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(ALLYLTHIO)ACETATE DIANION AS A NEW AND CONVENIENT REAGENT FOR THE STEREOSELECTIVE SYNTHESIS OF (2*E*,4*E*)DIENOATES FROM ALKYL HALIDES

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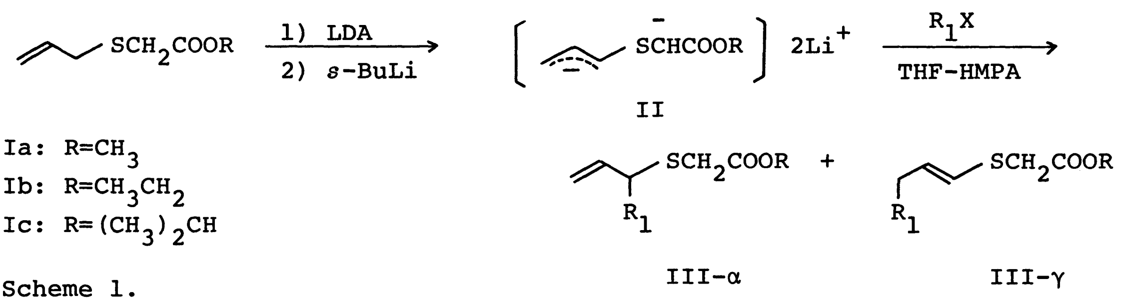
Treatment of (allylthio)acetate with lithium diisopropylamide followed by the addition of *s*-butyllithium produced a new dianion which could react with a variety of alkyl halides exclusively at the allylic position. The high regioselectivity of the allylic alkylation could be realized in the case of methyl (allylthio)acetate dianion. A convenient and general method for the stereoselective synthesis of (2*E*,4*E*)dienoates from alkyl halides has been developed.

As (2*E*,4*E*)dienoates are valuable synthetic intermediates for naturally occurring compounds such as insecticide,1) insect pheromone,2) and prostaglandin nucleus,3) the method which allows for their construction has been a topic of current interest.1,4)

We now report the highly efficient stereoselective synthesis of (2*E*,4*E*)dienoates starting from a new dianion derived from readily available (allylthio)acetate5) and alkyl halides. The dianion can be efficiently prepared by treatment of (allylthio)acetate (I) with lithium diisopropylamide (LDA) and then *s*-butyllithium in THF at -78°C (Scheme 1).



II

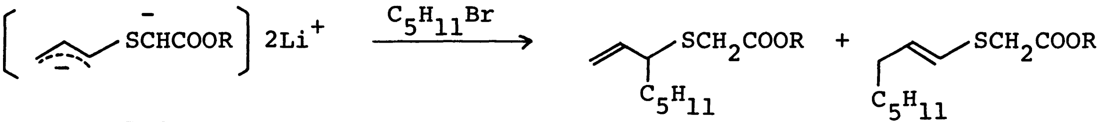
Ia: R=CH_3
Ib: R=CH_3CH_2
Ic: R=$(CH_3)_2CH$

III-α

III-γ

Scheme 1.

The dianion thus formed reacted with a variety of alkylating agents at -78°C exclusively at the allylic position to give monoalkylated products of type III after aqueous workup. We have found that the α- and γ-regioselectivity of allylic alkylation is strongly dependent on the size of ester groups (R) (Scheme 2).



IIa: R=CH_3
IIb: R=CH_3CH_2
IIc: R=$(CH_3)_2CH$
IId: R=$(CH_3)_3C$

Scheme 2.

	α-isomer(%)	γ-isomer(%)
IIIa:	90	10
IIIb:	80	20
IIIc:	72	28
IIId:	0[6]	0[6]

The high α-regioselectivity could be realized in the reaction of methyl (allylthio)acetate dianion (IIa). The ratio of α- vs. γ-substituted products and the yields are summarized in Table 1.

Table 1. Regioselectivity in the alkylation of dianion II

Dianion	Alkyl halide[a] R_1X	Yield of III[b] (%)	III-α/III-γ[c] Ratio
IIa	$CH_3(CH_2)_4Br$	68	90/10
IIa	$CH_3(CH_2)_4Cl$	60	93/7
IIa	$CH_3(CH_2)_5Br$	75	90/10
IIa	$CH_3(CH_2)_6Br$	70	88/12
IIa	$(CH_3)_2CHCH_2CH_2Br$	67	85/15
IIa	$CH_3(CH_2)_2CH(CH_3)Br$	52	80/20
IIa	$c\text{-}C_6H_{11}Br$	54	87/13
IIb	$CH_3(CH_2)_4Br$	69	80/20
IIb	$CH_3(CH_2)_4Cl$	42	84/16
IIb	$CH_3(CH_2)_4I$	54	71/29
IIb	$CH_3(CH_2)_6Br$	57	82/18
IIc	$CH_3(CH_2)_4Br$	48	72/28

a) Alkylation reactions were carried out at -78°C in THF in the presence of HMPA as a cosolvent. b) Isolated yields. c) Determined by GLC and ^{1}H-NMR analyses of the isolated products.

