

# Anomeric spironucleosides of $\beta$ -D-glucofuranosyl uracil as potential inhibitors of glycogen phosphorylase

Aggeliki Stathi<sup>1</sup>, Michael Mamais<sup>1,2</sup>, Evangelia D. Chrysina<sup>2</sup> and Thanasis Gimisis<sup>1,\*</sup>

<sup>1</sup> Organic Chemistry Laboratory, Department of Chemistry, National and Kapodistrian University of Athens, 10571, Athens, Greece. e-mail: [gimisis@chem.uoa.gr](mailto:gimisis@chem.uoa.gr).

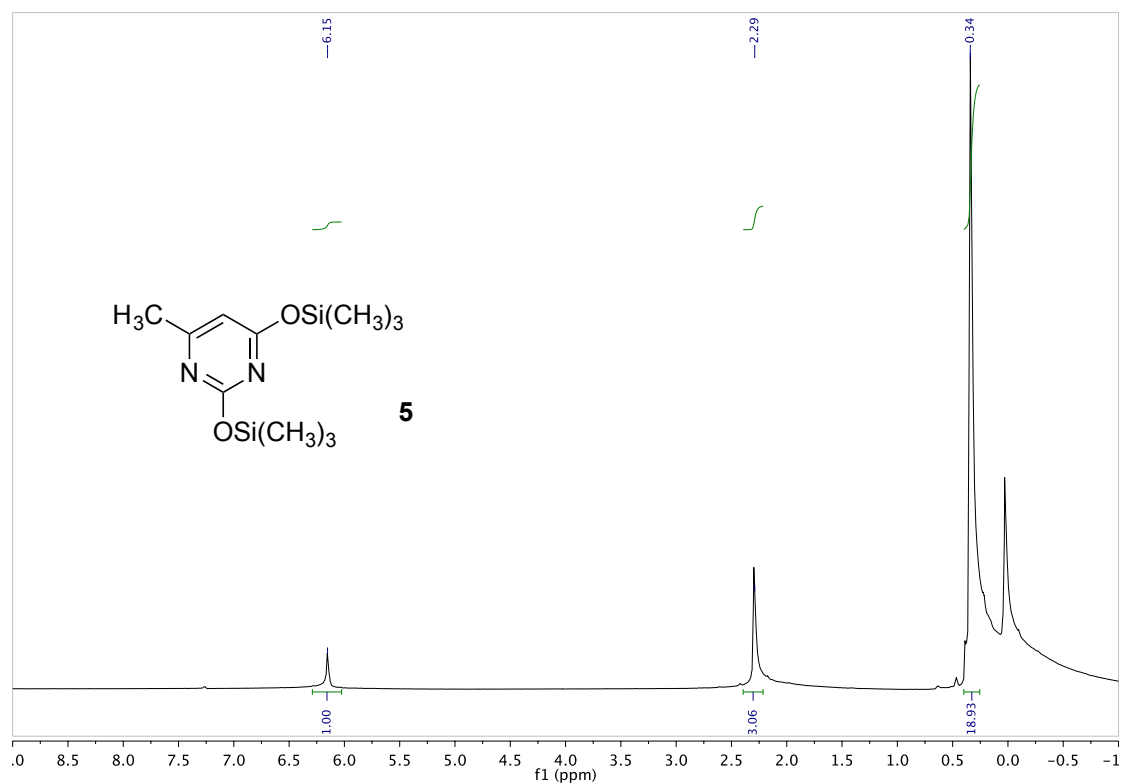
<sup>2</sup> Institute of Biology, Medicinal Chemistry & Biotechnology, National Hellenic Research Foundation, Athens (Greece). e-mail: [echrysina@ie.gr](mailto:echrysina@ie.gr).

## Supplementary Materials

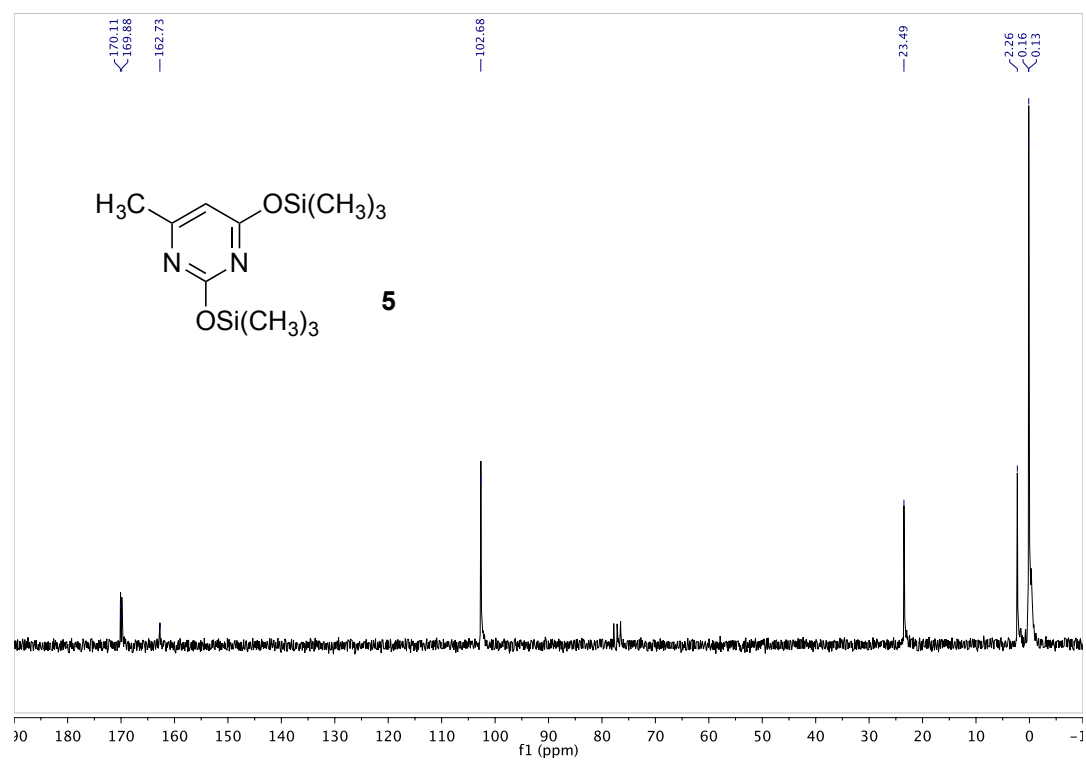
### Contents

<b>Figures S1-S21.</b> NMR spectra of compounds <b>5</b> , <b>6a-c</b> , <b>7</b> , <b>8</b> , <b>9a,b</b> and <b>4a,b</b> .	<b>2-12</b>
<b>Tables S1-2.</b> Enzyme kinetics for compounds <b>4a,b</b> and RMGPb.	<b>13</b>

