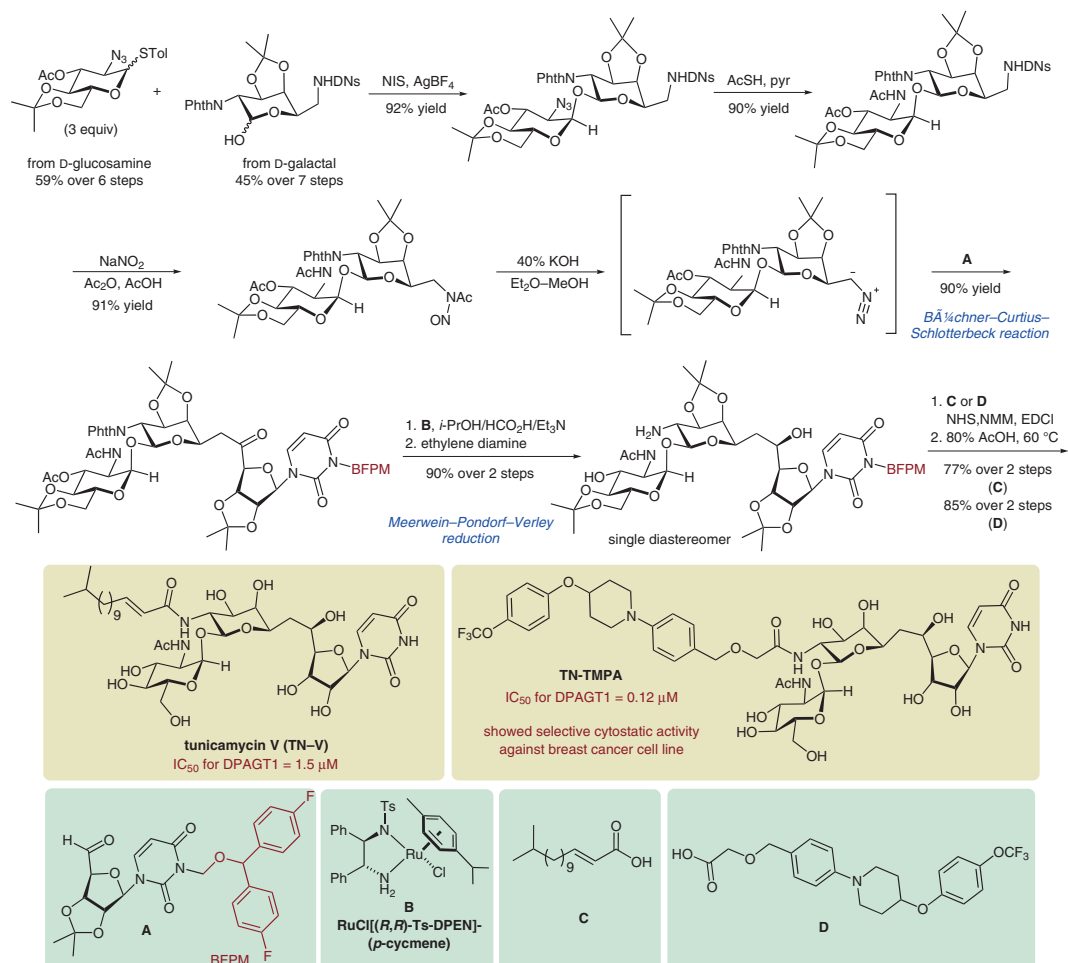


K. MITACHI, D. MINGLE, W. EFFAH, A. SÁNCHEZ-RUIZ, K. E. HEVENER, R. NARAYANAN, W. M. JR. CLEMONS, F. SARABIA, M. KUROSU* (UNIVERSITY OF TENNESSEE HEALTH SCIENCE CENTER, MEMPHIS, USA)

Concise Synthesis of Tunicamycin V and Discovery of a Cytostatic DPAGT1 Inhibitor

Angew. Chem. Int. Ed. **2022**, *61*, e202203225 DOI: 10.1002/anie.202203225.

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–Ponndorf–Verley reduction and *N*-acylation yields **TN-V** or **TN-TMPA**.

SYNFACTS Contributors: Dirk Trauner, Tufan K. Mukhopadhyay
Synfacts 2022, 18(09), 1027 Published online: 18.08.2022
DOI: 10.1055/s-0041-1738566; Reg-No.: T11222SF

© 2022, Thieme. All rights reserved.
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Category

Innovative Drug
Discovery and
Development

Key words

Büchner–Curtius–
Schlotterbeck
reaction

Meerwein–
Ponndorf–Verley
reduction

DPAGT1 inhibition

Synfact
of the
Month

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.