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A high yielding preparation of α-trimethylsilyloxyphosphonates by silylation of α-hydroxyphosphonates with HMDS catalyzed by iodine

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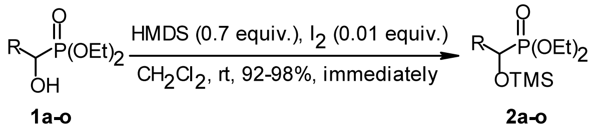
Abstract—A general, versatile, high yielding and convenient procedure for the immediate conversion of various α-hydroxyphosphonates to α-trimethylsilyloxyphosphonates under neutral conditions using HMDS in the presence of a catalytic amount of iodine is described. © 2002 Elsevier Science Ltd. All rights reserved.

α-Trimethylsilyloxyphosphonates show properties that make them attractive in biology, industry and organic chemistry.[1] The interest in the preparation of α-trimethylsilyloxyphosphonates arises on the one hand from the existence of an α-acidic hydrogen in these compounds, which can be metalated by lithium diisopropylamide to afford relatively stable α-carbanionic species.[2] On the other hand, the C–P and Si–O bonds of α-trimethylsilyloxyphosphonates are readily cleaved under alkaline and acidic conditions.[3] Therefore, α-lithiated α-trimethylsilyloxyphosphonates have become important synthons in organic synthesis as masked acyl anions. They react with various ketones to produce the corresponding α-trimethylsilyloxy ketones.[4] Unsymmetrical ketones, β,γ-unsaturated ketones and carboxylic acids could be obtained by means of alkylation of α-lithiated α-trimethylsilyloxyphosphonates followed by cleavage of the Si–O bond and elimination of dialkyl phosphate in alkaline media.[5] α-Lithiated α-trimethylsilyloxyphosphonates can also undergo facile acylation with various acylating agents to afford the corresponding α-acylated products, which could be converted to α-hydroxy ketones after cleavage of the Si–O bond and elimination of dialkyl phosphate in alkaline media.[2]



Scheme 1.

A survey of the literature indicates that a practical, general and high yielding method for the synthesis of pure α-trimethylsilyloxyphosphonates has not yet been described. Diethyl trimethylsilyloxyphosphite (DTMSP)[5] or triethylphosphite and trimethylsilyl chloride[1b,c] are the most common silicon–phosphorous reagents which have been reacted with aldehydes to produce α-trimethylsilyloxyphosphonates under harsh reaction conditions and require rather long reaction times. Another reported procedure for the preparation of these compounds is the reaction of silyl phenyl ketones with trialkylphosphites at a rather high temperature (80°C) with a long reaction time (12 h).[6] Hexamethylsilathiane has been used for the direct silylation of α-hydroxyphosphonates[7] at 50–70°C with moderate yields (55–78%).[8] Trimethylsilyl chloride has also been used for the preparation of the diethyl α-trimethylsilyloxybenzylphosphonate sodium salt of diethylphosphite and benzaldehyde in moderate yield (67%).[5a]

The reactions of α-hydroxyphosphonates have been under investigation in our laboratory in recent years.[9] A recent report on the silylation of alcohols with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) and iodine as a catalyst[10] prompted us to apply this method to the direct silylation of α-hydroxyphosphonates. Reactions of various α-hydroxyphosphonates (**1a**–**o**) occurred immediately at room temperature with excellent yields using this reagent system (Scheme 1, Table 1).

