Pergamon

Tetrahedron, Vol. 52, No. 40, pp. 12979-12992, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00779-X

Regiochemistry in Addition of Grignard Reagents to *N,N'*-Dibenzylated 2-Purinones

Geir Andresen, Lise-Lotte Gundersen, and Frode Rise

Department of Chemistry, University of Oslo, P. O. Box 1033, Blindern, *N*-0315 Oslo, Norway

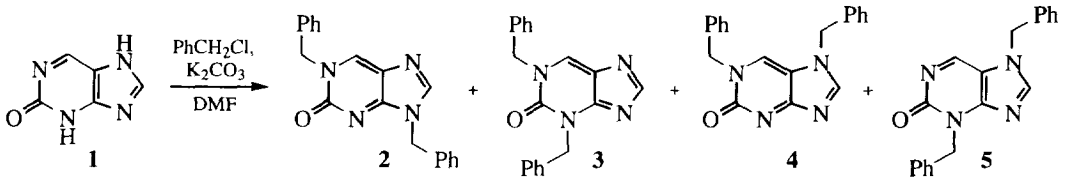
Abstract: 1,3-, 1,7-,1,9- and 3,7-dibenzylpurin-2-one form stable adducts when reacted with Grignard reagents. Reaction took place in the purine 6- or 8-position, and substantial differences in the regiochemical outcome of the reactions were found among the isomers. Several new classes of purinones are described here for the first time. The structure elucidations of the products were accomplished by HETCOR, COLOC, GA-HMQC and GA-HMBC NMR spectroscopy. Copyright © 1996 Elsevier Science Ltd

6-Amino-2-purinone (isoguanine) and derivatives are found in nature and several of these purinones and synthetic analogues are associated with interesting medicinal or other biological properties.[1,2] 6-Alkylamino-2-purinones have recently been isolated from both higher plants and microorganisms,[2] and identified as cytokinins (plant growth stimulators).[3] This kind of biological activity is also found among synthetic 6-alkylamino-2-purinones.[4] Several potent cytokinins containing a 6-alkyl or 6-alkenyl substituent, instead of an alkylamino group, have been prepared.[5] 6-Alkyl or 6-alkenyl-2-purinones may possess cytokinin activity, or other fascinating biological effects. However, synthetic methods for *C* - *C* bond formation in the 2-purinone 6-position are still rather limited.

2-Purinone is a highly polarized compound,[6] and it has been known for quite some time that this purine forms adducts with nucleophiles like barbituric acid[7] and potassium hydrogen sulfite.[8] These results indicated to us that carbon substituents may be introduced to the 2-purinone ring system by addition of organometallic reagents followed by rearomatization of the heterocyclic adduct, if desired. We have previously demonstrated the electrophilicity of 2-purinone; tribenzylated hydroxy, alkoxy and alkylthio adducts were formed when the purinone was alkylated with an excess of benzyl bromide in the presence of oxygen or sulfur nucleophiles,[9] and recently we reported regioselective addition of Grignard reagents to a 2-oxopurinium salt.[10] The only study of adduct formation on dialkylated 2-purinones involves addition of organometallic reagents in the 6- or 8-position to 3,7-methylated 2-purinones.[11] Calculations on 2-purinone itself show dramatic differences in dipole moment and electronic distribution among the tautomers,[6] which indicate substantial differences in reactivity between the *N,N'*-dialkylated isomers. This area is, however, unexplored. We are currently studying carbon - carbon bond formations in purines mediated by organometallic reagents,[10,12] and we report herein our results from addition of Grignard reagents to *N,N'*-dibenzylated 2-purinones, and the synthesis of several new classes of 6- and 8-substituted 2-purinones.

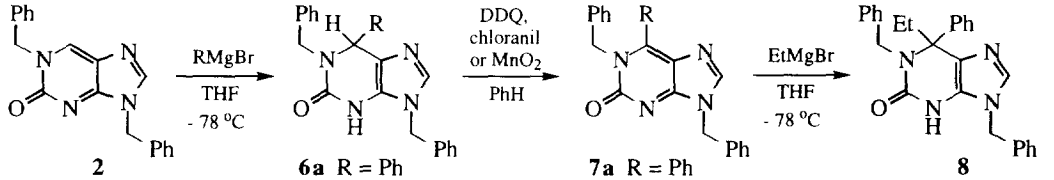
In this study, we chose to work with *N*-benzylated purinones. The benzyl group was selected due to the NMR diagnostic value of the benzylic AB resonance quartets in the addition products,[9,10] as well as to ensure sufficient lipophilicity for chromatographic handling of the products. 2-Purinone **1** was alkylated with 2 equiv. of benzyl chloride or benzyl bromide employing potassium carbonate as base (Scheme 1). Among the 5 possible *N,N'*-dialkylated isomers, **2**, **3**, **4** and **5** could be isolated after careful chromatography. The substitution patterns of the isomers were revealed by long range H-C correlated NMR spectroscopy (COLOC).

This two dimensional technique proved superior to long range INEPT. The structure of compound **2** was previously misassigned to 1,3-dibenzyl-2-purinone by the latter method, since the extremely narrow resonances of the two benzylic CH_2 protons prevented selective irradiation.[9]



Scheme 1

Grignard reagents may, in theory, attack the dibenzylated 2-purinones in the 6- or 8-position. Calculations of the N(1)-N(9)H tautomer of the parent 2-purinone indicate that the 6-position is somewhat more π-electron deficient than the 8-position.[6,13] We found that the 1,9-dibenzylated 2-purinone **2** reacted readily with Grignard reagents at -78 °C. In all cases examined, addition took place in the 6-position exclusively, giving the adducts **6** in high yields (Scheme 2, Table 1). COLOC NMR as well as gradient accelerated HMBC NMR (*vide infra*) were used for structure elucidation of the products **6**, and all other new compounds reported herein.



Scheme 2

Table 1. Additions of Grignard Reagents to the purinone **2** and rearomatization of the adducts **6**.

R-	Yield (%) **6** and **8**	Yield (%) **7**		
		DDQ	Chloranil	MnO_2
Ph-	88 (**6a**)	67 (**7a**)	50 (**7a**)	69 (**7a**)
Ph-C≡C-	85 (**6b**)	60 (**7b**)	70 (**7b**)	50 (**7b**)
CH_3-	93 (**6c**)	68 (**7c**)	81 (**7b**)	n.r.
$(CH_3)_2CH$-	93 (**6d**)	52 (**7d**)	55 (**7d**)	n.r.
CH_3CH_2-	81 (**8**)			

Attempts to add organolithium reagents to the purinone **2** resulted only in a complex mixture. This might be rationalized by lithiation of the purine **2** followed by decomposition. Another possible explanation may be that partial debenzylation took place. Debenzylation employing organolithium reagents has recently been

reported for *N*-benzylated indole derivatives,[14] and we suspect debenzylation to occur when lithiation of other *N*-benzylated purine derivatives is attempted.[15]

Rearomatization of the adducts **6a** - **6d** was achieved by smooth DDQ mediated oxidation to give the compounds **7a** - **7d**. Chloranil also affected these oxidations, but activated MnO_2, on the other hand, failed to oxidize the alkyl adducts **6c** and **6d**.

The 6-phenylpurinone **7a** was subjected to a second Grignard addition. In spite of the steric hindrance, ethylmagnesium bromide added cleanly in the 6-position to give the product **8** in 81 % yield. As an example of the combined power of the structure elucidation techniques GA-HMQC[16] (gradient accelerated heteronuclear multiple quantum correlation) ("inverse HETCOR") and GA-HMBC[17] (gradient accelerated heteronuclear multiple bond correlation) ("inverse COLOC") employed for structure elucidation of several of the structures reported in this paper, the spectra of structure **8** is included here, Fig. 1. and Fig. 2. The spectra in Fig. 1 and 2. are recorded on a 5 mg sample in 0.4 ml solvent in 18 and 30 minutes respectively. The spectrum in Fig 1. gives the direct C-H correlations and the correlations in Fig. 2 show long range C-H correlations up to 4 bond distances. Most noteworthy are the correlations from both of the N(1)C*H*$_2$ AB doublets and the correlations from both multiplets originating from the methylene protons in the ethyl group to C-6 at 70.3 ppm - thus confirming the structure of **8**. Another interesting feature of the HMBC spectrum is the N(3)H correlation to C-5 at 119 ppm. Furthermore it could be noted that initially the GA-HMBC of compound **17** (*vide infra*) showed no correlations from the low field benzylic CH_2 protons. The ^{1}H resonance of this CH_2 was very broad, possibly indicating a situation slightly above coalesence between different conformations. However raising the temperature from 300 to 330 K and moving into the fast exchange area, sharpened the ^{1}H resonance and all the expected long range correlations showed up in the GA-HMBC spectrum.

