COVALENT ANALOGUES OF DNA BASE-PAIRS AND TRIPLETS V+. SYNTHESIS OF PURINE-PURINE AND PURINE-PYRIMIDINE CONJUGATES CONNECTED BY DIVERSE TYPES OF ACYCLIC CARBON LINKAGES

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Dedicated to the memory of Professor Miloš Hudlický.

The title 1,2-bis(purin-6-yl)acetylenes, -diacetylenes, -ethylenes and -ethanes were prepared as covalent base-pair analogues starting from 6-ethynylpurines and 6-iodopurines by the Sonogashira cross-coupling or oxidative alkyne-dimerization reactions followed by hydrogenations. 6-[(1,3-Dimethyluracil-5-yl)ethynyl]purine (**11**) was prepared analogously and hydrogenated to the corresponding purine-pyrimidine conjugates linked *via* vinylene and ethylene linkers. Unlike the cytostatic bis(purin-6-yl)acetylenes and -diacetylenes, the purine-pyrimidine conjugates were inactive. Crystal structures of bis(purin-6-yl)acetylene **6a**, -diacetylene **8a** and -ethane **5a** were determined by single-crystal X-ray diffraction.

Keywords: Purines; Pyrimidines; Nucleobases; Alkynes; Cross-coupling reactions; Nucleosides; Sonogashira reaction; Hydrogen bonds.

The effect of many clinically used antitumor agents is based on DNA cross-linking[1] or on intercalation[2] to DNA. Numerous models and analogues of Watson–Crick base pairs consisting of annelated[3] or cross-linked[4] purine and pyrimidine heterocycles or even more simple aromatic rings[5,6] have been prepared. Such base-pairs analogues may interact with DNA (*e.g.* by intercalation); if incorporated into single stranded DNA, they are comple-

+ For Part IV, see ref.[17]

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mentary to abasic site of a damaged DNA strand; or, alternatively, if incorporated to duplex, they form permanent cross-links.

A number of diverse purine-purine conjugates containing linkage (9-9, 8-8, 9-8, 9-7, 9-6 and 6-6) of various lengths, including double- and triple-linked purinophanes, have been prepared[7] in order to study the π-π stacking of purine bases. A variety of N^6,$N^{6'}$-linked adenine-adenine dimers, trimers and tetramers with linkers of various lengths were prepared[8]; they exhibited diverse types of biological activity (inhibition of adenosine kinase, ribosomal peptidyltransferase, *etc.*).

Purines bearing carbon substituents in positions 2 or 6 possess a broad spectrum of biological activities. Thus 6-methylpurine is highly cytotoxic[9], while 2-alkynyladenosines are an important class of adenosine receptors agonists[10]. Recently, a cytokinin and antioxidant activity of 6-(arylalkynyl)-, 6-(arylalkenyl)- and 6-(arylalkyl)purines[11], a cytostatic activity of 6-(trifluoromethyl)purine riboside[12] and of 6-arylpurine ribonucleosides[13], a corticotropin-releasing hormone antagonist activity of some 2,8,9-trisubstituted 6-arylpurines[14] and an antimicrobial activity of 9-benzyl-6-arylpurines[15] were also reported.

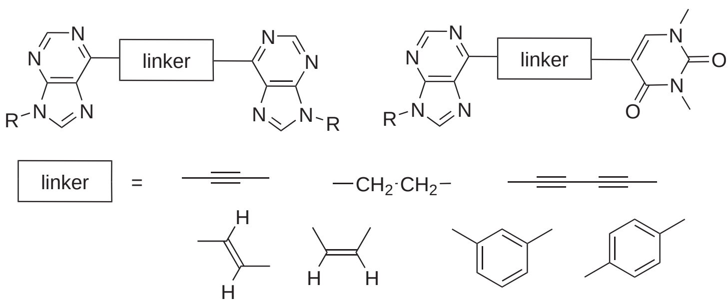


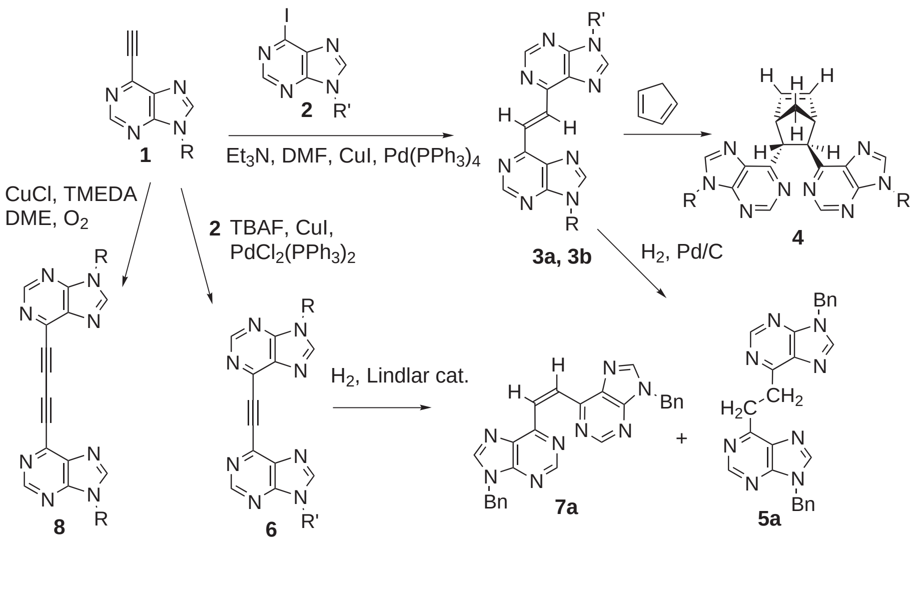
CHART 1

A combination of the unique structural features of the above mentioned classes of compounds led us to the design of a new group of base-pair and triplet analogues (Chart 1) based on conjugates of two or three purine and/or pyrimidine bases connected with diverse carbon linkages. Such carbon linkers connected to carbon atoms of the heterocycles were expected to be stable towards enzymatic degradation. Tris(purin-6-yl)- and tris-(pyrimidin-5-yl)benzenes were prepared[16,17] as triplet analogues by cyclotrimerization of 6-ethynylpurines or 6-ethynylpyrimidines. Bis(purin-6-yl)benzenes as well as (purin-6-yl)(pyrimidin-5-yl)benzenes were recently prepared by double cross-coupling of phenylenebis(stannanes)[18]. Very recently, we have reported a preliminary communication on purine dimers linked through positions 6 and 6′ by acetylene, diacetylene, vinylene and ethylene[19] linkers. A significant cytostatic activity has been found in some bis(purin-6-yl)acetylenes and diacetylenes[19], while the partially and fully saturated derivatives, as well as the phenylene-linked analogues were inactive. In this full-paper, the synthesis of the cytostatic purine-purine dimers linked by acyclic carbon chains is given in full detail and the study is extended to analogous purine-pyrimidine conjugates.

