CHEMISTRY LETTERS, pp. 1225-1228, 1982.

COMPOSITION OF "POLYPHOSPHORIC ACID TRIMETHYLSILYL ESTER (PPSE)" AND ITS USE AS A CONDENSATION REAGENT[1)]

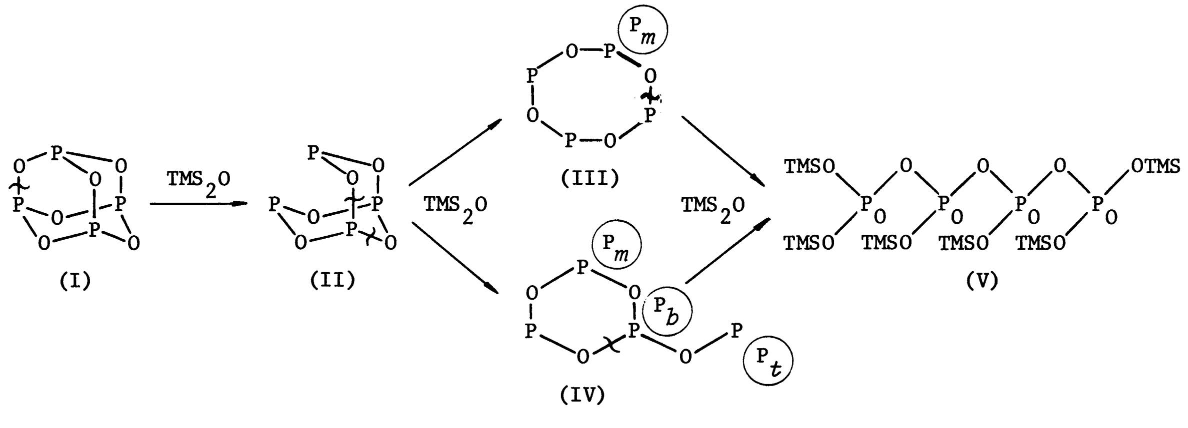
Keiji YAMAMOTO and Hiroyuki WATANABE
Department of Chemical Engineering, Tokyo Institute of Technology, Meguro, Tokyo 152

Phosphorus pentoxide reacts readily with anhydrous hexamethyldisiloxane (HMDSO) to form mixtures of tetraphosphoric acid trimethylsilyl esters (so-called PPSE), the composition of which being estimated from ^{31}P NMR data. PPSE was conveniently used as a condensation reagent for the syntheses of benzimidazoles, indoles, and isoquinoline derivatives. Heterogenized PPSE by using silica gel instead of HMDSO was found to be equally useful.

Phosphorus pentoxide, P_4O_{10}, which has an adamantane-like skeleton and is sparingly soluble in common organic solvents, has been known to react with excess hexamethyldisiloxane (HMDSO) to give tris(trimethylsilyl) orthophosphate,[2,3)] or even tetrakis(trimethylsilyl) pyrophosphate.[3)] However, the reaction is now found, in the strict absence of acid catalysts, to yield mainly mixtures of tetraphosphoric acid trimethylsilyl esters (PPSE) which are soluble in a variety of solvents. The composition of the mixture can reasonably be estimated on the basis of ^{31}P NMR measurements.

A recent report by Imamoto et al.[4)] concerning the Beckmann rearrangement in PPSE prompted us to disclose our investigations along these lines.

Ring opening of phosphorus pentoxide (I) with excess HMDSO is premised to proceed from bicyclotetraphosphate (II) to cyclotetraphosphate (III) and/or isocyclotetraphosphate (IV), and then to linear tetraphosphate (V) as shown in the Scheme.



Scheme. Only ring skeletons shown except V for clarity. TMS = Me_3Si-.