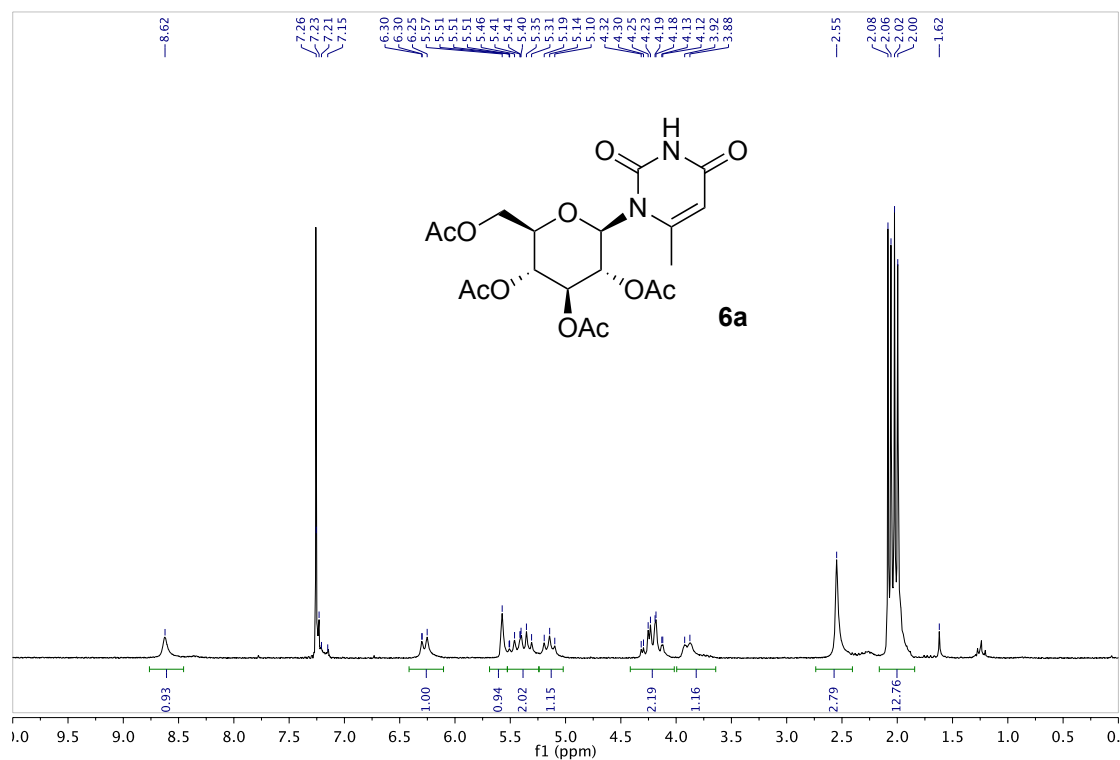
**Figure S1.**  $^1\text{H}$  NMR spectrum of compound **5** (200 MHz,  $\text{CDCl}_3$ ).



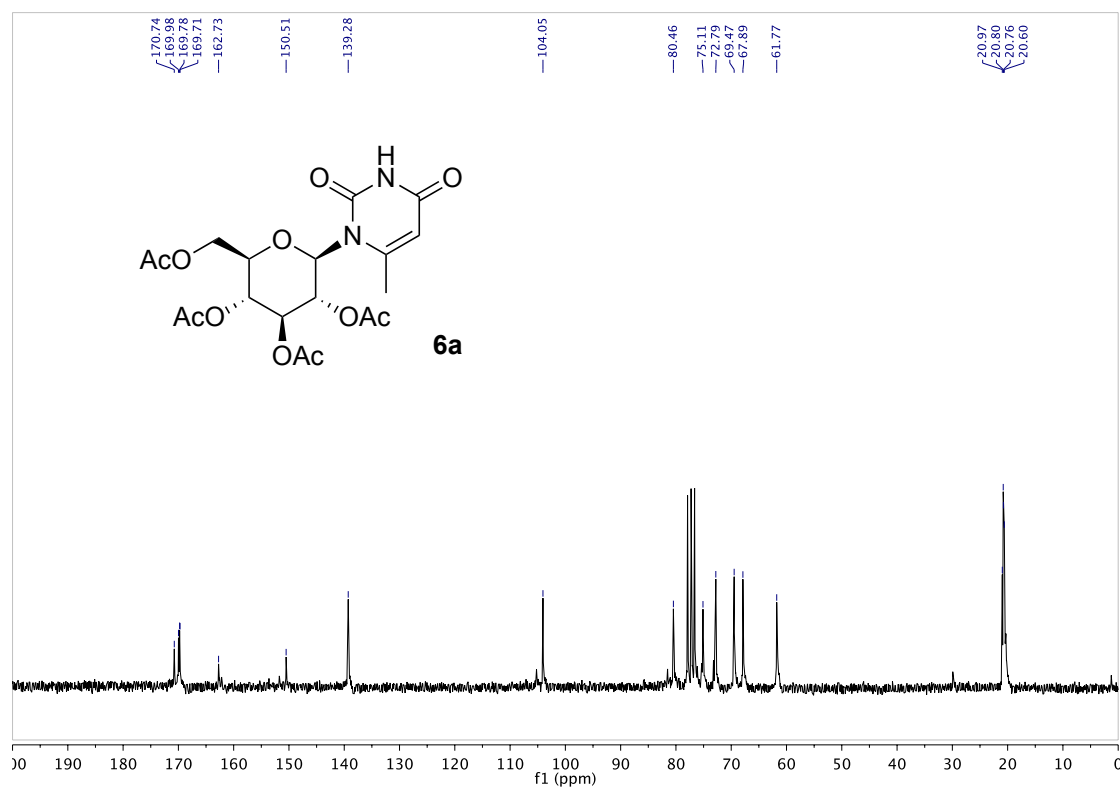
**Figure S2.**  $^{13}\text{C}$  NMR spectrum of compound **5** (50 MHz,  $\text{CDCl}_3$ ).



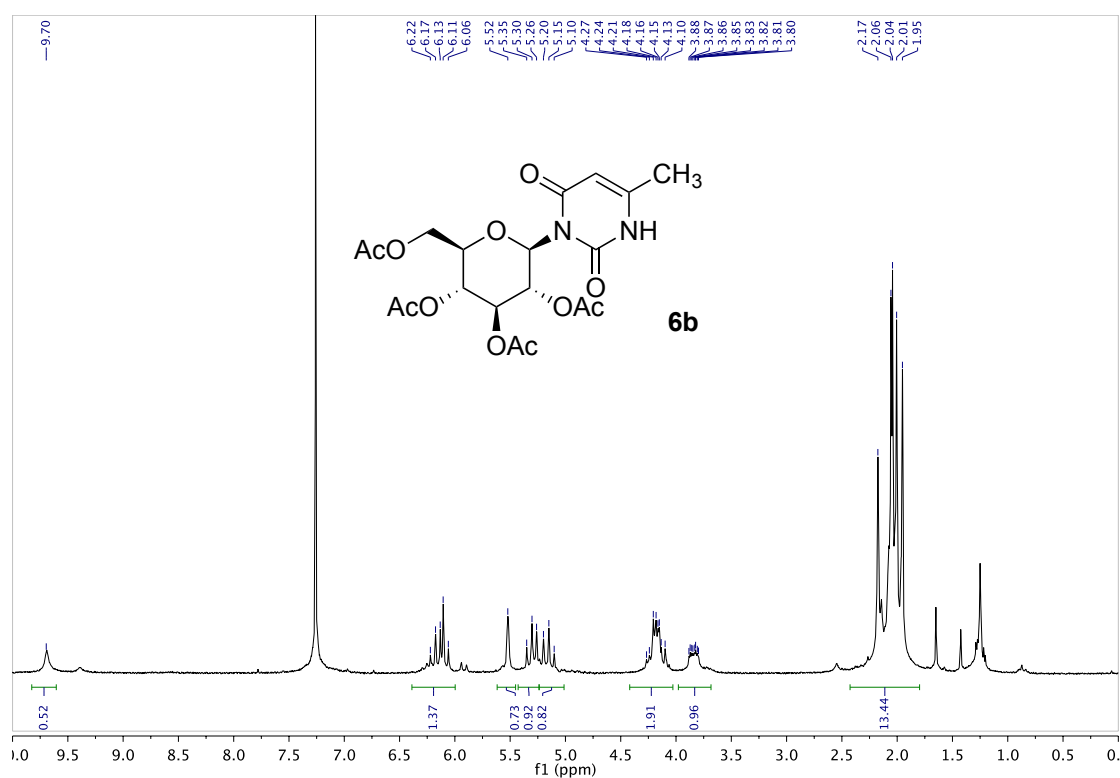
**Figure S3.**  $^1\text{H}$  NMR spectrum of compound **6a** (200 MHz,  $\text{CDCl}_3$ ).



