Synthesis of MK-5172

Significance: MK-5172 is a hepatitis C virus protease inhibitor. Key steps in the synthesis depicted are (1) the regioselective SNAr reaction of dichloroquinoxaline A with prolinol derivative B and (2) construction of the 18-membered macrocycle using a macrolactamization (F → G).

Comment: The medicinal chemistry route to MK-5172 is based on a ring-closing metathesis strategy. The best regioselectivity (20:1) and minimization of double substitution in the SNAr reaction of A with B were achieved using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base in polar solvents such as DMSO, NMP, or DMAc.