

## Chemical Shifts of Nucleosides of 4-Oxoquinoline-3-Carboxylic Acid Analogues

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**Abstract:** *Analogs of natural and synthetic nucleosides are potential chemotherapeutic agents in HIV treatment. This fact led to the synthesis of new nucleosides. NMR studies are very important in order to determine the conformational equilibrium of the glycoside ring relative to the nitrogenated bases when studying the activity of this kind of molecule. Recent work has shown that <sup>13</sup>C NMR calculated chemical shifts are very useful in solving spectral problems. Thus we have made calculations in order to verify their applicability for the nucleosides that were studied. Calculations were carried out for nucleosides with fluorine as substituent, as calculations with heavy atoms such as Cl and Br, may present problems. Geometry optimization was made by using the Gaussian 98 program with the GIAO method and B3LYP/6-31G(d,p) basis sets. <sup>1</sup>H and <sup>13</sup>C spectra were acquired in a 5 mm o.d. tube using DMSO as solvent and TMS as reference on a Varian Unity Plus 300MHz spectrometer (299.96 MHz for <sup>1</sup>H and 75.43MHz for <sup>13</sup>C) at room temperature. According to our results, <sup>13</sup>C chemical shifts are quite similar for substituents in position 6 or 7 except for the ring in which the substituent is present. Thus calculations are expected to distinguish the carbons in this ring. These assignments were confirmed by assigning the corresponding hydrogens by using their coupling constants with fluorine from HETCOR experiments.*

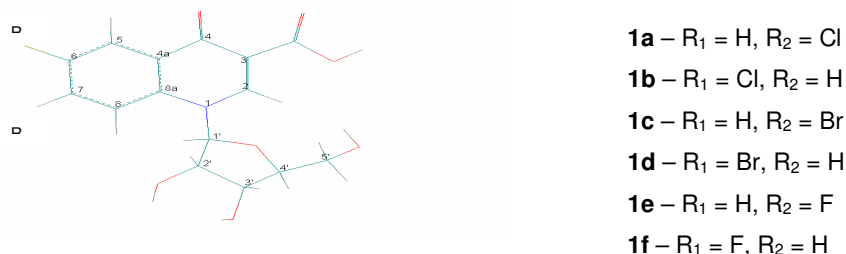
Analogs of natural and synthetic nucleosides are potential chemotherapeutic agents in HIV treatment. This fact led to the synthesis of new nucleosides (Figure 1).<sup>1</sup> NMR studies play an important role in determining the conformational equilibrium of the glycoside ring relative to nitrogenated bases when studying the activity of this kind of molecule.<sup>2</sup> Recent work has shown that <sup>13</sup>C NMR calculated chemical shifts are very useful in solving spectral problems.<sup>3,4</sup> Thus, we have made calculations in order to verify their

applicability to the nucleosides under study. Calculations were made for nucleosides 1e and 1f given the problems with calculations on heavy atoms such as Cl and Br.<sup>5</sup> Geometry optimization was made by using the Gaussian 98 program with the GIAO method and B3LYP/6-31G(d,p) basis sets.

<sup>1</sup>H and <sup>13</sup>C spectra were acquired in a 5 mm o.d. tube using DMSO as solvent and TMS as reference on a Varian Unity Plus 300MHz spectrometer (299.96 MHz for <sup>1</sup>H and 75.43MHz for <sup>13</sup>C) at room temperature.

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**Figure 1.** Substituted Nucleosides from 4-Oxoquinolin-3-Carboxylic Acid

According to Table 1, <sup>13</sup>C chemical shifts are very similar for substituents in position 6 or 7 for all carbons but the ones in the ring in which

the substituent is present. Thus the calculations are expected to distinguish the carbons from this ring.

**Table 1.** <sup>13</sup>C chemical shifts observed and calculated by Gaussian 98 program

		<b>1e</b>	<b>1f</b>
	<b>Obs.</b>	<b>Calc.</b>	<b>Calc.</b>
<b>C2</b>	143.8	136.8	136.1
<b>C3</b>	107.5	108.3	107.1
<b>C4</b>	177.0	164.4	164.4
<b>C4a</b>	127.2	123.4	129.4
<b>C5</b>	110.4	128.7	112.7
<b>C6</b>	159.8	108.4	156.3
<b>C7</b>	122.7	160.7	114.4
<b>C8</b>	120.9	98.6	112.6
<b>C8a</b>	135.8	134.6	129.3
<b>C1'</b>	93.5	95.0	94.7
<b>C2'</b>	75.2	82.5	82.8
<b>C3'</b>	69.0	73.7	73.6
<b>C4'</b>	85.4	91.3	91.1
<b>C5'</b>	59.9	61.5	61.7
<b>COOH</b>	165.6	152.8	152.8

Except for C<sub>8a</sub>, which showed practically the same calculated chemical shift as that of C<sub>4a</sub>, we found that the observed <sup>13</sup>C chemical shifts values correspond to structure 1f. These assignments were confirmed by assigning the corresponding hydrogens from their coupling constants with fluorine and HETCOR experiments.

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