RESULTS AND DISCUSSION

Chemistry

The synthesis of the target compounds was based on standard acetylene chemistry (Scheme 1) using 9-benzyl-6-ethynylpurine[17] (**1a**) as a key starting compound. The attempted Sonogashira reaction of this compound with



1, 2 and 8	R (or R')
a	benzyl
b	tetrahydropyran-2-yl
c	pentyl

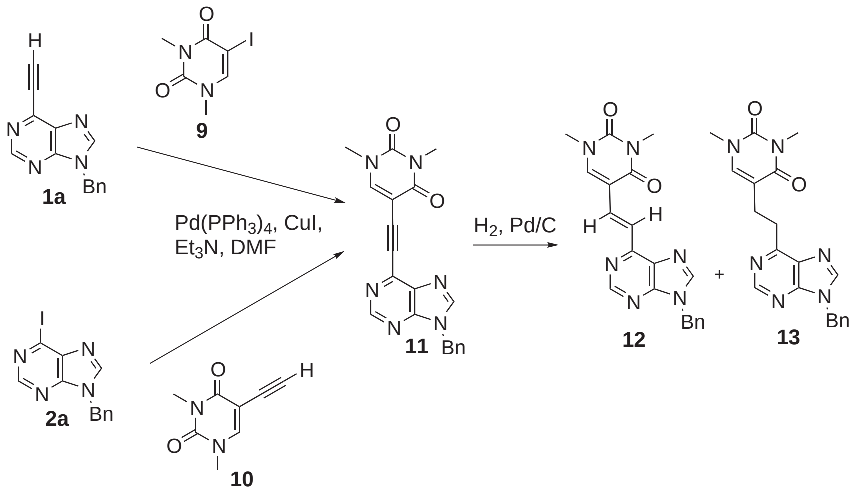
3 and 6	R	R'
a	benzyl	benzyl
b	tetrahydropyran-2-yl	benzyl
c	pentyl	pentyl

SCHEME 1

9-benzyl-6-iodopurine (**2a**) in the presence of CuI, $Pd(PPh_3)_4$ and Et_3N in DMF did not give the expected bis(purin-6-yl)acetylene **6a** but its partly reduced ethylene derivative **3a** in 27% yield. The formation of this product could be explained by a reductive addition[20] of the iodopurine **2a** on the acetylene **1a**. The presence of triethylamine and catalytic amounts of CuI and $Pd(PPh_3)_4$ is crucial for this reaction, while in the absence of DMF the reaction proceeds with lower conversion (probably due to low solubility of starting compounds in Et_3N). Therefore, though the mechanism has not been studied thoroughly, we suppose that triethylamine might be the reducing agent responsible for the formation of the disubstituted ethylene. Analogously, 6-iodo-9-THP-purine (**2b**) and 9-benzyl-6-ethynylpurine (**1a**) gave under the same conditions the heterodisubstituted ethylene **3b**. In order to determine the configuration of the compound **3a** (*vide infra*), its cycloaddition with cyclopentadiene has been performed to give the cycloadduct **4**. Catalytic hydrogenation of the ethylene derivative **3a** on Pd/C gave the fully saturated ethane derivative **5a** in a good yield of 80%.

For the synthesis of the acetylene derivative **6a**, an alternative method based on a recently published procedure[21] has been used. The reaction of the 6-iodopurine **2a** with the terminal acetylene **1a** was performed in the presence of tetrabutylammonium fluoride (TBAF) as base, catalytic amounts of CuI and $PdCl_2(PPh_3)_2$ in THF at room temperature to give the desired acetylene **6a** in a good yield of 57%. This approach has also been used for the synthesis of other related symmetrically and asymmetrically disubstituted acetylenes **6b** and **6c** differing by the substituents in positions 9 and 9′, starting from the appropriate iodopurines **2a** and **2c** and ethynylpurines **1b** and **1c**. Catalytic hydrogenation of the acetylene **6a** on Lindlar catalyst afforded the complementary (*Z*)-ethylene derivative **7a** in a low yield of 11% accompanied by the fully saturated compound **5a** (19%). Oxidative homo-coupling[22] of the terminal acetylenes **1a**–**1c** in the presence of CuCl and TMEDA [23] afforded 1,4-bis(purin-6-yl)diacetylenes **8a**–**8c** in good yields of 50–60%.

Unlike with 6-iodopurines, the Sonogashira reaction of 6-ethynylpurine **1a** with 5-iodo-1,3-dimethyluracil (**9**) under standard conditions (CuI, $Pd(PPh_3)_4$ and Et_3N in DMF at 120 °C) gave the expected disubstituted acetylene **11** in 68% yield (Scheme 2). The same product was alternatively prepared in 70% yield by cross-coupling of 5-ethynyl-1,3-dimethyluracil (**10**) with 9-benzyl-6-iodopurine (**2a**). Due to much easier access to 6-ethynylpurines than to 5-ethynyluracil, the former approach is more practical. The acetylene **11** was subjected to catalytic hydrogenation on Pd/C. Due to low solubility of the starting compound, the reaction was sluggish and even after 5 days the conversion was not complete. Nevertheless, from the reaction mixture, (*E*)-ethylene **12** and fully saturated ethane **13** derivatives were isolated in 15 and 40% yields, respectively. Attempted hydrogenation of **11** on Lindlar catalyst led to a complex mixture of **13** and some unidentified oligomeric and/or cycloadduct species.



SCHEME 2

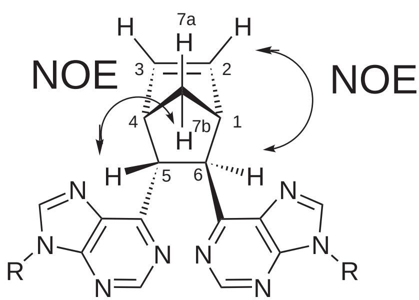
Spectroscopy

A combination of standard ^{1}H and ^{13}C NMR and IR spectroscopies as well as MS and microanalyses was used for identification and full characterization of compounds. Due to high symmetry it was not easy to determine the configuration on the double bond in compound **3a** (only one proton signal of the vinylene system with no significant interaction to any other proton). Even in the unsymmetrically disubstituted compound **3b**, the signals were overlapped and did not allow to determine the configuration by direct NMR methods. Therefore, we have desymmetrized the system by cycloaddition of cyclopentadiene. If the configuration of the starting disubstituted alkene was *E*, one racemic unsymmetrical cycloadduct should be formed, while for *Z*-isomer, a mixture of *endo* and *exo* symmetrical *meso*-forms was expected. The cycloadduct **4** was a single unsymmetrical compound which was the proof of *E*-configuration of the starting alkene **3a**. The configuration of **4** was also unequivocally proved by NOE experiments. The key evidence for the determination of the *E*-configuration of the original alkene was based on NOE connectivities of protons H-5, H-6 and H-7 of the bicyclic adduct: strong NOE contacts between protons H-7b and H-5 and between protons H-2 and H-6 (see Fig. 1). The complementary symmetrically disubstituted alkene **7a** prepared by hydrogenation of **5a** on Lindlar catalyst was assigned as *Z*-isomer. The assignment of *E*-configuration of the heterodisubstituted alkene **12** was based on the coupling constant of the vinylene protons ($^3J_{H,H}$ = 16 Hz).

Crystal Structures

Compounds **5a**, **6a** and **8a** (compound **8a** in two crystal modifications denoted as **A** and **B**) gave crystals suitable for X-ray diffraction (Table I). A single-crystal X-ray analysis showed bond lengths and angles of the purine moiety in these crystals (Fig. 2) to be rather standard, leaving geometrical parameters of linkers as a point of interest (Table II). The electron delocalization in linear acetylene linkage is well apparent from comparison of C6–C17 bond lengths being significantly shorter (0.060 Å in average) than for the saturated ethylene linker. In all molecules purine planes are parallel, and dihedral angles are zero for **8aA**, **8aB** and **5a** as a consequence of the center of symmetry in the molecules or 2.9(2)° for **6a**. As can be expected, the orientation of benzyl groups is flexible, the range of dihedral angles between least-square planes defined by the atoms N1–N9 and C11–C16 for presented structures being almost 20°.

