

Palladium(0)-catalyzed syntheses of cyclopentenyl-nucleoside analogues

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Abstract

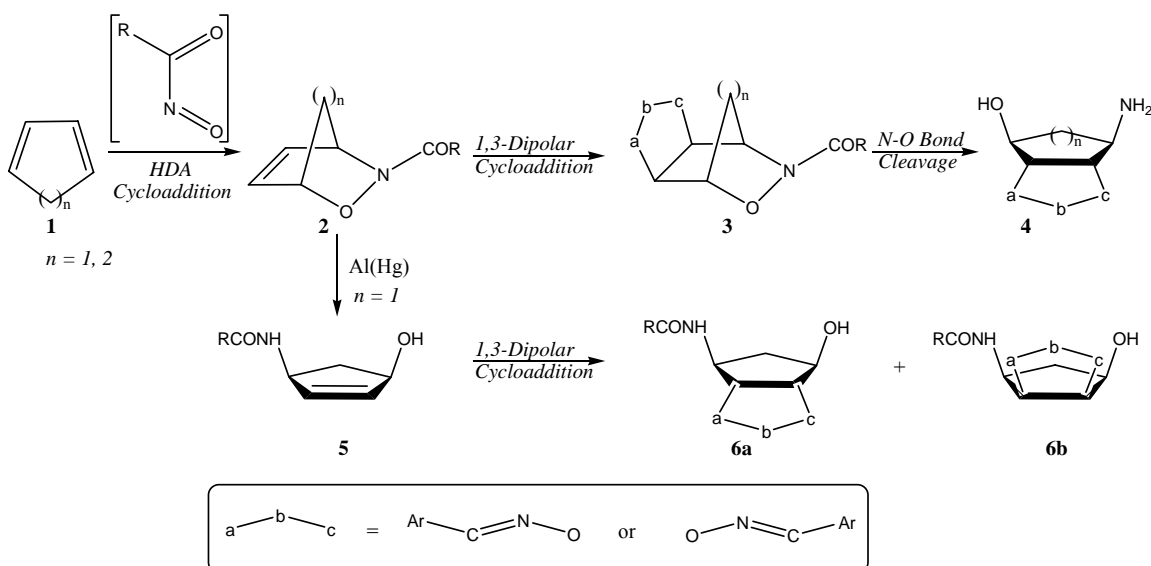
The *N*-benzoylamino-2-cyclopenten-1-ol, derived from the nitrosocarbonyl hetero Diels-Alder cycloaddition reaction followed by the mild reductive N-O bond cleavage, allows for the preparation of cyclopentenyl-nucleoside analogues through the palladium(0)-catalyzed addition of both purine and pyrimidine heterobases to the allylic acetate derivative with retention of the starting material stereochemistry. A systematic study is performed on different heterobases to test the general application of the protocol.

Keywords: Nitrosocarbonyl, hetero Diels-Alder cycloaddition, palladium(0)-catalyzed reactions, heterobases, nucleoside analogues

Introduction

Because of the imperative defence from infections, there is the never ending demand of new antagonists and the intense current interest in the synthesis of carbocyclic nucleoside analogues, that are widely preferred due to their metabolic stability.¹ During recent years, nucleoside targets have been investigated in the search of effective treatment for various herpes type viruses² yielding a profusion of synthetic activity that helped both the understanding in action mechanisms and in widening the pharmacological applications.³ In fact, carbocyclic nucleosides have been the focus also in the development of new antitumor therapeutic agents⁴ as well as in the selective inhibition of human immunodeficiency virus (HIV).⁵ Moreover these compounds were taken into consideration as agrochemicals⁶ and as antifungal drugs⁷ because of their wide range of biological properties. The development of further effective therapeutic agents against Hepatitis C virus (HCV) is also an urgent public health requirement.⁸ Nevertheless, due to the not ignored toxicity, the use of these nucleosides has been limited in the clinical applications of human diseases.⁹

The discovery of new structures displaying increased activities and low toxicities is challenging various research groups and we have recently proposed a rapid access to carbocyclic nucleosides containing a fused isoxazoline ring starting from cyclopentadiene or 1,3-cyclohexadiene.¹⁰ The route involves an hetero Diels-Alder (HDA) cycloaddition reaction of nitrosocarbonyl intermediates (R-CONO) followed by a 1,3-dipolar cycloaddition of nitrile oxides, cleavage of the N-O tether and elaboration of the heterocyclic aminols into nucleosides *via* the linear construction of purine and pyrimidine heterocycles. The pivotal step is represented by the chemistry of nitrosocarbonyls that are fleeting intermediates and powerful dienophiles in HDA reactions.¹¹ Cyclic dienes **1** efficiently trap these intermediates affording the HDA adducts **2** (Scheme 1) which were found highly reactive dipolarophiles. From the 1,3-dipolar cycloadducts **3** the stereoregulate anti aminols **4** were easily obtained and the heterobases were build up through appropriate reagents.



Scheme 1

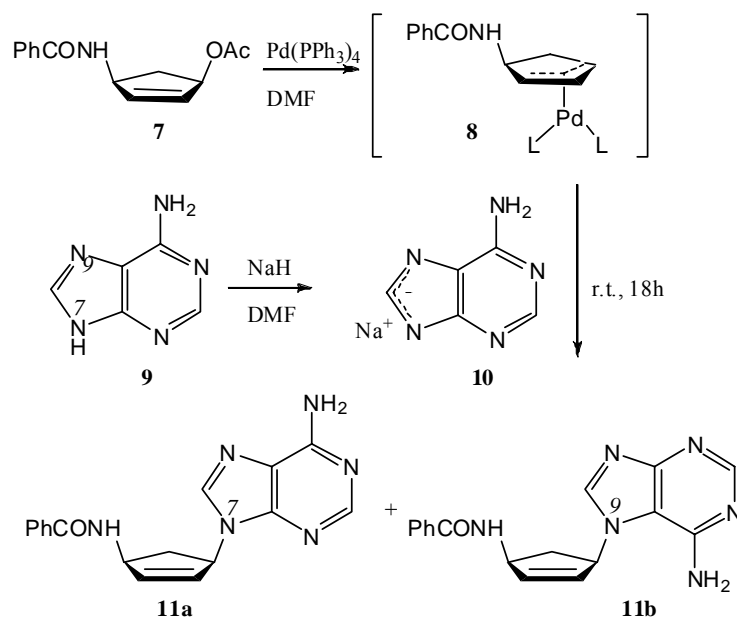
Starting from the 2,3-oxazanorborn-5-ene HDA cycloadduct **2** ($n = 1$), the mild reductive cleavage of the N-O bond with Al(Hg) afforded the stereodefined *cis* 4-amido-2-cyclopenten-1-ol **5** whose 1,3-dipolar cycloadditions with nitrile oxides have been thoroughly investigated.¹² It was found that the *syn* directing effect of the allylic OH and NHCOR groups is completely offset by a strong intramolecular hydrogen bond favoring the formation of cycloadducts **6a**. Removal of the intramolecular hydrogen bond by OH protection or oxidation of the alcoholic functionality activated the *syn*-directing ability of the amido substituent and provided a convenient *syn* stereoselective approach to cycloadduct **6b**.

