Preparation of 7-Methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones and their 1,3-Dipolar Cycloadditions towards Isoxazolinyl and Isoxazolidinyl Spironucleosides

[a]R. FISCHER, [a]E. HÝROŠOVÁ, [a]Ľ. FIŠERA*, [b]C. HAMETNER, and [c]M. K. CYRAŃSKI

[a]*Department of Organic Chemistry, Faculty of Chemical and Food Technology, Slovak University of Technology, SK-812 37 Bratislava*
e-mail: lubor.fisera@stuba.sk

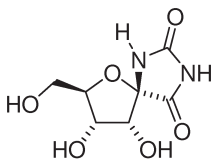
[b]*Institute of Applied Synthetic Chemistry, University of Technology, A-1060 Vienna, Austria*

[c]*Department of Chemistry, University of Warsaw, PL-02-093 Warsaw, Poland*

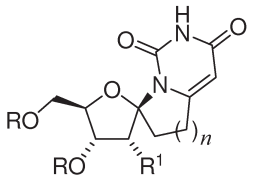
Received 5 August 2004

Novel 6,7-dihydro-5-hydroxy-3-methoxy-7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones were prepared from orotic acid. Their 1,3-dipolar cycloadditions with mesitonitrile oxide and methoxycarbonyl nitrone proceed with complete regioselectivity, the approach of the dipole taking place predominantly from the less sterically hindered side of the dipolarophiles. The isoxazolidinyl spironucleoside, bearing a primary hydroxyl group on methyl in C-3 position of the isoxazolidinyl ring, was prepared in three steps from the major isoxazolidine.

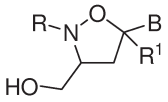
The improved knowledge of the HIV virus and its replication mechanism have suggested in recent years the synthesis of new molecules able to block the viral replication [1]. Structural modifications at the level of the sugar moiety and/or the heterocyclic base in nucleosides have long been recognized to improve their antiviral or anticancer activities: in this context, the synthesis of nucleoside analogues has recently received a great deal of attention [2]. Spironucleosides are useful modifications of the natural nucleosides possessing defined architecture around the *N*-glycosidic bond. In connection with the discovery of hydantocidin (*I*) [3], a natural spiro compound possessing herbicidal and plant growth regulatory activi-



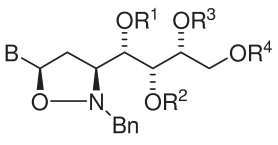
I



II $n = 1$, R, R^1=H
III $n = 2$, R=H, R^1=OH

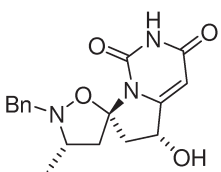


IV R^1 = H
V $R^1 = CH_2OH$

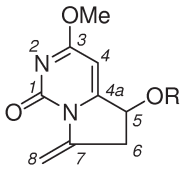


VI R^1, R^2=R^3, R^4=CMe_2
VII R^1, R^2=CMe_2, R^3=Bz, R^4=TBDPS

B = nucleoside base

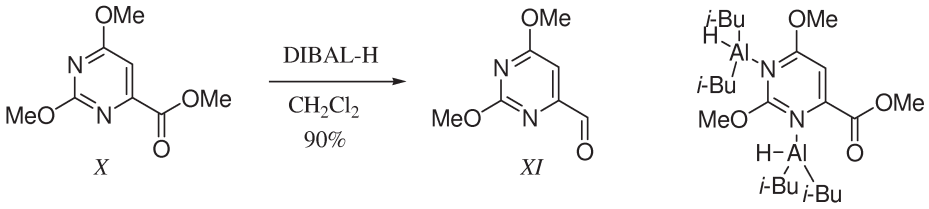


(±)-*VIII*

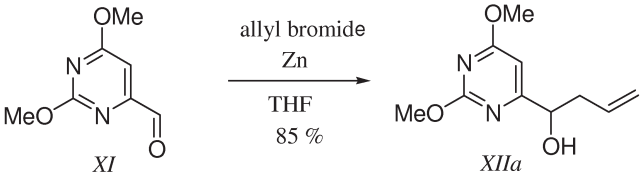


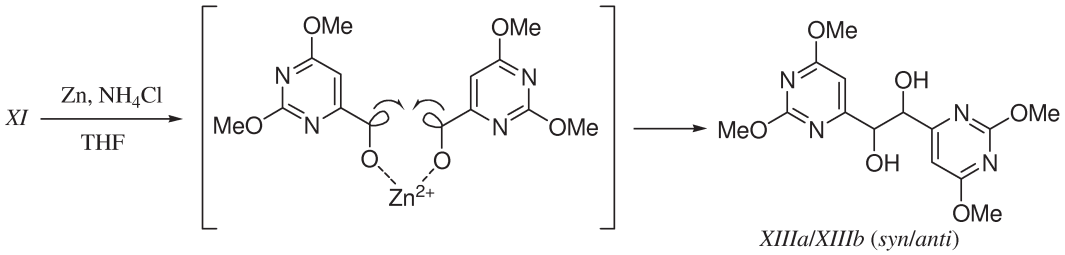
IXa R = H
IXb R = Bz
IXc R = TBDPS

*The author to whom the correspondence should be addressed.



Scheme 1





Scheme 2

ties, new spiro structures 6,1′-ethanouridine *II* [4—6] and 6,1′-propanouridine *III* [7] were synthesized. In the search for effective, selective, and nontoxic agents, a variety of strategies has been devised to design nucleoside analogues.

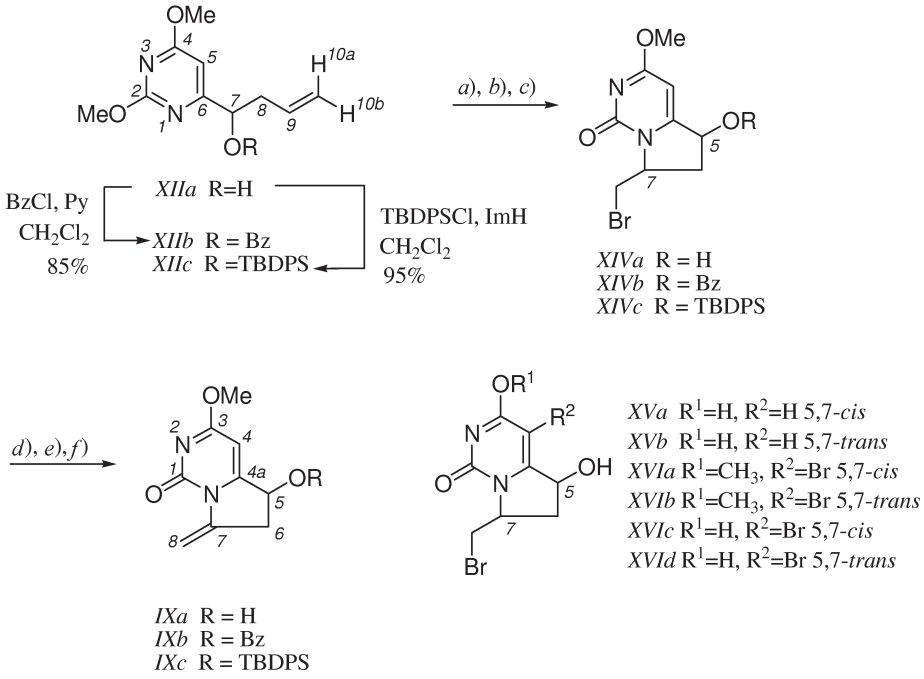
Insertion of a nitrogen atom into the furanosyl ring gives the possibility of constructing new isoxazolidinyl nucleosides *IV* [8, 9], which have received considerable interest for their potential anti-HIV activity over the last 10 years [10—15]. The first example of an isoxazolidinyl nucleoside (*V*) branched in the C-5 anomeric position was synthesized by *Chiacchio* and *Romeo* [16, 17].

Previously we have been interested in the preparation of *N*,*O*-modified nucleosides *VI* and *VII* [18—20]. In this paper we focus our attention onto the preparation of spiro isoxazolidine *VIII via* 1,3-dipolar cycloadditions of the 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones *IXa—IXc*. Our preliminary results in this area have been the subject of a recent communication [20].

For the preparation of the dipolarophiles *IXa—IXc* we decided to use methyl ester *X* as a starting compound (Scheme 1), prepared by the literature procedure from orotic acid [21]. In place of the two-step preparation of aldehyde *XI* by oxidation of the corresponding alcohol [22], we carried out direct reduction of the ester moiety with 3 equivalents of DIBAL-H in CH_2Cl_2 at −78 °C in 90 % yield.

With less than two equivalents of DIBAL-H, the ester group was not reduced completely, what could be caused by the possible complexation between the aluminium atom and the nitrogen atoms of the pyrimidine ring. Reaction of aldehyde *XI* with allyl bromide in the presence of Zn dust in anhydrous THF under reflux afforded homoallyl alcohol *XIIa* in 85 % yield (Scheme 2). Moreover, when the reaction was performed in the presence of solid NH_4Cl, two secondary 1,2-ethanediols *XIIIa* and *XIIIb* were isolated as by-products. Their formation can be explained by the reductive coupling of aldehyde *XI*.

Cyclization of allyl chain to the N-1 nitrogen in anhydrous $CHCl_3$ at 60 °C gave a mixture of two isomers *XIVa* (n(5,7-*cis*) : n(5,7-*trans*) = 70 : 30, Scheme 3), which were separated by column chromatography on silica. In addition to the desired products *XIVa* the unprotected pyrimidinones *XVa*, *XVb* were also isolated. It was noted that more than one equivalent of bromine results in formation of C-4 brominated derivatives of *XIIa—XIId*. For example, using 2 equivalents of Br_2, the amount of substance ratio 5,7-*cis* *XIVa* : 5,7-*trans* *XIVa* : *XVa* : *XVb* : *XVIa* : *XVIb* : *XVIc* : *XVId* = 9 : 6: 16 : 6 : 13 : 6 : 31 : 13 was obtained by ^{13}C NMR/125 MHz integration of the crude reaction mixture (C-4 signal of the pyrimidine ring). Finally, 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one *IXa* was prepared by elimination of HBr with DBU [23] in 1,4-dioxane at 80 °C



Scheme 3. *a*) For *XIIa*: Br_2, $CHCl_3$, 60 °C, 4 h, 80 %; *b*) for *XIIb*: Br_2, $CHCl_3$, 60 °C, 4 h, 82 %; *c*) for *XIIc*: Br_2, $CHCl_3$, 60 °C, 4 h, 80 %; *d*) for *XIVa*: DBU, 1,4-dioxane, 80 °C, 2 h, 44 %; *e*) for *XIVb*: DBU, 1,4-dioxane, reflux, 1 h, 70 %; *f*) for *XIVc*: DBU, 1,4-dioxane, reflux, 1 h, 70 %.

Table 1. ^{1}H NMR Characteristics of 7-Methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones *IX*

Dipolarophile	H-8a δ	H-8b δ	$J_{8a,8b}$ Hz	$J_{6a,8a}$ Hz	$J_{6b,8a}$ Hz	$J_{6a,8b}$ Hz	$J_{6b,8b}$ Hz
IXa	4.89 dd	6.14 dd	–	2.1	1.5	2.3	1.8
IXb	5.01 ddd	6.46 ddd	1.2	1.8	2.1	1.8	2.1
IXc	4.82 ddd	6.28 ddd	1.2	1.2	2.1	1.2	2.3

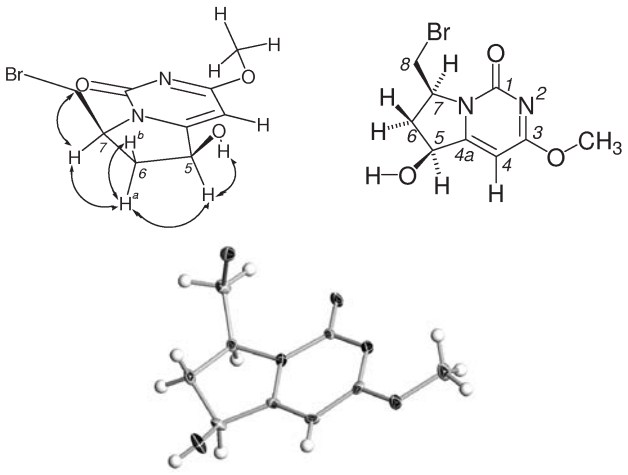
from the mixture of both 5,7-*cis* and 5,7-*trans* isomers of *XIVa* in 44 % yield.

In the light of our interest in the effect of the nature of the R-substituents onto diastereoselectivity of 1,3-dipolar cycloadditions of 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones *IXa*—*IXc*, we decided to protect the C-5 hydroxy group of *IXa* with the suitable bulk substituents. Lack of success in direct silylation of the free hydroxy group of *IXa* with TBDPSCl in the presence of imidazole in CH_2Cl_2 at reflux and in DMF at 100 °C, caused us to turn our attention to the similar silylation of homoallyl alcohol *XIIa*, which gave compound *XIIc* in 95 % yield (Scheme 3). Reaction of silyl ether *XIIc* with bromine afforded a mixture of two isomers *XIVc* (80 % yield) in the amount of substance ratio 60 : 40, these were not separated and their relative configuration was not determined. 7-Methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one *IXc* was prepared by subsequent elimination of HBr from the mixture of two isomers *XIVc* with DBU in dry 1,4-dioxane under reflux in 70 % yield. By the same means benzoylated pyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one *IXb* was prepared from *XIIa* in a total yield of 49 %.