Because of the lack of competition of strong hydrogen bonds, the presented crystals afford a good opportunity to study the non-conventional C–H···N hydrogen bonds[24]. For structures **8aA**, **8aB** and **5a**, these bonds in-



4

FIG. 1
NMR numbering system and significant NOE interactions in compound **4**

TABLE I
Crystal data, measurement and refinement details

Parameters	**6a**	**8aA**	**8aB**	**5a**
Formula	$C_{26}H_{18}N_8$	$C_{28}H_{18}N_8$	$C_{28}H_{18}N_8$	$C_{26}H_{22}N_8$
Crystal system	monoclinic	monoclinic	triclinic	monoclinic
Space group	$P2_1$ (No. 4)	$P2_1/n$ (No. 14)	P-1 (No. 2)	$P2_1/c$ (No. 14)
a, Å	11.854(1)	14.8085(4)	4.6720(3)	13.1008(5)
b, Å	5.7150(6)	4.7182(2)	10.6500(6)	4.5407(1)
c, Å	15.604(1)	15.9372(4)	11.5210(7)	18.4198(7)
α, °			89.245(3)	
β, °	95.491(5)	94.527(2)	97.530(4)	93.998(2)
γ, °			90.120(3)	
Z	2	2	1	2
V, $Å^3$	1 052.25(16)	1 110.05(5)	568.26(6)	1 093.07(6)
D_c, g cm^{-3}	1.397	1.396	1.363	1.357
Temperature, K	150(2)	150(2)	150(2)	150(2)
Crystal size, mm	0.5×0.1×0.025	0.4×0.2×0.1	0.57×0.075×0.05	0.3×0.1×0.08
Colour	colourless	yellow	blue	colourless
μ, mm^{-1}	0.089	0.088	0.086	0.086
θ_{max}, °	27.1	27.5	27.9	27.16
h range	–15,15	–19,19	–6,6	–16,16
k range	–7,7	–6,6	–13,13	–5,5
l range	–20,19	–20,20	–14,14	–23,23
Reflections measured	12 369	20 985	7 537	16 273
– independent (R_{int})[a]	2 520 (0.094)	2 534 (0.027)	2 497 (0.076)	2 408 (0.036)
– observed [$I > 2\sigma(I)$]	1 525	2 045	1 835	1 809
No. of parameters	307	199	199	198
GOF[b]	1.014	1.030	1.051	1.045
R_1, $wR(F^2)$[c]	0.066, 0.127	0.0375, 0.099	0.056, 0.133	0.047, 0.104
$\Delta\rho_{max}$, $\Delta\rho_{min}$, e $Å^{-3}$	0.214, –0.243	0.173, –0.195	0.227, –0.285	0.159, –0.214

[a] $R_{int} = \Sigma|F_o^2 - F_{o,mean}^2|/\Sigma F_o^2$. [b] GOF = $[\Sigma(w(F_o^2 - F_c^2)^2)/(N_{diffrs} - N_{params})]^{1/2}$. [c] $R(F) = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ for observed reflections, $wR(F^2) = [\Sigma(w(F_o^2 - F_c^2)^2)/(\Sigma w(F_o^2)^2)]^{1/2}$ for all data.

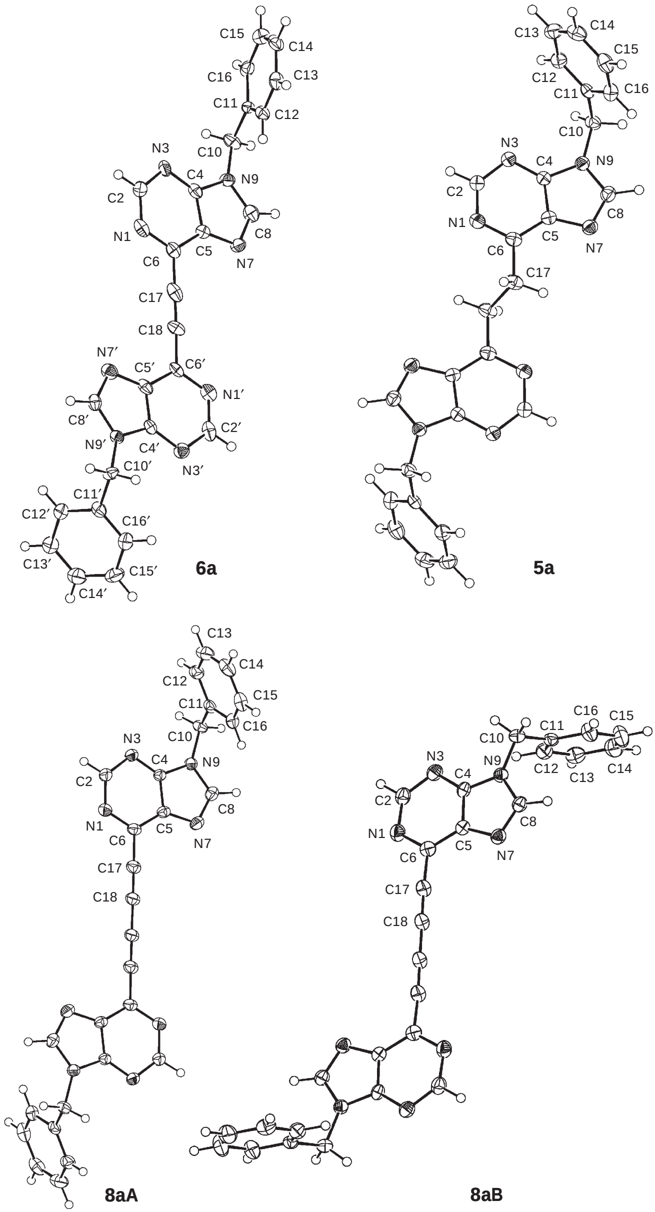


FIG. 2
Molecular structures of **6a**, **5a**, **8aA** and **8aB**, respectively. Thermal ellipsoids are drawn at 50% probability level

volve C8–H and N7 atoms, whereas in **6a**, it is the intramolecular interaction between C12–H and N9 (for details see Table III). The orientation of molecules bonded by intermolecular bonds is inclined in **8aA** and **5a**, but molecules of **8aB** are parallel, each purine moiety being connected to its partner by two centrosymmetrically related bonds.

The second important force is T-shaped C–H···π-electrons interaction, common for all structures; again **6a** is exceptional with >C(phenyl)–H purine contacts, contrary to $–CH_2–$ phenyl interaction for other compounds (Table III). As regards π–π interactions of aromatic rings, common features cannot be outlined. Molecules of **5a** are parallel and mutually slipped, which enables a π–π interaction between five- and six-membered rings of purines at centroid distances 3.5837(8) Å. Similar interaction occurred also

TABLE II
Selected bond lengths (in Å) and angles (in °) and atom distance (in Å) in compounds **6a**, **8aA**, **8aB** and **5a**

Parameter[a]	**6a**	**8aA**	**8aB**	**5a**
C6–C17	1.443(8)	1.429(2)	1.433(2)	1.495(2)
$C17–C17^{i}$	–	–	–	1.526(3)
C17–C18	1.208(5)	1.205(2)	1.200(2)	–
$C18–C18^{ii}$	–	1.368(2)	1.370(3)	–
C18–C6′	1.416(8)	–	–	–
$C6–C17–C17^{i}$	–	–	–	112.3(2)
C6–C17–C18	177.7(4)	177.5(2)	176.3(2)	–
C17–C18–C6′	176.2(4)	–	–	–
$C17–C18–C18^{i}$	–	179.4(2)	178.6(3)	–
t_1	81.5(6)	74.2(1)	–114.1(2)	73.8(2)
φ_1	82.3(1)	86.93(2)	79.64(4)	79.32(3)
φ_1'	67.7(1)	–	–	–
$N9–N9^{b}$	10.385(4)	12.800(2)	12.669(3)	10.477(2)

[a] t_1 torsion angle C4–N9–C10–C11; φ_1 dihedral angle between least-squared planes N1–N9 and C11–C16, φ_1' dihedral angle between planes N1′–N9′ and C11′–C16′; symmetry code: i = 1 – x, 1 – y, 1 – z for **8aA** and **5a**, i = 1 – x, 2 – y, 1 – z for **8aB**. [b] ′ for **6a** and i for **8aA**, **8aB** and **5a**.

in **8a** with the distances of 3.6143(6) Å. However, in the other modification of this compound (**8aB**), two parallel purine planes are oriented head to tail and slipped at such a degree that only electrons at the C8 atoms can efficiently interact. On the other hand, this interaction brings them to an unexpectedly short distance from each other (C8···C8 3.110(2) Å). In the crystal of **6a** the purine planes are oriented almost perpendicularly, atom N7 pointing towards C8 and the short N7–C8 distances being 3.037(7) Å.

