Conjugate Addition of Tris(phenylthio)methyl-lithium to αβ-Unsaturated Ketones. Synthesis of γ-Keto-esters

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Summary Conjugate addition of (**1**) to unhindered αβ-unsaturated ketones proceeds in good yield to produce γ-keto-orthothioesters.

Carbanions, stabilized by adjacent sulphur atoms, have been extensively used in organic synthesis.[1] Their reaction with αβ-unsaturated ketones generally results in carbonyl (1,2) addition rather than conjugate (1,4) addition.[2] We report that tris(phenylthio)methyl-lithium (**1**) reacts in a conjugate fashion with unhindered αβ-unsaturated ketones producing γ-keto-orthothioesters which are in turn readily hydrolysed to γ-keto-esters. Thus the anion of reagent (**1**) can be considered as an ester carbanion equivalent (*i.e.* $RO\bar{C}{=}O$).

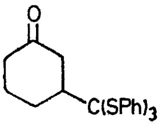
Triphenyl orthothioformate (**2**)[3] is rapidly deprotonated to the anion (**1**)[3–5] by treatment with n-butyl-lithium in tetrahydrofuran at −78 °C under nitrogen. Addition of cyclohex-2-enone (1 equiv.) to this solution followed by hydrolytic workup affords compound (**3**) in good yield (Table) which is converted into the ester (**4**)[6] (95%) by Hg^{2+} catalysed methanolysis[7] followed by acid treatment.[8]

Table

Reaction of αβ-unsaturated ketones with (**1**).

Substrate	Yield (%)[a]
Cyclohex-2-enone	95, 50[b,c]
2-Methylcyclohex-2-enone . .	85
5,5-Dimethylcyclohexenone . .	65
PhCH=CHCOMe	60
PhCH=CHCOPh	95
$PhCH{=}CHCOCMe_3$	85
MeCH=CHCOMe	65
3-Methylcyclohex-2-enone . .	<5[b]
$Me_2C{=}CHCOMe$	<5[b]

[a] Isolated yield of γ-keto-orthothioester unless otherwise stated. [b] Determined by n.m.r. analysis of the crude reaction product mixture. [c] Using the sodium salt (**5**).



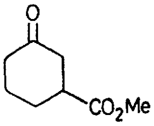
(3)

(PhS)$_3$CX

(1) X = Li

(2) X = H

(5) X = Na



(4)

Reduction of (**3**) with Raney nickel gives 3-methylcyclohexanone (70%).

Results of the reaction of (**1**) with various $\alpha\beta$-unsaturated ketones are listed in the Table. The yields of γ-keto-orthothioesters are satisfactory except for hindered $\beta\beta$-disubstituted enones. The use of the sodium salt (**5**), prepared from (**2**) and sodium bistrimethylsilylamide,[9] gives significantly lower yields of orthothioester. Reaction of (**1**) with unsaturated aldehydes gives products resulting from 1,2 addition.[10]

The ready availability of (**2**) combined with the variety of possible transformations[11] of the orthothioester unit make (**1**) and related compounds potentially useful synthetic reagents.

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[2] For other reports of 1,4 addition of sulphur-stabilized carbanions to $\alpha\beta$-unsaturated ketones see: T. Mukaiyama, K. Narasaku, and M. Furusato, *J. Amer. Chem. Soc.*, 1972, **94**, 8641; J. E. Richman, J. L. Herrmann, and R. H. Schlessinger, *Tetrahedron Letters*, 1973, 3271.

[3] A. Fröling and J. F. Arens, *Rec. Trav. Chim.*, 1962, **81**, 1009.

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[5] G. A. Wildschut, H. J. T. Bos, L. Brandsma, and J. F. Arens, *Monatsh.*, 1967, **98**, 1043.

[6] D. K. Banerjee, J. Dutta, and G. Bagavant, *Proc. Indian Acad. Sci.*, 1957, **46**A, 80; H. O. House, R. A. Latham, and C. D. Slater, *J. Org. Chem.*, 1966, **31**, 2667.

[7] R. A. Elisson, W. D. Woessner, and C. C. Williams, *J. Org. Chem.*, 1972, **37**, 2757.

[8] M. Janot, X. Lusinchi, and R. Goutarel, *Bull. Soc. chim. France*, 1961, 2109.

[9] U. Wannagat and H. Niederprum, *Chem. Ber.*, 1961, **94**, 1540.

[10] For the reaction of (**1**) with saturated aliphatic and aromatic aldehydes see ref. 4.

[11] *E.g.* R. H. DeWolfe, 'Carboxylic Ortho Acid Derivatives,' Academic Press, New York, 1970, ch. 6.