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Synthesis of 6-Alkenyl- and 6-Alkynylpurines with Cytokinin Activity

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Abstract: Analogs of the cytokinins *trans*-zeatin and benzylaminopurine have been prepared by Heck coupling on 6-vinylpurines or Sonogashira coupling on 6-halopurines as key-steps, and their cytokinin activity has been evaluated based on their ability to stimulate increased growth in radish cotyledons.

Cytokinins are plant hormones with a wide range of biological effects.[1] They promote cell division and cell growth and they are involved in the retardation of senescence. The cytokinins found in nature are 6-alkylaminopurines. Examples of important cytokinins and analogs are shown in Fig. 1.

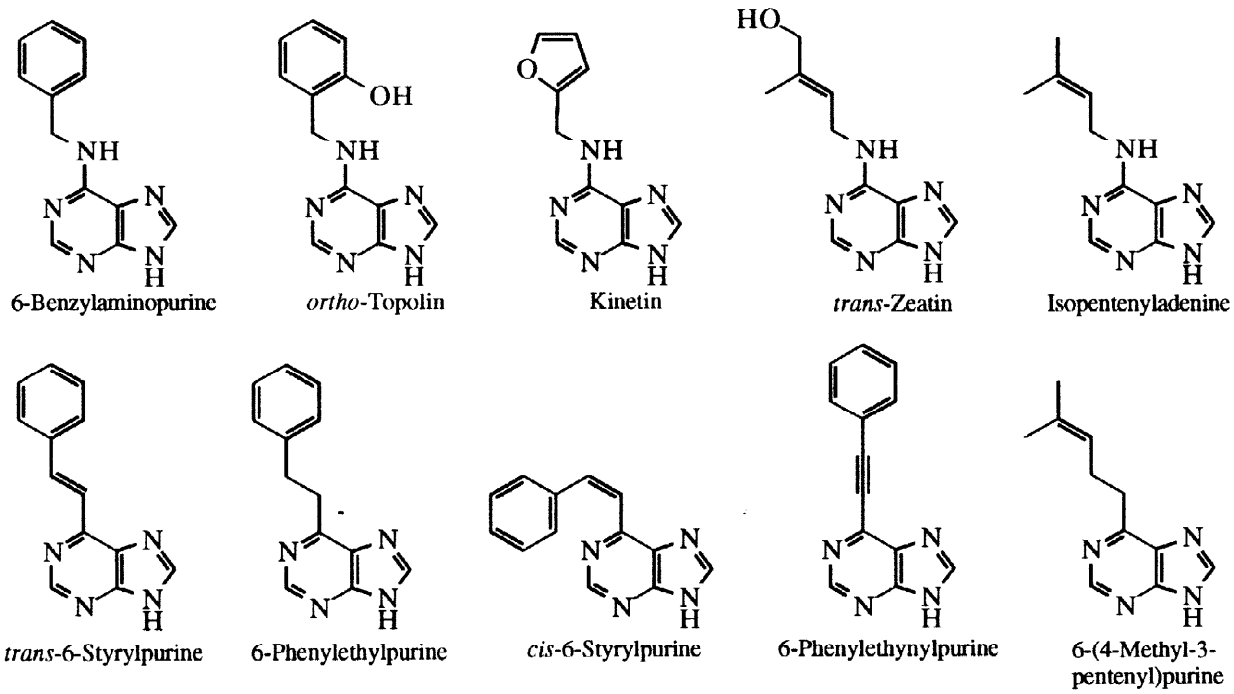

Fig. 1

trans-Zeatin is probably the most potent naturally occurring cytokinin growth hormone.[1] The closely related structure isopentenyladenine is also a widespread and active cytokinin[1] and high activity is found for

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benzylaminopurine[2] and the *ortho* and *meta* isomers of topolin[3] as well. These latter compounds are, however, less frequently detected in plant material. A great number of adenine derivatives have been synthesized and tested for phytohormonal activity. Maybe the most prominent example of a synthetic cytokinin is kinetin, which was the first plant growth stimulating purine ever discovered.[4]

Among the purine derivatives screened for cytokinin properties, high activity is reported for *trans*-6-styrylpurine[5-7] and the saturated analog,[5,6] demonstrating that the amino group is not essential for the promotion of all kinds of cytokinin effects. The spatial arrangement of the side chain appears to be important; *cis*-6-styrylpurine[6,7] and the corresponding alkyne[8] are only weakly active. In the zeatin series, development of non-adenine analogs have received much less attention. 6-(4-Methyl-3-pentenyl)purine has, however, been examined.[5,6]

Metabolism of zeatin and isopentenyladenine involves cytokinin oxidase promoted cleavage of the side chain and adenine, which exhibits practically no phytohormone activity, is irreversibly formed.[1b,9] Also benzylaminopurine and analogs are metabolized to adenine, but the enzyme system responsible for this conversion is less understood.[2] Compounds like *trans*-styrylpurine are not likely to be substrates for cytokinin oxidase or related enzymes, and hence this class of purine derivatives may exhibit a prolonged cytokinin action.

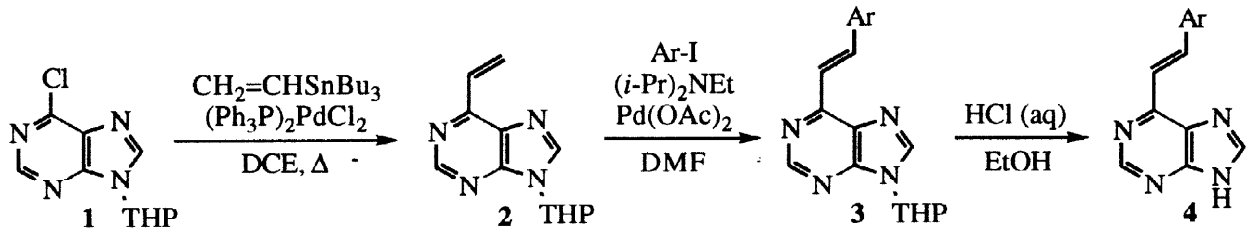
Studies of biological properties of conformationally restricted 6-alkenyl- or 6-alkynylpurines, may reveal important information about receptors responsible for cytokinin action. The difference in activity between *trans* styrylpurine and the saturated analog compared to *cis*-styrylpurine and the corresponding alkyne, strongly indicate that the orientation around the NH-CH_2 bond in "active conformations" of adenine cytokinins are close to anti. This contradicts the earlier theory that the biologically active conformations should resemble the X-ray structures of the compounds,[10] where C(6)-N(6)-CH_2-C torsion angles of ca. 80-100 ° are found.[10,11]

We have previously demonstrated that *trans*-alkenylpurines,[12] including *trans*-6-styrylpurine,[12a] are readily available from Stille couplings with the corresponding chloropurines. However, this method requires easy access to geometrically pure *trans*-alkenyltin reagents. Retention of alkenylstannane double bond stereochemistry is preferred in Stille reactions,[13] and couplings with a mixture of *cis*- and *trans*-alkenylstannane gives isomeric mixtures of alkenylpurines.[14] In two recent papers, we reported on the versatility of 6-vinylpurines as intermediates in syntheses of various purine derivatives.[15] As we continue to explore the reactivity of vinylpurines, we herein describe Heck coupling[16] between 6-vinylpurines and aryl iodides to give *trans*-6-arylalkenylpurines, compounds which may be regarded as analogs of 6-benzylaminopurine. Furthermore, we report the first *trans*-zeatin analogs where the NH group has been replaced by sp- or sp^2 hybridized carbon.

Pd-Catalyzed coupling between the *N*-9 THP-protected 6-chloropurine **1** and ethenyl(tributyl)tin afforded the 6-vinylpurine **2** (Scheme 1). An *N*-9 protecting group was required. Even though *N*-9 protection by acetylation may be beneficial in Sonogashira type couplings of 6-chloropurines,[17] we have shown that 6-chloropurine it self readily participate in Stille coupling with a variety of organotin reagents.[12a] Also unprotected 6-chloropurine appeared to react with the vinyltin reagent, but all attempts to isolate the desired product failed. Compound **2** is prone to decomposition upon extensive drying under high vacuum or upon storage, and in the couplings described below, we therefore used freshly prepared vinylpurine, and the yields of the Heck reaction products **3** are calculated from the chloropurine **1**. The THP-protecting group used in this work was not only chosen because it is easily introduced into the purine 9-position[18] and readily removed under acidic conditions,[19] also 9-THP protected purines have been associated with cytokinin activity. In some bio assays the THP-protected compounds were even more active than the parent purine with free NH function in the imidazole ring.[20] Compound **2** could also be generated from Pd-catalyzed coupling with vinylzinc bromide. However, as we previously have noted,[12b] this zinc reagent required the more reactive THP-protected 6-iodopurine. Vinyluracils have been prepared by Pd-mediated coupling with vinyl acetate,[21] but the chloropurine **1** or the corresponding 6-iodopurine, showed no reactivity towards vinyl acetate even at high reaction temperatures.

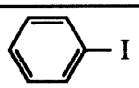
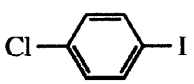
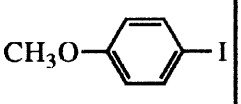
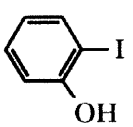
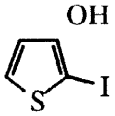
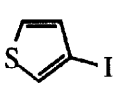
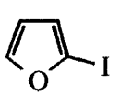
The vinylpurine **2** was subjected to Heck coupling with aryl iodides, and the THP-protecting groups in the products **3** were easily cleaved under acidic conditions[19] to give compounds **4** (Scheme 1, Table 1). As seen from Table 1, both aryl- and heteroaryl iodides participated in the Heck reaction to afford the

alkenylpurines **3** in good yields, calculated from the chloropurine **1**. We obtained better results when $Pd(OAc)_2$ alone was employed as catalyst compared with catalysts containing phosphine ligands like triphenylphosphine. Reduced yields in Heck reactions in the presence of phosphine ligands have also been noted by others.[22]



Scheme 1

Table 1. Synthesis of *trans* 6-Alkenylpurines **3** and **4**.