All structures were determined by ^{1}H and ^{13}C NMR spectroscopic analysis. The ^{1}H NMR spectrum of homoallyl alcohol *XIIa* demonstrated multiplets for H-10a, H-10b, and H-9 at δ = 5.13—5.81. The proton of the free hydroxy group appeared as a doublet at δ = 3.37. Disappearance of the methyl group and the appearance of new signals for the bromomethyl group as two double doublets in the δ region 3.80—4.20 confirmed the formation of pyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones *XIVa*—*XIVc*. For the final dipolarophiles *IXa*—*IXc* having an exocyclic double bond, signals for H-8a and H-8b were diagnostic at the positions described in Table 1.

In the case of target pyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one *XIVa*, the stereochemistry was deduced by means of NOE experiments. No enhancements were detectable between protons H-5 and H-7. On the other hand, irradiation of H-7 induced a positive NOE effect on proton H-6a and when the proton H-5 was irradi-

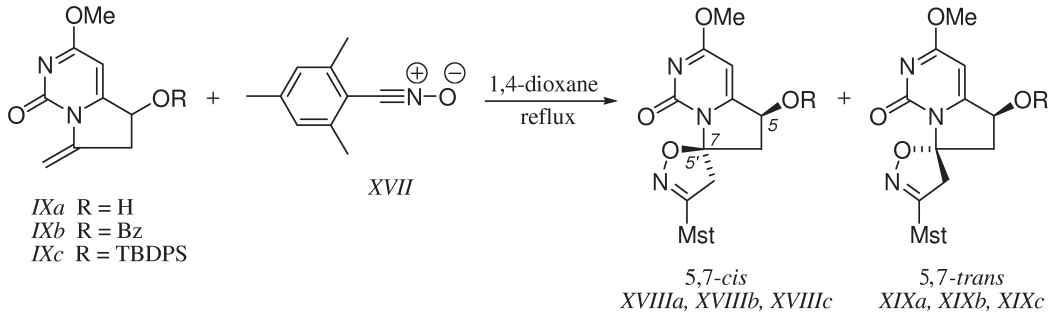
ated, NOE effect was observed for H-6a. These data clearly indicate a 5,7-*cis* relationship between the substituents in the C-5 and C-7 positions, which was subsequently confirmed by X-ray crystallographic analysis [24].



1,3-Dipolar cycloadditions of 7-methylenepyrrolo-[1,2-*c*]pyrimidin-1(5*H*)-ones *IXa*—*IXc* with mesitonitrile oxide *XVII* proceeded with complete regioselectivity to provide 5-isoxazolines *XVIII* and *XIX* in good yields (Scheme 4, Table 2). The approach of the dipole takes place predominantly from the less sterically hindered side of dipolarophiles *IXa* and *IXb* providing a mixture of two 5,7-*cis* *XVIIIa*, *XVIIIb* and 5,7-*trans* *XIXa*, *XIXb* isomers (entry 1 and 2). On the other hand, cycloaddition of the dipolarophile *IXc* bearing a bulky silyl group proceeded with high stereoselectivity providing 5,7-*trans* isoxazoline *XIXc* exclusively [20]. The structures of pure spiroisoxazolines *XVIIIa*, *XVIIIb*, and *XIXa*—*XIXc* were determined by spectroscopic analysis. Based on NOE experiments of H-5, H-6a, H-6b, H-4a′, and H-4b′ protons for the major isomers *XIXa*—*XIXc* we assigned the C-5/C-7 *trans* configuration.

Based on our main interest to deal with the preparation of the isoxazolidinyl spironucleoside *VIII* bearing a primary hydroxymethyl group in C-3 position of the isoxazolidinyl ring, we decided to focus attention onto 1,3-dipolar cycloadditions of alkoxycarbonyl nitrones as the suitable dipoles for the electron-rich dipolarophiles 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones. The synthetic utility of glyoxylic acid derived nitrone *XX* has been widely demonstrated in our laboratory and by other groups [25—28]. 1,3-Dipolar cycloaddition of methoxycarbonyl nitrone *XX* with dipolarophile *IXc* (Scheme 5), which achieved the highest diastereoselectivity in the cycloaddition with mesitonitrile oxide (*XVII*, Scheme 4), was carried out in refluxed toluene with 2 equivalents of nitrone. Cycloaddition proceeded with complete regioselectivity to provide 5-isoxazolidines *XXI* as a mixture of four isomers *XXIa*—*XXId* in the ratio of $a : b : (c + d) = 72 : 21 : (7)$. The two major isoxazolidines *XXIa* (3′,5′-*trans*) and *XXIb* (3′,5′-*cis*) were isolated in pure form by column chromatography and identified by spectroscopic analysis.

The stereochemical configuration of cycloadduct *XXIb* was determined by NOE experiments. Irradiation of H-3′ induced a positive NOE effect on the proton H-4a′ and no effect on H-4b′. When H-4a′ was

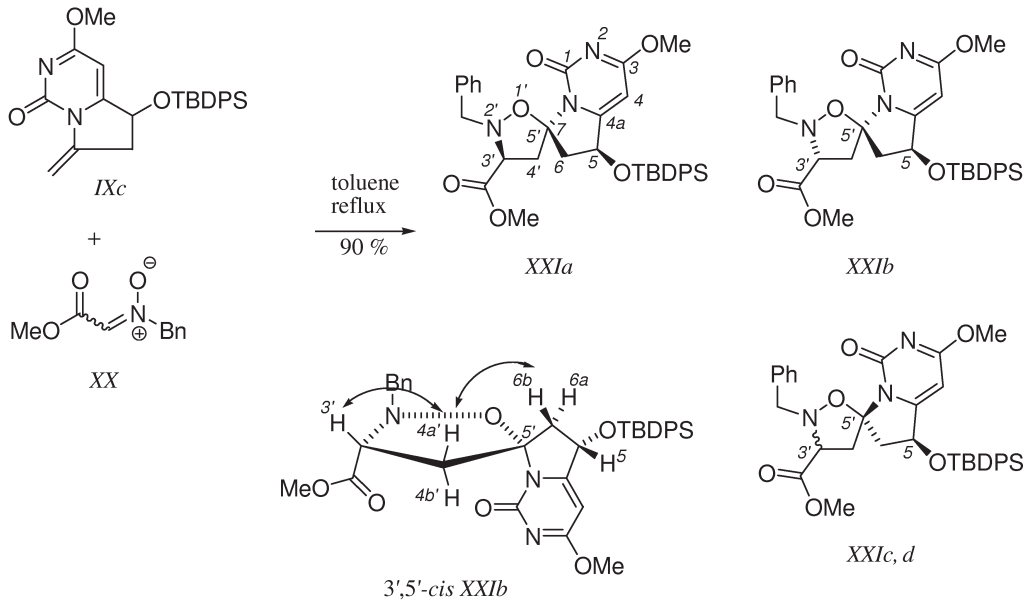


Scheme 4

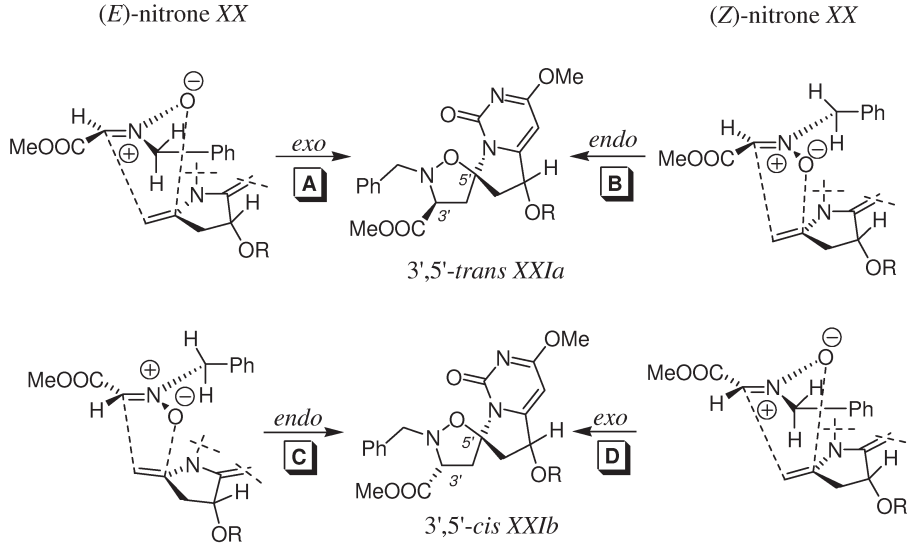
Table 2. 1,3-Dipolar Cycloadditions of Mesitonitrile Oxide to Methylenepyrrolo[1,2-*c*]pyrimidinones *IXa*—*IXc*

Entry	Dipolarophile	Total yield/%	n(*cis XVIII*) : n(*trans XIX*)[a]
1	*IXa*	60	30 : 70
2	*IXb*	83	17 : 83
3	*IXc*	79	< 5 : > 95

a) Ratios were obtained by ^{13}C NMR (125 MHz) integration of the crude reaction mixture (C-5′ signal of the isoxazolinyl ring).



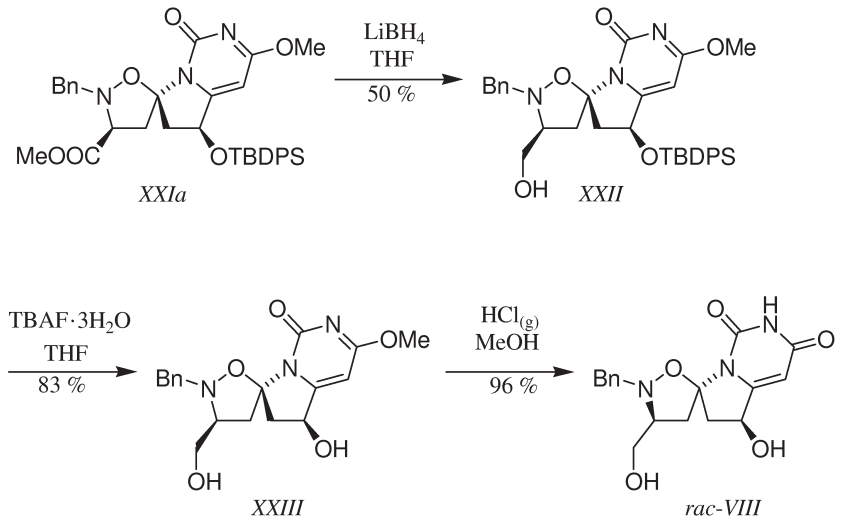
Scheme 5. NOE effects in the case of H-3′, H-4′, and H-6.



Scheme 6

irradiated, NOE enhancements between H-3′, H-4a′ and H-4a′, H-6a and H-6b were detectable. No enhancements were observed between the protons H-3′, H-4b′ and H-6. These data indicate the C-3′/C-5′ *cis* relative configuration between the methoxycarbonyl group and pyrimidine base. In the case of the major isomer *XXIa*, a NOE effect was observed between the protons H-3′ and H-4a′.

It is well known that alkoxycarbonyl nitrones can spontaneously isomerize and the ratio between *E*- and *Z*-isomer is dependent upon the nature of the solvent [25—28]. As a consequence of the interconversion between *E*/*Z* izomers, parallel models are always proposed for cycloaddition of nitrone *XX*. The formation of both major isoxazolidines *XXIa* (C-3′/C-5′ *trans* relationship) and *XXIb* (C-3′/C-5′ *cis* relative configuration) could be explained through the *endo* and *exo* approach as shown in Scheme 6. The isoxazolidine *XXIa* arises from cycloaddition of *Z*-nitrone through an *endo* transition state and *E*-nitrone through an *exo* transition state. On the other hand, the adduct *XXIb* could be formed by the *Z*-nitrone and *E*-nitrone reacting in the *exo*- and *endo*-fashion, respectively. For the cycloaddition with electron-rich alkene *IXc* an *exo* approach of the dipolarophile can be predicted [28]. The aforementioned obtained results on the cycloaddition of the nitrone *XX* with *IXc* are in agreement with DFT calculations, where the predominance of 3,5-*trans* adducts was predicted [28], as well as with experimental results



Scheme 7

reported in literature for analogue reactions [25—28].

In the case of major isomer *XXIa* the ester group was reduced with $LiBH_4$ in THF at room temperature to afford spiroisoxazolidine *XXII*, bearing the required hydroxymethyl group in the C-3 position of the isoxazolidinyl ring, in a yield of 50 % (Scheme 7). Finally, after deprotection of the silyl group with TBAF · $3H_2O$ in THF and demethylation under acid conditions, the isoxazolidinyl spironucleoside *VIII* was prepared in the total yield 80 %.

