Isoxazolinyl Spironucleosides: Stereoselectivity of 1,3-Dipolar Cycloadditions of 7-Methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones

Róbert Fischer,[a] Eva Hýrošová,[a] Alexandra Drucková,[a] Lubor Fišera,*[a] Christian Hametner,[b] Michał K. Cyrański[c]

[a] Department of Organic Chemistry, Slovak University of Technology, 812 37 Bratislava, Slovak Republic
E-mail: fisera@cvt.stuba.sk

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

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

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Abstract: Novel 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones **11a–c** were synthesized from commercially available orotic acid (**6**). 1,3-Dipolar cycloadditions of mesitonitrile oxide to the exocyclic double bond of the dipolarophiles **11** proceed with complete regioselectivity and lead to the spiroisoxazolinyl nucleosides **13** and **14** in good yields. Attack of the dipole from the less sterically hindered side of the dipolarophile affords C-5/C-7 *trans* isoxazolines as major isomers predominantly. The protection of the free hydroxyl group by the bulky substituent (TBDPS) leads to formation C-5/C-7 *trans* isomer **14c** exclusively.

Key words: pyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones, dipolar cycloadditions, nitrile oxides, isoxazolines, modified spironucleosides

Spironucleosides are useful modifications of the natural nucleosides with defined architecture around the *N*-glycosidic bond. Stereochemical factors such as *cis*/*trans* glycosyl configuration are important for biological activity and can be changed when the molecules are bound to an enzyme, but not in nucleosides, whose torsion angles are fixed. In connection with the discovery of hydantocidin (**1**),[1] a natural spiro compound possessing herbicidal and plant growth regulatory activities, new spiro structures 2′-deoxy-6,1′-ethanouridine **2**[2] and 6,1′-propanouridine **3**[3] were synthesised (Figure 1).

Insertion of a nitrogen atom into the furanosyl ring gives the possibility of constructing new modified nucleosides (isoxazolidines **4** and isoxazolines **5**).[4] Nucleosides containing nitrogen as the second heteroatom have received considerable interest for their potential anti-HIV activity over the last 10 years.[5,6] The first example of an isoxazolidinyl nucleoside branched in the C-5 anomeric position was synthesized by Chiacchio and Romeo. (Figure 1, **4;** R = Me, R^1 = H, R^2 = CH_2OH, B = thymine, adenine).[7] 1,3-Dipolar cycloadditions of nitrile oxides and nitrones with *N*-vinylated bases represents a means of accessing modified isoxazolinyl and isoxazolidinyl nucleosides directly. Based on our previous results from this area,[8] we focused our attention onto the preparation of spiroisoxazolines via 1,3-dipolar cycloaddition of mesitonitrile oxide **12** with the 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones **11a–c**.

