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Nucleoside analogues with photoremovable protecting groups for efficient light-controlled inhibition of viral infection

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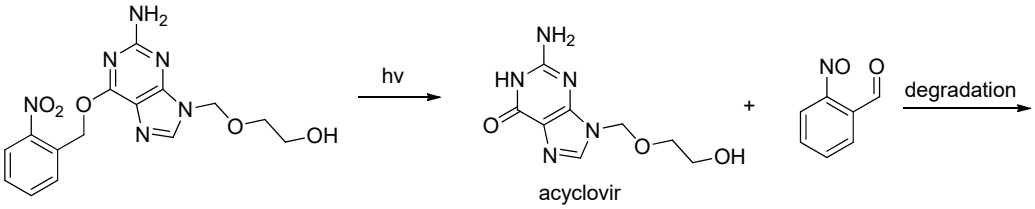
Motivation and Aim: Recent covid-19 pandemic showed that the development of antiviral drugs is of great importance. Many antiviral drugs are nucleoside analogues. They undergo phosphorylation inside cells and then inhibit the synthesis of viral nucleic acids. To begin its action, the nucleoside analogue should be able to enter the cell. It is often a bottleneck for drugs of this family.
Methods and Algorithms: Our idea is to conjugate the nucleoside analogue with the photoremovable protecting group (PPG, [1]), which renders the compound cell-permeable. Then the group can be dissociated by light inside cell, thereby liberating the antiviral drug. Apart from delivery into the cytoplasm, our approach will enable on-demand, local *in vivo* application. In this work, we used nitrobenzyl PPG responsive to UV light, but we also plan to use BODIPY-based PPG which efficiently absorbs green light.
Results: As a model compound, we used acyclovir in place of nucleoside analogue. It has been conjugated with PPG using the Mitsunobu reaction. The resulting compound and the scheme of photolysis are shown in the figure.



The presence of free acyclovir after photolysis was confirmed using the HPLC technique.
Conclusion: Our results indicate that the approach is viable. Further research will be aimed at the conjugation of visible-light PPGs with anti-coronavirus drugs such as molnupiravir, favipiravir and GS-441524 (metabolite of remdesivir).
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References

1. Vorobev A.Y., Moskalensky A.E. Long-wavelength photoremovable protecting groups: On the way to *in vivo* application. *Comput Struct Biotechnol J.* 2020;18:27-34.