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Synthesis of Purinecarbonitriles by Pd(0)-Catalysed Coupling of Halopurines with Zinc Cyanide

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Pd(0)-catalysed coupling of halopurines with zinc cyanide allows the smooth introduction of the cyano group into the purine 2-, 6- and 8-positions. Pronounced ligand effects were observed, and tetrakis(tri-2-furylphosphine)palladium(0) was found to be the catalyst of choice in reactions where tetrakis(triphenylphosphine)-palladium(0) failed.

Modified purines or purine nucleosides containing carbon substituents in the 2-, 6- or 8-position may exhibit several interesting biological properties including antiviral effects,[1] anticancer effects,[1] antihypertensive effects[2] or cytokinin activity.[3] Furthermore, high affinity for A_1- and/or A_2-adenosine receptors has been reported for a number of 8-substituted xanthine derivatives.[4]

Cyanopurines are versatile intermediates for the synthesis of a large number of purine derivatives.[5] Classical aromatic cyanation, treatment of an aryl halide with copper(I) cyanide,[6] is only partly effective for the cyanation of purines. 6-Iodopurines participate in this type of reaction to give the corresponding 6-cyanopurine,[5a,c,e] but often in moderate yields. 6-Chloropurines are generally more readily available than their 6-iodo analogues, but chloropurines are unreactive towards copper(I) cyanide. Other methods for the preparation of purinenitriles include reaction of halopurines or pseudohalopurines with potassium cyanide[5h] or sodium cyanide,[5d,j,7] and Pd catalysis has been employed in couplings with potassium cyanide[5k] and tributyltin cyanide.[8] Halopurines participate in reactions with tetraethylammonium cyanide in the presence of trimethylamine.[5i,5l] Generally, the methods listed above suffer from various disadvantages. Often only low yields of the desired cyanopurine are obtained, and several reactions require especially reactive purines, such as iodopurines or sulfonylpurines.

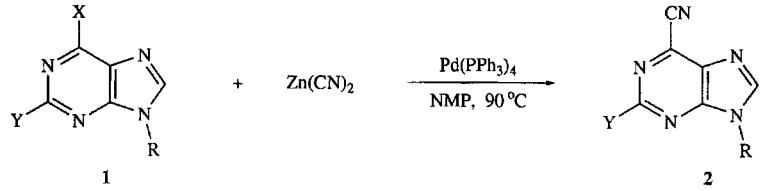
It has recently been shown that aryl bromides, in addition to aryl iodides, can be effectively converted into nitriles when reacted with zinc cyanide in the presence of a catalytic amount of Pd(0).[9] Zinc cyanide compares favourably with other cyanation agents known to participate in Pd-catalysed cross-couplings. $Zn(CN)_2$ is much less expensive than tributyltin cyanide, and it is effective in cases where, for instance, potassium cyanide fails.

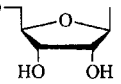
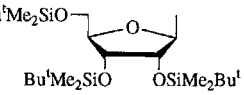
In connection with our on-going project directed towards development of methods for C–C bond formation in purines,[10] we have recently reported the first cross-couplings between halopurines and organozinc reagents.[10c,d] In this paper, results from Pd(0)-catalysed reactions of different halopurines with zinc cyanide are presented.

Several *N*-9-alkylated 6-halopurines **1a–f** were reacted with zinc cyanide in the presence of tetrakis(triphenylphosphine)palladium(0) at 90°C (Scheme 1). Pd(II)-complexes are known to catalyse coupling between KCN and aryl halides,[5k,11] but the coupling reactions with $Zn(CN)_2$ were not catalysed by Pd(II)-complexes such as $Pd(PPh_3)_2Cl_2$. In all cases examined, only 0.6 equiv. of zinc cyanide were necessary, showing that both cyano groups are transferred from the zinc.[9] The reaction required polar aprotic solvents, such as DMF or *N*-methylpyrrolidin-2-one (NMP), and NMP was generally the solvent of choice. No coupling took place in less polar solvents such as dichloroethane or dioxane.