In conclusion, novel 6,7-dihydro-5-hydroxy-3-methoxy-7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones *IXa*—*IXc* were prepared from orotic acid. Their 1,3-dipolar cycloadditions with mesitonitrile oxide *XVII* proceeded with complete regioselectivity to provide 5-isoxazolines *XVIII*, *XIX* in good yields. The approach of the dipole took place predominantly from the less sterically hindered side of the dipolarophiles. The isoxazolidinyl spironucleoside *VIII*, bearing a primary hydroxyl group on methyl in C-3 position of the isoxazolidinyl ring, was prepared in three steps from the isoxazolidine *XXIa*. The isoxazolidine *XXIa* was obtained by 1,3-dipolar cycloaddition of methoxycarbonyl nitrone *XX* to 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one *IXc*. Cycloaddition proceeded with complete regioselectivity to provide isoxazolidines *XXI* as a mixture of four isomers *XXIa*—*XXId*.

EXPERIMENTAL

All melting points were measured on a Kofler apparatus. NMR spectra were recorded on a Varian VRX-300 (^{1}H, 300 MHz and ^{13}C, 75 MHz) and a Bruker DRX-400 (^{1}H, 400 MHz and ^{13}C, 125 MHz) spectrometers in $CDCl_3$ and DMSO-d_6 using TMS as the internal standard. Elemental analyses were carried out at the Microanalytical Laboratory of the Institute of Physical Chemistry, Vienna University. All reactions were monitored by TLC Alugram SIL 50/UV_{254} (Macherey Nagel) with detection by UV, with ethanolic solution of *p*-anisaldehyde (0.5 cm^3 of *p*-anisaldehyde, 0.5 cm^3 of concentrated sulfuric acid, 9 cm^3 of ethanol, and few drops of acetic acid) or aqueous potassium permanganate (2.0 g of $KMnO_4$, 20.0 g of K_2CO_3, 5 cm^3 of 5 % aqueous solution of NaOH, and 300 cm^3 of water) followed by heating. Merck silica gel 60 (0.040—0.064 mm) was employed for column chromatography. All solvents were purified by standard methods. Orotic acid was purchased from Avocado, 1.5 M-DIBAL-H solution in toluene from Aldrich, zinc (powder) from Merck.

2,4-Dimethoxypyrimidine-6-carbaldehyde (*XI*)

To a stirred solution of methyl ester *X* (1.93 g; 9.7 mmol) in anhydrous CH_2Cl_2 (40 cm^3), 1.5 M-DIBAL-H solution in toluene (15.6 cm^3, 29.1 mmol) was added at −78 °C dropwise under argon. The reaction mixture was stirred for 4 h. Excess of DIBAL-H was quenched with CH_3OH (4 cm^3) and the temperature was allowed to arise to room temperature. Hydrochloric acid (1 M, 20 cm^3) was added slowly, followed by stirring for 15 min. The separated aqeuous layer was extracted with CH_2Cl_2 (2 × 20 cm^3). Combined organic layers were dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The product was purified by the column chromatography on silica (hexane—ethyl acetate, $\varphi_r = 70 : 30$) giving aldehyde *XI* as a colourless solid (1.38 g), 90 % yield, $R_f = 0.43$ (hexane—ethyl acetate, $\varphi_r = 70 : 30$), m.p. = 105—106 °C after crystallization from hexane (Ref. [29] gives m.p. = 107 °C. For $C_7H_8N_2O_3$ ($M_r = 168.15$) w_i(calc.): 50.00 % C, 4.80 % H, 16.66 % N; w_i(found): 49.73 % C, 4.65 % H, 16.39 % N. ^{1}H NMR spectrum (300 MHz, $CDCl_3$),

δ: 4.04, 4.09 (s, 3H, OCH_3), 6.90 (s, 1H, H-5), 9.89 (s, 1H, H-7). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ: 54.6 (OCH_3), 99.6 (C-5), 160.3 (C-6), 166.4, 172.9 (C-2, C-4), 192.2 (C-7).

2,4-Dimethoxy-6-(1-hydroxybut-3-en-1-yl)-pyrimidine (*XIIa*) and By-Products *XIII*

To a stirred suspension of Zn dust (1.98 g; 7.3 mmol) in anhydrous THF (50 cm^3), allyl bromide (1.62 cm^3, 18.07 mmol) was added, followed by aldehyde *XI* (0.60 g; 3.57 mmol) and the mixture was stirred vigorously under reflux for 3 h. The reaction mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl and vigorously stirred with CH_2Cl_2 (30 cm^3) for 15 min. The solid was removed by filtration through Celite® and the organic layer was separated. The aqueous phase was extracted with CH_2Cl_2 (20 cm^3), the combined organic layers were dried over Na_2SO_4 and the solvent was removed by evaporation. The final product was purified by the column chromatography on silica (hexane—ethyl acetate, φ_r = 75 : 25) giving product *XIIa* as a colourless solid (0.63 g), 85 % yield, R_f = 0.22 (hexane—ethyl acetate, φ_r = 75 : 25), m.p. = 131—133 °C. For $C_{10}H_{14}N_2O_3$ (M_r = 210.23) w_i(calc.): 57.13 % C, 6.71 % H, 13.33 % N; w_i(found): 57.51 % C, 5.08 % H, 16.24 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.46 (ddddd, 1H, $J_{7,8a}$ = 7.3 Hz, $J_{8a,8b}$ = 14.3 Hz, $J_{8a,9}$ = 7.3 Hz, $J_{8a,10a}$ = 1.2 Hz, $J_{8a,10b}$ = 1.2 Hz, H-8a), 2.63 (ddddd, 1H, $J_{7,8b}$ = 4.7 Hz, $J_{8a,8b}$ = 14.0 Hz, $J_{8b,9}$ = 7.0 Hz, $J_{8b,10a}$ = 1.5 Hz, $J_{8b,10b}$ = 1.2 Hz, H-8b), 3.37 (d, 1H, $J_{7,OH}$ = 5.0 Hz, H—OH), 3.97, 4.00 (2 × s, 2 × 3H, OCH_3), 4.62 (ddd, 1H, $J_{7,OH}$ = 4.7 Hz, $J_{7,8a}$ = 7.6 Hz, $J_{7,8b}$ = 4.7 Hz, H-7), 5.13 (dddd, 1H, $J_{8a,10b}$ = 1.2 Hz, $J_{8b,10b}$ = 1.2 Hz, $J_{9,10b}$ = 10.2 Hz, $J_{10a,10b}$ = 1.8 Hz, H-10b), 5.14 (dddd, 1H, $J_{8a,10a}$ = 1.5 Hz, $J_{8b,10a}$ = 1.5 Hz, $J_{9,10a}$ = 17.0 Hz, $J_{10a,10b}$ = 2.0 Hz, H-10a), 5.81 (dddd, 1H, $J_{8a,9}$ = 7.0 Hz, $J_{8b,9}$ = 7.0 Hz, $J_{9,10a}$ = 17.0 Hz, $J_{9,10b}$ = 10.2 Hz, H-9), 6.39 (d, 1H, $J_{5,7}$ = 0.6 Hz, H-5). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 42.2 (C-8), 54.4, 55.2 (OCH_3), 72.2 (C-7), 97.9 (C-5), 119.0 (C-10), 133.9 (C-9), 165.4 (C-6), 172.5, 173.0 (C-2, C-4).

The column chromatography on silica (hexane—ethyl acetate, φ_r = 75 : 25) gave also the by-products, 1,2-bis(2,4-dimethoxypyrimidin-6-yl)-ethane-1,2-diols (*XIII*). Spectroscopic data are given for mixture of both isomers *XIIIa* and *XIIIb*, in which the stereochemistry was not defined.

XIIIa, R_f = 0.18 (hexane—ethyl acetate, φ_r = 70 : 30). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ: 3.67, 3.84 (s, 3H, OCH_3), 4.87 (d, 1H, $J_{7,OH}$ = 5.1 Hz, H-7), 5.74 (d, 1H, $J_{OH,7}$ = 4.5 Hz, H—OH), 6.43 (s, 1H, H-5). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ: 54.2, 54.5 (OCH_3), 76.6 (C-7), 99.3 (C-5), 164.6 (C-6), 172.0, 173.2 (C-2, C-4).

XIIIb, R_f = 0.13 (hexane—ethyl acetate, φ_r = 70 : 30). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ: 3.89, 3.90 (s, 3H, OCH_3), 4.89 (d, $J_{7,OH}$ = 5.0 Hz, 1H, H-7), 5.40 (d, $J_{OH,7}$ = 6.9 Hz, 1H, H—OH), 6.65 (s, 1H, H-5). ^{13}C NMR spectrum (75 MHz, DMSO-d_6), δ: 54.3, 55.0 (OCH_3), 75.7 (C-7), 99.1 (C-5), 165.1 (C-6), 172.3, 174.8 (C-2, C-4).

2,4-Dimethoxy-6-(1-benzoyloxybut-3-en-1-yl)-pyrimidine (*XIIb*)

Homoallyl alcohol *XIIa* (0.20 g; 1.0 mmol) was dissolved in CH_2Cl_2 (10 cm^3) and pyridine (0.17 cm^3, 2.1 mmol) followed by benzoyl chloride (0.13 cm^3, 1.1 mmol) were added. The reaction mixture was stirred under reflux for 48 h. After cooling to the room temperature, saturated aqueous K_2CO_3 was added and the stirring was continued for 10 min. Separated organic layer was washed with water and brine and dried over Na_2SO_4. The solvent was evaporated *in vacuo*. The product was isolated by the column chromatography on silica (hexane—ethyl acetate, φ_r = 95 : 5) giving compound *XIIb* as a colourless oil (0.25 g), 84 % yield, R_f = 0.35 (hexane—ethyl acetate, φ_r = 80 : 20). For $C_{17}H_{18}N_2O_4$ (M_r = 314.34) w_i(calc.): 64.96 % C, 5.77 % H, 8.91 % N; w_i(found): 64.82 % C, 5.51 % H, 8.72 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.77 (ddddd, 1H, $J_{7,8a}$ = 7.3 Hz, $J_{8a,8b}$ = 14.6 Hz, $J_{8a,9}$ = 7.3 Hz, $J_{8a,10a}$ = 1.2 Hz, $J_{8a,10b}$ = 1.2 Hz, H-8a), 2.88 (ddddd, 1H, $J_{7,8b}$ = 4.7 Hz, $J_{8a,8b}$ = 14.6 Hz, $J_{8b,9}$ = 6.7 Hz, $J_{8b,10a}$ = 1.5 Hz, $J_{8b,10b}$ = 1.2 Hz, H-8b), 3.94, 3.99 (s, 3H, OCH_3), 5.07 (dddd, 1H, $J_{8a,10b}$ = 1.2 Hz, $J_{8b,10b}$ = 1.2 Hz, $J_{9,10b}$ = 10.2 Hz, $J_{10a,10b}$ = 2.0 Hz, H-10b), 5.13 (dddd, 1H, $J_{8a,10a}$ = 1.5 Hz, $J_{8b,10a}$ = 1.5 Hz, $J_{9,10a}$ = 17.0 Hz, $J_{10a,10b}$ = 1.5 Hz, H-10a), 5.81 (dddd, 1H, $J_{8a,9}$ = 7.0 Hz, $J_{8b,9}$ = 7.0 Hz, $J_{9,10a}$ = 17.0 Hz, $J_{9,10b}$ = 10.2 Hz, H-9), 5.93 (ddd, 1H, $J_{5,7}$ = 0.9 Hz, $J_{7,8a}$ = 7.3 Hz, $J_{7,8b}$ = 4.7 Hz, H-7), 6.39 (d, 1H, $J_{5,7}$ = 0.9 Hz, H-5), 7.44—8.12 (m, 5H, COBz). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 38.8 (C-8), 54.3, 55.3 (OCH_3), 75.2 (C-7), 98.2 (C-5), 118.9 (C-10), 128.9, 130.2, 133.1, 133.7 (C-9, COBz), 165.7, 166.0 (COBz, C-6), 170.2, 172.6 (C-2, C-4).

