Reactions of the α-Carbanion Species of (Phenylthio)acetic Acid and its Ester with Carbonyl Compounds

By **Shûichi Yamagiwa, Nobuto Hoshi, Hitoshi Sato, Hiroshi Kosugi,** and **Hisachi Uda,*** Chemical Research Institute of Non-aqueous Solutions, Tohoku University, Sendai 980, Japan

Reactions of the (phenylthio)acetic acid dianion (2) and its ester monoanion (3) with carbonyl compounds are described. Both the carbanions (2) and (3) react well with saturated aldehydes and ketones to give the α-(1-hydroxyalkyl) substituted derivatives in excellent yields. In the reaction with conjugated enones, the dianion (2) undergoes exclusive 1,2-addition, while the monoanion (3) gives 1,4-addition. Reaction of the dianion (2) with saturated esters produces directly phenylthiomethyl ketones through decarboxylation of the intermediates, whereas the reaction with αβ-unsaturated esters was found to be unsatisfactory. On the other hand, unlike the reaction with saturated esters, the reaction of the monoanion (3) with αβ-unsaturated esters proceeds well to yield 1,4-addition products.

REACTION of the dianion (2) of (phenylthio)acetic acid (1), formed by a strong base (lithium di-isopropylamide = LDA), with epoxides [1] has been shown to be an attractive preparative route to α-phenylthio-γ-butyrolactones [2] and, subsequently, to furan-2(5*H*)-ones.[1] Additionally, a few examples of alkylation of the dianion (2) and the ester monoanion (3) have been

$PhSCH_2CO_2H$ (1) $PhS\bar{C}HCO_2^-$ (2) $PhS\bar{C}HCO_2Me$ (3)

reported. It was observed that the dianion (2) also reacted well with primary alkyl halides to give the α-phenylthiocarboxylic acids [1,3] which could further react with epoxides [1] and alkyl halides.[3] On the other hand, it was found that the reaction of the monoanion (3) was markedly affected by the counter cation, *i.e.* a base employed for the anion generation; the lithio-derivative of the monoanion (3) generated by LDA has been shown to react unsatisfactorily with epoxides [1]

[1] (*a*) K. Iwai, M. Kawai, H. Kosugi, and H. Uda, *Chem. Letters*, 1974, 385; (b) K. Iwai, H. Kosugi, H. Uda, and M. Kawai, *Bull. Chem. Soc. Japan*, 1977, **50**, 242.

[2] (*a*) For an alternative preparation of α-phenylthio-γ-butyrolactones by direct sulphenylation see B. M. Trost and T. N. Salzmann, *J. Amer. Chem. Soc.*, 1973, **95**, 6840; B. M. Trost and K. K. Leung, *Tetrahedron Letters*, 1975, 4197; B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Amer. Chem. Soc.*, 1976, **98**, 4887; (*b*) For direct sulphinylation see H. J. Monteiro and J. P. Souza, *Tetrahedron Letters*, 1975, 921; H. J. Monteiro and A. L. Gemal, *Synthesis*, 1975, 437.

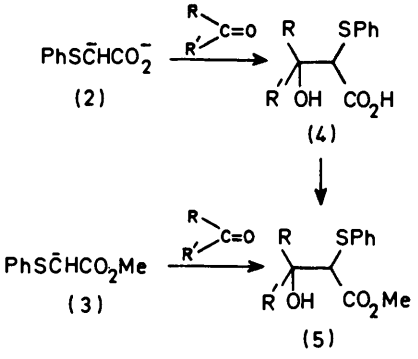
[3] (*a*) P. A. Grieco and C.-L. J. Wang, *J.C.S. Chem. Comm.*, 1975, 714; (*b*) For alkylation of (methylthio)acetic acid dianion see B. M. Trost and Y. Tamaru, *Tetrahedron Letters*, 1975, 3797.

and alkyl halides,[3] whereas the sodio-derivative generated by sodium hydride underwent smooth alkylation to give the homologous esters in high yields.[4]

Here we report our findings concerning reactions of the dianion (2), as well as the monoanion (3), with saturated and αβ-unsaturated aldehydes, ketones, and esters which demonstrate the usefulness of these α-carbanion species for a variety of functionalized compounds. In the present investigation, both the carbanions (2) and (3) were generated by treating with LDA in tetrahydrofuran and employed without the use of hexamethylphosphoric triamide.

(a) *Reaction with Saturated Aldehydes and Ketones.*—The reactions of the α-carbanion species (2) and (3) with saturated carbonyl compounds are outlined in Scheme 1. The dianion (2) reacted cleanly with saturated aldehydes and ketones initially at −60 °C and subsequently at −30 °C to room temperature to give the adducts (4) in high yields (Table 1). The products (6) (mixture of stereoisomers), (10), and (11) from isobutyraldehyde, acetone, and cyclopentanone (entries 1, 4, and 5) could be purified simply by recrystallization. On the other hand, others were converted into the methyl esters (5) and purified, since these did not crystallize. Each of the stereoisomers (racemates) of the esters (7), (9), (14), or (16) could be separated by column chromatography.

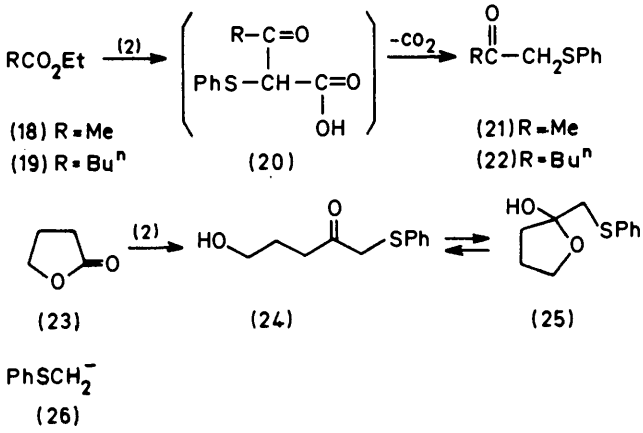
The reaction of the monoanion (3) with carbonyl compounds also proceeded well at −60 to −40 °C to yield directly the esters (5) (Table 1). It is observed that, however, the monoanion (3) is slightly less reactive than the dianion (2): no reaction with 2-methylcyclohexanone (entry 7) and acetophenone (entry 10) was observed under the conditions employed. Furthermore, in the



SCHEME 1

case of the reaction with cyclopentanone, the low temperature maintained for the reaction mixture before quenching was found to be essential to the optimum yield of the product (12). When the mixture was warmed to above −30 °C and worked up, cyclopentylidenecyclopentanone became the major product.

(b) *Reaction with Saturated Esters.*—The dianion (2) also reacted with saturated esters (1 molar equivalent), such as ethyl acetate (18) and ethyl valerate (19) at 0 °C to give directly the phenylthiomethyl ketones



SCHEME 2

(21) and (22) in 42 and 51% yields, respectively (Scheme 2). The initial adduct (20) is the β-oxo-carboxylic acid, and hence, decarboxylation should occur easily during reaction or work-up. Similarly, the reaction with γ-butyrolactone (23) afforded the expected phenylthiomethyl ketone (24) in 71% yield. In the n.m.r. spectrum of this compound the appearance of two singlets (almost equal intensity; total 2 H) at δ 3.21 and 3.58 assignable to the phenylthiomethyl protons suggests that the equilibration between the oxo-form (24) and the acetal form (25) exists in a carbon tetrachloride solution.

The fact that easy decarboxylation of the initial products (20) resulted in formation of the phenylthiomethyl ketones suggests that in the reaction with esters and lactones the dianion (2) reacts as the equivalent species to the thioanisole anion (26).[5] We have found that the dianion (2) seems to be superior to the thioanisole anion (26) for preparation of phenylthiomethyl ketones; the reaction of the anion (26) with γ-butyrolactone (23) produced a number of products, from which only a 25% yield of the phenylthiomethyl ketone (24) was isolated. Thus, the present reaction using the dianion (2) may provide a useful method for preparation of the phenylthiomethyl ketone derivatives.[6]

The reaction of the monoanion (3) with esters resulted in the formation of a complex mixture.

(c) *Reaction with Conjugated Enones.*—In view of the wide synthetic utility of conjugated enones in the elaboration of complex organic structures, the reactions of the present carbanions (2) and (3) with conjugated enones may be of considerable interest. The most important feature of the reaction of stabilized carbanions with conjugated enones is the selectivity on the reaction site of an enone system; both 1,2- (direct) and 1,4- (conjugate) additions may occur. Actually an equilibration between two anion species, such as (27) and (28)

[4] P. Brownbridge, I. Fleming, A. Pearce, and S. Warren, *J.C.S. Chem. Comm.*, 1976, 751; H. Kotake, K. Inomata, S. Aoyama, and H. Kinoshita, *Chem. Letters*, 1977, 73.

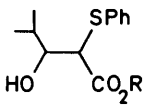
[5] E. J. Corey and D. Seebach, *J. Org. Chem.*, 1966, **31**, 4097; E. J. Corey and M. Jautelat, *Tetrahedron Letters*, 1968, 5787; R. L. Sowerby and R. M. Coats, *J. Amer. Chem. Soc.*, 1973, **94**, 4758.

[6] For an alternative preparation of phenylthiomethyl ketones see T. Cohen, D. Kuhn, and J. R. Falck, *J. Amer. Chem. Soc.*, 1975, **97**, 4749.

