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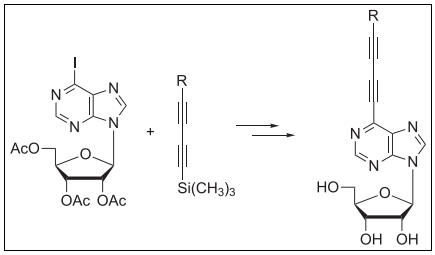

1,3-Alkadiynyl(trimethyl)silanes were prepared by the Negishi or Sonogashira reactions of bromoethynyl (trimethyl)silane with several terminal alkynes in 34–75% yield. However, the direct Hiyama coupling of these compounds with 6-iodopurine derivatives has not been successful. Therefore, a modified Sonogashira reaction using TBAF or CsF for *in situ* removal of the trimethylsilyl group has been utilized. This methodology afforded the desired 6-(1,3-butadiynyl)purines in 47–87% yield.

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INTRODUCTION

Many modified purines are biologically active [1]. Among them, 6-alkynyl derivatives play many important roles, and are reported to be cytotoxic [2] and also exhibit antimycobacterial [3] and cytokinin [4] activities. The biological activities of 6-alkynylpurines can be ascribed to their ability to undergo conjugate addition of a wide range of nucleophiles to the triple C–C bond activated by strongly electron-withdrawing purine nuclei [5]. Symmetrical bis (purin-6-yl)diacetylenes, prepared by oxidative dimerization of 6-alkynylpurines, were used for post-synthetic modification of oligodeoxynucleotides [6] and were designed and prepared as the covalent analogs of DNA base pairs [7]. However, the synthesis and biological evaluation of unsymmetrically substituted (purine-6-yl)buta-1,3-diynes has remained, to the best of our knowledge, unknown. Therefore, we developed the methodology for the synthesis of these hitherto unknown compounds. This new synthetic strategy can facilitate an access to the biological evaluation of these new compounds.

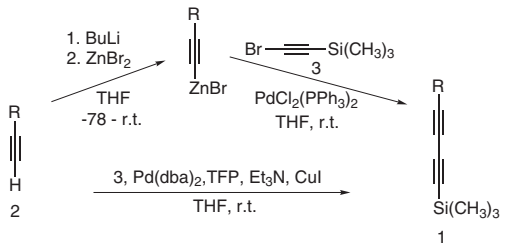
RESULTS AND DISCUSSION

The first attempts to synthesize 6-(1,3-butadiynyl)purines started from 9-benzyl-6-ethynylpurine, which is easily available by the Sonogashira coupling of 9-benzyl-6-chloropurine [8] with ethynyl(trimethyl)silane followed by deprotection. However, all attempts to couple 9-benzyl-6-ethynylpurine with 1-bromo-2-phenylethyne or 1-iodo-2-phenylethyne including Sonogashira coupling, Negishi coupling, and the Cadiot–Chodkiewicz reaction [9] have failed. Only formation of the symmetrical dimers, or in the case of the Cadiot–Chodkiewicz reaction adduct of the propylamine (used as the base) to the triple bond of the starting alkyne, was observed. An alternative approach, coupling of 9-benzyl-6-(2-haloethynyl)purine with alkyne, could not be used, because all attempts to prepare starting 9-benzyl-6-(2-haloethynyl)purines have been unsuccessful.

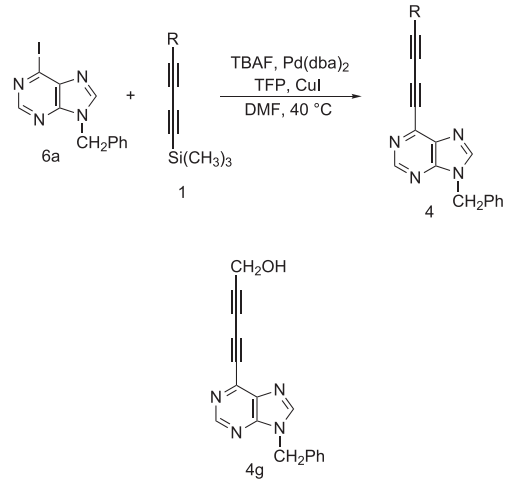
For that reason, we turned our attention to the coupling of 1-substituted buta-1,3-diynes with 6-halopurines. The synthesis of the key intermediates, 1,3-alkadiynyl(trimethyl) silanes **1**, has been addressed first. Diynes **1** can, in principle, be coupled directly with 6-halopurines using the Hyiama reaction. Alternatively, Sonogashira or Negishi couplings can be used after removal of the trimethylsilyl group. The reaction of ethynyl(trimethyl)silane with 1-bromo-2-phenylethyne under Cadiot–Chodkiewicz conditions [9] has not been successful, probably because of the instability of the trimethylsilylgroup under the reaction conditions. Fortunately, the Negishi coupling starting from phenylethyne **2a** and bromoethynyl(trimethyl)silane **3** was successful, giving the desired 4-phenylbuta-1,3-diyn-1-yl(trimethyl)silane **1a** in 63% yield (Scheme 1, Table 1, entry 1).

Alkynes bearing simple alkyl or diethylacetal groups (Table 1, entries 2, 4) reacted with **3** similarly smoothly. On the contrary, the alkynes bearing nitrogen-containing substituents (Table 1, entries 3, 5) gave only low yields of the desired diynes, presumably because of the formation of hardly soluble lithium salts. Additives such as TMEDA or HMPA had only limited influence on the yield in these cases. Because butyllithium used for the deprotonation of

Scheme 1. Preparation of alkadiynyl(trimethyl)silanes **1**.



Scheme 2. Preparation of 6-diynylpurines **4a–g**.



alkynes is not compatible with many functional groups, the Sonogashira reaction of alkynes **2a–f** with bromoethynyl (trimethyl)silane (**3**) was also attempted. The yields were in all cases, with the exception of phenylethyne (**2a**), somewhat higher compared with the Negishi coupling. Improvement of the yield was substantial in the case of imidazoyl derivative **1e** (Table 1, entry 5). This approach also allowed coupling of the propargyl acetate **2f** (Table 1, entry 6).

Attempts to prepare the target 6-diynylpurines **4** directly by Hiyama coupling of the prepared silylated diynes **1** with iodopurine **6a** were not successful. The reaction did not proceed at all, or at higher temperatures, complete decomposition of the diyne occurred. Therefore, a modified Sonogashira reaction was used, and the unprotected diyne was generated *in situ* from silanes **1** by gradual addition of the solution of TBAF to the solution of iodopurine **6a**, silylated diyne **1**, CuI, and the Pd catalyst in DMF (Scheme 2). The yields of the desired 6-diynylpurines **4** varied approximately in the range 50% to 90% (Table 2). Wihout the TBAF [10], the rection does not proceed. Isolation of the imidazoylderivative **4e** (Table 2, entry 5) was complicated by similar R_F of the product and TBAF. Therefore, CsF was used as the base in this case. The acetoxydiynyl derivative **4f** was then deprotected by the methanolysis, giving the hydroxymethyl derivative **4g** in 90% yield.

The acetylated ribosides **5a–f** have been prepared similarly, starting with acetylated riboside **6b**. The deprotection by the methanolysis then gave the nucleosides **7a–e** and **7g**, in high isolated yield (Scheme 3, Table 3). In the case of acetoxydiynyl derivative **5f**, the acetoxygroup of the diyne was deprotected simultaneously, giving the fully deprotected nucleoside **7g** in 90% yield (Table 3, entry 6).

CONCLUSIONS

The 6-butadiynylpurines can be easily prepared by the Sonogashira coupling of the 6-iodopurine derivatives with the substituted buta-1,3-diynes. The diynes are generated *in situ* in the reaction mixture by the deprotection of the

Table 1

Preparation of alkadiynyl(trimethyl)silanes **1** (Scheme 1).

