Use of Silyl Enol Ethers for the Synthesis of β-Acyl Anion Equivalents

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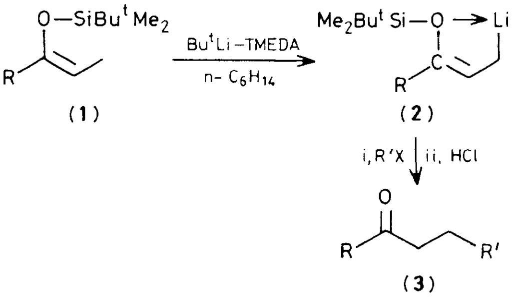
β-Acyl anion equivalents of certain ketones can be prepared directly from their silyl enol ethers by treatment with a strong base.

In recent years, a concerted effort has been made to develop reactive intermediates that would function as synthetic equivalents of β-acyl anions.[1] The recent publication of a multi-step procedure for the preparation of β-acyl anions of the general formula (**2**)[1a] prompts us to report that when R = Ph, the intermediate (**2**) can be obtained *directly* from the silyl enol ether (**1**) of the parent ketone, 1-phenylpropan-1-one, as shown below. The value of the present method resides not only in the fact that it provides the first direct procedure for the synthesis of a β-acyl anion equivalent from its parent ketone, but also because of its potential applicability to other carbonyl compounds.



Reaction of 1-phenylpropan-1-one with potassium hydride (1 equiv.) in tetrahydrofuran afforded the corresponding enolate which upon treatment with t-butyldimethylsilyl chloride in the presence of triethylamine gave the expected silyl enol ether (**1**; R = Ph)† [^{1}H n.m.r. ($CDCl_3$) δ 0.0 (s, 6H, Me), 1.1 (s, 9H, Bu^t), 1.8 (d, 3H, Me), 5.3 (q, 1H, vinylic), and 7.4 (m, 5H, ArH)] in virtually quantitative yield.

Conversion of the silyl enol ether (**1**) into its anion (**2**; R = Ph) was accomplished by treatment with t-butyl-lithium–tetramethylethylenediamine (TMEDA) in hexane or in hexane–cyclohexane.‡ In a typical experiment, t-butyl-lithium (20.2 mmol) and the silyl enol ether (**1**) (8.06 mmol) were added to hexane (or cyclohexane–hexane, 3 : 1) (50 ml) at −10 °C. To the resulting clear solution was added TMEDA (20.2 mmol) during 2 min. A yellow precipitate formed momentarily and subsequently dissolved to give a pale yellow solution. The mixture was stirred for 5 min at −10 °C; the cold bath was then removed and stirring was continued for an additional 30 min to give a clear orange-red solution. The mixture was then cooled to −5 °C, and 1-iodobutane (20.2 mmol) added. The mixture was stirred for 45 min, water (30 ml) added, and the organic layer treated with 6 M aqueous HCl to give heptanophenone in 62% yield.

The anion (**2**) was similarly treated with 1-iodopropane, 1-iodoethane, and iodomethane to give the expected β-substituted products (**4**) in good yields as shown.§

$PhC(:O)CH_2CH_2R$
(**4**)

	% Yield
a; R = Bu^n	62
b; R = Pr^n	68
c; R = Et	63
d; R = Me	66

It is clear that the successful overall transformation of 1-phenylpropan-1-one to its β-substituted derivatives (**4a**—**d**) depended critically on the efficient conversion of the silyl enol

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† New compounds were characterized on the basis of satisfactory elemental and spectroscopic analysis.

‡ All reactions involving air/moisture-sensitive compounds were carried out under an atmosphere of high purity nitrogen.

§ Yields are based on g.c. analysis (Hewlett–Packard, Model 5710A; thermal conductivity detector; 6 ft × 0.25 in column packed with 3% OV-17 on Chromosorb W HP 100/120) of several runs. In each case the products were further characterized by ^{1}H n.m.r. comparison with authentic samples.

ether (**1**) into its anion (**2**). By making use of the bulky t-butyldimethylsilyl group, it was possible to effect deprotonation of the allylic site of the intermediate (**1**) with virtually no cleavage of the silicon–oxygen bond.

1-Phenylbutan-1-one was also converted into its t-butyldimethylsilyl enol ether† [^{1}H n.m.r. ($CDCl_3$) δ 0.0 (s, 6H, Me), 1.1 (s, 9H, Bu^t), 1.25 (d, 3H, Me), 2.3 (m, 2H, CH_2), 5.2 (t, 1H, vinylic), and 7.5 (m, 5H, ArH)], which was treated with t-butyl-lithium–TMEDA as described above, except that the mixture was stirred for 3—6 h at room temperature, followed by excess of deuterium oxide. ^{1}H N.m.r. spectroscopy showed *ca.* 25% deuterium incorporation into the β-position of the product, indicating incomplete conversion of the silyl enol ether into the corresponding anion. Both steric and electronic effects are likely to have contributed to the lower acidity of the β-hydrogen atoms.

We are currently investigating the possible extension of this method to other carbonyl compounds, especially aldehydes.

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