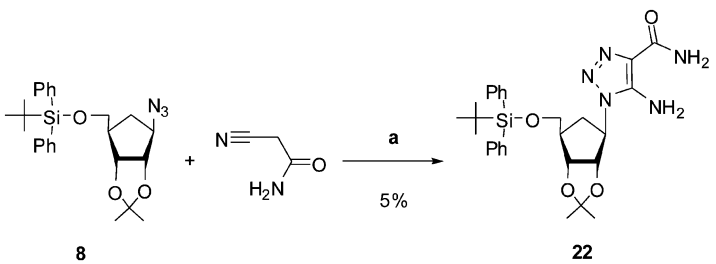
The synthesis of an optically pure 1,4,5-trisubstituted triazolo-carbanucleoside was also attempted. To achieve the synthesis of **22**, we applied our protocol previously optimized for 1,2,3-triazolo-3′-deoxy-carbanucleosides,[33] inspired by the reported 1,3-dipolar cycloaddition of azides and 2-cyanoacetamide.[34] In spite of reaction times of 48 h in refluxing ethanol, the starting material **8** was almost completely recovered (Scheme 2). Nevertheless, 5% of the expected compound **22** could be isolated and characterized.

Conclusions

In conclusion, we have explored the syntheses of D-configured 1,4-disubstituted 1,2,3-triazolo-carbanucleosides via optimized copper(I)-catalyzed microwave-assisted alkyne–azide Huisgen cycloaddition. The preparation of an enantiomerically pure cyclopentane azide derivative was achieved using an optically active enone intermediate, readily obtained by published procedure on a multi-gram scale. Final Mitsunobu azidation proved a superior method compared to traditional tosylation and S_N2 azidation sequence. The D-azide was then sucessfully reacted with different terminal alkynes to afford the corresponding 1,4-disubstituted D-(–)-1,2,3-triazolo-carbanucleosides, confirming the efficiency of the developed tool for different azido-carbanucleosidic substrates. Despite a carbocyclic 3-deazaadenosine-like carbocycle moiety, none of the synthesized compounds showed any cytotoxicity or significant antiviral activity on infected vaccinia virus cells. Comparing the evaluated compounds to known *anti*-pox nucleosides, the structure-activity relationship study suggests that 1,4-disubstituted 1,2,3-triazoles are not adequate bases for smallpox inhibition. In the domain of nucleoside chemistry, this original azido compound could be an important candidate and versatile precursor not only for cycloaddition with diverse dipolarophiles but also for various transformations involving azides.

Experimental Section

General: Commercially available chemicals were used as received. Microwave reactions were carried out in a Biotage Initiator with a maximum power of 300 W and temperatures were measured by IR sensor. Reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel plates (Kieselgel 60 F_{254}). Compounds were visualized by UV irradiation and/or spraying with ethanol solution 2.5% in phosphomolybdic acid, followed by charring at 150 °C. Column chromatography was performed on Silica Gel 60 M (0.040–0.063 mm). ^{1}H NMR spectra were recorded on 250 MHz or 400 MHz spectrometers, and ^{13}C NMR on 62.9 MHz or 125 MHz spectrometers at room temperature, using deuterated solvents as the internal standard. Chemical shifts are given in ppm



Scheme 2. Reagents and conditions: (a) EtONa, EtOH, reflux, N_2, 48 h.

and signals are reported as s (singlet), d (doublet), t (triplet), q (quartet), q_i (quintuplet) and m (multiplet). Assignments of NMR spectra follow standard nucleosides nomenclature: triazole bases are numbered from N-1 to C-5 and carbocycles are numbered from C-1′ to C-6′ with C-5′ for the 4-hydroxymethyl chain. Similar conventions apply for the corresponding hydrogen atoms.

(4*R*,5*R*)-(–)-4,5-Isopropylidenedioxy-2-cyclopenten-1-one (3): D-Ribose was converted into the diene **1** in six steps according to Chu's procedure.[19] A solution of diene **1** (7.0 g, 38 mmol) in anhydrous CH_2Cl_2 (200 mL) was added to [Ru] = catalyst **9** (0.48 g, 1.5 mol-%) under N_2 atmosphere. After 1 h of stirring at 24 °C, pyridinium chlorochromate (12.3 g, 57 mmol, 1.5 equiv.) was added to the resulting dark brown mixture. The reaction mixture was stirred at room temperature for 12 h and filtered through a silica gel pad (EtOAc). The filtrate was concentrated in vacuo, and the resulting residue was purified by column chromatography on silica gel (petroleum ether/EtOAc, 9:1), to give the unstable compound **3** (4.63 g, 79%) as a white crystalline solid. $[a]_D^{27}$ = –74.5 (*c* = 0.35, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (dd, *J* = 5.9 and 2.3 Hz, 1 H, H$^{3'}$), 6.21 (d, *J* = 5.9 Hz, 1 H, H$^{2'}$), 5.26 (dd, *J* = 5.5 and 2.3 Hz, 1 H, H$^{4'}$), 4.46 (d, *J* = 5.5 Hz, 1 H, H$^{5'}$), 1.42 (s, 6 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.9 (C, CO), 159.5 (CH, C$^{3'}$), 134.2 (CH, C$^{2'}$), 115.5 (C), 78.6 (CH, C$^{4'}$), 76.5 (CH, C$^{5'}$), 27.4 (CH_3), 26.1 (CH_3) ppm. MS (ESI): (M^+ + Na) *m*/*z* 177.0. CAS: 115509-13-2.

(1*S*,2*S*,3*R*,4*R*)-2,3-Isopropylidenedioxy-4-vinylcyclopentyl Benzoate (5): Compound **3** was converted into **4** according to Schneller's procedure.[22] A THF (40 mL) solution of **4** (4.46 g, 24.5 mmol) was added dropwise to a suspension of $LiAlH_4$ (1.67 g, 44.1 mmol, 1.8 equiv.) in THF (100 mL) at 0 °C under Ar. After 5 min of stirring, the reaction mixture was warmed to room temperature and stirred a further 3 h. H_2O (1 mL), 15% NaOH aqueous solution (1 mL) and H_2O (1 mL) were added in turn at 0 °C. The solution was filtered through a short celite pad and the filtrate was concentrated under reduced pressure. To a MeCN (40 mL) solution of the resulting residue, 4-(dimethylamino)pyridine (6.01 g, 49.0 mmol, 2 equiv.), *N*,*N*-diisopropylethylamine (8.54 mL, 49.0 mmol, 2 equiv.) and benzoyl chloride (5.6 mL, 49.0 mmol, 2 equiv.) were added at 0 °C under Ar. After 2 h of stirring at room temperature, the reaction mixture was diluted with EtOAc and then washed with aqueous saturated $NaHCO_3$ solution. The aqueous phases were extracted with EtOAc and the combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 5:1). **5** (5.54 g, 79% for 2 steps) was obtained as a colourless oil. $[a]_D^{27}$ = –66.6 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (d, *J* = 8.5 Hz, 2 H, H^{Ar}), 7.57 (t, *J* = 7.4 Hz, 1 H, H^{Ar}), 7.45 (t, *J* = 7.8 Hz, 2 H, H^{Ar}), 5.83 (ddd, *J* = 17.1, 10.5 and 6.6 Hz, 1 H, H$^{5'}$), 5.20–5.12 (m, 3 H, H_2C = +H$^{1'}$), 4.80 (t, *J* = 5.6 Hz, 1 H, H$^{2'}$), 4.54 (d, *J* = 5.6 Hz, 1 H, H$^{3'}$), 2.88 (br. s, 1 H, H$^{4'}$), 2.36–2.29 (m, 1 H, H$^{6'}$), 2.09–2.03 (m, 1 H, H$^{6'}$), 1.43 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3 (C, CO), 137.8 (CH, C$^{5'}$), 133.1 (CH, C^{Ar}), 130.3 (C, C^{Ar}), 129.9 (CH, 2C^{Ar}), 128.4 (CH, 2C^{Ar}), 115.8 (CH_2, H_2C=), 111.9 (C), 84.4 (CH, C$^{3'}$), 78.3 (CH, C$^{2'}$), 73.8 (CH, C$^{1'}$), 44.2 (CH, C$^{4'}$), 32.5 (CH_2, C$^{6'}$), 26.3 (CH_3), 24.7 (CH_3) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{17}H_{20}NaO_4$ (M^+ + Na) 311.1259, found 311.1259. IR (neat): $\tilde{\nu}$ = 1710 (C=O), 1637 (C=C), 1491, 1453, 1372 (C=C aromatic), 1268–1047 (C–O) cm^{-1}.