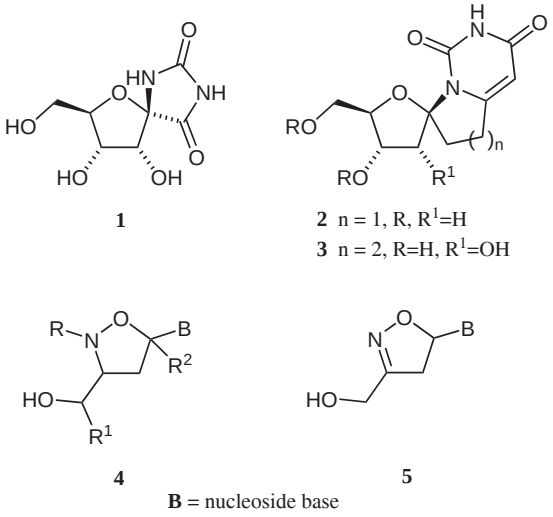

Figure 1

For the preparation of the final dipolarophiles **11a–c** (Scheme 1) we decided to use orotic acid (**6**) as a suitable and commercially available starting material in the synthesis of 6-substituted pyrimidinones. The corresponding methyl ester **7** was prepared by the procedure described in the literature.[9] Direct reduction with DIBAL-H/CH_2Cl_2/–78 °C gave aldehyde **8**[10] in 90% yield. According to the literature,[11] we carried out allylation of aldehyde **8** with allyl bromide and Zn dust in anhydrous THF. After column chromatography we obtained pure homoallyl alcohol **9a** as a colorless solid in 85% yield.[12] Cyclization to the more nucleophilic *N*-1 nitrogen through the bromonium ion gave a mixture of two difficult to separate isomers **10a** (5,7-*cis*:5,7-*trans* = 70:30). In addition to the desired product **10a** the unprotected pyrimidinone **15** was also isolated (Figure 2). Furthermore, more then one equivalent of bromine results in formation of C-4 brominated derivate **16** (Figure 2). Finally, 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)one **11a**[14] was prepared by elimination of HBr with DBU[11] in 44% yield from the mixture of 5,7-*cis* and 5,7-*trans* isomers of **10a**. Lack of success in direct silylation of the free hydroxyl group of **11a** caused us to turn our attention to the silylation of homoallyl alcohol **9a** using by TBDPSCl/imidazole in CH_2Cl_2, which gave compound **9c** in 95% yield. Cyclization and subsequent

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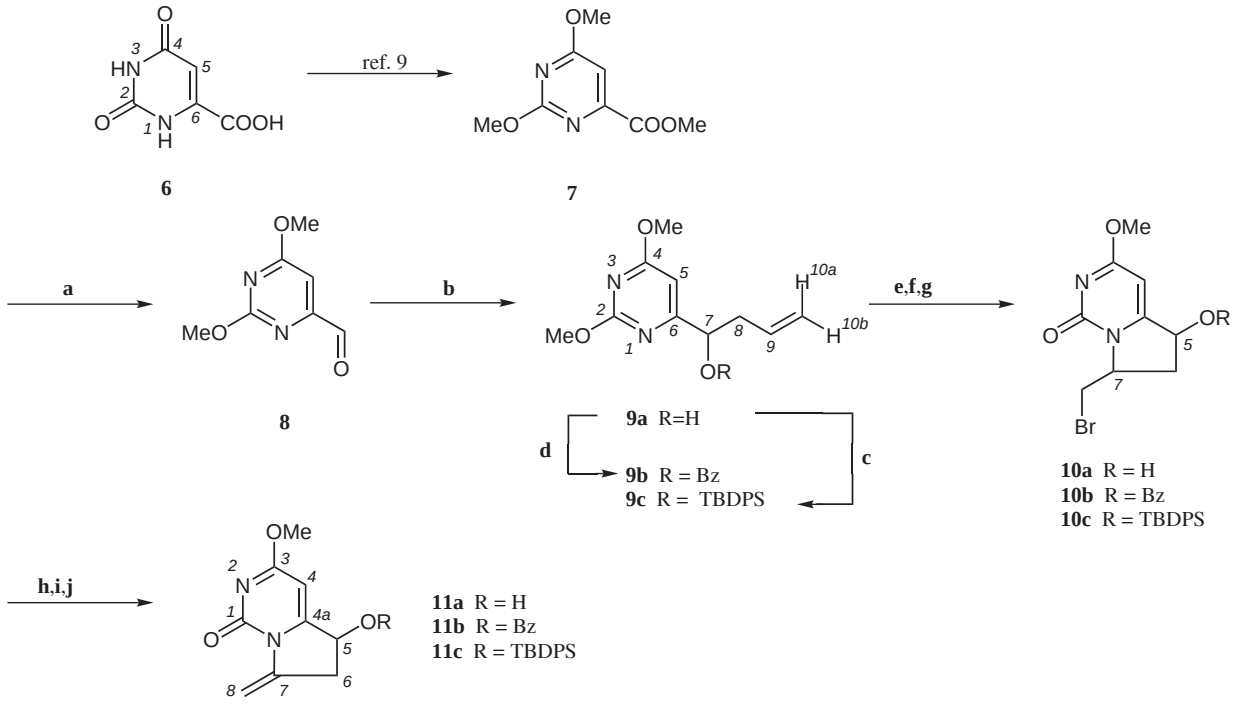


