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Addition and Cycloaddition to 2- and 8-Vinylpurines

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The reactivity of purines carrying an alkenyl substituent in the 2- or 8-position in nucleophilic addition and cycloaddition reactions has been studied. A vinyl substituent situated at C-8 is highly electrophilic and readily participates as a Michael acceptor in nucleophilic additions and as a dienophile in Diels–Alder reactions. 2-Vinylpurines may also give addition and cycloaddition products. When benzenethiol was added to 9-benzyl-2-vinylpurine, both the simple adduct as well as 9-benzyl-2-(2-phenylthio-1-hydroxyethyl)-9*H*-purine were formed. The structure of the latter compound was determined by single-crystal X-ray methods.

We have recently demonstrated that 6-vinylpurines are highly electron deficient alkenes which readily participate in nucleophilic additions,[1] Diels–Alder cycloadditions[2] and Heck couplings[3] to give a variety of 6-alkyl- or 6-alkenyl-purines including potent plant growth stimulators[3] as well as adenosine agonist analogs.[2] The potential of 8-vinylpurines as synthetic intermediates has, up till now, not been explored. However, the low stability reported for 8-vinyladenosine derivatives in the presence of nucleophilic reagents,[4] indicated to us that these compounds may also act as electron deficient alkenes in controlled synthetic transformations. 2-Vinylpurines have been utilized in the preparation of several C-2 modified purine nucleosides by catalytic hydrogenation, ozonolysis, dihydroxylation and hydroboration–oxidation,[5] but reactions requiring an electrophilic double bond have, to our knowledge, not been performed. It is, however, reported that 2-vinylinosinic acid inhibits inosine monophosphate dehydrogenase, probably by acting as a Michael acceptor towards cysteine in the enzyme.[6] In this paper we report our results from addition- and cycloaddition reactions on 2- and 8-vinylpurines.

The 8-vinylpurines **6a** and **6b** were prepared by iodination of the *N*-9 alkylated compounds **1a** and **1b** followed by Stille coupling with ethenyl(tributyl)tin (Scheme 1). The iodide **2b** was easily prepared in 93% yield by reaction of **1b** with lithium diisopropylamide (LDA) followed by iodine,[7] but when the same method was attempted on the benzylpurine **1a**, extensive decomposition of the starting material took place. We have also previously observed that certain *N*-benzylpurines do not tolerate butyllithium or LDA.[8] On the other hand, when 9-benzylpurine **1a** was treated with 2.5 equiv. of *N*-iodosuccinimide (NIS) in refluxing tetrahydrofuran (THF) for 2 days, 87% of the desired iodopurine **2a** was isolated together with 6% of the N^6 succinyl protected adenine **3**. When the amount of NIS was reduced to 2.0 equiv., compound **3** could not be detected but the reaction time was substantially prolonged; 75% of **2a** was isolated after 118 h. In order to confirm the structure of the by-product **3**, this compound was converted into the adenine derivatives **4** and **5**[9] as shown in Scheme 1. The structure of compounds **4** and **5** were easily determined by HMBC NMR spectroscopy.[8,10,11]

The 8-vinylpurines **6a** and **6b** were allowed to react with methanol, benzenethiol and diethyl malonate under various reaction conditions (Scheme 1, Table 1). The reactivity towards pure methanol was low (Table 1, entries 1, 2), but treatment with benzenethiol, sodium benzenethiolate or sodium methoxide resulted in clean conversion into the adducts **7a–7d** (Table 1, entries 3, 4, 6–9, 11–14). CSA-mediated addition of methanol or benzenethiol to vinylpurine **6a** resulted in quite moderate yield of adducts **7a** and **7c** and a complex mixture was formed (Table 1, entries 5 and 10). In contrast with CSA-mediated additions to the 6-vinyl isomer,[1] we were not able to isolate and determine the structure of any by-product. Compounds **7e** and **7f** were formed in high yields when compounds **6a** and **6b** were reacted with diethyl malonate in the presence of 0.5 equiv. of sodium hydride (Table 1, entries 12 and 14). As previously observed for 6-vinylpurines,[1] the use of a full equivalent of base resulted in addition of a second vinylpurine to the adducts **7e** or **7f**, giving the 1:2 adducts **8a** and **8b** (Table 1, entries 11 and 13). The reactivity of 8-vinylpurines towards the nucleophiles examined appears comparable to that of 6-vinylpurines.[1]

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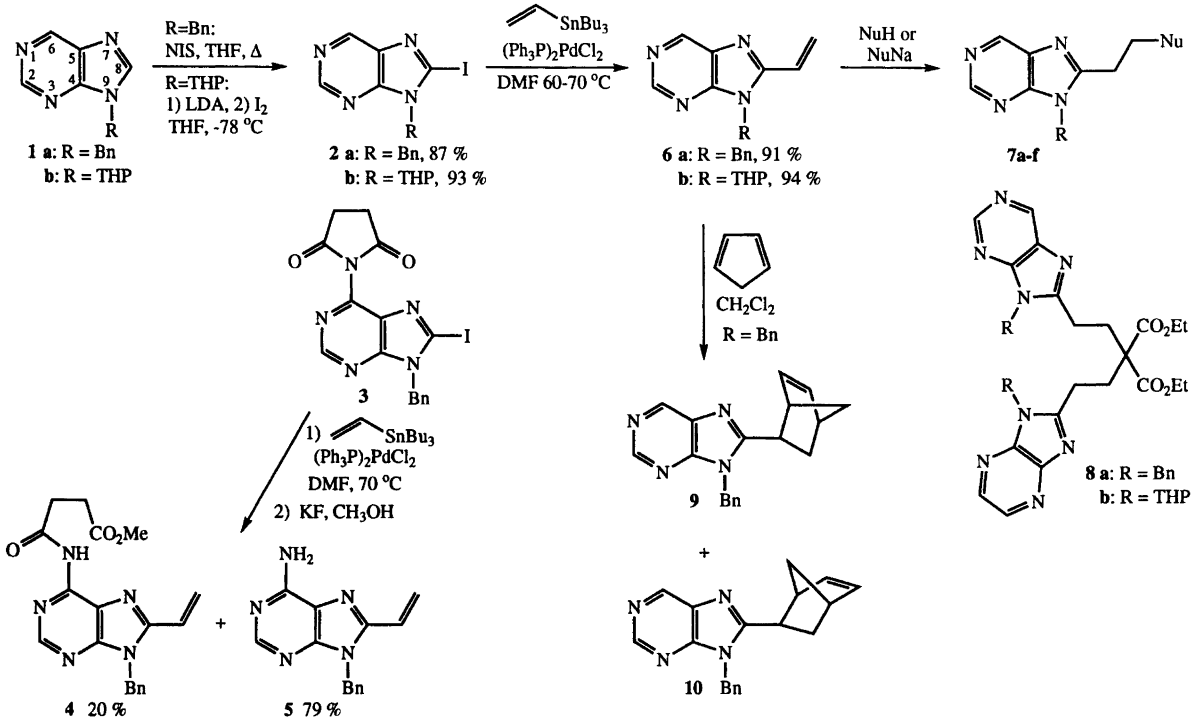


Scheme 1.

Table 1. Addition to 8-vinylpurines **6**.

Entry	Vinylpurine **6**	NuH	Co-reagent	Solvent	Time	Yield (%) **7**[a]
1	R=Bn, **6a**	MeOH	—	MeOH	6 weeks	7, **7a**[b]
2	R=THP, **6b**	MeOH	—	MeOH	6 weeks	4, **7b**[b]
3	R=Bn, **6a**	MeOH	NaH	DCE	4 h	85, **7a**
4	R=THP, **6b**	MeOH	NaH	DCE	4 h	91, **7b**
5	R=Bn, **6a**	MeOH	CSA	DCE	20 h	19, **7a**[c]
6	R=Bn, **6a**	PhSH	—	DCE	5 h	82, **7c**
7	R=THP, **6b**	PhSH	—	DCE	5 h	80, **7d**
8	R=Bn, **6a**	PhSH	NaH	DCE	4 h	84, **7c**
9	R=THP, **6b**	PhSH	NaH	DCE	4 h	85, **7d**
10	R=Bn, **6a**	PhSH	CSA	DCE	2 h	51, **7c**[c]
11	R=Bn, **6a**	$CH_2(CO_2Et)_2$	NaH (1.2 equiv.)	THF	3 h	63, **7e**[d]
12	R=Bn, **6a**	$CH_2(CO_2Et)_2$	NaH (0.5 equiv.)	THF	3 h	86, **7e**
13	R=THP, **6b**	$CH_2(CO_2Et)_2$	NaH (1.2 equiv.)	THF	3 h	62, **7f**[e]
14	R=THP, **6b**	$CH_2(CO_2Et)_2$	NaH (0.5 equiv.)	THF	3 h	84, **7f**

[a]Yields of isolated products unless otherwise stated. [b]From the ^{1}H NMR spectrum of the crude product. [c]Several unidentified products were also formed. [d]22% of compound **8a** was also isolated. [e]15% of compound **8b** was also isolated.