Entry	R	Product	Negishi[a] (Yield %)	Sonogashira[b] (Yield %)
1	C_6H_5	**1a**	63	55
2	C_5H_{11}	**1b**	75	74
3	$CH_2N(CH_3)_2$	**1c**	41[c,d]	48
4	$CH(OC_2H_5)_2$	**1d**	63	70
5		**1e**	11[c,e]	34
6	CH_2OCOCH_3	**1f**	–	44

[a]Reaction conditions: BuLi (1.25 eq.) and $ZnBr_2$ (1.3 eq.) were added successively to the solution of alkyne (1.25 eq.) in THF at −78°C. Then, bromoalkyne (1 eq.) and $PdCl_2(PPh_3)_2$ (2 mol.%) were added at room temperature.
[b]Reaction conditions: The solution of bromoalkyne (1 eq.), alkyne (1.2 eq.), Et_3N (3 eq.), CuI (2 mol.%.), $Pd(dba)_2$ (2 mol.%), and TFP (4 mol.%) in THF was stirred at room temperature.
[c]Formation of insoluble precipitate was observed.
[d]In the presence of 1 eq. of TMEDA.
[e]In the presence of 4 eq. of HMPA.

Table 2

Preparation of 6-diynylpurines **4a–g**[a] (Scheme 2).

Entry	R	Product	Yield %
1	C_6H_5	**4a**	66
2	C_5H_{11}	**4b**	62
3	$CH_2N(CH_3)_2$	**4c**	64
4	$CH(OC_2H_5)_2$	**4d**	55
5		**4e**[b]	47
6	CH_2OCOCH_3	**4f**	54
7	CH_2OH	**4g**[c]	90

[a]Reaction conditions: To the stirred mixture of iodopurine **6a**, $Pd(dba)_2$ (4 mol.%), TFP (8 mol.%), CuI (8 mol.%), and diyne **1** (1.5 eq.) in DMF (2 mL/mmol), the solution of 0.5*M* TBAF·3 H_2O (1 eq.) was added dropwise during 30 min at 40°C. The mixture was stirred at this temperature until all **6a** was consumed (TLC). After evaporation of the DMF, the product was isolated by chromatography.
[b]CsF was used instead of TBAF·3 H_2O.
[c]Preparation by methanolysis of **4f**: The acetate **4f** was dissolved in dry MeOH (5 mL/mmol), MeONa (0.1 eq.) was added, and the solution was stirred at room temperature until all **4f** was consumed (TLC). After quenching with AcOH (0.15 eq.) and evaporation of the solvent, **4g** was isolated by chromatography.

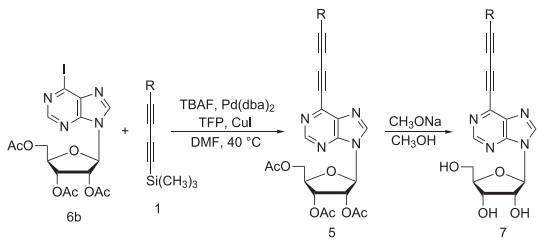
Table 3

Preparation of diynylpurine nucleosides **5**[a] and **7**[b] (Scheme 3).

Entry	R	Product (Yield %)	Product (Yield %)
1	C_6H_5	**5a** (87)	**7a** (86)
2	C_5H_{11}	**5b** (59)	**7b** (75)
3	$CH_2N(CH_3)_2$	**5c** (70)	**7c** (83)
4	$CH(OC_2H_5)_2$	**5d** (76)	**7d** (87)
5		**5e** (72)	**7e** (95)
6	CH_2OCOCH_3	**5f** (69)	**7g** (89) R = CH_2OH

[a]Reaction conditions: To a stirred mixture of iodopurine **6b**, $Pd(dba)_2$ (4 mol.%), TFP (8 mol.%), CuI (8 mol.%), and diyne **1** (1.5 eq.) in DMF (2 mL/mmol), the solution of 0.5*M* TBAF·3 H_2O (1 eq.) was added dropwise during 30 min at 40°C. The mixture was stirred at this temperature until all **6b** was consumed (TLC). After evaporation of the DMF, the product was isolated by the chromatography.
[b]Reaction conditions: The riboside **5** was dissolved in dry MeOH (5 mL/mmol), MeONa (0.1 eq.) was added, and the solution was stirred at room temperature until all starting compound was consumed (TLC). After quenching with AcOH (0.15 eq.) and evaporation of the solvent, pure **7** was isolated by chromatography.

Scheme 3. Preparation of diynylpurine nucleosides **7**.



corresponding buta-1,3-diynyl(trimethyl)silanes by TBAF or CsF. Methanolysis of the acetylated ribosides **5** then allows preparation of the unprotected nucleosides **7a–e**, **g**. Biological evaluation of the obtained diynylpurines **4** and **7** will be published elsewhere.

EXPERIMENTAL

Unless stated otherwise, all reactions were performed in flame-dried Schlenk flasks under argon. 9-Benzyl-6-iodopurine (**6a**) [11] and 9-(*O*,*O*,*O*-triacetyl-β-D-ribofuranosyl)-6-iodopurine (**6b**) [12] were prepared according to literature procedures. Other compounds were purchased. Tetrahydrofurane was dried using the standard benzophenone ketyl procedure, diethyl ether was distilled from sodium, and DMF was distilled from P_2O_5. Other solvents were purchased from Sigma-Aldrich or Acros Organics and used without further purification. TLC analyses were performed on Fluka silica plates (cat. no. 60778). Column chromatographies were performed using Merck Silica Gel 60 (40–63 μm). Melting points were measured on a Kofler bench and are not corrected. NMR spectra were recorded on Varian Gemini 300 (^{1}H 300.07 MHz, ^{13}C 75.46 MHz) and Bruker DRX 500 Avance (^{1}H 500 MHz, ^{13}C 125.77 MHz) spectrometers at 298 K. Chemical shifts are given in ppm with tetramethylsilane as a reference compound; coupling constants *J* are given in Hz. The unambiguous assignment of the signals (if noted) is supported by ^{13}C APT, ^{1}H COSY, ^{13}C(^{1}H) HMQC, and ^{13}C(^{1}H) HMBC spectra. High resolution mass spectra were recorded on an LTQ Orbitrap Velos spectrometer (Thermo Scientific). IR spectra were recorded on Nicolet FT-IR 740, Nicolet FT-IR 6700, and Nicolet FT-IR iS10 (Thermo Scientific) spectrometers; wavenumbers are given in cm^{-1}.

Bromoethynyl(trimethyl)silane (3). Ethynyltrimethylsilane (2.95 g, 30 mmol) was dissolved in Et_2O (20 mL), the solution was cooled to −78°C, and BuLi (15 mL of 2.0*M* solution) was added dropwise. The reaction mixture was stirred at −78°C for 30 min, and the temperature was allowed to reach −40°C. Bromine (4.8 g, 30 mmol) was added dropwise, and the temperature was allowed to reach room temperature while stirring. Subsequently, 10 mL of satd. NH_4Cl and 10 mL of satd. $Na_2S_2O_3$ were added. The aqueous layer was extracted with Et_2O (2 × 20 mL), and the combined organic layers were dried over $MgSO_4$. After the careful removal of the solvents (0°C), the residue was purified by distillation under reduced pressure. It was obtained 3.58 g (67%) of **3** as colorless liquid. Bp 61°C/81 Torr (lit. [13] 55°C/55 Torr). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.18 (s). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.3, 61.4, 86.9.

General procedure for preparation of alkadiynyl(trimethyl) silanes

Method A (Negishi reaction)

Preparation of the organzinc reagent. A solution of alkyne **2** (1 eq.) in THF (2 mL per mmol of alkyne) was cooled to −78°C. Subsequently, BuLi (1.05 eq.) was added, and the mixture was stirred for 10 min at −78°C and then slowly warmed up to

0°C. After 5 min at 0°C, the mixture was cooled down to −78°C, $ZnBr_2$ (1.05 eq., as 1*M* solution in THF) was added, and the mixture was warmed up to 0°C.

Reaction of organozinc reagents with bromoalkyne. Bromoethynyl(trimethyl)silane (**3**, 0.8 eq.) and $PdCl_2(PPh_3)_2$ (2 mol.%) were dissolved in THF (2 mL per mmol of **3**), and solution of the organozinc reagent was added dropwise during 30 min while stirring at room temperature. The reaction mixture was stirred at room temperature for an additional 2 h, and satd. NH_4Cl was added (cca half the volume of the reaxtion mixture). The organic layer was separated, and the aqueous layer was extracted twice with Et_2O. Combined organic layers were dried with $MgSO_4$, and after the removal of the solvents (max. 30°C), the product was isolated using column chromatography on silica gel.