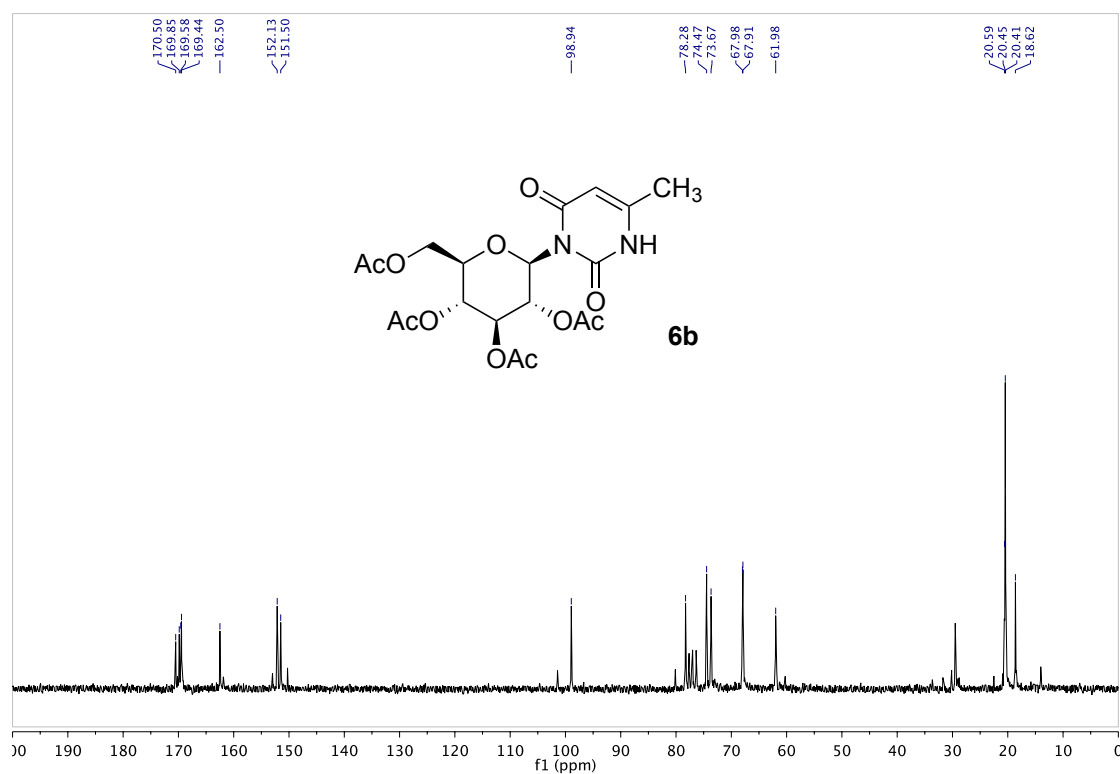
**Figure S4.**  $^{13}\text{C}$  NMR spectrum of compound **6a** (50 MHz,  $\text{CDCl}_3$ ).



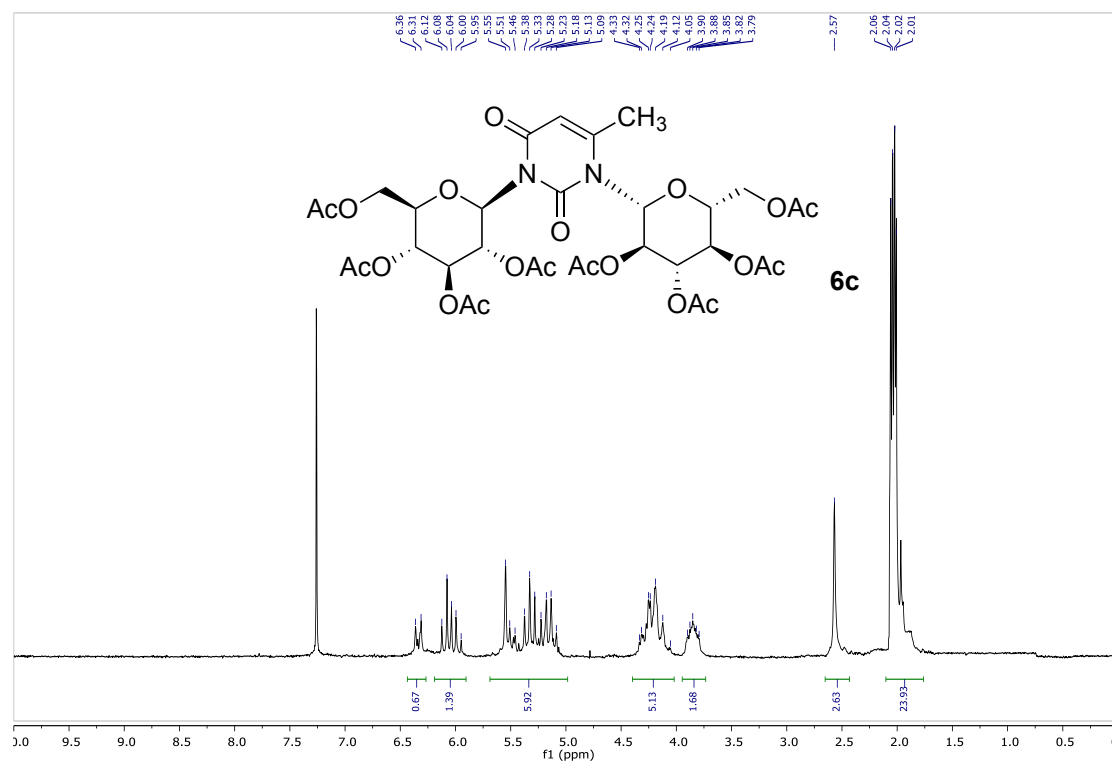
**Figure S5.**  $^1\text{H}$  NMR spectrum of compound **6b** (200 MHz,  $\text{CDCl}_3$ ).



**Figure S6.**  $^{13}\text{C}$  NMR spectrum of compound **6b** (50 MHz,  $\text{CDCl}_3$ ).



**Figure S7.**  $^1\text{H}$  NMR spectrum of compound **6c** (200 MHz,  $\text{CDCl}_3$ ).



**Figure S8.**  $^{13}\text{C}$  NMR spectrum of compound **6b** (50 MHz,  $\text{CDCl}_3$ ).

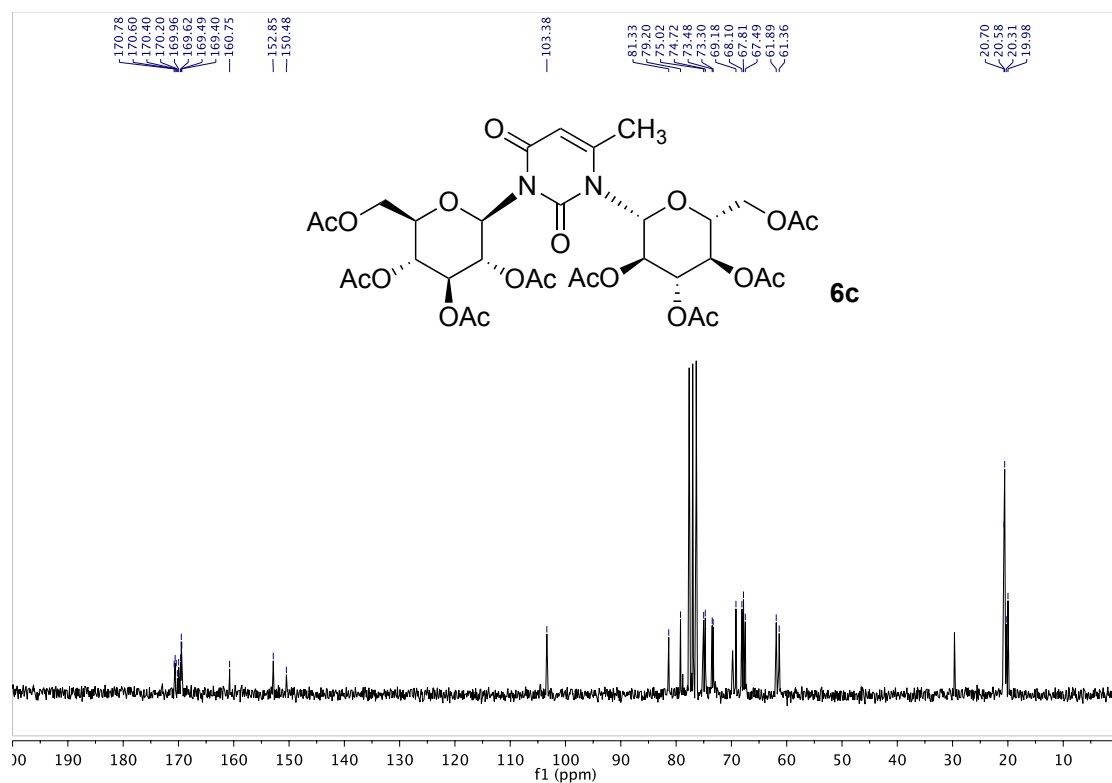


Figure S9.  $^1\text{H}$  NMR spectrum of compound **7** (200 MHz,  $\text{CDCl}_3$ ).

