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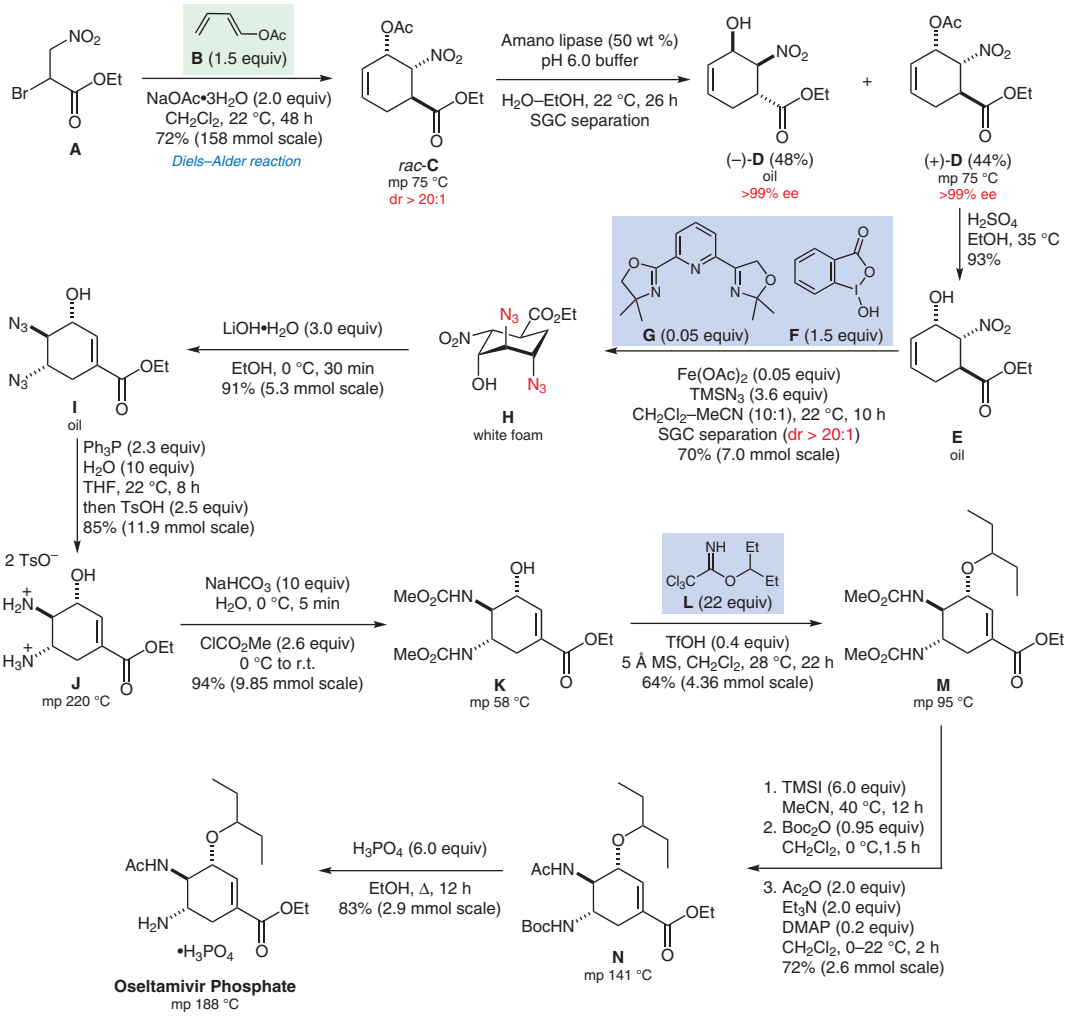
Enantioselective Synthesis of Oseltamivir Phosphate (Tamiflu) via the Iron-Catalyzed Stereoselective Olefin Diazidation

J. Am. Chem. Soc. **2018**, *140*, 10619–10626.

Synthesis of Oseltamivir Phosphate



Significance: Xu and co-workers report a gram-scale synthesis of the neuraminidase inhibitor oseltamivir phosphate (Tamiflu®), in which the *trans*-diamino moiety was installed through an iron-catalyzed, diastereoselective diazidation of enantiopure olefin **E** to give the 1,2-*trans*-diazide **H** in 70% yield (dr > 20:1). Electronically deactivated substrates, that have been otherwise problematic, are tolerated.

Comment: Mechanistic studies revealed that both the iron catalyst and the complex substrate cooperatively modulate the stereoselectivity of the diazidation. Process safety assessment using both differential scanning calorimetry and the drop weight test indicate that the diazidation reaction can be performed on large scale.

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Synfacts 2018, 14(11), 1109 Published online: 18.10.2018
DOI: 10.1055/s-0037-1609630; **Reg-No.:** K05918SF

Category

Synthesis of Natural Products and Potential Drugs

Key words

oseltamivir phosphate

neuraminidase inhibitor

olefin diazidation

iron catalysis

vicinal diazides

1,2-*trans*-diamines