Method B (Sonogashira reaction). A mixture of $Pd(dba)_2$ (2 mol.%), TFP (4 mol.%), CuI (2 mol.%), bromoethynyl (trimethyl)silane **3** (1 eq.), terminal alkyne **2** (1.2 eq.), THF (2 mL per mmol of **3**), and Et_3N (3 eq.) was stirred for 1 h at room temperature. The solvents were then evaporated (max. 30°C), and the oily residue was column chromatographed on silica gel.

Trimethyl(4-phenylbuta-1,3-diyn-1-yl)silane (1a)

Method A. From **3** (142 mg, 0.80 mmol) and phenylethyne (**2a**, 102 mg, 1.0 mmol) was obtained after chromatography (hexane, $R_F = 0.57$) 97 mg (61%) of the diyne **1a** as pale yellow colorless viscous oil.

Method B. From **3** (177 mg, 1.0 mmol) and phenylethyne (**2a**, 122 mg, 1.2 mmol) was obtained after chromatography (hexane, $R_F = 0.57$) 109 mg (55%) of the diyne **1a** as pale yellow colorless viscous oil. ^1H and ^{13}C NMR spectra are in a good agreement with published data [14].

Trimethyl(nona-1,3-diyn-1-yl)silane (1b)

Method A. From **3** (886 mg, 5.0 mmol) and hept-1-yne (**2b**, 577 mg, 6 mmol) was obtained after chromatography (hexane, $R_F = 0.61$) 720 mg (75%) of the diyne **1b** as colorless viscous oil.

Method B. From **3** (531 mg, 3.0 mmol) and hept-1-yne (**2b**, 346 mg, 5 mmol) was obtained after chromatography (hexane, $R_F = 0.61$) 426 mg (74%) of the diyne **1b** as colorless viscous oil. ^1H NMR (300 MHz, $CDCl_3$): δ 0.17 (s, 9 H, $Si(CH_3)_3$), 0.89 (t, $J = 7.0$, 3 H, CH_2CH_3), 1.24–1.42 (m, 4 H, 2 × CH_2), 1.46–1.60 (m, 2 H, CH_2), 2.26 (t, $J = 7.0$, 2 H, C≡C–CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.4, 13.9, 19.2, 22.1, 27.8, 30.9, 65.4, 80.2, 82.9, 88.4. IR (ATR): 2959 (m), 2933 (m), 2862 (w), 2225 (w), 2107 (w), 1722 (w), 1464 (w), 1426 (w), 1379 (w), 1328 (w), 1250 (m), 1182 (w), 1107 (w), 933 (w), 841 (s), 759 (w), 701 (w) cm^{-1}. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{12}H_{20}Si$ 192.1334; found 192.1326.

Dimethyl(5-(trimethylsilyl)penta-2,4-diyn-1-yl)amine (1c)

Method A. [note: 0.15 mL (1 eq.) TMEDA was added prior to BuLi addition]. From **3** (149 mg, 0.8 mmol) and dimethyl(prop-2-yn-1-yl)amine (**2c**, 83 mg, 1 mmol) was obtained after chromatography (EtOAc–hexane, 1:1, $R_F = 0.33$) 61 mg (41%) of the diyne **1c** as light brown viscous oil.

Method B. From **3** (354 mg, 2.0 mmol) and dimethyl(prop-2-yn-1-yl)amine (**2c**, 200 mg, 2.4 mmol) was obtained after chromatography (EtOAc–hexane, 1:1, $R_F = 0.33$) 173 mg (48%) of the diyne **1c** as light brown viscous oil. ^1H NMR (300 MHz, $CDCl_3$): δ 0.19 (s, 9 H, $Si(CH_3)_3$), 2.30 (s, 6 H, $N(CH_3)_2$), 3.36 (s, 2 H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.4, 44.0, 48.3, 70.3, 74.1, 85.1, 87.7. IR (ATR): 2958 (w), 2944 (w), 2902 (w), 2862 (w), 2824 (w), 2775 (w), 2212 (w), 2104 (w), 1455 (w), 1419 (w), 1536 (w), 1322 (w), 1251 (m), 1155 (w), 1097 (w), 1034 (w), 1027 (w), 840 (s), 788 (w), 759 (w), 701 (w) cm^{-1}. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{10}H_{17}NSi$ 179.1130; found 179.1124.

(5,5-Diethoxypenta-1,3-diyn-1-yl)trimethylsilane (1d)

Method A. From **3** (886 mg, 5.0 mmol) and 1,1-diethoxyprop-2-yne (**2d**, 769 mg, 6.0 mmol) was obtained after chromatography (EtOAc–hexane 1:1, $R_F = 0.33$) 461 mg (41%) of the diyne **1d** as light brown viscous oil.

Method B. From **3** (354 mg, 2.0 mmol) and 1,1-diethoxyprop-2-yne (**2d**, 200 mg, 2.4 mmol) was obtained after chromatography (EtOAc–hexane 1:1, $R_F = 0.33$) 173 mg (48%) of the diyne **1d** as light brown viscous oil.

^1H NMR (300 MHz, $CDCl_3$): δ 0.19 (s, 9 H, $Si(CH_3)_3$), 1.22 (t, $J = 6.9$, 6 H, CH_3), 3.54–3.78 (m, 4 H, CH_2), 5.28 (s, 1 H, C**H**$(OEt)_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.7, 14.9, 61.1, 69.9, 72.5, 86.7, 88.3, 91.3. IR (ATR): 2978 (m), 2932 (w), 2887 (w), 2111 (w), 1352 (w), 1326 (m), 1253 (w), 1089 (s), 1055 (s), 1016 (m), 916 (w), 866 (m), 845 (s), 761 (w), 702 (w), 634 (w) cm^{-1}. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{12}H_{20}O_2Si$ 224.3715; found 224.3720.

1-Methyl-5-(4-trimethylsilylbuta-1,3-diyn-1-yl)imidazole (1e)

Method A (modified). 1-Methyl-5-ethynylimidazole (**2e**, 106 mg, 1.0 mmol) was dissolved in THF (4 mL), HMPA (0.35 mL, 2 eq.) was added, and the solution was cooled to −78°C. Subsequently, LiHMDS (1.05 mL of 1*M* solution, 1.05 eq.) was added, and the reaction mixture was stirred for 1 h at −78°C. The mixture was then allowed to warm to 0°C, which led to precipitation of a small amount of solid. Therefore, two more equivalents of HMPA were added, which led to complete dissolution. Subsequently, $ZnBr_2$ (1.05 mL of 1*M* solution in THF, 1.05 eq.) was added, and the reaction mixture was stirred for 30 min at room temperature. $Pd(P(t\text{-}Bu)_3)_2$ (13 mg, 2 mol.%) was dissolved in THF (1 mL), and the solution was cooled to 0°C with stirring. Bromoethynyl(trimethyl)silane (**3**, 147 mg, 0.83 mmol) was dissolved in THF (7 mL), and both the solution of **3** and the solution of the organozinc were added simultaneously to the solution of the catalyst so that the added amount of both components remained the same. The addition took approx. 30 min. Subsequently, the water–ice bath was removed, and the reaction mixture was stirred overnight at room temperature. The reaction was quenched with satd. NH_4Cl (5 mL), which led to precipitation of solid material. Water (10 mL) was added, which led to the dissolution of the anorganic salts. The mixture was extracted with DCM (5 × 30 mL), and the combined organic layers were dried over $MgSO_4$. After the removal of the volatiles, the residue was column chromatographed (EtOAc, $R_F = 0.3$). It was obtained 18 mg (11%) of the diyne **1e** as pale yellow amorphous solid.

