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### Synthesis of 3'-Thioribouridine, 3'-Thioribocytidine, and Their Phosphoramidites

Sengen Sun<sup>a</sup> & Joseph A. Piccirilli<sup>a</sup>

<sup>a</sup> Howard Hughes Medical Institute, Department of Chemistry and Department of Biochemistry and Molecular Biology, The University of Chicago, 5841 South Maryland Avenue, Room N101, Chicago, Illinois, 60637

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SYNTHESIS OF 3'-THIORIBOURIDINE, 3'-THIO-RIBOCYTIDINE, AND THEIR PHOSPHORAMIDITES

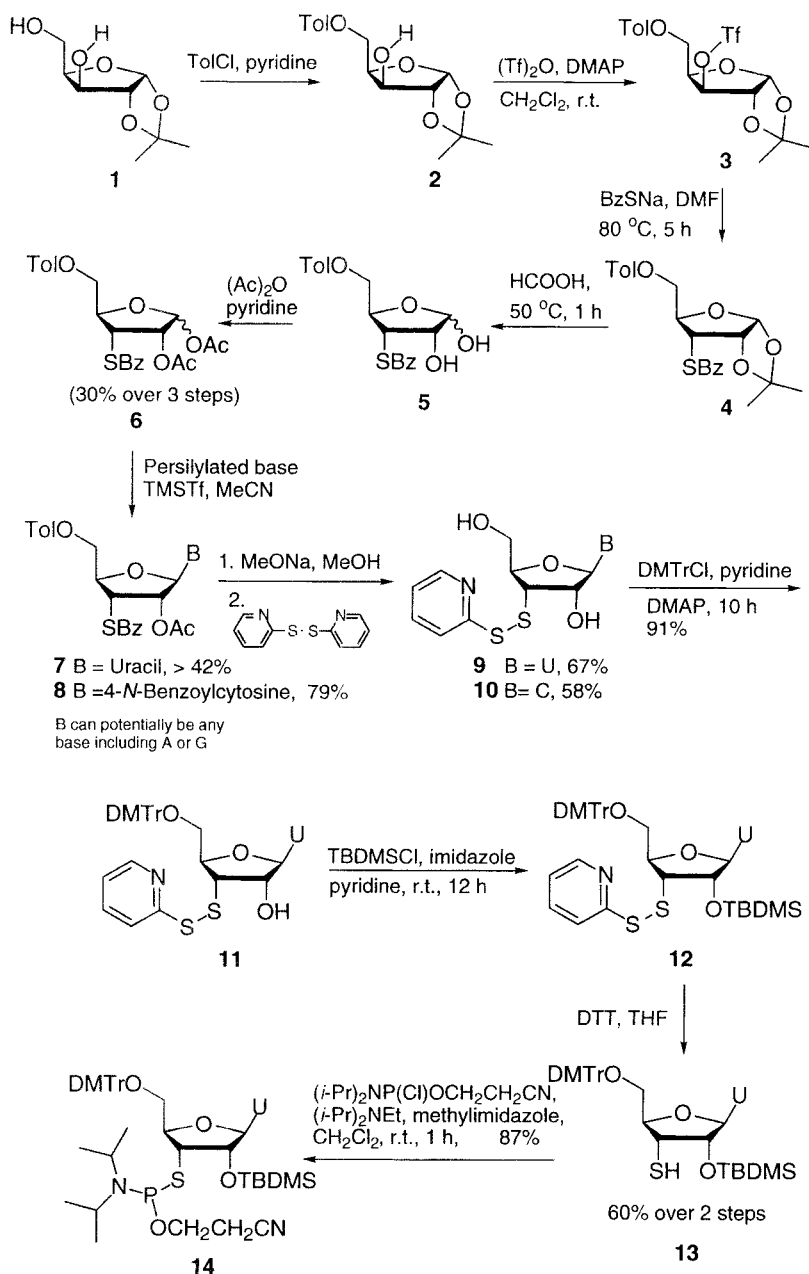
Sengen Sun and Joseph A. Piccirilli\*

Howard Hughes Medical Institute, Department of Chemistry and Department of Biochemistry and Molecular Biology, The University of Chicago  
5841 South Maryland Avenue, Room N101, Chicago, Illinois 60637

**ABSTRACT:** 3'-Thio-3'-deoxyribonucleosides (U and C) have been synthesized *via* Vorbruggen-type glycosylation with 3-*S*-benzoyl-5-*O*-toluoyl-1,2-*O*-diacetylfuranose, which was obtained from 1,2-*O*-isopropylidene-5-*O*-toluoyl-3-*O*-trifluoromethanesulfonyl- $\alpha$ -D-xylofuranose. 3'-Thio-3'-deoxyuridine has been converted to its phosphoramidite.

