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Synthesis of Cyclopentenyl Carbanucleosides *via* Palladium(0) Catalysed Reactions

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Abstract: Methyl 4-acetoxycyclopent-2-enylmethylcarboxylate (**2**) and the corresponding carbonate **3** have been treated with sodium salts and aluminum amides of pyrimidines, purines and methyl 1*H*-1,2,4-triazole-3-carboxylate with a catalyst formed from bis(dibenzylideneacetone)palladium(0) and triisopropyl phosphite to give the corresponding carbanucleosides in good to excellent yields. This method was also applied for a synthesis of carbovir (**31**).

INTRODUCTION

Carbocyclic nucleoside analogues exhibit a wide range of biological properties to take them into consideration as agrochemicals and pharmaceuticals.[1,2] An extensive methodology for their syntheses has been developed.[3] In 1988 *Trost et al.*[4] described the palladium(0) catalysed coupling reaction between an allylic epoxide and adenine for the synthesis of aristeromycin. A key intermediate of this allylic alkylation was the formation of a π-allylpalladium complex.[5] Nucleophilic addition of the salt of a heteroaromatic base, with formation of a carbon-nitrogen bond under inversion, affects the formation of the desired nucleoside analogue. The regiochemistry is mainly controlled by steric hindrance due to the side chain of the cyclopentene moiety,[6,7] thus nucleophilic attack takes place at the least hindered terminus of the π-allyl system.

During the last few years different palladium catalysts were employed for this reaction and the steric effect of ligands was studied.[8] However, if palladium bears bulky phosphine ligands, such as PPh_3, the energy necessary for the formation of the transition state increases due to the steric congestion. We decided to use triisopropyl phosphite, because phosphites are known to be good π-acceptor ligands.[9] The catalyst was always prepared *in situ* from bis(dibenzylideneacetone)palladium(0),[10] a non air sensitive complex, with four equivalents of $(i\text{-}C_3H_7O)_3P$ in THF.

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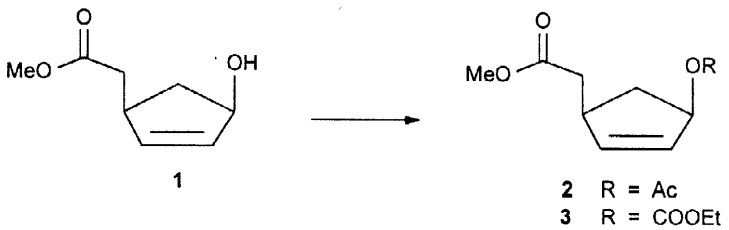
In this paper we want to present the application of this palladium catalyst in combination with aluminum amides of various heterocycles for the synthesis of carbocyclic nucleoside analogues in good to excellent yields, especially for pyrimidines.

RESULTS AND DISCUSSION

The known[11] starting material **2** for the palladium catalysed reaction was obtained from alcohol **1**, which is easily accessible from norborn-5-en-2-one. Compound **3** was yielded by the reaction of alcohol **1** with ethyl chloroformate in the presence of Et_3N.



Scheme 1. Reagents and conditions: Ac_2O/Pyr or ethyl chloroformate/Et_3N, respectively. All compounds are racemic, only one enantiomer is drawn.

The allylic acetate **2** and carbonate **3** were used as central intermediates in the synthesis of (±)-*cis*-[4-(methoxycarbonylmethyl)-2-cylcopenten-1-yl]-nucleosides.

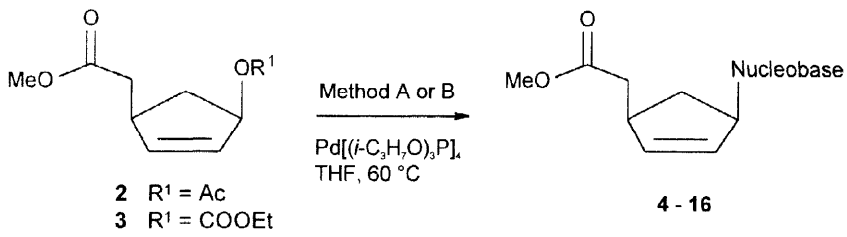
A decisive parameter in the reaction of the π-allylpalladium complex with anions of heteroaromatic bases as nucleophiles is the generation of the corresponding salts. For this purpose NaH, LiH, BuLi, or Cs_2CO_3 were mainly described in the literature.[3] A general problem is their low solubility and as a result long reaction times in polar and high boiling solvents are necessary.

Et_3Al was described as auxiliary base for the opening of epoxides with secondary amines.[12] We have applied this method to purines and pyrimidines for the synthesis of *xylo*-nucleoside analogues in good yields,[13] and so it was fair to assume that aluminum amides of heterocycles will also react in good yields under palladium catalysis.

The amides of various heterocycles were generated with Et_3Al in THF (Method A). This reaction requires 10-20 minutes until a clear solution is obtained. After addition of the freshly prepared catalyst and the allylic starting material the reaction mixture was stirred at 60 °C, depending on the amount of catalyst, for approximately 1 hour for 10% and 3-4 hours for 5% of catalyst. For comparison of yields also the sodium salts of thymine, uracil and methyl 1*H*-1,2,4-triazole-3-carboxylate were generated with NaH in DMF (Method B). The amount of the isolated product was lower in each case.

The nature of the leaving group had some consequences on reaction time and yield. When acetate **2** was used, the reaction time was about 10 times longer, but the yield was always better (see Table 1). The reason seems to be a different mechanism depending on the leaving group. Ethyl carbonate is known[14] to loose CO_2 during the reaction and the resulting ethoxy anion, a much better nucleophile than acetate, can react with the π-allylpalladium complex to unintended by-products.

Especially the yields of the cyclopentenyl nucleosides carbathymidine (**4**), -uridine (**5**) and N-benzoylcarbacytidine (**7**) synthesised by the aluminum amide method were excellent (see Table 1). The difference in the isolated yields regarding cytosine derivatives **6** and **7** did not result from the formation of by-products, but from the polarity of compound **6** and its difficult isolation besides aluminum hydroxide, formed during the hydrolysis of excess alkylaluminum cytosine (see Table 1). Optimisation of the workup procedure would increase the yield.



Scheme 2. Reagents and conditions: Method A: Et_3Al/THF/Nucleobase; Method B: NaH/DMF/Nucleobase. All compounds are racemic, only one enantiomer is drawn.

Methyl 1*H*-1,2,4-triazole-3-carboxylate, the heteroaromatic base of ribavirin,[15] reacted in 39% yield when the aluminum amide was used. The reaction course of purines (adenine, N^6-benzoyladenine, 6-chloropurine and N^2-acetylguanine) was similar to that of pyrimidines. Starting acetate **2** was shown to give better yields as compared to carbonate **3**. N-protection of the purines proved to be beneficial. The preparation of the aluminum amide was the method of choice, especially for 6-chloropurine (see Table 2).

To come from the *homo*-cyclopentenylcarbanucleosides **4** - **16** to target structures **29** - **31**, the side chain was shortened by one carbon atom applying the *Curtius* degradation. Carboxylic acid **17** was obtained by treatment of ester **1** with KOH in refluxing 1,4-dioxane, followed by addition of benzyl bromide to the reaction mixture. *Curtius* degradation of crude **17** afforded isocyanate **18**, which was treated with an aqueous solution of KOH at 0 °C in a THF/water system affording amine **19** and traces of the corresponding urea **19a** with two cyclopentenylmethyl moieties. For the replacement of an amino group by an oxygen functionality or a halide, which could be treated further on with suitable nucleophiles, several methods are known in the literature.[16] Unfortunately, one of the most simple and promising methods, the displacement of the corresponding di-tosylate of amine **19** with certain nucleophiles,[17] did not work satisfactory due to the sterical hindrance of the cyclopentene ring.