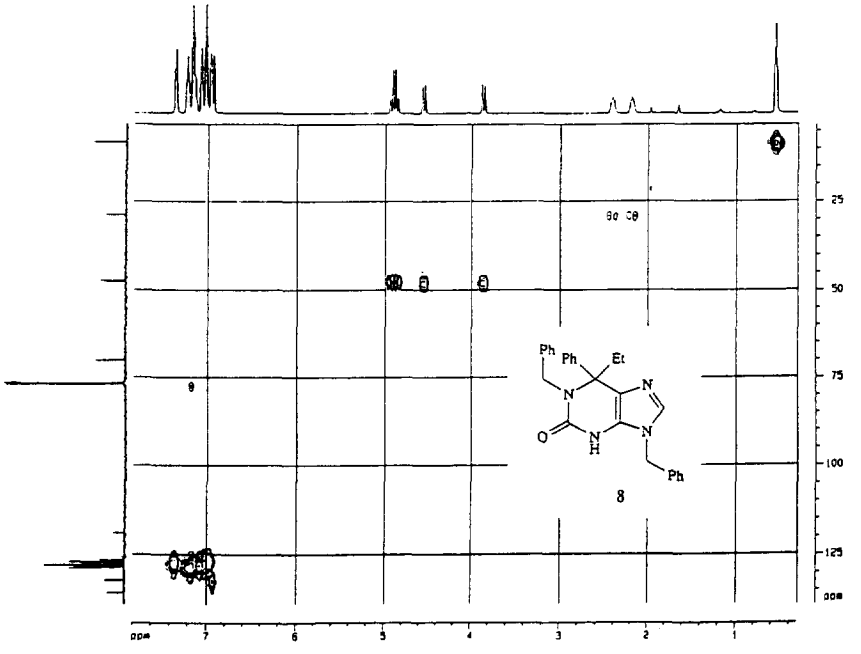


Fig. 1

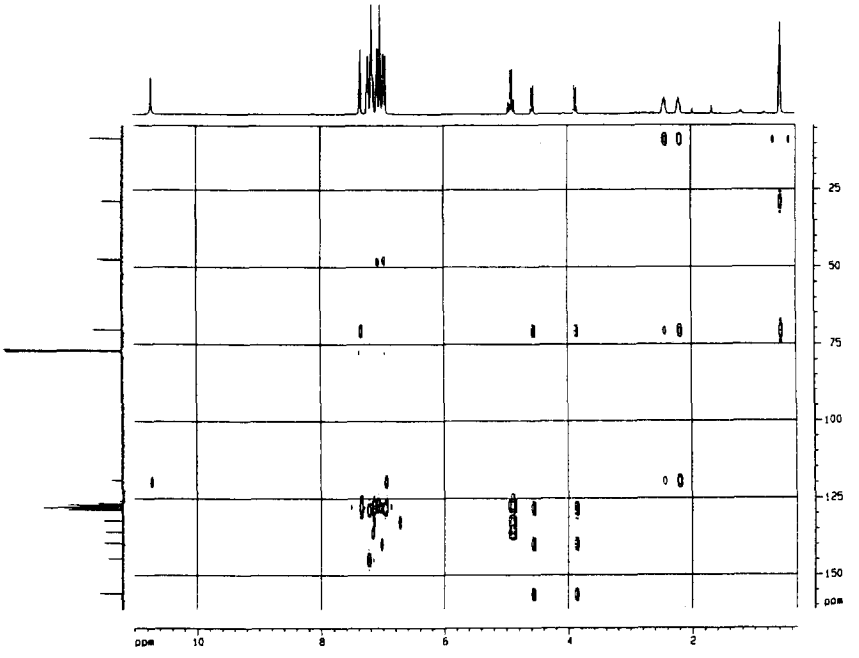
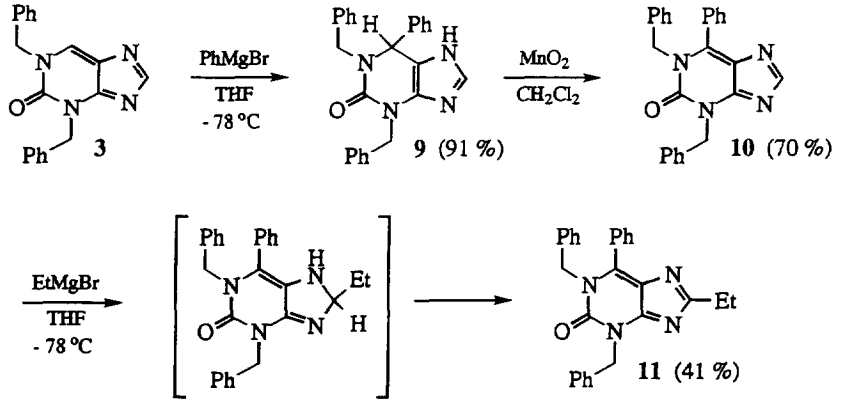


Fig. 2

The pseudoazulene structure of the 1,3-dibenzylated purinone **3** indicated that this compound was prone to nucleophilic attack in the 6-membered ring,[18] and phenylmagnesium bromide added cleanly in the 6-position of the purinone **3** to give the compound **9** (Scheme 3). The isolated yield, 91 %, was comparable to the yield of the 1,9-dibenzylated phenyl adduct **6a**.

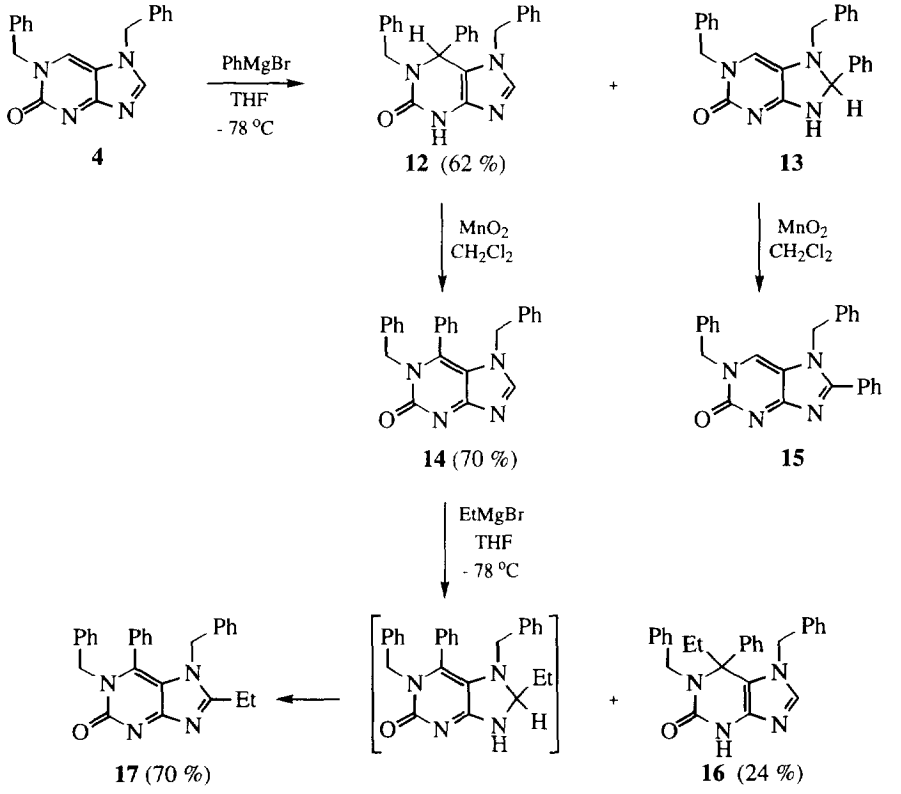


Scheme 3

Rearomatization of the adduct **9** was again achieved with DDQ, but chromatographic separation of the polar purinone **10** and residual $DDQH_2$ was tedious. The compound **10** was easily isolated in high yields when the adduct **9** was oxidized with MnO_2 in a polar solvent, DMSO or dichloromethane. When the 6-phenylpurinone **10** was treated with ethylmagnesium bromide, addition took place only in the 8-position. The

adduct was completely oxidized during work-up and chromatography, and the aromatic product **11** was isolated in 41 % yield. This reaction demonstrates the large reactivity differences between dibenzylated purinones. The 1,9-dibenzylated 6-phenylpurinone **7a** adds Grignard reagents selectively in the 6-position, whereas the 1,3-dibenzylated isomer **10** reacts exclusively at C-8.

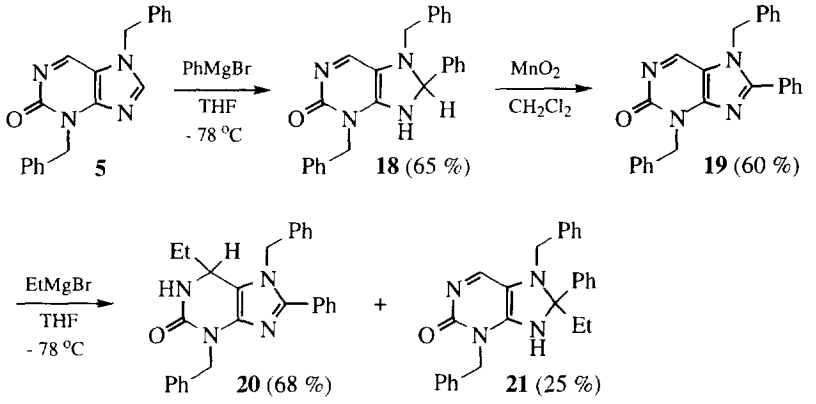
When the 1,7-dibenzylated purinone isomer **4** was reacted with phenylmagnesium bromide, a ca. 17:3 mixture of the 6-phenyl adduct **12** and the 8-adduct **13** was formed as judged by the ^{1}H NMR spectrum of the crude product (Scheme 4). This lack of selectivity might be attributed to the larger steric hindrance in the 6-position of the 1,7-dibenzylated purinone **4,** as well as to electronic factors. The 1,7-dibenzylated purinones are the only compounds examined in this study, where one would expect relatively large differences in steric hindrance between the 6- and 8-position. The product **12** was isolated in 62 % yield, and was easily oxidized to the compound **14**, when treated with MnO_2 in dichloromethane. The minor isomer, the 8-phenyl adduct **13**, could not be isolated in pure form, but oxidation of a mixture of **12** and **13**, gave the rearomatized isomers **14** and **15**, which were easily separated on silica gel. NMR structure elucidation of the compound **15** confirmed that the phenyl substituent was situated at C-8.