Even though aryl iodides are generally more reactive in Pd-catalysed couplings than the corresponding aryl chlorides, the 9-benzyl-6-chloropurine **1a** and the iodo analogue **1b** gave comparable yields of the 6-cyanopurine **2a**, showing that readily available 6-chloropurines are sufficiently activated for this reaction. Several functional groups, such as free amino or hydroxy groups, in the purine reaction partner are well tolerated. It is especially noteworthy that the nucleoside derivative 6-chloropurine riboside **1e** can be used without protection of the hydroxy groups in the sugar moiety. The yield of the coupling product **2d** was, however, somewhat reduced owing to the tedious separation from triphenylphosphine oxide.

The 7-benzyl-6-chloropurine **3a** appeared to be less reactive than the *N*-9 benzylated isomer **1a** in coupling with

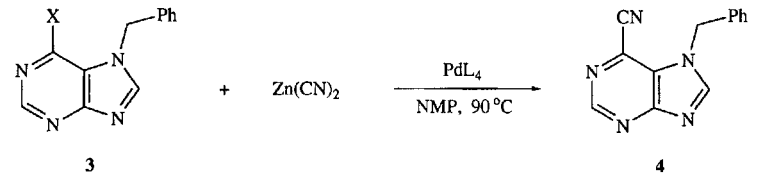


				Yield (%)	2
1a	Y = H	X = Cl	R = CH_2Ph	84	**2a**
1b	Y = H	X = I	R = CH_2Ph	89	**2a**
1c	Y = H	X = Cl	R = $CH_2CH{=}CH_2$	79	**2b**
1d	Y = NH_2	X = Cl	R = $CH_2CH{=}CH_2$	81	**2c**
1e	Y = H	X = Cl	R = 	48	**2d**
1f	Y = H	X = Cl	R = 	73	**2e**

Scheme 1.

zinc cyanide, and only 52% of the desired product **4** was obtained in the presence of $Pd(PPh_3)_4$ (Scheme 2). A similar reactivity difference between 9- and 7-alkylated 6-chloropurines in cross-couplings with other zinc reagents, has previously been noted.[10c]

The choice of ligands in Pd-catalysed reactions may have a profound effect on the reaction rate and yield, and more reactive Pd-catalysts were sought. Tri(*o*-tolyl)phosphine is superior to triphenylphosphine in Pd(0)-catalysed couplings between iodobenzene and KCN in NMP,[12] but no coupling took place between the chloropurine **3a** and $Zn(CN)_2$ when tri(*o*-tolyl)phosphine was used. In the Stille reaction, cross-couplings between aryl halides or aryl triflates and tin reagents, the use of triphenylarsine or tri(2-furyl)phosphine (TFP) is reported to enhance the reaction rate substantially, compared with triphenylphosphine.[13] The $Pd(AsPh_3)_4$ complex did not catalyse the coupling of the chloropurine **3a** at all, but the cyanopurine **4** could be isolated in 75% yield, when tri(2-furyl)phosphine was employed as the ligand. The reason why $Pd(AsPh_3)_4$ failed to catalyse the coupling is not completely understood. This catalyst is known to give higher reaction rate than $Pd(TFP)_4$ in many Stille reactions, but its stability is believed to be somewhat less than $Pd(TFP)_4$.[13a] It has also been recently reported that $Pd(AsPh_3)_4$ is ineffective in both Stille[14] and Heck couplings[15] where $Pd(TFP)_4$ works well. Changing to the more reactive 6-iodopurine analogue, **3b**, allowed isolation of the desired product **4** in 77% yield, even when $Pd(PPh_3)_4$ was used.



			Yield (%)	4
3a	X = Cl	L = PPh_3	52	
3a	X = Cl	L = P(*o*-tolyl)$_3$	n.r.	
3a	X = Cl	L = P(2-furyl)$_3$	75	
3a	X = Cl	L = $AsPh_3$	n.r.	
3b	X = I	L = PPh_3	77	

Scheme 2.