Method B. From **3** (334 mg, 1.9 mmol) and 1-methyl-5-ethynylimidazole (**2e**, 106 mg, 1.6 mmol) was obtained after chromatography (EtOAc, $R_F = 0.3$) 110 mg (34%) of the diyne **1e** as pale yellow amorphous solid. ^1H NMR (300 MHz, $CDCl_3$): δ 0.21 (s, 9 H, $Si(CH_3)_3$), 3.67 (s, 3 H, CH_3), 7.36 (s, 1 H), 7.48 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.6, 32.3, 63.9, 81.8, 87.0, 93.9, 115.2, 136.8, 138.7. IR (ATR): 3121 (w), 3088 (m), 2957 (m), 2898 (w), 2198 (s), 2105 (w), 1543 (w), 1490 (m), 1462 (w), 1414 (w), 1364 (w), 1289 (w), 1249 (s), 1242 (s), 1220 (w), 1127 (m), 1057 (w), 1031 (m), 1003 (w), 957 (w), 918 (m), 840 (s), 757 (m), 699 (w) cm^{-1}. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{11}H_{14}N_2Si$ 202.0926; found 202.0926.

5-Trimethylsilylpenta-2,4-diyn-1-yl acetate (1f)

Method B. From **3** (531 mg, 3.0 mmol) and propargyl acetate (**2f**, 353 mg, 3.6 mmol) was obtained after chromatography

(EtOAc–hexane, 1:10, $R_F = 0.5$) 257 mg (44%) of the diyne **1f** as pale yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (s, 9 H, $Si(CH_3)_3$), 2.06 (s, 3 H, CH_3), 4.69 (s, 2 H, CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ −0.7, 20.5, 52.2, 71.2, 71.4, 86.8, 88.0, 169.8. IR (ATR): 2961 (w), 2112 (m), 1746 (s), 1430 (w), 1376 (w), 1358 (w), 1251 (m), 1214 (s), 1026 (m), 969 (w), 840 (s), 759 (m), 703 (w), 634 (w), 603 (w), 539 (w), 489 (w) cm^{-1}. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{10}H_{14}O_2Si$ 194.0763; found 194.0754.

Reaction of butadiynyl(trimethyl)silanes with 6-iodopurines—general procedure. A solution of 6-iodopurine **6** (1 ekv.), $Pd(dba)_2$ (4 mol.%), TFP (8 mol.%), CuI (8 mol.%), and silylated diyne **1** (1.5 eq.) in DMF (2 mL per mmol of **6**) was stirred at 40°C. A 0.5*M* solution of TBAF·3 H_2O in DMF (1 eq.) was added dropwise during approx. 30 min, and the reaction mixture was stirred at 40°C until the conversion was complete according to TLC. The solvent was then evaporated, and the residue was column chromatographed on silica gel.

9-Benzyl-6-(4-phenylbuta-1,3-diyn-1-yl)purine (4a). From 9-benzyl-6-iodopurine (**6a**, 67 mg, 0.20 mmol) and diyne **1a** (60 mg, 0.30 mmol) was obtained after chromatography (hexane–EtOAc 2:1, $R_F = 0.24$) 44 mg (66%) of **4a** as yellow solid. Crystallization (hexane–EtOAc) afforded yellow needles, mp 151°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.44 (s, 2 H, CH_2), 7.26–7.40 (m, 8 H, Ph), 7.46–7.58 (m, 2 H, Ph), 8.11 (s, 1 H, H-8), 8.96 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 47.4 (**C**H_2Ph), 73.4 (C≡C), 75.2 (C≡C), 82.4 (C≡C), 85.7 (C≡C), 120.7 (C_q^{Ph}), 127.8 (CH^{Ph}), 128.4 (CH^{Ph}), 128.7 (CH^{Ph}), 129.1 (CH^{Ph}), 129.9 (CH^{Ph}), 132.8 (CH^{Ph}), 134.6 (C_q^{Ph}), 135.1 (C-5), 140.5 (C-6), 145.4 (C-8), 151.6 (C-4), 152.7 (C-2). IR (ATR): 3092 (w), 3047 (w), 2947 (w), 2208 (s), 1799 (w), 1745 (w), 1568 (s), 1491 (m), 1434 (m), 1402 (m), 1317 (m), 1263 (w), 1226 (w), 1193 (m), 1142 (w), 1078 (w), 1027 (w), 950 (w), 910 (w), 858 (w), 753 (m), 719 (m), 681 (m), 668 (m), 640 (m), 594 (w), 529 (w), 470 (w) cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{22}H_{14}N_4Na$ 357.1116; found 357.1108.

9-Benzyl-6-(nona-1,3-diyn-1-yl)purine (4b). From 9-benzyl-6-iodopurine (**6a**, 67 mg, 0.20 mmol) and diyne **1b** (57 mg, 0.30 mmol) was obtained after chromatography (hexane–EtOAc 2:1, $R_F = 0.32$) 41 mg (62%) of **4b** as pale yellow amorphous solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, $J = 7.5$, 3 H, CH_3), 1.25–1.42 (m, 4 H, CH_2), 1.52–1.62 (m, 2 H, CH_2), 2.37 (t, $J = 7.2$, 2 H, C≡C–C**H**$_2$), 5.43 (s, 2 H, C**H**$_2$Ph), 7.27–7.37 (m, 5 H, Ph), 8.08 (s, 1 H, H-8), 8.92 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9 (CH_3), 19.6 (CH_2), 22.1 (CH_2), 27.6 (CH_2), 30.9 (CH_2), 47.4 (**C**H_2Ph), 64.9 (C≡C), 68.5 (C≡C), 83.4 (C≡C), 89.9 (C≡C), 127.8 (CH^{Ph}), 128.7 (CH^{Ph}), 129.2 (CH^{Ph}), 134.7, 135.1, 141.0, 145.2, 151.5, 152.7. IR (ATR): 3057 (w), 2928 (m), 2859 (w), 2233 (m), 1573 (s), 1496 (w), 1438 (w), 1402 (w), 1323 (m), 1212 (w), 1162 (w), 1142 (w), 1078 (w), 979 (w), 803 (w), 722 (w), 696 (w), 640 (w) cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{20}N_4Na$ 351.1586; found: 351.1572.

9-Benzyl-6-(5-dimethylaminopenta-1,3-diyn-1-yl)purine (4c). From 9-benzyl-6-iodopurine (**6a**, 67 mg, 0.20 mmol) and diyne **1c** (51 mg, 0.25 mmol) was obtained after chromatography (EtOAc–MeOH–Et_3N, 18:2:1, $R_F = 0.67$) 40 mg (64%) of **4c** as brown, waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 6 H, CH_3), 3.48 (s, 2 H, CH_2N), 5.44 (s, 2 H, C**H**$_2$Ph), 7.25–7.38 (m, 5 H, Ph), 8.09 (s, 1 H, H-8), 8.94 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 43.9 (CH_3), 47.4 (CH_2), 48.5 (CH_2), 69.5 (C≡C), 70.1 (C≡C), 82.1 (C≡C), 83.7 (C≡C), 127.8 (CH^{Ph}), 128.7 (CH^{Ph}), 129.1 (CH^{Ph}), 134.6 (C_q^{Ph}), 135.1 (C-5), 140.4 (C-6), 145.5 (C-8), 151.6 (C-4), 152.6 (C-2). IR (ATR): 3059 (w), 2938 (w), 2778 (w), 2233 (w), 1574 (s), 1496 (w), 1439 (w), 1402 (w), 1319 (m), 1247 (w), 1213 (w), 1142 (w), 1028 (w), 974 (w), 908 (w), 804 (w), 725 (m), 697 (w), 642 (w), 544 (w) cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{19}H_{17}N_5Na$ 338.1382; found 338.1381.