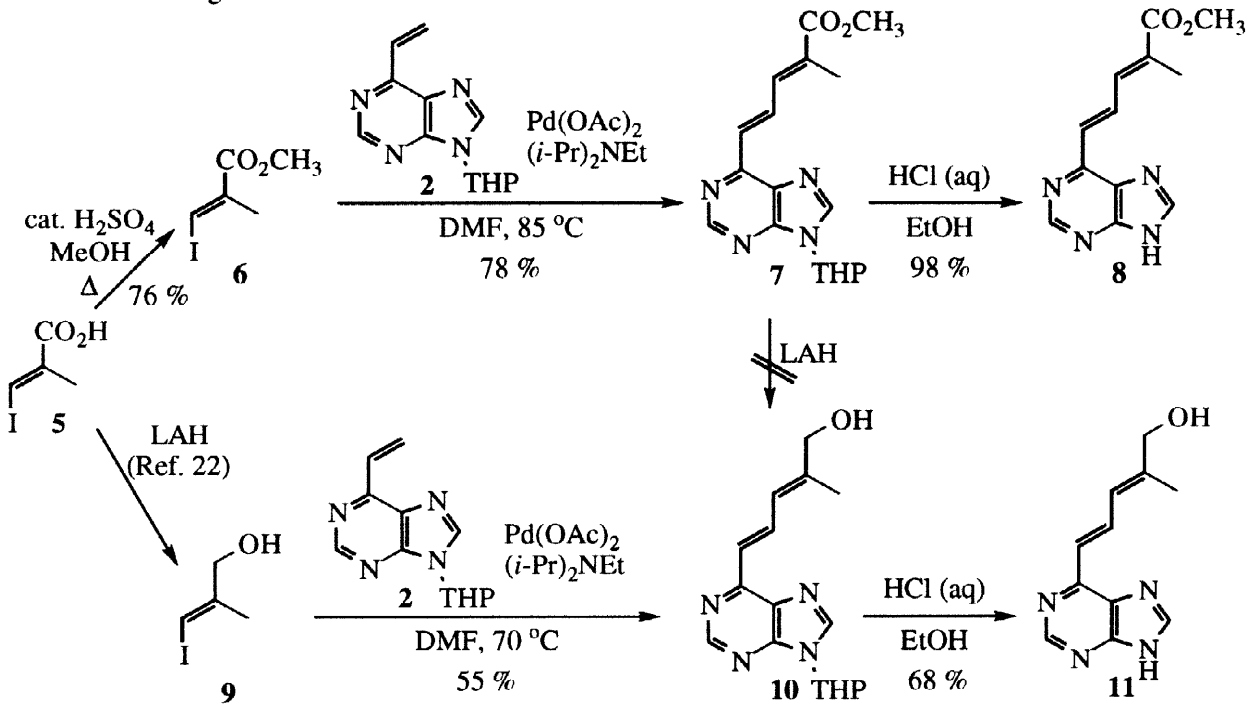
Entry	Ar-I	Time (h)[a]	Temp. (°C)[a]	Yield (%) **3**[b,c]	Yield (%) **4**[b]
1		3.5	60	67, **3a**	91, **4a**
2		20	75	82, **3b**	71, **4b**
3		20	55	74, **3c**	86, **4c**
4[d]		19	80	52, **3d**	77, **4d**
5		24	60	72, **3e**	97, **4e**
6		4.5	75	52, **3f**	77, **4f**
7		3.5	75	60, **3g**	82, **4g**

(a) Synthesis of compounds **3**; (b) Yield of isolated product; (c) Yield of two step conversion starting with the chloropurine **1**; (d) The phenol was protected as TMS-ether during the reaction, and the protecting group was cleaved during work up.

As expected, the couplings were highly stereoselective. In all cases examined, the *trans* alkenes were formed exclusively as judged by the ^1H NMR spectra of the crude products. However, the coupling with the reactive aryl halide 4-iodoanisol (Table 1, Entry 3) demanded only a small excess aryl halide in order to avoid a second coupling and the formation of the corresponding 2',2'-diarylethenylpurine. The 6-alkenylpurines **3** and **4** were tested for cytokinin effect and several compounds exhibited high activities (*vide infra*).

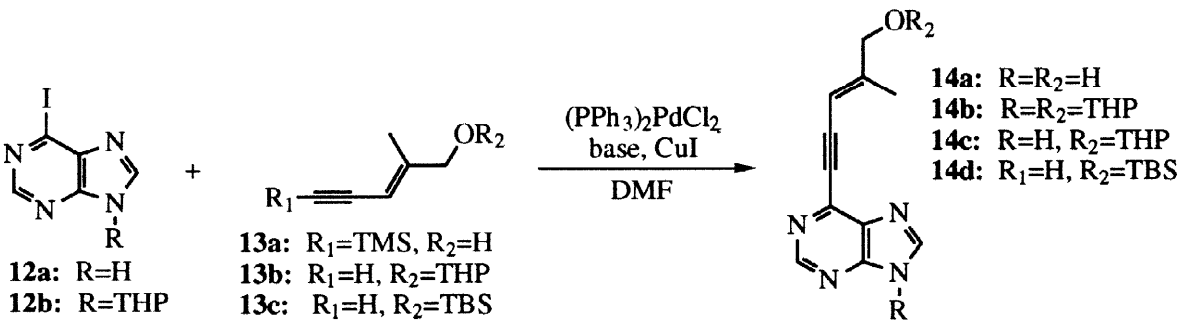
Two routes to the *trans*-zeatin analog **11** starting with the readily available (*E*)-vinyl iodide **5**[23] were evaluated (Scheme 2). The acid **5** was converted to the methyl ester **6**, which readily participated in Heck

coupling with the vinylpurine **2** to give compound **7** and the deprotected (*E,E*)-dienylpurine **8** were formed after cleavage of the THP protecting group. However, when selective reduction of the ester **7** to compound **10** was attempted, partial reduction of the carbon-carbon double bonds took place and a complex mixture of products were formed. Instead, the acid **5** was cleanly reduced to the hydroxymethyl compound **9** as described in the literature,[23] and Heck coupling of **9** with the vinylpurine **2** followed by deprotection resulted in the desired zeatin analog **11**.



Scheme 2

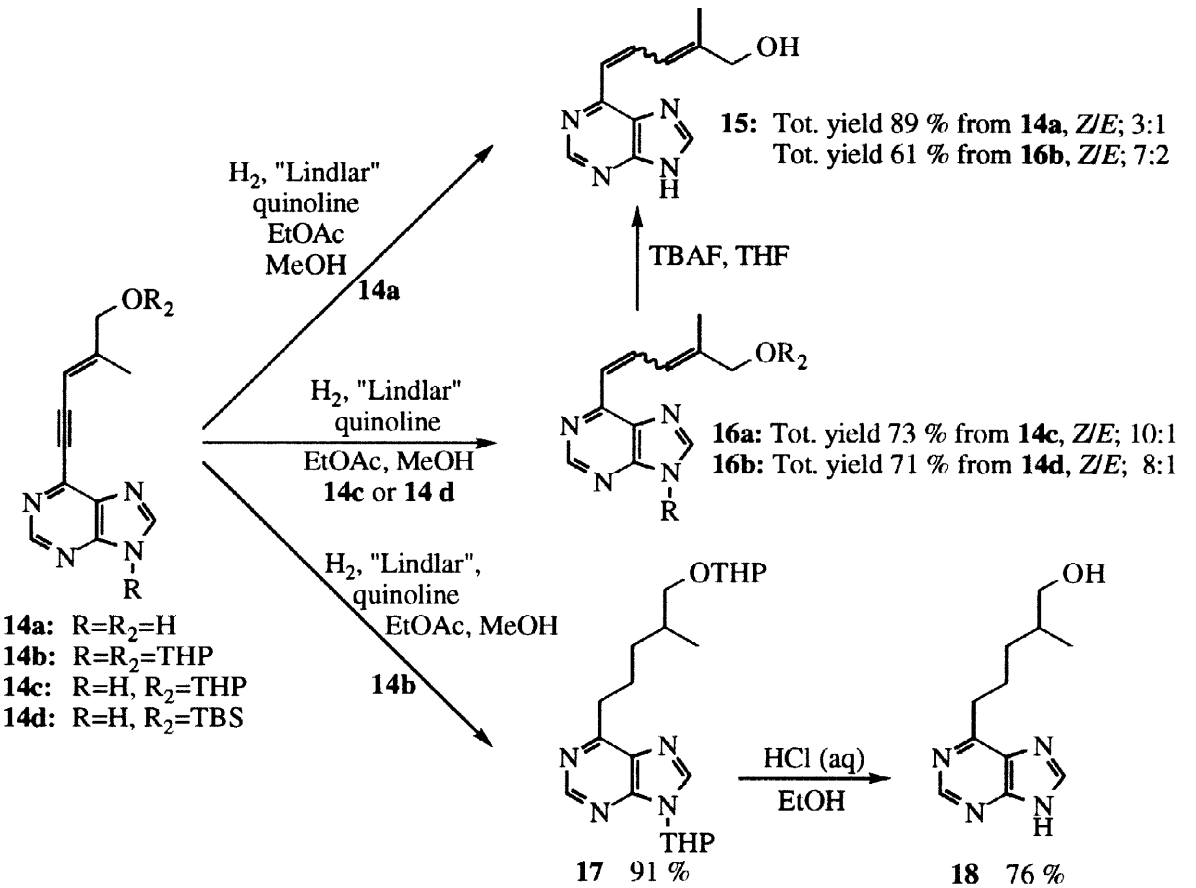
In order to evaluate the importance of the spatial arrangement of the C-6 substituent for cytokinin activity in the zeatin series, we needed analogs of compound **11** with a *cis* double bond or a triple bond as the linkage between the purine ring and the side chain. For alkyne synthesis, Sonogashira type coupling was chosen as the key-step (Scheme 3). Compound **9** was transformed to the enynes **13**,[24,25] and the enynes were coupled with purines **12** to give compounds **14** with various degree of OH- and NH-protection.



Temp. (°C)	Time (h)	Base	Co-Reagent	Yield (%) **14**
60	6	(*i*-Pr)$_2$NEt	Me_4NF	63, **14a**
65	14	(*i*-Pr)$_2$NEt	—	82, **14b**
65	24	Et_3N	—	75, **14c**
75	6.5	(*i*-Pr)$_2$NEt	—	80, **14d**

Scheme 3

Hydrogenation of 6-alkynylpurines to both (*E*)-[26] and (*Z*)-alkenes[27] have been reported and the alkynes **14** were subjected to catalytic hydrogenation employing the Lindlar catalyst (Pd on $CaCO_3$ poisoned with Pb) together with quinoline,[28] essentially as previously reported for selective syn hydrogenation of other alkynylpurines,[27] and the results are summarized in Scheme 4.

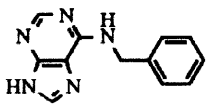
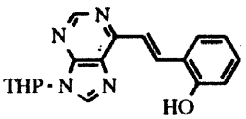
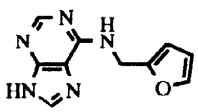
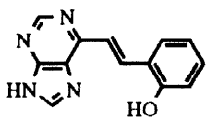
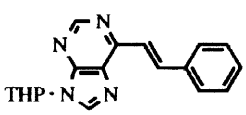
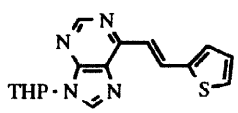
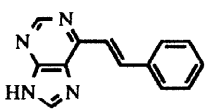
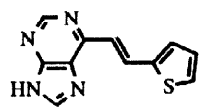
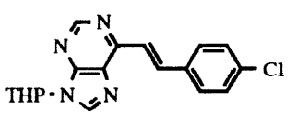
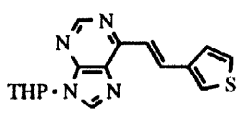
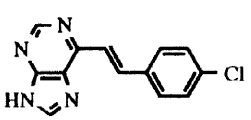
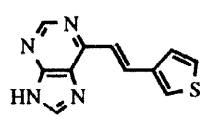
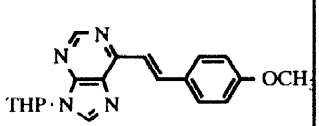
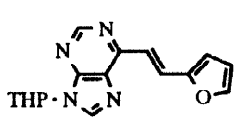
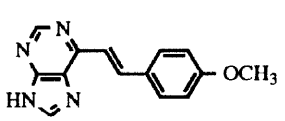
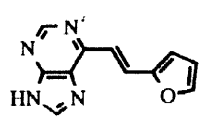


Scheme 4

Hydrogenation of the unprotected alkyne **14a** gave the desired diene **15** together with ca. 25 % of the *trans* isomer **11** as an inseparable mixture. On the other hand, when the same set of reaction conditions was applied to the fully protected alkyne **14b**, the reduction proceeded rapidly to the completely reduced compound **17** which could be isolated in a high yield. No dienes or monoenes were observed at all. High *Z* selectivity was obtained in Lindlar catalyzed hydrogenation of the *O*-THP protected compound **14c** and the silylprotected compound **14d**, but extensive decomposition and isomerisation took place during attempted cleavage of the THP protecting group. TBAF mediated deprotection of compound **16b** gave compound **15** with essentially the same *Z/E* ratio as obtained from direct hydrogenation of the unprotected alkyne **14a**.

