# **Supporting Information**

# Synthesis of the aminocyclitol units of (-) hygromycin A and

## methoxyhygromycin from myo-inositol

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Sr. No.	Starting material	No. of steps	Overall yield <sup>a</sup> (%)	Reference			
1	OH HOHO D-Glucose	20	2.7	1			
2	O=O 1,4-benzoquinone	13	10	2			
3	O H	14	12	3			
4		15	20	4			
5	HO HO HO HO HO HO OH <i>myo</i> -Inositol ( <b>5</b> )	11	31	Present work			
AcHN OAc AcO 20 OAc							
6	<i>myo</i> -Inositol (5)	11	4	5			
7	<i>myo</i> -Inositol (5)	10	56	Present work			

**Table S1:** Synthesis of aminocyclitol units of HMA and MHM; comparison with methods reported in the literature.

<sup>a</sup>Overall yield refers to aminocyclitol units (-)3 and 20



Comparison of the <sup>1</sup>H NMR spectroscopic data and specific rotation of (-)**3** with literature reports:

Trost <sup>2</sup> (300 MHz)	Donoho <sup>3</sup> (400 MHz)	Present work (500 MHz)
5.07 (s, 1H)	5.07 (s, 1H)	5.07 (s, 1H)
4.83 (s, 1H)	4.84 (s, 1H)	4.83 (s, 1H)
4.17 (dd, 1H, <i>J</i> 5.1,7.8)	4.17 (dd, 1H, J 4.8, 7.6)	4.17 (dd, 1H, <i>J</i> 4.9,7.7)
4.03 (m, 2H)	4.07 (dd, 1H, <i>J</i> 4.4,4.4)	4.06 (t, 1H, J 4.6)
	4.01 (dd, 1H, <i>J</i> 4.0,10.0)	4.01 (dd, 1H, <i>J</i> 4.2,9.7)
3.74 (dd, 1H, <i>J</i> 3.7,9.8)	3.73 (dd, 1H, <i>J</i> 3.6,10.0)	3.73 (dd, 1H, <i>J</i> 3.7,9.8)
3.61 (dd, 1H, J 3.4,7.8)	3.60 (dd, 1H, J 3.2,8.0)	3.60 (dd, 1H, J 3.1,7.7)
3.26 (t, 1H, J 3.4)	3.25 (t, 1H, J 3.3)	3.26 (t, 1H, J 3.1)
$[\alpha]_{\rm D}^{21} - 28.9^{\circ} (c = 0.85, \rm H_2O)$	$[\alpha]_{\rm D}^{20} -27.2^{\circ} (c = 0.45, {\rm H}_2{\rm O})$	$[\alpha]_{\rm D}^{25} - 29^{\circ} (c = 1.1, {\rm H}_2{\rm O})$



SI-4

Dept NMR, D <sub>2</sub> O, 125.76 MHz, (+) <b>3</b>				
	95.50	76.82 76.24 −70.55 −67.70	50.90	
HO HO OH OH (+)3	1946aya Santaka, dinaka Sangka			unte con actor actor interfaces dans
		80 70 66		30 20 10







SI-8



















SI-16









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![](_page_21_Figure_0.jpeg)

![](_page_22_Figure_0.jpeg)

![](_page_23_Figure_0.jpeg)

![](_page_24_Figure_0.jpeg)

![](_page_25_Figure_0.jpeg)

SI-26

![](_page_26_Figure_0.jpeg)

![](_page_27_Figure_0.jpeg)

![](_page_28_Figure_0.jpeg)

#### Single Crystal X-ray diffraction Data

X-ray intensity data measurements of all the comounds (9–12, 18 and 20) were carried out on a Bruker SMART APEX CCD diffractometer with graphitemonochromatized (MoK<sub> $\alpha$ </sub>= 0.71073Å) radiation. The X-ray generator was operated at 50 kV and 30 mA. Data were collected with  $\omega$  scan width of 0.3° at different settings of  $\varphi$ (0°, 90°, 180° and 270°) keeping the sample-to-detector distance fixed at 6.145 cm and the detector position (2 $\theta$ ) fixed at -28°. The X-ray data collection was monitored by SMART program (Bruker, 2003).<sup>6</sup>

