Electronic Supplementary Material (ESI) for MedChemComm.

Supporting Information

Design and synthesis of conformationally constraint Dyrk1A inhibitors by creating an intramolecular H-bond involving a benzothiazole core

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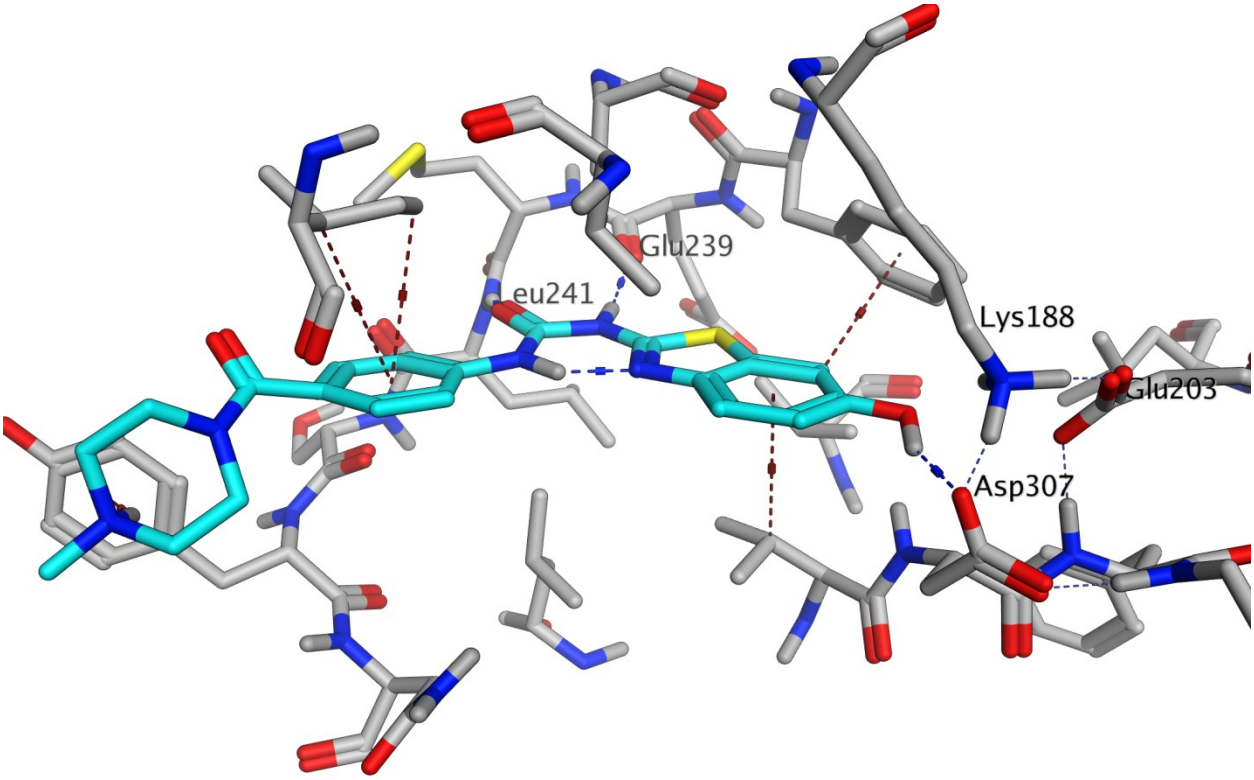
Figure S1



Potential inverted binding mode of **b5** in the ATP binding pocket of Dyrk1A. Compound **b5** was docked to the Dyrk1A coordinates derived from the co-crystal structure with 2-acetamido-5-methoxybenzothiazole (PDB code: 5A4E) using MOE.

Metabolic stability assay. The assay was performed using pooled human liver S9 fraction (Corning Life Sciences, cat. No. 452961). The incubation mix consisted of a S9 suspension of 0.33 mg/ml protein in phosphate buffer and an $NADP^+$-regenerating system ($NADP^+$, glucose-6-phosphate, glucose-6-phosphate dehydrogenase, $MgCl_2$). The reaction was initiated by the addition of test compound (final concentration 0.3 µM) to the pre-incubated microsomes/buffer mix at 37 °C. The samples were removed from the incubation mix after 0, 15, 30, and 60 min, and the reaction stopped by the addition of two volumes of ice-cold acetonitrile containing internal standard, followed by vortexing. The concentration of remaining test compound at the different time points was analyzed by LC-MS/MS.