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Table 1. Direct silylation of α-hydroxyphosphonates (**1a**–**o**) with HMDS and a catalytic amount of I_2

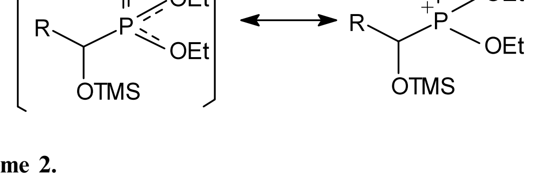
Product **2**[Ref.]	R-	Yield[a] (%)
a[1a,c,5a,6]	C_6H_5-	98
b[11]	4-$CH_3C_6H_4$-	97
c[12]	4-$CH_3OC_6H_4$-	97
d[14]	2,4,6-$(CH_3)C_6H_2$-	98
e[12]	2-ClC_6H_4-	97
f[12]	3-ClC_6H_4-	95
g[12]	4-ClC_6H_4-	98
h[14]	2,6-$Cl_2C_6H_3$-	97
i[12]	2-$O_2NC_6H_4$-	95
j[12]	3-$O_2NC_6H_4$-	94
k[12]	4-$O_2NC_6H_4$-	96
l[14]	2-Naphthyl	94
m[14]	3-Pyridyl	92
n[3]	PhCH=CH-	93
o[3]	CH_3CH=CH-	92

[a] Isolated yields; reaction occurred immediately at room temperature.

As shown in Table 1, various types of α-hydroxy-(phenylmethyl) phosphonates (**1a**–**k**) were cleanly converted into the corresponding α-trimethylsilyloxyphosphonates (**2a**–**k**) in excellent yields (94–98%). α-Hydroxy-2-naphthyl, 3-pyridyl and β,γ-unsaturated phosphonates (**1l**–**o**) were also silylated efficiently giving the corresponding α-trimethylsilyloxyphosphonates (**2l**–**o**) in 92–94% yields.

Due to the neutral nature of the reaction media, cleavage of O–Si and C–P bonds was not observed. Therefore, products of high purity were obtained after work-up and further purification was not required.[13] In order to show the unique catalytic behavior of iodine in these reactions, we have performed the silylation of **1a** with HMDS in the presence of NBS, NCS and Br_2 which possess electrophilic halogens. The results showed that the reaction times were long (9–10 h) and the cleavage of the C–P bond occurred to produce benzaldehyde in 40–60% yields. All spectral data of the isolated compounds confirm the structures that we have assigned to the products.

All mass spectral data[14] consist of molecular peaks with weak intensities due to the ready cleavage of $-P(O)(OEt)_2$ followed by loss of the $-Si(C\underline{H}_3)_3$ fragment. A common peak at *m*/*e* 73 due to formation of the $-Si(C\underline{H}_3)_3^+$ ion was also observed in the mass spectra of all the reported compounds. A strong peak at $M^+ + Si(C\underline{H}_3)_3$ was also observed which is the result of combination of M^+ and an $Si(C\underline{H}_3)_3^+$ ion. The formation of these peaks can be explained by the resonance-stabilized forms which are shown in Scheme 2.



Scheme 2.

Consequently, in this paper, we have described a simple procedure for the first general, versatile, and high yielding synthesis of a variety of α-trimethylsilyloxyphosphonates by direct silylation of α-hydroxyphosphonates with HMDS. Extension of this methodology for the preparation of α-trimethylsilyloxyphosphonates in the presence of other easily available catalysts is in progress in our laboratory.

Acknowledgements

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13. *Typical procedure for the preparation of α-trimethylsilyloxyphosphonates from α-hydroxyphosphonates*: A mixture of α-hydroxyphosphonate **1a** (5 mmol) and iodine (0.05 mmol) in CH_2Cl_2 (15 mL) was prepared. HMDS (3.5 mmol in 10 mL CH_2Cl_2) was added dropwise within 5 min to the reaction mixture. The reaction occurred immediately with the generation of ammonia gas. Then, finely powdered $Na_2S_2O_3$ (≅1 g, portionwise) was added to the mixture and after 10 min, the reaction mixture was

filtered and the filter cake was washed with $\mathrm{CH_2Cl_2}$ (3×5 mL). The resulting solution was washed with $\mathrm{H_2O}$ (5 mL) and the organic layer was separated and dried over anhydrous $\mathrm{Na_2SO_4}$. Evaporation of the solvent afforded the desired pure product **2a** in 98% yield (Table 1).