The vinylpurine **6a** was subjected to cycloaddition with cyclopentadiene to give the Diels–Alder adducts **9** and **10** with the *endo* isomer **9** as the major product (Scheme 1, Table 2). The stereochemical assignments of the *exo* and *endo* isomers were confirmed by NOESY spectroscopy.[2] Addition of zinc chloride to the reaction mixture resulted in considerably shorter reaction times and the *endo* selectivity was improved. When 4.0 equiv.

Table 2. Diels–Alder reactions on 8-vinylpurine **6a**.

Entry	Temp.	*t*/h	Catalyst	Yield (%) *endo* **9**[a]	Yield (%) *exo* **10**[a]
1	0 °C–rt	110	—	73[b]	12
2	0 °C–rt	24	$ZnCl_2$ (1 equiv.)	85	—[c]
3	0 °C	2.5	$ZnCl_2$ (4 equiv.)	83	—

[a]Yields of isolated products. [b]The *endo*: *exo* ratio in the crude product was 84 : 16 according to ^{1}H NMR. [c]Ca. 5% was present in the crude product according to the ^{1}H NMR spectrum.

of Lewis acid were present, the *exo* isomer **10** could no longer be detected. These findings closely resemble our results from Diels–Alder reactions on 6-vinylpurines,[2] but it appears that the 8-vinylpurine **6a** is somewhat more reactive and more *endo* selective in uncatalysed reaction with cyclopentadiene compared with the 6-vinyl isomer previously examined. With the latter compound more than 30% starting material remained unchanged after 4 days and the *endo*:*exo* ratio was close to 1:1.[2]

We next turned our attention to the 2-vinylpurine **14** (Scheme 2). For the preparation of compound **14** we utilized Nair's method for 2-vinylpurine nucleoside synthesis[5,12] starting from the 6-chloro-2-aminopurine **11**.[11c] The 6-chloro substituent was removed by catalytic hydrogenation and the resulting aminopurine **12** was converted into the iodopurine **13** by treatment with isopentyl nitrite, diiodomethane and CuI. Compound **13** readily participated in coupling with ethenyl(tributyl)tin to give the desired vinylpurine **14**.

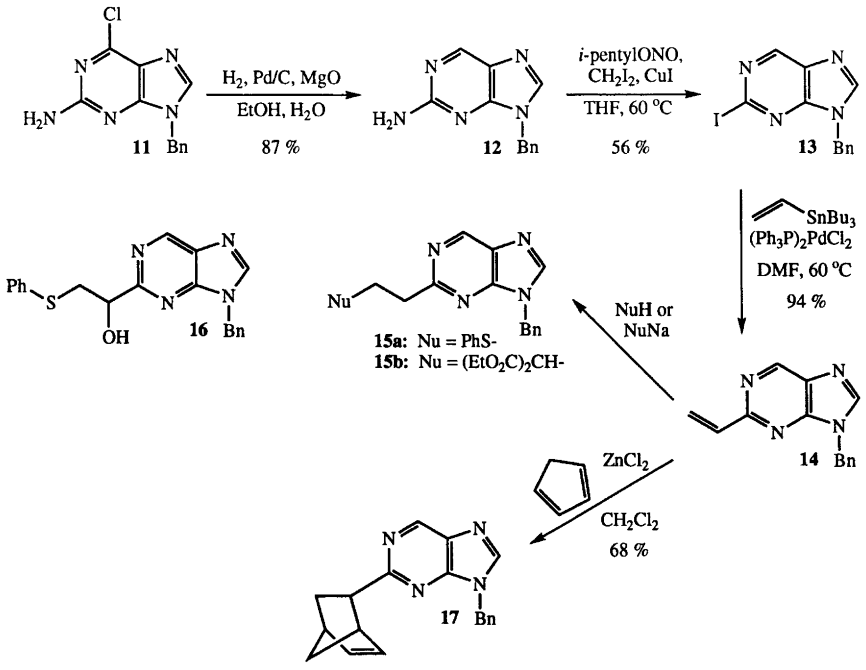
All attempts to add methanol alone or in the presence of CSA to the 2-ethenylpurine **14** failed even at elevated temperatures. This alkene was also completely inert towards excess sodium methoxide in DCE at ambient temperature as well as at 80 °C. On the other hand, when compound **14** was reacted with benzenethiol, the expected adduct **15a** could be isolated together with various amounts of the β-hydroxy sulfide **16** (Scheme 2, Table 3, entries 1–7). Single-crystal X-ray crystallography was used to determine the structure of compound **16** (*vide infra*). The formation of **16** may be the result of addition of benzenethiol and oxygen to the alkene **14**. β-Hydroxy sulfides are formed when oxidative addition of thiols is carried out in the presence of amines,[13] and in our reactions purines may have served as the source of base. This reaction pathway could account for the need for a substantial excess of thiol. Employing standard syringe and needle techniques and nitrogen or argon as an inert atmosphere, we were not able completely to suppress the formation of compound **16**.

The adduct **15b** was formed when the vinylpurine **14** was treated with the sodium salt of diethyl malonate, but an excess of the Michael donor as well as refluxing THF were required (Table 3, entries 8–11). Formation of a 1:2 adduct such as compound **8** (Scheme 1) was not observed.

The structure of compound **16** was determined by single-crystal X-ray crystallography and the asymmetric unit of **16** with atomic numbering is shown in Fig. 1. Final atomic coordinates and U_{eq} values are listed in Table 5, selected geometric parameters in Table 6. Tables of anisotropic displacement parameters, coordinates of hydrogen atoms and a listing of observed and calculated structure factors are available from the correspondence author upon request.

Even though the 2-ethenylpurine **14** was found to be a substantially less reactive dienophile than the 6- or 8-vinylated isomers, this compound did react with cyclopentadiene in the presence of 4 equiv. of zinc chloride to give the *endo* adduct **17** in 68% yield (Table 7, entry 3). The starting material was consumed after 2 days and no *exo* isomer could be detected.

The results presented in this and previous[1–3] papers, demonstrate that purines carrying an alkenyl substituent in the 2-, 6- or 8-position may be versatile intermediates in syntheses of modified purine derivatives. A vinyl substituent situated at C-6 or C-8 is highly electrophilic



Scheme 2.

Table 3. Addition to the 2-vinylpurine **14**.

Entry[a]	NuH	Co-reagent	Solvent	T/°C	t/h	% **14**[b]	**15**:**16**[b]	Yield (%) **15**[c]	Yield (%) **16**[c]
1[d]	PhSH (1.2 equiv.)	—	DCE	rt	24	31	60:40	32, **15a**	24
2	PhSH (2.4 equiv.)	—	DCE	rt	5	0	77:23	66, **15a**	19
3[d]	PhSH (2.4 equiv.)	—	DCE	rt	5	0	87:13	74, **15a**	10
4[d]	PhSH (2.4 equiv.)	—	THF	rt	5	0	51:49	41, **15a**	37
5[d]	PhSH (2.4 equiv.)	NaH (2.4 equiv.)	DCE	rt	40	55	44:56	23, **15a**	31
6[d]	PhSH (2.4 equiv.)	NaH (2.4 equiv.)	DCE	rt	40	62	36:64	12, **15a**	23
7	PhSH (2.4 equiv.)	CSA (1.0 equiv.)	DCE	rt	5	0[e]	78:22	23, **15a**	—[f]
8	$CH_2(CO_2Et)_2$ (6.0 equiv.)	NaH (6.0 equiv.)	THF	rt	120	—[f]	—	36, **15b**[g]	—
9	$CH_2(CO_2Et)_2$ (6.0 equiv.)	NaH (6.0 equiv.)	THF	Δ	96	15	—	70, **15b**	—
10	$CH_2(CO_2Et)_2$ (3.0 equiv.)	NaH (3.0 equiv.)	THF	Δ	96	27	—	62, **15b**	—
11	$CH_2(CO_2Et)_2$ (1.5 equiv.)	NaH (1.5 equiv.)	THF	Δ	96	83	—	14, **15b**	—

[a]Reactions were performed under an N_2-atmosphere unless otherwise stated. [b]From the ^1H NMR spectrum of the crude product. [c]Yields of isolated products. [d]Under an Ar-atmosphere. [e]Several unidentified products were also formed. [f]Not determined. [g]49% of the starting material **14** was recovered.