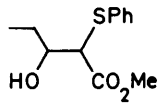
(Scheme 3) has been realised,[7] and the selectivity of two types of reactions depends not only on the nature of each substrate (carbanion and enone) but also on reaction conditions (temperature and time). Under the appropriate conditions, it would be expected that the 1,2-addition products might be produced predominantly from the reaction of highly nucleophilic carbanions, whereas the 1,4-addition products would be expected from weak nucleophilic carbanions. This is virtually the case for the reactions of the carbanions (2) and (3) with conjugated enones; the former gave predominantly the 1,2-adducts, the hydroxy-acids (29), and the latter the 1,4-adducts, the oxo-esters (30). The results are summarized in Tables 2 and 3. All the products from the dianion (2) were mixtures of stereoisomers and were purified as the methyl esters. After the completion of our study, a paper dealing with the reaction of the monoanion (3) with cyclohex-2-enone by Schultz and Yee [8] appeared.

TABLE 1

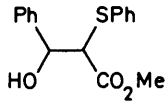
Reactions of the dianion (2) and monoanion (3) with saturated aldehydes and ketones



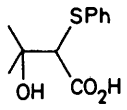
(6) R = H
(7) R = Me



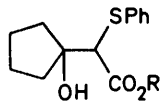
(8)



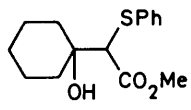
(9)



(10)



(11) R = H
(12) R = Me



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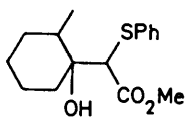

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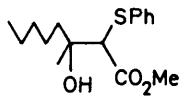
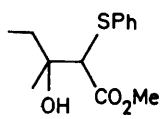


(15)



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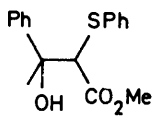
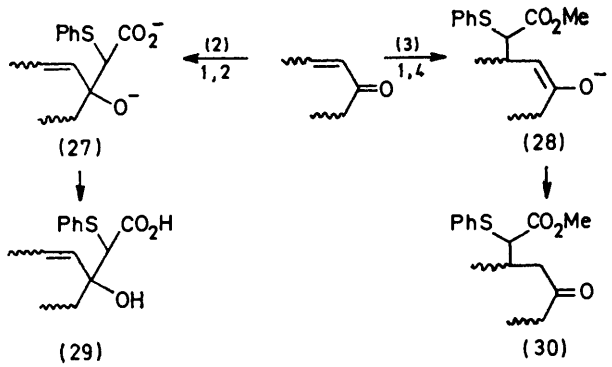


(17)

Entry	Aldehyde or ketone	Anion	Reaction time (h)	Product	% Yield
1	Isobutyraldehyde				
		(2)	5	(6) R = H	87
		(3)	0.5	(7) R = Me	88
2	Propionaldehyde	(3)	1	(8)	81
3	Benzaldehyde	(2)	15 (then CH_2N_2)	(9)	80
4	Acetone	(2)	0.7	(10)	96
5	Cyclopentanone				
		(2)	1.5	(11) R = H	100
		(3)	1.5	(12) R = Me	76
6	Cyclohexanone	(3)	1	(13)	88
7	2-Methylcyclohexanone	(2)	1 (then CH_2N_2)	(14)	96
		(3)			nil
8	Heptan-2-one	(2)	1.5 (then CH_2N_2)	(15)	93
9	Butan-2-one	(3)	1	(16)	87
10	Acetophenone	(2)	1 (then CH_2N_2)	(17)	90
		(3)			Nil

The low yields of the products from methyl vinyl ketone (Table 2, entry 2, and Table 3, entry 1) may be due to the instability of methyl vinyl ketone; a considerable amount of polymerized substance was formed.

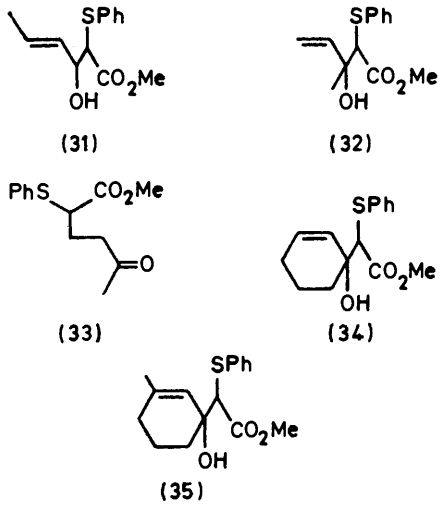
[7] G. Stork and L. Maldonado, *J. Amer. Chem. Soc.*, 1974, **96**, 5278, and references cited therein.
[8] A. G. Schultz and Y. K. Yee, *J. Org. Chem.*, 1976, **41**, 4044.



SCHEME 3

TABLE 2

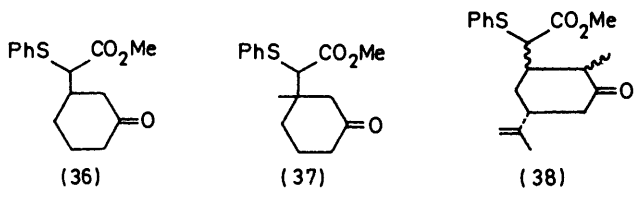
Reaction of the dianion (2) with conjugated enones



Entry	Enone	Reaction temp. and time (°)	(h)	Product (then CH_2N_2)	% Yield
1	Crotonaldehyde	−60	3	(31)	65
2	Methyl vinyl ketone	−78	2.5	(32)	48
				(33)	8
3	Cyclohex-2-enone	−30	2	(34)	86
4	3-Methylcyclohex-2-enone	−50	2	(35)	72

TABLE 3

Reaction of the monoanion (3) with conjugated enones

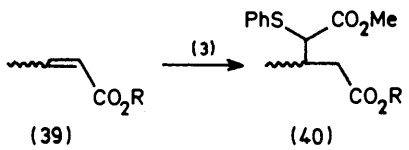


Entry	Enone	Reaction temp. and time (°)	(h)	Product	% Yield
1	Methyl vinyl ketone	−78	2	(33)	14
				(32)	31
	Methyl vinyl ketone	−78 (CuI)	1	(33)	42
2	Cyclohex-2-enone	−30	2	(36)	74
3	3-Methylcyclohex-2-enone	−60 to −10	6	(37)	83
4	*l*-Carvone	−50 to −20	2	(38)	76

For the reaction of the monoanion (3) with methyl vinyl ketone (Table 3, entry 1), the effect of cuprous iodide has been examined. When the reaction was conducted in the absence of cuprous iodide and quenched with glacial acetic acid, the 1,2-adduct (32) was the major product; it should be noted that in this case, the adduct (32) was not isolated by quenching with aqueous ammonium chloride (see Experimental section). On the other hand, the addition of cuprous iodide caused preferential conjugate addition, even for the short reaction time, thus giving rise to a moderate yield of the oxo-ester (33).

The result of the reaction of the monoanion (3) with cyclohex-2-enone was almost identical with the findings in the reactions carried out by Schultz and Yee[8] at −78 and 25 °C. However, it was found that the kinetic addition of the monoanion (3) at the carbonyl carbon atom also took place even at −78 °C. Thus, the aliquots at −78 °C were taken after 1 and 10 min, and the product fraction was separated by preparative t.l.c. on silica gel. From the analysis of the n.m.r. spectrum of each aliquot, the 1,2- (34) and 1,4-addition product (36) were formed in 28 and 13% yields after 1 min and in 18 and 16% yields after 10 min, respectively.

(d) *Reaction with αβ-Unsaturated Esters.*—Finally, the reactions of the carbanions (2) and (3) with αβ-unsaturated esters and lactones have been examined; the reaction of the dianion (2), however, was found to be unsatisfactory because of formation of an intractable mixture. In contrast, the reaction of the monoanion (3) with αβ-unsaturated esters and lactones (39) underwent smooth and preferential conjugate addition to yield the adducts (40); the results are presented in Scheme 4 and Table 4. The low yield of the adduct (43)



SCHEME 4

from furan-2(5*H*)-one (entry 3) may be due to competitive side-reaction; proton transfer from furan-2(5*H*)-one to the monoanion (3) occurred and the resulting 5-anion species or its equivalent of furan-2(5*H*)-one reacted with other furanone molecules to produce polymerized material. In the case of 3-phenylthiofuran-2(5*H*)-one (entry 4), however, the phenylthio-group effectively stabilized the α-carbanion intermediate arising from conjugate addition,[1b,9] and hence, the adduct (44) was obtained in good yield.