On the basis of these results, we considered the possibility to employ the cyclopentenyl derivative **5** as an alternative source of C-carbo nucleosides.¹³ The strategy relies on the metal-catalyzed functionalization of the esters of cyclic allylic alcohols with nucleophiles,¹⁴ heterobases in the specific case. P. M. Woster and N. S. Sirisoma reported the use of the acetates

of N-Boc protected 4-aminocycloalk-2-en-1-oles in Pd(0)-catalyzed amination with benzylamine or phthalimide to give the corresponding protected amines.¹⁵ B. M. Trost and co-workers described an enantioselective Pd-catalyzed desymmetrization of the benzoate of the *cis*-cyclopent-ene-1,4-diol as a key-step towards the synthesis of (-)-Neplanocin,^{3c} while M. von Janta-Lipinski *et al.* prepared adenosine analogues through the use of the 4-phosphonates of cyclopent-2-en-1,4-dioles using Pd-tetrakis as catalyst.^{5c} The acetates of 5-substituted derivatives of cyclopent-2-ene-1-ols were also used to prepare nucleoside analogues as anti-HIV agents under Pd-catalyzed conditions by R. A. MacKeith^{5e} and by M. T. Crimmins.^{5f} A single application has been reported from a N-Boc protected 4-aminocyclopent-2-ene-1-ol acetate derivative obtained from 2,3-oxazanorbornene compound by M. J. Miller who detailed the Pd-mediated functionalization with adenine.¹⁶ In all these as well as other cases¹⁴ Pd(0) catalysts were efficiently used in the pivotal steps of the syntheses and the ready stereoselective substitution of the alcoholic moiety with heterobases represents an interesting evolution in the field of anti-viral agents with low cytotoxicity.¹⁷ The stereodefined *cis* 4-amido-2-cyclopenten-1-ol **5** may be a useful synthon for the construction of nucleoside analogues and other derivatives through the easy functionalization of the C=C double bond. This paper gives a detailed account on the convergent approach to a variety of both purine and pyrimidine carbocyclic derivatives through the palladium(0)-catalyzed protocol. A systematic study is performed on different heterocyclic bases to test the general application of the method.

Results and Discussion

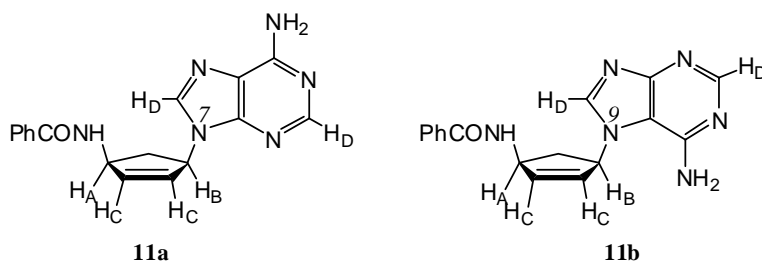
The 4-benzoylamino-2-cyclopenten-1-ol acetate **7** is prepared according to the reported^{14a} Ac₂O/Et₃N/DMAP procedure in anhydrous dichloromethane (DCM) solution in quantitative yield. The substrate **7**, now bearing a good leaving group (OAc), smoothly reacts in the presence of catalytic Pd(PPh₃)₄ (5% mol) in anhydrous dimethylformamide (DMF) solution at r.t. undergoing oxidative addition of the allylic cation, that coordinates to the Pd(0) complex (Scheme 2).^{5d-e,13,14f,g,18} The newly formed π -allylic complex **8** adds the adenine sodium salt **10**, previously generated *in situ* upon treatment of adenine **9** (1.2 equivs.) with a slight excess (1.5 equivs.) of NaH in DMF solution. The adenine salt addition occurs *syn* to the benzoylamine group as the Pd complex occupies the opposite face. As it is expected, the retention of the stereochemistry of the starting material **7** in the final products **11** is observed, which is in agreement with the reported examples.¹⁹ The reaction is left under stirring at r.t. for 18h and the choice of Pd tetrakis was done on the basis of the best results obtained in literature for similar substrates.^{13,14,16,19} Upon quenching of the reaction with water and extraction with DCM, the crude reaction mixture is submitted to chromatographic separation on silica gel column by eluting with CHCl₃ and then CHCl₃/MeOH 9/1 mixtures.



Scheme 2

Two isomeric adenine derivatives **11a,b** were isolated in 42 % and 35 % yields, respectively. Their structures rely upon the analytical and spectroscopic data. In particular, the ^1H - and ^{13}C -NMR spectra were consistent for a 1:1 ratio between the adenine and the cyclopentenyl moieties for compounds of general formula $\text{C}_{17}\text{H}_{16}\text{N}_6\text{O}$. The isomeric nature of products **11a,b** is related to the two possible orientations of the adenine salt **10** when adds the Pd complex, due to the anion delocalization between N7 and N9 in the heterobase moiety. Table 1 reports the representative chemical shifts for the two isomers **11a,b**.

Table 1. ^1H - and ^{13}C -NMR chemical shifts of compounds **11a,b**

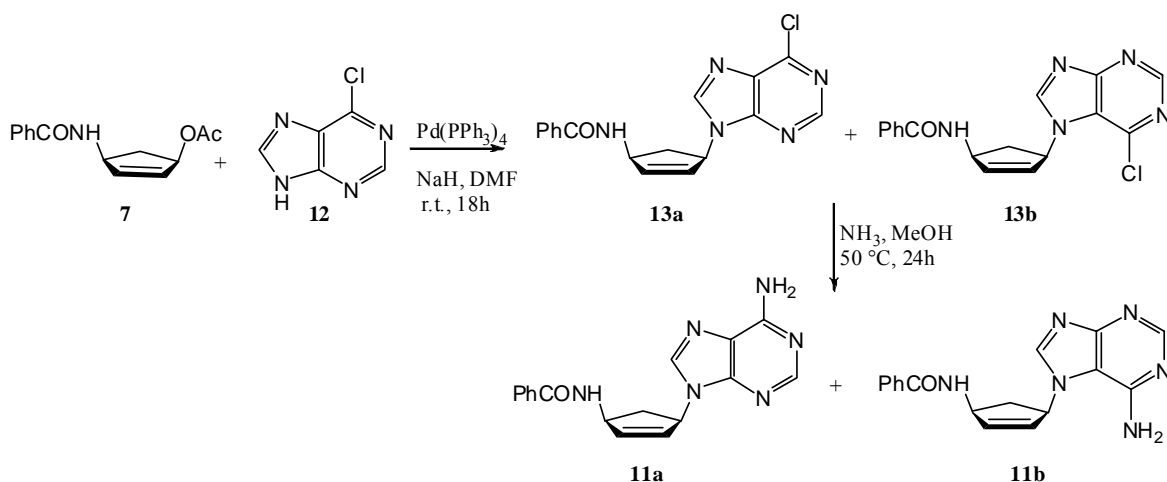


	^1H -NMR ^a				^{13}C -NMR ^b			
	A	B	C	D	A	B	C	D
11a	5.38	5.69	6.02	8.08	55.1	60.9	132.1	141.8
			6.20	8.19			136.6	153.4
11b	5.28	5.77	6.05	7.84	53.8	65.0	130.2	142.9
			6.20	8.42			137.8	151.6

^aProtons A, B and C are multiplets; protons D are singlets. ^bCarbons A-D are doublets.

None of these data allowed to assign the correct stereochemistry. More concrete evidences were gained from further appropriate experiments. NOESY experiments confirmed the *cis* relative position in both the isomers **11a,b** of the adenine moiety and the benzoylamino group. HMBC experiments allowed to find out the decisive connections via $^3J_{C-H}$ between the proton H_B at 5.69 δ and the C4 at 150.4 δ in the major isomer **11a** and the proton H_B at 5.77 δ and the C5 at 148.7 δ in the minor isomer **11b**.^{3f,14,16}

The 4-benzoylamino-2-cyclopenten-1-ol acetate **7** also reacts with the 6-chloropurine **12** under the same experimental conditions to afford, after the usual work-up and chromatographic separation, the chloropurine derivatives **13a,b** in 47 % and 13% yields, respectively (Scheme 3).