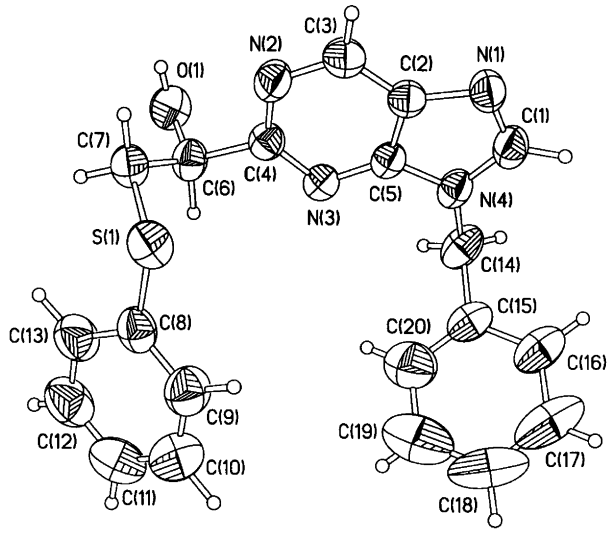


Fig. 1. Molecular structure of compound **16** with atomic numbering. Displacement ellipsoids drawn at the 50% propability level. H-atoms are arbitrarily scaled.

and reacts smoothly as a Michael acceptor in nucleophilic additions and as dienophile in Diels–Alder reactions. Only minor differences in reactivity between the 6-vinylpurine studied before[1–3] and the 8-vinylpurines described herein have been observed. Although less readily, 2-vinylpurines also give addition and cycloaddition products.

Experimental

General information. The ^1H NMR spectra were recorded at 500 MHz with a Bruker Avance DRX 500, at 300 MHz with a Bruker Avance DPX 300 or at 200 MHz with a Bruker Avance DPX 200 instrument. The ^{13}C NMR spectra were recorded at 125, 75 or 50 MHz using the above mentioned spectrometers. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane. Mass spectra were recorded at 70 eV ionising voltage with a VG Prospec instrument, and are presented as m/z (% rel. int.). Methane was used for chemical ionisation. 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). DMF was distilled from BaO. THF was distilled from sodium–benzophenone. Dichloroethane and dichloromethane were distilled from CaH_2. Methanol was distilled from magnesium and iodine and stored over molecular sieves. Benzenethiol was distilled at reduced pressure and stored over molecular sieves. A ca. 60% oily dispersion of sodium hydride was washed with hexane (×3) and dried *in vacuo* prior

Table 4. Crystal data, intensity collection and refinement data for compound **16**.

Formula	$C_{20}H_{18}N_4OS$
Formula weight/g mol^{-1}	362.44
Crystal size/mm	1.10 × 0.25 × 0.025
Colour, habit	Colourless plate
Crystal system	Monoclinic
Space group	*C*2/*c* (No. 15)
Cell dimensions/Å, °	*a* = 36.6951(11)
	b = 12.5877(5)
	c = 8.0725(2)
	β = 101.099(2)
Volume/Å^3	3659.0(2)
Z	8
D_{calc}/g cm^{-3}	1.316
F(000)	1520
Diffractometer	Siemens SMART[16]
Radiation	Mo Kα (λ = 0.71073 Å)
Monochromator	Graphite crystal
T/K	293
Scan mode	ω-scans
No. of sets of exposures	3
Exposure time per frame/s	60
Crystal to detector distance/cm	5.01
2θ range/°	3.42–52.84
Index ranges	$-32 \leqslant h \leqslant 45$
	$-15 \leqslant k \leqslant 14$
	$-10 \leqslant l \leqslant 10$
Absorption correction	Multi-scan[17]
No. of reflections measured	3715
No. of reflections used in refinement	3713
No. of reflections with $I > 2\sigma(I)n$	2046
Refinement	on F^2
No. of refined parameters *p*	251
$R = \Sigma\|\Delta F\|/\|F_o\|$ [a] $[I > 2\sigma(I)]$	0.0526
$R_w = \{\Sigma[w(\Delta F)^2/w(F_o)^2]\}^{1/2}$ [b] $[I > 2\sigma(I)]$	0.1187
$S = \{\Sigma[w(\Delta F)^2/(n-p)]\}^{1/2}$ $[I > 2\sigma(I)]$	1.081
Residual electron density/e Å^{-3}	+0.415, −0.333

[a] $\Delta F = |F_o| - |F_c|$. [b] $w = [\sigma^2(F_o^2) + (0.0544P)^2 + 4.1120P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$.

to use. All other reagents were commercially available and used as received.

Starting materials available by literature procedures. 9-Benzyl-9*H*-purine (**1a**),[14] 9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (**1b**)[15] and 2-amino-9-benzyl-6-chloro-9*H*-purine (**11**).[11c]

Crystallography. Single crystals suitable for X-ray analysis were obtained by crystallization of compound **16** from $CHCl_3$–hexane. Single-crystal X-ray data were collected with a Siemens SMART CCD diffractometer,[16] and nominally covered a hemisphere of reciprocal space. Data were corrected for Lorentz- and polarization-effects, and Sadabs[17] was used to correct for absorption. The data collection procedure is summarized in Table 4. The structure was solved by direct methods and refined by the least-squares method.[18] Positional parameters for all heavy atoms were refined. Hydrogen atoms were kept in idealized positions, refining a single C–H distance for all H atoms connected to the same C atom. Heavy atoms were refined anisotropically, whereas U_{iso} for the hydrogen atoms were fixed at $1.2U_{eq}$ of the bonded C atom. The hydroxy H(1) atom bonded to O(1) was localized using the rotating group refinement (AFIX card 147) of SHELXTL[18] and U_{iso} was set to $1.5U_{eq}$ for O(1). The refinement of the structure is summarized in Table 1. Atomic scattering factors are taken from Ref. 19.

Table 5. Fractional coordinates with e.s.d.s and equivalent temperature factors for all non-hydrogen atoms in compound **16**.

Atom	*x*	*y*	*z*	U_{eq} [a]
S1	0.14298(3)	0.12562(7)	−0.02808(11)	0.0634(3)
O1	0.19826(6)	0.1472(2)	0.4540(3)	0.0616(6)
N1	0.23399(7)	0.5585(2)	0.1117(3)	0.0533(7)
N2	0.22336(7)	0.2697(2)	0.1716(3)	0.0537(7)
N3	0.17512(6)	0.3697(2)	0.2588(3)	0.0425(6)
N4	0.18214(7)	0.5586(2)	0.2200(3)	0.0474(6)
C1	0.20814(9)	0.6155(3)	0.1585(4)	0.0548(8)
C2	0.22439(8)	0.4550(2)	0.1447(3)	0.0442(7)
C3	0.23945(9)	0.3571(2)	0.1264(4)	0.0542(8)
C4	0.19263(8)	0.2798(2)	0.2369(4)	0.0446(7)
C5	0.19215(8)	0.4543(2)	0.2120(3)	0.0401(7)
C6	0.17660(9)	0.1786(2)	0.2964(4)	0.0514(8)
C7	0.17321(9)	0.0903(2)	0.1685(4)	0.0552(8)
C8	0.09789(9)	0.1260(2)	0.0195(4)	0.0566(8)
C9	0.07343(11)	0.2044(3)	−0.0503(5)	0.0729(11)
C10	0.03698(13)	0.2038(4)	−0.0293(5)	0.0870(13)
C11	0.02486(13)	0.1260(4)	0.0659(5)	0.0844(13)
C12	0.04909(12)	0.0488(4)	0.1372(5)	0.0840(13)
C13	0.08517(11)	0.0474(3)	0.1136(5)	0.0732(11)
C14	0.15040(9)	0.5980(3)	0.2863(4)	0.0609(10)
C15	0.11595(9)	0.6114(3)	0.1559(4)	0.0556(8)
C16	0.10962(12)	0.7052(3)	0.0667(5)	0.0758(11)
C17	0.0779(2)	0.7196(5)	−0.0498(6)	0.115(2)
C18	0.0520(2)	0.6420(7)	−0.0764(8)	0.130(3)
C19	0.05780(15)	0.5476(6)	0.0077(9)	0.135(2)
C20	0.09031(12)	0.5328(4)	0.1252(6)	0.0930(14)

[a] $U_{eq} = S_i S_j U_{ij} a_i^* a_j^* \mathbf{a}_i \mathbf{a}_j$.

