Mechanism of Formation of α,β-Unsaturated Esters in the Reaction of Ethyl Mercaptoacetate Dianion with Carbonyl Compounds

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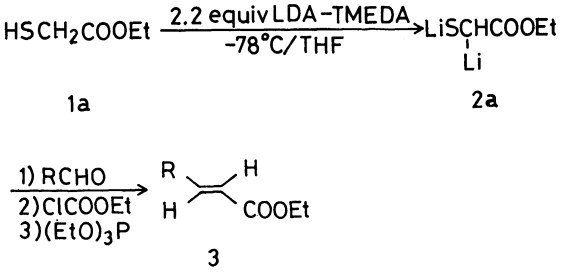
Dianion derived from ethyl mercaptoacetate undergoes aldol type reaction with a carbonyl compound to give an adduct, which exhibited low diastereoselectivity. However, the adducts obtained by the reaction with a variety of aldehydes were subsequently treated with ethyl chloroformate in the presence of trivalent phosphorus compound to give (*E*)-isomers of α,β-unsaturated esters in high yields with greater than 85% stereoselectivity regardless of the stereochemistry of the diastereomers of the adducts. The stereochemical mechanism and application of this reaction were studied in detail.

Recently, it has been reported in the communication[1] that, when trivalent phosphorus compound was used as a desulfurization agent, the (*E*)-products of α,β-unsaturated esters can be synthesized in high yields with high stereoselectivity by treating aldehydes with dianion derived from ethyl mercaptoacetate (**1a**). This finding would account for the mechanism of this reaction which involves the intramolecular cyclization to thiirane as an intermediate, followed by extrusion of sulfur to **3**.

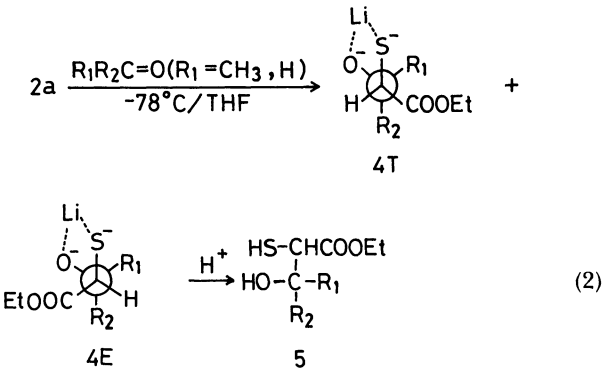


(1)

In the present study the author has observed that the aldol adducts were obtained in good yields by the reaction of **2a** with aldehydes, exhibiting consistently low diastereoselectivity. However, the reaction of the low diastereomeric mixture of the aldol products with 2.2 equiv of the base gave α,β-unsaturated esters of high stereoselectivity after treating with ethyl chloroformate and triethyl phosphite. In this paper the studies on the mechanism of the stereoselective formation of α,β-unsaturated esters and the application of this reaction to the synthesis of a component of royal jelly are described.

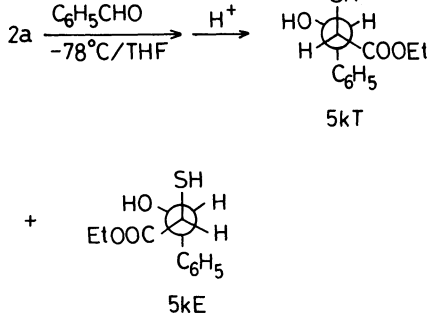
Results and Discussion

Aldol Condensation. Dianion (**2a**) undergoes aldol type reaction with a carbonyl compound to afford a mixture of diastereomers of an adduct (**4**). The conformations of aldol adduct, in which thiolate anion and alcoholate anion are gauche, are represented as **4T** and **4E** because of a chelation of lithium cation with both thiolate and alcoholate anion.[2] In order to determine the aldol diastereomer ratios (**4T** : **4E**), **2a** was treated with carbonyl compounds in THF at −78 °C for 2 h and quenched with saturated aqueous solution of ammonium chloride. The usual work-up and distillation afforded **5** in good yields.



(2)

Diastereomer ratios were determined by the ^{1}H-NMR spectra of the purified aldol product, using the well-established results that $J_{threo} > J_{erythro}$ and a chemical shift of threo isomer is higher than that of erythro isomer.[2a,3] For example, the ^{1}H-NMR spectrum of **5** derived from benzaldehyde shows the hydroxymethine proton at δ 4.70 (J=8.0 Hz) for threo isomer and at δ 4.82 (J=6.0 Hz) for erythro isomer. Integration of these protons showed that the ratio of threo isomer and erythro isomer was 60 : 40, being identical with the ratio obtained by capirally column GLC analysis (ratio=61 : 39). The stereochemical compositions of **5** prepared from various carbonyl compounds are summarized in Table 1. Next, the effect of reaction time of aldol condensation on the diastereomer ratio (**5kT** : **5kE**) of aldol adduct derived from benzaldehyde was investigated (Table 2).



(3)

Tables 1 (Entry 12) and 2 show that there is no obvious effect of reaction time and temperature on the diastereomer ratios. Thus, this aldol reaction was pre-

TABLE 1. ALDOL CONDENSATIONS OF DIANION (**2a**) WITH CARBONYL COMPOUNDS

Entry No.	$R_1R_2C=O$		Aldol product HS-CHCOOEt / HO-C-R_1 / R_2	Yield[a] %	erythro/threo[b] ratio
	R_1	R_2			
1	CH_3	n-C_4H_9	**5a**	73	38/62
2	CH_3	n-C_5H_{11}	**5b**	72	39/61
3	CH_3	n-C_6H_{13}	**5c**	85	43/57 (41/59)
4	CH_3	n-C_6H_{13}	**5d**	77[c]	54/46
5	CH_3	n-C_7H_{15}	**5e**	82	45/55
6	CH_3		**5f**	81	56/44
7	H	n-C_3H_7	**5g**	71	62/38 (62/38)
8	H	n-C_4H_9	**5h**	90	58/42 (54/46)
9	H	n-C_6H_{13}	**5i**	78	60/40
10	H	n-C_7H_{15}	**5j**	89	58/42 (59/41)
11	H		**5k**	73	40/60 (39/61)
12	H		**5k**	72[d]	31/69

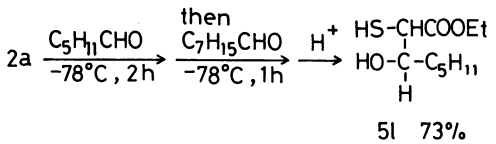
a) Isolated yields. b) Determined by ^{1}H-NMR. Values in parentheses were determined by GLC with a 30 m glass capirally column. c) Ethyl 2-mercaptopropionate dianion was used in the place of **2a**. d) Yield obtained by quenching the reaction after stirring at −78 °C for 1 h and then at room temperature for 1 h.

TABLE 2. EFFECT OF REACTION TIME ON THE DIASTEREOMER RATIO OF **5k**

Entry No.	Reaction time h	Yield of **5k**[a] %	**5kE**/**5kT**[b]
1	0.02	64	41/59
2	2	73	40/60
3	5	78	41/59
4	24	75	35/65

a) Isolated yields. b) Determined by ^{1}H-NMR.

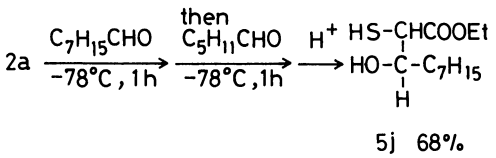
sumed to be kinetically controlled. Cross-over experiments which were attempted by adding another aldehydes to the reaction mixture produced no detectable cross-over product at −78 °C.