Scheme 4

1,7-Dibenzyl-6-phenyl-2-purinone **14** was reacted further with ethylmagnesium bromide. In this second Grignard addition, the major product was the 8-ethyl adduct, which was rearomatized to the compound **17** during work-up and purification. This oxidation was, however, somewhat slower than the corresponding oxidation of the 1,3-dibenzylated 8-ethyl adduct which gave the product **11**. In spite of the above discussed steric hindrance, some addition of the nucleophile to the 6-position also took place, and the compound **16** could be isolated in 24 % yield.

Finally the reactivity of the 3,7-benzylated 2-purinone **5** was examined. Due to the large difficulties in separation of this minor dibenzylated product from the 1,3-substituted isomer **3**, phenylmagnesium bromide was added to a mixture of the isomers **2** and **5**. The only adduct formed from the compound **5**, was the 8-phenyl adduct **18**, which was isolated in 65 % yield (Scheme 5). This result was surprising. Not only is the 3,7-dibenzylated isomer the only isomer studied, which preferably adds Grignard reagents in the 8-position when the 6-position is not substituted, but it is also reported previously that the corresponding 3,7-dimethylated analogoue of **5** prefers to react with Grignard reagents at C-6.[11] However, the reactions described in the literature were carried out in refluxing THF. We found that all the isomers studied readily reacted with Grignard reagents at low temperatures, and it has so far been outside the scope of this study to investigate the temperature dependency of the regiochemical outcome in the additions. The reaction of phenylmagnesium bromide at the purine 8-position of the compound **5** is also somewhat unexpected from an electronic point of view. Electron distribution calculations of the N(3)-N(7)H tautomer of the parent 2-purinone **1** shows that the 6-position is substantially more π-electron deficient than the 8-position.[6] The adduct **18** was easily oxidized to the compound **19**, when treated with activated MnO_2, and a second Grignard addition to **19** gave a ca 7:2 mixture of the regioisomers **20** and **21**.



Scheme 5

In summary, this paper reports the preparation and chemistry of the first examples of 16 new classes of 6- and / or 8-alkylated 2-purinones (compounds **6** - **21**). 1,9-, 1,3-, 1,7- and 3,7-Dibenzylpurin-2-one do form adducts when reacted with Grignard reagents and the reaction takes place either in the purine 6- or 8-position. Most of the adducts were stable enough for isolation, but some of the 8-adducts were prone to rearomatization during work-up and purification, in principle effecting a nucleophilic aromatic substitution of the hydrogen in the 8-position. All adducts were readily oxidized with DDQ or MnO_2. Substantial differences in the regiochemical outcome of the reactions were found among the isomers, and these differences made it possible to to introduce substituents by addition in the purine 6- or 8-position selectively, depending on the positions of the *N*-alkyl groups.

The synthetic strategy reported here, may be regarded as complementary to coupling of halopurines with organometallic reagents, a technique commonly used for *C* - *C* bond formation in the purine 6- or 8-position.[12,19] It is especially noteworthy that alkyl substituents, and even secondary alkyls, can easily be introduced. Moderate yields of the desired alkylpurines are often obtained in coupling reactions involving alkyl metal reagents, even though promising results are achieved employing organozinc reagents.[12b,c]

EXPERIMENTAL

The ^1H NMR spectra were recorded at 500 MHz with a Bruker Avance DRX 500, at 300 MHz with a Bruker Avance DPX 300 or at 200 MHz with a Varian Gemini 200 or a Bruker Avance DPX 200 instrument. The ^{13}C NMR spectra were recorded at 125, 75 or 50 MHz using the above mentioned instruments. $^1H\{^{13}C\}$ XHORR and COLOC experiments optimized for 10 Hz coupling constants, were performed on the Bruker DPX spectrometers. Gradient accelerated (z gradient) $^1H\{^{13}C\}$ HMBC (optimized for 10 Hz coupling constants) and gradient accelerated $^1H\{^{13}C\}$ HMQC spectra were recorded with the Bruker Avance DRX 500 spectrometer equipped with either a 5 mm triple resonance (^1H, ^{13}C, ^{15}N) inverse detection probe (TXI) or a 2.5 mm broad band inverse probe (BBI) equipped with actively shielded z-gradient coils, using the Bruker pulse programs; inv4gslplrndsw (GA-HMBC) and inv4gssw (GA-HMQC). The inverse gradient accelerated experiments were performed with 2-10 mg of sample dissolved in 0.4 ml or 0.1 ml of solvent. The F2 (^1H) acquisition parameters for the 10 Hz optimized GA-HMBC spectra includes 8 scans per increment, a time domain of 2048 complex points with an acquisition time of 0.23 seconds and an automatically adjusted ^1H sweep width. The F1 acquisition parameters include 128 increments with an automatically adjusted sweep width. The total acquisition time is approximately 30 minutes. The spectra in Fig. 1 and Fig. 2 were processed with a sine window function in both dimensions. The GA-HMQC spectra were recorded in 18 minutes with a time domain of 1024 complex points, employing garp decoupling of the ^{13}C atoms with 128 increments in the F1 dimension and sine window functions in both processing dimensions. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane. Mass spectra were recorded on a VG Prospec instrument at 70 eV ionizing voltage 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). THF was distilled from sodium / benzophenone, DMF from barium oxide and dichloromethane from calcium hydride. Benzene was dried over sodium wire. The Grignard reagents in Sure/Seal™ bottles, were purchased from Aldrich, Steinheim, Germany. 1,3-Dihydro-2*H*-purin-2-one[10,20] and activated manganese dioxide[21] were prepared according to the literature. All other reagents were commercially available and used as received.

*Benzylation of 1,3-dihydro-2*H*-purin-2-one* **1**. Benzyl chloride (0.92 ml, 8 mmol) was added to a mixture of 1,3-dihydro-2*H*-purin-2-one (544 mg, 4 mmol) and potassium carbonate (1.66 g, 12 mmol) in dry DMF (50 ml). After stirring for 48 h at ambient temperature under N_2, the reaction mixture was filtered and evaporated *in vacuo*, and the products were isolated by flash chromatography on silica gel eluting with MeCN, followed by mixtures of MeCN and EtOH, starting with MeCN-EtOH (10:1) and gradually increasing the amount of EtOH to MeCN-EtOH (2:1), and finally EtOH (100 %) to give compound **2** (464 mg, 37 %), a mixture of compound **3** and compound **5** and compound **4** (114 mg, 9 %). The compounds **3** and **5** were separated by flash chromatography eluting with MeCN followed by MeCN-EtOH (10:1) and MeCN-EtOH (6:1) to give *compound* **3** (350 mg, 26 %), and the compound **5** was purified further by chromatography eluting with EtOAc-EtOH (14:1).

*1,9-Dibenzyl-1,9-dihydro-2*H*-purinone* **2** was obtained as colourless powdery crystals, mp 226-228 °C (EtOAc-hexane). (Found: C, 72.27; H, 4.94, $C_{19}H_{16}N_4O$ requires C, 72.14; H, 5.10). ^1H NMR (300 MHz, DMSO-d_6): δ 8.94 (s, 1 H, H-6), 8.31 (s, 1 H, H-8), 7.4-7.2 (m, 10 H, Ph), 5.17 [s, 2 H, N(1)CH_2], 5.15 [s, 2 H, N(9)CH_2]. ^{13}C NMR (75 MHz, DMSO-d_6): δ 158.8 (C-4), 154.4 (C-2), 148.0 (C-8), 141.2 (C-6), 136.8 and 136.3 (C in Ph), 128.6-127.3 (CH in Ph), 122.9 (C-5), 53.7 [N(1)CH_2], 45.4 [N(9)CH_2]. MS (E.I.): 316 (76, M^+), 226 (16), 225 (100), 197 (4), 170 (4), 116 (6), 91 (72), 71 (4), 65 (14).

*1,3-Dibenzyl-1,3-dihydro-2*H*-purinone* **3** was obtained as colourless powdery crystals, mp 182-184 °C (EtOAc-hexane). ^1H NMR (300 MHz, DMSO-d_6): δ 8.96 (s, 1 H, H-6), 8.05 (s, 1 H, H-8), 7.4-7.2 (m, 10 H, Ph), 5.34 [s, 2 H, N(3)CH_2], 5.23 [s, 2 H, N(1)CH_2]. ^{13}C NMR (75 MHz, DMSO-d_6): δ 162.3 (C-8), 160.7 (C-4), 148.3 (C-2), 138.6 (C-6), 135.9 and 135.5 (C in Ph), 128.5-127.5 (CH in Ph, C-5), 53.9 [N(1)CH_2], 47.8 [N(3)CH_2].