(1*S*,2*S*,3*R*,4*R*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxycyclopentan-1-ol (6): To a solution of **5** (4.51 g, 15.6 mmol) and $NaIO_4$ (6.69 g, 31.3 mmol, 2 equiv.) in MeOH/acetone/H_2O (1:1:1, 240 mL), a solution of OsO_4 (2.5 wt.-% in *t*BuOH) (1 mL) was added at room temperature. After 1.5 h of stirring, the reaction mixture was filtered through a celite pad and concentrated. The resulting residue was diluted with CH_2Cl_2 and then washed with brine. The aqueous phases were extracted with CH_2Cl_2 and the combined organic layers were dried with $MgSO_4$. The crude **A** aldehyde was obtained as an oil and directly used in the next step without further purification. To a MeOH (100 mL) solution of crude **A**, $NaBH_4$ (1.18 g, 31.3 mmol, 2 equiv.) was added at –78 °C. After 40 min of stirring at room temperature, AcOH (2 mL) and acetone (100 mL) were added and the resulting reaction mixture was concentrated. The reaction mixture was diluted with CH_2Cl_2 and then washed with an aqueous saturated $NaHCO_3$ solution. The aqueous phases were extracted with CH_2Cl_2 and the combined organic layers were dried with $MgSO_4$. This crude alcohol **B** was used in the next step without further purification. To the MeCN (50 mL) solution of crude alcohol **B**, 4-(dimethylamino)pyridine (2.11 g, 17.2 mmol, 1.1 equiv.), imidazole (1.38 g, 20.3 mmol, 1.3 equiv.) and *tert*-butylchlorodiphenylsilane (5.26 mL, 20.3 mmol, 1.3 equiv.) were added at room temperature under N_2. After 1 h of stirring, the reaction mixture was diluted with EtOAc and then washed with an aqueous saturated $NaHCO_3$ solution. The aqueous phases were extracted with EtOAc and the combined organic layers were dried with $MgSO_4$, filtered and concentrated to give the crude **C**. Freshly prepared 0.5 M NaOMe solution in MeOH (100 mL) was added to crude **C** at 0 °C and stirred for 16 h at room temperature. AcOH (8.6 mL) was added and the reaction mixture was concentrated. The resulting residue was diluted with CH_2Cl_2 and then washed with an aqueous saturated $NaHCO_3$ solution. The aqueous phases were extracted with CH_2Cl_2 and the combined organic layers were dried with $MgSO_4$. The oily residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 3:1). Compound **6** (5.01 g, 76% for 4 steps) was obtained as a colourless oil. $[a]_D^{27}$ = –47.7 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.61 (m, 4 H, H^{Ar}), 7.45–7.36 (m, 6 H, H^{Ar}), 4.50 (d, *J* = 5.8 Hz, 1 H, H$^{3'}$), 4.44 (t, *J* = 5.8 Hz, 1 H, H$^{2'}$), 4.25–4.18 (m, 1 H, H$^{1'}$), 3.58 (dd, *J* = 10.3 and 5.6 Hz, 1 H, H$^{5'}$), 3.51 (dd, *J* = 10.3 and 5.6 Hz, 1 H, H$^{5'}$), 2.41 (d, *J* = 8.3 Hz, 1 H, OH), 2.24–2.23 (m, 1 H, H$^{4'}$), 1.93–1.82 (m, 2 H, H$^{6'}$), 1.50 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.04 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8 (CH, 2C^{Ar}), 135.7 (CH, 2C^{Ar}), 133.3 (C, 2C^{Ar}), 129.9 (CH, 2C^{Ar}), 127.9 (CH, 4C^{Ar}), 111.3 (C), 82.9 (CH, C$^{3'}$), 79.7 (CH, C$^{2'}$), 71.9 (CH, C$^{1'}$), 65.3 (CH_2, C$^{5'}$), 44.1 (CH, C$^{4'}$), 35.5 (CH_2, C$^{6'}$), 27.0 (*t*Bu), 26.3 (CH_3), 24.4 (CH_3), 19.3 (C-Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{34}O_4NaSi$ (M^+ + Na) 449.2124, found 449.2121. IR (neat): $\tilde{\nu}$ = 3520 (OH), 1471, 1427, 1381 (C=C aromatic), 1209–1040 (C–O) cm^{-1}. CAS: 112543-76-7.

(1*S*,2*R*,3*R*,4*R*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxy-1-tosyloxycyclopentane (7): To a CH_3CN (15 mL) solution of **6** (0.5 g, 1.17 mmol), 4-dimethylaminopyridine (0.2 g, 1.76 mmol, 1.5 equiv.) and *N*,*N*-diisopropylethylamine (0.3 mL, 1.76 mmol, 1.5 equiv.) at 0 °C, *p*-toluenesulfonyl chloride (0.34 g, 1.76 mmol, 1.5 equiv.) was added. After 10 min of stirring, the reaction mixture was warmed to room temperature. After 24 h of stirring, the reaction mixture was diluted with CH_2Cl_2 and then washed with an aqueous saturated $NaHCO_3$ solution. The aqueous phases were extracted with CH_2Cl_2 and the combined organic layers were dried with $MgSO_4$. The oily residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 6:1). **7** (0.59 g, 87%) was obtained as a colourless oil. The compound was pure enough by TLC to be directly engaged into the next reaction.

