



## ORIGINAL ARTICLE

# Selective removal of phenyl group from alkyl diphenyl phosphates



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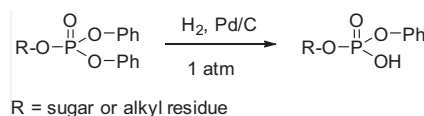
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## KEYWORDS

Alkyl diphenyl phosphates;  
Alkyl monophenyl phosphates;  
Catalytic hydrogenation;  
Hydrogenolysis

## Abstract



Selective removal of one phenyl group from alkyl diphenyl phosphates is reported. Catalytic hydrogenation on palladium catalyst (Pd/C) under atmospheric pressure provides the corresponding monophenyl phosphates in 70–89% yield. The method is efficient and mild, however, it cannot be applied for acid sensitive substrates.

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## 1. Introduction

Many natural products such as phospholipids, oligonucleotides, carbohydrate phosphates often possess in their structure a phosphorylated primary alcohol function [1–3]. Therefore, selective introduction of phosphate functionality is still a challenging task in organic synthesis [4]. Diphenyl chlorophosphate is used as one of more valuable reagents for the synthesis of alkyl dihydrogen phosphates. It reacts readily

with alcohols in pyridine to give the proper alkyl diphenyl phosphates [5]. Finally, both phenyl groups usually are removed by hydrogenolysis over platinum [6]. The reagent present in this paper we wish to report a mild method for partial deprotection of alkyl diphenyl phosphates. Hydrogenolytic removal of one phenyl group seems to be a good alternative for other methods conventionally used in the synthesis of mixed dialkyl phosphates.

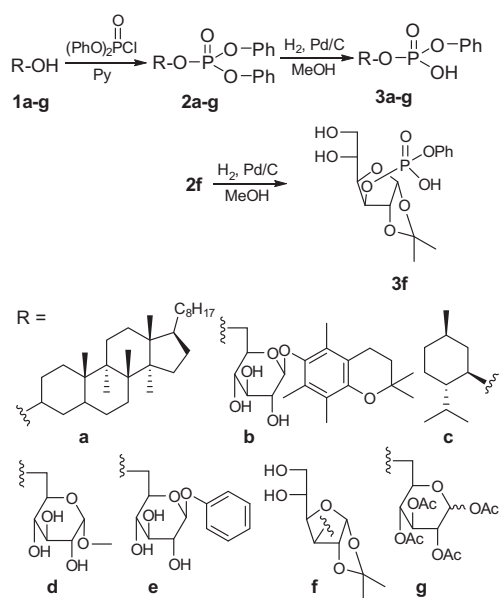
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Scheme 1

## 2. Results and discussion

Phenyl groups are used for protection of phosphates during introduction of this functionality in the natural product synthesis [7] when diphenyl chlorophosphate was used as reagent [8]. These groups are easily removable under mild conditions by catalytic hydrogenation on platinum catalyst [9–11]. For this purpose other more drastic hydrolytic methods are also used [7].

As part of a larger project, we developed an efficient and mild procedure for selective removal of only one phenyl group from alkyl diphenyl phosphoric esters. To our best knowledge, no similar transformation by means of catalytic hydrogenation has been described in the literature. Only Beven [12] and Folsch [13] in 1950s mentioned that during hydrogenolytic deprotection on Pd/C catalyst of *O*-diphenylphosphoryl-*N*-

carbobenzyoxy peptides, the removal of *N*-carbobenzyoxy group, was accompanied by the formation of *O*-monophenyl phosphorylated peptide as by-product.

In the more recent literature only a few examples of selective hydrogenation of diphenylphosphoryl derivatives ( $-\text{P}(\text{O})(\text{OPh})_2$ ) have been reported by Slepokura in 2006 [14] and Chelmecka et al. [15]. Such conversion takes place in the course of hydrogenolysis on palladium catalyst (Pd/C) when ammonium formate as a hydrogen source is used [10]. Unfortunately, no experimental details have been presented.

In the present paper a series of diphenyl phosphates **2a–g** (Scheme 1) were obtained by standard phosphorylation ( $(\text{Ph}_2\text{O})_2\text{POCl}$ , pyridine, [11]) of commercially available alcohols (**1c**, **1f** and **1g**). The deprotected *O*-glucosides **1a**, **1b**, **1d** and **1e** which were subjected to phosphorylation, were synthesized in our laboratory [16]. An introduction of diphenyl phosphoric residue to the alcohols **1a–g** resulted in deshielding of signals of neighboring carbon atom in  $^{13}\text{C}$  NMR of the alcoholic part by  $2.5 \pm 0.5$  ppm, as expected [16,17]. The position of the phosphate group in **2b**, **2d** and **2e** was conclusively determined in the presence of coupling constants  $^2J_{\text{P-O-C}}$  and  $^3J_{\text{P-O-C-C}}$  in  $^{13}\text{C}$  NMR spectra [16]. All phosphorylated substrates for hydrogenolysis **2a–g** were characterized by spectroscopic methods: IR,  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR.

Catalytic hydrogenation over platinum catalyst is a commonly used method for full deprotection of diphenyl phosphates [9,18,19]. Unexpectedly, the same reaction carried out over palladium on charcoal provided mono dephenylation products. The best results for transformation of diphenyl **2a–g** to monophenyl phosphates **3a–g** were achieved when methanolic solutions of substrates were hydrogenated over 5% Pd/C (Scheme 1). The reaction was tested on different types of substrates (**2a–g**) and the respective alkyl monophosphates **3a–e** were obtained in good yields (see Table 1). The products **3a–g** were characterized by  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  NMR and IR spectra as well as elemental analysis (see Supplementary Information). The selected  $^{31}\text{P}$  NMR chemical shift value and observed coupling constants  $^2J_{\text{P-O-C}}$  and  $^3J_{\text{P-O-C-C}}$  are listed in Table 1.

**Table 1**  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR data for diphenyl (**2a–g**) and monophenyl phosphates (**3a–g**); (**2a–g** in  $\text{CDCl}_3$  and **3a–g** in  $\text{CD}_3\text{OD}$  solutions).

Nr	$^{31}\text{P}$ NMR ( $\delta$ , ppm)	$^{13}\text{C}$ NMR (Hz)		Yield <sup>a</sup> (%)
		$^3J_{\text{P-O-C-C}}$	$^2J_{\text{P-O-C}}$	
<b>2a</b>	–11.40	5.7	5.8	70
<b>2b</b>	–11.41	5.7	5.8	81
<b>2c</b>	–12.29	not detected	7.1	82
<b>2d</b>	–11.15	6.8	6.2	50
<b>2e</b>	–11.25	7.6	6.1	92
<b>2f</b>	–11.97	6.3	8.3	79
<b>2g</b>	–11.54	7.8	5.5	68
<b>3a</b>	–3.40	5.7	5.8	70
<b>3b</b>	–3.11	5.7	5.8	7.9
<b>3c</b>	–5.25	<sup>b</sup>	6.7	78
<b>3d</b>	–4.10	6.7	6.2	75
<b>3e</b>	–4.37	4.6	5.9	77
<b>3f</b>	–4.02	5.2	8.3	89
<b>3g</b>	–4.58	7.4	5.2	78

<sup>a</sup> Isolated yields by MPLC.

<sup>b</sup> Overlapped by  $\text{CD}_3\text{OD}$  signals.

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