9-Benzyl-6-(5,5-diethoxypenta-1,3-diyn-1-yl)purine (4d). From 9-benzyl-6-iodopurine (**6a**, 168 mg, 0.50 mmol) and diyne **1d** (135 mg, 0.60 mmol) was obtained after chromatography (hexane–EtOAc 1:1, $R_F = 0.53$) 100 mg (55%) of **4d** as light brown, waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (t, $J = 7.2$, 6 H, CH_3), 3.58–3.84 (m, 4 H, CH_2), 5.39 (s, 1 H, C**H**$(OEt)_2$), 5.44 (s, 2 H, C**H**$_2$Ph), 7.27–7.38 (m, 5 H, Ph), 8.10 (s, 1 H, H-8), 8.96 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0 (CH_3), 47.5 (**C**H_2Ph), 61.4 (OCH_2), 69.0 (C≡C), 72.7 (C≡C), 80.8 (C≡C), 81.4 (C≡C), 91.4 (**C**$H(OEt)_2$), 127.9 (CH^{Ph}), 128.8 (CH^{Ph}), 129.2 (CH^{Ph}), 134.6 (C_q^{Ph}), 135.3 (C-5), 140.0 (C-6), 145.6 (C-8), 151.8 (C-4), 152.7 (C-2). IR (ATR): 3063 (w), 2977 (m), 2926 (m), 2159 (w), 1577 (s), 1491 (w), 1451 (m), 1395 (m), 1332 (s), 1242 (w), 1160 (m), 1101 (m), 1059 (s), 1014 (m), 978 (m), 912 (w), 802 (w), 724 (m), 699 (m), 644 (m), 540 (w) cm^{-1}. HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{20}N_4O_2Na$ 383.1484; found 383.1475.

9-Benzyl-6-(4-(1-methylimidazol-5-yl)buta-1,3-diyn-1-yl)purine (4e) *Modification: CsF (same molar amount) was used instead of TBAF.* From 9-benzyl-6-iodopurine (**6a**, 51 mg, 0.15 mmol) and diyne **1e** (30 mg, 0.15 mmol) was obtained after chromatography (EtOAc–MeOH 9:1, $R_F = 0.2$) 24 mg (47%) of **4e** as white powder, mp >160°C (dec.). ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 373 K): δ 3.75 (s, 3 H, CH_3), 5.47 (s, 2 H, CH_2), 7.28–7.45 (m, 5 H, Ph), 7.51 (s, 1 H, H-2′ or H-4′), 7.54 (s, 1 H, H-2′ or H-4′), 8.10 (s, 1 H, H-8), 9.00 (s, 1 H, H-2). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 373 K): δ 31.9 (CH_3), 47.3 (**C**H_2Ph), 77.7 (C≡C), 78.9 (C≡C), 81.17 (C≡C), 81.23 (C≡C), 114.6 (C-5′), 127.6 (CH^{Ph}), 128.5 (CH^{Ph}), 129.0 (CH^{Ph}), 134.5 (C-5 or C_q^{Ph}), 134.8 (C-5 or C_q^{Ph}), 138.4 (C-2′ or C-4′), 139.3 (C-2′ or C-4′), 140.0 (C-6), 145.2 (C-8), 151.8 (C-4), 152.6 (C-2). IR (ATR): 3348 (m), 3087 (w), 3042 (w), 2924 (w), 2210 (s), 1736 (w), 1680 (w), 1582 (s), 1546 (w), 1492 (m), 1438 (m), 1404 (m), 1367 (w), 1327 (m), 1278 (w), 1242 (w), 1225 (w), 1200 (m), 1119 (m), 1080 (w), 1058 (w), 967 (w), 938 (w), 902 (w), 858 (w), 843 (w), 802 (w), 774 (w), 735 (w), 700 (w) cm^{-1}. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{14}N_6$ 338.1280; found 338.1288.

5-(9-Benzylpurin-6-yl)penta-2,4-diyn-1-yl acetate (4f). From 9-benzyl-6-iodopurine (**6a**, 168 mg, 0.50 mmol) and diyne **1f** (97 mg, 0.50 mmol) was obtained after chromatography (hexane–EtOAc 1:1, $R_F = 0.34$) 90 mg (54%) of **4f** as yellow waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.12 (s, 3 H, CH_3), 4.83 (s, 2 H, C**H**$_2$OAc), 5.44 (s, 2 H, C**H**$_2$Ph), 7.28–7.39 (m, 5 H, Ph), 8.10 (s, 1 H, H-8), 8.96 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.6 (CH_3), 47.5 (**C**H_2Ph), 52.2 (OCH_2), 70.4 (C≡C), 72.4 (C≡C), 80.4 (C≡C), 81.0 (C≡C), 127.9 (CH^{Ph}), 128.8 (CH^{Ph}), 129.2 (CH^{Ph}), 134.6 (C_q^{Ph}), 135.3 (C-5), 140.0 (C-6), 145.6 (C-8), 151.8 (C-4), 152.8 (C-2), 169.9 (C=O). IR (ATR): 3104 (w), 3033 (w), 2923 (w), 2851 (w), 2242 (w), 2164 (w), 1742 (s), 1578 (s), 1491 (m), 1457 (w), 1445 (w), 1427 (w), 1399 (m), 1367 (m), 1358 (m), 1323 (s), 1249 (m), 1214 (m), 1168 (m), 1078 (w), 1016 (m), 982 (m), 903 (w), 883 (w), 825 (w), 732 (m), 697 (w), 641 (m), 595 (w), 549 (w), 526 (w), 459 (w), 417 (w) cm^{-1}. HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{19}H_{15}N_4O_2$ 331.1195; found 331.1189.

9-(O,O,O-Triacetyl-β-D-ribofuranosyl)-6-(4-phenylbuta-1,3-diyn-1-yl)purine (5a). From 9-(*O*,*O*,*O*-triacetyl-β-D-ribofuranosyl)-6-iodopurine (**6b**, 106 mg, 0.21 mmol) and diyne **1a** (50 mg,

0.25 mmol) was obtained after chromatography (hexane–EtOAc 1:1, $R_F = 0.29$) 92 mg (87%) of **5a** as pale yellow waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.07 (s, 3 H, $COCH_3$), 2.11 (s, 3 H, $COCH_3$), 2.14 (s, 3 H, $COCH_3$), 4.35–4.50 (m, 3 H, 2 × H-5′ + H-4′), 5.65 (t, $J = 4.7$, 1 H, H-3′), 5.95 (t, $J = 5.3$, 1 H, H-2′), 6.24 (d, $J = 5.3$, 1 H, H-1′), 7.30–7.46 (m, 3 H, Ph), 7.54–7.60 (m, 2 H, Ph), 8.31 (s, 1 H, H-8), 8.95 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3 ($CO\mathbf{C}H_3$), 20.5 ($CO\mathbf{C}H_3$), 20.7 ($CO\mathbf{C}H_3$), 62.9 (C-5′), 70.5 (C-3′), 73.0 (C-2′), 73.3 (C≡C), 74.9 (C≡C), 80.4 (C-4′), 83.0 (C≡C), 86.1 (C≡C), 86.5 (C-1′), 120.7 (C_q^{Ph}), 128.5 (CH^{Ph}), 130.1 (CH^{Ph}), 132.8 (CH^{Ph}), 135.9 (C-5), 141.1 (C-6), 143.9 (C-8), 151.1 (C-4), 152.9 (C-2), 169.3 (C=O), 169.5 (C=O), 170.2 (C=O). IR (ATR): 2921 (w), 2850 (w), 2213 (m), 1744 (s), 1575 (s), 1490 (w), 1438 (m), 1370 (m), 1321 (w), 1202 (s), 1151 (m), 1090 (m), 1063 (m), 1003 (m), 951 (w), 915 (w), 860 (w), 785 (w), 762 (w), 729 (w), 690 (w), 634 (w), 532 (w), 470 cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{26}H_{22}N_4O_7Na$ 525.1386; found 525.1369.