(1*R*,2*S*,3*R*,4*R*)-1-Azido-4-[(*tert*-butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxycyclopentane (8). Procedure from 7: A DMF (4 mL) solution of **7** (0.22 g, 0.38 mmol), sodium azide (0.12 g, 1.9 mmol, 5 equiv.) and 18-crown-6 ether (0.12 g, 0.46 mmol, 1.2 equiv.) was heated for 3 h at 140 °C. The reaction mixture was diluted with EtOAc and then washed with brine. The aqueous phases were extracted with EtOAc and the combined organic layers were dried with $MgSO_4$. The oily residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 9:1). **8** (0.12 g, 69%) was obtained as a yellow oil. **Procedure from 6:** To a THF (80 mL) solution of **6** (2.0 g, 4.72 mmol) and PPh_3 (3.82 g, 14.16 mmol, 3 equiv.), a mixture of diisopropyl azodicarboxylate (2.8 mL, 14.16 mmol, 3 equiv.) and diphenylphosphoryl azide (3.07 mL, 14.16 mmol, 3 equiv.) in THF (20 mL) was added dropwise at 0 °C under Ar. After 7 h of stirring at room temperature, EtOH (30 mL) was added and stirred for 30 min. After evaporation of all volatiles, the oily residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 100:1 to 50:1). **8** (2.03 g, 95%) was obtained as yellow oil. $[a]_D^{26}$ = –19.0 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68–7.65 (m, 4 H, H^{Ar}), 7.46–7.37 (m, 6 H, H^{Ar}), 4.46 (dd, *J* = 6.2 and 2.5 Hz, 1 H, $H^{3'}$), 4.31 (dd, *J* = 6.2 and 3.5 Hz, 1 H, $H^{2'}$), 3.92 (td, *J* = 6.0 and 2.8 Hz, 1 H, $H^{1'}$), 3.69 (dd, *J* = 10.3 and 7.0 Hz, 1 H, $H^{5'}$), 3.63 (dd, *J* = 10.3 and 7.0 Hz, 1 H, $H^{5'}$), 2.37 (q_id, *J* = 7.0 and 2.5 Hz, 1 H, $H^{4'}$), 2.22 (dt, *J* = 13.8 and 7.0 Hz, 1 H, $H^{6'}$), 1.75 (dt, *J* = 13.8 and 5.7 Hz, 1 H, $H^{6'}$), 1.46 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 1.07 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8 (CH, $2C^{Ar}$), 135.7 (CH, $2C^{Ar}$), 133.6 (C, $2C^{Ar}$), 129.9 (CH, $2C^{Ar}$), 127.9 (CH, $4C^{Ar}$), 111.7 (C), 85.1 (CH, $C^{2'}$), 82.1 (CH, $C^{3'}$), 67.0 (CH, $C^{1'}$), 64.3 (CH_2, $C^{5'}$), 47.0 (CH, $C^{4'}$), 31.7 (CH_2, $C^{6'}$), 27.0 (*t*Bu + CH_3), 24.6 (CH_3), 19.4 (C Si) ppm. ^{29}Si NMR (79.5 MHz, $CDCl_3$): δ = –104.4 (br. s, Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{25}H_{33}N_3NaO_3Si$ (M^+ + Na) 474.2189, found 474.2207. IR (neat): $\tilde{\nu}$ = 2102 (N_3), 1472, 1427, 1382 (C=C aromatic), 1160–1043 (C–O) cm^{-1}. CAS: 112543-78-9.

General Procedures for the 1,3-Dipolar Cycloaddition Under Microwave Irradiation. Synthesis of (–)-10–15: A solution of azide **8** (50 mg, 0.1 mmol) in a 1:1 mixture of water and *t*BuOH (1 mL) was prepared in a glass vial equipped with a magnetic stirring bar. Then, copper powder (5.6 mg, 80 mol-%), a water solution 1 M of copper sulfate (22 μL, 20 mol-%) and the alkyne (1.05 equiv.) were added in turn. The vial was sealed with an aluminum/Teflon® crimp cap and the reaction mixture was then irradiated at 125 °C. Upon completion of the reaction, the vial was cooled to 50 °C by air jet cooling before being opened. The reaction mixture was then filtered through a plug of celite (EtOAc) and the filtrate was concentrated under reduced pressure. The oily residue was then dissolved in 20 mL of EtOAc and washed twice with a saturated $NaHCO_3$ solution (5 mL) and once with brine (5 mL). The aqueous phases were extracted twice with EtOAc (20 mL) and the combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure.

(1*R*,2*S*,3*R*,4*R*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxy-1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)cyclopentane (10): The title compound was prepared from phenylacetylene (13 μL) after 5 min of microwave irradiation. Compound **10** (61 mg, >99%) was obtained as a colourless oil. $[a]_D^{27}$ = –25.7 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 8.5 and 1.4 Hz, 2 H, H^{Ar}), 7.84 (s, 1 H, H^5), 7.65 (dd, *J* = 7.8 and 1.4 Hz, 4 H, $H^{Ar–Si}$), 7.46–7.31 (m, 9 H, $6H^{Ar–Si}$ + $3H^{Ar}$), 4.86–4.77 (m, 2 H, $H^{2'}$ + $H^{1'}$), 4.61 (dd, *J* = 6.9 and 4.0 Hz, 1 H, $H^{3'}$), 3.82–3.75 (m, 2 H, $H^{5'}$), 2.64–2.42 (m, 3 H, $H^{4'}$ + $H^{6'}$), 1.57 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 1.08 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.9 (C, C^4), 135.7 (CH, $4C^{Ar–Si}$), 133.5 (C, $2C^{Ar–Si}$), 130.8 (C, C^{Ar}), 129.9 (CH, $2C^{Ar–Si}$), 128.9 (CH, $2C^{Ar}$), 128.3 (CH, C^{Ar}), 127.9 (CH, $4C^{Ar–Si}$), 125.9 (CH, $2C^{Ar}$), 119.4 (CH, C^5), 113.6 (C), 85.1 (CH, $C^{2'}$), 81.2 (CH, $C^{3'}$), 66.5 (CH, $C^{1'}$), 64.3 (CH_2, $C^{5'}$), 45.9 (CH, $C^{4'}$), 33.7 (CH_2, $C^{6'}$), 27.6 (CH_3), 27.0 (*t*Bu), 25.1 (CH_3), 19.5 (C Si) ppm. ^{29}Si NMR (79.5 MHz, $CDCl_3$): δ =-103.9 (br. s, Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{33}H_{39}N_3NaO_3Si$ (M^+ + Na) 576.2658, found 576.2642.

(1*R*,2*S*,3*R*,4*R*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxy-1-[4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl]cyclopentane (11): The title compound was prepared from 2-ethynyl pyridine (12 μL) after 1 min of microwave irradiation. Compound **11** (61 mg, >99%) was obtained as a light brown foam. $[a]_D^{27}$ = –25.7 (*c* = 0.16, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.58 (br. s, 1 H, N-CH), 8.24 (s, 1 H, H^5), 8.18 (d, *J* = 7.6 Hz, 1 H, =C-CH=), 7.78 (t, *J* = 7.6 Hz, 1 H, =C-CH=C*H*), 7.64 (dd, *J* = 6.4 and 1.2 Hz, 4 H, $H^{Ar–Si}$), 7.44–7.36 (m, 6 H, $H^{Ar–Si}$), 7.23 (br. s, 1 H, N-CH=C*H*), 4.87–4.81 (m, 2 H, $H^{2'}$ + $H^{1'}$), 4.59 (dd, *J* = 6.4 and 4.0 Hz, 1 H, $H^{3'}$), 3.81–3.74 (m, 2 H, $H^{5'}$), 2.66–2.59 (m, 1 H, $H^{6'}$), 2.49–2.40 (m, 2 H, $H^{4'}$ + $H^{6'}$), 1.55 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.07 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.5 (C, =C), 149.5 (CH, N-CH), 148.5 (C, C^4), 137.0 (CH, =C-CH=*C*H), 135.7 (CH, $4C^{Ar–Si}$), 133.5 (C, $2C^{Ar–Si}$), 129.9 (CH, $2C^{Ar–Si}$), 127.9 (CH, $4C^{Ar–Si}$), 123.0 (CH, N-CH=*C*H), 121.8 (CH, C^5), 120.4 (CH, =C-*C*H=), 113.7 (C), 85.0 (CH, $C^{2'}$), 81.1 (CH, $C^{3'}$), 66.6 (CH, $C^{1'}$), 64.2 (CH_2, $C^{5'}$), 45.8 (CH, $C^{4'}$), 33.9 (CH_2, $C^{6'}$), 27.6 (CH_3), 27.0 (*t*Bu), 25.1 (CH_3), 19.4 (C-Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{32}H_{38}N_4NaO_3Si$ (M^+ + Na) 577.2635, found 577.2629.

