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PREPARATION OF PHOSPHINIC ACIDS: MICHAEL ADDITIONS OF PHOSPHONOUS ACIDS/ESTERS TO CONJUGATED SYSTEMS.

John K. Thottathil*, Denis E. Ryono, Claire A. Przybyla,
Jerome L. Moniot and Richard Neubeck

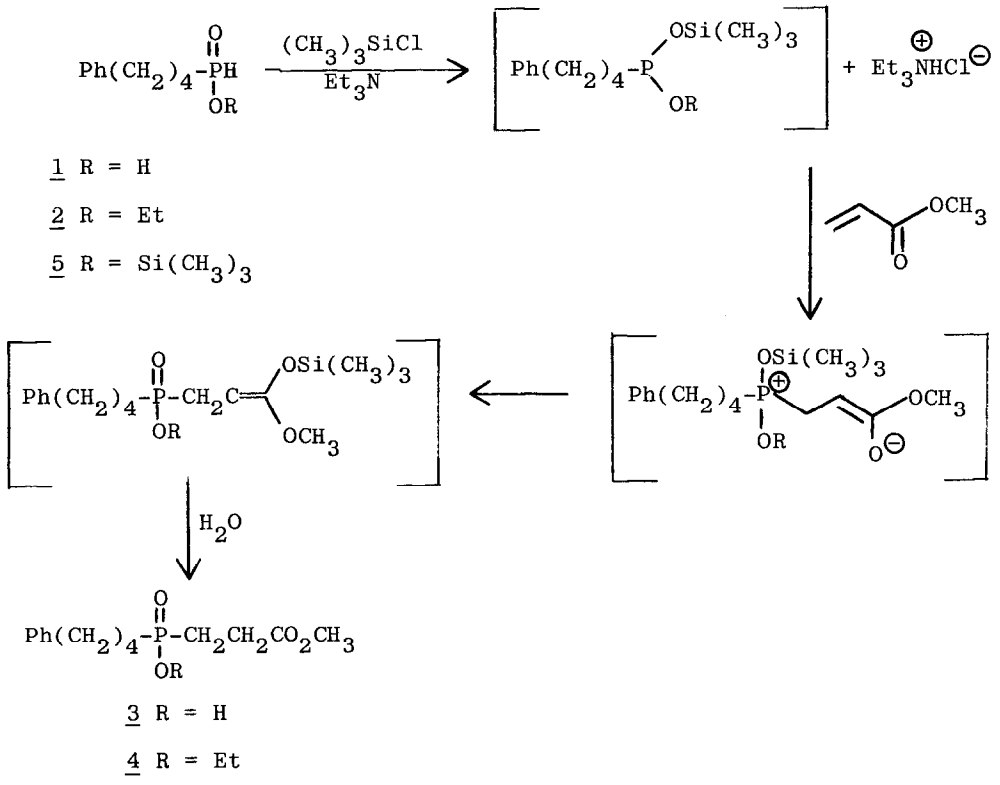
The Squibb Institute for Medical Research
P. O. Box 4000
Princeton, New Jersey 08540

Abstract: A very mild and facile method for the preparation of phosphinic acids *via* Michael addition of phosphonous acids as well as esters, through an intermediate silyl alkyl phosphonite, to activated conjugated systems is described.

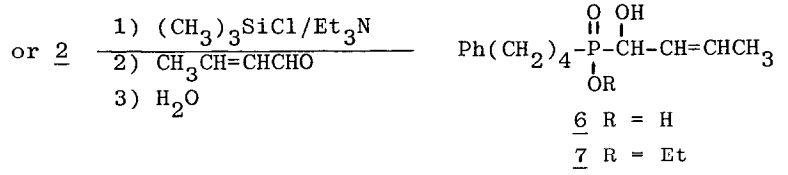
The preparation of phosphinic acid esters *via* Michael addition of phosphonous esters to activated double bonds is a known procedure that frequently requires the use of metal alkoxide bases in alcoholic solvents.[1,2] During the course of our continuing search for methods to prepare phosphinic acids, we reported a procedure[3] involving Arbuzov alkylation of phosphonous acids *via* an intermediate silyl phosphonite.