From the molecular packing, it can be concluded that the title compounds could exhibit a wide variety of possible interactions. Which of them is present in the crystal is affected even by small changes during crystallization as was demonstrated on **8a**, where two crystal modifications differing substantially in intermolecular packing crystallized together from the same solution.

For comparison of these extended analogues with Watson–Crick base-pairs, the N9–N9′ and N1–N9 distances in adenylyl-uridine[25] and guanylyl-cytidine[26] pairs can be used. It follows that even for the shortest analogue **6a** this dimension is almost 17% larger (8.825, 8.845 Å; 9.010 Å and 10.385(4) Å for AU; GC and **6a**, respectively).

TABLE III
Geometrical parameters for C–H···X interactions in **6a**, **8aA**, **8aB** and **5a**

Compound	Interaction[a]	H···N/π[b], Å	C···N/π, Å	C–H···N/π, °	γ[c], °
6a	sp^2 C12–H···N9(intra)	2.539	2.879(5)	101.9	
	sp^2 C14–H···π2	2.719	3.517(5)	144.3	3.27
	sp^2 C14′–H···π2′	2.735	3.581(5)	151.5	2.17
8aA	sp^2 C8–H···N7	2.57(1)	3.508(2)	161.(1)	
	sp^3 C10–H···π1	2.66(1)	3.481(1)	139.(1)	17.13
8aB	sp^2 C8–H···N7	2.47(2)	3.183(2)	129.(1)	
	sp^3 C10–H···π1	2.79(2)	3.443(2)	124.(1)	9.71
5a	sp^2 C8–H···N7	2.39(1)	3.331(2)	152.(1)	
	sp^3 C10–H···π1	2.62(2)	3.341(2)	128.(1)	9.65

[a] π1, centroid of the ring C11–C16; π2, centroid of the ring C1–C6; π2′, centroid of the ring C1′–C6′. [b] C–H lengths are within the range 0.93–1.03 Å. [c] γ, angle between H···π vector and normal of the aromatic ring.

Conclusion

In conclusion, Sonogashira-type cross-coupling reactions of 6-alkynylpurines or 5-alkynylpyrimidines with 6-halopurines or 5-halopyrimidines and oxidative homo-dimerizations of 6-ethynylpurines were developed as an efficient approach to the synthesis acetylene-linked purine-purine and purine-pyrimidine or diacetylene-linked purine-purine conjugates. Hydrogenations of these alkynes gave the partly or fully saturated derivatives in moderate yields. While the substituted bis(purin-6-yl)acetylenes **6** and -diacetylenes **8** exhibit significant cytostatic activity (for details, see ref.[19]), the saturated derivatives **3**, **5** and **7**, as well as the novel purine-pyrimidine conjugates **11**–**13** were inactive in these assays[27]. The synthesis of more hydrophilic water-soluble derivatives of these base-pair analogues and studies of their interactions with DNA will follow.

EXPERIMENTAL

Unless otherwise stated, solvents were evaporated at 40 °C/2 kPa and compounds were dried at 60 °C/2 kPa over P_2O_5. Melting points were determined on a Kofler block and are uncorrected. IR spectra (wavenumbers in cm^{-1}) were recorded on a Bruker IFS 88 spectrometer. NMR spectra were measured on a Bruker AMX-3 400 (400 MHz for ^1H and 100.6 MHz for ^{13}C) or a Bruker DRX 500 (500 MHz for ^1H and 125.8 MHz for ^{13}C) spectrometer. TMS was used as internal standard. Chemical shifts (δ) are given in ppm, coupling constants (*J*) in Hz. Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using FAB (ionization by Xe, accelerating voltage 8 kV, glycerol matrix). DMF was distilled from P_2O_5, degassed *in vacuo* and stored over molecular sieves under argon. Compounds **1a**, **1b**[17], **2a**[28], **2b**[29], **9**[30] and **10**[17] were prepared by known procedures.

N-Pentylation of 6-Chloropurine

A suspension of 6-chloropurine (6.2 g, 40 mmol) and K_2CO_3 (17 g, 123 mmol) in DMF (150 ml) was stirred at 50 °C for 1 h. Then the mixture was cooled to room temperature and 1-bromopentane (7.43 ml, 60 mmol) was added. The mixture was stirred at room temperature for 10 h. The volatiles were evaporated *in vacuo* and the residue was chromatographed on a silica gel column (300 g, ethyl acetate–light petroleum 1 : 2 to 2 : 1) to get 6-chloro-9-pentylpurine (5.35 g, 60%) followed by 6-chloro-7-pentylpurine (1.7 g, 19%).

6-Chloro-9-pentylpurine. Oil that crystallized on standing, m.p. 32–36 °C. EI MS, *m/z* (rel.%): 224 (44) [M], 168 (100), 154 (80). ^1H NMR (400 MHz, $CDCl_3$): 0.89 (t, 3 H, *J* = 6.9, CH_3); 1.30–1.42 (m, 4 H, 2 × CH_2); 1.93 (pent, 2 H, *J* = 7.2, CH_2); 4.29 (t, 2 H, *J* = 7.2, CH_2N); 8.11 (s, 1 H, H-8); 8.75 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 13.75 (CH_3); 22.02, 28.66, 29.51 and 44.49 (CH_2); 131.62 (C-5); 145.03 (CH-8); 151.02 (C-6 and C-4); 151.86 (CH-2). EI HRMS, found: 224.0836; $C_{10}H_{13}ClN_4$ [M] requires: 224.0829. For $C_{10}H_{13}ClN_4$ (224.4) calculated: 53.45% C, 5.83% H, 24.94% N; found: 53.14% C, 5.96% H, 24.78% N.

6-Chloro-7-pentylpurine. Oil that crystallized on standing, m.p. 38–41 °C. EI MS, *m/z* (rel.%): 224 (44) [M], 167 (100). ^{1}H NMR (400 MHz, $CDCl_3$): 0.90 (t, 3 H, *J* = 6.9, CH_3); 1.30–1.42 (m, 4 H, 2 × CH_2); 1.93 (pent, 2 H, *J* = 7.3, CH_2); 4.46 (t, 2 H, *J* = 7.3, CH_2N); 8.21 (s, 1 H, H-8); 8.87 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 13.77 (CH_3); 22.06, 28.46, 31.33 and 47.51 (CH_2); 122.34 (C-5); 142.96 (C-6); 148.87 (CH-8); 152.35 (CH-2); 162.05 (C-4). EI HRMS, found: 224.0837; $C_{10}H_{13}ClN_4$ [M] requires: 224.0829.

6-Iodo-9-pentylpurine (**2c**)

6-Chloro-9-pentylpurine (1.3 g, 5.8 mmol) was added portionswise into a stirred 57% aqueous HI (15 ml) at 0 °C and the resulting suspension was stirred at 0 °C for 2 h. Then water (50 ml) and 35% aqueous NH_3 (30 ml) were added and the suspension was stirred at room temperature for 20 min and filtered. The cake was dissolved in chloroform (200 ml) and washed with saturated aqueous $Na_2S_2O_3$ (300 ml), and water (300 ml). The solvent was evaporated and the residue chromatographed on a silica gel column (150 g, ethyl acetate–light petroleum 1 : 2) to give the 6-iodopurine **2c** (1.5 g, 82%) which was recrystallized from CH_2Cl_2/heptane. Colourless crystals, m.p. 49–52 °C. EI MS, *m/z* (rel.%): 316 (100) [M], 301 (13), 287 (25), 273 (14), 260 (63), 246 (25), 162 (70). IR ($CHCl_3$): 1 583, 1 554, 1 493, 1 428, 1 399, 1 333. ^{1}H NMR (400 MHz, $CDCl_3$): 0.90 (t, 3 H, *J* = 6.9, CH_3); 1.30–1.42 (m, 4 H, 2 × CH_2); 1.94 (pent, 2 H, *J* = 7.2, CH_2); 4.27 (t, 2 H, *J* = 7.2, CH_2N); 8.13 (s, 1 H, H-8); 8.63 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 13.75 (CH_3); 22.01, 28.65, 29.48 and 44.48 (CH_2); 122.08 (C-5); 138.58 (C-6); 144.36 (CH-8); 148.06 (C-4); 151.85 (CH-2). EI HRMS, found: 316.0167; $C_{10}H_{13}IN_4$ [M] requires: 316.0185. For $C_{10}H_{13}IN_4$ (316.1) calculated: 37.99% C, 4.14% H, 17.72% N; found: 38.37% C, 4.28% H, 17.68% N.

