NOTES *Bull. Chem. Soc. Jpn.*, 58, 3393—3394 (1985)

Synthesis of Alkyl Dihydrogenphosphate by the Reaction of Alcohols and Silyl Polyphosphate

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(Received June 27, 1985)

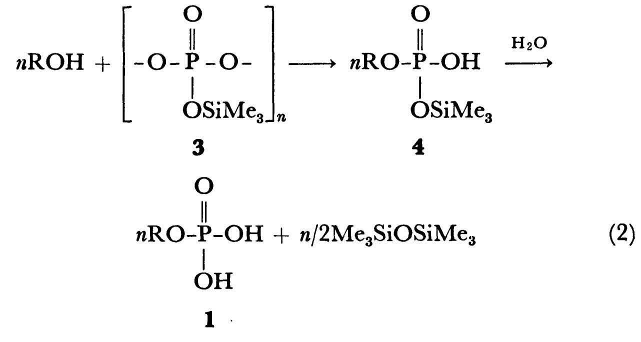
Synopsis. Alkyl dihydrogenphosphates were readily prepared by phosphorylation of alcohols with trimethylsilyl polyphosphate or polyphosphorylated silica-gel.

Various methods have been reported for phosphorylation of alcohols.[1] However, there are a few methods which are well suited to preparation of alkyl dihydrogenphosphate (**1**) for industrial use.[2] The cheapest and convenient method is the phosphorylation with powdery diphosphorus pentaoxide (Eq. 1),

$$3\mathrm{ROH} + 1/2\mathrm{P_4O_{10}} \longrightarrow \underset{\mathbf{1}}{\mathrm{(RO)P(O)(OH)_2}} + \underset{\mathbf{2}}{\mathrm{(RO)_2P(O)OH}} \qquad (1)$$

which has been widely used for industrial production of surfactants of **1**.[3] But, this reaction was always accompanied by the formation of considerable amounts (16—20%) of dialkyl hydrogenphosphate (**2**). Furthermore, vigorous stirring and careful control of the temperature are required, because the reaction is heterogeneous and much exothermic.

In this report, a new selective synthetic method of **1** by phosphorylation of alcohols with trimethylsilyl polyphosphate (**3**) is described. Trimethylsily polyphosphate (**3**) is readily prepared by refluxing the benzene solution of diphosphorus pentaoxide and hexamethyldisiloxane.[4,5] Alcohol reacts smoothly with **3** to give alkyl trimethylsilyl hydrogenphosphate (**4**), which is easily hydrolyzed with water into **1** (Eq. 2). For the purpose of synthesis of **1**, the trimethylsilyl polyphosphate (**3**),



$$n\mathrm{ROH} + \left[-\mathrm{O}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\underset{\underset{\displaystyle \mathrm{OSiMe_3}}{|}}{\mathrm{P}}}-\mathrm{O}- \right]_n \longrightarrow n\mathrm{RO}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\underset{\underset{\displaystyle \mathrm{OSiMe_3}}{|}}{\mathrm{P}}}-\mathrm{OH} \xrightarrow{\mathrm{H_2O}}$$

$$n\mathrm{RO}-\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\underset{\underset{\displaystyle \mathrm{OH}}{|}}{\mathrm{P}}}-\mathrm{OH} + n/2\mathrm{Me_3SiOSiMe_3} \qquad (2)$$

3 **4** **1**

R = C_8H_{17}, $C_{10}H_{21}$, $C_{12}H_{25}$, $C_{14}H_{29}$, $C_{16}H_{33}$, $C_6H_5CH_2$, 1-bornyl, and cholesteryl.

which was prepared by the use of diphosphorus pentaoxide (P_4O_{10}) and hexamethyldisiloxane at the mole ratio of 1/4, should be used. When the trimethylsilyl polyphosphates (**3**) prepared with less amounts of hexamethyldisiloxane was used, dialkyl hydrogenphosphate (**2**) formed in substantial quantity. On the other hand, when the trimethylsilyl polyphosphate (**3**) prepared with more excess amounts of hexamethyldisiloxane was used, the yield of **1** decreased. (Table 1) Hexamethyldisiloxane can be easily recovered by fractional distillation of the recovered solvent.

Polyphosphorylated silica-gel or heterogenized silyl polyphosphate (**5**) may be of great interest from a sythetic view-point. It was prepared by the reaction of diphosphorus pentaoxide and dry silica-gel.[5] Phosphorylation by the use of **5** was tried. Alkyl dihydrogenphosphate (**1**) containing a less amount of **2** (3.7%) was obtained, compared with the phosphorylation using only diphosphorus pentaoxide (21%). The polyphosphorylated silica-gel (**5**), prepared using diphosphorus pentaoxide and silica-gel at the ratio of 1/5 in weight was the best. (Table 3)

Experimental

Typical Procedure 1: Reaction With Trimethylsilyl Polyphosphate (3). In a dry, nitrogen-purged flask equipped with a reflux condenser, a magnetic stirrer, and a dropping funnel was placed 7.1 g (25 mmol) of diphosphorus pentaoxide. Benzene (100 ml) and 16.2 g (100 mmol) of hexamethyldisiloxane were added. The mixture was refluxed, until it became clear (*ca.* 1 h). After cooling, 15.8 g (100 mmol) of 1-decanol was added dropwise, and it was refluxed for 2 h. Removal of the solvent *in vacuo* left viscus oily residue. The residue was dissolved in 100 ml of ether. The ethereal solution was washed twice with 10 ml of water and, subsequently extracted three times with 20 ml of 5% sodium hydroxide solution. From this residual ether solution, hexamethyldisiloxane can be easily recovered quantitatively by fractional distillation (94%). The