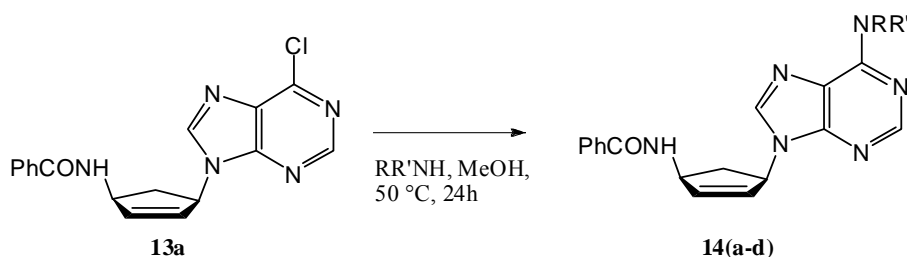


Scheme 3

The structure of compound **13a** relies upon the relative analytical and spectroscopic data. In particular, the ^1H - and ^{13}C -NMR spectra were consistent for a 1:1 ratio between the 6-chloroadenine **12** and the cyclopentenyl moieties for compounds of general formula $\text{C}_{17}\text{H}_{14}\text{N}_5\text{OCl}$. The protons of the purine ring are found at 8.74 and 8.59 δ while the rest of the signals belonging to the cyclopentenyl moiety are found in the usual range and the amide NH at 8.31 δ . NOESY experiments confirmed the *cis* relative position in the structure of **13a** of the purine moiety and the benzoylamino group. The structure of compound **13b** also relies upon the relative analytical and spectroscopic data. The ^1H - and ^{13}C -NMR spectra were consistent for a 1:1 ratio between the 6-chloroadenine **12** and the cyclopentenyl moieties for compounds of general formula $\text{C}_{17}\text{H}_{14}\text{N}_5\text{OCl}$. The protons of the purine ring are found at 8.77 and 8.65 δ while the signals belonging to the cyclopentenyl moiety are found in the usual range and the amide NH at 8.01 δ .

From the chloro-purine nucleosides **13a,b**, the adenine derivatives **11a,b** could be obtained by simple treatment with ammonia in methanol at 50 °C for 24h in a sealed flask.²⁰ Products **11a,b** were isolated in 89 % and 76 % yields, respectively, and found identical to the samples previously prepared.

From the major chloro-purine nucleoside **13a** a variety of derivatives can be obtained by nucleophilic substitution.²⁰ On heating MeOH solutions of **13a** at 50 °C in the presence of an excess of differently substituted primary and secondary amines, the amino derivatives **14(a-d)** could easily be obtained (Scheme 4).



Scheme 4

Table 2 reports the chemical yields and physical constants of purine nucleosides **14(a-d)** which have been fully characterized through their analytical and spectroscopic data.

Table 2. Yields and physical constants of purine derivatives **14(a-d)**

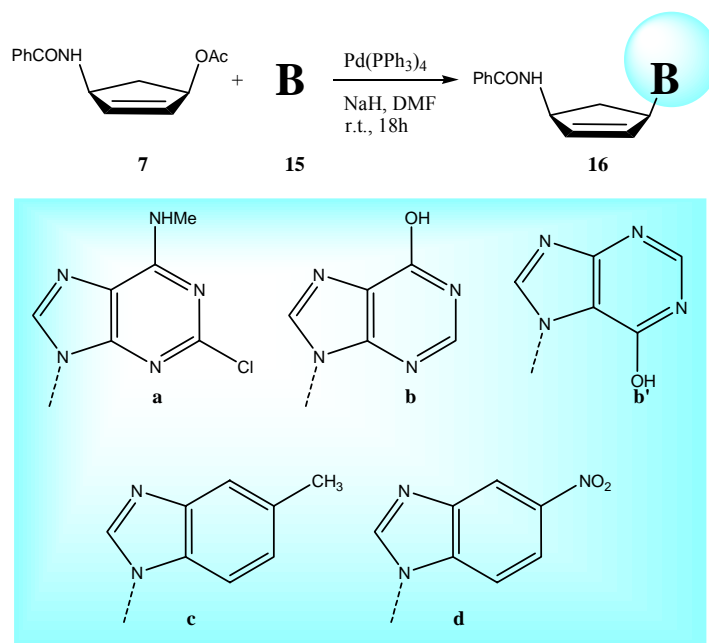
14	R	R'	mp °C (Solv.)	Yields %
a	H	Me	>210 (dec.) (<i>i</i> Pr ₂ O/EtOH)	99
b	Et	Et	127-130 (<i>i</i> Pr ₂ O/EtOH)	99
c	H	cPr [§]	193-195 (<i>i</i> Pr ₂ O/EtOH)	98
d	H	CH ₂ Ph	202-205 (<i>i</i> Pr ₂ O/EtOH))	97

[§]. cPr - cyclopropyl

In all the cases the products show the characteristic purine CH=N proton singlets ranging between 8.08 and 8.29 δ and the benzoyl amide NH deshielded at 9.1-9.3 δ . In compounds **14a,c** a second NH proton is found at 6.87 and 6.80 δ , respectively, because of the new substitution on the position 6 of the purine ring with primary amines. The same type of proton was expected in product **14d** where benzylamine was inserted on the 6-chloropurine ring; it is found deshielded on beneath the aromatic protons around 7.4 δ . The other proton belonging to the cyclopentenyl moiety and to the amine substituents are found in the usual ranges. To corroborate the *cis* relationship between the purine ring and the benzoylamido groups, NOESY experiments were performed showing cross-peaks between the amide NH proton and one of the two methylene

protons of the cyclopentene ring while the other relates with the two CH-N protons of the cyclopentene ring.

In order to test the application of the $\text{Pd}(\text{PPh}_3)_4$ catalyzed reactions as a general protocol for the synthesis of cyclopentenyl-nucleoside analogues, a few other purines **15a,b** as well as benzoimidazole derivatives **15c,d** have been tested in the reaction with the 4-benzoylamino-2-cyclopenten-1-ol acetate **7** under the usual conditions (Scheme 5). Upon quenching of the reactions with water and extraction with DCM, the crude reaction mixture is submitted to chromatographic separation on silica gel column by eluting with CHCl_3 - $\text{CHCl}_3/\text{MeOH}$ 9/1 mixtures. Table 3 reports the chemical yields and physical constants of purine nucleosides **16(a-d)** which have been fully characterized through their analytical and spectroscopic data.



Scheme 5

Table 3. Yields and physical constants of purine derivatives **16(a-d)**

16	mp °C (Solv.)	Yields %
a	>210 (dec.) (<i>i</i> Pr ₂ O)	60
b	>215 (dec.) (<i>i</i> Pr ₂ O)	37
b'	>215 (dec.) (<i>i</i> Pr ₂ O)	12
c	110-112 (<i>i</i> Pr ₂ O/EtOH)	10
d	179-181 (<i>i</i> Pr ₂ O/EtOH)	66