5l 73%

90%

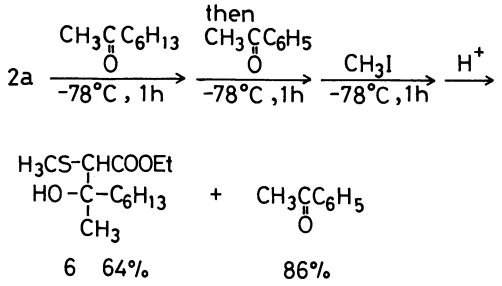
(4)



5j 68%

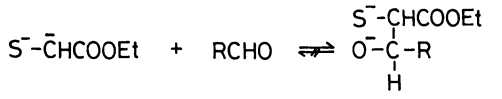
75%

(5)



(6)

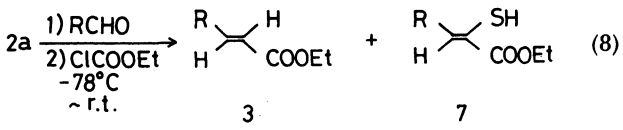
The carbonyl compound added first was always condensed with **2a** to afford **5l**, **5j**, and **6** in good yield, whereas the carbonyl compound added secondly was almost recovered. From these results, it is reasonable to consider that **4** is not in equilibrium with **2a** as follows (Eq. 7).



(7)

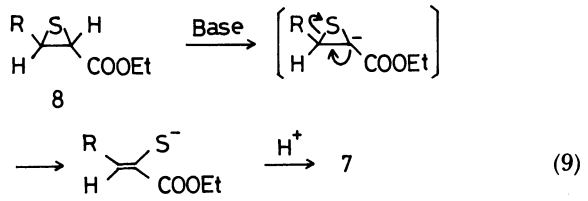
Generation of Thiirane Derivatives. It was found that a thioenol compound (**7**) could be isolated as a by-product in moderate yield in the reaction of **2a** with aldehydes, and that the formation of **7** was responsible for the low yield of **3** (Table 3). Yields of **7** were found to be strongly dependent on the reaction temperature after treating with ethyl chloroformate. For example, **7b** and **7d** were isolated in 41 and 68% yields respectively, by quenching the reaction at 10—15 °C after treating with ethyl chloroformate, whereas the yields of **7b** and **7d** were decreased to 22 and 53%, respectively, by quenching at 30—35 °C. On the other hand, **7** was not obtained by the reaction of **2a** with ketones. The structures of **7** were confirmed by their elemental analyses and spectral (IR, NMR) properties

(see Experimental). The *E*/*Z* ratio of **7** was determined by GLC and NMR analysis; *e.g.*, the ratio of (*E*)-isomer to (*Z*)-isomer of ethyl 2-mercapto-2-decenoate determined by integration of the olefinic proton at δ 6.59 and 5.83, respectively, is 93 : 7. Analysis of this material by GLC indicates a 94 : 6 mixture.



(8)

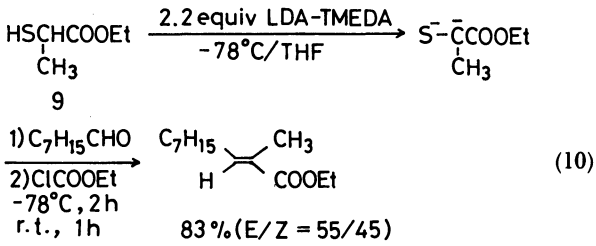
It is reasonable to assume that **7** is resulted from thiirane species (**8**) according to the following route (Eq. 9), since when trivalent phosphorus compound was added the formation of **7** was not observed and the yield of α, β-unsaturated ester (**3**) was increased.



(9)

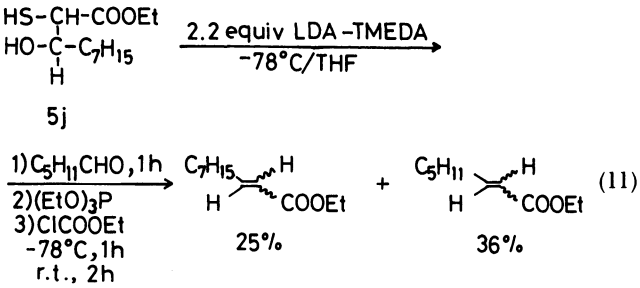
As anticipated, by the reaction of dianion derived from ethyl 2-mercaptopropionate (**9**) with aldehydes the thioenol compound was not obtained and α,β-unsaturated ester was isolated in high yield.

Attempts to isolate the thiirane species (**8**), however, were failed due to its unstability.



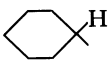
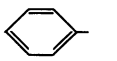
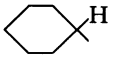
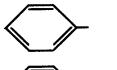
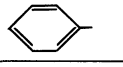
(10)

Retro-aldolization after Treating with ClCOOEt. When the adduct (**5j**) obtained by the reaction of **2a** with octanal was dilithiated with 2.2 equiv of LDA in the presence of TMEDA at −78 °C and followed by treating with hexanal and ethyl chloroformate in the presence of triethyl phosphite, ethyl 2-decenoate and ethyl 2-octenoate were obtained in 25 and 36% isolated yields, respectively. This scramble of carbonyl compound with **2a** demonstrates the retro-aldolization *after treating with ethyl chloroformate* (Eqs. 11, 12, 13, and 14).



(11)

TABLE 3. PRODUCT YIELDS OBTAINED BY THE REACTION OF DIANION (**2a**) AND MONOANIONS (**2b** AND **2c**)[a] WITH CARBONYL COMPOUNDS

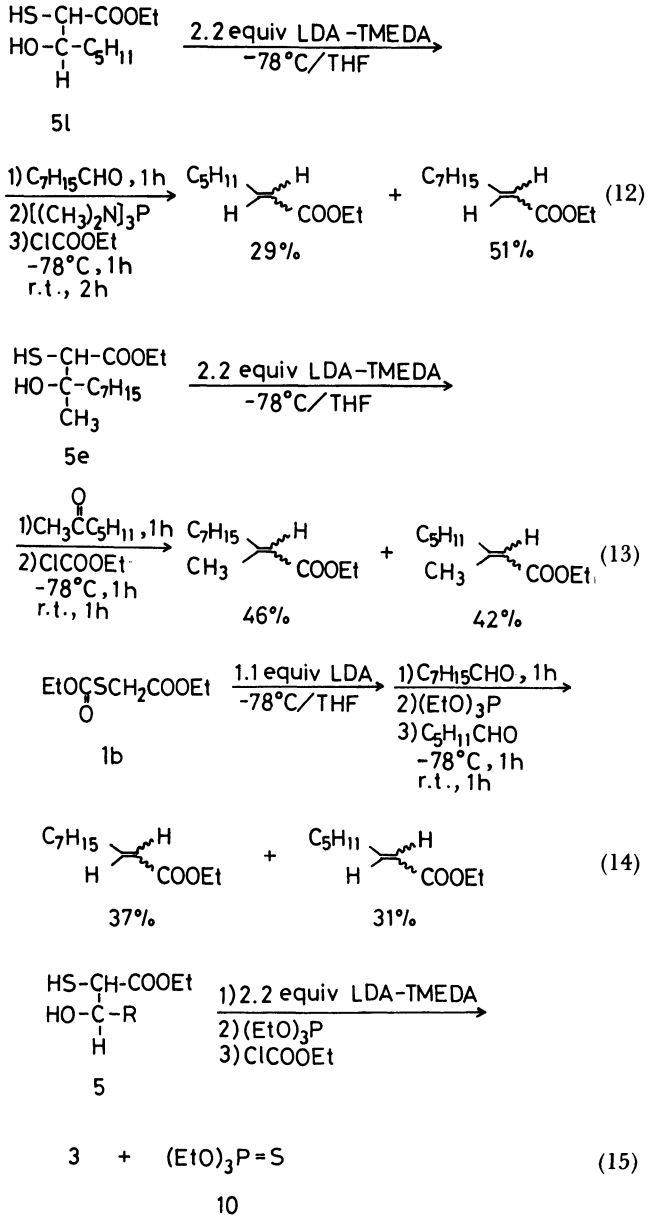
Entry No.	$XSCH_2COOEt$ X	$R_1R_2C=O$ R_1	R_2	Product (**3**)	Yield[b] %	*E*/*Z*[c] ratio	Product (**7**)	Yield[b] %	*E*/*Z*[c] ratio
1	H	H	*n*-C_5H_{11}	**3a**	51	92/8	**7a**	31	94/6
2	H	H	*n*-C_7H_{15}	**3b**	56 (54)[d]	91/9	**7b**	22 (41)[d]	94/6
3	H	H	*n*-C_9H_{19}	**3c**	50	90/10	**7c**	32	88/12
4	H	H		**3d**	35 (10)[d]	100/0	**7d**	53/(68)[d]	100/0
5	EtOC(=O)–	H	*n*-C_6H_{13}	**3e**	80	84/16	**7e**	18	82/18
6	EtOC(=O)–	H		**3f**	69	100/0	**7f**	11	100/0
7	EtOC(=O)–	H		**3d**	59	100/0	**7d**	27	100/0
8	$(EtO)_2P$(=O)–	H	*n*-C_9H_{19}	**3c**	78	93/7	**7c**	8	94/6
9	H	CH_3	*n*-C_3H_7	**3g**	72[e]	39/61		0	
10	H	CH_3	*n*-C_6H_{13}	**3h**	66	43/57		0	
11	H	CH_3		**3i**	61	100/0		0	
12	H	CH_2CH_3		**3j**	48	95/5		0	

