

Utilization of Oxidizing Character of TeCl_4 in the Reaction with Trialkyl Phosphite. A Novel Redox Phosphorylation

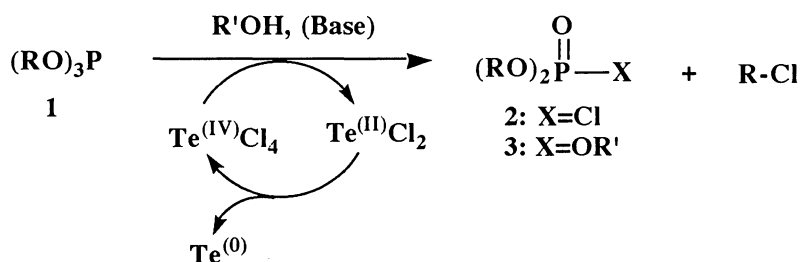
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Oxidation-reduction reaction of a trialkyl phosphite with TeCl_4 in the presence of an alcohol and *tert*-amine proceeded smoothly to afford the corresponding phosphorylation product in good yield.

As part of a program aimed at developing organic synthetic methods based on P(III) chemistry,¹⁾ we have found an efficient action of TeCl_4 on the reaction of glycosyl phosphites with alcohols giving rise to the corresponding glycoside.²⁾ During the reaction, metallic $\text{Te}(0)$ precipitated. The phenomena means that oxidation-reduction occurred in the reaction. Though the Lewis acidic character of TeCl_4 has been recently utilized in synthetic reactions^{3),4)} including chlorotelluration,⁵⁾ straightforward utilization of its oxidizing property has not been claimed so far in synthetic organic chemistry.⁶⁾ We were interested in the latter property of TeCl_4 and have now found a novel oxidative phosphorylation reaction which involves the oxidation-reduction reaction of a trialkyl phosphite with TeCl_4 as a driving force. Mukaiyama and co-workers reported a similar type of the reaction where trivalent phosphorus compounds were reacted with Hg(II) or Hg(I) resulting in the formation of P(V) and $\text{Hg}(0)$.⁷⁾ In particular, the condensation reagent system comprising tributylphosphine and diphenylmercury was employed for the preparation of respective acid anhydrides from carboxylic acids, phosphoric monoesters, and *p*-toluenesulfonic acid, and carboxylic esters and anilide from acids and alcohols or aniline.⁸⁾ Here, we describe the phosphorylation results and emphasize oxidation feature of TeCl_4 .

In order to understand the reaction of a phosphite with TeCl_4 such as the glycosylation mentioned above, NMR analysis of the reaction of tributyl phosphite (**1**, $\text{R}=\text{n-Bu}$) with an equimolar amount of TeCl_4 in CDCl_3 was first examined and the phosphite was found to disappear within 5 min resulting in the formation of dibutyl phosphorochloridate **2** ($\text{R}=\text{n-Bu}$, $\delta_{\text{p}} 5.60$)⁹⁾ and butyl

chloride [R=*n*-Bu, δ_{H} 3.55 (t, $J=6.72$ Hz) for α -CH₂]. The reaction was accompanied by precipitation of metallic Te which was generated along with TeCl₄ resulting from disproportionation of TeCl₂ first formed in the reaction.¹⁰ TeCl₄ thus regenerated can be incorporated again into the reaction with phosphite. Thus, the chloridate formation reaction would be expressed as shown in Scheme 1. Very recently, Koh and Oh reported the similar reaction of dialkyl or trialkyl phosphite with TeCl₄ as a preparative method of phosphorochloridates.¹¹ On the other hand, the reaction in the presence of 1-butanol proceeded also smoothly to yield the triester 3 (R=R'=*n*-Bu, δ_{p} -1.61)¹² in addition to a small amount of the chloridate 2 and Te(0). In the former experiment, when 1-butanol was added to the solution containing the chloridate thus formed 2 was hardly converted into tributyl phosphate 3. This finding indicates that the chloridate was not a key intermediate for the formation of the triester.



Scheme 1.

Based on the NMR experiments, we explored a phosphorylation of alcohols. Thus, 3-phenylpropanol in CH₂Cl₂ was treated with trimethyl phosphite and TeCl₄ in the presence of 2,6-dimethylpyridine (lutidine) which was added in order to increase the nucleophilicity of the alcohol and neutralize HCl generated in the reaction to afford dimethyl 3-phenylpropyl phosphate in 96% yield. The most suitable molar ratio of the phosphite to Te(IV) was 3:2 whereas 0.5 molar equivalent of TeCl₄ is stoichiometrically necessary according to Scheme 1. In place of TeCl₄, other oxidants such as TeBr₄, FeCl₃, CuCl₂, and Hg(OAc)₂ were examined, however, all cases gave poorer results. Triethylamine as well as lutidine was also effective as a base.