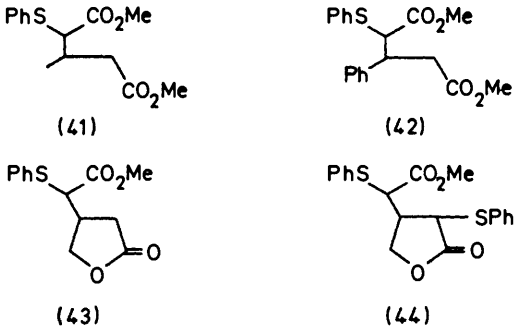
At this point a few remarks regarding the synthetic application of these reactions are appropriate. The hydroxy-esters (5) can be transformed into the α-phenylthioacrylate derivatives (47), which are the precursors

[9] K. Iwai, H. Kosugi, and H. Uda, *Chem. Letters*, 1974, 1237; 1975, 981.

of the synthetically useful compounds, α-phenylsulphinylacrylates.[10] The selective dehydration of the

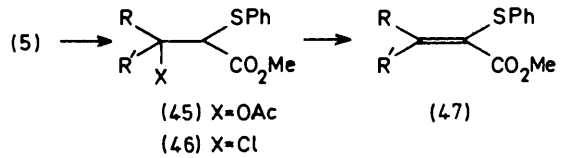
TABLE 4

Reaction of the monoanion (3) with conjugated esters and lactones



Entry	Conjugated ester or lactone	Reaction temp. (°)	Reaction time (h)	Product	% Yield
1	Methyl crotonate	−30 to −15	3	(41)	70
2	Methyl cinnamate	−60 to 0	9.5	(42)	75
3	Furan-2(5*H*)-one	−50 to −20	4	(43)	16
4	3-Phenylthiofuran-2(5*H*)-one	−60 to −40	2	(44)	70

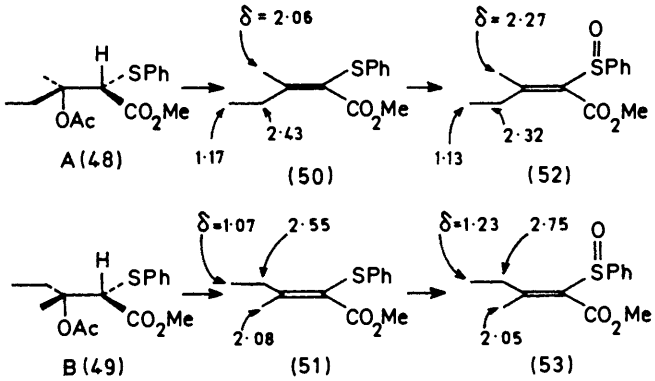
hydroxy-esters (5) to the acrylates (47) was accomplished by base-catalysed elimination through the acetoxy- (45) or chloro-ester (46), and among the various conditions examined (see Experimental section) the best results were obtained by the acetylation of the hydroxy-esters (5) and subsequent elimination of acetic acid by LDA or sodium hydride at room temperature (Scheme 5). Thus, the following acrylates (47) were



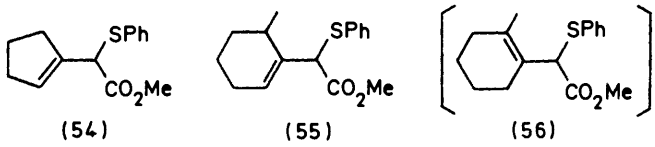
SCHEME 5

obtained in good yields: R or R′ = Et or H; R or R′ = Me_2CH or H; R = R′ = Me; R, R′ = $[CH_2]_4$; R, R′ = $[CH_2]_5$; R, R′ = $[CH_2]_4$·CH(Me). Furthermore, in the case of the hydroxy-ester (16), we have examined separately the dehydration of each diastereomer and found that the elimination of acetic acid of each acetate A (48) and B (49) proceeded stereospecifically to yield the geometrically isomeric acrylates (50) and (51), respectively. Assignment of the geometry of the substituents follows from comparison of the chemical shift values of the olefinic methyl and ethyl protons in the phenylthio-, (50) and (51), and the corresponding phenylsulphinyl-derivatives, (52) and (53). In the isomer (50), only the olefinic methyl signal is shifted markedly downfield (0.2 p.p.m.) upon conversion of the compound into the phenylsulphinyl derivative (52); in contrast, in the isomer (51) the ethyl signal is also shifted downfield, and hence, the relative geometry between the methyl and phenylthio-groups in the former compound (50) is *cis* and in the latter (51) *trans*.

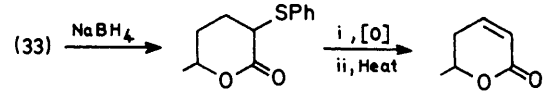
When the dehydration was conducted under acidic conditions (toluene-*p*-sulphonic acid–benzene, reflux), the cyclic hydroxy-ester (12) and (14) exclusively gave the *endo*-olefinic esters (54) and (55) in high yields. In the case of the hydroxy-esters (14) exclusive formation of the single isomer (55) is presumably attributable to



the fact that this is sterically less hindered than the double-bond isomer (56).



Reduction of the adduct (33) with sodium borohydride, followed by lactonization gave the δ-lactone (57), which was then transformed into parasorbic acid (58) in 56% overall yield by the usual dehydrosulphenylation procedure.[1,2a] Thus, the process provides a method for synthesis of αβ-unsaturated δ-lactones starting from acyclic conjugated enones.



In summary, both the (phenylthio)acetic acid dianion (2) and the ester monoanion (3) furnish highly efficient routes to a number of α-substituted (phenylthio)acetic acid derivatives which can be transformed into a wide variety of useful functional groups.

EXPERIMENTAL

All m.p.s are uncorrected. Liquid products were usually purified by evaporative short-path distillation; oil-bath temperatures are recorded. I.r. spectra of solutions in carbon tetrachloride (unless otherwise indicated) were

[10] H. Hagiwara, K. Nakayama, and H. Uda, *Bull. Chem. Soc. Japan*, 1975, **48**, 3769; H. Kosugi, H. Uda, and S. Yamagiwa, *J.C.S. Chem. Comm.*, 1975, 192; 1976, 71.

obtained with a Hitachi EPI-G2 or S2 spectrophotometer. N.m.r. spectra of solutions in carbon tetrachloride (unless otherwise indicated) were recorded with a JEOL C-60HL or PMX-60 instrument, with tetramethylsilane as internal standard; coupling constants are given in Hz. Microanalyses were carried out in the microanalytical laboratory of this Institute.

General Procedure for Reaction of the Dianion (2) *with Aldehydes and Ketones*.—To a freshly prepared solution of the (phenylthio)acetic acid dianion (2) [1] (0.005—0.03 mol) in tetrahydrofuran was added dropwise a solution of aldehyde or ketone (slight excess, 1.2—2.0 equiv.) in tetrahydrofuran (4—10 ml) at −60 °C under nitrogen, and the reaction mixture was stirred at −60 to −40 °C for a few hours (see Tables). A saturated solution of ammonium chloride and then chopped ice were added, and the resulting solution was washed with ether to remove neutral materials. The water layer was acidified with dilute sulphuric acid (6N) and thoroughly extracted with ether. The combined ether extracts were washed with water and brine. Evaporation of the ether left the crude product. The products from isobutyraldehyde, acetone, and cyclopentanone were purified by recrystallization, whilst the others were treated with an excess of ethereal diazomethane and the resulting methyl esters purified by distillation or chromatography on silica gel. Yields are based on (phenylthio)acetic acid used.

3-Hydroxy-4-methyl-2-phenylthiovaleric Acid (6).—Isobutyraldehyde (0.73 g, 0.01 mol) was treated with a solution of the dianion (2) (0.005 mol). The *hydroxy-acid* (6) (1.043 g, 87%; a mixture of stereoisomers) had m.p. 107.5—109 °C [from light petroleum–diethyl ether (1 : 1)], $\nu_{max.}$(KBr) 3 350, 1 705, and 1 230 cm^{-1}; δ($CDCl_3$) 0.95 (3 H, d, *J* 6.1), 1.00 (3 H, d, *J* 6.1), 2.15 (1 H, m), 3.78 (2 H, br,s), 6.30—6.80 (2 H, br,s, OH and CO_2H), and 7.25—7.80 (5 H, m) (Found: C, 59.8; H, 6.8. $C_{12}H_{16}O_3S$ requires C, 60.0; H, 6.7%).

Methyl β-Hydroxy-α-phenylthiodihydrocinnamate (9).—Benzaldehyde (1.04 g, 0.01 mol) was treated with a solution of the dianion (2) (0.005 mol). The crude *hydroxy-ester* (9) (1.29 g, 80%) was chromatographed on silica gel [35 g, light petroleum alone to light petroleum–diethyl ether (1 : 1)] to give the oily isomer A (0.08 g, 5.6%) and the crystalline isomer B (0.7 g, 48.2%). The oily isomer A had b.p. 130 °C at 2 mmHg, δ 3.25 (1 H, s, OH), 3.55 (3 H, s), 3.60 (1 H, d, *J* 7.3), 4.95 (1 H, d, *J* 7.3), and 7.15—7.55 (10 H, m) (Found: C, 66.9; H, 5.5. $C_{16}H_{16}O_3S$ requires C, 66.7; H, 5.6%). The crystalline isomer B had m.p. 99—100 °C (from carbon tetrachloride), $\nu_{max.}$ 3 450, 1 730, 1 710, 1 430, and 1 150 cm^{-1}; δ 3.45 (1 H, d, *J* 6.0, OH), 3.55 (3 H, s), 3.75 (1 H, d, *J* 9.0), 4.85 (1 H, dd, *J* 6.0 and 9.0), 7.13 (5 H, s), and 7.23 (5 H, s) (Found: C, 66.7; H, 5.6. $C_{16}H_{16}O_3S$ requires C, 66.7; H, 5.6%).

