Development of a Scalable Process for the Synthesis of a Next-Generation Statin

**Synthesis of BMS-644950**

**Significance:** BMS-644950 is a development candidate for the treatment of hypercholesterolemia. The route depicted delivered >70 kg of the API in 35% overall yield. The synthesis is noteworthy for the large-scale TEMPO oxidation (H → I, 83 mol scale) and Julia–Kocienski olefination (A + B → C, 78 mol scale).

**Comment:** The Julia–Kocienski olefination was performed by adding LiHMDS to a mixture of the aldehyde I and the sulfone J in THF at −70 °C (Barbier conditions). In this way the E-alkene product was obtained with high stereoselectivity (E/Z up to 200:1). Note the use of dimethyl carbonate and DABCO for the N-alkylation of G.

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**Synthesis of Natural Products and Potential Drugs**

**Key words**

BMS-644950  
HMG-CoA reductase inhibitors  
statins  
Biginelli reaction  
pyrimidines  
Julia–Kocienski olefination