MS (E.I.): 316 (38, M^+), 277 (5), 225 (45), 211 (4), 197 (5), 183 (12), 169 (4), 155 (3), 128 (2), 116 (3), 91 (100). Hrms: Found 316.1336, $C_{19}H_{16}N_4O$ requires 316.1324. R_F 0.17, EtOAc-EtOH (10:1), SiO_2.

1,7-Dibenzyl-1,7-dihydro-2H-purinone **4**[10] was obtained as colourless powdery crystals, mp 227-229 °C (EtOAc-hexane). ^1H NMR (300 MHz, DMSO-d_6): δ 9.05 (s, 1 H, H-6), 8.76 (s, 1 H, H-8), 7.5-7.2 (m, 10 H, Ph), 5.37 [s, 2 H, N(7)CH_2], 5.15 [s, 2 H, N(1)CH_2]. ^{13}C NMR (75 MHz, DMSO-d_6): δ 168.9 (C-4), 155.3 (C-8), 155.2 (C-2), 136.8 and 135.6 (C in Ph), 134.6 (C-6), 128.8-127.7 (CH in Ph), 115.4 (C-5), 53.8 [N(1)CH_2], 48.7 [N(7)CH_2]. MS (E.I.): 316 (70, M^+), 287 (5), 225 (30), 211 (16), 197 (3), 184 (3), 169 (3), 155 (2), 116 (5), 91 (100).

3,7-Dibenzyl-3,7-dihydro-2H-purinone **5** was obtained as colourless powdery crystals, mp 147-148 °C (EtOAc-hexane). ^1H NMR (500 MHz, $CDCl_3$): δ 8.52 (s, 1 H, H-6), 7.80 (s, 1 H, H-8), 7.5-7.3 (m, 10 H, Ph), 5.48 [s, 2 H, N(7)CH_2], 5.33 [s, 2 H, N(3)CH_2]. ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.2, 154.4 (C-2/C-4), 148.7 (C-6), 143.6 (C-8), 136.1 and 133.2 (C in Ph), 129.6-125.9 (CH in Ph), 115.5 (C-5), 50.6 [N(3)CH_2], 47.0 [N(7)CH_2]. MS (E.I.): 317 (17, M+1), 316 (77, M^+), 287 (7), 225 (26), 211 (20), 210 (7), 197 (6), 92 (9), 91 (100), 65 (17). Hrms: Found 316.1326, $C_{19}H_{16}N_4O$ requires 316.1324. R_F 0.17, EtOAc-EtOH (10:1), SiO_2.

General procedure for the addition of Grignard reagents to dibenzylated purin-2-ones. A 1 M solution of the desired Grignard reagent in THF (3.15 ml, 3.15 mmol) was added dropwise over 20 min to a solution of dibenzylated purin-2-one (0.63 mmol) in dry THF (10 ml) at - 78 °C under N_2-atmosphere, and the resulting mixture was stirred for 18 h while gradually reaching ambient temperature. Sat. aq. ammonium chloride (20 ml) was added, the phases separated and the aqueous layer extracted with EtOAc (3 x 20 ml). The combined organic extracts were dried ($MgSO_4$), evaporated *in vacuo*, and each product was isolated by flash chromatography on silica gel.

1,9-Dibenzyl-6-phenyl-1,3,6,9-tetrahydro-2H-purin-2-one **6a**. The compound **6a** was prepared from 1,9-dibenzyl-1,9-dihydro-2*H*-purin-2-one **2** and phenylmagnesium bromide as described above. The crude product was purified by flash chromatography eluting with EtOAc, to give compound **6a** (217 mg, 88 %) as colourless powdery crystals, mp 180-182 °C (EtOAc-hexane). (Found: C, 76.00; H, 5.38, $C_{25}H_{22}N_4O$ requires C, 76.12; H, 5.62). ^1H NMR (200 MHz, CD_2Cl_2): δ 11.10 (br s, 1 H, NH), 7.4-7.1 (m, 15 H, Ph), 7.07 (s, 1 H, H-8), 5.60 (s, 1 H, H-6), 5.35 [AB-doublet, J 15.3 Hz, 1 H, N(1)CH_2], 5.10 [s, 2 H, N(9)CH_2], 3.72 [AB-doublet, J 15.3 Hz, 1 H, N(1)CH_2]. ^{13}C NMR (50 MHz, CD_2Cl_2): δ 154.8 (C-2), 141.5, 136.9 and 135.9 (C in Ph), 132.1 (C-8), 128.8-126.3 (CH in Ph), 126.3 (C-4), 116.6 (C-5), 61.3 (C-6), 48.0 (CH_2), 47.4 (CH_2). MS (E.I.): 394 (10, M^+), 354 (2), 317 (9), 303 (8), 260 (10), 253 (27), 237 (11), 167 (18), 149 (46), 91 (100).

1,9-Dibenzyl-6-phenylethynyl-1,3,6,9-tetrahydro-2H-purin-2-one **6b**. The compound **6b** was prepared from 1,9-dibenzyl-1,9-dihydro-2*H*-purin-2-one **2** and phenylethynylmagnesium bromide (generated *in situ* from ethylmagnesium bromide and phenylacetylene) as described above. The crude product was purified by flash chromatography eluting with $CHCl_3$ followed by $CHCl_3$-MeCN (3:1) and $CHCl_3$-MeCN (1:1) to give compound **6b** (224 mg, 85 %) as colourless powdery crystals, mp 220-223 °C (dec., EtOAc-hexane). ^1H NMR (200 MHz, $CDCl_3$): δ 10.60 (br s, 1 H, NH), 7.5-7.2 (m, 15 H, Ph), 7.15 (s, 1 H, H-8), 5.58 (s, 1 H, H-6), 5.40 [AB-doublet, J 15.1 Hz, 1 H, N(1)CH_2], 5.07 [s, 2 H, N(9)CH_2] and 4.38 [AB-doublet, J 15.1 Hz, 1 H, N(1)CH_2]. ^{13}C NMR (50 MHz, $CDCl_3$): δ 153.9 (C-2), 136.4, 135.3 and 132.2 (C in Ph), 131.9 (C-8), 129.0-126.8 (CH in Ph), 122.4 (C-4), 112.6 (C-5), 85.7 and 85.2 (C≡), 49.3 (C-6), 48.6 [N(1)CH_2], 47.7 [N(9)CH_2]. MS (E.I.): 418 (10, M^+), 394 (12), 341 (7), 325 (12), 316 (20), 301 (8), 284 (22), 225 (29), 116 (5), 102 (68), 91 (100). Hrms: Found 418.1793, $C_{27}H_{22}N_4O$ requires 418.1794. R_F 0.55, $CHCl_3$-MeCN (1:1), SiO_2.

1,9-Dibenzyl-6-methyl-1,3,6,9-tetrahydro-2H-purin-2-one **6c**. The compound **6c** was prepared from 1,9-dibenzyl-1,9-dihydro-2*H*-purin-2-one **2** and methylmagnesium bromide as described above. The crude product was purified by flash chromatography eluting with $CHCl_3$-MeCN (1:1), to give compound **6c** (196 mg, 93 %)

as colourless powdery crystals, mp 174-176 °C (EtOAc-pentane). (Found: C, 72.60; H, 5.93, $C_{20}H_{20}N_4O$ requires C, 72.26; H, 6.07). ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.53 (br s, 1 H, NH), 7.4-7.1 (m, 10 H, Ph), 7.08 (s, 1 H, H-8), 5.08 [AB-doublet, *J* 15.6 Hz, 1 H, N(1)CH_2], 4.99 [s, 2 H, N(9)CH_2], 4.67 (q, *J* 6.2 Hz, 1 H, H-6), 4.25 [AB-doublet, *J* 15.6 Hz, 1 H, N(1)CH_2], 1.46 (d, *J* 6.2 Hz, 3 H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 154.8 (C-2), 137.4 and 135.7 (C in Ph), 131.5 (C-8), 128.8-127.2 (CH in Ph), 126.1 (C-4), 117.4 (C-5), 53.4 (C-6), 48.2 [N(1)CH_2], 47.4 [N(9)CH_2], 21.3 (CH_3). MS (E.I.): 332 (10, M^+), 330 (13), 317 (78), 239 (10), 225 (8), 199 (8), 91 (100), 65 (9).