2,4-Dimethoxy-6-(1-*tert*-butyldiphenylsilyl-oxybut-3-en-1-yl)pyrimidine (*XIIc*)

Homoallyl alcohol *XIIa* (0.20 g; 1.0 mmol) was dissolved in CH_2Cl_2 (10 cm^3) and imidazole (0.14 g; 2.1 mmol) followed by TBDPSCl (0.29 g; 1.1 mmol) were added. The reaction mixture was stirred under reflux for 24 h. The precipitate was removed by filtration, the filtrate was extracted with saturated NH_4Cl solution (10 cm^3) and the aqueous phase was subsequently extracted with CH_2Cl_2 (2 × 10 cm^3). The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The product was purified by the column chromatography (hexane—ethyl acetate,

φ_r = 95 : 5) as a colourless oil (0.41 g), 95 % yield, R_f = 0.23 (hexane—ethyl acetate, φ_r = 95 : 5). For $C_{26}H_{32}N_2O_3Si$ (M_r = 448.63) w_i(calc.): 69.61 % C, 7.19 % H, 6.24 % N; w_i(found): 70.08 % C, 6.98 % H, 6.61 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 1.14 (s, 9H, $OSiC(CH_3)_3$), 2.36 (ddddd, 1H, $J_{7,8a}$ = 5.6 Hz, $J_{8a,8b}$ = 14.0 Hz, $J_{8a,9}$ = 7.0 Hz, $J_{8a,10a}$ and $J_{8a,10b}$ = 1.2 Hz and 1.5 Hz, H-8a), 2.51 (ddddd, 1H, $J_{7,8b}$ = 4.4 Hz, $J_{8a,8b}$ = 14.0 Hz, $J_{8b,9}$ = 7.3 Hz, $J_{8b,10a}$ and $J_{8b,10b}$ = 1.5 Hz and 1.2 Hz, H-8b), 3.97, 4.00 (s, 3H, OCH_3), 4.82 (ddd, 1H, $J_{5,7}$ = 0.9 Hz, $J_{7,8a}$ = 5.6 Hz, $J_{7,8b}$ = 4.7 Hz, H-7), 4.87 (dddd, 1H, $J_{8a,10a}$ = 1.5 Hz, $J_{8b,10a}$ = 1.5 Hz, $J_{9,10a}$ = 17.0 Hz, $J_{10a,10b}$ = 2.3 Hz, H-10a), 4.94 (dddd, 1H, $J_{8a,10b}$ = 1.2 Hz, $J_{8b,10b}$ = 1.2 Hz, $J_{9,10b}$ = 10.2 Hz, $J_{10a,10b}$ = 2.3 Hz, H-10b), 5.67 (dddd, 1H, $J_{8a,9}$ = 7.0 Hz, $J_{8b,9}$ = 7.3 Hz, $J_{9,10a}$ = 17.2 Hz, $J_{9,10b}$ = 9.9 Hz, H-9), 6.62 (d, 1H, $J_{5,7}$ = 0.9 Hz, H-5), 7.30—7.76 (m, 10H, $OSiPh_2$). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 19.8 ($OSiC(CH_3)_3$), 27.5 ($OSiC(CH_3)_3$), 41.7 (C-8), 54.2, 55.0 (OCH_3), 75.1 (C-7), 98.7 (C-5), 118.1 (C-10), 128.0, 128.1, 130.1, 133.7, 134.1 ($OSiPh_2$), 135.2 (C-9), 136.2, 136.3 ($OSiPh_2$), 165.1 (C-6), 172.5, 174.6 (C-2, C-4).

5-Substituted 7-Bromomethyl-6,7-dihydro-3-methoxypyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones *XIVa*—*XIVc*, *XVa*—*XVc*, and *XVIa*—*XVId*

Method A

The stirred solution of the pyrimidines *XIIa*—*XIIc* (1 equivalent) in anhydrous chloroform was warmed to 60 °C and a solution of Br_2 (1 equivalent) in anhydrous chloroform was slowly added dropwise over 4 h. After this time, the solvent was removed *in vacuo* and the products were isolated by the column chromatography on silica giving pyrimidinones *XIVa*—*XIVc* as a mixture of *cis/trans* isomers in all cases.

Method B

At the reaction of *XIIa* with two equivalents of bromine, the stirred solution of the pyrimidine *XIIa* (0.60 g; 2.87 mmol) in anhydrous chloroform (50 cm^3) was warmed to 60 °C and a solution of Br_2 (0.92 g; 5.74 mmol, 0.30 cm^3) in anhydrous chloroform (20 cm^3) was slowly added dropwise over 4 h. After this time, the solvent was removed *in vacuo* and the products were isolated by the column chromatography on silica (CH_2Cl_2—CH_3OH, φ_r = 95 : 5), giving pyrimidinones *XIVa*, *XVa*, *XVb*, and *XVIa*—*XVId*.

7-Bromomethyl-6,7-dihydro-5-hydroxy-3-methoxypyrrolo[1,2-c]pyrimidin-1(5H)-one (XIVa): Prepared according to method *A*, pyrimidine *XIIa* (0.38 g; 1.8 mmol in 30 cm^3 of $CHCl_3$), Br_2 (0.1 cm^3, 1.8 mmol in 20 cm^3 of $CHCl_3$), column chromatography (CH_2Cl_2—CH_3OH, φ_r = 98 : 2), ratio *n*(5,7-*cis*)/*n*(5,7-*trans*) 70 : 30, 80 % total yield: 5,7-*cis* *XIVa*, R_f = 0.16 (CH_2Cl_2—CH_3OH, φ_r = 99 : 1, twice eluated), m.p. = 185—186 °C. For $C_9H_{11}BrN_2O_3$ (M_r = 275.10) w_i(calc.): 39.29 % C, 4.03 % H, 10.18 % N; w_i(found): 39.19 % C, 3.71 % H, 9.88 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 1.92 (ddd, 1H, $J_{5,6a}$ = $J_{6a,7}$ = 6.4 Hz, $J_{6a,6b}$ = 13.2 Hz, H-6a), 2.58 (ddd, 1H, $J_{5,6b}$ = $J_{6b,7}$ = 7.8 Hz, $J_{6a,6b}$ = 13.1 Hz, H-6b), 3.83 (s, 3H, OCH_3), 3.91 (dd, 1H, $J_{7,8a}$ = 2.1 Hz, $J_{8a,8b}$ = 9.9 Hz, H-8a), 4.18 (dd, 1H, $J_{7,8b}$ = 6.8 Hz, $J_{8a,8b}$ = 9.9 Hz, H-8b), 4.51 (m, 1H, H-7), 4.96 (m, 1H, H-5), 5.96 (s, 1H, H-4), 6.13 (d, 1H, $J_{5,OH}$ = 5.3 Hz, H—OH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 35.5 (C-8), 35.7 (C-6), 54.9 (OCH_3), 60.0 (C-7), 70.4 (C-5), 90.2 (C-4), 155.2 (C-4a), 165.1 (C-1), 173.0 (C-3); 5,7-*trans* *XIVa*, R_f = 0.10 (CH_2Cl_2—CH_3OH, φ_r = 99 : 1, two elutions), m.p. = 145—147 °C. For $C_9H_{11}BrN_2O_3$ (M_r = 275.10) w_i(calc.): 39.29 % C, 4.03 % H, 10.18 % N; w_i(found): 39.46 % C, 3.79 % H, 9.95 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.16 (ddd, 1H, $J_{5,6a}$ = $J_{6a,7}$ = 8.8 Hz, $J_{6a,6b}$ = 13.4 Hz, H-6a), 2.40 (ddd, 1H, J = 8.5 Hz, J = 2.3 Hz, $J_{6a,6b}$ = 13.4 Hz, H-6b), 3.81 (m, 1H, H-8a), 3.82 (s, 3H, OCH_3), 4.02 (dd, 1H, $J_{7,8b}$ = 5.6 Hz, $J_{8a,8b}$ = 10.2 Hz, H-8b), 4.80 (m, 1H, H-7), 5.25 (m, 1H, H-5), 5.95 (s, 1H, H-4), 6.14 (d, 1H, $J_{5,OH}$ = 6.1 Hz, H—OH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 34.7 (C-8), 35.5 (C-6), 54.1 (OCH_3), 59.3 (C-7), 70.2 (C-5), 89.1 (C-4), 154.0 (C-4a), 164.7 (C-1), 172.3 (C-3).

XIVa prepared by method *B*: 5,7-*cis* *XIVa*, 55 mg; 5,7-*trans* *XIVa* 45 mg.

7-Bromomethyl-5-benzoyloxy-6,7-dihydro-3-methoxypyrrolo[1,2-c]pyrimidin-1(5H)-one (XIVb): Pyrimidine *XIIb* (0.20 g; 0.6 mmol in 20 cm^3 of $CHCl_3$), Br_2 (0.03 cm^3, 0.6 mmol in 10 cm^3 of $CHCl_3$), column chromatography (hexane—ethyl acetate, φ_r = 70 : 30), amount of substance ratio 60 : 40, colourless foam, 0.20 g, 82 % total yield:

Major isomer, R_f = 0.13 (hexane—ethyl acetate, φ_r = 50 : 50). ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.49 (ddd, 1H, $J_{5,6a}$ = 7.3 Hz, $J_{6a,7}$ = 9.4 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6a), 2.82 (ddd, 1H, $J_{5,6b}$ = 8.8 Hz, $J_{6b,7}$ = 2.3 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6b), 3.70 (dd, 1H, $J_{7,8a}$ = 2.3 Hz, $J_{8a,8b}$ = 11.1 Hz, H-8a), 3.98 (s, 3H, OCH_3), 4.30 (dd, 1H, $J_{7,8b}$ = 4.1 Hz, $J_{8a,8b}$ = 11.1 Hz, H-8b), 5.07 (dddd, 1H, $J_{6a,7}$ = 9.1 Hz, $J_{6b,7}$ = 2.3 Hz, $J_{7,8a}$ = 2.3 Hz, $J_{7,8b}$ = 4.4 Hz, H-7), 6.04 (d, 1H, $J_{4,5}$ = 0.9 Hz, H-4), 6.57 (ddd, 1H, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 7.3 Hz, $J_{5,6b}$ = 8.8 Hz, H-5), 7.48—8.07 (m, 5H, COPh). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 34.4, 34.9 (C-6, C-8), 55.4 (OCH_3), 60.2 (C-7), 73.1 (C-5), 92.5 (C-4), 129.0, 129.1, 130.3, 134.4 (COPh), 155.4, 159.0 (C-4a, COPh), 165.9 (C-1), 173.5 (C-3).

Minor isomer, R_f = 0.11 (hexane—ethyl acetate, φ_r = 50 : 50). ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.57 (ddd, 1H, $J_{5,6a}$ = 2.6 Hz, $J_{6a,7}$ = 2.6 Hz, $J_{6a,6b}$ = 15.2 Hz, H-6a), 2.82 (ddd, 1H, $J_{5,6b}$ = 7.6 Hz, $J_{6b,7}$ = 8.2 Hz, $J_{6a,6b}$ = 14.9 Hz, H-6b), 3.85 (dd, 1H, $J_{7,8a}$

= 8.5 Hz, $J_{8a,8b}$ = 9.9 Hz, H-8a), 3.96 (s, 3H, OCH_3), 4.04 (dd, 1H, $J_{7,8b}$ = 2.9 Hz, $J_{8a,8b}$ = 9.9 Hz, H-8b), 4.84 (dddd, 1H, $J_{6a,7}$ = 2.9 Hz, $J_{6b,7}$ = 8.5 Hz, $J_{7,8a}$ = 8.5 Hz, $J_{7,8b}$ = 2.9 Hz, H-7), 6.12 (d, 1H, $J_{4,5}$ = 0.9 Hz, H-4), 6.22 (ddd, 1H, $J_{4,5}$ = 0.9 Hz, $J_{5,6a}$ = 2.6 Hz, $J_{5,6b}$ = 7.6 Hz, H-5), 7.48—8.04 (m, 5H, COPh). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 32.8, 33.0 (C-6, C-8), 55.4 (OCH_3), 60.6 (C-7), 72.5 (C-5), 94.1 (C-4), 129.0, 129.1, 130.2, 134.4 (COPh), 155.4, 157.5 (C-4a, COPh), 165.8 (C-1), 173.4 (C-3).

7-Bromomethyl-5-tert-butyldiphenylsilyloxy-6,7-dihydro-3-methoxypyrrolo[1,2-c]pyrimidin-1(5H)-one (XIVc): Pyrimidine *XIIc* (3.33 g; 7.4 mmol in 100 cm^3 of $CHCl_3$), Br_2 (0.38 cm^3, 7.4 mmol in 30 cm^3 of $CHCl_3$), column chromatography (hexane—ethyl acetate, φ_r = 50 : 50), amount of substance ratio 60 : 40, colourless foam, 2.96 g, 80 % total yield:

Major isomer, R_f = 0.28 (hexane—ethyl acetate, φ_r = 50 : 50). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ: 1.09 (s, 9H, $OSiC(CH_3)_3$), 2.20—2.32 (m, 1H, H-6a), 2.41 (ddd, 1H, $J_{5,6b}$ = 3.0 Hz, $J_{6b,7}$ = 3.4 Hz, $J_{6a,6b}$ = 14.1 Hz, H-6b), 3.87 (dd, 1H, $J_{7,8a}$ = 9.4 Hz, $J_{8a,8b}$ = 9.8 Hz, H-8a), 3.92 (s, 3H, OCH_3), 4.08 (dd, 1H, $J_{7,8b}$ = 3.4 Hz, $J_{8a,8b}$ = 9.8 Hz, H-8b), 4.59 (m, 1H, H-7), 4.91 (dd, 1H, $J_{5,6a}$ = 6.8 Hz, $J_{5,6b}$ = 3.0 Hz, H-5), 5.39 (s, 1H, H-4), 7.35—7.75 (m, $OSiPh_2$). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ: 19.1 ($OSiC(CH_3)_3$), 26.8 ($OSiC(CH_3)_3$), 32.5, 35.9 (C-6, C-8), 54.8 (OCH_3), 60.2 (C-7), 72.4 (C-5), 91.7 (C-4), 127.7—135.9 ($OSiPh_2$), 155.3 (C-4a), 160.7 (C-1), 172.8 (C-3).