No significant redistribution of V which should result in the formation of all possible linear polyphosphates was taken into account for the present reaction, because none of tris(trimethylsilyl) orthophosphate but a little pyrophosphate (VI) could be detected in the reaction mixture even after prolonged heating in a sealed NMR tube under an argon atmosphere. In addition, compounds I and II are thought to be too reactive to survive under the conditions employed. Therefore, the content of PPSE (III~VI) was calculated from ^{31}P NMR measurements with these assumptions according to the procedure of Burkhardt et al.[5] rather than that of Van Wazer et al.[6]

Each type of phosphorus atom as depicted in the Scheme, the branched unit (P_b), the middle unit (P_m), and the terminal unit (P_t), has a different chemical shift in the NMR spectrum, centering at 41, 38, and 32 ppm, respectively (from 85% H_3PO_4). The compositions of mixtures of III~VI in a few solvents were thus calculated and tabulated by solving simultaneous equations in terms of weighed number of P's in compounds III~VI and of their respective peak areas in NMR spectra (Table 1).

As can be seen from Table 1, the composition reflects significant solvent effects: In neat HMDSO, linear V is a major component presumably at the expense of IV with a branched unit P_b (entry 1 *vs.* 2). It is noteworthy that IV does exist as a major component in haloalkane solvents (entries 3 and 4), while the formation of III from intermediate II is preferred in xylene.

Table 1. Composition of Tetraphosphoric Acid Trimethylsilyl Ester (PPSE)

Entry	Solvent[a]	Temp (°C)	Time (h)	Composition[b] (%) III	IV	V	VI
1	neat	80	12	33	17	46	4
2	neat	80	36	26	8	59	7
3	CH_2Cl_2	80	36	29	52	15	4
4	$(ClCH_2)_2$	80	24	26	47	26	1
5	Xylene	80	24	60	18	21	1

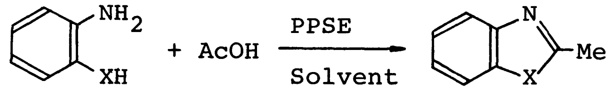
[a] P_4O_{10} (50 mg, 0.18 mmol) and HMDSO (0.4~2.8 mmol) in a given solvent.
[b] III, $4 \times P_m$; IV, $2 \times P_m + P_b + P_t$; V, $2 \times P_m + 2 \times P_t$.
VI, Tetrakis(trimethylsilyl) pyrophosphate, $2 \times P_t$.
(δ 31.6 ppm).

From the selected condensation reactions as described below, we might expect that the most effective reaction sites for dehydration would be the branched phosphorus atoms (P_b) formed only in compound IV, for which the use of haloalkanes as solvents was found to be advantageous.

A systematic investigation has been made of the several reactions using PPSE as condensation reagents in comparison with polyphosphoric acid (PPA) and polyphosphoric acid ethyl ester (PPE).

2-Methylbenzimidazole synthesis by means of PPSE (4 equiv, P_4O_{10} : HMDSO = 1 : 2, 10 min preheating) was carried out, the results being summarized in Table 2. Analogous 2-methylbenzoxazole and thiazole were also obtained with ease (Table 2).

Table 2. Phillips Benzimidazole Synthesis and Analogs

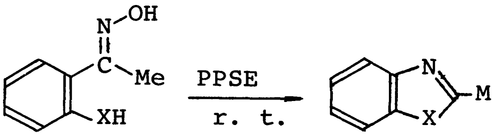


X	Reaction Conditions			Yield[a]
	Solvent	Temp(°C)	Time(m)	(%)
NH	$(ClCH_2)_2$	85	20	65
	Xylene	85	120	63
	PPA[b]	125	240	69
	PPE[c]	100	10	68
O	$(ClCH_2)_2$	85	10	68
	PPE[d]	100	10	75
S	$(ClCH_2)_2$	85	5	93
	PPE[d]	80	30	73

[a] Purified by column chromatography.
[b] Ref. 7. [c] Ref. 8. [d] Ref. 9.

The reaction conditions employed are obviously improved in all cases by the use of PPSE which is superior to PPE in ready availability.[8,9]

It should be noted that when one started with *o*-aminoacetophenone oxime (or with *o*-hydroxy and *o*-mercapto derivatives) the same compounds given in Table 2 were obtained *via* the Beckmann rearrangement[10] in satisfactory (38-86%) yields by using PPSE even at room temperature (eq. 1).



