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Lewis Acid Mediated Diels-Alder Reactions of 6-Vinylpurines

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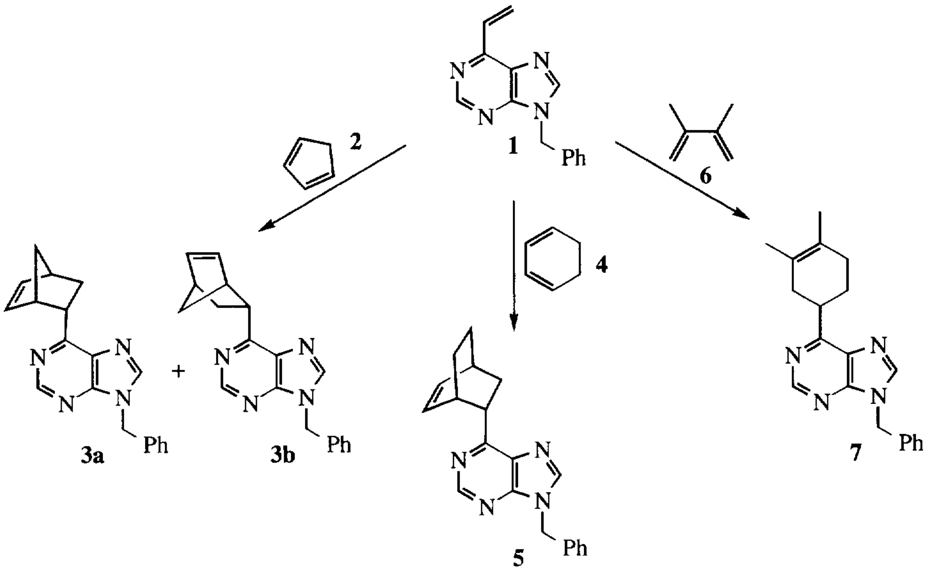
Abstract: 6-Vinylpurines readily undergo Diels-Alder reactions with dienes. Both reactivity and *endo* selectivity are greatly improved when the cycloadditions are performed in the presence of zinc chloride. Lewis acid mediated Diels-Alder reaction of 6-vinylpurine riboside was employed as a key step in the synthesis of a nucleoside with structural resemblance to potent A_1 adenosine agonists.

In connection with our on-going project directed towards synthesis of novel modified purine derivatives,[1] we recently identified 6-vinylpurines as electron poor alkenes which undergo smooth addition reactions, when treated with nucleophiles.[2] Electron deficient alkenes readily participate in Diels-Alder cycloadditions, often with high regio- and stereoselectivity.[3] We therefore envisaged that 6-vinylpurines may act as reactive dienophiles in Diels-Alder reactions giving purines with a variety of cycloalkyl substituents. Few convenient methods for the introduction of cycloalkyls, or secondary alkyls in general, in the purine 6-position have previously been reported.[1e,1i,4]

The vinylpurine **1** was readily available from Pd-catalyzed cross coupling between the corresponding 6-iodopurine and vinylzinc bromide, a technique for purine functionalisation previously developed by us.[1c] Diels-Alder reactions between the alkene **1** and dienes were studied (Scheme 1, Table 1). Initially, the reaction with cyclopentadiene **2** was slow and the *endo* selectivity was poor. The *endo*- and *exo* adducts **3a** and **3b** were formed in almost equal amounts and a considerable amount of the starting material **1** was recovered (Table 1. Entry 1). The preliminary stereochemical assignments of the products were made by comparing the NMR spectra with those of other isomeric norbornene *exo*- and *endo* adducts,[5] and confirmed by NOESY NMR spectroscopy (*vide infra*).

It is well known that coordination of a Lewis acid with a conjugated C=O or C=N moiety on the dienophile, may lower frontier orbital energies, and thereby increase both reaction rate and *endo* selectivity in Diels-Alder reactions with electron deficient dienophiles.[3,6] When the cycloaddition between the vinylpurine **1** and cyclopentadiene was performed in the presence of a catalytic amount of $ZnCl_2$, complete conversion of the alkene **1** was accomplished and the *endo* selectivity was clearly improved (Table 1, Entry 2). Increasing the amount of Lewis acid resulted in shorter reaction times, and nearly complete *endo* selectivity was achieved when 5 equiv. $ZnCl_2$ were employed (Table 1, Entries 3-4).

The cycloadditions of vinylpurine **1** with the dienes **4** and **6** were somewhat slower than with cyclopentadiene. In these latter reactions, an excess $ZnCl_2$ was required (Table 1, Entries 5-8). These dienes are also reported to be significantly less reactive compared with cyclopentadiene, in other Diels-Alder reactions.[7] Only one isomer, identified by NOESY as the *endo* compound **5**, was formed in the reaction with 1,3-cyclohexadiene **4** as judged by the ^1H NMR spectrum of the crude product.



Scheme 1

Table 1. Diels-Alder reactions of the vinylpurine **1**.

Entry	Diene	Solvent	Time (h)	Temp (°C)	Equiv. $ZnCl_2$	Yield (%)[a]
1	**2**	CH_2Cl_2	96	0 - RT	–	31 (**3a**) and 27 (**3b**)[b]
2	"	"	72	"	0.2	80 (**3a**) and 11 (**3b**)
3	"	"	24	"	1.0	91 (**3a**) and 8 (**3b**)
4	"	"	2.5	0	5.0	93 (**3a**) and 1 (**3b**)
5	**4**	DCE	8	50	–	n.r.
6	"	"	36	RT	5.0	50 (**5**)
7	**6**	"	48	50	–	n.r.
8	"	"	60	RT	5.0	57 (**7**)

(a) Yields of isolated products; (b) 36 % of the starting vinylpurine 1 was recovered.

