

The Effect of Bisphosphonate Acidity on the Activity of a Thymidyltransferase

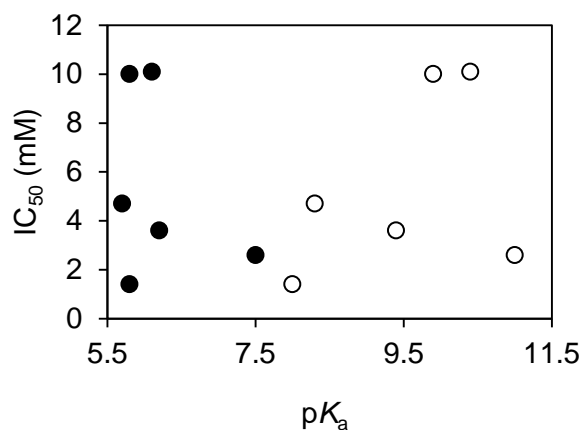
Stephen A. Beaton^a, Patricia M. Jiang^a, Jonathan C. Melong^b, Matthew W. Loranger^a, Samy Mohamady^a, Thomas I. Veinot^b and David L. Jakeman^{*a,b}

^aDepartment of Chemistry, Dalhousie University, 1459 Oxford St., Halifax, Nova Scotia, B3H 4R2

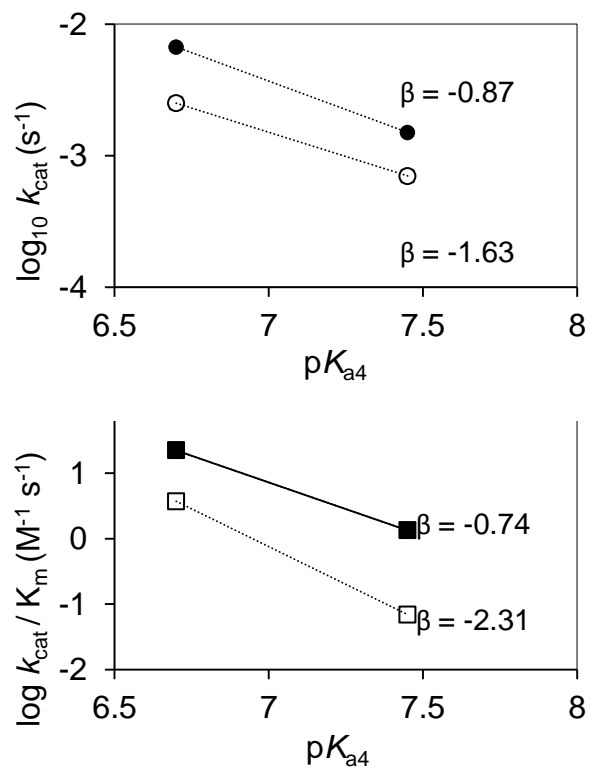
^bCollege of Pharmacy Dalhousie University, 5968 College St., Halifax, Nova Scotia, B3H 3J5 Canada. Fax: +1 902 494 1396; Tel: +1 902 494 7159; E-mail: david.jakeman@dal.ca

<i>Correlation between pKa and IC₅₀</i>	2
<i>Brønsted-type relationships for two UTP analogues</i>	2
<i>Michaelis-Menten and Lineweaver Burk plots for compounds evaluated as substrates for Cps2L</i>	3
<i>Effect of metal cations of percent conversion to dTDP-Glc</i>	5
<i>IC₅₀ data for 8-13 on the Cps2L-catalyzed production of dTDP-α-D-glucose</i>	6
<i>IC₅₀ plots for reverse reaction of Cps2L</i>	7