*1,9-Dibenzyl-6-isopropyl-1,3,6,9-tetrahydro-2*H*-purin-2-one* **6d**. The compound **6d** was prepared from 1,9-dibenzyl-1,9-dihydro-2*H*-purin-2-one **2** and isopropylmagnesium bromide as described above. The crude product was purified by flash chromatography eluting with $CHCl_3$ followed by $CHCl_3$-MeCN (4:1) and MeCN, to give *compound* **6d** (211 mg, 93 %) as colourless powdery crystals, mp 204-205 °C (EtOAc-hexane). (Found: C, 73.29; H, 6.69, $C_{22}H_{24}N_4O$ requires C, 73.30; H, 6.71). ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.54 (br s, 1 H, NH), 7.2-7.0 (m, 10 H, Ph), 6.97 (s, 1 H, H-8), 5.07 [AB-doublet, *J* 15.0 Hz, 1 H, N(1)CH_2], 4.94 [AB-doublet, *J* 16.5 Hz, 1 H, N(9)CH_2], 4.85 [AB-doublet, *J* 16.5 Hz, 1 H, N(9)CH_2], 4.38 (d, *J* 3.1 Hz, 1 H, H-6), 4.06 [AB-doublet, *J* 15.0 Hz, 1 H, N(1)CH_2], 2.1 (m, 1 H, CH), 0.96 (d, *J* 6.8 Hz, 3 H, CH_3), 0.66 (d, *J* 6.8 Hz, 3 H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.7 (C-2), 137.3 and 135.9 (C in Ph), 131.4 (C-8), 128.7-127.1 (CH in Ph and C-4), 113.9 (C-5), 62.2 (C-6), 48.9 [N(1)CH_2], 47.3 [N(9)CH_2], 31.5 (CH), 18.6 (CH_3), 15.3 (CH_3). MS (E.I.): 360 (30, M^+), 358 (58), 330 (16), 317 (74), 267 (3), 225 (11), 197 (2), 116 (2), 91 (100), 65 (11).

*6-Ethyl-1,9-dibenzyl-6-phenyl-1,3,6,9-tetrahydro-2*H*-purin-2-one* **8**. The compound **8** was prepared from 1,9-dibenzyl-6-phenyl-1,9-dihydro-2*H*-purin-2-one **7a** (150 mg, 0.38 mmol) and ethylmagnesium bromide as described above. The crude product was purified by flash chromatography eluting with EtOAc-hexane (3:1) followed by EtOAc, to give compound **8** (131 mg, 81 %) as colourless powdery crystals, mp 206-209 °C (EtOAc-hexane). (Found: C, 76.35; H, 6.11, $C_{27}H_{26}N_4O$ requires C, 76.75; H, 6.20). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 11.10 (br s, 1 H, NH), 7.6-7.0 (m, 16 H, Ph and H-8), 5.04 [AB-doublet, *J* 16.5 Hz, 1 H, N(9)CH_2], 4.97 [AB-doublet, *J* 16.5 Hz, 1 H, N(9)CH_2], 4.68 [AB-doublet, *J* 15.0 Hz, 1 H, N(1)CH_2], 4.01 [AB-doublet, *J* 15.0 Hz, 1 H, N(1)CH_2], 2.6-2.5 (m, 1 H, CH_2), 2.4-2.3 (m, 1 H, CH_2), 0.70 (t, *J* 7.0 Hz, 3 H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.1 (C-2), 144.5, 139.4 and 135.8 (C i Ph), 132.2 (C-8), 128.7-126.5 (CH in Ph and C-4), 119.0 (C-5), 70.3 (C-6), 47.7 [N(1)CH_2], 47.3 [N(9)CH_2], 28.7 (CH_2), 8.3 (CH_3). MS (E.I.): 422 (6, M^+), 393 (82), 345 (5), 315 (7), 288 (5), 224 (4), 198 (8), 91 (100), 65 (8).

*1,3-Dibenzyl-6-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one* **9**. The compound **9** was prepared from 1,3-dibenzyl-1,3-dihydro-2*H*-purin-2-one **3** (240 mg, 0.7 mmol) and phenylmagnesium bromide as described above. The crude product was purified by flash chromatography eluting with EtOAc-hexane (3:1), to give compound **9** (272 mg, 91 %) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.98 (br s, 1 H, NH), 7.6-7.0 (m, 15 H, Ph), 6.55 (s, 1 H, H-8), 5.33 (s, 1 H, H-6), 5.22 [AB-doublet, *J* 15.5 Hz, 1 H, N(1)CH_2], 4.98 [s, 2 H, N(3)CH_2], 3.44 [AB-doublet, *J* 15.5 Hz, 1 H, N(1)CH_2]. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.3 (C-2), 140.1, 138.3 and 136.8 (C in Ph), 136.3 (C-4), 132.8 (C-8), 128.8-126.9 (CH in Ph), 105.6 (C-5), 58.2 (C-6), 48.1 [N(1)CH_2], 45.5 [N(3)CH_2]. MS (E.I.): 394 (29, M^+), 317 (49), 303 (37), 260 (13), 198 (19), 170 (13), 128 (9), 91 (100), 77 (6), 65 (21). Hrms: Found 394.1792, $C_{25}H_{22}N_4O$ requires 394.1794. R_F 0.22, EtOAc-hexane (3:1), SiO_2.

*8-Ethyl-1,3-dibenzyl-1,3-dihydro-6-phenyl-*2H*-purin-2-one* **11**. The compound **11** was prepared from 1,3-dibenzyl-1,3-dihydro-6-phenyl-2*H*-purin-2-one **10** (35 mg, 0.089 mmol) and ethylmagnesium bromide as described above. The crude product was purified by flash chromatography eluting with EtOAc-EtOH (10:1) followed by EtOAc-EtOH (3:1) and EtOAc-EtOH (1:1), to give compound **11** (15 mg, 41 %) as a pale yellow

oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.7-6.9 (m, 15 H, Ph), 5.57 [s, 2 H, N(1)CH_2], 5.21 [s, 2 H, N(3)CH_2], 2.90 (q, *J* 7.5 Hz, 2 H, CH_2) and 1.39 (t, *J* 7.5 Hz, 3 H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 179.6 (C-8), 160.8 (C-4), 149.6 (C-2), 145.4, (C-6), 136.2 and 135.5 (C in Ph), 130.6-126.7 (CH in Ph, C in Ph, C-5), 50.6 [N(1)CH_2], 48.7 [N(3)CH_2], 26.2 (CH_2), 12.7 (CH_3). MS (E.I.): 421 (17, *M*+1), 420 (54, M^+), 419 (23), 343 (14), 330 (6), 329 (24), 286 (5), 92 (9), 91 (100), 65 (7). Hrms: Found 420.1951, $C_{27}H_{24}N_4O$ requires 420.1950. R_F 0.46, EtOAc-EtOH (10:1), SiO_2.

*1,7-Dibenzyl-6-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one* **12**. The compounds **12** and **13** were prepared from 1,7-dibenzyl-1,7-dihydro-2*H*-purin-2-one **4** (85 mg, 0.27 mmol) and phenylmagnesium bromide as described above. The products were separated by flash chromatography eluting with MeCN-EtOH (6:1) followed by MeCN-EtOH (4:1), to give the title compound **12** (66 mg, 62 %) and a mixture of compounds **12** and **13** (19 mg), which were oxidized to compounds **14** and **15** (*vide infra*).
The compound **12** was obtained as colourless powdery crystals, mp 239-240 °C (EtOAc-hexane). (Found: C, 76.10; H, 5.63, $C_{25}H_{22}N_4O$ requires C, 76.12; H, 5.62). ^{1}H NMR (DMSO-d_6, 300 MHz): δ 9.61 (br s, 1 H, NH), 7.44 (s, 1 H, H-8), 7.4-7.0 (m, 15 H, Ph), 5.20 (s, 1 H, H-6), 5.03 [AB-doublet, *J* 14.9 Hz, 1 H, N(1)CH_2], 4.98 [AB-doublet, *J* 15.4 Hz, 1 H, N(7)CH_2], 4.45 [AB-doublet, *J* 15.4 Hz, 1 H, N(7)-CH_2], 3.44 [AB-doublet, *J* 14.9 Hz, 1 H, N(1)CH_2]. ^{13}C NMR (DMSO-d_6, 75 MHz): δ 153.1 (C-2), 141.2 (C-4), 137.8 and 137.5 (C i Ph), 136.9 (C-8), 135.9 (C in Ph), 129.5-127.0 (CH in Ph), 106.8 (C-5), 58.0 (C-6), 48.4 [N(7)CH_2], 47.2 [N(1)CH_2]. MS (E.I.): 394 (58, M^+), 375 (2), 354 (8), 327 (2), 317 (100), 303 (29), 234 (2), 198 (7), 91 (51).