9-Pentyl-6-[(trimethylsilyl)ethynyl]purine

DMF (10 ml) and Et_3N (4 ml) were added through septum to an argon purged flask containing 6-chloro-9-pentylpurine (2.69 g, 12 mmol), TMS–C≡CH (3 ml, 21 mmol), CuI (200 mg, 1 mmol) and $Pd(PPh_3)_4$ (200 mg, 0.174 mmol). The mixture was then stirred at 120 °C for 7 h and left at ambient temperature overnight. The solvents were evaporated *in vacuo* and the residue was chromatographed on a silica gel column (150 g, ethyl acetate–light petroleum 1 : 2) to give compound 9-pentyl-6-[(trimethylsilyl)ethynyl]purine as amorphous solid (2.2 g, 64%). EI MS, *m/z* (rel.%): 286 (97) [M], 271 (60), 257 (17), 243 (11), 230 (50), 214 (65), 201 (100), 185 (28), 171 (18), 158 (66), 144 (50). IR ($CHCl_3$): 2 163, 1 583, 1 497, 1 402, 1 329, 1 252, 849. ^{1}H NMR (400 MHz, $CDCl_3$): 0.35 (s, 9 H, $(CH_3)_3Si$); 0.90 (t, 3 H, *J* = 6.9, CH_3); 1.25–1.42 (m, 4 H, 2 × CH_2); 1.93 (pent, 2 H, *J* = 7.2, CH_2); 4.29 (t, 2 H, *J* = 7.2, CH_2N); 8.13 (s, 1 H, H-8); 8.93 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): –0.44 ($(CH_3)_3Si$); 13.75 (CH_3); 22.02, 28.65, 29.48 and 44.05 (CH_2); 98.48 and 105.23 (C≡C); 134.32 (C-5); 141.10 (C-6); 145.35 (CH-8); 151.76 (C-4); 152.38 (CH-2). For $C_{15}H_{27}N_4Si$ (286.4) calculated: 62.89% C, 7.74% H, 19.56% N; found: 62.51% C, 7.81% H, 19.29% N.

6-Ethynyl-9-pentylpurine (**1c**)

A solution of 9-pentyl-6-[(trimethylsilyl)ethynyl]purine (1.88 g, 6.6 mmol) in saturated ethanolic ammonia (100 ml) was stirred for 2 h. The solvent was evaporated and the residue chromatographed on a silica gel column (150 g, ethyl acetate–light petroleum 1 : 1 to 3 : 1) to give the acetylene **1c** (1.15 g, 82%) which was recrystallized from CH_2Cl_2/heptane.

Brownis crystals, m.p. 66–69 °C. EI MS, *m/z* (rel.%): 214 (95) [M], 199 (20), 185 (35), 172 (22), 158 (100), 144 (75), 130 (18), 117 (20), 103 (20). IR ($CHCl_3$): 3 302, 2 119, 1 583, 1 497, 1 403, 1 329, 643. ^{1}H NMR (400 MHz, $CDCl_3$): 0.89 (t, 3 H, *J* = 7.0, CH_3); 1.28–1.40 (m, 4 H, 2 × CH_2); 1.94 (pent, 2 H, *J* = 7.3, CH_2); 3.73 (s, 1 H, ≡CH); 4.29 (t, 2 H, *J* = 7.3, CH_2N); 8.14 (s, 1 H, H-8); 8.95 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 13.75 (CH_3); 22.02, 28.66, 29.48 and 44.10 (CH_2); 77.99 (≡C-); 85.87 (≡CH); 134.91 (C-5); 140.49 (C-6); 145.59 (CH-8); 151.72 (C-4); 152.39 (CH-2). EI HRMS, found: 214.1207; $C_{12}H_{14}N_4$ [M] requires: 214.1218. For $C_{12}H_{14}N_4$ (214.3) calculated: 67.27% C, 6.59% H, 26.15% N; found: 67.09% C, 6.69% H, 25.90% N.

Reductive Addition of 6-Iodopurines to 6-Ethynylpurines. General Procedure

DMF (7 ml) and Et_3N (2 ml) were added through septum to an argon-purged flask containing a 6-iodopurine **2** (1.5 mmol), 6-ethynylpurine **1** (1.5 mmol), CuI (30 mg, 0.15 mmol) and $Pd(PPh_3)_4$ (150 mg, 0.130 mmol). The mixture was then stirred at 120 °C for 15 h. The solvents were evaporated *in vacuo* and the residue was chromatographed on a silica gel column (150 g, ethyl acetate–light petroleum 1 : 2 to pure ethyl acetate) to give the bis(purinyl)ethylenes **3**. Substantial amounts (*ca* 40%) of unreacted starting 6-iodopurines **2** were also isolated.

(E)-1,2-Bis(9-benzylpurin-6-yl)ethene (**3a**). Yield 27%; m.p. 245–247 °C (96% EtOH). EI MS, *m/z* (rel.%): 444 (57) [M], 399 (11), 353 (20) [M – Bn], 326 (7), 91 (100). IR ($CHCl_3$): 1 590, 1 579, 1 500, 1 454, 1 444, 1 401, 1 328, 982, 715. ^{1}H NMR (400 MHz, DMSO-d_6): 5.56 (s, 4 H, CH_2Ph); 7.30–7.40 (m, 10 H, H-arom.); 8.78 (s, 2 H, -CH=); 8.86 (s, 2 H, H-8); 9.00 (s, 2 H, H-2). ^{13}C NMR (125.8 MHz, DMSO-d_6): 46.53 (CH_2); 127.61, 127.90 and 128.72 (CH-arom.); 131.31 (C-5); 133.11 (-CH=); 136.36 (C-*ipso*-arom.); 147.24 (CH-8); 150.84 (C-6); 152.15 (CH-2 and C-4). EI HRMS, found: 444.1745; $C_{26}H_{20}N_8$ [M] requires: 444.1811. For $C_{26}H_{20}N_8$ (444.5) calculated: 70.26% C, 4.54% H, 25.21% N; found: 69.89% C, 4.47% H, 24.90% N.