14. *Spectral data and elemental analyses of unknown α-trimethylsilyloxyphosphonates*: **2d**: ^{1}H NMR ($\mathrm{CDCl_3}$, TMS): δ –0.04 (s, 9H, $\mathrm{Si(C\underline{H}_3)_3}$), 1.02 (t, 3H, $^2J_{\mathrm{HH}}=7$ Hz, 2-$\mathrm{OCH_2C\underline{H}_3}$), 1.22 (t, 3H, $^2J_{\mathrm{HH}}=7$ Hz, 2-$\mathrm{OCH_2C\underline{H}_3}$), 2.12 (s, 3H, $\mathrm{C\underline{H}_3}$), 2.25 (s, 3H, $\mathrm{C\underline{H}_3}$), 2.51 (s, 3H, $\mathrm{C\underline{H}_3}$), 3.58–3.68 (m, 1H, 2-$\mathrm{OC\underline{H}_2CH_3}$), 3.81–3.90 (m, 1H, 2-$\mathrm{OC\underline{H}_2CH_3}$), 3.98–4.10 (m, 2H, 2-$\mathrm{OC\underline{H}_2CH_3}$), 5.28 (d, 1H, $^1J_{\mathrm{PH}}=18.3$ Hz, $\mathrm{C\underline{H}}$), 6.66 (s, 1H, $\mathrm{C_6\underline{H}_2}$), 6.72 (s, 1H, -$\mathrm{C_6\underline{H}_2}$) ppm; ^{13}C NMR ($\mathrm{CDCl_3}$, TMS): 0.00 (s, -$\mathrm{Si(\underline{C}H_3)_3}$), 16.56 (d, $^3J_{\mathrm{CP}}=5.9$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 16.87 (d, $^3J_{\mathrm{CP}}=5.9$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 21.16 (s, -$\mathrm{\underline{C}H_3}$), 21.67 (s, -$\mathrm{\underline{C}H_3}$), 21.69 (s, -$\mathrm{\underline{C}H_3}$), 62.70 (d, $^2J_{\mathrm{CP}}=7.1$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 62.92 (d, $^2J_{\mathrm{CP}}=7.1$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 69.60 (d, $^1J_{\mathrm{CP}}=177.2$ Hz, -$\mathrm{\underline{C}H}$) 129.05 (d, $J_{\mathrm{CP}}=2$ Hz, -$\mathrm{\underline{C}_6H_2}$), 130.25 (s, -$\mathrm{\underline{C}_6H_2}$), 131.57 (d, $J_{\mathrm{CP}}=3.3$ Hz, -$\mathrm{\underline{C}_6H_2}$), 136.08 (d, $J_{\mathrm{CP}}=8.1$ Hz, -$\mathrm{\underline{C}_6H_2}$), 137.41 (d, $J_{\mathrm{CP}}=3.4$ Hz, -$\mathrm{\underline{C}_6H_2}$), 139.88 (d, $J_{\mathrm{CP}}=4.2$ Hz, -$\mathrm{\underline{C}_6H_2}$) ppm; IR (neat): OH peak was absent; MS (70 eV), *m*/*e* (relative intensity %): 431 ($\mathrm{M^+{+}Si(CH_3)_3}$, 19.3), 358 ($\mathrm{M^+}$, 3.2), 221 ($\mathrm{M^+}$–$\mathrm{P(O)(OEt)_2}$, 100), 147 (221-$\mathrm{Si(CH_3)_3}$, 12), 73 ($\mathrm{Si(CH_3)_3{}^+}$, 44.3);

$\mathbf{C_{17}H_{31}O_4PSi}$ requires C, 56.98; H, 8.66, found: C, 56.90; H, 8.70%.