The evaluation of cytokinin activity for the purines described herein were based on their ability to stimulate growth in radish cotyledons. The growth effect were measured as increase in weight of the cotyledons after 72 hours relative to a control sample, and the results for the benzylaminopurine analogs **3** and **4** are given as % of the increase obtained with benzylaminopurine (Table 2.) Also kinetin is included for comparison. Table 3 displays the results for the zeatin analogs. Many of the 6-(arylalkenyl)purines **3** and **4** exhibits cytokinin activity not far from benzylaminopurine in the bioassay chosen. Especially the thienyl derivatives **3e**, **3f** an **4f** were found to be potent growth stimulators. *N*-Alkylation in the purine ring generally lowers cytokinin activity,[1] but several of the 9-THP purines **3** examined stimulated cotyledon growth, some even more than their unprotected analogs **4**. Enhanced cytokinin activity by introduction of the THP-group in the purine 9-position has been reported before.[20]

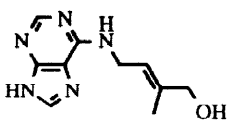
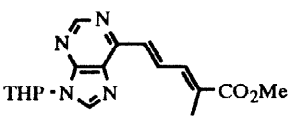
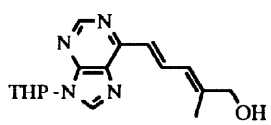
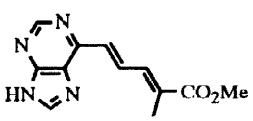
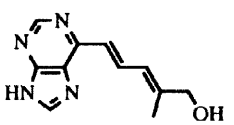
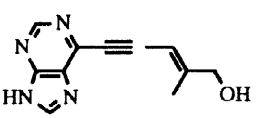
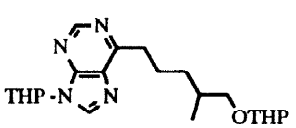
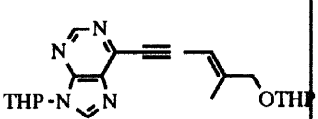
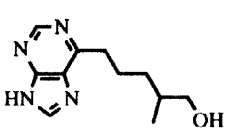
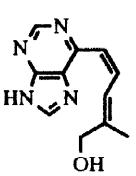
Table 2. Cytokinin Activity of Kinetin- and Benzylaminopurine analogs relative to BAP.

Compound	% Weight Increase Relative to BAP[a]	Compound	% Weight Increase Relative to BAP[a]
 Benzylaminopurine (BAP)	100	 **3d**	10
 Kinetin	88	 **4d**	17[c]
 **3a**	83	 **3e**	80
 **4a**	68	 **4e**	34
 **3b**	68[b]	 **3f**	85
 **4b**	–[c,d]	 **4f**	95
 **3c**	56	 **3g**	26
 **4c**	–[d]	 **4g**	58

(a) Comparison of weight gain between radish cotyledon grown in 0 μM and 100 μM purine solution, the results are given as % of the weight increase obtained with BAP; (b) 50 μM solution; (c) Low solubility of the compounds in the test medium, may be responsible for the low activity; (d) Weight retardation was observed.

In the zeatin series, we found the compounds with a free *NH*-function in the imidazole part quite able to increase growth in radish cotyledons (Table 3). Compounds **14a** and **18** exhibited an even greater effect than *trans*-zeatin. In contrast to what has previously been found for the benzylaminopurine analogs *cis*- and *trans*-6-styrylpurine and phenylethynylpurine[5-8] (*vide supra*), both the alkyne **14a** and the (*Z,E*)-diene **15**, as well as the saturated analog **18**, were all slightly more active than the (*E,E*)-diene **11**. Furthermore, a THP-substituent in the 9-position markedly reduces the cytokinin activity for all the zeatin analogs examined.

Table 3. Cytokinin Activity of *trans*-Zeatin and Analogs.

Compound	% Weight Increase Relative to BAP[a]	Compound	% Weight Increase Relative to BAP[a]
 *trans*-Zeatin	82	 **7**	6
 **10**	31	 **8**	61
 **11**	71	 **14a**	89
 **17**	–[c]	 **14b**	47
 **18**	91	 **15**	82[b]

(a) Comparison of weight gain between radish cotyledon grown in 0 μM and 100 μM purine solution, the results are given as % of the weight increase obtained with BAP; (b) *Z/E*; (3:1); (c) Weight retardation was observed.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded at 500 MHz with a Bruker Avance DRX 500 instrument, 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 instruments mentioned above. Unless otherwise stated, the spectra are recorded at ambient temperature. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane. IR spectra were recorded with a Perkin-Elmer 1310 Infrared Spectrophotometer. Mass spectra were recorded with a VG Prospec instrument at 70 eV ionizing voltage unless otherwise stated, and are presented as *m/z* (% rel. int.). 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) or Fluka, Buchs, Switzerland (Fluka No. 60752) and the Lindlar catalyst was purchased from Fluka, Buchs, Switzerland (Fluka No. 62145). DCE, CH_2Cl_2, DMF, pyrrolidine, diisopropylethylamine and triethylamine were distilled from CaH_2, and THF from Na/benzophenone. Tetramethylammonium fluoride trihydrate was dried by azeotropic distillation with abs. EtOH. 6-Chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine,[18] 2-iodothiophene,[29] 3-iodothiophene,[30] 2-iodofuran,[31] (*E*)-3-iodo-2-metylpropen-oic acid[23] (*E*)-3-iodo-2-methyl-2-propen-1-ol,[23] (*E*)-2-methyl-5-(trimethylsilyl)-2-penten-4-yn-1-ol,[24] (*E*)-2-methylpent-2-en-4-yn-1-ol,[24] 6-iodo-1*H*-purine,[32] 6-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine[18] and (*E*)-2-methyl-1-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2-penten-4-yne[25] were prepared according to literature procedures. All other reagents were commercially available and used as received.

*6-Ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (2).* A mixture of 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1** (239 mg, 1.0 mmol), bis(triphenylphosphine)palladium(II) chloride (35 mg, 0.05 mmol) and ethenyl(tributyl)tin (0.35 ml, 1.2 mmol) in dichloroethane (12 ml) was heated at reflux under N_2 for 5.5 h and cooled. The reaction mixture was evaporated *in vacuo* and a saturated solution of potassium fluoride in methanol (20 ml) added to the residue. The resulting mixture was stirred at ambient temperature for 2-3 h and evaporated *in vacuo* together with a small amount of silica gel. The residue was added on top of a silica gel column and the product was isolated by flash chromatography eluting with EtOAc/hexane 2:1; yellow oil used directly in Heck couplings. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.87 (s, 1 H, H-2), 8.24 (s, 1 H, H-8), 7.26 (dd, *J* 17.5 and 11.0 Hz, 1 H, CH=), 6.98 (dd, *J* 17.5 and 1.5 Hz, 1 H, CH_2=), 5.91 (dd, *J* 11.0 and 1.5 Hz, 1 H, CH_2=), 5.75 (dd, *J* 10.0 and 3.0 Hz, 1 H, H-2 in THP), 4.2-4.1 (m, 1 H, H-6 in THP), 3.7 (m, 1 H, H-6 in THP), 2.1-2.0 (m, 3 H, H-4 and H-3 in THP), 1.7-1.8 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR (C_6D_6, 75 MHz): δ 153.8 (C-6), 152.8 (C-2), 151.9 (C-4), 142.5 (C-8), 133.1 (CH=), 131.8 (C-5), 126.1 (=CH_2), 82.0 (C-2 in THP), 68.3 (C-6 in THP), 31.4 (C-3 in THP), 24.9 (C-5 in THP), 22.6 (C-4 in THP). MS (EI, 15 eV): 230 (100, M^+), 203 (9), 202 (63), 201 (6), 148 (9), 147 (81), 146 (6), 134 (5), 85 (25), 84 (23). Hrms (25 eV): Found 230.1167, $C_{12}H_{14}N_4O$ requires 230.1168.

*General procedure for Heck coupling between 6-ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine 2 and aryl iodides.* To a stirring solution of 6-ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2**, freshly prepared from 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1** (239 mg, 1.0 mmol) as described above, in dry DMF (8 ml) under N_2, was added palladium(II) acetate (11 mg, 0.05 mmol) in DMF (1 ml), aryl iodide (2.0 mmol) and *N,N*-diisopropylethylamine (510 μl, 3.0 mmol). The resulting mixture was heated at the temperatures and for the times given in Table 1. After cooling, saturated aqueous NH_4Cl (15 ml) was added and the mixture was extracted with EtOAc (3 x25 ml), dried (Na_2SO_4) and evaporated *in vacuo*. The product was isolated after flash chromatography on silica gel eluting with EtOAc-hexane (2:1).

*(E)-6-(2-Phenylethenyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine (3a).* Yield 206 mg (67 %) pale yellow powdery crystals. M.p. 129-131 °C. (Found: C, 70.45; H, 5.85. Calc. for $C_{18}H_{18}N_4O$: C, 70.57; H, 5.92 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.90 (s, 1 H, H-2), 8.39 (d, *J* 16.0 Hz, 1 H, CH=), 8.27 (s, 1 H, H-8), 7.7 (m, 3 H, Ph and CH=), 7.4-7.3 (m, 3 H, Ph), 5.79 (dd, *J* 10.0 and 3.0 Hz, 1 H, H-2 in THP), 4.2 (m, 1 H, H-6 in THP), 3.8 (m, 1 H, H-6 in THP), 2.1-2.0 (m, 3 H, H-4 and H-3 in THP), 1.8-1.7 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 153.7 (C-6), 152.3 (C-2), 151.0 (C-4), 141.8 (C-8), 139.8 (CH=), 136.0 (C in Ph), 131.0 (C-5), 129.4, 128.7 and 127.8 (CH in Ph), 122.1 (CH=), 81.8 (C-2 in THP), 69.7 (C-6 in THP), 31.7 (C-3 in THP), 24.8 (C-5 in THP), 22.7 (C-4 in THP). IR (KBr): ν_{max} 3070, 3020, 2990, 2930, 2840, 1620, 1570 cm^{-1}. MS (EI): 306 (10, M^+), 222 (39), 221 (100), 85 (5), 84 (10).

