2-Trimethylsilylprop-2-enyl, a New Protecting Group for Phosphoric and Related Acids

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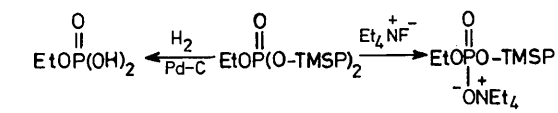
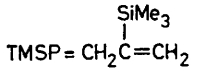
Summary 2-Trimethylsilylprop-2-enyl esters of phosphoric and related acids can be cleaved by tetraethylammonium fluoride or by catalytic hydrogenolysis to give the tetraethylammonium salts or the free acids, respectively.

A NEW protecting group for phosphoric and related acids[1] should preferably have the following characteristics: (i) it should be stable to existing methods of deprotection of other groups, (ii) it should be removable by conditions to which other groups are insensitive, (iii) no extensive purification should be necessary after removal of the protecting group, and (iv) when the phosphoric acid is protected as the disubstituted derivative, the two protecting groups should be removable either singly or together. The latter point is especially relevant to the triester method of nucleotide synthesis.[2] We have examined the possibility of using 2-trimethylsilylprop-2-enyl (TMSP) as a protecting group for phosphoric acid in the belief that it could meet many of the above requirements.



(3) (1) (2)

(4) R = EtO
(5) R = PhO
(6)



Ethyl bis-2-trimethylsilylprop-2-enyl phosphate (**1**), prepared from the reaction of ethyl phosphorodichloridate and 2 mol each of 2-trimethylsilylprop-2-enol[3] and pyridine in benzene at room temperature for 24 h, was used as a model substrate to evaluate the usefulness of the new protecting group. It was found that the TMSP group can be cleaved selectively by tetraethylammonium fluoride or by catalytic hydrogenation. Thus, when an equimolar amount of the phosphate (**1**) and tetraethylammonium fluoride (TEAF) were refluxed in acetonitrile (conc. 0·4 M) for 48 h under nitrogen, the salt (**2**) was obtained in good yield (*ca.* 90%) after removal of the solvent. The other products of the reaction, trimethylfluorosilane and allene,[4] were both volatile and removed during evaporation. On the other hand, when a solution of the phosphate (**1**) in absolute ethanol (conc. 0·15 M) was hydrogenated under atmospheric pressure of hydrogen with 10% palladium on charcoal as catalyst, ethyl dihydrogen phosphate (**3**) was obtained after removal of catalyst and evaporation.

Similarly, treatment of diethyl 2-trimethylsilylprop-2-enyl phosphate (**4**) with TEAF or catalytic hydrogenation gave the tetraethylammonium salt or the free acid of diethyl phosphate, respectively.

The TMSP protecting group is relatively stable to acid and to base. Thus, (**1**) is stable to 80% acetic acid at reflux for 10 min, conditions normally employed to cleave the *O*-trityl group.[5] Compound (**4**) is stable to methanolic ammonia for 20 h at room temperature, conditions under which acetate esters are cleaved.[6] The phosphate (**1**), however, is not stable to more basic conditions, *e.g.*, 0·5 M aqueous sodium hydroxide at room temperature for 3·5 h.

The ability to cleave the TMSP group either by fluoride ion or by hydrogenation has certain advantages, especially

when the phosphate in question may be sensitive to one of these conditions. For example, it is known that the phenoxy group of phenyl phosphates can be cleaved by fluoride ion.[7] Indeed, when diphenyl 2-trimethylsilylprop-2-enyl phosphate (**5**) was treated with TEAF, the products obtained were tetraethylammonium phenyl 2-trimethylsilylprop-2-enyl phosphate and phenol. The TMSP group in (**5**) could, however, be removed selectively by catalytic hydrogenation to give diphenyl phosphate. On the other hand, for the phosphonate ester (**6**), cleavage of the TMSP group had to be carried out with fluoride ion as the phenyl group was partially reduced under hydrogenation conditions.

The ease with which the TMSP groups can be removed under two different conditions, either singly or together [*e.g.*, (**1**) → (**2**) or (**3**)], and the fact that the deprotected phosphoric acid can be recovered without extensive purification render the TMSP group a useful addition to the arsenal of protective groups for phosphoric acid.

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