9-(O,O,O-Triacetyl-β-D-ribofuranosyl)-6-(nona-1,3-diyn-1-yl)purine (5b). From 9-(O,O,O-triacetyl-β-D-ribofuranosyl)-6-iodopurine (**6b**, 88 mg, 0.18 mmol) and diyne **1b** (40 mg, 0.21 mmol) was obtained after chromatography (hexane–EtOAc 1:1, $R_F = 0.47$) 51 mg (59%) of **5b** as colorless waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, $J = 7.0$, 3 H, $CH_2C\mathbf{H}_3$), 1.24–1.44 (m, 4 H, CH_2), 1.57 (m, 2 H, CH_2), 2.05 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 2.12 (s, 3 H, $COCH_3$), 2.38 (t, $J = 7.0$, 2 H, C≡C–CH_2), 4.32–4.48 (m, 3 H, 2 × H-5′ + H-4′), 5.63 (t, $J = 5.3$, 1 H, H-3′), 5.93 (t, $J = 5.3$, 1 H, H-2′), 6.21 (d, $J = 5.3$, 1 H, H-1′), 8.26 (s, 1 H, H-8), 8.96 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8 ($CH_2\mathbf{C}H_3$), 19.6 (CH_2), 20.3 ($CO\mathbf{C}H_3$), 20.4 ($CO\mathbf{C}H_3$), 20.7 ($CO\mathbf{C}H_3$), 22.0 (CH_2), 27.5 (CH_2), 30.9 (CH_2), 62.8 (C-5′), 64.7 (C≡C), 68.2 (C≡C), 70.4 (C-3′), 73.0 (C-2′), 80.4 (C-4′), 83.8 (C≡C), 86.4 (C-1′), 90.3 (C≡C), 135.8 (C-5), 141.5 (C-6), 143.7 (C-8), 151.0 (C-4), 152.7 (C-2), 169.2 (C=O), 169.5 (C=O), 170.2 (C=O). IR (ATR): 2930 (w), 2860 (w), 2235 (m), 1744 (s), 1576 (s), 1493 (w), 1440 (w), 1369 (w), 1330 (w), 1209 (s), 1093 (w), 1045 (m), 900 (w), 804 (w), 638 (w), 595 (w) cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{25}H_{28}N_4O_7Na$ 519.1856; found 519.1840.

9-(O,O,O-Triacetyl-β-D-ribofuranosyl)-6-(5-dimethylamino penta-1,3-diyn-1-yl)purine (5c). From 9-(*O*,*O*,*O*-triacetyl-β-D-ribofuranosyl)-6-iodopurine (**6b**, 202 mg, 0.40 mmol) and diyne **1c** (90 mg, 0.5 mmol) was obtained after chromatography (EtOAc–MeOH–Et_3N, 40:2:1, $R_F = 0.45$) 136 mg (70%) of **5c** as unstable brown wax. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.98 (s, 3 H, $COCH_3$), 2.02 (s, 3 H, $COCH_3$), 2.06 (s, 3 H, $COCH_3$), 2.25 (s, 6 H, $N(CH_3)_2$), 3.40 (s, 2 H, CH_2N), 4.24–4.43 (m, 3 H, 2 × H-5′ + H-4′), 5.57 (t, $J = 5.1$, 1 H, H-3′), 5.87 (t, $J = 5.3$, 1 H, H-2′), 6.16 (d, $J = 5.1$, 1 H, H-1′), 8.25 (s, 1 H, H-8), 8.84 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.1 ($CO\mathbf{C}H_3$), 20.3 ($CO\mathbf{C}H_3$), 20.5 ($CO\mathbf{C}H_3$), 43.8 (NCH_3), 48.3 (NCH_2), 62.7 (C-5′), 69.2 (C≡C), 69.7 (C≡C), 70.2 (C-3′), 72.8 (C-2′), 80.2 (C-4′), 82.3 (C≡C), 84.0 (C≡C), 86.3 (C-1′), 135.7 (C-5), 140.8 (C-6), 143.9 (C-8), 150.9 (C-4), 152.5 (C-2), 169.1 (C=O), 169.3 (C=O), 170.0 (C=O). IR (ATR): 2943 (w), 2826 (w), 2780 (w), 2232 (w), 2150 (w), 1743 (s), 1576 (s), 1493 (w), 1439 (w), 1405 (w), 1369 (m), 1329 (w), 1210 (s), 1095 (m), 1041 (m), 906 (w), 804 (w), 730 (w), 639 (w), 601 (w) cm^{-1}. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{26}N_5O_7$ 484.1832; found 484.1824.

9-(O,O,O-Triacetyl-β-D-ribofuranosyl)-6-(5,5-diethoxypenta-1,3-diyn-1-yl)purine (5d). From 9-(*O*,*O*,*O*-triacetyl-β-D-ribofuranosyl)-6-iodopurine (**6b**, 160 mg, 0.32 mmol) and diyne **1d** (85 mg, 0.38 mmol) was obtained after chromatography (EtOAc–hexane 1:1) 127 mg (76%) of **5d** as colorless waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.23 (t, $J = 7.2$, CH_3), 2.06 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$), 2.13 (s, 3 H, $COCH_3$), 3.57–3.81 (m, 4 H, CH_2), 4.32–4.48 (m, 3 H, 2 × H-5′ + H-4′), 5.38 (s, 1 H, $C\mathbf{H}(OEt)_2$), 5.63 (t, $J = 5.1$, 1 H, H-3′), 5.93 (t, $J = 5.4$, 1 H, H-2′), 6.22 (d, $J = 5.3$, 1 H, H-1′), 8.28 (s, 1 H, H-8), 8.93 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0 ($CH_2\mathbf{C}H_3$), 20.3 ($CO\mathbf{C}H_3$), 20.5 ($CO\mathbf{C}H_3$), 20.7 ($CO\mathbf{C}H_3$), 61.4 ($\mathbf{C}H_2CH_3$), 62.8 (C-5′), 68.8 (C≡C), 70.4 (C-3′), 72.4 (C≡C), 73.0 (C-2′), 80.4 (C-4′), 81.2 (C≡C), 81.8 (C≡C), 86.5 (C-1′), 91.4 ($\mathbf{C}H(OEt)_2$), 136.0 (C-5), 140.5 (C-6), 144.1 (C-8), 151.2 (C-4), 152.8 (C-2), 169.3 (C=O), 169.5 (C=O), 170.2 (C=O). IR (ATR): 2978 (w), 2934 (w), 2158 (w), 1754 (s), 1581 (m), 1493 (w), 1441 (w), 1404 (w), 1371 (w), 1331 (w), 1220 (s), 1140 (w), 1087 (m), 1050 (m), 902 (w), 804 (w) cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{25}H_{28}N_4O_9Na$ 551.1754; found 551.1742.

9-(O,O,O-Triacetyl-β-D-ribofuranosyl)-6-(4-(1-methylimidazol-5-yl)buta-1,3-diyn-1-yl)purine (5e). From 9-(*O*,*O*,*O*-triacetyl-β-D-ribofuranosyl)-6-iodopurine (**6b**, 160 mg, 0.32 mmol) and diyne **1e** (64 mg, 0.32 mmol) was obtained after chromatography (EtOAc–MeOH 20:1) 115 mg (72%) of **5e** as yellow waxy solid. ^{1}H NMR (500 MHz, $C_2D_2Cl_4$, 373 K): δ 2.09 (s, 3 H, $CO\mathbf{C}H_3$), 2.11 (s, 3 H, $CO\mathbf{C}H_3$), 2.17 (s, 3 H, $CO\mathbf{C}H_3$), 3.76 (s, 3 H, NCH_3), 4.38–4.50 (m, 3 H, 2 × H-5′ + H-4′), 5.66 (m, 1 H, H-3′), 5.99 (m, 1 H, H-2′), 6.25 (d, $J = 5.1$, 1 H, H-1′), 7.53 (s, 1 H, H-2″ or H-4″), 7.58 (s, 1 H, H-2″ or H-4″), 8.30 (s, 1 H, H-8), 8.97 (s, 1 H, H-2). ^{13}C NMR (125 MHz, $C_2D_2Cl_4$, 373 K): δ 19.9 ($CO\mathbf{C}H_3$), 20.0 ($CO\mathbf{C}H_3$), 20.2 ($CO\mathbf{C}H_3$), 32.0 (NCH_3), 62.6 (C-5′), 70.5 (C-3′), 72.8 (C-2′), 78.6 (C≡C), 80.5 (C-4′), 81.2 (C≡C), 81.7 (C≡C), 86.6 (C-1′), 114.4 (C-5″), 135.4 (C-5), 138.5 (C-2″ or C-4″), 139.3 (C-2″ or C-4″), 140.5 (C-6), 143.9 (C-8), 151.2 (C-4), 152.6 (C-2), 168.9 (C=O), 169.1 (C=O), 169.7 (C=O). IR (ATR): 3114 (w), 2949 (w), 2208 (m), 1745 (s), 1578 (s), 1539 (w), 1491 (w), 1439 (w), 1405 (w), 1373 (w), 1332 (w), 1242 (s), 1122 (m), 1098 (w), 1050 (m), 927 (w), 857 (w), 824 (w), 804 (w), 732 (w) cm^{-1}. HRMS (EI): m/z $[M]^+$ calcd for $C_{24}H_{22}N_6O_7$ 506.1550; found 506.1556.