a) Monoanions **2d** and **2c** were prepared by adding *O*-ethyl *S*-ethoxycarbonylmethyl thiocarbonate and *S*-ethoxycarbonylmethyl diethyl phosphorothioate to 1.1 equiv LDA in THF at −78 °C, respectively.[1] b) Isolated yields by column chromatography. c) Determined by ^{1}H-NMR and GLC. d) All reactions were quenched at −30—35 °C after treating with ethyl chloroformate. Yields in parentheses were obtained by quenching the reaction at 10—15 °C. e) A mixture of THF and TMEDA (8.0 equiv) was used as a solvent.

Table 4. Prepartion of α, β-unsaturated esters (3) from aldol adducts (5)

Entry No.	Aldol adduct (5)	erythro/threo[a] ratio	Product (3)	Yield[b] %	E/Z[c] ratio
1	**5g**	62/38	**3k**	70	88/12
2	**5h**	58/42	**3l**	88	90/10
3	**5i**	60/40	**3e**	81	89/11
4	**5j**	58/42	**3b**	73	92/8
5	**5k**	40/60	**3f**	80	100/0

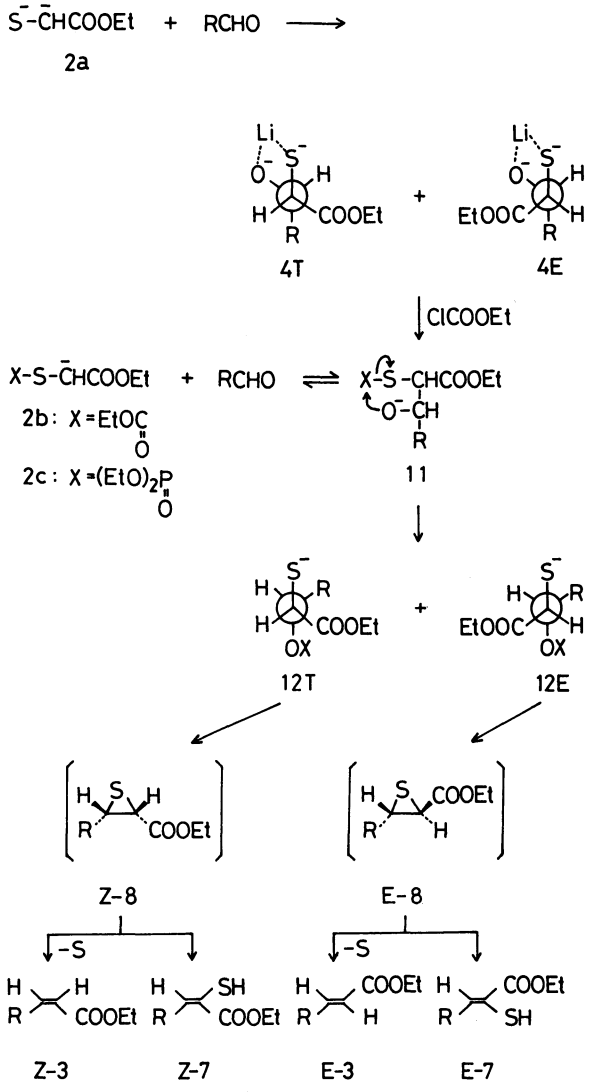
a) Determined by ^{1}H-NMR. b) Isolated yields. c) Determined by ^{1}H-NMR and GLC.



The aldol adducts (**5**) derived from carbonyl compounds afforded **3** in the following manner. These results were summarized in Table 4.

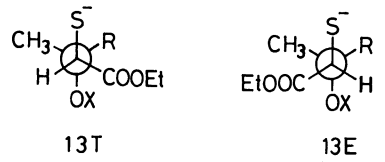
The substantial difference between the stereochemistry of **5** and the geometry of **3** was observed, that is, the predominant formation of (*E*)-α,β-unsaturated esters was observed.

Reaction Mechanism. It has been previously reported[4] that the mechanism of the reaction of **2a** with carbonyl compounds involves aldol type condensation, rearrangement of an adduct (**11**) to **12**, subsequent conversion of **12** to thiirane species (**8**), and elimination of sulfur to give α,β-unsaturated esters (**3**). The observations presented here would lead to the mechanism of the stereoselective formation of (*E*)-α,β-unsaturated esters.



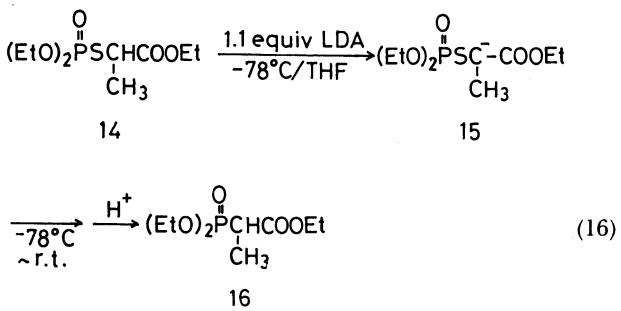
Scheme 1.

The aldol type condensation of **2a** with aldehydes exhibited low diastereoselectivity due to the kinetically controlled process, whereas the reaction after treating with ethyl chloroformate proceeded with high stereoselectivity to give (*E*)-isomer of **3**. This result can be rationalized by considering that a retroaldolization of **11** to **2b** is in competition with rearrangement of **11** to **12**, that is, the reaction after treating with ethyl chloroformate is the thermodynamically controlled process. In two possible stereoisomeric precursors (**12T** and **12E**) leading to **3** as shown in Scheme 1, if the conformer, in which the OCOEt and S^- groups are antiperiplaner, is favorable one for the subsequent intramolecular attack of S^- group and elimination of the OCOEt species, the orientation of R group is thus represented as **12T** and **12E**. The equiliblium between the stereoisomers **12T** and **12E** would surely favor **12E**, since the steric interaction between a bulky R group and an ethoxycarbonyl group is minimized in **12E**. On the other hand, the stereoisomer **12T**, in which the alkyl and ethoxycarbonyl group are gauche, would exhibit serve interactions. Thus, even if **12T** and **12E** should convert to (*Z*)-**3** and (*E*)-**3** stereospecifically, respectively,[5] the (*E*)-isomers of monosubstituted α,β-unsaturated esters would be predominantly obtained regardless of the stereochemistry of the aldol adduct (**4**) in the reaction of **2a** with aldehydes. On the other hand, in the reaction of **2a** with ketones, almost 1 : 1 mixture of geometrical isomers of disubstituted analogue was obtained.[4] Since in the conformers **13T** and **13E** (Scheme 2), the difference in steric interaction would be diminished by an introduction of methyl group in the place of hydrogen atom.



