SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 2-FLUOROALKYLTHIOPENEMS

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In the course of our synthetic studies on ß-lactam antibiotics having penem skelton, we have prepared new penem derivatives having halogenoalkylthio group, particularly fluoroalkylthio group, at 2-position.

Several useful routes were applied for the preparation. Alkylation of (5S, 6S)-6-[1-(R)]-thioxopenam 2 gave 5,6-cis compound 3, which was isomerized to 5,6-trans derivative by heating in xylene and then the protecting group was removed to give the desired compound 1a,b,f.

Alternatively, 4-acetoxyazetidin-2-one 4 was converted to the trithiocarbonate 5, which was transformed into phosphoranyl derivative 6 in three steps. Intramolecular Wittig reaction of 6 followed by deprotection afforded compound 1a,c,d,e. Also, the transformation of compound 5 to 1a has been achieved via compound 7 in short steps.

These penem derivatives had high activity against both gram-positive organisms and gram-negative organisms. Especially, compound 1a had *in vitro* activities 2 to 8 times higher than the known compound, Sch 29482.