Minor isomer, R_f = 0.24 (hexane—ethyl acetate, φ_r = 50 : 50). ^{1}H NMR spectrum (300 MHz, $CDCl_3$), δ: 1.11 (s, 9H, $OSiC(CH_3)_3$), 2.14 (ddd, $J_{5,6a}$= 8.1 Hz, $J_{6a,7}$ = 1.7 Hz, $J_{6a,6b}$ = 13.2 Hz, 1H, H-6a), 2.20—2.32 (m, 1H, H-6b), 3.48 (dd, $J_{7,8a}$ = 2.6 Hz, $J_{8a,8b}$ = 10.7 Hz, 1H, H-8a), 3.95 (s, 3H, OCH_3), 4.01 (dd, $J_{7,8b}$ = 4.3 Hz, $J_{8a,8b}$ = 10.7 Hz, 1H, H-8b), 4.85 (m, 1H, H-7), 5.46 (dd, $J_{5,6a}$ = 8.1 Hz, $J_{5,6b}$ = 8.5 Hz, 1H, H-5), 5.79 (s, 1H, H-4), 7.35—7.75 (m, $OSiPh_2$). ^{13}C NMR spectrum (75 MHz, $CDCl_3$), δ: 19.1 ($OSiC(CH_3)_3$), 26.8 ($OSiC(CH_3)_3$), 34.1, 37.0 (C-6, C-8), 54.8 (OCH_3), 59.4 (C-7), 72.8 (C-5), 90.9 (C-4), 127.7—135.9 ($OSiPh_2$), 155.3 (C-4a), 162.6 (C-1), 173.1 (C-3).

7-Bromomethyl-6,7-dihydro-5-hydroxypyrrolo[1,2-c]pyrimidin-1,3(5H)-dione (XV): 5,7-*cis XVa*: 125 mg, R_f = 0.18 (CH_2Cl_2—CH_3OH, φ_r = 95 : 5), m.p. = 223—226 °C. For $C_8H_9BrN_2O_3$ (M_r = 261.07) w_i(calc.): 36.80 % C, 3.47 % H, 10.73 % N; w_i(found): 36.96 % C, 3.26 % H, 10.52 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 1.91 (ddd, 1H, $J_{5,6a}$ = 6.3 Hz, $J_{6a,7}$ = 6.7 Hz, $J_{6a,6b}$ = 13.3 Hz, H-6a), 2.50 (m, 1H, H-6b), 3.85 (dd, 1H, $J_{7,8a}$ = 2.3 Hz, $J_{8a,8b}$ = 10.2 Hz, H-8a), 4.08 (dd, 1H, $J_{7,8b}$ = 7.0 Hz, $J_{8a,8b}$ = 10.2 Hz, H-8b), 4.43 (dddd, 1H, $J_{6a,7}$ = 7.0 Hz, $J_{6b,7}$ = 5.7 Hz, $J_{7,8a}$ = 2.3 Hz, $J_{7,8b}$ = 7.0 Hz, H-7), 4.86 (dddd, 1H, $J_{4,5}$ = 1.2 Hz, $J_{5,OH}$ = 5.5 Hz, $J_{5,6a}$ = 6.3 Hz, $J_{5,6b}$ = 7.0 Hz, H-5), 5.51 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-5), 6.06 (d, 1H, $J_{5,OH}$ = 5.1 Hz, H—OH), 11.18 (brs, 1H, H—NH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 35.6 (C-8), 35.8 (C-6), 59.0 (C-7), 70.0 (C-5), 96.1 (C-4), 150.4 (C-4a), 161.6, 165.3 (C-1, C-3).

5,7-*trans XVb*: 39 mg, R_f = 0.15 (CH_2Cl_2—CH_3OH, φ_r = 95 : 5), m.p. = 220—224 °C. For $C_8H_9BrN_2O_3$ (M_r = 261.07) w_i(calc.): 36.80 % C, 3.47 % H, 10.73 % N; w_i(found): 36.67 % C, 3.21 % H, 10.43 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.13 (ddd, 1H, $J_{5,6a}$ = $J_{6a,7}$ = 9.0 Hz, $J_{6a,6b}$ = 13.3 Hz, H-6a), 2.35 (ddd, 1H, $J_{5,6b}$ = 8.2 Hz, $J_{6b,7}$ = 2.0 Hz, $J_{6a,6b}$ = 13.3 Hz, H-6b), 3.75 (dd, 1H, $J_{7,8a}$ = 2.7 Hz, $J_{8a,8b}$ = 10.6 Hz, H-8a), 3.89 (dd, 1H, $J_{7,8b}$ = 6.3 Hz, $J_{8a,8b}$ = 10.6 Hz, H-8b), 4.68 (dddd, 1H, $J_{6a,7}$ = 9.2 Hz, $J_{6b,7}$ = 2.0 Hz, $J_{7,8a}$ = 2.7 Hz, $J_{7,8b}$ = 6.3 Hz, H-7), 5.15 (dddd, 1H, $J_{4,5}$ = 1.2 Hz, $J_{5,OH}$ = 6.3 Hz, $J_{5,6a}$ = $J_{5,6b}$ = 8.6 Hz, H-5), 5.50 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.05 (d, 1H, $J_{5,OH}$ = 6.3 Hz, H—OH), 11.18 (brs, 1H, H—NH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 35.6 (C-8), 36.3 (C-6), 58.6 (C-7), 70.2 (C-5), 95.7 (C-4), 150.2 (C-4a), 162.1, 165.2 (C-1, C-3).

4-Bromo-7-bromomethyl-6,7-dihydro-5-hydroxy-3-methoxypyrrolo[1,2-c]pyrimidin-1(5H)-one (XVIa, XVIb): 5,7-*cis XVIa*: 110 mg, R_f = 0.51 (CH_2Cl_2—CH_3OH, φ_r = 99 : 1, two elutions), m.p. = 183—185 °C. For $C_9H_{10}Br_2N_2O_3$ (M_r = 354.00) w_i(calc.): 30.54 % C, 2.85 % H, 7.91 % N; w_i(found): 30.54 % C, 2.65 % H, 7.64 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.06 (ddd, 1H, $J_{5,6a}$ = $J_{6a,7}$ = 2.3 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6a), 2.60 (ddd, 1H, $J_{5,6b}$ = $J_{6b,7}$ = 7.8 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6b), 3.75 (dd, 1H, $J_{7,8a}$ = $J_{8a,8b}$ = 9.5 Hz, H-8a), 3.90 (dd, 1H, $J_{7,8b}$ = 3.3 Hz, $J_{8a,8b}$ = 9.4 Hz, H-8b), 3.91 (s, 3H, OCH_3), 4.60 (m, 1H, H-7), 5.03 (ddd, 1H, $J_{5,OH}$ = 5.9 Hz, $J_{5,6a}$ = 2.3 Hz, $J_{5,6b}$ = 7.3 Hz, H-5), 6.33 (d, 1H, $J_{5,OH}$ = 5.8 Hz, H—OH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 34.1 (C-8), 35.8 (C-6), 56.4 (OCH_3), 62.5 (C-7), 72.2 (C-5), 84.6 (C-4), 153.5 (C-4a), 161.2 (C-1), 168.3 (C-3).

5,7-*trans XVIb*: 54 mg, R_f = 0.25 (CH_2Cl_2—CH_3OH, φ_r = 99 : 1, twice eluated), m.p. = 158—160 °C. For $C_9H_{10}Br_2N_2O_3$(M_r = 354.00) w_i(calc.): 30.54 % C, 2.85 % H, 7.91 % N; w_i(found): 30.33 % C, 3.01 % H, 7.98 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.25 (ddd, 1H, $J_{5,6a}$ = 5.2 Hz, $J_{6a,7}$ = 8.5 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6a), 2.42 (ddd, 1H, $J_{5,6b}$ = 8.2 Hz, $J_{6b,7}$ = 4.4 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6b), 3.85 (dd, 1H, $J_{7,8a}$ = 2.1 Hz, $J_{8a,8b}$ = 10.3 Hz, H-8a), 3.91 (s, 3H, OCH_3), 4.17 (dd, 1H, $J_{7,8b}$ = 5.2 Hz, $J_{8a,8b}$ = 10.4 Hz, H-8b), 4.87 (m, 1H, H-7), 5.20 (ddd, 1H, $J_{5,6a}$ = 5.2 Hz, $J_{5,OH}$ = $J_{5,6b}$ = 8.1 Hz, H-5), 6.17 (d, 1H, $J_{5,OH}$ = 8.2 Hz, H—OH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 36.1 (C-8), 37.2 (C-6), 56.4 (OCH_3), 61.1 (C-7), 72.3 (C-5), 84.3 (C-4), 153.5 (C-4a), 161.7 (C-1), 168.4 (C-3).

4-Bromo-7-bromomethyl-6,7-dihydro-5-hydroxypyrrolo[1,2-c]pyrimidin-1,3(5H)-dione (XVIc, XVId):

5,7-*cis XVIc*: 204 mg, R_f = 0.14 (CH_2Cl_2—CH_3OH, φ_r = 99 : 1, two elutions), m.p. = 194—197 °C. For $C_8H_8Br_2N_2O_3$(M_r = 339.97) w_i(calc.): 28.26 % C, 2.37 % H, 8.24 % N; w_i(found): 28.55 % C, 2.39 % H, 7.92 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.06 (ddd, 1H, $J_{5,6a} = J_{6a,7}$ = 1.7 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6a), 2.51 (ddd, 1H, $J_{5,6b} = J_{6b,7}$ = 7.5 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6b), 3.68 (dd, 1H, $J_{7,8a} = J_{8a,8b}$ = 9.8 Hz, H-8a), 3.84 (dd, 1H, $J_{7,8b}$ = 3.1 Hz, $J_{8a,8b}$ = 9.5 Hz, H-8b), 4.54 (m, 1H, H-7), 4.95 (ddd, 1H, $J_{5,OH}$ = 5.3 Hz, $J_{5,6a}$ = 1.7 Hz, $J_{5,6b}$ = 7.0 Hz, H-5), 6.29 (d, 1H, $J_{5,OH}$ = 5.6 Hz, H—OH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 34.1 (C-8), 35.8 (C-6), 61.8 (C-7), 72.4 (C-5), 92.6 (C-4), 149.4 (C-4a), 157.5, 161.5 (C-1, C-3).

5,7-*trans XVId*: 141 mg (fraction together with the isomer *XVIc*), R_f = 0.12 (CH_2Cl_2—CH_3OH, φ_r = 99 : 1, two elutions). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.22 (ddd, 1H, $J_{5,6a}$ = 5.0 Hz, $J_{6a,7}$ = 8.5 Hz, $J_{6a,6b}$ = 13.7 Hz, H-6a), 2.36 (ddd, 1H, $J_{5,6b}$ = 7.9 Hz, $J_{6b,7}$ = 4.7 Hz, $J_{6a,6b}$ = 13.7 Hz, H-6b), 3.78 (dd, 1H, $J_{7,8a}$ = 2.1 Hz, $J_{8a,8b}$ = 10.5 Hz, H-8a), 4.07 (dd, 1H, $J_{7,8b}$ = 5.6 Hz, $J_{8a,8b}$ = 10.5 Hz, H-8b), 4.77 (m, 1H, H-7), 5.08 (dd, 1H, $J_{5,6a}$ = 5.0 Hz, $J_{5,6b}$ = 7.6 Hz, $J_{5,OH}$ = 0 Hz, H-5), 6.08 (brs, 1H, H—OH). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 36.3 (C-8), 37.2 (C-6), 60.0 (C-7), 72.0 (C-5), 92.4 (C-4), 149.3 (C-4a), 158.0, 161.5 (C-1, C-3).

5-Substituted 6,7-Dihydro-3-methoxy-7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones (*IXa*—*IXc*)

The mixture of both 5,7-*cis*/5,7-*trans* isomers of the corresponding pyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones *XIVa*—*XIVc* (1 equivalent) was dissolved in anhydrous 1,4-dioxane (10 cm^3) and DBU (1.5 equivalents) was added. The mixture was stirred at corresponding temperature. After cooling, water (10 cm^3) and ethyl acetate (20 cm^3) were added and the mixture was vigorously stirred for 10 min, followed by filtration through Celite®. The aqueous phase was further extracted with ethyl acetate (2 × 10 cm^3). The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The product was isolated by the column chromatography.