3-Hydroxy-2-phenylthioisovaleric Acid (10).—Acetone (3 g, 0.052 mol) was treated with a solution of the dianion (2) (0.03 mol). The *hydroxy-acid* (10) (7.26 g, 96%) had m.p. 87—88° (from carbon tetrachloride), $\nu_{max.}$($CHCl_3$) 3 400, 1 715, 1 620, and 1 260 cm^{-1}; δ 1.40 (6 H, br,s), 3.60 (1 H, s), 7.15—7.65 (5 H, m), and 7.72 (2 H, br,s, OH and CO_2H) (Found: C, 58.5; H, 6.4. $C_{11}H_{14}O_3S$ requires C, 58.4; H, 6.2%).

α-Phenylthio-(1-hydroxycyclopentyl)acetic Acid (11).—Cyclopentanone (3.4 g, 0.0405 mol) was treated with a solution of the dianion (2) (0.03 mol). The *hydroxy-acid* (11) (9.76 g, 100%) had m.p. 132—132.5 °C (from chloroform), $\nu_{max.}$(KBr) 3 350, 1 695, and 1 240 cm^{-1}; δ($CDCl_3$) 1.50—2.40 (8 H, m), 3.70 (1 H, s), 7.13 (2 H, br,s, OH and CO_2H), and 7.20—7.85 (5 H, m) (Found: C, 61.8; H, 6.5. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%).

Methyl 1-Hydroxy-2-methylcyclohexyl-(α-phenylthio)acetate (14).—2-Methylcyclohexanone (1.51 g, 0.0134 mol) was treated with a solution of the dianion (2) (0.01 mol). The *hydroxy-ester* (14) (2.8 g, 96%) had b.p. 140 °C at 1.5 mmHg, $\nu_{max.}$ 3 450, 1 720, 1 440, and 1 320 cm^{-1} (Found: C, 65.1; H, 7.6. $C_{16}H_{22}O_3S$ requires C, 65.3; H, 7.5%). Chromatography on silica gel [60 g, light petroleum alone to light petroleum–diethyl ether (2 : 1)] gave the isomer A (0.59 g, 20%) and the isomer B (1.83 g, 62%). The minor isomer A had δ 0.95 (3 H, d, *J* 6.0), 1.10—2.00 (9 H, m), 2.36 (1 H, s), 3.61 (3 H, s), 3.99 (1 H, s), and 7.18—7.65 (5 H, m). The major isomer B had δ 0.84 (3 H, d, *J* 6.6), 1.00—2.30 (9 H, m), 2.70 (1 H, s), 3.61 (3 H, s), 3.95 (1 H, s), and 7.20—7.60 (5 H, m).

Methyl 3-Hydroxy-3-methyl-2-phenylthio-octanoate (15).—Heptan-2-one (4 g, 0.035 mol) was treated with a solution of the dianion (2) (0.03 mol). The *hydroxy-ester* (15) (8.9 g, 93%; a mixture of stereoisomers) had b.p. 110—130 °C at 1 mmHg, $\nu_{max.}$ 3 450, 1 720, and 1 155 cm^{-1}; δ 0.60—2.10 (14 H, m), 3.02 and 3.15 (total 1 H, each s, OH), 3.64 (4 H, s, OMe and α-H), and 7.20—7.70 (5 H, m) (Found: C, 65.0; H, 8.0. $C_{16}H_{24}O_3S$ requires C, 64.8; H, 8.2%).

Methyl β-Hydroxy-β-phenyl-α-phenylthiobutyrate (17).—Acetophenone (2.3 g, 0.019 mol) was treated with a solution of the dianion (2) (0.015 mol). The *hydroxy-ester* (17) (4 g, 90%; a mixture of stereoisomers) had b.p. 130 °C at 2 mmHg, $\nu_{max.}$ 3 450, 1 720, and 1 210 cm^{-1}; δ 1.63 and 1.69 (total 3 H, each s), 3.38 and 3.68 (total 3 H, each s), 3.86 and 4.06 (total 1 H, each s), 3.92 and 4.15 (total 1 H, each s, OH), and 7.20—7.70 (10 H, m) (Found: C, 67.7; H, 6.1. $C_{17}H_{18}O_3S$ requires C, 67.5; H, 6.0%).

Methyl 3-Hydroxy-2-phenylthiohex-4-enoate (31).—Crotonaldehyde (0.7 g, 0.01 mol) was treated with a solution of the dianion (2) (0.005 mol). The crude *hydroxy-ester* (31) (1.07 g, 65%) was chromatographed on silica gel [40 g, light petroleum alone to light petroleum–diethyl ether (1 : 1)] to give the isomer A (0.28 g, 22.2%) and B (0.53 g, 42%), both of which were purified by distillation, b.p. 140 °C at 2 mmHg. The isomer A had $\nu_{max.}$ 3 500, 1 735, and 1 435 cm^{-1}; δ 1.68 (3 H, d, *J* 5.4), 3.05 (1 H, d, *J* 4.6, OH), 3.60 (3 H, s), 4.25 (1 H, m), 5.20—6.07 (2 H, m), and 7.10—7.60 (5 H, m) (Found: C, 61.7; H, 6.4. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%). The isomer B had $\nu_{max.}$ 3 500, 1 725, and 1 435 cm^{-1}; δ 1.68 (3 H, d, *J* 5.4), 3.10 (1 H, d, *J* 6.0, OH), 3.60 (3 H, s), 4.25 (1 H, m), 5.20—6.06 (2 H, m), and 7.10—7.60 (5 H, m) (Found: C, 61.6; H, 6.5. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%).

Methyl 3-Hydroxy-3-methyl-2-phenylthiopent-4-enoate (32).—Methyl vinyl ketone (0.53 g, 0.0075 mol) was treated with a solution of the dianion (2) (0.005 mol). The crude esterified product was chromatographed on silica gel [preparative t.l.c.; light petroleum–diethyl ether (3 : 1)] to give the *hydroxy-ester* (32) (0.21 g, 48%) and the *oxo-ester* (33) (0.034 g, 8%).

The hydroxy-ester (32) could be further separated into the isomers A and B. The isomers A and B were purified by distillation, b.p. 140 °C at 2 mmHg. The isomer A had $\nu_{max.}$ 3 500, 1 725, 1 155, and 930 cm^{-1}; δ 1.40 (3 H, s), 3.35 (1 H, s, OH), 3.60 (4 H, s, OMe and α-H), 5.05 (1 H, dd, *J* 10.5 and 1.5), 5.28 (1 H, dd, *J* 16.5 and 1.5), 6.00 (1 H, dd, *J* 16.5 and 10.5), and 7.10—7.60 (5 H, m) (Found:

C, 61.7; H, 6.1. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%). The isomer B had $\nu_{max.}$ 3 500, 1 720, 1 150, and 925 cm^{-1}; δ 1.40 (3 H, s), 3.10 (1 H, s, OH), 3.60 (4 H, s, OMe and α-H), 5.10 (1 H, dd, *J* 10.5 and 1.5), 5.35 (1 H, dd, *J* 16.5 and 1.5), and 5.91 (1 H, dd, *J* 16.5 and 10.5), and 7.10—7.70 (5 H, m) (Found: C, 61.8; H, 6.9. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%). The physical properties of the oxo-ester (33) are described below.

Methyl 1-*Hydroxycyclohex*-2-*enyl*-(α-*phenylthio*)*acetate* (34).—Cyclohex-2-enone (0.23 g, 0.0024 mol) was treated with a solution of the dianion (2) (0.002 mol). In this case, ethyl acetate was used for extraction of the crude acid and evaporation of the solvent was carried out under reduced pressure without heating. The crude esterified product was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (2 : 1)] to give the *hydroxy-ester* (34) (0.48 g, 86%), which was further separated into the isomers A and B (2 : 1) by preparative t.l.c. [light petroleum–diethyl ether (4 : 1)] four times. The isomer A had b.p. 140 °C at 2.5 mmHg, m.p. 34—36 °C (crystallized distillate), $\nu_{max.}$ 3 500, 1 735sh, 1 720, 1 310, and 1 155 cm^{-1}; δ 1.50—2.50 (6 H, m), 2.88 (1 H, br,s, OH), 3.62 (4 H, s, OCH_3 and CH), 5.50—6.30 (2 H, m), and 7.10—7.60 (5 H, m) (Found: C, 64.8; H, 7.0. $C_{15}H_{18}O_3S$ requires C, 64.7; H, 6.5%). The isomer B had $\nu_{max.}$ 3 500, 1 740sh, 1 720, 1 370, and 1 160 cm^{-1}; δ 1.20—2.50 (6 H, m), 3.31 (1 H, br,s, OH), 3.62 (4 H, s, OCH_3 and CH), 5.30—6.00 (2 H, m), and 7.10—7.60 (5 H, m) (Found: C, 64.7; H, 6.8. $C_{15}H_{18}O_3$ requires C, 64.7; H, 6.5%).

