

Electronic Supplementary Information

Largazole: From Discovery to Broad-Spectrum Therapy

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Contents

Structure–Activity Relationships of Largazole

Page Number

S2

Table S1. HDAC Inhibitory Activity (nM)

(Y. Ying, Y. Liu, S. R. Byeon, H. Kim, H. Luesch and J. Hong, *Org. Lett.*, 2008, **10**, 4021–4024)

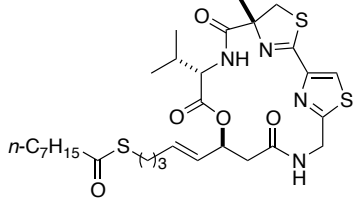
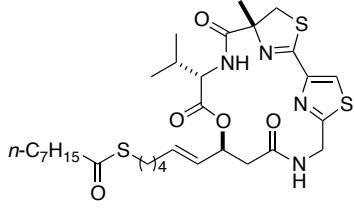
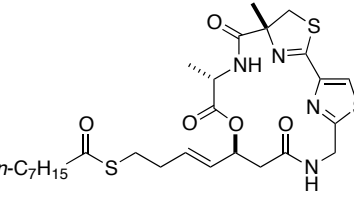
	HDAC1	HDAC6
largazole	7.6	1800
	690	> 10000
	1900	> 10000
	44	3300

Table S2. HDAC Inhibitory Activity (nM)

(A. A. Bowers, T. J. Greshock, N. West, G. Estiu, S. L. Schreiber, O. Wiest, R. M. Williams and J. E. Bradner, *J. Am. Chem. Soc.*, 2009, **131**, 2900–2905)

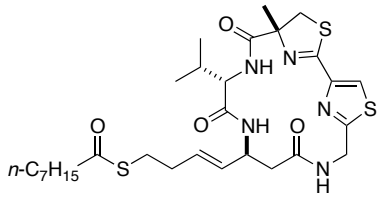
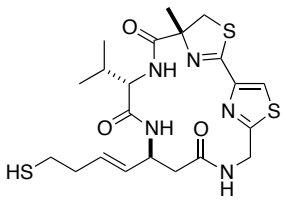
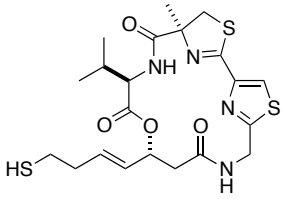
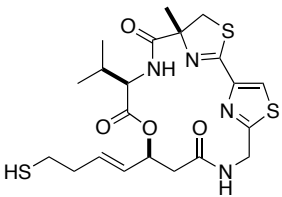
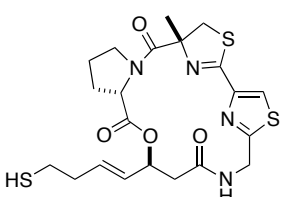
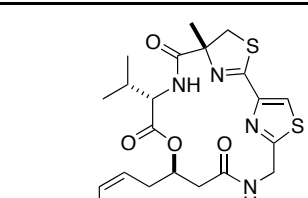
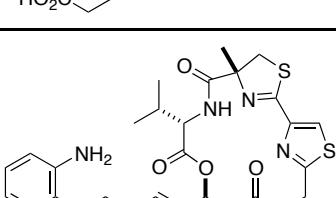
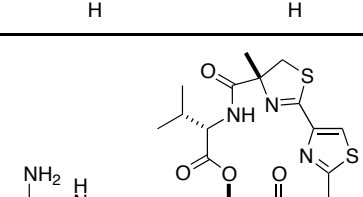
	HDAC1	HDAC2	HDAC3	HDAC6
largazole	40	42	96	>1000
largazole thiol	0.1	0.8	1	40
	>3000	>3000	>3000	>3000
	0.9	4	4	1500

Table S3. HDAC Inhibitory Activity (μM)

(A. A. Bowers, N. West, T. L. Newkirk, A. E. Troutman-Youngman, S. L. Schreiber, O. Wiest, J. E. Bradner and R. M. Williams, *Org. Lett.*, 2009, **11**, 1301–1304)

