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<th><strong>Title</strong></th>
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De Novel Synthesis of Tamiflu

Introduction
With increasing fear of a potential new influenza pandemic, the anti-influenza drug Tamiflu become more and more important. Tamiflu is an antiviral drug which acts as a transition-state analogue inhibitor of influenza neuraminidase, preventing new viruses from emerging from infected cells.

Results and Discussion
The retro-synthetic analysis is shown in Scheme 1. It is an auxiliary assistant 4+2 Diels-Alder cyclization. The sugar auxiliary is introduced to control the stereo selectivity of 3R,4R,5S (Tamiflu).

The X-ray structure of azide-D-galactose is shown below:

Two different methods were tried to do the job as shown in Scheme 5. The possible reason was supposed that there is an intramolecular hydrogen bond which could stabilize the Z configuration.

Conclusion
We are seeking a concise method to synthesis Tamiflu and the key intermediates have already been made. The future work is to study the stereoselectivity of the Diels-Alder reaction by using the sugar auxiliary.

Related Reagent
Pd/C
H2, 40 Psi
r.t., 3h, 90%

r.t., 4h, 95%

80 oC, 12h, 80%

Scheme 5. Synthesis of the sugar 10,Z-form

Route 1

Route 2

10, Z-form