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Supporting Information

Synthesis of novel pentacyclic triterpene-Neu5Ac2en derivatives and investigation of their in vitro anti-influenza entry activity

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Dedicated to Professor Lihe Zhang on the Occasion of His 80th Birthday.

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1. SI Figure 1. The NA inhibition assay

2. Selected ¹H, ¹³C NMR and HRMS spectra

NMR or HRMS	Page
¹ H NMR of compound 6	4
¹³ C NMR of compound 6	4
¹ H NMR of compound 7	5
¹³ C NMR of compound 7	5
¹ H NMR of compound 8a	6
¹³ C NMR of compound 8a	6
HRMS of compound 8a	7
¹ H NMR of compound 8b	7
¹³ C NMR of compound 8b	8
HRMS of compound 8b	8
¹ H NMR of compound 8c	9
¹³ C NMR of compound 8c	9

HRMS of compound 8c	10
¹ H NMR of compound 8d	10
¹³ C NMR of compound 8d	11
HRMS of compound 8d	11
¹ H NMR of compound 9a	12
¹³ C NMR of compound 9a	12
HRMS of compound 9a	13
¹ H NMR of compound 9b	13
¹³ C NMR of compound 9b	14
HRMS of compound 9b	14
¹ H NMR of compound 9c	15
¹³ C NMR of compound 9c	15
HRMS of compound 9c	16

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¹ H NMR of compound 9d	16
¹³ C NMR of compound 9d	17
HRMS of compound 9d	17
¹ H NMR of compound 10a	18
¹³ C NMR of compound 10a	18
HRMS of compound 10a	19
¹ H NMR of compound 10b	19
¹³ C NMR of compound 10b	20
HRMS of compound 10b	20
¹ H NMR of compound 11	21
¹³ C NMR of compound 11	21
¹ H NMR of compound 15a	22
¹³ C NMR of compound 15a	22
HRMS of compound 15a	23
¹ H NMR of compound 15b	23
¹³ C NMR of compound 15b	24
HRMS of compound 15b	24
¹ H NMR of compound 15c	25

¹³ C NMR of compound 15c	25
HRMS of compound 15c	26
¹ H NMR of compound 15d	26
¹³ C NMR of compound 15d	27
HRMS of compound 15d	27
¹ H NMR of compound 16a	28
¹³ C NMR of compound 16a	28
HRMS of compound 16a	29
¹ H NMR of compound 16b	29
¹³ C NMR of compound 16b	30
HRMS of compound 16b	30
¹ H NMR of compound 16c	31
¹³ C NMR of compound 16c	31
HRMS of compound 16c	32
¹ H NMR of compound 16d	32
¹³ C NMR of compound 16d	33
HRMS of compound 16d	33

1. SI Figure 1. The NA inhibition assay of compound 15a.



SI Figure 1. Compounds **15a** had no inhibitory effect on the influenza virus NA activity. Compound or zanamivir with two-fold serial dilution with PBS were mixed with influenza virus. The substrate solution (4-MUNANA) was mixed with the test compounds/virus mixture and incubated for 30 min at 37 °C. NA activity was measured by fluorescence of 4-methylumbelliferone with fluorescence spectrophotometer. Each point represents the mean \pm S.E.M. for three independent experiments.

2. Selected ¹H, ¹³C NMR and HRMS spectra

Figure 1. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 6



Figure 2. ¹³C NMR (100 MHz, CDCl₃) spectrum of compound 6





Figure 3. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 7



Figure 5. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 8a



Figure 7. HR-ESI-MS spectrum of compound 8a HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-24	C51 H75 N5 O12	C51 H75 N5 Na	972.5309	972.5304	-0.39
		O12			
x10 ⁵ + Scan (7.371) 6.5- 6- 5- 5- 4.5- 4- 3.5- 3- 2.5- 2.5- 1.5- 1- 0.5-	5 min) HX3-24.d Subtract (2)	972.530 (M+Na)+ 950.5490			
0-L860 8	, 70 880 890 900 910 920	930 940 950 960 970 Counts vs. Mass-to-Charge (r	980 990 1000 1010 n/z)		1050 1060 1070

Figure 8. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 8b





Figure 9. ¹³C NMR (100 MHz, CDCl₃) spectrum of compound 8b



Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-23	C51 H75 N5 O12	C51 H76 N5 O12	950.5493	950.5485	-0.97





Figure 11. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 8c



Figure 13. HR-ESI-MS spectrum of compound 8c HIGH RESLUTION MASS SPECTROMETRY REPORT

Figure 14. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 8d



Figure 15. ¹³C NMR (100 MHz, CDCl₃) spectrum of compound 8d



Figure 16. HR-ESI-MS spectrum of compound 8d HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-26	C51 H75 N5 O12	C51 H75 N5 Na O12	972.5298	972.5304	0.85
x10 ⁵ + Scan (7.354	9 min) HX3-26.d Subtract (2)	070 5000			