*6-Ethyl-1,7-dibenzyl-6-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one* **16** *and 8-ethyl-1,7-dibenzyl-1,7-dihydro-6-phenyl-2*H*-purin-2-one* **17**. The compounds **16** and **17** were prepared from 1,7-dibenzyl-6-phenyl-1,7-dihydro-2*H*-purin-2-one **14** (44 mg, 0.11 mmol) and ethylmagnesium bromide as described above. The isomers were separated by flash chromatography eluting with EtOAc-EtOH (10:1) followed by EtOAc-EtOH (3:1) and EtOAc-EtOH (1:1), to give **16** (11 mg, 24 %) and **17** (32 mg, 70 %).
*6-Ethyl-1,7-dibenzyl-6-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one* **16** was obtained as colourless powdery crystals, mp 179-180 °C (EtOAc-hexane). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.4-6.8 (m, 16 H, Ph and H-8), 4.44 [AB-doublet, *J* 15.6 Hz, 1 H, N(7)CH_2], 4.34 [AB-doublet, *J* 15.5 Hz, 1 H, N(1)CH_2], 4.12 [AB-doublet, *J* 15.5 Hz, 1 H, N(1)CH_2], 3.99 [AB-doublet, *J* 15.6 Hz, 1 H, N(7)CH_2], 2.2 (m, 1 H, CH_2), 1.3 (m, 1 H, CH_2) and 0.64 (t, *J* 7.1 Hz, 3 H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 154.3 (C-2), 142.3 and 139.6 (C in Ph), 138.3 (C-4), 135.7 (C-8), 135.1 (C in Ph), 128.7-126.4 (CH in Ph), 108.3 (C-5), 67.8, (C-6), 48.9 [N(7)CH_2], 46.5 [N(1)CH_2], 28.7 (CH_2), 7.71 (CH_3). MS (E.I.): 422 (4, M^+), 395 (4), 394 (29), 393 (100), 289 (4), 198 (4), 92 (8), 91 (92), 77 (3), 65 (6). Hrms: Found 422.2118, $C_{27}H_{26}N_4O$ requires 422.2107. R_F 0.24, EtOAc-EtOH (9:1), SiO_2.
*8-Ethyl-1,7-dibenzyl-1,7-dihydro-6-phenyl-2*H*-purin-2-one* **17** was obtained as colourless powdery crystals, mp 208-211 °C (EtOAc-hexane). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.4-6.4 (m, 15 H, Ph), 5.12 [s, 2 H, N(1)CH_2], 4.57 [s, 2 H, N(7)CH_2], 2.75 (q, *J* 7.4 Hz, 2 H, CH_2), 1.40 (t, *J* 7.4, Hz 3 H, CH_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.5 (C-8), 167.5, 157.1, 143.6 (C-2/C-4/C-6), 136.9, 130.5 and 134.9 (C in Ph), 128.7-124.6 (CH in Ph), 116.1 (C-5), 50.1 [N(1)CH_2], 47.2 [N(7)CH_2], 21.4 (CH_2), 11.1 (CH_3). MS (E.I.): 420 (44, M^+), 329 (23) 281 (9), 120 (9), 92 (22), 91 (100), 89 (13), 65 (24). Hrms: Found 420.1926, $C_{27}H_{24}N_4O$ requires 420.1950. R_F 0.17, EtOAc-EtOH (9:1), SiO_2.

*3,7-Dibenzyl-8-phenyl-1,3,7,8-tetrahydro-2*H*-purin-2-one* **18**. The compound **18** was prepared from a mixture of 3,7-dibenzyl-3,7-dihydro-2*H*-purin-2-one **5** (25 mg, 0.078 mmol), 1,3-dibenzyl-1,3-dihydro-2*H*-purin-2-one and phenylmagnesium bromide as described above. The crude product was purified by flash chromatography eluting with hexane followed by EtOAc-hexane (1:1), EtOAc-hexane (2:1) and EtOAc-hexane (3:1), to give compound **18** (20 mg, 65 %) as a colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.5-7.1 (m, 15 H, Ph), 6.23 (s, 1 H, H-6), 5.10 [s, 2 H, N(3)CH_2], 5.1 (m, 1 H, H-8), 4.15 [AB-doublet, *J* 15.5, 1 H, N(7)CH_2], 3.92 [AB-

doublet, *J* 15.5, 1 H, N(7)CH_2]. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 157.8 (C-4), 150.7 (C-2), 139.6, 136.8 and 136.6 (C in Ph), 127.4-129.0 (CH in Ph and C-5), 96.3 (C-6), 92.0 (C-8), 49.9 [N(7)CH_2], 45.1 [N(3)CH_2]. MS (E.I.): 395 (9, *M*+1), 394 (34, M^+), 393 (10), 392 (7), 318 (7), 317 (26), 303 (16), 92 (10), 91 (100), 65 (10). Hrms: Found 394.1788, $C_{25}H_{22}N_4O$ requires 394.1794. R_F 0.36, EtOAc-hexane (3:1), SiO_2.

*6-Ethyl-3,7-dibenzyl-8-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one* **20** and *8-ethyl-3,7-dibenzyl-8-phenyl-1,3,7,8-tetrahydro-2*H*-purin-2-one* **21**. The compounds **20** and **21** were prepared from 3,7-dibenzyl-8-phenyl-3,7-dihydro-2*H*-purin-2-one **19** (11 mg, 0.03 mmol) and ethylmagnesium bromide as described above. The isomers were separated by flash chromatography eluting with EtOAc followed EtOH, to give **20** (8 mg, 68 %) and **21** (3 mg, 25 %).

*6-Ethyl-3,7-dibenzyl-8-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one* **20** was obtained as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.7-6.8 (m, 15 H, Ph), 5.33 [AB-doublet, *J* 15.5 Hz, 1 H, N(3)CH_2], 5.16 [AB-doublet, *J* 16.7 Hz, 1 H, N(7)CH_2], 4.87 [AB-doublet, *J* 16.7 Hz, 1 H, N(7)CH_2], 4.24 (m, 1 H, H-6), 3.97 [AB-doublet, *J* 15.5 Hz, 1 H, N(3)CH_2], 1.9-1.8 (m, 1 H, CH_2), 1.3-1.2 (m, 1 H, CH_2), 0.78 (t, *J* 7.4 Hz, 3 H, CH_3). MS (E.I.): 422 (8, M^+), 395 (5), 394 (31), 393 (100), 301 (3), 132 (3), 104 (4), 92 (8), 91 (92), 65 (7). Hrms: Found 422.2099, $C_{27}H_{26}N_4O$ requires 422.2107.

*8-Ethyl-3,7-dibenzyl-8-phenyl-1,3,7,8-tetrahydro-2*H*-purin-2-one* **21** was obtained as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.6-6.8 (m, 16 H, Ph and H-6), 4.45 [AB-doublet, *J* 15.4 Hz, 1 H, N(7)CH_2], 4.33 [AB-doublet, *J* 15.4 Hz, 1 H, N(3)CH_2], 4.18 [AB-doublet, *J* 15.4 Hz, 1 H, N(3)CH_2], 4.03 [AB-doublet, *J* 15.4 Hz, 1 H, N(7)CH_2], 2.3-2.2 (m, 1 H, CH_2), 1.6-1.5 (m, 1 H, CH_2), 0.65 (t, *J* 7.1 Hz, 3 H, CH_3). MS (E.I.): 422 (7, M^+), 421 (6), 394 (29), 393 (100), 289 (4), 198 (4), 132 (4), 92 (8), 91 (100), 65 (7).

General procedure for the oxidation of the purin-2-one adducts with DDQ. A solution of the desired purin-2-one adduct and DDQ (1.1 equiv.) in dry benzene was stirred at ambient temperature. The precipitated hydroquinone was filtered off and triturated with benzene. The combined solutions were evaporated *in vacuo*, and each product isolated by flash chromatography on silica gel.

*1,9-Dibenzyl-1,9-dihydro-6-phenyl-2*H*-purin-2-one* **7a**. The compound **7a** was prepared from 1,9-dibenzyl-6-phenyl-1,3,6,9-tetrahydro-2*H*-purin-2-one **6a** (62 mg, 0.15 mmol) and DDQ (37 mg, 0.16 mmol) in benzene (25 ml) as described above. The crude product was purified by flash chromatography eluting with $CHCl_3$-MeCN (4:1), to give compound **7a** (39 mg, 67 %) as colourless powdery crystals, mp 184-186 °C. (Found: C, 76.00; H, 5.02, $C_{25}H_{20}N_4O$ requires C, 76.51; H, 5.14). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.75 (s, 1 H, H-8), 7.6-7.0 (m, 15 H, Ph), 5.37 (s, 2 H, CH_2), 5.27 (s, 2 H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 158.7 (C-2), 156.3 (C-4), 152.7 (C-6), 146.7 (C-8), 137.5, 135.8 and 129.8 (C in Ph), 130.9-127.0 (CH in Ph), 123.7 (C-5), 50.9 (CH_2), 46.8 (CH_2). MS (E.I.): 392 (55, M^+), 391 (100), 350 (3), 315 (4), 301 (62), 287 (5), 258 (5), 223 (3), 198 (3), 91 (100).

*1,9-Dibenzyl-1,9-dihydro-6-phenylethynyl-2*H*-purin-2-one* **7b**. The compound was prepared from 1,9-dibenzyl-6-phenylethynyl-1,3,6,9-tetrahydro-2*H*-purin-2-one **6b** (62 mg, 0.15 mmol) and DDQ (37 mg, 0.16 mmol) in benzene (25 ml) as described above and the reaction time was 46 h. The crude product was purified by flash chromatography eluting with $CHCl_3$-MeCN (4:1), to give compound **7b** (37 mg, 60 %) as colourless powdery crystals, mp 169-171 °C. (Found: C, 77.77; H, 4.95, $C_{27}H_{20}N_4O$ requires C, 77.49; H, 5.30). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.68 (s, 1 H, H-8), 7.5-7.1 (m, 15 H, Ph), 5.54 (s, 2 H, CH_2), 5.11 (s, 2 H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$): δ 158.2 (C-2), 155.9 (C-4), 146.8 (C-8), 136.2 (C in Ph), 134.8 (C-6), 133.5 (C in Ph), 132.4-127.7 (CH in Ph), 126.1 (C-5), 119.9 (C in Ph), 107.9 and 79.0 (C≡), 51.7 (CH_2), 46.5 (CH_2). MS (E.I.): 416 (20, M^+), 391 (51), 358 (8), 325 (26), 301 (100), 235 (11), 198 (12), 167 (6), 156 (10), 91 (100).