Methyl 1-*Hydroxy*-3-*methylcyclohex*-2-*enyl*-(α-*phenylthio*)-*acetate* (35).—3-Methylcyclohex-2-enone (0.40 g, 0.0036 mol) was treated with a solution of the dianion (2) (0.003 mol). In this case, the crude adduct was extracted with ethyl acetate and the extract was concentrated under reduced pressure without heating. The crude esterified product (thermally unstable) was purified by preparative t.l.c. [silica gel, light petroleum–diethyl ether (2 : 1)] to give the mixed stereoisomeric *hydroxy-ester* (35) (0.63 g, 72%), $\nu_{max.}$ 3 500, 1 740, 1 720, 1 435, 1 310, and 1 155 cm^{-1}; δ 1.00—2.50 (9 H, m), 2.80 and 3.15 (total 1 H, each br,s, OH), 3.62 (4 H, s, OCH_3 and CH), 5.20 and 5.82 (total 1 H, each s), and 7.00—7.70 (5 H, m). This sample decomposed on distillation, and hence, the elemental analysis was not carried out.

General Procedure for Reaction of the Monoanion (3) *with Aldehydes, Ketones, and Unsaturated Esters*.—To a freshly prepared solution of lithium di-isopropylamide (0.003—0.05 mol) in tetrahydrofuran was added dropwise a solution of methyl (phenylthio)acetate (equimolar amount) in tetrahydrofuran at −60 °C under nitrogen, and the mixture was stirred at −60 °C for 1 h. A solution of a carbonyl compound (slightly excess) in tetrahydrofuran was added to the above monoanion (3) solution. For saturated compounds, the reaction mixture was stirred at −60 °C for an appropriate time. For conjugated enones, the reaction temperatures and times are shown in Table 3. A saturated solution of ammonium chloride and chopped ice were added to the reaction mixture at the same temperature, and the mixture was thoroughly extracted with ether. The combined extracts were washed with water and brine. Evaporation of the ether left the crude product which was purified by distillation or by combination of chromatography and distillation. The yields were based on the starting phenylthioacetate.

Methyl β-*Hydroxy*-γ-*methyl*-α-*phenylthiovalerate* (7).—Isobutyraldehyde (2 g, 0.028 mol) was treated with a solution of the monoanion (3) (0.02 mol). The crude *hydroxy-ester* (7) (5.46 g) was chromatographed on silica gel [100 g, light petroleum alone to light petroleum–diethyl ether (1 : 1)] to give isomer A (1.42 g, 28%) and B (3.05 g, 60%), both of which were purified by distillation, b.p. 110 °C at 2 mmHg. Isomer A had $\nu_{max.}$ 3 500, 1 735, and 1 155 cm^{-1}; δ 0.93 (6 H, d, *J* 6.0), 1.81 (1 H, m), 2.93 (1 H, br,s, OH), 3.60 (5 H, br,s, OCH_3, and α- and β-CH), and 7.07—7.50 (5 H, m) (Found: C, 61.8; H, 6.7. $C_{13}H_{18}O_3S$ requires C, 61.4; H, 7.1%). Isomer B had $\nu_{max.}$ 3 500, 1 730, and 1 155 cm^{-1}; δ 0.83 (3 H, d, *J* 7.0), 0.95 (3 H, d, *J* 7.0), 2.03 (1 H, m), 2.47 (1 H, br,s, OH), 3.60 (5 H, s, OCH_3, and α- and β-CH), and 7.07—7.50 (5 H, m) (Found: C, 61.6; H, 7.1. $C_{13}H_{18}O_3S$ requires C, 61.4; H, 7.1%).

Methyl β-*Hydroxy*-α-*phenylthiovalerate* (8).—Propionaldehyde (3.5 g, 0.06 mol) was treated with a solution of the monoanion (3) (0.04 mol). The *hydroxy-ester* (8) (7.8 g, 81%; a mixture of stereoisomers) had b.p. 129—133 °C at 1 mmHg, $\nu_{max.}$ 3 500, 1 725, 1 435, and 1 155 cm^{-1}; δ 0.98 (3 H, t, *J* 7.0), 1.17—2.10 (2 H, m), 2.76 (1 H, br, OH), 3.40—4.00 (2 H, m), 3.65 (3 H, s), and 7.00—7.63 (5 H, m) (Found: C, 59.7; H, 6.8. $C_{12}H_{16}O_3S$ requires C, 60.0; H, 6.7%).

Methyl 1-*Hydroxycyclopentyl*-(α-*phenylthio*)*acetate* (12).—Cyclopentanone (4.5 g, 0.053 mol) was treated with a solution of the monoanion (3) (0.04 mol). Chromatography of the crude product [silica gel, 150 g, light petroleum alone to light petroleum–diethyl ether (1 : 1)] gave the pure *hydroxy-ester* (12) (8.12 g, 76%), b.p. 120—130 °C at 2 mmHg, $\nu_{max.}$ 3 450, 1 720, and 1 150 cm^{-1}; δ 1.40—2.20 (8 H, m), 3.00 (1 H, s, OH), 3.62 (4 H, s, OCH_3 and CH), and 7.10—7.60 (5 H, m) (Found: C, 63.3; H, 6.9. $C_{14}H_{18}O_3S$ requires C, 63.1; H, 6.8%).

Methyl 1-*Hydroxycyclohexyl*-(α-*phenylthio*)*acetate* (13).—Cyclohexanone (1.2 g, 0.012 mol) was treated with a solution of the monoanion (3) (0.01 mol). Chromatography of the crude product [silica gel, 35 g, light petroleum alone to light petroleum–diethyl ether (2 : 1)] gave the pure *hydroxy-ester* (13) (2.47 g, 88%), b.p. 100—130 °C at 2 mmHg, $\nu_{max.}$ 3 500, 1 720, and 1 155 cm^{-1}; δ 0.90—2.40 (10 H, m), 3.05 (1 H, br,s, OH), 3.60 (4 H, s, OCH_3 and CH), and 7.10—7.60 (5 H, m) (Found: C, 64.1; H, 7.4. $C_{15}H_{20}O_3S$ requires C, 64.3; H, 7.2%).

Methyl β-*Hydroxy*-β-*methyl*-α-*phenylthiovalerate* (16).—Butan-2-one (4 g, 0.055 mol) was treated with a solution of the monoanion (3) (0.04 mol). The *hydroxy-ester* (16) (8.82 g, 87%) had b.p. 123—125 °C at 3 mmHg, $\nu_{max.}$ 3 500, 1 720, 1 435, 1 315, and 1 155 cm^{-1} (Found: C, 61.5; H, 7.0. $C_{13}H_{18}O_3S$ requires C, 61.4; H, 7.1%). Chromatography on silica gel [200 g, light petroleum–diethyl ether (20 : 1) to (2 : 1)] gave the isomer A (4.88 g) and B (1.92 g). The isomer A had δ 0.92 (3 H, t, *J* 7.0), 1.27 (3 H, s), 1.74 (2 H, q, *J* 7.0), 3.00 (1 H, s, OH), 3.64 (4 H, s, OCH_3 and CH), and 7.00—7.60 (5 H, m). The isomer B had δ 0.89 (3 H, t, *J* 7.0), 1.33 (3 H, s), 1.60 (2 H, q, *J* 7.0), 2.79 (1 H, s, OH), 3.60 (4 H, s,OCH_3 and CH), and 6.90—7.70 (5 H, m).

Methyl 5-*Oxo*-2-*phenylthiohexanoate* (33).—(a) *Without cuprous iodide*. Methyl vinyl ketone (1.54 g, 0.022 mol) was treated with a solution of the monoanion (3) (0.02 mol). In this case, the reaction was quenched with glacial acetic acid (4 ml), and the excess of acetic acid was removed by washing the ethereal extract with sodium hydrogen carbonate solution. The crude product (5.02 g) was chromatographed on silica gel [50 g, light petroleum–

diethyl ether (4 : 1) to (2 : 1)] to give the *hydroxy-ester* (32) (1.54 g, 31%) and the *oxo-ester* (33) (0.70 g, 14%).

(b) *With cuprous iodide.* To a solution of the monoanion (3) (0.01 mol) was added cuprous iodide (0.91 g, 0.005 mol), and the mixture was stirred at −78 °C for 1 h. Then, a solution of methyl vinyl ketone (0.88 g, 0.011 mol) in tetrahydrofuran (10 ml) was added to the above mixture. The crude product was chromatographed on silica gel [60 g, light petroleum to light petroleum–diethyl ether (gradient) to diethyl ether] to give the *oxo-ester* (33) (1.06 g, 42%), b.p. 110—130 °C at 2 mmHg, $\nu_{max.}$ 1 730, 1 715, and 1 155 cm^{-1}; δ 2.00 (3 H, s), 2.00 (2 H, q, *J* 6.7), 2.55 (2 H, t, *J* 6.7), 3.59 (3 H, s), 3.68 (1 H, t, *J* 6.7), and 7.18—7.60 (5 H, m) (Found: C, 62.0; H, 6.6. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%).

Methyl 3-*Oxocyclohexyl*-(α-*phenylthio*)*acetate* (36).—Cyclohex-2-enone (0.35 g, 0.0036 mol) was treated with a solution of the monoanion (3) (0.003 mol). The crude product (0.84 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (2 : 1)] to give the *oxo-ester* (36) (0.62 g, 74%; a mixture of stereoisomers), b.p. 140—150 °C at 1 mmHg, $\nu_{max.}$ 1 720, 1 265, and 1 155 cm^{-1}; δ 1.10—2.80 (9 H, m), 3.40—3.80 (1 H, m), 3.58 (3 H, s), and 7.10—7.50 (5 H, m) (Found: C, 64.5; H, 6.2. $C_{15}H_{18}O_3S$ requires C, 64.7; H, 6.5%).