Table 1. Reaction of allylic acetate **2** (R^1 = Ac) and allylic carbonate **3** (R^1 = COOEt) with pyrimidines and methyl 1*H*-1,2,4-triazole-3-carboxylate

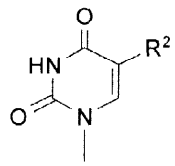
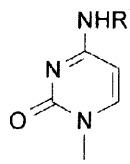
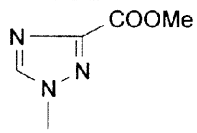
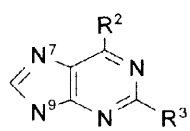
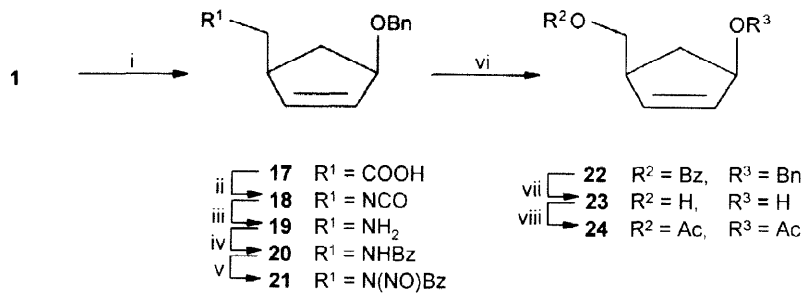
Nucleobase	R^1	R^2	Method	Yield (%)	Product
	Ac	CH_3	A	95	**4**
	Ac	CH_3	B	76	**4**
	COOEt	CH_3	A	91	**4**
	Ac	H	A	82	**5**
	Ac	H	B	40	**5**
	Ac	H	A	69	**6**
	COOEt	H	A	61	**6**
	Ac	Bz	A	98	7
	COOEt	Bz	A	86	7
	Ac	—	A	39	**8**
	Ac	—	B	21	**8**

Table 2. Reaction of allylic acetate **2** (R^1 = Ac) and allylic carbonate **3** (R^1 = COOEt) with purines

Nucleobase	Entry	R^1	R^2	R^3	Position	Method	Yield (%)	Product
	1	Ac	NH_2	H	N^9	A	45	**9**
		Ac	NH_2	H	*	A	20	**10**
		Ac	NHAc	H	N^9	A	5	**11**
	2	Ac	NH_2	H	N^9	B	36	**9**
	3	COOEt	NH_2	H	N^9	A	34	**9**
		COOEt	NH_2	H	*	A	30	**10**
	4	Ac	Cl	H	N^9	A	67	**12**
	5	Ac	Cl	H	N^9	B	9	**12**
	6	Ac	NHBz	H	N^9	A	81	**13**
		Ac	NHBz	H	N^7	A	7	**14**
	7	Ac	OH	NHAc	N^9	A	61	**15**
		Ac	OH	NHAc	N^7	A	17	**16**

* unseparable mixture of two nucleoside analogues, N^3 and N^7?

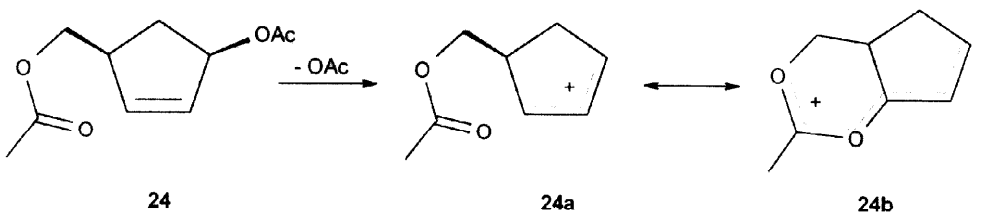


Scheme 3. Reagents and conditions: i KOH/benzyl bromide/1,4-dioxane/reflux; ii a) ethyl chloroformate/Et_3N/acetone, b) NaN_3/H_2O, c) toluene/reflux; iii KOH/H_2O/THF/0 °C; iv $BzCl/Et_3N/CH_2Cl_2$; v a) N_2O_4/CCl_4, b) NaOAc; vi petrol ether/80 °C; vii $NH_{3,liq.}$/Na; viii Ac_2O/Pyr/CH_2Cl_2. All compounds are racemic, only one enantiomer is drawn.

However, it is long known that the decomposition of nitrosamides can afford esters.[18] The mechanism and the thermal rearrangement of N-nitrosamides was studied by *White*[19] and *Huisgen*.[20] Therefore, amine **19** was treated with benzoyl chloride in the presence of Et_3N to yield benzoate **20** in 75% overall yield. The thermally unstable N-nitrosobenzamide **21** was obtained by the reaction of **20** with N_2O_4 and was immediately transformed further on by refluxing in petrol ether (bp 80 °C) overnight to yield 86% of the side chain shortened benzoate **22**. The benzoate as well as the benzyl ether were cleaved with Na/NH_3, but the intermediate diol **23** was not isolated due to its high polarity. Acetylation *in situ* with Ac_2O/Pyr afforded compound **24**, the starting material for the syntheses of carbanucleoside analogues **25 - 28**.

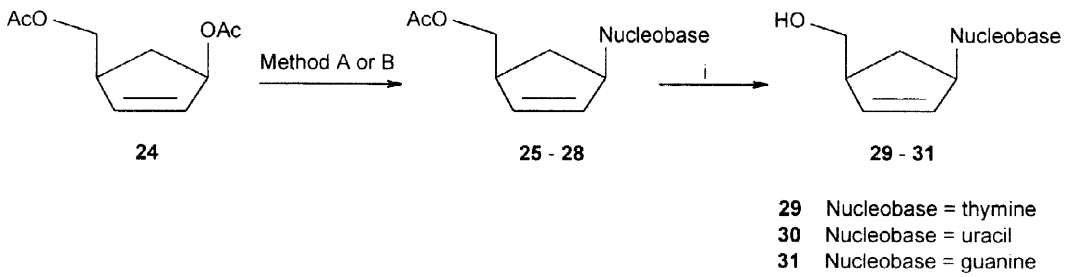
Diacetate **24** was submitted to palladium(0) catalysed reactions with the aluminum amides of thymine, uracil, N^2-acetylguanine as selected examples for pyrimidines and purines. In comparison to the side chain elongated compound **2** yields were lower. In particular for the pyrimidines investigated a dramatic decrease in isolated product has to be mentioned (see Table 3). Better yields are to be expected by protecting the hydroxy functionality at carbon atom 5 instead of acetate with trityl[21] or silyl moieties, e.g. *t*-butyldimethylsilyl[22] or thexyldimethylsilyl,[23] but we wanted to show the applicability of aluminum amides of heteroaromates using palladium(0) catalysis even with non optimised substrates.

An explanation for the low yields might be given if a participation of the acetate moiety is assumed. For the synthesis of diacetate **24** *via* the *Prins* reaction between cyclopentadiene and an acetylmethyleneoxonium species the allylic cation **24a** and the intramolecularly cyclised cation **24b** were assumed to be intermediates.[6] A participation of the carbonyl functionality would decrease the electrophilic character of the π-allylpalladium complex and poor nucleophiles, e.g. a salt of thymine, would react only slowly and be inclined to the formation of by-products.



Scheme 4

Starting material **24** was treated in the same manner as described for ester **2**. For comparison of yields the aluminum amide and the sodium salt of thymine were treated with $Pd[(i\text{-}C_3H_7O)_3P]_4$ in THF. The aluminum amide again gave better yields. The reaction of the aluminum amide of uracil afforded nucleoside **26** and the reaction with N^2-acetylguanine gave N^2,O-acetylated carbovir **27**.



Scheme 5. Reagents and conditions: Method A: Et_3Al/THF/Nucleobase; Method B: NaH/DMF/Nucleobase; i MeONa/MeOH; for N^2-acetylguanine: $NH_{3,\,liq.}/NaNH_2$All compounds are racemic, only one enantiomer is drawn.