(1*R*,2*S*,3*R*,4*R*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxy-1-(4-pentyl-1*H*-1,2,3-triazol-1-yl)cyclopentane (12): The title compound was prepared from 1-heptyne (15 μL) after 15 min of microwave irradiation. Compound **12** (60 mg, >99%) was obtained as a colourless oil. $[a]_D^{27}$ = –22.5 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (dd, *J* = 7.8 and 1.4 Hz, 4 H, $H^{Ar–Si}$), 7.45–7.35 (m, 6 H, $H^{Ar–Si}$), 7.33 (s, 1 H, H^5), 4.80–4.77 (m, 1 H, $H^{2'}$), 4.74–4.70 (m, 1 H, $H^{1'}$), 4.56 (dd, *J* = 6.8 and 4.0 Hz, 1 H, $H^{3'}$), 3.79–3.74 (m, 2 H, $H^{5'}$), 2.70 (t, *J* = 7.6 Hz, 2 H, =C-CH_2), 2.56–2.52 (m, 1 H, $H^{6'}$), 2.51–2.37 (m, 2 H, $H^{4'}$ + $H^{6'}$), 1.68–1.64 (m, 2 H, =C-CH_2-CH_2), 1.54 (s, 3 H, CH_3), 1.37–1.33 [m, 4 H, $(CH_2)_2$-CH_3], 1.29 (s, 3 H, CH_3), 1.06 (s, 9 H, *t*Bu), 0.89 [t, *J* = 7.2 Hz, 3 H, $(CH_2)_2$-CH_3] ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.6 (C, C^4), 135.7 (CH, $4C^{Ar–Si}$), 133.5 (C, $2C^{Ar–Si}$), 129.9 (CH, $2C^{Ar–Si}$), 127.9 (CH, $4C^{Ar–Si}$), 120.2 (CH, C^5), 113.5 (C), 85.1 (CH, $C^{2'}$), 81.2 (CH, $C^{3'}$), 66.2 (CH, $C^{1'}$), 64.3 (CH_2, $C^{5'}$), 45.8 (CH, $C^{4'}$), 33.9 (CH_2, $C^{6'}$), 31.6 (CH_2, *C*H_2-CH_2-CH_3), 29.3 (CH_2, =C-CH_2-*C*H_2), 27.6 (CH_3), 27.0 (*t*Bu), 25.8 (CH_2, =C-*C*H_2), 25.1 (CH_3), 22.5 (CH_2, *C*H_2-CH_3), 19.4 (C-Si), 14.1 (CH_2, CH_2-*C*H_3) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{32}H_{45}N_3NaO_3Si$ (M^+ + Na) 570.3128, found 570.3125.

(1*R*,2*S*,3*R*,4*R*)-1-[4-(Acetoxymethyl)-1*H*-1,2,3-triazol-1-yl]-4-[(*tert*-butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxycyclopentane (13): The title compound was prepared from propargyl acetate (12 μL) after 1 min of microwave irradiation. Compound **13** (60 mg, >99%) was obtained as a colourless oil. $[a]_D^{27}$ = –20.7 (*c* = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.63 (m, 5 H, H^5 + $H^{Ar–Si}$), 7.45–7.36 (m, 6 H, $H^{Ar–Si}$), 5.21 (s, 2 H, =C-CH_2), 4.8–4.70 (m, 2 H, $H^{2'}$ + $H^{1'}$), 4.57 (dd, *J* = 6.8 and 4.4 Hz, 1 H, $H^{3'}$), 3.80–3.73 (m, 2 H, $H^{5'}$), 2.57–2.52 (m, 1 H, $H^{6'}$), 2.48–2.35 (m, 2 H, $H^{4'}$ + $H^{6'}$), 2.08 (s, 3 H, CO-CH_3), 1.54 (s, 3 H, CH_3), 1.29 (s, 3 H, CH_3), 1.07 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0 (CO), 142.9 (C, C^4), 135.7 (CH, $4C^{Ar–Si}$), 133.4

(C, 2C$^{Ar–Si}$), 129.9 (CH, 2C$^{Ar–Si}$), 127.9 (CH, 4C$^{Ar–Si}$), 123.5 (CH, C^5), 113.7 (C), 85.0 (CH, C$^{2'}$), 81.1 (CH, C$^{3'}$), 66.6 (CH, C$^{1'}$), 64.3 (CH$_2$, C$^{5'}$), 57.7 (CH$_2$, =C-*C*H$_2$), 45.7 (CH, C$^{4'}$), 33.9 (CH$_2$, C$^{6'}$), 27.6 (CH$_3$), 27.0 (*t*Bu), 25.1 (CH$_3$), 21.0 (CH$_3$, CO-*C*H$_3$), 19.4 (C-Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{30}H_{39}N_3NaO_5Si$ (M^+ + Na) 572.2557, found 572.2554. IR (neat): $\tilde{\nu}$ = 1741 (C=O), 1471, 1427, 1381 (C=C aromatic), 1229 (C–O), 1111–1030 (C–O) cm^{-1}.

(1*R*,2*S*,3*R*,4*R*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[4-(2-hydroxyethyl)-1*H*-1,2,3-triazol-1-yl]-2,3-isopropylidenedioxycyclopentane (14): The title compound was prepared from 3-butyn-1-ol (9 μL) after 1 min of microwave irradiation. Compound **14** (57 mg, >99%) was obtained as a colourless oil. $[\alpha]_D^{27}$ = –13.3 (*c* = 0.17, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (dd, *J* = 8.0 and 1.2 Hz, 4 H, H$^{Ar–Si}$), 7.46 (s, 1 H, H^5), 7.44–7.36 (m, 6 H, H$^{Ar–Si}$), 4.80–4.69 (m, 2 H, H$^{2'}$ + H$^{1'}$), 4.57 (dd, *J* = 6.8 and 4.0 Hz, 1 H, H$^{3'}$), 3.95 (t, *J* = 5.4 Hz, 2 H, C*H*$_2$-OH), 3.80–3.73 (m, 2 H, H$^{5'}$), 2.95 (t, *J* = 5.4 Hz, 2 H, =C-C*H*$_2$), 2.63 (s, 1 H, OH), 2.57–2.52 (m, 1 H, H$^{6'}$), 2.48–2.35 (m, 2 H, H$^{4'}$ + H$^{6'}$), 1.54 (s, 3 H, CH$_3$), 1.29 (s, 3 H, CH$_3$), 1.07 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.7 (C, C^4), 135.7 (CH, 4C$^{Ar–Si}$), 133.4 (C, 2C$^{Ar–Si}$), 129.9 (CH, 2C$^{Ar–Si}$), 127.9 (CH, 4C$^{Ar–Si}$), 121.3 (CH, C^5), 113.6 (C), 85.0 (CH, C$^{2'}$), 81.1 (CH, C$^{3'}$), 66.4 (CH, C$^{1'}$), 64.3 (CH$_2$, C$^{5'}$), 61.8 (CH$_2$, CH$_2$-OH), 45.8 (CH, C$^{4'}$), 33.8 (CH$_2$, C$^{6'}$), 28.8 (CH$_2$, =C-*C*H$_2$), 27.6 (CH$_3$), 27.0 (*t*Bu), 25.1 (CH$_3$), 19.4 (C-Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{39}N_3NaO_4Si$ (M^+ + Na) 544.2608, found 544.2614. IR (neat): $\tilde{\nu}$ = 3390 (OH), 1471, 1427, 1380 (C=C aromatic), 1210–1064 (C–O) cm^{-1}.

