Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications

Identification of a Novel Nanomolar Inhibitor of hIcmt via a Carboxylate Replacement Approach

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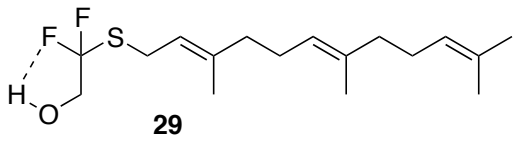
SUPPORTING INFORMATION



29

Figure S1: Possible intra-molecular hydrogen bonding in compound **29** could result in lack of activity *vis-à-vis* compound **12**.

Figure S2: Compound **12** is a mixed competitive Icmt inhibitor with a predominant competitive component (alpha value greater than 1). Procedure: K_i determinations were completed using a modified *in vitro* vapor diffusion assay. Briefly, 5 µg of protein was incubated with 10 mM Tris-HCl (pH 7.5), 0-200 µM AFC and 20 µM [^{14}C-methyl]SAM (50-60 mCi/mmol). Compound **12** was incubated with protein at a final concentration of 0.5, 1.5 and 3 µM. The reaction was continued as previously described. Lineweaver-Burk plots were used to illustrate the mode of inhibition (mixed-competitive) with an α-value greater than 1, describing predominantly competitive properties.

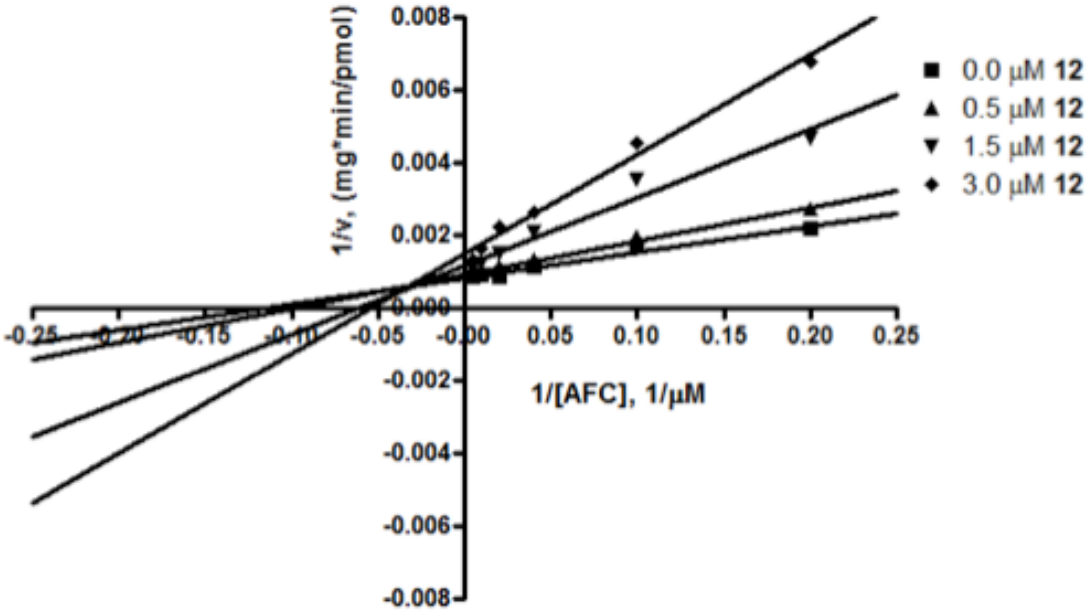


Figure S3: Compound **12** alters the subcellular localization of GFP K-Ras in Jurkat T cells. Jurkat T cells were transiently transfected with GFP K-Ras and treated with DMSO as a control, simvastatin (45 μM) or compound **12** at the indicated concentration for 24 hours. The histogram depicts the differences in GFP K-Ras localization after indicated treatment. Differences were defined as partial or complete loss of normal localization. Representative images for Jurkat cells transiently transfected with GFP-K-Ras, exhibiting normal localization, partial mislocalization, and full mislocalization, are shown in: Majmudar *et. al. Bioorg Med Chem* **2012** *20,* 283–295.