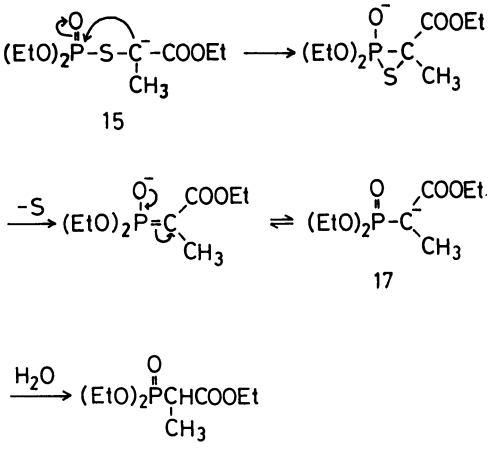
Scheme 2.

Reactivity of S-[1-(Ethoxycarbonyl)ethyl] Diethyl Phosphorothioate Carbanion. An already-published report described the efficient synthesis of trisubstituted α,β-unsaturated esters, starting from *S*-[1-(ethoxycarbonyl)ethyl] diethyl phosphorothioate (**14**).[6] To study the reactivity of **14**, the author treated *S*-[1-(ethoxycarbonyl)ethyl] diethyl phosphorothioate with 1.1 equiv of LDA in THF at −78 °C. The resulting carbanion (**15**) afforded ethyl 2-(diethoxyphosphinyl)-propionate (**16**) in 88% yield upon quenching with saturated aqueous solution of ammonium chloride after warming to room temperature (Eq. 16).



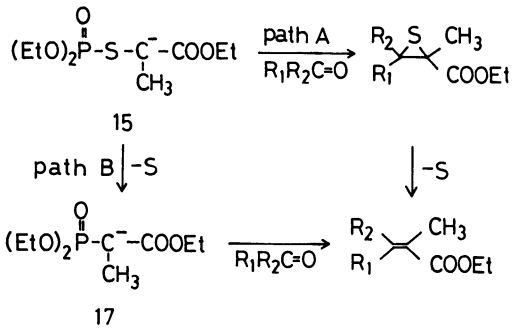
(16)

The mechanism of the formation of **16** is proposed as follows (Scheme 3).



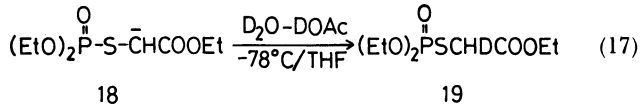
Scheme 3.

Therefore, two routes are taken into consideration for the reaction of **15** with carbonyl compounds to afford α,β-unsaturated esters (Scheme 4).



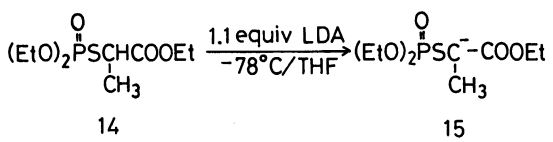
Scheme 4.

One is path A that proceeds *via* thiirane species as intermediate, another is path B where the product (**16**) acts as Emmons-Wadsworth reagent[7] and undergoes Wittig reaction.[8] In order to clarify the mechanism, the carbanion **18** was quenched with deuterium oxide and acetic acid-*d* at −78 °C, giving **19** in 89% yield (Eq. 17).

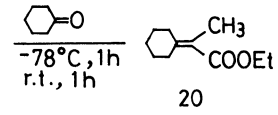


(17)

Furthermore, when **15** was treated with cyclohexanone at −78 °C for 1 h and at room temperature for 1 h, ethyl 2-cyclohexylidenepropionate (**20**) was isolated in 90% yield. Whereas **20** was obtained in only 33% yield from Emmons-Wadsworth reagent (**16**) under the same reaction conditions as those used for **14**.



14 15



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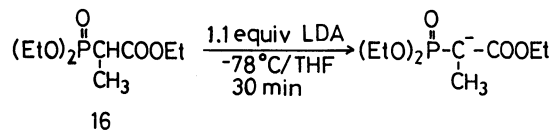

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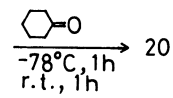
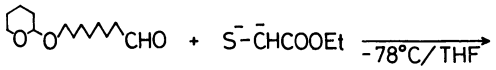


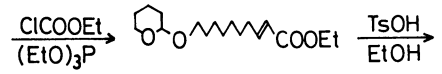
(19)

These results suggest that the reaction of *S*-[1-(ethoxycarbonyl)ethyl] diethyl phosphorothioate carbanion (**15**) with carbonyl compounds proceeds *via* path A.

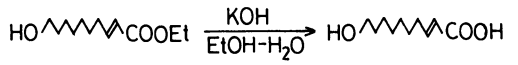
Synthesis of (E)-*10-Hydroxy-2-decenoic Acid.* To demonstrate the utility of our novel methodology,[1] the author has carried out the synthesis of (*E*)-10-hydroxy-2-decenoic acid, a component of royal jelly from *Apis Melifica*.[9] Reaction of **2a** with **21** in the presence of triethyl phosphite gave pure **22** as a pale yellow oil in 63% isolated yield (*E*/*Z*=94/6). Acid hydrolysis of **22**[10] produced pure ethyl (*E*)-10-hydroxy-2-decenoate (**23**) as a viscous oil in 79% isolated yield after purification by silica-gel chromatography. Alkali hydrolysis of **23**[11] produced pure (*E*)-10-hydroxy-2-decenoic acid (**24**) in 73% isolated yield after recrystallization from ether.



21 2a



22



(20)

23 24

Experimental

General. Boiling points were determined during distillation and are uncorrected. Infrared spectra were determined on a Hitachi Model 260-30 spectrophotometer. Nuclear magnetic resonance spectra were determined on a JEOLCO MH-100 spectrometer. Gas chromatograms were obtained using a Varian Aerograph Model 920 instrument with a 0.15 cm×120 cm glass column (20% Silicone DC-550 on Celite 545). Tetrahydrofuran (THF) was dried by distillation from calcium hydride and by subsequent distillation from lithium aluminum hydride under a nitrogen atmosphere. Diisopropylamine and *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) were distilled from calcium hydride and stored over molecular sieves. Triethyl phosphite and carbonyl compounds were purified by distillation under a nitrogen atmosphere. All reactions were performed under a nitrogen atmosphere. The glassware was dried by flaming in a nitrogen stream.

Preparation of Aldol Adduct (5). To a mixture of lithium diisopropylamide (LDA) (44 mmol) and TMEDA (44 mmol) in 40 ml of THF was added a solution of 2.4 g (20 mmol) of ethyl mercaptoacetate (**1a**) in 5 ml of THF at −78 °C. After being stirred for 1 h, a solution of 22 mmol of a carbonyl compound in 5 ml of THF was added and the reaction mixture was stirred at −78 °C for 2 h. The cooling bath was removed and the reaction mixture was quenched with 10 ml of saturated aqueous solution of ammonium chloride, poured into dilute hydrochloric acid, and extracted with ether (50×4 ml). The combined organic layer was washed twice with brine, dried on anhydrous sodium sulfate, and concentrated under reduced pressure. Distillation of the resulting oil gave **5**.