Coupling between halopurines and zinc cyanide can also be used for the introduction of the nitrile function into the purine 8-position, as demonstrated by the Pd-$(PPh_3)_4$-catalysed reaction of 8-bromocaffeine **5** with zinc cyanide under the same reaction conditions as described above (Scheme 3). The coupling product **6** was isolated in 70% yield.

The *O*-silylated 8-bromoadenosine **7a** showed almost no reactivity towards zinc cyanide in the presence of Pd-$(PPh_3)_4$ (Scheme 4). Only ca. 8% of the desired 8-cyanoadenosine **8** was formed, as judged from the ^{1}H NMR spectrum of the crude product. This was somewhat surprising, since other 8-bromoadenosine derivatives participate in a number of Pd-catalysed couplings.[1,2b,16] The effect of the palladium ligands was investigated, and as with the 6-chloropurine **3a**, no reaction took place when Pd[P(*o*-tolyl)$_3$]$_4$ was used. Again Pd(TFP)$_4$ was the catalyst of choice. All the starting material was consumed after 19 h at 90°C, and the coupling product **8** was isolated in 81% yield. The 8-iodoadenosine **7b** reacted with $Zn(CN)_2$ in the presence of $Pd(PPh_3)_4$ under the same reaction conditions as described above, but ca. 20% of the iodide **7b** remained and ca. 15% of the dehalogenated purine **9**[17] was formed, according to the ^{1}H NMR spectrum of the crude product. The isolated yield of the desired product **8** was 46%. In the Pd(TFP)$_4$-catalysed coupling of **7b** ca. 8% of **9** was formed and the isolated yield of the cyanopurine **8** was 75%.

Finally, coupling between a 2-halopurine and $Zn(CN)_2$ was performed. Even though 2-chloropurines are substantially less reactive than 6-chloropurines in Pd-catalysed couplings,[10d] the chloropurine **10** participated in the reaction to give the 2-cyanopurine **11** in 72% yield (Scheme 5).

In conclusion, it is demonstrated that smooth introduction of the cyano group into the purine 2-, 6- and 8-positions can be achieved by Pd(0)-catalysed coupling between halopurines and zinc cyanide. In many instances, tri(2-furyl)phosphine was a superior ligand, compared with the more conventional triphenylphosphine.

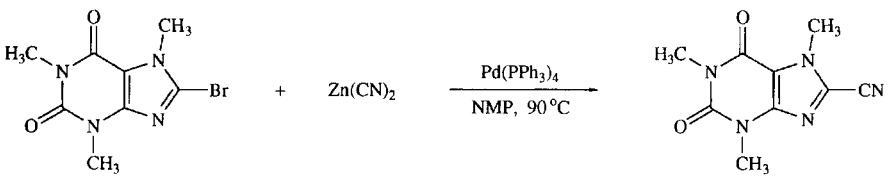
Experimental

The ^{1}H NMR spectra were recorded at 200 MHz with a Varian Gemini 200 instrument and the ^{13}C NMR spectra were recorded at 50 MHz at the same instrument. Mass spectra were recorded at 70 eV ionising voltage and are presented as *m/z* (% rel. int.). Methane was used for chemical ionization. Elemental analyses were performed by *Ilse Beetz Mikroanalytisches Laboratorium*, Kronach, Germany. Melting points are uncorrected. Silica gel for flash chromatography was purchased from Merck, Darmstadt, Germany (Merck No. 9385). *N*-Methylpyrrolidin-2-one (NMP), in Sure/Seal™ bottles, was purchased from Aldrich, Steinheim, Germany. DMF was distilled from BaO. Zinc cyanide was purchased from Fluka, Buchs, Switzerland, and dried at ca. 150°C under high vacuum for 2–4 h prior to use. All other reagents were commercially available and used as received.