Methyl 1-*Methyl*-3-*oxocyclohexyl*-(α-*phenylthio*)*acetate* (37).—3-Methylcyclohex-2-enone (0.40 g, 0.0036 mol) was treated with a solution of the monoanion (3) (0.003 mol). The crude product (0.90 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (2 : 1)] to give the *oxo-ester* (37) (0.73 g, 83%; a mixture of stereoisomers), b.p. 110—125 °C at 3 mmHg, $\nu_{max.}$ 1 730, 1 710, and 1 140 cm^{-1}; δ 1.11 and 1.15 (total 3 H, each s), 1.50—2.90 (8 H, m), 3.42 (1 H, s), 3.60 (3 H, s), and 7.10—7.60 (5 H, m) (Found: C, 65.5; H, 6.9. $C_{16}H_{20}O_3S$ requires C, 65.7; H, 6.9%).

Methyl 5-*Isopropenyl*-2-*methyl*-3-*oxocyclohexyl*-(α-*phenylthio*)*acetate* (38).—(−)-Carvone (0.54 g, 0.0036 mol) was treated with a solution of the monoanion (3) (0.003 mol). The crude product (1.04 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (2 : 1)] to give two fractions A (0.52 g, 52%) and B (wax-like solid, 0.24 g, 24%) of the mixed stereoisomeric *oxo-esters* (38). The minor waxy fraction had b.p. 160—170 °C at 2 mmHg, $\nu_{max.}$ 1 740, 1 715, 1 270, and 1 160 cm^{-1}; δ 1.05 (3 H, d, *J* 7.0), 1.72 and 1.78 (total 3 H, each s), 1.90—3.30 (7 H, m), 3.40—4.10 (4 H, m), 4.74 (2 H, br,s), and 7.00—7.70 (5 H, m) (Found: C, 68.9; H, 7.3. $C_{19}H_{24}O_3S$ requires C, 68.7; H, 7.3%). The major fraction had $\nu_{max.}$ 1 740, 1 715, 1 265, and 1 155 cm^{-1}; δ 0.99 (3 H, t like), 1.74 (3 H, d like), 1.90—3.10 (7 H, m), 3.20—4.00 (1 H, m), 3.67 (3 H, d like), 4.74 (2 H, d like), and 7.00—7.70 (5 H, m) [*m/e* 332 (M^+). $C_{19}H_{24}O_3S$ requires *M* 332, determined with a Shimadzu LKB-9000 instrument]. This sample did not give the satisfactory combustion analysis, probably because of impurities.

Dimethyl β-*Methyl*-α-*phenylthioglutarate* (41).—Methyl crotonate (0.36 g, 0.0036 mol) was treated with a solution of the monoanion (3) (0.003 mol). The crude product (0.84 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (3 : 2)] to give the *diester* (41) (0.59 g, 70%; a mixture of stereoisomers), b.p. 120 °C at 1.0 mmHg, $\nu_{max.}$ 1 735, 1 430, and 1 160 cm^{-1}; δ 1.10 (3 H, t like), 2.10—3.00 (3 H, m), 3.50—3.90 (1 H, m), 3.60 (6 H, s), and 7.10—7.50 (5 H, m). This sample still contained a trace of methyl crotonate, as detected by n.m.r. spectroscopy and, hence, the elemental analysis was not carried out. Mass spectrum showed the molecular ion peak at *m/e* 282 ($C_{14}H_{18}O_4S$ requires *M*, 282).

Dimethyl β-*Phenyl*-α-*phenylthioglutarate* (42).—Methyl cinnamate (0.59 g, 0.0036 mol) was treated with a solution of the monoanion (3) (0.003 mol). The crude product (1.09 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (2 : 1)] to give the *diester* (42) (0.78 g, 75%; a mixture of stereoisomers), b.p. 160 °C at 2.5 mmHg, m.p. 48.5—50.0 °C (crystallized); $\nu_{max.}$ 1 740, 1 265, and 1 155 cm^{-1}; δ 2.78 (2 H, d, *J* 7.0), 3.30—4.10 (2 H, m), 3.44 (3 H, s), 3.57 (3 H, s), and 7.00—7.60 (10 H, m) (Found: C, 66.4; H, 5.8. $C_{19}H_{20}O_4S$ requires C, 66.3; H, 5.9%).

4-[*Methoxycarbonyl*(*phenylthio*)*methyl*]*tetrahydrofuran*-2-*one* (43).—Furan-2(5*H*)-one (0.30 g, 0.0036 mol) was treated with a solution of the monoanion (3) (0.003 mol). The crude product (0.61 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (2 : 1)] to give the *ester-lactone* (43) (0.13 g, 16%; a mixture of stereoisomers), b.p. 120 °C at 1 mmHg, $\nu_{max.}$ 1 785, 1 740, and 1 160 cm^{-1}; δ 2.00—3.10 (3 H, m), 3.56 (3 H, s), 3.20—4.60 (3 H, m), and 7.00—7.70 (5 H, m) (Found: C, 58.6; H, 5.1. $C_{13}H_{14}O_4S$ requires C, 58.6; H, 5.3%).

4-[*Methoxycarbonyl*(*phenylthio*)*methyl*]-3-*phenylthiotetrahydrofuran*-2-*one* (44).—3-Phenylthiofuran-2(5*H*)-one (0.19 g, 0.001 mol) was treated with a solution of the monoanion (3) (0.001 mol). The crude product (0.36 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (2 : 1)] to give the *ester-lactone* (44) (0.26 g, 70%; a mixture of stereoisomers), b.p. 180 °C at 2 mmHg, $\nu_{max.}$($CHCl_3$) 1 780, 1 735, and 1 160 cm^{-1}; δ 2.50—3.20 (1 H, m), 3.61 (3 H, d like), 3.40—4.80 (4 H, m), 6.90—7.80 (10 H, m) (Found: C, 60.8; H, 4.8. $C_{19}H_{18}O_4S$ requires C, 61.0; H, 4.9%).

Methyl Phenylthiomethyl Ketone (21).—To a solution of the dianion (2) (0.006 mol) was added dropwise a solution of ethyl acetate (0.53 g, 0.006 mol) in tetrahydrofuran (6 ml) at 0 °C under nitrogen, and the reaction mixture was stirred for 20 h. Chopped ice and then water were added, and the resulting solution was extracted twice with ether. The water layer was acidified with 6N-hydrochloric acid and again extracted with ether twice. The combined extracts were washed with water and brine. Evaporation of the solvent, and distillation of the oil remaining gave the *phenylthiomethyl ketone* (21) (0.42 g, 42%), b.p. 120—150 °C at 5 mmHg, $\nu_{max.}$ 1 710, 1 480, and 1 315 cm^{-1}; δ 2.18 (3 H, s), 3.52 (2 H, s), and 7.00—7.38 (5 H, m).[11]

Butyl Phenylthiomethyl Ketone (22).—To a solution of the dianion (2) (0.003 mol) was added dropwise a solution of ethyl valerate (0.39 g, 0.003 mol) in tetrahydrofuran (3 ml) at 0 °C under nitrogen, and the reaction mixture was stirred for 22 h. Chopped ice and 3N-hydrochloric acid were added, and the resulting mixture was extracted twice with ether. The combined extracts were washed with water and brine, and evaporated. The residual oil (0.76 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (5 : 1)] to give, in addition to the recovered phenylthioacetic acid (0.24 g, 47%), the *phenylthiomethyl ketone* (22) (0.32 g, 51%), m.p. below room temperature (crystallized on ice-cooling), $\nu_{max.}$ 1 710, 1 480, and 1 440 cm^{-1}; δ 0.60—1.80 (7 H, m), 2.51 (2 H, t, *J* 6.2),

[11] A. Delisle, *Ann.*, 1890, **260**, 250.

3.51 (2 H, s), and 7.08 (5 H, m) (Found: C, 69.4; H, 8.0. $C_{12}H_{16}OS$ requires C, 69.2; H, 7.7%).

3-*Hydroxypropyl Phenylthiomethyl Ketone* (24).—(a) *From the dianion* (2). To a solution of the dianion (2) (0.003 mol) was added dropwise a solution of γ-butyrolactone (0.31 g, 0.0036 mol) in tetrahydrofuran (4 ml) at 0 °C under nitrogen, and the reaction mixture was stirred for 18 h. Saturated ammonium chloride solution was added, and the resulting solution was extracted twice with ether. The combined extracts were washed with water and brine. Evaporation of the solvent gave the crystalline *phenylthiomethyl ketone* (24) (0.45 g, 71%), m.p. 38—39 °C [from light petroleum–diethyl ether (1 : 2)], $\nu_{max.}$(KBr) 3 250 and 1 700 cm^{-1}; δ 1.47—2.20 (2 H, m), 2.65 and 3.48 (total 2 H, each t, *J* 6.3 and 6.0), 3.21 and 3.58 (total 2 H, each s), 3.65—4.08 (2 H, m), and 7.00—7.50 (5 H, m) (Found: C, 62.8; H, 6.7. $C_{11}H_{14}O_2S$ requires C, 62.7; H, 6.8%).

