A Tunicamycin Analogue Inhibits Human Phosphotransferase, DPAGT1

**Significance:** The naturally occurring nucleoside antibiotics, tunicamycins are of potential synthetic interest due to their nonselective cytotoxic and cytostatic activities. The authors report a 15-step synthesis of a tunicamycin analogue, TN-TMPA, which shows selective cytostatic activity against breast cancer cell lines. When compared to the natural analogue TN-V, TN-TMPA shows 12.5 times higher inhibition of dolichyl-phosphate N-acetylglucosamine-phosphotransferase (DPAGT1) – a protein responsible for abnormal N-linked glycosylation in cancer cells.

**Comment:** The molecule contains a disaccharide fragment and a uridine fragment. The key reaction in the synthesis is a Büchner–Curtius–Schlotterbeck-type reaction to couple the disaccharide with the uridine moiety. This reaction occurs via a diazoalkane intermediate. Deprotonation and nucleophilic addition to aldehyde following a 1,2-hydride shift afford the ketone product. Finally, a highly stereoselective Meerwein–Pondorf–Verley reduction and N-acylation yields TN-V or TN-TMPA.