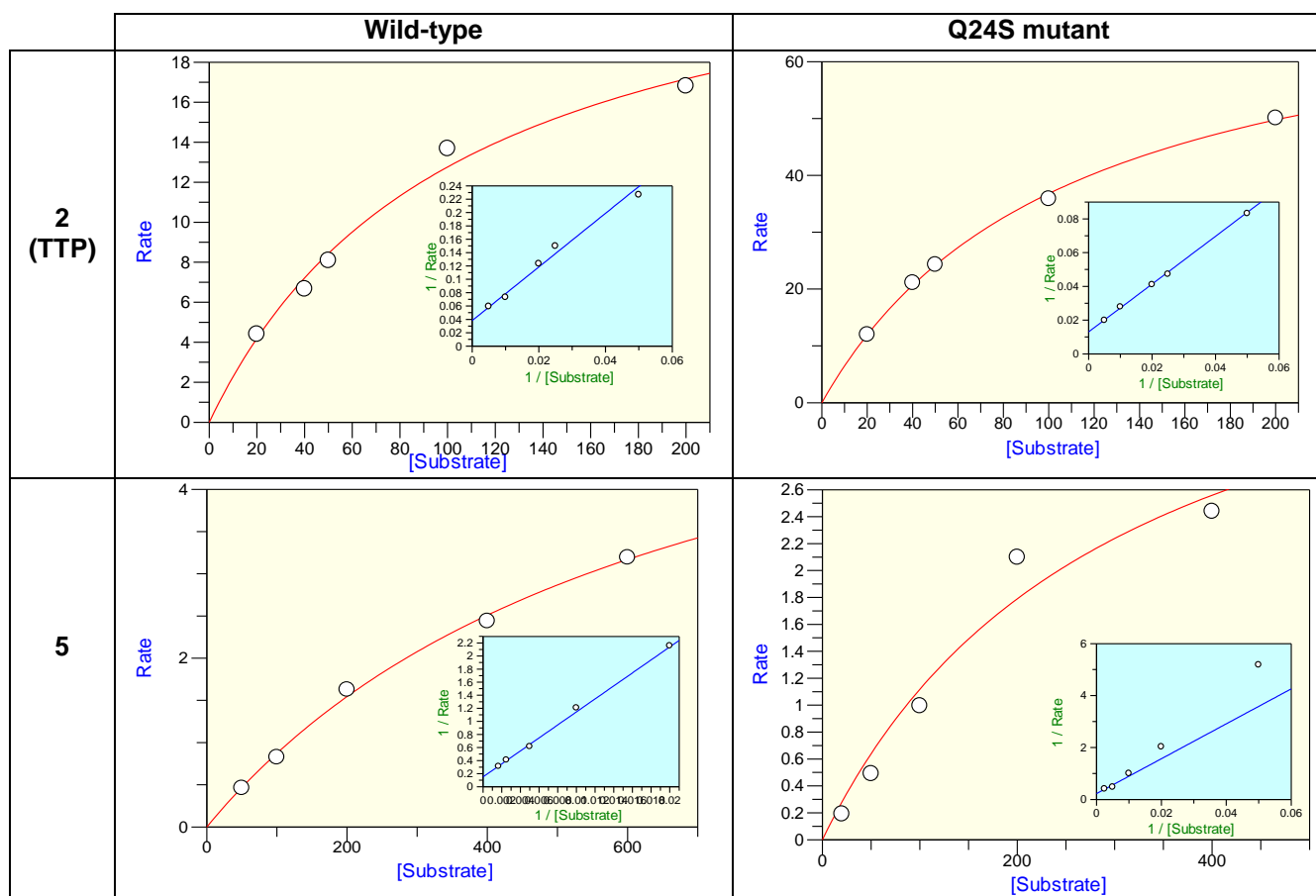
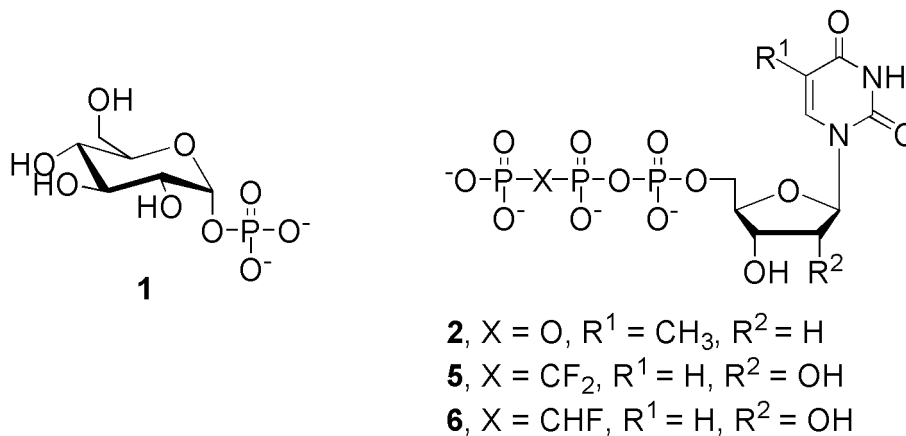
A relationship between IC_{50} values and the pK_{a3} (●) or pK_{a4} (○) for bisphosphonates (8-13)