The stereochemical assignments of the *exo* and *endo* products **3a**, **3b** and **5** were confirmed by NOESY spectroscopy as shown for the isomers **3a** and **3b** in Fig. 1.

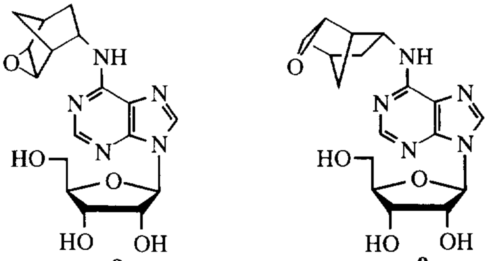
3a **3b**

R: 9-Benzylpurin-6-yl

Fig. 1. Selected correlations from the NOESY spectra of compounds **3a** and **3b**.

The ^{1}H NMR resonances from the norbornene ring systems were determined from gradient selected HMQC (GS-HMQC)[8] and gradient selected COSY (GS-COSY)[9] NMR spectroscopy. The NOESY spectrum of the *endo* isomer **3a** showed correlations between the H-7_a and the H-2_{exo} and H-3_{exo} protons. The presence of a hydrogen in the 2_{exo}-position, proved that the purine ring was situated in the 2_{endo}-position. In the NOESY spectrum of the *exo* isomer **3b**, no correlation between the H-7_a and the hydrogen in the norbornene 2-position was observed.

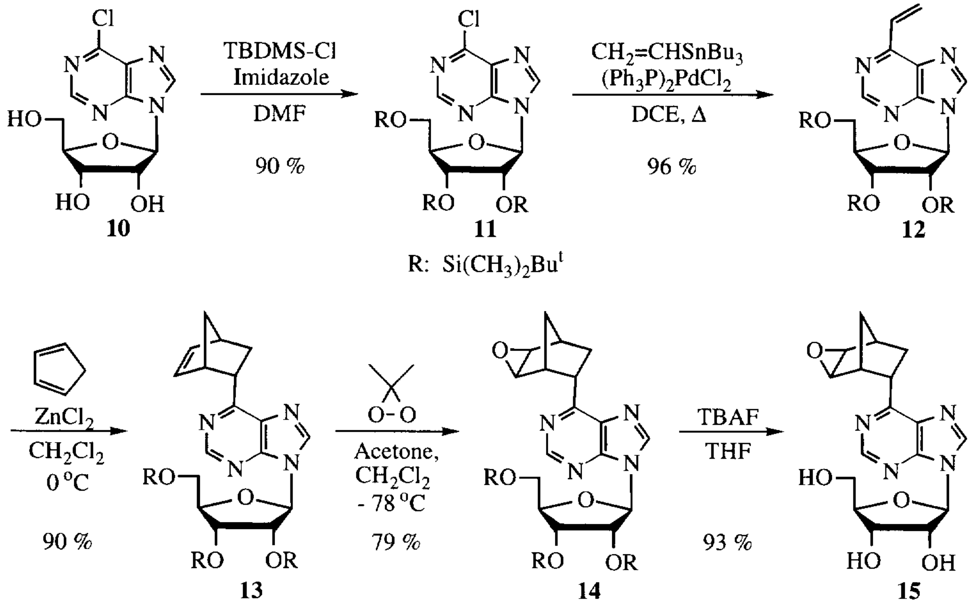
The epoxynorbornyladenosines **8** and **9** (Fig. 2) are recently shown to be potent agonists for the A_1 adenosine receptor.[10] We are now reporting the synthesis of an analogue of the *endo* norbornane derivative **8** lacking the NH-bridge between the purine and norbornane rings. Zinc chloride mediated Diels-Alder reaction of a 6-vinylpurine is the key-step in the synthesis.



8 **9**

Fig. 2. A_1 Adenosine receptor agonists.