*9-Benzyl-8-iodo-9*H*-purine* (**2a**) *and 9-benzyl-8-iodo-*N^6*-succinyladenine* (**3**). A mixture of 9-benzyl-9*H*-purine **1a** (315 mg, 1.5 mmol) and *N*-iodosuccinimide (844 mg, 3.8 mmol) in dry THF (10 ml) was heated at reflux under N_2 for 48 h, cooled and evaporated. The residue was stirred in dichloromethane (10 ml) and 10 M aq. $NaHSO_3$ was gradually added until the pink colour disappeared. 5% aq. K_2CO_3 (25 ml) was added and the mixture was stirred for 10 min, before the phases were separated. The aqueous layer was extracted with dichloromethane (4 × 10 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo*, and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (4:1) followed by EtOAc–hexane (20:1); yield 440 mg (87%) of compound **2a** as colourless crystals and 41 mg (6%) of compound **3** as colourless crystals.

2a. M.p. 195–196 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.45 (s, 2 H, CH_2), 7.30 (s, 5 H, Ph), 8.92 (s, 1 H, H-2), 9.04 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 48.9 (CH_2), 108.3 (C-8), 127.8, 128.4 and 128.9 (CH in Ph), 134.7, 136.3 (C in Ph/C-5), 147.1

Table 6. Selected bond lengths (Å) and torsion angles (°) with e.s.d.s in compound **16**, torsion angles refering to the *S* enantiomer.

S1–C7	1.808(3)	C6–C7	1.505(4)
S1–C8	1.769(4)	C8–C9	1.380(5)
O1–C6	1.420(4)	C8–C13	1.383(5)
N1–C1	1.302(4)	C9–C10	1.380(5)
N1–C2	1.389(3)	C10–C11	1.371(6)
N2–C3	1.332(4)	C11–C12	1.367(6)
N2–C4	1.340(4)	C12–C13	1.374(5)
N3–C4	1.330(3)	C14–C15	1.491(4)
N3–C5	1.326(3)	C15–C16	1.379(5)
N4–C1	1.361(3)	C15–C20	1.355(5)
N4–C5	1.368(4)	C16–C17	1.361(6)
N4–C14	1.459(4)	C17–C18	1.350(8)
C2–C3	1.370(4)	C18–C19	1.365(8)
C2–C5	1.394(4)	C19–C20	1.386(7)
C4–C6	1.519(4)		
C(5)–N(4)–C(14)–C(15)	−92.8(3)	C(4)–C(6)–C(7)–S(1)	−60.5(3)
N(4)–C(14)–C(15)–C(16)	−87.2(4)	C(6)–C(7)–S(1)–C(8)	−71.3(3)
N(4)–C(14)–C(15)–C(20)	93.8(4)	C(7)–S(1)–C(8)–C(9)	140.4(3)
N(3)–C(4)–C(6)–O(1)	−101.7(3)	C(7)–S(1)–C(8)–C(13)	−44.2(3)
N(3)–C(4)–C(6)–C(7)	133.5(3)		

Table 7. Diels–Alder reactions on the 2-vinylpurine **14**.

Entry	Temp.	*t*/h	Catalyst	**14**:**17**[a]	Yield (%) **17**[b]
1	0 °C–rt	120	—	89:11[c]	—
2	0 °C–rt	96	$ZnCl_2$ (1 equiv.)	65:35[c]	30
3	0 °C–rt	52	$ZnCl_2$ (4 equiv.)	—[d]	68

[a]From the ^1H NMR spectrum of the crude product. [b]Yields of isolated products. [c]Less than 10% of the *exo* isomer may have been present. [d]No starting material or *exo* isomer could be observed.

(C-6), 152.5 (C-4), 152.8 (C-2). MS (EI): 336 (68, M^+), 289 (10), 209 (100), 104 (8), 91 (99), 77 (10), 65 (22).

3. M.p. 224–226 °C. Anal.: C, H. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.98 (s, 4 H, CH_2CH_2), 5.50 (s, 2 H, CH_2N), 7.2–7.4 (m, 5 H, Ph), 8.93 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.0 (CH_2CH_2), 49.5 (CH_2N), 109.8 (C-8), 128.0, 128.6 and 128.9 (CH in Ph), 131.9 (C-5), 134.2 (C in Ph), 142.7 (C-6), 152.5 (C-2), 155.1 (C-4). MS (EI): 433 (70, M^+), 306 (68), 250 (7), 224 (30), 91 (100), 65 (15).

*8-Iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine* (**2b**). A solution of 9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1b** (408 mg, 2.0 mmol) in dry THF (3 ml) was added dropwise over 10 min to a stirred solution of LDA [prepared *in situ* from butyllithium (1.6 M in hexane, 2.5 ml, 4.0 mmol) and diisopropylamine (0.66 ml, 4.6 mmol) in THF (4 ml)] under N_2 at −78 °C. After 1 h, a solution of iodine (4.0 mmol) in THF (2 ml) was added dropwise over 10 min. The resulting mixture was stirred at −78 °C for 1 h before sat. aq. NH_4Cl (1.2 ml) was added. The mixture was warmed to ambient temperature and evaporated *in vacuo*, and the product was purified by flash chromatography eluting with EtOAc–hexane (20:1); yield 615 mg (93%) pale yellow crystals. M.p. 128–129 °C. Anal.: C, H. ^1H NMR ($CDCl_3$, 300 MHz): δ 1.6–1.9 (m, 4 H, THP), 2.1 (m, 1 H, THP), 3.1–3.2 (m, 1 H, THP), 3.7 (m, 1 H, H-6 in THP), 4.1–4.2 (m, 1 H, H-6 in THP), 5.62 (dd, *J* 11.2 and 2.4 Hz, 1 H, H-2 in THP), 8.85 (s, 1 H, H-2), 8.96 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.3, 24.6 and 28.8 (CH_2 in THP), 69.3 (C-6 in THP), 86.9 (C-2 in THP), 106.7 (C-8), 136.7 (C-5), 147.2 (C-6), 152.1 (C-4), 152.2 (C-2). MS (EI): 330 (3, M^+), 246 (100), 127 (6), 119 (9), 92 (25), 85 (31), 65 (16).

*9-Benzyl-*N^6*-(3-methoxycarbonylpropionyl)-8-ethenyladenine* (**4**) *and 9-benzyl-8-ethenyladenine* (**5**). A mixture of 9-benzyl-8-iodo-*N*^{6}-succinyladenine (**3**) (87 mg, 0.20 mmol), bis(triphenylphosphine)palladium(II) chloride (7 mg, 0.01 mmol) and ethenyl(tributyl)tin (84 µl, 0.28 mmol) in dry DMF (2 ml) was heated under N_2 at 70 °C for 1.5 h. The reaction mixture was evaporated *in vacuo* and a sat. solution of potassium fluoride in methanol (5 ml) was added to the residue. The resulting mixture was stirred at ambient temperature for 45 min and evaporated *in vacuo*, and the crude product was purified by flash chromatography eluting with EtOAc–hexane (20:1) followed by EtOAc–acetone (6:1); yield 15 mg (20%) of compound **4** as colourless crystals and 40 mg (79%) of compound **5** as colourless crystals.

