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SIMPLE CONVERSION OF γ- AND δ-LACTONES INTO 5-(OR 6)-SILYLOXY-3-KETO-PHOSPHONATES

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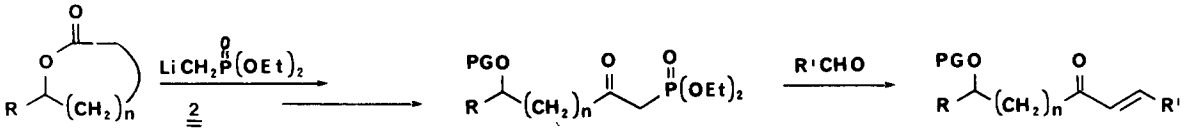
Abstract: A reliable one pot procedure for the conversion of γ- and δ-lactones 1 into the β-keto-phosphonates 10 is presented.

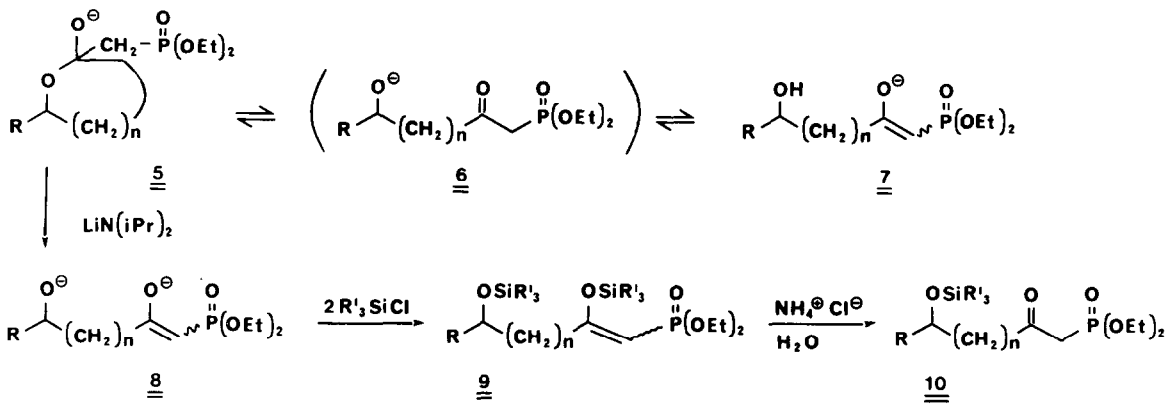
Lactones are versatile building blocks in syntheses. The chain extension 1 → 3 → 4 would provide a particularly useful example.



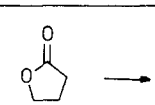
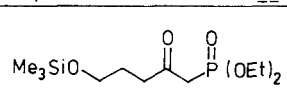
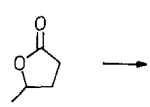
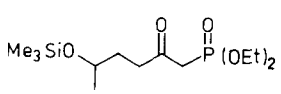
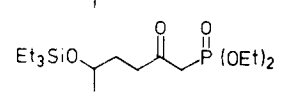
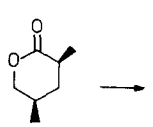
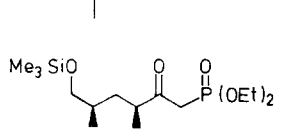
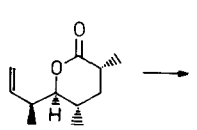
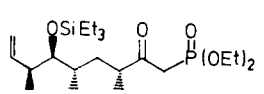
1 3 4

Yet, in situations where such transformation was required, quite circuitous routes have been used instead [1]. Obviously, the transformation of the lactones 1 into the β-keto-phosphonates 3 must have some moot points. The more it was desireable to develop a reliable high yielding procedure for this conversion.

