SIMPLIFYING THE SYNTHESIS OF VIRGINIAMYCIN MII ANALOGUES FOR CRYO-EM GUIDED DRUG DEVELOPMENT

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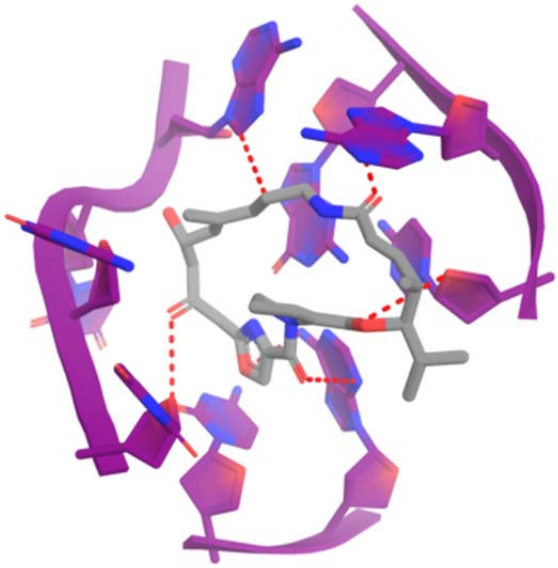
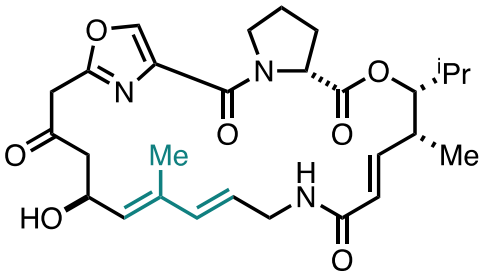
The development of novel antibiotics has been at the forefront of medicinal chemistry, with the threat of widespread antibiotic resistance looming. The binding of virginiamycin MII to the bacterial ribosome provides an opportunity to probe the possibilities of rational drug design through synthesis. Herein we report our preliminary studies focused on this topic.

In this project we have addressed the more synthetically challenging aspects of the molecule, in particular the *E,E* bis-alkene motif, through replacement with simpler aryl and heteroaryl functionality as guided by cryo-EM analysis. By replacing with a similarly planar triazole or phenyl ring, a more straightforward synthetic pathway is possible. Synthetic studies to this end are reported.





virginiamycin MII