6,7-Dihydro-5-hydroxy-3-methoxy-7-methylenepyrrolo[1,2-c]pyrimidin-1(5H)-one (IXa): *XIVa* (0.16 g; 0.6 mmol in 10 cm^3 of 1,4-dioxane), DBU (0.13 g; 0.9 mmol), reaction temperature 80 °C, reaction time 2 h, column chromatography (CH_2Cl_2—CH_3OH, φ_r = 99 : 1), colourless solid, 0.05 g, yield 44 %, R_f = 0.34 (CH_2Cl_2—CH_3OH, φ_r = 95 : 5), m.p. = 192—193 °C. For $C_9H_{10}N_2O_3$ (M_r = 194.19) w_i(calc.): 55.67 % C, 5.19 % H, 14.43 % N; w_i(found): 55.85 % C, 5.24 % H, 14.56 % N. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.60 (dddd, 1H, $J_{5,6a}$ = 6.1 Hz, $J_{6a,6b}$ = 16.1 Hz, $J_{6a,10a}$ = 2.1 Hz, $J_{6a,10b}$ = 2.4 Hz, H-6a), 3.07 (dddd, 1H, $J_{5,6b}$ = 8.2 Hz, $J_{6a,6b}$ = 16.1 Hz, $J_{6b,10a}$ = 1.5 Hz, $J_{6b,10b}$ = 1.8 Hz, H-6b), 3.86 (s, 3H, OCH_3), 4.89 (dd, 1H, $J_{6a,10a}$ = 2.1 Hz, $J_{6b,10a}$ = 1.5 Hz, H-10a), 4.98 (dddd, 1H, $J_{5,OH}$ = 6.1 Hz, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 6.1 Hz, $J_{5,6b}$ = 8.2 Hz, H-5), 6.08 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.10 (d, 1H, $J_{5,OH}$ = 6.1 Hz, H—OH), 6.14 (dd, 1H, $J_{6a,10b}$ = 2.3 Hz, $J_{6b,10b}$ = 1.8 Hz, H-10b). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 38.2 (C-6), 55.1 (OCH_3), 68.0 (C-5), 91.5 (C-4), 99.1 (C-10), 143.1 (C-7), 154.2 (C-1), 164.7 (C-8), 171.6 (C-3).

6,7-Dihydro-5-benzoyloxy-3-methoxy-7-methylenepyrrolo[1,2-c]pyrimidin-1(5H)-one (IXb): *XIVb* (0.15 g; 0.4 mmol in 10 cm^3 of 1,4-dioxane), DBU (0.09 g; 0.6 mmol), under reflux, reaction time 1 h, column chromatography (hexane—ethyl acetate, φ_r = 70 : 30), colourless syrup, 0.08 g, yield 70 %, R_f = 0.35 (hexane—ethyl acetate, φ_r = 70 : 30). ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.96 (dddd, 1H, $J_{5,6a}$ = 4.6 Hz, $J_{6a,6b}$ = 16.9 Hz, J = 1.8 Hz, J = 2.1 Hz, H-6a), 3.33 (dddd, 1H, $J_{5,6b}$ = 8.2 Hz, $J_{6a,6b}$ = 16.9 Hz, J = 1.8 Hz, J = 2.1 Hz, H-6b), 3.98 (s, 3H, OCH_3), 5.01 (ddd, 1H, $J_{10a,10b}$ = 1.2 Hz, J = 1.8 Hz, J = 2.1 Hz, H-10a), 6.13 (d, 1H, $J_{4,5}$ = 0.9 Hz, H-4), 6.19 (ddd, 1H, $J_{4,5}$ = 0.9 Hz, $J_{5,6a}$ = 4.6 Hz, $J_{5,6b}$ = 8.2 Hz, H-5), 6.46 (ddd, 1H, $J_{10a,10b}$ = 1.2 Hz, J = 1.8 Hz, J = 2.1 Hz, H-10b), 7.44—8.04 (m, 5H, COPh). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 35.4 (C-6), 55.4 (OCH_3), 69.8 (C-5), 94.0 (C-4), 101.1 (C-10), 129.1, 130.3, 134.3 (COPh), 141.0 (C-7), 154.8 (C-1), 157.5 (COPh), 166.0 (C-8), 171.5 (C-3).

6,7-Dihydro-5-tert-butyldiphenylsilyloxy-3-methoxy-7-methylenepyrrolo[1,2-c]pyrimidin-1(5H)-one (IXc): *XIVc* (0.70 g; 1.4 mmol in 20 cm^3 of 1,4-dioxane), DBU (0.31 g; 2.1 mmol), under reflux, reaction time 1 h, column chromatography (hexane—ethyl acetate, φ_r = 80 : 20), colourless syrup, which after standing at low temperature crystallized, 1.2 g, yield 70 %, R_f = 0.23 (hexane—ethyl acetate, φ_r = 70 : 30), m.p. = 100—102 °C. For $C_{25}H_{28}N_2O_3Si$(M_r = 432.59) w_i(calc.): 69.41 % C, 6.52 % H, 6.48 % N; w_i(found): 69.14 % C, 6.54 % H, 6.46 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 1.10 (s, 9H, $OSiC(CH_3)_3$), 2.68 (dddd, 1H, $J_{5,6a}$ = 7.9 Hz, $J_{6a,6b}$ = 15.2 Hz, $J_{6a,10a} = J_{6a,10b}$ = 1.2 Hz, H-6a), 2.76 (dddd, 1H, $J_{5,6b}$ = 7.3 Hz, $J_{6a,6b}$ = 15.2 Hz, $J_{6b,10a} = J_{6b,10b}$ = 2.3 Hz, H-6b), 3.95 (s, 3H, OCH_3), 4.82 (ddd, 1H, $J_{6a,10a} = J_{10a,10b}$ = 1.2 Hz, $J_{6b,10a}$ = 2.1 Hz, H-10a), 4.98 (ddd, 1H, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 7.9 Hz, $J_{5,6b}$ = 7.3 Hz, H-5), 5.77 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.28 (ddd, 1H, $J_{6a,10b} = J_{10a,10b}$ = 1.2 Hz, $J_{6b,10b}$ = 2.3 Hz, H-10b), 7.40—7.68 (m, 10H, $OSiPh_2$). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 19.6 ($OSiC(CH_3)_3$), 27.2 ($OSiC(CH_3)_3$), 39.3 (C-6), 55.2 (OCH_3), 70.4 (C-5), 92.0 (C-4), 100.6 (C-10), 128.4, 128.5, 130.8, 132.7, 133.0, 136.1 ($OSiPh_2$), 141.3 (C-7), 154.8 (C-1), 161.9 (C-8), 171.6 (C-3).

1,3-Dipolar Cycloadditions of Mesitonitrile Oxide

Mesitonitrile oxide *XVII* and the corresponding 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one *IXa*—*IXc* were dissolved in anhydrous 1,4-dioxane (10 cm^3) and stirred under reflux. When no starting material remained (TLC), the solvent was removed *in vacuo* and the products *XVIII* and *XIX* of the cycloaddition were isolated by the column chromatography.

4′,5′,6,7-Tetrahydro-3′-(2,4,6-trimethylphenyl)-3-methoxy-5-hydroxyspiro[pyrrolo[1,2-c]pyrimidine-7(5H),5′-izoxazol]-1-one (XVIIIa, XIXa): *XVII* (0.08 g; 0.5 mmol), *IXa* (0.07 g; 0.3 mmol), reaction time 2 h, ratio 5,7-*cis XVIIIa*/5,7-*trans XIXa*, 30 : 70, 60 % total yield, column chromatography (CH_2Cl_2—CH_3OH, φ_r = 99 : 1).

XVIIIa isolated as a mixture of both isomers: 0.05 g, 43 % yield and 0.02 g, 18 % yield, R_f = 0.11 (CH_2Cl_2—CH_3OH, φ_r = 98 : 2). ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.25 (s, 3H, 4-CH_3—Ph), 2.30 (s, 6H, 2,6-CH_3—Ph), 2.36 (dd, 1H, $J_{5,6a}$ = 6.7 Hz, $J_{6a,6b}$ = 13.7 Hz, H-6a), 2.96 (dd, 1H, $J_{5,6b}$ = 7.9 Hz, $J_{6a,6b}$ = 13.7 Hz, H-6b), 3.45 (d, 1H, $J_{4'a,4'b}$ = 18.7 Hz, H-4′a), 3.85 (s, 3H, OCH_3), 3.86 (d, 1H, $J_{4'a,4'b}$ = 18.7 Hz, H-4′b), 4.96 (dddd, 1H, $J_{4,5}$ = 1.2 Hz, $J_{5,OH}$ = 5.8 Hz, $J_{5,6a}$ = 6.7 Hz, $J_{5,6b}$ = 7.9 Hz, H-5), 6.00 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.20 (d, 1H, $J_{5,OH}$ = 6.1 Hz, H—OH), 6.93 (s, 2H, H—Ph). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 20.4 (2,6-CH_3—Ph), 21.5 (4-CH_3—Ph), 46.5, 47.2 (C-6, C-4′), 55.0 (OCH_3), 68.0 (C-5), 90.4 (C-4), 102.8 (C-5′), 126.5 (C-4—Ph), 129.2 (CH—Ph), 137.7 (C-2,6—Ph), 139.1 (C-1—Ph), 153.8 (C-4a), 158.0 (C-3′), 164.1 (C-1), 173.1 (C-3).

XIXa 0.02 g, 17 % yield and 0.05 g, 42 % yield, colourless solid, R_f = 0.16 (CH_2Cl_2/CH_3OH, φ_r = 98 : 2), m.p. = 241—243 °C. ^{1}H NMR spectrum (400 MHz, DMSO-d_6), δ: 2.26 (s, 3H, 4-CH_3—Ph), 2.31 (s, 6H, 2,6-CH_3—Ph), 2.41 (dd, 1H, $J_{5,6a}$ = 8.8 Hz, $J_{6a,6b}$ = 13.7 Hz, H-6a), 2.87 (dd, 1H, $J_{5,6b}$ = 7.6 Hz, $J_{6a,6b}$ = 13.7 Hz, H-6b), 3.44 (d, 1H, $J_{4a',4b'}$ = 18.7 Hz, H-4a′), 3.85 (s, 3H, OCH_3), 4.22 (d, 1H, $J_{4a',4b'}$ = 18.7 Hz, H-4b′), 5.13 (dddd, 1H, $J_{4,5}$ = 1.5 Hz, $J_{5,OH}$ = 5.8 Hz, $J_{5,6a}$ = 8.8 Hz, $J_{5,6b}$ = 7.3 Hz, H-5), 6.05 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.29 (d, 1H, $J_{5,OH}$ = 5.8 Hz, H—OH), 6.93 (s, 2H, H—Ph). ^{13}C NMR spectrum (125 MHz, DMSO-d_6), δ: 20.4 (2,6-CH_3—Ph), 21.5 (4-CH_3—Ph), 46.3, 46.4 (C-6, C-4′), 55.1 (OCH_3), 68.4 (C-5), 90.7 (C-4), 102.6 (C-5′/C-7), 126.4 (C-4—Ph), 129.2 (CH—Ph), 137.7 (C-2,6—Ph), 139.1 (C-1—Ph), 153.8 (C-1), 158.4 (C-3′), 164.9 (C-4a), 173.1 (C-3).

4′,5′,6,7-Tetrahydro-3′-(2,4,6-trimethylphenyl)-3-methoxy-5-benzoyloxyspiro[pyrrolo[1,2-c]pyrimidine-7(5H),5′-izoxazol]-1-one (XVIIIb, XIXb): *XVII* (0.03 g; 0.2 mmol), *IXb* (0.04 g; 0.1 mmol), reaction time 3 h, ratio 5,7-*cis XVIIIb*/5,7-*trans XIXb* 17 : 83, 83 % total yield, column chromatography (hexane—ethyl acetate, φ_r = 75 : 25).

XVIIIb 0.10 g, 17 % yield and 0.08 g, 14 % yield, R_f = 0.18 (hexane—ethyl acetate, φ_r = 70 : 30), colourless solid, m.p. = 164—165 °C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.30 (s, 3H, 4-CH_3—Ph), 2.43 (s, 6H, 2,6-CH_3—Ph), 2.85 (dd, 1H, $J_{5,6a}$ = 7.0 Hz, $J_{6a,6b}$ = 15.1 Hz, H-6a), 2.99 (dd, 1H, $J_{5,6b}$ = 2.3 Hz, $J_{6a,6b}$ = 15.1 Hz, H-6b), 3.23 (d, 1H, $J_{4a',4b'}$ = 18.4 Hz, H-4a′), 3.97 (s, 3H, OCH_3), 4.50 (d, 1H, $J_{4a',4b'}$ = 18.4 Hz, H-4b′), 6.14 (d, 1H, $J_{4,5}$ = 0.9 Hz, H-4), 6.22 (ddd, 1H, $J_{4,5}$ = 0.9 Hz, $J_{5,6a}$ = 7.0 Hz, $J_{5,6b}$ = 2.3 Hz, H-5), 6.92 (s, 2H, H—Ph), 7.45—8.11 (m, 5H, COPh). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 20.4 (2,6-CH_3—Ph), 21.5 (4-CH_3—Ph), 44.5, 46.9 (C-6, C-4′), 55.5 (OCH_3), 69.8 (C-5), 94.4 (C-4), 102.9 (C-5′/C-7), 125.4 (C-4—Ph), 129.0, 130.5, 134.3 (CH—Ph, COPh), 137.9 (C-2,6—Ph), 139.5 (C-1—Ph), 154.2 (C-1), 156.9 (COPh), 158.0 (C-3′), 166.2 (C-4a), 173.3 (C-3).