Table 3. Reaction of allylic acetate **24** with nucleobases

Nucleobase	Entry	Position	Method	Yield (%)	Product
Thymine	1	—	A	40	**25**
	2	—	B	32	**25**
Uracil	3	—	A	37	**26**
N^2-Acetylguanine	4	N^9	A	61	**27**
		N^7	A	9	**28**

Deprotection of nucleoside analogues **25** and **26** was performed with MeONa/MeOH at room temperature to afford known[24] carbathymidine (**29**), and the unprotected carbauridine (**30**), respectively. Nucleoside **27** was treated with liquid ammonia/$NaNH_2$ to afford (±)-carbovir (**31**) in 95% yield.

EXPERIMENTAL

Melting points were obtained on a Büchi-Tottoli apparatus and are uncorrected. Column chromatography was performed on silica gel 60, 230-400 mesh (Merck, Darmstadt), and TLC on aluminium sheets coated with silica gel 60 F_{254} (Merck, Darmstadt). ^1H and ^{13}C NMR spectra were recorded on a Bruker MSL 300 instrument (TMS as internal standard, δ-values in ppm, $CDCl_3$ as solvent unless otherwise indicated). IR spectra were determined as film on KBr on a Bomem Michelson 100 FT-spectrophotometer. MS spectra were recorded on a Kratos Profile spectrometer. Solvents were dried prior to use under standard conditions. THF was freshly distilled from potassium. The elemental analyses were performed at the Institute of Organic Chemistry, University of Graz.

(±)-*cis*-Ethyl (4-methoxycarbonylmethylcyclopent-2-enyl)carbonate (3)

30.0 g (190 mmol) of alcohol **1** and 53.9 ml (380 mmol) of Et_3N in 500 ml of CH_2Cl_2 were cooled to -30 °C and under stirring 22.0 ml (230 mmol) of ethyl chloroformate was added dropwise within 1 h. The reaction was warmed to room temperature and after complete conversion water was added. The organic layer was separated, washed with 1 N aqueous HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated *in vacuo*. Bulb-to-bulb distillation yielded 40.0 g (91.3%) of compound **3** as a colourless oil.

^1H NMR ($CDCl_3$) δ 1.16 (t, J = 7.1 Hz, 3H), 1.43 (dt, J = 14.5, 4.2 Hz, 1H), 2.26 (dd, J = 15.9, 8.1 Hz, 1H), 2.36 (dd, J = 15.9, 6.9 Hz, 1H), 2.48 (dt, J = 14.5, 7.9 Hz, 1H), 2.93 (m, 1H), 3.54 (s, 3H), 4.04 (dd, J = 14.5, 7.1 Hz, 2H), 5.42 (m, 1H), 5.85 (dt, J = 5.6, 2.1 Hz, 1H), 6.02 (ddd, J = 5.6, 2.3, 1.0 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 14.24 (q), 36.28 (t), 40.23 (t), 40.52 (d), 51.43 (q), 63.66 (t), 82.77 (d), 129.68 (d), 140.16 (d), 154.81 (s), 172.44 (s); IR (KBr) ν 2966, 1739, 1438, 1369, 1259, 1165, 1061, 1003, 858, 793 cm^{-1}; Anal. Calcd for $C_{11}H_{16}O_5$ (228.25): C, 57.89; H, 7.07. Found: C, 58.13; H, 6.93.

General procedures for the Pd-catalysed introduction of the heteroaromatic bases

Method A

Under an atmosphere of dry nitrogen 10 mmol of the heteroaromatic base was suspended in 100 ml of THF and 10 ml of Et_3Al (1 N solution in hexane) was added at once. The reaction mixture was heated to 60 °C to obtain a clear solution, stirred for another 10-20 min and allowed to cool to room temperature. For the preparation of the catalyst 0.5 mmol of bis(dibenzylideneacetone)palladium(0) was dissolved in 4 ml of THF, and 2 mmol of triisopropyl phosphite was added and stirred until the dark purple colour changed into yellow.

To the aluminum amide of the heteroaromatic base were added 5 mmol of the starting materials **2**, **3** or **24** and the freshly prepared Pd-catalyst. The reaction mixture was heated to 60 °C until complete conversion (about 1-2 h) was achieved. The reaction mixture was cooled to 0 °C and 10 ml of 1 N aqueous HCl was added slowly, followed by 15 ml of water and 100 ml of CH_2Cl_2. The organic layer was separated and the

aqueous layer reextracted twice with 30 ml of CH_2Cl_2. The combined organic extracts were washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography ($CHCl_3$ to remove unpolar impurities, then $CHCl_3$/MeOH 19/1 v/v) and recrystallisation from 2-propanol/diisopropyl ether afforded the pure carbocyclic nucleoside analogues.

Method B

Under dry nitrogen 10 mmol of the heteroaromatic base was suspended in 10 ml of DMF and 10 mmol of NaH was added. The reaction mixture was heated to 60 °C and allowed to cool to room temperature. To the suspension of the sodium salt of the heteroaromatic base were added 5 mmol of the starting materials **2** or **24** and the freshly prepared Pd-catalyst (see method A). The reaction mixture was heated to 40 °C until complete conversion was reached.

Workup (DMF was first removed by bulb-to-bulb distillation at 80 °C and 0.1 mbar) and purification was done as described above.

(±)-*cis*-1-[4-(Methoxycarbonylmethyl)-2-cyclopenten-1-yl]thymine (4)

mp: 138-9 °C; ^{1}H NMR ($CDCl_3$) δ 1.27 (dt, J = 13.7, 7.1 Hz, 1H), 1.92 (s, 3H), 2.45 (dd, J = 15.7, 7.5 Hz, 1H), 2.54 (dd, J = 15.7, 6.8 Hz, 1H), 2.84 (dt, J = 13.7, 8.2 Hz, 1H), 3.14 (m, 1H), 3.69 (s, 3H), 5.65-5.73 (m, 2H), 6.11 (dt, J = 5.7, 2.1 Hz, 1H), 7.03 (s, 1H), 9.70 (bs, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 12.73 (q), 37.60 (t), 39.63 (t), 41.05 (d), 51.88 (q), 61.38 (d), 111.39 (s), 129.76 (d), 136.69 (d), 140.31 (d), 151.34 (s), 164.08 (s), 172.38 (s); MS m/z (% rel int) 246 ($M^{+\cdot}$, 12), 233 (3), 191 (4), 148 (4), 139 (64), 127 (9), 107 (27), 97 (9), 79 (100), 66 (9), 59 (14), 39 (9); IR (KBr) ν 3173, 3042, 1732, 1685, 1456, 1365, 1250, 865, 766 cm^{-1}; Anal. Calcd for $C_{13}H_{16}N_2O_4$ (264.28): C, 59.08; H, 6.10; N, 10.60. Found: C, 58.93; H, 6.17; N, 10.54.

(±)-*cis*-1-[4-(Methoxycarbonylmethyl)-2-cyclopenten-1-yl]uracil (5)

mp: 125-6 °C; ^{1}H NMR ($CDCl_3$) δ 1.24 (dt, J = 13.8, 7.1 Hz, 1H), 2.39 (dd, J = 15.7, 7.5 Hz, 1H), 2.48 (dd, J = 15.7, 6.7 Hz, 1H), 2.82 (dt, J = 13.8, 8.2 Hz, 1H), 3.10 (m, 1H), 3.64 (s, 3H), 5.61-5.68 (m, 2H), 5.71 (d, J = 8.0 Hz, 1H), 6.08 (dt, J = 5.5, 1.7 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 9.50 (bs, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 37.48 (t), 39.33 (t), 40.87 (d), 51.71 (q), 61.48 (d), 102.72 (d), 129.16 (d), 140.84 (d), 140.86 (d), 151.38 (s), 163.90 (s), 172.22 (s); MS m/z (% rel int) 250 ($M^{+\cdot}$, 14), 219 (6), 190 (3), 177 (16), 153 (7), 139 (34), 107 (47), 97 (8), 79 (100), 67 (9), 53 (9), 39 (11); IR (KBr) ν 3183, 3052, 1696, 1459, 1376, 1249, 1174, 1032, 991, 815, 766, 713 cm^{-1}; Anal. Calcd for $C_{12}H_{14}N_2O_4$ (250.25): C, 57.59; H, 5.64; N, 11.19. Found: C, 57.89; H, 4.74; N, 10.87.