Table 1. Results of phosphorylation of 1-decanol with trimethylsilyl polyphosphates(**3**), prepared at several reagent ratios[a)]

Trimethylsilyl polyphosphate(**3**) Reagent ratio (mole ratio) $P_4O_{10}/Me_3SiOSiMe_3$ [c)]	Yields of phosphates/%[b]	
	$C_{10}H_{21}OP(O)(OH)_2$(**1b**)	$(C_{10}H_{21}O)_2P(O)OH$(**2b**)
1/2.0	67	12
1/2.5	66	9
1/3.0	68	5.4
1/4.0	73	trace
1/5.0	71	trace

a) With trimethylsilyl polyphosphate (**3**) prepared from P_4O_{10} 7.1 g (25 mmol) and prescribed amounts of $Me_3SiOSiMe_3$, 1-decanol 15.8 g (100 mmol) was phosphorylated in benzene (100 ml) at the refluxing temperature for 2 h. b) Yields are based on P_4O_{10} used. c) Phosphorylation using only P_4O_{10}, **1b** and **2b** were obtained in 69 and 18% yields, respectively.

Table 2. Preparation of several alkyl dihydrogenphosphates (**1a**—**h**) by the reaction of trimethylsilyl polyphosphate (**3**)[a]

Compd. No.	ROH	Yield %	Mp θ_m/°C	Lit, Mp(θ_m/°C)
1a	$CH_3(CH_2)_6CH_2OH$	76	129—130[b]	129—130[6]
1b	$CH_3(CH_2)_8CH_2OH$	73	45—47	45—46[7]
1c	$CH_3(CH_2)_{10}CH_2OH$	72	54—56[d]	—
1d	$CH_3(CH_2)_{12}CH_2OH$	75	67—69	66—68[2]
1e	$CH_3(CH_2)_{14}CH_2OH$	76	75—77	74—75[8]
1f	$C_6H_5CH_2OH$	61	152—154[c]	150—153[6]
1g	Borneol	65	195—197[b]	194—196[6]
1h	Cholesterol	82	185—187	186—188[9]

a) With trimethylsilyl polyphosphate(**3**) prepared from P_4O_{10} 7.1 g (25 mmol) and $Me_3SiOSiMe_3$ 16.2 g (100 mmol), alcohol (100 mmol) was phosphorylated in benzene (100 mmol) at the refluxing temperature for 2 h. b) Monoanilinium salts. c) Dianilinium salt. d) Elemental analysis, Found: C, 54.40; H, 10.42; P, 11.33%. Calcd for $C_{12}H_{27}O_4P$: C, 54.12; H, 10.22; P, 11.63%.

Table 3. Results of phosphorylation of 1-decanol with polyphosphorylated silica-gel (**5**)[a]

Polyphosphorylated silica-gel (**5**) Reagent ratio (weight ratio) P_4O_{10}/Silica-gel	Yields of phosphates/%	
	$C_{12}H_{21}OP(O)(OH)_2$(**1b**)	$(C_{12}H_{21}O)_2P(O)OH$(**2b**)
1/8	52	2
1/5	58	4.5
1/2	64	9
Without silica-gel	69	18

a) With polyphosphorylated silica-gel (**5**) prepared from P_2O_{10} 7.1 g (25 mmol) and prescribed amounts of silica-gel, 1-decanol 15.8 g (100 mmol) was phosphorylated in benzene (100 ml) at the refluxing temperature for 4 h.

combined alkaline extacts were acidified with 60 ml of 10% hydrochloric acid solution, and again extacted three times with 100 ml of ether. The ethereal solution was dried (Na2SO4), and evaporation of the ether gave 17.0 g of colorless crystalline product (76% yield) in an almost pure state. However, the product **1a**, **f**, and **g**, which did not crystalize, were characterized as anilinium salts. The **1**/**2** ratios of these products were determined by elemental analysis or alkalimetry.[10]

Typical Procedure 2: Reaction With Polyphosphorylated Silica-gel (5). The mixture of dry silica-gel (20 g, Kieselgel 60, 70—230 mesh, Merck for chromatography, calcinated at 900 °C for 4 h), diphosphorus pentaoxide (7.1 g, 25 mmol), and 100 ml of benzene was stirred at refluxing temperature for 3 h. 1-Decanol (15.8 g, 100 mmol) was added to the mixture and it was stirred at the same temperature for 4 h. After the reaction, the solvent was removed off, and 100 ml of water was added into the residue to hydrolyze the silyl phosphate. The mixture was filtered, and the silica-gel was washed twice with 100 ml of ether. The combined ether solutions were extracted three times with 20 ml of 5% sodium hydroxide solution. The combined alkaline extracts were acidified with 60 ml of 1 mol dm^3 hydrochloric acid solution, and again extracted three times with 100 ml of ether. The ethereal solution was dried and evaporation of the ether gave a mixture of decyl dihydrogenphosphate (**1b**) and didecyl hydrogenphosphate (**2b**) in 58% and 4.5% yields, respectively.

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