(E)-9-Benzyl-6-{2-[9-(tetrahydropyran-2-yl)purin-6-yl]vinyl}purine (**3b**). Yield 15%. FAB MS, *m/z* (rel.%): 439 (8) [M + H], 91 (100). ^{1}H NMR (500 MHz, $CDCl_3$): 1.68–1.85 and 2.06–2.35 (2 × m, 6 H, CH_2-THP); 3.81 (brt, 1 H, *J* = 11.5, CH_2Oa); 4.20 (brd, 1 H, *J* = 11.2, CH_2Ob); 5.48 (s, 2 H, CH_2Ph); 5.84 (dd, 1 H, *J* = 10.2 and 2.2, NCHO); 7.31–7.38 (m, 5 H, H-arom.); 8.12 (s, 1 H, H-8-PuBn); 8.35 (s, 1 H, H-8-PuTHP); 8.93 (d, 1 H, *J* = 16.0, -CH=); 8.97 (d, 1 H, *J* = 16.0, -CH=); 9.01 (s, 1 H, H-2-PuTHP); 9.04 (s, 1 H, H-8-PuBn). ^{13}C NMR (125.8 MHz, $CDCl_3$): 22.77, 24.85 and 31.79 (CH_2-THP); 47.28 (CH_2Ph); 68.83 (CH_2O); 81.98 (OCHN); 127.81, 128.57 and 129.14 (CH-arom.); 131.97 (C-5-PuBn); 132.16 (C-5-PuTHP); 133.68 (2 × -CH=); 135.13 (C-*ipso*-arom.); 142.68 (CH-8-PuTHP); 144.76 (CH-8-PuBn); 151.59 (C-4-PuTHP); 152.42 (C-6); 152.52 (CH-2-PuTHP); 152.63 (C-4-PuBn); 152.67 (C-6); 152.72 (CH-2-PuBn). FAB HRMS, found: 439.2008; $C_{24}H_{23}N_8O$ [M + H] requires: 439.1995.

trans-5,6-Bis(9-benzylpurin-6-yl)bicyclo[2.2.1]hept-2-ene (**4**)

A mixture of ethylene **3a** (160 mg, 0.36 mmol), freshly prepared cyclopentadiene (1 ml) and toluene (20 ml) was refluxed for 4 h. Then the solvent was evaporated and the residue was chromatographed on silica gel (100 g, ethyl acetate–light petroleum 1 : 1 to 2 : 1) to give the cycloadduct **4** as brownish oil (120 mg, 65%) (*ca* 95% purity). EI MS, *m/z* (rel.%): 510 (3) [M], 444 (23), 353 (15), 326 (5), 91 (69), 66 (100). ^{1}H NMR (500 MHz, $CDCl_3$): 1.60 (d, 1 H, *J* = 7.9, H-7a-BCH); 2.33 (d, 1 H, *J* = 8.2, H-7b-BCH); 3.34 (brs, 1 H, H-1-BCH); 3.91 (brs, 1 H, H-4-BCH); 4.71 and 5.33 (2 × m, 2 × 1 H, H-5 and H-6-BCH); 5.41 and 5.44 (2 × s, 2 × 2 H, 2 × CH_2Ph); 5.96 and 6.56 (2 × m, 2 × 1 H, H-2 and H-3-BCH); 7.28–7.35 (m, 10 H, H-arom.); 7.95 and 8.00 (2 × s, 2 × 1 H, 2 × H-8-Pu); 8.88 and 8.95 (2 × s, 2 × 1 H, 2 × H-2-Pu). ^{13}C NMR (125.8 MHz, $CDCl_3$): 45.51 and 46.34 (CH-5,6-BCH); 47.12 and 47.19 (CH_2-7-BCH and CH_2Ph); 48.25 (CH-4-BCH); 50.64 (CH-1-BCH); 127.88, 128.48 and 129.06 (CH-arom.); 132.58 (C-5-Pu); 135.28 (C-*ipso*-arom.); 135.63 and 137.95 (CH-2,3-BCH); 142.97 and 143.21 (CH-8-Pu); 150.56 and 150.79 (C-4-Pu); 152.19 and 152.34 (CH-2-Pu); 163.37 and 164.00 (C-6-Pu). EI HRMS, found: 510.2284; $C_{31}H_{26}N_8$ [M] requires: 510.2280.

Cross-Coupling of 6-Iodopurines with 6-Ethynylpurines. General Procedure

A degassed 0.165 M solution of TBAF trihydrate in THF (24 ml, 4 mmol) was added dropwise to an argon purged flask containing 6-ethynylpurine **1** (1.67 mmol), 6-iodopurine **2** (1.67 mmol), CuI (60 mg, 0.3 mmol), $PdCl_2(PPh_3)_2$ (100 mg, 0.14 mmol) at ambient temperature and the mixture was stirred for 4 h. The solvent was evaporated and the residue was chromatographed on silica gel (200 g, ethyl acetate–light petroleum 1 : 1) to give the bis(purinyl)acetylenes **6** which were recrystallized from CH_2Cl_2/heptane.

1,2-Bis(9-benzylpurin-6-yl)ethyne (**6a**). Yield 57%; m.p. 254–257 °C. FAB MS, *m/z* (rel.%): 443 (5) [M + H], 91 (100). IR ($CHCl_3$): 1 583, 1 448, 1 403, 1 330. ^{1}H NMR (500 MHz, $CDCl_3$): 5.49 (s, 4 H, CH_2Ph); 7.30–7.40 (m, 10 H, H-arom.); 8.15 (s, 2 H, H-8); 9.07 (s, 2 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 47.52 (CH_2Ph); 90.89 (C≡); 127.89, 128.80 and 129.28 (CH-arom.); 134.83 and 135.09 (C-5 and C-*ipso*-arom.); 140.40 (C-6); 145.83 (CH-8); 152.04 (C-4); 152.84 (C-2). EI HRMS, found: 442.1691; $C_{26}H_{18}N_8$ [M] requires: 442.1654. For $C_{26}H_{18}N_8$ (446.5) calculated: 70.58% C, 4.10% H, 25.32% N; found: 70.80% C, 4.05% H, 25.02% N.

6-[(9-Benzylpurin-6-yl)ethynyl]-9-(tetrahydropyran-2-yl)purine (**6b**). Yield 56%; yellow microcrystals, m.p. 83–85 °C. FAB MS, *m/z* (rel.%): 437 (6) [M + H], 352 (30) [M + H – THP], 91 (100). IR (KBr): 2 223, 1 582, 1 498, 1 445, 1 404, 1 323. ^{1}H NMR (500 MHz, $CDCl_3$): 1.65–1.85 and 2.04–2.20 (2 × m, 6 H, CH_2-THP); 3.80 (t, 1 H, *J* = 11.3, OCH_2a); 4.19 (d, 1 H, *J* = 11.5, OCH_2b); 5.49 (s, 2 H, CH_2Ph); 5.81 (d, 1 H, *J* = 8.8, NCHO); 7.27–7.36 (m, 5 H, H-arom.); 8.18 and 8.38 (H-8); 9.01 and 9.04 (H-2). ^{13}C NMR (125.8 MHz, $CDCl_3$): 22.61, 24.74, 31.74 and 47.47 (CH_2-THP); 68.80 (CH_2Ph); 82.16 (OCHN); 90.70 and 90.73 (C≡C); 127.83, 128.69, 129.16 (CH-arom.); 134.66, 134.84, 135.07 (C-*ipso*-arom. and C-5); 140.06 (C-6); 143.87 and 145.90 (CH-8); 151.05 and 151.89 (C-4); 152.55 and 152.73 (CH-2). FAB HRMS, found: 437.1858; $C_{24}H_{21}N_8O_1$ [M + H] requires: 437.1838. For $C_{24}H_{20}N_8O$ (436.5): 66.04% C, 4.62% H, 25.67% N; found: 65.80% C, 4.84% H, 25.39% N.

1,2-Bis(9-pentylpurin-6-yl)ethyne (**6c**). Yield 66%; m.p. 183–185 °C. EI MS, *m/z* (rel.%): 402 (25) [M], 346 (12), 277 (100). IR (KBr): 1 587, 1 578, 1 502, 1 439, 1 402, 1 321. ^{1}H NMR (500 MHz, $CDCl_3$): 0.85 (t, 3 H, *J* = 7.0, CH_3); 1.25–1.38 (m, 4 H, 2 × CH_2); 1.91 (pent, 2 H, *J* = 7.3, CH_2); 4.29 (t, 2 H, *J* = 7.3, CH_2N); 8.16 (s, 1 H, H-8); 8.98 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 13.76 (CH_3); 22.02, 28.67, 29.48 and 44.12 (CH_2); 90.74 (≡C-); 135.07 (C-5); 140.06 (C-6); 145.96 (CH-8); 151.92 (C-4); 152.43 (CH-2). EI HRMS, found: 402.2270; $C_{22}H_{26}N_8$ [M] requires: 402.2280. For $C_{22}H_{26}N_8$ (402.5) calculated: 65.65% C, 6.51% H, 27.84% N; found 65.73%: C, 6.58% H, 27.70% N.