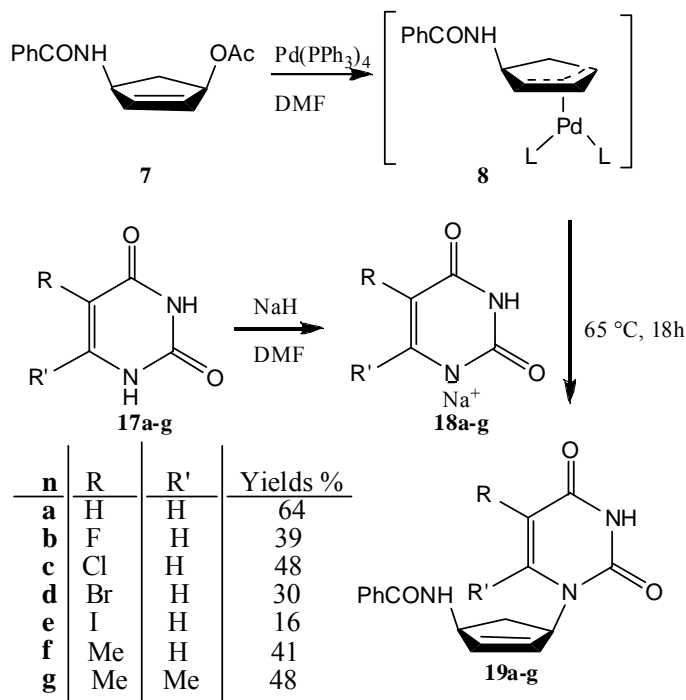
The ¹H-NMR spectra of compound **16a** nicely account for the reported structure with the two different NH groups, the more deshielded at 8.19 δ corresponding to the amide moiety and the

one at 7.81 δ relative to the methylamine substituent of the purine ring, which gives also a singlet at 7.75 δ for the imidazolic CH=N. The reaction with the 6-purinol gave two products **16b,b'**, regioisomeric at the N7 and N9 of the purine ring. The IR spectra of both the products show neat OH bands at 3277 (s) and 3250 (br) cm^{-1} . In the $^1\text{H-NMR}$ spectra (DMSO) the OH groups are strongly deshielded and are found at 12.34 and 11.75 δ and the structure of the purinol ring is completed by the presence of the CH=N protons in the expected region. However, we were unable to distinguish between the two possible structures of compounds **16b,b'** beyond any reasonable doubt. All the HMBC experiments performed in order to establish which one is connected to the cyclohexene moiety through the N7 or N9 failed.

Finally two benzoimidazole derivatives **16c,d** were prepared in variable yields. In **16c** the CH=N proton of the benzoimidazole ring is found at 7.50 δ along with other aromatic signals. The methyl group is also found at 2.45 δ . In **16d** the CH=N proton of the benzoimidazole ring is deshielded at 8.68 δ . For both **16c** and **16d** all the other signals are found in the expected regions.

Other heterobases, such as the 2-amino-6-chloropurine, guanine and hypoxanthine, have been tried under different conditions but without success. Presumably, the catalytic system has to be tuned up to perform the reactions with these or similar heterobases.

Besides the syntheses of the purine and benzoimidazole derivatives, we explored the application of the protocol for the preparation of pyrimidine nucleoside analogues. The experimental conditions previously introduced were not successful and the reactions took place only after heating overnight.^{14c} The uracils **17a-e** and the thymines **17f,g** were completely dissolved in anhydrous DMF at 65 $^\circ\text{C}$ and transformed into the corresponding sodium salts **18a-g** upon addition of a slight excess (1.2 equivs.) of NaH at r.t. (Scheme 6).

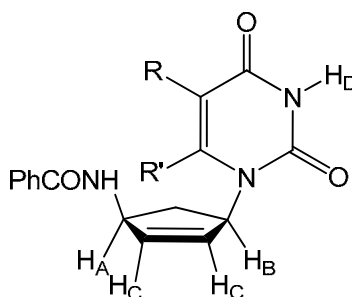


Scheme 6

After stirring for 30 minutes at 65 °C to complete the reaction, the solution is cooled down and 1 equiv. of the substrate **7** is added along with one half equiv. of Pd(PPh₃)₄, both dissolved in anhydrous DMF. The reaction goes to completion by keeping at 65 °C for 18h. After this period of time, quenching was done by addition of water and the solution was extracted with DCM. The residue, obtained upon evaporation of the solvent, was submitted to column chromatography (eluant: CHCl₃ - CHCl₃/MeOH 9/1) to purify the products **19a-g**, which were isolated from fair to good yields.

The analytical and spectroscopic data of **19a-g** were consistent with the assigned structures. Table 4 reports the physical data and the most significant spectroscopic data. In the FT-IR spectra the bands corresponding to the NHCOPh and the CONHCO groups are clearly shown. In the ¹H-NMR spectra the proton signals belonging to the cyclopentenyl moiety (H_{A,B,C}) are in the range between 5.0-6.2 δ. When R'=H, the uracil moieties showed significantly the protons around 7.5-8.7 δ depending on the adjacent substitution. In the case of simple uracil derivative **14a** an additional olefinic proton (R = H) signal is shown at 5.67 δ as a double doublet coupled with that (R'=H) at 7.56 δ (J = 8 and 1.5 Hz). Finally, the CONHCO is characterized by the H_D proton signals highly deshielded in the region around 11-12 δ.

Table 4. Physical and spectroscopic data of compounds **19a-g**



19	m.p. (°C)	FT-IR ν _{NH} (cm ⁻¹)	¹ H-NMR (δ, ppm in DMSO)				
			H _A	H _B	H _C	R'	H _D
a	217-220	3425 (br), 3223 (br)	5.00	5.51	5.87, 6.11	7.56	11.29
b	78-80	3370 (br), 3185 (br)	5.04	5.75	5.87, 6.11	8.32	11.12
c	147-150	3310 (br), 3167 (br)	5.03	5.52	5.91, 6.13	8.67	11.85
d	230 (dec.)	3250 (br), 3150 (br)	5.02	5.52	5.91, 6.15	8.69	11.84
e	194 (dec.)	3310 (br), 3167 (br)	5.00	5.49	5.92, 6.14	8.67	11.69
f	>210 (dec.)	3265 (m), 3163 (w)	5.01	5.51	6.12, 5.88	7.37	11.28
g	>210 (dec.)	3293 (s), 3217 (w)	5.07	5.83	5.83	/	10.98

When the thymine is introduced (R'=Me), the ¹H-NMR spectrum of **19f** shows an additional signal at 1.80 δ corresponding to the methyl on the pyrimidine ring. In the parent compound **19g** two methyls are found at 2.06 and 1.78 δ.

Despite the variable yields of the products **19a-g** obtained, a remarkable selectivity was achieved since in all the cases the pyrimidine rings are linked through the N1 to the cyclopentenyl moiety.

Conclusions

In summary, an efficient preparation of novel carbocyclic nucleoside analogues was achieved and the scope and the limitations of the methods have been displayed. The starting allylic acetate **7** is easily prepared by HDA cycloaddition of nitrosocarbonyl benzene to cyclopentadiene **1** followed by the mild reductive cleavage of the N-O bond with Al(Hg) and expedite acetylation with Ac₂O/Et₃N/DMAP procedure. The palladium(0)-catalyzed addition of both purine, pyrimidine and various heterobases to the allylic acetate allowed to prepare nucleoside compounds with retention of the initial substrate stereochemistry. Further derivatizations are currently developed in order to extend the range of heterobases which can be inserted on the cyclopentenyl ring. The double bond of the nucleosides is also suitable for synthetic elaboration, such as reduction by hydrogenation, oxidation to get the relative diols.¹⁰ The application of the described protocol to the parent cycloadducts **6a,b** is expect to broad the way to a family of nucleosidic compounds and analogues whose application as agonists or antagonists in selected biological targets is actually pursued.

Experimental Section

General Procedures. All melting points are uncorrected. Elemental analyses were done on a C. Erba 1106 elemental analyzer. IR spectra (nujol mulls) were recorded on an FT-IR Perkin-Elmer RX-1. ¹H- and ¹³C-NMR spectra were recorded on a Bruker AVANCE 300 in the specified deuterated solvents. Chemical shifts are expressed in ppm from internal tetramethylsilane (δ). Column chromatography and tlc: silica gel 60 (0.063-0.200 mm) (Merck); eluant CHCl₃. The identification of samples from different experiments was secured by mixed mps and superimposable IR spectra.