*1,9-Dibenzyl-1,9-dihydro-6-methyl-2*H*-purin-2-one* **7c**. The compound **7c** was prepared from 1,9-dibenzyl-6-methyl-1,3,6,9-tetrahydro-2*H*-purin-2-one **6c** (40 mg, 0.12 mmol) and DDQ (34 mg, 0.15 mmol) in benzene (10 ml) as described above. The crude product was purified by flash chromatography eluting with $CHCl_3$ followed by $CHCl_3$-MeCN (1:1), to give compound **7c** (27 mg, 68 %) as colourless powdery crystals, mp 122-124 °C (EtOAc-hexane). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.57 (s, 1 H, H-8), 7.3-7.1 (m, 10 H, Ph), 5.36 (s, 2 H, CH_2), 5.10 (s, 2 H, CH_2), 2.66 (s, 3 H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$): δ 156.6 (C-2), 156.5 (C-4), 151.9 (C-6), 144.7 (C-8), 135.5 and 135.0 (C in Ph), 128.9-126.5 (CH in Ph), 123.3 (C-5), 49.2 [N(1)CH_2], 46.2 [N(9)CH_2], 15.0 (CH_3). MS (E.I.): 330 (100, M^+), 315 (9), 301 (3), 256 (2), 239 (85), 225 (10), 198 (10), 184 (3), 142 (2), 91 (62). Hrms: Found 330.1477, $C_{20}H_{18}N_4O$ requires 330.1481. R_F 0.25, $CHCl_3$-MeCN (1:1), SiO_2.

*1,9-Dibenzyl-1,9-dihydro-6-isopropyl-2*H*-purin-2-one* **7d**. The compound **7d** was prepared from 1,9-dibenzyl-6-isopropyl-1,3,6,9-tetrahydro-2*H*-purin-2-one **6d** (110 mg, 0.3 mmol) and DDQ (70 mg, 0.3 mmol) in benzene (30 ml) as described above and the reaction time was 19 h. The crude product was purified by flash chromatography eluting with EtOAc, to give compound **7d** (57 mg, 52 %) as colourless powdery crystals, mp 165-167 °C (EtOAc-hexane). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.64 (s, 1 H, H-8), 7.4-7.1 (m, 10 H, Ph), 5.59 (s, 2 H, CH_2), 5.20 (s, 2 H, CH_2), 3.29 (m, 1 H, CH), 1.43 (d *J* 6.9 Hz, 6 H, CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.4 (C-6), 157.5 (C-4), 156.6 (C-2), 143.6 (C-8), 136.5 and 135.1 (C in Ph), 129.0-126.2 (CH in Ph), 121.9 (C-5), 49.2 [N(1)CH_2], 46.3 [N(9)CH_2], 31.8 (CH), 21.1 (CH_3). MS (E.I.): 358 (31, M^+), 343 (9), 330 (6), 316 (5), 302 (7), 267 (67), 253 (6), 91 (100). Hrms: Found 358.1800, $C_{22}H_{22}N_4O$ requires 358.1794. R_F 0.31, EtOAc, SiO_2.

*1,3-Dibenzyl-1,3-dihydro-6-phenyl-2*H*-purin-2-one* **10**. A mixture of 1,3-dibenzyl-6-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one **9** (115 mg, 0.29 mmol) and MnO_2 (1.15 g) in dichloromethane (50 ml) was stirred under N_2 at ambient temperature for 20 h, before the reaction mixture was filtered, and the filtrate evaporated *in vacuo*. The crude product was purified by flash chromatography eluting with EtOAc-hexane (3:1) followed by EtOAc and EtOH, to give compound **10** (80 mg, 70 %) as colourless powdery crystals, mp 188-190 °C (EtOAc-hexane). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.12 (s, 1 H, H-8), 7.7-6.9 (m, 15 H, Ph), 5.57 [s, 2 H, N(3)CH_2], 5.28 [s, 2 H, N(1)CH_2]. ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.3 (C-8), 159.7 (C-4), 149.5 (C-2), 149.1 (C-6), 135.7 135.1 and 131.0 (C in Ph), 129.3-126.7 (CH in Ph and C-5), 50.9 (CH_2), 48.9 (CH_2). MS (E.I.): 392 (64, M^+), 391 (90), 350 (4), 315 (6), 302 (25), 301 (100), 287 (5), 198 (28), 91 (100) and 65 (17). Hrms: Found 392.1618, $C_{25}H_{20}N_4O$ requires 392.1637. R_F 0.14, $CHCl_3$-MeCN (4:1), SiO_2.

*1,7-Dibenzyl-1,7-dihydro-6-phenyl-2*H*-purin-2-one* **14**. A mixture of 1,7-dibenzyl-6-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one **12** (99 mg, 0.25 mmol) and activated MnO_2 (485 mg) in dichloromethane (50 ml) was stirred under N_2 at ambient temperature for 20 h, before the mixture was filtered and the filtrate evaporated *in vacuo*. The crude product was purified by flash chromatography eluting with MeCN-EtOH (4:1) followed by EtOH, to give compound **14** (69 mg, 70 %) as colourless powdery crystals, mp 221-224 °C (EtOAc-hexane). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.95 (s, 1 H, H-8), 7.5-6.5 (m, 15 H, Ph), 5.13 [s, 1 H, N(1)CH_2], 4.57 [s, 1 H, N(7)CH_2]. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.1 (C-4), 156.4 (C-2), 155.4 (C-8), 145.5 (C-6), 136.4, 133.9 and 130.5 (C in Ph), 128.6-125.9 (CH in Ph), 114.7 (C-5), 50.2 (CH_2), 50.1 (CH_2). MS (E.I.): 392 (55, M^+), 363 (8), 350 (5), 317 (9), 301 (34), 287 (21), 210 (8), 198 (12), 144 (11), 91 (100), 65 (20). Hrms: Found 392.1632, $C_{25}H_{20}N_4O$ requires 392.1637. R_F 0.18, MeCN-EtOH (4:1), SiO_2.

*1,7-Dibenzyl-1,7-dihydro-8-phenyl-2*H*-purin-2-one* **15**. A mixture of 1,7-dibenzyl-6-phenyl-1,3,6,7-tetrahydro-2*H*-purin-2-one **12**, 1,7-dibenzyl-8-phenyl-1,3,7,8-tetrahydro-2*H*-purin-2-one **13** (10 mg) and activated MnO_2 (100 mg) in dichloromethane (5 ml) was stirred under N_2 at ambient temperature for 5 days, before the mixture was filtered and the filtrate evaporated *in vacuo*. The products were separated by flash chromatography on silica gel eluting with MeCN followed by MeCN-EtOH (4:1) to give compounds **14** (4 mg)

(data, see above) and **15** (2 mg) as colourless crystals, mp 220-224 °C (EtOAc-hexane). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.6-6.9 (m, 16 H, Ph and H-6), 5.33 [s, 2 H, N(7)CH_2], 5.11 [s, 2 H, N(1)CH_2]. ^{13}C NMR (125 MHz, $CDCl_3$): δ 168.5 (C-4), 165.8 (C-8), 156.5 (C-2), 135.4-125.9 (Ph and C-6), 118.4 (C-5), 54.3 [N(1)CH_2], 49.7 [N(7)CH_2]. MS (E.I.): 393 (29, *M*+1), 392 (57, M^+), 303 (22), 302 (18), 301 (46), 287 (13), 91 (100), 65 (21). Hrms: Found 392.1658, $C_{25}H_{20}N_4O$ requires 392.1637. R_F 0.23, MeCN-EtOH (4:1), SiO_2.

3,7-Dibenzyl-3,7-dihydro-8-phenyl-2H-purin-2-one **19**. A mixture of 3,7-dibenzyl-8-phenyl-1,3,7,8-tetrahydro-2*H*-purin-2-one **18** (20 mg, 0.05 mmol) and activated MnO_2 (200 mg) in dichloromethane (30 ml) was stirred under N_2 at ambient temperature for 20 h, before the mixture was filtered and the filtrate evaporated *in vacuo*. The crude product was purified by flash chromatography eluting with MeCN followed by MeCN-EtOH (4:1), to give compound **19** (12 mg, 60 %) as a colourless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.40 (s, 1 H, H-6), 7.6-7.1 (m, 15 H, Ph), 5.53 [s, 2 H, N(3)CH_2], 5.44 [s, 2 H, N(7)CH_2]. ^{13}C NMR ($CDCl_3$, 125 MHz): δ 156.2 (C-2), 155.3 (C-8), 153.8 (C-4), 148.5 (C-6), 136.3, 134.5 and 131.2 (C in Ph), 129.6-126.2 (CH in Ph), 117.4 (C-5), 49.6 [N(7)CH_2], 46.9 [N(3)CH_2]. MS (E.I.): 393 (21, *M*+1), 392 (57, M^+), 303 (8), 302 (11), 301 (27), 287 (12), 92 (8), 91 (100), 79 (11). Hrms: Found 392.1636, $C_{25}H_{20}N_4O$ requires 392.1637. R_F 0.43, MeCN-EtOH (4:1), SiO_2.