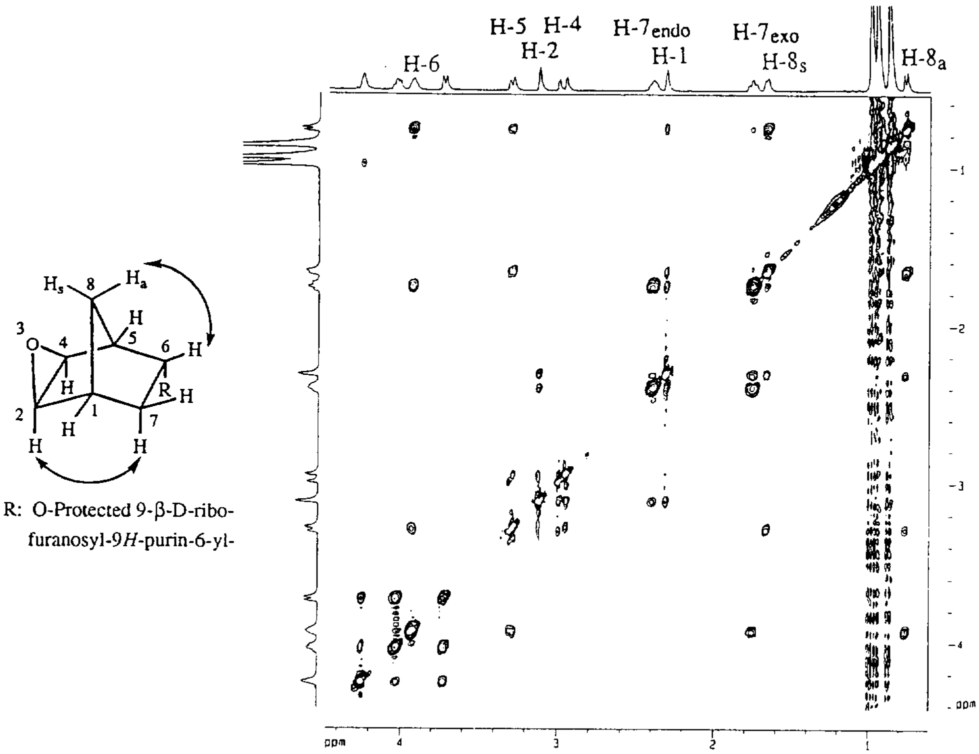
6-Chloropurine riboside **10** was *O*-silylated in order to minimize undesired complexation with Lewis acid in the Diels-Alder step and the nucleoside **11** was coupled with vinyl(tributyl)stannane to give the vinylpurine **12** in nearly quantitative yield (Scheme 2). The co-product Bu_3SnCl formed in the Stille reaction, was converted to the readily removable tin fluoride when the crude product was treated with potassium fluoride in methanol for a short time. Prolonged exposure to the KF-solution resulted however, in partial desilylation of the protected nucleoside. Smooth $ZnCl_2$ mediated cycloaddition with cyclopentadiene afforded the *endo* norbornenylpurine **13** in 90 % yield. ^{1}H NMR and TLC analysis of the crude product indicated that traces of the *exo* isomer was formed, but the amount was too small for isolation. The vinyl nucleoside **12** appears to be somewhat more reactive towards cyclopentadiene than the corresponding *N*-benzylated compound **1** (*vide supra*). Epoxidation of norbornenes employing dimethyldioxirane (DMD)[11] is reported to be *exo* selective.[12] Even though DMD oxidize azines to the corresponding *N*-oxides[12a,13] and purines are generally prone to oxidation of *N*-1 or *N*-3 by various oxidation agents[10a,14] including DMD,[15] we found that the norbornene **13** was epoxidized cleanly at -78 °C. The ^{13}C NMR spectra of the product **14** indicated that the expected *exo* epoxide was formed,[16] and the stereochemistry was once more confirmed by NOESY spectroscopy. On the other hand, DMD mediated epoxidation at 0 °C as reported for the synthesis of the epoxides **8** and **9**,[10] resulted in the formation of a small amount of an unidentified product, together with the desired product **14**. The target compound **15** was isolated after cleavage of the silyl protecting groups with TBAF.



Scheme 2

Again NOESY spectroscopy was employed to unambiguously determine the stereochemistry of the products **13** - **15** after previous assignment of the ^1H NMR resonances by GS-HMQC and GS-COSY NMR spectroscopy. The NOESY spectrum of compound **14** in Fig. 3 shows correlation between the H-8_a and H-6 demonstrating that the *endo* isomer **13** was formed in the Diels-Alder step. No correlation between the H-8_s and H-2 or H-4 is observed as would be expected for the isomeric *endo* epoxide, and the definite proof for the stereochemistry of the epoxide is the correlation between H-2 and H-7_{endo} which shows that both hydrogens are situated on the same side of the norbornane ring.

The results described herein demonstrate that 6-vinylpurines readily participate in stereoselective Diels-Alder cycloadditions in the presence of a Lewis acid, and open up a new route to purine derivatives carrying a variety of alkyl substituents in the 6-position.



R: O-Protected 9-β-D-ribofuranosyl-9*H*-purin-6-yl-

Fig. 3. NOESY spectrum of compound **14**.

EXPERIMENTAL

The ^1H 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 with 5 mm QNP, BBO and TXI probes. The ^{13}C NMR spectra were recorded at 125, 75 or 50 MHz using instruments mentioned above with 5 mm QNP or BBO probes. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane. The NOESY spectra were recorded at 500 MHz using the Bruker pulse program noesytp (phase sensitive, TPPI), the mixing time (d8) were optimized with the program t1irld (T1 inversion recovery pulse program). For the spectrum shown in Fig. 3 degassed benzene-d_6 was used as solvent and a mixing time (d8) of 1.7 s was chosen. The spectrum was processed with sine functions and zero filling in both dimensions. The GS-COSY[9] and GS-HMQC[8] spectra were recorded with the sweep optimized pulse programs cosygssw and inv4gssw under the Set and Run automation routine with the 5 mm triple resonance (^1H, ^{13}C, ^{15}N) inverse detection probe (TXI) equipped with a actively shielded z-gradient coil. The GS-HMQC spectra were recorded in 18 minutes employing garp decoupling of the ^{13}C atoms using sine window functions in both processing dimensions. All NMR acquisition and processing were performed with the program Xwinnmr 1.1. Mass spectra were recorded with a VG Prospec instrument at 70 eV ionizing voltage and are presented as *m/z*

(% rel. int.). Isobutane was used for chemical ionization (C.I.). 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). DCE and dichloromethane were distilled from CaH_2, DMF from BaO and THF from Na/benzophenone. Zinc chloride was dried at 200 °C under high vacuum for 3-4 h. Zinc bromide was dried at 125 °C under high vacuum for 5-6 h, weighed out and dissolved in dry THF to give a 1 M solution which was stored under N_2. An 0.1 M solution of dimethyldioxirane in acetone was prepared and titrated as described in the literature.[17] Tetrabutylammonium fluoride trihydrate was dried by azeotropic distillation with benzene and the residue was dissolved in dry THF to give a 0.5 M solution. All other reagents were commercially available and used as received.