Crystal data of **9**: C<sub>29</sub>H<sub>31</sub>N<sub>3</sub>O<sub>6</sub>, M=517.57, colorless plate, 0.12 x 0.10 x 0.08 mm<sup>3</sup>, monoclinic, space group *C*2/*c*, *a* =33.130(5), *b*=10.4844(17), *c*=16.523(3) Å,  $\beta$  = 111.386(3), V = 5344.0(15) Å<sup>3</sup>, Z = 8, T = 297(2) K,  $2\theta_{max} = 50.00^{\circ}$ ,  $D_{calc}$  (g cm<sup>-3</sup>) = 1.287, F(000) = 2192,  $\mu$  (mm<sup>-1</sup>) = 0.091, 13185 reflections collected, 4681 unique reflections ( $R_{int} = 0.0341$ ), 2867 observed ( $I > 2\sigma$  (I)) reflections, multi-scan absorption correction,  $T_{min} = 0.989$ ,  $T_{max} =$ 0.993, 448 refined parameters, S = 1.011, R1 = 0.0437, wR2 = 0.0872 (all data R = 0.0859, wR2= 0.1026), maximum and minimum residual electron densities;  $\Delta \rho_{max} = 0.131$ ,  $\Delta \rho_{min} = -0.170$ (eÅ<sup>-3</sup>).

Crystal data of **10**: C<sub>29</sub>H<sub>31</sub>N<sub>3</sub>O<sub>6</sub>, M=517.57, colorless needle, 0.22 x 0.19 x 0.12 mm<sup>3</sup>, triclinic, space group *P*-1, *a* = 9.3727(19), *b*= 10.020(2), *c*= 15.193(3) Å, *a* = 102.788(4)°,  $\beta$  = 104.677(3)°,  $\gamma$  = 99.305(4)°, *V* = 1309.8(5) Å<sup>3</sup>, *Z* = 2, *T* = 100(2) K, 2 $\theta_{max}$ =50.00°, *D<sub>calc</sub>* (g cm<sup>-3</sup>) = 1.312, *F*(000) = 548,  $\mu$  (mm<sup>-1</sup>) = 0.093, 12730 reflections collected, 4585 unique reflections (*R*<sub>int</sub>=0.0253), 3474 observed (*I* > 2 $\sigma$  (*I*)) reflections, multi-scan absorption correction, *T<sub>min</sub>* = 0.980, *T<sub>max</sub>* = 0.989, 376 refined parameters, *S* = 1.097, *R*1=0.0673,

wR2=0.1576 (all data R = 0.0865, wR2 = 0.1703, maximum and minimum residual electron densities;  $\Delta \rho_{\text{max}} = 0.392$ ,  $\Delta \rho_{\text{min}} = -0.187$  (eÅ<sup>-3</sup>).

Crystal data of **11:** C<sub>23</sub>H<sub>26</sub>N<sub>4</sub>O<sub>5</sub>, M=438.48, colorless needle, 0.37 x 0.06 x 0.04 mm<sup>3</sup>, orthorhombic, space group  $P2_12_12_1$ , a = 7.564(3), b=15.725(7), c=18.913(8) Å, V = 2249.7(16) Å<sup>3</sup>, Z = 4, T = 100(2) K,  $2\theta_{max}=50.00^{\circ}$ ,  $D_{calc}$  (g cm<sup>-3</sup>) = 1.295, F(000) = 928,  $\mu$  (mm<sup>-1</sup>) = 0.093, 16193 reflections collected, 3957 unique reflections ( $R_{int}=0.0510$ ), 3787 observed ( $I > 2\sigma$  (I)) reflections, multi-scan absorption correction,  $T_{min} = 0.967$ ,  $T_{max} = 0.997$ , 365 refined parameters, S = 1.190, R1=0.0420, wR2=0.0871 (all data R = 0.0447, wR2 = 0.0882, maximum and minimum residual electron densities;  $\Delta \rho_{max} = 0.197$ ,  $\Delta \rho_{min} = -0.162$  (eÅ<sup>-3</sup>).