XIXb 0.4 g, 66 % yield and 0.42 g, 69 % yield, R_f = 0.33 (hexane—ethyl acetate, φ_r = 70 : 30), colourless solid, m.p. = 210—212 °C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.30 (s, 3H, 4-CH_3—Ph), 2.42 (s, 6H, 2,6-CH_3—Ph), 2.57 (dd, 1H, $J_{5,6a}$ = 7.3 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6a), 3.25 (d, 1H, $J_{4a',4b'}$ = 18.4 Hz, H-4a′), 3.34 (dd, 1H, $J_{5,6b}$ = 7.6 Hz, $J_{6a,6b}$ = 14.0 Hz, H-6b), 3.98 (s, 3H, OCH_3), 4.58 (d, 1H, $J_{4a',4b'}$ = 18.1 Hz, H-4b′), 6.06 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.37 (ddd, 1H, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 7.3 Hz, $J_{5,6b}$ = 7.6 Hz, H-5), 6.92 (s, 2H, H—Ph), 7.46—7.65 (m, 5H, COPh). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 20.3 (2,6-CH_3—Ph), 21.5 (4-CH_3—Ph), 44.9, 47.0 (C-6, C-4′), 55.5 (OCH_3), 70.4 (C-5), 93.1 (C-4), 102.3 (C-5′/C-7), 125.4 (C-4—Ph), 129.0, 129.1, 130.3, 134.5 (CH—Ph, COPh), 137.9 (C-2,6—Ph), 139.6 (C-1—Ph), 154.2 (C-1), 157.7 (COPh), 158.2 (C-3′), 165.8 (C-4a), 173.2 (C-3).

4′,5′,6,7-Tetrahydro-3′-(2,4,6-trimethylphenyl)-3-methoxy-5-tert-butyldiphenylsilyloxyspiro[pyrrolo[1,2-c]pyrimidine-7(5H),5′-izoxazol]-1-one (XIXc): *XVII* (0.03 g; 0.2 mmol), *IXc* (0.03 g; 0.1 mmol), reaction time 4 h, ratio 5,7-*cis XVIIIc*/5,7-*trans XIXc* <5 : >95, 79 % total yield, column chromatography (hexane—ethyl acetate, φ_r = 80 : 20).

XIXc 0.03 g, 79 % yield, R_f = 0.52 (hexane—ethyl acetate, φ_r = 70 : 30), colourless solid, m.p. = 214—215 °C. For $C_{35}H_{39}N_3O_4Si$ (M_r = 593.79) w_i(calc.): 70.80 % C, 6.62 % H, 7.08 % N; w_i(found): 70.88 % C, 6.56 % H, 6.84 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 1.12 (s, 9H, $OSiC(CH_3)_3$), 2.28 (s, 3H, 4-CH_3—Ph), 2.37 (s, 6H, 2,6-CH_3—Ph), 2.32 (dd, 1H, $J_{5,6a}$ = 8.8 Hz, $J_{6a,6b}$ = 13.2 Hz, H-6a), 2.67 (dd, 1H, $J_{5,6b}$ = 7.3 Hz, $J_{6a,6b}$ = 13.2 Hz, H-6b), 3.09 (d, 1H, $J_{4a',4b'}$ = 18.4 Hz, H-4a′), 3.94 (s, 3H, OCH_3), 4.52 (d, 1H, $J_{4a',4b'}$ = 18.4 Hz, H-4b′), 5.25 (ddd, 1H, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 8.8 Hz, $J_{5,6b}$ = 7.3 Hz, H-5), 5.77 (d, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 6.89 (s, 2H, H—Ph), 7.41—7.70 (m, 10H, $OSiPh_2$). ^{13}C NMR spectrum (125 MHz, $CDCl_3$),

δ: 19.6 ($OSiC(CH_3)_3$), 20.4 (2,6-CH_3—Ph), 21.5 (4-CH_3—Ph), 27.3 ($OSiC(CH_3)_3$), 46.5, 47.6 (C-6, C-4′), 55.3 (OCH_3), 70.4 (C-5), 91.7 (C-4), 101.6 (C-5′/C-7), 125.5 (C-4—Ph), 128.5, 128.6, 129.0, 130.9, 131.0, 132.4, 132.8, 136.1 (CH—Ph, $OSiPh_2$), 137.8 (C-2,6—Ph), 139.4 (C-1—Ph), 154.3 (C-1), 158.2 (C-3′), 162.2 (C-4a), 173.2 (C-3).

2′-Benzyl-5-*tert*-butyldiphenylsilyloxy-3-methoxy-3′-methyloxycarbonyl-3′,4′,6-trihydrospiro[pyrrolo[1,2-*c*]pyrimidin-7(5*H*),5′-isoxazol]-1-one (*XXI*)

N-Benzyl-*C*-methoxycarbonyl nitrone *XX* (0.09 g; 0.5 mmol) and *IXc* (0.10 g; 0.2 mmol) were dissolved in anhydrous toluene (10 cm^3) and the mixture was stirred under reflux for 5 h. The solvent was evaporated *in vacuo* and the cycloadducts were isolated by column chromatography on silica (hexane—ethyl acetate, $\varphi_r = 75 : 25$) giving isoxazolidines *XXIa*—*XXId* in a total yield of 90 %. Only two major isomers *XXIa* and *XXIb* were isolated in the pure form:

(3′,5′-*trans*),(5′,5-*trans*) *XXIa* 0.07 g, 62 % yield, $R_f = 0.55$ (hexane—ethyl acetate, $\varphi_r = 70 : 30$), colourless uncrystalline stuff foam. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 1.12 (s, 9H, $OSiC(CH_3)_3$), 2.15 (dd, 1H, $J_{5,6a} = 9.4$ Hz, $J_{6a,6b} = 13.2$ Hz, H-6a), 2.63 (dd, 1H, $J_{5,6b} = 7.3$ Hz, $J_{6a,6b} = 13.2$ Hz, H-6b), 2.65 (dd, 1H, $J_{3',4a'} = 9.4$ Hz, $J_{4a',4b'} = 13.2$ Hz, H-4a′), 3.63 (s, 3H, $COOCH_3$), 3.69 (dd, 1H, $J_{3',4b'} = 7.6$ Hz, $J_{4a',4b'} = 13.2$ Hz, H-4b′), 3.96 (s, 3H, OCH_3), 4.07 (d, 1H, $J = 13.7$ Hz, NCH_2Ph), 4.24 (d, 1H, $J = 13.7$ Hz, NCH_2Ph), 4.40 (dd, 1H, $J_{3',4a'} = 9.4$ Hz, $J_{3',4b'} = 7.9$ Hz, H-3′), 5.03 (ddd, 1H, $J_{4,5} = 1.2$ Hz, $J_{5,6a} = 9.4$ Hz, $J_{5,6b} = 7.3$ Hz, H-5), 5.80 (d, 1H, $J_{4,5} = 1.2$ Hz, H-4), 7.25—7.68 (m, 15H, NCH_2Ph, $OSiPh_2$). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 21.0 ($OSiC(CH_3)_3$), 26.8 ($OSiC(CH_3)_3$), 41.2 (C-4′), 46.5 (C-6), 52.2 ($COOCH_3$), 54.6 (OCH_3), 61.9 (NCH_2Ph), 67.0 (C-3′), 70.4 (C-5), 91.0 (C-4), 98.8 (C-5′/C-7), 127.2—136.5 (NCH_2Ph, $OSiPh_2$), 153.9 (C-1), 162.8 (C-4a), 170.4, 172.6 (C-3, $COOCH_3$).

(3′,5′-*cis*),(5′,5-*trans*) *XXIb* 0.02 g, 20 % yield, $R_f = 0.26$ (hexane—ethyl acetate, $\varphi_r = 70 : 30$), colourless solid, m.p. = 70—74 °C. For $C_{35}H_{39}N_3O_6Si$ ($M_r = 625.79$) w_i(calc.): 67.18 % C, 6.28 % H, 6.71 % N; w_i(found): 66.98 % C, 6.30 % H, 6.31 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 1.10 (s, 9H, $OSiC(CH_3)_3$), 2.15 (dd, 1H, $J_{5,6a} = 9.1$ Hz, $J_{6a,6b} = 12.6$ Hz, H-6a), 2.20 (dd, 1H, $J_{5,6b} = 7.6$ Hz, $J_{6a,6b} = 12.6$ Hz, H-6b), 2.62 (dd, 1H, $J_{3',4a'} = 10.5$ Hz, $J_{4a',4b'} = 13.4$ Hz, H-4a′), 3.72 (dd, 1H, $J_{3',4a'} = 10.2$ Hz, $J_{3',4b'} = 4.4$ Hz, H-3′), 3.81 (s, 3H, $COOCH_3$), 3.88 (dd, 1H, $J_{3',4b'} = 4.4$ Hz, $J_{4a',4b'} = 13.4$ Hz, H-4b′), 3.91 (s, 3H, OCH_3), 4.01 (d, 1H, $J = 14.0$ Hz, NCH_2Ph), 4.27 (d, 1H, $J = 14.3$ Hz, NCH_2Ph), 5.06 (ddd, 1H, $J_{4,5} = 1.5$ Hz, $J_{5,6a} = 8.8$ Hz, $J_{5,6b} = 7.6$ Hz, H-5), 5.81 (d, 1H, $J_{4,5} = 1.5$ Hz, H-4), 7.21—7.66 (m, 15H, NCH_2Ph, $OSiPh_2$). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 19.1 ($OSiC(CH_3)_3$), 26.8 ($OSiC(CH_3)_3$), 39.8 (C-4′), 46.1 (C-6), 52.3 ($COOCH_3$), 54.6 (OCH_3), 60.7 (NCH_2Ph), 64.4 (C-3′), 70.1 (C-5), 90.6 (C-4), 98.7 (C-5′/C-7), 127.3—135.8 (NCH_2Ph, $OSiPh_2$), 154.1 (C-1), 162.5 (C-4a), 170.1, 172.1 (C-3, $COOCH_3$).

(3′,5′-*trans*),(5′,5-*trans*)-2′-Benzyl-5-*tert*-butyldiphenylsilyloxy-3′-hydroxymethyl-3-methoxy-3′,4′,6-trihydrospiro[pyrrolo[1,2-*c*]pyrimidin-7(5*H*),5′-isoxazol]-1-one (*XXII*)

The solution of *XXIa* (1.00 g; 1.6 mmol) in anhydrous THF (50 cm^3) was cooled to 0 °C and $LiBH_4$ (0.06 g; 3.2 mmol) was added. The reaction mixture was stirred at 0 °C for 12 h. After dilution with water, the solution was acidified with 0.5 M-HCl to pH $\approx$ 6 and extracted with ether (3 × 10 cm^3). The combined organic layers were washed with saturated $NaHCO_3$ solution and brine and dried over Na_2SO_4. The solvent was evaporated *in vacuo* and the product was purified by the column chromatography on silica (CH_2Cl_2—CH_3OH, $\varphi_r = 99 : 1$) giving product as a colourless solid (0.48 g) 50 % yield, $R_f = 0.49$ (CH_2Cl_2/CH_3OH, $\varphi_r = 95 : 5$), m.p. = 64—67 °C. For $C_{34}H_{39}N_3O_5Si$ ($M_r = 597.78$) w_i(calc.): 68.31 % C, 6.58 % H, 7.03 % N; w_i(found): 68.38 % C, 6.55 % H, 6.85 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 1.09 (s, 9H, $OSiC(CH_3)_3$), 1.99 (brs, 1H, OH), 2.16 (dd, 1H, $J_{5,6a} = 9.4$ Hz, $J_{6a,6b} = 12.6$ Hz, H-6a), 2.45 (dd, 1H, $J_{5,6b} = 7.0$ Hz, $J_{6a,6b} = 12.6$ Hz, H-6b), 2.46 (dd, 1H, $J_{3',4a'} = 9.1$ Hz, $J_{4a',4b'} = 13.4$ Hz, H-4a′), 3.37 (dd, 1H, $J_{3',6a'} = 2.9$ Hz, $J_{6a',6b'} = 11.7$ Hz, H-6a′), 3.45 (dd, 1H, $J_{3',6b'} = 3.5$ Hz, $J_{6a',6b'} = 11.7$ Hz, H-6b′), 3.54 (dd, 1H, $J_{3',4b'} = 8.2$ Hz, $J_{4a',4b'} = 13.4$ Hz, H-4b′), 3.90 (m, 1H, H-3′), 3.94 (s, 3H, OCH_3), 4.10 (d, 1H, $J = 13.7$ Hz, NCH_2Ph), 4.17 (d, 1H, $J = 13.7$ Hz, NCH_2Ph), 5.05 (ddd, 1H, $J_{4,5} = 1.2$ Hz, $J_{5,6a} = 9.4$ Hz, $J_{5,6b} = 7.0$ Hz, H-5), 5.81 (d, 1H, $J_{4,5} = 1.2$ Hz, H-4), 7.23—7.66 (m, 15H, NCH_2Ph, $OSiPh_2$). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 19.1 ($OSiC(CH_3)_3$), 26.8 ($OSiC(CH_3)_3$), 39.8, 46.8 (C-6, C-4′), 54.6 (OCH_3), 61.3, 61.6 (C-6′, NCH_2Ph), 66.5 (C-3′), 70.2 (C-5), 90.9 (C-4), 99.6 (C-5′/C-7), 127.2—137.0 (NCH_2Ph, $OSiPh_2$), 154.0 (C-1), 163.0 (C-4a), 170.4, 172.5 (C-3, $COOCH_3$).