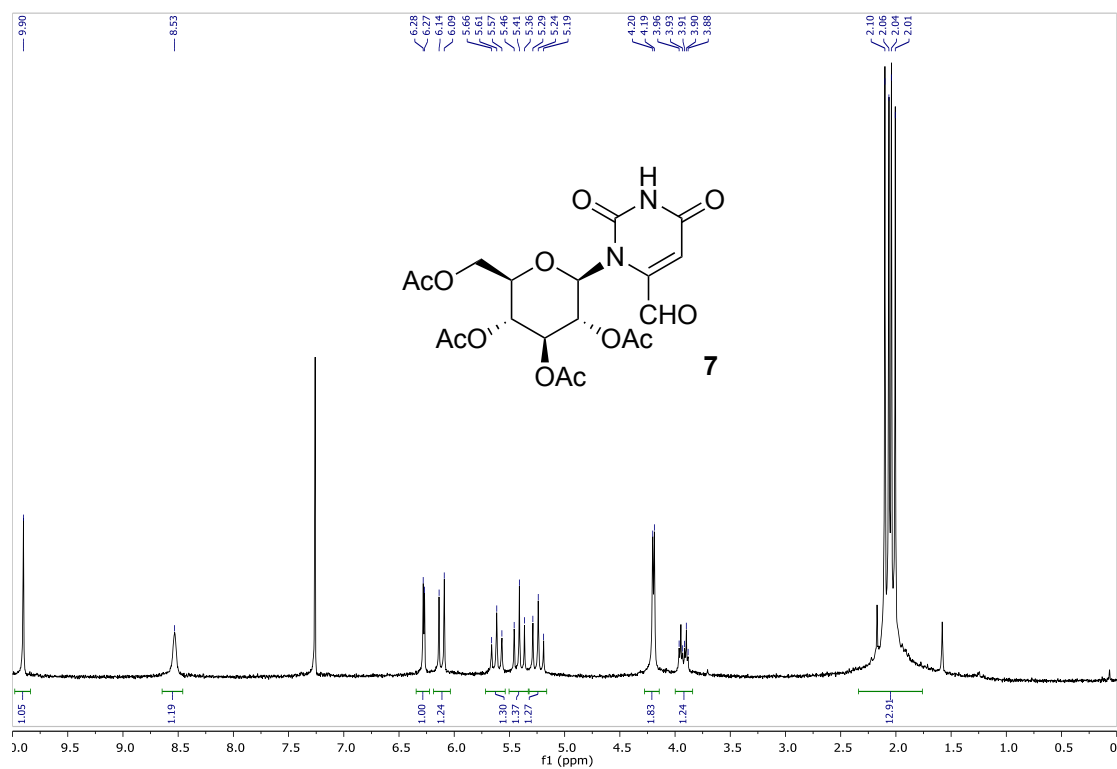
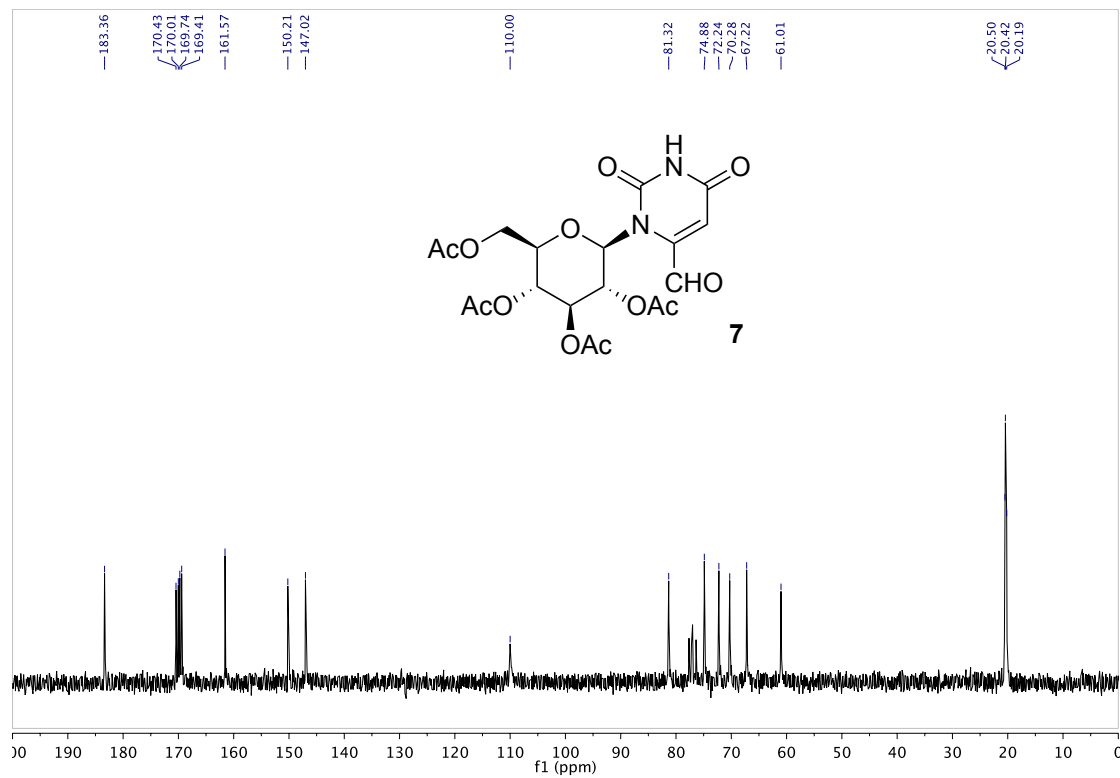
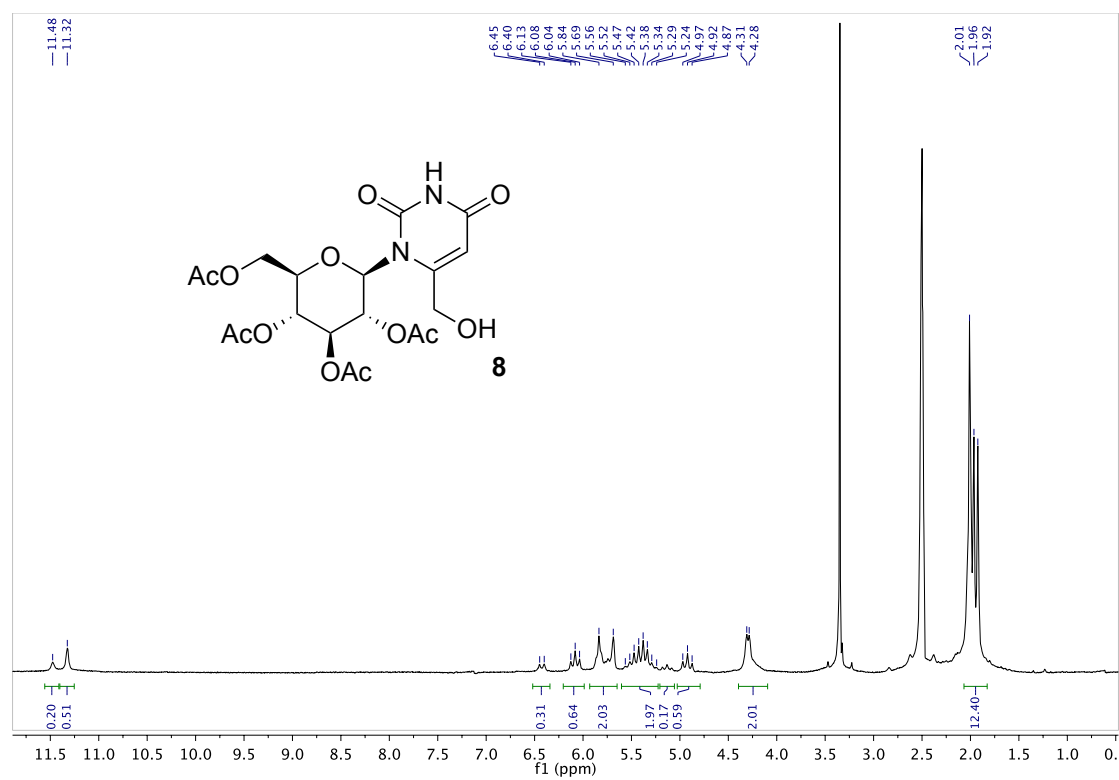