Crystal data of **12:**  $C_{14}H_{17}N_3O_5$ , M=307.31, colorless plate, 0.29 x 0.14 x 0.11 mm<sup>3</sup>, triclinic, space group *P*-1, *a* = 10.2239(8), *b* = 10.7231(9), *c* =15.4953(13) Å, *a* = 91.7140(10), *β* = 103.3900(10),  $\gamma$  = 117.7640(10) °, *V* = 1443.5(2) Å<sup>3</sup>, *Z* = 4, *T* = 297(2) K, 2 $\theta_{max}$ =50.00°, *D<sub>calc</sub>* (g cm<sup>-3</sup>) = 1.414, *F*(000) = 648,  $\mu$  (mm<sup>-1</sup>) = 0.109, 13362 reflections collected, 5061 unique reflections ( $R_{int}$ =0.0136), 4416 observed (*I* > 2 $\sigma$  (*I*)) reflections, multi-scan absorption correction, *T*<sub>min</sub> = 0.969, *T*<sub>max</sub> = 0.988, 401 refined parameters, *S* = 1.031, *R*1=0.0374, *wR*2=0.0941 (all data *R* = 0.0430, *wR*2 = 0.0987), maximum and minimum residual electron densities;  $\Delta \rho_{max} = 0.188$ ,  $\Delta \rho_{min} = -0.164$  (eÅ<sup>-3</sup>).

Crystal data of **18:**  $C_{31}H_{31}N_{3}O_{8}$ , M=573.59, colorless prism, 0.27 x 0.07 x 0.05 mm<sup>3</sup>, monoclinic, space group  $P2_{1}$ , a = 7.4388(5), b = 26.4633(17), c = 14.6237(10) Å,  $\beta = 93.580(3)$ , V = 2873.1(3) Å<sup>3</sup>, Z = 4, T = 100(2) K,  $2\theta_{max}=50.00^{\circ}$ ,  $D_{calc}$  (g cm<sup>-3</sup>) = 1.326, F(000) = 1208,  $\mu$  (mm<sup>-1</sup>) = 0.097, 16623 reflections collected, 6962 unique reflections ( $R_{int}=0.0248$ ), 5841 observed ( $I > 2\sigma$  (I)) reflections multi-scan absorption correction,  $T_{min} =$  0.975,  $T_{\text{max}} = 0.995$ , 799 refined parameters, 115 restraints applied, S = 1.047, R1=0.0375, wR2=0.0752 (all data R = 0.0527, wR2 = 0.0821, maximum and minimum residual electron densities;  $\Delta \rho_{\text{max}} = 0.155$ ,  $\Delta \rho_{\text{min}} = -0.251$  (eÅ<sup>-3</sup>).

Crystal data of **20**:  $C_{17}H_{25}N_1O_{10}$ , M=403.38, colorless rhombic crystals, 0.57 x 0.36 x 0.30 mm<sup>3</sup>, monoclinic, space group *Cc*, *a* = 15.345(2), *b* = 11.1876(18), *c* = 12.2187(19) Å,  $\beta$  = 103.406(2)°, *V* = 2040.5(6) Å<sup>3</sup>, *Z* = 4, *T* = 133(2) K,  $2\theta_{max}$ =50.00°,  $D_{calc}$  (g cm<sup>-3</sup>) = 1.313, F(000) = 856,  $\mu$  (mm<sup>-1</sup>) = 0.109, 7131 reflections collected, 3525 unique reflections ( $R_{int}$ =0.0245), 3475 observed ( $I > 2\sigma$  (I)) reflections, multi-scan absorption correction,  $T_{min}$  = 0.941,  $T_{max}$  = 0.968, 287 refined parameters, 2 restraints applied, S = 1.087, R1=0.0351, wR2=0.0889 (all data R = 0.0355, wR2 = 0.0894, maximum and minimum residual electron densities;  $\Delta\rho_{max} = 0.240$ ,  $\Delta\rho_{min} = -0.165$  (eÅ<sup>-3</sup>).

