

--- SUPPORTING INFORMATION ---

Entropy as a Driver of Selectivity for Inhibitor Binding to Histone

Deacetylase 6

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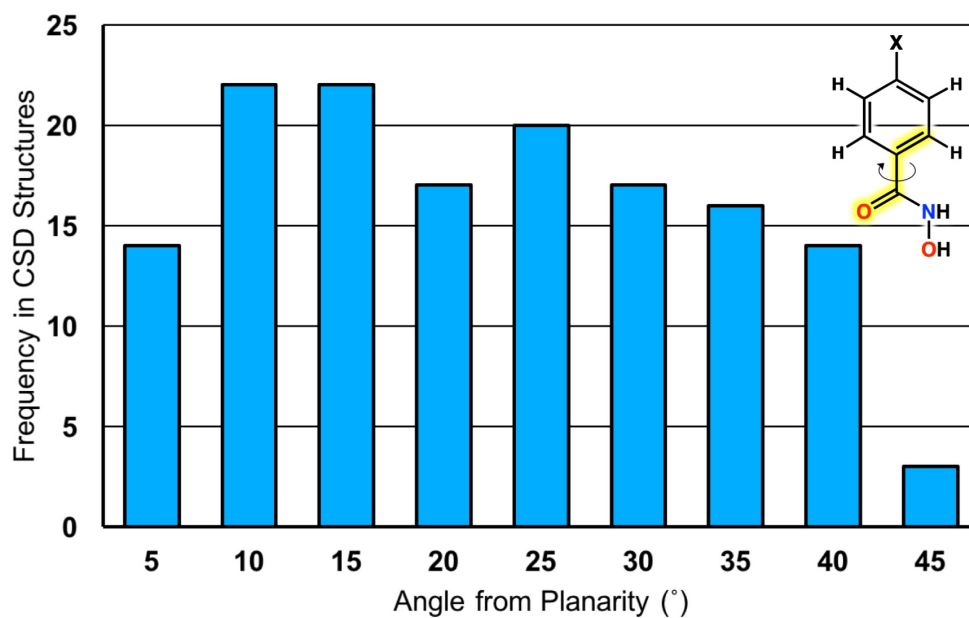


Figure S1. Deviations from planarity observed in conjugated aromatic hydroxamic acids. A total of 145 independent examples were found in 87 structures retrieved from the Cambridge Structural Database. The search query is shown as an inset structure and the angle measured is highlighted in yellow.

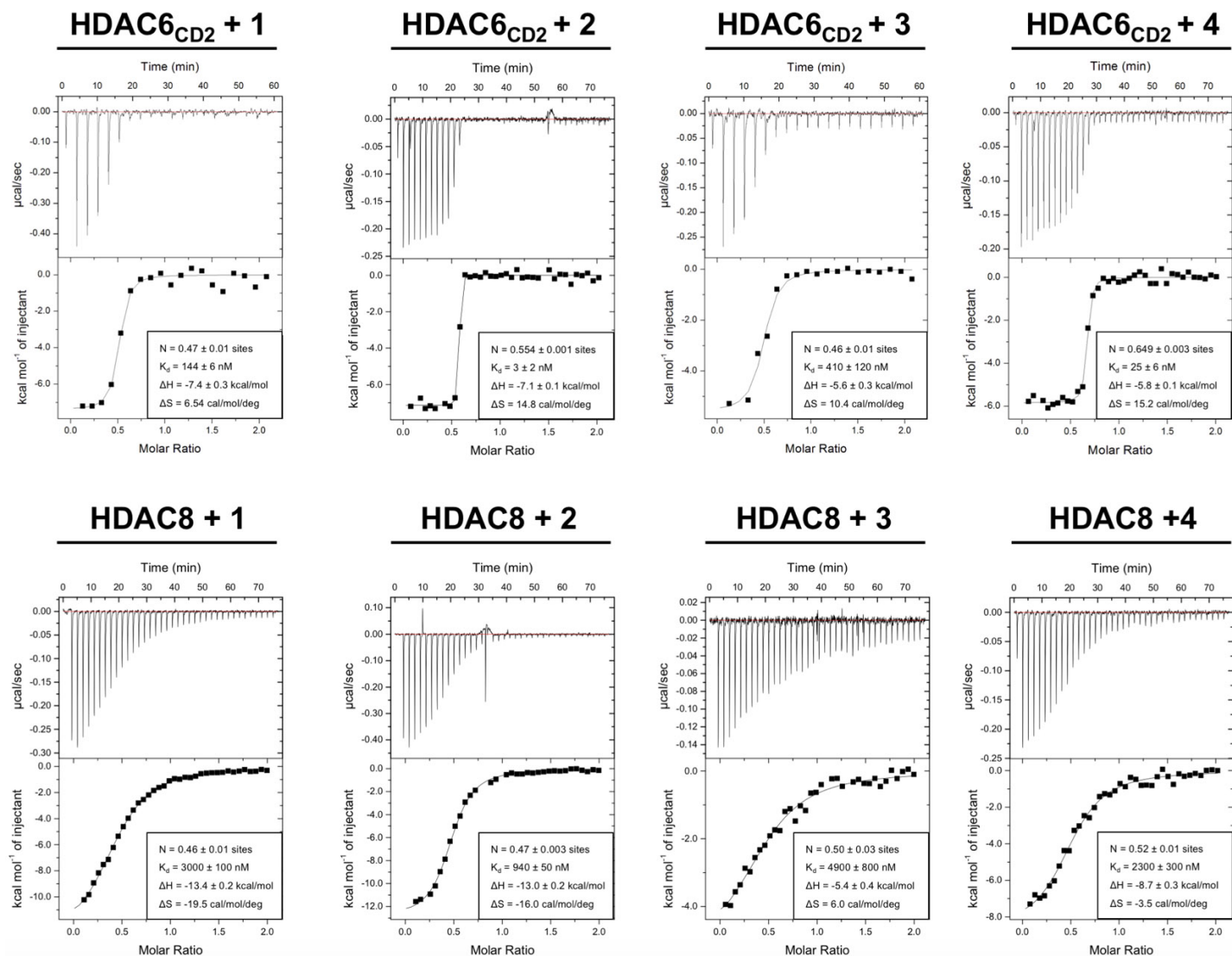
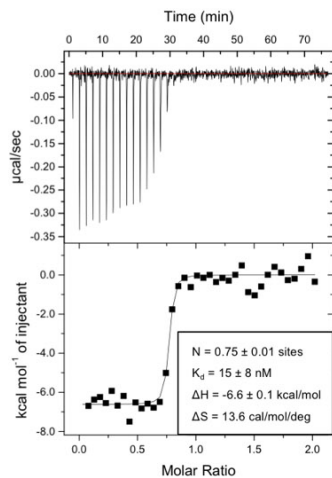
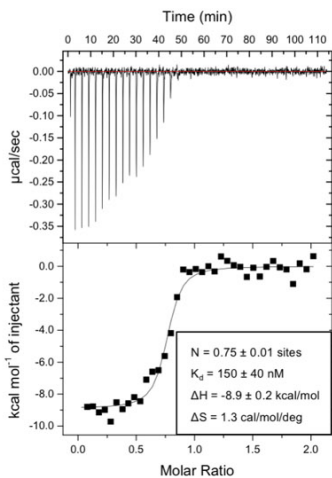