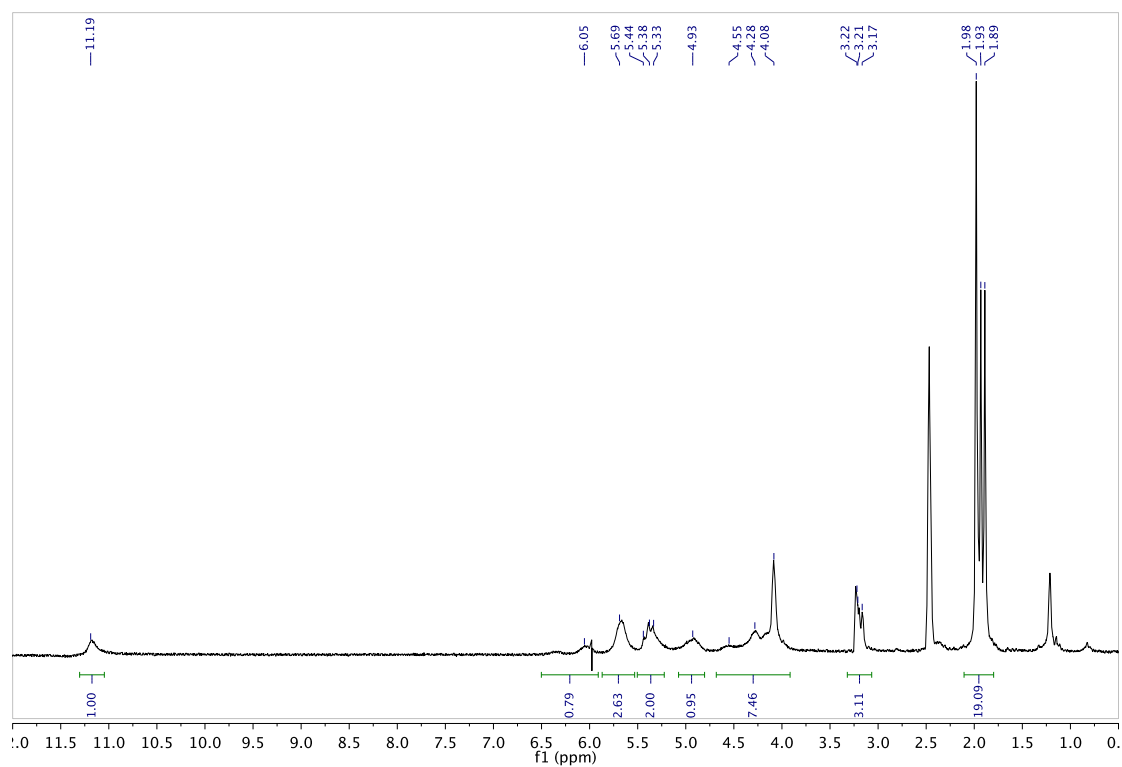
Figure S10.  $^{13}\text{C}$  NMR spectrum of compound **7** (50 MHz,  $\text{CDCl}_3$ ).



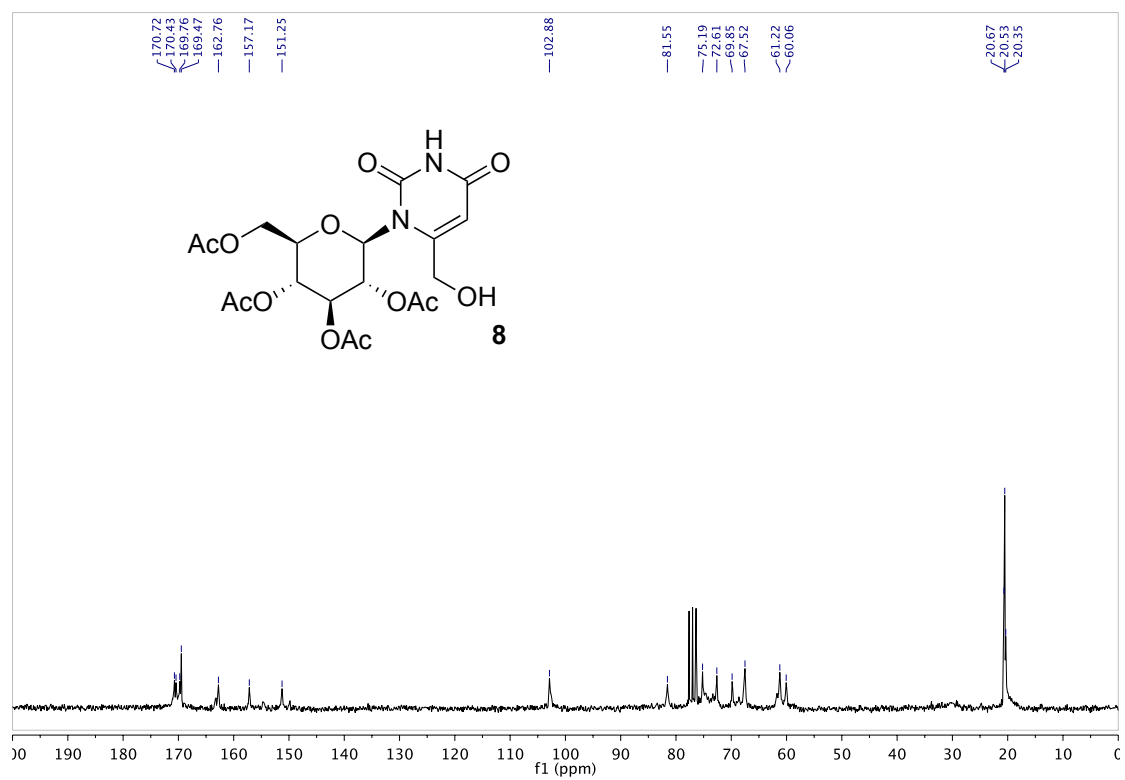
**Figure S11.**  $^1\text{H}$  NMR spectrum of compound **8** (200 MHz, DMSO- $d_6$ ).