2h: ^{1}H NMR ($\mathrm{CDCl_3}$, TMS): δ 0.00 (s, 9H, -$\mathrm{Si(C\underline{H}_3)_3}$), 1.07–1.24 (m, 6H, 2-$\mathrm{OCH_2C\underline{H}_3}$), 3.89–4.15 (m, 4H, 2-$\mathrm{OC\underline{H}_2CH_3}$), 5.81 (d, 1H, $^1J_{\mathrm{PH}}=19.3$ Hz, -$\mathrm{C\underline{H}}$), 7.03–7.10 (m, 1H, -$\mathrm{C_6\underline{H}_3}$), 7.20–7.25 (m, 2H, -$\mathrm{C_6\underline{H}_3}$), ppm; ^{13}C NMR ($\mathrm{CDCl_3}$, TMS): 0.00 (s, -$\mathrm{Si(\underline{C}H_3)_3}$), 16.86 (d, $^3J_{\mathrm{CP}}=6.8$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 16.96 (d, $^3J_{\mathrm{CP}}=6.8$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 63.35 (d, $^2J_{\mathrm{CP}}=7.1$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 63.60 (d, $^2J_{\mathrm{CP}}=7.1$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 70.02 (d, $^1J_{\mathrm{CP}}=179.8$ Hz, -$\mathrm{\underline{C}H}$), 128.60 (d, $J_{\mathrm{CP}}=2.0$ Hz, -$\mathrm{\underline{C}_6H_3}$), 129.99 (d, $J_{\mathrm{CP}}=2.9$ Hz, -$\mathrm{\underline{C}_6H_3}$), 131.31 (d, $J_{\mathrm{CP}}=2.8$ Hz, -$\mathrm{\underline{C}_6H_3}$), 135.73 (d, $J_{\mathrm{CP}}=8.2$ Hz, -$\mathrm{\underline{C}_6H_3}$), 136.87 (d, $J_{\mathrm{CP}}=4.9$ Hz, -$\mathrm{\underline{C}_6H_3}$) ppm; IR (neat): OH peak was absent.; MS (70 eV), *m*/*e* (relative intensity %): 457 ($\mathrm{M^+{+}Si(CH_3)_3}$, 100), 389 ($\mathrm{M^+}$+4, 2.3), 387 ($\mathrm{M^+}$+2, 10.8), 385 ($\mathrm{M^+}$, 14), 247 ($\mathrm{M^+}$–$\mathrm{P(O)(OEt)_2}$, 52.2), 173 (247-$\mathrm{Si(CH_3)_3}$, 2.4), 73 ($\mathrm{Si(CH_3)_3{}^+}$, 93.5);

$\mathbf{C_{14}H_{23}Cl_2O_4PSi}$ requires C, 43.64; H, 5.97, found: C, 43.60; H, 5.91%.

2l: ^{1}H NMR ($\mathrm{CDCl_3}$, TMS): δ 0.00 (s, 9H, -$\mathrm{Si(C\underline{H}_3)_3}$), 1.10 (t, 6H, $^1J_{\mathrm{HH}}=7.1$ Hz, 2-$\mathrm{OCH_2C\underline{H}_3}$), 3.79–3.99 (m, 4H, 2-$\mathrm{OC\underline{H}_2CH_3}$), 5.03 (d, 1H, $^1J_{\mathrm{PH}}=14.5$ Hz, -$\mathrm{C\underline{H}}$), 7.33–7.37 (m, 2H, -$\mathrm{C_{10}\underline{H}_7}$), 7.49–7.52 (m, 1H, -$\mathrm{C_{10}\underline{H}_7}$), 7.69–7.84 (m, 4H, -$\mathrm{C_{10}\underline{H}_7}$) ppm; ^{13}C NMR ($\mathrm{CDCl_3}$, TMS): 0.00 (s, -$\mathrm{Si(\underline{C}H_3)_3}$), 16.39 (d, $^3J_{\mathrm{CP}}=5.6$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 16.48 (d, $^3J_{\mathrm{CP}}=5.6$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 62.77 (d, $^2J_{\mathrm{CP}}=7.3$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 63.22 (d, $^2J_{\mathrm{CP}}=7.3$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 72.13 (d, $^1J_{\mathrm{CP}}=174.4$ Hz, -$\mathrm{\underline{C}H}$), 125.23–126.44, 127.61–128.06, 133.07–133.21, 134.94–135.48 (-$\mathrm{\underline{C}_{10}H_7}$) ppm; IR (neat): OH peak was absent; MS (70 eV), *m*/*e* (relative intensity %): 439 ($\mathrm{M^+{+}Si(CH_3)_3}$, 16.2), 366 ($\mathrm{M^+}$, 4.8), 229 ($\mathrm{M^+}$–$\mathrm{P(O)(OEt)_2}$, 100), 155 (229-$\mathrm{Si(CH_3)_3}$, 18.8), 73 ($\mathrm{Si(CH_3)_3}$, 87.5);