Starting material available by literature procedures. 9-Benzyl-6-chloro-9*H*-purine (**1a**),[10c] 9-benzyl-6-iodo-9*H*-purine (**1b**),[18] 2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-6-chloro-9*H*-purine (**1f**),[19] 7-benzyl-6-chloro-7*H*-purine (**3a**),[10c] 7-benzyl-6-iodo-7*H*-purine (**3b**),[10c] 8-bromo-3,7-dihydro-1,3,7-trimethyl-1*H*-purine-2,6-dione (**5**),[20] 8-iodo-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine (**7b**),[21] 9-benzyl-2-chloro-6-methyl-9*H*-purine (**10**).[10d]

*9-Allyl-6-chloro-9*H*-purine (**1c**).* Potassium carbonate (2.073 g, 15.0 mmol) was added to a stirred solution of 6-chloropurine (789 mg, 5.10 mmol) in dry DMF (20 ml) at ambient temperature under N_2. After 20 min, allyl bromide (0.84 ml, 10.2 mmol) was added and the resulting mixture was stirred at ambient temperature for 17 h, filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (1:1); yield 666 mg (67%) of a colourless powder. M.p. 163–166°C (Lit.[22] 163–167°C). ^{1}H NMR (DMSO-d_6): δ 4.9–5.0 (m, 2 H, CH_2), 5.0–5.2 (m, 2 H, CH_2=), 6.0–6.1 (m, 1 H, CH=), 8.69 (s, 1 H, H-8), 8.77 (s, 1 H, H-2).

*9-Allyl-2-amino-6-chloro-9*H*-purine (**1d**).*[23] Potassium carbonate (2.073 g, 15.0 mmol) was added to a stirred solution of 2-amino-6-chloropurine (808 mg, 4.76 mmol) in dry DMF (70 ml) at ambient temperature under N_2. After 20 min, allyl bromide (0.78 ml, 9.53 mmol) was added and the resulting mixture was stirred at ambient temperature for 17 h, filtered and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel eluting with MeOH–CH_2Cl_2 (1:20); yield 712 mg (71%) of a colourless powder. M.p. 151–154°C. ^{1}H NMR (DMSO-d_6): δ 4.7 (m, 2 H, CH_2), 4.9–5.2 (m, 2 H,



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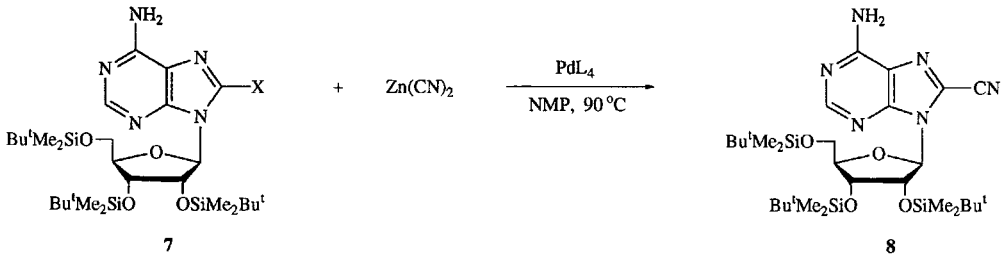
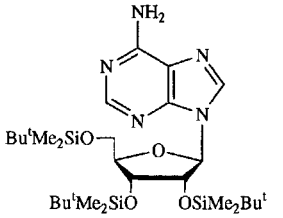
Scheme 3.



