

The structures of the anti-tuberculosis antibiotics viomycin and capreomycin bound to the 70S ribosome

Robin E. Stanley^{1,2*}, Gregor Blaha^{1*}, Robert L. Grodzicki^{1,3}, Michael D. Strickler^{1,3}, & Thomas A. Steitz^{1,3,4}

¹*Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT 06520, USA.*

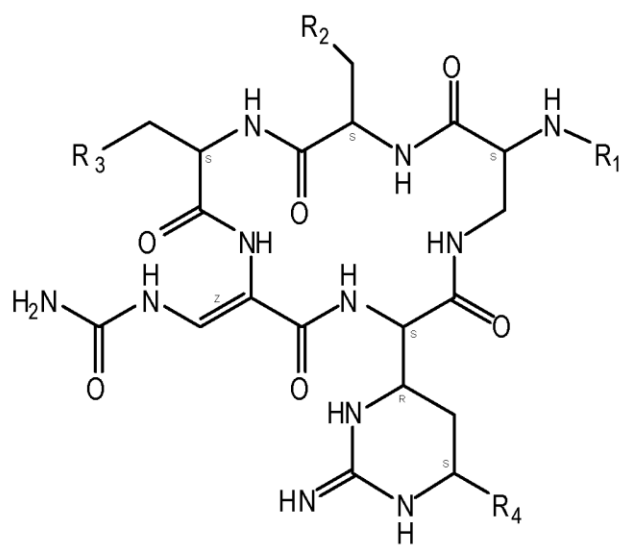
²*Present address: Laboratory of Molecular Biology, NIDDK, NIH, Bethesda, Maryland 20892, USA.*

³*Howard Hughes Medical Institute, New Haven, CT 06520, USA*

⁴*Department of Chemistry, Yale University, New Haven CT 06520, USA*

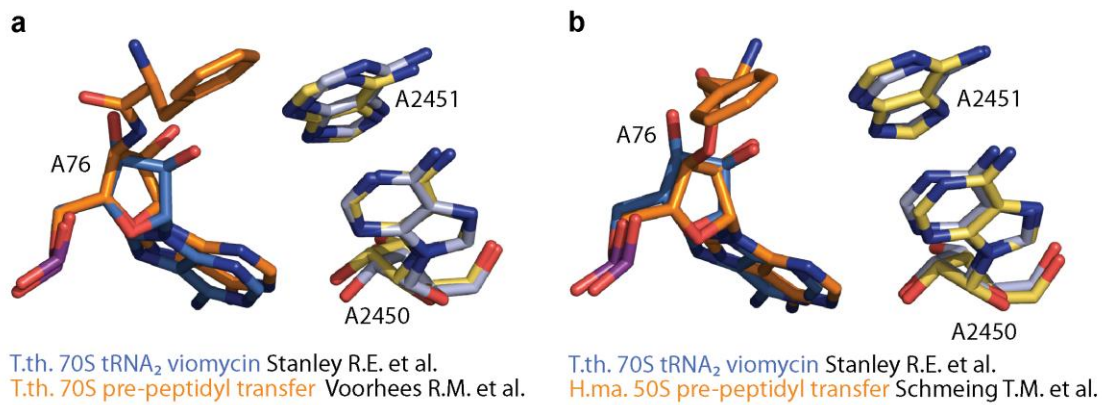
** These authors contributed equally to this work*

Correspondence to: Thomas A. Steitz e-mail: thomas.steitz@yale.edu



Antibiotic	R ₁	R ₂	R ₃	R ₄
Viomycin		-OH	-OH	-OH
Tuberactinomycin A		-OH	-OH	-OH
Tuberactinomycin B		-OH	-OH	-OH
Tuberactinomycin N		-OH	-OH	-H
Tuberactinomycin O		-OH	-OH	-H
Tuberactinamine	-H	-OH	-OH	-H
Capreomycin IA	-H	-OH		-H
Capreomycin IB	-H	-H		-H
Capreomycin IIA	-H	-OH	-NH ₂	-H
Capreomycin IIB	-H	-H	-NH ₂	-H

Supplemental figure 1: chemical structure of naturally occurring tuberactinomycins.



Supplemental figure 2: Comparison of the relative positions of A2450 and A2451 of the 23S rRNA to the A76 of a P-site substrate from structures of different ribosomal complexes. All structures were superimposed on the peptidyl transferase centre as defined by residues 2049-2074, 2244-2261, 2435-2466, 2484-2520, and 2545-2619 of 23S rRNA. (a) Comparison between *T.th.* 70S complex of a pre-peptidyl transfer reaction from the structure of Ramakrishnan and co-workers (2WDL and 2WDK)¹² and the viomycin structure reported here. Residues of 23S rRNA are in gold and gray, the terminal residue of the P-site tRNA is in orange and blue, for the complex of the pre-peptidyl transfer reaction and for the viomycin complex, respectively.

(b) Comparison between the structure of a *H.ma.* 50S complex of a pre-peptidyl transfer reaction (1VQN)¹¹ and the viomycin structure reported here. Residues of 23S rRNA are in gold and gray, the terminal residue of the P-site tRNA is in orange and blue, for the complex of the pre-peptidyl transfer reaction and for the viomycin complex, respectively.