(±)-*cis*-1-[4-(Methoxycarbonylmethyl)-2-cyclopenten-1-yl]cytosine (6)

mp: 178-9 °C; ^{1}H NMR ($CDCl_3$) δ 1.21 (dt, *J* = 13.5, 6.8 Hz, 1H), 2.32 (dd, *J* = 15.3, 7.5 Hz, 1H), 2.41 (dd, *J* = 15.3, 6.8 Hz, 1H), 2.79 (dt, *J* = 13.5, 6.1 Hz, 1H), 3.04 (m, 1H), 3.61 (s, 3H), 5.60 (m, 1H), 5.66 (m, 1H), 5.93 (d, *J* = 7.3 Hz, 1H), 6.01 (m, 1H), 7.18 (d, *J* = 7.3 Hz, 1H), 6.7-7.1 (1H), 7.7-8.1 (1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 38.24 (t), 39.77 (t), 40.92 (d), 51.65 (q), 62.03 (d), 95.61 (d), 130.21 (d), 139.64 (d), 142.11 (d), 157.04 (s), 166.03 (s), 172.42 (s); MS m/z (% rel int) 249 ($M^{+\cdot}$, 19), 218 (4), 191 (7), 176 (100), 139 (11), 122 (38), 79 (91), 67 (34), 52 (29), 41 (38); IR (KBr) ν 3338, 3148, 1729, 1633, 1604, 1485, 1397, 1362, 1272, 1186, 788, 598 cm^{-1}; Anal. Calcd for $C_{12}H_{15}N_3O_3$ (249.27): C, 57.82; H, 6.07; N, 16.86. Found: C, 57.76; H, 6.15; N, 16.51.

(±)-*cis*-N^4-Benzoyl-1-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]cytosine (7)

mp: 119-20 °C; ^{1}H NMR ($CDCl_3$) δ 1.26 (dt, *J* = 13.8, 6.7 Hz, 1H), 2.38 (dd, *J* = 15.7, 7.4 Hz, 1H), 2.46 (dd, *J* = 15.7, 6.8 Hz, 1H), 2.92 (dt, *J* = 13.8, 8.3 Hz, 1H), 3.12 (m, 1H), 3.65 (s, 3H), 5.76 (dt, *J* = 5.5, 1.9 Hz, 1H), 5.71-5.77 (m, 1H), 6.13 (dt, *J* = 5.5, 1.9 Hz, 1H), 7.41 (m, 3H), 7.51 (d, *J* = 7.3 Hz, 1H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.86 (m, 2H), 9.0-9.4 (m, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 38.18 (t), 39.48 (t), 41.04 (d), 51.67 (q), 63.15 (d), 97.25 (d), 127.78 (d), 128.91 (d), 129.11 (d), 133.00 (s), 133.39 (d), 140.98 (d), 145.29 (s), 155.58 (s), 161.98 (s), 172.17 (s); MS m/z (% rel int) 353 ($M^{+\cdot}$, 3), 323 (0.3), 280 (2), 262 (0.4), 206 (0.4), 138 (19), 103 (28), 94 (11), 79 (100); Anal. Calcd for $C_{19}H_{19}N_3O_4$ (353.38): C, 64.58; H, 5.42; N, 11.89. Found: C, 64.48; H, 5.52; N, 12.07.

(±)-*cis*-Methyl 1-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]-1*H*-1,2,4-triazole-3-carboxylate (8)

^{1}H NMR ($CDCl_3$) δ 1.74 (dt, *J* = 14.0, 6.0 Hz, 1H), 2.46 (dd, *J* = 16.0, 8.1 Hz, 1H), 2.56 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.96 (dt, *J* = 14.0, 8.4 Hz, 1H), 3.24 (m, 1H), 3.68 (s, 3H), 4.00 (s, 3H), 5.55 (m, 1H), 5.91 (dt, *J* = 5.5, 1.9 Hz, 1H), 6.22 (m, 1H), 8.19 (s, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 38.23 (t), 39.62 (t), 41.40 (d), 51.88 (q), 52.88 (q), 66.63 (d), 128.06 (d), 141.36 (d), 143.00 (d), 155.20 (s), 169.44 (s), 172.41 (s); Anal. Calcd for $C_{12}H_{15}N_3O_4$ (265.27): C, 54.33; H, 5.70; N, 15.84. Found: C, 54.53; H, 5.64; N, 15.59.

(±)-*cis*-9-[4-(Methoxycarbonylmethyl)-2-cyclopenten-1-yl]adenine (9)

mp: 191-2 °C; ^{1}H NMR ($CDCl_3$) δ 1.61 (dt, *J* = 13.8, 6.5 Hz, 1H), 2.48 (dd, *J* = 15.8, 8.1 Hz, 1H), 2.59 (dd, *J* = 15.8, 6.8 Hz, 1H), 3.01 (dt, *J* = 13.8, 8.4 Hz, 1H), 3.27 (m, 1H), 3.69 (s, 3H), 5.65 (bs, 2H), 5.72 (m, 1H), 5.93 (dt, *J* = 5.5, 2.2 Hz, 1H), 6.22 (dt, *J* = 5.5, 2.0 Hz, 1H), 7.84 (s, 1H), 8.38 (s, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 38.53 (t), 39.57 (t), 41.17 (d), 51.62 (d), 59.58 (q), 119.69 (s), 129.05 (d), 138.34 (d), 139.81 (d), 149.63 (s), 152.83 (d), 156.01 (s), 172.31 (s); MS m/z (% rel int) 273 ($M^{+\cdot}$, 36), 242 (7), 214 (11), 200 (12), 173 (5), 135 (100), 119 (3), 108 (21), 97 (6), 79 (48), 66 (7); IR (KBr) ν 3150, 1728, 1656, 1617, 1448,

1411, 1169, 1020, 775, 654 cm^{-1}; Anal. Calcd for $C_{13}H_{15}N_5O_2$ (273.29): C, 57.13; H, 5.53; N, 25.63. Found: C, 57.20; H, 5.72; N, 24.60.

(±)-*cis*-N^6-Acetyl-9-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]adenine (11)

^{1}H NMR ($CDCl_3$) δ 1.64 (dt, *J* = 13.8, 6.4 Hz, 1H), 2.48 (dd, *J* = 16.2, 7.5 Hz, 1H), 2.59 (dd, *J* = 16.2, 6.7 Hz, 1H), 2.62 (s, 3H), 3.01 (dt, *J* = 13.8, 8.4 Hz, 1H), 3.28 (m, 1H), 3.67 (s, 3H), 5.77 (m, 1H), 5.93 (dd, *J* = 5.6, 2.2 Hz, 1H), 6.23 (dd, *J* = 5.6, 2.2 Hz, 1H), 8.12 (s, 1H), 8.69 (s, 1H), 9.39 (s, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 25.84 (q), 38.61 (t), 39.68 (t), 41.46 (d), 51.85 (d), 60.16 (q), 122.40 (s), 128.93 (d), 140.48 (d), 141.56 (d), 149.53 (s), 151.55 (s), 152.34 (d), 171.09 (s), 172.39 (s); MS m/z (% rel int) 315 ($M^{+\cdot}$, 41), 284 (13), 273 (10), 256 (4), 242 (9), 214 (4), 200 (11), 178 (54), 135 (100), 107 (35), 79 (47); Anal. Calcd for $C_{15}H_{17}N_5O_3$ (315.33): C, 57.14; H, 5.43; N, 22.21. Found: C, 57.31; H, 5.41; N, 22.15.

