An easy Route to 2-Substituted-2,3-dihydro-5(7)*H*-oxazolo[3,2-*a*]pyrimidin-5-ones and 7-ones Starting from the Corresponding 2-Amino-2-oxazolines

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The isomeric 2-substituted-7(5)-methyl-2,3-dihydro-5(7)*H*-oxazolo[3,2-*a*]pyrimidin-5-ones **3a-b** and 7-ones **2a-b**,**7a** were synthesized by cyclocondensation from the 5-substituted-2-amino-2-oxazolines **1a-b** with biselectrophiles. In boiling ethanol, the reaction of **1a-b** with acetylenic esters led to a mixture of **2a-b**,**7a** with a small amount of *(E)*-2-*N*-(2-ethoxycarbonylethylene)-5-substituted-2-iminooxazolines **5a-b**. The ring annulation between **1a-b** and diketene gave the 2-substituted-7-hydroxy-7-methyl-2,3,6,7-tetrahydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-ones **4a-b** which can be easily dehydrated to provide the 2-substituted-7-methyl-2,3-dihydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-ones **3a-b**.

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Interest in the synthesis of nucleoside analogues stems from their antiviral and antitumoral activities [1-4]. Much effort has been devoted to simplify the structures leading to the synthesis of various acyclonucleosides. New pyrimidinones have been defined as synthons to produce new classes of acylnucleosides by reaction with the appropriate nucleophiles [5-7]. We have recently developed the preparation of related bicyclopyrimidinones based on the reactivity of the amidine moiety of 2-amino-2-oxazolines [8-9].

In this work we report the one-step ring-annulation of 5-[(2-methylphenoxy)methyl]- **1a** and 5-[(1-phenyl-4-piperazinyl)methyl]-2-amino-2-oxazoline **1b** with potent biselectrophiles, acetylenic esters or diketene, leading to the isomeric 2-substituted-5-methyl-2,3-dihydro-7(5)*H*-oxazolo[3,2-*a*]pyrimidin-7-ones **2a-b**,**7a** and -5-ones **3a-b**. The raw materials **1a-b** were prepared according to the method previously described by the authors [10-11].

In refluxing ethanol, the condensation of **1a-b** with ethyl 2-butynoate afforded the corresponding 2-substituted-5-methyl-2,3-dihydro-7*H*-oxazolo[3,2-*a*]pyrimidin-7-ones **2a-b** in 48% and 57% yield respectively, and to the (*E*)-2-*N*-(1-methyl-2-ethoxycarbonylethylene)-5-substituted-2-iminooxazolines **5a-b** in lower yields (10-11%). The corresponding pyrimidin-5-ones **3a-b** were easily obtained