Materials. Adenine **9**, 6-chloropurine **12**, uracils **17a-e**, thymines **17f,g**, purines **15a,b**, benzoimidazole **15c,d** and Pd(PPh₃)₄ were purchased from SIGMA-ALDRICH. *Cis* 4-benzoylamino-2-cyclopenten-1-ol **5** was prepared according to the previously reported synthesis.¹² *Cis* 4-benzoylamino-2-cyclopenten-1-ol acetate **7** was prepared upon treatment of **5** with Ac₂O in the presence of Et₃N and catalytic DMAP in anhydrous DCM solution.^{14a}

Synthesis of the adenine derivatives **11a,b**

To an anhydrous DMF solution (10 mL) of adenine **9** (132 mg, 0.98 mmol), 33 mg (1.39 mmol) of NaH (70% in mineral oil) were added under nitrogen atmosphere. After 3-4h under stirring, a

DMF solution (10 mL) of 200 mg (0.82 mmol) of the acetate **7** and 47 mg (0.04 mmol) of Pd(PPh₃)₄ was added and the reaction was continued overnight at r.t. After addition of water, the solution was extracted with DCM and the organic phase dried over anhydrous Na₂SO₄. The crude residue, obtained upon evaporation of the solvent, was then submitted to column chromatography. The products **11a,b** were isolated in 42% and 35% yield, respectively.

11a. (110 mg, 42%) as white crystals from benzene/petrol ether, m.p. 154-6 °C; [Found C, 63.7; H, 5.1; N, 26.3. C₁₇H₁₆N₆O (MW = 320.35) requires C, 63.73; H, 5.04; N, 26.24 %]; ν_{\max} (Nujol) 3310 (br), 3146 (br), 1670 (s) cm⁻¹; δ_{H} (300 MHz, CD₃COCD₃) 9.19 (1H, d, *J* 8 Hz, NH), 8.19 (1H, s, CH=N), 8.08 (1H, s, CH=N), 7.90 (2H, m, Ph), 7.50 (3H, m, Ph), 6.73 (2H, s, NH₂), 6.20 (1H, m, CH=), 6.02 (1H, m, CH=), 5.69 (1H, m, CH-N_{base}), 5.38 (1H, m, CH-N), 3.20 (1H, dt, *J* 15, 9 Hz, CH₂), 2.19 (1H, dt, *J* 15, 2.8 Hz, CH₂); δ_{C} (75 MHz, CD₃COCD₃) 166.8 (s), 157.7 (s), 153.4 (d), 150.4 (s), 141.8 (d), 137.9 (d), 136.6 (d), 132.4 (s), 132.1 (d), 129.7 (d), 128.4 (d), 121.7, 60.9 (d), 55.1 (d), 38.4 (t).

11b. (91 mg, 35%) as white crystals from benzene/petrol ether, m.p. 144-6 °C; [Found C, 63.6; H, 5.0; N, 26.2. C₁₇H₁₆N₆O (MW = 320.35) requires C, 63.73; H, 5.04; N, 26.24 %]; ν_{\max} (Nujol) 3310 (br), 3150 (br), 1675 (m) cm⁻¹; δ_{H} (300 MHz, CD₃COCD₃) 9.93 (1H, d, *J* 8 Hz, NH), 8.42 (1H, s, CH=N), 8.03 (2H, s, NH₂), 7.91 (2H, m, Ph), 7.84 (1H, s, CH=N), 7.55 (3H, m, Ph), 6.20 (1H, m, CH=), 6.05 (1H, m, CH=), 5.77 (1H, d, *J* 8 Hz, CH-N_{base}), 5.28 (1H, m, CH-N), 3.12 (1H, dt, *J* 15, 9 Hz, CH₂), 2.11 (1H, dt, *J* 15, 2.8 Hz, CH₂); δ_{C} (75 MHz, CD₃COCD₃) 165.1 (s), 155.3 (s), 151.6 (d), 148.7 (s), 142.9 (d), 137.8 (d), 134.7 (d), 131.2 (s), 130.2 (d), 128.4 (d), 127.1 (d), 120.8 (s), 65.0 (d), 53. (d), 36. (t).

Synthesis of the 6-chloropurine derivatives **13a,b**

To an anhydrous DMF solution (10 mL) of 6-chloropurine **12** (152 mg, 0.98 mmol), 33 mg (1.39 mmol) of NaH (70% in mineral oil) were added under nitrogen atmosphere. After 2h under stirring, a DMF solution (10 mL) of 200 mg (0.82 mmol) of the acetate **7** and 47 mg (0.04 mmol) of Pd(PPh₃)₄ was added and the reaction was continued overnight at r.t. After addition of water, the solution was extracted with DCM and the organic phase dried over anhydrous Na₂SO₄. The crude residue, obtained upon evaporation of the solvent, was then submitted to column chromatography. The products **13a,b** were isolated in 47% and 13% yields, respectively.

13a. (131 mg, 47%) as white crystals from diisopropyl ether, m.p. 136-140 °C; [Found C, 60.1; H, 4.1; N, 20.4. C₁₇H₁₄N₅OCl (MW = 339.78) requires C, 60.09; H, 4.15; N, 20.61 %]; ν_{\max} (Nujol) 3330 (br), 1645 (m) cm⁻¹; δ_{H} (300 MHz, CD₃COCD₃) 8.74 (1H, s, CH=N), 8.59 (1H, s, CH=N), 8.31 (1H, bs, NH), 7.91 (2H, m, Ph), 7.50 (3H, m, Ph), 6.33 (1H, m, CH=), 6.18 (1H, m, CH=), 5.89 (1H, m, CH-N_{base}), 5.36 (1H, m, CH-N), 3.32 (1H, m, CH₂), 2.22 (1H, m, CH₂); δ_{C} (75 MHz, CD₃COCD₃) 167.2 (s), 153.0 (d), 152.4 (s), 151.2 (d), 147.0 (d), 138.9 (d), 136.2 (s), 132.5 (d), 131.7 (d), 129.7 (d), 129.4 (s), 128.4 (d), 60.9 (d), 55.6 (d), 39.4 (t).

13b. (36 mg, 13%) as white crystals from diisopropyl ether, m.p. 110-112 °C; [Found C, 60.0; H, 4.0; N, 20.4. C₁₇H₁₄N₅OCl (MW = 339.78) requires C, 60.09; H, 4.15; N, 20.61 %]; ν_{\max} (Nujol) 3272 (br), 1654 (m) cm⁻¹; δ_{H} (300 MHz, CD₃COCD₃) 8.77 (1H, s, CH=N), 8.65 (1H, s, CH=N),

8.01 (1H, b, NH), 7.83 (2H, m, Ph), 7.52 (3H, m, Ph), 6.43 (1H, m, CH=), 6.36 (1H, m, CH=), 6.18 (1H, m, CH-N_{base}), 5.30 (1H, m, CH-N), 3.38 (1H, m, CH₂), 2.12 (1H, m, CH₂); δ_C (75 MHz, CD₃COCD₃) 167.5 (s), 163.6 (s), 152.8 (d), 149.0 (d), 140.0 (d), 136.0 (s), 133.0 (d), 131.7 (s), 131.2 (d), 129.6 (d), 129.5 (s), 128.5 (d), 62.6 (d), 56.0 (d), 41.9 (t).

Synthesis of the purine derivatives **14a-e**. General procedure

Solutions of chloro-nucleosides **13a** (30 mg, 0.09 mmol) in MeOH (2 mL) were saturated with gaseous amines and kept in a sealed tube at 50 °C for 24 h. In the case of liquid amines, an excess (50 equiv.) was added to the solutions. The solutions are then cooled and in most cases the products crystallize from the methanolic solutions. Otherwise, concentration of the solutions allows the amino derivatives to crystallize. Table 2 reports the physical constants (solvent of crystallization) and yields of the amino nucleosides **14(a-e)**.