Acknowledgements. The authors thank The Norwegian Academy of Science and Letters; The Nansen Foundation and Affiliated founds, *N*-0205 Oslo for financial support. The Norwegian Research Council and The Norwegian Cancer Foundation are greatly acknowledged for partial financing of the 200, 300 and 500 MHz Bruker Avance instruments at the Department of Chemistry, University of Oslo, Norway.

REFERENCES

1. See for instance: (a) Cherbuliez, E.; Bernhard, K. *Helv. Chim. Acta* **1932**, *15*, 464-471; (b) Pettit, G. R.; Ode, R. H.; Coomes, R. M.; Ode, S. L. *Lloydia* **1976**, *39*, 363-367; (c) Cook, A. F.; Bartlett, R. T.; Gregson, R. P.; Quinn, R. J. *J. Org. Chem.* **1980**, *45*, 4020-4025; (d) Fuhrman, F. A.; Fuhrman, G. J.; Kim, Y. H.; Pavelka, L. A.; Mosher, H. S. *Science* **1980**, *207*, 193-195; (e) Bartlett, R. T.; Cook, A. F.; Holman, M. J.; McComas, W. W.; Nowoswait, E. F.; Poonian, M. S. *J. Med. Chem.* **1981**, *24*, 947-954; (f) Cafieri, F.; Fattorusso, E.; Mangoni, A.; Taglialatela-Scafati, O. *Tetrahedron Lett.* **1995**, *36*, 7893-7896; (g) De Napoli, L.; Montesarchio, D.; Piccialli, G.; Santacroce, C.; Varra, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 15-17, and refs. therein; (h) Seela, F.; Wei, C.; Kazimierczuk, Z. *Helv. Chim. Acta* **1995**, *78*, 1843-1854, and refs. therein.
2. (a) Farooqi, A. H. A.; Shukla, Y. N.; Shukla, A.; Bhakuni, D. S. *Phytochemistry* **1990**, *29*, 2061-2063; (b) Dahiya, J. S.; Tewari, J. P. *Phytochemistry* **1991**, *30*, 2825-2828; (c) Fujii, T.; Ohba, M.; Haneishi, T.; Matsubara, S.; Farooqi, A. H. A.; Shukla, Y. N. *Heterocycles* **1992**, *34*, 21-24; (d) Fujii, T.; Ohba, M.; Kawamura, H.; Haneishi, T.; Matsubara, S. *Chem. Pharm. Bull.* **1993**, *41*, 1362-1365; (e) Farooqi, A. H. A.; Shukla, Y. N.; Sharma, S.; Bansal, R. P. *Plant Growth Regul.* **1994**, *14*, 109-113.
3. For a recent review on cytokinins, see for instance: Matsubara, S. *Crit. Rev. Plant Sci.* **1990**, *9*, 17-57.
4. (a) Hecht, S. M.; Leonard, N. J.; Schmitz, R. Y.; Skoog, F. *Phytochemistry* **1974**, *13*, 329-336; (b) Chen, C.-m.; Smith, O. C.; McChesney, J. D. *Biochemistry* **1975**, *14*, 3088-3093.
5. (a) Henderson, T. R.; Frihart, C.; Leonard, N. L.; Schmitz, R. Y.; Skoog, F. *Phytochemistry* **1975**, *14*, 1687-1690; (b) Nishikawa, S.; Kumazawa, Z.; Mizutani, H.; Kondo, H. *Agric. Biol. Chem.* **1985**, *49*, 3353-3354; (c) Nishikawa, S.; Kumazawa, Z.; Mizutani, H.; Kashimura, N. *Agric. Biol. Chem.* **1986**, *50*, 1089-1091.
6. Pullman, B.; Pullman, A. *Adv. Heterocycl. Chem.* **1971**, *13*, 77-159.
7. Pendergast, W. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2759-2763.
8. Pendergast, W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2240-2243.

9. Gogoll, A.; Gundersen, L.-L.; Rise, F.; Valli, M. *Heterocycles* **1993**, *36*, 231-235.
10. Andresen, G.; Gundersen, L.-L.; Lundmark, M.; Rise, F.; Sundell, S. *Tetrahedron* **1995**, *51*, 3655-3664.
11. Iwamura, T.; Okamoto, Y.; Yokomoto, M.; Shimizu, H.; Hori, M.; Kataoka, T. *Synthesis* **1994**, 203-206.
12. Gundersen, L.-L. *Tetrahedron Lett.* **1994**, *35*, 3155-3158; (b) Gundersen, L.-L.; Bakkestuen, A. K.; Aasen, A. J.; Øverås, H.; Rise, F. *Tetrahedron* **1994**, *50*, 9743-9756; (c) Gundersen, L.-L., Langli, G. and Rise, F. *Tetrahedron Lett.* **1995**, *36*, 1945-1948; (d) Gundersen, L.-L. *Acta Chem. Scand.* **1996**, *50*, 58-63; (e) Langli, G.; Gundersen, L.-L.; Rise, F. *Tetrahedron* **1996**, *52*, 5625-5638; (f) Gundersen, L.-L. *Acta Chem. Scand.* **1996**, *50*, 462-465.
13. (a) Song, P.-S.; Moore, T. A. *Intern. J. Quantum Chem.* **1967**, *1*, 699-719; (b) Song, P.-S. *Intern. J. Quantum Chem.* **1968**, *2*, 281-296.
14. Suzuki, H.; Tsukuda, A.; Kondo, M.; Aizawa, M.; Senoo, Y.; Nakajima, M.; Watanabe, T.; Yokohama, Y.; Murakami, Y. *Tetrahedron Lett.* **1995**, *36*, 1671-1672.
15. Gundersen, L.-L. Unpublished results.
16. Rinaldi, P. L.; Keifer, P. *J. Magn. Reson. Ser. A*, **1994**, *108*, 259-262.
17. (a) Hurd, R. E.; John, B. K. *J. Magn. Reson.* **1991**, *91* 648-653; (b) Vuister, G. W.; Boelens, R.; Kaptein, R.; Hurd, R. E.; John, B.; Van Zijl, P. C. M. *J. Am. Chem. Soc.* **1991**, *113*, 9688-9690; (c) Tyburn, J.-M.; Brereton, I. M.; Doddrell, D. M. *J. Magn. Reson.* **1992**, *97*, 305-312.
18. Timpe, H.-J.; El'tsov, A. V. *Adv. Heterocycl. Chem.* **1983**, *33*, 185-239.
19. (a) Công-Danh, N.; Beaucourt, J.-P.; Pichat, L. *Tetrahedron Lett.* **1979**, 3159-3162; (b) Bergstrom, D. E.; Reday, P. A. *Tetrahedron Lett.* **1982**, *23*, 4191-4194; (c) Moriarty, R. M.; Epa, W. R.; Awasthi, A. K. *Tetrahedron Lett.* **1990**, *31*, 5877-5880; (d) Estep, K. G.; Josef, K. A.; Bacon, E. R.; Carabateas, P. M.; Rumney IV, S.; Pilling, G. M.; Krafte, D. S.; Volberg, W. A.; Dillon, K.; Dugrenier, N.; Briggs, G. M.; Canniff, P. C.; Gorczyca, W. P.; Stankus, G. P.; Ezrin, A. M. *J. Med. Chem.* **1995**, *38*, 2582-2595; (e) Mamos, P.; Van Aerschot, A. A.; Weyns, N. J.; Herdewijn, P. A. *Tetrahedron Lett.* **1992**, *33*, 2413-2416; (f) Hirota, K.; Kitade, Y.; Kanbe, Y.; Maki, Y. *J. Org. Chem.* **1992**, *57*, 5268-5270; (g) Van Aerschot, A. A.; Mamos, P.; Weyns, N. J.; Ikeda, S.; De Clercq, E; Herdewijn, P. A. *J. Med. Chem.* **1993**, *36*, 2938-2942; (h) Manfredini, S.; Baraldi, P. G.; Bazzanini, R.; Marangoni, M.; Simoni, D.; Balzarini, J.; De Clercq, E. *J. Med. Chem.* **1995**, *38*, 199-203; (i) Ozola, V.; Persson, T.; Gronowitz, S.; Hörnfeldt, A.-B. *J. Heterocycl. Chem.* **1995**, *32*, 863-866; (j) Tu, C.; Keane, C.; Eaton, B. E. *Nucleosides, Nucleotides* **1995**, *14*, 1631-1638; (k) Dvořáková, H.; Dvořák, D.; Holý, A. *Tetrahedron Lett.* **1996**, *37*, 1285-1288.
20. Holý, A. *Coll. Czech. Chem. Commun.* **1979**, *44*, 2846-2853.
21. Attenburrow, J.; Cameron, A. F. B.; Chapman, J. H.; Evans, R. M.; Hems, B. A.; Jansen A. B. A.; Walker, T. *J. Chem. Soc.*, **1952** 1094-1111.

(*Received in UK* 6 *June* 1996; *revised* 27 *August* 1996; *accepted* 29 *August* 1996)