(1*R*,2*S*,3*R*,4*R*)-4-[(*tert*-Butyldiphenylsilyloxy)methyl]-2,3-isopropylidenedioxy-1-(4-methoxycarbonyl-1*H*-1,2,3-triazol-1-yl)cyclopentane (15): The title compound was prepared from methyl propiolate (10 μL) after 1 min of microwave irradiation. Compound **15** (59 mg, >99%) was obtained as an orange oil. $[\alpha]_D^{27}$ = –20.8 (*c* = 0.15, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (s, 1 H, H^5), 7.63 (dd, *J* = 6.4 and 1.2 Hz, 4 H, H$^{Ar–Si}$), 7.45–7.36 (m, 6 H, H$^{Ar–Si}$), 4.80–4.73 (m, 2 H, H$^{2'}$ + H$^{1'}$), 4.57 (dd, *J* = 6.2 and 4.2 Hz, 1 H, H$^{3'}$), 3.95 (s, 3 H, OCH$_3$), 3.77–3.76 (m, 2 H, H$^{5'}$), 2.62–2.54 (m, 1 H, H$^{6'}$), 2.49–2.37 (m, 2 H, H$^{4'}$ + H$^{6'}$), 1.54 (s, 3 H, CH$_3$), 1.29 (s, 3 H, CH$_3$), 1.07 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3 (C, CO), 140.0 (C, C^4), 135.7 (CH, 4C$^{Ar–Si}$), 133.4 (C, 2C$^{Ar–Si}$), 130.0 (CH, 2C$^{Ar–Si}$), 127.9 (CH, 4C$^{Ar–Si}$), 127.3 (CH, C^5), 113.8 (C), 85.0 (CH, C$^{2'}$), 81.1 (CH, C$^{3'}$), 67.0 (CH, C$^{1'}$), 64.1 (CH$_2$, C$^{5'}$), 52.3 (OCH$_3$), 45.6 (CH, C$^{4'}$), 33.7 (CH$_2$, C$^{6'}$), 27.6 (CH$_3$), 27.0 (*t*Bu), 25.1 (CH$_3$), 19.5 (C-Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{29}H_{37}N_3NaO_5Si$ (M^+ + Na) 558.2400, found 558.2394. IR (neat): $\tilde{\nu}$ = 1727 (C=O), 1471, 1427, 1382 (C=C aromatic), 1239 (C–O), 1066–1042 (C–O) cm^{-1}.

General Procedure for Deprotection. Synthesis of (–)-16–21: The protected triazole (0.1 mmol) was stirred overnight in an aqueous solution of trifluoroacetic acid (60% v/v) (2 mL) at room temperature. After evaporation of all volatiles, the resulting oil was dissolved in THF (2 mL) and tetrabutyl ammonium fluoride trihydrate (33 mg, 0.1 mmol, 1.05 equiv.) was added. The reaction mixture was stirred for 1 h at room temperature. After evaporation of all volatiles, the residue was purified by silica gel column chromatography (EtOAc/MeOH, 98:2).

(1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-(4-phenyl-1*H*-1,2,3-triazol-1-yl)cyclopentane (16): The title compound was prepared from **10** (55 mg, 0.1 mmol) and was obtained as a white solid **16** (24 mg, 86%). $[\alpha]_D^{27}$ = –65.0 (*c* = 0.2, CH_3OH). ^{1}H NMR (500 MHz, CD_3OD): δ = 8.39 (s, 1 H, H^5), 7.81 (d, *J* = 7.5 Hz, 2 H, H^{Ar}), 7.43 (t, *J* = 7.5 Hz, 2 H, H^{Ar}), 7.34 (t, *J* = 7.5 Hz, 1 H, H^{Ar}), 4.95–4.90 (m, 1 H, H$^{1'}$), 4.29 (dd, *J* = 8.0 and 5.0 Hz, 1 H, H$^{2'}$), 4.03 (dd, *J* = 5.0 and 3.5 Hz, 1 H, H$^{3'}$), 3.67 (d, *J* = 6.0 Hz, 2 H, H$^{5'}$), 2.52 (dt, *J* = 13.5 and 8.5 Hz, 1 H, H$^{6'}$), 2.29–2.23 (m, 1 H, H$^{4'}$), 1.99–1.93 (m, 1 H, H$^{6'}$) ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 148.6 (C, C^4), 131.7 (C, C^{Ar}), 130.0 (CH, 2C^{Ar}), 129.3 (CH, C^{Ar}), 126.6 (CH, 2C^{Ar}), 121.7 (CH, C^5), 78.2 (CH, C$^{2'}$), 73.8 (CH, C$^{3'}$), 66.7 (CH, C$^{1'}$), 64.4 (CH$_2$, C$^{5'}$), 46.8 (CH, C$^{4'}$), 31.0 (CH$_2$, C$^{6'}$) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{14}H_{17}N_3NaO_3$ (M^+ + Na) 298.1168, found 298.1181.

(1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-[4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl]cyclopentane (17): The title compound was prepared from **11** (59 mg, 0.1 mmol). After purification by column chromatography, the obtained precipitate was washed with CH_2Cl_2 to eliminate the colour. Compound **17** (29 mg, 98%) was isolated as a white solid. $[\alpha]_D^{27}$ = –33.6 (*c* = 0.3, CH_3OH). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 8.65 (s, 1 H, H^5), 8.59 (d, *J* = 4.4 Hz, 1 H, N-CH), 8.02 (d, *J* = 7.6 Hz, 1 H, =C-CH=), 7.89 (td, *J* = 7.6 and 1.6 Hz, 1 H, =C-CH=C*H*), 7.34 (ddd, *J* = 7.6, 4.4 and 0.8 Hz, 1 H, N-CH=C*H*), 5.09 (d, *J* = 6.8 Hz, 1 H, C$^{2'}$-OH), 4.87–4.82 (m, 1 H, H$^{1'}$), 4.78–4.76 (m, 2 H, C$^{3'}$-OH + C$^{5'}$-OH), 4.16–4.10 (m, 1 H, H$^{2'}$), 3.84–3.81 (m, 1 H, H$^{3'}$), 3.47–3.42 (m, 2 H, H$^{5'}$), 2.35 (dt, *J* = 13.2 and 8.6 Hz, 1 H, H$^{6'}$), 2.10–2.03 (m, 1 H, H$^{4'}$), 1.81–1.73 (m, 1 H, H$^{6'}$) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ= 150.2 (C, =C), 149.8 (CH, N-CH), 147.3 (C, C^4), 137.6 (CH, =C-CH=*C*H), 123.3 (CH, N-CH=*C*H), 122.7 (CH, C^5), 119.8 (CH, =C-*C*H=), 76.9 (CH, C$^{2'}$), 72.2 (CH, C$^{3'}$), 65.0 (CH, C$^{1'}$), 63.0 (CH$_2$, C$^{5'}$), 45.5 (CH, C$^{4'}$), 30.0 (CH$_2$, C$^{6'}$) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{16}N_4NaO_3$ (M^+ + Na) 299.1120, found 299.1120.