14a. (29 mg, 99%) as white crystals from diisopropyl ether/ethanol, m.p. >210 °C (dec.); [Found C, 64.7; H, 5.2; N, 25.2. C₁₈H₁₈N₆O (MW = 334.37) requires C, 64.65; H, 5.43; N, 25.14 %]; ν_{\max} (Nujol) 3261 (m), 3222 (m), 1646 (s), 1630 (s) cm⁻¹; δ_H (300 MHz, CD₃COCD₃) 9.26 (1H, b, NH), 8.27 (1H, s, CH=N), 8.04 (1H, s, CH=N), 7.94 (2H, m, Ph), 7.56 (3H, m, Ph), 6.87 (1H, s, NH), 6.19 (1H, m, CH=), 6.01 (1H, m, CH=), 5.67 (1H, m, CH-N_{base}), 5.37 (1H, m, CH-N), 3.22 (1H, m, CH₂), 3.14 (3H, bs, CH₃-N), 2.20 (1H, m, CH₂); δ_C (75 MHz, CD₃COCD₃) 166.8 (s), 157.1 (s), 153.4 (d), 141.4 (d), 137.9 (d), 136.7 (s), 136.3 (d), 132.4 (d), 132.2 (d), 129.7 (d), 128.4 (d), 61.0 (d), 55.1 (d), 38.3 (t), 31.0 (q).

14b. (32 mg, 99%) as white crystals from diisopropyl ether/ethanol, m.p. 127-130 °C; [Found C, 67.1; H, 6.3; N, 22.2. C₂₁H₂₄N₆O (MW = 376.45) requires C, 67.00; H, 6.43; N, 22.33 %]; ν_{\max} (Nujol) 3342 (br), 1647 (s), 1582 (s) cm⁻¹; δ_H (300 MHz, CD₃COCD₃) 9.17 (1H, d, *J* 7.2 Hz, NH), 8.21 (1H, s, CH=N), 8.08 (1H, s, CH=N), 7.94 (2H, m, Ph), 7.55 (3H, m, Ph), 6.20 (1H, m, CH=), 6.01 (1H, m, CH=), 5.71 (1H, m, CH-N_{base}), 5.37 (1H, m, CH-N), 3.20 (2H, m, N-CH₂), 2.19 and 2.08 (1H + 1H, m, CH₂), 1.26 (3H, t, *J* 7 Hz, CH₃); δ_C (75 MHz, CD₃COCD₃) 166.9 (s), 155.0 (s), 152.8 (d), 151.2 (s), 140.7 (d), 136.9 (d), 136.7 (s), 134.0 (s), 132.4 (d), 132.2 (d), 129.7 (d), 128.4 (d), 121.7 (s), 60.8 (d), 55.2 (d), 43.9 (t), 43.1 (t), 38.4 (t), 14.2 (q), 11.9 (q).

14c. (31 mg, 98%) as white crystals from diisopropyl ether/ethanol, m.p. 193-195 °C; [Found C, 66.7; H, 5.6; N, 23.2. C₂₀H₂₀N₆O (MW = 360.41) requires C, 66.65; H, 5.59; N, 23.32 %]; ν_{\max} (Nujol) 3214 (m), 1645 (s), 1620 (s) cm⁻¹; δ_H (300 MHz, CD₃COCD₃) 9.22 (1H, b, NH), 8.29 (1H, s, CH=N), 8.05 (1H, s, CH=N), 7.94 (2H, m, Ph), 7.55 (3H, m, Ph), 6.80 (1H, b, NH), 6.20 (1H, m, CH=), 6.00 (1H, m, CH=), 5.68 (1H, m, CH-N_{base}), 5.38 (1H, m, CH-N), 3.19 (2H, m, CH₂), 2.17 (1H, m, N-CH), 0.82 (2H, m, CH₂), 0.70 (2H, m, CH₂); δ_C (75 MHz, CD₃COCD₃) 166.8 (s), 157.4 (s), 153.3 (d), 141.5 (d), 137.9 (d), 136.7 (s), 136.2 (s), 133.4 (s), 132.4 (d), 132.1 (d), 129.7 (d), 128.4 (d), 122.1 (s), 60.9 (d), 55.1 (d), 38.4 (t), 32.4 (d), 25.1 (t), 7.8 (t).

14d. (36 mg, 97%) as white crystals from diisopropyl ether/ethanol, m.p. 202-205 °C; [Found C, 70.3; H, 5.5; N, 20.3. C₂₀H₂₀N₆O (MW = 410.46) requires C, 70.22; H, 5.40; N, 20.48 %]; ν_{\max} (Nujol) 3326 (br), 3266 (br), 1628 (vs) cm⁻¹; δ_H (300 MHz, CD₃COCD₃) 9.22 (1H, b, NH), 8.26 (1H, s, CH=N), 8.08 (1H, s, CH=N), 7.93 (2H, m, Ph), 7.2-7.6 (9H, m, Ph and NH), 6.20 (1H, m,

CH=), 6.01 (1H, m, CH=), 5.69 (1H, m, CH-N_{base}), 5.38 (1H, m, CH-N), 4.83 (2H, m, CH₂), 3.20 (1H, m, CH₂), 2.18 (1H, m, CH₂); δ_C (75 MHz, CD₃COCD₃) 166.7 (s), 152.9 (d), 147.2 (d), 141.2 (s), 137.5 (d), 132.0 (d), 131.7 (d), 129.4 (s), 129.3 (d), 129.1 (d), 128.2 (d), 127.9 (d), 127.6 (d), 121.1 (s), 60.5 (d), 54.6 (d), 37.9 (t).

Synthesis of compounds 16(a-d)

To an anhydrous DMF solution (10 mL) of the heterobases **15** (0.98 mmol), 33 mg (1.39 mmol) of NaH (70% in mineral oil) were added under nitrogen atmosphere. After 2h under stirring, a DMF solution (10 mL) of 200 mg (0.82 mmol) of the acetate **7** and 47 mg (0.04 mmol) of Pd(PPh₃)₄ was added and the reaction was continued overnight at r.t. After addition of water, the solution was extracted with DCM and the organic phase dried over anhydrous Na₂SO₄. The crude residue, obtained upon evaporation of the solvent, was then submitted to column chromatography. The products **16(a-d)** were isolated fully characterized.

16a. (181 mg, 60%) as white crystals from diisopropyl ether, m.p. >210 °C (dec.); [Found C, 58.6; H, 4.7; N, 22.7. C₁₈H₁₇N₆OCl (MW = 368.83) requires C, 58.62; H, 4.65; N, 22.79 %]; ν_{\max} (Nujol) 3436 (br), 3276 (s), 1634 (s) cm⁻¹; δ_H (300 MHz, DMSO) 8.19 (1H, d, *J* 7.7 Hz, NH-CO), 7.81 (1H, d, *J* 4.5 Hz, NH-Me), 7.75 (1H, s, CH=N), 7.39 (2H, m, Ph), 7.04 (3H, m, Ph), 5.73 (1H, m, CH=), 5.62 (1H, m, CH=), 5.08 (1H, m, CH-N_{base}), 4.68 (1H, m, CH-N), 2.90 (3H, s, CH₃), 2.65 (1H, m, CH₂), 1.43 (1H, m, CH₂); δ_C (75 MHz, DMSO) 165.9 (s), 155.5 (s), 153.2 (s), 149.1 (s), 139.4 (d), 137.0 (d), 134.3 (d), 131.3 (d), 131.0 (d), 128.2 (d), 127.3 (d), 118.3 (s), 57.5 (d), 53.9 (d), 38.9 (t), 27.2 (q).