*9-Benzyl-6-ethenyl-9*H*-purine (1).* A 1 M solution of anhydrous zinc bromide in THF (3.25 ml, 3.25 mmol) was added dropwise to a stirred solution of ethenylmagnesium bromide (3.25 mmol) in THF (9 ml) under N_2 at - 78 °C. After 1 h, 9-benzyl-6-iodo-9*H*-purine[18] (841 mg, 2.50 mmol) and tetrakis(triphenylphosphine)-palladium(0) (29 mg, 0.025 mmol) in THF (10 ml) were added and the resulting mixture heated at 50 °C for 10 min and cooled. Sat. aq. ammonium chloride (20 ml) was subsequently added and the mixture extracted with EtOAc (4 x 50 ml). The combined organic extracts were washed with brine (2 x 50 ml), dried ($MgSO_4$) and evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel eluting with EtOAc/hexane (2:1); yield 441 mg (75 %) clourless powdery crystals. M.p. 83-84 °C (Lit.[1c] 76-79 °C). ^{1}H NMR (CD_2Cl_2, 200 MHz): δ 5.43 (s, 2 H, CH_2N), 5.91 (dd, *J* 2.1 and 10.7 Hz, 1 H, $=CH_2$), 7.03 (dd, *J* 2.1 and 17.6 Hz, 1 H, $=CH_2$), 7.2 - 7.3 (m, 6 H, Ph and CH=), 8.07 (s, 1 H, H-8), 8.88 (s, 1 H, H-2). MS (E.I.): 236 (78, M^+), 91 (100).

endo *9-Benzyl-6-(bicyclo[2.2.1.]hept-5-en-2-yl)-9*H*-purine (3a) and* exo *9-benzyl-6-(bicyclo[2.2.1.]hept-5-en-2-yl)-9*H*-purine (3b).* Freshly cracked cyclopentadiene (420 mg, 6.35 mmol) was added dropwise to a stirring mixture of 9-benzyl-6-ethenyl-9*H*-purine **1** (300 mg, 1.27 mmol) and dry zinc chloride (865 mg, 6.35 mmol) in dichloromethane (13 ml) at 0 °C under N_2. The resulting mixture was stirred for 2.5 h and evaporated *in vacuo*. The products were separated by flash chromatography on silica gel eluting with EtOAc/hexane (1:1). The *exo* isomer eluted first.

endo *9-Benzyl-6-(bicyclo[2.2.1.]hept-5-en-2-yl)-9*H*-purine (3a).* Yield 356 mg (93 %) colourless crystals. M.p. 89-92 °C. (Found: C, 75.84; H, 5.75. Calc. for $C_{19}H_{18}N_4$: C, 75.47; H, 6.00 %). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.48 (m, 2 H, H-7'), 1.98 (m, 1 H, H-3'$_{endo}$), 2.12 (m, 1 H, H-3'$_{exo}$), 2.94 (m, 1 H, H-4'), 3.54 (m, 1 H, H-1'), 4.03 (m, 1 H, H-2'), 5.33 (s, 2 H, CH_2N), 5.61 (dd, 1 H, H-6', *J* 2.9 Hz and 5.6 Hz), 6.16 (dd, 1 H, H-5', *J* 3.1 Hz and 5.6 Hz), 7.2 - 7.3 (m, 5 H, Ph), 7.91 (s, 1 H, H-8), 8.78 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 30.3 (C-3'), 42.5 (C-2'), 43.4 (C-4'), 47.6 (CH_2N), 48.4 (C-1'), 50.7 (C-7'), 128.7, 128.9 and 129.5 (CH in Ph), 132.9 (C-6'), 133.1 (C-5), 135.7 (C in Ph), 137.8 (C-5'), 143.3 (C-8), 150.8 (C-4), 152.5 (C-2), 164.8 (C-6). MS (E.I.): 302 (82, M^+), 287 (19), 275 (8), 261 (9), 248 (9), 235 (49), 224 (38), 211 (16), 183 (13), 91 (100).

exo *9-Benzyl-6-(bicyclo[2.2.1.]hept-5-en-2-yl)-9*H*-purine (3b).* Yield 3 mg (1 %) colourless crystals. M.p. 72-75 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.33 (m, 1 H, H-7'$_s$), 1.55 (m, 1 H, H-3'$_{endo}$) 1.90 (m, 1 H, H-7'$_a$), 2.35 (m, 1 H, H-3'$_{exo}$), 2.99 (m, 1 H, H-4'), 3.05 (m, 1 H, H-1'), 3.44 (m, 1 H, H-2'), 5.36 (s, 2 H, CH_2N), 6.19

(m, 1 H, H-5'), 6.26 (m, 1 H, H-6'), 7.2 - 7.3 (m, 5 H, Ph), 7.92 (s, 1 H, H-8), 8.85 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 31.6 (C-3'), 41.6 (C-2'), 42.6 (C-4'), 46.3 (C-7'), 47.6 (CH_2N), 49.2 (C-1'), 128.2, 128.9 and 129.5 (CH in Ph), 132.8 (C-5), 135.5 (C in Ph), 137.2 (C-6'), 138.8 (C-5'), 143.5 (C-8), 150.8 (C-4), 152.8 (C-2), 166.1 (C-6). MS (E.I.): 302 (17, M^+), 261 (7), 237 (94), 224 (11), 211 (12), 159 (7), 145 (7), 91 (100), 77 (6), 66 (35). Hrms: Found 302.1529, calcd. for $C_{19}H_{18}N_4$: 302.1531.