(1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-(4-pentyl-1*H*-1,2,3-triazol-1-yl)cyclopentane (18): The title compound was prepared from **12** (58 mg, 0.1 mmol). The residue was purified by silica gel column chromatography (EtOAc). Compound **18** (25 mg, 88%) was obtained as a white solid. $[\alpha]_D^{27}$ = –13.2 (*c* = 0.2, CH_3OH). ^{1}H NMR (250 MHz, CD_3OD): δ = 7.81 (s, 1 H, H^5), 4.94–4.77 (m, 1 H, H$^{1'}$), 4.21 (dd, *J* = 8.0 and 5.0 Hz, 1 H, H$^{2'}$), 3.99 (dd, *J* = 5.3 and 3.5 Hz, 1 H, H$^{3'}$), 3.65 (d, *J* = 6.0 Hz, 2 H, H$^{5'}$), 2.69 (t, *J* = 7.5 Hz, 2 H, =C-CH$_2$), 2.46 (dt, *J* = 13.5 and 8.5 Hz, 1 H, H$^{6'}$), 2.26–2.19 (m, 1 H, H$^{4'}$), 1.91–1.84 (m, 1 H, H$^{6'}$), 1.70–1.62 (m, 2 H, =C-CH$_2$-C*H*$_2$), 1.38–1.32 [m, 4 H, (C*H*$_2$)$_2$-CH$_3$], 0.91 [t, *J* = 6.6 Hz, 3 H, (CH$_2$)$_2$-C*H*$_3$] ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 149.0 (C, C^4), 122.5 (CH, C^5), 78.0 (CH, C$^{2'}$), 73.8 (CH, C$^{3'}$), 66.4 (CH, C$^{1'}$), 64.4 (CH$_2$, C$^{5'}$), 46.7 (CH, C$^{4'}$), 32.5 (CH$_2$, *C*H$_2$-CH$_2$-CH$_3$), 31.0 (CH$_2$, C$^{6'}$), 30.3 (CH$_2$, =C-CH$_2$-*C*H$_2$), 26.3 (CH$_2$, =C-*C*H$_2$), 23.4 (CH$_2$, *C*H$_2$-CH$_3$), 14.3 (CH$_2$, CH$_2$-*C*H$_3$) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{23}N_3NaO_3$ (M^+ + Na) 292.1637, found 292.1626.

(1*R*,2*S*,3*R*,4*R*)-1-[4-(Acetoxymethyl)-1*H*-1,2,3-triazol-1-yl]-2,3-dihydroxy-4-(hydroxymethyl)cyclopentane (19): The title compound was prepared from **13** (58 mg, 0.1 mmol). The residue was purified by silica gel column chromatography (EtOAc). Compound **19** (22 mg, 76%) was obtained as a colorless oil. ^{1}H NMR (250 MHz, CD_3OD): δ = 8.09 (s, 1 H, H^5), 5.18 (s, 2 H, =C-CH$_2$), 4.92–4.81 (m, 1 H, H$^{1'}$), 4.22 (dd, *J* = 8.3 and 5.3 Hz, 1 H, H$^{2'}$), 3.99 (dd, *J* = 5.3 and 3.5 Hz, 1 H, H$^{3'}$), 3.64 (d, *J* = 5.6 Hz, 2 H, H$^{5'}$), 2.47 (dt, *J* = 13.2 and 8.5 Hz, 1 H, H$^{6'}$), 2.29–2.16 (m, 1 H, H$^{4'}$), 2.06 (s, 3 H, CO-CH$_3$), 1.97–1.83 (m, 1 H, H$^{6'}$) ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 172.3 (CO), 143.8 (C, C^4), 125.3 (CH, C^5), 78.2 (CH, C$^{2'}$), 73.8 (CH, C$^{3'}$), 66.6 (CH, C$^{1'}$), 64.4 (CH$_2$, C$^{5'}$), 58.2 (CH$_2$, =C-*C*H$_2$), 46.8 (CH, C$^{4'}$), 31.0 (CH$_2$, C$^{6'}$), 20.6 (CH$_3$, CO-*C*H$_3$) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{11}H_{17}N_3NaO_5$ (M^+ + Na) 294.1066, found 294.1073. IR (neat): $\tilde{\nu}$ = 3360 (OH), 1731 (C=O), 1229 (C–O), 1160–1042 (C–O) cm^{-1}.

(1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-1-[4-(2-hydroxyethyl)-1*H*-1,2,3-triazol-1-yl]-4-(hydroxymethyl)]cyclopentane (20): The title compound was prepared from **14** (57 mg, 0.1 mmol). After purification by column chromatography, the obtained precipitate was washed with CH_2Cl_2 to eliminate the colour. Compound **20** (21 mg, 80%) was obtained as a white solid. $[\alpha]_D^{27}$ = –26.6 (*c* = 0.15, CH_3OH). ^1H NMR (400 MHz, CD_3OD): δ = 7.87 (s, 1 H, H^5), 4.87–4.80 (m, 1 H, $H^{1'}$), 4.21 (dd, *J* = 8.4 and 5.3 Hz, 1 H, $H^{2'}$), 3.99 (dd, *J* = 5.3 and 3.6 Hz, 1 H, $H^{3'}$), 3.82 (br. s, 2 H, CH_2-OH), 3.65 (d, *J* = 6.0 Hz, 2 H, $H^{5'}$), 2.91 (t, *J* = 6.6 Hz, 2 H, =C-CH_2), 2.46 (dt, *J* = 13.2 and 8.5 Hz, 1 H, $H^{6'}$), 2.27–2.19 (m, 1 H, $H^{4'}$), 1.93–1.85 (m, 1 H, $H^{6'}$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.3 (C, C^4), 123.4 (CH, C^5), 78.2 (CH, $C^{2'}$), 73.9 (CH, $C^{3'}$), 66.5 (CH, $C^{1'}$), 64.4 (CH_2, $C^{5'}$), 62.1 (CH_2, CH_2-OH), 46.7 (CH, $C^{4'}$), 31.0 (CH_2, $C^{6'}$), 29.9 (CH_2, =C-*C*H_2) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{10}H_{17}N_3NaO_4$ (M^+ + Na) 266.1117, found 266.1111. IR (neat): $\tilde{\nu}$ = 3294 (OH), 1201–1050 (C–O) cm^{-1}.

(1*R*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)-1-[4-(methoxycarbonyl)-1*H*-1,2,3-triazol-1-yl]cyclopentane (21): The title compound was prepared from **15** (59 mg, 0.1 mmol). After purification by column chromatography, the obtained precipitate was washed with CH_2Cl_2 to eliminate the colour. Compound **21** (15 mg, 52%) was obtained as a white solid. $[\alpha]_D^{27}$ = –28.0 (*c* = 0.2, CH_3OH). ^1H NMR (250 MHz, CD_3OD): δ = 8.62 (s, 1 H, H^5), 4.97–4.78 (m, 1 H, $H^{1'}$), 4.25 (dd, *J* = 8.5 and 5.3 Hz, 1 H, $H^{2'}$), 4.00 (dd, *J* = 5.3 and 3.2 Hz, 1 H, $H^{3'}$), 3.92 (s, 3 H, OCH_3), 3.65 (d, *J* = 6.0 Hz, 2 H, $H^{5'}$), 2.57–2.45 (m, 1 H, $H^{6'}$), 2.30–2.19 (m, 1 H, $H^{4'}$), 1.99–1.87 (m, 1 H, $H^{6'}$) ppm. ^{13}C NMR (62.9 MHz, CD_3OD): δ = 162.4 (C, CO), 140.3 (C, C^4), 129.2 (CH, C^5), 78.2 (CH, $C^{2'}$), 73.8 (CH, $C^{3'}$), 66.9 (CH, $C^{1'}$), 64.3 (CH_2, $C^{5'}$), 52.5 (OCH_3), 46.8 (CH, $C^{4'}$), 30.8 (CH_2, $C^{6'}$) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{10}H_{15}N_3NaO_5$ (M^+ + Na) 280.0909, found 280.0913. IR (neat): $\tilde{\nu}$ = 3363 (OH), 1731 (C=O), 1226 (C–O), 1142–1055 (C–O) cm^{-1}.