**Figure S12.**  $^1\text{H}$  NMR spectrum of compound **8** (200 MHz, DMSO- $d_6$ ) at 75  $^\circ\text{C}$ .

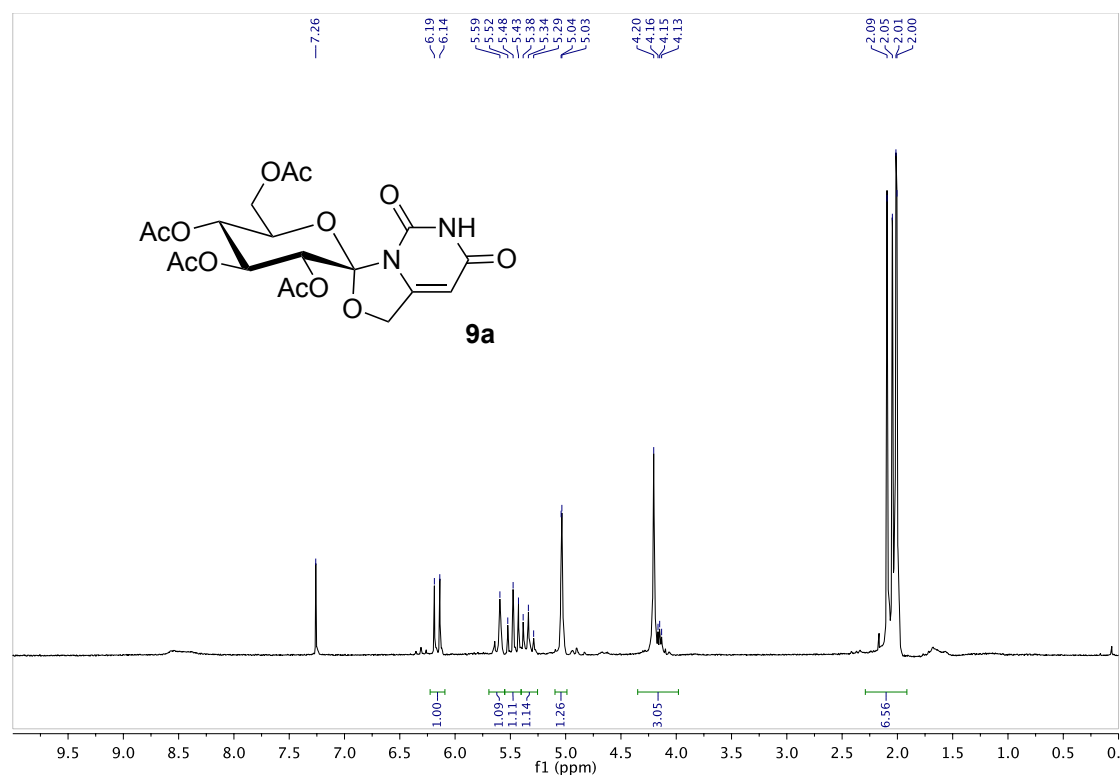


**Figure S13.**  $^{13}\text{C}$  NMR spectrum of compound **8** (50 MHz,  $\text{CDCl}_3$ ).





**Figure S14.**  $^1\text{H}$  NMR spectrum of compound **9a** (200 MHz,  $\text{CDCl}_3$ ).



**Figure S15.**  $^{13}\text{C}$  NMR spectrum of compound **9a** (50 MHz,  $\text{CDCl}_3$ ).

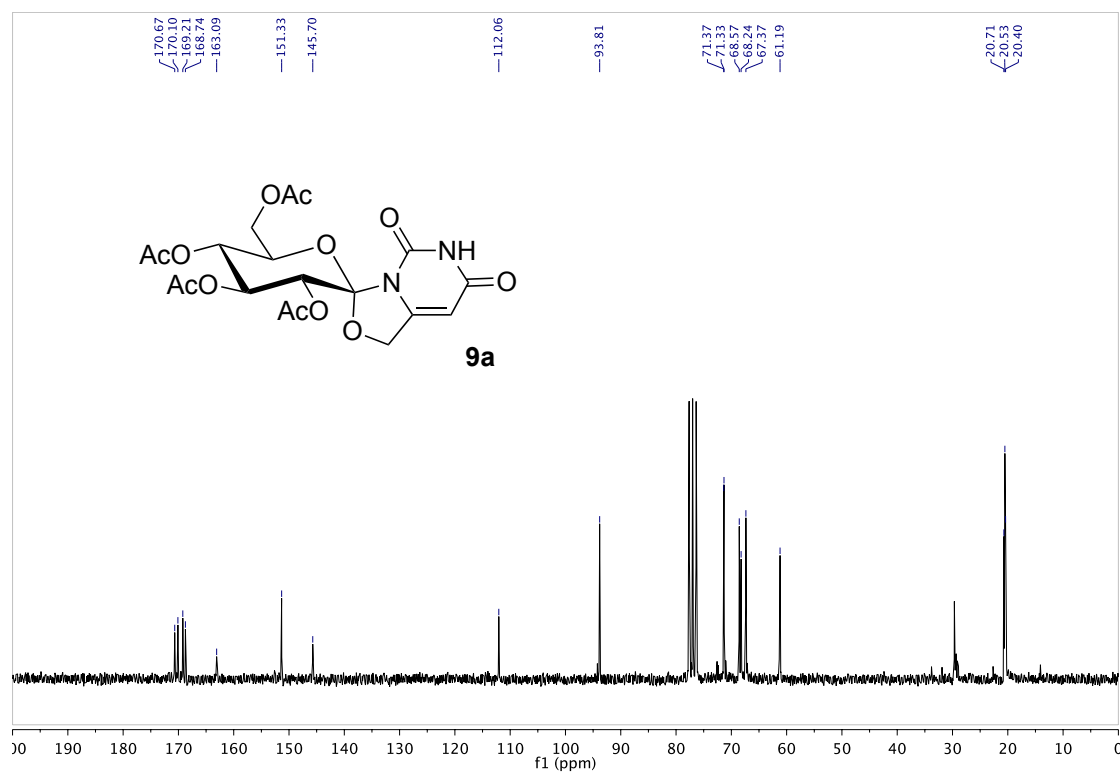


Figure S16.  $^1\text{H}$  NMR spectrum of compound **9b** (200 MHz,  $\text{CDCl}_3$ ).