Scheme 1 (a) DIBAL-H (3 equiv), CH_2Cl_2, –78 °C, 4 h, 90%; (b) allyl bromide, Zn-dust, THF, reflux, 3 h, 85%; (c) TBDPSCl, imidazole, CH_2Cl_2, reflux, 24 h, 95%; (d) BzCl, CH_2Cl_2, reflux, 48 h, 85%; (e) from **9a**: Br_2, $CHCl_3$, 60 °C, 4 h, 80%; (f) from **9b**: Br_2, $CHCl_3$, 60 °C, 4 h, 82%, ref.[13]; (g) from **9c**: Br_2, $CHCl_3$, 60 °C, 4 h, 80%; (h) from **10a**: DBU, 1,4-dioxane, 80 °C, 2 h, 44%; (i) from **10b**: DBU, 1,4-dioxane, reflux, 1 h, 70%; (j) from **10c**: DBU, 1,4-dioxane, reflux, 1 h, 70%

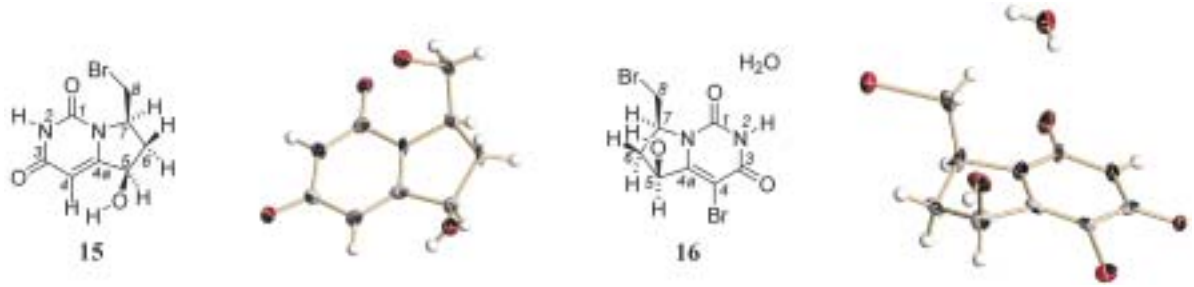
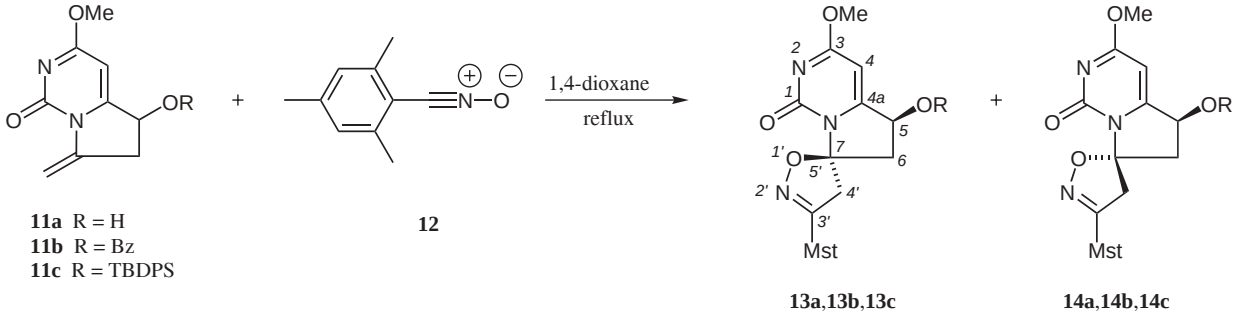


Figure 2

elimination afforded 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one **11c** in 56% yield over two steps.[14] By the same means benzoylated pyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one **11b** was prepared from **9a** in total yield of 49%.[14]

Cycloadditions of 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-ones **11a–c** with mesitonitrile oxide **12** proceeded with complete regioselectivity to provide 5-isoxazolines **13** and **14** in good yields (Scheme 2, Table 1).[15] The approach of the dipole takes place predominantly from the less sterically hindered side of dipolarophiles **11a** and **11b** providing a mixture of two 5,7-*cis* **13a**, **13b** and 5,7-*trans* **14a**, **14b** isomers (Table 1, entries 1 and 2). On the other



Scheme 2

Table 1 1,3-Dipolar Cycloadditions of Mesitonitrile Oxide **12** to Methylenepyrrolo[1,2-*c*] pyrimidinones **11a–c**

Entry	Dipolarophile	Total yield (%)	*cis* **13**:*trans* **14**[a]
1	**11a**	60	30:70
2	**11b**	83	17:83
3	**11c**	79	<5:95

[a] Ratios were obtained by ^{13}C NMR (125 MHz) integration of the crude reaction mixture.

bulky silyl group proceeded with high stereoselectivity providing 5,7-*trans* isoxazoline **14c** exclusively. All isomers were purified by column chromatography and were identified by NMR spectroscopic analysis and NOE difference experiments.