(±)-*cis*-6-Chloro-9-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]-9*H*-purine (12)

^{1}H NMR ($CDCl_3$) δ 1.66 (dt, *J* = 13.9, 6.6 Hz, 1H), 2.49 (dd, *J* = 16.0, 7.8 Hz, 1H), 2.62 (dd, *J* = 16.0, 6.6 Hz, 1H), 3.05 (dt, *J* = 13.9, 8.4 Hz, 1H), 3.30 (m, 1H), 3.69 (s, 3H), 5.81 (tt, *J* = 6.5, 2.1 Hz, 1H), 5.93 (dt, *J* = 5.4, 2.1 Hz, 1H), 6.26 (dt, *J* = 5.8, 2.1 Hz, 1H), 8.18 (s, 1H), 8.77 (s, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 38.55 (t), 39.55 (t), 41.52 (d), 51.91 (q), 60.67 (d), 128.54 (d), 132.45 (s), 140.97 (d), 143.62 (d), 151.45 (s), 152.09 (2 x C, s and d), 172.13 (s); Anal. Calcd for $C_{13}H_{16}ClN_4O_2$ (295.75): C, 52.80; H, 5.45; Cl, 11.99; N, 18.94. Found: C, 52.24; H, 5.42; Cl, 11.88; N, 19.23.

(±)-*cis*-N^6-Benzoyl-9-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]adenine (13)

mp: 162-3 °C; ^{1}H NMR ($CDCl_3$) δ 1.67 (dt, *J* = 13.7, 6.5 Hz, 1H), 2.50 (dd, *J* = 16.2, 7.7 Hz, 1H), 2.61 (dd, *J* = 16.2, 6.7 Hz, 1H), 3.05 (dt, *J* = 13.7, 8.4 Hz, 1H), 3.30 (m, 1H), 3.69 (s, 3H), 5.81 (m, 1H), 5.95 (m, 1H), 6.25 (m, 1H), 7.50-7.61 (m, 3H), 8.00 (m, 3H), 8.81 (s, 1H), 9.01 (s, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 38.65 (t), 39.79 (t), 41.49 (d), 51.91 (d), 60.22 (q), 123.68 (s), 128.16 (d), 128.93 (d), 129.06 (d), 132.91 (d), 134.09 (s), 140.58 (d), 141.30 (d), 142.00 (s), 149.78 (s), 152.73 (d), 164.94 (s), 172.41 (s); IR (KBr) ν 3060, 1734, 1636, 1554, 1430, 1394, 1316, 1285, 872, 695, 720, 788 cm^{-1}; Anal. Calcd for $C_{20}H_{19}N_5O_3$ (377.40): C, 63.65; H, 5.07; N, 18.56. Found: C, 63.43; H, 4.97; N, 18.66.

(±)-*cis*-6-Benzamido-7-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]-7*H*-purine (14)

mp: 148-9 °C; ^{1}H NMR ($CDCl_3$) δ 1.61 (dt, *J* = 13.8, 5.8 Hz, 1H), 2.41 (dd, *J* = 15.8, 7.6 Hz, 1H), 2.52 (dd, *J* = 15.8, 6.8 Hz, 1H), 3.18 (dt, *J* = 13.8, 8.5 Hz, 1H), 3.33 (m, 1H), 3.65 (s, 3H), 6.05 (m, 1H), 6.34 (m, 1H), 6.61 (m, 1H), 7.44-7.56 (m, 3H), 8.17-8.31 (m, 4H), 9.50 (bs, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 39.88 (t), 40.24 (t), 41.43 (d), 51.88 (d), 63.72 (q), 116.00 (s), 128.42 (d), 128.77 (d), 129.32 (d), 132.20 (d), 137.48

(s), 141.11 (d), 143.75 (d), 151.09 (s), 159.14 (s), 172.38 (s), 177.91 (s); Anal. Calcd for $C_{20}H_{19}N_5O_3$ (377.40): C, 63.65; H, 5.07; N, 18.56. Found: C, 63.20; H, 5.13; N,7 18.47.

(±)-*cis*-N^2-Acetyl-9-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]guanine (15)

^{1}H NMR ($CDCl_3$) δ 1.48 (dt, J = 13.8, 6.6 Hz, 1H), 2.36 (s, 3H), 2.39 (dd, J = 15.8, 6.6 Hz, 1H), 2.51 (dd, J = 15.8, 8.0 Hz, 1H), 2.79 (dt, J = 13.8, 8.3 Hz, 1H), 3.16 (m, 1H), 3.61 (s, 3H), 5.39 (m, 1H), 5.59 (m, 1H), 6.09 (m, 1H), 7.70 (s, 1H), 11.16 (s, 1H), 12.20 (s, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.57 (q), 38.52 (t), 39.81 (t), 51.93 (d), 60.13 (q), 121.54 (s), 129.25 (d), 137.34 (d), 140.00 (d), 147.70 (s), 148.71 (s), 156.27 (s), 172.71 (s), 172.86 (s); MS m/z (% rel int) 331 ($M^{+\cdot}$, 0.6), 309 (0.2), 295 (0.5), 281 (3), 263 (1), 193 (3), 138 (19), 97 (20), 79 (56), 69 (30), 55 (42), 36 (100); Anal. Calcd for $C_{15}H_{17}N_5O_4$ (331.33): C, 54.38; H, 5.17; N, 21.14. Found: C, 54.63; H, 5.11; N, 21.31.

(±)-*cis*-2-Acetamido-1,7-dihydro-7-[4-(methoxycarbonylmethyl)-2-cyclopenten-1-yl]-6*H*-purin-6-one (16)

^{1}H NMR ($CDCl_3$) δ 1.54 (dt, J = 13.7, 6.3 Hz, 1H), 2.38 (m, 4H), 2.51 (dd, J = 15.7, 6.8 Hz, 1H), 3.01 (dt, J = 13.7, 8.2 Hz, 1H), 3.20 (m, 1H), 3.63 (s, 3H), 5.93 (m, 2H), 6.18 (m, 1H), 7.81 (s, 1H), 11.62 (s, 1H), 12.35 (bs, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.84 (q), 39.84 (2 x C: C-5', C-4a'), 41.42 (d), 51.82 (d), 63.08 (q), 112.17 (s), 128.61 (d), 140.76 (2 x C: C-2', J_{CH} = 174.7 Hz, and C-8, J_{CH} = 212.7 Hz), 148.25 (s), 153.52 (s), 157.08 (s), 172.38 (s), 173.70 (s); Anal. Calcd for $C_{15}H_{17}N_5O_4$ (331.33): C, 54.38; H, 5.17; N, 21.14. Found: C, 54.31; H, 5.22; N, 21.28.

(±)-*cis*-(4-Benzyloxycyclopent-2-enyl)acetic acid (17)

A mixture of 37.1 g (238 mmol) of alcohol **1** and 80 g (1.4 mol) of powdered KOH in 500 ml of 1,4-dioxane was refluxed under stirring for 1 h. After cautious addition of 113 ml (950 mmol) of benzyl bromide in four portions refluxing was continued overnight. Water was added and the reaction mixture was extracted with diethyl ether (5 x 100 ml) to remove benzyl alcohol and dibenzyl ether. The aqueous layer was acidified with conc. HCl to pH 2 and extracted with diethyl ether (6 portions of 100 ml). The combined latter organic extracts were dried (Na_2SO_4), and concentrated *in vacuo* to yield 52.4 g (95%) of crude **17** as dark red oil. An analytical sample was purified by flash chromatography (ethyl acetate/toluene 1/2 v/v to remove traces of by-products, then ethyl acetate).