*(E)-6-[2-(4-Chlorophenyl)ethenyl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (**3b**).* 6-Ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2**, freshly prepared from 1.0 mmol 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1**, and 1-chloro-4-iodobenzene (286 mg, 1.2 mmol) was subjected to Heck coupling as described above. Yield 281 mg (82 %) pale yellow powdery crystals. M.p. 178-180 °C. (Found: C, 63.31; H, 5.08. Calc. for $C_{18}H_{17}ClN_4O$: C, 63.44; H, 5.03 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.88 (s, 1 H, H-2), 8.30 (d, *J* 16.0Hz, 1 H, CH=), 8.24 (s, 1 H, H-8), 7.64 (d, *J* 16.0 Hz, 1 H, CH=), 7.6 (m, 2 H, Ar), 7.3 (m, 2 H, Ar), 5.78 (dd, *J* 9.5 and 4.0 Hz, 1 H, H-2 in THP), 4.2 (m, 1 H, H-6 in THP), 3.8 (m, 1 H, H-6 in THP), 2.1-2.0 (m, 3 H, H-4 and H-3 in THP), 1.8-1.7 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.3 (C-6), 152.3 (C-2), 151.1 (C-4), 141.9 (C-8), 138.2 (CH=), 135.0 and 134.5 (C in Ar), 131.0 (C-5), 128.9 (2×CH in Ar) 122.8 (CH=), 81.8 (C-2 in THP), 68.7 (C-6 in THP), 31.7 (C-3 in THP), 24.7 (C-5 in THP), 22.7 (C-4 in THP). IR (KBr): ν_{max} 3100, 3020, 2910, 2840, 1620, 1570 cm^{-1}. MS (EI): 341 (9, *M*+1), 340 (25, *M*$^+$), 258 (22), 257 (45), 256 (57), 255 (100), 221 (9), 85 (25).

*(E)-6-[2-(4-Methoxyphenyl)ethenyl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (**3c**).* 6-Ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2**, freshly prepared from 2.0 mmol 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1**, and 4-iodoanisol (468 mg, 2.0 mmol) was subjected to Heck coupling as described above. Yield 496 mg (74 %) yellow powdery crystals. M.p. 159-162 °C. (Found: C, 67.96; H, 5.98. Calc. for $C_{19}H_{20}N_4O_2$: C, 67.84; H, 5.99 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.86 (s, 1 H, H-2), 8.32 (d, *J* 16.0 Hz, 1 H, CH=), 8.24 (s, H, H-8) 7.6 (m, 2 H, Ar), 7.56 (d, *J* 16.0 Hz, 1 H, CH=), 6.9 (m, 2 H, Ar), 5.77 (dd, *J* 10.0 and 3.0 Hz, 1 H, H-2 in THP), 4.2 (m, 1 H, H-6 in THP), 3.81 (s, 3 H, CH_3), 3.8 (m, 1 H, H-6 in THP), 2.1-2.0 (m, 3 H, H-4 and H-3 in THP), 1.8-1.6 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.7 (C-4 in Ar), 154.1 (C-6), 152.3 (C-2), 150.9 (C-4), 141.5 (C-8), 139.4 (CH=), 130.7 (C-5), 129.4 (CH in Ar), 128.8 (C-1 in Ar), 119.8 (CH=), 114.2 (CH in Ar), 81.8 (C-2 in THP), 68.7 (C-6 in THP), 55.2 (CH_3O), 31.7 (C-3 in THP), 24.8 (C-5 in THP), 22.7 (C-4 in THP). IR (KBr): ν_{max} 3080, 3020, 2980, 2930, 2820, 1620, 1590, 1570, 1500 cm^{-1}. MS (EI): 336 (63, *M*$^+$), 335 (16), 254 (17), 253 (90), 252 (100), 238 (16), 210 (9), 209 (28), 208 (22), 128 (12).

*(E)-6-[2-(2-Hydroxyphenyl)ethenyl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (**3d**).* A mixture of 2-iodophenol (1.026 g, 4.55 mmol) *N,N*-dimethylaminopyridine (28 mg, 0.227 mmol), triethylamine (0.950 ml 6.82 mmol) and chloro(trimethyl)silane (0.69 ml, 5.45 mmol) in dry CH_2Cl_2 (15 ml) was stirred at ambient temperature under N_2 for 16 h. The reaction mixture was diluted with CH_2Cl_2 (20 ml) and washed with water (2 x 20 ml) and saturated aqueous NH_4Cl (2×20 ml). The dried ($MgSO_4$) solution was evaporated to give 1.172 g (88 %) of TMS-protected phenol. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.73 (dd, *J* 8.0 and 1.5 Hz, 1 H, Ar), 7.18 (m, 1 H, Ar), 6.81 (m, 1 H, Ar), 6.68 (m, 1 H, Ar), 0.30 (s, 9 H, $SiMe_3$). 6-Ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2** and 2-iodo(trimethylsilyloxy)benzene was subjected to Heck coupling as described above. The cooled reaction mixture was evaporated *in vacuo* and the residue was stirred with a 0.14 M solution of anhydrous tetrabutylammonium fluoride in THF (12 ml) over night. Sat. aq. NH_4Cl (10 ml) and water (10 ml) was added and the mixture was extracted with $CHCl_3$ (3×30 ml). The combined organic extracts were washed with brine, dried (Na_2SO_4) and evaporated *in vacuo*. The product was isolated by flash chromatography on silica gel eluting with EtOAc-hexane (3:1); yield 169 mg (52 %) yellow powdery crystals. M.p > 220 °C (dec.). (Found: C, 66.89; H, 5.52. Calc. for $C_{18}H_{18}N_4O_2$: C, 67.07; H, 5.63 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.22 (s, 1 H, OH), 8.64 (s, 1 H, H-2), 8.48 (d, *J* 16.0 Hz, 1 H, CH=), 8.08 (s, 1 H, H-8), 7.56 (d, *J* 16.0 Hz, 1 H, CH=), 7.43 (dd, *J* 7.5 and 1.5 Hz, 1 H, Ar), 6.93 (dt, *J* 7.5 and 1.5 Hz, 1 H, Ar), 6.71 (dd, *J* 7.5 and 1.0 Hz, 1 H, Ar), 6.63 (t, *J* 7.5 Hz, 1 H, Ar), 5.56 (t, *J* 7.5 Hz, 1 H, H-2 in THP), 3.9 (m, 1 H, H-6 in THP), 3.6 (m, 1 H, H-6 in THP), 1.9-1.8 (m, 3 H, H-4 and H-3 in THP), 1.6-1.4 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$/DMSO-d_6, 50 MHz): δ 155.3 (C-2 in Ar), 152.7 (C-6), 150.7 (C-2), 149.7 (C-4), 141.1 (C-8), 134.1 (CH=), 129.3, 129.8 (C-5/C-4 in Ar) , 126.6 (C-6 in Ar), 121.6 (C-1 in Ar), 120.3 (CH=), 118.1 (C-5 in Ar), 115.0 (C-3 in Ar), 80.3 (C-2 in THP), 67.1 (C-6 in THP), 29.6 (C-3 in THP), 23.4 (C-5 in THP), 21.3 (C-4 in THP). IR (KBr): ν_{max}

3380, 3090, 3020, 2920, 2830, 1610, 1570 cm^{-1}. MS (EI): 322 (0.3, M^+), 238 (20), 237 (24), 236 (28), 222 (16), 221 (100), 220 (6), 84 (25), 83 (12).

(E)-6-[2-(2-Thienyl)ethenyl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (3e). 6-Ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2**, was prepared from 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1** (0.8 mmol). Yield 179 mg (72 %) pale yellow powdery crystals. M.p. 165-168 °C. (Found: C, 61.19; H, 5.10. Calc. for $C_{16}H_{16}N_4OS$: C, 61.55; H, 5.16 %). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.87 (s, 1 H, H-2), 8.51 (d, *J* 16.0 Hz, 1 H, CH=), 8.26 (s, 1 H, H-8), 7.47 (d, *J* 16.0 Hz, 1 H, CH=), 7.4-7.3 (m, 2 H, thienyl), 7.1-7.0 (m, 1 H, thienyl), 5.79 (dd, *J* 10.0 and 3.0 Hz, 1 H, H-2 in THP), 4.2 (m, 1 H, H-6 in THP), 3.8 (m, 1 H, H-6 in THP), 2.1 (m, 3 H, H-3 and H-4 in THP), 1.8-1.6 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 153.5 (C-6), 152.3 (C-2), 150.9 (C-4), 141.7 (C-8 and C-2 in thienyl), 132.6 (CH=), 130.8 (C-5), 129.7, 127.9 and 127.5 (CH in thienyl), 121.5 (CH=), 81.8 (C-2 in THP), 68.7 (C-6 in THP), 31.7 (C-3 in THP), 24.8 (C-5 in THP), 22.7 (C-4 in THP). IR (KBr): ν_{max} 3060, 3020, 2990, 2920, 2840, 1610, 1570, 1500 cm^{-1}. MS (EI): 312 (11, M^+), 229 (13), 228 (55), 227 (100), 195 (5), 120 (11), 85 (7), 81 (5).

(E)-6-[2-(3-Thienyl)ethenyl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (3f). Yield 162 mg (52 %) yellow powdery crystals. M.p. 149-151 °C. (Found: C, 61.37; H, 5.19. Calc. for $C_{16}H_{16}N_4OS$: C, 61.55; H, 5.16 %). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.88 (s, 1 H, H-2), 8.40 (d, 1 H, *J* 16.0 Hz, 1 H, CH=), 8.26 (s, 1 H, H-8), 7.56 (dd, *J* 3.0 and 1.0 Hz, 1 H, H-2 in thienyl), 7.502 (d, *J* 16.0 Hz, 1 H, CH=), 7.498 (dd, *J* 5.0 and 1.0 Hz, 1 H, H-5 in thienyl), 7.35 (dd, *J* 5.0 and 3.0 Hz, 1 H, H-4 in thienyl), 5.79 (dd, *J* 10.0 and 3.0 Hz, 1 H, H-2 in THP), 4.2 (m, 1 H, H-6 in THP), 3.8 (m, 1 H, H-6 in THP), 2.1-2.0 (m, 3 H, H-3 and H-4 in THP), 1.8-1.7 (m, 3 H, H-4 and H-5). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 153.9 (C-6), 152.2 (C-2), 151.0 (C-4), 141.8 (C-8), 139.2 (C-3 in thienyl), 134.0 (CH=), 130.8 (C-5), 127.0, 126.6 and 125.2 (thienyl), 121.9 (CH=), 81.9 (C-2 in THP), 68.8 (C-6 in THP), 31.8 (C-3 in THP), 24.8 (C-5 in THP), 22.7 (C-4 in THP). IR (KBr): ν_{max} 3060, 3020, 2990, 2920, 2890, 2840, 1610, 1570, 1500 cm^{-1}. MS (EI): 312 (3, M^+), 229 (10), 228 (44), 227 (100), 195 (4), 173 (4), 84 (11), 83 (5).

(E)-6-[2-(2-Furanyl)ethenyl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (3g). Yield 177 mg (60 %) yellow powdery crystals. M.p. 116-118 °C. (Found: C, 64.75; H, 5.70. Calc. for $C_{16}H_{16}N_4O_2$: C, 64.85; H, 5.44 %). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.85 (s, 1 H, H-2), 8.25 (s, 1 H, H-8), 8.19 (d, *J* 16.0 Hz, 1 H, CH=), 7.54 (d, *J* 16.0 Hz, 1 H, CH=), 7.48 (br s, 1 H, H-5 in furanyl), 6.64 (d, *J* 3.5 Hz, 1 H, H-3 in furanyl), 6.45 (dd, *J* 3.5 and 1.5 Hz, 1 H, H-4 in furanyl), 5.76 (dd, *J* 10.0 and 2.5 Hz, 1 H, H-2 in THP), 4.2-4.1 (m, 1 H, H-6 in THP), 3.8-3.7 (m, 1 H, H-6 in THP), 2.1-2.0 (m, 3 H, H-3 and H-4 in THP), 1.8-1.6 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.6 (C-6), 152.5 (C-2 in furanyl), 152.3 (C-2), 150.9 (C-4), 144.2 (C-5 in furanyl), 141.7 (C-8), 130.9 (C-5), 126.9 (CH=), 120.4 (CH=), 113.4 (C-3 in furanyl), 112.2 (C-4 in furanyl), 81.9 (C-2 in THP), 68.8 (C-6 in THP), 31.7 (C-3 in THP), 24.8 (C-5 in THP), 22.7 (C-4 in THP). IR (KBr): ν_{max} 3090, 3060, 3020, 2910, 2830, 1615, 1575, 1560 cm^{-1}. MS (EI): 296 (9, M^+), 213 (12), 212 (74), 184 (40), 183 (18), 171 (27), 159 (11), 158 (100), 149 (10), 84 (22).