16b (or 16b'). (97 mg, 37%) as white crystals from diisopropyl ether, m.p. >215 °C (dec.); [Found C, 63.6; H, 4.7; N, 21.7. C₁₇H₁₅N₅O₂ (MW = 321.33) requires C, 63.54; H, 4.70; N, 21.80 %]; ν_{\max} (Nujol) 3277 (s), 1697 (s), 1683 (s), 1632 (s) cm⁻¹; δ_H (300 MHz, DMSO) 12.34 (1H, s, OH), 8.84 (1H, d, *J* 7.6 Hz, NH-CO), 8.26 (1H, s, CH=N), 8.22 (1H, s, CH=N), 8.00 (2H, m, Ph), 7.58 (3H, m, Ph), 6.22 (1H, m, CH=), 6.10 (1H, m, CH=), 5.92 (1H, m, CH-N_{base}), 5.23 (1H, m, CH-N), 3.00 (1H, m, CH₂), 2.25 (1H, m, CH₂); δ_C (75 MHz, DMSO) 165.6 (s), 157.3 (s), 151.5 (s), 148.1 (d), 135.9 (d), 134.6 (d), 134.1 (s), 131.8 (d), 131.2 (d), 128.3 (d), 127.3 (d), 105.9 (s), 60.3 (d), 53.6 (d), 37.7 (t).

16b' (or 16b). (32 mg, 12%) as white crystals from diisopropyl ether, m.p. >215 °C (dec.); [Found C, 63.5; H, 4.6; N, 21.8. C₁₇H₁₅N₅O₂ (MW = 321.33) requires C, 63.54; H, 4.70; N, 21.80 %]; ν_{\max} (Nujol) 3250 (br), 1688 (s), 1640 (m) cm⁻¹; δ_H (300 MHz, DMSO) 11.75 (1H, s, OH), 8.76 (1H, d, *J* 7.9 Hz, NH-CO), 8.61 (1H, s, CH=N), 7.96 (1H, s, CH=N), 7.89 (2H, m, Ph), 7.47 (3H, m, Ph), 6.16 (1H, m, CH=), 6.09 (1H, m, CH=), 5.58 (1H, m, CH-N_{base}), 5.13 (1H, m, CH-N), 3.02 (1H, m, CH₂), 2.03 (1H, m, CH₂); δ_C (75 MHz, DMSO) 165.6 (s), 158.7 (s), 158.5 (s), 146.9 (d), 137.0 (d), 134.2 (s), 131.3 (d), 131.2 (d), 128.3 (d), 127.5 (d), 127.3 (d), 107.0 (s), 66.5 (d), 53.6 (d), 38.6 (t).

16c. (26 mg, 10%) as white crystals from diisopropyl ether/ethanol, m.p. 110-112 °C; [Found C, 75.6; H, 6.1; N, 13.3. C₂₀H₁₉N₃O (MW = 317.38) requires C, 75.68; H, 6.03; N, 13.24 %]; ν_{\max} (Nujol) 3196 (br), 1652 (m) cm⁻¹; δ_H (300 MHz, CD₃COCD₃) 8.06 (1H, b, NH), 8.05 (1H, d, *J*

6.1 Hz, CH_{benzoimid.}), 7.90 (2H, m, Ph), 7.50 [m, 1H (CH=N), 3H (Ph), 1H (CH_{benzoimid.})], 7.07 (1H, m, CH_{benzoimid.}), 6.32 (1H, m, CH=), 6.22 (1H, m, CH=), 5.67 (1H, m, CH-N_{base}), 5.29 (1H, m, CH-N), 3.26 (1H, m, CH₂), 2.45 (3H, m, CH₃), 2.02 (1H, m, CH₂); δ_C (75 MHz, CD₃COCD₃) 167.5 (s), 142.5 (s), 138.0 (d), 136.4 (d), 132.7 (s), 132.4 (d), 129.5 (s), 128.5 (d), 124.9 (d), 124. (d), 120.7 (d), 111.5 (s), 60.5 (d), 55.8 (d), 40.5 (t), 21.9 (q).

16d. (188 mg, 66%) as white crystals from diisopropyl ether/ethanol, m.p. 179-181 °C; [Found C, 65.5; H, 4.7; N, 16.2. C₁₉H₁₆N₄O₃ (MW = 348.35) requires C, 65.51; H, 4.63; N, 16.08 %]; ν_{\max} (Nujol) 3279 (br), 1630 (s), 1377 (m) cm⁻¹; δ_H (300 MHz, CD₃COCD₃) 8.68 (1H, s, CH=N), 8.51 (1H, s, CH=N), 8.17 (1H, d, *J* 7.9 Hz, NH-CO), 7.89 (2H, m, Ph), 7.47 (3H, m, Ph), 6.41 (1H, m, CH=), 6.30 (1H, m, CH=), 5.94 (1H, m, CH-N_{base}), 5.32 (1H, m, CH-N), 3.40 (1H, m, CH₂), 2.12 (1H, m, CH₂); δ_C (75 MHz, CD₃COCD₃) 167.6 (s), 150.0 (s), 148.3, 144.7 (s), 139.0 (d), 136.0 (d), 132.4 (s), 132.0 (d), 129.5 (d), 128.5 (d), 121.2 (d), 118.5 (d), 109.0 (s), 61.3 (d), 55.9 (d), 40.5 (t).

Synthesis of the pyrimidine derivatives **19a-g**

A clear solution of pyrimidines **17a-g** (0.87 mmol) in anhydrous DMF (10 mL) was made by heating at 65 °C for 10 minutes. To the cooled solution, 1.2 mmol of NaH (70% in mineral oil) were added under nitrogen atmosphere and heating is carried on for 30 minutes under stirring. The solution was then cooled down to room temperature and a DMF solution (10 mL) of 0.87 mmol of the acetate **7** and 0.43 mmol of Pd(PPh₃)₄ was added. The reaction was continued overnight at 65 °C. After filtration and addition of water, the solution was extracted with DCM and the organic phase dried over anhydrous Na₂SO₄. The crude residue, obtained upon evaporation of the solvent, was then submitted to column chromatography. The products **19a-g** were isolated in the reported yields.

19a. (166 mg, 64%) as white crystals from benzene/petrol ether, m.p. 217-220 °C; [Found C, 64.7; H, 5.1; N, 14.3. C₁₆H₁₅N₃O₃ (MW = 297.30) requires C, 64.63; H, 5.09; N, 14.14 %]; ν_{\max} (Nujol) 3425 (br), 3223 (br), 1683 (m) cm⁻¹; δ_H (300 MHz, DMSO) 11.29 (1H, s, CONHCO), 8.63 (1H, d, *J* 7.9 Hz, NH), 7.84 (2H, m, Ph), 7.56 (1H, dd, *J* 8, 1.5 Hz, N-CH=), 7.48 (3H, m, Ph), 6.11 (1H, m, CH=), 5.87 (1H, m, CH=), 5.87 (1H, dd, *J* 8, 1.5 Hz, CO-CH=), 5.51 (1H, m, CH-N_{base}), 5.00 (1H, m, CH-N), 2.89 (1H, dt, *J* 14, 7 Hz, CH₂), 1.58 (1H, dt, *J* 14, 7 Hz, CH₂); δ_C (75 MHz, DMSO) 165.8 (s), 163.3 (s), 150.9 (s), 141.9 (d), 137.7 (d), 134.4 (s), 131.3 (d), 131.0 (d), 128.3 (d), 127.3 (d), 101.7 (d), 58.7 (d), 53.7, 37.5 (t).