Based on the results from the NOE experiments protons H-5, H-6 and H-4′, for the major isomers **14a–c** we assigned the C-5/C-7 *trans* relative configuration (Figure 3). Thus, attack of the dipole to the exocyclic double bond of **11** occurs from the less sterically hindered side of the ring (Figure 3).[16] With a bulky hydroxyl protecting group at C-5, stereoselectivity of the cycloaddition was increased in favor of major isomers **14**.

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(10) Aldehyde **8** was prepared from **7** by a two-steps process via selective oxidation of the corresponding alcohol in 84% yield: Snider, B. B.; Chaoyu, X. *Tetrahedron Lett.* **1998**, *39*, 7021.

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(12) **Procedure for 2,4-Dimethoxy-6-(1-hydroxybut-3-en-1-yl)pyrimidine (9a):** To a stirred suspension of Zn dust (1.98 g, 7.33 mmol) in anhyd THF (50 mL), allyl bromide (1.62 mL, 18.07 mmol) was added, followed by 2,4-dimethoxy-6-pyrimidinecarbaldehyde (**8**, 0.60 g, 3.57 mmol) and the mixture was stirred vigorously under reflux for 3 h. The reaction mixture was cooled to r.t., quenched with sat. aq NH_4Cl and vigorously stirred with CH_2Cl_2 (30 mL) for 15 min. The solid was removed by filtration through the Celite® and the organic layer was separated. The aq phase was extracted with CH_2Cl_2 (20 mL) and the combined organic layers were dried with Na_2SO_4, filtered and the solvent removed. The final product was purified by the column

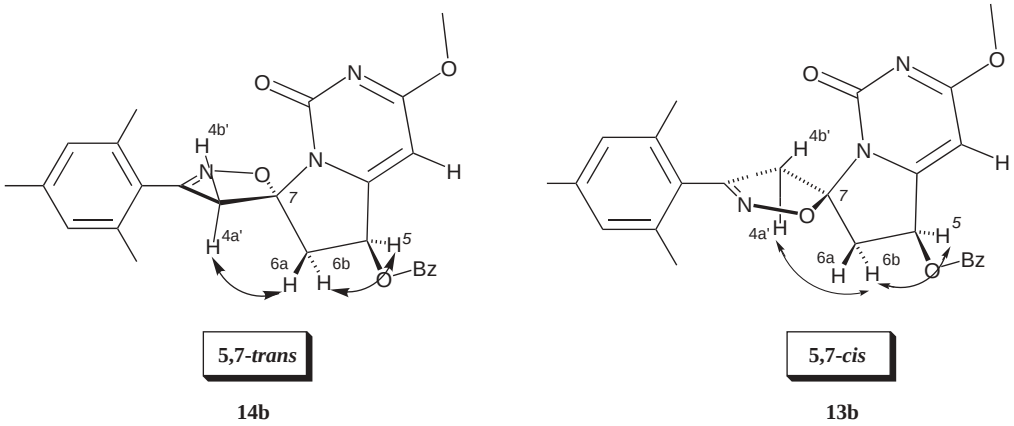

Figure 3 Positive NOE's for the protons H-4′, H-5 and H-6 in the case of the both isomers **13b** and **14b**