(E)-6-(2-Phenylethenyl)-1H-purine (4a). A mixture of (*E*)-6-(2-phenylethenyl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **3a** (168 mg, 0.55 mmol), CH_2Cl_2 (1.5 ml), 96% EtOH (18 ml) and 1 M HCl (12 ml) was stirred at ambient temperature for 4 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with $CHCl_3$ followed by MeOH-$CHCl_3$ (2:98); yield 111 mg (91 %) colourless powdery crystals. M.p. 252-254 °C (Lit.[5] 250-251 °C). ^1H NMR (DMSO-d_6, 500 MHz): δ 13.50 (br s, 1 H, NH), 8.85 (s, 1 H, H-2), 8.64 (s, 1 H, H-8), 8.33 (br d, 1 H, CH=), 7.76 (d, *J* 7.5 Hz, 2 H, Ph), 7.67 (d, *J* 16.0 Hz, 1 H, CH=), 7.46 (t, *J* 7.5 Hz, 2 H, Ph), 7.39 (t, *J* 7.5 Hz, 1 H, Ph). MS (EI): 222 (26, M^+), 221 (100) 167 (3), 141 (2), 128 (6), 111 (4), 66 (3).

(E)-6-[2-(4-Chlorophenyl)ethenyl]-1H-purine (4b). A mixture of (*E*)-6-[2-(4-chlorophenyl)ethenyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **3b** (139 mg, 0.41 mmol), 96% EtOH (15 ml) and 1 M HCl (10 ml) was stirred at ambient temperature for 5.5 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc-EtOH (1:20); yield 69 mg (74 %). M.p. 310-311 °C. (Found: C, 60.40; H, 3.75. Calc. for $C_{13}H_9ClN_4$ C, 60.83; H, 3.53 %). ^{1}H NMR (DMSO-d_6, 500 MHz): δ 13.51 (br s, 1 H, NH), 8.89 (s, 1 H, H-2), 8.65 (s, 1 H, H-8), 8.33 (br d, 1 H, CH=), 7.83 (d, *J* 8.0 Hz, 2 H, Ar), 7.72 (d, *J* 16.0 Hz, 1 H, CH=), 7.54 (d, *J* 8.0 Hz, 2 H, Ar). ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 155.8 (C-4), 153.3 (C-2), 152.9 (C-6), 146.4, (C-8) 139.3 (CH=), 136.3 (C in Ar), 136.2 (C-5), 136.2 (C in Ar), 130.3 (CH in Ar), 130.2 (CH in Ar), 124.3 (CH=). IR (KBr): ν_{max} 3050, 3010, 2940, 2770, 1615, 1565 cm^{-1}. MS (EI): 257 (37, *M*$^+$), 256 (34), 255 (100), 162 (4), 140 (6), 93 (6), 75 (4), 66 (6).

(E)-6-[2-(4-Methoxyphenyl)ethenyl]-1H-purine (4c). A mixture of (*E*)-6-[2-(4-methoxyphenyl)ethenyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **3c** (130 mg, 0.39 mmol), 96% EtOH (15 ml) and 1 M HCl (10 ml) was stirred at ambient temperature for 1 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc-EtOH (20:1); yield 84 mg (86 %) colourless powdery crystals. M.p. 239-242 °C. (Found: C, 66.72; H, 4.60. Calc. for $C_{14}H_{12}N_4O$ C, 66.65; H, 4.79 %). ^{1}H NMR (CD_3OD/DMSO-d_6, 200 MHz): δ 8.84 (s, 1 H, H-2), 8.54 (s, 1 H, H-8), 8.31 (d, *J* 16.0 Hz, 1 H, CH=), 7.7 (m, 2 H, Ar), 7.58 (d, *J* 16.0 Hz, 1 H, CH=), 7.0 (m, 2 H, Ar), 3.88 (s, 3 H, CH_3). ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 162.7 (C-4 in Ar), 155.5 (C-4/C-6), 154.0 (C-4/C-6), 153.3 (C-2), 145.8 (C-8), 141.1 (CH=), 130.5 (CH in Ar), 130.2 (C-1 in Ar), 129.5 (C-5), 120.5 (CH=), 115.6 (CH in Ar), 56.0 (CH_3). IR (KBr): ν_{max} 3060, 3020, 2950, 2810, 1620, 1575 cm^{-1}. MS (EI): 252 (55, *M*$^+$), 251 (100), 236 (5), 210 (3), 209 (10), 208 (15), 128 (4), 126 (4), 102 (3).

(E)-6-[2-(2-Hydroxyphenyl)ethenyl]-1H-purine (4d). A mixture of (*E*)-6-[2-(2-hydroxyphenyl)ethenyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **3d** (81 mg, 0.25 mmol), 96% EtOH (15 ml) and 1 M HCl (10 ml) was stirred at ambient temperature for 4 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc containing 0-40 % EtOH; yield 46 mg (77 %) colourless powdery crystals. M.p. >220 °C (dec.). ^{1}H NMR (CD_3OD, 300 MHz): δ 8.80 (s, 1 H, H-2), 8.60 (d, *J* 16.5 Hz, 1 H, CH=), 8.47 (s, 1 H, H-8), 7.80 (d, *J* 16.5 Hz, 1 H, CH=), 7.7 (m, 1 H, Ar), 7.2 (m, 1 H, Ar), 6.9 (m, 2 H, Ar). ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 157.9 (C-2 in Ar), 156.0 (C-6), 153.9 (C-4), 153.2 (C-2), 146.3 (C-8), 136.7 (CH=), 131.8 (C-4 in Ar), 129.7 (C-5), 129.3 ((C-6 in Ar), 124.6 (C-1 in Ar), 122.9 (CH=), 121.0 ((C-5 in Ar), 117.4 (C-3 in Ar). IR (KBr): ν_{max} 3060, 2950, 2820, 1615, 1590, 1570, 1555 cm^{-1}. MS (EI): 238 (16, *M*$^+$), 237 (17), 236 (3), 222 (16), 221 (100), 209 (4), 208 (4), 128 (4), 105 (6), 93 (5). Hrms: Found 238.0881, $C_{13}H_{10}N_4O$ requires 238.0855.

(E)-6-[2-(2-Thienyl)ethenyl]-1H-purine (4e). A mixture of (*E*)-6-[2-(2-thienyl)ethenyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **3e** (181 mg, 0.58 mmol), CH_2Cl_2 (2 ml), 96% EtOH (10 ml) and 1 M HCl (6 ml) was stirred at ambient temperature for 4 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with $CHCl_3$ followed by EtOH-$CHCl_3$ (5:95); yield 125 mg (97 %) pale yellow powdery crystals. M.p. 272-274 °C. (Found: C, 57.66; H, 3.80. Calc. for $C_{11}H_8N_4S$: C, 57.88; H, 3.53 %). ^{1}H NMR (DMSO-d_6, 500 MHz): δ 12.5 (br s, 1 H, NH), 8.81 (s, 1 H, H-2), 8.58 (s, 1 H, H-8), 8.48 (d, *J* 16.0 Hz, 1 H, CH=), 7.68 (d, *J* 5.0 Hz, 1 H, thienyl), 7.51 (d, *J* 3.5 Hz, 1 H, thienyl), 7.34 (d, *J* 16.0 Hz, 1 H, CH=), 7.16 (dd, *J* 5.0 and 3.5 Hz, 1 H, H-4 in thienyl). ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 155.4 (C-4), 153.3 (C-2), 153.3 (C-6), 145.8 (C-8), 142.7 (C-2 in thienyl), 134.0 (CH=), 131.1 (C-3 or C-5 in thienyl), 129.5 (C-5), 129.3 (C-4 in thienyl), 129.0 (C-3 or C-5

in thienyl), 122.0 (CH=). IR (KBr): ν_{max} 3070, 3020, 2960, 2820, 1615, 1590, 1570, 1535 cm^{-1}. MS (EI): 228 (7, M^+), 149 (50), 84 (20), 44 (100).

(E)-6-[2-(3-Thienyl)ethenyl]-1H-purine (4f). A mixture of (*E*)-6-[2-(3-thienyl)ethenyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **3f** (59 mg, 0.19 mmol), CH_2Cl_2 (1 ml), 96% EtOH (15 ml) and 1 M HCl (10 ml) was stirred at ambient temperature for 2.5 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with $CHCl_3$ followed by EtOH-$CHCl_3$ (5:95); yield 33 mg (77 %) pale yellow powdery crystals. M.p. 264-267 °C. ^1H NMR (DMSO-d_6, 500 MHz, 50 °C): δ 13.49 (br s, 1 H, NH), 8.75 (s, 1 H, H-2), 8.48 (s, 1 H, H-8), 8.29 (d, *J* 16.0 Hz, 1 H, CH=), 7.84 (m, 1 H, H-2 in thienyl), 7.54 (m, 2 H, H-4 and H-5 in thienyl), 7.41 (d, *J* 16.0 Hz, 1 H, CH=). ^{13}C NMR (DMSO-d_6, 125 MHz, 50 °C): δ 153.8 (C-4), 151.5 (C-2), 151.2 (C-6), 144.4 (C-8), 138.8 (C-3 in thienyl), 132.5 (C-2'), 127.9 (C-5), 127.2 (thienyl), 126.8 (C-2 in thienyl), 125.2 (thienyl), 122.6 (C-1'). IR (KBr): ν_{max} 3080-3020, 2950, 2800, 1615, 1585, 1565 cm^{-1}. MS (EI): 228 (35, M^+), 227 (100), 200 (4), 195 (5), 173 (5), 146 (5), 134 (4), 114 (4), 93 (4). Hrms: Found 228.0452, $C_{11}H_8N_4S$ requires 228.0470.

(E)-6-[2-(2-Furanyl)ethenyl]-1H-purine (4g). A mixture of (*E*)-6-[2-(2-furanyl)ethenyl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **3g** (279 mg, 0.94 mmol), 96% EtOH (15 ml) and 1 M HCl (10 ml) was stirred at ambient temperature for 0.5 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc followed by EtOH-EtOAc (1:20) and EtOH-EtOAc (1:10); yield 154 mg (77 %) yellow crystals. M.p. 250-251 °C (Lit.[33] 244-245 °C). ^1H NMR (CD_3OD, 300 MHz): δ 8.78 (s, 1 H, H-2), 8.46 (s, 1 H, H-8), 8.11 (d, *J* 16.0 Hz, 1 H, CH=), 7.66 (d, *J* 1.5 Hz, 1 H, furanyl), 7.48 (d, *J* 16.0 Hz, 1 H, CH=), 6.77 (d, *J* 3.5 Hz, 1 H, furanyl), 6.57 (dd, *J* 3.5 and 1.5 Hz, 1 H, furanyl). MS (EI): 212 (53, M^+), 211 (9), 184 (24), 183 (16), 171 (21), 159 (11), 158 (100), 156 (8), 129 (8), 77 (6).