Ethyl 3-Hydroxy-2-mercapto-3-methylheptanoate (5a): Bp 93—96 °C/1 Torr (1 Torr≈133.322 Pa). ^{1}H-NMR (CCl_4); δ=4.16 (q, J=7 Hz, 2H, CH_2), 3.22 (s, 0.38H, erythro CH), 3.10 (s, 0.62H, threo CH), 2.93 (brs, 1H, OH), 2.23 and 2.14 (each d, J=6 and 5 Hz, total 1H, SH), 1.00—1.60 (m, 12H, $3CH_2$ and $2CH_3$), 0.70—1.00 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1710 cm^{-1} (COO). Found: C, 54.27; H, 9.16%. Calcd for $C_{10}H_{20}O_3S$: C, 54.51; H, 9.15%.

Ethyl 3-Hydroxy-2-mercapto-3-methyloctanoate (5b): Bp 96—100 °C/1 Torr. ^{1}H-NMR (CCl_4); δ=4.02 (q, J=7 Hz, 2H, CH_2), 3.10 (s, 0.39H, erythro CH), 2.99 (s, 0.61H, threo CH), 2.90 (brs, 1H, OH), 2.22 and 2.06 (each d, J=5 and 5 Hz, total 1H, SH), 1.12—1.58 (m, 14H, $4CH_2$ and $2CH_3$), 0.72—1.06 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1720 cm^{-1} (COO). Found: C, 56.17; H, 9.53%. Calcd for $C_{11}H_{22}O_3S$: C, 56.38; H, 9.46%.

Ethyl 3-Hydroxy-2-mercapto-3-methylnonanoate (5c): Bp 108—112.5 °C/1 Torr. ^{1}H-NMR (CCl_4); δ=4.16 (q, J=7 Hz, 2H, CH_2), 3.20 (s, 0.43H, erythro CH), 3.09 (s, 0.57H, threo CH), 2.96 (brs, 1H, OH), 2.30 and 2.18 (each d, J=6 and 5 Hz, total 1H, SH), 1.18—1.60 (m, 16H, $5CH_2$ and $2CH_3$), 0.80—0.96 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1720 cm^{-1} (COO). Found: C, 57.87; H, 9.69%. Calcd for $C_{12}H_{24}O_3S$: C, 58.03; H, 9.74%.

Ethyl 3-Hydroxy-2-mercapto-2,3-dimethylnonanoate (5d): Bp 125—128 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=4.10 (q, J=7 Hz, 2H, CH_2), 3.54 (brs, 1H, OH), 2.82 (brs, 0.54H, erythro SH), 2.66 (brs, 0.46H, threo SH), 1.10—1.60 (m, 19H, $5CH_2$ and $3CH_3$), 0.74—0.94 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1710 cm^{-1} (COO). Found: C, 59.47; H, 10.05%. Calcd for $C_{13}H_{26}O_3S$: C, 59.50; H, 9.99%.

Ethyl 3-Hydroxy-2-mercapto-3-methyldecanoate (5e): Bp 111.5—118 °C/1 Torr. ^{1}H-NMR (CCl_4); δ=4.14 (q, J=7 Hz, 2H, CH_2), 3.18 (s, 0.45H, erythro CH), 3.02 (s, 0.55H, threo CH), 2.95 (brs, 1H, OH), 2.28 and 2.12 (each d, J=6 and 5 Hz, total 1H, SH), 1.14—1.60 (m, 18H, $6CH_2$ and $2CH_3$), 0.82—1.00 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1720 cm^{-1} (COO). Found: C, 59.38; H, 10.11%. Calcd for $C_{13}H_{26}O_3S$: C, 59.50; H, 9.99%.

Ethyl 3-Hydroxy-2-mercapto-3-phenylbutanoate (5f): Bp 123.0—126.5 °C/1 Torr. ^{1}H-NMR (CCl_4); δ=7.16—7.48 (m, 5H, aromatic), 4.18 (q, J=7 Hz, 2H, CH_2), 3.48—3.96 (m, 2H, CH and OH), 2.54 (d, J=2 Hz, 0.56H, erythro SH), 2.44 (d, J=3 Hz, 0.44H, threo SH), 1.40—1.70 (m, 3H, CH_3), 0.76—1.34 (m, 3H, CH_3). IR (neat); 3840 (OH), 2550 (SH), 1700 cm^{-1} (COO). Found: C, 59.92; H, 6.85%. Calcd for $C_{12}H_{16}O_3S$: C, 59.98; H, 6.71%.

Ethyl 3-Hydroxy-2-mercaptohexanoate (5g): Bp 83—86 °C/3 Torr. ^{1}H-NMR (CCl_4); δ=4.15 (q, J=7 Hz, 2H, CH_2), 3.50—3.88 (m, 1H, CH-OH), 3.00—3.30 (m, 2H, CH-SH and OH), 2.18 (d, J=4 Hz, 0.62H, erythro SH), 2.07 (d, 5 Hz, 0.38H, threo SH), 1.16—1.60 (m, 7H, $2CH_2$ and CH_3), 0.80—1.00 (m, 3H, CH_3). IR (neat): 3490 (OH), 2560 (SH), 1720 cm^{-1} (COO). Found: C, 49.72; H, 8.45%. Calcd for $C_9H_{18}O_3S$: C, 49.97; H, 8.39%.

Ethyl 3-Hydroxy-2-mercaptoheptanoate (5h): Bp 93.5—97 °C/2 Torr ^{1}H-NMR (CCl_4); δ=4.18 (q, J=7 Hz, 2H, CH_2), 3.52—3.84 (m, 1H, CH-OH), 3.04—3.30 (m, 2H, CH-SH and OH), 2.22 (d, J=4 Hz, 0.58H, erythro SH), 2.10 (d, J=5 Hz, 0.42H, threo SH), 1.20—1.60 (m, 9H, $3CH_2$ and CH_3), 0.80—1.00 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1710 cm^{-1} (COO). Found: C, 52.28; H,8.85%. Calcd for $C_9H_{18}O_3S$: C, 52.40; H, 8.79%.

Ethyl 3-Hydroxy-2-mercaptononanoate (5i): Bp 110—114.5 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=4.14 (q, J=7 Hz, 2H, CH_2), 3.50—3.90 (m, 1H, CH-OH), 2.86—3.24 (m, 2H, CH-SH and OH), 2.18 (d, J=4 Hz, 0.60H, erythro SH), 2.08 (d, J=5 Hz, 0.40H, threo SH), 1.18—1.62 (m, 13H, $5CH_2$ and CH_3), 0.78—0.96 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1710 cm^{-1} (COO). Found: C, 56.31; H, 9.60%. Calcd for $C_{11}H_{22}O_3S$: C, 56.38; H, 9.46%.

Ethyl 3-Hydroxy-2-mercaptodecanoate (5j): Bp 114—118 °C/1 Torr. ^{1}H-NMR (CCl_4); δ=4.16 (q, J=7 Hz, 2H, CH_2), 3.54—3.90 (m, 2H, CH-OH and OH), 3.02—3.28 (m, 1H, CH-SH), 2.20 (d, J=4 Hz, 0.58H, erythro SH), 2.09 (d, J=5 Hz, 0.42H, threo SH), 1.18—1.70 (m, 15H, $6CH_2$ and CH_3), 0.76—1.00 (m, 3H, CH_3). IR (neat); 3500 (OH), 2560 (SH), 1700 cm^{-1} (COO). Found: C, 58.01; H, 9.79%. Calcd for $C_{12}H_{24}O_3S$: C, 58.03; H, 9.74%.