chromatography on silica gel (hexane–EtOAc, 3:1) giving homoallyl alcohol **9a** (0.63 g) as a colourless solid; yield 85%; mp 131–133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.46 (ddddd, $J_{7,8a}$ = 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, 1 H, H-8a), 2.63 (ddddd, $J_{7,8b}$ = 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, 1 H, H-8b), 3.37 (d, $J_{7,OH}$ = 5.0 Hz, 1 H, OH), 3.97, 4.00 (2 × s, 2 × 3 H, OCH_3), 4.62 (ddd, $J_{7,OH}$ = 4.7 Hz, $J_{7,8a}$ = 7.6 Hz, $J_{7,8b}$ = 4.7 Hz, 1 H, H-7), 5.13 (dddd, $J_{8a,10b}$ = 1.2 Hz, $J_{8b,10b}$ = 1.2 Hz, $J_{9,10b}$ = 10.2 Hz, $J_{10a,10b}$ = 1.8 Hz, 1 H, H-10b), 5.14 (dddd, $J_{8a,10a}$ = 1.5 Hz, $J_{8b,10a}$ = 1.5 Hz, $J_{9,10a}$ = 17.0 Hz, $J_{10a,10b}$ = 2.0 Hz, 1 H, H-10a), 5.81 (dddd, $J_{8a,9}$ = 7.0 Hz, $J_{8b,9}$ = 7.0 Hz, $J_{9,10a}$ = 17.0 Hz, $J_{9,10b}$ = 10.2 Hz, 1 H, H-9), 6.39 (d, $J_{5,7}$ = 0.6 Hz, 1 H, H-5). ^{13}C NMR (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).

(13) **Procedure for 10a:** The stirred solution of the homoallyl alcohol **9b** (0.20 g, 0.64 mmol) in $CHCl_3$ (20 mL) was warmed to 60 °C and a solution of Br_2 (0.10 g, 0.03 mL, 0.64 mmol) in $CHCl_3$ (10 mL) was slowly added dropwise over 4 h. The solvent was removed in vacuo and the reaction products were isolated by column chromatography on silica gel (hexane–EtOAc, 1:1) giving pyrimidinone **10b** as a mixture of *cis*/*trans* isomers (0.20 g, 82%) as colorless foam.

(14) **Selected data: 6,7-Dihydro-5-hydroxy-3-methoxy-7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one (11a):** Yield 44%; colorless solid; mp 192–193 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.60 (dddd, $J_{5,6a}$ = 6.1 Hz, $J_{6a,6b}$ = 16.1 Hz, $J_{6a,10a}$ = 2.1 Hz, $J_{6a,10b}$ = 2.4 Hz, 1 H, H-6a), 3.07 (dddd, $J_{5,6b}$ = 8.2 Hz, $J_{6a,6b}$ = 16.1 Hz, $J_{6b,10a}$ = 1.5 Hz, $J_{6b,10b}$ = 1.8 Hz, 1 H, H-6b), 3.86 (s, 3 H, OCH_3), 4.89 (dd, $J_{6a,10a}$ = 2.1 Hz, $J_{6b,10a}$ = 1.5 Hz, $J_{10a,10b}$ = 0 Hz, 1 H, H-10a), 4.98 (dddd, $J_{5,OH}$ = 6.1 Hz, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 6.1 Hz, $J_{5,6b}$ = 8.2 Hz, 1 H, H-5), 6.08 (d, $J_{4,5}$ = 1.2 Hz, 1 H, H-4), 6.10 (d, $J_{5,OH}$ = 6.1 Hz, 1 H, OH), 6.14 (dd, $J_{6a,10b}$ = 2.3 Hz, $J_{6b,10b}$ = 1.8 Hz, 1 H, H-10b). ^{13}C NMR (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-*tert*-butyldiphenylsilyloxy-3-methoxy-7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one (11b): Yield 66%; colorless syrup. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 [s, 9 H, $OSiC(CH_3)_3$], 2.68 (dddd, $J_{5,6a}$ = 7.9 Hz, $J_{6a,6b}$ = 15.2 Hz, $J_{6a,10a}$ = $J_{6a,10b}$ = 1.2 Hz, 1 H, H-6a), 2.76 (dddd, $J_{5,6b}$ = 7.3 Hz, $J_{6a,6b}$ = 15.2 Hz, $J_{6b,10a}$ = $J_{6b,10b}$ = 2.3 Hz, 1 H, H-6b), 3.95 (s, 3 H, OCH_3), 4.82 (ddd, $J_{6a,10a}$ = $J_{10a,10b}$ = 1.2 Hz, $J_{6b,10a}$ = 2.1 Hz, 1 H, H-10a), 4.98 (ddd, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 7.9 Hz, $J_{5,6b}$ = 7.3 Hz, 1 H, H-5), 5.77 (d, $J_{4,5}$ = 1.2 Hz, 1 H, H-4), 6.28 (ddd, $J_{6a,10b}$ = $J_{10a,10b}$ = 1.2 Hz, $J_{6b,10b}$ = 2.3 Hz, 1 H, H-10b), 7.40–7.68 (m, 10 H, $OSiPh_2$). ^{13}C NMR (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).

