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Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713618290>

Stereoselective Synthesis of [Rp]-Dinucleoside (3',5')-Methanephosphonates

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To cite this Article Wozniak, Lucyna A. , Chworos, Arkadiusz and Stec, W. J.(1999) 'Stereoselective Synthesis of [Rp]-Dinucleoside (3',5')-Methanephosphonates', *Phosphorus, Sulfur, and Silicon and the Related Elements*, 147: 1, 437

To link to this Article: DOI: 10.1080/10426509908053698

URL: <http://dx.doi.org/10.1080/10426509908053698>

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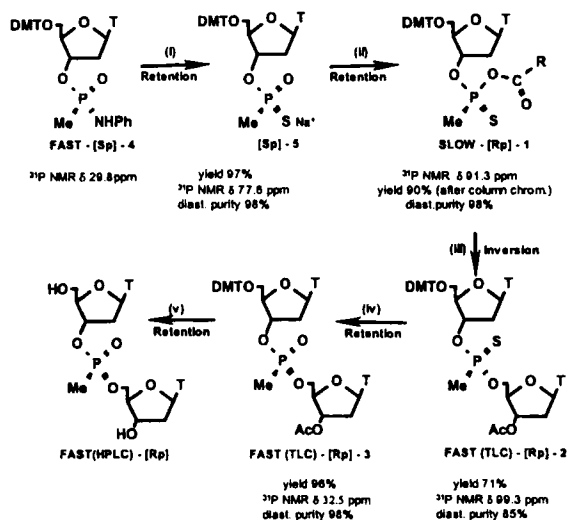
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Stereoselective Synthesis of [Rp]-Dinucleoside (3', 5')-Methanephosphonates

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DBU-assisted phosphonylating properties of diastereomerically pure 5'-O-DMT-thymidine (O-2,4,6-trimethylbenzoyl methanephosphonothiate)(1) towards alcohols [1] have been used for the synthesis of [Rp]-dithymidylyl (3',5')-methanephosphonothioates (2) and methanephosphonates (3). Substrates (4) and (5) have been obtained according to the previously described methods [2].



Reaction conditions: (I) NaH/CS₂, DMF; (II) RC(O)Cl, Py (R = 2,4,6-trimethylphenyl); (III) 3'-O-Ac-thymidine, DBU, MeCN; (IV) OXONE; (V) NH₂/MeOH-H₂O (1:1)

It has been found that the reaction of condensation (1) → (2) proceeds with predominant inversion of configuration. Dimer (2) was oxidized by means of oxone, leading to (3) [2].

References

- [1] L.A. Wozniak, A. Chworos, W.J. Stec, *J.Org.Chem.* submitted.
- [2] W.J. Stec, *et al. Antisense and Nucleic Drug Development* 7 (1997) 381.