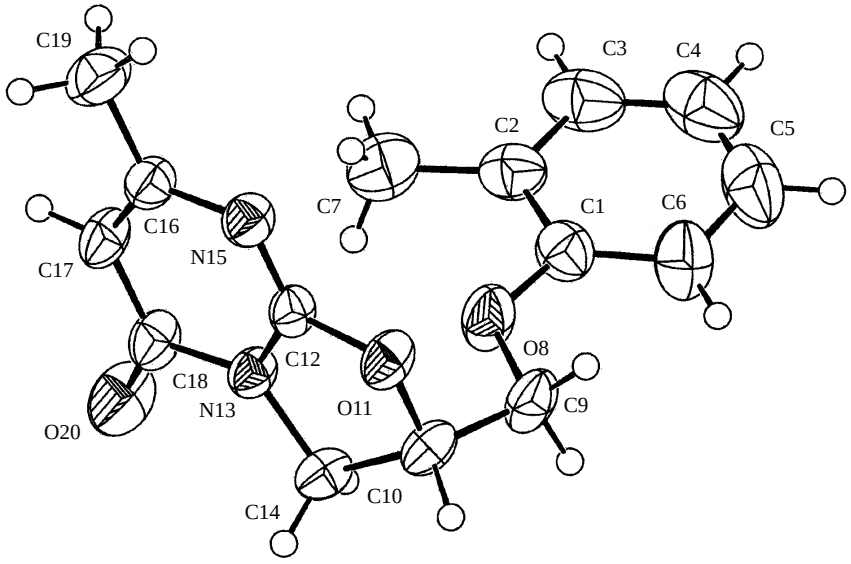
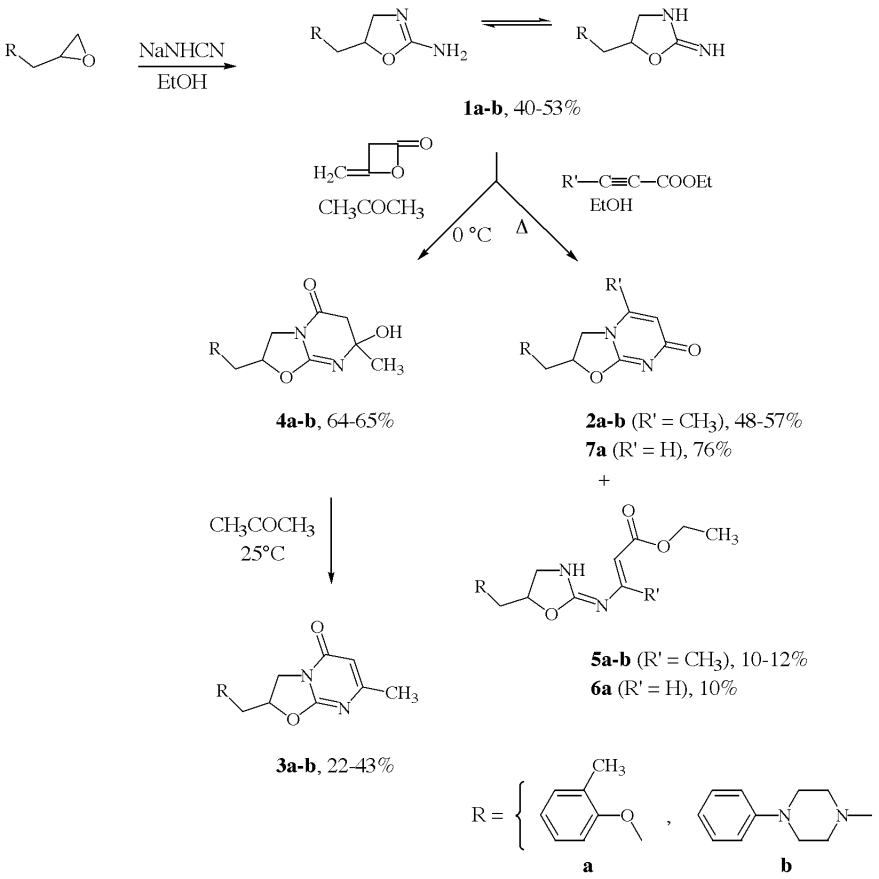


Figure 1. Side view of the crystal structure of **3a** with our numbering scheme, displacement ellipsoids are drawn at the 30% probability level.

Scheme 1



Synthesis of compounds **2a-b** and **3a-b**.

Table 1

Crystal Data and Structure Refinement for Compound **3a**

Formula	$C_{15}H_{16}N_2O_3$
Molecular weight	272.30
Crystal size (mm)	0.40 x 0.15 x 0.10
Lattice	monoclinic
Sp. Gr.	$P2_1/c$
a (Å)	12.817(2)
b (Å)	14.5120(10)
c (Å)	7.487(2)
b (°)	99.86(2)
D (mg/m^{-3})	1.318
F(000)	576
Z	4
Temperature	296(2) K
μ (mm^{-1})	0.763
h, k, l	0 15, 0 17, -8 +8
l (Å)	1.54178
No. of reflections	2330
No. of observed reflections	2330
Volume ($Å^3$)	1372.0(4)
No. of variables	182
R (F)	0.0457
Rw (F)	0.1329

by reaction of **1a-b** with diketene *via* the intermediates 2-substituted-7-hydroxy-7-methyl-2,3,6,7-tetrahydro-*5H*-oxazolo[3,2-*a*]pyrimidin-5-ones **4a-b**. By performing the reaction at 0 °C in acetone, we succeded in isolating these unstable cyclic hemiaminals **4a-b**, which result from a concerted addition [12-13].