5-(9-(O,O,O-Triacetyl-β-D-ribofuranosyl)purin-6-yl)penta-2,4-diyn-1-yl acetate (5f). From 9-(*O*,*O*,*O*-triacetyl-β-D-ribofuranosyl)-6-iodopurine (**6b**, 101 mg, 0.20 mmol) and diyne **1f** (50 mg, 0.26 mmol) was obtained after chromatography (EtOAc–hexane 2:1, $R_F = 0.57$) 69 mg (69%) of **5f** as pale yellow waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.07 (s, 3 H, $COCH_3$), 2.11 (s, 3 H, $COCH_3$), 2.12 (s, 3 H, $COCH_3$), 2.14 (s, 3 H, $COCH_3$), 4.33–4.49 (m, 3 H, 2 × H-5′ + H-4′), 4.83 (s, 2 H, C≡C–CH_2), 5.64 (t, $J = 5.1$, 1 H, H-3′), 5.94 (t, $J = 5.3$, 1 H, H-2′), 6.22 (d, $J = 5.0$, H-1′), 8.28 (s, 1 H, H-8), 8.94 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4 ($CO\mathbf{C}H_3$), 20.5 ($CO\mathbf{C}H_3$), 20.6 ($CO\mathbf{C}H_3$), 20.7 ($CO\mathbf{C}H_3$), 52.2 (C≡C–CH_2), 62.9 (C-5′), 70.3 (C≡C), 70.5 (C-3′), 72.0 (C≡C), 73.0 (C-2′), 80.5 (C-4′), 80.8 (C≡C), 81.5 (C≡C), 86.6 (C-1′), 136.0 (C-5), 140.6 (C-6), 144.1 (C-8), 151.2 (C-4), 152.8 (C-2), 169.3 (C=O), 169.5 (C=O), 169.9 (C=O), 170.2 (C=O). IR (ATR): 2939 (w), 2243 (w), 2162 (w), 1739 (s), 1577 (m), 1492 (w), 1429 (w), 1372 (w), 1332 (w), 1209 (s), 1144 (w), 1093 (w), 1029 (m), 909 (w), 804 (w), 730 (w), 638 (w) cm^{-1}. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{23}H_{22}N_4O_9Na$ 521.1284; found 521.1276.

General procedure of methanolysis of ribosides 5a–f and diynyl acetate **4f**. Acetylated riboside **5a–f** (acetate **4g**) was dissolved in dry MeOH (5 mL per mmol), then MeONa (0.1 eq.,

as 0.1*M* solution in MeOH) was added and the reaction mixture was stirred at room temperature until the conversion was complete (TLC). Subsequently, AcOH (0.15 eq., as 0.1*M* solution in MeOH) was added, and after evaporation of the volatiles, the residue was chromatographed.

9-β-D-Ribofuranosyl-6-(4-phenylbuta-1,3-diyn-1-yl)purine (7a). From **5a** (51 mg, 0.10 mmol) was obtained after chromatography (EtOAc–MeOH 20:1, R_F = 0.43) 33 mg (86%) of **7a** as beige amorphous powder. ^{1}H NMR (300 MHz, DMSO): δ 3.53–3.63 (m, 1 H, H-5′), 3.64–3.74 (m, 1 H, H-5′), 3.98 (m, 1 H, H-4′), 4.19 (m, 1 H, H-3′), 4.60 (m, 1 H, H-2′), 5.09 (t, *J* = 5.3, 1 H, OH-5′), 5.25 (d, *J* = 5.3, 1 H, OH), 5.56 (d, *J* = 5.9, 1 H, OH), 6.04 (d, *J* = 5.3, 1 H, H-1′), 7.42–7.57 (m, 3 H, Ph), 7.68–7.73 (m, 2 H, Ph), 8.96 (s, 2 H, H-8 + H-2). ^{13}C NMR (75 MHz, DMSO): δ 61.3, 70.3, 72.7, 74.1, 76.3, 80.4, 85.8, 85.9, 88.1, 119.6, 129.3, 131.1, 133.1, 135.8, 138.6, 146.7, 151.7, 152.5. IR (ATR): 3626 (w), 3296 (m), 3091 (m), 3055 (m), 2936 (m), 2212 (s), 1580 (s), 1494 (w), 1450 (m), 1443 (m), 1409 (w), 1389 (w), 1329 (m), 1211 (m), 1130 (w), 1095 (m), 1064 (m), 1025 (w), 983 (w), 950 (w), 866 (w), 852 (w), 809 (w), 762 (w), 687 (w), 636 (w), 593 (w), 528 (w), 475 (w) cm^{-1}. HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{20}H_{16}N_4O_4Na$ 399.1069; found 399.1055.

9-β-D-Ribofuranosyl-6-(nona-1,3-diyn-1-yl)purin (7b). From **5b** (32 mg, 0.064 mmol) was obtained after chromatography (EtOAc–MeOH 9:1, R_F = 0.58) 18 mg (75%) of **7b** as white amorphous powder. ^{1}H NMR (300 MHz, DMSO): δ 0.87 (t, *J* = 7.0, 3 H, CH_3), 1.26–1.42 (m, 4 H, CH_2), 1.50–1.60 (m, 2 H, CH_2), 2.51 (t, *J* = 7.0, 2 H, C≡C–CH_2), 3.51–3.61 (m, 1 H, H-5′), 3.63–3.73 (m, 1 H, H-5′), 3.96 (m, 1 H, H-4′), 4.17 (m, 1 H, H-3′), 4.58 (m, 1 H, H-2′), 5.09 (t, *J* = 5.3, 1 H, OH-5′), 5.25 (d, *J* = 5.0, 1 H, OH), 5.56 (d, *J* = 5.6, 1 H, OH), 6.01 (d, *J* = 5.3, 1 H, H-1′), 8.91 (s, 1 H, H-2 or H-8), 8.92 (s, 1 H, H-2 or H-8). ^{13}C NMR (75 MHz, DMSO): δ 14.0, 19.0, 21.8, 27.2, 30.7, 61.3, 64.2, 69.5, 70.3, 74.0, 81.4, 85.9, 88.0, 91.0, 135.8, 139.1, 146.5, 151.6, 152.4. IR (ATR): 3285 (s), 2927 (s), 2858 (s), 2233 (s), 1578 (s), 1492 (w), 1444 (m), 1403 (m), 1329 (m), 1211 (m), 1093 (m), 1058 (m), 981 (w), 866 (w), 802 (w), 724 (w), 637 (w), 593 (w) cm^{-1}. HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{19}H_{22}N_4O_4Na$ 393.1539; found 393.1534.

9-β-D-Ribofuranosyl-6-(5-(dimethylamino)penta-1,3-diynyl) purine (7c). From **5c** (107 mg, 0.22 mmol) was obtained after chromatography (EtOAc–MeOH–Et_3N 18:2:1) 66 mg (83%) of **7c** as unstable light brown waxy solid. ^{1}H NMR (300 MHz, DMSO): δ 2.23 (s, 6 H, $N(CH_3)_2$), 3.50–3.76 (m, 2 H, H-5′), 3.97 (m, 1 H, H-4′), 4.18 (m, 1 H, H-3′), 4.58 (m, 1 H, H-2′), 5.2 (br s, 3 H, 3 × OH), 6.02 (d, *J* = 5.1, 1 H, H-1′), 8.93 (s, 1 H, H-2 or H-8), 8.94 (s, 1 H, H-2 or H-8). ^{13}C NMR (75 MHz, DMSO): δ 44.3, 48.4, 61.7, 69.0, 70.8, 71.3, 74.5, 81.0, 86.0, 86.4, 88.5, 136.3, 139.2, 147.1, 152.1, 152.9. IR (ATR): 3268 (m), 3104 (m), 2924 (m), 2871 (m), 2783 (m), 2234 (w), 2149 (w), 1641 (w), 1576 (s), 1491 (m), 1441 (m), 1400 (m), 1327 (m), 1257 (w), 1211 (m), 1110 (m), 1082 (m), 1053 (m), 978 (w), 893 (w), 863 (w), 838 (w), 803 (w), 744 (w), 705 (w), 639 (w), 556 (w), 477 (w) cm^{-1}. HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{19}N_5O_4Na$ 380.1335; found 380.1324.

