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A NEW AND CONVENIENT SYNTHESIS OF TRISUBSTITUTED α,β-UNSATURATED CARBOXYLIC ESTERS

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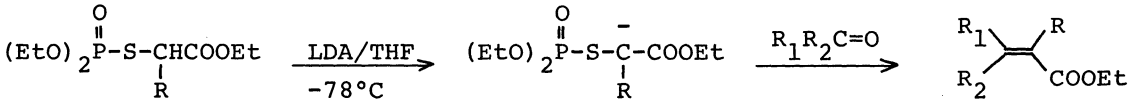
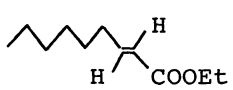
A new and single-step method for the synthesis of trisubstituted α,β-unsaturated esters using the lithium enolates of *S*-1-ethoxycarbonylethyl diethyl phosphorothioate (Ib) and *S*-1-ethoxycarbonylbutyl diethyl phosphorothioate (Ic) has been developed.

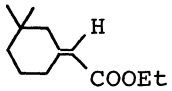
The widespread occurrence of the α,β-unsaturated esters and their derivatives in a variety of biological active natural products has stimulated considerable interest in the development of new synthetic methods for their construction. Although a number of methods for preparing mono- and disubstituted esters are known,[1] synthetic approaches to trisubstituted analogues are few in number and for the most part of limited applicability.[2] We report here an extremely facile method for preparation of a variety of trisubstituted α,β-unsaturated esters utilizing the lithium enolates IIb and IIc.

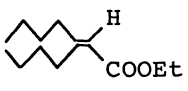


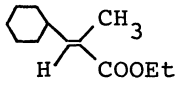
Ia: R=H IIa: R=H
Ib: R=CH_3 IIb: R=CH_3
Ic: R=$CH_3CH_2CH_2$ IIc: R=$CH_3CH_2CH_2$

The following is a typical experimental procedure. To a solution of LDA (22 mmol) in 40 ml of dry THF at -78°C was added dropwise under nitrogen a solution of Ib (20 mmol) in 5 ml of dry THF. After stirring for 30 min, a solution of cyclohexanone (25 mmol) in 3 ml of THF was added and the reaction mixture was stirred at -78°C for 1 h and at room temperature for 1 h. Aqueous workup gave a 90% yield of ethyl 2-cyclohexylidenepropionate. Table I summarized the trisubstituted α,β-unsaturated esters prepared in this way. The lithium enolates (IIa-IIc), of course, are effective reagents for the synthesis of mono- and disubstituted α,β-unsaturated esters as shown below.

 (65%; *E*/*Z*=79/21)

 (81%; *E*/*Z*=48/52)

 (72%)

 (90%; *E*/*Z*=55/45)

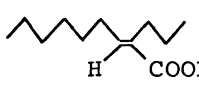
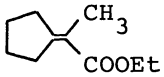
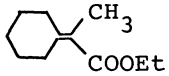
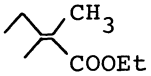
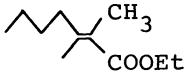
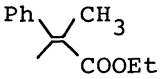
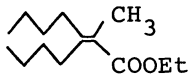
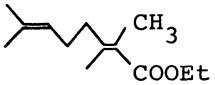
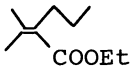
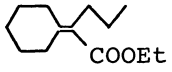
 (95%; *E*/*Z*= 54/46)

Table I. Product yields obtained by reaction of carbanion II with carbonyl compounds

Carbanion (II) R	Carbonyl compound	Reaction (°C), (h)	Product	Yield [%]	*E/Z* Ratio	b.p. °C/Torr
CH_3	Cyclopentanone	-78, 1 25, 4		60		67/1.3
CH_3	Cyclohexanone	-78, 1 25, 1		90		71-72/1.0
CH_3	2-Butanone	-78, 1 25, 4		74	50/50	73.5/13
CH_3	2-Hexanone	-78, 1 25, 4		74	45/55	88-100/10
CH_3	Acetophenone	-78, 1 25, 4		77	71/29	86/1.2
CH_3	5-Nonanone	-78, 1 25, 4		38		92/1.2
CH_3	6-Methyl-5-hepten-2-one	-78, 1 25, 4		85	45/55	86.5-88.5/1.3
$CH_3CH_2CH_2$	Acetone	-78, 1 25, 4		40		91-92/22
$CH_3CH_2CH_2$	Cyclohexanone	-78, 3.5 25, 3		60		85/0.9

The present route to trisubstituted α,β-unsaturated esters is attractive because of the mild reaction conditions, experimental simplicity, and reasonable yields (isolated).

References and Notes

1) a) G. Wittig and W. Haag, Chem. Ber., 88, 1654 (1955). b) W. S. Wadsworth, Jr. and W. D. Emmons, J. Am. Chem. Soc., 83, 1733 (1961). c) S. L. Hartzell, D. F. Sullivan, and M. W. Rathke, Tetrahedron Lett., 1974, 1403. d) K. Shimoji, H. Taguchi, K. Oshima, H. Yamamoto, and H. Nozaki, J. Am. Chem. Soc., 96, 1620 (1974); H. Taguchi, K. Shimoji, H. Yamamoto, and H. Nozaki, Bull. Chem. Soc. Jpn., 47, 2529 (1974). e) K. Tanaka, R. Tanikaga, and A. Kaji, Chem. Lett., 1976, 917.

2) a) G. Gallagher, Jr. and R. L. Webb, Synthesis, 1974, 122, and references cited therein. b) K. Tanaka, N. Yamagishi, R. Tanikaga, and A. Kaji, Chem. Lett., 1977, 471.

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