A Silicon-based Protecting Group for the αβ-Unsaturation of αβ-Unsaturated Ketones†

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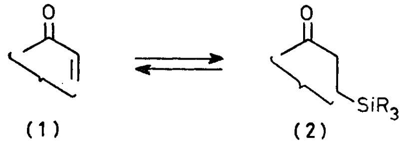
Summary Silyl-lithium reagents add to the β-position of αβ-unsaturated enones in the presence of copper(I) iodide, and the enone can be regenerated by treatment with copper(II) bromide.



(1) (2)

Still has reported[1] that trimethylsilyl-lithium adds at −78 °C in the presence of hexamethylphosphoric triamide to the conjugate position of αβ-unsaturated ketones (**1**) to give β-silyl ketones (**2**). We find that trimethylsilyl-lithium,[2] or the more easily prepared dimethylphenylsilyl-lithium,[3] add in the conjugate position of αβ-unsaturated ketones, aldehydes, and esters in the presence of copper(I) iodide (Table, column 2). Because our reaction takes place at −23 °C, a higher temperature than Still's, it works in some cases where his does not. Thus we find that cholestenone gives only 12% of the β-silyl ketone under Still's conditions, but 83% under ours; and Still himself

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† Reprints of this paper will not be available.

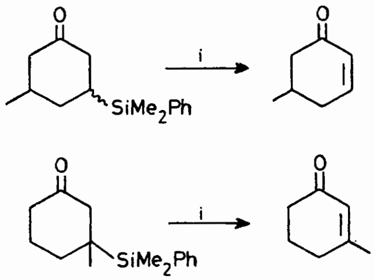
reported that isophorone gave recovered starting material, whereas we get 68% yield of the β-silyl ketone. Otherwise, his yields are comparable to or slightly better than ours.

TABLE. Yields of β-silylcarbonyl compounds (**2**) from enones (**1**) and of enones (**1**) regenerated from β-silyl ketones (**2**).

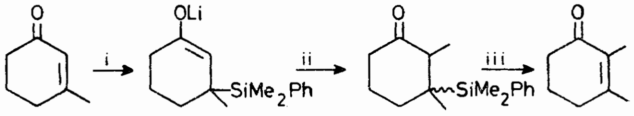
Starting material (**1**)	Yield of β-dimethyl-phenylsilyl carbonyl compound (**2**)[a] %	Yield of enone (**1**) from β-silyl ketone (**2**)[b] %
Methyl vinyl ketone . .	42	
Pent-3-en-2-one	85 (60[c])	
Mesityl oxide	84 (60[c])	69[d]
4-Phenylpent-3-en-2-one . .	68	43[d]
Cyclohex-2-enone	65 (64[c])	
3-Methylcyclohex-2-enone	99[e] (69[c])	72 (74[f])
5-Methylcyclohex-2-enone	97	70 (66[f])
Isophorone	68	
3-Methylcyclopent-2-enone	94	66 (68[f])
Cholest-4-en-3-one . .	83 (65[c])	
Ethyl crotonate	87	
Ethyl cinnamate	89	
Cinnamaldehyde	71	

[a] The silyl-lithium reagent (2 equiv.) and the copper(I) iodide (1 equiv.) were kept in tetrahydrofuran at −23 °C for 4 h, the enone (1 equiv.) was then added, and the mixture kept at −23 °C for 0·5 h. Should the silyl group to be transferred be precious, the yield based on silyl reagent can be improved by using only 1 equiv. and adding triethylamine after the reaction mixture has been kept at −23 °C for 0·5 h. The yield based on enone is usually rather lower with this method. [b] $CuBr_2$ (2 equiv.) at reflux for 0·75 h in 1 : 1 $CHCl_3$–EtOAc. [c] Yield for the corresponding reaction using trimethylsilyl-lithium and copper(I) iodide. [d] The β-bromoketone produced by treatment with $CuBr_2$ was converted into the enone by refluxing it in aqueous ethanol containing $NaHCO_3$. [e] Optimised yield; this product was crystalline, m.p. 66—67 °C. [f] Yield for the same reaction except that 1 equiv. of $CuBr_2$ was used together with 1 equiv. of benzoyl peroxide, and tetrahydrofuran was used as the solvent. These conditions avoid the production of HBr [N. Inukai, H. Iwamoko, T. Tamura, I. Yanagisawa, Y. Ishii, and N. Murakami, *Chem. and Pharm. Bull.* (*Japan*), 1976, **24**, 820].

As described in the preceding paper,[4] β-silyl ketones (**2**) are masked $\alpha\beta$-unsaturated ketones. Bromination should therefore convert the products of the copper-induced additions back into $\alpha\beta$-unsaturated ketones. We find that copper(II) bromide is particularly effective in the case of cyclic ketones, giving $\alpha\beta$-unsaturated ketones (**1**) directly (Table, column 3). With open-chain ketones, the products were the β-bromoketones, but these could be converted into the $\alpha\beta$-unsaturated ketones by treatment with mild base. Thus the easy addition and removal of a silyl group is *a way of protecting the $\alpha\beta$-unsaturation of an $\alpha\beta$-unsaturated ketone.*



SCHEME 1. Reagent: i, $CuBr_2$–$CHCl_3$–EtOAc



(**3**) (**4**)

SCHEME 2. Reagents: i, $PhMe_2SiLi$–CuI; ii, MeI; iii, $CuBr_2$

The two cases shown in Scheme 1 also demonstrate that the double bond is restored specifically to the side on which the silyl group is placed, and the sequence shown in Scheme 2 shows how the intermediate (**3**), produced by the addition of the silyl group, can be used for further synthetic steps without interference from the silyl group. The alkylation step, (**3**) → (**4**), is, however, limited to reactive halides like methyl iodide and allyl bromide, a common observation with relatively hindered enolates.

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[4] I. Fleming and J. Goldhill, *J.C.S. Chem. Comm.*, 1978, 176 (preceding communication).