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NEW REAGENTS FOR THE SYNTHESIS OF α,β-UNSATURATED ESTERS: LITHIATED *O*-ALKYL *S*-ETHOXYCARBONYLMETHYL DITHIOCARBONATE AND THIOCARBONATE

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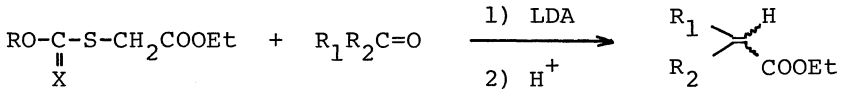
α,β-Unsaturated esters have been easily synthesized in good yields by treating carbonyl compounds with *O*-alkyl *S*-ethoxycarbonylmethyl dithiocarbonates or thiocarbonate in the presence of lithium diisopropylamide. The key intermediates for the synthesis of the recently isolated boll weevil sex pheromone were prepared in good yields by this method.

In the preceding papers, we have reported the several new routes to thiiranes from carbonyl compounds using sulfur-stabilized carbanions.[1,2] Especially, the procedure utilizing the lithium derivatives of *O*-alkyl *S*-methyl dithiocarbonates has the following advantages: (1) the starting materials are cheap and easily prepared in high yields; (2) carbanions are smoothly generated on treatment of the dithiocarbonates with lithium diisopropylamide (LDA), and are highly reactive to aldehydes and ketones; (3) chiral lithium reagent derived from (-)-menthol is also readily available;[2] and (4) work-up is quite simple because by-product (COS) is virtually eliminated.

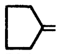
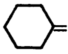
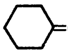
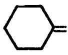
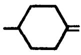
We wish to report here a new and useful method for the synthesis of α,β-unsaturated esters from carbonyl compounds by the use of lithium reagents derived from *O*-alkyl *S*-ethoxycarbonylmethyl dithiocarbonates or thiocarbonate (I).



I (R=Et, i-Pr; X=O, S)

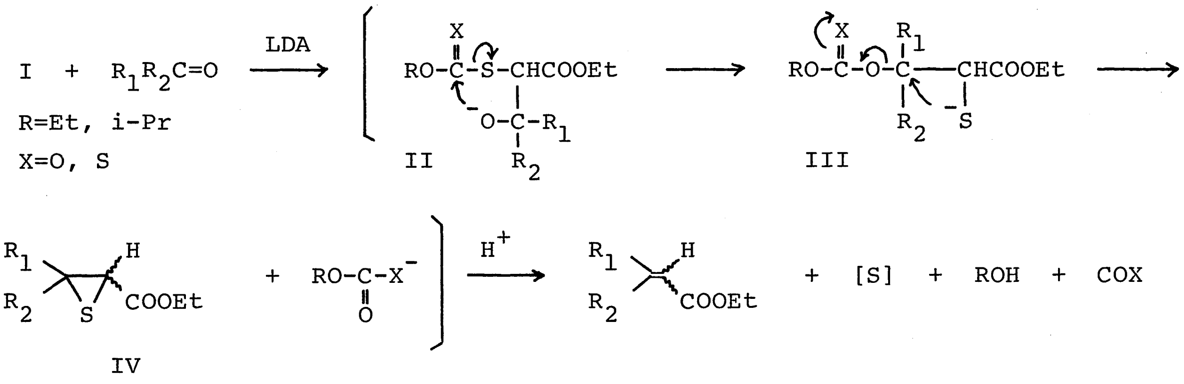
The typical procedure is described for the synthesis of ethyl cyclopentylideneacetate. To a stirred solution of LDA (20 mmol) in dry THF (40 ml) was added the readily available *O*-ethyl *S*-ethoxycarbonylmethyl dithiocarbonate$^{3)}$ (20 mmol) in 3 ml of dry THF at -78°C under nitrogen. After 30 min at -78°C, cyclopentanone (24 mmol) in 2 ml of dry THF was added dropwise. The reaction mixture was stirred at -78°C for 1 hr and at room temperature for 1 hr, diluted with ether, poured into dilute hydrochloric acid, and extracted with ether. The combined organic extracts were washed successively with water and brine, then dried over Na_2SO_4 and concentrated. Distillation under reduced pressure gave ethyl cyclopentylideneacetate in 88% yield; none of the isomerized β,γ-unsaturated esters were detected. In a similar manner, various α,β-unsaturated esters were synthesized in good yields as shown in Table 1.

Table 1. Reaction of carbonyl compounds with carbanions (I).