Oxidative Dimerizations of Ethynylpurines. General Procedure

A solution of CuCl (20 mg, 0.2 mmol), TMEDA (37 μl, 0.25 mmol) in DME (2 ml) was stirred at ambient temperature while a solution of an ethynylpurine **1** (1 mmol) in DME

(8 ml) was added dropwise. The stirring of the mixture in air atmosphere was continued for 4 h and it was allowed to stand overnight. Then the solvent was evaporated and the residue was chromatographed on silica gel (100 g, ethyl acetate–light petroleum 1 : 1) to give the diacetylenes **8** which were recrystallized from CH_2Cl_2/heptane.

1,4-Bis(9-benzylpurin-6-yl)butadiyne (**8a**). Yield 59%; m.p. 215 °C (dec.). FAB MS, *m/z* (rel.%): 467 (8) [M + H], 91 (100). IR ($CHCl_3$): 2 157, 1 575, 1 497, 1 491, 1 457, 1 435 1 404, 1 330. ^{1}H NMR (400 MHz, $CDCl_3$): 5.46 (s, 4 H, CH_2Ph); 7.26–7.38 (m, 10 H, H-arom.); 8.12 (s, 2 H, H-8); 9.01 (s, 1 H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): 47.55 (CH_2Ph); 78.59 and 80.68 (C≡C); 127.96, 128.83 and 129.27 (CH-arom.); 134.62 and 135.52 (C-arom. and C-5); 139.72 (C-6); 145.80 (CH-8); 151.98 (C-4); 152.81 (CH-2). FAB HRMS, found: 467.1700; $C_{28}H_{19}N_8$ [M + H] requires: 467.1732. For $C_{28}H_{18}N_8$ (466.5) calculated: 72.10% C, 3.89% H, 24.02 N; found: 71.96% C, 3.82% H, 23.81% N.

1,4-Bis[9-(tetrahydropyran-2-yl)purin-6-yl]butadiyne (**8b**). Yield 50%; m.p. 220 °C (dec.). FAB MS, *m/z* (rel.%): 455 (5) [M + H], 371 (8) [M + H – THP], 287 (24) [M + H – 2 THP], 57 (100). IR ($CHCl_3$): 2 157, 1 576, 1 489, 1 435, 1 407, 1 333. ^{1}H NMR (400 MHz, $CDCl_3$): 1.64–1.81 and 2.00–2.18 (m, 12 H, CH_2-THP); 3.77 (dt, 2 H, *J* = 11.4 and 2.4, CH_2Oa); 4.17 (brd, 2 H, *J* = 11.4, CH_2Ob); 5.78 (dd, 2 H, *J* = 10.3 and 2.3, NCHO); 8.35 (s, 2 H, H-8); 8.94 (s, 2 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 22.65, 24.81 and 31.81 (CH_2-THP); 68.86 (CH_2O); 78.60 and 80.65 (C≡C); 82.27 (NCHO); 135.76 (C-5); 139.62 (C-6); 143.95 (CH-8); 151.14 (C-4); 152.59 (CH-2). For $C_{24}H_{22}N_8O_2$ (454.5) calculated: 63.43% C, 4.88% H, 24.66% N; found: 63.05% C, 4.86% H, 24.29% N.

1,4-Bis(9-pentylpurin-6-yl)butadiyne (**8c**). Yield 73%; m.p. 202–204 °C. EI MS, *m/z* (rel.%): 426 (6) [M], 91 (100). IR (KBr): 2 157, 1 574, 1 494, 1 434, 1 398, 1 329. ^{1}H NMR (400 MHz, $CDCl_3$): 0.91 (t, 3 H, *J* = 7.0, CH_3); 1.30–1.41 (m, 4 H, 2 × CH_2); 1.96 (pent, 2 H, *J* = 7.3, CH_2); 4.32 (t, 2 H, *J* = 7.3, CH_2N); 8.18 (s, 1 H, H-8); 8.98 (s, 1 H, H-2). ^{13}C NMR (100.6 MHz, $CDCl_3$): 13.75 (CH_3); 22.03, 28.69, 29.49 and 44.16 (CH_2); 78.59 and 80.50 (≡C-); 135.62 (C-5); 139.50 (C-6); 146.00 (CH-8); 151.96 (C-4); 152.47 (CH-2). EI HRMS, found: 426.2274; $C_{24}H_{26}N_8$ [M] requires: 426.2280. For $C_{24}H_{26}N_8$ (426.5) calculated: 67.58% C, 6.14% H, 26.27% N; found: 67.47% C, 6.14% H, 26.26% N.

1,2-Bis(9-benzylpurin-6-yl)ethane (**5a**)

Compound **3a** (150 mg, 0.34 mmol) was hydrogenated at room temperature under atmospheric pressure in the presence of 10% Pd/C (100 mg) in MeOH (20 ml) for 10 h. Then the suspension was filtered through Celite and the filtrate evaporated. The residue was chromatographed on silica gel (100 g, ethyl acetate–light petroleum 1 : 1) to give the product **5a** which was recrystallized from EtOH. Yield 120 mg (80%); colourless needles, m.p. 219–221 °C. EI MS, *m/z* (rel.%): 446 (40) [M], 368 (8), 355 (38), 237 (11), 149 (25), 91 (100). IR ($CHCl_3$): 1 595, 1 437, 1 407, 1 333. ^{1}H NMR (400 MHz, $CDCl_3$): 3.88 (s, 4 H, CH_2CH_2); 5.43 (s, 4 H, CH_2Ph); 7.26–7.37 (m, 10 H, H-arom.); 7.95 (s, 2 H, H-8); 8.88 (s, 2 H, H-2). ^{13}C NMR (100 MHz, $CDCl_3$): 30.88 (CH_2CH_2); 47.19 (CH_2Ph); 127.80, 128.53 and 129.11 (CH-arom.); 132.59 (C-5); 135.24 (C-arom.); 143.49 (CH-8); 150.78 (C-4); 152.53 (C-2); 161.38 (C-6). EI HRMS, found: 446.1962; $C_{26}H_{22}N_8$ [M] requires: 446.1967. For $C_{26}H_{22}N_8$ (446.5) calculated: 69.94% C, 4.79% H, 25.10% N; found: 69.63% C, 4.93% H, 24.83% N.

(*Z*)-1,2-Bis(9-benzylpurin-6-yl)ethene (**7a**)

Compound **6a** (250 mg, 0.57 mmol) was hydrogenated at room temperature under atmospheric pressure in presence of Lindlar catalyst (100 mg) in a mixture of DMF (20 ml), EtOH (50 ml) and ethyl acetate (50 ml) for 8 days. Then the suspension was filtered through Celite and the filtrate evaporated. The residue was chromatographed on silica gel (100 g, ethyl acetate–light petroleum 1 : 1) to give compound **7a** (27 mg, 11%), **5a** (48 mg, 19%), starting compound **6a** (32%) and an inseparable mixture of some oligo- or polymeric materials. Compound **7a**: Yellow microcrystals, m.p. 242–244 °C (EtOH). FAB MS, *m/z* (rel.%): 445 (3) [M + H], 91 (100). IR ($CHCl_3$): 1 580, 1 498, 1 454, 1 403, 1 326, 717. ^{1}H NMR (500 MHz, $CDCl_3$): 5.51 (s, 4 H, CH_2Ph); 7.30–7.40 (m, 10 H, H-arom.); 8.14 (s, 2 H, H-8); 8.97 (s, 2 H, -CH=); 9.07 (s, 2 H, H-2). ^{13}C NMR (125.8 MHz, DMSO-d_6): 47.33 (CH_2); 127.87, 128.62 and 129.18 (CH-arom.); 132.01 (C-5); 133.84 (-CH=); 135.16 (C-*ipso*-arom.); 144.72 (CH-8); 152.47 (C-6 and C-4); 152.77 (CH-2). EI HRMS, found: 444.1770; $C_{26}H_{20}N_8$ [M] requires: 444.1811.