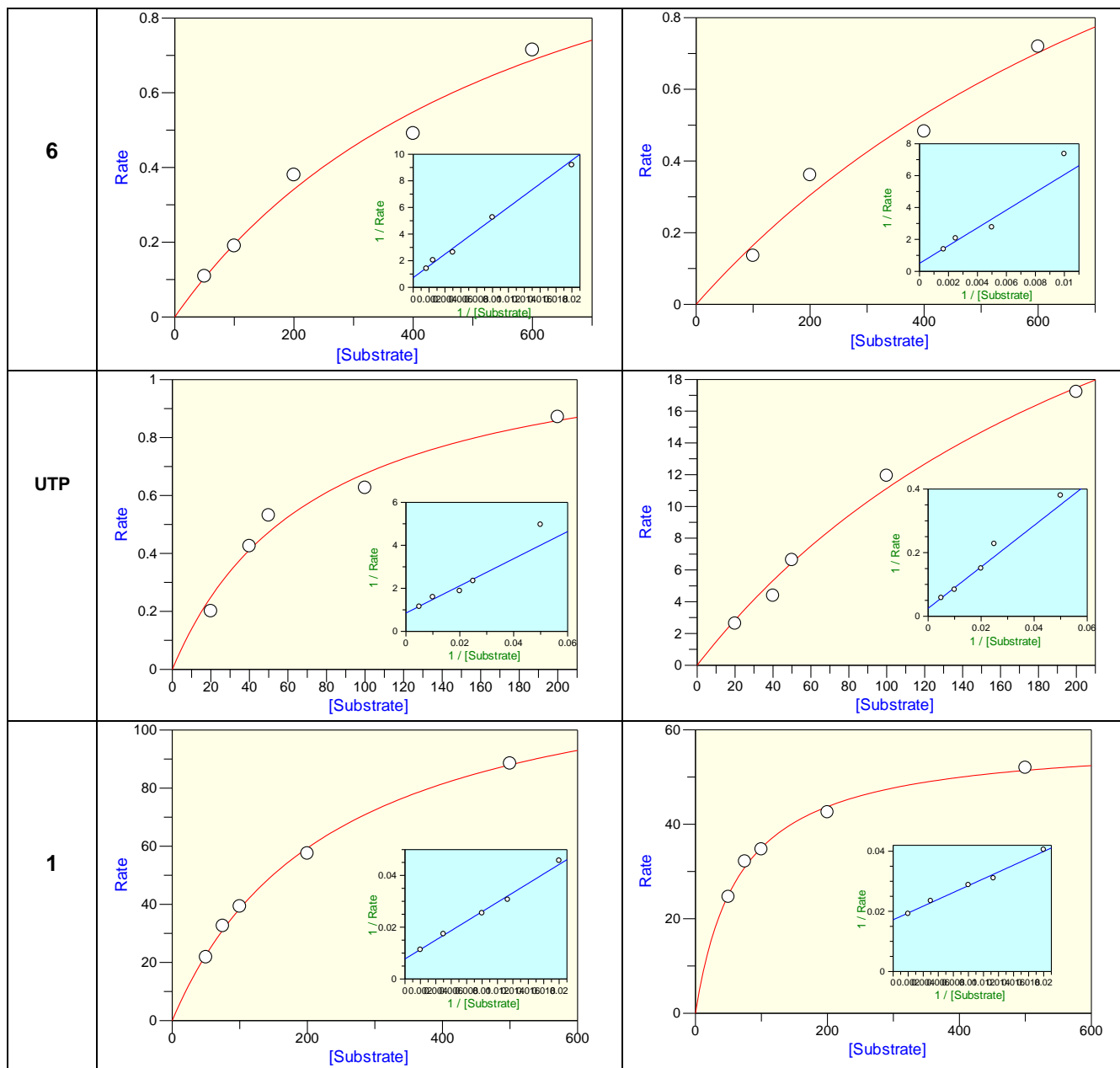


Brønsted-type relationships for two UTP analogues (5, 6) with Cps2L wild-type (○, □) and Q24S mutant (●, ■). Plots of $\log(k_{cat})$ (a) and $\log(k_{cat}/K_m)$ (b) against pK_{a4}