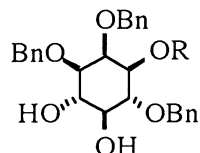
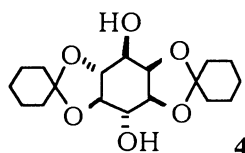
Typically, a solution of trimethyl phosphite (0.85 mmol), 3-phenylpropyl alcohol (0.72 mmol), and lutidine (0.99 mmol) in CH₂Cl₂ (4 ml) was treated with TeCl₄ (0.57 mmol) for 1 h at room temperature. Filtration of the black precipitate and chromatography on silica gel afforded dimethyl 3-phenylpropyl phosphate (96% yield). In a similar manner, various phosphates were prepared in good yields as shown in Table 1. An olefinic alcohol, 3-*cis*-hexenol was phosphorylated in good yield although alkenes are known to react at room

temperature with TeCl_4 forming 1,2-chlorotelluration products.^{3a),13)} Employment of tributyl phosphite in place of the methyl ester in the reaction with 3β -cholestanol yielded dibutyl 3β -cholestanyl phosphate in a completely selective manner while the phosphorylation product from less hindered (\pm)-2-octanol was accompanied by some extent of the tributyl phosphate, which may be formed by the Arbuzov-type decomposition of the 2-octyl moiety in an unidentified intermediate.¹⁴⁾ The inositol derivative **5** was regioselectively phosphorylated at the isolated hydroxyl group by treatment with trimethyl phosphite (2.4 equiv), TeCl_4 (1.8 equiv), and lutidine (4.2 equiv) at room temperature for 2 h to give monophosphate **6** in 56% yield (80% based on the recovered alcohol) as a sole product.

Table 1. Synthesis of Phosphoric Triesters^{a)}

Run	R in 1	R'OH	Reaction time/h	Yield/% of 3
1	Me	3-Phenylpropanol	1	96
2	Me	1-Octanol	2	88
3	Me	(\pm)-2-Octanol	2	84
4	ⁿ Bu	(\pm)-2-Octanol	3	70 ^{b)}
5	Me	<i>cis</i> -3-Hexenol	1	87 ^{c)}
6	Me	3β -Cholestanol	1	93
7	ⁿ Bu	3β -Cholestanol	1	93
8	Bn ^{d)}	3β -Cholestanol	2	67 ^{c)}
9	<i>p</i> -ClPhCH ₂ ^{e)}	3β -Cholestanol	2	68
10	Me	4	3	91 ^{f),g)}

a) An alcohol was treated with phosphite (1.2 eq) and TeCl_4 (0.8 eq) in the presence of lutidine (1.4 eq) in CH_2Cl_2 at room temperature unless otherwise noted. b) Tributyl phosphate was obtained in 30% yield based on the phosphite used. c) The reaction was conducted at 0 °C. d) Bn=benzyl. e) *p*-ClPhCH₂=*p*-Chlorophenylmethyl. f) The molar quantity of each reagent was double the amount employed generally for monols as shown at footnote a. g) Yield of 3,6-bis(dimethyl phosphate).



The present phosphorylation is a novel type of the redox reaction accompanying reduction of Te(IV) to Te(II) and an alternative method to the previously reported phosphonium salt approach which involved the transformation of phosphite with pyridinium hydrobromide perbromide.^{1b),1c)} Versatility and mechanism of the reaction are under investigation.

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- 12) Tributyl phosphate itself and its complex with TeCl_4 showed δ_p 0.13 and -1.28 respectively. The latter chemical shift changed depending on quantities of Te(IV).
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- 14) In the ^{31}P NMR experiments mentioned in the text, a resonance peak corresponding to the intermediate was observed at 23.70 ppm and its intensity decreased gradually with increase of the product 2 or 3. This signal had satellite (ca. 7.7% obtained from integral ratio,¹⁵) $J=2389$ Hz), suggesting P-Te bond. Tri(butyloxy)chlorophosphonium chloride (δ_p 16.7 at -80°C)¹⁶) might be an another possible intermediate.
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