3'-Thionucleosides have proven useful as mechanistic probes in phosphoryl transfer reactions in both protein enzymes<sup>1</sup> and ribozymes.<sup>2</sup> However, studies have been restricted to 2'-deoxy versions of these molecules. The 3'-thiol derivatives of adenosine<sup>3,4</sup> and uridine<sup>5</sup> have been previously reported, but not get incorporated into oligonucleotides by solid phase synthesis.

We have recently synthesized 3'-thio-3'-deoxyriboinosine and incorporated it at the 3'-splice site of a nuclear premessenger RNA *via* phosphoramidite chemistry followed by enzymatic ligation.<sup>6</sup> Our interest in the mechanism of catalysis of RNA-mediated phosphoryl transfer reactions inspired us to develop a general procedure to access efficiently any of the 3'-thioribonucleoside analogs and their phosphoramidites (Scheme 1). The commercially available 1,2-*O*-isopropylidene- $\alpha$ -D-xylofuranose was transformed to 1,2-*O*-isopropylidene-5-*O*-toluoyl-3-*O*-trifluoromethanesulfonyl- $\alpha$ -D-xylofuranose.<sup>7,8</sup> The triflate group was easily displaced by thiobenzoate to give the 3-*S*-benoylfuranose derivative. Removal of the isopropylidene group followed by acetylation gave a product **6**, which was used successfully in Vorbruggen-type reactions to glycosylate uridine and 4-*N*-benzoylcytosine. Removal of the acyl protecting groups followed by protection of the sulfhydryl as the pyridyl disulfide allowed 5'-dimethoxytritylation and 3'-silylation. Reduction of the disulfide followed by phosphitylation gave the phosphoramidite in very good yield.<sup>9</sup>



SCHEME 1

In conclusion, we have developed a useful procedure to synthesize 3'-thioribonucleosides. We are working to extend the procedure to prepare the corresponding guanosine and cytidine analogs.

## REFERENCES

1. Curley, J. F.; Joyce, C. M.; Piccirilli, J. A.; manuscript in preparation.
2. Piccirilli, J. A.; Vyle, J. S.; Caruthers, M. H.; Cech, T. R. *Nature* **1993**, *361*, 85.
3. Krahmer, U.; Griesser, H.; Mengel, R. *Nucleic Acid Chemistry, Part 3*, edited by L. B. Townsend & R. S. Tipson, John Wiley & Sons, 1986, p203.
4. Ryan, K. J.; Acton, E. M.; Goodman, L. *J. Org. Chem.* **1968**, *33*, 1783.
5. Liu, X; Reese, C. B. *Tetrahedron Lett.* **1996**, *37*, 925.
6. Sontheimer, E. J.; Sun, S; Piccirilli, J. A.; manuscript in preparation.
7. Ozols, A. M.; Azhayev, A. V.; Dyatkina, N. B.; Krayevsky, A. A. *Synthesis*, **1980**, 557.
8. Dempcy, R. O.; Luo, J.; Bruice, T. C. *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 4326.
9. Every new compound was characterized by  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR, and either a satisfactory molecular weight from high resolution mass spectrometry or a satisfactory elemental analysis was obtained. For the final thiouridine phosphoramidite **14**,  $^{31}\text{P}$ -NMR (90 MHz, in  $\text{CDCl}_3$ , using 85%  $\text{H}_3\text{PO}_4$  as external standard):  $\delta = 168.6, 157.4$ ; Anal. calcd for  $\text{C}_{45}\text{H}_{61}\text{N}_4\text{O}_8\text{PSSi}$ : C, 61.64; H, 6.96; N, 6.39; S, 3.65. Found: : C, 61.38; H, 6.95; N, 6.62; S, 3.49.