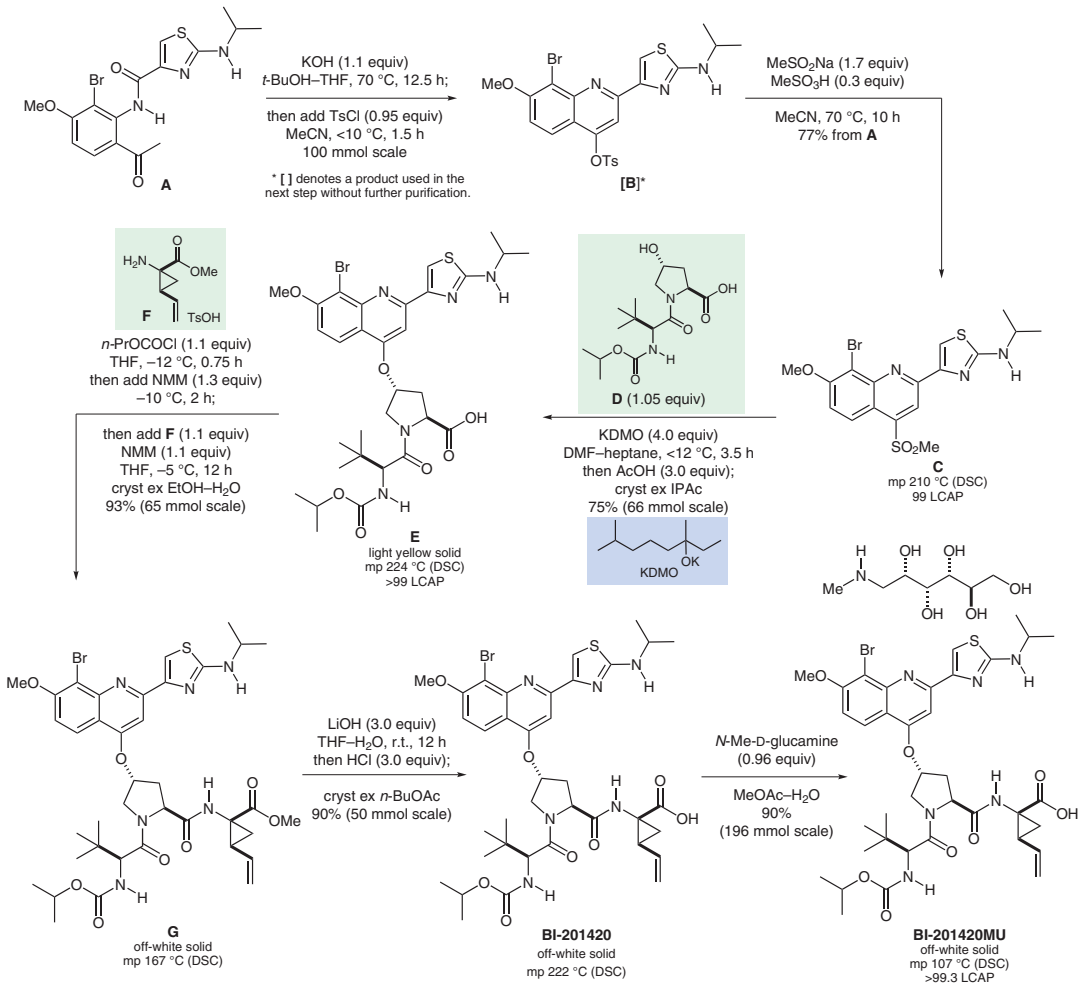
N. D. PATEL*, X. WEI* ET AL. (BOEHRINGER-INGELHEIM PHARMACEUTICALS INC., RIDGEFIELD, USA)

Sulfone-Mediated S_NAr Reaction as a Powerful Tool for the Synthesis of 4-Quinolinyl Ethers and More – Application to the Synthesis of HCV NS3/4a Protease Inhibitor BI 201420
J. Org. Chem. **2020**, *85*, 8339–8351.

Synthesis of BI 201420



Significance: A new method for the synthesis of 4-quinolinyl ethers has been applied to BI 201420, an HCV NS3/4a protease inhibitor. In the key step, methylsulfone **C** underwent an S_NAr reaction with alcohol **D** in the presence of potassium 3,7-dimethyloctan-3-oxide (KDMO, 4.0 equiv) to give 4-quinolyl ether **E** in 75% yield. Scoping studies revealed that 1°, 2°, 3°, allylic, and propargylic alcohols participate (20 examples).

Comment: The corresponding S_NAr reaction of 4-chloroquinolines with alcohols is sluggish, even with excess base (>5.0 equiv), and significant decomposition of starting material and product are observed during the long reaction times (12–24 h). Extensive optimization of solvent and reaction conditions failed to produce the desired 4-quinolinyl ethers in reasonable yield and quality.

SYNFACTS Contributors: Philip Kocienski
Synfacts 2020, 16(09), 1009 Published online: 18.08.2020
DOI: 10.1055/s-0040-1705870; **Reg-No.:** K05920SF

© 2020. Thieme. All rights reserved.
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Category

Synthesis of Natural Products and Potential Drugs

Key words

BI 201420

HCV NS3/4a protease inhibitor

4-methylsulfonyl quinolines

quinoline ring formation

S_NAr reaction

Synfact of the Month

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