Figure S2. Isothermal titration calorimetry (ITC) thermograms for the binding of compounds 1, 2, 3, and 4 to HDAC6 and HDAC8.

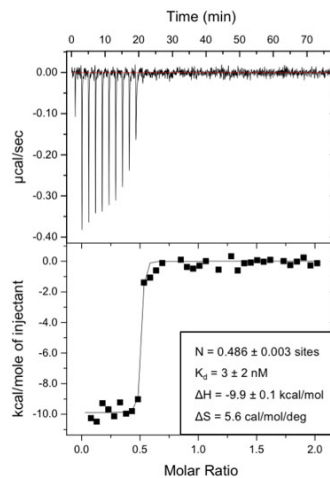
HDAC6_{CD2} + SAHA



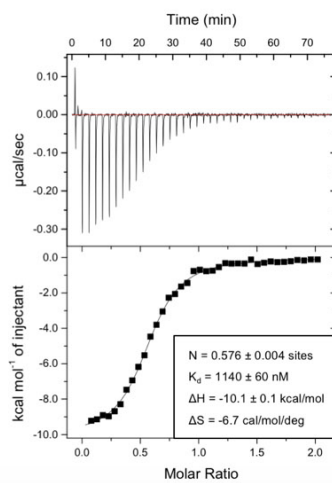
HDAC6_{CD2} + R'stat



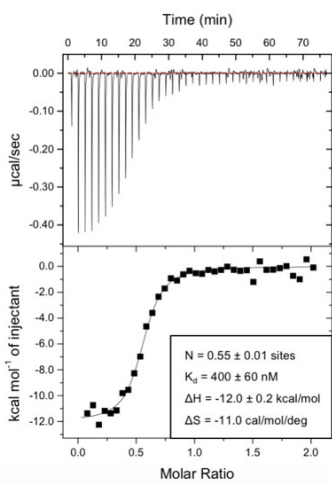
HDAC6_{CD2} + HPB



HDAC8 + SAHA



HDAC8 + R'stat



HDAC8 + HPB

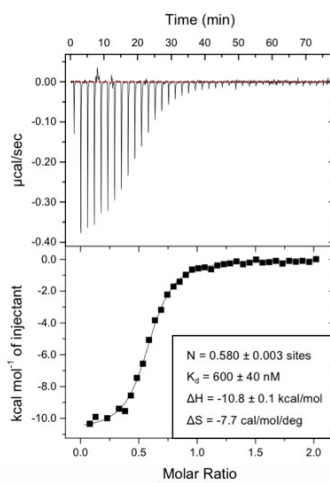


Figure S3. Isothermal titration calorimetry (ITC) thermograms for the binding of **SAHA**, Ricolinostat (**R'stat**), and **HPB** to HDAC6 and HDAC8.