6,7-Dihydro-5-benzoyloxy-3-methoxy-7-methylene-pyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one (11c): Yield 80%; colorless syrup. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.96 (dddd, $J_{5,6a}$ = 4.6 Hz, $J_{6a,6b}$ = 16.9 Hz, J = 1.8 Hz, J = 2.1 Hz, 1 H, H-6a), 3.33 (dddd, $J_{5,6b}$ = 8.2 Hz, $J_{6a,6b}$ = 16.9 Hz, J = 1.8 Hz, J = 2.1 Hz, 1 H, H-6b), 3.98 (s, 3 H, OCH_3), 5.01 (ddd, $J_{10a,10b}$ = 1.2 Hz, J = 1.8 Hz, J = 2.1 Hz, 1 H, H-10a), 6.13 (d, $J_{4,5}$ = 0.9 Hz, 1 H, H-4), 6.19 (ddd, $J_{4,5}$ = 0.9 Hz, $J_{5,6a}$ = 4.6 Hz, $J_{5,6b}$ = 8.2 Hz, 1 H, H-5), 6.46 (ddd, $J_{10a,10b}$ = 1.2 Hz, J = 1.8 Hz, J = 2.1 Hz, 1 H, H-10b), 7.44–8.04 (m, 5 H, COPh). ^{13}C NMR (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).

(15) **General Procedure:** Mesitonitrile oxide **12** and 7-methylenepyrrolo[1,2-*c*]pyrimidin-1(5*H*)-one **11** were dissolved in 1,4-dioxane and stirred under reflux. When no starting material remained (TLC), the solvent was removed in vacuo and the products of the cycloaddition were isolated by column chromatography (hexane–ethyl acetate).

Selected data: (5,7-*trans*)-4′,5′,6,7-Tetrahydro-3′-(2,4,6-trimethylphenyl)-3-methoxy-5-hydroxyspiro[pyrrolo[1,2-*c*]pyrimidine-7(5*H*),5′-izoxazol]-1-one (14a): Yield 42%; colorless solid; mp 241–243 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.26 (s, 3 H, 4-CH_3Ph), 2.31 (s, 6 H, 2,6-CH_3Ph), 2.41 (dd, $J_{5,6a}$ = 8.8 Hz, $J_{6a,6b}$ = 13.7 Hz, 1 H, H-6a), 2.87 (dd, $J_{5,6b}$ = 7.6 Hz, $J_{6a,6b}$ = 13.7 Hz, 1 H, H-6b), 3.44 (d, $J_{4a',4b'}$ = 18.7 Hz, 1 H, H-4a′), 3.85 (s, 3 H, OCH_3), 4.22 (d, $J_{4a',4b'}$ = 18.7 Hz, 1 H, H-4b′), 5.13 (dddd, $J_{4,5}$ = 1.5 Hz, $J_{5,OH}$ = 5.8 Hz, $J_{5,6a}$ = 8.8 Hz, $J_{5,6b}$ = 7.3 Hz, 1 H, H-5), 6.05 (d, $J_{4,5}$ = 1.2 Hz, 1 H, H-4), 6.29 (d, $J_{5,OH}$ = 5.8 Hz, 1 H, OH), 6.93 (s, 2 H, Ph). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.4 (2,6-CH_3Ph), 21.5 (4-CH_3Ph), 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).