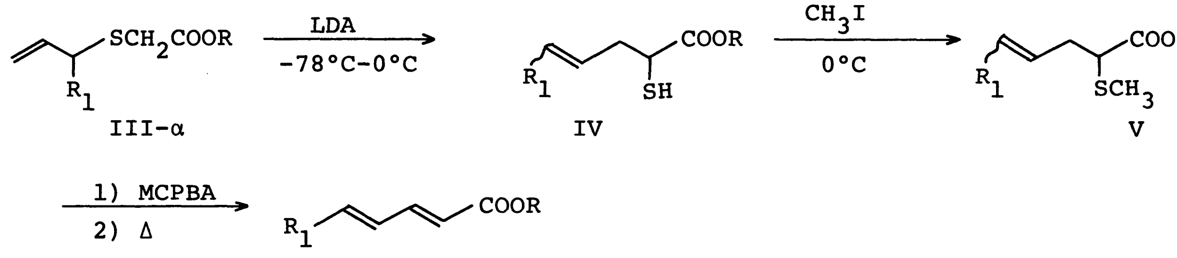
In contrast to the facile alkylation of dianions IIa-IIc, no alkylated products were observed by ^{1}H-NMR and GLC when ethyl (allyloxy)acetate (Ie) was treated in the similar manner as described above.

$OCH_2COOC_2H_5$

Ie

Conversion of the alkylated products III to the corresponding (2*E*,4*E*)dienoates VI was accomplished in the following manner. Treatment of III with LDA at -78°C for 30 min and then at 0°C for 5h in THF resulted in

[2,3]-sigmatropic rearrangement[7)] and formation of 2-mercaptocarboxylic esters IV. Reaction of IV with methyl iodide in the presence of sodium alkoxide at 0°C gave 2-(methylthio)carboxylic esters V in high yields (Scheme 3). We have found that the *E*/*Z* ratio of esters V could be unequivocally determined by GLC *with a 30 m glass capillary column.*[8)] Oxidation of V with *m*-chloroperbenzoic acid at -78°C in dichloromethane gave sulfoxides, and dehydrosulfenylation[9)] of the resulting sulfoxides in refluxing benzene solution containing powdered calcium carbonate for 24h afforded the desired (2*E*,4*E*)dienoates VI[10)] in good isolated yields.



Scheme 3.

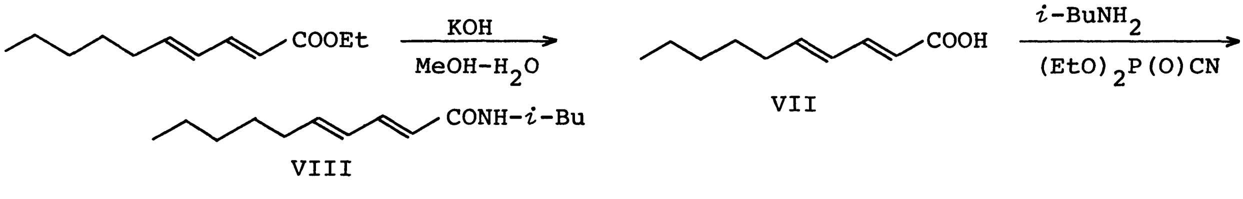
The results of these sequences are summarized in Table 2.

Table 2. Yields of compounds IV, V, and VI

III-α R	R$_1$	IV[a)] Yield(%)	V Yield(%)	V *E*/*Z* Ratio	VI[a)] Yield(%)	VI 2*E*,4*E*/other isomers[b)]
CH_3	$CH_3(CH_2)_4$	87	95	93/7[b)]	89	87/13
CH_3	$CH_3(CH_2)_5$	66	95	92/8[b)]	79	88/12
CH_3	$CH_3(CH_2)_6$	72	95	92/8[b)]	75	83/17
CH_3	$(CH_3)_2CHCH_2CH_2$	76	100	95/5[b)]	61	91/9
CH_3	$CH_3(CH_2)_2CH(CH_3)$	74	100	95/5[b)]	78	93/7
CH_3	c-C_6H_{11}	66	100	100/0[b)]	78	84/16
C_2H_5	$CH_3(CH_2)_4$	84	98	93/7[c)]	81	86/14
C_2H_5	$CH_3(CH_2)_6$	89	95	d	79	89/11

a) Isolated yields. b) Determined by GLC with a 30 m glass capillary column. c) Determined by HPLC and ^{13}C-NMR. d) Not determined.

Ethyl (2*E*,4*E*)decadienoate can serve as a valuable precursor for the synthesis of pellitorine, an insecticidal compound from *Anacyclus pyrethrum.*[1)] Thus, alkaline hydrolysis of ethyl (2*E*,4*E*)decadienoate[11)] produced pure acid VII, mp 48.5-49.5°C, in 69% yield after recrystallization.



Reaction of VII with isobutylamine in the presence of diethyl phosphorocyanidate in DMF gave pure pellitorine in 60% isolated yield,12) which exhibited spectral properties in agreement with the published data.1)

The present methodology allows an efficient route to the synthesis of highly functionalized materials from the readily available starting substances. In these synthetic sequences, the dianion II provides the structural equivalent of δ-carbanion of (*2E*,*4E*)pentadienoate.

Synthetic applications of these new dianions are under investigation.

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5) Methyl (allylthio)acetate was prepared in 83% yield from allyl bromide and methyl mercaptoacetate. Other (allylthio)acetates were prepared in a similar manner.
6) *t*-Butyl 2-pentylthio-4-pentenoate was isolated in 41% yield and the starting ester Id was recovered (31%).
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8) GLC analyses were performed on a Simadzu Model GC-6AM gas chromatograph with a flame ionization detector using a 30 m x 0.3 mm SS-4 glass capillary column.
9) For an excellent review, see: B. M. Trost, Chem. Rev., 78, 363 (1978).
10) The stereochemistry of the dienoates was firmly assigned from the ^{1}H-NMR (δ 5.62, d, 1H, J=15Hz, olefin)4b) and IR spectra.1b)
11) Purified by silica gel chromatography (>95% pure).
12) Mp 90.5-91.5°C. Anal. Found: C, 75.16; H, 11.23; N, 6.32%. Calcd for $C_{14}H_{25}NO$: C, 75.28; H, 11.28; N, 6.27%.

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