Ethyl 3-Hydroxy-2-mercapto-3-phenylpropionate (5k): Bp 128-131 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=7.20 (s, 5H, aromatic), 4.82 (d, J=6 Hz, 0.40H, erythro CH-OH), 4.70 (d, J=8 Hz, 0.60H, threo CH-OH), 4.04 (q, J=7 Hz, 2H, CH_2), 3.72—3.84 (m, 1H, OH), 3.30—3.60 (m, 1H, CH-SH), 2.10 (d, J=9 Hz, 0.40H, erythro SH), 1.95 (d, J=10 Hz, 0.60H, threo SH), 1.00—1.30 (m, 3H, CH_3). IR (neat); 3490 (OH), 2560 (SH), 1730 cm^{-1} (COO). Found: C, 58.25; H, 6.39%. Calcd for $C_{11}H_{14}O_3S$: C, 58.39; H, 6.24%.

Ethyl 3-Hydroxy-2-mercaptooctanoate (5l): Bp 96.5—100 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=4.16 (q, J=7 Hz, 2H, CH_2), 3.52—3.86 (m, 1H, CH-OH), 3.00—3.26 (m, 2H, CH-SH and OH), 2.20 (d, J=4 Hz, 0.60H, erythro SH), 2.08 (d, J=5 Hz, 0.40H, threo SH), 1.20—1.60 (m, 11H, $4CH_2$ and CH_3), 0.80—1.00 (m, 3H, CH_3). IR (neat): 3500 (OH), 2560 (SH), 1710 cm^{-1} (COO). Found: C, 54.35; H, 9.20%. Calcd for $C_{10}H_{20}O_3S$: C, 54.51; H, 9.15%.

Cross-over Experiment. Preparation of Ethyl 3-Hydroxy-3-methyl-2-(methylthio)nonanoate (6): Into a solution of 20 mmol of the dianion (**2a**) in 40 ml of THF, was added at −78°C a solution of 22 mmol of 2-octanone in 3 ml of THF. After being stirred for 1 h, a solution of 22 mmol of acetophenone in 3 ml of THF was added and the reaction mixture was stirred at −78 °C for 1 h. A solution of 22 mmol of methyl iodide in 3 ml of THF was then added with a syringe over a 3 min period. The resulting solution was stirred at −78 °C for 1 h before quenching with saturated aqueous solution of ammonium chloride (10 ml). The work-up similar to the preparation of **5** and silica-gel chromatography(benzene) gave 2.27 g of acetophenone and 3.36 g (64%) of **6**. ^{1}H-NMR (CCl_4); δ=4.28 (q, J=7 Hz, 2H, CH_2), 3.08 (s, 1H, CH), 3.07 (brs, 1H, OH), 2.20 (s, 3H, SCH_3), 1.20—1.72 (m, 16H, $5CH_2$ and $2CH_3$), 0.86—1.20 (m, 3H, CH_3). IR (neat); 3500 (OH), 1720 cm^{-1}(COO). Found: C, 59.39; H, 9.98%. Calcd for $C_{13}H_{26}O_3S$: C, 59.50; H, 9.99%.

General Procedure. Reaction of Dianion (2a) with Carbonyl Compounds: Into a solution of 20 mmol of the dianion (**2a**) in 40 ml of THF, was added at −78 °C a solution of 22 mmol of a carbonyl compound in 5 ml of THF. After being stirred for 2 h, ethyl chloroformate (20 mmol) in 3 ml of THF was added and the mixture was stirred at −78 °C for 30 min and at 30—35 °C or 15 °C for 1 h before it was quenched with saturated aqueous solution of ammonium chloride solution (10 ml). The reaction mixture was poured into dilute hydrochloric acid and extracted with ether (50× 4 ml). The combined organic layer was washed twice with brine, dried on anhydrous sodium sulfate, and concentrated under reduced pressure. Product isolation and purification by chromatography on silica-gel column (benzene) gave **3** and **7**. The dianion (**2a**) was treated with aldehydes in the presence of triethyl phosphite in a similar manner as described above to give **3** in high yields.

Reaction of Monoanions (2b, 2c) with Carbonyl Compounds: A solution of 20 mmol of *O*-ethyl *S*-ethoxycarbonylmethyl thiocarbonate (**1b**) or *S*-ethoxycarbonylmethyl diethyl phosphorothioate (**1c**) in 3 ml of THF was added to a stirred solution of 22 mmol of LDA in 40 ml of THF at −78 °C. The resulting solution was treating with 24 mmol of aldehydes in a similar manner as described above.

Ethyl (E)-2-Mercapto-2-octenoate (7a): ^{1}H-NMR (CCl_4); δ=6.72 (t, J=7 Hz, 1H, CH=C), 4.18 (q, J=7 Hz, 2H, CH_2), 3.94 (s, 1H, SH), 2.18 (q, J=7 Hz, 2H, CH_2), 1.10—1.60 (m, 9H, $3CH_2$ and CH_3), 0.86 (m, 3H, CH_3). IR (neat); 2560 (SH), 1710 (COO), 1610 cm^{-1} (C=C). Found: C, 59.31; H, 9.13%. Calcd for $C_{10}H_{18}O_2S$: C, 59.37; H, 8.97%.

Ethyl (E)-2-Mercapto-2-decenoate (7b): ^{1}H-NMR (CCl_4); δ=6.59 (t, J=7 Hz, 1H, CH=C), 4.06 (q, J=7 Hz, 2H, CH_2), 3.87 (s, 1H, SH), 2.14 (q, J=7 Hz, 2H, CH_2), 1.10—1.80 (m, 13H, $5CH_2$ and CH_3), 0.85 (m, 3H, CH_3). IR (neat); 2560 (SH), 1720 (COO), 1610 cm^{-1} (C=C). MS (20 eV); m/z 230 (M^+). Found: C, 62.60; H, 9.66%. Calcd for $C_{12}H_{22}O_2S$: C, 62.57; H, 9.63%.

Ethyl (E)-2-Mercapto-2-dodecenoate (7c): ^{1}H-NMR (CCl_4); δ=6.80 (t, J=7 Hz, 1H, CH=C), 4.24 (q, J=7 Hz, 2H, CH_2), 3.99 (s, 1H, SH), 2.20 (q, J=7 Hz, 2H, CH_2), 1.10—1.90 (m, 17H, $7CH_2$ and CH_3), 0.86 (m, 3H, CH_3). IR (neat); 2560 (SH), 1720 (COO), 1605 cm^{-1} (C=C). Found: C, 64.81; H, 10.22%. Calcd for $C_{14}H_{20}O_2S$: C, 65.07; H, 10.14%.

Ethyl (E)-3-Cyclohexyl-2-mercapto-2-propenoate (7d): ^{1}H-NMR (CCl_4); δ=6.40 (d, J=9 Hz, 1H, CH=C), 4.08 (q, J=7 Hz, 2H, CH_2), 3.87 (s, 1H, SH), 2.00—2.32 (m, 1H, CH), 0.80—1.80 (m, 13H, $5CH_2$ and CH_3). IR (neat); 2560 (SH), 1710 (COO), 1610 cm^{-1} (C=C). Found: C, 61.57; H, 8.35%. Calcd for $C_{11}H_{18}O_2S$: C, 61.65; H, 8.46%.

Ethyl (E)-2-Mercapto-2-nonenoate (7e): ^{1}H-NMR (CCl_4); δ=6.60 (t, J=7 Hz, 1H, CH=C), 4.08 (q, J=7 Hz, 2H, CH_2), 3.88 (s, 1H, SH), 2.14 (q, J=7 Hz, 2H, CH_2), 1.10—1.80 (m, 11H, $4CH_2$ and CH_3), 0.90 (m, 3H, CH_3). IR (neat); 2560 (SH), 1710 (COO), 1610 cm^{-1} (C=C). Found:C, 61.05; H, 9.41%. Calcd for $C_{10}H_{20}O_2S$: C, 61.07; H, 9.32%.