^{1}H NMR ($CDCl_3$) δ 1.54 (dt, J = 13.6, 5.0 Hz, 1H), 2.55 (m, 3H), 2.56 (d, 2H), 2.61 (m, 1H), 3.02 (m, 1H), 5.96 (s, 2H), 7.34 (m, 5H), 8.50 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 36.77, 40.14, 40.42, 70.80, 83.71, 127.48, 127.71, 128.29, 131.79, 137.50, 138.45, 176.95.

(±)-*cis*-(4-Benzyloxycyclopent-2-enyl)methyl isocyanate (18)

52.0 g (224 mmol) of carboxylic acid **17** was dissolved in 700 ml of acetone and cooled to -30 °C. 53 ml (380 mmol) of Et_3N was added and 32 ml (330 mmol) of ethyl chloroformate was dropped in slowly within 10 min. After complete conversion the corresponding mixed anhydride was treated with 31 g (480 mmol) of NaN_3, dissolved in 50 ml of water, and the reaction was warmed to room temperature and stirred for about 30 min (until the carboxylic azide was formed quantitatively). 300 ml of water and 300 ml of toluene were added, the reaction mixture filtered over a pad of Celite® and the aqueous layer was reextracted three times with 200 ml of toluene. The combined organic extracts were dried ($MgSO_4$), concentrated *in vacuo* to a volume of about 600 ml and dropped into a flask with boiling toluene (200 ml). After the liberation of nitrogen had ceased refluxing was continued for 15 min and then the solution was evaporated *in vacuo*. Bulb-to-bulb distillation yielded 44.1 g (86%) of isocyanate **18** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.59 (dt, J = 13.7, 4.7 Hz, 1H), 2.43 (dt, J = 13.7, 7.7 Hz, 1H), 2.88 (m, 1H), 3.28-3.40 (ABX, J_{AB} = 12.9 Hz, J_{AX} = 6.4 Hz, 2H), 4.54-4.63 (AB, J = 11.8 Hz, 2H), 4.64 (m, 1H), 5.94 (m, 1H), 6.06 (dt, J = 5.7, 1.9 Hz, 1H), 7.27-7.39 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.21 (t), 45.76 (d), 47.43 (t), 70.98 (t), 83.40 (d), 122.21 (s), 127.53 (d), 127.88 (d), 128.36 (d), 133.97 (d), 134.81 (d), 138.62 (s); MS m/z (% rel int) 229 ($M^{+\cdot}$, 0.6), 211 (0.3), 172 (0.8), 138 (10), 123 (60), 107 (83), 91 (100), 79 (65), 65 (43), 56 (39), 51 (31), 39 (38); IR (KBr) ν 3046, 2896, 2275, 1720, 1496, 1454, 1360, 1079, 869, 738, 699, 592 cm^{-1}; Anal. Calcd for $C_{14}H_{15}NO_2$ (229.28): C, 73.34; H, 6.59; N, 6.11. Found: C, 73.27; H, 6.69; N, 6.10.

(±)-*cis*-(4-Benzyloxycyclopent-2-enyl)methylamine (19)

44.0 g of isocyanate **16** was dissolved in 300 ml of THF and 150 ml of water and cooled to 0 °C. To the vigorously stirred solution was added a cooled (0 °C) solution of 6.8 g (170 mmol) of KOH in 50 ml of water within 2 min and vigorous stirring was continued until complete conversion was achieved. The reaction mixture was evaporated *in vacuo* to remove THF, acidified to pH 9-10, extracted with CH_2Cl_2, dried (Na_2SO_4), and concentrated *in vacuo*. Purification by bulb-to-bulb distillation yielded 37.4 g (95%) of amine **19** as a colourless oil. Flash chromatography (petrol ether/ethyl acetate 3/1 v/v) of the residue yielded 1.4 g (3%) of the corresponding urea **19a**.

^{1}H NMR ($CDCl_3$) δ 1.51 (dt, J = 13.6, 4.1 Hz, 1H), 2.37 (dt, J = 13.6, 7.4 Hz, 1H), 2.61 (bs, 2H, -NH_2), 2.74 (m, 3H), 4.50-4.59 (AB, J = 11.8 Hz, 2H and m, 1H), 5.91 (d, J = 5.7 Hz, 1H), 5.96 (d, J = 5.7 Hz, 1H), 7.25-7.35 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.30 (t), 46.07 (t), 46.71 (d), 70.86 (t), 83.62 (d), 127.47 (d), 127.69 (d), 128.31 (d), 132.41 (d), 136.47 (d), 138.59 (s); MS m/z (% rel int) 203 ($M^{+\cdot}$, 0.2), 156 (0.2), 138 (5), 107 (7), 95 (56), 91 (77), 77 (26), 66 (100), 51 (28), 39 (66), 31 (7); IR (KBr) ν 3043, 2880, 1573, 1473, 1369, 1321, 1075, 1028, 740, 698, 611 cm^{-1}; Anal. Calcd for $C_{13}H_{17}NO$ (203.28): C, 76.81; H, 8.43; N, 6.89. Found: C, 77.02; H, 8.37; N, 6.87.

(±)-*cis*-N,N'-Bis[(4-benzyloxycyclopent-2-enyl)methyl]urea (19a)

mp: 114-5 °C; ^{1}H NMR ($CDCl_3$) δ 1.50 (dt, J = 13.9, 3.2 Hz, 2H), 2.26 (dt, J = 13.9, 7.7 Hz, 2H), 2.78 (m, 2H), 3.14 (m, 4H), 4.47-4.56 (m, 6H), 4.83 (m, 2H), 5.82 (m, 2H), 5.92 (m, 2H), 7.27-7.35 (m, 10H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.38 (t), 44.08 (t), 44.50 (d), 70.99 (t), 83.63 (d), 127.79 (d), 127.90 (d), 128.58 (d), 132.26 (d), 137.35 (d), 138.74 (s), 159.02 (s); MS m/z (% rel int) 433 (MH^+, 0.1), 367 (0.4), 324 (0.7), 259 (8), 151 (23), 106 (37), 91 (100), 77 (65), 66 (61), 51 (68), 39 (65); IR (KBr) ν 3332, 2861, 1631, 1571, 1453, 1364, 1258, 1094, 1063, 738, 697 cm^{-1}; Anal. Calcd for $C_{27}H_{32}N_2O_3$ (432.56): C, 74.97; H, 7.46; N, 6.48. Found: C, 75.38; H, 7.33; N, 6.59.

(±)-*cis*-N-(4-Benzyloxycyclopent-2-enyl)methyl benzamide (20)

To 37.0 g of amine **19** (182 mmol) was added 40 ml (290 mmol) of Et_3N, dissolved in 300 ml of CH_2Cl_2, and cooled to 0 °C. 29 ml (250 mmol) of benzoyl chloride dissolved in 50 ml of CH_2Cl_2 was added and the reaction was stirred overnight. 30 ml of methanol was added and stirred for 30 min to react excess benzoyl chloride. The reaction mixture was washed with 1 N aqueous HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), evaporated *in vacuo* and purified by flash chromatography (ethyl acetate/petrol ether 1/4 v/v) to yield 54.6 g (98%) of compound **20**, which crystallised on standing, the overall yield, calculated from starting material **1**, was 75%.

mp: 72-3 °C; ^{1}H NMR ($CDCl_3$) δ 1.77 (d, J = 14.3 Hz, 1H), 2.38 (dt, J = 14.3, 8.3 Hz, 1H), 3.12 (m, 1H), 3.46 (dt, J = 13.5, 4.1 Hz, 1H), 3.67 (dt, J = 13.5, 5.3 Hz, 1H), 4.55 (m, 3H), 5.96 (m, 1H), 6.04 (m, 1H), 6.99 (bs, 1H, -NH), 7.15 (m, 2H), 7.29 (m, 6H), 7.72 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.40 (t), 42.87 (t), 43.40 (d), 71.60 (t), 83.57 (d), 127.12 (d), 127.89 (d), 128.03 (d), 128.41 (d), 128.65 (d), 131.19 (d), 132.62 (d), 134.81 (s), 137.71 (d), 138.40 (s), 168.06 (s); MS m/z (% rel int) 307 ($M^{+\cdot}$, 0.3), 242 (11), 201 (15), 134 (61), 105 (100), 91 (51), 77 (39), 66 (57), 51 (15), 39 (6); IR (KBr) ν 3322, 2889, 1643, 1539, 1489, 1367, 1305, 1092, 1068, 1027, 738, 699 cm^{-1}; Anal. Calcd for $C_{20}H_{21}NO_2$ (307.39): C, 78.15; H, 6.89; N, 4.56. Found: C, 77.91; H, 6.90; N, 4.65.

