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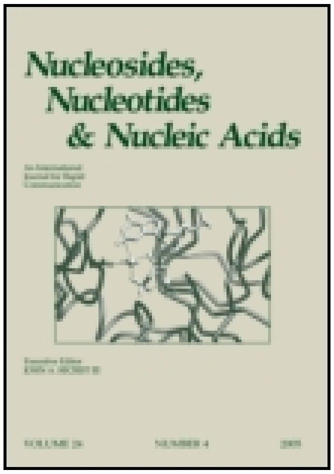

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9-Fluorenemethyl H-Phosphonoselenoate—A Versatile Reagent for Transferring an H-Phosphonoselenoate Group

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9-Fluorenemethyl H-Phosphonoselenoate—A Versatile Reagent for Transferring an H-Phosphonoselenoate Group

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ABSTRACT

This paper expands the available methods for preparation of H-phosphonoselenoate using a new reagent, 9-fluorenemethyl H-phosphonoselenoate.

Key Words: H-Phosphonates; H-Phosphonoselenoates; Reagent.

To expand synthetic methodologies available for the preparation of H-phosphonoselenoates, we have developed a new reagent for transferring an H-phosphonoselenoate moiety, 9-fluorenemethyl H-phosphonoselenoate **1**. The previous method for the preparation of H-phosponoselenoate monoesters,[1] although efficient in general sense, required excess of a hydroxylic component and this can be considered a drawback, especially for alcohols that are expensive and difficult to prepare.

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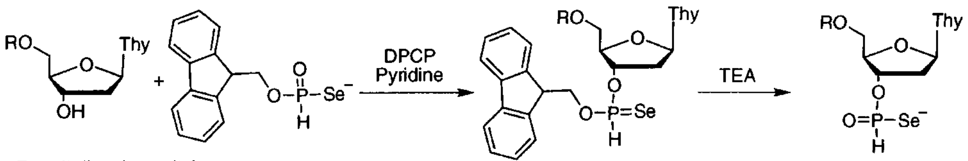
Chemistry of reagent **1** is based on the same principle as that for other reagents previously developed for transferring of H-phosphonate[2] and H-phosphonothioate groups[3] to various hydroxylic components, however, the presence of selenium required some cautions during handling.



R=4,4'-dimethoxytrityl
Thy=thymin-1-yl

1 **2** **3**

9-Fluorenemethyl H-phosphonoselenoate monoester **1** can easily be prepared using standard phosphinate approach previously developed for synthesis H-phosphonothioate monoesters.[4] Treatment of 9-fluorenemethanol with triethylammonium phosphinate in the presence of pivaloyl chloride, followed by selenization of the produced phosphinate intermediate with elemental selenium for 2 hours afforded **1** as a major product, which was isolated by silica gel chromatography as an oily, triethylammonium salt. A crystalline, stable, white solid was obtained in 88% overall yield upon replacement of the triethylammonium cation by S-(p-chlorobenzyl)-isothiuronium cation.

Utility of **1** has an H-phosponoselenoate group transferring reagent was assessed by reacting 5′-protected thymidine with a slight excess of **1** in acetonitrile containing pyridine (5 equiv.) in the presence of diphenyl chlorophosphate (2.5 equiv).[1] ^{31}P NMR spectroscopy indicated clean formation of H-phoshonoselenoate diester **2** ($>90\%$). Crude product **2** upon treatment with triethylamine in methylene chloride could be directly converted into H-phosphonoselenoate monoester **3** that was isolated as triethylammonium salt by precipitation (yield 83%).

It is worth noting that 9-fluorenemethyl H-phosphonoselenoate **2** can be easily separated into individual diastereoisomers by silica gel column chromatography, and after removal of the 9-fluorenemethyl group, diastereomerically pure H-phosphonoselenoate monoesters **3** can be obtained. Alternatively, diastereomerically pure H-phosphonoselenoate diesters **2** can be subjected to various oxidative transformations prior to deprotection. Further studies are in progress in this laboratory.

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