Ethyl (E)-2-Octenoate (3a): Bp 64—65 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=6.82 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 5.70 (d, J=16 Hz, 1H, CH=C), 4.08 (q, J=7 Hz, 2H, CH_2), 2.16 (m, 2H, CH_2), 1.47 (m, 9H, $3CH_2$ and CH_3), 0.90 (m, 3H, CH_3). IR (neat); 1640 cm^{-1} (C=C). Found: C, 70.38; H, 10.75%. Calcd for $C_{10}H_{18}O_2$:C, 70.55; H, 10.66%.

Ethyl 2-Decenoate (3b): Bp 87—88.5 °C/2 Torr. The *(E)*- and *(Z)*-isomers of **3b** were separated by silica-gel chromatography using benzene as eluent. *(E)*-isomer: ^{1}H-NMR (CCl_4); δ=6.76 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 5.72 (d, J=16 Hz, 1H, CH=C), 4.12 (q, J=7 Hz, 2H, CH_2), 2.00—2.20 (m, 2H, CH_2), 1.10—1.80 (m, 13H, $5CH_2$ and CH_3), 0.90 (m, 3H, CH_3). IR (neat); 1645 cm^{-1} (C=C). Found: C, 72.51; H, 10.87%. Calcd for $C_{12}H_{22}O_2$: C, 72.67; H, 11.18%. *(Z)*-isomer: ^{1}H-NMR (CCl_4); δ=6.10 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 5.72 (d, J=16 Hz, 1H, CH=C), 4.10 (q, J=7 Hz, 2H, CH_2), 1.98—2.00 (m, 2H, CH_2), 1.00—1.70 (m, 13H, $5CH_2$ and CH_3), 0.88 (m, 3H, CH_3).

Ethyl (E)-*2-Dodecenoate (3c)*: Bp 93—95 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=6.88 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 5.74 (d, J=16 Hz, 1H, CH=C), 4.12 (q, J=7 Hz, 2H, CH_2), 2.14 (m, 2H, CH_2), 1.45 (m, 17H, $7CH_2$ and CH_3), 0.90 (m, 3H, CH_3). IR (neat); 1650 cm^{-1} (C=C). Found: C, 74.03; H, 11.93%. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58%.

Ethyl (E)-*3-Cyclohexyl-2-propenoate (3d)*: Bp 57—58 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=6.83 (dd, J=7 Hz, 16 Hz, 1H, CH=C), 5.70 (d, 16 Hz, 1H, CH=C), 4.13 (q, J=7 Hz, 2H, CH_2), 2.09 (m, 1H, CH), 1.75 (m, 4H, $2CH_2$), 0.90 (m, 9H, $3CH_2$ and CH_3). IR (neat); 1640 cm^{-1} (C=C). Found: C, 72.47; H, 9.95%. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95%.

Ethyl (E)-*2-Nonenoate (3e)*: Bp 71.5—73.5 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=6.84 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 5.70 (d, J=16 Hz, 1H, CH=C), 4.10 (q, J=7 Hz, 2H, CH_2), 2.17 (m, 2H, CH_2), 1.49 (m, 11H, $4CH_2$ and CH_3), 0.90 (m, 3H, CH_3). IR (neat); 1645 cm^{-1} (C=C). Found: C, 71.50; H, 11.02%. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94%.

Ethyl (E)-*3-Phenyl-2-propenoate (3f)*: Bp 99—100 °C/2 Torr. ^{1}H-NMR (CCl_4); δ=7.62 (d, J=16 Hz, 1H, CH=C), 7.40 (m, 5H, aromatic), 6.34 (d, J=16 Hz, 1H, CH=C), 4.18 (q, J=7 Hz, 2H, CH_2), 1.31 (t, J=7 Hz, 3H, CH_3). IR (neat); 1630 cm^{-1}(C=C). Found: C, 74.88; H, 6.87%. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86%.

Ethyl 3-Methyl-2-hexenoate (3g): Bp 51—55 °C/5 Torr. ^{1}H-NMR (CCl_4); δ=5.55 (brs, 1H, CH=C), 4.05 (q, J=7 Hz, 2H, CH_2), 2.56 (t, J=8 Hz, 1.22H, CH_2 for *(Z)*-isomer), 1.96—2.25 (m, 1.95H, CH_2 and CH_3 for *(E)*-isomer), 1.84 (m, 1.83H, CH_3 for *(Z)*-isomer), 1.30—1.72 (m, 2H, CH_2), 1.24 (t, J=7 Hz, 3H, CH_3), 0.94 (m, 3H, CH_3). IR (neat); 1640 cm^{-1} (C=C). Found: C, 69.07; H, 10.55%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%.

Ethyl 3-Methyl-2-nonenoate (3h): Bp 90—93.5 °C/6 Torr. ^{1}H-NMR (CCl_4); δ=5.60 (brs, 1H, CH=C), 4.06 (q, J=7 Hz, 2H, CH_2), 2.56 (m, 1.14H, CH_2 for *(Z)*-isomer), 1.92—2.32 (m, 2.15H, CH_2 and CH_3 for *(E)*-isomer), 1.86 (m, 1.71H, CH_3 for *(Z)*-isomer), 1.20—1.84 (m, 11H, $4CH_2$ and CH_3), 0.90 (m, 3H, CH_3). IR (neat); 1640 cm^{-1} (C=C). Found: C, 72.56; H, 11.25%. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18%.

Ethyl (E)-*3-Phenyl-2-butenoate (3i)*: Bp 115—116 °C/5 Torr. ^{1}H-NMR (CCl_4); δ=7.24 (m, 5H, aromatic), 6.05 (m, 1H CH=C), 4.10 (q, J=7 Hz, 2H, CH_2), 2.50 (s, 3H, CH_3), 1.24 (t, J=7 Hz, 3H, CH_3). IR (neat); 1625 cm^{-1} (C=C). Found: C, 75.65; H, 7.55%. Calcd for $C_{12}H_{14}O_2S$: C, 75.76; H, 7.42%. This product was judged as *(E)*-isomer by NMR spectra which is consistent with that of ethyl *(E)*-3-phenyl-2-butenoate reported previously.[4]

Ethyl (E)-*3-Phenyl-2-pentenoate (3j)*: Bp 91—94.5 °C/1 Torr. ^{1}H-NMR (CCl_4); δ=7.20—7.50 (m, 5H, aromatic), 5.96 (s, 1H, CH=C), 4.12 (q, J=7 Hz, 2H, CH_2), 3.08 (q, J=7 Hz, 2H, CH_2), 1.26 (t, J=7 Hz, 3H, CH_3), 1.04 (t, J=7 Hz, 3H, CH_3). IR (neat); 1620 cm^{-1} (C=C). Found: C, 76.38; H, 8.01%. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.89%.

Ethyl (E)-*2-Hexenoate (3k)*: Bp 64—65 °C/10 Torr. ^{1}H-NMR (CCl_4); δ=6.80 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 5.70 (d, J=16 Hz, 1H, CH=C), 4.08 (q, J=7 Hz, 2H, CH_2), 1.30—1.90 (m, 5H, CH_2 and CH_3), 0.97 (t, J=7 Hz, 3H, CH_3). IR (neat); 1650 cm^{-1} (C=C). Found: C, 67.51; H, 9.97%. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92%.

Ethyl (E)-*2-Heptenoate (3l)*: Bp 59—60 °C/5 Torr. ^{1}H-NMR (CCl_4); δ=6.82 (dt, J=7 Hz, 16 Hz, CH=C), 5.70 (d, J=16 Hz, 1H, CH=C), 4.08 (q, J=7 Hz, 2H, CH_2), 2.20 (m, 2H, CH_2), 1.50 (m, 7H, $2CH_2$ and CH_3), 0.90 (m, 3H, CH_3). IR (neat); 1640 cm^{-1} (C=C). Found: C, 69.03; H, 10.37%. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32%.