4. M.p. 133–134 °C. ^1H NMR ($CDCl_3$, 500 MHz): δ 2.73 (t, *J* 6.7 Hz, 2 H, CH_2), 3.27 (t, *J* 6.4 Hz, 2 H, CH_2), 3.64 (s, 3 H, CH_3), 5.42 (s, 2 H, CH_2N), 5.65 (dd, *J* 10.8 and 1.0 Hz, 1 H, $=CH_2$), 6.49 (dd, *J* 17.4 and 1.0 Hz, 1 H, $=CH_2$), 6.65 (dd, *J* 17.4 and 10.8 Hz, 1 H, =CH), 7.1 (m, 2 H, Ph), 7.2–7.3 (m, 3 H, Ph), 8.60 (s, 2 H, H-2 and NH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 28.7 (CH_2), 32.9 (CH_2), 45.8 (CH_2N), 51.8 (CH_3), 121.3

(C-5), 122.5 (=CH_2), 125.3 (=CH), 126.8, 128.2 and 129.0 (CH in Ph), 135.4 (C in Ph), 148.2 (C-6), 150.7 (C-8), 152.1 (C-2), 152.5 (C-4), 171.7, 173.1 (C=O). MS (EI): 365 (3, M^+), 361 (7), 333 (37), 292 (8), 251 (12), 197 (8), 182 (37), 122 (19), 91 (60), 44 (100). HRMS: Found: 365.1501. Calc. for $C_{19}H_{19}N_5O_3$: 365.1488.

5. M.p. 194 °C. Anal.: C, H. ^{1}H NMR (DMSO-d_6–C_6D_6, 500 MHz): δ 5.38 (s, 2 H, CH_2), 5.45 (dd, *J* 11.2 and 1.8 Hz, 1 H, =CH_2), 6.27 (dd, *J* 17.0 and 1.8 Hz, 1 H, =CH_2), 6.84 (dd, *J* 17.0 and 11.2 Hz, 1 H, =CH), 7.1–7.2 (m, 5 H, Ph), 7.32 (s, 2 H, NH_2), 8.15 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 44.9 (CH_2), 118.9 (C-5), 122.2 (=CH_2), 124.1 (=CH), 127.2, 127.9 and 129.1 (CH in Ph), 137.5 (C in Ph), 147.8 (C-8), 150.9 (C-4), 153.0 (C-2), 156.0 (C-6). MS (EI): 251 (100, M^+), 236 (11), 224 (7), 208 (7), 149 (8), 91 (98), 65 (18).

*9-Benzyl-8-ethenyl-9*H*-purine* (**6a**). A mixture of 9-benzyl-8-iodo-9*H*-purine **2a** (336 mg, 1.0 mmol), bis(triphenylphosphine)palladium(II) chloride (36 mg, 0.05 mmol) and ethenyl(tributyl)tin (420 µl, 1.40 mmol) in dry DMF (4 ml) was heated at 70 °C under N_2 for 25 h and cooled. A sat. solution of potassium fluoride in methanol (20 ml) was added and the resulting mixture was stirred at ambient temperature for 4 h and evaporated *in vacuo* together with a small amount of silica gel. The residue was added to the top of a silica gel column and the product was isolated by flash chromatography eluting with EtOAc–hexane (10:1); yield 215 mg (91%) colourless crystals. M.p. 140–141 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.50 (s, 2 H, CH_2), 5.75 (dd, *J* 9.9 and 2.5 Hz, 1 H, =CH_2), 6.7 (m, 2 H, =CH_2 and CH=), 7.1 (m, 2 H, Ph), 7.3 (m, 3 H, Ph), 8.93 (s, 1 H, H-2), 9.07 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 45.5 (CH_2), 122.5 (=CH_2), 126.3 (CH=), 126.8, 128.2 and 129.0 (CH in Ph), 133.7, 135.3 (C in Ph/C-5), 147.5 (C-6), 152.5 (C-2), 152.6, 152.9 (C-4/C-8). MS (EI): 236 (89, M^+), 221 (9), 209 (10), 182 (10), 149 (13), 134 (11), 105 (15), 91 (100), 77 (12), 65 (20).

*8-Ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine* (**6b**). A mixture of 8-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2b** (660 mg, 2.0 mmol) bis(triphenylphosphine)-palladium(II) chloride (72 mg, 0.10 mmol), and ethenyl-(tributyl)tin (830 µl, 2.8 mmol) in dry dichloroethane (10 ml) was heated at 60 °C under N_2 for 5 h and cooled. The reaction mixture was evaporated *in vacuo* and a sat. solution of potassium fluoride in methanol (40 ml) was added to the residue. The resulting mixture was stirred at ambient temperature for 4 h and evaporated *in vacuo* together with a small amount of silica gel. The residue was added to the top of a silica gel column and the product was isolated by flash chromatography eluting with EtOAc–hexane (2:1) followed by EtOAc–hexane (4:1); yield 431 mg (94%) colourless crystals. M.p. 99–100 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.7–1.9 (m, 4 H, THP), 2.1–2.4 (m, 2 H, THP), 3.7–3.8 (m, 1 H, H-6 in THP), 4.2 (m, 1 H, H-6 in THP), 5.78 (dd, *J* 11.2 and 1.5 Hz, 1 H, CH_2=), 5.95 (dd, *J* 11.2 and 2.5 Hz, 1 H, H-2 in THP), 6.63 (dd, *J* 17.2 and 1.5 Hz, 1 H, CH_2=), 7.19 (dd, *J* 17.2 and 11.2 Hz, 1 H, CH=), 8.89 (s, 1 H, H-2), 9.03 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 23.1, 24.9 and 31.4 (CH_2 in THP), 69.3 (C-6 in THP), 82.3 (C-2 in THP), 124.9, 125.3 (CH_2=/CH=), 133.4 (C-5), 147.5 (C-6), 151.7 (C-4), 152.1 (C-2), 152.9 (C-8). MS (EI): 230 (25, M^+), 147 (100), 120 (9), 85 (88), 67 (22).

*9-Benzyl-8-(2-methoxyethyl)-9*H*-purine* (**7a**). 9-Benzyl-8-ethenyl-9*H*-purine (59 mg, 0.25 mmol) was dissolved in dry dichloroethane (3 ml) and the mixture was stirred at ambient temperature under N_2 for 10 min before a 25% solution of sodium methoxide in methanol (69 µl, 0.30 mmol) was added. The reaction was quenched with glacial acetic acid (22 µl, 0.38 mmol) after being stirred at ambient temperature for 4 h. The resulting mixture was evaporated *in vacuo* and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–acetone (6:1); yield 57 mg (85 %) pale yellow oil. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.06 (t, *J* 4.3 Hz, 2 H, CH_2), 3.29 (s, 3 H, CH_3), 3.80 (t, *J* 4.3 Hz, 2 H, CH_2O), 5.49 (s, 2 H, CH_2N), 7.1 (m, 2 H, Ph), 7.3 (m, 3 H, Ph), 8.92 (s, 1 H, H-2), 9.02 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 28.9 (CH_2), 45.5 (CH_2N), 58.9 (CH_3), 69.6 (CH_2O), 127.0, 128.1 and 129.0 (CH in Ph), 133.3 (C-5), 135.4 (C in Ph), 146.9 (C-6), 152.2 (C-2), 152.8 (C-4), 156.2 (C-8). MS (EI): 268 (22, M^+), 253 (31), 238 (43), 223 (10), 91 (100), 65 (13).

*8-(2-Methoxyethyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine* (**7b**). 8-Ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **6b** (115 mg, 0.50 mmol) was dissolved in dry dichloroethane (5 ml) and the mixture was stirred at ambient temperature under N_2 for 10 min before a 25% solution of sodium methoxide in methanol (137 µl, 0.60 mmol) was added. The reaction was quenched with glacial acetic acid (45 µl, 0.76 mmol) after 4 h, the resulting mixture was evaporated *in vacuo*, and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–acetone (6:1); yield 120 mg (91%) colourless crystals. M.p. 64–65 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.8 (m, 4 H, THP), 2.1 (m, 1 H, THP), 2.5–2.7 (m, 1 H, THP), 3.3–3.4 (m, 5 H, CH_3 and CH_2), 3.7 (m, 1 H, H-6 in THP), 3.9–4.1 (m, 2 H, CH_2O), 4.1–4.2 (m, 1 H, H-6 in THP), 5.78 (dd, *J* 11.3 and 2.5 Hz, 1 H, H-2 in THP), 8.87 (s, 1 H, H-2), 8.96 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.2, 24.8, 29.8, 30.1 (CH_2 in THP and CH_2Pur), 58.9, 69.2 (CH_2O/CH_3O), 69.7 (C-6 in THP), 83.1 (C-2 in THP), 133.2 (C-5), 147.0 (C-6), 151.8 (C-2), 152.1 (C-4), 155.7 (C-8). MS (EI): 262 (7, M^+), 247 (11), 179 (51), 163 (46), 148 (64), 85 (72), 67 (21).