The addition of lithium diethyl methane-phosphonate 2 [2] to γ- or δ-lactones 1 [3] generates the hemiketalides 5. It turned out to be irrelevant for the present purpose that the reaction remained incomplete using only one equivalent of 2, since 5 is partially deprotonated by 2 to 8, cf. the similar observation by Altenbach [4]. It can be assumed that the hemiketalide 5 is in equilibrium with the open chain alkoxides 6 and 7. The intended conversion of 5 into the ß-ketophosphonate 3 requires that the alkoxide function of the anion 6 can be selectively protected, e.g. by silylation. While 5 may be favored in the equilibrium by chelation of the metal counter ion, or 7 due to its lowest basicity, 6 should be present in only minute concentration, rendering its

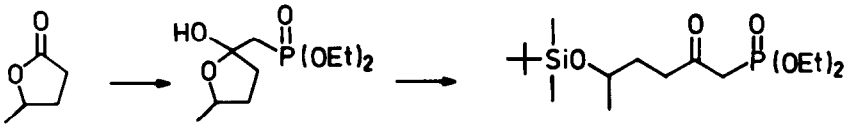


selective silylation precarious. We felt it therefore to be advantageous to convert all of the material into a reactive open chain alkoxide. This can be achieved by a second deprotonation [5] of 5 leading to the dianion 8, for instance by adding an additional equivalent of either n-butyllithium or lithium diisopropylamide. Rather than trying to achieve a selective silylation of the alkoxide function in 8, we found it convenient to add two equivalents of chlorotrimethyl-silane resulting in the bis-silyl ether 9, because the enolsilyl ether group of the latter could be selectively hydrolysed during workup with aqueous NH_4Cl solution. All these operations could be carried out without isolation of intermediates to give the β-ketophosphonates 10 in overall yields of > 80 % from 1, cf. table.

Starting Lactone	β-Ketophosphonate 10	overall yield
		86 %
		91 %
		96 %
		82 %
		96 %

a) All new compounds gave correct elemental analyses and had the expected ^{13}C- and ^{1}H nmr data. b) Cleavage of the enolsilane was effected with 1n aqueous HCl.

While this procedure worked well for the trimethylsilyl- or triethylsilyl-protected derivatives 10, extension to the preparation of the tert.-butyl-dimethylsilyl-derivative 12 resulted in lower yields, the difficulties arising probably in the step 8 → 9. A change to the more reactive potassium alkoxides 8 proved to be advantageous: For this purpose the lithium hemiketalide generated from 1b was hydrolysed to the hemiketal 11 (78 %). This was deprotonated in a subsequent step by 2,5 equivalents of potassium tert.-butoxide. Silylation of the dianion 8 proceeded readily to give the desired 12 in 89 %. It should be noted that in this instance we used only one equivalent of the more expensive silylating agent. This demonstrates that the alkoxide function in 8 is silylated more rapidly than the enolate function.



11 12

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2) E.J. Corey and G.T. Kwiatkowski, J. Am. Chem. Soc. 88, 5654 (1966).
3) cf. P.A. Aristoff, J. Org. Chem. 46, 1954 (1981); M.I. Lim and V.E. Marquez, Tetrahedron Lett. 24, 5559 (1983).
4) cf. the accompanying paper by H.J. Altenbach.
5) H.J. Gais and T. Lied, Angew. Chem. 96, 143 (1984); Angew. Chem., Int. Ed. Engl. 23, 145 (1984); S. Cavicchioli, S. Savoia, C. Trombini and U. Umani-Ronchi, J. Org. Chem. 49, 1246 (1984), and references quoted.
6) cf. J. Orban, J.V. Turner and B. Twitchin, Tetrahedron Lett. 25, 5099 (1984).

