Synthesis of loganVir, a New Carbocyclic Nucleoside Analog
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**Abstract**

Starting from a natural cyclopentanoid monoterpenone belonging to the class of iridoid glucosides called Loganin, we performed the synthesis of a new carbocyclic nucleoside, allowing the preparation of a new lead compound, with a potential HIV antiviral activity as a RT competitive inhibitor that we named LoganVir. The stereocontrol of the coupling reaction was completed utilizing the procedure described by Mitsunobu with a purinic base.

**Key words:** Antiviral agents / Terpenoids / Rearrangements / Chiral intermediates / synthons

**Spectrometric identification**

\`H and \textsuperscript{13}C NMR spectra were recorder on Varian Mercury 300 MHz instrument using CDCl\textsubscript{3}, CD\textsubscript{3}OD and D\textsubscript{2}O as deuterated solvents, the chemical shift was expressed in ppm from TMS (the signal of HDO at 4.78 ppm is used as reference for spectra in D\textsubscript{2}O) MS spectra were performed on a Q-TOF MICRO spectrometer (Micromass, now Waters, Manchester UK) equipped with an ESI source, that was operated in the negative and/or positive ion mode. The flow rate of sample injection was 10µL/min. With 100 acquisition per spectrum. Data were analyzed using Masslynx software developed by Waters.

**Chromatography**

Products were purified by solid-liquid column chromatography on Merck 0.063-0.20 mm silica gel; eluent was chosen case by case. TLC on plates precoated with Kiegel-
Gel 60 F<sub>254</sub> (Merck) was used to monitor the progress of the reaction; spots were developed by spraying with 2 N H<sub>2</sub>SO<sub>4</sub> and heating to 120 °C for 1 min.

**Compound 1**

(Loganic Acid)

(1S,6S,7R)-6-hydroxy-7-methyl-1-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-1,4a,5,6,7,7a-hexahydrocyclopenta[c]pyran-4-carboxylic acid.

<sup>1</sup>H-NMR, (300 MHz, D<sub>2</sub>O), δ : 0.88 (3H, d, J=6.1 Hz, H-10), 1.60 (1H, m, H-8), 1.74 (1H, m, H-9), 1.97 (1H, m, H-5), 2.86 (1H, m, H-5’), 3.13 (1H, m, H-3’), 3.25 (1H, m, H-4’), 3.58 (2H, m, H-5’’), 3.98 (1H, m, H-7), 4.58 (1H, d, J=9.2 Hz, H-1’), 5.22 (1H, d, J=9.0 Hz, H-1), 6.90 (1H, s, H-3). <sup>13</sup>C-NMR, (75 MHz, D<sub>2</sub>O), δ : 14.4 (C-10), 32.9 (C-5), 42.3 (C-6), 42.7 (C-8), 47.9 (C-9), 63.3 (C-6’), 72.2 (C-4’), 75.2 (C-2’), 76.9 (C-7), 78.1 (C-3’), 78.7 (C-5’), 98.2 (C-1), 100.8 (C-1’), 121.4 (C-4), 147.4 (C-3), 178.3 (C-11).

ESI-MS: m/z = 399.1060 [M+Na]<sup>+</sup> (calculated mass C<sub>16</sub>H<sub>24</sub>O<sub>10</sub> (376.5580)).

**Compound 2** (Loganin)

(1S,6S,7R)-methyl-6-hydroxy-7-methyl-1-(((2S,3R,4S)-3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)-1,4a,5,6,7,7‘hexahydrocyclopenta[c]pyran-4-carboxylate.

S.1  <sup>1</sup>H-NMR spectrum of 2
$^1$H-NMR, (330 MHz, CD$_3$OD), $\delta$: 1.08 (H-10, d, J=7.5 Hz), 1.60 (H-6, ddd, J=14.0 Hz, J=7.5 Hz, J=4.5 Hz), 1.86 (H-8, m), 2.03 (H-9, m), 2.25 (H-6, ddd, J=14 Hz, J=8.0 Hz, J=1.5 Hz), 3.10 (H-5, m), 3.20 (H-2’, d, J=8.1 Hz), 3.67 (-OMe), 4.04 (H-7, m), 4.65 (H-1’, d, J=8.0 Hz), 5.73 (H-1, d, J=4.5 Hz), 7.37 (H-3, d, J=0.5 Hz).

S.2 $^{13}$C-NMR spectrum of 2

$^{13}$C-NMR, (75 MHz, CD$_3$OD), $\delta$: 12.8 (C-10), 30.7 (C-5), 40.1 (C-8), 40.3 (C-6), 45.0 (C-9) 52.6 (-OMe), 61.5 (C-6’), 70.4 (C-4’), 73.6 (C-2’), 74.4 (C-7), 76.5 (C-3’), 77.1 (C-5’), 97.6 (C-1), 99.4 (C-1’), 113.2 (C-4), 151.0 (C-3).

S.3 ESI-MS spectrum of 2
ESI-MS: m/z = 413.1824 [M+Na]^+ (calculated mass C_{17}H_{26}O_{10} 390.3850).

S.4 $^1$H-NMR spectrum of 3

![Image of $^1$H-NMR spectrum of 3]

S.5 $^{13}$C-NMR spectrum of 3

![Image of $^{13}$C-NMR spectrum of 3]

S.6 ESI-MS spectrum of 3

![Image of ESI-MS spectrum of 3]
S.7 $^1$H-NMR spectrum of 4

S.8 $^{13}$C-NMR spectrum of 4 ($^{13}$C-NMR original format)

S.9 ESI-MS spectrum of 4
S.10 $^1$H-NMR spectrum of 5

S.11 $^{13}$C-NMR spectrum of 5

S.12 ESI-MS spectrum of 5
S.13 $^1$H-NMR spectrum of **6**

S.14 $^1$H-NMR spectrum of **6**
S.15 ESI-MS spectrum of 6

S.16 $^1$H-NMR spectrum of 7
S.17 $^{13}$C-NMR spectrum of 7

S.18 ESI-MS spectrum of 7

S.19 $^1$H-NMR spectrum of 8
$^{13}$C-NMR spectrum of 8

ESI-MS spectrum of 8