*9-Benzyl-8-(2-phenylthioethyl)-9*H*-purine* (**7c**). Sodium hydride (8 mg, 0.33 mmol) was added to a solution of benzenethiol (31 µl, 0.30 mmol) in dry dichloroethane

(1 ml) at ambient temperature under N_2. After 10 min, a solution of 9-benzyl-8-ethenyl-9*H*-purine (59 mg, 0.25 mmol) in dry dichloroethane (2 ml) was added and the resulting mixture was stirred for 4 h before glacial acetic acid (20 µl, 0.35 mmol) was added. The mixture was evaporated *in vacuo* and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (2:1); yield 73 mg (84%) pale yellow oil. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.1 (m, 2 H, CH_2), 3.4 (m, 2 H, CH_2S), 5.35 (s, 2 H, CH_2N), 7.0–7.3 (m, 10 H, Ph), 8.93 (s, 1 H, H-2), 9.03 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 28.3 (CH_2), 30.8 (CH_2S), 45.5 (CH_2N), 126.6–129.9 (CH in Ph), 133.3 (C-5), 134.8 and 135.1 (C in Ph), 147.0 (C-6), 152.3 (C-2), 152.7 (C-4), 156.2 (C-8). MS (EI): 346 (45, M^+), 313 (11), 277 (38), 255 (12), 237 (22), 224 (41), 201 (7), 121 (9), 109 (11), 91 (100).

*8-(2-Phenylthioethyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine* (**7d**). Sodium hydride (14 mg, 0.60 mmol) was added to a solution of benzenethiol (62 µl, 0.61 mmol) in dry DCE (2 ml) at ambient temperature under N_2. After 10 min, a solution of 8-ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **6b** (115 mg, 0.50 mmol) in dry dichloroethane (5 ml) was added and the resulting mixture was stirred for 4 h before glacial acetic acid (40 µl, 0.69 mmol) was added. The mixture was evaporated *in vacuo* and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (2:1); yield 145 mg (85%) pale yellow oil. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.6–2.4 (m, 6 H, THP), 3.3–3.7 (m, 5 H, CH_2CH_2 and H-6 in THP), 4.1 (m, 1 H, H-6 in THP), 5.72 (dd, *J* 11.2 and 2.5 Hz, 1 H, H-2 in THP), 7.2–7.4 (m, 5 H, Ph), 8.87 (s, 1 H, H-2), 8.98 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.0 and 24.7 (CH_2 in THP), 29.7 (CH_2), 30.4, 31.1, (CH_2 in THP/CH_2S), 69.1 (C-6 in THP), 82.7 (C-2 in THP), 126.5, 129.0 and 129.8 (CH in Ph), 133.1 (C-5), 135.3 (C in Ph), 147.1 (C-6), 151.9 (C-2), 152.1 (C-4), 156.1 (C-8). MS (EI): 339 (5, M^+), 277 (24), 256 (72), 223 (45), 210 (19), 147 (100), 134 (88), 123 (26), 109 (12), 85 (25).

*9-Benzyl-8-[3,3-bis(ethoxycarbonyl)propyl]-9*H*-purine* (**7e**) *and diethyl bis[(9-benzyl-8-purinyl)ethyl]malonate* (**8a**). Diethyl malonate (46 µl, 0.30 mmol) was added to a stirred suspension of sodium hydride (7.5 mg, 0.30 mmol) in dry THF (2 ml) at ambient temperature under N_2. After 10 min, a solution of 9-benzyl-8-ethenyl-9*H*-purine **6b** (59 mg, 0.25 mmol) in THF (2 ml) was added and the resulting mixture stirred at ambient temperature for 3 h. The reaction was quenched with glacial acetic acid (22 µl, 0.38 mmol), evaporated *in vacuo* and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (3:1) followed by EtOAc–MeOH (10:1); yield 62 mg (63%) of compound **7e** as colourless crystals and 17 mg (22%) of compound **8a** as a colourless oil.

7e. M.p. 70–71 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.21 (t, *J* 7.1 Hz, 6 H, 2 × CH_3), 2.41 (q, *J* 7.4 Hz, 2 H, CH_2), 2.90 (t, *J* 7.3 Hz, 2 H, CH_2), 3.55 [t, *J* 7.2 Hz, 1 H, $CH(CO_2Et)_2$], 4.14 (m, 4 H, 2 × CH_2CH_3), 5.45 (s, 2 H, CH_2N), 7.1–7.4 (m, 5 H, Ph), 8.94 (s, 1 H, H-2), 9.03 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.0 (CH_3), 25.3 (CH_2), 25.4 (CH_2), 45.5 (CH_2N), 50.6 [$CH(CO_2Et)_2$], 61.5 (CH_2CH_3), 127.0, 128.2 and 129.0 (CH in Ph), 133.3 (C-5), 135.2 (C in Ph), 146.9 (C-6), 152.2 (C-2), 152.9 (C-4), 156.7 (C-8), 168.8 (C=O). MS (EI): 396 (23, M^+), 351 (15), 277 (8), 237 (100), 223 (8), 159 (4), 91 (96), 65 (7).

8a. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.13 (t, *J* 7.1 Hz, 6 H, 2 × CH_3), 2.44 (m, 4 H, 2 × CH_2), 2.82 (m, 4 H, 2 × CH_2), 4.07 (q, *J* 7.1 Hz, 4 H, 2 × CH_2CH_3), 5.43 (s, 4 H, 2 × CH_2N), 7.0–7.3 (m, 10 H, Ph), 8.93 (s, 2 H, H-2), 9.00 (s, 2 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.0 (CH_3), 23.4 (CH_2), 30.3 (CH_2), 45.4 (CH_2N), 56.4 [$C(CO_2Et)_2$], 61.7 (CH_2CH_3), 127.0, 128.2 and 129.0 (CH in Ph), 133.2 (C-5), 135.3 (C in Ph), 146.8 (C-6), 152.3 (C-2), 152.9 (C-4), 157.0 (C-8), 170.4 (C=O). MS (EI): 632 (9, M^+), 587 (6), 396 (17), 237 (27), 224 (82), 209 (5), 91 (100), 65 (5).

*8-[3,3-Bis(ethoxycarbonyl)propyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine* (**7f**) *and diethyl bis[(9-(tetrahydro-2*H*-pyran-2-yl)-8-purinyl)ethyl]malonate* (**8b**). Diethyl malonate (46 µl, 0.30 mmol) was added to a stirred suspension of sodium hydride (7.3 mg, 0.30 mmol) in dry THF (2 ml) at ambient temperature under N_2. After 10 min, a solution of 8-ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **6b** (58 mg, 0.25 mmol) in THF (2 ml) was added and the resulting mixture stirred at ambient temperature for 3 h. The reaction was quenched with glacial acetic acid (22 µl, 0.38 mmol), the mixture was evaporated *in vacuo* and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (3:1 followed by 1:1); yield 60 mg (62 %) of compound **7f** as pale yellow crystals and 12 mg (15 %) of compound **8b** as colourless crystals.

7f. M.p. 58–59 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.23 (t, *J* 7.1 Hz, 6 H, 2 × CH_3), 1.6–2.1 (m, 5 H, THP), 2.5 (m, 2 H, CH_2), 2.5–2.7 (m, 1 H, THP), 3.1–3.2 (m, 2 H, CH_2), 3.60 [t, *J* 7.2 Hz, 1 H, $CH(CO_2Et)_2$], 3.7–3.8 (m, 1 H, H-6 in THP), 4.1–4.2 (m, 5 H, 2 × CH_2CH_3 and H-6 in THP), 5.77 (dd, *J* 11.3 and 2.5 Hz, 1 H, H-2 in THP), 8.87 (s, 1 H, H-2), 8.97 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.0 (CH_3), 23.2 and 24.8 (CH_2 in THP), 26.0 (CH_2), 26.6 (CH_2), 30.1 (CH_2 in THP), 50.9 [$CH(CO_2Et)_2$], 61.5 (CH_2CH_3), 69.1 (C-6 in THP), 82.9 (C-2 in THP), 133.2 (C-5), 146.9 (C-6), 151.9 (C-2), 152.2 (C-4), 156.8 (C-8), 169.0 (C=O). MS (EI): 390 (0.3, M^+), 306 (19), 224 (50), 215 (21), 159 (10), 147 (100), 134 (14), 85 (18).