(b) *From the thioanisole anion* (26). A solution of butyllithium in hexane (1.6N; 2 ml) was added dropwise to a solution of thioanisole (0.37 g, 0.003 mol) and triethylenediamine (0.34 g, 0.003 mol) in tetrahydrofuran (4.5 ml) at 0 °C under nitrogen. After 10 min the reaction mixture was warmed to room temperature and stirred for 1 h. The thioanisole anion solution was then added dropwise to a solution of γ-butyrolactone (0.26 g, 0.003 mol) in tetrahydrofuran (3 ml) at −40 °C under nitrogen. After being stirred at −40 °C for 2.2 h, the reaction mixture was acidified with 3N-hydrochloric acid and extracted with ether. The combined ether extracts were washed with water and brine, and evaporated. The residual oil (0.49 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (1 : 3)] to give the *phenylthiomethyl ketone* (24) (0.16 g, 25%).

Procedures for Dehydration of the Hydroxy-esters (5) *to the Acrylates* (47).—(a) *Acetylation of the hydroxy-esters* (5). (i) *With acetic anhydride*. A solution of the hydroxy-ester (5) in acetic anhydride (*ca.* 10 ml for 0.013 mol) was heated under reflux for 3 h. The reaction mixture was basified by addition of chopped ice and 30% sodium hydroxide solution, and was then extracted twice with ether. The combined extracts were washed with water and brine, and evaporated to give the *acetoxy-ester* (45).

(ii) *With acetic anhydride–pyridine*. A solution of the secondary hydroxy-ester (5) in acetic anhydride and pyridine (*ca.* 9 ml each for 0.02 mol) was allowed to stand at room temperature for several hours. The reaction mixture was poured into ice–water and extracted with ether twice. The combined extracts were washed successively with dilute sodium hydroxide solution, dilute sulphuric acid, water, and brine, and evaporated to give the *acetoxy-ester* (45).

(iii) *With acetyl chloride–diethylaniline*. A solution of the tertiary hydroxy-ester (5) in a mixture of acetyl chloride and diethylaniline (*ca.* 9 and 6 ml for 0.02 mol) was allowed to stand at 0 °C–room temperature for 1—2 h and then at 50 °C for several hours. The reaction mixture was poured into ice–water and extracted twice with ether. The combined extracts were washed successively with dilute sodium hydroxide solution, water, and brine, and evaporated to give the *acetoxy-ester* (45).

(b) *Elimination of acetic acid*. (i) *Method A* (*pyridine*). The acetoxy-ester (45) was dissolved in pyridine (*ca.* 10 ml for 0.013 mol), and the resulting solution was heated under reflux for 6 h. The reaction mixture was acidified by addition of chopped ice and 6N-sulphuric acid, and was then extracted twice with ether. The combined extracts were washed with water and brine, and evaporated to give the crude *acrylate* (47).

(ii) *Method B* (*LDA*). A solution of the acetoxy-ester (45) in tetrahydrofuran was added to a freshly prepared solution of LDA (*ca.* 1.2 equiv.) at 0 °C under nitrogen, and the mixture was stirred at room temperature for 1—2 h. The solution was then cooled at −30 to −40 °C and a saturated solution of ammonium chloride was added. The mixture was twice extracted with ether. The combined extracts were washed with water and brine, and evaporated to give the crude *acrylate* (47).

(iii) *Method C* (*sodium hydride*). A solution of the acetoxy-ester (45) in tetrahydrofuran was added to a slurry of sodium hydride (*ca.* 1.2—1.4 equiv.) in tetrahydrofuran (total *ca.* 7—30 ml for 0.0004—0.01 mol) at 0 °C under nitrogen, and the reaction mixture was stirred at room temperature for several hours (for the tertiary acetoxy-compound) and then at 50 °C for *ca.* 10 h (for the secondary acetoxy one). The mixture was poured into ice–water and extracted twice with ether. The combined extracts were washed with water and brine, and evaporated to give the *acrylate* (47).

(c) *Chlorination and dehydrochlorination: Method D*. To a solution of the hydroxy-ester (5) in pyridine [*ca.* 5 ml for 0.01 mol of (5)] was added dropwise thionyl chloride (1.5 equiv.) at 0 °C, and the mixture was then stirred for 2—3 h. This reaction mixture was then worked up in two different ways. (i) The mixture was acidified by addition of chopped ice and 6N-sulphuric acid and extracted twice with ether. The combined extracts were washed with water and brine, and then evaporated to give a mixture of the *chloro-ester* (46) and *acrylate* (47). This mixture was dissolved in pyridine, and the solution was heated under reflux for 1.5—3 h. After cooling, the mixture was worked up in the same manner as described above (acidification and extraction).

(ii) The reaction mixture was directly, without isolation of the products, heated under reflux for 1.5—3 h, and worked up in the same manner. The ethereal extracts thus obtained was evaporated to give the *acrylate* (47).

Methyl E- *or* Z-2-*Phenylthiopent*-2-*enoate* (47; R or R′ = Et or H).—The *acetoxy-ester* (45; R or R′ = Et or H) (5.13 g, 96%) was prepared by treating the mixed stereoisomeric hydroxy-ester (8) (4.56 g) with acetic anhydride and pyridine. Elimination of acetic acid from the acetoxy-ester (2.42 g, 0.0086 mol) was carried out according to Method C to give the crude product (1.93 g). A portion of the product (0.17 g) was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (4 : 1)] to give the individual isomers of the *acrylate* (47; R or R′ = Et or H) [0.13 g, 76% from (8)] (the definite geometry of the substituents has not yet been established), b.p. 60—70° at 1 mmHg, $\nu_{max.}$ 1 715, 1 610, 1 475, 1 435, and 1 240 cm^{-1}; δ 1.10 (3 H, t, *J* 7.0), 2.51 (2 H, quint., *J* 7.0), 3.57 (3 H, s), 7.11 (5 H, s), and 7.30 (1 H, t, *J* 7.0) (Found: C, 64.6; H, 6.1. $C_{12}H_{14}O_2S$ requires C, 64.9; H, 6.4%).

Methyl E- *and* Z-4-*Methyl*-2-*phenylthiopent*-2-*enoate* (47; R or R′ = Me_2CH or H).—The *acetoxy-ester* (45; R or R′ = Me_2CH or H) was prepared by treating the mixed stereoisomeric hydroxy-ester (7) (6.72 g) with acetic anhydride and pyridine. The elimination of acetic acid from the acetoxy-ester was carried out according to Method B to give the *acrylate* (47; R or R′ = Me_2CH or H) (3.60 g, 58%), b.p. 60—90° at 2 mmHg, $\nu_{max.}$ 1 715, 1 605, 1 585, 1 475,

1 435, and 1 240 cm^{-1}; δ 1.07 (6 H, d, *J* 7.0), 2.70—3.50 (1 H, m), 3.50 (3 H, s), 7.03 (1 H, d, *J* 10.0), and 7.04 (5 H, br,s) (Found: C, 66.2; H, 6.9. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8%).

Methyl α-Phenylthiosenecioate (47; R = R′ = Me).—The *acrylate* (47; R = R′ = Me) (1.34 g, 74%) was prepared from the hydroxy-acid (10) (2.0 g) according to Method D and had b.p. 130° at 3 mmHg, $\nu_{max.}$ 1 715, 1 580, 1 435, and 1 245 cm^{-1}; δ 2.07 (6 H, s), 3.50 (3 H, s), and 7.10 (5 H, s) (Found: C, 64.6; H, 6.5. $C_{12}H_{14}O_2S$ requires C, 64.9; H, 6.4%).

Methyl Cyclopentylidene(phenylthio)acetate (47; R, R′ = $[CH_2]_4$).—(i) The *acetoxy-ester* (45; R, R′ = $[CH_2]_4$) was prepared by treating the hydroxy-ester (12) (3.4 g) with acetic anhydride. The elimination of acetic acid from the acetoxy–ester was carried out according to Method A to give the *acrylate* (47; R, R′ = $[CH_2]_4$) (3.0 g, 94%), b.p. 130—150 °C at 1 mmHg; $\nu_{max.}$ 1 715, 1 600, 1 235, and 1 032 cm^{-1}; δ 1.40—2.20 (4 H, m), 2.20—3.10 (4 H, m), 3.52 (3 H, s), and 6.98—7.50 (5 H, m) (Found: C, 68.0; H, 6.7. $C_{14}H_{16}O_2S$ requires C, 67.7; H, 6.5%).

(ii) The *acrylate* (47; R, R′ = $[CH_2]_4$) (3.0 g, 96%) was prepared from the hydroxy-ester (12) (3.37 g) according to Method D.

Methyl Cyclohexylidene(phenylthio)acetate (47; R, R′ = $[CH_2]_5$).—(i) The *acetoxy-ester* (45; R, R′ = $[CH_2]_5$) was prepared by treating the hydroxy-ester (13) (5.0 g) with acetyl chloride and diethylaniline. Elimination of acetic acid from the acetoxy-ester was carried out according to Method B to give the *acrylate* (47; R, R′ = $[CH_2]_5$) (2.7 g, 59%), b.p. 90—110 °C at 1 mmHg, $\nu_{max.}$ 1 715, 1 580, 1 435, and 1 205 cm^{-1}; δ 1.20—1.90 (6 H, m), 2.20—2.80 (4 H, m), 3.50 (3 H, s), and 6.90—7.40 (5 H, m) (Found: C, 68.7; H, 6.7. $C_{15}H_{18}O_2S$ requires C, 68.7; H, 6.9%).