7 8

			Yield (%) 8
7a	X = Br	L = PPh_3	8[a]
7a	X = Br	L = P(*o*-tolyl)$_3$	n.r.
7a	X = Br	L = P(2-furyl)$_3$	81
7b	X = I	L = PPh_3	46
7b	X = I	L = P(2-furyl)$_3$	75

a) From ^{1}H NMR of the crude product



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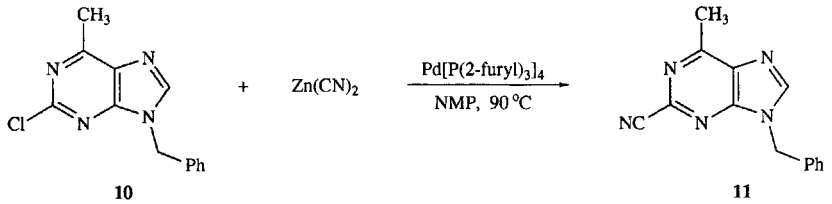
Scheme 4.

CH_2 =), 6.0–6.1 (m, 1 H, CH =), 6.92 (br s, 2 H, NH_2), 8.09 (s, 1 H, H-8).

*8-Bromo-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine* (**7a**). A mixture of 8-bromoadenosine (346 mg, 1.0 mmol), imidazole (545 mg, 8.0 mmol) and *tert*-butyldimethylchlorosilane (604 mg, 4.0 mmol) in dry DMF (4 ml) was stirred under N_2 at ambient temperature for 24 h. Sat. aq. NH_4Cl (10 ml) was added, and the mixture was extracted with ethyl acetate (2 × 20 ml). The combined organic extracts were washed with water (10 ml), dried ($MgSO_4$), and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (1:2); yield 664 mg (96%) to give colourless needles. M.p. 196–197°C (hexane). Found: C 49.40; H 8.06. Calc. for $C_{28}H_{54}BrN_5O_4Si_3$: C 48.82; H 7.90. ^{1}H NMR ($CDCl_3$): δ −0.34, −0.06, −0.01 and 0.03 (s, $SiCH_3$), 0.80, 0.84 and 0.96 (s, 9 H, Bu^t), 3.7–3.8 (m, 1 H), 4.0–4.1 (m, 2 H), 4.6 (m, 1 H), 5.5 (m, 1 H), 5.89 (br s, 2 H, NH_2), 5.96 (d, *J* 5.9 Hz, 1 H, H-1′), 8.26 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$): δ −5.6, −5.5 and −5.3 ($SiCH_3$), 17.7, 18.0 and 18.2 (C in Bu^t), 25.6, 25.7 and 25.8 (CH_3 in Bu^t), 62.1 (C-5′), 71.7 (C-3′), 72.1 (C-2′), 85.5 (C-4′), 90.5 (C-1′), 120.3 (C-5), 128.4 (C-8), 150.6 (C-4), 152.4 (C-2), 154.7 (C-6). MS (CI): 690/688 (6/5, *M* + 1), 343 (13), 315 (24), 171 (24), 164 (51), 150 (11), 136 (100), 133 (15), 117 (26), 115 (55).

General procedure for the coupling of halopurines with zinc cyanide. To a mixture of halopurine (1.0 mmol) in NMP (6 ml) were added zinc cyanide (70 mg, 0.6 mmol) and tetrakis(triphenylphosphine)palladium(0) (81 mg, 0.07 mmol), and the resulting mixture was stirred at 90°C under N_2 for 20 h and cooled, before 2 M aq. ammonia (10 ml) was added. The mixture was extracted with ethyl acetate (3 × 20 ml), and the combined organic extracts were washed with 2 M aq. ammonia (15 ml) and brine (20 ml), dried ($MgSO_4$) and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel.

*9-Benzyl-9*H*-purine-6-carbonitrile* (**2a**). The compound was prepared from 9-benzyl-6-chloro-9*H*-purine or 9-benzyl-6-iodo-9*H*-purine as described above. EtOAc–hexane (3:4) was used for flash chromatography; yield 197 mg (84%) from 9-benzyl-6-chloro-9*H*-purine and 209 mg (89%) from 9-benzyl-6-iodo-9*H*-purine, colourless needles. M.p. 99–101°C (hexane) (Lit.[51] 99–100.5°C). ^{1}H NMR ($CDCl_3$): δ 5.51 (s, 2 H, CH_2), 7.3–7.4 (m, 5 H, Ph), 8.28 (s, 1 H, H-8), 9.10 (s, 1 H,



10 11

Scheme 5.