Methyl (E)-3-iodo-2-methylpropenoate (6). Conc. sulfuric acid (5 drops) was added to a solution of (*E*)-3-iodo-2-methylpropenoic acid **5** (2.00 g, 9.43 mmol) in methanol (20 ml) and the resulting mixture was stirred at reflux for 16 h and cooled. 10 % aqueous K_2CO_2 (20 ml) was added and the mixture was extracted with CH_2Cl_2 (5×40 ml). The dried (Na_2SO_4) solution was evaporated *in vacuo* and the product was purified by bulb to bulb distillation (0.2 mm Hg, 60 °C); yield 1.624 g (76 %) colourless liquid. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.78 (q, *J* 1.5 Hz, 1 H, CH=), 3.73 (s, 3 H, OCH_3), 2.03 (d, *J* 1.5 Hz, 3 H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.2 (CO), 139.4 and 98.7 (C=), 52.3 (CH_3O), 20.3 (CH_3). IR (film): ν_{max} 3050, 2970, 2930, 1705, 1585 cm^{-1}. MS (EI): 226 (100, M^+), 195 (49), 167 (55), 127 (24), 126 (14), 99 (96), 69 (23), 67 (17). Hrms: Found 225.9501, $C_5H_7IO_2$ requires 225.9491.

(E,E)-6-(5-Carbomethoxy-4-methyl-1,3-pentadien-1-yl)-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (7). To a stirring solution of 6-ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2**, freshly prepared from 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1** (358 mg, 1.5 mmol) as described above, and palladium(II) acetate (17 mg, 0.075 mmol) in dry DMF (9 ml) under N_2, was added methyl (*E*)-3-iodo-2-methylpropenoate **6** (678 mg, 3.0 mmol) and *N,N*-diisopropylethylamine (770 µl, 4.5 mmol). The resulting mixture was heated at 85 °C for 22 h and evaporated *in vacuo*. The product was isolated after flash chromatography on silica gel eluting with EtOAc-hexane (2:1); yield 383 mg (78 %) off-white powdery crystals. M.p. 149-150 °C. (Found: C, 62.04; H, 6.12. Calc. for $C_{17}H_{20}N_4O_3$: C, 62.18; H, 6.14 %). ^1H NMR ($CDCl_3$, 200 MHz): δ 8.82 (s, 1 H, H-2), 8.24 (dd, *J* 15.5 and 12.0 Hz, 1 H, CH=), 8.22 (s, 1 H, H-8), 7.36 (dq, *J* 12.0 and 1.0 Hz, 1 H, CH=), 7.32 (d, *J* 15.5 Hz, 1 H, CH=), 5.7 (m, 1 H, H-2 in THP), 4.1 (m, 1 H, H-6 in THP), 3.8-3.7 (m, 1 H, H-6 in THP), 3.72 (s, 3 H, CH_3O), 2.08 (s, 3 H, CH_3), 2.1-2.0 (m, 3 H, H-3 and H-4 in THP), 1.7-1.6 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 168.2 (CO), 152.6 (C-2), 152.2 (C-4/C-6), 151.2 (C-4/C-6), 142.3 (C-8), 136.9

(C-3'), 134.3 (C-2'), 132.5 (C-4'), 131.9 (C-1'), 131.3 (C-5), 81.8 (C-2 in THP), 68.7 (C-6 in THP), 51.9 (CH_3O), 31.6 (C-3 in THP), 24.7 (C-5 in THP), 22.6 (C-4 in THP), 13.3 (CH_3). IR (KBr): ν_{max} 3080, 3020, 2920, 2830, 1695, 1625, 1575 cm^{-1}. MS (EI): 328 (3, M^+), 229 (20), 201 (11), 186 (7), 185 (100), 149 (13), 84 (21), 83 (10).

(E,E)-6-(5-Carbomethoxy-4-methyl-1,3-pentadien-1-yl)-1H-purine (***8***). A mixture of (*E,E*)-6-(5-carbomethoxy-4-methyl-1,3-pentadien-1-yl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **7** (207 mg, 0.63 mmol), MeOH (15 ml) and 1 M HCl (10 ml) was stirred at ambient temperature for 4 h and neutralized by addition of solid $NaHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with $CHCl_3$ containing 0-50 % EtOH; yield 131 mg (98 %) pale yellow crystals. M.p. 227-230 °C. ^1H NMR (DMSO-d_6, 300 MHz): δ 13 (br s, 1 H, NH), 8.84 (s, 1 H, H-2), 8.59 (s, 1 H, H-8), 8.28 (t, *J* 14.0 Hz, 1 H, CH=), 7.4 (m, 2 H, 2×CH=), 3.65 (s, 3 H, OCH_3), 2.06 (s, 3 H, CH_3). ^{13}C NMR (CD_3OD, 125 MHz): δ 169.9 (C-5'), 155.7 (C-4), 153.3 (C-2), 152.5 (C-6), 146.4 (C-8), 137.9 (C-3'), 135.4 (C-2'), 134.0 (C-4'), 132.7 (C-51), 130.3 (C-5), 52.5 (OCH_3), 13.3 (CH_3). IR (KBr): ν_{max} 3080-3020, 2920, 2780, 1695, 1600, 1580, 1560 cm^{-1}. MS (EI): 244 (11, M^+), 229 (15), 186 (8), 185 (54), 92 (6), 56 (6). Hrms: Found 244.0947, $C_{12}H_{12}N_4O_2$ requires 244.0960.

(E,E)-6-(5-Hydroxy-4-methyl-1,3-pentadien-1-yl)-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (***10***). To a stirring solution of 6-ethenyl-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **2**, freshly prepared from 6-chloro-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **1** (239 mg, 1.0 mmol) as described above, and palladium(II) acetate (11 mg, 0.05 mmol) in dry DMF (8 ml) under N_2, was added (*E*)-3-iodo-2-methyl-2-propen-1-ol **9** (396 mg, 2.0 mmol) and *N,N*-diisopropylethylamine (510 μl, 3.0 mmol). The resulting mixture was heated at 70 °C for 50 h and evaporated *in vacuo*. The product was isolated after flash chromatography on silica gel eluting with EtOAc-hexane (2:1) followed by EtOAc-hexane (3:1) and finally EtOAc; yield 165 mg (55 %) colourless powdery crystals. M.p. 146-149 °C. (Found: C, 63.57; H, 6.31. Calc. for $C_{18}H_{18}N_4O_2$: C, 63.98; H, 6.71 %). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.79 (s, 1 H, H-2), 8.24 (dd, *J* 15.0 and 11.5 Hz, 1 H, CH=), 8.21 (s, 1 H, H-8), 7.06 (d, *J* 15.0 Hz, 1 H, CH=), 6.48 (d, *J* 11.5 Hz, 1 H, CH=), 5.73 (dd, *J* 10.0 and 2.5 Hz, 1 H, H-2 in THP), 4.20 (s, 2 H, CH_2), 4.2-4.1 (m, 1 H, H-6 in THP), 3.88 (br s, 1 H, OH), 3.78 (dt, *J* 11.5 and 2.5 Hz, 1 H, H-6 in THP), 2.2-2.0 (m, 3 H, H-3 and H-4 in THP), 1.97 (s, 3 H, CH_3), 1.8-1.6 (m, 3 H, H-4 and H-5 in THP). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.4 (C-6), 152.4 (C-2), 150.8 (C-4), 146.0 (C=), 141.7 (C-8), 136.1 (CH=), 130.6 (C-5), 124.9 (CH=), 123.6 (CH=), 81.8 (C-2 in THP), 68.8 (C-6 in THP), 67.4 (CH_2OH), 31.7 (C-3 in THP), 24.8 (C-5 in THP), 22.7 (C-4 in THP), 14.8 (CH_3). IR (KBr): ν_{max} 3200, 3060, 2920, 2840, 1625, 1595, 1560 cm^{-1}. MS (EI): 300 (21, M^+), 216 (17), 187 (45), 186 (13), 185 (100), 159 (19), 158 (13), 134 (16), 85 (23).

(E,E)-6-(5-Hydroxy-4-methyl-1,3-pentadien-1-yl)-1H-purine (***11***). A mixture of (*E,E*)-6-(5-hydroxy-4-methyl-1,3-pentadien-1-yl)-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **10** (80 mg, 0.27 mmol), 96 % EtOH (15 ml) and 1 M HCl (12 ml) was stirred at ambient temperature for 15 h and neutralized by addition of solid $KHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc containing 10-40 % EtOH; yield 39 mg (68 %) colourless powdery crystals. M.p. 205-207 °C. ^1H NMR (CD_3OD, 300 MHz): δ 8.79 (s, 1 H, H-2), 8.50 (s, H, H-8), 8.38 (dd, *J* 15.5 and 11.5 Hz, 1 H, CH=), 7.06 (d, *J* 15.5 Hz, 1 H, CH=), 6.5 (m, 1 H, CH=), 4.15 (s, 2 H, CH_2), 1.99 (s, 3 H, CH_3). ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 155.1 (C-4/C-6), 154.0, (C-4/C-6) 153.2 (C-2), 147.8 (C-4'), 145.7 (C-8), 137.7 (C-2'), 129.5 (C-5), 125.4 (C-1'), 124.6 (C-3'), 67.9 (CH_2), 14.7 (CH_3). IR (KBr): ν_{max} 3080-3020, 2960-2920, 2790, 1580, 1555 cm^{-1}. MS (EI): 216 (18, M^+), 199 (10), 187 (43), 186 (14), 185 (100), 173 (11), 171 (17), 159 (23), 158 (28), 134 (25). Hrms: Found 216.1020, $C_{11}H_{12}N_4O$ requires 216.1011.

(E)-1-(tert-Butyldimethylsilyloxy)-2-methyl-2-penten-4-yne (***13c***). A mixture of (*E*)-2-methylpent-2-en-4-yn-1-ol (258 mg, 2.68 mmol), *tert*-butyldimethylsilyl chloride (607 mg, 4.02 mmol) and triethylamine (0.750 ml,

5.37 mmol) in dry dichloromethane (7 ml) and dry DMF (4 ml) was stirred under N_2 for 2 h before sat. aq. NH_4Cl (50 ml) was added and the mixture was extracted with dichloromethane (4×25 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated *n vacuo* and the product was isolated by flash chromatography on silica gel eluting with hexane followed by EtOAc-hexane (5:95); yield 470 mg (83 %). ^1H NMR ($CDCl_3$, 200 MHz): δ 5.59 (m, 1 H, H-3), 4.08 (t, *J* 1.0 Hz, 2 H, H-1), 3.05 (d, *J* 2.0 Hz, 1 H, H-5), 1.82 (s, 3 H, CH_3), 0.88 (s, 9 H, *t*-Bu), 0.05 [s, 6 H, Si(CH_3)]. ^{13}C NMR ($CDCl_3$, 50 MHz) δ 152.2 (C-2), 102.3 (C-3), 81.4 (C-4), 80.5 (C-5), 66.3 (C-1), 25.8 (CH_3 in *t*-Bu), 18.3 (C in *t*-Bu), 16.1 (CH_3), -5.5 [Si(CH_3)]. IR (film): ν_{max} 3270, 2920-2900, 2350, 1580 cm^{-1}. MS (EI): 210 (8, M^+), 155 (5), 154 (14), 153 (100), 125 (13), 109 (5), 83 (21), 77 (19), 75 (88), 73 (18). Hrms: Found 210.1417, $C_{12}H_{22}OSi$ requires 210.1440.