8b. M.p. 129–131 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.2–1.3 (m, 6 H, 2 × CH_3), 1.6–2.1 (m, 10 H, THP), 2.5–2.6 (m, 6 H, 3 × CH_2), 3.1 (m, 4 H, 2 × CH_2), 3.7 (m, 2 H, H-6 in THP), 4.2 (m, 2 H, H-6 in THP), 4.2–4.3 (m, 4 H, 2 × CH_2CH_3), 5.82 (d, *J* 10.8 Hz, 2 H, H-1 in THP), 8.88 (s, 2 H, H-2), 8.96 (s, 2 H, H-6).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.0 (CH_3), 23.1 (CH_2 in THP), 24.5 (CH_2), 24.7 and 30.2 (CH_2 in THP), 30.9 (CH_2), 56.6 [$C(CO_2Et)_2$], 61.6 (CH_2CH_3), 69.1 (C-6 in THP), 82.8 (C-2 in THP), 133.5 (C-5), 146.8 (C-6), 151.8 (C-2), 152.2 (C-4), 157.1 (C-8), 170.7 (C=O). MS (EI): 620 (3, M^+), 536 (10), 452 (23), 407 (17), 360 (17), 333 (27), 306 (32), 215 (21), 147 (69), 134 (100).

endo-*9-Benzyl-8-(bicyclo[2.2.1.]hept-5-en-2-yl)-9*H-*purine* (**9**) *and* exo-*9-benzyl-8-(bicyclo[2.2.1.]hept-5-en-2-yl)-9*H-*purine* (**10**). Freshly cracked cyclopentadiene (132 mg, 2.0 mmol) was added to a stirred solution of 9-benzyl-8-ethenyl-9*H*-purine (94 mg, 0.4 mmol) in dry dichloromethane (5 ml) at 0 °C under N_2. The resulting mixture was stirred for 110 h, during which it gradually reached ambient temperature, and evaporated *in vacuo*. The products were separated by flash chromatography on silica gel eluting with EtOAc–hexane (1:1); yield 88 mg (73%) of compound **9** as a colourless oil and 15 mg (12 %) of compound **10** as a pale yellow oil. The *exo* isomer **10** eluted first.

9. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.4 (m, 1 H, H-7′), 1.5 (m, 1 H, H-7′), 1.8 (m, 1 H, H-3′), 2.1 (m, 1 H, H-3′), 3.0 (m, 1 H, H-4′), 3.1 (m, 1 H, H-1′), 3.4 (m, 1 H, H-2′), 5.48 (d, *J* 16.2 Hz, 1 H, H_A in CH_2N), 5.51 (d, *J* 16.2 Hz, 1 H, H_B in CH_2N), 5.76 (dd, *J* 5.6 and 2.9 Hz, 1 H, H-6′), 6.30 (dd, *J* 5.6 and 3.1 Hz, 1 H, H-5′), 7.1 (m, 2 H, Ph), 7.3 (m, 3 H, Ph), 8.87 (s, 1 H, H-2), 9.00 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.4 (C-3′), 37.2 (C-2′), 42.6 (C-4′), 45.4 (CH_2N), 46.8 (C-1′), 50.1 (C-7′), 126.5, 128.1 and 129.0 (CH in Ph), 131.9 (C-6′), 133.0 (C-5), 135.6 (C in Ph), 137.7 (C-5′), 146.8 (C-6), 152.0 (C-2), 153.2 (C-4), 160.4 (C-8). MS (EI): 302 (74, M^+), 287 (4), 261 (7), 235 (28), 224 (14), 211 (13), 182 (5), 91 (100), 65 (16).

10. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.4 (m, 1 H, H-7′), 1.5 (m, 1 H, H-3′), 1.9 (m, 1 H, H-7′), 2.2 (m, 1 H, H-3′), 2.7–2.8 (m, 2 H, H-2′ and H-1′), 3.0 (m, 1 H, H-4′), 5.38 (d, *J* 15.9 Hz, 1 H, H_A in CH_2N), 5.56 (d, *J* 15.9 Hz, 1 H, H_B in CH_2N), 6.06 (dd, *J* 3.0 and 2.6 Hz, 1 H, H-6′), 6.19 (dd, *J* 3.0 and 2.7 Hz, 1 H, H-5′), 7.1 (m, 2 H, Ph), 7.3 (m, 3 H, Ph), 8.93 (s, 1 H, H-2), 9.04 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 32.2 (C-3′), 37.3 (C-2′), 42.1 (C-4′), 45.6 (CH_2N), 46.1 (C-7′), 47.7 (C-1′), 127.1, 128.3 and 129.0 (CH in Ph), 133.2 (C-5), 135.5 (C in Ph), 135.8 (C-6′), 138.7 (C-5′), 146.3 (C-6), 151.8 (C-2), 153.3 (C-4), 162.0 (C-8). MS (EI): 302 (23, M^+), 237 (100), 235 (30), 221 (5), 209 (8), 182 (4), 134 (4), 91 (89), 65 (13). HRMS: Found: 302.1532. Calc. for $C_{19}H_{18}N_4$: 302.1531.

*2-Amino-9-benzyl-9*H-*purine* (**12**). A mixture of 2-amino-9-benzyl-6-chloro-9*H*-purine (779 mg, 3.0 mmol), magnesium oxide (486 mg, 12.1 mmol) and 5% Pd–C (340 mg) in EtOH (50 ml) and H_2O (50 ml) was reduced in a Parr apparatus for 5 h at ambient temperature and a 40–50 psi pressure of H_2. The reaction mixture was filtered and evaporated to dryness *in vacuo*, and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–MeOH (10:1); yield 589 mg (87%) colourless crystals. M.p. 180–182 °C. Anal.: C, H. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 5.28 (s, 2 H, CH_2N), 6.53 (s, 2 H, NH_2), 7.3 (m, 5 H, Ph), 8.15 (s, 1 H, H-8), 8.59 (s, 1 H, H-6). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 45.4 (CH_2N), 126.7 (C-5), 127.1, 127.6 and 128.7 (CH in Ph), 137.0 (C in Ph), 142.8 (C-8), 149.1 (C-6), 152.9 (C-4), 160.7 (C-2). MS (EI): 225 (73, M^+), 148 (4), 91 (100), 65 (14).

*9-Benzyl-2-iodo-9*H-*purine* (**13**). To a stirred solution of 2-amino-9-benzyl-9*H*-purine (225 mg, 1.0 mmol) in dry THF (12 ml) at ambient temperature under N_2 was added copper(I) iodide (25 mg, 0.13 mmol), diiodomethane (0.85 ml, 10.2 mmol) and isopentyl nitrite (0.82 ml, 6.2 mmol). The resulting mixture was heated at 60 °C for 2 h, cooled and evaporated *in vacuo*. The residue was stirred in dichloromethane (5 ml) and 1 M aq. $NaHSO_3$ was gradually added until the pink colour disappeared. The phases were separated and the aqueous layer was extracted with dichloromethane (4 × 5 ml). The combined organic extracts were dried ($MgSO_4$) and evaporated, and the product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (2:1); yield 189 mg (56%) colourless crystals. M.p. 174–175 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.37 (s, 2 H, CH_2N), 7.3–7.4 (m, 5 H, Ph), 7.91 (s, 1 H, H-8), 8.84 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 47.3 (CH_2N), 119.6 (C-2), 128.1, 128.8 and 129.2 (CH in Ph), 133.8 (C-5), 134.4 (C in Ph), 145.1 (C-8), 149.7 (C-6), 152.6 (C-4). MS (EI): 336 (72, M^+), 297 (4), 272 (5), 243 (17), 209 (36), 167 (6), 141 (6), 127 (7), 115 (15), 91 (100).

