A New, Efficient Synthesis of ω-NBD Sphingosine
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Abstract
ω-NBD sphingosine is a biologically active derivative of sphingosine that is tagged with a fluorescent nitrobenzoxadiazole (NBD) group. Sphingosine-1-phosphate is an important precursor to sphingolipids and sphingolipid derivatives. In this study, we have developed a new and efficient synthesis of ω-NBD sphingosine that is only six steps long.

Introduction
Sphingosine is a bioactive lipid that is formed from the breakdown of ceramide and is the precursor to sphingosine-1-phosphate. Sphingosine has been known to induce apoptosis when added exogenously to cells. Sphingosine also inhibits protein kinase C and phosphatidic acid phosphohydrolase, and activates diacylglycerol (DAG) kinase and phospholipase D. When sphingosine is phosphorylated by the sphingosine kinase enzyme, it becomes sphingosine-1-phosphate. Sphingosine-1-phosphate has anti-apoptotic and proliferative activity. The enzyme sphingosine kinase has two isoforms, SPHK1 and SPHK2. SPHK1 and SPHK2 are expressed in all human tissues. The highest levels of SPHK1 are found in the lungs, spleen, and leukocytes. The highest levels of SPHK2 are expressed in all human tissues. The highest levels of SPHK1 are found in the lungs, spleen, and leukocytes. However, other studies demonstrated that SPHK2 has a similar role to SPHK1 in promoting cancer. The role that SPHK2 plays in inflammation is controversial in that many studies suggest that SPHK2 may be anti-inflammatory.

Methods
There were three critical steps to creating the shortened synthesis of ω-NBD sphingosine. The first step that was crucial for keeping the synthesis as short as possible was the direct transformation of the bromo-alcohol (1) with the NBD moiety (2) to give compound 3. The second crucial step in our approach was the application of protected L-serine (5) as a building block. The final crucial reaction was the diastereoselective reduction of the enone (7), which provided alcohol (8) without affecting the double bond.

Results and Discussion
Overall, creating a shortened synthesis of ω-NBD sphingosine was successful. We have proven that the attachment of the NBD moiety did not interfere with the rest of the synthesis. Some of the key steps in this shortened synthesis include: a) the coupling of amino NBD to 14-bromo-1-tetradecanol, b) the conversion of 5 to 6, and c) the Luche reduction of the enone (7 to 8). There are still some improvements that need to be made to the synthesis. Further work will be done in the future to optimize the coupling of amino NBD to 14-bromo-1-tetradecanol to increase the yield of the reaction. The other reaction that we would like to improve the yield on is the transformation of 5 to 6.

Conclusion
We have demonstrated that the introduction of the NBD moiety at the beginning of the synthesis allowed us to construct a shorter path for the synthesis of ω-NBD sphingosine. We have proven that the attachment of the NBD did not interfere with the remainder of the synthesis. The application of protected L-serine (5) also contributed to a significant simplification of the synthesis of the final product.

Synthesis of NBD Sphingosine

Reference

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