(E)-6-(5-Hydroxy-4-methyl-3-penten-1-yn-1-yl)-1H-purine (14a). (*E*)-2-Methyl-5-(trimethylsilyl)-2-penten-4-yn-1-ol **13a** (100 mg, 0.6 mmol) was added to a stirring solution of dry tetramethylammonium fluoride (70 mg, 0.75 mmol) in THF (1 ml) at ambient temperature under N_2. After 15 min, 6-iodo-1*H*-purine **12a** (123 mg, 0.5 mmol), bis(triphenylphosphine)palladium(II) chloride (18 mg, 0.025 mmol), cuprous iodide (10 mg, 0.05 mmol), *N,N*-diisopropylethylamine (257 µl, 1.5 mmol) and DMF (7 ml) were added and the resulting mixture was heated at 60 °C for 6 h. After cooling, water (2 ml) was added and the mixture was evaporated *in vacuo* together with a small amount of silica gel. The residue was added on top of a silica gel column and the product was isolated by flash chromatography eluting with EtOH-EtOAc (1:10); yield 67 mg (63 %) off-white powdery crystals. M.p. 213-214 °C. (Found: C, 61.27; H, 4.96. Calc. for $C_{11}H_{10}N_4O$: C, 61.67; H, 4.71 %). ^1H NMR (CD_3OD, 300 MHz): δ 8.83 (s, 1 H, H-2), 8.53 (s, 1 H, H-8), 6.0 (m, 1 H, CH=), 4.15 (s, 2 H, CH_2), 2.0 (m, 3 H, CH_3). ^{13}C NMR (DMSO-d_6, 125 MHz, 50 °C): δ 157.8 (C-4'), 153.7 (C-4), 151.8 (C-2), 145.6 (C-8), 138.9 (C-6), 131.4 (C-5), 101.1 (C-3'), 95.1 (C-2'), 87.9 (C-1'), 64.5 (C-5'), 16.5 (CH_3). IR (KBr): ν_{max} 3090-3020, 2930, 2790, 2180, 1585, 1565 cm^{-1}. MS (EI): 214 (76, M^+), 212 (19), 198 (24), 197 (26), 196 (19), 186 (26), 185 (100), 184 (19), 183 (25), 171 (28).

(E)-6-[4-Methyl-5-[(tetrahydro-2H-pyran-2-yl)oxy]-3-penten-1-yn-1-yl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine (14b). A mixture of 6-iodo-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **12b** (1.651 g, 5.0 mmol), (*E*)-2-methyl-1-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2-penten-4-yne **13b** (1.08 g, 6.0 mmol), bis(triphenylphosphine)-palladium(II) chloride (175 mg, 0.25 mmol), cuprous iodide (95 mg, 0.5 mmol), *N,N*-diisopropylethylamine (2.6 ml, 15 mmol) and DMF (30 ml) was heated at 65 °C under N_2 for 14 h. The reaction mixture was evaporated *in vacuo* and the product was isolated by flash chromatography eluting with EtOAc-hexane (2:1); yield 1.566 g (82 %) yellow oil. ^1H NMR ($CDCl_3$, 500 MHz): δ 8.69 (s, 1 H, H-2), 8.14 (s, 1 H, H-8), 5.80 (m, 1 H, H-3'), 5.57 (dd, *J* 10.0 and 2.5 Hz, 1 H, H-2 in NTHP), 4.44 (t, *J* 3.5 Hz, 1 H, H-2 in OTHP), 4.07 (d, *J* 15.0 Hz, 1 H, H_A in H-5'), 3.94 (m, 1 H, H-6 in NTHP), 3.84 (d, *J* 15.0 Hz, 1 H, H_B in H-5'), 3.63 (m, 1 H, H-6 in OTHP), 3.56 (m, 1 H, H-6 in NTHP), 3.31 (m, 1 H, H-6 in OTHP), 1.79-1.94 (m, 4 H, H-3 and H-4 in NTHP), 1.90 (m, 3 H, CH_3), 1.30-1.64 (m, 8 H, H-3, H-4 and H-5 in OTHP and H-5 in NTHP). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 153.3 (C-4'), 152.5 (C-2), 150.6 (C-4), 142.2 (C-8), 134.2 (C-5), 104.1 (C-3'), 97.7 (C-2 in OTHP), 96.5 (C-2'), 87.9 (C-1'), 82.0 (C-2 in NTHP), 69.8 (C-5'), 68.8 (C-6 in NTHP), 62.0 (C-6 in OTHP), 31.7 (C-3 in NTHP), 30.3 (C-3 in OTHP), 25.3 (C-5 in OTHP), 24.7 (C-5 in NTHP), 22.6 (C-4 in NTHP), 19.0 (C-4 in OTHP), 17.5 (CH_3). IR (KBr): ν_{max} 3090, 3030, 2920, 2830, 2190, 1650, 1560 cm^{-1}. MS (EI): 382 (2, M^+), 298 (25), 215 (18), 214 (100), 213 (17), 198 (18), 197 (38), 186 (11), 185 (74), 85 (71). Hrms: Found 382.1996, $C_{21}H_{26}N_4O_3$ requires 382.2005.

(E)-6-[4-Methyl-5-[(tetrahydro-2H-pyran-2-yl)oxy]-3-penten-1-yn-1-yl]-1H-purine (14c). A mixture of 6-iodo-1*H*-purine **12a** (492 mg, 2.0 mmol), (*E*)-2-methyl-1-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2-penten-4-yne **13b** (397 mg, 2.2 mmol), bis(triphenylphosphine)palladium(II) chloride (70 mg, 0.10 mmol), cuprous iodide (38 mg, 0.20 mmol), triethylamine (0.85 ml, 6.1 mmol) and DMF (10 ml) was heated at 65 °C under N_2 for 24 h. The reaction mixture was evaporated *in vacuo* and the product was isolated by flash chromatography eluting

with EtOAc; yield 445 mg (75 %) yellow crystals. M.p. 66-68 °C. ^{1}H NMR (CD_3OD, 200 MHz): δ 8.84 (s, 1 H, H-2), 8.54 (s, 1 H, H-8), 6.0 (m, 1 H, CH=), 4.7 (m, 1 H, H-2 in THP), 4.30 (d, *J* 15.0 Hz, 1 H, H_A in CH_2), 4.08 (d, *J* 15.0 Hz, 1 H, H_B in CH_2), 3.9 (m, 1 H, H-6 in THP), 3.6 (m, 1 H, H-6 in THP), 2.1 (m, 3 H, CH_3), 1.8-1.5 (m, 6 H, THP). ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 155.8 (C-4 or C-6), 155.5 (C-4 or C-6), 153.4 (C-2), 147.2 (C-4'), 140.6 (C-8), 131.9 (C-5), 104.7 (C-3'), 99.8 (C-2 in THP), 97.6 (C-1' or C-2'), 88.3 (C-1' or C-2'), 71.3 (C-5'), 63.4 (C-6 in THP), 31.6 (THP), 26.6 (THP), 20.4 (THP), 17.5 (CH_3). IR (KBr): ν_{max} 3080-3020, 2910, 2830, 2190, 1565 cm^{-1}. MS (EI): 298 (7, *M*$^+$), 215 (18), 214 (96), 213 (18), 198 (24), 197 (51), 186 (15), 185 (100), 171 (15), 85 (71). Hrms: Found 298.1415, $C_{16}H_{18}N_4O_2Si$ requires 298.1430.

*(E)-6-[5-(*tert*-Butyldimethylsilyloxy)-4-methyl-3-penten-1-yn-1-yl]-1*H*-purine (**14d**).* A mixture of 6-iodo-1*H*-purine **12a** (517 mg, 2.1 mmol), (*E*)-1-(*tert*-butyldimethylsilyloxy)-2-methyl-2-penten-4-yne **13c** (462 mg, 2.2 mmol), bis(triphenylphosphine)palladium(II) chloride (74 mg, 0.11 mmol), cuprous iodide (40 mg, 0.21 mmol), *N,N*-diisopropylethylamine (1.10 ml, 6.3 mmol) and DMF (13 ml) was heated at 75 °C under N_2 for 6.5 h. The reaction mixture was evaporated *in vacuo* and the product was isolated by flash chromatography eluting with EtOAc; yield 549 mg (80 %) colourless powdery crystals. M.p. 187-188 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.99 (s, 1 H, H-2), 8.38 (s, 1 H, H-8), 5.96 (m, 1 H, H-3'), 4.15 (s, 2 H, H-5'), 1.96 (s, 3 H, CH_3), 0.88 (s, 9 H, *t*-Bu), 0.05 [s, 6 H, Si(CH_3)]. ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 157.1 (C-4'), 154.4 (C-4), 152.7 (C-2), 145.8 (C-8), 140.7 (C-6), 131.2 (C-5), 102.5 (C-3'), 97.9 (C-2'), 87.7 (C-1'), 66.9 (C-5'), 26.1 (CH_3 in *t*-Bu), 18.7 (C in *t*-Bu), 16.9 (CH_3), -5.3 [Si(CH_3)]. IR (KBr): ν_{max} 3110-3010, 2920, 2900, 2830, 2190, 1585, 1565 cm^{-1}. MS (EI): 328 (11, *M*$^+$), 313 (4), 272 (22), 271 (100), 257 (6), 256 (25), 255 (4), 201 (12), 197 (15), 73 (10). Hrms: Found 328.1725, $C_{17}H_{24}N_4OSi$ requires 328.1719.

*(1Z,3E)-6-(5-Hydroxy-4-methyl-1,3-pentadien-1-yl)-1*H*-purine (**15**).* A mixture of (*E*)-6-(5-hydroxy-4-methyl-3-penten-1-yn-1-yl)-1*H*-purine **14a** (70 mg, 0.33 mmol), quinoline (0.84 ml) and Lindlar catalyst (131 mg) in EtOAc (16 ml) and MeOH (16 ml) was stirred under H_2-atmosphere at ambient temp for 3 h. The reaction mixture was filtered through Celite and evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc-hexane (2:1) followed by EtOAc containing 0-25 % EtOH; yield 62 mg (89 %) pale yellow powdery crystals containing 25 % of the (*E,E*) isomer. M.p. 90-95 °C. ^{1}H NMR (CD_3OD, 300 MHz): δ 8.86 (s, 1 H, H-2), 8.44 (s, 1 H, H-8), 7.78 (d, *J* 12.0 Hz, 1 H), 7.06 (t, *J* 12.0 Hz, 1 H, H-2'), 6.86 (d, *J* 12.0 Hz, 1 H), 4.11 (s, 2 H, H-5'), 1.92 (s, 3 H, CH_3). ^{13}C NMR (CD_3OD, 75 MHz): δ 155.5 (C-4/C-6), 154.2 (C-4/C-6), 153.2 (C-2), 147.6 (C-4'), 145.7 (C-8), 135.8, 129.6 (C-5), 123.0, 120.0, 68.5 (C-5'), 13.9 (CH_3). IR (KBr): ν_{max} 3080-3020, 2960-2910, 2800, 1575 cm^{-1}. MS (EI): 216 (10, *M*$^+$), 199 (12), 198 (14), 197 (13), 187 (27), 185 (100), 171 (15), 159 (19), 158 (25), 134 (35). Hrms: Found 216.1014, $C_{11}H_{12}N_4O$ requires 216.1011.

