

“Synthesis of Building Blocks for the Introduction of Cis-Syn Thymine Dimers onto Oligonucleotides”

Jonathan Waits
Chemistry 345
October 27, 2003

When DNA is exposed to ultraviolet light, a variety of photoproducts called photolesions result from the interaction. These photolesions can cause disease but their study is limited by the lack of well-characterized, isolated photoproducts. This study dealt with the synthesis of a compound used in the sequence-specific process of introducing the cis-syn thymine dimer onto an oligonucleotide using solid-phase DNA synthesis technology. The starting material, a phosphoradimite thymine (pT) called pT-O₃-(*tert*-butyldimethylsilyl)thymidylyl-(3' → 5')-thymidine, R,S-O-methyl phosphate or HO-TPO(OMe)T-OTBDMS, was photolyzed to produce a mixture of four major products: A, B, C, D. Products A and C have the formula HO-T[*t,s*]PO(OMe)T-OTBDMS. Products B and D have the formula HO-T[*c,s*]PO(OMe)T-OTBDMS. After separation by preparative isocratic reverse phase HPLC, B was converted in three steps to DMTO-T[*c,s*]PO(OMe)T-OP(OMe)(NC₄H₈O). This product was condensed using DNA synthesis to the cis-syn thymine dimer TpT[*c,s*]pTpT which could be photoreversed to TpTpTpT. In order to certify the character of the photoreversed TpTpTpT, a direct synthesis of TpTpTpT was performed for comparison. This positively identified the cis-syn thymine dimer. After testing the chemical stability of the dimer by subjecting it to conditions necessary to remove protective groups, DMTO-T[*c,s*]PO(OMe)T-OP(OMe)(NC₄H₈O) was certified as an appropriate building block for the production of cis-syn thymine dimer oligonucleotides.

Bibliography

Taylor, J.; Brockie, I. R and O'Day, C. L. *J. Am. Chem. Soc.* 1987, 109, 6735—6742

Taylor, J and Cohrs, M. P. *J. Am. Chem. Soc.* 1987, 109, 2834—2835

Taylor, J and O'Day, C. L. *J. Am. Chem. Soc.* 1989, 111, 401—402

Taylor, J. *J. Chem. Ed.* 1990, 67, 835—841