endo *9-Benzyl-6-(bicyclo[2.2.2]oct-5-en-2-yl)-9H-purine (5).* 1,3-Cyclohexadiene (0.25 ml, 2.62 mmol) was added dropwise to a stirring mixture of 9-benzyl-6-ethenyl-9*H*-purine **1** (122 mg, 0.52 mmol) and dry zinc chloride (352 mg, 2.58 mmol) in dichloroethane (6 ml) under N_2. The resulting mixture was stirred for 36 h at ambient temperature and evaporated *in vacuo*. The product was isolated by flash chromatography on silica gel eluting with EtOAc/hexane (2:1); yield 81 mg (50 %) colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.38 (m, 2 H, H-8' and H-7'), 1.68 (m, 1 H, H-8'), 1.91 (m, 1 H, H-7'), 2.05 (m, 1 H, H-3'$_{exo}$), 2.17 (m, 1 H, H-3'$_{endo}$), 2.75 (m, 1 H, H-4'), 3.08 (m, 1 H, H-1'), 3.91 (m, 1 H, H-2'$_{exo}$), 5.42 (s, 2 H, CH_2N), 6.12 (m, 1 H, H-6'), 6.44 (m, 1 H, H-5'), 7.3 - 7.4 (m, 5 H, Ph), 7.99 (s, 1 H, H-8), 8.93 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.2 (C-8'), 26.9 (C-7'), 29.8 (C-4'), 31.5 (C-3'), 34.9 (C-1'), 40.4 (C-2'), 47.1 (CH_2N), 127.7, 128.4 and 129.0 (CH in Ph), 131.7 (C-6'), 132.1 (C-5), 134.6 (C-5'), 135.2 (C in Ph), 142.9 (C-8), 150.4 (C-4), 152.3 (C-2), 165.6 (C-6). MS (E.I.): 316 (50, M^+), 301 (3), 287 (10), 261 (21), 249 (10), 238 (48), 225 (11), 210 (7), 147 (20), 91 (100). Hrms: Found 316.1696, calcd. for $C_{20}H_{20}N_4$: 316.1688.

9-Benzyl-6-(3,4-dimethylcyclohex-3-en-1-yl)-9H-purine (7). 2,3-Dimethyl-1,3-butadiene (0.425 ml, 3.76 mmol) was added dropwise to a stirring mixture of 9-benzyl-6-ethenyl-9*H*-purine **1** (178 mg, 0.75 mmol) and dry zinc chloride (513 mg, 3.75 mmol) in dichloroethane (7.5 ml) under N_2. The resulting mixture was stirred for 72 h at ambient temperature and evaporated *in vacuo*. The product was isolated by flash chromatography on silica gel eluting with EtOAc/hexane (1:1); yield 137 mg (57 %) colourless crystals. M.p. 97-99 °C. (Found: C, 75.70; H, 6.95. Calc. for $C_{20}H_{22}N_4$: C, 75.44; H, 6.96 %). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.67 (s, 6 H, CH_3), 2.08 (m, 3 H, H-5' and H-6'), 2.25 (m, 2 H, H-2' and H-6'), 2.65 (m, 1 H, H-2'), 3.68 (m, 1 H, H-1'), 5.44 (s, 2 H, CH_2N), 7.3 - 7.4 (m, 5 H, Ph), 8.00 (s, 1 H, H-8), 8.95 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 18.7 and 18.9 (CH_3), 28.0 (C-5'), 31.8 (C-6'), 36.1 (C-2'), 38.6 (C-1'), 47.0 (CH_2N), 124.5 , 125.0 (C-3'/C-4'), 127.7, 128.3 and 128.9 (CH in Ph), 131.7 (C-5), 135.1 (C in Ph), 143.1 (C-8), 150.7 (C-4), 152.5 (C-2), 166.0 (C-6). MS (E.I.): 318 (100, M^+), 303 (38), 289 (10), 275 (7), 263 (3), 237 (8), 224 (81), 211 (12), 199 (9), 91 (94).

*6-Chloro-2',3',5'-tris-O-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-9H-purine (11).*[19] A mixture of 6-chloropurine riboside **10** (256 mg, 0.95 mmol), imidazole (778 mg, 11.4 mmol) and *tert*-butyldimethylsilyl chloride (862 mg, 5.72 mmol) in DMF (2 ml) was stirred at ambient temperature under N_2 for 18 h, before EtOAc (25 ml) and sat. aq. NH_4Cl (10 ml) were added. The phases were separated and the aqueous phase extracted with EtOAc (10 ml). The combined organic layers were washed with water (10 ml), dried ($MgSO_4$) and evaporated *in vacuo*, and the product was isolated by flash chromatography on silica gel eluting with EtOAc/hexane (1:7); yield 539 mg (90 %) colourless crystals. M.p. 147-149 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ -0.27, -0.05, 0.07, 0.08, 0.12 and 0.13 (s, 3 H, $SiCH_3$), 0.77, 0.91 and 0.94 (s, 9 H, Bu^t), 3.78 (dd, 1 H, H-5', *J* 2.4 and 11.5 Hz), 4.00 (dd, 1 H, H-5', *J* 3.5 and 11.5 Hz), 4.14 (m, 1 H, H-4'), 4.28 (t, 1 H, H-3', *J* 4.0 Hz), 4.57 (t, 1 H, H-2', *J* 4.6 Hz), 6.10 (d, 1 H, H-1', *J* 4.9 Hz), 8.52 (s, 1 H, H-8), 8.72 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ -5.41, -5.37, -5.1, -4.8, -4.7 and -4.4 ($SiCH_3$), 17.8, 18.0 and 18.5 (C in Bu^t), 25.6, 25.8 and 26.1 (CH_3 in Bu^t), 62.3 (C-5'), 71.8 (C-3'), 76.3 (C-2'), 85.7 (C-4'), 88.5 (C-1'), 132.1 (C-5), 144.0 (C-8), 151.0 (C-4), 151.5 (C-6), 151.9 (C-2). MS (C.I.): 629 (68, *M*+1), 571 (15), 343 (100), 285 (24), 211 (31), 171 (24), 155 (66), 133 (95), 121 (38), 89 (15).