H-2). ^{13}C NMR ($CDCl_3$): δ 47.9 (CH_2), 113.5 (CN), 128.0, 129.1, and 129.4 (CH in Ph), 131.0 (C-6), 134.0 (C in Ph), 134.9 (C-5), 147.8 (C-8), 152.8, 152.9 (C-2/C-4). MS (EI): 235 (79, M^+), 234 (64), 209 (4), 208 (11), 207 (7), 158 (5), 92 (8), 91 (100), 89 (5), 77 (5), 65 (22).

*9-Allyl-9*H*-purine-6-carbonitrile (***2b***).* The compound was prepared from 9-allyl-6-chloro-9*H*-purine as described above. EtOAc–hexane (1:1) was used for flash chromatography; yield 146 mg (79%), colourless oil. ^{1}H NMR ($CDCl_3$): δ 4.9–5.0 (m, 2 H, CH_2), 5.3–5.4 (m, 2 H, CH_2 =), 6.0–6.2 (m, 1 H, CH =), 8.32 (s, 1 H, H-8), 9.06 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$): δ 46.4 (CH_2), 113.3 (CN), 120.3 (CH_2 =), 130.1 (CH =), 130.5 (C-6), 134.6 (C-5), 147.5 (C-8), 152.1, 152.2 (C-2/C-4). MS (EI): 185 (100, M^+), 184 (92), 159 (9), 158 (44), 157 (24), 149 (12), 146 (9), 84 (19), 77 (13), 76 (10). HRMS: Found 185.0702, calc. for $C_9H_7N_5$ 185.0701.

*9-Allyl-2-amino-9*H*-purine-6-carbonitrile (***2c***).* The compound was prepared from 9-allyl-2-amino-6-chloro-9*H*-purine as described above. EtOAc–hexane (1:1) was used for flash chromatography; yield 161 mg (81%), cream-coloured foam. ^{1}H NMR (DMSO-d_6): δ 4.7 (m, 2 H, CH_2), 5.0–5.2 (m, 2 H, CH_2 =), 6.0–6.1 (m, 1 H, CH =), 7.10 (br s, 2 H, NH_2), 8.33 (s, 1 H, H-8). ^{13}C NMR (DMSO-d_6): δ 44.7 (CH_2), 114.4 (CN), 117.4 (CH_2 =), 128.0 (C-5), 129.5 (C-6), 132.5 (CH =), 146.2 (C-8), 154.8 (C-4), 160.3 (C-2). MS (EI): 200 (100, M^+), 199 (48), 173 (18), 172 (14), 160 (11), 158 (6), 146 (6), 133 (8), 132 (7), 80 (5). HRMS: Found 200.0813, calc. for $C_9H_8N_6$ 200.0810.

*9-β-*D*-Ribofuranosyl-9*H*-purine-6-carbonitrile (***2d***).* The compound was prepared from 9-β-D-ribofuranosyl-6-chloro-9*H*-purine as described above. $CHCl_3$, followed by MeOH–$CHCl_3$ (1:10), was used for flash chromatography; yield 132 mg (48%). M.p. 196–198°C (EtOH) (Lit.[5e] 198–199°C). ^{1}H NMR (DMSO-d_6): δ 3.6–3.8 (m, 2 H), 4.0 (m, 1 H), 4.2–4.3 (m, 1 H), 4.6–4.7 (m, 1 H), 5.15 (t, *J* 5.3 Hz, 1 H, OH), 5.32 (d, *J* 5.3, 1 H, OH), 5.65 (d, *J* 5.6 Hz, 1 H, OH), 6.12 (d, *J* 5.1 Hz, 1 H, H-1′), 9.18 (s, 1 H, H-8), 9.21 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6): δ 60.8 (C-5′), 69.9 (C-3′), 74.0 (C-2′), 85.7 (C-4′), 88.1 (C-1′), 114.2 (CN), 129.7 (C-6), 135.3 (C-5), 148.7 (C-8), 152.3, 152.5 (C-2/C-4). MS (EI): 277 (100, M^+), 251 (3), 239 (4), 224 (9), 215 (2), 195 (5), 161 (3), 141 (5), 139 (7), 127 (6), 125 (6).