(±)-*cis*-N-[(4-Benzyloxycyclopent-2-enyl)methyl]-N-nitrosobenzamide (21)

CAUTION: This reaction has to be carried out in a well working hood and appropriate safety clothing has to be worn!

Preparation of N_2O_4

To a flask with 200 ml of preheated (about 150 °C) and well stirred conc. sulphuric acid were added **cautiously** 100 g of $NaNO_2$ in small portions *via* a Normag® powder addition funnel and 50 ml of conc. sulphuric acid within about 1 h. The produced mixture of NO_2 and NO was removed by a N_2-stream, washed with glacial acetic acid, dried in a cooled (0 °C) funnel filled with *Raschig* rings and condensed in a four-neck

flask cooled with liquid N_2. The amount of N_2O_4, produced by this method is sufficient for the reaction of about 130 mmol of amides, in this case of benzamide **20**.

To the produced N_2O_4 dissolved in 100 ml of carbon tetrachloride was added slowly (the solution was dark green; the cooling bath with liquid N_2 was removed and an ice bath was used instead) 40 g (130 mmol) of benzamide **20** dissolved in 80 ml carbon tetrachloride. After 5 min 100 g of NaOAc was added *via* a Normag® powder addition funnel. Through the bright yellow solution was bubbled N_2 for 30 min, and the mixture was then poured into 200 ml of ice-water. Extraction with CH_2Cl_2 (3 x 100 ml), washing the organic layer with saturated aqueous $NaHCO_3$, drying over Na_2SO_4, and evaporation *in vacuo* yielded the thermally unstable N-nitrosobenzamide as a yellow oil, which has to be reacted immediately to the corresponding benzoate **22**.

^{1}H NMR ($CDCl_3$) δ 1.60 (dt, J = 13.8, 4.5 Hz, 1H), 2.32 (dt, J = 13.8, 7.9 Hz, 1H), 2.93 (m, 1H), 4.06-4.20 (ABX, J_{AB} = ≈12 Hz, J_{AX} = 5.6 Hz, 2H), 4.54 (m, 1H), 4.55-4.65 (AB, J = 11.8 Hz, 2H), 5.82 (m, 1H), 5.93 (m, 1H), 7.30-7.56 (m, 7H), 7.77 (m, 1H), 8.13 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.48 (t), 43.50 (d), 68.05 (t), 71.06 (t), 83.44 (d), 127.83 (d), 128.06 (d), 130.17 (d), 130.71 (d), 132.27 (d), 132.85 (d), 133.46 (d), 135.40 (d), 138.71 (s), 173.67 (s).

(±)-*cis*-(4-Benzyloxycyclopent-2-enyl)methyl benzoate (22)

The crude N-nitrosobenzamide **21** was dissolved in 6 l of petrol ether (boiling point 80 °C) and refluxed overnight. Evaporation under reduced pressure and flash chromatography (ethyl acetate/petrol ether 1/9 v/v) yielded 34.3 g (86%) of benzoate **22** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.78 (dt, J = 13.6, 4.9 Hz, 1H), 2.49 (dt, J = 13.6, 7.9 Hz, 1H), 3.09 (m, 1H), 4.32-4.40 (ABX, J_{AB} = 10.5 Hz, J_{AX} = 6.3 Hz, 2H), 4.56-4.65 (AB, J = 11.8 Hz, 2H), 4.70 (m, 1H), 6.04 (d, J = 6.0 Hz, 1H), 6.08 (d, J = 6.0 Hz, 1H), 7.26-7.47 (m, 7H), 7.57 (m, 1H), 8.14 (d, J = 7.9 Hz, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 33.86 (t), 43.92 (d), 68.08 (t), 71.02 (t), 83.81 (d), 127.54 (d), 127.74 (d), 128.38 (d), 129.71 (d), 130.49 (s), 132.88 (d), 133.36 (d), 135.01 (d), 138.86 (s), 166.52 (s); MS m/z (% rel int) 308 (M^+, 0.1), 256 (1), 202 (6), 186 (2), 123 (13), 105 (99), 91 (100), 77 (64), 66 (20), 51 (29), 39 (16); IR (KBr) ν 2870, 1717, 1453, 1273, 1107, 1067, 1026, 712 cm^{-1}; Anal. Calcd for $C_{20}H_{20}O_3$ (308.38): C, 77.90; H, 6.54. Found: C, 78.04; H, 6.58.

(±)-*cis*-1-Acetoxy-4-(acetoxymethyl)cyclopent-2-ene (24)

Into a flask equipped with a mechanical stirrer about 700 ml of ammonia was condensed and cooled to about -70 °C. 6.7 g (290 mmol) of sodium was added in small portions and stirred for 5 min. 20 g (64.9 mmol) of benzyl ether **22**, diluted in 50 ml of 1,4-dioxane was dropped slowly into the dark blue solution and stirred for an additional 10 min. Saturated NH_4Cl solution was added until the blue colour disappeared and ammonia was evaporated. The residue was coevaporated with toluene to dryness to yield crude alcohol **23**.

This residue was treated with 30 ml (370 mmol) of pyridine and 300 ml of CH_2Cl_2, cooled to 0 °C and 25 ml (265 mmol) of acetic anhydride was added slowly. After complete conversion 10 ml of methanol was added. The reaction was stirred for further 30 min and evaporated *in vacuo*. 1 N aqueous HCl was added until pH 1 was reached, the layers were separated, the organic phase was washed with water and aqueous $NaHCO_3$ solution, dried (Na_2SO_4), and evaporated *in vacuo*. Flash chromatography (ethyl acetate/hexane 1/3 v/v) yielded 9.0 g (70%) of acetate **24** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.52 (dt, J = 14.4, 4.1 Hz, 1H), 1.99 (s, 3H), 2.02 (s, 3H), 2.44 (dt, J = 14.4, 8.0 Hz, 1H), 2.88 (m, 1H), 3.99 (d, J = 6.7 Hz, 2H), 5.59 (m, 1H), 5.86 (m, 1H), 5.95 (m, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 20.91 (q), 21.25 (q), 33.57 (t), 43.91 (d), 67.44 (t), 79.27 (d), 131.56 (d), 137.04 (d), 170.80 (s), 170.97 (s); IR (KBr) ν 3417, 2952, 1734, 1438, 1370, 1242, 1032, 764 cm^{-1}; Anal. Calcd for $C_{10}H_{14}O_4$ (198.22): C, 60.59; H, 7.12. Found: C, 60.15; H, 7.09.