*6-Ethenyl-2',3',5'-tris-O-(*tert-*butyldimethylsilyl)-9-β-D-ribofuranosyl-9*H*-purine (12).* A mixture of 6-chloro-2',3',5'-tris-O-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-9*H*-purine **11** (637 mg, 1.0 mmol), bis(triphenylphosphine)palladium(II) chloride (36 mg, 0.05 mmol) and tributyl(vinyl)tin (0.415 ml, 1.42 mmol) in dichloroethane (20 ml) was heated at reflux under N_2 for 2.5 h and cooled. The reaction mixture was evaporated *in vacuo* and a sat. solution of potassium fluoride in methanol (20 ml) was added to the residue. The resulting mixture was stirred at ambient temperature for 15 min 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 on silica gel eluting with EtOAc/hexane 1:7; yield 604 mg (96 %) colourless oil. (Found: C, 58.60; H, 9.14. Calc. for $C_{30}H_{56}N_4O_4Si_3$: C, 58.02; H, 9.09 %). ^{1}H NMR ($CDCl_3$, 500 MHz): δ -0.28, -0.07, 0.08, 0.09, 0.11 and 0.12 (s, 3 H, $SiCH_3$), 0.76, 0.92 and 0.93 (s, 9 H, Bu^t), 3.78 (m, 1 H, H-5'), 4.01 (m, 1 H, H-5'), 4.12 (m, 1 H, H-4'), 4.31 (t, 1 H, H-3', *J* 3.9 Hz), 4.67 (t, 1 H, H-2', *J* 4.7 Hz), 5.92 (dd, 1 H, CH_2=, *J* 10.6 and 1.0 Hz), 6.10 (d, 1 H, H-1', *J* 5.2 Hz), 7.00 (dd, 1 H, CH_2=, *J* 17.6 and 0.9 Hz), 7.11 (dd, 1 H, CH=, *J* 17.5 and 11.0 Hz), 8.40 (s, 1 H, H-8), 8.87 (s, 1 H, H-2). ^{13}C NMR ($CDCl_3$, 75 MHz): δ -5.38, -5.38, -5.1, -4.71, -4.67 and -4.4 ($SiCH_3$), 17.8, 18.1 and 18.5 (C in Bu^t), 25.6, 25.8 and 26.1 (CH_3 in Bu^t), 62.5 (C-5'), 72.0 (C-3'), 75.8 (C-2'), 85.6 (C-4'), 88.2 (C-1'), 126.1 (CH_2=), 131.6 (C-5), 131.9 (CH=), 143.5 (C-8), 151.9 (C-4), 152.3 (C-2), 153.5 (C-6). MS (C.I.): 621 (100, *M*+1), 563 (26), 417 (6), 394 (36), 359 (6), 343 (23), 171 (5), 147 (7), 133 (5), 89 (6).

endo *6-(Bicyclo[2.2.1.]hept-5-en-2-yl)-2',3',5'-tris-O-(*tert-*butyldimethylsilyl)-9-β-D-ribofuranosyl-9*H*-purine (13).* Freshly cracked cyclopentadiene (150 mg, 2.27 mmol) was added dropwise to a stirring mixture of 6-ethenyl-2',3',5'-tris-O-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-9*H*-purine **12** (248 mg, 0.40 mmol) and dry zinc chloride (110 mg, 0.81 mmol) in dichloromethane (8 ml) at 0 °C under N_2. The resulting mixture was stirred for 2 h and evaporated *in vacuo*. The product was isolated by flash chromatography on silica gel eluting with EtOAc/hexane (1:9); yield 248 mg (90 %) colourless oil. (Found: C, 61.53; H, 9.28. Calc. for $C_{35}H_{62}N_4O_4Si_3$: C, 61.18; H, 9.09 %). ^{1}H NMR (C_6D_6, 500 MHz): δ -0.14 , -0.01, 0.06, 0.07, 0.10 and 0.11 (s, 3 H, $SiCH_3$), 0.88, 0.95 and 0.99 (s, 9 H, Bu^t), 1.37 (m, 1 H, H-7''$_a$), 1.51 (m, 1 H, H-7''$_s$), 2.10 (m, 1 H, H-3''$_{exo}$), 2.45 (m, 1 H, H-3''$_{endo}$), 2.82 (m, 1 H, H-4''), 3.72 (m, 1 H, H-5'), 3.92 (m, 1 H, H-1''), 4.04 (m, 1 H, H-5'), 4.19 (m, 1 H, H-2''$_{exo}$), 4.24 (m, 1 H, H-4'), 4.55 (m, 1 H, H-3'), 5.02 (m, 1 H, H-2'), 5.79 (m, 1 H, H-6''), 6.17 (m, 2 H, H-5'', H-1'), 8.20 (d, 1 H, H-8, purin), 8.95 (s, 1 H, H-2, purin). ^{13}C NMR (C_6D_6, 75 MHz): δ -5.34, -5.29, -4.8, 4.61, -4.55 and -4.2 ($SiCH_3$), 18.1, 18.3 and 18.6 (C in Bu^t), 26.0, 26.1 and 26.2 (CH_3 in Bu^t), 29.7 (C-3''), 42.8 (C-2''), 43.4 (C-4''), 48.1 (C-1''), 50.4 (C-7''), 62.4 (C-5'), 72.1 (C-3'), 75.5 (C-2'), 85.2 (C-4'), 89.3 (C-1'), 132.9 (C-6''), 134.4 (C-5), 137.3 (C-5''), 142.7 (C-8), 150.6 (C-4), 152.0 (C-2), 164.7 (C-6). MS (E.I.): 686 (8, M^+), 605 (3), 563 (80), 417 (7), 303 (14), 285 (14), 261 (23), 147 (22), 89 (42), 73 (100).