*2′,3′,5′-Tris-*O*-(*tert*-butyldimethylsilyl)-9-β-*D*-ribofuranosyl-9*H*-purine-6-carbonitrile (***2e***).* The compound was prepared from 2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-6-chloro-9*H*-purine (0.43 mmol) as described above. EtOAc–hexane (1:12) was used for flash chromatography; yield 195 mg (73%), colourless needles. M.p. 154–156°C (hexane). Anal.: C, H. ^{1}H NMR ($CDCl_3$): δ −0.25, 0.01, 0.106, 0.110, 0.17 and 0.18 (s, 3 H, $SiCH_3$), 0.79, 0.94 and 0.98 (s, 9 H, Bu^t), 3.8–3.9 (m, 1 H), 4.0–4.1 (m, 1 H), 4.2 (m, 1 H), 4.3 (m, 1 H), 4.5–4.6 (m, 1 H), 6.18 (d, *J* 5.0 Hz, 1 H, H-1′), 8.76 (s, 1 H, H-8), 9.07 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$): δ −5.4, −5.0, −4.7 and −4.4 ($SiCH_3$), 17.8, 18.1 and 18.6 (C in Bu^t), 25.6, 25.8 and 26.1 (CH_3 in Bu^t), 62.2 (C-5′), 71.7 (C-3′), 76.6 (C-2′), 85.8 (C-4′), 88.4 (C-1′), 113.3 (CN), 130.9 (C-6), 135.4 (C-5), 146.8 (C-8), 152.5 (C-2 and C-4). MS (CI): 620 (24, M + 1), 562 (8), 475 (6), 345 (12), 344 (28), 343 (100), 303 (6), 261 (6), 146 (24), 115 (6).

*7-Benzyl-7*H*-purine-6-carbonitrile (***4***).* The compound was prepared from 7-benzyl-6-chloro-7*H*-purine or from 7-benzyl-6-iodo-7*H*-purine as described above. EtOAc–hexane (2:1) was used for flash chromatography; yield 123 mg (52%) from 7-benzyl-6-chloro-7*H*-purine and 180 mg (77%) from 7-benzyl-6-iodo-7*H*-purine, colourless needles. M.p. 189–190°C (PhH). Anal.: C, H. ^{1}H NMR (CD_2Cl_2): δ 5.70 (s, 2 H, CH_2), 7.3–7.4 (m, 5 H, Ph), 8.44 (s, 1 H, H-8), 9.19 (s, 1 H, H-2). ^{13}C NMR (CD_2Cl_2): δ 50.5 (CH_2), 114.3 (CN), 123.5 (C-6), 125.7 (C-5), 127.9, 129.6 and 129.7 (CH in Ph), 133.9 (C in Ph), 151.4 (C-8), 153.5 (C-2), 163.1 (C-4). MS (EI): 235 (38, M^+), 234 (7), 167 (4), 149 (4), 110 (5), 92 (12), 91 (100), 84 (4), 77 (4), 65 (13).

*2,3,6,7-Tetrahydro-1,3,7-trimethyl-2,6-dioxo-1*H*-purine-8-carbonitrile (***6***).* The compound was prepared from 8-bromo-3,7-dihydro-1,3,7-trimethyl-1*H*-purine-2,6-dione as described above. EtOAc–hexane (3:4) was used for flash chromatography; yield 153 mg (70%), colourless needles. M.p. 152–154°C (acetone) (Lit.[24] 151–153°C). ^{1}H NMR ($CDCl_3$): δ 3.35, 3.52 and 4.13 (s, 3 H, CH_3). ^{13}C NMR ($CDCl_3$): δ 28.7, 30.3 and 34.4 (CH_3), 109.0, 109.2, 124.0, 146.4, 150.1, 153.6. MS (EI): 219 (100, M^+), 190 (11), 162 (13), 135 (13), 134 (86), 133 (30), 107 (16), 93 (13), 82 (15), 67 (45).

