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STEREOSPECIFIC OXIDATION OF R_p - AND S_p -DINUCLEOSIDE H-PHOSPHONATES TO PHOSPHOROTHIOATES

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ABSTRACT: 8 H-Phosphonate dimers with dA, dC, dG or dT at the 5'- and dA or dT at the 3'-end were synthesized and separated into their diastereoisomers. Sulfur oxidation of the optically pure compounds proved to be stereospecific leading to R_p or S_p phosphorothioates.

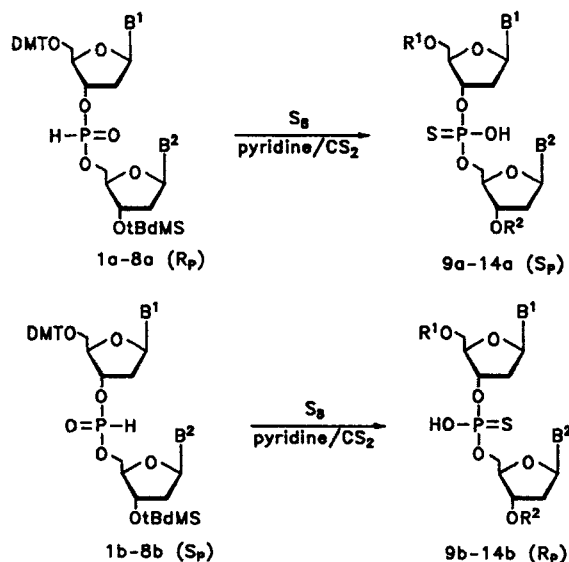
The diastereomeric H-phosphonates **1a,b** - **8a,b** were prepared (pyridine, adamantanoyl chloride)¹ and separated by preparative column chromatography (silica gel 60 H, EtOAc/AcOH; 998:2). The content of the slow migrating zones exhibited low field ^{31}P NMR signals compared to those of the faster migrating diastereoisomers (Table).

Direct oxidation of compounds **1a,b**; **4a,b** and **5a,5b** with octameric sulfur [pyridine/ CS_2 ; 1:1] or of presilylated intermediates $[(\text{CH}_3)_3\text{SiCl}$,

Table: ^{31}P NMR Chemical Shifts of Diastereomeric H-Phosphonates **1a,1b** - **8a,8b** in d_6 -DMSO.²

Compd.	a (R_p); fast zone	b (S_p); slow zone
1	9.79	10.25
2	9.86	10.30
3	9.93	10.37
4	9.87	10.34
5	9.83	10.52
6	9.89	10.59
7	9.92	10.56
8	9.94	10.82

pyridine]³ was stereospecific leading to compounds **9a,b** - **11a,b**. Upon deprotection the stereochemically pure R_P or S_P phosphorothioates **12a,b** - **14a,b** were obtained. According to the enzymic specificity⁴ only the slow migrating diastereoisomers (**12a** - **14a**) were hydrolyzed by nuclease PI. This confirmed S_P configuration for **12a** - **14a** and R_P for **12b** - **14b**. Earlier observations have shown that oxidation of similar P(III) derivatives with sulfur proceeds with retention of configuration.⁵ Therefor the configuration of the H-phosphonates **1b** - **8b** was assigned as S_P (**1a** - **8a** = R_P).



	1	2	3	4	5	6	7	8
B ¹	A	C	G	T	A	C	G	T
B ²	A	A	A	A	T	T	T	T

	B ¹	B ²	R ¹	R ²
9	T	A	DMT	tBdMS
12	T	A	H	H
10	A	A	DMT	tBdMS
13	A	A	H	H
11	A	T	DMT	tBdMS
14	A	T	H	H

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REFERENCES AND NOTES

1. P. Garegg, T. Regberg, J. Stawinski and R. Strömberg, *Chemica Scripta* **25**, 280 (1985).
2. Values are given in ppm, relative to phosphoric acid (85%) as external standard.
3. A. Kume, M. Fujii, M. Sekine and T. Hata, *J. Org. Chem.* **49**, 2139 (1984).
4. F. Eckstein, *Ann. Rev. Biochem.* **54**, 367 (1985).
5. L. Horner und H. Winkler, *Tetrahedron Lett.* **3**, 175 (1964).