Figure 17. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 9a







Figure 20. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 9b





Figure 21. ¹³C NMR (100 MHz, CD₃OD) spectrum of compound 9b





Figure 23. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 9c





Figure 25. HR-ESI-MS spectrum of compound 9c HIGH RESLUTION MASS SPECTROMETRY REPORT

Figure 26. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 9d





Figure 27. ¹³C NMR (100 MHz, CD₃OD) spectrum of compound 9d

Figure 28. HR-ESI-MS spectrum of compound 9d HIGH RESLUTION MASS SPECTROMETRY REPORT



Figure 29. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 10a



Figure 31. HR-ESI-MS spectrum of compound 10a HIGH RESLUTION MASS SPECTROMETRY REPORT



Figure 32. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 10b







Figure 34. HR-ESI-MS spectrum of compound 10b HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-25-1	C45 H69 N5 O9	C45 H69 N5 Na	846.4988	846.4987	-0.69
		O9			
x10 ⁵ + Scan (7.238) 3.4- 3.2- 3-		846.4988 (M+Na)+			



Figure 35. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 11



Figure 36. ¹³C NMR (100 MHz, CD₃OD) spectrum of compound 11



0.000 A 2,223 2,056 7.2725 HX3-57 SOLVENT CDC13 200 200 200 038 038 0 200 0 200 0 ppm 1.00 2.96 1.97 2.97 59.23 Figure 38. ¹³C NMR (100 MHz, CDCl₃) spectrum of compound 15a 10.40 12.42 HX3-57 SOLVENT CDC13



ppm

Figure 39. HR-ESI-MS spectrum of compound 15a HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-57	C48 H72 N2 O12	C48 H72 N2 Na	891.4984	891.4977	-0.66
		O12			
x10 ⁵ + Scan (7.614	3 min) HX3-57.d Subtract (2)				
3.4- 3.2-		891.4984 (M+Na)+			
3- 28-					
2.6-					
2.4-					
2-					
1.6-	000 515				
1.4-					
1-					
0.8-					
0.4-					
0.2-		<u> II</u>	<u>n. h</u>		h
790 800	810 820 830 840 850 860 870	880 890 900 910 920 930 94	10 950 960 970 980	990 1000 1010 1020	1030 1040 1050 1060

Figure 40. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 15b





Figure 41. ¹³C NMR (100 MHz, CDCl₃) spectrum of compound 15b

Figure 42. HR-ESI-MS spectrum of compound 15b HIGH RESLUTION MASS SPECTROMETRY REPORT





Figure 43. ¹H NMR (400 MHz, CDCl₃) spectrum of compound 15c



Figure 45. HR-ESI-MS spectrum of compound 15c HIGH RESLUTION MASS SPECTROMETRY REPORT







Figure 47. ¹³C NMR (100 MHz, CDCl₃) spectrum of compound 15d

Figure 48. HR-ESI-MS spectrum of compound 15d HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-58	C48 H72 N2 O12	C48 H73 N2 O12	869.5160	869.5158	-0.14





Figure 49. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 16a

90 80 70 60 50 40 30 20 10

0 ppm

220 210 200 190 180 170 160 150 140 130 120 110 100

Figure 51. HR-ESI-MS spectrum of compound 16a HIGH RESLUTION MASS SPECTROMETRY REPORT

Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-61	C42 H66 N2 O9	C42 H66 N2 Na	765.4669	765.4661	-1.61
		O9			
x10 ⁵ + Scan (7.193	3 min) HX3-61.d Subtract (2)				
6-		765.4669 (M+Na)+			
5.5-	743.4847				
4.5-					
4- 3.5-					
3-					
2.5-					



Figure 52. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 16b





Figure 53. ¹³C NMR (100 MHz, CD₃OD) spectrum of compound 16b





Figure 55. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 16c





781.4614

660 670 680 690 700 710 720 730 740 750 750 770 790 800 810 820 830 840 850 860 870 880 900 910 Counts vs. Massto-Charge (m/z)

Figure 57. HR-ESI-MS spectrum of compound 16c HIGH RESLUTION MASS SPECTROMETRY REPORT

Figure 58. ¹H NMR (400 MHz, CD₃OD) spectrum of compound 16d

1.2

0.8

0.6· 0.4· 0.2· 0·





Figure 59. ¹³C NMR (100 MHz, CD₃OD) spectrum of compound 16d



Sample No.	Formula (M)	Ion Formula	Measured	Calc m/z	Diff
			m/z		(ppm)
HX3-62	C42 H66 N2 O9	C42 H66 N2 Na	765.4667	765.4661	-0.82
		O9			

