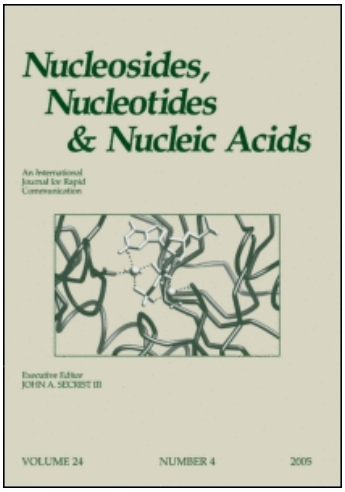


## Nucleosides, Nucleotides and Nucleic Acids

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# Development of a Nucleoside Analog UV Light Sensor

**Shiyue Fang,[1,3] Yousheng Guan,[1] Ernest R. Blatchley III,[2] Lian-Shin Lin,[2] Cheng Yue Shen,[2] and Donald E. Bergstrom[1,3,*]**

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## ABSTRACT

Conjugation of the photosensitive nucleoside (***E***)-5-(2-methoxycarbonylethenyl)-cytidine to biotin provided a means to attach this analogue to microparticles for dosimetry applications that require uv sensor mobility.

*Key Words:* Biotin; Nucleoside; Photosensor; Fluorescence.

The nucleoside analog (***E***)-5-(2-methoxycarbonylethenyl) cytidine (**1**) undergoes photon mediated isomerization to the ***Z***-isomer, which rapidly ring closes to the highly fluorescent 3-β-D-ribofuranosyl-2,7-dioxopyrido[2,3-*d*]pyrimidine, **2**.[1] We were interested in exploiting this photo-mediated reaction to develop sensors for applications requiring in-situ uv-light dosimetry. This required finding a way to

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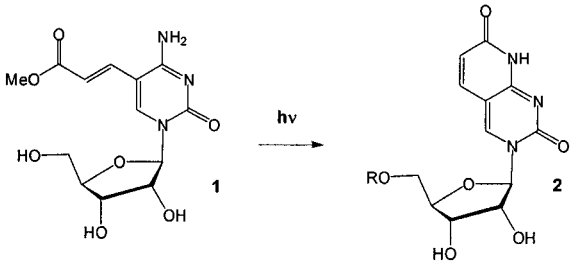
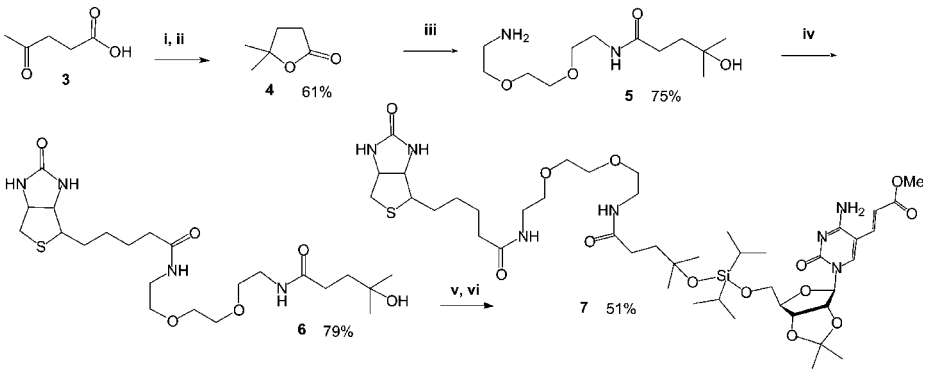
conjugate nucleoside **1** to biomolecules and




microparticles that would not interfere with the uv-mediated reaction. To accomplish this goal we chose to link biotin to nucleoside **1**. Biotin can irreversibly bind to streptavidin via a non-covalent interaction by simple incubation in buffer at room temperature, and a variety of streptavidin functionalized solid microspheres are




***Scheme 1.*** Reagents and conditions: i. MeMgBr, THF, −78°C to 50°C, overnight. ii. AcOH, water, 12 h. iii. 2,2′-(Ethylenedioxy)bis(ethylamine), water, 90°C, overnight. iv. Isobutyl chloroformate, DMF, $Et_3N$, biotin; then **5**. v. $iPr_2SiCl_2$, DMF, Py, −60°C to RT, 5h. vi. 2′,3′-Isopropylidene derivative of **1** in DMF, Py, −60°C to RT, 12 h.

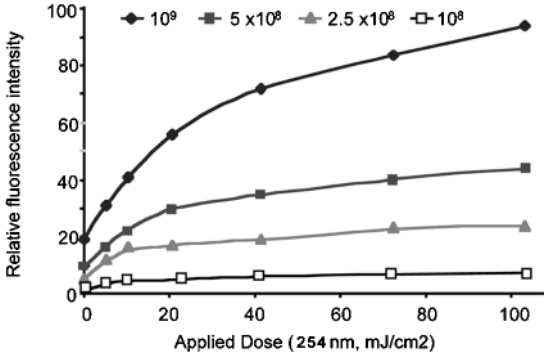



***Figure 1.*** Dose response as a function of initial beads concentrations (Beads/L).





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commercially available. The combination of functional groups on nucleoside **1** presented a significant synthetic challenge for conjugation to biotin. To accomplish this we synthesized nucleoside **7** (Sch. 1) in which the key structural feature is a stable silicon linkage. Nucleoside **7** was a single diastereomer and proved easy to purify and stable in water because of the tertiary alcohol linkage to the silicon.

Incubation of **7** with streptavidin coated beads (~5 μm in diameter, Bangs Laboratories, Inc.) in TTL buffer for 20 min at room temperature yielded derivatized beads whose fluorescence, when suspended in water, increased proportionally to uv dose (Fig. 1). The fluorescence was measured using a fluorescence spectrophotometer at 385 nm excited at 330 nm. Attachment of nucleoside **7** to streptavadin coated magnetic microparticles, which would allow retrieval from complex systems, is under investigation.

## ACKNOWLEDGMENTS

Grant support from the National Institutes of Health (GM53155) and the Showalter Trust Fund and assistance from the National Cancer Institute Grant (P30 CA23168) awarded to Purdue University are gratefully acknowledged.

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