19b. (107 mg, 39%) as white crystals from benzene/n-hexane, m.p. 78-80 °C; [Found C, 60.9; H, 4.5; N, 13.3. C₁₆H₁₄N₃O₃F (MW = 315.31) requires C, 60.95; H, 4.48; N, 13.33 %]; ν_{\max} (Nujol) 3370 (br), 3185 (br), 1709 (s) cm⁻¹; δ_H (300 MHz, DMSO) 11.12 (1H, s, CONHCO), 8.63 (1H, d, *J* 8.1 Hz, NH), 8.32 (1H, d, *J* 8 Hz, N-CH=), 7.82 (2H, m, Ph), 7.50 (3H, m, Ph), 6.11 (1H, m, CH=), 5.87 (1H, m, CO-CH=), 5.75 (1H, m, CH-N_{base}), 5.04 (1H, m, CH-N), 2.89 (1H, dt, *J* 13, 5 Hz, CH₂), 2.03 (1H, dt, *J* 13, 5 Hz, CH₂); δ_C (75 MHz, DMSO) 165.8 (s), 157.6 (s), 149.9 (s), 141.6 (d), 138.5 (d), 134.4 (s), 131.3 (d), 130.9 (d), 127.2 (d), 127.0 (d), 79.2 (d), 59.1 (d), 53.6 (d), 37.2 (t).

19c. (138 mg, 48%) as white crystals from benzene/n-hexane, m.p. 147-150 °C; [Found C, 57.9; H, 4.3; N, 12.7. C₁₆H₁₄N₃O₃Cl (MW = 331.76) requires C, 57.93; H, 4.25; N, 12.67 %]; ν_{\max} (Nujol) 3310 (br), 3167 (br), 1696 (s) cm⁻¹; δ_{H} (300 MHz, DMSO) 11.85 (1H, s, CONHCO), 8.63 (1H, d, *J* 8 Hz, NH), 8.67 (1H, d, *J* 8 Hz, N-CH=), 7.85 (1H, s, N-CH=), 7.84 (2H, m, Ph), 7.50 (3H, m, Ph), 6.13 (1H, m, CH=), 5.91 (1H, m, CH=), 5.52 (1H, m, CH-N_{base}), 5.03 (1H, m, CH-N), 2.89 (1H, dt, *J* 14, 6 Hz, CH₂), 1.60 (1H, dt, *J* 14, 6 Hz, CH₂); δ_{C} (75 MHz, DMSO) 166.1 (s), 159.5 (s), 150.4 (s), 139.6 (d), 138.6 (d), 134.7 (s), 131.7 (d), 131.2 (d), 128.7 (d), 127.6 (d), 107.4 (d), 59.7 (d), 54.0 (d), 37.9 (t).

19d. (98 mg, 30%) as white crystals from benzene/n-hexane, m.p. 230 °C (dec.); [Found C, 51.1; H, 3.8; N, 11.1. C₁₆H₁₄N₃O₃Br (MW = 376.21) requires C, 51.08; H, 3.75; N, 11.17 %]; ν_{\max} (Nujol) 3250 (br), 3150 (br), 1690 (s) cm⁻¹; δ_{H} (300 MHz, DMSO) 11.84 (1H, s, CONHCO), 8.63 (1H, d, *J* 8 Hz, NH), 7.89 (1H, s, N-CH=), 7.85 (2H, m, Ph), 7.51 (3H, m, Ph), 6.15 (1H, m, CH=), 5.91 (1H, m, CH=), 5.51 (1H, m, CH-N_{base}), 5.02 (1H, m, CH-N), 1.93 (1H, dt, *J* 14, 6 Hz, CH₂), 1.62 (1H, dt, *J* 14, 6 Hz, CH₂); δ_{C} (75 MHz, DMSO) 165.8 (s), 159.3 (s), 150.3 (s), 141.6 (d), 138.2 (d), 134.4 (s), 131.3 (d), 130.8 (d), 128.3 (d), 127.3 (d), 95.6 (d), 59.4 (d), 53.6 (d), 37.6 (t).

19e. (59 mg, 16%) as white crystals from benzene/n-hexane, m.p. 194 °C (dec.); [Found C, 45.4; H, 3.4; N, 10.0. C₁₆H₁₄N₃O₃I (MW = 423.21) requires C, 45.41; H, 3.33; N, 9.93 %]; ν_{\max} (Nujol) 3310 (br), 3167 (br), 1703 (s) cm⁻¹; δ_{H} (300 MHz, DMSO) 11.69 (1H, s, CONHCO), 8.65 (1H, d, *J* 8 Hz, NH), 7.88 (1H, s, N-CH=), 7.86 (2H, m, Ph), 7.51 (3H, m, Ph), 6.14 (1H, m, CH=), 5.92 (1H, m, CH=), 5.49 (1H, m, CH-N_{base}), 5.00 (1H, m, CH-N), 2.86 (1H, dt, *J* 14, 6 Hz, CH₂), 1.51 (1H, dt, *J* 14, 6 Hz, CH₂); δ_{C} (75 MHz, DMSO) 165.8 (s), 160.7 (s), 150.6 (s), 146.1 (d), 138.2 (d), 134.4 (s), 131.3 (d), 130.9 (d), 128.3 (d), 127.3 (d), 69.4 (d), 59.2 (d), 53.6 (d), 37.7 (t).

19f. (111 mg, 41%) as white crystals from diisopropyl ether/ethanol, m.p. > 210 °C (dec.); [Found C, 65.5; H, 5.4; N, 13.5. C₁₇H₁₇N₃O₃ (MW = 311.33) requires C, 65.58; H, 5.50; N, 13.50 %]; ν_{\max} (Nujol) 3265 (m), 3163 (w), 1697 (s), 1676 (m), 1646 (s) cm⁻¹; δ_{H} (300 MHz, DMSO) 11.28 (1H, s, CONHCO), 8.62 (1H, d, *J* 7.6 Hz, NH), 7.84 (2H, m, Ph), 7.52 (3H, m, Ph), 7.37 (1H, s, CH=_{thym.}), 6.12 (1H, m, CH=), 5.88 (1H, m, CH=), 5.51 (1H, m, CH-N_{base}), 5.01 (1H, m, CH-N), 2.87 (1H, m, CH₂), 1.80 (3H, s, CH₃), 1.57 (1H, m, CH₂); δ_{C} (75 MHz, DMSO) 165.9 (s), 163.8 (s), 150.9 (s), 137.5 (d), 137.4 (d), 134.4 (s), 131.3 (d), 128.3 (d), 127.3 (d), 109.3 (d), 58.4 (d), 53.7 (d), 37.5 (t), 12.3 (q).

19g. (136 mg, 48%) as white crystals from benzene/n-hexane, m.p. >210 °C (dec.); [Found C, 66.4; H, 5.8; N, 13.0. C₁₇H₁₉N₃O₃ (MW = 325.36) requires C, 66.44; H, 5.89; N, 12.92 %]; ν_{\max} (Nujol) 3293 (s), 3217 (w), 1712 (m), 1685 (w), 1629 (s) cm⁻¹; δ_{H} (300 MHz, DMSO) 10.98 (1H, s, CONHCO), 8.45 (1H, d, *J* 8.3 Hz, NH), 7.81 (2H, m, Ph), 7.50 (3H, m, Ph), 5.83 (3H, m, CH=CH, CH-N_{base}), 5.07 (1H, m, CH-N), 2.70 (1H, m, CH₂), 2.06 (3H, s, CH₃), 1.96 (1H, m, CH₂), 1.78 (3H, s, CH₃); δ_{C} (75 MHz, DMSO) 164.8 (s), 163.7 (s), 150.7 (s), 146.4 (d), 134.4 (s), 132.6 (d), 132.3 (d), 128.4 (d), 126.9 (d), 104.1 (d), 54.9 (d), 53.7 (d), 34.7 (t), 16.0 (q), 10.3 (q).

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