(3′,5′-*trans*),(5′,5-*trans*)-2′-Benzyl-5-hydroxy-3′-hydroxymethyl-3-methoxy-3′,4′,6-trihydrospiro[pyrrolo[1,2-*c*]pyrimidin-7(5*H*),5′-isoxazol]-1-one (*XXIII*)

To the solution of *XXII* (0.20 g; 0.3 mmol) in THF (10 cm^3), the solution of TBAF · $3H_2O$ (0.10 g; 0.4 mmol) in THF (5 cm^3) was added dropwise and the mixture was stirred at room temperature for 1 h. Saturated $NaHCO_3$ solution was added and the stir-

ring was continued for 10 min. The separated aqueous phase was extracted with CH_2Cl_2 (2 × 10 cm^3), the combined organic layers were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The product residue was purified by column chromatography on silica (CH_2Cl_2—CH_3OH, φ_r = 95 : 5) giving product as a colourless solid (0.10 g), 83 % yield, R_f = 0.41 (CH_2Cl_2/CH_3OH, φ_r = 95 : 5), m.p. = 74—77 °C. For $C_{18}H_{21}N_3O_5$ (M_r = 359.38) w_i(calc.): 60.16 % C, 5.89 % H, 11.69 % N; w_i(found): 60.34 % C, 5.55 % H, 11.87 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 1.92 (brs, 1H, CH_2OH), 2.16 (dd, 1H, $J_{5,6a}$ = 10.0 Hz, $J_{6a,6b}$ = 13.2 Hz, H-6a), 2.48 (dd, 1H, $J_{3',4a'}$ = 9.0 Hz, $J_{4a',4b'}$ = 13.2 Hz, H-4a′), 2.82 (dd, 1H, $J_{6b,5}$ = 7.4 Hz, $J_{6b,6a}$ = 13.2 Hz, H-6b), 3.47—3.53 (m, 3H, H-4b′, H-6a′, H-6b′), 3.82—3.91 (m, 1H, H-3′), 3.87 (s, 3H, OCH_3), 4.09 (d, 1H, J = 13.7 Hz, NCH_2Ph), 4.20 (d, 1H, J = 13.7 Hz, NCH_2Ph), 4.40 (brs, 1H, CHOH), 5.31 (m, 1H, H-5), 6.04 (d, 1H, $J_{4,5}$ = 1.1 Hz, H-4), 7.27—7.29 (m, 5H, NCH_2Ph). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 40.0 (C-4′), 46.4 (C-6), 54.7 (OCH_3), 61.5, 61.8 (C-6′, NCH_2Ph), 67.0 (C-3′), 68.8 (C-5), 91.3 (C-4), 99.7 (C-5′/C-7′), 127.4, 128.4, 128.8 (CH—NCH_2Ph), 137.2 (C—NCH_2Ph), 154.5 (C-4a), 163.5 (C-1), 172.8 (C-3).

(3′,5′-*trans*),(5′,5-*trans*)-2′-Benzyl-5-hydroxy-3′-hydroxymethyl-3′,4′,6-trihydrospiro[pyrrolo-[1,2-*c*]pyrimidin-7(5*H*),5′-isoxazol]-1,3-dione (*VIII*)

XXIII (0.038 g; 0.1 mmol) was dissolved in CH_3OH (5 cm^3) and a solution of HCl in CH_3OH (5 cm^3) was added. The reaction mixture was stirred at room temperature for 3 h. The solvent was evaporated *in vacuo* giving pure isoxazolidine (0.035 g), 96 % yield, R_f = 0.25 (CH_2Cl_2—CH_3OH, φ_r = 90 : 10), m.p. = 241—243 °C. For $C_{17}H_{19}N_3O_5$ (M_r = 345.35) w_i(calc.): 59.12 % C, 5.55 % H, 12.17 % N; w_i(found): 59.18 % C, 5.22 % H, 12.50 % N. ^{1}H NMR spectrum (400 MHz, $CDCl_3$), δ: 2.15 (dd, 1H, $J_{5,6a}$ = 10.2 Hz, $J_{6a,6b}$ = 13.3 Hz, H-6a), 2.36 (m, 1H, H-4a′), 2.82 (dd, 1H, $J_{5,6a}$ = 7.4 Hz, $J_{6a,6b}$ = 13.3 Hz, H-6b), 3.32 (dd, 1H, $J_{3',4b'}$ = 7.0 Hz, $J_{4a',4b'}$ = 13.7 Hz, H-4b′), 3.70—3.79 (m, 2H, H-6a′, H-6b′), 3.90—4.00 (m, 1H, H-3′), 4.17 (d, 1H, J = 14.5 Hz, NCH_2Ph), 4.61 (d, 1H, J = 14.9 Hz, NCH_2Ph), 4.76 (m, 1H, H-5), 4.80—5.80 (brs, CH_2OH, CHOH), 5.55 (s, 1H, H-4), 7.29—7.40 (m, 5H, NCH_2Ph), 11.23 (s, 1H, NH). ^{13}C NMR spectrum (125 MHz, $CDCl_3$), δ: 38.5 (C-4′), 45.0 (C-6), 59.6, 59.8 (C-6′, NCH_2Ph), 66.9, 67.7 (C-3′, C-5), 95.6 (C-4), 99.1 (C-5′/C-7), 127.9, 128.1, 129.6 (NCH_2Ph), 148.1 (C-4a), 160.5, 163.8 (C-1, C-3).

X-Ray Crystallographic Study of Compound *XIVa*

The X-ray measurement of 7-bromomethyl-6,7-dihydro-5-hydroxy-3-methoxypyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one (*XIVa*) was performed at 100 (2) K on a Kuma CCD *k*-axis diffractometer with graphite-monochromated Mo$K\alpha$ radiation (0.71073 Å). The crystal was positioned at 62.25 mm from the KM4CCD camera; 600 frames were measured at 1.0° intervals on a counting time of 40 s. Data reduction and analysis were carried out with the Kuma Diffraction programs. The data were corrected for Lorentz and polarization effects, and the analytic absorption correction (T_{min} = 0.40155 and T_{max} = 0.63831) was applied. The structure was solved by direct methods [30] and refined by using SHELXL [31]. The refinement was based on F^2 for all reflections except for those with very negative F^2. The weighted R factor, wR and all goodness-of-fit S values are based on F^2. The nonhydrogen atoms were refined anisotropically, whereas the H-atoms were placed in the calculated positions. The atomic scattering factors were taken from the International Tables [32]. $C_9H_{11}BrN_2O_3$, colourless crystal, 0.1 mm × 0.1 mm × 0.15 mm, relative molecular mass M_r = 275.11, monoclinic, space group $P2_1/c$, a = 6.984(1) Å, b = 15.359(3) Å, c = 9.486(2) Å, β = 94.82(3)°, V = 1013.9(4) $Å^3$, Z = 4, D_x = 1.802 Mg/m^3, $F(000)$ = 552, absorption coefficient μ = 4.042 mm^{-1}. The collected data range was $3.42 < \Theta < 24.99°$. ($-8 \leqq h \leqq 8$, $-18 \leqq k \leqq 18$, $-10 \leqq l \leqq 11$), 7270 reflections collected, 1780 (R(int) = 0.0398) unique reflections, goodness-of-fit on F^2= 1.023, final R = 0.0240, wR^2 = 0.0510 (for all 1532 $F_o > 4\ \sigma(F_o)$), R = 0.0309, wR^2 = 0.0537 (for all data), weight = $1/[\sigma^2(F_o^2) + (0.0306\ P)^2 + 0.00\ P]$ where $P = (F_o^2 + 2\ F_c^2)/3$, extinction coefficient = 0.0000(6), maximum and minimum difference electron densities were 0.466 $Å^{-3}$ and −0.347 $Å^{-3}$. Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC 230933. Copies of the data can be obtained on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements. The authors are grateful to the Slovak Grant Agency (No. 1/0057/03), APVT (No. 20-010702), and the Deutsche Forschungsgemeinschaft (L. F. stay at FU Berlin). The X-ray measurements were undertaken in the Crystallographic Unit of the Physical Chemistry Laboratory at the Chemistry Department of the University of Warsaw.

REFERENCES

1. De Clercq, E., *Biochim. Biophys. Acta 1587*, 258 (2002).
2. Chiacchio, U., Genovese, P., Iannazzo, D., Librando, V., Merino, P., Rescifina, A., Romeo, R., Procopio, A., and Romeo, G., *Tetrahedron 60*, 441 (2004).
3. Haruyama, H., Takayama, T., Kinoshita, T., Kondo, M., Nakajima, M., and Haneishi, T., *J. Chem. Soc., Perkin Trans. 1 1991*, 1637.

4. Kittaka, A., Tanaka, H., Odanaka, Y., Ohnuki, K., Yamaguchi, K., and Miyasaka, T., *J. Org. Chem. 59*, 3636 (1994).
5. Kittaka, A., Asakura, T., Kuze, T., Tanaka, H., Yamada, N., Nakamura, K. T., and Miyasaka, T., *J. Org. Chem. 64*, 7081 (1999).
6. Chatgilialoglu, C., Gimisis, T., and Spada, G. P., *Chem. Eur. J. 5*, 2866 (1999).
7. Yoshimura, Y., Otter, B. A., Ueda, T., and Matsuda, A., *Chem. Pharm. Bull. 40*, 1761 (1992).
8. Merino, P., *Curr. Med. Chem. – Anti-Infective Agents 1*, 389 (2002).
9. Pan, S., Amankulor, N. M., and Zhao, K., *Tetrahedron 54*, 6587 (1998).
10. Merino, P., Franco, S., Merchan, F. L., and Tejero, T., *J. Org. Chem. 65*, 5575 (2000).
11. Merino, P., Del Alamo, E. M., Franco, S., Merchan, F. L., Simon, A., and Tejero, T., *Tetrahedron: Asymmetry 11*, 1543 (2000).
12. Colacino, E., Coverso, A., Liguori, A., Napoli, A., Siciliano, C., and Sindona, G., *Tetrahedron 57*, 8551 (2001).
13. Dalpozzo, R., De Nino, A., Maiuolo, L., Procopio, A., De Munno, G., and Sindona, G., *Tetrahedron 57*, 4035 (2001).
14. Iannazzo, D., Piperno, A., Pistara, V., Rescifina, A., and Romeo, R., *Tetrahedron 58*, 581 (2002).
15. Chiacchio, U., Corsaro, A., Iannazzo, D., Piperno, A., Pistara, V., Procopio, A., Rescifina, A., Romeo, G., Romeo, R., Siciliano, M. C. R., and Valveri, E., *ARKIVOC 2002*, 159.
16. Chiacchio, U., Corsaro, A., Iannazzo, D., Piperno, A., Rescifina, A., Romeo, R., and Romeo, G.,*Tetrahedron Lett. 42*, 1777 (2001).
17. Iannazzo, D., Piperno, A., Pistara, V., Rescifina, A., and Romeo, R., *Tetrahedron 58*, 581 (2002).
18. Fischer, R., Drucková, A., Fišera, L., Rybár, A., Hametner, C., and Cyránski, M. K., *Synlett 2002*, 1113.
19. Fischer, R., Drucková, A., Fišera, L., and Hametner, C., *ARKIVOC 2002*, 80.
20. Fischer, R., Hýrošová, E., Drucková, A., Fišera, L., Hametner, C., and Cyránski, M. K., *Synlett 2003*, 2364.
21. Gershon, H., *J. Org. Chem. 27*, 3507 (1962).
22. Snider, B. B. and Chaoyu, X., *Tetrahedron Lett. 39*, 7021 (1998).
23. Danel, K., Pedersen, E. B., and Nielsen, C., *Synthesis 1997*, 1021.
24. Crystallographic data for the 5,7-*cis* isomer of *XIVa* have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).
25. Ondruš, V., Orság, M., Fišera, L., and Prónayová, N., *Tetrahedron 55*, 10425 (1999).
26. Jensen, K. B., Hazell, G. R., and Jørgensen, K. A., *J. Org. Chem. 64*, 2353 (1999).
27. Li, X., Takahashi, H., Ohtake, H., and Ikegami, S., *Heterocycles 59*, 547 (2003).
28. Merino, P., Revuelta, J., Tejero, T., Chiacchio, U., Rescifina, A., and Romeo, G., *Tetrahedron 59*, 3581 (2003).
29. Stogryn, E. L., *J. Heterocycl. Chem. 11*, 251 (1974).
30. Sheldrick, G. M., *Acta Crystallogr. A46*, 467 (1990).
31. Sheldrick, G. M., SHELXL93. Program for the Refinement of Crystal Structures. University of Göttingen, Germany.
32. *International Tables for Crystallography*, Vol. C. (Wilson, A. J. C., Editor.) Kluwer, Dordrecht, 1992.