Structural elucidation of **2a-b** was achieved by ^1H and ^{13}C nmr on the basis of previous results for the 2-aryl-2,3-dihydrooxazole[3,2-*a*]pyrimidin-7-one series published by Agami *et al*. [5-7]. The ^1H nmr spectrum of **2a** showed, at 5.75 ppm, the characteristic singlet for the proton at position 6, whereas it was found at 5.89 ppm for **3a**. In the ^{13}C nmr spectrum, the signals at 107.0 ppm (C-6), 160.8 ppm (C=N) and 172.5 ppm (C=O) confirmed the structure of **2a**. Different values of the C=O were also noticed in the ^{13}C nmr spectra of both compounds **2a** and **3a**, at 172.5 ppm for the first one and at 166.1 ppm for the second one.

Some differences were observed in the ^1H nmr spectra of the two regioisomers **2b** and **3b**, *i.e.*, the H-6 signal was observed at 5.72 ppm for **2b** and at 5.64 ppm for **3b**. The pyrimidin-5-one structure of **3a** has been confirmed by

Table 2

Atomic Coordinates (x 10^4) and Equivalent Isotropic Displacement Parameters ($Å^2$ x 10^3) for Compound **3a**

atom	x	y	z	U(eq)
C(1)	4267(2)	1253(1)	10505(3)	50(1)
C(2)	4777(2)	1092(2)	12267(3)	55(1)
C(3)	5872(2)	1100(2)	12596(4)	73(1)
C(4)	6448(2)	1263(2)	11226(5)	79(1)
C(5)	5930(2)	1440(2)	9519(5)	80(1)
C(6)	4829(2)	1444(2)	9134(4)	70(1)
C(7)	4140(2)	924(2)	13749(3)	81(1)
O(8)	3179(1)	1214(1)	10281(2)	57(1)
C(9)	2572(2)	1360(2)	8539(2)	51(1)
C(10)	1444(2)	1156(1)	8695(2)	43(1)
O(11	1331(1)	158(1)	8899(2)	43(1)
C(12)	1310(1)	-24(1)	10657(2)	33(1)
N(13)	1181(1)	756(1)	11565(2)	35(1)
C(14)	1093(2)	1561(1)	10380(2)	41(1)
N(15)	1383(1)	-848(1)	11284(2)	40(1)
C(16)	1336(1)	-901(1)	13121(2)	40(1)
C(17)	1222(2)	-157(1)	14154(2)	45(1)
C(18)	1131(2)	752(1)	13413(2)	43(1)
C(19)	1432(2)	-1853(2)	13885(3)	60(1)
O(20)	1014(2)	1481(1)	14186(2)	66(1)