*9-Benzyl-2-ethenyl-9*H-*purine* (**14**). A mixture of 9-benzyl-2-iodo-9*H*-purine (336 mg, 1.0 mmol), bis(triphenylphosphine)palladium(II) chloride (36 mg, 0.05 mmol) and ethenyl(tributyl)tin (420 µl, 1.4 mmol) in dry DMF (4 ml) was heated at 60 °C under N_2 for 20 h and evaporated *in vacuo*. A sat. solution of potassium fluoride in methanol (20 ml) was added to the residue and the resulting mixture was stirred at ambient temperature for 4 h and evaporated *in vacuo* together with a small amount of silica gel. The residue was added to the top of a silica gel column and the product was isolated by flash chromatography eluting with EtOAc–hexane (2:1); yield 222 mg (94%) colourless crystals. M.p. 77–78 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.42 (s, 2 H, CH_2N), 5.70 (dd, *J* 10.5 and 1.7 Hz, 1 H, $=CH_2$), 6.64 (dd, *J* 17.3 and 1.8 Hz, 1 H, $=CH_2$), 6.98 (dd, *J* 17.3 and 10.5 Hz, 1 H, CH=), 7.3 (m, 5 H, Ph), 7.98 (s, 1 H, H-8), 9.09 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 47.0 (CH_2N), 122.7 (CH_2=), 128.0, 128.6 and 129.1 (CH in Ph), 132.5 (C-5), 135.1 (C in Ph), 136.7 (CH=), 145.1 (C-8), 148.5 (C-6), 151.9 (C-4), 159.2 (C-2). MS (EI): 236 (82, M^+), 208 (5), 183 (8), 159 (11), 118 (5), 91 (100), 65 (20).

*9-Benzyl-2-(2-phenylthioethyl)-9*H*-purine* (**15a**) *and 9-benzyl-2-(2-phenylthio-1-hydroxyethyl)-9*H*-purine* (**16**). A mixture of 9-benzyl-2-ethenyl-9*H*-purine (47 mg, 0.2 mmol) and benzenethiol (50 µl, 0.48 mmol) in dry dichloroethane (3 ml) was stirred for 24 h at ambient temperature under Ar. The mixture was evaporated *in vacuo* and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (2:1) followed by EtOAc–hexane (10:1); yield 51 mg (74%) of compound **15a** as a pale yellow oil and 7 mg (10%) of compound **16** as colorless crystals.

15a. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.4 (m, 2 H, CH_2), 3.5 (m, 2 H, CH_2), 5.38 (s, 2 H, CH_2N), 7.1–7.4 (m, 10 H, Ph), 7.97 (s, 1 H, H-8), 9.03 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 32.4 (CH_2), 38.9 (CH_2), 47.0 (CH_2N), 126.0, 128.0, 128.6, 128.8, 129.1, and 129.5 (CH in Ph), 132.1 (C-5), 135.1 (C in Ph), 136.2 (C in PhS), 144.6 (C-8), 148.5 (C-6), 151.9 (C-4), 163.4 (C-2). MS (EI): 346 (24, M^+), 313 (14), 269 (8), 237 (59), 224 (65), 169 (6), 123 (13), 109 (5), 91 (100), 77 (6).

16. M.p. 124-125 °C. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.54 (dd, *J* 15.1 and 5.6 Hz, 1 H, H_A in CH_2), 3.64 (dd, *J* 15.1 and 4.2 Hz, 1 H, H_B in CH_2), 4.52 (d, *J* 6.0 Hz, 1 H, OH), 5.2 (m, 1 H, CH), 5.36 (s, 2 H, CH_2N), 7.0–7.1 (m, 3 H, Ph), 7.2–7.4 (m, 7 H, Ph), 8.01 (s, 1 H, H-8), 9.00 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 41.8 (CH_2), 47.2 (CH_2N), 72.1 (CH), 125.8, 128.0, 128.5, 128.8, 129.2 and 129.6 (CH in Ph), 132.8 (C-5), 134.7 and 136.0 (C in Ph), 145.2 (C-8), 148.0 (C-6), 151.5 (C-4), 163.1 (C-2). MS (EI): 362 (3), 346 (4), 345 (14), 344 (38), 311 (5), 267 (22), 253 (6), 239 (61), 167 (7), 123 (8), 91 (100), 65 (12).

*9-Benzyl-2-[3,3-bis(ethoxycarbonyl)propyl]-9*H*-purine* (**15b**). Diethyl malonate (184 µl, 1.2 mmol) was added to a stirred suspension of sodium hydride (30 mg, 1.2 mmol) in dry THF (1.5 ml) at ambient temperature under N_2. After 10 min, a solution of 9-benzyl-2-ethenyl-9*H*-purine (47 mg, 0.2 mmol) in THF (3 ml) was added and the resulting mixture was stirred at ambient temperature for 96 h. The reaction was quenched with glacial acetic acid (88 µl, 1.5 mmol), the resulting mixture was evaporated *in vacuo* and the crude product was purified by flash chromatography on silica gel eluting with EtOAc–hexane (2:1) followed by EtOAc–hexane (10:1); yield 56 mg (70%) colourless oil. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.24 (t, *J* 7.1 Hz, 6 H, $2\times CH_3$), 2.50 (q, *J* 7.5 Hz, 2 H, CH_2), 3.13 (t, *J* 7.5 Hz, 2 H, CH_2), 3.53 [t, *J* 7.5 Hz, 1 H, $CH(CO_2Et)_2$], 4.17 (q, *J* 7.0 Hz, 4 H, $2\times CH_2CH_3$), 5.39 (s, 2 H, CH_2N), 7.1–7.4 (m, 5 H, Ph), 7.96 (s, 1 H, H-8), 9.03 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.1 (CH_3), 27.3 (CH_2), 36.4 (CH_2), 47.0 (CH_2N), 51.3 [$CH(CO_2Et)_2$], 61.3 (CH_2CH_3), 128.1, 128.6 and 129.1 (CH in Ph), 132.0 (C-5), 135.2 (C in Ph), 144.5 (C-8), 148.5 (C-6), 151.9 (C-4), 164.1 (C-2), 169.4 (C=O). MS (EI): 396 (9, M^+), 351 (15), 323 (9), 305 (11), 277 (9), 237 (100), 224 (25), 91 (62).

endo-*9-Benzyl-2-(bicyclo[2.2.1.]hept-5-en-2-yl)-9*H*-purine* (**17**). Freshly cracked cyclopentadiene (66 mg, 1.0 mmol) was added to a stirred solution of 9-benzyl-2-ethenyl-9*H*-purine (47 mg, 0.2 mmol) and zinc chloride (109 mg, 0.8 mmol) in dry dichloromethane (3 ml) at 0 °C under N_2. The resulting mixture was stirred for 52 h, during which it reached ambient temperature, and evaporated *in vacuo*. The product was isolated by flash chromatography on silica gel eluting with EtOAc–hexane (10:1); yield 41 mg (68%) colourless oil. Anal.: C, H. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.2 (m, 2 H, H-7′), 1.5 (m, 1 H, H-3′), 1.9 (m, 1 H, H-3′), 3.0 (m, 1 H, H-4′), 3.5 (m, 1 H, H-1′), 3.8 (m, 1 H, H-2′), 5.39 (d, *J* 15.0 Hz, 1 H, H_A in CH_2N), 5.41 (d, *J* 15.0 Hz, 1 H, H_B in CH_2N), 5.66 (dd, *J* 5.6 and 2.8 Hz, 1 H, H-6′), 6.13 (dd, *J* 5.6 and 3.0 Hz, 1 H, H-5′), 7.3 (m, 5 H, Ph), 7.97 (s, 1 H, H-8), 9.01 (s, 1 H, H-6). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 31.0 (C-3′), 43.0 (C-4′), 47.0 and 47.1 (C-2′/CH_2N), 47.9 (C-1′), 59.9 (C-7′), 128.2, 128.6 and 129.0 (CH in Ph), 131.5 (C-5), 132.9 (C-6′), 135.3 (C in Ph), 137.0 (C-5′), 144.5 (C-8), 147.5 (C-6), 151.6 (C-4), 167.1 (C-2). MS (EI): 302 (73, M^+), 287 (14), 248 (7), 235 (53), 224 (24), 209 (6), 183 (7), 159 (7), 91 (100), 65 (17).

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