(1*R*,2*S*,3*R*,4*R*)-1-(5-Amino-4-carbamoyl-1*H*-1,2,3-triazol-1-yl)-2,3-isopropylidenedioxy-4-[(*tert*-butyldiphenylsilyloxy)methyl]cyclopentane (22): In a dry flask, sodium metal (11 mg, 0.48 mmol, 2 equiv.) was dissolved in dry EtOH (1 mL) under N_2. To a solution of 8 (100 mg, 0.22 mmol) in dry EtOH (10 mL) under N_2, the prepared sodium ethoxide solution was added dropwise. After the addition of 2-cyanoacetamide (21 mg, 0.25 mmol, 1.1 equiv.), the reaction mixture was refluxed for 48 h. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 1:3). Compound **22** (6 mg, 5%) was obtained as a colourless oil. $[\alpha]_D^{27}$ = –32.4 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.66 (dd, *J* = 7.6 and 1.6 Hz, 4 H, $H^{Ar–Si}$), 7.46–7.37 (m, 6 H, $H^{Ar–Si}$), 6.68 (br. s, 1 H, CON*H*H), 5.64 (s, 2 H, NH_2), 5.30 (br. s, 1 H, CONH*H*), 4.57 (dd, *J* = 7.2 and 4.4 Hz, 1 H, $H^{3'}$), 4.52–4.49 (m, 1 H, $H^{2'}$), 4.33 (dt, *J* = 12.4 and 6.4 Hz, 1 H, $H^{1'}$), 3.84–3.76 (m, 2 H, $H^{5'}$), 2.76 (dd, *J* = 25.2 and 12.4 Hz, 1 H, $H^{6'}$), 2.61–2.54 (m, 1 H, $H^{6'}$), 2.52–2.46 (m, 1 H, $H^{4'}$), 1.59 (s, 3 H, CH_3), 1.30 (s, 3 H, CH_3), 1.07 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7 (CO), 145.5 (C, C^4), 135.7 (CH, $4C^{Ar–Si}$), 133.5 (C, $2C^{Ar–Si}$), 130.0 (CH, $2C^{Ar–Si}$), 127.9 (CH, $4C^{Ar–Si}$), 122.9 (C, C^5), 114.2 (C), 85.1 (CH, $C^{2'}$), 81.5 (CH, $C^{3'}$), 64.3 (CH_2, $C^{5'}$), 63.7 (CH, $C^{1'}$), 45.3 (CH, $C^{4'}$), 31.2 (CH_2, $C^{6'}$), 27.6 (CH_3), 27.0 (*t*Bu), 25.1 (CH_3), 19.5 (C-Si) ppm. HRMS (ESI) *m*/*z* calcd. for $C_{28}H_{37}N_5O_4NaSi$ (M^+ + Na) 558.2513, found 558.254. IR (neat): $\tilde{\nu}$ = 3325 (NH), 1654 (C=O), 1458, 1421, 1380 (C=C aromatic), 1254 (C–N), 1210–1003 (C–O) cm^{-1}.

Supporting Information (see also the footnote on the first page of this article): ^1H and ^{13}C NMR spectra of all new compounds.

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[1] a) J. Zemlicka, *Pharmacol. Therapeut.* **2000**, *85*, 251–266; b) G. Y. Song, V. Paul, H. Choo, J. Morrey, R. W. Sidwell, R. F. Schinazi, C. K. Chu, *J. Med. Chem.* **2001**, *44*, 3985–3993; c) G. Gumina, S. Olgen, C. K. Chu, *Antivir. Nucleos.* **2003**, 77–189; d) L. A. Agrofoglio, *Curr. Org. Chem.* **2006**, *10*, 333–362.

[2] For the synthesis of carbocyclic nucleosides: a) V. E. Marquez, M. I. Lim, *Med. Res. Rev.* **1986**, *6*, 1–40; b) D. M. Huryn, M. Okabe, *Chem. Rev.* **1992**, *92*, 1745–1768; c) L. A. Agrofoglio, E. Suhas, A. Farese, R. Condom, S. R. Challand, R. A. Earl, R. Guedj, *Tetrahedron* **1994**, *50*, 10611–10684; d) M. T. Crimmins, *Tetrahedron* **1998**, *54*, 9229–9272; e) L. A. Agrofoglio, S. R. Challand, In; *Acyclic, Carbocyclic and L-Nucleosides*; Kluwer Academic Publishers: Dordrecht, **1998**; f) E. Ichikawa, K. Kato, *Curr. Med. Chem.* **2001**, *8*, 385–423; g) O. R. Ludek, C. Meier, *Synthesis* **2006**, *13*, 2101–2109.

[3] For the antiviral activities of carbocyclic nucleosides: a) J. Balzarini, E. De Clercq, *Pharmacochemistry Library* **1990**, *14*, 175–194; b) V. E. Marquez, *Adv. Antivir. Drug Des.* **1996**, *2*, 89–146; c) S. W. Schneller, *Curr. Top. Med. Chem.* **2002**, *2*, 1087–1092; d) J. Neyts, E. De Clercq, *Antivir. Res.* **2003**, *57*, 25–33; e) R. O. Baker, M. Bray, J. W. Huggins, *Antivir. Res.* **2003**, *57*, 13–23; f) E. De Clercq, J. Neyts, *Rev. Med. Virol.* **2004**, *14*, 289–300.

[4] a) M. S. Wolfe, R. T. Borchardt, *J. Med. Chem.* **1991**, *34*, 1521–1530; b) S. L. Mosley, B. A. Bakke, J. M. Sadler, N. K. Sunkara, K. M. Dorgan, Z. S. Zhou, K. L. Seley-Radtke, *Bioorg. Med. Chem.* **2006**, *14*, 7967–7971.

[5] a) C. K. Chu, Y. H. Jin, R. O. Baker, J. Huggins, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 9–12; b) C. Simons, Q. Wu, T. T. Htar, *Curr. Top. Med. Chem.* **2005**, *5*, 1191–1203; c) B. Arumugham, H.-J. Kim, M. N. Prichard, E. R. Kern, C. K. Chu, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 285–287.

[6] a) E. De Clercq, *Antimicrob. Agents Chemother.* **1985**, *28*, 84–89; b) S. R. Narayanan, B. T. Keller, D. R. Borcherding, S. A. Scholtz, R. T. Borchardt, *J. Med. Chem.* **1988**, *31*, 500–503.

[7] a) B. M. Trost, R. Madsen, S. D. Guile, A. E. H. Elia, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1569–1572; b) M. T. Crimmins, *Tetrahedron* **1998**, *54*, 9229–9272; c) J. B. Rodriguez, M. J. Comin, *Mini-Rev. Med. Chem.* **2003**, *3*, 95–114.

[8] For a comprehensive review about the versatility of organoazides in modern synthetic chemistry, see: S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188–5240. For a review on the synthesis of azido-nucleosides, see: T. Pathak, *Chem. Rev.* **2002**, *102*, 1623–1668.

[9] a) R. Huisgen, *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 565–598; b) R. Huisgen, in *1,3-Dipolar Cycloaddition Chemistry*, vol. 1; A. Padwa (Eds.), Wiley, New York, **1984**.

[10] R. G. Gish, *J. Antimicrob. Chemother.* **2006**, *57*, 8–13.

[11] a) J. T. Witkowski, R. K. Robins, G. P. Khare, R. W. Sidwell, *J. Med. Chem.* **1973**, *16*, 935–937; b) W. Markland, T. J. McQuaid, J. Jain, A. D. Kwong, *Antimicrob. Agents Chemother.* **2000**, *44*, 859–866; c) J. Z. Wu, C.-C. Lin, Z. J. Hong, *J. Antimicrob. Chemother.* **2003**, *52*, 543–546.