Table 3

Bond lengths (Å) and Angles (°) for Compound **3a**

C(1)-C(6)	1.379(3)	C(10)-C(14)	1.528(3)
C(1)-O(8)	1.378(2)	O(11)-C(12)	1.347(2)
C(1)-C(2)	1.389(3)	C(12)-N(15)	1.283(2)
C(2)-C(3)	1.383(3)	C(12)-N(13)	1.345(2)
C(2)-C(7)	1.505(4)	N(13)-C(18)	1.396(2)
C(3)-C(4)	1.383(4)	N(13)-C(14)	1.460(2)
C(4)-C(5)	1.360(4)	N(15)-C(16)	1.389(2)
C(5)-C(6)	1.391(4)	C(16)-C(17)	1.352(3)
O(8)-C(9)	1.415(2)	C(16)-C(19)	1.492(3)
C(9)-C(10)	1.499(3)	C(17)-C(18)	1.428(3)
C(10)-O(11)	1.467(2)	C(18)-O(20)	1.226(2)
C(6)-C(1)-O(8)	124.4(2)	N(15)-C(12)-N(13)	127.4(2)
C(6)-C(1)-C(2)	121.4(2)	N(15)-C(12)-O(11)	121.8(2)
O(8)-C(1)-C(2)	114.2(2)	N(13)-C(12)-O(11)	110.79(14)
C(1)-C(2)-C(3)	117.7(2)	C(12)-N(13)-C(18)	121.9(2)
C(1)-C(2)-C(7)	120.1(2)	C(12)-N(13)-C(14)	111.67(14)
C(3)-C(2)-C(7)	122.1(2)	C(18)-N(13)-C(14)	126.43(14)
C(4)-C(3)-C(2)	121.6(3)	N(13)-C(14)-C(10)	101.03(14)
C(5)-C(4)-C(3)	119.5(2)	C(12)-N(15)-C(16)	113.72(14)
C(4)-C(5)-C(6)	120.7(3)	C(17)-C(16)-N(15)	123.3(2)
C(1)-C(6)-C(5)	119.1(3)	C(17)-C(16)-C(19)	122.1(2)
C(1)-O(8)-C(9)	119.4(2)	N(15)-C(16)-C(19)	114.6(2)
O(8)-C(9)-C(10)	106.5(2)	C(16)-C(17)-C(18)	121.8(2)
O(11)-C(10)-C(9)	108.5(2)	O(20)-C(18)-N(13)	119.6(2)
O(11)-C(10)-C(14)	104.20(14)	O(20)-C(18)-C(17)	128.4(2)
C(9)-C(10)-C(14)	114.4(2)	N(13)-C(18)-C(17)	112.0(2)
C(12)-O(11)-C(10)	108.26(13)		

X-ray crystallography (Figure 1). Bond lengths and angles (Table 3) do not show surprising features. The 2,3-dihydro-7*H*-oxazolo[3,2-*a*]pyrimidin-5-one moiety is almost planar, the maximum deviation from planarity is found for C(12) lying 0.007(2) Å from the plane C(12), N(13), N(15), C(16), C(17) and C(18).

During the addition of ethyl butynoate, we obtained a slight part of the non-cyclized esters **5a-b** isolated as the (*E*) conformers. This structural result was established by analyzing the spectrum of the corresponding compound **6a** obtained from **1a** with ethyl propiolate. This reaction led to the major pyrimidin-7-one **7a** (76%) with **6a** in poor yield (10%). The ^{1}H nmr spectrum of **6a** exhibited the presence of two typical *trans* olefinic protons at 8.13 and 5.03 ppm with a coupling constant *J* of 14 Hz. This conformation could explain the relative stability of **5a-b**,**6a** towards an ulterior intramolecular cyclization involving the second nucleophilic nitrogen atom [14]. A comparable behavior of related amidines towards other biselectrophiles was previously described [15-17].

In conclusion, we studied the reactivity of 5-substituted-2-amino-2-oxazolines **1a-b** as synthons to provide new pyrimidinones **2a-b**,**3a-b**,**7a**. The 2-substituted-7-methyl-2,3-dihydro-*5H*-oxazolo[3,2-*a*]pyrimidin-5-ones **3a-b** were easily obtained from diketene after dehydratation of the intermediates **4a-b**. On the other hand, the second regioisomers 2-substituted-5-methyl-2,3-dihydro-*7H*-oxazolo[3,2-*a*]pyrimidin-7-ones **2a-b**,**7a** were generated from acetylenic esters by a ring-annulation involving the endocyclic nitrogen atom of the 2-amino-2-oxazolines **1a-b**. During this reaction, the non-cyclized (*E*)-2-*N*-(2-ethoxycarbonylethylene)-5-substituted-2-iminooxazolines **5a-b**,**6a** were isolated in slight yields. These methodologies are particulary adapted to the synthesis of such heterocycles which may find applications either as bioactive compounds or as useful intermediates for further transformations.

EXPERIMENTAL

Melting points were determined with a Kofler hot stage apparatus and are uncorrected. The ir spectra were obtained with a Bruker IFS 25 spectrophotometer. The nmr data were recorded with a Bruker AC-200 spectrometer. Chemical shifts (δ in ppm) and coupling constants (J in Hz) were measured using TMS as the internal standard. Silica gel SDS 60 (70-230 mesh) was used for column chromatography. Microanalyses were carried out at the Service central d'analyse CNRS, Vernaison, France.