Typical procedure: To a cold (-78 °C) solution of 11.41 g (75 mmol) diethyl methanephosphonate in 50 ml of THF were added over 10 min 75 mmol of n-butyl-lithium in n-hexane. After stirring for 15 min a solution of 6.46 g (75 mmol) butyrolactone in 5 ml of THF was added dropwise over 10 min. To this solution

was added after 30 min at -78 °C a solution of 75 mmol lithium diisopropylamide in 100 ml of THF/hexane (1:1). After another 30 min at -78 °C 16.30 g (150 mmol) of chloro-trimethyl-silane were added and the mixture was allowed to reach room temperature over night. After hydrolysis with 50 ml of saturated aqueous NH_4Cl-solution the phases were separated and the aqueous phase was extracted twice with 30 ml of ether each. The combined organic extracts were washed once each with 20 ml of saturated aqueous $NaHCO_3$-solution, water and saturated NaCl-solution. After drying over Na_2SO_4 the solvents were removed i.vac. to give 20.1 g (86 %) of diethyl 2-oxo-5-trimethylsilyloxy-1-pentane-phosphonate as colourless oil of b.p. 107 - 110 °C/10^{-1} Torr. - ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 9H), 1.31 (dt, J = 7.0 and 0.4 Hz, 6H), 1.78 (dq, J = 6.7 and 0.8 Hz, 2H), 2.66 (t, J = 7.2 Hz, 2H), 3.07 (d, J = 22.7 Hz, 2H), 3.57 (t, J = 6.2 Hz, 2H), 4.07 - 4.16 (m, 4H). - ^{13}C NMR ($CDCl_3$, proton decoupled): δ = -0.94 (s), 15.9 (d, J = 6.2 Hz), 26.2 (s), 40.2 (d, J = 1.0 Hz), 42.0 (d, J = 128.0 Hz), 61.0 (s), 62.2 (d, J = 6.5 Hz), 201.4 (d, J = 6.1 Hz).

Diethyl (3R*,5S*)-3,5-dimethyl-2-oxo-6-trimethylsilyloxy-1-hexanephosphonate: b.p. 117 - 120 °C/10^{-1} Torr. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08 (s, 9H), 0.88 (d, J = 6.6 Hz, 3H), 0.75 - 1.07 (m, 1H), 1.09 (d, J = 6.9 Hz, 3H), 1.31 (t, J = 7.0 Hz, 6H), 1.56 - 1.78 (m, 2H), 2.83 - 2.89 (m, 1H), 3.06 - 3.17 (m, 2H), 3.30 - 3.42 (m, 2H), 4.02 - 4.18 (m, 4H). - ^{13}C NMR ($CDCl_3$, proton decoupled): δ = -0.9 (s), 15.8 (s), 16.1 (s), 16.7 (d, J = 9.6 Hz), 33.0 (s), 36.1 (s), 40.1 (d, J = 130.1 Hz), 44.6 (s), 62.0 (d, J = 6.8 Hz), 67.1 (s), 205.3 (d, J = 6.9 Hz).

Diethyl (3R,5S,6S,7S)-2-oxo-6-triethylsilyloxy-3,5,7-trimethyl-non-8-en-1-phosphonate: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.54 - 0.60 (m, 6H), 0.74 - =.79 (m, 15H), 1.08 (d, J = 6.9 Hz, 3H), 1.29 (t, J = 7.1 Hz, 6H), 1.36 - 1.59 (m, 2H), 1.83 - 1.93 (m, 1H), 2.25 - 2.35 (m, 1H), 2.77 - 2.87 (m, 1H), 3.02 and 3.10 (ABX-System, J_{AB} = 13.9 Hz, J_{AX} = J_{BX} = 22.8 Hz, 2H), 3.27 (dd, J = 6.9 and 3.3 Hz, 1H), 4.05 - 4.14 (m, 4H), 4.90 - 4.97 (m, 2H), 5.65 - 5.74 (m, 1H). - ^{13}C NMR ($CDCl_3$, proton decoupled): δ = 5.2 (s), 6.8 (s), 16.0 (d, J = 6.2 Hz), 16.3 (s), 17.1 (s), 17.5 (s), 34.6 (s), 34.7 (s), 40.4 (d, J = 129.3 Hz), 41.5 (s), 44.7 (s), 62.1 (d, J = 6.3 Hz), 80.6 (s), 113.7 (s), 142.1 (s), 205.3 (d, J = 6.3 Hz).

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