	HDAC1	HDAC2	HDAC3	HDAC6
largazole thiol	0.0012	0.0035	0.0034	0.049
	1.2	3.1	1.9	2.2
	0.030	0.082	0.084	0.68
	0.11	0.80	0.58	13
	>30	>30	>30	>30
	0.27	4.1	4.1	>30
	23	29	14	>30

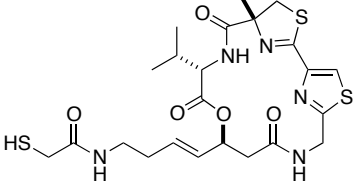
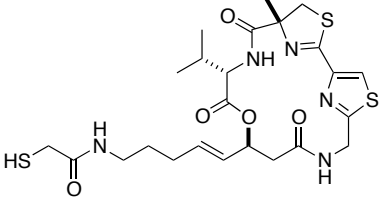
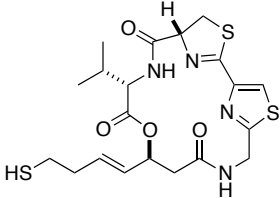
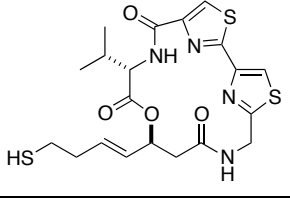
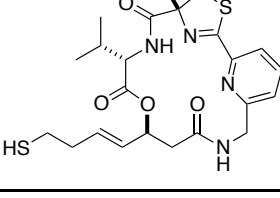
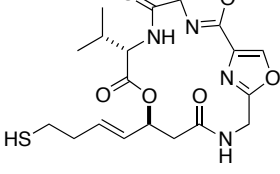
	0.67	1.6	0.96	0.7
	1	1.9	1.5	0.24
	0.0019	0.0048	0.0038	0.13
	0.077	0.12	0.085	>30
	0.00032	0.00086	0.0011	0.029
	0.00069	0.0017	0.0015	0.045

Table S4. HDAC Inhibitory Activity (μM)
 (F. Chen, A.-H. Gao, J. Li and F.-J. Nan, *ChemMedChem*, 2009, **4**, 1269–1272)

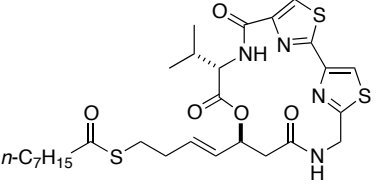
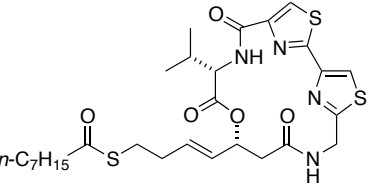
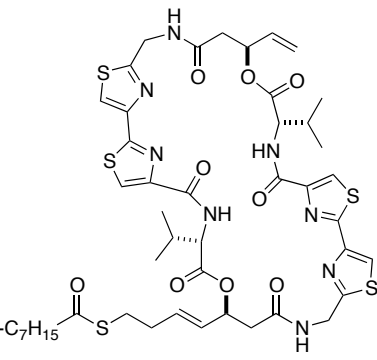
	HDAC1	HDAC2	HDAC3	HDAC6
largazole	0.0137	0.190	0.245	11.5
	2.0	18.5	16.8	14.7
	Not Determined	Not Determined	Not Determined	Not Determined
	Not Determined	51.8	22.6	Not Determined

Table S5. HDAC Inhibitory Activity (nM)

(J. A. Souto, E. Vaz, I. Lepore, A.-C. Poppler, G. Franci, R. Alvarez, L. Altucci and A. R. de Lera, *J. Med. Chem.*, 2010, **53**, 4654–4667)