(5,7-*trans*)-4′,5′,6,7-Tetrahydro-3′-(2,4,6-trimethyl-phenyl)-3-methoxy-5-*tert*-butyldiphenylsilyloxy-spiro[pyrrolo[1,2-*c*]pyrimidine-7(5*H*),5′-izoxazol]-1-one (14c): Yield 79%; colorless solid; mp 214–215 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 [s, 9 H, $OSiC(CH_3)_3$], 2.28 (s, 3 H, 4-CH_3Ph), 2.37 (s, 6 H, 2,6-CH_3Ph), 2.32 (dd, $J_{5,6a}$ = 8.8 Hz, $J_{6a,6b}$ = 13.2 Hz, 1 H, H-6a), 2.67 (dd, $J_{5,6b}$ = 7.3 Hz, $J_{6a,6b}$ = 13.2 Hz, 1 H, H-6b), 3.09 (d, $J_{4a',4b'}$ = 18.4 Hz, 1 H, H-4a′), 3.94 (s, 3 H, OCH_3), 4.52 (d, $J_{4a',4b'}$ = 18.4 Hz, 1 H, H-4b′), 5.25 (ddd, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 8.8 Hz, $J_{5,6b}$ = 7.3 Hz, 1 H, H-5), 5.77 (d, $J_{4,5}$ = 1.2 Hz 1 H, H-4), 6.89 (s, 2 H, H-Ph), 7.41–7.70 (m, 10 H, $OSiPh_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.6 [$OSiC(CH_3)_3$], 20.4 (2,6-CH_3Ph), 21.5 (4-CH_3Ph), 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 (CHPh, $OSiPh_2$), 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).

(5,7-*cis*)-4′,5′,6,7-Tetrahydro-3′-(2,4,6-trimethylphenyl)-3-methoxy-5-benzoyloxyspiro[pyrrolo[1,2-*c*]pyrimidine-7(5*H*),5′-izoxazol]-1-one (13b): Yield 14%; colorless solid; mp 164–165 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, 4-CH_3Ph), 2.43 (s, 6 H, 2,6-CH_3Ph), 2.85 (dd, $J_{5,6a}$ = 7.0 Hz, $J_{6a,6b}$ = 15.1 Hz, 1 H, H-6a), 2.99 (dd, $J_{5,6b}$ = 2.3 Hz, $J_{6a,6b}$ = 15.1 Hz, 1 H, H-6b), 3.23 (d, $J_{4a',4b'}$ = 18.4 Hz, 1 H, H-4a′), 3.97 (s, 3 H, OCH_3), 4,50 (d, $J_{4a',4b'}$ = 18.4 Hz, 1 H, H-4b′), 6.14 (d, $J_{4,5}$ = 0.9 Hz, 1 H, H-4), 6.22 (ddd, $J_{4,5}$ = 0.9 Hz, $J_{5,6a}$ = 7.0 Hz, $J_{5,6b}$ = 2.3 Hz, 1 H, H-5), 6.92 (s, 2 H, Ph), 7.45–8.11 (m, 5 H, COPh). ^{13}C NMR (125 MHz, $CDCl_3$), δ = 20.4 (2,6-CH_3Ph), 21.5 (4-CH_3Ph), 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 (CHPh, 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).

(5,7-*trans*)-4′,5′,6,7-Tetrahydro-3′-(2,4,6-trimethyl-phenyl)-3-methoxy-5-benzoyloxyspiro[pyrrolo[1,2-*c*]pyrimidine-7(5*H*),5′-izoxazol]-1-one (14b): Yield 69%; colorless solid; mp 210–212 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.30 (s, 3 H, 4-CH_3Ph), 2.42 (s, 6 H, 2,6-CH_3Ph), 2.57 (dd, $J_{5,6a}$ = 7.3 Hz, $J_{6a,6b}$ = 14.0 Hz, 1 H, H-6a), 3.25 (d, $J_{4a',4b'}$ = 18.4 Hz, 1 H, H-4a′), 3.34 (dd, $J_{5,6b}$ = 7.6 Hz, $J_{6a,6b}$ = 14.0 Hz, 1 H, H-6b), 3.98 (s, 3 H, OCH_3), 4.58 (d, $J_{4a',4b'}$ = 18.1 Hz, 1 H, H-4b′), 6.06 (d, $J_{4,5}$ = 1.2 Hz, 1 H, H-

4), 6.37 (ddd, $J_{4,5}$ = 1.2 Hz, $J_{5,6a}$ = 7.3 Hz, $J_{5,6b}$ = 7.6 Hz, 1 H, H-5), 6.92 (s, 2 H, H-Ph), 7.46–7.65 (m, 5 H, COPh). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.3 (2,6-CH_3Ph), 21.5 (4-CH_3Ph), 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 (CHPh, 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).

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(17) Crystallographic data for the structure **15** and **16** 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 (email: deposit@ccdc.cam.ac.uk).