All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2003). SHELX-97 was used for structure solution and full matrix least-squares refinement on  $F^{2,7}$  Hydrogen atoms for compounds **11** were located in difference Fourier map and refined isotropically whereas for compounds **12** and **18** they were placed in geometrically idealized position and constrained to ride on their parent atoms. In compounds **10** and **20** inositol ring H-atoms as well as acetal H-atoms in **10** and H-atom bound to N atom in **20** were located in difference Fourier map and refined is difference Fourier map and refined is otropically idealized position and constrained to ride on their parent atoms. In compound **9** methylene H-atoms bound to C8 and methyl H-atoms bound to C29 were placed in geometrically idealized position and constrained to ride on their parent atoms whereas all other H-atoms located in difference Fourier map and refined to ride on their parent atoms whereas all other H-atoms located in difference Fourier map and refined to ride on their parent atoms whereas all other H-atoms located in difference Fourier map and refined to ride on their parent atoms whereas all other H-atoms located in difference Fourier map and refined isotropically. All ORTEPs were generated using ORTEP-32.<sup>8</sup>

![](_page_32_Figure_0.jpeg)

**Figure S1.** ORTEP of **9**. Thermal ellipsoids are drawn at 30% probability and hydrogen atoms are depicted as small spheres of arbitrary radii.

![](_page_33_Figure_0.jpeg)

**Figure S2.** ORTEP of **10**. Thermal ellipsoids are drawn at 30% probability and hydrogen atoms are depicted as small spheres of arbitrary radii.

![](_page_34_Figure_0.jpeg)

**Figure S3.** ORTEP of **11**. Thermal ellipsoids are drawn at 50% probability and hydrogen atoms are depicted as small spheres of arbitrary radii.

![](_page_35_Figure_0.jpeg)

Figure S4. ORTEP of  $(\pm)12$ . Thermal ellipsoids are drawn at 30% probability and hydrogen atoms are depicted as small spheres of arbitrary radii.

![](_page_36_Figure_0.jpeg)

**Figure S5.** ORTEP of **18**. Thermal ellipsoids are drawn at 50% probability and hydrogen atoms are depicted as small spheres of arbitrary radii.

![](_page_37_Figure_0.jpeg)

**Figure S6.** ORTEP of **20**. Thermal ellipsoids are drawn at 30% probability and hydrogen atoms are depicted as small spheres of arbitrary radii.

### References

- Chida, N.; Ohtsuka, M.; Nakazawa, K.; Ogawa, S. J. Chem. Soc., Chem. Commun. 1989, 7, 436–438.
- 2. Trost, B. M.; Dudash, J. Chem. Eur. J. 2001, 7, 1619–1629.
- 3. Donohoe, T. J.; Johnson, P. D.; Pye, R. J.; Keenan, M. Org. Lett. 2005, 7, 1275–1277.
- Donohoe, T. J.; Flores, A.; Battaille, C. J. R.; Churruca, F. Angew. Chem. Int. Ed. 2009, 48, 6507–6510.
- Chida, N.; Nakazawa, N.; Ohtsuka, M.; Suzuki, M.; Ogawa, S. Chem. Lett. 1990, 423–426.
- Bruker (2003). SADABS (Version 2.05), SMART (Version 5.631), SAINT (Version 6.45) and SHELXTL (Version 6.14). Bruker AXS Inc., Madison, Wisconsin, USA.
- 7. Sheldrick, G. M. Acta Crystallogr. 2008, A64, 112-122.
- 8. Farrugia, L. J. J. Appl. Crystallogr. 1997, 30, 565-565.