Crystal Structure Determinations.

Colourless single crystal of **3a** was obtained by slow evaporation from methanol solution. The crystallographic data are presented in Table 1. In both cases, the unit cell dimensions were determined using the least-squares fit from 25 reflections (q < 25°). Intensities were collected with an Enraf-Nonius CAD-4 diffractometer using monochromated CuKα radiation by the w/2q scan technique to a limit of 65°. The intensities were corrected for Lorentz and polarization effects, and empirical (Ψ scans) absorption correction was applied. Both structures were determined by direct methods using MULTAN 80 [18]. The

scattering factors were taken from [19]. C, N and O Atoms were refined anisotropically. The H-atoms were placed in theoritical positions or were located from difference Fourier maps were refined isotropically. The convergence largest D/s, were <1 (on Bs), the highest peaks in final difference maps were 0.318 and -0.300 e.Å^{-3}. The atomic coordinates presented in Table 2 have been deposited at the Cambridge Crystallographic Data Centre. University Chemical Laboratory, 12 Union Road, Cambridge CB2 IEZ, U.K.

General Procedure for Preparation of 2-Substituted-2,3-dihydro-7*H*-oxazolo[3,2-*a*]pyrimidin-7-one **2a-b**/**7a** and (*E*)-2-*N*-(2-Ethoxycarbonylethylene)-5-substituted-2-iminooxazolines **5a-b**/**6a**.

To a solution of 2-amino-2-oxazoline (**1a-b**) (30 mmol) in ethanol (50 mL) was added ethyl 2-butynoate or ethyl propiolate (40 mmol). The reaction mixture was heated at reflux for 6 hours. The ethanol was evaporated *in vacuo* and the residue was separated by column chromatography on silica gel (chloroform/-methanol: 90/10 – v/v) to give **2a-b/7a** and **5a-b/6a**.

2-[(2-Methylphenoxy)methyl]-5-methyl-2,3-dihydro-7*H*-oxazolo[3,2-*a*]pyrimidin-7-one (**2a**).

Compound **2a** was obtained as colourless crystals (Toluene), yield 48%; mp 148-149 °C; ir (potassium bromide): ν 1660 (CO). ^{1}H nmr (deuteriochloroform): δ 7.10 (t, 1H, J = 7.90 Hz, H-5'), 7.08 (d, 1H, J = 7.90 Hz, H-6'), 6.86 (t, 1H, J = 7.90 Hz, H-4'), 6.75 (d, 1H, J = 7.90 Hz, H-3'), 5.75 (s, 1H, H-6), 5.28 (m, 1H, H-2), 4.43 (m, 1H, H-3), 4.26 (m, 2H, H-3 and OCH_2), 4.17 (m, 1H, OCH_2), 2.19 (s, 3H, CH_3), 1.98 (s, 3H, CH_3); ^{13}C nmr: δ 172.5 (CO), 160.8 (C=N), 155.6 (C-5), 146.7 (C-1'), 130.9 (C-3'), 126.9 (C-5'), 126.5 (C-2'), 121.5 (C-4'), 110.8 (C-6'), 107.0 (C-6), 75.4 (C-2), 67.6 (OCH_2), 46.2 (C-3), 17.6 (CH_3), 15.7 (CH_3).

Anal. Calcd. for $C_{15}H_{16}N_2O_3$: C, 66.18; H, 5.88; N, 10.29. Found: C, 66.40; H, 5.95; N, 10.15.

2-(1-Phenyl-4-piperazinylmethyl)-5-methyl-2,3-dihydro-7*H*-oxazolo[3,2-a]pyrimidin-7-one (**2b**).

