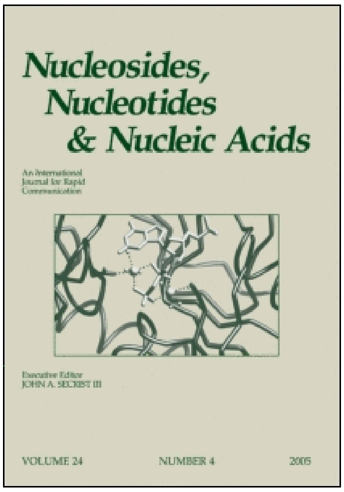


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Studies Towards Synthesis of Dinucleoside Arylphosphonates with Metal Complexing Properties

Tommy Johansson[a]; Jacek Stawinski[ab]
[a] Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Stockholm, Sweden
[b] Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznan, Poland

To cite this Article Johansson, Tommy and Stawinski, Jacek(2003) 'Studies Towards Synthesis of Dinucleoside Arylphosphonates with Metal Complexing Properties', Nucleosides, Nucleotides and Nucleic Acids, 22: 5, 1459 — 1461
To link to this Article: DOI: 10.1081/NCN-120023010
URL: http://dx.doi.org/10.1081/NCN-120023010

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, Nos. 5–8, pp. 1459–1461, 2003

Studies Towards Synthesis of Dinucleoside Arylphosphonates with Metal Complexing Properties

Tommy Johansson[1] and Jacek Stawinski[1,2,*]

[1]Department of Organic Chemistry, Arrhenius Laboratory,
Stockholm University, Stockholm, Sweden
[2]Institute of Bioorganic Chemistry, Polish Academy of Sciences,
Poznan, Poland

ABSTRACT

An efficient and stereospecific synthesis of dinucleoside 4′-(2,2′:6′,2″-terpyridyl)-phosphonate **2** and 5-(2,2′-bipyridyl)phosphonate **3** via a palladium(0) cross coupling strategy has been developed.

Key Words: H-Phosphonates; C-Phosphonates; Arylphosphonates; Terpyridine; Palladium cross coupling.

We have recently developed efficient and general methods for the preparation of dinucleoside 2-pyridyl-,[1] 3-pyridyl-,[2] and 4-pyridylphosphonates.[3] As a continuation of this work, we were aiming towards synthesis of various pyridylphosphonate derivatives with metal complexing properties. Since oligonucleotides appended with

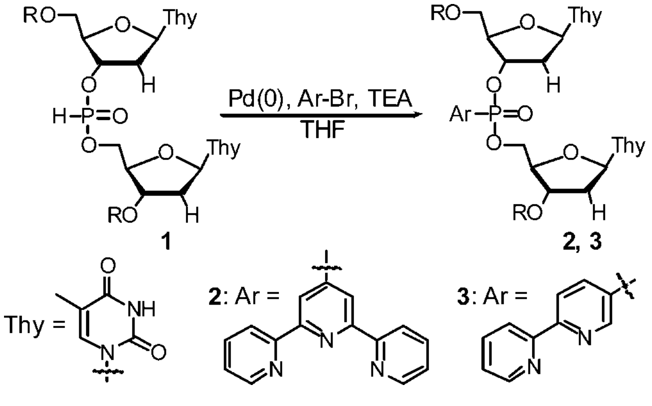
---

*Correspondence: Jacek Stawinski, Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-10691 Stockholm, Sweden; Fax: +46 8 154 908; E-mail: js@organ.su.se.

DOI: 10.1081/NCN-120023010 1525-7770 (Print); 1532-2335 (Online)

www.dekker.com

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016



Scheme 1.

2,2′:6′,2″-terpyridine or 2,2′-bipyridine moieties exhibit in the presence of metal ions promising properties as artificial nucleases,[4] we investigated the possibility of attaching these functionalities directly to the phosphorus centre using the recently developed palladium(0) cross coupling strategy[1] (Sch. 1).

When equimolar amounts of dinucleoside H-phosphonate **1** and 4′-bromo-(2,2′:6′,2″-terpyridine) in the presence of 1.2 equiv. of triethylamine (TEA) and 0.2 equiv. of $Pd(PPh_3)_4$ were refluxed in THF for 5 hours, the desired dinucleoside 4′-terpyridylphosphonate **2** was formed as a sole product (^{31}P NMR spectroscopy). When the separate diastereomers of H-phosphonate **1** were subjected to the same reaction conditions, a fully stereospecific conversion into 4′-terpyridylphosphonate **2** derivatives was observed and the products were isolated by silica gel chromatography in good yields (**2**-R_P: 73%, **2**-S_P: 66%).

Attempted preparation of dinucleoside 5-(2,2′-bipyridyl) phosphonate **3** in the reaction of equimolar amounts of H-phosphonate **1** and 5-bromo-2,2′-bipyridine, TEA (1.2 equiv.) and $Pd(PPh_3)_4$ (0.2 equiv.) under reflux in THF (5 h), resulted in only 60% conversion of **1** into 5-bipyridylphosphonate **3** (^{31}P NMR spectroscopy). However, by changing the catalytic system to $Pd(OAc)_2$ and 1,1′-bis(diphenylphosphino)-ferrocene (DPPF), almost quantitative formation of **3** could be achieved. This reaction also, when carried out on separate diastereomers of H-phosphonate **1**, proved to be completely stereospecific and the diastereomers of 5-bipyridylphosphonate **3** were isolated in good yields (R_P: 64%, S_P: 61%).

Among other ligands investigated only 2,2′-bis(diphenylphosphino)-1,1′-binaphtyl (BINAP) turned out to be as efficient as DPPF. Neither 1,2-bis(diphenylphosphino)ethane (DPPE) nor 1,3-bis(diphenylphosphino)propane (DPPP) promoted any detectable formation of bipyridylphosphonates **3**, probably due to inactivation of the palladium(0) catalyst by a 2,2′-bipyridine moiety (from the substrate or from product **3**). The efficacy of rigid and sterically demanding bidentate ligands (DPPF, BINAP) in promoting synthesis of **3** can probably be due to their high complexing affinity that prevents the bipyridine moiety to replace these ligands in active palladium complexes.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

ACKNOWLEDGMENTS

The financial support from the Swedish Research Council and the Swedish Foundation for Strategic Research is gratefully acknowledged.

REFERENCES

1. Johansson, T.; Kers, A.; Stawinski, J. 2-Pyridylphosphonates: a new type of modification for nucleotide analogues. Tetrahedron Lett. **2001**, *42*, 2217–2220.
2. Johansson, T.; Stawinski, J. Synthesis of dinucleoside pyridylphosphonates involving palladium(0) – catalysed phosphorus-carbon bond formation as a key step. Chem. Commun. **2001**, 2564–2565.
3. Kers, A.; Stawinski, J. A new type of nucleotide analogue with 4-pyridylphosphonate internucleotide linkage. Tetrahedron Lett. **1999**, *40*, 4263–4266.
4. Trawick, B.N.; Daniher, A.T.; Bashkin, J.K. Inorganic mimics of ribonucleases and ribozymes: from random cleavage to sequence-specific chemistry of catalytic anitsense drugs. Chem. Rev. **1998**, *98*, 939–960.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016