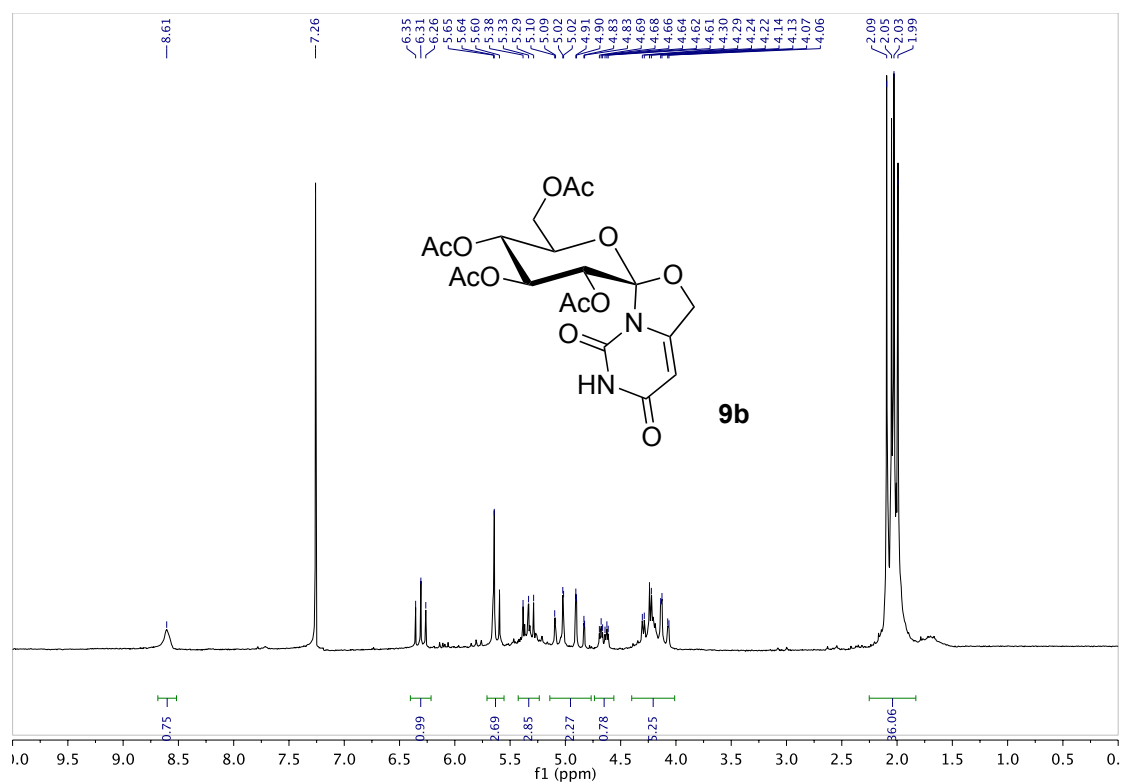
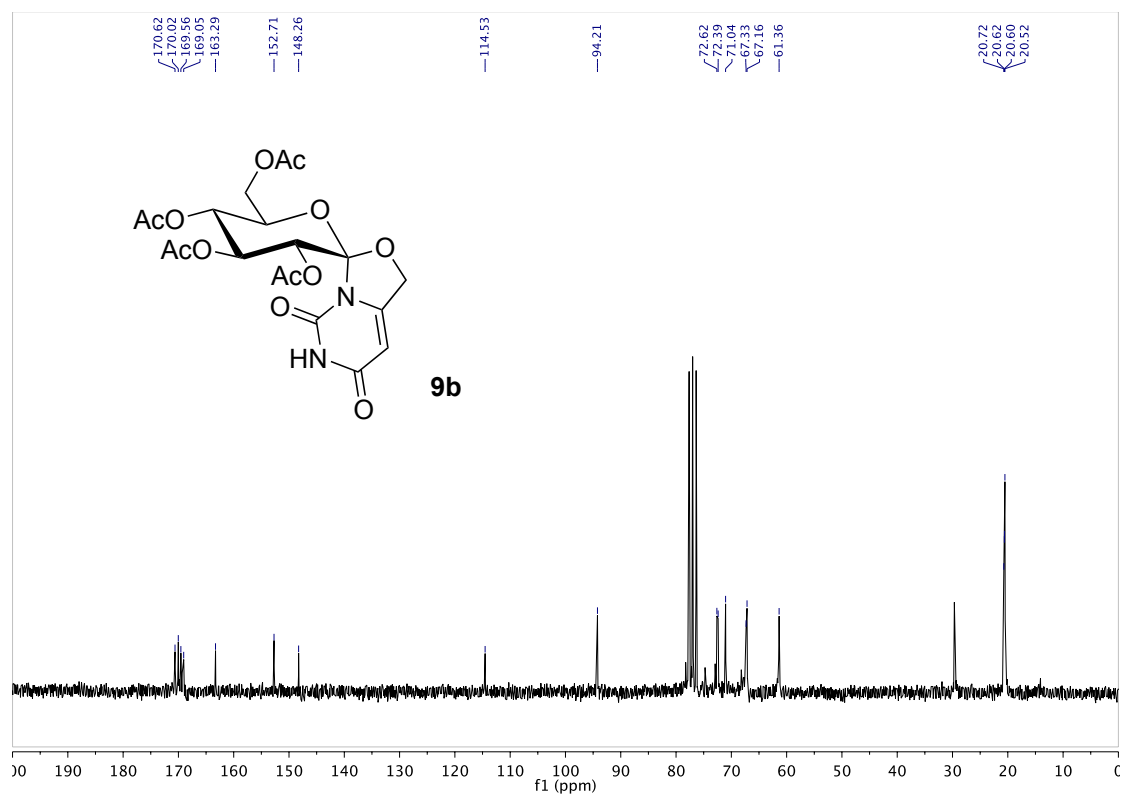
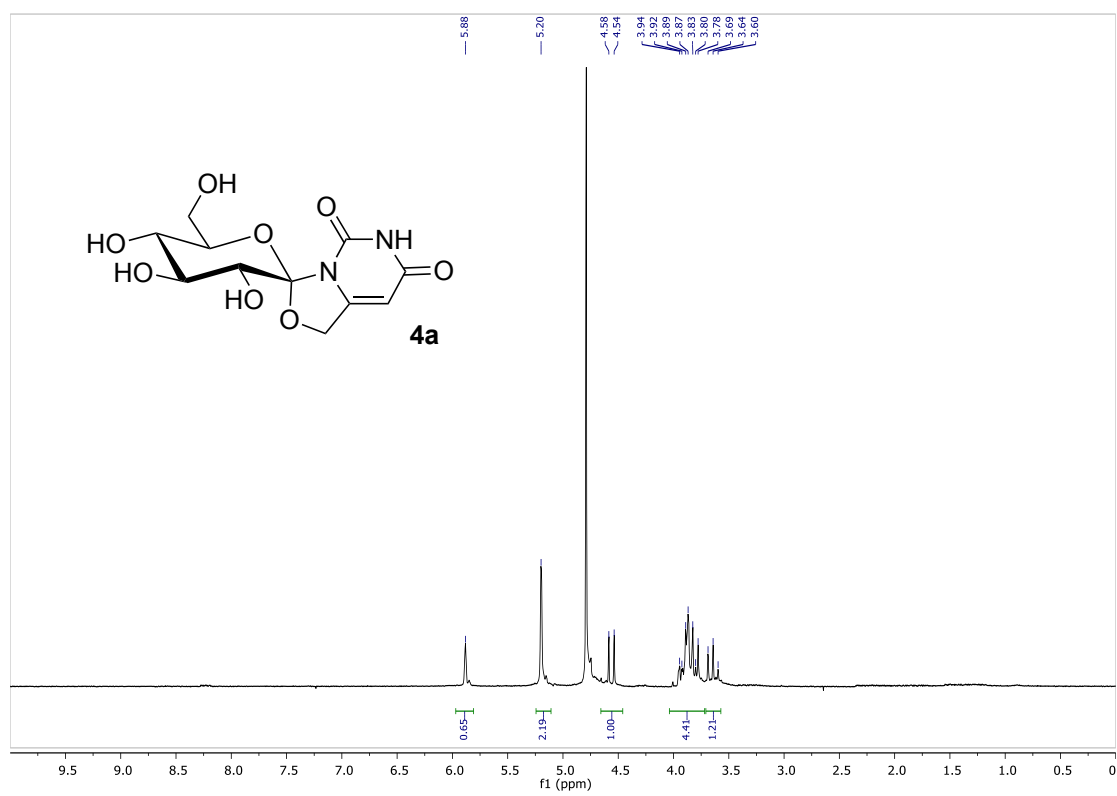


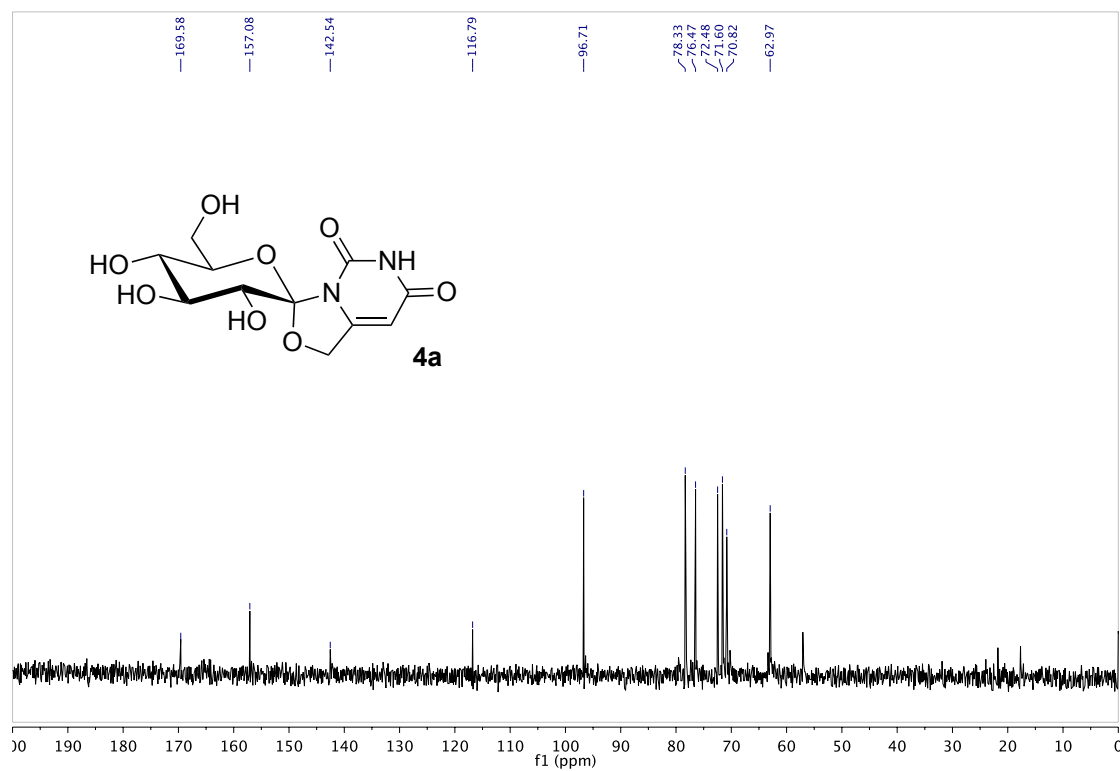
Figure S17.  $^{13}\text{C}$  NMR spectrum of compound **9b** (50 MHz,  $\text{CDCl}_3$ ).