Compound **2b** was obtained as colourless crystals, yield 36%; mp 93-95 °C; ir (potassium bromide): ν 1660 (CO). ^{1}H nmr (deuteriochloroform): δ 7.23 (t, 2H, J = 7.60 Hz, H-3' and H-5'), 6.87 (d, 2H, J = 7.60 Hz, H-2' and H-6'), 6.83 (t, 1H, J = 7.60 Hz, H-4'), 5.72 (s, 1H, H-6), 5.07 (m, 1H, H-2), 4.30 (dd, 1H, J = 11.55 and 8.90 Hz , H-3a), 4.02 (dd, 1H, J = 11.55 and 7.10 Hz, H-3b), 3.13 (t, 4H, J = 4.85 Hz, CH_2 pip.), 2.84 (d, 2H, J = 5.25 Hz, NCH_2), 2.73 (m, 4H, CH_2 pip.), 2.18 (s, 3H, CH_3); ^{13}C nmr: δ 166.2 (CO), 161.2 (C=N), 152.0 (C-7), 143.5 (C-1'), 129.1 (C-3' and C-5'), 120.0 (C-4'), 116.2 (C-2' and C-6'), 105.7 (C-6), 77.5 (C-2), 60.3 (NCH_2), 54.2 (CH_2 pip.), 49.2 (CH_2 pip.), 45.8 (C-3), 24.0 (CH_3).

Anal. Calcd. for $C_{18}H_{22}N_4O_2$: C, 66.18; H, 6.74; N, 17.16. Found: C, 66.50; H, 6.73; N, 17.28.

2-[(2-Methylphenoxy)methyl]-2,3-dihydro-7*H*-oxazolo[3,2-*a*]-pyrimidin-7-one (**7a**).

Compound **7a** was obtained as colourless crystals (Toluene), yield 76%; mp 51-52 °C; ir (potassium bromide): ν 1650 (CO). ^{1}H nmr (deuteriochloroform): δ 7.31 (d, 1H, J = 7.40 Hz, H-5), 7.05 (m, 2H, H-3' and H-4'), 6.87 (t, 1H, J = 7.50 Hz, H-5'), 6.71 (d, 1H, J = 7.50 Hz, H-6'), 5.93 (d, 1H, J = 7.40 Hz, H-6), 5.30 (m, 1H, H-2), 4.50-4.11 (m, 4H, $2CH_2$), 1.94 (s, 3H, CH_3).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85. Found: C, 65.18; H, 5.51; N, 10.78.

(*E*)-2-*N*-(1-Methyl-2-ethoxycarbonylethylene)-5-[(2-methylphenoxy)methyl]-2-iminooxazolines (**5a**).

Compound **5a** was obtained as pale yellow oil, yield 10%; ir (potassium bromide): ν 3320 (NH), 1765 (CO). ^{1}H nmr (deuteriochloroform): δ 7.13 (m, 2H, H-5' and H-6'), 6.90 (m, 1H, H-4'), 6.75 (m, 1H, H-3'), 5.61 (s, 1H, CH=), 4.79 (m, 1H, CH), 4.20-3.81 (m, 6H, $3CH_2$), 2.77 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 1.25 (t, 3H, J = 7.0 Hz, CH_3).

Anal. Calcd. for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.96; N, 8.80. Found: C, 64.27; H, 7.05; N, 8.92.

(*E*)-2-*N*-(1-Methyl-2-ethoxycarbonylethylene)-5-(1-phenyl-4-piperazinylmethyl)-2-iminooxazolines (**5b**).

Compound **5b** was obtained as a yellow oil, yield 11%; ir (potassium bromide): ν 3325 (NH), 1720 (CO). ^{1}H nmr (deuteriochloroform): δ 7.24 (t, 2H, J = 7.50 Hz, H-3' and H-5'), 6.89 (d, 2H, J = 7.50 Hz, H-2' and H-6'), 6.84 (t, 1H, J = 7.50 Hz, H-4'), 5.59 (s, 1H, CH=), 4.60 (m, 1H, CH), 4.25-4.07 (m, 4H, $2CH_2$), 3.85 (m, 1H, CH_2), 3.59 (dd, 1H, J = 9.30 and 7.25 Hz, CH_2), 3.16 (m, 4H, CH_2 pip.), 2.71 (s, 3H, CH_3), 2.65 (m, 4H, CH_2 pip.), 1.29 (t, 3H, J = 7.10 Hz, CH_3).