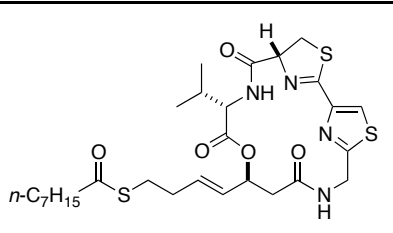
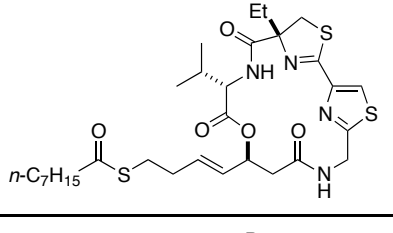
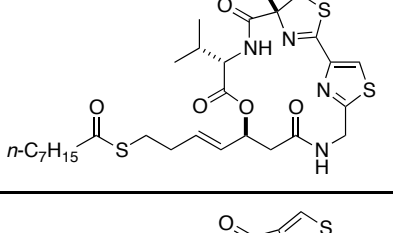
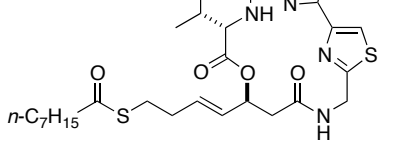
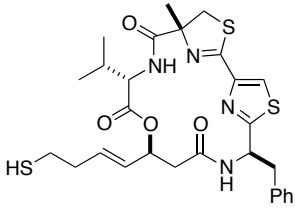
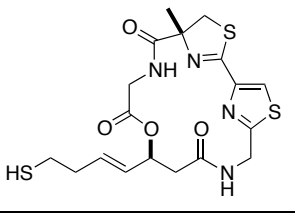
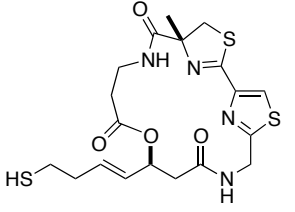
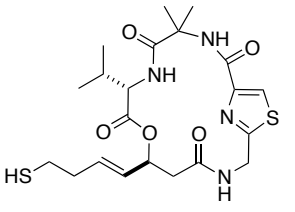
	HDAC1	HDAC4
largazole	11.4	3000
	13.7	7500
	161.3	4900
	4.5	3000
	4.7	3000

Table S6. HDAC Inhibitory Activity (nM)

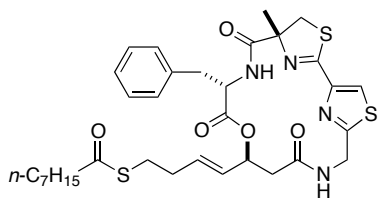
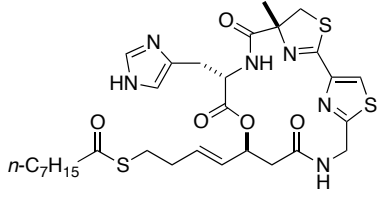
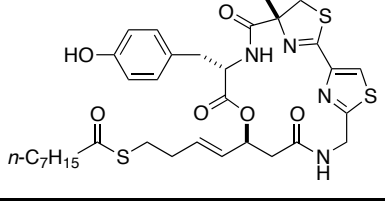
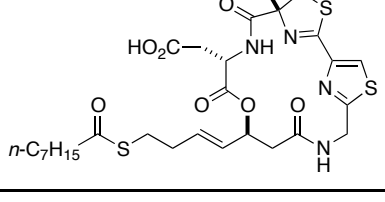
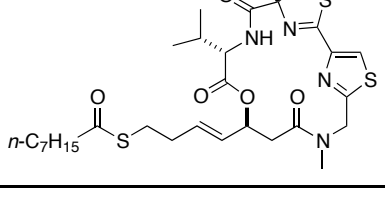
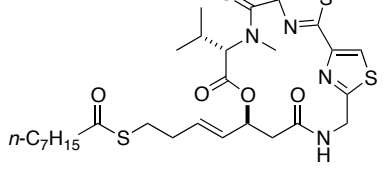
(H. Benelkebir, S. Marie, A. L. Hayden, J. Lyle, P. M. Loadman, S. J. Crabb, G. Packham and A. Ganesan, *Bioorg. Med. Chem.*, 2011, **19**, 3650–3658)

	HDACs ^a
largazole	572±29
largazole thiol	0.043±0.026
	17.2±2.3
	0.17±0.05
	3.15±0.35
	0.99±0.07

^a From HeLa cell extracts

Table S7. HDAC Inhibitory Activity (nM)

(Y. Liu, L. A. Salvador, S. Byeon, Y. Ying, J. C. Kwan, B. K. Law, J. Hong and H. Luesch, *J. Pharmacol. Exp. Ther.*, 2010, **335**, 351–361)

	HDAC1
largazole	7.6
	54
	44
	23
	61
	Not Determined
	Not Determined

