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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, 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.

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%).

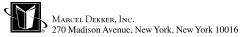
It is worth noting that 9-fluorenemethyl H-phosphonoselenoate 2 can be easily separated into individual diastereoisomers by silica gel column chromatography, and after removal of the 9-fluorenemethyl group, diastereomerically pure H-phosphonoselenoate monoesters 3 can be obtained. Alternatively, diastereomerically 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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