Anal. Calcd. for $C_{20}H_{28}N_4O_3$: C, 64.49; H, 7.58; N, 15.04. Found: C, 64.57; H, 7.63; N, 14.91.

(*E*)-2-*N*-(2-Ethoxycarbonylethylene)-5-[(2-methylphenoxy)methyl]-2-iminooxazolines (**6a**).

Compound **6a** was obtained as a pale yellow oil, yield 10%; ir (potassium bromide): ν 3340 (NH), 1770 (CO). ^{1}H nmr (deuteriochloroform): δ 8.14 (d, 1H, J = 14.0 Hz, CH=), 7.20 (m, 2H, H-3' and H-4'), 6.88 (t, 1H, J = 7.70 Hz, H-5'), 6.75 (d, 1H, J = 7.70 Hz, H-6'), 5.54 (bs, 1H, NH), 5.03 (d, 1H, J = 14.0 Hz, CH=), 4.93 (m, 4H, $2CH_2$), 3.75 (m, 2H, CH_2), 2.14 (s, 3H, CH_3), 1.27 (t, 3H, J = 7.10 Hz, CH_3).

Anal. Calcd. for $C_{16}H_{20}N_2O_4$: C, 63.14; H, 6.62; N, 9.20. Found: C, 63.27; H, 6.81; N, 8.97.

General Procedure for Preparation of 2-Substituted-7-methyl-2,3-dihydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-one (**3a-b**).

A solution of 2-substituted-7-hydroxy-7-methyl-2,3,6,7-tetrahydro-5*H*-oxazolo[3,2-a]pyrimidin-5-one (**4a-b**) (30 mmoles) in 50 ml of acetone was stirred at 25 °C during 24 hours. The solvent was removed and the oily residue was triturated in diethyl ether to provide **3a** and **3b**.

2-[(2-Methylphenoxy)methyl]-7-methyl-2,3-dihydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-one (**3a**).

Compound **3a** was obtained as colourless crystals (Toluene), yield 43%; mp 125-127 °C; ir (potassium bromide): ν 1685 (CO). ^{1}H nmr (deuteriochloroform): δ 7.09 (t, 1H, J = 7.50 Hz, H-5'), 7.07 (d, 1H, J = 7.50 Hz, H-6'), 6.85 (t, 1H, J = 7.50 Hz, H-4'), 6.72 (d, 1H, J = 7.50 Hz, H-3'), 5.89 (s, 1H, H-6), 5.24 (m, 1H, H-2), 4.31 (m, 3H, H-3 and OCH_2), 4.13 (dd, 1H, J = 10.70 and 3.05 Hz, OCH_2), 2.19 (s, 3H, CH_3), 1.97 (s, 3H, CH_3); ^{13}C nmr: δ 166.1 (CO), 160.9 (C=N), 158.9 (C-7), 155.6 (C-1'), 130.9 (C-3'), 126.8 (C-2' and C-5'), 121.5 (C-4'), 110.7 (C-6'), 105.5 (C-6), 76.2 (C-2), 67.8 (OCH_2), 44.1 (C-3), 23.9 (CH_3), 15.6 (CH_3).

Anal. Calcd. for $C_{15}H_{16}N_2O_3$: C, 66.18; H, 5.88; N, 10.29. Found: C, 66.39; H, 6.13; N, 10.42.

2-(1-Phenyl-4-piperazinyl)methyl-7-methyl-2,3-dihydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-one (**3b**).