Carbonate, I R	 X	$R_1R_2C=O$	Product	Yield$^{a)}$ %	E/Z$^{b)}$
Et	S	Propionaldehyde	H(Et)C=CHCOOEt	52	E only
Et	S	Acetone	Me(Me)C=CHCOOEt	85	
Et	S	Ethyl methyl ketone	Me(Et)C=CHCOOEt	74	39/61
Et	O	Ethyl methyl ketone	Me(Et)C=CHCOOEt	71	61/39
i-Pr	S	Ethyl methyl ketone	Me(Et)C=CHCOOEt	67	47/53
Et	S	Diethyl ketone	Et(Et)C=CHCOOEt	69	
Et	S	Acetophenone	Ph(Me)C=CHCOOEt	76	43/57
Et	S	Cyclopentanone	=CHCOOEt	88	
Et	S	Cyclohexanone	=CHCOOEt	78	
Et	O	Cyclohexanone	=CHCOOEt	61	
i-Pr	S	Cyclohexanone	=CHCOOEt	81	
Et	S	4-Methylcyclohexanone	CH_3=CHCOOEt	87$^{c)}$	

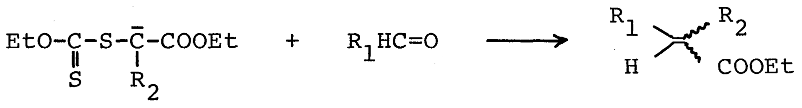
a) Isolated yields. b) Determined by GLPC and NMR. c) THF-HMPA (8:1) was used as a solvent.

The proposed mechanism for this reaction involves: (1) rearrangement of an adduct (II) to III; (2) subsequent conversion of III to thiirane species (IV); and (3) elimination of sulfur to give α,β-unsaturated esters.



The intermediate 2-hexyl thiirane was isolated in 71% yield, when heptanal was treated with lithium salt of *O*-(4-*t*-butylcyclohexyl) *S*-methyl dithiocarbonate.[1] The electron-withdrawing groups such as COOR and C=O promote a facile elimination of sulfur to form olefins.[4,5]

We also found that the sterically hindered carbanions derived from α-alkylated dithiocarbonates (V) reacted smoothly with aldehydes[6] to afford α,β-unsaturated esters in good yields as shown in Table 2.



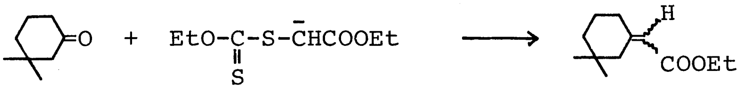
V (R_2=Me, Et)

Table 2. Reaction of aldehydes with carbanions (V).

Carbanion V, R_2	$R_1HC=O$	Product	Yield %	E/Z[b]
Me	Benzaldehyde	Ph(H)C=C(Me)COOEt	82	21/79
Et	Benzaldehyde	Ph(H)C=C(Et)COOEt	82	37/63
Me	Isobutyraldehyde	i-Pr(H)C=C(Me)COOEt	78	59/41
Me	Isobutyraldehyde	i-Pr(H)C=C(Me)COOEt	84[c]	11/89
Et	Isobutyraldehyde	i-Pr(H)C=C(Et)COOEt	82	42/58
Et	Isobutyraldehyde	i-Pr(H)C=C(Et)COOEt	91[c]	46/54

a) Isolated yields. b) Determined by GLPC and NMR. c) THF-HMPA (8:1) was used as a solvent.

To demonstrate the efficiency of our new reagents, we have carried out the synthesis of the key intermediates for the synthesis of components of the boll weevil sex pheromone, which have recently isolated and identified.[7)] When 3,3-dimethylcyclohexanone was treated with the carbanion derived from I (R=Et, X=S) in a similar procedure described above, the corresponding ester (VI) was isolated in 84% yield; bp 124-128°C/22 mmHg; IR(neat) 1715 (ester), 1645 cm^{-1} (C=C); MS (m/e) 196(M^+); NMR(CCl_4) δ 0.95 (two CH_3), 5.45, 5.60 (C=CH). The spectral data of VI agreed with the reported literature values.[7)] Separation of VI and conversion to components of the target pheromone have been already established.[8)]



VI

84% (E/Z=73/27)

In conclusion, it is noted that our procedure reported here provides the unique and new route to α,β-unsaturated esters from carbonyl compounds in a simple manner.

Studies on the scope and limitations of this reaction are now in progress in our laboratory.

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References and Notes

(1) C. R. Johnson, A. Nakanishi, N. Nakanishi, and K. Tanaka, Tetrahedron Lett., 1975, 2865.

(2) C. R. Johnson and K. Tanaka, Synthesis, 1976, in press.

(3) *O*-Ethyl *S*-ethoxycarbonylmethyl dithiocarbonate was prepared from ethanol, KOH, carbon disulfide, and ethyl bromoacetate in 92% yield.

(4) T. Hayashi, Bull. Chem. Soc. Jpn., 45, 1507 (1972).

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(6) Unfortunately, lithium reagents (V) failed to react with ketones under similar conditions, probably due to the steric hindrance.

(7) S. W. Pelletier and N. V. Mody, J. Org. Chem., 41, 1069 (1976), and references cited therein.

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