*(1Z,3E)-6-[4-Methyl-5-[(tetrahydro-2*H*-pyran-2-yl)oxy]-1,3-pentadien-1-yl]-1*H*-purine (**16a**).* A mixture of (*E*)-6-[4-methyl-5-[(tetrahydro-2*H*-pyran-2-yl)oxy]-3-penten-1-yn-1-yl]-1*H*-purine **14c** (134 mg, 0.45 mmol), quinoline (0.48 ml, 4.1 mmol) and Lindlar catalyst (270 mg) in EtOAc (12 ml) and MeOH (12 ml) was stirred under H_2-atmosphere at ambient temp for 5 h. The reaction mixture was filtered through Celite and evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc-hexane (2:1) followed by EtOAc-EtOH (9:1); yield 98 mg (73 %) pale yellow powdery crystals containing 9 % of the (*E,E*) isomer. M.p. 68-70 °C. ^{1}H NMR (CD_3OD, 200 MHz): δ 8.84 (s, 1 H, H-2), 8.39 (s, 1 H, H-8), 7.77 (d, *J* 11.5 Hz, 1 H, CH=), 7.05 (t, *J* 11.5 Hz, 1 H, CH=), 6.88 (d, *J* 11.5 Hz, 1 H, CH=), 4.66 (m, 1 H, H-2 in THP), 4.24 (d, *J* 14.0 Hz, 1 H, H_A in H-5'), 4.06 (d, *J* 14.0 Hz, 1 H, H_B in H-5'), 3.9 (m. 1 H, H-6 in THP), 3.5 (m, 1 H, H-6 in THP), 1.91 (s, 3 H, CH_3), 1.9-1.5 (m, 6 H, H-3, H-4 and H-5 in THP). ^{13}C NMR (CD_3OD, 75 MHz, 50 °C): δ 155.8 (C-4 or C-6), 154.2 (C-4 or C-6), 153.2 (C-2), 145.7 (C-4'), 144.3 (C-8), 135.5 (C-2'), 124.3 (C-3'), 120.5 (C-1'), 99.4 (C-2 in THP), 73.0 (C-5'), 63.3 (C-6 in THP), 31.8 (THP), 26.6 (THP), 20.4 (THP), 14.2 (CH_3). IR (KBr): ν_{max} 3080-3020, 2920, 2820, 1570 cm^{-1}. MS (EI, 15 eV): 300 (6, *M*$^+$), 269 (1), 216 (26), 215

(4), 200 (7), 199 (26), 198 (15), 188 (7), 187 (8), 186 (22), 185 (100), 85 (14). Hrms: Found 300.1581, $C_{16}H_{20}N_4O_2$ requires 300.1586.

*(1Z,3E)-6-[5-(*tert*-Butyldimethylsilyloxy)-4-methyl-1,3-pentadien-1-yl]-1H-purine* ***(16b)***. A mixture of (*E*)-6-[5-(*tert*-butyldimethylsilyloxy)-4-methyl-3-penten-1-yn-1-yl]-1*H*-purine **14d** (89 mg, 0.27 mmol), quinoline (0.29 ml, 2.5 mmol) and Lindlar catalyst (163 mg) in EtOAc (7 ml) and MeOH (7 ml) was stirred under H_2-atmosphere at ambient temp for 14 h. The reaction mixture was filtered through Celite and evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc-hexane (2:1) followed by EtOAc; yield 64 mg (71 %) pale yellow oil containing 11 % of the (*E,E*) isomer. M.p. 127-128 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 12.9 (br s, 1 H, NH), 8.95 (s, 1 H, H-2), 8.27 (s, 1 H, H-8), 8.03 (d, *J* 7.0 Hz, 1 H, CH=), 7.07 (m, 2 H), 4.21 (s, 2 H, H-5'), 2.02 (s, 3 H, CH_3), 0.93 (s, 9 H, *t*-Bu), 0.09 [s, 6 H, Si(CH_3)]. ^{13}C NMR (CD_3OD, 125 MHz, 50 °C): δ 154.3 (C-4 or C-6), 152.6 (C-2), 152.5 (C-4 or C-6), 146.8 (C-4'), 144.5 (C-8), 135.5 (C-2'), 129.4 (C-5), 121.5 (C-3'), 119.3 (C-1'), 68.3 (C-5'), 26.2 (CH_3 in *t*-Bu), 18.8 (C in *t*-Bu), 13.9 (CH_3), -5.2 [s, 6 H, Si(CH_3)]. IR (KBr): ν_{max} 3080-3020, 2930, 2910, 2830, 1600, 1575, 1540 cm^{-1}. MS (EI, 15 eV): 331 (1, M^+), 314 (5), 273 (25), 257 (8), 199 (34), 198 (21), 197 (24), 186 (13), 185 (100), 158 (16), 73 (12). Hrms: Found 330.1891, $C_{17}H_{26}N_4OSi$ requires 330.1876.

6-[4-Methyl-5-[(tetrahydro-2H-pyran-2-yl)oxy]pent-1-yl]-9-(tetrahydro-2H-pyran-2-yl)-9H-purine ***(17)***. A mixture of (*E*)-6-[4-methyl-5-[(tetrahydro-2*H*-pyran-2-yl)oxy]-3-penten-1-yn-1-yl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **14b** (665 mg, 1.7 mmol), quinoline (1.0 ml, 8.5 mmol) and Lindlar catalyst (980 mg) in EtOAc (25 ml) and MeOH (25 ml) was stirred under H_2-atmosphere at ambient temp for 4 h. The reaction mixture was filtered through Celite and evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc-hexane (1:4) followed by EtOAc-hexane (1:1) and finally EtOAc-hexane (2:1); yield 613 mg (91 %) of an isomeric mixture as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.85 (s, 1 H, H-2), 8.21 (s, 1 H, H-8), 5.77 (dd, *J* 9.5, and 3.5 Hz, 1 H, H-2 in NTHP), 4.52 (br s, 1 H, H-2 in OTHP), 4.1 (m, 1 H, H-6 in NTHP), 3.8 (m, 2 H, H-6 in NTHP and H-5'), 3.6-3.4 (m, 2 H, H-6 in OTHP and H-5'), 3.2-3.1 (m, 3 H, H-6 in OTHP and H-1'), 2.1-1.5 (m, 16 H, H-2', H-3' and THP), 1.2 (m, 1 H, H-4'), 0.90 (dd, *J* 6.5 and 4.0 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.0 (C-6), 163.0 (C-6), 152.4 (C-2), 149.9 (C-4), 141.4 (C-8), 132.7 (C-5), 98.8 (C-2 in OTHP), 98.7 (C-2 in OTHP), 81.9 (C-2 in NTHP), 72.8 (C-5' or C-6 in OTHP), 72.8 (C-5' or C-6 in OTHP), 68.8 (C-6 in NTHP), 62.0 (C-5' or C-6 in OTHP), 62.0 (C-5' or C-6 in OTHP), 33.6 (C-1' and C-4'), 33.6 (C-1' and C-4'), 33.5 (C-1' and C-4'), 33.4 (C-1' and C-4'), 33.3 (C-1' and C-4'), 31.8, 30.7, 26.1, 26.0, 25.5, 24.9), 22.8 and 19.5 (C-3, C-4, and C-5 in OTHP and NTHP, C-2' and C-3'), 17.1 (CH_3), 17.0 (CH_3). IR (film): ν_{max} 3070, 3030, 2920, 2840, 1580 cm^{-1}. MS (EI): 388 (4, M^+), 303 (10), 287 (11), 220 (12), 219 (43), 204 (21), 203 (61), 201 (15), 189 (11), 161 (14), 147 (30), 135 (15), 134 (100). Hrms: Found 388.2483, $C_{21}H_{32}N_4O_3$ requires 388.2474.

6-(5-Hydroxy-4-methylpent-1-yl)-1H-purine ***(18)***. A mixture of 6-[4-methyl-5-[(tetrahydro-2*H*-pyran-2-yl)oxy]pent-1-yl]-9-(tetrahydro-2*H*-pyran-2-yl)-9*H*-purine **17** (274 mg, 0.71 mmol), 96 % EtOH (18 ml), water (20 ml) and 1 M HCl (10 ml) was stirred at ambient temperature for 5.5 h and neutralized by addition of solid $NaHCO_3$. The resulting mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc containing 0-30 % EtOH; yield 118 mg (76 %) pale yellow oil. ^{1}H NMR (CD_3OD, 200 MHz): δ 8.64 (s, 1 H, H-2), 8.34 (s, 1 H, H-8), 3.2 (m, 2 H, H-5'), 2.99 (t, *J* 7.5 Hz, 2 H, H-1'), 1.8 (m, 2 H, H-2'), 1.4 (m, 2 H, H-3'), 1.0 (m, 1 H, H-4'), 0.74 (d, *J* 7.0 Hz, 3 H, CH_3). ^{13}C NMR (CD_3OD, 75 MHz): δ 161.5 (C-6), 155.2 (C-4), 153.2 (C-2), 145.9 (C-8), 130.6 (C-5), 68.3 (C-5'), 36.7 (C-3'), 34.4 (C-1' or C-4'), 34.2 (C-1' eller C-4'), 27.0 (C-2'), 16.9 (CH_3). IR (film): ν_{max} 3250, 3080-3020, 2940-2900, 2840, 2450, 1585, 1550 cm^{-1}. MS (EI): 220 (2, M^+), 218 (4), 203 (5), 190 (4), 189 (5), 161 (13), 159 (4), 148 (6), 147 (25), 135 (15), 134 (100). Hrms: Found 220.1320, $C_{11}H_{16}N_4O$ requires 220.1324.

Procedure for determination of cytokinin activity. The cytokinin activity of the compounds was determined using a bioassay method described by Letham.[34] Radish (*Raphanus sativus* L. cv. Cherry belle) cotyledons were used as the cytokinin sensitive plant material. Seeds were germinated in petri dishes (14 cm) between layers of wet cellulose paper for 30 hours at 30 °C. Six pairs of cotyledons of uniform size were excised and their fresh weight determined. The leaves were randomly placed on filter paper (Whatman no. 1, 9 cm) in petri dishes (9 cm). To the filter paper 3 mL 2m*M* potassium phosphate buffer (pH 6) with different concentrations of either benzylaminopurine (BAP) or cytokinin analogs had been added. Before dissolving in buffer, the BAP and cytokinin analogs were dissolved in 1 mL ethanol, or in some cases in 1 mL methanol, 0.1 M NaOH or dimethyl sulfoxide (DMSO). The closed petri dishes with cotyledons were placed at constant temperature (23 °C) and continuous light (intensity: 4 μmol/m ^{2}s) from fluorescent tubes (Aura 530 G2, 58 W, Sweden). To obtain the low light intensity, two layers of gaz covered the dishes. After 48 hours, 1 mL potassium phospate buffer was added to each dish to keep constant wet conditions in the dishes. The experiment was finished after 72 hours. Each cotyledon was carefully blotted dry and the fresh weight was determined. To determine the cytokinin effect of the purines, the weight gain of cotyledons treated with the 100 μ*M* cytokinin analogs was subtracted the weight gain of control cotyledons (0 μ*M* purine). This effect on growth of radish cotyledons was compared to the effect of BAP (100 μ*M*), and is expressed as percent of the effect of BAP. The results are based on the mean of three replicate dishes of each treatment.

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