Structural Studies of Human Cathepsin B Inhibitors: Tellurooxetanes

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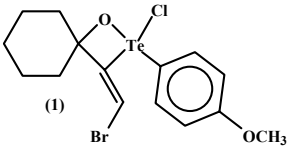

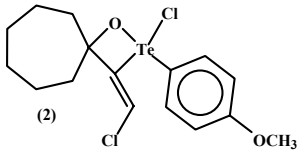

The inhibition of cathepsin B has been postulated to be directly responsible for the abrogation of the invasion process in several tumor cells lines [1], and, as it was shown that AS-101 [2], a Te^{IV} compound, was a cathepsin B inhibitor, compounds (1) and (2) were synthesized and studied.

In both compounds, if intra and two intermolecular secondary bonds and the electron lone pair are considered, then the Te^{IV} is coordinated in a ψ-pentagonal bipyramidal fashion. The secondary interactions join the molecules in chains of centrosymmetric dimmers. These compounds, have higher second-order rate constants for the inactivation of cathepsin B, than that of AS-101. Moreover, the compound with a cyclohexane ring is 20-fold more active than (**2**) and 4-fold than (**1**), so that it can be postulated that these differences are due to the nature of the halogens, or to the increase of the cycloalkane ring, which modify their electronic and steric characteristics.

FAPESP, CNPq, CAPES, FUNDUNESP

[1]Sinha A.A., Jaumar M.P., Wilson M.J., Rozhin J., Sloane B.F., *Prostate*, 2001, **49**, 172. [2] Albeck A., Weitman H., Sredni B., Albeck M., *Inorg. Chem.*, 1998, **37**, 1704.

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