Preparation of S-[1-(Ethoxycarbonyl)ethyl] Diethyl Phosphorothioate (14):[12] To a stirred solution of 50.0g (0.36 mol) of diethyl phosphite in 250 ml of benzene was added 8.5 g (0.37 mol) of sodium metal under a nitrogen atmosphere. After the mixture has been stirred at room temperature for 2 h, 11.6 g (0.36 mol) of sulfur was added. Stirring was continued at room temperature for overnight and a solution of 65.2 g (0.36 mol) of ethyl 2-bromopropionate in 50 ml of benzene was added over a 20 min period. The reaction mixture was then refluxed for 3 h and the resulting precipitate was filtered. Evaporation and distillation under reduced pressure of the filtrate gave 35.3 g (36%) of **14**. Bp 126.5—127.5 °C/1.2—1.3 Torr. ^{1}H-NMR (CCl_4); δ=3.60—4.30 (m, 7H, $3CH_3\underline{CH_2}$ and CH), 1.00—1.70 (m, 12H, $4CH_3$). IR (neat); 1735 (C=O), 1015 cm^{-1} (P-O). MS (20 eV) m/z 270 (M^+).

Decomposition of S-[1-(Ethoxycarbonyl)ethyl] Diethyl Phosphorothioate Carbanion (15): The carbanion (**15**) was generated by treatment of 5.41g (20 mmol) of **14** with 22 mmol of LDA in 40 ml of THF at −78 °C. After being stirred for 30 min, the reaction mixture was allowed to warm from −78 °C to room temperature before it was quenched with saturated aqueous solution of ammonium chloride (10 ml). The usual work-up and distillation gave 4.1 g (88%) of ethyl 2-(diethoxyphosphinyl)propionate (**16**), bp 101—103 °C/1 Torr. The product was identified by comparison of ^{1}H-NMR and mass spectrum with the corresponding data for independently synthesized material.[7]

Generation of S-(Ethoxycarbonylmethyl-1-d) Diethyl Phosphorothioate (19): To a solution of 9.5 mmol of LDA in 40 ml of THF was added a solution of 8.6 mmol of *S*-(ethoxycarbonylmethyl) diethyl phosphorothioate in 5 ml of THF at −78 °C. After stirring for 30 min, the cooling bath was removed, and a mixture of 30 mmol of acetic acid-*d* and 10 ml of deuterium oxide was added. The reaction mixture was then stirred for 15 min before it was quenched with saturated aqueous solution of ammonium chloride (20 ml), and extracted with ether (50×4 ml). The combined organic layer was washed with brine, dried on anhydrous sodium sulfate, and concentrated under reduced pressure. Distillation of the resulting oil gave 4.6 g (89%) of **19**, bp 129—131 °C/1.3 Torr. The degree of deuteration determined by means of ^{1}H-NMR was 87%.

Synthesis of Ethyl 2-Cyclohexilidenepropionate (20): To a solution of LDA (22 mmol) in 40 ml of THF was added dropwise a solution of 5.41 g (20 mmol) of **14** in 5 ml of THF at −78 °C. After being stirred for 30 min, a solution of 2.45 g (25 mmol) of cyclohexanone in 5 ml of THF was added dropwise over a 5 min period and stirred at −78 °C for 1 h and at room temperature for 1 h. The usual work-up and distillation gave 3.27 g (90%) of **20**. Bp 71—72 °C/1 Torr. ^{1}H-NMR (CCl_4); δ=4.06 (q, 2H, CH_2), 2.22—2.43 (m, 4H, $2CH_2$), 1.82 (s, 3H, $C=CCH_3$), 1.59 (m, 6H, $3CH_2$), 1.28 (t, J=7 Hz, 3H, $OCH_2\underline{CH_3}$). IR (neat); 1710 (C=O), 1635 cm^{-1} (C=C). MS (20 eV) m/z 182 (M^+). Found: C, 72.56; H, 10.00%. Calcd for $C_{11}H_{18}O_2$: C, 72.46; H, 9.95%.

Preparation of Ethyl 10-(2-Tetrahydropyranyloxy)-2-decenoate (22): 8-(2-Tetrahydropyranyloxy)octanal (**21**) was prepared from 8-(2-tetrahydropyranyloxy)-1-octanol by using chromium trioxide-pyridine complex by the reported procedure.[13] To a mixture of LDA (44 mmol) and TMEDA (44 mmol) in 40 ml of THF was added a solution of 2.4 g (20 mmol) of ethyl mercaptoacetate (**1a**) in 5 ml of THF at −78 °C. After being stirred for 1 h, a solution of 5.02 g (22 mmol) of **21** in 5 ml of THF was added and the reaction mixture was stirred in the presence of triethyl phosphite (30 mmol) at −78 °C for 2 h. Ethyl chloroformate (20 mmol) in 5 ml of THF was then added to the above solution with stirring and the mixture was kept at −78 °C for 30 min and at 30—35 °C for 1 h before it was quenched with saturated aqueous solution of ammonium chloride (10 ml). The usual work-up and silica-gel chromatography (benzene) gave **22** in 63% (3.75 g) isolated yield (*E*/*Z* =94/6). The *(E)*- and *(Z)*-isomers of **22** were separated by silica-gel chromatography using benzene as eluent.

Preparation of Ethyl (E)*-10-Hydroxy-2-decenoate (23)*: A solution of 3.50 g (16 mmol) of **22** and 0.35 g of *p*-toluensulfonic acid in 100 ml of ethanol was refluxed for 1 h, concentrated to half volume, diluted with water, and extracted with ether (50×4 ml). The combined organic layer was dried on anhydrous sodium sulfate and concentrated under reduced pressure. Silica-gel chromatography (ethyl acetate: chloroform=1 : 1) gave **23** as a viscous oil in 79% (2.70 g) isolated yield. ^{1}H-NMR (CCl_4); δ=6.65 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 5.52 (d, 16 Hz, 1H, CH=C), 3.96 (q, J=7 Hz, 2H, CH_2), 3.40 (t, J=6 Hz, 2H, CH_2), 3.02 (brs, 1H, OH), 1.96—2.22 (m, 2H, CH_2), 1.08—1.62 (m, 13H, $5CH_2$ and CH_3).

Preparation of (E)*-10-Hydroxy-2-decenoic Acid (24)*: A solution of 2.57 g (12 mmol) of **23** and 1.40 g of potassium hydroxide in 16 ml of ethanol was refluxed for 1.5 h under a nitrogen atmosphere, concentrated to half volume, diluted with water, and acidified to pH 4.0 with 2.5 M sulfuric acid (1 M=1 mol dm^{-3}). The reaction solution was then extracted with ether (50×4 ml), dried on anhydrous sodium sulfate, and concentrated under reduced pressure. Silica-gel chromatography (ethyl acetate and chloroform) and recrystallization from ether gave pure **24** in 73% (1.63 g) isolated yield. Mp 62.5—63.5 °C. ^{1}H-NMR (CCl_4); δ=6.80 (dt, J=7 Hz, 16 Hz, 1H, CH=C), 6.07 (brs, 2H, OH and COOH), 5.58 (d, J=16 Hz, 1H, CH=C), 3.47 (t, J=6 Hz, 2H, CH_2), 2.05—2.24 (m, 2H, CH_2), 0.92—1.16 (m, 10H, $5CH_2$). IR (disk); 3420 (OH), 1685 (COOH), 1640 cm^{-1} (C=C). Found: C, 64.08; H, 9.51%. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74%.

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