Herein we describe yet another mild and convenient procedure to access phosphinic acids, involving Michael addition of phosphonous acids and esters to activated conjugated systems involving the same silyl phosphonite intermediate.[3] When phosphonous ester 2 is treated with methyl acrylate in chloroform in the presence of trimethylsilyl chloride (TMS-Cl) and triethylamine, the 1,4-addition product 4 is obtained in 82% yield. Similar treatment of acid 1 with methyl acrylate afforded the 1,4-addition product 3 in 88% yield when two equivalents each of TMS-Cl and triethylamine were present; with one equivalent of each reagent, no 3 was obtained.

Due to the above requirement, the silyl ester 5 is presumed to be the initial intermediate in the conversion of 1 to 3. These transformations may well proceed through the same mechanistic pathway previously described for the reaction of silicon phosphite esters with conjugated systems.[4]



Examples of this procedure utilizing a variety of Michael acceptors are summarized in the Table. While acrylonitrile, acrylic acid, and acrylic esters react with 1 or 2 to give the 1,4-addition product, crotonaldehyde reacted with 1 and 2 to give primarily the 1,2-addition products 6 and 7, respectively, as shown below. While cyclopentenone afforded mainly 1,4-addition products, mesityloxide gave a misture of both 1,2-

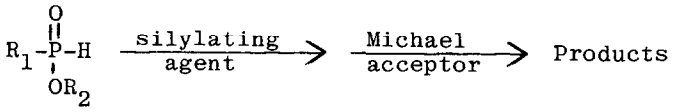


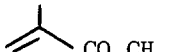
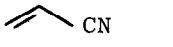
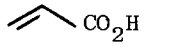
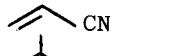
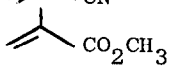
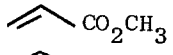
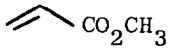
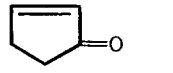
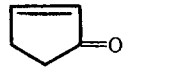
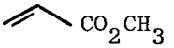
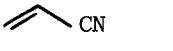
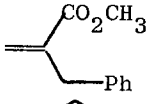
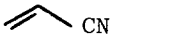
and 1.4-addition products. As can be seen in entries 13 to 16, alternate silylation reagents, *eg*. bis-trimethylsilyl acetamide (BSA) are also suitable.[5a]

Typical Experimental Procedures

(a) Using trimethylsilyl chloride (run #4): To a solution of phosphonous acid 1 (0.44 g, 0.0022 moles) in chloroform (15 ml) was added

Table 1



Run	R_1	R_2	Silylating Agent	Michael Acceptor	Product	Yield[a]
1	$Ph(CH_2)_4$	Et	$(CH_3)_3SiCl$		1,4[e]	93%
2	$Ph(CH_2)_4$	Et	$(CH_3)_3SiCl$		1,4	97%
3	$Ph(CH_2)_4$	Et	$(CH_3)_3SiCl$[b]		1,4	61%
4	$Ph(CH_2)_4$	H	$(CH_3)_3SiCl$[b]		1,4	90%
5	$Ph(CH_2)_4$	H	$(CH_3)_3SiCl$[b]		1,4	88%
6	$Ph(CH_2)_4$	H	$(CH_3)_3SiCl$[b]		1,4	88%
7	$Ph(CH_2)_4$	Et	$(CH_3)_3SiCl$		1,4	87%
8	$Ph(CH_2)_4$	Et	$(CH_3)_3SiCl$		1,4[e]	89%
9	$Ph(CH_2)_4$	H	$(CH_3)_3SiCl$[b]		1,4	77%
10	$Ph(CH_2)_4$	Et	$(CH_3)_3SiCl$	$CH_3CH=CHCHO$	1,2[e]	92%
11	$Ph(CH_2)_4$	H	$(CH_3)_3SiCl$[b]	$CH_3CH=CHCHO$	1,2	88%
12[c]	$Ph(CH_2)_4$	H	$(CH_3)_3SiCl$[b]	$(CH_3)_2C=CHCOCH_3$	1,2[e] 1,4	52% 37%
13	$Ph(CH_2)_4$	Et	BSA[d]		1,4	69%
14	$Ph(CH_2)_4$	H	BSA[b,d]		1,4	74%
15	CH_3	Et	BSA[d]		1,4[e]	81%
16	CH_3	Et	BSA[d]		1,4	63%