*2′,3′,5′-Tris-*O*-(tert-butyldimethylsilyl)-8-cyanoadenosine (***8***).* The compound was prepared from 8-bromo-2′,3′,5′-tris-*O*-(*tert*-butyldimethylsilyl)adenosine (0.38 mmol) as described above, except that tetrakis[tri(2-furyl)phosphine]palladium(0) [generated *in situ* from tris(dibenzylideneacetone)dipalladium–chloroform adduct (13 mg, 0.013 mmol) and tri(2-furyl)phosphine (25 mg, 0.11 mmol)] was used as the catalyst. EtOAc–hexane (1:6), followed by EtOAc–hexane (1:2), was used for flash chromatography; yield 196 mg (81%), colourless needles. M.p. 183–185°C (hexane). Anal.: C, H. ^{1}H NMR ($CDCl_3$): δ −0.37, −0.05, 0.04, 0.06 and 0.16 (s, $SiCH_3$), 0.78, 0.87 and 0.97 (s, 9 H, Bu^t), 3.7–3.8 (m, 1 H), 4.0–4.2 (m, 2 H), 4.5 (m, 1 H), 5.2–5.3 (m, 1 H), 5.76 (br s, 2 H, NH_2), 6.09 (d, *J* 6.2 Hz, H-1′), 8.42 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$): δ −5.5, −5.4, −5.3, −4.6 and −4.5 ($SiCH_3$), 17.8, 18.1 and 18.3 (C in Bu^t), 25.6 and 25.9 (CH_3 in Bu^t), 62.4 (C-5′), 72.3 (C-3′), 72.9 (C-2′), 86.4 (C-4′), 89.4 (C-1′), 110.4 (CN), 120.5 (C-5), 124.6 (C-8), 149.5 (C-4), 155.5 (C-2), 156.5 (C-6). MS

(CI): 635 (13, $M+1$), 343 (36), 303 (12), 175 (53), 171 (68), 161 (61), 117 (69), 115 (93), 89 (48), 75 (100).

*9-Benzyl-6-methyl-9*H*-purine-2-carbonitrile (***11***).* The compound was prepared from 9-benzyl-2-chloro-6-methyl-9*H*-purine (0.47 mmol) as described above, except that tetrakis[tri(2-furyl)phosphine]palladium(0) [generated *in situ* from tris(dibenzylideneacetone)dipalladium–chloroform adduct (17 mg, 0.016 mmol) and tri(2-furyl)phosphine (30 mg, 0.13 mmol)] was used as the catalyst. EtOAc–hexane (1:6), followed by EtOAc–hexane (2:1), was used for flash chromatography; yield 84 mg (72%), colourless oil. ^{1}H NMR ($CDCl_3$): δ 2.86 (s, 3 H, CH_3), 5.44 (s, 2 H, CH_2), 7.3 (m, 5 H, Ph), 8.20 (s, 1 H, H-8). ^{13}C NMR ($CDCl_3$): δ 19.3 (CH_3), 47.7 (CH_2), 116.4 (CN), 128.0 and 128.8 (CH in Ph), 129.1 (C-2), 129.2 (CH in Ph), 137.1 (C-5), 146.2 (C-8), 150.2 (C-4), 160.7 (C-6). MS (EI): 249 (48, M^+), 248 (42), 234 (4), 221 (2), 175 (2), 172 (4), 164 (11), 92 (8), 91 (100), 65 (15). HRMS: Found 249.1005, calc. for $C_{14}H_{11}N_5$ 249.1014.

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