Functional Selectivity in Phosphonate Ester Dealkylation with Bromotrimethylsilane

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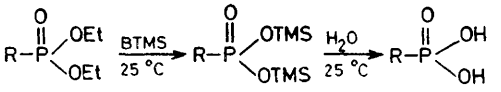
Summary Bromotrimethylsilane is highly selective for P–O silyldealkylation of mixed carboxylate–phosphonate alkyl esters and can be used to prepare trimethylsilyl amido-, alkynyl-, and iodoalkyl-phosphonates in good yield, thus making the corresponding phosphonic acids readily available *via* hydrolysis with neutral H_2O.

WE have previously shown that bromotrimethylsilane (BTMS) cleanly and quantitatively converts the alkyl phosphonates $RP(O)(OR')_2$ (**1**) into the corresponding trimethylsilyl phosphonates $RP(O)(OTMS)_2$ (**2**), which are readily transformed into the phosphonic acids $RP(O)(OH)_2$ (**3**) by hydrolysis with neutral H_2O. It was found that the BTMS reagent was compatible with benzyl, benzoyl, alkoxyalkyl, alkenyl, trichloromethyl, and α-diazomethyl functionalities in the R group of (**1**).[1,2] These results have been confirmed and extended by other workers.[3] Subsequently, alternative procedures based on iodotrimethylsilane (ITMS)[4,5] or chlorotrimethylsilane (CTMS)–NaI[6] have been proposed. Olah[7] originally described the use of ITMS for non-saponicative hydrolysis of carboxylate esters and he[8] and others[9] have since developed further applications of this and equivalent reagents, including CTMS–NaI.[10] Although Olah found BTMS to be markedly less reactive than ITMS with carboxylate esters,[7,11] it has been asserted[4] that BTMS was incompletely selective at 25 °C for the dealkylation of phosphonate esters in compounds having both carboxylate and phosphonate groups, while total selectivity was reportedly achieved with ITMS.

We have systematically examined selectivity using BTMS in ester dealkylation of mixed alkyl carboxylate–phosphonate esters. These included a series of diethyl alkoxycarbonylalkylphosphonates with 0—2 intervening methylene groups (**1a**—**1c**); the diethyl acyloxyalkylphosphonate (**1d**); and the bisethoxycarbonylalkylphosphonate (**1e**).[4] The compounds were treated at 25 °C with 2—3 equiv. of distilled BTMS added dropwise with stirring over 1 h. Reaction progress was monitored by ^1H and ^{31}P n.m.r. spectroscopy for 2 h. In all cases the reaction proceeded to completion with essentially complete selectivity for P–O dealkylation. The expected TMS esters (**2a**—**2e**) were distilled at reduced pressure [except (**3e**)] and characterized by i.r. and n.m.r. spectroscopy and high resolution mass spectrometry. The corresponding acids (**3a**—**3e**) were readily prepared by treatment in dry acetone with a small excess of H_2O and isolation *in vacuo*. The acids were characterized both directly and [except (**3e**)] as the corresponding dicyclohexylamine salts.



(**1**) (**2**) (**3**)

a; R = EtO_2C
b; R = EtO_2CCH_2
c; R = $EtO_2CCH_2CH_2$
d; R = $MeCO_2CH_2CH_2$
e; R = $(EtO_2C)_2CHCH_2$
f; R = $MeC{\equiv}C$
g; R = $MeNHCOCH_2$
h; R = MeCO
i; R = ICH_2
j; R = $BrCH_2$

We also found that selective TMS silyldealkylation of dialkyl prop-1-ynyl- (**1f**), *N*-methylcarbamoylmethyl (**1g**), acyl- (**1h**), and iodomethyl- (**1i**) phosphonates proceeds smoothly at 25 °C to give the corresponding TMS esters (**2**) in excellent yield. No exchange of the iodine atom in (**1i**) was detectable with BTMS, but CTMS–NaI treatment[6] of diethyl bromomethylphosphonate (**1j**) produced a mixture of (**1j**) and a mixture of 3 products (by ^{31}P n.m.r. spectroscopy).

Our earlier observation[1,2] of mixed alkyl TMS phosphonate intermediates in BTMS dealkylations of the symmetrical compound (**1**) has been reproduced with ITMS.[5] Competitive experiments with BTMS indicate that the relative reactivities of dimethyl, diethyl and di-isopropyl-acylphosphonates are *ca.* 1 : 0·25 : 0·04. This suggests that monosilyldealkylation of methyl isopropyl phosphonates should be a useful route to isopropyl phosphonic acids.

We have here demonstrated that BTMS is in fact quite selective in P–O *vs.* C–O dealkylation and that it is compatible with alkyne and other functionalities. Olah has recently summarized the various problems associated with the iodosilane reagent.[10] Unlike ITMS, BTMS is readily prepared in pure form at reasonable cost, is highly selective at room temperature, and can be stored without decomposition. It also can be more convenient to use than CTMS–NaI, which requires a dry solvent and filtration of the moisture-sensitive TMS phosphonate prior to isolation, and which presents a potential danger of halogen substitution in phosphonates such as (**1j**).

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