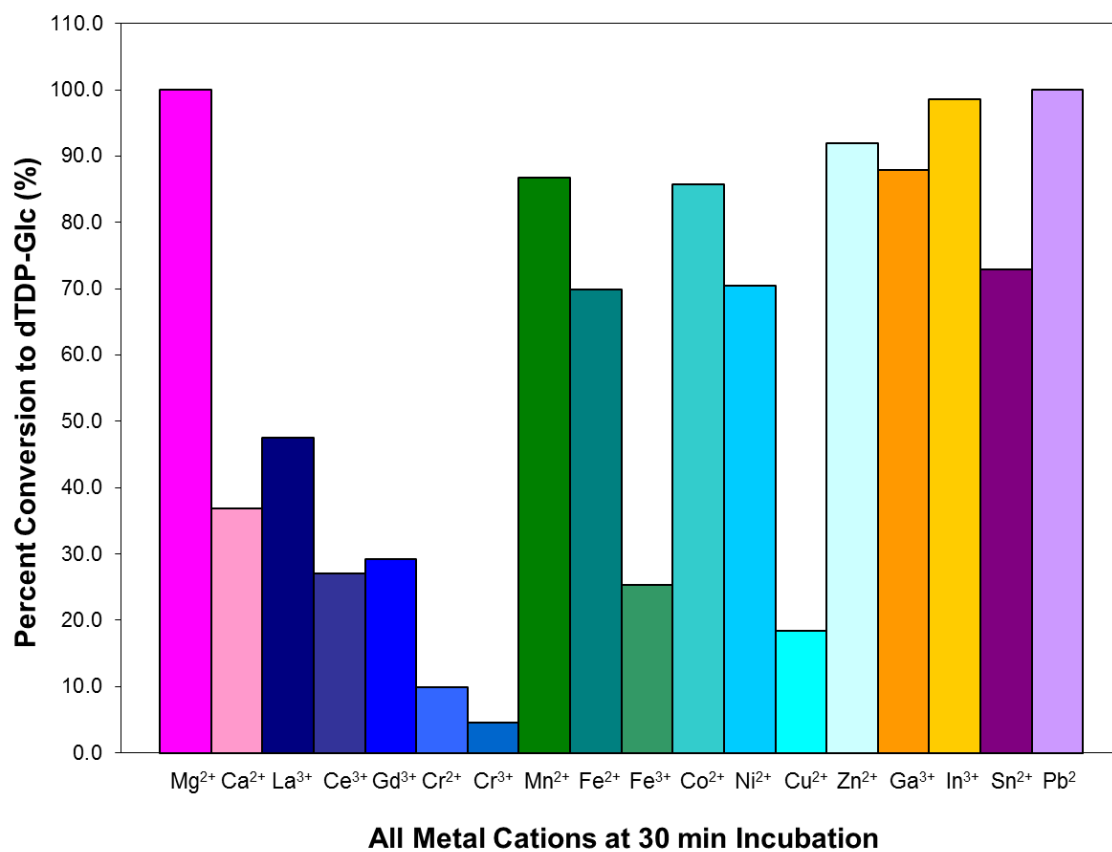


Michaelis-Menten and Lineweaver Burk plots for compounds evaluated as substrates for Cps2L

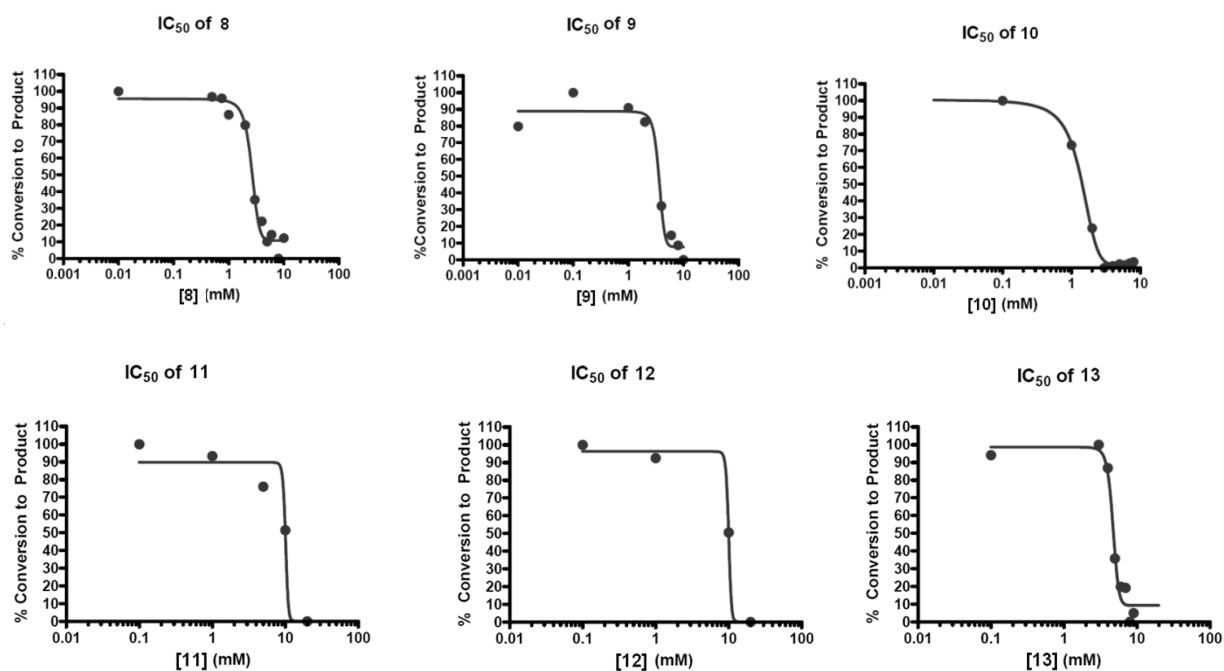




Effect of metal cations of percent conversion to dTDP-Glc



IC₅₀ data illustrating the effect of bisphosphonates **8-13** on the Cps2L-catalyzed production of dTDP- α -D-glucose



IC₅₀ data for reverse reaction of Cps2L

