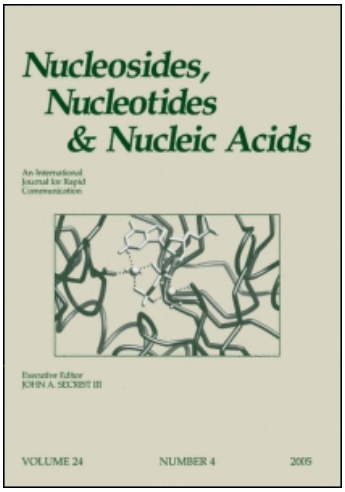


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Aryl Nucleoside H-Phosphonates—Novel Derivatives of Controlled Reactivity

J. Cieślak[a]; J. Jankowska[a]; M. Szymczak[a]; A. Kers[b]; I. Kers[b]; J. Stawiński[b]; A. Kraszewski[a]
[a] Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznań, Poland [b] Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Stockholm, Sweden

To cite this Article Cieślak, J. , Jankowska, J. , Szymczak, M. , Kers, A. , Kers, I. , Stawiński, J. and Kraszewski, A.(1999) 'Aryl Nucleoside H-Phosphonates—Novel Derivatives of Controlled Reactivity', Nucleosides, Nucleotides and Nucleic Acids, 18: 4, 937 — 938
To link to this Article: DOI: 10.1080/15257779908041603
URL: http://dx.doi.org/10.1080/15257779908041603

NUCLEOSIDES & NUCLEOTIDES, 18(4&5), 937–938 (1999)

ARYL NUCLEOSIDE H-PHOSPHONATES - NOVEL DERIVATIVES OF CONTROLLED REACTIVITY

J. Cieślak[a], J. Jankowska[a], M. Szymczak[a], A. Kers[b], I. Kers[b], J. Stawiński[b*] and A. Kraszewski[a*]

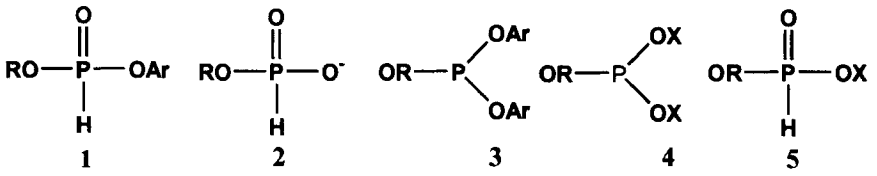
[a]Institute of Bioorganic Chemistry, Polish Academy of Sciences, Noskowskiego 12/14, 61-704 Poznań, Poland
[b]Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden

ABSTRACT: The most essential factors influencing the formation of aryl nucleoside H-phosphonates are discussed.

Recently, aryl nucleoside H-phosphonates (**1**) (Scheme 1) emerged as a new type of intermediates in the synthesis of phosphate derivatives[1]. In contradistinction to other reactive species derived from H-phosphonate monoesters, these compounds bear only one electrophilic centre (located on phosphorus) and their reactivity can be modulated by substituents on the aromatic ring[2].

In this report we wish to discuss factors influencing the formation of aryl nucleoside H-phosphonates under various experimental conditions. Reactivity of phenols in a coupling reaction with H-phosphonate monoesters **2** varied, and sometimes provided different products depending on a pKa value of the phenol used. In a standard condensation promoted by pivaloyl chloride in pyridine phenols with pKa values higher than 9.0 (*e.g.* 4-chlorophenol, phenol and 4-methylphenol)[3] produced exclusively the expected aryl nucleoside H-phosphonate **1**. Phenols with 9.0 > pKa > 6.0 (*e.g.* 2,4-dichloro-, 4-nitro-, 2,4,6-trichloro) afforded under these conditions variable amounts of tervalent bis-aryl nucleoside phosphites of type **3**, along with the desired **1**. Pentachlorophenol (pKa < 6), however, produced in a coupling reaction with **2** exclusively **3**.

SCHEME1



R = suitably protected nucleoside; **Ar** = aryl; **X** = pivaloyl or diphenylphosphate residue

The coupling reaction with phenols of moderate acidity (pKa > 6) performed in less basic media, *e.g.* CH_2Cl_2/pyridine 9 : 1 (v/v) produced exclusively aryl nucleoside H-phosphonates **1**. This is most likely due to suppression of a double activation of **2** (to produce **4**[4]) under these conditions and thus, predominantly monoactivated species **5** are formed. Besides pivaloyl chloride, the most convenient condensing agent for this purpose was found to be diphenyl phosphorochloridate. With this reagent (1.5 molar equiv.) aryl nucleoside H-phosphonates **1** were formed fast (ca. 3 min) and quantitatively.

Very acidic phenols (pKa < 6, *e.g.* pentachloro-, pentafluorophenol and 2,4-dinitrophenol) in CH_2Cl_2/pyridine 9 : 1 (v/v) also produced aryl nucleoside H-phosphonates of type **1**. These, however, were not completely stable under the reaction conditions and underwent a gradual disproportionation towards bis-aryl nucleoside phosphite of type **3** and the initial nucleoside H-phosphonate **2**, according to the mechanism we have described earlier[5].

ACKNOWLEDGEMENTS

Financial support from State Committee for Scientific Research, Republic of Poland (**3 T09A 118 14**) and the Swedish Natural Science Research Council for is gratefully acknowledged

REFERENCES

1. Cieślak, J., Jankowska, J., Kers, A., Kers, I., Sobkowska, A., Sobkowski, M., Stawiński, J. and Kraszewski, A. *Collect. Czech. Chem. Commun.* **1996**, *61*, 242-245.
2. Sobkowska, A., Sobkowski, M., Cieślak, J., Kers, I., Stawiński, J. and Kraszewski, A. *J. Org. Chem.*, **1997**, *62*, 4791-4794.
3. Kostrum, G., Vogel, W. and Andrussow, K. in *Dissociation Constants of Organic Acids in Aqueous Solution*, Butterworth, London, **1961**.
4. For review see - Stawiński, J. in *Handbook of Organophosphrus Chemistry*, Engel,R. Ed., Marcel Dekker, Inc. New York **1992**, 377-434.
5. Kers, A., Kers, I., Sobkowski, M., Kraszewski, A. and Stawiński, J. *Tetrahedron*, **1996**, *52* (29), 9931-9944.