[a]Crystallized or chromatographed. [b]2 equivalents of silylating agent. [c]The corresponding phosphonous ethyl ester gave 75% yield of a mixture of 1,2- and 1,4-addition products with an undetermined ratio. [d]Bis-trimethylsilylacetamide. [e]Mixture of two diastereomers.

triethylamine (0.68 ml, 0.0049 mole), trimethylsilyl chloride (0.61 ml, 0.0049 moles) and acrylonitrile (0.17 ml, 0.0024 mole), and the reaction mixture was stirred at room temperature for 18 hours. Standard extractive aqueous work-up followed by crystallization from ether produced phosphinic acid, the 1,4-addition adduct in 90% (0.5 g) yield, m.p. 80-82°C.[5b]

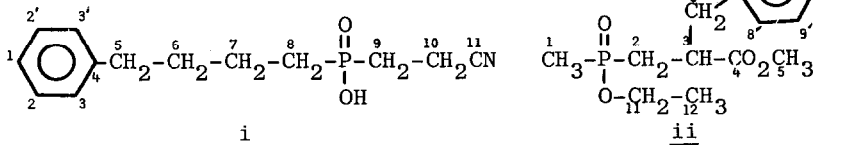
(b) Using bis-trimethylsilyl acetamide (run #15): To a solution of phosphonous ester (0.66 g, 0.006 mole) in methylene chloride (7.5 ml) was added the acrylate (0.9 g, 0.0047 moles) and bis-trimethylsilyl acetamide (1.03 g, 0.00474 moles) and the reaction mixture was stirred at room temperature overnight. Standard extractive aqueous work-up followed by chromatographic purification (neutral alumina activity 3) produced 1,4-addition adduct in 80.7% yield (1.14 g).[5b]

Acknowledgment

We thank Drs. R. H. Mueller, E. W. Petrillo, Jr., and C. M. Cimarusti for their interest in this work, and Dr. M. A. Porubcan and the Squibb Institute Analytical Department for assistance during the course of this work.

References and Notes

1. G. M. Kosolapoff and L. Maier, "Organic Phosphorous Compounds", Wiley-Interscience, New York, 1973, Vol. 6, page 28.
2. M. J. Gallagher and J. Sussman, *Phosphorous*, 5, 91 (1975).
3. Preceeding paper.
4. D. A. Evans, K. Hurst and J. M. Takacs, *J. Am. Chem. Soc.*, 100, 3467 (1978).
5a. Satisfactory IR, NMR (^{1}H and ^{13}C), MS and/or elemental analysis were obtained for all new compounds.
5b. ^{13}C NMR (15 MHz, INEPT) data for i and ii.



i

ii

i ($CDCl_3$): δ 141.35 (C_4,s); 128.04 (C_2,C_3,$C_{2'}$,$C_{3'}$,s); 125.57 (C_1,s); 118.81 (C_{11},d,14.64 Hz); 39.98 (C_5,s); 31.9 (C_7,d,14.65 Hz); 28.29 (C_8,d,28.29 Hz); 24.07 (C_9,d,91.80 Hz); 20.88 (C_6,d,3.91 Hz); 10.14 (C_{10},d,3.0 Hz). ii ($CDCl_3$): 174.15 (C_4,b.d); 137.4 (C_7,s); 128.70 and 128.20 (C_8,C_9,$C_{8'}$,$C_{9'}$,s); 126.50 (C_{10},s); 59.7 (C_{11},d,7 Hz); 51.4 (C_5,s); 41.2 (C_3,b.s); 39.80 and 39.0 (C_6,s); 30.7 (C_2,d,93.0 Hz), 16.15 (C_{12},d,6.0 Hz); 14.30 and 14.10 (C_1,d,93.0 Hz).

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