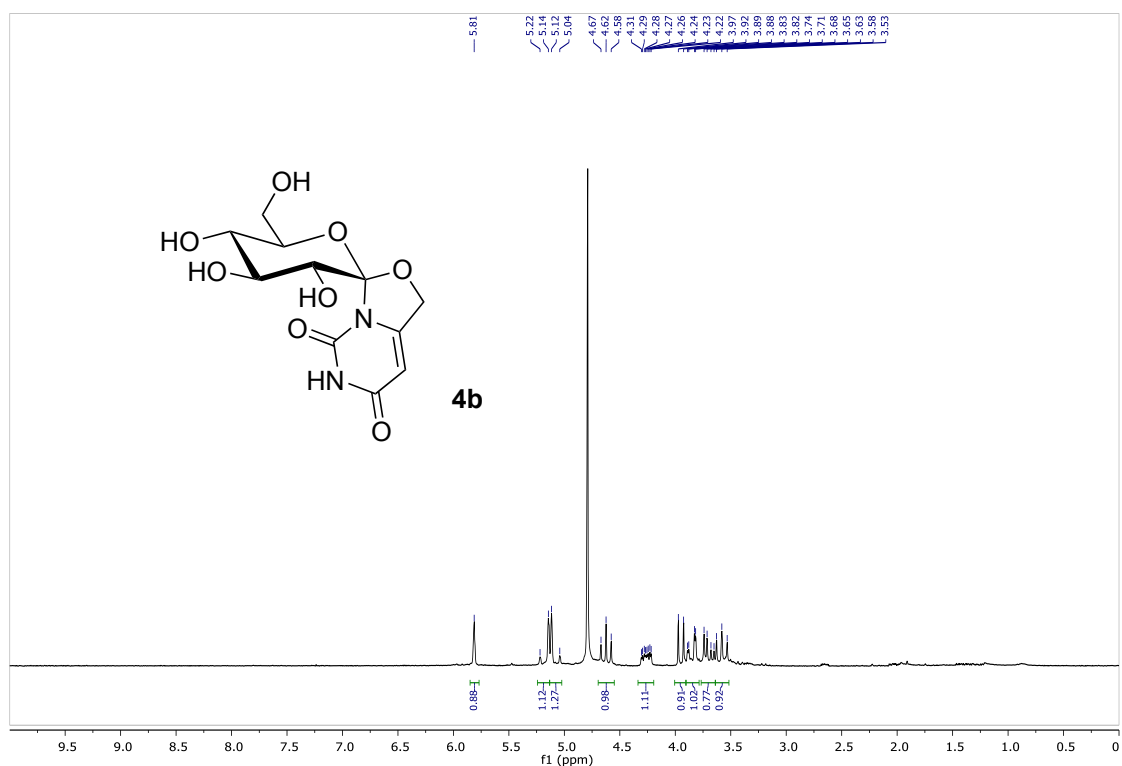
**Figure S18.**  $^1\text{H}$  NMR spectrum of compound **4a** (200 MHz,  $\text{CDCl}_3$ ).



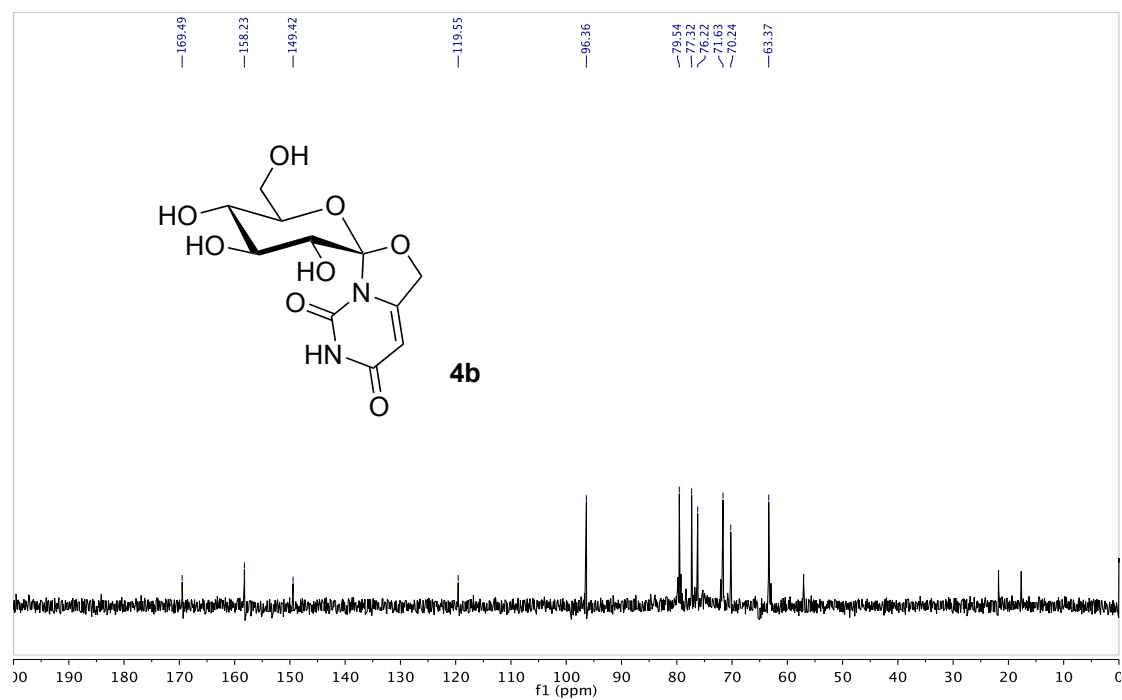
**Figure S19.**  $^{13}\text{C}$  NMR spectrum of compound **4a** (50 MHz,  $\text{CDCl}_3$ ).



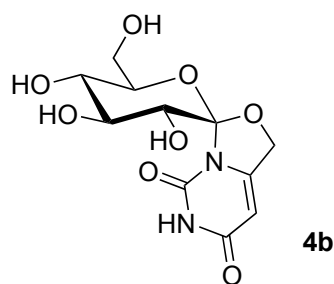
**Figure S20.**  $^1\text{H}$  NMR spectrum of compound **4b** (200 MHz,  $\text{D}_2\text{O}$ ).



**Figure S21.**  $^{13}\text{C}$  NMR spectrum of compound **4b** (50 MHz,  $\text{D}_2\text{O}$ ).



## 2. Enzyme Kinetics



RMGPb = 5  $\gamma$ /ml

G1p = 2 mM

AMP = 1 mM

Gly = 0.2%

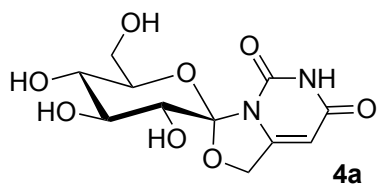
Buffer =

$\beta$ -glycerophosphate:mercaptoethanol:EDTA  
0.5 : 0.5 : 0.01

Km = 3 mM

**Table S1.** Inhibition vs **4b** concentration.

[ <b>4b</b> ] ( $\mu$ M)	% Inhibition
200	6.9
400	19.7
600	25.0
1000	35.0



RMGPb = 5  $\gamma$ /ml

G1p = 2 mM

AMP = 1 mM

Gly = 0.2%

Buffer =

$\beta$ -glycerophosphate:mercaptoethanol:EDTA  
0.5 : 0.5 : 0.01

Km = 3 mM

**Table S2.** Inhibition vs **4a** concentration.

[ <b>4a</b> ] ( $\mu$ M)	% Inhibition
200	1.7
400	9.4
600	18.3
1000	25.8