[12] Y. Saito, V. Escuret, D. Durantel, F. Zoulim, R. F. Schinazi, L. A. Agrofoglio, *Bioorg. Med. Chem.* **2003**, *11*, 3633–3639.

[13] I. Pérez-Castro, O. Caamaño, F. Fernández, M. D. García, C. López, E. De Clercq, *Org. Biomol. Chem.* **2007**, *5*, 3805–3813.

[14] H. Cho, D. L. Bernard, R. W. Sidwell, E. R. Kern, C. K. Chu, *J. Med. Chem.* **2006**, *49*, 1140–1148.

[15] a) K. Tadano, H. Maeda, M. Hoshino, Y. Iimura, *Chem. Lett.* **1986**, 1081–1084; K. Tadano, H. Maeda, M. Hoshino, Y. Iimura, *J. Org. Chem.* **1987**, *52*, 1946–1956; b) K. Tadano, M. Hoshino, S. Ogawa, T. Suami, *J. Org. Chem.* **1988**, *53*, 1427–1432.
[16] a) H. J. Bestmann, D. Roth, *Synlett* **1990**, 751–753; b) D. R. Borcherding, S. A. Scholtz, R. T. Borchardt, *J. Org. Chem.* **1987**, *52*, 5457–5461.
[17] a) W. J. Choi, J. G. Park, S. J. Yoo, H. O. Kim, H. R. Moon, M. W. Chun, Y. H. Jung, L. S. Jeong, *J. Org. Chem.* **2001**, *66*, 6490–6494; b) H. R. Moon, W. J. Choi, H. O. Kim, L. S. Jeong, *Tetrahedron: Asymmetry* **2002**, *13*, 1189–1193.
[18] For recent reviews on RCM: a) J. C. Conrad, D. E. Fogg, *Curr. Org. Chem.* **2006**, *10*, 185–202; b) A. Michaut, J. Rodriguez, *Angew. Chem. Int. Ed.* **2006**, *45*, 5740–5750; c) S. K. Chattopadhyay, S. Karmakar, T. Biswas, K. C. Majumdar, H. Rahaman, B. Roy, *Tetrahedron* **2007**, *63*, 3919–3952.
[19] a) Y. H. Jin, P. Liu, J. Wang, R. Baker, J. Huggins, C. K. Chu, *J. Org. Chem.* **2003**, *68*, 9012–9018; b) Y. H. Jin, C. K. Chu, *Tetrahedron Lett.* **2002**, *43*, 4141–4143.
[20] P. Schwab, M. B. France, J. W. Ziller, R. H. Grubbs, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2039–2041; b) P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc.* **1996**, *118*, 100–110.
[21] a) J. Huang, E. D. Stevens, S. P. Nolan, J. L. Petersen, *J. Am. Chem. Soc.* **1999**, *121*, 2674–2678; b) M. Scholl, T. M. Trnka, J. P. Morgan, R. H. Grubbs, *Tetrahedron Lett.* **1999**, *40*, 2247–2250.
[22] M. Yang, W. Ye, S. W. Schneller, *J. Org. Chem.* **2004**, *69*, 3993–3996.
[23] C. R. Johnson, Y. F. Chen, *J. Org. Chem.* **1991**, *56*, 3344–3351.
[24] a) H. Gilman, R. G. Jones, L. A. Woods, *J. Org. Chem.* **1952**, *17*, 1630–1634; b) J. F. Normant, *Synthesis* **1972**, 63–80.
[25] a) E. J. Corey, N. W. Boaz, *Tetrahedron Lett.* **1985**, *26*, 6015–6018; E. J. Corey, N. W. Boaz, *Tetrahedron Lett.* **1985**, *26*, 6019–6022; b) A. Alexakis, J. Berlan, Y. Besace, *Tetrahedron Lett.* **1986**, *27*, 1047–1050; c) E. Nakamura, S. Matsuzawa, Y. Horiguchi, I. Kuwajima, *Tetrahedron Lett.* **1986**, *27*, 4029–4032.
[26] a) M. T. Reett, F. Wang, K. Harms, *J. Chem. Soc., Chem. Commun.* **1991**, 1309–1311; b) M. Kanai, Y. Nakagawa, K. Tomioka, *Tetrahedron* **1999**, *55*, 3831–3842.
[27] a) O. Mitsunobu, Y. Yamada, *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380–2382; b) O. Mitsunobu, *Synthesis* **1981**, 1–28; c) Y. Yoshimura, K. Kitano, K. Yamada, H. Satoh, M. Watanabe, S. Miura, S. Sakata, T. Sasaki, A. Matsuda, *J. Org. Chem.* **1997**, *62*, 3140–3152.
[28] J. Broggi, S. Díez-González, J. L. Petersen, S. Berteina-Raboin, S. P. Nolan, L. A. Agrofoglio, *Synthesis* **2008**, 141–148.
[29] a) A. Deiters, T. A. Cropp, M. Mukerji, J. W. Chin, J. C. Anderson, P. G. Schultz, *J. Am. Chem. Soc.* **2003**, *125*, 11782–11783; b) L. V. Lee, M. L. Mitchell, S.-J. Huang, V. V. Fokin, K. B. Sharpless, C.-H. Wong, *J. Am. Chem. Soc.* **2003**, *125*, 9588–9589; c) P. Appukkuttan, W. Dehaen, V. V. Fokin, E. A. Van der Eycken, *Org. Lett.* **2004**, *6*, 4223–4225; d) W.-H. Zhan, H. N. Barnhill, K. Sivakumar, H. Tian, Q. Wang, *Tetrahedron Lett.* **2005**, *46*, 1691–1695; e) S. Quader, S. E. Boyd, I. D. Jenkins, T. A. Houston, *J. Org. Chem.* **2007**, *72*, 1962–1979.
[30] a) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596–2599; b) C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057–3064.
[31] a) U. Pradere, V. Roy, T. R. McBrayer, R. F. Schinazi, L. A. Agrofoglio, *Tetrahedron* **2008**, *64*, 9044–9051; b) J. Broggi, N. Joubert, V. Aucagne, S. Berteina-Raboin, S. Díez-González, S. P. Nolan, D. Topalis, D. Deville-Bonne, J. Balzarini, J. Neyts, G. Andrei, R. Snoeck, L. A. Agrofoglio, *Nucleosides Nucleic Acids* **2007**, *26*, 1391–1394; c) K. El Akri, K. Bougrin, J. Balzarini, A. Faraj, R. Benhida, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 6656–6659; d) R. Guezguez, K. Bougrin, K. El Akri, R. Benhida, *Tetrahedron Lett.* **2006**, *47*, 4807–4811 (and ref. 29); e) P. Appukkuttan, W. Dehaen, V. V. Fokin, E. Van der Eycken, *Org. Lett.* **2004**, *6*, 4223–4225.
[32] H. C. Kolb, M. G. Finn, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2001**, *40*, 2004–2021.
[33] N. Joubert, R. F. Schinazi, L. A. Agrofoglio, *Tetrahedron* **2005**, *61*, 11744–11750.
[34] a) D. F. Ewing, G. Goethals, G. Mackenzie, P. Martin, G. Ronco, L. Vanbaelinghem, P. Villa, *J. Carbohydr. Chem.* **1999**, *18*, 441–450; D. F. Ewing, G. Goethals, G. Mackenzie, P. Martin, G. Ronco, L. Vanbaelinghem, P. Villa, *Carbohydr. Res.* **1999**, 190–196.

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