(±)-*cis*-1-[4-(Acetoxymethyl)-2-cyclopenten-1-yl]thymine (25)

^{1}H NMR ($CDCl_3$) δ 1.34 (dt, J = 14.0, 6.7 Hz, 1H), 1.89 (s, 3H), 2.05 (s, 3H), 2.74 (dt, J = 14.0 Hz, 8.6 Hz, 1H), 3.05 (m, 1H), 4.05 (dd, J = 10.9, 5.5 Hz, 1H), 4.14 (dd, J = 10.9, 5.7 Hz, 1H), 5.67-5.74 (m, 2H), 6.06 (dt, J = 5.6, 2.2 Hz, 1H), 7.03 (s, 1H), 9.81 (bs, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 12.71 (q), 20.98 (q), 34.15 (t), 44.24 (d), 61.06 (d), 66.59 (t), 111.27 (s), 130.84 (d), 136.51 (d), 138.17 (d), 151.45 (s), 164.23 (s), 170.99 (s); Anal. Calcd for $C_{13}H_{16}N_2O_4$ (264.28): C, 59.08; H, 6.10; N, 10.60. Found: C, 58.81; H, 6.13; N, 10.60.

(±)-*cis*-1-[4-(Acetoxymethyl)-2-cyclopenten-1-yl]uracil (26)

^{1}H NMR ($CDCl_3$) δ 1.32 (m, 1H), 2.04 (s, 3H), 2.76 (dt, J = 14.3, 8.9 Hz, 1H), 3.06 (m, 1H), 4.03 (dd, J = 11.1, 5.4 Hz, 1H), 4.12 (dd, J = 11.1, 5.7 Hz, 1H), 5.70 (m, 2H and d, J = 8.2 Hz, 1H), 6.08 (dt, J = 5.7, 2.8 Hz, 1H), 7.27 (d, J = 8.2 Hz, 1H), 10.2 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 21.82 (q), 34.25 (t), 44.30 (d), 61.39 (d), 66.51 (t), 102.70 (d), 130.36 (d), 138.86 (d), 140.90 (d), 151.38 (s), 163.98 (s), 170.95 (s); Anal. Calcd for $C_{12}H_{14}N_2O_4$ (250.25): C, 57.59; H, 5.64; N, 11.19. Found: C, 57.74; H, 5.69; N, 11.13.

(±)-*cis*-N^2-Acetyl-9-[4-(acetoxymethyl)-2-cyclopenten-1-yl]guanine (27)

^{1}H NMR ($CDCl_3$) δ 1.83 (dt, J = 13.9, 3.4 Hz, 1H), 2.10 (s, 3H), 2.34 (s, 3H), 2.78 (dt, J = 13.9, 9.1 Hz, 1H), 3.19 (m, 1H), 4.19 (dd, J = 10.2, 6.5 Hz, 1H), 4.48 (dd, J = 10.2, 6.5 Hz, 1H), 5.10 (bs, 1H), 5.48 (m, 1H), 5.82 (m, 1H), 6.06 (m, 1H), 7.69 (s, 1H), 12.10 (bs, 1H, -NH); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.01 (q), 24.17 (q), 33.51 (t), 44.50 (d), 60.82 (d), 66.15 (t), 121.79 (s), 130.16 (d), 136.96 (d), 137.96 (d), 147.27 (s), 148.11 (s), 155.90 (s), 171.61 (s), 172.49 (s); Anal. Calcd for $C_{15}H_{17}N_5O_4$ (331.33): C, 54.38; H, 5.17; N, 21.14. Found: C, 54.23; H, 5.28; N, 21.04.

(±)-*cis*-2-Acetamido-7-[4-(acetoxymethyl)-2-cyclopenten-1-yl]-1,7-dihydro-6*H*-purin-6-one (28)

^{1}H NMR ($CDCl_3$) δ 1.65 (dt, J = 14.0, 5.6 Hz, 1H), 2.03 (s, 3H), 2.43 (s, 3H), 2.97 (dt, J = 14.0, 8.7 Hz, 1H), 3.16 (m, 1H), 4.03-4.16 (ABX, J_{AB} = 9.3 Hz, J_{AX} = 5.5 Hz, 2H), 6.00 (m, 2H), 6.18 (m, 1H), 7.84 (s, 1H), 11.5 (bs, 1H), 12.4 (bs, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.03 (q), 24.91 (q), 36.69 (t), 44.86 (d), 62.95 (d), 66.61 (t), 112.28 (s), 129.72 (d), 138.76 (d), 140.79 (d), 148.24 (s), 153.67 (s), 157.25 (s), 171.05 (s), 173.54 (s); Anal. Calcd for $C_{15}H_{17}N_5O_4$ (331.33): C, 54.38; H, 5.17; N, 21.14. Found: C, 54.33; H, 5.27; N, 21.01.

(±)-*cis*-1-[4-(Hydroxymethyl)-2-cyclopenten-1-yl]thymine (29)

0.4 g (1.51 mmol) of **25** was treated with 0.05 g of sodium in 10 ml of dry methanol at room temperature until complete conversion was achieved. CO_2 was bubbled through the solution and the solvent was removed *in vacuo*. Flash chromatography ($CHCl_3$/MeOH 9/1 v/v) yielded 0.32 g (97%) of thymine **29** as viscous oil.

^{1}H NMR (DMSO-d_6) δ 1.39 (dt, J = 13.9, 5.9 Hz, 1H), 1.79 (s, 3H), 2.52 (dt, J = 13.9, 8.7 Hz, 1H), 2.83 (m, 1H), 3.45 (dd, J = 10.6, 5.2 Hz, 1H), 3.53 (dd, J = 10.5, 5.1 Hz, 1H), 3.2-3.8 (1H), 5.55 (m, 1H), 5.72 (m, 1H), 6.12 (d, J = 4.2 Hz, 1H), 9.60 (s, 1H) ^{13}C NMR and DEPT (DMSO-d_6) δ 12.37 (q), 33.20 (t), 47.53 (d), 60.52 (d), 63.82 (t), 109.18 (d), 130.05 (d), 137.62 (d), 139.40 (s), 151.20 (s), 164.14 (s); Anal. Calcd for $C_{11}H_{14}N_2O_3$ (222.24): C, 59.45; H, 6.35; N, 12.60. Found: C, 59.24; H, 6.33; N, 12.66.

(±)-*cis*-1-[4-(Hydroxymethyl)-2-cyclopenten-1-yl]uracil (30)

0.4 g (1.60 mmol) of **26** was treated as described for **29** to yield after flash chromatography ($CHCl_3$/MeOH 9/1 v/v) 0.32 g (95%) of **30** as viscous oil.

^{1}H NMR ($CDCl_3$) δ 1.38 (dt, J = 13.7, 6.0 Hz, 1H), 2.54 (dt, J = 13.9, 9.0 Hz, 1H), 2.82 (m, 1H), 3.42 (m, 1H), 4.77 (t, J = 4.9 Hz, 1H), 5.55 (m, 2H), 5.72 (m, 1H), 5.61 (d, J = 7.9 Hz, 1H), 6.13 (dt, J = 5.3, 2.6 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 11.30 (bs, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 33.26 (t), 47.52 (d), 60.79 (t), 63.83 (d), 101.55 (d), 129.72 (d), 139.67 (d), 141.92 (d), 151.20 (s), 163.53 (s); Anal. Calcd for $C_{10}H_{12}N_2O_3$ (208.22): C, 57.69; H, 5.81; N, 13.45. Found: C, 57.97; H, 5.76; N, 13.53.

(±)-*cis*-9-[4-(Hydroxymethyl)-2-cyclopenten-1-yl]guanine (31)

To a solution of 0.05 g of $NaNH_2$ in 10 ml of liquid ammonia was added 0.3 g (0.91 mmol) of **27** and stirred for 5 min. 0.5 ml of saturated aqueous NH_4Cl solution was added and the ammonia allowed to evaporate. The residue was evaporated *in vacuo*. Flash chromatography ($CHCl_3$/MeOH 3/1 v/v) yielded 0.2 g (90%) of carbovir (**31**).

Analytical data in accordance with those published by *Vince*;[1b] Anal. Calcd for $C_{11}H_{13}N_5O_2$ (247.26): C, 53.43; H, 5.30; N, 28.32. Found: C, 53.15; H, 5.16; N, 27.88.

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