9-Benzyl-6-[(1,3-dimethyluracil-5-yl)ethynyl]purine (**11**)

Method A: DMF (7 ml) and Et_3N (2 ml) were added through septum to an argon purged flask containing 9-benzyl-6-ethynylpurine (**1a**; 490 mg, 2 mmol), 1,3-dimethyl-5-iodouracil (**9**; 650 mg, 2.4 mmol), CuI (40 mg, mmol) and $Pd(PPh_3)_4$ (120 mg, 0.1 mmol). The mixture was stirred at 120 °C for 15 h. The solvents were evaporated *in vacuo* and the residue was chromatographed on a silica gel column (150 g, ethyl acetate–light petroleum 1 : 2 to pure ethyl acetate) to give the product **11** (670 mg, 90%).

Method B: Analogously to method *A*, starting from 5-ethynyl-1,3-dimethyluracil (**10**; 82 mg, 0.5 mmol) and 9-benzyl-6-iodopurine (**2a**; 168 mg, 0.5 mmol) product **11** (130 mg, 70%) was prepared. Brownish crystals, m.p. 224–227 °C (96% EtOH). EI MS, *m/z* (rel.%): 372 (30) [M], 254 (22), 91 (89), 57 (94), 43 (100). IR ($CHCl_3$): 2 220, 1 714, 1 666, 1 637, 1 579, 1 498, 1 481, 1 457, 1 440, 1 404, 1 374, 1 334. ^{1}H NMR (500 MHz, $CDCl_3$): 3.38 (s, 3 H, CH_3); 3.47 (s, 3 H, CH_3); 5.46 (s, 2 H, CH_2Ph); 7.27–7.36 (m, 5 H, H-arom.); 7.87 (s, 1 H, H-6-U); 8.16 (s, 1 H, H-8-Pu); 8.95 (s, 1 H, H-2-Pu). ^{13}C NMR (125.8 MHz, $CDCl_3$): 28.43 and 37.60 (CH_3); 47.45 (CH_2); 88.21 and 90.51 (C≡C); 97.41 (C-5-U); 127.87, 128.69 and 129.17 (CH-arom.); 133.91 (C-5-U); 134.79 (C-*ipso*-arom.); 141.23 (C-6-Pu); 145.35 (CH-8-Pu); 147.87 (CH-6-U); 150.76 (C=O-2-U); 151.49 (C-4-Pu); 152.79 (CH-2-Pu); 160.87 (C=O-4-U). EI HRMS, found: 372.1341; $C_{20}H_{16}N_6O_2$ [M] requires: 372.1335. For $C_{20}H_{16}N_6O_2$ (372.4) calculated: 64.51% C, 4.33% H, 22.57% N; found: 64.23% C, 4.53% H, 22.27% N.

Hydrogenation of **11**

Compound **11** (350 mg, 0.94 mmol) was hydrogenated at room temperature under atmospheric pressure in presence of 10% Pd/C (500 mg) in MeOH (100 ml) for 5 days. Then the suspension was filtered through Celite and the filtrate evaporated. The residue was chromatographed on silica gel (100 g, ethyl acetate–light petroleum 1 : 1 to pure ethyl acetate) to give the ethene **12** (52 mg, 15%), ethane **13** (140 mg, 40%) and unreacted starting compound (100 mg, 29%).

(E)-9-Benzyl-6-[2-(1,3-dimethyluracil-5-yl)vinyl]purine (**12**). Yellow crystals, m.p. 247–250 °C. EI MS, *m/z* (rel.%): 374 (75) [M], 283 (36) [M – Bn], 260 (12), 226 (10), 198 (7), 180 (7), 171 (7), 129 (10), 91 (100). IR ($CHCl_3$): 1 705, 1 653, 1 629, 1 581, 1 497, 1 480, 1 452, 1 401, 1 324,

984, 728. ^{1}H NMR (500 MHz, $CDCl_3$): 3.42 and 3.48 (2 × s, 2 × 3 H, 2 × CH_3); 5.44 (s, 2 H, CH_2Ph); 7.26–7.37 (m, 5 H, H-arom.); 7.57 (s, 1 H, H-6-U); 8.01 (s, 1 H, H-8-Pu); 8.06 (d, 1 H, J = 16.0, CH=); 8.15 (d, 1 H, J = 16.0, CH=); 8.91 (s, 1 H, H-2-Pu). EI HRMS, found: 374.1496; $C_{20}H_{18}N_6O_2$ [M] requires: 374.1491. For $C_{20}H_{18}N_6O_2$ (374.4) calculated: 64.16% C, 4.85% H, 22.45% N; found: 63.88% C, 4.69% H, 22.32% N.

9-Benzyl-6-[2-(1,3-dimethyluracil-5-yl)ethyl]purine (**13**). Yellowish crystals, m.p. 70–74 °C. EI MS, *m/z* (rel.%): 376 (77) [M], 285 (100) [M – Bn], 91 (95). IR ($CHCl_3$): 1 700, 1 664, 1 642, 1 596, 1 498, 1 457, 1 406, 1 333. ^{1}H NMR (500 MHz, $CDCl_3$): 2.95 (t, 2 H, J = 7.4, CH_2); 3.26 and 3.31 (2 × s, 2 × 3 H, 2 × CH_3); 3.43 (t, 2 H, J = 7.4, CH_2); 5.42 (s, 2 H, CH_2Ph); 7.05 (H-6-U); 7.28–7.35 (m, 5 H, H-arom.); 8.01 (s, 1 H, H-8-Pu); 8.89 (s, 1 H, H-2-Pu). ^{13}C NMR (125.8 MHz, $CDCl_3$): 25.78 (CH_2); 27.89 (CH_3); 31.49 (CH_2); 36.67 (CH_2); 47.28 (CH_2Ph); 112.35 (C-5-U); 127.83, 128.59 and 129.12 (CH-arom.); 132.57 and 135.09 (C-*ipso*-Ph and C-5-Pu); 139.67 (CH-6-U); 143.82 (CH-8-Pu); 150.84 and 151.73 (C-4-Pu and C-6-Pu); 152.50 (CH-2-Pu); 161.15 and 163.48 (C=O). EI HRMS, found: 376.1646; $C_{20}H_{20}N_6O_2$ [M] requires: 376.1648. For $C_{20}H_{20}N_6O_2$ (376.4) calculated: 63.82% C, 5.36% H, 22.33% N; found: 63.97% C, 5.04% H, 22.13% N.

X-Ray Crystallographic Study

Crystals of **6a**, **8a** (crystal modifications **A** and **B**) and **5a** were mounted on a glass capillary with epoxy glue and measured on a Nonius KappaCCD diffractometer using monochromatized MoKα radiation (λ = 0.71073 Å). Absorption was neglected for all structures (μ = 0.086–0.089 mm^{-1}). Crystal data are summarized in Table I. The structures were solved by direct methods[31] (SIR92, Altomare, 1994) and refined by full-matrix least squares based on F^2 (SHELXL97)[32].

The hydrogen atoms of **8aA**, **8aB** and **5a** were found on difference Fourier maps and refined without restrictions with isotropic thermal parameters.

The hydrogen atoms of **6a** were fixed into idealised positions (riding model) and assigned temperature factors either H_{iso}(H) = 1.2 U_{eq}(pivot atom), since extremely thin, poorly diffracted crystal of this compound did not provide data of sufficient quality for their refinement. The final difference map of all structures displayed no peaks of chemical significance.

CCDC 188845–188848 contain the supplementary crystallographic data for structures **6a**, **8aA**, **8aB** and **5a**, respectively. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

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