*6-[(1α,2β,4β,5α,6β)-3-Oxatricyclo[3.2.1.0^{2,4}]oct-6-yl]-2',3',5'-tris-O-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-9*H*-purine (14).* A 0.1 M solution of dimethyldioxirane in acetone[17] (30 ml, 3.0 mmol) was added slowly to a stirred solution of *endo* 6-(bicyclo[2.2.1.]hept-5-en-2-yl)-2',3',5'-tris-O-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-9*H*-purine **13** (559 mg, 0.81 mmol) in dichloromethane (15 ml) under N_2 at -78 °C, and the resulting mixture was stirred for 5.5 h while reaching -20 °C. The reaction mixture was evaporated *in vacuo* and the product isolated by flash chromatography on silica gel eluting with EtOAc/hexane/Et_3N (10:50:1); yield 454 mg (79 %) colourless crystals. M.p. 48-50 °C. (Found: C, 59.81; H, 8.83. Calc. for $C_{35}H_{62}N_4O_5Si_3$: C, 59.79 ; H, 8.89 %). ^{1}H NMR (C_6D_6, 500 MHz): δ -0.13, 0.01, 0.07, 0.08, 0.09 and 0.11 (s, 3 H, $SiCH_3$), 0.77 (m, 1 H, H-8''$_a$), 0.88, 0.96 and 1.00 (s, 9 H, Bu^t), 1.68 (m, 1 H, H-8''$_s$), 1.76 (m, 1 H, H-7''$_{exo}$), 2.31 (m, 1 H, H-1''), 2.39 (m, 1 H, H-7''$_{endo}$), 2.99 (m, 1 H, H-4''$_{endo}$), 3.13 (m, 1 H, H-2''$_{endo}$), 3.31 (m, 1 H, H-5''), 3.74 (m, 1 H, H-5'), 3.94 (m, 1 H, H-6''$_{exo}$), 4.04 (m, 1 H, H-5'), 4.27 (m, 1 H, H-4'), 4.55 (m, 1 H, H-3'), 5.01 (m, 1 H, H-2'), 6.22 (m, 1 H, H-1'), 8.24 (d, 1 H, H-8, purin), 8.94 (d, 1 H, H-2, purin). ^{13}C NMR (C_6D_6, 75 MHz): δ -5.4, -5.3, -4.8, -4.62, -4.56 and -4.2 ($SiCH_3$), 18.1, 18.3 and 18.6 (C in Bu^t), 25.9, 26.1 and 26.2 (CH_3 in Bu^t), 28.5 (C-7'', C-8''), 37.9 (C-1''), 42.4 (C-5''), 44.4 (C-6''), 49.5 (C-4''), 51.3 (C-2''), 62.5 (C-5'), 72.1 (C-3'), 75.7 (C-2'), 85.3 (C-4'), 89.2 (C-1'), 134.4 (C-5), 143.0 (C-8), 150.8 (C-4), 151.9 (C-2), 163.0 (C-6). MS (E.I.): 702 (36, M^+), 687 (5), 645 (72), 417 (44), 285 (49), 226 (10), 211 (24), 147 (79), 89 (37), 73 (100).

*6-[(1α,2β,4β,5α,6β)-3-Oxatricyclo[3.2.1.0^{2,4}]oct-6-yl]-9-β-D-ribofuranosyl-9*H*-purine (15).* A 0.5 M solution of TBAF i THF (5.0 ml, 2.5 mmol) was added dropwise to a stirred solution of 6-[(1α,2β,4β,5α,6β)-3-oxatricyclo[3.2.1.0^{2,4}]oct-6-yl]-2',3',5'-tris-O-(*tert*-butyldimethylsilyl)-9-β-D-ribofuranosyl-9*H*-purine **14** (394 mg, 0.56 mmol) in THF (4 ml) at ambient temperature under N_2. After stirring for 11 h, the reaction mixture was evaporated *in vacuo* and the product was isolated by flash chromatography on silica gel eluting with EtOAc/MeOH/conc. NH_3(aq) (60:40:1); yield 187 mg (93 %) colourless crystals. M.p. 106-108 °C (dec.). (Found: C, 54.04; H, 5.80. Calc. for $C_{17}H_{20}N_4O_5$ x 1 H_2O: C, 53.96; H, 5.86%). ^{1}H NMR (DMSO-d_6, 500 MHz): δ 1.43 (d, 1 H, H in norbornane, J 10.1 Hz), 1.90 (m, 3 H, H in norbornane), 1.97 (d, 1 H, H in norbornane, *J* 10.1 Hz), 2.27 (m, 2 H, H in norbornane), 3.55 (m, 1 H, H-5'), 3.67 (m, 1 H, H-5'), 3.86 (m, 1 H, H in norbornane), 3.96 (m, 1 H, H-4'), 4.16 (m, 1 H, H-3'), 4.57 (m, 1 H, H-2'), 4.81 (d, 1 H, H in norbornane, *J* 3.9 Hz), 5.14 (t, 1 H, OH, C-5', *J* 5.6 Hz), 5.23 (d, 1 H, OH, C-3', *J* 4.9 Hz), 5.50 (d, 1 H, OH, C-2', *J* 6.0 Hz), 5.98 (d, 1 H, H-1', *J* 5.7 Hz), 8.64 (s, 1 H, H-8), 8.67 (s, 1 H, H-2). ^{13}C NMR (DMSO-d_6, 75 MHz): δ 26.0 (CH in norbornane), 30.1 (CH in norbornane), 30.2 (CH_2 in norbornane), 31.1 (CH in norbornane), 32.0 (CH_2 in norbornane), 36.5 (CH in norbornane), 61.3 (C-5'), 70.3 (C-3'), 73.7 (C-2'), 74.9, (CH in norbornane), 85.6 (C-4'), 87.5 (C-1'), 131.0 (C-5), 143.1 (C-8), 150.0 (C-4), 151.4 (C-2), 161.8 (C-6). MS (E.I.): 360 (2, M^+), 343 (2), 303 (3), 228 (20), 211 (48), 199 (52), 185 (34), 171 (100), 158 (15). Hrms: Found 360.1436, calcd. for $C_{17}H_{20}N_4O_5$: 360.1434.