(1)

(X = NH, O, and S)

PPSE in the Fischer indole synthesis,[11] Bischler-Napieralski isoquinoline synthesis,[12] and Pechmann coumarin synthesis[13] were also found to be of use under milder conditions than those by conventional condensation reagents.

Finally, heterogenized PPSE may be of great interest from both synthetic and mechanistic viewpoints. Preliminary experiments were carried out as follows: Phosphorus pentoxide (5 mmol) was heated at reflux in 1,2-dichloroethane (15 mL) for 1 h with stirring with dry silica gel (5 g, 100-200 mesh) instead of HMDSO to give pale yellow sands which could be referred to as "heterogenized PPSE". Calcinated silica gel at 900°C for 4 h appeared to have too reactive surface to be used at the present time. To the resulting "heterogenized PPSE" were added phenylhydrazine and diethyl ketone (1.5 mmol each) and the mixture was heated at 85°C for 20 min to give 2-ethyl-3-methylindole in 88% yield simply by eluting the reaction mixture through a short silica gel column with dichloromethane. Thus, the simplest procedure given here must find many applications to synthetic purposes.

The significant features of the use of PPSE in haloalkanes may be; (1) high reactivity for dehydration which most likely stems from higher content of branched unit (P_b) in the homogeneous mixtures of tetraphosphates than that in other solvents or even in PPE and (2) ready migratory tendency of trimethylsilyl group of the silyl phosphates, as is often encountered in a trimethylsilyl esters of inorganic acid,[14] may assist the expected activation of oxygen functionalities such as carbonyl groups in the substrates of the condensation reaction. Tris(trimethylsilyl) orthophosphate was found to be almost ineffective for the present reactions.

We thank Mr. Y. Nakamura for ^{31}P NMR measurements and Toshiba Silicone Co., Ltd. for the gift of chlorotrimethylsilane.

References

1) Presented in part at the 45th General Meeting of the Chemical Society of Japan, April, 1982 (Tokyo). Abstr. 1H04.
2) R. O. Sauer, J. Am. Chem. Soc., 66, 1707 (1944).
3) V. P. Mileshkevich and A. V. Karlin, Zhur. Obshch. Khim., 40, 2573 (1970); see also, M. G. Voronkov, ibid., 25, 437 (1955).
4) T. Imamoto, H. Yokoyama, and M. Yokoyama, Tetrahedron Lett., 22, 1803 (1981).
5) G. Burkhardt, M. P. Klein, and M. Calvin, J. Am. Chem. Soc., 87, 591 (1965).
6) J. R. Van Wazer and S. Norval, J. Am. Chem. Soc., 88, 4415 (1966).
7) D. W. Hein, R. J. Alheim, and J. J. Leavitt, J. Am. Chem. Soc., 79, 427 (1957).
8) Y. Kanaoka, O. Yonemitsu, K. Tanizawa, and Y. Ban, Chem. Pharm. Bull., 12, 773 (1964).
9) Y. Kanaoka, T. Hamada, O. Yonemitsu, Chem. Pharm. Bull., 18, 587 (1970).
10) S. Fujita, K. Koyama, and Y. Inagaki, Synthesis, 1982, 68.
11) For example, 2-ethyl-3-methylindole (88% yield) from phenylhydrazine and diethyl ketone in PPSE (4 equiv)/$(ClCH_2)_2$ at 85°C for 10 min.
12) 1-Phenyl-3,4-dihydroisoquinoline (82% yield) from *N*-(2-phenylethyl)benzamide in PPSE/$(Cl_2CH)_2$ at 147°C for 3 h.
13) 7-Methoxy-4-methylcoumarin (52% yield) from resorcinol monomethyl ether and methyl acetoacetate in PPSE/$(ClCH_2)_2$ at 85°C for 2 h.
14) H. H. Hergott and G. Simchen, Justus Liebigs Ann. Chem., 1980, 1718.

(Received May 15, 1982)