## Thiol-ene "click" synthesis and pharmacological evaluation of C-glycoside sp<sup>2</sup>-iminosugar glycolipids

Elena M. Sánchez-Fernández<sup>1,\*</sup>, M. Isabel García-Moreno<sup>1</sup>, Raquel García-Hernández<sup>2</sup>, José M. Padrón<sup>3</sup>, José M. García Fernández<sup>4</sup>, Francisco Gamarro<sup>2</sup>, Carmen Ortiz Mellet<sup>1,\*</sup>

**Supplementary Information** 

## List of contents

S1 to S28	NMR spectra of new C-glycoside sp <sup>2</sup> -iminosugars.
S29 to S45	Dixon and Lineweaver-Burk plots for <i>K</i> <sub>i</sub> determination
S46	Anti-proliferative activity (GI <sub>50</sub> ) of new C-glycoside sp <sup>2</sup> -iminosugars



**Figure S1.** <sup>1</sup>H and <sup>13</sup>C NMR spectra (500 MHz and 125.7 MHz, CDCl<sub>3</sub>) of **14**.



Figure S2. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of **15**.



Figure S3.  $^{1}$ H and  $^{13}$ C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of 16.



Figure S4. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of **17**.



Figure S5. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of **18**.



Figure S6.  $^{1}$ H and  $^{13}$ C NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of **1**.



Figure S7.  $^{1}$ H and  $^{13}$ C NMR spectra (400 MHz and 100.6 MHz, CD<sub>3</sub>OD) of **2**.



Figure S8.  $^{1}$ H and  $^{13}$ C NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of **3**.







Figure S10.  $^{1}$ H and  $^{13}$ C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of 20.



Figure S11. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of **21**.







Figure S13.  $^{1}$ H and  $^{13}$ C NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of 5.



Figure S14. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of 6



Figure S15. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of 23.



Figure S16. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of 24.







Figure S18.  $^{1}$ H and  $^{13}$ C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of **26**.



Figure S19. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz,  $CDCl_3$ ) of 27.



Figure S20.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of 7.







Figure S22.  $^{1}$ H and  $^{13}$ C NMR spectra (300 MHz and 75.5 MHz, CD<sub>3</sub>OD) of 9.



Figure S23. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz,  $CDCl_3$ ) of 28.



Figure S24. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, CDCl<sub>3</sub>) of 29.



Figure S25. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz,  $CDCl_3$ ) of **30**.



Figure S26.  $^{1}$ H and  $^{13}$ C NMR spectra (500 MHz and 125.7 MHz, 7:3 CD<sub>3</sub>OD-CDCl<sub>3</sub>) of **10**.



Figure S27. <sup>1</sup>H and <sup>13</sup>C NMR spectra (500 MHz and 125.7 MHz, 7:3  $CD_3OD$ -CDCl<sub>3</sub>) of **11**.



Figure S28. <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 MHz and 75.5 MHz, 7:3 CD<sub>3</sub>OD-CDCl<sub>3</sub>) of **12**.



Figure S29. Dixon Plot for  $K_i$  determination (79  $\mu$ M) of 15 against yeast maltase  $\alpha$ -glucosidase.



Figure S30. Lineweaver-Burk Plot for  $K_i$  determination (0.34  $\mu$ M) of 1 against yeast maltase  $\alpha$ -glucosidase.



Figure S31. Lineweaver-Burk Plot for  $K_i$  determination (0.74  $\mu$ M) of 2 against yeast maltase  $\alpha$ -glucosidase.



Figure S32. Lineweaver-Burk Plot for  $K_i$  determination (0.28  $\mu$ M) of 3 against yeast maltase  $\alpha$ -glucosidase.



Figure S33. Lineweaver-Burk Plot for  $K_i$  determination (2.6  $\mu$ M) of 4 against yeast maltase  $\alpha$ -glucosidase.



Figure S34. Lineweaver-Burk Plot for  $K_i$  determination (2.5  $\mu$ M) of 5 against yeast maltase  $\alpha$ -glucosidase.



Figure S35. Lineweaver-Burk Plot for  $K_i$  determination (0.75  $\mu$ M) of 6 against yeast maltase  $\alpha$ -glucosidase.



Figure S37. Dixon Plot for  $K_i$  determination (54  $\mu$ M) of 2 against bovine liver  $\beta$ -glucosidase.



Figure S38. Dixon Plot for  $K_i$  determination (151  $\mu$ M) of 3 against bovine liver  $\beta$ -glucosidase.



Figure S39. Dixon Plot for  $K_i$  determination (172  $\mu$ M) of 4 against bovine liver  $\beta$ -glucosidase.



Figure S40. Dixon Plot for  $K_i$  determination (85  $\mu$ M) of 5 against bovine liver  $\beta$ -glucosidase.



Figure S41. Dixon Plot for  $K_i$  determination (342  $\mu$ M) of 6 against bovine liver  $\beta$ -glucosidase.



Figure S42. Lineweaver-Burk Plot for  $K_i$  determination (53  $\mu$ M) of 8 against bovine liver  $\beta$ -glucosidase.



Figure S43. Dixon Plot for  $K_i$  determination (422  $\mu$ M) of **10** against bovine liver  $\beta$ -glucosidase.



Figure S44. Dixon Plot for  $K_i$  determination (134  $\mu$ M) of 11 against bovine liver  $\beta$ -glucosidase.



FigureS45. Dixon Plot for  $K_i$  determination (770  $\mu$ M) of **12** against bovine liver  $\beta$ -glucosidase.



**FigureS46.** Anti-proliferative activity (GI<sub>50</sub>) of **1**, **2**, **5**, **7**, **8**, **11** against different human solid tumor cell lines. Compounds **3**, **4**, **6**, **9**, **10** and **12** did not achieved 50% growth inhibition at the highest concentration tested (100  $\mu$ M).