(ii) Elimination of acetic acid from the acetoxy-ester (0.12 g) was carried out according to Method C to give the *acrylate* (47; R, R′ = $[CH_2]_5$) (0.07 g, 73%).

Methyl (E)- and (Z)-Methylcyclohexylidene(phenylthio)acetate (47; R, R′ = $[CH_2]_4$·CHMe).—The *acetoxy-ester* (45; R, R′ = $[CH_2]_4$·CHMe) was prepared by treating the hydroxy-ester (14) (7.24 g) with acetyl chloride and diethylaniline. Elimination of acetic acid from the acetoxy-ester was carried out according to Method B to give the *acrylate* (47; R, R′ = $[CH_2]_4$·CHMe) (2.0 g, 29%), b.p. 90—110 °C at 1 mmHg, $\nu_{max.}$ 1 715, 1 580, 1 435, and 1 215 cm^{-1}; δ 1.08 and 1.20 (total 3 H, each d, *J* 7.0), 0.50—3.50 (9 H, m), 3.45 and 3.49 (total 3 H, each s), and 6.80—7.20 (5 H, m) (Found: C, 69.5; H, 7.2. $C_{16}H_{20}O_2S$ requires C, 69.5; H, 7.3%).

Methyl (E)-3-*Methyl*-2-*phenylthiopent*-2-*enoate* (50).—The *acetoxy-ester* (48) was prepared by treating the isomer A of the hydroxy-ester (16) (4.88 g) with acetyl chloride and diethylaniline. Elimination of acetic acid from the acetoxy-ester was carried out according to Method B, and the crude product was chromatographed on silica gel [40 g, light petroleum alone to light petroleum–diethyl ether (5 : 1)] to give the (E)-*acrylate* (50) (2.62 g, 56%), b.p. 75—100 °C at 1 mmHg, $\nu_{max.}$ 1 715, 1 580, 1 430, and 1 240 cm^{-1}; δ 1.17 (3 H, t, *J* 7.0), 2.06 (3 H, s), 2.43 (2 H, q, *J* 7.0), 3.51 (3 H, s), and 7.13 (5 H, br,s) (Found: C, 66.2; H, 6.8. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8%).

Methyl (Z)-3-*Methyl*-2-*phenylthiopent*-2-*enoate* (51).—The Z-*acrylate* (51) (1.0 g, 56%) was prepared from the isomer B of the hydroxy-ester (16) (1.92 g) in the same manner as described in the preceding experiment and had $\nu_{max.}$ 1 715, 1 580, 1 435, and 1 230 cm^{-1}; δ 1.07 (3 H, t, *J* 7.0), 2.08 (3 H, s), 2.55 (2 H, q, *J* 7.0), 3.50 (3 H, s), and 7.13 (5 H, br,s) (Found: C, 65.9; H, 7.0. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8%).

Methyl (E)-3-*Methyl*-2-*phenylsulphinylpent*-2-*enoate* (52).—A solution of the *E*-phenylthioacrylate (50) (0.24 g) and *m*-chloroperbenzoic acid (0.26 g, 1.1 equiv.) in dichloromethane (25 ml) was allowed to stand at 0° for 20 min. The reaction mixture was washed with sodium bicarbonate solution, water, and brine, and evaporated. The residual oil (0.22 g) was chromatographed on silica gel (preparative t.l.c., ether) to give the E-*phenylsulphinylacrylate* (52) (0.17 g, 68%), $\nu_{max.}$ 1 715, 1 615, 1 245, and 1 050 cm^{-1}; δ 1.13 (3 H, t, *J* 7.0), 2.27 (3 H, s), 2.32 (2 H, q, *J* 7.0), 3.47 (3 H, s), and 7.40 (5 H, s) (Found: C, 62.1; H, 6.6. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%).

Methyl (Z)-3-*Methyl*-2-*phenylsulphinylpent*-2-*enoate* (53).—The Z-*phenylsulphinylacrylate* (53) (0.17 g, 78%) was prepared from the *Z*-phenylthioacrylate (51) (0.19 g) in the same manner as described in the preceding experiment and had $\nu_{max.}$ 1 715, 1 615, 1 235, and 1 050 cm^{-1}; δ 1.23 (3 H, t, *J* 7.0), 2.05 (3 H, s), 2.75 (2 H, q, *J* 7.0), 3.43 (3 H, s), and 7.43 (5 H, br,s) (Found: C, 62.1; H, 6.5. $C_{13}H_{16}O_3S$ requires C, 61.9; H, 6.4%).

Methyl α-Phenylthio(cyclopent-1-enyl)acetate (54).—A solution of the hydroxy-ester (12) (0.36 g) and toluene-*p*-sulphonic acid (trace) in benzene (10 ml) was heated under reflux for 1 h. The reaction mixture was poured into a mixture of ether and ice–water, and the water layer was extracted with ether. The combined organic layers were washed with water and brine, and evaporated to give the *unsaturated ester* (54) (0.34 g, 89%), b.p. 100—120 °C at 1 mmHg, $\nu_{max.}$ 1 740, 1 715, and 1 225 cm^{-1}; δ 1.50—2.70 (6 H, m), 3.63 (3 H, s), 4.38 (1 H, s), 5.63 (1 H, br,s, $w_{1/2}$ 6.0), and 7.10—7.60 (5 H, m) (Found: C, 67.9; H, 6.4. $C_{14}H_{16}O_2S$ requires C, 67.7; H, 6.5%).

Methyl α-Phenylthio(6-methylcyclohex-1-enyl)acetate (55).—The *unsaturated ester* (55) (0.134 g, 100%) was prepared from the hydroxy-ester (14) (0.136 g) in the same manner as described in the preceding experiment and had $\nu_{max.}$ 1 740, 1 440, and 1 150 cm^{-1}; δ 1.08 (3 H, d, *J* 8.0), 0.70—2.70 (7 H, m), 3.60 (3 H, s), 4.17 (1 H, s), 5.78 (1 H, m), and 7.10—7.60 (5 H, m) (Found: C, 69.8; H, 7.0. $C_{16}H_{20}O_2S$ requires C, 69.5; H, 7.3%).

δ-Methyl-α-phenylthio-δ-valerolactone (57).—To a solution of the oxo-ester (33) (2.74 g, 0.0109 mol) in methanol (150 ml) was added portionwise sodium borohydride (0.41 g, 0.0109 mol) at 0 °C, and the mixture was stirred at 0 °C for 1 h. Potassium hydroxide solution (40%, 2 ml) and water were added to the mixture which was then further stirred at room temperature for 2—3 h. The reaction mixture was concentrated (*ca.* 70 ml of methanol was removed) under ordinary pressure, acidified by addition of chopped ice and 10% hydrochloric acid, and extracted with chloroform. The combined extracts were washed with water and brine, and evaporated. The oil remaining (2.43 g) was dissolved in benzene containing a catalytic amount of toluene-*p*-sulphonic acid, and the solution was heated under reflux for 2.5 h using a Dean–Stark water separator. After the removal of benzene, the concentrate was passed through a short column of active charcoal (upper) and silica gel with the aid of ether, and evaporated to give the mixed stereoisomeric *lactones* (57) (2.18 g). A small portion of the product was chromatographed on silica gel [preparative t.l.c., light petroleum–diethyl ether (5 : 1)] to give an

analytical sample, b.p. 110—135 °C at 2 mmHg, $\nu_{max.}$ 1 740, 1 430, and 1 380 cm^{-1}; δ 1.32 (3 H, d, *J* 6.0), 1.50—2.50 (4 H, m), 3.73 and 3.83 (total 1 H, each t, *J* 6.0), 4.00—4.80 (1 H, m), and 7.00—7.60 (5 H, m) (Found: C, 65.1; H, 6.6. $C_{12}H_{14}O_2S$ requires C, 64.9; H, 6.4%).

Parasorbic Acid (58).—To a solution of the total crude lactone (57) in methanol (15 ml) was added dropwise a solution of sodium metaperiodate (2.52 g) in water (15 ml) at 0 °C, and the reaction mixture was stirred at room temperature for 13 h. Inorganic salts were filtered off, and the filtrate was extracted with chloroform. The combined extracts were washed with water and brine, and evaporated to give the sulphoxide (2.34 g). A portion of the sulphoxide (0.17 g) was dissolved in toluene (15 ml), and the resulting solution was heated under reflux for 3 h. Evaporation of the solvent and chromatography of the residue on silica gel [preparative t.l.c., light petroleum–diethyl ether (3 : 1)] gave *parasorbic acid* (58) [0.055 g, 56% from the oxo-ester (33)], $\nu_{max.}$ 1 738, 1 245, and 1 060 cm^{-1}; δ 1.41 (3 H, d, *J* 7.0), 2.31 (1 H, ddd, *J* 9.0, 4.0, and 2.0), 2.33 (1 H, ddd, *J* 7.0, 4.0, and 2.0), 4.52 (1 H, ddq, *J* 9.0, 7.0, and 7.0), 5.87 (1 H, dt, 10.0 and 2.0), and 6.82 (1 H, dt, *J* 10.0 and 4.0) identical with the authentic sample.[12]

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[12] R. Kuhn and D. Jerchel, *Ber.*, 1943, **76**, 413.