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# NEW SYNTHESIS OF β-KETO PHOSPHONATES

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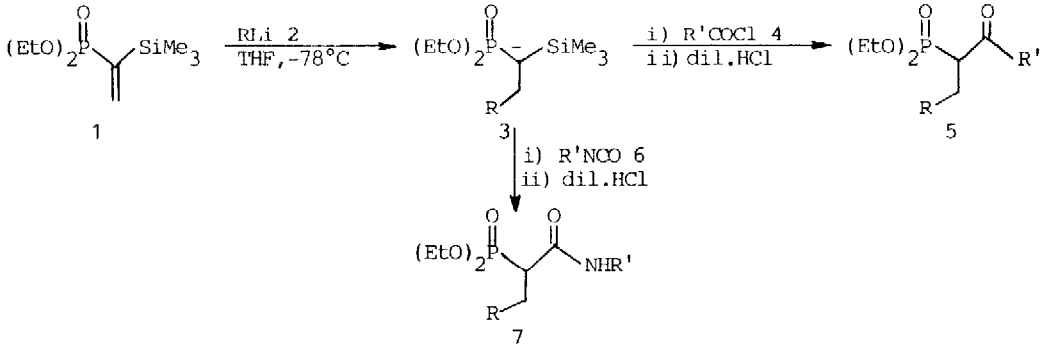
**Summary** : A new synthetic route to β-keto phosphonates from diethyl 1-(trimethylsilyl)vinylphosphonate **1** is described. This involves nucleophilic addition of the organolithium reagents toward **1** followed by quenching with acid chlorides and alkyl isocyanates.

β-Keto phosphonates are valuable intermediates in organic synthesis, especially for the preparation of α, β-unsaturated carbonyl compounds by the Wadsworth-Emmons condensation.[1] Unfortunately, synthetic routes to β-keto phosphonates and related phosphonates are rather limited in contrast with the significant progress[2] that has expanded the original scope of the Wadsworth-Emmons condensation. The commonly used method for the preparation of β-keto phosphonates is the Arbuzov reaction[3] of trialkyl phosphite and α-halo ketone. This method is restricted to the highly reactive α-halo ketones, due to the poor nucleophilicity of phosphites and the Perkow reaction to give enol phosphates. The acylation of alkylphosphonate anions[4] suffers from the limited availability of alkylphosphonates, and low reactivities resulting from the proton exchange between β-keto phosphonates generated and 1-lithioalkylphosphonates are always problematic since the α-protons of β-keto phosphonates are more acidic than that of the starting alkylphosphonates. Recently developed rearrangement[5] of vinyl phosphates to β-keto phosphonates via a 1,3-phosphorus migration is a good candidate for the preparation of β-keto phosphonates, especially of cyclic β-keto phosphonates.

Here we report a new facile synthesis of β-keto phosphonates **5** and β-oxoamido phosphonates **7** from the readily available diethyl 1-(trimethylsilyl)vinylphosphonate **1**.[6] Our approach for the synthesis of **5** is based on that vinyl phosphonates with trimethylsilyl group at α-position are sufficiently activated toward nucleophilic addition of organolithium




Scheme I

reagents by virtue of the polarizing trimethylsilyl group[7] (Scheme 1). α-Trimethylsilyl phosphonate anion **3** was quenched with freshly distilled acid chlorides and subsequent treatment with dil. HCl solution provided the protodesilylated products, β-keto phosphonates **5**. Inverse addition of **3** to acid chlorides did not improve the yield of **5**. The results were summarized in Table I. Quenching **3** with alkyl isocyanates yielded β-oxoamido phosphonates **7** in good yields. **5** and **7** were confirmed by $^1$H nmr, ir, ms, and elemental analysis.[8] In this process, trimethylsilyl group served to accelerate nucleophilic addition of the organolithium reagents toward **1** and stabilized α-silylated phosphonate anion **3** by α-effect[9] of the trimethylsilyl group which was easily removed by acidic hydrolysis at the final step. Thus β-keto phosphonates are facilely synthesized from **1** and moreover the α-silylated phosphonate anions **3** are considered to be versatile for further transformation into other functionalized organophosphonates.

Table I. Synthesis of β-keto phosphonates **5** and β-oxoamido phosphonates **7**.

| Entry | R | R' | Product | Yield (%) |
|---|---|---|---|---|
| 1 | Me | Ph | 5a | 80 |
| 2 | n-Bu | Me | 5b | 78 |
| 3 | n-Bu | c-Pr | 5c | 73 |
| 4 | n-Bu | Ph | 5d | 75 |
| 5 | t-Bu | Ph | 5e | 73 |
| 6 | Me | Et | 7a | 80 |
| 7 | n-Bu | Et | 7b | 71 |
| 8 | n-Bu | n-Pr | 7c | 70 |
| 9 | n-Bu | Ph | 7d | 85 |

**References and Notes**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6. **1** was synthesized by a modification of the method of Hirao. Hirao, T., Masunaga, T., Yamada, N., Ohsiro, Y., Agawa, T., Bull. Chem. Soc. Japan, 1982, **55**, 909.
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8. Synthesis of **5**. Typical procedure; To a stirred solution of **1** (1 mmol, 236 mg) in THF (5 ml), was added dropwise MeLi (1.1 mmol, 0.69 ml, 1.6 M in ether) at -78°C. After warming up to -50°C, benzoyl chloride (2.0 mmol, 281 mg) was added fast. Stirring was continued for 1.5 hr at rt, then hydrolysis was performed by addition of 30% HCl solution. Extractive work up and $SiO_2$ column chromatography ($Et_2O$) gave **5a** in 80% yield. **5a**; $R_f$ ($Et_2O$) 0.5; $^1$H nmr ($CDCl_3$) δ 0.9 (t, 3H), 1.35 (t, J=7Hz, 6H), 2.20 (m, 2H), 4.20 (m, 5H), and 7.80 (m, 5H); ir (film) 1695, 1260, and 1050 cm$^{-1}$; ms (70ev), m/e(%) 284 ($M^+$, 1.4) 105 (100). Anal. Calcd for $C_{14}H_{21}O_4P$: C, 59.15, H, 7.39; O, 22.54; P, 10.92. Found: C, 58,92; H, 7.50.
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