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REFERENCES

1. (a) Gogoll, A.; Gundersen, L.-L.; Rise, F.; Valli, M. *Heterocycles* **1993**, *36*, 231-235; (b) Gundersen, L.-L. *Tetrahedron Lett.* **1994**, *35*, 3155-3158; (c) Gundersen, L.-L.; Bakkestuen, A. K.; Aasen, A. J.; Øverås, H.; Rise, F. *Tetrahedron* **1994**, *50*, 9743-9756; (d) Gundersen, L.-L.; Langli, G.; Rise, F. *Tetrahedron Lett.* **1995**, *36*, 1945-1948; (e) Andresen, G.; Gundersen, L.-L.; Lundmark, M.; Rise, F.; Sundell, S. *Tetrahedron* **1995**, *51*, 3655-3664; (f) Gundersen, L.-L. *Acta Chem. Scand.* **1996**, *50*, 58-63; (g) Langli, G.; Gundersen, L.-L.; Rise, F. *Tetrahedron* **1996**, *52*, 5625-5638; (h) Gundersen, L.-L. *Acta Chem. Scand.* **1996**, *50*, 462-465; (i) Andresen, G.; Gundersen, L.-L.; Rise, F. *Tetrahedron* **1996**, *52*, 12979-12992.
2. Øverås, A. T.; Gundersen, L.-L.; Rise, F. Manuscript under preparation.
3. See for instance: (a) March, J. *Advanced Organic Chemistry*, 4th ed; Wiley & Sons: New York, 1992; pp. 839-852; (b) Oppolzer, W. In *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I. Eds.; Pergamon Press: Oxford, 1991; vol 5; chap. 4.1.
4. For recent references, see for instance: (a) Désaubry, L.; Bourguignon, J.-J. *Tetrahedron Lett.* **1995**, *36*, 7875-7876; (b) Dvoráková, H.; Dvorák, D.; Holy, A. *Tetrahedron Lett.* **1996**, *37*, 1285-1288.
5. (a) Fisher, J.; Gradwell, M. J. *Magn. Reson. Chem.* **1992**, *30*, 338-346; (b) Fisher, J.; Gradwell, M. J. *Magn. Reson. Chem.* **1991**, *29*, 1068-1069.
6. Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, *93*, 741-761, and references therein.
7. Sauer, J.; Lang, D.; Mielert, A. *Angew. Chem.* **1962**, *74*, 352-353.
8. Rinaldi, P. L.; Keifer, P. *J. Magn. Reson., Ser. A* **1994**, *108*, 259-262.
9. (a) Barker, P.; Freeman, R. *J. Magn. Reson.* **1985**, *64*, 334-338; (b) Hurd, R. E. *J. Magn. Reson.* **1990**, *87*, 422-428; (c) Brereton, I. M.; Crozier, S.; Field, J.; Doddrell, D. M. *J. Magn. Reson.* **1991**, *93*, 54-62; (d) von Kienlin, M.; Moonen, C. T. W.; van der Thorn, A.; van Zijl, P. C. M. *J. Magn. Reson.* **1991**, *93*, 423-429.
10. (a) Scammells, P. J.; Baker, S. P.; Bellardinelli, L.; Olsson, R. A.; Russels, R. A.; Wright, D. M. J. *Tetrahedron* **1996**, *52*, 4735-4744; (b) Scammells, P. J.; Bellardinelli, L.; Olsson, R. A.; Russel, R. A.; Knevitt, S. A. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 811-814.
11. For reviews on dioxirane mediated oxidations, see for instance: (a) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187-1201; (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205-211; (c) Adam, W.; Hadjiarapoglou, L. P. *Top. Curr. Chem.* **1993**, *164*, 45-62.
12. (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847-2853; (b) Murray, R. W.; Pillay, M. K.; Jeyaraman, R. *J. Org. Chem.* **1988**, *53*, 3007-3011.
13. Adam, W.; Golsch, D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 737-739.
14. Shaw, G. In *Comprehensive Heterocyclic Chemistry*, Katritzky, A. R.; Rees, C. W. Eds.; Pergamon Press: Oxford, 1984; vol 2; pp. 539-40, and references therein.
15. Adam, W.; Briviba, K.; Duschek, F.; Golsch, D.; Kiefer, W.; Sies, H. *J. Chem. Soc., Chem. Commun.* **1995**, 1831-1862.
16. Zimmermann, D.; Reisse, J.; Coste, J.; Plénat, F.; Christol, H. *Org. Magn. Reson.* **1974**, *6*, 492-493.
17. Adam, W. A.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.
18. McKenzie, T. C.; Epstein J. W. *J. Org. Chem.* **1982**, *47*, 4881-4884.
19. Bergstrom, D. E.; Reday, P. A. *Tetrahedron Lett.* **1982**, *23*, 4191-4194.

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