$\mathbf{C_{18}H_{27}O_4PSi}$ requires C, 59.02; H, 7.38, found: C, 59.04; H, 7.35%.

2m: ^{1}H NMR ($\mathrm{CDCl_3}$, TMS): δ 0.00 (s, 9H, -$\mathrm{Si(C\underline{H}_3)_3}$), 1.13 (t, 6H, $^1J_{\mathrm{HH}}=7.0$ Hz, 2-$\mathrm{OCH_2C\underline{H}_3}$), 3.91–3.99 (m, 4H, 2-$\mathrm{OC\underline{H}_2CH_3}$), 4.89 (d, 1H, $^1J_{\mathrm{PH}}=14.5$ Hz, -$\mathrm{C\underline{H}}$), 7.15–7.21 (m, 1H, -$\mathrm{C_5\underline{H}_4N}$), 7.74 (d, 1H, $J_{\mathrm{PH}}=7.3$ Hz, -$\mathrm{C_5\underline{H}_4N}$), 8.43 (d, H, $J_{\mathrm{PH}}=4.1$ Hz, -$\mathrm{C_5\underline{H}_4N}$), 8.54 (s, 1H, -$\mathrm{C_5\underline{H}_4N}$) ppm; ^{13}C NMR ($\mathrm{CDCl_3}$, TMS): 0.00 (s, -$\mathrm{Si(\underline{C}H_3)_3}$), 16.51 (d, $^3J_{\mathrm{CP}}=5.1$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 16.58 (d, $^3J_{\mathrm{CP}}=5.1$ Hz, 2-$\mathrm{OCH_2\underline{C}H_3}$), 63.06 (d, $^2J_{\mathrm{CP}}=7.3$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 63.43 (d, $^2J_{\mathrm{CP}}=7.3$ Hz, 2-$\mathrm{O\underline{C}H_2CH_3}$), 69.88 (d, $^1J_{\mathrm{CP}}=175.8$ Hz, -$\mathrm{\underline{C}H}$), 123.31 (d, $J_{\mathrm{CP}}=2.6$ Hz, -$\mathrm{\underline{C}_5H_4N}$), 133.53 (s, -$\mathrm{\underline{C}_5H_4N}$), 135.14 (d, $J_{\mathrm{CP}}=4.9$ Hz, -$\mathrm{\underline{C}_5H_4N}$), 148.69 (d, $J_{\mathrm{CP}}=6.7$ Hz, -$\mathrm{\underline{C}_5H_4N}$), 149.43 (d, $J_{\mathrm{CP}}=3.3$ Hz, -$\mathrm{\underline{C}_5H_4N}$) ppm; IR (neat): OH peak was absent; MS (70 eV), *m*/*e* (relative intensity %): 390 ($\mathrm{M^+{+}Si(CH_3)_3}$, 62.1), 317 ($\mathrm{M^+}$, 1.2), 180 ($\mathrm{M^+}$–$\mathrm{P(O)(OEt)_2}$, 86.2), 108 (180-$\mathrm{Si(CH_3)_3}$, 48.8), 73 ($\mathrm{Si(CH_3)_3}$, 100);

$\mathbf{C_{13}H_{24}NO_4PSi}$ requires C, 49.21; H, 7.57, found: C, 49.18 H, 7.51%.