Compound **3b** was obtained as colourless crystals, yield 57%; mp 130-131 °C; ir (potassium bromide): ν 1695 (CO). ^{1}H nmr (deuteriochloroform): δ 7.26 (t, 2H, J = 7.65 Hz, H-3' and H-5'), 6.92 (d, 2H, J = 7.65 Hz, H-2' and H-6'), 6.86 (t, 1H, J = 7.65 Hz, H-4'), 5.64 (s, 1H, H-6), 4.68 (m, 1H, H-2), 3.87 (dd, 1H, J = 11.60 and 9.00 Hz , H-3a), 3.62 (dd, 1H, J = 11.60 and 7.20 Hz, H-3b), 3.20 (t, 4H, J = 4.95 Hz, CH_2 pip.), 2.76 (s, 3H, CH_3), 2.70 (m, 4H, CH_2 pip.), 2.65 (d, 2H, J = 5.20 Hz, NCH_2); ^{13}C nmr: δ 168.1 (CO), 155.9 (C=N), 154.1 (C-5), 151.1 (C-1'), 129.2 (C-3' and C-5'), 119.9 (C-4'), 116.2 (C-2' and C-6'), 99.6 (C-6), 72.3 (C-2), 60.9 (NCH_2), 54.0 (CH_2 pip.), 50.9 (C-3), 49.1 (CH_2 pip.), 16.5 (CH_3).

Anal. Calcd. for $C_{18}H_{22}N_4O_2$: C, 66.18; H, 6.74; N, 17.16. Found: C, 66.32; H, 6.76; N, 17.25.

General Procedure for the Preparation of 2-Substituted-7-hydroxy-7-methyl-2,3,6,7-tetrahydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-one (**4a-b**).

A solution of the required 2-amino-2-oxazoline **1a-b** (30 mmoles) in 50 ml of acetone was cooled to 0 °C. Then, diketene (40 mmoles) was slowly added. After the addition was complete, the mixture was stirred at 0 °C. A precipitate was observed after 30 minutes. It was isolated by filtration and dried to yield **4a-b**.

2-[2-(Methoxyphenoxy)methyl]-7-hydroxy-7-methyl-2,3,6,7-tetrahydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-one (**4a**) (racemic form).

Compound **4a** was obtained as colourless crystals, yield 64%; mp 139-141 °C; ir (potassium bromide): ν 3185 (OH), 1710 (CO). ^{1}H nmr (deuteriochloroform): δ 7.11 (m, 2H, H-5' and H-6'), 6.91 (m, 1H, H-4'), 6.75 (m, 1H, H-3'), 5.18 and 5.01 (2m, 1H, H-2), 4.36-4.01 (m, 4H, CH_2), 2.85-2.56 (m, 2H, CH_2), 2.13 (m, 4H, CH_3 and OH), 1.52 (2s, 3H, CH_3).

Anal. Calcd. for $C_{15}H_{18}N_2O_4$: C, 62.07; H, 6.21; N, 9.65. Found: C, 62.15; H, 6.15; N, 9.73.

2-(1-Phenyl-4-piperazinyl)methyl-7-hydroxy-7-methyl-2,3,6,7-tetrahydro-5*H*-oxazolo[3,2-*a*]pyrimidin-5-one (**4b**) (racemic form).

Compound **4b** was obtained as colourless crystals, yield 65%; mp 133-134 °C; ir (potassium bromide): ν 3200 (OH), 1700 (CO). ^{1}H nmr (deuteriochloroform): δ 7.40 (m, 2H, H-3' and H-5'), 7.05 (m, 2H, H-2' and H-6'), 7.01 (m, 1H, H-4'), 4.83 (m, 1H, H-2), 3.73 (m, 1H, H-3a), 3.47(m, 1H, H-3b), 3.17 (m, 4H, NCH_2), 2.65 (m, 6H, NCH_2), 1.80 (bs, 1H, OH), 1.66 and 1.65 (2s, 3H, CH_3); ^{13}C nmr: δ 167.3 and 167.2 (CO), 153.6 and 153.5 (C=N), 150.9 and 150.8 (C-1'), 128.9 (C-3' and C-5'), 119.6 (C-4'), 115.9 and 115.8 (C-2' and C-6'), 83.5 and 83.4 (C-7), 75.9 and 75.7 (C-2), 60.1 and 60.0 (NCH_2), 53.9 and 53.8 (CH_2 pip.), 49.0 and 48.9 (CH_2 pip.), 44.5 and 44.4 (C-3), 42.2 and 42.1 (C-6), 30.4 (CH_3).

Anal. Calcd. for $C_{18}H_{24}N_4O_3$: C, 62.71; H, 6.97; N, 16.26. Found: C, 62.95; H, 7.13; N, 16.34.

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