9-β-D-Ribofuranosyl-6-(5,5-diethoxypenta-1,3-diyn-1-yl)purine (7d). From **5d** (71 mg, 0.13 mmol) was obtained after chromatography (EtOAc–MeOH 9:1) 47 mg (87%) of **7d** as pale yellow waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (dt, *J* = 1.8, 7.2, 6 H, CH_3), 3.57–3.82 (m, 5 H), 3.94 (m, 1 H), 4.11 (m, 1 H), 4.31 (m, 1 H), 4.51 (d, *J* = 4.1, 1 H), 4.97 (m, 1 H), 5.22 (m, 2 H), 5.40 (s, 1 H, C**H**$(OEt)_2$), 6.00 (d, *J* = 6.4, 1 H, H-1′), 8.43 (s, 1 H, H-8), 8.76 (s, 1 H, H-2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.0, 61.7, 62.7, 68.5, 71.8, 72.0, 74.1, 82.2, 82.7, 87.3, 90.9, 91.4, 136.1, 139.9, 146.3, 150.3, 151.9. IR (ATR): 3312 (s), 3107 (m), 2976 (m), 2929 (m), 2886 (m), 2241 (w), 2155 (w), 1579 (s), 1492 (m), 1443 (m), 1400 (m), 1328 (m), 1256 (w), 1211 (m), 1179 (w), 1114 (m), 1080 (s), 1044 (s), 977 (m), 899 (m), 864 (w), 802 (w), 740 (w), 702 (w), 636 (w), 596 (w), 551 (w), 494 (w) cm^{-1}. HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{19}H_{22}N_4O_6Na$ 425.1437; found 425.1431.

9-β-D-Ribofuranosyl-6-(4-(1-methylimidazol-5-yl)buta-1,3-diyn-1-yl)purin (7e). From **5e** (45 mg, 0.09 mmol) was obtained after chromatography (EtOAc–MeOH 9:1) 32 mg (95%) of **7e** as pale yellow amorphous solid. ^{1}H NMR (DMSO, 373 K): δ 3.61–3.66 (m, 1 H, H-5′), 3.71–3.74 (m, 1 H, H-5′), 3.75 (s, 3 H, CH_3), 4.01–4.06 (m, 1 H, H-4′), 4.23–4.27 (m, 1 H, H-3′), 4.62–4.66 (m, 1 H, H-2′), 6.07 (d, *J* = 5.2, 1 H, H-1′), 7.58 (s, 1 H, H-4″), 7.82 (s, 1 H, H-2″), 8.87 (s, 1 H, H-8), 8.94 (s, 1 H, H-2). ^{13}C NMR (DMSO, 373 K): δ 31.5 (CH_3), 60.9 (C-5′), 69.9 (C-3′), 73.6 (C-2′), 73.8 (C≡C), 78.9 (C≡C), 79.7 (C≡C), 79.8 (C≡C), 85.5 (C-4′), 87.9 (C-1′), 113.4 (C-5″), 135.5 (C-5), 138.2 (C-6), 138.4 (C-4″), 140.6 (C-2″), 145.9 (C-8), 151.7 (C-2 or C-4), 151.9 (C-2 or C-4). IR (ATR): 3110 (s), 3091 (s), 2925 (m), 2871 (m), 2214 (s), 1882 (w), 1758 (w), 1678 (w), 1584 (s), 1545 (w), 1493 (m), 1461 (m), 1439 (m), 1418 (m), 1400 (m), 1331 (s), 1277 (m), 1253 (m), 1223 (s), 1201 (s), 1178 (m), 1124 (s), 1079 (s), 1059 (s), 941 (w), 901 (w), 857 (m), 840 (w), 803 (w), 736 (w), 709 (w), 686 (w) cm^{-1}. HRMS (EI): *m/z* $[M]^+$ calcd for $C_{18}H_{16}N_6O_4$ 380.1233; found 380.1236.

5-(9-β-D-Ribofuranosylpurin-6-yl)penta-2,4-diyn-1-ol (7g). From **5f** (75 mg, 0.15 mmol) was obtained after chromatography (EtOAc–MeOH 20:1, R_F = 0.20) 44 mg (89%) of **7g** as white amorphous solid. ^{1}H NMR (300 MHz, DMSO): δ 3.54–3.75 (m, 2 H, H-5′), 3.97 (m, 1 H, H-5′), 4.18 (m, 1 H, H-4′), 4.34 (d, *J* = 6.2, 2 H, C≡C–CH_2), 4.58 (m, 1 H, H-3′), 5.09 (t, *J* = 5.3, OH-5′), 5.24 (d, *J* = 5.3, 1 H, OH), 5.56 (d, *J* = 5.9, 1 H, OH), 5.63 (t, *J* = 6.4, 1 H, OH), 6.03 (d, *J* = 5.3, 1 H, H-1′), 8.94 (s, 1 H, H-2 or H-8), 8.942 (s, 1 H, H-2 or H-8). ^{13}C NMR (75 MHz, DMSO): δ 49.8 (C≡C–**C**H_2), 61.2 (C-5′), 67.3 (C≡C), 70.3 (C-3′), 72.1 (C≡C), 74.1 (C-2′), 80.3 (C≡C), 85.9 (C-4′), 88.0 (C-1′), 88.6 (C≡C), 135.8 (C-5), 138.7 (C-6), 146.6 (C-8), 151.7 (C-4), 152.4 (C-2). IR (ATR): 3273 (s), 3104 (s), 2923 (m), 2237 (m), 2153 (w), 1730 (w), 1580 (s), 1491 (m), 1445 (m), 1402 (m), 1330 (m), 1256 (w), 1211 (m), 1111 (m), 1081 (m), 1056 (m), 1025 (m), 979 (m), 892 (w), 864 (w), 815 (w), 802 (w), 748 (w), 706 (w), 635 (w), 595 (w), 535 (w), 471 (w) cm^{-1}. HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{15}H_{14}N_4O_5Na$ 353.0862; found 353.0859.

5-(9-Benzylpurin-6-yl)penta-2,4-diyn-1-ol (4g). From **4f** (66 mg, 0.2 mmol) was obtained after chromatography (EtOAc) 52 mg (90%) of **4g** as white powder, mp >150°C (dec.). ^{1}H NMR (300 MHz, DMSO) δ 4.33 (d, *J* = 6.2, 2 H, C**H**$_2$OH), 5.50 (s, 2 H, C**H**$_2$Ph), 5.63 (t, *J* = 6.2, 1 H, OH), 7.22–7.36 (m, 5 H, Ph), 8.84 (s, 1 H, H-2 or H-8), 8.91 (s, 1 H, H-2 or H-8). ^{13}C NMR (75 MHz, DMSO) δ 46.9 (**C**H_2Ph), 49.8 (CH_2OH), 67.3 (C≡C), 72.2 (C≡C), 80.1 (C≡C), 88.4 (C≡C), 127.9 (CH^{Ph}), 128.2 (CH^{Ph}), 129.0 (CH^{Ph}), 135.3 (C-5), 136.3 (C_q^{Ph}), 138.5 (C-6), 148.4 (C-8), 151.8 (C-4), 152.4 (C-2). IR (ATR): 3193 (m), 3065 (m), 2925 (w), 2852 (w), 2229 (m), 1577 (s), 1499 (m), 1450 (m), 1431 (m), 1403 (m), 1333 (m), 1321 (m), 1249 (m), 1217 (m), 1166 (m), 1031 (m), 983 (m), 963 (w), 884 (w), 804 (w), 731 (m), 694 (m), 639 (m), 596 (w), 552 (w), 537 (w), 455 (w) cm^{-1}. HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{12}N_4ONa$ 311.0909; found 311.0917.

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